Press Release

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2014 Annual Report – DTR 6.3.5 Disclosure

March 26, 2015 - Shire plc (LSE: SHP, NASDAQ: SHPG) (the "Company") announces that the following documents have today been posted or otherwise made available to shareholders:

- 2014 Annual Report
- Notice of the 2015 Annual General Meeting
- Form of Proxy

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

The 2014 Annual Report and Notice of the 2015 Annual General Meeting are also available on Shire's website www.shire.com.

Disclosure & Transparency Rule ("DTR") 6.3.5 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. Accordingly, the Appendix to this announcement contains a management report and the Directors' responsibility statement. It should be read in conjunction with the Company's unaudited full year results for the year ended December 31, 2014, issued on February 12, 2015, which comprises the Company's consolidated financial statements prepared under US GAAP. The Appendix together with the unaudited full year results constitute the material required by DTR 6.3.5 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 2014 Annual Report.

The information included in the Appendix is extracted from the 2014 Annual Report which was approved by the Directors on February 24, 2015. Defined terms used in the Appendix refer to terms as defined in the 2014 Annual Report unless the context otherwise requires.

Tony Guthrie
Deputy Company Secretary

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NOTES TO EDITORS

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

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

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

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

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

- Shire's products may not be a commercial success;
- product sales from ADDERALL XR and INTUNIV are subject to generic competition;
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payers in a timely manner for Shire's products may affect future revenues, financial condition and results of operations;
- Shire conducts its own manufacturing operations for certain of its products and is reliant on third party contract manufacturers to manufacture other products and to provide goods and services. Some of the Shire's products or ingredients are only available from a single approved source for manufacture. Any disruption to the supply chain for any of the Shire's products may result in Shire being unable to continue marketing or developing a product or may result in Shire being unable to do so on a commercially viable basis for some period of time;
- the manufacture of Shire's products is subject to extensive oversight by various regulatory agencies. Regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- Shire has a portfolio of products in various stages of research and development. The successful development of these products is highly uncertain and requires significant expenditures and time, and there is no guarantee that these products will receive regulatory approval;
- the actions of certain customers could affect Shire's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect Shire's revenues, financial conditions or results of operations;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to Shire's activities in the highly regulated markets in which it operates may result in significant legal costs and the payment of substantial compensation or fines;
- adverse outcomes in legal matters and other disputes, including Shire's ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on Shire's revenues, financial condition or results of operations;
- Shire faces intense competition for highly qualified personnel from other companies and organizations. Shire is undergoing a corporate reorganization and was the subject of an unsuccessful acquisition proposal and the consequent uncertainty could adversely affect Shire's ability to attract and/or retain the highly skilled personnel needed for Shire to meet its strategic objectives;
- failure to achieve Shire's strategic objectives with respect to the acquisition of NPS Pharmaceuticals Inc. ("NPS Pharma") may adversely affect Shire's financial condition and results of operations; and

other risks and uncertainties detailed from time to time in Shire's filings with the Securities and Exchange Commission, including those risks outlined on pages 30 to 37 of the Appendix to this announcement.

APPENDIX

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1. Chairman's review

At Shire we focus on people. Those that work for us, partner with us, invest in our strategy and, above all, those who depend on the medicines we make every day. Our purpose is to help people with life-altering conditions lead better lives. We ask the questions that are raised by rare and specialty diseases and pursue new possibilities through thoughtful and innovative science.

Creating exceptional value
When we do what is good, we believe good follows. Value is created not just for the patients, but for physicians, caregivers, employees, communities, payers, policymakers, and shareholders—for anyone or any institution that our global company can touch. And value, we were reminded this year, can be created—and recognized—in so many ways.

Extraordinary results
We had an eventful year in 2014. We had unprecedented financial results as you'll see in the pages to come. We completed our acquisition of ViroPharma and successfully integrated this organization, serving new patients with the product CINRYZE®, a medicine for the inflammatory condition known as Hereditary Angioedema. At the same time, we acquired two rare diseases entities—Lumena and Fibrotech. We fortified our presence in established therapies and opened doors to new ones, including Ophthalmics. We moved into our new International Operational Headquarters in Zug, Switzerland and reinvigorated our presence in Europe, Asia and Latin America. We continued to streamline operations and to put the right people into the right jobs to complement the immediate impact of mergers and acquisitions with our focus on continuing organic growth. On behalf of adults with Binge Eating Disorder, we filed in the US for a supplemental new drug application for VYVANSE® which the Food and Drug Administration ("FDA") approved on January 30, 2015 as the first and only medication for the treatment for this disorder. And, most recently, we acquired NPS Pharma bringing two exciting rare disease therapies into our product portfolio.

We were again recognized as a constituent of the FTSE4Good Index Series, a leading responsibility investment index, and also earned the distinction from Corporate Knights in their ranking of the 2015 Global 100 Most Sustainable Corporations in the World.

We accomplished all this while responding to AbbVie as it considered the role that Shire might play within its own strategic framework. We never lost sight of the company that Shire is throughout the process.

We have a strong, independent future. And we're passionate about building it.

Executing our strategy
Our plan moving forward is to emerge as a leading global biotech focused on rare diseases and other speciality conditions. To get there, we'll continue our investment in our four key strategic drivers: growth, innovation, efficiency, and people. Under the leadership of our Chief Executive Officer, Dr. Flemming Ornskov, we'll strengthen—and sustain—our platform through our focused approach to mergers and acquisitions, pipeline advancement, and cash management. We'll rely on the people who make Shire what it is—a diversified team representing many skills and broad experiences.

Outstanding contributions
Our Board of Directors made significant contributions to Shire throughout 2014—going far above and beyond expectations to render opinions and weigh choices. I have the distinct pleasure of working with Board members who bring the full complement of scientific, medical, financial, organizational and commercial insights to bear on complex opportunities.

In closing, I would like to extend my gratitude to the people of Shire who remained focused on what mattered most throughout the year—our patients. The world is a healthier place, thanks to Shire. Our people are the reason.

Susan Kilsby
Chairman

2. Chief Executive Officer's review

In 2014 we delivered record sales and profitability, and continued to strengthen our pipeline of important medicines to enable people with life altering conditions to lead better lives.

At the same time we embarked on our course with the aim of becoming a leading global biotech building on the foundation laid by our One Shire reorganization. For us, it was a year of delivering outstanding results and superior shareholder returns, setting a clear direction and gaining momentum.

Moving forward
One of the highlights of 2014 for me was the ongoing journey to transform Shire into a high-growth, more efficient, more innovative organization with a streamlined structure.

We made great progress in this regard and our success was the result of a tremendous team effort to achieve a step change in growth, profitability, cash generation and to increase the value of our pipeline.

We were also focused. A prime example was our rapid and effective integration of ViroPharma following completion of the $4 billion acquisition early in the year. We successfully accelerated the growth of CINRYZE which came to us through the ViroPharma acquisition while obtaining operational synergies and advancing the acquired pipeline.

A clear direction
Our aspiration is to become a leading global biotech delivering innovative medicines to patients with rare diseases and other specialty conditions. We are prioritizing those areas that enable us to realize our purpose and maintain leading positions in the therapeutic areas in which we compete. Our commercial excellence is driving superior top-line results and our operational efficiency is enabling us to reinvest for the future. We have highly effective business development capabilities and a robust and innovative pipeline. Simply put, we are a high-growth, highly innovative company making a real difference in people's lives.

The best of two worlds
We are uniquely placed to make a difference in people's lives due to our distinctive mix of complementary business units and capabilities. I like to think of it as a triangle with our Rare Diseases business unit at the center, where we are increasingly focusing our R&D dollars, supported by the strength of the products in our specialty business units – Neuroscience, Gastrointestinal (GI) and Internal Medicine, and our recently added Ophthalmics business unit. Through this combination we get the best of two worlds – the future long-term growth and opportunities of Rare Diseases, which was our fastest growing business (+46%[1]) in 2014, and the continued foundation and growth of our cash-generating specialty products, which contribute significantly to our Rare Disease R&D dollars.

Moreover, there is an interplay between our business units that aids our current and future innovation and growth as we adapt our existing therapeutic area expertise to a rare disease focus. We are leveraging our domain expertise in rare diseases in the development of an intrathecal delivery device for enzyme replacement therapies and this year we partnered with ArmaGen to conduct research into therapies that can cross the blood-brain barrier for Hunter syndrome. We have added to our Ophthalmics pipeline with the acquisition of the specialist biotech company BIKAM Pharmaceuticals with its preclinical asset, SHP630, in development for the potential treatment of autosomal dominant retinitis pigmentosa. In addition, through our acquisition of Lumena we have added late stage pipeline assets for rare GI/hepatic conditions, and through our acquisition of Fibrotech we added an antifibrotic agent for focal segmental glomerulosclerosis. Our most recent acquisition of NPS Pharma further builds upon our rare disease expertise with therapies for Short Bowel Syndrome ("SBS") and Hyperparathyroidism ("HPT").

Our domain expertise in rare diseases is a key differentiator for Shire. It enables us to make the most of our belief that those living with rare conditions are just as deserving of treatment as those living with more common conditions.

To build on our distinctive focus and strengths, we have four strategic drivers: growth, innovation, efficiency and people. In 2014 we hit significant milestones across all four.

Driving strong growth across all our businesses
Shire delivered growth through commercial excellence across all of our business units.

[1] Product sales growth including CINRYZE product sales acquired in January 2014 with ViroPharma.

2. Chief Executive Officer's review

In Rare Diseases, through our acquisition of ViroPharma, we added and accelerated the sales growth of CINRYZE (+30%) on a pro forma basis[2], an innovative product for the prophylactic treatment of Hereditary Angiodema (HAE) attacks. FIRAZYR®, our treatment for acute HAE attacks, also grew strongly (+55%). In our GI business, LIALDA® has become the number one prescribed 5-ASA in the US[3] in 2014 and gained an additional 5% of market share in 2014. In Neuroscience, VYVANSE sales grew 18% as more patients continued to use VYVANSE to treat their Attention Deficit Hyperactivity Disorder ("ADHD").

We grew around the world too – continuing to expand our footprint with products available in 68 countries including the launch of two products, VPRIV® and AGRYLIN®, in Japan. Sales outside of the US were $1.75 billion, an increase of 11% versus 2013.

Much of our growth outside of the US was driven by our Rare Diseases business unit, particularly in Europe and the Middle East and Africa, with these regions accounting for more than 50% of our revenues outside the US. Despite the clinical, regulatory, and commercial challenges with bringing a rare disease treatment to market, we reached eight new international markets in 2014. In addition, the launch of ELVANSE® (marketed at VYVANSE in the US) has been a success launching in four countries this year, making the product available in 12 markets outside of the US. Our international GI business unit has also shown strong growth this year, with MEZAVANT® (marketed as LIALDA in the US) net sales growing by 12% and RESOLOR® net sales increasing by 26%.

Enhancing our innovation
Through 2014 we continued to concentrate our R&D on rare diseases – the majority of our research dollars now goes into this area. Overall, we invested $840 million on a Non GAAP basis in R&D[4] and we hosted our first R&D Day showcasing the innovation in our pipeline. In 2014, we have 27 programs in clinical development, 22 of them distinct, the balance relating to new markets or new indications – the most in Shire's history.

Mixing internal and external innovation, we have built a strong rare diseases platform in several areas, including enzyme replacement, plasma-derived products, kidney and fibrotic related conditions, and now in rare gastrointestinal/hepatic diseases, with the acquisition of Lumena. This enables us to develop products that can be brought to market in new areas where there is high medical need.

Alongside our strong research capability in rare diseases, we made excellent progress in enhancing our specialty pipeline. In Neuroscience for example, we explored product candidates such as SHP465, a potential treatment for ADHD in adults. We are also entering new markets with VYVANSE, having received FDA approval on January 30, 2015 for the treatment of Binge Eating Disorder ("BED") in adults. BED affects an estimated 2.8 million[5] US patients and VYVANSE is the only FDA approved treatment for this condition.

