

Notice of Annual General Meeting

Please read the "Important Notice re COVID-19" set out in the Explanatory Notes below. In particular, in light of the UK Government's response to the ongoing COVID-19 outbreak, the Company and the Executive Chairman have determined that the Resolutions to be proposed at the annual general meeting shall be voted on through a poll rather than on a show of hands; and, accordingly, shareholders are strongly encouraged to either submit their Form of Proxy or use the CREST Proxy Voting Service, rather than attend the meeting in person.

Notice is hereby given that the annual general meeting of Open Orphan Plc ("Company") will be held at the offices of Arden Partners PLC, 125 Old Broad St, London EC2N 1AR on 21 July 2021 at 12 noon for the purposes of considering and voting on the resolutions below ("AGM"). Resolutions 1 to 6 will be proposed as ordinary resolutions and Resolutions 7 and 8 will be proposed as special resolutions. Relevant documentation can also be consulted on the Investor section of the Company's website.

Ordinary Business

Resolution 1

THAT the Audited Accounts for the 12 months ended 31 December 2020, together with the Directors' Report and Auditors' Report thereon, be received and adopted.

Resolution 2

THAT Jeffrey's Henry LLP be re-appointed as auditors of the Company to hold office from the conclusion of the AGM until the conclusion of the next annual general meeting at which accounts are laid before the Company.

Resolution 3

THAT the directors of the Company ("Directors") be authorised to fix the remuneration of Jeffrey's Henry LLP as auditors of the Company.

Resolution 4

THAT Professor Brendan Buckley be re-elected as a Director of the Company retiring by rotation in accordance with the Articles of Association.

Resolution 5

THAT Dr Elaine Sullivan be elected as an Independent Director of the Company, having been appointed by the Board since the last annual general meeting of the Company.

Resolution 6

THAT in accordance with the requirements of section 551 of the Companies Act 2006 ("Act"), and in substitution for any existing authority (but without prejudice to any allotment of shares or grant of rights already made, offered or agreed to be made pursuant to such authority), the Directors be and they are hereby generally and unconditionally authorised to exercise all powers of the Company to allot Relevant Securities (as defined in the notes to this Resolution):

6.1 comprising equity securities (as defined by section 560 of the Act) up to an aggregate nominal amount of £223,618 (such amount to be reduced by the nominal amount of any Relevant Securities allotted pursuant to the authority in paragraph 6.2 below) in connection with an offer by way of a rights issue or open offer:

(a) to holders of ordinary shares in proportion (as nearly as may be practicable) to their respective holdings; and

(b) to holders of other equity securities as required by the rights of those securities or as the Directors otherwise consider necessary,

but subject to such exclusions or other arrangements as the Directors may deem necessary or expedient in relation to treasury shares, fractional entitlements, record dates, legal or practical problems in or under the laws of any territory or the requirements of any regulatory body or stock exchange; and

- 6.2 in any other case, up to a maximum aggregate nominal amount of £223,618 (223,618,334 new ordinary shares in the capital of the Company) (such amount to be reduced by the nominal amount of any equity securities allotted pursuant to the authority in paragraph 6.1 above),

PROVIDED that such authority shall expire on the earlier of (i) the conclusion of the annual general meeting of the Company to be held in 2022; and (ii) the date falling 18 months from the date of the passing of this Resolution unless any such authorities are renewed, varied or revoked by the Company prior to or on that date and provided also that the Company may, before such expiry, make an offer or agreement which would or might require shares in the Company or rights to be allotted or granted after such expiry and Directors may allot shares in the Company or grant rights pursuant to any such offer or agreement as if the authority conferred by this Resolution had not expired.

