

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 Shire Long Term Incentive Plan 2015 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 May 8, 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 Shire Long Term Incentive Plan 2015 (the "**LTIP**" and such awards being "**LTIP Awards**") and the decisions you need to make.

Please read everything in this letter and its Appendices. **Their contents are very important.** If you hold an award in the form of a Stock Appreciation Right granted under the LTIP (a "**SAR**"), you should log onto your EquatePlus account and make a pre-election under your TASK section in respect of your SARs by no later than 4p.m. (Eastern time) on December 24, 2018 if you would like to receive cash in lieu of Shire Shares/Shire ADSs in the earliest possible timeframe. You will be contacted if this deadline changes.

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 Shares at the Scheme Record Time will be entitled to receive, for each Shire Share they own:

- **USD30.33 in cash**; and
- either **0.839 New Takeda Shares** OR **1.678 Takeda ADSs**,

A person who holds Shire ADSs will instead be entitled to receive, for each Shire ADS they own:

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

Please note that a Shire ADS is equal to three Shire Shares. This means the cash payment for one Shire ADS is three times the amount payable for one Shire Share. Similarly, the amount of Takeda ADSs receivable are three times those that a person holding Shire Shares could potentially receive.

Please note that the above sets out what Shire Shareholders and 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 Shares and/or 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 LTIP Awards?

The Acquisition will affect different types of LTIP Awards differently. Please read the section(s) relevant to you below.

Restricted Stock Units (RSUs)

Normally, your RSUs would vest according to the timetable notified to you at grant.

However, as a result of the Acquisition, your RSUs will automatically vest on Court Sanction subject to time-based proration, and will include any dividend equivalents accrued to that date.

To the extent your RSU vests, you will be entitled to receive the RSU/PSU Cash Consideration less any necessary deductions for tax and social security contributions. Please see Appendix A for further details.

To the extent your RSU does not vest, it will be forfeited on Court Sanction but you may become eligible for a Transition Award (see *All LTIP Awards* and Appendix A).

Stock Appreciation Rights (SARs)

Please be aware that if you hold a SAR, you will need to take certain actions to realize value from it as this will NOT happen automatically.

Where your SARs are exercisable prior to Court Sanction

If you are already able, or will become able, to exercise your SARs prior to Court Sanction, your SARs will, subject to the rules of the LTIP, remain exercisable until the earlier of any lapse date specified in your EquatePlus account, and the date falling 60 days from Court Sanction.

You will have 4 choices:

1. You can exercise your SARs in the normal course prior to Court Sanction until 4p.m. (Eastern Time) on December 24, 2018 (or such later date as may be notified to you) (following which a blackout period will commence) and receive Shire Shares/Shire ADSs (as relevant), less any necessary deductions for tax and social security contributions. You will then be treated like any other Shire Shareholder, meaning that any Shire Shares or Shire ADSs acquired on exercise and not subsequently sold by you will be acquired by Takeda on completion of the Acquisition for the consideration set out in *What are the terms of the Acquisition for Shire Shareholders?* above. The Proposals set out in this letter will not be available to you. You will not be able to exercise your SARs prior to Court Sanction if they become exercisable during the trading blackout period but you can make a pre-election to exercise on Court Sanction (see 2 below).
2. You can pre-elect to exercise your SARs on Court Sanction and receive either the SAR Sanction Cash Consideration for each Shire Share/Shire ADS you would have been entitled to or, if your SARs are “underwater” on Court Sanction (see below) the Compensation Payment, in each case less any necessary deductions for tax and social security contributions. Please see Appendix A for further details.
3. You can wait and exercise your SARs after Court Sanction and receive the SAR Post-Sanction Cash Consideration for each Shire Share/Shire ADS you would have been entitled to, less any necessary deductions for tax and social security contributions. You will not be eligible to receive the Compensation Payment if your SARs are “underwater” as this is only available to those who pre-elect to exercise under choice 2 above. Please see Appendix A for further details.
4. You can do nothing. Your SARs will lapse on the earlier of any lapse date specified in your EquatePlus account, and the date falling 60 days from Court Sanction, and you will receive no consideration for them. This applies regardless of whether you have previously been told that your SARs will lapse on a later date. The Proposals set out in this letter will not be available to you.