Increasing efficiency throughout our organization
Our ongoing drive to increase efficiency gained momentum through the year as we took advantage of the significant reorganization undertaken in 2013 to streamline and simplify Shire. This was a contributor to our achievements in the year, notably our profitability, which is at an all-time high with a Non GAAP EBITDA margin of 44%[4]; our ability to generate cash, with cash generation of $2.4 billion[4] in 2014; and our sales per employee, $1.2 million. We also simplified our global footprint by establishing our US Operational Headquarters in Lexington, Massachusetts and our International Operational Headquarters in Zug, Switzerland.

Attracting, rewarding and retaining great people
Throughout 2014 we continued to hire and retain excellent talent at all levels. Our performance in a year which included the uncertainty and distraction resulting from the offer from AbbVie, is a testament to the great commitment, skills and resilience of our people, who continued to focus on their work and delivered record revenue and Non GAAP earnings. This reflects not only the dedication of our people but also the

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2 2013 CINRYZE product sales reported by ViroPharma.

3 IMS SFSS Attribute Ranking Table Study.

4 This is a Non GAAP financial measure. For reconciliation to US GAAP please see page 166 to the 2014 Annual Report.

5 Hudson JI, Hiripi E, Pope HG, Kessler RC. The prevalence and correlates of eating disorder in the National Comorbidity Survey Replication. *Biol Psychiatry*. 2007;61(3):348-358. Erratum in *Biol Psychiatry*. 2012;72(2):164 and Howden LM, et al. Age and sex composition: 2010. US Census Bureau; 2011.

strength of our patient-focused culture. I'm proud that we are increasingly recognized as a company where great people do great work to help transform lives around the world.

I am thankful for the leadership of our employees and their outstanding contributions through such a successful and eventful year. Shire has become a place that attracts people because it has the things they are looking for – low hierarchy, quick decision making, interesting products, and collaborative colleagues. As we continue to grow and pursue our goal to be a leader in biotech, Shire is a place which offers increasing opportunities and rewards for everyone involved.

I would also like to thank our investors for their continued loyalty. I am very pleased and proud of the fact that we attract investors who continue to support us on our journey.

Aiming to lead in biotech
Our four strategic drivers – growth, efficiency, innovation and people – are the engines propelling us forward on our journey to become a leading global biotech with a focus on rare diseases and specialty conditions. We have made significant progress this year but we also recognize that we are still in the early stages of our journey. We remain committed to being a lean, streamlined, innovation-driven and growth-focused company. A company that is big on ideas and value, rather than simply big. This is as much a mentality shift as an operational shift – it's about thinking differently and acting differently to get where we want to go.

10 x 20: a journey and a goal
To guide and encourage us, we have set the target of achieving $10 billion in product sales by 2020. Our 10 x 20 goal acts as our compass as we navigate excellent commercial execution across our business units, and strong innovation in our pipeline. This is the direction we have set for ourselves.

10 x 20 is a new and galvanizing target for us, but in many ways it is very much in character – we are a high performance company setting another high bar to meet and exceed. It is also as much about the journey as the goal. I like both the ambition of 10 x 20 and the adventure of getting there.

Transforming lives
Looking ahead, we will continue to build on our strong foundation and achievements. We have a clear growth strategy and a streamlined organization. We know where we are heading and, in great measure, how we are going to get there. But we also know that the year ahead will feature new opportunities and challenges that we are ready to make the most of so we continue to strive to strengthen and improve.

Through all of our change and progress one thing above all remains constant – our patients. We're on this journey for them and we are inspired to make a difference because we want to deliver innovative medicines that have the potential to transform their lives.

Flemming Ornskov, MD, MPH
Chief Executive Officer

3. Financial Review

Overview

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

The Company's purpose is to enable people with life altering conditions to lead better lives. The Company will execute on its purpose through its strategy and business model. For further details of Shire's strategy and business model, refer to pages 10 and 11 of Shire's 2014 Annual Report.

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

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

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

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

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

- 97% (2013: 96%) of total revenues are derived from product sales; and
- 3% of total revenues are derived from royalties (2013: 3%).

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

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

Markets

Shire's current portfolio of approved products focuses on the following markets: Rare Diseases, Neuroscience, and GI and Internal Medicine. Shire also has a number of marketed products for other therapeutic areas from which it generates product revenues or royalties from third parties. In 2014 Shire

derived 40% of product sales from Rare Diseases products, 31% from Neuroscience products and 29% from GI and Internal Medicine products. Shire's early stage research is primarily focused on rare diseases.

Shire has grown in part through acquisition which has brought therapeutic, geographic and pipeline growth and diversification. For example, the recent acquisitions of Lumena and Fibrotech in 2014, and Lotus Tissue Repair, Premacure and SARcode in 2013 provide potential access to new markets such as ophthalmology and neonatology. The acquisition of ViroPharma, which closed in January 2014, expanded Shire's Rare Diseases portfolio including adding CINRYZE, a leading currently marketed product for the prophylactic treatment of HAE.

In February 2015 Shire also completed the acquisition of NPS Pharma. This acquisition adds global rights to an innovative product portfolio with multiple growth catalysts, including, GATTEX/REVESTIVE with growing sales for the treatment of adults with SBS, a rare GI condition; and NATPARA/NATPAR, the only bioengineered hormone replacement therapy for use in the treatment of HPT, a rare endocrine disease, which received FDA approval in January 2015.

In 2014 Shire derived 30% (2013: 30%) of product sales from outside of the US. Shire has ongoing commercialization and late-stage development activities, which are expected to further supplement the diversification of revenues in the future, including the following:

- submission of an MAA to the EMA for once-daily, non-stimulant guanfacine extended release of INTUNIV in the EU;
- the approval of a marketing authorization by the MHLW in Japan for AGRYLIN (marketed as XAGRID in the EU) in adult essential thrombocythaemia patients; and
- the launch of VPRIV in Japan, for the improvement of symptoms of Gaucher disease, following approval of a marketing authorization on July 4, 2014 by the MHLW in Japan.

R&D

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

Evidence of the successful progression of the late stage pipeline can be seen in the granting of approval and associated launches of the Company's products over the last five years. In this time several products have received regulatory approval including: in the US, VPRIV in 2010, FIRAZYR in 2011, and VYVANSE for BED in 2015; in the EU, VPRIV in 2010 and ELVANSE/TYVENSE® in 2012; in Canada, VYVANSE in 2010.

Prior to the One Shire R&D reorganization, the Company's management reviewed R&D expenditure by operating segment. Following the One Shire R&D reorganization, Shire's management reviews direct costs for all R&D projects by development phase.

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

Year to December 31,	**2014 $'M**	**2013 $'M**
Early stage programs	170	102
Late stage programs	253	327
Currently marketed products	143	179
Total	566	608

In addition to the above, the Company recorded R&D employee costs of $270 million in 2014 (2013: $282 million) and other indirect R&D costs of $232 million (2013: $43 million), comprising depreciation and impairment charges.

3. Financial Review

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, and are generally able to sell a generic version of the Company's products at a much lower price.

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

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

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

Shire is engaged in various legal proceedings with generic manufacturers with respect to its VYVANSE and LIALDA patents. For more detail of current patent litigation, see Note 19, "Commitments and Contingencies, 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 which offer a strategic fit and have the potential to deliver demonstrable value to all of the Company's stakeholders.

Recent mergers or acquisitions

In February 2015 Shire completed the acquisition of NPS Pharma. This acquisition adds global rights to an innovative product portfolio with multiple growth catalysts, including, GATTEX/REVESTIVE with growing sales for the treatment of adults with SBS, a rare GI condition; and NATPARA/NATPAR, following its US approval on January 23, 2015, the only bioengineered hormone replacement therapy for use in the treatment of HPT, a rare endocrine disease.

In February 2015 Shire also acquired Meritage Pharma, Inc ("Meritage"). This acquisition provides Shire with worldwide rights to Meritage's Phase 3-ready compound Oral Budesonide Suspension ("OBS") for the potential treatment of adolescents and adults with eosinophilic esophagitis ("EoE"), a rare, chronic inflammatory GI disease.

In 2014, Shire acquired:

- ViroPharma which added a leading marketed product for the prophylactic treatment of HAE, CINRYZE, as well as a number of other marketed products and a pipeline of product candidates in the rare disease area;
- Lumena which added global rights to two late stage pipeline assets, SHP625 (formerly LUM001), in Phase 2 clinical development with four potential orphan indications; and SHP626 (formerly LUM002), ready to enter a Phase 1b multiple dose trial in the first half of 2015;
- Fibrotech which added global rights to SHP627 (formerly FT011) in Phase 1b, a new class of oral drug with a novel mechanism of action which has the potential to address both the inflammatory and fibrotic components of disease processes. In addition Shire has acquired Fibrotech's library of novel molecules including SHP628 (formerly FT061), which is in preclinical development; and
- BIKAM which added global rights to SHP630 (formerly BIK-406) in preclinical development, for the potential treatment of autosomal dominant retinitis pigmentosa (adRP).

3. Financial Review

In 2013, Shire acquired:

- SARcode which added SHP606 to the Shire portfolio (SHP606 is currently in Phase 3 development for the treatment of DED).
- Premacure which added SHP607 to the Shire portfolio (SHP607 is currently in Phase 3 for the prevention of ROP).
- Lotus Tissue Repair which added global rights to a protein replacement therapy in preclinical development, for the treatment of Dystrophic Epidermolysis Bullosa ("DEB").

Collaboration and licensing activity

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

- A worldwide licensing and collaboration agreement with ArmaGen in 2014 to develop and commercialize AGT-182, an investigational enzyme replacement therapy for the potential treatment of both the central nervous system and somatic manifestations in patients with Hunter syndrome;
- A collaboration and license agreement with Sangamo to develop therapeutics for hemophilia and other monogenic diseases based on Sangamo's ZFP technology in 2012; and
- An agreement with Shionogi in 2012 to co-develop and co-commercialize VYVANSE and INTUNIV in Japan.

Organization and structure

In 2013 the Company integrated its operations into a simplified One Shire organization in order to drive future growth and innovation. Shire now comprises a single operating and reportable segment. For further details see Note 25 "Segment reporting" to the consolidated financial statements. As part of the One Shire reorganization, the Company undertook a review of all of its pipeline programs and identified those projects that fit with the Company's new strategic direction and have an acceptable likelihood of success. Following that review and overall streamlining of the R&D organization, several clinical and preclinical projects were discontinued which resulted in the elimination of a significant number of R&D roles and functional roles that support R&D in Basingstoke, and some positions were re-located.

In addition the Company also relocated its international commercial hub from Nyon, Switzerland to Zug, Switzerland in 2013. All Nyon-based employees were affected by the move to Zug. Shire is now operating from its new Zug office and is providing employees with a reasonable period of time to manage their relocations.

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

For further details see Note 6 "Reorganization costs" to the consolidated financial statements.

On October 22, 2013 Shire discontinued the construction of its new manufacturing facility in San Diego. Subsequently on January 16, 2014, the Company sold and transferred certain of the assets relating to the manufacturing, marketing, sale and distribution of DERMAGRAFT to Organogenesis Inc. For further information, see Note 10 "Results of discontinued operations and assets held for sale" to the consolidated financial statements.

