ViiV Healthcare investor & analyst update

Wednesday, 15 February 2017

David Redfern, GSK Chief Strategy Officer and Chairman, ViiV Healthcare

Good afternoon everyone, if you are in Europe, and good morning to all of you who are in the US; we really appreciate you taking the time and the trouble to dial-in to this call this afternoon or this morning.

I am joined on this call by Dr Dominique Limet who, as you know, is the Chief Executive Officer of ViiV Healthcare, and Dr John Pottage, who is the Chief Scientific Officer of ViiV; both of those are in Seattle attending CROI, I am based here in London.

The main purpose of this call is to take you through the details of the data that we presented at CROI in the last few days, which is the first of our Phase III read-outs for investigational two drug regimes, including dolutegravir. This study with rilpivirine is evaluating the safety and efficacy of switching virology suppressed patients the bulk of our slides will cover this, and John Pottage will take you through that data. Clearly it is also an opportunity to discuss the HIV market generally and Dominique, John and I are available to do that.

I remind you, the slides for this session are on our website, they have been posted on our website, GSK.com; we will refer to those as we go through. We will try and keep our prepared remarks to around about 30 minutes and then we will have a Q&A session and obviously feel free to ask questions specifically about SWORD, but if you have broader questions on HIV, scientifically or commercially, we would be pleased to take those as well.

All I want to say by way of introduction is it is now the seventh year since we established ViiV Healthcare. I think an enormous amount has been achieved by ViiV scientifically and commercially during those seven years, but nonetheless, there remains very significant unmet medical need in HIV across both the developed and undeveloped or developing world and certainly we at ViiV remain 100% focussed on HIV and 100% focussed on continuing to invest in innovation, sales and our general reputation with all the stakeholders, and that remains critical to us and critical to our mission.

With that, I would like to hand over to Dominique, who will make some general remarks about the marketplace and where we are and then we will move onto the scientific data. Dominique.

Dr Dominique Limet, Chief Executive Officer, ViiV Healthcare

Thank you, David. Good morning, good afternoon everyone. I am delighted to be with you to share our views about the HIV market and, more importantly, how this first stage of our two-regimen strategy will transform the HIV landscape.

An ambitious vision

I would like to go to slide 2 and just to remind you the ambition that we set up in 2009, which is to establish ViiV Healthcare as a leading company in the HIV market in terms of innovation, sales and reputation.

What I would like to highlight is the word "Innovation", because innovation is not only discovering and commercialising new chemical entities, we really strongly believe that it means also developing new treatment regimens, new formulations, which can really transform the HIV landscape. If we want to become the leading company in HIV, it is clear that we need to transform the HIV landscape, we need to transform the market, we need to transform the future of treatment regimens, but also the future of HIV patients. That is why I am particularly pleased to be at CROI today and this week, because this is the moment where we start really building that long term vision we have, based on dolutegravir, which has been a successful product so far. We are here at CROI where we released I would say transformational data, transformational data results with the first pivotal Phase III trial results which will end up in filing a regulatory dossier in the first-half of this year with a single tablet regimen based on dolutegravir and rilpivirine.

The HIV epidemic remains a substantial challenge of our time

This is what our objective is, but I would like to, on slide 3, just remind everyone that, despite the huge progress we have made in terms of treatment of HIV, it is clear that the problem of HIV remains extremely serious.

You have seen on the slide that almost 37 million people are HIV positive. 2.1 million new infections every year and there are still, as you mentioned, David, significant unmet medical needs. Why is that? It is because the treatment lasts much longer now, thanks to the quality of treatment. We need more, better tolerated products which have a better toxicity profile because of the very long duration of treatment that the patients have now. That is particularly significant because we see, particularly in the developed world, an ageing HIV population, both in Europe and in the States.

Ageing populations means more comorbidities, more need for additional treatments and that is why it is so important to make sure that, on the HIV side, we can have the best optimal treatment for those patients.

With that in mind, can I go to the slide number 4, to give you a picture of where we stand today as an HIV company globally?

ViiV is the second largest HIV company globally, and the fastest-growing

As you see on this slide, in a market which is almost worth £20 billion, we have a 20% market share. On this slide, these are IMS data, but you know the actual data are slightly different, but we are £4 billion in IMS terms, £3.6 billion in actual terms in the GSK books and we have grown by 46%. We have done a fantastic performance over the past few years, in a market which is continuously outpaced by our growth in 2013 and you might remember that we delivered £1 billion of sales in the last quarter. We are number one in the naive segment, we are number one STR in Europe. Wherever we are, dolutegravir has been a fantastic success and dolutegravir is the engine of our growth, which is substantial, but the market will continue to grow. For the time being, the integrase-inhibitor market segment only represents 40% of the total of the third agents, so that means that there are reasons to believe that the gross momentum will carry on for years.

