

November 12, 2018

Citibank, N.A.
388 Greenwich Street
New York, New York 10013
USA
Attention: Citi Depository Receipts Services

Equiniti Limited
Corporate Advice
Aspect House, Spencer Road
Lancing, West Sussex BN99 8AH
UK
Attention: Andrew Farley

Takeda Pharmaceutical Company Limited
1-1 Nihonbashi-Honcho 2-Chome,
Chuo-ku, Tokyo 103-8668
Japan
Attention: Atsuhiko Nagano

The Bank of New York Mellon, as Depository for the Takeda ADS Program
240 Greenwich Street - 22 Floor West
New York, New York 10286
USA
Attention: Joanne DiGiovanni Hawke

Shire – Takeda Scheme of Arrangement

Ladies and Gentlemen:

Reference is made to the Amended and Restated Deposit Agreement, dated as of May 23, 2011 (the “Shire Deposit Agreement”), by and among Shire plc (“Shire”), Citibank, N.A., a national banking association organized under the laws of the United States of America (“Citibank”), as Depository (the “Shire Depository”), and all holders and beneficial owners from time to time of American depository receipts issued thereunder evidencing American depository shares (“Shire ADSs”) representing deposited Shire ordinary shares (“Shire Shares”). Terms used herein without definition shall have the meanings ascribed to such terms in the Shire Deposit Agreement.

The purpose and intent of this instructions letter (the “Instructions Letter”) is to supplement the Shire Deposit Agreement in connection with the scheme of arrangement proposed to be made under Article 125 of the Companies (Jersey) Law 1991, as amended from time to time (the “Jersey Companies Law”), between Shire’s shareholders and Shire to implement the acquisition of Shire by Takeda Pharmaceutical Company Limited, a joint-stock corporation incorporated under the laws of Japan (“Takeda”), pursuant to which Shire will become a wholly-owned subsidiary of Takeda (the “Scheme”). Pursuant to the Scheme, holders

of Shire Shares will receive (i) \$30.33 in cash, and (ii) *either* 0.839 newly issued ordinary shares of Takeda with no par value (the “Takeda Shares”) *or*, depending on their valid election (a) 1.678 American depositary shares representing Takeda Shares (the “Takeda ADSs”) to be issued pursuant to the Deposit Agreement (as amended and restated from time to time) (the “Takeda Deposit Agreement”) by and among Takeda, The Bank of New York Mellon (“BNY Mellon”) as depositary (the “Takeda Depositary”), and all owners and holders of Takeda ADSs, or (b) CREST depository interests representing Takeda ADSs, in each case in exchange for each Shire Share held as of the Scheme Record Time (as defined in the scheme document published by Shire on November 12, 2018) (the “Share Scheme Consideration”).

The Shire Depositary will, in accordance with the terms hereof, elect to receive Takeda ADSs in respect of all Shire Shares represented by Shire ADSs outstanding as at the “Scheme Record Time” (as defined in the Scheme Document, and hereinafter used so defined). Consequently, as a result of the exchange of Shire Shares for the Share Scheme Consideration, holders of Shire ADSs will be entitled to receive (i) \$90.99 in cash (the “ADS Cash Consideration”) and (ii) 5.034 Takeda ADSs to be issued pursuant to the Takeda Deposit Agreement (the “Takeda ADS Consideration”, and together with the ADS Cash Consideration, the “ADS Scheme Consideration”) in exchange for each Shire ADS held as of the ADS Effective Date (as herein after defined). Holders of Shire ADSs entitled to receive a fraction of a Takeda ADS will receive, in lieu thereof, an amount in cash equal to the net cash proceeds from the sale of the fractional entitlements to Takeda ADSs (net of applicable fees, taxes and expenses, and rounded down to the nearest whole cent) by the Shire Depositary.

The Scheme is more fully described in the document to be dispatched to the holders of Shire Shares setting out, among other things, the details of the Scheme and the terms and conditions of the Scheme (the “Scheme Document”) and is subject to, among others, the sanctioning of the Scheme by the Royal Court of Jersey.

In connection with the Scheme, the parties agree to the following:

1. **Solicitation of Votes from Shire ADS Holders.** In connection with the solicitation of the votes of holders of Shire Shares to approve the Scheme, the Shire Depositary shall (i) establish November 7, 2018 as the record date (the “ADS Record Date”) to determine holders of Shire ADSs entitled to instruct the Shire Depositary to vote, or cause to be voted, the Shire Shares represented by the Shire ADSs and (ii) close the books to the issuance and cancellation of Shire ADSs at the close of business (New York City time) on November 23, 2018 (the “November ADS Book Closure Date”). The books will subsequently be reopened to the issuance and cancellation of Shire ADSs at 8:00 a.m. (New York City time) on the day immediately following the date on which the Voting Record Time (as defined in the Scheme Document) falls (which Voting Record Time is, as of the date of this Instructions Letter, scheduled for 6:30 p.m. (United Kingdom time) on December 3, 2018) or such other time as may be agreed between Shire and the Shire Depositary (the “December ADS Book Re-Opening Date”). The Shire Depositary shall, in accordance with the Shire Deposit Agreement and subject to receipt of the “no registration” opinion referred to in the following paragraph: (a) mail to holders of Shire ADSs and (b) cause to be distributed to beneficial owners of Shire ADSs (via electronic delivery for those beneficial owners that have elected such delivery method), in each case, as of the ADS Record Date, each of the following: (i) the Depositary Notice of Court

Meeting and General Meeting for Shire which sets out notice of the Court Meeting (as defined in the Scheme Document) (the “Court Meeting”) and the Shire General Meeting (as defined in the Scheme Document) (the “Shire General Meeting”), substantially in the form of Exhibit I attached hereto, and which shall contain the web address where all holders and beneficial owners of Shire ADSs may access an electronic version of the Scheme Document (the “Depositary Notice”) and (ii) the Court Meeting and General Meeting 2018 Voting Instructions Card substantially in the forms of Exhibit II attached hereto (the “Voting Instructions Card”, and together with the Depositary Notice, the “Voting Materials”). Shire hereby advises and confirms to the Shire Depositary that the Scheme Document has not been furnished to the Shire Depositary by Shire for the purposes of Section 14 of the Shire Deposit Agreement. Shire hereby confirms to the Shire Depositary that: (i) it wishes for the discretionary proxy contemplated under paragraph of Exhibit A to the Shire Deposit Agreement (the “Discretionary Proxy”) to be given to it by the Shire Depositary for the purposes of the Shire General Meeting; and (ii) it does not wish for the Discretionary Proxy to be given to it by the Shire Depositary for the purposes of the Court Meeting. The Shire Depositary hereby confirms that it shall give the Discretionary Proxy to a person nominated by Shire in respect of any unvoted ADSs pursuant to paragraph 12 of Exhibit A to the Shire Deposit Agreement for use at the Shire General Meeting and, in respect thereto, confirms that it has received an opinion, as contemplated in paragraph 12 of Exhibit A to the Shire Deposit Agreement, in a form satisfactory to the Shire Depositary. The Shire Depositary shall require each person presenting Shire ADSs for cancellation after the ADS Record Date and prior to the November ADS Book Closure Date to deliver a duly completed and signed Withdrawal Certification substantially in the form of Exhibit III attached hereto (which may be collected by the Shire Depositary in electronic format).

Takeda shall cause its U.S. counsel to deliver to the Shire Depositary and to the Takeda Depositary promptly after the date of this Instructions Letter and prior to the distribution of the Voting Materials a “no registration” opinion under the U.S. Securities Act of 1933, as amended, in a form reasonably satisfactory to the Shire Depositary and the Takeda Depositary. In addition, Takeda shall cause its Japanese counsel to deliver an opinion to the Takeda Depositary, in a form reasonably satisfactory to the Takeda Depositary, dated the Effective Date (as defined in the Scheme Document, and hereinafter used as so defined), to the effect that (i) the Takeda Shares deposited with the Takeda Depositary in connection with the Scheme are duly authorized, validly issued, fully paid and non-assessable and were not issued in violation of any pre-emptive or similar rights of the holders of any Takeda securities and (ii) the issue and deposit of Takeda Shares in connection with the Scheme and the delivery of Takeda ADSs representing those Takeda Shares (A) will not violate the articles of association or similar documents of Takeda or any Japanese laws or regulations, (B) do not require any consents or approvals of or filings with, any Japanese governmental or regulatory authority that have not been obtained or made, or that are not in full force and effect, and (C) will not give rise to any stamp or similar Japanese transactional taxes or governments charges that are or may become payable by the Takeda Depositary or its Japanese custodian.

2. **ADS Exchange.** Shire hereby instructs the Shire Depositary, and the Shire Depositary hereby agrees, to make an ADS Election (as defined in the Scheme Document) to receive Takeda ADSs pursuant to the terms of the Scheme Document on behalf of the holders of Shire ADSs (the “ADS Election”). In accordance with Section 5 of the Shire Deposit Agreement and paragraph 10 of Exhibit A to the Shire Deposit Agreement, Shire hereby requests

that the Shire Depository distribute, and the Shire Depository agrees to establish the applicable procedures to distribute to the holders of Shire ADSs as of close of business in New York on the date which falls two “Business Days” (as defined in the Scheme Document, and hereinafter used as so defined) after the Scheme Record Time (the date falling two Business Days after the Scheme Record Time, as of the date of this Instructions Letter, being contemplated to be January 8, 2019) or such other time as Shire and the Shire Depository shall agree (the “ADS Effective Date”), the ADS Cash Consideration and the Takeda ADS Consideration in exchange for each Shire ADS held, upon the terms described in the Scheme Document (the “ADS Exchange”), promptly after the receipt of the corresponding amount of ADS Cash Consideration and Takeda ADS Consideration, respectively, and the Cancellation Fees and the Cash Distribution Fee described in Section 5 below.

In connection with the ADS Exchange, the Shire Depository shall deliver to the holders of Shire ADSs as of the ADS Effective Date the following documents: (i) to The Depository Trust Company (“DTC”), by e-mail, a Depository Notice of ADS Exchange substantially in the form of Exhibit IV attached hereto (the “Depository Notice of ADS Exchange”), (ii) to the holders of uncertificated Shire ADSs, by mail, the Depository Notice of ADS Exchange, and, subsequently, a check for the applicable cash portion of the ADS Scheme Consideration and any net cash-in-lieu of fractional entitlements to Takeda ADSs, and (iii) to holders of certificated Shire ADSs, by mail, the Depository Notice of ADS Exchange, together with a letter of transmittal substantially in form of Exhibit V attached hereto (the “Letter of Transmittal”). The Shire Depository shall close the books to issuance and cancellation of Shire ADSs at the close of business (New York City time) on the date (the “December ADS Book Closure Date”) falling six Business Days prior to the Scheme Record Time (the date falling six Business Days prior to the Scheme Record Time is contemplated, as of the date of this Instructions Letter, to be December 26, 2018) or such other time as Shire and the Shire Depository shall agree, in anticipation of the Scheme Record Time and the ADS Effective Date. To the extent reasonably possible, Shire will endeavor to provide notice of any revision to the proposed effectiveness of the Scheme at least twelve (12) calendar days prior to the revised effective date of the Scheme to the Shire Depository so as to enable the Shire Depository to provide to DTC a draft copy of the Depository Notice of the ADS Exchange at least ten (10) calendar days prior to the revised effective date of the Scheme. The failure by Shire to provide notice of any revision to the proposed effectiveness of the Scheme, as contemplated in the preceding sentence, shall not prevent the Scheme from becoming effective.

The ADS Cash Consideration and the Takeda ADS Consideration will be delivered by the Shire Depository after the ADS Effective Date as follows: (i) to DTC, promptly after receipt of the requisite amount of ADS Cash Consideration and Takeda ADS Consideration, respectively, the Cancellation Fees and the Cash Distribution Fee described in Section 5 below, and surrender by DTC of the applicable Shire ADSs to the Shire Depository (by SCL Draw-Down), (ii) to holders of uncertificated Shire ADSs, promptly after receipt of the requisite amount of ADS Cash Consideration and Takeda ADS Consideration, respectively, the Cancellation Fees and the Cash Distribution Fee described in Section 5 below, and proceeds from the sale of fractional entitlements to Takeda ADSs, and (iii) to holders of certificated Shire ADSs, promptly after receipt of the requisite amount of ADS Cash Consideration and Takeda ADS Consideration, respectively, the Cancellation Fees and the Cash Distribution Fee described in Section 5 below, a duly completed Letter of Transmittal, the relevant certificated Shire ADSs

(or applicable affidavit of loss or similar instrument), and applicable supporting documentation and payments (if any).