3. Financial Review

Results of operations for the years to December 31, 2014 and 2013

Financial highlights for the year to December 31, 2014 are as follows:

- Product sales grew strongly in 2014, up 23% to $5,830 million (2013: $4,757 million). Product sales in 2014 included $538 million for products acquired with ViroPharma, primarily $503 million from CINRYZE. The inclusion of ViroPharma contributed 12 percentage points to reported product sales growth in the year. Excluding products acquired with ViroPharma, product sales were up 11%. This growth was driven by VYVANSE (up 18% to $1,449 million), LIALDA/ MEZAVANT (up 20% to $634 million), ELAPRASE (up 9% to $593 million), REPLAGAL (up 7% to $500 million), VPRIV (up 7% to $367 million), and FIRAZYR (up 55% to $364 million). The strengthening of the US dollar during the fourth quarter of 2014 negatively affected the growth in product sales for a number of the Company's products, notably ELAPRASE, REPLAGAL and VPRIV. The US dollar has remained strong during the early part of 2015 and exchange rates as at January 31, 2015 were $1.13:€1.00 and $1.51:£1.00 (average exchange rates for the year to December 31, 2014 were $1.33:€1.00 and $1.65:£1.00). If exchange rates remain at these levels throughout 2015, or if the US dollar strengthens further against the Euro and the Pound Sterling, the Company's product sales growth in 2015 will be adversely impacted, particularly for ELAPRASE, REPLAGAL and VPRIV.
- Total revenues were up 22% to $6,022 million (2013: $4,934 million), due to the Company's strong product sales growth and higher royalties and other revenues (up 8%). The higher royalty income included $22 million of INTUNIV royalties following generic entry in December and other revenues included the receipt of a $13 million milestone relating to FOSRENOL.
- Operating income from continuing operations in 2014 was down 2% to $1,698 million (2013: $1,734 million). Operating income from continuing operations includes $190 million of intangible asset impairment charges (2013: $20 million), integration and acquisition costs of $159 million (2013: a net credit of $134 million), One Shire reorganization costs of $181 million (2013: $88 million), and costs associated with AbbVie's terminated offer for Shire of $96 million (2013: $nil). Excluding these items, operating income grew strongly in 2014, up 36%, due to higher total revenues (up 22%) and only a 9% increase in combined R&D and SG&A, demonstrating the Company's focus on delivering efficient growth.
- Diluted earnings per Ordinary Share from continuing operations increased 125% to $5.52 (2013: $2.45) primarily due to the receipt of a $1,635 million break fee in relation to AbbVie's terminated offer for Shire and a lower effective tax rate of 2% (2013: 16%), which was partially offset by the lower operating income.

Total revenues

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

Year to December 31,	2014	2013	Change
	$'M	$'M	%
Product sales	5,830.4	4,757.5	+23%
Royalties	160.8	153.7	+5%
Other revenues	30.9	23.1	+34%
Total	6,022.1	4,934.3	+22%

3. Financial Review

Product sales[1]

	Year to December 31, 2014 $'M	Year to December 31, 2013 $'M	Product sales growth %	Non-GAAP CER growth[5] %	US prescription growth[2] %	Exit market share[2] %
Net product sales:						
VYVANSE	1,449.0	1,227.8	+18	+18	+4	16
LIALDA/MEZAVANT	633.8	528.9	+20	+20	+25	33
ELAPRASE	592.8	545.6	+9	+11	n/a[3]	n/a[3]
CINRYZE	503.0	-	n/a	n/a	n/a[3]	n/a[3]
REPLAGAL	500.4	467.9	+7	+10	n/a[4]	n/a[4]
ADDERALL XR	383.2	375.4	+2	+3	+7	5
VPRIV	366.7	342.7	+7	+8	n/a[3]	n/a[3]
FIRAZYR	364.2	234.8	+55	+55	n/a[3]	n/a[3]
INTUNIV	327.2	334.9	-2	-2	-3	2
PENTASA	289.7	280.6	+3	+3	-4	13
FOSRENOL	183.0	183.4	-	-1	-8	4
XAGRID	108.5	99.4	+9	+6	n/a[3]	n/a[3]
Other product sales	128.9	136.1	-5	-4	n/a	n/a
Total product sales	5,830.4	4,757.5	+23	+23		

(1) Product sales from continuing operations, including ViroPharma acquired on January 24, 2014, and excluding DERMAGRAFT which has been treated as discontinued operations following divestment on January 17, 2014.

(2) Data provided by IMS Health National Prescription Audit ("IMS NPA"). Exit market share represents the average US market share in the month ended December 31, 2014.

(3) IMS NPA Data not available.

(4) Not sold in the US in the year to December 31, 2014.

(5) The Company's management analyzes product sales and revenue growth for certain products sold in markets outside of the US on a constant exchange rate ("CER") basis, so that product sales and revenue growth can be considered excluding movements in foreign exchange rates. Product sales and revenue growth on a CER basis is a Non-GAAP financial measure ("Non-GAAP CER"), computed by comparing 2014 product sales and revenues restated using 2013 average foreign exchange rates to 2013 actual product sales and revenues. This Non-GAAP financial measure is used by Shire's management, and is considered to provide useful information to investors about the Company's results of operations, because it facilitates an evaluation of the Company's year on year performance on a comparable basis. Average exchange rates for the year to December 31, 2014 were $1.65:£1.00 and $1.33:€1.00 (2013: $1.56:£1.00 and $1.33:€1.00).

3. Financial Review

VYVANSE – ADHD

VYVANSE product sales grew strongly (up 18%) in 2014 primarily due to the benefit of price increases and to a lesser extent higher US prescription demand and growth in ex-US product sales. This growth was partially offset by a lower level of stocking in 2014 as compared to 2013.

Litigation proceedings regarding VYVANSE are ongoing. Further information about this litigation can be found in Note 19, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements.

LIALDA/MEZAVANT – Ulcerative colitis

The 20% growth in product sales for LIALDA/MEZAVANT in 2014 was primarily driven by higher prescription demand (up 25%) and to a lesser extent a price increase[6] taken at the beginning of 2014. The growth was partially offset by a lower level of stocking and higher sales deductions as a percentage of sales in 2014 as compared to 2013.

Litigation proceedings regarding LIALDA are ongoing. Further information about this litigation can be found in Note 19, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements.

ELAPRASE – Hunter syndrome

ELAPRASE sales growth was up 9% (up 11% on a Non GAAP CER basis), driven by continued growth in the number of treated patients, especially in emerging markets. Sales growth was negatively affected by foreign exchange.

CINRYZE – for the prophylactic treatment of HAE

Shire acquired CINRYZE through its acquisition of ViroPharma on January 24, 2014. CINRYZE sales were $503 million in 2014, growing 30% on a pro forma basis on 2013 primarily driven by more patients on therapy and to a lesser extent the impact of a price increase[7] in the US and an increase in channel inventory.

REPLAGAL – Fabry disease

REPLAGAL sales were up 7% compared to 2013 (up 10% on a Non GAAP CER basis), driven primarily by higher unit sales as the Company continues to see an increase in the number of patients on therapy, with good growth in emerging markets and to a lesser extent in Europe. The benefit of the higher unit sales was partially offset by foreign exchange.

ADDERALL XR – ADHD

ADDERALL XR product sales were up 2% in 2014, as a result of higher prescription demand, partially offset by lower stocking in 2014 compared to 2013.

Litigation proceedings regarding ADDERALL XR are ongoing. Further information about this litigation and the Impax settlement, can be found in Note 19, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements.

VPRIV – Gaucher disease

VPRIV sales were up 7% (up 8% on a Non GAAP CER basis), driven by a strong performance in the EU and US as we continue to add naïve patients and gain patients switching from other therapies. Sales growth was also negatively impacted by foreign exchange.

FIRAZYR – Hereditary Angioedema

FIRAZYR sales growth was up 55% compared to 2013, driven by a higher number of patients on therapy and the effect of a price increase[6] in the US market.

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[6] The actual net effect of price increases on current period net sales compared to the comparative period is difficult to quantify due to the various managed care rebates, Medicaid discounts, other discount programs in which the Company participates and fee for service agreements with wholesalers customers.

[7] 2013 CINRYZE sales were recorded by ViroPharma prior to acquisition of ViroPharma by Shire.

3. Financial Review

INTUNIV – ADHD

INTUNIV product sales were down 2% compared to 2013, reflecting the impact of generic competition from December 2014, which resulted in lower prescription demand, significantly higher sales deductions as a percentage of product sales and destocking as compared to a slight level of stocking in 2013. This was partially offset by price increases taken in 2014. The impact of generic competition saw INTUNIV market share fall to 2.3% at the end of 2014 from 4.6% at the beginning of the year.

Further information about litigation proceedings regarding INTUNIV can be found in Note 19, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements.

PENTASA – Ulcerative Colitis

PENTASA product sales were up 3% as the benefit of price increases[8] was partially offset by higher sales deductions and a lower prescription demand in 2014 compared to 2013.

Royalties

	Year to December 31, 2014 $'M	Year to December 31, 2013 $'M	Change %
FOSRENOL	51.4	48.1	7%
3TC and ZEFFIX	33.9	46.7	-27%
ADDERALL XR	28.9	27.6	5%
INTUNIV	22.0	-	n/a
Other	24.6	31.3	-21%
Total	160.8	153.7	5%

Shire has received royalty income from Actavis following INTUNIV generic competition from December 2014. Royalty income is based on 25% of Actavis' gross profits from INTUNIV sales.

Cost of product sales from continuing operations

Cost of product sales increased to $979.3 million for the year to December 31, 2014 (17% of product sales), up from $670.8 million in the corresponding period in 2013 (14% of product sales). Cost of product sales as a percentage of product sales was three percentage points higher compared to the same period in 2013. In the year to December 31, 2014 Cost of product sales was impacted by loss and expiry provisions, the inclusion of lower margin CINRYZE acquired with ViroPharma and charges of $91.9 million on the unwind of the fair value adjustment on acquired ViroPharma inventories.

For the year to December 31, 2014 cost of product sales included depreciation of $57.1 million (2013: $37.5 million).

R&D from continuing operations

[8] The actual net effect of price increases on current period net sales compared to the comparative period is difficult to quantify due to the various managed care rebates, Medicaid discounts, other discount programs in which the Company participates and fee for service agreements with wholesalers customers.

3. Financial Review

R&D expenditure increased to $1,067.5 million for the year to December 31, 2014 (18% of product sales), compared to $933.4 million in the corresponding period in 2013 (20% of product sales). R&D expenditure in 2014 includes impairment charges of $190.3 million, primarily relating to the SHP602 IPR&D intangible asset of $166.0 million, following the current Phase 2 trial being placed on clinical hold and $22.0 million relating to the SHP613 IPR&D intangible asset, following the decision to discontinue further development based on portfolio prioritization as well as unexpected challenges and complexities with the development program. Also included in 2014 R&D expenditure is a payment of $12.5 million in respect of in-licensed and acquired products. In 2013 R&D expenditure included impairment charges of $19.9 million related to IPR&D intangible assets acquired with Movetis N.V. Excluding these costs , R&D expenditure in the year to December 31, 2014 decreased by 5% or by $49 million, due to the completion/termination of several large Phase 3 programs which were ongoing during 2013, including new uses for LDX, the effect of portfolio prioritization decisions taken during 2013 and lower overheads due to the One Shire reorganization, partially offset by the inclusion of programs acquired with ViroPharma and Lumena, and increased spend on the SHP607 (prevention of ROP), SHP608 (DEB) and SHP606 (DED) programs.

R&D in the year to December 31, 2014 included depreciation of $24.5 million (2013: $23.3 million).

SG&A from continuing operations

SG&A expenditure increased to $2,025.8 million for the year to December 31, 2014 from $1,651.3 million, due to the inclusion of ViroPharma SG&A costs from January 24, 2014, higher intangible asset amortization, costs incurred in connection with AbbVie's terminated offer for Shire and commercial spending in advance of anticipated product launches for certain products, which offset lower overheads following the One Shire reorganization. SG&A as a proportion of product sales remained constant at 35% of product sales for the year to December 31, 2014 compared with 35% of product sales in the corresponding period in 2013, as the Company continues to see benefits from the One Shire reorganization and the focus on operational discipline in the year to December 31, 2014.

For the year to December 31, 2014 SG&A included depreciation of $81.9 million (2013: $66.8 million) and amortization of $243.8 million (2013: $152.0 million).

