

# FINAL TRANSCRIPT

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## **SHP.L - Q2 2010 Shire Plc Earnings Conference Call**

**Event Date/Time: Aug. 04. 2010 / 1:00PM GMT**



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*Shire Plc - CEO*

**Graham Hetherington**

*Shire Plc - CFO*

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## PRESENTATION

**Operator**

Good day, ladies and gentlemen, and welcome to the Shire's 2010 second-quarter results conference call hosted by Eric Rojas. My name is Grant, and I am your event manager. (Operator Instructions). I would also like to advise all parties this conference is also being recorded for replay purposes, and now I would like to hand the call over to Eric. Please go ahead.

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**Eric Rojas** - *Shire Plc - IR - North America*

Thank you. Good morning and good afternoon, everyone. Thank you for joining us today for Shire's second-quarter 2010 financial results. By now you should have all received our press release and should be viewing our presentation via our website on Shire.com. If for some reason you have not received the press release or are unable to access our website, please contact Souheil Salah in our UK Investor Relations department, +44-1256-894-160 as he will be happy to assist you.

Our speakers today are Angus Russell, Graham Hetherington, Sylvie Gregoire and Mike Cola. 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 as follows on slide three. 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 review of our Specialty Pharma business performance, and Sylvie Gregoire will update you on the latest developments in our HGT business. Angus will then summarize the key points for this presentation, and we will then open up for your questions.

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

And now I will pass it on to Angus.

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**Angus Russell** - *Shire Plc - CEO*

Okay. Thanks, Eric, and hello, everyone. Let's turn to the opening slide, which is number five. As you can see from the title, I believe these results and what you will hear throughout this conference call will demonstrate that Shire is performing really well on all fronts. These financial results, I believe, are truly excellent, and you can see that with the revenues up 35% to \$849 million in the quarter.

As you can see from the sub-bullet point here, revenues are now ahead of pre-ADDERALL XR authorized generic levels just after 15 months. That is a remarkable achievement and one that I don't think I have ever seen in this industry. If you remember, ADDERALL XR was almost 50% still of our revenues just over two years ago. So to be back so quickly to sales in excess of that level and with a tremendous growth platform ahead for many years to come, truly a remarkable performance.

Core product sales -- and those are the ones excluding ADDERALL XR -- were up 39% to \$684 million. Non-GAAP diluted earnings per ADS were \$1.03, well ahead, I believe, of market expectations, and that is up 71% versus the same quarter last year, and the strong cash generation has also been very strong this quarter at \$416 million. And on the basis of all of these results, I'm happy to say the board has authorized an increase in the first interim dividend of 5% in US dollar terms.

Let me turn to the next slide now and talk a little bit broader about the strategy, which, again, I believe, from these results is showing clear evidence of delivering. We have now eight global products driving growth, and they are all very much focused on specialist prescribers meeting customers' very high unmet medical needs.

We continue to extend our geographic reach. The proposed acquisition of Movetis NV adds to our core GI business in this respect and hopefully will soon allow us to say that we have nine global products driving growth well into the future.

We've got a lot of pipeline progress on key development programs, and both Mike and Sylvie will make some comments on that in their presentations. I believe we are very well placed to absorb industry macro challenges, and these have been quite numerous in the year to date. We have had US healthcare reform proposals. We have had some adverse pricing impacts in

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Europe, not to mention other macroeconomic effects moving against us such as exchange rates. And despite all of that, we have not only been able to just maintain the guidance you have seen from these results, we have actually upgraded our guidance while taking on board all those adverse changes.

Full-year earnings, therefore, we believe, are now tending towards \$4.00 per ADS. If we had hit that \$4.00 mark, it will indeed represent a 15% increase on our 2009 earnings. And I believe that gives us a great platform to achieve our aspirational target, which remains the midteens sales growth on average between 2009 and 2015. So having made those opening remarks, let me now hand over to Graham who will take you through these financial results in a little bit more detail.

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**Graham Hetherington - Shire Plc - CFO**

Thank you, Angus. Good morning. Good afternoon. I will be covering three themes today. The first are drivers of another very strong earnings performance that Angus has just described. Second, reinforcing how these results represent a real breakthrough in Shire's journey. That is the growth of our core portfolio is now fully visible in our total results. Third, I will reinforce what Angus has just been saying, that despite some external headwinds why we were able to increase expectations for earnings in 2010.

So first on slide eight, an overview of our reported requirements in the first clean quarter since losing exclusivity of ADDERALL XR. It is an outstanding result. Total revenues are up 35%. EBITDA up over 100%, demonstrating value-enhancing operating leverage, and EPS increasing by over 70% despite an unusually low tax charge last year.

Significantly we double cash generation compared to last year.

The next chart, nine, breaks out our revenue growth in more detail. The big story is that growth of our core portfolio generating nearly \$200 million more sales compared to last year with growth of 39%. You can see that the impacts of foreign exchange on our revenues has started to move into negative territory in the second quarter. This is a trend we are seeing continue into the second half.

ADDERALL XR has benefited from its sustained market share. Sales deductions were high at 74%, offset by some stocking compared to last year when we saw significant destocking following the launch of the authorized generics. I expect the contribution from ADDERALL XR to reduce in the second half, and we will give you more specifics later in the presentation.

We benefited from another healthy contribution from royalties. The royalty we now will receive from Impax is higher than the receipts from Teva last year. Again, I will touch more on the dynamics for the balance of 2010 later.

So moving to chart 10 where you can see the sources of our growth, it is broadly based both by product and geography. We now have six products with annualized sales of over \$200 million.

From the ADHD franchise, which Mike will expand on, we saw further market share gains from VYVANSE. Sales deductions for VYVANSE spiked at 37% in the quarter. I expect them to return to nearer 35% for the balance of the year.

We achieved significant gains from the successful launch of INTUNIV. Prescription demand allowed us to recognize the last \$90 million of deferred launch sales, and demand also pulled through an additional \$29 million of pipeline inventory.

In GI LIALDA continued to gain market share, and we saw significant growth from our HGT franchise. Sylvie will be expanding on this, but looking at this chart here, ELAPRASE continued to deliver double-digit growth despite foreign exchange headwinds.

REPLAGAL is clearly benefiting from the significant patient switches we supported. In the second quarter specifically, we also saw accelerated sales of product that physicians were securing for their patients. Some of this will be used for treatments in the second half, so we will see a reduced rate of growth for the rest of the year.



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VPRIV is now generating accelerated revenues from commercialization, following the approval in the US and pre-approval reimbursement in other parts of the world. Our young portfolio represents an exceptionally strong foundation and now visible demonstration of our future growth prospects.

Turning to the next chart, 11, our actual dollar spend on R&D and SG&A increased compared to last year when we were managing down expenditure as we faced authorized generic competition from ADDERALL XR. You can now see operating leverage from the total business, and critically this reinforces Shire's breakthrough this quarter. Both R&D and SG&A percentages are now starting to reduce as a percentage of total product sales, as well as a percentage of core product sales.

