Press Release

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2015 Annual Report – DTR 6.3.5 Disclosure

March 29, 2016 - Shire plc (LSE: SHP, NASDAQ: SHPG) (the "Company") announces that the following documents have today been posted or otherwise made available to shareholders:

> 2015 Annual Report
> Notice of the 2016 Annual General Meeting
> Form of Proxy

In accordance with Listing Rule 9.6.1R, a copy of each of these documents has been uploaded to the National Storage Mechanism and will be available for viewing shortly.

The 2015 Annual Report and Notice of the 2016 Annual General Meeting are also available on Shire's website: www.shire.com

Disclosure & Transparency Rule ("DTR") 6.3.5R requires the Company to disclose to the media certain information from its Annual Report if that information is of a type that would be required to be disseminated in a half-yearly report. The information contained in the Appendix to this announcement, together with the Company's unaudited full year results for the year ended December 31, 2015, issued on February 11, 2016, constitute the materials required by DTR 6.3.5R to be communicated to the media in unedited full text through a Regulatory Information Service. This material is not a substitute for reading the full 2015 Annual Report.

The information included in the Appendix is extracted from the 2015 Annual Report which was approved by the Board of Directors on February 23, 2016. Defined terms used in the Appendix refer to terms as defined in the 2015 Annual Report, unless the context otherwise requires.

Oliver Strawbridge
Senior Assistant Company Secretary

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NOTES TO EDITORS

Shire enables people with life-altering conditions to lead better lives.

Our strategy is to focus on developing and marketing innovative specialty medicines to meet significant unmet patient needs.

We focus on providing treatments in Rare Diseases, Neuroscience, Gastrointestinal and Internal Medicine and we are developing treatments for symptomatic conditions treated by specialist physicians in other targeted therapeutic areas, such as Ophthalmics.

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Forward-Looking Statements

Statements included herein that are not historical facts, including without limitation statements concerning our announced business combination with Baxalta and the timing and financial and strategic benefits thereof, our 20x20 ambition that targets $20 billion in combined product sales by 2020, as well as other targets for future financial results, capital structure, performance and sustainability of the combined company, the combined company's future strategy, plans, objectives, expectations and intentions, the anticipated timing of clinical trials and approvals for, and the commercial potential of, inline or pipeline products 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 "ITEM 1A: Risk Factors" in Shire's and Baxalta's Annual Reports on Form 10-K for the year ended December 31, 2015.

All forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by this cautionary statement. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Except to the extent otherwise required by applicable law, we do not undertake any obligation to republish revised forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

APPENDIX

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1. Chairman's review

Throughout 2015, I've had the privilege of listening to Shire people as they talk about the future. I've heard the stories that are driving our business forward. I've also watched as one Shire team after another presented ideas and possibilities, often in novel, even moving ways. This is a passionate and highly promising organization. I see and hear this passion and promise in my daily interactions. Our purpose as a company is to enable people with life-altering conditions to lead better lives. Our focus is on building long-term sustainable value for shareholders as a global biotechnology company while balancing the needs of all our stakeholders including patients, employees, partners, payers, physicians and regulators.

We aim to be the world leader in rare diseases and a leading global biotechnology and as a result of our clear focus on innovation, efficiency, growth and people, we are well on our way to achieving this goal.

Looking ahead, our announced combination with Baxalta Incorporated ("Baxalta"), which at closing would create the world's leading biotech company focused on rare diseases, and provide a platform for sustainable innovation, growth and value creation. This is an exciting time for Shire and Baxalta alike, and is great news for our current and future rare disease patients.

The Shire 2015 Annual Report provides details of our key activities for the year. In this letter I highlight those events and accolades that I believe demonstrate our leadership and our commitment to our patients.

We have been successful in driving the business forward through original research, creative acquisitions and novel licensing agreements, advancing our innovative pipeline. In 2016, our pipeline will be comprised of 29 programs in clinical development, with 14 in Phase 3 or planned to enter Phase 3 in 2016.

Completed acquisitions including NPS Pharmaceuticals, Inc. ("NPS Pharma"), Dyax Corp. ("Dyax"), Foresight Biotherapeutics Inc. ("Foresight"), and Meritage Pharma, Inc. ("Meritage"), and new research partnerships such as those with Foundation Fighting Blindness and the Cincinnati Children's Hospital, will help us make a real difference to the lives of patients.

2015 brought good news for the millions of adults in the US with Binge Eating Disorder ("BED"). With the Food and Drug Administration ("FDA") approval of VYVANSE for the treatment of moderate to severe BED in adults, physicians now have an effective treatment for a widely unmet need.

We at Shire take a responsible, transparent and sustainable approach to our business. In 2015 we were once again confirmed as a constituent company in the FTSE4Good Index, which measures globally recognized standards for corporate responsibility. We were also ranked as the #2 "greenest" company in the world according to *Newsweek* magazine. This year we held our first Global Day of Service, raised awareness for rare diseases, improved access to our therapies, participated in industry-wide roundtables, presented new research at world conferences, and furthered the dialogue about patient health.

I'd like to welcome the many individuals who have joined Shire around the world since the beginning of the year. They have joined a company with a strong identity and sense of purpose, and a high performance culture that rewards creativity, innovation and delivering results. The perspectives and experiences of these new colleagues will no doubt add new dimensions and depth to the innovation we are seeing across the business.

Shire also has great leadership. Our CEO, Flemming Ornskov, MD was named by Harvard Business Review in October as one of the 100 Best-Performing CEOs in the World. I would like to thank Flemming for his vision, leadership and exceptional dedication to the company.

I'd also like to recognize the Board of Directors for their contributions, insights and rigorous approach in challenging and assessing Shire's activities over the course of the year. In particular, I'd like to thank David Kappler, Deputy Chairman and Senior Independent Director, who will retire at the 2016 AGM, for his many years of exceptional service.

In 2015, two Non-Executive Directors joined our Board — Olivier Bohuon, Chief Executive Officer at Smith & Nephew, plc, and Sara Mathew, who, until 2013, served as Chairman, President, and Chief Executive Officer of Dun & Bradstreet. Jeffrey Poulton also joined the Board this year on his promotion to Chief Financial Officer. You can read more about the Board in my corporate governance report on page 64 of Shire's Annual Report.

1. Chairman’s review

We’ve had a remarkable year at Shire, and I’ve felt extraordinarily privileged to play a role in this company’s emergence as a true global leader. I wish to thank all of those who are making this company what it is — and what it will continue to become.

Susan Kilsby
Chairman

2. Chief Executive Officer's review

DRIVING CHANGE

2015 has been a year of transformation. With our streamlined One Shire organization in place, we advanced our ambition to become a leading global biotechnology company.

We built category leadership, launched multiple products in our core therapeutic areas, greatly expanded our global footprint and strengthened our innovative pipeline, now the most robust in Shire's history. We did all this while delivering excellent results, investing in future growth drivers and announcing several, game-changing deals.

Our achievements are grounded in our clear and focused strategy of growth, innovation, efficiency and people. In 2015, we made significant progress across each of these strategic drivers. These achievements reflect the contributions of our people who work passionately every day to help those with life-altering conditions to lead better lives, and to whom I am extremely grateful.

Becoming a leading global biotechnology company

We are transforming into a fast-growing, leading global biotech with best-in-class products for patients with rare diseases and specialty conditions. We strive to become leaders within the categories where we have product offerings, which are Neuroscience, Gastrointestinal/Endocrinology, hereditary angioedema ("HAE")/ lysosomal storage disorders ("LSDs"), and Ophthalmics. Rare Diseases are at the center of our strategy and the mindset we bring to our work every day. Today, approximately 45% of product sales come from rare diseases and biologics, with over 75% of our 29 R&D clinical programs in rare conditions.

As we advance our portfolio, business development continues to play an important role. In 2015, we added promising rare disease assets and technologies through complimentary, highly strategic, mid-sized acquisitions. These bolt-on acquisitions benefit from our domain leadership, commercial and R&D expertise, and our proven abilities in integration and advancing assets through development to commercialization. I describe this as our "string of pearls" approach to transactions.

There were many times during 2015 when we were able to put this into action. We started the year with the acquisition of NPS Pharma, adding Natpara and Gattex/Revestive to our innovative portfolio of products, and supporting our GI franchise past the eventual loss of Lialda exclusivity.

With the acquisition of Meritage, we acquired the global rights to Oral Budesonide Suspension (SHP621), for the treatment of adolescents and adults with eosinophilic esophagitis, a rare, chronic inflammatory GI disease, further bolstering our GI/IM portfolio.

Our acquisition of Foresight underscored our commitment to building a leadership position in ophthalmology, with the potential for SHP640 (formerly FST-100), if approved, to become the first agent to treat both viral and bacterial conjunctivitis.

The $6 billion acquisition of Dyax expands and extends our industry-leading portfolio in HAE, a rare, debilitating genetic inflammatory condition that causes episodes of swelling in the face, extremities and GI tract, and can be life threatening. With Dyax we bring into our portfolio DX-2930. If approved, this therapy has the potential to expand HAE-treated patients and achieve worldwide sales of up to $2 billion with exclusivity beyond 2030.

As we add to our "string of pearls," we have pursued transformational transactions with the potential to lead the industry. Our announced combination with Baxalta, pending shareholder and certain regulatory approvals, would create the global leader in rare diseases with a strong strategic fit and a leading, diversified portfolio. The combined company would have the ability to deliver an anticipated $20 billion in product sales by 2020, multiple $1+ billion disease franchises, and over 50 inline and pipeline rare disease products and programs, more than any other company. Assuming the necessary approvals, this transaction is expected to close in mid-2016.

Delivering growth through new launches and commercial excellence

This year we showed our launch capabilities with several new products successfully entering markets around the globe. We launched VYVANSE for moderate to severe BED in adults, and VYVANSE outperformed the adult attention deficit hyperactivity disorder ("ADHD") market and grew 19% over the prior year. The recently launched NPS products, NATPARA® and GATTAX/REVESTIVE®, have shown early promise. Internationally, we achieved 25 in-market launches and expanded our international presence, with Shire medicines now available in 72 countries.

2. Chief Executive Officer's review

Throughout, we continued to execute across our core commercial business. Our HAE portfolio, CINRYZE and FIRAZYR, grew 23% and 22%, respectively. In our GI franchise, LIALDA continued to gain market share and now represents 36% of the 5-ASA US market.

Looking ahead, we will continue to prioritize investment in our future growth drivers. We are especially excited by the potential for leadership in Ophthalmics, with SHP640 from Foresight and lifitegrast (SHP606) which has potential to be the only product approved in the US in the past decade indicated for the treatment of signs and symptoms of Dry Eye Disease ("DED") in adults. Today, there are an estimated 29 million people living with the symptoms of DED in the US. Only about half are diagnosed, and only a small fraction of these are treated. Following the positive results of OPUS-3, we have been working on advancing lifitegrast through the regulatory process by addressing the FDA's complete response letter and resubmitted the New Drug Application ("NDA") for lifitegrast on January 22, 2016. We expect to remain on track for potential US approval in 2016.

Progressing our innovative pipeline — the most robust in our history

We entered 2016 with the strongest pipeline in Shire's 30-year history, with 29 clinical development programs, including 14 in Phase 3 or planned to enter Phase 3 in 2016. Just a few highlights from our Phase 3 programs include SHP620 (maribavir) for CMV infection in transplant patients; SHP621 for Eosinophilic Esophagitis; and SHP609 for Hunter syndrome-intrathecal delivery (phase 2/3); all in areas of high unmet medical need.

Having worked for years in pediatrics, I am personally excited by the potential of SHP607 for the prevention of Retinopathy of Prematurity ("ROP"), a disorder of the retinal blood vessels in the eyes of premature infants weighing 2¾ pounds or less and typically born before 31 weeks of gestation. ROP is a leading cause of visual loss in childhood and can lead to lifelong vision impairment and blindness. Shire is investigating SHP607, an experimental insulin-like growth factor 1 (IGF-1) protein replacement therapy, specifically to determine whether it may prevent ROP. Phase 2 results are expected in the second half of 2016. If successful, SHP607 will add to our growing category leadership in Ophthalmics.

Ensuring a streamlined, efficient organization

We continued to look critically at how we work and where we can improve our core processes and systems to do things better and faster. Much was achieved in this area over the past year. This includes consolidating our US operational headquarters in Massachusetts. We also worked to strengthen our manufacturing position through renegotiation of our agreement with Sanquin. We are now in a position to seek a second source of supply to boost production of CINRYZE, an important treatment for HAE.

Aligning and engaging our people

We had amazing growth last year — hiring many new employees — reflecting our dynamism as an organization and the attractiveness of our culture: high performing, patient-focused, and one that rewards innovation and results. This year we integrated our new colleagues from NPS Pharma, adding to Shire's deep expertise in rare diseases. We look forward to doing the same with our colleagues from Dyax now that the deal has been closed.

Supporting our local communities and giving back has long been one of Shire's key strengths and passions. This year, on October 2nd, we held our First Global Day of Service. More than 1,700 Shire employees donated 8,000 volunteer hours in more than 20 locations around the world. Because of the positive feedback from employees and our community partners, plans are underway to hold our second Global Day of Service in 2016. Our corporate responsibility efforts also received more formal recognition in 2015, for example, through our continued inclusion on the FTSE4Good Index.

Shaping what's next

In 2016, we mark the 30th anniversary of Shire. It was three decades ago, in 1986, that we opened our doors with our first product. Like many journeys, ours has not been a straight road. It's had many twists and turns — and there will certainly be many more. This is the reality of our industry — with advances in science, and with shifts in the healthcare environment — the journey is never quite linear. But one thing that's defined Shire since day one is its forward-looking mindset. We are never complacent.

Our journey for the past 30 years has been shaped by a shared focus on what's next — on how we can be ahead of what's needed or expected — to do things better and faster so we can meet the needs of our patients, our physicians, our employees and our business, not just today but also tomorrow. Throughout the years, we set bold aspirational goals and did what was needed to achieve them.

But of course, we're not stopping there. We're already looking ahead to what's next for Shire — which is the opportunity we have to shape what's next as a leading global biotech.

2. Chief Executive Officer’s review

As we look toward the next 30 years (and beyond), I want to express my appreciation and gratitude to our employees for the impact they have every day on the growth of our business — and most importantly to our patients who inspire us to keep pushing forward.

I look forward to working with all of Shire’s stakeholders on shaping what’s to come.

Flemming Ornskov, MD, MPH
Chief Executive Officer

3. Review of our business

Overview
The Company has grown both organically and through acquisition, completing a series of major transactions that have brought therapeutic, geographic and pipeline growth and diversification. The Company will continue to conduct its own research and development, focused on rare diseases, as well as evaluate companies, products and pipeline opportunities that offer a strategic fit and have the potential to deliver value to all of the Company's stakeholders: patients, physicians, policy makers, payers, investors and employees.

The Company's purpose is to enable people with life altering conditions to lead better lives. The Company will execute on its purpose through its strategy and business model. For further details of Shire's strategy and business model, refer to pages 12 to 15 of Shire's 2015 Annual Report.

Through deep understanding of patients' needs, the Company is able to:

- Serve patients with high unmet needs in select, commercially attractive specialty TAs;
- Drive optimum performance of its marketed products — to serve patients today;
- Build its pipeline of innovative specialist treatments through both R&D and Corporate Development activities — to enable the Company to serve patients in the future.

Shire's in-licensing and acquisition efforts are focused on products in specialist markets with strong intellectual property protection or other forms of market exclusivity and global rights. Shire believes that a carefully selected and balanced portfolio of products with strategically aligned and relatively small-scale sales forces will deliver strong results.

Company revenues, expenditures and net assets are attributable to the R&D, manufacture, sale and distribution of pharmaceutical products within one reportable segment. The Company also earns royalties (where Shire has out-licensed products to third parties) which are recorded as royalty revenues.

Revenues are derived primarily from two sources — sales of the Company's own products and royalties:

- 95% (2014: 97%) of total revenues are derived from product sales; and
- 5% of total revenues are derived from royalties (2014: 3%).

The markets in which the Company conducts its business are intensely competitive and highly regulated.

The health-care industry is also experiencing:

- Pressure from governments and healthcare providers to keep prices low while increasing access to drugs;
- Increased discount liability due to the population of "baby boomers" covered under Medicare, specifically those beneficiaries receiving drug cost offset through the Medicare Part D Coverage Gap (the "Donut Hole");
- Increasing challenges from third party payers for products to have demonstrable clinical benefit, with pricing and reimbursement approval becoming increasingly linked to a product's clinical effectiveness and impact on overall costs of patient care;
- Increased R&D costs, because development programs are typically larger and take longer to get approval from regulators;
- Challenges to existing patents from generic manufacturers;
- Governments and healthcare systems favoring earlier entry of low cost generic drugs; and
- Higher marketing costs, due to increased competition for market share.

