

FINAL TRANSCRIPT

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SHP.L - Q4 2009 Shire Plc Earnings Conference Call

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CORPORATE PARTICIPANTS

Clea Rosenfeld

Shire Plc - Director, IR

Angus Russell

Shire Plc - CEO

Graham Hetherington

Shire Plc - CFO

Mike Cola

Shire Plc - President, Specialty Pharmaceuticals

Sylvie Gregoire

Shire Plc - President, Human Genetic Therapies

CONFERENCE CALL PARTICIPANTS

Frank Pinkerton

SunTrust - Analyst

David Evans

JPMorgan - Analyst

Gary Nachman

Leerink Swann - Analyst

Alex Blakely

Sanford Bernstein - Analyst

Mesha Deerman

Piper Jaffray - Analyst

Matthew Weston

Credit Suisse - Analyst

Tom Russo

Baird & Co. - Analyst

Graham Parry

Merrill Lynch - Analyst

David Steinberg

Deutsche Bank - Analyst

Florent Cespedes

Exane BNP Paribas - Analyst

David Buck

Buckingham Research - Analyst

PRESENTATION

Operator

Good day, ladies and gentlemen, and welcome to Shire's 2009 full-year and fourth-quarter results hosted by Clea Rosenfeld. My name is Kevin, and I am your event manager. (Operator Instructions). I would like to advise all parties this conference is being recorded for replay purposes, and now I would like to hand over to your host, Clea Rosenfeld. Please proceed.



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Clea Rosenfeld - *Shire Plc - Director, IR*

Thank you very much, operator. Good morning and good afternoon, everyone. Thank you for joining us today for Shire's fourth-quarter and full-year 2009 financial results. By now you should all have received your press release, our press release, and should be viewing our presentation via our website on shire.com. But if for some reason, you have not received the press release or are unable to access our website, please contact Souheil in the UK Investor Relations department on 44-1256-894-160, and she will be happy to assist you.

Our speakers today are Angus Russell, Graham Hetherington, Sylvie Gregoire, and Michael Cola. Before we begin, I would refer you to slide number 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 could materially affect our results.

Today's agenda is as follows. We begin with opening remarks of Shire's performance and highlights from Angus. Then Graham will continue with the financial review. Mike will follow with a real of our Specialty Pharma business performance, and Sylvie Gregoire will update you on the latest developments of our HGT business. Angus will then summarize the key points for this presentation, and we will then open up for Q&A. As always, we are requesting please that you ask a maximum of two questions -- not a minimum -- so that everyone gets the chance to ask their questions. As always, Eric and I will be more than happy to follow-up offline for any subsequent queries or clarifications.

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

Angus Russell - *Shire Plc - CEO*

Thanks very much, Clea, and good afternoon or good morning to you all. I'm just going to turn to slide five, the opening slide. It is headed excellent results in a Transformational year, and I think for us, as you know, 2009 was both a challenging but ultimately transformational year for Shire. Our core product sales -- and, as you can see from the footnotes on this slide we define those to be our sales, excluding ADDERALL XR -- those product sales were up 25% to over \$2 billion at \$2.1 billion. They were up 28% on a like-for-like basis at constant currencies.

In Q4 2009 these core product sales were actually up 36% versus the same quarter in 2008. Full-year 2009 non-GAAP diluted earnings per ADS were \$3.49, and Q4 2009 non-GAAP diluted earnings per ADS were \$1.11. These results, I believe, also show that we are clearly leveraging our existing infrastructure very effectively. We have decreased our full-year SG&A expense versus 2008. Also, cash generation has been very strong in the year, up to \$921 million.

So turning to the next page, I just wanted to take a step back from today's results and talk a bit about what underpins these kinds of results. For me I believe the success comes from our very focused business model, and this has been key to our success. Our business model, I will remind you, is the focus on Specialty Biopharmaceuticals, the treatment of symptomatic diseases where we can use small sales force to build very strong relationships with physicians and patient groups, and our focus on lower risk projects with relatively fast development timelines and strong IP protection.

On the right-hand side of your slide, you can see the kind of success that has resulted from this business model over many years now. I remember that we first came out with our aspirational target in 2003 where again we talked about the opportunity of growing our business by 15% both top and bottom line. And here you can see, if we measure now the seven-year period from 2003 when we first came out with those kinds of targets to 2009, you see that our revenues grew by 190% or compound average growth of 16%. And our EBITDA was up 169% or 15% compound annual growth. So we actually did deliver on those promises.

Turning the page to the next slide, we believe this strategy will continue to deliver. This is a strategy I break down into these five different boxes. We are primarily focused on our patients' needs. VPRIV, or velaglucerase alfa as it was formally known, and



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REPLAGAL currently address very high unmet needs in a period of some shortage of treatments for these very rare and debilitating diseases. We have been very happy to be able to step up and provide these patients with alternative treatments.

We are also launching further new products. INTUNIV was just launched, as you know, last November and is the first and only selective alpha-2 agonist indicated for the treatment of ADHD.

Acquisitions and geographic expansion will continue to play a major part of our growth over the next few years, but already we have rapidly expanded our geographical presence into 28 countries, and we have other countries that we plan to move into during 2010 and beyond.

The acquisition of EQUASYM also facilitates our immediate access to the European ADHD market, and beyond that, we have other global filings for VYVANSE and in time other drugs in ADHD.

We also have great pipeline opportunities for future long-term growth. We are continuing to progress many programs in development, including programs for anti-thrombotic treatments, CARRIERWAVE technology, early-stage HGT research, and new technologies such as the collaboration recently with Santaris.

We continue through all these periods of time to actually sustain our financial performance, and, as I said, whilst in history we had an aspirational target to grow midteens, which we readily achieved, we continue to have that same aspirational target going forward beyond the end of 2009 where, as you know, we aspire to grow our revenues on average by midteens through the periods 2015.

So with those introductory remarks, let me now past over to our CFO, Graham Hetherington, to take you through the financial results in more detail.

Graham Hetherington - *Shire Plc - CFO*

Thank you, Angus, and good morning and good afternoon. Today I will be covering first the 2009 EPS. We delivered ahead of expectations. Second, the growth dynamics of our core product portfolio. Third, the operational leverage developing from this new business, and fourthly, to underline the key dynamics that will support our growth into 2010 and beyond.

So first, looking at chart nine, our EPS was by any definition toward the top end of our guidance range. At \$3.49 in 2009, our EPS was 10% down on 2008, but significantly is 23% up on our 2008 EPS result.

One key item we have not included in setting our long-term long-standing guidance framework was the potential change in best estimate for ADDERALL XR Medicaid rebates. Our fourth-quarter results did benefit by \$0.32 from this change, and I have excluded this change in the second box here on this chart. This is a variable that I flagged at the third quarter. You will recall that we have effectively been booking zero net revenues for sales of ADDERALL XR through Medicaid in the US. This was not sustainable and did not reflect the actual economics of these sales. We are now confident that movings providing for these rebates based on the invoiced amounts from the states is now the right approach.

We also had a strong fourth quarter without this, which I have highlighted in the third box. Most importantly, the year-on-year rate of growth of our portfolio of core products exceeded expectations.

ADDERALL XR was a very uncertain variable all the way until the end of the year, and we ended up with stronger than expected product sales and royalties. These both help to offset increased R&D and SG&A spending in the quarter behind some of our key new products.