75% of the new brand prescriptions are made of INIs these days, and we have a very significant share of the INI market now, with *~40% [corrected]* of the total. We are in a market which is growing, which will continue to grow because of the longer duration of life expectancy for patients and because we have new infected patients. So this is an attractive market, but this is a market which is now driven by two companies, and it is clear that we want to become the leading company.

Guideline updates drive market evolution

On slide 5 you can see in a way why we have been successful too, because we have developed such a comprehensive set of data, such a compelling set of data that over the last four years we have continuously seen dolutegravir becoming part of the key guidelines and becoming absolute first priority for many of these guidelines. Some of these guidelines have led to shipping very early on in Africa in 2016, and also to have a fantastic success in Brazil recently in a first-line position thanks to these guidelines which were set up by a number of these bodies.

Why? What explains the very good performance of dolutegravir amongst the ARVs?

Amongst integrase inhibitors, dolutegravir stands out

Slide 6 is a slide which summarises in some form why. What are the unique product characteristics of dolutegravir? What is the body of evidence that we started building early on and I would like to focus on one or two of those characteristics.

One, the element which is unique in dolutegravir, which differentiates dolutegravir from all others, including PIs, the protease inhibitors, is that we have a very potent drug which is associated with a very high barrier to resistance. On top of that, and that is so important in the future, we have very little drug-drug interaction. In a population which is ageing with 70% of US HIV patients who will be above 50 by 2030, with today 23% of patients in Florida who are already above 50, it is absolutely critical to make sure we have products which do not harm patients for the long term.

This has led to developing a set of clinical trials which are really unprecedented. We have trials which we performed from naïve to experienced patients, in males and in females, from paediatric indications to the adult ones, in naïve to resistant patients, so we have covered and that is why the product is so broadly used nowadays; *more than [corrected]* 300,000 patients are taking dolutegravir now. We have built the evidence that we can start thinking about a new approach for treating HIV patients.

DTG leads the market as the #1 core agent in the US

These results, which are clinical results, helped by a good commercial execution all across the world have, as I said earlier, led dolutegravir to take the first place as a core agent in the US, on slide 7, with 23% of the market of the third agent and STR.

DTG leads the market as the #1 core agent in the top 5 European markets and Japan

If you look on slide 8, being in Europe or in Japan, we occupy also a leading position with dolutegravir, with 18% of the total volume in days of treatment in Europe and up to 40% in Japan. ViiV Japan has 40% market share, which is the number one position in the world.

A growing body of evidence to support two drug regimens (2DR)

To summarise, slide 9: we have now built a body of evidence which supports that we can really move into a new treatment era. That is why I use the word “transformational period” that we leave this week in Seattle. We really believe that less can do more. We believe that if you have less long term toxicity, you can improve the quality of life. We believe that, if we have less hassle for the two drug regimen for prescribers because of less drug-drug interactions in order to cope with comorbidities, it is better for the patient. We can do more because we maintain options, treatment options for the future of patients and, eventually, we will be able to deliver more value for money in developing the next generation of the two drug regimen.

What is the rationale for developing the two drug regimen? One, we have demonstrated now with several trials that it is a scientifically viable option. We started, remember, with the LATTE trial, cabotegravir plus rilpivirine, because we had the long term vision of the injectable formulation, but nowadays, with the SWORD study, we have the demonstration that our strategic vision, our long term approach about a two-drug regimen can work, and will work.

We are anchored as well by a number of investigator sponsored studies, which are done with dolutegravir as the core regimen, being with darunavir, with lamivudine, with rilpivirine; this evidence has become absolutely huge. In addition to that, as I said, there are a number of unmet medical needs. If you interview patients in the US, 50% of the patients are still concerned about their treatments. 44% of them are really concerned by the long term side effect profile, the long term toxicity of the ARVs that they take and two-thirds of the US patients are ready to consider reducing the number of drugs. So the simplification of the treatment regimen, de-escalation of the treatment regimen is something which is actually required by more and more patients. To the point that if you look at Europe, for instance, up to 11% of the patients in Europe, in Italy, are already treated by a two drug regimen and 50% of these two drug regimens are made of dolutegravir. Yes, there is an unmet medical need.

Eventually, I think the market demands it. There is, as we see during this conference, as we saw in the last conferences a lot of activities around the two drug regimen, that is something that physicians wanted to develop for years now and I am absolutely convinced in looking at how the market has reacted to dolutegravir/rilpivirine data in the US that there is a positive reception of that simplification.

