

FINAL TRANSCRIPT

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SHP.L - Full Year 2010 Shire Plc Earnings Conference Call

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PRESENTATION

Operator

A very good day to you, ladies and gentlemen. Welcome to the Shire 2010 full-year results conference call hosted by Angus Russell. My name is Nancy. I'm the operator for the call today. Your lines will remain on listen-only throughout the conference. (Operator Instructions). I would like to advise all parties this call is being recorded for replay purposes.

I would now like to hand the call over to Eric Rojas. Please go ahead.

Eric Rojas - Shire Plc - IR

Thanks, Nancy. Good morning and good afternoon, everyone. Thank you for joining us today for Shire's full-year 2010 financial results.

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By now you should have all received our 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 our website, please contact Souheil Salah in our UK Investor Relations department on 1256-894-160, and he will be happy to assist you. Our speakers today are Angus Russell and Graham Hetherington. Mike Cola and Sylvie Gregoire will be available for Q&A as well.

Before we begin, I would refer you to slide two 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 can materially affect our results.

Today's agenda is as follows. We begin with opening remarks on Shire's performance and highlights from Angus, and then Graham will continue with a financial review. Angus will then summarize the key priorities for 2011, and we will then open up for your questions.

As always, we are requesting that you ask a maximum of two questions per person so that everyone gets a chance to ask their questions. I will be more than happy to follow up off-line for any subsequent questions or clarifications.

Now I will hand the call over to our CEO, Angus Russell.

Angus Russell - Shire Plc - CEO

Thanks, Eric, and good morning or good afternoon to everyone. I'm going to turn now to the first slide in the presentation, which is number five.

These results, as you can see, are very much characterized by strong topline growth. Total revenues for the year were up 15% to \$3.5 billion, and product sales were up 16% to \$3.1 billion. It's something of a landmark for Shire. That's the first time we've actually had product sales exceed \$3 billion.

Turning to slide six and looking at the earnings, you can see those earnings -- that sales growth has actually driven strong earnings performance as well. Earnings were up 21% for the full year, up \$4.23 per ADS. We've also produced strong cash generation of \$1.4 billion during the year, and that's up 48% on 2009. That gives us a very strong balance sheet, which is also supported by newly renewed banking facilities. These financial results clearly underpin our aspirational target of midteens growth that we put out there some three years ago and said would be our target through 2015.

So let's turn to the next slide and just have a little look at some of the business highlights for this past year. So going through this product by product and starting with VYVANSE, recently we received an approval for the use of VYVANSE in adolescents. That's an important segment of the market in our minds given the recent changes in US healthcare reform, which allows younger people to stay on their family insurance for a much longer period of time. And that does carry over very much this adolescent period of people's lives.

We've also had the pediatric indication launched in Canada, and recently again we gained approval for adolescents and adults in Canada. And we were approved in Brazil, and it will be our intent to try and launch the product there the middle of 2011.

We also got our labeling indication for 14-hour efficacy in adults. Mind you, this is very clear differentiation in the market. No other drug in the marketplace has that kind of duration of effect. And that's extremely important in the adult community where adults obviously metabolize drugs faster or have a longer working day and need that kind of coverage.

And we also announced for the first time obviously some headline data around signal finding studies on our non-ADHD indications of VYVANSE, and this, we believe, will over the next few years potentially create new value in our pipeline.



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But INTUNIV, it's now approaching pretty much a 3% US market share in just its first full year of launch and is being prescribed by about 28,000 physicians across the US. LIALDA continues to have a great performance, although it's one of the products now that's been out there a little longer. It still is producing very, very good growth, and it recently achieved a 20% US market share.

And to the GI portfolio, as you know through the acquisition of Movetis, we recently added a new product RESOLOR, which addresses a symptomatic unmet medical need of chronic constipation. It both expands the acquisition first of Movetis, both expands our ex-US GI franchise and our R&D pipeline. RESOLOR itself is now launched in three countries and recently had a strong recommendation for payments and reimbursement by NICE in the UK.

Turning to slide eight and looking at our HGT business, VPRIV obviously its first full year of launch has done exceptionally well. It's now approved in 35 countries worldwide, including both countries in North America and the EU. We ended the year at about just over 1000 patients on therapy globally, and by our calculations that represents something around an 18% global market share -- tremendous performance in just its first full year.

REPLAGAL tremendous growth over this past year, and that left us at the end of the year treating something just over 2300 patients globally. In Western Europe we, again, estimate that to be something like an 80% market share.

ELAPRASE continues to show good growth having been launched now for a few years, but we have over 1000 patients on treatment globally. In FIRAZYR obviously we again headlined recently for you the positive efficacy and safety from the second US Phase III study, and we hope very shortly to be filing the response with the FDA. That as a second response will have a six-month review period, and so we hope to be in a position to launch this drug later in the year in the US.

And, in addition, today we can actually announce also that we recently in the last couple of weeks received a positive opinion from the CHMP for the self-administration label in Europe, and that's a major advance, we believe, for this product. As you remember, it's in a pre-filled syringe. It was designed to be self-administered, and we believe this will now give patients full benefit by this convenience of use.

Also, M&A activity in the HGT segment. As you know, we signed a partnership arrangement with Acceleron for an exciting range of new compounds called ActR2B. We have secured the exclusive ex-North American rights to those products, and at the moment, the first of those, ACE-031 is undergoing a proof of concept study (technical difficulty) for the treatment of Duchenne muscular dystrophy. Again, if you couple that with our own internal work on intra-fecal delivery of proteins crossing the blood brain barrier, that would be unique if it was to work for Shire, and that with the Acceleron platform gives us the prospect here, too, of two great new platforms for growth in the future.

All of this can be seen really on the next chart on page nine, which shows that we are not only just delivering really strong growth in revenues from the current nine products that we have in our product portfolio globally, but we have a lot of things moving again into the later stages of development in our pipeline and then some exciting, as I call them, platform technologies being tested in the early stages of research and development. If you couple with that the investment in new manufacturing facilities and the buildup of our global operations over the past year that are shown on this chart, all of this speaks to a very strong performance not only now, but obviously the ability to sustain and grow the business well into the future. For me personally, this is one of the most exciting prospects I ever saw for Shire.

So turning over the page, it's very clear to me that the business model that we've used now for many years is actually delivering tremendous results. You can see here that from 2003 to 2010 inclusive we have delivered a compound average growth rate of 16% in revenues and 15% in EBITDA, absolutely in line with our aspirational targets, not only in the past but also going forward. We are driving growth from a balanced portfolio of products, and we're also delivering tangible stakeholder value, not just for you as investors but also for patients, physicians, payers, and policymakers. To me that's extremely important. That's going to be the new world standard for this industry. It's no longer just about the physician. We have to be able to prove to all these



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audiences that we are demonstrably bringing value to the table. I believe we are in Shire, and I believe we will continue to do so in the future.

So with that, let me hand over to Graham to just take you through a few more details of these Q4 and year-end results.

Graham Hetherington - *Shire Plc - CFO*

Thank you, Angus, and good morning and good afternoon, everyone. I'll be taking you through three key things today. First, our outstanding full-year results and some of the dynamics shaping our fourth-quarter performance. Second, the continued growth of our product portfolio, which combined with our operating leverage will support our earnings growth from 2011 and beyond. And finally, I will be providing direction on the dynamics beyond 2010 and specifically the emerging shape of the 2011 income statement, which underpins market expectations for earnings in 2011.

Angus has highlighted the outstanding progress we've made on revenues and EPS and advancing the pipeline in 2010. It's worth reiterating again on slide 12 the strong results we have delivered throughout the year, while absorbing amongst other things US healthcare reform, European pricing pressures, foreign exchange and the impacts of recent transactions.

Product sales are ahead of expectations with 16% growth on a reported basis and 17% after stripping out the impact of foreign exchange. This really is an outstanding result when you consider that we are comparing against 2009, which included a peak quarter of sales from Adderall XR. Earnings per ADS were up 21% to \$4.23, marginally ahead of the guidance I provided at the end of the third quarter, and we generated almost \$1.4 billion of cash in the year, up 48% compared to 2009.

Turning now to slide 13 and our performance in the fourth quarter, our topline momentum continued through to the last quarter of the year. You'll recall that in the fourth quarter of 2009 we revised our estimates of the Adderall XR Medicaid rebates downwards, resulting in a large one-time benefit in the quarter. After adjusting for this item and stripping out the impact of foreign exchange, product sales were up 23% on a like-for-like basis in the quarter. We've laid out the quarterly numbers for last year adjusted for this item on chart 31 in the appendix.

It's also worth reinforcing that we have delivered this growth despite the adverse impacts of the disposal of Daytrana at the beginning of the fourth quarter. Daytrana sales were \$19 million in the fourth quarter of 2009.

As expected, royalties and other revenues were down approximately 30% compared to last year. When royalties were boosted by Impax's authorized generic version of Adderall XR, they sold into the wholesale and retail channels for the first time. [EBITDAR] in the quarter was up 5% compared to last year after adjusting for the 2009 Medicaid estimate change and foreign exchange movements.

We chose to accelerate some R&D activities and investments in our support infrastructure at the end of 2009. This combined with approximately \$25 million of nonrecurring expenditure, and the inclusion of Movetis for the first time resulted in higher year-on-year growth in operating costs in the quarter than we expect to see going forward.

I will be expanding on our increased investment in growing the business later.

Despite this additional investment, EPS for the quarter was in line with expectations as a result of higher than expected sales and a lower tax rate than we forecast at around 16% for the quarter.

On slide 14, you can see how our core portfolios continue to grow strongly, up 30% this quarter and 34% for the full year on a reported basis. Overall, our core products have generated an additional \$700 million of sales this year, substantially offsetting the decline in Adderall XR revenues that we have experienced in this our first full calendar year since losing exclusivity. It's a great growth story and, as you can see from the chart, one that is broadly based across our young portfolio.

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Picking out some of the highlights from our ADHD franchise, INTUNIV reached a market share approaching 3% by the year end, and total sales for its full-year were \$166 million. VYVANSE exited the year with a share of almost 15%, up 2 percentage points year on year. Sales have grown 26%, helped by strong growth in the ADHD market, which grew 12% year on year and a higher share of the market.

As we expected, we saw some modest stocking of VYVANSE in the fourth quarter to leave the stocking flat year on year and gross to net approached 40% in the last quarter, primarily driven by higher Medicaid utilization. We expect this level of gross to net to continue into 2011.

In our GI franchise, LIALDA continues to gain market share and generate double-digit sales growth, along with the useful contribution from MEZAVANT in Europe. The fourth quarter also saw our first sales of RESOLOR, following completion of the acquisition of Movetis. Sales from RESOLOR will grow as launches continue across Europe.

In our HGT business, REPLAGAL and VPRIV's momentum continued with REPLAGAL posting sales growth of 87% for the full year on a like-for-like basis and VPRIV ending the year with sales of \$143 million. ELAPRASE finished the year strongly, too, with sales up 16% on a like-for-like basis in the full year.

Turning to the next chart, 15. At the top, you can see how sales for the full year have grown ahead of the increase in R&D and SG&A spend. As I explained earlier, R&D and SG&A were particularly high in the fourth quarter. Even with these investments, we are able to show continual operating leverage for the full year with our EBITDA margin increasing to 26% for the full year.

As we invest in advancing our pipeline and supporting our expansion, we will continue to manage our cost progression closely to deliver further operating leverage as our product revenues continue to grow.

Let's look at our cash flow on chart 16. We generated almost \$1.4 billion of cash during the year, which compares to \$900 million in 2009. This cash flow has allowed us to make some key investments for the future -- strengthening our portfolio of marketing products in our pipeline through the acquisition of Movetis and the Acceleron license and investing in our rare disease R&D and manufacturing capabilities through the purchase and development of our Lexington facility. We finished the year with cash of \$550 million and net debt of \$530 million (sic - See Press Release). We continue to have a strong and flexible funding position supported by our recently negotiated bank facility.

Turning to chart 17, 2010 has been a really significant year for Shire, not just in terms of the financial progress we've made, but also in the emergence of new activities that both underpin our existing strong growth profile but also represent key sources of incremental growth in the future. This chart shows where the investment through increases in R&D and SG&A spend have started to be made.

You can see in the green where we've been supporting the launches of INTUNIV in the US, the first launch of VYVANSE outside of the US and Canada, VPRIV around the world and RESOLOR in Europe. We've also supported the exceptional level of share gain that REPLAGAL has experienced in the year.

At the beginning of September, we also established our Swiss hub. This includes teams heading our commercial operations outside of the US, along with important R&D functions and represents another significant step in the ongoing internationalization of the business and one that also supports our effective tax rate.

Our already strong pipeline also grew progressively during the year, reinforced by the activities that you can see in the bottom half of the chart. It now represents a broad portfolio of opportunities which have an above-average likelihood of success as we leverage the potential of existing products and proven technology platforms through our investment in R&D. These were exciting investments, and initiatives do come, and they do come at a cost, and you've seen us increase our operating costs during 2010 to reflect this. We look forward to demonstrating the benefits of these investments in the future.



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So, moving on to chart 18, let's build on this and look at the dynamics as we look beyond 2010. The growth of our portfolio will continue to be a key feature with most of these products still at an early stage in their life cycle. We'll continue to invest in the future growth of the business, and from 2011 we will be absorbing the impacts of the number of transactions, including the Movetis acquisition and the Daytrana disposal. However, taking these things together, we are confident that continuing operating leverage will drive expanded operating margins, good earnings growth and strong cash generation for the future.

Finally, let's look at 2011 specifically on chart 19. As I outlined earlier, we are entering 2011 with strong momentum following an outstanding performance in 2010. We have a young growing portfolio from which we expect to see continued strong growth despite the impact of the sale of Daytrana in October last year, remembering that Daytrana generated \$49 million of sales in 2010. We remain confident that in 2011 and in all likelihood beyond, there will only be two authorized generic competitors to Adderall XR. My best estimate is that Adderall XR's product sales will be somewhere between the actual levels recorded in 2010 and the currently low market consensus forecast for 2011.

As a result, I'm expecting expecting total product sales -- that is including Adderall XR growth in 2011 -- to be at least in line with the reported growth of total product sales in 2010. The royalties from Impax will be based on their own market performance. We are seeing other royalties as expected start to decline as the related products face increasing generic competition. We expect those trends to continue through 2011, and my best estimate is that total royalties and other revenues combined are likely to be about 10% lower than in 2010.

I'm expecting our product percentage gross margins to be in line with 2010, and depreciation will be about \$110 million in the current financial year. As I highlighted earlier, we do expect our investments in the business to continue to be a feature in 2011. Specifically, we'll be absorbing a number of additional cost streams, including first the full year of Movetis' operating costs as we launch RESOLOR in new markets and invest in new indications for RESOLOR and its promising pipeline.

Second, a full year of our new Swiss hub, a key benefit of which will be underpinning a tax rate in 2011 of between 22% and 24%. And third, the impact of the new industrywide US excise fee. As I outlined earlier in the year, this will be relatively limited for Shire. Our latest estimate is that we'll be in the range of \$10 million to \$20 million in 2011.

After absorbing all of these and continuing the investment to support the future growth of the business, I expect based on our current plans combined R&D and SG&A to increase by between 10% and 13% compared to 2010. These dynamics taken together will see continued topline growth through 2011, which combined with operating leverage will drive good earnings growth, underpinning market expectation to 2011, and our aspirational growth targets. And with that, I'll hand you back to Angus.

Angus Russell - Shire Plc - CEO

Thanks, Graham, and just turning to my wrap-up section of the presentation, which continues to really look at the new year and our agenda from a business point of view. So what I tried to do if you turn to slide 21 is bracket and highlight the key priorities for us in this business in 2011. You can see them put between these various categories. We will be launching further new products this year and getting new indications for some of our existing products. We're going to see, I believe, further advances in the R&D pipeline, and we will keep you updated of those through the year. And, of course, we have invested in biologic manufacturing and global operations, and we hope later this year to see the start-up of many of those facilities.

So turning to page 22 and just looking in a bit more detail at some of the issues under launching new products and new indications, firstly, VYVANSE again. I mentioned at the beginning we are going to probably launch the product in Brazil around the middle of this year. We'll see the adolescent launch now in both the US and Canada and the adult launch in Canada.

We're going to be filing, we hope, the MMA, the MAA in Europe, obviously gearing ourselves towards what we hope 2012 will be a launch in Europe for VYVANSE. And we'll continue to develop the new uses of VYVANSE, and as we said when we gave you the top headline news on that, basically we'll be talking with regulators in the first part of the year on both the results of major



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depressive disorder and excessive daytime sleepiness, and I hope that Mike will be able to share with you later this year the results of the impact on the negative symptoms of schizophrenia.

With regard to INTUNIV, I mentioned earlier co-administration with stimulants, and as you know, we have an upcoming PDUFA date at the end of February. If approved, this will allow us to promote for the use of INTUNIV in this way, which will be a complete new paradigm of therapy and one that we're hearing back from physicians who have tried it this way that this is having extremely good benefits for many of the patients. We believe this will be a useful upside possibility for the use of INTUNIV.

Then we'll continue to progress obviously our Phase III program for the EU for INTUNIV so that we can bring our two leading drugs to the European market in the next two to three years.

FIRAZYR, I mentioned earlier the self-administration label and the importance of that in Europe, and also obviously, as I said, we will be hopefully shortly filing the package with the FDA, and looking forward we hope later this year to full US launch of that product.

LIALDA we will actually we hope to be able to extend a maintenance indication on that product, which we hope will give us renewed growth potential to add to the already good steady growth that we've seen over recent years. And with RESOLOR, I also mentioned earlier this continued rollback of the product across Europe following on from the initial launches in three markets.

Turning over the page and looking at what we expect to see advancing in the pipeline, again, in perhaps the next quarter, Mike will be giving you some headline date on SPD 535, which is a platelet-lowering agent, and so we will give you some further information on the results of some proof of concept work we've been doing with that product and looking forward to the potential utility for that drug based on the results of that study.

One foreseen, Carrierwave continues to make good progress. Mike has told you in the past that the lead compound we have some backups, but the lead compound is continuing to perform very well. And again, perhaps later this year, we will have some data for you from the results of those studies.

Movetis programs we also recently approved progression of drug for GERD into Phase III. This was a Phase II compound at the point of acquisition, but we've now reviewed that in detail. And again, Mike can give us a bit more information, if you will, in the Q&A, but he and his team have agreed now to advance that into Phase III studies, and that will hopefully be a very good prospect for the future.

And then the HGT business I mentioned earlier, the intrathecal programs which are now directed at three different rare genetic diseases -- Hunter-CNS, Sanfilippo A, and metachromatic leukodystrophy -- and we have human studies begun now in each of those areas.

Also, we have a new project here on the horizon, HGT 4510 for DMD, which, again, still we could give you some more information if you want to ask questions at the Q&A on that.

As I mentioned earlier and as you are well aware, we are investing in our new biological manufacturing capability in Lexington, Boston and continue to expand our global operations most notably with the buildout of our EU hub in Nyon in Switzerland.

So moving to the penultimate slide, we believe all of this speaks to a very solid foundation for what we believe will be sustained good growth in line, as Graham said earlier, with our aspirational targets in the future. I think it's most noticeable that not only are we producing that good growth, but we are producing it at a time of what the industry sees as significant headwinds. So sustaining this tremendous double-digit performance in a challenging macroeconomic environment is even more of an outstanding performance in my view.



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As I said earlier, we are continuing to build our global presence, and we've now in recent years become a very international business. And you will see us continue with that push into new markets on this global basis. Most importantly, in doing this and the way we run our business, we feel we are meeting the needs of patients and families with innovative, truly valued products.

So turning to the last slide, just to leave you with what we all believe here passionately in Shire, that we enable people with life-altering conditions to lead better lives. With that, I'll turn back to the operator, and we would be very pleased to answer your questions.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions). Ken Cacciatore, Cowen and Company.

Ken Cacciatore - Cowen and Company - Analyst

Thanks, Angus. Just two questions for you. First, the Lexington facility, you indicated on your slide here that you are completing the submissions for new plan approval. Can you just give us a little more context, or maybe Sylvie can give us a little more context on how that's progressing and any update in terms of timing? And then also, Angus, you were talking about your global presence. I'm just wondering if you could indicate any of the countries that you find particularly interesting that maybe we've not been paying attention to as you go about this process and describe to us what some of those opportunities may be.

Angus Russell - Shire Plc - CEO

Maybe I will take the second one first, and then I will, of course, pass the question to Sylvia for an update on the Lexington facility.

So, I think you can bracket the global expansion in a number of ways. I mean obviously the HGT portfolio stating the blindingly obvious does pretty well all over the world because it just follows obviously population size, and it is -- we are treating rare genetic diseases. So there is always good potential across all these markets, and I wouldn't necessarily single any one market out. Our economics tend to be pretty much the same all over the world for those kind of products.

Maybe in ADHD, I indicated earlier it's going to be an excited I think 12 months for us in ADHD, not only because of launch in Brazil, which, as I said earlier, will be the first launch outside of North America for us as a company with ADHD treatments, but obviously Europe is a big opportunity for us in the future. So, finishing up the program there on VYVANSE and filing, continuing to progress INTUNIV, I think that's a really exciting prospect in store. We are going to be looking to obviously continue educating those new markets to the importance of treating ADHD via treating the awareness of ADHD. And we said it before, some of these North European markets are growing quite quickly now, and we were in Germany as a team before Christmas, and I tell you there are presentations there that remind me exactly of the sort of presentations I listened to 10 years ago in the US from KOLs, talking about the need to treat and the importance of treating what's been a not very well treated or identified population. And then the reason we're launching in Brazil is, Latin America and Brazil particularly has been already a market that's growing reasonably quickly in terms of ADHD.

So, maybe those are kind of some of the highlights. Generally we're finding good growth around the world. Maybe turn it the other way. The markets that we are still thinking of with our kind of niche portfolio that's treating these rare and high-margin kind of products that we have, then China and India are markets that at the moment we're not exactly rushing into. And we're



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taking our time to think when is a good entry point, what kind of entry point. So I think you won't see us rushing in, buying generics and branded generics in those markets like many other industry players.

We don't really have an appetite. We don't think that's our model. We don't think we have core competencies there, and we're preferring to other folks on the market, as I said, where we see awareness of the kind of diseases we treat and where we can secure the kind of economics consistent with our model. So, with that, let me just hand over to Sylvie and ask her to pick up on the Lexington facility.

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

Sure. Hi, Ken. I'm going to update you regarding the status of what's happening in the plant and the facility. The update we provided in the last quarter is we are still on target with that. So I'll just remind you of the specific activities regarding REPLAGAL and VPRIV in the plant. So, we had told you in the last quarter that we were doing the [QBRs] or the qualifying batches for submission for REPLAGAL, and those have been completed. So we expect to be able to submit those in short order. And therefore, then the regulatory submission will go to the EMA in this instance, as you know, since this is the authority that has oversight over the major market of Europe where the product is available in large quantity. And so we should expect the authorities to come and inspect and review the application and then give approval later this year most likely.

For VPRIV, what has happened the last quarter is what we have started, the engineering runs in the facility, and we will be completing those as in the beginning of the year. And then similarly, we'll file them for approval and then in the US and Europe in this instance. And the timing of approval, I think we've said, was expected early 2012, and it a bit depends on the authorities' viewpoint of how fast they will review this particular application. So, those -- we are on track relative to the activities in the plant, and you will hear, I'm sure, more about it as the year progresses.

Operator

Peter Verdult, Morgan Stanley.

Peter Verdult - *Morgan Stanley - Analyst*

It's Peter Verdult here from Morgan Stanley. Just two questions. Basically just on REPLAGAL, (inaudible) I was going to ask the same question about the timelines. I realize that it's not going to be an exact date, but could REPLAGAL, given the particular following, be an H1 event, or should we just more likely think of it as an H2 event?

And then just to turn to Graham, in terms of the attentional negative surprise of this year, we see an enforcement risk rising in the industry. You've talked about a legal provision in the SG&A line for the fourth quarter. I just wanted to know, could you tell me what the exact dollar amount is for legal provisions currently on Shire's balance sheet?

And then quickly, Angus, on ADHD outside the US, could you just remind me and hand some numbers as to market sizes in Europe and Brazil and potential growth rates. Thanks.

Angus Russell - *Shire Plc - CEO*

Okay. Some of those statistics I think (inaudible) over the markets are difficult. I mean what I can say, Mike, can add if he's got further detail.

I mean certainly in Europe we've been on record many times as saying, if you you are tracking the growth rates, it does vary a bit market by market. But the last two or three years we've seen compound growth in some of those markets of 25%, 30%, kind

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of percent rates in some of the -- certainly some of the North European markets. But let me pass to Mike in a minute and perhaps ask him to finish off that, and then maybe we'll go to Sylvie where we probably needs sand by sand. If so, we need to also remind people we have the potential to make more product off our existing plant and deliver some good growth this year off existing patients. So, there seems to be a big emphasis on obviously the new plant, which I understand, and we're looking forward to that. But probably worth just running through all those numbers again, Sylvie, as well on what we can do from our existing facilities to make it clear we're not exactly capped at the moment this year.

So, Mike, anything else on ADHD?

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

Just real briefly, if you look at Europe, it's about \$400 million, and as Angus said, it's not a homogenous market. Some of the markets are growing much faster than others. But still, it's mid-20s percent growth annually. I think we need to look at those markets differently than the way you guys generally view the US market. As Angus said, it reminds him of the US market maybe 10 or 15 years ago. It's really a market development activity for Shire going forward. So, we have to drive that market. We have to build that market.

So, today's starting point to me is a good place, but, it's really about market creation and not taking share, and we are really looking at it from a very long perspective. We have IP on VYVANSE out through 2024, and we have at least 10 years with INTUNIV. So we can take that long perspective.

Outside of Europe, again, market creation, particularly down in Brazil with VYVANSE, we're excited for our first non-North American launch. That's a big step for Shire in ADHD. We've never done that before. So, it's a first step for us in South America, and we think it will be good for that team. Sylvie?

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

Yes, to answer your specific question, Peter, relative to the timing, yes, I would factor more H2 than H1 in terms of the planned approval for REPLAGAL. But to pick up on what Angus was mentioning and to put it in perspective, we're going to be very focused on the plant, but the reality is, of course, that we can still add what we had said the last quarter. And we can still add at least 300 patients on REPLAGAL this year. And if you think of the market dynamics as they exist today, we cover about 70% of the Fabry market worldwide, and supplies from the competitor cover about the other 30%.

The majority of the growth this year will come we expect from the patients that are new patients and that require therapy as there is no other alternative therapy. And, in fact, in the last quarter, we were able to add just a little less than 100 patients on REPLAGAL. It was a mix of both switches and naive in that particular quarter. But over the course of the year, one would anticipate that the majority of the new patients, again, if the market size to existing patients are treated would come from the naive patients now being diagnosed.

And that's a very important market for us going forward. The Fabry market grows. It is expected to grow over the next 10 years at a compounded rate of about 4% to 5%. And so one can envisage the Fabry market, total Fabry market, to be well above \$1 billion by 2020. So, it's an important driver for the growth of the HGT franchise over a long period of time.

Angus Russell - *Shire Plc - CEO*

And then Graham?

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Graham Hetherington - *Shire Plc - CFO*

Finally, on the legal and litigation side, we are not immune from the emerging enforcement risk profile that you were describing. But actually Shire's exposure to litigation from an industry perspective is incredibly low. And that's explicitly measured by the provision levels that we have, which are not on the balance sheet at the moment for round number of \$34 million where we have an explicit settlement or fine that is likely. So it's \$34 million is the answer to your question.

Operator

David Buck, Buckingham Research.

David Buck - *Buckingham Research - Analyst*

Thanks. Just a couple of questions. First, on the outlook for tax rate in the 22% to 24% range, can you talk a little bit about what's driving that? Specifically the change from 2010 and how sustainable do you think that is, and do you think there is further improvement as you put in an intellectual property for new products?

And then secondly, for Sylvie, just a couple of questions. FIRAZYR with the new label in Europe, do you see that as a major growth driver, or do you think we need to wait for the US approval to really see meaningful growth in that product? And then, for the assumptions on switchbacks, can you talk about what the assumption is in terms of patients perhaps lost to your competitor, and what's the assumption in the product sales guidance on that front? Thanks.

Angus Russell - *Shire Plc - CEO*

So, Graham, tax rate?

Graham Hetherington - *Shire Plc - CFO*

Well, let me start on tax rate. You may recall at the beginning of this year, our guidance for tax rate was 25%, and we are managing through three key dynamics. The first one is in certain parts of the world where we are earning profits, there is upward pressure on the tax rate, and the mix of the business puts some upward pressure on our tax rates as well.

The second dynamic is the fact that we have established this hub in Switzerland, and that helps us manage that upward pressure that we've benefited from in the fourth quarter. You can see us benefiting from that as we guide to a tax rate in the range of 22% to 24% going into 2011.

Then the third dynamic is actually very specific to the fourth quarter of 2010 where yes, we experienced some small benefit from the establishment of the Swiss hub in September, but we also had a one-off tax credit we experienced. But what you can see is that from the start of 2010 where we are working on a 25% level, we're able to give you a guide in the range of 22% to 24%, and that, I think, is a good number for the next couple of years.

David Buck - *Buckingham Research - Analyst*

And was there an R&D tax credit in the fourth quarter? Was that the one time you talked about?

Graham Hetherington - *Shire Plc - CFO*

It was.

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David Buck - *Buckingham Research - Analyst*

Okay. Thanks.

Angus Russell - *Shire Plc - CEO*

So, Sylvie, FIRAZYR?

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

FIRAZYR, yes. FIRAZYR, indeed, the ability to be able to self-administer FIRAZYR will then be able to exploit the true value or the true advantages of this product over the competitive products. And so, it's like in the countries in Europe where the product is at the hand of the patient, we can see a much better uptake. So, in some instance, if even though the patients couldn't administer themselves, they could get it themselves at the pharmacy and travel around with it. So we do anticipate that this will be an important advantage for the growth of the market in Europe.

And you talked about the US opportunity, which is, of course, a very significant one for us because it has several advantages relative to Europe. First of all, the competitors that are there have been there for less long duration. So, there's less well entrenched competition as opposed to the EU, and then the competitors have established a higher price actually point in the US compared to Europe.

So, those are two very important factors. And then we anticipate the launch of FIRAZYR with self-administration obviously in the US. And so, all these combined make the US market a very interesting market for FIRAZYR.

Then, I think you asked about the switchbacks for I'm assuming REPLAGAL and VPRIV, and we've seen very little switchback -- I'll start with VPRIV -- well, for both products actually, but especially for VPRIV in the US, which is important since Cerezyme is somewhat coming back onto the market at this point, and we've seen very little switchbacks. So, handfuls. We've even seen people who have switched to another therapy and then come back onto VPRIV. But, again, very small numbers.

And as for REPLAGAL, of course, we've seen very little switchbacks as well because it's almost impossible to switch at the moment and offer Cerezyme to really -- there's more Fabrazyme around to switch to.

David Buck - *Buckingham Research - Analyst*

And just to close that out for Graham, I guess the product sales guidance for this year, what does that assume on switchbacks, particularly for VPRIV?

Graham Hetherington - *Shire Plc - CFO*

On VPRIV at the moment, it assumes that there will be some small amount of switchback at the back end of this year.

Angus Russell - *Shire Plc - CEO*

I think the other thing, David, just to add a little postscript there is the JPMorgan conference, Genzyme indicated that they wouldn't begin to even come back on Cerezyme until the second half of this year. People perceive that as a further delay, and you know, if that's true and they don't appear until kind of second half of the year sometime, some of our patients there will have been switched and on REPLAGAL for something like two years now. So they are all doing well. We've had, to Sylvie's point,

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no real feedback with any concerns or any problems, and consequently that's what supports our thesis of, we wouldn't expect patients or, indeed, their physicians to advise a switchback.

Operator

Kerry Holford, Credit Suisse.

Kerry Holford - *Credit Suisse - Analyst*

A couple of questions on ADHD. The growth of the market in the US continues to be way ahead of other disease categories. Q4 in particular looked very strong. I wonder if you could just talk about what you think are the key drivers here and how sustainable that growth is going forward? And then moving on to ADHD in Europe, you talk about reinvesting in the business. I presume presumably a lot of it's going to be for expansion of the sales force and sales in Europe. Should we expect those costs to come through this year or primarily in 2012? Thank you.

Angus Russell - *Shire Plc - CEO*

Okay. So, Mike is obviously well positioned to answer both of those questions.

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

Kerry, it's Mike. On the fourth quarter, it was very strong. I think the most telling thing for me in the fourth quarter was that strength was not just in the adult market where we've seen it for the last few years, but it was also in the pediatric market, which for the first time was up around 10% year-over-year growth. That's unusual. That's about twice what we have generally forecast for that (inaudible) market.

I don't have a full analysis of exactly why that accelerated the way it did and to Angus' point earlier gave us a 12%, 13% overall growth. But I can give you some anecdotal thoughts on that.

One is, as we continue to promote INTUNIV, we believe we are bringing more folks that have been sitting on the sideline have been being diagnosed with ADHD, but have not sought treatment because they are unhappy with the current treatments or they have tried a treatment and did not like it. We think there is upwards of 700,000 patients, pediatric patients sitting on the sideline waiting for the right therapy. So we think that's helped grow that pediatric market.

We also think that as we get a better safety profile of around VYVANSE as people become more comfortable with it, we really are driving the market growth. When I look forward this year, I think we will continue to see that growth. You look at the events that are out there for us this year, we have still a long way to go with some very interesting activities. We have co-administration. We have the adolescence launch, and we have a direct to mom campaign for the only product without a blackbox warning on it, INTUNIV, this year.

And so I think it will continue to -- you'll continue to see a really nice growth in the entire ADHD market. We get questions all the time, can the adult continue to grow 20% forever? By our estimate, it's still only about 35% penetrated. So forever? No. But for the foreseeable future, could it grow at that rate? Yes, I think it could.

Turning to Europe, I think if you think of the timing of the spend, we are looking for a very much an end of 2012 approval for VYVANSE. So you'll see the buildup I think most of the cost in 2012 on the commercial side. Just so you know, that has been our single largest drug development investment over the last three years both in INTUNIV and in VYVANSE for Europe. So it has been a significant investment. It will grow slightly and move more towards a commercial bent in 2012.

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Angus Russell - *Shire Plc - CEO*

Yes, and as Mike said, Kerry, in his previous answer on one of those earlier questions, we're not expecting a rapid takeoff, so throwing huge resources or something that is sort of supposed to explode out of the gate. What will be looking to do, as Mike said, is put the resources behind as we see the market respond to our education, our growing awareness programs, and invest behind that.

So we'll be looking at that very carefully, but I wouldn't think of it as how we launch the US where we went out there, put big salesforce relative to our size, and launch there because the market in a sense was much more receptive, already well-established. So this will be a gradual build of costs behind as we see the value proposition emerge.

Kerry Holford - *Credit Suisse - Analyst*

Lovely. Thank you.

Operator

David Steinberg, Deutsche Bank.

David Steinberg - *Deutsche Bank - Analyst*

First question on PENTASA. I know the drug is not an insignificant product for you now at a \$0.25 billion run rate. Yet the patents have expired, and I was wondering if you could share with us your most recent thinking about when generics may come into the market? Has the FDA come up with any new bioequivalency standards? Do you know of any filers out there? What's the timeline you're currently thinking when competition may emerge?

Angus Russell - *Shire Plc - CEO*

Okay. David. No new news. Mike can run you through it. You're right. I mean the patents went as long ago I think it was 2001 or something like that. So nine years ago now or 10 years ago this year, I guess.

But, Mike, there obviously has been a lot of debate. There has been quite a bit of sort of published information out that is probably worth just recapping on that. David is pretty familiar with it. That probably helps.

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

David, you could probably answer this question better than I could, but, as you know, there was a white paper in 2007 that looked like the goalposts for clinical trials, and those goalposts have shifted now. It's still not completely clear. It's not policy, but the guidance out there is more around partial AUC. It looks consistent with long-acting products across the board, including CNS products.

We think that's a fairly hard standard to meet for both PENTASA and LIALDA. We don't see any possibility of a PENTASA generic in our imminent future. But, as you know, with the IP actually played out on this product, we will not be informed. We will not know when there is a Paragraph IV filer. But we're fairly confident that the latest guidance, again, is a pretty high barrier to entry for generics.



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Angus Russell - *Shire Plc - CEO*

I think, as you know, David, there has been a pretty public kind of playout of something we have worn a -- want to choke off because they have obviously a similar drug with Asacol that they got from P&G. I mean it's interesting, you know as well as I do, probably the generic there had gone down the path that was established, that Mike talked about, the 2007 kind of where we are doing trials to then kind of find they've been wrongfooted. The FDA changed the goalpost, and I said no, it's this dissolution study thing and multiple dissolutions of different pH levels, and we are still awaiting kind of clarity of exactly what that means in terms of how many studies.

So, again, in terms of someone commencing right now, I don't know. You can never say never. But, with what Mike just said, pretty gray area still, not entire clarity yet on what the new standard is in terms of how many studies and how many different levels of pH you are going to have to file those dissolution studies around. But, as Mike said, our view is that is tougher. It's gray, and it's certainly been a complete revision and a new standard achieved in that wrongfooted one generic already in terms of going up against one choke up.

David Steinberg - *Deutsche Bank - Analyst*

Okay. Fair enough. And then the question on HGT facility, in a couple of weeks, there will be -- there's a PDUFA date for a potentially new competitor in the Gaucher market, Protalix. I was wondering, there is a wide-ranging view on whether the product is efficacious or safe, but wanted to get your view on, number one, do you think it will be approved at that point in time? Number two, do you see it as significant competition? Number three, if it is approved, any thoughts on how you would deal if, for example, Pfizer cut price, how you would react to that, and what your response would be?

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

Wow. A lot of questions on that. (multiple Speakers). So yes, we, of course, know that their PDUFA date is coming up, and so we'll be watching with you in terms of what happens relative to the label mostly that they obtain if approval is given. Because I think that label will be an important differentiator between the products. We already know of some differences at least, and for instance, they haven't been conducting any pediatric studies and we have. So, there certainly will be differences if there is an approval.

In terms of the uptake and whether or not it will be approved, I cannot comment. I'll just tell you that anecdotally, the product has been available for a while, and the usage of it has been limited from what we hear from the KOLs perspective.

In terms of pricing, well, we have to see again what they come out with from a pricing perspective. We already have a benefit in terms of the US in terms of pricing relative to what we offer to patients from a discount perspective with Cerezyme's product, and then we'll have to see what happens in the market dynamics once there is a third player in the market.

Operator

Graham Parry, Merrill Lynch.

Graham Parry - *Merrill Lynch - Analyst*

Just, firstly, on the guidance, I was just wondering what scenarios lead to be 10% versus 13% growth in R&D and SG&A cost growth. And what I'm thinking here is, is this purely sales dependent and you will see as you go through the year, or are there nondiscretionary elements of this that might be beyond your control? So we could see 13% R&D SG&A growth regardless of what happens on the top line.

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Secondly, I just wanted to clarify exactly again that you are expecting to see growth from the HGT business, and in particular, you are assuming that REPLAGAL does grow in 2011 in that guidance. And if you clarify, are you actually assuming any capacity from Lexington for REPLAGAL and VPRIV in your guidance?

And then lastly, regarding the comments you have made about HGT sales in 2011, could you just clarify whether they would represent an increase, a decrease or unchanged versus your prior comments about I think it was 200 more patients on VPRIV? I think so you did just reconfirm the 300 more on REPLAGAL in 2011. Thanks.

Angus Russell - *Shire Plc - CEO*

Graham, you want to do the costs and then Sylvie-- (Multiple Speakers)

Graham Hetherington - *Shire Plc - CFO*

Let me start on costs. The driving feature there of the increase is about key activities that we have planned. We can't be certain that all of the trials go at the rate that we expect. There will be some programs, some activities which are either accelerated or decelerated because of the way that they are going. That's why there's a range out there. It really isn't related to sales. It's about activities and just giving a sensible range of potential outcomes at this stage.

Angus Russell - *Shire Plc - CEO*

Yes, I mean, for instance, Graham, we talked already about the new indications for VYVANSE. I said in my introduction that we are going to be having discussions at the beginning of the year or the first half of the year with regulators. That's what we told you when we headlined these results. That's a classic case in point. We can't predict the timing of the start of those. They are penciled in -- put it that way -- for a second half, assuming it will take the first half. But Mike and his team will have to have those meetings, see where they end up with FDA, and then that will determine both the shape, cost, and timing of starting those studies. That's just a classic case in point. So we have to make those kind of assumptions and build that in, and that's why it's not a precise art. It makes those sort of estimates. So Sylvie -- (Multiple Speakers)

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

Yes?

Graham Parry - *Merrill Lynch - Analyst*

I'm sorry. So it's fair to say then that most of the variability is in R&D as opposed to SG&A?

Angus Russell - *Shire Plc - CEO*

It's on both actually. Because in the SG&A side, we got very significant programs going in developing IT programs, which have a P&L component as well. But, a large part of the swing, yes, your right is in R&D.

Graham Hetherington - *Shire Plc - CFO*

There are other launches, remember? So go back, Graham, to looking at the back of the pack what I went through in terms of new launches. So, we got Brazil coming up. But these are all planned. We've got FIRAZYR in the US. All of these things we are

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assuming we've given you the kind of rough timelines. But again, they're not absolutely sort of cast in stone yet. And something like FIRAZYR will be again dependent on the six-month review with FDA.

Sylvie Gregoire - Shire Plc - President, Human Genetic Therapies

And, Graham, you were asking about the growth, whether the guidance included some growth on the HGT products such as REPLAGAL and VPRIV. So, on REPLAGAL, yes, we do anticipate some growth of that product in 2011, and in the same way that I talked about it, it will mainly be driven by, I guess, the naive patients that come on to therapy, and you can have an estimate of what that -- how many naive patients come per quarter. If you look at last year our presentations throughout the year, we kind of highlighted to the proportion of patients from the growth of the market for REPLAGAL, which ones claimed from the naive group. And so those patients we anticipate taking.

But, if you look at that market potential growth based on last year's figures, you can see that when I say we can add 300 patients as of now of REPLAGAL throughout the year 2011, that that number would be able to cover sort of this demand that one would see from the naive market. And it is from our existing facility that we can cover this.

And so, having the approval of the new facility in Lexington, we just add flexibility and improve our ability to move around production of the purification from one plant to the other.

From a VPRIV perspective, of course, the competitor being back in the market throughout the year and as of the beginning of this year, we would imagine potentially the market dynamics to stabilize, and growth from the patients certainly that are now coming around full year this year, you'll see growth in the numbers and in the dollar numbers for sure. And then we can still add 200 patients on VPRIV this year. So, there is -- we certainly have -- we are not capacity limited in terms of the potential growth of product throughout the year. But, of course, it is the new facility in Lexington that will allow us to significantly increase our potential to make both of these products in the future. But for this year, we can anticipate having enough capacity to cover both the growth of these products.

Graham Hetherington - Shire Plc - CFO

And then just on the guidance and whether the plant is in there, I mean clearly you have been saying start-up is underway where we're in the throes of commissioning the plant with both VPRIV and REPLAGAL. So, you can imagine, Graham, there are costs baked in this year for commissioning the plant, getting it up and running. But, Sylvie, any assumptions about upsides on revenue because of the plant? Is that in the guidance that we gave out? I don't believe it is.

Sylvie Gregoire - Shire Plc - President, Human Genetic Therapies

No.

Graham Hetherington - Shire Plc - CFO

So, there you are. Affirmation, Graham, there's nothing in the guidance in terms of assumption of revenues at the moment, any upside from being able to have extra quantities of VPRIV or REPLAGAL. But there are costs in there because we are up and running on the plant. We're producing material off REPLAGAL certainly at this stage and commissioning batches now on both products. So, the cost is in, but no revenue.

Operator

[Graham Bardot], Barclays.



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Graham Bardot - Barclays - Analyst

Thanks very much. Just wondering, on the ADHD market, there will be a cheaper version of Concerta launched midyear with an authorized generic. Do you foresee any impact on market dynamics in terms of volumes or pricing for VYVANSE as a result?

And secondly, I know it's not your study, and we're all waiting for an update from the FDA and the AHRQ about the release of their findings, and it doesn't sound like there's been any update, and there is still Q1. But I just wondering if you've heard anything in terms of timing on that or on the other study being conducted by the University of Pennsylvania group? Thank you.

Graham Hetherington - Shire Plc - CFO

Let me deal with the second one, AHRQ, we have no further update. We have no dialogue with the FDA on that. That's an industrywide study. It's not likely that they are going to talk to one player as such in the space. And so, we've got nothing more in terms of timeline in use. So to reiterate, the latest view was end of the first quarter this year. That is almost probably a full year away from when the initial idea was publishing this.

So I think it's interesting. I said it last time and I will say it again. Because there has been obviously another approval given to VYVANSE in Canada now through adolescent and ADHD. Those that remember the history of this concern around cardiovascular events all started in Canada and then spread back into the FDA announcing they would do this very long-term matter analysis.

So, it's interesting to me that in the last few months we've both been given an expanded label on VYVANSE for adolescent, and now in Canada we get an expanded label to cover not just adolescent but adults as well.

If there was something significant, I mean this is, if you want to call it me just postulating, but in my experience that would be great strange of regulators to give those expanded labels if they had any kind of serious concern certainly around the use of VYVANSE. So, that I would say is at least an encouraging sign, and we'll await to see what happens at the end of the first quarter this year.

The Penn study, we are not associated with in terms of anything to do with publications or whatever. Clearly there's been nothing published formally yet. I think all we know is that Penn are trying to do that. We know no more because I say, it's their study, not ours, and we are not involved in the publication or the process of getting it published. You'd need to talk about talk to Penn about that.

Concerta, Mike, perhaps you want to give an idea that maybe that won't be as cheap as some people fear, if you might run people through that.

Mike Cola - Shire Plc - President, Specialty Pharmaceuticals

Yes, Ken, I will just add to Angus' point that -- what was I going to say -- I will move on to Concerta. Concerta AG will be coming in the market this spring, but, again, I don't think it's going to be as cheap as everyone is concerned about. They've been taking very aggressive price. If you look at the top 10 price movers over the last year, Concerta is in that and top of the pack. So whatever discounting is done off of that price, I still think it will be quite expensive and most likely still well above VYVANSE.

The only other thing I would add to Angus' comment on AHRQ is that ADHD treatment guidelines came out over the last six months, and I actually think they really validated the value of stimulants in the class. And, I don't know that they would be coming out with treatment guidelines like that if they really had safety concerns.

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So they are only guidelines again. They're not actually policy. But, in fact, they are on the website. You can read them. I think they are pretty good for the whole class of drugs.

Angus Russell - *Shire Plc - CEO*

The FDA website you're talking about?

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

That is on the AHRQ.

Angus Russell - *Shire Plc - CEO*

Just to make it clear for people, yes. So it's a great point. Thanks for adding that. I had forgotten that has been a further significant development as well, which speaks to what you just said.

Okay. Operator, I will take one more question in the interest of time. We been going over an hour now. So let me just take one final question, and then we will wrap up.

Operator

Frank Pinkerton, SunTrust.

Frank Pinkerton - *SunTrust - Analyst*

Thanks for taking the question, and I will try to sneak in a couple.

The first one is, can you speak to the sustainability of the 3TC franchise? And then, following your comments on the ADHD pipeline, was it possible to run combination pills to put INTUNIV in combination with VYVANSE or another product if it does get this approval in February? And then finally, Angus, I've asked in the past about board directors and turnovers. It looks like the R&D hiring has been pretty robust over the last year. Does that mean that Shire is much more internally focused now, and we should see the internal pipeline with business development being secondary? Thank you.

Angus Russell - *Shire Plc - CEO*

Let me deal with that last one maybe first, and I might at least kick off the 3TC thing as well as others can add if they want. And then, Mike, I'm sure we will take the ADHD/INTUNIV combination question.

I wasn't sure about Board of Directors relating unless you're using that as -- you did ask me a question, Frank, I remember, on that about the high turnover. That was the timing of certain directors coming to the end of their contracts and time on our board, and I'm delighted to say, we've got tremendous additions to the board, people with, as you know, a lot of experience in this industry, a lot of experience internationally. They have run big international pharma companies, and with the existing members of the board, I think that gives us a really high-quality board that's giving us great value and advice at what is a critical time for the entire industry now in terms of where the industry heads in the future.

In terms of R&D, yes, we've made some great hires there recently. I mean we don't publish those internal hires. Maybe some of those are out in the street, but certainly Jeff Jonas or maybe we press release them. Yes, we did. I'm getting a nod from Mike.



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So, as you know, we've hired Lawson Macartney, many people know who was in GSK. He's going to head up our Emerging Business unit group, which will mainly operate now out of the new Nyon facility in Switzerland. And then, also, we just bought in a senior ex-Abbott person. He will be running clinical development in the specialty side of things. We also had Phil recently join us in Sylvie's business in HGT and is running then -- has moved quickly into getting up to speed and bringing a lot of value already. So we have some high quality.

And to your answer, it doesn't mean no at all. We are certainly not abandoning our M&A strategy. We continue to do bolt-on acquisitions, continue to look for new opportunities to potentially push into new areas that fit our business model.

I think like most companies it's a mix at the end of the day. It is a blend. What I would say is that Shire has evolved over time. We have actually established more of an earlier stage capability. We still assume, if you like, complete blue sky discovery research. So let me just try and differentiate that and spend a moment as I think it is an important thing about where we are all heading in the future.

It's very clear, as I said in my round-up comments on the presentation, that we're moving into a world where payers, patients, everybody is going to demand real value from this industry. So, let me say something very kind of bold but very clear is, the world of marginal improvement and "me too" drugs is over. And if you don't realize that yet, you're going to be in serious problems in the next few years.

So the world of clear invention, bringing clear benefits to patients and physicians, more importantly bringing real value to payers is going to be the mantra or the real thing, the standard you have to meet, the new standard.

I think Shire has a great track record of doing that already. We stressed off in our business model being based, and that's why you've heard us saying that maybe the significance of that has been missed. But in a world that demands those kind of standards, I think having a business model that focuses on real symptomatic diseases and chronic conditions where you've shown physical changes in patients that both they and the physicians can see and most important importantly the payers see a real benefit from savings that come from treating those people effectively, you know, that's what you get paid for, and that's what you will increasingly only get paid for in the future. So, we have to gear up, and we have to get a competency and a capability that allows us to do that.

I think of our world very much as being one of platforms. We have platform technologies in Shire that we've leveraged multiple times. In the past, that was simple kind of proprietary oral drug delivery that produced CARBATROL, Adderall XR and then INTUNIV -- three, as you know, great drugs for Shire. Two or three of them are still there and going on very strongly still.

And then we moved into the world of HGT five or six years ago, a platform that has seen us bring REPLAGAL, VPRIV and ELAPRASE to the market off that platform. We have a platform with FIRAZYR. You've only seen FIRAZYR, but we have other drugs that may come through our earlier stages and be new treatments leveraging the peptide technology and the knowledge we came with that business in R&D.

Most recently -- and that's why I stressed it again in the press release -- you've seen us get two more potential platforms -- Movetis with their knowledge of that GI space, and then the work we're doing on intrathecal delivery. That would be unique. If that works -- and we pointed it out on the last call -- by the end of this year, we may be able to start assessing whether that's having a real clinical benefit. We're in, as we said, three sets of human studies in three different diseases. Sorry, two different human studies in two diseases. But we're going to address a third one shortly with that same technology. And, basically, that and the Acceleron partnership have the prospect of establishing more technology platforms, which can be leveraged multiple times.

So once you have those proof of concepts, the point is, it becomes slightly lower risk to then leverage known technology. That's the bit we're focused on is trying to develop these new platforms, not just going straight in with a compound that's never been used and a disease where it has never been treated. Those are kind of different blue sky, and as I say, we are still not wholly into



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that kind of side of things where we're really focused on these platforms very much in ways we can invest in sensible early-stage ideas. So you will see us do more of that.

M&A, though, still a big part of our model. We will continue to be very active as we've always been in the M&A space, and with business development, I often say it's not an event for us. It's a process. It's part of our everyday life. It is part of our business model.

So with that, let me just say 3TC. I said I would cover that a little bit. 3TC is an amazing drug. I mean I always call it the drug that always keeps on giving. It is a tremendous drug. You know, HIV has been an interesting world the way it has evolved, and many forecasted long ago -- maybe five or more years ago -- the new treatments would completely displace 3TC.

What we have tended to find -- and you know that as most of the HIV treatments are cocktails of products and those cocktails have tended to add on top of 3TC. And because of that, 3TC has remained very much a benchmark and gold standard of many regimens and many forms of treatment for HIV.

Obviously we are not the commercial arm in this. If you have very direct questions about the developments of the markets and the prospects, probably better go and ask our partner GSK, but certainly, as I say, from our perspective, we know enough as being their partner and inventor of the drug to know to say, it's a tremendous product that's held up with a great side effect profile. That's what's kept it there for so many years. Many of these other drugs have toxicity, and they can't be tolerated over long periods of time. 3TC can.

So, it is in decline, but it's, as Graham indicated, with other things coming in and 3TC on somewhat of a decline, we are still only seeing sort of relatively slowish decline in the royalties line of 10%. That was in the guidance. That is what is leading to that outcome.

So with that, let me just hand over to Mike on probably hopefully the final answer, ADHD and INTUNIV in combination, whether we will ever go to a combination.

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

Yes, Frank, just real briefly, the study that we did and hopefully the label that we get will be about adjunctive therapy to stimulants, which are the gold standards. So, just so you know, it wasn't just VYVANSE that INTUNIV was studied with.

We are looking at the whole idea of a fixed dose combo. But it's tough. It's tough to make it work, and you have a fixed dose titration on both products, and then to study the permutations of all of those fixed doses is not easy, particularly when you have to study each drug separately, and then you have to study them together.

So, we're looking at it. It's a good part of the market. It's the fastest-growing part of the market. It's growing in 20% plus this adjunctive therapy. But we will see. I think it's going to be hard for us to make the numbers work for this to be a good investment.

We still like the area. We can still promote it in combination with VYVANSE, but I don't know that we will actually create a set of pills to make that more convenient.

Angus Russell - *Shire Plc - CEO*

Okay, Frank. So, with that, I just wrap up by saying again I hope you agree with us that 2010 was a great year. Outstanding performance, as I said, before. A landmark for us with going over \$3 billion of product sales in this very young and vibrant new portfolio of drugs. One that delivered growth in EPS this year of -- past year of 21%. Not only have we exceeded our aspirational targets 2010, but, as how you got clear indication of our guidance on the call for 2011, we were able to continue to meet our



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aspirational growth target for 2011, and we have every confidence that we are well on track now to hitting that aspirational growth target. But, as you know, we extended out there until 2015.

So, with that summing up, I wish you all a very good day, and we look forward to talking to you all again soon. Thank you.

Operator

Thank you. Thank you all for joining, ladies and gentlemen. That concludes your call for today. You may now disconnect.

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