

We enable people
with life-altering
conditions to lead
better lives.



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Shire trademarks

The following are trademarks either owned or licensed by Shire plc or companies within the Shire Group which are the subject of trademark registrations in certain territories, or which are owned by third-parties as indicated and referred to in this Annual Review.

ADDERALL XR[®] (mixed salts of a single-entity amphetamine)
AGRYLIN[®] (anagrelide hydrochloride)
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[®] XL (mesalamine)
REPLAGAL[®] (agalsidase alfa)
VYVANSE[®] (lisdexamfetamine dimesylate)
XAGRID[™] (anagrelide hydrochloride)

Third-party trademarks

The following are trademarks of third-parties referred to in this document.

AMIGAL (migalastat hydrochloride) (trademark of Amicus)
ASACOL (mesalamine) (trademark of Procter & Gamble Pharmaceuticals)
COLAZAL (balsalazide disodium) (trademark of Salix Pharmaceuticals, Inc)
DIPENTUM (olsalazine sodium) (trademark of Celltech Pharmaceuticals, Inc)
DYNEPO (epoetin delta) (trademark of Sanofi-Aventis)
PENTASA (mesalamine) (trademark of Ferring)
PLICERA (isofagomine tartrate) (trademark of Amicus)

Cover picture: Sara Logan with daughter, Sara suffers from ulcerative colitis and is currently taking LIALDA.

We enable people with life-altering conditions to lead better lives.

That's a brave claim, but it's one that inspires everyone at Shire. By harnessing that energy and dedication, we can make a real difference to patients and their families, and generate profitable long-term growth for the people who invest in us.

The more successful we are at generating returns for our shareholders, the more cash we will be able to invest in new therapies that will change more peoples' lives.

In the next few pages, we'll look at how that works, and share some of the stories that show it in action.





VYVANSE

Revenues have reached
\$319 million this year.

*"VYVANSE helps me to
concentrate and I'm making
friends and enjoying school."
Macey Owens*

VYVANSE is an innovative new pro-drug
therapy for Attention Deficit Hyperactivity
Disorder (ADHD), which only becomes
active when it is metabolized in the body.
This means it offers a steady benefit
throughout the day.

For more information on Shire products
visit <http://www.shire.com/shire/products/>

We focus on *meeting unmet needs*,
and developing effective treatments
for *specialist physicians*, and *rare diseases*.



LIALDA/MEZAVANT XL
US ASA market share is now
14.1% as at December 2008*.

*"Having medication that
I take just once a day has
helped me regain control
and enjoy quality time
with my young daughter."
Sara Logan*

LIALDA/MEZAVANT XL is the first and only oral once a day treatment for the induction of remission in patients with active mild to moderate ulcerative colitis. For more information on Shire products visit <http://www.shire.com/shire/products/>

*Source: IMS NPA



FOSRENOL
Is approved in 42 countries
and is now available in Japan.

*"My life has improved; I now
don't have as much stomach
discomfort and am able to
enjoy the time I spend with
my grandson."
Shirley Pinckney*

FOSRENOL is our first global product, and the first compound that we took from the test tube to approval. It helps in the reduction of high phosphorus levels which occur in patients with end-stage kidney disease. For more information on Shire products visit <http://www.shire.com/shire/products/>

We organize our business around our patients, and around the type and prevalence of the diseases we treat.





ELAPRASE

Is now approved and launched
in 43 countries.

*"Since I started taking
ELAPRASE, I have more
energy to enjoy things that
I wouldn't have been able
to, and this has made my
life better."*

Andrew Watkins

ELAPRASE is the first and only enzyme
replacement therapy for Hunter syndrome—
a rare, progressive and life-threatening
condition that primarily affects boys.

*For more information on Shire products
visit <http://www.shire.com/shire/products/>*

We have *a delivery model* that reflects the different market dynamics of our two businesses, and helps us meet our patients' needs more effectively.

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REPLAGAL
Has had revenue growth
of 22%.

*"The constant pains I had are
much better; it's wonderful
to go through the day
not dreading such pain."
Mathieu Pauly*

REPLAGAL replaces the enzyme which
is missing or deficient in people suffering
from Fabry disease. It's been shown to help
improve both kidney function and heart size.
For more information on Shire products
visit <http://www.shire.com/shire/products/>



FIRAZYR

Has been launched and is now available in the UK, Germany and Austria.

"I want to be able to control my condition and not have to worry about when my next attack might be."

FIRAZYR is a pioneering new treatment for acute attacks of hereditary angioedema in adults, a rare, debilitating and potentially life-threatening genetic disease.

For more information on Shire products visit <http://www.shire.com/shire/products/>

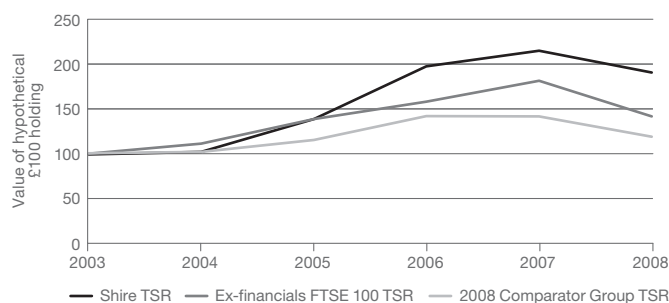
We have the right people and the right resources, in the right places, to address our immediate challenges, *and seize the opportunities that are opening up for us across the world.*

Five year performance

Revenue growth over the past five years \$M

2008	\$3,022M
2007	\$2,436M
2006	\$1,797M
2005	\$1,599M
2004	\$1,363M

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



2008

Product sales—\$2.75 billion

Total revenues—\$3 billion

Sources of revenue %

up **27%**

up **24%**

ADDERALL XR	36%
VYVANSE	11%
ELAPRASE	10%
PENTASA	6%
REPLAGAL	6%
FOSRENOL	5%
LIALDA	5%
DAYTRANA	3%
CARBATROL	2%
XAGRID	2%
Royalties	8%
Others	6%
Total	100.0%

New product sales
 36% of total sales

Total revenue
 \$3,022 million

Product sales

2008	36%
2007	22%

2008	\$3,022M
2007	\$2,436M

	2008 \$M
Established products	\$653M
VYVANSE	\$319M
ELAPRASE	\$305M
FOSRENOL	\$155M
LIALDA	\$140M
DAYTRANA	\$79M
FIRAZYR	\$1M
New product sales	\$999M
ADDERALL XR	\$1,102M
Total product sales	\$2,754M

2008—New market product launches

Shire Australia

Specialty Pharmaceuticals ('SP') (FOSRENOL and XAGRID) and Human Genetic Therapies ('HGT') products (REPLAGAL) taken back from local distributors and re-launched under Shire.

Shire Brazil

HGT products to be commercialized directly via the Local Operating Company ('LOC').

Shire Czech Republic

HGT products—ELAPRASE and REPLAGAL.

Shire Greece

HGT products—ELAPRASE and REPLAGAL.

Shire Japan

Local rep office will work with existing partners to optimize commercialization of Shire portfolio: Genzyme Corporation for ELAPRASE, Dainippon Sumitomo Pharma Co., Ltd for REPLAGAL, Mochida Pharmaceutical Co., Ltd for LIALDA, Bayer Yakuhin Ltd for FOSRENOL, Kirin Brewery Company Ltd for XAGRID.

Shire Mexico

HGT products to be commercialized directly via the LOC, FOSRENOL commercialization plans through a local distributor.

Shire Russia

HGT products to be commercialized directly via the rep office; FOSRENOL, AGRYLIN and MEZAVANT to be commercialized via relationship with commercial partner.

Shire remains in the hunt for new technologies—fully focused on unmet patient needs and thoroughly committed to making the right difference.

The future of healthcare, many say, lies in personalized medicine—in helping physicians optimize outcomes for patients through individualized treatments that make a measurable difference to their lives. The industry will continue to experience enormous pressures—on prices, through regulations, by virtue of new leaders and legislators, by the hard reality that there is a worldwide shortage of cash. But the future is bright for biopharmaceutical companies with financial resources and with product portfolios that can deliver tangible benefits to patients and their caregivers, and Shire is one of those companies.

In 2008, Shire once again demonstrated the value of its specialty-focused business model and unique culture. Since succeeding me as Chief Executive Officer ('CEO') in June, Angus Russell has exercised consistently good judgment. He has brought new focus, enthusiasm, and creativity to the Shire business while leading a team that has overseen the continued flawless execution of its strategy. He has revisited Shire's mission and values, developed a corporate brand that asserts the importance of being brave, and looked ahead to the coming seven years with the conviction that Shire will continue to develop into one of the world's most valuable specialty biopharmaceutical companies.

At the same time, Angus and his team have paid careful attention to the Shire pipeline, bolstering a diverse and innovative product development program. Priority has also been given to fully globalizing Shire, a strategy that Shire—which can enter new markets through Human Genetic Therapies ('HGT') products that require relatively little infrastructure—undertakes with extreme efficiency. An increasing emphasis has also been placed, over the course of the year, on Shire's role as a global corporate citizen intent on acting responsibly and protecting the precious resources of our planet.

At the end of 2008, Shire remains a cash generative company capable of pursuing new technologies and products that boast good supportive data and can be acquired for the right price. These factors, combined with Shire's robust balance sheet, leave the company unusually well positioned for our current economic environment. It remains a Company that can not only measurably improve lives, but sometimes contribute to saving them.

I am grateful to Angus Russell, his management team, and all the people of Shire who come to work each day determined to make the most of the opportunities that present themselves, and the opportunities that Shire people create. Shire is leading the way to a brighter future. I look forward to the year ahead.



Matthew Emmens
Chairman

"The future is bright;
we have the financial
resources and a products
portfolio that can deliver
tangible results..."



Over the course of the past two years at Shire, we've broadened our pipeline/portfolio with eight new products, while successfully bolstering our existing franchises.

US GAAP highlights

Revenues	\$3,022M
Operating income	\$412M
Net income	\$156M
Diluted earnings per ADS	86¢

Risks—wisely measured and judiciously taken—are part and parcel of every successful company, and certainly we've taken our fair share at Shire. In our brightest moments we have stood at a critical juncture, made defining, not-always-obvious decisions, and redefined the future, not just for ourselves, but for the physicians and patients we serve.

Since succeeding Matt Emmens as CEO in June, I have been particularly keen on staying true to those aspects of our culture that brought us to our present state as one of the most effective biopharmaceutical companies in the world: the willingness to take measured risks; the courage to challenge one another; and the unyielding commitment to the patients, physicians, and communities we serve. We spent the time, in 2008, to look around and to project forward—to set the targets that will enable us to emerge, by 2015, as one of the most valuable specialty biopharmaceutical companies in the world. We committed to the underlying thesis that now forms the core of our corporate brand—that we strive to be as brave as the people we help.

