

# FINAL TRANSCRIPT

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## **SHP.L - Q1 2010 Shire Plc Earnings Conference Call**

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## PRESENTATION

**Operator**



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Good day, ladies and gentlemen, and welcome to Shire's 2010 first-quarter results conference call hosted by Clea Rosenfeld. My name is Sam, and I am the event manager today. (Operator Instructions). I would like to inform our participants this conference is being recorded.

And now without further ado, I'll hand it over to Clea. Please go ahead.

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**Clea Rosenfeld** - *Shire plc - IR*

Thank you very much, operator. Good morning and good afternoon, everyone. Thank you for joining us today for Shire's first-quarter 2010 financial results. By now, you should all have received your press release and should be viewing our presentation via our website on shire.com. If for some reason you have not received the press release or are unable to access it through our website, please contact Sue Hale in the UK on 01256 894 160, and they will be happy to assist you.

Our speakers today are Angus Russell and Graham Hetherington. Sylvie Gregoire and Michael Cola are also on line to answer your questions at the end of the presentation.

Before we begin, I would refer you to slide 2 of our presentation and remind you that any statements made during this call which 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.

Today's agenda is as follows -- begin with opening remarks of Shire's performance and business update from Angus, and then Graham will continue with the financial review. Angus will then summarize the key points for the presentation, and then we will open up for your questions. As always, we are requesting that you ask a maximum of two questions per person so that we can give the chance to everybody to ask their questions. And as always, Eric and I will be more than happy to follow up offline for any subsequent queries or clarifications you guys may have.

Thanks for your understanding, and I will pass you now on to our CEO, Angus Russell.

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**Angus Russell** - *Shire plc - CEO*

Thanks, Clea. Hello, everyone. Welcome to the call. Before we get into the slides, I just thought it would be useful to talk a little bit about healthcare reform in the US. There's obviously been a lot of headline news over the last few days. And I'm sure everybody would have an interest in understanding how that may impact Shire.

Graham is going to give you some more details on some of the financial impacts in the shorter term, but I thought I would talk more qualitatively about some of the key areas of the reform and how, as I say, that impacts our business.

I would add at this stage that a lot about Shire's business model over the past few years has been really working towards dealing with these kind of reform issues. Our strategy of focus on specialist and rare diseases was always a model that was built around a company that would obviously be a winner in the 21st century and, as I say, one that could meet these kind of reforms and actually potentially benefit from them as well.

It's for that reason, therefore, that we feel there will be minimal impacts on our business going forward, in contrast to many other players in the industry. And that, as I say, has a lot to do with our focus on specialist and rare diseases, and our very low exposure, therefore, to both federal and state programs in the case of Medicare/Medicaid.

Let me talk a bit about some of the benefits, and basically, obviously, we welcome the extension of universal coverage now and the inclusion of another 32 million Americans. I am sure over the next few years that will enhance and allow us to treat patients who have not been able to be treated in the past.

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Some more specific issues in regard to that are, if you look at our ADHD business particularly, I think the area of insurance coverage and family coverage, which has only ever covered kids and young adults up to the age of 22, family members, that has meant sometimes we have seen people drop off treatment when they've graduated from college, maybe. And until they're employed and they have insurance coverage through their employer, there may be a few years where they feel they can't pay for the cost of these medicines.

Now, as you know, there is an extension of family coverage on insurance up to the age of 26, and hopefully that will bridge that gap and allow these people to continue with their ADHD treatment.

In regards to our specialist and rare disease portfolio, obviously, stating the obvious, with a rare genetic disease, mostly these people are diagnosed from birth, and you know there has been provisions for exclusion of patients from insurance coverage where they've got a preexisting condition. So, obviously, the removal of that now will allow those people insurance coverage from day one.

And as we look forward over their life's treatment, with those kind of more costly treatments, as you know, sometimes there are issues around the caps being imposed on lifetime -- caps on coverage for insurance. And again, those are now specifically removed, and that will presumably allow people to enjoy insurance cover for these treatments for as long as they survive.

In regard to our portfolio being orphan drugs and biological in nature of the products, clearly, again, some major benefits in the reform in regard to biologics. As you know, in other areas of the world, in the EU and in Japan, we have orphan drug exclusivity for 10 years from launch. In the US historically, this has been seven years, and now under this reform there will be a further five years' data exclusivity added to that market exclusivity for seven years, which means in effect we should enjoy in our biological products 12 years' exclusivity from launch in the US market. So that is obviously, again, a very welcome development for us with our particular focus on these rare genetic diseases.

As I said, the areas of Medicaid and Medicare and the prospects of an industry levy, I will leave those to Graham to comment on in a little bit more detail during his financial presentation.

So now let's turn to these results, and slide 5, which has a heading, Replenished Portfolio Drives Excellent First-Quarter Results. And that really is the story. I'll remind you that this was always going to be the toughest quarter of the year. Simply put, it's the comparison to a quarter last year where we still had ADDERALL XR on an exclusive basis. And since then, as you know, there are now two authorized generics in the market, which combined share about just over 60% of the market between them.

But despite that loss of exclusivity in the comparison to this quarter, I am very pleased to say that our revenues were in total flat for the quarter, and just about all of the revenue, therefore, loss from ADDERALL XR has been made up by products and a bit of royalty income as well.

So if we look at the core products sales statistic, and that core products we define to be all the product portfolio excluding ADDERALL XR, we saw tremendous growth again in this quarter, up 36% to \$626 million, on a like-for-like basis almost the same kind of growth, so currency impact has been relatively small. I'm sure Graham is going to make a few more remarks about that later. As you can see, 33% growth on a like-for-like basis.

Our non-GAAP diluted earnings per ADS came in at \$1.01 per ADS, and that is substantially ahead of the consensus, which we believe is about \$0.83 for the quarter.

We are obviously able now to leverage our existing infrastructure. Graham has talked about that in the past. He will be mentioning that again today. But you know we put out some operating margin aspirational targets a year or two ago, and you can see that we are beginning our path along closing the gap towards those improved operating margins. So a lot of operating leverage still to come going forward. And in terms of cash generation, a very strong quarter, up 19% to \$278 million.



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So if we turn the page, and looking at the two business segments, and turning to Specialty Pharma first, on slide 6, VYVANSE had a tremendously strong quarter. We now have a 14% market share in the US, based on the last script data last week. We also launched in our first international market, in Canada, at the end of January, beginning of February, and we have had very good reception in that market, too. So it is the start of the global rollout of VYVANSE for ADHD.

Revenue in the US was up 32% compared to the same quarter last year. And I will remind you that we have a number of new indications we are looking at with VYVANSE that Mike has referred to in past presentations. Clinical trial enrollment is now well underway. And as we said before, we hope to share with you some of the results of those early trials later this year.

INTUNIV, also doing extremely well. You can see on the latest weekly data, again, 1.8% of the US ADHD market. If you look at the subbullet there, it really addresses the fact that we are very much focused on a subgroup of physicians, so where we've put most of our sales effort to date is amongst the child and adolescent psychiatrists. And in that community, we're actually enjoying a 4.3% share in terms of the patients that they address. Most commercial managed care plans are now providing unrestricted access for INTUNIV, and Medicaid reimbursement is very much in line with what we expected.

