Press Release

www.shire.com

2017 Annual Report – DTR 6.3.5 and LR 9.6.1 Disclosures

March 22, 2018 - Shire plc (LSE: SHP, NASDAQ: SHPG) (the "Company") announces that the following documents will today be posted to shareholders:

- 2017 Annual Report
- Notice of the 2018 Annual General Meeting
- Form of Proxy

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

The 2017 Annual Report and Notice of the 2018 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, 2017, issued on February 14, 2018, 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 2017 Annual Report. Page and note references in the Appendices below refer to page and note references in the 2017 Annual Report.

The information included in the Appendix is extracted from the 2017 Annual Report which is dated February 16, 2018. Defined terms used in the Appendix refer to terms as defined in the 2017 Annual Report, unless the context otherwise requires.

Sarah Rixon
Company Secretarial Assistant

For further information please contact:

Investor Relations

Christoph Brackmann	christoph.brackmann@shire.com	+41 795 432 359
Sun Kim	sun.kim@shire.com	+1 617 588 8175
Robert Coates	rcoates@shire.com	+44 203 549 0874

Media

Katie Joyce	kjoyce@shire.com	+1 781 482 2779

NOTES TO EDITORS

About Shire

Shire is the global leader in serving patients with rare diseases. We strive to develop best-in-class therapies across a core of rare disease areas including hematology, immunology, genetic diseases, neuroscience, and internal medicine with growing therapeutic areas in ophthalmics and oncology. Our diversified capabilities enable us to reach patients in more than 100 countries who are struggling to live their lives to the fullest.

We feel a strong sense of urgency to address unmet medical needs and work tirelessly to improve people's lives with medicines that have a meaningful impact on patients and all who support them on their journey.

www.shire.com

Forward-Looking Statements

Statements included herein that are not historical facts, including without limitation statements concerning future strategy, plans, objectives, expectations and intentions, projected revenues, 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:

- Shire's products may not be a commercial success;
- increased pricing pressures and limits on patient access as a result of governmental regulations and market developments may affect Shire's future revenues, financial condition and results of operations;
- Shire 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. Any disruption to the supply chain for any of Shire's products may result in Shire being unable to continue marketing or developing a product or may result in Shire being unable to do so on a commercially viable basis for some period of time;
- the manufacture of Shire's products is subject to extensive oversight by various regulatory agencies. Regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to, among other things, significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- the nature of producing plasma-based therapies may prevent Shire from timely responding to market forces and effectively managing its production capacity;
- Shire has a portfolio of products in various stages of research and development. The successful development of these products is highly uncertain and requires significant expenditures and time, and there is no guarantee that these products will receive regulatory approval;
- the actions of certain customers could affect Shire's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect Shire's revenues, financial conditions 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;
- Shire's products and product candidates face substantial competition in the product markets in which it operates, including competition from generics;
- Shire's patented products are subject to significant competition from generics;
- adverse outcomes in legal matters, tax audits and other disputes, including Shire's ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on the Shire's revenues, financial condition or results of operations;
- Shire may fail to obtain, maintain, enforce or defend the intellectual property rights required to conduct its business;
- Shire faces intense competition for highly qualified personnel from other companies and organizations;

- failure to successfully execute or attain strategic objectives from Shire's acquisitions and growth strategy may adversely affect the Shire's financial condition and results of operations;
- Shire's growth strategy depends in part upon its ability to expand its product portfolio through external collaborations, which, if unsuccessful, may adversely affect the development and sale of its products;
- a slowdown of global economic growth, or economic instability of countries in which Shire does business, could have negative consequences for Shire's business and increase the risk of non-payment by Shire's customers;
- changes in foreign currency exchange rates and interest rates could have a material adverse effect on Shire's operating results and liquidity;
- Shire is subject to evolving and complex tax laws, which may result in additional liabilities that may adversely affect the Shire's financial condition or results of operations;
- if a marketed product fails to work effectively or causes adverse side effects, this could result in damage to Shire's reputation, the withdrawal of the product and legal action against Shire;
- Shire 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 Shire's revenues, financial condition or results of operations;
- Shire faces risks relating to the expected exit of the United Kingdom from the European Union;
- Shire incurred substantial additional indebtedness to finance the Baxalta acquisition, which has increased its borrowing costs and may decrease its business flexibility;
- Shire's ongoing strategic review of its Neuroscience franchise may distract management and employees and may not lead to improved operating performance or financial results; there can be no guarantee that, once completed, Shire's strategic review will result in any additional strategic changes beyond those that have already been announced; and

a further list and description of risks, uncertainties and other matters can be found on pages 18 to 21 of the 2017 Annual Report.

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 update or revise forward- looking statements, whether as a result of new information, future events or otherwise.

APPENDIX

Contents

1. **Chairman's Review** (Pages 4 – 5 2017 Annual Report)

In 2017, Shire started its first full financial year as a transformed company: the undisputed global leader in treating rare diseases.

As we began the year, the integration of Baxalta was well under way. A company that had commercial operating units in 22 countries in 2013 is now in more than 60 countries. A clinical pipeline with 20 programs in 2013, ended 2017 with 40 such active programs. And our therapeutic footprint had expanded into three new dynamic areas: immunology, hematology, and oncology.

Shire has transformed itself, but with this transformation came obvious challenges. We had a global manufacturing portfolio that required careful pruning and disciplined, efficient management. In many countries we had to consolidate two offices into one, moving and reassigning experienced staff, while maintaining commercial momentum. And we set aggressive targets for our teams, pushing ourselves to meet the highest possible financial goals, some of which were clearly aspirational.

At the end of 2017, the people of Shire could look back with pride. The implementation of our Network Manufacturing Study laid the foundation for efficient and effective supply operations. And at the same time, Shire exceeded its challenging integration synergy targets for the year, saving money and managing its global procurement systems in the most cost-effective and efficient manner.

Despite these many achievements, Shire's share price performance was disappointing. For a Board, management team, and company focused on improving shareholder value, the challenge is clear and we have strengthened our resolve to improve and succeed in 2018.

For Shire, success means delivering more innovative solutions to the patients who depend on us. We know that if patients, physicians, and caregivers appreciate and value our products, then shareholders will also benefit. In this way 2017 was not just a year of integration, but also one of preparation for the future.

In 2017, we launched 50 products in 25 countries with therapies to treat diseases such as short bowel syndrome, hypoparathyroidism and attention deficit hyperactivity disorder (ADHD). We significantly advanced our Research and Development (R&D) pipeline with 54 major market filings around the world and continued to invest in areas where we see great need and opportunity such as immunology.

We maintained our dedication to our environment and the communities in which we serve. In 2017, Shire developed our new Responsibility strategy with commitments and long-term goals to be achieved by 2025. We also held our third annual Global Day of Service, during which more than 7,300 Shire employees from around the world dedicated more than 29,000 hours of their time to volunteering in their communities. A detailed description of Shire's commitment to Responsibility can be found on page 35.

The accomplishments — focused squarely on delivering benefits to patients in need and the communities in which we live — came during a year of substantial external regulatory and macroeconomic challenge. The hemophilia market landscape shifted, and continues to change rapidly. The global political, tax, and regulatory environment in which we operate is constantly in motion. And the pharmaceutical industry must still manage societal challenges in funding, pricing, and identifying ways to support future innovation.

These challenges will continue in 2018, making it essential that Shire maintains its efficient and nimble business strategy. Towards that end, we continue to evaluate the strategic and operational direction of the Company, including an assessment of our neuroscience business. While this review continues, we are creating two distinct business divisions within Shire: one focused on rare disease and the other focused on neuroscience. This will enable sharper management focus, greater strategic clarity, and distinct investment opportunities for both parts of the business. We expect the conclusion of our strategic review of these two business segments in the second half of 2018. Additional details on the divisions can be found on page 12.

For our employees, 2017 was a period of challenge and change. But it was also a year in which they all showed their grit, resolve, and unwavering dedication to the patients we serve. The Board and I would like to thank everyone at Shire, not just for their hard work, but also for their drive, focus, and commitment during a period of transformation. We would also like to thank our CEO, Dr. Flemming Ornskov, who has led the Shire

team through this integration with great skill and has kept everyone focused on the goal of building a more resilient Shire for the long-term.

Finally, I'd like to express my sincere appreciation to Bill Burns, Senior Independent Director; Anne Minto, the previous Chairman of our Remuneration Committee; and Dominic Blakemore, previous chair of the Audit, Compliance & Risk Committee, all of whom will be retiring from the Board after the 2018 AGM.

Thank you also to former Shire CFO Jeff Poulton who left the Company at the end of 2017. The contributions of Bill, Anne, Dominic, and Jeff cannot be overstated. Shire is a better company because of their work; we are grateful for their dedication and wish them all the best in the future.