Where your SARs will not be or become exercisable prior to Court Sanction

Normally, your SARs would vest in full and become exercisable on the timetable notified to you at grant. However, as a result of the Acquisition, your SARs will vest on Court Sanction subject to time-based proration. Please see Appendix A for further details.

To the extent your SARs vest on Court Sanction, you will have 3 choices:

1. You can pre-elect to exercise your SARs on Court Sanction and receive either the SAR Sanction Cash Consideration for each Shire Share/Shire ADS you would have been entitled to or, if your SARs are “underwater” on Court Sanction (see below) the Compensation Payment, in each case less any necessary deductions for tax and social security contributions. Please see Appendix A for further details.
2. You can wait and exercise your SARs after Court Sanction and receive the SAR Post-Sanction Cash Consideration for each Shire Share/Shire ADS you would have been entitled to, less any necessary deductions for tax and social security contributions. You will not be eligible to receive the Compensation Payment if your SARs are underwater as this is only available to those who pre-elect to exercise under choice 1 above. Please see Appendix A for further details.
3. You can do nothing. Your SARs will, unless they lapse earlier under the rules of the LTIP, lapse on the date falling 60 days from Court Sanction and you will receive no consideration for them. The Proposals set out in this letter will not be available to you.

To the extent your SARs do not vest, they will be forfeited on Court Sanction but you may become eligible for a Transition Award (see *All LTIP Awards* and Appendix A).

Performance Share Units (PSUs)

Normally, your PSUs would vest on the third anniversary of grant, subject to satisfaction of performance conditions.

However, as a result of the Acquisition, your PSUs will vest on Court Sanction, subject to time-based proration and the Shire Remuneration Committee’s determination as to the extent to which performance conditions are satisfied as at that date, and will include any dividend equivalents accrued to that date. Shire has agreed with Takeda that the current performance conditions may, in line with the rules of the LTIP, be amended. You will be contacted shortly after the date of this letter with confirmation of the extent to which such performance conditions have been met.

To the extent your PSU vests, you will be entitled to receive the RSU/PSU Cash Consideration less any deductions for tax and social security contributions. Please see Appendix A for further details.

To the extent your PSU does not vest, it will be forfeited on Court Sanction but you may become eligible for a Transition Award.

All LTIP Awards

Following completion of the Acquisition, Takeda has agreed that it will grant a cash award to each participant whose award is unvested and will be forfeited due to time-based pro-ration, over the value of such forfeited award (in the case of PSUs, after performance assessment has been applied) on the condition that the participant is still employed by the Shire Group on the date of Court Sanction (the “**Transition Award**”). Please see Appendix A for further details.

If the Acquisition does not happen for any reason, your LTIP Awards will continue as normal – this means they will vest, subject to the rules of the LTIP and, in the case of PSUs, subject to performance conditions, on the timetable notified to you at grant and you will not receive a Transition Award. However, if you do choose to exercise your SARs (other than by way of a pre-election to exercise on Court Sanction), you will not be able to revoke such exercise i.e. your exercise will be effective and you will receive Shire Shares/Shire ADSs.

A detailed explanation of the way in which your LTIP 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 LTIP Awards and, if you hold SARs, what you have to do.
- Appendix B explaining some key definitions.

What do you need to do?

