

This letter and its appendices are important and require your immediate attention.

If you are in any doubt as to the action you should take, you are recommended to seek your own independent financial advice immediately from a 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 in a territory outside the United Kingdom.

November 20, 2018



Dear Participant

The Baxalta Incorporated 2015 Incentive Plan and the Governing Terms of the Substitute Awards and the recommended cash and share offer for Shire plc by Takeda Pharmaceutical Company Limited

Shire plc (“**Shire**”) and Takeda Pharmaceutical Company Limited (“**Takeda**”) announced on 8 May 2018 that they had reached agreement on the terms of a recommended cash and share offer for the entire issued and to be issued share capital of Shire by Takeda (the “**Acquisition**”).

Why are we writing to you?

We are writing to explain how the Acquisition will affect your awards under the Baxalta Incorporated 2015 Incentive Plan and the Governing Terms of the Substitute Awards (the “**Baxalta Exchange Awards**”) and such awards being “**Baxalta Awards**”).

Please read everything in this letter and its Appendices. **Their contents are very important.**

If you participate in other Shire share plans you are also being written to separately about the effect of the Acquisition on your other options or awards. Please read those letters carefully.

The Acquisition

The Acquisition will result in Shire and its subsidiaries becoming wholly-owned subsidiaries of Takeda.

The Acquisition will take place through what is called a “scheme of arrangement” (the “**Scheme**”). This is a procedure that is subject to approval by Shire Shareholders and the Court. In particular, as part of the Acquisition, the Court will sanction the Scheme on a date known throughout this letter as **Court Sanction**. This date is not the date on which the Acquisition will be completed. The Acquisition is currently due to complete a few days after “Court Sanction” on the **Effective Date**. Please see Appendix A for further detail.

Further information on the Scheme is set out in the Scheme Document dated November 12, 2018 sent to Shire Shareholders on November 12, 2018. Copies of the Scheme Document and this letter are also available on the Shire website at <http://investors.shire.com/takeda> and on the Takeda website at <https://www.takeda.com/investors/offer-for-shire/offer-for-shire-details/>.

This letter and its Appendices should be read together with the Scheme Document. A brief explanation of some of the terms used in this letter is given in Appendix B to this letter. Terms

defined in the Scheme Document will have the same meaning in this letter and its Appendices unless otherwise defined.

What are the terms of the Acquisition for Shire Shareholders?

The terms of the Acquisition are set out in full in the Scheme Document. However, in summary, a person who holds Shire ADSs at the Scheme Record Time will be entitled to receive, for each Shire ADS they own:

- **USD90.99 in cash;** and
- **5.034 Takeda ADSs.**

Please note that the above sets out what persons who hold Shire ADSs at the relevant record time for the Scheme are entitled to receive under the Scheme and is provided for reference. You are being written to because you participate in a Shire share plan, and will not necessarily receive the above consideration unless you hold Shire ADSs at the relevant record time for the Scheme – in which case, you should read the Scheme Document for further information.

When is the Acquisition likely to take place?

The Acquisition is currently expected to become effective on January 8, 2019. The expected timeline is set out in Appendix A.

How does the Acquisition affect your Baxalta Awards?

Normally, your Baxalta Awards would vest on the timetable notified to you at grant.

Restricted Stock Units (RSUs)

As a result of the Acquisition, any RSUs that are outstanding on Court Sanction will be cancelled on Court Sanction in accordance with the terms of the Baxalta Exchange Awards. You will be entitled to receive the Cash Consideration less any necessary deductions for tax and social security contributions as a consequence. Please see Appendix A for further details. Please be aware that in order to calculate the relevant values, certain foreign exchange rates as at the relevant dates may need to be applied (please see Appendix A for further detail).

Options

If you hold an Option that can be exercised prior to December 24, 2018 (or such later date as may be notified to you), you can either:

- (i) accept the Cancellation Proposal by doing nothing. This means your Option (if it remains outstanding on Court Sanction) will be cancelled on Court Sanction in accordance with the terms of the Baxalta Exchange Awards. You will, unless your Option is “underwater” (i.e. its strike price is equal to or higher than the market value of a Shire ADS on Court Sanction) be entitled to receive the Cash Consideration less any necessary deductions for tax and social security contributions as a consequence. However, if your Option is “underwater”, your Option will be cancelled without payment of any consideration in accordance with the terms of the Baxalta Exchange Awards. If you accept the Cancellation Proposal, you will not be eligible to participate in the Scheme in respect of any Shire ADSs subject to your Option. Please see Appendix A for further details. Please be aware that in order to calculate the relevant values, certain foreign exchange rates as at the relevant dates may need to be applied (please see Appendix A for further detail);
or

- (ii) exercise your Option prior to 4p.m. (Eastern Time) on December 24, 2018 by logging onto www.etrade.com, and electing to exercise your Option and thus receive Shire ADSs, less any necessary deductions for tax and social security contributions. You will be contacted if this deadline changes. As always, you will then be required to sell your Shire ADSs. Consequently, you will not receive the Cash Consideration nor will you be able to participate in the Scheme, and this decision will be irrevocable.