3. **Receiving Agent Instruction and Agreement.** Shire, Takeda, and Equiniti Limited (“Equiniti”) confirm that Equiniti has been appointed as receiving agent in connection with the Scheme and the distribution of the Share Scheme Consideration (the “Receiving Agent”). The Shire Depository will procure that Citibank, N.A. (London Branch), the custodian for the Shire ADS program (the “Custodian”), via the Custodian’s nominee, National City Nominees Limited (the “Nominee”), to make an ADS Election in respect of all of the Shire Shares represented by Shire ADSs outstanding as at the Scheme Record Time by completing and returning to the Receiving Agent a CREST Form of Election, substantially in the form of Exhibit VI attached hereto, in accordance with the instructions therein, which will include instruction to deposit the Takeda Shares to be issued as Share Scheme Consideration for the Shire Shares represented by Shire ADSs with Sumitomo Mitsui Banking Corporation, the custodian appointed by the Takeda Depository, for credit to JASDEC Participant Code 0000980; JASDEC Shareholder Participant Code 00009809340000000000, for issuance of the corresponding Takeda ADSs in the name of Citibank, N.A., as Depository of the Shire ADS Program, 388 Greenwich Street, New York, New York 10013 (Attn.: Global Structuring), by no later than the Election Return Time (as defined in the Scheme Document). Subject to such CREST Form of Election being validly completed and returned by such time, in accordance with the terms of the Scheme, Equiniti will process the ADS Election by the Nominee on behalf of the Custodian in accordance with the terms of the Scheme such that the Takeda Shares to be issued as Share Scheme Consideration for the Shire Shares represented by Shire ADSs will be deposited with the Takeda Depository.

In accordance with the terms of the Scheme, the cash portion of the Share Scheme Consideration for the Shire Shares represented by Shire ADSs will be deposited into the CREST account of the Nominee (on behalf of the Custodian).

Shire and Takeda confirm, and Equiniti acknowledges, that, pursuant to the terms of the Scheme, the Shire Shares shall be automatically transferred to Takeda upon the Scheme becoming “Effective” (as defined in the Scheme Document, and hereinafter used so defined) and, as to the Shire Shares represented by Shire ADSs, the Shire Depository shall have no obligation to take any other action in connection therewith.

4. **Takeda Depository Instructions and Agreement.** Takeda and BNY Mellon hereby confirm that BNY Mellon has been appointed as the Takeda Depository. Takeda hereby instructs the Takeda Depository to act upon the instructions of the Shire Depository in respect of the Takeda ADSs to be issued as part of the ADS Scheme Consideration. Takeda hereby instructs the Takeda Depository, and the Takeda Depository agrees, to deliver the Takeda ADSs to be issued as part of the ADS Scheme Consideration to the Shire Depository (or its nominee) as promptly as practicable after receipt of confirmation of deposit of the requisite Takeda Shares.

The Shire Depository instructs the Takeda Depository, and the Takeda Depository agrees, to deliver the Takeda ADSs representing the Takeda Shares deposited by the Receiving Agent pursuant to Section 3 above, as soon as practicable following receipt of such deposit in its

custody account in Japan, in uncertificated form, to the following account: Citibank, N.A., as Depositary of the Shire ADS Program, 388 Greenwich Street, New York, New York 10013 (Attn.: Global Structuring). The Takeda Depositary agrees to act upon the instructions of the Shire Depositary for the delivery of the Takeda ADSs so registered in the name of the Shire Depositary. The Shire Depositary will give the Takeda Depositary proper instructions to register transfers of those Takeda ADSs to the names of the registered holders of Shire ADSs, or to Cede & Co., as nominee of DTC, for allocation by DTC to the accounts of the DTC participants entitled to those Takeda ADSs. DTC will notify the Shire Depositary when that allocation is completed. Upon receipt of such notice, the Shire Depositary shall notify the New York Stock Exchange. The Shire Depositary expects to be able to provide such notification by 3.30 p.m. (New York City time) on the relevant day.

The Takeda Depositary confirms that no Takeda ADS issuance fees will be payable in respect of the Takeda ADSs to be issued as ADS Scheme Consideration to the Shire Depositary.

The Shire Depositary will give written instructions to the Takeda Depositary for the registration of the transfer of the Takeda ADSs to the holders of Shire ADSs entitled thereto pursuant to draw-down letters substantially in the form of Exhibit VII attached hereto (each, a “Drawn-Down Letter”), and the Takeda Depositary agrees to register the transfer of the specified Takeda ADSs upon the instruction of the Shire Depositary as soon as practicable after receipt of the applicable Draw-Down Letter.

5. **Shire Depositary Fees.** Takeda and Shire agree that, in accordance with the terms of the Shire Deposit Agreement and in connection with the “Acquisition” (as defined in the Scheme Document, and hereinafter used so defined), the Shire Depositary will be entitled to the following fees in respect of the Scheme:

- Shire ADS cancellation fee - US\$0.05 per Shire ADS cancelled (i) on or after the date falling 16 Business Days prior to the December ADS Book Closure Date (such date, as of the date of this Instructions Letter, being contemplated to be December 4, 2018) and up to and including the sooner of: (x) the December ADS Book Closure Date (which date, as of the date of this Instructions Letter, is contemplated to be December 26, 2018), and (y) the date that the Acquisition lapses, terminates or is withdrawn in accordance with its terms; and (ii) in connection with the distribution of the Takeda ADS Consideration if the Scheme becomes Effective (the sum of such fees being the “Cancellation Fees”); provided, however, that in the event either Shire or Takeda announce, after the December ADS Book Re-Opening Date (such date, as of the date of this Instructions Letter, being contemplated to be December 4, 2018) and prior to the December ADS Book Closure Date, that the date on which the Scheme is expected to become Effective is delayed, ADS cancellation fees (US\$0.05 per Shire ADS) will be payable to the Shire Depositary by Shire, Takeda or the Shire ADS holders in respect of Shire ADSs which were cancelled in the period between the December ADS Book Re-Opening Date and the date of such announcement upon terms to be agreed by the Shire Depositary,

Shire and Takeda; provided, however, further, that the Shire ADS holders will be solely responsible for any ADS cancellation fees for Shire ADSs that are cancelled prior to, and including, the November ADS Book Closure Date; and

- Shire ADS cash distribution fee for the distribution of the ADS Cash Consideration - US\$0.02 per Shire ADS (the sum of such fees being the “Cash Distribution Fee”).

(A) Subject to Section 5(B) below, and subject to the Scheme becoming Effective, Shire agrees to pay the Cancellation Fees and the Cash Distribution Fee which have fallen due in accordance with the terms of the Shire Deposit Agreement and this Instructions Letter as a single amount, which amount shall be invoiced by the Shire Depository to Shire no later than the close of business in New York on the date falling four Business Days prior to the expected Scheme Record Time (the date falling four Business Days prior to the Scheme Record Time is, as of the date of this Instructions Letter, expected to be December 28, 2018) and which invoice shall include instructions to pay to the following account: Citibank, N.A., ABA# 021000089, A/C# 3685-8172, Re: Shire Cancellation Fees, Att.: Brian M. Teitelbaum. Subject to receipt of such invoice, Shire shall remit complete payment of such fees to the Shire Depository’s account designated therein by no later than the close of business in New York on the date falling one Business Day after the Effective Date (the date falling one Business Day after the Effective Date is, as of the date of this Instructions Letter, expected to be January 9, 2019).

(B) Notwithstanding Section 5(A) above, but subject to Section 5(C) below, in the event that the Scheme does not become Effective, Takeda agrees to pay the Cancellation Fees which have fallen due in accordance with the terms of the Shire Deposit Agreement and this Instructions Letter as a single amount, which amount shall be invoiced by the Shire Depository to Takeda no later than the close of business in New York on the date falling four Business Days after the date on which Shire announces publicly that the Co-Operation Agreement between Takeda and Shire has been terminated in accordance with its terms, and which invoice shall include instructions to pay to the following account: Citibank, N.A., ABA# 021000089, A/C# 3685-8172, Re: Shire Cancellation Fees, Att. Brian M. Teitelbaum. Subject to receipt of such invoice, Takeda shall remit complete payment of such fees to the Shire Depository’s account designated therein by no later than the close of business in New York on the date falling seven Business Days after the date on which such invoice is received.

(C) Notwithstanding Section 5(B) above, in the event that the Acquisition lapses, terminates or is withdrawn in accordance with its terms because a competing transaction is recommended by, or becomes effective with the recommendation of, the Shire Directors (as defined in the Scheme Document), Shire agrees to pay the Cancellation Fees which have fallen due in accordance with the terms of the Shire Deposit Agreement and this Instructions Letter as a single amount, which amount shall be invoiced by the Shire Depository to Shire no later than the close of business in New York on the date falling four Business Days after the date on which Shire announces publicly that the Co-Operation Agreement between Takeda and Shire has been terminated in accordance with its terms, and which invoice shall include instructions to pay to the following account: Citibank, N.A., ABA# 021000089, A/C# 3685-8172, Re: Shire

Cancellation Fees, Att. Brian M. Teitelbaum. Subject to receipt of such invoice, Shire shall remit complete payment of such fees to the Shire Depository's account designated therein by no later than the close of business in New York on the date falling seven Business Days after the date on which such invoice is received.

In addition, Shire shall reimburse the Shire Depository, upon the terms contemplated in the Shire Deposit Agreement (and related ancillary agreements between Shire and the Shire Depository), for all incurred out-of-pocket expenses incurred by it in connection with the Scheme (and any ancillary corporate actions related to, or deriving from, the Scheme), including, without limitation, all fees and expenses of its legal counsel and all fees and expenses of the transfer/exchange agent for the Shire ADSs.

Separately, Shire confirms its agreement that the Shire Depository shall, in accordance with the Shire Deposit Agreement, be entitled to receive, and that it shall be responsible for the prompt payment of, all other fees and expenses of the transfer/exchange agent incurred by the Shire Depository upon the terms contemplated in the Shire Deposit Agreement (and related ancillary agreements between Shire and the Shire Depository).

For the avoidance of doubt, the Shire ADS holders shall be responsible for the payment of fees and expenses in connection with the sale of fractional entitlements to Takeda ADSs.

6. **U.S. Tax Reporting and Withholding.**

(i) **U.S. Federal Income Tax Treatment.** The parties will treat the exchange of Shire ADSs for the ADS Scheme Consideration by a U.S. citizen or resident (as determined for U.S. federal income tax purposes), a corporation organized under the laws of the United States of America or any other person treated as a U.S. person for U.S. federal income tax purposes (a "**U.S. Holder**") as a taxable transaction for U.S. federal income tax purposes. Furthermore, Shire has confirmed in the Scheme Document that receipt of the ADS Cash Consideration by U.S. Holders will likely be subject to Section 304 of the Internal Revenue Code of 1986, as amended (the "**Code**"). The Shire Depository shall mail to U.S. Holders receiving ADS Scheme Consideration any tax reports, and file any reports with the U.S. Internal Revenue Service ("**IRS**") in respect of the Shire ADSs surrendered as specified below or as required pursuant to the Code and the U.S. Treasury Regulations thereunder.

(ii) **U.S. Tax Reporting.** On or before February 15 of the year following the year of the Scheme, the Shire Depository will prepare and mail to each holder of Shire ADSs who has received ADS Scheme Consideration from the Shire Depository in accordance with the terms hereof, other than holders of Shire ADSs who demonstrate their status as nonresident aliens (or who are not otherwise U.S. Holders) by providing a properly completed Form W-8 in accordance with U.S. Treasury Regulations (such person, a "**Non-U.S. Holder**") or other recipients providing evidence of exempt status, a Form 1099-B reporting the ADS Scheme Consideration delivered to such holders as of the year of payment, to the extent required by, and in accordance with, U.S. Treasury Regulations. The Shire Depository will also prepare and timely file copies of such Forms 1099-B by electronic filing with the IRS. For U.S. tax reporting purposes, Takeda will provide to the Shire Depository and to the Takeda Depository, promptly

after the Effective Date, and in any event prior to the open of business in New York on the first Business Day after the Effective Date (the date, as of the date of this Instructions Letter, being contemplated to be January 9, 2019), in a signed officer's certificate, the calculation of the fair market value as of the Effective Date of the Takeda ADSs received in exchange for a single Shire ADS in the Scheme, and the related "acquisition date", both of which will be used by the Shire Depository for purposes of the tax reporting on Form 1099-B.

(iii) U.S. Backup Withholding. If the Shire Depository has not received notice from the surrendering holder of Shire ADSs such holder's Taxpayer Identification Number ("TIN"), including on a properly completed Form W-9, or if such TIN has not been certified as correct (*i.e.*, by the registrar or transfer agent of Shire) or such holder otherwise fails to comply with applicable backup withholding provisions under the U.S. Treasury Regulations, the Shire Depository shall deduct and withhold backup withholding with respect to the ADS Scheme Consideration (to the extent required by, and at the applicable rate or rates specified by, the Code and U.S. Treasury Regulations thereunder) from any cash consideration (including cash in lieu of fractional Takeda ADS) delivered to such holder (other than a Non-U.S. Holder that provides a properly completed Form W-8 or other exempt recipient) and remit such funds to the IRS in accordance with the Shire Depository's standard procedures.