1. You should read the enclosed Appendices.
2. If you hold RSUs or PSUs, you do **not** need to do anything for your LTIP Awards to vest and to receive the RSU/PSU Cash Consideration. This will happen automatically, and you will receive the RSU/PSU Cash Consideration payment from Equatex within the month following the Court Sanction, less any necessary deductions for tax and social security contributions.
3. If you hold SARs that are or become exercisable prior to Court Sanction and wish to exercise them prior to Court Sanction, you should log onto your EquatePlus account and exercise your SARs in the normal way until 4p.m. (Eastern Time) on December 24, 2018. You will be contacted if this deadline changes. You will not be able to exercise your SARs prior to Court Sanction if they become exercisable during the trading blackout period but can make a pre-election to exercise (see below).
4. If you hold SARs and wish to pre-elect to exercise them on Court Sanction, then you should log onto your EquatePlus account and complete your pre-election to exercise your SARs, located in the TASK section of your EquatePlus account. Your pre-election to exercise your SARs must be completed by no later than 4p.m. (Eastern Time) on December 24, 2018. You will receive the SAR Sanction Cash Consideration payment for each Shire Share/Shire ADS you would have been entitled to (or, if your SAR is underwater, the Compensation Payment) from Equatex within one month of Court Sanction, in each case less any necessary deductions for tax and social security contributions. You will be contacted if this deadline changes.
5. If you hold SARs and wish to exercise them after Court Sanction, you will be able to do so by logging onto your EquatePlus account and completing your election to exercise under the SAR tile of your EquatePlus account after Court Sanction. If you wish to exercise your SAR after Court Sanction, you will need to wait until after the blackout period has ended, post Court Sanction (please see Appendix A). Please do **not** attempt to make an election or pre-election now or before Court Sanction. You will receive the SAR Post-Sanction Cash Consideration payment for each Shire Share/Shire ADS you would have been entitled to from Equatex within one month of exercise, less any necessary deductions for tax and social security contributions.

What if you have questions?

If you have any questions that relate to your LTIP Awards, what your choices are or how to complete your pre-election to exercise your SARs within your EquatePlus account, please refer to the FAQs that can be found in your EquatePlus account as well as the Shire HRConnect 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 LTIP 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 LTIP Awards.

Important notes

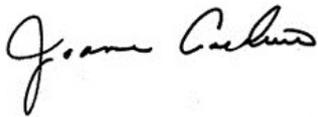
The Shire Board, which has been so advised by Citi, Goldman Sachs and Morgan Stanley, considers the terms of the Proposals described in this letter and its Appendices to be fair and reasonable in the context of the Acquisition. In providing their advice to the Shire Board, Citi, Goldman Sachs and Morgan 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 if you hold SARs, you exercise these before they lapse. If you hold SARs, you should consider your own personal circumstances, including your tax position, when deciding your preferred timing for exercising your SARs.

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 rules of the LTIP or any relevant legislation, the rules 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 LTIP Awards

1. The impact on your LTIP 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.

As a result of the Acquisition, your LTIP Awards, to the extent not already vested, will vest on Court Sanction, subject to the Shire Remuneration Committee’s determination as to, in the case of PSUs, whether performance conditions are satisfied as at Court Sanction and, in the case of all LTIP Awards, application of the following time-based proration formula:

- where between two and three years of the vesting period remain at Court Sanction, your LTIP Award will, subject to satisfaction of any applicable performance conditions, vest as to one-third of the amount of Shire Shares or Shire ADSs subject to the LTIP Award;
- where between one and two years of the vesting period remain your LTIP Award will, subject to satisfaction of any applicable performance conditions, vest as to two-thirds of the amount of Shire Shares or Shire ADSs subject to the LTIP Award; and
- where one year or less of the vesting period remains at Court Sanction, your LTIP Award will vest in full (though the extent to which PSUs vest will remain subject to satisfaction of performance conditions).

Please note that if your LTIP Award vests in tranches, the above formula applies independently in respect of each tranche. A chart demonstrating the above will be set out in the FAQs that can be found in your EquatePlus account.

To the extent an LTIP Award does not vest, it will be forfeited on Court Sanction. However, Takeda has agreed that it will grant a cash award to each participant whose award is forfeited due to time-based proration (in the case of PSUs, after performance assessment has been applied) on the condition that the participant is still employed by the Shire Group on the date of Court Sanction (the “**Transition Award**”). Please see below for further details.

If the Acquisition does not happen for any reason, all of your LTIP Awards will continue as normal, subject to the rules of the LTIP.

RSUs/PSUs

If you hold RSUs or PSUs that vest on Court Sanction then, in accordance with the rules of the LTIP, in lieu of the Shire Shares or Shire ADSs to which you would normally have been entitled (which would include any dividend equivalents accrued at Court Sanction), the Shire Remuneration Committee has determined that you will receive the RSU/PSU Cash Consideration for each Shire Share/Shire ADS you would have been entitled to, less any necessary deductions for tax and social security contributions. This is a cash amount equal to the market value of each Shire Share or Shire ADS you would have been entitled to on Court Sanction. This value is calculated as the higher of: (i) USD30.33 in cash; and the value of 0.839 Takeda Shares (if your SAR is over Shire Shares); or USD90.99 in cash; and 5.034 Takeda ADSs (if your SAR is over Shire ADSs), each on the Court Sanction date; and (ii) the average closing middle market Shire Share or Shire ADS (as relevant) price over the 30 calendar days prior to Court Sanction. This

will be paid to you by Equatex within one month of Court Sanction, less any necessary deductions for tax and social security contributions.