Given the strong performance of the business and the opportunities we see for future growth, we are continuing to make investments in 2010 and beyond. And even with this investment, we will continue to generate operational leverage from the growth of our core portfolio, coupled with solid cost management.

Let's look at our cash generation on chart 12. Again, this is a reinforcement of this breakthrough quarter for Shire. \$0.4 billion of cash generated in the quarter, which compares with \$0.2 billion last year. The key drivers of this increase is the additional \$200 million of core product sales this year. This cash generation has funded the acquisition of our HGT side in Lexington, and with this, we have secured a significant strategic asset while creating significant value from the use of our cash resources. Even with this investment, we saw a further reduction of our net debt, which is now less than \$400 million. We continue to have a strong and flexible funding position to manage future refinancing and support investment to further enhance the quality of our business as we have demonstrated yesterday with the proposed acquisition of Movetis for cash.

Turning now to the balance of 2010 and the dynamics that will support the growth in full-year earnings, on chart 13 I'm focusing on ADDERALL XR. Sales in the second quarter reflect high sales deductions offset by increased inventories pulled through following supply shortages we experienced in the first quarter when inventories fell to 15 days. With 27 days of inventory at the end of the second quarter, we are now inside our normal range of 20 to 30 days.

As we move forward, there are a number of dynamics over which we have limited influence. These include the continued potential to some brand erosion and constant destocking and our reliance on sufficient DA quotas to support supply for the brand and the two authorized generics. My working assumption now is that ADDERALL XR product sales and related royalties together will be around \$400 million in 2010.

Looking out beyond 2010, we increasingly believe that it is more likely than not that there will only be authorized generics. The ADDERALL XR franchise is likely to generate significantly greater value over time than the market is currently forecasting.

Finally, let's look at the dynamics of the total business on chart 14 that support our increased earnings expectations. We now see, as Angus said, EPS per ADS trending towards \$4.00, which represents a 15% growth compared to last year. And just to reinforce, this guidance includes (technical difficulty) to the proposed acquisition of Movetis.

It is important to reinforce that we have been able to increase our guidance despite a number of external dynamics that have emerged in the last six months, and these are highlighted at the top of the chart. Firstly, US healthcare reform, which I have covered in some detail on the first-quarter call. Secondly, European pricing, where our sturdy measures are putting pressure on reimbursement and pricing in the EU. Shire's exposure is limited since only a quarter of our product sales are into Europe, and nearly two-thirds of these sales are orphan drugs, which in most cases are excluded from the measures being taken. We are absorbing between a \$15 million and \$20 million impact in 2010.

And thirdly, foreign exchange rates. Shire remains a dollar reporting company with 70% of our revenues generated in dollars, so our exposure is limited. You can see from the update of RESOLOR at the bottom of the page, that our most significant exposure is the movements in the euro to the dollar.



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It is worth reinforcing that our guidance assumes the current depreciated spot rate of around EUR1.30 to the dollar for the second half, which is lower than the average rates we experienced in the second half last year and the first half of this year.

Despite all of these factors, the broad-based underlying strength of the business is allowing us to increase earnings expectations for the year. We would continue to see significant growth from our core product portfolio, but the rate of quarterly year-on-year growth will moderate compared to the strengthening comparatives in 2009.

And, as I've said, the sales trajectory of REPLAGAL will moderate in the second half.

Royalties will benefit from the continued Impax royalties. That said, we expect the level of royalties from Impax will be lower, are likely to be lower in the second half as we will no longer benefit from the Impax launch shipments of the authorized generic.

The net result is that we expect full-year total royalties to be slightly up on last year. I still expect our full-year gross margins to be in line with the end of 2009 at approximately 86%. You have seen our R&D expense start to increase year on year, and you will see SG&A doing the same in the second half. Our strong performance is enabling us to increase investment in 2010 and beyond in the long-term growth of the business. And, as a result, in 2010 the aggregate dollar increase in R&D and SG&A will be around 10%, at the top end of our previous guidance range of between 5% and 10%.

Finally, our tax rate. We are still looking to rates in 2010, broadly in line with last year's 25% rate. So another great quarter that has given us the confidence to increase the expectations for earnings in 2010. It also demonstrates that Shire has really broken out from the impact of losing exclusivity on ADDERALL XR and reinforces the sustained growth potential of the business going forward.

I will now hand you over to Mike. Mike?

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

Thank you, Graham. Good morning and good afternoon to everyone. In light of our proposed acquisition of Movetis, we thought now would be a good time to step back and take a look at the strategic imperatives that we faced in specialty only five years ago and take a look at how we have progressed against those challenges. If you think back to 2005, the specialty business was primarily a one product, ADDERALL XR, one market, US, and really one patient type, mostly pediatric-focused organization. Obviously there is tremendous risk there. We had multiple generic filers at that time, and we knew we needed to broaden our remit in order to be successful.

As Graham has discussed, we have been able to protect the XR franchise to some extent, but really today's performance is driven by three major areas. And they are multiple products that are growing rapidly in a very dynamic ADHD market, our globalization efforts to bring our products to more patients outside of the US, and investments we have made in new uses for our existing products, coupled with the current new pipeline candidates, which I will discuss in more detail today.

First, let's look at our ADHD portfolio. Obviously the cornerstone of that portfolio is VYVANSE. It continues to grow quite nicely with net sales and TRX volume up almost 30%. It's in a very dynamic market -- year-over-year growth of 12%, year-to-date growth of 10% -- and I would like to think that Shire gets most of the credit for that market growth. Good progress in an extremely fast-growing market, particularly the adult ADHD market.

Let's move on to INTUNIV. Our launch continues to make progress and meet our expectations. Our national share has gone up almost a full point since we last talked to 2.6. We have a significantly higher percentage of the market in the very important child and adolescent psych area with over 18,000 physicians having now prescribed INTUNIV.



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Earlier in the year we had a lot of questions about where is that source of business coming from; will it hurt VYVANSE; are you going to pull mainly from Strattera? And until the data settled down a bit, we thought it would be best not to share that, and now we feel confident based on the last few months that, in fact, it is relatively stable and worth discussing.

About 10% of our patients are new starts to INTUNIV. They are new to the market patients. I think that is good. It helps us grow the market. 37% are switches, and I will talk a little bit more about the source of those switches. And 53%, roughly half are add-on therapy, so used in combination with another product.

40% of our switches come from Strattera, which is not surprising, although we are not directly targeting Strattera. The others come from the short-acting Alpha 2s and the atypical antipsychotics. So we are pulling very broadly from all parts of the market, and in fact, we are being used in concert with many other products in this market. I think that bodes very well for INTUNIV long-term. I will come back at the end and give you a bit of an update on our co-administration data, which I think is an important to the future.

