Shire's 2015 Full Year and Fourth Quarter Results Conference Call Transcript

Shire PLC

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Presentation participants

Flemming Ornskov – CEO
Phil Vickers – Head of R&D
Jeff Poulton – CFO
Matt Osborne – Head of IR

QAs participants

Kerry Holford, Exane BNP Paribas
Ronny Gal, Bernstein
Keyur Parekh, Goldman Sachs
Ken Cacciatore, Cowen & Company
Graham Parry, Bank of America Merrill Lynch
John Boris, SunTrust
Douglas Miehm, RBC Capital Markets

Presentation

Matt Osborne – Head of IR

Thank you. Good morning and good afternoon, everyone. Thank you for joining us to discuss the press release Shire issued earlier today announcing our 2015 year-end results.

You should have received our press release and can view the presentation via the link on Shire's website. For those not able to view the webcast, slides that accompany today's call are located on the presentations and webcasts page of Shire's corporate website at Shire.com.

Our speakers today are Chief Executive Officer Dr. Flemming Ornskov, Dr. Phil Vickers, Head of Research and Development, and Jeff Poulton, Shire's Chief Financial Officer.

Before we begin, please refer to slides 2 and 3 of our presentation, which provide information about certain statements to be made today that are forward-looking statements within the meaning of the securities laws, including those regarding our development programs, future financial results and statements regarding the potential impact of our announced combination with Baxalta. Statements made during this call that are not historical statements will be forward-looking statements and, as such, will be subject to risks and uncertainties which, if they materialize, could materially affect our results. The forward-looking statements in this presentation speak only as of today and we undertake no obligation to update or revise any of these statements. Additional information regarding these factors appears in our SEC filings.

Following our presentation today, we will also open up the call to your questions. We request that you ask only one to two questions so that everyone has a chance to participate. We will also be available to follow up with you after the call.

I will now hand the presentation over to Flemming.

Flemming Ornskov – CEO

Thank you, Matt and hello everyone. We're pleased to be with you today to discuss our fourth quarter and full year results.

During today's call, I will provide you with a greater understanding of our significant achievements made during 2015, one of the most remarkable in the Company's 30-year history. I will then hand the call over to Phil to highlight some important advances in our innovative pipeline. Jeff will then take you through what was a strong Q4 2015 and full-year financial performance for 2015. Finally, I will make a few closing remarks before we move into Q&A.

Let's now turn to slide 5

In 2013, we laid out a strategy for long-term growth and global biotechnology leadership with a focus on rare diseases and other specialty conditions. In 2015, we fast-tracked our progress on this journey. We executed significant acquisitions to build category leadership and deliver best-in-class therapies in our core therapeutic areas. We accelerated the growth of key rare diseases assets and built the best pipeline we have ever had.

We also advanced lifitegrast, our innovative and promising dry eye treatment, laying the foundation for ophthalmics leadership.

It is important to note that as we transformed our business in 2015, we also achieved record full year revenues, and strong double digit earnings growth as measured by Non GAAP diluted earnings per ADS.

Let me briefly take you through what I see are the defining moments for us in 2015.

So with that, please turn to slide number 6

Side 6 highlights four accomplishments that distinguished 2015 and significantly transformed the company. Each of these events is meaningful in its own right.

First, early in the year, we acquired NPS, which strengthened our GI business and brought in rare disease products, Gattex/Revestive and Natpara;

Next, we successfully completed and reported positive, top-line results from the lifitegrast Phase 3 study, called OPUS-3. We resubmitted the NDA, and last week FDA accepted the NDA, establishing a PDUFA date of July 22 of this year for this submission. We are working towards a potential approval and launch in the second half of 2016.

The third key milestone was Dyax. We recently completed the acquisition of Dyax, which extended our leadership position in hereditary angioedema with the addition of SHP643, formerly DX-2930. You will hear more about this compound later in the presentation.

Finally, we announced a proposed combination with Baxalta. This transaction advances our goal of becoming the biotechnology global leader in rare diseases and expands our category leadership to include franchises in hematology and immunology, as well as a growing franchise in oncology.
I want to take a brief moment to remind you why we are so excited about this combination with Baxalta. Together, we expect that Shire and Baxalta:

- will generate double-digit topline growth, with revenues projected to exceed $20 billion by 2020 - 65% of total annual revenues will be from rare diseases;
- We will have more than 60 programs in development, of which over 50 address rare diseases;
- Will launch over 30 products, if approved, from this pipeline by 2020, contributing a projected $5 billion in annual new product revenue by 2020;
- We will deliver annual operating cash flow of approximately $6B beginning in 2018, and
- We will achieve an attractive ROIC; projected to exceed Shire cost of capital in 2020.

The integration planning has started and is proceeding well. Numerous teams are in place to design and plan the new organization. I am pleased by the progress and will keep you updated as this moves forward and more information becomes available.

Please now go to slide number 7

As this slide shows, amid all the M&A, we maintained focus and executed forcefully: delivering record annual revenues and strong double digit earnings growth as measured by Non GAAP diluted earnings per ADS.

We exceeded the upgraded full-year guidance as provided at Q2, and Jeff will take you through the finances in greater detail later in the presentation.

As shown, top-line growth was primarily driven by Vyvanse, Lialda, Cinryze, and Firazyr, as well as by the assets we acquired from NPS --- Gattex/Revestive and Natpara.

In addition, during the year, we continued to progress our innovative pipeline, which now includes 26 programs in clinical development with 14 programs in Phase-3, or Phase 3 ready.

And, as mentioned, we continue to be very excited about our planned combination with Baxalta which we expect to close in mid-this year.

Moving to slide 8…

Shire's underlying business delivered on both the top- and bottom-line during 2015.

- On a reported basis, the company delivered 5% year-over-year growth in product sales, largely driven by volume, which was at the upper end of our guidance.

- At constant exchange rates and excluding the impact of generic INTUNIV, product sales for the year grew even higher, at 14%.
- We delivered a 43% Non GAAP EBITDA margin while investing in the launches of Vyvanse for the binge-eating disorder indication and Natpara for hypoparathyroidism, as well as investing in lifitegrast as we prepare for its potential approval and launch for dry eye disease later this year.
- Shire's continued focus on generating sustainable growth through efficiency resulted in Non GAAP diluted earnings per ADS growth of 10%, which exceeded our previous guidance of mid-to-high single-digit earnings growth in 2015 compared to 2014.
- At constant exchange rates, Shire's Non GAAP diluted earnings per ADS growth was even higher for the year, 14%.