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On chart 10 you can see how the fourth quarter contributed to our full-year performance. EBITDA for the full year was just 5% down on 2008, and this reduction is a result of the loss of the incremental percentage margin that ADDERALL XR was contributing through 2008.

As you can see, our total revenues were flat on the year, an exceptional performance in a year where our number one product lost exclusivity. And chart 11 breaks out our revenue in more detail.

Our core product portfolio is now our core value driver and was up 36% in the fourth quarter, driving a 25% year-on-year growth for the full year. The performance from the core portfolio reinforces the strength and momentum of our business.

You can see that the impact to foreign exchange on our revenues also became marginally positive in the fourth quarter, although for the full year, growth at constant exchange rates of 28% exceeded reported growth by 3 percentage points.

Royalties were boosted by the receipt of royalties from Impax in relation to their authorized generic version of ADDERALL XR. I have included a detailed analysis later, but we estimate that 75% of this royalty related to initial stocking of the wholesaler and retailer channel.

One statistic I would like to pause on is total revenues. In the year in which our historically largest drug faced generic competition, our total revenues of \$3 billion in 2009 were in line with the \$3 billion we recorded in 2008.

As I said earlier, this is an outstanding result, and I would like to move on to chart 12 which highlights this.

In 2008 ADDERALL XR generated \$1.1 billion of net revenues. With the actions Mike and his team put in place with managed care providers and state Medicaid agencies, we successfully limited the loss of product sales in 2009 to just short of \$0.5 billion. This is partially offset by the receipt of royalties from the two authorized generics. Most significantly, we generated over \$400 million of additional product sales growth from the balance of the portfolio.

Chart 13 reinforces my second big point -- the strength of our core product portfolio. We have delivered a growth of over 25% across this portfolio. And if we annualize our fourth-quarter sales, we now have six products, which are each delivering or very close to delivering annualized sales of over \$200 million. This is a real reinforcement of our current portfolio strength to which we are adding FIRAZYR, INTUNIV, and VPRIV.

Mike and Sylvie will be talking you through some of the growth dynamics behind these brands, but in the meantime I will reinforce that this performance is after backing out \$38 million of launch sales of INTUNIV.

Chart 14 further demonstrates the strength of our portfolio, our core value driver. We have invested significantly in building this portfolio over the last few years. It has nearly doubled in size over the last two years, and the growth has been consistent. This group of products, which generated half of our product sales in 2007, generated over 75% by the end of 2009. The pie on the right reinforces the balanced portfolio we have developed.

Turning to chart 15, the decline in ADDERALL XR has never to be distorted our overall financial ratios in relation to R&D and SG&A during 2009 and is masking the underlying operational leverage we are already achieving.

During the year we increased our dollar investment in R&D by 10%. This accelerated in the second half because of our increased investment behind ADHD in Europe also on diverticulitis for LIALDA. We have also invested in supporting the accelerated filings for VPRIV and REPLAGAL that Sylvie's team has been achieving.

We successfully managed the 3% reduction in SG&A in the full year. We did, however, see SG&A increase year on year in the fourth quarter. About a third of this increase over the quarterly run-rate in the first three quarters related to one-off items in the



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fourth quarter, but we also increased sales and marketing spend behind new products, particularly the launch of INTUNIV and the integration of EQUASYM.

In addition, we have ramped up commercial costs targeted at optimizing the opportunities for VPRIV and REPLAGAL. This resulted in combined R&D and SG&A as a percentage of total sales increasing only marginally year on year for this really masks the operating leverage we are generating over time. If you look at the same ratios on the bottom of the chart based on our core product portfolio, you can see a 4 percentage point improvement on R&D and a 16 percentage point improvement on SG&A. This reinforces the trends we expect to deliver over the next few years.

Before I move on to looking at our outlook for 2010 and beyond, let's recap on our strong cash generation through the year on chart 16. We generated a further \$250 million of cash in the fourth quarter, taking us to over \$920 million in the year. This strong cash generation has funded significant capital expenditure in 2009 of just over \$250 million, particularly on the expansion of our HGT manufacturing capability. I expect us to be investing at this sort of level again in 2010 before it falls to more normal levels after that.

With the net cash inflow in the year of \$285 million, we now have \$0.5 billion of cash, and with that our only significant borrowings are the \$1.1 billion convertible. We have an unused \$1.2 billion facility and no refinancing 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.

Turning to chart 17, there are a number of dynamics that underpin our expectation that reported non-GAAP EPS will grow in 2010. And to be clear, that is reported, i.e. the \$3.49 level that we had planned to grow from.

Let's take a look at ADDERALL XR, first. As you can see on the left-hand side of the chart, XR has the potential to generate ongoing revenues. This chart now includes both product sales and royalties. The macro assumptions that support this are firstly our increasingly strong assumption that the Citizen's Petition will hold through 2010, and second, that the states continue to invoice for Medicaid rebates at current levels.

On the right-hand side of the chart, I have tried to help with the detailed dynamics we are likely to see as we move from the fourth quarter of 2009 into 2010. There is more backup in the appendix slide 40.

To date the second authorized generic from Impax has almost exclusively been taking share from the other generic, but we should assume that there will be further erosion of the brand in 2010.

In the fourth quarter, we saw the sustained demand for branded XR due through an additional \$23 million of wholesaler inventory. But we are expecting to see reductions of inventory going forward as demand has eroded through 2010.

Sales deductions were distorted in the fourth quarter by the change of best estimate from Medicaid rebates. As I said earlier, we have been booking rebates at around 100%, so we were not recognizing any contribution from Medicaid XR sales. We're now booking rebates at the 75% level at which the states have been invoicing through this year.

As we move through 2010, we will see an increasing proportion of our product sales of XR coming through contracts and managed care and Medicaid in 2010 than in 2009. These attract high levels of rebates. This will lead to gross to net deduction levels in 2010 of between 60% and 70% compared to the underlying level of 55% that we have seen in the last three quarters of 2009.

Finally, XR royalties. In the fourth quarter, we benefited from \$52 million of royalties from Impax, of which we estimate around \$40 million related to pipeline fill, which will not be repeated in 2010.

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Let's look at the core business on chart 18. The key message is that supported by the dynamics I have just been outlining we expect to see growth in reported EPS in 2010 compared to 2009 and again to confirm that is against our \$3.49 EPS that we reported. This is despite having to absorb the inevitable down first quarter when we will be comparing to 2009's first quarter, which was the last quarter before XR faced generic competition.

Foreign exchange rates will remain a variable. That said, our most significant exposure is the Eurodollar rate, and I have updated the simple Ready Reckoner we provided last year at the bottom of the chart. We are still a dollar reporting company generating over 70% of our revenues in dollars. So the sensitivity for Shire to its earnings is limited, and we will keep you updated throughout the year.

Our expected growth in EPS will be delivered by continued significant growth from our core product portfolio, which has the potential to accelerate as we gain more traction and visibility from new product launches. This growth should offset the further reductions in 2010 XR revenues in the full year. Royalties will benefit from the ongoing Impax royalty, but this will be more than offset by the ongoing decline of other royalties.

Gross margins, which ended the year at 86%, should be at a similar level through 2010.

As we have seen, there has been an uplift in our R&D investment in the last two quarters, supporting the progression of our pipeline, and these investments will also continue into 2010.

As I mentioned earlier, SG&A increased in the last quarter. While some of this was one-offed, we are planning some targeted investment in SG&A during 2010 to support the fast-growing core business and increased internationalization of our business. This includes the strengthening of our operations outside the US, including the establishment of a mainland Europe international hub. Taken together I could see R&D and SG&A dollars increasing by between 5% and 10% year on year.

Finally, our tax rate, which I currently expect to be in line with the level in 2009.

Before I hand you over to Mike, on chart 19 I would like to recap on the significant drivers of growth and value in 2010 and beyond. First, the sustained growth from our core portfolio, which is now being supported by new product launches. Second, we will be able to continue to leverage our existing infrastructure. We have demonstrated our ability to proactively manage our cost base, and I have outlined the emerging operational leverage that we will benefit from in the future. Finally, we will continue to invest in developing our pipeline.

I will update you on all of these dynamics throughout the year. Mike?

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

Thank you, Graham, and hello, everyone. We are all in slide 21, Specialty Pharma key highlights 2009.

As Angus said earlier, this was really a transformational year for us. If I think back a year ago when we sat here on this call, there was a lot of skepticism as to whether we would be able to transform in 2009, particularly with the loss of exclusivity on XR and our ability to grow VYVANSE sales. A lot of concern about potentially therapeutic substitution, loss of managed-care status, etc., and I'm happy to report that we have made it through that period, and, in fact, we have performed quite well with VYVANSE, which I will walk you through briefly.

As you know, we've gained FDA approval for INTUNIV we launched in November. It is early. I will walk you through what early statistics we have. Again, last year we initiated the VYVANSE non-ADHD programs, which we think brings new opportunity to the brand, and you should be seeing data by the end of 2010 and early 2011.

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2009 also saw us make a commitment to Europe both for the development of VYVANSE for the European markets and also an early start with the acquisition of EQUASYM, to really learn the market, to get there, understand the KOLs, understand the unmet need, and that has gone quite well.

Also in 2009, we approached almost \$0.5 billion of sales in our G.I. portfolio. We don't talk that much about it. It just keeps ticking along. They continue to make great progress with LIALDA while maintaining our PENTASA brand.

And finally, throughout this year you're going to hear about the programs that were started last year in our early stage pipeline around CARRIERWAVE and specifically 535, which is our anagrelide analog, and I will touch on them briefly at the end of this presentation.

Slide 22, VYVANSE performance at the top level between 2008, 2009. Net up of 58, script volume up 65%, good performance. We ended the year at 13.3. We had a nice January, a 0.3 share point gain to 13.6. I think we are off to a good start for the year.

The market continues to grow strongly, similar to what we have seen over the last year. At 9.2% it is a very robust market, and it is, as you know, mostly driven by the adult market, which has been in the high teens, low 20s. We, along with our colleagues at GSK, I think have done a great job of building awareness, particularly in that adult market, getting that market to grow robustly. 2010 and beyond is really about capturing a disproportionate share of that market growth.

If you move on to slide 23, a quick update on the INTUNIV launch again. It is really too early to start to share a lot of data with you. You have seen our weeklies running at 1.2 for the week of February five. We are quite pleased with our progress. The people who really lead this market, adult -- I'm sorry adolescent and child psychs -- are really leading the way with INTUNIV. That is a good sign as they are generally the early adopters and drive adoption of products in this market.

We have about 7500 physicians that are currently prescribing, and that is growing daily. And we continue to make progress on our formulary status. As you know from VYVANSE, we have an approach where we get the product in the market, we grow the share, we get advocacy from both patients and physicians, and then we sit down generally with the payers and discuss formulary status. I think it worked out quite well for us on VYVANSE. Again, I think we have a unique value proposition for these plans with INTUNIV, and I think we will do well over the course of this year with our payers.

Move on to slide 24, selected opportunities in our portfolio that you will be hearing about throughout the year. We have had some questions about INTUNIV and its lifecycle. I think we currently -- we have not really highlighted the fact that currently we have a very important study that should be on display at ACAP in May. It is Study 310. It is our combination study with all the major stimulants. We think it really will optimize therapy for our patients. It will give physicians tremendous flexibility between the stimulants and INTUNIV, and it also will provide them confidence to do nighttime dosing. Nighttime dosing we think reduces the somnolence and sedation side effects you see the first two weeks with INTUNIV. So that is an important study for us. Look for that to be coming out sometime in the May timeframe.

VYVANSE non-ADHD again started last year. You should be seeing these studies read out end of this year, beginning of next year. Adjunctive therapy in depression, cognitive impairment in depression, and negative symptoms of schizophrenia are the three major ones. You also see at least one other additional indication started this year for VYVANSE.

Finally, on globalization of the ADHD portfolio, we continue to make a large investment in Europe. If you think about our biggest investment in ADHD over the next couple of years, it's really building our European base over the next two years in anticipation for the VYVANSE launch. While we are doing that, we are also expanding the global footprint for VYVANSE with the launch in Canada this year and the filings that are under review in Mexico and Brazil hopefully with approval end of this year, beginning of next year.



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Also, LIALDA, we continue to work our diverticulitis trials. We think that is a great opportunity for us. There is a note out there today that you may want to look at if you want to learn more about diverticulitis. I think it describes the opportunity for Shire with LIALDA quite well.

Turning to slide 25, progress in the pipeline. Just a little more color on these programs. 535, which is the follow-on disaggregate, the platelet lowering product that actually eliminates the PDE 3 inhibition which creates cardiotoxicity, is underway and doing well. We have our multiples ending dose Phase I study finishing up, and we should be able to talk about that data in a way that is very clear by the middle of the year. Obviously our first proof of principle program is limited to a really well-defined indication, thrombotic complications in AV grafts. But obviously if this product works and you can reduce thrombosis without increasing bleeding time, it has much broader utility, and that data should be available mid-2010.

And CARRIERWAVE we continue to make progress on CARRIERWAVE. Again, we are very much focused on ADHD in pain right now with CARRIERWAVE. The first products you will be hearing about in CARRIERWAVE are likely to be the guaifenesin-based products. We have a number of molecules in development. We actually have one in man today, and we hope to make a decision by, say, the middle of the second half of this year on which molecule goes forward. That would be for both lifecycle in the US and a new development in Europe. Also, pain, we have two products in man right now and data available mid-year.

And I will turn it over to Sylvie.

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

Thank you, Mike. Good afternoon and good morning, everyone. We're now on page 27, and I will give you the highlights for 2009 of the HGT business and talk a little bit about what we see coming to us in 2010.

And I will start with our currently marketed products and ELAPRASE for Hunter syndrome. This product has been on the market since 2006 and has grown since then nicely and again last year has grown 20% at constant exchange rate relative to 2008.

We continue to expect growth in 2010, mostly coming from the regions where the product is less well penetrated. So Latin America and Eastern Europe where our penetration is less than 50% in these markets.

Important to the future of ELAPRASE and the continued growth of the product and to support that is the Lexington Roller Bottle facility. You will recall that we built another facility in Lexington to accommodate long-term growth of the product and to support it, and it has been approved now in the EU in the first quarter and in January. And then we expect approval in the US or shortly between now and the middle of the year. And then, of course, this will allow us to support the long-term growth of the product.

FIRAZYR in HAE is now launched in 12 countries, including the five largest European countries. And recent market research indicates that FIRAZYR has nearly 100% awareness among physicians who manage HAE patients in these large countries. In addition, more than 60% of these physicians have now tried FIRAZYR at least once.

The physicians who have used FIRAZYR report that the product is delivering strong efficacy in clinical practice. So, as experience builds and that is positive experience, we expect the utilization rates to increase in 2010.

REPLAGAL in the Fabry franchise. There has been a lot of activity around that Fabry market, so I'm going to give you a bit of color as to how we ended 2009 so you can have a perspective as to how we enter 2010 in this market. REPLAGAL has been on the market, of course, over eight years in Western Europe and this year grew again at 16% at constant exchange rates relative to 2008. And in this market in general in the Fabry market, the growth of the market comes from new patients, patients that have never been treated that go on to therapy on enzymal patient therapy. So we have seen 60% of 2009 patients, however,



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grow in the fourth quarter with the majority coming from switches from Fabrazyme. And so that is a new phenomenon in the last quarter and, of course, directly related to the shortage supply of Fabrazyme.

The fourth-quarter revenue or the third-quarter revenue, therefore, increased at 26%. We, therefore, exited the market in Western Europe as leader, and, of course, that is self-reported data. There is no IMS data on these products. But we feel we ended the year last year at 44% of the market and now have about 53% of the market in Western Europe with REPLAGAL.

We have, of course, also made the product available in the US through FDA-approved treatment protocol and emergency IND treatment, and patients are enrolled in both of these programs in the US as well. We filed a BLA at the end of December last year, and we are awaiting confirmation of our acceptance of the file by the FDA within the next weeks or so. And, of course, we will make sure to update you when that happens.

The next page on page 28 is where we -- again, we decided that it might be helpful to you at this stage to have a bit more visibility on the number of patients or the dynamics of the market. And, of course, that is -- we decided to exceptionally give you numbers. So we have more than 300 patients that actually started REPLAGAL in 2009. And so this chart here shows you by quarter how many patients came on. And the light blue boxes show the net -- the naive-treated patients that come on to therapy. And so you see quarter one and quarter two represent the usual addition of patients in this market. Mostly naive patients come on board, and there is a little switch activity during that time.

However, as you can see in Q4, there is a dramatic increase in the number of new patients on REPLAGAL, and the vast majority of them come from switching from Fabrazyme. There is also, though, a nice increase in the naive patients since physicians tend to start the new patients now on REPLAGAL since there is the availability of that product as opposed to the competitor product.

And I wanted to point out that this trend that we see here in the fourth quarter we have continued to see in January of this year.

Page 29, we have also been able to progress our velaglucerase alfa program very quickly this year for Gaucher patients. We responded to demand in the market mid-year last year. And we filed and so we are happy to tell you about the commercial -- Angus and Graham have already mentioned it -- it is VPRIV, and it will be the name used in the US and in Europe upon commercialization.

So mid-year there was an acute shortage of the product, and the FDA asked us to help out and make the product available pre-approval in the US. And, of course, we have made it also available pre-approval in the rest of the world. And then we quickly took the results from our three Phase III studies and filed on these results, and these results, as you know, some of them were presented last week at LDN. They were the patients that were naive. There were children and adults in that study. The details -- the results of this study were presented last week, and physicians were -- the results were well received by physicians.

We also presented at LDN data on the low antibody rate of velaglucerase and the cellular uptake that is very rapid and efficient for this product.

There has been five years now of experience in the practice with velaglucerase based on the Phase II trials, and then I thought we would give you an idea of how many patients to date we have that in combination with the clinical trial patients and the early access program patients, and over 400 patients now have received VPRIV all-in-all around the world.

And just to give you an idea of the distribution of these patients, that represents about 10% of the treated Gaucher market in the US that has been treated with velaglucerase and 5% to 6% in Eastern Europe, and, of course, we have patients in the rest of the world and a significant amount of patients in Israel.

So we have submitted, as you know, the file, and we are awaiting decisions from the FDA out February 28, and we are in constant communication with them and expect no specific delays at this point. We have also submitted the MAA at the end of the year



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and expect a response from them in the third quarter of this year, and, of course, the manufacturing and clinical site inspections now in the US have been completed.

So we are firmly ready for launch, I guess, at this point, and so I would like to take this time now on page 30 to tell you about our commercialization strategy. We very much see our purpose to provide patients with access to life-altering therapies. And during the past year, we have been very happy to demonstrate our commitment to the Gaucher patient community by bringing forward our VPRIV program and providing the treatment in the US for no charge.

We are pleased that we have been able to help so many patients to receive treatment for their condition during these last several months, and really we are quite touched actually to have the many letters and messages that we have received from patients thanking us for our support.

And now that we're ready to launch our focus is no different, frankly. The patients' needs are at the forefront of our minds. And in determining our commercial strategy, we have carefully considered the input received from the physicians and patients in what they believe is a hurdle to access to treatment. And so, therefore, today we are announcing that we will price VPRIV at \$1350 per 400 unit vial. This offer is a considerable savings of 15% over Cerazyme. And, of course, we have plenty of supply to support patients that have already started on VPRIV and have ample supply to support several hundred more patients this year, and they can be assured that we will not have to worry about interruptions in their treatment.

In addition, as further ongoing commitment to help these patients, we are announcing that this year we will provide direct co-pay assistance to cover the first three months of out-of-pocket prescriptions for eligible patients in the US.

In 2011 we will continue to support patients in a similar fashion in that we will also plan to cap the out-of-pocket prescription costs for these patients at \$500 again for the eligible patients in the US. And, of course, we will not forget and will continue to provide significant support to the Gaucher and the NORD community through our support to patient associations.

I would also like to say that this program will start March 1, and patients on ELAPRASE will also be eligible for co-pay assistance this year and next year in the same fashion.

REPLAGAL, of course, we continue to focus on market growth and switch in the markets where the product is available, and we will continue to address the unmet needs in the US. Ongoing discussions with the FDA are going relative to the filing that we have made, and as soon as we have a response from them, of course, we will let you know.

I've talked a lot about the programs that are near commercial or commercial today, but we're also continuing to focus in 2010 on our products in development. And on page 31 you will see the highlights of our programs that are going to make progress this year.

FIRAZYR, there is a Phase III trial, the Phase III trial to support US registration and the self administration trial that are ongoing, and studies are going to be completed this year, allowing us to file a complete response to the FDA by the end of this year and to also file for a labeling change for self administration in Europe.

An important program for us is idursulfase-IT for Hunter CNS. We are pleased to announce that we have dosed the first patient in that program, and, as you know, many of our products in our pipeline are enzyme replacement therapies to be delivered through the central nervous system. And so this is a milestone for us in our pipeline progress. So importantly, Sanfilippo A, which is a disease of the central nervous system for which there are no available therapies at all, also is meant to be administered through an intrathecal port, the same port that is being used in the Hunter CNS program, and the patient studies will start in the first half of this year for that population as well.

You have heard us talk about the MLD program, the metachromatic leukodystrophy program, and we have had some delays in starting our pivotal trial, mostly associated with difficulties in our contract manufacturing producing the enzyme there.



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However, we have taken advantage of that time to look at the longer-term impact on the patients that have already been in the clinical trial and will continue in treatment and looked at the peripheral nerve response, as well as through MRI, the central nervous system response to the enzyme delivered intravenously, and have found that there is probably a better way to bring better treatment to these patients via a central nervous system delivery of the (technical difficulty)-- that will more efficiently bring benefits to the patients.

And, therefore, we have decided to shift our focus from the intravenous treatment to the central nervous system delivery treatment, and studies are ongoing in preclinical studies in order to allow us to start human studies next year. We will also be starting studies next year with products made in our own facility with -- in a human cell line. So that is now called HGT-1110.

We have now got here on the slide a mention of our Krabbe program or our GLD program, which is also another central nervous system disease, that is in preclinical development and making its way. And, of course, ADHD research group, as well as the Santaris collaboration, we expect will continue to work on preclinical programs that will further our pipeline in the future.

The next page is an overview of where we are located in the world, and it is, of course, important to bring our treatments to patients all around the world. And through the HGT product line, we have been in a position to establish small but direct presence in 28 countries. Now this allows us to enhance our global presence of Shire around the world, and we will be able to announce FIRAZYR and velaglycerase to these local entities this year and, therefore, leverage these new sites.

As well, the Specialty Pharma portfolio, as it expands internationally, we will be able to benefit from these local presences that we have established.

Page 33, my last comment here for the HGT business is to talk about our capabilities and capacity that we have in manufacturing. So today just to recap we have manufacturing going on in Cambridge where we make ELAPRASE, velaglycerase and REPLAGAL, with REPLAGAL and velaglycerase made in bioreactors and in serum free containing media. We have just mentioned to you we have added a manufacturing site for Roller Bottles in Lexington; therefore, we now have two sites for manufacturing of ELAPRASE, which always reduces the risk in the supply chain.

And then what you see here is a picture of our large-scale manufacturing facility in Lexington. It will, as you can see, it is nearly completed. It is undergoing validation, and we will start manufacturing there in the middle of this year. This, of course, adds a lot of capacity, up to four 2000 liter bioreactors. These are profusion method bioreactors, using single use technology or disposable technology, which again reduces the risk of contamination. And it provides also, of course, an additional manufacturing site and ensures that we have enough capacity and the most modern possible capabilities to support the growth of our portfolio again for many years to come.

I will now pass the mic to Angus who will give us some closing remarks.

Angus Russell - Shire Plc - CEO

Thank you, Sylvie. So having heard from Mike and Sylvie a review of both of their performances for excellence in 2009 and the prospects for 2010 and beyond, I just wanted to turn to slide 35 and remind everybody that whilst we have great growth prospects for the future, and I think it's a very important differentiating feature of Shire, we have our aspirational targets that I mentioned at the start of the presentation out until 2015. Very often in this industry those kinds of targets are dependent on pipeline evolution and regulatory approvals. As we look at our long-range plan, we see that most of that growth comes from the eight key products that you see in the market today -- six of those at \$200 million of sales or more and the other two products in that group are well on their way to becoming more than \$200 million, too.

But beyond that, we have obviously a lot more going on in the pipeline as Mike and Sylvie just alluded to. And so on this slide you can see that will in our eyes lead to potential launches right from 2010 through 2016. Obviously Mike highlighted the



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continued internationalization of the ADHD pipeline going forward or products. We have FIRAZYR in its early stages of launch in our [W] markets, and then you can see in 2011 our expectation of getting a US launch for FIRAZYR. And then VPRIV will actually go out on a formal launch both in the US, but also in all of the international markets over the next couple of years. So still plenty of activity on the launch front for some years to come.

So turning to the final slide, 36, I believe what you have heard today is a story which shows a very solid foundation for future growth. And for me Shire is in the most robust shape it has ever been. We have delivered a very strong financial performance in 2009 with the core product sales excluding ADDERALL XR up 25%. Allied to that, we have had very proactive cost management, and that has helped us to deliver a very good earnings performance, too.

In addition, we continue to have strong cash generation, and that gives us a strengthening balance sheet again to further our aspirations to bring in more good assets now to our pipeline in the future. So, as I said at the outset, I believe the strategy is very evidentially delivering. Driving growth from a balanced portfolio of eight key products, the INTUNIV launch is off to a strong start, VPRIV is now available on a preapproval basis, and we are awaiting obviously the final decision from FDA in a few days time and we would hope to formally launch thereafter.

The REPLAGAL BLA was filed in December 2009 as planned, and again, we look forward to continuing our discussions with the FDA with moving towards what we hope will ultimately be a formal approval in the US market for REPLAGAL.

We continue to increase our global reach, as Sylvie mentioned, in 28 countries. A very different geographic picture now for Shire from just a few years ago, and we will continue, as she said, to add to what are some small operations in some of these countries. These will be added to with products and people over the next few years.

And we continue to develop and enhance and advance our strong pipeline, and this year there will be many opportunities in the next few quarters' calls to actually update you on the progression of what I believe is a very exciting future product pipeline in R&D.

So all of that gives us a lot of confidence in the Shire management team about our ability to deliver what is an aspirational goal, but one that we feel is readily achievable over the next few years from 2009 up to 2015 where we aspire to grow our sales in the mid-teens range on average year on year.

So with those comments, I thank you very much for your attention, and we are now available to answer your questions. So I will hand back to the operator to moderate the question and answer session.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions). Frank Pinkerton, SunTrust.

Frank Pinkerton - SunTrust - Analyst

Sylvie, can you start and please just talk about the patients that switched over? What do you expect or how can we think about potential switchbacks given what some doctors view as a different dosing range and abilities between REPLAGAL and Fabrazyme?

Sylvie Gregoire - Shire Plc - President, Human Genetic Therapies

So you're referring to REPLAGAL? I just want to make sure --

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Frank Pinkerton - SunTrust - Analyst

I'm sorry, yes. I'm sorry, REPLAGAL and Fabrazyme and the switches we saw in the fourth quarter, are there any expectations, or can you give us any guidance on what would be switchbacks?

Sylvie Gregoire - Shire Plc - President, Human Genetic Therapies

Well, we have not seen any switchbacks obviously, but the supply constraints on the Fabrazyme side have been announced I think until midyear this year. So I guess people will wait until switching back that product, the other product is available.

So there is not normally a lot of switchbacks from here. People when they are satisfied with their therapy don't normally switch back, but, of course, we expect that some amount of patients might switch back. But we currently don't know to which degree the switches will be. We just continue that January saw a similar pattern as we saw in the fourth quarter of last year that you saw in the slide.

Frank Pinkerton - SunTrust - Analyst

Okay. Great. And then, Angus, one for you. I know I brought this up to you a little while back, but can you just speak generally to the board? Two medical doctors, I think, have taken leave in the last couple of months, and what's the plans on replacing the board members and the focus of the board and the strategic plan going forward?

Angus Russell - Shire Plc - CEO

Yes, I think you are referring to -- let me just cover the reasons why just so we are all clear, so there's no any sort of red herrings going here. But Barry Price was the first person that you're referring to. Barry was a very long-term serving member of the Shire board. We thank Barry very much for all the input he has given us over very many years. Under corporate governance rules in the UK, Barry was seen to be well beyond his term of office, and it is a mark of the advice he has given us over the years that he stayed so long on the Shire board. But this year he indicated on personal grounds he was going to step down from the Shire board. So we wish Barry all the best in the future.

And then Michael Rosenblatt, who had recently joined the Shire board, was given a great opportunity to actually join Merck, where Merck were looking for a Medical Director, and obviously Mike fitted that bill very readily. And those of you that don't know, Mike Rosenblatt originally came from Merck. So in a sense he is returning to a management team there that he knows very well, and I think Dick Clark personally asked him to join the management team there at Merck. So again, we wish him well for the future.

So those are the circumstances. And you're right, Frank. It is of concern to the Shire board. We have a lot of medical expertise in the Company all the way up through, and we do have still Jeff Leiden on the board, and those that don't know Jeff is, a qualified medic, and he is vice-Chairman of the Company and again adds tremendous value to the Shire Board. He is actually the Chairman of our Science & Technology Subcommittee of the board as well.

But it's a good point, Frank, and the board is well onto this. Clearly Mike Rosenblatt's circumstances came about quite rapidly, and since then we have actually initiated a global search for someone with a medical background to add to what I say is already tremendous skill sets that we have from Jeff Leiden. But obviously Jeff is by himself there. We would like to supplement that.

Operator

David Evans, JPMorgan.

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David Evans - JPMorgan - Analyst

Firstly, on manufacturing capacities, for velaglucerase you are currently saying you're treating about 400 patients and could probably treat a few hundred more patients. So does this imply that the dosing, the current dosing, is at the bottom end of the range that you assume in your 300 to 600 patient range, or have you managed to increase the productivity for this product?

And then also reading across to REPLAGAL and given the limitations on Vela manufacturing, is your REPLAGAL Manufacturing reaching any kind of limitations? Should we expect your switching patients at any point to be limited by how much REPLAGAL you can actually manufacture?

And then the second question, just on core product sales growth, looking at full-year growth rates of 25% and then the Q4 rate of 36%, what kind of rate do you look at for 2010? Are we kind of looking at 25% plus, or is 36% realistic for your growth rate?

Sylvie Gregoire - Shire Plc - President, Human Genetic Therapies

Yes, I will take the first question on manufacturing and the supplies of velaglucerase and REPLAGAL. Recall that we were not meant to file so quickly and did not anticipate launch of velaglucerase until the end of this year. And this will all be because of the -- heating up of all of the activities regarding the launch of the activities in the US, we have, of course, altered the manufacturing schedule in the US and moved things around in order to accelerate the build of inventory of velaglucerase. We already had some, which is how the 400 patients were able to come online, and we are manufacturing as we go throughout the year, which allows us then now to add more patients, like I said several hundred patients this year, and it is not related to the dose. The average dose actually across all products, across all patients around the world is the 45 units per kilogram. Of course, there is a range of utilization, but if one averages out for those 400 patients, that is the dose that is being utilized.

So it is really about becoming manufacturing of the capacity that we had anticipated but just earlier. Therefore, for REPLAGAL there is no manufacturing or inventory issues that we see. We were already working with important files to inventory for REPLAGAL, and therefore, we can support the anticipated growth of this product with the manufacturing capacity that we have that.

Of course, the large-scale facility will come online again in the middle of this year and will ensure the future growth of all of our products and even at a probably over time a reduced cost because it will be done at a better scale.

Graham Hetherington - Shire Plc - CFO

Yes, David, on chart 17 and 18 I tried to lay out the 2010 dynamics. For XR I was using intentionally the fourth quarter -- (multiple speakers). I'm assuming we are still on. I'm sorry, I was interrupted there. David, what I was saying that chart 17 and 18 highlighted the dynamics going into 2010. For XR on chart 17 I was using the fourth quarter intentionally as a reference point. For the rest of the business, I was using the 2010 full year, and I would just reinforce what I included on that chart, which is that the 2009 full-year growth continues as a dynamic into 2010 with the potential to accelerate. So going back to your question in terms of using the 25% as a reference point rather than the 36%.

Operator

Gary Nachman, Leerink Swann.



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Gary Nachman - *Leerink Swann - Analyst*

So the first question is for Sylvie. On the decision to price Vela at a discount, are you concerned at all that this will set a precedent for more substantial pricing pressure when infant (inaudible) ultimately enters the market? And should we also assume that you would price REPLAGAL at a discount if that gets approved in the US? Just a little bit more on your strategy of the discounting versus Cerazyme.

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

Well, as I have mentioned, our strategy on pricing or the commercialization of the product takes into consideration what we see is a hurdle to access. And we believe that patients are sensitive to price, as well as the amount of co-pay that they have to pay and, therefore, believe that the best way to bring the product onto the market is to bring Vela, as you call it, on a discounted price that provides some savings, I think, for the patients and the healthcare community. We are not necessarily announcing that we will do the same for REPLAGAL, but we will let you know of our commercialization strategy on that product at the time of approval.

Gary Nachman - *Leerink Swann - Analyst*

Okay. And then second question for Graham. As far as the EPS growth in 2010, I know there's a lot of moving parts, but can you frame that a little bit more in terms of range? Is it going to be single-digit, mid or high or even double-digit, and does that factor all of the new launches that you guys highlighted, Vela, REPLAGAL in the US and whatever else that you're planning for 2010?

Graham Hetherington - *Shire Plc - CFO*

Gary, I'm afraid I'm not going to repeat the one-off guidance, EPS guidance framework or range that we did us as a one-off last year. We have tried to be as helpful as we can in terms of the shape so that you can make your own judgments as to how you want to get to an EPS number, but with that been trying to give a very clear floor to the EPS guidance sort of 349 for 2010.

Angus Russell - *Shire Plc - CEO*

I think it is clear, Gary, that Graham made that statement a number of times saying the growth that we are projecting in 2010 is growth of 349.

Gary Nachman - *Leerink Swann - Analyst*

Right. No, that is clear. And also, just to confirm that is factoring the new product launches and investment in those new launches?

Graham Hetherington - *Shire Plc - CFO*

Yes, by definition it includes obviously everything that we are highlighting here. I mean we build that into our plans obviously over time.

Operator

[Alex Blakely], Sanford Bernstein.

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Alex Blakely - Sanford Bernstein - Analyst

I have got just one question. You have your aspirational midteens annual sales growth target, and this seems a little bit above market expectations. Could you help us understand what you think is causing this difference? Are estimates too conservative across the board, or are there specific areas we should focus on, or is there some acquisitive growth maybe that you are expecting?

Angus Russell - Shire Plc - CEO

No, I told you. It is aspirational. Usually aspirational means it's yet to be delivered. So I cannot speak to the street. You would have to ask every single analyst as to why they forecast what they forecast. That is the whole point. It is an aspirational target that we are driving towards. I mean it's a normal pharmaceutical company. So over time basically you get things like pipeline progression, but I come back to most of this, as I said before, can be achieved what we believe by the growth of our existing portfolio of approved drugs that you see in the market today.

Now some of those like we just highlighted are things like VPRIV and REPLAGAL in the US, which still have to have their formal approvals, but already available on a preapproved access basis. And then we have VYVANSE international launches in that timeframe and diverticulitis, as Mike highlighted, as a good note out this morning that I think highlights the upside opportunity. That could be possible with good clinical results on diverticulitis. But they will not be available until the end of this year or beginning of next year for reporting out.

So, as ever with a pharma company, there are a number of things that can happen. And then because we are very active always in in-licensing and M&A, it is not inconceivable that we bring other assets in when you're looking at a six-year long-range plan. So we stretch ourselves to obviously the achievement of those kind of goals, and that is why we use the word aspirational. But you would have to speak to everybody else. Obviously I cannot speak for the market. Everybody does their own sales forecasts. They come out with their own assumptions and conclusions.

Operator

David Ansellem, Piper Jaffray.

Mesha Deerman - Piper Jaffray - Analyst

This is actually [Mesha Deerman] for David. I just have a question on INTUNIV. Do you have a sense right now how many of the patients on drug you are seeing now are switched from antipsychotics and/or from [Serta]? Also, are you getting traction in treatment naive patients?

Mike Cola - Shire Plc - President, Specialty Pharmaceuticals

That's a very good question. I think we are way too early to answer that question with meaningful data. We have data from November from the launch. I just think the sample size is too small right now to really comment on that.

I think you look out a couple of months we will have three months of real data, and we will know where those patients are. I think the answer is the same as prelaunch. We do expect to draw an awful lot of patients that are currently not part of the market definition that are using atypical antipsychotics and generic guaifenesin today. But I hesitate to share those numbers with you because I just think the sample size is too small at this point.



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Operator

Matthew Weston, Credit Suisse.

Matthew Weston - Credit Suisse - Analyst

A couple of questions if I may. Firstly, with respect to the 400 patients who received velaglucerase that you noted in the presentation, can you let us know how many of those are subsequently switched back to Cerazyme as Genzyme product comes back online? In other words, how many of those 400 are still on Vela?

And then secondly, does your indication for the increase in SG&A include the co-pay assistance charges for both Vela and ELAPRASE and REPLAGAL assuming US approval midyear?

Sylvie Gregoire - Shire Plc - President, Human Genetic Therapies

We have seen some switchback but at a very small order in terms of velaglucerase back to Cerazyme. We have less than 20 patients that have switched back in four centers and all in the US. We have seen no switchbacks in the rest of the world thus far, so small numbers of patients have switched back.

We have also continued to see people coming on to the preapproval program as this week several patients came on in the US, as well as in the rest of the world.

And relative to the co-pay that you and the contributions that we will see to the cost side, those are included in the forecasts this year. As you know, they apply in the US to only patients that are eligible, so not all treated patients are eligible to this co-pay, and therefore, they can be included in the forecasts that we have.

Angus Russell - Shire Plc - CEO

Equally I would add the pricing we have announced today is, of course, again incorporated in our projections. So the 15% discount to Cerazyme and the announced price, I mean all of that clearly has been factored into all of these numbers.

Operator

Tom Russo, Baird & Co.

Tom Russo - Baird & Co. - Analyst

Sylvie thanks for the patient numbers and the average dosing for Vela. Can you comment, if you're willing to, what percentage of your available product was taken up until this point, and also to confirm is that additional several hundred patient capacity available now, or at what point this year will it be available?

Sylvie Gregoire - Shire Plc - President, Human Genetic Therapies

Yes, we had announced, as you will recall, that we had up to enough sufficient inventory for 300 to 600 patients by the end of the year, and therefore, we have sufficient capacity now and inventory to add now more patients. And, of course, that inventory builds over the year, this year as we continue to make the product and build until, therefore, more products -- more patients can come on. But today we can supply many more patients that would come on at the rate that we anticipate over the year. At



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launch, of course, we anticipate some patients taking advantage or have waited perhaps for the availability of a commercial product to come on to velaglucerase.

But recall that of the 400 patients or so that are on therapy today, 100 of those are in clinical trials, and then a portion of those are in the US. So when you think about your models and at what point these patients come onto commercial product, I think it is important to factor in that it does take a few weeks to a few months for patients to transfer in the US from product that is in a trial or as it is today provided in order to be reimbursed in the system. And so I hope that is helpful that you have got a lot of points to calculate or triangulate your forecasts with this type of information. But be reassured that the patients once the product is approved in the US will continue. We will continue to provide drug until they can switch over. There will be a gradual increase over the year between now and the end of the year, and you will see that in the revenues.

Tom Russo - *Baird & Co. - Analyst*

Okay and then maybe over on REPLAGAL. Knowing that that supply constraint there is now going to continue at a 30% level through at least May, is there anything you plan to do differently or more aggressively on your new treatment protocol as a result of that?

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

Well, of course, this is probably new news also for some of the patients in the US in terms of the delayed comeback of Fabrazyme. So we anticipate that the protocols both in the emergency treatment and the protocols will enroll until at least the supply can be revived.

Now physicians in the US have also started to understand better, but recall the product is not available in the US. So the information available and the knowledge about REPLAGAL in the US is building now to advisory boards and presentations that are done at meetings. It was last week at the LDN the presentation done on the Canadian study, which looks at Fabrazyme and REPLAGAL side-by-side, if you will, over three years that showed no difference between the outcomes for these patients. And so this information now is getting to be known into the medical community in the US, and, of course, now also it will become more balanced at the time that there are two commercial products on the market.

Tom Russo - *Baird & Co. - Analyst*

Thanks, great quarter.

Unidentified Participant

Great quarter. See, that is what you would expect from [Tony Bacall], great quarter. Great quarter.

Operator

Graham Perry, Merrill Lynch.

Graham Parry - *Merrill Lynch - Analyst*

I'm just wondering when the Medicaid rebate situation is actually likely to become resolved? So you have indicated obviously that Medicaid can still come off, CMS could still come back and reverse the situation. So does this just sit as an overhang now, or do you have a fixed timeline on that?



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And then also related to that, I was just wondering why you decided to change now and not when you have 100% certainty from CMS about what the correct rebate levels should be?

Angus Russell - *Shire Plc - CEO*

The reality is it could take many, many years before you get absolute conclusive certainty, and that is not in -- our gift is to make sure the way that CMS worked. We had two scenarios.

One was to continue not to recognize the revenues, and that could have gone on for many, many years or to do what we have done now. Based on the fact that we have gone through 2009 with the states invoicing us at the level that we believe is right with the 75% level and based on our judgment as to what response we would make to CMS in the event that they did challenge us, we now believe this is the absolutely right approach to take, and I hope that helps.

Operator

David Steinberg, Deutsche Bank.

David Steinberg - *Deutsche Bank - Analyst*

I have a few questions on the Specialty Pharma business for Mike. On INTUNIV you launched it right after the back-to-school season was over, and I was wondering -- and you put it on first detail taking VYVANSE off first detail. The question is, when would it go back to second detail, and when it does, do you see any change in the trajectory?

Second, with regards to sampling, are you still sampling, and if so, is it aggressive, or what level are you sampling? And are the current scripts reflecting the true nature of demand, or are they understated given the sampling?

And finally, given the strong launch to date, any thoughts on peak sales? Any change? I think you indicated \$250 million at peak.

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

First of all, on first line versus second line, we did launch the product in what is traditionally a slow, period, even though the launch has been strong the end of the year, and really now through the end of the school year in the US, things start to ramp down. So it's some point it makes sense to think about moving it off of first line since it is a pediatric drug and thinking about VYVANSE sometime this spring.

We're not going to give a definitive answer on that right now. We are still debating it. But it would make sense to move back to VYVANSE at some point because, in fact, there's not that many doctor-patient visits, particularly from, let's say, the beginning of May through the end of June. It really starts ramping back up after July 4. So we will toggle the switches on the salesforce depending on what each product needs.

It is hard to say on the sampling levels without giving you exact numbers what is aggressive and what is moderate. For Shire this is a very aggressive sampling program, and it is reflected, as you know, in the early scripts. Unlike the launch of VYVANSE, the samples do not count as a script. We are actually able to give drug where we are not with the controlled substances. So you do get a little bit of a dampening and a delay of your initial scripts. And we are out there trying to do this quite aggressively, particularly for a company that has traditionally come from a C2 background.



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And then peak sales, I don't know, we don't have any more comments on that. Graham, I don't know if you want to say anything. We are happy with the progress. We think there's a lot of room to run with this thing. We have a long-term strategy with it. Study 310 on coadministration, I do believe opens up a new opportunity with all of the folks on the stimulant side of ADHD, and we will just watch it and keep working it.

David Steinberg - *Deutsche Bank - Analyst*

Okay and then one question on the G.I. business. With regard to PENTASA, you had said you're maintaining the brand. It is now pretty sizable, \$0.25 billion. But it has been off-patent for a number of years. Can you update us on what kind of bioequivalent guidelines there are for this drug? Should we think about it going generic this year, or could it be one of these products where there is just no generic for years to come?

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

It is really tough to see a generic pathway, even with doing clinical trials for both of these drugs. There is guidance out there, and I think you can do clinical trials. You can do a 505 B2 type program. But then when you get to the point where you have to ask the agency for an AB rating, I think that becomes very sticky because I don't see how bioequivalents will ever work in this category.

As you know, these are topical drugs in the gut. PK is not very meaningful. So doing noninferiority trials, again I think we will see other mesalamine-based products coming forward, but it's hard for me to see how they get AB rating, and it really has stymied people in PENTASA land to date. It does not mean there will not be more products based on this mesalamine, but I don't see an AB rated product anytime soon for PENTASA.

Operator

Florent Cespedes, Exane BNP Paribas.

Florent Cespedes - *Exane BNP Paribas - Analyst*

The first question for Angus. Back on the aspirational target, when we look at slide 35 with the potential product launches, if we compare to what you presented in Lexington almost one year and a half ago, it seemed that most of the growth drivers are products which are now approved or almost preapproved. So does that mean that aspirational targets may be now conservative, or is there any risk that we should be aware of like maybe the appetite from large pharma companies like Pfizer or Glaxo?

My second question is for Sylvie. A quick one. Could we have an update on FIRAZYR, maybe an update on your view on the potential sale of this product given the relatively slow

Angus Russell - *Shire Plc - CEO*

Yes, just going back then to the aspirational targets, I think, as I said at the beginning, one of what I feel very strongly now and our management team feel here at Shire very strongly about is a differentiating feature for Shire is, as I said before, we believe we are well on the way to delivering our aspirational targets over the next six years based on the fact that that will be -- that period will be driven very much by the eight key products, meaning the entire core product portfolio, but very much the eight new products that have come out in the last three or four years, which to your point have long periods of exclusivity ahead of them and are at a fairly early stage still of their lifers' products in this industry.



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So unusually yes, we think we are a long way on our highly probable outcome toward meeting those kind of aspirational targets. I highlighted, though, and you referred to that slide of all of the launches on slide 35, and what I was highlighting earlier is there are things that add to that along the way, and I highlight -- and I will not go through those again now, you have got the slide -- but as ever those have to be probability adjusted. There in Phase III studies, many of them, some of them are in slightly earlier stage than that. But these have the normal kind of pipeline and then regulatory and commercial probabilities attaching to them.

But I believe probably if you were to say -- if you asked me a different question, say, if all of those things come to pass and they all achieve 100% probability outcomes, then I think there is obviously every chance of us achieving the aspirational target we have out there.

Your question about Pfizer and Glaxo and because you picked on those two companies, I can only assume -- I will elaborate and assume that you're driving at the fact that their recent acquisitions of players in rare disease, the orphan drug space --

Florent Cespedes - *Exane BNP Paribas - Analyst*

Yes, of course.

Angus Russell - *Shire Plc - CEO*

Yes, what I would say Protalex people know quite a lot about, I mean just to remind you it is a different technology. They are still waiting their formal approvals, and we will wait to hear more about that in due course. But I would remind you it is the first plant cell-based products. I will remind you, as Sylvie said earlier, and that was the published data in our Phase III programs, we have the only human cell-based products in the markets, and they show obviously very, very low levels of antiviral antibody activity. So we will wait and all see and watch with interest what happens when that product comes to market, Protalex's product.

As regards the GSK acquisition, I mean when you look at that acquisition all of those drugs are at the very, very early stage. They are all in pre-clinical, and from our experience as a player for many years now in this arena, we know it takes at least five to seven years to get the commercialization of these kind of drugs. So again, I think in that aspect you are looking at a different issue, which is the competition rising from that acquisition is many, many years away yet. So the simple answer is I don't think today we are particularly distracted or concerned about new entrants into the market.

Florent Cespedes - *Exane BNP Paribas - Analyst*

Thank you.

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

And you had a question on FIRAZYR. And slow progress from the first two, yes, it has been a little slower than we would have liked, but there's a reason for that, and that is due to the fact that it is not an enzyme replacement therapy. And, therefore, pricing reimbursement and formulary listing does not occur at the same pace as it does when (inaudible). It rather follows a normal product launch, and the slow growth -- the usual gradual growth of the product and launches across Europe.

So we continue to work toward maximizing the reimbursement coverage for FIRAZYR and are awaiting several actions from reimbursements in the European countries where it has not been launched yet. And also, we have filed for marketing authorizations in other countries outside Europe -- Argentina, Mexico, Australia and Israel -- and are preparing additional files for other submissions outside in other countries. So we are committed to make FIRAZYR a global market leader in HAE, and therefore, we will continue to work to that progress.

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Angus Russell - *Shire Plc - CEO*

Operator, I think we will take one final question. We have been on the call almost an hour and a half now. So, in the interest of time, I will just take one more question on the call and then remind, please, if you have any more questions, please follow up with Clea or Eric afterwards.

Operator

David Buck, Buckingham Research.

David Buck - *Buckingham Research - Analyst*

A couple of quick ones. First for Mike on LIALDA. Have you seen any change in behavior from your largest competitor, and are you assuming any generic of Asacol this year? And one for either Sylvie or Graham, whoever wants to answer on VPRIV. Can you remind us where the free product was booked whether that was in R&D or part of gross margin, and how does that factor into the 5% to 10% growth? Because obviously you are saving when that product is going to be reimbursed and approved. That pre-product will go away.

Graham Hetherington - *Shire Plc - CFO*

Well, I will just take the free product. The cost of that is relatively small, David, and it was booked in the R&D line.

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

I will start on LIALDA. Obviously a lot has changed with the former P&G group that sold Asacol, and I do not really feel comfortable talking about those changes. But needless to say, it is a completely different group and a different approach, which I do think creates an opportunity for us.

I think you have seen some strength the last few months, and I think we will continue to make progress in that marketplace. The launch of Asacol 800 obviously made some noise, but that seems to be slowing down. And I don't see, like as we talked about PENTASA, I do not see a generic Asacol this year. I'm not aware of any clinical trials that are underway for Asacol. That does not mean they are not happening, but, in fact, I just don't see an easy pathway to Asacol.

Angus Russell - *Shire Plc - CEO*

Okay. So with that, we thank you very much for your time and attention. I apologize. There were a few background noises I think by some of the banks' lines on this call today. We had some interference from some background noise, so apologies for that. Background noise to some of the answers.

And again, thank you. I believe these are a tremendous set of results in 2009. We have come through what I would characterized in my opening remarks to be both a challenging but yet transformational year in terms of where we have arrived at the end of 2009. And the leadership team here at Shire looked forward very much with our colleagues to a great platform for our future growth, not only in 2010 but through until 2015 and beyond.

So thank you, have a great day, and we look forward to talking to you again soon.



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Operator

Thank you, ladies and gentlemen. That concludes your conference call for today. You may now disconnect. Thank you for joining, and have a great day. Thank you.

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