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

FORM 6-K

**REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO RULE 13a-16 OR 15d-16
UNDER THE SECURITIES EXCHANGE ACT OF 1934**

For the Month of September 2022

Commission File Number: 001-39992

Immunocore Holdings plc

(Translation of registrant's name into English)

**92 Park Drive
Milton Park
Abingdon, Oxfordshire OX14 4RY
United Kingdom
(Address of principal executive office)**

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

Sales Agreement

On September 9, 2022, Immunocore Holdings plc (the “Company”) entered into an Open Market Sale AgreementSM (the “Sales Agreement”) with Jefferies LLC (“Jefferies”), pursuant to which the Company may issue and sell American Depositary Shares, each representing one ordinary share, nominal value £0.002 per share, in the capital of the Company, having an aggregate offering price of up to \$250,000,000 (the “ADSs”), from time to time, in an at-the-market offering pursuant to which Jefferies will act as sales agent and/or principal.

Subject to the terms and conditions of the Sales Agreement, Jefferies has agreed to use its commercially reasonable efforts, consistent with its normal sales and trading practices, to sell all of the ADSs so designated by the Company with respect to which Jefferies has agreed to act as sales agent subject to, and in accordance with the information specified in, a written notice from the Company. The sales, if any, of the ADSs under the Sales Agreement, will be made (i) in privately negotiated transactions with the consent of the Company or (ii) by any other method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended (the “Securities Act”), including block transactions, sales made directly on the Principal Market (as defined in the Sales Agreement) or sales made into any other existing trading market of the ADSs. The Sales Agreement provides that the commission payable to Jefferies for sales of the ADSs with respect to which Jefferies acts as sales agent shall be up to 3.0% of the gross sales price for such ADSs sold pursuant to the Sales Agreement.

The Sales Agreement contains customary representations and warranties of the parties and indemnification and contribution provisions under which the Company and Jefferies have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act. Jefferies and the Company have the right, by giving written notice as specified in the Sales Agreement, to terminate the Sales Agreement.

The foregoing description of the Sales Agreement is not complete and is qualified in its entirety by reference to the full text of the Sales Agreement, a copy of which is filed herewith as Exhibit 1.1 hereto and is incorporated by reference herein.

The offering has been registered under the Securities Act pursuant to the Company’s automatic shelf registration statement on Form F-3ASR (File No. 333-264105), as supplemented by the prospectus supplement (the “Prospectus Supplement”) dated September 9, 2022, relating to the sale of the ADSs pursuant to the Sales Agreement. The Prospectus Supplement contains an updated summary description of the Company’s business under the heading “Recent Developments” in the section titled “Prospectus Supplement Summary” in the Prospectus Supplement, which disclosure is filed herewith as Exhibit 99.1 hereto and is incorporated by reference herein.

A copy of the opinion of Cooley (UK) LLP relating to the validity of the securities to be issued pursuant to the Sales Agreement is filed herewith as Exhibit 5.1 hereto.

This Report on Form 6-K shall not constitute an offer to sell or solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities law of such state or jurisdiction.

Incorporation by Reference

This Report on Form 6-K (the “Report”), including all Exhibits hereto, shall be deemed to be incorporated by reference into the Company’s registration statement on Form F-3ASR (File No. 333-264105) and the Company’s registration statements on Form S-8 (File Nos. 333-255182 and 333-265000), including any prospectuses forming a part of such registration statements, and to be a part thereof from the date on which this Report is filed, to the extent not superseded by documents or reports subsequently filed or furnished.

EXHIBIT INDEX

| Exhibit No. | Description |
|-----------------------------|--|
| <u>1.1</u> | Sales Agreement, dated as of September 9, 2022, by and between the Company and Jefferies LLC. |
| <u>5.1</u> | Opinion of Cooley (UK) LLP. |
| <u>23.1</u> | Consent of Cooley (UK) LLP (included in Exhibit 5.1). |
| <u>99.1</u> | Recent Developments section of the Prospectus Supplement Summary included in the Company's Prospectus Supplement dated September 9, 2022 to the Registration Statement on Form F-3ASR (File No. 333-264105). |

SIGNATURES

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

IMMUNOCORE HOLDINGS PLC

Date: September 9, 2022

By: /s/ Bahija Jallal, Ph.D.

Name: Bahija Jallal, Ph.D.

Title: Chief Executive Officer

OPEN MARKET SALE AGREEMENTSM

September 9, 2022

JEFFERIES LLC
520 Madison Avenue
New York, New York 10022

Ladies and Gentlemen:

Immunocore Holdings plc, a public limited company incorporated under the laws of England and Wales with registered number 13119746 (the “**Company**”), proposes, subject to the terms and conditions stated herein, to issue and sell from time to time through Jefferies LLC, as sales agent and/or principal (the “**Agent**”), American Depositary Shares, each representing one ordinary share, nominal value £0.002 per share, in the capital of the Company (the “**Ordinary Shares**”), having an aggregate offering price of up to \$250,000,000 (the “**ADSs**”), on the terms set forth in this agreement (this “**Agreement**”).

The ADSs to be sold from time to time hereunder will be issued, pursuant to a deposit agreement (the “**Deposit Agreement**”), dated February 9, 2021, among (inter alia) the Company, Citibank, N.A., as depositary (the “**Depositary**”) and holders from time to time of the ADSs (or any American Depositary Receipts (“**ADRs**”) issued by the Depositary and evidencing the ADSs). The Company will, following a sale by the Agent of the ADSs, deposit, on behalf of the Agent, the Ordinary Shares represented by such ADSs (the “**Underlying Shares**”) with Citibank, N.A., London Branch as custodian for the Depositary (the “**Custodian**”), pursuant to which the Depositary (or the Custodian acting on behalf of the Depositary) will deliver the ADSs (or ADRs evidencing ADSs) to the Agent.

References in this Agreement to (1) the Company issuing and selling ADSs through the Agent, and similar or analogous expressions, shall be understood to include references to the Company allotting and issuing the Underlying Shares to the Depositary or its nominee and procuring the issue of ADSs representing such Underlying Shares by the Depositary or its nominee to the Agent (acting as agent and/or principal); and (2) the purchase of, or payment for, any ADSs, and similar or analogous expressions, shall be understood to refer to the subscription for the Underlying Shares, as well as the acquisition of the ADSs representing such Underlying Shares deposited therefor, and the payment of the subscription monies in respect of such Underlying Shares.

Section 1. DEFINITIONS

- (a) Certain Definitions. For purposes of this Agreement, capitalized terms used herein and not otherwise defined shall have the following respective meanings:

“**Affiliate**” of a Person means another Person that directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with, such first-mentioned Person. The term “control” (including the terms “controlling,” “controlled by” and “under common control with”) means the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a Person, whether through the ownership of voting securities, by contract or otherwise.

SM “Open Market Sale Agreement” is a service mark of Jefferies LLC

“**Agency Period**” means the period commencing on the date of this Agreement and expiring on the earliest to occur of (x) the date on which the Agent shall have placed the Maximum Program Amount pursuant to this Agreement and (y) the date this Agreement is terminated pursuant to Section 7(b).

“**CA 2006**” means the UK Companies Act 2006, as amended.

“**Commission**” means the U.S. Securities and Exchange Commission.

“**Exchange Act**” means the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission thereunder.

“**Floor Price**” means the minimum price set by the Company in the Issuance Notice below which the Agent shall not sell Shares (as defined below) during the applicable period set forth in the Issuance Notice, which may be adjusted by the Company at any time during the period set forth in the Issuance Notice by delivering written notice of such change to the Agent and which in no event shall be less than \$1.00 without the prior written consent of the Agent, which may be withheld in the Agent’s sole discretion (and in no event shall be less than the nominal value per Underlying Share).

“**Issuance Amount**” means the aggregate Sales Price of the ADSs to be sold by the Agent pursuant to any Issuance Notice.

“**Issuance Notice**” means a written notice delivered to the Agent by the Company in accordance with this Agreement in the form attached hereto as Exhibit A that is executed by its Chief Executive Officer, President or Chief Financial Officer.

“**Issuance Notice Date**” means any Trading Day during the Agency Period that an Issuance Notice is delivered pursuant to Section 3(b)(i).

“**Issuance Price**” means the Sales Price less the Selling Commission.

“**Maximum Program Amount**” means the lesser of (a) ADSs with an aggregate Sales Price of the lesser of (1) the dollar amount of Ordinary Shares in the form of ADSs registered under the effective Registration Statement (defined below) pursuant to which the offering is being made, (2) the dollar amount of Ordinary Shares in the form of ADSs permitted to be sold under Form F-3 (including General Instruction I.B.5 thereof, if applicable), and (3) the number or dollar amount of ADSs for which the Company has filed a Prospectus (defined below) and (b) ADSs representing the pound sterling nominal amount of Ordinary Shares that the Company’s board of directors or a duly authorized committee thereof is authorized to allot from time to time, in accordance with the Company’s articles of association and pursuant to a valid authority under section 551 of the CA 2006 and a valid power under section 570 of the CA 2006 or, if applicable, section 571 of the CA 2006 to allot Ordinary Shares as if section 561 of the CA 2006 did not apply (less any Ordinary Shares issued or rights to subscribe for or to convert any security into Ordinary Shares granted pursuant to such authorities and powers).

“**Person**” means an individual or a corporation, partnership, limited liability company, trust, incorporated or unincorporated association, joint venture, joint stock company, governmental authority or other entity of any kind.

“**Principal Market**” means The Nasdaq Global Select Market or such other national securities exchange on which the ADSs are then listed.

“**Rule 462(b) Registration Statement**” means any registration statement filed by the Company pursuant to Rule 462(b) under the Securities Act in connection with the offer and sale of Shares.

“**Sales Price**” means the actual sale execution price of each ADS placed by the Agent pursuant to this Agreement.

“**Securities Act**” means the Securities Act of 1933, as amended, and the rules and regulations of the Commission thereunder.

“**Selling Commission**” means up to three percent (3%) of the gross proceeds of ADSs sold pursuant to this Agreement, or as otherwise agreed between the Company and the Agent with respect to any ADSs sold pursuant to this Agreement.

“**Settlement Date**” means the second business day following each Trading Day during the period set forth in the Issuance Notice on which ADSs are sold pursuant to this Agreement, when the Company shall deliver to the Agent the amount of ADSs sold on such Trading Day and the Agent shall deliver to the Company the Issuance Price in respect of such sales.

“**Shares**” means the ADSs and Underlying Shares issued or issuable pursuant to this Agreement or either of the above, as the context may require.

“**Trading Day**” means any day on which the Principal Market is open for trading.

Section 2. REPRESENTATIONS AND WARRANTIES OF THE COMPANY

The Company represents and warrants to, and agrees with, the Agent that as of (1) the date of this Agreement, (2) each Issuance Notice Date, (3) each Settlement Date, (4) each Triggering Event Date on which a certificate under Section 4(o) is delivered and (5) each Time of Sale (each of the times referenced above is referred to herein as a “**Representation Date**”), except as may be disclosed in the Prospectus (including any documents incorporated by reference therein and any amendments or supplements thereto) on or before a Representation Date:

(a) **Registration Statement.** The Company has prepared and filed with the Commission a shelf registration statement on Form F-3 (File No. 333-264105) that contains a base prospectus (the "**Base Prospectus**"). Such registration statement registers the issuance and sale by the Company of the Shares under the Securities Act. The Company may file one or more additional registration statements from time to time that will contain a base prospectus and related prospectus or prospectus supplement, if applicable, with respect to the Shares. Except where the context otherwise requires, such registration statement(s), including any information deemed to be a part thereof pursuant to Rule 430B under the Securities Act, including all financial statements, exhibits and schedules thereto and all documents incorporated or deemed to be incorporated therein by reference pursuant to Item 6 of Form F-3 under the Securities Act as from time to time amended or supplemented, is herein referred to as the "**Registration Statement**," and the prospectus constituting a part of such registration statement(s), together with any prospectus supplement filed with the Commission pursuant to Rule 424(b) under the Securities Act relating to a particular issuance of the Shares, including all documents incorporated or deemed to be incorporated therein by reference pursuant to Item 6 of Form F-3 under the Securities Act, in each case, as from time to time amended or supplemented, is referred to herein as the "**Prospectus**," except that if any revised prospectus and/or prospectus supplement is provided to the Agent by the Company for use in connection with the offering of the Shares that is not required to be filed by the Company pursuant to Rule 424(b) under the Securities Act, the term "**Prospectus**" shall refer to such revised prospectus and/or prospectus supplement, as applicable, from and after the time it is first provided to the Agent for such use. The registration statement on Form F-6 (File No. 333-252487) relating to the ADSs has been filed with the Commission (such registration statement on Form F-6, including all exhibits thereto, as amended at the time such registration statement became effective, is herein referred to as the "**ADS Registration Statement**").

As used in this Agreement, the terms "amendment" or "supplement" when applied to the Registration Statement, the ADS Registration Statement or the Prospectus shall be deemed to include the filing by the Company with the Commission of any document under the Exchange Act after the date hereof that is or is deemed to be incorporated therein by reference. All references in this Agreement to financial statements and schedules and other information which is "contained," "included" or "stated" in the Registration Statement, the ADS Registration Statement or the Prospectus (and all other references of like import) shall be deemed to mean and include all such financial statements and schedules and other information which is or is deemed to be incorporated by reference in or otherwise deemed under the Securities Act to be a part of or included in the Registration Statement, the ADS Registration Statement or the Prospectus, as the case may be, as of any specified date; and all references in this Agreement to amendments or supplements to the Registration Statement, the ADS Registration Statement or the Prospectus shall be deemed to mean and include, without limitation, the filing of any document under the Exchange Act which is or is deemed to be incorporated by reference in or otherwise deemed under the Securities Act to be a part of or included in the Registration Statement, the ADS Registration Statement or the Prospectus, as the case may be, as of any specified date .

At the time the Registration Statement was or will be originally declared effective and at the time the Company's most recent annual report on Form 20-F was filed with the Commission, if later, the Company met the then-applicable requirements for use of Form F-3 under the Securities Act. During the Agency Period, each time the Company files an annual report on Form 20-F, the Company will meet the then-applicable requirements for use of Form F-3 under the Securities Act.

(b) Compliance with Registration Requirements. The ADS Registration Statement has been declared effective by the Commission under the Securities Act, and the Registration Statement and any Rule 462(b) Registration Statement have been declared effective by the Commission under the Securities Act. The Company has complied to the Commission's satisfaction with all requests of the Commission for additional or supplemental information. No stop order suspending the effectiveness of the Registration Statement, the ADS Registration Statement or any Rule 462(b) Registration Statement is in effect and no proceedings for such purpose have been instituted or are pending or, to the best knowledge of the Company, are contemplated or threatened by the Commission.

The Prospectus, when filed, complied or will comply in all material respects with the Securities Act and, if filed with the Commission through its Electronic Data Gathering, Analysis and Retrieval system ("**EDGAR**") (except as may be permitted by Regulation S-T under the Securities Act), was identical to the copy thereof delivered to the Agent for use in connection with the issuance and sale of the Shares. Each of the Registration Statement, the ADS Registration Statement, any Rule 462(b) Registration Statement and any post-effective amendment thereto conforms, at the time each was declared effective, and the Prospectus and any further amendments or supplements to the Registration Statement, ADS Registration Statement and the Prospectus on the date when such prospectus, amendment or supplement is filed will conform, in all material respects to the requirements of the Securities Act and the rules and regulations of the Commission thereunder. The Registration Statement and the ADS Registration Statement do not and will not, as of the applicable effective date as to each part of the Registration Statement and ADS Registration Statement and any amendment thereto, contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading; provided, however, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with the information furnished by the Agent to the Company described in Section 6 below. The Prospectus, as of the date hereof did not, and as of each Time of Sale will not, include any untrue statement of a material or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, however, that this representation and warranty shall not apply to statements or omissions made in reliance upon and in conformity with the information furnished by the Agent to the Company described in Section 6 below. As of the date of this Agreement, the Prospectus and any Free Writing Prospectus (as defined below) considered together (collectively, the "**Time of Sale Information**") did not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading. The Prospectus, as amended or supplemented, as of its date and at each Representation Date, did not and will not contain any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The representations and warranties set forth in the three immediately preceding sentences do not apply to statements in or omissions from the Registration Statement, the ADS Registration Statement, any Rule 462(b) Registration Statement, or any post-effective amendment thereto, or the Prospectus, or any amendments or supplements thereto, made in reliance upon and in conformity with information relating to the Agent furnished to the Company in writing by the Agent expressly for use therein, it being understood and agreed that the only such information furnished by the Agent to the Company consists of the information described in Section 6 below. There are no contracts or other documents required to be described in the Prospectus or to be filed as exhibits to the Registration Statement which have not been described or filed as required. The Registration Statement and the offer and sale of the Shares as contemplated hereby meet the requirements of Rule 415 under the Securities Act and comply in all material respects with said rule.

(c) Ineligible Issuer Status. The Company is not an “ineligible issuer” in connection with the offering of the Shares pursuant to Rules 164, 405 and 433 under the Securities Act. Any Free Writing Prospectus that the Company is required to file pursuant to Rule 433(d) under the Securities Act has been, or will be, filed with the Commission in accordance with the requirements of the Securities Act. Each Free Writing Prospectus that the Company has filed, or is required to file, pursuant to Rule 433(d) under the Securities Act or that was prepared by or behalf of or used or referred to by the Company complies or will comply in all material respects with the requirements of Rule 433 under the Securities Act including timely filing with the Commission or retention where required and legending, and each such Free Writing Prospectus, as of its issue date and at all subsequent times through the completion of the issuance and sale of the Shares did not, does not and will not include any information that conflicted, conflicts with or will conflict with the information contained in the Registration Statement or the Prospectus, including any document incorporated by reference therein. Except for the Free Writing Prospectuses, if any, and electronic road shows, if any, furnished to the Agent before first use, the Company has not prepared, used or referred to, and will not, without the Agent’s prior consent, prepare, use or refer to, any Free Writing Prospectus.

