Goldman Sachs seminar on HIV and ViiV Healthcare

Monday 19 September 2016

Keyur Parekh: Good morning, and thank you all for joining us. My name's Keyur Parekh and I cover Glaxo for Goldman Sachs. I'm going to pass it over straight to Dr Limet and Dr Pottage for the remarks.

Dominique Limet: Thank you, Keyur. Ladies and gentlemen, good morning. I am delighted to be with you today. I'm delighted to be with you to tell the story about ViiV Healthcare. You might think that I'm a bit partisan or too positive about this business, but I have had the privilege with John Pottage to be in charge of that JV for almost seven years now. And the story that we will tell you – the past and the future story – is a story that we built with a great supporter of the GSK company and I'm delighted to share some of those elements with you.

Overview

We will split the presentation in two parts. I'll do the presentation up to the point four, included, and then John will tell you a bit more about the R&D strategy, and then, obviously, we'll have the Q&A and the conclusions.

ViiV Healthcare vision

An ambitious vision

ViiV Healthcare ambition and vision – I think because it's the first time, possibly that we meet, it's important for us to go back to the model that we have created, which is very unique, and which is partially, I think, responsible for the success we have made. Then I will talk about the HIV market, which is not completely known, possible, and relatively complex because there are numerous drugs, numerous combinations, fewer and fewer partners or competitors. Then we will spend some time on dolutegravir, which is a key element of our growth, which is also the key element not only of the past but of the future. And throughout the dolutegravir, let's say, vision,

you'll better understand why we are so positive about the future – in the presentation that I do, but also that John Pottage will do.

So just about our vision: we have a very ambitious vision. Simply, we want to become the leading company in HIV and we are 100% focused on HIV. We want to do that in terms of sales, innovation, and reputation. The three components are important for us. You might say, what matters to you is sales and profits, but we believe that the two other elements are very important. Innovation, that's what John and I, we wanted to really reenergise from 2009, and we have developed not only new drugs but we are also developing new regimens and we are changing the world and trying to transform the life of HIV patients. So it's pretty ambitious just by that. Sales, obviously we have grown tremendously in the last three years, and we have still a lot to grow. And obviously we want to catch up with the big leaders of the HIV field today. It will take some time, but we are very confident that we can grow even further. And reputation. You could say reputation is not only the corporate social responsibility activity. It's not how we deal with the press and so forth, it's making sure that we do good and we do well. Because we are absolutely convinced that in a world which is very close to the patients needs, close to activities, close to societal problems, it is important for us to serve well this community. It is important to make sure that we have a fair pricing strategy – responsible strategy – for payers, patients and healthcare systems. We want to have high standards because we know and we have seen that when competitors do stupid things, it might impact the whole industry. So we want to be the one who leads the way in these three dimensions.

ViiV Healthcare history and operating model

A rich history joined under a unique model

So let's – let's look at what has been our journey so far. So we started almost seven years ago, as a joint venture which was created between GSK and Pfizer, and the goal was very simply to pull together the two R&D pipelines and some of the expertise that both companies had in HIV. And you know Wellcome, Glaxo Wellcome, GlaxoSmithKline, are really the companies which

have paved the way of the HIV treatment, starting with AZT long ago. And we have, for long now, transformed the lives of HIV patients. So GSK and Pfizer, you will see, originally owned 85% to 15%. But in 2012 we were able to swap some of the rights that Shionogi had on dolutegravir and the integrase franchise into an equity share, and that's why today Shionogi is one of the three shareholders with 10% of the total equity. By 2013 we come into the dolutegravir era, we got the first phase-III trials in 2009, and then we developed the vast program of clinical trials and we ended up with the first launch in the US in 2013. And then last piece of news which is important – the first time we had a big acquisition at ViiV Healthcare – in 2016 when we acquired BMS HIV, let's say, franchise in the pipeline, the discovery asset and also some team in the discovery world.

