Shire plc

Half Yearly Report 2015

Registered in Jersey, No. 99854, 22 Grenville Street, St Helier, Jersey JE4 8PX

Half Yearly Report

Contents

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, that:

- Shire's products may not be a 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 Shire's products may affect future revenues, financial condition and results of operations;
- Shire conducts its own manufacturing operations for certain of its products and is reliant on third party contract manufacturers to manufacture other products and to provide goods and services. Some of Shire's products or ingredients are only available from a single approved source for manufacture. Any disruption to the supply chain for any of Shire's products may result in Shire being unable to continue marketing or developing a product or may result in Shire being unable to do so on a commercially viable basis for some period of time;
- the manufacture of Shire's products is subject to extensive oversight by various regulatory agencies. Regulatory approvals or interventions associated with 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;
- Shire has a portfolio of products in various stages of research and development. The successful development of these products 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 Shire's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect Shire's revenues, financial condition or results of operations;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to Shire'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 Shire's ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on Shire's revenues, financial condition or results of operations;
- Shire faces intense competition for highly qualified personnel from other companies and organizations. Shire is undergoing a corporate reorganization and was the subject of an unsuccessful acquisition proposal and the consequent uncertainty could adversely affect Shire's ability to attract and/or retain the highly skilled personnel needed for Shire to meet its strategic objectives;
- failure to achieve Shire's strategic objectives with respect to the acquisition of NPS Pharmaceuticals Inc. ("NPS Pharma") may adversely affect Shire's financial condition and results of operations; and

other risks and uncertainties detailed from time to time in Shire's filings with the Securities and Exchange Commission, including those risks outlined in "Item 1A: Risk Factors" in Shire's Annual Report on Form 10-K for the year ended December 31, 2014.

TRADE MARKS

All trade marks designated ® and ™ used in this press release are trade marks of Shire plc or companies within the Shire group except for 3TC® and ZEFFIX® which are trade marks of GlaxoSmithKline, PENTASA® which is a trade mark of FERRING B.V. Corp, LIALDA® which is a trade mark of Nogra International Limited, MEZAVANT® which is a trade mark of Guiliani International Limited, CALCICHEW® which is a trade mark of Takeda, DERMAGRAFT® which is a trademark of Organogenesis Inc., VANCOCIN® which is a trademark of ANI Pharmaceuticals Inc. and DAYTRANA® which is a trade mark of Noven Pharmaceutical Inc. Certain trade marks of Shire plc or companies within the Shire group are set out in Shire's most recent Annual Report and Accounts for the year ended December 31, 2014.

Half Yearly Report

Chief Executive Officer's review

We are pleased to enclose our financial results for the six-month period ended June 30, 2015. This Half Yearly Report includes condensed consolidated financial statements prepared in accordance with generally accepted accounting principles in the United States of America ("US GAAP").

Flemming Ornskov, M.D., Shire's Chief Executive Officer, commented:

"During the first half of 2015, we delivered double-digit underlying product sales growth (on a Non GAAP CER[(1)] basis and excluding INTUNIV) amid continued investment in our pipeline and future growth drivers.

Total reported product sales in the first half of 2015 were $2.9 billion, up 4%, and Non GAAP EBITDA[(2)] reached $1.4 billion, growing 5%. We are especially pleased by the performance of VYVANSE, with total product sales growing 18% to $842 million. This includes the market expansion of VYVANSE for adults with ADHD and the launch of the new adult indication for moderate to severe Binge Eating Disorder. The Rare Disease Business Unit continues to be our largest, with product sales of approximately $1.1 billion. LIALDA has also performed well, gaining market share and generating product sales of $306 million, up 12%.

During the first half of the year, we further strengthened our focus on rare diseases through the acquisition of NPS Pharma, the largest acquisition in Shire's history. NPS Pharma enabled us to leverage our GI commercial capabilities and global footprint while gaining access to two exciting rare disease assets, GATTEX®/REVESTIVE® and NATPARA®. GATTEX/REVESTIVE is off to a strong start and we are pleased with the early progress of NATPARA. This positive momentum underscores the strength of our M&A capabilities to effectively identify, acquire and integrate assets and deliver value. The NPS Pharma commercial integration has been completed.

Our innovative pipeline saw several key developments in the first half of 2015. We received a Priority Review designation for lifitegrast for Dry Eye Disease and in July 2015 we completed enrolment of the OPUS 3 study for lifitegrast. In addition, we initiated a Phase 3 study for SHP465 ahead of plan and we received favourable FDA feedback on a path forward for a potential Phase 3 study for maribavir. Shire now has the broadest and deepest pipeline in its history."

Flemming Ornskov, M.D.
Chief Executive Officer

(1) The Non GAAP CER financial measures included within this release is explained on page 59.

(2) Non GAAP earnings before interest, tax, depreciation and amortization ("EBITDA"). A reconciliation to US GAAP net income is provided on page 60.

Half Yearly Report

Business overview for the six months to June 30, 2015

The following discussion should be read in conjunction with the unaudited condensed consolidated financial statements and related notes appearing elsewhere in this Half Yearly Report for Shire plc and its subsidiaries (collectively "Shire" or "the Group").

Significant events in the six months to June 30, 2015 and recent developments

Products

INTUNIV for the treatment of attention deficit hyperactivity disorder ("ADHD") in the EU

- The Committee for Medicinal Products for Human Use ("CHMP") of the European Medicines Agency ("EMA") has adopted a positive opinion at its July 2015 meeting recommending marketing authorization approval of INTUNIV (guanfacine) extended release drug product, a non-stimulant indicated as part of a comprehensive treatment programme for ADHD in children and adolescents 6 to 17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective.

  The CHMP positive opinion will be reviewed by the European Commission ("EC") with the expectation that the EC will then grant a centralized marketing authorization with unified labeling that is valid in the 28 countries that are members of the European Union, as well as European Economic Area members, Iceland, Liechtenstein and Norway.

RESOLOR – for the Symptomatic Treatment of Chronic Constipation in Men

- On May 27, 2015, Shire received the EC decision amending the terms of the RESOLOR Marketing Authorisation to the use of RESOLOR in adults for the symptomatic treatment of chronic constipation for whom laxatives fail to provide adequate relief. In Europe, RESOLOR was initially approved for use in women only, so the new variation extends the use of this treatment to male patients.

VYVANSE – for the treatment of moderate to severe Binge Eating Disorder ("BED") in adults

- Topline results from a 39-week, long-term maintenance of efficacy study (SPD489-346) in adults with moderate to severe BED showed VYVANSE superior to placebo ($p<.001$) on the primary efficacy endpoint of time to relapse of binge eating symptoms. At the conclusion of the trial, patients continuing on VYVANSE had a lower proportion of relapse of 5/136 (3.7%) as compared to patients continuing on placebo 42/131 (32.1%).
- The results of a separate, 12-month open-label safety extension study (SPD489-345) were generally consistent with the safety profile currently outlined in the United States Prescribing information.
- Based on the results of these studies, the Group plans to submit a supplemental New Drug Application by year end to the US Food and Drug Administration ("FDA"). The FDA will evaluate adding this data to the current labeling for VYVANSE.
- On January 30, 2015 Shire launched VYVANSE for the treatment of adults with moderate to severe BED.

VYVANSE – for the treatment of ADHD

- On March 23, 2015 Shire announced VYVANSE was available in a 10mg strength capsule. This new titration dose, which was approved by the FDA on October 30, 2014, is the seventh VYVANSE dosage strength available in addition to the 20mg, 30mg, 40mg, 50mg, 60mg, and 70mg capsule strengths. On April 7, 2015 Health Canada approved the 10mg dose strength for incremental titration adjustments.

NATPARA – for the treatment of hypoparathyroidism

- On January 23, 2015 it was announced that the FDA had approved NATPARA as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism. Hypoparathyroidism is a rare endocrine disorder characterized by insufficient levels of parathyroid hormone, or PTH. NATPARA is a bioengineered replica of human PTH. NATPARA was launched on April 1, 2015.

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