(d) Exchange Act Compliance. The documents incorporated or deemed to be incorporated by reference in the Prospectus, at the time they were or hereafter are filed with the Commission, and any Free Writing Prospectus or amendment or supplement thereto complied and will comply in all material respects with the requirements of the Exchange Act, and, when read together with the other information in the Prospectus, at the time the Registration Statement and any amendments thereto become effective and at each Time of Sale (as defined below), as the case may be, will not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(e) Incorporated Documents. The documents incorporated or deemed to be incorporated by reference in the Registration Statement and the Prospectus, at the time they were filed with the Commission, complied in all material respects with the requirements of the Exchange Act, as applicable, and, when read together with the other information in the Prospectus, do not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances under which they were made, not misleading.

(f) No Material Adverse Effect. Neither the Company nor any of its subsidiaries, taken as a whole, has, since the date of the latest audited financial statements included or incorporated by reference in the Prospectus, (i) sustained any material loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree or (ii) entered into any transaction or agreement (whether or not in the ordinary course of business) that is material to the Company and its subsidiaries taken as a whole or incurred any liability or obligation, direct or contingent, that is material to the Company and its subsidiaries taken as a whole, in each case otherwise than as set forth or contemplated in the Prospectus; and, since the respective dates as of which information is given in the Registration Statement and the Prospectus, there has not been (x) any change in the share capital (other than as a result of (i) the issuance of ADSs representing Ordinary Shares and non-voting ordinary shares through a private investment in public equity pursuant to that certain share purchase agreement between the Company and certain investors dated July 15, 2022, as described in the Prospectus, (ii) the exercise, if any, of share options or the award, if any, of share options or restricted shares in the ordinary course of business pursuant to the Company's equity plans that are described in the Prospectus, or (iii) the issuance, if any, of shares upon conversion of Company securities as described in the Prospectus) or long-term debt of the Company or any of its subsidiaries or (y) any Material Adverse Effect (as defined below); as used in this Agreement, "**Material Adverse Effect**" shall mean any material adverse change or effect, or any development involving a prospective material adverse change or effect, in or affecting (i) the business, properties, general affairs, management, financial position, shareholders' equity or results of operations of the Company and its subsidiaries, taken as a whole, except as set forth or contemplated in the Prospectus, or (ii) the ability of the Company to perform its obligations under this Agreement, including the issuance and sale of the Shares, or to consummate the transactions contemplated in the Prospectus.

(g) Title to Properties. The Company and its subsidiaries have good and marketable title in fee simple (or its jurisdictional equivalent) to, or has valid rights to lease or otherwise use, all items or real and personal property that are material to its business, in each case free and clear of all liens, encumbrances and defects except (i) such as are described in the Prospectus, (ii) those that do not materially interfere with the use made and proposed to be made of such property by the Company or (ii) those that would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect.

(h) Incorporation and Good Standing. The Company and each of its subsidiaries has been (i) duly organized and is validly existing and in good standing (where such concept exists) under the laws of its jurisdiction of organization, (ii) has the requisite power and authority (corporate and other) to own its properties and conduct its business as described in the Prospectus, and (iii) has been duly qualified as a foreign corporation for the transaction of business and is in good standing (where such concept exists) under the laws of each other jurisdiction in which it owns or leases properties or conducts any business so as to require such qualification, except, in the case of clauses (ii) and (iii), where the failure to have such authority or be so qualified or in good standing would not, individually or in the aggregate, be reasonable expected to have a Material Adverse Effect, and each subsidiary of the Company has been listed in the Registration Statement.

(i) Capitalization. The Company has an issued share capital as set forth in the Registration Statement and the Prospectus and all of the existing issued shares in the capital of the Company have been duly and validly authorized and issued and are fully paid and are not subject to any call for the payment of further capital and conform in all material respects to the description of the Ordinary Shares contained in the Prospectus; and all of the existing issued shares of each subsidiary of the Company have been duly and validly authorized and issued, are fully paid and are not subject to any call for the payment of further capital and (except, in the case of any foreign subsidiary, for directors' qualifying shares) are owned directly or indirectly by the Company, free and clear of all liens, encumbrances, equities or claims, except for such liens or encumbrances described in the Prospectus.

(j) The Underlying Shares. The Underlying Shares have been duly and validly authorized and, when issued, delivered and paid for in accordance with the terms of this Agreement, will be duly and validly issued and fully paid and not subject to any call for the payment of further capital, and will conform to the description of the Ordinary Shares contained in the Prospectus; the issuance of the Underlying Shares is not subject to any preemptive or similar rights (save for such rights that have been validly waived or disappplied); the Underlying Shares, when issued and delivered against payment therefor, may be freely deposited by the Company with the Depositary or its nominee against issuance of the ADSs; and the ADSs when issued and delivered, will be freely transferable by the Company to or for the account of the Agent and the initial purchasers thereof.

(k) Non-Contravention. The issue and sale of the Shares and the compliance by the Company with this Agreement and the consummation of the transactions contemplated in this Agreement and the Prospectus will not conflict with or result in a breach or violation of any of the terms or provisions of, or constitute a default under, (A) any indenture, mortgage, deed of trust, loan agreement or other agreement or instrument to which the Company or any of its subsidiaries is a party or by which the Company or any of its subsidiaries is bound or to which any of the property or assets of the Company or any of its subsidiaries is subject, (B) the articles of association or by-laws (or other applicable organizational document) of the Company or any of its subsidiaries, or (C) any statute or any judgment, order, rule or regulation of any court or governmental agency or body having jurisdiction over the Company or any of its subsidiaries or any of their properties (including, without limitation, the CA 2006 and the Financial Services and Markets Act 2000 of the United Kingdom and EU Regulation (No. 596/2014) as it forms part of domestic law in the United Kingdom by virtue of the European Union (Withdrawal) Act 2018 (as amended) and as amended from time to time), except, in the case of clauses (A) and (C) for such defaults, breaches, or violations that would not, individually or in the aggregate, be reasonably expected to have a Material Adverse Effect; and no consent, approval, authorization, order, registration or qualification of or with any such court or governmental agency or body is required for the issue and sale of the Shares or the consummation by the Company of the transactions contemplated by this Agreement, except such as have been obtained under the Securities Act, the approval by the Financial Industry Regulatory Authority (“FINRA”) of the underwriting terms and arrangements and such consents, approvals, authorizations, registrations or qualifications as may be required under state securities or Blue Sky laws in connection with the purchase and distribution of the ADSs by the Agent.

(l) No Violation or Default. Neither the Company nor any of its subsidiaries is (i) in violation of its articles of association or by-laws (or other applicable organizational document), (ii) in violation of any statute or any judgment, order, rule or regulation of any court or governmental agency or body having jurisdiction over the Company or any of its subsidiaries or any of their properties, or (iii) in default in the performance or observance of any obligation, agreement, covenant or condition contained in any indenture, mortgage, deed of trust, loan agreement, lease or other agreement or instrument to which it is a party or by which it or any of its properties may be bound, except, in the case of the foregoing clauses (ii) and (iii), for such violations or defaults as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect.

(m) The statements set forth in the Registration Statement and the Prospectus under the caption “Description of Share Capital and Articles of Association” and “Description of American Depositary Shares,” insofar as they purport to constitute a summary of the terms of the ADSs and Ordinary Shares, under the caption “Taxation” and under the caption “Plan of Distribution,” insofar as they purport to describe the provisions of the laws and documents referred to therein, are accurate and complete in all material respects.

(n) No Material Proceedings. Other than as set forth in the Prospectus, there are no legal or governmental proceedings pending to which the Company or any of its subsidiaries or, to the Company’s knowledge, any officer or director of the Company, is a party or of which any property of the Company or any of its subsidiaries or, to the Company’s knowledge, any officer or director of the Company, is the subject which, if determined adversely to the Company or any of its subsidiaries (or such officer or director), would individually or in the aggregate reasonably be expected to have a Material Adverse Effect; and, to the Company’s knowledge, no such proceedings are threatened or contemplated by governmental authorities or threatened by others.

(o) No Additional Documents. There are no contracts or documents which are required to be described in the Registration Statement or the Prospectus or to be filed as exhibits to the Registration Statement or the Prospectus which have not been so described and filed as required.

(p) No Transfer Taxes. No stamp, documentary, issuance, registration, transfer or other similar taxes or duties (including United Kingdom stamp duty and stamp duty reserve tax and excluding, for the avoidance of doubt, any income taxes on commissions earned by the Agent under this Agreement) (“**Transfer Taxes**”) are required to be paid by or on behalf of the Agent in the United Kingdom or the United States or to any taxing authority thereof or therein in connection with (i) the execution or delivery of this Agreement or the Deposit Agreement or (ii) the issuance and allotment of the Underlying Shares and the delivery of the ADSs (and any corresponding ADRs evidencing such ADSs) to the Agent or purchasers procured by the Agent in the manner contemplated in this Agreement and in the Deposit Agreement or (iii) the initial sale and delivery by the Agent of the ADSs (and any corresponding ADRs evidencing such ADSs) through the facilities of the Depository Trust Company (“**DTC**”) to the initial purchasers thereof in the manner contemplated in this Agreement and in the Deposit Agreement.

(q) Dividends. Except as disclosed in the Registration Statement or the Prospectus, no approvals are currently required in the United Kingdom in order for the Company to pay dividends or other distributions declared by the Company to the holders of Ordinary Shares. Under current laws and regulations of England and Wales and any political subdivision thereof, any amount payable with respect to the Ordinary Shares upon liquidation of the Company or upon redemption thereof and dividends and other distributions declared and payable on the share capital of the Company may be paid by the Company in United States dollars and freely transferred out of the United Kingdom and without the necessity of obtaining any governmental authorization in the United Kingdom or any political subdivision or taxing authority thereof or therein.

(r) Legality. The legality, validity, enforceability or admissibility into evidence of any of the Registration Statement, the Prospectus, this Agreement or the Shares in any jurisdiction in which the Company is organized or does business is not dependent upon such document being submitted into, filed or recorded with any court or other authority in any such jurisdiction on or before the date hereof.

(s) Legal Action. A holder of the Shares and the Agent are each entitled to sue as plaintiff in the court of the jurisdiction of formation and domicile of the Company for the enforcement of their respective rights under this Agreement and the Underlying Shares and such access to such courts will not be subject to any conditions which are not applicable to residents of such jurisdiction or a company incorporated in such jurisdiction except that plaintiffs not residing in England and Wales may be required to guarantee payment of a possible order for payment of costs or damages at the request of the defendant.

(t) Foreign Private Issuer. The Company is a “foreign private issuer” as defined in Rule 405 under the Securities Act.

(u) No Immunity. Neither the Company nor any of its subsidiaries or their properties or assets has immunity under English, U.S. federal or New York state law from any legal action, suit or proceeding, from the giving of any relief in any such legal action, suit or proceeding, from set-off or counterclaim, from the jurisdiction of any English, U.S. federal or New York state court, from service of process, attachment upon or prior to judgment, or attachment in aid of execution of judgment, or from execution of a judgment, or other legal process or proceeding for the giving of any relief or for the enforcement of a judgment, in any such court with respect to their respective obligations, liabilities or any other matter under or arising out of or in connection herewith; and, to the extent that the Company or any of its subsidiaries or any of its properties, assets or revenues may have or may hereafter become entitled to any such right of immunity in any such court in which proceedings arising out of, or relating to the transactions contemplated by this Agreement, may at any time be commenced, the Company has, pursuant to Section 8(g) of this Agreement, waived, and it will waive, or will cause its subsidiaries to waive, such right to the extent permitted by law.

(v) Company Not an “Investment Company”. The Company is not and, after giving effect to the deposit with the Depository or its nominee of the Underlying Shares and offering and sale of the ADSs and the application of the proceeds thereof as described in the Prospectus, will not be required to register as an “investment company,” as such term is defined in the Investment Company Act of 1940, as amended.

(w) Independent Accountants. KPMG LLP, who have audited certain financial statements of the Company and its subsidiaries, are independent public accountants as required by the Securities Act.

(x) Internal Control Over Financial Reporting. The Company maintains a system of internal control over financial reporting (as such term is defined in Rule 13a-15(f) under the Exchange Act) that (i) complies with the applicable requirements of the Exchange Act, (ii) has been designed by the Company's principal executive officer and principal financial officer, or under their supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and (iii) are effective in all material respects to perform the functions for which they were established. Since the date of the latest audited financial statements of the Company included in the Prospectus, except as described in the Prospectus, there have been no changes in the Company's internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting and the Company is not aware of any material weaknesses in its internal control over financial reporting (it being understood that, until December 31, 2022, the Company is not required to comply with Section 404(b) of the Sarbanes-Oxley Act of 2002).

(y) Disclosure Controls and Procedures. The Company maintains disclosure controls and procedures (as such term is defined in Rule 13a-15(e) under the Exchange Act) that are designed to comply with the applicable requirements of the Exchange Act; such disclosure controls and procedures have been designed to ensure that material information relating to the Company and its subsidiaries is made known to the Company's principal executive officer and principal financial officer by others within those entities; and such disclosure controls and procedures are effective.

(z) This Agreement. This Agreement has been duly authorized, executed and delivered by the Company.

(aa) Deposit Agreement. The Deposit Agreement has been duly authorized, executed and delivered by the Company, and assuming due authorization, execution and delivery by the Depository, constitutes a valid and legally binding obligation of the Company, enforceable in accordance with its terms, subject, as to enforceability, to bankruptcy, insolvency, reorganization, moratorium and similar laws of general applicability relating to or affecting creditors' rights and to general equity principles; upon due issuance by the Depository of the ADSs against the deposit of the Underlying Shares in respect thereof in accordance with the provisions of the Deposit Agreement, such ADSs will be duly and validly issued, and the persons in whose names the ADSs are registered will be entitled to the rights specified therein, respectively, and in the Deposit Agreement; the Deposit Agreement conforms in all material respects to the description thereof contained in the Registration Statement and the Prospectus.

(bb) Anti-Bribery and Anti-Corruption Laws. Except as described in the Prospectus, none of the Company or any of its subsidiaries nor, to the knowledge of the Company, any director, officer, agent, employee, affiliate or other person associated with or acting on behalf of the Company or any of its subsidiaries has (i) made, offered, promised or authorized any unlawful contribution, gift, entertainment or other unlawful expense or taken any act in furtherance thereof; (ii) made, offered, promised or authorized any direct or indirect unlawful payment; or (iii) violated or is in violation of any applicable provision of the Foreign Corrupt Practices Act of 1977, the Bribery Act 2010 of the United Kingdom or any other applicable anti-bribery or anti-corruption law.

(c c) Anti-Money Laundering Laws. The operations of the Company and its subsidiaries are and have been conducted at all times in compliance with the requirements of applicable anti-money laundering laws and financial recordkeeping and reporting requirements, including, but not limited to, the Bank Secrecy Act of 1970, as amended by the USA Patriot Act of 2001, and the rules and regulations promulgated thereunder, and the anti-money laundering laws of the various jurisdictions in which the Company and its subsidiaries conduct business (collectively, the “**Money Laundering Laws**”) and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any of its subsidiaries with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(dd) Sanctions. None of the Company or any of its subsidiaries nor, to the knowledge of the Company, any director, officer, agent, employee or affiliate of the Company or any of its subsidiaries is currently the subject or the target of any sanctions administered or enforced by the U.S. Government, including, without limitation, the Office of Foreign Assets Control of the U.S. Department of the Treasury (“**OFAC**”), or the U.S. Department of State and including, without limitation, the designation as a “specially designated national” or “blocked person,” the European Union, Her Majesty’s Treasury, the United Nations Security Council, or other relevant sanctions authority (collectively, “**Sanctions**”), nor is the Company or any of its subsidiaries located, organized or resident in a country or territory that is the subject or target of comprehensive Sanctions (currently, Cuba, Iran, North Korea, Syria, the so-called Donetsk People’s Republic, the so-called Luhansk People’s Republic, any other Covered Region of Ukraine identified pursuant to Executive Order 14065 and the Crimea Region) (“**Sanctioned Countries**”), and the Company will not directly or indirectly use the proceeds of the offering of the Shares hereunder, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity (i) to fund or facilitate any activities of or business with any person, or in any country or territory, that, at the time of such funding, is the subject or the target of Sanctions or a Sanctioned Country or (ii) in any other manner that will result in a violation by any person (including any person participating in the transaction, whether as underwriter, advisor, investor or otherwise) of Sanctions.

(ee) Recognition of Judgments. Any final judgment for a fixed or determined sum of money rendered by any U.S. federal or New York state court located in the State of New York having jurisdiction under its own laws in respect of any suit, action or proceeding against the Company based upon this Agreement or the Deposit Agreement would be declared enforceable against the Company by the courts of England and Wales, without reconsideration or reexamination of the merits, except as disclosed in the Registration Statement and the Prospectus.

(ff) Choice of Law. The choice of laws of the State of New York as the governing law of this Agreement is a valid choice of law under the laws of England and Wales and will be honored by the courts of England and Wales, subject to the restrictions described under the caption “Service of Process and Enforceability of Liabilities” in the Registration Statement and the Prospectus. The Company has the power to submit, and pursuant to Section 8(g) of this Agreement, has legally, validly, effectively and irrevocably submitted, to the personal jurisdiction of each New York state and United States federal court sitting in the City of New York and has validly and irrevocably waived any objection to the laying of venue of any suit, action or proceeding brought in such court.

(gg) Brokers. Except pursuant to this Agreement, neither the Company nor any of its subsidiaries is a party to any contract, agreement or understanding with any person (other than this Agreement) that would give rise to a valid claim against any of them or any agent or underwriter for a brokerage commission, finder’s fee or like payment in connection with the offering and sale of the Shares.

(hh) Financial Information. The financial statements included in the Registration Statement and the Prospectus, together with the related schedules, if any, and notes, present fairly, in all material respects, the financial position of the Company and its consolidated subsidiaries at the dates indicated and the statement of loss, changes in equity and cash flows of the Company and its consolidated subsidiaries for the periods specified; said financial statements have been prepared in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board (“**IFRS**”) applied on a consistent basis throughout the periods involved. The supporting schedules, if any, present fairly in accordance with IFRS the information required to be stated therein. The selected financial data and the summary financial information included in the Registration Statement and the Prospectus, if applicable, present fairly the information shown therein and have been compiled on a basis consistent with that of the audited financial statements included therein. Except as included therein, no historical or pro forma financial statements or supporting schedules are required to be included in the Registration Statement or the Prospectus under the Securities Act. All disclosures contained in the Registration Statement and the Prospectus regarding “non-IFRS financial measures” (as such term is defined by the rules and regulations of the Commission) comply with Regulation G of the Exchange Act and Item 10 of Regulation S-K of the Securities Act, to the extent applicable.