Finally, EQUASYM continues to provide an excellent footprint for the European ADHD business that expands -- as it expands. Globalization is important to us at SP, and I think we are actually starting to execute against our globalization plans. VYVANSE is off to an extremely strong start in Canada with a 4 share after five months -- just a great job by the Canadian team. VYVANSE, which will be known as VENVANSE in Brazil, was approved in July, and we are looking for a first half of 2011 launch. Although it is a relatively small market and it is growing rapidly, it really is a major milestone for the ADHD franchise as it is our first VYVANSE approval outside of North America. VYVANSE European trials are now more than 50% enrolled and on target for a second half of 2011 submission. That is going as planned. And we will advance a guanfacine-based product in the EU for ADHD, and that will either be INTUNIV, as we think we will get 10 years data exclusivity for INTUNIV, or one of the CarrierWave guanfacine programs, which I will discuss at the end of this presentation.

And lastly, we don't talk much about it, but, in fact, we have the rights for XAGRID back in Japan, and we think there is a real market opportunity, and we continue to progress our Phase III efforts. We are looking at potential partners to take that Phase III forward since we are now terminated with Kirin, our former partner.

I would like to move to slide 19 of the proposed Movetis acquisition, which we feel is an extremely strong fit with our core GI business. If you think back just five years ago, GI at Shire was a relatively small nascent business. It was a little over \$100 million. It was based on PENTASA. It was completely US-focused. Spinning off a reasonable amount of cash, but again no real direction.

Since the formation of the GI business unit and the addition of LIALDA, we have grown that business fivefold. Last year LIALDA was our fastest growing product at 68%. And, in fact, we felt that we needed to invest in this business in a way that filled in some of the gaps that they had in their business. They were the pipeline, not really having a pipeline besides diverticulitis, organizational capabilities around discovering and developing new products or licensing in new products, and finally, creating a much more global footprint outside of the US.

Movetis ticks most of those boxes. It is a Belgian GI specialty company created in 2006 as a spinoff of J&J. This group has tremendous pedigree. They are the foremost experts on motility disorders in the gut in the world today, and their lead product is RESOLOR, which is an exciting addition for us. RESOLOR is for meeting the symptomatic unmet need for chronic idiopathic constipation. It has a unique MOA. It's a selective 5-HT4. It does not appear to have any of the cardiovascular issues that have plagued this class of drugs, and it has a patent that will protect it through 2020.

We think there is significant upside potential for RESOLOR in new populations, peds and males, and other indications, opioid-induced constipation.

Also, there is a substantial library of both new chemical entities and potential new products for us that are, I will say, early stage but still exciting. We have [MV002], [MV003], and then a whole library of new products that we will be working with Movetis to evaluate over the coming months.



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So very exciting for us. We are very happy to get this. It fills in a great strategic need for the GI business unit.

Moving on to slide 20, the R&D pipeline. We are going to focus on new indications first. As you know, over the last 12 to 18 months, we have had many signal finding studies underway for VYVANSE. With the long patent life, we can invest in VYVANSE in a way that we have not been able to invest in old 505b2s in the past.

We have not discussed it very much, but we have a pending indication for VYVANSE in the adolescent area, which is 13 to 17 that we think is important and will launch in the first half of next year. Why is it important? We know that we lose a significant number of patients in the late teen years, early 20s as they kind of fall out of the system based on the fact that they no longer go to a pediatrician and they move on to a primary care physician. And, in fact, we don't see those patients show up again until their mid-to-late 20s.

So this is exciting for us. We think it is a way for us to promote directly to those patients and keep them in the system.

We will have top-line results for depression augmentation the second half of this year. I hope to be able to discuss them in October on our next quarterly call, and then we have a number of signifying studies underway, which actually headlined in 2011. Those are negative symptoms of schizophrenia, cognitive impairment and depression, and excessive daytime sleepiness.

As I spoke about earlier, we have some very exciting results with INTUNIV in the coadministration study. It met all of its primary and secondary endpoints, and we have submitted an sNDA to seek approval as adjunctive therapy, along with [all-comers'] long-acting stimulants. We hope to get this thing approved first half of next year and launched.

Why is it important to us? Well, stimulants and non-stimulants consist of about 12% of the market today. They are coadministered, and that segment of the market is growing 20% annually, which is significant. We think we can be the player in that coadministration market. When you look at the data, it looks as if the coadministered product VYVANSE -- I am sorry, INTUNIV and long-acting stimulants outperforms stimulants alone or INTUNIV alone. So very exciting data. Look for the first half of next year to launch that.

Finally, diverticulitis with LIALDA. The trial is fully enrolled, and we expect to have headline data in 2012 for a 2013 launch.

On to the early-stage products and I think the program we've had the most questions about is known as SPD 547. This is Guanfacine CarrierWave, obviously important to us as we have 2015 exclusivity on INTUNIV. We have had a number of people asking, how are you going to continue that franchise, that non-stimulant franchise? And obviously this is an important part of that strategy.

We have completed a feasibility study in humans using micro doses under an experimental IND. These are very small doses. But they are generally predictive of how a product will perform under normal dosing conditions. The results indicate characteristics suitable for entering formal Phase I studies and really a product that we think can be successful in the marketplace. Those studies will initiate this quarter, and we will have more detailed results throughout 2011.

The premise for a Guanfacine CarrierWave product is that we can actually improve on the INTUNIV profile. We think we can minimize the known food effect, which is high fat meals causing inconsistent dosing. Inconsistency and the delivery due to PDH and transit time in the gut, very similar for what we did for amphetamine with VYVANSE. And then the hope is that we can possibly reduce the somnolence and sedation side effects.

Obviously our target is back-to-school 2014. We think we can go a little beyond that if we have to.

Finally, I would like to end with SPD 535. It is a novel platelet-lowering agent. The initial proof of concept program targets thrombotic complications from AV graphs in hemodialysis patients. We have the proof of principle data, and we are looking at it is potentially a much broader anticoagulant. We have to review that data with you in October.



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And with that, I will turn it over to Sylvie.

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

Good morning, everybody; good afternoon. It has been a very successful quarter obviously at HGT, and today what I will do is I will try to provide you, and perhaps exceptionally, with a fair amount of details regarding our products so that we can be as clear as possible with what we expect of these products from a supply and demand perspective going forward. And so will start on page 23 with VPRIV.

VPRIV has had a really strong market uptake since it has been available to patients, and we have now about 850 patients that are currently on therapy. So you have the bar chart represents -- if I can guide you to it for a moment -- in the fourth quarter of last year was when the product was made available preapproval, and we have received approval in the US in February of this year, and we have received the positive CHMP opinion in the EU in June.

So these 850 patients represent close to 20% of the market for the Gaucher disease in the EU and over 20% of the market in the US.

We do have capacity to support approximately 1000 patients with VPRIV patients in 2010, and the potential to add more patients is linked really to the ability to use material made in the new plant at Lexington.

So what we have done is since we see continued strong demand for the product, we have implemented a program to monitor and manage requests for new patients and are managing our supply and demand in that fashion for new patients.

