

AMENDED AND RESTATED DEPOSIT AGREEMENT, dated as of May 23, 2011 (this “Deposit Agreement”), among SHIRE plc (the “Company”) and its successors, CITIBANK, N.A., as successor depositary hereunder (the “Depositary”), and all Holders and Beneficial Owners from time to time of American Depositary Receipts (“ADRs”) issued hereunder evidencing American Depositary Shares (“ADSs”) representing deposited Shares (as defined below).

W I T N E S S E T H

WHEREAS, the Company and JPMorgan Chase Bank, N.A. (the “Old Depositary”) and all Holders from time to time of ADRs issued thereunder evidencing ADSs entered into a Deposit Agreement, dated as of November 21, 2005 (the “Old Deposit Agreement”), to provide for the deposit of Shares of the Company with the Old Depositary, as predecessor depositary, for the creation of American depositary shares (“Old ADSs”) representing the Shares (as hereinafter defined) so deposited and for the execution and delivery of American depositary receipts (“Old ADRs”) evidencing the Old ADSs; and

WHEREAS, pursuant to the terms of Section 13 of the Old Deposit Agreement and paragraphs (15) and (16) of the Old ADRs, the Company now wishes to (i) remove the Old Depositary as depositary under the Old Deposit Agreement and replace the Old Depositary with Citibank, N.A., as successor depositary, and (ii) amend and restate the Old Deposit Agreement and the Old ADRs in accordance with the terms and conditions set forth in this Deposit Agreement;

NOW THEREFORE, in consideration of the premises, the parties hereto hereby amend and restate the Old Deposit Agreement and the Old ADRs in their entireties as follows:

1. Certain Definitions.

- (a) “ADR Register” is defined in paragraph (3) of the form of ADR.
- (b) “ADRs” means the American Depositary Receipts evidencing ADSs executed and delivered hereunder. ADRs shall be executed and delivered in physical certificated form or in the form of uncertificated Direct Registration ADRs. ADRs in physical certificated form shall be substantially in the form of Exhibit A annexed hereto (the “form of ADR”). References to “ADRs” shall include uncertificated Direct Registration ADRs, unless the context otherwise requires.
- (c) “ADSs” means American depositary shares representing beneficial interests in the Deposited Securities. Subject to paragraphs (10) and (13) of the form of ADR, each ADS represents the right to receive three (3) Shares.
- (d) “Articles” means the Articles of Association of the Company, as amended from time to time.
- (e) “Beneficial Owner” means, as to any ADS, any person or entity having a beneficial interest deriving from the ownership of such ADS. A Beneficial Owner of ADSs may or may not be the Holder of such ADSs. A Beneficial Owner shall be able to

exercise any right or receive any benefit hereunder solely through the person who is the Holder of the ADSs owned by such Beneficial Owner. Unless otherwise identified to the Depository, a Holder shall be deemed to be the Beneficial Owner of all the ADSs registered in his/her/its name.

(f) “Custodian” means Citibank, N.A. (London Branch), in its capacity as such, as the agent of the Depository for the purposes of this Deposit Agreement named as Custodian in the form of ADR and any additional or substitute Custodian appointed pursuant to Section 9 hereof.

(g) The terms “deliver”, “execute”, “issue”, “register”, “surrender”, “transfer” or “cancel”, when used with respect to uncertificated Direct Registration ADRs, shall refer to an entry or entries or an electronic transfer or transfers in the Direct Registration System.

(h) “Delivery Order” is defined in Section 3 hereof.

(i) “Deposited Securities” as of any time means all Shares at such time deposited under this Deposit Agreement and any and all other Shares, securities, property and cash at such time held by the Depository or the Custodian in respect or in lieu of such deposited Shares and other Shares, securities, property and cash.

(j) “Direct Registration ADR” means an uncertificated ADR, the ownership of which is recorded on the Direct Registration System.

(k) “Direct Registration System” means the direct registration system maintained by the Depository, pursuant to which the Depository may record the ownership of uncertificated ADRs, which ownership shall be evidenced by periodic statements issued by the Depository to the Holders entitled thereto.

(l) “DTC” shall mean The Depository Trust Company, a national clearinghouse and the central book-entry settlement system for securities traded in the United States and, as such, the custodian for the securities of DTC Participants maintained in DTC, and any successor thereto.

(m) “DTC Participant” shall mean any financial institution (or any nominee of such institution) having one or more participant accounts with DTC for receiving, holding and delivering the securities and cash held in DTC. A DTC Participant may or may not be a Beneficial Owner. If a DTC Participant is not the Beneficial Owner of the ADSs credited to its account at DTC, or of the ADSs in respect of which the DTC Participant is otherwise acting, such DTC Participant shall be deemed, for all purposes hereunder, to have all requisite authority to act on behalf of the Beneficial Owner(s) of the ADSs credited to its account at DTC or in respect of which the DTC Participant is so acting.

(n) “Holder” means the person or persons in whose name an ADR is registered on the ADR Register. A Holder may or may not be a Beneficial Owner. If a Holder is not the Beneficial Owner of the ADS(s) registered in its name, such person

shall be deemed, for all purposes hereunder, to have all requisite authority to act on behalf of the Beneficial Owners of the ADSs registered in its name.

(o) “Pre-released ADRs” has the meaning set forth in paragraph (1) of the form of ADR.

(p) “Securities Act of 1933” means the United States Securities Act of 1933, as from time to time amended.

(q) “Securities Exchange Act of 1934” means the United States Securities Exchange Act of 1934, as from time to time amended.

(r) “Shares” mean the Ordinary Shares of the Company and shall include the rights to receive Shares specified in paragraph (1) of the form of ADR.

(s) “Transfer Office” is defined in paragraph (3) of the form of ADR.

(t) “Withdrawal Order” is defined in Section 6.

2. Appointment of Depositary; Form of ADR; Incorporation by Reference.

(a) Appointment of Depositary. The Company hereby appoints the Depositary as successor depositary for the Deposited Securities and hereby authorizes and directs the Depositary to act in accordance with the terms and conditions set forth in this Deposit Agreement and the form of ADR. Each Holder and each Beneficial Owner, upon acceptance of any ADSs (or any interest therein) issued in accordance with the terms and conditions of this Deposit Agreement shall be deemed for all purposes to (a) be a party to and bound by the terms of this Deposit Agreement and the applicable ADR(s), and (b) appoint the Depositary its attorney-in-fact, with full power to delegate, to act on its behalf and to take any and all actions contemplated in this Deposit Agreement and the applicable ADR(s), to adopt any and all procedures necessary to comply with applicable law and to take such action as the Depositary in accordance with this Deposit Agreement in its sole discretion may deem necessary or appropriate to carry out the purposes of this Deposit Agreement and the applicable ADR(s), the taking of such actions to be the conclusive determinant of the necessity and appropriateness thereof. The issuer of the ADSs is deemed to be the legal entity resulting from this Deposit Agreement for the purpose of U.S. securities laws.

(b) Form of ADR. ADRs in certificated form shall be engraved, printed or otherwise reproduced at the discretion of the Depositary in accordance with its customary practices in its American depositary receipt business, or at the request of the Company typewritten and photocopied on plain or safety paper, and shall be substantially in the form set forth in the form of ADR, with such changes as may be required by the Depositary or the Company to comply with their obligations hereunder, any applicable law, regulation or usage or to indicate any special limitations or restrictions to which any particular ADRs evidencing ADSs are subject. ADRs may be issued in denominations of any whole number of ADSs. ADRs in certificated form shall be dated, executed and countersigned by the Depositary by the manual or facsimile signature of a duly

authorized officer of the Depository and registered in the ADR Register. ADRs in certificated form bearing the manual or facsimile signature of anyone who was at the time of execution a duly authorized officer of the Depository shall bind the Depository, notwithstanding that such officer has ceased to hold such office prior to the delivery of such ADRs. Holders and Beneficial Owners shall be bound by the terms and conditions of this Deposit Agreement and of the form of ADR, as incorporated by reference herein, regardless of whether their ADRs are uncertificated Direct Registration ADRs or certificated ADRs.

(c) Incorporation by Reference. The terms and conditions set forth in the form of ADR are hereby incorporated by reference herein and made a part hereof as if set forth herein, and shall be binding upon the parties hereto.

(d) Direct Registration ADRs. Notwithstanding anything in this Deposit Agreement or in the form of ADR to the contrary, ADSs may be evidenced by uncertificated Direct Registration ADRs, unless certificated ADRs are specifically requested by the Holder or ADSs are to be issued and delivered pursuant to the terms and conditions of (f) below.