3. Review of our business

Shire's strategy has been developed to address these industry-wide competitive pressures. This strategy has resulted in a series of initiatives in the following areas:

Markets

Shire's current portfolio of approved products focuses on the following markets: HAE/LSD, Neuroscience, and GI and Internal Medicine. Shire has also established an Ophthalmics commercial unit in preparedness for the commercialization of Shire's ophthalmic pipeline candidates. In addition, Shire has a number of marketed products for other TAs from which it generates product revenues or royalties from third parties. In 2015 Shire derived approximately 45% of product sales from rare disease products, 36% from Neuroscience products and 19% from GI and Internal Medicine products. Shire's early stage research is primarily focused on rare diseases.

Shire has grown in part through acquisition which has brought therapeutic, geographic and pipeline growth and diversification. In 2015 Shire acquired NPS Pharma, Meritage and Foresight. On January 11, 2016, Shire announced that the Boards of Directors of Shire and Baxalta had reached an agreement under which Shire will combine with Baxalta. On January 22, 2016, Shire announced the closing of the acquisition of Dyax.

The acquisition of NPS Pharma added global rights to an innovative product portfolio with multiple growth catalysts, including GATTEX/REVESTIVE and NATPARA. The acquisition of Meritage provided global rights to OBS, a Phase 3-ready asset for the treatment of adolescents and adults with EoE, a rare, chronic inflammatory GI disease. This enhances Shire's late-stage pipeline and builds upon the Company's rare disease and GI commercial infrastructure and expertise. With the acquisition of Foresight Shire acquired the global rights to FST-100 (topical ophthalmic drops combining 0.6% povidone iodine (PVP-I) and 0.1% dexamethasone), a therapy in late-stage development for the treatment of infectious conjunctivitis, an ocular surface condition commonly referred to as pink eye. This acquisition further strengthens Shire's late-stage pipeline, has a clear strategic fit with lifitegrast, which is in late-stage development for treatment of dry eye disease, and further demonstrates Shire's commitment to building a leadership position in ophthalmics.

The acquisition of Dyax and their lead pipeline product, DX-2930, alongside Dyax's currently marketed product KALBITOR, expands and extends Shire's industry-leading HAE portfolio (FIRAZYR and CINRYZE), advancing its leadership position in rare diseases and enhancing the Company's growth profile.

The proposed combination with Baxalta will enable Shire to become a global leader in rare diseases.

In 2015 Shire derived 27% (2014: 30%) of product sales from outside of the US. Shire has ongoing commercialization and late-stage development activities, which are expected to further supplement the diversification of revenues in the future, including the following:

- Launch of INTUNIV in the EU for children and adolescents and the submission of INTUNIV NDA in Japan;
- Continued launch of REVESTIVE across Europe;
- Review of MAA for NATPAR in the EU.

R&D

In 2013 Shire combined the R&D organizations of its former divisions into a single One Shire R&D organization, focused around a prioritized portfolio of clinical development and research programs. Shire has focused its R&D efforts on five TAs: Neuroscience, GI/Metabolic Diseases, Renal/Fibrotic Diseases, Ophthalmic Diseases, and Diseases of the Complement Cascade. Shire concentrates its resources on obtaining regulatory approval for later-stage pipeline products within these therapeutic areas and focuses its early stage research activities in rare diseases.

Evidence of the successful progression of the late stage pipeline can be seen in the granting of approval and associated launches of the Company's products over the last five years. In this time several products have received regulatory approval including: in the US, FIRAZYR in 2011, VYVANSE for BED and NATPARA in 2015; in the EU, ELVANSE/TYVENSE for adults, INTUNIV for children and adolescents in 2015.

3. Review of our business

Shire's management reviews direct costs for all R&D projects by development phase.

Shire's R&D costs in 2015 and 2014 included expenditure on programs in all stages of development. The following table provides an analysis of the Company's direct R&D spend categorized by development stage, based upon the development stage of each program as at December 31, 2015 and 2014:

Year to December 31,	**2015 $'M**	2014 $'M
Early stage programs	**177**	170
Late stage programs	**225**	253
Currently marketed products	**179**	143
Total	**581**	566

In addition to the above, the Company recorded R&D employee costs of $303 million in 2015 (2014: $270 million) and other indirect R&D costs of $680 million (2014: $232 million), comprising depreciation and impairment charges.

For a discussion of the Company's current development projects see pages 20 to 21 of Shire's 2015 Annual Report.

Patents and market exclusivity The loss or expiration of patent protection or regulatory exclusivity with respect to any of the Company's major products could have a material adverse effect on the Company's revenues, financial condition and results of operations, as generic or biosimilar products may enter the market. Companies selling generic products often do not need to complete extensive clinical studies when they seek registration of a generic or biosimilar product and accordingly, are generally able to sell a generic version of the Company's products at a much lower price.

As expected, in 2009 Teva and Impax commenced commercial shipments of their authorized generic versions of ADDERALL XR, which led to lower sales of branded ADDERALL XR compared to the periods prior to the authorized generic launches.

In 2011 generic versions of the Company's CARBATROL and REMINYL products respectively were launched, which led to lower sales of these branded products compared to the period before loss of exclusivity.

In 2014 and 2015 generic versions of the Company's INTUNIV product was launched, which led to lower sales of Shire's INTUNIV product compared to the period before loss of exclusivity.

Shire is engaged in various legal proceedings with generic manufacturers with respect to its VYVANSE and LIALDA patents. For more detail of current patent litigation, see Note 18, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements set forth in Shire's 2015 Annual Report.

Corporate development

Shire focuses its corporate development activity on the acquisition and in-licensing of businesses, products or compounds which offer a strategic fit and have the potential to deliver demonstrable value to all of the Company's stakeholders.

Recent mergers or acquisitions

On January 22, 2016 Shire completed the acquisition of Dyax which has expanded and extended Shire's industry-leading HAE portfolio by adding the currently approved product, KALBITOR, SHP643 (formerly DX-2930), a Phase 3 program for the treatment of HAE as well as other programs in early stages of development.

On January 11, 2016 Shire announced that the Boards of Directors of Shire and Baxalta had reached an agreement under which Shire will combine with Baxalta, creating the global leader in rare diseases. Under the agreement Baxalta shareholders are to receive $18.00 in cash and 0.1482 Shire ADS per Baxalta share. Closing of the transaction is subject to approval by Baxalta and Shire shareholders, certain regulatory

approvals, redelivery of tax opinions delivered at signing and other customary closing conditions. For further details, see “Risks Related to the Proposed Merger with Baxalta Incorporated” included within Principal Risks and Uncertainties and “The January 2016 Facilities Agreement” in the Liquidity and Capital Resources section.

In 2015, Shire acquired:

- NPS Pharma which added global rights to an innovative product portfolio with multiple growth catalysts, including GATTEX/REVESTIVE with growing sales for the treatment of adults with SBS, a rare GI condition; and NATPARA, the only bioengineered hormone replacement therapy for use in the treatment of HPT, a rare endocrine disease;

- Meritage which provided Shire with worldwide rights to Meritage’s Phase 3-ready compound OBS for the potential treatment of adolescents and adults with EoE, a rare, chronic inflammatory GI disease; and

- Foresight which added global rights to SHP640 (formerly FST-100), a Phase-3 ready therapy for the treatment of infectious conjunctivitis, an ocular surface condition commonly referred to as pink eye.

In 2014, Shire acquired:

- ViroPharma which added a leading marketed product for the prophylactic treatment of HAE, CINRYZE, as well as a number of other marketed products and a pipeline of product candidates in the rare disease area;

- Lumena which added global rights to two late stage pipeline assets: SHP625, in Phase 2 clinical development with potential orphan indications; and SHP626, in Phase 1b clinical development;

- Fibrotech which added global rights to SHP627 in Phase 1b, a new class of oral drug with a novel mechanism of action which has the potential to address both the inflammatory and fibrotic components of disease processes. In addition Shire has acquired rights to Fibrotech’s library of novel molecules including SHP628, which is in pre-clinical development; and

- BIKAM which added global rights to SHP630 in pre-clinical development, for the potential treatment of autosomal dominant retinitis pigmentosa (adRP).

Collaboration and licensing activity

Shire has also entered into a number of collaboration and license agreements in recent years, including:

- A worldwide licensing and collaboration agreement with ArmaGen in 2014 to develop and commercialize AGT-182, an investigational ERT for the potential treatment of both the central nervous system and somatic manifestations in patients with Hunter syndrome;

- A collaboration and license agreement with Sangamo to develop ZFP Therapeutic clinical leads for Huntington’s disease and a ZFP Therapeutic for one additional gene target; and

- An agreement with Shionogi in 2012 to co-develop and co-commercialize VYVANSE and INTUNIV in Japan.

Organization and structure

In 2013 the Company integrated its operations into a simplified One Shire organization in order to drive future growth and innovation. Shire now comprises a single operating and reportable segment. For further details see Note 24 “Segmental reporting” to the consolidated financial statements set forth in Shire’s 2015 Annual Report. As part of the One Shire reorganization, the Company undertook a review of all of its pipeline programs and identified those projects that fit with the Company’s new strategic direction and have an acceptable likelihood of success. Following that review and overall streamlining of the R&D organization, several clinical and pre-clinical projects were discontinued which resulted in the elimination of a significant number of R&D roles and functional roles that support R&D in Basingstoke, and some positions were re-located.

In addition the Company also relocated its international commercial hub from Nyon, Switzerland to Zug, Switzerland.

In 2014 certain aspects of the One Shire program were temporarily put on hold due to AbbVie's offer for Shire, which was terminated in October 2014. Subsequent to the termination of AbbVie's offer, Shire announced on November 10, 2014 its plans to relocate over 500 positions to Lexington, Massachusetts from its Chesterbrook, Pennsylvania, site and establish Lexington as the Company's US operational headquarters in continuation of the One Shire efficiency program. This relocation streamlines business globally through two principal locations, Massachusetts and Switzerland, with support from regional and country-based offices around the world.

For further details see Note 5 "Reorganization costs" to the consolidated financial statements set forth in Shire's 2015 Annual Report.

On October 22, 2013 Shire discontinued the construction of its new manufacturing facility in San Diego. Subsequently on January 16, 2014, the Company sold and transferred certain of the assets relating to the manufacturing, marketing, sale and distribution of DERMAGRAFT to Organogenesis Inc. For further information, see Note 9, "Results of discontinued operations" to the consolidated financial statements included in Shire's 2015 Annual Report.

Results of operations for the years to December 31, 2015 and 2014

Financial highlights for the year to December 31, 2015 are as follows:

> Product sales excluding INTUNIV were up 10% (up 14% on a Non GAAP CER[1] basis), with growth driven by VYVANSE[2] (up 19% to $1,722 million), CINRYZE (up 23% to $618 million), LIALDA/MEZAVANT (up 8% to $684 million) and FIRAZYR (up 22% to $445 million). GATTEX/REVESTIVE and NATPARA acquired with NPS Pharma contributed 3 percentage points, or $166 million of product sales growth.

> Product sales growth in 2015 was held back, as expected, by 4 percentage points due to the foreign exchange headwinds from the strong US dollar, primarily affecting sales of ELAPRASE, REPLAGAL and VPRIV.

> Total product sales were up 5% on 2014 (up 9% on a Non GAAP CER basis[1]) to $6,100 million (2014: $5,830 million). Total product sales were held back by significantly lower INTUNIV sales (down 80% to $65 million) following the introduction of generic competition from December 2014.

> Total revenues were up 7% to $6,417 million (2014: $6,022 million), due to our product sales growth and higher royalties and other revenues (up 65%), primarily $115 million of SENSIPAR royalties acquired with NPS Pharma.

> Operating income in 2015 was down 16% to $1,420 million (2014: $1,698 million), as higher total revenues in 2015 were offset by higher operating costs as we advance our pipeline, invest behind current and anticipated product launches and include NPS Pharma operating costs for the first time. Operating income in 2015 was held back by higher IPR&D impairment charges ($644 million in 2015 relating to SHP625 and SHP608), and higher intangible asset amortization charges following the acquisition of NPS Pharma, which were in part offset by a net credit from changes in the fair value of contingent consideration liabilities ($150 million).

> Diluted earnings per ordinary share from continuing operations decreased 62% to $2.20 (2014: $5.76) primarily as a result of comparison to strong diluted earnings per ordinary shares in 2014 which benefited from the $1,635 million break fee received following AbbVie's terminated offer for Shire.

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[1] CER, a Non GAAP financial measure. CER performance is determined by comparing 2015 performance (restated using 2014 exchange rates) to actual 2014 reported performance.

[2] Lisdexamfetamine dimesylate ("LDX") currently marketed as VYVANSE in the US and Canada, VENVANSE in Latin America and ELVANSE in certain territories in the EU for the treatment of Attention Deficit Hyperactivity Disorder ("ADHD") ADHD and in the US for the treatment of moderate to severe BED.

3. Review of our business

Total revenues

The following table provides an analysis of the Company's total revenues by source:

Year to December 31,	**2015 $'M**	2014 $'M	Change $'M
Product sales	**6,099.9**	5,830.4	+5%
Royalties	**300.5**	160.8	+87%
Other revenues	**16.3**	30.9	-47%
Total	**6,416.7**	6,022.1	+7%

Product sales

Year to December 31,	**Year to December 31, 2015 $'M**	Year to December 31, 2014 $'M	Product sales growth %	Non GAAP CER growth[1] %	US prescription growth[2] %	Exit market share[2] %
Net product sales:						
VYVANSE	**1,722.2**	1,449.0	+19	+21	+8	17
LIALDA/MEZAVANT	**684.4**	633.8	+8	+10	+10	36
CINRYZE	**617.7**	503.0	+23	+24	n/a[3]	n/a[3]
ELAPRASE	**552.6**	592.8	-7	+4	n/a[3]	n/a[3]
FIRAZYR	**445.0**	364.2	+22	+25	n/a[3]	n/a[3]
REPLAGAL	**441.2**	500.4	-12	+1	n/a[4]	n/a[4]
ADDERALL XR	**362.8**	383.2	-5	-4	+10	5
VPRIV	**342.4**	366.7	-7	+1	n/a[3]	n/a[3]
PENTASA	**305.8**	289.7	+6	+6	-7	12
FOSRENOL	**177.6**	183.0	-3	+4	-9	3
GATTEX/REVESTIVE	**141.7**	–	n/a	n/a	n/a[3]	n/a[3]
XAGRID	**100.8**	108.5	-7	+7	n/a[3]	n/a[3]
INTUNIV	**65.1**	327.2	-80	-79	-70	1
NATPARA	**24.4**	–	n/a	n/a	n/a[3]	n/a[3]
Other product sales	**116.2**	128.9	-10	-1	n/a	n/a
Total product sales	**6,099.9**	5,830.4	+5	+9		

[1] On a Constant Exchange Rate ("CER") basis, which is a Non GAAP measure, computed by comparing 2015 product sales and revenues restated using 2014 average foreign exchange rates to 2014 actual product sales and revenues. Average exchange rates for the year to December 31, 2015 were $1.53:£1.00 and $1.11:€1.00 (2014: $1.65:£1.00 and $1.33:€1.00). For reconciliation to US GAAP please see page 159 of Shire's 2015 Annual Report.

[2] This information is an estimate derived from the use of information under license from the following IMS Health information service: IMS NPA Weekly for the period January 17, 2014 to January 22, 2016. IMS expressly reserves all rights, including rights of copying, distribution and republication. Exit market share represents the average US market share in the month ended December 31, 2015.

[3] IMS NPA Data not available.

[4] Not sold in the US in the year to December 31, 2015.

VYVANSE — ADHD and Binge Eating Disorder (BED)

VYVANSE product sales grew strongly (up 19%) in 2015. Growth was driven by prescription growth in the US (up 8%), the benefit of price increases[1] and to a lesser extent the benefit of stocking in 2015 as compared to destocking in 2014 and growth from international markets. This growth was partially offset by higher sales deductions as a percentage of product sales in 2015 as compared to 2014.

Litigation proceedings regarding VYVANSE are ongoing. Further information about this litigation can be found in Note 18, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements included in Shire's 2015 Annual Report.

LIALDA/MEZAVANT — Ulcerative Colitis (UC)

The 8% growth in product sales for LIALDA/MEZAVANT in 2015 was primarily driven by higher prescription demand (up 10%) and, to a lesser extent, a price increase[1] taken at the beginning of 2015. The growth was partially offset by higher sales deductions as a percentage of sales in 2015 as compared to 2014 and, to a lesser extent the impact of destocking in 2015 compared to stocking in 2014.

Litigation proceedings regarding LIALDA are ongoing. Further information about this litigation can be found in Note 18, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements included in Shire's 2015 Annual Report.

CINRYZE — prophylactic treatment of HAE

CINRYZE sales were up 23% on 2014, primarily driven by strong growth in patients on therapy and, to a lesser extent, sales also benefited from a price increase[1] taken since 2014.

ELAPRASE — Hunter syndrome

ELAPRASE product sales were down 7% (up 4% on a Non GAAP CER basis[2]) reflecting the negative impact of foreign exchange movements and to a lesser extent a lower average price due to pricing pressures and geographic mix. These negative factors were partially offset by higher volumes primarily due to an increase in the number of patients on therapy.

FIRAZYR — HAE

FIRAZYR product sales growth was up 22% compared to 2014, driven by a higher number of patients on therapy and, to a lesser extent, the effect of a price increase[1] in the US market.