Our duty is very simple: initially it was to develop a product where we can define clearly what is the minimum effective dose. Nowadays, with the two drug regimen, what are we doing? We are trying to develop the minimum effective treatment regimen, and that is why it is transformational for patients, that is why it is transformational for the HIV landscape, that is why it can be transformational for the market dynamics because, in a way, what we are demonstrating with dolutegravir/rilpivirine, dolutegravir/lamivudine in the future, cabotegravir and rilpivirine, is that we can live with almost no backbone because we have dolutegravir and cabotegravir which are so critical, great co-agents that we can revisit the way we treat HIV patients.

What John Pottage in a minute will describe is what we have done in order to demonstrate the validity of the two drug regimen. There are four key ingredients of that: proving efficacy, proving that we have a high barrier to resistance, proving that the durability of the two drug regimen exists and eventually, with the next generation of our two drug regimen, demonstrate the value for money

of these two drug regimens. With the SWORD data, we have the demonstration that yes, the product is efficacious, yes, we have a good barrier to resistance. The full 144-week data on cabotegravir, LATTE, that we also present here, are a good illustration of the sustainability and durability of the two drug regimen efficacy. That is why, before I give you the floor, John, I am really confident, very excited by this opportunity because it can really transform ViiV, it can transform the life of HIV patients and, eventually, it can transform for our shareholders.

John.

John Pottage, Chief Scientific and Medical Officer

Thank you, Dominique. It is a great pleasure to be here on a rainy morning here in Seattle. I will start out with slide 10.

Our belief in the market evolution

I just want to take a couple of seconds to give a little bit of a perspective on how we treat patients and how we have done it over the last 20 years of therapy for HIV patients. If you recall, in the middle of the 1990s, the real transformational change of having treatments where patients could live long lives happened with the introduction of three drug therapy. It was the introduction of protease inhibitors, it was the introduction of non-nucleoside reverse transcriptase inhibitors combined with nucleosides. At that time, if you think about the language that was used there, we had a two-nucleoside drug backbone, combined with what was called a third agent and so it was different mechanisms of drugs composing that third agent category mixing with the nucleosides and, as I said, the success I think everyone is well familiar with that.

As time has moved on, drugs have become better and better and it really was with the introduction of dolutegravir that transformational changes have occurred, which we think has changed the way we think about how we treat patients. As Dominique outlined, we are thinking about treating patients for decades, so many years, so you have to really think about what the medicines are doing to the patient, how they are improving their lives, how they are suppressing the virus over this long period of time and, as we know, there can be some morbidities or side effects of the medicines that interfere with a patient's lifestyle and also there are interactions with other medicines they may be taking. As was mentioned, people are getting older and there is an ageing of the HIV population such that other diseases are becoming manifest – people developing diabetes or hypertension, or disease that need other medicines and drug interactions do become a real problem.

As we think about the therapy for HIV, as I show on the slide there, the middle or the present time we have really moved dolutegravir as a core agent, so when one is considering what medicines you are going to put together, based on that huge body of evidence that Dominique outlined and with our multiple superiority studies, our position on treatment guidelines, we look at dolutegravir as the key agent to form the core of therapy. At present time, people add other drugs to it and, typically, for most patients they will receive two nucleosides or two nucleoside drug backbone.

As we think about it going forward, and again, taking into account the work of others that have looked at two drug regimens, the LATTE study, as Dominique mentioned, we see that having three drugs isn't necessarily necessary and perhaps we can move to a two drug regimen, again with the idea of reducing long term toxicities, reducing long term drug interaction issues, interference with other conditions that the patients are developing over time.

It has really come to what we view as the future of combining a core agent, dolutegravir, with one other agent, or the two drug regimens going forward. This meeting is the start of our journey with that, so we are really excited because the data is great and what we are presenting here is the first data from the SWORD study.

Phase III SWORD 1 & 2:

Switch to DTG + RPV

Maintains virologic suppression through 48 weeks

A bit on perspective as we go forward, and I will move forward to slide 12, so the introduction of the SWORD study.

Introduction

I have a number of slides; I am not going to go through them in detail, I will try to give the highlights from them. A couple of points I want to make clear from this, this is the first study of a whole programme of two drug regimens that we have moving forward in clinical development. This is dolutegravir and rilpivirine in patients who are on stable medication and fully virologically suppressed, and this is a switch study for them.

We are also looking at dolutegravir in combination with lamivudine or 3TC in treatment naïve patients, so to start out therapy. That is a study that will be *fully enrolled [corrected]* in 2017. Then we are also looking at long-acting drugs, so cabotegravir, another integrase closely related to

dolutegravir, combined with long-acting rilpivirine in a long acting regimen in which we give the medicine once monthly as an injectable. We are really looking at this at the start.