(e) Book-Entry Systems. The Depository shall make arrangements for the acceptance of the ADSs into DTC. A single ADR in the form of a "Balance Certificate" will evidence all ADSs held through DTC and will be registered in the name of the nominee for DTC (currently "Cede & Co.") and will provide that it represents the aggregate amount of ADSs from time to time indicated in the records of the Depository as being issued hereunder and held through DTC and that the aggregate amount of ADSs represented thereby may from time to time be increased or decreased by making adjustments on such records of the Depository and of DTC or its nominee as hereinafter provided. The nominee for DTC will be the only "Holder" of the ADR evidencing all ADSs held through DTC. Citibank, N.A. (or such other entity as is appointed by DTC or its nominee) may hold the "Balance Certificate" as custodian for DTC. Each Beneficial Owner of ADSs held through DTC must rely upon the procedures of DTC and the DTC Participants to exercise or be entitled to any rights attributable to such ADSs. The DTC Participants shall for all purposes be deemed to have all requisite power and authority to act on behalf of the Beneficial Owners of the ADSs held in the DTC Participants' respective accounts in DTC and the Depository shall for all purposes be authorized to rely upon any instructions and information given to it by DTC Participants on behalf of Beneficial Owners of ADSs. So long as ADSs are held through DTC or unless otherwise required by law, ownership of beneficial interests in the ADR registered in the name of the nominee for DTC will be shown on, and transfers of such ownership will be effected only through, records maintained by (i) DTC or its nominee (with respect to the interests of DTC Participants), or (ii) DTC Participants or their nominees (with respect to the interests of clients of DTC Participants).

3. Deposit of Shares. In connection with the deposit of Shares hereunder, the Depository or the Custodian may require the following in form satisfactory to it: (a) a written order directing the Depository to execute and deliver to, or upon the written order of, the person or persons designated in such order (i) uncertificated Direct Registration ADRs or ADRs

evidencing the number of ADSs representing such deposited Shares or (ii) ADSs representing such Shares to the DTC Participant account number designated in such order by making the appropriate adjustments on the records of the Depository and of DTC and its nominee (a “Delivery Order”); (b) proper endorsements or duly executed and stamped (if necessary) instruments of transfer in respect of such deposited Shares; (c) instruments assigning to the Depository or its nominee any distribution on or in respect of such deposited Shares or indemnity therefor; and, (d) proxies entitling the Depository to vote such deposited Shares. As soon as practicable after the Custodian receives Deposited Securities pursuant to any such deposit or pursuant to paragraph (10) or (13) of the form of ADR, the Custodian shall present such Deposited Securities for registration of transfer into the name of the Depository or its nominee or the Custodian or its nominee, to the extent such registration is practicable, at the cost and expense of the person making such deposit (or for whose benefit such deposit is made) and shall obtain evidence satisfactory to it of such registration. Deposited Securities shall be held by the Custodian for the account and to the order of the Depository at such place or places and in such manner as the Depository shall determine. Deposited Securities may be delivered by the Custodian to any person only under the circumstances expressly contemplated in this Deposit Agreement.

4. Issue of ADRs. After any such deposit of Shares, the Custodian shall notify the Depository of such deposit and of the information contained in any related Delivery Order by letter, first class airmail postage prepaid, or, at the request, risk and expense of the person making the deposit, by cable, telex or facsimile transmission. After receiving such notice from the Custodian, the Depository, subject to this Deposit Agreement, shall issue and deliver at the Transfer Office, to or upon the order of any person named in such notice, the aggregate ADSs to which such person is entitled and, if applicable, ADR(s) evidencing ADSs so issued, in each case registered as requested. ADRs may be issued by the Depository only under circumstances contemplated in this Deposit Agreement.

5. Distributions on Deposited Securities; Conversion of Foreign Currency.

(a) Distributions on Deposited Securities. Following timely written notice to the Depository and to the extent that the Depository determines in its discretion that any distribution pursuant to paragraph (10) of the form of ADR is practicable with respect to any Holder, the Depository may make such distribution as it so deems practicable, including the distribution of foreign currency, securities or property (or appropriate documents evidencing the right to receive foreign currency, securities or property) or the retention thereof as Deposited Securities with respect to such Holder’s ADRs (without liability for interest thereon or the investment thereof). To the extent any holder of Deposited Securities is permitted to elect to receive distributions from Shire Biopharmaceutical Holdings, a subsidiary of the Company resident for tax purposes in the United Kingdom, or from the Company, a company resident for tax purposes in the Republic of Ireland, the Holders and Beneficial Owners shall be deemed to have instructed the Depository to elect and the Depository hereby elects, on behalf of Holders and Beneficial Owners, to receive all such distributions from Shire Biopharmaceutical Holdings. The Depository agrees to execute all further documentation reasonably requested by the Company to implement the foregoing election. The Depository shall not be deemed to exercise any discretion in connection with such election and shall be

entitled to any and all protections afforded to the Depositary under this Deposit Agreement in connection with such election.

(b) Conversion of Foreign Currency. Upon receipt by the Depositary or the Custodian of any foreign currency, if at the time of its receipt such foreign currency can in the judgment of the Depositary be converted on a reasonable basis into U.S. dollars and the resulting U.S. dollars transferred to the United States for distribution to Holders entitled thereto, the Depositary shall as promptly as practicable convert or cause to be converted such foreign currency into U.S. dollars by sale or in any other manner that it may determine, and shall transfer the resulting U.S. dollars (net of its charges and expenses in effecting such conversion) to the United States and shall distribute such U.S. dollars to the Holders entitled thereto in accordance with paragraph (10) of the form of ADR. If such conversion or distribution can be effected only with the approval or license of any government or agency thereof, the Depositary shall have discretion to file such application for approval or license as it may deem desirable. If the Depositary determines in its reasonable judgment that such foreign currency is not convertible, in whole or in part, on a reasonable basis into U.S. dollars transferable to the United States, or if any approval or license which is required for such conversion is denied or in the opinion of the Depositary, after consultation with the Company to the extent practicable, is not obtainable or is not obtained within a reasonable period or at a reasonable cost, the Depositary may distribute all or part of the foreign currency (or an appropriate document evidencing the right to receive such foreign currency) to, or in its discretion may hold such foreign currency uninvested and without liability for interest thereon for the respective accounts of, the Holders entitled thereto. All expenses of any such conversion shall be deducted from the proceeds thereof.

6. Withdrawal of Deposited Securities. In connection with any surrender of an ADS for withdrawal of the Deposited Securities represented by the ADSs evidenced thereby, the Depositary may require proper endorsement in blank of such ADR (or duly executed instruments of transfer thereof in blank) and the Holder's written order directing the Depositary to cause the Deposited Securities represented by the ADSs evidenced by such ADR to be withdrawn and delivered to, or upon the written order of, any person designated in such order (a "Withdrawal Order"). Directions from the Depositary to the Custodian to deliver Deposited Securities shall be given by letter, first class airmail postage prepaid, or, at the request, risk and expense of the Holder, by cable, telex or facsimile transmission. Delivery of Deposited Securities may be made by the delivery of certificates (which, if required by law shall be properly endorsed or accompanied by properly executed instruments of transfer or, if such certificates may be registered, registered in the name of such Holder or as ordered by such Holder in any Withdrawal Order) or by such other means as the Depositary may deem practicable.

7. Substitution of ADRs. The Depositary shall execute and deliver a new ADR of like tenor in exchange and substitution for any mutilated ADR upon cancellation thereof or in lieu of and in substitution for such destroyed, lost or stolen ADR, unless the Depositary has notice that such ADR has been acquired by a bona fide purchaser, upon the Holder thereof filing with the Depositary a request for such execution and delivery and a sufficient indemnity bond and satisfying any other reasonable requirements imposed by the Depositary.

8. Cancellation and Destruction of ADRs. All ADRs surrendered to the Depositary shall be canceled by the Depositary. The Depositary is authorized to destroy ADRs so canceled in accordance with its customary practices.