The next page is 24. We will now discuss REPLAGAL. We have seen again a substantial increase in the number of Fabry patients treated with REPLAGAL this quarter, and over 320 patients have either initiated therapy, and about 25% of these patients are new patients, new to enzyme replacement therapy.

So on the graph, what we have tried to illustrate for you is again the progression of new added patients by quarter since the first quarter of 2009, and the dark portion represents really the switches from Fabrazyme, and the light color blue represents the new patients.

So from that graph, you can see that we have as of today, I should say, about 2000 patients currently on therapy. Again, the demand was very strong again in July. And REPLAGAL these patients represent patients that are either on therapy that is reimbursement of patients where the product is commercially available or IND patients or clinical trial patients.

Shire can support about another 150 to 250 patients between now and the end of this year, 2010. We still have the strong demand in July, so we anticipate really reaching that maximum number of patients sometime in the early fall. Our primary goal is to ensure the long-term and uninterrupted supply of REPLAGAL to patients on therapy. So we are carefully monitoring the demand relative to our inventory, and we implemented a wait list system once we have reached that maximum number of patients this year.

Now next year, based on our current inventory consumption and our manufacturing schedules, we will be able to offer REPLAGAL to about 250 to 350 more patients over the course of 2011. And again, our ability to substantially increase manufacturing capacity for REPLAGAL is linked to our ability to shift manufacturing for some of our enzymes to our new facility in Lexington. Process validation runs for REPLAGAL are scheduled for September of 2010, and we are, of course, exploring avenues with authorities, several regulatory authorities, to determine whether timelines can be accelerated ahead of the currently forecasted early 2012 planned approval.

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So recall that we filed at the request of the agency about a year ago now a treatment IND for the product in the US. That led to the filing of a BLA at that time or in the October timeframe. At that time we filed with the data that we had, and I think we have explained to you before that this data represented the controlled trial data that existed from the original data and observational longitudinal data on REPLAGAL.

The situation has changed quite significantly as we stand today. The prolonged and severe shortage of Fabrazyme has provided really an opportunity for Shire to consider gathering additional pharmacodynamic and clinical data for REPLAGAL beyond what was originally provided to the FDA at the time of the filing of the BLA. We have, therefore, decided to withdraw the current ruling application and not complete the application at this stage of the BLA to allow us to gather this data in addition to the pharmacokinetic data that was required by the agency in order to really enhance the clinical portion of the application for review and enhance our competitive position in the marketplace with potentially a better label. We really see now the market dynamics allowing us to have an opportunity to develop a more robust and standardized package of clinical data for review by the agency, as well as really a better labeling outcome. The timing of additional clinical data will be based on the timing of the accumulation of this data and the discussions with the FDA regarding the willingness or intent on how long they would like the observations to occur.

In the meantime in the US, we will continue to provide REPLAGAL to patients who have been enrolled in the treatment IND and who have obtained REPLAGAL under emergency use.

So, in conclusion, the strong demand for REPLAGAL worldwide is anticipated to continue for several months, and whilst ensuring that patients who are receiving therapy have no interruptions in their treatments, we will manage supply and demand to approximately 2200 patients this year and 250 to 350 more throughout the 2011 timeframe.

In the current market conditions for the product being prolonged for several months, we will take advantage of this time to collect additional clinical data in order to bolster the clinical portion of the BLA and enhance our ability to compete in the marketplace.

All right. Let me switch my queue to switch to page 25 and talk about a little bit and give you an overview of ELAPRASE. ELAPRASE continues to grow nicely. It has grown 17% year over year and 20% at constant exchange rates, and that is mainly driven by increased penetration in new markets due to geographic expansion.

The bar chart actually is intended to show you that if you focus on the dark portion of the chart, that explains or shows the proportion of patients coming from patients such as Eastern Europe, the Middle East and Latin America. We now have over 1000 patients on therapy in a disease where there is about 1500 patients diagnosed, and the revenues were, therefore, about \$100 million this quarter.

You will recall that we had added rollerball manufacturing capacity in Lexington in the facility. That facility has been approved in Europe a few months ago, and it was also approved by the FDA in this quarter. And in the future, we continue to see the growth of the product being driven by these products, by these territories where the product is less well penetrated.

There were other significant highlights in the second quarter, and those will be discussed on page 26 relative to our pipeline of products. Our pipeline is progressing well, and here are some of the milestones that occurred in this quarter.

FIRAZYR, by the way, has launched now in 18 countries, including the five largest European countries. But, importantly, the self-administration study has now been completed. You will recall that this is a study that we are performing that will allow stations to have the drugs -- carry the drugs with themselves and administer them when they have the first symptoms of HAE. And, therefore, this is an important competitive advantage over the existing therapies in that market. So this will lead us to be able to file for a labeling change in the EU in the fourth quarter, and we expect about a six-month review for this indication.



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In the US the Phase III trial is continuing to enroll, and we expect it to be completed at the end of the year for a targeted complete filing of a complete response at the FDA in the first half of 2011.

In addition to the enzyme replacement therapy that we have, that trial is ongoing for the central nervous system aspect of Hunter syndrome, we initiated this quarter a trial of another enzyme replacement therapy for the treatment of another rare disease that has no treatment available, and that is Sanfilippo A. Sanfilippo Syndrome, or MPS III, is a severe, progressive neurodegenerative disease that is caused by a missing enzyme just like our other enzyme replacement diseases. And this will be -- the treatment here will be administered intrathecally using the same port that is being used for Hunter syndrome.

So there are -- essentially [Guoa] is the most prevalent of four different forms of Sanfilippo, and it occurs at a rate of about one in 115,000 lives.

You will probably be interested in knowing where we stand on our manufacturing facility in Lexington. We have, therefore, started, as I said, the REPLAGAL batches, engineering batches on the purification side, and the validation batches will be produced in the fall. We have also initiated the engineering batches on the cell culture side of the facility, and we expect to start the validation batches also for the cell culture part of the facility in the fall. And, as I've mentioned, we are looking to work with regulatory authorities to see if the material produced from these batches can be accelerated for use into the various markets around the world.

So at this point I think I will hand over to Angus who will give you some concluding remarks.

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**Angus Russell - Shire Plc - CEO**

Thanks very much, Sylvia. So turning to slide 28, I just wanted to highlight a number of key events to look out for in the second half of this year. You have heard from both Mike and Sylvie that there is tremendous progress with our pipeline. We are hitting a number of milestones within the pipeline, and this is very important obviously in providing great opportunities that will start to kick in towards the end of our current envisioned strategy target period of 2015. This will provide us, we believe, with a great platform to sustain and grow our business well beyond 2015.

So things to look out for are listed on this slide. Mike already mentioned VYVANSE. There will be an update from the Phase II non-ADHD trials in depression. Also, the novel platelet-lowering agent he highlighted where he said that we had begun work on proof of concept studies, SPD 535, there will be a further update in the second half of the year as that goes through its proof of concept.

