

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549
FORM 10-K

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2008
- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission file number 0-29630

SHIRE PLC

(Exact name of registrant as specified in its charter)

Jersey (Channel Islands)

(State or other jurisdiction of incorporation or organization)

98-0601486

(I.R.S. Employer Identification No.)

**5 Riverwalk, Citywest Business Campus, Dublin
24, Republic of Ireland**

(Address of principal executive offices and zip code)

+353 1 429 7700

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class

Name of exchange on which registered

American Depositary Shares, each representing three
Ordinary Shares 5 pence par value per share

NASDAQ Global Select Market

Securities registered pursuant to Section 12(g) of the Act:

None

(Title of class)

Indicate by check mark whether the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act

Yes No

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act

Yes No

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the Registrant's knowledge, in definitive proxy or information statements incorporated by reference to Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes No

As at June 30, 2008, the last business day of the Registrant's most recently completed second quarter, the aggregate market value of the ordinary shares, £0.05 par value per share of the Registrant held by non-affiliates was approximately \$9,173 million. This was computed using the average bid and asked price at the above date.

As at February 20, 2009, the number of outstanding ordinary shares of the Registrant was 560,222,583.

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, the Company's results could be materially adversely affected. The risks and uncertainties include, but are not limited to, risks associated with: the inherent uncertainty of research, development, approval, reimbursement, manufacturing and commercialization of the Company's Specialty Pharmaceuticals and Human Genetic Therapies products, as well as the ability to secure and integrate new products for commercialization and/or development; government regulation of the Company's products; the Company's ability to manufacture its products in sufficient quantities to meet demand; the impact of competitive therapies on the Company's products; the Company's ability to register, maintain and enforce patents and other intellectual property rights relating to its products; the Company's ability to obtain and maintain government and other third-party reimbursement for its products; and other risks and uncertainties detailed from time to time in the Company's filings with the Securities and Exchange Commission.

The following are trademarks of Shire plc or its subsidiaries, which are the subject of trademark registrations in certain territories.

ADDERALL XR[®] (mixed salts of a single entity amphetamine)
ADDERALL[®] (mixed salts of a single entity amphetamine)
AGRYLIN[®] (anagrelide hydrochloride)
CALCICHEW[®] range (calcium carbonate with or without vitamin D₃)
CARBATROL[®] (carbamazepine extended-release capsules)
DAYTRANA[®] (methylphenidate transdermal system)
ELAPRASE[®] (idursulfase)
FIRAZYR[®] (icatibant)
FOSRENOL[®] (lanthanum carbonate)
INTUNIV[™] (guanfacine extended release)
LIALDA[®] (mesalamine)
METAZYM[™] (arylsulfatase-A)
MEZAVANT[®] (mesalazine)
REMINYL[®] (galantamine hydrobromide) (United Kingdom (“UK”) and Republic of Ireland)
REMINYL XL[™] (galantamine hydrobromide) (UK and Republic of Ireland)
REPLAGAL[®] (agalsidase alfa)
VYVANSE[®] (lisdexamfetamine dimesylate)
XAGRID[™] (anagrelide hydrochloride)

The following are trademarks of third parties referred to in this Form 10-K.

3TC (trademark of GlaxoSmithKline (“GSK”))
AMIGAL (trademark of Amicus Therapeutics (“Amicus”))
ASACOL (trademark of Proctor and Gamble)
ATRIPLA (trademark of Bristol Myers Squibb Company (“BMS”) and Gilead Sciences (“Gilead”))
BERINERT P (trademark of CSL Behring)
CEREZYME (trademark of Genzyme Corporation (“Genzyme”))
CLAVERSAL (trademark of Merckle Recordati)
COLAZAL (trademark of Salix)
COMBIVIR (trademark of GSK)
CONCERTA (trademark of Alza Corporation)
DIPENTUM (trademark of UCB S.A. (“UCB”))
DYNEPO (trademark of Sanofi-Aventis)
EPIVIR (trademark of GSK)
EPIVIR-HBV (trademark of GSK)
EPZICOM/KIVEXA (EPZICOM) (trademark of GSK)
EQUASYM[®] IR (trademark of UCB)
EQUASYM[®] XL (trademark of UCB)
EQUETRO (trademark of Validus Pharmaceuticals)
FABRAZYME (trademark of Genzyme)
FOCALIN XR (trademark of Novartis)
FUZEON (trademark of Roche)
HEPTOVIR (trademark of GSK)
JUVISTA (trademark of Renovo)

KALETRA (trademark of Abbott Laboratories (“Abbott”))
METADATE CD (trademark of UCB)
MICROTROL (trademark of Supernus)
PENTASA (trademark of Ferring)
PLICERA (trademark of Amicus)
RAZADYNE (trademark of Johnson & Johnson)
RAZADYNE ER (trademark of Johnson & Johnson)
REMINYL (trademark of Johnson & Johnson, excluding UK and Republic of Ireland)
REMINYL XL (trademark of Johnson & Johnson, excluding UK and Republic of Ireland)
RETROVIR (trademark of GSK)
REYATAZ (trademark of BMS)
RHUCIN (trademark of Pharming Group)
RITALIN LA (trademark of Novartis)
SALOFALK (trademark of Dr Falk Pharma)
SEASONIQUE (trademark of Barr Laboratories)
SOLARAZE (trademark of Laboratorios Almirall (“Almirall”))
STRATTERA (trademark of Eli Lilly)
SUSTIVA (trademark co-owned DuPont Pharmaceuticals and Merck)
TRIZIVIR (trademark of GSK)
TRUVADA (trademark of Gilead)
VANIQA (trademark of Almirall)
VIDEX (trademark of BMS)
VIRAMUNE (trademark of Boehringer-Ingelheim)
VIREAD (trademark of Gilead)
ZEFFIX (trademark of GSK)

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PART I

ITEM 1: Business

General

Shire plc and its subsidiaries (collectively referred to as either “Shire” or the “Company”) is a leading specialty biopharmaceutical company that focuses on meeting the needs of the specialist physician.

Shire plc (formerly known as Shire Limited) was incorporated under the laws of Jersey (Channel Islands) on January 28, 2008 and is a public limited company. Following the implementation of a court sanctioned Scheme of Arrangement, on May 23, 2008 Shire plc (formerly known as Shire Limited) replaced the former Shire plc, which was a public limited company incorporated in England and Wales, as the new holding company for Shire.

The Company has grown through acquisition, completing nine major mergers or acquisitions in a fourteen-year period from 1994 to 2008. Divestments of non-core assets over the past four years have streamlined the Company’s operations. The Company will continue to evaluate companies, products and project opportunities that offer a good strategic fit and enhance shareholder value.

Strategy

Shire’s strategic goal is to become the leading specialty biopharmaceutical company that focuses on meeting the needs of the specialist physician. Shire focuses its business on attention deficit and hyperactivity disorder (“ADHD”), human genetic therapies (“HGT”), and gastrointestinal (“GI”) diseases as well as opportunities in other therapeutic areas to the extent they arise through acquisitions. Shire’s in-licensing, merger and acquisition efforts are focused on products in specialist markets with strong intellectual property protection and global rights. Shire believes that a carefully selected and balanced portfolio of products with strategically aligned and relatively small-scale sales forces will deliver strong results.

2008 Highlights

For a full discussion of the 2008 Product, Pipeline and Business Highlights, including:

- the approval by the US Food and Drug Administration (“FDA”) of the adult indication of VYVANSE for the treatment of ADHD in the US market in April 2008 and the launch of the additional 20mg, 40mg, and 60mg dosage strengths in July 2008;
- the completion, in May 2008, of the court sanctioned Scheme of Arrangement through which Shire plc, a Jersey incorporated and Irish tax resident company, became the holding company for Shire;
- the acquisition in June 2008 of the global rights to METAZYM, for the treatment of Metachromatic Leukodystrophy, from Zymenex A/S (“Zymenex”); and
- the acquisition of more than 98% of Jerini AG (“Jerini”) during the second half of 2008, adding Jerini’s hereditary angioedema (“HAE”) product FIRAZYR, an approved product in the EU, to the portfolio,

see ITEM 1: Business and ITEM 5: Market for Registrant’s common equity, related stockholder matters and issuer purchases of equity securities.

Liquidity

Shire’s robust balance sheet includes \$218.2 million of cash and cash equivalents at December 31, 2008. We generated \$800.1 million of cash from operating activities during the year. Shire has no debt or facilities maturing in the next three years and substantially all of Shire’s debt relates to its \$1.1 billion 2.75% convertible bond which matures in 2014, although these include a put option which could require repayment in 2012. In addition, Shire has a committed facility until 2012 of \$1.2 billion, which is currently undrawn. For a full discussion see Liquidity and Capital Resources in ITEM 7: Management’s Discussion and Analysis of Financial Condition and Results of Operations.

Financial information about operating segments

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 two operating segments: Specialty Pharmaceuticals and HGT. The Company also earns royalties (where Shire has out-licensed products to third parties) which are recorded as revenues within "All Other" in the segmental analysis. Segment revenues, profits or losses and assets for 2008, 2007 and 2006 are presented in Note 27 to the Company's consolidated financial statements contained in Part IV of this Annual Report.

Sales and marketing

At December 31, 2008, the Company employed 1,596 (2007: 1,563) sales and marketing staff to service its operations throughout the world, which included its major markets in the US, Europe and Canada.

Currently marketed products

The table below lists the Company's key marketed products as at December 31, 2008, indicating the owner, licensor, disease area and the key territories in which Shire markets the product.

Specialty Pharmaceuticals

<u>Products</u>	<u>Disease area</u>	<u>Owner/licensor</u>	<u>Key territory</u>
Treatments for ADHD			
VYVANSE (lisdexamfetamine dimesylate)	ADHD	Shire	US
DAYTRANA (methylphenidate transdermal system)	ADHD	Noven Pharmaceuticals, Inc. ("Noven")	US
ADDERALL XR (mixed salts of a single-entity amphetamine)	ADHD	Shire	US and Canada
Treatments for GI diseases			
PENTASA (mesalamine)	Ulcerative colitis	Shire	US
LIALDA (mesalamine)/MEZAVANT(mesalazine)	Ulcerative colitis	Giuliani SpA	US and Europe ⁽¹⁾
Treatments for diseases in other therapeutic areas			
FOSRENOL (lanthanum carbonate)	Hyperphosphatemia in end stage renal disease	Shire	US and Europe ⁽²⁾
CALCICHEW (calcium carbonate range)	Adjunct in osteoporosis	Nycomed Pharma AS	UK and Republic of Ireland
CARBATROL (carbamazepine extended-release capsules)	Epilepsy	Shire	US
REMINYL/REMINYL XL (galantamine hydrobromide)	Alzheimer's disease	Synaptech, Inc. ("Synaptech")	UK and Republic of Ireland ⁽³⁾
XAGRID (anagrelide hydrochloride)	Elevated platelet counts in at risk essential thrombocythemia patients	Shire	Europe ⁽²⁾

Human Genetic Therapies

<u>Products</u>	<u>Disease area</u>	<u>Owner/licensor</u>	<u>Key territory</u>
REPLAGAL (algalsidase alfa)	Fabry disease	Shire	Europe, Canada, Latin America and Asia Pacific ⁽⁴⁾
ELAPRASE (idursulfase)	Hunter syndrome (Mucopolysaccharidosis Type II)	Shire	US, Europe, Latin America and Asia Pacific ⁽⁵⁾
FIRAZYR (icatibant)	Hereditary angioedema	Shire	Europe

⁽¹⁾ Marketed in US as LIALDA and Europe as MEZAVANT XL, MEZAVANT, OR MEZAVANT LP

⁽²⁾ Marketed by distributors in certain markets

⁽³⁾ Marketed in rest of world ("ROW") under license from Shire by Janssen Pharmaceutica N.V. ("Janssen") (part of the Johnson & Johnson group of companies)

⁽⁴⁾ Marketed in Japan under license from Shire by Dainippon Sumitomo Pharma Co., Ltd. ("DSP")

⁽⁵⁾ Marketed in Japan under license from Shire by Genzyme

Specialty Pharmaceuticals

Treatments for ADHD

ADHD is estimated to affect 7.8% of US children aged 4 to 17, according to the US Centers for Disease Control and Prevention ("the CDC"). Symptoms present themselves as impulsivity/hyperactivity, inattention or both. In up to 65% of children affected by this disorder, symptoms will persist into adulthood (according to the CDC), with estimates of approximately 9.9 million adults in the United States having ADHD (according to IMS Health ("IMS")). According to IMS, a leading global provider of business intelligence for the pharmaceutical and healthcare industries, the US market for ADHD treatments was valued at approximately \$4.0 billion for the year to December 31, 2008, an increase of 7% from the year to December 31, 2007.

VYVANSE

VYVANSE is a new chemical entity for the treatment of ADHD and is the first pro-drug stimulant, where the amino acid l-lysine is linked to d-amphetamine, which is therapeutically inactive until metabolized in the body.

VYVANSE was approved by the FDA in February 2007 for the treatment of ADHD in pediatric patients aged 6 to 12. VYVANSE was launched in the US in July 2007 in three dosage strengths: 30mg, 50mg and 70mg, all indicated for once-daily dosing.

In December 2007 the FDA approved VYVANSE in 20mg, 40mg and 60mg dosage strengths, which are designed to increase the dosing flexibility of VYVANSE. The new dosage strengths were made available in retail pharmacies in July 2008.

In April 2008 the FDA approved the adult indication for VYVANSE, making it the first and only once-daily pro-drug stimulant approved to treat adults with ADHD. Shire launched VYVANSE for adult ADHD in June 2008.

On February 24, 2009 Actavis Elizabeth LLC brought a lawsuit against the FDA seeking to overturn the FDA's decision granting new chemical entity exclusivity to VYVANSE. Shire believes the FDA's decision was correct. VYVANSE has new chemical entity exclusivity through February 23, 2012 and patents listed in the Orange Book which expire on June 29, 2023.

DAYTRANA

DAYTRANA is a methylphenidate transdermal delivery system for the once daily treatment of ADHD. DAYTRANA, launched in the US in June 2006, is the first and only patch medication approved by the FDA to treat the symptoms of pediatric ADHD. It is available in four dosage strengths of 10mg, 15mg, 20mg and 30mg, all designed for once-daily use. When worn for the recommended nine hours, efficacy has been demonstrated from the first time point measured (at two hours) through the 12-hour time point. Shire in-licensed the worldwide royalty-free sales and marketing rights to DAYTRANA from Noven in 2003.

In January 2008 the FDA issued a Warning Letter to Noven relating to Noven's manufacture of DAYTRANA and the difficulties that had been experienced in removing the release liner of the patch. Noven submitted a response to the FDA on January 30, 2008. The FDA is currently working with Noven to resolve the issues cited in the Warning Letter.

In June and August, 2008 Shire announced voluntary recalls of a limited portion of DAYTRANA patches because certain patches did not meet their release liner removal specifications which may have resulted in some patients and caregivers having difficulties removing the liners. The voluntary recall was not due to safety issues. Shire and Noven continue to pursue enhancements to the product and to work closely with the FDA to implement changes that may improve the usability of DAYTRANA. There has been no interruption in the production of DAYTRANA.

ADDERALL XR

ADDERALL XR is an extended release treatment for ADHD, which uses MICROTROL drug delivery technology and is designed to provide once daily dosing. It is available in 5mg, 10mg, 15mg, 20mg, 25mg and 30mg capsules and can be administered either as a capsule or sprinkled on soft food.

The FDA approved ADDERALL XR as a once-daily treatment for children aged 6 to 12 with ADHD in October 2001, for adults in August 2004 and for adolescents (aged 13 to 17) in July 2005.

In October 2005 the Company filed a Citizen Petition with the FDA requesting that the FDA require more rigorous bioequivalence testing or additional clinical testing for generic or follow-on drug products that reference ADDERALL XR before they can be approved. The Company received correspondence from the FDA in April 2006 stating that, due to the complex issues raised, which require extensive review and analysis by the FDA's officials, a decision cannot yet be reached by the FDA. The FDA did not provide any guidance as to when that decision may be reached.

Litigation proceedings relating to the Company's ADDERALL XR patents are in progress. For further information see ITEM 3: Legal Proceedings. In addition the US Federal Trade Commission ("FTC") is reviewing the ADDERALL XR patent litigations settlement with Barr Laboratories, Inc. ("Barr") and Impax Laboratories, Inc. ("Impax"). For further information see ITEM 7: Management's Discussion and Analysis of Financial Condition and Results of Operations.

Treatments for GI diseases

Ulcerative Colitis was estimated to affect approximately 1.2 million patients worldwide in 2007 according to Decision Resources, Immune and Inflammatory Disorders Study #4, Ulcerative Colitis, (August 2008). Ulcerative colitis is a serious chronic inflammatory disease of the colon in which part, or all, of the large intestine becomes inflamed and often ulcerated. Typically, patients go through periods of relapse and remission and can suffer from diarrhea, bleeding and abdominal pain. Once diagnosis is confirmed, patients are usually treated for life. The first line treatment for inflammatory bowel disease is with mesalamine (5-aminosalicylic acid ("5-ASA")) based products.

PENTASA

PENTASA controlled release capsules are indicated for the induction of remission and for the treatment of patients with mild to moderately active ulcerative colitis.

PENTASA is an ethylcellulose-coated, controlled release capsule formulation designed to release therapeutic quantities of mesalamine throughout the gastrointestinal tract. PENTASA is available in the US in 250mg and 500mg capsules.

In September 2008 the Company filed a Citizen Petition with the FDA requesting that the FDA require more rigorous bioequivalence testing for generic or follow-on drug products that reference PENTASA before they can be approved. To date, there has been no substantive action on this Citizen Petition by the FDA.

LIALDA/MEZAVANT

LIALDA is indicated for the induction of remission in patients with mild to moderately active ulcerative colitis. LIALDA is the first and only FDA-approved once-daily oral formulation of mesalamine for induction of remission. Once-daily LIALDA contains the highest mesalamine dose per tablet (1.2g), so patients can take as few as two tablets once daily.

LIALDA was approved by the FDA in January 2007 and was launched in the US in March 2007. Following completion of the EU decentralized registration procedure, the product received national approval in 15 EU countries. The first EU launch was in the UK in November 2007. By the end of 2008 LIALDA/MEZAVANT was available in a total of six countries. Preparations are underway for further European launches, subject to the successful conclusion of pricing and reimbursement negotiations.

In April 2008, TAP Pharmaceutical Products Inc. ("TAP") commenced co-promotion of LIALDA in the US in accordance with the co-promotion agreement entered into in March 2008. This agreement adds more than 500 additional sales representatives from TAP which will increase the reach and frequency of sales calls covering an additional 22,000 doctors

The Company has in-licensed the exclusive royalty-bearing rights to LIALDA/MEZAVANT in the US, Canada, Europe (excluding Italy) and the Pacific Rim from Giuliani S.p.A.

Treatments for diseases in other therapeutic areas

FOSRENOL

FOSRENOL is a phosphate binder that is indicated for use in end-stage renal failure patients receiving dialysis. It is estimated that there are approximately 1.5 million patients worldwide with end-stage renal disease on dialysis. In this condition the kidneys are unable to regulate the balance of phosphate in the body. If untreated, the resultant retention and elevated blood phosphate levels (hyperphosphatemia) can combine with other biochemical disturbances and result in bone disorders described as chronic kidney disease mineral bone disorders ("CKD-MBD"). Research also suggests that hyperphosphatemia is associated with the development of cardiovascular disease which accounts for nearly 50% of deaths in dialysis patients.

FOSRENOL binds dietary phosphate in the gastrointestinal tract to prevent it from passing through the gut lining and, based upon this mechanism of action, phosphate absorption from the diet is decreased. Formulated as a convenient chewable tablet, FOSRENOL is available in 500mg, 750mg and 1,000mg dosage strengths in the US.

The FDA approved the 500mg dosage strength in October 2004, which launched in the US in January 2005 and the 750mg and 1,000mg dosage strengths were approved by the FDA in November 2005. At December 31, 2008 FOSRENOL was available in 30 countries worldwide.

In April 2008 Shire and Abbott Laboratories Inc. mutually agreed to terminate their Co-Promotion Agreement for FOSRENOL in the US. Shire will continue to promote FOSRENOL on its own in the US and throughout Europe.

In February 2009, Shire received three Paragraph IV Notice letters, from Barr, Mylan Inc. ("Mylan") and NATCO Pharma Limited ("NATCO") advising the filing of Abbreviated New Drug applications ("ANDA") for generic versions of 500mg, 750mg and 1,000mg FOSRENOL. Shire is currently reviewing the details of these notice letters and, under the Hatch-Waxman regulations, has 45 days from the date of each notice letter to determine if it will file a patent infringement suit. If Shire brings suit pursuant to the Hatch-Waxman regulations a 30 month stay of approval, commencing on October 26, 2009, will be imposed on the FDA on each ANDA which is the subject of such a lawsuit.

CALCICHEW range

The CALCICHEW range of calcium and calcium/vitamin D3 supplements are indicated for the adjunctive treatment of osteoporosis in the UK and Republic of Ireland. Osteoporosis is characterized by a progressive loss of bone mass that renders bone fragile and liable to fracture. More than 3 million people in the UK are estimated to suffer from this condition.

Shire has licensed from Nycomed Pharma AS the exclusive rights to distribute the CALCICHEW range of products in the UK and Republic of Ireland until December 31, 2012.

CARBATROL

CARBATROL is an anti-convulsant for individuals with epilepsy. Approximately 2.7 million people in the United States suffer from epilepsy, a disorder that is characterized by a propensity for recurrent seizures and is defined by two or more unprovoked seizures.

CARBATROL is an extended release formulation of carbamazepine that uses MICROTROL drug delivery technology. It is available in 100mg, 200mg and 300mg capsules and can be administered either as a capsule or sprinkled on food and delivers consistent blood levels of the drug over 24 hours, when taken twice daily. Carbamazepine is one of the most widely prescribed anti-epileptic drugs.

The FDA approved CARBATROL in September 1997 and it was launched in the US in June 1998. Pursuant to a promotional services agreement, Impax has promoted CARBATROL for the Company in the US since July 2006.

In October 2008 the Company filed a Citizen Petition with the FDA requesting that the FDA require more rigorous bioequivalence testing for generic or follow-on drug products that reference CARBATROL before they can be approved. To date, there has been no substantive action on this Citizen Petition by the FDA.

Litigation proceedings relating to the Company's CARBATROL patents are in progress. For further information see ITEM 3: Legal Proceedings.

REMINYL and REMINYL XL

REMINYL and REMINYL XL are indicated for the symptomatic treatment of mild to moderately severe dementia of the Alzheimer type. It is estimated in a report produced by King's College London and the London School of Economics that approximately 0.4 million people in the UK suffer from Alzheimer's disease ("AD"), which affects the ability to carry out normal daily activities and affects memory, language and behavior. The disease is progressive, with death usually occurring within eight to ten years following the onset of symptoms.

REMINYL and REMINYL XL are marketed by the Company in the UK and Republic of Ireland under a royalty-bearing license from Synaptech. In the rest of the world, they are marketed by Janssen, an affiliate of Johnson & Johnson and the Company receives royalties on Janssen's sales. REMINYL XL is a once-daily prolonged release formulation of REMINYL, which was launched by the Company in the UK and Republic of Ireland in June 2005.

Litigation proceedings relating to the REMINYL patents in the UK are in progress. For further information see ITEM 3: Legal Proceedings

XAGRID

Myeloproliferative disorders ("MPDs"), including essential thrombocythemia ("ET") and polycythemia vera, are a group of diseases in which one or more blood cell types are overproduced. In the case of platelets, which are involved in the blood clotting process, excess numbers can result in abnormal blood clot formation giving rise to events such as heart attack and stroke. Excessive platelet production can also lead to the formation of abnormal platelets, which may not be as effective in the clotting process. This can lead to events such as gastrointestinal bleeding.

Anagrelide hydrochloride is marketed as XAGRID in Europe for the reduction of elevated platelet counts in at risk ET patients. It was granted a marketing authorization in the EU in November 2004. XAGRID has been granted orphan drug status in the EU, providing it with up to ten years market exclusivity from November 2004.

In the US anagrelide hydrochloride is marketed (under the trade name AGRYLIN) for the treatment of thrombocythemia secondary to a MPD. Generic versions of AGRYLIN (anagrelide hydrochloride) have been available in this market since expiration of marketing exclusivity in 2005.

Human Genetic Therapies

REPLAGAL

REPLAGAL is a treatment for Fabry disease. Fabry disease is a rare, inherited genetic disorder resulting from a deficiency in the activity of the lysosomal enzyme alpha-galactosidase A, which is involved in the breakdown of fats. Although the signs and symptoms of Fabry disease vary widely from patient to patient, the most common include severe pain of the extremities, impaired kidney function often progressing to full kidney failure, early heart disease, stroke and disabling gastrointestinal symptoms. The disease is estimated to affect 1 in 40,000 males and is less frequent in females.

REPLAGAL is a fully human alpha-galactosidase A protein that replaces the deficient alpha-galactosidase A with an active enzyme to ameliorate the clinical manifestations of Fabry disease. In August 2001, REPLAGAL was granted marketing authorization and co-exclusive orphan drug status in the European Union with up to ten years market exclusivity.

REPLAGAL was launched in Japan in February 2007. As part of an agreement with DSP, DSP will manage the sale and distribution of REPLAGAL in Japan. As at December 31, 2008 REPLAGAL was approved in 43 countries.

ELAPRASE

ELAPRASE is a treatment for Hunter syndrome (also known as Mucopolysaccharidosis Type II or MPS II). Hunter syndrome is a rare, inherited genetic disorder mainly affecting males that interferes with the body's ability to break down and recycle waste substances called mucopolysaccharides, also known as glycosaminoglycans or GAGs. Hunter syndrome is one of several related lysosomal storage diseases. In patients with Hunter syndrome, cumulative buildup of GAGs in cells throughout the body interferes with the way certain tissues and organs function, leading to severe clinical complications and early mortality.

ELAPRASE was approved by the FDA in July 2006 and launched in the US during August 2006.

In January 2007 the European Medicines Agency ("EMA") granted marketing authorization for the use of ELAPRASE for the long-term treatment of patients with Hunter syndrome.

In October 2007 ELAPRASE received approval from the Ministry of Health, Labour and Welfare for the sale and marketing of ELAPRASE in Japan and in January 2008 ELAPRASE received approval for sale and marketing by the Therapeutic Goods Administration in Australia. As part of an agreement with Genzyme, Genzyme will manage the sales and distribution of ELAPRASE in Japan as well as certain other countries in the Asia Pacific region.

As at December 31, 2008 ELAPRASE was approved in 43 countries. ELAPRASE has been granted orphan drug status by both the FDA and the EMEA, providing it with up to seven and ten years market exclusivity in the US and EU, respectively, from the date of the grant of the relevant marketing authorization.

FIRAZYR

During the third quarter of 2008 Shire acquired a majority voting interest in Jerini and now owns more than 98% of its outstanding shares. The acquisition has added Jerini's HAE product, FIRAZYR, to the Shire portfolio. FIRAZYR is a first-in-class peptide-based therapeutic developed for the symptomatic treatment of acute attacks of HAE. HAE is a debilitating and potentially life-threatening genetic disease characterized by unpredictable recurring swelling attacks in the hands, feet, face, larynx, or abdomen.

Launches of FIRAZYR were initiated in some countries in Europe during 2008, following the receipt of marketing authorization from the EMEA in July 2008. Launches will continue across Europe once reimbursement negotiations conclude. FIRAZYR has orphan designation and is the first HAE product to receive approval throughout the European Union.

Royalties received from other products

Antiviral products

The Company receives royalties on antiviral products based on certain of the Company's patents licensed to GlaxoSmithKline plc ("GSK"). These antiviral products are for Human Immunodeficiency Virus ("HIV") and Hepatitis B. The table below lists these products, indicating the principal indications, the company responsible for marketing the product and the relevant territory.

<u>Products</u>	<u>Principal indications</u>	<u>Marketed by/relevant territory</u>
3TC/EPIVIR	HIV	Shire & GSK / Canada; GSK / RoW
COMBIVIR	HIV	Shire & GSK / Canada; GSK / RoW
TRIZIVIR	HIV	Shire & GSK / Canada; GSK / RoW
EPZICOM/KIVEXA	HIV	Shire & GSK / Canada; GSK / RoW
ZEFFIX/EPIVIR-HBV/ HEPTOVIR ⁽¹⁾	Hepatitis B infection	Shire & GSK / Canada; GSK / RoW

⁽¹⁾ This is not a comprehensive list of trademarks for this product. The product is also marketed under other trademarks in some markets.

HIV/AIDS

HIV is a retrovirus that has been isolated and recognized as the causative agent of Acquired Immunodeficiency Syndrome ("AIDS"). There are many strains of HIV throughout the world, although they all exhibit the same disease mechanism.

According to UNAIDS (a joint United Nations program on AIDS), in 2007 there were an estimated 33.2 million people worldwide living with HIV/AIDS, including 15.4 million women and 2.5 million children under the age of 15. In 2007 an estimated 2.7 million people became newly infected with HIV and there were 2 million AIDS related deaths. Of the new infections in 2007, 1.9 million occurred in Sub-Saharan Africa, and this region accounted for 1.5 million of the deaths. In an effort to combat the AIDS epidemic in Africa and reduce the cost of medicines used to treat AIDS in sub-Saharan Africa, the Company has waived a significant proportion of its royalty entitlements on sales of products containing lamivudine in this region.

Lamivudine was originally discovered by Shire Canada, Inc. (formerly Shire BioChem, Inc.), a wholly-owned subsidiary of the Company. Since 1990, Shire has licensed to GSK the worldwide rights, with the exception of Canada, to develop manufacture and sell lamivudine (now marketed in various single and combination formulations including 3TC/EPIVIR, COMBIVIR, TRIZIVIR and EPZICOM/KIVEXA). In Canada lamivudine is sold by Shire in partnership with GSK.

In 2007, generic drug companies filed ANDAs seeking approval for EPIVIR, COMBIVIR, ZEFFIX and EPZICOM in the US. Several tentative approvals of generic lamivudine have been issued by the FDA. Pursuant to the GSK/Shire license for lamivudine products, GSK has the right to enforce the licensed patents. In November 2007 GSK filed a patent infringement lawsuit against Teva Pharmaceuticals, Inc. ("Teva") in the US District Court for the District of Delaware for infringement of one of the patents relating to COMBIVIR. The patent, which covers the combination of zidovudine ("AZT") and lamivudine to treat HIV, expires in May 2012. Teva had filed an ANDA with the FDA with a certification of invalidity, unenforceability and non-infringement of that combination patent. Teva did not challenge two other patents relating to COMBIVIR that expire in 2010 and 2016. The case is in its early stages.

3TC/EPIVIR

3TC (lamivudine) is indicated in combination with other anti-retrovirals for the treatment of HIV-1 infection and was first approved in the US in November 1995. It is now marketed in the US as EPIVIR. Approval in Canada followed shortly after in December 1995 and in the EU in August 1996.

The safety and efficacy of 3TC together with 3TC's ease of administration has successfully established 3TC as the cornerstone of combination therapy in HIV infection. In combination with other anti-retrovirals, 3TC is used in the majority of triple and quadruple combination therapies with other nucleoside analog, protease inhibitors and non-nucleoside reverse transcriptase inhibitors ("NNRTI"). It was also part of the pivotal clinical trials used as the basis for approval of five other HIV anti-retroviral agents: the nucleoside analog abacavir, the NNRTI efavirenz, and the protease inhibitors indinavir, nelfinavir and amprenavir.

COMBIVIR

In September 1997, the FDA authorized the marketing of COMBIVIR, the first product to combine two anti-retroviral drugs in a single tablet formulation. Each tablet of COMBIVIR contains 3TC and AZT and can be taken twice daily, offering the advantage of reducing significantly the number of tablets a person on a 3TC/AZT based treatment regimen needs to take. COMBIVIR was approved for use in Europe in March 1998 and in Canada in December 1998.

TRIZIVIR

In November 2000, the FDA authorized the marketing of TRIZIVIR in the US in combination with other antiretrovirals or alone in the treatment of HIV-1 infection. Each tablet of TRIZIVIR contains 3TC, AZT and abacavir (“ABC”) and can be taken twice daily. TRIZIVIR was the first tablet to combine three anti-HIV agents. TRIZIVIR was approved for use in the EU in December 2000 and in Canada in October 2001.

EPZICOM/KIVEXA

In August 2004, the FDA authorized the marketing of EPZICOM in the US. Each tablet of EPZICOM contains 3TC and ABC and can be taken once a day. EPZICOM, in combination with other antiretroviral agents, is indicated for the treatment of HIV-1 infection in adults. In December 2004, EPZICOM was granted a marketing authorization for adults and adolescents in the EU. KIVEXA was approved in Canada in July 2005.

Hepatitis B infection

Hepatitis B virus (“HBV”) is the causative agent of both acute and chronic forms of Hepatitis B, a liver disease that is a major cause of death and disease throughout the world. According to the Hepatitis B Foundation two billion people worldwide have been infected with HBV. Of those infected, 400 million people are chronically infected. An estimated 1 million people die each year from HBV and its complications. Although vaccines to prevent infection by HBV are currently available, they have not been shown to be effective in those already infected with the virus.

ZEFFIX/EPIVIR-HBV/HEPTOVIR

ZEFFIX (lamivudine) is an orally available treatment for chronic hepatitis B infection associated with evidence of hepatitis B viral replication and active liver inflammation. Use of lamivudine in Hepatitis B was approved in Canada in November 1998, followed by US approval in December 1998 and EU approval in July 1999.

The Company has licensed to GSK the worldwide rights, with the exception of Canada, to develop manufacture and sell ZEFFIX, EPIVIR-HBV and HEPTOVIR. In Canada HEPTOVIR is sold by the Company in partnership with GSK.

Dementia

REMINYL and REMINYL XL

REMINYL and REMINYL XL are indicated for the symptomatic treatment of mild to moderately severe dementia of the Alzheimer type and are marketed by the Company in the UK and Republic of Ireland. In the rest of the world, they are marketed by Janssen, an affiliate of Johnson & Johnson (under the name RAZADYNE and RAZADYNE ER in the US). The Company receives royalties on Janssen's sales.

Following patent litigation in the US in respect of RAZADYNE, a decision on August 28, 2008 rendered the relevant patent invalid and generic versions of RAZADYNE were permitted to enter the US market.

REMINYL XL is a once-daily prolonged release formulation of REMINYL, which was launched by Janssen in the US in May 2005 as RAZADYNE ER. Patent litigation proceedings relating to RAZADYNE ER are in progress in the US. For further information see ITEM 7: Management's Discussion and Analysis of Financial Condition and Results of Operations.

Products under development

The Company focuses its development resources on projects within its core therapeutic areas of ADHD, GI and HGT.

The table below lists the Company's key products under development as at December 31, 2008 by disease areas indicating the most advanced development status reached in key markets and the Company's territorial rights in respect of each key product.

<u>Product</u>	<u>Disease area</u>	<u>Most advanced development status</u>	<u>The Company's territorial rights</u>
Specialty Pharmaceuticals			
Treatments for ADHD			
VYVANSE (lisdexamfetamine dimesylate)	ADHD	Registration in Canada Phase 3 in EU	Global
DAYTRANA (methylphenidate transdermal system)	ADHD	Registration in EU and Canada	Global
INTUNIV (formerly SPD503) (extended release guanfacine)	ADHD	Registration in the US	Global
Treatments for GI diseases			
LIALDA (mesalamine)	Maintenance of remission in ulcerative colitis	Phase 3 in the US	Global (excluding Italy and Latin America) ⁽¹⁾
LIALDA (mesalamine)	Diverticulitis	Phase 3	Global (excluding Italy and Latin America) ⁽¹⁾
SPD550 (Iarazotide-acetate)	Celiac disease	Phase 2	Global (excluding US and Japan)
Treatments for diseases in other therapeutic areas			
FOSRENOL (lanthanum carbonate)	Chronic kidney disease in patients pre-dialysis	Pre-registration in the US	Global
JUVISTA	Prevention and reduction of scarring in connection with both cosmetic and therapeutic surgery	Phase 3	Global (excluding EU)
Human Genetic Therapies			
Treatment for Angioedema			
FIRAZYR (icatibant)	Acute HAE	Phase 3 in the US	Global
Enzyme Replacement Therapies ("ERT")			
Velaglucerase alfa (GA-GCB)	Gaucher disease	Phase 3	Global
HGT-1111	MLD	Phase 1/2	Global
HGT-2310	Hunter Syndrome with central nervous system symptoms, idursulfase-IT	Pre-clinical	Global ⁽²⁾
HGT-1410	Sanfilippo Syndrome (Mucopolysaccharidosis IIIA)	Pre-clinical	Global
HGT-2610	Krabbe Disease	Pre-clinical	Global
Chaperone Technology			
PLICERA (HGT-3410) (isofagomine tartrate)	Gaucher disease	Phase 2	Global (excluding US)

AMIGAL (HGT-3310) (migalastat hydrochloride)	Fabry disease	Phase 2	Global (excluding US)
AT2220 (HGT-3510) (deoxynojirimycin)	Pompe disease	Phase 2	Global (excluding US)

⁽¹⁾ Mochida Pharmaceutical Co., Ltd has rights to develop and sell LIALDA in Japan under license with Shire

⁽²⁾ Genzyme has rights to manage marketing and distribution in Japan and certain other Asia Pacific countries under licenses with Shire

Specialty Pharmaceuticals

Treatments for ADHD

VYVANSE for ADHD in EU and Canada

In March 2008 the Canadian new drug submission was accepted for filing for the treatment of ADHD in children. Review is ongoing.

VYVANSE for the treatment of ADHD in children aged 6 to 17 in the EU is in Phase 3 development and Shire expects to submit the regulatory filing for VYVANSE in Europe in 2010.

DAYTRANA for ADHD in EU & Canada

Regulatory submissions were filed for approval of the product with Health Canada in November 2007 and in the EU via the decentralized procedure, with the Netherlands as the reference member state in December 2007. Reviews are ongoing.

INTUNIV for ADHD in US

In June 2007 Shire received an approvable letter from the FDA for INTUNIV. Shire is conducting additional clinical work which is designed to enhance the label. The New Drug Application (“NDA”) was resubmitted in January 2009 and it is anticipated that launch for use in the treatment of ADHD in children and adolescents in the US will occur in the second half of 2009.

SPD487 (Amphetamine transdermal system)

In November 2008 Shire terminated the agreement with Noven for the development of the amphetamine transdermal system.

Treatments for GI diseases

LIALDA/MEZAVANT for the maintenance of remission in ulcerative colitis in the US

Phase 3 trials investigating the use of the product to maintain remission in patients who have ulcerative colitis were initiated in 2006 for the US market and are continuing. The product was given this indication on approval in the EU.

LIALDA/MEZAVANT for the treatment of diverticulitis

Phase 3 worldwide clinical trials investigating the use of the product for the treatment of diverticulitis were initiated in 2007 and are continuing.

Diverticulosis is among the most common diseases in developed countries and manifests as weaknesses or out-pouches of the bowel wall primarily in elderly populations. Approximately 15-20% of people with diverticulosis go on to develop diverticulitis which is an acute inflammation, infection and micro or macro-perforation of these out-pouches. The current standard of care requires treatment with antibiotics and depending on the frequency or severity of attacks frequently may require surgery. LIALDA is being investigated as a treatment to prevent recurrent attacks of diverticulitis.

SPD550 (Larazotide Acetate; also known as AT-1001) for the treatment of Celiac disease

SPD550 is being developed for the treatment of Celiac disease. Celiac disease is a T-cell mediated auto-immune disease that occurs in genetically susceptible individuals and is characterized by small intestinal inflammation triggered by gluten. SPD550 is a novel peptide that inhibits intestinal paracellular permeability by inhibiting stimulus-induced cytoskeletal rearrangement in epithelial cells that leads to the disassembly of tight junctions. There are currently no approved pharmaceutical treatments to reduce the risk of recurrent attacks.

In December 2007 Shire acquired the worldwide rights to SPD550 (Larazotide Acetate; also known as AT-1001) in markets outside of the US and Japan from Alba Therapeutics Corporation (“Alba”). The two parties have established

Joint Committees which will guide the development, manufacture and commercialization of the product. Alba has initiated and is responsible for executing the ongoing Phase 2 program and certain non-clinical studies. Additional development studies may be conducted jointly or by the individual companies prior to or after initiation of Phase 3.

Treatments for diseases in other therapeutic areas

FOSRENOL for the treatment of pre-dialysis chronic kidney disease (“CKD”)

Following the FDA Cardiovascular and Renal Drugs Advisory Committee recommendation in October of 2007 on the use of phosphate binders, including FOSRENOL, to treat hyperphosphatemia in pre-dialysis CKD patients, Shire continues to work with the FDA to determine whether FOSRENOL can launch in the pre-dialysis CKD market in the US without conducting additional clinical outcomes trials.

JUVISTA

Renovo Limited (“Renovo”) initiated its first pivotal European Phase 3 trial in scar revision in the fourth quarter of 2008 to support the filing of a European regulatory dossier. If the outcome from Renovo’s multi centre, EU Phase 3 study is suitably positive, the data will be used to inform the strategy and design of Shire’s US development plan and to strengthen the chances of regulatory and commercial success in the US.

SEASONIQUE an extended cycle oral contraceptive

In August 2006 Shire entered into a license agreement in respect of Duramed Pharmaceuticals, Inc’s (“Duramed”) oral contraceptive, SEASONIQUE. Duramed markets SEASONIQUE in the US. Shire has the rights to market this product in a number of territories outside of North America, including the larger European markets.

On February 24, 2009, Shire and Duramed amended this agreement and it will terminate on December 31, 2009. Pursuant to this amendment, Shire agreed to return to Duramed its rights under the agreement effective February 24, 2009. For further details on this amendment see ITEM 7: Management’s Discussion of Financial Condition and Results of Operations.

Projects in pre-clinical development

A number of projects are underway in the early stages of pre-clinical development for the Specialty Pharmaceuticals area.

Human Genetic Therapies

Treatments for Angioedema

FIRAZYR for HAE in the US

FIRAZYR is a treatment for acute HAE which Shire added to the portfolio through its acquisition of a majority voting interest in Jerini during 2008. FIRAZYR is a first-in-class peptide-based therapeutic developed for the symptomatic treatment of acute attacks of HAE. HAE is a debilitating and potentially life-threatening genetic disease characterized by unpredictable recurring swelling attacks in the hands, feet, face, larynx, or abdomen.

Jerini received a not approvable letter for FIRAZYR for use in the US from the FDA in April 2008, and met with FDA in December 2008 to discuss the development of FIRAZYR. It was agreed that an additional clinical study would be required before approval could be considered and that a complete response to the not approvable letter would be filed after completion of this study. This additional study will be initiated during the third quarter of 2009.

ERT

Velaglucerase alfa (GA-GCB)

Velaglucerase alfa is an enzyme replacement therapy being developed for the treatment of Gaucher disease. Gaucher disease is the most common of the inherited lysosomal storage diseases and is caused by a deficiency of the enzyme glucocerebrosidase. As a result of this deficiency, certain lipids accumulate in specific cells of the liver, spleen and bone marrow causing significant clinical symptoms in the patient, including enlargement of the liver and spleen, hematological abnormalities and bone disease.

Shire has completed enrolment in a worldwide Phase 3 clinical program for velaglucerase alfa. This comprehensive development program includes the evaluation of velaglucerase alfa in naïve patients and patients previously treated with imiglucerase across three clinical studies. It is anticipated that this development program will support global filings in the second half of 2009.

HGT-1111 / METAZYM

Shire has an ongoing enzyme replacement therapy program for the treatment of MLD, which is a lysosomal storage disorder that results from a deficiency in the enzyme arylsulfatase-A (“ASA”). In June 2008 Shire completed its acquisition from Zymenex of the global rights to a clinical candidate ASA, known as METAZYM. METAZYM has completed a Phase 1b clinical trial in 12 MLD patients in Europe and an extension to this study is ongoing. The product has been granted orphan drug designation in the US and in the EU. The current plan is to initiate a Phase 2/3 clinical trial in the first half of 2009. This product is now referred to as HGT-1111.

HGT-1110 was in development at Shire for the treatment of MLD following successful pre-clinical proof of concept studies. The HGT-1110 program was replaced with the HGT-1111 development program upon completion of the acquisition from Zymenex.

HGT-2310 - Hunter syndrome with central nervous system symptoms, idursulfase-IT

Following the acceptance by the FDA in January 2008 of Shire’s Investigational New Drug application for idursulfase-IT (HGT-2310 -formerly referred to as ELAPRASE for Hunter syndrome patients with significant central nervous system symptoms - “Hunter CNS”) the Company plans to initiate a Phase 1 clinical trial in the first quarter of 2009.

HGT-1410 for Sanfilippo Syndrome (Mucopolysaccharidosis IIIA)

HGT-1410 is in development as an enzyme replacement therapy for the treatment of Sanfilippo Syndrome (Mucopolysaccharidosis IIIA), a lysosomal storage disorder. Sanfilippo is an autosomal recessive genetic disease caused by a deficiency of heparan-N-sulfatase, an enzyme that degrades heparan sulfate. The accumulation of heparan sulfate in tissues causes a neurodegenerative disorder in children in which the central nervous system is primarily affected. The product has been granted orphan drug designation in the US and in the EU. Pre-clinical development for this product is continuing.

HGT-2610 for the treatment of Krabbe Disease (Globoid Cell Leukodystrophy, (“GLD”))

In November 2008 Shire announced that an enzyme replacement therapy was being developed for the treatment of Krabbe Disease, a lysosomal storage disorder. Krabbe is a rare, inherited lysosomal disorder resulting from a deficiency in the enzyme galactosylcerebrosidase. This neurodegenerative disease primarily affects infants, but can occur in adolescents and adults. GLD is caused by degradation of the myelin sheath that normally covers nerve fibers, which leads to rapid degeneration of mental and motor function in these patients. This program is in early development and preclinical studies.

Pharmacological Chaperone Technology

In November 2007 Shire entered into a license agreement with Amicus under which it received the rights to three compounds, PLICERA, AMIGAL and AT2220, in markets outside the US.

PLICERA (HGT-3410 for the treatment of Gaucher disease)

PLICERA is an orally-administered, small molecule pharmacological chaperone that is being developed for the treatment of Gaucher disease. PLICERA has received orphan drug designation by the EMEA, which may provide it with up to ten years market exclusivity in the EU.

In March 2008 Amicus announced positive data from its Phase 2 clinical trial. Results from the Phase 2 trial support the previously reported interim findings that PLICERA was generally safe and well tolerated at all doses and increased target enzyme activity levels in a majority of patients. Shire has rights to PLICERA in markets outside the US.

AMIGAL (HGT-3310 for the treatment Fabry disease)

AMIGAL is an orally-administered, small molecule pharmacological chaperone being developed for the treatment of Fabry disease. AMIGAL has received orphan drug designation by the EMEA, which may provide it with up to ten years market exclusivity in the EU.

Amicus met with the FDA to discuss the AMIGAL development program in June 2008, and discussions are ongoing. Discussions are also ongoing with the EMEA. A final decision on the global development strategy will follow the conclusion of the discussions with both agencies. Shire has rights to AMIGAL in markets outside the US.

HGT-3510 for the treatment of Pompe disease

HGT-3510 is an orally-administered, small molecule pharmacological chaperone being developed for the treatment of Pompe disease. Pompe disease, also known as glycogen storage disease type II or acid maltase deficiency, is a

relatively rare neuromuscular and lysosomal storage disorder caused by inherited genetic mutations in a key enzyme called acid α -glucosidase (GAA) which result in deficient activity of the enzyme GAA. The deficient activity of the GAA enzyme, which normally breaks down glycogen, results in lysosomal glycogen accumulation in skeletal, cardiac and smooth muscle tissue.

In June 2008 Amicus initiated a Phase 2 clinical trial of HGT-3510, an orally administered, small molecule pharmacological chaperone being jointly developed for the treatment of Pompe disease by Shire and Amicus. This trial was placed on clinical hold in February 2009 in response to reports of two serious adverse events probably related to treatment with HGT-3510. Shire has rights to HGT-3510 in markets outside the US.

Early Research Products

A number of additional projects are underway in the early stages of development for the HGT business area.

Manufacturing and distribution

Manufacturing

The Company sources its products from third party contract manufacturers, and for certain products has its own manufacturing capability. All products marketed by the International sales and marketing operation are either manufactured and supplied by the licensor of the product under supply arrangements or are manufactured for Shire by third parties under contract.

The Company currently has dual sources for VYVANSE, ADDERALL XR, FOSRENOL, ELAPRASE and REPLAGAL and is developing a second source of manufacture for LIALDA. The Company sources FIRAZYR, DAYTRANA, CARBATROL, PENTASA and XAGRID from a single contract manufacturer. The Company manages the risks associated with reliance on single sources of production by carrying additional inventories or developing second sources of supply.

Active pharmaceutical ingredient ("API") sourcing

The Company sources API from third party suppliers for its Specialty Pharmaceuticals products and the HGT product FIRAZYR. Shire has manufacturing capability for agalsidase alfa and idursulfase at its protein manufacturing plant in Cambridge, Massachusetts, US for its HGT products, REPLAGAL and ELAPRASE.

The Company currently has a dual source of API for VYVANSE, DAYTRANA, ADDERALL XR, PENTASA and is developing one for LIALDA. The Company manages the risks associated with reliance on single sources of API by carrying additional inventories or developing second sources of supply. A second source of supply of idursulfase for ELAPRASE is being developed.

In order to support the rapid growth of ELAPRASE, additional manufacturing capacity is currently being added in Lexington, Massachusetts, US. Manufacturing will start in the first quarter of 2009, with submission to regulatory authorities expected in the fourth quarter of 2009. Shire's supply is sufficient to support all existing patients and allow for forecasted growth in 2009. Inventory will be managed in order to meet forecasted demand.

Distribution

The Company's US distribution center, which includes a large vault to house US Drug Enforcement Agency ("DEA") regulated Schedule II products, is located in Kentucky. From there, the Company primarily distributes its Specialty Pharmaceuticals products through the three major wholesalers who have a hub or distribution centers that stock Schedule II drugs in the US, providing access to nearly all pharmacies in the US.

The distribution and warehousing of HGT products for the US market are contracted out to specialist third party contractors.

Outside the US, where the Company has local operations, physical distribution of Specialty Pharmaceuticals and HGT products is contracted out to third parties.

Outside the US, where the Company does not have local operations, distribution agreements are in place for certain territories in respect of both certain Specialty Pharmaceuticals and HGT products.

Material customers

The Company's two largest trade customers are Cardinal Health Inc. and McKesson Corp., both of which are in the US. In 2008, these wholesale customers accounted for approximately 32% and 24% of product sales, respectively.

Intellectual Property

An important part of the Company's business strategy is to protect its products and technologies through the use of patents and trademarks, to the extent available. The Company also relies on trade secrets, unpatented know-how, technological innovations and contractual arrangements with third parties to maintain and enhance its competitive position where it is unable to obtain patent protection or where marketed products are not covered by specific patents. The Company's commercial success will depend, in part, upon its ability to obtain and enforce strong patents, to maintain trade secret protection, to operate without infringing the proprietary rights of others and to comply with the terms of licenses granted to it. The Company's policy is to seek patent protection for proprietary technology whenever possible in the US, Canada, major European countries and Japan. Where practicable, the Company seeks patent protection in other countries on a selective basis. In all cases the Company endeavors to either obtain patent protection itself or support patent applications by its licensors.

In the regular course of business, the Company's patents may be challenged by third parties. The Company is a party to litigation or other proceedings relating to intellectual property rights. Details of ongoing litigation are provided in ITEM 3: Legal Proceedings.

The degree of patent protection afforded to pharmaceutical inventions around the world is uncertain. If patents are granted to other parties that contain claims having a scope that is interpreted by the relevant authorities to cover any of the Company's products or technologies, there can be no guarantee that the Company will be able to obtain licenses to such patents or make other arrangements at reasonable cost, if at all.

The existence, scope and duration of patent protection varies among the Company's products and among the different countries where the Company's products may be sold. It may also change over the course of time as patents are granted or expire, or become extended, modified or revoked. The following non-exhaustive list sets forth details of the granted US and EU patents pertaining to the Company's key marketed products, material products from which the Company receives a royalty and major products in later stages of development, or technology relating to those products, which are owned by or licensed to the Company and that are material to an understanding of the Company's business taken as a whole. The Company also holds patents in other jurisdictions, such as Canada and Japan and has patent applications pending in such jurisdictions, as well as in the US and the EU.

	Granted US and EP Patents	Expiration Date
ADDERALL XR	US 6,322,819	October 21, 2018
	US 6,605,300	October 21, 2018
	US 6,913,768	January 29, 2023
CARBATROL	US 5,326,570	July 23, 2011
	US 5,912,013	June 15, 2016
	EP 0660705	July 23, 2012
DAYTRANA	US 5,958,446	December 12, 2012
	US 6,210,705	September 30, 2018
	US 6,348,211	September 30, 2018
	EP 591432	June 22, 2012
	EP 1037615	December 14, 2018
ELAPRASE	US 5,728,381	March 17, 2015
	US 5,798,239	August 25, 2015
	US 5,932,211	September 3, 2019
	US 6,153,188	November 12, 2011
	US 6,541,254	November 12, 2011
FIRAZYR	US 5,648,333	July 15, 2014
	EP 370453	November 14, 2009 ⁽¹⁾

FOSRENOL	US 5,968,976	October 26, 2018
	US 7,078,059	July 5, 2021
	US 7,381,428	August 26, 2024
	US 7,465,465	August 26, 2024
	EP 0817639	March 19, 2016
Velaglucerase-alfa (GA-GCB)	US 5,641,670	June 24, 2014
	US 5,733,761	March 31, 2015
	US 6,270,989	November 5, 2011
	US 6,565,844	November 5, 2011
	US 6,566,099	September 12, 2017
	US 7,138,262	August 18, 2020
	EP 0750044	November 5, 2012
INTUNIV	US 5,854,290	September 21, 2015
	US 6,287,599	December 20, 2020
	US 6,811,794	July 4, 2022
JUVISTA (SPD538)	US 6,331,298	December 18, 2018
	US 6,425,769	July 30, 2019
	US 5,693,489	December 2, 2014
	US 5,869,320	February 9, 2016
LIALDA/MEZAVANT	US 6,773,720	June 8, 2020
	EP 1198226	June 8, 2020
	EP 1183014	June 9, 2020
	EP 1287822	June 8, 2020
REMINYL & REMINYL XL	US 6,099,863	June 6, 2017
	US 6,358,527	June 6, 2017
	US 7,160,559	December 20, 2019
	EP 236684	January 15, 2007
	EP 915701	June 6, 2017
	EP1140105	December 20, 2019
REPLAGAL	US 5,641,670	June 24, 2014
	US 5,733,761	March 31, 2015
	US 6,270,989	November 5, 2011
	US 6,565,844	November 5, 2011
	US 6,083,725	September 12, 2017
	US 6,395,884	September 12, 2017
	US 6,458,574	September 12, 2017
	EP 0750044	November 5, 2012
	EP 0935651	September 12, 2017
VYVANSE	US 7,105,486	June 29, 2023
	US 7,223,735	June 29, 2023

EPZICOM	US 5,047,407	May 17, 2010
	US 5,693,787	December 2, 2014
	US 5,663,320	September 2, 2014
	US 5,696,254	December 9, 2014
	US 6,180,639	July 30, 2018
	US 7,119,202	February 8, 2009
	EP 382 526	February 8, 2010
	EP 565 549	January 3, 2012
	EP 515 157	May 20, 2012
LAMIVUDINE: EPIVIR/EPIVIR-ZEFFIX/3TC	US 5,047,407	May 17, 2010
	US 5,693,787	December 2, 2014
	US 5,663,320	September 2, 2014
	US 5,696,254	December 9, 2014
	US 6,180,639	July 30, 2018
	RE 39155	January 2, 2014
	US 7,119,202	February 8, 2009
	EP 382 526	February 8, 2010
	EP 565 549	January 3, 2012
EP 515 157	May 20, 2012	
TRIZIVIR	US 5,047,407	May 17, 2010
	US 5,693,787	December 2, 2014
	US 5,663,320	September 2, 2014
	US 5,696,254	December 9, 2014
	US 6,180,639	July 30, 2018
	EP 382 526	February 8, 2010
	EP 565 549	January 3, 2012
	EP 515 157	May 20, 2012

Note:

- The EP patents listed above do not necessarily have a corresponding national patent registered in each EU member state. In some cases, national patents were obtained in only a limited number of EU member states. The rights granted to an EP patent are enforceable in any EU member state where the EP patent has been registered as a national patent.
- The EP patents listed above do not reflect term extensions afforded by supplementary protection certificates (SPC's) which are available in many EU member states.

⁽¹⁾ Subject to SPC application which will extend patent expiry to November 14, 2014 when granted.

The loss of patent protection following a legal challenge may result in third parties commencing commercial sales of their own versions of the Company's products before the expiry of the patents. The Company's sales of such product(s) may decrease in consequence. In many cases, however, the Company's products have more than one patent pertaining to them. In such cases, or where the Company enjoys trade secrets, manufacturing expertise, patient preference or regulatory exclusivity, the Company may continue to market its own products without its commercial sales of those products being adversely affected by the loss of any given patent.

Competition

Shire believes that competition in its markets is based on, among other things, product safety, efficacy, convenience of dosing, reliability, availability and price. Companies with more resources and larger R&D expenditures than Shire have a greater ability to fund the research and clinical trials necessary for regulatory applications, and consequently may have a better chance of obtaining approval of drugs that would then compete with Shire's products. Other products now in use or being developed by others may be more effective or have fewer side effects than the Company's current or future products. The market share data provided below is sourced from IMS.

ADHD market

Competition in the US ADHD market has increased as several products that compete with the Company's products have been launched in recent years. The Company has also introduced two new entrants to the market: VYVANSE, the Company's stimulant pro-drug product, launched in 2007 and DAYTRANA, the Company's methylphenidate transdermal product, launched in 2006. Additional competition will result in 2009 from the anticipated launch of generic ADDERALL XR beginning in April 2009, and other ADHD products could face generic competition in the future.

Many of the competing products contain methylphenidate. In 2000, Johnson & Johnson (in conjunction with ALZA) launched CONCERTA, a once-daily formulation of methylphenidate. For the month of December 2008, CONCERTA had a 19.4% share of the US ADHD market. In 2001, UCB launched METADATE CD, a once-daily formulation of methylphenidate. In December 2008, METADATE CD had a 2.4% share of the US ADHD market. In 2002, Novartis (in conjunction with Elan) launched RITALIN LA, an extended release formulation of methylphenidate, and in 2005 Novartis launched FOCALIN XR in conjunction with Celgene Corporation ("Celgene"), a long-acting formulation of dexamethylphenidate, the active ingredient of traditional methylphenidate preparations. In December 2008 RITALIN LA and FOCALIN XR had a 1.7% and 6.0% share, respectively, of the US ADHD market.

In 2002, Barr launched a generic version of ADDERALL. Subsequently, five additional companies have launched generic versions. Total ADDERALL generic prescriptions accounted for about 14.7% of the US ADHD market for the month of December 2008. In September 2006, Duramed purchased the product rights to the Company's ADDERALL product for \$63 million. For further information see ITEM 7: Management's Discussion and Analysis of Financial Condition and Results of Operations.

In 2003, Eli Lilly launched STRATTERA, a non-stimulant, non-scheduled treatment for ADHD. As of December 2008, STRATTERA had a 7.4% share of the US ADHD market. The Company's non-stimulant product INTUNIV is in registration in the US.

The Company is also aware of clinical development efforts by GlaxoSmithKline (in collaboration with Neurosearch), Cortex Pharmaceuticals Inc., Eisai Inc., BMS (in collaboration with Otsuka), AstraZeneca (in collaboration with Targacept), CoMentis, Shionogi/Sciele (in collaboration with Addrenex), Eli Lilly, Johnson & Johnson, Pfizer, Merck, Schering-Plough/Organon, PsychoGenics, Supernus and Abbott to develop additional indications and new non-stimulant treatment options for ADHD.

GI /Ulcerative Colitis market

Ulcerative colitis is a type of Inflammatory Bowel Disease. The primary treatments for patients with ulcerative colitis are 5-ASA containing formulations. More than 88% of all ulcerative colitis patients receive treatment with 5-ASA. Competition in the oral 5-ASA market has remained relatively constant with the Company's LIALDA/MEZAVANT being the only new branded market entrant for patients with mild to moderate ulcerative colitis since the launch of the mesalamine pro-drug COLAZAL in 2001. Shire defines the 5-ASA competitive set as the non-sulfasalazine, oral mesalamine and mesalamine pro-drug products.

The US oral 5-ASA market is led by Proctor and Gamble's ASACOL. In December 2008, ASACOL had a 58.9% share of the oral 5-ASA market, declining from 63.2% in December of 2007. In December 2008 Salix's COLAZAL had a 1.8% market share, while UCB's DIPENTUM had a 0.9% market share.

The EU oral 5-ASA market is somewhat more fragmented. Major competitors in the UK include Proctor and Gamble's ASACOL which had a 45.8% share of the UK oral 5-ASA market and Ferring's PENTASA tablets had an 18.7% market share in November 2008. The German oral 5-ASA market is led by Dr Falk's SALOFALK, with 56.7% market share, followed by Merckle's CLAVERSAL with 20.0% share in November 2008. CLAVERSAL and PENTASA are the leaders in the oral 5-ASA market in Spain with 42.6% and 41.0% market shares respectively in November 2008. PENTASA sachets are the market leader in France with 42.8% market share of the oral 5-ASA market. Norgine's FIV-ASA had a 15.1% share of the French oral 5-ASA market. Overall, Proctor and Gamble's ASACOL had a 22.0% share of the EU G5 oral 5-ASA market.

Mesalamine and balsalazide products are generally protected by formulation patents only. In December 2007, the FDA denied Salix's Citizen Petition for COLAZAL and Salix subsequently announced the launch of an authorized generic version by Watson Laboratories. This was followed by the introduction of three other generic versions of COLAZAL.

The Company is aware of other 5-ASA formulation development efforts by Salix and Proctor and Gamble and other non-5-ASA biologic treatments in development for Inflammatory Bowel Disease by UCB and Abbott.

Market for the treatment of rare genetic diseases

The Company believes that the primary competition with respect to its products for rare genetic diseases is from smaller pharmaceutical and biotechnology companies. Competitors for lysosomal storage disorders include BioMarin Pharmaceutical Inc. (“BioMarin”), Actelion Ltd. (“Actelion”), and Genzyme. Specifically, REPLAGAL competes with Genzyme’s FABRAZYME, and, if approved, velaglucerase alfa would compete with Genzyme’s CEREZYME. Shire does not know of any party developing an enzyme replacement therapy for the treatment of Hunter syndrome.

FIRAZYR competes in certain European countries with CSL Behring’s Berinert P, a human plasma-derived C1-esterase inhibitor (C1-INH) product; CSL Behring is in the process of seeking regulatory approval for Berinert P in additional European countries. Other competitive products in development for HAE include Dyax Corporation’s DX-88, a plasma kallikrein inhibitor, and Pharming Group’s RHUCIN, a recombinant version of C1-INH.

The markets for some of the potential products for rare genetic diseases caused by protein deficiencies are quite small, and consequently the Company has sought orphan drug designation for certain of such products.

REPLAGAL and FABRAZYME were granted co-exclusive orphan drug status in the EU for up to ten years. Genzyme has orphan drug exclusivity for FABRAZYME in the United States until April 2010. ELAPRASE has orphan drug designation in the United States and the EU. FIRAZYR has orphan exclusivity in the EU until 2018.

For more information on orphan drug designation, see Part I – ITEM 1: Business – Government regulation.

HIV Market

The HIV competitive landscape is becoming more crowded and complicated as treatment trends evolve.

NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS

3TC/EPIVIR is part of the Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (“NRTI”) market. TRIZIVIR, COMBIVIR and EPZICOM/KIVEXA are part of the combined NRTI market. TRUVADA (tenofovir/emtricitabine), sold by Gilead, is the market leader combination NRTI. TRUVADA and VIREAD (tenofovir), also sold by Gilead, both represent the most direct competition to lamivudine.

OTHER HIV COMPETITION

In addition to the two NRTI HIV markets in which lamivudine operates, there is competition from:

- *NNRTIs.* Of the branded NNRTIs available, SUSTIVA (efavirenz) sold by BMS and VIRAMUNE (nevirapine) sold by Boehringer-Ingelheim are the class leaders. INTELENCE (etravirine) was launched by Tibotec in the US in January 2008.
- *Protease Inhibitors (PIs).* Of the branded PIs available, REYATAZ (atazanavir), sold by BMS, and KALETRA (lopinavir/ritonavir), sold by Abbott, dominate this class. PREZISTA (darunavir), sold by Tibotec, was initially approved by the FDA in June 2006 and had its label extended in October 2008.
- *Entry inhibitors and others.* Of the branded drugs available, ATRIPLA (efavirenz/emtricitabine/tenofovir), a cross-class fixed dose combination sold by Gilead and BMS, is the market leader in this class. FUZEON (enfuvirtide), an injectable integrase inhibitor sold by Roche/Trimeris, is the other current significant product in this class. ISENTRESS (raltegravir) was launched by Merck in the US in October 2007.

GENERIC HIV COMPETITORS

BMS’s VIDEX EC (didanosine) became the first generic HIV product in the United States in 2004. GSK’s RETROVIR (AZT) came off patent in the US in September 2005 and in Europe in March 2006. Several zidovudine generics have been approved by the FDA starting in September 2005.

A generic tenofovir (NRTI competitor) by Matrix Labs received tentative approval by the FDA in November 2007.

Furthermore in 2007 generic drug companies have filed ANDAs seeking approval for EPIVIR, COMBIVIR, ZEFFIX and EPZICOM in the US (see further information within “Royalties received from other products” above). Several tentative approvals of generic lamivudine have been issued by the FDA.

Government regulation

The clinical development, manufacturing and marketing of Shire's products are subject to governmental regulation in the US, the EU and other territories. The Federal Food, Drug, and Cosmetic Act, the Prescription Drug Marketing Act and the Public Health Service Act in the US, and numerous directives and guidelines in the EU, govern the testing, manufacture, safety, efficacy, labeling, storage, record keeping, approval, advertising and promotion and pricing of the Company's products. Product development and approval within these regulatory frameworks take a number of years and involves the expenditure of substantial resources.

In general, for a new chemical entity, the product needs to undergo rigorous preclinical testing. Clinical trials for new products are typically conducted in three sequential phases that may overlap. In Phase 1, the initial introduction of the pharmaceutical compound into healthy human volunteers, the emphasis is on testing for safety (adverse effects), dosage tolerance, metabolism, distribution, excretion and clinical pharmacology. Phase 2 involves studies in a limited patient population to determine the initial efficacy of the pharmaceutical compound for specific targeted indications, to determine dosage tolerance and optimal dosage and to identify possible adverse side effects and safety risks. Once a compound is found to be effective and to have an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken with a larger number of patients to provide enough data to statistically evaluate the efficiency and safety of the product and to evaluate more fully clinical outcomes. The failure to demonstrate adequately the quality, safety and efficacy of a therapeutic drug under development can delay or prevent regulatory approval of the product.

In order to gain marketing approval the Company must submit to the relevant regulatory authority for review information on the quality (chemistry, manufacturing and pharmaceutical) aspects of the product as well as the non-clinical and clinical data. The FDA undertakes the review for the US. In the EU the review may be undertaken by the following: (i) members of the EMEA's Committee for Medicinal Products for Human Use ("CHMP") as part of a centralized procedure; (ii) an individual country's agency, followed by "mutual recognition" of this review by a number of other countries' agencies, depending on the process applicable to the drug in question; or (iii) a competent member state's authorities through a decentralized procedure, an alternative authorization procedure to the "mutual recognition" procedure for those drugs that are ineligible for a "centralized" review.

Approval can take from several months to several years, or be denied. The approval process can be affected by a number of factors - for example additional studies or clinical trials may be requested during the review and may delay marketing approval and involve unbudgeted costs. As a condition of approval, the regulatory agency will require post-marketing surveillance to monitor for adverse effects, and may require other additional studies as deemed appropriate. After approval for the initial indication, further clinical studies are usually necessary to gain approval for any additional indications. The terms of any approval, including labeling content, may be more restrictive than expected and could affect the marketability of a product.

As a condition of approval, the regulatory agency will require that the product continue to meet regulatory requirements as to safety, efficacy and quality and will require strict procedures to monitor and report any adverse effects. Where adverse effects occur or may occur, the regulatory agency may require additional studies or changes to prescribing advice or to product licences. Additional data may result in a product authorization being withdrawn at any stage.

Some jurisdictions, including the EU and the US, may designate drugs for relatively small patient populations as "orphan drugs". Generally, if a product that has an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity means that applications to market the same drug for the same indication may not be approved, except in limited circumstances, for a period of up to ten years in the EU and for up to seven years in the US. These laws are particularly pertinent to Shire's HGT business unit.

