Press Release

www.shire.com

2012 Annual Report – DTR 6.3.5 Disclosure

March 28, 2013 - Shire plc (LSE: SHP, NASDAQ: SHPGY), the global specialty biopharmaceutical company, announces that the following documents have today been posted or otherwise made available to shareholders:

- 2012 Annual Report and Accounts
- Notice of the 2013 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 2012 Annual Report and Accounts and Notice of the 2013 Annual General Meeting are also available on Shire's website at 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, 2012, issued on February 14, 2013 which comprises the Company's consolidated financial statements prepared under U.S. 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 Regulated Information Service. This material is not a substitute for reading the full 2012 Annual Report.

The information included in the Appendix is extracted from the 2012 Annual Report which was approved by the Directors on February 25, 2013.

Tony Guthrie
Deputy Company Secretary

For further information please contact:

Investor Relations	Eric Rojas (erojas@shire.com)	+1 781 482 0999
	Sarah Elton-Farr (seltonfarr@shire.com)	+44 1256 894 157

Notes to editors

Shire plc (the "Company") and its subsidiaries (collectively "Shire" or the "Group") develop and provide healthcare in the areas of:

- Behavioral Health and Gastro Intestinal conditions;
- Rare Genetic Diseases; and
- Regenerative Medicine;

as well as other symptomatic conditions treated by specialist physicians. To serve different patient groups, Shire operates in three distinct business units: Specialty Pharmaceuticals ("SP"), Human Genetic Therapies ("HGT") and Regenerative Medicine ("RM").

For further information about Shire, please visit our website: www.shire.com.

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;
- revenues from ADDERALL XR® are subject to generic erosion;
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payors in a timely manner for Shire's products may impact future revenues and earnings;
- Shire relies on a single source for manufacture of certain of its products and a disruption to the supply chain for those 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;
- Shire uses third party manufacturers to manufacture many of its products and is reliant upon third party contractors for certain goods and services, and any inability of these third party manufacturers to manufacture products, or any failure of these third party contractors to provide these goods and services, in each case in accordance with its respective contractual obligations, could adversely affect Shire's ability to manage its manufacturing processes or to operate its business;
- the development, approval and manufacturing of Shire's products is subject to extensive oversight by various regulatory agencies and regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- the actions of certain customers could affect Shire's ability to sell or market products profitably and fluctuations in buying or distribution patterns by such customers could adversely impact 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 the distraction of senior management, significant legal costs and the payment of substantial compensation or fines;
- adverse outcomes in legal matters and other disputes, including Shire's ability to obtain, maintain, 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;

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 26 to 32.

APPENDIX

Contents

1. Chairman's review

At Shire we have always embraced change as an opportunity to become even better. Our ability to anticipate and adapt has been at the heart of our success - from the earliest days right through to the present. Looking ahead, we are well prepared to enjoy the next chapter of growth and change in our ongoing story.

2012 highlights

- We have enjoyed another strong year
- We have a solid foundation for going forward
- We are well positioned for continued global growth

We have enjoyed another strong year at Shire. This is particularly pleasing, given the backdrop of challenges across the pharmaceuticals industry and the world economy.

Over the years we have established a fantastic record of growth, built on the vision and leadership of successive Chief Executives and the talent, skills and dedication of all our employees. Our success is a credit to both the individuals involved and the unique culture of Shire.

Focusing on patients

We continue to follow our strategy of focusing on meeting the needs of selected groups of patients with conditions where we have products and expertise. We have always had this specialized approach and continue to believe it is the right strategy for the future. But around this core principle is the need to adapt and evolve. We are never complacent and we will continue to change, to keep the company competitive, keep it growing and moving forward. This is everyone's job in Shire.

Change is our strength

The ability of the company to change is its greatest strength. It has enabled Shire to progress from a small company only offering one treatment in one market to becoming a multifaceted specialist company offering patient solutions around the world. For us change is the responsible thing to do. By changing in the right way we maintain and live up to our role as an industry leader but more importantly offer patients medicines and hope not there before.

Change has also been a feature of the Board in recent years. We now have a complex multinational business and the Board has evolved accordingly. We have the right balance of skill sets and experience to enable continued success. Membership includes pharmaceutical backgrounds, as well as those with depth in finance, international banking, private equity, medicine and science.

Courage and wisdom

Change takes courage – it's a key outcome of our brave culture. Change takes wisdom, too. You need to know what to change and how to change it and you need to have the right people in place, with the right attitude at the right time.

Speaking of the right people, we have been very fortunate to have had Angus Russell as Chief Executive over the last several years – his contributions have been many. On behalf of the Board I would like to thank Angus for his excellent leadership that has brought the company to where it stands today and we wish him and his family well in his retirement.

With the retirement of Angus, I am confident that his successor, Dr. Flemming Ornskov, will lead us to the next level of success and international growth. Flemming comes with an impressive set of skills and considerable international experience, including working with both large and small companies. And his background as a physician will be a great asset to ensure we keep our patient focus. I look forward to working closely with Flemming in the months and years ahead. We also welcomed Dr. Steven Gillis to the Board of Directors this year, he brings deep technical and scientific knowledge as well as an entrepreneurial approach.

1. Chairman’s review

Continuing to grow and succeed

Looking ahead, we have a sound strategy and we are committed to continue to grow internationally, to increase our patient focus and add even greater value. For us, a changing world is a good thing. It’s an opportunity to see the world differently; to seize the initiative and ultimately strengthen the business and ensure continued growth and success.

Mathew Emmens
Chairman

2. Chief Executive Officer's review

This year saw us continue to deliver on our growth commitments and further advance our pipeline. We articulated a 2020 vision and built on our unique culture of aspiring to be as brave as the people we help.

2012 highlights

- We continued to deliver growth
- We advanced our pipeline, creating significant opportunities for growth beyond 2015
- We distilled and communicated where we want to take the company: our 2020 vision

Continuing to deliver

We achieved our target of mid-teens earnings growth again this year, having delivered ahead of expectations for the last couple of years with growth rates of over 20%.

The business continued to perform extremely well. VYVANSE® and INTUNIV®, our treatments for attention deficit hyperactivity disorder ("ADHD"), both increased their share of the growing US market, further consolidating our leading position in this area. FIRAZYR®, our treatment for hereditary angiodema, launched strongly in the US and we continued robust global sales of our other rare disease treatments: ELAPRASE®, for Hunter syndrome, VPRIV®, for Gaucher disease, and REPLAGAL®, for Fabry disease. We underlined our belief in our Regenerative Medicine business through announcing investment in a new campus in California and the rollout of a new commercial strategy.

Looking to extend our treatments

During the year we had continued successes in our clinical milestones for our program of new uses for VYVANSE.

We are undertaking late stage studies for lisdexamfetamine dimesylate ("LDX"), the active ingredient in VYVANSE, as a treatment for major depressive disorder and recently initiated our Phase 3 programs for binge eating disorder and negative symptoms of schizophrenia.

In addition, we have identified potential new indications for FIRAZYR and DERMAGRAFT®. Our intrathecal trials for Hunter CNS, SanFilippo A and Metachromatic Leukodystrophy are also progressing as anticipated. So through this year we managed to build a very good late stage pipeline to fuel our growth in the years ahead.

We also added to our expertise in hematology through our acquisition of FerroKin Biosciences, Inc., ("FerroKin") and strengthened our regenerative medicine pipeline with the acquisition of Pervasis Therapeutics, Inc., ("Pervasis"), bringing us the Phase 2 product in development, VASCUGEL®.

Preparing to launch ELVANSE across Europe

We received approval of ELVANSE® (currently marketed in the US as VYVANSE) and we are now preparing for launch in eight European markets. We already have experience of the ADHD market in Europe through our EQUASYM® product and we know that there is a patient need for a product with the profile of ELVANSE. The launch will be a significant milestone in the globalization of our major ADHD franchise and the company overall. It follows our successful launch of VYVANSE (marketed as VENVANSE®) in Brazil.