(iv) Section 6045B Reporting. Notwithstanding any other provision herein, any U.S. tax returns or information statements required to be filed with respect to the Scheme pursuant to Code Section 6045B or the U.S. Treasury Regulations promulgated thereunder shall be prepared, and timely filed, by Takeda, and neither the Shire Depository nor the Takeda Depository shall be responsible for preparing or filing any such U.S. tax returns or information statements. Takeda shall timely post an IRS Form 8937 on its website in accordance with applicable U.S. Treasury Regulations to provide information to former holders of Shire ADSs and shall furnish, or cause to be furnished, a copy of the IRS Form 8937 to the Shire Depository within 15 days of posting the form on its website. The Shire Depository shall not be required to mail to U.S. Holders any tax reports or forms except as specified in paragraph (ii) of this Section 5.

(v) Further Assistance. Should any issue arise regarding U.S. federal income tax reporting or withholding, the Shire Depository will take such action consistent with the terms of the Shire Deposit Agreement and this Instructions Letter, as Shire instructs the Shire Depository in writing. Shire agrees to reimburse the Shire Depository for any reasonable costs incurred in connection with such actions.

7. **Jersey, Japan, and United Kingdom Tax Withholding.** Shire confirms that it has been advised by: (a) Jersey counsel that (other than in the case of holders or Beneficial Owners of Shire ADSs resident in Jersey for tax purposes) the exchange of Shire Shares represented by Shire ADSs for Share Scheme Consideration is not subject to Jersey taxation, and that, as a result, there will be no Jersey tax withheld or payable (including any stock transfer tax) with respect to the Share Scheme Consideration received by the Depository in the Scheme in respect of the Shire ADSs; (b) Japanese counsel that no stamp, registration or other issuance or transfer taxes or duties and no capital gains, income, withholding or other taxes are payable in Japan by or on behalf of the Depository or the holders of Shire ADSs who are individual non-residents of Japan or non-Japanese corporations, each having no permanent establishment in

Japan for Japanese tax purposes, in connection with the exchange of Shire Shares represented by Shire ADSs for ADS Scheme Consideration received by the Depository on behalf of the holders of Shire ADSs in the Scheme in respect of the Shire ADSs; and (c) English counsel that the Shire Depository shall not be required to pay UK tax (including any UK stock transfer tax) with respect to the ADS Scheme Consideration received by the Shire Depository under the Scheme in exchange for the Shire Shares represented by Shire ADSs on behalf of the holders of Shire ADSs.

8. **Termination of Shire Deposit Agreement.** Shire hereby instructs the Shire Depository to terminate the Shire Deposit Agreement effective upon the expiration of six months after the ADS Effective Date; provided that the other provisions of the Shire Deposit Agreement regarding indemnification, liability and limits thereon shall survive the termination of the Shire Deposit Agreement.

9. **Indemnity/Survival.** Shire acknowledges and agrees that the indemnities provided in Section 16 of the Shire Deposit Agreement shall apply to any acts performed or omitted by the Shire Depository, the Custodian and any of their respective directors, employees, agents and affiliates pursuant to the (a) instructions provided, and confirmations contained, in this Instructions Letter, or (b) the Scheme generally. For avoidance of doubt, Shire and Takeda confirm that the obligations of Shire hereunder (including, without limitation, the indemnity obligations) shall survive the Scheme and be the surviving obligations of Takeda.

10. **Governing Law/Jurisdiction.** This Instructions Letter shall be governed by, and construed in accordance with, the laws of the State of New York. Shire, Takeda and the Shire Depository agree that the federal or state courts in the Borough of Manhattan, The City of New York shall have jurisdiction to hear and determine any suit, action or proceeding and to settle any dispute between them that may arise out of, or in connection with, this Instructions Letter and, for such purposes, each irrevocably submits to the non-exclusive jurisdiction of such courts.

Shire hereby irrevocably designates, appoints and empowers Shire Pharmaceuticals LLC (the "**Shire Agent**"), whose Delaware registered office address is at Corporation Trust Center, 1209 Orange Street, Wilmington, DE 19801 and whose business address is 730 Stockton Drive, Exton, PA 19341, as its authorized agent to receive and accept for and on its behalf, and on behalf of its properties, assets and revenues, service by mail of any and all legal process, summons, notices and documents that may be served in any suit, action or proceeding brought against Shire in any federal or state court as described in the first paragraph of this Section 10. If for any reason the Shire Agent shall cease to be available to act as such, Shire agrees to designate a new agent in the U.S. on the terms and for the purposes of this paragraph reasonably satisfactory to the Depository. Shire further hereby irrevocably consents and agrees to the service of any and all legal process, summons, notices and documents in any suit, action or proceeding against Shire, by service by mail of a copy thereof upon the Shire Agent (whether or not the appointment of the Shire Agent shall for any reason prove to be ineffective or the Shire Agent shall fail to accept or acknowledge such service), with a copy mailed to Shire by registered or certified air mail, postage prepaid, to its address at 1 Kingdom Street, London, W2 6BD, United Kingdom. Shire agrees that the failure of the Shire Agent to

give any notice of such service to it shall not impair or affect in any way the validity of such service or any judgment rendered in any action or proceeding based thereon.

Takeda hereby irrevocably designates, appoints and empowers CT Corporation System (the “Takeda Agent”) whose registered office is at 111 Eighth Avenue, New York, NY 10011 as its authorized agent to receive and accept for and on its behalf, and on behalf of its properties, assets and revenues, service by mail of any and all legal process, summons, notices and documents that may be served in any suit, action or proceeding brought against Takeda in any federal or state court as described in the first paragraph of this Section 10. If for any reason the Takeda Agent shall cease to be available to act as such, Takeda agrees to designate a new agent in U.S. on the terms and for the purposes of this paragraph reasonably satisfactory to the Depository. Takeda further hereby irrevocably consents and agrees to the service of any and all legal process, summons, notices and documents in any suit, action or proceeding against Takeda, by service by mail of a copy thereof upon the Takeda Agent (whether or not the appointment of the Takeda Agent shall for any reason prove to be ineffective or the Takeda Agent shall fail to accept or acknowledge such service), with a copy mailed to Takeda by registered or certified air mail, postage prepaid, to its address at 1-1 Nihonbashi-Honcho 2-Chome, Chuo-ku, Tokyo 103-8668, Japan, Attn: Atsuhiko Nagano. Takeda agrees that the failure of the Takeda Agent to give any notice of such service to it shall not impair or affect in any way the validity of such service or any judgment rendered in any action or proceeding based thereon.

Shire, Takeda and the Shire Depository each irrevocably waives, to the fullest extent permitted by law, any objection that it may now or hereafter have to the laying of venue of any actions, suits or proceedings brought in any court as provided in this Section 10, and hereby further irrevocably and unconditionally waives, and agrees not to plead or claim in any such court, that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum. Shire, Takeda and the Shire Depository each further irrevocably and unconditionally waives, to the fullest extent permitted by law, and agrees not to plead or claim, any right of immunity from legal action, suit or proceeding, from setoff or counterclaim, from the jurisdiction of any such court, from service of process, from attachment upon or prior to judgment, from attachment in aid of execution or judgment, from execution of judgment, or from any other legal process or proceeding for the giving of any relief or for the enforcement of any judgment, and consents to such relief and enforcement against it, its assets and its revenues in any jurisdiction, in each case with respect to any matter arising out of, or in connection with, this Instructions Letter.

EACH OF SHIRE, TAKEDA AND THE SHIRE DEPOSITARY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF, OR RELATING TO, THIS INSTRUCTIONS LETTER AND ANY ACTIONS AND TRANSACTIONS CONTEMPLATED THEREIN (WHETHER BASED ON CONTRACT, TORT, COMMON LAW OR OTHERWISE).

This Instructions Letter may be executed in one or more counterparts, each of which shall be deemed an original and all of such counterparts shall constitute the same agreement.

Shire and the Shire Depositary have caused this Instructions Letter to be executed and delivered on their behalf by their respective officers thereunto duly authorized as of the date set forth above. Takeda joins in the execution for purposes of Sections 1, 4, 5, 6, 9, and 10 hereof. The Takeda Depositary joins in the execution for purposes of Sections 1, 4, and 6 hereof. The Receiving Agent joins in the execution for purposes of Section 3 hereof.

[Signature pages follow]

Kind regards,

Shire plc

By: _____ /s/ Thomas Dittrich

Name: Thomas Dittrich
Title: Chief Financial Officer

Agreed and Accepted

CITIBANK, N.A. – ADS DEPOSITARY

By: _____ /s/ Brian M Teitelbaum

Name: Brian M Teitelbaum
Title: Vice President

Joined in solely for purposes of Sections 1, 4, 5, 6, 9, and 10

Takeda Pharmaceutical Company Limited

By: _____ /s/ Mitsuhiro Okada _____

Name: Mitsuhiro Okada

Title: Head of Global Treasury & Finance Management

Joined in solely for purposes of Sections 1, 4, and 6

The Bank of New York Mellon, as Takeda Depositary

By: _____ /s/ Joanne DiGiovanni Hawke

Name: Joanne DiGiovanni Hawke

Title: Managing Director

Joined in solely for purposes of Section 3

Equiniti Limited, as Receiving Agent

By: _____ /s/ Paul Matthews _____

Name: Paul Matthews

Title: CEO, EQ Boardroom

EXHIBITS

Exhibit I	Depository Notice
Exhibit II	Voting Instructions Card
Exhibit III	Withdrawal Certification
Exhibit IV	Depository Notice of ADS Exchange
Exhibit V	Letter of Transmittal
Exhibit VI	CREST Form of Election
Exhibit VII	Draw-Down Letter

Exhibit I

Depository Notice



**Depository's Notice of
Court Meeting and Extraordinary General Meeting
for
SHIRE PLC**

ADSs:	American Depositary Shares.
ADS CUSIP No.:	82481R106.
ADS Record Date:	November 7, 2018.
Meeting Specifics:	Court Meeting – December 5, 2018 at 11:15 a.m. (London time). Extraordinary General Meeting – December 5, 2018 at 11:30 a.m. (London time) (or as soon thereafter as the Court Meeting shall have been concluded or adjourned).
Meeting Agenda:	Please refer to the Company's Notice of Court Meeting and General Meeting available on the Company's website www.shire.com .
ADS Voting Instructions Deadline:	Prior to 10:00 a.m. (New York City time) on November 29, 2018.
Deposited Securities:	Ordinary Shares of 5 pence each (the " <u>Shares</u> ") in the capital of Shire plc, a corporation organized under the laws of Jersey (the " <u>Company</u> ").
ADS Ratio:	Three (3) Shares to one (1) ADS.
Depository:	Citibank, N.A.
Custodian of Deposited Securities:	Citibank, N.A. (London Branch).
Deposit Agreement:	Amended and Restated Deposit Agreement, dated as of May 23, 2011, by and among the Company, the Depository and all Holders and Beneficial Owners from time to time of American Depositary Receipts (" <u>ADRs</u> ") issued thereunder evidencing American Depositary Shares (" <u>ADSs</u> ") representing Deposited Securities.

To be counted, your Voting Instructions need to be received by the
Depository prior to **10:00 a.m.** (New York City time) on **November 29, 2018.**

**The Depository's books will be closed for ADS issuances and cancellations from
November 23, 2018 until December 4, 2018.**

The Company has announced that the Court Meeting and Extraordinary General Meeting will be held at the date and time identified above. The Court Meeting and Extraordinary General Meeting will both be held at Block 3, Miesian Plaza, 50-58 Baggot Street Lower, Dublin 2, Ireland. **Full details of the Court Meeting and the Extraordinary General Meeting, with explanatory notes, are set out in the “Notice of Court Meeting” and the “Notice of Shire General Meeting”, each of which is contained in the scheme document published by Shire plc on November 12, 2018 (the “Scheme Document”). It is recommended that you read the Scheme Document in full (including Part X (Further information for Shire ADS Holders)). A copy of the Scheme Document is available at the ‘Investors’ section of www.shire.com.**

If you are unable to access the internet or would like a copy of the Scheme Document sent to you, please call +1-866-395-6421 from within the US or +1-781-575-4555 if calling from outside the US between 8.30 a.m. and 6.00 p.m. (New York time) Monday to Friday (except public holidays in the US). Calls are charged at the standard geographic rate and will vary by provider. Calls outside the US will be charged at the applicable international rate. Alternatively, please write to Citibank Shareholder Services, PO Box 43099, Providence RI 02940-5000, USA.

Holders of ADSs wishing to give Voting Instructions to the Depositary by mail must complete, sign and return the enclosed Voting Instructions Card, prior to the ADS Voting Instructions Deadline, in the enclosed pre-addressed envelope. Alternatively, Holders of ADSs may give Voting Instructions to the Depositary by internet or telephone, as set out in the instructions below.