This is data that we will be rolling out over the next several years as I think we hope to transform how we think about treating patients over their lifespans, so it is really keeping in mind that long treatment scheme that we want to put going forward.

If I can move to slide 13, just to set up the design of the SWORD study?

SWORD-1 and SWORD-2 Phase III Study Design

This is two studies, so they are identical studies. SWORD-1 and SWORD-2; these were done globally and what we have presented here is we have pooled the data from these two studies and these are Phase III pivotal studies which will form the basis of a submission to regulatory authorities for a fixed dose combination of dolutegravir and rilpivirine as a full treatment regimen. That is unique and has not been done before, where we have a two drug regimen as a full treatment regimen for patients. This is forming the key data for them. The study looked at patients – as I mentioned, these are people on stable therapy, they have been fully suppressed and so they entered into the study and they were randomised to either continuing that therapy or they were switched over to receiving dolutegravir and rilpivirine as a two drug regimen.

The primary endpoint is at week 48, and that is the substance of the presentation that I will go over and what was presented at the meeting.

As you can see this is a long study that goes out to week 148, so it is answering a number of questions that Dominique listed that we have to show from these two drug regimens. The key here is that, by going to a two drug regimen, do we continue the virologic control that these patients have continued with their previous therapy? The demonstration here is that you can safely, successfully switch over to the two drug regimen and also not lose control and also not see emergence of resistance with that change of therapy.

We will also be looking at the adverse events, side effects, how the tolerability of this regimen compares, but importantly, as we talk about why you want to use the two drug regimen, it really is the long term, and really the later stages of this study will help to inform the comparison of side effects associated with the drug. We will continue to report on this study as it develops. I think at the next upcoming meeting we will have some more data, particularly on areas of health outcomes, how the patients feel with this type of regimen as well as studies related to effects on the bone and renal markers.

The study, as I mentioned, is a comparison of these two groups. If we go to the next slide, slide 14.

Subject Disposition: Early Switch Phase (Through Wk 52)

I am not going to look at that. Again, the data I am showing here is the pooled data from the two studies, so it accounts for a little more than 1,000 patients enrolled in the two studies.

Demographics and Baseline Characteristics

If we move to slide 15, the baseline characteristics I think are important. As you see in this we have roughly 30%, a little less than 30% of the patients are over 50 years of age, so again we are targeting, and it is important to keep in mind, a long term treatment for patients and as they get older we want to see how the drug works in those patients.

We have roughly a little more than 20% women enrolled in the study and, importantly, the other aspect is that these patients were fairly treatment experienced; they had been on prior therapy for about 4.5 years.

Snapshot Outcomes at Week 48 (Pooled)

If we look at slide 16, and looking at the outcome here. As I said, the week 48 outcome. Here is the pooled data and you can see the great success of this. Basically, the two groups are essentially 95% of the patients who had an HIV RNA less than 50 copies at week 48. This is the FDA snapshot analysis, so it is what it says; it is a picture of what is happening at week 48. Then you can see a smaller percentage of the patients did not achieve that virologic outcome and we will look at those patients in a moment, but the 95% success rate is quite impressive. You can see statistically that the two drug regimen is non-inferior to the continued antiretroviral regimen.

Snapshot Outcomes at Week 48 (SWORD-1&2)

The next slide, slide 17, shows the breakdown of the two studies. You can see again very similar results that you see from the pooled data. One important point is that when we think about switch studies, the FDA has tightened up the bar that you have to show in terms of having that confidence that it is giving you the right answer and so the non-inferiority margin of the pooled data is at 8% of the two, SWORD 1 and SWORD 2 – it is 10%, but even if you look at those individual studies, they also achieve the 8% margin. It is really quite solid, the statistics that we see of the success here.

Snapshot Outcomes at Week 48

An important slide is the next one, which is slide 18, looking at those snapshot outcomes. Again, this is the picture at week 48, and we already know that 95% of the patients in both groups were less than 50 copies. There is a small number of patients that, when we tested for the virology that we did not achieve less than 50 copies, an important line to look at, that were discontinued for lack of efficacy and we see two patients in each group, so that is less than 1%, so that is quite impressive with that.

Moving to those patients who, when we did the snapshot, that there is no virologic data, these are generally people who have left the study early, so generally they leave due to adverse events. In this study, there were two patients who died – one in each group, and both those cases were patients with advanced cancer and that was not considered to be related to their treatment regimen.