Special Business

Resolution 7

THAT, subject to Resolution 6 being passed, in accordance with section 570(1) of the Act, and in substitution for any existing authority, the Directors be and they are hereby empowered to allot equity securities (within the meaning of section 560 of the Act) for cash pursuant to the authorities conferred by Resolution 6 as if section 561 of the Act did not apply to such allotment, PROVIDED that this power shall be limited to:

- 7.1 the allotment of equity securities in connection with an offer of equity securities (but, in the case of the authority granted under Resolution 6.1, by way of a rights issue or open offer only):

(a) to the holders of ordinary shares in proportion (as nearly as may be practicable) to their respective holdings; and

(b) to holders of other equity securities as required by the rights of those securities or as the Directors otherwise consider necessary,

but subject to such exclusions or other arrangements as the Directors may deem necessary or expedient in relation to treasury shares, fractional entitlements, record dates, legal or practical problems in or under the laws of any territory or the requirements of any regulatory body or stock exchange; and

- 7.2 the allotment of equity securities (otherwise than pursuant to paragraph 7.1 of this Resolution) to any person up to a maximum aggregate nominal amount of £67,086.

PROVIDED ALSO that such powers shall expire on the earlier of (i) the conclusion of the annual general meeting of the Company to be held in 2022; and (ii) the date falling 18 months from the date of the passing of this Resolution unless any such power is renewed, revoked or varied by special resolution and that the Company may, before such expiry make an offer or agreement which

would or might require equity securities to be allotted after such expiry, and the Directors may allot equity securities pursuant to any such offer or agreement as if such powers had not expired.

Resolution 8

THAT the Company be and is hereby generally and unconditionally authorised for the purposes of Section 701 of the Act to make one or more market purchases (within the meaning of Section 693(4) of the Act) on the London Stock Exchange of ordinary shares of 0.1 pence each in the capital of the Company PROVIDED THAT:

- (a) the maximum aggregate number of shares hereby authorised to be purchased is 67,085,500 ordinary shares of 0.1 pence each (representing approximately 10% of the Company's issued ordinary share capital as at 23 June 2021, the latest practicable date prior to publication of this Notice of AGM);
- (b) the minimum price (exclusive of expenses) which may be paid for such shares is 0.1 pence per share;
- (c) the maximum price (exclusive of expenses) which may be paid for an ordinary share shall not be more than 105% of the average closing middle market quotation for an ordinary share as derived from the London Stock Exchange plc for the five business days immediately preceding the date on which the ordinary share is purchased;

- (d) unless previously renewed, varied or revoked, the authority hereby conferred shall expire at the conclusion of the Company's next annual general meeting; and
- (e) the Company may make a contract or contracts to purchase ordinary shares under the authority hereby conferred prior to the expiry of such authority, which will or may be executed wholly or partly after the expiry of such authority, and may make a purchase of ordinary shares in pursuance of any such contract or contracts.

By order of the Board

Beach Secretaries Limited
Company secretary

Registered office:-
Queen Mary BioEnterprises Innovation Centre
42 New Road
London
E1 2AX

Registered number:- 07514939

23 June 2021

Notice of Annual General Meeting (continued)

Explanatory Notes

Resolution 1

The Directors are required by law to lay the Audited Accounts and the Directors' Report and Auditors' Report for the 12 months ended 31 December 2020 before a general meeting of the Company. At the AGM, these documents will be presented to shareholders.

Resolution 2

The auditors are required to be re-appointed at each annual general meeting at which Accounts are laid. The Directors, on the recommendation of the Audit Committee (which has evaluated the effectiveness and independence of the external auditors) are proposing the re-appointment of Jeffreys Henry LLP as auditors.

Resolution 3

This resolution authorises the Directors to fix the auditors' remuneration. It is considered best practice to provide for this authority in a separate resolution and not link it to the appointment of the auditors in Resolution 2.

Resolution 4

The Articles of Association require the number nearest to, but not greater than, one third of the Directors for the time being of the Company to retire at each annual general meeting, with the longest in office since their appointment or last re-election retiring first.

Currently, the Board of Directors has five Directors. Of the current Directors, Dr Elaine Sullivan is excluded from the calculation of the number of directors to retire, which means that one of the other four directors must retire and offer himself for re-election. Brendan Buckley was last re-elected at the 2019 AGM and he therefore offers himself for re-election.

Resolution 5

The Articles of Association require any Director who has been appointed by the Board since the last annual general meeting of the Company to retire and such person may offer himself for re-election.