In the US, the Drug Price Competition and Patent Restoration Term Act of 1984, known as the US Hatch-Waxman Act, established a period of marketing exclusivity for brand name drugs as well as abbreviated application procedures for generic versions of those drugs. Approval to manufacture these drugs is sought by filing an ANDA. As a substitute for conducting full-scale pre-clinical and clinical studies, the FDA can accept data establishing that the drug formulation, which is the subject of an abbreviated application, is bio-equivalent and has the same therapeutic effect as the previously approved drug, among other requirements. EU legislation also contains data exclusivity provisions. All products will be subject to an "8+2+1" exclusivity regime. A generic company may file a marketing authorization application for that product with the health authorities eight years after the innovator has received its first community authorization for a medicinal product. The generic company may not commercialize the product until after either ten (8+2) or eleven years (8+2+1) have elapsed from the date of grant of the initial marketing authorization. The one-year extension is available if the innovator obtains an additional indication during the first eight years of the marketing authorization that is of significant advancement in clinical benefit.

In the US, the DEA also regulates the national production and distribution in the US of Scheduled drugs (i.e. those drugs containing controlled substances) by allocating production quotas based, in part, upon the DEA's view of national demand. As Schedule II drugs, the production and distribution of Shire's ADHD products are strictly controlled.

The branch of the FDA responsible for drug marketing oversight routinely reviews company marketing practices and also may impose pre-clearance requirements on materials intended for use in marketing of approved products. Shire is also subject to various US federal and state laws pertaining to healthcare fraud and abuse, including anti-kickback and false claims laws. Similar review and regulation of advertising and marketing practices exists in the other geographic areas where the company operates.

Regulatory Developments

In the US various legislative proposals at the federal and state levels could bring about major changes in the affected health care systems. Some states have passed such legislation, and further federal and state proposals are possible. Such proposals and legislation include, and future proposals could include, price controls, patient access constraints to medicines and increases in required rebates or discounts. Similar issues exist in the EU. The Company cannot predict the outcome of such initiatives, but will work to maintain patient access to its products and to oppose price constraints. Additionally, legislation is being debated at the federal level in the US that could allow patient access to drugs approved in other countries – most notably Canada. This is generally referred to as drug re-importation. Although there is substantial opposition to this potential legislation within areas of the federal government, including the FDA, the Company cannot predict the outcome of such legislative activities pertaining to drug re-importation.

Additionally, US federal and state proposals have called for substantial changes in the Medicaid program. US law requires the Company to give rebates to state Medicaid agencies based on each state's reimbursement of pharmaceutical products under the Medicaid program. Rebates potentially could be viewed as price discounts without appreciable increases in Shire's product sales volume as an offset. The Company must also give discounts or rebates on purchases or reimbursements of pharmaceutical products by certain other federal and state agencies and programs.

In September, 2007 the Food and Drug Administration Amendments Act of 2007 was signed into law. It contains a wide range of changes affecting the pharmaceutical industry covering issues relating to fees associated with application approval, drug safety and risk management, direct to consumer advertising, clinical trial and clinical trial result disclosure. Implementing regulations and guidance will be forthcoming from the FDA and other agencies, and the Company is monitoring the situation closely to assure that it meets the new requirements.

Similar regulatory and legislative issues are encountered in Europe and other international markets where governments regulate pharmaceutical prices and patient reimbursement levels. The differing approach to price regulation has led to some parallel trade within the EU where Shire's products are imported into markets with higher prices from markets with lower prices. Exploitation of price differences between countries in this way can impact sales in those markets with higher prices.

Third party reimbursement and pricing

The Company's revenue depends, in part, upon the price third parties, such as health care providers and governmental organizations are willing to reimburse patients and physicians for the cost of the Company's products or the Company's competitors' similar products and related treatment. These third party payers are increasingly challenging the pricing of pharmaceutical products and/or seeking pharmaco-economic data to justify their negotiated reimbursement prices. In the US, several factors outside Shire's control could significantly influence the sale price of pharmaceutical products, including: Medicare Part D prescription drug plans; new Medicare Part B reimbursement rules; the increase in states seeking supplemental Medicaid rebates; the ongoing trend toward managed healthcare; and the renewed focus on reducing costs and reimbursement rates in Medicaid, Medicare and other government insurance programs. For example, revisions or clarification from the Centers for Medicare and Medicaid Services ("CMS") related to Medicaid and other government reimbursement programs may have retroactive application which may result in changes to management's estimated rebate liability reported in a prior period. At the time of sale, revenues from the Company's products are reasonably estimable with the aid of historical trend analysis and consideration of any current period changes in pricing practices. The rebates can be reasonably determinable at the time of sale to the initial customers. These factors would not impact our revenue recognition policy under generally accepted accounting principles.

The Medicare Prescription Drug Improvement and Modernization Act of 2003 established a voluntary drug benefit for Medicare beneficiaries and created the new Medicare Part D and Medicare Part B. Medicare Part D gives elderly and disabled people, already on Medicare, access to subsidized prescription drug coverage from January 2006 onwards. Medicare Part B establishes new rules to lower Medicare's reimbursement rate for physician administered drugs. It is difficult to predict the long-term impact of this expansion of Medicare on pharmaceutical companies. Usage of pharmaceutical products may increase as the result of expanded access to medications afforded by partial reimbursement under Medicare. However, such potential sales increases may be offset by increased pricing pressures due to enhanced purchasing power of the private sector that will negotiate on behalf of Medicare beneficiaries.

Similar developments may take place in the EU markets, where the emphasis will likely be on price controls and non-reimbursement for new and highly priced medicines for which the economic as well as the therapeutic rationales are not established. Significant uncertainty exists about the reimbursement status of newly approved pharmaceutical products in the EU. Limits on reimbursement available from third party payers may reduce the demand for the Company's products. Price applications in Europe have delayed product launches of products otherwise approved in some countries for up to two years and, in occasional situations, prevented launch. As a consequence the Company's estimated dates for product launches may be subject to change.

Corporate Responsibility ("CR")

The Company continues to develop its approach to CR; the Shire CR Committee guides the overall direction and sets and monitors objectives. Members of the Committee include representatives from, among others, R&D, HR, Environment Health & Safety, Compliance & Risk Management, Facilities, Marketing and Corporate Communications. The Chairman of the Committee is Shire's General Counsel, Tatjana May. The Committee meets at least three times a year to discuss and monitor progress. An annual CR report is published in hard copy and is also available on the Company's website.

Employees

In the pharmaceutical industry, the Company's employees are vital to its success. The Company believes that it has a good relationship with its employees. At December 31, 2008 the Company had 3,769 employees.

Available information

The Company maintains a website on the World Wide Web at www.shire.com. The Company makes available on its website its Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as soon as reasonably practicable after such reports are electronically filed with, or furnished to, the Securities and Exchange Commission ("SEC"). Shire's reports filed with, or furnished to, the SEC are also available on the SEC's website at www.sec.gov. The information on the Company's website is neither part of nor incorporated by reference in this Annual Report on Form 10-K.

ITEM 1A: Risk Factors

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

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

RISK FACTORS RELATED TO THE COMPANY'S BUSINESS

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

Shire has launched a number of new products in the last four years, including key new products ELAPRASE, VYVANSE, LIALDA, FIRAZYR and FOSRENOL (ROW). The commercial success of these new products, as well as 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 timing of the receipt of marketing approvals, the scope of marketing approvals as reflected in the product's label, the countries in which such approvals are obtained, the authorization of price and reimbursement 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 may not be able to grow revenues in its new products as quickly as anticipated if any or all of the following occur:

- if competitive products are genericised and the impact on the market negatively affects the prescribing of branded treatments for the indications that the Company's new products treat;
- if there are unanticipated adverse events experienced with the Company's new products not seen in clinical trials that impact the physician's willingness to prescribe the Company's new products;
- if issues arise from clinical trials being conducted for post marketing purposes or for registration in another country or regulatory agencies in one country act in a way that causes concern for prescribers or patients in another country;
- if patients, payors or physicians favor older treatments over newer treatments;
- if government regulation is stricter for the Company's new products than for existing treatments;
- if the new products suffer a loss of patent protection or competitors successfully challenge or circumvent the Company's patents or regulatory exclusivity (See ITEM 3: Legal Proceedings of this Form 10-K for details of current patent litigation);
- if planned geographical expansion into emerging markets is not successful; or
- if the size of the patient population for the new product is less than expected or the Company fails to identify new patients for the new products.

If the Company is unable to commercialize ELAPRASE, VYVANSE, LIALDA, FIRAZYR, FOSRENOL (ROW) or any of its new products successfully, there may be a material adverse effect on the Company's revenues, financial condition and results of operations.

Any decrease in the combined sales of VYVANSE and ADDERALL XR will significantly reduce revenues and earnings

In 2008, the combined sales of VYVANSE and ADDERALL XR were \$1,420.6 million, representing approximately 47% of the Company's total revenues. Sales of ADDERALL XR are expected to decrease significantly due to generic competition that is anticipated to commence on April 1, 2009. Any factors that decrease the sales of ADDERALL XR more significantly than expected could have a material adverse effect on the Company's financial condition and results of operations. In addition, the entrance of generic competitors for ADDERALL XR or other leading ADHD medications could impact the sales of VYVANSE. Other factors that could impact the sales of VYVANSE or ADDERALL XR include, but are not limited to:

- faster than anticipated erosion of ADDERALL XR sales by generic competitors;
- the development and marketing of competitive pharmaceuticals to VYVANSE and ADDERALL XR;
- issues impacting the production of VYVANSE or ADDERALL XR or the supply of amphetamine salts including, but not limited to, the ability to get sufficient quota from the DEA;

- technological advances (including the approval of new competing products for ADHD treatments);
- changes in reimbursement policies of third-party payers;
- government action/intervention;
- marketing or pricing actions by competitors;
- public opinion towards ADHD treatments;
- any change in the label or other such regulatory intervention;
- product liability claims; and
- changes in prescription-writing practices.

Any decrease in the sales of 3TC could significantly reduce earnings

The Company receives royalties from GSK on the worldwide sales of 3TC. In 2008, the Company's royalty income relating to 3TC sales was \$140.2 million (2007: \$145.3 million; 2006: \$150.9 million). This royalty stream generates a larger proportion of net income relative to the Company's own product sales as there are minimal costs associated with its generation.

Any factors that decrease sales of 3TC by GSK could significantly reduce the Company's earnings. These include:

- development and marketing of competitive pharmaceuticals, including generic versions;
- loss of patent protection or ability of competitors to challenge or circumvent patents (see ITEM 3: Legal Proceedings of this Form 10-K for details of current patent litigation);
- reduction in the production of 3TC;
- technological advances;
- government action/intervention;
- marketing or pricing actions by GSK's competitors;
- any change in the label or other such regulatory intervention;
- public opinion towards AIDS treatments; and
- product liability claims.

The failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payers in a timely manner for certain of the Company's products and parallel importation 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 pharmaceutical products. Changes to governmental policy or practices could adversely affect the Company's sales, financial condition and results of operations. In addition, the cost of treatment established by health care providers, private health insurers and other organizations, such as health maintenance organizations and managed care organizations are under downward pressure and this, in turn, could impact on the prices at which the Company can sell its products.

The market for pharmaceutical 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:

- the ongoing trend toward managed health care, particularly in the US;
- legislative proposals to reform health care and government insurance programs in many of the Company's markets; and
- price controls and non-reimbursement of new and highly priced medicines for which the economic and therapeutic rationales are not established.

The prices for certain of the Company's products when commercialized, in particular products for the treatment of rare genetic diseases such as REPLAGAL and ELAPRASE, may be high compared to other pharmaceutical products. The Company may encounter particular difficulty in obtaining satisfactory pricing and reimbursement for its products, including those that are likely to have a high annual cost of therapy. The failure to obtain and maintain pricing and reimbursement at satisfactory levels for such products may adversely affect revenues and earnings.

Parallel importation occurs when an importer finds a cheaper price for a product or equivalent product on the world market and imports that product from the lower price jurisdiction to the higher price jurisdiction. If the parallel

importation of lower priced drugs is permitted in the US, it could have the effect of reducing sales of equivalent drugs in the US. To the extent that parallel importation increases, the Company may receive less revenue and earnings from its commercialized products. The parallel importation of prescription drugs is relatively common within the EU.

A disruption to the product supply chain 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 its products from third party contract manufacturers, and for certain products has its own manufacturing capability. In the event of either the Company's failure or the failure of any third party contract manufacturer to comply with mandatory manufacturing standards (often referred to as 'Current Good Manufacturing Standards' or cGMP) in the countries in which the Company intends to sell or have its products sold, the Company may experience a delay in supply or be unable to market or develop its products.

The Company dual-sources certain key products and/or active ingredients. However, the Company currently relies on a single source for production of the final drug product for each of DAYTRANA, FIRAZYR, LIALDA, PENTASA, REMINYL and XAGRID and relies on a single active ingredient source for each of ELAPRASE, FIRAZYR, FOSRENOL, REMINYL, REPLAGAL and XAGRID.

In the event of financial failure of a third party contract manufacturer, the Company may experience a delay in supply or be unable to market or develop its products. This could have a material adverse affect on the Company's financial condition and results of operations.

There is no assurance that suppliers will continue to supply on commercially viable terms, or be able to supply components that meet regulatory requirements. The Company is also subject to the risk that suppliers will not be able to meet the quantities needed to meet market requirements

The development and approval of the Company's products depends on the ability to procure active ingredients and special packaging materials from sources approved by regulatory authorities. As the marketing approval process requires manufacturers to specify their own proposed suppliers of active ingredients and special packaging materials in their applications, regulatory approval of a new supplier would be required if active ingredients or such packaging materials were no longer available from the supplier specified in the marketing approval. The need to qualify a new supplier could delay the Company's development and commercialization efforts.

The Company uses bovine-derived serum sourced from New Zealand and North America in the manufacturing processes for REPLAGAL and ELAPRASE. The discovery of additional cattle in North America or the discovery of cattle in New Zealand with bovine spongiform encephalopathy, or mad cow disease, could cause the regulatory agencies in some countries to impose restrictions on these products, or prohibit the Company from using these products at all in such countries.

The actions of certain customers can affect the Company's ability to sell or market products profitably, as well as impact net sales and growth comparisons

A small number of large wholesale distributors control a significant share of the US and European markets. In 2008, for example, approximately 56% of the Company's product sales were attributable to two customers; McKesson Corp. and Cardinal Health, Inc. In the event of financial failure of any of these customers, the Company may suffer financial loss and a decline in revenues and earnings. In addition, the number of independent drug stores and small chains has decreased as retail pharmacy consolidation has occurred. Consolidation or financial difficulties could cause customers to reduce their inventory levels, or otherwise reduce purchases of the Company's products. Such actions could have an adverse effect on the Company's revenues, financial condition and results of operations. A significant portion of the Company's Specialty Pharmaceuticals product sales are made to major pharmaceutical wholesale distributors as well as to large pharmacies in both the US and Europe. Consequently, product sales and growth comparisons may be affected by fluctuations in the buying patterns of major distributors and other trade buyers. These fluctuations may result from seasonality, pricing, wholesaler buying decisions, or other factors. In addition, 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 financial condition and results of operations.

The outsourcing of services can create a significant dependency on third parties, the failure of whom can affect the ability to operate the Company's business and to develop and market products

The Company has entered into many agreements with third parties for the provision of services to enable it to operate its business. If the third party can no longer provide the service on the agreed basis, the Company may not be able to continue the development or commercialization of its products as planned or on a commercial basis. Additionally, it may not be able to establish or maintain good relationships with the suppliers.

The Company has also entered into licensing and co-development agreements with a number of parties. There is a risk that, upon expiration or termination of a third party agreement, the Company may not be able to renew or extend the agreement with the third party as commercial interests may no longer coincide. In such circumstances, the

Company may be unable to continue to develop or market its products as planned and could be required to abandon or divest a product line.

In the event of breakdown, failure or breach of security on any of the Company's IT systems, the Company may be unable to maintain its business operations

The Company operates several complex information systems upon which it is dependent. The Company has back-up procedures and disaster recovery plans in place to enable the business to continue its normal operations and to mitigate any loss in the event of a failure. However, in the event of breakdown, failure or breach of security of any of these systems or the associated suppliers, the Company may be unable to maintain its business operations.

This could lead to loss of revenue and delay in product development. In addition, the Company is in the process of installing enterprise-wide information systems in its operations throughout the world. Any failure in the operation of these systems could have an adverse effect on the Company's business operations.

The Company may incur unexpected expenditure in order to comply with US environmental laws

The Company's manufacturing sites are situated in the US and are subject to national, state and local environmental laws. Compliance with environmental laws requires ongoing expenditure and any spillage or contamination found to be caused by the Company may result in clean up costs and financial penalties for the Company which could adversely affect the Company's revenues, financial condition and results of operations.

Contracts are used in all areas of operation of the business. They may contain provisions that do not protect the Company's position or with which it cannot comply

Contracts form the basis of agreement in many key activities such as mergers and acquisitions, arrangements with suppliers, outsourcing, product licensing and marketing. These contracts may contain provisions that impose duties on the parties involved or may fail to contain adequate conditions to protect the Company's position. The Company may be unable to meet its obligations under a contract or may be unable to require other parties to comply with their obligations and, therefore, may suffer financial loss or penalty.

RISK FACTORS RELATED TO THE PHARMACEUTICAL INDUSTRY IN GENERAL

The actions of governments, industry regulators and the economic environments in which the Company operates may adversely affect its ability to develop and market its products profitably

Changes to laws or regulations impacting the pharmaceutical industry, in any country in which the Company conducts its business, may adversely impact the Company's sales, financial condition and results of operations. In particular, changes to the regulations relating to orphan drug status may affect the exclusivity granted to products with such designation. Changes in the general economic conditions in any of the Company's major markets may also affect the Company's sales, financial condition and results of operations.

The introduction of new products by competitors may impact future revenues

The manufacture and sale of pharmaceuticals is 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 fall.

The pharmaceutical and biotechnology 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, technological advances in manufacturing or production by its competitors.

If the Company's projects or clinical trials for the development of products are unsuccessful, its products will not receive authorization for manufacture and sale

Due to the complexity of the formulation and development of pharmaceuticals, the Company cannot be certain that it or its collaborative partners will successfully complete the development of new products, or, if successful, that such products will be commercially viable.

Before obtaining regulatory approvals for the commercial sale of each product under development, the Company or its collaborative partners must demonstrate through clinical and other studies that the product is of appropriate quality and is safe and effective for the claimed use. Clinical trials of any product under development may not demonstrate the quality, safety and efficacy required to result in an approvable or a marketable product. Failure to demonstrate adequately the quality, safety and efficacy of a therapeutic drug under development would delay or

prevent regulatory approval of the product. In addition, regulatory authorities in Europe, the US, Canada and other countries may require additional studies, which could result in (a) increased costs and significant development delays, or (b) termination of a project if it would no longer be economically viable. The completion rate of clinical trials is dependent upon, among other factors, obtaining adequate clinical supplies and recruiting patients. Delays in patient enrolment in clinical trials may also result in increased costs and program delays. Additional delays can occur in instances in which the Company shares control over the planning and execution of product development with collaborative partners. The Company cannot be certain that, if clinical trials are completed, either the Company or its collaborative partners will file for, or receive, required authorizations to manufacture and/or market potential products (including a marketing authorization application or ANDA) or that such application will be reviewed and approved by the regulatory authorities in a timely manner, if at all.

If the Company is unable to meet the requirements of regulators in relation to a particular product, it may be unable to develop the product or obtain or retain the necessary marketing approvals

Drug companies are required to obtain regulatory approval before manufacturing and marketing most drug products. Regulatory approval is generally based on the results of:

- quality testing (chemistry, manufacturing and controls);
- non-clinical testing; and
- clinical testing.

The clinical development, manufacture, marketing and sale of pharmaceutical products is subject to extensive regulation, including separate regulation by each member state of the EU, the EMEA itself and federal, state and local regulation in the US. Unanticipated legislative and other regulatory actions and developments concerning various aspects of the Company's operations and products may restrict its ability to sell one or more of its products or to sell those products at a profit. The generation of data is regulated and any generated data is susceptible to varying interpretations that could delay, limit or prevent regulatory approval. Required regulatory approvals may not be obtained in a timely manner, if at all. In addition, other regulatory requirements for any such proposed products may not be met.

Even if the Company obtains regulatory approvals, the terms of any product approval, including labeling, may be more restrictive than desired and could affect the marketability of its products. Regulatory authorities also have the power amongst other things, to:

- revoke or suspend approvals of previously approved products;
- require the recall of products that fail to meet regulatory requirements; and
- close manufacturing plants that do not operate in conformity with cGMP and/or other regulatory requirements or approvals.

Such delays or actions could affect the Company's ability to manufacture and sell its products.

The failure of a strategic partner to develop and commercialize products could result in delays in 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 dependent on its partner to deliver results. While these partnerships are supported by contracts, the Company does not exercise direct control. If a partner fails to perform or experiences financial difficulties, the Company may suffer a delay in the development, a delay in the approval or a reduction in sales or royalties of a product.

The failure to secure new products or compounds for development, either through in-licensing, acquisition or internal research and development efforts, 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 in-license, acquire or develop new products or compounds. The Company also expends significant resources on research and development. The failure to in-license or acquire new products or compounds, on a commercially viable basis, could have a material adverse effect on the Company's financial position. The failure of these efforts to result in the development of products appropriate for testing in human clinical trials could have a material adverse effect on the Company's revenues, financial condition and results of operations.

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

The Company's success depends upon its ability and the ability of its partners and licensors to protect their intellectual property rights. Where possible, the Company's strategy is to register intellectual property rights, such as

patents and trademarks. The Company also relies variously on trade secrets, unpatented know-how and technological innovations and contractual arrangements with third parties to maintain its competitive position.

Patents and patent applications covering a number of the technologies and processes owned or licensed to the Company have been granted, or are pending in various countries, including the US, Canada, major European countries and Japan. The Company intends to enforce vigorously its patent rights and believes that its partners intend to enforce vigorously patent rights they have licensed to the Company. However, patent rights may not prevent other entities from developing, using or commercializing products that are similar or functionally equivalent to the Company's products or technologies or processes for formulating or manufacturing similar or functionally equivalent products. The Company's patent rights may be successfully challenged in the future or laws providing such rights may be changed or withdrawn. The Company cannot assure investors that its patents and patent applications or those of its third party manufacturers will provide valid patent protection sufficiently broad to protect the Company's products and technology or that such patents will not be challenged, revoked, invalidated, infringed or circumvented by third parties. In the regular course of business, the Company is party to litigation or other proceedings relating to intellectual property rights. (See ITEM 3 of this Form 10-K for details of current patent litigation).

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. If third parties are the first to invent a particular product or technology, it is possible that those parties will obtain patent rights that will be sufficiently broad to prevent the Company or its strategic partners from developing, manufacturing or selling its products. The Company may need to obtain licenses for intellectual property rights from others to develop, manufacture and market commercially viable products and may not be able to obtain these licenses on commercially reasonable terms, if at all. In addition, any licensed patents or proprietary rights may not be valid and enforceable.

The Company also relies on trade secrets and other un-patented proprietary information, which it generally seeks to protect by confidentiality and nondisclosure agreements with its employees, consultants, advisors and partners. These agreements may not effectively prevent disclosure of confidential information and may not provide the Company with an adequate remedy in the event of unauthorized disclosure of such information. 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. Protracted and costly litigation could be necessary to enforce and determine the scope of the Company's proprietary rights. The failure to obtain or maintain patent and trade secret protection, for any reason, could allow other companies to make competing products and reduce the Company's product sales.

The Company has filed applications to register various trademarks for use in connection with its products in various countries including the US and countries in Europe and Latin America and intends to trademark new product names as new products are developed. In addition, with respect to certain products, the Company relies on the trademarks of third parties. These trademarks may not afford adequate protection or the Company or the third parties may not have the financial resources to enforce any rights under any of these trademarks. The Company's inability or the inability of these third parties to protect their trademarks because of successful third party claims to those trademarks could allow others to use the Company's trademarks and dilute their value.

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 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 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, 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.

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 in a number of jurisdictions around the world. The promotion, marketing and sale of pharmaceutical products 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 FDA, the US Department of Justice and the DEA in the US. Any inquiries or investigations into the operations of, or enforcement or other regulatory action against, the Company by such regulatory authorities could result in the distraction of senior management for prolonged periods of time, significant defense costs and substantial monetary penalties.

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

The Company faces intense competition for highly qualified management and scientific 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 scientific and management 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.

ITEM 1B: Unresolved Staff Comments

None.

ITEM 2: Properties

The following are the principal premises of the Company, as at December 31, 2008:

Location	Use	Approximate Square Footage	Owned or Leased
Dublin, Ireland	Office accommodation	16,000	Leased
Basingstoke, Hampshire, UK	Office accommodation	88,500	Owned/Leased
Wayne, Pennsylvania, USA	Office accommodation (Specialty Pharmaceuticals Headquarters)	375,000	Leased
Florence, Kentucky, USA	Warehousing and distribution facility	96,000	Leased
Owings Mills, Maryland, USA	Manufacturing facility and technology center	90,000	Leased
Cambridge, Massachusetts, USA	Office accommodation (Shire HGT Headquarters) and laboratories	181,000	Leased
Cambridge, Massachusetts, USA	Laboratories and manufacturing facility	29,000	Leased
Cambridge, Massachusetts, USA	Office accommodation	34,000	Leased
Lexington, Massachusetts, USA	Office accommodation, laboratories and manufacturing, warehousing and distribution facility	218,000	Leased
Belmont, Massachusetts, USA	Warehousing facility	16,000	Leased

The Company also has other smaller locations in some of the countries listed above and in several other countries around the world. At December 31, 2008 all the above sites were utilized by the Company with the exception of part of the sites at Lexington, Massachusetts and Wayne, Pennsylvania, which are undergoing significant alterations or new construction of additional facilities. In addition, Shire has properties at Newport, Kentucky and Rockville, Maryland which are not fully utilized.

ITEM 3: Legal Proceedings

The information required by this Item is incorporated herein by reference to Note 23(d), "Commitments and Contingencies, Legal proceedings" in our notes to the consolidated financial statements listed under ITEM 15: Exhibits and Financial Statement Schedules of Part IV of this Annual Report on Form 10-K.

In addition, information on legal proceedings relating to products from which the Company receives royalties is included within ITEM 1: Business of this Annual Report on Form 10-K.

ITEM 4: Submission of matters to a vote of security holders

Shire did not submit any matters to the vote of security holders during the fourth quarter of 2008.

PART II

ITEM 5: Market for Registrant's common equity, related stockholder matters and issuer purchases of equity securities

Ordinary shares

The Company's ordinary shares are traded on the London Stock Exchange ("LSE"). On May 23, 2008 a Scheme of Arrangement (the "Scheme") approved by the High Court of England and Wales and the shareholders of Shire plc, a company incorporated in England and Wales, ("Old Shire") became effective. Under the terms of the Scheme, Shire Limited (now known as Shire plc), a public company incorporated in Jersey (Channel Islands) and tax resident in the Republic of Ireland, became the holding company of Old Shire (the former holding company of the Shire Group). Pursuant to the Scheme, holders of ordinary shares of Old Shire received one ordinary share of Shire Limited for each ordinary share of Old Shire held at 5.30pm (GMT) on May 22, 2008. The Shire Limited ordinary shares carry substantially the same rights as the Old Shire ordinary shares, and the Scheme did not involve any payment for the Shire Limited ordinary shares.

The ordinary shares of Shire Limited were admitted to the Official List and to trading on the LSE at 8.00am (GMT) on May 23, 2008. The listing of the ordinary shares of Old Shire was cancelled at the same time. Shire Limited changed its name to Shire plc on October 1, 2008.

The following table presents the per share closing mid-market quotation for ordinary shares of Shire plc (or as applicable prior to May 23, 2008 the ordinary shares of Old Shire) as quoted in the Daily Official List of the LSE for the periods indicated.

	High £ per ordinary share	Low £ per ordinary share
Year to December 31, 2008		
1 st Quarter	11.94	8.60
2 nd Quarter	10.30	7.67
3 rd Quarter	10.00	7.12
4 th Quarter	10.34	6.91
Year to December 31, 2007		
1 st Quarter	11.44	10.36
2 nd Quarter	12.43	10.33
3 rd Quarter	13.16	11.18
4 th Quarter	12.68	10.27

The total number of record holders of ordinary shares of Shire plc on February 20, 2009 was 7,071. Since certain of the ordinary shares are held by broker nominees, the number of record holders may not be representative of the number of beneficial owners.

American Depositary Shares

American Depositary Shares ("ADSs") each represent three ordinary shares of Shire plc. An ADS is evidenced by an American Depositary Receipt ("ADR") issued by JPMorgan Chase Bank, N.A. (formerly known as Morgan Guaranty Trust Company of New York) as depositary, and is listed on the NASDAQ Global Select Market. On February 20, 2009 the proportion of ordinary shares represented by ADRs was 29% of the outstanding ordinary shares.

As a result of the Scheme, ADSs representing three ordinary shares of Old Shire were replaced by ADSs representing three ordinary shares of Shire Limited (now known as Shire plc) on a one-for-one basis. Dealings in ADSs representing ordinary shares of Shire Limited on NASDAQ Global Select Market commenced at 9.30am (EST) on May 23, 2008. ADSs representing ordinary shares of Old Shire were cancelled at the same time.

The following table presents the high and low market quotations for ADSs quoted on the NASDAQ Global Select Market for the periods indicated, (prior to May 23, 2008 the ADSs represented ordinary shares of Old Shire).

	<u>High \$ per ADS</u>	<u>Low \$ per ADS</u>
Year to December 31, 2008		
1 st Quarter	69.72	51.95
2 nd Quarter	60.60	45.12
3 rd Quarter	55.50	43.63
4 th Quarter	48.48	32.74
Year to December 31, 2007		
1 st Quarter	67.73	60.55
2 nd Quarter	75.37	61.62
3 rd Quarter	81.00	68.28
4 th Quarter	77.34	64.16

The number of record holders of ADSs in the United States on February 20 2009 was 752. Since certain of the ADSs are held by broker nominees, the number of record holders may not be representative of the number of beneficial owners.

Canadian exchangeable shares

On February 12, 2008, a subsidiary of Shire exercised a redemption call right and purchased all remaining exchangeable shares of Shire Acquisition Inc. in public ownership. Exchangeable shareholders received either three ordinary shares of Old Shire or one ADS representing three ordinary shares of Old Shire for each exchangeable share held. Exchangeable shares were issued to Canadian resident shareholders of Biochem Pharma Inc. (now Shire Canada, Inc.) in 2001 as consideration for the acquisition by the Shire group of Biochem Pharma Inc. The exchangeable shares have now been de-listed from the Toronto Stock Exchange.

Dividend policy

A first interim dividend for the first half of 2008 of 2.15 US cents (1.08 pence) per ordinary share, equivalent to 6.44 US cents per ADS, was paid in October 2008. The Board has resolved to pay a second interim dividend of 7.76 US cents (5.47 pence) per ordinary share equivalent to 23.28 US cents per ADS for the six months to December 31, 2008.

A first interim dividend for the first half of 2007 of 2.15 US cents (1.05 pence) per ordinary share, equivalent to 6.44 US cents per ADS and 6.72 Canadian cents per Exchangeable Share, was paid in October 2007. A second interim dividend for the second half of 2007 of 6.47 US cents (3.33 pence) per ordinary share equivalent to 19.41 US cents per ADS was paid in April 2008.

This is consistent with Shire's stated policy of paying a dividend semi-annually, set in US cents per ordinary share. It is intended that the first interim payment each year should be constant in US dollar terms. Dividend growth for the full year will be reviewed by the Board when the second interim dividend is determined. Any dividend growth will come through increasing the second interim dividend in a financial year.

Income Access Share ("IAS Trust") Arrangements

Shire has put into place income access share arrangements which enable Shire ordinary shareholders, other than Shire ADS holders, to elect to receive their dividends from a company resident for tax purposes in the Republic of Ireland or receive their dividends under the income access share arrangements from a Shire Group company resident for tax purposes in the UK.

Old Shire has issued one income access share which is held by the income access share trustee pursuant to the IAS Trust. The IAS Trust is constituted pursuant to a trust deed which provides that:

(i) the income access share trustee will hold any dividends paid (not just declared) on the income access share on trust for the Shire ordinary shareholders who have elected (or are deemed to have elected) to receive dividends pursuant to these arrangements;

(ii) the income access share itself will be held on trust for Shire; and

(iii) each registered holder of Shire ordinary shares on a dividend record date who has made (or is deemed to have made) a valid income access share election (described below) will be entitled to receive from the income access share trustee an amount equal to the dividend it would have received from Shire, to the extent the income access share trustee has actually received an amount equal to such amount by way of dividend from Old Shire.

To ensure compliance with technical trust law rules, the period during which the income access share trust may continue will be restricted. However, the income access share trust should be able to continue for 80 years.

This mechanism is reflected in the articles of association of both Shire plc and Old Shire; the mechanics of the arrangements are as follows:

The Shire plc articles of association provide that if (i) a dividend is announced or declared by Shire plc on the Shire ordinary shares, (ii) an amount is paid by Old Shire by way of a dividend on the income access share to the income access share trustee, and (iii) such amount is paid by the income access share trustee to the Shire ordinary shareholders who have elected (or are deemed to have elected) to receive dividends under these arrangements, the dividend which would otherwise be payable by Shire to such Shire ordinary shareholders will be reduced by an amount equal to the amount paid to such Shire ordinary shareholders by the income access share trustee.

If the dividend paid on the income access share and on-paid by the income access share trustee to the Shire ordinary shareholders is less than the total amount of the dividend announced or declared by Shire on the Shire ordinary shares in respect of which an election has been made (or is deemed to have been made) to receive dividends under these arrangements, Shire will be obliged to pay a dividend on the Shire ordinary shares to those Shire ordinary shareholders who have so elected (or are deemed to have so elected) of the amount of the shortfall. In such a case, any dividend paid on the Shire ordinary shares will generally be subject to Irish withholding tax at the rate of 20% or such lower rate as may be applicable under exemptions from withholding tax contained in Irish law.

A Shire ordinary shareholder is entitled to make an income access share election such that he will receive his dividends (which would otherwise be payable by Shire) under these arrangements from Old Shire.

A Shire ordinary shareholder who held 25,000 or fewer Shire ordinary shares at the time he became a Shire ordinary shareholder pursuant to the court sanctioned Scheme of Arrangement, and who did not make a contrary election, is deemed to have made an election (pursuant to the Shire articles of association) such that he will receive his dividends under these arrangements from Old Shire.

Equally, where a Shire ordinary shareholder who first acquires his Shire ordinary shares after the date of the Scheme of Arrangement, who holds 25,000 or fewer Shire ordinary shares on the first dividend record date after he becomes a Shire ordinary shareholder, and who does not make a contrary election, will be deemed to have made an election (pursuant to the Shire articles of association) such that he will receive his dividends under these arrangements from Old Shire.

In accordance with the provisions of the Shire ADS deposit agreement, the Depositary has made an election on behalf of all holders of Shire ADSs such that they will receive dividends from Old Shire under the income access share arrangements. Dividends paid by Old Shire under the income access share arrangements will not under current legislation be subject to any UK or Irish withholding taxes. If a holder of Shire ADSs does not wish to receive dividends from Old Shire under the income access share arrangements, he must withdraw his Shire ordinary shares from the Shire ADS program prior to the dividend record date set by the Depositary and request delivery of the Shire ordinary shares. This will enable him to receive dividends from Shire (if necessary, by making an election to that effect).

It is the expectation, although there can be no certainty, that dividends will be paid by Old Shire through the income access share trustee to Shire ordinary shareholders who make (or are deemed to make) an income access share election.

It is the expectation, although there can be no certainty, that Old Shire will distribute dividends on the income access share to the income access share trustee for the benefit of all Shire ordinary shareholders who make (or are deemed to make) an income access share election in an amount equal to what would have been such Shire ordinary shareholders' entitlement to dividends from Shire in the absence of the income access share election. To the extent that any dividend paid on the income access share to the income access share trustee and on-paid by the income access share trustee to the Shire ordinary shareholders is less than an amount equal to what would have been such Shire ordinary shareholders' entitlement to dividends from Shire in the absence of the income access share election, the dividend on the income access share received by the income access share trustee will be allocated pro rata to such Shire ordinary shareholders and Shire will pay the balance by way of dividend. In such circumstances, there will be no grossing up by Shire in respect of, and Old Shire and Shire will not compensate those Shire ordinary shareholders for, any adverse consequences including any Irish withholding tax consequences.

Shire will be able to suspend or terminate these arrangements at any time, in which case the full Shire dividend will be paid directly by Shire to those Shire ordinary shareholders (including the Depositary) who have made (or are deemed to have made) an income access share election. In such circumstances, there will be no grossing up by Shire in respect of, and Old Shire and Shire will not compensate those Shire ordinary shareholders for, any adverse consequences including any Irish withholding tax consequences.

On October 7, 2008 Old Shire paid dividends totaling \$7.2 million on the income access share to the income access share trustee in an amount equal to the dividend Shire ordinary shareholders would have received from Shire.

Reduction of Capital and Distributable Reserves

On June 11, 2008 the Jersey Court approved a reduction of Shire plc's (then known as Shire Limited) share capital to take effect on June 12, 2008. The reduction increased the distributable reserves potentially available to Shire plc at the time of reduction to approximately \$3.7 billion by recharacterizing amounts standing to the credit of Shire plc's share premium account as a distributable reserve. The purpose of the reduction of capital is to create a distributable reserve which would be available to be distributed as dividends, at the discretion of the Directors of Shire plc, from time to time or for any other lawful purpose to which such a reserve may be applied (including share buy backs). The reduction of capital was designed to create in Shire plc a level of distributable reserves similar to that previously available in Old Shire and to enable Shire plc to continue Shire's existing dividend policy in a financially and operationally efficient manner.

Since Shire plc is a Jersey company, the payment of dividends by Shire plc is governed by Jersey law. Under Jersey law, Shire plc is entitled to make payments of dividends from its accumulated profits and other distributable reserves. Prior to making any dividend payment, the Directors of Shire plc who authorize the payment of the dividend must make a solvency statement to the effect that Shire plc will be able to continue to carry on its business and discharge its debts as they fall due immediately after the payment is made and for the twelve month period following the making of the payment. Shire plc's future dividend policy will be dependent upon the amount of its distributable reserves, its financial condition, the terms of its then existing debt facilities and other relevant factors existing at the time.

For dividends paid by Old Shire prior to the Scheme, and for those dividends paid by Old Shire on the income access share to the income access share trustee subsequent to the Scheme, the ability of Old Shire to pay dividends is determined under English law. As a matter of English law Old Shire can only pay dividends out of its distributable profits, which are the accumulated realized profits under generally accepted accounting principles in the United Kingdom, (including reserves arising from a reduction of share capital), of Old Shire and not the consolidated group, so far as not previously utilized by distribution or capitalization, less accumulated realized losses, so far as not previously written off in a reduction of capital duly made.

Equity Compensation Plan Information

Equity compensation plan information is incorporated herein by reference to ITEM 12: Security Ownership of Certain Beneficial Owners and Management and Related Stock Holder Matters of Part IV of this Annual Report on Form 10-K.

Performance Graph

For a graph comparing the cumulative total return to our stockholders during the five years ending December 31, 2008 to that of the FTSE 100 index and a comparator group of companies, please refer to ITEM 11: Executive Compensation – Directors' Remuneration Report.

ITEM 6: Selected financial data

The selected consolidated financial data presented below at December 31, 2008 and 2007 and for each of the three years in the period ended December 31, 2008 were derived from the audited consolidated financial statements of the Company, included herein. The selected consolidated financial data presented below at December 31, 2006, 2005 and 2004 and for each of the two years in the period ended December 31, 2005 were derived from the audited consolidated financial statements of the Company, which are not included herein.

The selected consolidated financial data should be read in conjunction with ITEM 7: Management's Discussion and Analysis of Financial Condition and Results of Operations and with the consolidated financial statements and related notes appearing elsewhere in this report.

Year to December 31,	2008 \$'M	2007 \$'M	2006 \$'M	2005 \$'M	2004 \$'M
Statement of Operations:					
Total revenues	3,022.2	2,436.3	1,796.5	1,599.3	1,363.2
Total operating expenses ⁽¹⁾⁽²⁾	(2,610.2)	(3,815.4)	(1,513.3)	(2,124.2)	(950.3)
Operating income/(loss)	412.0	(1,379.1)	283.2	(524.9)	412.9
Total other (expense)/income, net ⁽³⁾	(146.4)	(19.0)	33.6	33.2	13.5
Income/(loss) from continuing operations before income taxes, minority interest and equity in earnings/(losses) of equity method investees					
Income taxes	265.6	(1,398.1)	316.8	(491.7)	426.4
Minority Interest	(98.0)	(55.5)	(84.9)	(88.8)	(128.3)
Equity in earnings/(losses) of equity method investees, net of taxes	3.6	-	-	-	-
Income/(loss) from continuing operations	2.4	1.8	5.7	(1.0)	2.5
(Loss)/gain from discontinued operations, net of tax	173.6	(1,451.8)	237.6	(581.5)	300.6
Gain/(loss) on disposition of discontinued operations, net of tax	(17.6)	-	40.6	-	(20.1)
Net income/(loss)	-	-	-	3.1	(44.2)
Earnings per share – basic	156.0	(1,451.8)	278.2	(578.4)	236.3
Income/(loss) from continuing operations	32.1c	(268.7c)	47.2c	(116.2c)	60.6c
(Loss)/gain from discontinued operations	(3.3c)	-	8.1c	-	(4.1c)
Gain/(loss) on disposition of discontinued operations	-	-	-	0.6c	(8.9c)
Earnings/(loss) per ordinary share - basic	28.8c	(268.7c)	55.3c	(115.6c)	47.6c
Earnings per share – diluted					
Income/(loss) from continuing operations	31.8c	(268.7c)	46.6c	(116.2c)	59.4c
(Loss)/gain from discontinued operations	(3.2c)	-	8.0c	-	(3.9c)
Gain/(loss) on disposition of discontinued operations	-	-	-	0.6c	(8.6c)
Earnings/(loss) per ordinary share - diluted	28.6c	(268.7c)	54.6c	(115.6c)	46.9c

(1) Total operating expenses include: an in-process research and development ("IPR&D") write-off of \$263.1 million in 2008 resulting from the acquisition of Jerini and METAZYM from Zymenex, \$1,866.4 million in 2007 resulting from the acquisition of New River Pharmaceuticals Inc ("New River") and \$815.0 million in 2005 resulting from the acquisition of TKT; costs of \$149.9 million in 2008 relating to the write down of inventory, intangible asset impairment charges and other exit costs in respect of DYNEPO which the Company has decided to stop commercializing; costs of \$14.8 million and \$4.5 million associated with the introduction of the new holding company in 2008 and 2005 respectively; integration costs arising on the acquisitions of Jerini, New River and TKT of \$10.3 million, \$1.3 million, \$5.6 million and \$9.7 million in 2008, 2007, 2006 and 2005 respectively; and reorganization costs of \$9.4 million and \$48.5 million in 2005 and 2004 respectively relating to the implementation of the new business model in 2005 and 2004.

(2) Total operating expenses include gains on sale of product rights of \$20.7 million in 2008, \$127.8 million in 2007 and \$63.0 million in 2006. See Note 5 to the consolidated financial statements in Part IV of this Annual Report for further details.

(3) Total other (expense)/ income, net includes interest income and expense, the gain or loss on the sale of investments, impairment of long-term investments and transactional foreign exchange. See Note 29 to the consolidated financial statements in Part IV of this Annual Report. Significant components of Total other (expense) / income, net include:

- a. Interest expense in respect of the TKT appraisal rights litigation of \$87.3 million, \$28.0 million, \$24.6 million and \$7.7 million in 2008, 2007, 2006 and 2005 respectively. This litigation was settled in November 2008: prior to this the Company had accrued interest based on a reasonable estimate of an award made by the Court to those former TKT shareholders who requested appraisal. After reaching the settlement, the Company accrued additional interest expense of \$73.0 million in the year to

December 31, 2008 consistent with the terms of the settlement agreement. Further information on the settlement of this litigation can be found in Note 23(d) of ITEM 15: Exhibits and Financial Statement Schedules of Part IV of this Annual Report.

- b. Other than temporary impairment charges in respect of available for sale securities totaling \$58.0 million, \$3.0 million, \$0.3 million, \$0.4 million, and \$1.6 million, in 2008, 2007, 2006, 2005 and 2004 respectively. Other than temporary impairment charges in the year to December 31, 2008 includes \$44.3 million relating to the Company's investment in Renovo Group plc. These amounts reflect unrealized holding losses that have been reclassified out of other comprehensive income into the statement of operations in the period, as management have concluded that the impairment is other than temporary. See Note 12 of Item 15 of Part IV of this Annual Report for further details.
- c. Gains of \$9.4 million, \$0.1 million, \$3.9 million and \$14.8 million on the sale of portfolio investments in 2008, 2007, 2005 and 2004 respectively; and
- d. A gain of \$3.6 million in 2005 on the sale of the drug formulation business

Weighted average number of shares (millions):

	2008	2007	2006	2005	2004
Basic	541.6	540.3	503.4	500.2	496.3
Diluted	545.4	540.3	509.3	500.2	511.3
<hr/>					
Cash dividends declared and paid per ordinary share	8.6160c	7.3925c	6.3536c	5.6746c	1.8246c
<hr/>					

December 31,

	2008	2007	2006	2005	2004
	\$'M	\$'M	\$'M	\$'M	\$'M
<hr/>					
Balance sheets:					
Total current assets	1,044.4	1,696.8	1,810.3	1,312.2	1,928.9
Total assets	3,933.7	4,330.1	3,326.4	2,656.2	2,714.9
Total current liabilities	823.8	1,262.2	1,332.0	965.4	432.0
Non-current liabilities	1,811.4	1,840.9	52.1	43.5	32.2
Total liabilities	2,635.2	3,103.1	1,384.1	1,008.9	464.2
Minority interest	0.3	-	-	-	-
Total shareholders' equity	1,298.2	1,227.0	1,942.3	1,647.3	2,250.7
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ITEM 7: Management's discussion and analysis of financial condition and results of operation

The following discussion should be read in conjunction with the Company's consolidated financial statements contained in Part IV of this Annual Report.

Overview

Shire's strategic goal is to become the leading specialty biopharmaceutical company that focuses on meeting the needs of the specialist physician. Shire focuses its business on ADHD, HGT and GI diseases as well as opportunities in other therapeutic areas to the extent they arise through acquisitions. Shire's in-licensing, merger and acquisition efforts are focused on products in specialist markets with strong intellectual property protection and global rights. Shire believes that a carefully selected and balanced portfolio of products with strategically aligned and relatively small-scale sales forces will deliver strong results.

Substantially all of the Company's revenues, expenditures and net assets are attributable to the R&D, manufacture, sale and distribution of pharmaceutical products within two operating segments: Specialty Pharmaceuticals and HGT. The company also earns royalties (where Shire has out-licensed products to third parties) which are recorded as revenues within "All Other" in the segmental analysis.

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

- 91% (2007: 89%) of total revenues are derived from product sales, of which 75% (2007: 76%) are within the Specialty Pharmaceuticals operating segment and 16% (2007: 13%) are within the HGT operating segment;
- 8% of total revenues are derived from royalties (2007: 10%).

Shire's strategic objectives are set using a balanced scorecard approach. Objectives are also set at the business, functional and therapeutic area levels and are aligned with the Company-wide strategic and operational objectives. The Company therefore takes a fully integrated approach to strategic management. Key performance indicators ("KPIs") are used to measure achievement of the objectives. Strategic objectives are categorized into fields - 'financial', 'customers', 'people & capabilities' and 'operational excellence'. For 2008, Shire's corporate objectives included: target net revenue and defined levels of revenue growth; target sales and contributions for core products; development of a strategy to improve customer care and customer service levels; drug application filing and launch targets for new products; development of a strategy to achieve the optimum Shire product portfolio; development of optimal manufacturing and supply chain strategy; development and communication of career development tools for employees; development and commencement of rollout of Corporate brand positioning; and maintenance of robust risk management practices including internal controls.

The markets in which the Company conducts its business are highly competitive and highly regulated. The health care industry is experiencing:

- pressure from governments and healthcare providers to keep prices low while increasing access to drugs;
- increased R&D costs as development programs are typically larger and take longer to get approval from regulators;
- challenges to existing patents from generic manufacturers;
- low cost generic drugs entering the market on expiration of patent protection; and
- higher marketing costs due to the use of direct to consumer campaigns in the US and competition for market share.

Shire's strategy to become the leading specialty biopharmaceutical company 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. With the acquisition of TKT in 2005 and the establishment of our HGT business, Shire has substantially increased its presence in Europe and thereby diversified the risk associated with being reliant on one geographic market. Through the TKT acquisition, Shire acquired ELAPRASE (global rights) and REPLAGAL (which is presently sold only outside the US) and through the Jerini acquisition, FIRAZYR (global rights). In addition, 2008 saw the European launch of FIRAZYR and the continued roll out of MEZAVANT and FOSRENOL in Europe.

For 2008, sales outside North America represented approximately 24% of product sales (2007: 24%). Shire's late stage development pipeline contains a number of products with rights outside of the US, including VYVANSE, DAYTRANA, velaglucerase alfa (GA-GCB), SPD550, PLICERA, AMIGAL, AT2220 and METAZYM.

Shire's continued expansion beyond North America will be driven by the development of products with patent protection in both the North and Latin American and European markets wherever possible. In 2009 and the 2010, subject to obtaining the relevant regulatory/governmental approvals, regions outside the US should see:

- the continued roll out of MEZAVANT in certain European Union ("EU") countries;
- the launch of DAYTRANA (EU and Canada);
- the continued roll out of FIRAZYR in certain European and Latin American countries;
- the launch of VYVANSE in Canada; and
- the launch of Velaglucerase alfa in the EU.

This program of new product launches will require significant investment in advertising, promotional spend and in some cases, additional sales representatives.

The orphan disease nature of HGT products means that relatively low associated SG&A and sales infrastructure investment is required, making them ideal products for Shire to launch into new markets. In markets outside North America and Europe where products require significant SG&A and infrastructure investment, Shire will assess opportunities for internal investment versus distribution and/or out-license partners on a country-by-country basis.

R&D

Over the last five years Shire has focused its R&D efforts on products in its core therapeutic areas, which meet the needs of the specialist physician. The Company has also concentrated its resources on obtaining regulatory approval for later-stage pipeline products within its core therapeutic areas.

Evidence of the successful execution of this strategy can be seen from the progression of the Company's development pipeline over the last five years. Since January 2004, nine products have received regulatory approval; six in the US (FOSRENOL and EQUETRO in 2004, DAYTRANA and ELAPRASE in 2006, LIALDA and VYVANSE in 2007) and three in Europe (FOSRENOL in 2005, ELAPRASE and MEZAVANT in 2007). The Company has another one product in registration in the US (INTUNIV) and one in registration in the EU (DAYTRANA).

Shire's strategy is focused on the development of product candidates that have a lower risk profile. R&D costs in 2009 will include expenditure on several pre-clinical to Phase 3 studies and Phase 3(b) and Phase 4 studies to support recently launched products in the Specialty Pharmaceuticals and HGT businesses, and the development of new projects in both the Specialty Pharmaceuticals and HGT businesses. For a full discussion of these projects see ITEM 1: Business.

Patents and Market Exclusivity

The loss or expiration of patent protection or market exclusivity with respect to any of the Company's major products could have a material adverse effect on future revenues and net income as generic manufacturers may produce similar drugs and be able to sell the Company's drugs at a lower price as their costs of development are significantly lower than Shire's.

The Company anticipates that there will be one or more generic competitors to ADDERALL XR in the ADHD market beginning April 2009. ADDERALL XR is, in revenue terms, Shire's most significant product representing 36% of total revenues in 2008 (2007: 42%). The Company expects that sales of VYVANSE will partially offset any decline in sales of ADDERALL XR and that VYVANSE prescriptions will come from a number of sources, including patients who are new to ADHD treatment, patients who previously were taking ADDERALL XR, and patients who were taking another ADHD medication.

Shire is engaged in various legal proceedings with generic manufacturers with respect to its ADDERALL XR and CARBATROL patents, as well as the patents for certain other products. These legal proceedings are discussed in more detail in ITEM 3: Legal Proceedings.

Business Development

As a result of the issues associated with the loss or expiry of patent protection or market exclusivity, Shire seeks to focus its business development activity on the acquisition and in-licensing of products and projects which have the benefit of long-term patent protection and market exclusivity.

The Company remains active in seeking out opportunities to acquire new products or companies that fit its business strategy, its existing therapeutic areas or are in complementary therapeutic areas. During 2008 Shire:

- acquired more than 98% of Jerini, adding Jerini's HAE product, FIRAZYR, to the portfolio; and
- acquired the global rights to METAZYM, a clinical candidate arylsulfatase-A, from Zymenex.

In 2007, the Company acquired New River, allowing Shire to capture the full economic value of VYVANSE and gain control of the development and commercialization of this product. In 2007 Shire also in-licensed the rights to AMIGAL, PLICERA and AT-2220, three pharmacological chaperone compounds for lysosomal storage disorders in markets outside the US; SPD550 for Celiac disease in markets outside of the US and Japan; and worldwide rights (excluding EU member states) to JUVISTA.

As part of its strategy of focusing on drugs with long term patent protection in its core therapeutic areas, the Company will continue to evaluate opportunities to dispose of non-core assets. In 2007 the Company divested a portfolio of non-core products, including SOLARAZE and VANIQA, to Almirall and sold EQUETRO and transferred post-approval study commitments to Validus Pharmaceuticals Inc.

Organization and Structure

During 2008, the Company undertook a court sanctioned Scheme of Arrangement, establishing Shire plc as the new Shire holding company. For further details on the Scheme of Arrangement see Note 3 to the Company's consolidated financial statements in Part IV to this Annual Report.

In 2008, Shire acquired more than 98% of Jerini and is in the process of integrating Jerini into the Company: integration and acquisition related costs expensed during the year to December 31, 2008 totaled \$10.3 million.

Results of operations for the years to December 31, 2008 and 2007

For the year to December 31, 2008 the Company's total revenues increased by 24% to \$3,022.2 million, compared to \$2,436.3 million in 2007. Net income for the year to December 31, 2008 was \$156.0 million compared to a net loss of \$1,451.8 million in 2007.

Total revenues

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

Year to December 31,	2008 \$'M	2007 \$'M	Change %
Product sales	2,754.2	2,170.2	27
Royalties	245.5	247.2	-1
Other revenues	22.5	18.9	19
Total	3,022.2	2,436.3	24

Product sales

Year to December 31,	2008 \$'M	2007 \$'M	Product sales growth %	US prescription growth %
Specialty Pharmaceuticals				
ADHD				
ADDERALL XR	1,101.7	1,030.9	7	-5
VYVANSE	318.9	76.5	317	388
DAYTRANA	78.7	64.2	23	-11
GI				
PENTASA	185.5	176.4	5	-1
LIALDA / MEZAVANT	140.4	50.5	178	204
General Products				
FOSRENOL	155.4	102.2	52	-4
CALCICHEW	52.8	54.2	-3	n/a
CARBATROL	75.9	72.3	5	-4
REMINYL/REMINYL XL	34.4	31.2	10	n/a
XAGRID	78.7	66.8	18	n/a
Other product sales	50.1	119.3	-58	n/a
	2,272.5	1,844.5	23	
Human Genetic Therapies				
ELAPRASE	305.1	181.8	68	n/a
REPLAGAL	176.1	143.9	22	n/a
FIRAZYR	0.5	-	n/a	n/a
	481.7	325.7	48	
Total	2,754.2	2,170.2	27	

The following discussion includes references to US prescription and US market share data for key products. The source of this data is IMS, December 2008.

Specialty Pharmaceuticals

US ADHD market share

The continued growth in market share of VYVANSE helped Shire grow its average annual share of the US ADHD market to 32.6% for the year to December 31, 2008 compared to 29.4% in 2007. Shire has the leading portfolio of products in the US ADHD market.

ADDERALL XR

ADDERALL XR's average share of the US ADHD market for 2008 fell to 22.6% (2007: 25.5%). US prescriptions for ADDERALL XR for the year to December 31, 2008 decreased by 5% compared to 2007 due to an 11% fall in average market share offset by a 7% growth in the US ADHD market.

Sales of ADDERALL XR for the year to December 31, 2008 were \$1,101.7 million, an increase of 7% compared to the same period in 2007 (2007: \$1,030.9 million), with the decline in prescriptions being more than offset by price increases.

As previously disclosed, the United States Federal Trade Commission ("FTC") informed Shire on October 3, 2006 that it was reviewing the ADDERALL XR patent litigation settlement agreement between Shire and Barr. On June 22, 2007 the Company received a civil investigative demand requesting that it provide information to the FTC relating to its settlement with Barr and its earlier settlement with Impax Laboratories, Inc. The Company is cooperating fully with this investigation and believes that the settlements are in compliance with all applicable laws.

Litigation proceedings concerning Shire's ADDERALL XR patents are ongoing. For further information see ITEM 3: Legal Proceedings.

VYVANSE

VYVANSE was launched in the US in July 2007 and product sales for the year to December 31, 2008 were \$318.9 million (2007: \$76.5 million). Product sales growth was driven by the increase in average share of the US ADHD market (8.2% for the year to December 31, 2008 compared to 1.8% in 2007) and a price increase in April 2008.

DAYTRANA

Product sales for the year to December 31, 2008 were \$78.7 million (2007: \$64.2 million). DAYTRANA's average annual share of the US ADHD market decreased to 1.8% in 2008 compared to 2.1% in 2007.

Despite the 11% decrease in prescriptions compared to 2007, sales of DAYTRANA grew 23% compared to the same period last year due to growth in the US ADHD market of 7% and lower sales deductions in 2008 over 2007, primarily due to reduced coupon expense.

During 2008 Shire announced two voluntary market recalls of a limited portion of DAYTRANA patches because certain patches did not meet their release liner removal specifications which may have resulted in some patients and caregivers having difficulties removing the liners. The voluntary recalls were not due to safety issues. Shire and Noven (the manufacturer of DAYTRANA) continue to pursue enhancements to the product and to work closely with the FDA to implement changes that may improve the usability of DAYTRANA. There has been no interruption in the production of DAYTRANA.

US oral mesalamine market share

Shire's average annual market share of the US oral mesalamine market rose to 28.4% for the year to December 31, 2008 (2007: 21.1%), driven by the growth of LIALDA since its launch in March 2007.

PENTASA

US prescriptions of PENTASA for the year to December 31, 2008 were down 1% compared to 2007 primarily due to a small decrease in PENTASA's average annual market share from 17.2% in 2007 to 16.7% in 2008, offset by a 2% increase in the US oral mesalamine prescription market.

Sales of PENTASA for the year to December 31, 2008 were \$185.5 million, an increase of 5% compared to 2007 (2007: \$176.4 million). Sales growth is higher than prescription growth primarily due to the impact of price increases.

LIALDA/MEZAVANT

US prescriptions of LIALDA for the year to December 31, 2008 were up 204% compared to the prior year and LIALDA's average market share for 2008 increased to 11.7% (2007: 3.9%). LIALDA's US product sales for the year to December 31, 2008 were \$134.8 million compared to \$50.3 million in 2007.

Sales of MEZAVANT outside the US for the year to December 31, 2008 were \$5.6 million (2007: \$0.2 million). By December 31, 2008 MEZAVANT was available in five EU countries. Launches are planned in other countries during 2009, subject to the successful conclusion of pricing and reimbursement negotiations.

FOSRENOL

At December 31, 2008 FOSRENOL was available in 30 countries and global sales grew by 52% to \$155.4 million for the year to December 31, 2008 (2007: \$102.2 million). Sales of FOSRENOL outside the US for the year to December 31, 2008 were \$69.5 million (2007: \$40.1 million).

US sales of FOSRENOL for the year to December 31, 2008 were up 38% to \$85.9 million compared to 2007 (2007: \$62.1 million). FOSRENOL's average prescription share of the US phosphate binder retail market decreased to 8.1% for the year to December 31, 2008 (2007: 8.6%). Product sales increased despite the decrease in prescriptions due to price increases and a 34% increase in FOSRENOL's share of the non retail market resulting from Shire's continued focus on specialist physicians, clinics and dialysis centers.

In February 2009, Shire received three Paragraph IV Notice letters, from Barr, Mylan and NATCO advising the filing of Abbreviated New Drug applications ("ANDA") for generic versions of 500mg, 750mg and 1,000mg FOSRENOL. Shire is currently reviewing the details of these notice letters and, under the Hatch-Waxman regulations, has 45 days from the date of each notice letter to determine if it will file a patent infringement suit. If Shire brings suit pursuant to the Hatch-Waxman regulations a 30 month stay of approval, commencing on October 26, 2009, will be imposed on the FDA on each ANDA which is the subject of such a lawsuit.

XAGRID

Sales for the year to December 31, 2008 were \$78.7 million, an increase of 18% compared to the same period in 2007 (2007: \$66.8 million). Expressed in transaction currencies (XAGRID is primarily sold in Euros and Pounds sterling) sales increased by 16%, with exchange rate movements against the US dollar accounting for the remaining 2% increase.

DYNEPO

In July 2008 Shire announced that it had made the decision to cease the commercialization of DYNEPO, effective at the end of 2008, and recorded charges of \$149.9 million to cover intangible asset impairment, inventory write downs and other exit costs. Sales for the year to December 31, 2008 were \$20.9 million (2007: \$14.2 million).

Human Genetic Therapies

ELAPRASE

Sales for the year to December 31, 2008 were \$305.1 million, an increase of 68% compared to the same period in 2007 (2007: \$181.8 million). The sales growth was driven by increased unit sales across all regions where ELAPRASE is sold: Europe, North America, Latin America, and Asia Pacific. Expressed in transaction currencies (ELAPRASE is primarily sold in US dollars and Euros) sales increased by 64%, with exchange rate movements against the US dollar accounting for the remaining 4% increase.

REPLAGAL

Sales for the year to December 31, 2008 were \$176.1 million, an increase of 22% compared to the same period in 2007 (2007: \$143.9 million). The sales growth was primarily driven by increased unit sales in Europe and Asia Pacific. Expressed in transaction currencies (REPLAGAL is primarily sold in Euros and Pounds sterling) sales increased by 18%, with exchange rate movements against the US dollar accounting for the remaining 4% increase.

FIRAZYR

During the second half of 2008 FIRAZYR was launched in some countries in Europe, and sales of \$0.5 million were recognized (2007: \$nil). Launches will continue across Europe through 2009 as reimbursement negotiations successfully conclude.

Foreign exchange effect

Revenues reported in US dollars include the impact of translating sales made in local currency (primarily Euros and Pounds sterling) into US dollars. The table below shows the effect of foreign exchange translations on the revenue growth of the key affected products (for the principal currencies for each product) as well as the underlying performance of those products in their local currency:

	2008 sales in US dollars \$'M	2008 sales growth in local currency %	2008 sales growth in US dollars %	Impact of translation to US dollars %
XAGRID				
- sales in Euros	53.0	+18	+26	+8
- sales in Pounds Sterling	25.4	+11	+3	-8
REPLAGAL				
- sales in Euros	100.9	+15	+23	+8
- sales in Pounds Sterling	24.5	+5	-3	-8
ELAPRASE				
- sales in Euros	137.3	+41	+51	+10
- sales in Pounds Sterling	28.0	+43	+31	-12
CALCICHEW sales in Pounds Sterling	47.8	+6	-2	-8
REMINYL and REMINYL XL sales in Pounds Sterling	32.2	+21	+11	-10

Royalties

Royalty revenue decreased by 1% to \$245.5 million for the year to December 31, 2008 (2007: \$247.2 million).

Year to December 31,	2008 \$'M	2007 \$'M	Change %
3TC	140.2	145.3	-4
ZEFFIX	40.3	41.0	-2
Others	65.0	60.9	7
Total	245.5	247.2	-1

3TC

Royalties from sales of 3TC for the year to December 31, 2008 were \$140.2 million, a decrease of 4% compared to the same period in 2007 (2007: \$145.3 million). Excluding favorable foreign exchange movements of 2%, there has been a decline of 6% compared to the same period in 2007.

Shire receives royalties from GSK on worldwide 3TC sales. GSK's worldwide sales of 3TC for the year to December 31, 2008 were \$1,060 million, a decrease of 5% compared to the same period in 2007 (2007: \$1,110 million), but a decrease of approximately 7% on a constant exchange rate basis. While the nucleoside analogue market for HIV has continued to grow, competitive pressures within the market have increased, leading to a decline in 3TC sales.

In 2007 generic drug companies filed ANDAs seeking approval for EPIVIR, COMBIVIR, ZEFFIX and EPZICOM in the US. Pursuant to the GSK/Shire license for lamivudine products, GSK has the right to enforce the licensed patents. In November 2007 GSK filed a patent infringement lawsuit against Teva in the US District Court for the District of Delaware for infringement of one of the patents relating to COMBIVIR. The patent, which covers the combination of AZT and lamivudine to treat HIV, expires in May 2012. Teva had filed an ANDA with the FDA with a certification of invalidity, unenforceability and non-infringement of that combination patent. Teva did not challenge two other patents relating to COMBIVIR that expire in 2010 and 2016. The case is in its early stages.

ZEFFIX

Royalties from sales of ZEFFIX for the year to December 31, 2008 were \$40.3 million, a decrease of 2% compared to the same period in 2007 (2007: \$41.0 million). The impact of foreign exchange movements has contributed 6% growth; excluding favorable foreign exchange movements there has been a decrease of 8% compared to the same period in 2007.

OTHER

Other royalties are primarily in respect of REMINYL and REMINYL XL (known as RAZADYNE and RAZADYNE ER in the US). REMINYL and REMINYL XL are indicated for the symptomatic treatment of mild to moderately severe dementia of the Alzheimer type and are marketed by the Company in the UK and Republic of Ireland. In the rest of the world, they are marketed by Janssen, an affiliate of Johnson & Johnson (under the name RAZADYNE and RAZADYNE ER in the US). The Company receives royalties on Janssen's sales.

Certain companies filed ANDAs with the FDA for generic versions of RAZADYNE. Janssen and Synaptch filed lawsuits against some of those ANDA filers. A trial was held during the week of May 21, 2007. Following a decision on August 28, 2008 which rendered the relevant patent invalid, generic versions of RAZADYNE were permitted to enter the US market.

REMINYL XL is a once-daily prolonged release formulation of REMINYL, which was launched by Janssen in the US in May 2005 as RAZADYNE ER. Patent litigation proceedings relating to RAZADYNE ER are in progress in the US. Certain companies filed ANDAs with the FDA for generic versions of RAZADYNE ER. Janssen and Synaptch filed lawsuits against some of those ANDA filers for infringement of their patent rights relating to RAZADYNE ER as a result of the ANDA filing.

Sales of the REMINYL/RAZADYNE range continue to grow in most countries, however the entry of generic versions of RAZADYNE and RAZADYNE ER into the US market has significantly decreased sales in that region.

Cost of product sales

The Cost of product sales increased by 27% to \$408.0 million for the year to December 31, 2008 (15% of product sales), up from \$320.3 million in the corresponding period in 2007 (2007: 15% of product sales). For the year to December 31, 2008 Cost of product sales included charges of \$48.8 million (2% of product sales) (2007: \$nil) relating to the write down of inventory and other exit costs in respect of DYNEPO which the Company has decided to stop commercializing, depreciation of \$16.2 million (2007: \$11.8 million) and amortization of \$1.7 million (2007: \$1.2 million). Cost of product sales as a percentage of product sales benefited from the impact of price increases on the Company's product sales and favorable changes in product mix in 2008 over 2007.

R&D

R&D expenditure decreased to \$526.6 million for the year to December 31, 2008 (19% of product sales), from \$576.4 million in the year to December 31, 2007 (27% of product sales). For the year to December 31, 2007 R&D included upfront and milestone payments totaling \$155.9 million (Renovo \$75.0 million, Amicus \$50.0 million, Alba \$25.0 million and Noven \$5.9 million) for the in-licensing of pipeline products (7% of product sales). For the year to December 31, 2008 R&D included \$6.5 million (2007: \$nil) relating to the cost of exiting post-approval marketing commitments for DYNEPO, which the Company has decided to stop commercializing. R&D also includes depreciation of \$12.5 million (2007: \$11.3 million).

R&D in 2008 over 2007 includes higher expenditure on projects in-licensed and acquired since the second half of 2007 including SPD 550, PLICERA, AMIGAL, FIRAZYR and METAZYM together with Phase 3(b) and Phase 4 studies to support new product launches.

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

SG&A expenses increased 21% to \$1,422.9 million in the year to December 31, 2008 from \$1,178.8 million in the year to December 31, 2007. This increase in SG&A expenses was less than the product sales increase of 27%, and as a percentage of product sales SG&A expenses in 2008 compared to the same period in 2007 fell by two percentage points to 52% (2007: 54%).