Sylvie mentioned VPRIV. We expect to get the final approval from the EU Commission and go to a full launch situation across the EU with VPRIV. And then with FIRAZYR, obviously self-administration is, as Sylvie highlighted, a key to continuing to grow that product over the coming years.

So turning to the final slide in the deck, 29, I just wanted to pull all this together and say that I hope by now at the end of our formal presentation you clearly see that we are not only delivering great growth now, but we have the platform to deliver and sustain that growth well into the future. We are delivering excellent results, I believe. Total revenues up 35% in this market with a number of adverse challenges and companies within our sector facing even greater challenges of their own. 35% stands out as a tremendous top quartile performance. 2010 full-year earnings, therefore, are now being raised, and as Graham and I have both highlighted, we believe they are trending now towards \$4.00. And, as Graham highlighted in his presentation, if we achieve that mark, it will already put us well on the road to achieving our aspirational target. That will represent 15% growth over 2009.

In terms of executing on our strategy, I believe now that there is very, very clear evidence of our ability to now derived growth from this balanced portfolio of 8 global products. The proposed acquisition of Movetis NV, we are looking forward to completing that deal and bringing those people on board to join Shire. And, as Mike highlighted, that will give us a ninth product. So soon



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hopefully we will be able to talk about nine global products driving growth into the future. And we continue, as I said earlier, to develop and progress our pipeline and hit many key milestone dates.

At the same time, we are increasing our global reach. You know that is a key target for us over the next three, five-year period. We have offices now in 28 different countries, and all of these products are now being rolled out across those various markets. And, as I said a moment ago, I believe that where we are today coming back so quickly from the loss of ADDERALL XR exclusivity and having this tremendous portfolio of new drugs with good strong exclusivity gives us obviously a very strong platform to achieve future growth. And with that in mind, we still feel tremendously confident about achieving our aspirational growth target of growing this Company around the midteens on average between 2009 and 2015.

So with those formal remarks, let me now hand back to Grant and have him coordinate the Q&A session.

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## QUESTIONS AND ANSWERS

### Operator

(Operator Instructions). David Amsellem.

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### David Amsellem - Analyst

Just a couple. On VYVANSE maybe you can shed some light on why you saw a spike in sales deductions, and was this a function of negotiations of contracts with managed care organizations, or is there something else we should be thinking about?

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### Graham Hetherington - Shire Plc - CFO

The first one, the primary driver of that is the fact that we announced a price increase on July 1 and that that spike was driven by us having to accrue higher rebates relating to that price increase in the second quarter. And that is why I think it will return to nearer 35% for the balance of the year.

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### David Amsellem - Analyst

Okay. That is helpful. And then the second quarter, I'm a little surprised that you would see a big ADDERALL XR stocking number going into the summer season. So maybe you can explain what drove the stocking in the quarter.

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### Graham Hetherington - Shire Plc - CFO

Well, what we saw was destocking taking place in the first quarter. And, as I highlighted earlier, that destocking resulted from supply shortages, and as a result, our wholesale inventories dropped to 15 days. We actually experienced some stock outs as a result of that, and with the sustained subscription demand, the supply has returned, and we have been able to move the wholesaler inventories back to more normal levels. They ended up at the end of the second quarter at 27 days, which is in the normal range of 20 to 27 days. So the stocking, frankly, is as much a function of the fact that we were short of products in the first product, and we just had to reestablish the supply chain.

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### Operator

Brian White.

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**Brian White** -- Analyst

I've got a couple of questions. Firstly, one for Sylvie with regard to REPLAGAL manufactured. Just if it was possible to accelerate REPLAGAL availability from the Lexington plant, I just wonder how many additional patients that would mean in 2011?

And the second question is, could you just remind us where we are with respect to the first and second detail on VYVANSE and INTUNIV, just given that there were [indications] moving towards the back-to-school season?

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

So the manufacturing, as soon as we can use material from the manufacturing plant in Lexington, that bottlenecks actually our ability to produce REPLAGAL. So we could supply then several hundred more patients as soon as we can ramp up and utilize the manufacturing facility in [Elwhite] where REPLAGAL is being made. So, in fact, for both products, the underpinning of our ability to increase capacity is linked to our ability to use material that is made in Lexington.

**Angus Russell** - Shire Plc - CEO

So maybe, Sylvie, it is just worth clarifying so there is no misunderstanding the numbers you gave out about 2011 next year, the range that you gave out to 250 to 350 extra, does that assume this, or would there be (multiple speakers) that is where Brian is going with the question.

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

(multiple speakers) So, Brian, the number I provided is with our current manufacturing capacity.

**Angus Russell** - Shire Plc - CEO

Mike, the VYVANSE and INTUNIV.

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

Yes, as we move from the slower pediatric summer season to back-to-school, we obviously ramp up our VYVANSE back-to-school initiatives on the ped side. Mix of business as far -- or mix of detailing remains about the same. I don't think we see any substantial changes going forward. It is just the focus turns from that adult population to the peds as we get into the July/August/September timeframe.

**Brian White** -- Analyst

Okay. And just finally, in terms of we don't hear much on the GSK co-promote, is that still adding substantially to the other indication?

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

I don't know that it has added substantially. It has definitely added. Obviously they are going through a whole set of changes. We are trying to work with them through those changes to figure out the best course. They continue to make effort against the original deal, and we monitor it.



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**Operator**

Bill Tanner.

**Bill Tanner** - - Analyst

Sylvie, a couple of questions for you, number one on VPRIV. What is the earliest that you might have an idea from the FDA about the ability to release data that are being manufactured in the Lexington plant? And then as it relates to REPLAGAL, just if you could comment on what kind of differential data you would like to try to tease out in clinical trials and if there is any comment on the PK comparability study?

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

Yes, so your question on VPRIV I think it maybe relates to what point do we expect to make -- to manufacture really VPRIV at the Lexington facility. So, as I indicated, we have started the engineering runs, and in the fall we expect to do the engineering and validation runs for VPRIV. So through the fall the material would be sort of made and available early next year, but it needs to be released and then generally the stability of these data needs to be accumulated, and then there is filing of the agency. So that is all -- if all done with the normal timelines, that would lead us to an early 2012 approval for the plant for this material.

**Bill Tanner** - - Analyst

Sorry, but if it could be released more on a compassionate basis, the potential for that and the timeline along that?

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

Well, so, there are many sort of ways to accelerate to try to negotiate with agencies regarding acceleration of the use of the material, and one is compassionate use. But it really has to do with the availability of the material, and so, as I mentioned, it will be available sometime in the first quarter next year with release data and be able to sneak sales in and hopefully then used somewhere.

**Bill Tanner** - - Analyst

Right, right.