Let's now turn to slide number 9

Multiple products contributed to our strong growth in 2015 reflecting the investments made in recent years to bring these innovative products to market. Jeff will provide more detail on the performance of our portfolio but it is worth highlighting the strength of the following products:

- Vyvanse continues to perform very well in the adult market which includes both ADHD and the Binge Eating Disorder indication.
- Lialda continues to build on its market share leading position.
- Our two hereditary angioedema products, Cinryze and Firazyr, surpassed $1 billion in combined annual revenue during 2015;
- The two rare disease products that we acquired from NPS, Gattex and Natpara, both performed very well.

Let's now go to slide number 10

Refinement of our market segmentation and messaging has increased Vyvanse's ability to compete, particularly in the adult ADHD market which is growing above the overall market. This above-market growth is also being driven by the use of Vyvanse in adults with moderate to severe binge-eating disorder.

In December, we submitted a supplemental NDA to the FDA with 6-month data for Vyvanse demonstrating long-term maintenance of efficacy and safety in adults with moderate to severe binge-eating disorder. Following FDA's feedback, we look forward to potentially including these data into Vyvanse's product label for this indication later this year, therefore enhancing the efficacy and safety label.

Please now go to slide number 11

Previously, we have demonstrated our ability to leverage our Rare Disease infrastructure to accelerate the growth of CINRYZE post the ViroPharma acquisition. Similarly, we are now demonstrating our ability to accelerate the growth of both GATTEX and NATPARA, which were assets we acquired through NPS.

Focusing first on GATTEX, our strategy to grow product sales in the U.S. including identifying, converting, and supporting patients, and in the third quarter, we also began to leverage our 100 Lialda sales reps to drive enhanced awareness of short bowel syndrome among GI physicians.

The result in 2015 was an increase in GATTEX patient start forms in the U.S. and a steady increase in GATTEX patients on therapy, reaching 564 in the U.S. at the end of 2015.

REVESTIVE, as GATTEX is known outside the U.S., is currently launched in Germany, France, Norway, Sweden and Canada and 75 patients from these combined regions are already on therapy at the end of 2015.

Please now move to slide number 12

Natpara is also demonstrating strong patient growth from the approximate 200 patients on therapy at the end of Q2 2015 to the approximate **700** patients on therapy at the end of 2015.

Natpara has been well received by physicians and patients as the only FDA approved medicine to treat hypocalcemia for patients with hypoparathyroidism who are not well controlled on calcium and vitamin D. We are also making progress with the approval of NATPAR, as Natpara is known in the EU, which Phil will discuss I more details.

Let me now turn the call over to Phil Vickers, Shire's Head of R&D, who will highlight our pipeline progress and key pipeline programs.

Phil…

Phil Vickers – Head of R&D

Thank you, Flemming.

I am very pleased to highlight key aspects of Shire's innovative pipeline that continues to grow and advance. Our pipeline now includes 26 programs in clinical development, and is the most robust pipeline in Shire's history. The vast majority of these programs are focused on the treatment of rare diseases.

Moving on to slide 15…

We now have 14 programs that are in Phase 3, or are Phase 3-ready. Three programs recently advanced to Phase 3. These are:

- SHP616 (or 'CINRYZE' for AMR): this is an additional indication for CINRYZE for antibody-mediated rejection in patients receiving a kidney transplant. Clinical trial sites are open and we expect to begin dosing patients imminently in this area of high unmet medical need;
- Next program is Subcutaneous CINRYZE: this is a subcutaneous formulation of CINRYZE for prophylactic treatment of hereditary angioedema, where we recently initiated patient dosing;

- Finally there is SHP621: for the treatment of Eosinophilic Esophagitis, or EoE, one of the programs obtained through the acquisition of Viropharma. Although a rare disease, the prevalence of EoE approaches approximately 180,000 individuals in the U.S. alone, and represents a significant unmet medical need. SHP621 has the potential to be the first approved product in this indication.

The Dyax acquisition added one further Phase 3 program:

- SHP643, previously known as DX-2930, is being developed for the prophylaxis of Hereditary Angioedema. SHP643 remains on track to start patient dosing in March of this year. It has the potential to lower rates of HAE attacks and significantly improve patient convenience, based on the clinical data reported to date.

Additionally, one more program will enter Phase 3 in the near future:

- SHP620, or maribavir, an additional program acquired through our acquisition of Viropharma, is on track to enter a Phase 3 trial next quarter for cytomegalovirus infection in transplant patients. This is another area of high unmet need, particularly for those patients resistant or refractory to the current standard of care.

Turning now to slide 16…

In addition to progressing a number of studies into Phase 3, we expect a number of key topline data read-outs during the first half of the year. These include data from:

- a Phase 3 study of SHP465 for the treatment of ADHD, designed for the adult population
- a Phase 2b study of SHP610 for the treatment of the rare lysosomal storage disease San Filippo A
- a Phase 2 study of SHP607 for the prevention of Retinopathy of Prematurity, which is another rare disease.

SHP465, a three-bead formulation of mixed amphetamine salts, has the potential to provide ADHD symptom control from 4-16 hours post-dose.

An efficacy and safety study in pediatric patients, a requirement of the FDA, has rapidly enrolled, as did a study in adults investigating additional dose strengths of SHP465. Top-line data from the pediatric study, along with the Phase 3 data in adults, will form the basis of the planned resubmission to the FDA for this program, and this is projected to occur later this year.

If it reaches the market, SHP465 could offer a new effective treatment for ADHD patients seeking a longer duration therapy, one of the largest unmet needs in adult ADHD.

We are also expecting Top Line Phase 2 results from our exciting program, SHP607, for the prevention of Retinopathy of Prematurity or ROP in mid-2016.

As a reminder, babies born prematurely are at risk of developing ROP, which is characterized by vision impairment and blindness. An estimated 30,000 babies are born at less than 28 weeks gestational age every year in the US alone, and so the opportunity for an effective therapy is significant. As well as evaluating the impact of SHP607 in ROP, we are also assessing it in a number of key secondary endpoints associated with prematurity.