9. The Custodian. Any Custodian in acting hereunder shall be subject to the directions of the Depositary and shall be responsible solely to it. The Depositary may from time to time, after consultation with the Company, appoint one or more agents to act for it as Custodian hereunder in addition to or in lieu of the Custodian appointed hereunder. Each Custodian so appointed (other than Citibank, N.A. (London Branch)) shall give written notice to the Company and the Depositary accepting such appointment and agreeing to be bound by the applicable terms hereof. Any Custodian may resign from its duties hereunder by at least 30 days written notice to the Depositary. The Depositary may discharge any Custodian at any time upon notice to the Custodian being discharged. Any Custodian ceasing to act hereunder as Custodian shall deliver, upon the instruction of the Depositary, all Deposited Securities held by it to a Custodian so continuing to act.

10. Co-Registrars and Co-Transfer Agents. The Depositary may appoint and remove (i) co-registrars to register ADRs and transfers, combinations and split-ups of ADRs and to countersign ADRs in accordance with the terms of any such appointment and (ii) co-transfer agents for the purpose of effecting transfers, combinations and split-ups of ADRs at designated transfer offices in addition to the Transfer Office on behalf of the Depositary. Each co-registrar or co-transfer agent (other than Citibank, N.A.) shall give notice in writing to the Company and the Depositary accepting such appointment and agreeing to be bound by the applicable terms of this Deposit Agreement.

11. Lists of Holders. The Company shall have the right to inspect transfer and registration records of the Depositary and its agents and the ADR Register, take copies thereof and require the Depositary and its agents to supply copies of such portions of such records as the Company may request. The Depositary or its agent shall furnish to the Company promptly upon the written request of the Company, a list of the names, addresses and holdings of ADSs by all Holders as of a date within seven days of the Depositary's receipt of such request.

12. Depositary's Agents. The Depositary may perform its obligations under this Deposit Agreement through any agent appointed by it, provided that the Depositary shall notify the Company of such appointment and shall remain responsible for the performance of such obligations as if no agent were appointed.

13. Successor Depositary. If the Depositary acting hereunder shall resign or be removed, the Company shall, unless it elects to terminate this Agreement in accordance with paragraph (17) of the form of ADR, use its best efforts to appoint a bank or trust company having an office in the Borough of Manhattan, The City of New York, as successor depositary hereunder. Every successor depositary shall execute and deliver to its predecessor and to the Company written acceptance of its appointment hereunder, and thereupon such successor depositary, without any further act or deed, shall become Depositary hereunder; but such predecessor, upon payment of all sums due it and on the written request of the Company, shall execute and deliver an instrument transferring to such successor all rights and powers of such predecessor hereunder and assigning all interest in the Deposited Securities to such successor,

and shall deliver to such successor a copy of its records in respect of all outstanding ADRs issued hereunder and a list of the Holders. Any bank or trust company into or with which the Depositary may be merged or consolidated, or to which the Depositary shall transfer substantially all its American depositary receipt business (including the ADR facility established pursuant to this Agreement), shall be the successor of the Depositary without the execution or filing of any document or any further act; provided, however, that such bank or trust company shall give a written notice thereof to the Company. Upon the appointment of any successor depositary hereunder, any agent of the Depositary then acting hereunder shall forthwith become such agent hereunder of such successor depositary and such successor depositary shall, on the written request of any such agent, execute and deliver to such agent any instruments necessary to give such agent authority as such agent hereunder of such successor depositary. Notwithstanding the foregoing, any appointment of a successor Depositary shall not relieve the predecessor Depositary or the Company from those obligations and liabilities to each other under Section 16 hereof which arose prior to the appointment of such successor Depositary. A predecessor Depositary shall not have any liability or incur any expense as a result of any action or inaction on the part of a successor Depositary.

14. Reports and Communications. The Depositary shall make available for inspection by Holders at the Transfer Office any reports and communications received by the Company which are both (a) received by the Depositary as the holder of the Deposited Securities and (b) made generally available to the holders of such Deposited Securities by the Company. The Depositary shall also promptly send to the Holders copies of such reports and communications when furnished by the Company. Any such reports and communications furnished to the Depositary by the Company shall be furnished in English.

15. Additional Shares. Neither the Company nor any company controlled by the Company shall issue additional Shares, rights to subscribe for Shares, securities convertible into or exchangeable for Shares or rights to subscribe for any such securities or shall deposit any Shares under this Deposit Agreement, except under circumstances complying in all respects with, and not in violation of, the Securities Act of 1933. The Company shall use its best efforts to ensure that any company controlling or under common control with the Company shall abide by the restrictions set forth in the preceding sentence. The Depositary will use reasonable efforts to comply with written instructions of the Company not to accept for deposit hereunder any Shares identified in such instructions at such times and under such circumstances as may reasonably be specified in such instructions in order to facilitate the Company's compliance with securities laws in the United States.

16. Indemnification.

(a) The Company shall indemnify, defend and save harmless each of the Depositary and its agents against any loss, liability or expense (including reasonable fees and expenses of counsel) that may arise out of (a) its acceptance and performance of its powers and duties in respect of this Deposit Agreement, except to the extent such loss, liability or expense is due to the negligence or bad faith of the Depositary or its agents, as the case may be, or (b) any offer or sale of ADRs, ADSs, Shares or other Deposited Securities or any registration statement under the Securities Act of 1933 in respect thereof filed by the Company (including any Form F-6 registration statement to which

this Deposit Agreement has been, and may hereafter be, filed or incorporated by reference therein as an exhibit), except to the extent such loss, liability or expense arises out of information (or omissions from such information) relating to it furnished in writing to the Company by the Depositary or its agents expressly for use in any such registration statement. The Depositary shall indemnify, defend and save harmless the Company against any loss, liability or expense (including reasonable fees and expenses of counsel) incurred by the Company in respect of this Deposit Agreement to the extent such loss, liability or expense is due to the negligence or bad faith of the Depositary or its agents.

(b) Any person seeking indemnification hereunder (an “indemnified person”) shall notify the person from whom it is seeking indemnification (the “indemnifying person”) of the commencement of any indemnifiable action or claim promptly after such indemnified person becomes aware of such commencement (provided that the failure to make such notification shall not affect such indemnified person’s rights otherwise than under this Section 16 and shall only affect its rights hereunder to the extent such failure is prejudicial) and shall consult in good faith with the indemnifying person as to the conduct of the defense of such action or claim, which shall be reasonable in the circumstances. No indemnified person shall compromise or settle any indemnifiable action or claim without the prior written consent of the indemnifying person (which consent shall not be unreasonably withheld or delayed).

(c) The obligations set forth in this Section 16 shall survive the termination of this Deposit Agreement and the succession or substitution of any indemnified person.

17. Notices. Notice to any Holder shall be deemed given when first mailed, first class postage prepaid, to the address of such Holder on the ADR Register. Notice to the Depositary or the Company shall be deemed given when first received by it at the address or facsimile transmission number set forth below, or at such other address or facsimile transmission number as either may specify to the other by written notice:

Citibank, N.A.  
388 Greenwich Street, 14<sup>th</sup> Floor  
New York, NY 10013  
Attention: Depositary Receipts Department  
Fax: +1 212 816 6865

Shire plc  
Hampshire International Business Park  
Chineham Basingstoke Hampshire RG24 8EP  
United Kingdom  
Attention: Corporate Counsel  
Fax: + 44 1256 894 710

18. Miscellaneous. This Deposit Agreement is for the exclusive benefit of the Company, the Depositary, the Holders, the Beneficial Owners and their respective successors hereunder, and shall not give any legal or equitable right, remedy or claim whatsoever to any other person. The Holders and Beneficial Owners of ADRs from time to time shall be parties to

this Deposit Agreement and shall be bound by all of the provisions hereof. If any such provision is invalid, illegal or unenforceable in any respect, the remaining provisions shall in no way be affected thereby. This Deposit Agreement may be executed in any number of counterparts, each of which shall be deemed an original and all of which shall constitute one instrument.

19. Amendment and Restatement of Old Deposit Agreement. This Deposit Agreement amends and restates the Old Deposit Agreement in its entirety to consist exclusively of this Deposit Agreement, and Old ADRs are hereby deemed amended and restated to substantially conform to the form of ADR set forth in Exhibit A annexed hereto, except that, to the extent any portion of such amendment and restatement would prejudice any substantial existing right of Holders of Old ADRs, such portion shall not become effective as to such Holders with respect to such Old ADRs until thirty (30) days after such Holders shall have received notice thereof, such notice to be conclusively deemed given upon the mailing to such Holders of notice of such amendment and restatement which notice contains a provision whereby such Holders can receive a copy of the form of ADR.

