

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2015

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission file number 0-29630

SHIRE PLC

(Exact name of registrant as specified in its charter)

Jersey (Channel Islands)

98-0601486

(State or other jurisdiction of incorporation or organization)

(I.R.S. Employer Identification No.)

**5 Riverwalk, Citywest Business Campus, Dublin 24,
Republic of Ireland**

+353 1 429 7700

(Address of principal executive offices and zip code)

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class
American Depositary Shares, each representing three
Ordinary Shares 5 pence par value per share

Name of exchange on which registered
NASDAQ Global Select Market

Securities registered pursuant to Section 12(g) of the Act:

None
(Title of class)

Indicate by check mark whether the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act

Yes No

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act

Yes No

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the Registrant's knowledge, in definitive proxy or information statements incorporated by reference to Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes No

Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (232,405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

Yes No

As at June 30, 2015, the last business day of the Registrant's most recently completed second quarter, the aggregate market value of the ordinary shares, £0.05 par value per share of the Registrant held by non-affiliates was approximately \$47.3 billion. This was computed using the average bid and asked price at the above date.

As at February 12, 2016, the number of outstanding ordinary shares of the Registrant was 601,127,241.

THE “SAFE HARBOR” STATEMENT UNDER THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995

Statements included herein that are not historical facts are forward-looking statements. Such forward-looking statements involve a number of risks and uncertainties and are subject to change at any time. In the event such risks or uncertainties materialize, Shire's results could be materially adversely affected. The risks and uncertainties include, but are not limited to, the following:

- the proposed combination with Baxalta may not be completed due to a failure to satisfy certain closing conditions, including any shareholder or regulatory approvals or the receipt of applicable tax opinions;
- disruption from the proposed transaction with Baxalta may make it more difficult to conduct business as usual or maintain relationships with patients, physicians, employees or suppliers;
- the combined company may not achieve some or all of the anticipated benefits of Baxalta's spin-off from Baxter International, Inc. (“Baxter”) and the proposed transaction may have an adverse impact on Baxalta's existing arrangements with Baxter, including those related to transition, manufacturing and supply services and tax matters;
- the failure to achieve the strategic objectives with respect to the proposed combination with Baxalta may adversely affect the combined company's financial condition and results of operations;
- products and product candidates may not achieve commercial success;
- product sales from ADDERALL XR and INTUNIV are subject to generic competition;
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payers in a timely manner for the combined company's products may affect future revenues, financial condition and results of operations, particularly if there is pressure on pricing of products to treat rare diseases;
- supply chain or manufacturing disruptions may result in declines in revenue for affected products and commercial traction from competitors; regulatory actions associated with product approvals or changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- the successful development of products in various stages of research and development is highly uncertain and requires significant expenditures and time, and there is no guarantee that these products will receive regulatory approval;
- the actions of certain customers could affect the combined company's ability to sell or market products profitably, and fluctuations in buying or distribution patterns by such customers can adversely affect the combined company's revenues, financial condition or results of operations;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to the combined company's activities in the highly regulated markets in which it operates may result in significant legal costs and the payment of substantial compensation or fines;
- adverse outcomes in legal matters and other disputes, including the combined company's ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on the combined company's revenues, financial condition or results of operations;
- Shire is undergoing a corporate reorganization and was the subject of an unsuccessful acquisition proposal and the consequent uncertainty could adversely affect the combined company's ability to attract and/or retain the highly skilled personnel needed to meet its strategic objectives;
- failure to achieve the strategic objectives with respect to Shire's acquisition of NPS Pharmaceuticals Inc. or Dyax Corp. (“Dyax”) may adversely affect the combined company's financial condition and results of operations;
- the combined company will be dependent on information technology and its systems and infrastructure face certain risks, including from service disruptions, the loss of sensitive or confidential information, cyber-attacks and other security breaches or data leakages that could have a material adverse effect on the combined company's revenues, financial condition or results of operations;
- the combined company may be unable to retain and hire key personnel and/or maintain its relationships with customers, suppliers and other business partners;
- difficulties in integrating Dyax or Baxalta into Shire may lead to the combined company not being able to realize the expected operating efficiencies, cost savings, revenue enhancements, synergies or other benefits at the time anticipated or at all; and

other risks and uncertainties detailed from time to time in Shire's, Dyax's or Baxalta's filings with the Securities and Exchange Commission ("SEC"), including those risks outlined in Baxalta's current Registration Statement on Form S-1, as amended, and in "ITEM 1A: Risk Factors" in Shire's Annual Report on Form 10-K for the year ended December 31, 2015.