REPLAGAL — Fabry disease

REPLAGAL sales were down 12% compared to 2014 (up 1% on a Non GAAP CER basis[2]), as the benefit of more patients on therapy was more than offset by the negative impact of foreign exchange and to a lesser extent, pricing pressures.

ADDERALL XR — ADHD

ADDERALL XR product sales were down 5% in 2015, as growth in prescription demand (up 10%) was more than offset by higher sales deductions as a percentage of product sales in 2015 compared to 2014.

VPRIV — Gaucher disease

VPRIV product sales were down 7% (up 1% on a Non GAAP CER basis[2]), as sales growth was negatively impacted by foreign exchange and the impact of new competition in the US market partially offset by higher utilization per patient.

PENTASA — UC

PENTASA product sales were up 6% as the benefit of price increases[1] was partially offset by higher sales deductions as a percentage of product sales and lower prescription demand in 2015 compared to 2014.

GATTEX — SBS

Shire acquired GATTEX/REVESTIVE through its acquisition of NPS Pharma on February 21, 2015, and recorded sales of $142 million in 2015 (up 51% on a pro-forma basis[3]).

INTUNIV — ADHD

INTUNIV product sales were down 80% compared to 2014, reflecting the impact of generic competitors since December 2014.

NATPARA — Hypocalcemia in Hypoparathyroidism

Shire made NATPARA available on April 1, 2015, after acquiring the product through its acquisition of NPS, and following a strong US launch, sales of $24 million were recorded in 2015.

1. The actual net effect of price increases on current period net sales compared to the comparative period is difficult to quantify due to the various managed care rebates, Medicaid discounts, other discount programs in which the Company participates and fee for service agreements with wholesalers customers.
2. CER, a Non GAAP financial measure. CER performance is determined by comparing 2015 performance (restated using 2014 exchange rates) to actual 2014 reported performance.
3. Sales prior to February 21, 2015 were recorded by NPS Pharma, prior to the acquisition by Shire.

Royalties

	Year to December 31, 2015 $'M	Year to December 31, 2014 $'M	Change %
SENSIPAR	**114.5**	–	n/a
3TC and ZEFFIX	**49.1**	33.9	45%
FOSRENOL	**46.1**	51.4	-10%
INTUNIV	**27.8**	22.0	26%
ADDERALL XR	**26.0**	28.9	-10%
Other	**37.0**	24.6	50%
Total	**300.5**	160.8	87%

Royalty income increased by 87% in 2015 due primarily to the inclusion of royalty income receivable from Amgen Inc. for SENSIPAR (following the acquisition of NPS Pharma by Shire).

Cost of product sales from continuing operations

Cost of product sales decreased to $969.0 million for the year to December 31, 2015 (16% of product sales), down from $979.3 million in the corresponding period in 2014 (17% of product sales). Cost of product sales as a percentage of product sales was one percentage point lower compared to the same period in 2014, as the impact of the inclusion of lower margin products acquired with NPS Pharma was more than offset by lower charges on the unwind of fair value adjustments on acquired inventories.

For the year to December 31, 2015 cost of product sales included depreciation of $46.1 million (2014: $57.1 million).

R&D from continuing operations

R&D expenditure increased to $1,564.0 million for the year to December 31, 2015 (26% of product sales), compared to $1,067.5 million in the corresponding period in 2014 (18% of product sales). R&D expenditure in 2015 includes impairment charges of $467 million relating to the SHP625 IPR&D intangible asset, due to a lower probability of regulatory approval following trial results and revised commercial potential, and $176.7 million relating to the SHP608 IPR&D intangible asset, following preclinical toxicity findings. R&D expenditure in 2014 includes impairment charges of $190.3 million, primarily relating to the SHP602 IPR&D intangible asset of $166.0 million, following the Phase 2 trial being placed on clinical hold and $22.0 million relating to the SHP613 IPR&D intangible asset, following the decision to discontinue further development based on portfolio prioritization as well as unexpected challenges and complexities with the development program. Also included in 2014 R&D expenditure is a payment of $12.5 million in respect of in-licensed and acquired products. Excluding these costs, R&D expenditure in the year to December 31, 2015 increased by 6% or by $56 million, due to the inclusion of NPS Pharma costs since February 2015 and increased investment in existing pipeline programs, partially offset by lower spend on certain programs in 2014 which was not repeated in 2015.

R&D expenditure in the year to December 31, 2015 included depreciation of $21.7 million (2014: $24.5 million).

SG&A from continuing operations

3. Review of our business

SG&A expenditure increased to $2,341.2 million for the year to December 31, 2015 from $2,025.8 million. SG&A expenditure as a proportion of product sales also increased by three percentage points to 38% of product sales for the year to December 31, 2015 compared with 35% of product sales in the corresponding period in 2014, due to the inclusion of NPS Pharma's SG&A costs, higher amortization of intangible assets acquired with NPS Pharma and increased sales and marketing spend supporting the launch of VYVANSE for the treatment of BED and the anticipated launch of lifitegrast for the treatment of Dry Eye Disease (DED).

For the year to December 31, 2015 SG&A included depreciation of $70.7 million (2014: $81.9 million) and amortization of $498.7 million (2014: $243.8 million).

Gain on sale of product rights

For the year to December 31, 2015 Shire recorded a net gain on sale of product rights of $14.7 million (2014: $88.2 million) due primarily to the re-measurement of the contingent consideration receivable relating to the divestment of DAYTRANA. In 2014 Shire additionally recorded a net gain on sale of product rights following the divestment of CALCICHEW, VANCOCIN, ESTRACE and EXPUTEX.

Reorganization costs

For the year to December 31, 2015 Shire recorded reorganization costs of $97.9 million (2014: $180.9 million) primarily related to the relocation of roles from Chesterbrook to Lexington. 2014 also included costs relating to the One Shire reorganization, which included termination benefits and other reorganization costs.

Integration and acquisition costs

For the year to December 31, 2015 Shire recorded net integration and acquisition costs of $39.8 million, representing acquisition and integration costs of $189.7 million, primarily related to NPS Pharma, ViroPharma, Baxalta and Dyax. These costs were offset by a net credit of $149.9 million on the change in fair value of contingent consideration liabilities, primarily relating to SHP625 (acquired with Lumena) and SHP608 (acquired with Lotus Tissue Repair, Inc.).

In 2014 Shire recorded integration and acquisition costs of $158.8 million, comprising acquisition and integration costs of $144.1 million, primarily related to ViroPharma, and a $14.7 million charge relating to the change in fair values of contingent consideration.

Interest expense

For the year to December 31, 2015 Shire incurred interest expense of $41.6 million (2014: $30.8 million). Interest expense in 2015 principally relates to interest and financing costs incurred on facilities drawn down in respect of the acquisition of NPS Pharma.

Taxation from continuing operations

The effective tax rate on income from continuing operations was 3% (2014: 2%).

The effective rate of tax on income from continuing operations in 2015 is low primarily due to the deferred tax accounting for acquisitions in higher tax territories, including the amortization and impairments of acquired intangible assets and changes in the fair values of contingent consideration liabilities, which do not reduce the Company's cash tax liability. In addition, the effective rate of tax on income from continuing operations is reduced by increased R&D credits, the effect of the finalization of various tax returns and changes in profit mix including the benefit in higher tax territories of significant reorganization and integration costs.

The effective rate of tax on income from continuing operations in 2014 includes the receipt of the break fee from AbbVie and recognition of a net credit to income taxes of $235 million, following the settlement of certain tax positions with the Canadian revenue authorities in 2014. The Company has obtained advice that the break fee should not be taxable in Ireland. The Company has therefore concluded that no tax liability should arise and did not recognize a tax charge in the income statement in 2014. The relevant tax return was submitted on September 23, 2015.

Discontinued operations

The loss from discontinued operations for the year to December 31, 2015 was $34.1 million net of tax (2014: gain of $122.7 million) primarily relating to a change in estimate for onerous lease provisions.

2014 included a tax credit of $211.3 million primarily driven by a tax benefit arising following a reorganization of the Regenerative Medicine business undertaken in Q4 2014, associated with the divestment of the DERMAGRAFT business in Q1 2014. The gain was partially offset by costs associated with the divestment of the DERMAGRAFT business, including a loss on re-measurement of contingent consideration receivable from Organogenesis to its fair value.

Financial condition at December 31, 2015 and 2014

Cash & cash equivalents

Cash and cash equivalents decreased by $2,846.9 million to $135.5 million at December 31, 2015 (December 31, 2014: $2,982.4 million), primarily due to the use of existing cash and cash equivalents to partially fund the acquisitions of NPS Pharma, Foresight and Meritage.

In the year to December 31, 2014 Cash and cash equivalents included the receipt of the $1,635 million break fee in relation to AbbVie's terminated offer for Shire, the benefit of the $417 million repayment received from the Canadian revenue authorities and the net proceeds of $554.5 million from Shire's line of credit and other borrowings. These inflows were offset by the cost of acquiring ViroPharma, Lumena and Fibrotech.

Accounts receivable, net

Accounts receivable, net increased by $166.1 million to $1,201.2 million at December 31, 2015 (December 31, 2014: $1,035.1 million), primarily due to the inclusion of NPS Pharma's accounts receivable and an increase in revenue. Days sales outstanding slightly decreased to 42 days (December 31, 2014: 43 days).

Inventories

Inventories increased by $90.6 million to $635.4 million at December 31, 2015 (December 31, 2014: $544.8 million), primarily due to the inventories acquired as part of the acquisition of NPS Pharma and an increase in inventories of certain products following continued sales growth.

Goodwill

Goodwill increased by $1,672.9 million to $4,147.8 million at December 31, 2015 (December 31, 2014: $2,474.9 million), principally due to the acquisitions of NPS Pharma, Meritage and Foresight.

Other intangible assets, net

Other intangible assets increased by $4,238.9 million to $9,173.3 million at December 31, 2015 (December 31, 2014: $4,934.4 million), principally due to the intangible assets acquired with NPS Pharma, Meritage and Foresight, offset by IPR&D intangible asset impairment charges and intangible asset amortization.

Short term borrowings

Short term borrowings increased by $661.5 million to $1,511.5 million at December 31, 2015 (December 31, 2014: $850.0 million), reflecting the utilization of short term debt facilities to partially fund the acquisition of NPS Pharma and the recognition of secured non-recourse debt liabilities assumed as part of the NPS Pharma acquisition.

Other current liabilities

Other current liabilities decreased by $118.5 million to $144.0 million at December 31, 2015 (December 31, 2014: $262.5 million) principally due to the reduction in the fair value of contingent consideration payable associated with the SHP625 IPR&D intangible asset.

Non-current deferred tax liabilities

Non-current deferred tax liabilities increased by $995.3 million to $2,205.9 million at December 31, 2015 (December 31, 2014: $1,210.6 million) primarily due to deferred tax liabilities arising on intangible assets partially offset by deferred tax assets arising on tax attributes both acquired with NPS Pharma, Meritage and Foresight.

Other non-current liabilities

Other non-current liabilities increased by $62.1 million to $798.8 million at December 31, 2015 (December 31, 2014: $736.7 million) principally due to a change in estimate in respect of onerous lease liabilities and

recognition of contingent consideration payable in respect of the Meritage acquisition, offset by a reduction in the fair value of contingent consideration payable associated with the SHP608 and SHP625 IPR&D intangible assets.

Liquidity and capital resources

General

The Company's funding requirements depend on a number of factors, including the timing and extent of its development programs; corporate, business and product acquisitions; the level of resources required for the expansion of certain manufacturing and marketing capabilities as the product base expands; increases in accounts receivable and inventory which may arise with any increase in product sales; competitive and technological developments; the timing and cost of obtaining required regulatory approvals for new products; the timing and quantum of milestone payments on business combinations, in-licenses and collaborative projects; the timing and quantum of tax and dividend payments; the timing and quantum of purchases by the Employee Benefit Trust of Shire shares in the market to satisfy awards granted under Shire's employee share plans; and the amount of cash generated from sales of Shire's products and royalty receipts.

An important part of Shire's business strategy is to protect its products and technologies through the use of patents, proprietary technologies and trademarks, to the extent available. The Company intends to defend its intellectual property and as a result may need cash for funding the cost of litigation.

The Company finances its activities through cash generated from operating activities; credit facilities; private and public offerings of equity and debt securities; and the proceeds of asset or investment disposals.

Shire's balance sheet includes $135.5 million of cash and cash equivalents at December 31, 2015.

Shire has a revolving credit facility of $2,100 million which matures in 2020, $750 million of which was utilized as December 31, 2015.

In connection with the acquisitions of NPS Pharma and Dyax and the proposed combination with Baxalta, Shire entered into a number of facility arrangements in the year to December 31, 2015 and subsequently in 2016. The details of these facility arrangements are presented below. Shire also assumed non-recourse secured debt obligations as part of the NPS Pharma acquisition with a carrying value of $81.4 million as at December 31, 2015. See Note 16, "Borrowings" to the consolidated financial statements included in Shire's 2015 Annual Report.

In addition Shire has access to certain short-term uncommitted lines of credit which it utilizes from time to time to provide short-term flexibility in cash management. At December 31, 2015, these lines of credit were not utilized.

Revolving Credit Facilities Agreement

On December 12, 2014, Shire entered into a $2,100 million revolving credit facilities agreement (the "RCF") with a number of financial institutions, for which Abbey National Treasury Services PLC (trading as Santander Global Banking and Markets), Bank of America Merrill Lynch International Limited, Barclays Bank PLC, Citigroup Global Markets Limited, Lloyds Bank PLC, The Royal Bank of Scotland PLC and Sumitomo Mitsui Banking Corporation acted as mandated lead arrangers and bookrunners and DNB Bank ASA, The Bank of Tokyo-Mitsubishi UFJ, Ltd., Credit Suisse AG, London Branch, Deutsche Bank Luxembourg S.A., Goldman Sachs Bank USA, Mizuho Bank, Ltd. and Morgan Stanley Bank International Limited acted as arrangers. Shire is an original borrower and original guarantor under the RCF. Shire has agreed to act as guarantor for any of its subsidiaries that become additional borrowers under the RCF. As at December 31, 2015 the Company utilized $750 million of the RCF.

The RCF, which terminates on December 12, 2020, may be applied towards financing the general corporate purposes of Shire. The RCF incorporates a $250 million US dollar and euro swingline facility operating as a sub-limit thereof.

Interest on any loans made under the RCF is payable on the last day of each interest period, which may be one week or one, two, three or six months at the election of Shire, or as otherwise agreed with the lenders. The interest rate for the RCF is: LIBOR (or, in relation to any revolving loan in euro, EURIBOR); plus 0.30% per year subject to change depending upon (i) the prevailing ratio of Net Debt to EBITDA (each as defined in

the RCF) in respect of the most recently completed financial year or financial half year and (ii) the occurrence and continuation of an event of default in respect of the financial covenants or the failure to provide a compliance certificate.

Shire shall also pay (i) a commitment fee equal to 35% of the applicable margin on available commitments under the RCF for the availability period applicable thereto and (ii) a utilization fee equal to (a) 0.10% per year of the aggregate of all outstanding loans up to an aggregate base currency amount equal to $700 million, (b) 0.15% per year of the amount by which the aggregate base currency amount of all outstanding loans exceeds $700 million but is equal to or less than $1,400 million and (c) 0.30% per year of the amount by which the aggregate base currency amount of all outstanding loans exceeds $1,400 million.

The RCF includes customary representations and warranties, covenants and events of default, including requirements that Shire's (i) ratio of Net Debt to EBITDA in respect of the most recently ended 12-month relevant period (each as defined in the RCF) must not, at any time, exceed 3.5:1 except that, following an acquisition fulfilling certain criteria, Shire may on a once only basis elect to increase this ratio to (a) 5.5:1 for the relevant period in which the acquisition was completed (b) 5.0:1 in respect of the first relevant period following the relevant period in which the acquisition was completed and (c) 4.5:1 in respect of the second relevant period following the relevant period in which the acquisition was completed, and (ii) ratio of EBITDA to Net Interest for the most recently ended 12-month relevant period (each as defined in the RCF) must not be less than 4.0:1.

The RCF restricts subject to certain exceptions, Shire's ability to incur additional financial indebtedness, grant security over its assets or provide loans/grant credit. Further, any lender may require mandatory prepayment of its participation if there is a change of control of Shire, subject to certain exceptions for schemes of arrangement and analogous schemes.

Events of default under the RCF include, subject to customary grace periods and materiality thresholds: (i) non-payment of any amounts due under the finance documents (as defined in the RCF), (ii) failure to satisfy any financial covenants, (iii) material misrepresentation in any of the finance documents, (iv) failure to pay, or certain other defaults, under other financial indebtedness, (v) certain insolvency events or proceedings, (vi) material adverse changes in the business, operations, assets or financial condition of Shire as a whole, (vii) if it becomes unlawful for Shire (or any successor parent company) or any of their respective subsidiaries that are parties to the RCF to perform their obligations thereunder or (viii) if Shire (or any successor parent company) or any subsidiary thereof which is a party to the RCF repudiates such agreement or other finance document, among others.

The RCF is governed by the English law.