20. Fees and Charges of Depositary. The Company, the Holders, the Beneficial Owners, and persons depositing Shares or surrendering ADSs for cancellation and withdrawal of Deposited Securities shall be required to pay to the Depositary the Depositary's fees and related charges identified as payable by them respectively in the form of ADR. All fees and charges so payable may, at any time and from time to time, be changed by agreement between the Depositary and the Company, but, in the case of fees and charges payable by Holders and Beneficial Owners, only in the manner contemplated in paragraph (16) of the form of ADR. The Depositary shall provide, without charge, a copy of its latest fee schedule to anyone upon request. Depositary fees payable upon (i) deposit of Shares against issuance of ADSs and (ii) surrender of ADSs for cancellation and withdrawal of Deposited Securities will be charged by the Depositary to the person to whom the ADSs so issued are delivered (in the case of ADS issuances) and to the person who delivers the ADSs for cancellation to the Depositary (in the case of ADS cancellations). In the case of ADSs issued by the Depositary into DTC or presented to the Depositary via DTC, the ADS issuance and cancellation fees will be payable to the Depositary by the DTC Participant(s) receiving the ADSs from the Depositary or the DTC Participant(s) surrendering the ADSs to the Depositary for cancellation, as the case may be, on behalf of the Beneficial Owner(s) and will be charged by the DTC Participant(s) to the account(s) of the applicable Beneficial Owner(s) in accordance with the procedures and practices of the DTC participant(s) as in effect at the time. Depositary fees in respect of distributions and the Depositary services fee are payable to the Depositary by Holders as of the applicable record date, as described in paragraph (11) of the form of ADR, established by the Depositary. In the case of distributions of cash, the amount of the applicable Depositary fees is deducted by the Depositary from the funds being distributed. In the case of distributions other than cash and the Depositary service fee, the Depositary will invoice the applicable Holders as of the applicable record date, as described in paragraph (11) of the form of ADR, established by the Depositary. For ADSs held through DTC, the Depositary fees for distributions other than cash and the Depositary service fee are charged by the Depositary to the DTC Participants in accordance with the procedures and practices prescribed by DTC from time to time and the DTC Participants in turn charge the amount of such fees to the Beneficial Owners for whom they hold ADSs. The Depositary may reimburse the Company for certain expenses incurred by the Company in respect of the ADR program established pursuant to this Deposit Agreement, by making

available a portion of the Depositary fees charged in respect of the ADR program or otherwise, upon such terms and conditions as the Company and the Depositary agree from time to time. The Company shall pay to the Depositary such fees and charges and reimburse the Depositary for such out-of-pocket expenses as the Depositary and the Company may agree from time to time. Responsibility for payment of such charges and reimbursements may from time to time be changed by agreement between the Company and the Depositary. Unless otherwise agreed, the Depositary shall present its statement for such expenses and fees or charges to the Company once every three months. The charges and expenses of the Custodian are for the sole account of the Depositary. The right of the Depositary to receive payment of fees, charges and expenses as provided above shall survive the termination of this Deposit Agreement. As to any Depositary, upon the resignation or removal of such Depositary as described in paragraph (15) of the form of ADR, such right shall extend for those fees, charges and expenses incurred prior to the effectiveness of such resignation or removal.

21. Governing Law; Submission to Jurisdiction. This Deposit Agreement and any and all ADRs shall be governed by and construed in accordance with the laws of the State of New York. Notwithstanding anything contained in this Deposit Agreement, an ADR or any present or future provisions of the laws of the State of New York, the rights of holders of Shares and of any other Deposited Securities and the obligations and duties of the Company in respect of the holders of Shares and other Deposited Securities, as such, shall be governed by the laws of Jersey (or, if applicable, such other laws as may govern the Deposited Securities).

Except as set forth herein, the Company and the Depositary agree that the federal or state courts in the Borough of Manhattan, The City of New York shall have jurisdiction to hear and determine any suit, action or proceeding and to settle any dispute between them that may arise out of or in connection with this Deposit Agreement and, for such purposes, each irrevocably submits to the non-exclusive jurisdiction of such courts. The Company hereby irrevocably designates, appoints and empowers Shire Pharmaceuticals Inc. (the "Agent") whose registered office is at 2711 Centerville Road, Suite 400, Wilmington DE 19808 and whose business address is 725 Chesterbrook Boulevard, Wayne, PA 19087 as its authorized agent to receive and accept for and on its behalf, and on behalf of its properties, assets and revenues, service by mail of any and all legal process, summons, notices and documents that may be served in any suit, action or proceeding brought against the Company in any federal or state court as described in the preceding sentence or in the next paragraph. If for any reason the Agent shall cease to be available to act as such, the Company agrees to designate a new agent in New York on the terms and for the purposes of this paragraph reasonably satisfactory to the Depositary. The Company further hereby irrevocably consents and agrees to the service of any and all legal process, summons, notices and documents in any suit, action or proceeding against the Company, by service by mail of a copy thereof upon the Agent (whether or not the appointment of such Agent shall for any reason prove to be ineffective or such Agent shall fail to accept or acknowledge such service), with a copy mailed to the Company by registered or certified air mail, postage prepaid, to its address provided in this Deposit Agreement. The Company agrees that the failure of the Agent to give any notice of such service to it shall not impair or affect in any way the validity of such service or any judgment rendered in any action or proceeding based thereon.

Notwithstanding the foregoing, the Depositary and the Company unconditionally agree that in the event that a Holder or Beneficial Owner brings a suit, action or proceeding against (a)

the Company, (b) the Depositary in its capacity as Depositary under this Deposit Agreement or (c) against both the Company and the Depositary, in any such case, in any state or federal court of the United States, and the Depositary or the Company have any claim, for indemnification or otherwise, against each other arising out of the subject matter of such suit, action or proceeding, then the Company and the Depositary may pursue such claim against each other in the state or federal court in the United States in which such suit, action, or proceeding is pending and, for such purposes, the Company and the Depositary irrevocably submit to the non-exclusive jurisdiction of such courts. The Company agrees that service of process upon the Agent in the manner set forth in the preceding paragraph shall be effective service upon it for any suit, action or proceeding brought against it as described in this paragraph.

The Company irrevocably and unconditionally waives, to the fullest extent permitted by law, any objection that it may now or hereafter have to the laying of venue of any actions, suits or proceedings brought in any court as provided in this section, and hereby further irrevocably and unconditionally waives and agrees not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum. The Company irrevocably and unconditionally waives, to the fullest extent permitted by law, and agrees not to plead or claim, any right of immunity from legal action, suit or proceeding, from setoff or counterclaim, from the jurisdiction of any court, from service of process, from attachment upon or prior to judgment, from attachment in aid of execution or judgment, from execution of judgment, or from any other legal process or proceeding for the giving of any relief or for the enforcement of any judgment, and consents to such relief and enforcement against it, its assets and its revenues in any jurisdiction, in each case with respect to any matter arising out of, or in connection with, this Deposit Agreement, any ADR or the Deposited Securities.

IN WITNESS WHEREOF, SHIRE plc and CITIBANK, N.A. have duly executed this Deposit Agreement as of the day and year first above set forth and all Holders and Beneficial Owners of ADSs shall become parties hereto upon acceptance by them of ADSs issued in accordance with the terms hereof.

SHIRE plc

By: /s/ Graham Hetherington  
Name: Graham Hetherington  
Title: Chief Financial Officer

CITIBANK, N.A.