In closing, I am proud of the contributions of our more than 23,000 employees and our Board, and I am grateful to our patient communities for their partnership. And importantly, I remain excited and optimistic about the future of our Company. It is our privilege to continue working on behalf of the patients who inspire us every day.

Susan Kilsby
Chairman

2. Chief Executive Officer's Review (Pages 6 – 9 2017 Annual Report)

2017 is the year Shire solidified its position as the global leader in rare diseases. With approximately 70 percent of revenues coming from rare disease products, and the most robust pipeline in Shire's history — 60 percent of which are biologic therapies we continue to make significant progress in the Company's evolution.

As we evolved, we also put the Company on solid financial footing. Key to Shire's performance has been the ability to achieve strong financial results while managing our largest integration. We grew by approximately 17,000 employees and consolidated 28 country sites globally — and remain on track to deliver on our Baxalta cost synergy goal of $700 million by the third year post-close. We achieved sales growth of 33 percent and delivered a strong operating cash flow of $4.3 billion enabling us to realize our 2017 leverage ratio target.

We are proud that we now have five of our seven franchises contributing more than $1 billion in revenue annually. Immunology delivered outstanding performance in 2017, driven by the success of our sub-cutaneous immunoglobulin products and growth in International markets. Ophthalmics, our newest franchise, generated sales of $259 million in 2017 as XIIDRA, the only therapy approved in the U.S. to treat the signs and symptoms of dry eye disease (DED), reached more than one million prescriptions written since launch in late 2016. I am greatly appreciative of what our talented and focused team has delivered, in many cases, exceeding our performance expectations in 2017.

Two distinct market-leading businesses
Since I arrived at Shire five years ago, we have grown from an ADHD-focused company to a global biotech with two distinct market-leading businesses — rare disease and neuroscience. To enable these two businesses to reach their full potential, in early 2018 we announced that the neuroscience business warranted additional sharpened focus and increased investment and that there was a strong strategic rationale for creating separate Rare Disease and Neuroscience divisions. For more information about the two divisions, please see page 12.

Innovation at the heart of our vision and culture
Our long-term vision is to be an innovation- driven biotech company focused on rare diseases and specialized conditions across our core scientific platforms and therapeutic areas. Shire has an excellent record of accessing external innovation and delivering late-stage products to market. Going forward, we plan to build on these capabilities by taking our internal research to a new level. To accelerate this goal, we have appointed a new Head of Research and Development and Chief Scientific Officer, Andreas Busch, PhD, an accomplished scientist with an extensive background and impressive track record in research.

At the same time, we continue to complement our R&D innovation with new advances in health information technologies and precision medicine. Shire is utilizing artificial intelligence (AI) as well as pursuing wearables and sensor technology, particularly in clinical trials. We are partnering with new, cutting-edge companies to improve the time it takes for rare disease patients to find a diagnosis, tailor our treatment options for smaller patient groups, and help us identify hard to find patients for clinical trials. More information about these efforts can be found on page 30.

We are also working to enhance our manufacturing network with an eye towards optimizing our reliability and growth. We're making important changes to our internal and external networks to reduce redundancy while also ensuring supply continuity. Among the benefits of these changes, we anticipate savings of $100 million annually beginning in 2019 and $300 million annually by 2023. Additionally, we are modernizing the manufacturing network with new facilities in Georgia (U.S.) and Dublin (Ireland). Our Georgia plant will expand manufacturing capacity for our plasma-derived products by approximately 30 percent, while our Dublin facility will focus on production of antibody-based therapies.

An industry-leading pipeline

Our R&D organization continues to fuel our robust pipeline with innovative therapies. In 2017, our R&D team completed 54 major market regulatory filings around the world. In addition, Shire received two U.S. FDA Fast Track Designations, two Orphan Drug Designations, and one Breakthrough Therapy Designation. We completed nine Phase 3 clinical trials, and received 126 product approvals globally. These accomplishments are major strides forward on behalf of our patients. Additional details about our pipeline can be found on page 24.

New product launches fueled growth

As we advanced programs through the pipeline, we also developed a team that excels at product launches and ensures patients have access to these important therapies. We executed 50 product launches globally in 2017, including the initial launch of MYDAYIS in the U.S. and expanded into multiple new geographies for products such as CUVITRU, NATPARA/N ATPAR, and GATTEX/REVESTIVE. In total, Shire generated $1.6 billion in sales in 2017 from products launched since 2013. Our products are now available in more than 100 countries enabling us to reach more patients than ever before. For more details about Shire's launch excellence, please see page 28.

Patient and customer focus

The main reason I believe our Company has performed so well is because the Shire team is driven by a clear mission, a shared purpose, and strong values—all of which put the patient at the center of all that we do. We know we are most successful when we have patients front of mind, inspiring our thinking, and guiding our work every single day.

Central to our mission at Shire is being close to our patients and our partners, which allows us to not only serve them better, but also to innovate based on their insights. We are often with patients for the long-term, given that half of rare diseases are diagnosed in childhood. From diagnosis to finding appropriate treatment options, securing access, and supporting patients on treatment, we are committed to the wellbeing of our patients for life. The inspiration they provide to our team is second-to-none. I'd like to take this opportunity to thank our patients, their families, and their healthcare providers for allowing us to be part of their journey.

Navigating challenges

While I am extremely proud of Shire's accomplishments in 2017, the year was not without its challenges. We faced generic competition for LIALDA (for the treatment of ulcerative colitis) for the first time. We also faced a supply interruption during the summer for CINRYZE (for the treatment of hereditary angioedema (HAE)) related to issues with a third-party manufacturer. We thank HAE patients and the HAE community for their patience while we worked diligently to address this issue and have taken steps to mitigate this risk in the future, including bringing additional manufacturing of drug product in-house beginning in 2018.

We also experienced increased competition in the Hematology franchise, but continue to be confident in our leadership position. Shire is committed to innovating and building for the future — as it can be seen with ADYNOVI receiving a positive opinion and, early this year, the marketing authorization from the European Medicines Agency (EMA) and with the recent approval of myPKFiT, a registered software-based medical device for personalized hemophilia A dosing in the U.S. And, we continue to invest in and expand our pipeline of innovative Hematology programs.

While we are proud of our accomplishments in 2017, we also acknowledge that we need to work even harder on improving shareholder value throughout 2018.

Despite these challenges, Shire performed very well financially in 2017 — delivering 8% pro forma product sales growth to $14.4 billion, an increase of over $1 billion. We also improved our operating margin and operating cash flow of $4.3 billion which enabled us to reach our debt target.

Employees and culture
I would like to thank Shire employees and the Board of Directors who has provided invaluable guidance for the organization. We've grown from fewer than 6,000 employees to more than 23,000, and everyone continues to focus on our mission to serve the needs of patients. The accomplishments achieved in 2017 are incredible and I look forward to an equally impressive 2018.

Outlook and summary
We left 2017 stronger than we've ever been before with leadership positions in many of the therapeutic areas in which we compete. In particular, we now have a leading high-growth Immunology franchise, which will be the foundation of our rare disease business as we move into 2018. Our neuroscience business will soon benefit from increased investment and focus as we look to broaden our expertise beyond ADHD.

2018 will be a year of continued focus on commercial execution and targeted investment in our manufacturing infrastructure, new product launches, and pipeline to drive future growth. We expect to deliver mid-single digit product sales growth in 2018 after absorbing the anticipated impact of generics. Based on current assumptions, we also expect margins to be impacted by the start-up of our new U.S. plasma manufacturing site, intensifying genericization, and lower royalties. But, I remain confident that Shire will continue to build on our leadership position in both rare disease and neuroscience and we are committed to achieving our 2020 goal of $17-$18 billion in revenues and mid-forties Non GAAP EBITDA margin.

I am energized and excited about Shire's future as we look forward to growing our franchises, especially Immunology; executing on our many launches; leveraging our robust international footprint in key markets such as China to expand access to our 40+ marketed products; and, building an innovative, results-oriented, patient-centric culture. I am confident that our team and our partners will continue to execute on our priorities and serve as champions for our patients.