For Natpar in the EU, recent meetings with the CHMP have confirmed allowance for additional time to assess the Natpar Marketing Authorization Application. We anticipate that the additional time will allow for a satisfactory resolution of outstanding items related to this application, and we expect a CHMP decision in the third quarter of this year, potentially leading to launch in Europe during 2017.

Moving now to slide 17…

Shire is quickly becoming recognized among physicians, key opinion leaders and within the industry for our commitment towards driving true innovation in ophthalmology, having created an exciting portfolio of programs in just a few short years. I mentioned earlier the SHP607 program for ROP, but in our pipeline we also have SHP640, a treatment for infectious conjunctivitis, or pink-eye - a potentially significant opportunity in one of the largest areas of ophthalmic medicine. This approach has the potential to address both the bacterial and viral causes of disease and will enter Phase 3 trials later this year. Other ophthalmology programs in earlier stage development include treatments for glaucoma and autosomal dominant retinitis pigmentosa, which recently received Orphan Drug Designation in the U.S.

Turning now to slide 18…

As mentioned, a tremendous focus this year for the entire team will be to advance lifitegrast, which is in registration in the US. Lifitegrast is the subject of the largest clinical trial program for an investigational compound for dry eye disease, having been studied in over 2,500 patients in three rigorously designed Phase 3 trials as well as a separate safety study.

On January 22, we resubmitted the New Drug Application to the FDA for lifitegrast for the treatment of the signs and symptoms of dry eye disease in adults. The FDA recently acknowledged receipt of the resubmission, determined it complete, and established a PDUFA date of July 22, 2016.

We look forward to moving this program closer towards patients as we approach this date.

I'll now turn the call over to Jeff Poulton, who will review the fourth quarter and year-end financials.

Jeff Poulton – CFO

Thank you, Phil.

Good Morning and Good Afternoon Everyone.

As Flemming has indicated, we delivered strong top and bottom line growth during 2015, demonstrating continued positive momentum in our business as we enter 2016. Consistent with our previous calls discussing 2015 results, I will focus on four key areas today:

- First, I will provide detail on the drivers of the continued double digit sales growth from our core underlying business.
- Second, I will talk about delivering a 43% non-GAAP EBITDA margin in a year when we invested significantly in new future growth drivers.
- Third, I will cover our continued strong cash generation.
- Finally, I will discuss our outlook for 2016 for the current business which now includes Dyax.

Starting with slide 20, we delivered product sales of $6.1 billion in 2015, a 5% increase over 2014 on a reported basis, at the top end of our guidance range. On a CER basis, the year-over-year growth is 9%, and was a robust 14% excluding the impact of the Intuniv loss of exclusivity in the US. I will cover the drivers of this growth on the next slide which did include pricing actions on a variety of our products in the US. While this was a contributor to overall growth in 2015, the majority of US growth was driven by volume increases.

Royalties and Other Revenues increased by 65% over 2014, a bit higher than what we anticipated for the full year. The year-over-year increase is primarily due to the benefit of the Sensipar royalty which delivered more than $100 million in revenue in 2015 following the acquisition from NPS in Q1.

Total revenues were just over $6.4 billion, up 7% on a reported basis and 11% on a CER basis.

Non-GAAP EBITDA increased by approximately 6% on a reported basis and 10% on a CER basis. Our non-GAAP EBITDA margin was 43% during a year in which we invested in the US launches of Vyvanse for BED and Natpara as well as investing in Gattex in the US or Revestive in International markets. As we will show, we are pleased with the growth we are driving from these investments. We also made investments to prepare for the anticipated launch of Lifitegrast for dry eye disease – a key driver of future growth.

Non-GAAP diluted EPS per ADS was $11.68 or 10% higher than the $10.60 reported in the prior year and higher than the upgraded full-year guidance that we issued at Q2. At constant exchange rates, this represents 14% year-over-year growth, although it is worth noting that 2015 did benefit from a non-GAAP effective tax rate of 16%, or 2% lower than the comparable rate for 2014.

We have a highly cash generative business and our non-GAAP cash generation was approximately $2.4 billion in 2015.

As you can see on the slide, in comparison to the upgraded full-year guidance that we issued at Q2, we delivered double digit Non-GAAP diluted EPS growth, slightly better than we expected. We consider 2015 another strong year of performance for Shire.

Turning to slide 21, let’s take a more detailed look at product sales.

As noted on the slide, core product sales were up approximately $800 million in 2015 or 14% at constant exchange rates. This growth was driven by Vyvanse, our HAE products and our GI franchise which includes the recently acquired NPS products – Gattex and Natpara.

Vyvanse continues to show very strong growth. Vyvanse's 2015 sales slightly exceeded $1.7 billion, delivering growth of 21% at constant exchange rates. The increase was driven by US prescription growth of 8% outpacing ADHD market growth of 6%. Vyvanse's performance continues to be particularly strong in the adult segment which includes both ADHD patients as well as BED patients. Vyvanse exited 2015 at a 16.7% market share, up a half share point from December of 2014. 2015 performance also benefited from growth from international markets, stocking of approximately $30 million on a net sales basis during the year compared with approximately $25 million of destocking in 2014, and price increases taken since the end of 2014.

We are also pleased with the performance of our HAE products.

Cinryze sales increased approximately $115 million, or 24% on a constant exchange rate basis, to $618 million for the year. The addition of more patients on therapy was the primary driver of Cinryze's growth during the year. For the 4th quarter, Cinryze de-stocked by approximately $20 million following stocking in Q3 of a similar amount.

Firazyr sales were $445 million in 2015 up 25% on a constant exchange rate basis from 2014. Sales benefited primarily from an increased number of patients on therapy.

Turning now to our lysosomal storage disease products, which given their significant international mix, were the products most impacted by the strengthening of the US dollar. Elaprase sales increased 4% on a constant exchange rate basis. Higher unit sales volumes for Elaprase driven by an increase in patients on therapy were partially offset by a lower average price due to modest price reductions in international markets and geographic mix. Replagal sales increased 1% on a constant exchange rate basis as the benefit of more patients on therapy was partially offset by modest price reductions in international markets and geographic mix. For Replagal in particular, we are focused on and optimistic about driving improved growth during 2016. VPRIV sales also increased by 1% on a constant exchange rate basis as competitive pressures in the US market reduced the impact of growth in patients on therapy in international markets.