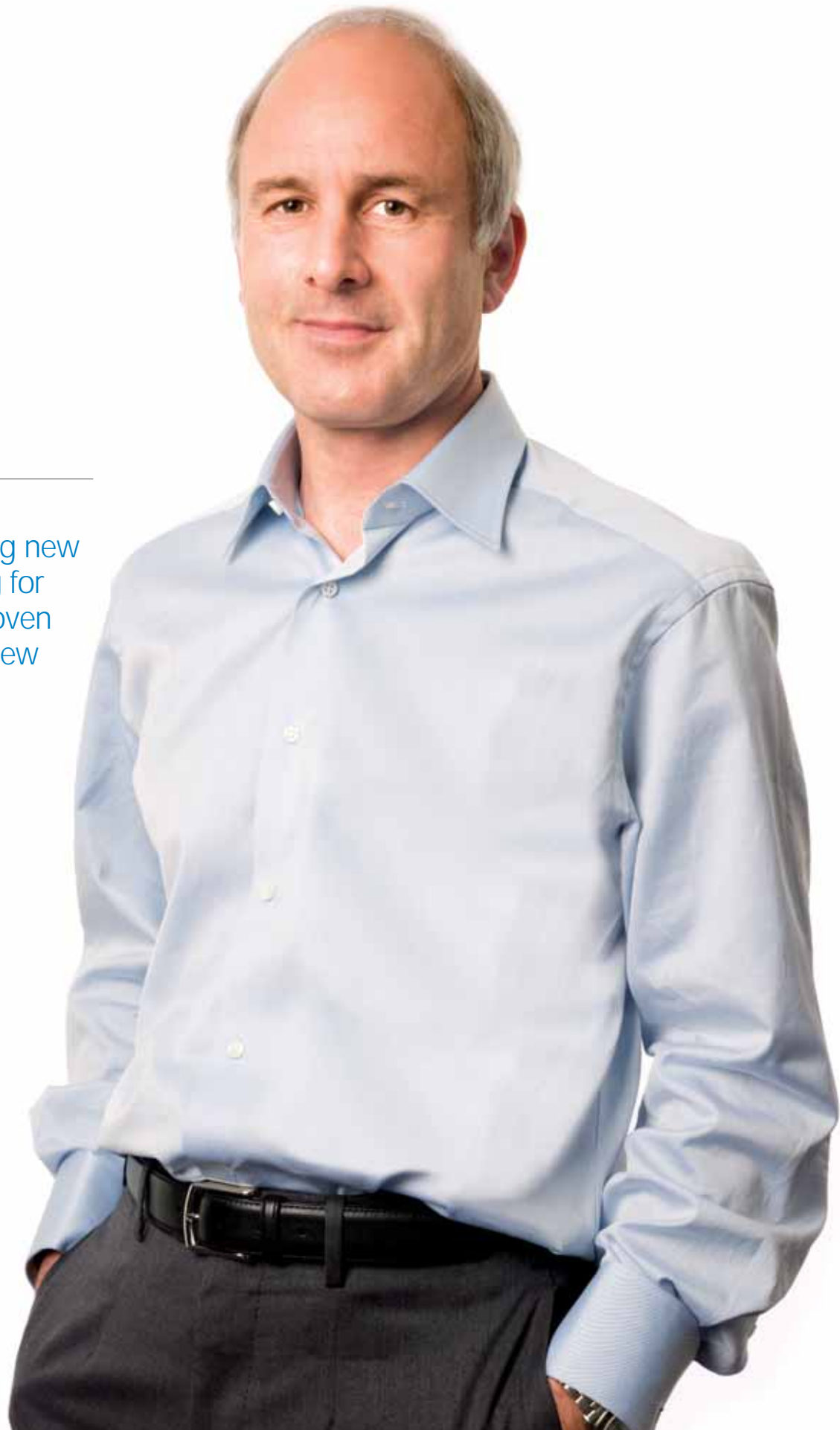
Of course, achieving our mission demands quite a lot of Shire's pipeline as well as its marketed portfolio, and I am very pleased with the steps that

we have taken to further leverage both. Consider this: over the course of the last two years alone, we've successfully completed six deals that have yielded eight new products in our pipeline/portfolio. Consider, also, this: the combined sales of new products launched in the past four years achieved \$1 billion of sales in 2008.

We're committed to going the distance with every product at Shire—asking hard questions, exploring new indications, looking for ways to extend proven technologies into new treatments; always with the patients' needs most at heart. The acquisition of New River, for example, didn't just provide Shire with VYVANSE, a next-generation treatment for ADHD; it opened the door to new possibilities associated with 'CarrierWave' technology, which enhances drug metabolism and may well have applications for other medicines. At the same time we're expanding our patient populations with plans to expand our presence in markets outside the US and the proposed launch in the US of INTUNIV, our first non-stimulant ADHD drug.

In the gastrointestinal business unit, we are taking similar strides—leveraging our success with LIALDA, our expertise in ulcerative colitis, and our relationships with gastro-enterologists to explore

"We're asking hard questions, exploring new indications, looking for ways to extend proven technologies into new treatments."



*We've come together with one overriding purpose:
to be as brave as the people we help.*

new options for patients suffering from an entire range of Inflammatory Bowel diseases. We're currently in the midst of Phase 2 trials for SPD550, a compound we licensed in from Alba Therapeutics Corporation ('Alba') because we believe that it can have important implications for patients suffering from Celiac disease.

Three and a half years ago, when Shire acquired what has since become known as Shire Human Genetic Therapies, there were only four projects in the pipeline and there were many questions about this relatively small company's future. Three deals later—with Amicus Therapeutics, Inc. ('Amicus'), Zymenex A/S ('Zymenex') and Jerini AG ('Jerini')—HGT is 1,000 people strong, with three marketed drugs in its portfolio (REPLAGAL, ELAPRASE and FIRAZYR) and a number of very exciting Phase 2 and 3 products designed to treat such debilitating conditions as Gaucher disease, Fabry disease, and Metachromatic Leukodystrophy. HGT now occupies an entire campus in Lexington, Massachusetts—a campus that we opened to investors in November during our first-ever HGT Business Day.

Moreover, HGT products are helping Shire meet its goal of global diversification, with REPLAGAL and ELAPRASE together now approved and in use in more than 40 countries, and 70% of HGT sales now generated outside the United States. Our world really is expanding rapidly at Shire, and we are taking aggressive steps to capitalize on—and to create—opportunities for patients around the world who do not yet have access to the life-altering medicines that we manufacture and sell.

Pressures abound in the current economy, but at Shire we're not just merely biding our time. We are moving forward—bolstering our pipeline through business-enhancing acquisitions, anticipating breakthroughs helping new patient populations with unmet needs, capitalizing on new patient populations, and looking for commonalities between our Specialty and HGT businesses. It's been an exciting time and the future promises even more. I thank my colleagues for continuing to help Shire live up to its promise.



Angus Russell
Chief Executive Officer

R&D projects.

Shire has a total of 17 projects in full development of which 14 are in Phase 2 or beyond.

Indication	Project	Phase	Estimated submission	Estimated launch
SPECIALTY PHARMA				
ADHD	INTUNIV	Registration	H1-2009	2009
ADHD—EU	DAYTRANA—EU	Registration		2009
ADHD—US adolescent	DAYTRANA—US	3	H2-2009	2010
ADHD—EU	VYVANSE	3		2011
Chronic Kidney disease	FOSRENOL	3		2009
Diverticulitis	LIALDA	3		2012–2015
Celiac disease	SPD550	2		2012–2015
Prevention and reduction of scarring	AVOTERMIN	2		2012–2015
HUMAN GENETIC THERAPIES				
Hereditary angioedema	FIRAZYR (US)	3		2011
Gaucher disease	VELAGLUCERASE ALFA	3	H2-2009	2010
Metachromatic Leukodystrophy	HGT-1111 (METAZYM)	2		2012–2015
Fabry disease	HGT-3310 (AMIGAL)	2		2012–2015
Gaucher disease	HGT-3410 (PLICERA)	2		2012–2015
Pompe disease	HGT-3510*	2		2012–2015
Hunter syndrome CNS	HGT-2310	1		2012–2015
Sanfilippo A syndrome	HGT-1410	Pre-clinical		2012–2015
Krabbe disease	HGT-2610	Pre-clinical		2012–2015

*Currently on clinical hold in the US.

Shire's business strategy.

We focus on *meeting unmet needs*, and developing effective treatments for *specialist physicians*, and *rare diseases*.

There are common threads that run through everything we do. One is a focus on specialist physicians, many of them working in a small number of centers of excellence in their own particular country. Another is a focus on symptomatic conditions where our drugs can make a real difference.

So what does this mean in practice? Shire has never wanted to be a big pharma company; we don't think that way, and we don't act that way. Our special expertise lies in finding niche markets, and making the most of them. These might be areas of medical need that other products aren't yet addressing, or rare life-threatening conditions where there is as yet no treatment, and no hope for the people who suffer from them.

There are common threads that run through everything we do. One is a focus on specialist physicians, many of them working in a small number of centers of excellence in their own particular country. Another is a focus on symptomatic conditions where our drugs can make a real difference, and where healthcare providers can see tangible value from the money they spend—what you might call a higher 'return on treatment'.

ADHD is, of course, where the whole Shire story began, and for a long time we were known as 'the ADHD company'. These days there's a lot more to our business than that, even if we still remain a serious force in that market. It still provides a significant proportion of our revenue, but it also gives us something else: the experience

of growing a whole therapeutic area almost from scratch. We were instrumental in growing the US ADHD market from \$278 million in 1994 to the \$4.4 billion it is now. Some of that was achieved by developing the right drugs, some of that was by working with specialists, patient groups, and opinion-formers to raise awareness of the impact of the condition, and how the right treatment can improve the lives of patients and their families. These days markets move much faster than they did ten years ago, but the learning we gained is still valid, and we're using it not only to develop and launch completely new ADHD treatments, like DAYTRANA and INTUNIV, but to expand into new therapeutic areas.

Something else that's shared across the whole Company is a collaborative way of working that's distinctively 'Shire'. However large we become, we want to remain as agile as we are now, so that we can move fast, and have the courage to seize new opportunities. Three years ago, we were one of the first to move into the biopharma space, with our acquisition of what is now Shire HGT. Many other pharmaceutical companies have since followed our lead, but we think we have the people and resources to exploit it to the full. We want our shareholders to be

confident that we are rigorous in deciding what we invest in, and will work for the maximum return on our investment—and theirs.

Whether it's through HGT, or our Specialty Pharma business, we're expanding our business by growing our international presence, and adding new products to our portfolio that are late stage and low risk, or use proven technologies that we can take through the approval process quickly, and start to commercialize. And while their aims might be the same, the way these two businesses operate is different, and recognizing that difference, and capitalizing on the advantages it gives us, is going to be crucial to our next stage of growth.