Another interesting development in terms of how INTUNIV may be use going forward is not only its initial approved indication for aggressive behavior in children, but we're shortly going to be publishing abstracts at the SOBP meeting in May on coadministration data showing it being used in coadministration with stimulants. We believe, as physicians do, that that adds another useful dimension to treating patients with ADHD.

Looking at LIALDA for ulcerative colitis, again, another strong performance. It now has an 18.9% share of the US oral mesalamine market. I'll remind you that we have an ongoing study there. The enrollment is now completed in regard to our Phase III study for diverticulitis, an extended indication for LIALDA. We anticipate to have the data -- it is a two-year study -- we anticipate that data will be available at the beginning of 2012.

Turning to the next slide and looking at product highlights for our Human Genetic Therapies segment, ELAPRASE, again, very strong quarter. We have seen, as Sylvie predicted, an uptick in growth this quarter, with plenty of supply of material now. We have revenue up 22% versus the same quarter last year.

VPRIV, I know always a keen area of attention at the moment in terms of a very dynamic and ever-changing situation with Genzyme. We are now approaching 500 patients treated globally with VPRIV. I just remind you again that it does take a little while to gain reimbursement for these patients. You know in the US, as it says here, we were formally approved, and we launched at the end of February. But it still takes probably a period of several weeks to actually get the insurance coverage up and running and gain reimbursement and payment, so still some patients who are receiving drug free of charge.

That is also true on a global basis. About half the patients here are in RoW markets. And there, whilst we have preapproved access, many of those markets do pay for treatment, but again, some don't. So although there's only \$6 million of sales during the quarter, one would expect that this will gain momentum throughout the year as we get more and more patients reimbursed and covered.

You can see some statistics on this. In the US right now, we have a 13% share of the Gaucher market. 80% of patients on VPRIV have initiated commercial access, started on the IND, but now they have commercial access to the drugs. They have begun the process to get reimbursed.

And of those that we are seeing move through that commercial access program, 25% of them are new patients who are initiating treatment on VPRIV. So everything going extremely well. I am sure maybe some follow-up questions that Sylvie can deal with in terms of supply situation, which remains very good in terms of our ability to supply growing number of patients.

FIRAZYR for hereditary angioedema has now launched in 13 countries, including the five largest European countries. I remind you, this is a mainly hospital-used drug at the moment, and therefore, expecting a slowish rollout, something that is probably



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more historically looking at a drug like FOSRENOL. So it is a slow rollout. We have to get it on the formulary, get it reimbursed. But as you can see, more and more countries coming onstream. We also have the two studies ongoing in terms of self-administration in the EU, and then in the US a second registration study, which is enrolling.

REPLAGAL, revenue up 69%. Again, an outstanding performance versus Q1 last year for a drug that has been several years in the market now. And with that, we have achieved a very clear lead, in our minds, in the EU, where we estimate to have a 60% market share.

Turning to the next page, slide 8, you can see a bit more detail on where that growth is coming from with REPLAGAL. So in this quarter, you can see almost exactly the same performance as you saw in Q4 last year. That is 190 additional patients being added to REPLAGAL. And something around just over a quarter of that is new business, but almost three-quarters has, again, come from product switching from Fabrazyme.

So we are seeing the kind of performance that we saw in the fourth quarter, I think in reaction to further announcements of further ongoing shortages from Genzyme. We are seeing a lot more patients switching, again, into REPLAGAL.

So turning to the next page and my final slide in this introductory section of the presentation, just wanted to highlight some of the key upcoming events for the rest of this year and particularly the second half. As I said, it's a lot about pipeline data on early studies. On VYVANSE, I already said that we should see the results of some Phase II studies in regard to new indications, non-ADHD indications.

There is the CARRIERWAVE programs, specifically in looking at INTUNIV with CARRIERWAVE. We also have a pain project, remember, ON CARRIERWAVE. So we hope to have data available on some of the early work on that to talk about later this year, and Mike will be taking you through both those first two items. And he'll also be looking at SPD 535, which, as we said before, is an analog of anagrelide. [That's XAGRELIN] or XAGRID as you know it at the moment. This is an analog of that product where we're doing, again, some proof-of-concept work, and we should have data later this year to share with you.

We anticipate getting EU full approval for VPRIV, which will allow us to move forward, as we are in the US right now, with full reimbursement and a formal launch in all the EU. And in REPLAGAL, I remind you, we have a BLA, a Biologics License Application, under a rolling submission at the moment. And basically, we hope to hear something back from the FDA, again, later this year.

We also initiated manufacturing in our new large-scale facility at Lexington, on our major site in Lexington in Massachusetts. So work has begun there, and obviously there's a longish period of commissioning until we get commercial drug, but we are effectively now producing product.

So with those opening remarks, let me pass over to Graham, who is going to take you through the financials in some more detail.

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**Graham Hetherington** - *Shire plc - CFO*

Thank you, Angus, and good morning. Good afternoon. Today, I will be covering firstly the drivers of our strong EPS performance in the first quarter; secondly, the growth dynamics of our core product portfolio; and thirdly, how ADDERALL XR generated income very much at the top end of our expectations in the quarter; and pulling these three strands together, how these dynamics and our accelerated investment in the future growth of the business are likely to play out during 2010.

I will also be summarizing the limited financial impact of the US healthcare reform, which Angus identified, on our business, which is incorporated in both the first-quarter results and our outlook and our guidance.

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So turning to the first quarter, on chart 11, in this quarter it was inevitable that EPS and EBITDA would be down versus 2009 as we are comparing against a quarter that had the maximum ADDERALL XR margin contribution and low levels of operating expense.

Despite this, it's an outstanding result, but the total revenues were broadly in line with last year. EBITDA was down just \$60 million, and an EPS delivered of just over \$1. But I think most significantly, we delivered an increase in cash generation of 19% compared to the first quarter last year.

The next chart breaks out our revenue in more detail. Our core product portfolios continued to deliver the same rate of growth we saw out of last year, up 36% in the quarter. This performance underlines the strength and momentum of the business. And as you can see, the impact of foreign exchange on our revenues continued to be marginally positive this quarter.

ADDERALL XR has generated product sales at the top end of expectations in the quarter, driven by a number of factors -- the ADHD market, where prescription volumes grew by 10% year on year in the first quarter. This was helped by the branded ADDERALL XR's market share in the US, which has held up well. In the quarter, we have also included the impact of the healthcare reform provisions on ADDERALL XR, which include the movement of the base Medicaid rebate from 15.1% to 23%, and significantly, the cap on the rebates to the average manufacturers' price.

The already-high levels of rebates we are paying, factoring in both federal and state elements, overshadow the 8% increase in the base rebate, headline base rebate, which you have all been hearing about. Keep in mind that the best Medicaid rebate -- base Medicaid rebate is the higher of 23.1% or the best commercial discount. And for ADDERALL XR, our base commercial discount is well above 23%.

