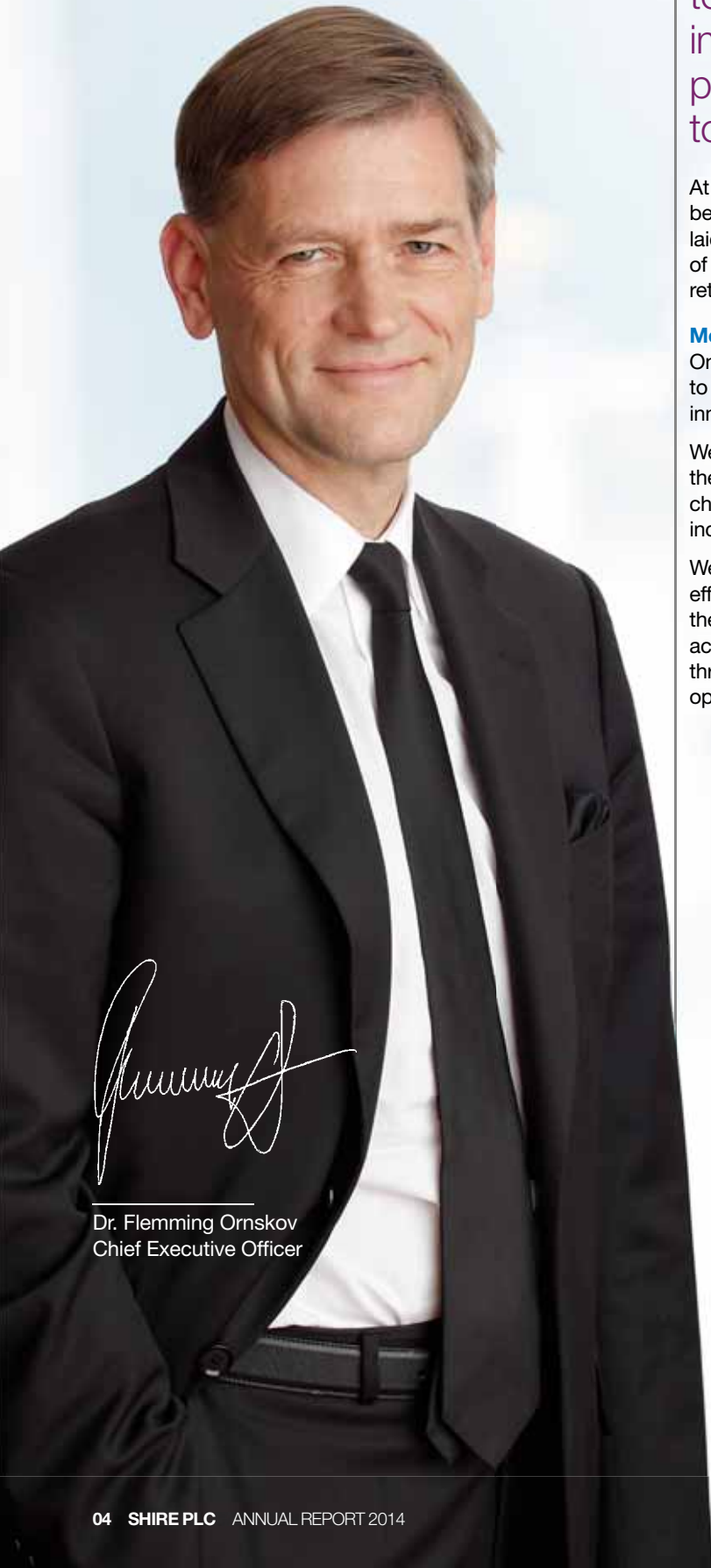


Chief Executive Officer's review



Dr. Flemming Ornskov
Chief Executive Officer

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

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

Moving forward

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

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

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

A clear direction

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

The best of two worlds

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

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

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

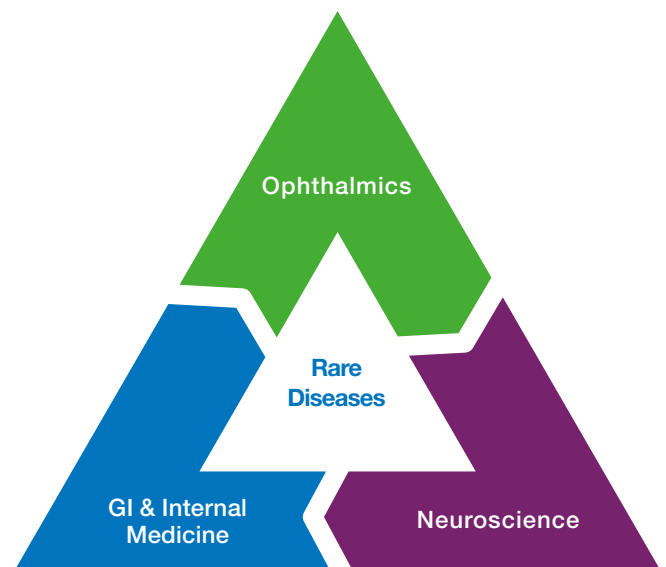
To build on our distinctive focus and strengths, we have four strategic drivers: growth, innovation, efficiency and people. In 2014 we hit significant milestones across all four.