Our strategy principles

- Specialist focus; symptomatic diseases; high unmet needs; niche markets.
- Remain agile, move fast and seize opportunities that present themselves.
- Focus on our best opportunities and be prepared to exit underperforming or low priority assets and businesses.
- Strong bias towards outsourcing non-differentiating capabilities.
- Strong bias towards projects and technologies that have proof of concept in man, are low risk and allow for a quick development decision point.
- Need to diversify business concentration through addition of bolt-on products and 'corner lots' (self supporting business opportunities) and through international expansion.

Putting it into practice.

We organize our business around our patients, and around the type and prevalence of the diseases we treat.

Working in the orphan drug field differs markedly from operating in the more mainstream Specialty Pharma business.

The key difference between Specialty Pharma and HGT is the prevalence of the conditions they treat.

As Mike Cola, the President of Specialty Pharma, says, "A typical product for us will treat a condition that affects around 100,000 people in a major market like the US; in HGT's case there may be less than 10,000 patients across the whole world." Such small patient populations mean that HGT is, in effect, an 'orphan drug' enterprise. The volumes for such a business will always be low, but it does have special advantages of its own. Approval processes can often be quicker and smoother, and many governments will offer tax advantages to offset the high development costs. Add to that strong intellectual property and regulatory protections and you see a stronger deterrent to the development of generic alternatives. The result is good investment returns, even though volumes are low. And because there is often no other treatment available, a drug that can offer genuine benefits will not only generate very good returns, but make an enormous difference to the people who use it.

Working in the orphan drug field also differs markedly from operating in the more mainstream Specialty Pharma business. Not just the regulatory and approval structure but the sales model is quite different, and most healthcare providers have a very different approach to paying for these drugs. Many orphan treatments are reimbursed straightaway, for example, without the sometimes protracted pricing negotiations that can apply to more conventional products.

This is one key reason why we organize ourselves into two businesses. There are also other practical factors that make the two business models quite distinct. For example, HGT drugs tend to cost less to develop and less to sell; as a result the reinvestment rate in R&D in HGT will be something like the 25% typical of a biotech venture, whereas in Specialty Pharma it will be closer to the 14% you might expect in a big pharma operation. This results in quite different sales structures, and a different approach to R&D that starts with the science and extends right through the approval process.

2008 key developments

Q1

Reaffirming our full year 2008 guidance—
2008 revenue growth expected to be in
the mid to high teens range and positive
revenue growth through 2010

LIALDA co-promotion agreement with TAP
Pharmaceutical Products, Inc. ('TAP')

Global expansion continues with product
approvals in Spain, Russia, Mexico,
Australia, South Korea and Hong Kong

Q3

Voluntary public takeover of Jerini AG

—FIRAZYR approved in EU
—FIRAZYR launched by Jerini in Austria,
Germany and the UK

New product portfolio* representing
39% of Q3 product sales and exceeding
ADDERALL XR sales for the first time

VYVANSE now third highest prescribed
ADHD brand

ELAPRASE sales driven by swift geographic
expansion and strong patient demand

Discontinuation of DYNEPO

—Redirecting resources into faster growing
core products

Q2

New UK/US listed holding company to protect
Shire's tax position

VYVANSE approved for treatment in adults

Acquisition of new orphan drug for
Metachromatic Leukodystrophy ('MLD')

VYVANSE for adults launched in June

— Two million VYVANSE Rx written since
product launched

Q4

Strong portfolio of new high growth
products with long patent protection and
regulatory exclusivity

—Achieved \$1 billion of combined annual sales

Shire now has over 98% of Jerini's
shareholding and has initiated compulsory
purchase in relation to minority shareholders

Robust pipeline with focus on orphan
drugs and specialist products treating
symptomatic disorders

—Eight products acquired since beginning
of 2007

FOSRENOL approved in Japan

—Shire will receive royalties via an exclusive
agreement with Bayer

—Bayer are responsible for product development,
approval and commercialization

*New products: DAYTRANA, ELAPRASE, FIRAZYR,
FOSRENOL, LIALDA/MEZAVANT XL AND VYVANSE.

Focus on the science.

Drug development at Specialty Pharma.

In many ways the research and development activity in our Specialty Pharma business looks very similar to what you would expect to find in a traditional pharmaceutical R&D department. The same protocols apply, and there's exactly the same need to take a new product through all the phases of pre-clinical and clinical trials. The most notable difference will be in the fact that Shire Specialty Pharma's R&D team focuses on late-stage products that can be brought to market quickly, and carry far lower risk, both for the Company, and its investors.

Specialty Pharma has also developed a significant expertise in applying proven technologies to produce new treatments. For example, we acquired the so-called 'CarrierWave' process as part of our acquisition of New River in 2007. Our main objective in buying that company was to develop a next-generation ADHD product to succeed ADDERALL XR, and we're already seeing the proof of that in the successful launch, and huge potential, of VYVANSE. But the technology that makes VYVANSE so effective, by

using peptide chains and amino-acids to enhance the metabolism of the drug, could also have many other uses in other therapeutic areas. The Specialty Pharma Emerging business unit is actively seeking new opportunities to exploit 'CarrierWave' technology.

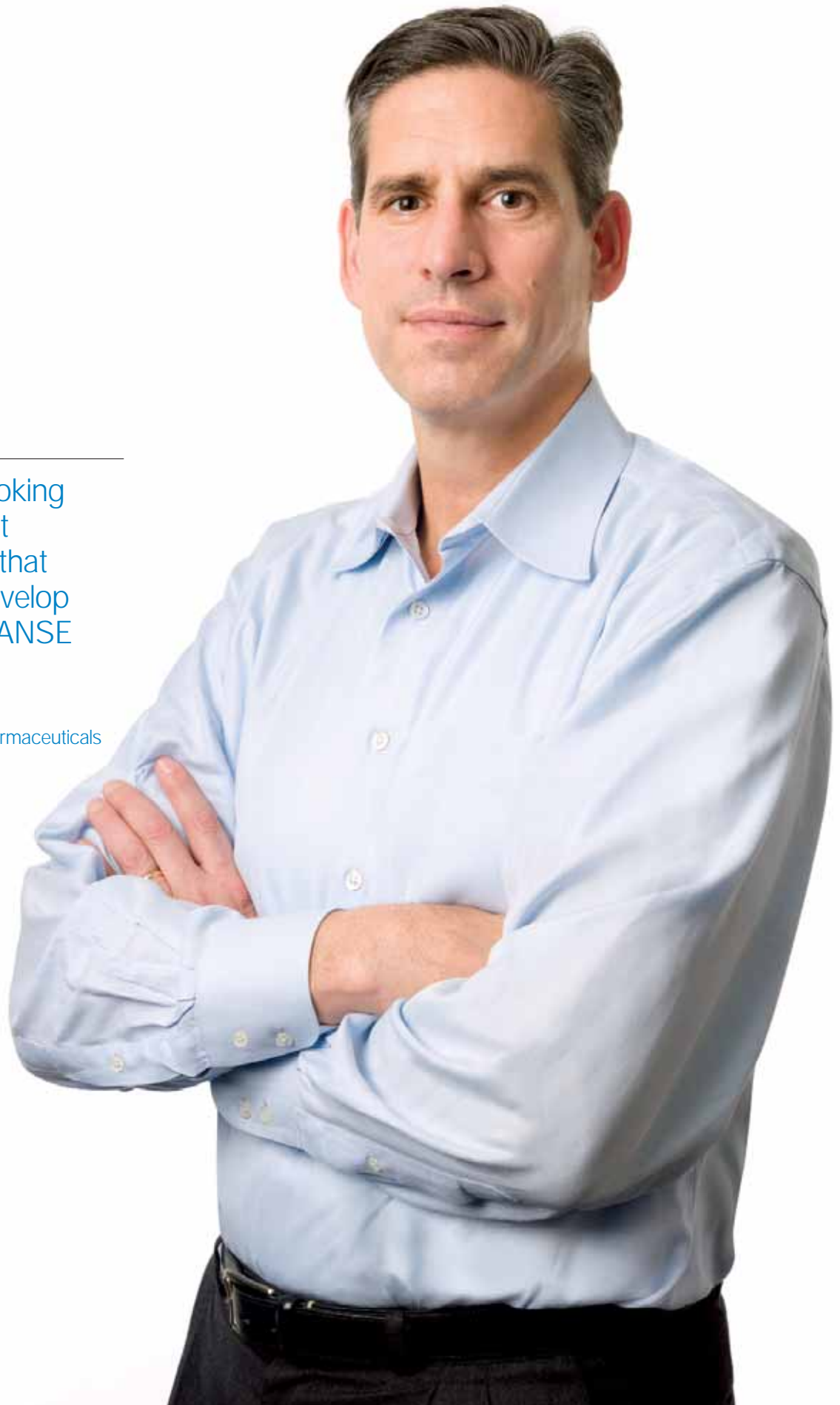
The gastrointestinal business unit is another good example. Specialty Pharma has particular expertise in the treatment of ulcerative colitis, with the number two treatment in the US Oral 5-ASA market*, but there are opportunities for Shire across the whole range of Inflammatory Bowel diseases, which are all treated by the same specialist gastro-enterologists. This might range from liver disease, to pancreatic enzyme replacement, which is particularly crucial for Cystic Fibrosis patients. The only treatment currently available here is derived from pig enzymes, but a human-derived compound might well be more effective. There could be a real opportunity for us here, which might also generate opportunities for Specialty Pharma and HGT to work collaboratively together.

SPD550, currently in Phase 2 of clinical development for Celiac disease and licensed during 2007, could provide the first available treatment for this condition. As Roger Adsett, Senior Vice President of the gastrointestinal business unit, says, "Our track record in developing and launching successful ulcerative colitis treatments, like PENTASA and LIALDA, make us an attractive business partner for companies who are looking to commercialize new compounds for this segment of the market." It's also possible that LIALDA could prove to be an effective treatment for Diverticulitis, which is an acute and very painful condition affecting the bowel wall, and which can often only be relieved by surgery. There is no other drug treatment available, so if LIALDA can indeed help to prevent recurrent attacks, it would meet an important unmet need. It's currently in Phase 3 trials, and if successful we would hope to launch sometime between 2012 and 2015.

*Oral 5-ASA Market Definition: LIALDA, PENTASA, ASACOL, COLAZAL and DIPENTUM.

“We’re actively looking for the same sort of opportunities that allowed us to develop and launch VYVANSE so successfully.”

Mike Cola
President of Specialty Pharmaceuticals



Focus on the science. *Drug research at HGT.*

Turning to HGT, the picture looks quite different. Enzyme replacement therapy is still a relatively new area, but a very successful one in R&D terms. An extremely high proportion—around 75%—of development projects succeed in the clinic and HGT aims to run this process for three to five new products with the expectation that one product per year can move into development. The enzyme replacement therapy developed at Shire is unique in so far as they are almost all derived from human cells. This proprietary technology is ground breaking. As Sylvie Grégoire, the President of HGT says, “So far no drug using this technology has ever reached a peak level of sales, which shows how much potential there is for Shire in the future. However, it does make extra demands on us as a company. For example, while we would always prefer to outsource aspects of our business that others can do more cheaply, like manufacturing and some aspects of distribution, you can’t always do that with orphan disease treatments. This means you have to manage more of the process yourself, but low volumes keep the costs under control. There are also special challenges in manufacturing enzyme replacement therapies. Specialty Pharma can do much of their manufacturing under license, but we need to invest in our own production facilities for HGT, so that we can retain

full control of the quality and the impact this has on the efficacy of the final product.”