Gain on sale of product rights from continuing operations

For the year to December 31, 2014 Shire recorded a net gain on sale of product rights of $88.2 million (2013: $15.9 million) following the divestment of CALCICHEW, VANCOCIN, ESTRACE® rights also included the loss on re-measurement of the contingent consideration receivable relating to the divestment of DAYTRANA®.

Reorganization costs from continuing operations

For the year to December 31, 2014 Shire recorded reorganization costs of $180.9 million (2013: $88.2 million) comprising costs relating to the One Shire reorganization, which included involuntary termination benefits and other termination costs. Amounts recorded in 2014 also include certain costs associated with moving more than 500 positions from Chesterbrook to Lexington, which will be effected over 2015 and 2016.

Integration and acquisition costs from continuing operations

For the year to December 31, 2014 Shire recorded integration and acquisition costs of $158.8 million, comprising acquisition and integration costs of $144.1 million, primarily related to ViroPharma, and a $14.7 million charge relating to the change in fair value of contingent consideration liabilities.

In 2013 Shire recorded a net credit of $134.1 million in integration and acquisition costs primarily related to the change in fair values of contingent consideration liabilities offset by the costs of integrating SARcode, and Lotus Tissue Repair Inc..

Interest expense from continuing operations

For the year to December 31, 2014 Shire incurred interest expense of $30.8 million (2013: $38.1 million). Interest expense in 2014 principally relates to interest and financing costs incurred on facilities drawn down in respect of the acquisition of ViroPharma.

Receipt of Break Fee

On July 18, 2014, the Boards of AbbVie and Shire announced that they had agreed the terms of a recommended combination of Shire with AbbVie, subject to a number of conditions including approval by shareholders and regulators. On the same date Shire and AbbVie entered into a co- operation agreement in connection with the recommended combination. On October 16, 2014, the Board of AbbVie confirmed that it

had withdrawn its recommendation of its offer for Shire as a result of the anticipated impact of a US Treasury Notice on the benefits that AbbVie expected from its offer. As AbbVie's offer was conditional on the approval of its stockholders, and given their Board's decision to change its recommendation and to advise AbbVie's stockholders to vote against the offer, there was no realistic prospect of satisfying this condition. Accordingly, Shire's Board agreed with AbbVie to terminate the cooperation agreement on October 20, 2014. The Company entered into a termination agreement with AbbVie, pursuant to which AbbVie paid the break fee due under the cooperation agreement of approximately $1,635.4 million. The Company has obtained advice that the break fee should not be taxable in Ireland. The Company has therefore concluded that no tax liability should arise and has not recognized a tax charge in the income statement in the current accounting period. However, this has not been agreed with the tax authorities.

Taxation from continuing operations

The effective tax rate on income from continuing operations was 2% (2013: 16%). The effective rate of tax on income from continuing operations is lower than 2013 primarily due to the receipt of the break fee from AbbVie and recognition of a net credit to income taxes of $235 million, following the settlement of certain tax positions with the Canadian revenue authorities in 2014. The accounting treatment for tax purposes of the Break Fee is outlined in the immediately preceding paragraph.

Excluding the effect of these two items the effective tax rate in 2014 would have been 17%.

Discontinued operations

The gain from discontinued operations for the year to December 31, 2014 was $122.7 million net of tax (2013: loss of $754.5 million). The gain from discontinued operations includes a tax credit of $211.3 million primarily driven by a tax benefit arising following a reorganization of the former RM business undertaken in the fourth quarter of 2014, associated with the divestment of the DERMAGRAFT business in the first quarter of 2014. This gain was partially offset by costs associated with the divestment of the DERMAGRAFT business, including a loss on re-measurement of contingent consideration receivable from Organogenesis to its fair value.

Results of operations for the year to December 31, 2013 and 2012

Financial highlights for the year to December 31, 2013 are as follows:

- Product sales from continuing operations in 2013 were up 12% to $4,757 million (2012: $4,253 million). The strong growth in product sales from continuing operations was driven by VYVANSE (up 19% to $1,228 million), LIALDA/MEZAVANT (up 32% to $529 million), VPRIV (up 12% to $343 million), INTUNIV (up 16% to $335 million) and FIRAZYR (up 102% to $235 million).
- Total revenues from continuing operations were up 9% to $4,934 million (2012: $4,527 million) as the growth in product sales was partially offset, as expected, by lower royalties and other revenues (down 36%).
- Operating income from continuing operations in 2013 was up 66% to $1,734 million (2012: $1,045 million), primarily due to the strong growth in product sales and an overall reduction in total operating expenses in 2013 compared to 2012 as the Company focuses on delivering efficient growth. Operating expenses in 2013 include a net credit of $159 million due to change in the fair value of contingent consideration liabilities, in particular relating to the acquisition of SARcode following the release of top-line Opus-2 data. Operating expenses in 2012 included impairment charges of $197.9 million related to RESOLOR intangible assets. Research and Development expenditure decreased by 2%. SG&A expenditure decreased by 15%.
- Diluted earnings per Ordinary Share from continuing operations increased 74% to $2.45 (2012: $1.41) due to the higher operating income from continuing operations and a lower effective tax rate of 16% (2012: 20%).

3. Financial Review

Total revenues

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

Year to December 31,	2013	2012	Change
	$'M	$'M	%
Product sales	4,757.5	4,252.9	+12%
Royalties	153.7	241.6	-36%
Other revenues	23.1	32.9	-30%
Total	4,934.3	4,527.4	+9%

Product sales

	Year to December 31, 2013 $'M	Year to December 31, 2012 $'M	Product sales growth %	Non-GAAP CER growth[4] %	US prescription growth[1] %	Exit market share[1] %
Net product sales:						
VYVANSE	1,227.8	1,029.8	+19	+19	+6	16
ELAPRASE	545.6	497.6	+10	+11	n/a[2]	n/a[2]
LIALDA/MEZAVANT	528.9	399.9	+32	+32	+18	28
REPLAGAL	467.9	497.5	-6	-4	n/a[3]	n/a[3]
ADDERALL XR	375.4	429.0	-12	-12	-9	5
VPRIV	342.7	306.6	+12	+12	n/a[2]	n/a[2]
INTUNIV	334.9	287.8	+16	+16	+8	5
PENTASA	280.6	265.8	+6	+6	-1	14
FIRAZYR	234.8	116.3	+102	+101	n/a[2]	n/a[2]
FOSRENOL	183.4	172.0	+7	+6	-18	4[3]
XAGRID	99.4	97.2	+2	+1	n/a[2]	n/a[2]
Other product sales	136.1	153.4	-11	-11	n/a	n/a
Total product sales	4,757.5	4,252.9	+12	+12		

(1) Data provided by IMS Health National Prescription Audit ("IMS NPA"). Exit market share represents the average US market share in the month ended December 31, 2013.
(2) IMS NPA Data not available.
(3) Not sold in the US in the year to December 31, 2013.
(4) Average exchange rates for the year to December 31, 2013 were $1.56:£1.00 and $1.33:€1.00 (2012: $1.59:£1.00 and $1.29:€1.00).

3. Financial Review

VYVANSE – ADHD

VYVANSE product sales grew strongly (+19%) in 2013 primarily as a result of price increases[9] as well as higher prescription demand, primarily due to growth in the US ADHD market (+6%).

Litigation proceedings regarding VYVANSE are ongoing. Further information about this litigation can be found in Note 19 to the consolidated financial statements.

ELAPRASE – Hunter syndrome

Reported ELAPRASE sales growth (+10%) was driven by an increase in the number of patients on therapy.

LIALDA/MEZAVANT – Ulcerative colitis

The growth in product sales for LIALDA/MEZAVANT (+32%) in 2013 was primarily driven by higher market share in the US, the effects of which were partially offset by higher sales deductions in 2013 as compared to 2012.

Litigation proceedings regarding LIALDA/MEZAVANT are ongoing. Further information about this litigation can be found in Note 19 to the consolidated financial statements.

REPLAGAL – Fabry disease

REPLAGAL sales were down 6% compared to 2012 (down 4% on a Non GAAP CER basis) as sales in 2013 were impacted by foreign exchange, pricing pressure (primarily in Europe) and slightly lower volumes due to the return of competition to the Fabry market.

ADDERALL XR – ADHD

ADDERALL XR product sales decreased 12% in 2013 as a result of higher sales deductions, partially offset by the effect of higher stocking in 2013 compared to 2012.

Litigation proceedings regarding ADDERALL XR are ongoing. Further information about this litigation and the Impax settlement, can be found in Note 19 to the consolidated financial statements.

VPRIV – Gaucher disease

Reported VPRIV sales growth of 12% was driven by an increase in the number of patients on therapy.

INTUNIV – ADHD

INTUNIV product sales were up 16% compared to 2012, driven by growth in US prescription demand (up 9% compared to 2012), together with price increases[9]. These positive factors were partially offset by higher sales deductions in 2013 compared to 2012.

Further information about litigation proceedings regarding INTUNIV can be found in see Note 19 to the consolidated financial statements.

PENTASA – Ulcerative Colitis

PENTASA product sales were up 6% as the benefit of price increases[9] was partially offset by higher sales deductions in 2013 as compared to 2012.

FIRAZYR – Hereditary Angioedema

FIRAZYR sales growth (+102% compared to 2012) was primarily driven by the US market, where we continue to see both good growth in new patients and increased levels of repeat usage by existing patients.

[9] The actual net effect of price increases on current period net sales compared to the comparative period is difficult to quantify due to the various managed care rebates, Medicaid discounts, other discount programs in which the Company participates and fee for service agreements with wholesalers customers.

3. Financial Review

Royalties

	Year to December 31, 2013 $'M	Year to December 31, 2012 $'M	Change %
FOSRENOL	48.1	53.3	-10%
3TC and ZEFFIX	46.7	91.6	-49%
ADDERALL XR	27.6	70.3	-61%
Other	31.3	26.4	+19%
Total	153.7	241.6	-36%

Royalties from ADDERALL XR in 2013 were significantly impacted by the lower royalty rate payable on sales of authorized generic ADDERALL XR by Impax, following the launch of a new generic version of ADDERALL XR late in the second quarter of 2012 as well as by Impax's lower market share in 2013 versus 2012.

Royalties from 3TC and ZEFFIX in 2013 were lower, as 2012 included one-time royalty income of $38 million in respect of prior periods due to resolution of a disagreement with GlaxoSmithKline and ViiV Healthcare.

Cost of product sales from continuing operations

Cost of product sales increased to $670.8 million for the year to December 31, 2013 (14% of product sales), up from $585.8 million in the corresponding period in 2012 (14% of product sales). The costs of product sales as a percentage of product sales remained broadly constant in 2013 as compared to 2012.

For the year to December 31, 2013 cost of product sales included depreciation of $37.5 million (2012: $29.0 million).

R&D from continuing operations

R&D expenditure decreased to $933.4 million for the year to December 31, 2013 (20% of product sales), compared to $953.0 million in the corresponding period in 2012 (22% of product sales). In the year to December 31, 2012 R&D included up-front payments of $13.0 million to Sangamo and $10.0 million to acquire the US rights for prucalopride (marketed in certain countries in Europe as RESOLOR) and IPR&D impairment charges in respect of RESOLOR of $71.2 million (2013: $19.9 million). Excluding these costs R&D increased by $54.7 million or 6% in the year to December 31, 2013 due to the Company's continuing investment in a number of targeted R&D programs, particularly new uses for LDX and other recently acquired assets including SHP606 (Lifitegrast), SHP607 (for the prevention of ROP) and SHP608 (for the treatment of DEB).

R&D in the year to December 31, 2013 included depreciation of $23.3 million (2012: $22.5 million).