Driving strong growth across all our businesses

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

In Rare Diseases, through our acquisition of ViroPharma, we added and accelerated the sales growth of CINRYZE (+30%) on a pro forma basis², an innovative product for the prophylactic treatment of Hereditary Angiodema (HAE) attacks. FIRAZYR[®], our treatment for acute HAE attacks, also grew strongly (+55%). In our GI business, LIALDA[®] has become the number one prescribed 5-ASA in the US³ in 2014 and gained an additional 5% of market share in 2014. In Neuroscience, VYVANSE sales grew 18% as more patients continued to use VYVANSE to treat their Attention Deficit Hyperactivity Disorder ("ADHD").

Our distinctive mix of complementary business units and capabilities



¹ Product sales growth including CINRYZE products sales acquired in January 2014 with ViroPharma.

² 2013 CINRYZE product sales reported by ViroPharma.

³ IMS SFSS Attribute Ranking Table Study.

Chief Executive Officer's review

(continued)

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

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

Enhancing our innovation

Through 2014 we continued to concentrate our R&D on rare diseases – the majority of our research dollars now goes into this area. Overall, we invested \$840 million on a Non GAAP basis in R&D² and we hosted our first R&D Day showcasing the innovation in our pipeline. In 2014, we have 27 programs in clinical development, 22 of them distinct, the balance relating to new markets or new indications – the most in Shire's history.

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

Alongside our strong research capability in rare diseases, we made excellent progress in enhancing our specialty pipeline. In Neuroscience for example, we explored product candidates such as SHP465, a potential treatment for ADHD in adults. We are also entering new markets with VYVANSE, having received FDA approval on January 30, 2015 for the treatment of Binge Eating Disorder ("BED") in adults. BED affects an estimated 2.8 million¹ US patients and VYVANSE is the only FDA approved treatment for this condition.

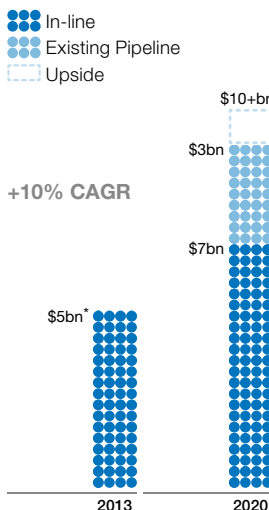
Increasing efficiency throughout our organization

Our ongoing drive to increase efficiency gained momentum through the year as we took advantage of the significant reorganization undertaken in 2013 to streamline and simplify Shire. This was a contributor to our achievements in the year, notably our profitability, which is at an all-time high with a Non GAAP EBITDA margin of 44%²; our ability to generate cash, with cash generation of \$2.4 billion² in 2014; and our sales per employee, \$1.2 million. We also simplified our global footprint by establishing our US Operational Headquarters in Lexington, Massachusetts and our International Operational Headquarters in Zug, Switzerland.

Attracting, rewarding and retaining great people

Throughout 2014 we continued to hire and retain excellent talent at all levels. Our performance in a year which included the uncertainty and distraction resulting from the offer from AbbVie, is a testament to the great commitment, skills and resilience of our people, who continued to focus on their work and delivered record revenue and Non GAAP earnings. This reflects not only the dedication of our people but also the strength of our patient-focused culture. I'm proud that we are increasingly recognized as a company where great people do great work to help transform lives around the world.

Product sales; Percent CAGR



10 x 20 Details

- > **In-Line:** \$7 billion expected from on-market products³
- > **Pipeline:** \$3 billion expected from existing pipeline³
- > **Upside:** NPS Pharma, Lumena, Fibrotech, BIKAM, CINRYZE new uses, early stage pipeline and future business development provide additional upside to 10 x 20

* \$5bn represents sales from continuing operations.

¹ Hudson JI, Hiripi E, Pope HG, Kessler RC. The prevalence and correlates of eating disorder in the National Comorbidity Survey Replication. *Biol Psychiatry*. 2007;61(3):348-358. Erratum in *Biol Psychiatry*. 2012;72(2):164 and Howden LM, et al. Age and sex composition: 2010. US Census Bureau; 2011.

² This is a Non GAAP financial measure. For reconciliation to US GAAP please see page 166.

³ Shire announced its 10x20 aspiration on June 23, 2014 and seeks to achieve 2020 product sales of \$10 billion from its In-line and Pipeline portfolio as at May 2014.

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

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

Aiming to lead in biotech

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

10 x 20: a journey and a goal

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

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

Transforming lives

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

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

Flemming Ornskov, MD, MPH

Chief Executive Officer

\$5.8bn

2014 record product sales

44%

Non GAAP EBITDA margin¹

Sales in **68** countries

We've continued to expand our footprint

\$840m

Investment in Non GAAP R&D¹

¹ This is a Non GAAP financial measure. For reconciliation to US GAAP please see page 166.