We did benefit from a one-off change in estimates in the quarter. And as a result, gross discounts were at the bottom end of our expectations of 60% to 70%. And I will give you an update on the forward-looking dynamics for ADDERALL XR later in the presentation.

Total royalties were also at the top end of our expectations. Our royalty stream from Impax's sales of authorized generic XR generated a very strong \$41 million in revenues. This was driven by Impax's authorized generic market share growth, lower levels of discounting than we expected -- than we saw in the fourth quarter, and further increases in Impax's wholesale and retail channel stocking. Again, I will touch on the dynamics for the balance of 2010 later.

In addition, in terms of royalties, we didn't see the year-on-year erosion of other royalties in the first quarter that we are expecting to see for the full year.

On the next chart, 13, you can see how the loss of sales from ADDERALL XR is almost fully being replenished by other sources. This has been primarily driven by significant growth in product sales across our core product portfolio, generating over \$160 million of additional product sales year on year.

Let's look at that in more detail on chart 14. This chart reinforces my second main point, the strength of our core product portfolio. We delivered growth of 36%. Importantly, this growth has been broadly driven from our young products like VYVANSE, ELAPRASE and LIALDA; the step-up in revenues from REPLAGAL; the contributions from more recent product launches, including INTUNIV and VPRIV; as well as continued growth from the more mature elements of the portfolio.

I'd just like to pause on a couple of specifics. The first one is INTUNIV. As you'll recall, at the end of the fourth quarter, we didn't recognize early launch shipments of INTUNIV. And in the first quarter, we were able to release some of -- we were able to recognize some of those launch shipment supported by demand. And in net terms, that contributed to our net revenues by \$16 million in the quarter. That leaves a further \$15 million of net shipment -- launch shipments to be recognized in the second quarter.

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The second point is, as I've already mentioned, these first-quarter revenues take account of the US healthcare reform. And you can see that the impact has been very limited. We have seen a step-up in sales deductions compared to the fourth quarter for VYVANSE and also for LIALDA, which was in part influenced by the increase in Medicaid rebate rates. However, for the quarter, the total impact of healthcare reform on this portfolio of products was less than \$10 million.

Chart 15 further demonstrates how the strength and diversity of the core portfolio has evolved over the last two years. The compound growth over this period I think speaks for itself. And we expect our core portfolio will continue to grow and be supported by further product launches going forward.

Turning now to the next chart, 16, our actual dollar spend on R&D and SG&A increased by 9% and 14%, respectively, compared to the first quarter of 2009. The increase in headline ratios was driven by two factors -- first, the decline of ADDERALL's sales year on year, and secondly, the relatively low levels of spend on R&D and SG&A we incurred in the first quarter last year.

However, these headline ratios masked the underlying operational leverage we were already achieving. And if you look at the same ratios at the bottom of the chart in relation to our core product sales, you can see a 5 percentage point reduction on R&D and a 10% point improvement on SG&A.

Our confidence in Shire's outlook has increased, and we have decided this year to accelerate further the investment we're making behind the future growth of the business. And as a result, you will see increases in the quarterly run rates of R&D and SG&A over the course of 2010.

To give you some ideas, we are making -- idea of what we are doing, we are making key investments to further progress our pipeline, including VYVANSE in Europe, LIALDA for diverticulitis, and also selectively advancing candidates to exploit the potential for CARRIERWAVE technology.

We have been investing more to support the growth of our young product portfolio, specifically INTUNIV and VPRIV. And we'll also be making investments in infrastructure supporting our fast-growing international business. This includes the development of our South American hub in Brazil and a Swiss-based mainland European hub. Even with this investment, we will continue to generate significant operational leverage from the growth of our core portfolio.

Before I move on to looking at the income statement dynamics for the balance of 2010, let's look at our cash generation on chart 17. We generated \$278 million of cash from operations in the quarter, an increase of 19%. This resulted in a net cash inflow of \$152 million in the quarter.

This is particularly strong, both reflecting our operational performance, but we also benefited from the phasing of capital expenditure. We expect capital expenditure for the year to be about \$230 million, and this will complete the investments of our state-of-the-art manufacturing capacity in Lexington to support current and future therapeutic protein products.

As you can see, our net debt is now less than \$0.5 billion, comprising our \$1.1 billion convertible and \$0.7 billion of cash. Our \$1.2 billion facility remains unutilized, and no refinancing is due until 2012. We continue to have a strong and flexible funding position to manage future refinancing and to support investment to further enhance the quality of our business and pipeline.

On the next chart, 18, you can see on the left-hand side the potential for ADDERALL XR to continue to generate ongoing revenues from both product sales and royalties. I have updated the top end of the range of potential outcomes for ADDERALL XR to reflect the strong revenue generation achieved in the first quarter. And I have overlaid this range on the range of current market expectations.

That said, the variables that will influence the actual outcome in 2010 and beyond remain broadly the same as before. The key macro assumption remains that there will only be two authorized generics in the market through 2010, and increasingly likely beyond that.



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In terms of the detailed dynamics, on the right-hand side of the chart, there has been little change despite the strong result in the fourth quarter -- in the first quarter. There is more backup supporting this analysis in the Appendix 27 and Appendix 28.

Running through the dynamics here on chart 18, though, we have seen limited further erosion of the branded ADDERALL XR's market share in the first quarter. We are assuming some further erosion during the balance of 2010. As result, we also expect to see reductions of pipeline inventory for branded XR in the balance of the year.

As I've said earlier, sales deductions in the first quarter of 61% were at the lower end of our expectations. For the balance of the year, I expect to see gross to net deduction levels nearer to 70%. This includes any increase in rebates as a result of healthcare reform.

Turning now to the royalty stream relating to ADDERALL XR, royalties from Impax were again very strong in the first quarter. There are a number of dynamics over which we don't have control, but as we move forward, we expect to see Impax's pipeline inventory stabilizing and higher gross-to-net deductions on Impax's gross sales. Both of these factors contribute to our view that the likely future quarterly run rate will reduce to something close to half the level of the last two quarters.

Finally, let's look at the dynamics of the total business on chart 19. Our performance in the first quarter has increased our confidence in the outlook for revenues and for earnings for 2010. This reinforces the prospects for growth in reported EPS in 2010 compared to 2009. And we are comfortable with small increases to EPS estimates for the year, which would result in a small increase in our published EPS per ADS consensus of \$3.65. And this is even with the impact of US healthcare reform. As I said earlier, the impact of this reform is relatively limited for Shire.

What I would like to do -- I'm just going to pause for a short while and just drill into this. There are a number of factors that educate why we have a limited exposure. The impact on any company will be dependent on a number of variables, and these include the types of products it sells, the proportion of sales made through US government channels, and its contracting strategy, along with the level of federal and, significantly, state rebates which it's already paying on its products.

Specifically for Shire, sales through Medicaid, managed Medicaid, and Medicare represent only around 15% of our US specialties business, excluding ADDERALL XR, which I have already covered. For HGT, the impact is very low, as only 13% of its sales are from the US market, of which only a fraction are made through government programs.