Collaborating for quicker better outcomes

Our collaborative culture is a key Shire strength. We're moving into a world where more people are seeing the benefits of partnerships and collaboration with outside agencies, companies and academia. It's a much better model, because it gives you access to a wider range of opportunities and skill sets that can enhance the solutions we develop for our patients. At Shire, partnering and collaborating with third parties has always been a core capability and it fits the increasingly changing and dynamic world in healthcare, where you have to make a lot of quick decisions and timeframes tend to be shorter in terms of product development and opportunity. We have worked with partners from day one. It's just more of the same for us. We're building our collaborations, with academia, with institutions, with companies that work in the areas of expertise that we're focused on, such as rare genetic diseases. In doing this we are investing in the best ideas.

2. Chief Executive Officer's review

Putting patients at the heart of everything we do

Over the past few years the world of healthcare has completely changed – aligning with our objectives and business model. Markets are much more heterogeneous now, and one size does not fit all. You have to tailor your innovation, your capabilities and your treatments to suit individual needs. This is where our focus of putting the patient at the centre of everything we do and focusing on specialist treated and rare diseases with small patient numbers puts us in a strong position. It allows us to understand the needs of the patients and the relatively small number of physicians who help them. Our relationships with them provide us with real insights into how patients live their lives – the challenges they face and how we can help and add value around beyond the provision of treatments. Educating people so they really understand a rare disease for example, or helping patients treat themselves at home rather than having to travel long distances to specialists centers. There's a lot more we can do to help patients and their physicians, building greater value for everyone involved along the way. And this is what our new 2020 vision is about. Being a responsible business goes to the heart of our vision and for us is distilled to a single core consideration: What is the right thing to do? This guides everything we do from day-to-day across our business.

Taking brave steps to do more for our patients

Our view of the world, with the patient at the centre, has directly driven our shared culture of aspiring to be as brave as the people we help. Our decentralized, market-driven and increasingly international business is united by this shared commitment to identify new ways to help our patients as much as we possibly can.

Transforming the business

Our shared culture will continue to be fundamental as we enter our next stage of global expansion. The globalization of our business is one of the most exciting development opportunities since I joined the company 13 years ago. When I came to the company in 1999 we were dependent on one product for ADHD in the US. Now we have a strong portfolio of products across behavioral health, gastro intestinal diseases, rare genetic diseases and regenerative medicine, which we sell in over 50 markets around the world. Looking ahead, we have a huge global opportunity with a very strong platform and a proven strategy and business model for future growth.

Our highly specialized, patient-focused, collaborative approach is increasingly seen as the way forward in our industry – we have led the way. As I prepare to retire from the business, I am extremely proud of what we have achieved together and look forward to seeing the continued growth and success of the company in the years ahead.

Angus Russell
Chief Executive Officer

3. Financial review

Overview

Shire plc is a leading specialty biopharmaceutical company that focuses on meeting the needs of the specialist physician. The Company has grown through acquisition, completing a series of major transactions that have brought therapeutic, geographic and pipeline growth and diversification. The Company will continue to evaluate companies, products and pipeline opportunities that offer a good strategic fit and have the potential to deliver demonstrable value to all of the Company's stakeholders: patients, physicians, policy makers, payors, investors and employees.

Substantially all of the Company's revenues, expenditures and net assets are attributable to the research and development ("R&D"), manufacture, sale and distribution of pharmaceutical products within three reportable segments: SP, HGT and RM. The Company also earns royalties (where Shire has out-licensed products to third parties) which are recorded as revenues.
Revenues are derived primarily from two sources - sales of the Company's own products and royalties:

- 94% (2011: 93%) of total revenues are derived from product sales, of which 64% (2011: 66%) are within SP, 32% (2011: 31%) are within HGT and 4% (2011: 3%) are within RM; and
- 5% of total revenues are derived from royalties (2011: 6%).

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

There is increasing legislation both in the US and the rest of the world which is placing downward pressure on the net pricing of pharmaceutical products and medical devices. For example the US government passed healthcare reform legislation in 2010 which included an increase in Medicaid rebate rates and extended Medicaid rebates to those products provided through Medicaid managed care organizations. The legislation also imposed excise fees to be paid by both pharmaceutical manufacturers (from 2011) and medical device companies (from 2013). The impact of these recent changes to US healthcare legislation, and other healthcare reforms in the rest of the world, has not to date had a material impact on the Company's results of operations.

The healthcare industry is also experiencing:

- pressure from governments and healthcare providers to keep prices low while increasing access to drugs;
- increasing challenges from third party payors 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

Historically, Shire's portfolio of approved products has been heavily weighted towards the North American market. The acquisition in 2005 of Transkaryotic Therapies Inc. ("TKT") and the consequent establishment of the Company's HGT business, together with the acquisitions of New River Pharmaceuticals in 2007 (which brought full rights to ADHD product VYVANSE), Jerini AG ("Jerini") in 2008 (which brought the HAE product FIRAZYR), EQUASYM in 2009 (which facilitated Shire's immediate access to the European ADHD market) and Movetis NV ("Movetis") in 2010 (which brought EU rights to RESOLOR®). The acquisition of Advanced BioHealing, Inc. ("ABH") in 2011 (which subsequently became RM), and FerroKin in 2012 (which brought a new hematology drug to the SP portfolio) provided Shire with platforms to increase its presence in Europe and the rest of the world ("RoW"), thereby working towards diversifying the risk associated with reliance on one geographic market. In 2012 the SP and HGT businesses derived 15% and 75%, respectively, of their product sales from outside of the US. Currently all RM product sales are generated in 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:

- continued launch of VYVANSE in Brazil (marketed as VENVANSE) and the potential approval and launch of VYVANSE in Mexico;
- approval of ELVANSE/TYVENSE® in certain countries in the EU for treatment of ADHD in children;
- filing in 2012 of an application to expand the label of FIRAZYR in the EU to include the treatment of attacks of ACE-inhibitor induced Angioedema;
- filing in 2012 of an application in Europe for the VPRIV label to be updated with data regarding the impact of VPRIV on certain parameters of bone disease in Type 1 Gaucher patients;
- INTUNIV Phase 3 clinical program to support submission of an MAA in the EU; and
- continued roll-out of DERMAGRAFT in Canada and RESOLOR in the EU.

R&D

Over the last five years Shire has focused its R&D efforts on products in its core therapeutic areas and concentrated its resources on obtaining regulatory approval for later-stage pipeline products within these core therapeutic areas. In addition to continued efforts in its late stage pipeline for the ADHD, Gastro Intestinal ("GI"), HGT and RM therapeutic areas, Shire has also progressed work on an earlier stage pipeline.

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, INTUNIV in 2009, VPRIV in 2010, and FIRAZYR in 2011; in the EU, VPRIV in 2010 and ELVANSE/TYVENSE in 2012; in Canada, VYVANSE in 2010 and DERMAGRAFT in 2012.

Shire's strategy is focused on the development of product candidates that have a lower risk profile. As Shire further expanded its earlier phase pipeline, R&D costs in 2012 included expenditure on several pre-clinical to Phase 3 studies for products in development as well as Phase 3(b) and Phase 4 studies to support recently launched products in the SP and HGT businesses, together with the development of new projects in the SP, HGT and RM businesses.

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 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, they are generally able to sell 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 period prior to the authorized generic launch. In June 2012 the US Food and Drug Administration ("US") reached a decision on the Citizen Petition for ADDERALL XR which was filed in October 2005. The FDA also approved an abbreviated new drug application ("ANDA")for a generic version of ADDERALL XR. Sales of AXR decreased in 2012 due to the launch of a new generic product.

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.

Shire is engaged in various legal proceedings with generic manufacturers with respect to its VYVANSE, INTUNIV, FOSRENOL®, LIALDA® and ADDERALL XR patents.

Business Development

Shire seeks to focus its business development activity on the acquisition and in-licensing of products which offer a good strategic fit and have the potential to deliver demonstrable value to all of the Company's stakeholders.