Confirmed Virologic Withdrawals

Moving to the next slide, looking more carefully at the confirmed virologic withdrawals, this is a very important item, as I said. The purpose of the study is to emphasise the safety of switching and not losing virologic control. When we look at, here we see a very small number of patients in the same, in each group and so when we looked at them in more detail, one of the patients in the dolutegravir/rilpivirine arm did show an emergence of resistance to rilpivirine. There were no patients who developed integrase resistance mutations in the study. The other patient we weren't able to detect any resistance mutations and so I think, very importantly here, we have a good success with the virology at this timepoint.

Adverse Events with Onset through Week 52

When we look at the adverse events with the study that out through 52 weeks we see that most of the adverse events were what we expected, so there was nothing unusual; both drugs are well studied and you see that most of the patients had low grade adverse events that led to them perhaps being discontinued.

Adverse Events Leading to Withdrawal

The next slide just lists the number of adverse events and again a number of events, about a third of them aren't even related to the drug, but again did lead to removal or withdrawal from the study.

Change in Serum Lipids at Week 48

Moving to the next slide just quickly, there was not much of an effect on serum lipids through this time period; both dolutegravir/rilpivirine are fairly benign in terms of the effects on lipids, so this is what we would expect.

Change in Bone Markers at Week 48

The following slide is slide 23; importantly, here, as I said previously, we will develop some subsequent publications and presentations on the effect on the bone in patients with DEXA studies, where we look at bone mineralisation, but here are some serum markers which are markers of bone turnover. You do see significant decreases in these markers in the patients who switch to dolutegravir/rilpivirine, indicating improvement of the osteopenic processes that often occur in patients with HIV who are treated with nucleosides.

Here we have very encouraging signs and again, putting this in the perspective of long term treatment, I think is very important.

Conclusions

In conclusion, as I said the data is quite impressive, we have been able to really show that the virology stands up. We have not seen emergence of any kind of integrase resistance mutations in these patients, and switching of it looks to be quite well demonstrated here. As I said at the beginning, this is a study part-way through, so we will be looking at the patients, the patients who were on the continued antiretroviral therapy are switched over to the two drug regimen, so we will have another tranche of data coming up at subsequent meetings.

Emerging clinical support on 2DR

If we move to the next slide, it just looks at the emerging clinical support on multiple two drug regimens. We have listed a number of studies and, as I have mentioned, SWORD is our study of dolutegravir/rilpivirine, we have data being generated for dolutegravir/3TC in treatment naïve patients, the cabotegravir/rilpivirine in long-acting treatment of patients, both in naïve and switch situations and a whole host of investigator sponsored studies with large groups, such as the ACTG or ANRS, looking at these two types of regimens. I think you will see a lot of data over the next several years looking to support this type of approach to patients.

Innovative pipeline addressing unmet patient needs

The final slide I just want to mention looks at the pipeline from ViiV as we go forward, really addressing the unmet patient need, but really thinking about long term treatment and again, we are in the middle of this. As you see the dolutegravir two drug regimen is really the core of what we are

kicking off here at the CROI meeting, but we are also very interested in developing the long acting treatment regimens both, as I said, for treatment, but also for prevention, but also developing new drugs with new mechanisms of action and really the search for ultimately remission and cure for patients.

With that I will conclude and move to Q&A.

Question & Answer Session

David Redfern: Thanks John, thanks, Dominique. Operator, I think we are open to take questions.

Steve Scala (Cowen & Co): Thank you. I have two questions: what is ViiV's view of the Gilead Phase II data which showed numerically higher virologic outcomes for bictegravir versus dolutegravir, and how shall we think about that drug as a competitive threat?

The second question is the exclusion criteria for SWORD study seems extensive with patients with hep B co-infection, hepatic impairment or a need of HCV therapy all excluded. What % of the market do these patients represent and what was the screening failure rate in the study? Thank you.

David Redfern: Thanks, Steve. John, I think both of those are for you.

John Pottage: Okay – although, Dominique, did you want to make a comment?

Dominique Limet: First of all, what we saw two days ago, is a very preliminary set of data from a competitor. This is a small study result, it is a Phase II and by no means the results demonstrated any difference between dolutegravir and bictegravir, which was statistically significant, by no means.

We believe that the jury is still out. It is a Phase II study. It is done with 75mg dose. The Phase III programme that our competitors have started is based on the 50mg and actually there is absolutely no data which has been released on 50mg, so that is why it is early days. The jury is out. I am sorry to say that the uncertainty of the value of that product remains.

John Pottage: The only comment I would add to it, if you look at the randomisation of that study it was small, but it was a two-to-one randomisation so they had twice as many patients as bictegravir versus dolutegravir, so one or two patients drives the dolutegravir number and, as Dominique mentioned, statistically there was no difference that we saw in the study.