Please be aware that in order to calculate the relevant values, certain foreign exchange rates on the relevant dates may need to be applied (see below).

SARs

Exercising prior to Court Sanction

If you already are able, or will become able, to exercise your SARs prior to Court Sanction, and wish to exercise your SAR in the normal course prior to Court Sanction, you may do so within your EquatePlus account until the earlier of any lapse date specified in your EquatePlus account and 4p.m. (Eastern Time) on December 24, 2018. You will be treated like any other Shire Shareholder, meaning that any Shire Shares or Shire ADSs acquired on exercise and not subsequently sold by you will be acquired by Takeda on completion of the Acquisition for the consideration set out in the main body of this letter. The Proposals set out in this letter will not be available to you. You will be contacted if this deadline changes. Please be aware that there will be a trading blackout period before Court Sanction and you will not be able to exercise your SARs prior to Court Sanction if they become exercisable during this time (see the current expected timetable below) though you will be able to make a pre-election.

If you decide to exercise prior to Court Sanction, your decision will be irrevocable.

Exercising on or after Court Sanction

Regardless of whether your SAR is or becomes exercisable prior to Court Sanction, and provided that it has not lapsed prior to Court Sanction, you may (unless your SAR is due to lapse earlier) make a pre-election to exercise on Court Sanction by logging onto your EquatePlus account and pre-electing to exercise your SARs under your TASK section. Your pre-election to exercise your SARs must be completed by no later than 4p.m. (Eastern Time) on December 24, 2018 (or such later deadline as may be notified to you). The consideration you receive will depend on the strike price of your SAR compared to the value of the underlying Shire Shares/Shire ADSs on Court Sanction:

- if the strike price of your SAR is less than the value per Shire Share/Shire ADS of the SAR Sanction Cash Consideration then you will receive a cash amount equal to the SAR Sanction Cash Consideration in lieu of each Shire Share/Shire ADS you would have been entitled to, less any necessary deductions for tax and social security contributions. The SAR Sanction Cash Consideration is a cash amount equal to the market value of each Shire Shares or Shire ADS you would have been entitled to on Court Sanction. This value is calculated as the higher of: (i) USD30.33 in cash; and the value of 0.839 Takeda Shares (if your SAR is over Shire Shares); or USD90.99 in cash; and 5.034 Takeda ADSs (if your SAR is over Shire ADSs), each on the Court Sanction date; and (ii) the average closing middle market Shire Share or Shire ADSs (as relevant) price over the 30 calendar days prior to Court Sanction (a sample calculation of how your SARs will be valued will be outlined in the FAQs); and
- if the strike price of your SAR means your SAR is “underwater” i.e. the strike price is equal to or more than the value per Shire Share/Shire ADS of the SAR Sanction Cash Consideration, then you will not receive the SAR Sanction Cash Consideration as your SARs would be of nil value, nor will you be eligible for a Transition Award. Instead, Shire (with Takeda’s consent) has agreed that you will receive a cash amount for each Shire

Share/Shire ADS subject to the SAR (without any reduction to reflect time-based proration) equal to approximately 10% (or such other percentage as Shire may determine) of the strike price (the “**Compensation Payment**”), less any necessary deductions for tax and social security contributions. A sample calculation will be set out in the FAQs. **If you pre-elect to exercise your SAR on Court Sanction and your SAR is underwater on Court Sanction, you will agree to cancel the relevant SAR in return for the Compensation Payment. This means you will have no further entitlement under your SAR on and from Court Sanction.**