HGT is also expanding its expertise into other new technologies. The agreement recently signed with Amicus doesn’t only allow us the worldwide (excluding US) rights to three exciting new small molecule compounds for Fabry disease, Gaucher disease, and Pompe disease, but gives us access to their new ‘chaperone technology’ which could open up other possibilities in future.

The HGT business has changed out of all recognition since it was acquired by Shire in 2005. The investments we’ve made have accelerated its growth to a whole new level. HGT now has 43 approvals for ELAPRASE, our treatment for Hunter syndrome. Five new products were taken through the business development process, and there’s the possibility of a further nine new products in the next seven years. At the same time, HGT now has the strength and breadth to take on joint venture partnerships, like the one with Amicus, which it would never have been able to contemplate before. As Sylvie Grégoire says, “HGT now has one of the strongest pipelines in the rare diseases sector. That’s the beauty of this business. The challenge now is to execute it, and execute it well.”

This brings new challenges for the HGT team. For the first time, HGT now has a number of different products at different stages of the development, approval and marketing process, and this demands new skills from the people who manage them. Having the US business on one site outside Boston, which will be completed by 2011 will be a significant advantage here, and in the meantime there’s a new focus on developing people, and standardizing some of the management and sales processes, so that they can cope with a more complex business model. Looking forward, the scope for growth in HGT is substantial, with up to 300 genetic diseases that might be amenable to treatment some day.

Taking Specialty Pharma and HGT together, we’re now seeing the results of a planned and considered period of pipeline growth. We now have a portfolio of products across all the phases of development, from lab, to trials, to marketing and sales. Some of these—like ELAPRASE and FIRAZYR—are providing hope for patients who previously had little to turn to; others—like VYVANSE and FOSRENOL—are offering effective treatments with clear benefits over previous alternatives. At Shire the objective is to seek global marketing approval whenever feasible.

“HGT now has one of the
strongest pipelines in
the rare diseases sector.”

Sylvie Grégoire
President of Shire HGT



From science to sales.

We have *a delivery model* that reflects the different market dynamics of our two businesses, and helps us meet our patients' needs more effectively.

The phrase often used for orphan drug sales is an 'advocacy model'. In other words an approach in which sales tend to be generated in response to active demands from patients and a small number of highly-specialized physicians working in regional and national centers of excellence and telling us what their treatment needs are. In practice this means that HGT has a very cost-effective sales infrastructure—for example, it only needs ten sales representatives across the whole of the US. HGT can also open sales operations in new markets at low cost, that can generate returns, and comparatively high volumes per sales person employed. As the maximum global turnover for each drug will probably be in the range of \$300–\$500 million.

Specialty Pharma, by contrast, will always generate higher absolute sales volumes than HGT, and needs more conventional sales structures as a result. While HGT salespeople are often trained scientists or medics in their own right, Specialty Pharma sales people have a more traditional sales background.

Specialty Pharma has a much wider range of sales approaches, from those that resemble the big pharma format, to one closer to that which HGT might take. At one end of the scale there are around 43,000 specialists treating ADHD in the US, and Shire has 550 salespeople in the US, backed up by an extensive program of investment in medical education, and public information targeted directly at the consumer in the US. At the other extreme a drug like XAGRID is closer to the orphan model, and has around 36 sales reps who target a small number of specialist haematologists. FOSRENOL, our treatment to reduce high phosphorus levels in late-stage kidney disease, is somewhere in the middle, with around 60 US reps, and a similar number in Europe.

US sales of FOSRENOL did not grow quite so quickly from its 2005 launch as we had expected, but the European roll-out is progressing extremely well. The US launch of LIALDA, our ulcerative colitis treatment, has been so successful in the US that it is now positioned to be the market leader in its segment, which has proved the value of the Specialty Pharma model. It's already been launched in Canada, Germany, Ireland and the Netherlands, under the brand name MEZAVANT XL, and there are filings in place in Australia and fifteen approvals in Europe.

Whether in HGT or Specialty Pharma, our challenge going forwards is to leverage our existing sales infrastructure, and grow revenues at the lowest possible cost. One way we're already doing this is by using HGT's overseas representative offices as a bridgehead for the Specialty Pharma business. As Joseph Rus, Executive Vice President of Market Alliance and New Product Development, says, "Specialty Pharma will typically enter a new market through a distributor arrangement, and then take over its own sales a few years later, once volumes reach an appropriate level. At that stage the sales infrastructure already in place for HGT can be a really valuable shared resource."

Whether in HGT or Specialty Pharma, our challenge going forwards is to leverage our existing sales infrastructure, and grow revenues at the lowest possible cost.

Leveraging Shire's portfolio

- Specialty Pharmaceuticals and HGT business models can be utilized synergistically to facilitate geographic expansion into targeted territories.
- HGT model offers near-term growth potential with relative ease of market access. Low cost infrastructure supports high value products and near-term cash flow. Longer-term growth is limited by patient populations.
- Specialty Pharmaceuticals model offers longer-term growth potential based on larger patient populations. Broader infrastructure investment supports long-term presence for both portfolios.
- Together the businesses drive long-term growth and contribution for Shire.

Looking to the future.

We have the *platform* to address our *immediate challenges*, and *exploit the opportunities* that are opening up for us across the world.

Today we have a physical presence in over 20 markets, and sell our products in more than 40. We've already stated that our ambition is to generate 50% of our sales from outside the US, and 25% of those sales from what's become known as the 'pharmerging' countries like Brazil, China and India, rather than the more established markets within Europe.

There are both immediate and long-term challenges that we need to address to achieve this goal. In the long term it's all about growing the business in the right way, which protects the qualities of bravery and nimbleness that have made Shire a special place to work, and have been directly responsible for so much of our success. In the short term there are issues relating to the ADHD business in the US over the next year, which we are well positioned to address, but which still need to be actively managed in the next few months.

A pivotal year for ADHD

There's no question that the next twelve months will see huge changes in the worldwide ADHD market, which will also have implications for Shire. An authorized generic version of ADDERALL XR, Shire's longstanding market leader, will probably be available in the early part of 2009, which raises inevitable questions about the impact of this on the price of our other drugs, and on our overall revenue.

But as Mike Yasick, Senior Vice President of the ADHD business unit, says, "We are as prepared as we can be for this event. We have known this would happen for a long time, and we've been planning for it by developing a whole new generation of ADHD treatments. ADDERALL XR is a great product so our challenge has been to improve upon it. VYVANSE is the first example of the fruits of that effort and has significant benefits for patients with ADHD. VYVANSE has a novel mechanism of action based on 'CarrierWave' technology. The effects are consistent throughout the day and they can last up to 13 hours—meaning VYVANSE may improve ADHD symptoms beyond work and school hours to important home time."

At the same time the number of prescriptions for adults in North America is accelerating, making it the fastest-growing segment of the market: there are up to ten million adults with the condition in the US, compared with only five million children, but while 80% of those children are receiving medication, the figure for adults is as low as 25%. There's also a growing awareness of the condition elsewhere in the world, and a new willingness to consider medication as well as behavioral therapies. This is especially true in Europe, which is currently quite a small market of around

Total market estimates for sales and growth for the eight developed markets in 2008

	Growth in 2008	Size of market
A. US	1.5%	\$291.6BN
B. Canada	5.9%	\$18.5BN
C. France	3.3%	\$45.9BN
D. Germany	5.3%	\$43.6BN
E. UK	2.4%	\$23.5BN
F. Italy	2.1%	\$26.6BN
G. Spain	6.8%	\$21.9BN
H. Japan	1.3%	\$77.1BN
Total (8 developed markets)	2.3%	\$548.7BN

Source: IMS Health Market Prognosis, Total Market Estimates for 2008, Sep 2008 edition



It's all about growing the business in the right way, which protects the qualities of bravery and nimbleness that have made Shire a special place to work, and have been directly responsible for so much of our success.

\$350 million, but could eventually become as significant as the US, where total annual turnover is around \$4.4 billion. If the industry is to achieve that Shire will need to help grow the whole market, as well as our own share within it, just as we did so successfully in the US in the 90s. That will mean more investment in raising awareness of the condition among physicians, opinion-formers, patients and carers. We've done it before, and we're well-placed to do it again.

The benefits of VYVANSE should also be attractive for the European market. There's still a lot to do in terms of filings and registration for VYVANSE, but Shire now has a significant advantage of a full portfolio of ADHD products, some of which are further along with the approval process.

DAYTRANA, our methylphenidate patch, is one of these, and a part of our overall strategy for ADHD. It has its own distinct advantages—it's not only provided in a format that's well understood in the US, but the effects of the drug can be easily regulated by simply removing the patch. Launching DAYTRANA in Europe ahead of VYVANSE will enable us to start developing the relationships with key physicians that will be key to long-term success.

We're also in the process of developing INTUNIV, which is a completely new type of ADHD drug, because it's a non-stimulant treatment for ADHD. After four years as the market leader, we're still at the cutting edge of the science for this important and still under-appreciated condition. As Mike Yasick says, "This is a good time to be in this business. In fact it's a perfect storm of opportunity."

Shire tomorrow. *Towards a global business.*

“By 2015 we want to see at least half our sales coming from markets from outside the US, and a significant proportion of these from new ‘pharmerging’ markets in regions like Asia and Latin America. We’ve already launched successfully in Russia, Australia and Japan, and our next priority is China, where the opportunities for us are enormous.”

Joseph Rus
Executive Vice President
Market Alliance and
New Product Development

There’s no doubt that, in the near term, ADHD remains a hugely important aspect of our business. It’s a relatively mature market—albeit with real possibilities for growth in both geographical and product terms—and one that we understand so well that it reduces our overall risk profile significantly from our investors’ point of view. At the same time, as Mike Cola says, “Many of the opportunities we now have, are only possible if the ADHD franchise steps up to the plate. It’s a generator of cash for investment in our future pipeline, and a platform for our international growth.”

Expanding our business internationally is absolutely central to achieving our long-term potential. North America and Europe will always remain important markets for us, but most of the industry agrees that overall sales growth is likely to be limited in the next few years, even without factoring in the effects of a worldwide economic downturn. That makes opening up new markets for Shire outside these regions even more crucial. For example, in 2008 total pharmaceutical industry sales in the main European and North American markets grew by between 2% and 5%, while the eight key emerging markets of Russia, China, India, Brazil, South Korea, Mexico and Turkey grew between 12% and 13%, and now

account for nearly \$80 billion of annual sales. China is forecasting that 90% of its population will have universal healthcare by 2012, and 100% by 2020, which means a population equal to the US and Europe put together. Likewise Russia is putting huge new investment into healthcare, and spent \$14 billion in 2008 alone.