In terms of the set-up of the SWORD study, one thing I wanted to point out is there have been issues with two drug regimens in the past when we haven't had as good drugs in terms of tolerability or potency and there has been a lack of success. With the newer drugs, and particularly with dolutegravir, we feel much more confident, but as we study this we are looking forward to doing this in a very systematic but safe way for patients and so we are starting with the patients who are stable and suppressed and seeing how they do. Obviously, we have had data from the LATTE study as mentioned and from this study and we are also moving into more of the treatment naïve patients, so again patient safety is of utmost importance for us.

In terms of hepatitis B, it does cause a bit of an issue because a number of the nucleosides for the treatment of HIV have hepatitis B activity, so tenofovir as well as 3TC or FTC and so again, as this was the first large study here, we felt that patients needed to not have a history of hepatitis B, so again it would become much more complicated if they had a flare or something along that line. That is one of the reasons for that.

David Redfern: John, is it worth being a little bit more specific just on the dolutegravir lamivudine studies and broader viral load entry criteria that we now have as we recruit patients into that?

John Pottage: Yes, so treatment naïve patients as we are going forward in the GEMINI study, so these are Phase III studies going forward that began in August of 2016, we are studying patients with viral loads up to 500,000 copies. Again, I think we are doing it in a prudent fashion and ultimately, we may extend to where you can treat larger amounts of patients, but really those patients with those high viral loads above a million are only a small percentage of patients. It is systematically going forward for them.

Luisa Hector (Exane): Thank you very much for the call. I just wonder if you can talk a little bit more about where you might expect to take market share with the dual therapy? Is it very much the switches and would you expect patients on a dolutegravir regime to move to the dual before others?

Are you considering doing any monotherapy studies with dolutegravir? Thank you.

Dominique Limet: I will start. No, actually. No, we do not envisage doing a monotherapy trial with dolutegravir. The first question you raised is about what are the patients eligible to a dual regimen and here it is clear that our intent is to enhance the market share of dolutegravir within the third agent market and to build on what we have done, not to replace what

we have. As I said, we have only 40% of patients who are today on integrase inhibitors. Dolutegravir has 50% of that 40% of the market and there are plenty of patients who have been treated for some time who are eligible for simplification for this escalation and this will be our focus. Our focus is to add to what we currently have. Some might speak about cannibalisation, but when we want cannibalisation it is very difficult to get and here, moving from three to two, is not as simple as a conversion from, let's say one old backbone to a new backbone, so that is why we really believe that is what is core of our strategy is to build on those patients who want to simplify treatment, who want to preserve the long term, who want to have less long term toxicity effect of their products, and it will be in addition to what we currently have with *Tivicay* and *Triumeq.*

David Redfern: Thanks, Dominique. I think the only thing I would add is just remember in at least the West, certainly in the US and Europe, about 90% of patients that are treated are properly virologically suppressed. Obviously they are consistent to the most part with the SWORD study.

James Gordon (JP Morgan): Hello and thanks for taking my questions - a few please. One of them is on GEMINI, so dolutegravir plus lamivudine doublet: how confident are you in showing non-inferiority to the triple and what is the pooled margin in non-inferiority? Is it the same 8% non-inferiority margin as the SWORD programme?

I have another question about potency of integrases. Last year, I think you suggested that bictegravir might be less potent than dolutegravir, which might be why you could do doublets and Gilead couldn't. Do you still think that dolutegravir is more potent?

Thirdly, where is the integrases ceiling in terms of what proportion of patients could eventually get an integrase? I believe you said 40% is where you are now but what do you see as the ceiling and how much do doublets or injectables raise the ceiling up?

Dominique Limet: I shall start with the last question because it is a market question and David and John can elaborate on the two others. It is 40% today but, as I told you in my introductory remarks, 75% of the new brand prescriptions for naïve patients are made of integrase inhibitors. I would say our ambition is likely to be at 75% of INIs, which, on the one hand, is ambitious but it is also reasonable when taking into account the value and added value of integrase inhibitors, particularly dolutegravir and cabotegravir.

John Pottage: Starting way back at the beginning, then we shall come to the bictegravir question in the middle, in terms of the GEMINI study, the basis for feeling that this will be

successful comes from another study called the GARDEL study done by Pedro Cahn. That was a combination of Kaletra, a protease inhibitor, plus 3TC in which it showed that it was as good as a three-drug regimen, and numerically it was better. That was a very substantial study which gave us a good basis for going forward with this.