3. Financial review

Recent mergers or acquisitions

In 2012 Shire acquired FerroKin which added SPD602 to the SP business unit (SPD 602 is in Phase 2 for treatment of iron overload following numerous blood transfusions).

Through the acquisition of ABH in 2011 Shire obtained DERMAGRAFT, which is currently marketed in the US for the treatment of DFU, and established the RM business unit. In 2012 Shire acquired substantially all the assets and certain liabilities of Pervasis which added VASCUGEL (now SRM003) to the RM business unit (SRM003 is in Phase 2 development for acute vascular repair).

Through the acquisition of Movetis in 2010, Shire obtained RESOLOR, which is approved for the treatment of chronic constipation in women in the EU and Switzerland. In addition, in 2012 Shire acquired the rights to market RESOLOR in the US.

Collaboration and licensing activity

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

- a collaboration and license agreement with Sangamo to develop therapeutics for hemophilia and other monogenic diseases based on Sangamo's ZFP technology in 2012;
- an exclusive license in markets outside of North America for the ActRIIB class of molecules being developed by Acceleron in 2010. The collaboration with Acceleron will initially focus on further developing HGT-4510 (also called ACE-031) for the treatment of patients with Duchenne muscular dystrophy ("DMD");
- a worldwide exclusive license from IGAN Biosciences, Inc. to develop and commercialize protease-based therapeutics for the treatment of IgA nephropathy, a rare kidney disease;
- Shionogi co-development and co-commercialization agreement for VYVANSE and INTUNIV in Japan.

Organization and Structure

Shire's internal financial reporting is in line with its business unit and management reporting structure. The Company has three business units and three reporting segments: SP, HGT and RM. During 2010, to support the Company's geographical expansion and diversification, Shire established an international commercial hub in Switzerland.

On January 23, 2013 Shire announced that it had decided to proceed with a collective dismissal and business closure at its site in Turnhout, Belgium. This decision follows the conclusion of an information and consultation process. Shire will continue to sell RESOLOR in Europe and the supply of RESOLOR for patients in Europe who rely on the medicine will not be affected. The collective dismissal and business closure of the Turnhout site is not expected to have a material impact on the Company's consolidated financial position and results of operations in future periods.

3. Financial review

Results of operations for the years to December 31, 2012

Financial highlights for the year to December 31, 2012 are as follows:

- Product sales in 2012 were up 12% to $4,407 million (2011: $3,950 million). On a Constant Exchange Rate ("CER")[1] basis, which is a Non GAAP measure, product sales were up 13%.

  Product sales excluding ADDERALL XR grew strongly and were up 16% particularly driven by growth from VYVANSE (up 28% to $1,030 million), VPRIV (up 20% to $307 million), INTUNIV (up 29% to $288 million) and FIRAZYR (up 252% to $116 million).

  ADDERALL XR product sales were down 19% to $429 million primarily due to lower prescription volumes following the approval of a new generic version of ADDERALL XR in the second quarter of 2012. Reported product sales were also impacted by the accounting for the settlement of the Impax Laboratories, Inc. ("Impax") litigation.

- Total revenues increased by 10% (up 12% on a Non GAAP CER basis) as the growth in product sales was partially offset by lower royalties and other revenues (down 12%), primarily ADDERALL XR royalties following the launch of a new generic competitor in the second quarter of 2012. The decline in ADDERALL XR royalties was partially offset by the recognition of one-time royalty income of $38 million following resolution of a disagreement with GlaxoSmithKline ("GSK") and ViiV Healthcare ("Viiv") relating to royalty payments for 3TC® and ZEFFIX®.

- Operating income in 2012 was down 14% to $949 million (2011: $1,109 million) primarily resulting from charges to impair intangible assets for RESOLOR in the EU ($198 million). The impairments were due to lower actual and projected performance for the product given the increasingly challenging European reimbursement environment. Operating income in 2012 was also impacted by a charge of $58 million in relation to the agreement in principle with the US Government to resolve a previously disclosed civil investigation. Excluding these charges operating income in 2012 was up by 9%.

- Diluted earnings per ordinary share decreased by 13% to $1.31 (2011: $1.51) primarily due to the lower operating income, partially offset by a lower effective tax rate of 18% (2011: 21%).

1. 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 2012 product sales and revenues restated using 2011 average foreign exchange rates to 2011 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, 2012 were $1.59:£1.00 and $1.29:€1.00 (2011: $1.60:£1.00 and $1.39:€1.00).

Total revenues

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

Year to December 31,	2012 $'M	2011 $'M	Change %
Product sales	4,406.7	3,950.2	+12%
Royalties	241.6	283.5	-15%
Other revenues	32.9	29.7	+11%
Total	4,681.2	4,263.4	+10%

3. Financial review

Product sales

	Year to December 31, 2012 $'M	Year to December 31, 2011 $'M	Product sales growth %	Non-GAAP CER growth %	US prescription growth[1] %	Exit market share[1] %
SP						
Behavioral Health						
VYVANSE	1,029.8	805.0	+28	+28	+17	17
ADDERALL XR	429.0	532.8	-19	-19	-11	5
INTUNIV	287.8	223.0	+29	+29	+34	5
EQUASYM	29.2	19.9	+47	+53	n/a[2]	n/a[2]
GI						
LIALDA / MEZAVANT®	399.9	372.1	+7	+8	+5	22
PENTASA®	265.8	251.4	+6	+6	-5	14
RESOLOR	11.8	6.1	+93	n/a	n/a[3]	n/a[3]
General Products						
FOSRENOL	172.0	166.9	+3	+6	-19	4
XAGRID®	97.2	90.6	+7	+14	n/a[2]	n/a[2]
Other product sales	112.4	147.8	-24	-23	n/a	n/a
	2,834.9	2,615.6	+8			
HGT						
ELAPRASE	497.6	464.9	+7	+11	n/a[3]	n/a[3]
REPLAGAL	497.5	475.2	+5	+10	n/a[2]	n/a[2]
VPRIV	306.6	256.2	+20	+23	n/a[2]	n/a[2]
FIRAZYR	116.3	33.0	+252	+258	n/a[2]	n/a[2]
	1,418.0	1,229.3	+15			
RM						
DERMAGRAFT	153.8	105.3	+46	+46[4]	n/a[2]	n/a[2]
Total RM product sales	153.8	105.3	+46			
Total product sales	4,406.7	3,950.2	+12			

(1) Data provided by IMS. Exit market share represents the average US market share in the month ended December 31, 2012.
(2) IMS NPA Data not available.
(3) Not sold in the US in the year to December 31, 2012.
(4) DERMAGRAFT was acquired by Shire on June 28, 2011 (sales growth above reflects full year 2012 sales compared to post acquisition sales for 2011).

3. Financial review

Specialty Pharmaceuticals

VYVANSE – ADHD

VYVANSE product sales grew strongly (28%) in 2012 as a result of higher prescription demand, due to growth in US ADHD market (+9%) and VYVANSE's share of that market, and as a result of a price increase taken in 2012. These positive factors, together with lower sales deductions in 2012, more than offset the effect of higher retailer destocking in 2012 compared to 2011 and some shipment slippage at the end of the fourth quarter.

Litigation proceedings regarding VYVANSE are ongoing.

ADDERALL XR – ADHD

ADDERALL XR product sales decreased (-19%) in 2012 as a result of lower US prescription demand following the introduction of a new generic competitor and the impact of the accounting for the legal settlement with Impax, which reduced reported product sales by $42 million in 2012, in addition to the effect of product destocking in 2012 compared to stocking in 2011 and, higher sales deductions. These negative factors were partially offset by the benefit of a price increase taken during 2012.

On February 7, 2013 Shire and Impax settled all litigation relating to Shire's contract to supply Impax with authorized generic ADDERALL XR. Under the terms of the settlement Shire will make a one-time cash payment to Impax of $48 million, which has been recorded as a liability at December 31, 2012. In accordance with US GAAP, as this represents a payment to a customer, the amount has been recorded in the Income Statement as a reduction in reported ADDERALL XR product sales and royalties ($42 million and $6 million respectively) in 2012.