Flemming Ornskov, MD, MPH
Chief Executive Officer

Diagram on pages 8 – 9 of 2017 Annual Report:

Q1

- Ian Clark is appointed as a Non-Executive Director
- Receipt of New Drug Application for SHP465 for ADHD is acknowledged by U.S. FDA

- EU Conditional Marketing Authorization is recommended for NATPAR for patients with chronic hypoparathyroidism by CHMP
- European approval is received for label extension of CINRYZE to prevent and treat attacks in pediatric patients with HAE

- New data from Shire that aim to help close the diagnosis and treatment gap for people with hemophilia are presented

- Seventh annual scholarship for individuals with ADHD is announced

- U.S. FDA Fast Track Designation is received for SHP655 for treatment of congenital thrombotic thrombocytopenic purpura

- INTUNIV, a non-stimulant for the treatment of ADHD, is approved in Japan

- “Rare Count” campaign to personalize the global impact of Rare Diseases is launched

- Data are released showing improved treatment satisfaction for patients on CUVITRU relative to previous immunoglobulin therapy

Q2

- #PIPostsThanks Social Campaign is launched to raise awareness of primary immunodeficiency

- VYVANSE is made available in a new chewable tablet formulation

- Lanadelumab is shown to reduce HAE monthly attack rate by 87% versus placebo in Phase 3 26-week pivotal trial

- EU Conditional Marketing Authorization is received for NATPAR for treatment of patients with chronic hypoparathyroidism

- Collaborative license agreement is entered into with Parion Sciences, Inc., to advance SHP659 for ophthalmic indications

- New headquarters office is opened in Dublin City Center

- EMA validation of VEYVONDI Marketing Authorization Application is received for treatment of von Willebrand disease

- U.S. FDA approval is received for MYDAYIS (formerly SHP465), a new once-daily option for ADHD symptom control in patients 13 years and older

Q3

- Investigational New Drug Application is submitted to U.S. FDA for gene therapy candidate SHP654 for treatment of hemophilia A

- Licensing agreement is entered into with Novimmune S.A. for bi-specific antibody to expand Shire’s monoclonal antibody research platform

- It is announced that Jeff Poulton will step down as CFO at end of 2017

- Joanne Cordeiro is appointed Chief Human Resources Officer and a member of the Executive Committee

- Collaboration with MicroHealth is launched to address unique needs of hemophilia patients with inhibitors

- MYDAYIS is launched in the U.S.

- Lifitegrast Marketing Authorization Application for treatment of dry eye disease is submitted in Europe

- Positive topline results for INTUNIV in Phase 3 clinical trial in adults with ADHD are released

- SHP616 is shown to significantly reduce HAE monthly attack rate versus placebo in a Phase 3 pivotal trial

- U.S. FDA Fast Track Designation is received for SHP607 for prevention of chronic lung disease in extremely premature infants

Q4

- The appointments of Thomas Dittrich as CFO and Andreas Busch, PhD as Head of R&D and CSO are announced

- European approval for label extension of FIRAZYR for symptomatic treatment of acute HAE attacks in paediatric patients is received

- U.S. FDA Orphan Drug Designation is received for gene therapy candidate SHP654 for treatment of hemophilia A

- Topline results for SHP609 are announced showing Phase 2/3 clinical trial in children with Hunter syndrome and cognitive impairment did not meet its primary endpoint

- OnePath patient portal and mobile application are launched

- EU Marketing Authorization is recommended by CHMP for ADYNOVI for adults and adolescents with hemophilia A

- U.S. FDA clearance is received for myPKFiT for ADVATE to help personalize care for hemophilia A

- Positive CHMP opinion is received in Europe for new formulation of ONCASPAR for patients with acute lymphoblastic leukemia (ALL)

- Submission is filed with U.S. FDA for approval of new plasma manufacturing facility near Covington, Georgia

3. Financial Review (Pages 44 – 55 2017 Annual Report)

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 and specialized conditions,

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, partners, 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 and 14.

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

- serve patients with high unmet needs in specialty therapeutic areas;
- drive optimum performance of its marketed products — to serve patients today; and
- 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 and other revenues (where Shire has out-licensed products to third parties) that are recorded as royalty and other revenues.

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

- 95.3% (2016: 95.5%) of total revenues are derived from Product sales; and
- 4.7% (2016: 4.5%) of total revenues are derived from royalties and other revenues, including upfront payments from out-license arrangements.

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

The healthcare industry is also experiencing:

- pressure from governments and healthcare providers to keep prices low while increasing access to drugs;
- increased discounts, which reduce revenue, due to the population of "baby boomers" covered under Medicare, specifically those beneficiaries receiving drug cost offset through the Medicare Part D Coverage Gap;
- 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 health-care systems favoring earlier entry of low cost generic drugs; and
- higher marketing costs, due to increased competition for market share.

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 spans seven key therapeutic areas (TA): Immunology, Hematology, Neuroscience, Internal Medicine, Genetic Diseases, Oncology and Ophthalmics. In 2017, the contribution of each TA to overall Product sales was as follows:

	Product sales $'M	Percentage %
Immunology	4,370.3	30.2
Hematology	3,785.6	26.2
Neuroscience	2,664.1	18.4
Internal Medicine	1,670.3	11.6
Genetic Diseases	1,437.7	10.0
Oncology	261.7	1.8
Opthalmics	259.2	1.8
	14,448.9	100.0

Shire has grown in part through acquisition which has brought therapeutic, geographic and pipeline growth and diversification.

The acquisition of Baxalta in June 2016 added the Hematology, Immunology and Oncology franchises and enabled Shire to become the global leader in rare diseases and highly specialized conditions.

The acquisition of Dyax in January 2016, with its lead pipeline product, SHP643, and marketed product KALBITOR, expanded and extended Shire's industry-leading HAE portfolio (FIRAZYR and CINRYZE).

In July 2016, Shire licensed the global rights to all indications for SHP647 from Pfizer Inc. SHP647 is an investigational biologic being evaluated for the treatment of moderate-to- severe inflammatory bowel disease.

In 2015, Shire acquired NPS Pharma, Meritage Pharma, Inc. (Meritage Pharma) and Foresight Biotherapeutics Inc. (Foresight).

The acquisition of NPS Pharma added global rights to an innovative product portfolio with multiple growth catalysts, including GATTEX/REVESTIVE and NATPARA/NATPAR. The acquisition of Meritage Pharma provided global rights to SHP621, a Phase 3 ready asset for the treatment of adolescents and adults with EoE, a rare, chronic inflammatory GI disease. This builds upon the Company's rare disease and GI commercial infrastructure and expertise. With the acquisition of Foresight, Shire acquired the global rights to SHP640 (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 has a clear strategic fit with XIIDRA, which is approved in the U.S. for the treatment of the signs and symptoms of dry eye disease, and further demonstrates Shire's commitment to building a leadership position in ophthalmics.

In 2017, Shire derived 34% (2016: 32%) of Product sales from outside of the U.S. 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:

- the launch of MYDAYIS in the U.S.;
- continued launch of INTUNIV, REVESTIVE and ONIVYDE across Europe;
- the approvals of NATPAR and ADYNOVI in the EU;
- submission of SHP643 in the U.S.;
- submission of CALPEG NDA for ALL in the U.S.;
- submission of VONVENDI MAA in Europe; and
- geographic expansion of XIIDRA with the recent approval in Canada and submissions in other key markets.

R&D

Shire's R&D efforts are focused on core therapeutic areas including Immunology, Hematology, Neuroscience, Internal Medicine, Genetic Diseases, Oncology and Ophthalmics. 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 three years. In this time, several products have received regulatory approval including: in the U.S., MYDAYIS in 2017, XIIDRA and CUVITRU in 2016, NATPARA and VYVANSE for BED in 2015; in the EU, ONIVYDE and CUVITRU in 2016, ELVANSE/TYVENSE for adults, INTUNIV for children and adolescents in 2015.

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

Shire's R&D expenses in 2017 and 2016 include costs on programs in all stages of development. The following table summarizes the Company's direct R&D spend categorized by development stage, based upon the development stage of each program for the years ended December 31, 2017 and 2016:

For years ended December 31	2017 $M	2016 $M
Early stage programs	275.3	325.7
Late stage programs	507.5	291.1
Currently marketed products	275.0	238.1
Total	1,057.8	854.9

Early stage programs also include pre- clinical and research programs. In addition to the above, the Company recorded R&D employee costs of $506.9 million in 2017 (2016: $431.9 million) and other indirect R&D costs of $198.6 million (2016: $153.0 million), comprising mainly of depreciation and up-front and milestone payments for in-licensed development projects.

For a discussion of the Company's current development projects see pages 24 and 25.

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.

In 2017, a generic version of the Company's LIALDA product was launched, which led to lower sales of Shire's LIALDA product compared to the period before loss of exclusivity. In 2017, a generic version of the Company's FOSRENOL product was launched, which led to lower sales of FOSRENOL compared to the period before loss of exclusivity.

Shire is engaged in various legal proceedings with generic manufacturers.
For information regarding current patent litigation, refer to Note 25, Legal and Other Proceedings, to the consolidated financial statements.

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

Results of operations for the years ended December 31, 2017 and 2016
Financial highlights for the year ended December 31, 2017 are as follows:

Revenues

- Product sales increased 33% to $14,448.9 million (2016: $10,885.8 million), primarily driven by the inclusion of a full year of legacy Baxalta product sales, with strong sales from immunoglobulin therapies and bio therapeutics.
- Royalties and other revenues increased 39% to $711.7 million (2016: $510.8 million), primarily due to the receipt of an upfront license fee and a full year of contract manufacturing revenue acquired with Baxalta.