SG&A for the year to December 31, 2008 includes intangible asset impairment charges of \$97.1 million (4% of product sales) (2007: \$0.4 million) of which \$94.6 million relates to DYNEPO which the Company has decided to stop commercializing. Amortization of intangible assets in 2008 increased by \$31.6 million to \$126.2 million (2007: \$94.6 million); this increase resulted from a full year's amortization in 2008 of the Company's VYVANSE intangible asset, of \$55.8 million (2007: \$28.9 million), and amortization in the second half of 2008 of the FIRAZYR intangible

asset acquired through the Jerini business combination. SG&A expenses also include depreciation charges of \$48.5 million (2007: \$42.1 million).

The year to December 31, 2008 also included costs associated with the introduction of a new holding company in 2008 totaling \$14.8 million (2007: \$nil). Other increases in SG&A expenses in 2008 over 2007 principally relate to the increase in advertising, promotional and marketing spend to support commercialization of the Company's new products.

SG&A for the year to December 31, 2007 included a net charge of \$17.0 million in respect of legal settlements, being a charge of \$27.0 million for settlement of the TKT purported securities fraud class action shareholder suit partially offset by a \$10.0 million release of existing legal provisions. SG&A expenses in the year to December 31, 2007 further included a share-based compensation catch-up charge of \$22.5 million for the 2005 awards: for further details on this catch-up charge, see "Results of Operations for the years to December 31, 2007 and 2006" in ITEM 7 of this Annual Report on Form 10-K.

In-Process R&D ("IPR&D")

For the year to December 31, 2008 the Company recorded an IPR&D charge of \$263.1 million: this charge related to FIRAZYR in markets outside of the EU acquired through the Jerini business combination (\$128.1 million) and the acquisition from Zymenex of the global rights to the clinical candidate arylsulfatase-A currently known as METAZYM (HGT-1111), being investigated for the treatment of MLD (\$135.0 million).

The IPR&D charge in respect of FIRAZYR of \$128.1 million relates to the US (\$64.1 million) and the Rest of the World ("ROW") (\$64.0 million) markets. In the US FIRAZYR received a not approvable letter from the FDA in April 2008, and in ROW it has not been approved by the regulatory authorities. At December 31, 2008 Shire's management estimated that future R&D costs until regulatory approval would be approximately \$30 million. This estimate can be affected by various factors, both internal and external, and is part based upon management estimates and assumptions. For this reason, amongst others, the actual cash flows may vary from future estimated cash flows.

METAZYM (HGT-1111) has completed a Phase 1b clinical trial in 12 MLD patients in Europe and an extension to this study is ongoing. The product has been granted orphan drug designation in the US and in the EU. At December 31, 2008 Shire's management estimated that future R&D costs until regulatory approval for METAZYM for the treatment of MLD in the US and the EU will be approximately \$80 to \$90 million. This estimate can be affected by various factors both internal and external and is, in part, based on management's estimate and assumptions. For this reason, among others, the actual cash flows may vary from forecast future cash flows.

During the year to December 31, 2007 Shire expensed the portion of the New River purchase price allocated to IPR&D totaling \$1,866.4 million. This amount represented the value of those acquired development projects which, at the acquisition date, had not been approved by the FDA or other regulatory authorities, including the adult indication of VYVANSE. On April 23, 2008 Shire announced that the FDA had approved the adult indication of VYVANSE and Shire launched VYVANSE for adult ADHD in the US in June 2008. In March 2008 the Canadian new drug submission was accepted for filing for the treatment of ADHD in children, and Shire expects to submit the regulatory filing for VYVANSE in Europe for the treatment of ADHD in children aged 6 to 17 in 2010. At December 31, 2008 management estimated that future R&D costs until regulatory approval for VYVANSE for ADHD in markets outside the US are approximately \$60 to \$80 million. These estimates can be affected by various factors and are, in part, based on management's estimate and assumptions. For these reasons, among others, the actual cash flows may vary from forecast future cash flows.

Gain on sale of product rights

For the year to December 31, 2008 Shire recognized gains of \$20.7 million on the sale of non-core products (2007: \$127.8 million). For the year to December 31, 2008 these gains primarily relate to the sale of non core products, including the dermatology products SOLARAZE and VANIQA, to Almirall in 2007, which were deferred at December 31, 2007 pending the transfer of relevant consents.

The gains of \$127.8 million recognized in the year to December 31, 2007 comprise \$114.8 million arising from the sale of non-core products to Almirall and \$13.0 million of gains on the sale of other non-core products during 2007.

Integration costs

For the year to December 31, 2008 Shire incurred \$10.3 million of costs associated with the integration of Jerini into the Company and acquisition related advisory fees incurred by Jerini (2007: \$1.3 million relating to the New River acquisition).

Interest income

For the year to December 31, 2008 Shire received interest income of \$25.5 million (2007: \$50.6 million). Interest income primarily relates to interest received on cash and cash equivalents. Interest income for the year to December 31, 2008 is lower than the same period in 2007 due to lower average cash balances and lower average US dollar interest rates.

Interest expense

For the year to December 31, 2008 Shire incurred interest expense of \$139.0 million (2007: \$70.8 million).

Interest expense for the year to December 31, 2008 includes \$87.3 million (2007: \$28.0 million) in respect to the TKT appraisal rights litigation. On November 5, 2008 Shire announced that it had successfully settled all aspects of this litigation with all parties. Shire paid the same price of \$37 per share originally offered to all TKT shareholders at the time of the July 2005 merger, plus interest. The Delaware Chancery Court has approved dismissal of the case and Shire made payment to the dissenting shareholders on November 7, 2008. The settlement represents a total payment of \$567.5 million, representing consideration at \$37 per share of \$419.9 million and an interest cost of \$147.6 million.

Prior to reaching this settlement, the Company accrued interest based on a reasonable estimate of the amount that may be awarded by the Court to those former TKT shareholders who requested appraisal. This estimate of interest was based on Shire's cost of borrowing. Between the close of the merger and November 5, 2008 the Company applied this interest rate on a quarterly compounding basis to the \$419.9 million of consideration to calculate its provision for interest.

Upon reaching agreement in principle with all the dissenting shareholders, the Company determined that settlement had become the probable manner through which the appraisal rights litigation would be resolved. Under current law, (although not applicable in this case because the merger was entered into before the relevant amendment to the law became effective) the court presumptively awards interest in appraisal rights cases at a statutory rate that is 5 percentage points above the Federal Reserve discount rate (as it varies over the duration of the case). In connection with the settlement, the Company agreed to an interest rate that approximates to this statutory rate. Based on the settlement, the Company amended the method of determining its interest provision to reflect this revised manner of resolution, and upon reaching settlement with the dissenting shareholders recorded an additional interest expense of \$73.0 million in its consolidated financial statements for the year to December 31, 2008. For further details on the settlement of this litigation, see Note 23(d) of ITEM 15 of this Form 10-K.

Other (expense)/income, net

Year to December 31,	2008 \$'M	2007 \$'M
Impairment of long-term investments	(58.0)	(3.0)
GeneChem Funds management fee	1.9	3.6
Gain on sale of available-for-sale security	9.4	0.1
Foreign exchange ⁽¹⁾	14.1	(0.8)
Other	(0.3)	1.3
	<u>(32.9)</u>	<u>1.2</u>

⁽¹⁾ Includes gains and losses arising on translation of foreign currency transactions and balances and gains and losses on swap and forward foreign exchange contracts

Other (expense)/ income, net for the year to December 31, 2008 includes impairment charges in respect of available for sale securities totaling \$58.0 million (2007: \$3.0 million), including \$44.3 million relating to the Company's investment in Renovo Group plc. The impairment of the investment in Renovo Group plc was recognized at the end of the third quarter of 2008. These amounts reflect unrealized holding losses that have been reclassified out of other comprehensive income into earnings in the period, as management have concluded that the impairment is other than temporary.

The decline in the market value of the Company's investment in Renovo Group plc initially arose from the results of clinical trials for JUVISTA announced over 2007 and 2008. During the third quarter of 2008, in considering whether the decline in value was temporary or "other than temporary" under US GAAP the Company considered the following factors: the severity of the decline from historical cost (87%) and its duration (eleven months); market analysts' targets of Renovo Group plc's share price for the next 18-24 months; and the revised expected filing date for JUVISTA due to the adoption of a sequential rather than parallel Phase 3 development plan.

These factors, together with the significant decline in global equity markets during the third quarter of 2008 meant that the Company was unable to reasonably estimate the period over which a full recovery in the value of its investment in Renovo Group plc could occur. As such, the Company concluded that for US GAAP purposes the decline in value was "other than temporary".

In such circumstances US GAAP requires the full difference between the book value of the investment and the fair (market) value be recognized as an other than temporary impairment. Accordingly the Company recognized an impairment charge of \$44.3 million for its investment in Renovo Group plc through the Statement of Operations in the third quarter of 2008. For purposes of computing the impairment charge fair value was assumed to be £0.26 per share, representing the closing price of Renovo Group plc securities on the London Stock Exchange on September 30, 2008. If in the future JUVISTA's Phase 3 trials report positively and Renovo Group plc's other products progress through development, Renovo Group plc's share price could react favorably and the Company may recover some or all of this impairment loss. Any future potential increases in the value of Renovo Group plc will be recognized through other comprehensive income. The closing price of Renovo Group plc securities on the London Stock Exchange on December 31, 2008 was £0.20, and the carrying value of the Company's investment in Renovo Group plc was \$3.6 million.

Other (expense)/income, net also includes a gain of \$9.4 million arising from the sale of Shire's minority equity investment in Questcor Pharmaceutical Inc., a specialty pharmaceutical company focused on providing prescription drugs for central nervous system (CNS) disorders. Shire received cash consideration of \$10.3 million in respect of the sale.

Income taxes

The effective tax rate for the year to December 31, 2008 was 36.9% (2007: -4.0%). Excluding IPR&D charges of \$263.1 million (2007: \$1,866.4 million) which are either not tax deductible or for which no tax benefit is currently recognized, the effective tax rate for the year to December 31, 2008 has increased by 6.6% to 18.5% (2007: 11.9%). This increase in 2008 over 2007 is primarily due to the combined effects of (a) in 2008, significant unfavorable rate impacts related to other than temporary impairment charges on available-for-sale securities and an increase in the valuation allowance and, (b) in 2007, favorable impacts recognized related to non-taxable gains on the sale of non-core products rights which were partially offset by an increase in the FIN 48 provision. The 2008 effective tax rate was also unfavorably impacted by exchange losses recorded in continuing operations.

For further information, see Note 31 to the Company's consolidated financial statements contained in Part IV of this Annual Report.

Equity in earnings of equity method investees

Net earnings of equity method investees of \$2.4 million were recorded for the year to December 31, 2008 (2007: \$1.8 million). This comprised earnings of \$5.8 million from the 50% share of the anti-viral commercialization partnership with GSK in Canada (2007: \$6.5 million), offset by losses of \$3.4 million being the Company's share of losses in the GeneChem, AgeChem and EGS Healthcare Funds (2007: losses of \$4.7 million).

Discontinued Operations

Losses from discontinued operations in the year to December 31, 2008 totaled \$17.6 million, (2007: \$ nil), relating to those businesses acquired through the Jerini business combination that have been deemed by Shire and Jerini to be non strategic to the combined business. The loss from discontinued operations in the year to December 31, 2008 includes a charge of \$12.9 million arising on the re-measurement of assets held for sale to their fair value less costs to sell at December 31, 2008. At December 31, 2008 these assets held-for-sale had a carrying value of \$14.9 million.

Results of operations for the years to December 31, 2007 and 2006

For the year to December 31, 2007 the Company's total revenues increased by 36% to \$2,436.3 million, compared to \$1,796.5 million in 2006. Net loss for the year to December 31, 2007 was \$1,451.8 million compared to a net income of \$278.2 million in 2006. The Company's net loss for 2007 was primarily attributable to the IPR&D write-off of \$1,866.4 million following the acquisition of New River.

Total revenues

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

Year to December 31,	2007 \$'M	2006 \$'M	Change %
Product sales	2,170.2	1,535.8	41
Royalties	247.2	242.9	2
Other revenues	18.9	17.8	6
Total	2,436.3	1,796.5	36

Product sales

Year to December 31,	2007 \$'M	2006 \$'M	Product sales growth %	US prescription growth %
Specialty Pharmaceuticals				
<u>ADHD</u>				
ADDERALL XR	1,030.9	863.6	19	3
VYVANSE	76.5	-	n/a	n/a
DAYTRANA	64.2	25.1	156	166
ADDERALL	-	23.6	n/a	n/a
<u>GI</u>				
PENTASA	176.4	137.8	28	3
LIALDA	50.5	-	n/a	n/a
<u>General Products</u>				
FOSRENOL	102.2	44.8	128	5
DYNEPO	14.2	-	n/a	n/a
CALCICHEW	54.2	45.5	19	n/a
CARBATROL	72.3	68.3	6	-5
XAGRID	66.8	53.3	25	n/a
REMINYL/REMINYL XL	31.2	21.5	45	n/a
Other	105.1	111.0	-5	
	1,844.5	1,394.5	32	
<u>Human Genetic Therapies</u>				
REPLAGAL	143.9	117.7	22	n/a
ELAPRASE	181.8	23.6	670	n/a
	325.7	141.3	131	
Total	2,170.2	1,535.8	41	

The following discussion includes references to US prescription and US market share data for key products. The source of this data is IMS, December 2007.

Specialty Pharmaceuticals

ADDERALL XR

As a result of the launch of VYVANSE in July 2007 ADDERALL XR's average share of the US ADHD market for 2007 fell to 25.5% (2006: 26.1%). US prescriptions for ADDERALL XR for the year to December 31, 2007 increased by 3% compared to the same period in 2006 due to a 6% growth in the US ADHD market offset by the 0.6% fall in average market share.

Sales of ADDERALL XR for the year to December 31, 2007 were \$1,030.9 million, an increase of 19% compared to the same period in 2006 (2006: \$863.6 million). Product sales growth was higher than prescription growth due primarily to price increases in January and October 2007.

As previously disclosed, the FTC informed Shire on October 3, 2006 that it was reviewing the ADDERALL XR patent litigation settlement agreement between Shire and Barr. On June 22, 2007 the Company received a civil investigative demand requesting that it provides information to the FTC relating to its settlement with Barr and its earlier settlement with Impax. The Company is cooperating fully with this investigation and believes that the settlements are in compliance with all applicable laws.

Patent litigation proceedings relating to ADDERALL XR are in-progress. For further information see ITEM 3: Legal Proceedings.

VYVANSE

VYVANSE was launched in the US market in July 2007 and at December 31, 2007 its market share had reached 5.2% (average annual market share 2%). Product sales of \$76.5 million for the year to December 31, 2007 were net of \$42 million sales deductions, primarily coupons, wholesaler discounts and rebates.

All initial launch stocks of VYVANSE totaling \$57.8 million were recognized into revenue during the year to December 31, 2007.

DAYTRANA

Product sales for the year to December 31, 2007 were \$64.2 million (2006: \$25.1 million). DAYTRANA's average share of the US ADHD market increased to 2.1% in 2007 compared to 0.8% in 2006 (DAYTRANA was launched in June 2006). US prescriptions of DAYTRANA for the year to December 31, 2007 over 2006 benefited from a full year of demand, 6% growth in the US ADHD market and higher market share. For the six month period to December 31, 2007 prescriptions of DAYTRANA were up 31% compared to the same period in 2006. During September 2007 Shire announced a voluntary market withdrawal of a limited quantity of DAYTRANA patches following feedback from patients and caregivers who had experienced difficulty in removing the release liner. Patches are now being manufactured using an enhanced process, which Shire believes offers improved ease of use when peeling off the release liner.

The addition of VYVANSE combined with ADDERALL XR and DAYTRANA's market share helped Shire grow its total share of the US ADHD market to 31.1% at December 31, 2007 compared to 28.0% at December 31, 2006. Shire has the leading portfolio of products in the US ADHD market.

PENTASA

US prescriptions of PENTASA for the year to December 31, 2007 were up 3% compared to the same period in 2006 primarily due to a 4% increase in the US oral mesalamine prescription market, offset by a 0.1% decrease in PENTASA's average market share from 17.3% in 2006 to 17.2% in 2007.

Sales of PENTASA for the year to December 31, 2007 were \$176.4 million, an increase of 28% compared to the same period in 2006 (2006: \$137.8 million). Sales growth is higher than prescription growth primarily due to restocking to normal levels in 2007 and the impact of price increases in November 2006 and August 2007.

LIALDA

Shire launched LIALDA in the US oral mesalamine market in March 2007, and by December 31, 2007 LIALDA had reached a market share of 8.0% (average annual market share 3.9%). LIALDA's product sales for the year to December 31, 2007 were \$50.5 million. All initial launch stocks of LIALDA totaling \$34.3 million were recognized into revenue during the year to December 31, 2007.

The product was launched in the UK in November 2007, Canada in January 2008 and further launches are planned in the EU during 2008, subject to the successful conclusion of pricing and reimbursement negotiations. In the UK and Ireland the product will be called MEZAVANT XL and Shire plans to market the product in most other EU countries as MEZAVANT.

Since the launch of LIALDA in March 2007, PENTASA and LIALDA's combined share of the US oral mesalamine prescription market had grown to 24.9% as at December 31, 2007, up from 17.6% as at December 31, 2006.

FOSRENOL

Global sales totaled \$102.2 million for the year to December 31, 2007 (2006: \$44.8 million). Sales of FOSRENOL outside the US for the year ended December 31, 2007 were \$40.1 million compared to the same period in 2006 (2006: \$4.6 million).

US sales of FOSRENOL for the year to December 31, 2007 were up 54% to \$62.1 million compared to the same period in 2006 (2006: \$40.2 million). FOSRENOL's average market share of the US phosphate binder market increased from 8.5% in 2006 to 8.6% in 2007. The increase in product sales is due to a small wholesaler stocking increase in 2007 compared to significant wholesaler de-stocking of initial launch stocks in 2006, the continued shift to the 1 gram strength tablet launched in 2006, partially offset by higher sales deductions in 2007 compared to the same period in 2006 (relating to a one-off provision made in 2007 for returns of the 750mg dose).

DYNEPO

DYNEPO was launched in March 2007 in Germany and later in the year in the UK, France, Italy, and Ireland with sales for 2007 reaching \$14.2 million.

CARBATROL

US prescriptions for CARBATROL for the year to December 31, 2007 were down 5% compared to the same period in 2006. This was primarily due to a comparable decline in the US extended release carbamazepine prescription market; CARBATROL's average market share remained constant.

Sales of CARBATROL for the year to December 31, 2007 were \$72.3 million, an increase of 6% compared to the same period in 2006 (2006: \$68.3 million). Product sales increased despite the decrease in prescriptions, due to a sales price increase in April 2007 and restocking to normal levels, partially offset by higher sales deductions.

Patent litigation proceedings relating to CARBATROL are in-progress. For further information see ITEM 3: Legal Proceedings.

XAGRID

Sales for the year to December 31, 2007 were \$66.8 million, an increase of 25% compared to the same period in 2006 (2006: \$53.3 million). Expressed in transaction currencies (XAGRID is primarily sold in Euros and Pounds sterling), sales increased by 15% due to growth in many of Shire's existing markets, with exchange rate movements against the US dollar accounting for the remaining 10% increase.

Human Genetic Therapies

REPLAGAL

Sales for the year to December 31, 2007 were \$143.9 million, an increase of 22% compared to the same period in 2006 (2006: \$117.7 million). Expressed in transaction currencies (REPLAGAL is primarily sold in Euros and Pounds sterling) sales increased by 13% due to higher unit sales in Europe and Canada and the continued roll out of REPLAGAL to new countries, including those in Latin America. Exchange rate movements against the US dollar accounted for the remaining 9% increase in sales.

ELAPRASE

Sales for the year to December 31, 2007 were \$181.8 million (2006: \$23.6 million). Sales growth in 2007 was driven primarily by a full year of sales in the US (ELAPRASE was launched in the US in August 2006), sales in Europe (ELAPRASE was launched in several European markets in the first half of 2007), and pre-approval sales in several Latin American markets. ELAPRASE was approved for sale and marketing in Japan in October 2007.

Foreign exchange effect

Revenues reported in US dollars include the impact of translating sales made in local currency (primarily Euros and Pounds sterling) into US dollars. The table below shows the effect of foreign exchange translations on the revenue growth of the key affected products as well as the underlying performance of those products in their local currency:

	2007 sales in US dollars \$'M	2007 sales growth in local currency %	2007 sales growth in US dollars %	Impact of translation to US dollars %
XAGRID				
- sales in Euros	42.2	+19	+29	+10
- sales in Pounds sterling	24.6	+9	+18	+9
REPLAGAL				
- sales in Euros	82.5	+7	+17	+10
- sales in Pounds sterling	25.2	+14	+24	+10
CALCICHEW sales in Pounds sterling	48.8	+10	+19	+9
REMINYL and REMINYL XL sales in Pounds sterling	28.8	+35	+46	+11

Royalties

Royalty revenue increased by 2% to \$247.2 million for the year to December 31, 2007 (2006: \$242.9 million).

Year to December 31,	2007 \$'M	2006 \$'M	Change %
3TC	145.3	150.9	-4
ZEFFIX	41.0	34.8	+18
Others	60.9	57.2	+6
Total	247.2	242.9	+2

3TC

Royalties from sales of 3TC for the year to December 31, 2007 were \$145.3 million, a decrease of 4% compared to the same period in 2006 (2006: \$150.9 million). Excluding favorable foreign exchange movements of 4%, there has been a decline of 8% compared to the same period in 2006.

Shire receives royalties from GSK on worldwide 3TC sales. GSK's worldwide sales of 3TC for the year to December 31, 2007 were \$1,110 million, a decrease of 2% compared to the same period in 2006 (2006: \$1,138 million), but a decrease of approximately 7% on a constant exchange rate basis. While the nucleoside analogue market for HIV has continued to grow, competitive pressures, such as new entrants to the market and products in competing markets, have increased leading to a decline in 3TC sales.

In 2007 generic drug companies filed ANDAs seeking approval for EPIVIR, COMBIVIR, ZEFFIX and EPZICOM in the US. Pursuant to the GSK/Shire license for lamivudine products, GSK has the right to enforce the licensed patents. In November 2007 GSK filed a patent infringement lawsuit against Teva in the US District Court for the District of Delaware for infringement of one of the patents relating to COMBIVIR. The patent, which covers the combination of AZT and lamivudine to treat HIV, expires in May 2012. Teva had filed an ANDA with the FDA with a certification of invalidity, unenforceability and non-infringement of that combination patent. Teva did not challenge two other patents relating to COMBIVIR that expire in 2010 and 2016. The case is in its early stages.

ZEFFIX

Royalties from sales of ZEFFIX for the year to December 31, 2007 were \$41.0 million, an increase of 18% compared to the same period in 2006 (2006: \$34.8 million). The impact of foreign exchange movements has contributed 8% to the reported growth; excluding favorable foreign exchange movements there has been an increase of 10% compared to the same period in 2006.

Shire receives royalties from GSK on worldwide ZEFFIX sales. GSK's worldwide sales of ZEFFIX for the year to December 31, 2007 were \$341 million, an increase of 13% compared to the same period in 2006 (2006: \$301 million). This increase was mainly due to strong growth in the Chinese market and favorable foreign exchange rate movements.

OTHER

Other royalties are primarily in respect of REMINYL and REMINYL XL (known as RAZADYNE and RAZADYNE ER in the US), a product marketed worldwide (excluding the UK and the Republic of Ireland) by Janssen, an affiliate of Johnson & Johnson. Shire has the exclusive marketing rights in the UK and the Republic of Ireland.

Barr and other companies have filed ANDAs with the FDA for generic versions of RAZADYNE. Janssen and Synaptich have filed lawsuits against some of those ANDA filers. A trial was held during the week of May 21, 2007. Following a decision on August 28, 2008 which rendered the relevant patent invalid, generic versions of RAZADYNE were permitted to enter the US market.

Janssen and Synaptich filed lawsuits against Barr and Sandoz Inc. ("Sandoz") for infringement of their patent rights relating to RAZADYNE ER as a result of Barr and Sandoz filing ANDAs with the FDA for generic versions of RAZADYNE ER. No court dates have been set.

Cost of product sales

For the year to December 31, 2007 the Cost of product sales was 15% of product sales (2006: 17%). The Cost of product sales for REPLAGAL in 2006 included a \$47.0 million (3% of product sales) adjustment in respect of inventories acquired through the acquisition of TKT. Excluding the impact of this fair value adjustment, Cost of product sales as a percentage of product sales in 2006 was 14%. The increase in Cost of product sales as a percentage of products sales in 2007 over 2006 was primarily due to a shift in product mix resulting from increased sales of launched products, which had lower margins than existing products, and the write-off of inventory following the voluntary market withdrawal of a limited quantity of DAYTRANA patches.

For the year to December 31, 2007 Cost of product sales included a charge of \$5.5 million for share-based compensation (2006: \$3.2 million) which included a \$2.1 million cumulative catch up charge (2006: \$nil) in respect of the 2005 awards, for further information see SG&A below.

R&D

R&D expenditure increased to \$576.4 million for the year to December 31, 2007 (27% of product sales), up from \$385.4 million in the year to December 31, 2006 (25% of product sales). For the year to December 31, 2007 R&D included upfront and milestone payments totaling \$155.9 million (Renovo \$75.0 million, Amicus \$50.0 million, Alba \$25.0 million and Noven \$5.9 million) for the in-licensing of pipeline products (7% of product sales). For the year to December 31, 2006 R&D included \$80.5 million (New River \$50.0 million, Duramed \$25.0 million and Warren Pharmaceuticals Inc ("Warren") \$5.5 million) of upfront and milestone payments (5% of product sales).

Excluding these upfront and milestone payments, the increase in R&D expenditure in 2007 was due to Phase 3(b) and Phase 4 studies to support new product launches; the continuation of Phase 3 trials on velaglucerase alfa; the development of the Women's Health franchise and JUVISTA; and the pre-clinical development of three HGT projects and the Amicus products in-licensed in 2007.

For the year to December 31, 2007 R&D included a charge of \$17.0 million for share-based compensation (2006: \$5.4 million) which included a \$4.6 million cumulative catch up charge in respect of 2005 awards, for further information see SG&A below.

SG&A expenses

Total SG&A costs increased 27% to \$1,178.8 million in the year to December 31, 2007 from \$926.6 million in the year to December 31, 2006, which was substantially less than the product sales increase of 41%. As a percentage of product sales, total SG&A costs were 54% (2006: 60%).

The increase in SG&A expenses in 2007 over 2006 included the impact of the following: an increase in the ADHD sales force to promote VYVANSE; the cost of the new GI sales force in the US; the increase in advertising, promotional and marketing spend to support VYVANSE, LIALDA/MEZAVANT and ELAPRASE; and a net charge of \$17.0 million in respect of legal settlements, being a charge of \$27.0 million for settlement of the TKT securities

class action shareholder suit partially offset by a \$10.0 million release of existing legal provisions (1% of product sales).

For the year to December 31, 2007 SG&A included a charge of \$52.7 million for share-based compensation (2006: \$34.4 million), which included a \$22.5 million cumulative catch up charge (2006: \$nil) in respect of 2005 awards.

The depreciation charge for the year to December 31, 2007 was \$42.1 million (2006: \$43.3 million), inclusive of impairment charges of \$1.8 million (2006: \$0.5 million). The increase in depreciation follows investment in Shire's infrastructure to support the continuing growth of the Company.

The amortization charge for the year to December 31, 2007 was \$95.0 million (2006: \$57.4 million), inclusive of impairment charges of \$0.4 million (2006: \$1.1 million). The increased charge is primarily due to the amortization of DAYTRANA, DYNEPO and VYVANSE intangible assets following the product launches in June 2006, March 2007 and July 2007 respectively.

The cumulative share-based compensation catch up charge related to options issued by Shire in 2005 under the 2000 Executive Scheme. These options were exercisable subject to certain performance criteria, including growth in Option EPS (being reported diluted earnings per share as adjusted for one-off items agreed by the Company's Remuneration Committee between 2004 and 2007).

At the start of 2007 forecast Option EPS for the year was such that the Company thought it improbable that these 2005 awards would vest in 2008; rather it was thought that the awards would vest, based upon service conditions, in 2015. Since then, business performance has improved over the course of the year particularly in the fourth quarter in which the business generated \$144 million of additional net income over the same period in 2006, equivalent to 209% growth for the fourth quarter. This strong performance in 2007 enabled the Remuneration Committee to conclude that the 2005 awards vested in 2008. Accordingly the compensation charge for these awards based on the revised grant date fair value, was accrued over the three year vesting period to 2008 rather than the ten year period to 2015. The catch-up charge has been recognized in the fourth quarter of 2007, split \$2.1 million to Cost of product sales, \$4.6 million to R&D and \$22.5 million to SG&A.

IPR&D

On April 19, 2007 Shire completed its acquisition of New River by way of a short-form merger, in an all-cash transaction. The acquisition of New River allows Shire to capture the full economic value of VYVANSE, and gain control of the future development and commercialization of this product.

During the year to December 31, 2007 Shire expensed the portion of the New River purchase price allocated to IPR&D of \$1,866.4 million. This amount represents the value of those acquired development projects which, at the acquisition date, had not been approved by the FDA or other regulatory authorities, specifically VYVANSE indicated for ADHD in non-pediatric patients in the US (\$1,786.8 million) and VYVANSE in RoW (\$79.6 million). During the fourth quarter of 2007 the Company reduced the values ascribed to intangible assets by \$17.4 million and IPR&D by \$29.7 million from amounts previously assigned in the preliminary purchase price allocation as a result of changes to preliminary estimates of deferred taxes in the purchase price allocation exercise.

On the acquisition date, VYVANSE had only achieved regulatory approval for use in pediatric patients in the US. On June 29, 2007 Shire submitted a sNDA to the FDA for VYVANSE for the treatment of ADHD in adults in the US. On April 23, 2008 Shire announced that the FDA had approved the adult indication for VYVANSE, and Shire launched VYVANSE for adult ADHD in the US in June 2008. At December 31, 2007, management estimated that future R&D costs until regulatory approval for VYVANSE for ADHD in non-pediatric patients in the US are approximately \$35 to \$45 million. This estimate can be affected by various factors and is, in part, based on management's estimate and assumptions. For these reasons, among others, the actual cash flows may vary from forecast future cash flows.

On the acquisition date VYVANSE in RoW had not received regulatory approval. Planning is underway for submission of VYVANSE for the RoW. In March 2008 the Canadian new drug submission was accepted for filing for the treatment of ADHD in children, and Shire expects to submit the regulatory filing for VYVANSE in Europe for the treatment of ADHD in children aged 6 to 17 in 2010. Management estimates that material net cash inflows would be anticipated one to two years after the approval and at December 31, 2007 management estimated that future R&D costs until regulatory approval for VYVANSE for ADHD in RoW are approximately \$35 to \$45 million. These estimates can be affected by various factors and are, in part, based on management's estimate and assumptions. For these reasons, among others, the actual cash flows may vary from forecast future cash flows.

The Company considers that these IPR&D assets have no alternative future use outside their current development projects and these assets have therefore been charged to expense in the Consolidated Statement of Operations as of the acquisition date in accordance with Financial Accounting Standards Board ("FASB") Interpretation ("FIN") No. 4 "Applicability of FASB Statement No. 2 to Business Combinations Accounted for by the Purchase method" ("FIN 4").

Gain on sale of product rights

For the year to December 31, 2007 Shire recognized gains of \$127.8 million on the sale of non-core products.

Shire received \$209.6 million (net of \$2.2 million of costs associated with the transfer of product rights) from Almirall for a portfolio of non core products comprising the dermatology products SOLARAZE and VANIQA and six non-promoted products across a range of indications, which were sold by Shire primarily in the UK, France, Germany, Italy, Spain and Ireland. This sale realized a total gain of \$139.2 million, of which \$114.8 million was recognized during Q4 2007. The remaining deferred gain of \$24.4 million will be recognized after the transfer of the relevant consents.

Shire received \$24.8 million on the sale of other non-core products, realizing a total gain of \$17.2 million, of which \$13.0 million was recognized during 2007. The remaining deferred gain of \$4.2 million relating to these disposals will be recognized on the transfer of marketing authorizations.

During the year to December 31, 2006 Shire recognized a gain of \$63.0 million on the disposal of ADDERALL to Duramed.

Integration costs

For the year to December 31, 2007 Shire incurred \$1.3 million of costs associated with the integration of the New River business (2006: \$5.6 million relating to the TKT acquisition). New River is now fully integrated and no further integration costs are anticipated.

Interest income

For the year to December 31, 2007 Shire received interest income of \$50.6 million (2006: \$50.5 million). Interest income primarily relates to interest received on cash balances. Included in 2006 was interest of \$6.5 million received from IDB Biomedical Inc. ("IDB") on repayment of injectable flu development drawings arising on the disposal of the vaccines business in 2004. Excluding this one-off item, interest income in 2007 is higher than in 2006 due to slightly higher average cash balances and higher average US dollar interest rates.

Interest expense

For the year to December 31, 2007 Shire incurred interest expense of \$70.8 million (2006: \$26.4 million). The increase in interest expense follows the acquisition of New River in April 2007 which was partly funded by \$1.3 billion of term loans, utilized under the \$2.3 billion Multicurrency Term and Revolving Facilities Agreement. These term loans were subsequently partially repaid using the proceeds from Shire's \$1.1 billion 2.75% convertible bond issued in May 2007. The remaining \$200 million of the term loans was also repaid during June 2007. Interest expense for the year to December 31, 2007 includes a \$7.9 million write-off of deferred financing costs following the repayment of these term loans.

In the years to December 31, 2007 and 2006 interest expense included a provision for interest (2007: \$28.0 million; 2006: \$24.6 million) which had been accrued based on a reasonable estimate that may be awarded by the Court to those former TKT shareholders who requested appraisal. On November 5, 2008 Shire announced that it had successfully settled all aspects of this litigation with all parties. For further details on the settlement of this litigation, see Note 23(d) of ITEM 15 of this Form 10-K.

Other income, net

Year to December 31,	2007 \$'M	2006 \$'M
Impairment of long-term investments	(3.0)	(2.1)
GeneChem Funds management fee	3.6	4.6
Gain on sale of available-for-sale security	0.1	-
Foreign exchange ⁽¹⁾	(0.8)	3.2
Other	1.3	3.8
	1.2	9.5

⁽¹⁾ Includes gains and losses arising on translation of foreign currency transactions and balances and gains and losses on swap and forward foreign exchange contracts

The impairment of long-term investments in 2007 and 2006 resulted from events and circumstances that indicated there was an other-than-temporary impairment of the relevant investment and, accordingly, management recorded an impairment based on its assessment of fair value.

For further details see Note 12 to the Company's consolidated financial statements contained in Part IV of this Annual Report.

Income taxes

The effective tax rate for the year to December 31, 2007 was -4.0% (2006: 26.8%). Excluding the IPR&D charge of \$1,866.4 million which is not tax deductible, the effective tax rate for the year to December 31, 2007 has reduced by 14.9% to 11.9% compared to the year to December 31, 2006 as a result of an increase in favorable permanent differences of \$32.8 million compared to the same period in 2006 (including the tax effect of Shire plc's 2.75% convertible bonds, an increase in R&D tax credits, and the tax effect of the gain on disposal of product rights) and a net reduction in valuation allowances of \$4.7 million (2006: \$125.5 million), partially offset by an increase in the provision for uncertain tax benefits and associated interest and penalties of \$38.1 million (2006: an increase in tax contingencies of \$187 million).

For further information, see Note 31 to the Company's consolidated financial statements contained in Part IV of this Annual Report.

Equity in earnings/(losses) of equity method investees

Net earnings of equity method investees of \$1.8 million were recorded for the year to December 31, 2007 (2006: \$5.7 million). This comprised earnings of \$6.5 million from the 50% share of the anti-viral commercialization partnership with GSK in Canada (2006: \$6.2 million), offset by losses of \$4.7 million being the Company's share of losses in the GeneChem, AgeChem and EGS Healthcare Funds (2006: losses of \$0.5 million).

Liquidity and capital resources

General

The Company's funding requirements depend on a number of factors, including the timing and number of its development programs; corporate, business and product acquisitions; the level of resources required for the expansion of manufacturing and marketing capabilities as the product base expands; increases in accounts receivable and inventory which may arise with any increase in product sales; competitive and technological developments; the timing and cost of obtaining required regulatory approvals for new products; the timing and quantum of milestone payments on collaborative projects; the timing and quantum of tax and dividend payments; the timing and quantum of purchases by the Employee Share Ownership Trust, ("ESOT") of Shire shares in the market to satisfy option exercises and the continuing cash generated from sales of Shire's key products.

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

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

Shire's robust balance sheet includes \$218.2 million of cash and cash equivalents at December 31, 2008. We generated \$800.1 million of cash from operating activities during the year. Shire has no debt maturing in the next three years and substantially all of Shire's debt relates to its \$1.1 billion 2.75% convertible bond which matures in 2014, although these include a put option which could require repayment in 2012. In addition, Shire has a committed facility until 2012 of \$1.2 billion, which is currently undrawn. However, the current financial situation which is affecting the banking system and financial markets, together with the current uncertainty in global economic conditions, have resulted in a tightening in the credit markets and a low level of liquidity in many financial markets. As a result, the Company may not be able to access new equity or debt finance at the same level or cost as it has done previously.

Shire 2.75% Convertible Bonds due 2014

On May 9, 2007 Shire plc issued \$1,100 million in principal amount of 2.75% convertible bonds due 2014 and convertible into fully paid ordinary shares of Shire plc of par value £0.05 each. The net proceeds of issuing the Bonds, after deducting the commissions and other direct costs of issue, totaled \$1,081.7 million.

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 rateably, 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 (the "Call Option") 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 plc's ordinary shares underlying each Bond in the principal amount of \$100,000 would exceed \$130,000; or (ii) at any time conversion rights shall 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 may also be redeemed at the option of the Bond holder at their principal amount including accrued but unpaid interest on May 9, 2012 (the "Put Option"), or following the occurrence of change of control. 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 and following exercise of the Put Option, by delivery of the underlying Shire plc ordinary shares and a cash top-up amount.

The Bonds are convertible into Shire plc 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 Shire plc ordinary shares at the initial conversion price of \$33.5879 per Shire plc ordinary share, (subject to adjustment as outlined below), being 2,977.26265 shares per \$100,000 denomination. The initial 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 Shares issued on conversion will be delivered credited as fully paid, and will rank pari passu in all respects with all fully paid Shares in issue on the relevant conversion date.

Direct costs of issue of the Bonds paid in the year to December 31, 2007 totaled \$18.3 million. These costs are being amortized to interest expense using the effective interest method over the five year period to the Put Option date. At December 31, 2008 \$12.6 million of these costs remained deferred (\$3.8 million within other current assets and \$8.8 million within other non-current assets).

In May 2008, pursuant to a court sanctioned Scheme of Arrangement, Shire Limited (now known as Shire plc) replaced Shire plc (the former holding company of the Shire Group, "Old Shire") as the holding company of Shire and its subsidiaries. Immediately prior to the Scheme of Arrangement becoming effective, Shire Limited was substituted for Old Shire as the principal obligor under the Bonds, and the terms and conditions of the Bonds accordingly amended. In connection with the Scheme of Arrangement the following documents were entered into:

- (i) a supplemental trust deed dated April 15, 2008 between Old Shire, Shire plc and BNY Corporate Trustee Services Limited as Trustee (the "Supplemental Trust Deed") relating to a trust deed dated May 9, 2007 (the "Trust Deed") constituting the US \$1,100,000,000 2.75% Convertible Bonds due 2014 (the "Convertible Bonds") originally issued by Shire; and
- (ii) an accession and amendment agreement dated April 15, 2008 between Shire plc, Old Shire, BNY Corporate Trustee Services Limited as Trustee and The Bank of New York as Paying and Conversion Agent (the "Accession and Amendment Agreement") relating to a paying and conversion agency agreement dated May 9, 2007 (the "Agency Agreement") between Old Shire, BNY Corporate Trustee Services Limited as Trustee and The Bank of New York as Paying and Conversion Agent.

As a result of amendments to the Trust Deed, effected pursuant to the Supplemental Trust Deed, and to the Agency Agreement, effected pursuant to the Accession and Amendment Agreement, in connection with the Scheme, Shire plc was substituted in place of Old Shire as principal obligor under, and issuer of, the Convertible Bonds, and Shire plc acceded to, and assumed all Old Shire obligations under, the Trust Deed and the Agency Agreement. Old Shire ceased to be a party to the Trust Deed and the Agency Agreement. The Trust Deed, the Agency Agreement and the terms and conditions of the Convertible Bonds were amended and restated in order to, among other things, provide that the Convertible Bonds will, following the substitution, be convertible into ordinary shares of Shire plc.

Multicurrency Term and Revolving Facilities Agreement

In connection with the acquisition of New River, Shire plc entered into a Multicurrency Term and Revolving Facilities Agreement (the "Facilities Agreement") with ABN AMRO Bank N.V., Barclays Capital, Citigroup Global Markets Limited and The Royal Bank of Scotland plc (the "Arrangers") on February 20, 2007. The Facilities Agreement comprised three credit facilities: (i) a committed multicurrency five year term loan facility in an aggregate amount of \$1,000 million ("Term Loan A"), (ii) a committed multicurrency 364 day term (with a further 364 day extension option) loan facility in an aggregate amount of \$300 million ("Term Loan B") and (iii) a committed five year revolving loan facility in an aggregate amount of \$1,000 million (the "RCF" and, together with Term Loan A and Term Loan B, the "Facilities"). Shire plc has agreed to act as guarantor for any of its subsidiaries that borrow under the Facilities Agreement.

On April 18, 2007 the Company fully utilized Term Loan A of \$1,000 million and Term Loan B of \$300 million to partially fund the acquisition of New River. In May 2007 Shire issued \$1,100 million principal amount of the Bonds. The proceeds of the issue were used to repay and cancel \$800 million of Term Loan A and all of Term Loan B in accordance with the terms of the Facilities Agreement. The remaining \$200 million drawn down under Term Loan A was repaid on June 29, 2007.

On July 19, 2007, the Company entered into a syndication and amendment agreement in relation to the Facilities Agreement (the "Amended Facilities Agreement"), which increased the RCF to an aggregate amount of \$1,200 million, amended the covenant relating to the ratio of Net Debt to EBITDA and syndicated the RCF between the banks with the following commitments: ABN Amro Bank N.V., (\$200 million); Barclays Capital, (\$200 million); Citigroup Global Markets Limited, (\$200 million); The Royal Bank of Scotland plc, (\$200 million); Lloyds TSB Bank plc, (\$200 million); Bank of America N.A., (\$100 million); and Morgan Stanley Bank (\$100 million).

The RCF, which includes a \$250 million swingline facility, may be used for general corporate purposes and matures on February 20, 2012. The availability of loans under the RCF is subject to customary conditions, including the absence of any defaults thereunder and the accuracy (in all material respects) of Shire's representations and warranties contained therein.

The interest rate on each loan drawn under the RCF for each interest period, as determined by the Company, is the percentage rate per annum which is the aggregate of the applicable margin (ranging from 0.40 to 0.80 per cent per annum, depending on the ratio of Net Debt to EBITDA for the preceding period) 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.

The Amended Facilities Agreement includes requirements that (i) Shire's ratio of Net Debt to EBITDA (as defined in the Amended Facilities 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; and (ii) that the ratio of EBITDA to Net Interest (as defined in the Facilities 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.

Upon a change of control of Shire or upon the occurrence of an event of default and the expiration of any applicable cure period, the total commitments under the Facilities may be canceled and/or all or part of the loans, (together with accrued interest and all other amounts accrued or outstanding) may become immediately due and payable. Events of default under the Amended Facilities Agreement include: (i) non-payment of any amounts due under the Facilities; (ii) failure to satisfy any financial covenants; (iii) material misrepresentation in any of the finance documents; (iv) failure to pay, or certain other defaults under other financial indebtedness; (v) certain insolvency events or proceedings; (vi) material adverse changes in the business, operations, assets or financial condition of the group; (vii) certain US Employee Retirement Income Security Act breaches which would have a material adverse effect; (viii) if it becomes illegal for Shire or any of its subsidiaries that are parties to the Amended Facility Agreement to perform their obligations or (ix) if Shire or any subsidiary of Shire which is party to the Amended Facility Agreement repudiates the Amended Facility Agreement or any Finance Document (as defined in the Amended Facility Agreement).

In connection with the Scheme of Arrangement, with effect from May 23, 2008, Old Shire entered into an accession and amendment deed dated April 15, 2008 between Shire plc (formerly Shire Limited), Old Shire, certain subsidiaries of Shire plc and Barclays Bank plc as Facility Agent (the "Accession and Amendment Deed") relating to the Amended Facilities Agreement. The following is a description of the material amendments to the Amended Facilities Agreement, affected pursuant to the Accession and Amendment Deed, which took effect on May 23, 2008, immediately prior to the Scheme of Arrangement becoming effective.

Shire plc acceded to the Facility Agreement as a borrower and guarantor, and Shire Holdings UK Limited, a wholly-owned subsidiary of Old Shire, acceded to the Facility Agreement as a borrower. Old Shire ceased to be a party to the Facility Agreement as a guarantor (although it remains a party to the Facility Agreement as a borrower). The Amended Facilities Agreement was amended and restated in order to take account of the fact that Shire plc is incorporated in Jersey and tax resident in the Republic of Ireland, to exclude the Scheme of Arrangement between Shire plc and its shareholders from the mandatory prepayment provisions contained in the Amended Facilities Agreement, and amend the financial covenants contained in the Amended Facilities Agreement in order to ensure that if any amount of interest awarded in the TKT appraisal rights litigation differs from that provided for in Shire's accounts, any excess or shortfall would be treated as if it had been provided for on a pro rata basis in accounting periods up to the time of judgement. This amendment was made to avoid a technical breach of the Amended Facilities Agreement in the accounting period in which the any judgement occurs.

During the year ended December 31, 2007 the Company paid \$14.5 million for the arrangement of the Facilities of which \$1.2 million has been amortized in the year to December 31, 2008 (\$9.4 million amortized in the year to December 31, 2007). Arrangement costs of \$3.9 million, which relate to the RCF, remain deferred at December 31, 2008 and are being amortized over the estimated term of the facility (\$1.2 million within other current assets and \$2.7 million within other non-current assets).

On November 7, 2008 Shire utilized \$190.0 million of the facility to part fund the TKT appraisal rights litigation settlement. The loan was repaid in full prior to December 31, 2008. For further information see Note 23(d) in ITEM 15: Exhibits and Financial Statement Schedules.

Sources and uses of cash

The following table provides an analysis of the Company's gross and net debt (excluding restricted cash) at December 31, 2008 and 2007:

December 31,	2008 \$'M	2007 \$'M
Cash and cash equivalents	218.2	762.5
Shire 2.75% Convertible bonds	1,100.0	1,100.0
Building financing obligation	45.6	32.9
Total debt	1,145.6	1,132.9
Net debt	(927.4)	(370.4)

Cash flow activity

Net cash provided by operating activities for the year to December 31, 2008 was \$800.1 million resulting from a net profit of \$156.0 million, non-cash items not affecting 2008 operating cash flows of \$616.6 million, a decrease in working capital of \$32.2 million and cash flows used in discontinued operations of \$4.7 million. Cash flow from operating activities increased by \$325.4 million to \$800.1 million (2007: \$474.7 million). The increased cash flow

from operating activities primarily resulted from higher revenues and cash collection in 2008 over 2007, together with cash inflows from forward foreign exchange contracts in 2008. These cash inflows were partially offset by interest payments to the TKT dissenting shareholders (\$147.6 million), cash paid to Zymenex for METAZYM (\$135.0 million) and higher cash tax payments in 2008 over 2007.

Net cash provided by operating activities for the year to December 31, 2007 was \$474.7 million resulting from a net loss of \$1,451.8 million, non-cash items not affecting 2007 operating cash flows of \$1,962.8 million (predominately the IPR&D charge of \$1,866.4 million) and an increase in working capital of \$36.3 million.

Net cash used in investing activities was \$1,154.5 million in the year to December 31, 2008 and includes the cash outflows associated with purchasing over a 98% interest in Jerini (\$499.4 million, net of cash acquired), the payment of \$419.9 million at \$37 per share on settlement of the TKT appraisal rights litigation, expenditure on purchases of property, plant and equipment of \$236.0 million, the final sales milestone payment of \$25.0 million for DAYTRANA to Noven and purchases of long-term investments of \$2.2 million. These investing outflows which were partially offset by receipts of \$10.3 million from the sale of long term assets and \$5.0 million received from the sale of product rights.

Capital expenditure on property, plant and equipment included \$136.0 million on construction work at Shire's office and manufacturing facilities in Lexington, Massachusetts and \$4.7 million on construction work at the Basingstoke, UK Office. This capital expenditure was funded from the Company's existing cash resources and operating cash flows, and the Company expects to fund 2009 capital expenditure which is committed at December 31, 2008 from operational cash flows generated in 2009.

Net cash used in investing activities was \$2,468.1 million in the year to December 31, 2007 and includes expenditure on the acquisition of New River of \$2,519.6 million, net of cash acquired; purchases of long term investments of \$63.2 million (which includes expenditure of \$50.0 million on an equity investment in Renovo Group plc); purchases of property, plant and equipment of \$110.4 million and purchases of intangible assets of \$59.0 million were partially offset by \$234.4 million received as proceeds/deposits for the sale of certain product rights and \$55.8 million received on maturity of New River's short term investments. Capital expenditure on property, plant and equipment included \$36.1 million on IT projects at the Wayne, Pennsylvania US headquarters; \$12.4 million on IT at the Basingstoke, UK headquarters; \$8.2 million on construction work at Shire's manufacturing facility at Owings Mills, Maryland; and \$35.1 million and \$8.2 million on leasehold improvements and IT equipment, respectively at Shire's site in Cambridge, Massachusetts. Capital expenditure on intangible assets included \$50.0 million of sales milestones paid to Noven for DAYTRANA.

Net cash used in financing activities was \$178.1 million for the year to December 31, 2008 of which \$146.6 million related to payments to acquire shares by the ESOT and \$46.8 million to the dividend payment. During the year to December 31, 2008 the Company additionally drew down \$190.0 million of its revolving credit facility to part fund the TKT appraisal rights settlement, this amount was subsequently repaid during the period.

Net cash provided by financing activities was \$1,623.0 million for the year to December 31, 2007. On April 18, 2007 the Company fully utilized Term Loan A of \$1,000 million and Term Loan B of \$300 million to partially fund the acquisition of New River, which, as described above, have subsequently been repaid in 2007. Shire incurred \$14.5 million of arrangement costs in respect of these facilities in the year to December 31, 2007. In May 2007 Shire issued \$1.1 billion principal amount of 2.75% convertible bonds due 2014. The net proceeds of the issue of the Bonds were \$1.1 billion with associated issue costs of \$18.3 million. On February 20, 2007 Shire plc raised \$877.3 million, net of associated costs, through the private placement of 42.9 million new ordinary shares to certain institutional investors at a price of 1075 pence per share. In addition, Shire plc received \$13.0 million from the exercise of warrants and \$30.4 million from the exercise of stock options, made payments to acquire treasury stock of \$186.0 million and paid a dividend of \$41.3 million. Shire also paid \$279.4 million to holders of New River's 3.5% Convertible Subordinated Notes due 2013 and received \$141.8 million from Merrill Lynch in settlement of a purchased call option entered into by New River prior to the acquisition in April 2007.

Outstanding Letters of credit

At December 31, 2008, the Company had irrevocable standby letters of credit in the amount of \$10.5 million, including letters of credit with Barclays Bank plc in the amount of \$4.0 million providing security on the recoverability of insurance claims, and with Citigroup in the amount of \$4.2 million, providing security on the payment of lease obligations.

Cash Requirements

At December 31, 2008, the Company's cash requirements for contractual obligations and long-term liabilities reflected on the Balance Sheet were as follows:

Payments due by period

	Total \$'M	Less than 1 year \$'M	1 – 3 years \$'M	3 – 5 years \$'M	More than 5 years \$'M
Long-term debt obligations ⁽ⁱ⁾	1,266.4	30.3	60.5	60.5	1,115.1
Building financing obligation ⁽ⁱⁱ⁾	34.3	2.5	4.6	4.4	22.8
Operating leases obligation ⁽ⁱⁱⁱ⁾	172.4	34.2	49.9	30.7	57.6
Purchase obligations ^(iv)	310.2	251.2	45.5	13.5	-
Other long-term liabilities reflected on the Balance Sheet ^(v)	233.2	11.6	221.6	-	-
Total	2,016.5	329.8	382.1	109.1	1,195.5

- (i) Shire's \$1,100 million principal amount of 2.75% convertible bonds due 2014 issued in May 2007 and the interest on the convertible bonds has been included based on the contractual payment dates. The principal amount of \$1,100 million has been included within payments due in more than 5 years based on the Final Maturity Date of the convertible bonds. The bondholders have the option to redeem the convertible bonds at the principal amount in May 2012 and the Company has the option to call the bonds subject to certain conditions after May 2012. Further details are included within Liquidity and capital resources: Shire 2.75% Convertible Bonds due 2014 above.
- (ii) The Company has entered into a building financing arrangement for certain laboratory and office space for its HGT business unit in Massachusetts expiring in 2023. For further information see Note 20, "Other long-term debt" in our notes to the consolidated financial statements in Part IV of this Annual Report on Form 10-K.
- (iii) The Company leases certain land, facilities, motor vehicles and certain equipment under operating leases expiring through 2025.
- (iv) Purchase obligations include agreements to purchase goods, investments or services (including clinical trials, contract manufacturing and capital equipment) that are enforceable and legally binding and that specify all significant terms, including open purchase orders. Shire expects to fund these commitments with cash flows from operations.
- (v) Unrecognized tax benefits and associated interest and penalties of \$11.6 million and \$221.6 million are included within payments due in less than one year and payments due in one to three years, respectively.

The contractual obligations table above does not include payments yet to fall due upon the occurrence of certain milestones and other contractual commitments. The most significant payments are as follows:

(i) Alba Therapeutics Corporation ("Alba")

On December 14, 2007 Shire acquired worldwide rights to SPD550 (also known as AT-1001), in markets outside of the US and Japan, from Alba. SPD550 is Alba's lead inhibitor of barrier dysfunction in various gastrointestinal disorders that is currently in Phase 2 development for the treatment of Celiac disease. Shire paid an upfront payment of \$25 million (expensed as R&D in 2007) and will pay further development and sales milestones up to a maximum of \$300 million. Shire will also pay tiered royalties on net sales of the product. Tiered royalty rates will be single or double digit dependent on annual net sales.

Alba and Shire have formed a joint development committee to monitor R&D activities of SPD550. Alba will fund all development until SPD550 has completed Proof of Concept, which is expected to be in the first half of 2009, after which Shire and Alba will share equally development costs under a joint development plan.

(ii) Amicus Therapeutics, Inc. ("Amicus")

On November 7, 2007 Shire licensed from Amicus the rights to three pharmacological chaperone compounds in markets outside of the US: AMIGAL for Fabry disease (Phase 2), PLICERA for Gaucher disease (Phase 2) and AT2220 for Pompe disease (Phase 2). Shire paid Amicus an upfront license fee of \$50 million (expensed as R&D in 2007), and will pay further development and sales based milestones to a maximum of \$390 million. Shire will also pay tiered, double digit, royalties on net sales of the products. Shire and Amicus will pursue a joint development program toward market approval in the US and Europe; expenses for this program will be shared equally.

(iii) JUVISTA

On June 19, 2007 Shire signed an agreement with Renovo to develop and commercialize JUVISTA, Renovo's novel drug candidate being investigated for the reduction of scarring in connection with surgery. Under the terms of the agreement Shire has the exclusive right to commercialize JUVISTA worldwide, with the exception of EU member states.

Shire has remaining obligations to pay Renovo \$25 million on the filing of JUVISTA with the FDA; up to \$150 million on FDA approval; royalties on net sales of JUVISTA; and up to \$525 million on the achievement of very significant sales targets. Shire will bear the cost of clinical trials designed specifically for obtaining US regulatory approval. Renovo will bear the costs of clinical trials designed specifically for obtaining EU regulatory approval. Shire and Renovo will share equally the costs of conducting global clinical trials that are designed for obtaining both US and EU regulatory approvals.

(iv) Women's Health Products

In August 2006, Shire and Duramed (an affiliate of Barr) entered into an agreement related to SEASONIQUE, a number of products using Duramed's transvaginal ring technology and other oral products (the "Collaboration Products"). Under this agreement, Shire was required to reimburse Duramed for US development expenses incurred in respect of the Collaboration Products up to a maximum of \$140 million over eight years from September 2006, and Shire had the right to commercialize these products in a number of markets outside of North America, including the larger European markets.

US development expenses reimbursed in the year ended December 31, 2008 totaled \$30.0 million, and at December 31, 2008 the maximum future reimbursement for Duramed incurred US development expenditures was \$95.6 million.

On February 24, 2009, Shire and Duramed amended this agreement and it will terminate on December 31, 2009. Pursuant to this amendment, Shire agreed to return to Duramed its rights under the agreement effective February 24, 2009. Shire also agreed to reimburse Duramed for incurred US development expenditures in 2009 up to a maximum of \$30.0 million. In addition, Shire agreed to a one-time payment to Duramed of \$10.0 million and to forego royalties receivable from Barr and cost of goods otherwise payable by Barr to Shire in 2009 under the License Agreement between the parties for the supply of the authorized generic of ADDERALL XR up to a maximum of \$25.0 million.

(v) EQUASYM IR and XL

On February 20, 2009, Shire announced that it has signed an agreement with UCB to acquire the worldwide rights to EQUASYM IR and XL (methylphenidate hydrochloride) (excluding the USA, Canada and Barbados) used for the treatment of ADHD. Shire will make a cash payment to UCB of €55 million for the acquisition of global rights (ex-USA, Canada and Barbados) on completion of the transaction subject to standard closing conditions. In addition, small milestone payments may become payable in 2009 and 2010 if certain net sales targets are met.

(vi) Other R&D and sales milestones

In addition to the commitments set out in (i) to (iv), at December 31, 2008 the Company had commitments payable on achievement of specified milestones and fees payable for products under development in-licensed from third parties of \$1.0 million (2007: \$5.3 million).

(vii) Capital commitments

At December 31, 2008, the Company has committed to spend \$95.4 million in respect of capital projects, including commitments for the expansion and improvements to office space at the Basingstoke UK headquarters and improvements to laboratory and office space leased by the HGT business at Lexington, Massachusetts which is expected to be all payable in 2009.

Off-balance sheet arrangements

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

Foreign currency fluctuations

A number of the Company's subsidiaries have functional currencies other than the US dollar. As such, the consolidated financial results are subject to fluctuations in exchange rates, particularly those between the US dollar, Canadian Dollar, Pounds Sterling and the Euro. The accumulated foreign currency translation differences at December 31, 2008 of \$101.5 million are reported within accumulated other comprehensive income in the

consolidated balance sheet and foreign exchange gains for the year to December 31, 2008 of \$4.6 million are reported in the consolidated statement of operations.

At December 31, 2008, the Company had outstanding swap and forward foreign exchange contracts to manage the currency risk associated with inter-company transactions. For further information, see ITEM 7A to this Annual Report. At December 31, 2008 the fair value of these contracts was a liability of \$44.2 million.

Concentration of credit risk

Financial instruments that potentially expose Shire to concentrations of credit risk consist primarily of short-term cash investments, trade accounts receivable (from product sales and from third parties for which the Company receives royalties) and derivative contracts. Excess 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 and the US onshore funds participate in the US Treasury Department's Temporary Guarantee Program.

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 require counterparties to have a long term credit rating of A+ / A1 or better from 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 the derivative are major international financial institutions.

The Company's revenues from product sales 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, 2008 there were two customers in the US who accounted for 56% of the Company's total revenues. However, such clients typically have significant cash resources and as such the risk from concentration of credit is considered minimal. The Company has taken positive steps to manage any credit risk associated with these transactions and operates clearly defined credit evaluation procedures.

Inflation

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

Critical accounting estimates

The preparation of consolidated financial statements, in conformity with US GAAP and SEC regulations, requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. Estimates and assumptions are primarily made in relation to the valuation of intangible assets, the valuation of equity investments, sales deductions, income taxes and provisions for litigation.

(i) Valuation of intangible assets

(a) General

The Company has acquired and continues to acquire significant intangible assets, recorded at acquisition cost. At December 31, 2008, the carrying value of such intangibles was \$1,824.9 million, which primarily related to the Company's DAYTRANA (\$130.1 million), FIRAZYR (\$280.4 million), FOSRENOL (\$22.9 million), PENTASA (\$71.8 million), REMINYL (\$13.9 million), REPLAGAL (\$298.9 million), VYVANSE (\$988.5 million) and XAGRID (\$10.5 million) products. Those assets which do not yet have a defined revenue stream and for which there is no alternative future use are expensed upon acquisition, and those that do have a defined revenue stream (namely commercial products or rights to products awaiting final regulatory approval) are capitalized and amortized over their estimated useful life.

Whenever events or circumstances suggest that the carrying value of intangible assets may not be recoverable, the Company reviews the intangible asset for impairment using an undiscounted net cash flow approach. If the undiscounted cash flows resulting from the use and ultimate disposition of the intangible asset is less than its carrying value, the intangible asset is written down to its fair value, based on estimated discounted cash flows. When cash flows cannot be identified for an individual asset, the impairment review is applied at the lowest level for which cash flows are identifiable.

The events or circumstances that may suggest that its intangible assets may not be recoverable, and which would lead to the Company evaluating its intangible assets for impairment, include the following:

- any change to the commercialization strategy in respect of a product;
- the loss of patent protection or challenge or circumvention by competitors of the Company's patents;
- the development and marketing of competitive products, including generic entrants into the marketplace;
- any changes to the product labels, or other regulatory intervention;
- sustained government pressure on prices and, specifically, competitive pricing;
- the occurrence of significant adverse events in respect to the Company's products; and
- a significant deterioration in a product's operating performance compared to expectations.

The occurrence of any such events, combined with changes in interest rates, could adversely affect Shire's valuation of the estimated future net cash flows generated by its long-lived assets. Following the identification of such events and the resultant impairment review, the Company recognized impairment charges of \$97.1 million in respect to its intangible assets in the year to December 31, 2008 (2007: \$0.4 million, 2006: \$1.1 million), of which \$94.6 million related to DYNEPO which the Company has decided to stop commercializing. Dependent on the occurrence of future events or circumstances, the Company's operating results could be materially and adversely affected by impairment charges related to the recoverability of its long-lived assets.

Management's estimate of the useful life of its intangible assets considers, inter alia, the following factors: the expected use of the asset by the Company; any legal, regulatory, or contractual provisions that may limit the useful life and the effects of demand; competition, including the launch of generic products; and other economic factors (such as the stability of the industry, known technological advances, legislative action that results in an uncertain or changing regulatory environment, and expected changes in distribution channels).

The Company reviews the useful life of its intangible assets subject to amortization at each reporting period, and revises its estimate of useful life if events or circumstances warrant. In the year to December 31, 2005 the Company decreased the estimated life of a product, which resulted in an additional amortization charge of \$5.9 million in each of the years to December 31, 2006, 2007 and 2008. Any future changes to the useful life of the Company's intangible assets could result in additional or lesser amortization expense in future periods which could materially affect operating results.

(b) Intangible assets acquired through business combinations

The fair values of all of the identifiable intangible assets acquired through business combinations, (primarily the acquisitions of TKT in 2005, New River in 2007 and the acquisition of more than a 98% interest in Jerini in 2008)

have been determined using an income approach on a project-by-project basis using the multi-period excess earnings method. This method starts with a forecast of all of the expected future net cash flows either generated or saved as a result of ownership of the intellectual property, the customer relationships and the other intangible assets. These cash flows are then adjusted to present value by applying an appropriate discount rate that reflects the risk factors associated with the cash flow streams (to the extent the underlying cash flows have not similarly been risk adjusted).

The forecast of future cash flows requires various assumptions to be made, including:

- revenue that is reasonably likely to result from the sale of products including the estimated number of units to be sold, estimated selling prices, estimated market penetration and estimated market share and year-over-year growth rates over the product life cycles;
- royalty or license fees saved by owning the intellectual property associated with the products;
- cost of sales for the products using historical data, industry data or other sources of market data;
- sales and marketing expense using historical data, industry data or other sources of market data;
- general and administrative expenses;
- research and development expenses;
- the estimated life of the products; and
- the tax amortization benefit available to a market participant purchasing the assets piecemeal.

The valuations are based on information at the time of the acquisition and the expectations and assumptions that (i) have been deemed reasonable by the Company's management and (ii) are based on information, expectations and assumptions that would be available to and made by a market participant. No assurance can be given, however, that the underlying assumptions or events associated with such assets will occur as projected. For these reasons, among others, the actual cash flows may vary from forecasts of future cash flows.

(c) Valuation of IPR&D acquired through business combinations

IPR&D is defined by FIN 4 as being a development project that has been initiated and achieved material progress but (i) has not yet reached technological feasibility or has not yet reached the appropriate regulatory approval, (ii) has no alternative future use, and (iii) the fair value is estimable with reasonable certainty.

As required by FIN 4, the portion of the purchase price ascribed to IPR&D has been immediately expensed to the Statement of Operations in the year of the acquisition. The Company has expensed as IPR&D the following amounts in respect of its significant business combinations: \$128 million on acquisition of a majority voting interest in Jerini in 2008; \$1,866 million on acquisition of New River in 2007; and \$815 million on acquisition of TKT in 2005. Significant IPR&D projects expensed to income include FIRAZYR for the treatment of acute HAE in the US and the rest of the world (excluding the US and EU) for the Jerini acquisition; VYVANSE indicated for ADHD in non-pediatric patients in the US and VYVANSE indicated for ADHD in the rest of the world on acquisition of New River. In the year to December 31, 2008 the Company also expensed IPR&D totaling \$135 million for the acquisition of METAZYM from Zymenex.

In the identification of intangible assets, consideration is given to whether any technology that is identified is developed or in-process. In making this determination the Company considers the factors in the American Institute of Certified Public Accountants Practice Aid "Assets Acquired in a Business Combination to Be Used in Research and Development Activities: A Focus on Software, Electronic Devices and Pharmaceutical Industries", which gives guidance on the factors that should be considered when identifying IPR&D.

The fair value of IPR&D acquired through business combinations is determined using the income approach on a project-by-project basis using the multi-period excess earnings method. The fair value of the acquired IPR&D assets has been based on the present value of probability adjusted incremental cash flows expected to be generated by the IPR&D projects after the deduction of contributory asset charges for other assets employed in these projects. This method includes risk factors, which include applying an appropriate discount rate that reflects the project's stage of completion, the nature of the product, the scientific data associated with the technology, the current patent situation and market competition.

The forecast of future cash flows required the following assumptions to be made:

- revenue that is likely to result from specific IPR&D projects, including the likelihood of approval of the product, estimated number of units to be sold, estimated selling prices, estimated market penetration, estimated market share and year-over-year growth rates over the product life cycles;
- cost of sales related to the potential products using historical data, industry data or other sources of market data;
- sales and marketing expense using historical data, industry data or other market data;

- general and administrative expenses;
- R&D expenses to complete the development of the acquired products; and
- the tax amortisation benefit available to a market participant purchasing the assets piecemeal.

The valuation process for IPR&D involves a number of inter-relating assumptions, such that the Company does not consider it meaningful to quantify the sensitivity to change for any individual assumption. The major risks and uncertainties associated with the timely completion of the acquired IPR&D projects consist of the ability to confirm the safety and efficacy of the technology based on the data from ongoing clinical trials and obtaining the necessary regulatory approvals. The valuations have been based on information at the time of the acquisition and expectations and assumptions that (i) have been deemed reasonable by Shire's management, and (ii) are based on information, expectations and assumptions that would be available to and made by a market participant. However, no assurance can be given that the underlying assumptions or events associated with such assets will occur as projected. For these reasons, among others, the actual cash flows may vary from forecast future cash flows.

(ii) Valuation of Equity Investments

The Company has investments in certain public and private pharmaceutical and biotechnology companies. The carrying values of these investments are periodically reviewed for other-than-temporary impairments whenever certain events or circumstances suggest that the cost of an investment exceeds the fair market value of the investment. Indicators of other-than-temporary impairment considered by the Company, include, inter alia:

- the market value of a quoted investment being below the cost of the investment;
- adverse news on a company's progress in scientific technology/development of compounds; and
- recent stock issuances at a price below the investment price.

If the fair value appears to be below the cost of an investment the Company considers all available evidence in assessing whether there is an other-than-temporary impairment. This evidence would include:

- the length of time and/or the extent to which the market value of the investee is less than the cost of the investment;
- the level of progress in the investee's scientific technology/development of compound
- ongoing activity in collaborations with the investee;
- whether or not other substantial investee-specific adverse events have occurred which may cause a decline in value;
- analysis and valuation of comparable companies; and
- the overall financial condition and near term prospects of the investee.

In instances when this review indicates that there is an other-than-temporary impairment, for private companies the Company writes down the investment to the fair value of the investment. For investments in public companies accounted for as available-for-sale securities any unrealized holding loss is reclassified from other comprehensive income by recording an other than temporary impairment charge in the consolidated statement of operations.

The determination of the fair value of private company investments and the determination of whether an unrealized loss on a publicly quoted investment is other-than-temporary requires significant judgment and can have a material impact on the reported results. During 2008, Shire recorded impairments on long-term investments in private companies of \$nil (2007: \$nil, 2006: \$1.8 million) and an other-than-temporary impairment charge of \$58.0 million (2007: \$3.0 million, 2006: \$0.3 million) for its available-for-sale securities, including \$44.3 million for its investment in Renovo Group plc. During the third quarter of 2008, the Company considered the following factors in its determination of whether its impairment in Renovo Group plc was temporary or other-than-temporary: the severity of the decline from historical cost (87% decline) and its duration (eleven months); market analysts' targets of Renovo Group plc's share price for the next 18-24 months; and the revised expected filing date for JUVISTA due to the adoption of a sequential rather than parallel Phase 3 development plan. These factors, together with the significant decline in global equity markets during the third quarter of 2008 meant that the Company was unable to reasonably estimate the period over which a full recovery in the value of its investment in Renovo Group plc could occur. As such, at the end of the third quarter of 2008 the Company concluded that the decline in value was other-than-temporary. During the fourth quarter of 2008, the value of the Company's investment in Renovo Group plc further declined to \$3.6 million by December 31, 2008: the Company has recognized this decline of \$2.2 million as a temporary impairment within Other Comprehensive Income during the fourth quarter of 2008.

(iii) Sales Deductions

Sales deductions consist of statutory rebates to state Medicaid and other government agencies, contractual rebates with health-maintenance organizations (“HMOs”), product returns, sales discounts (including trade discounts and distribution service fees), wholesaler chargebacks, and allowances for coupon sampling programs. These deductions are recorded as reductions to revenue in the same period as the related sales with estimates of future utilization derived from historical experience adjusted to reflect known changes in the factors that impact such reserves.

The Company accounts for these sales deductions in accordance with Emerging Issues Task Force Issue No. 01-9, *Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor’s Products)*, and Statement of Financial Accounting Standards (“SFAS”) No. 48, *Revenue Recognition When Right of Return Exists*, as applicable.

The Company has the following significant categories of sales deductions, all of which involve estimates and judgments which the Company considers to be critical accounting estimates, and require the Company to use information from external sources:

Medicaid and HMO Rebates

Statutory rebates to state Medicaid agencies and contractual rebates to HMOs under managed care programs are based on statutory or negotiated discounts to the selling price. Medicaid rebates generally increase as a percentage of the selling price over the life of the product (if prices increase faster than inflation).

As it can take up to six months for information to reach the Company on actual usage of the Company’s products in managed care and Medicaid programs and on the total discounts to be reimbursed, the Company maintains reserves for amounts payable under these programs relating to sold products.

The amount of the reserve is based on historical experience of rebates, the timing of payments, the level of reimbursement claims, changes in prices (both normal selling prices and statutory or negotiated prices), changes in prescription demand patterns, and the levels of inventory in the distribution channel.

Shire’s estimates of the level of inventory in the distribution channel are based on product-by-product inventory data provided by wholesalers; results of independently commissioned retail inventory surveys and third-party prescription data (such as IMS Health National Prescription Audit data).

Revisions or clarification of guidelines from CMS related to state Medicaid and other government program reimbursement practices with retroactive application can result in changes to management’s estimates of the rebates reported in prior periods. However, since the prices of the Company’s products are fixed at the time of sale and the quantum of rebates is therefore reasonably determinable at the outset of each transaction, these factors would not impact the recording of revenues in accordance with generally accepted accounting principles.

The accrual estimation process for Medicaid and HMO rebates involves in each case a number of interrelating assumptions, which vary for each combination of product and Medicaid agency or HMO. Accordingly, it would not be meaningful to quantify the sensitivity to change for any individual assumption or uncertainty. However, Shire does not believe that the effect of uncertainties, as a whole, significantly impacts the Company’s financial condition or results of operations.

At the balance sheet date, accruals for Medicaid and HMO rebates were \$222.5 million in 2008, \$146.6 million in 2007 and \$126.4 million in 2006, or 8%, 7%, and 8%, respectively, of net product sales. Historically, actual returns have not varied significantly from the reserves provided.

Product Returns

The Company typically accepts customer product returns in the following circumstances: a) expiration of shelf life; b) product damaged while in the possession of Shire; or c) under sales terms that allow for unconditional return (guaranteed sales).

Shire estimates the proportion of recorded revenue that will result in a return by considering relevant factors, including:

- past product returns activity;
- the duration of time taken for products to be returned;
- the estimated level of inventory in the distribution channel;
- product recalls and discontinuances;
- the shelf life of products;
- the launch of new drugs or new formulations; and
- the loss of patent protection or new competition.

Shire's estimate of the level of inventory in the distribution channel is based on product-by-product inventory data provided by wholesalers, third-party prescription data and, for some product return provisions, market research of retail pharmacies.

Returns for new products are more difficult for the Company to estimate than for established products. For shipments made to support the commercial launch of a new product (which are typically guaranteed sales), as the Company cannot determine customer acceptance of the new product, the Company's policy is therefore to defer recognition of the sales revenue until there is evidence of end-patient acceptance (primarily third-party prescription data), in accordance with SAB No. 104, *Revenue Recognition*. For shipments after launch under standard terms (ie not guaranteed sales), the Company's initial estimates of sales return accruals are primarily based on the historical sales returns experience of similar products shortly after launch. Once sufficient historical data on actual returns of the product are available, the returns provision is based on this data and any other relevant factors as noted above.

The accrual estimation process for product returns involves in each case a number of interrelating assumptions, which vary for each combination of product and customer. Accordingly, it would not be meaningful to quantify the sensitivity to change for any individual assumption or uncertainty. However, Shire does not believe that the effect of uncertainties, as a whole, significantly impacts the Company's financial condition or results of operations.

At the balance sheet date, provisions for product returns were \$47.1 million in 2008, \$39.5 million in 2007 and \$36.5 million in 2006, or 2%, 2% and 2%, respectively, of net product sales. Historically, actual rebates have not varied significantly from the reserves provided.

Sales Coupon accrual

For certain products, primarily VYVANSE, LIALDA, and DAYTRANA, the Company uses coupons as a form of sales incentive. These coupons reimburse part or all of the cost of the first prescription. Each coupon can only be used once and coupons typically expire three to 15 months after the date of issuance. The Company's management calculates an accrual for the estimated value of coupons that will be redeemed against sold products, based on the rebate value per coupon, the timing and volume of coupon distributions, the estimated level of inventory in the distribution channel and expected coupon redemption rates, using historical trends and experience.

Shire's estimate of the level of inventory in the distribution channel is based on product-by-product inventory data provided by wholesalers and third-party prescription data.

Shire believes that historical redemption rates, adjusted for known changes in coupon programs (such as length of coupon life and redemption conditions) are an appropriate basis for predicting future redemption rates. For coupon programs open at December 31, 2008 the redemption rates assumed by Shire range between 22% and 43% of coupons distributed (depending on the life of the coupons). A one percentage point increase in estimated coupon redemption rates would increase the provision at December 31, 2008 by \$0.1 million.

At December 31, 2008 the accrual for coupon redemptions was \$4.0 million (2007: \$9.0 million, 2006: \$13.0 million). The accrual levels at December 31 and within each financial year fluctuate according to the timing and volume of coupon distributions, in addition to changes in estimated redemption rates.

For rebates, returns and sales coupons the actual experience and the level of these deductions to revenue may deviate from the estimate. Shire reviews its estimates every quarter and may be required to adjust the estimate in a subsequent period. Historically, actual payments have not varied significantly from the reserves provided.

(iv) Income Taxes

In the application of FIN 48, "Accounting for Uncertainty in Income Taxes—an interpretation of FASB Statement No. 109" ("FIN 48") management is required to develop estimates as to whether a tax benefit should be recognized in the consolidated financial statements, based on whether it is more likely than not that the technical merits of the position will be sustained based on audit by the tax authorities. The measurement of the tax benefit recognized in the consolidated financial statements is based upon the largest amount of tax benefit that, in management's judgment, is greater than 50% likely to be realized based on a cumulative probability assessment of the possible outcomes. In applying FIN 48, management is required to make judgments in the determination of the unit of account, the evaluation of the facts, circumstances and information in respect of the tax position taken, together with the estimates of amounts that the Company may be required to pay in ultimate settlement with the tax authority.

Shire operates in numerous countries where its income tax returns are subject to audit and adjustment by local tax authorities. Because Shire operates globally, the nature of the uncertain tax positions is often very complex and subject to change and the amounts at issue can be substantial. Shire develops its cumulative probability assessment of the measurement of uncertain tax positions using internal expertise, experience, judgment and assistance from professional advisors. Estimates are refined as additional information becomes known. Any outcome upon settlement that differs from Shire's best estimate may result in additional or lower tax expense in future periods.

At December 31, 2008 the Company recognized a liability of \$228.7 million for total unrecognized tax benefits (2007: \$292.2 million) and had accrued \$76.2 million (2007: \$63.7 million) for the payment of interest and penalties.

The Company has significant deferred tax assets due to net operating losses (“NOLs”) in the United States, the UK, Ireland, Germany and other countries. The realization of these assets is not assured and is dependent on the generation of sufficient taxable income in future periods. Management is required to exercise judgment in determining whether it is more likely than not that it would realize these losses, based upon the availability of prudent and feasible tax planning strategies and estimates of future taxable income in the various jurisdictions in which these NOLs exist. Where there is an expectation that on the balance of probabilities there will not be sufficient taxable profits to utilize these NOLs a valuation allowance is held against these deferred tax assets. If actual events differ from management’s estimates, or to the extent that these estimates are adjusted in the future, any changes to the valuation allowance could materially impact the Company’s financial position and results.

At December 31, 2008, the Company had deferred tax liabilities of \$533 million and gross deferred tax assets of \$472 million, against which the Company had recorded valuation allowances of \$119 million.

At December 31, 2007, the Company had deferred tax liabilities of \$539 million and gross deferred tax assets of \$587 million, against which the Company had recorded valuation allowances of \$105 million.

At December 31, 2006, the Company had deferred tax liabilities of \$197 million and gross deferred tax assets of \$568 million, against which the Company had recorded valuation allowances of \$110 million.

(v) **Litigation**

The Company has a number of lawsuits pending that relate to product liability and intellectual property infringement claims, see ITEM 3: Legal Proceedings of Part II of this Annual Report on Form 10-K for further details. Shire accounts for litigation losses in accordance with SFAS No. 5, “Accounting for Contingencies” (“SFAS No 5”). Under SFAS No. 5, loss contingency provisions are recorded for probable losses when management is able to reasonably estimate the loss. Where the estimated loss lies within a range and no particular amount within that range is a better estimate than any other amount, the minimum amount is recorded. In other cases management’s best estimate of the loss is recorded. These estimates are developed substantially earlier than the ultimate loss is known, and the estimates are refined each accounting period, as additional information becomes known. Best estimates are reviewed quarterly and estimates are changed when expectations are revised. Any outcome upon settlement that deviates from Shire’s best estimate may result in an additional or lesser expense in a future accounting period.

On November 5, 2008 the Company announced that it had successfully settled all aspects of the TKT appraisal rights litigation with all parties. Shire paid the same price of \$37 per share originally offered to all TKT shareholders at the time of the July 2005 merger, plus interest. The settlement represents a total payment of \$567.5 million, representing consideration at \$37 per share of \$419.9 million and an interest cost of \$147.6 million. Prior to reaching this settlement, the Company accrued interest based on a reasonable estimate of the amount that may be awarded by the Court to those former TKT shareholders who requested appraisal. This estimate of interest was based on Shire’s cost of borrowing. Between the close of the merger and November 5, 2008 the Company applied this interest rate on a quarterly compounding basis to the \$419.9 million of consideration to calculate its provision for interest.

Upon reaching agreement in principle with all the dissenting shareholders, the Company determined that settlement had become the probable manner through which the appraisal rights litigation would be resolved. Under current law, (although not applicable in this case because the merger was entered into before the relevant amendment to the law became effective) the court presumptively awards interest in appraisal rights cases at a statutory rate that is 5 percentage points above the Federal Reserve discount rate (as it varies over the duration of the case). In connection with the settlement, the Company agreed to an interest rate that approximates to this statutory rate. Based on the settlement, the Company amended the method of determining its interest provision to reflect this revised manner of resolution, and recorded additional interest expense of \$73.0 million in its consolidated financial statements for the year to December 31, 2008 on reaching settlement with the dissenting shareholders. For further details on the settlement of this litigation, see Note 23(d) of ITEM 15: Exhibits and Financial Statement Schedules of this Annual Report on Form 10-K.

Recent accounting pronouncements update

See Note 2(y) to the consolidated financial statements contained in ITEM 15: Exhibits and Financial Statement Schedules of Part IV of this Annual Report on Form 10-K for a full description of recent accounting pronouncements, including the expected dates of adoption and effects on financial condition, results of operations and cash flows.

Financial Information Relating to the Shire IAS Trust

The results of operations and the financial position of the IAS Trust are included in the Consolidated Financial Statements of the Company. An explanation of the IAS Trust is included in ITEM 5: Market for Registrant's common equity, related stockholder matters and issuer purchases of equity securities of Part II of this Annual Report on Form 10-K. Separate, audited financial statements of the IAS Trust are included in ITEM 15: Exhibits and Financial Statement Schedules of Part IV of this Annual Report of Form 10-K.

For the period from August 29, 2008 to December 31, 2008 the IAS Trust recorded income before tax of \$7.2 million. This income reflected dividends received on the Income Access Share.

At December 31, 2008 the IAS Trust had total equity of \$nil. In future periods, to the extent that dividends are unclaimed on the expiry of checks, or to the extent they are returned unrepresented, the IAS Trust will record a liability for these unclaimed dividends.

The movements in cash and cash equivalents of the IAS Trust consist of dividends received on the Income Access Share, (\$7.2 million), and distributions made on behalf of Shire to shareholders (\$7.2 million).

ITEM 7A: Quantitative and qualitative disclosures about market risk

Treasury policies and organization

The Company's principal treasury operations are coordinated by its corporate treasury function, which is based in the UK. All treasury operations are conducted within a framework of policies and procedures approved annually by the Board. As a matter of policy, the Company does not undertake speculative transactions that would increase its 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 swaps on which interest is at floating rate. This exposure is primarily to US dollar and Euro interest rates. As the Company maintains all of its investments and foreign exchange swaps on a short term basis for liquidity purposes, this risk is not actively managed. In the year to December 31, 2008 the average interest rate received on cash and liquid investments was approximately 3% per annum. The largest proportion of investments was in US dollar money market and liquidity funds.

At December 31, 2008 the Company had debt totaling \$1,145.6 million outstanding, comprising Shire plc's \$1,100 million in principal amount of 2.75% convertible bonds, due 2014 which were issued in May 2007 and \$45.6 million of building financing obligations. The company incurs interest at a fixed rate on both the convertible bonds and on the building financing obligation.

No derivative instruments have been entered into to manage interest rate exposure by February 20, 2009.

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 exposure.

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, the Canadian Dollar, Pounds Sterling 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.

Translational foreign exchange exposure arises on the translation into US dollars of the balance sheet and income statement of non-US dollar functional subsidiaries. These foreign exchange exposures are generally managed through natural hedging via the currency denomination of foreign currency assets and liabilities. The consolidated financial statements of foreign entities are translated using the accounting policies described in Note 2 to the Company's consolidated financial statements contained in Part IV of this Annual Report.

At December 31, 2008, the Company had swap and forward foreign exchange contracts outstanding to manage the currency risk associated with inter-company loans. At December 31, 2008 the fair value of these contracts was a net liability of \$44.2 million. Further details are included below.

Foreign exchange risk sensitivity

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, 2008	Principal Value of Amount Receivable \$'M	Weighted Average Exchange Rate	Fair Value \$'M
Swap foreign exchange contracts			
Receive USD/Pay EUR	795.7	1.31	(45.6)
Receive USD/Pay GBP	38.3	1.49	1.4
Receive USD/Pay SEK	2.2	8.13	-

Market risk of investments

As at December 31, 2008 the Company has \$42.9 million of investments comprising equity investment funds (\$17.5 million), private companies (\$19.3 million) and publicly quoted equities (\$6.1 million). The investment in public

quoted companies and equity investment funds are exposed to market risk. No financial instruments or derivatives have been employed to hedge this risk.

Credit risk

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 and the US onshore funds participate in the US Treasury Department's Temporary Guarantee Program.

The Company is exposed to the credit risk of the counterparties with which it enters into derivative contracts. The Company limits this exposure through a system of internal credit limits which require counterparties to have a long term credit rating of A+ / A1 or better from 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 the derivative contracts are major international financial institutions.

The Company has entered into many agreements with third parties for the provision of services to enable it to operate its business. If the third party can no longer provide the service on the agreed basis, the Company may not be able to continue the development or commercialization of its products as planned or on a commercial basis. Additionally, it may not be able to establish or maintain good relationships with the suppliers.

ITEM 8: Financial statements and supplementary data

The consolidated financial statements and supplementary data called for by this item are submitted as a separate section of this report. See ITEM 15: Exhibits and financial statement schedules.

ITEM 9: Changes in and disagreements with accountants on accounting and financial disclosure

Not applicable.

ITEM 9A: Controls and procedures

Disclosure Controls and Procedures

The Company, under the supervision and with the participation of the Company's management, including the Chief Executive Officer and the Chief Financial Officer, has performed an evaluation of the effectiveness of the Company's disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e)), as at December 31, 2008.

In 2008, the Shire Income Access Share Trust was established. See ITEM 5: Market for Registrant's common equity, related stockholder matters and issuer purchases of equity securities - Income Access Share Arrangements. The daily operations of the Income Access Share Trust are administered on behalf of Shire by Lloyds TSB Offshore Trust Company Limited, an established trustee services company. Material financial information of the Income Access Share Trust is included in Shire's consolidated financial statements and is subject to Shire's disclosure controls and procedures. As a result, the Company's evaluation of the effectiveness of the Company's disclosure controls and procedures included those applicable to the Income Access Share Trust.

The Company's management necessarily applied its judgment in assessing the costs and benefits of such controls and procedures, which by their nature can provide only reasonable assurance regarding management's control objectives. Based on this evaluation, the Company's Chief Executive Officer and Chief Financial Officer concluded that the Company's disclosure controls and procedures are effective for gathering, analyzing and disclosing the information that the Company is required to disclose in the reports it files under the Securities Exchange Act of 1934, within the time periods specified in the SEC's rules and forms.

Management's Report on Internal Control Over Financial Reporting

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13(a)-15(f) or 15(d)-15(f) promulgated under the US Securities Exchange Act of 1934.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In 2008, the Shire Income Access Share Trust was established. See ITEM 5: Market for Registrant's common equity, related stockholder matters and issuer purchases of equity securities— Income Access Share Arrangements. The daily operations of the Income Access Share Trust are administered on behalf of Shire by Lloyds TSB Offshore Trust Company Limited, an established trustee services company. Material financial information of the Income Access Share Trust is included in Shire's consolidated financial statements and is subject to Shire's internal control over financial reporting. As a result, the Company's assessment of the effectiveness of the Company's internal control over financial reporting included those controls applicable to the Income Access Share Trust.

The Company's management assessed the effectiveness of the Company's internal control over financial reporting as at December 31, 2008. In making this assessment, the Company's management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework.

Based on its assessment, management believes that, as at December 31, 2008, the Company's internal control over financial reporting is effective based on those criteria.

Deloitte LLP, an independent registered public accounting firm, has issued an audit report on the Company's internal control over financial reporting, including those controls applicable to the Income Access Share Trust. This report appears on page F-3 of the Company's consolidated financial statements contained in Part IV of this Annual Report.

Changes in Internal Control Over Financial Reporting

The Company has an integrated information system covering financial processes, production, logistics and quality management. Various upgrades and new implementations were made to the information system during 2008 and more are planned for 2009. The Company reviewed each system change as it was implemented together with any

internal controls affected. Alterations were made to affected controls at the time the system changes were implemented. Management believes that the controls as modified are appropriate and functioning effectively.

ITEM 9B: Other Information

None

PART III

ITEM 10: Directors and executive officers of the registrant

Directors of the Company

Name	Age	Position
Matthew Emmens	57	Non-Executive Chairman
Angus Russell	53	Chief Executive Officer ("CEO")
Graham Hetherington	50	Chief Financial Officer ("CFO")
David Kappler	61	Senior Non-Executive Director
Dr Barry Price	65	Non-Executive Director
Robin Buchanan ⁽¹⁾	56	Non-Executive Director
Patrick Langlois	63	Non-Executive Director
Kate Nealon	55	Non-Executive Director
Dr Jeffrey Leiden	53	Non-Executive Director
David Mott	43	Non-Executive Director
Dr Michael Rosenblatt ⁽²⁾	61	Non-Executive Director

⁽¹⁾ Mr Buchanan retired from the Board with effect from July 29, 2008

⁽²⁾ Dr Rosenblatt was appointed with effect from April 24, 2008

Executive Officers of the Company

Name	Age	Position
Angus Russell	53	Chief Executive Officer
Graham Hetherington	50	Chief Financial Officer
Mike Cola	49	President of Specialty Pharmaceuticals
Dr Sylvie Grégoire	47	President of Shire Human Genetic Therapies
Tatjana May	43	General Counsel, Company Secretary and Executive Vice President Global Legal Affairs
Joseph Rus	63	Executive Vice President Alliance Management & New Product Development
Anita Graham	37	Executive Vice President Corporate Business Services and Chief Administrative Officer
Barbara Deptula	54	Executive Vice President and Chief Corporate Development Officer

For the purposes of the NASDAQ corporate governance rules, the independent directors are Dr Barry Price, David Kappler, Patrick Langlois, Kate Nealon, Dr Jeffrey Leiden, David Mott, Dr Michael Rosenblatt and prior to his retirement in July 2008, Robin Buchanan. There is no family relationship between or among any of the directors or executive officers.

The Company's Directors, including Non-Executive Directors, are subject to the "retirement by rotation" provisions of the Company's Articles of Association. These are designed to ensure that all directors are re-elected by shareholders at least every three years, a common practice for UK public companies.

In addition to the requirements of the Articles of Association, the Non-Executive Directors are appointed to office pursuant to individual letters of appointment for a term of two years (with the exception of Dr Barry Price who has a one year term), subject to invitation to serve further terms at the discretion of the Board. At the expiration of the two-year term, the Non-Executive Directors are not required to be re-elected by shareholders (unless the expiration of the term coincides with a particular Non-Executive Directors turn to retire by rotation), but may be re-appointed by the Board. Non-Executive Directors who have served on the Board for nine or more years are appointed to office for a term of one year, subject to annual re-election by shareholders, and by invitation to serve further terms at the discretion of the Board.

The current terms of the Non-Executive Directors are as set out below:

Name	Date of Term Expiration
Matthew Emmens	June 17, 2010
Dr Barry Price	January 24, 2010
David Kappler	April 4, 2010
Patrick Langlois	November 10, 2009
Kate Nealon	July 26, 2010
Dr Jeffrey Leiden	December 31, 2010
David Mott	October 30, 2009
Dr Michael Rosenblatt	April 23, 2010

Executive Officers are appointed pursuant to service agreements, which are not limited in term.

Biographical details of directors and executive officers of the Company

Matthew Emmens ***Chairman***

Mr Emmens succeeded Dr Cavanaugh as Non-Executive Chairman on June 18, 2008 and has been a member of the Board since March 12, 2003. He is also a member of the Company's Nomination Committee. He was Chief Executive Officer from March 2003 to June 2008. Mr Emmens also serves as a Non-Executive Director and President of Vertex Pharmaceuticals Inc. and will become Chairman and Chief Executive Officer in May 2009. He is a former board member of Incyte Corporation. Mr Emmens began his career in international pharmaceuticals with Merck & Co, Inc. in 1974, where he held a wide range of sales, marketing and administrative positions. In 1992, he helped to establish Astra Merck, a joint venture between Merck and Astra AB of Sweden, becoming President and Chief Executive Officer. In 1999, he joined Merck KGaA and established EMD Pharmaceuticals, the company's US prescription pharmaceutical business. He was later based in Germany as President of Merck KGaA's US prescription pharmaceutical business and was a Board member. Mr Emmens holds a degree in Business Management from Fairleigh Dickinson University.

Angus Russell ***Chief Executive Officer***

Mr Russell succeeded Mr Emmens as Chief Executive Officer on June 18, 2008 and has been a member of the Board since December 13, 1999. He was the Company's Chief Financial Officer from December 1999 to June 2008. He is also the Chairman of the Company's Leadership Team. Mr Russell also serves as a Non-Executive Director of the City of London Investment Trust plc. Between 1980 and 1999, he held a number of positions of increasing responsibility at ICI, Zeneca and AstraZeneca PLC, including Vice President, Corporate Finance at AstraZeneca and Group Treasurer at Zeneca. Mr Russell is a Chartered Accountant, having qualified with Coopers & Lybrand, and is a Fellow of the Association of Corporate Treasurers.

Graham Hetherington ***Chief Financial Officer***

Mr Hetherington has been the Company's Chief Financial Officer and a member of the Board since July 1, 2008. He is also a member of the Company's Leadership Team. Mr Hetherington most recently held positions as the Chief Financial Officer of Bacardi in 2007 and Allied Domecq plc from 1999-2005. Mr Hetherington is a Fellow of the Chartered Institute of Management Accountants.

David Kappler

Deputy Chairman and Senior Independent Non-Executive Director

Mr Kappler has been a member of the Company's Board since April 5, 2004. He is Chairman of the Company's Nomination Committee and Audit, Compliance & Risk Committee. Mr Kappler also serves as the Non-Executive Chairman of Premier Foods plc and as a Non-Executive Director of Intercontinental Hotels Group plc. Mr Kappler was a Director of Camelot Group plc from 1996-2002 and of HMV Group plc from 2002-2006. Mr Kappler retired from Cadbury Schweppes plc in April 2004 after serving as Chief Financial Officer since 1995. He worked for the Cadbury Schweppes group between 1965 and 1984 and rejoined the company in 1989 following its acquisition of Trebor Group, where he was Financial Director. Mr Kappler is a Fellow of the Chartered Institute of Management Accountants.

Patrick Langlois

Non-Executive Director

Mr Langlois has been a member of the Company's Board since November 11, 2005. He is also a member of the Company's Audit, Compliance & Risk Committee and Remuneration Committee. Mr Langlois is a Non-Executive Director of Scynexis Inc., Nanobiotix S.A., and Exonhit S.A. Mr Langlois previously served as Vice Chairman of the Management Board of Aventis S.A., Strasbourg, having been Group Executive Vice President and Chief Financial Officer for several years. He also spent many years in senior financial roles with the Rhone-Poulenc Group, including three years as a member of the Executive Committee and Chief Financial Officer. Mr Langlois holds a PhD in Economics and a diploma in banking studies.

Dr Jeffrey Leiden

Non-Executive Director

Dr Leiden has been a member of the Company's Board since January 1, 2007. He is a member of the Company's Remuneration Committee and Nomination Committee and Chairman of the Company's Science & Technology Committee. Dr Leiden served as President and Chief Operating Officer, Pharmaceutical Products Group and Chief Scientific Officer at Abbott Laboratories from 2001-2006; during this time he was also a member of the Boards of Directors of Abbott and TAP Pharmaceutical Products, Inc. Prior to joining Abbott, Dr Leiden served as the Elkan R. Blout Professor of Biological Sciences, Harvard School of Public Health and Professor of Medicine, Harvard Medical School. Previously, he was the Frederick H. Rawson Professor of Medicine and Pathology and Chief of the Section of Cardiology at the University of Chicago. His extensive business and consulting experience includes both the pharmaceutical and medical device areas. Dr Leiden was a founder of Cardiogene, Inc., a biotechnology company specializing in cardiovascular gene therapy. Dr Leiden earned a bachelor's degree in biological sciences, a doctorate in virology and a medical degree, all from the University of Chicago. He is a Fellow of the American Academy of Arts and Sciences and an elected member of the Institute of Medicine of the National Academy of Sciences. Dr Leiden is currently a Managing Director at Clarus Ventures LLC.

David Mott

Non-Executive Director

Mr Mott has been a member of the Company's Board since October 31, 2007. He is also a member of the Company's Audit, Compliance & Risk Committee. Mr Mott joined venture capital firm New Enterprise Associates ('NEA') in September 2008 as a General Partner focused on biopharmaceutical investments. Prior to joining NEA, Mr Mott was President and Chief Executive Officer of MedImmune Inc., a subsidiary of AstraZeneca PLC, and Executive Vice President of AstraZeneca. He joined MedImmune in 1992 and served in roles of increasing responsibility including Chief Operating Officer, Chief Financial Officer, President and Chief Executive Officer. Prior to joining MedImmune, Mr Mott was a Vice President in the Health Care Investment Banking Group at Smith Barney, Harris Upham & Co. Inc. Mr Mott is a member of the board of Rib-x Pharmaceuticals and of the St. Albans School. He is a former board member of Ambit Biosciences, Conceptis Technologies, and MedImmune, Inc. and has served on numerous industry trade group and not-for-profit boards. Mr Mott holds a bachelor's degree in economics and government from Dartmouth College.

Kate Nealon

Non-Executive Director

Ms Nealon has been a member of the Company's Board since July 27, 2006. She is Chair of the Company's Remuneration Committee and also a member of the Audit, Compliance & Risk Committee. Ms Nealon is a Non-Executive Director of Cable & Wireless plc and a former Non-Executive Director of HBOS plc. She is also a Senior Associate at the Judge Business School at Cambridge University. Ms Nealon was previously Group Head of Legal & Compliance at Standard Chartered plc until 2004. She is a US qualified lawyer and spent several years in her early career practising law in New York.

Dr Barry Price
Non-Executive Director

Dr Price has been a member of the Company's Board since January 16, 1996. He is a member of the Company's Nomination Committee and Science & Technology Committee. He also serves as Chairman of Antisoma plc and Summit Corporation plc. Dr Price worked for Glaxo for 28 years, where he held positions of increasing responsibility with the company's research group.

Dr Michael Rosenblatt
Non-Executive Director

Dr Rosenblatt has been a member of the Company's Board since April 24, 2008 and is a member of the Company's Science & Technology Committee. Dr Rosenblatt is the Dean of Tufts University School of Medicine, Boston, Massachusetts. He was previously Professor of Medicine at Harvard Medical School and has served in senior research positions at the Beth Israel Deaconess Medical Center in Boston. He was the founding director of the Carl J. Shapiro Institute for Education and Research at Harvard Medical School and Beth Israel Deaconess Medical Center. In addition, Dr Rosenblatt has served as Director of the Harvard-MIT Division of Health Sciences and Technology and as Senior Vice President for Research at Merck Research Laboratories where he headed a worldwide development team as well as directing drug discovery efforts in the United States, Japan and Italy. In Japan, he was responsible for Merck's clinical research and development; he also headed Merck Research's worldwide University and Industry Relations Department. He is a graduate of Columbia University and gained his medical qualification at Harvard Medical School.

Executive officers

Mike Cola has been with Shire since July 2005. He is President of Specialty Pharmaceuticals and a member of Shire's Leadership Team. Mr Cola has over 20 years of international biopharmaceutical industry experience. He was previously President of the Life Sciences Group of Safeguard Scientifics, Inc. He also held progressively senior management positions in product development and commercialization at AstraMerck/AstraZeneca. Mr Cola received his Master of Science degree in biomedical engineering from Drexel University.

Dr Sylvie Grégoire joined Shire in September 2007. She is President of Shire Human Genetic Therapies and a member of Shire's Leadership Team. Dr Gregoire has over 20 years of pharmaceutical and biotechnology experience. She most recently served as Executive Chairwoman of the Board of IDM Pharma, a biotechnology company in California. Prior to this she was CEO of GlycoFi, and has also held numerous leadership positions at Biogen Inc., in the United States and France. She also worked for Merck & Co. in various positions in clinical research and in European regulatory affairs both in the US and abroad. She received her Doctor of Pharmacy degree from the State University of New York at Buffalo, and her pharmacy degree from Université Laval, Québec City, Canada.

Tatjana May has been with Shire since May 2001. She is General Counsel, Company Secretary and Executive Vice President Global Legal Affairs and a member of Shire's Leadership Team. Ms May was previously Assistant General Counsel at the corporate headquarters of AstraZeneca plc and prior to that she worked at the law firm Slaughter and May.

Joseph Rus has been with Shire since 1999. He is Executive Vice President Alliance Management & New Product Development and a member of Shire's Leadership Team. Following the merger of Shire Pharmaceuticals and BioChem Pharma in May 2001, Mr Rus was appointed President and CEO of Shire BioChem Inc. (now known as Shire Canada Inc.) He has more than 25 years of experience in the international pharmaceutical industry including European country management with both Warner Lambert and Hoffmann La Roche.

Anita Graham has been with Shire since January 2004. She is Executive Vice President Corporate Business Services and Chief Administrative Officer and a member of Shire's Leadership Team. Ms Graham was previously Vice President of Human Resources at Cytoc Corporation. She also held senior HR positions at Serono, Inc. and Scudder Kemper Investments, Inc. (now part of Deutsche Bank) and has extensive experience in all aspects of HR, both in Europe and the US.

Barbara Deptula has been with Shire since September 2004. She is Executive Vice President and Chief Corporate Development Officer and a member of Shire's Leadership Team. Ms Deptula was previously President of the biotechnology division of Sicor Inc. and Senior Vice President for commercial and product development at Coley Pharmaceutical Group. She also held senior management positions focused on marketing, product development, licensing and business development at US Bioscience, Schering-Plough, American Cyanamid, and Genetics Institute.

Audit, Compliance & Risk Committee Financial Expert

The members of the Audit, Compliance & Risk Committee as at December 31, 2008 were Mr Kappler, Mr Langlois, Ms Nealon and Mr Mott.

The Board of Directors has determined that Mr Kappler is the serving member of the Audit, Compliance & Risk Committee who is the Audit, Compliance & Risk Committee's financial expert and that he is independent as defined under applicable SEC rules. A description of Mr Kappler's relevant experience is provided above.

Code of Ethics

Shire's Board of Directors has adopted a Code of Ethics that applies to all its directors, officers and employees, including its Chief Executive Officer, Chief Financial Officer and Group Financial Controller. The Code of Ethics is posted on Shire's internet website at www.shire.com.

NASDAQ Corporate Governance Exemption

As a foreign private issuer incorporated in Jersey with its principal listing on the London Stock Exchange, Shire follows its "home country" corporate governance practices in lieu of the provisions of The NASDAQ Stock Market's Marketplace Rule 4350 that apply to the nomination of directors and the constitution of a quorum for any meeting of shareholders.

The NASDAQ Stock Market's rules require that new directors are selected, or recommended for the board's selection, by a majority of independent directors or a nominations committee comprised solely of independent directors. In compliance with Jersey law and the provisions of the UK Combined Code on Corporate Governance (the "Combined Code"), new directors at Shire are nominated by a nomination committee comprised of four members. Mr Matthew Emmens, who is a member of the committee, is not regarded as "independent" under The NASDAQ Stock Market's rules.

Shire also complies with the laws of Jersey and the Combined Code in lieu of The NASDAQ Stock Market's rules regarding the constitution of a quorum for any meeting of shareholders. The NASDAQ Stock Market's rules provide for a quorum of no less than 33 1/3% of Shire's outstanding shares. However, Shire's By-laws provide that a quorum has been established when two members are present in person or by proxy and entitled to vote except where the rights attached to any existing class of shares are proposed to be varied, and then the quorum shall be two persons entitled to vote and holding or representing by proxy not less than one-third in nominal value of the issued shares of the class.

ITEM 11: Executive compensation

In respect of the financial year to December 31, 2008, the total compensation paid to Shire plc's directors and executive officers as a group for the periods during which they served in any capacity was \$19.5 million. The total amounts set aside or accrued by the Company to provide pension, retirement or similar benefits for this group was \$1.3 million. During 2008, members of the group were granted options over ordinary shares and ADSs of the Company. All such holdings were issued pursuant to the various executive share option plans described in Note 33 to the Company's consolidated financial statements contained in Part IV of this Annual Report.

The Company provides information on the individual compensation of its directors in the Directors' Remuneration Report included within its financial statements filed with the United Kingdom Listings Authority ("UKLA"). As the remuneration report is made publicly available, it is reproduced in full below. As at the time of filing this Form 10-K, the Directors' Remuneration Report is subject to approval by Shire plc's shareholders at the Annual General Meeting.

Introduction

This report meets the relevant requirements of the Listing Rules of the Financial Services Authority and describes how the Board has applied the principles relating to directors' remuneration in the Combined Code.

Directors' Remuneration Report

Dear Shareholder

The year 2008 was an active one for Shire's Remuneration Committee due to the change in leadership in the Company. The retirement of James Cavanaugh as Chairman and the succession of Matthew Emmens to that role resulted in a series of changes. These included the promotion of Angus Russell to CEO, and the appointment of Graham Hetherington as CFO.

Shareholders overwhelmingly supported the appointment of each executive to his new position and the Remuneration Committee was responsible for ensuring each individual was paid competitively in his new role.

The Remuneration Committee reviewed competitive remuneration levels for the aforementioned executive directors, as well as below board executive vice presidents, and confirmed that Shire's approach to the remuneration package is well positioned relative to its competitive market. In addition, the Committee is satisfied that awards are commensurate with corporate and individual performance.

Upon assuming the leadership of the Company, Angus Russell began a review of Company strategy and vision. When the strategy was approved by the Board, the Remuneration Committee ensured that the goals set forth in the strategy were closely aligned with the metrics of the short-term incentive plan and the competitive peer group used in assessing long-term performance. The Remuneration Committee will continue this work in 2009, as a comprehensive review of total rewards strategy and remuneration programs will be undertaken.

The Remuneration Committee remains committed to a continuing dialogue with shareholders and we take account of your views. We hope that this report provides helpful context and explanation of the policies and practical considerations that influence our decisions.

Sincerely,

Kate Nealon
Chair of the Remuneration Committee

Pound sterling denominated amounts are converted to US dollar amounts at the average exchange rates for the year ended December 31, 2008 of £1:\$1.8542 (2007: £1:\$2.0010) unless otherwise stated.

The Remuneration Committee

The Remuneration Committee (the "Committee") is responsible for developing, reviewing and overseeing the implementation of the Company's compensation and benefits policy. The Committee is responsible for all elements of the Executive Directors' remuneration, and reviews and approves broad policy for the remuneration of senior management and the employee population.

The constitution of the Committee complies with the Combined Code. During 2008 the Committee reviewed and updated its Terms of Reference to ensure that these effectively reflect its responsibilities.

The Company considers all members of the Committee to be independent. The members during 2008 were:

- Kate Nealon, an Independent Non-Executive Director and Chair of the Committee;
- Patrick Langlois, an Independent Non-Executive Director;
- Dr Jeffrey Leiden, an Independent Non-Executive Director; and
- Robin Buchanan, an Independent Non-Executive Director, who served on the Committee through July 28, 2008. His tenure on the Committee ended concurrent with the end of his Board membership. The Committee extends its gratitude to Mr. Buchanan for his contribution during his years of service.

The Chairman and the CEO attend meetings of the Committee at its invitation, but neither is involved in any decisions relating to his own remuneration.

The Committee was materially assisted in 2008 by Anita Graham, EVP, Chief Administrative Officer. The following external advisors were appointed by and materially assisted the Committee:

- PricewaterhouseCoopers LLP served as the independent advisor to the Committee beginning in March 2008. In addition, PricewaterhouseCoopers LLP also provided a broad range of consultancy services to Shire in accounting and related areas in 2008;
- Deloitte LLP (who also provided audit and some tax services to the Company), served as the independent advisors to the Committee through February 2008 and provided data and advice on general issues around the operation of the Company's incentive schemes;
- Slaughter and May (who also provided general legal advice to the Company) provided legal advice on Directors' service contracts and the Group's incentive plans.

Key Committee Activities for 2008

The Committee met seven times in 2008 and completed the following key activities:

- Approved remuneration arrangements for Matthew Emmens in his new role as Chairman and Angus Russell in his new role as CEO, both effective June 18, 2008. The Committee also approved remuneration for Graham Hetherington, who joined the Company as CFO effective July 1, 2008.
- Conducted benchmarking studies for below-board executive vice president positions and approved a blended US/UK pay approach for benchmarking for their base salaries and total compensation.
- Conducted a review of reward program effectiveness for senior management. Outcomes from this study will be used in a comprehensive review of reward strategy in 2009.

In addition, the Committee discussed, among other items, the following standing agenda items:

- Review of Executive Directors' performance and all components of remuneration
- Review of Company performance for 2007 against the previously agreed corporate objectives for 2007 and determination of the corporate component of the Company's annual incentive plan

- Remuneration for members of senior management
- Performance measures for the 2008 Annual Incentive Plans
- Long-term incentive grants for current employees and new hires throughout 2008
- Employee Stock Purchase Plan and Sharesave scheme offerings

Executive remuneration policy

The Committee considers that an effective remuneration policy, aligned to the Company's business needs, is important to the Company's success. It directly impacts the Company's ability to recruit, retain and motivate executives of the highest calibre who will be able to deliver sustained value to shareholders, even in the most challenging times. The Committee also recognizes shareholders' focus on the delivery of results and the creation of long-term value and, as such, the remuneration policy reflects a pay-for-performance philosophy and alignment to shareholder interests.

The Company's compensation and benefits policy for Executive Directors achieves the above goals through a balanced remuneration program based on the following principles:

- base pay is market and performance driven, with reference to a blended US/UK market comparison group. It is targeted at or around the median relative to the comparison group, and varies based on individual performance;
- the Executive Annual Incentive Plan is performance-based and is linked to the achievement of an appropriate mix of corporate and individual performance targets. The Executive Annual Incentive Plan allows the Company to measure and reward progress against its strategic goals and is closely tied to delivery of sustained shareholder value;
- share-based compensation is a key element of the Company's remuneration policy as it aligns the interests of the Company's executives with the interests of its shareholders. This element of compensation also utilises a blended US/UK market comparison to determine the face value of awards to Executive Directors;
- benefits programs are locally competitive and provide for the welfare and well-being of the Company's employees and their families;
- the Committee currently aims for variable compensation to represent over two-thirds of total remuneration; and
- the Committee believes that Executive Directors should be encouraged to own shares in the Company in order to ensure the alignment of their interests with those of the Company's shareholders. Share ownership guidelines have been in effect since 2006.

In its assessment of corporate and Executive Director performance, the Committee utilizes a Balanced Scorecard ("Scorecard") set of objectives which consider both financial and non-financial measures. Financial measures include revenue growth, net sales and contribution, as well as management of expense ratios. Among the non-financial measures are customer care and satisfaction, operational excellence, and the development of people and organizational capabilities.

The Committee regularly monitors the effectiveness of the remuneration policy and reviews this policy based on independent analysis and advice, an understanding of the business drivers and competitive environment in which the Company operates, and on-going dialogue with shareholders. In 2008, the Committee maintained the above principles for Executive Directors and, in addition, agreed to adopt the blended US/UK benchmarking approach for base pay, total cash and total compensation for the below-board executive vice presidents of the Company. This approach will be used for benchmarking remuneration with effect from 2009.

The remuneration package

The main elements of the remuneration package for Executive Directors and senior management are:

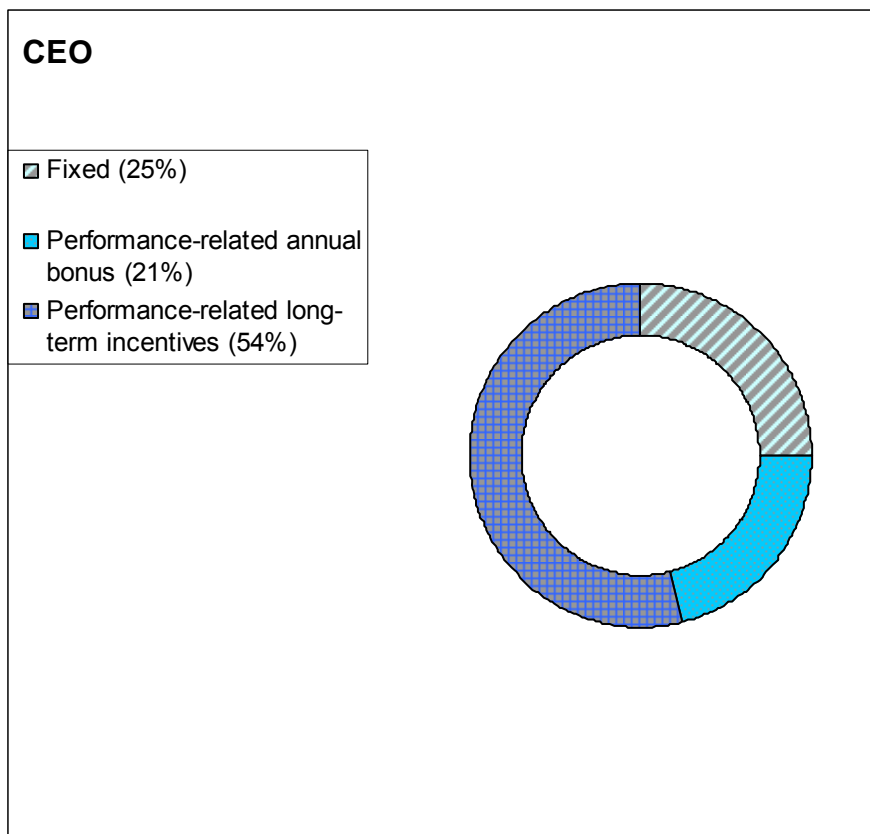
1. Salary
2. Executive Annual Incentive Plan
 - (a) Cash Component
 - (b) Share Component
3. Long-term incentives

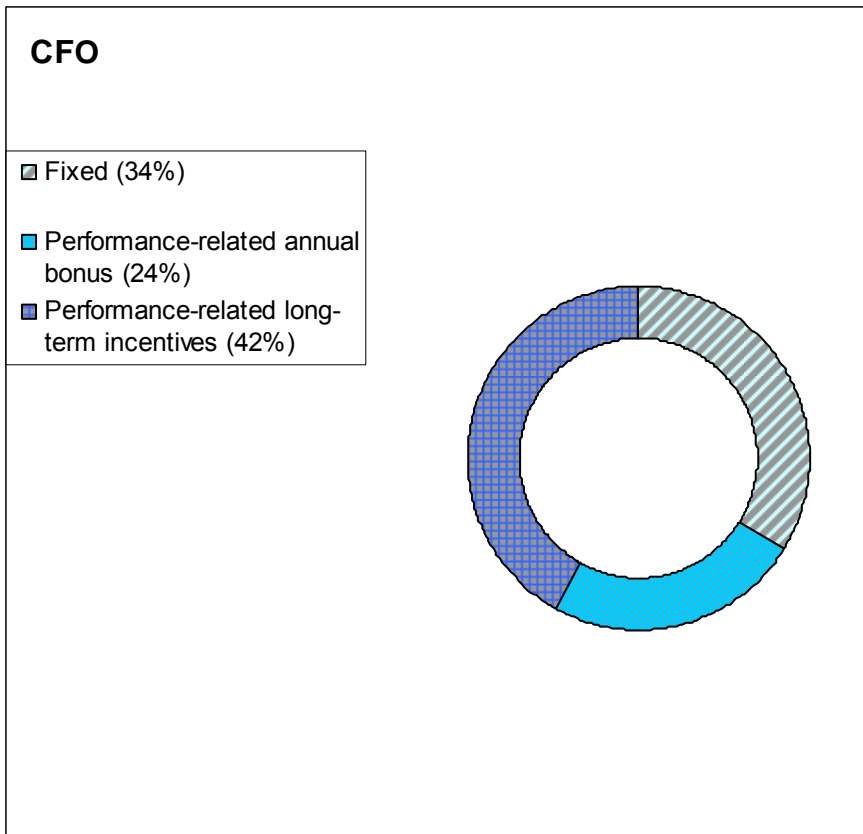
(a) Portfolio Share Plan

4. Pension and other benefits

While each element of remuneration is reviewed and determined separately, the Committee also considers a total compensation approach when establishing each executive's remuneration package.

An appropriate balance is maintained between fixed and performance-related remuneration and between elements linked to short-term financial performance and long-term shareholder value creation. The Executive Annual Incentive Plan and long-term incentive plans are considered performance-related elements, while base salary is essentially "fixed", although performance is considered when determining annual increases. Assuming on-target performance, the CEO's remuneration is 25% fixed and 75% variable, and the CFO's remuneration is 34% fixed and 66% variable. The aforementioned fixed percentages exclude pension and other benefits.





1. Salary

The Committee reviews salaries annually and utilizes a comparator group that is a blend of US and UK companies with sector, size, complexity, and international characteristics similar to those of the Company. The Committee’s policy is for salary to be targeted at or around the median of the blend of US/UK comparators. This approach positions pay comparably to those companies with whom the Company competes for business and talent.

As part of its normal annual salary review process, the Committee reviews competitive market data provided by independent external consultants and US and UK market conditions. Base salary levels and salary increase decisions for senior management take into account the competitive market data, the Company’s budget for performance-related pay increases, and the skills, performance and results achieved by each individual. Salaries may be positioned below median for employees who are new to their role or under-performing, while salaries for consistently strong performers may be positioned at median or higher.

Based on a review of competitive market data, and on corporate and individual performance results, the following salaries for the CEO and CFO were determined in 2008:

- Angus Russell received a salary increase to £602,000 (\$1,116,228) concurrent with his promotion to CEO effective June 18, 2008. This pay level is below median for comparable roles within the peer group. Effective January 1, 2009, Mr. Russell received a salary increase to £682,000 (\$1,264,564), which will place him in the bottom quartile for his position. This increase is a step toward moving his salary to the median over the course of two years, dependent upon continued satisfactory performance.
- Graham Hetherington’s salary was set at £400,000 (\$741,680) when he joined the Company on July 1, 2008. Effective January 1, 2009 he received a salary increase to £416,000 (\$771,347), which reflects overall solid performance and an excellent transition into his role.

2. Executive Annual Incentive Plan

Executive Directors and senior management participate in an Executive Annual Incentive Plan (“EAIP” or “Plan”), which rewards Company performance based on achievement of pre-defined, Committee-approved corporate objectives. The EAIP is delivered in a combination of cash, which is delivered shortly after the close of the fiscal year, and restricted shares, which are payable in three years. The Plan design is meant to provide a strong performance/shareholder value orientation and reward executives for the creation of shareholder value. Both the cash and share-based components of the award are determined based on the achievement of corporate, business and individual objectives.

Corporate objectives are organized in a Scorecard format, which focuses on all areas that drive the success of the business: financial, customer, people and capabilities, and operational excellence. These objectives include a description of the objective and key performance indicators (“KPIs”), including targets and deadlines.

The extent of the awards under the Plan is determined by the Committee only when exacting levels of performance specified by the KPI have been achieved. Objectives measured by the Company’s financial performance are assessed on the Company’s results, as reported in the Company’s Annual Report on Form 10-K under US GAAP.

2008 individual objectives for Executive Directors were approved by the Committee. The detailed objectives and performance standards contain commercially sensitive information and therefore are not detailed here. However, some of the objectives are summarised below according to the four Scorecard areas for 2008. Weightings for each of the four Scorecard areas are also provided:

- Financial Targets (40% of Weighting)
 - Year on year revenue growth
 - Net sales and contribution of each Business
 - Management of expense ratios

- Customers (15% of Weighting)
 - Improve customer care and customer service levels across the entire business

- People and Capabilities (15% of Weighting)
 - Employee retention
 - Programs to support leadership and career development for high potential talent

- Operational effectiveness (30% of Weighting)
 - Successful product filings, approvals and launches
 - Determination of strategies for therapeutic areas
 - Strategies for investment in Company infrastructure

The Committee assesses performance against annual objectives in the first quarter of the following year. The target incentive is paid where Executive Directors have fully achieved their individual objectives and the corporate objectives have been met. The maximum incentive is paid when the Committee determines that individual and/or corporate performance has been exceptional. Maximum incentive payments for 2008 were capped at 115% of salary in cash and 65% of salary in restricted shares for the CEO and 100% of salary in cash and 55% of salary in restricted shares for the CFO.

For 2008, the Committee made award determinations for Matthew Emmens, pro-rated for his tenure as CEO through June 17, 2008, for Angus Russell, taking into account his performance as CFO until June 17, 2008 and his subsequent transition to CEO and for Graham Hetherington who joined the Company as CFO on July 1, 2008. In alignment with the rules of the Executive Annual Incentive Plan, Mr. Russell received the CEO incentive target for the full year. The table below outlines the incentive opportunities for each:

	Target incentive (as a % of salary)	Maximum incentive (as a % of salary)	Weighting of target incentive objectives	
			Corporate	Individual
Matthew Emmens CEO (January 1 – June 17, 2008)	65% cash 20% restricted shares	115% cash 65% restricted shares	100%	Will be taken into account in determining final award
Angus Russell CFO (January 1 – June 17, 2008) CEO (June 18 – December 31, 2008)	65% cash 20% restricted shares	115% cash 65% restricted shares	100%	Will be taken into account in determining final award
Graham Hetherington CFO (July 1 – December 31, 2008)	55% cash 15% restricted shares	100% cash 55% restricted shares	70%	30%

In 2008, Shire's performance was very strong in a very challenging market. The incentive payments awarded to each Executive Director for 2008 reflect that strong corporate performance and individual achievements:

- Mr Emmens was granted a cash award of 90% of base salary and a share award of 51% of base salary to recognize his performance in 2008. This award was, in accordance with his employment contract, pro-rated to June 17, 2008 and was based on year to date Company performance as at the time of Mr Emmens stepping down as CEO.
- Mr Russell was awarded a cash award of 95% of base salary and a share award of 54% of base salary based on his performance as CFO and CEO.
- Mr Hetherington was awarded a cash award of 69% of base salary and a share award of 39% of base salary based on his performance as CFO from July 1 to December 31, 2008. His incentive award is pro-rated based on his tenure with the Company.

These incentive awards are consistent with the overall performance of the Company in 2008, which included:

- Total revenue growth of 24%;
- Net sales and contribution of each business exceeding its targets;
- Approval and launch of VYVANSE for Adult ADHD;
- Successful M&A activities designed to expand both the marketed and pipeline product set (including the acquisition of Jerini);
- Geographical expansion for marketed products into Mexico, Argentina, Brazil, Australia, and Russia; and
- The highly successful implementation of other Scorecard objectives focused on the continuing growth of the Company.

Employees below senior management participate in a cash-based annual incentive plan that applies the same Scorecard format used for senior management. Personal objectives were developed for each employee based on 2008 corporate objectives and individual awards are determined based on achievement of individual and corporate objectives.

3. Long-term incentives

Long-term incentives in 2008 were granted under the Portfolio Share Plan. Details are also provided below on legacy incentive plans. No awards were granted to Executive Directors or any other employee under these legacy plans in 2008; however, awards from grants in previous years continue to vest.

(a) The Portfolio Share Plan

The purpose of the Portfolio Share Plan (the “Plan”) is to enable the Company to motivate and reward selected employees by reference to share price performance, and to align the interests of these employees with long-term value creation for shareholders. Participation in the Plan is discretionary.

Under the Plan, awards granted to Executive Directors will be subject to a performance target, which must, in normal circumstances, be met before the award vests. Performance targets will normally be measured over a period of not less than three years. Special rules apply if the participant’s employment terminates early or on a change in control of the Company.

The Plan is comprised of two parts, which can be operated separately:

Part A

- A **Stock Appreciation Right (“SAR”) Award** is the right to receive shares or American Depositary Shares (“ADSs”) in Shire plc linked to the increase in value of a specified number of shares over a period between three and five years from the date of grant and, in the case of Executive Directors, subject to the satisfaction of performance targets. SAR Awards will normally vest three years after the date of grant, subject to the satisfaction of performance targets in the case of Executive Directors, and can be exercised up to the fifth anniversary of the date of grant.

Part B

- A **Performance Share (“PSA”) Award** is the right to receive a specified number of shares or ADSs three years from the date of grant. In the case of Executive Directors, performance targets must be satisfied before a PSA Award vests. Upon vesting of the PSA Award, shares will be released to the participant automatically without any action on the part of the participant.

The Plan contains individual grant limits set at a face value of six times base salary for SAR awards in any one year and four times base salary for PSA awards in any one year. It is the Company’s intention for awards granted under the Plan to Executive Directors to comprise either or both a SAR Award and a PSA Award. Ordinarily, it is the Company’s intention to provide annual grants to the CEO and CFO with face values (calculated by reference to the average share price over the prior 12 month calendar period) as follows:

- for the CEO, equivalent to approximately 4 times base salary in SARs and 3 times base salary in PSAs; and
- for the CFO, equivalent to approximately 2.2 times base salary in SARs and 1.65 times base salary in PSAs.

Performance criteria

Awards under the Plan normally vest on the third anniversary of the date of grant. In the case of Executive Directors, awards will only vest if the Committee determines that the performance conditions have been satisfied and that, in the opinion of the Committee, the underlying performance of the Company is sufficient to justify the vesting of the award.

Performance criteria are based on relative Total Shareholder Return (“TSR”) measured against two comparator groups. Vesting of one-third of an Award will depend upon the Company’s performance relative to the TSR performance of FTSE 100 constituents, excluding financial institutions. The vesting of the remaining two-thirds of an Award will depend upon the Company’s performance relative to the TSR performance of a group of international companies from the pharmaceutical sector (see below). Vesting will be as follows:

Percent Vesting	Performance Level Achieved
0% Vesting	Performance below the median versus the comparator companies and the FTSE 100
33% Vesting	Performance at median versus the comparator companies and the FTSE 100
100% Vesting	Performance at or above upper quartile performance versus the comparator companies and the FTSE 100

Performance between median and upper quartile versus the comparator companies and the FTSE 100 is calculated from 33% to 100% on a straight-line basis.

For 2008, the comparator group of international companies from the pharmaceutical sector comprised the following companies:

Allergan, Inc. ("Allergan"), Altana Aktiengesellschaft ("Altana"), Biovail Corporation ("Biovail"), Cephalon Inc. ("Cephalon"), Forest Laboratories Inc. ("Forest Labs"), King Pharmaceuticals Inc ("King"), Kos Pharmaceuticals Inc ("Kos"), H. Lundbeck A/S ("Lundbeck"), Medicis Pharmaceutical Corporation ("Medicis"), Novo Nordisk A/S ("Novo Nordisk"), Schering AG, Sepracor Inc. ("Sepracor"), Merck Serono S.A. ("Merck Serono"), UCB S.A. ("UCB"), Valeant Pharmaceuticals International ("Valeant"), and Watson Pharmaceuticals Inc ("Watson").

The Committee has the discretion to amend this group of companies to ensure that the group stays both relevant and representative; however, the change must not have the effect of making the performance criteria either materially easier or materially more difficult to achieve, in the opinion of the Committee, than it was or they were immediately before the circumstance in question.

For the 2009 award, the Committee has decided that the comparator group will comprise the following international companies from the pharmaceutical sector. These companies are aligned with competitors identified in the Company's definition of the strategy in 2008 referred to in ITEM 7: Management's Discussion and Analysis of Financial Condition and Results of Operations:

Actelion Pharmaceuticals Ltd, Amgen Inc, Biogen Idec Inc., BioMarin, Biovail, Celgene Corporation, Cephalon, Endo Pharmaceuticals Holdings Inc., Forest Labs, Genzyme, Gilead, Ipsen Ltd, King, Lundbeck, Novo Nordisk, UCB.

TSR performance will be measured using an averaging period of three months. In addition, the Committee will have regard to the same calculation using an averaging period of six months as part of a fairness review to ensure that vesting properly reflects underlying performance.

If the performance conditions are not met, awards will lapse.

Awards made to Executive Directors under the Plan in 2008 are set out in the audited information below.

(b) Legacy long-term incentive plans

The three legacy long-term incentive plans in which some members of senior management participate include the Shire Pharmaceuticals Executive Share Option Scheme, Shire 2000 Executive Share Option Scheme and the Long Term Incentive Plan. No awards have been granted under these plans in 2008; however, awards from grants in previous years continue to vest.

(i) Shire Pharmaceuticals Executive Share Option Scheme ("Executive Scheme")

The last options were granted under the Executive Scheme in 2000. The Executive Scheme was replaced by the Shire 2000 Executive Share Option Scheme.

(ii) Shire 2000 Executive Share Option Scheme ("2000 Executive Scheme")

The last options were granted under the 2000 Executive Scheme in 2005. All options granted under the 2000 Executive Scheme have vested, with the exception of those granted in 2000. The 2000 Executive Scheme was replaced by the Portfolio Share Plan in 2005.

Details of the performance conditions attached to options granted under the above schemes are set out in Note 33 to the consolidated financial statements.

(iii) Long Term Incentive Plan ("LTIP")

The LTIP was adopted in 1998 and amended in 2000. The last awards were granted under this plan in 2005.

Performance tied to the vesting of the 2005 LTIP grants resulted in a vesting percentage of 88.54%. Awards will be satisfied by the transfer of shares in May 2009. The awards for each of the Executive Directors are as follows:

- Matthew Emmens will receive 86,298 shares.
- Angus Russell will receive 55,972 shares.

Details of the performance condition attached to awards made under the LTIP are set out in Note 33 to the consolidated financial statements.

4. Share Ownership Guidelines

The Committee believes that Executive Directors and certain other members of senior management should be encouraged to own shares in Shire plc in order to ensure the alignment of their interests with those of Shire plc's shareholders.

The Executive Share Ownership Guidelines are administered by the Committee and are based on the following principles:

- The Committee believes that share ownership is an important element of an executive's role in leading the Company and represents both a commitment by the executive as well as an alignment of the executive's interests with those of shareholders.
- The Committee believes that share ownership by executives should be strongly encouraged, but not mandated.
- The Committee understands that, depending on personal and other circumstances, an executive may not be able to achieve the desired level of share ownership.
- The Committee believes that executives should understand the importance of share ownership in the stewardship of the Company, and both appropriate time and latitude will be provided to executives to achieve desired share ownership levels, where possible.
- Share ownership levels will be reviewed annually for each executive.

Executives are encouraged, within a five-year period following the later of either the initiation of these guidelines, or their appointment or election, to attain and hold an investment position no less than the multiples of base salary set forth below.

The following are the guideline share ownership levels for the Executive Directors:

- CEO: 2 x base salary
- CFO: 1.5 x base salary

All shares beneficially owned by an executive (excluding unexercised vested Stock Options or SARs) count towards achieving these guidelines.

The Committee reviews share ownership levels for each executive on an annual basis. The Committee will discuss with each Executive Director their plans for share ownership on a regular basis; the CEO will discuss with each of the remaining executives their plans for share ownership on a regular basis.

5. Pension and other benefits

The Company's policy is to ensure that pension benefits are competitive in the markets in which Shire operates.

For Mr Emmens, who was based in the US, Shire contributed 30% of his annual salary to a Supplemental Employee Retirement Plan (SERP) and 401(k) Plan in the US. The SERP is an unfunded defined contribution scheme; the benefits are payable to certain senior US employees as lump sums on leaving the Company's employment or earlier due to death, disability or termination. The amount of benefit is based on the value of notional contributions adjusted for 'earned' investment returns as if they were invested in investments of the employees' choice.

In the UK, Shire operates a defined contribution scheme. The Company contributed 25% of salary towards pension benefits for Mr. Russell during his time as CFO and 30% during his time as CEO. The Company contributed 25% of salary towards pension benefits for Mr. Hetherington for his time as CFO. In addition to pension benefits, the Executive Directors receive certain benefits in kind, principally a car or car allowance, life insurance, private medical insurance and dental cover. These benefits are not pensionable.

Service contracts

The Committee believes that Executive Directors' service contracts should be for a rolling term and, for UK contracts, incorporate notice periods of 12 months. The Committee also believes that the Company should retain the right to make a payment in lieu of notice to a Director. The contracts contain obligations on the Executive Directors in respect of intellectual property, together with post-termination restrictions. The Committee's view is that, in the event of early termination, Executive Directors should be treated fairly but paid no more than is necessary. Moreover, there should be no element of reward for failure.

Mr Emmens was CEO of Shire until June 18, 2008 and then became Non-Executive Chairman. His terms of appointment are set out in a letter dated June 11, 2008. Mr Emmens was entitled to receive his base salary and

annual bonus for the period up to the date on which he became non-executive Chairman but not other payments. As Chairman he is not entitled to bonus or to be granted further awards under Shire share schemes. He continues to participate in the group medical plan.

Mr Russell's contract is dated July 2, 2008. His previous contract was revised to reflect his new role as CEO and incorporated contract provisions reflecting current best practice for Executive Directors' contracts. Mr Hetherington's contract is dated July 2, 2008. Mr Russell's and Mr Hetherington's contracts require them to give Shire 12 months' notice. Shire is required to give Mr Russell and Mr Hetherington 12 months' notice of termination, other than if termination is for cause.

The contracts contain phased payment provisions which would entitle Shire to terminate an Executive Director's employment and make a severance payment not as a lump sum but in monthly instalments over the length of the notice period. These provisions allow the payments to be reduced, or eliminated entirely, by income obtained by the director from a new post.

In the event of termination of employment within 12 months of a change in control, the amount payable to Mr Russell and Mr Hetherington is one year's salary and the cash equivalent of one year's pension, car and other contractual benefits. Any annual bonus payable is at the discretion of the Committee and is capped at the contractual maximum level.

The amount of annual bonus payable upon termination of employment in any other circumstances, other than for cause, is at the discretion of the Committee and is capped at the contractual target level.

Non-Executive Directors and the Chairman

Each Non-Executive Director is paid a fee for serving as a Director and additional fees are paid for membership or chairmanship of the Audit, Risk & Compliance, Remuneration, Nomination and Science & Technology Committees. The Chairman of the Company receives an inclusive fee. Fees are determined by the Executive Directors and the Chairman, with the exception of the Chairman's fee which is determined by the Committee and confirmed by the Board. Fees are benchmarked against Non-Executive Director fees of comparable companies. The fees paid to Non-Executive Directors are not performance-related. Details of fees paid to the Chairman and Non-Executive Directors in 2008 are set out in the table below.

The Non-Executive Directors are not eligible to join the Company's pension scheme. Non-Executive Directors do not participate in any of the Company share schemes or other employee benefit schemes and no options have been granted to Non-Executive Directors in their capacity as Non-Executive Directors of Shire plc.

Non-Executive Directors are appointed ordinarily for a term of two years, subject to shareholder approval. Non-Executive Directors who have served on the Board for nine years or more are appointed for one year terms and, in accordance with the Combined Code on Corporate Governance, are subject to annual re-election by shareholders. Re-appointment of Non-Executive Directors following the expiry of their term of appointment is subject to Board approval. Non-Executive Directors are not entitled to compensation for loss of office.

Details of the unexpired terms of the letters of appointment and notice periods are as follows:

Director	Date of appointment	Date of term expiry	Notice period
Matthew Emmens	06.18.08	06.17.10	3 months
Dr Barry Price	01.25.09	01.24.10	3 months
David Kappler	04.05.08	04.04.10	3 months
Patrick Langlois	11.11.07	11.10.09	3 months
Kate Nealon	07.27.08	07.26.10	3 months
Dr Jeffrey Leiden	01.01.09	12.31.10	3 months
David Mott	10.31.07	10.30.09	3 months
Dr Michael Rosenblatt	04.24.08	04.23.10	3 months

The fee policy structure for Non-Executive Directors ("NED"), effective January 1, 2008 and January 1, 2009 is presented in the table below.

Annual Fees	2008 \$	2009 \$
Board membership		
Chairman of the Board (inclusive of all committees)	546,989	630,428
Deputy Chairman and Senior Independent Non-Executive Director (inclusive of NED fee)	120,523	152,972
Non-Executive Director	97,346	129,794
Committee Membership		
Audit, Compliance & Risk Committee Chair	37,084	37,084
Remuneration Committee Chair	23,178	23,178
Nomination Committee Chair	23,178	23,178
Science & Technology Committee Chair	23,178	23,178
Audit, Compliance & Risk Committee member	18,542	18,542
Remuneration Committee member	13,907	13,907
Nomination Committee member	9,271	9,271
Science & Technology Committee member	13,907	13,907

The fee policy structure was updated for 2009 to reflect a blended US/UK approach to benchmarking, consistent with that applied to the Executive Directors. Base fees for Non-Executive Directors were increased to \$129,794 and the fee for the Chairman of the Board was increased to \$630,428; Committee chair and membership fees remain unchanged. In addition, to recognize the travel required for Directors to attend meetings in Ireland or the US, a \$9,271 travel allowance was instituted for travel exceeding four hours.

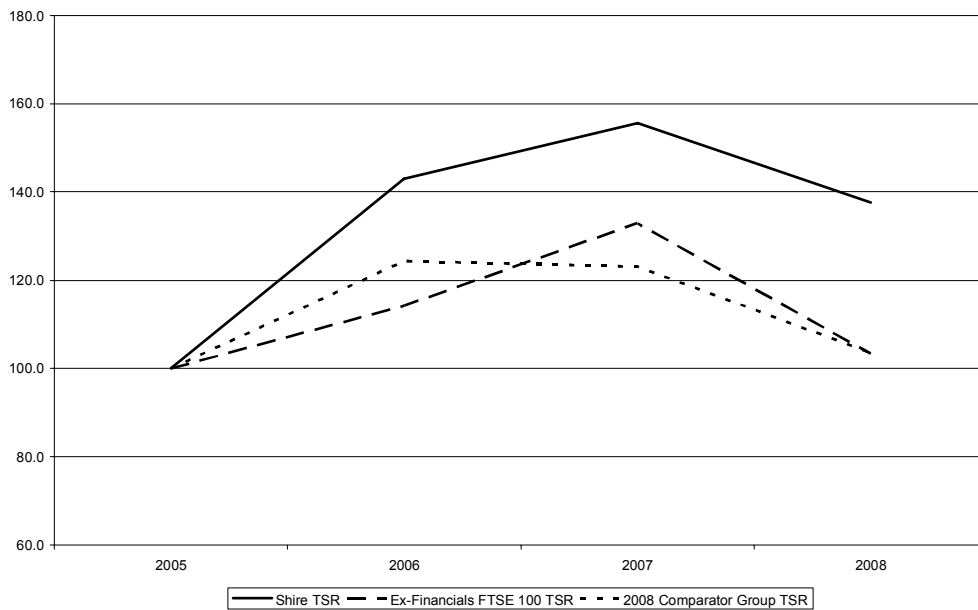
Related party transactions

Details of transactions relating to Dr James Cavanaugh are given in Note 25 in ITEM 15: Exhibits and financial statement schedules.

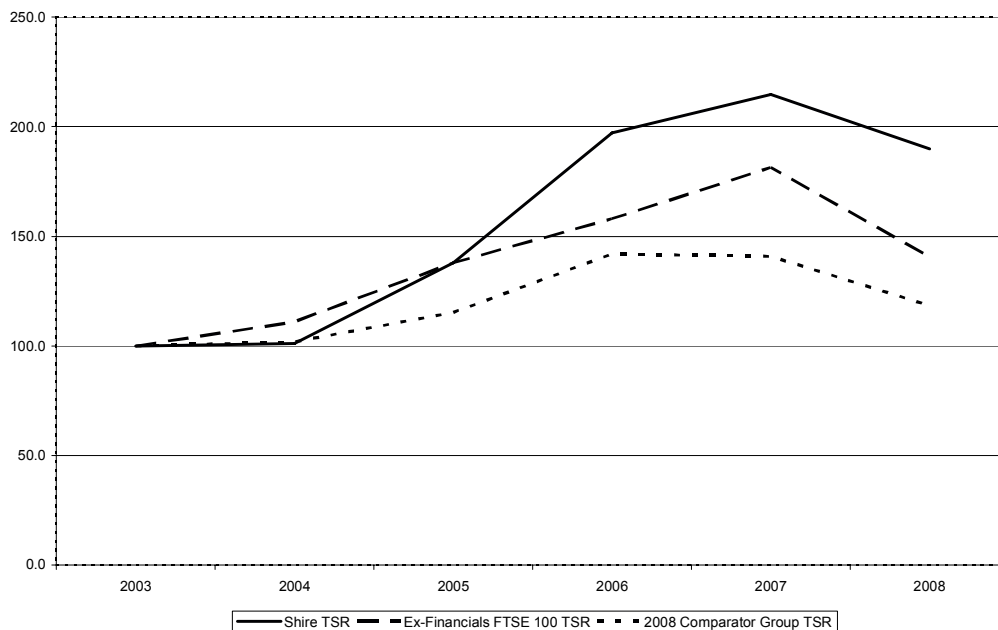
Performance graph

The graphs below set out the TSR for the three and five years ending December 31, 2008. The graphs compare the performance of a hypothetical £100 holding of Shire plc's shares with that of a holding of shares in the FTSE 100 index (excluding financial institutions) and with a holding in a group comprised of the following pharmaceutical companies: Allergan, Altana, Biovail, Cephalon, Forest, King, Kos, Lundbeck, Medicis, Novo Nordisk, Schering AG, Sepracor, Merck Serono, UCB, Valeant and Watson. This comparator group is a blend of US and UK companies with sector, size, complexity and international characteristics similar to those of the Company. The Company is a member of the FTSE 100 Index and consequently, for the purpose of the graphs which are set out below, we have selected the FTSE 100 Index (excluding financial institutions) as the appropriate index. These comparisons will also be used to determine achievement of performance conditions relating to the Portfolio Share Plan.

Three-year historical TSR performance. Change in value of a hypothetical £100 holding over three years.



Five-year historical TSR performance. Change in value of a hypothetical £100 holding over five years.



Other remuneration

The Company believes there are benefits to Executive Directors' participation at the Board level at other companies, including cross-industry and cross-company exposure and the added perspective of outside views. It is therefore the Company's policy to allow Executive Directors to take up Non-Executive positions at other companies and retain associated earnings, as long as such appointments are expressly permitted by the Board of Directors.

Mr Emmens served as a Non-Executive Director of Vertex Pharmaceuticals Inc. and Incyte Corporation during 2008. In this capacity he was paid \$68,298 and \$32,500 in 2008, respectively in 2008, which he retained.

Mr Russell is a Non-Executive Director of The City of London Investment Trust plc (and its associated companies, The City of London European Trust Limited, The City of London Investments Limited and The City of London Finance Company Limited). In this capacity, he was paid £23,000 (\$42,647 equivalent) in 2008, which he retained.

Mr Hetherington was appointed as a Supervisory Board member of Jerini AG in 2008. Mr. Hetherington has assigned all rights to fees due to Shire.

Audited information

Aggregate Directors' remuneration

The total amounts for Directors' remuneration were as follows:

	2008	2007
	\$'000	\$'000
Emoluments	6,609	6,846
Money purchase pension contributions	696	542
Gains on exercise of share options	304	4,442
Gains on maturity of LTIP Awards	2,530	-
	10,139	11,830

Executive Directors' Emoluments

	Salary		Incentive				Cash benefits		Benefits in kind		Total		Pension contributions	
	2008	2007	Cash element		Deferred share element		2008	2007	2008	2007	2008	2007	2008	2007
			2008	2007	2008	2007								
	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000	\$'000
Matthew Emmens ⁽ⁱ⁾⁽ⁱⁱⁱ⁾	625	1,156	583	1,334	330	750	137	421	-	-	1,675	3,661	187	347
Angus Russell ^{(ii)(iv)}	971	781	1,061	620	599	396	29	28	20	8	2,680	1,833	414	195
Graham Hetherington ^{(ii)(iv)}	371	-	257	-	143	-	11	-	2	-	784	-	95	-

⁽ⁱ⁾ Mr Emmens was paid a pro-rated bonus under his contract as CEO, which was based on his 2008 performance whilst CEO and represented his final bonus as CEO prior to him standing down and becoming Chairman on June 18, 2008.

⁽ⁱⁱ⁾ Pound sterling salary and cash benefits translated into US dollars.

⁽ⁱⁱⁱ⁾ Pension contributions were made by the Group to a SERP and 401(k) Plan in the US up to the date Mr. Emmens stepped down as CEO.

^(iv) Pension contributions were made by the Company into defined contribution schemes.

Mr Emmens' cash benefits include holiday pay, car allowance, executive financial planning and tax return preparation. Mr Russell's and Mr Hetherington's cash benefits comprise car allowances. Benefits in kind consist of private medical insurance and tax return preparation.

Details of the exercise of share options are disclosed below.

Non-Executive Directors Emoluments*

	Fees	
	2008 \$'000	2007 \$'000
Dr James Cavanaugh ⁽ⁱ⁾⁽ⁱⁱⁱ⁾	265	530
Matthew Emmens ^{(i)(iv)}	292	-
Dr Barry Price ⁽ⁱⁱ⁾	107	136
Robin Buchanan ^{(ii)(v)}	65	109
David Kappler ⁽ⁱⁱ⁾	167	165
Patrick Langlois ⁽ⁱⁱ⁾	130	129
Dr Jeffrey Leiden ⁽ⁱ⁾	121	104
Kate Nealon ⁽ⁱⁱ⁾	139	125
David Mott ⁽ⁱ⁾	117	16
Dr Michael Rosenblatt ^{(i)(vi)}	67	-
The Hon. James Grant ^{(i)(vii)}	-	38

* Non-Executive Directors' fees are to/from the date of retirement/appointment.

⁽ⁱ⁾ US dollars fees.

⁽ⁱⁱ⁾ Pound sterling fees translated into US dollars.

⁽ⁱⁱⁱ⁾ Dr Cavanaugh retired on June 18, 2008.

^(iv) Mr Emmens was appointed Chairman on June 18, 2008.

^(v) Mr Buchanan stepped down from the Board on July 29, 2008

^(vi) Dr Michael Rosenblatt was appointed a Non-Executive Director on April 24, 2008.

^(vii) The Hon. James Grant stepped down from the Board on May 10, 2007.

Directors' shareholdings

Directors' interests in the share capital of the Company are as follows (all interests are beneficial):

Name of Director	At December 31, 2008: Number of Ordinary shares	At January 1, 2008: Number of Ordinary shares	At December 31, 2008: Number of ADSs	At January 1, 2008: Number of ADSs
Matthew Emmens	39,434	2,212	5,670	5,670
Angus Russell	17,219	17,219	2,000	-
Graham Hetherington	4,000	-	-	-
Dr Barry Price	31,350	31,350	-	-
David Kappler	10,000	10,000	-	-
Patrick Langlois	-	-	-	-
Dr Jeffrey Leiden	-	-	-	-
Kate Nealon	2,251	2,251	-	-
David Mott	-	-	20,000	-
Dr Michael Rosenblatt	-	-	385	-

Since December 31, 2008 Mr Mott acquired an additional 5,000 ADSs increasing his interest to 25,000 ADSs. There were no further changes to the Directors' interests since December 31, 2008 and the date of this report.

Directors' share options

Aggregate emoluments disclosed above do not include any amounts for the value of options to acquire ordinary shares in the Company granted to or held by the Directors.

Directors have been granted options over ordinary shares under the Shire Pharmaceuticals Executive Share Option Scheme (Parts A and B) (Executive Scheme), the Shire 2000 Executive Share Option Scheme (Parts A and B)

(2000 Executive Scheme), the Shire Sharesave Scheme (Sharesave Scheme) and the Shire Employee Stock Purchase Plan (Stock Purchase Plan).

Details of options over ordinary shares exercised during the year are as follows:

Director	Scheme	Number of options	Exercise price £	Market price at exercise date £	Gains on exercise 2008 \$'000
Matthew Emmens	2000 Executive Scheme B	17,279	3.683	9.01	171
		10,432	5.26	9.01	73
		9,511	5.585	9.01	60

Details of the options of Directors who served during the year are as follows:

Director	Scheme	Number of ADSs*				At December 31, 2008	Exercise price \$	Exercise dates	
		At January 1, 2008	Granted	Exercised	Lapsed			Earliest	Latest
Matthew Emmens	Stock Purchase Plan ^(iv)	166	-	-	166	-	62.58	11.01.08	11.01.08

*One ADS is equal to three ordinary shares.

Director	Scheme	Number of ordinary shares				At December 31, 2008	Exercise price £	Exercise dates	
		At January 1, 2008	Granted	Exercised	Lapsed			Earliest	Latest
Matthew Emmens	2000 Executive Scheme B ⁽ⁱⁱⁱ⁾	945,010	-	17,279	-	927,731	3.68	03.18.06	03.17.13
		315,777	-	10,432	-	305,345	5.26	03.25.07	03.24.14
		295,000	-	9,511	-	285,489	5.585	05.11.08	05.10.15
	Stock Purchase Plan ^(iv)	713	-	-	713	-	7.48	11.21.08	11.21.08
		1,556,500	-	37,222	713	1,518,565			
Angus Russell	Executive Scheme A ⁽ⁱ⁾	4,181	-	-	-	4,181	7.175	12.13.02	12.12.09
	2000 Executive Scheme B ⁽ⁱⁱⁱ⁾	69,213	-	-	-	69,213	12.57	06.05.04	06.04.11
		284,024	-	-	-	284,024	3.38	03.04.06	03.03.13
		195,000	-	-	-	195,000	5.585	05.11.08	05.10.15
	Sharesave ⁽ⁱⁱ⁾	2,342	-	-	-	2,342	6.99	12.01.11	05.31.12
		554,760	-	-	-	554,760			

Graham Hetherington	Sharesave ⁽ⁱⁱ⁾	-	1,240	-	-	1,240	7.74	12.01.11	05.31.12
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⁽ⁱ⁾ Options granted under this scheme are subject to performance criteria and cannot be exercised in full, unless Shire's ordinary share price increases at a compound rate of at least 20.5% per annum over a minimum three-year measurement period. If Shire's share price increases at a

compound rate of 14.5% per annum over a minimum three-year measurement period, 60% of the options may be exercised. If these conditions are not met after the initial three years, they are thereafter tested quarterly by reference to share price growth over the extended period. If the share price does not meet these conditions at any time, none of the options granted become exercisable.

(ii) Options granted under the Sharesave Scheme are granted with an exercise price equal to 80% of the mid-market price on the day before invitations are issued to employees. Employees may enter into three or five-year savings contracts.

(iii) Options granted under the 2000 Executive Scheme are exercisable subject to certain performance criteria. In respect of any option granted prior to August 2002, if Shire's ordinary share price increases at a compound rate of at least 20.5% per annum over a minimum three-year measurement period, the option becomes exercisable in full. If it increases by at least 14.5% per annum over the same three-year period, 60% of the options granted become exercisable. If these conditions are not met after the initial three-year measurement period, they will thereafter be tested quarterly by reference to compound annual share price growth over an extended period.

The performance criteria were reviewed in 2002 to ensure the criteria reflected the market in which Shire operates. Given Shire's development, it was considered appropriate that an earnings per share-based measure should be adopted in place of share price growth targets. The performance criteria are based on real growth in the diluted earnings per share reported in the Company's Form 10-K under US GAAP, adjusted to ensure a consistent basis of measurement, as approved by the Remuneration Committee, including the add back of significant one-time items (option EPS). Therefore, the performance criteria were amended so that an option would become exercisable in full if Shire plc's option EPS growth over a three-year period from the date of award exceed the UK Retail Prices Index (RPI) for the following tranches of grants:

Options with a grant value of up to 100% of salary	RPI plus 9% (Directors, RPI plus 15%)
Between 101% and 200% of salary	RPI plus 15%
Between 201% and 300% of salary	RPI plus 21%
Over 301% of salary	RPI plus 27%

The RPI based earnings per share performance criteria applied to options granted under the 2000 Executive Scheme from August 2002. After consultation with certain institutional shareholders, the Company decided that, for options granted under the scheme from 2004 onwards, the performance condition will be retested once only, at five years after the grant, if Shire's option EPS growth falls short of the minimum annual average percentage increase over the three year period from grant. Hence the level of option EPS growth in the next two years needs to be consequentially higher to meet the test.

In December 2006 the Committee exercised its powers to amend the performance conditions for options granted under the 2000 Executive Scheme which had not vested. The RPI based growth rate was replaced with an equivalent fixed growth rate based on historical and forecast inflation.

Under Part B of the scheme, six weeks prior to the expiration date, any options that have not become exercisable at an earlier date, automatically vest without reference to the performance criteria.

(iv) Under the Stock Purchase Plan, options are granted with an exercise price equal to 85% of the fair market value of a share on the enrolment date (the first day of the offering period) or the exercise date (the last day of the offering period), whichever is the lower. Following approval by shareholders at the AGM held on June 20, 2007 the 2007 Shire Employee Stock Purchase Plan was adopted on similar terms to the predecessor plan save that participants agree to save for a period up to 27 months, rather than a fixed 27 months, as set by the Committee. The offering period set for plan grants in 2008 was 12 months.

Directors' share awards

Details of the SARs granted under Part A and PSAs granted under Part B of the Portfolio Share Plan of Directors who served during the year are as follows:

Director	Scheme	Number of ADSs*				At December 31, 2008	Market price at the date of the award \$	Exercise dates	
		At January 1, 2008	Granted	Exercised	Lapsed			Earliest	Latest
Matthew Emmens	PSP part A	126,831	-	-	-	126,831	49.36	08.17.09	08.16.11
	PSP part B	92,671	-	-	-	92,671	49.36	08.17.09	09.16.09
	PSP part A	93,840	-	-	-	93,840	64.10	02.27.10	02.26.12
	PSP part B	70,380	-	-	-	70,380	64.10	02.27.10	03.29.10
	PSP part A	-	35,126	-	-	35,126	58.51	03.28.11	03.27.13
	PSP part B	-	26,345	-	-	26,345	58.51	03.28.11	04.27.11
		383,722	61,471	-	-	445,193			

*One ADS is equal to three ordinary shares.

Director	Scheme	Number of ordinary shares				At December 31, 2008	Market price at the date of the award £	Exercise dates	
		At January 1, 2008	Granted	Exercised	Lapsed			Earliest	Latest
Angus Russell	PSP part A	128,542	-	-	-	128,542	8.65	08.17.09	08.16.11
	PSP part B	96,406	-	-	-	96,406	8.65	08.17.09	09.16.09
	PSP part A	117,495	-	-	-	117,495	10.99	02.27.10	02.26.12
	PSP part B	80,000	-	-	-	80,000	10.99	02.27.10	03.29.10
	PSP part A	-	85,000	-	-	85,000	9.97	02.22.11	02.21.13
	PSP part B	-	60,000	-	-	60,000	9.97	02.22.11	03.24.11
	PSP part A	-	123,547	-	-	123,547	8.13	06.18.11	06.17.13
	PSP part B	-	96,410	-	-	96,410	8.13	06.18.11	07.18.11
		422,443	364,957	-	-	787,400			
Graham Hetherington	PSP part A	-	100,000	-	-	100,000	8.675	08.01.11	07.31.13
	PSP part B	-	75,000	-	-	75,000	8.675	08.01.11	08.31.11
			175,000	-	-	175,000			

Details of the Portfolio Share Plan and vesting criteria are set out in Note 33 to the consolidated financial statements.

The market price of the ordinary shares at December 31, 2008 was £10.12 and the range during the year was £7.20 to £11.80. The market price of the ADSs at December 31, 2008 was \$44.78 and the range during the year was \$32.88 to \$69.35.

Executive Annual Incentive Plan

Under the Executive Annual Incentive Plan, part of the executive's annual incentive is delivered in the form of ordinary shares or ADSs. The deferred ordinary shares/ADSs are released on the third anniversary of the day on which the payment of the corresponding cash award was made.

Details of deferred ordinary shares/ADSs of Directors who served during the year are as follows:

Director	Number of ADSs*			Market price at date of award \$	At December 31, 2008
	At January 1, 2008	Date of award	No of ADSs conditionally awarded during 2008		
Matthew Emmens	11,534	-	-	-	11,534
	-	April 1, 2008	12,881	58.3524	12,881
	-	July 31, 2008	6,471 ⁽ⁱ⁾	50.9298	6,471
	11,534		19,352		30,886

*One ADS is equal to three ordinary shares.

⁽ⁱ⁾ Share-based element of Mr. Emmens's 2008 pro-rated bonus which was based on his 2008 performance whilst Chief Executive Officer of the Company. The value of the ADS award is also disclosed in the Executive Directors' Emoluments table above.

Number of ordinary shares

Director	At January 1, 2008	Date of award	No of ordinary shares conditionally awarded during 2008	Market price at date of award £	At December 31, 2008
Angus Russell	18,140	-	-	-	18,140
	-	April 1, 2008	20,068	9.93	20,068
	18,140		20,068		38,208

Long Term Incentive Plan⁽ⁱ⁾

Details of current and outstanding awards under the Long Term Incentive Plan of Directors who served during the year are as follows:

Director	At January 1, 2008	Date of award	Number of ordinary shares vested during 2008	Number of ordinary shares lapsed during 2008	Value of award at grant date \$'000	At December 31, 2008	Earliest date on which an award can be transferred
Matthew Emmens	105,259	March 25, 2004	(75,408)	(29,851)	1,032	-	-
	97,468	May 11, 2005	-	-	1,025	97,468	05.11.09
	202,727		(75,408)	(29,851)	2,057	97,468	

Angus Russell	65,059	March 25, 2004	(46,634)	(18,425)	638	-	-
	63,217	May 11, 2005	-	-	664	63,217	05.11.09
	128,276		(46,634)	(18,425)	1,302	63,217	

⁽ⁱ⁾ The performance criteria attaching to awards made under the Long Term Incentive Plan are detailed above.

Details of awards which vested during the year are as follows:

Director	Date of Award	Number of ordinary shares vested	Market price at date of award £	Market price at date of release £	Value at date of release \$'000⁽ⁱ⁾
Matthew Emmens	March 25, 2004	75,408	5.26	10.36	1,563
Angus Russell	March 25, 2004	46,634	5.26	10.36	967

⁽ⁱ⁾ The Pound sterling value of the award has been translated into US dollars using the exchange rate of £1:\$ 2.0012, being the exchange rate at the close of business on the date of release.

Approval

This report was approved by the Board of Directors on February 17, 2009 and signed on its behalf by:

Kate Nealon

Chair of the Remuneration Committee

ITEM 12: Security ownership of certain beneficial owners and management and related stockholder matters

Set forth in the following table is the beneficial ownership of ordinary shares on February 20, 2009 for (i) each person (or group of affiliated persons) known to the Company to be the beneficial owner of more than 5% of ordinary shares, (ii) all current directors, (iii) certain of the Company's named executive officers in 2008, where applicable, and (iv) all other current directors and executive officers as a group. Except as indicated by the notes to the following table, the holders listed below have sole voting power and investment power over the shares beneficially held by them. The address of each of Shire plc's directors and executive officers is that of Shire plc's.

Name	Number of ordinary shares beneficially owned on February 20, 2009	Percent of ordinary shares ⁽¹⁾
Beneficial owner		
FMR LLC	30,466,066	5.4%
Management		
Matthew Emmens ⁽²⁾	1,575,009	*
Angus Russell ⁽³⁾	575,637	*
Graham Hetherington	4,000	*
Dr Barry Price	31,350	*
David Kappler	10,000	*
Patrick Langlois	-	-
Jeffrey Leiden	-	-
David Mott	75,000	*
Kate Nealon	2,251	*
Michael Rosenblatt	1,155	*
Mike Cola	250,000	*
Tatjana May	432,693	*
Joseph Rus	24,000	*
All Directors and Executive Officers of the Company (16 persons)	3,256,403	*

* Less than 1%

(1) For the purposes of this table, a person or a group of persons is deemed to have "beneficial ownership" as at a given date of any shares, which that person has the right to acquire within 60 days after that date. For purposes of computing the percentage of outstanding shares held by each person or a group of persons named above on a given date, any shares which that person or persons has the right to acquire within 60 days after that date are deemed to be outstanding.

(2) Includes 1,518,565 ordinary shares issuable upon exercise of options.

(3) Includes 552,418 ordinary shares issuable upon exercise of options.

Equity Compensation Plan Information

Set forth in the following table are the details, for the year to December 31, 2008, in respect of compensation plans (including individual compensation arrangements) under which equity securities of the Company are authorized for issuance.

Plan category	Number of securities to be issued upon exercise of outstanding equity awards	Weighted-average price of outstanding equity awards	Number of securities remaining available for future issuance under equity compensation plans ⁽¹⁾
Equity compensation plans approved by security holders	38,694,742	\$15.33	9,140,247
Equity compensation plans not approved by security holders	-	-	-
Total	38,694,742		9,140,247

(1) This number reflects the maximum number of ordinary shares remaining available for issuance (excluding the number of ordinary shares reflected in column (a)) upon the exercise of options that may be issued under the Company's equity compensation plans that have specific limits. However, the certain of the Company's plans do not provide for a maximum amount of options or SARS that may be issued under those plans. Consequently, it is not possible to calculate the maximum number of ordinary shares that may be required to settle the exercise of any future options or SARS issued under those plans. However, the Company follows the Executive Remuneration - Association of British Insurers ("ABI") Guidelines on Policies and Practices that recommend that newly issued shares when aggregated with awards under all of the company's other equity compensation plans, must not exceed 10% of the issued ordinary share capital in any rolling 10 year period. As a result, the maximum number of ordinary shares that the Company may issue to satisfy the option and SAR exercises under its equity compensation plans in accordance with the ABI guidelines is 4,358,927. Any requirement to settle option or SAR exercises in excess of such limits will be met by the open market purchase of securities by the Shire Employee Share Ownership Trust.

ITEM 13: Certain relationships and related transactions

None.

ITEM 14: Principal accountant fees and services

The Audit, Compliance & Risk Committee reviews the scope and results of the audit and non-audit services, including tax advisory and compliance services, provided by the Company's Independent Registered Public Accountants, Deloitte LLP, the cost effectiveness and the independence and objectivity of the Registered Public Accountants. In recognition of the importance of maintaining the independence of Deloitte LLP, a process for pre-approval has been in place since July 1, 2002 and has continued through to the end of the period covered by this Report.

The following table provides an analysis of the amount paid to the Company's Independent Registered Public Accountants, Deloitte LLP, all fees having been pre-approved by the Audit, Compliance & Risk Committee.

Year to December 31,	2008 \$'000	2007 \$'000
Audit fees ⁽¹⁾	4,512	3,625
Audit-related fees ⁽²⁾	435	1,432
Tax fees ⁽³⁾	544	1,142
All other fees ⁽⁴⁾	140	346
Total fees	5,631	6,545

(1) Audit fees consisted of audit work only the Independent Registered Public Accountant can reasonably be expected to perform, such as statutory audits.

(2) Audit related fees consist of work generally only the Independent Registered Public Accountant can reasonably be expected to perform, such as procedures relating to regulatory filings.

(3) Tax fees consisted principally of assistance with matters related to compliance, planning and advice in various tax jurisdictions.

(4) All other fees relate to assisting the remuneration committee and corporate responsibility.

Policy on Audit, Compliance & Risk Committee pre-approval of audit and permissible non-audit services of Independent Registered Public Accountant

Consistent with SEC policies regarding auditor independence, the Audit, Compliance & Risk Committee has responsibility for appointing, setting compensation and overseeing the work of the Independent Registered Public Accountant. In recognition of this responsibility, the Audit, Compliance & Risk Committee pre-approves all audit and permissible non-audit services provided by the Independent Registered Public Accountant.

Certain services have been pre-approved by the Audit, Compliance & Risk Committee as part of its pre-approval policy, including:

- audit services, such as audit work performed in the preparation of consolidated financial statements, as well as work that generally only the Independent Registered Public Accountant can reasonably be expected to provide, including comfort letters, statutory audits and consultation regarding financial accounting and/or reporting standards;
- audit-related services, such as the audit of employee benefit plans, and special procedures required to meet certain regulatory requirements; and
- tax services, such as tax compliance services and tax advice on employee remuneration strategies.

Where it is necessary to engage the Independent Registered Public Accountant for services not contemplated in the pre-approval policy, the Audit, Compliance & Risk Committee must pre-approve the proposed service before engaging the Independent Registered Public Accountant. For this purpose, the Audit, Compliance & Risk Committee has delegated pre-approval authority to the Chairman of the Audit, Compliance & Risk Committee. The pre-approval policy is reviewed and updated periodically and was last updated on April 24, 2008. The Chairman must report any pre-approval decisions to the Audit, Compliance & Risk Committee at its next scheduled meeting.

PART IV

ITEM 15: Exhibits, financial statement schedules

The following documents are included as part of this Annual Report on Form 10-K

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Consolidated Balance Sheets as at December 31, 2008 and 2007

Consolidated Statements of Operations for each of the three years in the period ended December 31, 2008

Consolidated Statements of Changes in Shareholders' Equity for each of the three years in the period ended December 31, 2008

Consolidated Statements of Comprehensive Income/(Loss) for each of the three years in the period ended December 31, 2008

Consolidated Statements of Cash Flows for each of the three years in the period ended December 31, 2008

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Statement of Changes in Equity for the period to December 31, 2008

Statement of Cash Flows for the period to December 31, 2008

Notes to the Shire Income Access Share Trust Financial Statements

Financial statement schedule

The following schedule is filed as part of this Form 10-K:

Schedule II – Valuation and Qualifying Accounts for each of the three years in the period ended December 31, 2008.

All other schedules are omitted as the information required is inapplicable or the information is presented in the consolidated financial statements or the related notes.

Exhibits

Exhibit number	Description
2.01	Agreement and Plan of Merger by and among Shire Pharmaceuticals Group plc, Transkaryotic Therapies, Inc. and Sparta Acquisition Corporation, dated as of April 21, 2005. ⁽¹⁾
2.02	Agreement of Merger dated as of February 20, 2007 among Shire plc, Shuttle Corporation and New River Pharmaceuticals, Inc. ⁽²⁾
2.03	Business Combination Agreement dated as of July 3, 2008 between Maia Elfte Vermögensverwaltungs GmbH and Jerini AG. ⁽³⁾
3.01	Form of Amended Memorandum and Articles of Association of Shire plc as adopted by special resolution passed on April 10, 2008 and amended by special resolution on September 24, 2008. ⁽⁴⁾
4.01	Form of Assignment and Novation Agreement between Shire Limited, Shire plc, JPMorgan Chase Bank, N.A. dated April 16, 2008 relating to the Deposit Agreement among Shire plc, JPMorgan Chase Bank, N.A. as depositary and all holders from time to time of ADRs issued thereunder dated November 21, 2005. ⁽⁵⁾
4.02	Form of Deposit Agreement among Shire plc, JPMorgan Chase Bank, N.A. as depositary and all

- holders from time to time of ADRs issued thereunder dated November 21, 2005. ⁽⁶⁾
- 4.03 Form of Ordinary Share Certificate of Shire Limited. ⁽⁷⁾
- 4.04 Form of American Depositary Receipt Certificate of Shire Limited. ⁽⁸⁾
- 4.05 Trust Deed for the New Shire Income Access Trust, dated August 29, 2008.
- 10.01 Tender and Support Agreement dated as of February 20, 2007 among Shire plc, Mr. Randal J. Kirk and the other parties named therein. ⁽⁹⁾
- 10.02 Multicurrency Term and Revolving Facilities Agreement as of February 20, 2007 by and among Shire plc, ABN AMRO Bank N.V., Barclays Capital, Citigroup Global Markets Limited, The Royal Bank of Scotland plc, and Barclays Bank plc. ⁽¹⁰⁾
- 10.03 Accession and Amendment Deed dated April 15, 2008 between Shire Limited, Shire plc, certain subsidiaries of Shire plc and Barclays Bank plc as Facility Agent relating to a US \$1,200,000,000 facility agreement dated February 20, 2007 (as amended by a syndication and amendment agreement dated July 19, 2007). ⁽¹¹⁾
- 10.04 Subscription Agreement dated May 2, 2007 relating to the 2.75% Convertible Bonds due 2014 between Shire plc and ABN AMRO Bank N.V. and NM Rothschild & Sons Limited (trading together as ABN AMRO Rothschild, an unincorporated equity capital markets joint venture) and Barclays Bank plc and Citigroup Global Markets Limited and Goldman Sachs International and Morgan Stanley & Co. International plc and others. ⁽¹²⁾
- 10.05 Amending Subscription Agreement dated May 8, 2007 relating to the 2.75% Convertible Bonds due 2014 between Shire plc and ABN AMRO Bank N.V. and NM Rothschild & Sons Limited (trading together as ABN AMRO Rothschild, an unincorporated equity capital markets joint venture) and Barclays Bank plc and Citigroup Global Markets Limited and Goldman Sachs International and Morgan Stanley & Co. International plc and others. ⁽¹³⁾
- 10.06 Trust Deed dated May 9, 2007 relating to the 2.75% Convertible Bonds due 2014 between Shire plc and BNY Corporate Trustee Services Limited. ⁽¹⁴⁾
- 10.07 Supplemental Trust Deed dated April 15, 2008 between Shire Limited, Shire plc and BNY Corporate Trustee Services Limited relating to a trust deed dated May 9, 2007 relating to US \$1,100,000,000 2.75% Convertible Bonds due 2014. ⁽¹⁵⁾
- 10.08 Accession and Amendment Agreement dated April 15, 2008 between Shire Limited, Shire plc, BNY Corporate Trustee Services Limited and The Bank of New York relating to a paying and conversion agency agreement dated May 9, 2007 relating to US \$1,100,000,000 2.75% Convertible Bonds due 2014. ⁽¹⁶⁾
- 10.09* Revised and Restated Master License Agreement dated November 20, 1995 among Shire BioChem Inc (f/k/a BioChem Pharma Inc.), Glaxo Group Limited, Glaxo Wellcome Inc. (formerly Glaxo Canada Inc.), Glaxo Wellcome Inc. (formerly Glaxo Inc.), Tanaud Holdings (Barbados) Limited, Tanaud International B.V. and Tanaud LLC. ⁽¹⁷⁾
- 10.10* Settlement Agreement, dated August 14, 2006 by and between Shire Laboratories Inc. and Barr Laboratories, Inc. ⁽¹⁸⁾
- 10.11* Product Development and License Agreement, dated August 14, 2006 by and between Shire LLC and Duramed Pharmaceuticals, Inc. ⁽¹⁹⁾
- 10.12* Product Acquisition and License Agreement, dated August 14, 2006 by and among Shire LLC, Shire plc and Duramed Pharmaceuticals, Inc. ⁽²⁰⁾
- 10.13 Service Agreement between Shire plc and Mr Angus Russell, dated March 10, 2004. ⁽²¹⁾
- 10.14 Novation Agreement dated November 21, 2005 relating to the Employment Agreement of Angus Russell dated March 10, 2004. ⁽²²⁾
- 10.15 Novation Agreement dated April 11, 2008 relating to the Employment Agreement of Angus Russell dated March 10, 2004, as previously novated on November 21, 2005. ⁽²³⁾
- 10.16 Form of Amended and Restated Employment Agreement between Shire plc and Mr Matthew Emmens, dated March 12, 2004. ⁽²⁴⁾
- 10.17 Amendment Agreement dated November 21, 2005 relating to the Amended and Restated Employment Agreement of Matthew Emmens dated March 12, 2004. ⁽²⁵⁾
- 10.18 Ratification and Guaranty dated November 21, 2005 relating to the Amended and Restated Employment Agreement of Matthew Emmens dated March 12, 2004. ⁽²⁶⁾

- 10.19 Amendment Agreement dated May 20, 2008 relating to the Amended and Restated Employment Agreement of Matthew Emmens dated March 12, 2004, as amended on November 21, 2005.⁽²⁷⁾
- 10.20 Ratification and Guaranty dated May 20, 2008 relating to the Amended and Restated Employment Agreement of Matthew Emmens dated March 12, 2004.⁽²⁸⁾
- 10.21 Form of Indemnity Agreement for Directors of Shire Limited.⁽²⁹⁾
- 10.22 Service Agreement between Shire Limited and Mr Angus Russell, dated July 2, 2008.⁽³⁰⁾
- 10.23 Service Agreement between Shire Limited and Mr Graham Hetherington, dated July 2, 2008.⁽³¹⁾
- 10.24 Form of Settlement Agreement and Mutual Release in re: *Transkaryotic Therapies, Inc.*, by and between Shire Human Genetic Therapies, Inc., Shire plc and the parties set forth therein.⁽³²⁾
- 21 List of Subsidiaries.
- 23.1 Consent of Deloitte LLP.
- 23.2 Consent of Deloitte LLP.
- 31.1 Certification of Angus Russell pursuant to Rule 13a – 14 under The Exchange Act.
- 31.2 Certification of Graham Hetherington pursuant to Rule 13a – 14 under The Exchange Act.
- 32.1 Certification of Angus Russell and Graham Hetherington pursuant to Section 906 of the Sarbanes – Oxley Act of 2002.

* Certain portions of this exhibit have been omitted intentionally, subject to a confidential treatment request. A complete version of this agreement has been filed separately with the Securities and Exchange Commission.

- (1) Incorporated by reference to Exhibit 99.02 to Shire's Form 8-K filed on April 25, 2005.
- (2) Incorporated by reference to Exhibit 2.1 to Shire's Form 8-K filed on February 23, 2007.
- (3) Incorporated by reference to Exhibit 2.1 to Shire's Form 8-K filed on July 10, 2008.
- (4) Incorporated by reference to Exhibit 99.02 to Shire's Form 8-K filed on October 1, 2008.
- (5) Incorporated by reference to Exhibit 4.01 to Shire's Form 8-K filed on May 23, 2008.
- (6) Incorporated by reference to Exhibit 4.02 to Shire's Form 8-K filed on May 23, 2008.
- (7) Incorporated by reference to Exhibit 4.03 to Shire's Form 8-K filed on May 23, 2008.
- (8) Incorporated by reference to Exhibit 4.04 to Shire's Form 8-K filed on May 23, 2008.
- (9) Incorporated by reference to Exhibit 99.1 to Shire's Form 8-K filed on February 23, 2007.
- (10) Incorporated by reference to Exhibit 10.2 to Shire's Form 10-Q filed on May 1, 2007.
- (11) Incorporated by reference to Exhibit 10.01 to Shire's Form 8-K filed on May 23, 2008.
- (12) Incorporated by reference to Exhibit 10.1 to Shire's Form 10-Q filed on August 2, 2007.
- (13) Incorporated by reference to Exhibit 10.2 to Shire's Form 10-Q filed on August 2, 2007.
- (14) Incorporated by reference to Exhibit 10.3 to Shire's Form 10-Q filed on August 2, 2007.
- (15) Incorporated by reference to Exhibit 10.02 to Shire's Form 8-K filed on May 23, 2008.
- (16) Incorporated by reference to Exhibit 10.03 to Shire's Form 8-K filed on May 23, 2008.
- (17) Incorporated by reference to Exhibit 10.09 to Shire's Form 10-K/A filed on May 30, 2008.
- (18) Incorporated by reference to Exhibit 10.1 to Shire's Form 10-Q filed on November 7, 2006.
- (19) Incorporated by reference to Exhibit 10.2 to Shire's Form 10-Q filed on November 7, 2006.
- (20) Incorporated by reference to Exhibit 10.3 to Shire's Form 10-Q filed on November 7, 2006.
- (21) Incorporated by reference to Exhibit 10.11 to Shire's Form 10-K filed on March 12, 2004.
- (22) Incorporated by reference to Exhibit 10.03 to Shire's Form 8-K filed on November 25, 2005.
- (23) Incorporated by reference to Exhibit 10.06 to Shire's Form 8-K filed on May 23, 2008.
- (24) Incorporated by reference to Exhibit 10.13 to Shire's Form 10-K filed on March 12, 2004.
- (25) Incorporated by reference to Exhibit 10.01 to Shire's Form 8-K filed on November 25, 2005.
- (26) Incorporated by reference to Exhibit 10.02 to Shire's Form 8-K filed on November 25, 2005.
- (27) Incorporated by reference to Exhibit 10.04 to Shire's Form 8-K filed on May 23, 2008.
- (28) Incorporated by reference to Exhibit 10.05 to Shire's Form 8-K filed on May 23, 2008.
- (29) Incorporated by reference to Exhibit 10.07 to Shire's Form 8-K filed on May 23, 2008.
- (30) Incorporated by reference to Exhibit 10.22 to Shire's Form 10-Q filed on November 10, 2008.
- (31) Incorporated by reference to Exhibit 10.23 to Shire's Form 10-Q filed on November 10, 2008.
- (32) Incorporated by reference to Exhibit 10.24 to Shire's Form 10-Q filed on November 10, 2008.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Shire plc

We have audited the accompanying consolidated balance sheets of Shire plc and subsidiaries (the "Company") as of December 31, 2008 and 2007, and the related consolidated statements of operations, shareholders' equity, comprehensive income/(loss) and cash flows for each of the three years in the period ended December 31, 2008. Our audits also included the financial statement schedule listed in the Index at Item 15. These consolidated financial statements and financial statement schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements and financial statement schedule based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Shire plc and subsidiaries as of December 31, 2008 and 2007, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2008, in conformity with accounting principles generally accepted in the United States of America. Also, in our opinion, such financial statement schedule, when considered in relation to the consolidated financial statements taken as a whole, present fairly, in all material respects, the information set forth therein.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Company's internal control over financial reporting as of December 31, 2008, based on the criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 27, 2009 expressed an unqualified opinion on the Company's internal control over financial reporting.

DELOITTE LLP

London, United Kingdom
February 27, 2009

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Shire plc

We have audited the internal control over financial reporting of Shire plc and subsidiaries (the "Company") as of December 31, 2008, based on criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting, including those controls applicable to the Income Access Share Trust (the "Trust") based on our audit.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed by, or under the supervision of, the company's principal executive and principal financial officers, or persons performing similar functions, and effected by the company's board of directors, management, and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of the inherent limitations of internal control over financial reporting, including the possibility of collusion or improper management override of controls, material misstatements due to error or fraud may not be prevented or detected on a timely basis. Also, projections of any evaluation of the effectiveness of the internal control over financial reporting to future periods are subject to the risk that the controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting, including those controls applicable to the Trust, as of December 31, 2008, based on the criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated financial statements and financial statement schedule as of and for the year ended December 31, 2008 of the Company and the financial statements as of and for the period from August 29, 2008 to December 31, 2008 of the Trust and our reports dated February 27, 2009 expressed an unqualified opinion on those financial statements and financial statement schedule.

DELOITTE LLP

London, United Kingdom
February 27, 2009

CONSOLIDATED BALANCE SHEETS
(In millions of US dollars, except share data)

	Notes	December 31, 2008 \$'M	December 31, 2007 \$'M
ASSETS			
Current assets:			
Cash and cash equivalents		218.2	762.5
Restricted cash		29.2	39.5
Accounts receivable, net	8	395.0	441.5
Inventories	9	154.5	174.1
Assets held-for-sale	10	16.6	10.6
Deferred tax asset	31	89.5	143.3
Prepaid expenses and other current assets	11	141.4	125.3
Total current assets		1,044.4	1,696.8
Non current assets:			
Investments	12	42.9	110.2
Property, plant and equipment, net	13	534.2	368.6
Goodwill	14	350.8	219.4
Other intangible assets, net	15	1,824.9	1,764.5
Deferred tax asset	31	118.1	143.7
Other non-current assets	16	18.4	26.9
Total assets		3,933.7	4,330.1
LIABILITIES AND SHAREHOLDERS' EQUITY			
Current liabilities:			
Accounts payable and accrued expenses	17	708.6	674.2
Deferred tax liability	31	10.9	11.3
Liability to dissenting shareholders	23	-	480.2
Other current liabilities	18	104.3	96.5
Total current liabilities		823.8	1,262.2
Non-current liabilities:			
Convertible bonds	19	1,100.0	1,100.0
Other long-term debt	20	43.1	32.9
Deferred tax liability	31	377.0	332.4
Other non-current liabilities	21	291.3	375.6
Total liabilities		2,635.2	3,103.1
Commitments and contingencies	23		

CONSOLIDATED BALANCE SHEETS (continued)
(In millions of US dollars, except share data)

	Notes	December 31, 2008 \$'M	December 31, 2007 \$'M
		<hr/>	<hr/>
Minority interest		0.3	-
Shareholders' equity:			
Common stock of 5p par value; 1,000.0 million shares authorized; and 560.2 million shares issued and outstanding (2007: 750.0 million shares authorized; and 556.8 million shares issued and outstanding)	24	55.5	55.2
Exchangeable shares: nil shares issued and outstanding (2007: 0.7 million)		-	33.6
Treasury stock: 20.7 million shares (2007: 14.0 million shares)	24	(397.2)	(280.8)
Additional paid-in capital		2,594.6	2,503.4
Accumulated other comprehensive income		97.0	55.7
Accumulated deficit		(1,051.7)	(1,140.1)
Total shareholders' equity		<hr/> 1,298.2	<hr/> 1,227.0
Total liabilities and shareholders' equity		<hr/> 3,933.7	<hr/> 4,330.1

The accompanying notes are an integral part of these consolidated financial statements.

CONSOLIDATED STATEMENTS OF OPERATIONS
(In millions of US dollars, except share and per share data)

Year to December 31,	Notes	2008 \$'M	2007 \$'M	2006 \$'M
Revenues:				
Product sales		2,754.2	2,170.2	1,535.8
Royalties		245.5	247.2	242.9
Other revenues		22.5	18.9	17.8
Total revenues		3,022.2	2,436.3	1,796.5
Costs and expenses:				
Cost of product sales ⁽¹⁾	2(w)	408.0	320.3	258.7
Research and development	2(w)	526.6	576.4	385.4
Selling, general and administrative ⁽¹⁾	2(w)	1,422.9	1,178.8	926.6
In-process R&D charge	4	263.1	1,866.4	-
Gain on sale of product rights	5	(20.7)	(127.8)	(63.0)
Integration costs	6	10.3	1.3	5.6
Total operating expenses		2,610.2	3,815.4	1,513.3
Operating income/(loss)		412.0	(1,379.1)	283.2
Interest income		25.5	50.6	50.5
Interest expense	28	(139.0)	(70.8)	(26.4)
Other (expense)/income, net	29	(32.9)	1.2	9.5
Total other (expense)/income, net		(146.4)	(19.0)	33.6
Income/(loss) from continuing operations before income taxes, minority interest and equity in earnings of equity method investees				
		265.6	(1,398.1)	316.8
Income taxes	31	(98.0)	(55.5)	(84.9)
Minority interest		3.6	-	-
Equity in earnings of equity method investees, net of taxes	32	2.4	1.8	5.7
Income/(loss) from continuing operations		173.6	(1,451.8)	237.6
(Loss)/gain from discontinued operations (net of income tax expense of \$nil, \$nil and \$nil respectively)	4,7	(17.6)	-	40.6
Net income/(loss)		156.0	(1,451.8)	278.2

(1) Cost of product sales includes amortization of intangible assets relating to favorable manufacturing contracts of \$1.7 million for the year to December 31, 2008 (2007: \$1.2 million; 2006: \$nil) and Selling, general and administrative ("SG&A") costs includes amortization of intangible assets relating to intellectual property rights acquired of \$223.3 million for the year to December 31, 2008 including impairments of intangible assets of \$97.1 million (2007: \$95.0 million including impairments of intangible assets of \$0.4 million; 2006: \$57.4 million including impairments of intangible assets of \$1.1 million).

CONSOLIDATED STATEMENTS OF OPERATIONS (continued)

(In millions of US dollars, except share and per share data)

Year to December 31,	Notes	2008	2007	2006
Earnings per share – basic	26			
Income/(loss) from continuing operations		32.1c	(268.7c)	47.2c
(Loss)/gain from discontinued operations		(3.3c)	-	8.1c
Earnings/(loss) per share – basic		28.8c	(268.7c)	55.3c
Earnings per share – diluted	26			
Income/(loss) from continuing operations		31.8c	(268.7c)	46.6c
(Loss)/gain from discontinued operations		(3.2c)	-	8.0c
Earnings/(loss) per share – diluted		28.6c	(268.7c)	54.6c
Weighted average number of shares (millions):				
Basic		541.6	540.3	503.4
Diluted		545.4	540.3	509.3

The accompanying notes are an integral part of these consolidated financial statements.

CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY

(In millions of US dollars except share data)

	Common stock \$'M	Common stock number shares M's	Exchange- able shares \$'M	Exchange- able shares number shares M's	Treasury stock \$'M	Additional paid-in capital \$'M	Accumulated other compre- hensive income \$'M	Retained earnings \$'M	Total share- holders' equity \$'M
As at December 31, 2005	42.7	495.7	101.2	2.2	(2.8)	1,327.5	71.5	107.2	1,647.3
Effect of Scheme of Arrangement (cancellation) ⁽¹⁾	(42.7)	-	-	-	-	(1,327.5)	-	-	(1,370.2)
Effect of Scheme of Arrangement (issue) ⁽¹⁾	49.1	-	-	-	-	1,321.1	-	-	1,370.2
As at December 31, 2005 (restated)	49.1	495.7	101.2	2.2	(2.8)	1,321.1	71.5	107.2	1,647.3
Net income	-	-	-	-	-	-	-	278.2	278.2
Foreign currency translation	-	-	-	-	-	-	18.1	-	18.1
Exchange of exchangeable shares	0.3	2.7	(41.8)	(0.9)	-	41.5	-	-	-
Options exercised	0.8	8.3	-	-	-	81.1	-	-	81.9
Share-based compensation	-	-	-	-	-	43.0	-	-	43.0
Shares purchased by the Employee Share Ownership Trust ("ESOT")	-	-	-	-	(92.0)	-	-	-	(92.0)
Unrealized holding loss on available-for-sale securities, net of taxes	-	-	-	-	-	-	(2.1)	-	(2.1)
Other than temporary impairment of available-for-sale securities, net of taxes	-	-	-	-	-	-	0.3	-	0.3
Dividends	-	-	-	-	-	-	-	(32.4)	(32.4)
As at December 31, 2006	50.2	506.7	59.4	1.3	(94.8)	1,486.7	87.8	353.0	1,942.3

(1) Net increase to common stock of \$6.4 million as a result of court sanctioned Scheme of Arrangement, see Note 3 for further details.

The accompanying notes are an integral part of these consolidated financial statements.

Dividends per share

During the year to December 31, 2006 the Company paid dividends totaling 6.35 US cents per ordinary share, equivalent to 19.06 US cents per American Depositary Share ("ADS"), and 21.81 Canadian cents per exchangeable share.

CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY (continued)
(In millions of US dollars except share data)

	Common stock \$'M	Common stock Number of shares M's	Exchange- able shares \$'M	Exchange- able Number of shares M's	Treasury stock \$'M	Additional paid-in capital \$'M	Accumulated other compre- hensive income \$'M	Retained Earnings/ (Accumu- lated deficit) \$'M	Total share- holders' equity \$'M
As at December 31, 2006	50.2	506.7	59.4	1.3	(94.8)	1,486.7	87.8	353.0	1,942.3
Net loss	-	-	-	-	-	-	-	(1,451.8)	(1,451.8)
Foreign currency translation	-	-	-	-	-	-	(15.5)	-	(15.5)
Shares issued, net of issue costs	4.3	42.8	-	-	-	873.0	-	-	877.3
Exchange of exchangeable shares	0.1	1.7	(25.8)	(0.6)	-	25.7	-	-	-
Warrants exercised	0.2	1.3	-	-	-	12.8	-	-	13.0
Options exercised	0.4	4.3	-	-	-	30.0	-	-	30.4
Share-based compensation	-	-	-	-	-	75.2	-	-	75.2
Shares purchased by ESOT	-	-	-	-	(186.0)	-	-	-	(186.0)
Unrealized holding loss on available-for-sale securities, net of taxes	-	-	-	-	-	-	(19.5)	-	(19.5)
Realized gain on available-for-sale securities, net of taxes	-	-	-	-	-	-	(0.1)	-	(0.1)
Other than temporary impairment of available-for-sale securities, net of taxes	-	-	-	-	-	-	3.0	-	3.0
Dividends	-	-	-	-	-	-	-	(41.3)	(41.3)
As at December 31, 2007	55.2	556.8	33.6	0.7	(280.8)	2,503.4	55.7	(1,140.1)	1,227.0

The accompanying notes are an integral part of these consolidated financial statements.

Dividends per share

During the year to December 31, 2007 the Company paid dividends totaling 7.39 US cents per ordinary share, equivalent to 22.18 US cents per ADS, and 25.32 Canadian cents per exchangeable share.

CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY (continued)
(In millions of US dollars except share data)

	Common stock \$'M	Common stock Number of shares M's	Exchange- able shares \$'M	Exchange- able shares Number of shares M's	Treasury stock \$'M	Additional paid-in capital \$'M	Accumulated other compre- hensive income \$'M	Retained Earnings/ (Accumu- lated deficit) \$'M	Total share- holders' equity \$'M
As at December 31, 2007	55.2	556.8	33.6	0.7	(280.8)	2,503.4	55.7	(1,140.1)	1,227.0
Net income	-	-	-	-	-	-	-	156.0	156.0
Foreign currency translation	-	-	-	-	-	-	36.6	-	36.6
Exchange of exchangeable shares	0.2	2.3	(33.6)	(0.7)	-	33.4	-	-	-
Costs associated with shares issued through Scheme of Arrangement	-	-	-	-	-	(5.6)	-	-	(5.6)
Options exercised	0.1	1.1	-	-	-	2.0	-	-	2.1
Share-based compensation	-	-	-	-	-	65.2	-	-	65.2
Tax deficit associated with exercise of stock options	-	-	-	-	-	(3.8)	-	-	(3.8)
Shares purchased by the ESOT	-	-	-	-	(146.6)	-	-	-	(146.6)
Shares released by ESOT to satisfy exercise of stock options	-	-	-	-	30.2	-	-	(20.8)	9.4
Unrealized holding loss on available-for-sale securities, net of taxes	-	-	-	-	-	-	(47.9)	-	(47.9)
Realized gain on available-for-sale securities, net of taxes	-	-	-	-	-	-	(5.4)	-	(5.4)
Other than temporary impairment of available-for-sale securities, net of taxes	-	-	-	-	-	-	58.0	-	58.0
Dividends	-	-	-	-	-	-	-	(46.8)	(46.8)
As at December 31, 2008	55.5	560.2	-	-	(397.2)	2,594.6	97.0	(1,051.7)	1,298.2

The accompanying notes are an integral part of these consolidated financial statements.

Dividends per share

During the year to December 31, 2008 the Company paid dividends of 8.62 US cents per ordinary share (equivalent to 25.85 US cents per ADS), totaling \$46.8 million.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME/(LOSS)
(In millions of US dollars)

Year to December 31,	2008 \$'M	2007 \$'M	2006 \$'M
Net income/(loss)	156.0	(1,451.8)	278.2
Other comprehensive income/(loss):			
Foreign currency translation adjustments	36.6	(15.5)	18.1
Unrealized holding loss on available-for-sale securities, net of taxes of \$nil (2007: \$5.2 million; 2006: \$nil)	(47.9)	(19.5)	(2.1)
Other than temporary impairment of available-for-sale securities, net of taxes of \$nil (2007: \$nil; 2006: \$nil)	58.0	3.0	0.3
Realized gain on available-for-sale securities, net of taxes of \$4.0 million (2007: \$nil; 2006: \$nil)	(5.4)	(0.1)	-
Comprehensive income/(loss)	197.3	(1,483.9)	294.5

The components of accumulated other comprehensive income as at December 31, 2008 and 2007 are as follows:

	December 31, 2008 \$'M	December 31, 2007 \$'M
Foreign currency translation adjustments	101.5	64.9
Unrealized holding loss on available-for-sale securities, net of taxes	(4.5)	(9.2)
Accumulated other comprehensive income	97.0	55.7

The accompanying notes are an integral part of these consolidated financial statements.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In millions of US dollars)

Year to December 31,	2008	2007	2006
	\$'M	\$'M	\$'M
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net income/(loss)	156.0	(1,451.8)	278.2
Adjustments to reconcile net income/(loss) to net cash provided by operating activities:			
Loss/(gain) from discontinued operations	17.6	-	(40.6)
Depreciation and amortization	202.9	158.3	102.8
Amortization of deferred financing charges	5.0	11.9	-
Interest on building financing obligation	3.3	0.5	-
Share-based compensation	65.2	75.2	43.0
In-process research and development charge	128.1	1,866.4	-
Impairment of intangible assets	97.1	0.4	1.1
Impairment of available-for-sale securities	58.0	3.0	0.3
Impairment of long-lived assets	2.2	1.8	3.5
Gain on sale of product rights	(20.7)	(127.8)	(63.0)
(Gain)/loss on sale of long-lived assets	(10.1)	0.3	(0.3)
Movement in deferred taxes	74.0	(25.4)	(142.4)
Equity in earnings of equity method investees	(2.4)	(1.8)	(5.7)
Minority interest	(3.6)	-	-
Changes in operating assets and liabilities, net of acquisitions:			
Decrease/(increase) in accounts receivable	9.4	(120.7)	27.6
Increase in sales deduction accrual	84.3	24.1	24.8
Decrease/(increase) in inventory	36.4	(45.9)	7.2
Increase in prepayments and other current assets	(9.6)	(10.3)	(6.2)
Decrease in other assets	3.6	1.2	0.7
(Decrease)/increase in accounts and notes payable and other liabilities	(108.0)	103.5	297.0
Increase/(decrease) in deferred revenue	9.0	5.0	(1.9)
Returns on investments from joint ventures	7.1	6.8	5.8
Cash flows used in discontinued operations	(4.7)	-	-
Net cash provided by operating activities ^(A)	<u>800.1</u>	<u>474.7</u>	<u>531.9</u>

CONSOLIDATED STATEMENTS OF CASH FLOWS (continued)
(In millions of US dollars)

Year to December 31,

	2008 \$'M	2007 \$'M	2006 \$'M
CASH FLOWS FROM INVESTING ACTIVITIES:			
Movement in short-term investments	-	55.8	6.9
Movements in restricted cash	10.3	(9.7)	0.7
Purchase of subsidiary undertaking, net of cash acquired	(499.4)	(2,519.6)	(0.8)
Payment on settlement of TKT appraisal rights litigation	(419.9)	-	-
Purchase of long-term investments	(2.2)	(63.2)	(9.8)
Purchase of property, plant and equipment	(236.0)	(110.4)	(100.3)
Purchase of intangible assets	(25.0)	(59.0)	(58.8)
Proceeds from sale of long-term investments	10.3	0.5	-
Proceeds from sale of property, plant and equipment	1.8	0.8	0.9
Proceeds/deposits received from sale of product rights	5.0	234.4	63.4
Proceeds from loan repaid by ID Biomedical Corporation ("IDB")	-	-	70.6
Returns of equity investments	0.6	2.3	0.3
Net cash used in investing activities ^(B)	(1,154.5)	(2,468.1)	(26.9)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from drawings under bank facilities	190.0	1,300.0	-
Repayment of drawings under bank facilities	(190.0)	(1,300.0)	-
Proceeds from issue of Shire plc 2.75% convertible bonds due 2014	-	1,100.0	-
Redemption of 2% convertible loan notes due 2011	-	-	(0.1)
Redemption of New River 3.5% convertible note due 2013	-	(279.4)	-
Proceeds from exercise of New River purchased call option	-	141.8	-
Payment of debt arrangement and issue costs	-	(32.8)	-
Proceeds from building finance obligation	11.3	-	-
Payment under building finance obligation	(1.8)	-	-
Proceeds from exercise of options	11.4	30.4	81.9
(Costs)/proceeds from issue of common stock, net	(5.6)	877.3	-
Proceeds from exercise of warrants	-	13.0	-
Payments to acquire shares by ESOT	(146.6)	(186.0)	(92.0)
Payment of dividend	(46.8)	(41.3)	(32.4)
Net cash (used in)/provided by financing activities ^(C)	(178.1)	1,623.0	(42.6)
Effect of foreign exchange rate changes on cash and cash equivalents ^(D)	(11.8)	6.0	8.0
Net (decrease)/increase in cash and cash equivalents ^(A+B+C+D)	(544.3)	(364.4)	470.4
Cash and cash equivalents at beginning of year	762.5	1,126.9	656.5
Cash and cash equivalents at end of year	218.2	762.5	1,126.9

CONSOLIDATED STATEMENTS OF CASH FLOWS (continued)
(In millions of US dollars)

**Supplemental information associated with continuing operations:
Year to December 31,**

	2008	2007	2006
	\$'M	\$'M	\$'M
Interest paid	191.3	25.8	1.8
Income taxes paid	117.0	33.5	5.6
Non cash activities:			
Building financing obligation	-	32.3	-
Proceeds from product out licensing:			
Equity in Avexa Limited ("Avexa").	5.0	2.9	-

The accompanying notes are an integral part of these consolidated financial statements.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

(In millions of US dollars, except where indicated)

1. Description of operations

Shire plc (formerly Shire Limited) and its subsidiaries (collectively referred to as either “Shire” or the “Company”) is a leading specialty biopharmaceutical company that focuses on meeting the needs of the specialist physician.

Historically, the Company has grown through acquisition, completing nine major mergers or acquisitions in a fourteen-year period from 1994 to 2008. Divestments of non-core assets over the past four years have streamlined the Company’s operations. The Company will continue to evaluate companies, products and project opportunities that offer a good strategic fit and enhance shareholder value in the future.

Shire focuses its business on attention deficit and hyperactivity disorder (“ADHD”), human genetic therapies (“HGT”), and gastrointestinal (“GI”) diseases as well as opportunities in other therapeutic areas to the extent they arise through acquisitions. Shire’s in-licensing, merger and acquisition efforts are focused on products in specialist markets with strong intellectual property protection and global rights. Shire believes that a carefully selected and balanced portfolio of products with strategically aligned and relatively small-scale sales forces will deliver strong results.

2. Summary of significant accounting policies

(a) Basis of preparation

The accompanying consolidated financial statements include the accounts of Shire plc, all of its subsidiary undertakings and the Income Access Share trust, after elimination of inter-company accounts and transactions. Minority interests in the net assets and earnings or losses of a consolidated subsidiary are reflected in “Minority interest” in the Company’s consolidated balance sheet and statement of operations. Minority interest adjusts the Company’s consolidated results of operations to reflect only the Company’s share of the earnings or losses of the consolidated subsidiary.

(b) Use of estimates in consolidated financial statements

The preparation of consolidated financial statements, in conformity with US generally accepted accounting principles (“GAAP”) and Securities and Exchange Commission (“SEC”) regulations, requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. Estimates and assumptions are primarily made in relation to the valuation of intangible assets, the valuation of equity investments, sales deductions, income taxes and provisions for litigation.

(c) Revenue recognition

The Company recognizes revenue when:

- there is persuasive evidence of an agreement or arrangement;
- delivery of products has occurred or services have been rendered;
- the seller’s price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

Where applicable, all revenues are stated net of value added tax and similar taxes, and trade discounts.

No revenue is recognized for consideration, the value or receipt of which is dependent on future events or future performance.

The Company’s principal revenue streams and their respective accounting treatments are discussed below:

Product sales

Revenue for the sales of products is recognized upon shipment to customers or at the time of delivery to the customer depending on the terms of sale. Provisions for rebates, product returns and discounts to customers are provided for as reductions to revenue in the same period as the related sales are recorded. The Company monitors and tracks the amount of sales deductions based on historical experience to estimate the amount of reduction to revenue.

Royalty income

Royalty income relating to licensed technology is recognized when the licensee sells the underlying product. The Company receives sales information from the licensee on a monthly basis. For any period that the information is not available, the Company estimates sales amounts based on the historical product information.

Licensing and development fees

Licensing and development fees represent revenues derived from product out-licensing agreements and from contract research and development agreements.

Initial license fees received in connection with product out-licensing agreements, even where such fees are non-refundable and not creditable against future royalty payments, are deferred and recognized over the period of the license term, or the period of the associated collaborative assistance if that period is reasonably estimable. In circumstances where initial license fees are not for a defined period, revenues are deferred until the period of associated collaborative assistance is either reasonably estimable or any performance obligations are inconsequential: thereafter revenues are deferred and recognized over the period to the expiration of the relevant patent to which the license relates.

Revenue from contract research and development agreements is recognized as the services are performed.

Milestones

During the term of certain research and development agreements and licensing agreements, the Company receives non-refundable milestones as certain technical and regulatory targets are achieved. Revenues are recognized either on achievement of such milestones or over the relevant performance period if the Company has substantive performance obligations.

The Company also receives non-refundable clinical milestones when certain targets are achieved during the clinical phases of development, such as the submission of clinical data to a regulatory authority. These clinical milestones are either recognized when receivable (i.e. on completion of the relevant phase) or over the relevant performance period if the Company has substantive performance obligations. If milestone payments are creditable against future royalty payments, the milestones are deferred and released over the period in which the royalties are anticipated to be paid.

(d) Sales deductions

(i) Rebates

Rebates primarily consist of statutory rebates to state Medicaid agencies and contractual rebates with health-maintenance organizations. These rebates are based on price differentials between a base price and the selling price. As a result, rebates generally increase as a percentage of the selling price over the life of the product (as prices increase). Provisions for rebates are recorded as reductions to revenue in the same period as the related sales are recorded, with estimates of future utilization derived from historical trends.

(ii) Returns

The Company estimates the proportion of recorded revenue that will result in a return, based on historical trends and when applicable, specific factors affecting certain products at the balance sheet date. The accrual is recorded as a reduction to revenue in the same period as the related sales are recorded.

(iii) Coupons

The Company uses coupons as a form of sales incentive. An accrual is established based on the Company's expectation of the level of coupon redemption, using historical trends. The accrual is recorded as a reduction to revenue in the same period as the related sales are recorded.

(iv) Discounts

The Company offers cash discounts to customers for the early payment of receivables. Those discounts are recorded as reductions to revenue and accounts receivable in the same period that the related sale is recorded.

(v) Wholesaler chargebacks

The Company has contractual agreements whereby it supplies certain products to third parties at predetermined prices. Wholesalers acting as intermediaries in these transactions are reimbursed by the Company if the predetermined prices are less than the prices paid by the wholesaler to the Company. Accruals for wholesaler chargebacks, which are based on historical trends, are recorded as reductions to revenue in the same period as the related sales are recorded.

(e) Cost of product sales

Cost of product sales includes the cost of purchasing finished product for sale, the cost of raw materials and manufacturing for those products that are manufactured by the Company, shipping and handling costs, depreciation and amortization of intangible assets in respect of favorable manufacturing contracts. Royalties that are payable on those products that the Company does not own the rights to are also included in Cost of product sales.

(f) Leased assets

The costs of operating leases are charged to operations on a straight-line basis over the lease term, even if rental payments are not made on such a basis.

Assets acquired under capital leases are included in the balance sheet as property, plant and equipment and are depreciated over the shorter of the period of the lease or their useful lives. The capital elements of future lease payments are recorded as liabilities, while the interest element is charged to operations over the period of the lease to produce a level yield on the balance of the capital lease obligation.

(g) Advertising expense

The Company expenses the cost of advertising as incurred. Advertising costs amounted to \$134.5 million, \$92.3 million, and \$91.6 million for the years to December 31, 2008, 2007 and 2006 respectively and were included within Selling, general and administrative expenses.

(h) Research and development ("R&D") expense

R&D costs are expensed as incurred. Upfront and milestone payments made to third parties for products that have not yet received marketing approval and for which no alternative future use has been identified are also expensed as incurred.

Milestone payments made to third parties subsequent to regulatory approval are capitalized as intangible assets, and amortized over the remaining useful life of the related product.

(i) Valuation and impairment of long-lived assets other than goodwill and investments

The Company evaluates the carrying value of long-lived assets other than goodwill and investments for impairment whenever events or changes in circumstances indicate that the carrying amounts of the assets may not be recoverable. When such a determination is made, management's estimate of undiscounted cash flows to be generated by the use and ultimate disposition of these assets is compared to the carrying value of the assets to determine whether an impairment is indicated. If an impairment loss is indicated, the amount of the impairment recognized in the consolidated financial statements is determined by estimating the fair value of the assets and recording a loss for the amount that the carrying value exceeds the estimated fair value. This fair value is usually determined based on estimated discounted cash flows.

(j) Finance costs of debt

Finance costs of debt are recorded as a deferred cost and amortized to the statement of operations over the period to the earliest redemption date of the debt, using the effective interest rate method. On extinguishment of the related debt, any unamortized deferred financing costs are written off and charged to interest expense in the consolidated statement of operations.

(k) Foreign currency

Monetary assets and liabilities in foreign currencies are translated into the relevant functional currency at the rate of exchange ruling at the balance sheet date. Transactions in foreign currencies are translated into the relevant functional currency at the rate of exchange ruling at the date of the transaction. Transaction gains and losses, other than those related to current and deferred tax assets and liabilities, are recognized in arriving at income/(loss) from continuing operations before income taxes, minority interests, equity in earnings of equity method investees and discontinued operations. Transaction gains and losses arising on foreign currency denominated current and deferred tax assets and liabilities are included within income taxes in the statement of operations.

The results of operations for affiliates, whose functional currency is not the US dollar, are translated into the US dollar at the average rates of exchange during the period, with the balance sheets translated at the rates ruling at the balance sheet date. The cumulative effect of exchange rate movements is included in a separate component of other comprehensive income.

Foreign currency exchange transaction gains and losses included in consolidated net income/(loss) in the years to December 31, 2008, 2007, and 2006, amounted to a \$4.6 million gain, \$4.4 million gain and \$3.2 million gain, respectively.

(l) Income taxes

The Company provides for income taxes in accordance with Statement of Financial Accounting Standards ("SFAS") No.109, "Accounting for Income Taxes" ("SFAS No. 109") and Financial Accounting Standards Board ("FASB") Interpretation No. 48, "Accounting for Uncertainty in Income Taxes - an interpretation of FASB Statement No. 109" ("FIN 48").

Uncertain tax positions are recognized in the consolidated financial statements for positions which are considered more likely than not of being sustained based on the technical merits of the position on audit by the tax authorities. The measurement of the tax benefit recognized in the consolidated financial statements is based upon the largest amount of tax benefit that, in management's judgement, is greater than 50% likely of being realized based on a cumulative probability assessment of the possible outcomes.

Deferred tax assets and liabilities are recognized for differences between the carrying amounts of assets and liabilities in the consolidated financial statements and the tax bases of assets and liabilities that will result in future taxable or deductible amounts. The deferred tax assets and liabilities are measured using the enacted tax laws and rates applicable to the periods in which the differences are expected to affect taxable income.

Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will not be realized.

The Company recognizes interest relating to unrecognized tax benefits and penalties within income taxes.

(m) Earnings per share

Earnings per share is computed in accordance with SFAS No. 128, "Earnings per Share" ("SFAS No. 128"). Basic earnings per share is based upon net income/(loss) available to ordinary shareholders divided by the weighted average number of ordinary shares outstanding during the period. Diluted earnings per share is based upon net income/(loss) available to ordinary shareholders (adjusted for the impact of interest expense on convertible debt on an "if-converted" basis) divided by the weighted average number of ordinary share equivalents outstanding during the period, adjusted for the effect of all dilutive potential ordinary shares that were outstanding during the year. Such potentially dilutive shares are excluded when the effect would be to increase earnings per share or reduce a loss per share.

(n) Share-based compensation

Share-based compensation represents the cost of share-based awards granted to employees. The Company measures share-based compensation cost for awards classified as equity at the grant date, based on the estimated fair value of the award, and recognizes the cost as an expense on a straight-line basis (net of estimated forfeitures) over the employee requisite service period. The Company estimates the fair value of share-based awards without market-based performance conditions using a Black-Scholes valuation model and awards with market-based performance conditions are valued using a binomial valuation model. The following assumptions were used to value share-based awards:

- Risk-free interest rate – For awards granted over ADSs, the US Federal Reserve treasury constant maturities rate with a term consistent with the expected life of the award is used. For awards granted over ordinary shares, the yield on UK government bonds with a term consistent with the expected life of the award is used.
- Expected dividend yield – measured as the average annualised dividend estimated to be paid by the Company over the expected life of the award as a percentage of the share price at the grant date;
- Expected life – the average of the vesting period and the expiration period from the date of issue of the award; and
- Weighted average expected volatility – measured using historical daily price changes of the Company's share price over the respective expected life of the share-based awards at the date of the award.

The forfeiture rate is estimated using historical trends of the number of awards forfeited prior to vesting.

The expense is recorded in Cost of product sales; R&D; and SG&A in the statement of operations based on the employees' respective functions.

The Company records deferred tax assets for awards that result in deductions on the Company's income tax returns, based on the amount of compensation cost recognized and the Company's statutory tax rate in the jurisdiction in

which it will receive a deduction. Differences between the deferred tax assets recognized for financial reporting purposes and the actual tax deduction reported on the Company's income tax return are recorded in additional paid-in capital (if the tax deduction exceeds the deferred tax asset) or in the statement of operations (if the deferred tax asset exceeds the tax deduction and no additional paid-in capital exists from previous awards).

At December 31, 2008 the Company had seven share-based employee compensation plans, which are described more fully in Note 33.

(o) Cash and cash equivalents

Cash and cash equivalents are defined as short-term highly liquid investments with original maturities of ninety days or less.

(p) Financial instruments - derivatives

The Company uses derivative financial instruments to manage its exposure to foreign exchange risk associated with third party and inter-company loan transactions. These instruments consist of swap and forward foreign exchange contracts. The Company has not elected to apply hedge accounting for these instruments and accordingly the movements in the fair values of these instruments are recognized in the statement of operations. The fair values of these instruments are included on the balance sheet in current assets/liabilities and the cash flows relating to these instruments are presented within Net cash provided by operating activities in the consolidated statement of cash flows.

(q) Inventories

Inventories are stated at the lower of cost (including manufacturing overheads, where appropriate) or market. Cost incurred in bringing each product to its present location and condition is based on purchase costs calculated on a first-in, first-out basis, including transportation costs.

Inventories include costs relating to both marketed products and certain products prior to regulatory approval. Inventories are capitalized prior to regulatory approval if the Company considers that it is probable that the FDA or another regulatory body will grant commercial and manufacturing approval for the relevant product, and it is probable that the value of capitalized inventories will be recovered through commercial sale.

Inventories are written down for estimated obsolescence or unmarketable inventory equal to the difference between the cost of inventory and estimated market value based upon assumptions about future demand and market conditions. If actual market conditions are less favorable than those anticipated, inventory adjustments may be required.

(r) Assets held-for-sale

An asset is classified as held-for-sale when, amongst other things, the Company has committed to a plan of disposition, the asset is available for immediate sale, and the plan is not expected to change significantly. Assets held-for-sale are carried at the lower of their carrying amount or fair value less cost to sell.

Assets acquired in a business combination that will be sold rather than held and used are classified as held-for sale at the date of acquisition when it is probable that the Company will dispose of the assets within one year. Newly acquired assets held-for-sale are carried at their fair value less cost to sell at the acquisition date. The Company does not record depreciation or amortization on assets classified as held-for-sale.

(s) Investments

The Company has certain investments in pharmaceutical and biotechnology companies.

Investments are accounted for using the equity method of accounting if the investment gives the Company the ability to exercise significant influence, but not control over, the investee. Significant influence is generally deemed to exist if the Company has an ownership interest in the voting stock of the investee between 20% and 50%, although other factors, such as representation on the investee's Board of Directors and the nature of commercial arrangements, are considered in determining whether the equity method of accounting is appropriate. Under the equity method of accounting, the Company records its investments in equity-method investees in the consolidated balance sheet under Investments and its share of the investees' earnings or losses together with other-than-temporary impairments in value under Equity in earnings of equity method investees in the consolidated statement of operations.

All other equity investments, which consist of investments for which the Company does not have the ability to exercise significant influence, are accounted for under the cost method or at fair value. Investments in private companies are carried at cost, less provisions for other-than-temporary impairment in value. For public companies that have readily determinable fair values, the Company classifies its equity investments as available-for-sale and, accordingly, records these investments at their fair values with unrealized holding gains and losses included in the consolidated statements

of comprehensive income/(loss), net of any related tax effect. Realized gains and losses and declines in value of available-for-sale securities judged to be other-than-temporary are included in Other (expense)/income, net (see Note 29). The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included as interest income.

(t) Property, plant and equipment

Property, plant and equipment is shown at cost, less accumulated depreciation and any impairment losses. The cost of significant assets includes capitalized interest incurred during the construction period. Depreciation is provided on a straight-line basis at rates calculated to write off the cost less estimated residual value of each asset over its estimated useful life as follows:

Buildings	15 to 50 years
Office furniture, fittings and equipment	3 to 10 years
Warehouse, laboratory and manufacturing equipment	3 to 10 years

The cost of land is not depreciated. Assets under the course of construction are not depreciated until the relevant assets are available and ready for their intended use.

Expenditures for maintenance and repairs are charged to the statement of operations as incurred. The costs of major renewals and improvements are capitalized. At the time property, plant and equipment is retired or otherwise disposed of, the cost and accumulated depreciation are eliminated from the asset and accumulated depreciation accounts. The profit or loss on such disposition is reflected in operating income/(loss).

(u) Goodwill and other intangible assets

(i) Goodwill

In a business combination, goodwill represents the excess of the fair value of the consideration given over the fair value of the identifiable assets and liabilities acquired. An excess of the fair value of assets acquired and liabilities assumed over the cost of acquisition is, in accordance with SFAS No. 141, "Accounting for Business Combinations" ("SFAS No. 141") allocated as a pro rata reduction of amounts that would otherwise have been ascribed to identifiable intangible assets and in process R&D ("IPR&D"), (such IPR&D being immediately charged to expense, having no alternative future use).

Goodwill is not amortized to operations, but instead is reviewed for impairment, at least annually or whenever events or changes in circumstances indicate that the carrying value may not be recoverable. Some factors the Company considers important which could trigger an impairment review include the following: (i) significant underperformance of a reporting unit relative to expected historical or projected future operating results; (ii) significant changes in the manner of the Company's use of acquired assets or the strategy for the overall business; and (iii) significant negative industry trends.

In accordance with SFAS No. 142 "Goodwill and Other Intangible Assets" ("SFAS No. 142"), goodwill is reviewed for impairment by comparing the carrying value of each reporting unit's net assets (including allocated goodwill) to the fair value of those net assets. If the reporting unit's carrying amount is greater than its fair value, then a second step is performed whereby the portion of the fair value that relates to the reporting unit's goodwill is compared to the carrying value of that goodwill. The Company recognizes a goodwill impairment charge for the amount by which the carrying value of goodwill exceeds the fair value. The Company has determined that there are no impairment losses in respect of goodwill for any of the reporting periods covered by these consolidated financial statements.

(ii) Other intangible assets

Other intangible assets, which principally comprise intellectual property including trademarks for products with a defined revenue stream, are recorded at cost and amortized over the estimated useful life of the related product, which ranges from 5 to 35 years (weighted average 18 years). Intellectual property with no defined revenue stream, where the related product has not yet completed the necessary approval process and has no alternative future use, is written off to the statement of operations on acquisition.

The following factors are considered in estimating the useful lives of other intangible assets:

- expected use of the asset;
- regulatory, legal or contractual provisions, including the regulatory approval and review process, patent issues and actions by government agencies;

- the effects of obsolescence, changes in demand, competing products and other economic factors, including the stability of the market, known technological advances, development of competing drugs that are more effective clinically or economically; and
- actions of competitors, suppliers, regulatory agencies or others that may eliminate current competitive advantages.

When a number of factors apply to an intangible asset, these factors are considered in combination when determining useful life.

(v) Non-monetary transactions

The Company enters into certain non-monetary transactions that involve either the granting of a license over the Company's patents or the disposal of an asset or group of assets in exchange for a non-monetary asset, usually equity. The Company accounts for these transactions at fair value if the Company is able to determine the fair value within reasonable limits. To the extent that the Company concludes that it is unable to determine the fair value of a transaction, that transaction is accounted for at the recorded amounts of the assets exchanged. Management is required to exercise its judgment in determining whether or not the fair value of the asset received or that given up can be determined.

(w) Reclassifications

For the year to December 31, 2007 depreciation of \$17.2 million was reclassified from SG&A costs to Cost of product sales (\$7.4 million) and R&D (\$9.8 million). For the year to December 31, 2006 depreciation of \$9.5 million was reclassified from SG&A costs to Cost of product sale (\$4.6 million) and R&D costs (\$4.9 million).

(x) New accounting pronouncements

Adopted during the period

SFAS No. 162

In May 2008 the FASB issued SFAS No. 162, "The Hierarchy of Generally Accepted Accounting Principles" ("SFAS No. 162"). SFAS No. 162 identifies the sources of accounting principles and the framework for selecting the principles to be used in the preparation of financial statements under US GAAP. SFAS No. 162 became effective 60 days following the SEC's approval of the Public Company Accounting Oversight Board amendments to AU Section 411, "The Meaning of Present Fairly in Conformity With Generally Accepted Accounting Principles" on September 16, 2008. The adoption of SFAS No. 162 did not have an impact on the Company's consolidated financial statements.

SFAS No. 157

On January 1, 2008 the Company adopted SFAS No. 157, "Fair Value Measurements" ("SFAS No. 157") for financial assets and liabilities, which provides a single definition of fair value, establishes a framework for the measurement of fair value and expands disclosure about the use of fair value to measure assets and liabilities. The adoption of SFAS No. 157 for financial assets and liabilities did not have a material impact on the Company's consolidated financial statements as at January 1, 2008.

SFAS No. 159

On January 1, 2008 the Company adopted SFAS No. 159, "The Fair Value Option for Financial Assets and Financial Liabilities - Including an Amendment of FASB Statement No. 115" ("SFAS No. 159"). This standard permits an entity to choose to measure many financial instruments and certain other items at fair value. The unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings at each subsequent reporting date. The fair value option: (a) may be applied instrument by instrument, with a few exceptions, such as investments otherwise accounted for by the equity method; (b) is irrevocable (unless a new election date occurs); and (c) is applied only to entire instruments and not to portions of instruments. The Company did not elect to fair value any items on adoption, therefore the adoption of SFAS No. 159 did not have an impact on the Company's consolidated financial statements.

EITF 07-3

In June 2007 the Emerging Issues Task Force ("EITF") reached a consensus regarding EITF 07-3, "Accounting for Non-refundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities" ("EITF 07-3"). The scope of this Issue is limited to non-refundable advance payments for goods and services to be used or rendered in future research and development activities. The EITF concluded that non-refundable advance payments for future research and development activities should be deferred and capitalized on

the balance sheet. Such amounts should be recognized as an expense as the related goods are delivered or the related services are performed. Entities should continue to evaluate whether they expect the goods to be delivered or services to be rendered. If an entity does not expect the goods to be delivered or services to be rendered, the capitalized advance payment should be charged to expense. On January 1, 2008 the Company adopted EITF 07-3. The adoption of EITF 07-3 had no impact on the Company's consolidated financial statements as at January 1, 2008.

To be adopted in future periods

EITF 07-5

In June 2008 the FASB issued EITF 07-5 "Determining whether an Instrument (or Embedded Feature) is indexed to an Entity's Own Stock" ("EITF No. 07-5"). EITF 07-5 is effective for consolidated financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years. Early application is not permitted. Paragraph 11(a) of SFAS No. 133 "Accounting for Derivatives and Hedging Activities" ("SFAS 133") specifies that a contract that would otherwise meet the definition of a derivative but is both (a) indexed to the Company's own stock and (b) classified in stockholders' equity in the statement of financial position would not be considered a derivative financial instrument. EITF 07-5 provides a new two-step model to be applied in determining whether a financial instrument or an embedded feature is indexed to an issuer's own stock and thus able to qualify for the SFAS No. 133 paragraph 11(a) scope exception. The Company does not expect the adoption of EITF 07-5 to have an impact on the Company's consolidated financial statements.

FASB Staff Position ("FSP") No. APB 14-1

In May 2008 the FASB issued FSP No. APB 14-1, "Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement)" ("FSP No. APB 14-1"). This FSP clarifies that convertible debt instruments that may be settled in cash upon conversion (including partial cash settlement) do not fall within the scope of paragraph 12 of Accounting Principles Board (APB) Opinion No. 14, "Accounting for Convertible Debt and Debt Issued with Stock Purchase Warrants" ("APB 14"). It requires issuers of such instruments to separately account for the liability and equity components of those instruments by allocating the proceeds from issuance of the instrument between the liability component and the embedded conversion option (i.e., the equity component). FSP No. APB 14-1 is effective for fiscal years beginning after December 15, 2008 and for interim periods within those fiscal years. It is required to be applied retrospectively to convertible debt instruments that are within the scope of the guidance and were outstanding during any period presented in the financial statements. A cumulative effect adjustment must be recognized as of the beginning of the first period presented. Early adoption of the guidance is not permitted. The Company does not expect the adoption of FSP No. APB 14-1 to have an impact on the Company's consolidated financial statements.

FSP No. FAS 142-3

In April 2008 the FASB issued FSP No. FAS 142-3, "Determination of the Useful Life of Intangible Assets" ("FSP No. FAS 142-3"). This FSP amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of a recognized intangible asset under FASB Statement No. 142, "Goodwill and Other Intangible Assets" ("SFAS No. 142"). The intent of FSP No. FAS 142-3 is to improve the consistency between the useful life of an intangible asset determined under SFAS No. 142 and the period of expected cash flows used to measure the fair value of the asset under FASB Statement No. 141, "Business Combinations", ("SFAS No. 141"). FSP No. FAS 142-3 is effective for financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years. Early adoption is prohibited. The Company is currently evaluating the impact of the adoption of FSP No. FAS 142-3.

SFAS No. 161

In March 2008 the FASB issued SFAS No. 161, "Disclosures about Derivative Instruments and Hedging Activities – an amendment of FASB No. 133" ("SFAS No. 161"). SFAS No. 161 requires enhanced disclosures about an entity's derivative and hedging activities and thereby improves the transparency of financial reporting. SFAS No. 161 is effective for financial statements issued for fiscal years and interim periods beginning after November 15, 2008 with early application encouraged. This Statement encourages, but does not require, comparative disclosures for earlier periods at initial adoption. The Company is currently evaluating the impact of the adoption of SFAS No. 161.

FSP No. FAS 157-2

In February 2008 the FASB issued FSP No. FAS 157-2, "Effective Date of FASB Statement No. 157" ("FSP No. FAS 157-2"). This FSP delays the effective date of SFAS No. 157 for non-financial assets and non-financial liabilities, except for items that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually). SFAS No. 157 will therefore be applicable to non-financial assets and liabilities for the Company's fiscal

year commencing January 1, 2009. The Company does not expect the adoption of SFAS 157 to have an impact on the Company's consolidated financial statements.

EITF 07-1

In December 2007 the EITF reached a consensus regarding EITF 07-1, "Accounting for Collaborative Arrangements" ("EITF 07-1"). The objective of this EITF 07-1 is to define collaborative arrangements and to establish reporting requirements for transactions between participants in a collaborative arrangement and between participants in the arrangement and third parties. EITF 07-1 is effective for financial statements issued for fiscal years beginning after December 15, 2008 and interim periods within those fiscal years. EITF 07-1 shall be applied retrospectively to all prior periods presented for all collaborative arrangements existing as of the effective date. The Company is currently evaluating the impact of the adoption of EITF 07-1.

SFAS No. 160

In December 2007 the FASB issued SFAS No. 160, "Non-controlling Interests in Consolidated Financial Statements - An Amendment of ARB No. 51" ("SFAS No. 160"). SFAS No. 160 establishes new accounting and reporting standards for the non-controlling interest in a subsidiary and for the deconsolidation of a subsidiary. Specifically, this statement requires the recognition of a non-controlling interest (minority interest) as equity in the consolidated financial statements, separate from the parent's equity. The amount of net income attributable to the non-controlling interest will be included in consolidated net income on the face of the income statement. SFAS No. 160 also includes expanded disclosure requirements regarding the interests of the parent and its non-controlling interest. SFAS No. 160 is effective for fiscal years, and interim periods beginning after December 15, 2008. The Company is currently evaluating the impact of the adoption of SFAS No. 160.

SFAS No. 141(R)

In December 2007 the FASB issued SFAS No. 141 (Revised 2007), "Business Combinations" ("SFAS No. 141(R)"). SFAS No. 141(R) will significantly change the accounting for business combinations. Under SFAS No. 141(R), an acquiring entity will be required to recognize all the assets acquired and liabilities assumed in a transaction at the acquisition-date fair value with limited exceptions. It also amends the accounting treatment for certain specific items including acquisition costs and non-controlling minority interests and includes a substantial number of new disclosure requirements. SFAS No. 141(R) applies prospectively to business combinations for which the acquisition date is on or after December 15, 2008. The Company is currently evaluating the impact of the adoption of SFAS No. 141(R).

(y) Statutory accounts

The consolidated financial statements as at December 31, 2008 and 2007, and for each of the three years in the period to December 31, 2008, do not comprise statutory accounts within the meaning of Section 240 of the UK Companies Act 1985 or Article 104 of the Companies (Jersey) Law 1991.

Statutory accounts prepared in accordance with International Financial Reporting Standards, as adopted for use in the EU for the years ended 31 December 2007 and 2006 have been delivered to the Registrar of Companies for England and Wales. The auditors' reports on those accounts were unqualified.

Statutory accounts of Shire, consisting of the solus accounts of Shire plc, for the period to December 31, 2008 prepared under UK GAAP and in compliance with Jersey law will be delivered to the Registrar of Companies for Jersey in 2009. The Company further expects to file the consolidated accounts of the Company, prepared in accordance with US GAAP, in fulfillment of the Company's UKLA annual reporting requirements with the UKLA in 2009.

3. Change in reporting entity

Shire Limited (now known as Shire plc) was incorporated under the laws of Jersey (Channel Islands) on January 28, 2008 and is a public company limited by shares and tax resident in the Republic of Ireland. On May 23, 2008 Shire Limited became the holding company of Shire plc (the former holding company of the Shire Group) ("Old Shire"), a public limited company incorporated in England and Wales, pursuant to a scheme of arrangement under Sections 895 to 899 of the UK Companies Act 2006 that was approved by the High Court of Justice in England and Wales and the shareholders of Old Shire (the "Scheme of Arrangement"). Prior to May 23, 2008 Shire Limited had not commenced trading or made any profits or trading losses. On October 1, 2008 Shire Limited (herein referred as Shire plc) changed its name to Shire plc following the approval of the change of name by shareholders at the Company's Annual General Meeting.

Pursuant to the Scheme of Arrangement, ordinary shares, each having a nominal value of £0.05, of Old Shire (“Shire Ordinary Shares”) were exchanged for ordinary shares, each having a nominal value of £0.05, of Shire plc (“Shire plc Ordinary Shares”), on a one-for-one basis. As a result of the Scheme of Arrangement, Old Shire became a wholly-owned subsidiary of Shire plc. The Shire plc Ordinary Shares carry substantially the same rights as did the Shire Ordinary Shares. The Scheme of Arrangement did not involve any payment for the Shire plc Ordinary Shares.

Shire plc immediately after the effectiveness of the Scheme of Arrangement had the same Board of Directors, management and corporate governance arrangements as Old Shire had immediately prior thereto. The consolidated assets and liabilities of Shire plc immediately after the effective time of the Scheme of Arrangement were substantially the same as the consolidated assets and liabilities of Old Shire immediately prior thereto.

The Shire Ordinary Shares underlying the Shire American Depositary Shares (the “Shire ADSs”), each representing three Shire Ordinary Shares, participated in the Scheme of Arrangement like all other Shire Ordinary Shares. Upon the Scheme of Arrangement becoming effective, the Shire ADSs remained outstanding but became Shire plc ADSs, each representing three Shire plc Ordinary Shares. The Scheme of Arrangement did not involve any payment for the Shire plc ADSs.

In accordance with SFAS No. 141, the corporate restructuring has been accounted for as a reorganization of entities under common control. Accordingly, the historical consolidated financial statements prior to the reorganization are labeled as those of Shire plc, but continue to represent the operations of Old Shire.

Earnings per share were unaffected by the reorganization.

All Old Shire stock options granted to directors and employees under stock option plans that were in existence immediately prior to the Scheme of Arrangement were exchangeable for stock options in Shire plc on a one-for-one basis with no change in any terms or conditions, other than the acceleration of the vesting date of certain awards granted under the Shire plc 2000 Executive Share Option Scheme (“2000 Executive Scheme”) to the date of the Scheme of Arrangement, May 23, 2008. The number of stock options for which this exchange did not take place was not material.

For presented periods prior to the 2008 corporate restructuring, the equity of Shire plc represents the historical equity of Old Shire, restated to reflect the change in the nominal value of common stock as expressed in US dollars resulting from the corporate restructuring. The \$6.4 million increase in the value of common stock at January 1, 2006 (being the earliest period presented) to \$49.1 million on restatement is due to differences between the historic exchange rates used to convert Shire’s Sterling denominated nominal share capital into US dollars, and the exchange rate at the time of the corporate restructuring. The offset is recorded in additional paid in capital.

4. Business combinations

Jerini AG acquisition

On July 3, 2008 the Company announced that it was launching a voluntary public takeover offer for all outstanding shares in Jerini AG (“Jerini”), a German corporation, at a price of EUR 6.25 per share. During the second half of 2008 the Company, through its indirect wholly owned subsidiary, Shire Deutschland Investments GmbH, acquired a 98.6% voting interest in Jerini. The acquisition added Jerini’s hereditary angiodema (“HAE”) product FIRAZYR (icatibant) to Shire’s portfolio.

By August 6, 2008 the Company had acquired 80.1% of the voting interests in Jerini for a cash consideration of \$456.3 million, by (i) subscribing for new Jerini shares; (ii) acquiring voting interests through the completion of sale and purchase agreements entered into with institutional shareholders and certain members of Jerini’s Management and Supervisory Boards; and (iii) acquiring voting interests through market purchases.

Between acquiring this controlling voting interest in early August 2008 and December 31, 2008, the Company acquired additional voting interests totaling 18.5% of Jerini’s issued share capital, for a cash consideration of \$100.2 million obtained by shares tendered during the Offer process, and on and off market purchases. These additional voting interests have been accounted for as step-acquisitions using the purchase method of accounting. By December 31, 2008 Shire had acquired a 98.6% voting interest in Jerini for a total consideration of \$556.5 million, represented by Jerini shares, (\$539.8 million), the cash cost of cancelling Jerini stock options (\$9.4 million) and direct costs of acquisition (\$7.3 million).

The acquisition of Jerini has been accounted for as a purchase business combination in accordance with SFAS No. 141. Under the purchase method of accounting, the assets acquired and the liabilities assumed from Jerini are recorded at the date of acquisition at their fair value. Consolidated financial statements and reported results of operations of Shire issued after the acquisition of this majority holding will reflect these values, with the results of Jerini

included from August 1, 2008, for convenience purposes, in the consolidated statement of operations. The purchase price has been allocated on a preliminary basis to the fair value of assets acquired and liabilities assumed. The final fair values of assets acquired and liabilities assumed will be determined as soon as possible and, in any event, no later than one year from the acquisition date if such fair values can be measured in this period. To the extent that estimates need to be adjusted, Shire will do so in future periods in accordance with SFAS No. 141.

The following table presents the Company's preliminary allocation of the purchase price to the assets acquired and liabilities assumed at their fair values based on the Company's 80.1% voting interest acquired by August 6, 2008:

	Fair value \$'M
ASSETS	
Current assets:	
Cash and cash equivalents	56.7
Restricted cash	0.4
Inventories, net	1.9
Assets held-for-sale	24.4
Other current assets	4.9
Total current assets	88.3
Property, plant and equipment	3.6
Goodwill	121.0
Other intangible assets	
- currently marketed product	257.6
- in-process R&D	104.1
Deferred tax asset	0.5
Total assets	575.1
LIABILITIES	
Current liabilities:	
Deferred tax liability	31.3
Other long-term liabilities	76.3
	0.8
Total liabilities	108.4
Estimated fair value of identifiable assets acquired and liabilities assumed	466.7
Minority interests	(10.4)
Cost of 80.1% voting interest acquired	456.3

In respect of the step acquisitions made subsequent to the acquisition of the 80.1% majority voting interest the Company has recognized additional goodwill of \$27.0 million, intangible assets in respect of the currently marketed product of \$58.1 million and IPR&D of \$24.0 million.

(a) Other intangible assets, currently marketed product

Other intangible assets includes \$315.7 million (being \$257.6 million acquired as of August 6, 2008 and \$58.1 million in the subsequent step acquisitions) relating to intellectual property rights in respect of Jerini's currently marketed product, FIRAZYR, which received marketing authorization from the European Commission in July 2008 for the treatment of acute HAE in the EU. These intellectual property rights include the right to develop, use, market, sell and/or offer for sale the technical processes, intellectual property and institutional understanding (including the way in which FIRAZYR reacts in body, an understanding of the mechanisms of action which allow FIRAZYR to work and the knowledge related to the associated clinical and marketing studies performed to obtain approval of FIRAZYR). The fair value of FIRAZYR in the EU has been determined using an income approach applying the multi-period excess earnings method, based on the present value of incremental after tax cash flows attributable to the asset after the

deduction of contributory asset charges for the assets employed (including working capital, the assembled workforce and other fixed assets).

This intangible asset has an estimated useful life of 17 years, will be amortized on a straight line basis, and has been allocated to the HGT reporting segment.

(b) Other intangible assets, IPR&D

IPR&D is defined by FASB Interpretation No. 4, "Applicability of FASB Statement No. 2 to Business Combinations Accounted for by the Purchase Method" ("FIN 4"), as being a development project that has been initiated and has achieved material progress but (i) has not yet reached technological feasibility or has not yet received the appropriate regulatory approval, (ii) has no alternative future use, and (iii) the fair value is estimable with reasonable certainty. A project-by-project valuation using the guidance in SFAS No. 141 and the American Institute of Certified Public Accountants Practice Aid "Assets Acquired in a Business Combination to Be Used In Research and Development Activities: A Focus on Software, Electronic Devices and Pharmaceutical Industries" (the "AICPA Practice Aid") has been performed to determine the fair value of research and development projects of Jerini which were in-process, but not yet completed as of the acquisition date.

The IPR&D assets of \$128.1 million (being \$104.1 million acquired as of August 6, 2008 and \$24.0 million in the subsequent step acquisitions) relate to FIRAZYR for the treatment of acute HAE in the US (\$64.1 million), and the rest of the world excluding the US and EU ("RoW"), (\$64.0 million). These IPR&D assets have not yet received approval from the relevant regulatory authorities at the acquisition date. In the US FIRAZYR received a not approvable letter from the US Food and Drug Administration in April 2008. The Company considers that these IPR&D assets have no alternative future use outside of their current development projects and the fair value of these IPR&D assets has therefore been charged to the consolidated statement of operations as of the acquisition date in accordance with FIN 4.

The fair value of the FIRAZYR IPR&D assets was determined using the income approach applying the multi-period excess earnings method. The fair value of the IPR&D assets has been based on the incremental cash flows expected to be generated by the development projects after the deduction of contributory asset charges in respect of other assets employed in these research projects (including working capital, the assembled workforce and other fixed assets). These estimated future cash flows were then probability adjusted to take into account the stage of completion and the remaining risks and uncertainties surrounding the future development and commercialization of FIRAZYR. These estimated probability adjusted, after tax cash flows were then discounted at 17-18% to determine a present, or fair, value.

The major risks and uncertainties associated with the timely completion of the acquired IPR&D projects consist of the ability to confirm the efficacy of the technology based on data from the clinical trials, and obtaining the relevant regulatory approvals. The valuations have been based on information at the time of the acquisition and expectations and assumptions that (i) have been deemed reasonable by the Company's management, and (ii) are based on information, expectations and assumptions that would be available to and be made by a market participant. However, no assurance can be given that the underlying assumptions or events associated with such assets will occur as projected. For these reasons, among others, the actual cash flows may vary from forecast future cash flows.

(c) Assets held-for-sale

On acquisition of Jerini the Company and Jerini commenced a strategic review of the acquired assets to identify which of the assets were non strategic to the newly combined business. In October 2008 Jerini announced that its Supervisory and Management Boards had concluded that it was in the best interests of Jerini to divest Jerini Ophthalmic, Inc. ("JOI"), Jerini Peptide Technologies GmbH ("JPT") and Jerini's pre clinical projects. Consistent with SFAS No. 144, *Accounting for the Impairment or Disposal of Long Lived Assets* ("SFAS No. 144") the Company has presented the fair value less costs to sell of those businesses that met the SFAS No. 144 criteria, being JOI and JPT, as assets held-for-sale at the acquisition date. These held-for-sale assets are recorded at their aggregate fair value less costs to sell of \$27.8 million (for the Company's 98.6% voting interest) within the purchase price allocation, the carrying value being primarily represented by the fair value of IPR&D. These held-for-sale assets are reported in "All Other" in the Company's segmental analysis, see Note 27.

In accordance with SFAS No. 144 the Company has presented JOI and JPT as discontinued operations, recording a loss of \$17.6 million from these businesses in the year to December 31, 2008, (2007: \$ nil; 2006: \$nil). Revenues and the pre-tax loss from discontinued operations for the year to December 31, 2008 totaled \$3.6 million and \$17.6 million respectively. The loss from discontinued operations in the year to December 31, 2008 also includes a charge of \$12.9 million arising on the re-measurement of assets held for sale to their fair value less costs to sell at December 31, 2008.

(d) Goodwill

Goodwill of \$148.0 million resulting from the acquisition of 98.6% of the voting interests in Jerini has been wholly allocated to the HGT reporting segment and is not deductible for tax purposes.

METAZYM acquisition

On June 4, 2008 Shire completed the acquisition of the global rights to METAZYM, a clinical candidate arylsulfatase-A, from Zymenex for \$135.0 million in cash. Upon completion Shire recognized an IPR&D charge of \$135.0 million in respect of the acquired development project.

New River acquisition

On April 19, 2007 Shire completed its acquisition of New River by way of a short-form merger, in an all-cash transaction. The acquisition was effected by merging Shuttle Corporation, an indirect wholly owned subsidiary of Shire, with and into New River, with New River continuing as the surviving corporation. As consideration, Shire paid to New River's shareholders \$64 in cash for each share of New River common stock outstanding at the time of the acquisition.

The acquisition of New River allowed Shire to capture the full economic value of VYVANSE, and gain control of the future development and commercialization of this product.

VYVANSE for ADHD in pediatric populations was approved by the FDA on February 23, 2007 and the Company received notification from the Drug Enforcement Agency ("DEA") of the final Schedule II classification for VYVANSE on May 3, 2007.

The acquisition of New River was accounted for using the purchase method in accordance with SFAS No. 141. Under the purchase method of accounting, the assets and liabilities of New River were recorded at their fair values at the acquisition date. The consolidated financial statements and reported results of operations of Shire issued after the completion of the acquisition reflect these fair values, with the results of New River being included within the consolidated statement of operations from April 19, 2007.

Total consideration, including amounts payable in respect of stock options, share appreciation rights ("SARs"), warrants over New River's common stock and costs directly attributable to the business combination was approximately \$2.6 billion at the price of \$64 per share of New River's common stock, as analyzed below:

	\$'M
Cash consideration for 37.1 million outstanding shares of New River common stock at \$64 per share (net of 1.5 million of common stock repurchased through a prepaid forward purchase contract ⁽¹⁾)	2,276.0
Cash cost of settling New River's stock options and SARs	124.5
Cash cost for settling sold warrants over 4.0 million shares of New River's common stock	133.0
Direct acquisition costs	61.0
	<hr/> 2,594.5 <hr/>

(1) New River entered into this prepaid forward purchase contract with Merrill Lynch in July 2006.

Accounting for the Effective Settlement of the New River Collaboration Agreement

Prior to the acquisition of New River, on January 31, 2005 Shire entered into a collaboration agreement with New River which governed the development, manufacture and commercialization of VYVANSE for the treatment of ADHD in the US and RoW territories. In March 2005, this collaboration agreement was split into two separate agreements, the US Collaboration Agreement and the RoW Territory Licence Agreement (together the "New River Collaboration Agreements").

Under the terms of the New River Collaboration Agreements, the parties were required to collaborate on the development, manufacturing, marketing and sales of VYVANSE in the US. Profits from the collaboration arising in the

US were to be divided according to a predetermined formula, based on the scheduling of VYVANSE by the DEA. Post-approval milestones were due under the New River Collaboration Agreements if the product received favorable scheduling (schedule III, IV or V or unscheduled) and on the achievement of certain sales milestones.

Through the New River Collaboration Agreements Shire also acquired the license in the RoW territory to develop and commercialize VYVANSE, in consideration of a low double-digit royalty.

Shire paid an initial sum of \$50 million to New River in January 2005 on signing the original collaboration agreement and a further \$50 million was paid by Shire to New River following acceptance of the filing of a New Drug Application ("NDA") by the FDA in January 2006.

As Shire had a pre-existing relationship with New River, Shire applied EITF 04-1, "Accounting for Pre-existing Relationships between the Parties to a Business Combination" ("EITF 04-1"), in accounting for the effective settlement of the New River Collaboration Agreements.

In accordance with EITF 04-1, Shire measured the effective settlement of the New River Collaboration Agreements resulting from its pre-existing relationship with New River and determined that, in respect of the US Collaboration Agreement, it was less favorable to the Company when compared with pricing for current market transactions for similar items. The RoW Territory License Agreement was determined to be at current market rates. The valuation of the New River Collaboration Agreements and their current market comparators was based upon information available at the time of the acquisition and using the expectations and assumptions that were deemed reasonable by the Company's management.

Although the US Collaboration Agreement was deemed less favorable to the Company at the time of the acquisition when compared with pricing for current market transactions for similar items, the Company did not record a loss on the effective settlement of the pre-existing relationship in the consolidated statement of operations, nor did the Company adjust its purchase price for New River to reflect any such loss resulting from this effective settlement, as settlement provisions in the US Collaboration Agreement available to the Company enabled effective settlement of the New River Collaboration Agreements at no cost to the Company.

(a) Purchase price allocation

Shire's cost of acquiring New River of approximately \$2.6 billion has been allocated to the assets acquired and liabilities assumed according to their estimated fair values at the date of acquisition. Based on this allocation, and at the end of the allocation period, an excess of the fair value of assets acquired and liabilities assumed over the cost of acquisition totaling \$122.2 million has arisen which management, in accordance with SFAS No. 141, allocated as a pro rata reduction of amounts that would otherwise have been ascribed to identifiable intangible assets and IPR&D, (such IPR&D being immediately charged to expense, having no alternative future use). The value of other intangible assets and IPR&D below are presented after this pro-rata allocation.

During the second half of 2008, after the end of the allocation period, the Company reduced the values ascribed to other intangible assets by \$24.1 million from amounts previously assigned to these assets in the purchase price allocation. The change to the values ascribed arose from changes to estimates of deferred taxes: accordingly the excess of the fair value of net assets acquired and liabilities assumed over the cost of the acquisition increased by \$24.1 million. In accordance with SFAS 141 this excess was allocated to intangible assets.

The following table presents the Company's allocation of the purchase price to the assets acquired and liabilities assumed, including the post-allocation period adjustment as outlined above, based on their fair values.

	<u>\$'M</u>
ASSETS	
Current assets:	
Cash and cash equivalents	74.9
Short-term investments	55.8
Accounts receivable, net	0.3
Inventories	11.4
Purchased call option	141.8
Deferred tax asset	68.1
Prepaid expenses and other current assets	0.2
Total current assets	<u>352.5</u>
Property, plant and equipment, net	0.8
Other intangible assets, net	
- Intellectual property - developed technology	1,064.5
- Favorable manufacturing contracts	8.7
- In process research and development	1,866.4
Total assets	<u>3,292.9</u>
LIABILITIES	
Current liabilities:	
Accounts payable and accrued expenses	33.3
Convertible loan notes	279.4
	<u>312.7</u>
Non-current liabilities:	
Deferred tax liability	385.7
Total liabilities	<u>698.4</u>
Net assets acquired	<u>2,594.5</u>

(b) IPR&D

A project-by-project valuation using the guidance in SFAS No. 141 and the AICPA Practice Aid was performed to determine the fair values of research and development projects of New River which were in-process, but not completed as at the completion of the acquisition.

IPR&D assets totaling \$1,866.4 million were identified relating to VYVANSE indicated for ADHD in non-pediatric patients in the US (\$1,786.8 million) and VYVANSE indicated for ADHD in RoW, (\$79.6 million). Both of these IPR&D assets had not received approval, (either from the FDA or from the relevant regulators in the RoW) at the acquisition date. The Company considered that these IPR&D assets have no alternative future use outside their current development projects, as outlined in the AICPA Practice Aid, and these assets were therefore charged to expense in the consolidated statement of operations as of the acquisition date in accordance with FIN 4.

The fair value of the VYVANSE IPR&D assets was determined through the income approach using the multi-period excess earnings method. The fair value of the acquired IPR&D assets was based on the present value of the probability adjusted incremental cash flows expected to be generated by the research and development projects, after the deduction of contributory asset charges for other assets employed in these projects (such other assets include

working capital, the assembled workforce, and the favorable manufacturing contract identified below). The valuation assumed that, consistent with EITF 04-1, the effective settlement of the pre-existing New River Collaboration Agreements had occurred and Shire had purchased 100% of the forecast future cash flows.

Estimated future cash flows were probability adjusted to take into account the stage of completion and the risks surrounding the successful development and commercialization of the acquired projects. The estimated after tax cash flows were discounted to present value using risk adjusted discount rates between 10% and 12%.

The forecast of future cash flows required various assumptions to be made including:

- revenue that is likely to result from sales of VYVANSE for non-pediatric patients in the US and sales of VYVANSE in RoW, including estimated number of units to be sold, estimated selling prices, estimated market penetration, estimated ADHD market share and year-over-year growth rates over VYVANSE's life cycle;
- cost of sales for VYVANSE using historical data from similar products, industry data or other sources of market data;
- sales and marketing expenses using historical data, industry data or other market data;
- general and administrative expenses;
- future research and development expenses to complete the development of VYVANSE in the US and RoW; and
- the tax amortization benefit which would be available to a market participant purchasing the assets piecemeal.

In addition Shire considered:

- the stage of completion of VYVANSE development in the US and RoW;
- the costs incurred to date;
- the projected costs to complete;
- the contribution, if any, of the acquired identifiable intangible assets, including the favorable manufacturing contract (see below);
- the projected launch date of VYVANSE; and
- the estimated life of VYVANSE.

The major risks and uncertainties associated with the timely completion of the acquired IPR&D projects consist of the ability to confirm the safety and efficacy of the technology based on the data from ongoing clinical trials and obtaining the necessary regulatory approvals. The valuations were based on information at the time of the acquisition and expectations and assumptions that (i) were deemed reasonable by Shire's management, and (ii) were based on information, expectations and assumptions that would have been available to and made by a market participant. However, no assurance can be given that the underlying assumptions or events associated with such assets will occur as projected. For these reasons, among others, the actual cash flows may vary from forecast future cash flows.

(c) Identifiable intangible assets

The acquired identifiable intangible assets were attributable to the following categories:

	Fair value \$'M	Asset life Years
Intellectual property – developed technology ⁽¹⁾	1,064.5	20 ⁽³⁾
Other (finite-lived assets) ⁽²⁾	8.7	5
	<u>1,073.2</u>	

(1) Relates to VYVANSE approved for the treatment of ADHD in pediatric patients.

(2) Relates to a favorable manufacturing contract for VYVANSE.

(3) The asset life of 20 years represents the period over which management believe the asset will contribute to the future cash flows of Shire, being the expected commercial lifespan of VYVANSE (VYVANSE has patent protection in the US until September 2023 and until September 2024 in Europe).

Acquired identifiable intangible assets primarily represent the value ascribed to developed technology, represented by VYVANSE for the treatment of ADHD in pediatric populations in the US. These rights include the rights to develop, use, market, sell and/or offer for sale the technical processes, intellectual property and institutional understanding (including the way in which VYVANSE reacts in body, an understanding of the mechanisms of action which allow VYVANSE to work and the knowledge related to the associated clinical and marketing studies performed for VYVANSE).

The fair value of this intellectual property in respect of VYVANSE for the treatment of ADHD in pediatric populations was determined through the income approach using the multi-period excess earnings method. The valuation assumes that, consistent with EITF 04-1, the effective settlement of the pre-existing New River Collaboration Agreements has occurred and Shire has purchased 100% of the cash flows of VYVANSE for the treatment of ADHD in pediatric populations in the US. Using the multi-period excess earnings method, the fair value of intellectual property in respect of VYVANSE for the treatment of ADHD in pediatric populations in the US was based on the present value of the incremental after-tax cash flows attributable to the asset, after the deduction of contributory asset charges for other assets employed (including working capital, the assembled workforce, and the favorable manufacturing contract).

The forecast of future cash flows in respect of the VYVANSE intellectual property requires various assumptions to be made, including:

- revenue that is likely to result from sales of VYVANSE for the treatment of ADHD in pediatric populations, including the estimated number of units to be sold, estimated selling prices, estimated ADHD market penetration, estimated ADHD market share and year-over-year growth rates over VYVANSE's life cycle;
- cost of sales for the products using historical data, industry data or other sources of market data;
- sales and marketing expenses using historical data, industry data or other market data;
- general and administrative expenses;
- research and development expenses; and
- the tax amortization benefit which would be available to a market participant purchasing the assets piecemeal.

The fair value of the favorable manufacturing contract represents the cost savings over market rates negotiated by New River under a five year contract for supply of the active pharmaceutical ingredient used in the manufacture of VYVANSE.

The valuations were based on information available at the time of the acquisition and the expectations and assumptions that (i) were deemed reasonable by Shire's management, and (ii) were based on information, expectations and assumptions that would have been available to and made by a market participant. However, no assurance can be given that the underlying assumptions or events associated with such assets will occur as projected. For these reasons, among others, the actual cash flows may vary from forecast future cash flows.

(d) Convertible Notes

In July 2006, New River issued \$137.8 million of 3.5% Convertible Subordinated Notes due 2013 (the "Notes"). On conversion of the Notes New River was obligated to pay the principal amount of the Notes to the Note holders in cash, with any excess of the fair value over their principal amount (the "Excess Conversion Value") being payable either in cash, shares of New River common stock or a combination of shares of New River common stock and cash at the election of New River.

On April 3, 2007 New River announced that it had elected to settle any Excess Conversion Value in cash. Following the change of control of New River as a result of the business combination, Note holders were entitled to a make-whole premium in the form of an increase in the conversion rate if they tendered their Notes for conversion prior to May 17, 2007.

In accordance with SFAS No. 141 and EITF Issue No. 98-1, "Valuation of Debt Assumed in a Purchase Business Combination", the Notes were valued at their fair value, being the present value of the estimated future cash flows in respect of the Notes as at the date of acquisition.

All the outstanding Notes were tendered for conversion in the period between the acquisition and May 17, 2007 and were therefore settled in cash during the second quarter of 2007 at a value of \$279.4 million which equates to the fair value of the Notes at the acquisition date including the make-whole premium.

(e) Purchased Call Option

Concurrent with the issue of the Notes, New River also entered into a purchased call option with Merrill Lynch at a cost to New River of \$43.5 million, being a convertible note hedge transaction for the Excess Conversion Value of the

Notes. The purchased call options covered, subject to customary anti-dilution adjustments, 4,005,811 shares of New River common stock at strike prices which correspond to the conversion price of the Notes. New River had recorded the cost of acquiring the purchased call option to additional paid in capital.

As a result of New River's election on April 3, 2007 to settle the Excess Conversion Value in cash, Merrill Lynch was obligated to settle the purchased call option in cash. The fair value of the purchased call option represents the Excess Conversion Value of the Notes, including the make-whole premium. This fair value of \$141.8 million was recorded by the Company as an asset within the purchase price allocation.

(f) Deferred taxes

A net current deferred tax asset of \$68.1 million and a net non current deferred tax liability of \$385.7 million were recognized in the purchase price allocation, as analyzed below:

	\$'M
Deferred tax asset on New River net operating loss carryforwards	59.5
Other deferred tax assets - current	8.6
Net deferred tax asset - current	68.1
Deferred tax liabilities on intangible assets – non current ⁽¹⁾	386.1
Other deferred tax liabilities	2.8
Deferred tax liability – non current	388.9
Other deferred tax assets – non current	(3.2)
Net deferred tax liability – non current	385.7

(1) Principally relating to temporary differences arising in respect of the acquired intangible asset for developed technology (representing VYVANSE for the treatment of ADHD in pediatric populations in the US) which is not deductible for tax purposes. The deferred tax liability will be credited to the statement of operations in line with the amortization of the intangible asset.

(g) Deferred revenue

In accordance with the requirements of EITF Issue No. 01-3, "Accounting in a Business Combination for Deferred Revenue of an Acquiree", deferred revenue of \$3.1 million previously included within New River's other current liabilities and \$59.5 million included within other non-current liabilities relating to the New River Collaboration Agreements were eliminated from the acquisition balance sheet through the purchase price allocation exercise, as the enlarged Shire group had no external performance obligations in respect of this deferred revenue following the acquisition.

(h) Restructuring costs

An estimate of restructuring costs of \$3.6 million accounted for in accordance with EITF Issue No. 95-3 "Recognition of Liabilities in Connection with Purchase Business Combinations", was recognized as a liability assumed in the purchase business combination within Accounts payable and accrued expenses. These costs primarily relate to employee severance costs and the cost of exiting New River's Virginia facilities. These costs were paid in 2007.

Supplemental Disclosure of Pro Forma Information

The following unaudited pro forma financial information for the years ended December 31, 2008 and 2007 assumes the Jerini acquisition occurred on January 1, 2007, and for the years ended December 31, 2008, 2007 and 2006 assumes the New River acquisition occurred on January 1, 2006. The unaudited pro-forma financial information which includes Jerini is based upon Shire's ownership interest of 98.6% of Jerini at December 31, 2008. The unaudited pro forma financial information is not necessarily indicative of what the consolidated results of operations actually would have been had the acquisition been completed at the dates indicated. In addition, the unaudited pro forma financial information does not purport to project the future results of operations of the combined Company.

	2008	2007	2006
	\$'M	\$'M	\$'M
Revenues	3,031.6	2,461.7	1,796.5
Net income from continuing operations before cumulative effect of change in accounting principles	114.7	204.6	105.1
Net income from continuing operations	114.7	204.6	104.4
Net income	97.1	204.6	145.0
Per share amounts:			
Net income from continuing operations per share - basic	21.2c	37.0c	19.2c
Net income per ordinary share – basic	18.0c	37.0c	26.5c
Net income from continuing operations per share - diluted	21.0c	36.4c	19.0c
Net income per ordinary share – diluted	17.8c	36.4c	26.3c

The unaudited pro forma financial information above reflects the following pro forma adjustments applied using the principles of SFAS No. 141.

Jerini

- (i) An adjustment to decrease interest income by \$9.1 million and \$29.0 million in the years to December 31, 2008 and 2007 respectively, to reflect the interest foregone on the Company's cash resources used to fund the acquisition of a majority voting interest in Jerini; and
- (ii) An adjustment to increase amortization expense by approximately \$12.1 million and \$18.2 million for the year to December 31, 2008 and 2007 respectively, to reflect amortization of intangible assets relating to the currently marketed product, over the estimated useful life of 17 years.

New River

- (iii) An adjustment to eliminate revenues recognized by New River of \$3.0 million and \$34.3 million for the years to December 31, 2007 and 2006 respectively and expenses incurred by Shire of \$50.0 million for the year to December 31, 2006 in connection with the New River Collaboration Agreements;
- (iv) An adjustment to increase interest expense by \$25.3 million and \$67.2 million for the years to December 31, 2007 and 2006 respectively, to reflect the interest expense and amortization of deferred issue costs associated with the \$1,300 million drawn down under the Facilities Agreement (as defined in Note 19), which was entered into by Shire on February 21, 2007 for the purpose of financing the acquisition of New River;
- (v) An adjustment to decrease interest income by \$6.5 million and \$18.6 million in the years to December 31, 2007 and 2006 respectively, to reflect the interest foregone on the Company's cash resources used to part fund the acquisition of New River;
- (vi) an adjustment to increase amortization expense based on the estimated fair value of identifiable intangible assets from the purchase price allocation, which are being amortized over their estimated useful lives over a range of 5 to 20 years, of approximately \$28.1 million and \$56.2 million for the years to December 31, 2007 and 2006 respectively; and

- (vii) an adjustment to the weighted average number of shares used in the pro forma EPS calculation to reflect the private placement of 42.9 million new ordinary shares of Shire plc on February 20, 2007, the proceeds of which were used to partially fund the acquisition of New River, as if the private placement took place on January 1, 2006.

The unaudited pro forma financial information above does not include the New River IPR&D charge of \$1,866.4 million and the IPR&D charge of \$128.1 million in respect of FIRAZYR outside of the EU, both of which formed part of the preliminary purchase price allocations because they are non-recurring in nature. The unaudited pro forma financial information includes a charge of \$81.8 million for the year to December 31, 2007 in respect of New River cash settled SARs. Pursuant to SFAS No 123(R), "Share-based payments" ("SFAS No. 123(R)"), the liability for the cash settled SARs was revalued to fair value at each balance sheet date; these cash settled SARs were extinguished as a result of the acquisition.

5. Gain on sale of product rights

Disposal of the Beta range

In the year to December 31, 2008 Shire received cash consideration of \$5.0 million from the divestment of the Beta range of hormone replacement products to Meda AB, realizing a gain of \$5.0 million.

Disposal of non-core products to Laboratorios Almirall S.A ("Almirall")

On December 18, 2007 the Company received cash consideration of \$209.6 million, net of costs of \$2.2 million arising on the transfer of product licences, in respect of the divestment of a portfolio of its non-core products, including SOLARAZE and VANIQA, to Almirall. The Company recognizes gains in respect of these divested product rights when the relevant regulatory or other consents for the transfer of these product rights are obtained.

Following receipt of the relevant regulatory or other consents the Company recognized gains of \$15.7 million and \$114.8 in the year to December 31, 2008 and 2007 respectively on disposal of assets and liabilities with a carrying value of \$4.5 million and \$62.1 million, including goodwill, intangibles and inventory.

At December 31, 2008 the Company recorded as a deposit within Other current liabilities \$12.5 million (2007: \$32.7 million) of proceeds from these products where regulatory or other consents have yet to be obtained. See Note 10 for further information.

Disposal of EQUETRO

In September 2007 Shire sold EQUETRO to Validus Pharmaceuticals Inc. ("Validus") for a cash consideration of \$7.5 million and transferred to Validus all post approval study commitments, resulting in a gain of \$7.1 million being recorded in the year to December 31, 2007.

Other disposals

In the year to December 31, 2007 Shire also received cash consideration of \$11.2 million in respect of the divestment of other non-core products resulting in a gain of \$5.9 million being recorded. In addition, the Company received cash consideration of \$6.1 million for divested non-core products where regulatory or other consents were yet to be obtained. At December 31, 2007 these proceeds were recorded as a deposit within Other accrued liabilities pending transfer of the relevant regulatory authorizations for the products.

Disposal of ADDERALL in the year to December 31, 2006

In September 2006, Shire disposed of its ADDERALL (immediate release mixed amphetamine salts) product to Duramed Pharmaceuticals Inc ("Duramed") for \$63.0 million in cash, resulting in a gain of \$63.0 million being recorded.

All assets disposed of during 2008, 2007 and 2006 formed part of the Specialty Pharmaceuticals segment.

6. Integration costs

Jerini Integration

Integration costs of \$10.3 million, primarily acquisition related advisory fees incurred by Jerini and costs relating to the integration of Jerini into Shire, have been incurred in the year to December 31, 2008.

New River Integration

Integration costs of \$1.3 million in connection with the Company's acquisition of New River were incurred in the year to December 31, 2007. At December 31, 2007 the integration of New River was completed and no further integration costs will be incurred.

Transkaryotic Therapies Inc. ("TKT") integration costs

In connection with the Company's acquisition of TKT in July 2005, the Company's management approved and initiated plans to restructure the operations of the enlarged Company to eliminate duplicate facilities and reduce costs.

Integration costs represent incremental costs incurred by the Company directly related to the absorption of the TKT business into the Company, including expenditures for consulting and systems integration. The charges have been presented as integration costs in the statement of operations and are accounted for solely within the HGT operating segment. Total costs of \$5.6 million were incurred in the year to December 31, 2006 and these related to employee severance and retention payments for key TKT employees (\$3.0 million), Information technology costs (\$1.2 million) and other costs relating to the integration of TKT (\$1.4 million).

7. Discontinued operations and reorganizations

Disposition of the vaccines business

On September 9, 2004 the Company completed the disposition of its vaccines business to IDB for a consideration of \$120 million. As part of the transaction, Shire entered into an agreement to provide IDB with a loan facility of up to \$100 million, which could be drawn down over the four years following completion. As at December 31, 2005, IDB had drawn down the entire \$100 million loan.

The transaction gave rise to an overall loss on disposition of the vaccines business of \$41.1 million, recorded as a loss on disposition at completion in 2004 of \$44.2 million and a subsequent provision release of \$3.1 million being recognized during the year to December 31, 2005.

This net loss on disposition of \$41.1 million comprised a gain on disposition of net assets of \$28.9 million together with a provision for a loss of \$70 million out of the \$100 million loan facility available to IDB. On February 14, 2006 the Company received \$78.7 million from IDB, being the full repayment of the \$70.6 million injectable flu development drawings, together with accrued interest of \$8.1 million. The repayment followed the acquisition of IDB by GlaxoSmithKline ("GSK"), after which IDB was provided with resources by GSK to fund the early repayment of the injectable flu tranche.

At the time of the disposal, a provision of \$70.0 million was charged to discontinued operations on the basis that there was no certainty of recovery of this amount. The \$70.0 million provision was allocated against all of the pipeline development tranche (\$29.4 million) and against \$40.6 million of the \$70.6 million injectable flu development tranche.

Accordingly, the \$78.7 million received in 2006 was recorded as follows:

- a gain on disposition of discontinued operations of \$40.6 million (being the amount previously provided against the injectable flu development tranche);
- settlement of the loan receivable balance of \$31.6 million (being the unprovided component of the injectable flu development loan, plus recognized and accrued interest); and
- interest income of \$6.5 million (being interest earned in the year of \$1.0 million and \$5.5 million of interest earned but provided for in previous periods).

The repayment of the \$70.6 million injectable flu tranche had no tax effect.

On March 28, 2008 the Company agreed to a final settlement with IDB of \$4.0 million for the outstanding pipeline development tranche and interest. The amount received was recorded within interest income for the year to December 31, 2008 in accordance with the method of allocating receipts between interest and advances in the loan agreement.

8. Accounts receivable, net

Accounts receivable at December 31, 2008 of \$395.0 million (December 31, 2007: \$441.5 million), are stated net of a provision for sales discounts and doubtful accounts of \$20.2 million (December 31, 2007: \$9.8 million).

The movement in the provision for sales discounts and doubtful accounts is as follows:

	2008 \$'M	2007 \$'M	2006 \$'M
As at January 1,	9.8	8.8	9.7
Charged to operations	95.0	60.1	47.1
Utilization	(84.6)	(59.1)	(48.0)
As at December 31,	20.2	9.8	8.8

Revenues are mainly derived in North America (76% of total revenues) from agreements with major pharmaceutical companies and relationships with pharmaceutical wholesale distributors and retail pharmacy chains. Material customers are disclosed in Note 27.

9. Inventories

Inventories at December 31, 2008 of \$154.5 million (December 31, 2007: \$174.1 million) are stated at the lower of cost or market and are analyzed as follows:

	December 31, 2008 \$'M	December 31, 2007 \$'M
Finished goods	41.4	67.6
Work-in-process	78.7	66.2
Raw materials	34.4	40.3
	154.5	174.1

During the year to December 31, 2008 the Company wrote down the value of its DYNEPO inventory to the lower of cost or market, a write down of \$48.8 million. Changes in the external environment during the year, including the launch of several competing bio-similars at lower prices has made DYNEPO uneconomic for the Company. Accordingly during the year to December 31, 2008 the Company decided to stop commercializing DYNEPO. Product sales were wound down over the second half of 2008 as all patients were transferred off DYNEPO by the end of 2008.

At December 31, 2008 inventories included \$11.5 million (2007: \$nil) of costs related to inventories capitalized prior to the regulatory approval of the relevant product.

10. Assets held-for-sale

At December 31, 2008 assets held-for-sale had a carrying value of \$16.6 million (December 31, 2007: \$10.6 million) principally comprising JOI and JPT acquired through the Jerini acquisition which the Company intends to divest (\$14.9 million). For further details in respect of these assets, see Note 4.

Other assets held-for-sale of \$1.7 million (2007: \$10.6 million) primarily represent intangible assets and attributed goodwill for certain products divested to Almirall in 2007 of \$1.7 million (2007: \$8.3 million). The recognition of the gains arising on the disposal of these products and the de-recognition of the related assets have been deferred pending the completion of the transfer of the relevant regulatory and other consents to the acquirer. For further details see Note 5. These assets form part of the Specialty Pharmaceuticals operating segment.

11. Prepaid expenses and other current assets

	December 31, 2008 \$'M	December 31, 2007 \$'M
Prepaid expenses	47.6	38.1
Income tax receivable	33.2	19.2
Value added taxes receivable	19.3	10.8
Supplemental Executive Retirement Plan ("SERP") investment (see Note 30)	7.2	0.9
Other current assets	34.1	56.3
	<u>141.4</u>	<u>125.3</u>

At December 31, 2007 Other current assets included \$23.0 million, payable by Shire's insurance companies as a contribution towards the settlement of the TKT Class Action Shareholder Suit, see Note 23(d). This amount was paid into escrow by the insurance companies during the year to December 31, 2008. The settlement was approved by the Court on June 11, 2008.

12. Investments

	December 31, 2008 \$'M	December 31, 2007 \$'M
Investments in private companies	19.3	23.2
Available-for-sale securities	6.1	62.1
Equity method investments	17.5	24.9
	<u>42.9</u>	<u>110.2</u>

The Company recorded impairments of \$58.0 million on its investments in private companies and available-for-sale securities during the year to December 31, 2008 (2007: \$3.0 million; 2006: \$2.1 million). See Note 29.

(i) *Investments in private companies*

During the year to December 31, 2008 there were no additions to investments in private companies. During the years to December 31, 2007 and 2006 the Company had additions to investments of \$6.2 million and \$8.0 million respectively in respect of increased equity interests in ViroChem Pharma Inc.

During the year to December 31, 2008 the Company recorded impairments of \$nil million (2007: \$nil; 2006: \$1.8 million) against its investments in private companies. The 2006 impairment was based on a decline in the estimates of the fair value of certain private companies that the Company concluded were other-than-temporary.

(ii) *Available-for-sale securities*

Renovo Group plc

On June 19, 2007 Shire signed a development and license agreement with Renovo Limited ("Renovo"), an affiliate of Renovo Group plc to develop and commercialize JUVISTA, Renovo's novel drug candidate which at the time of entering into the development and license agreement was in late Phase 2 development, outside the EU. In accordance with this agreement, on August 20, 2007 Shire made an equity investment of \$50.0 million for 12.4 million ordinary shares in Renovo Group plc, which represented 6.5% of the total outstanding shares in Renovo Group plc immediately after the issue. The Company has accounted for this investment as an available-for-sale security in accordance with SFAS No. 115 "Accounting for Certain Investments in Debt and Equity Securities". For further information on the development and license agreement, see Note 23.

Avexa Limited ("Avexa")

On January 22, 2007 Shire amended its out-license agreement with Avexa relating to the investigational HIV compound SPD754, to extend Avexa's exclusive commercialization rights to include the US and Canadian markets. In return, Shire received an up-front cash payment of \$10 million, eight million additional Avexa shares valued at \$2.9 million (taking its shareholding in Avexa to just over 8%) and will receive further milestones and royalty payments upon approval and commercialization of the product.

In March 2007, Avexa reported positive Phase 2b results for SPD754 and initiated a capital raising program, including a rights issue, to fund Phase 3 trials. Shire has fully participated in the rights issue and accordingly has recognized an additional investment of \$3.6 million.

In August 2008, Shire granted Avexa an option for 18 months to amend the license agreement to reduce the sales royalties and to remove future milestone payments for an aggregate payment of \$19.0 million in cash upon exercise of the option. Shire received \$5.0 million of additional Avexa shares for the option grant, (equal to 18.6 million shares) taking its holding in Avexa to just over 11%.

Other-than-temporary impairment of available-for-sale securities

The Company recorded other-than-temporary impairments of \$58.0 million, \$3.0 million and \$0.3 million against its available-for-sale securities in the years to December 31, 2008, 2007, and 2006 respectively.

During the year to December 31, 2008 the Company recognized impairment charges in respect of its available-for-sale securities totaling \$58.0 million, including \$44.3 million for the Company's investment in Renovo Group plc. These amounts represent unrealized holding losses that have been reclassified out of other comprehensive income into earnings in the period, as management has concluded that the impairment is other than temporary.

The decline in the market value of the Company's investment in Renovo Group plc initially arose from the results of clinical trials for JUVISTA announced over 2007 and 2008. During the third quarter of 2008, in considering whether the decline in value was temporary or "other than temporary" under US GAAP the Company considered the following factors: the severity of the decline from historical cost (87%) and its duration (eleven months); market analysts' targets of Renovo Group plc's share price for the next 18-24 months; and the revised expected filing date for JUVISTA due to the adoption of a sequential rather than parallel Phase 3 development plan.

These factors, together with the significant decline in global equity markets during the third quarter of 2008 meant that the Company was unable to reasonably estimate the period over which a full recovery in the value of its investment in Renovo Group plc could occur. As such, the Company concluded that for US GAAP purposes the decline in value was "other than temporary".

In such circumstances US GAAP requires the full difference between the book value of the investment and the fair (market) value be recognized as an other than temporary impairment. Accordingly the Company recognized an impairment charge of \$44.3 million for its investment in Renovo Group plc through the Statement of Operations in the third quarter of 2008. For purposes of computing the impairment charge fair value was assumed to be £0.26 per share, representing the closing price of Renovo Group plc securities on the London Stock Exchange on September 30, 2008. If in the future JUVISTA's Phase 3 trials report positively and Renovo Group plc's other products progress through development, Renovo Group plc's share price could react favorably and the Company may recover some or all of this impairment loss. Any future potential increases in the value of Renovo Group plc will be recognized through other comprehensive income. The closing price of Renovo Group plc securities on the London Stock Exchange on December 31, 2008 was £0.20, and the carrying value of the Company's investment in Renovo Group plc was \$3.6 million.

Realized gain on divestment of available-for-sale securities

Other (expense)/income net includes a gain of \$9.4 million from the sale of Shire's available-for-sale investment in Questcor Pharmaceutical Inc., a specialty pharmaceutical company focused on providing prescription drugs for central nervous system (CNS) disorders. Shire received cash consideration of \$10.3 million on the sale of this investment.

During 2007, Shire sold an investment in part of its portfolio of available-for-sale securities, valued at \$0.4 million, realizing a gain on the sale of \$0.1 million. In 2006, there were no sales of available-for-sale securities.

Equity method investments

	December 31, 2008 \$'M	December 31, 2007 \$'M
GSK Partnership	5.1	7.6
GeneChem Funds	6.1	10.4
Other	6.3	6.9
	<u>17.5</u>	<u>24.9</u>

(a) *GSK Partnership*

The Company has accounted for its commercialization partnership with GSK (through which the products 3TC and ZEFFIX are marketed in Canada), using the equity method of accounting. The Company's 50% share of the partnership is included within Equity in earnings of equity method investees.

(b) *GeneChem Funds*

The GeneChem Technologies Venture Fund and the GeneChem Therapeutics Venture Fund ("the Funds") are Canadian limited partnerships investing in healthcare research and development companies, in which the Company owns 30% and 11% of the issued shares respectively. At December 31, 2008 the Funds' net assets totaled approximately \$46.8 million (2007: \$68.8 million; 2006: \$72.0 million). The Company is involved as a limited partner and has been involved in the Funds since 1997. In August 2008, Shire sold GeneChem Financial Corporation to its management for CAN\$2.4 million, payable over 2 years. Accordingly, Shire has ceased to be the general partner of the Funds. The Company's exposure to loss as a result of its involvement with the Funds is limited to the carrying value of the investment, \$6.1 million at December 31, 2008.

13. Property, plant and equipment, net

	December 31, 2008 \$'M	December 31, 2007 \$'M
Land and buildings	267.6	198.0
Office furniture, fittings and equipment	228.2	177.1
Warehouse, laboratory and manufacturing equipment	80.1	54.8
Assets under construction	164.3	94.4
	<u>740.2</u>	<u>524.3</u>
Less: Accumulated depreciation	(206.0)	(155.7)
	<u>534.2</u>	<u>368.6</u>

Depreciation expense for the years to December 31, 2008, 2007 and 2006 was \$77.2 million, \$65.3 million, and \$48.1 million respectively. The expense included impairment losses of \$2.2 million, \$1.8 million and \$0.5 million in the years to December 31, 2008, 2007 and 2006 respectively.

14. Goodwill

	December 31, 2008 \$'M	December 31, 2007 \$'M
Goodwill arising on businesses acquired	350.8	219.4

The changes in the net book value of goodwill for the years to December 31, 2008 and 2007 are shown in the table below:

	2008 \$'M	2007 \$'M
As at January 1,	219.4	237.4
Acquisitions	148.0	-
Adjustments relating to prior year acquisitions	-	(15.0)
Reclassified to assets held-for-sale	-	(1.0)
Disposals	-	(5.0)
Foreign currency translation	(16.6)	3.0
As at December 31,	350.8	219.4

During the year to December 31, 2008 the Company acquired more than a 98% voting interest in Jerini for cash consideration of \$556.5 million which resulted in goodwill of \$148.0 million (see Note 4). This goodwill has been attributed to the HGT reporting segment.

During the year to December 31, 2007 the Company attributed \$6.0 million of goodwill to the divested portfolio of non-core product rights sold to Almirall, of which \$0.4 million remains within assets held-for-sale at December 31, 2008, (see Note 10). Goodwill attributed to the divestment arose in the Specialty Pharmaceuticals segment.

During the year to December 31, 2007 the Company acquired New River for \$2.6 billion through a purchase business combination. No goodwill arose on the acquisition, as pursuant to SFAS No. 141, the excess of the fair value of assets acquired and liabilities assumed over the cost of the acquisition totaling \$146.3 million (including those adjustments arising in the second half of the year to December 31, 2008 as outlined in Note 4) has been allocated pro-rata to reduce the values that would otherwise have been ascribed to acquired intangible assets and IPR&D (see Note 4).

In the year to December 31, 2007 the Company reduced goodwill arising on the acquisition of TKT by \$15.0 million. In accordance with SFAS No. 109, the Company is required to first reduce goodwill to zero and then to reduce non-current intangible assets arising on acquisition for all changes in estimates related to tax contingencies and the elimination of valuation allowances established at the time of the acquisition, regardless of the time elapsed since the date of acquisition. Accordingly the Company reduced the goodwill in respect of the TKT acquisition by \$11.0 million due to the elimination of a valuation allowance established against acquired deferred tax assets and the goodwill was further reduced by \$4.0 million due to a change in estimate in respect of pre-acquisition income tax contingencies.