Lialda sales increased 10% at constant exchange rates. This growth reflects script growth of 10% year-over-year as well as a price increase taken at the beginning of 2015 offset by higher sales deductions and inventory destocking. Lialda sales did benefit in the 4th quarter from approximately $15 million of stocking, but destocked slightly for the full year 2015 compared with approximately $15 million of stocking in 2014. Lialda's exit share in the US market was approximately 36%, a 3 point increase from the 2014 exit share – an impressive share gain as Lialda continues to bolster its market leading position.

The products acquired with our NPS acquisition earlier this year contributed $166 million of sales in 2015 which favorably impacted Shire's total product sales growth rate by 3%. Gattex contributed $142 million and Natpara contributed $24 million. For Gattex, as noted previously, we believe we are seeing positive results from leveraging our existing GI sales force to raise awareness of short bowel syndrome and to help identify eligible patients as our ~ 100 Lialda sales reps in the US began making calls for Gattex for the first time during the third quarter. For Natpara, the number of REMS certified physicians has increased to

approximately 2,500 and we ended the year with approximately 700 patients on therapy – a 66% increase in the number of patients on therapy since the end of the third quarter.

We are pleased with the performance of both products and believe our rare disease expertise has benefited these products in the same way that we were able to accelerate growth in our HAE franchise following the acquisition of Cinryze from Viropharma.

As you can see on the far right side of the chart Intuniv and FX headwinds continued to hold back reported performance. Intuniv, which lost exclusivity in the US in December 2014, held back reported full year sales growth by approximately 5 percentage points as US sales were impacted by the entry of multiple generics during the year. We were also impacted by foreign exchange headwinds from a stronger US dollar which held back reported growth by another 4 percentage points.

Turning to slide 22, we have covered product sales so I will turn my attention to operating expenses and ratios.

R&D spend increased 5% from the prior year as we advanced our pipeline during the year. Phil took you through the significant progress we are making as lifitegrast has been refiled with the FDA, and we are now positioned with the most Phase 3 programs in our history.

SG&A was up 8% from the prior year as 2015 was a year of investment for us. We launched the B.E.D. indication for Vyvanse in the U.S. and made investments to help prepare for an anticipated 2016 launch of Lifitegrast. We also assumed the costs associated with NPS, acquired in the first quarter of this year. As part of that transaction, we successfully launched Natpara and invested in accelerating the growth of Gattex.

Taken together, we achieved a non-GAAP EBITDA margin of 43% in 2015, particularly impressive during a year when we invested significantly behind future growth drivers.

Turning to slide 23, my final slide focused on 2015.

Given our strong operating performance, our cash generation remained strong in 2015. We generated approximately $2.4 billion of cash in 2015 up 1% from prior year. Free cash flow was down 12% to $2.2 billion as 2014 free cash flow benefited from a repayment of over $400 million from the Canadian revenue authorities. Excluding the Canadian repayment, free cash flow increased 5% in 2015. We expect our business to continue to generate strong cash flow going forward.

We ended 2015 in a net debt position of approximately $1.5 billion. This has increased to $7 billion as of the end of January as we closed on the Dyax acquisition, which was financed with a new $5.6 billion term loan bank facility, in late January.

Turning to slide 24, I will finish up with our outlook for 2016.

Before moving into the detail I'd like to make three points. First, the outlook includes the impact of the Dyax acquisition, which closed on January 22, 2016. Second, our outlook does not include the impact of our announced combination with Baxalta. We expect the transaction to close mid-2016 and we will update our guidance thereafter. Third, our outlook assumes FX rates based on the January month end exchange rates which are noted at the bottom of our guidance slide.

Starting at the top, we are expecting product sales to grow double digits. On a reported basis, we expect year-over-year growth between 11% and 14% in 2016. This includes the benefit of Kalbitor, the marketed product acquired as part of the Dyax transaction. Based on current FX rates, we expect product sales to be held back approximately 2 to 3 percentage points by FX headwinds in 2016 -- so on a constant exchange rate basis we expect product sales to grow between 13% and 17%.

Royalties and Other Revenues are anticipated to increase in the 5% to 10% range. This is less than the growth achieved in 2015 which benefited from the initial year of the Sensipar royalty stream and from royalties associated with the Intuniv authorized generic sales in the US in the first half of 2015.

Our non-GAAP gross margin is expected to be similar to 2015 levels.

Our non-GAAP combined R&D and SG&A expense is expected to increase between 12% and 14% in 2016. The increase is primarily due to investment associated with the anticipated launch of Lifitegrast, operating costs supporting the Dyax business from January 22, 2016, and investment in 14 programs in late stage clinical development.

Given the increase in our debt position since the close of the Dyax acquisition, we are expecting our non-GAAP interest and other expense to increase by approximately 1.5x to 2.0x 2015 levels.

We finished 2015 with a full year non-GAAP effective tax rate of approximately 16% and expect a slightly higher rate in 2016 of between 16% and 18%.

Taken together, we expect reported non-GAAP diluted earnings per ADS growth of between 7% and 10% in 2016. On a constant currency basis we anticipate non-GAAP diluted earnings per ADS growth of between 9% and 13%.

The final comment I will make regarding our outlook for 2016 relates to capital expenditures. As you see, we are expecting capex of approximately $300 million in 2016. We expect this will be our level of capex investment over the next three years as we enhance and expand our manufacturing capabilities including our plan to break ground on a new biologics greenfield manufacturing site during 2016. The new greenfield site will ensure full redundancy capability for our Biologics portfolio and will more than double our current capacity.

And with that, I will hand you back to Flemming.

Flemming Ornskov – CEO

Thanks Jeff. 2015 was indeed a remarkable year for Shire.

In 2015 we not only transformed our business and advanced our pipeline but did so while delivering record revenue and strong earnings growth as measured by Non GAAP diluted earnings per ADS. We delivered top and bottom-line growth during a year when we continued to invest in future growth drivers and achieved four significant milestones: NPS, lifitegrast, Dyax, and, of course, Baxalta.