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

And so your second question related to REPLAGAL. And so the type -- basically since we filed originally, hundreds of patients have switched on to from Fabrazyme to REPLAGAL giving us really the opportunity to gather a lot of clinical data that is of that demeanor into switch. We also have a number of new patients that were naive to therapy that came on to REPLAGAL. So this really affords us an ability to bolster significantly the clinical data that was relative to what was filed at the time of a year ago double the number of patients on REPLAGAL. So we want to take advantage of this in order to be able to really create a better -- (technical difficulty) if you will, for the product, and enhance or reduce the uncertainties of regulatory approval also for the product. The PK study is not complete, but would be part, of course, of the filing also at that time.



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**Bill Tanner** - - Analyst

But this does not suggest that there is an increased concern about the success of the PK study, I guess?

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

No, it is not linked to the PK study. It is linked to the fact that we see this opportunity to gather significantly more clinical data -- (technical difficulty) to provide to the agency in a way a more standard package and certainly an enhanced number of patients treated experience in the package. And, therefore, that is the reason to withdraw and really refile with a clinical section that is rewritten with this information contained in the filing.

**Operator**

Florent Cespedes.

**Florent Cespedes** - Exane BNP Paribas - Analyst

Exane BNP Paribas. First of all, to come back on VYVANSE, can you maybe give more color on the adult market? Do we have to anticipate some acceleration of the sales growth due to the contribution of this market? How do you stand compared to the roadmap with the GlaxoSmithKline agreement on that?

Secondly, on the stocking effect, could you confirm that about REPLAGAL and ADDERALL XR there is no significant stocking impact in Q2, and could you quantify the REPLAGAL stocking impact in Q2?

**Angus Russell** - Shire Plc - CEO

Okay. I think we have answered some of those questions already, but maybe we will do a quick recap. So Mike, do you want to do something about the ADDERALL growth?

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

Yes, I can just briefly talk about the ADDERALL XR growth. I don't have anything really new to report for, let's say, maybe four quarters now. It has averaged between 18% and 20% growth, which is remarkable. Does that go on forever? Maybe not forever, but it could go on for a long time because of the fact the market is still less than 30% penetrated.

So I think we have created a lot of awareness there, and we are reaping the benefit. VYVANSE continues to make progress. We are at about 11% market share in adult. Remember it launched a year after the peds indication. It is starting to catch up, but it's going to catch up slowly because the market is growing so much faster than peds.

Again, I don't have much else to say about GSK.

**Florent Cespedes** - Exane BNP Paribas - Analyst

Just to come back on VYVANSE, my point was to ask, how does this compare to your initial expectations of the penetration of the product?

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

I think it is absolutely on target. I think we all are a little surprised at the market growth, if you look at it year over year, is 12%. That is above our internal expectations. And if you think about where the market was trending a year ago, it was closer to that 7% to 8%, 6% to 8%. So it does look like the ADHD market is accelerating in the US, and again, I think that has a lot to do with Shire's efforts to educate people.

**Angus Russell** - *Shire Plc - CEO*

So GSK, I think you were about to say you have nothing to add really to what you said earlier. You just said your back in discussing with them. I mean our feeling is that the majority of what we are achieving is down to Shire, and they are helping us a little bit, but you are discussing all that kind of stuff with them right now again.

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

Yes, and it is a particularly sensitive time. They are going through a lot of changes. I don't really think it is my place to talk about their changes.

**Angus Russell** - *Shire Plc - CEO*

Okay. So then stocking. Graham, I guess that is back in your court.

**Graham Hetherington** - *Shire Plc - CFO*

Again, I have described how we saw destocking in the first quarter. That equates it to about \$22 million worth of destocking in the first quarter, and that took us down to 15 -- an unsustainable 15 days of wholesaler inventory. And taking it back up to 27 days of wholesaler inventory meant that there was \$33 million worth of increase inventory being drawn into the channel.

**Angus Russell** - *Shire Plc - CEO*

I think, Graham, as you were stressing earlier, I mean the point here is that sometimes people worry that we are at way beyond normal levels. And your point is that 27 days was slap bang in the middle of the normal 25 to 30. It was more that Q1 fell to outside that range on the downside.

**Graham Hetherington** - *Shire Plc - CFO*

Absolutely.

**Florent Cespedes** - *Exane BNP Paribas - Analyst*

And with REPLAGAL, is there any new color they can provide on the effect in Q2?

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

There is generally not a lot of stocking of these products because they are drop shipped upon demand. However, there have been some ordering patterns in the end of the quarter that just occurred where hospitals have called on some products to

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cover the new patients that have been coming on, and I think Graham referred to the fact that, therefore, these products that have been ordered will be used in the second quarter -- in the third quarter on these patients.

We will be monitoring. Because the supply and demand situation is so tight for these products, we are going to monitor carefully to make sure there is no stocking in the channel anywhere actually so that from an equity perspective patients can receive products as efficiently as possible and fairly.

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**Operator**

Ken Cacciatore.

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**Ken Cacciatore** -- Analyst

A question on FIRAZYR. Could you talk about the timing of releasing maybe even topline results? You indicated when you are planning on making your regulatory filing, but maybe would you be releasing the results a little bit early?

And the second question on Sanfilippo, Sylvie, is this possible that this is a pivotal study, or is this -- do we have to wait for the unusual small results here before moving into pivotal? And maybe talk about timing of a potential launch -- maybe I'm getting way ahead of myself -- and the size of that opportunity.

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

Yes, so on Sanfilippo certainly I can answer that this is a Phase I/II trial the first time in patients. It is a dose-ranging study in a very small number of patients. So it is unlikely that it would be a pivotal trial at all based on the fact that we would want to establish a right dose before we move on -- you know, not a large trial obviously, but a pivotal trial nevertheless or a status nevertheless.

So from a timing perspective, I think it would be between -- I think we've had a (inaudible) for the period after 2015, sometime after that. However, it is an important product for us in a sense that it represents another disease where there is no therapy at all and, therefore, an interesting opportunity for us, and of course, for patients it is an important step.

Your first question?

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**Ken Cacciatore** -- Analyst

FIRAZYR.

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

The self-administration data is really a safety trial, so there is not a lot of information to publish, other than to say that patients have been monitored from having administrations from the healthcare professional to themselves having administered the product. I suppose the product -- the data will be published somewhere, but it certainly may be that we will file the data before it is presented as there is not a lot of clinical data. It is mostly a safety trial.



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**Ken Cacciatore** -- Analyst

And I guess just following up on a lot of the questions concerning your capacity, just to make sure I understand this correctly. It is theoretically possible that you could be supplying additional product from Lexington in Q1. And I know we are all going to the most optimistic point here and you're not bringing us there, but is that what you are saying, is that we could, in fact, see -- the kind of guidance you have given on patient starts here increase if the regulatory agencies are willing to accept that product?