So that's history. But the model that we have is pretty unique because we have a combination of a form of biotech mind-set, we try as much as we can, but associated with big pharma – GSK, Pfizer and Shionogi. We try to be agile, we try to be faster, quicker to act, and very focused on the area of HIV. This is part of the foundation of the success that we have had. So in the middle [of the slide], I start with ViiV Healthcare, we are in charge of the strategy, the narrative – we have drug discovery, the development is directed from these, but obviously extremely well supported by the GSK organisation. And we have, a number of activities, which are the ones that you would find in any company. But on the right and left-hand side, you see the other partners that we have. And it is extremely important to notice that GSK is playing a major role in supporting us in many support functions, but more importantly in helping us, implementing our clinical trial development, manufacturing, and addressing the needs of the business in most of the territories, even if they represent only a small part of our business. And Shionogi/Pfizer are mostly involved in the R&D, and more importantly in manufacturing for Shionogi today.

End to end operation reliant on the scale and infrastructure of large Pharma shareholders

So how are we organised? We have three regions. We have 15 affiliates – that means 15 local ViiV Healthcare entities across the world – and we have partnership as well with GSK, and that

means in 2009 we put in place distribution agreement with GSK for all other markets, except the ones where we have a local entity. So we are close to 900 people, but we have grown up from the beginning. And if you look at the other numbers, it means that we have a lot of people who are fully dedicated to our business, our development activities and discovery, and through a number of service agreements. So we have, let's say, 900 people within ViiV Healthcare, but we have about 600 people who work within GSK – mainly; a bit of Pfizer and Shionogi – who support the mainstream of our activity and our strategy. And if you look at the last bit on the right-hand side of the slide, 450 trials – that means that we, because we wanted really to pave the way of innovation in the field of HIV, we have invested a lot in HIV trials, we have developed very, very comprehensive data packages – particularly for dolutegravir, and John Pottage will speak about that later, We have done a lot to really strengthen our understanding of the disease, understanding of the patient needs, understanding of our products.

ViiV Healthcare success to date has evolved in two phases – First Phase: 2009 – 2013

So I'll distinguish two phases into the ViiV Healthcare development. One, is between 2009 and 2013 – 2009, so it's the moment where we created the JV, and 2013 that the first launch in the US of dolutegravir. So on the left-hand side, that's what we have been doing. We have been able to stop the erosion of *Kivexa/Epzicom* particularly in the US, and to regain some momentum. And that came before we had dolutegravir. So that means that we have been able to offset some of the competitive pressure and to regain momentum, because over time we gathered more data about that product, which helped us support the product. But on the right-hand side, you see that we have developed absolutely fantastic set of data to support the dolutegravir launch. We wanted to really demonstrate the value of the new integrase inhibitor. And that was the first time that we had such a large set of data. And actually it's important not only from a differentiation standpoint, but also from a pricing standpoint because we were able, thanks to this big body of evidence of clinical trial results, to navigate the pricing and access dimension pretty nicely and that's something which has delivered a lot of good results.

ViiV Healthcare success to date has evolved in two phases – Second Phase: 2013 – Today

So the second stage is from 2013 to now and the future. So you see on the left-hand side that dolutegravir-based regimens – *Tivicay* and *Triumeq*. I think those combination have really transformed the way we grew our business. So for a couple of years, we were able – which was already a challenge – to maintain our performance, more or less. And then, from 2013, we were really growing tremendously. And what is important to notice there is that the part that *Epzicom*/ *Kivexa* are playing into the global turnover is reducing month after month, which actually is good news, as this product will be out of patent in the months or weeks or days to come. So, that's the trend, and you are all familiar with the sales performance we achieved last year, and we are growing at a very high pace. You saw, we are still growing, by June at a very high pace in new prescriptions, and that means that this growth will carry on. On the right-hand side, we have started building the next stage of our development. And you see this arrow that we all like, because it really creates the ambition. And, as you can see on that slide, we are not only developing new drugs, but we are developing new treatment regimens. We are caring about more dimensions regarding the HIV condition and how patients progress – John Pottage will go into more details later.