All of this would not be possible without the focus, dedication and drive of our employees who continue to outperform in challenging environments. Before we take your questions, I'd like to emphasize the key drivers that all of us at Shire are most focused on delivering during 2016:

- Integrate the recently closed acquisition of Dyax and advance SHP643 for HAE prophylaxis;
- Progress lifitegrast towards approval and launch for the second half of this year;
- Work toward closing the combination with Baxalta in the middle of this year and begin the process of integrating our two companies;
- And finally, expand and strengthen manufacturing to support our global growth; and, importantly; and importantly execute and deliver forcefully across our entire portfolio and business.

We are committed to delivering another strong set of results in 2016, and to having our customer-facing colleagues stay laser focused on delivering. I look forward to keeping you updated on our performance during 2016.

Operator, we are now ready to take questions from the audience.

Q&A

Operator:
Thank you. [Operator Instructions]

First from the line of Kerry Holford at Exane BNP Paribas. Please go ahead, Kerry. Your line is open.

<Q - Kerry Holford>: Thank you. Two questions, please. Firstly, on tax rate gave in guidance, is for it to increase a little this year but still be lower than your long-term guidance, the 17% to 19%. So if you could just provide details as to why that is not yet stepping up. Is it - are you expecting further tax provision releases in 2016? And then on NATPAR, you talk about a delay in Europe, and essentially CHMP seemingly stopping the clock, and I wonder if you could just detail what's caused that and how quickly you can think that can be rectified? Thank you.

<A - Flemming Ornskov>: Thanks very much, Kerry. I noted questions one and two - one on tax and us also not predicting to be at a 17% to 19% level next year. So Jeff, I'll ask you in a second to answer that. And then NATPAR, what is holding us up there. I think, Phil, that fits perfectly into your expertise. So Jeff, do you want to talk about tax and outlook?

<A - Jeff Poulton>: Sure. So you're correct, Kerry. We have guided to long-term tax guidance of 17% to 19%, and what I just guided to for this year is 16% to 18%. A fairly modest difference, I would say, between the two, but the favorable change in guidance for 2016 reflects changes to our profit mix as we invest in product launches in high-tax jurisdictions. That's probably the biggest driver of the slight improvement from what we had previously issued.

<A - Flemming Ornskov>: And the other question was on NETPAR, which is a product we're very excited about. We see great uptake in the U.S. of NETPARA.

So what's holding us back in Europe, Phil?

<A - Phil Vickers>: Yeah, we're looking forward to bringing the product forward to patients in Europe. The discussions with the regulatory authorities in Europe have really focused in three areas, two of which are very standard. That is the definition of the patient population where we'll get benefit - that would get benefit, so those discussions are ongoing. And the second is obviously around manufacturing questions that they have.
I'd say the third area, which is a little bit more unusual for this product, is around the device, because you have to have a device with a CE Mark in Europe if you're going to move forward in Europe, and so that's really where much of the discussion has been with the regulatory authorities. We've had some very positive and frequent discussions with them. They continue this quarter. We're aiming to resolve all of the scientific issues in the first half of the year. And the ongoing discussions about the device, we're aiming for resolution of those as we go into the third quarter. So we're looking for a decision on the overall program by third or fourth quarter of this year.

<Q - Kerry Holford>: Thank you.

<A - Flemming Ornskov>: Thanks so much, Kerry. Maybe the next question or two?

Operator:
Yes. The next is over to Ronny Gal at Bernstein. Please go ahead. Your line is open.

<Q - Ronny Gal>: Good morning. Congratulations on a nice quarter.

<A - Flemming Ornskov>: Thanks, Ronny.

<Q - Ronny Gal>: A couple of questions here. First on the NASH program, can you just give us an update where you stand on this? And then, second, as you kind of look at your mix of product, it looks like the specialty pharma products that have delivered most of the growth in this year. And the question is if we kind of think about your mix of products going forward, is there more comfort with expanding that franchise? Or still the focus is primarily going to be on orphan drugs?

<A - Flemming Ornskov>: So a good observation and good questions. And maybe I take the first questions on specialty, and then we'll talk about SHP626, which is the NASH compound we acquired from Lumena, which is a bile acid reuptake inhibitor.
So maybe talk about specialty. Shire does not differentiate between specialty and rare diseases. We're focused on rare diseases and highly specialized conditions, and we expect everybody within Shire to deliver phenomenal results. This year, VYVANSE had delivered phenomenal results, as have some other areas. VYVANSE, of course, given we're in the launch mode there, is penetrating the adult ADHD market, significantly outgrowing the market. Market's growing 10% adult; they're growing, I think, almost 50%, overall market growing 5.8%. We're growing almost 2% more than that. So clearly a very strong performance. And also points to the fact that there's a significant unmet need in binge-eating disorder in the U.S. We're also continuing to see very strong growth of VYVANSE ex U.S. So whether they're in specialty or rare diseases,

it's quite clear that if people perform and they have phenomenal growth franchises, we always will look at whether we should supplement the franchise. The good news for ADHD - we have our own supplement, a phenomenal product which is called SHP465. We have three studies, 111, then we have 305 and 306 that is ongoing. They're five to nine months ahead of schedule respectively. We plan by the end of year to file that. That's a product that has long-acting - from four to 16 hours, I think it is. And we think that will go into a significant unmet need, particularly in the adult marketplace. So we don't differentiate, but we're very pleased when our businesses and I think most of them if not all, continue to deliver.What about NASH, Phil?

<A - Phil Vickers>: Yep. So you're right. I mean, this is 626, which we got from the Lumena acquisition, along with 625. We've recently completed a Phase 1 study successfully with that program. We're now engaging regulatory authorities. We're planning to move towards a Phase 2 study, and we're planning to initiate that, which will probably be third quarter of this year, I would anticipate.

<A - Flemming Ornskov>: So the profile here - the 626 has a very attractive profile both on its impact on lipids and plasma glucose, but it's too early. And we want to see the Phase 2 data before we get too excited. But it's, of course, a significant unmet need with a very attractive compound with strong IP status.

<Q - Ronny Gal>: Do we understand now what happened with 625? Do you understand what's the issue with the ASBT mechanism?

