

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



Annual General Meeting 2018 - Shire plc

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

A Issues

	Vote		
	For	Against	Withheld
Resolution 1	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 3	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 4	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 5	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 6	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 7	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 8	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Vote		
	For	Against	Withheld
Resolution 9	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 10	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 11	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 12	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 13	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 14	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 15	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 16	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Vote		
	For	Against	Withheld
Resolution 17	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 18	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 19	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Resolution 20	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



B Authorized Signatures — This section must be completed for your vote to be counted — Date and Sign Below

Please sign your name exactly as it appears on the face of this card. When signing in a fiduciary or representative capacity, give full title as such. Where more than one owner, each MUST sign. Voting Instruction Card(s) executed by a corporation should be in full name by a duly authorized officer with full title as such. **Please be sure to sign and date this Voting Instruction Card.**

If this Voting Instruction Card is signed and 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 a "Vote Withheld" voting instruction for such issue.

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

Signature 1 — Please keep signature within the box.

Signature 2 — Please keep signature within the box.

/ /



1 Annual Report and Accounts

To receive the Company's Annual Report and Accounts for the year ended December 31, 2017.

2 Directors' Remuneration Report

To approve the Directors' Remuneration Report, excluding the Directors' Remuneration Policy, set out on pages 78 to 108 of the Annual Report and Accounts for the year ended December 31, 2017.

3 Directors' Remuneration Policy

To approve the Directors' Remuneration Policy, contained within the Directors' Remuneration Report and set out on pages 86 to 95 of the Annual Report and Accounts for the year ended December 31, 2017, to take effect after the end of the Annual General Meeting on April 24, 2018.

Election and re-election of Directors

- 4 To re-elect Olivier Bohuon as a Director.
- 5 To re-elect Ian Clark as a Director.
- 6 To elect Thomas Dittrich as a Director.
- 7 To re-elect Gail Fosler as a Director.
- 8 To re-elect Steven Gillis as a Director.
- 9 To re-elect David Ginsburg as a Director.
- 10 To re-elect Susan Kilsby as a Director.
- 11 To re-elect Sara Mathew as a Director.
- 12 To re-elect Flemming Ornskov as a Director.
- 13 To re-elect Albert Stroucken as a Director.

Auditor

14 To re-appoint Deloitte LLP as the Company's Auditor until the conclusion of the next Annual General Meeting of the Company.

15 To authorize the Audit, Compliance & Risk Committee to determine the remuneration of the Auditor.

16 Authority to allot shares

That the authority to allot Relevant Securities (as defined in the Company's Articles of Association (the "Articles")) conferred on the Directors by Article 10 paragraph (B) of the Articles be renewed and for this purpose the Authorised Allotment Amount shall be:

- (a) £15,187,600.85 of Relevant Securities; and
- (b) solely in connection with an allotment pursuant to an offer by way of a Rights Issue (as defined in the Articles, but only if and to the extent that such offer is implemented by way of rights), £30,375,201.70 of Relevant Securities (after deducting from such limit any Relevant Securities allotted under paragraph (a) above),

and the Allotment Period (as defined in the Articles) shall be the period commencing on April 24, 2018, and ending on the earlier of the close of business on July 23, 2019, and the conclusion of the Annual General Meeting of the Company to be held in 2019, save that the Company may before such expiry make an offer or agreement which would or might require Relevant Securities to be allotted after such expiry and the Directors may allot Relevant Securities pursuant to any such offer or agreement as if the authority conferred hereby had not expired.

17 General authority to disapply pre-emption rights

That, subject to the passing of Resolution 16, the authority to allot equity securities (as defined in the Company's Articles of Association (the "Articles")) wholly for cash conferred on the Directors by Article 10 paragraph (D) of the Articles be renewed and for this purpose the Non Pre-emptive Amount (as defined in the Articles) shall be £2,278,140.10 and the

Allotment Period shall be the period commencing on April 24, 2018, and ending on the earlier of the close of business on July 23, 2019, and the conclusion of the Annual General Meeting of the Company to be held in 2019, save that the Company may before such expiry make an offer or agreement which would or might require equity securities to be allotted after such expiry and the Directors may allot equity securities pursuant to any such offer or agreement as if the authority conferred hereby had not expired.

18 Specific authority to disapply pre-emption rights in connection with an acquisition or specified capital investment

That, subject to the passing of Resolutions 16 and 17 and for the purpose of the authority to allot equity securities (as defined in the Company's Articles of Association (the "Articles")) wholly for cash conferred on the Directors by Article 10 paragraph (D) of the Articles and renewed by Resolution 17, the Non Pre-emptive Amount (as defined in the Articles) shall be increased from £2,278,140.10 to £4,556,280.20 and the Allotment Period shall be the period commencing on April 24, 2018, and ending on the earlier of the close of business on July 23, 2019, and the conclusion of the Annual General Meeting of the Company to be held in 2019, provided that (a) the Company may before such expiry make an offer or agreement which would or might require equity securities to be allotted after such expiry and the Directors may allot equity securities pursuant to any such offer or agreement as if the authority conferred hereby had not expired, and (b) only up to £2,278,140.10 of such increased Non Pre-emptive Amount may be used other than for the purposes of financing (or refinancing, if the authority is to be used within six months after the original transaction) a transaction which the Board of the Company determines to be an acquisition or other capital investment of a kind contemplated by the Statement of Principles on Disapplying Pre-emption Rights most recently published by the Pre-emption Group prior to the date of this notice.