Dr Elaine Sullivan has been appointed as a Director of the Company since the Company's last annual general meeting and will accordingly retire in accordance with the terms of the Company's Articles of Association and offer herself for re-election.

Biographies

Professor Brendan Buckley (aged 71) – Non-Executive Director

Professor Brendan Buckley is a medical graduate of University College Cork and a doctoral graduate in Biochemistry of Oxford University. Brendan has over 30 years' experience in clinical research. He is one of the founders of Open Orphan as well as being Adjunct Professor at University College Dublin. He was the Chief Medical Officer of ICON plc until 2017. In 2009, Brendan co-founded Firecrest Clinical Ltd, a company which focussed on improving the performance of clinical trial sites. Brendan was a Director of the Health Products Regulatory Authority of Ireland between 2004 and 2011. He was also a member of the EMA's Committee for Orphan Medicinal Products (COMP) from 2000-2003 and the EMA's Scientific Advisory Committee on Diabetes and Metabolism until 2011.

Dr Elaine Sullivan (aged 60) – Non-Executive Director

Elaine is a business leader and senior scientist with international experience in the pharmaceutical industry and Biotech and is the CEO of Curadh Pharmaceuticals. Elaine has an in-depth background and knowledge of virology having received a PhD from the University of Edinburgh in Molecular Virology. She has been a member of the most senior R&D management teams in Lilly and AstraZeneca. Elaine also has extensive start-up experience having been a founder of Carrick Therapeutics and helped to raise over €100m of investor funds as CEO of Carrick in recent years. Elaine is a Non-Executive Director at IP Group plc and Active Biotech AB and is a member of the Supervisory Board at Evotec which is listed on the Frankfurt Stock Exchange.

Resolution 6

This is an ordinary resolution that deals with the Directors' authority to allot Relevant Securities in accordance with section 551 of the Act and is in place of any and all existing authorities.

If passed, the resolution will authorise the Directors to allot: (i) in relation to a rights issue or open offer only, equity securities (as defined by section 560 of the Act) up to a maximum nominal amount of £223,618 which represents approximately one-third of the Company's issued ordinary shares as at 23 June 2021. This maximum is reduced by the nominal amount of any Relevant Securities allotted under the authority set out in paragraph 6.2 of Resolution 6; and (ii) in any other case, Relevant Securities up to a maximum nominal amount of £223,618 which represents approximately one-third of the Company's issued ordinary shares as at 23 June 2021. This maximum is reduced by the nominal amount of any equity securities allotted under the authority set out paragraph 6.1 of Resolution 6.

The authority granted by this resolution will expire on the earlier of (i) the conclusion of the annual general meeting of the Company to be held in 2022, and (ii) the date falling 18 months from the date of the passing of the resolution, unless any such authorities are renewed, varied or revoked by the Company prior to or on that date. In this regard, it should be noted that the authority conferred at the general meeting of the Company held in July 2020 will expire at the end of the AGM.

In Resolution 6, Relevant Securities means (i) shares in the Company, other than shares allotted pursuant to: (a) an employee share scheme (as defined in section 1166 of the Act); (b) a right to subscribe for shares in the Company where the grant of the right itself constitutes a Relevant Security; or (c) a right to convert securities into shares in the Company where the grant of the right itself constitutes a Relevant Security; and (ii) any right to subscribe for or to convert any security into shares in the Company other than rights to subscribe for or convert any security into shares allotted pursuant to an employee share scheme (as defined in section 1166 of the Act). References to the allotment of Relevant Securities in Resolution 6 includes the grant of such rights.

Resolution 7

This is a special resolution to disapply statutory pre-emption rights otherwise applicable to the Company in respect of Resolution 6. In this regard, it should be noted that the authority conferred at the general meeting of the Company held in July 2020 will expire at the end of the AGM.

This resolution will, if passed, give the Directors power, pursuant to the authority to allot granted by Resolution 6, to allot equity securities (as defined by section 560 of the Act) for cash without first offering them to existing shareholders in proportion to their existing holdings: (a) in connection with a rights issue or open offer subject to any arrangements that the Directors consider appropriate to deal with fractions and overseas requirements; and (b) in any other case, up to a maximum nominal amount of £67,086 which represents approximately 10% of the Company's issued ordinary share capital as at 23 June 2021.