<A - Phil Vickers>: Yeah, we're continuing to look at that, Ronny. And as you know, we still have studies ongoing. There were two pediatric studies and two adult studies. And one of the adult studies is still ongoing. So we're still getting data in from the studies with 625. It was one of those programs where we didn't see everything that we wanted in the pediatric studies. But in the PFIC patients, we saw very profound activity where we saw effects on biomarkers and really affecting the course of the disease, as measured by liver markers, for example. So where we saw activity, we saw very profound activity. So we're now going through engaging world leaders in this space, and in the very near future we anticipate coming up with a plan to move forward. So certainly in PFIC, we plan to move forward with that program. And we're considering how broad we want that program to be as we move forward initially, but we do plan to move forward.

<A - Flemming Ornskov>: And the guiding principle for us in this category and other categories are the same. One is that we innovate for our patients; there's significant unmet need among these patients, many of which go into transplants. So we'll do everything we can to find a treatment that is safe and efficacious. And, secondly, we shy no obstacle, if look at our ophthalmics, Lifitegrast and others, we don't jump away just because we run to an initial obstacle. For our patients, we do everything we can to find a product that works. But with that maybe we move on to the next question.

Operator:
Okay. We now go to the line of Keyur Parekh at Goldman Sachs. Please go ahead; your line is open.

<Q - Keyur Parekh>: Good afternoon. Two questions, please. One, Flemming, if you can just highlight for us kind of how you see the steps forward for Lifitegrast in Europe, kind of any conversations you might have had with the CHMP post OPUS-3? And then separately, as you think about the focus for Shire over the next

12 to 18 months, can you help us think about what's of priority from your perspective, what it is that you need to get absolutely spot on?
Thank you.

<A - Flemming Ornskov>: Thanks, Keyur. This is quite clear. Let me start with the last question, because that will lead into the other question. The next 12 to 18 months, as I outlined, is an absolutely sharp and undiminishing focus on customer-facing commercial execution for all the products we have.
That also means in particular that the launches of NATPARA and ongoing strong growth of GATTEX and binge-eating disorder have to continue, and that's an absolutely key focus for the company.
Number two is integrating Dyax and making sure that SHP643, their lead compound, that quickly gets into Phase 3. We're on track for that in a few months to start that. And then with Baxalta that we as quickly as possible set out the framework and make a smooth integration and start capturing the $500 million plus in synergies that we set out as a goal and deliver the double-digit top line growth through commercial focus. So that's the absolute focus.
And the final, and not least is of course on the commercial side, is going to be Lifitegrast. That is absolutely a bellwether for us. We have come a long way since 2013. I think we have now an excellent a package that's gone to the FDA in record time. January 22 we submitted that. People had to work over the holidays; they know how important it is to get quickly to market. We're ready manufacturing wise; we have the commercial infrastructure almost fully ready. We have the plants ready. We do tons of market research that reconfirms to us how strong a product this potentially could be. In Europe we've had meetings with one or two regulators, and after Santen got their product approved based on a, I would say mainly signs data, they are very interested in our products, and I think we will finalize these discussions and then look at that market. We've also had engagements in Japan with those, and of course also Canada.
Anything you want to supplement, Phil?

<A - Phil Vickers>: No. I think - well, you're right, Flemming. We've got a laser-like focus on moving forward in the U.S. towards approval. That's where our focus has been. Now we've had some discussions with European regulatory authorities, and I think those - characterize those as being very positive and productive discussions. Now we've resubmitted in the U.S., we will again turn our focus to Europe with a plan to move forward.

<A - Flemming Ornskov>: Our absolute goal is to make this a leading global ophthalmic brand in this category. So we will pursue down that path.

Operator:
Okay. We're now over to the line of Ken Cacciatore at Cowen & Company. Please go ahead. Your line is open.

<Q - Ken Cacciatore>: Great, thanks. A question on 607 - just wondering if you could remind us on those secondary endpoints what we should be looking at? And then also maybe discuss if you're successful on hitting the secondary - clearly we're all fingers crossed on the primary - but if you're not successful on the primary and do hit the secondaries, can you just talk about whether those could be made primary in a Phase 3 program?

And then my second question is, Flemming, clearly we understand what's in front of you over the next 12 to 18 months, but just if you could put a little bit of context into your really broader vision for the company. Now that you're hopefully going to be closing on Baxalta, hopefully launching Lifitegrast, where are we in terms of the transformation of the company? Do you see yourself with - this is midway through, meaning we could have just as large a transformational deal as a Baxalta, if we look 24 months forward, or do you think we're going to be focused on more smaller, orphan assets? Can you give us a broader perspective of kind of where we stand in the evolution of the company in your head? Thank you.

<A - Flemming Ornskov>: Thanks very much, Ken. So on 607, as you know, given that I started off working in a neonatal intensive care unit in my training as a physician in Denmark, this is close to my heart. I know what the significant unmet need is. This is clearly a challenging program. There's a significant unmet need. We're going for a first primary endpoint of retinopathy of prematurity, but there are a number of very attractive secondary endpoints. This is at Phase 2. I don't think we want to be indicating that we think that's enough. There's clearly probably going to be a need for additional data. We think it's one of our most challenging but also our most attractive programs just given the sheer size of neonates in the U.S. that would fall under this category and globally 65,000-plus and significant unmet need and particularly in the category of 24 to 28 weeks preemies.
But - do you want to say a little bit about what you think we're going to do?

<A - Phil Vickers>: Yeah, well, thanks for asking about the program, Ken. I am personally very excited about this program, just as the company is. You're right; we're focusing on retinopathy of prematurity. We're fully enrolled in this program now, and by the middle of this year we will get the top line data from that Phase 2 study. We are looking at other endpoints that - you can have a rationale that IGF-1, which is what 607 is, with its binding protein, could have an effect, for example, on lung function, on growth.
There's a variety of different endpoints. So we are looking at those, and of course if we saw benefit there, then that would be tremendous. But we should say we obviously cannot power for those endpoints, so if we don't see those and we saw a trend but we didn't get statistical significance, then that in itself would be encouraging. And of course, as always, we will respond to the data that we get. So if we saw a trend in some of those that looked exciting and we think could demonstrate benefits to patients, then we would factor that into the design of future studies and either have co-primary endpoints or indeed as you're suggesting, we would be free to switch the endpoints in a future clinical study. So we're excited about it. Wait till we get the data, and then decide how to move forward. But it is an exciting program.