So, if you start by the bottom of the arrow on the left hand side, this legacy ARV drug portfolio is the one that we know today. It's *Kivexa/Epzicom* – and we have built our momentum thanks to this product. But thanks to dolutegravir we're able to think about the ways to really transform, radically transform, the way we treat HIV patients. So, we are at the next stage of our development, which is based on two drug regimens. We will spend some time going into that, it is based on science, mainly, and we have a strong growing body of evidence for that. So, dolutegravir two drug regimen: it's firstly with rilpivirine, and then we have another one coming, in development, which is with lamivudine. So, you see, dolutegravir-based regimens, two drug regimens, based on dolutegravir. And then, we have another way of transforming life for HIV patients, which is to look at the long-acting treatment. As you reported — the HIV disease is one

of the worst disease, worst condition, but what you could have added is that when you start at the age of 20 or 25, today you are forced to consider that you have a product for 40, 50 years. It has become a chronic condition. So, a number of patients would love HIV to have less impact on their daily life. That's why we are developing these long-acting formulations which can potentially reduce the number of intakes from one pill a day to one injection every month, every two months, which could transform the way the patients live their lives. Then, we are also looking at the long-acting in prevention, possibly at a even less frequent scale, once every two months, every three months. That means the dolutegravir injectable can also relatively transform the way we prevent the emergence of the condition. On top of that, we have, thanks to the acquisition of the BMS [development and discovery HIV pipeline], but also thanks to the GSK discovery efforts, a number of new product in discovery phase, which are new mechanisms of action, which are really, again, trying to transform the way we approach the HIV condition. So, you see, we move from a relatively simple portfolio to a broadened portfolio, addressing more and more of the needs of the HIV patient.

The HIV market

The HIV epidemic remains a substantial challenge of our time

So, why are we so interested to grow even further? Because we believe that the HIV market is still a very attractive market, both from a medical need but also from a business need. There are, 37 million people living with the condition. Obviously, a large part of that population lives in developing world, but note that we have 2.4 million people living with HIV in the Western world. And, unfortunately, in fact, the infection rate carries on growing. And so, it's far from being a disease which is behind us. So, a huge number of patients, but what is interesting, too, is to consider that guidelines have changed in the recent months, meaning that today the guidelines tell something which is radically different from the past, which is to treat every single HIV positive individual, rather than to wait until they become really sick. So, that means that we can expect, slowly — it's not a radical shift — but we can expect more of those patients who are waiting for

treatment to come on to treatment. It's mainly the case in Europe, but in some of the Western world market, it can increase the value of the respective markets.

A highly dynamic market

So, now we get into a bit more details about the HIV market and about our performance and penetration in the naïve market. So, I wanted to give you a clear highlight about what the market is about, and in what respect some segments are more important than others. So, first of all, we define the market with three segments. We have the initiation segment. That means new patients coming for a new drug for the first time. There is also a pretty large switch segment. That means people who have been already treated for some time, but for a number of reasons that you can see on the right hand side need a change of their treatments. So, naïve and switch. Most of the data that we have focus on those two elements, because they are indicative of how much value can we gain from the market. So, we are looking at our share in the naïve segment, our share in the switch segment, and the total of those two segments, switch and initiation or naïve, we present would be called the dynamic segment, because everybody doesn't change every day. We need to look at how much dynamism do we have in the pool of the patients already treated or to be treated. And so, the dynamic segment varies according to countries, to new launches, etc. We've seen that it's about 15 to 35% of the market per year. We have seen that recently in the US – with a peak of a dynamic market increase, which is now slowing down – the peak is just following the introduction of new products with, in fact, a lot of conversions from the old product into the, let's say, new product. A large part of the market is in the stable segment. That means people who are happy with what they have. So we market our product into the 15 or 35% of the market.

The market has been receptive to innovation and remains a strong opportunity for growth

Now we move from patients to products. And I guess this slide is not too familiar to you, because I'm not too sure that you always see the market divided the same way as we do. So, first of all, you see two pictures, one from 2013, the other one from 2015. The market has tremendously

increased, about 10% CAGR. But you see that it's divided, in some form, into two or three buckets. Let's say two, because we have what we call a third agent, like dolutegravir, and we have what we call the NRTI backbones. And there are only two or three backbones on the market, which are the Gilead and the ViiV Healthcare ones, but, as you see the NRTI backbone represents today almost 40% of the total sales. These two classes of products are combined into what we call STRs, which are the single-tablet regimens.