So drilling into the core specialty business, the impact on our core portfolio is also limited, because our ADHD portfolio is already rebating above the 23.1% level, and the rest of the portfolio has very limited sales through Medicaid. Overall, the impact on the core portfolio was less than \$10 million in the first quarter and is likely to be between \$25 million and \$30 million in the full year of 2010.

In terms of the industry levy, which applies from 2011, and this applies on prescriptions through government channels, it's still very early days. But just to give you some idea of quantum, we are talking about a few tens of millions of dollars in 2011, to give you some order of magnitude.

Turning to foreign exchange, we've benefited to a small extent on the revenue line, which has been offset by negative movements on costs. The ready reckoner at the bottom of the slide captures at a high level our exposure to the euro- and sterling-dollar rates. That said, it is worth repeating that we are still a dollar-reporting company, generating nearly 70% of our revenues in dollars. So the sensitivity to earnings is limited. And I will continue to update you throughout the year.

We're going to continue to see significant growth from our core product portfolio, which will drive growth in total revenues. Total royalties will benefit from the continued royalty from Impax in relation to ADDERALL XR. As I said earlier, the level of this royalty will be lower than we have experienced to date. We will also see ongoing declines of other royalties, specifically 3TC in the US.



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In the first quarter, favorable mix of some one-time items pushed gross margins marginally up to 87%. I still expect our full-year gross margins in 2010 to be in line with the end of 2009 at approximately 86%.

While we've seen the first-quarter spend on both R&D and SG&A fall compared to the fourth quarter of 2009, I expect the aggregate spend to increase year on year, reflecting the accelerated investment we are making in our growing business. On the fourth-quarter call, I said I could see R&D and SG&A dollars together increasing by between 5% and 10% year on year. I expect the dollar increase, taken together, to be at the top end of this range this year.

Finally, our tax rate, which I still expect to be broadly in line with the level in 2009 of 25%. So a great start to the year, which has really increased our confidence in our outlook and which includes the minimal impact the US healthcare reform has on Shire's products. The momentum of the business will drive growth in total revenue and earnings growth this year and beyond.

Angus?

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**Angus Russell - Shire plc - CEO**

Thanks very much, Graham. So turning to the last slide in the deck on page 21, and it says A Solid Foundation for Future Growth, and I believe we have a tremendous platform now for realizing our growth ambitions going forward.

I have never seen the business in better shape, and I think these are truly excellent results in the first quarter, with our core product sales portfolio up strongly at 36%, very strong cash generation also, up 19%, and operating margins already improving, with still a lot of operational leverage to be had.

I think these results also demonstrate that we've successfully replenished our portfolio just barely one year on from the loss of exclusivity of ADDERALL XR. And we are now driving growth in this Company from a very balanced portfolio in which eight key products are global, they have very strong exclusivity and are at very early stage of their launch and product life.

INTUNIV, as I said, approaching something like a 2% market share in the US, with a lot of potentializing to continue to grow, and a new study, as I said, coming up in May.

VPRIV launch is off to a great start. We now have, as I said, the formal approval this last quarter in the US. And we're looking forward to gaining approval in the EU in the second half of the year.

REPLAGAL, that sustained performance in the first quarter in line with the fourth quarter, and we expect with continued shortages of Fabrazyme to see more patients switching into REPLAGAL as we go forward.

As Graham said, we are taking the opportunity to continue to develop and invest in our strong product pipeline and the product portfolio. And as you saw from one of my earlier charts, we should have a lot of pipeline results and data to share with you later in the second half of this year.

And at the same time, we are increasing our global reach. We have direct business presence now in 28 countries, and I think probably add at least a couple more markets this year. So I expect that to be 30 or more markets by the end of the year.

As Graham and I have touched on, there is very minimal effect in the short term from any downside from healthcare reform in the US. As I've said before, we have been for many years planning to build a company that is fit to survive these kind of reforms and can meet the new challenges of healthcare delivery in the 21st century.

So with all of that, as we said, we expect and are comfortable, Graham and I, in seeing forecasts of earnings for the current year, in 2010, move up a little bit from the previous consensus. We do expect to see that. And overall, we think we are rapidly beginning



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to close the gap on our aspirational target of growing both our top and bottom line in the midteens range on average between the end of last year, 2009, and 2015.

So with that, let me pass back to Simon, the operator, and have him coordinate the Q&A session, and just remind you we will have Mike and Sylvie available as well with us now to answer your questions. Simon?

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## QUESTIONS AND ANSWERS

### Operator

(Operator Instructions). Jack Scannell.

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### Jack Scannell - Sanford Bernstein - Analyst

Just one question. If Genzyme continues only supplying 50% of the Gaucher market and only 30% of the Fabry market, what degree of the shortfall can you fill with your current manufacturing capacity? And how long would it take you to fill the entire shortfall if Genzyme's manufacturing rates remained what they are today?

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### Angus Russell - Shire plc - CEO

Okay, Jack, well, I knew we'd get -- thank you very much. I knew we would have a manufacturing or supply question, so I am going to ask Sylvie to obviously give you some more information on that particular question. Sylvie?

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### Sylvie Gregoire - Shire plc - President, Human Genetic Therapies

Yes, Jack, regarding (technical difficulty). Regarding VPRIV, we can supply for several hundred more patients relative to what we have today with the current manufacturing plans and inventory that we have today. We can treat the whole market once we have the large facility, if you will, approved here in Lexington, Massachusetts, which, as Angus mentioned, is starting manufacturing really proper in July of this year. We are doing some test runs at this stage.

So that is the forecast for VPRIV. We can supply many hundreds more than we have today, and then even more once we add this facility.

As for REPLAGAL, we have no -- we don't see any limited supply that would prevent us from gaining market share as the demand grows due to the supply shortages of Fabrazyme over time. Again, to supply the whole market as well, the large facility would be of benefit and necessary in order to supply the entire Fabry market, but that would come online. These are products that would go first, of course, very first in our facility, in our large facility.

I hope that is helpful.

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### Angus Russell - Shire plc - CEO

Yes, and Sylvie, it's probably worth just mentioning, the large facility, as we've said, it has begun, but it's commissioning work at the moment. And I think target is probably end of 2011 kind of timeframe, [2000], to have a lot of material available off that plant.

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**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

That's right. On the standard approval base for the FDA, that would be the timeframe.

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**Operator**

David Evans.

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**David Evans** - *JPMorgan - Analyst*

Just a question about really one of your minor products, EQUASYM. I was just wondering what happened with that in Europe over the quarter. And then also, on FIRAZYR, just wondering when we might expect to see an uptick in sales, really, if you could give any guidance on where you expect to be by the end of 2010, for instance. Thanks very much.

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**Angus Russell** - *Shire plc - CEO*

Okay, thanks, David. So first one, I will ask Mike -- I will just remind you that EQUASYM is not really a core strategic product going forward. It was very much a bridge to enable us to get into the European ADHD market and start having a product which covered our ability to build infrastructure ready for VYVANSE and hopefully INTUNIV in the longer term.