INTUNIV – ADHD

INTUNIV product sales were up 29% compared to 2011, primarily driven by strong growth in US prescription demand (up 34% compared to 2011), together with price increases taken during 2012. These positive factors were partially offset by lower stocking in 2012 and higher sales deductions in 2012 compared to 2011.

Litigation proceedings relating to the Company's INTUNIV patents are in progress.

LIALDA/MEZAVANT – Ulcerative colitis

The growth in product sales for LIALDA/MEZAVANT (7%) in 2012 was primarily driven by higher market share in the US and a price increase taken since the fourth quarter of 2011, the effects of which were partially offset by product destocking in 2012 compared to a small amount of product stocking in 2011 and higher sales deductions in 2012. Growth in US net product sales was partially offset by the impact of lower priced imports into certain European markets.

Litigation proceedings regarding LIALDA/MEZAVANT are ongoing.

PENTASA – Ulcerative colitis

PENTASA product sales were up 6% as the benefit of price increases was partially offset by lower prescription demand, a small amount of destocking in 2012 and higher sales deductions as compared to 2011.

FOSRENOL – Hyperphosphatemia

Product sales of FOSRENOL in the US increased (3%) due to the effect of price increases in 2012 and lower sales deductions compared to 2011, which more than offset the decline in prescription demand. Product sales of FOSRENOL outside the US decreased marginally primarily because of the impact of unfavorable foreign exchange.

Litigation proceedings regarding Shire's FOSRENOL patents are ongoing.

3. Financial review

Human Genetic Therapies

ELAPRASE – Hunter syndrome

Reported ELAPRASE sales growth (7%) was driven by an increase in the number of patients on therapy. On a Non GAAP CER basis, ELAPRASE sales grew by 11% as reported sales were held back by unfavorable foreign exchange (amounting to approximately $20 million) primarily due to weaker European currencies in 2012 compared to 2011. The increase in ELAPRASE sales between the third quarter and fourth quarter of 2012 was partly driven by the timing of certain large orders from markets which order less frequently.

REPLAGAL – Fabry disease

Reported REPLAGAL sales growth (5%) was driven by an increase in the number of patients on therapy. On a Non GAAP CER basis, REPLAGAL sales grew by 10%, as reported sales were impacted by unfavorable foreign exchange (amounting to approximately $26 million), primarily due to weaker European currencies in 2012 compared to 2011. The reduction in REPLAGAL sales between the third and fourth quarter of 2012 was partly driven by the timing of certain large orders from markets which order less frequently.

Litigation proceedings regarding REPLAGAL are ongoing.

VPRIV – Gaucher disease

Reported VPRIV sales growth (20%) was driven by an increase in the number of patients on therapy. On a Non GAAP CER basis, VPRIV sales increased by 23% as reported sales were also held back by unfavorable foreign exchange (amounting to approximately $8 million).

FIRAZYR – HAE

Reported FIRAZYR sales growth (252%) was driven largely by the first full year of sales in the US market, following launch of FIRAZYR in the market in fourth quarter of 2011.

Regenerative Medicine

DERMAGRAFT – DFU

DERMAGRAFT product sales were up 46%[(1)] compared to sales reported by Shire subsequent to acquisition in 2011. On a full year basis, sales for DERMAGRAFT were down 21% reflecting the impact of an ongoing restructuring of the RM sales and marketing organization and the implementation of a new commercial model, all of which is expected to position DERMAGRAFT for future sales growth.

1. Shire acquired DERMAGRAFT through its acquisition of ABH on June 28, 2011 and reported revenues from DERMAGRAFT of $105.3m relating to the post acquisition period in 2011.

Royalties

	Year to December 31, 2012 $'M	Year to December 31, 2011 $'M	Change %
3TC and ZEFFIX	91.6	82.7	+11%
ADDERALL XR	70.3	107.1	-34%
FOSRENOL	53.3	46.5	+15%
Other	26.4	47.2	-44%
Total	241.6	283.5	-15%

Royalties from 3TC and ZEFFIX include one-time royalty income of $38 million in respect of prior periods due to resolution of the disagreement between Shire, GSK and ViiV as to how the royalty rate for these products should be applied. This one-time income more than offset the underlying decline in 3TC and ZEFFIX royalties as a result of increased competition and the expiry of patents in certain territories in 2012.

Royalties from ADDERALL XR in 2012 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 in late second quarter of 2012.

FOSRENOL royalties increased primarily due to higher royalties received on sales in Japan.

Other royalties decreased primarily due to increased generic competition.

Cost of product sales

Cost of product sales increased to $645.4 million for the year to December 31, 2012 (15% of product sales), up from $588.1 million in the corresponding period in 2011 (2011: 15% of product sales). The costs of product sales as a percentage of product sales remained constant as the impact of lower gross margins in 2012 was offset by the fair value adjustment relating to DERMAGRAFT inventories and costs incurred on the transfer of manufacturing from Owings Mills in 2011 which were not repeated in 2012.

For the year to December 31, 2012 cost of product sales included depreciation of $31.5 million (2011: $39.8 million) and amortization of $0.7 million (2011: $1.7 million).

R&D

R&D expenditure increased to $965.5 million for the year to December 31, 2012 (22% of product sales), compared to $770.7 million in the corresponding period in 2011 (20% of product sales). In the year to December 31, 2012 R&D included up-front payment of $13.0 million to Sangamo, $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 (2011: $16.0 million). Excluding these costs R&D increased by $100.6 million or 20% in the year to December 31, 2012 due to the Company's continued investment in a number of targeted R&D programs, particularly new uses of LDX and recently acquired assets including SPD602 for iron overload (acquired with FerroKin). R&D in 2012 also included a full year of ABH's R&D costs (ABH was acquired in late June 2011).

R&D in the year to December 31, 2012 included depreciation of $22.5 million (2011: $25.2 million).

Selling, general and administrative ("SG&A")

SG&A expenditure increased to $2,114.0 million (48% of product sales) for the year to December 31, 2012 from $1,751.4 million (44% of product sales) in the corresponding period in 2011. In the year to December 31, 2012 SG&A increased by $362.6 million, or 21%, as 2012 included higher intangible asset amortization, the impact of impairment charges and higher legal and litigation costs, which included a charge of $57.5 million in relation to the agreement in principle with the US Government and settling the litigation related to the termination of co-promotion agreement for VYVANSE.

Impairment charges of $126.7 million relate to RESOLOR intangible assets as the actual and projected performance for RESOLOR has been adversely affected by the challenging European reimbursement environment. Shire has evaluated alternative sales and marketing strategies for RESOLOR in response to these challenges but has judged that projected profitability levels will continue to be below the level forecast at the time of the acquisition of Movetis.

For the year to December 31, 2012 SG&A included depreciation of $59.8 million (2011: $63.1 million) and amortization of $194.1 million (2011: $165.0 million).

(Gain)/loss on sale of product rights

For the year to December 31, 2012 Shire recorded a gain on sale of product rights of $18.1 million (2011: loss of $6.0 million) following re-measurement of the contingent consideration receivable from the divestment of DAYTRANA®.

Integration and acquisition costs

For the year to December 31, 2012 Shire recorded integration and acquisition costs of $25.2 million (2011: $13.7 million), primarily associated with the acquisition of FerroKin and the integration of ABH. In 2011 integration and acquisition costs primarily related to the acquisition of ABH.

3. Financial review

Interest expense

For the year to December 31, 2012 Shire incurred interest expense of $38.2 million (2011: $39.1 million). Interest expense principally relates to the coupon and amortization of issue costs on Shire's $1,100 million 2.75% convertible bonds due 2014.

Taxation

The effective rate of tax in 2012 was 18% (2011: 21%). The effective tax rate in 2012 is lower than 2011 due to favorable changes in profit mix in 2012 and the benefit of the recognition of foreign tax credits.