By: /s/ Robert Franz  
Name: Robert Franz  
Title: Vice President

EXHIBIT A  
ANNEXED TO AND INCORPORATED IN  
AMENDED AND RESTATED DEPOSIT AGREEMENT

[FORM OF FACE OF ADR]

Number

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CUSIP NUMBER: 82481R106

American Depositary Shares (each  
American Depositary Share  
representing the right to receive three  
(3) fully paid ordinary shares)

AMERICAN DEPOSITARY RECEIPT

evidencing

AMERICAN DEPOSITARY SHARES

representing

ORDINARY SHARES, NOMINAL VALUE 5P EACH

of

SHIRE plc

(Incorporated under the laws of Jersey)

Citibank, N.A., a national banking association organized and existing under the laws of the United States of America, as depository (the "Depository"), hereby certifies that \_\_\_\_\_ is the registered owner (a "Holder") of \_\_\_\_\_ American Depositary Shares ("ADSs"), each (subject to paragraphs (10) and (13)) representing three ordinary shares ("Shares") (including the rights to receive Shares described in paragraph (1), and, together with any other securities, cash or property from time to time held by the Depository in respect or in lieu of deposited Shares, the "Deposited Securities"), of Shire plc, a corporation organized under the laws of Jersey (the "Company"), deposited with the Custodian appointed under the Deposit Agreement (subject to paragraph (15), the "Custodian"), under the Amended and Restated Deposit Agreement, dated as of May 23, 2011 (as amended from time to time, the "Deposit Agreement") among the Company, the Depository and all Holders and Beneficial Owners from time to time of American Depositary Receipts evidencing ADSs issued thereunder ("ADRs"), each of whom, by accepting an ADR becomes a party thereto. The Deposit Agreement and this ADR (which includes the provisions set forth on the reverse hereof) shall be governed by and construed in accordance with the laws of the State of New York. Notwithstanding anything contained in the Deposit Agreement, this ADR or any present or future provisions of the laws of the State of New York, the rights of holders of Shares and of any other Deposited Securities and

the obligations and duties of the Company in respect of the holders of Shares and other Deposited Securities, as such, shall be governed by the laws of Jersey (or, if applicable, such other laws as may govern the Deposited Securities). The terms and conditions of the Deposit Agreement are hereby incorporated by reference and all capitalized terms used herein which are not otherwise defined herein shall have the meanings ascribed thereto in the Deposit Agreement.

(1) Issuance of ADRs. This ADR is one of the ADRs issued under the Deposit Agreement to evidence ADSs outstanding thereunder. Subject to paragraph (4), the Depositary may so issue ADRs for delivery at the Transfer Office (defined in paragraph (3)) only against deposit with the Custodian of: (a) Shares in form satisfactory to the Custodian; (b) rights to receive Shares from the Company or any registrar, transfer agent, clearing agent or other entity recording Share ownership or transactions on behalf of the Company; or, (c) unless requested in writing by the Company to cease doing so at least two business days in advance of the proposed deposit, other rights to receive Shares (until such Shares are actually deposited pursuant to (a) or (b) above, "Pre-released ADRs"), only if (i) Pre-released ADRs are fully collateralized (marked to market daily) with cash or U.S. government securities held by the Depositary for the benefit of Holders (but such collateral shall not constitute Deposited Securities), (ii) each recipient of Pre-released ADRs agrees in writing with the Depositary that such recipient (a) owns such Shares, (b) assigns all beneficial right, title and interest therein to the Depositary in its capacity as such, (c) holds such Shares for the account of the Depositary, (d) will deliver such Shares to the Custodian as soon as practicable and promptly upon demand therefor and (e) will not take any action with respect to the Pre-released ADRs and Shares that is inconsistent with the transfer of the Depositary's beneficial ownership thereof, and (iii) no new Pre-released ADRs will be issued if the total outstanding Pre-released ADRs is or would become more than 20% of the outstanding ADR balance (excluding then outstanding Pre-released ADRs) at the time of issuance, unless the Depositary: 1) determines that unusual market conditions require the issuance of Pre-released ADRs in addition to 20% of all such ADRs and 2) receives the prior written approval of the Company. The Depositary may retain for its own account any earnings on collateral for Pre-released ADRs and its charges for issuance thereof. At the request, risk and expense of the person depositing Shares, the Depositary may accept deposits for forwarding to the Custodian and may deliver ADRs at a place other than its office. Every person depositing Shares under the Deposit Agreement represents and warrants that such Shares are free and clear of any lien, encumbrance, security interest, charge, mortgage, pledge or restriction on transfer, validly issued and outstanding, fully paid, nonassessable and free of pre-emptive rights, that the person making such deposit is duly authorized so to do and that such Shares (A) are not "restricted securities" as such term is defined in Rule 144 under the Securities Act of 1933 unless at the time of deposit they may be freely transferred in accordance with Rule 144 and may otherwise be offered and sold freely in the United States or (B) have been registered under the Securities Act of 1933. Such representations and warranties shall survive the deposit of Shares and issuance of ADRs. The Depositary will not knowingly accept for deposit under the Deposit Agreement any Shares required to be registered under the Securities Act of 1933 and not so registered; the Depositary may refuse to accept for such deposit any Shares identified by the Company in order to facilitate the Company's compliance with such Act.

(2) Withdrawal of Deposited Securities. Subject to paragraphs (4) and (5), upon surrender of this ADR in form satisfactory to the Depositary at the Transfer Office, the Holder hereof is entitled to delivery at the Custodian's office of the Deposited Securities at the

time represented by the ADSs evidenced by this ADR. At the request, risk and expense of the Holder hereof, the Depositary may deliver such Deposited Securities at such other place as may have been requested by the Holder. Notwithstanding any other provision of the Deposit Agreement or this ADR, the withdrawal of Deposited Securities may be restricted only for the reasons set forth in General Instruction I.A.(1) of Form F-6 (as such instructions may be amended from time to time) under the Securities Act of 1933.

(3) Transfers of ADRs. The Depositary or its agent will keep, at a designated transfer office in the Borough of Manhattan, The City of New York (the “Transfer Office”), (a) a register (the “ADR Register”) for the registration, registration of transfer, combination and split-up of ADRs, which at all reasonable times will be open for inspection by Holders and the Company for the purpose of communicating with Holders in the interest of the business of the Company or a matter relating to the Deposit Agreement and (b) facilities for the delivery and receipt of ADRs. Title to this ADR (and to the Deposited Securities represented by the ADSs evidenced hereby), when properly endorsed or accompanied by proper instruments of transfer, is transferable by delivery with the same effect as in the case of negotiable instruments under the laws of the State of New York; provided that the Depositary, notwithstanding any notice to the contrary, may treat the person in whose name this ADR is registered on the ADR Register as the absolute owner hereof for all purposes. Subject to paragraphs (4) and (5), this ADR is transferable on the ADR Register and may be split into other ADRs or combined with other ADRs into one ADR, evidencing the same number of ADSs evidenced by this ADR, by the Holder hereof or by duly authorized attorney upon surrender of this ADR at the Transfer Office properly endorsed or accompanied by proper instruments of transfer and duly stamped as may be required by applicable law; provided that the Depositary may close the ADR Register at any time or from time to time when deemed expedient by it or requested by the Company. At the request of a Holder, the Depositary shall, for the purpose of substituting a certificated ADR with uncertificated Direct Registration ADRs, or vice versa, execute (if applicable) and deliver a certificated ADR or uncertificated Direct Registration ADRs, as the case may be, for any authorized number of ADSs requested, evidencing the same aggregate number of ADSs as those evidenced by the certificated ADR or designated as uncertificated Direct Registration ADRs, as the case may be, substituted.

(4) Certain Limitations. Prior to the issue, registration, registration of transfer, split-up or combination of any ADR, the delivery of any distribution in respect thereof, or, subject to the last sentence of paragraph (2), the withdrawal of any Deposited Securities, and from time to time in the case of clause (b)(ii) of this paragraph (4), the Company, the Depositary or the Custodian may require: (a) payment with respect thereto of (i) any stamp duty, stamp duty reserve tax or other transfer duty or stock transfer or other tax or other governmental charge, (ii) any stock transfer or registration fees in effect for the registration of transfers of Shares or other Deposited Securities upon any applicable register and (iii) any applicable charges as provided in paragraph (7) of this ADR; (b) the production of proof satisfactory to it of (i) the identity and genuineness of any signature and (ii) such other information, including without limitation, information as to citizenship, residence, exchange control approval, beneficial ownership of any securities, compliance with applicable law, regulations, provisions of or governing Deposited Securities and terms of the Deposit Agreement and this ADR, as it may deem necessary or proper; and (c) compliance with such regulations as the Depositary may establish consistent with the Deposit Agreement. The issuance of ADRs, the acceptance of deposits of Shares, the

registration, registration of transfer, split-up or combination of ADRs or, subject to the last sentence of paragraph (2), the withdrawal of Deposited Securities may be suspended, generally or in particular instances, when the ADR Register or any register for Deposited Securities is closed or when any such action is deemed advisable by the Depositary or the Company.