The following are trademarks either owned or licensed by Shire plc or its subsidiaries, which are the subject of trademark registrations in certain territories, or which are owned by third parties as indicated and referred to in this Form 10-K:

ADDERALL XR[®] (mixed salts of a single entity amphetamine)
ADUVANZ[™] (lisdexamfetamine dimesylate)
AGRYLIN[®] (anagrelide hydrochloride)
APRISO[®] (trademark of Salix Pharmaceuticals, Ltd. ("Salix"))
ASACOL[®] (trademark of Medeva Pharma Suisse AG (used under license by Warner Chilcott Company, LLC ("Warner Chilcott")))
BERINERT[®] (trademark of CSL Behring GmbH)
BERINERT P[®] (trademark of Aventis Behring GmbH)
BUCCOLAM[®] (midazolam hydrochloride oromucosal solution)
CALCICHEW[®] (trademark of Takeda Nycomed AS)
CARBATROL[®] (carbamazepine extended-release capsules)
CERDELGA[®] (trademark of Genzyme Corporation ("Genzyme"))
CEREZYME[®] (trademark of Genzyme)
CINRYZE[®] (C1 esterase inhibitor [human])
CLAVERSAL[®] (trademark of Merckle Recordati)
COLAZAL[®] (trademark of Salix Pharmaceuticals, Inc)
CONCERTA[®] (trademark of Alza Corporation ("Alza"))
DAYTRANA[®] (trademark of Noven Pharmaceutical Inc. ("Noven"))
DELZICOL[®] (trademark of Warner Chilcott)
DERMAGRAFT[®] (trademark of Organogenesis Inc. ("Organogenesis"))
ELAPRASE[®] (idursulfase)
ELELYSO[®] (trademark of Pfizer Inc.)
ELVANSE[®] (lisdexamfetamine dimesylate)
ELVANSE ADULT[®] (lisdexamfetamine dimesylate)
ELVANSE VUXEN[®] (lisdexamfetamine dimesylate)
EPIVIR[®] (trademark of GlaxoSmithKline ("GSK"))
ESTRACE[®] (trademark of Trimel Pharmaceuticals Inc.)
EQUASYM[®] (methylphenidate hydrochloride)
EQUASYM XL[®] (methylphenidate hydrochloride)
EXPUTEX[®] (trademark of Phoenix Labs)
FABRAZYME[®] (trademark of Genzyme)
FIRAZYR[®] (icatibant)
FOCALIN XR[®] (trademark of Novartis AG)
FOSRENOL[®] (lanthanum carbonate)
GATTEX[®] (teduglutide [rDNA origin])
HUNTERASE[™] (trademark of Green Cross Corp.)
INTUNIV[®] (guanfacine extended release)
KALBITOR[®] (ecallantide)
KAPVAY[®] (trademark of Shionogi Pharma, Inc. ("Shionogi"))
LIALDA[®] (trademark of Nogra International Limited)
MEDIKINET[®] (trademark of Medice Arzneimittel Pütter GmbH & Co. KG ("Medice"))
MEZAVANT[®] (trademark of Giuliani International Limited)
MIMPARA[®] (cinacalcet HCl)
MICROTROL[®] (trademark of Supernus Pharmaceuticals, Inc. ("Supernus"))
NATPAR[®] (parathyroid hormone)
NATPARA[®] (parathyroid hormone (rDNA))
PENTASA[®] (trademark of Ferring B.V. Corp ("Ferring"))
PLENADREN (hydrocortisone, modified release tablet)
QUILLIVANT[®] (trademark of Next Wave Pharmaceuticals, Inc.)
REMINYL[®] (galantamine hydrobromide) (United Kingdom ("UK") and Republic of Ireland) (trademark of Johnson & Johnson ("J&J")), excluding UK and Republic of Ireland)
REGPARA[®] (cinacalcet HCl)
REPLAGAL[®] (agalsidase alfa)
RESOLOR[®] (prucalopride)
REVESTIVE[®] (teduglutide)

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