Term Loan Facilities Agreement

January 2016 Facilities Agreement

On January 11, 2016, Shire (as original guarantor and original borrower), entered into, an $18.0 billion bridge facilities agreement with, among others, Barclays Bank PLC ("Barclays") and Morgan Stanley Bank International Limited, acting as mandated lead arrangers and bookrunners (the "January 2016 Facilities Agreement"). The January 2016 Facilities Agreement comprises two credit facilities: (i) a $13.0 billion term loan facility which, subject to a one year extension option exercisable at Shire's option, matures on January 11, 2017 ("January 2016 Facility A") and (ii) a $5.0 billion revolving loan facility which, subject to a one year extension option exercisable at Shire's option, matures on January 11, 2017 ("January 2016 Facility B"). Shire has agreed to act as guarantor for any of its subsidiaries that become additional borrowers under the January 2016 Facilities Agreement. As of February 23, 2016 the January 2016 Facility was undrawn.

January 2016 Facility A may be used to finance the cash consideration payable in respect of the proposed combination with Baxalta and certain costs related to the proposed combination. January 2016 Facility B may be used to finance the redemption of all or part of Baxalta's senior notes upon completion of the proposed combination.

Interest on any loans made under the January 2016 Facilities Agreement will be payable on the last day of each interest period, which may be one week or one, two, three or six months, or as otherwise agreed with the lenders. The interest rate applicable to the January 2016 Facilities Agreement is LIBOR plus 1.25 percent per annum, increasing by: (i) 0.25 percent per annum on July 11, 2016 and on each subsequent

date falling at three month intervals thereafter until (and excluding) April 11, 2017 and (ii) 0.50 percent per annum on April 11, 2017 and on each subsequent date falling at three month intervals thereafter.

Shire shall also pay a commitment fee on the available but unutilized commitments under the January 2016 Facilities Agreement for the availability period applicable to each facility. With effect from first utilization, the commitment fee rate will be 35 percent of the applicable margin. Before first utilization, the commitment fee rate shall be increased in stages from 10 percent to 35 percent of the applicable margin over the period to May 11, 2016.

The January 2016 Facilities Agreement includes customary representations and warranties, covenants and events of default, including requirements that Shire's (i) ratio of Net Debt to EBITDA in respect of the most recently ended 12-month relevant period, (each as defined in the January 2016 Facilities Agreement), must not, at any time, exceed 3.5:1, except that following the combination with Baxalta, or any other acquisition fulfilling certain criteria, Shire may elect on a once only basis to increase this ratio to (a) 5.5:1 for the relevant period in which the acquisition was completed, (b) 5.0:1 in respect of the first relevant period following the relevant period in which the acquisition was completed and (c) 4.5:1 in respect of the second relevant period following the relevant period in which the acquisition was completed, and (ii) ratio of EBITDA to Net Interest, for the most recently ended 12-month relevant period (each as defined in the January 2016 Facilities Agreement), must not be less than 4.0:1.

The January 2016 Facilities Agreement restricts, subject to certain exceptions, Shire's ability to incur additional financial indebtedness, grant security over its assets or provide loans/grant credit. Further, any lender may require mandatory prepayment of its participation if there is a change of control of Shire, subject to certain exceptions for schemes of arrangement and analogous schemes. In addition, in certain circumstances and subject to certain broad exceptions, the net cash proceeds of disposals and certain issues, loans, sales or offerings of debt securities by any member of Shire's group must be applied in cancellation of the available commitments under the January 2016 Facilities Agreement and, if applicable, mandatory prepayment of any loans made under the January 2016 Facilities Agreement.

Events of default under the January 2016 Facilities Agreement include, subject to customary grace periods and materiality thresholds: (i) non-payment of any amounts due under the finance documents (as defined in the January 2016 Facilities Agreement), (ii) failure to satisfy any financial covenants, (iii) material misrepresentation in any of the finance documents, (iv) failure to pay, or certain other defaults, under other financial indebtedness, (v) certain insolvency events or proceedings, (vi) material adverse changes in the business, operations, assets or financial condition of Shire as a whole, (vii) if it becomes unlawful for Shire (or any successor parent company) or any of their respective subsidiaries that are parties to the January 2016 Facilities Agreement to perform their obligations thereunder or (viii) if Shire (or any successor parent company) or any subsidiary thereof which is a party to the January 2016 Facilities Agreement repudiates the January 2016 Facilities Agreement or any other finance document, among others.

The January 2016 Facilities Agreement is governed by English law.

November 2015 Facilities Agreement

On November 2, 2015, Shire (as original guarantor and original borrower) entered into a $5.6 billion facilities agreement with, among others, Morgan Stanley Bank International Limited and Deutsche Bank AG, London Branch acting as mandated lead arrangers and bookrunners (the "November 2015 Facilities Agreement"). The November 2015 Facilities Agreement comprises three credit facilities: (i) a $1.0 billion term loan facility which, subject to a one year extension option exercisable at Shire's option, matures on November 2, 2016 ("November 2015 Facility A"), (ii) a $2.2 billion amortizing term loan facility which matures on November 2, 2017 ("November 2015 Facility B") and (iii) a $2.4 billion amortizing term loan facility which matures on November 2, 2018 ("November 2015 Facility C").

As of December 31, 2015, the November 2015 Facilities Agreement was undrawn. In January 2016 the November 2015 Facilities Agreement was utilized in full to finance the purchase price payable in respect of Shire's acquisition of Dyax and certain costs related to the acquisition.

Interest on any loans made under the November 2015 Facilities Agreement is payable on the last day of each interest period, which may be one week or one, two, three or six months, or as otherwise agreed with the lenders. The interest rate applicable is LIBOR plus, in the case of November 2015 Facility A, 0.55% per annum, in the case of November 2015 Facility B, 0.65% per annum and, in the case of November 2015

Facility C, 0.75% per annum, in each case until delivery of the first compliance certificate required to be delivered after the date of the November 2015 Facilities Agreement and is subject to change thereafter depending on (i) the prevailing ratio of Net Debt to EBITDA (each as defined in the November 2015 Facilities Agreement) in respect of the most recently completed financial year or financial half year and (ii) the occurrence and continuation of an event of default in respect of the financial covenants or failure to provide a compliance certificate.

The November 2015 Facilities Agreement includes customary representations and warranties, covenants and events of default, including requirements that Shire's (i) ratio of Net Debt to EBITDA in respect of the most recently ended 12-month relevant period, (each as defined in the November 2015 Facilities Agreement) must not, at any time, exceed 3.5:1, except that following an acquisitions fulfilling certain criteria, Shire may elect on a once only basis to increase this ratio to (a) 5.5:1 for the relevant period in which the acquisition was completed, (b) 5.0:1 in respect of the first relevant period following the relevant period in which the acquisition was completed and (c) 4.5:1 in respect of the second relevant period following the relevant period in which the acquisition was completed, and (ii) the ratio of EBITDA to Net Interest in respect of the most recently ended 12-month relevant period (each as defined in the November 2015 Facilities Agreement) must not be less than 4.0:1.

The November 2015 Facilities Agreement restricts, subject to certain exceptions, Shire's ability to incur additional financial indebtedness, grant security over its assets or provide loans/grant credit. Further, any lender may require mandatory prepayment of its participation if there is a change of control of Shire, subject to certain exceptions for schemes of arrangement and analogous schemes.

Events of default under the November 2015 Facilities Agreement include, subject to customary grace periods and materiality thresholds: (i) non-payment of any amounts due under the finance documents (as defined in the November 2015 Facilities Agreement), (ii) failure to satisfy any financial covenants, (iii) material misrepresentation in any of the finance documents, (iv) failure to pay, or certain other defaults, under other financial indebtedness, (v) certain insolvency events or proceedings, (vi) material adverse changes in the business, operations, assets or financial condition of Shire as a whole, (vii) if it becomes unlawful for Shire (or any successor parent company) or any of their respective subsidiaries that are parties to the November 2015 Facilities Agreement to perform their obligations thereunder or (viii) if Shire (or any successor parent company) or any subsidiary thereof which is a party to the November 2015 Facilities Agreement repudiates the November 2015 Facilities Agreement or any other finance document, among others.

The November 2015 Facilities Agreement is governed by English law.

January 2015 Facility Agreement

On January 11, 2015, Shire entered into an $850 million term facility agreement with, among others, Citigroup Global Markets Limited (acting as mandated lead arranger and bookrunner) (the "January 2015 Facility Agreement") with an original maturity date of January 10, 2016. The maturity date was subsequently extended to July 11, 2016 in line with the provisions within the January 2015 Facility Agreement allowing the maturity date to be extended twice, at Shire's option, by six months on each occasion.

The January 2015 Facility Agreement was available to finance the purchase price payable in respect of Shire's acquisition of NPS Pharma (including certain related costs). On September 28, 2015 the Company reduced the January 2015 Facility Agreement by $100 million. As at December 31, 2015 the January 2015 Facility Agreement, was fully utilized in the amount of $750 million. In January 2016 and at various points thereafter, the Company canceled parts of the January 2015 Facility Agreement. On February 22, 2016, the Company repaid in full the remaining balance of $100 million.

2013 Facilities Agreement

On November 11, 2013, Shire entered into a $2,600 million facilities agreement with, among others, Morgan Stanley Bank International Limited (acting as mandated lead arranger and bookrunner) (the "2013 Facilities Agreement"). The 2013 Facilities Agreement comprised two credit facilities: (i) a $1,750 million term loan facility and (ii) an $850 million term loan facility.

On December 13, 2013 and at various points thereafter, the Company cancelled parts of the 2013 Facilities Agreement. On September 28, 2015 the Company repaid in full the remaining balance of $350 million under the 2013 Facilities Agreement.

3. Review of our business

Short-term uncommitted lines of credit ("Credit lines")

Shire has access to various Credit lines from a number of banks which provide flexibility to short-term cash management procedures. These Credit lines can be withdrawn by the banks at any time. The Credit lines are not relied upon for core liquidity. As at December 31, 2015 these Credit lines were not utilized.

Financing

Shire anticipates that its operating cash flow together with available cash, cash equivalents and the RCF will be sufficient to meet its anticipated future operating expenses, capital expenditures, tax and interest payments, lease obligations, repayment of the term loans and milestone payments as they become due over the next twelve months.

Shire's existing cash, January 2016 Facilities Agreement and the RCF are sufficient to finance Shire's proposed combination with Baxalta.

If the Company decides to acquire other businesses, it expects to fund these acquisitions from cash resources, the RCF, term loan facilities and through new borrowings (including issuances of debt securities) or the issuance of new equity if necessary.

Sources and uses of cash

The following table provides an analysis of the Company's gross and net cash (excluding restricted cash), as at December 31, 2015 and 2014:

Year to December 31,	**2015 $'M**	2014 $'M
Cash and cash equivalents[1]	**135.5**	2,982.4
Long term borrowings	**(69.9)**	–
Short term borrowings	**(1,511.5)**	(850.0)
Other debt	**(13.4)**	(13.7)
Total debt	**(1,594.8)**	(863.7)
Net (debt)/cash[2]	**(1,459.3)**	2,118.7

[1] Substantially all of the Company's cash and cash equivalents are held by foreign subsidiaries (i.e, those subsidiaries incorporated outside of Jersey, Channel Islands, the jurisdiction of incorporation of Shire plc, Shire's holding company). The amount of cash and cash equivalents held by foreign subsidiaries has not had, and is not expected to have, a material impact on the Company's liquidity and capital resources.

[2] Net (debt)/cash is a Non GAAP measure. The Company believes that Net (debt)/cash is a useful measure as it indicates the level of net cash/borrowings after taking account the cash and cash equivalents that could be utilized to pay down the outstanding borrowings. See above for reconciliation to cash and cash equivalents.

Cash flow activity

Net cash provided by operating activities for the year to December 31, 2015 decreased by $1,891.4 million or 45% to $2,337.0 million (2014: $4,228.4 million). Net cash provided by operating activities in 2014 included the receipt of the $1,635 million break fee in relation to AbbVie's terminated offer for Shire, and the benefit of the $417 million repayment received from the Canadian revenue authorities. Excluding these items net cash provided by operating activities in 2015 increased by $160.6 million as a result of higher cash receipts from gross product sales and royalties, which were partially offset by higher operating expense payments, including payments in relation to integration, reorganization activities and employee retention payments following AbbVie's terminated offer for Shire.

Net cash provided by operating activities for the year to December 31, 2014 increased by $2,765.4 million or 189% to $4,228.4 million (2013: $1,463.0 million) primarily due to the receipt of the $1,635 million break fee in relation to AbbVie's terminated offer for Shire, the benefit of the $417 million repayment received from the Canadian revenue authorities and higher cash receipts from gross product sales, offset by payments for sales deductions, payments of acquisition and integration costs in respect of the acquisitions of ViroPharma, Lumena and Fibrotech, costs in connection with Abbvie's terminated offer for Shire and cash payments in respect of the One Shire reorganization.

3. Review of our business

Net cash used in investing activities was $5,619.9 million in the year to December 31, 2015, principally relating to the cash paid for the acquisition of NPS Pharma of $5,220 million (excluding cash acquired with NPS Pharma of $42 million) and for the acquisitions of Foresight ($299 million) and Meritage ($75 million).

Net cash used in investing activities was $4,030.6 million in the year to December 31, 2014, principally relating to the cash paid for the acquisition of ViroPharma of $3,997 million (excluding cash acquired with ViroPharma of $233 million) and for the acquisition of Lumena of $300 million (excluding cash acquired with Lumena of $46 million), offset by the proceeds received on the sale of non-core product rights.

Net cash provided by financing activities was $439.0 million for the year to December 31, 2015, principally due to the drawings, net of subsequent repayments, made under Shire's various borrowing facilities to partially fund the NPS Pharma, Meritage and Foresight acquisitions. In addition the Company made dividend payments of $134.4 million.

Net cash provided by financing activities was $554.5 million for the year to December 31, 2014, principally due to the drawings, net of subsequent repayments, made under the facilities to partially fund the ViroPharma acquisition. In addition the Company paid cash of $551.4 million to settle the convertible debt assumed with ViroPharma, received cash of $346.7 million upon settlement of a purchased call option acquired with ViroPharma and made dividend payments of $121.2 million.

Outstanding letters of credit

At December 31, 2015, the Company had irrevocable standby letters of credit and guarantees with various banks totaling $48 million, providing security for the Company's performance of various obligations. These obligations are primarily in respect of the recoverability of insurance claims, lease obligations and supply commitments.

Cash Requirements

At December 31, 2015 the Company's cash requirements for short and long term liabilities reflected on the Balance Sheet and other contractual obligations were as follows:

	Payments due by period				
	Total $'M	Less than 1 year $'M	1-3 years $'M	3-5 years $'M	More than 5 years $'M
Long-term debt obligation	69.9	–	69.9	–	–
Short-term debt obligation	1,511.5	1,511.5	–	–	–
Operating leases obligation[1]	372.3	51.5	75.4	59.6	185.8
Purchase obligations[2]	1,406.4	934.3	304.1	167.3	0.7
Other long term liabilities reflected on the Balance Sheet[3]	624.8	–	416.9	191.5	16.4
Total	3,984.9	2,497.3	866.3	418.4	202.9

[1] The Company leases certain land, facilities, motor vehicles and certain equipment under operating leases expiring through 2021.
[2] Purchase obligations include agreements to purchase goods, investments or services (including clinical trials, contract manufacturing and capital equipment), including open purchase orders, that are enforceable and legally binding and that specify all significant terms. Shire expects to fund these commitments with cash flows from operating activities.
[3] Unrecognized tax benefits and associated interest and penalties of $201.2 million are included within payments due in one to three years.

In addition to the above contractual obligations, the Company is committed to make milestone payments (principally arising from the in-licensing or acquisition of products, assets and businesses), contingent upon the occurrence of future events (and therefore payment is not yet due). At December 31, 2015, the Company is contingently committed to pay up to approximately $0.8 billion (aggregate contractual amount) in respect of potential future research and development milestone payments and up to approximately $1.1 billion (aggregate contractual amount) in respect of commercial milestones as a result of prior business combinations and in-licensing agreements. Payments under these agreements are generally due and payable only upon achievement of certain development, regulatory and commercial milestones.

From a business perspective, these payments signify that the product is successfully moving through development and is now generating or is more likely to generate cash flows from product sales. However, it

is not possible to predict with reasonable certainty whether these milestones will be achieved or the timing of their achievement. As a result, these potential payments are not included in the table of contractual obligations.

Off-balance sheet arrangements

There are no off-balance sheet arrangements, aside from those outlined above, that have, or are reasonably likely to have, a current or future material effect on the Company's financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources.

Foreign currency fluctuations

A number of the Company's subsidiaries have a functional currency other than the US Dollar. As such, the consolidated financial results are subject to fluctuations in exchange rates, particularly in the Euro, Swiss Franc and Pound Sterling against the US Dollar.

The accumulated foreign currency translation differences at December 31, 2015 of $156.4 million are reported within accumulated other comprehensive income in the consolidated balance sheet and foreign exchange losses for the year to December 31, 2015 of $26.5 million are reported in the consolidated statements of income.