SG&A from continuing operations

SG&A expenditure decreased to $1,651.3 million (35% of product sales) for the year to December 31, 2013 from $1,948.0 million (46% of product sales) in the corresponding period in 2012. In the year to December 31, 2012 SG&A included impairment charges of $126.7 million related to RESOLOR intangible assets and higher legal and litigation costs, including a charge of $57.5 million in relation to the agreement in principle with the US Government. Excluding these costs SG&A decreased by $43.1 million or 3% due to the Company's continuing focus on simplifying its business and delivering efficient growth.

For the year to December 31, 2013 SG&A included depreciation of $66.8 million (2012: $57.5 million) and amortization of $152.0 million (2012: $153.6 million).

3. Financial Review

Goodwill impairment charges from continuing operations

In the first quarter of 2013 Shire recorded a goodwill impairment charge of $198.9 million (2012: $nil) in relation to the former RM business unit. Following a review of future forecasts for the RM business unit, management determined in the first quarter of 2013 that future sales were expected to be lower than anticipated at the time of acquisition and consequently in accordance with US GAAP, it was determined that the goodwill attributable to the RM business unit was impaired. Following the divestment of DERMAGRAFT on January 16, 2014 the Company has reclassified $191.8 million of the impairment charge (being the portion of the RM reporting unit goodwill impairment charge that related to the DERMAGRAFT business) to discontinued operations.

Reorganization costs from continuing operations

For the year to December 31, 2013 Shire recorded reorganization costs of $88.2 million (2012: $nil) comprising costs relating to the "One Shire" reorganization ($64.6 million), which included involuntary termination benefits and other reorganization costs (of which approximately $42 million was paid in cash during 2013) as the Company transitions to a new operating structure, and the cost of closing the Company's facility at Turnhout, Belgium ($23.6 million).

Integration and acquisition costs from continuing operations

For the year to December 31, 2013 the Company recorded a net credit of $134.1 million in integration and acquisition costs (2012: $13.5 million charge). This comprised a credit of $159.1 million (2012: $9.2 million charge) relating to the change in fair values of contingent consideration liabilities, in particular relating to the acquisition of SARcode, partially offset by $25.0 million of acquisition and integration costs, primarily for the acquisition of ViroPharma and integration of SARcode and Lotus Tissue Repair. In 2012 integration and acquisition costs was primarily related to the acquisition of FerroKin.

Interest expense from continuing operations

For the year to December 31, 2013 the Company incurred interest expense of $38.1 million (2012: $38.2 million). Interest expense principally related to the coupon and amortization of issue costs on the Bonds which were fully redeemed or converted in the year, and to a lesser extent costs incurred on facilities related to the purchase of ViroPharma.

Taxation from continuing operations

The effective tax rate was 16% (2012: 20%).

The effective tax rate is lower than 2012 primarily due to the impact of changes in the fair values of contingent consideration liabilities which have no tax impact and impairment charges in 2012 which had no tax benefit and were not repeated in 2013.

Discontinued operations

The loss from discontinued operations for the year to December 31, 2013 was $754.5 million net of tax (2012: $60.3 million), which included impairment charges in respect of the assets held for sale ($636.9 million), goodwill impairment charges ($191.8 million), net losses on the discontinued DERMAGRAFT business ($252.2 million including reorganization costs) and related taxes (credits) of $326.4 million.

Financial condition at December 31, 2014 and 2013

Cash & cash equivalents

Cash and cash equivalents increased by $743.0 million to $2,982.4 million at December 31, 2014 (December 31, 2013: $2,239.4 million). Cash provided by operating activities was up by 189% to $4,229 million, due to the receipt of the $1,635 million break fee in relation to AbbVie's terminated offer for Shire, the benefit of the $417 million repayment received from the Canadian revenue authorities and the Company's continued strong cash receipts from gross product sales. In addition cash provided by financing activities in 2014 of $554.5 million primarily reflected the net proceeds from Shire's line of credit and other borrowings. These inflows were offset by the cost of acquiring ViroPharma, Lumena and Fibrotech.

Accounts receivable, net

Accounts receivable, net increased by $73.9 million to $1,035.1 million at December 31, 2014 (December 31, 2013: $961.2 million), primarily due to the increase in revenue. Days sales outstanding decreased to 43 days (December 31, 2013: 46 days).

3. Financial Review

Inventories

Inventories increased by $89.5 million to $544.8 million at December 31, 2014 (December 31, 2013: $455.3 million), primarily due to the inclusion of CINRYZE inventories following the acquisition of ViroPharma.

Goodwill

Goodwill increased by $1,850.3 million to $2,474.9 million at December 31, 2014 (December 31, 2013: $624.6 million), principally due to the acquisitions of ViroPharma, Fibrotech and Lumena.

Other intangible assets, net

Other intangible assets increased by $2,621.8 million to $4,934.4 million at December 31, 2014 (December 31, 2013: $2,312.6 million), principally due to the intangible assets acquired with ViroPharma, Lumena and Fibrotech, offset by the impairments of the SHP602 and SHP613 IPR&D assets, intangible asset amortization and the divestments of VANCOCIN, EXPUTEX and ESTRACE.

Short term borrowing

Short term borrowings increased from $nil at December 31, 2013 to $850.0 million at December 31, 2014 reflecting the utilization of a short term debt facility to part fund the acquisition of ViroPharma.

Other current liabilities

Other current liabilities increased by $143.0 million to $262.5 million at December 31, 2014 (December 31, 2013: $119.5 million) principally due to the recognition of contingent consideration liabilities in respect of the Lumena acquisition.

Non-current deferred tax liabilities

Non-current deferred tax liabilities increased by $650.0 million to $1,210.6 million at December 31, 2014 (December 31, 2013: $560.6 million), primarily due to deferred tax liabilities arising on the intangible assets acquired with ViroPharma and Lumena.

Other non-current liabilities

Other non-current liabilities increased by $148.2 million to $736.7 million at December 31, 2014 (December 31, 2013: $558.5 million) principally due to the recognition of contingent consideration payable in respect of the Lumena and Fibrotech acquisitions and changes in the fair value of contingent consideration payable in respect of prior acquisitions.

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 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; and the amount of cash generated from sales of Shire's products and royalty receipts.

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

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

Shire's balance sheet includes $2,982.4 million of cash and cash equivalents at December 31, 2014.

Shire also has a revolving credit facility of $2,100 million which matures in 2019, which was undrawn at December 31, 2014.

In connection with its acquisition of ViroPharma, on November 11, 2013 the Company also entered into a $2,600 million term loan facilities agreement with, among others, Morgan Stanley Bank International Limited (acting as lead arranger and agent) (the "2013 Facilities Agreement"). Amounts drawn under the 2013

Facilities Agreement were subsequently reduced to $850 million. At December 31, 2014 the 2013 Facilities Agreement comprises an $850 million term loan facility which matures on November 11, 2015, which was fully utilized and recorded within short term borrowings.

On January 24, 2014 ViroPharma commenced a tender offer to repurchase, at the option of each holder, any and all of ViroPharma's outstanding 2.00% Convertible Senior Notes Due 2017 (the "Convertible Notes") and notified the holders of their separate right to convert the Convertible Notes. As of December 31, 2014, Convertible Note holders had voluntarily converted approximately $205 million aggregate principal amount of the Convertible Notes for a total consideration of $551.5 million. The remaining outstanding Convertible Notes total an aggregate principal amount of $26,000.

Following the Company's announcement to acquire NPS Pharma, on January 11, 2015 the Company entered into an $850 million term loan facilities agreement which matures on January 10, 2016.

Revolving Credit Facilities Agreement

On December 12, 2014, Shire entered into a $2,100 million revolving credit facilities agreement (the "RCF") with a number of financial institutions, for which Abbey National Treasury Services PLC (trading as Santander Global Banking and Markets), Bank of America Merrill Lynch International Limited, Barclays Bank PLC, Citigroup Global Markets Limited, Lloyds Bank PLC, The Royal Bank of Scotland PLC and Sumitomo Mitsui Banking Corporation acted as mandated lead arrangers and bookrunners and DNB Bank ASA, The Bank of Tokyo-Mitsubishi UFJ, Ltd., Credit Suisse AG, London Branch, Deutsche Bank Luxembourg S.A., Goldman Sachs Bank USA, Mizuho Bank, Ltd. and Morgan Stanley Bank International Limited acted as arrangers. Shire is an original borrower under the RCF and has agreed to act as guarantor for its subsidiaries, which are also original borrowers and for any other of its subsidiaries that become additional borrowers thereunder. At December 31, 2014 the RCF was undrawn. On February 21, 2015 Shire requested the utilization of $1,300 million under the RCF to partially finance the purchase price payable in respect of Shire's acquisition of NPS Pharma (including certain related costs).

The RCF, which terminates on December 12, 2019, may be applied towards financing the general corporate purposes of Shire. The RCF incorporates a $250 million US dollar and Euro swingline facility operating as a sub-limit thereof.

The RCF became immediately available for general corporate purposes as outlined above, on satisfaction of certain customary conditions precedent including the cancellation of Shire's multicurrency term and revolving facilities agreement dated November 23, 2010 (the "2010 RCF") with a number of financial institutions, for which Abbey National Treasury Services PLC, Bank of America Merrill Lynch International Limited (formerly Banc of America Securities Limited), Barclays Bank PLC (formerly Barclays Capital), Citigroup Global Markets Limited, Lloyds Bank PLC (formerly Lloyds TSB Bank PLC) and The Royal Bank of Scotland PLC acted as lead arrangers (the facilities under which at such time were undrawn).

Interest on any loans made under the RCF will be 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 will be: LIBOR (or, in relation to any revolving loan in Euro, EURIBOR); plus 0.30% per year until delivery of the first compliance certificate required to be delivered after the date of the RCF, subject to change thereafter depending upon (i) the prevailing ratio of Net Debt to EBITDA (each as defined in the RCF) in respect of the most recently completed financial year or financial half year and (ii) the occurrence and continuation of an event of default in respect of the financial covenants or the failure to provide a compliance certificate.

Shire shall also pay (i) a commitment fee equal to 35% per year 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 the amount requested by the borrower in a utilization request (the "Base Currency Amount") of all outstanding loans up to an aggregate Base Currency Amount equal to $700 million, (b) 0.15% per year of the amount by which the aggregate Base Currency Amount of all outstanding loans exceeds $700 million but is equal to or less than $1,400 million and (c) 0.30% per year of the amount by which the aggregate Base Currency Amount of all outstanding loans exceeds $1,400 million.

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

EBITDA to Net Interest for the most recently-ended 12-month Relevant Period (each as defined in the RCF) must not be less than 4.0:1.

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

Events of default under the facilities include, among others:

(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.

Term Loan Facilities Agreement

2015 Facilities Agreement

On January 11, 2015, Shire entered into an $850 million Facility Agreement with, among others, Citi Global Markets Limited (acting as mandated lead arranger and bookrunner) (the "2015 Facility Agreement"). The 2015 Facility Agreement comprises a $850 million term loan facility. Shire has agreed to act as guarantor for any of its subsidiaries that are or become additional borrowers under the 2015 Facility Agreement.

The 2015 Facility agreement, which matures on January 10, 2016, may be used only to finance the purchase price payable in respect of Shire's acquisition of NPS Pharma (including certain related costs). The maturity date may be extended twice, at Shire's option, by six months on each occasion. On February 23, 2015 Shire requested the utilization of $850 million under the 2015 Facilities Agreement to partially finance the purchase price payable in respect of Shire's proposed acquisition of NPS Pharma (including certain related costs).

Interest on any loans made under the 2015 Facility Agreement will be 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 applicable to the 2015 Facility Agreement is LIBOR plus 0.50% per annum and increases by 0.25% per annum on six months after the date of the agreement and on each subsequent date falling at three-month intervals thereafter.

Shire shall also pay a commitment fee on the available but unutilized commitments under the 2015 Facility Agreement for the availability period applicable to each facility. With effect from first utilization, the commitment fee rate will be 35% of the applicable margin. Before first utilization, the commitment fee rate will increase in stages from 0% to 35% of the applicable margin over a period of three months.