But with that, Mike, why don't you give a bit more detail about the quarter on EQUASYM?

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**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

Yes, I think EQUASYM continues to roll out. We are quite pleased with the performance overall. We have obviously got our footprint in place based on EQUASYM. We have worked out some supply chain issues, and it continues to move along.

As Angus said, this was more for a learning experience for us, a first-to-market event. And it is serving the purpose that we had hoped it would.

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**Angus Russell** - *Shire plc - CEO*

And Sylvie, if you would like to pick up FIRAZYR in terms of what we expect in terms of the studies, maybe reiterate -- I touched on them briefly, but what are our longer-term kind of ambitions with FIRAZYR.

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**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

Yes, I think you asked what we expected in 2010. We don't really give product-specific guidance, as you know. The product, though, is approved now in many countries, and there's growing reimbursement available in these countries. So we are seeing a nice acceptance from the market of this product, and market research continues to show that patients and physicians are satisfied.

But importantly, we are going to have the self-administration study results later this year, which will allow us to amend the labeling in the EU and have the product formally approved for self-administration, which I think will be an important step for the patients as well in that territory.

And as you know, in the US, we're going to be completing the complete response submission probably early next year so that we can gain approval in that territory as well, which will be an important contributor to the overall FIRAZYR market.

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**Operator**

Martin Wales.

**Martin Wales - UBS - Analyst**

Just to help me understand, could you explain precisely what happened with the ADDERALL XR inventory, your revenue recognition that you talk about in the press release?

**Graham Hetherington - Shire plc - CFO**

ADDERALL -- sorry, Martin -- are you asking about ADDERALL XR or INTUNIV?

**Martin Wales - UBS - Analyst**

I'm talking about -- asking about ADDERALL XR. You made reference to -- I am trying to find the precise (multiple speakers) in your press release (multiple speakers).

**Graham Hetherington - Shire plc - CFO**

Okay, let me try and be really quite specific. We have to make accruals on Medicaid and other rebates based on estimates of product in the pipeline. That is a recurring estimate that we have to make quarter after quarter. It has to be based on assumptions, and we are only able to test whether those assumptions are like -- are correct after the date.

In the case of ADDERALL XR, we discovered that our estimates on the pipeline weren't correct. It meant that we had been accruing for a larger pipeline than was actually out there. And therefore, there was a one-time correction reducing the rebate provision, reflecting that lower pipeline estimate.

And that, linking back to what I was saying in the presentation, is what I was referring to when I said that there was a one-time benefit in the quarter, which actually benefited us by 8 percentage points on the gross-to-net deductions, which moved our underlying gross-net deductions on ADDERALL XR of 69% down to the reported 61%.

And it is on the basis of that, removing that one-off true-up, that I am guiding to closer to the 70% for the final three quarters of the year.

I hope that makes it clearer.

**Martin Wales - UBS - Analyst**

Yes, thank you. I just have one quick question in relation to REPLAGAL. Obviously, the European Medicines Agency, they seem to be suggesting that patients who aren't responding well to a 30% dosing of Fabrazyme effectively get switched to REPLAGAL about a week ago. Firstly, is that interpretation correct? And secondly, any early comments on any impact that is having, or is it just too early?



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**Angus Russell** - *Shire plc - CEO*

Sure. I will ask Sylvie. You're right in that there was an EMEA guidance came out on that, which is very interesting, given there has been a lot of controversy, I would say, out there about the relative dosing of Fabrazyme and REPLAGAL. So, Sylvie, what do you say?

**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

Yes, so the EMEA all along during the shortage has been updating their guidance for use of Fabrazyme, and in this last one indicated what you have just stated, like you, that some patients who have switched to the lower dose of Fabrazyme are not doing as well as they could.

What we have seen, however, and you can refer to the chart that Angus showed a little bit earlier, there's clearly been along quite a bit of switching from Fabrazyme to REPLAGAL in the fourth quarter last year and the first quarter this year. So we anticipate that this will continue to occur in the next quarters, as long as there is a shortage of Fabrazyme in these markets where the drug is in low supply.

**Operator**

Ken Cacciatore.

**Ken Cacciatore** - *Cowen and Company - Analyst*

A question on INTUNIV first. Graham, if you can just clarify, or Mike, the inventory versus the actual prescription demand number, just so we make sure we have our prescription price correct? And maybe also just update again on the timing of the CARRIERWAVE, how quickly we could enroll, if this formulation is correct, how quickly you could roll into clinical studies, and timing of that potential filing as well?

**Angus Russell** - *Shire plc - CEO*

So, Mike, then, if you can answer those, and Graham can chip in on the first one, if you don't have the figures to hand. But Mike, why don't you answer both of those? We will get Graham maybe to do this one on the split, on the inventory uptake versus true demand.

**Graham Hetherington** - *Shire plc - CFO*

Yes, let me just address that. In the Q1 numbers, and on the call there, I was talking to the fact that we had recognized \$16 million worth of revenues in the first quarter in relation to launch shipments. That was at the net level. Ken, I think what you're looking for is that at the gross level to help you get to pricing, which is \$20 million in the first quarter.

And then at the end of the first quarter, we are left at a net level with \$15 million, which is in all likelihood going to be recognized in the second quarter. At the gross level, that is \$19 million still to go.

**Angus Russell** - *Shire plc - CEO*

Okay. And then, Mike, you want to say something about CARRIERWAVE? Anything more you can say for now? I said we expect to share more information later this year, but --

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**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

Sure. It's Mike. As I have said in the past, we continue to work on a CARRIERWAVE guanfacine, which we believe will have new molecular entity status. We have had some success. We have the first molecule in the clinic. We have two backup molecules along the way. As I said, we hope to make a decision sometime after the midpoint of the year as to which molecule goes forward.

I would also say that this could be a very good product for Europe. We are focused on retaining our revenue in the US, obviously, but if you look at the attributes of this product, it plays very well in the European markets.

**Operator**

David Steinberg.

**David Steinberg** - *Deutsche Bank - Analyst*

I know a couple weeks ago, the FDA had an advisory committee on bioequivalents for extended-release, controlled-release drugs. And the FDA hasn't issue any statement on it, but based on the conclusions of the panel, I'm wondering what you thought about the implications for your citizens' petition. Do you have any change in your view on how long that may be in place based on this panel?

**Angus Russell** - *Shire plc - CEO*

David, a very interesting, perceptive question. So I think Graham said in his remarks that one of the key assumptions on ADDERALL XR in the tail is that the CP continues. And he said we believe that this year, and then he said, and it may be some years to come. And I think that was the pointer towards what has been, as you say, a very interesting series of developments over just the last week or two in regard to the FDA, where they were specifically looking at Ambien and Concerta.

But I will ask Mike to perhaps summarize a little bit more of the detail, how that might read over into our own citizens' petition. But you can gather, our confidence is being raised based on that very recent advisory panel. Mike?

**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

We would agree with what has been written out there, that in fact this really does support our core arguments in the CP. And again, it is a read-over from what was discussed around Concerta.