Please be aware that you can only exercise your Option if it is or becomes exercisable prior to December 24, 2018 (or such later deadline as may be notified to you). If your Option is not and does not become exercisable prior to December 24, 2018 (or such later date as may be notified to you), but remains outstanding at Court Sanction, you will be treated as though you accepted the Cancellation Proposal.

All Baxalta Awards

If the Acquisition does not happen for any reason and (if you hold an Option) you do not exercise your Option, your Baxalta Awards will continue as normal, subject to the terms of the Baxalta Exchange Awards – this means they will not be cancelled but will continue to be exercisable or vest on the timetable notified to you at grant. However, if you do choose to exercise an Option, you will not be able to revoke such exercise i.e. your exercise will be effective and you will receive Shire ADSs.

A detailed explanation of the way in which your Baxalta Awards will be affected is set out in Appendix A to this letter.

Attachments to this letter

The following are provided as attachments to this letter:

- Appendix A explaining how the Acquisition affects Baxalta Awards;
- Appendix B explaining some key definitions.

What do you need to do?

1. You should read the enclosed Appendices.
2. If you either hold RSUs, Options that will not be exercisable prior to December 24, 2018 (or such later date as may be notified to you), or you wish to accept the Cancellation Proposal, you do **not** need to do anything for your Baxalta Awards to be cancelled and to receive the Cash Consideration. This will happen automatically, and you will receive the Cash Consideration payment within a month following Court Sanction, less any necessary deductions for tax and social security contributions.
3. If you do hold Options that you are able to, or become able to, exercise prior to December 24, 2018 (or such later deadline as may be notified to you) and wish to do so, you may do so in the usual manner via your E*TRADE account until 4p.m. (Eastern Time) on December 24, 2018. You will be required to sell any Shire ADSs received as a result of such exercise in the usual manner.

What if you have questions?

If you have any questions that relate to your Baxalta Awards or the Proposals, please refer to the FAQs that can be found on your E*TRADE account portal. If these do not answer your question, please contact the general helpline number set out on the last page of the FAQs. Please note that

no legal, tax or financial advice on the merits of the Acquisition or its effect on your Baxalta Awards or your choices can be provided.

You are strongly advised to seek your own independent financial and/or tax advice regarding your personal circumstances and the effect of the Acquisition in relation to your Baxalta Awards.

Important notes

The Shire Board, which has been so advised by Citi, Goldman Sachs and Morgan Stanley, considers the terms of the Proposal described in this letter and its Appendices to be fair and reasonable in the context of the Acquisition. In providing their advice to the Shire Board, Citi, Goldman Sachs and Morgan Stanley have taken into account the commercial assessments of the Shire Board. Citi, Goldman Sachs and Morgan Stanley are providing independent financial advice to the Shire Board for the purposes of Rule 3 of the City Code on Takeovers and Mergers.

The Shire Board recommends that you either exercise your Options or accept the Cancellation Proposal. If you hold Options, you should consider your own personal circumstances, including your tax position, when deciding your preferred timing for exercising your Options and whether you wish to exercise your Options.

Nothing in this letter and its Appendices constitutes financial advice to any holder of shares, share awards or share options in Shire or Takeda.

If there is a conflict between the information in this letter and appendices and the terms of the Baxalta Exchange Awards or any relevant legislation, the terms and the legislation will prevail.

Yours faithfully



Joanne Cordeiro
Chief Human Resources Officer

For and on behalf of
Shire plc

Yours faithfully



Padma Thiruvengadam
Chief Human Resources Officer

For and on behalf of
Takeda Pharmaceutical Company Limited

Appendix A

Impact of the Acquisition on Baxalta Awards

1. The impact on your Baxalta Awards

As part of the Acquisition, the Court will sanction the Scheme on a date known throughout this letter as **Court Sanction**. This date is not the date on which the Acquisition will be completed. The Acquisition is currently due to complete a few days after “Court Sanction” on the **Effective Date**. Please see the timetable below for further detail.