(ii) Emerging Growth Company. From the time of initial confidential submission of a registration statement relating to the Shares with the Commission through the date of this Agreement and through each Representation Date that occurs prior to December 31, 2022, the Company has been and is an “emerging growth company” as defined in Section 2(a)(19) of the Act (an “**Emerging Growth Company**.”)

(jj) No Price Stabilization or Manipulation; Compliance with Regulation M. Neither the Company nor any of its subsidiaries has taken, directly or indirectly, any action designed to or that might cause or result in stabilization or manipulation of the price of the ADSs or of any “reference security” (as defined in Rule 100 of Regulation M under the Exchange Act (“**Regulation M**”)) with respect to the ADSs, whether to facilitate the sale or resale of the Shares or otherwise, and has taken no action which would directly or indirectly violate Regulation M.

(kk) Compliance with Regulations. Neither the issuance, sale and delivery of the Shares nor the application of the proceeds thereof by the Company as described in each of the Registration Statement and the Prospectus will violate Regulation T, U or X of the Board of Governors of the Federal Reserve System or any other regulation of such Board of Governors.

(ll) Forward-Looking Statements. No forward-looking statement (within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act) contained in any of the Registration Statement or the Prospectus has been made or reaffirmed without a reasonable basis or has been disclosed other than in good faith.

(mm) Statistical and Market-Related Data. Nothing has come to the attention of the Company that has caused the Company to believe that the statistical and market-related data included in each of the Registration Statement and the Prospectus is not based on or derived from sources that are reliable and accurate in all material respects.

(nn) Sarbanes-Oxley. There is and has been no failure on the part of the Company or any of the Company's directors or officers, in their capacities as such, to comply with any material provision of the Sarbanes-Oxley Act of 2002, as amended and the rules and regulations promulgated in connection therewith, including Section 402 related to loans and Sections 302 and 906 related to certifications.

(oo) No Applicable Registration Rights. There are no persons with registration rights or other similar rights to have any securities registered for sale pursuant to the Registration Statement or otherwise registered for sale or sold by the Company under the 1933 Act pursuant to this Agreement, other than rights that have been disclosed in the Prospectus.

(pp) Insurance Matters. The Company and its subsidiaries have insurance covering their respective properties, operations, personnel and businesses, including business interruption insurance, which insurance is in amounts and insures against such losses and risks as are adequate to protect the Company and its subsidiaries and their respective businesses; and neither the Company nor any of its subsidiaries has (i) received notice from any insurer or agent of such insurer that capital improvements or other expenditures are required or necessary to be made in order to continue such insurance or (ii) any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage at reasonable cost from similar insurers as may be necessary to continue its business.

(qq) Tax Law Compliance. The Company and its subsidiaries (i) have paid all taxes (ii) have filed all tax returns required to be paid or filed through the date hereof; and (iii) except as otherwise disclosed in the Registration Statement and the Prospectus, do not have any tax deficiency that has been asserted against them or any of their respective properties or assets except those, in each of the cases described in (i), (ii) and (iii) above that (a) are being contested in good faith and for which reserves in accordance with IFRS have been made or (b) would not, individually or in the aggregate, have a Material Adverse Effect.

(rr) All Necessary Permits, etc. The Company and its subsidiaries possess all licenses, sub-licenses, certificates, permits and other authorizations issued by, and have made all declarations and filings with, the appropriate federal, state, local or foreign governmental or regulatory authorities that are necessary for the ownership or lease of their respective properties or the conduct of their respective businesses as described in each of the Registration Statement and the Prospectus, except where the failure to possess or make the same would not, individually or in the aggregate, have a Material Adverse Effect; and except as described in each of the Registration Statement and the Prospectus, neither the Company nor its subsidiaries has received notice of any revocation or modification of any such license, sub-license, certificate, permit or authorization or has any reason to believe that any such license, sub-license, certificate, permit or authorization will not be renewed in the ordinary course.

(ss) Intellectual Property Rights. The Company and its subsidiaries own or have valid and enforceable rights to use all patents, trademarks, service marks, trade names, domain names and other source indicators, copyrights and copyrightable works, licenses, know-how (including trade secrets and other unpatented or unpatentable proprietary or confidential information, systems or procedures) and all other similar intellectual property and proprietary rights (including all registrations and applications for registration of, and all goodwill associated with, the foregoing) (collectively, “**Intellectual Property**”) used in or necessary for the conduct of their respective businesses as conducted and as proposed to be conducted. Except as disclosed in the Prospectus and except as would not reasonably be expected to, individually or in the aggregate, have a Material Adverse Effect, (i) the Company’s and its subsidiaries’ conduct of their respective businesses has not infringed, misappropriated or otherwise violated any Intellectual Property of any third party; (ii) none of the product candidates of the Company or its subsidiaries would, upon commercialization, infringe, misappropriate or otherwise violate any Intellectual Property of any third party; and (iii) the Company and its subsidiaries have not received any written notice and are not otherwise aware of any pending or threatened claim alleging infringement, misappropriation or other violation of any Intellectual Property of any person, or challenging the validity, enforceability, scope or ownership of any Intellectual Property owned by or exclusively licensed to the Company or its subsidiaries. To the knowledge of the Company, no Intellectual Property owned by or exclusively licensed to the Company and its subsidiaries has been infringed, misappropriated or otherwise violated by any person. To the knowledge of the Company, all Intellectual Property owned by or exclusively licensed to the Company and its subsidiaries is valid and enforceable, except as would not reasonably be expected to, individually or in the aggregate, have a Material Adverse Effect. The Company and its subsidiaries have taken reasonable steps in accordance with normal industry practice to maintain the confidentiality of all Intellectual Property, the value of which to the Company or its subsidiaries is contingent upon maintaining the confidentiality thereof.

(tt) Preclinical Studies and Clinical Trials. (i) Except as described in the Registration Statement and the Prospectus, the preclinical studies and clinical trials conducted by or, to the knowledge of the Company, on behalf of or sponsored by the Company or its subsidiaries, or in which the Company or its subsidiaries have participated, that are described in the Registration Statement and the Prospectus, or the results of which are referred to in the Registration Statement and the Prospectus, as applicable, were, and if still pending are, being conducted in accordance with the protocols submitted to the U.S. Food and Drug Administration (the “**FDA**”), the European Medicines Agency (the “**EMA**”), and other applicable regulatory authorities (including, without limitation, any foreign, federal, state or local governmental or regulatory authority performing functions similar to those performed by the FDA and EMA) (collectively, the “**Regulatory Authorities**”), the applicable rules and regulations of the Regulatory Authorities, and current Good Clinical Practices and Good Laboratory Practices; (ii) the descriptions in the Registration Statement and the Prospectus of the results of such studies and trials are accurate and fairly present the data derived therefrom; (iii) the Company has no knowledge of any other studies or trials not described in the Registration Statement and the Prospectus, the results of which are inconsistent with or call into question the results described or referred to in the Registration Statement and the Prospectus; (iv) the Company and its subsidiaries have operated at all times and are currently in compliance, in all material respects, with all applicable statutes, rules and regulations of the Regulatory Authorities; (v) the Company has provided the Agent with all material written notices, correspondence and summaries of all other communications from the Regulatory Authorities; and (vi) neither the Company nor any of its subsidiaries have received any written notices, correspondence or other communications from the Regulatory Authorities or any other governmental agency requiring or threatening the termination, material modification or suspension of any preclinical studies or clinical trials that are described in the Registration Statement and the Prospectus or the results of which are referred to in the Registration Statement and the Prospectus, other than ordinary course communications with respect to modifications in connection with the design and implementation of such studies or trials, and, to the Company’s knowledge, there are no reasonable grounds for the same.

(u) Regulatory Filings. The Company has not failed to file with the Regulatory Authorities any required filing, declaration, listing, registration, report or submission with respect to the Company's product candidates that are described or referred to in the Registration Statement and the Prospectus; all such filings, declarations, listings, registrations, reports or submissions, as applicable, were to the Company's knowledge in compliance, in all material respects, with applicable laws when filed; and to the Company's knowledge no deficiencies regarding compliance with applicable law have been asserted by any applicable Regulatory Authority with respect to any such filings, declarations, listings, registrations, reports or submissions.

(vv) Compliance with Health Care Laws. Except as described in each of the Registration Statement or the Prospectus and except as would be reasonably expected to have a Material Adverse Effect on the Company and its subsidiaries, taken as a whole, the Company and its subsidiaries are, and at all times have been, in compliance with all applicable Health Care Laws. For purposes of this Agreement, "**Health Care Laws**" means: (i) the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §§ 301 et seq.), the Public Health Service Act (42 U.S.C. §§ 201 et seq.); (ii) all applicable federal, state, local and all applicable foreign health care related fraud and abuse laws, including, without limitation, the U.S. Anti-Kickback Statute (42 U.S.C. § 1320a-7b(b)), the U.S. False Statements Law (42 U.S.C. § 1320a-7b(a)), the Civil Monetary Penalties Law (42 U.S.C. § 1320a-7a), the U.S. Civil False Claims Act (31 U.S.C. § 3729 et seq.), all criminal laws relating to health care fraud and abuse, including but not limited to 18 U.S.C. §§ 286 and 287, and the health care fraud criminal provisions under the U.S. Health Insurance Portability and Accountability Act of 1996 ("**HIPAA**") (42 U.S.C. §§ 1320d et seq.), the Physician Payments Sunshine Act (42 U.S.C. § 1320a-7h), the exclusion law (42 U.S.C. § 1320a-7); (iii) HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (42 U.S.C. §§ 17921 et seq.); (iv) regulations promulgated pursuant to such statutes; and (v) any and all other applicable federal, state, or foreign health care laws and regulation applicable to the ownership, testing, development, manufacture, packaging, processing, use, distribution, marketing, advertising, labeling, promotion, sale, offer for sale, storage, import, export or disposal of any product manufactured or distributed by the Company. Neither the Company nor its subsidiaries has received written notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any court or arbitrator or governmental or regulatory authority or third party alleging that it is in violation of any Health Care Laws, and, to the Company's knowledge, no such claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action is threatened. Neither the Company nor its subsidiaries, nor their respective officers, directors, employees, contractors or agents, is a party to any corporate integrity agreements, monitoring agreements, consent decrees, settlement orders, or similar agreements with or imposed by any governmental or regulatory authority. Additionally, neither the Company nor any of its employees, officers, directors, contractors or agents, nor its subsidiaries or any of the subsidiary's employees, officers, directors, contractors or agents, has been excluded, suspended or debarred from participation in any U.S. federal health care program (as defined in 42 U.S.C. § 1320a-7b(f)) or human clinical research or, to the knowledge of the Company, is subject to a governmental inquiry, investigation, proceeding, or other similar action that could reasonably be expected to result in such debarment, suspension, or exclusion. The Company and its subsidiaries have filed, obtained, maintained or submitted all material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by the Health Care Laws, and all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were timely, complete, accurate and not misleading on the date filed in all material respects (or were corrected or supplemented by a subsequent submission).

(ww) Cybersecurity. The Company and its subsidiaries' information technology assets and equipment, computers, systems, networks, hardware, software, websites, applications, and databases (collectively, "**IT Systems**") are adequate for, and operate and perform in all material respects as required in connection with the operation of the business of the Company and its subsidiaries, and, to the knowledge of the Company, free and clear of all material bugs, errors, defects, Trojan horses, time bombs, malware and other corruptants. The Company and its subsidiaries have implemented and maintained commercially reasonable controls, policies, procedures, and safeguards designed to maintain and protect their material confidential information and the integrity, continuous operation, redundancy and security of their IT Systems and data (including all personal, personally identifiable, sensitive, confidential or regulated data) used in connection with their businesses (including the data of their respective customers, employees, suppliers, vendors and any third-party data in the possession, custody or control of the Company or its subsidiaries, in each case, as applicable to the Company and its subsidiaries and to the knowledge of the Company) ("**Data**"), and, to the knowledge of the Company, there have been no material breaches, violations, outages, losses or unauthorized modifications or other uses of or accesses to same, except for those that have been remedied without material cost or liability or, to the knowledge of the Company, the duty to notify any other person, nor any incidents under internal review or investigations relating to the same.

(xx) Compliance with Data Security Obligations. In all material respects, the Company and its subsidiaries have complied and are presently in compliance with all of the Company or its subsidiaries governing privacy policies, contractual obligations, applicable laws, statutes, judgments, orders, rules and regulations of any court or arbitrator or other governmental or regulatory authority and any other applicable legal obligations regarding the collection, use, transfer, import, export, storage, disposal, processing and disclosure by the Company and its subsidiaries of Data and the privacy and security of IT Systems ("**Data Security Obligations**"), except where the violation of such Data Security Obligations would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect. Neither the Company nor its subsidiaries have received any written notification of or complaint regarding, and are aware of any other facts that, individually or in the aggregate, would reasonably indicate material non-compliance with any applicable Data Security Obligation. There is no pending, or to the knowledge of the Company, threatened, action, suit or proceeding by or before any court or governmental agency, authority or body alleging material non-compliance with any applicable Data Security Obligation. The Company and its subsidiaries have at all times taken commercially reasonable steps in accordance with normal industry practice designed to protect Data against loss and unauthorized access, use, modification, disclosure or other misuse (such as, implementing and monitoring compliance with commercially reasonable measures with respect to technical and physical security), except in each case to the extent that the failure to do so would not reasonably be expected to have a Material Adverse Effect. To the knowledge of the Company, except as disclosed in the Registration Statement, the Time of Sale Information or the Prospectus or as would not individually or in the aggregate have a Material Adverse Effect, there has been no unauthorized access to such information.

(yy) Compliance with Environmental Laws. (i) The Company and its subsidiaries (x) are in compliance with all, and have not violated any, applicable federal, state, local and foreign laws (including common law), rules, regulations, requirements, decisions, judgments, decrees, orders and other legally enforceable requirements relating to pollution or the protection of human health or safety, the environment, natural resources, hazardous or toxic substances or wastes, pollutants or contaminants (collectively, "**Environmental Laws**"); (y) have received and are in compliance with all, and have not violated any, permits, licenses, certificates or other authorizations or approvals required of them under any Environmental Laws to conduct their respective businesses; and (z) have not received notice of any actual or potential liability or obligation under or relating to, or any actual or potential violation of, any Environmental Laws, including for the investigation or remediation of any disposal or release of hazardous or condition that would reasonably be expected to result in any such notice, and (ii) there are no costs or liabilities associated with Environmental Laws of or relating to the Company or its subsidiaries, except in the case of each of (i) and (ii) above, for any such matter as would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect; and (iii) except as described in the Prospectus, (x) there is no proceeding that is pending, or that is known to be contemplated, against the Company or any of its subsidiaries under any Environmental Laws in which a governmental entity is also a party, other than such proceeding regarding which it is reasonably believed no monetary sanctions of \$100,000 or more will be imposed, (y) the Company and its subsidiaries are not aware of any facts or issues regarding compliance with Environmental Laws, or liabilities or other obligations under Environmental Laws or concerning hazardous or toxic substances or wastes, pollutants or contaminants, that could reasonably be expected to have a material effect on the capital expenditures, earnings or competitive position of the Company and its subsidiaries, and (z) none of the Company or its subsidiaries anticipates material capital expenditures relating to any Environmental Laws.

Section 3. ISSUANCE AND SALE OF SHARES

(a) Sale of Securities. On the basis of the representations, warranties and agreements herein contained, but subject to the terms and conditions herein set forth, the Company and the Agent agree that the Company may from time to time seek to sell Shares through the Agent, acting as sales agent, or directly to the Agent, acting as principal, as follows, with an aggregate Sales Price of up to the Maximum Program Amount, based on and in accordance with Issuance Notices as the Company may deliver, during the Agency Period.

(b) Mechanics of Issuances.

(i) Issuance Notice. Upon the terms and subject to the conditions set forth herein, on any Trading Day during the Agency Period on which the conditions set forth in Section 5(a) and Section 5(b) shall have been satisfied, the Company may exercise its right to request an issuance of Shares by delivering to the Agent an Issuance Notice; *provided, however*, that (A) in no event may the Company deliver an Issuance Notice to the extent that (I) the sum of (x) the aggregate Sales Price of the requested Issuance Amount, plus (y) the aggregate Sales Price of all Shares issued under all previous Issuance Notices effected pursuant to this Agreement, would exceed the Maximum Program Amount; and (B) prior to delivery of any Issuance Notice, the period set forth for any previous Issuance Notice shall have expired or been terminated. An Issuance Notice shall be considered delivered on the Trading Day that it is received by e-mail by the persons set forth in Schedule A hereto and confirmed by the Company by telephone (including a voicemail message to the persons so identified), with the understanding that, with adequate prior written notice, the Agent may modify the list of such persons from time to time.

(ii) Agent Efforts. Upon the terms and subject to the conditions set forth in this Agreement, upon the receipt of an Issuance Notice, the Agent will use its commercially reasonable efforts consistent with its normal sales and trading practices to place the Shares with respect to which the Agent has agreed to act as sales agent, subject to, and in accordance with the information specified in, the Issuance Notice, unless the sale of the Shares described therein has been suspended, cancelled or otherwise terminated in accordance with the terms of this Agreement. For the avoidance of doubt, the parties to this Agreement may modify an Issuance Notice at any time provided they both agree in writing to any such modification.

(iii) Method of Offer and Sale. The Shares may be offered and sold (A) in negotiated transactions with the consent of the Company; or (B) by any other method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act, including block transactions, sales made directly on the Principal Market or sales made into any other existing trading market of the ADSs. Nothing in this Agreement shall be deemed to require either party to agree to the method of offer and sale specified in the preceding sentence, and (except as specified in clause (A) above) the method of placement of any Shares by the Agent shall be at the Agent’s discretion.

(iv) Confirmation to the Company. If acting as sales agent hereunder, the Agent will provide written confirmation to the Company no later than the opening of the Trading Day next following the Trading Day on which it has placed Shares hereunder setting forth the number of Shares sold on such Trading Day, the corresponding Sales Price and the Issuance Price payable to the Company in respect thereof.