The 2015 Facility Agreement includes customary representations and warranties, covenants and events of default, including requirements that the ratio of Net Debt to EBITDA of the Group (each as defined in the 2015 Facility Agreement) must not, at any time, exceed 3.5:1 for the Relevant Period (as defined in the 2015 Facility Agreement), except that following certain acquisitions, including the merger with NPS Pharma, Shire may elect to increase the ratio to 4.0:1 in the relevant period in which the acquisition was completed and the immediately following relevant period. In addition, for each 12-month period ending December 31 or June 30, the ratio of EBITDA of the Group to Net Interest (each as defined in the 2015 Facility Agreement) must not be less than 4.0:1.

The 2015 Facility Agreement restricts (subject to certain exceptions) Shire's ability to incur additional financial indebtedness, grant security over its assets or provide or guarantee loans. Further, any lender may require mandatory prepayment of its participation if there is a change of control of Shire. In addition, in certain circumstances, the net proceeds of certain shares, undertakings or business disposals by Shire must be applied towards the mandatory prepayment of the facility, subject to certain exceptions.

Events of default under the facility include: (i) non-payment of any amounts due under the facility, (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 and its subsidiaries, (vii) if it becomes unlawful for Shire or any of its subsidiaries that are parties to the 2015 Facility Agreement to perform their obligations or (viii) if Shire or any subsidiary of Shire which is a party to

the 2015 Facility Agreement repudiates the 2015 Facility Agreement or any other finance document, among others. The 2015 Facility Agreement is governed by English law.

2013 Facilities Agreement

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

On December 13, 2013 and at various points during the year to December 31, 2014, the Company cancelled part of the $2,600 million term loan facility. At December 31, 2014 the 2013 Facilities Agreement comprised an $850 million term loan facility which matures on November 11, 2015 and was fully utilized. All other terms and conditions remain unchanged.

The $850 million term loan facility has been used to finance the purchase price payable in respect of Shire's acquisition of ViroPharma (including certain related costs).

Interest on any loans made under the facilities will be 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 applicable to the $850 million term loan facility commenced at LIBOR plus 1.15% per annum until delivery of the compliance certificate for the year ending December 31, 2013 and is subject to change depending upon the prevailing ratio of Net Debt to EBITDA of the Group (each as defined in the 2013 Facilities Agreement), in respect of the most recently completed financial year or financial half year.

The 2013 Facilities Agreement includes customary representations and warranties, covenants and events of default, including requirements that the ratio of Net Debt to EBITDA of Shire (each as defined in the 2013 Facilities Agreement) must not, at any time, exceed 3.5:1 for the Relevant Period (as defined in the 2013 Facilities Agreement), except that following certain acquisitions, including the ViroPharma acquisition, Shire may elect to increase the ratio to 4.0:1 in the relevant period in which the acquisition was completed and the immediately following relevant period. In addition, for each 12-month period ending December 31 or June 30, the ratio of EBITDA of the Group to Net Interest (each as defined in the 2013 Facilities Agreement) must not be less than 4.0:1.

The 2013 Facilities Agreement restricts (subject to certain covenants) Shire's ability to incur additional financial indebtedness, grant security over its assets or provide or guarantee loans. Further, any lender may require mandatory prepayment of its participation if there is a change of control of Shire. In addition, in certain circumstances, the net proceeds of certain shares, undertakings or business disposals by Shire must be applied towards the mandatory prepayment of the facilities, subject to certain exceptions.

Events of default under the facilities include: (i) non-payment of any amounts due under the facilities, (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 and its subsidiaries, (vii) if it becomes unlawful for Shire or any of its subsidiaries that are parties to the 2013 Facilities Agreement to perform their obligations or (viii) if Shire or any subsidiary of Shire which is a party to the 2013 Facilities Agreement repudiates the 2013 Facilities Agreement or any other finance document, among others. The 2013 Facilities Agreement is governed by English law.

Financing

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

Shire's existing cash, the 2015 Facilities Agreement and the RCF are sufficient to finance the acquisition of NPS Pharma.

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

3. Financial Review

Sources and uses of cash

The following table provides an analysis of the Company's gross and net cash (excluding restricted cash), as at December 31, 2014 and 2013:

December 31,	2014 $'M	2013 $'M
Cash and cash equivalents[1]	2,982.4	2,239.4
Short term borrowings	(850.0)	-
Other debt	(13.7)	(8.9)
Total debt	(863.7)	(8.9)
Net cash[2]	2,118.7	2,230.5

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

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

Cash flow activity

Net cash provided by operating activities for the year to December 31, 2014 increased by $2,765.4 million or 189% to $4,228.4 million (2013: $1,463.0 million) primarily due to the receipt of the $1,635.4 million break fee in relation to AbbVie's terminated offer for Shire, the benefit of the $417 million repayment received from the Canadian revenue authorities and higher cash receipts from gross product sales, offset by payments for sales deductions, payments of acquisition and integration costs in respect of the acquisitions of ViroPharma, Lumena and Fibrotech, costs in connection with AbbVie's terminated offer for Shire and cash payments in respect of the One Shire reorganization.

Net cash provided by operating activities for the year to December 31, 2013 increased by $80.1 million or 6% to $1,463.0 million (2012: $1,382.9 million) as higher cash receipts from gross product sales were more than offset by payments made in relation to the One Shire reorganization (approximately $42 million), costs incurred on the closure of Shire's facility at Turnhout in Belgium (approximately $24 million) and the payment to settle the litigation with Impax ($48 million).

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

Net cash used in investing activities was $360.9 million in the year to December 31, 2013, principally relating to the cash paid (net of cash acquired) for the acquisitions of SARcode, Premacure and Lotus Tissue Repair and for purchases of PP&E.

Net cash provided by financing activities was $554.5 million for the year to December 31, 2014, principally due to the drawings, net of subsequent repayments, made under the facilities to partially fund the ViroPharma acquisition. In addition the Company paid cash of $551.4 million to settle the convertible debt

assumed with ViroPharma, received cash of $346.7 million upon settlement of a purchased call option acquired with ViroPharma and made dividend payments of $121.2 million.

Net cash used in financing activities was $344.6 million for the year to December 31, 2013, principally due to the purchase of shares under the share buy-back program, purchase of shares by the EBT and the dividend payment.

Outstanding letters of credit

At December 31, 2014, the Company had irrevocable standby letters of credit and guarantees with various banks totaling $46 million, providing security for the Company's performance of various obligations. These obligations are primarily in respect of the recoverability of insurance claims, lease obligations and supply commitments.

Cash requirements

At December 31, 2014 the Company's cash requirements for short and long term liabilities reflected on the Balance Sheet and other contractual obligations were as follows:

Payments due by period

	Total $'M	Less than 1 year $'M	1 – 3 years $'M	3 – 5 years $'M	More than 5 years $'M
Short-term debt obligation	850.0	850.0	-	-	-
Operating leases obligation [(i)]	221.1	49.3	51.1	28.2	92.5
Purchase obligations [(ii)]	1,110.1	729.5	217.7	153.9	-
Other long term liabilities reflected on the Balance Sheet [(iii)]	675.1	-	283.6	290.1	101.4
Total	2,847.3	1,628.8	552.4	472.2	193.9

(i) The Company leases certain land, facilities, motor vehicles and certain equipment under operating leases expiring through 2021.

(ii) Purchase obligations include agreements to purchase goods, investments or services (including clinical trials, contract manufacturing and capital equipment), including open purchase orders, that are enforceable and legally binding and that specify all significant terms. Shire expects to fund these commitments with cash flows from operating activities.

(iii) Unrecognized tax benefits and associated interest and penalties of $199.2 million are included within payments due in one to three years.

In addition to the above contractual obligations, the Company is committed to make milestone payments (principally arising from the in-licensing or acquisition of products, assets and businesses), contingent upon the occurrence of future events (and therefore payment is not yet due). At December 31, 2014, the Company is contingently committed to pay up to approximately $1.4 billion (aggregate contractual amount) in respect of potential future research and development milestone payments and up to approximately $1.2 billion (aggregate contractual amount) in respect of commercial milestones as a result of prior business combinations and in-licensing agreements. Payments under these agreements are generally due and payable only upon achievement of certain development, regulatory and commercial milestones.

From a business perspective, these payments signify that the product is successfully moving through development and is now generating or is more likely to generate cash flows from product sales. However, it is not possible to predict with reasonable certainty whether these milestones will be achieved or the timing of

their achievement. As a result, these potential payments are not included in the table of contractual obligations.

On January 11, 2015 Shire also signed a definitive agreement to acquire all of the outstanding share capital of NPS Pharma for $46 per share in cash or approximately $5.2 billion. This acquisition was completed on February 21, 2015. This cash requirement did not exist as at December 31, 2014 and therefore is not reflected in the table above.

Off-balance sheet arrangements

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

Foreign currency fluctuations

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

The accumulated foreign currency translation differences at December 31, 2014 of $136.1 million are reported within accumulated other comprehensive (loss)/income in the consolidated balance sheet and foreign exchange losses for the year to December 31, 2014 of $15.6 million are reported in the consolidated statements of income.

At December 31, 2014, the Company had outstanding swap and forward foreign exchange contracts to manage the currency risk associated with intercompany transactions. At December 31, 2014 the fair value of these contracts was a net asset of $4.8 million.

Inflation

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

Treasury policies and organization

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

Interest rate risk

The Company is exposed to interest rate risk on its $2,100 million RCF, its $850 million 2013 Facilities Agreement and its $850 million 2015 Facilities Agreement, on which interest is at floating rates, to the extent any of these facilities are utilized. At December 31, 2014 the RCF was undrawn, and the Company had fully utilized $850 million of the 2013 Facilities Agreement. Shire's exposure under its $850 million 2013 Facilities Agreement is to US Dollar interest rates.

The Company has evaluated the interest rate risk on the RCF, the 2013 Facilities Agreement and the 2015 Facilities Agreement and considers the risks associated with floating interest rates on the instruments as appropriate. A hypothetical one percentage point increase or decrease in the interest rates applicable to drawings under the 2013 Facilities Agreement at December 31, 2014 would increase or decrease interest expense by approximately $8.5 million per annum.

The Company is also exposed to interest rate risk on its restricted cash, cash and cash equivalents and on foreign exchange contracts on which interest is at floating rates. This exposure is primarily to US Dollar, Pounds Sterling, Euro and Canadian Dollar interest rates. As the Company maintains all of its cash, liquid investments and foreign exchange contracts on a short term basis for liquidity purposes, this risk is not actively managed. In the year to December 31, 2014 the average interest rate received on cash and liquid investments was less than 1% per annum. The largest proportion of these cash and liquid investments was in US dollar money market and liquidity funds.

No derivative instruments were entered into during the year to December 31, 2014 to manage interest rate exposure. The Company continues to review its interest rate risk and the policies in place to manage the risk.

3. Financial Review

Foreign exchange risk

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

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

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

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

At December 31, 2014 the Company had 56 swap and forward foreign exchange contracts outstanding to manage currency risk. The swap and forward contracts mature within 90 days. The Company did not have credit risk related contingent features or collateral linked to the derivatives. The Company has master netting agreements with a number of counterparties to these foreign exchange contracts and on the occurrence of specified events, the Company has the ability to terminate contracts and settle them with a net payment by one party to the other. The Company has elected to present derivative assets and derivative liabilities on a gross basis in the consolidated balance sheet. As at December 31, 2014 the potential effect of rights of set off associated with the foreign exchange contracts would be an offset to both assets and liabilities of $4.2 million, resulting in net derivative assets and derivative liabilities of $8.4 million and $3.6 million, respectively. Further details are included below.