Resolution 8

A special resolution will be proposed to authorise the Directors to make one or more market purchases for the purposes of Section 701 of the Act. The maximum number of shares which may be acquired pursuant to this authority is 67,085,500, which is equal to approximately 10% of the issued ordinary share capital of the Company as at 23 June 2021, the latest practicable date prior to publication of this Notice of AGM. This authority will expire at the conclusion of the annual general meeting in 2022.

The Directors currently have no intention of using their authority to make market purchases. Should this change and the Directors decide to make market purchases, they will only do so if such market purchases are expected to result in an increase in the Company's earnings per share and are in the best interests of the Company's shareholders. The Directors must ensure that any market purchases made are made between a minimum price of 0.1 pence per ordinary share and a maximum price equal to 105% of the average of the middle market quotations for the ordinary shares of the Company derived from the London Stock Exchange plc for the five business days immediately preceding the date on which the ordinary share is purchased.

The Company may either cancel any ordinary shares it purchases under this authority or transfer them into treasury (and subsequently sell or transfer them out of treasury or cancel them).

Compliance with the QCA Code

The Board recognises the importance of sound corporate governance and applies the Corporate Governance Code 2018 published by the Quoted Companies Alliance ("QCA Code"), which the Directors believe is the most appropriate recognised governance code for a company with shares admitted to trading on AIM and Euronext Growth. It is believed that the QCA Code provides the Company with the framework to help ensure that a strong level of governance is maintained, enabling the Company to embed the governance culture that exists within the organisation as part of building a successful and sustainable business for all of its stakeholders.

Board and committee independence

The Board consists of the Executive Chairman, one Executive Director and three Non-Executive Directors. The Company regards two of the Non-Executive Directors as each being an "independent Non-Executive Director" within the meaning of the

QCA Code. The Board has determined that Mark Warne and Michael Meade are independent in character and judgement and that there are no relationships or circumstances which could materially affect or interfere with the exercise of their independent judgement. The Board believes this combination of Executive and Non-Executive Directors allows it to exercise objectivity in decision making and proper control of the Group's business and that this composition is appropriate in view of the size and requirements of the Group's business.

IMPORTANT NOTICE RE COVID-19

In light of the measures issued by the UK Government in view of the ongoing COVID-19 pandemic and the prohibition of large public gatherings, the Company and the Executive Chairman have determined that the Resolutions to be proposed at the AGM shall be voted on through a poll rather than on a show of hands. The Company believes that this is the best and fairest way to ensure that the votes of all shareholders can be taken into account, whilst also preventing the Company and shareholders breaching applicable regulations. Accordingly, the Company encourages all shareholders to either submit their Form of Proxy or use the CREST Proxy Voting Service, rather than attend the meeting in person. In accordance with the Company's articles of association, whilst completion and return of the Form of Proxy or using the CREST Proxy Voting Service would not preclude shareholders from attending, speaking and voting in person at the AGM should they so wish, shareholders are strongly encouraged to either submit their Form of Proxy or use the CREST Proxy Voting Service, rather than attend the AGM in person.

Notice of Annual General Meeting (continued)

NOTES:

1. As a member of the Company who is entitled to attend and vote at the AGM, you are entitled to appoint one or more proxies to exercise all or any of your rights to attend, speak and vote at the AGM and you should have received a Form of Proxy with this Notice of AGM. You can only appoint a proxy using the procedures set out in these notes and the notes to the Form of Proxy. Appointment of a proxy does not preclude you from attending the AGM and voting in person. If you have appointed a proxy and attend the AGM in person, your proxy appointment will automatically be terminated. However, please see the "Important Notice re COVID-19" set out above concerning the implications that COVID-19 will have on attendance at the AGM and the measures that the Company is putting in place in respect of the same.
2. A proxy does not need to be a member of the Company but must attend the AGM to represent you. Details of how to appoint the Chairman of the Meeting or another person as your proxy using the Form of Proxy are set out in the notes to the Form of Proxy. If you wish your proxy to speak on your behalf at the AGM you will need to appoint your own choice of proxy (not the Chairman) and give your instructions directly to them.
3. To appoint a proxy using the form accompanying this Notice of AGM, the Form of Proxy must be:
 - completed and signed;
 - sent or delivered to **SLC Registrars, P.O. Box 5222, Lancing , BN99 9FG**; or
 - scanned as a PDF file and sent by email to proxy@slcregistrars.com; and
 - received by SLC Registrars no later than 12 noon on 19th July 2021.
4. In the case of a member which is a company, the Form of Proxy must be executed under its common seal or signed on its behalf by an officer of the company or an attorney for the company. Any power of attorney or any other authority under which the Form of Proxy is signed (or a duly certified copy of such power or authority) must be included with the Form of Proxy.
5. A corporation which is a member can appoint one or more corporate representatives who may exercise, on its behalf, all its powers as a member provided that no more than one corporate representative exercises powers over the same share.
6. To change your proxy instructions, simply submit a new proxy appointment using the methods set out above. Note that the cut-off time for receipt of proxy appointments (see above) also applies in relation to amended instructions; any amended proxy appointment received after the relevant cut-off time will be disregarded.
7. In order to revoke a proxy instruction you will need to inform the Company by sending a signed hard copy notice clearly stating your intention to revoke your proxy appointment to **SLC Registrars, P.O. Box 5222, Lancing , BN99 9FG**, to be received by the Company's Registrars no later than 12 noon on 19th July 2021. In the case of a member which is a company, the revocation notice must be executed under its common seal or signed on its behalf by an officer of the company or an attorney for the company. Any power of attorney or any other authority under which the revocation notice is signed (or a duly certified copy of such power or authority) must be included with the revocation notice.
8. If you submit more than one valid proxy appointment, the appointment received last before the latest time for the receipt of proxies will take precedence.
9. CREST members who wish to appoint a proxy or proxies through the CREST electronic proxy appointment service may do so by using the procedures described in the CREST Manual. CREST personal members or other CREST sponsored members, and those CREST members who have appointed a voting service provider(s), should refer to their CREST sponsor or voting service provider(s), who will be able to take the appropriate action on their behalf.
10. In order for a proxy appointment or instruction made using the CREST service to be valid, the appropriate CREST message (a "CREST Proxy Instruction") must be properly authenticated in accordance with Euroclear UK & Ireland Limited's specifications, and must contain the information required for such instruction, as described in the CREST Manual (available via www.euroclear.com). The message, regardless of whether it constitutes the appointment of a proxy or is an amendment to the instruction given to a previously appointed proxy must, in order to be valid, be transmitted so as to be received by the Company's agent (ID 7RA01) by 12 noon on 19th July 2021. For this purpose, the time of receipt will be taken to be the time (as determined by the time stamp applied to the message by the CREST Application Host) from which the Company's agent is able to retrieve the message by enquiry to CREST in the manner

prescribed by CREST. After this time any change of instructions to proxies appointed through CREST should be communicated to the appointee through other means.

11. CREST members and, where applicable, their CREST sponsors, or voting service providers should note that Euroclear UK & Ireland Limited does not make available special procedures in CREST for any particular message. Normal system timings and limitations will, therefore, apply in relation to the input of CREST Proxy Instructions. It is the responsibility of the CREST member concerned to take (or, if the CREST member is a CREST sponsored member, or has appointed a voting service provider, to procure that his CREST sponsor or voting service provider(s) take(s)) such action as shall be necessary to ensure that a message is transmitted by means of the CREST system by any particular time. In this connection, CREST members and, where applicable, their CREST sponsors or voting system providers are referred, in particular, to those sections of the CREST Manual concerning practical limitations of the CREST system and timings.
12. The Company may treat as invalid a CREST Proxy Instruction in the circumstances set out in Regulation 35(5)(a) of the Uncertificated Securities Regulations 2001.
13. As at 23 June 2021 (being the last business day prior to the publication of this Notice of AGM) the Company's issued share capital consists of 670,855,002 ordinary shares of 0.1 pence each carrying one vote each. The total voting rights in the Company as at close of business on 23 June 2021 are therefore 670,855,002.
14. Pursuant to regulation 41(1) of the Uncertificated Securities Regulations 2001 (2001 No. 3755) the Company has specified that only those members registered on the Register of Members of the Company at 6.30pm on 19th July 2021 shall be entitled to attend and vote at the AGM in respect of the number of ordinary shares registered in their name at that time. Changes to the Register of Members after 6.30pm on 19th July 2021 shall be disregarded in determining the rights of any person to attend and vote at the AGM.