I think the most optimistic part of the discussion for us is the potential use of partial area under the curve as a measure for bioequivalence. We think that is a very high standard, and it is a standard that really supports and validates the citizens' petition that we have in place.

**David Steinberg** - *Deutsche Bank - Analyst*

So is it safe to say, then, that presumably, these companies would have to do two studies, and with all the timelines involved and filing, etc., and an FDA decision, that you're looking at two to three years down the road? Is that about right?

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**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

I think that is a good assumption, provided you can actually have a positive outcome on those studies. Again, the guidelines have not been written. We are actually gleaning this information from first-hand accounts of the meeting, including the folks from Shire that were there.

But if in fact they move towards a partial AUC for critically dosed drugs, obviously, not for all drugs, we think that is a very hard standard to meet, a very hard standard to meet. And whether you do those trials or not, I think if you do them, you could have a lot of problems having a successful outcome. It's not impossible, but I think it decreases the odds greatly.

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**Operator**

Martin Wales.

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**Martin Wales** - *UBS - Analyst*

Well, actually, your previous questioner just asked that question. But maybe I could ask another one, then, just coming back to where we started. Could you just take me through manufacturing of the Human Genetic Therapies, where we are today, where we are going to be by the end of this year, precisely where we will be by the end of 2011 in terms of your ability to supply demand at Genzyme? They keep finding problems with this manufacturing.

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**Angus Russell** - *Shire plc - CEO*

I can ask Sylvie to go through it again. I think we kind of covered it, but if you want to just highlight it again, Sylvie, just in terms of --

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**Martin Wales** - *UBS - Analyst*

(multiple speakers), just to make life easy.

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**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

I understand the interest in manufacturing, Martin, and making sure that we have enough supply to meet the demand that we have seen. We have seen a lot of patients come on to VPRIV and on to REPLAGAL. So remember that we are currently manufacturing in our Alewife facility in Cambridge. And so we have inventory for both these products and have had a planned manufacturing schedule that can always be, by the way, amended slightly upward by making certain shifts if we saw the demand even greater than what I have just talked about a little earlier.

The large facility will start manufacturing midyear this year, in July, formally the products on the purification side, as well as the cell culture side of that facility will be making product and submitting the batches that are made from these first batches to the agencies. And then the plant gets inspected by the agency, and generally that takes about 18 months. So that's where we end up at the end of 2011 or the beginning of 2012 and approval of the facility per se.

I hope that clarifies.

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**Martin Wales** - UBS - Analyst

Okay. And I think you've paid attention to the newspaper article recently suggesting that patients were losing their patience, if you excuse the phrasing, with Genzyme's inability to supply them with drug. Are you seeing much evidence of that yet in terms of your patient numbers in just the last month or so?

**Sylvie Gregoire** - Shire plc - President, Human Genetic Therapies

So in the US, that is to me represented in how well the launch is going on the onboarding of patients, and as well as the onboarding of patients overall around the world through our early access programs. And so, indeed, we continue to see patients coming on to VPRIV all around the world. And, yes, when sometimes Genzyme makes an announcement, we see a slightly uptick in the telephone calls relative to our products.

However, for REPLAGAL, again, in Europe, it is the same. We can measure patient demand or unmet medical need, if you will, by looking at the switch of patients, as well as, remember, in Europe, we tend to get all the new Fabry patients come on to REPLAGAL because of the supply shortage. And so we have seen, again, the softer numbers there that Angus presented a little earlier on. So I think those are the manifestations that we see with that frustration.

**Martin Wales** - UBS - Analyst

And with them having so little inventory of either drug --

**Clea Rosenfeld** - Shire plc - IR

Martin, we can take that offline. I think there's a lot of people -- I see the e-mails -- a lot of people waiting online, so if that is okay with you. You have had (multiple speakers) questions.

**Martin Wales** - UBS - Analyst

No problem, Clea. I'll be quiet. Cheers.

**Operator**

Tom Russo.

**Tom Russo** - Robert W. Baird - Analyst

First question, on operating margin, can you comment on whether operating margin expansion applies to total revenues in addition to relative to core product revenues in 2010? That is my first question.

**Angus Russell** - Shire plc - CEO

I will ask Graham to answer. It is a strange question. You are saying operating margins applies to revenues?

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**Tom Russo** - Robert W. Baird - Analyst

No, I think the specific comments was that operating margin expansion would be seen relative to core products. And I was wondering, is that true also relative to total Company revenues, operating (multiple speakers)

**Angus Russell** - Shire plc - CEO

You are more or less asking, is the operating margin leverage at the total business level including --

**Graham Hetherington** - Shire plc - CFO

Tom, directionally, I think in this transition year, on total revenues -- on total product revenues, they are broadly going to be in line. But we are going to see expansion on the core products. And as we move into 2011, it will be both on core and total.

**Tom Russo** - Robert W. Baird - Analyst

Okay. And then secondly, I know it's a smaller opportunity, but just to touch base on REPLAGAL for the US, do you expect at this point that FDA would take its full six months after you complete the BLA submission, or is there potential they could act more quickly since they have seen a lot of the data?

**Angus Russell** - Shire plc - CEO

As you say, it is a small opportunity, but one we are welcome to address, so, Sylvie?

**Sylvie Gregoire** - Shire plc - President, Human Genetic Therapies

As you know, it's very hard to speculate on what the FDA will or will not do. So at this stage, as you know, we are going to submit -- our next step is to submit the results of a pharmacokinetic study. That will complete the rolling BLA. And then we will be informed by the FDA what timing they view the PDUFA date to be established at. So we will keep you in the loop as we know more.

**Operator**

Brian White.

**Brian White** - Shore Capital - Analyst

Just two very brief questions. Wondered if you could update us on the timelines for taking VYVANSE to Europe, what has to be done there from a regulatory perspective. And just I note your interest in some additional investment in South America. Have you thought more broadly about emerging markets?

**Angus Russell** - Shire plc - CEO

Yes, sure. I am just back from a trip down under to Australia for a week, Brian, which was fascinating. We have 20 people in an office down there, and four or five products with the portfolio on the market, with a couple more probably to come in the next 12 months. So just as an add-on, that is also a growing and importantly growing region for us.

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But, Mike, in terms of timelines on VYVANSE in Europe, and then maybe that spills over into Latin America and also what is happening in the registering of the product there.

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**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

Yes, as far as Latin America, we are taking a good, hard look at Mexico and Brazil. We have talked about both of those countries launching VYVANSE. We are mostly on track for that for the beginning of the year, although there's regulatory issues in Mexico right now with the regulatory agencies themselves basically being shut down. And we are not quite sure when they are going to be up and revealing dossiers again.

In Europe, VYVANSE continues to be on track. We have had a little bit of a delay from our original timelines. We are looking at 2012, probably second half now, based on enrollment and number of patients per site. But I think we are largely on track for a launch there. The program has been underway for awhile. We feel like we know what we are doing there, and we look to have a great product launch sometime in that 2012, 2013 timeframe.

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**Operator**

David Amsellem.