Foreign exchange risk sensitivity

The following exchange rate sensitivity analysis summarises the sensitivity of the Company's reported revenues and net income to hypothetical changes in the average annual exchange rates of the Euro, Pound Sterling and Swiss Franc against the US Dollar, (assuming a hypothetical 10% strengthening of the US Dollar against each of the aforementioned currencies in the year to December 31, 2014):

	Increase/(reduction) in revenues	Increase/(reduction) in net income
	$M	$M
Euro	(73)	(46)
Pound Sterling	(16)	(5)
Swiss Franc	-	6

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

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

3. Financial Review

December 31, 2014	Principal Value of Amount Receivable $'M	Weighted Average Exchange Rate	Fair Value $'M
Swap foreign exchange contracts			
Receive USD/Pay EUR	364.7	1.24	10.5
Receive GBP/Pay USD	252.8	1.57	(2.1)
Receive USD/Pay JPY	5.5	0.01	-
Receive SEK/Pay USD	26.6	0.13	(1.3)
Receive USD/Pay MXN	11.4	0.07	0.9
Receive CAD/Pay USD[1]	407.3	0.87	(3.4)
Receive USD/Pay AUD	6.7	0.83	0.2

[1] Relates to the repayments received from the Canadian revenue authorities in 2014.

Concentration of credit risk

Financial instruments that potentially expose Shire to concentrations of credit risk consist primarily of short-term cash investments, derivative contracts and trade accounts receivable (from product sales and from third parties from which the Company receives royalties). Cash is invested in short-term money market instruments, including money market and liquidity funds and bank term deposits. The money market and liquidity funds in which Shire invests are all triple A rated by both Standard & 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 derivative instruments. The Company limits this exposure through a system of internal credit limits which vary according to ratings assigned to the counterparties by the major rating agencies. The internal credit limits are approved by the Board and exposure against these limits is monitored by the corporate treasury function. The counterparties to these derivatives contracts are major international financial institutions.

The Company's revenues from product sales in the US are mainly governed by agreements with major pharmaceutical wholesalers and relationships with other pharmaceutical distributors and retail pharmacy chains. For the year to December 31, 2014 there were three customers in the US that accounted for 47% of the Company's global product sales. However, such customers typically have significant cash resources and as such the risk from concentration of credit is considered acceptable. The Company has taken positive steps to manage any credit risk associated with these transactions and operates clearly defined credit evaluation procedures. However, an inability of one or more of these wholesalers to honor their debts to the Company could have a material adverse effect on Company's financial condition and results of operations.

A substantial portion of the Company's accounts receivable in countries outside of the United States is derived from product sales to government-owned or government-supported healthcare providers. The Company's recovery of these accounts receivable is therefore dependent upon the financial stability and creditworthiness of the relevant governments. In recent years global and national economic conditions have negatively affected the growth, creditworthiness and general economic condition of certain markets in which the Company operates. As a result, in some countries outside of US the Company is experiencing delays in the remittance of receivables due from government-owned or government-supported healthcare providers. In the year to December 31, 2014 the Company continued to receive remittances in relation to government-owned or government-supported healthcare providers, from all countries in which it operates, including receipts of $98 million and $143 million in respect of Spanish and Italian receivables, respectively.

3. Financial Review

The Company's aggregate accounts receivable, net of the allowance for doubtful accounts, in total from government-owned or government-supported healthcare providers in those territories in which the Company is experiencing the most significant delays, being Argentina, Greece, Italy, Portugal and Spain (collectively the "Relevant Countries") are as follows:

	December 31, 2014	December 31, 2013
	$'M	$'M
Total accounts receivable, net in the Relevant Countries	118	138
Total accounts receivable, net in the Relevant Countries as a percentage of total outstanding accounts receivable, net	11%	14%
Accounts receivable, net due from government-owned or government-supported healthcare providers for the Relevant Countries	77	128

Accounts receivable due from government-owned or government-supported healthcare providers in the Relevant Countries of $77 million (2013: $128 million) are split by country as follows: Greece $4 million (2013: $4 million); Italy $30 million (2013: $59 million); Portugal $11 million (2013: $14 million), Spain $15 million (2013: $39 million) and Argentina $17 million (2013: $12 million).

The Company continues to receive remittances in relation to government-owned or government-supported healthcare providers in the Relevant Countries and in the year to December 31, 2014 received $311 million in settlement of accounts receivable in the Relevant Countries - $7 million was from Greece; $143 million from Italy; $14 million from Portugal, $98 million from Spain and $49 million from Argentina.

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

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

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

4. Principal risks and uncertainties

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

Board of Directors: The Board is responsible for determining the Group's risk tolerance and for ensuring the maintenance of a sound system of internal control and risk management. In fulfilling this responsibility, the Board sets Shire's corporate risk culture; ensuring its dissemination throughout the organisation. This is achieved through interaction with key stakeholders which, in turn, enables the Board to monitor the Group's risks as well as its risk management and internal control systems; contributing to its annual review of their effectiveness. Stakeholders to the risk framework, which is overseen by the Board and designed to manage and mitigate the Group's risks, include:

> **Audit, Compliance & Risk Committee**: The Committee supports the Board by, on a biannual basis, reviewing and reporting on the principal risks faced by the Company. These risks are assessed on their likelihood of materialisation and potential impact and include those that would threaten the Company's business model, future performance, solvency or liquidity. Moreover, alongside the Board the Committee monitors and reviews the risk management and internal control systems; ensuring oversight through its interaction with functional stakeholders, through its review and challenge of key risk and control processes and through its evaluation of key strategy updates from management.

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

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

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

> **Chief Compliance and Risk Officer**: The Chief Compliance and Risk Officer is responsible for the global compliance program and for coordinating oversight of risk mitigation activity through the Enterprise Risk Management process. In addition to maintaining relationships with assurance functions outside of the Global Compliance and Risk Management Department, the Chief Compliance and Risk Officer has direct access to

the Board and the Audit, Compliance & Risk ("ACR") Committee; providing an independent mechanism of escalation, should the need arise. The Chief Compliance and Risk Officer provides twice-yearly updates to the ACR Committee in respect of risk and risk mitigation review, as well as ongoing compliance monitoring and investigation.

> **Internal Audit**: The Internal Audit function provides independent assurance to the Audit, Compliance & Risk Committee with respect to the operation of the internal control and risk management systems.

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

Risk factors
Set out below are the key risk factors associated with the business that have been identified through the Company's approach to risk management. Some of these risk factors are specific to the Company and others are more generally applicable to the pharmaceutical industry or specific markets in which the Company operates. The Company believes that these risk factors apply equally and therefore all should be carefully considered before any investment is made in Shire.

Risk factors related to the Company's business
The Company's products may not be a commercial success.
The commercial success of the Company's marketed products and other new products that the Company may launch in the future, will depend on their approval and acceptance by physicians, patients and other key decision- makers, as well as the receipt of marketing approvals in different countries, the time taken to obtain such approvals, the scope of marketing approvals as reflected in the product labels, approval of reimbursement at commercially sustainable prices in those countries where price and reimbursement is negotiated, and safety, efficacy, convenience and cost-effectiveness of the product as compared to competitive products.

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

> if the Company's products, or competitive products, are genericized;
> if the prices of the Company's products suffer forced reductions or if prices of competitor products are reduced significantly;
> if there are unanticipated adverse events experienced with the Company's products or those of a competitor's product not seen in clinical trials that impact physicians' willingness to prescribe the Company's products;
> if issues arise from clinical trials being conducted for post- marketing purposes or for registration in another country which raise questions or concerns about a product;
> if the regulatory agencies in one country act in a way that raises concerns for regulatory agencies or for prescribers or patients in another country;
> if patients, payers or physicians favor other treatments over the Company's products;
> if the Company's products are subject to more stringent government regulation than competitor products;
> if patent protection or other forms of exclusivity are lost or curtailed, or if competitors are able to successfully challenge or circumvent the Company's patents or other forms of exclusivity (see Note 19, "Commitments and Contingencies, Legal and other proceedings" to the consolidated financial statements);
> if launches of the Company's products in new markets are not successful;
> if the sizes of the patient populations for the Company's products are less than expected;
> if there are lawsuits filed against Shire, including but not limited to, product liability claims, consumer law claims, and payer or reimbursement litigation; or
> if the Company is unable to commercialize its products successfully, there may be a material adverse effect on the Company's revenues, financial condition or results of operations.

Product sales from ADDERALL XR and INTUNIV are subject to generic competition.
During 2012 the FDA clarified the regulatory pathway required for approval of generic versions of ADDERALL XR. Consequently in June 2012 and February 2013, Actavis and Teva, respectively, received approval to launch their own generic versions of ADDERALL XR. Shire currently sells authorized generic

versions of ADDERALL XR to Teva and also continues to sell the branded version of ADDERALL XR. Actavis makes and markets its own generic versions of ADDERALL XR.

In 2013, Shire settled a number of patent lawsuits in the United States against certain companies that had filed for approval of their generic versions of INTUNIV. Under the terms of the settlements, Actavis was granted a license to make and market Actavis' generic versions of INTUNIV in the United States on December 1, 2014. All other parties with whom Shire has settled will be able to enter the market with their respective ANDA-approved products after Actavis' 180 day exclusivity period has expired.

Product sales from INTUNIV have declined as a result of the December 2014 launch of Actavis' generic versions of INTUNIV and are expected to decline further following the anticipated launches of generic versions of INTUNIV by other companies after Actavis' 180 day exclusivity period expires.

Factors which could cause further or more rapid decline in ADDERALL XR and INTUNIV product sales include:

> generic or authorized generic versions of these products capture more of Shire's branded market share than expected;
> the FDA approves additional ANDAs for generic versions of these products which, if launched, further reduce branded market share or impact the amount of Shire's authorized generic product sales;
> the production of branded ADDERALL XR is disrupted by difficulties in obtaining a sufficient supply of amphetamine salts including, but not limited to, an inability to obtain sufficient quota from the DEA;
> there are changes in reimbursement policies of third-party payers; or
> there are changes to the level of sales deductions for branded ADDERALL XR or branded INTUNIV for private or public payers.

The failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payers in a timely manner for the Company's products may affect future revenues, financial condition and results of operations.
The Company's revenues are partly dependent on the level of reimbursement provided to the Company by governmental reimbursement schemes for its products. Changes to governmental policy or practices could adversely affect the Company's revenues, financial condition and results of operations. In addition, the reimbursement of treatments by health care providers, private health insurers and other organizations, such as health maintenance organizations and managed care organizations is under downward pressure and this, in turn, could adversely impact the prices at which the Company can sell its products. Factors affecting the Company's ability to obtain and maintain adequate reimbursement for its products include:

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

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

The Company conducts its own manufacturing operations for certain of its products and is reliant on third party contract manufacturers to manufacture other products and to provide goods and services. Some of the Company's products or ingredients are only available from a single approved source for manufacture. Any disruption to the supply chain for any of the Company's products may result in the Company being unable to continue marketing or developing a product or may result in the Company being unable to do so on a commercially viable basis for some period of time.
Although the Company dual-sources certain key products and/ or active ingredients, the Company currently relies on a single source for production of the final drug product for each of ADDERALL XR, CINRYZE, FIRAZYR, FOSRENOL®, INTUNIV, LIALDA and PENTASA, the Company currently relies on a single active ingredient source for each of ELAPRASE, FIRAZYR, FOSRENOL, INTUNIV and REPLAGAL and also relies

on limited third party sources to provide the donated human plasma necessary for the manufacture of CINRYZE. Following the completion of the acquisition of NPS Pharma in the first quarter of 2015, Shire has acquired GATTEX®/REVESTIVE®, which currently relies on a single active ingredient source and NATPARA®/NATPAR®, which currently relies on a single source for both production of the final drug product and supply of the active ingredient.

The Company may experience supply failures or delays beyond its control if it does not, or if any of its third party manufacturers do not, supply the Company on time with the required volumes, or supply products that do not meet regulatory requirements. Any such supply failures could lead to significant delays, increase in operating costs, lost product sales, an interruption of research activities, or the delay of new product launches, all of which could have a material adverse effect on the Company's revenues, financial condition or results of operations.

