

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



Court Meeting and Extraordinary General Meeting 2018 Voting Instructions Card

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

A Issues — Shire plc

Court Meeting*

For Against

Resolution

Extraordinary General Meeting**

For Against Abstain

Resolution



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

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

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

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

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

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

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

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

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

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

Signature 1 — Please keep signature within the box.

Signature 2 — Please keep signature within the box.



Court Meeting

To approve the Scheme of Arrangement.

Extraordinary General Meeting

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

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

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

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

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

Court Meeting and Extraordinary General Meeting

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

2018 VOTING INSTRUCTIONS

AMERICAN DEPOSITORY SHARES

Shire plc (the "Company")

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

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

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

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

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

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

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

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

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