Subsequently, Pedro has done a small pilot study with dolutegravir and 3TC - the PADDLE study - again done in very careful circumstances and the data from that have been presented and show good success. Therefore, as far as looking at those studies, and there is a whole host of other studies coming along, as I said, by the ACTG, the ANRS with dolutegravir and 3TC. We are emerging with a reasonable hope of success here and we are quite confident with this. Again, the GEMINI study is more than half enrolled, so it is moving forward and we shall have that [recruitment] completed in the next month or so. It is a large Phase III pivotal study, the inferiority margin there is 10%, so this is a treatment naïve study, and, as mentioned before, we are looking at patients up to 500,000 copies. Just to re-emphasise, those above really account for a very small number of patients who come into treatment for HIV.

Just a comment about bictegravir, we really have not seen a lot of data coming forward. We saw a Phase II study with 75mg used, their Phase III programmes are using 50mg, so we shall have to see what happens with that as far as whether it is able to support a two-drug regimen remains to be seen. These are early days and it is hard to really comment on that.

Richard Purkiss (Piper Jaffray): I have two questions. First, can you estimate for us what proportion of treated and suppressed HIV patients fit the specific inclusion criteria for the SWORD in developed market, as in no HBV, confirmed RNA below 50 copies and no change in the prior regimen?

Secondly, is the higher adverse event rate in the dolutegravir arm more likely down to the open label design of this switch study?

John Pottage: In terms of the adverse events, in all switch studies you are taking patients who are stable on a medicine, in this case for many years in most cases, and then you are introducing a new medicine, which introduces issues particularly a mild headache or gastrointestinal side-effects. That is commonly seen and expected in switch studies going forward for that. That is what we would expect and, as I said, there were no unusual adverse events to it.

As far as hepatitis B in the developed markets, in the United States it is 3-5% in patients with HBV. Dominique, do you want to comment?

Dominique Limet: On the eligible patients for the two-drug regime, it is a huge number and we estimate between 30-50% of the total population, so it is a very significant part of the total HIV market, which is why we are so upbeat about the value of the product.

John Pottage: Just to wrap up on the open label nature, that contributes to reporting and what people are looking out for, they know they are on a new medicine so they are more vigilant as far as reporting what they feel.

Damien Conover (Morningstar): I have a question on the bone marker reduction that we are seeing in SWORD. Can you talk a little about the clinical meaningfulness of this and how we should interpret the near-term data here and what will be potentially more important at the 148-week data point?

Then I have one bigger picture strategy question. When looking at the choice of the doublet in the SWORD studies versus the GEMINI studies, within SWORD using an NNRTI and then within GEMINI looking at an NRTI, can you talk about the pros and cons of using the different doublet within those different patient populations? Thank you.

John Pottage: Starting out with the data that we have shown here with bone markers, the better way to look at this is that it is more of a hint of what we see going on in terms of moving away from nucleoside regimens in the SWORD study. These are markers that have shown roughly a 15% reduction. They are markers that are elevated when you have the osteopenic effects of ARVs and also from HIV disease itself, and it is really a sign that the bone is not needing continually to fix itself or turning it over and repairing itself. It is an early sign, it is something that could lead into a more sensitive or a more important marker which is more radiologic. Those are DEXA scans where we look at the bone mineralisation of, say, the lumbar spine, the hips and that is where we are looking at that.

As far as the clinical significance of this, it ultimately means do you break your bones, do you have a fracture, and these are all leading to that. These are encouraging data that we see and, when we think about this regimen for the long term, this is what we want to see and this is what would be a reason to switch to the two drug regimen going forward.

What we are looking at here are options for patients; we are not looking at any one two-drug combination going forward. As I mentioned before, the choice of rilpivirine came from work we were doing for cabotegravir for the long-acting programme and our partnership with Janssen looking at that as a good combination.

Regarding the use of 3TC, again taking the example of what we saw with the GARDEL study and some other data being generated that led to its choice. We are open to other two-drug options as we go forward, so it is something that is a dynamic ongoing type of choice but it really is that word "choice" or "option" for patients as we treat them for many decades, and that is what led to the thinking there.

Dominique Limet: If I may add, John, with dolutegravir and lamivudine, we possibly had a fourth component of the value of that combination, which is value for money knowing that it will be affordable not only for the developed world but for the developing world.

Andrew Baum (Citi): Can I talk big picture for a second? You focused a lot on less hassle, lower toxicity associated with a long treatment duration to the two-drug regimen. If I think about your likely future competition with bictegravir TAF, the whole point there is TAF should not have the bone-related toxicity of tenofovir. No.1 it will be a single pill, so it will be no less hassle and not having to take the theoretical risk of a new regimen. How should I think about that within that context?