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

The manufacture of the Company's products is subject to extensive oversight by various regulatory agencies. Regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches. Pharmaceutical and device manufacturing sites must be inspected and approved by regulatory agencies such as the FDA, and similar agencies in other countries. Active ingredients, excipients and packaging materials used in the manufacturing process must be obtained from sources approved by regulatory agencies.

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

US-based manufacturers must be registered with the DEA and similar regulatory authorities in other countries if they handle controlled substances. Certain of the Company's products, including ADDERALL XR and VYVANSE, contain ingredients which are controlled substances subject to quotas managed by the DEA. As a result, the Company's procurement and production quotas may not be sufficient to meet commercial demand.

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

The failure to obtain regulatory approvals promptly or at all and/or regulatory interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, an increase in operating costs, lost product sales, an interruption of research activities, the delay of new product launches or constraints on manufacturing output, all of which could have a material adverse effect on the Company's revenues, financial condition and results of operations.

4. Principal risks and uncertainties

The Company has a portfolio of products in various stages of research and development. The successful development of these products is highly uncertain and requires significant expenditures and time, and there is no guarantee that these products will receive regulatory approval.
Products that initially appear promising in research or development may be delayed or fail to reach later stages of development as:

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

Success in preclinical and early clinical trials does not ensure that late stage clinical trials will be successful. Clinical results are frequently susceptible to varying interpretations that may delay, limit, or prevent regulatory approvals. The length of time necessary to complete clinical trials and to submit an application for marketing approval for a final decision by a regulatory authority varies significantly and may be difficult to predict. Moreover, once an application is submitted, additional data may be sought by regulators or an application may be rejected. If the Company's large-scale or late-stage clinical trials for a product are not successful, the Company will not recover its substantial investments in that product. The Company has a range of programs in late stage clinical development. For example, in Phase 3, SHP606 is being developed for the treatment of DED and SHP465 is being developed for the treatment of ADHD in adults.

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

The actions of certain customers could affect the Company's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect the Company's revenues, financial conditions or results of operations.
A considerable portion of the Company's product sales are made to major pharmaceutical wholesale distributors, as well as to large pharmacies, in both the US and Europe. In 2014, for example, 47% of the Company's product sales were attributable to three customers in the US: McKesson Corp., Cardinal Health, Inc and AmerisourceBergen Drug Corp. In the event of financial failure of any of these customers there could be a material adverse effect on the Company's revenues, financial condition or results of operations. The Company's revenues, financial condition or results of operations may also be affected by fluctuations in customer buying or distribution patterns. These fluctuations may result from seasonality, pricing, wholesaler inventory objectives, or other factors. A significant portion of the Company's revenues for certain products for treatment of rare diseases are concentrated within a small number of customers. Changes in the buying patterns of those customers may have an adverse effect on the Company's revenues, financial condition or results of operations.

Investigations or enforcement action by regulatory authorities or law enforcement agencies relating to the Company's activities in the highly regulated markets in which it operates may result in significant legal costs and the payment of substantial compensation or fines.
The Company engages in various marketing, promotional and educational activities pertaining to, as well as the sale of, pharmaceutical products and medical devices in a number of jurisdictions around the world. The promotion, marketing and sale of pharmaceutical products and medical devices is highly regulated and the operations of market participants, such as the Company, are closely supervised by regulatory authorities and law enforcement agencies, including the US Department of HHS, the FDA, the US Department of Justice,

the SEC and the DEA. These authorities and agencies and their equivalents in countries outside the US have broad authority to investigate market participants for potential violations of laws relating to the sale, marketing and promotion of pharmaceutical products and medical devices, including the False Claims Act, the Anti-Kickback Statute and the Foreign Corrupt Practices Act, among others, for alleged improper conduct, including corrupt payments to government officials, improper payments to medical professionals, off-label marketing of pharmaceutical products and medical devices, and the submission of false claims for reimbursement by the federal government. Healthcare companies may also be subject to enforcement actions or prosecution for such improper conduct. Any inquiries or investigations into the operations of, or enforcement or other regulatory action against, the Company by such authorities could result in significant defense costs, fines, penalties and injunctive or administrative remedies, distract management to the detriment of the business, result in the exclusion of certain products, or the Company, from government reimbursement programs or subject the Company to regulatory controls or government monitoring of its activities in the future. The Company is subject to certain ongoing investigations by governmental agencies. For further information, see Note 19, “Commitments and Contingencies, Legal and other proceedings” to the consolidated financial statements.

Adverse outcomes in legal matters and other disputes, including Shire’s ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on the Company’s revenues, financial condition or results of operations.
During the ordinary course of its business the Company may be involved in claims, disputes and litigation with third parties, employees, regulatory agencies, governmental authorities and other parties. The range of matters of a legal nature that might arise is extremely broad but could include, without limitation, intellectual property claims and disputes, product liability claims and disputes, regulatory litigation, contract claims and disputes, employment claims and disputes, and tax or other governmental agency audits and disputes.

Any unfavorable outcome in such matters could adversely impact the Company’s ability to develop or commercialize its products, adversely affect the profitability of existing products, subject the Company to significant defense costs, fines, penalties, audit findings and injunctive or administrative remedies, distract management to the detriment of the business, result in the exclusion of certain products, or the Company, from government reimbursement programs or subject the Company to regulatory controls or government monitoring of its activities in the future. Any such outcomes could have a material adverse effect on the Company’s revenue, financial condition or results of operations. For further information see Note 19, “Commitments and Contingencies, Legal and other proceedings” to the consolidated financial statements.

The Company faces intense competition for highly qualified personnel from other companies and organizations. The Company is undergoing a corporate reorganization and was the subject of an unsuccessful acquisition proposal and the consequent uncertainty could adversely affect the Company’s ability to attract and/or retain the highly skilled personnel needed for the Company to meet its strategic objectives.
The Company relies on recruiting and retaining highly skilled employees to meet its strategic objectives. The Company faces intense competition for highly qualified personnel and the supply of people with the requisite skills may be limited, generally or geographically. The range of skills required and the geographies in which they are required by the Company may also change over time as Shire’s business evolves. The Company’s ongoing One Shire reorganization, which aims to simplify the Company’s organizational structure and streamline operations through two principal locations, Massachusetts and Switzerland, involves changes to, and geographic relocation of, certain skilled roles. The unsuccessful proposed acquisition of the Company by AbbVie in 2014 created uncertainty in the employee population which could lead to further loss of certain skilled employees. If the Company is unable to retain key personnel or attract new personnel with the requisite skills and experience, it could adversely affect the implementation of the Company’s strategic objectives and ultimately adversely impact the Company’s revenues, financial condition or results of operations.

Failure to achieve the Company’s strategic objectives with respect to the acquisition of NPS Pharma may adversely affect the Company’s financial condition and results of operations.
On February 21, 2015, Shire completed the acquisition of NPS Pharma for a total cash consideration of approximately $5.2 billion.

The acquisition entails various risks, which, if they materialize, may adversely impact Shire’s revenues, financial condition or results of operations.

4. Principal risks and uncertainties

These risks include but are not limited to:

> failure to achieve the targeted growth and expected benefits of the acquisition if sales of NPS Pharma products, including GATTEX/REVESTIVE, are lower than anticipated;
> failure to successfully commercialize NPS Pharma's compound NATPARA/NATPAR in the US or to obtain regulatory approval in the EU;
> difficulties in integrating NPS Pharma into Shire may lead to the combined company not being able to realize the expected operating efficiencies, cost savings, revenue enhancements, synergies or other benefits in the timeframe anticipated, or at all;
> undiscovered or unanticipated risks and liabilities, including legal and compliance related liabilities, may emerge after closing the acquisition or may be higher than anticipated;
> the Company may be unable to retain key NPS Pharma personnel;
> the Company may not be able to retain the existing customers, suppliers and other business partners of NPS Pharma or attract new customers; and
> the business of NPS Pharma may be otherwise disrupted by the acquisition, including increased costs and diversion of management time and resources.

Any failure to achieve the Company's strategic objectives with respect to the NPS Pharma acquisition could result in slower growth, higher than expected costs, the recording of asset impairment charges and other actions which could adversely affect the Company's business, financial condition and results of operations.

General risk factors related to the Company and to the healthcare industry
The actions of governments, industry regulators and the economic environments in which the Company operates may adversely affect its ability to develop and profitably market its products.
The healthcare industry is heavily regulated. Changes to laws or regulations impacting the healthcare industry, in any country in which the Company conducts its business, may adversely impact the Company's revenues, financial condition or results of operations. For example, changes to the regulations relating to the exclusivity periods available for the Company's products may allow for the earlier entry of generic or biosimilar competitor products.

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

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

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

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

4. Principal risks and uncertainties

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

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

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

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

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

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

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

4. Principal risks and uncertainties

In the regular course of business, the Company is party to litigation or other proceedings relating to intellectual property rights. For details of current intellectual property litigation, see Note 19, “Commitments and Contingencies, Legal and other proceedings” to the consolidated financial statements.

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

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

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

5. Directors' responsibility statement

The following responsibility statement is repeated here solely for the purpose of complying with DTR 6.3.5. This statement relates to and is extracted from page 106 of the 2014 Annual Report.

These responsibilities are for the full 2014 Annual Report and not the extracted information presented in this announcement or otherwise.

The Directors confirm 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 Company and the undertakings included in the consolidation taken as a whole;

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

- the Annual Report and Financial Statements, taken as a whole, are fair, balanced and understandable and provide the information necessary for shareholders to assess the Group's performance, business model and strategy.

Approved by the Board and signed on its behalf by:

Dr. Flemming Ornskov
Chief Executive Officer
February 24, 2015

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

ADDERALL XR® (mixed salts of a single entity amphetamine)
AGRYLIN® (anagrelide hydrochloride)
BUCCOLAM® (midazolam hydrochloride oromucosal solution)
CALCICHEW® (trademark of Takeda Nycomed AS)
CARBATROL® (carbamazepine extended-release capsules)
CINRYZE® (C1 esterase inhibitor [human])
CONCERTA® (trademark of Alza Corporation)
DAYTRANA® (trademark of Noven Pharmaceutical Inc.)
DERMAGRAFT® (trademark of Organogenesis Inc.)
ELAPRASE® (idursulfase)
ELVANSE® (lisdexamfetamine dimesylate)
ESTRACE® (trademark of Trimel Pharmaceuticals Inc.)
EXPUTEX® (trademark of Phoenix Labs)
FIRAZYR® (icatibant)
FOSRENOL® (lanthanum carbonate)
GATTEX® (teduglutide recombinant)
INTUNIV® (guanfacine extended release)
LIALDA® (trademark of Nogra International Limited)
MEZAVANT® (trademark of Giuliani International Limited)
NATPAR® (parathyroid hormone (rDNA))
NATPARA® (parathyroid hormone)
PENTASA® (trademark of Ferring B.V. Corp)
PLENADREN® (hydrocortisone, modified release tablet)
PREMIPLEX® (IGF-I/IGFBP-3)
REMINYL® (galantamine hydrobromide) (United Kingdom ("UK") and Republic of Ireland) (trademark of Johnson & Johnson ("J&J")), excluding UK and Republic of Ireland)
REPLAGAL® (agalsidase alfa)
RESOLOR® (prucalopride)
REVESTIVE® (teduglutide)
TYVENSE® (lisdexamfetamine dimesylate)
VASCUGEL® (allogeneic aortic endothelial cells cultured in a porcine gelatin matrix [Gelfoam®] with cytokines, implanted)
VANCOCIN® (trademark of ANI Pharmaceuticals Inc.)
VPRIV® (velaglucerase alfa)
VYVANSE® (lisdexamfetamine dimesylate)
XAGRID® (anagrelide hydrochloride)
ZEFFIX® (trademark of GlaxoSmithKline ("GSK"))
3TC® (trademark of GSK)