19 Authority to purchase own shares

That the Company be and is hereby generally and unconditionally authorized:

- (a) pursuant to Article 57 of the Companies (Jersey) Law 1991 to make market purchases of Ordinary Shares in the capital of the Company, provided that:
 - (1) the maximum number of Ordinary Shares hereby authorized to be purchased is 91,125,605;
 - (2) the minimum price, exclusive of any expenses, which may be paid for an Ordinary Share is five pence;
 - (3) the maximum price, exclusive of any expenses, which may be paid for an Ordinary Share shall be the higher of:
 - (i) an amount equal to 105% of the average of the middle market quotations for the Company's Ordinary Shares as taken from the London Stock Exchange Daily Official List for the five business days immediately preceding the day on which such shares are contracted to be purchased; and
 - (ii) the higher of the price of the last independent trade and the highest current independent bid on the London Stock Exchange Daily Official List at the time the purchase is carried out;
- (4) the authority hereby conferred shall expire on the earlier of the close of business on July 23, 2019, and the conclusion of the Annual General Meeting of the Company to be held in 2019, save that the Company may make a contract to purchase Ordinary Shares under this authority before the expiry of this authority, which will or may be executed wholly or partly after the expiry of this authority, and may make purchases of Ordinary Shares in pursuance of any such contract as if such authority had not expired; and
- (b) pursuant to Article 58A of the Companies (Jersey) Law 1991, to hold as treasury shares any Ordinary Shares purchased pursuant to the authority conferred by paragraph (a) of this resolution.

20 Notice of general meetings

To approve that a general meeting of the Company, other than an annual general meeting, may be called on not less than 14 clear days' notice.

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Annual General Meeting 2018

The Voting Instruction Card must be completed, signed and received at the indicated address prior to 10:00 A.M. (New York City time) on April 17, 2018 for action to be taken.

2018 VOTING INSTRUCTIONS

Shire plc (the "Company")

AMERICAN DEPOSITARY SHARES

ADS CUSIP No.:	82481R106.
ADS Record Date:	March 22, 2018.
Meeting Specifics:	Annual General Meeting to be held on April 24, 2018 at 2:45 P.M. (Dublin time) at Block 3, Miesian Plaza, 50-58 Baggot Street Lower, Dublin 2, Ireland (the "Meeting").
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 holder, as of the ADS Record Date, of the American Depositary Shares issued under the Deposit Agreement and identified above (the "ADSs"), hereby authorizes and directs the Depository to cause to be voted at the Meeting (and any adjournment thereof) the Deposited Securities represented by the ADSs in the manner indicated on the reverse side hereof. If you want to deliver this Voting Instruction Card by mail, please deliver to Shire plc, c/o Citibank Shareholder Services, PO Box 43099, Providence RI 02940-5000. For a copy of the Annual Report and Accounts for the year ended December 31, 2017 and the Notice of Annual General Meeting 2018, please use the following links <http://investors.shire.com/ar-2017> and <http://www.shire.com/NoticeOfMeeting2018> respectively. If you have any questions regarding the proxy voting process, please contact Citibank, N.A. -ADR Shareholder Services at 1-866-395-6421.

If the Depository does not receive voting instructions from a Holder by 10:00 A.M. (New York City time) on April 17, 2018, such 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 Holder will be required, in accordance with DTR 5 of the UK Financial Conduct Authority's Disclosure Guidance and Transparency Rules, to notify the Company of such Holder's holdings in Deposited Securities represented by ADSs if the percentage of such Holder's voting rights falls below a notifiable threshold as a result of a person designated by the Company having been given such discretionary proxy. The 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 of Directors of the Company to direct such person to exercise votes under such discretionary proxy in favor of the resolutions proposed by the Board at the 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 Meeting.

The Depository confirms that it has been provided with an opinion of counsel to the Company, in form and substance satisfactory to the Depository, substantially to the effect that: (i) the granting of such discretionary proxy does not subject the Depository to any additional disclosure obligations related to interests in shares under the Company's Articles of Association or the laws of Jersey or the Listing Rules of the United Kingdom Listing Authority; (ii) the granting of such proxy does not result in a breach of the laws of Jersey or the Listing Rules of the United Kingdom Listing Authority; and (iii) the Depository or the Custodian, or the nominee of any of them, whichever is the registered holder entitled to attend and vote at meetings of the Company in respect of such shares, has the right to appoint the proxy to attend and vote in their stead.

Please indicate on the reverse side hereof how the Deposited Securities are to be voted.

The Voting Instruction Card must be completed, signed and returned on time in order to be counted.

By signing on the reverse side hereof, the undersigned represents to the Depository and the Company that the undersigned is duly authorized to give the voting instructions contained herein.