If, in respect of the Extraordinary General Meeting only, the Depositary does not receive Voting Instructions from a Holder by 10:00 a.m. (New York City time) on November 29, 2018 in respect of their entire holding of ADSs, such Holder will, subject to the terms of the Deposit Agreement, be deemed to have instructed the Depositary to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities represented by ADSs as to which the Depositary has not received Voting Instructions. In addition, such Holder will be required, in accordance with DTR 5 of the UK Financial Conduct Authority’s Disclosure Guidance and Transparency Rules, to notify the Company of such Holder’s holdings in Deposited Securities represented by ADSs if the percentage of such Holder’s voting rights falls below a notifiable threshold as a result of a person designated by the Company having been given such discretionary proxy. The Depositary will not itself exercise any voting discretion in respect of any Deposited Security.

In the event that a person designated by the Company is given such discretionary proxy, it is the intention of the Board of Directors of the Company (the “Board”) to direct such person to exercise votes under such discretionary proxy in favor of the resolution proposed by the Board at the Extraordinary General Meeting (as set out in the Notice of General Meeting) and, otherwise, in line with the voting recommendation of the Board for any other resolutions which may be proposed at the Extraordinary General Meeting.

If, in respect of the Court Meeting, the Depositary does not receive Voting Instructions from a Holder by 10:00 a.m. (New York City time) on November 29, 2018 in respect of their entire holding of ADSs, such Holder will, subject to the terms of the Deposit Agreement, not be deemed to have instructed the Depositary to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities represented by ADSs as to which the Depositary has not received Voting Instructions. Accordingly, such Deposited Securities will not be represented at the Court Meeting and will not be voted at the Court Meeting.

The enclosed materials are provided to allow you to vote at the Meetings of the Company. There are three alternative ways for voting:

- a) **Through the Internet:** if you are a registered ADS Holder, *i.e.*, you do not hold your ADSs through a custodian, broker or other agent, please follow these instructions:
- Access the website www.citi.com/dr.
 - Click on “Investors” and then click on “Voting by Internet”.
 - Enter your Proxy Access Number which is the circled number located on the front of the Voting Instructions Card in the shaded bar.
 - Complete the Voting Instructions provided on the Internet site by the ADS Voting Instructions Deadline.

If you hold your ADSs through a custodian, broker or other agent and you wish to vote through the Internet, you should refer to other information provided by your agent.

- b) **On the Telephone:** if you are a registered ADS Holder, *i.e.*, you do not hold your ADSs through a custodian, broker or other agent, please follow these instructions:
- Call the telephone voting access number: 1-800-652-Vote (8683).
 - Enter your Proxy Access Number which is the circled number located on the front of the Voting Instructions Card in the shaded bar.
 - Complete the Voting Instructions as indicated on a recording by the ADS Voting Instructions Deadline.

If you hold your ADSs through a custodian, broker or other agent and you wish to vote on the telephone, you should refer to other information provided by your agent.

- c) **By Mailing the Voting Instructions Card:**
- Complete all of the required information on the Voting Instructions Card.
 - Sign the Voting Instructions Card and return the card by the ADS Voting Instructions Deadline to Shire plc, c/o Citibank Shareholder Services, PO Box 43099, Providence RI 02940-5000.

If you hold your ADSs through a custodian, broker or other agent, you may have special instructions from your agent.

Please note that the Deposit Agreement provides that, in connection with the Meetings, the Depositary shall not be responsible for instructions not carried out or for the manner in which such instructions are carried out or the effect of any such action or omission, provided that such action or omission is without negligence and in good faith.

Holders of ADSs who wish to attend either or both of the Meetings must take steps to present their ADSs (and, to the extent that such ADSs are certificated, the certificates evidencing such ADSs) to the Depositary for cancellation before 5:00 p.m. (New York City time) on November 23, 2018 (subject to the relevant Holder’s compliance with the terms of the Deposit Agreement and payment of the Depositary’s fees), together with: (i) delivery instructions for the Deposited Securities represented by such ADSs (including, if applicable, the name and address of the person who will be the registered holder of such Deposited Securities); and (ii) if the cancellation is to take place before the Meetings, a certification that the Holder: (x) beneficially owned the relevant ADSs as of the ADS Record Date and has not given, and will not give, voting instructions to the Depositary in respect of such ADSs in relation to the Meetings (or has cancelled all voting instructions previously given); (y) beneficially owned the relevant ADSs as of the ADS Record Date and has given voting instructions to the Depositary in respect of such ADSs in relation to the Meetings, but undertakes not to vote the Deposited Securities represented by such ADSs at the Meetings; or (z) did not beneficially own the relevant ADSs as of the ADS Record Date, but undertakes not to vote the Deposited Securities represented by such ADSs at the Meetings. Holders of ADSs who hold their ADSs in a brokerage, bank, custodian or other nominee account should promptly contact their broker, bank or other nominee to find out what actions are required to instruct the broker, bank or other nominee to cancel the ADSs on their behalf. Holders of ADSs who present their ADSs to the Depositary for cancellation prior to 5.00 p.m. (New York City time) on November 23, 2018 in order to take delivery of Deposited Securities will be responsible for the payment of the Depositary’s fees associated with such cancellation.

You may also find additional information on the website www.citi.com/dr.

The information contained herein with respect to the Meetings has been provided by the Company. Citibank, N.A. is forwarding this information to you solely as Depositary and in accordance with the terms of the Deposit Agreement and disclaims any responsibility with respect to the accuracy of such information. Citibank, N.A. does not, and should not be deemed to, express any opinion with respect to the proposals to be considered at the Meetings. The rights and obligations of Holders and Beneficial Owners of ADSs, the Company and the Depositary are set forth in their entirety in the Deposit Agreement and summarized in the American Depositary Receipts. If you wish to receive a copy of the Deposit Agreement, please contact the Depositary at the number set forth below.

If you have any questions, please contact Citibank, N.A. - ADR Shareholder Services at 1-866-395-6421.

Citibank, N.A., as Depositary

Exhibit II

Voting Instructions Cards

Electronic Voting Instructions

You can vote by Internet or telephone!

Shire plc encourages you to take advantage of the convenient ways by which you can vote your American Depositary Shares ("ADSs"). You can vote your ADSs electronically through the Internet or by telephone up to the ADS Voting Instructions Deadline of 10:00 A.M. (New York City time) on November 29, 2018. This eliminates the need to return your Voting Instruction Card below.



Vote by Internet

- Log on to the Internet and go to www.citi.com/dr.
- Click on "Investors" and then click on "Voting by Internet".



Vote by telephone

- Call toll free 1-800-652 Vote (8683) within the United States, Canada & Puerto Rico any time on a touch tone telephone. There is **NO CHARGE** to you for the call.
- Follow the instructions provided by the recorded message.

If you choose to vote your ADSs electronically, there is no need to return your voting card.

Using a **black ink** pen, mark your votes with an **X** as shown in this example. Please do not write outside the designated areas.



**Court Meeting and Extraordinary General Meeting
2018 Voting Instructions Card**

▼ IF YOU HAVE NOT VOTED VIA THE INTERNET OR TELEPHONE, FOLD ALONG THE PERFORATION, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

A Issues – Shire plc

Court Meeting*

**Extraordinary
General Meeting****



For Against

For Against Abstain

Resolution

Resolution

B Authorized Signatures — Sign Here – This section must be completed for your instructions to be executed.

*For matters to be voted on at the Court Meeting:

If the Voting Instructions Card is signed and timely returned to the Depository but no specific direction as to voting is marked above as to an issue, the undersigned shall be deemed to have directed the Depository to give voting instructions "FOR" the unmarked issue.

If these voting instructions are signed and timely returned to the Depository but multiple specific directions as to voting are marked above as to an issue, the voting instructions with respect to such issue will be deemed defective and the Depository shall not vote the Deposited Securities represented by your ADSs on such issue.

**For matters to be voted on at the Extraordinary General Meeting:

If the Voting Instructions Card is signed and timely returned to the Depository but no specific direction as to voting is marked above as to an issue, the undersigned shall be deemed to have directed the Depository to give voting instructions "FOR" the unmarked issue.

If these voting instructions are signed and timely returned to the Depository but multiple specific directions as to voting are marked above as to an issue, the undersigned shall be deemed to have directed the Depository to give an "ABSTAIN" voting instruction for such issue.

Please be sure to sign and date this Voting Instructions Card.

Please sign your name to the Voting Instructions Card exactly as printed. When signing in a fiduciary or representative capacity, give full title as such. Where there is more than one owner, each owner MUST sign. Voting Instructions Cards executed by a corporation should be in the full name of such corporation and be executed by a duly authorized officer with full title as such.

Date (mm/dd/yyyy) — Please print date below.

Signature 1 — Please keep signature within the box.

Signature 2 — Please keep signature within the box.

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Court Meeting

To approve the Scheme of Arrangement.

Extraordinary General Meeting

Special Resolution THAT for the purpose of giving effect to the Scheme of Arrangement:

- the Board of Directors of the Company (the "Board") be authorized to take all such action as they may consider necessary or appropriate for carrying the Scheme of Arrangement into effect;
- the articles of association of the Company be amended by the adoption and inclusion of a new Article 154; and
- conditional upon and with effect from the sanctioning of the Scheme of Arrangement by the Court, the Company, or such other person as may be appointed by the Company, be appointed as agent of the Scheme Shareholders (as defined in the Scheme of Arrangement) for the purposes of undertaking and carrying into effect any and all such steps, actions, matters and procedures as may, in the opinion of the agent, be considered necessary, desirable or appropriate pursuant to Japanese law (including, in particular, under Articles 203 and 204 of the Japanese Companies Act (Act No. 86 2005) (*kaisha hou*)) in connection with the allotment, issue and settlement of the New Takeda Shares (as defined in the Scheme of Arrangement) pursuant to the Scheme of Arrangement.

Full details of the Court Meeting and the Extraordinary General Meeting, with explanatory notes, are set out in the "Notice of Court Meeting" and the "Notice of Shire General Meeting", each of which is contained in the scheme document published by Shire plc on November 12, 2018 (the "Scheme Document"). It is recommended that you read the Scheme Document in full (including Part X (Further information for Shire ADS Holders)). A copy of the Scheme Document is available at the 'Investors' section of www.shire.com.

If you are unable to access the internet or would like a copy of the Scheme Document sent to you, please call +1-866-395-6421 from within the US or +1-781-575-4555 if calling from outside the US between 8.30 a.m. and 6.00 p.m. (New York time) Monday to Friday (except public holidays in the US). Calls are charged at the standard geographic rate and will vary by provider. Calls outside the US will be charged at the applicable international rate. Alternatively, please write to Citibank Shareholder Services, PO Box 43099, Providence RI 02940-5000, USA.

To submit your proxy instructions electronically, please access the website www.citi.com/dr. You will need your Proxy Access Number which is the circled number on the shaded bar.

You can also call the telephone voting access number: 1-800-652-vote (8683). You will need your Proxy Access Number to proceed with the voting.

▼ IF YOU HAVE NOT VOTED VIA THE INTERNET OR TELEPHONE, FOLD ALONG THE PERFORATION, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

Court Meeting and Extraordinary General Meeting

The Voting Instructions Card must be completed, signed and received at the indicated address prior to 10:00 A.M. (New York City time) on November 29, 2018 for action to be taken.



2018 VOTING INSTRUCTIONS CARD

AMERICAN DEPOSITARY SHARES

Shire plc (the "Company")

CUSIP No.:	82481R106.
ADS Record Date:	November 7, 2018.
Meeting Specifics:	Court Meeting – December 5, 2018. Extraordinary General Meeting – December 5, 2018.
Depository:	Citibank, N.A.
Deposit Agreement:	Amended and Restated Deposit Agreement, dated as of May 23, 2011.
Deposited Securities:	Ordinary Shares of the Company.
Custodian:	Citibank, N.A. (London Branch).

The undersigned **Registered Holder**, as of the ADS Record Date, of the American Depositary Shares issued under the Deposit Agreement and identified on the reverse side hereof (such American Depositary Shares, the "ADSs"), acknowledges receipt of a copy of the Depository's Notice of Court Meeting and Extraordinary General Meeting (the "Meetings") for Shire plc enclosed herewith and hereby irrevocably authorizes and directs the Depository to cause to be voted at the Meetings (and any adjournment or postponement thereof) the Deposited Securities represented by the ADSs in the manner indicated on the reverse side hereof.