Financial condition at December 31, 2012

Cash & cash equivalents

Cash and cash equivalents increased by $862.2 million to $1,482.2 million (December 31, 2011: $620.0 million). Cash generated by operating activities of $1,382.9 million was offset by the cost of acquiring FerroKin, other capital expenditure, the purchase of shares (both by the employee benefit trust ("EBT") and under the share buy-back program) and dividend payments.

Other intangible assets, net

Other intangible assets have decreased by $104.9 million to $2,388.1 million (December 31, 2011: $2,493.0 million). Additions in the year of $281.6 million, principally relating to intangible assets acquired with FerroKin and from Pervasis and the license acquired from Mt. Sinai School of Medicine of New York University ("Mt. Sinai"), were offset by intangible asset amortization and impairment charges of $194.8 million and $197.9 million respectively.

Accounts payable and accrued expenses

Accounts payable and accrued expenses have increased by $131.0 million to $1,501.5 million (December 31, 2011: $1,370.5 million) mainly due to the recognition of liabilities in relation to the settlement of litigation with Impax Laboratories Inc. and the agreement in principle reached with the US Government regarding the investigation into the sales and marketing of ADDERALL XR, DAYTRANA and VYVANSE.

Convertible bonds

Convertible bonds – current liabilities have decreased by $1,100 million due to the reclassification of the Company's $1,100 million 2.75% convertible bonds due 2014 and convertible into fully paid Ordinary Shares of Shire plc (the "Bonds") from current to non-current liabilities in 2012 as the Company is no longer required to redeem the Bonds within twelve months of the balance sheet date.

Other non-current liabilities

Other non-current liabilities increased by $97.3 million to $241.6 million (December 31, 2011: $144.3 million) due primarily to the recognition of non-current contingent consideration payable totaling $120.4 million related to the FerroKin and Pervasis business combinations and the license agreement with Mt. Sinai.

3. Financial review

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 EBT of Shire shares in the market to satisfy awards granted under Shire's employee share plans; the timing and quantum of purchases of Shire shares under the share buy-back program; 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 trade marks, 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 $1,482.2 million of cash and cash equivalents at December 31, 2012. Substantially all of Shire's debt relates to the Bonds. The Bonds were potentially redeemable at the option of Bondholders at their principal amount including accrued and unpaid interest on May 9, 2012 (the "Put Option"), and remain redeemable following the occurrence of a change of control of Shire. On April 9, 2012 the deadline for Bondholders to choose to exercise the Put Option passed. No elections from the Bondholders were received by this date and the Bonds are now due on the Final Maturity date. In addition, Shire has a revolving credit facility of $1,200 million which matures in 2015 (the "RCF"), which is currently undrawn.

Shire 2.75% Convertible Bonds due 2014

On May 9, 2007 Shire issued the Bonds and the net proceeds of the issuance, after deducting the commissions and other direct costs of issue, totaled $1,081.7 million. In connection with the Scheme the Trust Deed was amended and restated in 2008 in order to provide that, following the substitution of Shire plc in place of Shire Biopharmaceutical Holdings as the principal obligor and issuer of the Bonds, the Bonds would be convertible into Ordinary Shares of Shire plc.

The Bonds were issued at 100% of their principal amount, and unless previously purchased and cancelled, redeemed or converted, will be redeemed on May 9, 2014 (the "Final Maturity Date") at their principal amount.

The Bonds bear interest at 2.75% per annum, payable semi-annually in arrears on November 9 and May 9. The Bonds constitute direct, unconditional, unsubordinated and unsecured obligations of the Company, and rank pari passu and ratably, without any preference amongst themselves, and equally with all other existing and future unsecured and unsubordinated obligations of the Company.

The Bonds may be redeemed at the option of the Company, at their principal amount together with accrued and unpaid interest if: (i) at any time after May 23, 2012 if on no less than 20 dealing days in any period of 30 consecutive dealing days the value of Shire's Ordinary Shares underlying each Bond in the principal amount of $100,000 would exceed $130,000; or (ii) at any time conversion rights have been exercised, and/or purchases and corresponding cancellations, and/or redemptions effected in respect of 85% or more in principal amount of Bonds originally issued. The Bonds are repayable in US dollars, but also contain provisions entitling the Company to settle redemption amounts in Pounds sterling, or in the case of the Final Maturity Date or any change of control Shire, by delivery of the underlying Ordinary Shares and a cash top-up amount.

The Bonds are convertible into Ordinary Shares during the conversion period, being the period from June 18, 2007 until the earlier of: (i) the close of business on the date falling fourteen days prior to the Final Maturity Date; (ii) if the Bonds have been called for redemption by the Company, the close of business fourteen days before the date fixed for redemption; (iii) the close of business on the day prior to a Bond holder giving notice of redemption in accordance with the conditions; and (iv) the giving of notice by the trustee that the Bonds are accelerated by reason of the occurrence of an event of default.

Upon conversion, the Bond holder is entitled to receive Ordinary Shares at the conversion price of $32.83 per ordinary share, (subject to adjustment as outlined below).

The conversion price is subject to adjustment in respect of (i) any dividend or distribution by the Company, (ii) a change of control and (iii) customary anti-dilution adjustments for, inter alia, share consolidations, share splits, spin-off events, rights issues, bonus issues and reorganizations. The initial conversion price of $33.5879 was adjusted to $33.17 with effect from March 11, 2009 as a result of cumulative dividend payments during the period from October 2007 to April 2009 inclusive, and was further adjusted to $32.83 with effect from March 11, 2011 as a result of cumulative dividend payments during the period April 2009 to April 2011 inclusive. The Ordinary Shares issued on conversion will be delivered credited as fully paid, and will rank pari passu in all respects with all fully paid Ordinary Shares in issue on the relevant conversion date.

Revolving Credit Facilities Agreement

On November 23, 2010 the Company entered into a committed multicurrency revolving and swingline facilities agreement with a number of financial institutions, for which Abbey National Treasury Services Plc (trading as Santander Global Banking and Markets), Bank of America Securities Limited, Barclays Capital, Citigroup Global Markets Limited, Lloyds TSB Bank plc and The Royal Bank of Scotland plc acted as mandated lead arrangers and bookrunners (the “new RCF”). The new RCF is for an aggregate amount of $1,200 million and cancelled the Company’s then existing committed revolving credit facility (the “old RCF”). The new RCF, which includes a $250 million swingline facility, may be used for general corporate purposes and matures on November 23, 2015.

The interest rate on each loan drawn under the new RCF for each interest period is the percentage rate per annum which is the aggregate of the applicable margin (ranging from 0.90 to 2.25 per cent per annum) and LIBOR for the applicable currency and interest period. Shire also pays a commitment fee on undrawn amounts at 35 per cent per annum of the applicable margin.

Under the new RCF it is required that (i) Shire’s ratio of Net Debt to EBITDA (as defined within the new RCF agreement) does not exceed 3.5 to 1 for either the 12 month period ending December 31 or June 30 unless Shire has exercised its option (which is subject to certain conditions) to increase it to 4.0 to 1 for two consecutive testing dates; (ii) the ratio of EBITDA to Net Interest (as defined in the new RCF agreement) must not be less than 4.0 to 1, for either the 12 month period ending December 31 or June 30, and (iii) additional limitations on the creation of liens, disposal of assets, incurrence of indebtedness, making of loans, giving of guarantees and granting security over assets. These financial and operating covenants have not had, and are not expected to have, an effect on the Company’s financial position and liquidity.

On entering into the new RCF in November 2010 the Company paid arrangement costs of $8.0 million, which have been recorded as deferred charges, with amortization of these costs to the Company’s income statement over the contractual term of the new RCF.

The availability of loans under the new RCF is subject to customary conditions.

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, share buy-back program, capital expenditures, tax and interest payments, lease obligations and milestone payments as they become due over the next twelve months.

If the Company decides to acquire other businesses, it expects to fund these acquisitions from existing cash resources, the RCF and possibly through new borrowings and the issue of new equity if necessary.

Share buy-back program

Shire has a strong balance sheet and continued robust cash generation, and considers efficient use of capital on behalf of shareholders an important objective. Therefore, during the year to December 31, 2012 the Company commenced a share buy-back program, for the purpose of returning funds to shareholders, of up to $500 million through both direct purchases of Ordinary Shares and through the purchase of Ordinary Shares underlying ADRs.