(v) Settlement. Each issuance of Shares will be settled on the applicable Settlement Date for such issuance of Shares and, subject to the provisions of Section 5, on each Settlement Date, the Company will, or will cause the Depository to, electronically transfer the ADSs being sold by crediting the Agent or its designee’s account at DTC through its Deposit/Withdrawal At Custodian (DWAC) System, or by such other means of delivery as may be mutually agreed upon by the parties hereto. Against issue to the Depository or its nominee of the Underlying Shares the Agent will deliver, by wire transfer of immediately available funds, the related Issuance Price in same day funds delivered to an account designated by the Company prior to the Settlement Date. Such ADSs shall be freely tradeable, transferable, registered shares in good deliverable form. The Company may sell Shares to the Agent as principal at a price agreed upon at each relevant time Shares are sold pursuant to this Agreement (each, a “**Time of Sale**”).

(vi) Suspension or Termination of Sales. Consistent with standard market settlement practices, the Company or the Agent may, upon notice to the other party hereto in writing or by telephone (confirmed immediately by verifiable email), suspend any sale of Shares, and the period set forth in an Issuance Notice shall immediately terminate; *provided, however*, that (A) such suspension and termination shall not affect or impair either party's obligations with respect to any Shares placed or sold hereunder prior to the receipt of such notice; (B) if the Company suspends or terminates any sale of Shares after the Agent confirms such sale to the Company, the Company shall still be obligated to comply with Section 3(b)(v) with respect to such Shares; and (C) if the Company defaults in its obligation to deliver Shares on a Settlement Date, the Company agrees that it will hold the Agent harmless against any loss, claim, damage or expense (including, without limitation, penalties, interest and reasonable and documented legal fees and expenses), as incurred, arising out of or in connection with such default by the Company. The parties hereto acknowledge and agree that, in performing its obligations under this Agreement, the Agent may borrow ADSs from stock lenders in the event that the Company has not delivered Shares to settle sales as required by subsection 3(b)(v) above, and may use the Shares to settle or close out such borrowings. The Company agrees that no such notice shall be effective against the Agent unless it is made to the persons identified in writing by the Agent pursuant to Section 3(b)(i).

(vii) No Guarantee of Placement, Etc. The Company acknowledges and agrees that (A) there can be no assurance that the Agent will be successful in placing Shares; (B) the Agent will incur no liability or obligation to the Company or any other Person if it does not sell Shares; and (C) the Agent shall be under no obligation to purchase Shares on a principal basis pursuant to this Agreement, except as otherwise specifically agreed by the Agent and the Company.

(viii) Material Non-Public Information. Notwithstanding any other provision of this Agreement, the Company and the Agent agree that the Company shall not deliver any Issuance Notice to the Agent, and the Agent shall not be obligated to place any Shares, during any period in which the Company is in possession of material non-public information.

(c) Fees. As compensation for services rendered, the Company shall pay to the Agent, on the applicable Settlement Date, the Selling Commission for the applicable Issuance Amount (including with respect to any suspended or terminated sale pursuant to Section 3(b)(vi)) by the Agent deducting the Selling Commission from the applicable Issuance Amount.

(d) Expenses. The Company agrees to pay all costs, fees and expenses incurred in connection with the performance of its obligations hereunder and in connection with the transactions contemplated hereby (in each case excluding any Transfer Taxes (and any interest and penalties imposed thereon) which shall be dealt with exclusively in accordance with Section 4(y) below and any VAT which shall be dealt with exclusively in accordance with Section 4(aa) below), including without limitation (i) all expenses incident to the issuance and delivery of the Shares (including all printing and engraving costs); (ii) all fees and expenses of the registrar and the Depositary, as applicable, of the Shares; (iii) all fees and expenses of the Company's counsel, independent public or certified public accountants and other advisors; (iv) all costs and expenses incurred in connection with the preparation, printing, filing, shipping and distribution of the Registration Statement (including financial statements, exhibits, schedules, consents and certificates of experts), the Prospectus, any Free Writing Prospectus (as defined below) prepared by or on behalf of, used by, or referred to by the Company, and all amendments and supplements thereto, and this Agreement; (v) all filing fees, attorneys' fees and expenses incurred by the Company or the Agent in connection with qualifying or registering (or obtaining exemptions from the qualification or registration of) all or any part of the Shares for offer and sale under the state securities or blue sky laws, and, if requested by the Agent, preparing and printing a "Blue Sky Survey" or memorandum, and any supplements thereto, advising the Agent of such qualifications, registrations, determinations and exemptions; (vi) the reasonable fees and disbursements of the Agent's counsel, including the reasonable fees and expenses of counsel for the Agent in connection with, FINRA review, if any, and approval of the Agent's participation in the offering and distribution of the Shares ; (vii) the filing fees incident to FINRA review, if any; and (viii) the fees and expenses associated with listing the Shares on the Principal Market). The fees and disbursements of Agent's counsel pursuant to subsections 3(d)(vi) and 3(d)(vii) above shall not exceed (A) \$95,000 with respect to United States counsel and \$20,000 with respect to United Kingdom counsel in connection with the execution of this Agreement and (B) \$30,000 with respect to United States and United Kingdom counsel in connection with each Triggering Event Date (as defined below) on which the Company is required to provide a certificate pursuant to Section 4(o).

Section 4. ADDITIONAL COVENANTS

The Company covenants and agrees with the Agent as follows, in addition to any other covenants and agreements made elsewhere in this Agreement:

(a) Exchange Act Compliance. During the Agency Period, the Company shall (i) file, on a timely basis, with the Commission all reports and documents required to be filed under Section 13, 14 or 15 of the Exchange Act in the manner and within the time periods required by the Exchange Act; and (ii) either (A) include in each report filed or furnished by the Company on Form 6-K that includes the Company's quarterly interim financial statements and its annual reports on Form 20-F, a summary detailing, for the relevant reporting period, (1) the number of Shares sold through the Agent pursuant to this Agreement and (2) the net proceeds received by the Company from such sales or, in the Company's sole discretion, (B) prepare a prospectus supplement containing, or include in such other filing permitted by the Securities Act or Exchange Act (each an "**Interim Prospectus Supplement**"), such summary information and, at least once a quarter and subject to this Section 4, file such Interim Prospectus Supplement pursuant to Rule 424(b) under the Securities Act (and within the time periods required by Rule 424(b) and Rule 430B under the Securities Act).

(b) Securities Act Compliance. After the date of this Agreement, the Company shall promptly advise the Agent in writing (i) of the receipt of any comments of, or requests for additional or supplemental information from, the Commission; (ii) of the time and date of any filing of any post-effective amendment to the Registration Statement, the ADS Registration Statement, any Rule 462(b) Registration Statement or any amendment or supplement to the Prospectus or any Free Writing Prospectus; (iii) of the time and date that any post-effective amendment to the Registration Statement, the ADS Registration Statement or any Rule 462(b) Registration Statement becomes effective; and (iv) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement, the ADS Registration Statement or any post-effective amendment thereto, any Rule 462(b) Registration Statement or any amendment or supplement to the Prospectus or of any order preventing or suspending the use of any Free Writing Prospectus or the Prospectus, or of any proceedings to remove, suspend or terminate from listing or quotation the ADSs from any securities exchange upon which they are listed for trading or included or designated for quotation, or of the threatening or initiation of any proceedings for any of such purposes. If the Commission shall enter any such stop order at any time, the Company will use its best efforts to obtain the lifting of such order as soon as practicable. Additionally, the Company agrees that it shall comply with the provisions of Rule 424(b) and Rule 433, as applicable, under the Securities Act and will use its reasonable efforts to confirm that any filings made by the Company under such Rule 424(b) or Rule 433 were filed in a timely manner with the Commission.

(c) Amendments and Supplements to the Prospectus and Other Securities Act Matters. If any event shall occur or condition exist as a result of which it is necessary to amend or supplement the Prospectus so that the Prospectus does not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances when the Prospectus is delivered to a purchaser, not misleading, or if in the opinion of the Agent or counsel for the Agent it is otherwise necessary to amend or supplement the Prospectus to comply with applicable law, including the Securities Act, the Company agrees (subject to Section 4(d) and Section 4(f)) to promptly prepare, file with the Commission and furnish at its own expense to the Agent, amendments or supplements to the Prospectus so that the statements in the Prospectus as so amended or supplemented will not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances when the Prospectus is delivered to a purchaser, not misleading or so that the Prospectus, as amended or supplemented, will comply with applicable law including the Securities Act. Neither the Agent's consent to, or delivery of, any such amendment or supplement shall constitute a waiver of any of the Company's obligations under Sections 4(d) and 4(f). Notwithstanding the foregoing, the Company shall not be required to file such amendment or supplement if there is no pending Issuance Notice and the Company believes that it is in its best interests not to file such amendment or supplement.

(d) Agent's Review of Proposed Amendments and Supplements. Prior to amending or supplementing the Registration Statement (including any registration statement filed under Rule 462(b) under the Securities Act), the ADS Registration Statement or the Prospectus (excluding any amendment or supplement through incorporation by reference of any report filed under the Exchange Act), the Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of each such proposed amendment or supplement, and the Company shall not file or use any such proposed amendment or supplement without the Agent's prior consent, and to file with the Commission within the applicable period specified in Rule 424(b) under the Securities Act any prospectus required to be filed pursuant to such Rule.

(e) Use of Free Writing Prospectus. Neither the Company nor the Agent has prepared, used, referred to or distributed, or will prepare, use, refer to or distribute, without the other party's prior written consent, any "written communication" that constitutes a "free writing prospectus" as such terms are defined in Rule 405 under the Securities Act with respect to the offering contemplated by this Agreement (any such free writing prospectus being referred to herein as a "**Free Writing Prospectus**").

(f) Free Writing Prospectuses. The Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of each proposed Free Writing Prospectus or any amendment or supplement thereto to be prepared by or on behalf of, used by, or referred to by the Company and the Company shall not file, use or refer to any proposed Free Writing Prospectus or any amendment or supplement thereto without the Agent's consent, which shall not be unreasonably withheld, conditioned or delayed. The Company shall furnish to the Agent, without charge, as many copies of any Free Writing Prospectus prepared by or on behalf of, or used by the Company, as the Agent may reasonably request. If at any time when a prospectus is required by the Securities Act (including, without limitation, pursuant to Rule 173(d)) to be delivered in connection with sales of the Shares (but in any event if at any time through and including the date of this Agreement) there occurred or occurs an event or development as a result of which any Free Writing Prospectus prepared by or on behalf of, used by, or referred to by the Company conflicted or would conflict with the information contained in the Registration Statement or included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances prevailing at that subsequent time, not misleading, the Company shall promptly amend or supplement such Free Writing Prospectus to eliminate or correct such conflict or so that the statements in such Free Writing Prospectus as so amended or supplemented will not include an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances prevailing at such subsequent time, not misleading, as the case may be; *provided, however*, that prior to amending or supplementing any such Free Writing Prospectus, the Company shall furnish to the Agent for review, a reasonable amount of time prior to the proposed time of filing or use thereof, a copy of such proposed amended or supplemented Free Writing Prospectus and the Company shall not file, use or refer to any such amended or supplemented Free Writing Prospectus without the Agent's consent, which shall not be unreasonably withheld, conditioned or delayed.

(g) Filing of Agent Free Writing Prospectuses. The Company shall not take any action that would result in the Agent or the Company being required to file with the Commission pursuant to Rule 433(d) under the Securities Act a Free Writing Prospectus prepared by or on behalf of the Agent that the Agent otherwise would not have been required to file thereunder.

(h) Copies of Registration Statement and Prospectus. After the date of this Agreement through the last time that a prospectus is required by the Securities Act (including, without limitation, pursuant to Rule 173(d)) to be delivered in connection with sales of the Shares, the Company agrees to furnish the Agent with copies (which may be electronic copies) of the Registration Statement, the ADS Registration Statement and each amendment thereto, and with copies of the Prospectus and each amendment or supplement thereto in the form in which it is filed with the Commission pursuant to the Securities Act or Rule 424(b) under the Securities Act, both in such quantities as the Agent may reasonably request from time to time; and, if the delivery of a prospectus is required under the Securities Act or under the blue sky or securities laws of any jurisdiction at any time on or prior to the applicable Settlement Date for any period set forth in an Issuance Notice in connection with the offering or sale of the Shares and if at such time any event has occurred as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made when such Prospectus is delivered, not misleading, or, if for any other reason it is necessary during such same period to amend or supplement the Prospectus or to file under the Exchange Act any document incorporated by reference in the Prospectus in order to comply with the Securities Act or the Exchange Act, to notify the Agent and to request that the Agent suspend offers to sell Shares (and, if so notified, the Agent shall cease such offers as soon as practicable); and if the Company decides to amend or supplement the Registration Statement, the ADS Registration Statement or the Prospectus as then amended or supplemented, to advise the Agent promptly by telephone (with confirmation in writing) and to prepare and cause to be filed promptly with the Commission an amendment or supplement to the Registration Statement, the ADS Registration Statement or the Prospectus as then amended or supplemented that will correct such statement or omission or effect such compliance; provided, however, that if during such same period the Agent is required to deliver a prospectus in respect of transactions in the Shares, the Company shall promptly prepare and file with the Commission such an amendment or supplement.

(i) Blue Sky Compliance. The Company shall cooperate with the Agent and counsel for the Agent to qualify or register the Shares for sale under (or obtain exemptions from the application of) the state securities or blue sky laws or Canadian provincial securities laws of those jurisdictions designated by the Agent, shall comply with such laws and shall continue such qualifications, registrations and exemptions in effect so long as required for the distribution of the Shares. The Company shall not be required to qualify as a foreign corporation or to take any action that would subject it to general service of process in any such jurisdiction where it is not presently qualified or where it would be subject to taxation as a foreign corporation. The Company will advise the Agent promptly of the suspension of the qualification or registration of (or any such exemption relating to) the Shares for offering, sale or trading in any jurisdiction or any initiation or threat of any proceeding for any such purpose, and in the event of the issuance of any order suspending such qualification, registration or exemption, the Company shall use its best efforts to obtain the withdrawal thereof as soon as practicable.

(j) Earnings Statement. As soon as practicable, the Company will make generally available to its security holders and to the Agent an earnings statement (which need not be audited) covering a period of at least twelve months beginning with the first fiscal quarter of the Company occurring after the date of this Agreement which shall satisfy the provisions of Section 11(a) of the Securities Act and Rule 158 under the Securities Act, which requirement may be satisfied by publicly filing the required information on EDGAR.

(k) Listing; Reservation of Shares. (a) The Company will use its best efforts to maintain the listing of the ADSs on the Principal Market; and (b) the Company will ensure it is able to allot and issue, free of preemptive rights, Ordinary Shares for the purpose of enabling the Company to satisfy its obligations under this Agreement.

(l) Registrar and Depositary. The Company shall engage and maintain, at its expense, a registrar for the Ordinary Shares and a depositary for ADSs.

(m) Due Diligence. During the term of this Agreement, the Company will reasonably cooperate with any reasonable due diligence review conducted by the Agent in connection with the transactions contemplated hereby, including, without limitation, providing information and making available documents and senior corporate officers, during normal business hours and at the Company's principal offices, as the Agent may reasonably request from time to time.

(n) Representations and Warranties. The Company acknowledges that each delivery of an Issuance Notice and each delivery of Shares on a Settlement Date shall be deemed to be (i) an affirmation to the Agent that the representations and warranties of the Company contained in or made pursuant to this Agreement are true and correct as of the date of such Issuance Notice or of such Settlement Date, as the case may be, as though made at and as of each such date, except as may be disclosed in the Prospectus (including any documents incorporated by reference therein and any supplements thereto); and (ii) an undertaking that the Company will advise the Agent if any of such representations and warranties will not be true and correct as of the Settlement Date for the Shares relating to such Issuance Notice, as though made at and as of each such date (except that such representations and warranties shall be deemed to relate to the Registration Statement and the Prospectus as amended and supplemented relating to such Shares).

(o) Deliverables at Triggering Event Dates: Certificates. The Company agrees that on or prior to the date of the first Issuance Notice and, during the term of this Agreement after the date of the first Issuance Notice, upon:

(A) the filing of the Prospectus or the amendment or supplement (other than any amendment or supplement through incorporation of any report filed under the Exchange Act) of any Registration Statement, the ADS Registration Statement or the Prospectus (other than a prospectus supplement relating solely to an offering of securities other than the Shares or a prospectus filed pursuant to Section 4(a)(ii)(B)), by means of a post-effective amendment, sticker or supplement, but not by means of incorporation of documents by reference into the Registration Statement, the ADS Registration Statement or the Prospectus;

(B) the filing with the Commission of an annual report on Form 20-F or a report on Form 6-K containing quarterly financial information (including any Form 20-F/A or Form 6-K/A containing amended financial information or a material amendment to the previously filed annual report on Form 20-F or quarterly financial information on Form 6-K), in each case, of the Company; or

(C) the filing with the Commission of a report on Form 6-K of the Company containing amended or new financial information that is material to the offering of securities of the Company in the Agent's reasonable discretion;

(any such event, a “**Triggering Event Date**”), the Company shall furnish to the Agent (but in the case of clause (C) above only if the Agent reasonably determines that the information contained in such report on Form 6-K of the Company is material) with a certificate in the form attached hereto as **Exhibit B** as of the Triggering Event Date, in the form and substance satisfactory to the Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel, modified, as necessary, to relate to the Registration Statement, the ADS Registration Statement and the Prospectus as amended or supplemented, (A) confirming that the representations and warranties of the Company contained in this Agreement are true and correct, (B) confirming that the Company has performed all of its obligations hereunder to be performed on or prior to the date of such certificate and as to the matters set forth in Section 5(a)(iii) hereof, and (C) containing any other certification that the Agent shall reasonably request. The requirement to provide a certificate under this Section 4(o) shall be waived for any Triggering Event Date occurring at a time when no Issuance Notice is pending or a suspension is in effect, which waiver shall continue until the earlier to occur of the date the Company delivers an Issuance Notice with instructions for the sale of Shares hereunder (which for such calendar quarter shall be considered a Triggering Event Date) and the next occurring Triggering Event Date. Notwithstanding the foregoing, if the Company subsequently decides to sell Shares following a Triggering Event Date when a suspension was in effect and did not provide the Agent with a certificate under this Section 4(o), then before the Company delivers an Issuance Notice with the instructions for the sale of Shares or the Agent sells any Shares pursuant to such instructions, the Company shall provide the Agent with a certificate in conformity with this Section 4(o) dated as of the date that an Issuance Notice with instructions for the sale of Shares is issued.

(p) Legal Opinions. On or prior to the date of the first Issuance Notice and on or prior to each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) for which no waiver is applicable and excluding the date of this Agreement, the Company shall cause to be furnished to the Agent a negative assurance letter and a written legal opinion of Cooley LLP, counsel to the Company, and written legal opinions of each of Cooley (UK) LLP, English counsel to the Company, Fenwick & West LLP and Kilburn & Strode LLP, intellectual property counsels to the Company, and Patterson Belknap Webb & Tyler, LLP, counsel for the Depositary, each dated the date of delivery, in form and substance reasonably satisfactory to Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel, modified, as necessary, to relate to the Registration Statement, the ADS Registration Statement and the Prospectus as then amended or supplemented. In lieu of such opinions for subsequent periodic filings, in the discretion of the Agent, the Company may furnish a reliance letter from such counsel to the Agent, permitting the Agent to rely on a previously delivered opinion letter, modified as appropriate for any passage of time or Triggering Event Date (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented as of such Triggering Event Date). The Company shall be required to furnish no more than one set of legal opinions hereunder per each filing of an annual report on Form 20-F or report on Form 6-K containing quarterly financial information.

(q) Comfort Letter. On or prior to the date of the first Issuance Notice and on or prior to each Triggering Event Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 4(o) for which no waiver is applicable and excluding the date of this Agreement, the Company shall cause KPMG LLP, the independent registered public accounting firm who has audited the financial statements included or incorporated by reference in the Registration Statement and the ADS Registration Statement, to furnish the Agent a comfort letter, dated the date of delivery, in form and substance reasonably satisfactory to the Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel; provided, however, that any such comfort letter will only be required on the Triggering Event Date specified to the extent that it contains financial statements filed with the Commission under the Exchange Act and incorporated or deemed to be incorporated by reference into a Prospectus. If requested by the Agent, the Company shall also cause a comfort letter to be furnished to the Agent on the date of occurrence of any material transaction or event requiring the filing of a report on Form 6-K containing material amended financial information of the Company, including the restatement of the Company's financial statements. The Company shall be required to furnish no more than one comfort letter hereunder per each filing of an annual report on Form 20-F or a report on Form 6-K containing quarterly financial information.

(r) Secretary's Certificate. On or prior to the date of the first Issuance Notice and on or prior to each Trigger Event Date, the Company shall furnish the Agent a certificate executed by the Secretary of the Company, signing in such capacity, dated the date of delivery (i) certifying that attached thereto are true and complete copies of the resolutions duly adopted by the Board of Directors of the Company authorizing the execution and delivery of this Agreement and the consummation of the transactions contemplated hereby (including, without limitation, the issuance of the Shares pursuant to this Agreement), which authorization shall be in full force and effect on and as of the date of such certificate, (ii) certifying and attesting to the office, incumbency, due authority and specimen signatures of each Person who executed this Agreement for or on behalf of the Company, and (iii) containing any other certification that the Agent shall reasonably request.

(s) Agent's Own Account; Clients' Account. The Company consents to the Agent trading, in compliance with applicable law, in the ADSs for the Agent's own account and for the account of its clients at the same time as sales of the Shares occur pursuant to this Agreement.

(t) Investment Limitation. The Company shall not invest, or otherwise use the proceeds received by the Company from its sale of the Shares in such a manner as would require the Company or any of its subsidiaries to register as an investment company under the Investment Company Act.

(u) Market Activities. The Company will not take, directly or indirectly, any action designed to or that might be reasonably expected to cause or result in stabilization or manipulation of the price of the Shares or any other reference security, whether to facilitate the sale or resale of the Shares or otherwise, and the Company will, and shall cause each of its affiliates to, comply with all applicable provisions of Regulation M. If the limitations of Rule 102 of Regulation M ("**Rule 102**") do not apply with respect to the Shares or any other reference security pursuant to any exception set forth in Section (d) of Rule 102, then promptly upon notice from the Agent (or, if later, at the time stated in the notice), the Company will, and shall cause each of its affiliates to, comply with Rule 102 as though such exception were not available but the other provisions of Rule 102 (as interpreted by the Commission) did apply. The Company shall promptly notify the Agent if it no longer meets the requirements set forth in Section (d) of Rule 102 or if the exemptive provisions set forth in Rule 101(c)(1) of Regulation M are not satisfied with respect to the Company or the Shares.

(v) Chief Financial Officer Certificate. On or prior to the date of the first Issuance Notice and on or prior to each Triggering Event Date, if the Agent reasonably requests, the Company shall furnish to the Agent a certificate executed by the Chief Financial Officer of the Company, signing in such capacity, dated the date of delivery with respect to certain financial data contained in the Registration Statement and the Prospectus, providing "management comfort" with respect to such information, in form and substance reasonably satisfactory to the Agent.

(w) Depository Actions. The Company shall cause the Depository to, on or prior to each Settlement Date, deliver to the Company certificates reasonably satisfactory to the Agent evidencing the deposit with the Depository or its nominee of the Underlying Shares being so deposited against issuance of ADRs evidencing the ADSs to be delivered by the Company at such Settlement Date.

(x) Notice of Other Sale. Without the written consent of the Agent, the Company will not, directly or indirectly, offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Ordinary Shares, ADSs or securities convertible into or exchangeable for Ordinary Shares or ADSs (other than Shares hereunder), warrants or any rights to purchase or acquire Ordinary Shares or ADSs, during the period beginning on the third Trading Day immediately prior to the date on which any Issuance Notice is delivered to the Agent hereunder and ending on the third Trading Day immediately following the Settlement Date with respect to Shares sold pursuant to such Issuance Notice; and will not directly or indirectly enter into any other “at the market” or continuous equity transaction, offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Ordinary Shares or ADSs (other than the Shares offered pursuant to this Agreement) or securities convertible into or exchangeable for Ordinary Shares or ADSs, warrants or any rights to purchase or acquire, Ordinary Shares or ADSs prior to the termination of this Agreement; provided, however, that such restrictions will not be required in connection with the Company’s (i) issuance of Ordinary Shares or ADSs upon conversion of the non-voting ordinary shares purchased in the private investment in public equity, pursuant to that certain share purchase agreement between the Company and certain investors dated July 15, 2022, as described in the Prospectus, (ii) issuance or sale of Ordinary Shares or ADSs, options to purchase Ordinary Shares or ADSs or Ordinary Shares or ADSs issuable upon the exercise of options or other equity awards pursuant to any employee or director share option, incentive or benefit plan, share purchase or ownership plan, long-term incentive plan, dividend reinvestment plan, inducement award under Nasdaq rules or other compensation plan of the Company or its subsidiaries, as in effect on the date of this Agreement, (iii) issuance or sale of Ordinary Shares or ADSs issuable upon exchange, conversion or redemption of securities or the exercise or vesting of warrants, options or other equity awards or rights outstanding at the date of this Agreement, (iv) modification of any outstanding options, warrants or any rights to purchase or acquire Ordinary Shares or ADSs, (v) offer, issue and sell Ordinary Shares or ADSs, or any securities convertible into or exercisable or exchangeable for Ordinary Shares or ADSs, in connection with any merger, acquisition or strategic investment (including any joint venture, strategic alliance or partnership) and (vi) offer, issue and sell Ordinary Shares or ADSs, or any securities convertible into or exercisable or exchangeable for Ordinary Shares or ADSs, on an arm’s-length basis to, to any unaffiliated collaborators, patient foundations or organizations, or any other similar parties pursuant to a collaboration, licensing agreement, strategic alliance or similar transaction; *provided however*, that the aggregate number of Ordinary Shares or ADSs, or any securities convertible into or exercisable or exchangeable for Ordinary Shares or ADSs, offered, issued or sold pursuant to clauses (v) and (vi) hereof, shall not exceed 5.0% of the aggregate number of Ordinary Shares outstanding immediately prior to giving effect to such issuance or sale.

(y) Indemnification for Transfer Taxes. The Company shall pay, and shall indemnify and hold the Agent harmless against, any Transfer Taxes (and any interest or penalties imposed thereon) that are payable by or on behalf of the Agent in respect of (i) the execution and delivery of this Agreement or the Deposit Agreement, (ii) the issuance and allotment of the Underlying Shares by the Company to the Depository in the manner contemplated herein and in the Deposit Agreement, (iii) the issuance and delivery of the ADSs (and any corresponding ADRs evidencing such ADSs) by the Depository to the Agent (or purchasers procured by the Agent) in the manner contemplated herein and in the Deposit Agreement, or (iv) the sale and delivery of the ADSs (and any corresponding ADRs evidencing such ADSs) by the Agent to the initial purchasers thereof in the manner contemplated herein and in the Deposit Agreement.

(z) Free and Clear Payments. All sums payable by the Company to the Agent under this Agreement shall be paid free and clear of and without any deduction or withholding for or on account of any current or future taxes or duties, unless the deduction or withholding is required by law, in which case the Company shall pay such additional amount as will result in the receipt by the Agent of the full amount that would have been received had no deduction or withholding been made other than to the extent that any deductions or withholdings of any present or future taxes or duties are imposed by a jurisdiction as a result of any present or former connection (other than any connection resulting from the transactions contemplated by this Agreement) between the Agent and such jurisdiction.

(aa) VAT. All sums payable to the Agent shall be considered to be exclusive of any value added tax chargeable pursuant to the Value Added Tax Act 1994 or any equivalent value added or sales tax whether imposed in the United Kingdom (instead of or in addition to value added tax) or elsewhere from time to time (“VAT”). Where VAT is or becomes chargeable in respect of any amount payable hereunder to the Agent, the Company shall in addition to the sum payable hereunder (and at the same time) pay an amount equal to any applicable VAT subject to receipt of a valid VAT invoice (or equivalent documentation in any jurisdiction other than the United Kingdom (to the extent required)) from the Agent. Where the Company is required by the terms of this Agreement to reimburse or indemnify the Agent for any cost or expense, the Company shall reimburse or indemnify the Agent for the full amount of such cost or expense, including such part thereof as represents VAT, save to the extent that the Agent (or any member of the Agent’s group for VAT purposes) is entitled to credit or repayment in respect of such VAT.

Section 5. CONDITIONS TO DELIVERY OF ISSUANCE NOTICES AND TO SETTLEMENT

(a) Conditions Precedent to the Right of the Company to Deliver an Issuance Notice and the Obligation of the Agent to Sell Shares. The right of the Company to deliver an Issuance Notice hereunder is subject to the satisfaction, on the date of delivery of such Issuance Notice, and the obligation of the Agent to use its commercially reasonable efforts to place Shares during the applicable period set forth in the Issuance Notice is subject to the satisfaction, on each Trading Day during the applicable period set forth in the Issuance Notice, of each of the following conditions:

(i) Accuracy of the Company's Representations and Warranties; Performance by the Company. The Company shall have delivered the certificate required to be delivered pursuant to Section 4(o) on or before the date on which delivery of such certificate is required pursuant to Section 4(o). The Company shall have performed, satisfied and complied with all covenants, agreements and conditions required by this Agreement to be performed, satisfied or complied with by the Company at or prior to such date, including, but not limited to, the covenants contained in Section 4(p), Section 4(q) and Section 4(r).

(ii) No Injunction. No statute, rule, regulation, executive order, decree, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any court or governmental authority of competent jurisdiction or any self-regulatory organization having authority over the matters contemplated hereby that prohibits or directly and materially adversely affects any of the transactions contemplated by this Agreement, and no proceeding shall have been commenced that may have the effect of prohibiting or materially adversely affecting any of the transactions contemplated by this Agreement.

(iii) Material Adverse Effects. Except as disclosed in the Prospectus and the Time of Sale Information, in the judgment of the Agent there shall not have occurred any Material Adverse Effect.

(iv) No Suspension of Trading in or Delisting of ADSs; Other Events. The trading of the ADSs (including without limitation the ADSs sold pursuant to this Agreement) shall not have been suspended by the Commission, the Principal Market or FINRA and the ADSs (including without limitation the ADSs sold pursuant to this Agreement) shall have been approved for listing or quotation on and shall not have been delisted from the Nasdaq Stock Market, the New York Stock Exchange or any of their constituent markets. There shall not have occurred (and be continuing in the case of occurrences under clauses (i) and (ii) below) any of the following: (i) trading or quotation in any of the Company's securities shall have been suspended or limited by the Commission or by the Principal Market or trading in securities generally on the Principal Market shall have been suspended or limited, or minimum or maximum prices shall have been generally established on any of such stock exchanges by the Commission or FINRA; (ii) a general banking moratorium shall have been declared by any United Kingdom, federal or New York authorities; or (iii) there shall have occurred any outbreak or escalation of national or international hostilities or any crisis or calamity, or any change in the United Kingdom, United States or international financial markets, or any substantial change or development involving a prospective substantial change in United Kingdom's, United States' or international political, financial or economic conditions, as in the judgment of the Agent is material and adverse and makes it impracticable to market the Shares in the manner and on the terms described in the Prospectus or to enforce contracts for the sale of securities.

(b) Documents Required to be Delivered on each Issuance Notice Date. The Agent's obligation to use its commercially reasonable efforts to place Shares hereunder shall additionally be conditioned upon the delivery to the Agent on or before the Issuance Notice Date of a certificate in form and substance reasonably satisfactory to the Agent, executed by the Chief Executive Officer or Chief Financial Officer of the Company, to the effect that all conditions to the delivery of such Issuance Notice shall have been satisfied as at the date of such certificate (which certificate shall not be required if the foregoing representations shall be set forth in the Issuance Notice).

(c) No Misstatement or Material Omission. The Agent shall not have advised the Company that the Registration Statement, the ADS Registration Statement, the Prospectus or the Time of Sale Information, or any amendment or supplement thereto, contains an untrue statement of fact that in the Agent's reasonable opinion is material, or omits to state a fact that in the Agent's reasonable opinion is material and is required to be stated therein or is necessary to make the statements therein not misleading.

(d) Deposit Agreement. The Deposit Agreement shall be in full force and effect.

Section 6. INDEMNIFICATION AND CONTRIBUTION

(a) Indemnification of the Agent. The Company agrees to indemnify and hold harmless the Agent, its officers and employees, and each person, if any, who controls the Agent within the meaning of the Securities Act or the Exchange Act against any loss, claim, damage, liability or expense, as incurred, to which the Agent or such officer, employee or controlling person may become subject, under the Securities Act, the Exchange Act, other federal or state statutory law or regulation, or the laws or regulations of foreign jurisdictions where Shares have been offered or sold or at common law or otherwise (including in settlement of any litigation), insofar as such loss, claim, damage, liability or expense (or actions in respect thereof as contemplated below) arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, or any amendment thereto, including any information deemed to be a part thereof pursuant to Rule 430B under the Securities Act, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading; or (ii) any untrue statement or alleged untrue statement of a material fact contained in any Free Writing Prospectus that the Company has used, referred to or filed, or is required to file, pursuant to Rule 433(d) of the Securities Act or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading, and to reimburse the Agent and each such officer, employee and controlling person for any and all expenses (including the reasonable and documented fees and disbursements of counsel chosen by the Agent) as such expenses are reasonably incurred by the Agent or such officer, employee or controlling person in connection with investigating, defending, settling, compromising or paying any such loss, claim, damage, liability, expense or action; provided, however, that the foregoing indemnity agreement shall not apply to any loss, claim, damage, liability or expense to the extent, but only to the extent, arising out of or based upon any untrue statement or alleged untrue statement or omission or alleged omission made in reliance upon and in conformity with written information furnished to the Company by the Agent expressly for use in the Registration Statement, any such Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto), it being understood and agreed that the only such information furnished by the Agent to the Company consists of the information described in subsection (b) below. The indemnity agreement set forth in this Section 6(a) shall be in addition to any liabilities that the Company may otherwise have.

(b) Indemnification of the Company and its Directors and Officers. The Agent agrees to indemnify and hold harmless the Company, each of its directors, each of its officers who signed the Registration Statement, and each person, if any, who controls the Company within the meaning of the Securities Act or the Exchange Act, against any loss, claim, damage, liability or expense, as incurred, to which the Company, or any such director, officer, or controlling person may become subject, under the Securities Act, the Exchange Act, or other federal or state statutory law or regulation, or at common law or otherwise (including in settlement of any litigation.), insofar as such loss, claim, damage, liability or expense (or actions in respect thereof as contemplated below) arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, or any amendment thereto, or any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading or (ii) any untrue statement or alleged untrue statement of a material fact included or incorporated by reference in any Free Writing Prospectus or the Prospectus that the Company has used, referred to or filed, or is required to file, pursuant to Rule 433 of the Securities Act or the Prospectus (or any such amendment or supplement) or the omission or alleged omission to state therein a material fact necessary in order to make the statements, in the light of the circumstances under which they were made, not misleading, in each case to the extent, but only to the extent, that such untrue statement or alleged untrue statement or omission or alleged omission was made in the Registration Statement, Free Writing Prospectus or the Prospectus (or any such amendment or supplement), in reliance upon and in conformity with information relating to the Agent furnished to the Company by the Agent in writing expressly for use therein; and to reimburse the Company, or any such director, officer, or controlling person for any and all expenses (including the fees and disbursements of counsel) as such expenses are incurred by the Company, or any such director, officer, or controlling person in connection with investigating, defending, settling, compromising or paying any such loss, claim, damage, liability, expense or action. The Company hereby acknowledges that the only information that the Agent have furnished to the Company expressly for use in the Registration Statement, any Free Writing Prospectus that the Company has filed, or is required to file, pursuant to Rule 433(d) of the Securities Act or the Prospectus (or any amendment or supplement to the foregoing) is the information set forth in the first sentence of the ninth paragraph under the caption "Plan of Distribution" in the Prospectus. The indemnity agreement set forth in this Section 6(b) shall be in addition to any liabilities that the Agent may otherwise have.