OPEN ORPHAN PLC

(Incorporated and registered in England and Wales with registered number 07514939)

FORM OF PROXY – ANNUAL GENERAL MEETING (continued)

1. As a member of the Company you are entitled to appoint a proxy or proxies to exercise all or any of your rights to attend, speak and vote at a general meeting of the Company. You can only appoint a proxy using the procedures set out in these notes. If the proxy is being appointed in relation to part of your holding only, please enter in the space next to the proxy's name the number of shares in relation to which they are authorised to act as your proxy. If this space is left blank they will be authorised in respect of your full voting entitlement. Appointment of a proxy does not preclude you from attending the meeting and voting in person. If you have appointed a proxy and attend the meeting in person and vote, your proxy appointment will automatically be terminated. However, please see the "Important Notice re COVID-19" set out above concerning the implications that COVID-19 will have on attendance at the AGM and the measures that the Company is putting in place in respect of the same.
2. A proxy does not need to be a member of the Company but must attend the meeting to represent you. To appoint as your proxy a person other than the Chairman of the Annual General Meeting, insert their full name in the space provided. If you sign and return this Form of Proxy with no name inserted in the space, the Chairman of the Annual General Meeting will be deemed to be your proxy. Where you appoint as your proxy someone other than the Chairman, you are responsible for ensuring that they attend the meeting and are aware of your voting intentions. If you wish your proxy to make any comments on your behalf, you will need to appoint someone other than the Chairman and give them the relevant instructions directly.
3. You may appoint more than one proxy provided each proxy is appointed to exercise rights attached to different shares. You may not appoint more than one proxy to exercise rights attached to any one share. To appoint more than one proxy you should contact **SLC Registrars, P.O. Box 5222, Lancing , BN99 9FG**. If you are appointing more than one proxy, please indicate in the space next to the proxy holder's name the number of shares in relation to which they are authorised to act as your proxy and indicate by ticking the relevant box that the proxy appointment is one of multiple appointments being made. Multiple proxies should be returned in the same envelope. For details of how to change your proxy instructions or revoke your proxy appointment, see the notes to the Notice of AGM.
4. To direct your proxy how to vote on the resolutions, mark the appropriate box with an 'X'. To abstain from voting on the resolution, select the "Vote Withheld" box. If no voting indication is given, your proxy will vote or abstain from voting at his or her discretion. Your proxy will vote (or abstain from voting) as he or she thinks fit in relation to any other matter which is put before the meeting. Please note that a vote withheld is not a vote in law and will not be counted in the proportion of votes "for" or "against" a resolution.
5. To appoint a proxy using the form accompanying this Notice of AGM, the Form of Proxy must be:
 - a. completed and signed;
 - b. sent or delivered to **SLC Registrars, P.O. Box 5222, Lancing , BN99 9FG**; or
 - c. scanned as a PDF file and sent by email to proxy@slcregistrars.com; and
 - d. received by SLC Registrars no later than 12 noon on 19th July 2021.
6. In the case of a member which is a company, this Form of Proxy must be executed under its common seal or signed on its behalf by an officer of the company or an attorney for the company.
7. Any power of attorney or any other authority under which this Form of Proxy is signed (or a duly certified copy of such power or authority) must be included with the Form of Proxy.
8. In the case of joint holders, where more than one of the joint holders purports to appoint a proxy, only the appointment submitted by the most senior holder will be accepted. Seniority is determined by the order in which the names of the joint holders appear in the Company's register of members in respect of the joint holding (the first named being the most senior).
9. If you submit more than one valid proxy appointment, the appointment received last before the latest time for the receipt of proxies will take precedence.