

FINAL TRANSCRIPT

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SHP.L - Q1 2011 Shire PLC Earnings Conference Call

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Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

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PRESENTATION

Operator

Good day, ladies and gentlemen, and welcome to the Shire's 2011 first-quarter results conference call hosted by Angus Russell. My name is Laura and I'm your event manager. During the presentation, your lines will remain on listen only (Operator instructions). I would like to advise all parties, this conference is being recorded for replay purposes and I would like to hand over to Sarah Elton-Farr. Please go ahead.

Sarah Elton-Farr - Shire plc - IR

Good morning and good afternoon, everyone. Thank you for joining us today for Shire's first quarter 2011 financial results. By now you should have received our press release and should be viewing our presentation via our website from Shire.com. If for

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

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 +44-1256-894-160, and he will be happy to assist you.

Our speakers today are Angus Russell, Graham Hetherington and Jeff Jonas. 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, could materially affect our results.

Today's agenda is on slide three. Angus will begin with opening remarks on Shire's Q1 performance and highlights, then Graham will continue with a financial review. Jeff Jonas will give a VYVANSE new uses update and then Angus will summarize our key messages. We will then open up for your questions. We request that you only ask one question so that everyone gets a chance for participation in the call. Eric Rojas and I will be more than happy to follow up off-line for any subsequent questions or clarifications. I will now hand over the call to Angus.

Angus Russell - Shire plc - CEO

Thanks, Sarah, and hello, everyone. So let's just flip to the presentation, page 5 and see here what I believe are very strong first-quarter results characterized, really, by a strong top-line performance, once again. Total revenues, you can see, were up 19% at \$972 million, driven by our, as you know, relatively young, strong portfolio of new products, which were up 24% to \$889 million in the quarter.

Turning to the next page, that strong top-line performance obviously has driven also very strong growth in earnings per share, and here you can see that our non-GAAP earnings were up 22% at \$1.23 per ADS.

Turning over to the next slide and just getting behind a few of the highlights for this quarter, starting with our Specialty Pharma business. Going through the products, VYVANSE -- obviously, we saw the launch this quarter of new indication for adolescents, an area of the market in the US that we believe has been a little bit neglected in the past. We didn't have a formal indication previously for VYVANSE to be promoted in this space. Now we do, and we are already seeing significant, I think, upside coming from the ability now to promote to adolescents.

Next point you can see, an exciting one -- this is the first launch ever of an ADHD drug for Shire outside of an amphetamine-based product outside of North America. You can see we have just launched what is now called VENVANSE in Brazil, and shipments actually have gone out this week. So we are looking for growth in the Latin American market based on that approval and launch.

As you know, we have a big clinical trial program underway in the EU; that is progressing as planned, and just highlight at the end and remind you that we hope to be following that before the end of the year.

And then, in regard to potential non-ADHD indications for VYVANSE, again significant advancements this quarter. You know we have also put out a press release with our results today summarizing the latest of these new indications, which is in the negative symptoms of schizophrenia. As Sarah said, Jeff Jonas is with us here today and he's going to be talking to you later about what actually are very significant and remarkable findings from a scientific point of view in regard to treating patients with negative symptoms of schizophrenia with VYVANSE.

INTUNIV -- you can see we are at 3% US market share now. Again, during -- towards the end of the quarter, we actually gained approval and have been launching a new indication for INTUNIV, and that's to use the drug co-administered as adjunctive therapy with an existing stimulant. And again, we believe this is a paradigm that doctors have been very keen to move towards that actually helps a lot control patients through the evening and into the night, when they suffered sleep disruption, historically,

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

and then wake in a controlled state next morning before they then probably dose with a stimulant again. So we expect, again, that this will continue to give you upside to INTUNIV going forward.

Once again, we remind you just that we have a significant, again, clinical program underway in Europe for INTUNIV, again progressing as planned. Remind you that what triggered us to do this was an agreement in principle with the regulators to gain 10 years of market exclusivity from launch for INTUNIV, which could be, again, another significant enhancement to the international growth of our ADHD franchise.

In regard to our intestinal, gastrointestinal franchise, again good growth in the quarter. LIALDA grew at 37% this quarter and has achieved now a 20% US market share, and that is to put alongside, as you know already, our strong position that has been there for years with PENTASA.

And then our newest drug in regard to GI is obviously RESOLOR, now launched in three markets -- the UK, Germany and Belgium. I believe next market to launch will probably be Ireland, very shortly. On top of that we have many other EU launches planned throughout the balance of this year and through into 2012, as soon as we can finalize pricing and reimbursement discussions.

And we have now initiated an ongoing trial in men with opioid-induced constipation as an expansion, the first expansion to the use of RESOLOR in noncancer pain patients.

So turning to the next slide and just doing similar review for our HCT business, FIRAZYR, as you know -- again, in this period we got a new approval for the use of FIRAZYR in the European markets in terms of self-administration for acute [AHE] (sic -- see presentation) attacks. This was, remember, the way the product was designed to be used, so now we will see the full potential, I believe, of FIRAZYR based on an increasingly easy use of its administration.

We mentioned before but just to reaffirm that we did complete the full response and filed that with the FDA. And as you remember, this is a second response, so it got a six-month review period, which gives us a PDUFA date now of August 25 this year. We believe that the data we submitted is a very significant Phase 3 program result that showed very positive efficacy and safety.

In regard to REPLAGAL, outside of the US you can see the market share is now 73%, and we -- probably of most significant interest to all of you out there is that during this quarter we have now filed for European approval for making REPLAGAL in the new Lexington manufacturing facility. And you can see on the third bullet, we have already had that facility inspected by the European authorities, and I can tell you they were very pleased with the new plants. And we had very little commentary back from them other than, I think, really an endorsement that the plant is in good shape to make REPLAGAL.

As regards VPRIV, now up to a 34% US share, which is pretty dramatic when you think the product has only been available in the US for probably about 18 months. And globally we have an 18% market share. So both on REPLAGAL and VPRIV, we have seen incremental numbers. Sylvie can talk about that, I'm sure, in the question-and-answer session. But on both products, we have gained additional patients and some switches during the quarter.

In regard to new Lexington manufacturing facility, again, as regards VPRIV, you remember that is running a little behind because we have to do a full transfer of the process into the new plant. I can tell you everything is on track according to the time lines that we gave you before, although that will result, as you know, as what we said previously, that VPRIV probably won't be available from that new plant until somewhere around the middle of next year.

So if you turn to the next page, what does all this mean? Well, it means Shire is in an increasingly, I believe, strong position. This chart, remember, shows you to the right the range of products that we have out there in the blue bubbles on this chart that are actually driving that tremendous top-line performance of 24% growth in product sales during the quarter. But behind that, even more exciting for me is the progression of our pipeline and the amount of late-stage opportunities that we are rebuilding. This is significant.



Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

As you know, this will actually give us a range of projects which I believe will give us great opportunities to stay in the kind of double-digit aspirational target we've got out there at the moment until 2015. But many of these things will be launching around the 2014, 2015, 2016 time frame, which will provide a great basis for continuing what we hope will be a sustainability position opposite our existing kind of growth.

So you can see there the sort of more turquoise bars, and we've talked about many of these on my summary so far -- FIRAZYR in the US, VYVANSE and INTUNIV programs in the EU. Let me remind you about our big study for LIALDA in diverticulitis -- a very, again, big market with high unmet need. And those results will report out probably around middle of next year, first half. And then we'll probably talk about them in the middle of next year.

And then the various new indications for VYVANSE -- we've got depressive disorder, excessive daytime sleepiness. And now we add to that, as I said earlier, the negative symptom of schizophrenia. As I said, Jeff and Mike will, between them, cover off what our plans are going forward in regard to what I believe is a very fast track now of moving things into Phase 3 development.

And behind that, a number of early-stage programs. In the interest of time, I won't go through those and reiterate them. But intrathecal is something I'll just remind you again that we are continuing to see interesting and encouraging results, I would say, on the intrathecal programs. And again, we would hope to be in a position to discuss those maybe at the end of the year or beginning of next year, some early findings from the human trials that we have underway there.

Later in the year -- and I'll cover that at the end, and just reminding you we will talk about guanfacine as well in terms of Carrier Wave in the second half of this year.

So with that opening set of remarks, let me hand over to Graham, who is going to take you through the financial numbers in a bit more detail.

Graham Hetherington - *Shire plc - CFO*

Thank you, Angus, good morning, good afternoon, everyone. I know that many of you have got a lot to cover today, so I'll be keeping it brief. I'll focus on, first, our strong results in the quarter; second, the investments we're making across the business, particularly in some of the exciting advances we are seeing in our R&D pipeline. And finally, I'll remind you of our expectations for the full year.

So turning to chart 11, Angus has shown you the strong top-line and earnings growth we have achieved this quarter. And this reiterates how we are continuing with the momentum we saw through 2010. Product sales were up 24% year on year. We've seen great performances across the business, demonstrating the robust positions of our products in their markets and their continuing growth potential. Total revenues are up 19%, lower than the growth in product sales due, as expected, to lower royalties. As I explained back in February, we expect to see royalties decline this year resulting from increasing generic competition.

Specifically, in the first quarter our ADDERALL XR royalties are comparing against very strong numbers in the first quarter last year, when we received much higher royalties from Impax as they completed their initial wholesale and retail channel stocking.

EBITDA is up 15% on a reported basis and 17% after stripping out the effects of foreign exchange. EBITDA as a percentage of product sales, which excludes royalties to give an underlying operating margin, has increased by 2 percentage points to 28%. I'll be touching on this operational leverage later.

Earnings per ADS are up 22% to \$1.23, an excellent start to 2011 and one that continues at the pace that we set last year.

Apr. 28, 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

And finally, we generated \$208 million of cash, down against the first quarter last year, primarily as a result of the timing and quantum of Medicaid payments this year and also reflecting lower ADDERALL XR royalty receipts compared to last year, which included the receipts of royalties from Impax's initial channel stocking.

Turning now to slide 12, you can see the outstanding performance of some of our key products and, in particular, VYVANSE, up 31% or \$48 million as both the ADHD market and VYVANSE's share of that market grew. This is particularly impressive, given that we saw about \$15 million of destocking in the first quarter of 2011 compared to \$5 million of stocking this time last year. This performance was supported by lower rebate levels in the quarter than we expect to see for the rest of the year.

INTUNIV reported growth of 21% in the year. It's worth recalling that in the first quarter of last year we booked \$17 million worth of deferred revenues from the initial launch of INTUNIV. So the underlying growth is significantly higher than the 20% that is reported.

LIALDA was up 37% or \$24 million, helped by LIALDA's market share gains in the US and growth of MEZAVANT in Europe. ELAPRASE's underlying growth of 10% was held back by a delayed shipment that slipped into the second quarter this year, to give a reported growth of 3%.

REPLAGAL, up 55% or \$37 million as we continue to add new Fabry patients, and VPRIV recording sales of nearly \$60 million, reflecting the strong performance of our global launches which continue across Europe this year.

In addition, product sales of ADDERALL XR are up 21% on the back of strong market growth and some favorable stocking in the quarter compared to the first quarter of last year, when we saw sizable destocking. We again saw lower rebate levels than we expect to see for the balance of the year. Total revenues from ADDERALL XR are down \$5 million due to lower royalties, as I explained earlier.

Overall, total revenues are up 19% or \$156 million, even after the divestment of DAYTRANA last year, which contributed \$18 million to the first quarter's revenues in 2010, along with the \$21 million of decline in royalties that I've spoken about. I believe this shows how strong our young portfolio is and how robust its growth drivers are, and I am also pleased to see the positive impact of our historic investment in these products.

Turning to the next slide, 13, overall we are seeing continuing operating leverage as combined R&D and SG&A grew at 20% compared to the 24% growth in product sales. In addition to our ongoing investment to support our growing sales base, this year we're also absorbing the operating costs on the basis of Swiss Hub, which came into operation in the second half of last year, and the new US healthcare reform excise fee.

We're also seeing positive progress from the investment we have made in our pipeline, particularly in potential new uses for VYVANSE, which Jeff Jonas will talk about shortly. We believe these pipeline developments represent great potential to future growth and excellent investment opportunities.

It's worth also keeping in mind the continued investment we are making in other therapeutic areas, for example, as Angus spoke about, in LIALDA for diverticular disease, in the Carrier Wave platform, in RESOLOR and the early-stage Novartis pipeline, in FIRAZYR self administration and the US market opportunity and in our intrathecal therapies at HDTV. We are excited by the potential of our promising, relatively low-risk pipeline and will be stepping up our investment this year to help drive growth over the medium term.

Let's look at our cash flow on slide 14. As I mentioned earlier, the timing and the content of sales deduction payments including Medicaid in the US combined with the expected lower ADDERALL XR royalty receipts in the quarter reduced our first-quarter cash generation, which came in at \$208 million. Despite that, our free cash flow is strong at \$155 million, up 9% compared to the first quarter last year as a result of lower cash tax payments and flat capital expenditure.



Apr. 28, 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

We finished the quarter with cash of \$712 million and net debt of \$366 million. We continue to have a strong and flexible funding position supported by our five-year, \$1.2 billion bank facility, which remains undrawn.