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**David Amsellem** - *Piper Jaffray - Analyst*

This is more of a business development question for Mike. You have talked about ways to better leverage your psychiatry and GI sales organizations. So to that end, I wanted to get a sense of how aggressively you're looking to add additional products to these businesses. And are you looking at commercial-stage products or products in late-stage clinical development, or both?

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**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

I will let Angus lead off, and then I will follow on.

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**Angus Russell** - *Shire plc - CEO*

The business development, just to pick it up generally, we never stop looking. We always try and make this point that what seems sometimes as an event to the outside world, given the only periodic deal announcements, to us is a continuous process and a key part of our business model, given that we have limited amount of in-house early-stage development or research activity. So we look across all the areas and all the therapeutic areas we currently have a presence in.

Mike will probably add to my comments, but generally, whilst we are always interested in the kind of CNS and all the related diseases of CNS, many of these have large primary care dimensions. I think you can see from some of the issues confronting the industry in some of those spaces right now, they are not always attractive areas to be in. They are potentially big areas, but in today's world, they are well supplied, and we have looked at them nonstop, really, for the past certainly more than 10 years that I have been with the Company. And we never stop looking at broad CNS indications.

So we are very interested always in specialist and niche areas. And probably with those kind of broader comments, let me hand over to Mike and see if you'd like to add any further remarks.

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**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

I would just reiterate that we have been very active over the last two years. I know you haven't seen a lot of deals consummated, but I think our deal flow has been good. We have done a lot of due diligence. And as Angus and Graham have said in the past, I think we have been extremely selective over the last two years. We don't feel the absolute need to get a deal done.

I would also say that besides expanding the portfolio and the number of products in the bag, we believe that the indication areas for VYVANSE, the additional lifecycle programs we are working on, will give us a lot more leverage with VYVANSE over the next five to seven years. If you think of MDD and some of the additional indications that we are working on, I think we get some leverage out of that salesforce, even with the current portfolio.

We are active out there. I don't know what else we could be doing. I think we know every product that has either gone to a company or has been looked at, and we just have not -- we have not consummated a deal. We haven't found anything particularly exciting that we are willing to stretch for.

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**David Amsellem** - *Piper Jaffray - Analyst*

And then one quick question on LIALDA. You have talked about the diverticulitis program. I guess the question here is, how would you quantify the opportunity in terms of patient numbers or expectations for penetration? And then I guess the second part of that is, what is the extent to which LIALDA and the 5-ASAs are already used off-label for diverticulitis?

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**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

Well, I don't think they are used very much for diverticulitis off-label today. If you search the literature, there are obviously some cases, which is one of the bases for this program, but I don't think there is a lot of off-label use.

I think the potential for a diverticulitis claim is much, much larger than our current UC indication. We have a fairly conservative set of estimates that takes you down to a patient population that I think makes it a much, much larger opportunity than ulcerative colitis.

Obviously, we have high hopes for this one, investing in it quite readily. It is, in GI, our single largest investment. And we look to see that pay off in the 2012 timeframe.

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**Angus Russell** - *Shire plc - CEO*

I think just to add to that, there have been one or two good notes come out in the market in the past from various sell-side brokers. So I am sure if you contact Clea or Eric, they would be happy to either direct you to those reports or supply you with a copy, if we still have them on file.

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**Operator**

Jack Scannell.

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**Jack Scannell** - *Sanford Bernstein - Analyst*

Thanks very much for taking a second one. Again, just to clarify, on the EMEA guidance, is the EMEA guidance simply going to follow what is happening in clinical practice, or do you think it's going to change clinical practice?



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**Angus Russell** - *Shire plc - CEO*

You're talking in regard to REPLAGAL (multiple speakers)?

**Jack Scannell** - *Sanford Bernstein - Analyst*

Yes.

**Angus Russell** - *Shire plc - CEO*

Okay. Sylvie?

**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

I think the EMEA has provided guidance to physicians relative to what they should be doing when facing a shortage of a product. So they respond to, basically, physician observations and the demand of physicians to see how they should be acting in the face of the shortage.

So I think the effect will be -- the decision is still in the hand of the physician of, obviously, of what to do. But it does provide some information and guidance to the physician as to what to do in the event that Fabrazyme does not work. And as you saw, they suggest that switching to REPLAGAL is certainly an option at this stage.

**Clea Rosenfeld** - *Shire plc - IR*

Operator, is it possible to actually make sure that we get questions from people that have not been on the call yet? That would be really helpful. We are short in time. So we're going to take a few last questions. But it would be helpful to ask them to those people waiting.

**Operator**

Okay. I will try to do that.

Jon Stephenson.

**Jon Stephenson** - *Summer Street Partners - Analyst*

Thanks for taking my question. I just wanted to get a little bit more clarity in terms of the update on enrollment for FIRAZYR. You alluded to a potential first-half-of-next-year filing and refile in the US. I just wanted to get a little more clarity.

And then as an adjunct, I was wondering whether or not you'd be able to utilize the self-administration European data when you resubmit the US application.

And then just a last question on that regarding the trial in the US. Because there's three products available now, have you seen any difference in the distribution of patients -- attach frequency of the patients being enrolled relative to what you would have liked?



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**Angus Russell** - *Shire plc - CEO*

Sylvie?

**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

Yes, FIRAZYR, FAST -- the FAST-3 trial in the US, as Angus mentioned, is enrolling. What we see in the trial, which was we revised, as you saw, our complete response date to early next year rather than the end of this year, is due not necessarily to enrollment, but there is a certain conversion rate that was observed in FAST-1 and -2. Remember, these patients are enrolled, and then we wait for them to have an attack in order to really participate in the trial.

So the average sort of rate was three to one in the FAST-1 and -2 trials. It's more like five to one. So we're onboarding patients, and they're not getting the attacks as fast as they were for the other two trials. And it may or may not be due to the availability of other products in the US. But remember, this product -- this trial is conducted worldwide, so there are plenty of other countries where the issue of having other products on the market is not part of that response.

But we do expect to be able to finish the enrollment in the study, do the analysis and be able to submit the complete response early next year. And with that, indeed, we will submit the self-administration data that is for this trial that is ongoing. And that will be part of the submission.

**Operator**

Karl Bradshaw.

**Karl Bradshaw** - *Morgan Stanley - Analyst*

Two quick questions. The first one is for Mike. Apologies if I missed this, but could you maybe give us any details on how INTUNIV is actually being used in the treatment of ADHD at the moment in terms of single-use versus combination?

And the second question relates to Sylvie. I think I may have missed this again, but could you give us the total number of patients on REPLAGAL globally at the moment? Thank you.

**Angus Russell** - *Shire plc - CEO*

Mike, do you want to talk about INTUNIV?

**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

Yes. As far as use in combination versus monotherapy, we are still looking through our data, and we have made a commitment to get back to you sometime midyear on the source of business and how it is being used. I would say it is being used in combination. I think you'll see more use in combination when we have our coadministration study out. Angus mentioned that will be out next month, and in fact, that will up our coadministration.