<A - Flemming Ornskov>: And I think on your second question, I think the team and I - since I arrived in 2013 - I think we've made good progress to make Shire into a leading candidate for being one of the premier biotechnology companies. We're not there yet; we clearly with Baxalta would be number one in rare diseases. We are in some very attractive specialty areas. For the next 18 months, I think, the focus is to integrate both Dyax and not least Baxalta, deliver on the many launches they have which are incredibly attractive, like HYQVIA, the product, VONVENDI for von Willebrand, and all the products that they have or will soon be launching, and all the launches we have with GATTEX, NETPARA, Lifitegrast coming up. And in many countries we're launching other products, so that's going to be the focus.
And I'm sure Jeff would want me to say - and I'll let him say something - is pay down the debt as fast as we can and stay disciplined and extract the $500 million-plus we have promised in synergies. Naturally, as an

acquisitory company, we'll keep an eye on what's going on, both small and larger, but the focus right now is clearly, clearly on integrating and delivering. So, Jeff, do you want to say something?

<A - Jeff Poulton>: You got the script right in terms of the focus on the next 12 to 18 months around the balance sheet and our focus on using free cash flow to pay down debt. When we announced the Baxalta deal on the call in January, we talked about being at five times or just under five times net debt to EBITDA when the deal closes, and we think, given the cash generation capability of the combined organization, we can pay it down fairly quickly, and we plan to do that and be two to three times by the end of 2017.

Operator:
Okay. We're now over to Graham Parry at Bank of America Merrill Lynch. Please go ahead. Your line is open.

<Q - Graham Parry>: Great, thanks for taking my questions. So, firstly, you mentioned some price pressure in ELAPRASE and REPLAGAL ex U.S.; just wondering if you could expand on that. Where is it? How much are you seeing?
Do you think it's a growing trend spreading to other products, and whether you're seeing any price pressure at all in the U.S.? And then secondly on cash and balance sheet again, only $135 million on the balance sheet at the end of the year, so in terms of the cash you need for operational needs after you've drawn on the debt facility, how much of that you actually have to hive off? And at which point you think the balance sheet will be in a position, for you to think about having any of the businesses that you could be looking at? So the two to three times that you've talked about, is that a point - sort of threshold point for you to think about future M&A?

<A - Flemming Ornskov>: Thanks very much, Graham. So I think there was maybe a potential misunderstanding on the cash available there, but I'll let Jeff comment on that. I think even at the close of this deal we still have, of course, sufficient cash and plenty of it to do all what we need to do. And maybe we take that as the first question, Jeff.

<A - Jeff Poulton>: Yeah, I think that's right, Flemming. You're correct that the short-term liquidity is in good shape. I think the focus of the question was really on the balance sheet, how leveraged will you be and, again, how quickly can you pay down and how quickly can you start to consider M&A again? Again, I'll repeat what I said previously, the focus - and Flemming said as well - the focus in the near term is going to be on integrating Baxalta and using free cash flow from the combined operations to pay down debt. We have talked about two to three times at the end of 2017, and I think that would certainly be a place where we would have multiple options to consider in terms of how to deploy cash. Could be M&A, could be share buybacks if that was something that looked attractive at that time, but that would be a good place, I think, to start to reconsider different ways to deploy cash.

<A - Flemming Ornskov>: Yeah, I think the most important thing here is to stay disciplined. The thing is also we don't - we have a number of key growth drivers that are in the launch phase, so we'll be focused on that. We are a company that constantly look both at tuck-ins on the product side, and we'll continue to do that, and we also look at M&A, of course. That's part of our DNA. But I think the focus right now is on the

integration, which will be the largest we've ever done. Actually the two largest we've ever done. So we're confident. We have all the plans in place, and I'm absolutely sure we will do it. We've shown with every other acquisition that we do it, we know how to do it, and we do it quickly. The other thing is of course with a combined company we'll take a look at all the franchises and just make sure we think that they're all franchises that should stay with us going forward.
On price, do you want to say a word or two about price?

<A - Jeff Poulton>: Yeah, I think the headwinds that we saw on the lysosomal storage disease products in terms of price in 2015 are fairly consistent with what we've seen for the last several years. So these are low single digit over the course of the year price reductions across the portfolio. Again, nothing specific or in particular to highlight or point out. I would say it's, again, fairly consistent with what we've seen for the last several years.

<Q - Graham Parry>: Thank you.

<A - Flemming Ornskov>: But I think the overall thing not to forget here is this is a company that is, I think, one of the very few that have delivered strong results this quarter in our space. Secondly, this is a company that has done more M&A and business development in 2015, and yet we come out and deliver record results, that we can both chew and walk at the same time, I think we've shown. So maybe with that we should get the next question.

Operator:
That's over to John Boris of SunTrust. Please do go ahead, John. Your line is open.

<Q - John Boris>: Thanks for taking the questions and congratulations on the very robust momentum of your business. First question has to do with Lifitegrast. You mentioned, Flemming, that you've done some market research and would like to focus on any blinded product concept testing that you've done and how that shapes intent to prescribe going forward. Obviously the brand has some features, advantages, and benefit to that of the current product, RESTASIS. And then if you have any commentary about the recent FDA draft guidance on cyclosporine ophthalmic and the possibility of a generic entering the market and influencing that, that would be very helpful. And then, secondly, any update from an intellectual property standpoint on LIALDA - there was a marketing hearing - and then also GATTEX and the IPR timing?

<A - Flemming Ornskov>: Yeah, so I count a bit more than two, but we're in a generous mood today given the general depressed markets, so we'll be optimistic and put them in two buckets.
So let's talk about Lifitegrast first. So our strategy to entering into the ophthalmic market is to bring innovation. Lifitegrast is a totally differentiated molecule. I think we've shown both in terms of symptoms and signs and onset of action that we have a very differentiated. I think the data shows a good tolerability and safety profile, so we think we absolutely have a product that is a very good match to the needs that we see in the marketplace. We don't see generic to being where we would be seeing competition from. We have to show the virtues of Lifitegrast. All our market research both shows clearly that we have a differentiated molecule. We know there's significant pent-up demand for a differentiated molecule. We know there's significant unmet needs. We know that the current product, which - doesn't meet all the needs of this

marketplace, so we think there's absolutely a clear place for Lifitegrast. And our focus right now is on getting the best and most differentiated label, but also have the best and most educated launch force in place, and I'm absolutely sure we have that.