(5) Taxes. If any tax or other governmental charge shall become payable by or on behalf of the Custodian or the Depositary with respect to this ADR, any Deposited Securities represented by the ADSs evidenced hereby or any distribution thereon, such tax or other governmental charge shall be paid by the Holder hereof to the Depositary and neither the Company nor the Depositary shall have any liability therefore. The Depositary may refuse to effect any registration, registration of transfer, split-up or combination hereof or, subject to the last sentence of paragraph (2), any withdrawal of such Deposited Securities until such payment is made. The Depositary may also deduct from any distributions on or in respect of Deposited Securities, or may sell by public or private sale for the account of the Holder hereof any part or all of such Deposited Securities (after attempting by reasonable means to notify the Holder hereof prior to such sale), and may apply such deduction or the proceeds of any such sale in payment of such tax or other governmental charge, the Holder and Beneficial Owner hereof remaining liable for any deficiency, and shall reduce the number of ADSs evidenced hereby to reflect any such sales of Deposited Securities. In connection with any distribution to Holders, the Company will remit to the appropriate governmental authority or agency all amounts (if any) required to be withheld and owing to such authority or agency by the Company; and the Depositary and the Custodian will remit to the appropriate governmental authority or agency all amounts (if any) required to be withheld and owing to such authority or agency by the Depositary or the Custodian. If the Depositary determines that any distribution in property other than cash (including Shares or rights) on Deposited Securities is subject to any tax that the Depositary or the Custodian is obligated to withhold, the Depositary may dispose of all or a portion of such property in such amounts and in such manner as the Depositary deems necessary and practicable to pay such taxes, by public or private sale, and the Depositary shall distribute the net proceeds of any such sale or the balance of any such property after deduction of such taxes to the Holders entitled thereto.

(6) Disclosure of Interests. To the extent that the provisions of or governing or to which such Deposited Securities are otherwise subject may require disclosure of or impose limits on beneficial or other ownership of Deposited Securities, other Shares and other securities and may provide for blocking transfer, voting or other rights to enforce such disclosure or limits, Holders, Beneficial Owners and all persons holding ADSs (or any interest therein) agree to comply with all such disclosure requirements and ownership limitations and to cooperate with the Depositary in the Depositary's compliance with any Company instructions in respect thereof, and the Depositary will use reasonable efforts to comply with such Company instructions.

Notwithstanding any provision of the Deposit Agreement or of this ADR and without limiting the foregoing, by being a Holder of an ADR, each such Holder and Beneficial Owner agrees to provide such information as the Company may request in a disclosure notice (a "Disclosure Notice") given pursuant to the Articles of the Company. By accepting or holding this ADR, each Holder and Beneficial Owner acknowledges that it understands that failure to comply with a Disclosure Notice may result in the imposition of sanctions against the holder of the Shares in respect of which the non-complying person is or was, or appears to be or has been,

interested as provided in the Articles which currently include, the withdrawal of the voting rights of such Shares and the imposition of restrictions on the rights to receive dividends on and to transfer such Shares. In addition, by accepting or holding this ADR each Holder and Beneficial Owner agrees to comply with the provisions of the Articles with regard to the notification to the Company of interests in Shares, which currently provide, inter alia, that any member must comply with certain notification obligations to the Company set forth in the Articles, as if the Company were a UK-issuer (and not a non-UK Issuer) for the purposes of these provisions. Such notification obligations are extended to each Holder and Beneficial Owner where such Holder and Beneficial Owner is aware that another person for whom it holds such ADRs is so interested.

(7) Charges of Depositary. The Depositary may charge the following fees:

(a) Issuance Fee: to any person depositing Shares or to whom ADSs are issued upon the deposit of Shares (excluding issuances as a result of distributions described in paragraph (iv) below), a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) so issued under the terms of the Deposit Agreement, *provided, however*, that the Depositary shall not charge an issuance fee to any person depositing Shares for purposes of the issuance of ADSs in connection with the Company's employee share plans;

(b) Cancellation Fee: to any person surrendering ADSs for cancellation and withdrawal of Deposited Securities or to any person to whom Deposited Securities are delivered, a fee not in excess of U.S. \$5.00 per 100 ADSs (or fraction thereof) surrendered;

(c) Cash Distribution Fee: to any Holder of ADSs, a fee not in excess of U.S. \$2.00 per 100 ADSs (or fraction thereof) held for the distribution of cash dividends or other cash distributions (*i.e.*, sale of rights and other entitlements);

(d) Stock Distribution /Rights Exercise Fee: to any Holder of ADS(s), a fee not in excess of U.S. \$2.00 per 100 ADSs (or fraction thereof) held for (a) the distribution of stock dividends or other free stock distributions or (b) the exercise of rights to purchase additional ADSs;

(e) Other Distribution Fee: to any Holder of ADS(s), a fee not in excess of U.S. \$2.00 per 100 ADSs (or fraction thereof) held for the distribution of securities other than ADSs or rights to purchase additional ADSs; and

(f) Depositary Services Fee: to any Holder of ADS(s), a fee not in excess of U.S. \$2.00 per 100 ADSs (or fraction thereof) held on the applicable record date(s) established by the Depositary.

In addition, in connection with any action to deposit Shares or surrender ADSs for cancellation for the purpose of withdrawal of Deposited Securities instigated by, or on behalf of, any Holders or Beneficial Owners, the Depositary shall be entitled to charge the following:

(a) taxes (including applicable interest and penalties) and other

governmental charges;

(b) such registration fees as may from time to time be in effect for the registration of Shares or other Deposited Securities on the share register and applicable to transfers of Shares or other Deposited Securities to or from the name of the Custodian, the Depository or any nominees upon the making of deposits and withdrawals, respectively;

(c) such cable, telex and facsimile transmission and delivery expenses as are expressly provided in the Deposit Agreement to be at the expense of the person depositing or withdrawing Shares or Holders and Beneficial Owners of ADSs;

(d) the expenses and charges incurred by the Depository in the conversion of foreign currency;

(e) such fees and expenses as are incurred by the Depository in connection with compliance with exchange control regulations and other regulatory requirements applicable to Shares, Deposited Securities, ADSs and ADRs; and

(f) the fees and expenses incurred by the Depository, the Custodian, or any nominee in connection with the delivery or servicing of Deposited Securities.

For the avoidance of doubt, any fees and charges incurred by the Depository in connection with its general operations and not triggered by a specific deposit or withdrawal transaction instigated for or on behalf of a Holder or Beneficial Owner shall be met by the Depository and not passed on to Holders or Beneficial Owners.

All fees and charges may, at any time and from time to time, be changed by agreement between the Depository and Company but, in the case of fees and charges payable by Holders or Beneficial Owners, only in the manner contemplated by paragraph 16 and as contemplated in the Deposit Agreement. The Depository will provide, without charge, a copy of its latest fee schedule to anyone upon request.

Depository fees payable upon (i) deposit of Shares against issuance of ADSs and (ii) surrender of ADSs for cancellation and withdrawal of Deposited Securities will be charged by the Depository to the person to whom the ADSs so issued are delivered (in the case of ADS issuances) and to the person who delivers the ADSs for cancellation to the Depository (in the case of ADS cancellations). In the case of ADSs issued by the Depository into DTC or presented to the Depository via DTC, the ADS issuance and cancellation fees will be payable to the Depository by the DTC Participant(s) receiving the ADSs from the Depository or the DTC Participant(s) surrendering the ADSs to the Depository for cancellation, as the case may be, on behalf of the Beneficial Owner(s) and will be charged by the DTC Participant(s) to the account(s) of the applicable Beneficial Owner(s) in accordance with the procedures and practices of the DTC participant(s) as in effect at the time. Depository fees in respect of distributions and the Depository services fee are payable to the Depository by Holders as of the applicable ADS Record Date established by the Depository. In the case of distributions of cash, the amount of the applicable Depository fees is deducted by the Depository from the funds being distributed. In the case of distributions other than cash and the Depository service fee, the Depository will

invoice the applicable Holders as of the ADS Record Date established by the Depositary. For ADSs held through DTC, the Depositary fees for distributions other than cash and the Depositary service fee are charged by the Depositary to the DTC Participants in accordance with the procedures and practices prescribed by DTC from time to time and the DTC Participants in turn charge the amount of such fees to the Beneficial Owners for whom they hold ADSs.

The Depositary may reimburse the Company for certain expenses incurred by the Company in respect of the ADR program established pursuant to the Deposit Agreement, by making available a portion of the Depositary fees charged in respect of the ADR program or otherwise, upon such terms and conditions as the Company and the Depositary agree from time to time. The Company shall pay to the Depositary such fees and charges and reimburse the Depositary for such out-of-pocket expenses as the Depositary and the Company may agree from time to time. Responsibility for payment of such charges and reimbursements may from time to time be changed by agreement between the Company and the Depositary. Unless otherwise agreed, the Depositary shall present its statement for such expenses and fees or charges to the Company once every three months. The charges and expenses of the Custodian are for the sole account of the Depositary.