Operating results

- Operating income increased 155% to $2,455.2 million (2016: $962.9 million), primarily due to the inclusion of a full year of legacy Baxalta operating income and lower expense related to the unwind of inventory fair value adjustments, partially offset by higher amortization of acquired intangible assets.

Earnings per share (EPS)

- Diluted earnings per American Depositary Share (ADS) increased to $14.05 (2016: $1.27). The increase is primarily due to a tax benefit in 2017 driven by U.S. tax reform, higher operating income, combined with lower discontinued operations losses related to the divested DERMAGRAFT business.

Cash flows

- Net cash provided by operating activities increased 60% to $4,256.7 million (2016: $2,658.9 million), primarily due to the inclusion of a full year of legacy Baxalta operating cash flows and strong cash receipts from higher legacy Shire sales and operating profitability, partially offset by a payment associated with the settlement of the DERMAGRAFT litigation and higher interest payments. Also, 2016 net cash provided by operating activities was negatively impacted by a payment associated with the termination of a biosimilar collaboration acquired with Baxalta.

Total revenues

The following table provides an analysis of the Company's total revenues by source. In 2017, Immunology includes HAE from Genetic Diseases; prior year amounts have been reclassified to conform with the current year presentation.

Years ended December 31	2017 $'M	2016 $'M	Product sales growth %
Product sales by franchise			
IMMUNOGLOBULIN THERAPIES	2,236.6	1,143.9	N/M
HEREDITARY ANGIOEDEMA	1,429.6	1,310.9	9
BIO THERAPEUTICS	704.1	372.2	N/M
Immunology	4,370.3	2,827.0	N/M
HEMOPHILIA	2,957.3	1,789.0	N/M
INHIBITOR THERAPIES	828.3	451.8	N/M
Hematology	3,785.6	2,240.8	N/M
VYVANSE	2,161.1	2,013.9	7
ADDERALL XR	348.0	363.8	(4)
MYDAYIS	21.6		N/M
Other Neuroscience	133.4	112.8	18
Neuroscience	2,664.1	2,490.5	7
LIALDA/MEZAVANT	569.4	792.1	(28)
GATTEX/REVESTIVE	335.5	219.4	53
PENTASA	313.2	309.4	1
NATPARA/NATPAR	147.4	85.3	73
Other Internal Medicine	304.8	349.3	(13)
Internal Medicine	1,670.3	1,755.5	(5)
ELAPRASE	615.7	589.0	5
REPLAGAL	472.1	452.4	4
VPRIV	349.9	345.7	1

Genetic Diseases	1,437.7	1,387.1	4
Oncology	261.7	130.5	N/M
Ophthalmics	259.2	54.4	N/M
Total Product sales	14,448.9	10,885.8	33
Royalties and other revenues			
Royalties	448.4	382.6	17
Other revenues	263.3	128.2	105
Total royalties and other revenues	711.7	510.8	39
Total revenues	15,160.6	11,396.6	33

N/M: Consolidated results include Baxalta sales as of June 3, 2016, the date of acquisition, or partial year product launches; therefore, Product sales growth as a percentage is not meaningful.

Immunology

Immunology product sales, which now include HAE product sales, were $4,370.3 million in 2017 compared to $2,827.0 million in 2016, primarily driven by the inclusion of a full year of immunoglobulin therapies and bio therapeutics product sales following the acquisition of Baxalta in June 2016. Immunoglobulin and bio therapeutics reported total product sales of $2,940.7 million.

HAE product sales for the year ended December 31, 2017 increased to $1,429.6 million or 9% from $1,310.9 million in 2016, primarily driven by FIRAZYR, up 15% to $663.0 and CINRYZE up 3% to $699.3 million. During the third quarter of 2017, CINRYZE had a supply constraint caused by a manufacturing interruption at a third-party supplier. The issue was addressed and production resumed in the fourth quarter of 2017. On January 24, 2018, FDA granted approval for the technology transfer of CINRYZE drug product manufacturing process to the Vienna, Austria manufacturing site. The Company expects to start manufacturing CINRYZE drug product in-house in Vienna in the first quarter of 2018, providing an additional supply source to meet patient demand.

Hematology

Hematology, acquired with Baxalta in June 2016, included sales of recombinant and plasma-derived hemophilia products (primarily Factor VIII and Factor IX) and inhibitor therapies. Hematology product sales were $3,785.6 million in 2017 compared to $2,240.8 million in 2016, primarily driven by the inclusion of a full year of Hematology product sales following the acquisition of Baxalta.

Neuroscience

Neuroscience product sales for the year ended December 31, 2017 increased to $2,664.1 million, or 7%, from $2,490.5 million in 2016, with growth primarily driven by VYVANSE and the inclusion of MYDAYIS.

VYVANSE product sales for the year ended December 31, 2017 increased to $2,161.1 million, or 7%, from $2,013.9 million in 2016, due to the benefit of a price increase[1] taken since 2016, increased demand resulting from growth in the U.S. ADHD market and strong performance in the Company's international markets, partially offset by lower U.S. stocking.

[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 wholesale customers.

MYDAYIS, which was made available to patients on August 28, 2017, contributed $21.6 million of product sales in 2017.

Information about litigation related to MYDAYIS can be found in Note 25, Legal and Other Proceedings, to the consolidated financial statements.

Internal Medicine
Internal Medicine product sales for the year ended December 31, 2017 decreased to $1,670.3 million, or 5%, from $1,755.5 million in 2016, primarily driven by the impact of LIALDA generic competition, partially offset by growth from GATTEX/ REVESTIVE and NATPARA.

LIALDA/MEZAVANT product sales decreased to $569.4 million, or 28%, for the year ended December 31, 2017 from $792.1 million in 2016, due to the impact of generic competition in 2017.

Information about litigation related to LIALDA can be found in ITEM 3: Legal Proceedings and Note 25, Legal and Other Proceedings, to the consolidated financial statements.

GATTEX/REVESTIVE and NATPARA/NATPAR product sales increased to $335.5 million, or 53%, and $147.4 million or 73%, respectively, for 2017, compared to product sales in 2016 primarily due to an increase in the numbers of patients on therapy and to a lesser extent, the benefit of price increases taken since 20161.

Genetic Diseases
Genetic Diseases product sales, which now excludes HAE product sales, for the year ended December 31, 2017 increased to $1,437.7 million, or 4%, from $1,387.1 million in 2016, primarily due to ELAPRASE and REPLAGAL, as both products benefited from an increase in the number of patients on therapy.

Oncology
Oncology, acquired with Baxalta in June 2016, reported product sales of $261.7 million for the year ended December 31, 2017 compared to $130.5 million for the year ended December 31, 2016. Oncology includes sales of ONCASPAR and ONIVYDE. ONIVYDE was approved in the EU on October 18, 2016.

Ophthalmics
Ophthalmic product sales relate to XIIDRA, which was made available to patients on August 29, 2016. XIIDRA product sales were $259.2 million for the year ended December 31, 2017 compared to $54.4 million for the year ended December 31, 2016.

Royalties and other revenues
Royalties and other revenues increased to $711.7 million or 39% for the year ended December 31, 2017 from $510.8 million in 2016, primarily due to an upfront license fee received, a full year of contract manufacturing revenue acquired with Baxalta, increase in SENSIPAR royalties and an increase in royalty streams acquired with Dyax.

Cost of sales
Cost of sales increased by $884.3 million to $4,700.8 million for the year ended December 31, 2017 (31% of Total revenues) from $3,816.5 million in 2016 (33% of Total revenues), due to the inclusion of a full year of legacy Baxalta costs. The decrease in Cost of sales as a percentage of Total revenues for the year ended

December 31, 2016 to December 31, 2017 is primarily due to the impact of lower expense related to the unwind of inventory fair value adjustments, partially offset by the inclusion of a full year of lower margin product franchises acquired with Baxalta.

For the year ended December 31, 2017, Cost of product sales included additional depreciation totaling $276.1 million (2016: $160.8 million), primarily due to the acquisition of Baxalta.

R&D

R&D expense increased by $323.5 million, or 22%, to $1,763.3 million for the year ended December 31, 2017 (12% of Total revenues) from $1,439.8 million in 2016 (13% of Total revenues), primarily due to the inclusion of a full year of legacy Baxalta costs.

R&D expense for the year ended December 31, 2017 included depreciation of $47.2 million (2016: $34.1 million).

SG&A

SG&A expense increased by $515.7 million, or 17%, to $3,530.9 million for the year ended December 31, 2017 (23% of Total revenues) from $3,015.2 million in 2016 (26% of Total revenues), primarily due to the inclusion of a full year of legacy Baxalta costs.

For the year ended December 31, 2017, SG&A expense included depreciation of $172.5 million (2016: $98.0 million).