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

Well, so the guidance I have given on the number of products we can add represents patients that we can add this year and next year has to do with our existing current manufacturing facility and the standard timelines of approval for the facility in Lexington. I'm just pointing out that, of course, based on the supply situation on these products, we will be trying to negotiate and see if authorities are willing to take less data or a different kind of data in order to allow us to use these products. But I think it would be rather premature before we even have some of these discussions with the agency at length to be able to put a prediction on that. And, indeed, you are jumping to the optimistic view that we could add patients for both VPRIV and REPLAGAL if that happened. But, indeed, if it did happen, we would be able to add a number of patients treated with both of those products. (multiple speakers)

**Angus Russell** - Shire Plc - CEO

Overall you are leading the witness if I understand it.

**Ken Cacciatore** -- Analyst

I know that. Okay. I will not ask a follow-up then to see how many patients that would be, so I will just stop there.

**Operator**

Peter Welford.

**Peter Welford** -- Analyst

I have got two questions. Firstly, a rather boring financial one, I guess, which is on the Movetis acquisition. Have you looked into whether or not you can keep the rather attraction Belgian tax rate for that, and have you also got any sort of insights in early stage into what the annual amortization charge could be for that acquisition?

And then secondly, on REPLAGAL, can you just give us some, I guess, into what is sort of the timeline of the endpoints you are looking at for this BLA package? So when you say the FDA you're reviewing with them what sort of data would they want? I mean are we looking here at the standard timelines for Fabry disease, or are these more short-term endpoints than typically used?

**Angus Russell** - Shire Plc - CEO

Okay. Peter, the first one I guess is in Graham's court in regards to a couple financials around Movetis.



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**Graham Hetherington** - *Shire Plc - CFO*

The first question was regarding the lower Belgian tax rate, which Movetis benefits from. And the simple answer to that question is yes. We will be able to benefit from Movetis' tax rate.

In terms of amortization, frankly, it is too early for us to be able to work that through, and as soon as we have completed the transaction, then we will be able to talk about it in the amortization at that point.

**Angus Russell** - *Shire Plc - CEO*

And so then the next one is REPLAGAL, and I think Peter is clarifying -- I mean Sylvie was talking about the fact we are withdrawing, which is what it said at the BLA. So she was talking about collecting fresh clinical data and going for something that should be tantamount to a normal filing package. So just to clarify, you said what additional data points, unless I'm misunderstanding you because are saying what additional clinical data to support the BLA or whatever?

**Peter Welford** - *Analyst*

I guess what I was asking, when you say you're talking and getting the FDA views on this, I realize you are refiling this. So I'm wondering if when you are trying to bolster the package with these switch and naive patients, will this be the traditional endpoint type data you're going to bolster the package with, or will this be sort of shorter-term type data points from those patients that you are adding to the tri-clinical trial set?

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

Right. So this is precisely what we have to discuss with the FDA is how long an ovulation period would they like to see for pharmacodynamic and clinical parameters on these patients. And so once we know that, we will be in a position to establish a timing for the refiling.

**Operator**

John Newman.

**John Newman** - *Analyst*

I actually have two questions. The first one is, given VP approval is coming in the EU most likely, do you see an opportunity for maybe a differential view from the FDA versus the EMEA in terms of the type of data they would need to see to be comfortable with the material from the Lexington facility?

And then the second question is actually a follow-up to the last question that was asked. When do you see yourself potentially being able to submit additional data on REPLAGAL to the FDA?

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

I will take the second question first because I think I've just said, we do have to discuss with the FDA relative to the observation period what they would like to see in order to make it the best possible package for them to review. And so that will determine, of course, the timing of when we provide the data through the agency what we file regarding REPLAGAL.

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Regarding VPRIV, I think you're relating do I see any differences in the authority's views relative to the amount of data that would be required to accelerate the approval of this facility? And at this stage I would not want to comment. We do know that in the past they have had different views on what data was required, and I will leave it at that until such time that we can provide more detail. It is useful to have the data when you have these discussions with the agency.

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**Operator**

Kevin Wilson.

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**Kevin Wilson** - - Analyst

At the risk of being really boring, I wanted ask a longer term strategic question of you, Angus, and thinking of the evolution of the business model in the medium term. I propose some comments I have read that you made in an interview.

So thinking about your strategic investment group where you're talking about making 10 to 15 investments over the next couple of years, questions would be, how early stage will you go? What impact might that have on your R&D spending, and can you tell me how a business model which involves an interest in genetics might work?

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**Angus Russell** - Shire Plc - CEO

Okay. Well, it's nice to get a kind of slightly different question around strategy on the call. But yes, so we call it the SIG, as you say, not the STIG, and it is the SIG, Strategic Investment Group. And it is what it infers.

So the first point, which picks up one of your points probably, is -- (technical difficulty) and what we see this being is largely small, and, as I said, 10, 15, that is kind of a normal portfolio to derisk a kind of portfolio investments of this nature. That would be the normal range of the number of individual investments you would make. And it infers by the word investment what it is, which is we see them as being equity investments where we sit alongside co-investors.

The concept came out of two or three lines of thought between myself and the leadership team here discussed in the past year, and that is we are seeing, as you know, a world where VCs have been very burned there. You know, walking away from a lot of investments in this sector, other traditional funders are also walking away, and big pharma, indeed, themselves seem to have less appetite to fund very early risky stage assets. That is leaving many of these companies who have potentially good quality ideas with no funding, no capability to bring these ideas forward. So we see a kind of window of opportunity there at a time when actually Shire has this great platform of growth for the next few years, and we need to be working on things that will kick in probably as we start to approach 2020. Because we can see a lot of growth coming out of our existing business and our existing pipeline between now and then. But, as ever, you need to reinvent, state the blinding yield of the pharma business every 10 years or so, 10 or 15 years.

So that is what we are focused on. So, again, by that, we would infer these are very early stage ideas. We are always looking at new technologies and new ideas. As you know, we have no blue sky discovery of our own, and we have certainly still no ambition -- we have tested that again -- to build blue sky discovery in the sense of investing in infrastructure. I see that world in a sense going away, and I see a lot of people doing what I think they should do, which is divest themselves of owning infrastructure in that early stage of the business model.

So our concept is something different. It is one where we make these investments and we get to see new ideas, breaking ideas. Because of our areas of interest, it would stand to reason that genetics would be of interest. I mean I think we all know in this industry again that genetics could represent the major next breakthrough rather like biotechnology 20 years ago. You know, genetics, we are on the cusp I would say again. As ever, like biotechnology, one can never exactly predict when it will start to

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have a significant impact, but rather like Shire did perhaps with the acquisition of TKT over five years ago now, we were one of the earlier adopters of commercializing biotechnology products. We would like to again try and be in that early group in terms of genetics.

So this gives us something, which will be limited in terms of size, so I will just tell you the total size of fund we are thinking is probably of the order of \$50 million. 10 to 15 investments would imply a range of \$3 million to \$5 million for each of those investments. They will be purely equity, so there will be no impact on R&D spend in terms of earnings in that period. This is really to say to give us an early insight on things that could then be of interest and could represent acquisition targets down the road for us. And by then we would hopefully understand a lot more about them having been a co-investor.

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**Operator**

Jon Stephenson.