If you believe your SAR will have a strike price that is equal to or more than the value of the SAR Sanction Cash Consideration and do not wish to receive the Compensation Payment described above, or if you otherwise do not wish to exercise your SAR on or before Court Sanction, you may choose to wait. You will have until the earlier of your normal lapse date (as specified in your EquatePlus account) and the date falling 60 days from Court Sanction to exercise your SAR using your EquatePlus account, following which your SAR will lapse (but please be aware that Shire will impose a trading blackout period after Court Sanction, during which you will not be able to exercise your SARs (see the current expected timetable below)). Please be aware that if you do exercise your SAR after Court Sanction, the Shire Remuneration Committee has determined that you will receive the SAR Post-Sanction Cash Consideration in lieu of each Shire Share/Shire ADS you would have been entitled to, in lieu of Shire Shares or Shire ADSs (as relevant). The SAR Post-Sanction Cash Consideration is a cash amount equal to the market value of each Shire Share or Shire ADS you would have been entitled to on the date of exercise, less any necessary deductions for tax and social security contributions. This value is calculated as: (i) USD30.33 in cash; and 0.839 New Takeda Shares (if your SAR is over Shire Shares); or (ii) USD90.99 in cash; and 5.034 Takeda ADSs (if your SAR is over Shire ADSs) – this is not calculated on the same basis as the SAR Sanction Cash Consideration. Please see the definition in Appendix B for further information.

Currency exchange rates and currencies

Other than participants in Argentina and Brazil (who will receive any cash proceeds in USD), all cash proceeds paid under the Proposals will be paid in your local currency, provided Equatex supports your country’s currency and subject to any restrictions on payments by third parties. You will be contacted if you will not be able to receive the proceeds in your local currency.

The following currency exchange rates will be used:

- in respect of determining the value of the Court Sanction Deal Consideration, the RSU/PSU Cash Consideration and the SAR Sanction Cash Consideration, the Bloomberg rate as at close on Court Sanction;
- in respect of determining the value of the SAR Post-Sanction Cash Consideration, the Bloomberg rate as at close on the day prior to exercise; and
- in respect of converting the value of any payment into your local currency, the currency exchange rate as determined by Equatex using their standard process.

Transition Awards

To the extent your LTIP Award is forfeited as a result of time-based proration and it was not eligible for the Compensation Payment, Takeda has agreed to grant you a cash award equivalent to the value of the LTIP Award that was forfeited due to time-based proration (after performance assessment) on the condition that you are still employed by the Shire Group on the date of Court

Sanction. The value of the forfeited award will be calculated per Shire Share/Shire ADS as the higher of: (i) the value of the Court Sanction Deal Consideration; and (ii) the average closing middle market Shire Share or Shire ADSs (as relevant) price over the 30 calendar days prior to Court Sanction. Further details of the terms of such grant will be set out in the relevant grant documentation. However, in outline, the terms will be:

- no performance conditions will apply to your Transition Award as your Transition Award will only be granted to the extent that any performance conditions on your LTIP Award are determined to be satisfied;
- the vesting schedule that would normally apply to your LTIP Awards will apply to the Transition Awards. This means that the Transition Awards will vest on the same date or dates that your LTIP Award would normally have vested on (had the Acquisition not occurred), in the same proportions as those LTIP Awards;
- notwithstanding the above, if your employment is terminated: (i) by your employer for any reason other than for Cause; (ii) due to death or disability; or (iii) by you, for Good Reason, then your Transition Award will vest in full on such termination;
- if your employment is otherwise terminated (other than for Cause) or you resign on or after 12 months from the Effective Date, your Transition Award will vest but shall be reduced to reflect the time between grant of the original LTIP Award and the date of termination of employment; and
- if you leave employment in the 12 months after the Effective Date without a Good Reason, or you are terminated for Cause, your Transition Award will lapse.

In addition, Takeda will maintain the terms of such award until the date on which your Transition Award vests.

2. Leaving Shire before or after Court Sanction

Leaving Shire before Court Sanction (current employees only)

The leaver arrangements under the LTIP will apply in the normal way if you leave Shire before Court Sanction. This means that if you leave employment and do not qualify as a “good leaver” under the LTIP rules, your unvested LTIP Awards will lapse on the date that your employment ceases.