If, in respect of the Extraordinary General Meeting only, the Depository does not receive voting instructions from a Registered Holder by 10:00 a.m. (New York City time) on November 29, 2018 in respect of their entire holding of ADSs, such Registered Holder will, subject to the terms of the Deposit Agreement, be deemed to have instructed the Depository to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities represented by ADSs as to which the Depository has not received voting instructions. In addition, such Registered Holder will be required, in accordance with DTR 5 of the UK Financial Conduct Authority's Disclosure Guidance and Transparency Rules, to notify the Company of such Registered Holder's holdings in Deposited Securities represented by ADSs if the percentage of such Registered Holder's voting rights falls below a notifiable threshold as a result of a person designated by the Company having been given such discretionary proxy. The Depository will not itself exercise any voting discretion in respect of any Deposited Security.

In the event that a person designated by the Company is given such discretionary proxy, it is the intention of the Board to direct such person to exercise votes under such discretionary proxy in favor of the resolution proposed by the Board at the Extraordinary General Meeting (as set out above) and, otherwise, in line with the voting recommendation of the Board for any other resolutions which may be proposed at the Extraordinary General Meeting.

If, in respect of the Court Meeting, the Depository does not receive voting instructions from a Registered Holder by 10:00 a.m. (New York City time) on November 29, 2018 in respect of their entire holding of ADSs, such Registered Holder will, subject to the terms of the Deposit Agreement, not be deemed to have instructed the Depository to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities represented by ADSs as to which the Depository has not received voting instructions. Accordingly, such Deposited Securities will not be represented at the Court Meeting and will not be voted at the Court Meeting.

Registered Holders of ADSs who wish to attend either or both of the Meetings must take steps to present their ADSs (and, to the extent that such ADSs are certificated, the certificates evidencing such ADSs) to the Depository for cancellation before 5:00 p.m. (New York City time) on November 23, 2018 (as the Depository's books will be closed for ADS cancellations after that date and will not reopen until December 4, 2018) subject to the relevant Registered Holder's compliance with the terms of the Deposit Agreement and payment of the Depository's fees, together with: (i) delivery instructions for the Deposited Securities represented by such ADSs (including, if applicable, the name and address of the person who will be the registered holder of such Deposited Securities); and (ii) if the cancellation is to take place before the Meetings, a certification that the Registered Holder: (x) beneficially owned the relevant ADSs as of the ADS Record Date and has not given, and will not give, voting instructions to the Depository in respect of such ADSs in relation to the Meetings (or has cancelled all voting instructions previously given); (y) beneficially owned the relevant ADSs as of the ADS Record Date and has given voting instructions to the Depository in respect of such ADSs in relation to the Meetings, but undertakes not to vote the Deposited Securities represented by such ADSs at the Meetings; or (z) did not beneficially own the relevant ADSs as of the ADS Record Date, but undertakes not to vote the Deposited Securities represented by such ADSs at the Meetings. Registered Holders of ADSs who hold their ADSs in a brokerage, bank, custodian or other nominee account should promptly contact their broker, bank or other nominee to find out what actions are required to instruct the broker, bank or other nominee to cancel the ADSs on their behalf. Registered Holders of ADSs who present their ADSs to the Depository for cancellation prior to 5.00 p.m. (New York City time) on November 23, 2018 in order to take delivery of Deposited Securities will be responsible for the payment of the Depository's fees associated with such cancellation.

To appoint the Depository's Nominee to vote on your behalf, your Voting Instructions Card must be signed, completed and received at the Depository's indicated address prior to 10:00 A.M. (New York City time) on November 29, 2018.

The undersigned Registered Holder(s) hereby appoint(s) the Depositary's Nominee as its/their proxy (the "Proxy") to attend, speak and vote in respect of all of the Deposited Securities represented by its/their ADSs at the Shire plc Court Meeting on December 5, 2018 at 11:15 A.M. (London time) to be held at Block 3, Miesian Plaza, 50-58 Baggot Street Lower, Dublin 2, Ireland, and at the Extraordinary General Meeting on December 5, 2018 at 11:30 A.M. (or as soon thereafter as the Court Meeting shall have been concluded or adjourned) at the same location.

Please indicate on the reverse side hereof how the Deposited Securities are to be voted. By signing on the reverse side hereof, the undersigned represents to the Proxy, the Depositary and the Company that the undersigned is duly authorized to give the voting instructions contained therein.



Using a **black ink** pen, mark your votes with an **X** as shown in this example. Please do not write outside the designated areas. 

Court Meeting and Extraordinary General Meeting 2018 Voting Instructions Card

▼ PLEASE FOLD ALONG THE PERFORATION, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

A Issues – Shire plc

Court Meeting*

Extraordinary General Meeting**



	For	Against		For	Against	Abstain
Resolution	<input type="checkbox"/>	<input type="checkbox"/>	Resolution	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

B Authorized Signatures — Sign Here – This section must be completed for your instructions to be executed.

*For matters to be voted on at the Court Meeting:

If the Voting Instructions Card is signed and timely returned to the Depository but no specific direction as to voting is marked above as to an issue, the undersigned shall be deemed to have directed the Depository to give voting instructions "FOR" the unmarked issue.

If these voting instructions are signed and timely returned to the Depository but multiple specific directions as to voting are marked above as to an issue, the voting instructions with respect to such issue will be deemed defective and the Depository shall not vote the Deposited Securities represented by your ADSs on such issue.

**For matters to be voted on at the Extraordinary General Meeting:

If the Voting Instructions Card is signed and timely returned to the Depository but no specific direction as to voting is marked above as to an issue, the undersigned shall be deemed to have directed the Depository to give voting instructions "FOR" the unmarked issue.

If these voting instructions are signed and timely returned to the Depository but multiple specific directions as to voting are marked above as to an issue, the undersigned shall be deemed to have directed the Depository to give an "ABSTAIN" voting instruction for such issue.

Please be sure to sign and date this Voting Instructions Card.

Please sign your name to the Voting Instructions Card exactly as printed. When signing in a fiduciary or representative capacity, give full title as such. Where there is more than one owner, each owner MUST sign. Voting Instructions Cards executed by a corporation should be in the full name of such corporation and be executed by a duly authorized officer with full title as such.

Date (mm/dd/yyyy) — Please print date below.

Signature 1 — Please keep signature within the box.

Signature 2 — Please keep signature within the box.

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01JG7J

Court Meeting

To approve the Scheme of Arrangement.

Extraordinary General Meeting

Special Resolution THAT for the purpose of giving effect to the Scheme of Arrangement:

- the Board of Directors of the Company (the "Board") be authorized to take all such action as they may consider necessary or appropriate for carrying the Scheme of Arrangement into effect;
- the articles of association of the Company be amended by the adoption and inclusion of a new Article 154; and
- conditional upon and with effect from the sanctioning of the Scheme of Arrangement by the Court, the Company, or such other person as may be appointed by the Company, be appointed as agent of the Scheme Shareholders (as defined in the Scheme of Arrangement) for the purposes of undertaking and carrying into effect any and all such steps, actions, matters and procedures as may, in the opinion of the agent, be considered necessary, desirable or appropriate pursuant to Japanese law (including, in particular, under Articles 203 and 204 of the Japanese Companies Act (Act No. 86 2005) (*kaisha hou*)) in connection with the allotment, issue and settlement of the New Takeda Shares (as defined in the Scheme of Arrangement) pursuant to the Scheme of Arrangement.

Full details of the Court Meeting and the Extraordinary General Meeting, with explanatory notes, are set out in the "Notice of Court Meeting" and the "Notice of Shire General Meeting", each of which is contained in the scheme document published by Shire plc on November 12, 2018 (the "Scheme Document"). It is recommended that you read the Scheme Document in full (including Part X (Further information for Shire ADS Holders)). A copy of the Scheme Document is available at the 'Investors' section of www.shire.com.

If you are unable to access the internet or would like a copy of the Scheme Document sent to you, please call +1-866-395-6421 from within the US or +1-781-575-4555 if calling from outside the US between 8.30 a.m. and 6.00 p.m. (New York time) Monday to Friday (except public holidays in the US). Calls are charged at the standard geographic rate and will vary by provider. Calls outside the US will be charged at the applicable international rate. Alternatively, please write to Citibank Shareholder Services, PO Box 43099, Providence RI 02940-5000, USA.

▼ PLEASE FOLD ALONG THE PERFORATION, DETACH AND RETURN THE BOTTOM PORTION IN THE ENCLOSED ENVELOPE. ▼

Court Meeting and Extraordinary General Meeting

The Voting Instructions Card must be completed, signed and received at the indicated address prior to 10:00 A.M. (New York City time) on November 29, 2018 for action to be taken.

2018 VOTING INSTRUCTIONS CARD

AMERICAN DEPOSITARY SHARES

Shire plc (the "Company")

CUSIP No.:	82481R106.
ADS Record Date:	November 7, 2018.
Meeting Specifics:	Court Meeting – December 5, 2018. Extraordinary General Meeting – December 5, 2018.
Depository:	Citibank, N.A.
Deposit Agreement:	Amended and Restated Deposit Agreement, dated as of May 23, 2011.
Deposited Securities:	Ordinary Shares of the Company.
Custodian:	Citibank, N.A. (London Branch).

The undersigned **Beneficial Owner**, as of the ADS Record Date, of the American Depositary Shares issued under the Deposit Agreement and identified on the reverse side hereof (such American Depositary Shares, the "ADSs"), acknowledges receipt of a copy of the Depository's Notice of Court Meeting and Extraordinary General Meeting (the "Meetings") for Shire plc enclosed herewith and hereby irrevocably authorizes and directs the Depository to cause to be voted at the Meetings (and any adjournment or postponement thereof) the Deposited Securities represented by the ADSs in the manner indicated on the reverse side hereof.

If, in respect of the Extraordinary General Meeting only, the Depository does not receive voting instructions from a registered holder of ADSs by 10:00 a.m. (New York City time) on November 29, 2018 in respect of their entire holding of ADSs, such registered holder of ADSs will, subject to the terms of the Deposit Agreement, be deemed to have instructed the Depository to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities represented by ADSs as to which the Depository has not received voting instructions. In addition, such registered holder of ADSs will be required, in accordance with DTR 5 of the UK Financial Conduct Authority's Disclosure Guidance and Transparency Rules, to notify the Company of such registered holder of ADSs' holdings in Deposited Securities represented by ADSs if the percentage of such registered holder of ADSs' voting rights falls below a notifiable threshold as a result of a person designated by the Company having been given such discretionary proxy. The Depository will not itself exercise any voting discretion in respect of any Deposited Security.

In the event that a person designated by the Company is given such discretionary proxy, it is the intention of the Board to direct such person to exercise votes under such discretionary proxy in favor of the resolution proposed by the Board at the Extraordinary General Meeting (as set out above) and, otherwise, in line with the voting recommendation of the Board for any other resolutions which may be proposed at the Extraordinary General Meeting.

If, in respect of the Court Meeting, the Depository does not receive voting instructions from a registered holder of ADSs by 10:00 a.m. (New York City time) on November 29, 2018 in respect of their entire holding of ADSs, such registered holder of ADSs will, subject to the terms of the Deposit Agreement, not be deemed to have instructed the Depository to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities represented by ADSs as to which the Depository has not received voting instructions. Accordingly, such Deposited Securities will not be represented at the Court Meeting and will not be voted at the Court Meeting.

Beneficial Owners of ADSs who wish to attend either or both of the Meetings must take steps to present their ADSs (and, to the extent that such ADSs are certificated, the certificates evidencing such ADSs) to the Depository for cancellation before 5:00 p.m. (New York City time) on November 23, 2018 (as the Depository's books will be closed for ADS cancellations after that date and will not reopen until December 4, 2018) subject to the relevant Beneficial Owner's compliance with the terms of the Deposit Agreement and payment of the Depository's fees, together with: (i) delivery instructions for the Deposited Securities represented by such ADSs (including, if applicable, the name and address of the person who will be the registered holder of such Deposited Securities); and (ii) if the cancellation is to take place before the Meetings, a certification that the Beneficial Owner: (x) beneficially owned the relevant ADSs as of the ADS Record Date and has not given, and will not give, voting instructions to the Depository in respect of such ADSs in relation to the Meetings (or has cancelled all voting instructions previously given); (y) beneficially owned the relevant ADSs as of the ADS Record Date and has given voting instructions to the Depository in respect of such ADSs in relation to the Meetings, but undertakes not to vote the Deposited Securities represented by such ADSs at the Meetings; or (z) did not beneficially own the relevant ADSs as of the ADS Record Date, but undertakes not to vote the Deposited Securities represented by such ADSs at the Meetings. Beneficial Owners of ADSs who hold their ADSs in a brokerage, bank, custodian or other nominee account should promptly contact their broker, bank or other nominee to find out what actions are required to instruct the broker, bank or other nominee to cancel the ADSs on their behalf. Beneficial Owners of ADSs who present their ADSs to the Depository for cancellation prior to 5:00 p.m. (New York City time) on November 23, 2018 in order to take delivery of Deposited Securities will be responsible for the payment of the Depository's fees associated with such cancellation.