3. Financial review

During the year ended December 31, 2012 the Company made on-market repurchases totaling 3,631,571 Ordinary Shares at a cost of $106.4 million (excluding transaction costs). This represents 0.65% of the issued share capital of the Company as at the year end. The program covers purchases of Ordinary Shares for cancellation or to be held as treasury shares, in accordance with the authority renewed by shareholders at the Company's AGM on April 24, 2012 when the Company was authorized to make market purchases of up to 56,253,208 of its own Ordinary Shares. That authority will expire at the 2013 AGM and in accordance with usual practice a resolution to renew it for another year will be proposed.

Sources and uses of cash

The following table provides an analysis of the Company's gross and net debt (excluding restricted cash), as at December 31, 2012 and 2011:

December 31,	**2012 $'M**	**2011 $'M**
Cash and cash equivalents[1]	1,482.2	620.0
Shire 2.75% Convertible bonds	1,100.0	1,100.0
Other debt	9.3	8.2
Total debt	1,109.3	1,108.2
Net cash/(debt)	372.9	(488.2)

(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.

Cash flow activity

Net cash provided by operating activities for the year to December 31, 2012 increased by $309.3 million or 29% to $1,382.9 million (2011: $1,073.6 million) as higher cash receipts from gross product sales and improved cash collections for aged European receivables more than offset higher operating expenses and sales deduction payments in the year.

Net cash used in investing activities was $271.0 million in the year to December 31, 2012, principally relating to the expenditure on property, plant and equipment of $149.6 million and the cash paid (net of cash acquired) of $97.0 million for the acquisition of FerroKin ($94.5 million) and Pervasis ($2.5 million). Capital expenditure on property, plant and equipment primarily includes expenditure of $65.0 million on computer software and hardware due to SAP upgrade and construction and leasehold improvements at different Company sites of $45.2 million.

Net cash used in financing activities was $244.3 million for the year to December 31, 2012, principally due to the purchase of shares by the EBT, the purchase of shares under the share buy-back program and dividend payments, offset by the tax benefit associated with the exercise of stock options.

Outstanding Letters of credit

At December 31, 2012, the Company had irrevocable standby letters of credit and guarantees with various banks totaling $38.2 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.

3. Financial review

Cash requirements

At December 31, 2011 the Group's cash requirement for 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
Convertible bonds[(i)]	1,145.4	30.3	1,115.1	-	-
Operating leases obligation [(ii)]	244.3	49.6	61.0	40.8	92.9
Purchase obligations [(iii)]	806.8	670.1	127.7	4.4	4.6
Other long-term liabilities reflected on the Balance Sheet [(iv)]	230.2	-	159.3	37.8	33.1
Total	2,426.7	750.0	1,463.1	83.0	130.6

(i) Shire's $1,100 million principal amount of 2.75% convertible bonds due 2014 and the interest on the Bonds has been included based on their contractual payment dates. The principal amount of $1,100 million has been included within payments due in one to three years based on the Final Maturity Date of the Bonds. On April 9, 2012 the deadline for Bondholders to choose to exercise their Put Option on May 9, 2012 passed. No elections from the Bondholders were received by this date and the Bonds are now due on the Final Maturity Date, subject to the certain exceptions. As the Company is no longer required to redeem the Bonds within twelve months of the balance sheet date, the Bonds have been presented as a non-current liability at December 31, 2012. Further details are included within Liquidity and capital resources: Shire 2.75% Convertible Bonds due 2014 above.

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

(iii) 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.

(iv) Unrecognized tax benefits and associated interest and penalties of $58.9 million are included within payments due in one to three years.

The contractual obligations table above does not include certain milestones and other contractual commitments where payment is contingent upon the occurrence of events which are yet to occur (and therefore payment is not yet due). At December 31, 2012 the most significant of the Company's milestone and contractual commitments which are contingent on the occurrence of future events are as follows:

(i) Collaboration with Acceleron for ActRIIB class of molecules

On September 9, 2010 Shire announced that it had expanded its HGT pipeline by acquiring an exclusive license in markets outside of North America for the ActRIIB class of molecules being developed by Acceleron. The collaboration will initially focus on further developing HGT-4510 (also called ACE-031), the lead ActRIIB drug candidate, which is in development for the treatment of patients with DMD. The Phase 2a trial is on hold and clinical safety is under review. HGT-4510 and the other ActRIIB class of molecules have the potential to be used in other muscular and neuromuscular disorders with high unmet medical need.

In the year to December 31, 2010 Shire made an upfront payment of $45 million to Acceleron which has been expensed to R&D.

In the year to December 31, 2012 Shire's share of R&D costs under this collaboration agreement was $4.5 million (2011: $10.1 million; 2010: $2.7 million) which were expensed to R&D. Shire will pay Acceleron up to

a further $165.0 million, subject to certain development, regulatory and sales milestones being met for HGT-4510 in DMD, up to an additional $288 million for successful commercialization of other indications and molecules, and royalties on product sales.

Shire and Acceleron will conduct the collaboration through a joint steering committee, with subcommittees including a joint manufacture committee, and a joint patent committee to monitor the development of HGT-4510 and other compounds.

(ii) Research Collaboration with Santaris Pharma A/S ("Santaris") on Locked Nucleic Acid ("LNA") Drug Platform

On August 24, 2009 Shire announced that it had entered into a research collaboration with Santaris, to develop its proprietary LNA technology in a range of rare diseases. LNA technology has the benefit of shortened target validation and proof of concept, potentially increasing the speed and lowering the cost of development. As part of the joint research project Santaris will design, develop and deliver pre-clinical LNA oligonucleotides for Shire-selected orphan disease targets, and Shire will have the exclusive right to further develop and commercialize these candidate compounds on a worldwide basis.

In the year to December 31, 2009 Shire made an upfront payment to Santaris of $6.5 million, for technology access and R&D funding, which was expensed to R&D.

In the year to December 31, 2012 Shire paid success milestones and other support costs of $3.0 million (2011: $2.5 million; 2010: $4.0 million) and $8.1 million (2011: $5.3 million; 2010: $2.3 million) to Santaris respectively, which were expensed to R&D. Shire has remaining obligations to pay Santaris $13.5 million subject to certain success criteria, and development and sales milestones up to a maximum of $69.0 million for each indication. Shire will also pay single or double digit tiered royalties on net sales of the product.

Shire and Santaris have formed a joint research committee to monitor R&D activities through preclinical lead candidate selection at which point all development and commercialization costs will be the responsibility of Shire.

(iii) Collaboration and license agreement with Sangamo to develop therapeutics for hemophilia

On February 1, 2012 Shire and Sangamo announced that they had entered into a collaboration and license agreement to develop therapeutics for hemophilia and other monogenic diseases based on Sangamo's ZFP technology. Sangamo is responsible for all activities through submission of Investigational New Drug Applications and European Clinical Trial Applications for each product and Shire will reimburse Sangamo for its internal and external research program-related costs. Shire is responsible for clinical development and commercialization of products arising from the collaboration.

In the year to December 31, 2012 Shire made an upfront payment to Sangamo of $13.0 million, for technology access and R&D funding, which was expensed to R&D.

In the year to December 31, 2012 Shire's share of R&D costs under this collaboration agreement was $8.9 million (2011: $nil; 2010: $nil) which were expensed to R&D. Shire may be required to pay research, regulatory, development and commercial milestone payments up to a maximum of $213.5 million and to pay royalties on net sales of the product.

(iv) Acquisition of FerroKin

On April 2, 2012 Shire completed the acquisition of 100% of the outstanding share capital of FerroKin. The acquisition-date fair value of consideration totaled $159.3 million, comprising cash consideration paid on closing of $94.5 million and the fair value of contingent consideration payable of $64.8 million. The maximum amount of contingent cash consideration which may be payable by Shire in future periods is $225.0 million. The amount of contingent cash consideration ultimately payable by Shire is dependent upon the achievement of certain clinical development, regulatory and net sales milestones.