Amortization of acquired intangible assets

For the year ended December 31, 2017, Shire recorded Amortization of acquired intangible assets of $1,768.4 million compared to $1,173.4 million in 2016. The increase of $595.0 million was primarily related to a full year of amortization of intangible assets acquired with Baxalta and the acceleration of CINRYZE amortization following positive SHP643 Phase 3 results.

Integration and acquisition costs

For the year ended December 31, 2017, Shire recorded Integration and acquisition costs of $894.5 million, primarily relating to the Baxalta acquisition. Costs included asset impairment charges, employee severance and expenses associated with facility consolidations.

For the year ended December 31, 2016, Shire recorded Integration and acquisition costs of $883.9 million, primarily relating to the Baxalta and Dyax acquisitions. Costs included employee severance, acceleration of stock compensation, third-party professional fees, contract terminations and other transaction-related fees.

Reorganization costs

For the year ended December 31, 2017, Shire recorded Reorganization costs of $47.9 million, primarily related to the closure of the Basingstoke, U.K. office.

For the year ended December 31, 2016, Shire recorded Reorganization costs of $121.4 million, primarily related to the closure of a facility at the Los Angeles, U.S. manufacturing site.

Other expense, net

Other expense, net increased by $85.0 million to $561.8 million for the year ended December 31, 2017 from $476.8 million in 2016, primarily due to a full year of interest expense incurred on borrowings used to fund the acquisition of Baxalta, reduced by repayments of borrowings and partially offset by lower amortization of one-time upfront borrowing costs for Baxalta and Dyax in 2017.

Taxation

The effective tax rate in 2017 was a tax credit of 125% (2016: tax credit of 26%). The effective tax rate in 2017 was lower due to the enactment of the U.S. Tax Cuts and Jobs Act (P.L. 115-97) (Tax Act), which was signed into law on December 22, 2017. Among the changes is a permanent reduction in the federal U.S. corporate income tax rate from 35% to 21% effective January 1, 2018.

As a result of the reduction in the U.S. corporate income tax rate, Shire revalued its net deferred tax positions for the year ending December 31, 2017.

This resulted in a decrease to the net deferred tax liability of approximately $2.5 billion, which was recorded as reduction to income tax expense for the fourth quarter of 2017. In addition, Shire has estimated an income tax liability of $621.7 million related to the transition tax which is applicable to certain non U.S. earnings previously untaxed in the U.S. The Company recorded a $90.1 million income tax expense related to the transition tax and reclassified a deferred tax liability which had been accrued for prior years' unremitted earnings to income tax payable for the remaining amount. Shire continues to analyze the Tax Act to determine the full effects the new law will have on its financial statements and all amounts recorded in the 2017 financial statements are provisional in nature.

Discontinued operations

The gain from discontinued operations for the year ended December 31, 2017 was $18.0 million, net of taxes, primarily the return of funds previously held in escrow related to the acquisition of the DERMAGRAFT business. The loss from discontinued operations for the year ended December 31, 2016 was $276.1 million, net of tax benefit of $98.9 million, primarily due to the establishment of legal contingencies related to the divested DERMAGRAFT business.

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 (EBT) of Shire shares in the market to satisfy awards granted under Shire's employee share plans; the timing and qualification of its refinancing obligations; 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 Consolidated Balance Sheets included $472.4 million of Cash and cash equivalents as of December 31, 2017.

Shire has a revolving credit facility (RCF) of $2.1 billion which matures in 2021, $810.0 million of which was utilized as of December 31, 2017. The RCF incorporates a $250 million U.S. dollar and Euro swingline facility operating as a sub-limit thereof.

In connection with the acquisition of Dyax, Shire entered into a $5.6 billion amortizing term loan facility in November 2015. As of December 31, 2017, $1.2 billion of this term loan facility was outstanding. The facility matures on November 2, 2018.

In connection with the acquisition of Baxalta, Shire assumed $5.0 billion of unsecured senior notes previously issued by Baxalta, of which $750.0 million is due within the next twelve months and issued $12.1 billion of unsecured senior notes in September 2016, of which none are due for repayment in the next twelve months.

The details of these debt agreements are described below and in Note 18, Borrowings and Capital Leases, to the consolidated financial statements.

In addition, Shire also has access to certain short-term uncommitted lines of credit which are available to utilize from time to time to provide short-term cash management flexibility. As of December 31, 2017, these lines of credit were not utilized.

The Company may also engage in financing activities from time to time, including accessing the debt or equity capital markets.

Senior Notes Issuance

On September 23, 2016, SAIIDAC, issued senior notes with a total aggregate principal value of $12.1 billion (SAIIDAC Notes), guaranteed by Shire plc and by Baxalta. SAIIDAC used the net proceeds to fully repay amounts outstanding under the January 2016 Facilities Agreement (discussed below), which was used to finance the cash consideration payable related to the Company's acquisition of Baxalta. Below is a summary of the SAIIDAC Notes as of December 31, 2017:

	Aggregate Amount $'M	Coupon rate %	Effective Interest Rate in 2017 %	Carrying amount as of December 31, 2017 $'M
Fixed-rate notes due 2019	3,300.0	1.900	2.05	3,291.9
Fixed-rate notes due 2021	3,300.0	2.400	2.53	3,286.4
Fixed-rate notes due 2023	2,500.0	2.875	2.97	2,489.5
Fixed-rate notes due 2026	3,000.0	3.200	3.30	2,982.4
	12,100.0			12,050.2

The costs and discount associated with this offering of $49.8 million have been recorded as a reduction to the carrying amount of the debt on the Consolidated Balance Sheets. These costs will be amortized as additional interest expense using the effective interest rate method over the period from issuance through maturity.

Baxalta Notes

Shire plc guaranteed senior notes issued by Baxalta with a total aggregate principal amount of $5.0 billion in connection with the Baxalta acquisition (Baxalta Notes). Below is a summary of the Baxalta Notes as of December 31, 2017:

	Aggregate Amount $'M	Coupon rate %	Effective Interest Rate in 2017 %	Carrying amount as of December 31, 2017 $'M

Variable-rate notes due 2018	375.0	LIBOR plus 0.78	2.60	373.9
Fixed-rate notes due 2018	375.0	2.000	2.00	374.9
Fixed-rate notes due 2020	1,000.0	2.875	2.80	1,001.3
Fixed-rate notes due 2022	500.0	3.600	3.30	506.8
Fixed-rate notes due 2025	1,750.0	4.000	3.90	1,770.2
Fixed-rate notes due 2045	1,000.0	5.250	5.10	1,030.6
Total Baxalta Notes	5,000.0			5,057.7

The effective interest rates above exclude the effect of any related interest rate swaps. The book values above include any premiums and adjustments related to hedging instruments. For further details related to the interest rate derivative contracts, please see Note 16, Financial Instruments, to the consolidated financial statements.

Revolving Credit Facilities Agreement

On December 12, 2014, Shire entered into a $2.1 billion revolving credit facilities agreement with a number of financial institutions. Shire plc and SAIIDAC are able to borrow under the RCF; Shire plc, SAIIDAC and Baxalta are guarantors under the RCF. As of December 31, 2017 SAIIDAC utilized $810.0 million of the RCF.

The RCF, which terminates on December 12, 2021, may be applied towards financing the general corporate purposes of Shire. The RCF incorporates a $250 million U.S. 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 annum 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 also will 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 $700.0 million, (b) 0.15% per year of the amount by which the aggregate base currency amount of all outstanding loans exceeds $700.0 million but is equal to or less than $1,400.0 million and (c) 0.30% per year of the amount by which the aggregate base currency amount of all outstanding loans exceeds $1,400.0 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 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. Shire elected to increase the Net Debt to EBITDA ratio in connection with the period ending June 30, 2016, following the completion of the acquisition of Baxalta during the period. The final relevant period ended June 2017.

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.

Term Loan Facilities Agreement
November 2015 Facilities Agreement
On November 2, 2015, Shire entered into a $5.6 billion facilities agreement with various financial institutions (November 2015 Facilities Agreement). Shire plc, SAIIDAC and Baxalta are guarantors under the November 2015 Facilities Agreement. SAIIDAC is the borrower under the November 2015 Facilities Agreement. The November 2015 Facilities Agreement comprises three credit facilities: (i) a $1.0 billion term loan facility of which, following the exercise of the one year extension option in the amount of $400.0 million, $600.0 million matured and was repaid on November 2, 2016 and $400.0 million was repaid on July 31, 2017 (November 2015 Facility A), (ii) a $2.2 billion amortizing term loan facility which was fully paid during 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), of which $1.2 billion remains outstanding as of December 31, 2017.