To appoint the Depository's Nominee to vote on your behalf, your Voting Instructions Card must be signed, completed and received at the Depository's indicated address prior to 10:00 A.M. (New York City time) on November 29, 2018.

The undersigned Beneficial Owner(s) hereby appoint(s) the Depository's Nominee as its/their proxy (the "Proxy") to attend, speak and vote in respect of all of the Deposited Securities represented by its/their ADSs at the Shire plc Court Meeting on December 5, 2018 at 11:15 A.M. (London time) to be held at Block 3, Miesian Plaza, 50-58 Baggot Street Lower, Dublin 2, Ireland, and at the Extraordinary General Meeting on December 5, 2018 at 11:30 A.M. (or as soon thereafter as the Court Meeting shall have been concluded or adjourned) at the same location.

Please indicate on the reverse side hereof how the Deposited Securities are to be voted. By signing on the reverse side hereof, the undersigned represents to the Proxy, the Depository and the Company that the undersigned is duly authorized to give the voting instructions contained therein.

Exhibit III

Withdrawal Certification

Certification and Agreement of Persons Surrendering ADSs
for the Purpose of Withdrawal of Deposited Securities
Pursuant to Section 6 of the Deposit Agreement

Citibank, N.A.
Depositary Receipts Department
388 Greenwich Street
New York, New York 10013

Re: Shire plc

We refer to the Amended and Restated Deposit Agreement, dated as of May 23, 2011 (as amended from time to time, the “Deposit Agreement”), by and among Shire plc (the “Company”), Citibank, N.A., as successor depositary thereunder (the “Depositary”), and all Holders and Beneficial Owners from time to time of American Depositary Receipts (“ADRs”) issued thereunder evidencing American Depositary Shares (“ADSs”) representing deposited Shares. Capitalized terms used but not defined herein shall have the meanings given them in the Deposit Agreement.

1. We are surrendering certain ADSs (such ADSs, the “Cancelled ADSs”) for cancellation for the purpose of withdrawal of the Deposited Securities represented thereby pursuant to Section 6 of the Deposit Agreement, and in connection with such cancellation of the Cancelled ADSs and withdrawal of the corresponding Deposited Securities, we are providing the information herein, as or on behalf of the Beneficial Owner of the Cancelled ADSs, with the understanding that the Company and the Depositary will rely upon the information provided herein in connection with the Jersey Court Meeting and the Extraordinary General Meeting to be held on December 5, 2018 (the “Meetings”), each Meeting in connection with the scheme of arrangement proposed to be made under Article 125 of the Companies (Jersey) Law 1991, as amended from time to time, between the Company’s shareholders and the Company to implement the acquisition of the Company by Takeda Pharmaceutical Company Limited, a joint-stock corporation incorporated under the laws of Japan.

2. We agree (or if we are acting for the account of another person, such person has confirmed to us that it agrees) to comply with all requests from the Company and/or the Depositary pursuant to the Deposit Agreement, applicable laws and regulations, and the Memorandum and Articles of Association of the Company, to provide information, *inter alia*, as to the capacity in which the Beneficial Owner held or owned, or holds or owns, the Cancelled ADSs or the Deposited Securities and regarding the identity of any other person then or previously interested in such ADSs or Deposited Securities, the nature of such interest and various related matters, whether or not we (they) are Holders and/or Beneficial Owners of ADSs or Deposited Securities at the time of such request.

3. We certify as (or on behalf of) the Beneficial Owner of the Cancelled ADSs that either (i) the Beneficial Owner beneficially owned the Cancelled ADSs as of 5:00 p.m., Eastern Standard Time, on November 7, 2018 (the “ADS Voting Record Date”) and that the Beneficial Owner has (x) not, directly or indirectly, given, and will not give, voting instructions to the

Depository as to the Cancelled ADSs, or (y) cancelled any voting instructions previously given to the Depository as to the Cancelled ADSs, or (z) given voting instructions to the Depository as to the Cancelled ADSs being cancelled but undertakes not to vote the corresponding Shares at the Meetings, or (ii) did not beneficially own the Cancelled ADSs as of the ADS Voting Record Date and undertakes not to vote the corresponding Shares at the Meetings.

As a result, the Beneficial Owner of the Cancelled ADSs undertakes that it will only vote on the Scheme (either directly as a holder of the Shares or indirectly as an ADS Holder) with respect to the Cancelled ADSs or the corresponding Shares if it held the Cancelled ADSs as of the ADS Voting Record Date and will only cast one such vote in respect of a Cancelled ADS and the underlying Share in respect of each Cancelled ADS held on the ADS Voting Record Date, notwithstanding any subsequent withdrawal of the underlying Share.

Date: _____

Very truly yours,

[NAME OF CERTIFYING ENTITY]

By: _____

Name

Title:

Exhibit IV

Depository Notice of ADS Exchange

Notice to Holders of Shire PLC American Depositary Shares

Depository Notice of ADS Exchange

SHIRE PLC

Shire Deposited Shares:	Ordinary Shares, each having a nominal value of £0.05 per share, of Shire plc, a company organized under the laws of Jersey, Channel Islands (“ <u>Shire</u> ”).
Shire ADSs:	American Depositary Shares issued under the Shire Deposit Agreement (as hereinafter defined), each such American Depositary Share representing three (3) Shire Deposited Shares.
Takeda Deposited Shares:	Ordinary Shares of no par value of Takeda Pharmaceutical Company Limited, joint stock corporation organized under the laws of Japan (“ <u>Takeda</u> ”).
Takeda ADSs:	American Depositary Shares issued under the Takeda Deposit Agreement (as hereinafter defined), each such American Depositary Share representing one-half (1/2) of one Takeda Deposited Share.
Shire plc ADS CUSIP No.:	82481R106.
Takeda Ltd ADS CUSIP No.:	874060205.
Shire Depository:	Citibank, N.A.
ADS Exchange Ratio:	\$90.99 in cash and 5.034 Takeda ADSs for each Shire ADS held as of the ADS Effective Time.
Shire Deposit Agreement:	Amended and Restated Deposit Agreement, dated as of May 23, 2011, by and among the Shire Depository, Shire, and all Holders and Beneficial Owners from time to time of American Depositary Receipts issued thereunder evidencing Shire ADSs representing Shire Deposited Shares.
Takeda Deposit Agreement:	Amended and Restated Deposit Agreement, dated as of [•], among Takeda, The Bank of New York Mellon, as depository, and all Owners and Holders from time to time of Takeda ADSs issued thereunder.
ADS Effective Time:	Close of business in New York on [•].

This notice is in respect of the offer for Shire by Takeda effected by means of a scheme of arrangement under Article 125 of the Companies (Jersey) Law 1991, as amended from time to time (the “Scheme”). The Shire Depository has been informed by Shire that all conditions to the

Scheme pursuant to the Scheme Document, dated as of [•], 2018, have been satisfied or waived and the Scheme became effective on [•], 201[•].

As a result of the Scheme, each Shire ADS as at the ADS Effective Time now represents the right to receive in exchange for the cancellation of such Shire ADS (the “ADS Exchange”), Scheme consideration (the “ADS Scheme Consideration”) per Shire ADS held as of the ADS Effective Time consisting of (i) \$90.99 in cash (the “ADS Cash Consideration”), and (ii) 5.034 Takeda ADSs (the “Takeda ADS Consideration”). Holders of Shire ADSs entitled to receive a fractional entitlement to a Takeda ADS will receive, in lieu thereof, an amount in cash equal to the net cash proceeds from the sale of the fractional entitlement to a Takeda ADS (net of applicable fees, taxes, and expenses, and rounded down to the nearest whole cent) by the Shire Depository.

No Shire Depository fees will be charged by the Shire Depository to holders of Shire ADSs in connection with the ADS Exchange. Takeda will be responsible for the fees that would otherwise have been charged by the Shire Depository to such holders.

Shire ADSs held in The Depository Trust Company (“DTC”).

No affirmative action is required on your part. DTC is requested to surrender its Shire ADSs to the Shire Depository in exchange for the applicable Takeda ADS Consideration (and applicable net cash in lieu of a fractional entitlement to a Takeda ADS, if any), and to credit the applicable ADS Cash Consideration so received to the applicable DTC participants. Your ADS Cash Consideration will be paid on a date later than your Takeda ADS Consideration.

Shire ADSs held in uncertificated form (other than in DTC).

No affirmative action is required on your part. The Shire Depository has arranged for the cancellation of the Shire ADSs registered in your name immediately following the effectiveness of the Scheme, and the delivery of the applicable ADS Scheme Consideration that you are entitled to receive as a former holder of Shire ADSs.

The Bank of New York Mellon, in its capacity as depository for the Takeda ADS program, will mail you a DRS advice confirming that a specified whole number of uncertificated ADSs (issuable to you as the Takeda ADS portion of the ADS Scheme Consideration) has been registered in your name. Separately, and on a later date, you will receive from the Shire Depository, by mail, a check representing (i) the cash portion of the ADS Scheme Consideration you are entitled to receive and (ii) net cash in lieu of a fractional entitlement to a Takeda ADS, if applicable, in each case net of applicable fees, taxes and expenses, and rounded down to the nearest whole cent.

Shire ADSs held in certificated form.

In order to receive the ADS Scheme Consideration and any entitlements to net cash in lieu of a fractional entitlement to a Takeda ADS, you will need to do each of the following:

- Complete, sign and deliver to the Shire Depository at the address specified therein, the Letter of Transmittal enclosed herewith (the “Letter of Transmittal”), in accordance with the accompanying instructions;

- Enclose the American Depositary Receipt(s) (“Shire ADR(s)”) that evidence(s) your Shire ADS(s) with the Letter of Transmittal; and
- Complete, sign and deliver to the Shire Depository at the address specified in the Letter of Transmittal, an applicable Form W-9 or Form W-8 enclosed with the Letter of Transmittal in accordance with the instructions.

Please read the instructions in the Letter of Transmittal carefully before completing and signing the Letter of Transmittal and the applicable Form W-9 or Form W-8 and forwarding each of them, together with the Shire ADR(s), to the Shire Depository to the address specified in the Letter of Transmittal.

When we receive the completed and signed Letter of Transmittal, together with the Shire ADRs evidencing your Shire ADSs, we will send you a check representing (i) the cash portion of the ADS Scheme Consideration you are entitled to receive, and (ii) cash in lieu of a fractional entitlement to a Takeda ADS, if applicable, in each case net of applicable fees, taxes and expenses, and rounded down to the nearest whole cent. You will receive separately a transaction advice from The Bank of New York Mellon confirming that a specified whole number of uncertificated ADSs (issuable to you as the Takeda ADS portion of the ADS Scheme Consideration) have been registered in your name. Depending on when you return your Letter of Transmittal and Shire ADR(s), your ADS Cash Consideration will be paid on a date later than your Takeda ADS Consideration.

The Shire Deposit Agreement (other than those provisions regarding indemnification, liability and limits thereon) shall, in accordance with its terms, terminate on [●]. Any actions you need to take to claim your ADS Scheme Consideration as a holder of certificated Shire ADSs need to be completed before that time. If you do not complete all actions to be so taken, the Shire Depository will sell the Takeda ADS portion of the ADS Scheme Consideration it holds on your behalf, and your Shire ADR(s) will thereafter represent the right to receive, upon surrender of the Shire ADR(s) to the Shire Depository, the cash portion of the ADS Scheme Consideration received on your behalf, any cash in lieu of a fractional entitlement to the Takeda ADS portion of the ADS Scheme Consideration received on your behalf, and the proceeds from the sale of the whole Takeda ADSs received as ADS Scheme Consideration on your behalf, in each case net of applicable fees, taxes, and expenses.

Any questions concerning the exchange of Shire ADSs for Takeda ADSs should be addressed to Citibank, N.A., in its capacity as Shire Depository at 1-800-308-7887. For holders outside the U.S. and Canada, please use 1-781-575-4555.

Citibank, N.A., as Shire Depository

[●], 2019

Exhibit V

Letter of Transmittal



Citibank, N.A.
 c/o Computershare Trust Company, N.A.
 462 South Fourth Street, Suite 1600
 Louisville, KY 40202
 Within USA, US territories & Canada 866 395 6421
 Outside USA, US territories & Canada 781 575 4555
 www.computershare.com



MR A SAMPLE
 DESIGNATION (IF ANY)
 ADD 1
 ADD 2
 ADD 3
 ADD 4
 ADD 5
 ADD 6



C 1234567890 J N T



Tax ID certification on file: <Certified Y/N>

TOTAL SHARES 12345678901234

Exchange Form - ACTION REQUIRED - The listed original certificates below MUST be returned with this Exchange Form

YOUR ACTION IS REQUIRED - PLEASE FOLLOW THESE INSTRUCTIONS

Our records indicate you currently hold Shire plc ("Shire") American Depositary Shares ("Shire ADS's") that now represent the right to receive \$90.99 in cash and [5.034] American Depositary Shares ("Takeda ADS's"), each Takeda ADS represents [] Ordinary Shares of Takeda (collectively, the ADS Merger Consideration) as a result of the acquisition of Shire by Takeda, effective [Date]. In order to receive your ADS Merger Consideration, cash-in-lieu of a fractional Takeda ADS, and any future dividend or distributions in respect of the Takeda ADSs, you MUST return these original certificates. Please note: If you also hold Shire ADSs in uncertificated form, they will be automatically exchanged upon the presentation of the below listed certificate(s), see "Shares Held in Book Entry by Us" below.