But the source of business today has been primarily from the nonstimulants, the short-acting guanfacines, the atypical antipsychotics and Strattera. But we do see coadministration as a big part of the future of this product. And I think the data will be exciting when you guys see it a month from now.

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**Angus Russell** - *Shire plc - CEO*

Sylvie, do you want to answer the comment that was asked for on REPLAGAL's numbers, total patient numbers?

**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

Yes, we have never given you total patient numbers, although with the last few quarters, I guess you can see how fast it is growing. Maybe I can speak in percentage of market share, however. Remember that the product for us is not available in the US. And even with that, we currently have an estimated 40% of the global market share at this point. And that is up from about 30%, 31% before the shortage of the product.

So I hope that is helpful in understanding where the product is.

**Operator**

Gary Nachman.

**Gary Nachman** - *Leerink Swann - Analyst*

Sylvie, a couple on VPRIV. First, on the 15% price discount that you guys took to Cerazyme, has there been any sort of response from Genzyme yet?

And for the 20% of patients from treatment IND that did not initiate commercial access yet, did they go back to Cerazyme, or are they waiting to get access to VPRIV? I am trying to get a sense if you've actually lost any patients back to Cerazyme. Thanks.

**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

These are good questions. We haven't seen any that we are aware of, any response from Genzyme on the pricing at this stage.

And in reference to the treatment IND, I think that Angus highlighted the fact that, yes, about 80% of the patients that were on the treatment IND to date have submitted access forms. The other ones have just, we assume, not initiated that process yet, and they are waiting, if you will, a little longer.

We have seen very few switch back to Cerazyme, no more than we had, I think, announced earlier on in the process. So there's still very few patients that elect to go on to Cerazyme.

And more importantly, I think in the US market, what we have seen is the 25% bullet that is on the slide 7 that Angus was talking -- was pointing to, is that of all the patients that submit what we call these access forms, or basically they have a prescription and they call us to gain access to the product, and there's many of those, 25% of those come from patients who were not on VPRIV before. So they were not on the treatment IND, and they were not on our protocols, so they're like straight switches from Cerazyme to VPRIV.

**Gary Nachman** - *Leerink Swann - Analyst*

And actually, just one quick one on ELAPRASE. What is the current penetration that you have of the Hunter's market? Thanks.



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**Sylvie Gregoire** - *Shire plc - President, Human Genetic Therapies*

Yes, well, globally, I don't think it's changed much from the percentages I have announced before. But basically, in the EU, it's about 75%, as well as in the US. In Latin America, it's about -- I am just looking at my notes -- 50% or so, and then in Eastern Europe about 34%, and then in the Asia-Pacific region it's around 85%.

**Gary Nachman** - *Leerink Swann - Analyst*

Okay, very helpful. Thanks.

**Operator**

Kerry Holford.

She seems to have disconnected. Sorry.

Justin Smith.

**Justin Smith** - *MF Global - Analyst*

Thanks for taking my question. I was just trying to understand what kind of bottlenecks there might be on the budgeting side [subsidiaries]. Revenues did surprise on the upside in later quarter this year. Could you guys raise investment further, or are we at a situation now, with the increase in the SG&A and the R&D spend so far, that you guys are investing the maximum for the year now?

**Angus Russell** - *Shire plc - CEO*

Not bottlenecks as such. Basically, what Graham gave you was an inference that what we are doing is investing behind the product growth and the pipeline development. So there are a number of features that will emerge over the course of the year. If we're seeing good growth opportunities or responses to the kind of promotional efforts we've put into SG&A -- Graham has made that point before -- we are investing behind the growth.

And in R&D, a lot of our investment is determined by progression of the pipeline, where we have a lot of things, as we indicated, going on, but we also have a lot of trigger points, a lot of decisions, which we based on the early results that we will share with you later in the year.

The significant point that Graham has made is we do have an expectation that sales will, over time, continue to outstrip the increases in costs, and that is what is leading to our statements about the ability for good operational leverage over time.

**Clea Rosenfeld** - *Shire plc - IR*

Operator, we're going to take one more question.

**Operator**

Matthew Weston.

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**Kerry Holford** - *Barclays Capital - Analyst*

Actually, it is Kerry Holford here. I just have a couple of questions. On FOSRENOL, the US prescriptions were down 12% in the quarter, market share down around 7%. Could you talk about what is driving this? Obviously, you've seen some price rises. But can they continue to support the progress there, or should we be seeing this as a revenue stream that is going to start declining shortly?

And then secondly, on SG&A, does that now include a profit payaway to GSK on VYVANSE and ADDERALL ADHD? Can you quantify that? Was it substantial in the quarter?

And then I have a very small follow-up question on ADDERALL XR royalty figure, and \$40 million or so in Q1. Was that from Impax? Was there any payments in from Teva? Thank you.

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**Angus Russell** - *Shire plc - CEO*

The last one we can deal with pretty quickly, is that Teva basically don't pay a royalty. It's only Impax that pay a royalty. So by definition, all that royalty income is Impax.

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**Graham Hetherington** - *Shire plc - CFO*

And the other question, in terms of GSK copromote, there is nothing in the first quarter significant, no.

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**Angus Russell** - *Shire plc - CEO*

And we are not disclosing the terms. And what we said before is it is in the form of a kind of gain share. In other words, they earn money on the performance. It was a small upfront originally in terms of striking that deal, but again, it was minimal in terms of the cost of it, and we are not disclosing any more terms other than to say they have to perform. They have to produce upside to our business plan to actually get paid.

In terms of FOSRENOL, Mike, don't know if you want to give a little bit more color on what is going on with FOSRENOL, the dynamics in the US?

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**Mike Cola** - *Shire plc - President, Specialty Pharmaceuticals*

Yes, Kerry, just to reiterate, it has been about a year and a half now since we have gone to this optimization of EBITDA strategy. So we are not really focused on driving the top line with FOS. We reduced our salesforce and our spend, and we really focus on what we think is the highest-margin activities in this product. And we are less concerned or less focused on growing that top line.

We are trying to maintain it. I would tell you it is difficult going up against a company that has a very high market share in Genzyme. And they use managed care leverage and Part D leverage on us. But in fact, I think we have done a great job of driving EBITDA, and we will continue to do that in the US. Outside the US, we continue to make great progress with FOSRENOL to become the leading noncalcium phosphate binder in Europe.

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**Angus Russell - Shire plc - CEO**

Okay, so I think we will call a halt there. If you do have any other follow-up questions, certainly Clea and Eric are available to follow up with you one on one on calls, so please do call them if you do have some follow-up. We apologize if we didn't get to all your questions. It was very busy, and we are on a bit of a time constraint. So we will call it a day there.

So thank you for your time and attention. It is great to be able to talk to you with these what I believe, as I said, are excellent results. Thanks for your questions. It was nice seeing none of those were bigoted in any way. And we wish you all a great day. Thanks.

**Operator**

Thank you, ladies and gentlemen. That concludes your call for today. You may now disconnect. Thank you very much for joining. Speakers, please remain online. Thank you.

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