If you leave Shire before Court Sanction as a “good leaver” (for example, because of injury or disability or qualified retirement), your LTIP Award will vest on:

- in respect of RSUs and SARs, the date on which your employment ends (or such later date as the Shire Remuneration Committee may determine); and
- in respect of PSUs, the date on which that PSU would normally vest (which would be Court Sanction if the Acquisition completes as anticipated), subject to performance conditions, unless the Shire Remuneration Committee determine that it will vest on the date on which your employment ends or another later date.

In each case, your LTIP Award will normally be reduced pro rata to reflect the period from your leaving date to the normal vesting date (unless the Shire Remuneration Committee decides otherwise). You will not be eligible for a Transition Award.

Leaving Shire and Takeda after Court Sanction (current employees only)

Other than unexercised SARs, your LTIP Awards will not be affected if you leave employment after Court Sanction because they will have vested or lapsed before you left employment.

Any SARs (whether they vested previously or vest on Court Sanction) that are not exercised on Court Sanction will remain outstanding until the earlier of any lapse date specified in your EquatePlus account and the date falling 60 days from Court Sanction, save that if you leave due to misconduct or breach of the terms of your employment, your SAR will lapse on the date of cessation of employment.

If you are eligible for a Transition Award, please see paragraph 1 above for an explanation of the effects on that Transition Award of leaving employment after Court Sanction.

3. Making your decision – SARs only

If you are able to exercise your SARs prior to Court Sanction and wish to do so, you may do so until 4p.m. (Eastern Time) on December 24, 2018 by logging onto your EquatePlus account and exercising your SAR in the normal way. You will be contacted if this deadline changes.

If you wish to pre-elect to exercise your SAR on Court Sanction and receive the SAR Sanction Cash Consideration for each Shire Share/Shire ADS you would have been entitled to at the earliest opportunity or, if your SAR is underwater, to receive the Compensation Payment, you should log on to your EquatePlus account and complete your pre-election to exercise your SARs which may be found within the TASK section of your EquatePlus account. You must complete your pre-election to exercise your SARs within your EquatePlus account by no later than 4p.m. (Eastern Time) on December 24, 2018. You will be contacted if this deadline changes.

If you wish to exercise your SARs after Court Sanction and receive the SAR Post-Sanction Cash Consideration for each Shire Share/Shire ADS you would have been entitled to, you will be able to do so by logging onto EquatePlus after the blackout period has ended (expected to be on January 13, 2019) and exercising your SARs under the SAR tile in the normal way. Please do not attempt to exercise your SARs now if you wish to exercise after Court Sanction. Please remember that if you do not choose to pre-elect to exercise your SARs on Court Sanction and the strike price of your SARs is, on the date on which you elect to exercise after Court Sanction, equal to or higher than the SAR Post-Sanction Cash Consideration, you will not be entitled to the Compensation Payment.

If you do not exercise your SARs at all, your SARs will lapse on the earlier of the lapse date specified in your EquatePlus account, and the date falling 60 days from Court Sanction.

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.

4. 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 notified if any deadlines change.

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	<p>Last date to exercise vested SARs prior to Court Sanction.</p> <p>If you hold SARs and wish to exercise on Court Sanction, last date that you may pre-elect to exercise your SARs within EquatePlus.</p> <p>This is also the last date on which you may sell your Shire Shares/Shire ADSs held within your EquatePlus account.</p>
December 24, 2018 – January 13, 2019	Blackout period. During this time, you will be restricted from taking certain actions such as exercising your SARs.
January 3, 2019 (the expected Court Sanction)	All LTIP Awards vest, subject to the Shire Remuneration Committee's determination in respect of performance conditions and time-based proration. Value of Transition Awards to be calculated based on this date
January 8, 2019 (the expected Effective Date)	Scheme becomes effective and the Acquisition completes.
February 3, 2019	Last date by which any RSU/PSU Compensation Payment, SAR Sanction Cash Consideration, and Compensation Payment payments which become due to participants on Court Sanction are expected to be made.
March 4, 2019 60 days after Court Sanction	Date on which unexercised SARs will lapse (subject to any earlier lapse date).