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 the November 2015 Facility A, 0.55% per annum, in the case of the November 2015 Facility B, 0.65% per annum and, in the case of the November 2015 Facility C, 0.75% per annum, in each case subject to change 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 acquisition fulfilling certain criteria, Shire may 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 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. Shire elected to increase the Net Debt to EBITDA ratio in connection with the period ending June 30, 2016, following the completion of the acquisition of Baxalta during the period. The final relevant period ended June 2017.

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.

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 various financial institutions (the January 2016 Facilities Agreement). The January 2016 Facilities Agreement comprised two credit facilities: (i) a $13.0 billion term loan facility originally maturing on January 11, 2017 (January 2016 Facility A) and (ii) a $5.0 billion revolving loan facility originally maturing on January 11, 2017 (January 2016 Facility B). On April 1, 2016, SAIIDAC became an additional borrower and additional guarantor under the January 2016 Facilities Agreement. The January 2016 Facility A was fully repaid in September 2016. The January 2016 Facility B was canceled effective July 11, 2016, in accordance with its terms.

Short-term uncommitted lines of credit (Credit lines)

Shire has access to various Credit lines from a number of banks which are available to be utilized from time to time to provide short- term cash management flexibility. These Credit lines can be withdrawn by the banks at any time. The Credit lines are not relied upon for core liquidity. As of December 31, 2017, 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, debt repayments and milestone payments as they become due over the next twelve months.

If the Company decides to acquire other businesses, it expects to fund these acquisitions from cash resources, the RCF 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 of December 31	2017 $'M	2016 $'M
Cash and cash equivalents	472.4	528.8
Long term borrowings (excluding capital leases)	16,410.7	19,552.6
Short term borrowings (excluding capital leases)	2,781.2	3,061.6

Capital leases	349.2	353.6
Total debt	19,541.1	22,967.8
Net debt	19,068.7	22,439.0

- 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). 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.

- Net debt is a Non GAAP measure. The Company believes that Net Debt is a useful measure as it indicates the level of net cash/borrowings after taking account of the Cash and cash equivalents that could be utilized to pay down the outstanding borrowings.

Cash flow activity

Net cash provided by operating activities for the year ended December 31, 2017 increased 60% to $4,256.7 million (2016: $2,658.9 million), primarily due to inclusion of a full year of Baxalta operating cash flows, increased cash receipts from higher sales and operating profitability, partially offset by a payment of $351.6 million associated with the settlement of the DERMAGRAFT litigation and higher interest payments.

Net cash provided by operating activities for the year ended December 31, 2016 increased 14% to $2,658.9 million (2015: $2,337.0 million), primarily due to increased cash receipts from higher sales, partially offset by higher tax and interest payments, costs related to the Baxalta integration and a payment associated with the termination of a biosimilar collaboration acquired with Baxalta.

Net cash used in investing activities was $700.9 million for the year ended December 31, 2017, primarily related to purchase of $798.8 million of PP&E due to continued investments in manufacturing operations, offset by $88.6 million of proceeds from the sale of investments.

Net cash used in investing activities was $18,092.2 million for the year ended December 31, 2016, primarily related to the cash paid for the acquisitions of Baxalta ($12,366.7 million, less cash acquired of $583.2 million) and Dyax ($5,934.0 million, less cash acquired of $241.2 million). The Company's investing activities also included the purchase of $648.7 million of PP&E due to the continued investment in manufacturing operations.

Net cash used in financing activities was $3,619.3 million for the year ended December 31, 2017, principally due to repayments of November Facilities of $3,800.0 million and dividend payments of $281.3 million, offset by monies borrowed under the RCF of $360.0 million and proceeds from the issuance of stock and share-based compensation arrangements of $134.1 million.

Net cash provided by financing activities was $15,825.8 million for the year ended December 31, 2016, principally due to monies borrowed under the January 2016 Facilities Agreement to partially fund the acquisition of Baxalta (repaid using the proceeds of the issuance of the SAIIDAC Notes) and drawings made under the RCF and the November 2015 Facilities Agreement to fund the acquisition of Dyax (net of subsequent repayments). In addition, the Company made dividend payments of $171.3 million.

Outstanding Letters of credit

As of December 31, 2017, the Company had irrevocable standby letters of credit and guarantees with various banks totaling $224.8 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

As of December 31, 2017, the Company's cash requirements for current and non-current liabilities reflected on the Consolidated Balance Sheets 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
Borrowings and capital lease obligations	23,626.5	3,330.5	5,294.7	4,555.0	10,446
Operating leases obligations	1,579.7	188.5	320.0	275.4	795.
Purchase obligations	3,946.6	2,113.4	1,501.4	281.1	50.
Other non-current liabilities	1,077.6	—	473.9	323.9	279.
Total	30,230.4	5,632.4	7,590.0	5,435.4	11,572

- Calculations of expected interest payments incorporate current period assumptions for interest rates, foreign currency translation rates and hedging strategies (refer to Note 16, Financial Instruments to these consolidated financial statements), and assume that interest is accrued through the maturity date or expiration of the related instrument.
- The Company leases certain land, facilities, motor vehicles and certain equipment under operating leases expiring through 2033.
- Purchase obligations include agreements to purchase goods, investments or services (including clinical trials, contract manufacturing and capital equipment), and 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.
- Unrecognized tax benefits and associated interest and penalties of $143.8 million are included within payments due in one to three years.

The following items have been excluded from the table above:

- Cash outflows related to the assumed pension and other post-employment benefit plans, in which timing of funding is uncertain and dependent on future movements in interest rates and investment returns, changes in laws and regulations and other variables.
- In connection with the Company's acquisitions, the Company recorded contingent consideration liabilities related to development, regulatory and commercial milestones and royalty payments. These liabilities were recorded at fair value on the respective acquisition dates and revalued each reporting period. The Company may pay up to approximately $2.7 billion, which excludes royalty related payments, upon achieving clinical, regulatory and commercialization milestones. For additional information, see Note 14, Fair Value Measurement.
- Milestone payments to third parties upon the achievement of development, regulatory and commercial milestones, as well as potential royalty payments, associated with in-licensing and collaboration agreements. Potential future milestone payments associated with these arrangements was approximately $5.5 billion, which excludes potential royalty payments. For additional information, see Note 4. Collaborative and Other Licensing Arrangements.
- Milestone payments related with collaboration agreements that become payable only if the Company chooses to exercise one or more of its options and potential contingent payments associated with R&D costs that may be funded by collaboration partners in the future.
- An unfunded commitment of $48.9 million as a limited partner in multiple investment companies, in which the timing of future payments is uncertain.

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 U.S. dollar. As such, the consolidated financial results are subject to fluctuations in exchange rates, particularly in the Euro, Swiss franc, Japanese yen and Pound sterling against the U.S. dollar.

Accumulated foreign currency translation differences of $1,279.6 million are reported within Accumulated other comprehensive income as of December 31, 2017. Foreign exchange losses for the year ended December 31, 2017 of $97.3 million are reported in the Consolidated Statements of Operations.

As of December 31, 2017, the Company had outstanding foreign exchange swap and forward contracts that manage the currency risk associated with intercompany transactions. As of December 31, 2017 the fair value of these contracts was a net asset of $11.4 million. For the year ended December 31, 2017, net gains on foreign exchange swaps and forwards of $93.6 million are reported in the Consolidated Statements of Operations.

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 exposed to the risk that its earnings and cash flows could be adversely impacted by fluctuations in benchmark interest rates relating to its debt obligations on which interest is set at floating rates. The Company's policy is to manage this risk to an acceptable level. The Company is principally exposed to interest rate risk on any borrowings under the Company's various debt facilities and on part of the senior notes assumed in connection with the acquisition of Baxalta. Interest on each of these debt obligations is set at floating rates, to the extent utilized. Shire's exposure under these facilities is to changes in U.S. dollar interest rates. For details refer to Note 15, Financial Instruments, to the consolidated financial statements.

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. 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. For the year ended December 31, 2017, the average interest rate received on cash and liquid investments was less than 1.0% per annum. These cash and liquid investments were primarily invested in U.S. dollar term deposits with banks and money market and liquidity funds or held as cash on account.

As of December 31, 2017, Shire estimates that a hypothetical increase and decrease of 100 basis points in interest rates would increase and decrease net interest costs on borrowings by approximately $30.0 million during 2018, and decrease and increase the fair value of long term interest rate sensitive instruments by approximately $870.7 million and $956.4 million, respectively, during the same period.

Foreign exchange risk

The Company operates in numerous countries and as a consequence has foreign exchange exposure. The main operating currencies of the Company are the U.S. dollar, Pounds sterling, Swiss franc, Canadian dollar,

Japanese yen 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 (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 Company has not elected hedge accounting for these transactions. Cash flows from derivative instruments are presented within net cash provided by operating activities in the Consolidated Statements of Cash Flows, unless the derivative instruments are economically hedging specific investing or financing activities.