At December 31, 2008 goodwill of \$202.4 million (2007: \$203.9 million) is held in the Specialty Pharmaceuticals segment and \$148.4 million (2007: \$15.5 million) in the HGT segment.

15. Other intangible assets, net

	December 31, 2008 \$'M	December 31, 2007 \$'M
Other intangible assets:		
Intellectual property rights acquired	2,389.9	2,116.8
Favorable manufacturing contracts	8.7	8.9
	<u>2,398.6</u>	<u>2,125.7</u>
Less:		
Accumulated amortization	(437.0)	(321.6)
Impairment charges	(136.7)	(39.6)
	<u>1,824.9</u>	<u>1,764.5</u>

Intellectual property rights relate to currently marketed products. At December 31, 2008 the net book value of these intellectual property rights for products with sales recorded in the Specialty Pharmaceuticals operating segment was \$1,244.9 million (December 31, 2007: \$1,440.6 million) and in the HGT operating segment was \$579.3 million (December 31, 2007: \$322.4 million).

The increase in the net book value of other intangible assets for the year to December 31, 2008 is shown in the table below:

	Other intangible assets \$'M
As at January 1, 2008	1,764.5
Acquisitions	350.8
Amortization charged	(127.9)
Assets transferred to held-for-sale	(0.1)
Impairment charges	(97.1)
New River purchase price allocation adjustment	(24.1)
Foreign currency translation	(41.2)
As at December 31, 2008	<u>1,824.9</u>

During the year to December 31, 2008 the Company acquired intangible assets totaling \$350.8 million, principally relating to FIRAZYR (\$315.7 million) for the treatment of acute HAE in the EU (acquired through the Jerini business combination), and DAYTRANA (\$25.0 million). The weighted average amortization period for acquired assets is 17 years. Intangible asset acquisitions exclude \$263.1 million of IPR&D acquired through the Jerini acquisition and the acquisition of METAZYM from Zymenex which was immediately charged to the Consolidated Statement of Operations at the acquisition date (see Note 4).

Amortization charged for the three years to December 31, 2008, 2007 and 2006 was \$127.9 million, \$95.8 million and \$56.3 million, respectively.

The Company recorded impairments of \$97.1 million, \$0.4 million and \$1.1 million in the years to December 31, 2008, 2007 and 2006 respectively, recorded within Selling, general and administrative costs. During the year to December 31, 2008 the Company recognized impairment charges of \$97.1 million, of which \$94.6 million relates to the write-down of its DYNEPO intangible asset to fair value (\$nil). Changes in the external environment, including the launch of several competing bio-similars at lower prices has made DYNEPO uneconomic for the Company. Accordingly the Company has decided to stop commercializing DYNEPO. Product sales were wound down over the second half of 2008 as all patients were transferred off DYNEPO by the end of 2008. The fair value of DYNEPO has been determined using an expected present value technique. The impairment charge relates to the Specialty Pharmaceuticals operating segment.

Following the resolution of uncertainties during the year to December 31, 2008 principally relating to the tax treatment of certain items incurred by New River, the Company changed its estimates of deferred taxes from those estimates made in the New River purchase price allocation. In accordance with EITF 93-7 "Uncertainties Related to Income Taxes in a Purchase Business Combination", the effect of resolving these uncertainties has been applied to decrease non current intangible assets by \$24.1 million as no goodwill arose on the acquisition of New River, (see Note 4).

The useful economic lives of all intangible assets that continue to be amortized under SFAS No. 142 have been assessed. Management estimates that the annual amortization charges in respect of intangible assets held at December 31, 2008 will be approximately \$137 million for each of the five years to December 31, 2013. Estimated amortization expense can be affected by various factors including future acquisitions, disposals of product rights, foreign exchange movements and the technological advancement and regulatory approval of competitor products.

16. Other non-current assets

	December 31, 2008 \$'M	December 31, 2007 \$'M
SERP investment (see Note 30)	-	7.0
Deferred financing costs (see Note 19)	11.5	16.6
Other assets	6.9	3.3
	18.4	26.9

Further details of the SERP investment are provided in Note 30. The amount shown above is the cash surrender value of life insurance policies, which is backed by short-term investments.

17. Accounts payable and accrued expenses

	December 31, 2008 \$'M	December 31, 2007 \$'M
Trade accounts payable	102.4	79.6
Accrued rebates – Medicaid	162.6	114.3
Accrued rebates – Managed care	59.9	32.3
Sales return reserve	47.1	39.5
Accrued bonuses	62.0	59.6
Accrued employee compensation and benefits payable	36.7	35.0
Accrued coupons	4.0	9.0
Research and development accruals	29.3	38.2
Marketing accruals	22.1	19.0
Deferred revenue	9.6	11.1
Accrued settlement costs	2.6	51.5
Other accrued expenses	170.3	185.1
	708.6	674.2

At December 31, 2007 Accrued settlement costs included \$50.0 million, for the settlement of the TKT Class Action Shareholder Suit, see Note 23(d). This amount was paid into escrow by Shire (\$27.0 million) and Shire's insurance companies (\$23.0 million – see Note 11) during the year to December 31, 2008. The settlement was approved by the Court on June 11, 2008.

18. Other current liabilities

	December 31, 2008 \$'M	December 31, 2007 \$'M
Income taxes payable	25.8	47.3
Value added taxes	4.4	6.0
Derivative financial instruments	46.9	2.8
Other accrued liabilities	27.2	40.4
	<u>104.3</u>	<u>96.5</u>

19. Long-term debt

Shire 2.75% Convertible Bonds due 2014

On May 9, 2007 Old Shire issued \$1,100 million in principal amount of 2.75% convertible bonds due 2014 and convertible into fully paid Shire Ordinary Shares of (the "Bonds"). The net proceeds of issuing the Bonds, after deducting the commissions and other direct costs of issue, totaled \$1,081.7 million.

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 rateably, 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, (the "Call Option"), 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 shall 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 may also be redeemed at the option of the Bond holder at their principal amount including accrued but unpaid interest on May 9, 2012 (the "Put Option"), or following the occurrence of change of control. 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 and following exercise of the Put Option, by delivery of the underlying Shire Ordinary Shares and a cash top-up amount.

The Bonds are convertible into Shire 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 Shire Ordinary Shares at the initial conversion price of \$33.5879 per Shire Ordinary Share, (subject to adjustment as outlined below), being 2,977.26265 shares per \$100,000 denomination. The initial 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 Shares issued on conversion will be delivered credited as fully paid, and will rank pari passu in all respects with all fully paid Shares in issue on the relevant conversion date.

On the issuance of the Bonds, the Company evaluated whether: (a) the conversion feature of such the issuance should be bifurcated from the debt host and separately accounted for as a derivative instrument in accordance with the requirements of SFAS No.133 or (b) the conversion feature meets the criteria within SFAS No. 133 for exemption from treatment as a derivative instrument. As the conversion feature in the Bonds qualifies for the SFAS No.133 exemption from treatment as a derivative instrument, the Bonds are accounted for by the Company in accordance with APB 14. In accordance with APB 14 no portion of the proceeds of the Bonds has been allocated to the conversion feature and the Bonds have been recorded at their principal amount within non-current liabilities.

In connection with the Scheme of Arrangement Shire entered into:

(i) a supplemental trust deed dated April 15, 2008 between Shire plc, Old Shire and BNY Corporate Trustee Services Limited as Trustee (the "Supplemental Trust Deed") relating to a trust deed dated May 9, 2007 (the "Trust Deed") constituting the US \$1,100,000,000 2.75% Convertible Bonds due 2014 (the "Convertible Bonds") originally issued by Shire; and

(ii) an accession and amendment agreement dated April 15, 2008 between Shire plc, Old Shire, BNY Corporate Trustee Services Limited as Trustee and The Bank of New York as Paying and Conversion Agent (the "Accession and Amendment Agreement") relating to a paying and conversion agency agreement dated May 9, 2007 (the "Agency Agreement") between Old Shire, BNY Corporate Trustee Services Limited as Trustee and The Bank of New York as Paying and Conversion Agent.

The following is a description of the material amendments to the Trust Deed, effected pursuant to the Supplemental Trust Deed, and to the Agency Agreement, effected pursuant to the Accession and Amendment Agreement, each of which took effect on May 23, 2008, immediately prior to the Scheme of Arrangement becoming effective.

Shire plc was substituted in place of Old Shire as principal obligor under, and issuer of, the Convertible Bonds, and Shire plc acceded to, and assumed all Old Shire obligations under, the Trust Deed and the Agency Agreement. Old Shire ceased to be a party to the Trust Deed and the Agency Agreement. The Trust Deed, the Agency Agreement and the terms and conditions of the Convertible Bonds were amended and restated in order to, among other things, provide that the Convertible Bonds will, following the substitution, be convertible into ordinary shares of Shire plc.

Direct costs of issue of the Bonds paid in the year to December 31, 2007 totaled \$18.3 million. These costs are being amortized to interest expense using the effective interest method over the five year period to the Put Option date. At December 31, 2008 \$12.6 million was deferred (\$3.8 million within other current assets and \$8.8 million within other non-current assets).

Multicurrency Term and Revolving Facilities Agreement

In connection with the acquisition of New River, Shire plc entered into a Multicurrency Term and Revolving Facilities Agreement (the "Facilities Agreement") with ABN AMRO Bank N.V., Barclays Capital, Citigroup Global Markets Limited and The Royal Bank of Scotland plc (the "Arrangers") on February 20, 2007. The Facilities Agreement comprised three credit facilities: (i) a committed multicurrency five year term loan facility in an aggregate amount of \$1,000 million ("Term Loan A"), (ii) a committed multicurrency 364 day term (with a further 364 day extension option) loan facility in an aggregate amount of \$300 million ("Term Loan B") and (iii) a committed five year revolving loan facility in an aggregate amount of \$1,000 million (the "RCF" and, together with Term Loan A and Term Loan B, the "Facilities"). Shire plc has agreed to act as guarantor for any of its subsidiaries that borrow under the Facilities Agreement.

On April 18, 2007 the Company fully utilized Term Loan A of \$1,000 million and Term Loan B of \$300 million to partially fund the acquisition of New River. In May 2007 Shire issued \$1,100 million principal amount of the Bonds. The proceeds of the issue were used to repay and cancel \$800 million of Term Loan A and all of Term Loan B in accordance with the terms of the Facilities Agreement. The remaining \$200 million drawn down under Term Loan A was repaid on June 29, 2007.

On July 19, 2007, the Company entered into a syndication and amendment agreement in relation to the Facilities Agreement dated February 20, 2007 (the "Amended Facilities Agreement"), which increased the RCF to an aggregate amount of \$1,200 million, amended the covenant relating to the ratio of Net Debt to EBITDA and syndicated the RCF between the following banks which have the following commitment: ABN Amro Bank N.V., (\$200 million); Barclays Capital, (\$200 million); Citigroup Global Markets Limited, (\$200 million); The Royal Bank of Scotland plc, (\$200 million); Lloyds TSB Bank plc, (\$200 million); Bank of America N.A., (\$100 million); and Morgan Stanley Bank, (\$100 million).

The RCF, which includes a \$250 million swingline facility, may be used for general corporate purposes and matures on February 20, 2012. The availability of loans under the RCF is subject to customary conditions, including the absence of any defaults thereunder and the accuracy (in all material respects) of Shire's representations and warranties contained therein.

The interest rate on each loan drawn under the RCF for each interest period, as determined by the Company, is the percentage rate per annum which is the aggregate of the applicable margin (ranging from 0.40 to 0.80 per cent per annum, depending on the ratio of Net Debt to EBITDA for the preceding period) 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.

The Amended Facilities Agreement includes requirements that (i) Shire's ratio of Net Debt to EBITDA (as defined in the Amended Facilities 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; and (ii) that the ratio of EBITDA to Net Interest (as defined in the Facilities 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.

Upon a change of control of Shire or upon the occurrence of an event of default and the expiration of any applicable cure period, the total commitments under the Facilities may be canceled and/or all or part of the loans, (together with accrued interest and all other amounts accrued or outstanding) may become immediately due and payable. Events of default under the Amended Facilities Agreement include: (i) non-payment of any amounts due under the Facilities; (ii) failure to satisfy any financial covenants; (iii) material misrepresentation in any of the finance documents; (iv) failure to pay, or certain other defaults under other financial indebtedness; (v) certain insolvency events or proceedings; (vi) material adverse changes in the business, operations, assets or financial condition of the group; (vii) certain US Employee Retirement Income Security Act breaches which would have a material adverse effect; (viii) if it becomes illegal for Shire or any of its subsidiaries that are parties to the Amended Facility Agreement to perform their obligations or (ix) if Shire or any subsidiary of Shire which is party to the Amended Facility Agreement repudiates the Amended Facility Agreement or any Finance Document (as defined in the Amended Facility Agreement).

In connection with the Scheme of Arrangement, with effect from May 23, 2008, Old Shire entered into an accession and amendment deed dated April 15, 2008 between Shire plc (formerly Shire Limited), Old Shire, certain subsidiaries of Shire plc and Barclays Bank plc as Facility Agent (the "Accession and Amendment Deed") relating to the Amended Facilities Agreement. The following is a description of the material amendments to the Amended Facilities Agreement, affected pursuant to the Accession and Amendment Deed, which took effect on May 23, 2008, immediately prior to the Scheme of Arrangement becoming effective.

Shire plc acceded to the Facility Agreement as a borrower and guarantor, and Shire Holdings UK Limited, a wholly-owned subsidiary of Old Shire, acceded to the Facility Agreement as a borrower. Old Shire ceased to be a party to the Facility Agreement as a guarantor (although it remains a party to the Facility Agreement as a borrower). The Amended Facilities Agreement was amended and restated in order to take account of the fact that Shire plc is incorporated in Jersey and tax resident in the Republic of Ireland, to exclude the Scheme of Arrangement between Shire plc and its shareholders from the mandatory prepayment provisions contained in the Amended Facilities Agreement, and amend the financial covenants contained in the Amended Facilities Agreement in order to ensure that if any amount of interest awarded in the TKT appraisal rights litigation differs from that provided for in Shire's accounts, any excess or shortfall would be treated as if it had been provided for on a pro rata basis in accounting periods up to the time of judgement. This amendment was made to avoid a technical breach of the Amended Facilities Agreement in the accounting period in which the any judgement occurs.

During the year ended December 31, 2007 the Company paid \$14.5 million for the arrangement of the Facilities of which \$1.2 million has been amortized in the year to December 31, 2008 (\$9.4 million amortized in the year to December 31, 2007). The remaining arrangement costs of \$3.9 million, which relate to the RCF, remain deferred at December 31, 2008 and are being amortized over the estimated term of the facility (\$1.2 million within other current assets and \$2.7 million within other non-current assets).

On November 7, 2008 Shire utilized \$190.0 million of the facility to part fund the TKT appraisal rights litigation settlement. The loan was repaid in full prior to December 31, 2008 (see Note 23).

New River 3.5% Convertible Subordinated Notes due 2013

During July 2006, New River issued \$137.8 million of 3.5% Convertible Subordinated Notes due 2013 (the "Notes"). Prior to the acquisition of New River during April 2007, the Notes were convertible according to their terms following the New River share price having exceeded predetermined levels. Following Shire's acquisition of New River, the Notes also became convertible as a result of the change of control of New River, entitling Note holders to a make-whole premium in the form of an increase in the conversion rate if the Notes were tendered for conversion prior to May 17, 2007.

All of the outstanding Notes were tendered for conversion in the period between the acquisition and May 17, 2007 and were settled at their fair value of \$279.4 million.

20. Other long-term debt

On August 17, 2007 Shire entered into a multi-year lease on laboratory and office space in Lexington, Massachusetts for its HGT business unit. The lease expires in 2023 although Shire has the option to extend the term of the lease for additional periods up to a total of 15 years.

Pursuant to the requirements of EITF 97-10, "The Effect of Lessee Involvement in Asset Construction", as the Company is in substance the owner of the property during the construction phase, the related asset and

corresponding financial obligation have been recorded within Property, plant and equipment, net and Other long-term debt, as a building financing obligation. The fair value of the building element at inception of the arrangement of \$32.7 million has been included in the balance sheet in Property, plant and equipment, net. In accordance with SFAS No. 13, "Accounting for Leases", the land element of the lease has been accounted for as an operating lease.

At the completion of the construction period, the Company will review the building for potential sale-leaseback treatment in accordance with SFAS No. 98, "Accounting for Leases: Sale-Leaseback Transactions Involving Real Estate, Sales-Type Leases of Real Estate, Definition of the Lease Term, and Initial Direct Costs of Direct Financing Leases—an amendment of FASB Statements No. 13, 66, and 91 and a rescission of FASB Statement No. 26 and Technical Bulletin No. 79-11". However, based on its preliminary analysis, the Company determined that the building will not qualify for sale-leaseback treatment. Therefore, the building, improvements and associated liabilities will remain on the Company's consolidated balance sheet throughout the lease term. The building and tenant improvements will be depreciated on a straight line basis over their estimated useful lives.

Concurrent with entering into the lease, Shire also entered into an agreement which provided Shire, *inter alia*, with the option to purchase or lease additional manufacturing, laboratory and office space in Lexington, Massachusetts. During 2008 Shire has purchased and leased additional manufacturing, laboratory and office space pursuant to this option agreement.

21. Other non-current liabilities

	December 31, 2008 \$'M	December 31, 2007 \$'M
Income taxes payable	220.4	320.8
SERP (see Note 30)	1.8	3.6
Deferred revenue	29.5	13.9
Deferred rent	16.1	16.8
Insurance provisions	18.1	14.7
Other accrued liabilities	5.4	5.8
	291.3	375.6

22. Financial instruments

Assets and Liabilities that are Measured at Fair Value on a Recurring Basis

As outlined in Note 2(x), on January 1, 2008 the Company adopted the provisions of SFAS No. 157 as they relate to financial assets and financial liabilities. The following are the major categories of financial assets and liabilities measured at fair value on a recurring basis during the year to December 31, 2008 using quoted prices in active markets for identical assets (Level 1); significant other observable inputs (Level 2); and significant unobservable inputs (Level 3).

	Total \$'M	Level 1 \$'M	Level 2 \$'M	Level 3 \$'M
Financial assets:				
Available-for-sale securities	6.1	6.1	-	-
Equity method investments	6.1	-	6.1	-
Derivatives ⁽¹⁾	2.7	-	2.7	-
Financial liabilities:				
Derivatives ⁽¹⁾	46.9	-	46.9	-

⁽¹⁾ Derivatives comprise swap and forward foreign exchange contracts

Certain estimates and judgments were required to develop the fair value amounts. The fair value amounts shown above are not necessarily indicative of the amounts that the Company would realize upon disposition, nor do they indicate the Company's intent or ability to dispose of the financial instrument.

The following methods and assumptions were used to estimate the fair value of each material class of financial instrument:

- Available-for-sale securities – The fair values of available-for-sale investments are estimated based on quoted market prices for those investments.
- Equity method investments – The Company's equity method investments comprise quoted and unquoted investments. The fair values of quoted investments within the funds are estimated based on quoted market prices for those investments. For unquoted investments within the fund, the fair value is estimated using directly observable inputs other than quoted prices.
- Derivatives – derivative instruments comprise swap and forward foreign exchange contracts. The fair value of the swap and forward foreign exchange contracts has been determined using an income approach based on current market expectations about the future cash flows.

Fair value of financial instruments: At December 31, 2008 and 2007, the Company's financial instruments included cash and cash equivalents, restricted cash, marketable securities, accounts receivable, investments, accounts payable and accrued expenses, convertible bonds, building finance obligations and derivative contracts. The carrying amounts of cash and cash equivalents, accounts receivable, accounts payable and accrued expenses approximate fair value because of the short-term maturity of these amounts. Available-for-sale marketable securities, investments and derivatives are recorded at fair values as indicated in the preceding disclosures. The estimated fair values of the Company's other financial instruments as at December 31, 2008 and 2007 are summarized below. Certain estimates and judgments were required to develop the fair value amounts. The fair value amounts shown below are not necessarily indicative of the amounts that the Company would realize upon disposition, nor do they indicate the Company's intent or ability to dispose of the financial instrument.

The following methods and assumptions were used to estimate the fair value of each material class of financial instrument:

- Convertible bonds – the fair value of the Shire plc's 2.75% convertible bonds due 2014 is estimated by reference to the market price of the instrument as the convertible bonds are publicly traded.
- Building financing obligations - the fair value of building financing obligations are estimated based on the discounted future cash flows using the Company's incremental borrowing rate.

The carrying amounts and corresponding fair values of financial instruments are as follows:

	December 31, 2008		December 31, 2007	
	Carrying amount \$'M	Fair value \$'M	Carrying amount \$'M	Fair value \$'M
Financial assets:				
Option over Avexa shares	-	-	-	0.7
Financial liabilities:				
Convertible bonds	1,100.0	892.9	1,100.0	1,110.1
Building financing obligation	45.6	40.7	32.9	36.4

23. Commitments and contingencies

(a) Operating Leases

Future minimum payments presented below include operating lease payments and other fixed executory fees under operating lease arrangements as at December 31, 2008:

	Operating leases
	\$'M
2009	34.2
2010	26.5
2011	23.4
2012	16.1
2013	14.6
Thereafter	57.6
	<hr/> 172.4 <hr/>

(i) Operating leases

The Company leases land, facilities, motor vehicles and certain equipment under operating leases expiring through 2025. Lease and rental expense amounted to \$32.6 million, \$28.0 million and \$23.7 million for the years to December 31, 2008, 2007 and 2006, which is predominately included in Selling, general and administrative expenses in the accompanying statements of operations.

(b) Letters of credit

As at December 31, 2008 the Company had the following letters of credit:

- (i) an irrevocable standby letter of credit with Barclays Bank plc, in the amount of \$4.0 million, providing security on the recoverability of certain insurance claims. The Company has restricted cash of \$4.0 million, as required by this letter of credit; and
- (ii) an irrevocable standby letter of credit with Citigroup in the amount of \$4.2 million, providing security on the payment of lease obligations. The Company has restricted cash of \$4.2 million, as required by this letter of credit.

(c) Commitments

(i) Alba Therapeutics Corporation ("Alba")

On December 14, 2007 Shire acquired rights to SPD550 (also known as AT-1001) in all markets outside of the US and Japan, from Alba. SPD550 is Alba's lead inhibitor of barrier dysfunction in various gastrointestinal disorders that is currently in Phase 2 development for the treatment of Celiac disease. Shire paid an upfront payment of \$25 million (expensed as R&D in 2007) and will pay further development and sales milestones up to a maximum of \$300 million. Shire will also pay tiered royalties on net sales of the product. Tiered royalty rates will be single or double digit dependent on annual net sales.

Alba and Shire have formed a joint development committee to monitor R&D activities of SPD550. Alba will fund all development until SPD550 has completed Proof of Concept, which is expected to be in the first half of 2009, after which Shire and Alba will share equally development costs under a joint development plan.

(ii) Amicus Therapeutics, Inc. ("Amicus")

On November 7, 2007 Shire licensed from Amicus the rights to three pharmacological chaperone compounds in markets outside of the US: AMIGAL for Fabry disease (Phase 2), PLICERA for Gaucher disease (Phase 2) and AT2220 for Pompe disease (Phase 2). Shire paid Amicus an upfront license fee of \$50 million (expensed as R&D in 2007), and will pay further development and sales based milestones to a maximum of \$390 million. Shire will also pay tiered, double digit, royalties on net sales of the products. Shire and Amicus will pursue a joint development program toward market approval in the US and Europe; expenses for this program will be shared equally.

(iii) JUVISTA

On June 19, 2007 Shire signed an agreement with Renovo to develop and commercialize JUVISTA, Renovo's novel drug candidate being investigated for the reduction of scarring in connection with surgery. Under the terms of the agreement Shire has the exclusive right to commercialize JUVISTA worldwide, with the exception of EU member states.

Shire has remaining obligations to pay Renovo \$25 million on the filing of JUVISTA with the FDA; up to \$150 million on FDA approval; royalties on net sales of JUVISTA; and up to \$525 million on the achievement of very significant sales targets. Shire will bear the cost of clinical trials designed specifically for obtaining US regulatory approval. Renovo will bear the costs of clinical trials designed specifically for obtaining EU regulatory approval. Shire and Renovo will share equally the costs of conducting global clinical trials that are designed for obtaining both US and EU regulatory approvals.

(iv) Women's Health Products

In August 2006, Shire and Duramed (an affiliate of Barr) entered into an agreement related to SEASONIQUE, a number of products using Duramed's transvaginal ring technology and other oral products (the "Collaboration Products"). Under this agreement, Shire was required to reimburse Duramed for US development expenses incurred in respect of the Collaboration Products up to a maximum of \$140 million over eight years from September 2006, and Shire had the right to commercialize these products in a number of markets outside of North America, including the larger European markets.

US development expenses reimbursed in the year ended December 31, 2008 totaled \$30.0 million, and at December 31, 2008 the maximum future reimbursement for Duramed incurred US development expenditures was \$95.6 million.

On February 24, 2009, Shire and Duramed amended this agreement and it will terminate on December 31, 2009. Pursuant to this amendment, Shire agreed to return to Duramed its rights under the agreement effective February 24, 2009. Shire also agreed to reimburse Duramed for incurred US development expenditures in 2009 up to a maximum of \$30.0 million. In addition, Shire agreed to a one-time payment to Duramed of \$10.0 million and to forego royalties receivable from Barr and cost of goods otherwise payable by Barr to Shire in 2009 under the License Agreement between the parties for the supply of the authorized generic of ADDERALL XR up to a maximum of \$25.0 million.

(v) Other R&D and sales milestones

In addition to the commitments set out in (i) to (iv), at December 31, 2008 the Company had commitments payable on achievement of specified milestones and fees payable for products under development in-licensed from third parties of \$1.0 million (2007: \$5.3 million).

(vi) Clinical testing

At December 31, 2008 the Company had committed to pay approximately \$99.5 million (2007: \$77.6 million) to contract vendors for administering and executing clinical trials. The Company expects to pay \$40.7 million in 2009 (2007: \$44.4 million in 2008). However, the timing of these payments is dependent upon actual services performed by the organizations as determined by patient enrollment levels and related activities.

(vii) Contract manufacturing

At December 31, 2008 the Company had committed to pay approximately \$67.0 million (2007: \$109.7 million) in respect of contract manufacturing. The Company expects to pay \$66.9 million of these commitments in 2009 (2007: \$91.3 million in 2008).

(viii) Purchase and service commitments

At December 31, 2008 the Company had committed to pay approximately \$42.6 million (2007: \$49.4 million) in respect of commitments for purchases and services, predominately relating to active pharmaceutical ingredients sourcing and IT outsourcing. The Company expects to pay \$42.4 million of these commitments in 2009 (2007: \$31.0 million in 2008).

(ix) Investment commitments

At December 31, 2008 the Company had outstanding commitments to subscribe for interests in companies and partnerships for amounts totaling \$5.7 million (2007: \$7.9 million) which may all be payable in 2009, depending on the timing of capital calls.

(x) Capital commitments

At December 31, 2008, the Company has committed to spend \$95.4 million in respect of capital projects, including commitments for the expansion and improvements to office space at the Basingstoke UK headquarters and improvements to laboratory and office space leased by the HGT business at Lexington, Massachusetts which is expected to be all payable in 2009.

(d) Legal proceedings

General

The Company accounts for litigation losses and insurance claims and provisions in accordance with SFAS No. 5, "Accounting for Contingencies" ("SFAS No. 5"). Under SFAS No. 5, loss contingency provisions are recorded for probable losses when management is able to reasonably estimate the loss. Where the estimated loss lies within a range and no particular amount within that range is a better estimate than any other amount, the minimum amount is recorded. In other cases management's best estimate of the loss is recorded. These estimates are developed substantially before the ultimate loss is known and the estimates are refined in each accounting period in light of additional information becoming known. In instances where the Company is unable to develop a reasonable estimate of loss, no litigation loss is recorded at that time. As information becomes known a loss provision is set up when a reasonable estimate can be made. The estimates are reviewed quarterly and the estimates are changed when expectations are revised. Any outcome upon settlement that deviates from the Company's estimate may result in an additional expense in a future accounting period.

As at December 31, 2008 provisions for litigation losses, insurance claims and other disputes totaled \$20.8 million (2007: \$66.2 million).

Specific

ADDERALL XR

(i) Sandoz

In December 2006, Shire was notified that Sandoz Inc. ("Sandoz") had submitted an Abbreviated New Drug Application ("ANDA") under the Hatch-Waxman Act seeking permission to market its generic versions of the 5mg, 10mg, 15mg, 20mg, 25mg and 30mg strengths of ADDERALL XR prior to the expiration of US Patent No. 6,322,819 ("the '819 Patent") and US Patent No. 6,605,300 ("the '300 Patent"), the Shire patents that cover ADDERALL XR. On January 26, 2007 Shire filed suit in the US District Court for the District of Colorado for infringement of the '819 and '300 Patents. Pursuant to the Hatch-Waxman Act, there is a 30 month stay with respect to Sandoz' proposed generic products. In response to the parties' summary judgment motions, the court, in a decision dated September 24th, 2008, (a) granted Shire's motion to strike Sandoz' affirmative defenses of alleged patent misuse and sham litigation; (b) denied Sandoz's motion of non-infringement; and (c) construed certain terms of the patent claims. Sandoz' motion for immediate appeal on the issue of whether a patentee who settles an earlier infringement case after a Markman ruling has issued is precluded under the doctrine of collateral estoppel from relitigating claim-construction issues determined in the prior case (in this instance, the prior case was Shire v Impax from the Delaware court) was granted by the Colorado court. On February 6, 2009, the Court of Appeals for the Federal Circuit ("CAFC") also granted Sandoz' petition for appeal as to this question. The Colorado case remains administratively closed until there is a decision from the CAFC.

CARBATROL

(i) Nostrum

In August 2003, the Company was notified that Nostrum Pharmaceuticals, Inc. ("Nostrum") had submitted an ANDA under the Hatch-Waxman Act seeking permission to market its generic version of the 300mg strength of CARBATROL (Nostrum's ANDA product) prior to the expiration date of the Company's US patents for CARBATROL, US patent No. 5,912,013 ("the '013 Patent") and US patent No. 5,326,570 ("the '570 Patent"). On September 18, 2003, Shire filed suit against Nostrum in the United States District Court for the District of New Jersey alleging infringement of these two patents by Nostrum's ANDA and ANDA product. Pursuant to the Hatch-Waxman Act, there was a 30-month stay with respect to Nostrum's ANDA product which expired in February, 2006. Nostrum could be in a position to market its 300mg extended-release carbamazepine product upon FDA final approval of its ANDA. On January 23, 2004 the Company amended the complaint to drop the allegations with respect to the '013 Patent while maintaining the suit with respect to the '570 Patent. On July 17, 2006 the Court entered an order staying discovery.

In May 2008, the Company was notified that Nostrum had submitted an amendment to the above referenced ANDA seeking permission to market its generic versions of the 100mg and 200mg strengths of CARBATROL prior to the expiration date of the Company's '013 and '570 Patents. On July 2, 2008 Shire filed suit against Nostrum in the United

States District Court for the District of New Jersey alleging infringement of these two patents by Nostrum's ANDA and ANDA products. Pursuant to the Hatch-Waxman Act, there is a 30-month stay with respect to Nostrum's 100mg and 200mg ANDA products which will expire in November 2010. This case was referenced as related to the earlier filed case on Nostrum's 300 mg product and has been assigned to the same Judge as the earlier ongoing case. In a December 15, 2008 decision the court decided that the two cases should proceed separately. No trial date has been set for either case.

(ii) Corepharma

On March 30, 2006 the Company was notified that Corepharma LLC ("Corepharma") had filed an ANDA under the Hatch-Waxman Act seeking permission to market its generic version of carbamazepine extended release products in 100mg, 200mg and 300mg strengths prior to the expiration date of the '013 and the '570 Patents. On May 17, 2006 Shire filed suit against Corepharma in the United States District Court for the District of New Jersey alleging infringement of these two patents by Corepharma's ANDA and ANDA products. Pursuant to the Hatch-Waxman Act, there was a 30 month stay with respect to Corepharma's proposed generic products which expired in October 2008. The Court rendered a claim construction ruling on March 26, 2008. On September 23, 2008 the Court issued a decision denying Corepharma's summary judgment motion for noninfringement of the '570 patent. In an order dated October 31, 2008 the Court granted Corepharma's motion for summary judgment of non-infringement of the '013 Patent. The parties submitted a joint pretrial order directed to the '570 Patent on December 5, 2008. A final pretrial conference has been set for March 3, 2009. No trial date has been set.

(iii) Teva

On March 20, 2007 the Company was notified that Teva USA had filed an ANDA under the Hatch-Waxman Act seeking permission to market its generic version of carbamazepine extended release products in 100mg, 200mg and 300mg strengths prior to the expiration date of the '013 and the '570 Patents. On May 2, 2007, Shire filed suit against Teva in the US District Court for the Southern District of New York alleging infringement of the '013 and the '570 Patents by Teva's ANDA and ANDA products. On August 23, 2007 Shire amended the complaint to drop the allegations with respect to the '013 Patent while maintaining the suit with respect to the '570 Patent. Teva USA raised counterclaims that the '570 and '013 Patents were not infringed. Shire has offered Teva USA a covenant not to sue with respect to the '013 Patent. The Court held a status conference on October 16, 2007. Teva withdrew its counterclaim directed to the '013 patent. The parties have submitted a discovery schedule to the Court. The Court conducted another status conference on June 19, 2008. The parties have submitted a revised discovery schedule for the Court's consideration. Fact and expert discovery is to be completed by February 27, 2009. No trial date has been set.

(iv) Apotex

In May 2008, Shire was notified that Apotex Inc. had submitted an ANDA under the Hatch-Waxman Act seeking permission to market its generic version of carbamazepine extended release products in 100mg, 200mg and 300mg prior to the expiration date of the '013 and the '570 Patents. On July 2, 2008, Shire filed a lawsuit in the U.S. District Court for the Eastern District of Texas against Apotex Inc., Apotex Corp. and Apotex Pharmaceutical Holdings Inc. (collectively; "Apotex") alleging infringement of the '013 and '570 Patents by Apotex ANDA and ANDA products. On July 17, 2008 Apotex Inc. filed a declaratory judgment complaint against Shire for noninfringement and invalidity of the '570 and '013 patents in the District of New Jersey. In a December 28, 2008 decision the Texas Court transferred the case to New Jersey.

(v) Actavis

Shire has been notified that Actavis South Atlantic LLC has submitted an ANDA under the Hatch-Waxman Act seeking permission to market its generic version of carbamazepine extended release products in 200mg and 300mg strengths prior to the expiration date of the '013 and the '570 Patents. On July 24, 2008, Shire filed a lawsuit in the U.S. District Court for the Eastern District of Texas against Actavis South Atlantic LLC and Actavis Inc. (collectively "Actavis") alleging infringement of the '013 and '570 Patents by the Actavis ANDA and ANDA products. By an Order dated December 30, 2008 the judge in the Texas case *sua sponte* transferred the case to the District Court of New Jersey. The litigation was settled on February 20, 2009. No payments to Actavis are involved in the settlement. As required by law, Shire will submit to the US Federal Trade Commission ("FTC") and the US Department of Justice ("DOJ") all of the agreements entered into as part of this settlement.

REMINYL

On January 29, 2008 Generics UK Ltd commenced a rectification action in the UK seeking a declaration that the duration of the Supplementary Protection Certificate ("SPC") for EP 236684, the patent that claims the use of

galantamine for the treatment of Alzheimer's disease, is zero (ie the period of exclusivity conferred by the patent has already expired). This SPC represents the primary patent protection for REMINYL in the EU. The current term of the SPC extension runs to January 2012. Absent the SPC extension, the patent would have expired in January 2007. REMINYL is entitled to ten years data exclusivity in the UK, which will not expire until March 2010. A trial was held on December 10, 2008. No decision has been rendered to date.

FOSRENOL

In February 2009, Shire received three Paragraph IV Notice letters, from Barr, Mylan and NATCO related to ANDA's for generic versions of 500mg, 750mg and 1,000mg FOSRENOL. Shire is currently reviewing the details of these notice letters and, under the Hatch-Waxman regulations, has 45 days from the date of each notice letter to determine if it will file a patent infringement suit. If Shire brings suit pursuant to the Hatch-Waxman regulations, a 30 month stay of approval, commencing on October 26, 2009, will be imposed on the FDA on each ANDA which is the subject of such a lawsuit.

VYVANSE

On February 24, 2009 Actavis Elizabeth LLC brought a lawsuit against the FDA seeking to overturn the FDA's decision granting new chemical entity exclusivity to VYVANSE. Shire believes the FDA's decision was correct. VYVANSE has new chemical entity exclusivity through February 23, 2012 and patents listed in the Orange Book which expire on June 29, 2023.

Appraisal Rights

In connection with Shire's merger with TKT, former holders of approximately 11.7 million shares of TKT common stock submitted written demands to the Delaware Court of Chancery for appraisal of those shares and, as a result, elected not to accept the \$37 per share merger consideration. On October 10, 2005 at the request of one of the holders to tender 365,000 shares at the merger price of \$37 per share, TKT filed a motion to dismiss the holder's demand. On October 12, 2005 the Delaware Court of Chancery granted this motion, and the holder tendered the shares at the merger consideration of \$37 per share. Therefore, during 2008 former holders of approximately 11.3 million shares of TKT common stock maintained written demands for appraisal of these shares and had elected not to accept the \$37 merger consideration. In November 2005, the Delaware Court of Chancery approved a stipulated consolidation order whereby actions brought by all petitioners were consolidated as one case.

Such former holders were entitled to receive the fair value of these shares as determined by the Delaware Court of Chancery. The determination of fair value is made excluding any element of value arising from the transaction, such as cost savings or business synergies. The Delaware Court of Chancery can ascribe a valuation to shares that is greater than, less than or equal to the merger price and may award interest on the amount determined in the appraisal process.

On March 8, 2007 certain of the former TKT shareholders who previously asserted appraisal rights in connection with the Shire/TKT merger filed a second suit in the Delaware Chancery Court alleging, among other claims, breaches of fiduciary duty by TKT and certain members of its board in connection with the merger with Shire. Shire and TKT have been named as defendants as are four former directors of TKT. The new complaint asserted a claim that the merger itself was not properly approved by a majority of the outstanding stock of TKT entitled to vote. The complaint sought rescissory damages with interest, attorneys' fees and costs. In January 2008 Shire and three of the other defendants (former TKT directors) filed a motion for summary judgment in respect of the five counts included in the second suit. In June 2008 the Court granted the motion in full with respect to the three other defendants and in part with respect to Shire. The remaining counts of the second suit relate to alleged breaches of fiduciary duty by Dr. Dennis Langer (a former TKT director) and Shire as well as the claim that the merger was not properly approved.

On November 5, 2008 Shire announced that it had successfully settled all aspects of this litigation with all parties. Shire paid the same price of \$37 per share originally offered to all TKT shareholders at the time of the July 2005 merger, plus interest. The Delaware Chancery Court approved dismissal of the case and Shire made payment to the dissenting shareholders on November 7, 2008. The settlement represents a total payment of \$567.5 million, representing consideration at \$37 per share of \$419.9 million and an interest cost of \$147.6 million.

Prior to reaching this settlement, the Company accrued interest based on a reasonable estimate of the amount that may be awarded by the Court to those former TKT shareholders who requested appraisal. This estimate of interest was based on Shire's cost of borrowing. Between the close of the merger and November 5, 2008 the Company applied this interest rate on a quarterly compounding basis to the \$419.9 million of consideration to calculate its provision for interest.

Upon reaching agreement in principle with all the dissenting shareholders, the Company determined that settlement had become the probable manner through which the appraisal rights litigation would be resolved. Under current law, (although not applicable in this case because the merger was entered into before the relevant amendment to the law

became effective) the court presumptively awards interest in appraisal rights cases at a statutory rate that is 5 percentage points above the Federal Reserve discount rate (as it varies over the duration of the case). In connection with the settlement, the Company agreed to an interest rate that approximates to this statutory rate. Based on the settlement, the Company amended the method of determining its interest provision to reflect this revised manner of resolution, and recorded additional interest expense of \$73.0 million in its consolidated financial statements for the year to December 31, 2008 on reaching settlement with the dissenting shareholders.

The interest cost of \$147.6 million has been recorded as interest expense in the Company's statement of operations since the time of the merger, including \$87.3 million recorded in the year to December 31, 2008 (2007: \$28.0 million; 2006: \$24.6 million), inclusive of the additional charge for interest recorded on reaching settlement with the dissenting shareholders.

Class Action Shareholder Suit

In January and February 2003, various parties filed purported securities fraud class action lawsuits against TKT and Richard Selden, TKT's former Chief Executive Officer, in the United States District Court for the District of Massachusetts. In April 2003, the Court appointed a Lead Plaintiff and Lead Counsel and consolidated the various matters under one matter: *In re Transkaryotic Therapies, Inc., Securities Litigation*, C.A. No. 03-10165-RWZ.

In July 2003, the plaintiffs filed a Consolidated and Amended Class Action Complaint (the "Amended Complaint") against TKT; Dr Selden; Daniel Geffken, TKT's former Chief Financial Officer; Walter Gilbert, Jonathan S. Leff, Rodman W. Moorhead, III, and Wayne P. Yetter, then members of TKT's board of directors; William R. Miller and James E. Thomas, former members of TKT's board of directors; and SG Cowen Securities Corporation, Deutsche Bank Securities Inc., Pacific Growth Equities, Inc. and Leerink Swann & Company, underwriters of TKT's common stock in prior public offerings.

The Amended Complaint alleged that the defendants made false and misleading statements and failed to disclose material information concerning the status and progress for obtaining United States marketing approval of REPLAGAL during the period between January 4, 2001 and January 10, 2003. The Amended Complaint asserted claims against Dr. Selden and TKT under Section 10(b) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder; and against Dr. Selden under Section 20(a) of the Exchange Act. The Amended Complaint also asserted claims based on TKT's public offerings of June 29, 2001, December 18, 2001 and December 26, 2001 against each of the defendants under Section 11 of the Securities Act of 1933 and against Dr. Selden under Section 15 of the Securities Act; and against SG Cowen Securities Corporation, Deutsche Bank Securities Inc., Pacific Growth Equities, Inc. and Leerink Swann & Company under Section 12(a) (2) of the Securities Act. The plaintiffs sought equitable and monetary relief, an unspecified amount of damages, with interest, and attorneys' fees and costs.

In May 2004, the Court granted in part and denied in part TKT's motion to dismiss. In particular, the Court dismissed allegations against TKT to the extent they arose out of certain forward-looking statements protected by the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 and dismissed claims based on the public offerings of June 29, 2001 and December 18, 2001. The Court allowed all other allegations to remain. In July 2004, the plaintiffs voluntarily dismissed all claims based on the third public offering dated December 26, 2001.

In November 2005, the Court granted the plaintiffs' motion for class certification. On May 23, 2005, the Court entered judgment on all claims alleged against SG Cowen Securities Corporation, Deutsche Bank Securities Inc., Pacific Growth Equities, Inc. and Leerink Swann & Company. On June 5, 2006, the Court entered judgment on all claims alleged against Messrs. Gilbert, Leff, Moorhead, Yetter, Miller, and Thomas. On November 9, 2006, Mr. Geffken filed an Agreement for Judgment on all claims alleged against him. On September 1, 2007 the SEC filed suit against Dr Selden. The case is entitled *Securities and Exchange Commission v. Richard F Selden*, Civil Action No. 05-11805-NMG (D. Mass.) ("the SEC Action"). On July 10, 2008 the Court entered a final judgment against Selden which permanently enjoins him from violating the anti-fraud and other provisions of the federal securities laws, and orders him to pay approximately \$1.2 million in penalties.

In October 2007, the parties reached an agreement in principle to resolve the Class Action Shareholder Suit, subject to Court approval, for \$50 million. In February 2008 the US District Court for the District of Massachusetts granted preliminary approval to the settlement. Shire contributed \$27 million towards the settlement and its insurance companies contributed the remaining \$23 million. The settlement was approved by the Court on June 11, 2008. Distribution of funds under the approved settlement is expected to occur in the first quarter of 2009.

24. Shareholders' equity

Reduction of Capital and Distributable Reserves

On June 11, 2008 the Jersey Court approved a reduction of Shire plc's share capital to take effect on June 12, 2008 (see Note 3). The reduction increased the distributable reserves potentially available to Shire plc at the time of reduction to approximately \$3.7 billion by recharacterizing amounts standing to the credit of Shire plc's share premium

account as a distributable reserve. The purpose of the reduction of capital is to create a distributable reserve which would be available to be distributed as dividends, at the discretion of the Directors of Shire plc, from time to time or for any other lawful purpose to which such a reserve may be applied (including share buy backs). The reduction of capital was designed to create in Shire plc a level of distributable reserves similar to that previously available in Old Shire, (see Note 3) and to enable Shire plc to continue Shire's existing dividend policy in a financially and operationally efficient manner.

Income Access Share Arrangements

Shire has put into place income access share arrangements which enable Shire plc ordinary shareholders, other than Shire plc ADS holders, to elect to receive their dividends from a company resident for tax purposes in the Republic of Ireland or receive their dividends under the income access share arrangements from a Shire Group company resident for tax purposes in the UK.

Old Shire has issued one income access share which is held by the income access share trustee pursuant to the income access share trust. The income access share trust is constituted pursuant to a trust deed which provides that (*inter alia*):

(i) the income access share trustee will hold any dividends paid (not just declared) on the income access share on trust for the Shire plc ordinary shareholders who have elected (or are deemed to have elected) to receive dividends pursuant to these arrangements;

(ii) the income access share itself will be held on trust for Shire plc; and

(iii) each registered holder of Shire plc ordinary shares on a dividend record date who has made (or is deemed to have made) a valid income access share election (described below) will be entitled to receive from the income access share trustee an amount equal to the dividend it would have received from Shire, to the extent the income access share trustee has actually received an amount equal to such amount by way of dividend from Old Shire.

To ensure compliance with technical trust law rules, the period during which the income access share trust may continue will be restricted. However, the income access share trust should be able to continue for 80 years.

This mechanism is reflected in the articles of association of both Shire plc and Old Shire that the mechanics of the arrangements will be as follows:

The Shire plc articles of association provide that if (i) a dividend is announced or declared by Shire plc on the Shire plc ordinary shares, (ii) an amount is paid by Old Shire by way of a dividend on the income access share to the income access share trustee, and (iii) such amount is paid by the income access share trustee to the Shire plc ordinary shareholders who have elected (or are deemed to have elected) to receive dividends under these arrangements, the dividend which would otherwise be payable by Shire plc to such Shire plc ordinary shareholders will be reduced by an amount equal to the amount paid to such Shire plc ordinary shareholders by the income access share trustee.

If the dividend paid on the income access share and on-paid by the income access share trustee to the Shire plc ordinary shareholders is less than the total amount of the dividend announced or declared by Shire plc on the Shire plc ordinary shares in respect of which an election has been made (or is deemed to have been made) to receive dividends under these arrangements, Shire plc will be obliged to pay a dividend on the Shire plc ordinary shares to those Shire plc ordinary shareholders who have so elected (or are deemed to have so elected) of the amount of the shortfall. In such a case, any dividend paid on the Shire plc ordinary shares will generally be subject to Irish withholding tax at the rate of 20% or such lower rate as may be applicable under exemptions from withholding tax contained in Irish law.

A Shire plc ordinary shareholder is entitled to make an income access share election such that he will receive his dividends (which would otherwise be payable by Shire plc) under these arrangements from Old Shire.

A Shire plc ordinary shareholder who held 25,000 or fewer Shire plc ordinary shares at the time he became a Shire plc ordinary shareholder pursuant to the Scheme of Arrangement, and who did not make a contrary election, is deemed to have made an election (pursuant to the Shire plc articles of association) such that he will receive his dividends under these arrangements from Old Shire.

Equally, where a Shire plc ordinary shareholder who first acquires his Shire plc ordinary shares after the date of the Scheme of Arrangement, who holds 25,000 or fewer Shire plc ordinary shares on the first dividend record date after he becomes a Shire plc ordinary shareholder, and who does not make a contrary election, will be deemed to have made an election (pursuant to the Shire plc articles of association) such that he will receive his dividends under these arrangements from Old Shire.

In accordance with the provisions of the Shire plc ADS deposit agreement, the Depositary has made an election on behalf of all holders of Shire plc ADSs such that they will receive dividends from Old Shire under the income access share arrangements. Dividends paid by Old Shire under the income access share arrangements will not under current legislation be subject to any UK or Irish withholding taxes. If a holder of Shire plc ADSs does not wish to receive

dividends from Old Shire under the income access share arrangements, he must withdraw his Shire plc ordinary shares from the Shire ADS program prior to the dividend record date set by the Depositary and request delivery of the Shire plc ordinary shares. This will enable him to receive dividends from Shire plc (if necessary, by making an election to that effect).

It is the expectation, although there can be no certainty, that dividends will be paid by Old Shire through the income access share trustee to Shire plc ordinary shareholders who make (or are deemed to make) an income access share election.

It is the expectation, although there can be no certainty, that Old Shire will distribute dividends on the income access share to the income access share trustee for the benefit of all Shire plc ordinary shareholders who make (or are deemed to make) an income access share election in an amount equal to what would have been such Shire plc ordinary shareholders' entitlement to dividends from Shire plc in the absence of the income access share election. To the extent that any dividend paid on the income access share to the income access share trustee and on-paid by the income access share trustee to the Shire plc ordinary shareholders is less than an amount equal to what would have been such Shire plc ordinary shareholders' entitlement to dividends from Shire plc in the absence of the income access share election, the dividend on the income access share received by the income access share trustee will be allocated pro rata to such Shire plc ordinary shareholders and Shire plc will pay the balance by way of dividend. In such circumstances, there will be no grossing up by Shire plc in respect of, and Old Shire and Shire plc will not compensate those Shire plc ordinary shareholders for, any adverse consequences including any Irish withholding tax consequences.

Shire plc will be able to suspend or terminate these arrangements at any time, in which case the full Shire plc dividend will be paid directly by Shire plc to those Shire plc ordinary shareholders (including the Depositary) who have made (or are deemed to have made) an income access share election. In such circumstances, there will be no grossing up by Shire plc in respect of, and Old Shire and Shire plc will not compensate those Shire plc ordinary shareholders for, any adverse consequences including any Irish withholding tax consequences.

On October 7, 2008 Old Shire paid dividends totalling \$7.2 million on the income access share to the income access share trustee in an amount equal to the dividend Shire plc ordinary shareholders would have received from Shire plc.

The consolidated financial statements of the Income Access Share Trust can be found on pages F-82 to F-87 of this Form 10-K.

Exchangeable shares

On February 12, 2008 a subsidiary of Shire exercised a redemption call right and purchased all remaining exchangeable shares of Shire Acquisition Inc. ("SAI") in public ownership. Exchangeable shareholders received either three ordinary shares of Shire plc or one Shire ADS representing three ordinary shares of Shire plc for each Exchangeable Share held. Exchangeable Shares were issued to Canadian resident shareholders of Biochem Pharma Inc. (now Shire Canada, Inc.) in 2001 as consideration for the acquisition by the Shire group of Biochem Pharma Inc. The Exchangeable Shares have now been de-listed from the Toronto Stock Exchange.

Authorized common stock

The authorized stock of Shire plc as at December 31, 2008 was 1,000,000,000 ordinary shares and 2 subscriber ordinary shares.

On February 20, 2007 the Company raised \$877.3 million, net of associated issue costs, through the private placement of 42.9 million new ordinary shares to certain institutional investors at a price of 1075 pence per share. The newly issued shares represent approximately 8.4 per cent of Shire plc's issued ordinary share capital prior to the placing.

Dividends

Under Jersey law, Shire plc is entitled to make payments of dividends from its accumulated profits and other distributable reserves. At December 31, 2008 Shire plc's distributable reserves were approximately \$3.7 billion.

Treasury stock

The Company records the purchase of its own shares by the ESOT as a reduction of shareholders' equity based on the price paid for the shares. At December 31, 2008, the ESOT held 7.3 million ordinary shares and 4.5 million ADSs. During the period to December 31, 2008 a total of 0.2 million (2007: 3.0 million) ordinary shares and 2.8 million (2007: 1.8 million) ADSs had been purchased for total consideration of \$146.6 million (2007: \$186.0 million), including stamp duty and broker commission.

25. Related parties

Xanodyne Pharmaceuticals Inc.

In October 2005, the Company sub-leased its office premises in Newport to Xanodyne Pharmaceuticals Inc. Dr James Cavanaugh, the Non-Executive Chairman of the Company, was the Chairman of the Board of Directors of Xanodyne Pharmaceuticals, Inc. up to February 9, 2007 and remains a Board Director. As a result of the transaction the Company will receive \$7.8 million (net of inducements) in lease income over the sub-lease period from Xanodyne Pharmaceuticals Inc.

26. Earnings per share

The following table reconciles income/(loss) from continuing operations and the weighted average ordinary shares outstanding for basic and diluted earnings/(loss) per share for the periods presented:

Year to December 31,

	2008 \$'M	2007 \$'M	2006 \$'M
Income/(loss) from continuing operations	173.6	(1,451.8)	237.6
(Loss)/gain from discontinued operations, net of tax	(17.6)	-	40.6
Numerator for basic and diluted earnings per share	156.0	(1,451.8)	278.2

Year to December 31,

	2008 No. of shares Millions	2007 No. of shares Millions	2006 No of shares Millions
Weighted average number of shares outstanding	541.6	540.3	503.4
Basic ⁽¹⁾	541.6	540.3	503.4
Effect of dilutive shares:			
Share options ⁽²⁾	3.8	-	5.3
Warrants ⁽²⁾	-	-	0.6
	3.8	-	5.9
Diluted	545.4	540.3	509.3

(1) Excludes shares purchased by the ESOT and presented by the Company as treasury stock.

(2) Calculated using the treasury stock method.

	2008	2007	2006
Basic earnings per share:			
Income/(loss) from continuing operations	32.1c	(268.7c)	47.2c
(Loss)/gain from discontinued operations	(3.3c)	-	8.1c
	<u>28.8c</u>	<u>(268.7c)</u>	<u>55.3c</u>
Diluted earnings per share:			
Income/(loss) from continuing operations	31.8c	(268.7c)	46.6c
(Loss)/gain from discontinued operations	(3.2c)	-	8.0c
	<u>28.6c</u>	<u>(268.7c)</u>	<u>54.6c</u>

The share options, warrants and the number of ordinary shares underlying the convertible bond not included in the calculation of the diluted weighted average number of shares are shown below:

	⁽¹⁾ ⁽²⁾ 2008	⁽³⁾ 2007	⁽²⁾ 2006
	No. of shares Millions	No. of shares Millions	No. of shares Millions
Stock options in the money	-	8.4	-
Stock options out of the money	17.3	2.9	7.7
Warrants	-	0.3	-
Convertible bonds 2.75% due 2014	32.7	21.2	-

⁽¹⁾ In 2008 the convertible bonds were not included in the calculation of the diluted weighted average number of shares, because their effect would be anti-dilutive in the period.

⁽²⁾ In 2008 and 2006 certain stock options have been excluded from the calculation of diluted EPS because their exercise prices exceeded Shire plc's average share price during the calculation period.

⁽³⁾ In 2007 all share options, warrants and the number of ordinary shares underlying the convertible bonds were excluded from the calculation of the diluted weighted average number of shares, because the Company made a net loss during the calculation period and the effect of their inclusion would be anti-dilutive.

27. Segment reporting

SFAS No. 131, "Disclosures about Segments of an Enterprise and Related Information" ("SFAS No. 131") establishes standards for reporting information about operating segments and related disclosures, products and services, geographic areas and major customers. Operating segments are components of an enterprise about which separate financial information is available that is evaluated regularly by the chief operating decision-maker to decide how to allocate resources and to assess performance.

Shire's internal financial reporting is in line with a business unit and management reporting structure based on two segments: Specialty Pharmaceuticals and HGT.

The Specialty Pharmaceuticals and HGT operating segments represent the Company's revenues and costs in respect of currently promoted and sold products, together with the costs of developing projects for future commercialization. 'All Other' has been included in the table below in order to reconcile the two operating segments to the total consolidated figures.

The Company evaluates performance based on revenue and operating income. The Company does not have inter-segment transactions. Assets that are directly attributable to the segments have been separately disclosed.

2008	Specialty Pharmaceuticals	HGT	All Other	Total
	\$'M	\$'M	\$'M	\$'M
Product sales	2,272.5	481.7	-	2,754.2
Royalties	1.5	-	244.0	245.5
Other revenues	8.2	4.0	10.3	22.5
Total revenues	2,282.2	485.7	254.3	3,022.2
Cost of product sales ^{(1) (2)}	329.0	58.9	20.1	408.0
Research and development ^{(1) (2)}	318.9	201.7	6.0	526.6
Selling, general and administrative ^{(1) (2)}	1,087.6	171.3	164.0	1,422.9
IPR&D	-	263.1	-	263.1
Gain on sale of product rights	(20.7)	-	-	(20.7)
Integration costs	-	-	10.3	10.3
Total operating expenses	1,714.8	695.0	200.4	2,610.2
Operating income/(loss)	567.4	(209.3)	53.9	412.0
Total assets	2,161.2	1,107.7	664.8	3,933.7
Long-lived assets ⁽³⁾	192.2	263.5	82.1	537.8
Capital expenditure on long-lived assets ⁽³⁾	54.1	169.5	30.6	254.2

(1) Stock-based compensation of \$65.2 million is included in: Cost of product sales (\$3.9 million), Research and development (\$18.9 million) and Selling, general and administrative (\$42.4 million).

(2) Depreciation from manufacturing plants (\$16.2 million) and amortization of favorable manufacturing contracts (\$1.7 million) is included in Cost of product sales; depreciation of research and development assets (\$12.5 million) is included in Research and development; and all other depreciation, amortization and intangible asset impairment charges (\$271.9 million) are included in Selling, general and administrative.

(3) Long-lived assets comprise all non-current assets, (excluding goodwill and other intangible assets, deferred tax assets, investments and financial instruments) based on the geographic location within which the economic benefits arise.

2007	Specialty Pharmaceuticals \$'M	HGT \$'M	All Other \$'M	Total \$'M
Product sales	1,844.5	325.7	-	2,170.2
Royalties	1.6	-	245.6	247.2
Other revenues	9.5	4.3	5.1	18.9
Total revenues	1,855.6	330.0	250.7	2,436.3
Cost of product sales ^{(1) (2)}	263.3	44.3	12.7	320.3
Research and development ^{(1) (2)}	362.1	214.3	-	576.4
Selling, general and administrative ^{(1) (2)}	864.5	124.2	190.1	1,178.8
IPR&D	1,866.4	-	-	1,866.4
Gain on sale of product rights	(127.8)	-	-	(127.8)
Integration costs	1.3	-	-	1.3
Total operating expenses	3,229.8	382.8	202.8	3,815.4
Operating (loss)/income	(1,374.2)	(52.8)	47.9	(1,379.1)
Total assets	2,394.5	586.6	1,349.0	4,330.1
Long-lived assets ⁽³⁾	174.8	114.6	79.2	368.6
Capital expenditure on long-lived assets ⁽³⁾	37.3	77.5	27.9	142.7

(1) Stock-based compensation of \$75.2 million is included in: Cost of product sales (\$5.5 million), Research and development (\$17.0 million) and Selling, general and administrative (\$52.7 million).

(2) Depreciation from manufacturing plants (\$11.8 million) and amortization of favorable manufacturing contracts (\$1.2 million) is included in Cost of product sales, depreciation of research and development assets (\$11.3 million) is included in Research and development, and all other depreciation and amortization and intangible asset impairment charges (\$136.2 million) are included in Selling, general and administrative.

(3) Long-lived assets comprise all non-current assets, (excluding goodwill and other intangible assets, deferred tax assets, investments and financial instruments) based on the geographic location within which the economic benefits arise.

2006	Specialty Pharmaceuticals \$'M	HGT \$'M	All Other \$'M	Total \$'M
Product sales	1,394.5	141.3	-	1,535.8
Royalties	2.3	-	240.6	242.9
Other revenues	16.0	1.8	-	17.8
Total revenues	1,412.8	143.1	240.6	1,796.5
Cost of product sales ^{(1) (2)}	180.9	66.6	11.2	258.7
Research and development ^{(1) (2)}	275.8	109.6	-	385.4
Selling, general and administrative ^{(1) (2)}	675.8	113.1	137.7	926.6
Gain on sale of product rights	(63.0)	-	-	(63.0)
Integration costs	-	5.6	-	5.6
Total operating expenses	1,069.5	294.9	148.9	1,513.3
Operating income/(loss)	343.3	(151.8)	91.7	283.2
Total assets	1,168.9	547.4	1,610.1	3,326.4
Long-lived assets ⁽³⁾	160.8	63.9	80.5	305.2
Capital expenditure on long-lived assets ⁽³⁾	51.4	21.9	35.0	108.3

(1) Stock-based compensation of \$43.0 million is included in: Cost of product sales (\$3.2 million), Research and development (\$5.4 million) and Selling, general and administrative (\$34.4 million).

(2) Depreciation from manufacturing plants (\$9.4 million) is included in Cost of product sales, depreciation of research and development assets (\$4.9 million) is included in Research and development, and all other depreciation and amortization and intangible asset impairment charges (\$93.1 million) are included in Selling, general and administrative.

(3) Long-lived assets comprise all non-current assets, (excluding goodwill and other intangible assets, deferred tax assets, investments and financial instruments) based on the geographic location within which the economic benefits arise.

Geographic Information

Revenues (based on the geographic location from which the sale originated):

Year to December 31,	2008 \$'M	2007 \$'M	2006 \$'M
Ireland	17.8	16.2	13.8
United Kingdom	160.0	177.0	187.5
North America	2,299.6	1,798.2	1,341.0
Rest of World	544.8	444.9	254.2
Total	3,022.2	2,436.3	1,796.5

Long-lived assets comprise all non-current assets, (excluding goodwill and other intangible assets, deferred tax assets, investments and financial instruments) based on the geographic location within which the economic benefits arise:

Year to December 31,	2008 \$'M	2007 \$'M
Ireland	1.0	1.4
United Kingdom	61.6	68.8
North America	468.6	294.8
Rest of World	6.6	3.6
Total	537.8	368.6

Material customers

In the periods set out below, certain customers, all within the Specialty Pharmaceuticals operating segment, accounted for greater than 10% of the Company's total revenues:

Year to December 31,	2008 \$'M	2008 % revenue	2007 \$'M	2007 % revenue	2006 \$'M	2006 % revenue
Cardinal Health Inc.	888.7	29	666.1	27	512.1	29
McKesson Corp.	674.3	22	546.0	22	338.6	19

Amounts outstanding as at December 31, in respect of these material customers were as follows:

December 31,	2008 \$'M	2007 \$'M
Cardinal Health Inc.	72.3	102.9
McKesson Corp.	69.6	79.6

Revenues by product

In the periods set out below, revenues by major product were as follows:

	2008 \$'M	2007 \$'M	2006 \$'M
Specialty Pharmaceuticals			
ADDERALL XR	1,101.7	1,030.9	863.6
CALCICHEW	52.8	54.2	45.5
CARBATROL	75.9	72.3	68.3
DAYTRANA	78.7	64.2	25.1
FOSRENOL	155.4	102.2	44.8
LIALDA / MEZAVANT	140.4	50.5	-
PENTASA	185.5	176.4	137.8
REMINYL/REMINYL XL	34.4	31.2	21.5
VYVANSE	318.9	76.5	-
XAGRID	78.7	66.8	53.3
Other	50.1	119.3	134.6
	<u>2,272.5</u>	<u>1,844.5</u>	<u>1,394.5</u>
Human Genetic Therapies			
ELAPRASE	305.1	181.8	23.6
FIRAZYR	0.5	-	-
REPLAGAL	176.1	143.9	117.7
	<u>481.7</u>	<u>325.7</u>	<u>141.3</u>
	<u>2,754.2</u>	<u>2,170.2</u>	<u>1,535.8</u>

28. Interest expense

Interest expense for the years to December 31, 2008, 2007 and 2006 was \$139.0 million, \$70.8 million and \$26.4 million respectively. Included in the amount for the year to December 31, 2008 is \$87.3 million (2007: \$28.0 million and 2006: \$24.6 million) in respect to the TKT appraisal rights litigation. For further details on this litigation see Note 23.

29. Other (expense)/income, net

Year to December 31,	2008 \$'M	2007 \$'M	2006 \$'M
Impairment of long-term investments (see Note 12)	(58.0)	(3.0)	(2.1)
GeneChem Funds management fee	1.9	3.6	4.6
Gain on sale of available-for-sale security (see Note 12)	9.4	0.1	-
Foreign exchange	14.1	(0.8)	3.2
Other	(0.3)	1.3	3.8
	<u>(32.9)</u>	<u>1.2</u>	<u>9.5</u>

30. Retirement benefits

(a) *Personal defined contribution pension plans*

The Company makes contributions to defined contribution retirement plans that together cover substantially all employees. The level of the Company's contribution is fixed at a set percentage of employee's pay.

Company contributions to personal defined contribution pension plans totaled \$26.3 million, \$22.3 million and \$15.0 million for the years to December 31, 2008, 2007 and 2006, respectively, and were charged to operations as they became payable.

Defined benefit pension plans

(i) The Roberts SERP

The Roberts SERP is for some US employees of Roberts Pharmaceutical Corporation ("Roberts") who met certain age and service requirements. Shire acquired Roberts in 1999, and the plan was discontinued in 2000. There were no contributions payable by the Company in respect of 2008, 2007 or 2006. In 1999, the Company paid a lump sum of \$18.0 million into the Roberts SERP, which was accounted for as a fair value adjustment, on the acquisition of Roberts to make good the deficit on this scheme at the time of acquisition. This lump sum payment has led to the Company having no future liability under the SERP, which is closed to new members with contributions no longer payable by existing members. Assets are set aside to fund these benefits in a "Rabbi Trust". The legal form of the trust is such that the assets held to cover the pension liabilities are available to the general creditors of the Company on winding up. Accordingly, the assets held by the trust are not plan assets and are recorded on the balance sheet.

In accordance with EITF 97-14, "Accounting for Deferred Compensation Arrangements Where Amounts Earned Are Held in a Rabbi Trust and Invested" the assets and liabilities of \$7.2 million and \$1.9 million, respectively, are shown on the balance sheet within the categories "Other current assets", "Other current liabilities" and "Other non-current liabilities".

(ii) The Shire SERP

The Shire SERP defined benefit scheme is an unfunded arrangement; the benefits are payable to certain senior US employees as lump sums on leaving the Company's employment or earlier due to death, disability or termination. The amount of benefit is based on the value of notional contributions increased with "earned" investment returns as if they were invested in investments of the employees' choice. The entire benefit liability has been recognized on the balance sheet.

31. Income taxes

The components of pre tax income/(loss) from continuing operations are as follows:

Year to December 31,

	2008	2007	2006
	\$'M	\$'M	\$'M
UK	39.2	94.7	20.5
US	238.7	27.6	(28.3)
Republic of Ireland	(83.5)	(99.5)	(69.0)
IPR&D	(263.1)	(1,866.4)	-
Other jurisdictions	334.3	445.5	393.6
	<u>265.6</u>	<u>(1,398.1)</u>	<u>316.8</u>

The provision/(benefit) for income taxes by location of the taxing jurisdiction for the years to December 31, consisted of the following:

Year to December 31,

	2008	2007	2006
	\$'M	\$'M	\$'M
Current income taxes:			
UK corporation tax	0.3	20.3	7.0
US federal tax	12.0	84.5	6.1
US state and local taxes	6.4	4.9	3.8
Republic of Ireland	-	0.2	(1.8)
Other	(10.8)	24.8	211.8
Total current taxes	<u>7.9</u>	<u>134.7</u>	<u>226.9</u>
Deferred taxes			
UK corporation tax	29.8	14.4	(81.0)
US federal tax	75.2	(91.4)	(57.8)
US state and local taxes	(17.2)	(5.2)	0.2
Republic of Ireland	(1.3)	9.1	(7.0)
Other	3.6	(6.1)	3.6
Total deferred taxes	<u>90.1</u>	<u>(79.2)</u>	<u>(142.0)</u>
Total income taxes ⁽¹⁾	<u>98.0</u>	<u>55.5</u>	<u>84.9</u>

⁽¹⁾ Total income taxes relate solely to continuing operations as there is no tax provision/(benefit) relating to discontinued operations for the years to December 31, 2008, 2007 or 2006

The reconciliation of income/(loss) from continuing operations before income taxes, minority interests and equity in earnings of equity method investees and discontinued operations to the provision for income taxes is shown in the table below:

Year to December 31,

	2008	2007	2006
	\$'M	\$'M	\$'M
Income/(loss) from continuing operations before income taxes, minority interests and equity in earnings of equity method investees and discontinued operations	265.6	(1,398.1)	316.8
Group tax rate ⁽¹⁾⁽²⁾	<u>25.0%</u>	<u>30.0%</u>	<u>30.0%</u>
Adjustments to derive effective rate:			
Non-deductible items:			
IPR&D	12.1%	(40.0%)	-
Permanent differences	(7.6%)	6.6%	(18.8%)
Other items:			
Change in valuation allowance	7.0%	0.3%	(30.0%)
Difference in taxation rates	3.1%	1.3%	(9.3%)
Change in provisions for uncertain tax positions ⁽³⁾	1.9%	(2.7%)	59.8%
Prior year adjustment	(9.2%)	0.8%	(6.5%)
Change in tax rates	(0.2%)	(0.5%)	-
Other	4.8%	0.2%	1.6%
Provision for income taxes on continuing operations	<u>36.9%</u>	<u>(4.0%)</u>	<u>26.8%</u>

⁽¹⁾ In addition to being subject to the Irish Corporation tax rate of 25% (2007 and 2006: UK Corporation tax rate of 30%), in 2008 the Company is also subject to income tax in other territories in which the Company operates, including: Canada (19.5%); France (33.3%); Germany (15%); Italy (27.5%); Malta (35%); the Netherlands (25.5%); Spain (30%); Sweden (28%); Switzerland (8.5%); United Kingdom (28.5%) and the US (35%). The rates quoted represent the headline federal income tax rates in each territory, and do not include any state taxes or equivalents or surtaxes or other taxes charged in individual territories, and do not purport to represent the effective tax rate for the Company in each territory.