Appendix B

A brief explanation of some definitions

“Cause” shall have the meaning prescribed for such term (or such similar term) in any contract of employment applicable to an employee provided such contract of employment was entered into before May 8 2018 and shall mean for any other employee: (A) material breach by the employee of the terms and conditions of the employee’s employment, including but not limited to (i) material breach by the employee of Shire’s or any relevant member of the Takeda Group’s (as applicable) code of business conduct; (ii) material breach by the employee of the employee’s employment contract (if any); (iii) commission by the employee of an act of fraud, embezzlement or theft in connection with the employee’s duties or in the course of the employee’s employment; (iv) wrongful disclosure by the employee of secret processes or confidential information of the Shire Group or the Takeda Group; or (v) failure by the employee to substantially perform the duties of the employee’s employment (other than any such failure resulting from the employee’s disability) provided that any such determination in respect of whether such a failure has occurred must be made on a reasonable basis; or (B) to the extent permitted by applicable law, engagement by the employee, directly or indirectly, for the benefit of the employee or others, in any outside activity, employment or business which is competitive with the Shire Group and/or the Takeda Group;

“Compensation Payment” means the cash payment to be made by Shire (with Takeda’s agreement) to LTIP participants who elect to exercise SARs on Court Sanction where the relevant SAR’s strike price is equal to or greater than the value of the SAR Sanction Cash Consideration, where the payment is calculated as an amount per Shire Share/Shire ADS equal to approximately 10% (or such other percentage as Shire may determine) of the strike price;

“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 (i) USD30.33 in cash; and the value of 0.839 Takeda Shares (calculated by reference to the mid-market closing price of a Takeda Share on Court Sanction) (if your LTIP Award is over Shire Shares); or (ii) USD90.99 in cash; and the value of 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) (if your LTIP Award is over Shire ADSs);

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

“Good Reason” shall have the meaning prescribed for such term (or such similar term) in any contract of employment applicable to an employee provided such contract of employment was entered into before 8 May 2018 and shall mean for any other employee: (i) any material reduction in an employee’s base salary or total variable compensation opportunity, (ii) a relocation in the principal place of an employee’s employment that increases his or her daily commute by more than 50 miles from that immediately prior to the Effective Date; or (iii) any material change in that employee’s role;

“LTIP” means the Shire Long Term Incentive Plan 2015;

“LTIP Award” means a PSU, RSU or SAR, as appropriate;

“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;

“Post-Completion Cash Settlement Determination” means Takeda’s commitment to honour the Shire Remuneration Committee’s determination that SARs exercised after Court Sanction will be settled in cash pursuant to the rules of the LTIP;

“Proposals” means the Compensation Payment, the Post-Completion Cash Settlement Determination and the Transition Awards, being the proposals made by Takeda for the purpose of Rule 15 of the City Code on Takeovers and Mergers;

“PSU” means a Performance Share Unit, being an award in the form of a Restricted Stock Unit granted subject to performance conditions under the LTIP;

“RSU” means an award in the form of a Restricted Stock Unit granted under the LTIP;

“RSU/PSU Cash Consideration” means an amount in cash per Shire Share/Shire ADS equal to the market value of a Shire Share/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 Share or Shire ADSs (as relevant) price over the 30 calendar days prior to Court Sanction;

“SAR” means an award in the form of a Stock Appreciation Right granted under the LTIP;

“SAR Post-Sanction Cash Consideration” means an amount in cash per Shire Share/Shire ADS equal to the market value of a Shire Share/Shire ADS on the relevant date of exercise, calculated as: (i) USD30.33 in cash; and 0.839 New Takeda Shares (calculated by reference to the mid-market closing price of a New Takeda Share on the last day on which such New Takeda Shares were traded falling immediately prior to the date of exercise) (if the SAR is over Shire Shares); or (ii) USD90.99 in cash; and 5.034 Takeda ADSs (calculated by reference to the mid-market closing price of a Takeda ADS on the last day on which such Takeda ADSs were traded falling immediately prior to the date of exercise) (if the SAR is over Shire ADSs);

“SAR Sanction Cash Consideration” means an amount in cash per Shire Share/Shire ADS equal to the market value of a Shire Share/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 Share or Shire ADS (as relevant) price over the 30 calendar days prior to Court Sanction;

“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;

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

“Transition Awards” means the cash awards Takeda has agreed to grant equivalent to the value of the LTIP Awards that lapse due to time proration (after performance assessment) in connection with the Acquisition (as described in Appendix A).

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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.