At December 31, 2015, the Company had outstanding swap and forward foreign exchange contracts to manage the currency risk associated with intercompany transactions. At December 31, 2015 the fair value of these contracts was a net liability of $9.6 million.

Inflation

Although at reduced levels in recent years, inflation continues to apply upward pressure on the cost of goods and services which are used in the business. However, the Company believes that the net effect of inflation on its revenues and operations has been minimal during the past three years.

Treasury policies and organization

The Company's principal treasury operations are coordinated by its corporate treasury function. All treasury operations are conducted within a framework of policies and procedures approved annually by the Board of Directors. As a matter of policy, the Company does not undertake speculative transactions that would increase its credit, currency or interest rate exposure.

Interest rate risk

The Company is principally exposed to interest rate risk on any borrowings under the Company's various debt facilities (see Liquidity and Capital Resources for details of each of the Company's facilities). Interest on each of these facilities is set at floating rates, to the extent utilized. Shire's exposure under these facilities is to US dollar interest rates. At December 31, 2015 the Company had fully utilized the January 2015 Facility Agreement and utilized $750 million of the RCF. Other facilities were not utilized at December 31, 2015.

The Company regularly evaluates the interest rate risk on its facilities. At December 31, 2015 the Company considered the risks associated with floating interest rates on borrowings under its facilities as appropriate. A hypothetical one percentage point increase or decrease in the interest rates applicable to drawings under the January 2015 Facility Agreement and the RCF at December 31, 2015 would increase interest expense by approximately $15 million per annum or would decrease the interest expense by approximately $7 million per annum.

The Company is also exposed to interest rate risk on its restricted cash, cash and cash equivalents and on foreign exchange contracts on which interest is set at floating rates. This exposure is primarily limited to US dollar, Pounds sterling and Euro interest rates. As the Company maintains all of its cash, liquid investments and foreign exchange contracts on a short term basis for liquidity purposes, this risk is not actively managed. In the year to December 31, 2015 the average interest rate received on cash and liquid investments was less than 1% per annum. These cash and liquid investments were primarily invested in US dollar term deposits with banks and money market and liquidity funds.

No derivative instruments were entered into during the year to December 31, 2015 to manage interest rate exposure. The Company continues to review its interest rate risk and the policies in place to manage the risk and may enter into derivative instruments to manage interest rate risk in the future.

3. Review of our business

Foreign exchange risk

The Company trades in numerous countries and as a consequence has transactional and translational foreign exchange exposures.

Transactional exposure arises where transactions occur in currencies different to the functional currency of the relevant subsidiary. The main trading currencies of the Company are the US dollar, Pounds Sterling, Swiss Franc, Canadian dollar and the Euro. It is the Company's policy that these exposures are minimized to the extent practicable by denominating transactions in the subsidiary's functional currency.

Where significant exposures remain, the Company uses foreign exchange contracts (being spot, forward and swap contracts) to manage the exposure for balance sheet assets and liabilities that are denominated in currencies different to the functional currency of the relevant subsidiary. These assets and liabilities relate predominantly to inter-company financing. The foreign exchange contracts have not been designated as hedging instruments. Cash flows from derivative instruments are presented within net cash provided by operating activities in the consolidated cash flow statement, unless the derivative instruments are economically hedging specific investing or financing activities.

Translational foreign exchange exposure arises on the translation into US dollars of the financial statements of non-US dollar functional subsidiaries.

At December 31, 2015 the Company had 39 swap and forward foreign exchange contracts outstanding to manage currency risk. The swap and forward contracts mature within 90 days. The Company did not have credit risk related contingent features or collateral linked to the derivatives. The Company has master netting agreements with a number of counterparties to these foreign exchange contracts and on the occurrence of specified events, the Company has the ability to terminate contracts and settle them with a net payment by one party to the other. The Company has elected to present derivative assets and derivative liabilities on a gross basis in the consolidated balance sheet. As at December 31, 2015 the potential effect of rights of set-off associated with the foreign exchange contracts would be an offset to both assets and liabilities of $1.4 million, resulting in net derivative assets and derivative liabilities of $0.5 million and $10.1 million, respectively. Further details are included below.

Foreign exchange risk sensitivity

The following exchange rate sensitivity analysis summarizes the sensitivity of the Company's reported revenues and net income to hypothetical changes in the average annual exchange rates of the Euro, Pound Sterling and Swiss Franc against the US Dollar (assuming a hypothetical 10% strengthening of the US Dollar against each of the aforementioned currencies in the year to December 31, 2015) (*see Table 1 below*).

A 10% weakening of the US Dollar against the aforementioned currencies would have an equal and opposite effect.

The table below provides information about the Company's swap and forward foreign exchange contracts by currency pair. The table presents the net principal amounts and weighted average exchange rates of all outstanding contracts. All contracts have a maturity date of less than three months (*see Table 2 below*).

Table 1

	Increase/ (reduction) in revenues $'M	Increase/ (reduction) in net income $'M
Euro	(71.0)	(45.0)
Pound Sterling	(17.0)	(9.0)
Swiss Franc	(3.1)	(2.0)

Table 2

December 31, 2015	Principal Value of Amount Receivable $'M	Weighted Average Exchange Rate	Fair Value $'M
Swap foreign exchange contracts			
Receive USD/Pay EUR	270.4	1.08	(1.1)
Receive GBP/Pay USD	258.1	1.52	(8.3)
Receive USD/Pay JPY	21.4	0.01	(0.3)
Receive USD/Pay SEK	14.4	0.12	(0.3)
Receive USD/Pay MXN	11.6	0.06	0.3
Receive USD/Pay AUD	7.4	0.72	0.1

Concentration of credit risk

Financial instruments that potentially expose Shire to concentrations of credit risk consist primarily of short-term cash investments, derivative contracts and trade accounts receivable (from product sales and from third parties from which the Company receives royalties). Cash is invested in short-term money market instruments, including money market and liquidity funds and bank term deposits. The money market and liquidity funds in which Shire invests are all triple A rated by both Standard and Poor's and by Moody's credit rating agencies.

The Company is exposed to the credit risk of the counterparties with which it enters into bank term deposit arrangements and derivative instruments. The Company limits this exposure through a system of internal credit limits which vary according to ratings assigned to the counterparties by the major rating agencies. The internal credit limits are approved by the Board and exposure against these limits is monitored by the corporate treasury function. The counterparties to these derivatives contracts are major international financial institutions.

The Company's revenues from product sales in the US are mainly governed by agreements with major pharmaceutical wholesalers and relationships with other pharmaceutical distributors and retail pharmacy chains. For the year to December 31, 2015 there were three customers in the US that accounted for 47% of the Company's product sales. However, such customers typically have significant cash resources and as such the risk from concentration of credit is considered acceptable. The Company has taken positive steps to manage any credit risk associated with these transactions and operates clearly defined credit evaluation procedures. However, an inability of one or more of these wholesalers to honor their debts to the Company could have an adverse effect on the Company's financial condition and results of operations.

A substantial portion of the Company's accounts receivable in countries outside of the United States is derived from product sales to government-owned or government-supported healthcare providers. The Company's recovery of these accounts receivable is therefore dependent upon the financial stability and creditworthiness of the relevant governments. In recent years global and national economic conditions have negatively affected the growth, creditworthiness and general economic condition of certain markets in which the Company operates. As a result, in some countries outside of the US, specifically, Argentina, Greece, Italy, Portugal and Spain (collectively the "Relevant Countries") the Company is experiencing delays in the remittance of receivables due from government-owned or government-supported healthcare providers. The Company continued to receive remittances in relation to government-owned or government-supported healthcare providers in the Relevant Countries in the year to December 31, 2015, including receipts of $116.0 million and $100.0 million in respect of Spanish and Italian receivables, respectively. The Company's exposure to Greece, both in terms of gross accounts receivable and annual revenues, is not material.

The Company's aggregate accounts receivable, net of the allowance for doubtful accounts, in total from government-owned or government-supported healthcare providers in those territories in which the Company

is experiencing the most significant delays, (i.e. in the "Relevant Countries") are as follows (*see Table 3 below*).

Table 3

	December 31, 2015 $'M	December 31, 2014 $'M
Total accounts receivable, net in the Relevant Countries	127	118
Total accounts receivable, net in the Relevant Countries as a percentage of total outstanding accounts receivable, net	11%	11%
Accounts receivable, net due from government-owned or government-supported healthcare providers for the Relevant Countries	106	77

Accounts receivable due from government-owned or government-supported healthcare providers in the Relevant Countries of $106 million (2014: $77 million) are split by country as follows:
Greece $7 million (2014: $4 million); Italy $49 million (2014: $30 million); Portugal $9 million (2014: $11 million); Spain $33 million (2014: $15 million); and Argentina $8 million (2014: $17 million).

The Company continues to receive remittances in relation to government-owned or government-supported healthcare providers in the Relevant Countries and in the year to December 31, 2015 received $294 million in settlement of accounts receivable in the Relevant Countries; $3 million was from Greece; $100 million from Italy; $13 million from Portugal; $116 million from Spain; and $62 million from Argentina.

To date the Company has not incurred material losses on accounts receivable in the Relevant Countries, and continues to consider that such accounts receivable are recoverable.

Other than the accounts receivable from government-owned or supported healthcare providers outlined above, the Company does not hold any other government debt from the Relevant Countries. Additionally the Company does not consider it is currently exposed to significant credit risk outside of the Relevant Countries.

The Company continues to evaluate all its accounts receivable for potential collection risks and has made provision for amounts where collection is considered to be doubtful. If the financial condition of the Relevant Countries or other countries suffer significant deterioration, such that their ability to make payments becomes uncertain, additional allowances for doubtful accounts may be required, and losses may be incurred, in future periods. Any such loss could have an adverse effect on the Company's financial condition and results of operations.

4. Principal risks and uncertainties

Risk management framework
As a highly regulated biopharmaceutical company with a keen patient focus, Shire has implemented policies and procedures intended to reduce risk and to ensure appropriate and lawful conduct within the increasing number of countries in which the Company operates. Success in these areas is of benefit to shareholders and other stakeholders alike. Shire's risk management strategy is to identify, assess and mitigate any significant risks that it faces. Despite this, it should be noted that no risk management strategy can provide absolute assurance against loss.

Board of Directors The Board is responsible for determining the Group's risk tolerance and for ensuring the maintenance of sound systems of risk management and internal control. In fulfilling this responsibility, the Board sets Shire's corporate risk culture; ensuring its dissemination throughout the organization. This is achieved through interaction with key stakeholders which, in turn, enables the Board to monitor and review the Group's risks as well as its risk management and internal control systems. During the year the Board undertook a robust assessment of the principal risks facing the Company, including those that might threaten its business model, future performance, solvency or liquidity. Stakeholders to the risk management framework, which is overseen by the Board and designed to manage and mitigate the Group's risks, are detailed below.

Audit, Compliance & Risk Committee The Committee supports the Board by, on a biannual basis, reviewing and reporting on the principal risks faced by the Company, with each assessed on likelihood of materialization and potential impact. Furthermore, alongside the Board the Committee monitors and reviews the risk management and internal control systems; ensuring oversight through its interaction with functional stakeholders, through its review and challenge of key risk and control processes and through its evaluation of key strategy updates from management.

Executive Committee The Committee is responsible for ensuring the implementation of the risk management and internal control infrastructure; overseeing its operation and ensuring it remains effective. Committee members receive regular updates from functional stakeholders and, along with the Chief Compliance and Risk Officer and the Head of Internal Audit, are responsible for elevating matters to the Board and Audit, Compliance & Risk ("ACR") Committee as required. In addition, on a biannual basis the Committee validates any significant risks put forward by the Risk Council; identifying and putting forward for review by the ACR Committee those that have the capacity to materially impact the Group's strategy.

Risk Council The Risk Council comprises senior members of the Company's business units and corporate functions, including the Head of Internal Audit, and is chaired by the Chief Compliance and Risk Officer. The Council is charged with overseeing risk management at an operational level; ensuring that each identified risk is allocated an "owner" within the business who is responsible for related management and mitigation activities. As part of the biannual risk review process the Council appraises risk schedules produced by individual business units and corporate functions; validating and revising assessments made and evaluating mitigation practices. A report is prepared for review by the Executive Committee detailing all risks meeting a prescribed threshold along with recommendations on their mitigation. The Chief Compliance and Risk Officer then presents these matters to the ACR Committee; highlighting those risks of strategic importance to the Company.

Global Compliance and Risk Management Department The Department, led by the Chief Compliance and Risk Officer, is made up of compliance, privacy, corporate security and risk management, and Health, Safety & Environment sub-teams. It is responsible for supporting the development, implementation and maintenance of effective compliance and risk management systems. This is achieved through policy development, the delivery of training programs and communications, and through the ongoing monitoring of compliance and risk-assessed activity, with follow-up investigation undertaken where necessary. Such activity provides for the timely undertaking of mitigation and/or remediation actions, as well for the escalation of matters to the ACR Committee and to the Board as appropriate. In addition, the Chief Compliance and Risk Officer provides regular updates to the ACR Committee on all matters falling within the Department's remit.

Chief Compliance and Risk Officer The Chief Compliance and Risk Officer is responsible for the global compliance program and for coordinating oversight of risk mitigation activity through the Enterprise Risk Management process. In addition to maintaining relationships with assurance functions outside of the Global Compliance and Risk Management Department, the Chief Compliance and Risk Officer has direct access to the Board and the ACR Committee; providing an independent mechanism of escalation, should the need

arise. The Chief Compliance and Risk Officer provides twice-yearly updates to the ACR Committee on risk and risk mitigation, as well as more regular updates regarding compliance monitoring and investigation.

Internal Audit The Internal Audit function provides independent assurance to the ACR Committee with respect to the operation of internal control and risk management systems.

Business units and corporate functions Business units and corporate functions are responsible for implementing risk management processes and establishing internal controls within their respective organizations in accordance with a centrally approved framework. In addition, each produces a schedule of material risks and associated mitigation plans as part of the Group's biannual review process for submission to the Risk Council.

Risk factors

Set out below are the principal risk factors associated with the business that have been identified through the Company's risk management and internal control systems. The Company believes that these risk factors apply equally and therefore all should be carefully considered before any investment is made in Shire.

The Company's products may not be a commercial success.

The commercial success of the Company's marketed products and other new products that the Company may launch in the future, will depend on their approval and acceptance by physicians, patients and other key decision-makers, as well as the receipt of marketing approvals in different countries, the time taken to obtain such approvals, the scope of marketing approvals as reflected in the product labels, approval of reimbursement at commercially sustainable prices in those countries where price and reimbursement is negotiated, and safety, efficacy, convenience and cost-effectiveness of the product as compared to competitive products.

The Company's revenues, financial condition or results of operations may be adversely affected if any or all of the following occur:

- if the Company's products, or competitive products, are genericized;
- if the prices of the Company's products suffer forced reductions or if prices of competitor products are reduced significantly;
- if there are unanticipated adverse events experienced with the Company's products or those of a competitor's product not seen in clinical trials that impact physicians' willingness to prescribe the Company's products;
- if issues arise from clinical trials being conducted for post-marketing purposes or for registration in another country which raise questions or concerns about a product;
- if the regulatory agencies in one country act in a way that raises concerns for regulatory agencies or for prescribers or patients in another country;
- if patients, payers or physicians favor other treatments over the Company's products;
- if the Company's products are subject to more stringent government regulation than competitor products;
- if patent protection or other forms of exclusivity are lost or curtailed, or if competitors are able to successfully challenge or circumvent the Company's patents or other forms of exclusivity (See Note 18, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements set forth in Shire's 2015 Annual Report;
- if launches of the Company's products in new markets are not successful;
- if the sizes of the patient populations for the Company's products are less than expected; or
- if there are lawsuits filed against Shire, including but not limited to, product liability claims, consumer law claims, and payer or reimbursement litigation.

If the Company is unable to commercialize its products successfully, there may be a material adverse effect on the Company's revenues, financial condition or results of operations.

Increased pricing pressures and limits on patient access as a result of governmental regulations and market developments may affect the Company's future revenues, financial condition and results of operations.

The Company's product revenues are subject to increasing pressures from governmental initiatives to regulate or influence prices and access to customers. Regulations in the United States, the European Union and other jurisdictions mandating price controls or imposing constraints on patients' ability to purchase Shire's

products significantly impacts its business, and the Company's financial condition and results of operations could be adversely affected in the future by changes in such regulations, practices or policies.

Regulatory measures that could have a material adverse effect on the Company include the imposition of government-approved drug pricing schedules, the use of drug formularies, prohibitions on direct-to-consumer advertising or drug marketing practices and caps or limits on the level of reimbursement provided to the Company by governmental reimbursement schemes for its products.

These pressures have also resulted in market developments, such as the consolidation of managed care organizations and private health insurers, that have increased the relative bargaining power of institutional drug purchasers and enhanced their ability to negotiate discounts and extract other concessions in exchange for purchasing Shire's products.

Such regulatory and market developments create downward pressures on the prices at which the Company can offer its products and on the level of reimbursement its treatments receive from health care providers, private health insurers and other organizations, such as health maintenance organizations and managed care organizations.