Lost Certificates: If you cannot locate some or all of your certificates, read and complete the Lost Securities Affidavit on the back of this form and also mark the boxes below with an X corresponding for the certificate numbers you cannot locate.

Step 1. Shire ADS certificates:

Locate and return the original certificate(s) listed below.

Lost	Certificate Numbers	Shire ADS	Lost	Certificate Numbers	Shire ADS
<input type="checkbox"/>	XXXX12345678	12345678901234	<input type="checkbox"/>	XXXX12345678	12345678901234
<input type="checkbox"/>	XXXX12345678	12345678901234	<input type="checkbox"/>	XXXX12345678	12345678901234
<input type="checkbox"/>	XXXX12345678	12345678901234	<input type="checkbox"/>	XXXX12345678	12345678901234
<input type="checkbox"/>	XXXX12345678	12345678901234	<input type="checkbox"/>	XXXX12345678	12345678901234
<input type="checkbox"/>	XXXX12345678	12345678901234	<input type="checkbox"/>	XXXX12345678	12345678901234

You hold more than 10 certificates, not all certificates can be listed on this form.

Other Certificate Total 12345678901234	Total Certificated Shire ADS 12345678901234	Shire ADS Held in Book Entry by Us 12345678901234	Total Shire ADS 12345678901234
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Step 2. Signatures: Sign and date this form. The names of the registered holders are listed in the Name and Address at the top of this form. All registered holders MUST sign exactly as your name(s) appears above.

Signature of Owner

Signature of Co-Owner (if more than one registered holder listed)

Date (mm/dd/yyyy)

1 2 3 4 5 6 7 8 9 0 1 2 EXOTFC

C O Y C C L S



Additional Instructions for Completing the Exchange Form and Surrendering Certificates

Delivery of Certificates: Your [Acquired Company Name and Class of Stock] stock certificate(s) and this Exchange Form must be sent or delivered to Computershare. The method of delivery of certificates to be surrendered to Computershare at one of the addresses set forth on the bottom of this page is at the option and risk of the surrendering stockholder. Delivery will be deemed effective only when received by Computershare. For your convenience, a return envelope is enclosed.

Authorization and Registration: The signature(s) on the reverse side represents that you have full authority to surrender these certificate(s) for exchange and warrants that the Shire ADSs represented by these certificates are free and clear of liens, restrictions, adverse claims and encumbrances.

Special Transfer Instructions: If you would like your [Surviving Company Name and Class of Stock] issued to a person(s) other than the registered owner(s), a transfer of ownership form must be completed. You may obtain transfer of ownership requirements and instructions from the internet at www.computershare.com or by calling Computershare at the number listed below.

Tax Forms and Backup Withholding: If your taxpayer identification number ("TIN") is not certified in our records, we have enclosed a Form W-9. If the payee is a "U.S. person" (as defined in the instructions to Form W-9), follow the instructions on the enclosed Form W-9 for completing and signing the form. If the payee is not a U.S. person and the form W-8BEN applies to your situation, follow the instructions on the enclosed Form W-8BEN for completing and signing such form. If a different form applies to your situation within the IRS suite of W-8 forms, refer to the IRS website for instructions on completing and signing such applicable form. Failure to provide a properly completed and signed Form W-9, Form W-8BEN or other applicable form to Computershare may subject the payee to backup withholding on any reportable payment under U.S. federal tax law.

Lost Securities Affidavit

IF YOU CANNOT LOCATE SOME OR ALL OF YOUR CERTIFICATE(S), PLEASE COMPLETE THE BELOW AFFIDAVIT
LIBERTY MUTUAL INSURANCE COMPANY
LOST SECURITIES AFFIDAVIT FOR ACCOUNTS WITH LESS THAN \$250,000.00 IN MARKET VALUE

By checking the lost certificates box and signing the bottom of this form, I (we) certify that (a) I (we) am (are) the lawful owner(s) ("Owner") of the Shire ADSs described on the front of this form; (b) I (we) reside at the address set forth on the front of this form; (c) I (we) am (are) entitled to possession of the lost certificate(s) (the "Lost Securities"); (d) the Lost Securities have been lost, mislaid, stolen or destroyed and cannot now be produced; (e) the Lost Securities WERE NOT ENDORSED and neither the Lost Securities nor the Owner(s)' rights therein have, in whole or in part, been cashed, negotiated, sold, transferred, hypothecated, pledged, disposed of, and to my (our) knowledge, no claim of right, like or interest, adverse to the Owner, in or to the Lost Securities, has been made or advanced by any person; (f) I (we) have made or caused to be made a diligent search for the Lost Securities and have been unable to find or recover the Lost Securities; (g) I (we) make this Affidavit of Lost Securities For Computershare Accounts for the purpose of inducing the issuance of new or replacement Securities ("Replacement Securities") (in book-entry form, unless unavailable through the issuer) in lieu of the said Lost Securities, or the distribution to the Owner(s) of proceeds (including liquidation) thereof; and (h) I (we) agree that this Lost Securities Affidavit for Computershare Accounts may be delivered to and made part of the Liberty Mutual Insurance Company Bond No. 285055966.

The Owner(s) hereby agree(s) in consideration of (1) the issuance of such replacement Securities in lieu of the Lost Securities, or of the distribution to the Owner of the proceeds there from, and (2) the assumption by Liberty Mutual Insurance Company of liability therefore under its Bond, the OWNER, his/her/its heirs, successors and assigns agree to indemnify, protect and save harmless Liberty Mutual Insurance Company, Computershare Inc., Computershare Trust Company, N.A., Citibank, N.A. and the issuer, jointly and severally, and their respective agents, representatives, successors, and assigns, from and against all losses, cost and damages (court costs and attorneys fees) to which they may be subject or liable arising out of or relating to the Lost Securities, the issuance of Replacement Securities, the Owner's requested action herein (or any other action arising out of or relating to the Replacement of Lost Securities), or Liberty Mutual Insurance Company's assumption of liability under its bond described above.

STEP 1. CALCULATE LOST CERTIFICATE BOND PREMIUM - FEE MUST BE ENCLOSED

LOST CERTIFICATE BOND PREMIUM CALCULATION: $\frac{\text{Shire ADSs Lost}}{\text{Bond premium Per share}} \times \frac{[\text{TBD}]}{\text{Total Premium Due (MINIMUM \$20.00)}} = \text{Total Check Amount} + \$80.00 \text{ processing fee}$

Multiply the number of shares lost by the Liberty Mutual Insurance Company Bond premium noted above to calculate the premium you owe. If you have Lost Securities representing [TBD] or fewer Shire ADSs, there is a minimum premium of \$20.00. There is also a processing fee of \$80.00. This premium is only valid until [DATE]. PLEASE MAKE YOUR CHECK PAYABLE TO "COMPUTERSHARE INSURANCE SERVICES" FOR THE BOND PREMIUM AND PROCESSING FEE AND ENCLOSE WITH THIS AFFIDAVIT. If your request is approved, Computershare Insurance Services will forward the Bond premium to Liberty Mutual Insurance Company. We cannot complete your exchange without a Surety Bond. NOTE: This premium is calculated based upon each lost share, not per each lost certificate.

STEP 2. SIGNATURES OF OWNERS - all registered owners MUST sign below exactly as the name(s) appear on the front of this form

If your lost certificate(s) is (are) part of an estate or trust, or are valued at more than \$250,000, please contact Computershare for additional instructions.

ANY PERSON WHO, KNOWINGLY AND WITH INTENT TO FRAUD ANY INSURANCE COMPANY OR OTHER PERSON, FILES A STATEMENT OF CLAIM CONTAINING ANY MATERIALLY FALSE INFORMATION OR CONCEALS FOR THE PURPOSE OF MISLEADING, INFORMATION CONCERNING ANY FACT MATERIAL THERETO, COMMITS A FRAUDULENT INSURANCE ACT, WHICH IS A CRIME.

By signing below, [I][we] acknowledge the processing fee listed above.

Signature of Owner _____ Signature of Co-Owner, if any _____

STEP 3. NOTARIZATION

You must have your signature(s) notarized if you have lost more than [TBD] shares.

State of _____ County of _____ Notary Signature _____

Printed Name of Notary _____ Sworn to and subscribed to me this (date) _____ (month/day/year)

My commission Expires (date) _____ (month/day/year) (Notary Seal)

Enclose all original certificates in the envelope provided and send with completed form to Computershare.

By Mail:
Citibank, N.A.
c/o Computershare
Computershare Trust Company, N.A.
PO Box 505004
Louisville, KY 40233-5004

By Overnight Delivery:
Citibank, N.A.
c/o Computershare
Computershare Trust Company, N.A.
462 South Fourth Street, Suite 1600
Louisville, KY 40202

For Assistance Please Call:
Within USA, US territories & Canada:
1-866-395-6421
Outside USA, US territories & Canada:
1-781-575-4555

Exhibit VI

CREST Form of Election

THIS DOCUMENT IS IMPORTANT AND REQUIRES YOUR IMMEDIATE ATTENTION. If you are in any doubt as to what 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 if you are in the United Kingdom, or from another appropriately authorised independent financial adviser if you are taking advice in a territory outside the United Kingdom. This document should be read in conjunction with the accompanying scheme document dated November 12, 2018 (the "Scheme Document"). Unless the context otherwise requires, the definitions used in the Scheme Document also apply to this CREST Form of Election. Please read carefully the terms of the Scheme, as set out in Part III (Scheme of Arrangement) of the Scheme Document, which are incorporated into, and form part of, this CREST Form of Election.

CREST FORM OF ELECTION

in respect of the recommended cash and share offer for

SHIRE PLC

by

TAKEDA PHARMACEUTICAL COMPANY LIMITED ("TAKEDA")

to be effected by means of a Scheme of Arrangement
under Article 125 of the Companies (Jersey) Law 1991, as amended

\$30.33 IN CASH AND EITHER 0.839 NEW TAKEDA SHARES OR 1.678 NEW TAKEDA ADSs

for each Scheme Share held at the Scheme Record Time

BEFORE COMPLETING THIS CREST FORM OF ELECTION, PLEASE READ:

- THE SCHEME DOCUMENT IN FULL (INCLUDING THE "ACTION TO BE TAKEN: MAKING AN ELECTION IN RESPECT OF THE CONSIDERATION" SECTION AND FLOWCHARTS AT PAGE 18 OF THE SCHEME DOCUMENT); AND
- THE SEPARATE "NOTES ON HOW TO COMPLETE THE CREST FORM OF ELECTION" DOCUMENT WHICH ACCOMPANY THIS CREST FORM OF ELECTION.

BACKGROUND

Scheme Shareholders whose names appear on the register of members of Shire at the Scheme Record Time will be entitled to receive for each Scheme Share held: (i) \$30.33 in cash; and (ii) either 0.839 New Takeda Shares or 1.678 New Takeda ADSs.

If you hold Scheme Shares in uncertificated form (that is, in CREST) (and are not a Restricted Scheme Shareholder), you may use this CREST Form of Election to make the following elections:

OPTIONS AVAILABLE TO ELECT FOR IN RESPECT OF YOUR CASH CONSIDERATION:

Currency Election – Receive the cash portion of your Consideration in pounds Sterling:

- You may elect to receive the cash portion of your Consideration in pounds Sterling (instead of US Dollars) in respect of SOME or ALL of the Scheme Shares which you hold by making a Currency Election. To make a Currency Election, you must submit a valid TTE Instruction through CREST by 6.00 p.m. (London time) on January 4, 2019 – see [Part 3](#) on page 2 of this form for further details.

OPTIONS AVAILABLE TO ELECT FOR IN RESPECT OF YOUR SHARE CONSIDERATION:

You may make a JASDEC Election, a Corporate Nominee Election and/or an ADS Election in relation to your holding of Scheme Shares, but you are not permitted to make multiple JASDEC Elections, Corporate Nominee Elections and/or ADS Elections in respect of your holding of Scheme Shares. You should in any event make at least one of the following Elections:

Option A: JASDEC Election – Hold your New Takeda Shares in a JASDEC Account

- If you: (i) have a direct account with JASDEC or an account with a JASDEC account management institution that has been admitted to JASDEC pursuant to the Book-Entry Act; and (ii) have a standing proxy or mailing address in Japan (or are resident in Japan), you may elect to hold your New Takeda Shares in that account. To elect for this option, please complete [Part 4A](#) on page 2 of this form.