The right of the Depositary to receive payment of fees, charges and expenses as provided above shall survive the termination of the Deposit Agreement. As to any Depositary, upon the resignation or removal of such Depositary as described in this ADR, such right shall extend for those fees, charges and expenses incurred prior to the effectiveness of such resignation or removal.

(8) Available Information. The Deposit Agreement, the provisions of or governing Deposited Securities and any written communications from the Company, which are both received by the Custodian or its nominee as a holder of Deposited Securities and made generally available to the holders of Deposited Securities, are available for inspection by Holders and Beneficial Owners at the offices of the Depositary and the Custodian and at the Transfer Office. The Depositary will mail copies of such communications (or English translations or summaries thereof) to Holders if and when furnished by the Company. The Company is subject to the periodic reporting requirements of the Securities Exchange Act of 1934 and accordingly files certain reports with the United States Securities and Exchange Commission (the "Commission"). Such reports and other information may be inspected and copied at public reference facilities maintained by the Commission located at the date hereof at 100 F Street, N.E., Washington, D.C. 20549.

(9) Execution. This ADR shall not be valid for any purpose unless executed by the Depositary by the manual or facsimile signature of a duly authorized officer of the Depositary.

Dated: May 23, 2011

CITIBANK, N.A., as Depositary

By: \_\_\_\_\_

Authorized Officer

The Depository's principal executive office is located at 388 Greenwich Street, New York, New York 10013.

[FORM OF REVERSE OF ADR]

(10) Distributions on Deposited Securities. Subject to paragraphs (4) and (5), to the extent practicable and provided timely written notice is delivered to the Depositary, the Depositary will distribute by mail to each Holder entitled thereto on the record date set by the Depositary therefor at such Holder's address shown on the ADR Register, in proportion to the number of Deposited Securities (on which the following distributions on Deposited Securities are received by the Custodian) represented by ADSs evidenced by such Holder's ADRs and, in each case, without unreasonable delay. (a) Cash: Any U.S. dollars available to the Depositary resulting from a cash dividend or other cash distribution or the net proceeds of sales of any other distribution or portion thereof authorized in this paragraph (10) ("Cash"), on an averaged or other practicable basis, subject to (i) appropriate adjustments for taxes withheld, (ii) such distribution being impermissible or impracticable with respect to certain Holders, and (iii) deduction of the Depositary's expenses in (1) converting any foreign currency to U.S. dollars by sale or in such other manner as the Depositary may determine to the extent that it determines that such conversion may be made on a reasonable basis, (2) transferring foreign currency or U.S. dollars to the United States by such means as the Depositary may determine to the extent that it determines that such transfer may be made on a reasonable basis, (3) obtaining any approval or license of any governmental authority required for such conversion or transfer, which is obtainable at a reasonable cost and within a reasonable time and (4) making any sale by public or private means in any commercially reasonable manner. If the Depositary determines in its reasonable judgment that such foreign currency is not convertible, in whole or in part, on a reasonable basis into U.S. dollars transferable to the United States, or if any approval or license which is required for such conversion is denied or in the opinion of the Depositary, is not obtainable or is not obtained within a reasonable period or at a reasonable cost, the Depositary may distribute all or part of the foreign currency (or an appropriate document evidencing the right to receive such foreign currency) to, or in its discretion may hold such foreign currency uninvested and without liability for interest thereon for the respective accounts of, the Holders entitled thereto. All expenses of any such conversion shall be deducted from the proceeds thereof. On the date on which the Company pays any cash dividend to the holders of Shares or other Deposited Securities, the Company may convert or cause to be converted, in a commercially reasonable manner, such foreign currency into U.S. dollars and distribute the same to the Depositary for distribution to Holders. No deductions shall be made by the Company from the proceeds of such conversion; provided that actual and customary commissions paid by the Company on account of such conversion shall not be considered a deduction by the Company. To the extent any holder of Deposited Securities is permitted to elect to receive distributions from Shire Biopharmaceutical Holdings, a subsidiary of the Company resident for tax purposes in the United Kingdom, or from the Company, a company resident for tax purposes in the Republic of Ireland, the Holders and Beneficial Owners shall be deemed to have instructed the Depositary to elect and the Depositary hereby elects, on behalf of Holders and Beneficial Owners, to receive all such distributions from Shire Biopharmaceutical Holdings. The Depositary agrees to execute all further documentation reasonably requested by the Company to implement the foregoing election. The Depositary shall not be deemed to exercise any discretion in connection with such election and shall be entitled to any and all protections afforded to the Depositary under the Deposit Agreement in connection with such election. (b) Shares. (i)

Additional ADRs evidencing whole ADSs representing any Shares available to the Depositary resulting from a dividend or free distribution on Deposited Securities consisting of Shares (a “Share Distribution”) and (ii) U.S. dollars available to it resulting from the net proceeds of sales of Shares received in a Share Distribution, which Shares would give rise to fractional ADSs if additional ADRs were issued therefor, as in the case of Cash. (c) Rights. (i) Warrants or other instruments in the discretion of the Depositary representing rights to acquire additional ADRs in respect of any rights to subscribe for additional Shares or rights of any nature available to the Depositary as a result of a distribution on Deposited Securities (“Rights”), to the extent that the Company timely furnishes to the Depositary evidence satisfactory to the Depositary that the Depositary may lawfully distribute the same (the Company has no obligation to so furnish such evidence), or (ii) to the extent the Company does not so furnish such evidence and sales of Rights are practicable, any U.S. dollars available to the Depositary from the net proceeds of sales of Rights as in the case of Cash, or (iii) to the extent the Company does not so furnish such evidence and such sales cannot practicably be accomplished by reason of the nontransferability of the Rights, whether by their terms, pursuant to applicable law or otherwise, limited markets therefor, their short duration or otherwise, nothing (and any Rights may lapse). (d) Other Distributions. (i) Securities or property available to the Depositary resulting from any distribution on Deposited Securities other than Cash, Share Distributions and Rights (“Other Distributions”), by any means that the Depositary may deem equitable and practicable, or (ii) to the extent the Depositary deems distribution of such securities or property not to be equitable and practicable, any U.S. dollars available to the Depositary from the net proceeds of sales of Other Distributions as in the case of Cash. Before effecting any such sale of a Share Distribution, Rights or Other Distribution, the Depositary will provide notice to the Company of its intended action. Such U.S. dollars available will be distributed by checks drawn on a bank in the United States for whole dollars and cents (any fractional cents being withheld without liability for interest and dealt with by the Depositary in accordance with its then current practices).

(11) Record Dates. The Depositary may, after consultation with the Company, if practicable, fix a record date (which shall be as near as practicable to any corresponding record date set by the Company) for the determination of the Holders who shall be entitled to receive any distribution on or in respect of Deposited Securities, to give instructions for the exercise of any voting rights, to receive any notice or to act in respect of other matters and only such Holders shall be so entitled.

(12) Voting of Deposited Securities. As soon as practicable after receipt from the Company of notice of any meeting or solicitation of consents or proxies of holders of Shares or other Deposited Securities, the Depositary shall fix a record date in accordance with paragraph (11) hereof and, unless otherwise requested in writing by the Company in order to comply with applicable law, mail to Holders a notice stating (a) such information as is contained in such notice and any solicitation materials, (b) that each Holder on the record date set by the Depositary therefor will be entitled to instruct the Depositary as to the exercise of the voting rights, if any, pertaining to the Deposited Securities represented by the ADSs evidenced by such Holder’s ADRs and (c) the manner in which such instructions may be given, including instructions to give a discretionary proxy to a person designated by the Company subject to any applicable provisions of the laws of Jersey and the Memorandum and Articles of the Company and the provisions of or governing Deposited Securities. Upon receipt of instructions of a Holder on such record date in the manner and on or before the date established by the Depositary

for such purpose, the Depositary shall endeavor insofar as practicable and permitted under the provisions of or governing Deposited Securities to vote or cause to be voted (or to grant a discretionary proxy to a person designated by the Company to vote) the Deposited Securities represented by the ADSs evidenced by such Holder's ADRs in accordance with such instructions. The Depositary will not itself exercise any voting discretion in respect of any Deposited Security. Subject to the provisions of the next succeeding paragraph, to the extent such instructions are not so received by the Depositary from any Holder, the Holder shall be deemed to have instructed the Depositary to give a discretionary proxy to a person designated by the Company to vote the Deposited Securities represented by ADSs as to which the Depositary has not received instructions from the Holders, provided that no such instruction shall be deemed to be given and no discretionary proxy shall be given with respect to which the Company informs the Depositary (and the Company agrees to provide such information promptly in writing) that the Company does not wish such proxy given.