Additional factors affecting the Company's ability to obtain and maintain adequate prices and levels of reimbursement for its products include:

- higher levels of controls on the use of the Company's products and/or requirements for further price concessions mandated or negotiated by managed health care organizations or government authorities;
- legislative proposals to reform health care and government insurance programs in many of the Company's markets; and
- price controls, unsuccessful government tenders, or non-reimbursement of new medicines or new indications.

Moreover, the cost of treatment for some of the Company's products is high, particularly those which are used for the treatment of rare diseases. The Company may encounter difficulty in obtaining or maintaining satisfactory pricing and reimbursement for such products. The failure to obtain and maintain pricing and reimbursement at satisfactory levels for its products may adversely affect the Company's revenues, financial condition or results of operations.

The Company depends on third parties to supply certain inputs and services critical to its operations including certain inputs, services and ingredients critical to its manufacturing processes.

The Company relies on third-party suppliers, vendors and outsourcing partners to, among other things, research, develop, manufacture and commercialize its products, to provide certain key ingredients and manufacturing inputs and to manage certain sales, distribution, marketing, information technology, accounting, transaction-processing and other business services. While the Company depends on these third parties for multiple aspects of its product development, manufacturing, commercialization and business activities, it does not control these third parties directly.

As a result, there is a possibility these third parties may not complete activities on schedule or in accordance with the Company's expectations, and their failure to meet certain contractual, regulatory or other obligations to Shire, or any disruption of Shire's relationship with these third parties could delay or prevent the development, approval, manufacture or commercialization of the Company's products, result in non-compliance with applicable laws and regulations, disrupt Shire's operations, or result in reputational or other harm to the Company.

This outsourcing risk is of particular concern with respect to third-party suppliers of key manufacturing inputs of Shire's drug products. Although the Company dual-sources certain key products and/or active ingredients, the Company currently relies on a single source for production of the final drug product for each of ADDERALL XR, CINRYZE, FIRAZYR, FOSRENOL, INTUNIV, LIALDA, PENTASA and NATPARA/NATPAR. The Company currently relies on a single active ingredient source for each of ELAPRASE, FIRAZYR, FOSRENOL, INTUNIV, REPLAGAL and GATTEX/REVESTIVE and also relies on limited third party sources to provide the donated human plasma necessary for the manufacture of CINRYZE. Following the completion of the acquisition of Dyax Corp on January 22, 2016 Shire acquired DX-2930, which currently relies on separate sole sources for both production of the final drug product and supply of the active ingredient for its Phase 3 trial. In addition, one of those drug substance sites has not been approved by the FDA and would

need to be approved prior to commercial launch. Any failure by a single-source supplier to provide the Company with the required volumes on time or at all, or to provide products that do not meet regulatory requirements, could lead to significant delays in the production of Shire's products, increases in operating costs, lost product sales, an interruption of research activities, or the delay of new product launches, all of which could have a material adverse effect on the Company's revenues, financial condition or results of operations.

Any disruption to the supply chain for any of the Company's products, or any difficulties or delays in the manufacturing, distribution and sale of its products may result in the Company being unable to continue marketing or developing a product, or may result in the Company being unable to do so on a commercially viable basis for some period of time.

A disruption, delay or other difficulties in the manufacturing, distribution and sale of Shire's products, or in the supply chain of any of its products, may have a material adverse effect on the Company and its revenues, financial condition and results of operations. Examples of such manufacturing and supply chain difficulties include, but are not limited to:

- regulatory or enforcement actions that result in shut-downs, delays in or withdrawal of regulatory approvals necessary to carry on manufacturing activities, product recalls and penalties or fines resulting in unanticipated costs in production, whether imposed directly on the Company or imposed indirectly through one or more of its third-party suppliers;
- the inability of the Company to increase its production capacity for certain drugs commensurate with market demand;
- the possibility that the supply of incoming materials may be delayed or become unavailable and that the quality of incoming materials may be substandard and not detected;
- the possibility that the Company may fail to maintain appropriate quality standards throughout its internal and third-party supply network, or to comply with current manufacturing best practices, rules or other applicable regulations;
- disruptions to supply chain continuity as a result of natural or man-made disasters at the Company's facilities or at one or more of its third-party suppliers' facilities; and
- failure to maintain the integrity of the Company's supply chains against fraudulent and criminal acts, such as intentional product adulteration, diversion, theft, or counterfeiting activities.

Also, as noted above, the Company has also entered into many agreements with third parties for the provision of goods and services to enable it to manufacture its products. If these third parties are unable to manufacture products, or provide these goods and services, in each case in accordance with its respective contractual obligations, the Company's ability to manage its manufacturing processes or to operate its business, including to continue the development or commercialization of its products as planned or on a commercial basis, may be adversely impacted.

The manufacture of the Company'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.

Pharmaceutical and device manufacturing sites must be inspected and approved by regulatory agencies such as the FDA, and similar agencies in other countries. Active ingredients, excipients and packaging materials used in the manufacturing process must be obtained from sources approved by regulatory agencies.

The development, approval and manufacturing of the Company's products depend on the ability to procure ingredients and packaging materials from approved sources and for the manufacturing process to be conducted at approved sites. Changes of manufacturer or changes of source of ingredients or packaging materials must generally be approved by the regulatory agencies, which will involve testing and additional inspections to ensure compliance with the applicable regulatory agency's regulations and standards. The need to qualify a new manufacturer or source of ingredients or packaging materials can take a significant amount of time. Should it become necessary to change a manufacturer or supplier of ingredients or packaging materials, or to qualify an additional supplier, the Company may not be able do so quickly, or at all, which could delay or disrupt the manufacturing process.

US-based manufacturers must be registered with the DEA and similar regulatory authorities in other countries if they handle controlled substances. Certain of the Company's products, including ADDERALL XR and

4. Principal risks and uncertainties

VYVANSE, contain ingredients which are controlled substances subject to quotas managed by the DEA. As a result, the Company's procurement and production quotas may not be sufficient to meet commercial demand.

CINRYZE, ELAPRASE, REPLAGAL and VPRIV are manufactured using highly complex biological processes. The complexity of the manufacturing results in a number of risks, including the risk of microbial contamination. Additionally, CINRYZE is derived from human plasma, and is therefore subject to the risk of biological contamination inherent in plasma-derived products. The sole manufacturer of CINRYZE has received observations on Form 483 and a warning letter from the FDA identifying issues with respect to the manufacturing process for CINRYZE which must be addressed to the satisfaction of the FDA. Any regulatory interventions, in relation to these, or any other issues, if they occur, may delay or disrupt the manufacture of the Company's products.

The failure to obtain regulatory approvals promptly or at all and/or regulatory 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, the delay of new product launches or constraints on manufacturing output, all of which could have a material adverse effect on the Company's revenues, financial condition and results of operations.

The Company 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.

Products that initially appear promising in research or development may be delayed or fail to reach later stages of development as:

- preclinical or clinical tests may show the product to lack safety or efficacy;
- delays may be caused by slow enrollment in clinical studies; regulatory requirements for clinical trial drug supplies; extended length of time to achieve study endpoints; additional time requirements for data analysis or dossier preparation; time required for discussions with regulatory agencies, including regulatory agency requests for additional preclinical or clinical data; delays at regulatory agencies due to staffing or resource limitations; analysis of or changes to study design; unexpected safety, efficacy, or manufacturing issues; delays may arise from shared control with collaborative partners in the planning and execution of the product development, scaling of the manufacturing process, or getting approval for manufacturing;
- manufacturing issues, pricing or reimbursement issues, or other factors may render the product economically unviable;
- the proprietary rights of others and their competing products and technologies may prevent the product from being developed or commercialized; or
- submission of an application for regulatory approval of any of the Company's product candidates may be subjected to lengthy review and ultimately rejected.

Success in preclinical and early clinical trials does not ensure that late stage clinical trials will be successful. Clinical results are frequently susceptible to varying interpretations that may delay, limit, or prevent regulatory approvals. The length of time necessary to complete clinical trials and to submit an application for marketing approval for a final decision by a regulatory authority varies significantly and may be difficult to predict. Moreover, once an application is submitted, additional data may be sought by regulators or an application may be rejected. If the Company's large-scale or late-stage clinical trials for a product are not successful, the Company will not recover its substantial investments in that product. The Company has a range of programs in or entering late stage clinical development. For example, an NDA for SHP606 for the treatment of signs and symptoms of adults with DED is currently in registration with the FDA and following the acquisition of Dyax in January 2016 the Company has acquired SHP643 (formerly DX-2930) for the treatment of HAE, which is in Phase 3.

In addition, even if the products receive regulatory approval, they remain subject to ongoing regulatory requirements, including, for example, obligations to conduct additional clinical trials or other non-clinical testing, changes to the product label (which could impact its marketability and prospects for commercial success), new or revised requirements for manufacturing, written notifications to physicians, or product recalls or withdrawals.

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The actions of certain customers could affect the Company's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect the Company's revenues, financial conditions or results of operations.

A considerable portion of the Company's product sales are made to major pharmaceutical wholesale distributors, as well as to large pharmacies, in both the US and Europe. In 2015, for example, 47% of the Company's product sales were attributable to three customers in the US: AmerisourceBergen Drug Corp., McKesson Corp. and Cardinal Health, Inc. In the event of financial failure of any of these customers there could be a material adverse effect on the Company's revenues, financial condition or results of operations. The Company's revenues, financial condition or results of operations may also be affected by fluctuations in customer buying or distribution patterns. These fluctuations may result from seasonality, pricing, wholesaler inventory objectives, or other factors. A significant portion of the Company's revenues for certain products for treatment of rare diseases are concentrated within a small number of customers. Changes in the buying patterns of those customers may have an adverse effect on the Company's revenues, financial condition or results of operations.

Failure to comply with laws and regulations governing the sales and marketing of its products could materially impact Shire's revenues and profitability.

The Company engages in various marketing, promotional and educational activities pertaining to, as well as the sale of, pharmaceutical products and medical devices in a number of jurisdictions around the world. The promotion, marketing and sale of pharmaceutical products and medical devices is highly regulated and the sales and marketing practices of market participants, such as the Company, have been subject to increasing supervision by governmental authorities, and Shire believes that this trend will continue.

In the United States, the Company's sales and marketing activities are monitored by a number of regulatory authorities and law enforcement agencies, including the US Department of HHS, the FDA, the US Department of Justice, the SEC and the DEA. These authorities and agencies and their equivalents in countries outside the US have broad authority to investigate market participants for potential violations of laws relating to the sale, marketing and promotion of pharmaceutical products and medical devices, including the False Claims Act, the Anti-Kickback Statute and the Foreign Corrupt Practices Act, among others, for alleged improper conduct, including corrupt payments to government officials, improper payments to medical professionals, off-label marketing of pharmaceutical products and medical devices, and the submission of false claims for reimbursement by the federal government. Healthcare companies may also be subject to enforcement actions or prosecution for such improper conduct. Any inquiries or investigations into the operations of, or enforcement or other regulatory action against, the Company by such authorities could result in significant defense costs, fines, penalties and injunctive or administrative remedies, distract management to the detriment of the business, result in the exclusion of certain products, or the Company, from government reimbursement programs or subject the Company to regulatory controls or government monitoring of its activities in the future. The Company is also subject to certain ongoing investigations by governmental agencies. For further information, see Note 18, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements set forth in Shire's 2015 Annual Report.

The Company's products are subject to intense competition from generics.

Shire faces significant competition from the manufacturers of generic drug products in all of its major markets. The introduction of lower-priced generics by the Company's competitors or their successful efforts in aggressively commercializing and marketing their alternative drug products pose significant challenges to maintaining Shire's market share, revenues and sales growth.

For example, since 2009, generic versions of ADDERALL XR have been marketed and, since 2014, generic versions of INTUNIV have been marketed in the United States. As a result, product sales of ADDERALL XR and INTUNIV have declined.

Factors which could cause further or more rapid declines in Shire's product sales include:

- the loss or earlier than expected expiration of intellectual property rights or regulatory exclusivity periods with respect to the Company's branded products;
- generic or authorized generic versions of these products capturing more of Shire's branded market share than expected;
- lower prices and the actual or perceived greater effectiveness or safety of generic drug products relative to Shire's branded products;

- the FDA approving additional ANDAs for generic versions of these products which, if launched, would further reduce branded market share or impact the amount of Shire's authorized generic product sales;
- changes in reimbursement policies of third-party payers; or
- changes to the level of sales deductions for branded Shire products for private or public payers.

Should any of the above developments occur, the resulting generic competition could reduce sales and market share of Shire's branded products and have a material adverse effect on the Company's revenues, financial condition or results of operations.

Adverse outcomes in legal matters and other disputes, including the 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 Company's revenues, financial condition or results of operations.

During the ordinary course of its business the Company may be involved in claims, disputes and litigation with third parties, employees, regulatory agencies, governmental authorities and other parties. The range of matters of a legal nature that might arise is extremely broad but could include, without limitation, intellectual property claims and disputes, product liability claims and disputes, regulatory litigation, contract claims and disputes, employment claims and disputes, and tax or other governmental agency audits and disputes.

Any unfavorable outcome in such matters could adversely impact the Company's ability to develop or commercialize its products, adversely affect the profitability of existing products, subject the Company to significant defense costs, fines, penalties, audit findings and injunctive or administrative remedies, distract management to the detriment of the business, result in the exclusion of certain products, or the Company, from government reimbursement programs or subject the Company to regulatory controls or government monitoring of its activities in the future. Any such outcomes could have a material adverse effect on the Company's revenue, financial condition or results of operations. For further information see Note 18, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements set forth in Shire's 2015 Annual Report.

The Company faces intense competition for highly qualified personnel from other companies and organizations.

The Company relies on recruiting and retaining highly skilled employees to meet its strategic objectives. The Company faces intense competition for highly qualified personnel and the supply of people with the requisite skills may be limited, generally or geographically. The range of skills required and the geographies in which they are required by the Company may also change over time as Shire's business evolves. If the Company is unable to retain key personnel or attract new personnel with the requisite skills and experience, it could adversely affect the implementation of the Company's strategic objectives and ultimately adversely impact the Company's revenues, financial condition or results of operations.

Failure to successfully execute or attain strategic objectives from the Company's acquisitions and growth strategy may adversely affect the Company's financial condition and results of operations.

The Company's business depends to a significant extent on its ability to improve and expand its product pipeline through strategic acquisitions. Such improvements and expansions, however, are subject to the ability of the Company's management to effectively identify appropriate strategic targets and effectuate the contemplated transactions, the availability and relative cost of acquisition opportunities as well as competition from other pharmaceutical companies seeking similar opportunities.

Moreover, even when such transactions are successfully executed, the Company may face subsequent difficulties in integrating the operations, infrastructure and personnel of acquired businesses and may experience unanticipated risks or liabilities that were not discovered, accurately disclosed or sufficiently assessed during the transactions' due diligence process. Finally, even successfully acquired and integrated businesses may ultimately fail or fall short of achieving the Company's strategic objectives for the transaction over the long term.

Any failures in the execution of a transaction, in the integration of an acquired business or in achieving the Company's strategic objectives with respect to such acquisitions could result in slower growth, higher than expected costs, the recording of asset impairment charges and other actions which could adversely affect the Company's business, financial condition and results of operations.

The Company has recently completed and is currently pursuing a number of strategic acquisitions. On February 21, 2015, Shire completed the acquisition of NPS Pharma for a total cash consideration of

approximately $5.2 billion. On January 22, 2016 Shire also completed the acquisition of all the outstanding share capital of Dyax for a total upfront cash consideration of approximately $5.9 billion and a further approximately $0.6 billion in cash consideration contingent upon the approval of DX-2930 for the prophylactic treatment of HAE. Finally, on January 11, 2016 Shire announced a combination with Baxalta Incorporated had been agreed by both Boards.

These proposed and completed acquisitions as well as future acquisitions each entail various risks, which include but are not limited to:

- a proposed acquisition may not be consummated due to the occurrence of an event, change or other circumstances that gives rise to the termination of the applicable merger agreement;
- a governmental, regulatory, board, shareholder or other approval required for a proposed acquisition may not be obtained, or may be obtained subject to conditions that are not anticipated, or another condition to the closing of a proposed acquisition may not be satisfied, resulting in delays or ultimate failure of consummating a proposed acquisition;
- shareholders may initiate legal action to prevent or delay consummation of a proposed acquisition or to seek judicial reevaluation of a proposed acquisition's consideration;
- a lengthy, uncertain process when pursuing a combination could disrupt relationships between Shire and a target company's customers, suppliers and employees, distract Shire's or a target's management from operating its business, and could lead to additional and unanticipated costs;
- a target company may be unable to retain and hire key personnel and/or maintain its relationships with customers, suppliers and other business partners pending the consummation of the proposed acquisition by Shire;
- after the consummation of an acquisition, the Company may be unable to retain the acquired company's key personnel, existing customers, suppliers and other business partners or attract new customers;
- the businesses of an acquired company may be otherwise disrupted by the acquisition, including increased costs and diversion of its respective management's time and resources;
- failure to achieve the targeted growth and expected benefits of the acquisition if sales of an acquired company's products are lower than anticipated, or these products cannot be successfully commercialized or cannot obtain necessary regulatory approvals;
- any integration of an acquired company into Shire could be complex and time-consuming, and difficulties in effectuating these integrations may lead to the combined companies not being able to realize the expected operating efficiencies, cost savings, revenue enhancements, synergies or other benefits in the timeframe anticipated, or at all;
- failure to successfully obtain regulatory approval of an acquired company's late stage pipeline assets in a timely manner or at all, or to successfully commercialize such products after regulatory approval has been obtained;
- undiscovered or unanticipated risks and liabilities, including legal and compliance related liabilities, may emerge in connection with an acquisition, or may be higher than anticipated; and
- even after successfully completing an acquisition and integrating the acquired company's businesses into Shire, the anticipated benefits of the combinations may ultimately prove less than anticipated.