(c) Notifications and Other Indemnification Procedures. Promptly after receipt by an indemnified party under this Section 6 of notice of the commencement of any action, such indemnified party will, if a claim in respect thereof is to be made against an indemnifying party under this Section 6, notify the indemnifying party in writing of the commencement thereof, but the omission so to notify the indemnifying party will not relieve it from any liability which it may have to any indemnified party for contribution or otherwise than under the indemnity agreement contained in this Section 6 or to the extent it is not prejudiced as a proximate result of such failure. In case any such action is brought against any indemnified party and such indemnified party seeks or intends to seek indemnity from an indemnifying party, the indemnifying party will be entitled to participate in, and, to the extent that it shall elect, jointly with all other indemnifying parties similarly notified, by written notice delivered to the indemnified party promptly after receiving the aforesaid notice from such indemnified party, to assume the defense thereof with counsel reasonably satisfactory to such indemnified party; provided, however, if the defendants in any such action include both the indemnified party and the indemnifying party and the indemnified party shall have reasonably concluded based on the advice of counsel that a conflict may arise between the positions of the indemnifying party and the indemnified party in conducting the defense of any such action or that there may be legal defenses available to it and/or other indemnified parties which are different from or additional to those available to the indemnifying party, the indemnified party or parties shall have the right to select separate counsel to assume such legal defenses and to otherwise participate in the defense of such action on behalf of such indemnified party or parties. Upon receipt of notice from the indemnifying party to such indemnified party of such indemnifying party's election so to assume the defense of such action and approval by the indemnified party of counsel, the indemnifying party will not be liable to such indemnified party under this Section 6 for any legal or other expenses subsequently incurred by such indemnified party in connection with the defense thereof unless (i) the indemnified party shall have employed separate counsel in accordance with the proviso to the preceding sentence (it being understood, however, that the indemnifying party shall not be liable for the fees and expenses of more than one separate counsel (together with local counsel), representing the indemnified parties who are parties to such action), which counsel (together with any local counsel) for the indemnified parties shall be selected by the indemnified party (in the case of counsel for the indemnified parties referred to in Section 6(a) and Section 6(b) above), (ii) the indemnifying party shall not have employed counsel satisfactory to the indemnified party to represent the indemnified party within a reasonable time after notice of commencement of the action or (iii) the indemnifying party has authorized in writing the employment of counsel for the indemnified party at the expense of the indemnifying party, in each of which cases the fees and expenses of counsel shall be at the expense of the indemnifying party and shall be paid as they are incurred.

(d) Settlements. The indemnifying party under this Section 6 shall not be liable for any settlement of any proceeding effected without its written consent, but if settled with such consent or if there be a final judgment for the plaintiff, the indemnifying party agrees to indemnify the indemnified party against any loss, claim, damage, liability or expense by reason of such settlement or judgment. Notwithstanding the foregoing sentence, if at any time an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for fees and expenses of counsel as contemplated by Section 6(d) hereof, the indemnifying party agrees that it shall be liable for any settlement of any proceeding effected without its written consent if (i) such settlement is entered into more than 30 days after receipt by such indemnifying party of the aforesaid request; and (ii) such indemnifying party shall not have reimbursed the indemnified party in accordance with such request prior to the date of such settlement. No indemnifying party shall, without the prior written consent of the indemnified party, effect any settlement, compromise or consent to the entry of judgment in any pending or threatened action, suit or proceeding in respect of which any indemnified party is or could have been a party and indemnity was or could have been sought hereunder by such indemnified party, unless such settlement, compromise or consent includes an unconditional release of such indemnified party from all liability on claims that are the subject matter of such action, suit or proceeding.

(e) Contribution. If the indemnification provided for in this Section 6 is for any reason held to be unavailable to or otherwise insufficient to hold harmless an indemnified party in respect of any losses, claims, damages, liabilities or expenses referred to therein, then each indemnifying party shall contribute to the aggregate amount paid or payable by such indemnified party, as incurred, as a result of any losses, claims, damages, liabilities or expenses referred to therein (i) in such proportion as is appropriate to reflect the relative benefits received by the Company, on the one hand, and the Agent, on the other hand, from the offering of the Shares pursuant to this Agreement; or (ii) if the allocation provided by clause (i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above but also the relative fault of the Company, on the one hand, and the Agent, on the other hand, in connection with the statements or omissions which resulted in such losses, claims, damages, liabilities or expenses, as well as any other relevant equitable considerations. The relative benefits received by the Company, on the one hand, and the Agent, on the other hand, in connection with the offering of the Shares pursuant to this Agreement shall be deemed to be in the same respective proportions as the total gross proceeds from the offering of the Shares (before deducting expenses) received by the Company bear to the total Selling Commissions received by the Agent. The relative fault of the Company, on the one hand, and the Agent, on the other hand, shall be determined by reference to, among other things, whether any such untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company, on the one hand, or the Agent, on the other hand, and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

The amount paid or payable by a party as a result of the losses, claims, damages, liabilities and expenses referred to above shall be deemed to include, subject to the limitations set forth in Section 6(c), any legal or other fees or expenses reasonably incurred by such party in connection with investigating or defending any action or claim. The provisions set forth in Section 6(c) with respect to notice of commencement of any action shall apply if a claim for contribution is to be made under this Section 6(e); *provided, however*, that no additional notice shall be required with respect to any action for which notice has been given under Section 6(c) for purposes of indemnification.

The Company and the Agent agree that it would not be just and equitable if contribution pursuant to this Section 6(e) were determined by pro rata allocation or by any other method of allocation which does not take account of the equitable considerations referred to in this Section 6(e).

Notwithstanding the provisions of this Section 6(e), the Agent shall not be required to contribute any amount in excess of the Selling Commissions received by the Agent in connection with the offering contemplated hereby. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 6(e), each officer and employee of the Agent and each person, if any, who controls the Agent within the meaning of the Securities Act or the Exchange Act shall have the same rights to contribution as the Agent, and each director of the Company, each officer of the Company who signed the Registration Statement, and each person, if any, who controls the Company within the meaning of the Securities Act and the Exchange Act shall have the same rights to contribution as the Company.

Section 7. TERMINATION & SURVIVAL

(a) Term. Subject to the provisions of this Section 7, the term of this Agreement shall continue from the date of this Agreement until the end of the Agency Period, unless earlier terminated by the parties to this Agreement pursuant to this Section 7.

(b) Termination; Survival Following Termination

(i) Either party may terminate this Agreement prior to the end of the Agency Period, by giving written notice as required by this Agreement, upon ten (10) Trading Days' notice to the other party; provided that, (A) if the Company terminates this Agreement after the Agent confirms to the Company any sale of Shares, the Company shall remain obligated to comply with Section 3(b)(v) with respect to such Shares and (B) Section 2, Section 6, Section 7 and Section 8 shall survive termination of this Agreement. If termination shall occur prior to the Settlement Date for any sale of Shares, such sale shall nevertheless settle in accordance with the terms of this Agreement.

(ii) In addition to the survival provision of Section 7(b)(i), the respective indemnities, agreements, representations, warranties and other statements of the Company, of its officers and of the Agent set forth in or made pursuant to this Agreement will remain in full force and effect, regardless of any investigation made by or on behalf of the Agent or the Company or any of its or their partners, officers or directors or any controlling person, as the case may be, and, anything herein to the contrary notwithstanding, will survive delivery of and payment for the Shares sold hereunder and any termination of this Agreement.

Section 8. MISCELLANEOUS

(a) Press Releases and Disclosure. The Company may issue a press release describing the material terms of the transactions contemplated hereby as soon as practicable following the date of this Agreement, and may file with the Commission a Report on Form 6-K, with this Agreement attached as an exhibit thereto, describing the material terms of the transactions contemplated hereby, and the Company shall consult with the Agent prior to making such disclosures, and the parties hereto shall use all commercially reasonable efforts, acting in good faith, to agree upon a text for such disclosures that is reasonably satisfactory to all parties hereto. No party hereto shall issue thereafter any press release or like public statement (including, without limitation, any disclosure required in reports filed with the Commission pursuant to the Exchange Act) related to this Agreement or any of the transactions contemplated hereby without the prior written approval of the other party hereto, except as may be necessary or appropriate in the reasonable opinion of the party seeking to make disclosure to comply with the requirements of applicable law or stock exchange rules. If any such press release or like public statement is so required, the party making such disclosure shall consult with the other party prior to making such disclosure, and the parties shall use all commercially reasonable efforts, acting in good faith, to agree upon a text for such disclosure that is reasonably satisfactory to all parties hereto.

(b) No Advisory or Fiduciary Relationship. The Company acknowledges and agrees that (i) the transactions contemplated by this Agreement, including the determination of any fees, are arm's-length commercial transactions between the Company and the Agent, (ii) when acting as a principal under this Agreement, the Agent is and has been acting solely as a principal and is not the agent or fiduciary of the Company, or its shareholders, creditors, employees or any other party, (iii) the Agent has not assumed nor will assume an advisory or fiduciary responsibility in favor of the Company with respect to the transactions contemplated hereby or the process leading thereto (irrespective of whether the Agent has advised or is currently advising the Company on other matters) and the Agent does not have any obligation to the Company with respect to the transactions contemplated hereby except the obligations expressly set forth in this Agreement, (iv) the Agent and its affiliates may be engaged in a broad range of transactions that involve interests that differ from those of the Company, and (v) the Agent has not provided any legal, accounting, regulatory or tax advice with respect to the transactions contemplated hereby and the Company has consulted its own legal, accounting, regulatory and tax advisors to the extent it deemed appropriate.

(c) Research Analyst Independence. The Company acknowledges that the Agent's research analysts and research departments are required to and should be independent from their respective investment banking divisions and are subject to certain regulations and internal policies, and as such the Agent's research analysts may hold views and make statements or investment recommendations and/or publish research reports with respect to the Company or the offering that differ from the views of their respective investment banking divisions. The Company understands that the Agent is a full service securities firm and as such from time to time, subject to applicable securities laws, may effect transactions for its own account or the account of its customers and hold long or short positions in debt or equity securities of the companies that may be the subject of the transactions contemplated by this Agreement.

(d) Notices. All communications hereunder shall be in writing and shall be mailed, hand delivered or telecopied and confirmed to the parties hereto as follows:

If to the Agent:

Jefferies LLC
520 Madison Avenue
New York, NY 10022
Attention: General Counsel

with a copy (which shall not constitute notice) to:

Davis Polk & Wardwell LLP
450 Lexington Avenue
New York, NY 10017
Attention: Yasin Keshvargar

If to the Company:

Immunocore Holdings plc
Six Tower Bridge, Suite 200
181 Washington Street
Conshohocken, PA 19428
Attention: Chief Financial Officer

with a copy (which shall not constitute notice) to:

Cooley LLP
500 Boylston Street
Boston, MA 02116
Attention: Courtney T. Thorne

Any party hereto may change the address for receipt of communications by giving written notice to the others in accordance with this Section 8(d).

(e) Successors. This Agreement will inure to the benefit of and be binding upon the parties hereto, and to the benefit of the employees, officers and directors and controlling persons referred to in Section 6, and in each case their respective successors, and no other person will have any right or obligation hereunder. The term “successors” shall not include any purchaser of the Shares as such from the Agent merely by reason of such purchase.

(f) Partial Unenforceability. The invalidity or unenforceability of any Article, Section, paragraph or provision of this Agreement shall not affect the validity or enforceability of any other Article, Section, paragraph or provision hereof. If any Article, Section, paragraph or provision of this Agreement is for any reason determined to be invalid or unenforceable, there shall be deemed to be made such minor changes (and only such minor changes) as are necessary to make it valid and enforceable.

(g) Governing Law Provisions.

(i) This Agreement shall be governed by and construed in accordance with the internal laws of the State of New York applicable to agreements made and to be performed in such state. Any legal suit, action or proceeding arising out of or based upon this Agreement or the transactions contemplated hereby (“**Related Proceedings**”) may be instituted in the federal courts of the United States of America located in the Borough of Manhattan in the City of New York or the courts of the State of New York in each case located in the Borough of Manhattan in the City of New York (collectively, the “**Specified Courts**”), and each party irrevocably submits to the exclusive jurisdiction (except for proceedings instituted in regard to the enforcement of a judgment of any such court, as to which such jurisdiction is non-exclusive) of such courts in any such suit, action or proceeding. Service of any process, summons, notice or document by mail to such party’s address set forth above shall be effective service of process for any suit, action or other proceeding brought in any such court. The parties irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the Specified Courts and irrevocably and unconditionally waive and agree not to plead or claim in any such court that any such suit, action or other proceeding brought in any such court has been brought in an inconvenient forum. To the extent that the Company has or hereafter may acquire any immunity (on the grounds of sovereignty or otherwise) from the jurisdiction of any court or from any legal process with respect to itself or its property, the Company irrevocably waives, to the fullest extent permitted by law, such immunity in respect of any such suit, action or proceeding.

(ii) The Company hereby irrevocably appoints Immunocore LLC, with offices at Six Tower Bridge, Suite 200, 181 Washington Street, Conshohocken, PA 19428, as its agent for service of process in any Related Proceeding and agrees that service of process in any such Related Proceeding may be made upon it at the office of such agent. The Company waives, to the fullest extent permitted by law, any other requirements of or objections to personal jurisdiction with respect thereto. The Company represents and warrants that such agent has agreed to act as the Company’s agent for service of process, and the Company agrees to take any and all action, including the filing of any and all documents and instruments, that may be necessary to continue such appointment in full force and effect.

(h) Judgment Currency. If for the purposes of obtaining judgment in any court it is necessary to convert a sum due hereunder into any currency other than United States dollars, the parties hereto agree, to the fullest extent permitted by law, that the rate of exchange used shall be the rate at which in accordance with normal banking procedures the Agent could purchase United States dollars with such other currency in The City of New York on the business day preceding that on which final judgment is given. The obligation of the Company with respect to any sum due from it to the Agent or any person controlling the Agent shall, notwithstanding any judgment in a currency other than United States dollars, not be discharged until the first business day following receipt by the Agent or controlling person of any sum in such other currency, and only to the extent that Agent or controlling person may in accordance with normal banking procedures purchase United States dollars with such other currency. If the United States dollars so purchased are less than the sum originally due to the Agent or controlling person hereunder, the Company agrees as a separate obligation and notwithstanding any such judgment, to indemnify the Agent or controlling person against such loss. If the United States dollars so purchased are greater than the sum originally due to the Agent or controlling person hereunder, the Agent or controlling person agrees to pay to the Company an amount equal to the excess of the dollars so purchased over the sum originally due to the Agent or controlling person hereunder.

(i) General Provisions. This Agreement constitutes the entire agreement of the parties to this Agreement and supersedes all prior written or oral and all contemporaneous oral agreements, understandings and negotiations with respect to the subject matter hereof. This Agreement may be signed in two or more counterparts, each of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument. The words "execution," "signed," "signature," and words of like import in this Agreement or in any other certificate, agreement or document related to this Agreement, if any, shall include images of manually executed signatures transmitted by facsimile or other electronic format (including, without limitation, "pdf," "tif" or "jpg") and other electronic signatures (including, without limitation, DocuSign and AdobeSign). The use of electronic signatures and electronic records (including, without limitation, any contract or other record created, generated, sent, communicated, received, or stored by electronic means) shall be of the same legal effect, validity and enforceability as a manually executed signature or use of a paper-based record-keeping system to the fullest extent permitted by applicable law, including the Federal Electronic Signatures in Global and National Commerce Act, the New York State Electronic Signatures and Records Act and any other applicable law, including, without limitation, any state law based on the Uniform Electronic Transactions Act or the Uniform Commercial Code. This Agreement may not be amended or modified unless in writing by all of the parties hereto, and no condition herein (express or implied) may be waived unless waived in writing by each party whom the condition is meant to benefit. The Article and Section headings herein are for the convenience of the parties only and shall not affect the construction or interpretation of this Agreement.

(j) Recognition of the U.S. Special Resolution Regimes In the event that the Agent is a Covered Entity and becomes subject to a proceeding under a U.S. Special Resolution Regime, the transfer from the Agent of this Agreement, and any interest and obligation in or under this Agreement, will be effective to the same extent as the transfer would be effective under the U.S. Special Resolution Regime if this Agreement, and any such interest and obligation, were governed by the laws of the United States or a state of the United States. In the event that the Agent that is a Covered Entity or a BHC Act Affiliate of the Agent becomes subject to a proceeding under a U.S. Special Resolution Regime, Default Rights under this Agreement that may be exercised against the Agent are permitted to be exercised to no greater extent than such Default Rights could be exercised under the U.S. Special Resolution Regime if this Agreement were governed by the laws of the United States or a state of the United States. As used in this Section 8:

(i) “BHC Act Affiliate” has the meaning assigned to the term “affiliate” in, and shall be interpreted in accordance with, 12 U.S.C. § 1841(k).

(ii) “Covered Entity” means any of the following:

(A) a “covered entity” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 252.82(b);

(B) a “covered bank” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 47.3(b); or

(C) a “covered FSI” as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 382.2(b).

(iii) “Default Right” has the meaning assigned to that term in, and shall be interpreted in accordance with, 12 C.F.R. §§ 252.81, 47.2 or 382.1, as applicable.

(iv) “U.S. Special Resolution Regime” means each of (i) the Federal Deposit Insurance Act and the regulations promulgated thereunder and (ii) Title II of the Dodd-Frank Wall Street Reform and Consumer Protection Act and the regulations promulgated thereunder.

[Signature Page Immediately Follows]

If the foregoing is in accordance with your understanding of our agreement, kindly sign and return to the Company the enclosed copies hereof, whereupon this instrument, along with all counterparts hereof, shall become a binding agreement in accordance with its terms

Very truly yours,

IMMUNOCORE HOLDINGS PLC

By: /s/ Brian Di Donato

Name: Brian Di Donato

Title: Chief Financial Officer

The foregoing Agreement is hereby confirmed and accepted by the Agent in New York, New York as of the date first above written.

JEFFERIES LLC

By: /s/ Donald Lynaugh

Name: Donald Lynaugh

Title: Managing Director

EXHIBIT A

FORM OF ISSUANCE NOTICE

[Date]

Jefferies LLC
520 Madison Avenue
New York, New York 10022

Attn: [_____]

Reference is made to the Open Market Sale Agreement between Immunocore Holdings plc (the “**Company**”) and Jefferies LLC (the “**Agent**”) dated as of September 9, 2022. The Company confirms that all conditions, including without limitation, the conditions set forth in Section 3(b)(i) and Section 5 of the Sales Agreement, to the delivery of this Issuance Notice are satisfied as of the date hereof.