Finally, let's look at our full-year outlook for 2011 on slide 15. Product sales continue to grow strongly. The rate of growth, however, is going to moderate over the course of the year as a result of tougher comparatives, but I continue to expect full-year growth to be in line with the mid-teens rate achieved in 2010. Our current forecast for total royalties and other revenues combined remains at about 10% lower than in 2010.

I'm expecting our product percentage gross margins for the full year to be in line with the first quarter, and I now expect depreciation to be around \$115 million for the full year. As I highlighted earlier, I'm expecting the growth in combined R&D and SG&A to be at the top end of the 10% to 13% range as we increase our investment in advancing the R&D pipeline, continue to support our sales growth and the international expansion of our portfolio, and absorb a full year of the operating costs from [Abatis], our Swiss Hub and the new US healthcare reform excise fee.

My expectation for our full-year tax rate remains 22% and 24%. It's early in the year, and these dynamics, together with the strong start we've made for the year, underpin our guidance from February of good earnings growth. And to help demonstrate the value of our continued R&D investments, I'll ask Jeff to provide an update on our research into the potential new uses for VYVANSE. Jeff?

Jeff Jonas - Shire plc - SVP, R&D

Thanks, Graham, and good morning and good afternoon. Before I begin my talk about an update on the new uses program, I just want your mind everyone on slide 17 that what I'm going to talk about today involves investigational studies and experimental data, and that VYVANSE is only approved for the treatment of ADHD, attention deficit/hyperactivity disorder. So obviously, we don't recommend the use of this product in other ways.

Turning now to slide 18, I just want to remind people why we are pursuing the new uses program. We've described to you before how VYVANSE impacts both dopamine and norepinephrine. And this impact on these neurotransmitters may affect a number of psychiatric symptoms that you can see on this slide -- mood, cognition, interest, inhibition, energy, motivation, wakefulness. We have decided, therefore, to explore illnesses where these symptoms are major components of the dysfunction.

As a result, we have looked at major depression, excessive daytime sleepiness, schizophrenia and binge eating. When I turn later to negative symptoms of schizophrenia, you will need to remember these symptoms because it's the absence of many of these symptoms that actually comprise the negative symptoms of schizophrenia.

Before I do that, though, I want to give you a brief update on where our other new uses programs are. You may recall that we reported positive results from major depressive disorder and excessive daytime sleepiness in the last six months. I'm happy to report that we will be commencing our Phase 3 program for the adjunct treatment of major depressive disorder in the second half of this year.

With respect to binge eating disorder, which you now see on the chart, we have had a productive dialogue with FDA and we expect to commence our Phase 2 study in this indication in the second half of this year. We are evaluating the EDS opportunity in the context of the other opportunities we now have, including the results you will hear later for the negative symptoms of schizophrenia.

One of the key theses of all these illnesses is that these are all illnesses that represent significant unmet medical need. There frequently are no available therapies, and as a result these represent large market opportunities that, in effect, for depression and schizophrenia may be larger than ADHD.

Apr. 28, 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Now let's turn to slide 19. Now, I know that many of you think and believe that large studies will be needed to approach these indications that represent significantly larger markets than ADHD and significant areas of unmet medical need and areas where we believe we can create true value. However, we intend to conduct these studies using the Shire model.

Basically, our plan is to only develop drugs where we have a large signal and a large effect size. We won't develop a drug if we require a large study to basically show a weak effect. So we have incorporated this thesis throughout our entire development program, and this is our means of managing risk in these indications.

So we are de-risking our development in a number of ways. First, from each of these indications we've demanded clear Phase 2 signals. We're looking for clear indications with clear diagnostic criteria. All the studies have been designed to minimize multiple forms of bias and to basically maintain internal discipline, we have required predefined go/no go criteria that demonstrates suitable value, large effect sizes and suitable safety and efficacy balance.

Therefore, we intend for each of the indications to have a potential value proposition established early, including, when possible, using comparator data. In each of these studies, we have used enriched or more homogeneous populations. So, for example, in major depression, we have studied patients who are already non-responders to SSRIs, or serotonin reuptake inhibitors. In our schizophrenia program, we studied patients who were already on stable atypical antipsychotics who still had residual negative symptoms.

These features basically combined together to reduce our Phase 3 investment risk. We can make small investments, looking for clear signals, and then move forward with studies that are Shire-sized studies that don't require large populations.

Finally, in all of these areas we believe we have significant overlap in synergies with our current central nervous system expertise and these diseases being treated by specialists.

Turning now to slide 20, I would like to get into our study for negative-symptom schizophrenia, but first I want to take a step back and talk about what patients with negative symptoms look like. Schizophrenia affects 1% of the population around the world, and most people are familiar with the so-called positive symptoms of schizophrenia -- hallucinations and delusions.

Less well-known but possibly more disabling and responsible for much of the morbidity in the workplace are the so-called negative symptoms, for which there is no established and well recognized therapy. These negative symptoms -- inability to communicate, loss of emotion, loss of interest and enjoyment and the loss of social interaction -- produce significant impairment and prevent these types of patients from being gainfully employed and make them a burden on society.

Again, recalling there are no approved treatments for either the cognitive or negative symptoms of schizophrenia, the slide above shows us that this is up to -- we believe is more than a \$1 billion opportunity. I have included this slide for your reference but won't go into it in detail.

As I now begin to turn to the study, I want to remind everyone that literally for decades there was a strong clinical belief, almost folklore, that agents like VYVANSE had no role in the treatment of schizophrenia and also might make the onus worse. So the results I'm going to talk about today are really quite remarkable and, we expect, will take some time to be accepted, possibly, by the scientific community because they are so -- frankly, so unexpected.

So let me turn now to slide 21. I need to emphasize that in many ways this was a unique and groundbreaking study. We have designed this study to assure and maximize patient safety, so we began with an open-label portion to allow us to observe the patients carefully. But in order to preserve the utility of this portion of the design, we used blinded raters who were unaware of the nature of the study or the treatment received. We studied patients who were on stable doses of atypical antipsychotics and then added doses of VYVANSE up to 70 milligrams for up to 10 weeks.



Apr. 28, 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

At the end of 10 weeks these patients then underwent a double-blind randomized withdrawal. We did this for two primary reasons. One, we were interested and wanted to be reassured that the discontinuation of our treatment would not result in exacerbation or relapse of the disorder. Also, we wanted to see how stable the response was to the open-label portion of the treatment.

Further, we wanted to fully characterize both the efficacy and the safety of VYVANSE in this population, and so included a large battery of measures, as you can see here on the slide, testing both many aspects of efficacy and safety in the treatment of negative-symptom schizophrenia.

Turning now to slide 22, I want to begin with safety first. As you can see from this slide, the adverse events observed in this study are really just those typically associated with VYVANSE. This was gratifying and frankly surprising because many people had predicted that this would exacerbate the illness or produce a significant safety finding. As you can see here, this treatment was as well tolerated as in other treatments of schizophrenia, and the dropout rate seen in this study is in line with other studies of other agents in schizophrenia.

Let me now talk about the efficacy. Turning now to slide 23 -- I mentioned earlier that our primary endpoint was the reduction of negative symptoms as measured by a validated rating scale, the SANS-18. In this slide you can see the score of the SAS-18 plotted against the week of therapy. This is the format we will use in the next few slides. In this slide, a lower score basically corresponds with patient improvement.

As you can see in this slide, there is a significant reduction from baseline in the SANS score. This was frankly a surprise to us and obviously quite gratifying. We intend to publish these data as well as to produce some of the more meaningful vignettes of the types of improvements we saw in these patients. We're also planning to review these data with regulatory agencies worldwide, but in our initial feedback with thought leaders there has been significant enthusiasm and encouragement about these findings.

On the left-hand side you see the acute effect, just basically almost a 15-point or more than 20% drop in the SANS score. On the right-hand side you see the results of a randomized discontinuation. Again, we were quite gratified to see that there was no evidence of relapse or rebound on abrupt discontinuation of VYVANSE. This is an issue in patients with schizophrenia, where compliance can be an issue.

Once we've had these data in hand, our next question was how did this treatment impact all the other symptoms of the disease? If the folklore was accurate and the conventional wisdom held, we would expect the positive symptoms to worsen.

What you can see on the next slide, 24, was that the conventional wisdom didn't hold. This is, again, a slide with a similar format that you saw in the previous slide, and that is a number of rating scales where lower score signify patient improvement versus the week of treatment.

The top score is what's called the PANSS General Psychopathology Score, and this measures a decrease in the general and non-psychotic symptoms of schizophrenia. And, what you can see here as well is a significant decrease in the PANSS. On discontinuation on the right-hand side of the slide, you see no evidence of rebound or relapse. The middle shows you again the PANSS negative score, which is another measure of negative symptoms which, gratifyingly, was also consistent with the SANS score, again showing a significant decrease from baseline.

I wanted to point out that these are clinically meaningful decreases which we believe will be exemplified in improved patient behavior, and hopefully in improved productivity.

Finally, I want to draw your attention to the bottom line, which is the PANSS Positive Score, or the psychosis score. One of the strong clinical beliefs is that the use of these types of agents in schizophrenia would cause an exacerbation of psychosis. What you can see here is that is not the case and that these patients remained stable throughout the course of the study.



Apr. 28, 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Finally, turning to the summary on slide 25, I want to make a few points. First, we believe we have a strong signal here that will allow us to conduct a Shire-type study of meaningful numbers in a population where clinical improvement can be measured and where we can meet a significant unmet medical need. We saw improvement with VYVANSE augmentation during an open-label blinder-rated phase and no worsening of rebound on the short double-blind withdrawal phase. And we believe these data suggest that we can produce and conduct a relatively straightforward clinical development program for these agents.

Safety was, frankly, prosaic, and there were no new or unexpected safety findings that were not already associated with the use of VYVANSE. And, the negative symptoms improvements were supported by other measures, some of which we didn't present today but which all remain consistent with the overall findings.

What will our next steps be? We intend to conduct a global program for this disorder and therefore schedule health authority interactions in the second half of this year. We will be looking for potential biomarkers and [producers] of response in this population, and in addition we will be looking for commercially viable diagnostic and maintenance tools to add to the value proposition of treating this very important disorder. If all goes well, we have the potential to initiate Phase 3 by the end of this year.

So thank you all for your attention. Now I would like to turn the conclusion over to Angus.

Angus Russell - Shire plc - CEO

Thanks very much, Jeff; what I think you might all agree are very remarkable, as we said, scientific findings and one that we are very keen now to discuss, as Jeff said, with the scientific community and also with regulators.

So just linking to the balance of this year, turning to slide 27, I said earlier, let me just try and give a few highlights of the key events for the rest of this year. First off is we have planned now the approval and launch, we hope, of the use of LIALDA for maintenance of remission in the US, be a new indication for LIALDA, which, again, we think is a significant potential further upside for LIALDA's ongoing growth.

VYVANSE -- I mentioned our EU programs and that we are targeting, as remember, a filing with the MAA before the end of this year. And as Jeff highlighted, just to reiterate, we will commence a Phase 2 study in regards to binge eating disorder.

FIRAZYR I highlighted earlier; PDUFA date upcoming on August 25 in the US, and then a planned launch following that action date.

Carrier Wave -- I said before and I think we will be planning this for the next quarterly call. We will give you an update on the guanfacine programs utilizing Carrier Wave. We are progressing with that, but we will give you a full summary on the lead compound and our expectations of that during the next quarter.

And, finally, the Lexington manufacturing plant, where we will continue to move forward with our plans there. Remind you, I'll say European authorities have already inspected the plant with, it seems, a resounding endorsement of it. And we will await, obviously, discussions with them on the approval to make REPLAGAL in that plant.

So let's just turn to the final slide, 28, and just really summarize what I think is clear evidence again in these results that the strategy that we adopt here in Shire of meeting high unmet needs but at the same time demonstrating real value to the healthcare systems are in the world, which is an increasing need these days this structure, I think, is very evidently delivering.

Obviously, as I said, these results were characterized by very strong revenue growth coming from that new, balanced product portfolio. We are continuing to find new indications and gain approvals for those, and that is leading to further launches, which provides more upside to many of those products. And at the same time, as you have heard today and we can talk a bit more



Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

about on this call, if you have interest, we are continuing to make great progression in our pipeline. Very exciting because that provides, as I said earlier, with now a pool of middle- to late-stage projects from which we can choose the very best. That will give us a great platform for sustaining the growth of the Company not only from here with the existing product portfolio, but, most importantly, in the period of beyond 2015.

And as I said a ago, we believe that through all of this we are demonstrating that we are bringing real valuable treatment to both patients and physicians which are helping their very serious acute and chronic conditions and, at the same time, demonstrating real value to the players and policymakers, which, as you all know, will be an increasing requirement in the next decade of the healthcare industry.

So with those comments, I'd like to hand back to the operator and invite you to ask questions.

QUESTIONS AND ANSWERS

Operator

(Operator instructions). Ken Cacciatore.

Ken Cacciatore - Cowen and Company - Analyst

Thanks, guys, I'll keep it to one question, as you asked. Some of the greatest value in the Company is still deep in the pipeline, I guess, with MLD and Sanfilippo. So I know there's not much you can give us, but if Sylvie could provide any updates, any progression, maybe discuss the device and any subtleties as you continue to progress forward with those programs?

Angus Russell - Shire plc - CEO

So yes, I'll ask Sylvie to tell you whatever she can about the current progress.

Sylvie Gregoire - Shire plc - President, Human Genetic Therapies

Hi, Ken, good morning, everyone. Yes, these programs -- we have two programs that are in the clinic, Hunter CNS and Sanfilippo. Both of them have started about a year ago and are in the middle phase. It's a multiple-dose, dose-escalating type trial, and we are in the middle of the second cohort.

I think I said earlier in the year we will be able to provide, I think, better guidance as to when the timing of these programs would transpire in terms of the next phase of start of the trial and duration of trial and so when it materializes, actually, in our commercial pipeline, at the end of the year. We are still looking. The data is open so we can see that the intrathecal port, when administered to patients, seems to be well tolerated and the infusion of proteins into the CSF seems also to be well tolerated to date. But let us advance a little bit more the data from the safety perspective and efficacy signaling, and then we will be able to give you an idea of the timing of the start of the next trials, how long they may be, which endpoints might be in these trials, which are all things I think will impact how and the time frame we can see these programs --

MLD we intend to start in the clinic before the year end, so those programs are slightly behind. But they all follow the same pattern, in a Phase 1-2 trial, and then the next phase should be the last trial. And they're all small trials, of course, because they are all fairly rare diseases.

I hope that answers your question, Ken.



Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Angus Russell - *Shire plc - CEO*

I think -- the question on the port, Smiths Industries -- I think we got -- the port is something that comes from Smiths. (Multiple speakers)

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

Yes, it's an existing port that's a commercially available device, and so we are just using something that's commercially available. We tried to minimize any risks by using or developing a port at the same time that we are developing a drug, so we went with the easy route and went with an existing port.

Ken Cacciatore - *Cowen and Company - Analyst*

Thanks, Sylvie.

Operator

Peter Verdult.

Peter Verdult - *Morgan Stanley - Analyst*

It's Peter Verdult here, Morgan Stanley. Angus and Jeff, just on what you have been talking about in VYVANSE, if we take you back to when VYVANSE was launched, you talked about aspirational peak sales guidance of \$1.5 billion to \$2 billion. So I just wanted to know, firstly, whether when you gave that guidance, indications such as MDD, NSS and EDS and binge eating formed part of that.

And then could you -- you have talked about what you think the addressable market opportunity is in schizophrenia, being a \$1 billion market. Could you give us some numbers that we could hang our hats on in terms of what you see as the addressable market in MDD and EDS and some of the other indications?

And if I could quickly slip in a question about just ADDERALL XR, the dynamics year-to-date. We are seeing a drug that should be in decline accelerating in growth. I just want to know, can you walk us through how we should think about that going forward, given the Concerta situation?

Angus Russell - *Shire plc - CEO*

Okay, so you snook in a few questions there under the cover of one question. I suppose it's all ADHD. Anyway, right, peak sales -- no, the \$1.5 billion to \$2 billion that we gave out some few years ago was obviously -- we contemplated the potential in the medium and longer-term of looking at VYVANSE. We always said that we would study it in other conditions, but we put nothing in those numbers. So that's purely what we estimated to be the global opportunity -- and, I think, very crudely. In our minds it was a potential of about, perhaps, \$1.5 billion in the US and \$0.5 billion outside the US, to break that sort of \$1.5 billion to \$2 billion range down, which is why we used \$1.5 billion to \$2 billion because it's US, and at the time we hadn't even begun the European trials and we hadn't discussed those. So now we know that the other \$500 million in [their assay].

I'll ask Jeff in a minute to come back on, perhaps, the opportunities for depression. All I would say, and I'm going to ask Mike then, just ordering things here, ask Mike to talk about ADDERALL XR. But something probably I should have summarized -- I'm sure Mike will mention it as well -- is that -- you've seen it, probably, in the press release already. What we are seeing generally



Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

in the ADHD market -- and this is significant, I think, in terms of the opportunity on peak sales for all of these drugs, is 13% prescription growth in the quarter, which is, again, up on the prior quarter and obviously higher than what we saw on average throughout the whole of last year.

So we are seeing at the moment, at least in the US, no let up to the continued growth of these markets. And I'll remind you that we are pretty much the only Company left there in the branded market now.

So Mike will cover, I'm sure, the ADDERALL XR and maybe talk, Mike, about some of those kind of competitive dynamics. But Jeff, why don't you just give us the answers on just potential size of some of these opportunities. (multiple speakers) yes, let Jeff do that.

Jeff Jonas - *Shire plc - SVP, R&D*

Well, for major depression we anticipate that the market, given what we understand about market dynamics, would -- arguably, anywhere in the \$2 billion-plus potential market opportunity, if not larger. Some of that would depend, obviously, on the effect size.

Binging disorder is interesting because right now, as currently potentially diagnosed, it could be at least 2% of the overall population. So that could be a market that's at least equal to the size of the schizophrenia market opportunity, if not larger. There are some estimates of binge eating disorder that have it up to 5% of the population at some point in time, so it could represent a larger market opportunity.

(multiple speakers) I'm being interrupted by Michael Cola. The other point for binge eating disorder is that there are no other approved treatments, so this would be a unique monotherapy and an opportunity. We believe that the profile for VYVANSE in terms of its activity might be ideal to treat binging disorder as well.

So we think all of these are potentially \$1 billion-plus opportunities. As I said at the beginning of my talk, we believe that they are opportunities that could eclipse the size of the ADHD market, but also are illnesses that likely to be treated by specialty physicians, so consistent with the Shire model.

Angus Russell - *Shire plc - CEO*

Thanks, Jeff, Mike?

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

I'm just going to pick up XR because the 20% growth that you are seeing in the first quarter -- yes, it is benefiting from the market growth. But it's actually dominated by a couple of key features. The first is that in the first quarter last year we saw de-stocking of ADDERALL XR of \$22 million, and through the phasing of shipments we actually saw stocking of \$9 million in the first quarter of this year, so a \$31 million swing year on year, which is a key driver of that 20% growth.

What we also saw in the first quarter was that rebating levels that we had to book dipped to 64% in the first quarter, and on the first-quarter call I was giving guidance that I expected it to be in the 65% to 70% range. Our citing now is that we are more likely to be nearer the 70% range.

So once you stripped out the stocking effect and the return to the expected level of discounting we expect to see for the balance of the year, I would expect the full year to see growth in ADDERALL XR in the really quite low single-digit percentage terms.

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Jeff Jonas - *Shire plc - SVP, R&D*

The only thing that I would add to Angus's point is that the market growth continues to be strong. We've talked a lot about the adult side of the market driving that, but we've seen an acceleration that has held up for the last few quarters in the pedes area as well. So it's actually a very good situation for us right now in ADHD.

Peter Verdult - *Morgan Stanley - Analyst*

And, Mike, anything worth mentioning just as we head into the northwestern launch for Concerta.

Jeff Jonas - *Shire plc - SVP, R&D*

Yes, I don't generally comment on that, but we don't see a huge market disruption there. They seem to have a very similar strategy to what we did with XR, so I don't see a real cheap alternative out there. But yes; I don't think it affects the market dynamic as it is today.

Peter Verdult - *Morgan Stanley - Analyst*

Thanks.

Operator

Brian Bourdot.

Brian Bourdot - *UBS - Analyst*

I'll stick to your rules and ask just one question. Now that you've had the inspection of Lexington or the REPLAGAL production at your Lexington facilities, do you have any transparency on time lines to potential approval, or is it rather vague? Thank you.

Angus Russell - *Shire plc - CEO*

That's a question to Sylvie. I'm sure she can walk you through, give you some guidelines on what the process would be from here, Sylvie, to get approval.

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

Yes; there's two steps right there. We filed the data required, demonstrating the production of the batches at the facility, and then the inspectors came, all this to the EMEA. And we therefore expect, as we said before, I think, approval before year end. And we will update you, of course, as soon as we have more information. But the filing occurred, the inspection was done. I think in the fourth quarter, surely, we can expect news from the agency.

Brian Bourdot - *UBS - Analyst*

Thank you.

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Operator

Gary Nachman.

Gary Nachman - *Susquehanna Financial Group/SIG - Analyst*

Just to follow up on the last question, Lexington facility, Sylvie, what are the latest plans for filing an NDA for REPLAGAL in the US? And then just confirm for us how far behind VPRIV is in getting approval in the EU and the US? You said mid-2012, but could it potentially be earlier?

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

So we are on plan with our activities that we had anticipated in the Lexington facility. I'll start with that question and then go back to the REPLAGAL BLA. We had announced that we would do the PVRs for REPLAGAL, and we filed those, as you've seen. So we are -- the VPRIV PVRs are ongoing, as mentioned by Angus. And we anticipate to file before the end of the year for those in the EU as well as at the EMA so that we -- and then the same process of having an inspection and can be anticipated and with the review of the application. So sometime in the first part of the year next year is when we anticipate the facility to be approved for VPRIV.

Remember, there's a little bit more data than there is for REPLAGAL in that there is a cell culture part as well as the purification part of the application. But that's -- we are on the same timing that we have announced, I think, the last two quarters, and the activities are progressing well on VPRIV in the plant as well.

In terms of REPLAGAL filing in the US, I think we said last quarter, and I can reassess that, that we're looking at the data coming in from these switch trials that are ongoing, the Canadian trial that's a head-to-head comparison trial as well as some data in Europe of the many patients that have switched from Fabrazyme to REPLAGAL. We're going to take a look at all of this over the summer and we will let you know in the back half of the year whether, based on what we see and the market opportunity and what other opportunities exist in terms of -- or the residual effort that would be required in the US, what our decision is relative to the filing of REPLAGAL in the US.

Angus Russell - *Shire plc - CEO*

Probably worth reiterating, just to give you a fully comprehensive answer in case anybody knew who didn't catch prior calls -- but the existing facility that we have (inaudible) is actually still producing material, remember, to give us the opportunity to supply more patients on both the VPRIV and REPLAGAL, so probably just worth reiterating about 300 patients is what we said, across the course of the year, for REPLAGAL, and about 200 more, potentially, for VPRIV is the capacity that we will increment across the year. And you've seen that already, that we've supplied and been able to take on more patients in the past quarter, and that will continue throughout this year until we build up to those kind of numbers.

Gary Nachman - *Susquehanna Financial Group/SIG - Analyst*

Okay, thanks guys.

Operator

(inaudible) [Parakh].

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Unidentified Participant

I actually have two, if I may. First of all, Graham, you have spoken about the opportunity for incremental operating leverage in 2011. Can you give us some flavor of what that might be? Are we looking at 100 basis points on an operating profit basis, 200 basis points? Some sort of flavor might be useful.

And secondly, for Jonas, as we look at the opportunity for VYVANSE in this other indications, I guess the one with schizophrenia -- Roche has recently started a Phase 3 program for one of their drugs which involves roughly about 4000 patients and is going to be a very, very expensive trial. What sort of cost are we looking at for running these Phase 3 trials?

Graham Hetherington - Shire plc - CFO

If we go back to the guidance I gave at the beginning of the year, that framework and your framework broadly hasn't changed; gave you operating leverage in the range of 100 to 200 basis points.

Angus Russell - Shire plc - CEO

Jeff, do you want to (multiple speakers) about these trials? You did indicate that we are not planning to do the same large-scale because we're looking at subsets of patients that have already been tried on many of these other products.

Jeff Jonas - Shire plc - SVP, R&D

Angus answered it.

Angus Russell - Shire plc - CEO

Kind of ballparked it.

Jeff Jonas - Shire plc - SVP, R&D

I think that it's probably a little premature to estimate, but I can tell you that, obviously, I'm familiar with the public data from the Roche program, and I'm pretty confident that we have a strong enough signal that it won't require that type size program. There are differences between the compounds and, I think, differences between how the studies were done. So with the caveat that we are going to have meetings with the FDA and global authorities, I'm pretty confident, given our signal size, that we will be able to do this with a smaller population. And that is our underlying thesis, that if the signal is not strong enough we won't continue the studies.

Unidentified Participant

Thank you.

Operator

Kerry Holford.

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Kerry Holford - *Credit Suisse - Analyst*

Hi, thank you, Kerry Holford of Credit Suisse. I wonder if I can ask a couple of questions on REPLAGAL and VPRIV. Can you tell us how many patients have been added on to both of those drugs during the first quarter? And, can you tell us whether you seen any switchbacks to the Genzyme products, particularly from VPRIV to Cerazyme, since they have then back on full capacity?

And then, quickly, on Lexington, the EU approval -- what could that mean in terms of additional patient capacity?

Angus Russell - *Shire plc - CEO*

Sylvie?

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

So I'll start with REPLAGAL, perhaps. So, as mentioned by, I think, Graham over the -- in his presentation, we have been able to add -- we've seen about 100 patients, new patients added on REPLAGAL. The majority of them were naive patients, as we anticipated. And there's very little, obviously, switchback to Fabrazyme at this stage because there's no Fabrazyme to switch to. And so I think that was the essence of your questions regarding REPLAGAL.

Regarding VPRIV, we've also added some patients. Obviously, the rate of growth on the VPRIV side now that there's a stabilization of the market, if you will, since, as you mentioned, there is more. Certainly Cerazyme or the market conditions in the US have stabilized and there is more Cerazyme in the US. But we still have -- and there are a few patients, a handful of patients have switched back or, I would say, stopped taking VPRIV. Some switched back to Cerazyme. A few went to in a trial, and a few just went off product. But, again, a very small amount of patients have done it. And overall -- or we have added patients; we are net positive on adding patients all over the world with the product, with small amounts of patients in each geography.

Angus Russell - *Shire plc - CEO*

The Lexington facility was how much bigger is the Lexington facility --

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

Oh, I see --

Angus Russell - *Shire plc - CEO*

(multiple speakers) and what could you envisage in terms of perhaps REPLAGAL? We've got [captures], as you said, now filed with the regulators. So probably just some feel of relative scale of the (inaudible).

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

So you will recall that for REPLAGAL the Lexington facility is being approved for the purification of REPLAGAL. And so what we -- that's the manufacturing step that's there. So the numbers, however, we have provided to you this year in terms of being able to add 300 patients, which, by the way, is about, relative to the demand quarter to quarter that we anticipate, it comes all from the Alewife facility. So the REPLAGAL from the facility, the new facility will be used when approved, and patients will be able to come on next year.



Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

And of course, being able to purify REPLAGAL at the new facility immensely enhances the flexibility of the utilization of these plants. The true enhancement of capacity from a cell culture side, of course, comes when VPRIV gets approved so that it can, or the cell culture of VPRIV can be removed from the Alewife facility and be put into the Lexington facility. But having REPLAGAL in the new facility does help a lot in terms of -- and we use the term debottlenecking. That's not a very elegant term, but just increasing the flexibility of the manufacturing on the purification side.

So I hope this answers your question.

Kerry Holford - *Credit Suisse - Analyst*

Understood, thank you, so just to clarify, you could add around 300 patients onto REPLAGAL this year?

Angus Russell - *Shire plc - CEO*

Yes, that's out of the Alewife system. That's our existing factory, just so -- you may not recognize the name. So that's not Lexington, that's in another part of Boston, just down the road, it's called Alewife is where we currently manufacture. So we said 300, and I mentioned earlier we can do another 200 patients from that facility during the course of this year on VPRIV.

Kerry Holford - *Credit Suisse - Analyst*

Understood, thank you.

Operator

James Gordon.

James Gordon - *JPMorgan - Analyst*

I was having a look at VYVANSE for negative symptoms of schizophrenia, and on clinical trials (inaudible) I can see a study designated 320, and it looks like a Phase 3 negative symptoms of schizophrenia study, so 500 patients, 26 weeks with a 213 readout. Is that the right study, or is that a clinical trials mix up?

And also just on schizophrenia as well, are we going to see a separate study in cognitive impairment?

Jeff Jonas - *Shire plc - SVP, R&D*

I'm sorry; I missed the last part of that question.

James Gordon - *JPMorgan - Analyst*

The first part was --

Angus Russell - *Shire plc - CEO*

We got the first part; it's the second part. I can't hear you, James. You are very faint. I don't know whether you are on a cell phone or something.

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

James Gordon - JPMorgan - Analyst

I picked up my handset, hope that helps. The second part was previous results. You've also referred to looking at the cognitive symptoms or treatment of the cognitive symptoms of schizophrenia as a Phase 2. I can't see that listed anymore. Is that something we are also going to see, or was that just part of this study?

Jeff Jonas - Shire plc - SVP, R&D

So the listing on clinicaltrials.gov had been an earlier study that was -- that I think we've rethought. We haven't started that, basically, I have to say, candidly, because the signal size was somewhat stronger than we had anticipated in this study.

With respect to cognition, we are looking right now at the cognitive improvement in this study. But these patients really were not selected for cognitive issues; they were selected for the negative symptoms. And we may still look at cognition. But again, the results for the negative symptoms were strong enough, in our view, that we are right now focusing our intentions there.

James Gordon - JPMorgan - Analyst

So, just to make sure I've got that right, the cognitive symptoms -- there wasn't a separate Phase 2; it was just something that you were going to look at as part of this Phase 2 that's reported today?

Jeff Jonas - Shire plc - SVP, R&D

Right. We have cognitive endpoints here, but we are not going to do that now, no.

James Gordon - JPMorgan - Analyst

And the study that's already on there, the Phase 3 that's already on there in schizophrenia, that's one that would eventually become the one you are talking about, potentially starting with the end of the year, or that's something else?

Jeff Jonas - Shire plc - SVP, R&D

It could be, yes, it could be. But it's likely -- we are waiting [to test it], yes. So -- pending discussions with regulatory authorities.

James Gordon - JPMorgan - Analyst

Okay, thank you.

Operator

Graham Parry.

Graham Parry - BofA Merrill Lynch - Analyst

Firstly, on ADDERALL XR, just wondering if you could confirm the duration of the authorized generic contracts with Impax and Teva. Presumably, they have a fixed duration. And discuss commercially what you would do in the event that you never did see generic launch by that time, if those contracts are actually expiring. Is there any way you can bifurcate the market, target some

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

patients with VYVANSE, some with ADDERALL XR, and whether you would actually put any promotional effort behind XR in that scenario.

Secondly, just can you give us a couple more details on the co-administration launch in terms of when, who, breadth of the launch and just remind us what you think the addressable population for co-administration is?

And then, thirdly, just a question on schizophrenia. Is 14 weeks long enough to detect whether we see any impact from positive symptoms of schizophrenia and what duration of (inaudible) trial do you think regulators will actually need for approval?

Angus Russell - *Shire plc - CEO*

I'll do the first and maybe ask Jeff to do the next two as kind of (inaudible).

Yes; the contracts, I mean, it has become a matter of public record, since I think some of the generics have talked about that both Impax and Teva's contracts were for five years, fixed-term contracts. That's very clear in both contracts. Obviously, they commenced -- if you remember, Teva came in on April 2009 and then Impax in October 2009, so five years fixed terms from those dates.

Because of that, we are actually in 2014, and that's some ways off. So I can tell you, whilst we have it at the back of our minds and the points you raised are all very interesting, Graham, I would say it's too early. We are just focused on the current business. But I guess, as we get nearer to those dates, I'm sure both we and our authorized generic colleagues will be focusing on those kind of issues.

So with that, let me just hand over to Jeff (multiple speakers).

Jeff Jonas - *Shire plc - SVP, R&D*

I'll take the co-ad. And then, James, we may have to ask you for the third part of the question. But anyway, on the co-ad, why do we care about it? If you look at the use of INTUNIV today, about 50% of the scripts are coming out of the adjunctive therapy between either a stimulant and INTUNIV or, in many cases, VYVANSE and INTUNIV.

We think that's good, but in fact if you look at the potential, the potential is that there are only one out of every five scripts, roughly 20% of co-administration patients coming to VYVANSE. So we think there's a lot of potential there. And you have seen this data before. What are the other agents that are being used out there? There's Tenex, there's other antipsychotics. We think those other four out of five scripts should be going to INTUNIV. We have the data to support that. We haven't been able to promote that since launch, so we think there's a fair amount of upside for us there.

It was launched a couple weeks ago. You should have potentially seen ads in the US. They were endorsed by CHADD and NAMI and ADDA, not prospecting for patients but actually taking a diagnosed patient who is not happy with the existing therapies and making them aware of INTUNIV. We will be following on with a more specific ad campaign later this year around adjunctive therapy. But the adjunctive therapy itself was launched with the sales force a couple weeks ago.

[Jeff], can we just asked for a clarification on question three? It was related to NSS.

Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Graham Parry - BofA Merrill Lynch - Analyst

So the question was just whether 14 weeks, i.e., what you saw in Phase 2, would actually be long enough to detect whether you were seeing any impact from positive symptoms, i.e., is there a risk that with longer duration of therapy you would have an impact, and what duration of therapy would be sufficient to satisfy a regulator of that?

Jeff Jonas - Shire plc - SVP, R&D

That's a good question. I think one of the reasons we're consulting with the agencies is just for that. I think the expectation, as you know from the clinical folklore, is that these patients will have very rapid exacerbations. That has not been the case. Now, one of the observations here that these are patients on stable antipsychotics. So in theory, we can argue that they have coverage in the areas that cause positive symptoms, the so-called subcortical D2 receptors, for those of you who care, and that the prefrontal receptors of what we are attacking or are implementing with VYVANSE. So there may not be a theoretical reason, in fact, to see those exacerbations.

I think in part of the study, we intend that when we go forward we will do a long-term safety program. It's likely it will be 12 months. But again, we intend to do a program based on the signal size that's more in line with meeting ICH criteria of 1500-2000 type of patients, or whatever is required for regulatory guidance but not farther or greater, because of the consistency of the signal.

I think -- so that long-term I suspect that the duration of the study was probably long enough to see any real exacerbations, especially because the behavior of the patients in the demographics was pretty consistent with the type of exacerbations one would see in a normal schizophrenia program.

Angus Russell - Shire plc - CEO

I'm conscious it's a busy day for you, and it is for us, too. So we've been running for well over an hour, and I will suggest we take one more question and then hopefully Sarah and Eric will be available to follow-up with your calls or we could take some other calls off-line. So let's just have one more question.

Operator

David Buck.

David Buck - Buckingham Research Group - Analyst

Just a quick question on progression of a couple of product sales for INTUNIV. Obviously, you have the co-administration that has now been launched, but it has been a little bit lumpy in terms of progression of sales. Can you talk about what you see for the rest of the year in terms of progression and what you think the ultimate opportunity for a non-stimulant might be in the ADHD market?

A similar question for Sylvie -- what should we be looking at for progression of REPLAGAL/VPRIV?

And just one quick question for Jeff -- on the study for schizophrenia, the timing to get the significance, at least as presented, looks like it was about week 10. Was that the first significance, or was it earlier but you just didn't show that data?



Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Angus Russell - *Shire plc - CEO*

Okay, so it's a good job we only allowed one more question because we got three there. Thank you, David. So, Mike, INTUNIV, I think?

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

Progression of [sales] INTUNIV -- yes, I think we've done quite a bit this year between the adjunctive launch and what we are doing for the existing claim that we had in the pedes market. I think you will continue to see it grow. It's something where it has met our expectations. I think, as you see these direct-to-mom ads, you will see it continue to see pickup. We have a 0.6 new to brand right now over the last month, which we think is strong, so we are confident that it will grow throughout the year.

I guess we did give peak year sales guidance; I don't think that has changed. I can't remember exactly what that was, but it was somewhere around \$600 million, I believe was our original guidance. And I think we are in line with that.

One thing we haven't talked about very much on our calls is the potential for Europe. Angus mentioned it in his opening remarks. I think we have a clear pathway to exclusivity, even though the IP is no longer with this product in Europe. So I think it has potential in Europe that you will see emerge over the next three to four years.

Angus Russell - *Shire plc - CEO*

Probably just to reiterate once again, Mike, it's just like even holding share in this market gets you, at the moment 13% (multiple speakers) volume growth plus a pricing benefit, which is usually an annual event for these products, at least (inaudible). So (multiple speakers) Mike said to me, we think with these new introductions just approved, that there's -- just to go for more upside there in market share gain, too. And remind you we're the only game in town now promoting these kind of drugs.

So Jeff, just on the timing issues around the study?

Jeff Jonas - *Shire plc - SVP, R&D*

In that study there are two points to make. One is the primary endpoint, which is what we presented today, was LOCF, change from baseline and endpoint. It does look like, and I don't have it in front of me, we achieved significance sooner.

One of the points to remember, though, is that we were tiptoeing with this program. So we started nations at very low doses and then titrated them up. And even though the majority ultimately got to 70 milligrams, 60 to 70 milligrams, it took a number of weeks because it was a forced and regimented titration.

It's likely that when we review this study we won't have to be quite as judicious in our up-titration so that we can probably see an effect more rapidly. So right now I think it's hard to judge how soon we can get that effect.

Angus Russell - *Shire plc - CEO*

Sylvie, I'm not sure what more we say. We gave out the patient numbers that we can supply this year in VPRIV and REPLAGAL. And if you have anything else you want --



Apr. 28. 2011 / 12:00PM, SHP.L - Q1 2011 Shire PLC Earnings Conference Call

Sylvie Gregoire - Shire plc - President, Human Genetic Therapies

Well, I'll just reiterate I think that the market growth for -- certainly in the Fabry market is mainly the naive patients at this stage, since the two companies are providing product to patients that are already treated. And that's about, we estimate, 75 to 100 patients per quarter and (inaudible) this quarter. And I think that, if I look at consensus, that's what everybody also carries somewhat in their models, and it corresponds to, therefore, also the supply projections that we said we could meet this demand. And the same for VPRIV; there's some small growth, slow growth of the product in terms of new patients this year. But relative to last year, of course, there's lots of growth. And I think that I would just say that whatever consensus is carrying, it seems that we are in line with that.

David Buck - Buckingham Research Group - Analyst

So just to follow up, sequential growth, then, for REPLAGAL and maybe flattish for VPRIV? Is that the way to look at it?

Sylvie Gregoire - Shire plc - President, Human Genetic Therapies

I would say small growth for VPRIV and the growth of between 75 and 100 patients for REPLAGAL -- again, in line -- both products in line with what (inaudible -- background noise).

David Buck - Buckingham Research Group - Analyst

Okay, thank you.

Angus Russell - Shire plc - CEO

Okay. So with that, folks, thank you all again for your time, particularly people in the UK, I know, have got a busy day, given that it's a holiday tomorrow. And with that event in mind, I guess we should wish everybody gets to the church on time tomorrow. So thanks very much, folks. Have a good day, bye.

Operator

Thank you. Ladies and gentlemen, that concludes your conference call for today.

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