The opportunities for us are clear, but there are risks to be addressed as well. Some of the new markets have a history of political instability, or laxer regulations on key issues like intellectual property. We need to manage these challenges actively, and develop a number of effective entry strategies for these valuable new markets. This might range from licensing our products in the near term, to gain a royalty stream, as we’ve done in Japan, to the use of an established distributor, to our own small office or representative office, as we are doing so successfully with HGT in markets like Brazil, Mexico and Russia. HGT now has over 1,000 people worldwide, an increase of 300 in only twelve months, and is already achieving its own stake in the overall Shire ambition of 25% of sales outside North America and Europe.

The market estimates for 'Pharmerging' markets sales and growth in 2008

	Growth in 2008	Size of market
A. Brazil	10.3%	\$20.2BN
B. Mexico	6.2%	\$11.9BN
C. Turkey	13.8%	\$10.7BN
D. Russia	13.3%	\$6.6BN
E. China	25.6%	\$24.3BN
F. South Korea	9.7%	\$10.7BN
G. India	11.5%	\$10.7BN
Total (7 'pharmerging' markets)	13.9%	\$95.1BN

Source: IMS Health Market Prognosis, Total Market Estimates for 2008, Sep 2008 edition 'Pharmerging' markets include: China, India, Brazil, Russia, Mexico, Turkey and South Korea



If we fulfil the goals we have set ourselves, 2015 will also see Shire as the most valuable Specialty biopharmaceutical company in the world.

International expansion is one key route to growth; together with planned portfolio diversification, and new strategic alliances or acquisitions. One key challenge for Shire as a whole is how best to analyze all the new opportunities open to us, whether from our own research, or from acquisitions or partnerships with outside third-parties. The Shire Business Development group actively explores all these new prospects, and teams from Specialty Pharma and HGT work together to decide where the most promising might fit, depending on which business model is the most appropriate to exploit it. The result? A pipeline of at least 16 new product launches between now and 2015.

like INTUNIV. For everyone in Shire it will mean dealing effectively with the complex market and regulatory challenges that this will entail, while retaining the agility, bravery, and flexibility that has always been at the heart of our success.

Which brings us back to where we started. A combination of strong international growth and pioneering new therapies is how we'll achieve strong, sustainable growth for our shareholders; but it's also how we'll achieve our fundamental purpose and *raison d'être*: to help people with life-altering conditions lead better lives.

If we fulfil the goals we have set ourselves, 2015 will also see Shire as the most valuable Specialty biopharmaceutical company in the world, with number one and number two positions in all our key therapeutic areas. That's a huge ambition, and if we're to achieve it, we will need to take measured risks, for maximum returns. In HGT this could mean going into disease areas we've never looked at before—that no-one may have ever looked at before; in Specialty Pharma it may mean looking at possibilities that are in a slightly earlier stage of development, and having the courage to operate at the cutting edge, just as we're already doing with a product

Corporate Responsibility at Shire.

Shire has always been a *responsible business*; our challenge now is to make it a *more sustainable one*.

Shire has had a corporate responsibility ('CR') strategy since it first began business—it just wasn't referred to as that. While our basic CR principles remain constant (and we set these out in detail on our dedicated CR website, www.shirecr.com) the focus and emphasis of our strategy has gradually evolved over time. This has been particularly noticeable in the last two or three years, as issues of climate change and sustainability have moved into the mainstream, and pressure has grown for companies and governments to take more concerted action.

Like many other companies of our size and prominence, we're finding that CR issues are becoming more and more closely integrated into the way we manage the Company day-to-day. We're not alone in this, but the pharmaceutical sector as a whole has particular challenges it needs to address, and many of the changes we're making to our corporate strategy and way of working at Shire are either in response to this, or, in some cases, in anticipation of it.

We have never wanted to be like 'big pharma', and most of the people who work at Shire do so for exactly that reason: they want to be part of a Company that has an agile entrepreneurial culture, and where their personal efforts can make a real difference. The whole Leadership Team

is passionately committed to retaining that spirit. This is one reason why our new purpose statement is to 'enable people with life-altering conditions to lead better lives': the core of our *raison d'être* is to help patients and their families.

We believe that this is what CR really means for a company like Shire. We want to be a responsible and ethical business, but also one that leads the way in its industry, and delivers strong returns for shareholders. In our view this is a sustainable business model in every sense of the word.

From CR to sustainability

We're also looking seriously at what 'sustainability' means for Shire, and the implications of the new drive towards corporate sustainability which has gained so much ground in the last year. We know that sustainability is much wider in its remit than CR, and we're developing a new sustainability strategy that takes these broader challenges into account. For example, it's clear to us that the sustainability agenda in our own industry is evolving from one focused on the direct impacts of operational activities, like drug safety and animal welfare, to a much wider remit covering the whole value chain, as well as an even broader range of social issues including healthcare systems, patent rights, and access to medicines.



To be as brave as the people we help.

Top: Tatjana May—Chair of CR Committee
Above: Shire's new 'Brave' brand

We know that sustainability is much wider in its remit than Corporate Responsibility, and we're developing a new sustainability strategy that takes these broader challenges into account.



Ask Angus—online chat session for Shire employees around the world

We see this new focus on sustainability as an evolution of what we're already doing, even if it might lead to some fairly revolutionary thinking in one or two areas. We want to know if there are changes we should be making in the way we operate, or new approaches we should consider that other companies are benefiting from. We also need to think about how we measure what we do more effectively, and set realistic and appropriate targets. This will be an important project for 2009.

A successful transition, and a new corporate brand

There have been many changes at Shire in the last year, not least the appointment of Angus Russell as the new CEO, and Matt Emmens' transition to Chairman. The process was managed extremely successfully, partly as a result of a comprehensive internal communications program. This has included a number of innovations such as a new employee blog by Angus Russell, the first online chat session, during which Shire employees all over the world had the chance to ask questions. Another important appointment was that of Tatjana May to the position of Chair of the CR Committee, which acts as a strategic steering group for all the Company's CR activities. There were also a number

of new members who joined the Committee this year, including Anne Marie Conway (R&D HGT), Susan Gavigan (Procurement), Ferdinand Massari (R&D HGT and Medical), Craig Lewis (US Commercial).

With the business embarking on the next phase of its overall business strategy in 2008, it was also felt to be a good time to review our overall mission, purpose and corporate brand. The aim was to reinforce our employees' commitment to our objectives, and ensure that everyone in the Company is aligned behind the same goals.

The new corporate brand captures the special character of the Shire culture in its aspiration to 'be as brave as the people we help'. This focuses quite deliberately on the patients and carers who rely on Shire's treatments, many of whom are dealing with life-threatening diseases, or conditions that can disrupt an entire family. 'Brave' has proved to be an extremely powerful unifying idea, from its initial launch at the strategy workshop for Shire's top 100 managers in September, to its wider roll-out to all Shire's employees across the world.

Corporate Responsibility at Shire.

Our commitment starts with our own *employees*, and extends outwards to our *customers* and *suppliers*, our *communities*, and the *environment*.

Customers and employees

In the 2007 report we talked about the work we were doing to improve our customer care, in the wake of the DAYTRANA voluntary withdrawal in September 2007. The result is a series of four separate but connected programs, each designed to improve a specific aspect of the way we manage our relationships with customers, from sales and marketing to our relationships with healthcare providers. Some of these are already underway, while others will get going later in 2009.

We continue to invest in our own people, and support their personal and professional development. Work/life balance remains an important issue for us, and we want to encourage a positive and healthy balance between home and work. In some cases this can include the flexibility to work from home, and our HR teams are supporting our managers so that this can be an option for more Shire employees where appropriate.

Shire and the environment

Shire has always been an environmentally responsible Company, and in the last two years we've drawn together all our efforts in this area into one umbrella initiative, Shire's Actions and Values for the Environment, or 'SAVE'. This covers everything from environmental performance at our operations, to the help and support we offer our own people to help them play their part in tackling climate change. This includes a dedicated site on the Shire intranet which offers a personal carbon footprint calculator, and practical advice throughout the year. 'SAVE for the holidays', for example, suggested ten tips for a greener Christmas, including suppliers of environmentally-friendly gifts. UK employees also received a packet of seeds to encourage them to grow their own Christmas tree for the future.

SAVE is run by teams of employees across the business, and is focused on the five most important areas for a business like Shire: product development, transport, buildings, recycling and procurement. Achievements in 2008 included reductions in the amount of packaging we use, the increasing use of hybrid cars in our sales fleet, new car-pooling schemes, a range of energy-saving modifications to our buildings, higher

levels of recycling, and the work we're doing to help our suppliers reduce their carbon footprint. We aim to reduce our own carbon footprint by 10% by the end of 2009.

One of the centerpieces of the SAVE program is Earth Day. Although it originated in the US, Earth Day is now a worldwide event involving 17,000 organizations in 174 countries. Shire's Earth Day events involve employees from across the world, and focus on raising environmental awareness and encouraging people to take part, whether that's by participating in conservation schemes or making changes to their own lifestyles to help combat climate change. Every employee was given an Earth Day environmentally-friendly re-usable shopping bag, and the day ended with the planting of trees at our Basingstoke, Philadelphia, and Massachusetts offices.



Top: Planting a tree for Earth Day
Above: Supporting science education

Earth Day events involve employees from across the world, and focus on raising environmental awareness.



Shire in the community

Shire took part in hundreds of different community activities in 2008, ranging from individual employee fundraising and volunteering, to bigger projects like World Kidney Day.

One of our community priorities is to support science education, which is why we've established a five-year partnership with the Royal Society of Chemistry in the UK. We're investing £50,000 a year in a scheme to encourage some of the UK's brightest young people to consider a career in science. Our support is funding an essay prize which is open to the best A-level chemistry students in the UK. The first set of winners flew to Boston in December 2008 during which they toured the HGT plant, and visited Harvard and MIT.

We're supporting education in a completely different way through our work on 'Project Playground'. We're working on this with Ty Pennington, the US TV personality; he suffers from ADHD and is committed to raising awareness of the effect the condition can have on both children and adults. This particular project focuses on an elementary school in Harlem, New York. There are 600 children at the school, but they had nowhere to play. We worked with Ty to design and build

a stunning new playground, including a running track, a jungle gym, a baseball area, and a basketball court.

In 2008 Shire donated £15,000 to the M-PACT program being run by the UK charity Action on Addiction. The name stands for 'Moving Parents and Children Together', and it aims to bring together families who've been affected by substance abuse, so they can help and support one another. M-PACT is a pilot project at present, but the aim is to roll it out to parents and children across the UK. Shire's support will help Action on Addiction to evaluate the program and train more professionals to deliver the program in their own areas.

Throughout the year staff from the HGT office in Massachusetts took part in sponsored walks and runs for the US National MPS Society. MPS stands for Mucopolysaccharidoses, which is the group of genetic diseases which includes Hunter syndrome. There were five walks throughout the year, and those who took part were also able to meet many patients and their families.

Full information about all our CR activities, including data, targets and objectives, can be found on our dedicated CR website: www.shirecr.com



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1
Matthew Emmens (57)
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.

2
Angus Russell (53)
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 a member 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.

3
Graham Hetherington (50)
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.

4
David Kappler (61)
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.

5
Patrick Langlois (63)
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 Rhône-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.



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6
Dr Jeffrey Leiden (53)
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.

7
David Mott (43)
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.

8
Kate Nealon (55)
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 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.

9
Dr Barry Price (65)
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.

10
Dr Michael Rosenblatt (61)
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.



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1
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 a member 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.

2
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.

3
Mike Cola
President, Specialty Pharmaceuticals

Mike joined Shire in July 2005 from Safeguard Scientifics, Inc., where he was President of its Life Sciences division. He joined Safeguard in 2000 and is on the board of several of its life science companies. Between 1992–2000, Mike worked for AstraMerck/AstraZeneca and, as one of the earliest employees of AstraMerck, was responsible for developing the new company's product development, medical affairs, business research, licensing and pharmaceutical business units. As Head of Product Development he was responsible for development and commercialization in the US.

4
Sylvie Grégoire
President, Human Genetic Therapies

Dr Grégoire 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. Dr Grégoire also worked for Merck & Co. in various positions in clinical research and in European regulatory affairs both in the US and abroad. Dr Grégoire 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.



5



6



7



8

5

Barbara Deptula

**Executive Vice President and
Chief Corporate Development Officer**

Barbara Deptula has been with Shire since September 2004. She was previously President of the biotechnology division of Sico Inc. and Senior Vice President for commercial and product development at Coley Pharmaceutical Group. She also held senior management positions focused on licensing and business development at US Bioscience, Schering-Plough, American Cyanamid, and Genetics Institute.

6

Anita Graham

**Executive Vice President, Corporate Business
Services and Chief Administrative Officer**

Anita Graham has been with Shire since January 2004. She is Executive Vice President Corporate Business Services and Chief Administrative Officer. In this role, Ms Graham leads the Company's Information Services, Human Resources & Talent Management, Corporate Communications and Corporate Shared Services groups. She was previously EVP, Global Human Resources. Prior to joining Shire Ms Graham was Vice President of Human Resources at Cytoc Corporation. She also held senior HR positions at Serono, Inc. and Scudder Kemper Investments, Inc.

7

Tatjana May

**General Counsel, Company Secretary and
Executive Vice President Global Legal Affairs**

Tatjana May has been with Shire since May 2001. She 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. Tatjana is also Chair of the Company's Corporate Responsibility Committee.

8

Joseph Rus

**Executive Vice President Market
Alliance & New Product Development**

Joseph Rus has been with Shire since 1999. Following the merger of Shire Pharmaceuticals and BioChem Pharma in May 2001, he was appointed President and Chief Executive Officer of Shire BioChem Inc. He has more than 25 years of experience in the international pharmaceutical industry including European country management.

Electronic communication

Shire will communicate with those shareholders who have elected or who are deemed to have elected to receive documents electronically by publishing documents on its website and will write to shareholders to inform them of the availability of these documents on the Company's website.

Alternatively, shareholders can elect to receive electronic notification of Company communications. Instead of a letter, an email will be sent to the shareholder's email address with a link to the documents on the Company's website. To effect this, you must register free of charge at www.shareview.co.uk by following the online instructions.

The advantages of electronic communication are:
—receiving shareholder information speedily and efficiently;
—reducing the demand on natural resources; and
—helping your Company reduce its costs.

Shareholders who do not elect to receive documents or notifications electronically will receive paper copies of materials.

Shareholder security

Over the last year, many companies have become aware that their shareholders have received unsolicited phone calls or correspondence concerning investment matters. These are typically from overseas based 'brokers' who target UK shareholders, offering to sell them what often turn out to be worthless or high risk shares in US or UK investments.

Shareholders are advised to be very wary of any unsolicited advice, offers to buy shares at a discount or offers of free company reports. If you receive any unsolicited investment advice:
—make sure you get the name of the person and organization;
—check that they are properly authorized by the FSA before getting involved by visiting www.fsa.gov.uk/Pages/register; and
—report the matter to the FSA either by calling 0845 606 1234 or visiting www.moneymadeclear.fsa.gov.uk

If you deal with an unauthorized firm, you will not be eligible to receive payment under the Financial Services Compensation Scheme. The FSA can be contacted by completing an online form at www.fsa.gov.uk/pages/doing/regulated/law/alerts/overseas.shtml

Details of any share dealing facilities that the Company endorses will be included in Company mailings.

More detailed information on this or similar activity can be found on the FSA website www.moneymadeclear.fsa.gov.uk

This warning has been issued by the Financial Services Authority and endorsed by the ICASA.

Financial calendar

Second interim dividend payment
April 2009

Annual General Meeting
April 2009

First quarter results' announcement
April 2009

Second quarter results' announcement
August 2009

First interim dividend payment
September/October 2009

Third quarter results' announcement
October 2009

Annual results' announcement
February 2010

Second interim dividend payment
April 2010

Dividends

Shareholders are able to choose how they receive their dividends:
—directly into their bank account* or
—by cheque.

*Shire preferred option:

The quickest and most efficient way to receive your dividends is to have them paid directly into your bank account. Those selecting this payment method receive a tax voucher with each payment. To change how you receive your dividends, either log on to www.shareview.co.uk or contact Equiniti.

Income Access Share (IAS) arrangements

Shareholders who elect, or are deemed to have elected, to receive their dividends via the IAS arrangements will receive their dividends from a UK source (rather than directly from the Company which is an Irish tax resident company) for UK tax purposes.

Shareholders who hold 25,000 or fewer shares (i) on the date of admission of the Company to the London Stock Exchange, being May 23, 2008, and (ii) in the case of shareholders who did not own shares at that time, on the first dividend record date after they became shareholders in the Company, unless they elect otherwise, will be deemed to have elected to receive their dividends under the IAS arrangements.

Shareholders who hold more than 25,000 shares and who wish to receive their dividends from a UK source must make an IAS election. All elections remain in force indefinitely unless revoked.

Unless shareholders have made an IAS election, or are deemed to have made an IAS election, dividends will be received from an Irish source and will be taxed accordingly.

ShareGift

Shareholders with a small number of shares, the value of which makes it uneconomical to sell, may wish to consider donating them to the charity ShareGift (registered charity no. 1052686). Donated shares are aggregated and sold by ShareGift, the proceeds being passed on to a wide range of charities. Find out more about ShareGift at www.sharegift.org or by telephoning ShareGift on +44 (0)20 7930 3737.

US Shareholders

(i) ADSs

The Company's American Depositary Shares (ADSs), each representing three Ordinary Shares, are listed on NASDAQ under the symbol 'SHPGY'. The Company files reports and other documents with the Securities and Exchange Commission (SEC) that are available for inspection and copying at the SEC's public reference facilities or can be obtained by writing to the Company Secretary.

(ii) ADS Depository

JPMorgan Chase Bank, N.A. is the depository for Shire ADSs. All enquiries concerning ADS records, certificates or transfer of Ordinary Shares into ADSs should be addressed to:

JPMorgan Chase & Co.
P.O. Box 64504
St Paul
MN 55164-0504
USA

General enquiries:

Toll free in US:
Tel: +1 800 990 1135

From outside the US:
Tel: +1 651 453 2128

Email: jpmorgan.adr@wellsfargo.com

Registrars

All administrative enquiries relating to shareholders should be addressed to Equiniti, clearly stating the registered shareholder's name and address.

Equiniti

Shire Shareholder Services
Equiniti (Jersey) Limited
PO Box 63
11-12 Esplanade
St Helier
Jersey JE4 8PH

Shareholder helpline

From overseas:
Tel: +44 (0)121 415 7047

In the UK:
Tel: 0871 384 2553*

*Calls to this number are charged at 8p per minute from a BT landline. Other telephone providers' charges may vary.

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CarrierWave process

A drug technology platform acquired as part of the New River Pharmaceuticals acquisition.

Pharmacological chaperone technology

Small molecule drugs called pharmacological chaperones are used to selectively bind to a target protein and increase its stability. The binding of the chaperone molecule helps the protein fold into its correct three-dimensional shape. This allows the protein to be trafficked from the endoplasmic reticulum to the appropriate location in the cell, thereby increasing protein activity and cellular function and reducing stress on cells. This approach was developed to address human genetic diseases resulting from misfolded proteins.

Enzyme replacement therapy

A medical treatment replacing an enzyme in patients whom that particular enzyme is deficient or absent. Usually this is done by giving the patient an intravenous (IV) infusion containing the enzyme.

FDA

US Food and Drug Administration

Oral-5 ASA

5-ASA (5-aminosalicylic acid) also known as Mesalazine or Mesalamine, is an anti-inflammatory drug used to treat inflammation of the digestive tract ulcerative colitis and mild to moderate Crohn's disease. Mesalazine is a bowel-specific aminosalicilate drug that acts locally in the gut and has its predominant actions there, thereby having few systemic side-effects.

Phase 1

Oral therapies usually conducted in healthy human volunteers to determine if a drug candidate is safe for more extensive testing.

Phase 2

Clinical trials conducted in patients with relevant disease to assess the safety and efficacy of the drug candidate.

Phase 3

Clinical trials conducted in the target patient population to comprehensively assess the safety and efficacy of the drug candidate.

Pivotal study

A major clinical trial that has a significant impact on the labeling (approved usage) of a drug.

Pre-clinical study

Studies of compounds conducted in the laboratory, in isolated tissues, or in living animals.

Symptomatic diseases

A disease is symptomatic when it is at a stage when the patient is experiencing symptoms. It is generally used in counter distinction of asymptomatic (when the disease is inapparent). Symptomatic treatment is the practice of treating a patient's symptom, rather than the disease or injury itself.

We enable people
with life-altering
conditions to lead
better lives.

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Shire trademarks

The following are trademarks either owned or licensed by Shire plc or companies within the Shire Group which are the subject of trademark registrations in certain territories, or which are owned by third-parties as indicated and referred to in this Report.

ADDERALL XR[®] (mixed salts of a single-entity amphetamine)
AGRYLIN[®] (anagrelide hydrochloride)
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[®] XL (mesalamine)
REPLAGAL[®] (agalsidase alfa)
VYVANSE[®] (lisdexamfetamine dimesylate)
XAGRID[™] (anagrelide hydrochloride)

Third-party trademarks

The following are trademarks of third-parties referred to in this Report.

AMIGAL (migalastat hydrochloride) (trademark of Amicus)
ASACOL (mesalamine) (trademark of Procter & Gamble Pharmaceuticals)
COLAZAL (balsalazide disodium) (trademark of Salix Pharmaceuticals, Inc)
DIPENTUM (olsalazine sodium) (trademark of Celltech Pharmaceuticals, Inc)
DYNEPO (epoetin delta) (trademark of Sanofi-Aventis)
PENTASA (mesalamine) (trademark of Ferring)
PLICERA (isofagomine tartrate) (trademark of Amicus)



Graham Hetherington
Chief Financial Officer

The following discussion should be read in conjunction with the Company's US GAAP consolidated financial statements included in the Company's Annual Report on Form 10-K for the year to December 31, 2008. A copy of the Company's Annual Report on Form 10-K is available on its website www.shire.com and is also available on the SEC's website at www.sec.gov.

Results of operations

For the year to December 31, 2008 the Company's total revenues increased by 24% to \$3,022 million, compared to \$2,436 million in 2007. Net income for the year to December 31, 2008 was \$156 million compared to a net loss of \$1,451 million in 2007.

Total revenues

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

Year to 31 December,	2008 \$'M	2007 \$'M	Growth %
Net product sales:			
SPECIALTY PHARMACEUTICALS ('Specialty')			
Attention Deficit Hyperactivity Disorder ('ADHD')			
ADDERALL XR	1,101.7	1,030.9	7%
VYVANSE	318.9	76.5	317%
DAYTRANA	78.7	64.2	23%
Gastrointestinal ('GI')			
PENTASA	185.5	176.4	5%
LIALDA/MEZAVANT	140.4	50.5	178%
General products			
FOSRENOL	155.4	102.2	52%
CALCICHEW	52.8	54.2	-3%
CARBATROL	75.9	72.3	5%
REMINYL/REMINYL XL	34.4	31.2	10%
XAGRID	78.7	66.8	18%
Other product sales	50.1	119.3	-58%
Total Specialty product sales	2,272.5	1,844.5	23%
HUMAN GENETIC THERAPIES ('HGT')			
ELAPRASE	305.1	181.8	68%
REPLAGAL	176.1	143.9	22%
FIRAZYR	0.5	—	—
Total HGT product sales	481.7	325.7	48%
Total product sales	2,754.2	2,170.2	27%
Royalty income:			
3TC	140.2	145.3	-4%
ZEFFIX	40.3	41.0	-2%
Other	65.0	60.9	7%
	245.5	247.2	-1%
Other revenues	22.5	18.9	19%
Total revenue	3,022.2	2,436.3	24%

The following discussion includes references to US prescription and US market share data for key products. The source of this data is IMS Health ('IMS').

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 29.7% in 2007. Shire has the leading portfolio of products in the US ADHD market.

ADDERALL XR—ADHD

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 co-operating 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. Further information on this litigation can be found in our filings with the Securities and Exchange Commission ('SEC'), including our Annual Report on Form 10-K for the year to December 31, 2008.

VYVANSE—ADHD

VYVANSE was launched in the US in July 2007 as the first and only once-daily pro-drug stimulant to treat ADHD.

In April 2008 VYVANSE was approved by the FDA for use in adults and Shire launched VYVANSE for adult ADHD in June 2008.

In July 2008 Shire launched VYVANSE in 20mg, 40mg and 60mg dosage strengths, which are designed to increase the dosing flexibility of VYVANSE.

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—ADHD

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 Pharmaceuticals Inc. (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 annual average market share of the US Oral Mesalamine market rose to 28.4% for the year to December 31, 2008 (2007: 21.1%) driven by growth of LIALDA since its launch in March 2007.

PENTASA—Ulcerative colitis

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.

Financial review**LIALDA/MEZAVANT—Ulcerative colitis**

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 re-imburement negotiations.

FOSRENOL—Hyperphosphatemia

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 ended 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 ending December 31, 2008 (2007: 8.6%). Product sales increased despite the decrease in prescriptions due to price 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.

On February 9, 2009 Shire announced that it had received Paragraph IV Notice letters from Barr Laboratories, Inc. ('Barr') and Mylan Inc. ('Mylan') advising the filing of Abbreviated New Drug Applications for generic versions of 500 mg, 750mg, and 1 gram FOSRENOL. Shire is currently reviewing the detail of the Paragraph IV Notice letters from Barr and Mylan, and under the Hatch Waxman Act has 45 days to determine if it will file patent infringement suits.

XAGRID—Thrombocytopenia

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). On a constant exchange rate basis, sales rose 15% (XAGRID is primarily sold in Euros and Pounds sterling).

DYNEPO—Anemia associated with chronic kidney disease

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—Hunter syndrome**

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. On a constant exchange rate basis, sales increased by 64%.

REPLAGAL—Fabry disease

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. On a constant exchange rate basis, sales rose by 19%.

FIRAZYR—Hereditary angioedema ('HAE')

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 re-imburement negotiations successfully conclude. FIRAZYR has orphan exclusivity in the EU until 2018.

Royalties

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

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.

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). On a constant exchange rate basis, royalties from sales of ZEFFIX fell 8%.

Other

Other royalties are primarily in respect of REMINYL and REMINYL XL (known as RAZADYNE and RAZADYNE ER in the US), for the symptomatic treatment of mild to moderately severe dementia of the Alzheimer's type.

Information on the RAZADYNE patent litigation (which rendered the relevant patent invalid in August 2008) and RAZADYNE ER patent litigation (which is ongoing) can be found in our filings with the SEC on our Annual Report on Form 10-K for the year to December 31, 2008.

Cost of product sales

The cost of product sales increased to \$408.0 million for the year to December 31, 2008 (15% of product sales), from \$320.3 million in the corresponding period in 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 exit costs for DYNEPO, which the Company has decided to stop commercializing, and depreciation of \$16.2 million (2007: \$11.8 million). Excluding these charges Cost of product sales as a percentage of product sales in the year to December 31, 2008 decreased by two percentage points compared to 2007 due to the impact of price increases on the Company's product sales and favorable changes in product mix.

Research and development ('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). The year to December 31, 2007 included up-front and milestone payments for in-licensed products of \$155.9 million representing 7% of product sales. R&D expenditure included \$6.5 million (2007:\$nil) of R&D commitments relating to DYNEPO and depreciation of \$12.5 million (2007: \$11.3 million).

Excluding these charges R&D expenditure increased over the same period in 2007, although decreasing as a percentage of product sales to 18% (2007: 19% of product sales). Contributing to the increase in R&D expenditure in 2008 over 2007 were projects in-licensed and acquired since the second half of 2007, including PLICERA, SPD550, AMIGAL, FIRAZYR and METAZYM together with Phase 3(b) and Phase 4 studies to support new product launches.

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

SG&A expenses increased by 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 Group 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). SG&A expenses in the year to December 31, 2008 also included costs associated with the introduction of a new holding company 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.

Financial review**Integration costs**

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

Gain on sale of product rights

For the year to December 31, 2008 Shire recognized gains of \$20.7 million on the sale of product rights, primarily relating to the sale of non-core products to Ammirall in 2007, for which some gains were deferred at December 31, 2007 pending the transfer of relevant consents. In the year to December 31, 2007 Shire recognized gains on the sale of product rights of \$127.8 million, of which \$114.8 million was for the products sold to Ammirall.

In-Process Research and Development ('IPR&D')

During the year to December 31, 2008 the Company recorded an IPR&D charge of \$263.1 million (2007: \$1,866.4 million). The charge in 2008 related to FIRAZYR in those markets outside of the EU (\$128.1 million) which had not been approved by the relevant regulatory authorities at the acquisition date, and for METAZYM (\$135.0 million). In the year to December 31, 2007 the Company recorded an IPR&D charge of \$1,866.4 million in respect of development projects acquired with New River, including VYVANSE for use in adults in the US market, which at the time of acquisition had yet to be approved by the FDA.

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 and cash equivalent balances and lower average 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: \$28.1 million) in respect of the TKT appraisal rights litigation. This litigation was settled in November 2008. 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. 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. For further details on the settlement of this litigation, see the Company's Annual Report on Form 10-K for the year to December 31, 2008.

Other income, net

Other (expenses)/income, net for the year to December 31, 2008 include other than temporary 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. These amounts reflect unrealized holding losses that have been reclassified from other comprehensive income to the statement of operations in 2008, as management have concluded that the impairment is other than temporary.

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) for which no tax benefit is currently recognized, the effective tax rate for the year to December 31, 2008 has increased by 7% to 19% (2007: 12%). The 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 provision for uncertain tax benefits. The 2008 effective tax rate was also unfavorably impacted by exchange losses.

Equity in earnings/(losses) 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 2008 of \$17.6 million (2007: \$nil) relate to those Jerini businesses that met the criteria for held for sale and discontinued operations at December 31, 2008, which Jerini announced in October 2008 that it intended to invest.

	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	395.0	441.5
Inventories	154.5	174.1
Assets held-for-sale	16.6	10.6
Deferred tax asset	89.5	143.3
Prepaid expenses and other current assets	141.4	125.3
Total current assets	1,044.4	1,696.8
Non-current assets:		
Investments	42.9	110.2
Property, plant and equipment, net	534.2	368.6
Goodwill	350.8	219.4
Other intangible assets, net	1,824.9	1,764.5
Deferred tax asset	118.1	143.7
Other non-current assets	18.4	26.9
Total assets	3,933.7	4,330.1
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued expenses	708.6	674.2
Deferred tax liability	10.9	11.3
Liability to dissenting shareholders	—	480.2
Other current liabilities	104.3	96.5
Total current liabilities	823.8	1,262.2
Non-current liabilities:		
Convertible bonds	1,100.0	1,100.0
Other long-term debt	43.1	32.9
Deferred tax liability	377.0	332.4
Other non-current liabilities	291.3	375.6
Total liabilities	2,635.2	3,103.1
Minority interest	0.3	—
Shareholders' equity:		
Common stock of 5p par value	55.5	55.2
Exchangeable shares	—	33.6
Treasury stock	(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	1,298.2	1,227.0
Total liabilities and shareholders' equity	3,933.7	4,330.1