Option B: Corporate Nominee Election – Hold your New Takeda Shares through the Corporate Nominee Facility managed by Equiniti Financial Services Limited

- If you will have a registered address in the EEA, Isle of Man, Gibraltar or Switzerland at the Scheme Record Time, you may elect to have your New Takeda Shares held through the Corporate Nominee Facility managed by Equiniti Financial Services Limited (subject to the Corporate Nominee Facility Terms and Conditions). To elect for this option, please complete [Part 4B](#) on page 3 of this form.

Option C: ADS Election – Receive New Takeda ADSs (or CDIs representing New Takeda ADSs) instead of New Takeda Shares

- You may elect to receive New Takeda ADSs (or CDIs representing New Takeda ADSs) instead of the New Takeda Shares which you would otherwise have been entitled to receive pursuant to the Scheme. As each New Takeda ADS represents 0.5 New Takeda Shares, you will receive 1.678 New Takeda ADSs (or an equivalent number of CDIs representing New Takeda ADSs) for each New Takeda Share which you would otherwise have been entitled to receive pursuant to the Scheme.
 - To elect to receive New Takeda ADSs issued under the terms of the Takeda Deposit Agreement through DTC or the Direct Registration System, please complete [Part 4C](#) on page 3 of this form.
 - To elect to receive CDIs representing New Takeda ADSs to be settled in CREST, make the relevant TTE Instruction through CREST (see Part IX (Notes for making settlement elections) of the Scheme Document for further details).

**The last time for Equiniti to receive this CREST Form of Election
is 6.00 p.m. (London time) on January 2, 2019**

Without prejudice to any other provision of this CREST Form of Election or Part IX (Notes on making Elections) of the Scheme Document, or otherwise, Shire and Takeda reserve the right (subject to the terms of the Scheme and the provisions of the Takeover Code) to treat as valid in whole or in part any Election which is not entirely in order.

DO NOT DETACH ANY PART OF THIS CREST FORM OF ELECTION

SHIRE SHAREHOLDER INFORMATION

Equiniti Reference

PART 1

Shire Shares held at 6.00 p.m. (London time) on November 6, 2018
Box 1A

Box 2A: CREST Participant ID:

Box 3A: CREST Member Account ID (If applicable):

If you purchase, transfer or sell Shire Shares between the above date and the Scheme Record Time, you should account for these transactions when returning the CREST Form of Election, as any Election should be made based on your holding as at the Scheme Record Time.

SHIRE SHAREHOLDER CONTACT INFORMATION – MANDATORY

PART 2

All the below fields are mandatory

Contact Name:

Phone Number:

Email:

This CREST Form of Election is specific to the CREST participant and CREST Member Account ID (if designated) stated in Boxes 2A and 3A above.

If you are a CREST member who holds multiple CREST Member Account IDs and intend to make the same Securities Election(s) and provide the same delivery instructions in relation to Scheme Shares under multiple CREST Member Account IDs (excluding any TTE Instructions in respect of a Currency Election or an ADS Election to receive CDIs representing New Takeda ADSs), you are required to complete this CREST Form of Election and attach the corporate "Multiple Account" continuation page (which allows up to 25 CREST Member Account IDs) which is supplied with this CREST Form of Election. The CREST Member Account ID stated in Box 3A above will be disregarded so should be added to the continuation page. If you need more than one continuation page, please photocopy the continuation page as required (prior to completing and signing it) or otherwise contact the Shareholder Helpline to request additional copies.

If you submit this CREST Form of Election with a "Multiple Account" continuation page, the Securities Election(s) specified below will apply to ALL of the Scheme Shares in the CREST Member Account ID(s) stated on the continuation page.

CURRENCY ELECTION – OPTIONAL

PART 3

Under the terms of the Scheme, Scheme Shareholders will receive USD30.33 for every Scheme Share held.

You may elect to receive SOME or ALL of the cash portion of your Consideration in pounds Sterling (net of any applicable customary transaction and dealing costs associated with the conversion) at the applicable market exchange rate on the latest reasonably practicable date for fixing such rate prior to the relevant payment date by making a Currency Election.

To make a Currency Election to receive pounds Sterling, you must submit a TTE Instruction through CREST in respect of the relevant number of Scheme Shares. Refer to Part IX (Notes for making Elections) of the Scheme document for further details. You cannot make a Currency Election in respect of your Scheme Shares by completing this CREST Form of Election.

SECURITIES ELECTION – MANDATORY

You may make a Securities Election in respect of some or all of your Scheme Shares.

OPTION A – JASDEC Election: To hold your New Takeda Shares in an existing account with either JASDEC or an account management institution that has been admitted to JASDEC pursuant to the Book-Entry Act.

IMPORTANT: You **MUST** have a standing proxy or mailing address in Japan (or be resident in Japan) to make a valid JASDEC Election.

PART 4A

Enter "ALL" or the number of Scheme Shares to which this election relates:

All the below fields are mandatory unless otherwise stated

JASDEC Participant Code (7 digits – numeric):

JASDEC Participant or AMI Contact Name:

The below information is mandatory if you hold indirectly through a JASDEC Account Management Institution ("AMI")

JASDEC AMI name in full:

JASDEC Participant or AMI contact e-mail:

JASDEC Shareholder Participant Code (21 digits – numeric)

JASDEC Participant or AMI telephone No.:

The last time for Equiniti to receive this CREST Form of Election is 6.00 p.m. (London time) on January 2, 2019

SHAREHOLDER HELPLINE

If you have any questions relating to these notes, the CREST Form of Election, the completion and return of the CREST Form of Election, or would like to receive an additional CREST Form of Election please call the Shareholder Helpline on 0330 123 5506 (if calling from within the UK) or on +44 (0)121 415 0856 (if calling from outside the UK).

Lines are open from 8.30 a.m. to 5.30 p.m. (London time) Monday to Friday (except for public holidays in England and Wales). Calls are charged at the standard geographic rate and will vary by provider. Calls outside the United Kingdom will be charged at the applicable international rate. Different charges may apply to calls from mobile telephones. Please note that calls may be recorded or monitored.

Please note that the Shareholder Helpline operators cannot provide advice on the merits of the Scheme or give financial, legal, tax or investment advice.

COMPLETION AND RETURN CHECKLIST

Signatures:

- **For your Election(s) to be valid, you MUST sign and date the CREST Form of Election in Part 5.**
- If signing under a power of attorney: (i) if the power of attorney has been registered with Shire's registrar, Equiniti (Jersey) Limited, this CREST Form of Election should be signed in accordance with the power and returned to Equiniti, Corporate Actions, Aspect House, Spencer Road, Lancing, West Sussex BN99 6DA, United Kingdom; or (ii) if the power of attorney has not been registered with Shire's registrar, you should contact the Shareholder Helpline stated above for further information
- If you are signing on behalf of a company (not an individual), remember to state the capacity in which you are signing. Please read the "NOTES ON HOW TO COMPLETE THE CREST FORM OF ELECTION" document which accompanies this CREST Form of Election for further information.

Please tick

Returning the CREST Form of Election

- Check that your Election(s) are made in accordance with the guidance in the Scheme Document and the "NOTES ON HOW TO COMPLETE THE CREST FORM OF ELECTION" document which accompanies this CREST Form of Election.
- **Return the original of this CREST Form of Election to Equiniti, Corporate Actions, Aspect House, Spencer Road, Lancing West Sussex BN99 6DA United Kingdom (facsimile signatures will not be accepted).** A pre-paid envelope is provided for use in the UK only. Unless notified otherwise by Shire and Takeda, the deadline for Equiniti to receive this CREST Form of Election is 6:00 p.m. (London time) on January 2, 2019. You should allow a minimum of four working days for the CREST Form of Election to be received. If you are resident outside the UK, you are advised to return this CREST Form of Election as soon as possible.
- If you have elected to hold your New Takeda Shares through the Corporate Nominee Facility (Option B), you MUST supply all applicable Customer Identification and Verification documents set out in the "NOTES ON HOW TO COMPLETE THE CREST FORM OF ELECTION" document which accompanies this CREST Form of Election for the Corporate Nominee Election to be valid.
- **If you hold Scheme Shares in certificated form (that is, not in CREST), contact the Shareholder Helpline immediately. Do not complete this CREST Form of Election.**
- **The last time for Equiniti to receive this CREST Form of Election is 6.00 p.m. (London time) on January 2, 2019.**
- **The last time for receipt of a TTE Instruction through CREST (applicable only for making a Currency Election an ADS Election to receive CDIs representing New Takeda Shares) is 6.00 p.m. (London time) on January 4, 2019.**

Please tick

IMPORTANT: If you do not validly complete and return any of Parts 4A, 4B or 4C of the CREST Form of Election or make a TTE Instruction to receive CDIs representing New Takeda ADSs, the New Takeda Shares to which you are entitled under the Scheme will be held in the name of the Representative as bare trustee for you for three months from the Effective Date. If, within that period, you do not make a valid Securities Election in relation to the action which should be taken in respect of the New Takeda Shares using this CREST Form of Election, the Representative will procure that the New Takeda Shares which it holds for you are sold and the net proceeds are remitted to you in cash.

If you sell, have sold or otherwise have transferred all of your Shire Shares, please send the Scheme Document, but not this CREST Form of Election, at once to the purchaser or transferee, or to the bank, stockbroker or other agent through whom the sale or transfer was effected, for transmission to the purchaser or transferee. If you have sold or otherwise transferred only part of your holding of Shire Shares, you should retain these documents and contact the bank, stockbroker or other agent through whom the sale or transfer was effected.

The release, publication or distribution of this CREST Form of Election (in whole or in part) in or into or from jurisdictions other than Jersey and the United Kingdom may be restricted by the laws of those jurisdictions and therefore persons into whose possession this CREST Form of Election comes should inform themselves about, and observe, any such restrictions. This CREST Form of Election should not be distributed in, forwarded to or transmitted into any jurisdiction where the availability of the Acquisition would breach any applicable law. Overseas Shareholders should read paragraph 27 of Part II (Explanatory Statement) of the Scheme Document and consult an appropriate independent professional adviser to ascertain whether the Acquisition will be subject to any restrictions or require compliance with any formalities imposed by the laws or regulations of the jurisdiction in which they are resident.

Exhibit VII

Draw-Down Letter

[Citibank Letterhead]

[Date], 2019

The Bank of New York Mellon – ADR Department
240 Greenwich Street – 22 Floor West
New York, New York 10286
USA

Attn:[_____]

Shire – Takeda Scheme

Ladies & Gentlemen,

Reference is made to the instructions letter agreement, dated as of [____], 2018 (the “Letter Agreement”), by and among Shire plc (“Shire”), Citibank, N.A. (“Citi”), as Depository for the Shire ADS Program (the “Shire Depository”), and for the limited purposes specified therein Takeda Pharmaceutical Company, Ltd. (“Takeda”), The Bank of New York Mellon (“BNY Mellon”), as Depository for the Takeda ADS Program (the “Takeda Depository”, and the American Depository Shares issued under the Takeda ADS Program the “Takeda ADSs”), and Equiniti Limited, as Receiving Agent, in connection with the scheme of arrangement pursuant to which Shire will become a wholly-owned subsidiary of Takeda (the “Scheme”). All capitalized terms used but not otherwise defined herein shall have the meaning given to such terms in the Letter Agreement.

In connection with the Scheme and under the terms of the Letter Agreement, Citi in its capacity as Shire Depository and as registered holder of Takeda ADSs, hereby instructs BNY Mellon, in its capacity as Takeda Depository, to register transfers of the specified Takeda ADSs from the Shire Depository’s registered ADS position on the books of the Takeda Depository [**Account #** _____] as promptly as practicable and as follows:

Number of Takeda ADSs	Transferee	Manner of Transfer/Issuance	Transaction
_____ Takeda ADSs	Cede & Co., as nominee for DTC	SCL Add to Balance	Scheme exchange with DTC as holder of Shire ADSs
_____ Takeda ADSs	[Computershare Trust Company] – DTC Participant Account # [_____]	[DWAC]	Settlement of sale of fractional entitlements to Takeda ADSs

_____ Takeda ADSs	See list of transferees attached hereto as <u>Schedule I</u>	DRS Format	Scheme exchange with DRS holders of Shire ADSs
_____ Takeda ADSs	See list of transferees attached hereto as <u>Schedule I</u>	DRS Format	Scheme exchange with holders of certificated Shire ADSs
_____ Takeda ADSs	[Computershare Trust Company] – DTC Participant Account # [_____]	[DWAC]	Settlement of termination sale for Shire ADS Program

If you have any questions about the above, please do not hesitate to call me at [_____].

Citibank, N.A., as Shire Depository

By: _____
Name:
Title:
Date: