

Dated 12 November 2018

EQUINITI FINANCIAL SERVICES LIMITED

and

EQUINITI LIMITED

and

NOMURA BANK (LUXEMBOURG) S.A.

and

NOMURA SECURITIES, CO., LTD.

and

SHIRE PLC

and

TAKEDA PHARMACEUTICAL COMPANY LIMITED

and

THE BANK OF NEW YORK MELLON

## MASTER FRAMEWORK AND CUSTODY AGREEMENT

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**This Agreement** is entered into on 12 November 2018, **between:**

- (1) **EQUINITI FINANCIAL SERVICES LIMITED**, a private limited company incorporated in England and Wales, with its registered address at Aspect House, Spencer Road, Lancing, West Sussex BN99 8AH and company number 06208699 (the “**Fiduciary**”);
- (2) **EQUINITI LIMITED**, a private limited company incorporated in England and Wales, with its registered address at Aspect House, Spencer Road, Lancing, West Sussex BN99 8AH and company number 06226088 (“**Equiniti**” or the “**Receiving Agent**”);
- (3) **NOMURA BANK (LUXEMBOURG) S.A.**, a public limited company (*société anonyme*) incorporated in the Grand Duchy of Luxembourg with its registered address at 33 rue de Gasperich, L-5826 Luxembourg and company number B32921 (the “**Global Custodian**” or the “**Nomura Sales Agent**”);
- (4) **NOMURA SECURITIES, CO., LTD.**, a company incorporated in Japan with its registered address at 9-1 Nihonbashi 1-chome, Chuo-ku, Tokyo 103-8011, Japan (the “**Nomura Broker**”, the “**Sub-Custodian**” or the “**Standing Proxy**”);
- (5) **SHIRE PLC**, a company incorporated in Jersey with its registered address at 22 Grenville Street, Jersey, JE4 8PX and registered number 99854 (“**Shire**” or the “**Representative**”, as applicable in the context);
- (6) **TAKEDA PHARMACEUTICAL COMPANY LIMITED**, a company incorporated in Japan with its registered address at 1-1 Doshomachi 4-chome, Chuo-ku, Osaka 540-8645, Japan (“**Takeda**”); and
- (7) **THE BANK OF NEW YORK MELLON**, a New York banking corporation, with its principal executive office at 240 Greenwich Street, New York, New York 10286 (the “**Takeda Depositary**”).

**Whereas:**

- (A) On May 8, 2018, the boards of Takeda and Shire announced that they had reached agreement on the terms of a recommended offer pursuant to which Takeda will acquire the entire issued and to be issued ordinary share capital of Shire to be effected by way of the Scheme. Under the terms of the Acquisition, each Scheme Shareholder will be entitled to receive:

for each Scheme Share	\$30.33 in cash
	and either
	0.839 New Takeda Shares
	or
	1.678 New Takeda ADSs

- (B) The Takeda Shares are (and the New Takeda Shares, once allotted, issued and admitted, will be) listed and traded on the Tokyo Stock Exchange and the Local Japanese Stock Exchanges. Pursuant to the Japanese book-entry system and the Book-Entry Act, all shares of Japanese listed companies, including those of Takeda, are dematerialised and all transfers of such shares are effected through an entry in the record maintained by JASDEC, which is Japan’s central securities depository and the only institution designated as a clearing house under the Book-Entry Act.

- (C) In order to hold and trade listed Japanese shares, investors must either have an account with JASDEC or, failing that, an account with an account management institution that has been admitted to JASDEC pursuant to the Book-Entry Act (a “**JASDEC Account**”). Under the Japanese Companies Act and the Book-Entry Act, it is also necessary for an investor to provide a name and address in Japan to be registered in a Japanese-listed company’s register of members. Accordingly, pursuant to Takeda’s articles of incorporation (as amended from time to time) (the “**Takeda Articles**”) and Takeda’s share handling regulations (the “**Share Handling Regulations**”), investors who are not resident in Japan are required to appoint a standing proxy in Japan or to provide a mailing address in Japan.
- (D) The purpose of this Agreement is to implement certain arrangements between the parties designed to: (i) give effect to Securities Elections made by Scheme Shareholders in respect of the non-cash portion of the Consideration which they are entitled to receive under the Scheme; and (ii) enable Scheme Shareholders without a JASDEC Account and a standing proxy or mailing address in Japan to receive the New Takeda Shares in settlement of Takeda’s obligation to pay the non-cash portion of the Consideration due under the Acquisition and in accordance with the terms of the Scheme.

It is agreed as follows:

## 1 Interpretation

1.1 In this Agreement, the following words and expressions have the meanings given below:

“**Acquisition**” means the proposed acquisition of the issued and to be issued ordinary share capital of Shire by Takeda;

“**ADS CDI Election**” means an election made by a Scheme Shareholder who holds Scheme Shares in uncertificated form to receive CDIs representing New Takeda ADSs (made by making a valid TTE Instruction before the Election Return Time);

“**ADS Election**” means an election to receive New Takeda ADSs or CDIs representing New Takeda ADSs (as applicable) under the ADS Election Facility;

“**ADS Election Facility**” means the facility provided for under the terms of the Scheme under which a Scheme Shareholder may elect to receive the non-cash portion of the Consideration payable to them in the form of New Takeda ADSs or (in the case of Scheme Shareholders who make a valid ADS CDI Election and who hold Scheme Shares in uncertificated form) CDIs representing New Takeda ADSs;

“**Agent**” has the meaning given in Clause 3.9;

“**Agreement**” means this agreement;

“**AMI**” means a JASDEC account management institution that has been admitted to JASDEC pursuant to the Book-Entry Act;

“**BNYM JASDEC Account**” means the JASDEC account to be held with SMBC in the name of the Takeda Depository;

“**Book-Entry Act**” means the Act on Book-Entry of Company Bonds, Shares, etc. of Japan, as amended from time to time;

“**Broker**” means the Nomura Broker or such other party as the Global Custodian shall engage to fulfil the role of the broker in accordance with the terms of this Agreement;

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**“Business Day”** means a day (other than a Saturday, Sunday or public holiday in London, Jersey, New York, Luxembourg or Tokyo) on which banks are open for business in London, Jersey, New York, Luxembourg and Tokyo;

**“CDI”** means a CREST depository interest, as defined in the CREST Manual;

**“Certificated Form of Election”** means the white form of election under which a Scheme Shareholder who holds Scheme Shares in certificated form may make: (i) a Currency Election; and/or (ii) a JASDEC Election, a Corporate Nominee Election and/or an ADS Election (excluding an ADS CDI Election); and/or (iii) a Dealing Facility Election, subject to the terms and conditions set out in the Scheme Document;

**“Citi”** means Citibank, N.A. acting as Shire ADS Depository;

**“Code”** means the City Code on Takeovers and Mergers as issued from time to time by or on behalf of the Panel;

**“Consideration”** means the consideration payable to Scheme Shareholders pursuant to the Acquisition, comprising \$30.33 in cash and either 0.839 New Takeda Shares or 1.678 New Takeda ADSs per Scheme Share;

**“Corporate Nominee Election”** means an election to receive New Takeda Shares through the Corporate Nominee Facility;

**“Corporate Nominee Facility”** means the facility provided for under the terms of the Scheme under which a Scheme Shareholder who has a registered address in the EEA, Channel Islands, Switzerland, Isle of Man or Gibraltar as at the Scheme Record Time may elect to have the Fiduciary hold on their behalf some or all of the New Takeda Shares which such Scheme Shareholder is entitled to receive as the non-cash portion of the Consideration for their Scheme Shares pursuant to the Scheme, subject to the Corporate Nominee Facility Terms and Conditions;

**“Corporate Nominee Facility Terms and Conditions”** means the terms and conditions governing the operation of the Corporate Nominee Facility, as appended to the Scheme Document;

**“Corporate Nominee Shareholders”** means the Scheme Shareholders who have validly completed and submitted a Corporate Nominee Election from time to time;

**“Corporate Nominee Termination Sales Process”** means the sales process to be undertaken pursuant to Clause 7.4 in respect of any New Takeda Shares which remain held in the Settlement Account on behalf of Corporate Nominee Shareholders on the date which is two years following the Effective Date;

**“Corporate Nominee Termination Sales Process Cut-Off Date”** means the date falling two years after the Effective Date;

**“Court”** means the Royal Court of Jersey;

**“Court Meeting”** means the meeting or meetings of Shire Shareholders as at the Voting Record Time or any class or classes thereof convened by order of the Court pursuant to Article 125(1) of the Jersey Companies Law for the purpose of considering and, if thought fit, approving the Scheme (with or without amendment), including any adjournment, postponement or reconvention thereof;

**“Court Sanction Hearing”** means the hearing at which the Court sanctions the Scheme;

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“**CREST**” means the relevant system (as defined in the CREST Regulations) in respect of which Euroclear is the Operator (as defined in the CREST Regulations) in accordance with which securities may be held and transferred in uncertificated form;

“**CREST Form of Election**” means the green form of election under which a Scheme Shareholder who holds Scheme Shares in uncertificated form (that is, in CREST) may make a JASDEC Election, Corporate Nominee Election and/or ADS Election (excluding an ADS CDI Election), or such other form of instruction as may be agreed between a Scheme Shareholder and the Receiving Agent, in each case subject to the terms and conditions set out in the Scheme Document;

“**CREST Manual**” means the CREST Manual published by Euroclear, as amended from time to time;

“**CREST Regulations**” means (i) in relation to Scheme Shares held in uncertificated form, the Companies (Uncertificated Securities) (Jersey) Regulations Order 1999, as amended from time to time; and (ii) in relation to CDIs representing New Takeda ADSs, the Uncertificated Securities Regulations 2001 (SI 2001 No.3755), as amended from time to time;

“**Currency Conversion Facility**” means the facility provided for under the terms of the Scheme under which a Scheme Shareholder may elect to receive the US Dollar cash portion of the Consideration which such Scheme Shareholder is entitled to receive pursuant to the Scheme 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 before the relevant payment date;

“**Currency Election**” means an election made pursuant to the Currency Conversion Facility;

“**Data Protection Legislation**” means the following legislation to the extent applicable from time to time: (i) national laws implementing the Directive on Privacy and Electronic Communications (2002/58/EC); (b) the General Data Protection Regulation (2016/679/EC) and any national law issued under that regulation; and (c) any other similar national privacy law;

“**Dealing Facility**” means the facility provided for under the terms of the Scheme under which a Scheme Shareholder who holds 200 or fewer Scheme Shares in certificated form as at the Scheme Record Time and has a registered address in the EEA, Channel Islands, Isle of Man, Switzerland or Gibraltar as at the Scheme Record Time may make an election to have all of the New Takeda Shares which they are entitled to receive pursuant to the Scheme sold on their behalf, subject to the Dealing Facility Terms and Conditions;

“**Dealing Facility Election**” means an election to sell New Takeda Shares through the Dealing Facility;

“**Dealing Facility Sales Process Cut-Off Date**” means each of: (i) the date which is the seventh Business Day after the Effective Date; (ii) the date which is every two weeks after the date set out in (i); and (iii) the No Action Sales Process Cut-Off Date;

“**Dealing Facility Sales Process**” means the sales process to be undertaken pursuant to Clause 7.2 in respect of all New Takeda Shares linked to the Dealing Facility;

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**“Dealing Facility Terms and Conditions”** means the terms and conditions governing the operation of the Dealing Facility, as set out on Takeda and Shire’s websites as at the date of publication of the Scheme Document;

**“DTC”** means the Depository Trust Company;

**“EEA”** means the European Economic Area as at the date of this Agreement;

**“Effective”** means the Scheme having become effective pursuant to its terms;

**“Effective Date”** means the date on which the Scheme becomes Effective;

**“Election Return Time”** means (i) in respect of a Form of Election, 6.00 p.m. (London time) on the date falling two calendar days before the Scheme Record Time, being the latest time for lodging a Form of Election, or such later date as Takeda and Shire may determine in accordance with the Scheme; and (ii) in respect of an ADS CDI Election (to be made by a TTE Instruction), 6.00 p.m. (London time) on the date of the Scheme Record Time, being the latest time for making a TTE Instruction;

**“Euroclear”** means Euroclear UK & Ireland Limited, incorporated in England with company number 02878738;

**“Excluded Shares”** means any Shire Shares:

- (a) registered in the name of, or beneficially owned by, Takeda or any member of the Takeda Group or their respective nominees;
- (b) represented by Shire ADSs which are registered in the name of, or beneficially owned by, Takeda or any member of the Takeda Group or their respective nominees; or
- (c) held in treasury by Shire;

**“Fiduciary Bank Account”** means the bank account(s) to be opened by the Global Custodian on behalf of the Fiduciary for the purpose of receiving the proceeds of the sale of New Takeda Shares and any dividends or other distributions (or returns of capital) made or paid by Takeda on behalf of the Representative (as bare trustee for the No Action Shareholders) and relevant Scheme Shareholders;

**“Forms of Election”** means the Certificated Form of Election and/or the CREST Form of Election, as the context requires;

**“Fractional Sales Process”** means the process to be undertaken pursuant to Clause 7.1 with respect to the sales of the Fractional Shares;

**“Fractional Shares”** means the maximum whole number of New Takeda Shares resulting from the aggregation of fractional entitlements to New Takeda Shares to which Scheme Shareholders are entitled pursuant to the Scheme and the maximum whole number of New Takeda Shares which represent the aggregate of fractional entitlements to New Takeda ADSs to which Scheme Shareholders are entitled pursuant to the Scheme;

**“Global Custodian Account”** has the meaning given to it in Clause 4.1.1;

**“Japanese Business Day”** means a day (other than a Saturday or Sunday) on which banks are open for general banking business in Tokyo, Japan;

**“Japanese Companies Act”** means the Japanese Companies Act (Act No. 86 2005), as amended from time to time;

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“**JASDEC**” means Japan Securities Depository Center, Inc.;

“**JASDEC Account**” has the meaning given to it in Recital (C);

“**JASDEC Election**” means an election by a Scheme Shareholder to receive some or all of the New Takeda Shares which such Scheme Shareholder is entitled to receive pursuant to the Scheme into a designated JASDEC Account;

“**Jersey**” means the Bailiwick of Jersey;

“**Jersey Companies Law**” means the Companies (Jersey) Law 1991, as amended from time to time;

“**Local Japanese Stock Exchanges**” means Nagoya Stock Exchange, Fukuoka Stock Exchange and Sapporo Stock Exchange;

“**London Business Day**” means a day (other than a Saturday or Sunday and public holidays in England) on which banks are open for general banking business in London, United Kingdom;

“**New Takeda ADSs**” means the new Takeda ADSs to be delivered pursuant to the Scheme to those Scheme Shareholders who have made a valid ADS Election to receive New Takeda ADSs (including any New Takeda ADSs underlying CDIs representing New Takeda ADSs);

“**New Takeda Shares**” means the new Takeda Shares to be delivered to Scheme Shareholders pursuant to the Scheme;

“**No Action Sales Process**” means the sales process to be undertaken pursuant to Clause 7.3 in respect of any No Action Shares remaining held in the Settlement Account on behalf of the Representative as bare trustee for and on behalf of No Action Shareholders as soon as practicable following the No Action Sales Process Cut-Off Date;

“**No Action Sales Process Cut-Off Date**” means the date which is three months following the Effective Date;

“**No Action Shareholders**” means Scheme Shareholders who have made (or have been deemed to have made) an invalid Securities Election, or have failed to make any Securities Election at all, in respect of some or all of their Scheme Shares, in each case as at the Election Return Time, and until the earlier of:

- (a) the date on which a valid Securities Election made by such Scheme Shareholder is received by the Receiving Agent; and
- (b) the date on which the relevant New Takeda Shares are sold pursuant to the No Action Sales Process;

“**No Action Shares**” has the meaning given in Clause 4.4.1(i);

“**No Action Sub-Account**” has the meaning given in Clause 4.4.1(i);

“**Panel**” means the UK Panel on Takeovers and Mergers;

“**Personal Sub-Account**” has the meaning given in Clause 4.4.1(ii);

“**Sales Manual**” has the meaning given in Clause 7.6;

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“**Sales Policy**” means the sales policy set out in Clause 7.5, which is to apply to any sale of New Takeda Shares to be arranged by the Nomura Sales Agent on the instruction of the Fiduciary as contemplated by this Agreement;

“**Scheme**” means the scheme of arrangement proposed to be made under Article 125 of the Jersey Companies Law between Shire and the Scheme Shareholders to implement the Acquisition, with or subject to any modification, addition or condition approved or imposed by the Court and agreed to by Shire and Takeda;

“**Scheme Document**” means the document to be dispatched to Shire Shareholders and persons with information rights setting out, among other things, the details of the Acquisition, the explanatory statement required under Article 125 of Jersey Companies Law, the full terms and conditions of the Scheme and containing the notices convening the Court Meeting and the Shire General Meeting (including any supplementary scheme document);

“**Scheme Effective Time**” means the time and date at which the Scheme becomes Effective;

“**Scheme Record Time**” means the date and time specified in the Scheme by reference to which the Scheme will be binding on the holders of Scheme Shares at such time;

“**Scheme Shareholder**” means a holder of Scheme Shares;

“**Scheme Shares**” means the Shire Shares:

- (a) in issue at the date of the Scheme Document;
- (b) (if any) issued after the date of this document but before the Voting Record Time; and
- (c) (if any) issued at, or after, the Voting Record Time and before the Scheme Record Time on terms that the original holder or any subsequent holder thereof shall be bound by the Scheme or in respect of which the original or any subsequent holder thereof shall have agreed in writing to be bound by the Scheme,

and in each case remaining in issue at the Scheme Record Time, but excluding any Excluded Shares;

“**Securities Election**” means a JASDEC Election, Corporate Nominee Election, ADS Election or Dealing Facility Election, as the context requires;

“**Settlement Account**” has the meaning given to it in Clause 4.1.1;

“**Settlement Date**” means the date on which the New Takeda Shares are recorded to the Settlement Account, which is expected to be two Japanese Business Days after the Effective Date;

“**Share Handling Regulations**” has the meaning given to it in Recital (C);

“**Shire ADS**” means an American Depositary Share issued under the Shire Deposit Agreement, such American Depositary Share representing three Shire Shares;

“**Shire ADS Instruction Letter**” means the ADS instruction letter entered into on or around the date of this Agreement between the Takeda Depositary, Citi, Equiniti, Shire and Takeda to supplement the Shire Deposit Agreement in connection with the Scheme;

“**Shire Articles**” means the articles of association of Shire as amended from time to time;

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**“Shire Deposit Agreement”** means the amended and restated deposit agreement dated 23 May 2011 between Shire, Citi and all holders and beneficial owners from time to time of American Depositary Receipts issued thereunder evidencing American Depositary Shares representing deposited Shire Shares, including the form of American Depositary Receipt for American Depositary Shares representing Shire Shares attached thereto, setting forth the terms of the Shire ADSs from time to time;

**“Shire General Meeting”** means the general meeting of Shire to be convened in connection with the Scheme for the purpose of considering, and, if thought fit, approving, the Shire Special Resolution (with or without amendment) and any adjournment, postponement or reconvention thereof;

**“Shire Meeting(s)”** means the Court Meeting and/or the Shire General Meeting, as the case may be;

**“Shire Shareholder”** means a holder of Shire Shares from time to time;

**“Shire Shares”** means the existing unconditionally allotted or issued and fully paid ordinary shares of 5 pence each in the capital of Shire and any further such ordinary shares which are unconditionally allotted or issued before the Scheme becomes Effective;

**“Shire Special Resolution”** means the special resolution to be proposed by Shire at the Shire General Meeting in connection with, among other things, the approval of the Scheme and the alteration of the Shire Articles and such other matters as may be necessary to implement the Scheme and the delisting of the Shire Shares;

**“SMBC”** means Sumitomo Mitsui Banking Corporation;

**“Takeda ADSs”** means an American Depositary Share issued under the Takeda Deposit Agreement, such American Depositary Share representing 0.5 Takeda Shares;

**“Takeda Articles”** has the meaning given to it in Recital (C);

**“Takeda Deposit Agreement”** means the deposit agreement dated as of May 10, 2010 (as amended from time to time, including without limitation the amendment and restatement anticipated to be effected prior to the Effective Date) between Takeda, the Takeda Depositary and all holders and beneficial owners from time to time of American Depositary Receipts issued thereunder evidencing American Depositary Shares representing deposited Takeda Shares, including the form of American Depositary Receipt for American Depositary Shares representing Takeda Shares attached thereto, setting forth the terms of the Takeda ADSs from time to time;

**“Takeda Group”** means Takeda and its subsidiaries and subsidiary undertakings from time to time and, where the context permits, each of them;

**“Takeda Shares”** means the shares of common stock with no par value in the capital of Takeda;

**“Tokyo Stock Exchange”** or **“TSE”** means Tokyo Stock Exchange, Inc (including its subsequent successors);

**“TTE Instruction”** means a transfer to escrow instruction as defined in the CREST Manual;

**“Voting Record Time”** means 6.30 p.m. (London time) on the day which is two calendar days before the date of the Shire Meetings or, if the Court Meeting and/or the Shire

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General Meeting is or are adjourned, 6.30 p.m. (London time) on the date falling two calendar days before the date appointed for such adjourned Shire Meeting (as the case may be); and

“**Working Hours**” has the meaning given in Clause 12.5.

**1.2** In this Agreement, except where the context otherwise requires:

- 1.2.1 a reference to an enactment or statutory provision shall include a reference to any subordinate legislation made under the relevant enactment or statutory provision and is a reference to that enactment, statutory provision or subordinate legislation as from time to time amended, consolidated, modified, re-enacted or replaced;
  - 1.2.2 words in the singular shall include the plural and vice versa;
  - 1.2.3 references to one gender include other genders;
  - 1.2.4 a reference to a “**person**” shall include a reference to an individual, an individual’s executors or administrators, a partnership, a firm, a body corporate, an unincorporated association, government, state or agency of a state, a local or municipal authority or government body, and a joint venture or association (in any case, whether or not having separate legal personality);
  - 1.2.5 references to a “**company**” shall be construed so as to include any company, corporation or other body corporate, wherever and however incorporated or established;
  - 1.2.6 a reference to a Recital, Clause, paragraph or schedule (other than to a schedule to a statutory provision) shall be a reference to a recital, clause, or paragraph of or schedule to (as the case may be) this Agreement;
  - 1.2.7 if a period of time is specified as from a given day, or from the day of an act or event, it shall be calculated exclusive of that day;
  - 1.2.8 any reference to a “**day**” (including within the phrase “**Business Day**”) shall mean a period of 24 hours running from midnight to midnight;
  - 1.2.9 references to any English legal term for any action, remedy, method of judicial proceeding, legal document, legal status, court, official or any legal concept or thing shall in respect of any jurisdiction other than England be deemed to include what most nearly approximates the English legal term in that jurisdiction;
  - 1.2.10 references to “**writing**” shall include any modes of reproducing words in any legible form and shall include email except where otherwise expressly stated;
  - 1.2.11 a reference to “**includes**” or “**including**” shall mean “includes without limitation” or “including without limitation” respectively;
  - 1.2.12 references to “**\$**”, “**USD**” and “**US Dollar**” are to the lawful currency of the United States;
  - 1.2.13 references to “**¥**”, “**JPY**” and “**Japanese Yen**” are to the lawful currency of Japan;
  - 1.2.14 references to “**£**”, “**GBP**” and “**Pounds Sterling**” are to the lawful currency of the United Kingdom;
  - 1.2.15 (i) the rule known as the *ejusdem generis* rule shall not apply and accordingly general words introduced by the word “other” shall not be given a restrictive
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meaning by reason of the fact that they are preceded by words indicating a particular class of acts, matters or things; and

- (ii) general words shall not be given a restrictive meaning by reason of the fact that they are followed by particular examples intended to be embraced by the general words;

1.2.16 a reference to any other document referred to in this Agreement is a reference to that other document as amended, varied, novated or supplemented at any time; and

1.2.17 references to this Agreement include this Agreement as amended or supplemented in accordance with its terms.

1.3 The headings in this Agreement are for convenience only and shall not affect the interpretation of this Agreement.

## 2 Condition Precedent

The obligations of the Representative under this Agreement shall be conditional upon the occurrence of the following:

2.1.1 the Scheme becoming Effective; and

2.1.2 the issue of the New Takeda Shares becoming effective under the Japanese Companies Act.

## 3 Appointment of Additional Parties

3.1 Shire confirms that it has engaged Equiniti (Jersey) Limited to act as the share registrar in connection with the Scheme and to fulfil such role in accordance with the terms of this Agreement.

3.2 Shire confirms that it has engaged Citi to act as the Shire ADS Depository and to fulfil such role in accordance with the terms of the Shire ADS Instruction Letter.

3.3 The Global Custodian confirms that it has engaged the Nomura Broker to act as the Broker, the Sub-Custodian and the Standing Proxy on behalf of the Global Custodian, and to fulfil such roles in accordance with the terms of this Agreement.

3.4 The Global Custodian undertakes and agrees that, if for any reason the Nomura Broker is unable to continue to act as the Broker, the Sub-Custodian and/or the Standing Proxy and to fulfil such roles in accordance with the terms of this Agreement, then the Global Custodian shall engage another party to fulfil the relevant role or roles in accordance with the terms of this Agreement as soon as reasonably practicable (with the intention that there shall be no disruption in the service provided pursuant to the relevant role) and shall notify the other parties to this Agreement of such change in accordance with Clause 12.

3.5 Takeda confirms that it has engaged Mitsubishi UFJ Trust and Banking Corporation as its shareholder registry administrator, with such engagement to also encompass the role of the "transfer agent" to the extent such role is required to be performed in order to implement the matters contemplated by this Agreement.

3.6 Takeda undertakes and agrees that if, for any reason, Mitsubishi UFJ Trust and Banking Corporation is unable to continue to act as shareholder registry administrator on behalf of

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Takeda, both generally and as "transfer agent" in relation to the matters contemplated by this Agreement, then Takeda shall engage another party to fulfil such roles as soon as reasonably practicable (with the intention that there shall be no disruption in the service provided pursuant to the relevant role) and shall notify the other parties to this Agreement of such change in accordance with Clause 12.

- 3.7** Takeda confirms that it has engaged BNYM to act as the Takeda Depositary and to fulfil such role in accordance with the terms of this Agreement and the Shire ADS Instruction Letter.
- 3.8** Takeda undertakes and agrees that if, for any reason BNYM is unable to continue to act the Takeda Depositary and to fulfil such role in accordance with the terms of this Agreement and the Shire ADS Instruction Letter, then Takeda shall engage another party to fulfil such role as soon as reasonably practicable (with the intention that there shall be no disruption in the service provided pursuant to the relevant role) and shall notify the other parties to this Agreement of such change in accordance with Clause 12.
- 3.9** The parties acknowledge that, subject to approval by the Shire Shareholders at the Shire General Meeting and conditional upon and with effect from the time and date at which the Scheme is sanctioned by the Court, Shire plc will be appointed as the agent of all Scheme Shareholders (the "**Agent**") for the purposes of undertaking any and all matters and procedures necessary or desirable to be undertaken pursuant to Japanese law (including, in particular, under Articles 203 and 204 of the Japanese Companies Act) in connection with the issuance and settlement of the New Takeda Shares pursuant to the Scheme.
- 3.10** The parties acknowledge and agree to each of the appointments and engagements referred to in this Clause 3.

## **4 Creation and Maintenance of Accounts and Records**

### **4.1 Settlement Account**

- 4.1.1** No later than 15 Business Days prior to the Effective Date, the Fiduciary shall instruct the Global Custodian to, and the Global Custodian shall, (i) open a JASDEC Account with the Sub-Custodian for the purposes of entering into the record maintained by JASDEC the issue of the New Takeda Shares and, as relevant, the transfers and continued holding of the New Takeda Shares in accordance with the Book-Entry Act (the "**Settlement Account**"), and (ii) open in its own books a securities account in the name of the Fiduciary as nominee for the Scheme Shareholders wherein all holdings and transfers of New Takeda Shares in and from the Settlement Account shall also be recorded (the "**Global Custodian Account**").
- 4.1.2** The Global Custodian Account shall be operated in accordance with the terms of the custody agreement entered into between the Fiduciary and the Global Custodian.
- 4.1.3** The Global Custodian shall provide details of the Settlement Account to the Fiduciary in writing no later than 5 Business Days prior to the Effective Date.
- 4.1.4** Following completion of the Corporate Nominee Termination Sales Process, the Global Custodian will procure that the Settlement Account and the Global Custodian Account are closed.
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#### 4.2 Fiduciary Bank Account

The Fiduciary shall open the Fiduciary Bank Account with the Global Custodian, for the purposes of receiving any sales proceeds or distributions in respect of the New Takeda Shares (on behalf of the Representative (as bare trustee for the No Action Shareholders) and relevant Scheme Shareholders) from the Global Custodian, by not later than three Business Days prior to the Effective Date.

#### 4.3 BNYM JASDEC Account

The Takeda Depository shall provide written confirmation of such details of the BNYM JASDEC Account as are necessary to enable settlement of the transfer of the relevant New Takeda Shares into the BNYM JASDEC Account, in the form agreed between BNYM, the Fiduciary and the Global Custodian, to the Receiving Agent by not later than three Business Days prior to the Effective Date.

#### 4.4 Fiduciary Records

4.4.1 The Fiduciary shall create and maintain up-to-date records, with effect from the Settlement Date, of:

- (i) the number of New Takeda Shares being held in the Settlement Account (through the Global Custodian Account) from time to time on behalf of the Representative as bare trustee for the No Action Shareholders (the “**No Action Shares**”) (and such record being referred to as the “**No Action Sub-Account**”), together with separate records of the number of New Takeda Shares to which each such underlying No Action Shareholder is ultimately entitled; and
- (ii) the number of New Takeda Shares being held in the Settlement Account (through the Global Custodian Account) from time to time on behalf of any Corporate Nominee Shareholder, each such record being referred to as a “**Personal Sub-Account**”.

4.4.2 All records maintained by the Fiduciary in accordance with Clause 4.4.1 shall be made available to Takeda and (in the case of Clause 4.4.1(i) only) the Representative on demand.

4.4.3 The parties acknowledge and agree that the records maintained by the Fiduciary in accordance with Clauses 4.4.1(i) and (ii) are maintained solely on behalf of, respectively, the Representative (and, as a consequence, the No Action Shareholders) and the Corporate Nominee Shareholders and that none of the aforementioned records is maintained on behalf of Takeda. Takeda hereby represents that the only register of Takeda Shares is maintained through JASDEC by Mitsubishi UFJ Trust and Banking Corporation in Japan.

### 5 Shire Shareholder Register

5.1 Equiniti shall (subject to compliance with applicable Data Protection Legislation) provide Takeda with a copy of the updated register of holders of Shire ordinary shares by email (in both excel format and PDF):

5.1.1 as at the Scheme Record Time, by no later than 03.00 GMT / 12.00 JST on the calendar day immediately following the date on which the Scheme Record Time occurs;

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- 5.1.2 updated to show Takeda as the sole registered holder of all of the Scheme Shares, by no later than two hours following the Scheme Effective Time, subject only to receipt of a pdf copy of the executed stock transfer form in respect of the Scheme Shares; and
- 5.1.3 upon reasonable written request from Takeda, as soon as possible (and in any event no later than two Business Days following any such request).

## **6 Elections and Settlement**

**6.1** The Receiving Agent shall be responsible for collecting the Forms of Election from Scheme Shareholders, which shall include the Securities Elections.

**6.2** The Global Custodian, in accordance with instructions from the Fiduciary, shall procure that the initial settlement of the New Takeda Shares is effected on the Settlement Date by crediting the Settlement Account with the total number of New Takeda Shares (including the Fractional Shares) to be issued pursuant to the Scheme.

**6.3** The Global Custodian shall record the Standing Proxy as standing proxy in respect of all New Takeda Shares held in the Settlement Account from time to time.

### **6.4 JASDEC Elections**

**6.4.1** In the case of all JASDEC Elections which Scheme Shareholders have validly completed and submitted to the Receiving Agent by no later than the Election Return Time:

- (i) the Receiving Agent, through the Fiduciary, shall provide a delivery schedule containing all of the relevant details contained in such JASDEC Elections, in the form agreed with the Global Custodian, to the Global Custodian as soon as practicable and in any event by the end of the London Business Day following the Scheme Record Time;
  - (ii) the Fiduciary shall send an instruction in the agreed form to the Global Custodian as soon as practicable and in any event within no later than two London Business Days of the Effective Date, instructing the Global Custodian to transfer on the Settlement Date the relevant number of New Takeda Shares from the Settlement Account to the JASDEC Accounts of the relevant Scheme Shareholders as notified on such Scheme Shareholders' completed JASDEC Elections;
  - (iii) the Global Custodian shall procure that the relevant transfers are made on or as soon as practicable after the Settlement Date in accordance with the instruction received; provided that, the Global Custodian shall notify the Fiduciary on a daily basis of any JASDEC transfer failures or delays and of the number of New Takeda Shares that remain in the Settlement Account as a consequence (such New Takeda Shares being classified by the Fiduciary as "in flight" shares until their successful transfer) and, if a transfer cannot be settled within 14 days of the Effective Date due to the provision of inadequate account details by the Scheme Shareholder or the failure by the Scheme Shareholder's AML to take any necessary steps to receive delivery or for any other reason, the relevant New Takeda Shares will be reclassified by the Fiduciary as No Action Shares; and
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- (iv) the Fiduciary will update its records with respect to the No Action Shares being held in the Settlement Account accordingly.

**6.4.2** In the case of all JASDEC Elections which No Action Shareholders have validly completed and submitted to the Receiving Agent after the Election Return Time and by no later than the No Action Sales Process Cut-Off Date:

- (i) the Receiving Agent, through the Fiduciary, shall provide a delivery schedule containing all of the relevant details contained in such JASDEC Elections, in the form agreed with the Global Custodian, to the Global Custodian on a weekly basis as applicable and in any event by the end of the London Business Day following the No Action Sales Process Cut-Off Date;
- (ii) the Fiduciary shall send a weekly instruction to the Global Custodian, in the form agreed with the Global Custodian, instructing the Global Custodian to transfer the relevant number of New Takeda Shares from the Settlement Account to the JASDEC Accounts of the relevant Scheme Shareholders as notified on any such Scheme Shareholders' completed JASDEC Elections received in the preceding week;
- (iii) the Global Custodian shall procure that such transfers are made as soon as practicable thereafter in accordance with the instruction received; provided that the Global Custodian shall notify the Fiduciary on a daily basis of any JASDEC transfer failures or delays and of the number of New Takeda Shares that remain in the Settlement Account as a consequence and, if a transfer cannot be settled within two weeks of the original transfer request date due to the provision of inadequate account details by the Scheme Shareholder or the failure by the Scheme Shareholder's AMI to take any necessary steps to receive delivery or for any other reason, the relevant New Takeda Shares will remain classified by the Fiduciary as No Action Shares; and
- (iv) the Fiduciary will update its records with respect to the No Action Shares being held in the Settlement Account accordingly.

**6.4.3** No JASDEC Elections will be accepted by the Receiving Agent after the No Action Sales Process Cut-Off Date.

## **6.5 Corporate Nominee Elections**

**6.5.1** In the case of all Corporate Nominee Elections which Scheme Shareholders have validly completed and submitted to the Receiving Agent by no later than the Election Return Time:

- (i) the Receiving Agent shall verify the information set out in all Corporate Nominee Elections collected and pass on all such Corporate Nominee Elections collected and verified, together with a summary of all details contained in such Corporate Nominee Elections, to the Fiduciary; and
  - (ii) the Fiduciary shall, as soon as practicable after the receipt of such Corporate Nominee Elections and in any event by the end of the London Business Day following the Scheme Record Time, notify the Global
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Custodian of the number of New Takeda Shares that will initially be held in the Settlement Account on behalf of Corporate Nominee Shareholders.

**6.5.2** In the case of all Corporate Nominee Elections which No Action Shareholders have validly completed and submitted to the Receiving Agent after the Election Return Time and by no later than the No Action Sales Process Cut-Off Date:

- (i) the Receiving Agent shall verify the information set out in all Corporate Nominee Elections collected and pass on all such Corporate Nominee Elections collected and verified, together with a summary of all details contained in such Corporate Nominee Elections, on a rolling basis to the Fiduciary;
- (ii) the Fiduciary shall, on a bi-weekly basis (or as otherwise agreed) as applicable and in any event by the end of the London Business Day following No Action Sales Process Cut-Off Date, notify the Global Custodian of the revised number of New Takeda Shares that are being held in the Settlement Account on behalf of Corporate Nominee Shareholders and the correspondingly revised number of No Action Shares; and
- (iii) the Fiduciary shall update its records with respect to the number of New Takeda Shares being held in the Settlement Account on behalf of Corporate Nominee Shareholders, and shall reduce its records of the number of No Action Shares accordingly.

**6.5.3** No Corporate Nominee Elections will be accepted by the Receiving Agent after the No Action Sales Process Cut-Off Date.

## **6.6 ADS Elections (other than ADS CDI Elections)**

**6.6.1** In the case of all ADS Elections (other than ADS CDI Elections) which Scheme Shareholders have validly completed and submitted to the Receiving Agent by no later than the Election Return Time:

- (i) the Receiving Agent, through the Fiduciary, shall provide a delivery schedule containing all of the relevant details contained in such ADS Elections, in the form agreed with the Takeda Depository, to the Takeda Depository as soon as practicable and in any event by the end of the London Business Day following the Scheme Record Time;
  - (ii) the Fiduciary shall send an instruction in the agreed form to the Global Custodian as soon as practicable and in any event within two London Business Days of the Effective Date instructing the Global Custodian to transfer the relevant number of New Takeda Shares from the Settlement Account to the BNYM JASDEC Account on the Settlement Date. The Global Custodian shall then procure that such transfer is made on or as soon as practicable after the Settlement Date; and
  - (iii) the Takeda Depository shall effect the credit of the relevant number of New Takeda ADSs through DTC to the securities deposit accounts specified in the delivery schedule for the ADS Elections (or issue and mail a direct registration system statement, if so directed by a Scheme Shareholder pursuant to its ADS Election) as soon as practicable after receipt of the New Takeda Shares into the BNYM JASDEC Account.
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- 6.6.2** In the case of all ADS Elections (other than ADS CDI Elections) which No Action Shareholders have validly completed and submitted to the Receiving Agent after the Election Return Time and by no later than the No Action Sales Process Cut-Off Date:
- (i) the Receiving Agent, through the Fiduciary, shall provide a weekly delivery schedule containing all of the relevant details contained in such ADS Elections, in the form agreed with the Takeda Depository, to the Takeda Depository on a weekly basis as applicable and in any event by the end of the London Business Day following the No Action Sales Process Cut-Off Date;
  - (ii) the Fiduciary shall send a weekly instruction to the Global Custodian, in the form agreed with the Global Custodian, instructing the Global Custodian to transfer the relevant number of New Takeda Shares from the Settlement Account to the BNYM JASDEC Account in accordance with the ADS Elections received in the preceding week. The Global Custodian shall then procure that such transfer is made as soon as practicable thereafter in accordance with the instruction received. The Fiduciary will update its records with respect to the No Action Shares being held in the Settlement Account accordingly; and
  - (iii) the Takeda Depository shall effect the credit of the relevant number of New Takeda ADSs through DTC to the securities deposit accounts specified in the ADS Elections (or issue and mail a direct registration system statement, if so directed by a Scheme Shareholder pursuant to its ADS Election) as soon as practicable after receipt of the relevant New Takeda Shares into the BNYM JASDEC Account.
- 6.6.3** No ADS Elections will be accepted by the Receiving Agent after the No Action Sales Process Cut-Off Date.
- 6.6.4** In the event that any attempted deliveries by the Takeda Depository of New Takeda ADSs through DTC are rejected, the Takeda Depository shall inform the Receiving Agent of such rejection as soon as practicable and the Receiving Agent shall use reasonable endeavours to re-verify the information in the relevant ADS Elections. If it has not been possible to complete delivery of any such New Takeda ADSs through DTC after 30 days from the Effective Date, the Takeda Depository shall request from the Receiving Agent, and the Receiving Agent shall provide to the Takeda Depository, such information as is available to the Receiving Agent and necessary in order for the Takeda Depository to issue and mail a direct registration system statement to the relevant Scheme Shareholders.
- 6.6.5** For the purposes of settlement of all ADS Elections validly completed and submitted to the Receiving Agent prior to the Election Return Time, the Takeda Depository shall post a notice to its website and send emails to its broker network stating that it intends to commence delivery of the New Takeda ADSs on the date on which it receives confirmation that the relevant New Takeda Shares have been deposited into the BNYM Account (such date currently expected to be the Settlement Date).
- 6.6.6** It is acknowledged that the Takeda Depository shall not be required to supply the US tax authorities with any tax reporting information or perform any tax withholding
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of any kind for any New Takeda ADSs being issued to former Scheme Shareholders.

## 6.7 ADS CDI Elections

6.7.1 In the case of all ADS CDI Elections validly made by the Election Return Time:

- (i) the Receiving Agent, through the Fiduciary, shall provide a delivery instruction to the Takeda Depository, in the form agreed with the Takeda Depository, containing all relevant details of the securities deposit account of CREST International Nominees Limited, as nominee for CREST Depository Limited within DTC, and the number of New Takeda ADSs which are to be issued in CDI form as soon as practicable and in any event by the end of the London Business Day following the Scheme Record Time;
- (ii) the Fiduciary shall send an instruction to the Global Custodian, in the form agreed with the Global Custodian, as soon as practicable and in any event within two London Business Days of the Effective Date instructing the Global Custodian to transfer the relevant number of New Takeda Shares from the Settlement Account to the BNYM JASDEC Account on the Settlement Date. The Global Custodian shall then procure that such transfer is made on or as soon as practicable after the Settlement Date;
- (iii) the Takeda Depository shall effect the credit of the relevant number of New Takeda ADSs through DTC to the securities deposit account of CREST International Nominees Limited, as nominee for CREST Depository Limited, as soon as practicable after receipt of the New Takeda Shares into the BNYM JASDEC Account; and
- (iv) the Receiving Agent shall procure that CREST Depository Limited will then issue the relevant number of CDIs representing New Takeda ADSs through CREST to the Receiving Agent for delivery to the securities deposit account in CREST in which each relevant Scheme Shareholder previously held Scheme Shares.

6.7.2 It is acknowledged that ADS CDI Elections can only be made through CREST by way of a TTE Instruction and, therefore, that no ADS CDI Elections will be capable of being made after the Election Return Time or by No Action Shareholders.

## 6.8 Dealing Facility Elections

6.8.1 In the case of all Dealing Facility Elections which Scheme Shareholders have validly completed and submitted to the Receiving Agent by no later than the Election Return Time:

- (i) the Receiving Agent shall verify the information set out in all Dealing Facility Elections collected;
  - (ii) the Receiving Agent shall, through the Fiduciary, provide to the Nomura Sales Agent, in the form agreed with the Nomura Sales Agent, notification of the number of New Takeda Shares to be sold pursuant to the Dealing Facility Elections as soon as practicable and in any event by the end of the London Business Day following the Scheme Record Time; and
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- (iii) as soon as practicable and in any event within two London Business Days of the Effective Date, the Fiduciary shall send an instruction in the agreed form (a) to the Nomura Sales Agent instructing it to sell the relevant number of New Takeda Shares from the Settlement Account and (b) to the Global Custodian instructing it to take all actions necessary to settle such sale from the Settlement Account. The Global Custodian shall then procure that such settlement is made on or as soon as practicable after the Settlement Date in accordance with the instruction received and the Dealing Facility Sales Process.

**6.8.2** In the case of all Dealing Facility Elections which No Action Shareholders have validly completed and submitted to the Receiving Agent after the Election Return Time and by no later than the No Action Sales Process Cut-Off Date:

- (i) the Receiving Agent shall verify the information set out in all Dealing Facility Elections collected;
- (ii) the Receiving Agent shall, through the Fiduciary, provide to the Nomura Sales Agent, in the form agreed with the Nomura Sales Agent, notification of the number of New Takeda Shares to be sold pursuant to the Dealing Facility Elections received in the preceding period by the end of the London Business Day following each Dealing Facility Sale Process Cut-Off Date; and
- (iii) as soon as practicable and in any event by no later than the end of the London Business Day following the relevant Dealing Facility Sales Process Cut-Off Date, the Fiduciary shall send an instruction in the agreed form (a) to the Nomura Sales Agent instructing it to sell the relevant number of New Takeda Shares as soon as practicable and (b) to the Global Custodian instructing it to take all actions necessary to settle such sale from the Settlement Account. The Global Custodian shall then procure that such settlement is made in accordance with the instruction received and the Dealing Facility Sales Process and the Fiduciary will update its records with respect to the No Action Shares being held in the Settlement Account on behalf of the Representative accordingly.

**6.8.3** No Dealing Facility Elections will be accepted by the Receiving Agent after the No Action Sales Process Cut-Off Date.

**6.9** Upon Takeda's request, the Receiving Agent, through the Fiduciary, shall provide Takeda with the results of the Securities Elections and a summary of all details contained in each of the Securities Elections, subject to compliance with applicable Data Protection Legislation.

**6.10** No transfers will be effected pursuant to this Clause 6 after the No Action Sales Process Cut-Off Date.

## **7 Sales Processes**

### **7.1 Fractional Sales Process**

**7.1.1** As soon as practicable following the Settlement Date, the Nomura Sales Agent shall, on instruction from the Fiduciary, arrange through the Nomura Broker for the sale of the Fractional Shares in accordance with the parameters of the Sales Policy

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and, after the necessary currency conversion through the Nomura Broker, shall pay the net proceeds of the sales of such Fractional Shares (after deduction of all applicable expenses, commissions and taxes incurred in connection with such sale and currency conversion as set out in "Dealing Charges" below) to the Fiduciary in United States Dollars and Pounds Sterling as directed by the Fiduciary.

- 7.1.2 The Fiduciary will procure that the proceeds of sale are paid in accordance with the procedures set forth in the Scheme Document, in due proportion to the Scheme Shareholders entitled to them, in the same currency as the cash portion of the Consideration which was payable to such Scheme Shareholders pursuant to the Scheme (save that if a Scheme Shareholder has made a valid Currency Election to receive some of the cash portion of the Consideration which is payable to them in Pounds Sterling, any amounts paid in respect of fractional entitlements to such Scheme Shareholder shall be paid in Pounds Sterling).
- 7.1.3 It is acknowledged that sales arranged pursuant to this Clause 7.1 may take more than one trading day.

## **7.2 Dealing Facility Sales Process**

- 7.2.1 As soon as practicable following the Settlement Date, the Nomura Sales Agent shall, on instruction from the Fiduciary, arrange through the Nomura Broker for the sale, in accordance with the parameters of the Sales Policy, of the New Takeda Shares in respect of which valid Dealing Facility Elections have been made and, after the necessary currency conversion through the Nomura Broker, shall pay the net proceeds of the sale of such New Takeda Shares (after deduction of all applicable expenses, commissions and taxes incurred in connection with such sale and currency conversion as set out in "Dealing Charges" below) to the Fiduciary in Pounds Sterling as directed by the Fiduciary.
- 7.2.2 If a Scheme Shareholder completes and submits a valid Dealing Facility Election after the Election Return Time but prior to the date falling three months after the Effective Date, the relevant New Takeda Shares will be sold through the Dealing Facility as soon as practicable after the next Dealing Facility Sales Process Cut-Off Date falling after the valid submission of the Dealing Facility Election.
- 7.2.3 In each case the Fiduciary will procure that the proceeds of sale are paid in accordance with the procedures set forth in the Dealing Facility Terms and Conditions, in due proportion to the Scheme Shareholders entitled to them.
- 7.2.4 It is acknowledged that sales arranged pursuant to this Clause 7.2 may take more than one trading day.

## **7.3 No Action Sales Process**

- 7.3.1 As soon as practicable after the date falling three months following the Effective Date, the Nomura Sales Agent shall, on instruction from the Fiduciary, arrange through the Nomura Broker for the sale of any remaining No Action Shares in accordance with the parameters of the Sales Policy and, after the necessary currency conversion through the Nomura Broker, shall pay the net proceeds of the sale of such No Action Shares (after deduction of all applicable expenses, commissions and taxes incurred in connection with such sale and currency conversion as set out in "Dealing Charges" below) to the Fiduciary in United States Dollars and Pounds Sterling as directed by the Fiduciary.
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- 7.3.2 The Fiduciary will procure that the proceeds of sale are paid in accordance with the procedures set forth in the Scheme Document for initial settlement of the cash portion of the Consideration, in due proportion to the Scheme Shareholders entitled to them. No Action Shareholders who held their Scheme Shares in certificated form and had a registered address in the United Kingdom, Channel Islands or Isle of Man as at the Scheme Record Time will be paid in Pounds Sterling. All other No Action Shareholders will be paid in United States Dollars.
- 7.3.3 It is acknowledged that any sales arranged pursuant to this Clause 7.3 may take more than one trading day.
- 7.3.4 The Fiduciary will update its records accordingly to reflect the sales of any No Action Shares pursuant to this Clause 7.3.

#### 7.4 Corporate Nominee Termination Sales Process

- 7.4.1 As soon as practicable after the date falling two years after the Effective Date, the Nomura Sales Agent shall, on instruction from the Fiduciary, arrange through the Nomura Broker for the sale of any remaining New Takeda Shares held in the Settlement Account on behalf of Corporate Nominee Shareholders in accordance with the parameters of the Sales Policy and, after the necessary currency conversion through the Nomura Broker, shall pay the net proceeds of the sale of such New Takeda Shares (after deduction of all applicable expenses, commissions and taxes incurred in connection with such sale and currency conversion as set out in “Dealing Charges” below) to the Fiduciary in Pounds Sterling as directed by the Fiduciary.
- 7.4.2 The Fiduciary will procure that the proceeds of sale are paid in accordance with the procedures set forth in the Corporate Nominee Facility Terms and Conditions, in due proportion to the Scheme Shareholders entitled to them.
- 7.4.3 It is acknowledged that any sales arranged pursuant to this Clause 7.4 may take more than one trading day

#### 7.5 Sales Policy

- 7.5.1 It is acknowledged that any sale of New Takeda Shares to be arranged by the Nomura Sales Agent on the instruction of the Fiduciary as contemplated by this Agreement shall be carried out in accordance with the following parameters:

Item	Details
Number of New Takeda Shares to be sold	Number of New Takeda Shares to be sold in each sale will be specified in each instruction by the Fiduciary.
Exchange	The Tokyo Stock Exchange (TSE)
Broker	Nomura Securities Co., Ltd.
Maximum aggregate order volume per day <sup>1</sup>	15% of the average daily trading volume during the four weeks preceding the week in which the relevant sales day falls.
Treatment of share units	Whole units of Takeda Shares (1 unit is 100 Takeda Shares) will be sold on the Tokyo Stock Exchange.

Item	Details
	Any partial unit (being any number of 1 to 99 New Takeda Shares) will be sold at the last traded price on the relevant trading day.
Dealing charges	(i) 0.3% transaction fee charged by the Broker; plus (ii) 0.25% currency conversion fee charged by the Broker; and (iii) in the case of sales made pursuant to requests by Corporate Nominee Shareholders (as envisaged by Clause 8.4) only, such additional charges as may be agreed from time to time under the Corporate Nominee Facility Terms and Conditions.

<sup>1</sup> This refers to all sales of New Takeda Shares instructed to be arranged by the Nomura Sales Agent on the instruction of the Fiduciary on a given day.

## 7.6 Sales Manual

Without prejudice to any of the provisions of this Clause 7, it is further acknowledged that any sale of New Takeda Shares to be arranged by the Nomura Sales Agent on the instruction of the Fiduciary as contemplated by this Agreement shall be carried out in accordance with the detailed procedures set out in the sales manual agreed between the Fiduciary, the Nomura Sales Agent and the Nomura Broker from time to time (the “**Sales Manual**”).

## 7.7 Limitation of obligation

7.7.1 It is acknowledged that in the absence of bad faith, fraud, wilful default or gross negligence, provided Nomura Bank (Luxembourg) S.A. (in any capacity under this Agreement) and Nomura Securities Co., Ltd. (in any capacity under this Agreement) (together, the “**Nomura Parties**”) perform the sales of New Takeda Shares, transfers of dividends and other distributions and returns of capital, and currency conversions (together, the “**Procedures**”) contemplated by this Agreement in accordance with this Agreement, the Sales Policy, the Sales Manual, the instructions of the Fiduciary and any other agreements, memorandums or manuals agreed with the Fiduciary from time to time, neither of the Nomura Parties shall be responsible for the results of such Procedures including the prices and/or timing thereof.

7.7.2 It is further acknowledged that if any of the Procedures cannot be carried out due to reasons outside the control of the Nomura Parties (including, without limitation, if trading on the Tokyo Stock Exchange and/or any relevant currency market is suspended or disabled for reasons outside the control of the Nomura Parties), then the Nomura Parties shall not be liable for any consequential delay in carrying out the relevant Procedures pursuant to this Agreement, and the time for performance of such obligations shall be extended accordingly.

## 7.8 Currency conversions

It is acknowledged that, subject always to the terms of this Agreement, the Sales Policy, the Sales Manual, the instructions of the Fiduciary and any other agreements, memorandums or manuals agreed with the Fiduciary from time to time, the Global

Custodian shall be entitled to determine the terms of any necessary currency conversions to be carried out or arranged by it under this Agreement.

## **8 Ongoing operation of the Settlement Account**

### **8.1 Notices of Meeting and Voting**

- 8.1.1 Takeda shall procure the prompt delivery to the Standing Proxy (who shall procure prompt delivery to the Global Custodian and to the Fiduciary) of all notices of meeting (including convocation notices) and other Takeda shareholder communications in respect of the New Takeda Shares that are held in the Settlement Account from time to time.
- 8.1.2 The Fiduciary shall ensure that all notices and other communications received by it pursuant to Clause 8.1.1 are passed on to the relevant underlying Corporate Nominee Shareholders in accordance with the Corporate Nominee Facility Terms and Conditions.
- 8.1.3 Each of Takeda, the Fiduciary and the Global Custodian agrees that, in circumstances in which the holders of New Takeda Shares held in the Settlement Account from time to time have the right to vote by proxy on a resolution, the Fiduciary shall, in accordance with the Corporate Nominee Facility Terms and Conditions, collect voting instructions from any underlying Corporate Nominee Shareholders in connection with the same, and shall separately aggregate the "For" and "Against" voting instructions received to enable the maximum number of "For" and "Against" votes to be exercised, and shall then communicate to the Global Custodian the votes with respect to such New Takeda Shares so that they can be cast accordingly.
- 8.1.4 It is acknowledged that no votes will be exercised in respect of any No Action Shares and, accordingly, that the Fiduciary will not be required to pass on any notices of meeting or other shareholder communications to either the Representative or the No Action Shareholders nor to collect any voting instructions from such persons.

### **8.2 Dividends**

- 8.2.1 Takeda shall procure that all dividends, distributions and other returns of capital made or paid with respect to the New Takeda Shares held in the Settlement Account on behalf of Corporate Nominee Shareholders from time to time are delivered to a bank account nominated by the Global Custodian, who shall transfer such amounts (subject to applicable withholding tax deductions and converted from Japanese Yen to Pounds Sterling) to the Fiduciary Bank Account such that the Fiduciary is able to remit the same to the underlying Corporate Nominee Shareholders in accordance with the Corporate Nominee Facility Terms and Conditions.
  - 8.2.2 Takeda shall procure that all dividends, distributions and other returns of capital made or paid with respect to the No Action Shares are delivered to a bank account nominated by the Global Custodian, who shall transfer such amounts (subject to applicable withholding tax deductions and converted from Japanese Yen to United States Dollars and Pounds Sterling) to the Fiduciary Bank Account (it being acknowledged that No Action Shareholders who held their Scheme Shares in
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certificated form and had a registered address in the United Kingdom, Channel Islands or Isle of Man as at the Scheme Record Time will receive Pounds Sterling and all other No Action Shareholders will receive United States Dollars). The Fiduciary shall remit such dividends, distributions and other returns of capital to No Action Shareholders pro rata to the number of No Action Shares held on their behalf at the relevant record time, no later than ten Business Days after such dividends, distributions and other returns of capital are received in the Fiduciary Bank Account.

- 8.2.3** The Fiduciary, the Global Custodian and the Sub-Custodian agree and acknowledge that Japanese withholding tax in respect of any dividends and other distributions treated as dividends for Japanese tax purposes made or paid with respect to the New Takeda Shares held in the Settlement Account from time to time, and transferred by the Sub-Custodian, through the Global Custodian, to the Fiduciary Bank Account in accordance with Clause 8.2.1 or 8.2.2, as the case maybe, and the Sales Manual, is intended to be withheld at a rate of 10 per cent. under the double taxation convention between the UK and Japan (to the extent applicable) and, to the extent practicable, at any other applicable treaty rate in accordance with the tax residency information (if any) supplied by underlying shareholders to the Fiduciary and communicated to the Global Custodian and the Sub-Custodian from time to time, and that the holdings in the Global Custodian Account and the Settlement Account may be segregated from time to time to facilitate the performance of such withholding.

### **8.3 Elections by No Action Shareholders**

Any Securities Elections (other than ADS CDI Elections) which are validly completed by a No Action Shareholder and submitted to the Receiving Agent after the Election Return Time and by no later than the No Action Sales Process Cut-Off Date shall be actioned in accordance with the provisions of Clause 6.

### **8.4 Sales Requests by Corporate Nominee Shareholders**

- 8.4.1** The Fiduciary shall implement a procedure which allows each Corporate Nominee Shareholder to instruct the Fiduciary to procure the sale of some or all of such Corporate Nominee Shareholder's New Takeda Shares on the market from time to time in accordance with the Corporate Nominee Facility Terms and Conditions, regardless of whether such Corporate Nominee Shareholder's New Takeda Shares form a part unit or a full unit under the Takeda Articles or for the purposes of Japanese law. Such process shall be open to Corporate Nominee Shareholders who hold New Takeda Shares in the Settlement Account until at least five Business Days prior to the Corporate Nominee Termination Sales Process Cut-Off Date.
- 8.4.2** Any sales pursuant to Clause 8.4.1 which are to be arranged by the Nomura Sales Agent, on instruction from the Fiduciary, shall be carried out in accordance with the parameters of the Sales Policy or as may otherwise be agreed under the Corporate Nominee Facility Terms and Conditions.

### **8.5 Reminders**

- 8.5.1** Promptly following the Settlement Date, and at regular agreed intervals until the No Action Sales Process Cut-Off Date, the Fiduciary shall procure that communications (in such form as may be agreed between Takeda and the
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Fiduciary from time to time) are issued to remind No Action Shareholders of the No Action Sales Process Cut-Off Date and the date on which the sales process under the No Action Sales Policy will commence.

**8.5.2** On or around the date which is 20 months following the Settlement Date, the Fiduciary will procure that a communication (in such form as may be agreed between Takeda and the Fiduciary) is issued to Corporate Nominee Shareholders, reminding them that:

- (i) a sales process in accordance with the Corporate Nominee Termination Sales Process will commence as soon as practicable after the date falling two years after the Effective Date; and
- (ii) any Corporate Nominee Shareholder on whose behalf any New Takeda Shares remain held in the Settlement Account who do not wish such New Takeda Shares to be sold in accordance with such Corporate Nominee Termination Sales Process must notify the Fiduciary of either:
  - (a) a JASDEC Account into which they wish their New Takeda Shares to be transferred and the details of their standing proxy or mailing address in Japan; or
  - (b) that they wish to convert their New Takeda Shares into Takeda ADSs and provide applicable and valid delivery instructions,

in each case, by no later than the Corporate Nominee Termination Sales Process Cut-Off Date.

## **9 Authority from the Representative**

The Representative shall grant a power of attorney, in a form to be agreed between the Representative and the Fiduciary, with effect from the Scheme Effective Time, authorising the Fiduciary to issue any and all instructions and notifications as may be required in order to implement (i) any Securities Elections (other than ADS CDI Elections) received from No Action Shareholders on whose behalf No Action Shares in the name of the Representative as bare trustee are being held in the Settlement Account; and (ii) any sales of No Action Shares in accordance with the No Action Sales Process.

## **10 Termination**

**10.1** This Agreement shall terminate on the date on which the completion of the Corporate Nominee Termination Sales Process occurs or, if earlier, the date on which the proceeds of the last New Takeda Share(s) to be transferred out of the Settlement Account are distributed by the Fiduciary to all the relevant Corporate Nominee Shareholders or No Action Shareholders, as applicable.

**10.2** Termination of this Agreement shall be without prejudice to the rights of any of the parties which have arisen before termination.

**10.3** The whole of this Clause 10 (Termination) and Clauses 12 (Notices) to 21 (Governing law and jurisdiction) (inclusive) shall survive termination of this Agreement.

## 11 Data protection

Each party to this Agreement shall comply with applicable Data Protection Legislation when processing any personal data (as such term is defined in Data Protection Legislation) under this Agreement.

## 12 Notices

**12.1** A notice under this Agreement shall only be effective if it is in writing.

**12.2** Notices under this Agreement shall be sent to a party by hand delivery or reputable international courier or by facsimile or by email at its physical address, facsimile number or email address respectively, and shall be marked for the attention of the individual(s) set out below:

### 12.2.1 Takeda:

Attention: Atsuhiko Nagano  
 Physical address: 1-1, Nihonbashi-Honcho 2-Chome, Chuo-ku, Tokyo 103-8668, Japan  
 Fax number: +81 3278 2268  
 Email address: atsuhiko.nagano@takeda.com

### 12.2.2 the Fiduciary:

Attention: Richard Warrington  
 Physical address: Equiniti Financial Services Limited, Level 6, The Broadgate Tower, 20 Primrose Street, London EC2A 2EW, United Kingdom  
 Fax number: +44 207 469 1969  
 Email address: richard.warrington@equiniti.com

### 12.2.3 the Receiving Agent:

Attention: Jon McLean, Senior Manager  
 Physical address: Equiniti Limited, Corporate Advice, Aspect House, Spencer Road, Lancing, West Sussex BN99 6DA, United Kingdom  
 Fax number: N/A  
 Email address: jonathan.mclean@equiniti.com

### 12.2.4 the Representative:

Attention: Company Secretary  
 Physical address: Block 2, Miesian Plaza, 50-58 Baggot Street Lower, Dublin 2, Ireland  
 Fax number: +353 1 6096001  
 Email address: receptionbaggotst@shire.com

### 12.2.5 the Global Custodian and the Nomura Sales Agent:

Attention: Depository Banking Division and Corporate Legal Department  
 Physical address: 33 rue de Gasperich, L-5826 Hesperange, G-D de Luxembourg  
 Fax number: N/A  
 Email address: Dept\_CorporateLegal-lu@lu.nomura.com

**12.2.6** the Nomura Broker:

Attention: Kent Yoshida, Corporate Finance Dept. V  
Physical address: Urbannet Otemachi Building, 2-2 Otemachi 2-chome,  
Chiyoda-ku, Tokyo 100-8130, Japan  
Fax number: +81 3 6838 4954  
Email address: kent.yoshida@nomura.com

**12.2.7** the Takeda Depositary:

Attention: Joanne DiGiovanni Hawke  
Physical address: The Bank of New York Mellon, Depositary Receipts  
240 Greenwich Street, New York NY 10286  
Fax number: +1 212 571 3050  
Email address: joanne.digiovanni@bnymellon.com

**12.3** A party may change its notice details on giving notice to the other party of the change in accordance with this Clause 12.3 and Clause 12.1. That notice shall only be effective on the date falling one Business Day after the notification has been received or such later date as may be specified in the notice.

**12.4** Any notice given under this Agreement shall, in the absence of earlier receipt, be deemed to have been duly given:

**12.4.1** if delivered by hand, on delivery;

**12.4.2** if sent by reputable international courier, on signature of a delivery receipt;

**12.4.3** if sent by facsimile, when the sender's facsimile system generates a message confirming successful transmission of the notice; or

**12.4.4** if sent by email, when acknowledged by the recipient.

**12.5** Any notice given under this Agreement outside the period between 9:00 a.m. and 5:00 p.m. (in the place to which that notice is addressed) on a Business Day ("**Working Hours**") shall be deemed not to have been given until the start of the next period of Working Hours.

**12.6** The provisions of this Clause 12 shall not apply in relation to the service of any claim form, application notice, order, judgment or other document relating to any proceedings, suit or action arising out of or in connection with this Agreement, whether contractual or non-contractual.

### **13 Remedies and Waivers**

**13.1** No delay or omission by any party to this Agreement in exercising any right, power or remedy provided by law or under this Agreement shall:

**13.1.1** affect that right, power or remedy; or

**13.1.2** operate as a waiver of it.

**13.2** The single or partial exercise of any right, power or remedy provided by law or under this Agreement shall not preclude any other or further exercise of it or the exercise of any other right, power or remedy.

**13.3** The rights, powers and remedies provided in this Agreement are cumulative and not exclusive of any rights, powers and remedies provided by law.

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**13.4** Without prejudice to any other rights and remedies which any party may have, each party acknowledges and agrees that damages would not be an adequate remedy for any breach by any party of the provisions of this Agreement and any party shall be entitled to seek the remedies of injunction, specific performance and other equitable remedies, for any threatened or actual breach of any such provision of this Agreement by any party and no proof or special damages shall be necessary for the enforcement by any party of the rights under this Agreement.

#### **14 Variation**

No variation of this Agreement shall be valid unless it is in writing (which, for this purpose, does not include email) and signed by or on behalf of each of the parties.

#### **15 Invalidity**

**15.1** If at any time any provision of this Agreement is or becomes illegal, invalid or unenforceable in any respect under the law of any jurisdiction, that shall not affect or impair:

**15.1.1** the legality, validity or enforceability in that jurisdiction of any other provision of this Agreement; or

**15.1.2** the legality, validity or enforceability under the law of any other jurisdiction of that or any other provision of this Agreement,

and, if such provision would be valid and enforceable if deleted in whole or in part or reduced in application, such provision shall apply with such deletion or modification as may be necessary to make it valid and enforceable.

**15.2** Nothing in this Agreement shall in any way limit the parties' obligations under the Code, and any uncontested rulings of the Panel as to the application of the Code in conflict with the terms of this Agreement shall take precedence over such terms.

#### **16 Language**

Each notice or other communication under or in connection with this Agreement shall be in English.

#### **17 Contracts (Rights of Third Parties) Act 1999**

**17.1** The parties do not intend that any term of this Agreement should be enforceable, by virtue of the Contracts (Rights of Third Parties) Act 1999, by any person who is not a party to this Agreement.

**17.2** The rights of the parties to terminate, rescind or agree any variation, waiver or settlement under this Agreement are not subject to the consent of any other person.

#### **18 Assignment**

No party shall be entitled to assign (whether absolutely or by way of security and whether in whole or in part), transfer, mortgage, charge, declare itself a trustee for a third party of, or otherwise dispose of (in any manner whatsoever) the benefit of this Agreement (or any part of it) or sub-contract in any manner whatsoever its performance under this Agreement

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without the prior written consent of each of Takeda, the Fiduciary, the Receiving Agent and the Representative.

## **19 Further Assurance**

Each party shall, at its own cost, use reasonable endeavours to do and execute and perform all such further deeds, documents, assurances, acts and things as may reasonably be required to give effect to this Agreement, and procure the doing of all such acts by any relevant third party.

## **20 Counterparts**

**20.1** This Agreement may be executed in any number of counterparts, and by the parties on separate counterparts, but shall not be effective until each party has executed at least one counterpart.

**20.2** Each counterpart shall constitute an original of this Agreement, but all the counterparts shall together constitute but one and the same instrument.

**20.3** Delivery of an executed counterpart signature page of this Agreement by email (pdf) or facsimile shall be as effective as delivery of a manually executed counterpart of this Agreement. In relation to each counterpart, upon confirmation by or on behalf of the signatory that the signatory authorises the attachment of such counterpart signature page on the final text of this Agreement, such counterpart signature page shall take effect with such final text as a complete authorised counterpart.

## **21 Governing Law and Jurisdiction**

**21.1** This Agreement is to be governed by and construed in accordance with English law. Any matter, claim or dispute arising out of or in connection with this Agreement, whether contractual or non-contractual, is to be governed by and determined in accordance with English law.

**21.2** The parties irrevocably submit to the exclusive jurisdiction of the Courts of England and Wales in respect of any matter, claim or dispute arising out of or in connection with this Agreement, whether contractual or non-contractual.

## **22 Service**

**22.1** Nomura Bank (Luxembourg) S.A. (in any capacity under this Agreement) hereby appoints Nomura International plc of 1 Angel Lane London EC4R 3AB to be its agent for service of process in England and Wales in connection with any claim form, application notice, order, judgment or other document relating to any proceedings, suit or action arising out of or in connection with this Agreement, whether contractual or non-contractual and it undertakes to maintain such an address at all times in the United Kingdom and to notify the other party in advance of any change from time to time of the details of such address.

**22.2** Nomura Securities Co., Ltd. (in any capacity under this Agreement) hereby appoints Nomura International plc of 1 Angel Lane London EC4R 3AB to be its agent for service of process in England and Wales in connection with any claim form, application notice, order, judgment or other document relating to any proceedings, suit or action arising out of or in connection with this Agreement, whether contractual or non-contractual and it undertakes

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to maintain such an address at all times in the United Kingdom and to notify the other party in advance of any change from time to time of the details of such address.

- 22.3** Takeda hereby appoints Hackwood Secretaries Limited of One Silk Street, London EC2Y 8HQ to be its agent for service of process in England and Wales in connection with any claim form, application notice, order, judgment or other document relating to any proceedings, suit or action arising out of or in connection with this Agreement, whether contractual or non-contractual and it undertakes to maintain such an address at all times in the United Kingdom and to notify the other party in advance of any change from time to time of the details of such address.
- 22.4** The Representative hereby appoints Shire Pharmaceuticals Group of 1 Kingdom Street, London, W2 6BD to be its agent for service of process in England and Wales in connection with any claim form, application notice, order, judgment or other document relating to any proceedings, suit or action arising out of or in connection with this Agreement, whether contractual or non-contractual and it undertakes to maintain such an address at all times in the United Kingdom and to notify the other party in advance of any change from time to time of the details of such address.
- 22.5** The Takeda Depository hereby appoints The Bank of New York Mellon, London Branch of 160 Queen Victoria Street, London EC4V 4LA to be its agent for service of process in England and Wales in connection with any claim form, application notice, order, judgment or other document relating to any proceedings, suit or action arising out of or in connection with this Agreement, whether contractual or non-contractual and it undertakes to maintain such an address at all times in the United Kingdom and to notify the other party in advance of any change from time to time of the details of such address.

**IN WITNESS WHEREOF** the parties have executed this Agreement on the date first set out above:

*{Signature pages follow}*

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*{Signature page to the Master Framework and Custody Agreement}*

SIGNED by Paul Matthews  
on behalf of  
**EQUINITI FINANCIAL SERVICES LIMITED:**

}

/s/ PAUL MATTHEWS

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*{Signature page to the Master Framework and Custody Agreement}*

SIGNED by Paul Matthews  
on behalf of  
**EQUINITI LIMITED:**

}

/s/ PAUL MATTHEWS

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*{Signature page to the Master Framework and Custody Agreement}*

SIGNED by François John  
on behalf of  
**NOMURA BANK (LUXEMBOURG) S.A.:**

}

/s/ FRANÇOIS JOHN

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*{Signature page to the Master Framework and Custody Agreement}*

SIGNED by  
on behalf of  
**NOMURA SECURITIES CO., LTD.:**

}

1-9-1 Nihonbashi, Chuo-ku, Tokyo;  
Nomura Securities Co.,Ltd.;  
President MORITA Toshio

REPRESENTATIVE EXECUTIVE  
OFFICER'S SEAL

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*{Signature page to the Master Framework and Custody Agreement}*

SIGNED by Thomas Dittrich  
on behalf of  
**SHIRE PLC:**

}

/s/ THOMAS DITTRICH

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*{Signature page to the Master Framework and Custody Agreement}*

SIGNED by Costa Saroukos  
on behalf of  
**TAKEDA PHARMACEUTICAL COMPANY LIMITED:**

}

/s/ COSTA SAROUKOS

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*{Signature page to the Master Framework and Custody Agreement}*

SIGNED by Joanne DiGiovanni Hawke  
on behalf of  
**THE BANK OF NEW YORK MELLON:**

} /s/ JOANNE DIGIOVANNI HAWKE