So, let's focus on the right-hand side, because that's closer to us today. The business is worth £16 billion. The third agents, as single agents, are worth £5.4 billion. The STR, single tablet regimen, which will present a combination of third agent and backbone, represent £5.9 billion. And the NRTI backbone represent £4.5 billion. The total of these three elements, third agent, STR, and NRTI backbone, equals ~£16 billion. But what you might not see regularly is the speed of backbones that use third agent. Because, to be clear, we are really a very strong competitor company in the field of third agents. And, actually, if you look at the value of the third agent, compared to the total value of the backbones which are, in part, included into STR, it's almost 50/50. So, that means another way to look at the HIV market is to consider that 50% of the market is made of third agents, and 50% is made of backbones. And in this latter segment of the backbone, we only have 20% of the total market. So, that means that being at 20%, with no NRTI to come from our pipeline, because we believe in the future of the drugs, we are focusing most of our activity on the third agent. And if we are successful with our two drug regimen, statistically, that it will be partially at the expense of the backbone segment.

Guideline updates drive market evolution

So, why are we focusing so much attention on the third agent? Because they are the ones who dictate the guidelines. And the proof of what I'm saying is that all guidelines focus their attention on the choice of the third agent for treating patients in the naïve or in the switch segments. And, as you can see on the slide — I will not go across all different years — but they have continuously evolved, and they are now, in 2016, consisting of an integrase inhibitor plus two NRTIs as the key

recommended treatment regimens for many patients. That means that, over time, the medical community, has displaced, in a way, the focus which was initially on these old NRTIs, like AZT. They have moved away from that as being the core point of discussion into selecting the third agent, which become their core agent. That's why we have this recommendation today. And you see, it's an evolving pattern, and it's an evolving transformation of the HIV market.

We have now entered the integrase inhibitor era

Just to give you two numbers, let's say, in 2013, protease inhibitors, represented 40%/45% of the total prescriptions per treatment days. Today, we have replaced PIs with more or less the same amount of newer treatment. That means that the PIs are slowly but continuously decreasing, while integrase inhibitors are slowly but continuously increasing. And that's what you can see on this slide, where you see very well the last almost 12-year history. And you see this green line which started in 2008 with the launch of Isentress, and which is continuously growing. And, just to give you a very important number, 70% of the new prescription today are made for an integrase inhibitor. We have a huge, huge increase of integrase inhibitors, and there is no reason, to our knowledge, to believe that any product could really go against that. I know that you can speculate about how much the integrase inhibitor class we represent by 2023. We don't give forecasts, but we are absolutely convinced that they will grow, and the integrase inhibitor will represent the dominant class within the HIV field.

dolutegravir

Among integrase inhibitors, DTG stands out

So, dolutegravir. dolutegravir is honestly an amazing product. Some years ago, in 2009, someone in the Financial Times, when I became CEO, said, ‘They have nominated a veteran of the pharma industry to lead.’ I'm seven years older now, but I'm still a veteran, still amazed by what I've seen with dolutegravir. I know the pharma industry a bit. I've never seen a product which is able to deliver that package of information. You follow the pharma industry. How many times have you seen one product with superiority over benchmark results? Not so often. From

time to time. One single trial of these clinical trial results which are superior to benchmark. And we have developed a package of information which has revealed that four trials have shown superiority over benchmark. That means, whatever the benchmark, whatever the comparator is, we have demonstrated that we have superior results with dolutegravir. It started in 2009, when some physicians commented on the unprecedented results that we had with the first round, and since then we have accumulated this absolute body of evidence that dolutegravir is special, and I could say outstanding. And looking at what others did, they have what I believe is a weak set of data when compared to ours. That's why we really believe that we have an unprecedented clinical trial programme.