(v) Acquisition of certain assets & liabilities of Pervasis

On April 19, 2012 Shire acquired substantially all the assets and certain liabilities of Pervasis. The acquisition date fair value of the consideration totaled $26.1 million, comprising cash consideration paid on closing of $2.5 million and the fair value of contingent consideration payable of $23.6 million. The maximum

amount of contingent cash consideration which may be payable by Shire in future periods is $169.5 million. The amount of contingent cash consideration ultimately payable by Shire is dependent upon achievement of certain clinical development, regulatory and net sales milestones.

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 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, 2012 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.

The Company incurs interest at a fixed rate of 2.75% on its $1,100 million in principal amount convertible bonds due 2014.

No derivative instruments were entered into during the year to December 31, 2012 to manage interest rate exposure. The Company continues to review its interest rate risk and the policies in place to manage the risk.

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 and specific external receivables. 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, 2012 the Company had 19 swap and forward foreign exchange contracts outstanding to manage currency risk. The swaps and forward contracts mature within 90 days. The Company did not have credit risk related contingent features or collateral linked to the derivatives. At December 31, 2012 the fair value of these contracts was a net liability of $1.7 million. 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, 2012):

	Increase/(reduction) in revenues $M	Increase/(reduction) in net income $M
Euro	(76)	(42)

Pound Sterling	(22)	(2)
Swiss Franc	-	30

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.

December 31, 2012	**Principal Value of Amount Receivable $'M**	**Weighted Average Exchange Rate**	**Fair Value $'M**
Swap foreign exchange contracts			
Receive USD/Pay EUR	213.7	1.30	(2.8)
Receive GBP/Pay USD	117.5	1.61	1.1
Receive USD/Pay CAD	7.8	1.01	0.1
Receive USD/Pay SEK	9.0	0.15	(0.2)
Receive USD/Pay AUD	2.5	1.04	-
Receive USD/Pay MXN	3.6	0.08	0.1

Concentration of credit risk

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

The Company is exposed to the credit risk of the counterparties with which it enters into 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, 2012 there were three customers in the US that accounted for 50% of the Company's product sales. However, such customers typically have significant cash resources and as such the risk from concentration of credit is considered acceptable. The Company has taken positive steps to manage any credit risk associated with these transactions and operates clearly defined credit evaluation procedures. However, an inability of one or more of these wholesalers to honor their debts to the Company could have an adverse effect on the Company's financial condition and results of operations.

A substantial portion of the Company's accounts receivable in countries outside of the United States is derived from product sales to government-owned or government-supported healthcare providers. The Company's recovery of these accounts receivable is therefore dependent upon the financial stability and creditworthiness of the relevant governments. In recent years the creditworthiness and general economic condition of the Relevant Countries has deteriorated. As a result, in some of these countries the Company is experiencing delays in the remittance of receivables due from government-owned or government-supported healthcare providers.

The Company's aggregate accounts receivable, net of the allowance for doubtful accounts, in total from government-owned or government-supported healthcare providers in the Relevant Countries are as follows:

3. Financial review

	December 31, 2012 $'M	December 31, 2011 $'M
Total accounts receivable, net in the Relevant Countries	137	184
Total accounts receivable, net in the Relevant Countries as a percentage of total outstanding accounts receivable, net	17%	22%
Accounts receivable, net due from government-owned or government-supported healthcare providers for the Relevant Countries	130	170

Accounts receivable due from government-owned or government-supported healthcare providers in the Relevant Countries of $130 million (2011: $170 million) are split by country as follows: Greece $6 million (2011: $4 million); Ireland $1 million (2011: $1 million); Italy $62 million (2011: $81 million); Portugal $13 million (2011: $14 million) and Spain $48 million (2011: $70 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, 2012 received $280.2 million in settlement of accounts receivable in the Relevant Countries - $4 million was from Greece; $142.3 million from Italy; $15.2 million from Portugal and $118.7 million from Spain.

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 sovereign 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 Eurozone countries suffer significant deterioration, such that their ability to make payments becomes uncertain, or if one or more Eurozone member countries withdraws from the Euro, 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.

Graham Hetherington
Chief Financial Officer

4. Principal risks and uncertainties

Principal risks and uncertainties

The Group has adopted a risk management strategy designed to identify, assess and manage the significant risks that it faces. While the Group aims to identify and manage such risks, no risk management strategy can provide absolute assurance against loss.

Mitigation of principal risks

The management and mitigation of risks are a key focus for the Group. The Group has established a Risk Council which is supported by the Global Compliance and Risk Management ("GCRM") Department to oversee the management and mitigation of the principal risks faced by the Group, as set out below.

Risk Council

The Risk Council is charged with overseeing the Group's risk management process and activities. Chaired by the Chief Compliance and Risk Officer, the Risk Council's membership includes senior members of the Group's business units and corporate functions, in addition to the Head of Internal Audit. Each business unit and corporate function is required to periodically review the significant risks facing their business or function, and are provided with a framework to use in their review. This review, which occurs biannually, includes identifying operational risks, compliance risks and risks to the achievement of goals and objectives. The Risk Council ensures that there is an owner who is responsible for the management or mitigation of each identified risk. Material risks and associated mitigation plans are recorded on a corporate risk schedule for ongoing review and assessment by the Risk Council.

The risk schedule is also reviewed and validated by the Leadership Team. In addition, the risk schedule is reviewed biannually by the Audit, Compliance and Risk ("ACR") Committee, and annually by the Board.

GCRM

The Risk Council is assisted by the GCRM Department, which is responsible for supporting the development and implementation of practices that facilitate employees' compliance with laws and Company policy. The GCRM Department provides assistance to help employees meet high ethical standards and comply with applicable laws and regulations.

The principal focus of Shire's compliance effort is to prevent and detect misconduct or non-compliance with laws or regulations through the promotion of ethical behavior, policy development, appropriate training, monitoring and audit. Shire employees are encouraged to seek help and to report suspected cases of misconduct and to do so without fear of retaliation. Employees can report suspected cases of misconduct to management or through the confidential reporting lines managed by the GCRM Department. Concerns and allegations are fairly and independently investigated and appropriate disciplinary action is taken if warranted.

The GCRM Department is managed by the Chief Compliance and Risk Officer, who reports directly to the CEO. The Chief Compliance and Risk Officer chairs the Risk Council and regularly provides summary reports on the Risk Council and Compliance activities to the ACR Committee. The Chief Compliance and Risk Officer has access at all times to the Chairman of the ACR Committee which provides a mechanism for bypassing the executive management should the need ever arise.

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

4. Principal risks and uncertainties

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 and the time taken to obtain them, the scope of marketing approvals as reflected in the product's label, 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 the physician's 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 or if 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, payors 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;
- loss of patent protection or other forms of exclusivity, or the ability of competitors to challenge or circumvent patents or other forms of exclusivity;
- if planned geographical expansion into new markets is not successful;
- if the sizes of the patient populations for the Company's products are less than expected; or
- if there are lawsuits filed against the Company, including but not limited to, product liability claims, consumer law claims, and payor or reimbursement litigation.

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

Revenues from ADDERALL XR are subject to generic erosion

During 2012 the FDA clarified the regulatory pathway required for approval of generic versions of ADDERALL XR and in June 2012 Actavis received approval to launch its own generic version of ADDERALL XR. Shire sells authorized generic versions of ADDERALL XR to Teva and Impax and also continues to sell the branded version of ADDERALL XR.

Revenues from ADDERALL XR have declined as a result of these developments and could decline further if:

- generic or authorized generic versions of ADDERALL XR capture more of Shire's branded market share;
- the FDA approves additional ANDAs for generic versions of ADDERALL XR which could further reduce branded market share;
- the production of 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 US Drug Enforcement Agency ("DEA");
- there are changes in reimbursement policies of third-party payors; or
- there are changes to the level of sales deductions for ADDERALL XR for private or public payors.