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**Jon Stephenson** - - Analyst

Just a follow-up on REPLAGAL. I was wondering if you might be able to comment on what proportion of the patients are really in the expanded access program in the US?

And then also, I don't know if I've missed this on the call, but if you could quantify the impact -- or the estimated impact of that kind of buying pattern fluctuation?

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

So, the extended access, there are about 120 patients in the US, a little over 120 patients that are in the extended access program in the US. You will recall that in the US the potential for the products in the US has always been limited. And so we will manage now going forward as opposed to, of course, the great strides that the products have made in the markets where it has actually improved. So we are going to continue to provide products to these patients in the US and those that are (inaudible) the products through the emergency use program. And then you have heard about how many we can add on throughout the rest of the year, and then we will manage that based on the demand and supply that we have forecasted.

And regarding --

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**Angus Russell** - Shire Plc - CEO

Yes, buying patterns I'm not sure in regards to what product you're thinking about when you said buying patterns?

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**Jon Stephenson** - - Analyst

Well, you had mentioned some buy-in at the hospital over the center level for REPLAGAL that might have basically taken some sales from Q3, and I was wondering -- and you talked a little bit about that, but I don't think you gave a dollar estimate.

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**Graham Hetherington** - Shire Plc - CFO

No, we did not. In this market it is very difficult to have a precise number. But it's nothing like the scale of numbers we have been talking elsewhere. It is just going to be single-digit millions.



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**Jon Stephenson** - - Analyst

Okay. So net net is you guys had pretty strong sequential growth, so a lot of that growth is really end market demand and not stocking on that?

**Graham Hetherington** - Shire Plc - CFO

Absolutely.

**Angus Russell** - Shire Plc - CEO

I think you should look in the charts Sylvie showed. It told you that. We had just under 200 patient starts, of which three-quarters are switches last quarter. This one it was over 320. It was over a 50% increase in patient starts on REPLAGAL in this queue compared to last. I think that tells you there is just huge underlying market demand being pulled through here.

**Jon Stephenson** - - Analyst

And just long-term, what proportion of that do you expect to ultimately keep?

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

Well, it is hard to know, but, of course, those patients, they are on therapy whether that's VPRIV or REPLAGAL for a long period of time, and we are satisfied that this therapy is the number of patients are likely to switch probably less over time. Because it is all about being satisfied on the therapy that you have. Also, for these patients it is not a small deal to switch from one therapy to another. It is a very big deal. And so if they are satisfied, again the likelihood of switching is minimized.

**Jon Stephenson** - - Analyst

Thanks. Great quarter.

**Angus Russell** - Shire Plc - CEO

Thanks. So I am conscious we have been on about an hour and a quarter, and we always like to answer your questions. But I am conscious it seems some of the questions are a little repetitive now. So I will take one more question, and then hopefully you will be able to follow up with Eric Rojas on the phone afterwards. So can we just take, operator, one last question?

**Operator**

Martin Wales.

**Martin Wales** - - Analyst

The Movetis acquisition obviously brings you some pipeline products away from RESOLOR. Is there anything there that particularly interests or intrigues you, and how should we think about having any impact on your (inaudible) development model given, I guess, it brings you some slightly earlier stage R&D than you have in your organization at the moment?



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And I guess my second question would simply be, what proportion of patients on VPRIV and REPLAGAL do you expect to be paying for the drug by year-end?

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

I can talk about Movetis a little bit. Obviously we have focused primarily on RESOLOR in this proposed acquisition. MV002 for ascites, which is a vasopressin, looks interesting, and then MV003 looks very interesting to me. That is an upper GI 5-HT4. For motility it would probably be used for gastroparesis and GERD or GORD in Europe.

The Company has not been able to invest in these programs the way they would like to because of the fact they have had to focus all their resources -- both money and people -- on RESOLOR and the additional indications and the postapproval commitments.

So we will go in, and we will evaluate the programs with Movetis, and they will decide how to go forward. I do think, when I look at the MV003, it has a lot of potential. I mean there have been some pretty big products in this area if you think back to Cisapride. But we are a long way from that. They had one fail proof of concept study a few years back, and we would have to look into why that study failed and figure out how we would move forward.

But overall we are very encouraged by what we see. We like the (inaudible) pipeline, and again, these are folks that have been bringing products forward to the GI area for many, many years. We think we can continue that tradition under Shire, and we hope to recapitalize and give them access to more resources similar to what we were able to do for TKT in '05.

**Angus Russell** - *Shire Plc - CEO*

Sylvie, paying patients at the end of year?

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

That is right. So let's start with VPRIV perhaps. As you know, as we have said, we can support about 1000 patients between now and the end of the year, and we think that we will have those patients. And we have shown you a chart of the proportion of paying and nonpaying patients. And the proportion of patients in the US are again slightly above the marketshare above 20%, but slightly around 25%, 26%. So I think you can make your calculation relative to the amount of revenues that we might garner from in the US where the product does continued switching from patients that were in the trial on to the therapy.

In Europe the product is, of course, being sold preapproval in many of the countries. And then there will be some gradual increase in revenues coming from Europe for the products where we will gain formal pricing reimbursement. But the vast majority of the patients in Europe are also currently paying for the product.

In terms of REPLAGAL, we have capped the treatment IND in the US to the number of patients that I have indicated are already being treated. And so the vast majority of the patients coming on, of course, will be -- in fact, all the patients coming on are likely to be paying patients. We are reserving a small amount of reserves for emergency use patients in the US, but this will be a small amounts of patients between now and the end of the year.

**Angus Russell** - *Shire Plc - CEO*

So the bottom line of all that, Sylvie, is what we're getting to is a large proportion of what we are seeing in patients numbers that you have quoted they are paying patients?



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

Paying patients, and gradually for (inaudible), there will be an increase. In this proportion that you see today, about 70% of the patients are being reimbursed that are on therapy, and that should increase gradually between now and the end of the year. Probably not 100%, but certainly gradually.

**Angus Russell** - Shire Plc - CEO

Okay. Folks, well, I am going to call it a wrap at that, so we thank you very much for your participation today and for all of your questions. As I said, Eric will be available on the phone to answer any follow-ups you have.

In conclusion, I would just like to say again that I believe these are tremendous results. I think they demonstrate that we really have bounced back from the loss of ADDERALL XR exclusivity quicker than pretty much anything I have ever seen before in the industry. And now we have a tremendous platform, as you know, for future growth, not only up to 2015 but with the evolution of this pipeline, and you will be hearing a lot more about that over the next 12 and 18 months. We believe we're already building a tremendous platform for sustaining that growth beyond 2015.

And this year, of course, we are very pleased on this call to have raised earnings guidance as we said, which we now believe was trending towards the \$4.00 per ADS level.

So with those closing remarks, again, thanks very much. Have a great day, and we will speak to you all again soon.

**Operator**

Thank you, ladies and gentlemen. That now concludes your conference call for today. You may now all disconnect. Thank you all for joining. Have a very good day.

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