Secondly, when I think about the ability of ViiV to use cost to your advantage with payors, because your competitors might discount TAF, to what extent does the lobby of patients mean that the pricing power in this particular market, or the ability to cut pricing to payors right now in the US is of limited value because patients and physicians will argue for access to drugs and, therefore, it may limit its potential? Thank you.

John Pottage: As you think about treating patients for the long term, the most important thing, which I know we take for granted, is the virologic efficacy of the drugs. We assume that we shall be able to treat them for a person's lifetime which, unfortunately, is not true. As we try to organise medicines going forward by reducing the number you are using, it does give you good, durable action, but ultimately you will need to switch. Therefore, by reserving medicines, it allows you to have further options for treating viruses that may develop resistance in the future and that is one way of thinking about it. That long-term organisation of medicines is important for that.

As I said, with the data we are developing for dolutegravir, we shall see about the drug interactions and, again, it gives options for those patients who are taking lots of other medications where there have to be drug interactions, or you have to do dose adjustments where it isn't just one pill which may be an issue. I feel pretty confident that, by dropping down to what is needed, that is

the best way to go forward and, again, we have multiple options down the line. We are playing a 40, 50, 60-year game here, not a five or 10-year timespan.

Dominique Limet: If I may add, John, that even if there is a likely improvement on some side-effects of the backbone competitor, we have not yet seen the long-term effect of that backbone. Having fewer side-effects does not mean there are no side-effects, which is why it is important to bear that in mind and why potentially getting rid of it is positive.

With regard to the ASO(AIDS Service Organisation), you are right that it is an important element of the prescribing patterns of prescribers, it is not about the STR. The STR does not resolve all the hassles of prescribing an ARV, and one key element of choice for ARVs is the lack or not of drug interaction, the convenience with regard to how to use the product, and drug-drug interaction is an element that we have to discover with our competitor now. We have not yet seen any data which demonstrate that there is an added value of that combination and, as I said initially, the jury is still out, which is why we feel confident with the data we have. We have with this two-drug regimen, with the SWORD data, demonstrated a 95% efficacy rate with the two-drug regimen instead of with a three or four-drug regimen. We are confident that, over time, the value of having less hassle because of having few drugs and not fewer pills will be demonstrated.

Regarding the value and the price, we are not saying that we shall highlight that as a key differentiating element. What we know is that in some places, the added benefit of lamivudine, for instance, as far as value for money will certainly be perceived as positive. However, we know that in the US, for the time being, this is not particularly relevant but, as we know, we have to be sensitive, we have to be aware, we have to be thoughtful about the long-term future of HIV treatment so, in that respect, we are preparing for the future.

David Redfern: It is worth adding, Dominique, as you alluded to earlier, there are big differences in the dynamics of the pricing environment between the US and Europe and, certainly, some parts of Europe are very price sensitive. You mentioned Italy where there is quite a lot of dual use. This will play out differently in different parts of the world and it is already doing so to some degree.

Next question?

Jo Walton (Credit Suisse): I want to follow on from Andrew's question on pricing. Could you tell us what the average co-pay is in the US and, as you are saying you are getting an older cohort of patients, presumably there aren't many in the dual-eligible bucket yet. I wonder whether

you can also give us some sense of the payment in the HIV market as far as Medicaid, VA, etc.? Thank you.

Dominique Limet: First of all, you may know that in the US the vast majority of patients are reimbursed through the public system: 64% of our patients are under the public system while many others benefit from subsidies and support. When we look at the patients in the government channels, they have little to no co-pay. When there are co-pays, we have a programme that we call a Commercial Health Sections plan which is able to help patients to get savings cards which reduce considerably the copay or the out of pocket expense. That is why, in the last few years, we have not faced any access issue neither for *Tivicay* nor for *Triumeq*, whatever combination we see with *Tivicay,* because *Tivicay* can be associated with any backbone, we have not seen any major complaint or constraint with the copay so far.

David Redfern: We shall probably draw a line at this point but, just before we finish the call, I would like to say that, as many of you may already know, Dominique is *stepping down [corrected]* at the end of March after seven years as Chief Executive of ViiV. As I said at the beginning, an enormous amount has been achieved during that time scientifically and commercially, and in the returns that have accrued to all three shareholders, not least to GSK as the majority shareholder, and on to all of you. This is the moment to thank him for his fantastic leadership not only in what he has driven for the business but also for the HIV community during the last seven years on behalf of the Board and on behalf of all of you.

Dominique will be succeeded by Deborah Waterhouse who takes over from the beginning of April, and we look forward to introducing Deborah to you over the coming weeks and months as this story and progress of ViiV unfolds. With that, we really appreciate your attention and time this afternoon, I hope it was helpful and thank you very much.

- Ends -