4. Principal risks and uncertainties

The failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payors in a timely manner for the Company's products may impact future revenues and earnings

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.

The market for the Company's products could be significantly influenced by the following, which could result in lower prices for the Company's products and/or a reduced demand for the Company's products:

- higher levels of controls on the use of the Company's products and/or requirements for additional price concessions 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; or
- price controls, unsuccessful government tenders, or non-reimbursement of new medicines or new indications for which the health economic (i.e. cost/benefit) rationales are not well established.

The cost of treatment for some of the Company's products is high, in particular REPLAGAL, ELAPRASE and VPRIV which are used for the treatment of certain rare genetic 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 relies on a single source for manufacture of certain of its products. A disruption to the supply chain for these 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

The Company sources some products from third party contract manufacturers, and for certain products has its own manufacturing capability. 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, FIRAZYR, FOSRENOL, INTUNIV, LIALDA, PENTASA, RESOLOR and VPRIV (in the US), relies on a single active ingredient source for each of ELAPRASE, FIRAZYR, FOSRENOL, INTUNIV, REPLAGAL, RESOLOR and VPRIV (in the US) and relies on a single source for certain serum reagents, the mesh framework and the manifold used in the manufacture of DERMAGRAFT.

The Company uses third party manufacturers to manufacture many of its products and is reliant upon third party contractors for certain goods and services. Any inability of these third party manufacturers to manufacture products, or any failure of these third party contractors to provide these goods and services, in each case in accordance with its respective contractual obligations, could adversely affect the Company's ability to manage its manufacturing processes or to operate its business

The Company may experience supply failures or delays beyond its control 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 third party 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 operate its business. If the third party does not provide the goods or services on the agreed basis and within the specified timeframe, the Company may not be able to continue the development or commercialization of its products as planned or on a commercial basis.

4. Principal risks and uncertainties

The development, approval and manufacturing of the Company's products is subject to extensive oversight by various regulatory agencies

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

The development and approval of the Company's products depends 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 which could delay the manufacturing process.

US-based manufacturers must be registered with the DEA and similar regulatory authorities 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.

The Company manufactures VPRIV, ELAPRASE, REPLAGAL, and DERMAGRAFT using complex biological processes. The complexity of the manufacturing results in a number of risks, including the risk of viral or other contamination.

Regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes 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 and results of operations.

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 impact 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 2012, for example, 50% of the Company's product sales were attributable to three customers in the US: McKesson Corp., Cardinal Health, Inc and AmerisourceBergen 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 could 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 genetic diseases are concentrated with 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 the distraction of senior management, 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 Health and Human Services, the FDA, the US Department of Justice, the US Securities and Exchange Commission 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 federal laws relating to the 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 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.

Adverse outcomes in legal matters and other disputes 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, employment claims and disputes, intellectual property claims and disputes, contract claims and disputes, product liability claims and disputes, regulatory litigation and tax 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.

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 continued instability of the Eurozone, 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 also reduce the level of reimbursement that governments 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.

Any slowing economic environment may also lead to financial difficulties for some of the Company's significant customers. In such situations, the Company could experience delays in payment or non-payment of amounts owed which may result in a rising level of contractual defaults by its contractual counterparties.

The Company does business, both directly (with government hospitals, clinics, pharmacies and other agencies) and indirectly (through wholesalers and distributors), with a number of Eurozone governments, including the governments of Greece, Ireland, Italy, Portugal and Spain. These and other countries have experienced, and may continue to experience, declines in their creditworthiness. These events could in turn result in these countries making significant cuts to their public spending, including national healthcare budgets, in an attempt to manage their budget deficits, or could result in a greater risk of default or non-payment of outstanding payment obligations, any of which could adversely affect the Company's revenues, financial condition or results of operations.

In addition, there are concerns for the overall stability and suitability of the Euro as a single currency, given the economic and political challenges facing individual Eurozone countries. Continuing deterioration in the creditworthiness of Eurozone countries, the withdrawal of one or more member countries from the EU, or the failure of the Euro as a common European currency could adversely affect the Company's revenues, financial condition or results of operations.

4. Principal risks and uncertainties

The introduction of new products by competitors may impact future revenues

The markets in which the Company operates are highly competitive. Many of the Company's competitors are large, well-known pharmaceutical, biotechnology, chemical and healthcare companies with considerable resources. Companies with more resources and larger R&D expenditures have a greater ability to fund clinical trials and other development work necessary for regulatory applications. They may also be more successful than the Company in acquiring or licensing new products for development and commercialization. If any product that competes with one of the Company's principal drugs is approved, the Company's sales of that drug could be negatively impacted.

The pharmaceutical, biotechnology and device industries are also characterized by continuous product development and technological change. The Company's products could, therefore, be rendered obsolete or uneconomic, through the development of new products, new methods of treatment, or technological advances in manufacturing or production by its competitors which may impact future revenues.

The successful development of products is highly uncertain and requires significant expenditures and time

Products that 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
- the product may fail to receive necessary regulatory approvals.

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. 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.

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

The Company enters into strategic partnerships with other companies in areas such as product development and 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.

4. Principal risks and uncertainties

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

In the regular course of business, the Company is party to litigation or other proceedings relating to intellectual property rights.

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.

Loss of highly qualified personnel could cause the Company subsequent financial loss

The Company faces competition for highly qualified personnel from other companies, academic institutions, government entities and other organizations. It may not be able to successfully attract and retain such personnel. The Company has agreements with a number of its key personnel for periods of one year or less. The loss of such personnel, or the inability to attract and retain the additional, highly skilled employees required for its activities could have an adverse effect on the Company's business.

5. Directors' responsibility statement

Each of the current Directors, whose names and functions are listed below, confirms that, to the best of his or her knowledge:

(i) the Group financial statements, which have been prepared under accounting principles generally accepted in the United States ("US GAAP"), present fairly, in all material respects, the financial condition, results of operations and cash flows of the Group; and

(ii) the Business review 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 they face.

Matthew Emmens	– Chairman
Angus Russell	– Chief Executive Officer
Dr. Flemming Ornskov	– Chief Executive Officer Designate
Graham Hetherington	– Chief Financial Officer
David Kappler	– Non-Executive Director
William Burns	– Non-Executive Director
Dr. Steven Gillis	– Non-Executive Director
Dr. David Ginsburg	– Non-Executive Director
Susan Kilsby	– Non-Executive Director
Anne Minto OBE	– Non-Executive Director
David Stout	– Non-Executive Director

The following are trade marks either owned or licensed by Shire plc or companies within the Shire group which are the subject of trade mark 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)
CARBATROL® (carbamazepine extended-release capsules)
DAYTRANA® (trade mark of Noven Pharmaceutical Inc.
DERMAGRAFT® (human fibroblast-derived dermal substitute)
ELAPRASE® (idursulfase)
ELVANSE® (lisdexamfetamine dimesylate)
EQUASYM® (methylphenidate hydrochloride)
EQUASYM XL® (methylphenidate hydrochloride)
FIRAZYR® (icatibant)
FOSRENOL® (lanthanum carbonate)
INTUNIV® (guanfacine extended release)
LIALDA® (trade mark of Nogra International Limited
MEZAVANT® (trade mark of Giuliani International Limited)
PENTASA® (trade mark of Ferring B.V. Corp
REMINYL® (galantamine hydrobromide) (United Kingdom and Republic of Ireland) (trade mark of Johnson & Johnson, excluding UK and Republic of Ireland)
REMINYL XL™ (galantamine hydrobromide) (UK and Republic of Ireland) (trade mark of J&J, excluding UK and Republic of Ireland)
REPLAGAL® (agalsidase alfa)
RESOLOR® (prucalopride)
TYVENSE® (lisdexamfetamine dimesylate)
VENVANSE® (lisdexamfetamine dimesylate)
VPRIV® (velaglucerase alfa)
VYVANSE® (lisdexamfetamine dimesylate)
XAGRID® (anagrelide hydrochloride)
ZEFFIX® (trade mark of GSK)
3TC® (trade mark of GSK)