Date of Delivery of Issuance Notice (determined pursuant to Section 3(b)(i)): _____

Issuance Amount (equal to the total Sales Price for such Shares):

\$ _____

Number of days in selling period: _____

First date of selling period: _____

Last date of selling period: _____

Settlement Date(s) if other than standard T+2 settlement: _____

Floor Price Limitation (in no event less than \$1.00 without the prior written consent of the Agent, which consent may be withheld in the Agent’s sole discretion): \$ ____ per Share

Comments: _____

IMMUNOCORE HOLDINGS PLC

By: _____

Name:

Title:

Schedule A
Notice Parties

The Company

Bahija Jallal: [***]

Brian Di Donato: [***]

Lily Hepworth: [***]

The Agent

Donald Lynaugh: [***]

Jack Fabbri: [***]

EXHIBIT B

FORM OF OFFICER'S CERTIFICATE PURSUANT TO SECTION 4(o)

[Date]

The undersigned, the duly qualified and elected Chief [Executive/Financial] Officer of Immunocore Holdings plc, a public limited company incorporated under the laws of England and Wales with registered number 13119746 (the "Company"), does hereby certify in such capacity and on behalf of the Company, pursuant to Section 4(o) of the Open Market Sale AgreementSM, dated September 9, 2022, between the Company and Jefferies LLC (the "Sales Agreement"), that to the knowledge of the undersigned:

(i) The representations and warranties of the Company in Section 2 of the Sales Agreement are true and correct on and as of the date hereof with the same force and effect as if expressly made on and as of the date hereof; provided, however that such representations and warranties are qualified by the disclosure included or incorporated by reference in the Registration Statement and Prospectus (including any documents incorporated by reference therein and any supplements thereto); and

(ii) The Company has complied with all agreements and satisfied all conditions on its part to be performed or satisfied pursuant to the Sales Agreement at or prior to the date hereof.

Cooley LLP, Cooley (UK) LLP and Davis Polk & Wardwell LLP are entitled to rely on this certificate in connection with the respective opinions such firms are rendering pursuant to the Sales Agreement. Capitalized terms used herein without definition shall have the meanings given to such terms in the Sales Agreement.

[The Remainder of This Page Is Intentionally Left Blank]

IN WITNESS WHEREOF, the undersigned has caused this certificate to be executed as of the date first written above.

IMMUNOCORE HOLDINGS PLC

By: _____

Name:

Title:



Claire Keast-Butler
+44 20 7556 4211
ckeastbutler@cooley.com

Immunocore Holdings plc
92 Park Drive
Milton Park
Abingdon
Oxfordshire OX14 4RY
United Kingdom

9 September 2022

Ladies and Gentlemen:

Re: Immunocore Holdings plc — Prospectus Supplement – Exhibit 5.1

1. INTRODUCTION

- 1.1 We have acted as English legal advisers to Immunocore Holdings plc, a public limited company incorporated in England and Wales (the “**Company**”), in connection with the preparation and filing on the date hereof with the U.S. Securities and Exchange Commission (the “**SEC**”) of a prospectus supplement (the “**Prospectus Supplement**”). We have taken instructions solely from the Company.
- 1.2 The Prospectus Supplement supplements a registration statement on Form F-3 that the Company filed with the SEC on 4 April 2022 (the “**Registration Statement**”). The Registration Statement relates to the registration for issue and sale by the Company of (a) ordinary shares with a nominal value of £0.002 each in the capital of the Company (“**Ordinary Shares**”), (b) American Depositary Shares representing Ordinary Shares (“**ADSs**”), (c) debt securities in one or more series, as either senior, senior subordinated or subordinated debt or as senior, senior subordinated or subordinated convertible debt and (d) warrants for the purchase of (i) Ordinary Shares, including Ordinary Shares represented by ADSs and (ii) debt securities, each in one or more series, in each case to the public in a registered offering or offerings.
- 1.3 The Prospectus Supplement relates to the offering, issuance and sale of an amount of ADSs (the “**Placement ADSs**”) with an aggregate offering price of up to US\$250,000,000 (the Ordinary Shares to be represented by such ADSs, the “**New Shares**”) that may be issued and sold under a sales agreement between the Company and Jefferies LLC dated 9 September 2022 (the “**Sales Agreement**”).
- 1.4 We are rendering this letter at the request of the Company in connection with the Prospectus Supplement.
- 1.5 Except as otherwise defined in this letter, capitalised terms used have the respective meanings given to them in the Registration Statement and the Prospectus Supplement and headings are for ease of reference only and shall not affect interpretation.
- 1.6 All references to legislation in this letter are to the legislation of England unless the contrary is indicated, and any reference to any provision of any legislation shall include any amendment, modification, re-enactment or extension thereof, as in force on the date of this letter.

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2. DOCUMENTS

For the purpose of issuing this letter, we have reviewed the following documents only:

- 2.1 a PDF copy of the Registration Statement;
- 2.2 a PDF copy of the Prospectus Supplement;
- 2.3 a PDF executed copy of the Sales Agreement; and
- 2.4 a PDF executed copy of a certificate dated 9 September 2022 (the “**Secretary’s Certificate**”) signed by the Company’s company secretary (the “**Company Secretary**”) relating to certain factual matters as at the date of the Secretary’s Certificate and having annexed thereto copies (certified by the Company Secretary as being true, complete, accurate and up-to-date in each case) of the following documents:
 - (a) a PDF copy of the certificate of incorporation of the Company dated 7 January 2021 and a PDF copy of the certificate of incorporation on re-registration of the Company as a public company dated 1 February 2021;
 - (b) a PDF copy of the current articles of association of the Company adopted on 9 February 2021 (the “**Articles**”);
 - (c) a PDF executed copy of the written resolutions of the board of directors of the Company (the “**Board**” or the “**Directors**”) passed in November 2021 constituting a financing and pricing committee of the Board (the “**Committee**”) with effect from 8 November 2021 (the “**Board Written Resolutions**”);
 - (d) a PDF executed copy of the minutes of a meeting of the Board held on 29 April 2022 at which it was resolved, *inter alia*, to appoint Siddharth Kaul to the Committee (the “**Board Minutes**”);
 - (e) a PDF executed copy of the minutes of a meeting of the Committee held on 31 August 2022 resolving, *inter alia*, to (i) approve the Prospectus Supplement and proceed with the execution and filing of the Prospectus Supplement with the SEC, (ii) approve the form of Sales Agreement subject to such finalisation and further modification as is deemed appropriate by the Chief Executive Officer and Chief Financial Officer of the Company, and any other officer or officers authorised by either of them (the “**Authorised Signatories**”), (iii) authorise the Authorised Signatories to execute and deliver the Sales Agreement on behalf of the Company and (iv) authorise the offer and sale by the Company of the Placement ADSs, and the allotment and issue of the New Shares, for an aggregate offering amount up to US\$250,000,000 in one or more “at-the-market” offerings pursuant to the Sales Agreement (each such offering, an “**Authorised Placement**”) (the “**Committee Minutes**”); and
 - (f) a PDF executed copy of the minutes of the general meeting of the Company held on 3 February 2021 (the “**General Meeting**”) at which it was resolved, *inter alia*, to authorise the Directors for the purposes of section 551 of the Companies Act 2006, as amended (the “**Companies Act**”) to allot shares in the Company or grant rights to subscribe for or to convert any security into shares in the Company up to an aggregate nominal amount of £150,000.00 for a period ending on 3 February 2026 and to allot equity securities for cash pursuant to such authority as if section 561 of the Companies Act did not apply to the allotment (the “**Shareholder Resolutions**”).

3. SEARCHES

In addition to examining the documents referred to in paragraph 2 (*Documents*), we have carried out the following searches only:

- 3.1 an online search at Companies House in England and Wales (“**Companies House**”) with respect to the Company, carried out at 9:41 a.m. (London time) on 9 September 2022 (the “**Online Search**”); and
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3.2 a telephone enquiry at the Companies Court in London of the Central Registry of Winding-up Petitions in England and Wales with respect to the Company, carried out at 10:13 a.m. (London time) on 9 September 2022 (the “**Telephone Enquiry**” and, together with the Online Search, the “**Searches**”).

4. **OPINIONS**

Subject to the assumptions set out in paragraph 5 (*Assumptions*), the scope of the opinions set out in paragraph 6 (*Scope of Opinions*) and the reservations set out in paragraph 7 (*Reservations*), we are of the opinion that as at the date of this letter:

4.1 The Company has been duly incorporated and is existing as a public company with limited liability under English law.

4.2 The Searches gave no indication that any winding-up, dissolution or administration order or appointment of a receiver, administrator, administrative receiver or similar officer has been made with respect to the Company, or that any petition for the winding-up of the Company has been presented.

4.3 The New Shares, when issued, delivered and paid for in accordance with the Sales Agreement and as provided in the Prospectus Supplement, will be validly issued, fully paid and will not be subject to any call for payment of further capital.

5. **ASSUMPTIONS**

In giving the opinions in this letter, we have assumed (without making enquiry or investigation) that:

5.1 all signatures, stamps and seals on all documents are genuine. All original documents are complete, authentic and up-to-date, and all documents submitted to us as a copy (whether by email or otherwise) are complete and accurate and conform to the original documents of which they are copies and that no amendments (whether oral, in writing or by conduct of the parties) have been made to any of the documents since they were examined by us;

5.2 where a document has been examined by us in draft or specimen form, it will be or has been duly executed in the form of that draft or specimen;

5.3 each of the individuals who signs as, or otherwise claims to be, an officer of the Company is the individual whom they claim to be and holds the office that they claim to hold;

5.4 where a document is required to be delivered, each party to it has delivered the same without it being subject to any escrow or similar arrangement;

5.5 all documents, forms and notices which should have been delivered to Companies House in respect of the Company have been and will be so delivered;

5.6 the information revealed by the Searches is true, accurate, complete and up-to-date in all respects, and there is no information which should have been disclosed by the Searches that has not been disclosed for any reason and there has been no alteration in the status or condition of the Company since the date and time that the Searches were made, and that the results of the Searches will remain true, complete, accurate and up-to-date as at each date on which the Company allots or issues New Shares (each, a “**Bring-Down Date**”);

5.7 no notice has been received by the Company which could lead to the Company being struck off the register of companies under section 1000 of the Companies Act and no such notice shall have been received as at each Bring-Down Date;

5.8 the Articles remain in full force and effect and no alteration has been made or will be made to the Articles as at the date of this letter and as at each Bring-Down Date;

5.9 to the extent that the obligations of the Company under the Sales Agreement may be dependent upon such matters, each of the parties to the Sales Agreement:

- (a) is duly organised, validly existing and in good standing (where such concept is legally relevant) under the laws of its jurisdiction of incorporation;
- (b) is in compliance, generally, with all applicable laws, rules and regulations to which it is subject, its constitutional documents and any judicial or administrative judgements, awards, injunctions or orders binding upon it or its property;
- (c) has the capacity, power and authority to execute, deliver and perform its obligations under the Sales Agreement;
- (d) is duly qualified to engage in the activities contemplated by the Sales Agreement and will not be in breach of any of its respective obligations under any document, contract, instrument or agreement as a result of its entry into and performance of its obligations under the Sales Agreement;
- (e) is authorised under all applicable laws of its jurisdiction and domicile to submit to the jurisdiction of the federal courts of the United States of America located in the Borough of Manhattan in the City of New York or the courts of the State of New York in each case located in the Borough of Manhattan in the City of New York as specified in the Sales Agreement and has validly submitted to such jurisdiction; and
- (f) has or will have validly authorised, executed and delivered all relevant documents;

and that each of the foregoing remains the case as at each Bring-Down Date;

- 5.10 the Sales Agreement (and any other documents referred to therein) constitutes legal, valid and binding obligations of each of the parties thereto enforceable under all applicable laws and that the Sales Agreement will remain in full force and effect at each Bring-Down Date;
 - 5.11 there is an absence of fraud or mutual mistake of fact or law or any other arrangements, agreements, understandings or course of conduct or prior or subsequent dealings amending, rescinding or modifying or suspending any of the terms of the Sales Agreement or which would result in the inclusion of additional terms therein, and that the parties have acted and will act in accordance with the terms of the Sales Agreement;
 - 5.12 in relation to the Registration Statement and the Prospectus Supplement and the transactions contemplated thereby, the Directors have acted and will act in the manner required by section 172 of the Companies Act and that each issuance of Placement ADSs and New Shares pursuant to the Prospectus Supplement will be made in good faith and on bona fide commercial terms and on arms' length terms and for the purposes of carrying on the business of the Company;
 - 5.13 the Company is, and the Company and each party to the Sales Agreement will at all relevant times remain, in compliance with all applicable anti-corruption, anti-money laundering, anti-terrorism, sanctions and human rights laws and regulations;
 - 5.14 the Registration Statement has become effective under the US Securities Act of 1933 (the "**Securities Act**") and such effectiveness shall not have been terminated or rescinded prior to each Bring-Down Date, and the Prospectus Supplement has been filed with the SEC;
 - 5.15 the Board Minutes and the Committee Minutes referred to in paragraph 2.4 (*Documents*) are a true record of the proceedings described therein, and that each meeting recorded in such minutes was duly conducted as described therein, duly constituted and convened and all constitutional, statutory and other formalities were duly observed (including, if applicable, those relating to the declaration of Directors' interests or the power of interested Directors to vote), a quorum was present throughout, the requisite majority of Directors voted in favour of approving the resolutions and the resolutions passed at that meeting of the Board or the Committee, as applicable, were duly adopted, have not been revoked or varied and remain in full force and effect as at the date of this letter and each Bring-Down Date;
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- 5.16 the resolutions set out in the Board Written Resolutions referred to in paragraph 2.4 (*Documents*) were validly passed as written resolutions in accordance with the Articles, that all eligible directors of the Company (being all the directors of the Company who would have been entitled to vote on the matter had it been proposed as a resolution at a directors' meeting, but excluding any director whose vote is not to be counted in respect of a particular matter) have signed one or more copies of the Board Written Resolutions, that all relevant provisions of the Companies Act and the Articles were complied with and the Articles were duly observed (including, if applicable, those relating to the declaration of Directors' interests or the power of interested Directors to vote) and such resolutions were duly adopted, and have not been revoked or varied and remain in full force and effect as at the date of this letter and each Bring-Down Date;
- 5.17 the General Meeting was duly convened and held on 3 February 2021 at which all constitutional, statutory and other formalities were duly observed, a quorum of shareholders was present throughout and the Shareholder Resolutions referred to in paragraph 2.4 (*Documents*) were duly passed and have not been revoked or varied and remain in full force and effect as at the date of this letter and each Bring-Down Date, and that all filings required to be made with Companies House in connection therewith have been made within the relevant time limits as at the date of this letter and each Bring-Down Date;
- 5.18 all of the New Shares will be allotted and issued pursuant to the authority and power granted to the Directors pursuant to section 551 and section 570 of the Companies Act, respectively, under the Shareholder Resolutions, and that authority and that power are and shall remain unutilised to a sufficient extent to enable the allotment and issue of any of the New Shares, and that the Directors shall not allot or issue (or purport to allot or issue) any Ordinary Shares and shall not grant rights (or purport to grant rights) to subscribe for any Ordinary Shares, or convert any security into Ordinary Shares, in excess of such authorities or powers or in breach of any other limitation on their authority or power to allot and issue shares or grant rights to subscribe for, or convert any security into, Ordinary Shares;
- 5.19 if any New Shares are to be allotted and issued or rights to subscribe for, or convert any security into, New Shares granted after the expiration date of the Shareholder Resolutions or if the Shareholder Resolutions have been fully utilised at the relevant time, such New Shares shall be allotted and issued and/or rights to subscribe for, or convert any security into, New Shares shall be granted pursuant to an authority and power granted to the Directors pursuant to section 551 and section 570 or 571 of the Companies Act at a general meeting of the Company duly convened and held at which all constitutional, statutory and other formalities will be duly observed, a quorum of shareholders will be present throughout and the relevant resolutions will have been duly passed and will not have been revoked or varied and will remain in full force and effect, and that all filings required to be made with Companies House in connection therewith will have been made within the relevant time limits;
- 5.20 any sales of Placement ADSs will be made in accordance with the limitations imposed by the Committee as set out in the Committee Minutes; the terms of any Authorised Placement will be approved by the Chief Executive Officer and/or the Chief Financial Officer of the Company and will be in accordance with the terms approved by the Committee as specified in the Committee Minutes;
- 5.21 the contents of the Secretary's Certificate were true and not misleading when given and remain true and not misleading as at the date of this letter and will remain so as at each Bring-Down Date, and there is no fact or matter not referred to in the Secretary's Certificate which would make any of the information in the Secretary's Certificate inaccurate or misleading;
- 5.22 no New Shares will be allotted or issued, or are or shall be committed to be allotted and issued, at a discount to their nominal value (whether in dollars or equivalent in any other currency);
- 5.23 at the time of each allotment and issue of New Shares, the Company shall have received in full payment for such shares in an amount of "cash consideration" (as defined in section 583(3) of the Companies Act) equal to the aggregate subscription price for such shares, such amount not being less than the aggregate nominal value for such shares, and the Company shall have entered the holder or holders thereof in the register of members of the Company showing that all such shares have been fully paid up as to their nominal value and any premium thereon as at the date of each such allotment;
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- 5.24 there will be no fact or matter (such as bad faith, coercion, duress, undue influence or a mistake or misrepresentation before or at the time any agreement or instrument is entered into, a subsequent breach, release, waiver or variation of any right or provision, an entitlement to rectification or circumstances giving rise to an estoppel) which might affect the allotment and issue of any Placement ADSs or New Shares that may be issued pursuant to the Registration Statement and the Prospectus Supplement;
- 5.25 as at the date of this letter and each Bring-Down Date, the Company has not and will not have taken any corporate or other action and no steps have been or will be taken or legal proceedings have been or will be started against the Company for the liquidation, winding-up, dissolution, reorganisation or bankruptcy of, or for the appointment of a liquidator, receiver, trustee, administrator, administrative receiver or similar officer of, the Company or all or any of its assets (or any analogous proceedings in any jurisdiction) and the Company is not and will not be unable to pay its debts as they fall due within the meaning of section 123 of the Insolvency Act 1986, as amended (the “**Insolvency Act**”) or will become unable to pay its debts within the meaning of that section as a result of any of the transactions contemplated in this letter, is or will become insolvent or has been or will be dissolved or declared bankrupt;
- 5.26 all agreements and documents examined by us that are governed by the laws of any jurisdiction other than England are on the date of this letter legal, valid and binding under the laws by which they are (or are expected to be) governed and will remain so on each Bring-Down Date;
- 5.27 there are no provisions of the laws of any jurisdiction outside England that would have any implication for the opinions which we express in this letter and that, insofar as the laws of any jurisdiction outside England may be relevant to this letter, such laws have been and will be complied with;
- 5.28 we note that Sales Agreement provides that it is to be governed by and construed in accordance with the laws of the State of New York. We express no opinion as to any matters governed by New York law. As lawyers not qualified in New York, we are not qualified or able to assess the true meaning or import of the terms of the Sales Agreement under New York law, and we have made no investigation of such meaning or import. Therefore, our review of the Sales Agreement has been limited to its terms as they appear to us on its face. We have assumed that the choice of New York law in the Sales Agreement is valid as a matter of New York law and the Sales Agreement and each of its provisions are valid, binding and enforceable under New York law and the law of any other jurisdiction whose law applies, other than law covered expressly in an opinion included in this letter. We have also assumed that, under New York law, any court named in the forum selection clause of the Sales Agreement will have jurisdiction over the parties and the subject matter of any action brought in that court under the Sales Agreement;
- 5.29 all statements of fact and representations and warranties as to matters of fact (except as to matters expressly set out in the opinions given in this letter) contained in or made in connection with any of the documents examined by us were true and correct as at the date given and are true and correct at today’s date and no fact was omitted therefrom which would have made any of such facts, representations or warranties incorrect or misleading;
- 5.30 all consents, licences, approvals, authorisations, notices, filings and registrations that are necessary under any applicable laws or regulations in connection with the transactions contemplated by the Registration Statement and the Prospectus Supplement have been or will be duly made or obtained and are, or will be, in full force and effect;
- 5.31 no Placement ADSs or New Shares have been or shall be offered to the public in the United Kingdom in breach of the Financial Services and Markets Act 2000, as amended (the “**FSMA**”), the EU Prospectus Regulation (Regulation (EU) 2017/1129) as it forms part of domestic law in the United Kingdom by virtue of the European Union (Withdrawal) Act 2018 (the “**Withdrawal Act**”) (the “**UK Prospectus Regulation**”) or of any other United Kingdom laws or regulations concerning offers of securities to the public, and no communication has been or shall be made in relation to the Placement ADSs in breach of section 21 (*Restrictions on financial promotion*) of the FSMA or any other United Kingdom laws or regulations relating to offers or invitations to subscribe for, or to acquire rights to subscribe for or otherwise acquire, shares or other securities;
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- 5.32 in issuing Placement ADSs and New Shares, the Company is not carrying on a regulated activity for the purposes of section 19 of FSMA and each person involved in or dealing with the Company in connection with the offering of the Placement ADSs which is carrying on, or purporting to carry on, a regulated activity (within the meaning of section 19 (*The general prohibition*) of the FSMA is an authorised person or exempt person under the FSMA;
- 5.33 all applicable provisions of the EU Market Abuse Regulation (Regulation (EU) No 596/2014) as it forms part of domestic law in the United Kingdom by virtue of the Withdrawal Act (“**UK MAR**”), the UK Prospectus Regulation, the FSMA, the Financial Services Act 2012 (the “**FS Act**”), and all rules and regulations made pursuant to UK MAR, the UK Prospectus Regulation, the FSMA and the FS Act, have been and will be complied with as regards anything done in relation to the Placement ADSs or otherwise in relation to the Registration Statement and the Prospectus Supplement and the transactions contemplated thereby in, from or otherwise involving England (including, without limitation, articles 14 (*Prohibition of insider dealing and of unlawful disclosure of inside information*) and 15 (*Prohibition of market manipulation*) of UK MAR, sections 19 (*The general prohibition*) and 21 (*Restrictions on financial promotion*) of the FSMA and sections 89 (*Misleading statements*), 90 (*Misleading impressions*) and 91 (*Misleading statements etc. in relation to benchmarks*) of the FS Act); and
- 5.34 no application has been or will be made for any Placement ADSs or New Shares to be listed or admitted to trading on a regulated market, multilateral trading facility or organised trading facility situated or operating in the United Kingdom.

6. SCOPE OF OPINIONS

- 6.1 The opinions given in this letter are limited to English law as it would be applied by English courts on the date of this letter
- 6.2 We express no opinion in this letter on the laws of any other jurisdiction. We have not investigated the laws of any country other than England and we assume that no foreign law affects any of the opinions stated in paragraph 4 (*Opinions*).
- 6.3 We express no opinion as to any agreement, instrument or other document other than as specified in this letter. For the purposes of giving the opinions in paragraph 4 (*Opinions*), we have only examined and relied on those documents set out in paragraph 2 (*Documents*) and made those searches and enquiries set out in paragraph 3 (*Searches*), respectively. We have made no further enquiries concerning the Company or any other matter in connection with the giving of the opinions in paragraph 4 (*Opinions*).
- 6.4 No opinion is expressed with respect to taxation in the United Kingdom or otherwise in this letter.
- 6.5 We have not been responsible for investigating or verifying the accuracy of the facts or the reasonableness of any statement of opinion or intention, contained in or relevant to any document referred to in this letter, or that no material facts have been omitted therefrom.
- 6.6 The opinions given in this letter are given on the basis of each of the assumptions set out in paragraph 5 (*Assumptions*) and are subject to each of the reservations set out in paragraph 7 (*Reservations*) to this letter. The opinions given in this letter are strictly limited to the matters stated in paragraph 4 (*Opinions*) and do not extend, and should not be read as extending, by implication or otherwise, to any other matters.
- 6.7 This letter only applies to those facts and circumstances which exist as at today’s date and we assume no obligation or responsibility to update or supplement this letter to reflect any facts or circumstances which may subsequently come to our attention, any changes in laws which may occur after today, or to inform the addressee of any change in circumstances happening after the date of this letter which would alter the opinion given in this letter.
- 6.8 We have not been responsible for investigation or verification of statements of fact (including statements as to foreign law) or the reasonableness of any statements of opinion in the Registration Statement and the Prospectus Supplement, or that no material facts have been omitted therefrom.
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- 6.9 This letter is given by Cooley (UK) LLP and no partner or employee assumes any personal responsibility for it nor shall owe any duty of care in respect of it.
- 6.10 This letter, the opinions given in it, and any non-contractual obligations arising out of or in connection with this letter and/or the opinions given in it, are governed by and shall be construed in accordance with English law as at the date of this letter.

7. RESERVATIONS

7.1 The Online Search described at paragraph 3.1 (*Searches*) is not capable of revealing conclusively whether or not:

- (a) a winding-up order has been made or a resolution passed for the winding-up of a company;
- (b) an administration order has been made; or
- (c) a receiver, administrative receiver, administrator or liquidator has been appointed,

since notice of these matters may not be filed with the Registrar of Companies in England and Wales immediately and, when filed, may not be entered on the public database or recorded on the public microfiches of the relevant company immediately.

In addition, such a company search is not capable of revealing, prior to the making of the relevant order, whether or not a winding-up petition or a petition for an administration order has been presented.

7.2 The Telephone Enquiry described at paragraph 3.2 (*Searches*) relates only to a compulsory winding-up and is not capable of revealing conclusively whether or not a winding-up petition in respect of a compulsory winding-up has been presented, since details of the petition may not have been entered on the records of the Central Registry of Winding-up Petitions in England and Wales immediately or, in the case of a petition presented to a County Court in England and Wales, may not have been notified to the Central Registry of Winding-up Petitions in England and Wales and entered on such records at all, and the response to an enquiry only relates to the period of approximately four years prior to the date when the enquiry was made. We have not made enquiries of any District Registry or County Court in England and Wales.

7.3 The opinions set out in this letter are subject to: (i) any limitations arising from applicable laws relating to insolvency, bankruptcy, administration, reorganisation, liquidation, moratoria, schemes or analogous circumstances; and (ii) an English court exercising its discretion under section 426 of the Insolvency Act (*co-operation between courts exercising jurisdiction in relation to insolvency*) to assist the courts having the corresponding jurisdiction in any part of the United Kingdom or any relevant country or territory.

7.4 We express no opinion as to matters of fact.

7.5 Save for the matters set out in the Secretary's Certificate, we have made no enquiries of any individual connected with the Company. We have relied entirely on the facts, statements and confirmations contained in the Secretary's Certificate and we have not undertaken any independent investigation or verification of the matters referred to in the Secretary's Certificate.

7.6 If (a) a party to the Sales Agreement is the target of economic or financial sanctions or other restrictive measures imposed in any jurisdiction ("**Sanctions**") or is owned or controlled (directly or indirectly) by or is acting on behalf of or at the direction of or is otherwise connected with a person who is a target of Sanctions or (b) a party to the Sales Agreement is incorporated or resident in or operating from a country or territory that is a target of Sanctions or (c) the rights or obligations of a party to the Sales Agreement is otherwise affected by Sanctions, then the rights and obligations of such person under the Sales Agreement may be void and/or unenforceable.

7.7 We express no opinion in this letter on the application or potential application of the National Security and Investment Act 2021 in relation to the Sales Agreement or any transaction contemplated thereby.

8. DISCLOSURE AND RELIANCE

8.1 This letter is addressed to you solely for your benefit in connection with the Registration Statement and the Prospectus Supplement and the transactions contemplated thereunder. We consent to the filing of this letter as an exhibit to the Prospectus Supplement. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under section 7 of the Securities Act or the rules and regulations thereunder.

8.2 This letter may not be relied upon by you for any other purpose, or furnished to, assigned to, quoted to, or relied upon by any other person, firm or other entity for any purpose without our prior written consent, which may be granted or withheld at our sole discretion.

Yours faithfully

/s/ Cooley (UK) LLP
Cooley (UK) LLP

Cautionary Note Regarding Forward Looking Statements

This Exhibit contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “may,” “can,” “will,” “believe,” “expect,” “plan,” “anticipate,” “project” and similar expressions (as well as other words or expressions referencing future events or circumstances) are intended to identify forward-looking statements. All statements, other than statements of historical facts, included in this Exhibit are forward-looking statements. These statements include, but are not limited to, statements regarding Immunocore’s anticipated cash runway and expectations regarding the development plan, design, progress, timing, scope and results of Immunocore’s existing and planned clinical trials, including statements regarding enrollment, randomization, upcoming cohorts, trial expansion and the timing of the availability of future clinical trial results. Any forward-looking statements are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements, many of which are beyond the Company’s control. These risks and uncertainties include, but are not limited to, the impact of the ongoing and evolving COVID-19 pandemic on the Company’s business, strategy, clinical trials and financial position, strategy and anticipated milestones, including Immunocore’s ability to conduct ongoing and planned clinical trials; Immunocore’s ability to obtain a clinical supply of current or future product candidates or commercial supply of KIMMTRAK or any future approved product, including as a result of the COVID-19 pandemic, war in Ukraine or global geopolitical tension; Immunocore’s ability to obtain and maintain regulatory approvals for its product candidates; Immunocore’s ability to develop, manufacture and commercialize its product candidates; Immunocore’s ability and plans in continuing to establish and expand a commercial infrastructure and to successfully launch, market and sell KIMMTRAK and any future approved products; the delay of any current or planned clinical trials, whether due to the COVID-19 pandemic, patient enrollment delays or otherwise; Immunocore’s ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; actions of regulatory agencies, which may affect the initiation, timing and progress of the Immunocore’s clinical trials or future regulatory approval; Immunocore’s need for and ability to obtain additional funding, on favorable terms or at all, including as a result of rising inflation, interest rates and general market conditions, and the impacts thereon of the COVID-19 pandemic, war in Ukraine and global geopolitical tension; Immunocore’s ability to obtain, maintain and enforce intellectual property protection for KIMMTRAK or any product candidates it is developing; unexpected safety or efficacy data observed during preclinical studies or clinical trials; clinical trial site activation or enrollment rates that are lower than expected; changes in expected or existing competition; and the success of Immunocore’s current and future collaborations, partnerships or licensing arrangements. These and other risks and uncertainties are described in greater detail in the section titled “Risk Factors” in Immunocore’s filings with the Securities and Exchange Commission, including Immunocore’s most recent Annual Report on Form 20-F for the year ended December 31, 2021 filed with the Securities and Exchange Commission on March 3, 2022, as well as discussions of potential risks, uncertainties, and other important factors in the Company’s subsequent filings with the Securities and Exchange Commission. Such risks may be amplified by the COVID-19 pandemic, war in Ukraine and global geopolitical tension, and their potential impacts on Immunocore’s business and the overall global economy. All forward-looking statements contained in this Exhibit speak only as of the date on which they were made and should not be relied upon as representing Immunocore’s views as of any subsequent date. Except to the extent required by law, Immunocore undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Recent Developments

Financing Update

July 2022 PIPE Transaction; Extension of Anticipated Cash Runway

On July 20, 2022, we issued and sold 2,000,000 American Depositary Shares, or ADSs, representing ordinary shares of nominal value of £0.002 each and 1,733,333 non-voting ordinary shares of nominal value £0.002 each, to certain institutional accredited investors, or the Investors, at a purchase price of \$37.50 per ADS/non-voting ordinary share as a private investment in public equity, or PIPE, pursuant to a securities purchase agreement with such Investors, generating gross proceeds of £116.7 million (\$140.0 million) before deducting estimated offering expenses payable by us of £0.3 million (\$0.4 million).

Following the receipt of PIPE proceeds, we believe we have cash and cash equivalents sufficient, together with anticipated revenue from sales of KIMMTRAK, to extend our anticipated cash runway and fund our operations through 2025.

Clinical Updates

Dosing of First Patient in Clinical Trial of IMC-M113V

On July 11, 2022, we announced the dosing of the first patient in our Phase 1/2 clinical trial evaluating IMC-M113V, our ImmTAV molecule targeting a HIV gag antigen bispecific TCR molecule. We expect to enroll further patients in this trial later in 2022.

Announcement of Trial Design for Planned Randomized Phase 2/3 Trial of Tebentafusp in Advanced Melanoma

On August 20, 2022, we announced our plans for evaluating tebentafusp in a randomized Phase 2/3 clinical trial in patients with previously treated advanced melanoma. Our plan is to enroll patients with advanced melanoma, excluding uveal melanoma, that have progressed on an anti-PD1, received prior ipilimumab and, if applicable, received TKI. We plan to start the randomization of this trial in the fourth quarter of 2022, and we designed the trial with input from global melanoma experts and from the FDA.

Presentation of Initial Phase 1 Data from Dose Escalation Trial of IMC-F106C at ESMO Congress 2022

Overview

IMC-F106C, our ImmTAC molecule targeting an optimal HLA-A*02:01 PRAME antigen, is currently being evaluated in a first-in-human, Phase 1/2 dose escalation trial in patients with multiple solid tumor cancers including NSCLC, SCLC, endometrial, ovarian, cutaneous melanoma, and breast cancers. PRAME is overexpressed in many solid tumors including NSCLC, SCLC, endometrial, ovarian, melanoma and certain breast cancers. We believe IMC-F106C is the first clinical stage bi-specific targeting PRAME.

Trial Design

The trial will be conducted in two phases, and we intend to enroll up to 170 patients. Patient eligibility for the dose escalation phase of the trial are HLA-A*02:01 positivity with either a high expression frequency tumor indication that does not require screening for PRAME positivity or a lower expression frequency tumor indication where PRAME positivity has been confirmed by immunohistochemistry staining. The primary endpoint in the Phase 1 portion of the clinical trial is to assess the safety and tolerability and identify the maximum tolerated dose and/or the recommended Phase 2 dose of IMC-F106C as a monotherapy and in combination with a checkpoint inhibitor. The primary endpoint in the Phase 2 portion of the clinical trial is to characterize the initial efficacy of IMC-F106C as monotherapy. Secondary endpoints include pharmacokinetics, immunogenicity, pharmacodynamic biomarkers, and antitumor efficacy of IMC-F106C as monotherapy and in combination with a checkpoint inhibitor.

Summary of Initial Results from Phase 1 Portion

Our IMC-F106C trial was initiated in May 2020 in the United States. As of July 18, 2022, the data cut-off date for the presentation, 55 patients have been treated across 10 dose cohorts. IMC-F106C was observed to be well-tolerated, with treatment-related adverse events, or AEs, that were manageable and consistent with the mechanism of action. The most frequent treatment-related AE reported was cytokine release syndrome, or CRS, which was mostly Grade 1 (none of were greater than Grade 3) and occurred predominantly during the time period where the initial three doses were administered. None of the related AEs led to treatment discontinuation or patient death.

Doses of greater than 20 mcg were observed in the trial to be clinically active and had consistent and robust interferon gamma induction, a specific marker of T cell activation. Most of the patients in these active dose cohorts were enrolled without prospective PRAME testing. In these patients, PRAME expression was analyzed retrospectively; the vast majority were positive, and the average expression was high (median H score 188).

In the clinically active dose cohorts, durable partial responses, or PR, were observed in 2 patients with cutaneous melanoma (6 patients enrolled), 2 patients with ovarian cancer (4 patients enrolled) and 3 patients with tebentafusp-naïve uveal melanoma (6 patients enrolled). We did not observe any PR responses in patients with UM who had progressed on prior tebentafusp. All ovarian patients in the trial were platinum-resistant, and all cutaneous melanoma patients had progressed on prior anti-PD1 and anti-CTLA4. Six of the seven PRs are still ongoing, including two patients with PRs for over seven months. Ten additional efficacy evaluable patients across four other tumor types had a best RECIST response of stable disease or progressive disease. A majority of patients evaluable for circulating tumor DNA had at least a 50% reduction.

Ongoing Expansion Arms in Four Cancer Types

We have initiated patient enrollment into four expansion arms in cutaneous melanoma, NSCLC, endometrial and ovarian cancers. The IMC-F106C-101 trial is adaptive and includes the option for Phase 2 expansion of over 100 patients per tumor type. Dose escalation continues in additional solid tumors as well as plans for expansion into combination arms with standards-of-care.