On IP, there are a lot of things going on in the IP space. I think you mentioned LIALDA. So Actavis/Watson, there was a trial recently which was in California which took place in January, and there's on the 11th of March, there's going to be final arguments in that particular case. Zydus still has the first filer status. There are other cases that have been staged, so I'd imagine that's what you focus on. The situation with the interpartes review, do you want to say something about that?

<A - Jeff Poulton>: Yeah, we don't expect anything, John, more in terms of additional information on the IPR until the second half of 2016, and the fourth quarter, I think, is the best guess in terms of timing.

<A - Flemming Ornskov>: And for GATTEX - we also had a question on GATTEX.

<A - Jeff Poulton>: I'm sorry, that was the question I was answering in terms of the next step in the IPR process. Should be second half of 2016.

<A - Flemming Ornskov>: Does that answer your questions?

<Q - John Boris>: Sure did. Thank you very much.

<A - Flemming Ornskov>: Okay. Thank you very much. Thanks for your questions.

Operator:
Over to Douglas Miehm of RBC Capital Markets. Please go ahead, Douglas, your line is open.

<Q - Douglas Miehm>: Yeah, perhaps you could go into a bit more detail on the eosinophilic esophagitis trial - when that might start, when you'd expect enrollment to be completed, and when we could see some data, if you don't mind?

<A - Flemming Ornskov>: So given the Phase 2 data, Phil is extremely excited about that. It's a total breakthrough in this category where there's no available treatment. So I'll limit him to two minutes. Is that okay, Phil?

<A - Philip Vickers>: Yes, that's fine. Yeah, but thanks for the question.
Yeah, we were excited to get this program. As you may remember, it came from ViroPharma. It was the acquisition of Meritage that resulted in this compound, SHP621. Pleased to say that effective the beginning of this year, we've now transitioned from Phase 2, where we'd looked at signs and symptoms of the disease, and we've seen some very encouraging data in both of those at Phase 2. So we therefore acquired the asset, and we've now started the Phase 3 study. We've got the first patients in the Phase 3 study in January of this year, so we are now moving forward with that program. So - and again, using co-primary endpoints,

looking at eosinophil counts and dysphagia. So program's started now, so you can expect to see some data from that as we move forward and towards 2017.

<Q - Douglas Miehm>: Perfect. And then just a follow-up question as it relates to the LSD products and the pricing, so probably proper [inaudible] model slight price decreases in that portfolio, offset by continued growth in the patient population, so net-net somewhere between the 1% and 5% CER growth that we saw with those products in 2015?

<A - Jeff Poulton>: So I'm not sure I - could you repeat the question? It was breaking up a little bit when you asked it. We couldn't quite hear it.

<Q - Douglas Miehm>: Oh, no, I just wanted to circle back to the LSD products. You indicated that we have the slight price decreases.

<A - Jeff Poulton>: Yes, okay.

<Q - Douglas Miehm>: I just want to know if it's fair to assume - yeah, to see a little bit more of that but offset by continued growth in patient population?

<A - Flemming Ornskov>: It was largely a mix issue in terms of which countries we had sales in.

<A - Jeff Poulton>: Yeah, I would say for the three products for 2016, as it relates to expectations, I'll take them one at a time.

I think VPRIV in Gaucher, I think, is probably the most competitive space with three enzyme replacement therapies currently marketed by three different companies. And you've got a couple of different oral products on the market. And the organic growth of Gaucher in terms of the number or percentage of new patients you'll see on therapy in a given year is generally low single digits. So we're probably going to see lower growth, maybe consistent with what we saw in 2015 as we move ahead.

ELAPRASE grew 4% at constant exchange rates. We've had ELAPRASE on the market in the U.S. since 2006, and then broadly in the main markets in Europe since 2007, so we're fairly well penetrated in terms of patients on therapy in the key markets around the world. We still are getting growth, primarily from developing markets, and I think we'll continue to see that. But I would say the kind of growth that we delivered in 2015 is what I would expect for the next couple of years on a constant exchange rate basis.

For REPLAGAL, I think we're more optimistic about the kind of growth that we might see, really for three or four different reasons. One is that the Fabry market growth from an organic perspective does grow mid to high single digit on an annual basis, so there's more opportunity for growth here. I also think that we've seen the switching from REPLAGAL to Fabrazyme really minimized over the course of the year, which I think will help our growth going forward. We also saw stronger second half performance out of REPLAGAL. If you look at it on a constant exchange rate basis, second half versus first half, we were up about 8%, and we also increased the number of diagnosed patients that we identified during 2015. It was up about 25% versus the number of patients we identified in 2014, and I think that's a precursor to good revenue growth going forward.

So, again, for a variety of reasons around Fabry and REPLAGAL, I think we're optimistic that we'll see better growth in 2016.

<Q - Douglas Miehm>: Thank you.

Flemming Ornskov:
So with that, I think we will thank you all for all your great questions, maybe leave you with a few thoughts. 2015 was clearly a record year for Shire. Record top line sales, very, very strong double-digit earnings growth.
You saw the best pipeline we've ever had, 14 products now in Phase 3 or just about to enter into Phase 3. We delivered both on the top line, the bottom line, very strong margin, 43%. We had more acquisitions in M&A and BD activity than ever before. You hardly can remember the full list but maybe repeat it to you. So we started off with NPS. We also had, of course, the Foresight acquisition. We've had Dyax. And we have Baxalta being announced in the beginning of this year and closing this year.
So despite all of that, that some people will call distraction, my team delivered phenomenal results. I think that speaks to the resilience and the ability to focus on customers and patients during this process. We absolutely are equally dedicated in 2016 to focus on our priorities, which is focused on delivering on the product launches we have or will be having, on the integration of Dyax and integration of Baxalta, making sure we have sufficient supply for our high-growth outlook. And I hope that you understand that you don't see that every day.
So on behalf of my colleagues, we're really proud of what we established and did in 2015, but the benchmark will be, I'm sure, higher in 2016, but we will make it as well. Thanks a lot.

Operator:
This now concludes today's webcast. Thank you all very much for attending, and you may now disconnect.