Restricted Stock Units (RSUs)

As a result of the Acquisition, any RSUs that are outstanding on Court Sanction will be cancelled on Court Sanction in accordance with the terms of the Baxalta Exchange Awards. You will be entitled to receive the Cash Consideration less any necessary deductions for tax and social security contributions as a consequence. Please be aware that in order to calculate the relevant values, certain foreign exchange rates as at the relevant dates may need to be applied (please see below for further detail).

The Cash Consideration is a cash amount equal to the market value of the aggregate of the Shire ADSs you would have been entitled to had your RSU vested in full on Court Sanction. This value is calculated as the higher of: (i) the value of USD90.99 in cash; and 5.034 Takeda ADSs (calculated by reference to the mid-market closing price of a Takeda ADS on the New York Stock Exchange or, if not listed on the New York Stock Exchange at the relevant time, on the relevant over-the-counter market, in either case on Court Sanction), on Court Sanction; and (ii) the average closing middle market Shire ADS price over the 30 calendar days prior to Court Sanction. This will be paid to you by E*TRADE within one month of Court Sanction in USD (unless you otherwise elect within your E*TRADE account to receive the proceeds in an alternative currency – this may mean certain fees are also deducted from payments made to you as per normal practice).

Please be aware that if you receive the Cash Consideration, the following currency exchange rates will be used:

- in respect of determining the value of the Court Sanction Deal Consideration and the Cash Consideration, the Bloomberg rate as at close on Court Sanction; and
- in respect of converting the value of any payment into the relevant currency, the currency exchange rate as determined by E*TRADE using their standard process.

Please be aware that if your RSU vests before Court Sanction, your resulting Shire ADSs will, unless you sell them, be subject to the Scheme and you will receive the consideration set out in *What are the terms of the Acquisition for Shire Shareholders?* (see above).

Options

If you hold an Option that can be exercised prior to December 24, 2018 (or such later deadline as may be notified to you), you can:

- (i) accept the Cancellation Proposal by doing nothing. This means your Option (if it remains outstanding on Court Sanction) will be cancelled on Court Sanction in accordance with the terms of the Baxalta Exchange Awards. You will, unless your Option is “underwater” (i.e. its strike price is equal to or higher than the

market value of a Shire ADS on Court Sanction) be entitled to receive the Cash Consideration less any necessary deductions for tax and social security contributions as a consequence.

- a. The Cash Consideration is a cash amount equal to the market value of the aggregate of the Shire ADSs you would have been entitled to had your Option been exercised on Court Sanction. This value is calculated as the higher of:
(i) the value of USD90.99 in cash; and 5.034 Takeda ADSs (calculated by reference to the mid-market closing price of a Takeda ADS on the New York Stock Exchange or, if not listed on the New York Stock Exchange at the relevant time, on the relevant over-the-counter market, in either case on Court Sanction), on Court Sanction; and (ii) the average closing middle market Shire ADS price over the 30 calendar days prior to Court Sanction.
 - b. However, if your Option is “underwater”, your Option may be cancelled without payment of any consideration in accordance with the terms of the Baxalta Exchange Awards. If you accept the Cancellation Proposal, you will not be eligible to participate in the Scheme in respect of any Shire ADSs subject to your Option; or
- (ii) elect to exercise your Option prior to 4p.m. (Eastern Time) on December 24, 2018 (or such later deadline as may be notified to you) and receive Shire ADSs (less any deductions for tax and social security contributions) which will then be sold on your behalf in the usual manner. You will not receive the Cash Consideration nor will you be able to participate in the Scheme. You may exercise your Option by logging onto www.etrade.com until the earlier of any lapse date previously communicated to you and 4p.m. (Eastern Time) on December 24, 2018 (or such later deadline as may be notified to you).

Please remember that if your Option is not and does not become exercisable prior to December 24, 2018 (or such later deadline as may be notified to you), but remains outstanding at Court Sanction, you will be treated as though you accepted the Cancellation Proposal.

If you receive the Cash Consideration, the following currency exchange rates will be used:

- in respect of determining the value of the Court Sanction Deal Consideration and the Cash Consideration, the Bloomberg rate as at close on Court Sanction; and
- in respect of converting the value of any payment into the relevant currency, the currency exchange rate as determined by E*TRADE using their standard process.

Shire and Takeda cannot give you investment advice. If you are in any doubt about the action you should take, you should consult your stockbroker, bank manager, solicitor, accountant or other independent legal or financial adviser, who (where relevant) is authorised and appropriately regulated under the Financial Services and Markets Act 2000, or an appropriately authorised financial adviser if you are in a territory outside the UK.

2. Expected timeline of principal events

The dates given below are indicative only and are based on Shire’s and Takeda’s current expectations as to the earliest possible date on which such events may occur, and may be subject to change. These dates will depend on various different factors. You will be contacted if any deadline for exercising your Options changes.

Date	Event
December 5, 2018	Shire Shareholder meetings to approve the Scheme; and Takeda Shareholder meetings to approve the issue of shares in connection with the Acquisition.
4p.m. (Eastern Time), December 24, 2018	Last date by which any Options that are exercisable may be exercised with any resulting Shire ADSs being sold.
January 3, 2019 (the expected Court Sanction)	All outstanding Baxalta Awards are cancelled in return for the Cash Consideration.
January 8, 2019 (the expected Effective Date)	Scheme becomes effective and the Acquisition completes.
February 3, 2019	Last date by which any Cash Consideration payments which become due to participants on Court Sanction are expected to be made.

Appendix B

A brief explanation of some definitions

“Baxalta Award” means an award granted under the Baxalta Exchange Awards in the form of either a Restricted Stock Unit or an Option;

“Baxalta Exchange Awards” means the Baxalta Incorporated 2015 Incentive Plan and the Governing Terms of the Substitute Awards;

“Cancellation Proposal” means the determination by Shire in accordance with the terms of the Baxalta Exchange Awards that participants holding a Baxalta Award outstanding on Court Sanction will have their Baxalta Award cancelled in return for the Cash Consideration (if such Baxalta Award is not an Option with a strike price equal to or greater than the value of the Cash Consideration);

“Cash Consideration” means an amount in cash per Shire ADS equal to the market value of a Shire ADS on Court Sanction, calculated as the higher of: (i) the value of the Court Sanction Deal Consideration; and (ii) the average closing middle market Shire ADS price over the 30 calendar days prior to Court Sanction;

“Court” means the Royal Court of Jersey;

“Court Sanction” means the date on which the Court sanctions the Scheme under Article 125 of the Companies (Jersey) Law 1991;

“Court Sanction Deal Consideration” means the value of USD90.99 in cash; and 5.034 Takeda ADSs (calculated by reference to the mid-market closing price of a Takeda ADS on the New York Stock Exchange or, if not listed on the New York Stock Exchange at the relevant time, on the relevant over-the-counter market, in either case on Court Sanction), on Court Sanction;

“Effective Date” means the date on which the Scheme becomes effective in accordance with its terms;

“New Takeda Shares” means the new allotted and issued and fully paid ordinary shares in the capital of Takeda, proposed to be issued to Shire Shareholders in connection with the Acquisition;

“Option” means an award granted under the terms of the Baxalta Exchange Awards in the form of an option;

“Proposal” means Takeda’s endorsement of the Cancellation Proposal being the proposal made by Takeda for the purpose of Rule 15 of the City Code on Takeovers and Mergers;

“RSU” means an award granted under the terms of the Baxalta Exchange Awards in the form of a restricted stock unit;

“Scheme” means the procedure by which Takeda will become the holder of the entire issued and to be issued ordinary share capital of Shire;

“Scheme Document” means the document setting out the terms of the Scheme dated November 12, 2018 sent to Shire Shareholders;

“Scheme Record Time” means the time and date specified as such in the Scheme Document or such later time as Shire and Takeda may agree;

“Shire” means Shire plc;

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

“Shire Board” means the board of directors of Shire;

“Shire Deposit Agreement” means the deposit agreement, 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 Directors” means the directors of Shire as at the date of this letter;

“Shire Group” means Shire and its subsidiaries and subsidiary undertakings from time to time;

“Shire Shareholders” means holders of Shire Shares;

“Shire Shares” means ordinary shares of 5p each in the capital of Shire;

“Takeda” means Takeda Pharmaceutical Company Limited;

“Takeda ADSs” means American Depositary Shares, each of which will represent 0.5 allotted and issued and fully paid ordinary shares in the capital of Takeda;

“Takeda Group” means Takeda and its subsidiaries and subsidiary undertakings from time to time; and

“Takeda Shares” means the shares of common stock of no par value in the capital of Takeda in the capital of Takeda.

The distribution of this document (in whole or in part) in jurisdictions other than the United Kingdom may be restricted by the laws of those jurisdictions and therefore persons into whose possession this document comes should inform themselves about and observe any such restrictions. Failure to comply with any such restrictions may constitute a violation of the securities laws of any such jurisdiction.