Translational foreign exchange exposure arises on the translation into U.S. dollars of the financial statements of non-U.S. dollar functional subsidiaries. For details refer to Note 16, Financial Instruments, to the consolidated financial statements.

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 U.S. dollar, (assuming a hypothetical 10% strengthening of the U.S. dollar against each of the aforementioned currencies in the year ended December 31, 2017):

	Reduction in revenues $'M	Reduction in net income $'M
Euro	(221.3)	(38.7)
Pound sterling	(31.0)	(7.5)
Swiss franc	(8.3)	(2.1)

A 10% weakening of the U.S. dollar against the aforementioned currencies would have an equal and opposite effect.

For more detail of foreign exchange forward contracts, refer to Note 16, Financial Instruments, to the consolidated financial statements.

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 or held on account. The money market and liquidity funds where 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 Shire's Board of Directors and exposure against these limits is monitored by the Company's corporate treasury function. The counterparties to these derivatives contracts are major international financial institutions.

The Company's revenues from Product sales in the U.S. are mainly governed by agreements with major pharmaceutical wholesalers and relationships with other pharmaceutical distributors and retail pharmacy chains. For the year ended December 31, 2017, there were three customers in the U.S. that accounted for 26% of the Company's Product sales. 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 U.S. 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 U.S., specifically, Argentina, Brazil, Greece, Italy, Portugal and Spain, the Company is experiencing delays in the remittance of receivables due from government-owned or government- supported healthcare providers. Of those, the only significant accounts receivable as of December 31, 2017 is $91.5 million from Brazil.

The Company will continue to evaluate all its accounts receivable for potential collection risks and has made provision for amounts where collection is considered to be doubtful. Any such loss could have an adverse effect on the Company's financial condition and results of operations. The Company does not consider it is currently exposed to significant credit risk outside of the countries listed above.

Strategic report
The Strategic report comprises pages 2 to 55 of this Annual Report.

Approved by the Board of Directors and signed on its behalf by:

Flemming Ornskov, MD, MPH

Chief Executive Officer

February 16, 2018

4. Principal risks and uncertainties (Pages 18 – 21 2017 Annual Report)

Risk management
As a highly regulated biopharmaceutical company focused on serving people with rare diseases, Shire has implemented policies, processes and procedures intended to manage risk and ensure appropriate and lawful conduct in the countries in which the Company operates. Successful risk management is of benefit to shareholders and other stakeholders alike. Shire's risk management strategy is to identify, assess, manage, and monitor significant risks that it faces. Despite this, no risk management strategy can provide absolute assurance against loss or unfavorable results.

Stakeholders in risk management, which is overseen by the Board of Directors and designed to enable the effective identification, assessment, management, and monitoring of the Group's risks, are detailed below.

Board of Directors
The Board of Directors is responsible for ensuring the development and maintenance of sound systems of risk management and internal control. In fulfilling this responsibility, the Board oversees Enterprise Risk Management (ERM), determines the Company's risk appetite, and ensures that an appropriate risk culture is embedded throughout the Company. The Board also interacts with key risk and internal control stakeholders on a frequent basis, enabling it to monitor and review the Company's principal risks and the effectiveness of its risk management and internal control systems. During the past year the Board conducted a robust assessment of the principal risks facing the Company, including those that could threaten its business model, future performance, solvency, or liquidity.

Audit, Compliance & Risk Committee The Audit, Compliance & Risk Committee supports the Board by overseeing and reviewing risk management, compliance, and internal control programs through its interaction with key stakeholders and periodic updates from management. The Committee reviews and monitors the principal risks facing the Company, with each risk assessed on the likelihood of materialization, potential financial and non-financial impacts, and overall risk mitigation effectiveness.

Executive Committee
The Executive Committee oversees the implementation and operation of risk management and internal control systems across the Company. The Committee reviews and monitors principal risks identified during the enterprise risk assessment process, before they are presented to the Audit, Compliance & Risk Committee. Committee members also receive regular risk updates from functional and business unit stakeholders. Along with both the Chief Compliance and Risk Officer and the Head of Internal Audit, Committee members are also responsible for escalating matters of risk management and internal control to the Audit, Compliance & Risk Committee and/or the Board of Directors, as appropriate.

Chief Compliance and Risk Officer
The Chief Compliance and Risk Officer leads the Global Compliance and Risk Management Department, and is responsible for overseeing compliance and risk management systems and programs, including ERM across the Company, and providing the Executive Committee, the Audit, Compliance & Risk Committee, and the Board with updates on risk management and compliance.

Global Compliance and Risk Management Department
The Global Compliance and Risk Management Department, led by the Chief Compliance and Risk Officer, is made up of compliance, assurance, monitoring, privacy, and risk management competencies. It is responsible for supporting the development, implementation, and maintenance of relevant risk management and compliance systems and programs across the Company. This is achieved through governance, policy, and procedures; awareness, training, and communications; as well as, audits, monitoring, and investigations. These activities provide for risk identification, assessment, management, and monitoring, as well as the

escalation of relevant matters to the Executive Committee, Audit, Compliance & Risk Committee, and the Board of Directors as appropriate.

Enterprise Risk Management Team
The ERM Team, led by the Chief Compliance and Risk Officer, includes the Head of Global Risk and Compliance Assurance, and the Head of Risk Management and Business Continuity, and is supported by external consultants as appropriate. The Team is charged with implementing and operating the ERM system. This consists of maintaining the enterprise risk universe and risk assessment methodology, identifying functional and executive risk owners, facilitating the enterprise risk assessment process, providing risk training and awareness to stakeholders across the Company, assisting with risk reporting, and supporting the Executive Committee and Audit, Compliance & Risk Committee as appropriate.

Internal Audit
Internal Audit provides independent assurance to the Audit, Compliance & Risk Committee that Shire's risk management, governance, and internal control processes are designed and operating effectively.

Business units, corporate functions, and franchises
Business units, corporate functions, and franchises participate in the enterprise risk assessment process by identifying and assessing their relevant risks. They are responsible for managing their risks; implementing controls, and monitoring, escalating, and reporting risk.

Global Issues and Crisis Management
Shire operates a Global Issues and Crisis Management framework, which assists in planning for, and responding to, disruptive events that could potentially jeopardize the Company's reputation and business operations, The guiding principles emphasize the health and safety of patients, customers, employees, and the community at large; safeguarding the Company's integrity, executing strategy, and supporting business continuity.

Principal areas of risk
The Company is subject to varying degrees of risk and uncertainty. The table below details the principal areas of risk that were identified and assessed through the Company's ERM system in 2017.

These principal areas of risk are listed in no particular order and, along with the detailed risk factors set out on pages 187 to 198 of this Annual Report (the "Risk Factors"), should be carefully considered before any investment is made in Shire. In addition, risks not presently known to the Company may also adversely affect its business. If any of these aforementioned risks were to materialize, the business, financial condition, results of operations, or prospects of the Company could be materially harmed. In such circumstances, the value of the Company's securities could decline and an investor could lose part or all of his or her investment. In addition, forward-looking statements that are contained in this Annual Report or in the Company's other reports, filings, or statements may be subject to the principal areas of risk described below and the Risk Factors.

Principal area of risk	Context	Trend[1]
Competition/exclusivity The market entry of competitor products, and increasing competition due to the loss of patent exclusivity and product genericization, could lead to reduced revenue.	The Company's products face competition in the markets in which we operate. Our products are subject to patent or regulatory expiration and emerging competition from generics or biosimilars. Shire continues to conduct relevant market research, analysis, and product risk assessments. We monitor the regulatory, legal, and industry environment to proactively anticipate and identify competitor products and plan accordingly.	Increased
Environment, health and safety (EHS) material compliance Failure to adhere to relevant laws, regulations, and policies, including Shire's Environment, Health & Safety Policy and Supplier Code of Conduct, may result in fines, business disruptions, increased operating costs, reduced revenue, interruption/postponement in research, delays of new product launches, and/or other environmental and reputational consequences.	The manufacture and distribution of the Company's products are subject to extensive laws, regulations and policies. Shire has established a cross-functional Product Stewardship Working Group that meets quarterly to review any changes to the various material compliance regulations and requirements as well as changes to the Company, products, and processes. Shire has implemented processes and supporting technology to provide a framework for oversight and governance.	Decreased
Anti-corruption/anti-bribery Failure to comply with anti-corruption/ anti-bribery laws, regulations, policies and standards governing the manufacturing, sales, and marketing of Shire products, could negatively impact the Company and/or its officers, Directors and employees, resulting in enforcement activity, civil and/or criminal liability, fines, penalties, imprisonment, business restrictions, or damage to our	We operate in numerous countries across the globe, with emergent markets having differing levels of infrastructure and legislative/regulatory frameworks. Our industry is also highly regulated. These circumstances increase our exposure to potential bribery or corruption risks. Shire has a well-defined Code of Ethics, a clear set of values, and pertinent policies/ procedures that guide our approach to Anti-Corruption/Anti-Bribery compliance, all of which are	Neutral