	12 months to December 31, 2008 \$'M	12 months to December 31, 2007 \$'M
Revenues:		
Product sales	2,754.2	2,170.2
Royalties	245.5	247.2
Other revenues	22.5	18.9
Total revenues	3,022.2	2,436.3
Costs and expenses:		
Cost of product sales	408.0	320.3
Research and development	526.6	576.4
Selling, general and administrative	1,422.9	1,178.8
Integration costs	10.3	1.3
Gain on sale of product rights	(20.7)	(127.8)
In-process R&D charge	263.1	1,866.4
Total operating expenses	2,610.2	3,815.4
Operating income/(loss)	412.0	(1,379.1)
Interest income	25.5	50.6
Interest expense	(139.0)	(70.8)
Other (expenses)/income, net	(32.9)	1.2
Total other expenses, net	(146.4)	(19.0)
Income/(loss) from continuing operations before income taxes, minority interest and equity in earnings of equity method investees	265.6	(1,398.1)
Income taxes	(98.0)	(55.5)
Minority interest	3.6	—
Equity in earnings of equity method investees, net of taxes	2.4	1.8
Income/(loss) from continuing operations	173.6	(1,451.8)
Loss from discontinued operations, net of taxes	(17.6)	—
Net income/(loss)	156.0	(1,451.8)
Earnings per share—basic		
Income/(loss) from continuing operations	32.1¢	(268.7¢)
Loss from discontinued operations	(3.3¢)	—
Earnings/(loss) per Ordinary share—basic	28.8¢	(268.7¢)
Earnings per share—diluted		
Income/(loss) from continuing operations	31.8¢	(268.7¢)
Loss from discontinued operations	(3.2¢)	—
Earnings/(loss) per Ordinary share—diluted	28.6¢	(268.7¢)
Earnings/(loss) per ADS—diluted	85.8¢	806.1¢
Weighted average number of shares:		
	Millions	Millions
Basic	541.6	540.3
Diluted	545.4	540.3

	12 months to December 31, 2008 \$'M	12 months to December 31, 2007 \$'M
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net income/(loss)	156.0	(1,451.8)
Adjustments to reconcile net income/(loss) to net cash provided by operating activities:		
Loss from discontinued operations	17.6	—
Depreciation and amortization	202.9	158.3
Share-based compensation	65.2	75.2
In-process R&D charge	128.1	1,866.4
Interest on building financing obligation and amortization of deferred financing charges	8.3	12.4
Impairment of intangible assets, long-lived assets and available-for-sale securities	157.3	5.2
Gain on sale of product rights and long-term assets	(30.8)	(127.5)
Movement in deferred taxes	74.0	(25.4)
Equity in earnings of equity method investees	(2.4)	(1.8)
Minority interest	(3.6)	—
Changes in operating assets and liabilities, (net of acquisitions), return on investment in joint venture and cash used by discontinued operations	27.5	(36.3)
Net cash provided by operating activities	800.1	474.7
CASH FLOWS FROM INVESTING ACTIVITIES:		
Movements in short-term investments	—	55.8
Movements in restricted cash	10.3	(9.7)
Purchases of subsidiary undertakings and long-term investments	(501.6)	(2,582.8)
Payment on settlement of TKT appraisal rights litigation	(419.9)	—
Purchases of property, plant and equipment and intangible assets	(261.0)	(169.4)
Proceeds from sale of long-term investments, property, plant and equipment and product rights	17.1	235.7
Returns from equity investments	0.6	2.3
Net cash used in investing activities	(1,154.5)	(2,468.1)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from drawings under bank facility	190.0	1,300.0
Repayment of drawings under bank facility	(190.0)	(1,300.0)
Proceeds from issue of 2.75% Convertible Bonds due 2014	—	1,100.0
Redemption of New River convertible notes	—	(279.4)
Proceeds from exercise of New River purchased call option	—	141.8
Payment of debt arrangement and issuance costs	—	(32.8)
Building finance obligations, net	9.5	—
Proceeds from exercise of options and warrants	11.4	43.4
(Costs)/proceeds from issue of common stock, net	(5.6)	877.3
Payments to acquire treasury stock	(146.6)	(186.0)
Payment of dividends	(46.8)	(41.3)
Net cash (used in)/provided by financing activities	(178.1)	1,623.0
Effect of foreign exchange rate changes on cash and cash equivalents	(11.8)	6.0
Net decrease in cash and cash equivalents	(544.3)	(364.4)
Cash and cash equivalents at beginning of period	762.5	1,126.9
Cash and cash equivalents at end of period	218.2	762.5

1 BASIS OF PREPARATION

This summary financial information has not been audited. It has been extracted from the Company's full consolidated financial statements for the year ended December 31, 2008, which were presented in accordance with accounting principles generally accepted in the United States of America and which were audited in accordance with standards of the Public Company Accounting Oversight Board (United States), filed with the SEC on Form 10-K on February 27, 2009.

This summary financial information does not contain sufficient information to allow a full understanding of the results and state of affairs of the Company and are not statutory accounts within the meaning of Section 240 of the Companies Act 1985 or Article 104 of the Companies (Jersey) Law 1991 or summary financial statements within the meaning of Section 251 of the UK Companies Act 1985.

For further information the full consolidated financial statements and the report of the independent registered public accounting firm that expressed an unqualified opinion on those consolidated financial statements included in the Company's Annual Report on Form 10-K for the year ended December 31, 2008 should be consulted. A copy of the Company's Annual Report on Form 10-K is available on its website and is also available on the SEC's website at www.sec.gov.

2 SHAREHOLDERS' EQUITY

	Total shareholders' equity \$'M
As at December 31, 2007	1,227.0
Net income for the period	156.0
Foreign currency translation	36.6
Costs associated with shares issued through Scheme of Arrangement	(5.6)
Options exercised	2.1
Tax deficit associated with the exercise of stock options	(3.8)
Stock-based compensation	65.2
Shares purchased by Employee Share Ownership Trust ('ESOT')	(146.6)
Shares released by ESOT to satisfy option exercises	9.4
Unrealized holding loss on available-for-sale securities, net of taxes	(47.9)
Realized gain on sale of available-for-sale securities, net of taxes	(5.4)
Other than temporary impairment of available for sale securities, net of taxes	58.0
Dividends	(46.8)
As at December 31, 2008	1,298.2

3 DIVIDENDS

During the year to December 31, 2008 the Company paid dividends totaling 8.62 US¢ per Ordinary share, equivalent to 25.85 US¢ per ADS, totalling \$46.8 million.

4 BUSINESS COMBINATIONS

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 6.25 Euros per share. 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 canceling 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.

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 (the date a controlling voting interest was obtained):

	Fair value \$'M
ASSETS	
Current assets:	88.3
Property, plant and equipment, net	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:	31.3
Deferred tax liability	76.3
Other long-term liabilities	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.

5 CHANGE IN REPORTING ENTITY

On May 23, 2008 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 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.

Introduction

This summary Directors' remuneration report outlines the Group's remuneration policy and approach as developed by the Remuneration Committee, and provides the annual remuneration of the Board in 2008.

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

Shire's executive remuneration policy and remuneration components

The Committee considers that an effective remuneration policy, aligned to the Group's business needs, is important to the Group's success. It directly impacts the Group'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 Group'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 Group 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 Group's remuneration policy as it aligns the interests of the Group'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 Group'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 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 Group 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 Group. This approach will be used for benchmarking remuneration with effect from 2009.

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 Group 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.

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 Group 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 Chairman and Non-Executive Director fees of comparable companies. The fees paid to the Chairman and 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 Group's pension scheme. Non-Executive Directors do not participate in any of the Group 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.

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.

Aggregate Directors' remuneration

The total amounts for Directors' remuneration were as follows:

	2008 \$'000	2007 \$'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 \$'000	2007 \$'000	Cash element		Deferred share element		2008 \$'000	2007 \$'000	2008 \$'000	2007 \$'000	2008 \$'000	2007 \$'000	2008 \$'000	2007 \$'000
			2008 \$'000	2007 \$'000	2008 \$'000	2007 \$'000								
Matthew Emmens ^{(i)(ii)(iv)}	625	1,156	583	1,334	330	750	137	421	—	—	1,675	3,661	187	347
Angus Russell ^{(iii)(v)}	971	781	1,061	620	599	396	29	28	20	8	2,680	1,833	414	195
Graham Hetherington ^{(iii)(v)}	371	—	257	—	143	—	11	—	2	—	784	—	95	—

(i) Paid in US dollars.

(ii) 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.

(iii) Pound sterling salary and cash benefits translated into US dollars.

(iv) Pension contributions were made to a SERP and 401(k) Plan in the US up to the date Mr Emmens stepped down as CEO.

(v) Pension contributions were made by the Group 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.

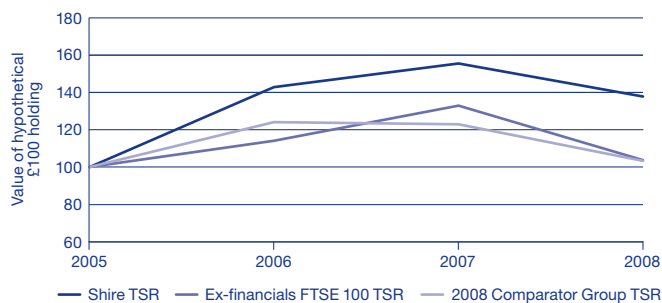
Non-Executive Directors' emoluments*

	Fees	
	2008 \$'000	2007 \$'000
Dr James Cavanaugh ⁽ⁱ⁾⁽ⁱⁱ⁾	265	530
Matthew Emmens ⁽ⁱ⁾⁽ⁱⁱⁱ⁾	292	—
Dr Barry Price ⁽ⁱ⁾	107	136
Robin Buchanan ^{(i)(iv)}	65	109
David Kappler ⁽ⁱ⁾	167	165
Patrick Langlois ⁽ⁱ⁾	130	129
Dr Jeffrey Leiden ⁽ⁱ⁾	121	104
Kate Nealon ⁽ⁱ⁾	139	125
David Mott ⁽ⁱ⁾	117	16
Dr Michael Rosenblatt ^{(i)(v)}	67	—
The Hon. James Grant ^{(i)(vi)}	—	38

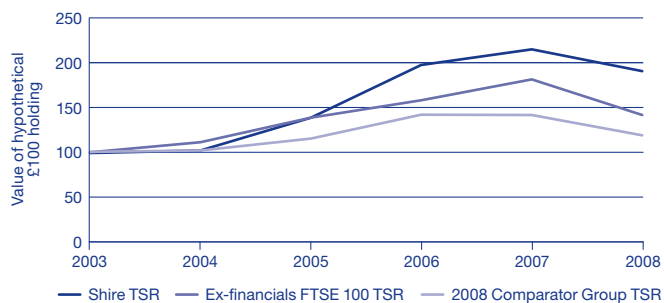
*Non-Executive Directors' fees are to/from the date of retirement/appointment.

- (i) Pound sterling fees translated into US dollars.
- (ii) Dr Cavanaugh retired on June 18, 2008.
- (iii) Mr Emmens was appointed Chairman on June 18, 2008.
- (iv) Mr Buchanan stepped down from the Board on July 29, 2008.
- (v) Dr Michael Rosenblatt was appointed a Non-Executive Director on April 24, 2008.
- (vi) The Hon. James Grant stepped down from the Board on May 10, 2007.

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



Five year historical TSR performance. Change in value of hypothetical £100 holding over three years (£)



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, re-imbursement, manufacturing and commercialization of the Company's Specialty Pharmaceutical 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 re-imbursement for its products; and other risks and uncertainties detailed from time to time in the Company's filings with the Securities and Exchange Commission.

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