Citigroup Global Markets Limited ("**Citi**"), which is authorised by the Prudential Regulation Authority ("**PRA**") and regulated by the Financial Conduct Authority ("**FCA**") and the PRA in the United Kingdom, is acting exclusively as financial adviser to Shire and no one else in connection with the Acquisition and will not be responsible to anyone other than Shire for providing the protections afforded to clients of Citi, or for providing advice in connection with the Acquisition or any matter referred to herein (including the Proposal). Neither Citi nor any of its subsidiaries, branches or affiliates owes or accepts any duty, liability or responsibility whatsoever (whether direct or indirect, whether in contract, in tort, under statute or otherwise) to any person who is not a client of Citi in connection with the Acquisition.

Citi has given and not withdrawn its written consent to the issue of this document with the inclusion of references to its name in the form and context in which they are included.

Goldman Sachs International ("**Goldman Sachs**"), which is authorised by the PRA and regulated by the FCA and the PRA in the United Kingdom, is acting exclusively as financial adviser to Shire and no one else in connection with the Acquisition and will not be responsible to anyone other than Shire for providing the protections afforded to clients of Goldman Sachs or for providing advice in connection with the Acquisition or the Proposal described in this document. Neither Goldman Sachs nor any of its subsidiaries, branches or affiliates owes or accepts any duty, liability or responsibility whatsoever (whether direct or indirect, whether in contract, in tort, under statute or otherwise) to any person who is not a client of Goldman Sachs in connection with the Acquisition or the Proposal described in this document.

Goldman Sachs has given and not withdrawn its written consent to the issue of this document with the inclusion of references to its name in the form and context in which they are included.

Morgan Stanley & Co. International plc ("**Morgan Stanley**"), which is authorised by the PRA and regulated by the FCA and the PRA in the United Kingdom, is acting exclusively as financial adviser to Shire and no one else in connection with the Acquisition and will not be responsible to anyone other than Shire for providing the protections afforded to clients of Morgan Stanley or for providing advice in connection with the Acquisition or the Proposal described in this document. Neither Morgan Stanley nor any of its subsidiaries, branches or affiliates owes or accepts any duty, liability or responsibility whatsoever (whether direct or indirect, whether in contract, in tort, under statute or otherwise) to any person who is not a client of Morgan Stanley in connection with the Acquisition or the Proposal described in this document..

Morgan Stanley has given and not withdrawn its written consent to the issue of this document with the inclusion of references to its name in the form and context in which they are included.

This document does not constitute, and may not be used for the purposes of, an offer to sell or an invitation or the solicitation of an offer to subscribe for or buy, any securities by any person in any jurisdiction (a) in which such offer or invitation is not authorised, (b) in which the person making such offer or invitation is not qualified to do so, or (c) in which, or to any person to whom, it is unlawful to make such offer, solicitation or invitation or where the making of such offer, solicitation or invitation would impose any unfulfilled registration, qualification, publication or approval requirements on Shire, Takeda or any of their respective directors, officers, agents,

affiliates and advisers. No action has been taken nor will be taken in any jurisdiction by any such person that would permit a public offering of any securities in any jurisdiction where action for that purpose is required, nor has any such action been taken with respect to the possession or distribution of this document other than in any jurisdiction where action for that purpose is required. Neither Shire nor Takeda nor their respective directors, officers, agents, affiliates or advisers accept any responsibility for any violation of any of these restrictions by any other person.

The Shire Directors, whose names are set out in Paragraph 2.1 of Part VIII of the Scheme Document, accept responsibility for the information contained in this letter (including, without limitation, all information in respect of Shire which had been incorporated by reference in this document), except for that information for which the Takeda Directors accept responsibility. To the best of the knowledge and belief of the Shire Directors (who have taken all reasonable care to ensure that such is the case), the information contained in this letter for which it is responsible is in accordance with the facts and does not omit anything likely to affect the import of such information.

The Takeda Directors, whose names are set out in Paragraph 2.2 of Part VIII of the Scheme Document, accept responsibility for the information contained in this letter relating to the Takeda Group (including, without limitation, all information in respect of the Takeda Group which has been incorporated by reference in this document) and the Takeda Directors, their close relatives, related trusts and other connected persons and persons acting in concert with Takeda. To the best of the knowledge and belief of the Takeda Directors (who have taken all reasonable care to ensure that such is the case), the information contained in this letter for which they are responsible is in accordance with the facts and does not omit anything likely to affect the import of such information.