⁽²⁾ During 2008 Shire introduced a new holding company resident in the Republic of Ireland, as a result the reconciliation of income from continuing operations before income taxes, minority interests and equity in earnings of equity method investees for the year to December 31, 2008 has been prepared using the Irish non-trading corporation tax rate of 25% which is the rate applicable to Shire plc. In prior reporting periods, the reconciliation of income from continuing operations before income taxes, minority interests and equity in earnings of equity method investees was prepared using the UK corporation tax rate of 30%.

⁽³⁾ The Company prospectively adopted FIN 48 from January 1, 2007. For the year ended December 31, 2006 the measurement and disclosure of changes in uncertain tax positions in the rate reconciliation has been determined in accordance with FAS No. 5. The change in provision for uncertain tax positions as disclosed in the above rate reconciliation includes interest and penalties associated with uncertain tax positions.

IPR&D

IPR&D charges arising on the acquisition of Jerini in 2008 (\$128.1 million), and New River in 2007 (\$1,866.4 million) are not tax deductible, and have resulted in significant fluctuations in the effective rate of tax for the years to December 31, 2008 and 2007. Tax deductions in respect of IPR&D for METAZYM acquired from Zymenex (\$135.0 million) are available but have not yet been recognized at 31 December 2008, as recognition is dependent upon projections of future earnings.

Permanent differences

Permanent differences decreased the effective tax rate by 7.6% or \$20.2 million in the year to December 31, 2008 (2007: increased by 6.6% or \$92.4 million; 2006: decreased by 18.8% or \$59.6 million). These permanent differences are composed of recurring items such as the tax effect of Shire's convertible bonds; research and development tax credits; and tax deductible amortization for which the recognition of a deferred tax asset is precluded by FAS 109. Other significant permanent differences over the period 2006 to 2008 include: the tax free gain on disposal of certain product rights in 2007 and non taxable capital receipts following an internal reorganization in 2005.

Permanent differences have decreased by \$72.2 million between 2008 and 2007 primarily due to non-taxable gains related to the sale of certain non-core product rights of \$114.8 million recognized in the fourth quarter of 2007 which

were not repeated in 2008, together with the other than temporary impairment charge on available-for-sale securities of \$58.0 million during 2008.

Change in valuation allowances

The net increase in valuation allowances of \$14.5 million in 2008 (\$4.7 million reduction in 2007) is principally due to an increase of \$20.3 million in respect of losses and other timing differences in European jurisdictions, as insufficient future taxable income to overcome cumulative losses led the Company's management to maintain the position taken in the fourth quarter of 2007 that it was more likely than not that the relevant deferred tax assets would not be realized. This is partially offset by a reversal of \$5.7 million of valuation allowances in place at January 1, 2008 in North America as a result of several factors including a U.S. State tax law change enacted in the fourth quarter of 2008, which led the Company's management to determine that it was now more likely than not that the relevant tax attributes would be realized.

The net reduction in valuation allowances of \$4.7 million in 2007 is principally due to a reversal of \$14.9 million of valuation allowances in place at January 1, 2007 in a European tax jurisdiction as a result of a law change enacted in the fourth quarter of 2007, which led the Company's management to determine that it was now more likely than not that the relevant tax loss carry-forwards would be realized, and utilization of a valuation allowance of \$10.9 million in another jurisdiction. This is partially offset by recognition of a valuation allowance totalling \$22.0 million in respect of losses in another European jurisdiction, as insufficient future taxable income to overcome cumulative losses led the Company's management to determine in the fourth quarter of 2007 that it was now more likely than not that the relevant tax loss carry-forwards would not be realized.

The change in valuation allowances in the year to December 31, 2006 included a reversal in the fourth quarter of \$120 million of valuation allowances in place at January 1, 2006 of which \$97 million related to the UK, \$8 million to the US and \$15 million to certain European affiliates. The Company recognized the reversal of these valuation allowances primarily following the implementation of tax planning strategies during the fourth quarter of the year to December 31, 2006 and revisions to projections of future earnings in certain European jurisdictions, which led the Company's management to determine that it was now more likely than not that the relevant tax loss carry-forwards would be realizable. The valuation allowances were not reversed until the fourth quarter of 2006 as the predominant tax planning strategies which triggered the recognition of the reversals were either not in place or did not provide a prudent and feasible source of taxable income until the fourth quarter. Prior to the reversal of these valuation allowances, the Company had determined that it was more likely than not that the related deferred tax assets would not be realized, primarily as a result of insufficient future taxable income being available to overcome cumulative losses.

Realization of deferred tax assets is dependent upon generating sufficient taxable income to utilize such assets. Although realization of these assets is not assured, the Company believes it is more likely than not that the amount recognized will be realized.

Change in provisions for uncertain tax positions

The Company adopted the provisions of FIN 48 on January 1, 2007. There was no cumulative effect adjustment to the opening balance of retained earnings arising as a result of the adoption of FIN 48.

The Company files income tax returns in the UK, the US (both federal and state) and various other jurisdictions (see footnote (1) to the table above for major jurisdictions). With few exceptions, the Company is no longer subject to income tax examinations by tax authorities for years before 1999. Tax authorities in various jurisdictions are in the process of auditing the Company's tax returns for fiscal periods from 1999; these tax audits cover a range of issues, including transfer pricing, potential restrictions on the utilization of net operating losses, potential taxation of overseas dividends and controlled foreign companies rules.

During the year to December 31, 2008 changes in the Company's provision for unrecognized tax benefits increased the effective rate by 1.9% or \$5.1 million (2007: 2.7%, or \$38.1 million), which relates to a decrease of \$21.0 million in the provision for unrecognized tax benefits offset by an increase of \$26.1 million for interest and penalties (2007: \$20.1 million increase in unrecognized tax benefits and \$18.0 million increase in interest and penalties).

During the year to December 31, 2007 changes in the Company's provision for unrecognized tax benefits reduced the effective rate by 2.7%, or \$38.1 million, which relates to an increase in the provision for unrecognized tax benefits of \$20.1 million and an increase in the provision for interest and penalties of \$18.0 million. The increase in the provision for unrecognized tax benefits of \$20.1 million was due to additional provisions of \$58.4 million recognized in relation to potential transfer pricing adjustments, the deductibility of expenses and availability of certain tax reliefs, which was partially offset by a reduction in the provision as a result of expiration of the statute of limitations of \$38.3 million.

The Company considers it reasonably possible that the total amount of unrecognized tax benefits recorded at December 31, 2008 could decrease by approximately \$11.6 million (2007: \$40.0 million) in the next twelve months. While tax audits remain open, the Company also considers it reasonably possible that issues may be raised by tax authorities resulting in increases to the balance of unrecognized tax benefits, however an estimate of such an increase cannot be made.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	2008	2007
	\$'M	\$'M
Balance at January 1	292.2	234.4
Increases based on tax positions related to the current year	30.5	25.6
Reductions based on tax positions taken in the current year	-	(12.5)
Increases for tax positions taken in prior years	3.9	51.7
Reductions for tax positions taken in prior years ⁽¹⁾	(17.4)	(10.4)
Decreases resulting from settlements with the taxing authorities	(16.6)	-
Reductions as a result of expiration of the statute of limitations	(13.8)	(38.3)
Foreign currency translation adjustments ⁽²⁾	(50.1)	41.7
Balance at December 31 ⁽³⁾	<u>228.7</u>	<u>292.2</u>

⁽¹⁾ Included within this amount in the year to December 31, 2008 is \$3.2 million increase (2007: reduction of \$4.0 million) in the provision affecting the purchase price allocation of New River

⁽²⁾ Recognized within Other Comprehensive Income, with the exception of \$4.4 million in 2008 included in the Statement of Operations

⁽³⁾ The full amount of which would affect the effective rate if recognized

The Company recognizes interest and penalties accrued related to unrecognized tax benefits within income taxes. During the years ended December 31, 2008, 2007 and 2006, the Company recognized approximately \$26.1 million, \$18.0 million and \$30.3 million in interest and penalties. The Company had approximately \$76.2 million, \$63.7 million and \$41.3 million for the payment of interest and penalties accrued at December 31, 2008, 2007, and 2006, respectively.

Additional tax contingencies (under SFAS No. 5)

The increase in current tax liabilities in the year to December 31, 2006 was primarily a result of additional tax contingencies of \$187 million recognized in the fourth quarter of 2006 as a result of the Company's assessment of the implications of ongoing audits by tax authorities (included in change in provision for uncertain tax positions above). The tax audits commenced in 2004 and relate to the years 1999 to 2006, covering a range of issues including transfer pricing, potential restrictions on the utilization of net operating loss carry-forwards ("NOLs"), potential taxation of overseas dividends and controlled foreign companies rules.

The Company had recognized a \$53 million contingency in respect of these tax audits at December 31, 2005, based on the Company's management's assessment of the probability of additional taxation payments at that time. However, during the fourth quarter of 2006, the tax authorities expanded the scope of their enquiries and proposed adjustments to certain tax positions previously filed by the Company. At this point, the Company retained third party advisors to assess the merits, quantum and implications of the adjustments proposed by the tax authorities, and to assist the Company's management in determining whether or not additional tax payments in excess of the existing provision of \$53 million were reasonably possible or probable.

Upon completion of the Company's review of these proposed adjustments in December 2006, including receipt of the expert third party's advice, the Company found it appropriate to recognize the additional tax contingencies of \$187 million, which included an estimate of potential interest due in respect of potential unpaid taxes. Following the recognition of these additional tax contingencies in the fourth quarter of 2006, the provision in respect of these ongoing tax audits totaled \$240 million. It was the opinion of the Company's management at December 31, 2006 that while tax audits remain open, additional tax payments in excess of those already provided which would have a material impact on the Company's consolidated financial statements, were not reasonably possible.

Deferred taxes

The significant components of deferred tax assets and liabilities and their balance sheet classifications, as at December 31, are as follows:

	December 31, 2008 \$'M	December 31, 2007 \$'M
Deferred tax assets:		
Deferred revenue	9.1	21.5
Inventory & warranty provisions	26.4	17.3
Losses carried forward (including tax credits)	295.0	357.7
Provisions for product returns and doubtful accounts	54.7	35.2
Restructuring	2.0	34.1
Intangible assets	17.7	34.6
Share-based compensation	38.7	30.4
Excess of tax value over book value of assets	8.7	-
Other	19.4	56.1
Gross deferred tax assets	<u>471.7</u>	<u>586.9</u>
Less: valuation allowance	(119.3)	(104.9)
	<u>352.4</u>	<u>482.0</u>
Deferred tax liabilities:		
Intangible assets	(532.7)	(533.1)
Excess of book value over tax value of assets	-	(5.6)
Net deferred tax liabilities	<u>(180.3)</u>	<u>(56.7)</u>
Balance sheet classifications:		
Deferred tax assets - current	89.5	143.3
Deferred tax assets - non-current	118.1	143.7
Deferred tax liabilities - current	(10.9)	(11.3)
Deferred tax liabilities - non-current	(377.0)	(332.4)
	<u>(180.3)</u>	<u>(56.7)</u>

Shire moved to a net deferred tax liability position at December 31, 2007 principally following the recognition of a deferred tax liability on acquisition of New River in respect of acquired intangible assets. During the year to December 31, 2008 the net deferred tax liability has increased primarily as a result of the utilisation of loss carryforward deferred tax assets during the year in the US, Netherlands, UK and Canada, but offset by the creation of deferred tax assets for additional loss carryforwards in other European affiliates. An additional deferred tax liability of \$85 million arose on the acquisition of Jerini in 2008 in respect of acquired intangible assets.

At December 31, 2008, the Company had a valuation allowance of \$119.3 million (2007: \$104.9 million) to reduce its deferred tax assets to estimated realizable value. These valuation allowances related primarily to operating loss, capital loss and tax-credit carry-forwards in the US (2008: \$65.5 million, 2007: \$67.0 million, 2006: \$79.9 million); Canada (2008: \$6.6 million, 2007: \$11.0 million, 2006: \$9.8 million); and other foreign tax jurisdictions (2008: \$47.2 million, 2007: \$26.9 million, 2006: \$19.9 million).

At December 31, 2008, based upon the profit history of the entities, projections for future taxable income over the periods in which temporary differences are anticipated to reverse, any restrictions on uses of loss carryforwards and prudent and feasible tax-planning strategies, management believes it is more likely than not that the Company will realize the benefits of these deductible differences, net of the valuation allowances. However, the amount of the deferred tax asset considered realizable could be adjusted in the future if estimates of taxable income are revised.

Valuation allowances related to the pre-acquisition NOLs are applied first to reduce goodwill and then to reduce non-current intangible assets arising from the acquisition as the related tax benefits are realized. During 2008 there were no reversals of valuation allowances applied to reduce goodwill (2007: \$11.0 million).

The approximate NOLs, capital losses and tax credit carry-forwards as at December 31, are as follows:

	2008	2007
	\$'M	\$'M
US federal tax NOLs	-	170.6
US state tax NOLs	94.2	69.9
UK NOLs	114.0	155.1
Republic of Ireland NOLs	238.4	175.8
Foreign tax jurisdictions	88.7	102.0
R&D tax credits	208.1	176.0
Capital losses	27.3	37.8

The NOLs, capital losses and tax credit carry-forwards shown above have the following expiration dates:

	December 31
	2008
	\$'M
Within 1 year	6.9
Within 1 to 2 years	12.9
Within 2 to 3 years	22.7
Within 3 to 4 years	14.5
Within 4 to 5 years	0.6
Within 5 to 6 years	1.3
After 6 years	332.2
Indefinitely	379.6

As at December 31, 2008, the Company had not recorded deferred taxes on approximately \$3.7 billion (2007: \$2.8 billion) of un-remitted earnings of the Company's foreign subsidiaries. At December 31, 2008 these earnings are expected to be permanently reinvested overseas. It is not practical to compute the estimated deferred tax liability on these earnings.

32. Equity in earnings of equity method investees

Year to December 31,	2008	2007	2006
	\$'M	\$'M	\$'M
GSK (see Note 12)	5.8	6.5	6.3
GeneChem Funds (see Note 12)	(3.4)	(4.6)	(1.3)
Other	-	(0.1)	0.7
	<u>2.4</u>	<u>1.8</u>	<u>5.7</u>

33. Share-based compensation plans

The Company applies the provisions of SFAS No. 123(R), which establishes accounting for share-based compensation to employees. The Company measures share-based compensation cost at the grant date, based on the fair value of the award, and recognizes the expense over the employee requisite service period. The following table shows the total share-based compensation expense (see below for types of share-based awards) included in the statements of operations:

	2008 \$'M	2007 \$'M	2006 \$'M
Cost of product sales	3.9	5.5	3.2
Research and development	18.9	17.0	5.4
Selling, general and administrative	42.4	52.7	34.4
Total	65.2	75.2	43.0
Less tax	(15.3)	(11.7)	(6.5)
	49.9	63.5	36.5

There were no capitalized share-based compensation costs at December 31, 2008 and 2007.

At December 31, 2008 \$40.7 million of total unrecognized compensation cost relating to non-vested awards, is expected to be recognized over a weighted average period of 1.9 years. The total fair value of share and share option awards vested during the year was \$34.4 million.

Share-based compensation plans

Historically the Company has granted options to directors and employees over ordinary shares under six stock option plans. On November 28, 2005 the ordinary shareholders of Shire approved the adoption of the Shire Portfolio Share Plan (Parts A and B), a new share-based compensation plan, which provides for stock-settled share appreciation rights and performance share awards to be made to directors and employees over ordinary shares and Shire ADSs. As of 28 November 2005, all awards were granted using the Portfolio Share Plan. No further awards will be made under the previous stock option plans (except for the Sharesave scheme).

The following awards were outstanding as at December 31, 2008:

	Compensation type	Number of awards	Expiration period from date of issue	Vesting period
Portfolio Share Plan - Part A	Stock-settled share appreciation rights – ordinary shares	7,264,481	5 years	3 years, subject to performance criteria for executive directors only
Portfolio Share Plan - Part A	Stock-settled share appreciation rights – ADSs ⁽¹⁾	18,972,372	5 years	3 years, subject to performance criteria for executive directors only
Total Portfolio Share Plan - Part A		26,236,853		
Portfolio Share Plan - Part B	Performance share awards - ordinary shares	933,633	3 years	3 years, subject to performance criteria for executive directors only
Portfolio Share Plan - Part B	Performance share awards - ADSs ⁽¹⁾	2,291,562	3 years	3 years, subject to performance criteria for executive directors only
Total Portfolio Share Plan - Part B		3,225,195		
Executive Scheme	Stock options	65,166	7 to 10 years	3-10 years, subject to performance criteria
2000 Executive Scheme	Stock options	8,043,869	10 years	3 -10 years, subject to performance criteria
Sharesave Scheme	Stock options	380,774	6 months after vesting	3 or 5 years
Stock Purchase Plan	Stock options	729,243	On vesting date	1 to 5 months
BioChem Plan	Stock options	13,642	10 years	Immediate on acquisition by Shire
Total stock option awards		9,232,694		

⁽¹⁾ For the purposes of this table ADSs have been converted into ordinary shares. One ADS is equivalent to three ordinary shares.

(a) Stock-settled share appreciation rights

Portfolio Share Plan – Part A

Stock-settled share appreciation rights granted under the Portfolio Share Plan – Part A are exercisable subject to certain performance criteria. In respect of any award made to executive directors performance conditions will be based on relative total shareholder return. Vesting will depend on relative total shareholder return performance against two comparator groups. For one-third of the award, the comparator group will be the Financial Times Stock Exchange 100 constituents (excluding financial institutions) and for two-thirds of the award the comparator group will be a group of international companies from the pharmaceutical sector. In addition, before awards granted to executive directors will vest, the Committee must be satisfied that the underlying performance of the Company is sufficient to justify this. Where median performance is achieved, 33 1/3 per cent of stock-settled share appreciation rights will vest, rising on a straight-line basis to full vesting at upper quartile performance.

Awards granted to employees below executive director level will not be subject to performance conditions.

Once awards have vested, participants will have until the fifth anniversary of the date of grant to exercise their awards.

A summary of the status of the Company's stock-settled share appreciation rights as at December 31, 2008 and of the related transactions during the periods then ended is presented below:

Year to December 31, 2008 Ordinary shares	Weighted average exercise price £	Number of shares	Intrinsic Value £' M
Outstanding as at beginning of period	9.89	5,680,361	
Granted	9.59	2,115,297	
Exercised	7.70	(132,243)	
Forfeited	10.16	(398,934)	
Outstanding as at end of period	9.90	7,264,481	4.6
Exercisable as at end of period	8.49	408,097	0.7

2.1 million stock-settled share appreciation rights were granted over ordinary shares under the Portfolio Share Plan – Part A. These options were granted with exercise prices equivalent to the market value on the date of grant. The weighted average fair value of options granted in the year to December 31, 2008 is £2.43.

A summary of the status of the Company's stock-settled share appreciation rights as at December 31, 2007 and of the related transactions during the periods then ended is presented below:

Year to December 31, 2007 Ordinary shares	Weighted average exercise price £	Number of shares	Intrinsic Value £' M
Outstanding as at beginning of period	8.54	2,919,223	
Granted	9.92	3,297,395	
Exercised	8.27	(9,539)	
Forfeited	9.18	(526,718)	
Outstanding as at end of period	9.89	5,680,361	9.2
Exercisable as at end of period	8.65	79,870	0.2

3.3 million stock-settled share appreciation rights were granted over ordinary shares under the Portfolio Share Plan – Part A. These options were granted with exercise prices equivalent to the market value on the date of grant. The weighted average fair value of options granted in the year to December 31, 2007 is £2.70.

A summary of the status of the Company's stock-settled share appreciation rights as at December 31, 2006 and of the related transactions during the periods then ended is presented below:

Year to December 31, 2006	Weighted average exercise price	Number of	Intrinsic Value
Ordinary shares	£	shares	£' M
Outstanding as at beginning of period	7.17	449,490	
Granted	8.74	2,561,292	
Exercised	-	-	
Forfeited	7.19	(91,559)	
Outstanding as at end of period	8.54	2,919,223	6.0
Exercisable as at end of period	7.86	6,015	-

2.6 million stock-settled share appreciation rights were granted over ordinary shares under the Portfolio Share Plan – Part A. These options were granted with exercise prices equivalent to the market value on the date of grant. The weighted average fair value of options granted in the year to December 31, 2006 is £2.58.

Stock-settled share appreciation rights over ordinary shares outstanding as at December 31, 2008 have the following characteristics:

Number of options outstanding	Exercise prices £	Weighted Average Remaining Contractual term Years	Weighted average exercise price of options outstanding £	Number of options exercisable	Weighted average exercise price of options exercisable £
4,197,809	6.01-10.00	3.4	9.03	322,720	7.84
3,066,672	10.01-11.90	3.2	11.09	85,377	10.96
7,264,481				408,097	

Year to December 31, 2008	Weighted average exercise price	Number of	Intrinsic Value
American depositary shares	\$	ADSs	\$' M
Outstanding as at beginning of period	56.29	5,414,024	
Granted	55.79	1,538,666	
Exercised	43.27	(25,097)	
Forfeited	57.82	(603,469)	
Outstanding as at end of period	56.09	6,324,124	5.3
Exercisable as at end of period	40.75	819,382	4.8

1.5 million stock-settled share appreciation rights were granted over American depositary shares (equivalent to 4.6 million ordinary shares) under the Portfolio Share Plan – Part A. These options were granted with exercise prices equivalent to the market value on the date of grant. The 6.3 million stock-settled share appreciation rights over ADSs outstanding at December 31, 2008 are equivalent to 19.0 million ordinary shares. The average fair value of options granted in the year to December 31, 2008 is \$14.10.

Year to December 31, 2007 American depositary shares	Weighted average exercise price \$	Number of ADSs	Intrinsic Value \$' M
Outstanding as at beginning of period	46.40	2,965,798	
Granted	49.79	2,782,413	
Exercised	46.04	(1,156)	
Forfeited	49.68	(333,031)	
Outstanding as at end of period	56.29	5,414,024	70.8
Exercisable as at end of period	52.83	30,201	0.5

2.8 million stock-settled share appreciation rights were granted over American depositary shares (equivalent to 8.3 million ordinary shares) under the Portfolio Share Plan – Part A. These options were granted with exercise prices equivalent to the market value on the date of grant. The 5.4 million stock-settled share appreciation rights over ADSs outstanding at December 31, 2007 are equivalent to 16.2 million ordinary shares. The average fair value of options granted in the year to December 31, 2007 is \$13.53.

Year to December 31, 2006 American depositary shares	Weighted average exercise price \$	Number of ADSs	Intrinsic Value \$' M
Outstanding as at beginning of period	37.80	937,392	
Granted	50.10	2,138,356	
Exercised	-	-	
Forfeited	41.71	(109,950)	
Outstanding as at end of period	46.40	2,965,798	45.3
Exercisable as at end of period	46.30	1,088	-

2.1 million stock-settled share appreciation rights were granted over American depositary shares (equivalent to 6.3 million ordinary shares) under the Portfolio Share Plan – Part A. These options were granted with exercise prices equivalent to the market value on the date of grant. The 3.0 million stock-settled share appreciation rights over ADSs outstanding at December 31, 2006 are equivalent to 9.0 million ordinary shares. The average fair value of options granted in the year to December 31, 2006 is \$14.70.

Stock-settled share appreciation rights over American depositary shares outstanding as at December 31, 2008 have the following characteristics:

Number of options outstanding	Exercise prices \$	Weighted Average Remaining Contractual term (years)	Weighted average exercise price of options outstanding \$	Number of options exercisable	Weighted average exercise price of options exercisable
2,485,686	35.01 – 50.00	2.6	45.50	752,687	38.75
3,838,438	50.01 – 75.00	3.6	62.95	66,695	63.30
6,324,124				819,382	

(b) Performance shares

Portfolio Share Plan – Part B

Performance share awards granted under the Portfolio Share Plan – Part B are exercisable subject to certain performance criteria. In respect of any award made to executive directors performance conditions will be based on relative total shareholder return. Vesting will depend on relative total shareholder return performance against two comparator groups. For one-third of an award, the comparator group will be the Financial Times Stock Exchange 100 constituents (excluding financial institutions) and for two-thirds of the award the comparator group will be a group of international companies from the pharmaceutical sector. In addition, before awards granted to executive directors will vest, the Committee must be satisfied that the underlying performance of the Company is sufficient to justify this. Where median performance is achieved, 33 1/3 per cent of performance shares will vest, rising on a straight-line basis to full vesting at upper quartile performance.

A summary of the status of the Company's stock-settled share awards as at December 31, 2008 and of the related transactions during the periods then ended is presented below:

	Number of shares	Aggregate intrinsic value £'M	Weighted average remaining life
Performance share awards - Ordinary shares			
Outstanding as at beginning of period	240,406		
Granted	710,482		
Exercised	(565)		
Forfeited	(16,690)		
Outstanding as at end of period	933,633	9.4	2.0
Exercisable as at end of period	-	N/A	N/A

The average fair value of options granted in the year to December 31, 2008 is £8.15.

	Number of ADSs	Aggregate intrinsic value \$'M	Weighted average remaining life
Performance share awards - American Depositary Shares			
Outstanding as at beginning of period	299,103		
Granted	530,571		
Exercised	(20,866)		
Forfeited	(44,954)		
Outstanding as at end of period	763,854	34.2	2.2
Exercisable as at end of period	-	N/A	N/A

The average fair value of options granted in the year to December 31, 2008 is \$57.27.

A summary of the status of the Company's stock-settled share awards as at December 31, 2007 and of the related transactions during the periods then ended is presented below:

Performance share awards - Ordinary shares	Number of shares	Aggregate intrinsic value £'M	Weighted average remaining life
Outstanding as at beginning of period	130,406		
Granted	110,000		
Outstanding as at end of period	240,406	2.8	1.9
Exercisable as at end of period	-	N/A	N/A

Performance share awards - American Depositary Shares	Number of ADSs	Aggregate intrinsic value \$'M	Weighted average remaining life
Outstanding as at beginning of period	175,341		
Granted	146,316		
Forfeited	(22,554)		
Outstanding as at end of period	299,103	20.6	1.9
Exercisable as at end of period	-	N/A	N/A

(c) Stock option plans

(i) Shire Pharmaceuticals Executive Share Option Scheme - Parts A and B (Executive Scheme)

Options granted under the Executive Scheme are subject to performance criteria and cannot be exercised in full, unless Shire's ordinary share price increases at a compound rate of at least 20.5% per annum over a minimum three-year measurement period. If Shire's ordinary share price increases at a compound rate of 14.5% per annum over a minimum three-year measurement period, 60% of the options may be exercised. If these conditions are not met after the initial three years, they are thereafter tested quarterly by reference to share price growth over the extended period. If the share price does not meet these conditions at any time, none of the options will become exercisable.

On February 28, 2000 the Remuneration Committee of the Board exercised its powers to amend the terms of the Executive Share Option Scheme so as to include a cliff vesting provision.

(ii) Shire 2000 Executive Share Option Scheme (2000 Executive Scheme)

Options granted under this scheme are exercisable subject to certain performance criteria. In respect of any option granted prior to August 2002, if Shire's ordinary share price increases at a compound rate of at least 20.5% per annum over a minimum three-year measurement period, the option becomes exercisable in full. If it increases by at least 14.5% per annum over the same three-year period, 60% of the options granted become exercisable. If these conditions are not met after the initial three-year measurement period, they will thereafter be tested quarterly by reference to compound annual share price growth over an extended period.

The performance criteria were reviewed in 2002 to ensure the criteria reflected the market in which Shire operates. Given Shire's development, it was considered appropriate that an earnings per share-based measure should be adopted. The performance criteria are based on real growth in the diluted earnings per share reported in the Company's Form 10-K under US GAAP, adjusted to ensure a consistent basis of measurement, as approved by the Remuneration Committee, including the add back of significant one time items (Option EPS). Therefore, the performance criteria were amended so that an option would become exercisable in full if Shire's Option EPS growth over a three year period from the date of award exceeds the UK Retail Prices Index (RPI) for the following tranches of grants:

Options with a grant value of up to 100% of salary	RPI plus 9% (directors, RPI plus 15%)
Between 101% and 200% of salary	RPI plus 15%
Between 201% and 300% of salary	RPI plus 21%
Over 301% of salary	RPI plus 27%

The new earnings per share performance criteria apply to options granted under the 2000 Executive Scheme from August 2002. After consultation with certain of its institutional shareholders, the Company has decided that for options granted under the scheme from 2004 onwards, the retest of the performance condition if Shire's option EPS growth has fallen short of the minimum annual average percentage increase over the three year period from grant, should be changed. The revised performance condition will be retested once only, at five years after the grant. Hence the level of option EPS growth in the next two years needs to be consequentially higher to meet the test.

Under Part B of the scheme, six weeks prior to the expiration date, any options that have not become exercisable at an earlier date, automatically vest without reference to the performance criteria.

In December 2006, the Remuneration Committee exercised its powers to amend the performance criteria for options granted under the 2000 Executive Scheme which had not vested. The RPI based growth rate was replaced with an equivalent fixed growth rate based on historical and forecast inflation. The fair values of the awards were unaffected by this change and no additional employee compensation cost was recorded as a result of the modification.

(iii) Shire Sharesave Scheme (Sharesave Scheme)

Options granted under the Sharesave Scheme are granted with an exercise price equal to 80% of the mid-market price on the day before invitations are issued to employees. Employees may enter into three or five-year savings contracts. No performance conditions apply.

(iv) Shire Employee Stock Purchase Plan (Stock Purchase Plan)

Under the Stock Purchase Plan, options are granted with an exercise price equal to 85% of the fair market value of a share on the enrolment date (the first day of the offering period) or the exercise date (the last day of the offering period), whichever is the lower. Following approval by shareholders at the AGM held on June 20, 2007, the 2007 Shire Employee Stock Purchase Plan was adopted on similar terms to the predecessor plan, save that participants agree to save for a period up to 27 months, rather than a fixed 27 months, as set by the Committee. The offering period set for plan grants in 2008 was 12 months. No performance conditions apply.

(v) BioChem Stock Option Plan (BioChem Plan)

Following the acquisition of BioChem Pharma Inc. on May 11, 2001, the BioChem Stock Option Plan was amended such that options over BioChem Pharma Inc.'s common stock became options over ordinary shares of Shire. All BioChem Pharma Inc. options, which were not already exercisable, vested and became exercisable as a result of the acquisition. It is intended that no further options will be granted under the BioChem Stock Option Plan.

(vi) *Long Term Incentive Plan*

The Long Term Incentive Plan (LTIP) was adopted by Shire at the Company's 1998 Annual General Meeting and amended in 2000. Under the LTIP, the Remuneration Committee has discretion to make awards to senior executives of shares subject to a maximum of 100% of salary a year. The last awards were granted under the LTIP in 2005.

Performance tied to the vesting of the 2005 LTIP grants, as detailed below, resulted in a vesting percentage of 88.54%. Awards will be satisfied by the transfer of shares in May 2009.

The performance condition attached to the vesting of the share awards made under the LTIP is Shire's Total Shareholder Return (TSR) relative to the FTSE 100 Index over a three-year period. The Committee considers that this measure is a reliable and appropriate measure of the Group's performance and that the FTSE 100 is an appropriate benchmark given that the Company is a member of the Index.

Under the LTIP:

- all shares vest if Shire's TSR is in the top 10% of the FTSE 100;
- 20% of the shares vest if Shire's TSR is at the median of the FTSE 100, with vesting between these points on a linear basis; and
- no shares vest if Shire's TSR is below the median of the FTSE 100.

The Remuneration Committee determines whether and to what extent the performance condition has been met on the basis of data provided by an independent third party. Whilst the performance period is measured over three years, an award is normally transferred after the fourth anniversary of grant, to the extent the performance condition has been met.

A summary of the status of the Company's stock option plans as at December 31, 2008, 2007 and 2006 and of the related transactions during the periods then ended is presented below:

Year to December 31, 2008

	Weighted average exercise price £	Number of shares	Aggregate Intrinsic Value £'M
Outstanding as at beginning of period	6.09	13,113,255	
Granted	7.12	879,049	
Exercised	7.01	(4,440,123)	
Forfeited	9.44	(319,487)	
Outstanding as at end of period	6.14	9,232,694	38.7
Exercisable as at end of period	5.98	8,098,635	35.5

0.2 million options were granted under the Sharesave Scheme at a price of £7.74. These options were granted with an exercise price equal to 80% of the mid-market price on the day before invitations were issued to employees. The weighted average fair value of options granted was £3.43.

0.7 million options were granted under the Stock Purchase Plan at prices of £6.96, £6.87 and £7.26. These options were granted with an exercise price equal to 15%, 20% and 25% of the mid-market price on the day before invitations were issued to employees. The weighted average fair value of options granted was £2.06.

Year to December 31, 2007

	Weighted average exercise price £	Number of shares	Aggregate Intrinsic Value £'M
Outstanding as at beginning of period	5.90	19,559,873	
Granted	9.93	287,762	
Exercised	5.78	(5,947,857)	
Forfeited	7.58	(786,523)	
Outstanding as at end of period	6.09	13,113,255	71.9
Exercisable as at end of period	6.02	5,132,646	29.1

0.1 million options were granted under the Sharesave Scheme at a price of £9.77. These options were granted with an exercise price equal to 80% of the mid-market price on the day before invitations were issued to employees. The weighted average fair value of options granted was £3.96.

0.2 million options were granted under the Stock Purchase Plan at a prices of £10.12 and £8.92. These options were granted with an exercise price equal to 15% and 20% of the mid-market price on the day before invitations were issued to employees. The weighted average fair value of options granted was £2.72.

Year to December 31, 2006

	Weighted average exercise price £	Number of shares	Aggregate Intrinsic Value £'M
Outstanding as at beginning of period	5.85	28,470,739	
Granted	7.33	386,159	
Exercised	5.21	(8,312,174)	
Forfeited	8.83	(984,851)	
Outstanding as at end of period	5.90	19,559,873	92.1
Exercisable as at end of period	6.77	5,742,106	24.2

0.1 million options were granted under the Sharesave Scheme at a price of £6.99. These options were granted with an exercise price equal to 80% of the mid-market price on the day before invitations were issued to employees. The weighted average fair value of options granted was £3.21.

0.3 million options were granted under the Stock Purchase Plan at a price of £7.48. These options were granted with an exercise price equal to 85% of the mid-market price on the day before invitations were issued to employees. The weighted average fair value of options granted was £3.71.

Options outstanding as at December 31, 2008 have the following characteristics:

Number of options outstanding	Exercise prices £	Weighted average remaining contractual term (years)	Weighted average exercise price of options outstanding £	Number of options exercisable	Weighted average exercise price of options exercisable £
1,785,273	0.01 – 4.00	4.1	3.54	1,757,709	3.54
4,284,635	4.01 – 6.00	5.8	5.44	4,269,262	5.44
2,298,210	6.01 – 10.00	4.3	7.11	1,262,647	6.97
864,576	10.01 – 13.00	2.3	12.46	809,017	12.56
9,232,694				8,098,635	

Exercises of employee share-based awards

The total intrinsic values of share-based awards exercised for the years to December 31, 2008, 2007 and 2006 were \$23.8 million, \$67.9 million and \$65.5 million, respectively. The total cash received from employees as a result of employee share option exercises for the period to December 31, 2008, 2007 and 2006 was approximately \$11.4 million, \$30.4 million and \$82.0 million, respectively. In connection with these exercises, the tax deficit charged to additional paid-in capital for the period to December 31, 2008 was \$3.8 million (2007: \$nil, 2006: \$nil).

The Company will settle future employee share award exercises with either newly listed common shares or with shares held in an ESOT. The number of shares to be purchased by the ESOT during 2009 will be dependent on the number of employee share awards granted and exercised during the year and Shire plc's share price. At December 31, 2008 the ESOT held 7.3 million ordinary shares and 4.5 million ADSs.

Valuation methodologies

The Company estimates the fair value of share-based awards without market-based performance conditions using a Black-Scholes valuation model and awards with market-based performance conditions are valued using a binomial valuation. This is consistent with the provisions of SFAS No. 123(R) and SEC Staff Accounting Bulletin No. 107. Key input assumptions used to estimate the fair value of share-based awards include the grant price of the award, the expected stock-based award term, volatility of the Company's share, the risk-free rate and the Company's dividend yield. The Company believes that the valuation technique and the approach utilized to develop the underlying assumptions are appropriate in estimating the fair values of Shire's stock-based awards. Estimates of fair value are not intended to predict actual future events or the value ultimately realized by employees who receive equity awards, and subsequent events are not indicative of the reasonableness of the original estimates of fair value made by the Company under SFAS No. 123(R).

The fair value of share awards granted was estimated using the following assumptions:

Period ended December 31,	2008	2007	2006
Risk-free interest rate ⁽¹⁾	1.3-5.3%	3.4-5.35%	4.7-5.0%
Expected dividend yield	0-0.5%	0-0.5%	0.5%
Expected life ⁽²⁾	4 years	4 years	4 years
Weighted average volatility	29%	27%	30%
Forfeiture rate	5%	5%	5%

(1) Risk free interest rate is for UK and US grants

(2) Stock awards made in the year to December 31, 2008, 2007 and 2006 expire 5 years from the date of issue

34. Subsequent events

Agreement to Acquire EQUASYM IR and XL

On February 20, 2009 the Company announced that it had signed an agreement with UCB to acquire the worldwide rights (excluding the USA, Canada and Barbados) to the currently marketed products EQUASYM[®] IR and XL (methylphenidate hydrochloride) used for the treatment of ADHD. The acquisition is subject to standard closing conditions.

On completion of the transaction approximately 20 sales and sales management personnel will transfer to the Company, providing an established sales force for EQUASYM and other potential ADHD products. Shire will make a cash payment to UCB of €55 million for the acquisition of these rights on completion of the transaction. In addition, small milestone payments may become due in 2009 and 2010 if certain net sales targets are met.

Agreement to Terminate Development of Women's Health Products

In August 2006, Shire and Duramed (an affiliate of Barr) entered into an agreement related to SEASONIQUE, a number of products using Duramed's transvaginal ring technology and other oral products (the "Collaboration Products"). Under this agreement, Shire was required to reimburse Duramed for US development expenses incurred in respect of the Collaboration Products up to a maximum of \$140 million over eight years from September 2006, and Shire had the right to commercialize these products in a number of markets outside of North America, including the larger European markets.

US development expenses reimbursed in the year ended December 31, 2008 totaled \$30.0 million, and at December 31, 2008 the maximum future reimbursement for Duramed incurred US development expenditures was \$95.6 million.

On February 24, 2009, Shire and Duramed amended this agreement and it will terminate on December 31, 2009. Pursuant to this amendment, Shire agreed to return to Duramed its rights under the agreement effective February 24, 2009. Shire also agreed to reimburse Duramed for incurred US development expenditures in 2009 up to a maximum of \$30.0 million. In addition, Shire agreed to a one-time payment to Duramed of \$10.0 million and to forego royalties receivable from Barr and cost of goods otherwise payable by Barr to Shire in 2009 under the License Agreement between the parties for the supply of the authorized generic of ADDERALL XR up to a maximum of \$25.0 million.

Quarterly results of operations (unaudited)

The following table presents summarized unaudited quarterly results for the years to December 31, 2008 and 2007

2008	Q1	Q2	Q3	Q4
	\$'M	\$'M	\$'M	\$'M
Total revenues	702.2	775.6	778.6	765.8
Operating income/(loss)	163.0	(67.3)	122.9	193.4
Net income/(loss)	128.6	(79.0)	(34.9)	141.3
Earnings per share - basic	23.6c	(14.6c)	(6.5c)	26.2c
Earnings per share - diluted	22.7c	(14.6c)	(6.5c)	26.0c
2007	Q1	Q2	Q3	Q4
	\$'M	\$'M	\$'M	\$'M
Total revenues	528.2	574.9	608.7	724.5
Operating income/(loss)	141.2	(1,775.1)	22.6	232.2
Net income/(loss)	112.7	(1,811.3)	34.7	212.1
Earnings per share - basic	21.6c	(331.0c)	6.4c	38.9c
Earnings per share - diluted	21.3c	(331.0c)	6.3c	36.9c

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To Lloyds TSB Offshore Trust Company Limited, Trustee of the Shire Income Access Share Trust and the Board of Directors and Stockholders of Shire plc

We have audited the accompanying Balance Sheet of the Shire Income Access Share Trust (the "Trust") as of December 31, 2008 and the related statement of income, statement of changes in equity and statement of cash flows for the period from August 29, 2008 to December 31, 2008. These financial statements are the responsibility of the Trustee and Shire plc's management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Trust is not required to have an audit of its internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the Trust's internal control over financial reporting. Accordingly, we express no such separate opinion. Our audit of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Shire Income Access Share Trust at December 31, 2008, and the results of its operations and cash flows for the period ended December 31, 2008, in conformity with accounting principles generally accepted in the United States of America.

DELOITTE LLP

London, United Kingdom

February 27, 2009

**SHIRE INCOME ACCESS SHARE TRUST
BALANCE SHEET**

	Notes	December 31, 2008 \$'M
ASSETS		
Total assets		-
LIABILITIES AND SHAREHOLDERS' EQUITY		
Total liabilities		-
Shareholders' equity:		
Capital account		-
Total shareholders' equity		-
Total liabilities and shareholders' equity		-

The notes on pages F-87 to F-88 are an integral part of these financial statements.

**SHIRE INCOME ACCESS SHARE TRUST
STATEMENT OF INCOME**

	Notes	Period to December 31, 2008 \$'M
Dividend income		7.2
Net income		7.2

The notes on page F-87 to F-88 are an integral part of these financial statements.

**SHIRE INCOME ACCESS SHARE TRUST
STATEMENT OF CHANGES IN EQUITY**

	Capital account \$'M	Revenue account \$'M	Total equity \$'M
At August 29, 2008	-	-	-
Net income for the period	-	7.2	7.2
Distributions made	-	(7.2)	(7.2)
As at December 31, 2008	-	-	-

The notes on page F-87 to F-88 are an integral part of these financial statements.

**SHIRE INCOME ACCESS SHARE TRUST
STATEMENT OF CASHFLOWS**

	Notes	Period to December 31, 2008 \$'M
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net income		7.2
Net cash provided from operating activities ^(A)		7.2
CASH FLOWS FROM INVESTING ACTIVITIES:		
Net cash provided by investing activities ^(B)		-
CASH FLOWS FROM FINANCING ACTIVITIES:		
Distributions made		(7.2)
Net cash used in financing activities ^(C)		(7.2)
Net increase in cash and cash equivalents ^(A+B+C)		-
Cash and cash equivalents at beginning of period		-
Cash and cash equivalents at end of period		-

The notes on page F-87 to F-88 are an integral part of these financial statements.

(a) The Trust

The Shire Income Access Share Trust (the "Trust") was established on August 29, 2008 by Shire Biopharmaceuticals Holdings (formerly Shire plc) ("Old Shire"). The Trust is governed by the applicable laws of England and Wales and is resident in Jersey. The Trustee of the Trust is Lloyds TSB Offshore Trust Company Limited, 25 New Street, St Helier, Jersey, JE4 8RG.

The Trust was established as part of the Income Access Share mechanism, as outlined on page F-53 to the financial statements of Shire plc and its subsidiaries (collectively referred to as either "Shire" or the "Company").

(b) Basis of preparation

The financial statements of the Trust have been prepared in accordance with US generally accepted accounting principles ("US GAAP"). The financial statements have been prepared under the historical cost convention.

The preparation of financial statements in conformity with US GAAP requires the use of certain accounting estimates. It also requires management to exercise its judgement in the process of applying the Trust's accounting policies. Actual results may differ from these estimates.

The results of operations, and the financial position and cash flows of the Trust are also consolidated in the Company's financial statements, as contained on pages F-1 to F-81.

(c) Summary of significant accounting policies

i) Functional currency

The functional currency of the Trust is US dollars.

ii) Foreign currency translation

Income and expense items denominated in currencies other than the functional currency are translated into the functional currency at the rate ruling on their transaction date. Monetary assets and liabilities recorded in currencies other than the functional currency have been expressed in the functional currency at the rates of exchange ruling at the respective balance sheet dates. Differences on translation are included in the Statement of Income.

iii) Dividend income

Interim dividends declared on the Income Access Share are recognised on a paid basis unless the dividend has been confirmed by a general meeting of Shire, in which case income is recognised on the record date of the dividend by Shire on its ordinary shares.

(d) Capital Account

The Capital account is represented by the Income Access Share of 5 pence settled in the Trust by Old Shire.

(e) Distributions Made

Distributions are made to those shareholders of Shire who have elected to receive dividends from the Trust in accordance with the Trust Deed. Unclaimed dividends are not included in distributions made. There were no unclaimed dividends at December 31, 2008. Amounts are recorded as distributed once a wire transfer or check is issued. All checks are valid for one year from the date of issue. Any wire transfers that are not completed are replaced by cheques. To the extent that cheques expire or are returned unrepresented, the Trust records a liability for unclaimed dividends and a corresponding amount of cash.

(f) Financial Instruments

The Trust, in its normal course of business, is not subject to market risk, credit risk or liquidity risk. The Trustees do not consider that any foreign exchange composure will materially affect the operations of the Trust.

SCHEDULE II

VALUATION AND QUALIFYING ACCOUNTS

	Beginning balance \$'M	Provision charged to income⁽¹⁾ \$'M	Costs incurred/ utilization⁽¹⁾ \$'M	Ending balance \$'M
Provision for sales rebates, returns and coupons				
2008 :				
Accrued rebates – Medicaid and Health Maintenance Organizations (HMOs)	146.6	396.9	(321.0)	222.5
Sales returns reserve	39.5	38.2	(30.6)	47.1
Accrued coupons	9.0	32.5	(37.5)	4.0
	<u>195.1</u>	<u>467.6</u>	<u>(389.1)</u>	<u>273.6</u>
2007 :				
Accrued rebates – Medicaid and HMOs	126.4	263.5	(243.3)	146.6
Sales returns reserve	36.5	46.0	(43.0)	39.5
Accrued coupons	13.0	50.2	(54.2)	9.0
	<u>175.9</u>	<u>359.7</u>	<u>(340.5)</u>	<u>195.1</u>
2006 :				
Accrued rebates – Medicaid and HMOs	105.4	263.3	(242.3)	126.4
Sales returns reserve	31.8	34.1	(29.4)	36.5
Accrued coupons	5.2	8.8	(1.0)	13.0
	<u>142.4</u>	<u>306.2</u>	<u>(272.7)</u>	<u>175.9</u>

⁽¹⁾ In the analysis above, due to systems limitations, it is not practical and has not been necessary to break out current versus prior year activity. When applicable, Shire has performed general ledger reviews of sales deduction provisions charged to income, and the utilization of these provisions in subsequent years. Shire has determined that adjustments made in each year as a result of changes to estimates that related to prior year sales, and adjustments made as a result of differences between prior period provisions and actual payments, did not have a material impact on the Company's financial performance or position either in each individual year, or in the Company's performance over the reported period.

SIGNATURES

Pursuant to the requirements of Section 13 of 15(d) of the Securities and Exchange Act of 1934, the Company has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SHIRE PLC

(Registrant)

Date: February 27, 2009

By: /s/ Angus Russell

Angus Russell, Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the date indicated.

Signature	Title	Date
/s/ Matthew Emmens MATTHEW EMMENS	Non-Executive Chairman	February 27, 2009
/s/ Angus Russell ANGUS RUSSELL	Chief Executive Officer	February 27, 2009
/s/ Graham Hetherington GRAHAM HETHERINGTON	Chief Financial Officer	February 27, 2009
/s/ David Kappler DAVID KAPPLER	Non-Executive Director	February 27, 2009
/s/ Barry Price BARRY PRICE	Non-Executive Director	February 27, 2009
/s/ Patrick Langlois PATRICK LANGLOIS	Non-Executive Director	February 27, 2009
/s/ David Mott DAVID MOTT	Non-Executive Director	February 27, 2009
/s/ Kate Nealon KATE NEALON	Non-Executive Director	February 27, 2009
/s/ Jeffrey Leiden JEFFREY LEIDEN	Non-Executive Director	February 27, 2009
/s/ Michael Rosenblatt MICHAEL ROSENBLATT	Non-Executive Director	February 27, 2009

LIST OF SUBSIDIARIES

Subsidiary/undertaking	Jurisdiction of incorporation
3829359 Canada Inc.	Canada
BioChem Vaccines BV	Netherlands
Monmouth Pharmaceuticals Limited	United Kingdom
Orpharm SA	Argentina
Pharma International Insurance Limited	Ireland
Rybar Laboratories Limited	United Kingdom
Shire 2005 Investments Limited	Cayman Islands
Shire Acquisition Inc	Canada
Shire Australia Pty Limited	Australia
Shire Belgium BVBA	Belgium
Shire Biopharmaceuticals Holdings	United Kingdom
Shire Biopharmaceuticals Ireland Limited	Ireland
Shire Biopharmaceuticals Ireland No.2 Limited	Ireland
Shire Canada Inc.	Canada
Shire Deutschland GmbH	Germany
Shire Deutschland Investments GmbH	Germany
Shire Development Inc	United States
Shire Europe Finance	United Kingdom
Shire Europe Limited	United Kingdom
Shire Executive Services LLC	United States
Shire Finance Limited	Cayman Islands
Shire France S.A.	France
Shire Global Finance	United Kingdom
Shire Holdings AG	Switzerland
Shire Holdings Europe B.V.	Netherlands
Shire Holdings Europe Limited	United Kingdom
Shire Holdings Europe No.2 S.a.r.l.	Luxembourg
Shire Holdings Ireland Limited	Ireland
Shire Holdings Ireland No.2 Limited	Ireland
Shire Holdings Limited	Bermuda
Shire Holdings UK Canada Limited	United Kingdom
Shire Holdings UK Limited	United Kingdom
Shire Holdings US AG	United States
Shire Human Genetic Therapies (Canada) Inc.	Canada
Shire Human Genetic Therapies AB	Sweden
Shire Human Genetic Therapies Inc	United States
Shire Human Genetic Therapies Limited	United Kingdom
Shire Human Genetic Therapies Ltda	Brazil
Shire Human Genetic Therapies Securities Corporation	United States
Shire Human Genetic Therapies UK Limited	United Kingdom
Shire Incorporated	United States
Shire Intellectual Property 2 SRL	Barbados
Shire Intellectual Property SRL	Barbados
Shire International Licensing BV	Netherlands
Shire Investments & Finance (U.K.) Company	United Kingdom
Shire IP Services Corporation	Canada
Shire Italia S.p.A.	Italy
Shire Jersey Limited	Jersey
Shire LLC	United States
Shire Luxembourg Sarl	Luxembourg
Shire Pharmaceutical Contracts Limited	United Kingdom
Shire Pharmaceutical Development Inc	United States
Shire Pharmaceutical Development Limited	United Kingdom
Shire Pharmaceutical Holdings Ireland Limited	Ireland

Shire Pharmaceutical Investment Holdings Limited	Malta
Shire Pharmaceutical Investment Limited	Malta
Shire Pharmaceutical Investment Trading Ireland	Ireland
Shire Pharmaceutical Investments 2008	Ireland
Shire Pharmaceuticals Group	United Kingdom
Shire Pharmaceuticals Iberica S.L.	Spain
Shire Pharmaceuticals Inc	United States
Shire Pharmaceuticals Investments (British Virgin Islands) Limited	Virgin Islands, British
Shire Pharmaceuticals Investments 2007 Limited	Ireland
Shire Pharmaceuticals Ireland Limited	Ireland
Shire Pharmaceuticals Limited	United Kingdom
Shire Pharmaceuticals Mexico SA de CV	Mexico
Shire Pharmaceuticals Services Limited	United Kingdom
Shire plc	Jersey
Shire Properties US	United States
Shire Regulatory Inc	United States
Shire Supplies U.S. LLC	United States
Shire UK Investments Limited	United Kingdom
Shire US Holdings Inc.	United States
Shire US Inc	United States
Shire US Investments	United Kingdom
Shire US Manufacturing Inc	United States
Sparkleflame Limited	United Kingdom
SPG Insurance Company Limited	Guernsey
Tanaud International BV	Netherlands
Tanaud Ireland Inc.	Ireland
The Endocrine Centre Limited	United Kingdom
TKT Argentina srl	Argentina
Jerini AG	Germany
Jerini US, Inc.	United States
JPT Peptide Technologies GmbH	Germany
JPT Peptide Technologies, Inc.	United States
Jerini Ophthalmic Holding GmbH	Germany
Jerini Ophthalmic, Inc.	United States
Jerini Beteiligungen GmbH	Germany
Jerini Holding Ltd	Malta
Jerini Trading Ltd	Malta

All subsidiary undertakings (with the exception of the Jerini subsidiaries which are held at 98.6%) of Shire plc are beneficially owned (directly or indirectly) as to 100% and are all consolidated in the consolidated financial statements of Shire plc.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Shire plc's Registration Statements on Form S-8 (Nos. 333-09168, 333-93543, 333-60952, 333-91552, 333-111579, 333-129961, 333-129960 and 333-111108), Form S-4 (No. 333-55696) and Form S-3 (Nos. 333-72862-01, 333-38662 and 333-39702) of our reports relating to the consolidated financial statements and financial statement schedule of Shire plc and the effectiveness of Shire plc's internal control over financial reporting dated February 27, 2009 appearing in this Annual Report on Form 10-K of Shire plc for the year ended December 31, 2008.

/s/ Deloitte LLP

DELOITTE LLP

London, United Kingdom

February 27, 2009

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Shire plc's Registration Statements on Form S-8 (Nos. 333-09168, 333-93543, 333-60952, 333-91552, 333-111579, 333-129961, 333-129960 and 333-111108), Form S-4 (No. 333-55696) and Form S-3 (Nos. 333-72862-01, 333-38662 and 333-39702) of our report relating to the financial statements of the Shire Income Access Share Trust dated February 27, 2009 appearing in this Annual Report on Form 10-K of Shire plc for the year ended December 31, 2008.

/s/ Deloitte LLP

DELOITTE LLP

London, United Kingdom

February 27, 2009

**CERTIFICATION OF ANGUS RUSSELL RELATING TO
FORM 10-K FOR THE YEAR TO
DECEMBER 31, 2008 OF
SHIRE PLC**

I, Angus Russell, certify that:

1. I have reviewed this Annual Report on Form 10-K of Shire plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Registrant as at, and for, the periods presented in this report;
4. The Registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Registrant and have:
 - (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) evaluated the effectiveness of the Registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as at the end of the period covered by this report based on such evaluation; and
 - (d) disclosed in this report any change in the Registrant's internal control over financial reporting that occurred during the Registrant's most recent fiscal quarter (the Registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the Registrant's internal control over financial reporting; and
5. The Registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Registrant's auditors and the audit committee of Registrant's board of directors (or persons performing the equivalent functions):
 - (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Registrant's ability to record, process, summarize and report financial information; and
 - (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the Registrant's internal control over financial reporting.

Date: February 27, 2009

/s/ Angus Russell
Angus Russell
Chief Executive Officer

**CERTIFICATION OF GRAHAM HETHERINGTON RELATING TO
FORM 10-K FOR THE YEAR TO
DECEMBER 31, 2008 OF
SHIRE PLC**

I, Graham Hetherington, certify that:

1. I have reviewed this Annual Report on Form 10-K of Shire plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Registrant as at, and for, the periods presented in this report;
4. The Registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Registrant and have:
 - (a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) evaluated the effectiveness of the Registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as at the end of the period covered by this report based on such evaluation; and
 - (d) disclosed in this report any change in the Registrant's internal control over financial reporting that occurred during the Registrant's most recent fiscal quarter (the Registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the Registrant's internal control over financial reporting; and
5. The Registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Registrant's auditors and the audit committee of Registrant's board of directors (or persons performing the equivalent functions):
 - (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Registrant's ability to record, process, summarize and report financial information; and
 - (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the Registrant's internal control over financial reporting.

Date: February 27, 2009

/s/ Graham Hetherington

Graham Hetherington

Chief Financial Officer

The certification set forth below is being submitted in connection with the Annual Report of the Registrant on the Form 10-K for the year to December 31, 2008 (the Report), for the purpose of complying with Rule 13a-14(b) or Rule 15d-14(b) of the Securities Exchange Act of 1934 (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code.

Angus Russell, the Chief Executive Officer and Graham Hetherington, the Chief Financial Officer of Shire plc (the Registrant), each certifies that, to the best of his knowledge:

1. the Report fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and
2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Registrant.

Dated: February 27, 2009

/s/ Angus Russell

Angus Russell
Chief Executive Officer

/s/ Graham Hetherington

Graham Hetherington
Chief Financial Officer

Exhibit Index

Exhibit number	Description
2.01	Agreement and Plan of Merger by and among Shire Pharmaceuticals Group plc, Transkaryotic Therapies, Inc. and Sparta Acquisition Corporation, dated as of April 21, 2005. ⁽¹⁾
2.02	Agreement of Merger dated as of February 20, 2007 among Shire plc, Shuttle Corporation and New River Pharmaceuticals, Inc. ⁽²⁾
2.03	Business Combination Agreement dated as of July 3, 2008 between Maia Elfte Vermögensverwaltungs GmbH and Jerini AG. ⁽³⁾
3.01	Form of Amended Memorandum and Articles of Association of Shire plc as adopted by special resolution passed on April 10, 2008 and amended by special resolution on September 24, 2008. ⁽⁴⁾
4.01	Form of Assignment and Novation Agreement between Shire Limited, Shire plc, JPMorgan Chase Bank, N.A. dated April 16, 2008 relating to the Deposit Agreement among Shire plc, JPMorgan Chase Bank, N.A. as depository and all holders from time to time of ADRs issued thereunder dated November 21, 2005. ⁽⁵⁾
4.02	Form of Deposit Agreement among Shire plc, JPMorgan Chase Bank, N.A. as depository and all holders from time to time of ADRs issued thereunder dated November 21, 2005. ⁽⁶⁾
4.03	Form of Ordinary Share Certificate of Shire Limited. ⁽⁷⁾
4.04	Form of American Depositary Receipt Certificate of Shire Limited. ⁽⁸⁾
4.05	Trust Deed for the New Shire Income Access Trust, dated August 29, 2008.
10.01	Tender and Support Agreement dated as of February 20, 2007 among Shire plc, Mr. Randal J. Kirk and the other parties named therein. ⁽⁹⁾
10.02	Multicurrency Term and Revolving Facilities Agreement as of February 20, 2007 by and among Shire plc, ABN AMRO Bank N.V., Barclays Capital, Citigroup Global Markets Limited, The Royal Bank of Scotland plc, and Barclays Bank plc. ⁽¹⁰⁾
10.03	Accession and Amendment Deed dated April 15, 2008 between Shire Limited, Shire plc, certain subsidiaries of Shire plc and Barclays Bank plc as Facility Agent relating to a US \$1,200,000,000 facility agreement dated February 20, 2007 (as amended by a syndication and amendment agreement dated July 19, 2007). ⁽¹¹⁾
10.04	Subscription Agreement dated May 2, 2007 relating to the 2.75% Convertible Bonds due 2014 between Shire plc and ABN AMRO Bank N.V. and NM Rothschild & Sons Limited (trading together as ABN AMRO Rothschild, an unincorporated equity capital markets joint venture) and Barclays Bank plc and Citigroup Global Markets Limited and Goldman Sachs International and Morgan Stanley & Co. International plc and others. ⁽¹²⁾
10.05	Amending Subscription Agreement dated May 8, 2007 relating to the 2.75% Convertible Bonds due 2014 between Shire plc and ABN AMRO Bank N.V. and NM Rothschild & Sons Limited (trading together as ABN AMRO Rothschild, an unincorporated equity capital markets joint venture) and Barclays Bank plc and Citigroup Global Markets Limited and Goldman Sachs International and Morgan Stanley & Co. International plc and others. ⁽¹³⁾
10.06	Trust Deed dated May 9, 2007 relating to the 2.75% Convertible Bonds due 2014 between Shire plc and BNY Corporate Trustee Services Limited. ⁽¹⁴⁾
10.07	Supplemental Trust Deed dated April 15, 2008 between Shire Limited, Shire plc and BNY Corporate Trustee Services Limited relating to a trust deed dated May 9, 2007 relating to US \$1,100,000,000 2.75% Convertible Bonds due 2014. ⁽¹⁵⁾
10.08	Accession and Amendment Agreement dated April 15, 2008 between Shire Limited, Shire plc, BNY Corporate Trustee Services Limited and The Bank of New York relating to a paying and conversion agency agreement dated May 9, 2007 relating to US \$1,100,000,000 2.75% Convertible Bonds due 2014. ⁽¹⁶⁾
10.09*	Revised and Restated Master License Agreement dated November 20, 1995 among Shire BioChem Inc (f/k/a BioChem Pharma Inc.), Glaxo Group Limited, Glaxo Wellcome Inc. (formerly Glaxo Canada Inc.), Glaxo Wellcome Inc. (formerly Glaxo Inc.), Tanaud Holdings (Barbados) Limited, Tanaud International B.V. and Tanaud LLC. ⁽¹⁷⁾

- 10.10* Settlement Agreement, dated August 14, 2006 by and between Shire Laboratories Inc. and Barr Laboratories, Inc. ⁽¹⁸⁾
- 10.11* Product Development and License Agreement, dated August 14, 2006 by and between Shire LLC and Duramed Pharmaceuticals, Inc. ⁽¹⁹⁾
- 10.12* Product Acquisition and License Agreement, dated August 14, 2006 by and among Shire LLC, Shire plc and Duramed Pharmaceuticals, Inc. ⁽²⁰⁾
- 10.13 Service Agreement between Shire plc and Mr Angus Russell, dated March 10, 2004. ⁽²¹⁾
- 10.14 Novation Agreement dated November 21, 2005 relating to the Employment Agreement of Angus Russell dated March 10, 2004. ⁽²²⁾
- 10.15 Novation Agreement dated April 11, 2008 relating to the Employment Agreement of Angus Russell dated March 10, 2004, as previously novated on November 21, 2005. ⁽²³⁾
- 10.16 Form of Amended and Restated Employment Agreement between Shire plc and Mr Matthew Emmens, dated March 12, 2004. ⁽²⁴⁾
- 10.17 Amendment Agreement dated November 21, 2005 relating to the Amended and Restated Employment Agreement of Matthew Emmens dated March 12, 2004. ⁽²⁵⁾
- 10.18 Ratification and Guaranty dated November 21, 2005 relating to the Amended and Restated Employment Agreement of Matthew Emmens dated March 12, 2004. ⁽²⁶⁾
- 10.19 Amendment Agreement dated May 20, 2008 relating to the Amended and Restated Employment Agreement of Matthew Emmens dated March 12, 2004, as amended on November 21, 2005. ⁽²⁷⁾
- 10.20 Ratification and Guaranty dated May 20, 2008 relating to the Amended and Restated Employment Agreement of Matthew Emmens dated March 12, 2004. ⁽²⁸⁾
- 10.21 Form of Indemnity Agreement for Directors of Shire Limited. ⁽²⁹⁾
- 10.22 Service Agreement between Shire Limited and Mr Angus Russell, dated July 2, 2008. ⁽³⁰⁾
- 10.23 Service Agreement between Shire Limited and Mr Graham Hetherington, dated July 2, 2008. ⁽³¹⁾
- 10.24 Form of Settlement Agreement and Mutual Release in re: *Transkaryotic Therapies, Inc.*, by and between Shire Human Genetic Therapies, Inc., Shire plc and the parties set forth therein. ⁽³²⁾
- 21 List of Subsidiaries.
- 23.1 Consent of Deloitte LLP.
- 23.2 Consent of Deloitte LLP.
- 31.1 Certification of Angus Russell pursuant to Rule 13a – 14 under The Exchange Act.
- 31.2 Certification of Graham Hetherington pursuant to Rule 13a – 14 under The Exchange Act.
- 32.1 Certification of Angus Russell and Graham Hetherington pursuant to Section 906 of the Sarbanes – Oxley Act of 2002.

* Certain portions of this exhibit have been omitted intentionally, subject to a confidential treatment request. A complete version of this agreement has been filed separately with the Securities and Exchange Commission.

- (1) Incorporated by reference to Exhibit 99.02 to Shire's Form 8-K filed on April 25, 2005.
- (2) Incorporated by reference to Exhibit 2.1 to Shire's Form 8-K filed on February 23, 2007.
- (3) Incorporated by reference to Exhibit 2.1 to Shire's Form 8-K filed on July 10, 2008.
- (4) Incorporated by reference to Exhibit 99.02 to Shire's Form 8-K filed on October 1, 2008.
- (5) Incorporated by reference to Exhibit 4.01 to Shire's Form 8-K filed on May 23, 2008.
- (6) Incorporated by reference to Exhibit 4.02 to Shire's Form 8-K filed on May 23, 2008.
- (7) Incorporated by reference to Exhibit 4.03 to Shire's Form 8-K filed on May 23, 2008.
- (8) Incorporated by reference to Exhibit 4.04 to Shire's Form 8-K filed on May 23, 2008.
- (9) Incorporated by reference to Exhibit 99.1 to Shire's Form 8-K filed on February 23, 2007.
- (10) Incorporated by reference to Exhibit 10.2 to Shire's Form 10-Q filed on May 1, 2007.
- (11) Incorporated by reference to Exhibit 10.01 to Shire's Form 8-K filed on May 23, 2008.
- (12) Incorporated by reference to Exhibit 10.1 to Shire's Form 10-Q filed on August 2, 2007.
- (13) Incorporated by reference to Exhibit 10.2 to Shire's Form 10-Q filed on August 2, 2007.
- (14) Incorporated by reference to Exhibit 10.3 to Shire's Form 10-Q filed on August 2, 2007.
- (15) Incorporated by reference to Exhibit 10.02 to Shire's Form 8-K filed on May 23, 2008.
- (16) Incorporated by reference to Exhibit 10.03 to Shire's Form 8-K filed on May 23, 2008.
- (17) Incorporated by reference to Exhibit 10.09 to Shire's Form 10-K/A filed on May 30, 2008.
- (18) Incorporated by reference to Exhibit 10.1 to Shire's Form 10-Q filed on November 7, 2006.
- (19) Incorporated by reference to Exhibit 10.2 to Shire's Form 10-Q filed on November 7, 2006.
- (20) Incorporated by reference to Exhibit 10.3 to Shire's Form 10-Q filed on November 7, 2006.

- (21) Incorporated by reference to Exhibit 10.11 to Shire's Form 10-K filed on March 12, 2004.
- (22) Incorporated by reference to Exhibit 10.03 to Shire's Form 8-K filed on November 25, 2005.
- (23) Incorporated by reference to Exhibit 10.06 to Shire's Form 8-K filed on May 23, 2008.
- (24) Incorporated by reference to Exhibit 10.13 to Shire's Form 10-K filed on March 12, 2004.
- (25) Incorporated by reference to Exhibit 10.01 to Shire's Form 8-K filed on November 25, 2005.
- (26) Incorporated by reference to Exhibit 10.02 to Shire's Form 8-K filed on November 25, 2005.
- (27) Incorporated by reference to Exhibit 10.04 to Shire's Form 8-K filed on May 23, 2008.
- (28) Incorporated by reference to Exhibit 10.05 to Shire's Form 8-K filed on May 23, 2008.
- (29) Incorporated by reference to Exhibit 10.07 to Shire's Form 8-K filed on May 23, 2008.
- (30) Incorporated by reference to Exhibit 10.22 to Shire's Form 10-Q filed on November 10, 2008
- (31) Incorporated by reference to Exhibit 10.23 to Shire's Form 10-Q filed on November 10, 2008
- (32) Incorporated by reference to Exhibit 10.24 to Shire's Form 10-Q filed on November 10, 2008