A slowdown of global economic growth, or economic instability of countries in which the Company does business, could have negative consequences for the Company's business and increase the risk of non-payment by the Company's customers.

Growth of the global pharmaceutical market has become increasingly tied to global economic growth. Accordingly a substantial and lasting slowdown of the global economy, or major national economies, could negatively affect growth in the markets in which the Company operates. Such a slowdown, or any resultant austerity measures adopted by governments in response to a slowdown, could result in national governments making significant cuts to their public spending, including national healthcare budgets, or reducing the level of reimbursement they are willing and able to provide to the Company for its products and, as a result, adversely affect the Company's revenues, financial condition or results of operations.

A slowdown of a nation's economy could also lead to financial difficulties for some of the Company's significant customers, including national governments, and result in a greater risk of delayed orders or payments, defaults or non-payments of outstanding payment obligations by the Company's customers in that country, which could adversely affect the Company's revenues, financial condition or results of operations.

4. Principal risks and uncertainties

The Company is subject to evolving and complex tax laws, which may result in additional liabilities that may adversely affect the Company's financial condition or results of operations.

The Company is subject to evolving and complex tax laws in the jurisdictions in which it operates, and routinely obtains advice on matters, including the tax treatment of the break fee received in connection with the terminated offer for Shire by AbbVie Inc. ("AbbVie") in 2014. Significant judgment is required in determining the Company's tax liabilities, and the Company's tax returns are periodically examined by various tax authorities. The Company regularly assesses the likelihood of outcomes resulting from these examinations to determine the adequacy of its accrual for tax contingencies; however, due to the complexity of tax contingencies, the ultimate resolution of any tax matters may result in payments greater or less than amounts accrued. In addition, the Company may be affected by changes in tax laws, including tax rate changes, new tax laws, and revised tax law interpretations in domestic and foreign jurisdictions.

The failure of a strategic partner to develop and commercialize products could result in delays in development, approval or loss of revenue.

The Company enters into strategic partnerships with other companies in areas such as product development, manufacturing, sales and marketing. In these partnerships, the Company is sometimes dependent on its partner to deliver results. While these partnerships are governed by contracts, the Company may not exercise direct control. If a partner fails to perform or experiences financial difficulties, the Company may suffer a delay in the development, a delay in the approval or a reduction in sales, or royalties of a product.

The failure to secure new products or compounds for development either through in-licensing, acquisition or internal research and development efforts, or the failure to realize expected benefits from acquisitions of businesses or products, may have an adverse impact on the Company's future results.

The Company's future results will depend, to a significant extent, upon its ability to develop, in-license or acquire new products or compounds, or to acquire other businesses. The expected benefits from acquired products, compounds or businesses may not be realized or may require significantly greater resources and expenditure than originally anticipated. The failure to realize expected benefits from acquisitions of businesses or products including those resulting from integration into the Company, or the failure to develop, in-license or acquire new products or compounds on a commercially viable basis, could have a material adverse effect on the Company's revenues, financial condition or results of operations.

The Company may fail to obtain, maintain, enforce or defend the intellectual property rights required to conduct its business.

The Company's success depends upon its ability and the ability of its partners and licensors to protect their intellectual property rights. Where possible, the Company's strategy is to register intellectual property rights, such as patents and trademarks. The Company also relies on various trade secrets, unpatented know-how and technological innovations and contractual arrangements with third parties to maintain its competitive position. The failure to obtain, maintain, enforce or defend such intellectual property rights, for any reason, could allow third parties to make competing products or impact the Company's ability to develop, manufacture and market its own products on a commercially viable basis, or at all, which could have a material adverse effect on the Company's revenues, financial condition or results of operations.

The Company intends to enforce its patent rights vigorously and believes that its commercial partners, licensors and third party manufacturers intend to enforce vigorously those patent rights they have licensed to the Company. However, the Company's patent rights, and patent rights that the Company has licensed, may not provide valid patent protection sufficiently broad to prevent any third party from developing, using or commercializing products that are similar or functionally equivalent to the Company's products or technologies. These patent rights may be challenged, revoked, invalidated, infringed or circumvented by third parties. Laws relating to such rights may in future also be changed or withdrawn.

Additionally, the Company's products, or the technologies or processes used to formulate or manufacture those products may now, or in the future, infringe the patent rights of third parties. It is also possible that third parties will obtain patent or other proprietary rights that might be necessary or useful for the development, manufacture or sale of the Company's products. The Company may need to obtain licenses for intellectual property rights from others and may not be able to obtain these licenses on commercially reasonable terms, if at all.

4. Principal risks and uncertainties

The Company also relies on trade secrets and other un-patented proprietary information, which it generally seeks to protect by confidentiality and nondisclosure agreements with its employees, consultants, advisors and partners. These agreements may not effectively prevent disclosure of confidential information and may not provide the Company with an adequate remedy in the event of unauthorized disclosure. In addition, if the Company's employees, scientific consultants or partners develop inventions or processes that may be applicable to the Company's products under development, such inventions and processes will not necessarily become the Company's property, but may remain the property of those persons or their employers.

The Company has filed applications to register various trademarks for use in connection with its products in various countries and also, with respect to certain products, relies on the trademarks of third parties. These trademarks may not afford adequate protection or the Company or the third parties may not have the financial resources to enforce their rights under these trademarks which may enable others to use the trademarks and dilute their value.

In the regular course of business, the Company is party to litigation or other proceedings relating to intellectual property rights. For details of current intellectual property litigation, See Note 18, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements set forth in Shire's 2015 Annual Report.

The introduction of new products by competitors may impact future revenues.

The pharmaceutical, biotechnology and device industries are highly competitive and are characterized by substantial investment in continuous product development and technological change. The Company faces significant competition from large pharmaceutical and biotechnology companies, many of whom have substantially greater resources than the Company. In addition, many of the Company's competitors have more products and have operated longer in the fields in which the Company competes. A number of companies are pursuing the development of technologies which compete with the Company's existing products or research programs. These competitors include specialized pharmaceutical firms and large pharmaceutical companies acting either independently or together with other pharmaceutical companies. Furthermore, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection and may establish collaborative arrangements for competitive products or programs. As a result of this competition the Company's products could be rendered obsolete or uneconomic or lose market share following the development of new products, new methods of treatment, or technological advances in manufacturing or production by competitors which could adversely affect the Company's revenues, financial condition, and results of operations.

If a marketed product fails to work effectively or causes adverse side effects, this could result in damage to the Company's reputation, the withdrawal of the product and legal action against the Company.

Unanticipated side effects or unfavorable publicity from complaints concerning any of the Company's products, or those of its competitors, could have an adverse effect on the Company's ability to obtain or maintain regulatory approvals or successfully market its products. The testing, manufacturing, marketing and sales of pharmaceutical products and medical devices entail a risk of product liability claims, product recalls, litigation and associated adverse publicity. The cost of defending against such claims is expensive even when the claims are not merited. A successful product liability claim against the Company could require the Company to pay a substantial monetary award. If, in the absence of adequate insurance coverage, the Company does not have sufficient financial resources to satisfy a liability resulting from such a claim or to fund the legal defense of such a claim, it could become insolvent. Product liability insurance coverage is expensive, difficult to obtain and may not be available in the future on acceptable terms. Although the Company carries product liability insurance when available, this coverage may not be adequate. In addition, it cannot be certain that insurance coverage for present or future products will be available. Moreover, an adverse judgment in a product liability suit, even if insured or eventually overturned on appeal, could generate substantial negative publicity about the Company's products and business and inhibit or prevent commercialization of other products.

4. Principal risks and uncertainties

The Company is 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 Company's revenues, financial condition or results of operations.

The Company relies to a large extent upon sophisticated information technology systems to operate its businesses. In the ordinary course of business, the Company collects, stores and transmits large amounts of confidential information (including, but not limited to, personal information and intellectual property), and it is critical that the Company does so in a secure manner to maintain the confidentiality and integrity of such confidential information. The size and complexity of the Company's information technology and information security systems, and those of third-party vendors with whom the Company contracts (and the large amounts of confidential information that is present on them), make such systems potentially vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by the Company's employees or vendors, or from attacks by malicious third parties.

The Company and its vendors' sophisticated information technology operations are spread across multiple, sometimes inconsistent platforms, which pose difficulties in maintaining data integrity across systems. The ever-increasing use and evolution of technology, including cloud-based computing, creates opportunities for the unintentional dissemination or intentional destruction of confidential information stored in the Company's systems. The Company and its vendors could also be susceptible to third party attacks on their information security systems, which attacks are of ever increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including criminal groups, "hackers" and others. While the Company has taken steps to protect such information and invested heavily in information technology, there can be no assurance that these efforts will prevent service interruptions or security breaches in its systems, the loss of data or other confidential information due to a lack of redundant backup systems, or the unauthorized or inadvertent wrongful use or disclosure of confidential information that could adversely affect the Company's business operations or result in the loss, dissemination, or misuse of critical or sensitive information.

A breach of the Company's security measures or the accidental loss, inadvertent disclosure, unapproved dissemination, misappropriation or misuse of trade secrets, proprietary information, or other confidential information, whether as a result of theft, hacking, fraud, trickery or other forms of deception, or for any other cause, could enable others to produce competing products, use the Company's proprietary technology or information, and/or adversely affect the Company's business position. Further, any such interruption, security breach, loss or disclosure of confidential information, could result in financial, legal, business, and reputational harm to the Company and could have a material adverse effect on the Company's revenues, financial condition or results of operations.

In addition, legislators and/or regulators in countries in which the Company operates are increasingly adopting or revising privacy, information security and data protection laws, as well as focusing on increased privacy-related enforcement activity, that potentially could have a significant impact on the Company's current and planned privacy, data protection and information security-related practices, its collection, use, sharing, retention and safeguarding of consumer and/or employee information, and some of its current or planned business activities.

Risks related to the proposed merger with Baxalta Incorporated

Failure to consummate the merger as contemplated could negatively impact the price of the Company's ordinary shares and ADSs and the future business and financial results of the Company and/or the combined company.

The consummation of the merger of BearTracks, Inc., a wholly-owned subsidiary of the Company ("Merger Sub") within and into Baxalta, with Baxalta surviving the merger as a wholly-owned subsidiary of the Company (the "merger") may be delayed, the merger may be consummated on terms different than those contemplated by Agreement and Plan of Merger, dated as of January 11, 2016, as it may be amended from time to time, ("the merger agreement") between the Company, Merger Sub and Baxalta, or the merger may not be consummated at all. Failure to consummate the merger would prevent the Company's ordinary shareholders from realizing the anticipated benefits of the merger. The current market price of the Company's ordinary shares and ADSs may reflect a market assumption that the merger will occur, and a failure to consummate the merger could result in a significant decline in the market price of the Company's ordinary shares and ADSs and a negative perception of the Company generally. Any delay in the consummation of the merger or any uncertainty about the consummation of the merger could also negatively

impact the share price and future business and financial results of the Company and/or the combined company following the proposed merger.

There is no assurance that Shire and Baxalta will be able to obtain the required governmental and regulatory approvals to consummate the merger, which, if delayed or not granted, may delay or jeopardize the merger.

The merger is conditioned on the expiration or termination of the applicable waiting period (or extension thereof) under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, merger control approval under the relevant merger control laws of the European Union and the consent of certain other merger control authorities and other governmental entities. The governmental and regulatory agencies from which Shire and Baxalta are seeking these approvals have broad discretion in administering the applicable governing regulations. As a condition to their approval of the transactions contemplated by the merger agreement, those agencies may impose requirements, limitations or costs or require divestitures or place restrictions on the conduct of the combined company's business. The required approvals may not be obtained or the required conditions to the merger may not be satisfied, or, even if the required approvals are obtained and the conditions to the consummation of the merger are satisfied, the terms, conditions and timing of such approvals are uncertain. Any delay in consummating the merger could cause Shire and/or the combined company not to realize some or all of the synergies that Shire expects to achieve if the merger is successfully consummated within the expected time frame.

The merger remains subject to additional conditions, some of which Shire and Baxalta cannot control, which could result in the merger not being consummated or being delayed, any of which could negatively impact the share price and future business and operating results of the Company and/or the combined company.

The merger is subject to the satisfaction or waiver of other conditions in addition to the approval of governmental authorities described above, including, but not limited to, (i) the approval of the issuance of ordinary shares and ADSs by the Company's ordinary shareholders; (ii) the adoption of the merger agreement by the stockholders of Baxalta; (iii) effectiveness of a registration statement on Form S-4 registering ordinary shares to be issued in the merger; (iv) the absence of any orders, injunctions or rulings, or laws that would have the effect of enjoining or preventing the consummation of the merger; (v) the approval of the United Kingdom Listing Authority (the "UKLA") of a prospectus relating to the ordinary shares and a circular convening a meeting of Shire's ordinary shareholders; (vi) approval from the NASDAQ Global Select Market to list the ADSs; (vii) approval of the UKLA and London Stock Exchange to list the ordinary shares; and (viii) Section 4.02 of the tax matters agreement dated as of June 30, 2015 (the "tax matters agreement"), by and between Baxter International Inc. ("Baxter") and Baxalta, shall have been waived with respect to the closing of the merger, pursuant to the terms of the letter agreement, dated as of January 11, 2016 (the "letter agreement"), among the Company, Baxter and Baxalta, and each of the Company and Baxalta shall have received from Baxter a certificate, as described in the letter agreement, to the effect that the tax advisor to Baxter has furnished an opinion in substantially the same form and substance as the tax opinion delivered by such advisor on the date immediately prior to the signing of the merger agreement. Certain conditions to the merger may not be satisfied or, if they are, the timing of such satisfaction is uncertain. If any conditions to the merger are not satisfied or, where waiver is permitted by applicable law, not waived, the merger will not be consummated.

The merger is not subject to a financing condition. While Shire has secured an $18 billion fully underwritten bank facility of which $13 billion is available to finance the cash component of the per share merger consideration, certain customary conditions precedent to funding must be satisfied in order for the Company to utilize its bank facility, and if such conditions are not satisfied or if the Company's lenders do not satisfy their funding commitment, the Company may be unable to obtain the funds necessary to consummate the merger.

If for any reason the merger is not completed, or the closing of the merger is significantly delayed, the market price of the Company's ordinary shares and ADSs and business and results of operations of the Company and/or the combined company may be adversely affected.

4. Principal risks and uncertainties

Lawsuits have been filed, and other lawsuits may be filed, against the Company and Baxalta and Baxalta's board of directors challenging the merger, and an adverse ruling in any such lawsuit may delay or prevent the completion of the merger or result in an award of damages against the Company.

Multiple putative class action complaints have been filed by purported Baxalta stockholders in connection with the merger. The complaints generally allege that the members of the Baxalta board breached their fiduciary duties to Baxalta stockholders by entering into the merger agreement and approving the merger, and that the Company, Baxalta and/or Merger Sub, aided and abetted such breaches of fiduciary duties. The complaints further allege that, among other things, the per share merger consideration undervalues Baxalta and certain provisions of the merger agreement inappropriately inhibit competing bids. The complaints seek, among other things, to enjoin the merger.

Additional lawsuits arising out of or relating to the merger agreement or the merger may be filed in the future. The results of complex legal proceedings are difficult to predict and could delay or prevent the completion of the merger. The existence of litigation relating to the merger could impact the likelihood of obtaining the stockholder approvals from either the Company or Baxalta. Moreover, the pending litigation is, and any future additional litigation could be, time consuming and expensive and could divert the Company's management's attention away from their regular business.

One of the conditions to completion of the merger is the absence of any law or judgment issued by any court or tribunal of competent jurisdiction that prevents, makes illegal or prohibits the closing of the merger. Accordingly, if a plaintiff is successful in obtaining a judgment prohibiting completion of the merger, then such judgment may prevent the merger from being completed, or from being completed within the expected time frame.

If the proposed merger is not completed, the Company will have incurred substantial costs that may adversely affect the Company's financial results and operations.

The Company has incurred and will continue to incur substantial costs in connection with the proposed merger with Baxalta. These costs are primarily associated with the fees of attorneys, accountants and financial advisors. In addition, the Company diverted significant management resources in an effort to complete the merger and are subject to restrictions contained in the merger agreement on the conduct of the Company's business during the pendency of the merger. If the merger is not completed, the Company will have received little or no benefit in respect of such costs incurred.

The merger agreement restricts the Company's ability to pursue alternatives to the merger, however, in specified circumstances, the Company may terminate the merger agreement to accept a superior proposal.