reputation.	available Group-wide. Shire continues to review, audit, and monitor compliance with relevant policies, procedures, systems, and controls. We deploy global anti-corruption/ anti-bribery measures including training and awareness initiatives and a third-party due diligence program.	
Cyber security In today's complex and ever-changing environment, failure to safeguard information, systems, applications, databases, and networks could result in cyber breaches and violations of privacy/consumer protection laws, business disruption, loss of intellectual property, damage to our reputation, fines, penalties and/or compromise of operations or financial condition.	The Company is dependent on the availability and integrity of our information and supporting technology platforms including systems, applications, databases, and networks. We have developed an internal cyber security capability, that provides information and assistance to the Company concerning compliance with Shire cybersecurity policies, guidance on cybersecurity standards, and recommendations on potential vulnerabilities. We provide training, awareness and monitoring of cybersecurity activities. We invest in cyber threat intelligence, security operations, and incidence response services to proactively predict, prevent, detect and respond to cyber risks.	Neutral
Data protection and privacy Failure to effectively identify, collect, and store, personal (sensitive) information in compliance with federal, state, and regional laws, contractual obligations, and policies, could result in regulator-imposed fines/ enforcement actions, damage to our reputation, and/or civil or criminal liability.	The Company is required to protect natural persons when processing their personal data, including maintaining the confidentially, integrity and availability of personal data relating to physicians, patients, employees and other individuals whose personal data is being processed by the Company. Shire continues to implement a data protection and privacy management program, including governance, policies, and procedures, to address global data protection and privacy	Neutral

	requirements. Our mitigation strategies are evolving to meet a dynamic regulatory environment. We monitor regulatory, environmental, and innovation key risk indicators, utilize data analytics, and promote employee awareness of data protection requirements.	
Pharmaceutical industry reform Failure to proactively identify and comply with industry laws and pharmaceutical regulatory changes across our value chain (including government mandated pricing), could result in fines, penalties, business disruption, reduced revenue, and/or potential exclusion from government programs.	The Company has a large portfolio of products in multiple countries across various therapeutic areas. We operate in a highly regulated industry, with the research and development, manufacturing, marketing, and sale of these products subject to regulatory oversight in various jurisdictions across the globe. The successful development, manufacturing, distribution, and sale of these products are highly uncertain due to the changing regulatory landscape. Shire continues to monitor the regulatory environment at large, and proactively plans for potential regulatory changes within our industry. We collaborate internally across global functions and business units, and externally with outside counsel and advisors, to understand potential industry reform, and its impact on our strategy, operations and performance.	Neutral
Clinical trial research, safety and efficacy Failure to demonstrate safety and efficacy in planned and ongoing clinical trials, unsuccessful clinical research, and failure to complete clinical research in a timely fashion, could result in penalties, fines, reduced revenue, and/or damage to our reputation.	The Company has a portfolio of products in various stages of research and development. The successful development of these products requires significant investment, with no guarantee that these products will receive regulatory approval. We continue to emphasize patient safety and a disciplined approach to research and development. We have governance structures in	Neutral

	place to monitor and evaluate our risk exposure in this area, and which also allow for engagement in external reviews with thought-leaders, key opinion leaders and other stakeholders. Our combined portfolio is subject to review by Shire's Quality Assurance and Control function for inspection readiness. We conduct various operational reviews of the programs ensuring targeted reviews of safety and efficacy profiles, including identification of programs where there is limited or no mechanistic, clinical or regulatory precedent.	
Intellectual property (IP) and patents Failure to obtain, maintain, enforce or defend our patents, regulatory data, or other IP may lead to the compromise of exclusivity periods and reduced revenue.	As a global biopharmaceutical company, our significant investments in research and development, and related intellectual property and patents, are extremely valuable corporate assets, and need to be protected. We face intense competition from manufacturers of branded and generic therapies who may challenge our patent protections in certain markets. We may be subject to 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 our business. Shire works with internal and external counsel to monitor threats, defend our patents and IP and prosecute violations.	Neutral
Public and private partnerships (PPP)/joint ventures (JV) Failure to effectively manage third-party alliances, geopolitical uncertainty, technology expropriation, foreign exchange exposure, payment/collections, and other risk areas could result in reduced revenue, damage to our	We operate a number of collaborative agreements and external alliances with various third-parties across the globe to expand our product portfolio and market share. Shire carefully evaluates new PPP/JV opportunities before entering into agreements.	Neutral

reputation, and/or loss of “license to operate” in certain jurisdictions.	We focus on support and alignment between our patients, healthcare professionals, and each PPP/JV. We oversee, monitor, audit, and report on these PPP/JV relationships on a regular basis. We review macroeconomic factors, manage relevant government relations, and enforce contractual terms.	
Tenders Failure to effectively execute and win major tenders in key markets could result in reduced revenue.	Procurement through tenders is standard practice in the majority of our international markets and we have developed capabilities to effectively manage tenders. We strive to shape tenders to include criteria beyond price so that the value of the therapy is recognized. We also encourage payers to partner with us on alternative, value-based models to move beyond tenders, where appropriate. We continue to manage tender relationships and monitor the tender landscape around the world, adjusting our approach as needed.	Neutral
Global drug safety tracking of patient support programs (PSP) Risk of non-compliance in safety reporting and interpretation, and incomplete safety information and documentation relative to Patient Support Programs (PSPs), could result in potential compromise of patient safety, loss of confidential data, fines, penalties, business disruptions, and/or damage to our reputation.	We manage an increasing number and variety of PSPs globally and aim to accurately and efficiently track and report their respective safety information. Shire has implemented a safety reporting policy, registration programs, personnel training, and detailed procedures for PSPs. We continue to improve and refine our system to ensure central approval and oversight of all global PSPs.	Neutral
Acquired product/company integration and strategic initiatives Failure to effectively integrate acquired products/companies, and achieve projected value from other strategic initiatives, could result in lost synergies, diversion	The integration of new products/companies and the implementation of other strategic initiatives can be complex, costly, and time-consuming. Important considerations include culture, personnel, product line synergy, operations, platform alignment,	Neutral

of management focus, time and resources, operational inefficiencies, increased costs, reduced revenue, and/or damage to our reputation.	compliance, and systems, while maintaining focus on patient safety, supply chain execution, customer service, sales, and business relationships. The Board has established a governance framework to enable the integration of Baxalta and the ongoing strategic review of the organization. These initiatives are being led by senior, experienced leaders. We continue to audit and monitor Baxalta integration activities in all functions, franchises, and business units, with the Board maintaining oversight. As of December 31, 2017, certain Baxalta integration activities, particularly in IT and Technical Operations, continue to progress, with the majority of integration work having been completed or being in the final phases of implementation. We continue to invest time, attention, and resources in the ongoing strategic review of the business.	

1 Illustrates overall risk exposure direction, based on an assessment of potential risk impact, likelihood of materialization, and risk mitigation effectiveness

5. Directors responsibilities statement (Page 113 2017 Annual Report)

The Directors are responsible for preparing the Annual Report and the financial statements in accordance with applicable law and regulations.

Company law requires the Directors to prepare financial statements for each financial year. Under that law the Directors are required to prepare the Group financial statements in accordance with accounting principles generally accepted in the United States of America. Under company law the Directors must not approve the accounts unless they are satisfied that they give a true and fair view of the state of affairs of the Group and of the profit or loss of the Group for that period.

In preparing the Group financial statements, the Directors are required to:

- properly select and apply accounting policies
- present information, including accounting policies, in a manner that provides relevant, reliable, comparable and understandable information
- provide additional disclosures when compliance with the specific requirements within accounting principles generally accepted in the United States of America are insufficient to enable users to understand the impact of particular transactions, other events and conditions on the Company's financial position and financial performance
- make an assessment of the Group's ability to continue as a going concern

The Directors are responsible for keeping proper accounting records that are sufficient to show and explain the Group's transactions and disclose with reasonable accuracy at any time the financial position of the Group and enable them to ensure that the financial statements comply with the Companies (Jersey) Law 1991. They are also responsible for safeguarding the assets of the Group and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Responsibilities statements
Each of the Directors confirms that to the best of their 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
- 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
- there is no relevant audit information of which the Company's auditor is unaware
- they have taken all the steps that they ought to have taken as Directors in order to make themselves aware of any relevant audit information and to establish that the Company's auditor is aware of that information

The Responsibilities Statements and the Directors' Report, which comprises pages 2 to 113 and pages 184 to 198 of this Annual Report, were approved by the Board of Directors and signed on its behalf by:

Flemming Ornskov, MD, MPH
Chief Executive Officer
February 16, 2018