Notwithstanding anything to the contrary contained in the preceding paragraph, the Depositary shall not be obligated to give any such discretionary proxy and the Holders shall not have been deemed to have so instructed the Depositary unless and until the Depositary has been provided with an opinion of counsel to the Company, which may be given at the time of entering into the Deposit Agreement, satisfactory to the Depositary (which may be internal counsel), in form and substance satisfactory to the Depositary, substantially to the effect that (i) the granting of such discretionary proxy does not subject the Depositary to any additional disclosure obligations related to interests in shares under the Articles 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 Depositary 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 instead of him. The Company undertakes to inform the Depositary of any substantial change in the Articles or the laws of Jersey which would subject the Depositary to disclosure obligations under the listing rules of the United Kingdom Listing Authority to which the Depositary, the Custodian or the nominee of any of them would not otherwise be subject but for the grant of such discretionary proxy.

(13) Changes Affecting Deposited Securities. Subject to paragraphs (4) and (5) the Depositary may, in its discretion, and after consultation with the Company if practicable, amend this ADR or distribute additional or amended ADRs or ADSs (with or without calling this ADR for exchange) or cash, securities or property on the record date set by the Depositary therefor to reflect any change in par value, split-up, consolidation, cancellation or other reclassification of Deposited Securities, any Share Distribution or Other Distribution not distributed to Holders or any cash, securities or property available to the Depositary in respect of Deposited Securities from (and the Depositary is hereby authorized to surrender any Deposited Securities to any person and to sell by public or private sale any property received in connection with) any recapitalization, reorganization, merger, consolidation, liquidation, receivership, bankruptcy or sale of all or substantially all the assets of the Company, and to the extent the Depositary does not so amend the terms and conditions of the ADRs or ADSs or make a distribution to Holders to reflect any of the foregoing, or the net proceeds thereof, whatever cash, securities or property results from any of the foregoing shall constitute Deposited Securities and

each ADS evidenced by this ADR shall automatically represent its pro rata interest in the Deposited Securities as then constituted.

(14) Exoneration. Without limiting Section 16 of the Deposit Agreement as between the Company and the Depositary, the Depositary, the Company, their respective officers, directors, employees and agents and each of them shall: (a) incur no liability (i) if any present or future law, regulation, the provisions of or governing any Deposited Securities, act of God, war or other circumstance beyond its control shall prevent, delay or subject to any civil or criminal penalty any act which the Deposit Agreement or this ADR provides shall be done or performed by it, or (ii) by reason of any exercise or failure to exercise any discretion given it in the Deposit Agreement or this ADR; (b) assume no obligation nor shall any of them be subject to any liability to any Holders or beneficial owners of ADSs or any other person except to perform its obligations to the extent they are specifically set forth in this ADR and the Deposit Agreement without gross negligence or bad faith; (c) in the case of the Depositary and its agents, be under no obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Securities or this ADR; or (d) in the case of the Company and its agents hereunder be under no obligation to appear in, prosecute or defend any action, suit or other proceeding in respect of any Deposited Securities or this ADR, which in its opinion may involve it in expense or liability, unless indemnity satisfactory to it against all expense (including fees and disbursements of counsel) and liability be furnished as often as may be required; (e) not be liable for any action or inaction by it in reliance upon the advice of or information from legal counsel, accountants, any person presenting Shares for deposit, any Holder, Beneficial Owner or any other person believed by it to be competent to give such advice or information; or (f) not be liable for any consequential or punitive damages for any breach of the terms of the Deposit Agreement or this ADR. The Depositary and the Company, their respective agents and their respective directors, officers and employees acting hereunder may rely and shall be protected in acting upon any written notice, request, direction or other document believed by them to be genuine and to have been signed or presented by the proper party or parties. The Depositary and its agents will not be responsible for any failure to carry out any instructions to vote any of the Deposited Securities, for the manner in which any such vote is cast or for the effect of any such vote. The Depositary and its agents may own and deal in any class of securities of the Company and its affiliates and in ADRs. The Company has agreed to indemnify the Depositary and its agents under certain circumstances and the Depositary has agreed to indemnify the Company under certain circumstances. No disclaimer of liability under the Securities Act of 1933 is intended by any provision hereof.

(15) Resignation and Removal of Depositary; the Custodian. The Depositary may resign as Depositary by written notice of its election to do so delivered to the Company, or be removed as Depositary by the Company by written notice of such removal delivered to the Depositary; such resignation or removal shall take effect upon the appointment of and acceptance by a successor depositary. The Depositary may appoint substitute or additional Custodians and the term "Custodian" refers to each Custodian or all Custodians as the context requires.

(16) Amendment. Subject to the last sentence of paragraph (2), the ADRs, the ADSs evidenced by the ADRs and the Deposit Agreement may be amended by the Company and the Depositary, provided that any amendment that imposes or increases any fees or charges

(other than stock transfer or other taxes and other governmental charges, transfer or registration fees for the registration of transfer of Deposited Securities on any applicable register in connection with the deposit or withdrawal of Deposited Securities, cable, telex or facsimile transmission costs, delivery costs or other such expenses), or that shall otherwise prejudice any substantial existing right of Holders or Beneficial Owners, shall become effective 30 days after notice of such amendment shall have been given to the Holders and Beneficial Owners. Every Holder and Beneficial Owner of an ADS (or any interest therein) at the time any amendment to the Deposit Agreement so becomes effective shall be deemed, by continuing to hold such ADS (or any interest therein), to consent and agree to such amendment and to be bound by the Deposit Agreement and, if applicable, the ADR(s), as so amended thereby. In no event shall any amendment impair the right of the Holder of any ADR to surrender such ADR and receive the Deposited Securities represented thereby, except in order to comply with mandatory provisions of applicable law. The parties hereto agree that any amendments or supplements which (i) are reasonably necessary (as agreed by the Company and the Depository) in order for (a) the ADSs to be registered on Form F-6 under the Securities Act of 1933 or (b) the ADSs or Shares to be traded solely in electronic book-entry form and (ii) do not in either such case impose or increase any fees or charges to be borne by Holders and Beneficial Owners, shall be deemed not to prejudice any substantial rights of Holders or Beneficial Owners. In no event shall any amendment or supplement impair the right of the Holder to surrender such ADR and receive therefor the Deposited Securities represented thereby except in order to comply with mandatory provisions of applicable law. Notwithstanding the foregoing, if any governmental body should adopt new laws, rules or regulations which would require amendment or supplement of the Deposit Agreement or the form of ADR to ensure compliance therewith, the Company and the Depository may amend or supplement the Deposit Agreement, the ADRs and the ADSs evidenced by the ADRs at any time in accordance with such changed rules. Such amendment or supplement to the Deposit Agreement and, if applicable, the ADR, in such circumstances may become effective before a notice of such amendment or supplement is given to Holders and Beneficial Owners or within any other period of time as required for compliance.

(17) Termination. The Depository shall at the written direction of the Company, terminate the Deposit Agreement and this ADR by mailing notice of such termination to the Holders at least 30 days prior to the date fixed in such notice for such termination. The Depository may terminate the Deposit Agreement by giving the notice set forth in the preceding sentence of this paragraph (17) at any time after 60 days has elapsed after the Depository shall have resigned hereunder, provided that no successor depository shall have been appointed and accepted its appointment hereunder before the end of such 60 days. After the date so fixed for termination, the Depository and its agents will perform no further acts under the Deposit Agreement and this ADR, except to advise Holders of such termination, receive and hold (or sell) distributions on Deposited Securities and deliver Deposited Securities being withdrawn. As soon as practicable after the expiration of six months from the date so fixed for termination, the Depository shall sell the Deposited Securities and shall thereafter (as long as it may lawfully do so) hold in a segregated account the net proceeds of such sales, together with any other cash then held by it under the Deposit Agreement, without liability for interest, in trust for the pro rata benefit of the Holders of ADRs not theretofore surrendered. After making such sale, the Depository shall be discharged from all obligations in respect of the Deposit Agreement and this ADR, except to account for such net proceeds and other cash. After the date so fixed for

termination, the Company shall be discharged from all obligations under the Deposit Agreement except for its obligations to the Depositary and its agents.