Under the merger agreement, the Company has agreed not to (1) take certain actions to solicit proposals relating to alternative business combination transactions or (2) subject to certain exceptions, including the receipt of a "parent superior proposal" (as such term is defined in the merger agreement), enter into discussions or an agreement concerning, or provide confidential information in connection with, any proposals for alternative business combination transactions. However, in specified circumstances, the Company may terminate the merger agreement to enter into a definitive agreement with response to a "parent superior proposal" prior to obtaining approval of the merger from its stockholders.

Upon termination of the merger agreement in specified circumstances, the Company would be required to disburse a termination fee equal to $369 million to Baxalta and/or reimburse Baxalta for its merger-related expenses in an amount not to exceed $65 million, which expense reimbursement would be offset against any termination fee subsequently disbursed. Following the disbursement of the termination fee and/or reimbursement of merger-related expenses, the Company will, other than in certain circumstances, have no further obligation or liabilities to Baxalta. Such termination would deny the Company and its respective stockholders any benefits from the merger and could negatively impact market price of the Company's ordinary shares and ADSs.

These provisions could discourage a third party that may have an interest in acquiring all or a significant part of the Company from considering or proposing that acquisition, even if such third party were prepared to enter into a transaction that is more favorable to the Company or the Company's ordinary shareholders than the merger.

4. Principal risks and uncertainties

In specified circumstances, Baxalta could terminate the merger agreement to accept an alternative proposal.

Under the merger agreement, Baxalta may terminate the merger agreement to enter into a definitive agreement with respect to a "company superior proposal" (as such term is defined in the merger agreement) prior to obtaining approval of the merger from its ordinary shareholders. In such event, Baxalta would be obligated to disburse a termination fee equal to $369 million, but would have no further obligation or liabilities to the Company. Such termination would deny the Company and its stockholders any benefits from the merger and could negatively impact the price of the Company's ordinary shares and ADSs.

Uncertainties associated with the merger may cause a loss of employees and may otherwise affect the future business and operations of Shire and the combined company.

Uncertainty about the effect of the merger on employees and customers may have an adverse effect on the Company and, if the proposed combination with Baxalta is consummated, on the combined company following the merger. These consequent uncertainties may impair the Company's, and following the closing of the merger, the combined company's, ability to retain and motivate key personnel and could also cause customers, suppliers, licensees, partners and other business partners to defer entering into contracts with, making other decisions concerning, or seeking to change existing business relationships with the Company, and following the closing of the merger, the combined company. Because the Company depends on the experience and industry knowledge of their executives and other key personnel to execute their business plans, the combined company may be unable to meet its strategic objectives.

While the merger is pending, the Company may not be able to hire qualified personnel to replace any key employees that may depart to the same extent that they have been able to in the past. In addition, if the merger is not completed, the Company may also encounter challenges in hiring qualified personnel to replace key employees that may depart the Company subsequent to the merger announcement.

Risks related to the combined company following the merger

The Company may not successfully integrate the businesses of Shire and Baxalta.

If the merger is consummated, achieving the anticipated benefits of the proposed combination of Shire and Baxalta will depend in part upon whether the two companies integrate their businesses in an effective and efficient manner. The Company may not be able to accomplish this integration process successfully. The integration of businesses is complex and time-consuming. The difficulties that could be encountered include the following:

- integrating personnel, operations and systems, while maintaining focus on selling and promoting existing and newly acquired or produced products;
- coordinating geographically dispersed organizations;
- distraction of management and employees from operations;
- changes or conflicts in corporate culture;
- management's inability to manage a substantial increase in the number of employees;
- management's inability to train and integrate personnel, who may have limited experience with the respective companies' business lines and products, and to deliver a consistent message regarding diseases treated by the combined company;
- retaining existing customers and attracting new customers;
- retaining existing employees and attracting new employees;
- maintaining business relationships; and
- inefficiencies associated with the integration and management of the operations of the combined company.

In addition, there will be integration costs and non-recurring transaction costs (such as fees paid to legal, financial, accounting and other advisors and other fees paid in connection with the merger) associated with the proposed merger, including costs associated with combining their operations and achieving the synergies the Company expects to obtain, and such costs may be significant.

An inability to realize the full extent of the anticipated benefits of the proposed combination of Shire and Baxalta, including estimated cost synergies, as well as any delays encountered in the integration process and realizing such benefits, could have an adverse effect upon the revenues, level of expenses and

operating results of the combined company, which may materially adversely affect the value of the Company's ordinary shares and ADSs after the consummation of the merger.

The Company will incur significant additional indebtedness in connection with the merger, which will decrease the combined company's business flexibility and increase its interest expense. All of the Company's debt obligations, and any future indebtedness the Company may incur, will have priority over the Company's ordinary shares and ADSs with respect to payment in the event of a liquidation, dissolution or winding up.

The Company has secured an $18 billion fully underwritten bank facility of which $13 billion is available to finance the cash component of the per share merger consideration. The Company has announced the that it intends to maintain an investment grade credit rating for the combined company, but one or more credit rating agencies may determine that the combined company's credit rating is below investment grade, which could increase the combined company's borrowing costs. The combined company's indebtedness following consummation of the merger could have the effect, among other things, of reducing the combined company's flexibility to respond to changing business and economic conditions as well as reducing funds available for capital expenditures, acquisitions, and creating competitive disadvantages for the combined company relative to other companies with lower indebtedness levels. The Company will also incur various costs and expenses associated with the debt financing.

The Company intends to refinance the bank facility through capital market debt issuances in due course. Its ability to refinance the indebtedness will depend on the condition of the capital markets and the combined company's financial condition at such time. Any refinancing of indebtedness could be at higher interest rates and may require the combined company to comply with more onerous covenants, which could further restrict business operations and such refinancing may not be available at all.

Moreover, the combined company may be required to raise substantial additional financing to fund capital expenditures and acquisitions. The combined company's ability to arrange additional financing and the costs of that financing will depend on, among other factors, the combined company's financial position and performance, as well as prevailing market conditions and other factors beyond Shire's control.

In any liquidation, dissolution or winding up of Shire, the Company's ordinary shares and ADSs would rank below all debt claims against Shire or any of its subsidiaries. In addition, any convertible or exchangeable securities or other equity securities that Shire may issue in the future may have rights, preferences and privileges more favorable than those of the Company's ordinary shares and ADSs. As a result, holders of the Company's ordinary shares and ADSs will not be entitled to receive any payment or other distribution of assets upon any liquidation or dissolution until after Shire's obligations to its debt holders and holders of equity securities, which rank senior to the Company's ordinary shares and ADSs, have been satisfied.

The merger could result in significant liability to Baxalta and the Company if the merger causes the spin-off of Baxalta from Baxter or a Later Distribution, as defined below, to be taxable.

Under the letter agreement, from and after the closing of the merger, Baxalta agreed to indemnify, and the Company agreed to guarantee such indemnity to, Baxter and each of its affiliates and each of their respective officers, directors and employees against certain tax-related losses attributable to, or resulting from, in whole or in part, the merger. If the contribution of property by Baxter in one or more transfers to Baxalta in exchange for shares of Baxalta common stock, cash, and the assumption of certain liabilities, together with the distribution or exchange by Baxter on July 1, 2015 of approximately 80.5% of the shares of Baxalta common stock to shareholders of Baxter (the "spin-off") and/or a Later Distribution, collectively the "Baxter Transactions", are determined to be taxable as a result, in whole or in part, of the merger (for example, if the merger is deemed to be part of a plan, or series of related transactions, that includes the Baxter Transactions), Baxter and its shareholders could incur significant tax liabilities, and under the tax matters agreement, and the letter agreement, Baxalta and the Company may be required to indemnify Baxter for any such tax liabilities. Baxter's waiver of the provisions under the tax matters agreement restricting Baxalta's ability to enter into and consummate the merger will not relieve Baxalta or the Company of its obligation to indemnify Baxter if the merger causes any of the Baxter Transactions to be taxable.

In connection with the signing of the merger agreement, the Company received an opinion from Cravath, Swaine & Moore LLP, tax counsel to the Company, to the effect that the merger will not cause Baxter's contribution of assets to Baxalta, Baxter's initial distribution of Baxalta shares on July 1, 2015, Baxter's distribution of cash received from Baxalta to its creditors or a Later Distribution to fail to qualify as tax-free to Baxter and its shareholders under Sections 355, 361 and 368(a)(1)(D) of the Internal Revenue Code of

1986, as amended. The merger is conditioned on the receipt by the Company at the time of the consummation of the merger of a tax opinion to the same effect.

The tax opinion referred to in the immediately preceding paragraph is based upon various factual representations and assumptions, as well as certain undertakings made by the Company, Baxter and Baxalta. If any of the factual representations or the assumptions in the tax opinion is untrue or incomplete in any material respect, an undertaking is not complied with or the facts upon which the tax opinion is based are materially different from the facts at the time of the merger, the opinion may not be valid. Moreover, opinions of counsel are not binding on the Internal Revenue Service (the "IRS"). As a result, the conclusions expressed in the tax opinion could be challenged by the IRS. None of the Company, Baxalta or Baxter has requested a ruling from the IRS regarding the impact of the merger on the tax treatment of the Baxter Transactions. Further, the tax opinion does not address all tax aspects of the spin-off, a Later Distribution and other related transactions and it is possible the Company may be obligated to indemnify Baxter despite the continuing validity of the tax opinion.

The Company's indemnification obligations to Baxter and its subsidiaries, officers, directors and employees under the tax matters agreement and letter agreement are not limited in amount or subject to any cap. If Baxalta or the Company is required to indemnify Baxter and its subsidiaries and their respective officers, directors and employees under the circumstances set forth in the tax matters agreement, as supplemented by the letter agreement, it could have a material adverse effect on Baxalta and the Company.

In this document, references to the "Later Distributions" includes the following transactions that may be undertaken by Baxter: (i) any debt-for-equity exchange (and related underwritten offering) with respect to Baxalta shares, (ii) any offer to exchange Baxter shares for Baxalta shares, (iii) a contribution of Baxalta shares to Baxter's U.S. pension fund, and/or (iv) a dividend of Baxalta shares to Baxter's stockholders, in each case, that are undertaken prior to the earlier of any Baxalta or Company stockholder vote with respect to the merger and that are intended to be part of a plan that includes the spin-off.

Certain Baxalta agreements may contain change of control provisions that may be triggered by the merger that, if not waived, could cause the combined company to lose the benefit of such agreement and incur liabilities or replacement costs, which could have material adverse effect on the combined company.

Baxalta and its affiliates are each party to various agreements with third parties, including certain license agreements, business development-related agreements, production and distribution related agreements, bonding/financing facilities, contracts for the performance of services material to the operations of Baxalta and/or its affiliates, IT contracts, technology licenses and employment agreements that may contain change of control provisions that could be triggered upon the closing of the merger. Agreements with change of control provisions typically provide for or permit the termination of the agreement upon the occurrence of a change of control of one of the parties which can be waived by the relevant counterparties. In the event that there is such a contract or arrangement requiring a consent or waiver in relation the merger, there can be no assurance that such consent will be obtained at all or on favorable terms. If such a waiver is not obtained from any such counterparty, the combined company could lose the benefit of the underlying agreement and incur liabilities or replacement costs, which could have an adverse effect on the combined company.

Sales of the Company's ordinary shares and/or ADSs in anticipation of the merger, and resales of such shares following the consummation of the merger may adversely affect the market price of the Company's ordinary shares and/or ADSs prior to, and following, the merger.

Certain Baxalta stockholders, such as index funds or funds with concentration, geographic or other limitations on their permitted investments, may be required to sell ordinary shares or ADSs of Shire that they receive in the merger. Other Baxalta stockholders may already hold ordinary shares or ADSs of Shire and those stockholders may decide not to hold the shares that they receive in the merger. Such sales of ordinary shares or ADSs could adversely affect the market price of the Company's ordinary shares and/or ADSs.

Upon consummation of the merger, the Company expects that it will issue up to approximately 311 million ordinary shares, based on the number of shares of Baxalta common stock outstanding as of December 31, 2015, in the aggregate. In addition, the per share merger consideration represents a premium of approximately 37.5% to the unaffected share price of Baxalta common stock on August 3, 2015, the day prior to the public announcement of the Company's initial offer for Baxalta, based on the closing price of the Company's ADSs on January 8, 2016, which may cause significant arbitrage activity by investors seeking to take advantage of the price differential. The risk of dilution coupled with the possibility of merger arbitrage

activity could result in downward pressure on the Company's ordinary shares and ADSs and encourage third parties to engage in short sales of the Company's shares.

In addition, these factors could also make it more difficult for the combined company to raise funds through future offerings of ordinary shares and ADSs. The issuance of ordinary shares and ADSs in the merger and the sale of additional ordinary shares or ADSs that may become eligible for sale in the public market from time to time upon exercise of options or the vesting of restricted securities will further dilute the combined company's ordinary shares and/or ADSs. Moreover, the increase in the number of ordinary shares or ADSs, or an increase in the number of such shares outstanding following a future issuance, sale or transfer of such ordinary shares or ADSs by the Company or the possibility of such an issue, sale or transfer may lead to sales of such shares or the perception that such sales may occur, either of which may adversely affect the market for, and the market price of, the Company's ordinary shares or ADSs.

The market price of the Company's ordinary shares and ADSs may be adversely affected by reports of third-party analysts published in connection with the consummation of the merger.

The trading market for the Company's ordinary shares and ADSs depends in part on the research and reports that third-party securities analysts publish about Shire and its industry. In connection with the consummation of the merger, one or more of these analysts could downgrade the Company's ordinary shares and ADSs or issue other negative commentary about Shire or its industry, which could cause the market price of the Company's ordinary shares and ADSs to decline.

The market price of the Company's ordinary shares and ADSs may be affected by factors different from those affecting the market price for shares of the Company's ordinary shares and ADSs prior to the merger.

If the merger is consummated, the risks associated with the combined company may affect the results of operations of the combined company and the market price of the Company's ordinary shares and ADSs following the merger differently than they could affect the results of operations of Shire and the market price of its securities while it is a separate company. Additionally, the results of operations of the combined company may be affected by additional or different factors than those that currently affect the results of operations of Shire, including, but not limited to: complexities associated with managing the larger, more complex, combined business; integrating personnel from the two companies while maintaining focus on providing products and services; and potential performance shortfalls resulting from the diversion of management's attention caused by integrating the companies' operations.

5. Directors' responsibility statement

The following responsibility statement is repeated here solely for the purpose of complying with DTR 6.3.5. This statement relates to and is extracted from page 105 of the 2015 Annual Report.

These responsibilities are for the full 2015 Annual Report and not the extracted information presented in this announcement or otherwise.

We confirm that to the best of our knowledge:

> the financial statements, prepared in accordance with the accounting principles generally accepted in the United States of America, give a true and fair view of the assets, liabilities, financial position and profit or loss of the Group and the undertakings included in the consolidation taken as a whole;

> the strategic report includes a fair review of the development and performance of the business and the position of the Group and the undertakings included in the consolidation taken as a whole, together with a description of the principal risks and uncertainties that they face; and

> the annual report and financial statements, taken as a whole, are fair, balanced and understandable and provide the information necessary for shareholders to assess the Group's performance, business model and strategy.

This responsibility statement was approved by the Board of Directors on February 23, 2016 and is signed on its behalf by:

Flemming Ornskov, MD, MPH

Chief Executive Officer
February 23, 2016

Jeffrey Poulton

Chief Financial Officer
February 23, 2016

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 document:

ADDERALL XR® (mixed salts of a single entity amphetamine)

BUCCOLAM® (midazolam hydrochloride oromucosal solution)

CALCICHEW® (trademark of Takeda Nycomed AS)

CARBATROL® (carbamazepine extended-release capsules)

CINRYZE® (C1 esterase inhibitor [human])

DAYTRANA® (trademark of Noven Pharmaceutical Inc. ("Noven"))

DERMAGRAFT® (trademark of Organogenesis Inc. ("Organogenesis"))

ELAPRASE® (idursulfase)

ELVANSE® (lisdexamfetamine dimesylate)

ELVANSE ADULT® (lisdexamfetamine dimesylate)

ESTRACE® (trademark of Trimel Pharmaceuticals Inc.)

EXPUTEX® (trademark of Phoenix Labs)

FIRAZYR® (icatibant)

FOSRENOL® (lanthanum carbonate)

GATTEX® (teduglutide [rDNA origin])

INTUNIV® (guanfacine extended release)

KALBITOR® (ecallantide)

LIALDA® (trademark of Nogra International Limited)

MEZAVANT® (trademark of Giuliani International Limited)

MIMPARA® (cinacalcet HCl)

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)

SENSIPAR® (cinacalcet HCl)

TYVENSE® (lisdexamfetamine dimesylate)

VANCOCIN® (trademark of ANI Pharmaceuticals Inc.)

VENVANSE® (lisdexamfetamine dimesylate)

VPRIV® (velaglucerase alfa)

VYVANSE® (lisdexamfetamine dimesylate)

XAGRID® (anagrelide hydrochloride)

ZEFFIX® (trademark of GSK)

3TC® (trademark of GSK)