THIS FORM IS IMPORTANT AND REQUIRES YOUR IMMEDIATE ATTENTION

If you are in any doubt about the Offer, the contents of the Offer Document or Letter or the action you should take, you are recommended to seek your own personal financial advice immediately from your stockbroker, bank manager, solicitor, accountant or other independent financial adviser authorised under the Financial Services and Markets Act 2000 (as amended) if you are resident in the United Kingdom or, if not, from another appropriately authorised independent financial adviser in the relevant jurisdiction.

This form of instruction ("**Form of Instruction**") should be read in conjunction with the accompanying letter dated 6 January 2020 ("**Letter**") and the Offer Document dated 9 December 2019 which are available, subject to certain restrictions applicable to persons in Restricted Jurisdictions, on the websites of hVIVO and Open Orphan at https://hvivo.com/investors/recommended-all-equity-offer-for-hvivo-to-merge-with-open-orphan-plc/ and https://www.openorphan.com/recommended-offer-for-hvivo-plc respectively.

Unless the context requires otherwise, words and expressions defined in the Offer Document and the Letter have the same meanings in this Form of Instruction. Please read carefully the terms and conditions of the Offer as set out in the Letter and the Form of Instruction, which are incorporated into, and form part of, this Form of Instruction.

Form of Instruction

RECOMMENDED SHARE OFFER

BY

OPEN ORPHAN PLC

("OPEN ORPHAN")

for

HVIVO PLC

("hVIVO")

If you wish to accept Choice 1 or Choice 2 as described in the Letter, you must send this Form of Instruction duly completed, together with the applicable Option certificate(s)/agreement(s), to Anesh Patel at hVIVO by post or by hand (during normal business hours) or by email to a.patel@hvivo.com as soon as possible, and in any event, to be received by no later than 5.00 p.m. on 27 January 2020. If you wish to proceed under Choice 1 and you return a duly completed Form of Instruction after this time, you will be able to proceed under Choice 1 provided your Form of Instruction is received before your Options lapse and while the Offer remains open for acceptance.

If you take no action, your Options, to the extent unexercised, will lapse and become worthless on the earliest to occur of (i) the date falling one month after the date on which the Offer becomes or is declared unconditional in all respects; and (ii) the expiry of the Exercise Period (as defined in the Share Option Scheme).

If you have any queries in relation to the Letter or how to complete this Form of Instruction, you should contact Anesh Patel at hVIVO on 020 7347 5335 without delay. However, please note that none of Anesh Patel, hVIVO, Open Orphan or Arden will able to provide you with any legal, financial, tax planning or investment advice on the merits of any particular choice or on the Offer itself.

To: ***Open Orphan plc and hVIVO plc***

Return of this Form of Instruction
Please return this Form of Instruction duly completed together with the original applicable Option certificate(s)/agreement(s) to Anesh Patel at hVIVO by post or by hand (during normal business hours) or by email to a.patel@hvivo.com **as soon as possible, and in any event, to be received by no later than 5.00 p.m. on 27 January 2020.**

Please insert your full name, address, work and home/mobile telephone numbers in BLOCK CAPITALS in the boxes below.

Name	
Address	
Work telephone number	
Home telephone or mobile number	

CHOICE 1 - Instructions to exercise and accept the Offer (Choice 1 pursuant to the Letter)

Before completing any of the following boxes you should read the Letter (together with the attached Schedule) which accompanies this Form of Instruction and the Offer Document. You should read all the pages and each of the boxes.

Having done so, I hereby irrevocably exercise my Options as detailed in the table below in respect of all the hVIVO Shares the subject of my Options, if, as and when they become exercisable, with such exercise to take effect:

1 where my duly completed Form of Instruction and related documentation is received before the Offer becomes or is declared unconditional in all respects, immediately following the Offer becoming or being declared unconditional in all respects; and

2 where my duly completed Form of Instruction and related documentation is received after the Offer becomes or is declared unconditional in all respects and before my Options lapse, as soon as reasonably practicable after receipt of my Form of Instruction and related documentation so long as the Offer remains open for acceptance at that time, and

I hereby irrevocably accept the Offer in respect of the hVIVO Shares I acquire on the exercise of my Options.

Box 1

Number of hVIVO Options	Grant Date	Exercise Price per hVIVO Share	Tick to acquire all the hVIVO Shares currently available under your Options and to accept the Offer under Choice 1 in respect of all the hVIVO Shares acquired on such exercise

Notes on completion of Box 1:

1 Tick the relevant box in the last column to exercise your Options **in full** and to accept the Offer in respect of all your hVIVO Shares acquired on such exercise of your Options, as contemplated by Choice 1. If you wish to exercise your Options but **not** accept the Offer in respect of the resulting hVIVO Shares, **DO NOT** complete this Form of Instruction and instead contact Anesh Patel at hVIVO on 020 7347 5335 without delay.

2 If you tick the relevant box in the last column you have irrevocably agreed to exercise your Options in full with such exercise and your acceptance of the Offer taking effect as applicable as set out in paragraphs 1 and 2 above Box 1, in accordance with Choice 1.

3 Subject to the below, if you complete this Form of Instruction and agree to exercise your Options and accept the Offer (i.e. under Choice 1) you **do not** need to send a cheque for the Aggregate Exercise Price to be paid to exercise your Options, or any Tax Liability payable on such exercise. You will be treated as agreeing to the terms of the Dealing Arrangement described in the Letter.

4 **Please note, if you are in any doubt as to your personal tax position, you should consult an appropriate independent professional tax adviser without delay.**

CHOICE 2 - Instructions to cancel and replace your hVIVO Options with Open Orphan Share Options (Choice 2 pursuant to the Letter)

Before completing any of the following boxes you should read the Letter (together with the attached Schedule) which accompanies this Form of Instruction and the Offer Document. You should read all the pages and each of the boxes.

Having done so, I hereby irrevocably agree to cancel all the hVIVO Options I hold in respect of hVIVO Shares as detailed in the table below and replace them with the Open Orphan Share Options as detailed in the table below I will acquire in accordance with Choice 2 on the cancellation of my hVIVO Options, subject to the vesting schedule for the Open Orphan Share Options detailed in the table below and following the Offer becoming or being declared unconditional in all respects, in accordance with paragraphs 9.1.1 and 9.1.2 of the Letter.

Box 2

Number of hVIVO Options and Grant Date	Number of Open Orphan Share Options and vesting schedule	Tick to cancel and replace all Options over hVIVO Shares with new Open Orphan Share Options

Notes on completion of Box 2:

5 Tick the relevant box in the last column to cancel and replace all of your hVIVO Options and to accept the applicable number of Open Orphan Share Options.

6 If you tick the relevant box in the last column, you have irrevocably agreed to cancel and replace your hVIVO Options with the applicable number of Open Orphan Share Options with effect in accordance with paragraphs 9.1.1 and 9.1.2 of the Letter.

7 If you complete this Form of Instruction and agree to cancel and replace your hVIVO Options with Open Orphan Share Options, you **do not** need to pay anything at this time.

8 **Please note, if you are in any doubt as to your personal tax position, you should consult an appropriate independent professional tax adviser without delay.**

NOW COMPLETE THE SIGNATURE BOX BELOW TO CONFIRM EITHER:

- **THE EXERCISE OF YOUR OPTIONS AND THE ACCEPTANCE OF THE OFFER ("CHOICE 1") IN RESPECT OF THE OPTIONS AND RESULTING HVIVO SHARES ACQUIRED PURSUANT TO THIS FORM OF INSTRUCTION; OR**

- **THE CANCELLATION AND REPLACEMENT OF YOUR OPTIONS WITH NEW OPEN ORPHAN SHARE OPTIONS ("CHOICE 2").**

FAILURE TO DO SO WILL RESULT IN THIS FORM OF INSTRUCTION BEING INEFFECTIVE, IN WHICH CASE YOU WILL INSTEAD BE TREATED AS HAVING ELECTED TO TAKE NO ACTION, IN WHICH EVENT YOUR OPTIONS WILL LAPSE AND CEASE TO BE OF ANY VALUE ON THE BASIS SET OUT IN SECTION 7 OF THE LETTER.

CHOICE 1

Box A—Option holder to sign

	SIGN HERE TO EXERCISE YOUR OPTIONS AND ACCEPT THE OFFER			
BOX 3	**Execution by individual(s)**			
	Signed and delivered as a deed by:	Witnessed by:	Witness name:	Date:
	Holder 1 signature _____	Witness 1 signature _____	_____	_____
	Holder 2 signature _____	Witness 2 signature _____	_____	_____
Note:	*The signature of each registered holder who is an individual should be witnessed. The witness must be over 18 years of age, not a member of your immediate family and must not be one of the joint holders.*			

CHOICE 2

Box A—Option holder to sign

	SIGN HERE TO ACCEPT THE CANCELLATION AND REPLACEMENT OF YOUR OPTIONS WITH OPEN ORPHAN SHARE OPTIONS			
BOX 4	**Execution by individual(s)**			
	Signed and delivered as a deed by:	Witnessed by:	Witness name:	Date:
	Holder 1 signature _____	Witness 1 signature _____	_____	_____
	Holder 2 signature _____	Witness 2 signature _____	_____	_____
Note:	*The signature of each registered holder who is an individual should be witnessed. The witness must be over 18 years of age, not a member of your immediate family and must not be one of the joint holders.*			

ADDITIONAL NOTES ON THE COMPLETION OF THIS FORM

Signing the signature box and returning the Form of Instruction duly completed is your confirmation that you want to make the choices indicated in Box 1 or Box 2 (as the case may be) above and take the above actions and agree to the terms of the Letter, the Terms and Conditions of this Form of Instruction and the terms and conditions of the Offer or, as the case may be, of the Open Orphan Option Scheme.

It is important that you read the Terms and Conditions of this Form of Instruction. **If you do not take any action your Options will eventually lapse and cease to be of any value.**

If you wish to: (i) exercise your Options and accept the Offer (i.e. proceed under Choice 1) or (ii) cancel and replace your Options with Open Orphan Share Options (i.e. proceed under Choice 2), you need to send this Form of Instruction using the enclosed reply-paid envelope and return it, together with the relevant Option certificate(s)/agreement(s), to Anesh Patel at hVIVO by post or by hand (during normal business hours only). You are requested to return this Form of Instruction as soon as possible and in any event so as to be received by no later than 5.00 p.m. (UK time) on 27 January 2020. If you have lost your Option certificate(s)/agreement(s), please see paragraphs 4.8 and 7 of the attached terms and conditions. Please take and retain a copy of your completed Form of Instruction for your records.

Terms and Conditions

1 Subject to the following paragraphs, this Form of Instruction will be of no effect unless it is duly completed and returned to Anesh Patel at hVIVO by post or by hand (during normal business hours only) or by email to a.patel@hvivo.com as soon as possible and in any event so as to be received by no later than 5.00 p.m. (UK time) on 27 January 2020.

2 The delivery of this Form of Instruction duly signed may, if hVIVO and Open Orphan so determine in their absolute discretion, be as effective as if it were duly completed and received despite the fact that it is not completed or received strictly in accordance with the Form of Instruction and these Terms and Conditions.

3 Provided that the Offer becomes or is declared unconditional in all respects, your Option certificate(s)/agreement(s) will cease to be valid after the exercise of your Options becomes effective or your Options are cancelled and replaced with Open Orphan Options (as the case may be).

4 By completing and signing this Form of Instruction and either (i) electing to exercise and accept the Offer (i.e. proceeding under Choice 1) or (ii) agreeing to cancel and replace your Options with Open Orphan Share Options (i.e. proceeding under Choice 2) and returning it by the method and date specified you hereby irrevocably:

4.1 confirm that you have read, understood and agree to the Terms and Conditions of this Form of Instruction and that you have had an opportunity to review the Offer Document and the Letter (including the Schedule);

4.2 in the case of Choice 1:

4.2.1 elect to exercise your Options;

4.2.2 accept the Offer in respect of your hVIVO Shares, as described in the Letter on the terms set out in the Offer Document and the Letter; such acceptance to take effect immediately following the exercise of your Options;

4.2.3 authorise each of hVIVO, Open Orphan and Arden Partners plc ("**Arden**") and any director of hVIVO, Open Orphan or Arden (from time to time) to, or to nominate any person to, execute on your behalf and as your agent and attorney a Form of Instruction (or similar documentation) having regard to the instructions listed in this Form of Instruction and a form of transfer or cancellation (and/or any other document) in favour of Open Orphan in respect of your hVIVO Shares, Open Orphan Shares, Options or Open Orphan Share Options;

4.2.4 authorise hVIVO to procure registration of the issue or transfer of hVIVO Shares and the delivery of a certificate (if necessary) in respect of those hVIVO Shares to Open Orphan or as Open Orphan may direct; and

4.2.5 you confirm that you hereby:

(a) authorise Open Orphan to allot and issue such number of Open Orphan Shares due to you or any other person under the Offer on your behalf in accordance with the terms of Choice 1;

(b) authorise Arden to sell such number of Open Orphan Shares you would otherwise acquire as is necessary to cover the amounts specified in paragraphs (c) and (d) below;

(c) authorise hVIVO to retain an amount equal to the Aggregate Exercise Price in discharge of your undertaking pursuant to the terms of the Dealing Arrangement (as more particularly described in the Letter);

(d) authorise hVIVO, your employer and/or former employer to deduct an amount equal to the Tax Liability and account for the same to HMRC (or any other relevant tax authority) on your behalf, and to do any other act as may be necessary or desirable to give effect to your instructions as set out in the Form of Instruction;

(e) authorise Arden to deduct a fee of 0.5% in respect of the Dealing Arrangement; and

(f) agree to indemnify and keep indemnified hVIVO (and, where relevant, your employing company) for any further income tax and employee's National Insurance contributions (or the overseas equivalent) in respect of the Options (whether pursuant to their exercise, the acquisition of hVIVO Shares or otherwise);

4.3 in the case of Choice 2:

4.3.1 elect to cancel and replace your Options with the applicable number of Open Orphan Share Options;

4.3.2 agree that the cancellation and replacement of your Options will take effect as set out in the Letter and this Form of Instruction;

4.3.3 authorise hVIVO and Open Orphan to deliver a deed or option certificate (if necessary) in respect of the award of any Open Orphan Share Options or as Open Orphan may direct;

4.3.4 authorise each of hVIVO, Open Orphan and any director of hVIVO or Open Orphan (from time to time) to nominate any person to execute on your behalf and as your agent and attorney a Form of Instruction (or similar documentation) having regard to the instructions listed in this Form of Instruction and a form of transfer in favour of Open Orphan;

4.4 acknowledge that if any of the Options have lapsed or lapse before exercise takes effect, completion of this Form of Instruction will be of **no** effect in respect of such lapsed Options;

4.5 acknowledge that neither hVIVO nor Open Orphan will be responsible for any loss incurred by any person in the event of the Form of Instruction being incorrectly completed or where either of them has been unable to obtain clarification of your instructions;

4.6 acknowledge that, save in the event of their own fraud, neither hVIVO nor the hVIVO Directors nor Open Orphan nor the Open Orphan Directors nor Arden nor J&E Davy nor MCF Ltd nor any person acting on behalf of any of them shall have any liability to any person for any loss or alleged loss arising from the price of, the timing of, or the manner of any sale or cancellation and replacement of hVIVO Shares or Options made in accordance with the terms of the Offer or the Letter or otherwise in connection with the Offer, the Letter, Choice 1 or Choice 2;

4.7 authorise that all correspondence, share certificates, consideration and any other item in connection with the Offer and the Letter may be sent to you at your own risk at the address to which the Letter was sent (or address provided above, if different) and that hVIVO and Open Orphan accept no responsibility for documentation lost or delayed in the postal system;

4.8 agree that unless hVIVO and Open Orphan decide otherwise, this Form of Instruction has no effect unless accompanied by the Option certificates/agreements;

4.9 waive all rights and/or claims you may have (current and future) in respect of the Options (other than the right to receive hVIVO Shares in respect of the exercise of your Options you exercise under Choice 1 or the right to receive Open Orphan Share Options under Choice 2) and any hVIVO Shares you acquire pursuant to the exercise of the Options, such waiver to take effect immediately upon the exercise of the Options; and

4.10 agree that hVIVO and Open Orphan may, but are not obliged to, rely on a duly completed PDF or faxed copy of this Form of Instruction if not accompanied by the original.

5 Your signature on this Form of Instruction constitutes:

5.1 a warranty that you are entitled to your Options, that they are valid and subsisting and free from all liens, charges and encumbrances of any nature whatsoever and that you are entitled to exercise the Options;

5.2 where relevant, your written consent to amendments to the Share Option Scheme; and

5.3 an irrevocable authority to and appointment of any director of hVIVO and/or Open Orphan and/or Arden or any person nominated by hVIVO and/or Open Orphan and/or Arden as your attorney (the "**Attorney**") with authority in your name and on your behalf to sign and execute any and all agreements, instruments, deeds or other papers and documents and do all things in your name as the Attorney may in its absolute discretion consider necessary or desirable in order to give effect to your instructions and authorities above and to facilitate (i) the exercise of your Options and the transfer of the hVIVO Shares that you shall hold as a result of the

exercise of your Options to Open Orphan (including the sale of such number of Open Orphan Shares as is necessary to cover the Aggregate Exercise Price and any Tax Liability arising on the exercise of your Options pursuant to the Dealing Arrangement, Arden's fee and anything else required to give effect to the Dealing Arrangement) or (ii) the cancellation and replacement of your Options with new Open Orphan Share Options, in each case, in accordance with the terms set out in this Form of Instruction, the Letter and the Offer Document AND you hereby undertake to ratify everything which the Attorney shall do or purport to do by virtue of this power of attorney and declare that this power of attorney having been given by you to the Attorney to secure your undertakings to it in connection with the Options and this Form of Instruction, shall be irrevocable in accordance with section 4 of the Powers of Attorney Act 1971.

6 **If you sign and return this Form of Instruction, but do not complete any of the boxes, or if you compete this Form of Instruction incorrectly, you will be** deemed **to have elected to take no action, in which event your options will lapse and cease to be of any value on the basis set out in section 7 of the Letter.**

7 If you have not enclosed your original Option certificates/agreements you agree to deliver such Option certificates/agreements to hVIVO for cancellation (if possible) as soon as such Option certificates/agreements become available to you. You also agree to indemnify hVIVO and/or Open Orphan against all claims, demands, liabilities and expense, howsoever arising as a consequence of exercise being permitted without production of the relevant Option certificates/agreements.