And what does it mean, and why do we have these results? That's because the product, by itself, is really a good product. We can spend some time on the fact that it's a very rapid and potent viral agent. You know, within ten days, we have 70% of the patients who are undetectable. No other product has demonstrated that. We have a very, very high barrier to resistance. That means, no patients initiated with this product during the clinical trials have demonstrated resistance, which is very, very good. We have a long binding tie, very long binding, to the integrase inhibitor. That means that the product sticks to the integrase sites and pockets and lasts on them. It's very well tolerated. Obviously, we have a number of side effects, like all these drugs, but it's normally extremely well tolerated, and we don't have significant drug-drug interactions. First, because the drug by itself doesn't create any interaction, and two, we don't have a booster, compared to many others, and being booster-free means there are much less drug interaction. And it's important to mention that by 2030 — so, it's not far from now — 70% of HIV patients in the US., will be over 50. So, that means that, being over 50, you have, naturally, and also because of the HIV condition, more co-morbidities, meaning more need for other drugs. And that's why being booster free and having no drug-drug interaction is so critical in the aging population that we see in the developed world. At the end of the day, what matters, what really makes a difference, is to be able to prove in clinical trials that a product delivers a promise, and that's what we have with dolutegravir.

dolutegravir leads the market as the #1 core agent

And so, this is obviously the reason why we are growing so well, and you see that we have become the number one third agent, number one third agent with almost 20% of the total prescriptions in the US. So, you know, the product is doing good. I would say, proudly, I think our teams have done good. We have done the right development package, as I said. We have implemented the right pricing policy, and I think we approach the market well, and that's why we are in this position with 20%. And that's why dolutegravir, for us, has become the core agent that we have to think about.

And the #1 agent in dynamic share in the US

If you look at other metrics of our success — so, on the left-hand side, we have the new patient share and you see that despite an active competitor, we are still number one with 27% of the naive patients. Obviously, thanks to *Triumeq*, which actually represents 50% of our sales globally. On the right-hand side, we have a slide which possibly requires some notes as we have excluded the conversions. By conversion, we mean when a patient is moved from one current regimen to another similar one , for example from TDF to TAF containing regimens, or from Tivicay+Epzicom/Kivexa to Triumeq. So, it is one for one. We do not really consider that as a true switch – a true switch meaning a true gain of new patients thanks to new drugs. And, we have done that for the competitors as well as for us. And, when you look at that, on dolutegravir-based regimens, in the US are still extremely well positioned, despite, I can tell you, their fierce competition with three products launched in a very recent time. So, we are proud about that.

Already #1 agent in dynamic share in many other key markets

But you could say that the US is where we are in good shape – actually, we are in good shape everywhere. So far as you see, we are the number one position in most in the key markets, and I think I am proud to say that in Japan, we have 37% of market share so that means that in one of

the countries of our shareholders, we are doing extremely well. So, number one in naïve and number one in switch.

ViiV Healthcare is the only company with increasing growth in HIV over the past 12 months (from +34% to +53%)

Here you have in total [HIV market] the position. We are still very high in terms of weight. We are the only company growing. It is clear that we have one big competitor, and it is still in play. But we have achieved, as you know £3.1 billion in annualized sales using performance through June – which is clearly a very strong performance and as you know the 3.1 billion represents a major chunk of GSK's total. So we spoke about dolutegravir globally. We spoke about the pace of performance, the model. Now I'd like to pass a thought to Dr John Pottage. John has been a key element of our R&D strategy for 7 years and he has done – with his team – a fantastic job for developing the products we have.

R&D Strategy

Committed to innovation and leadership in HIV

John Pottage: Thank you, Dominique. This is the slide I love the most because it really summarises what we do, where we are going and really centres on the innovations that we think will answer patient needs. And, I think as Dominique mentioned, there are continuing medical needs for the treatment of HIV. And so let us dive in a little bit more specifically than Dominique mentioned when he went through it very quickly. But, if we start on the left side of the slide down at the legacy ARV drug portfolio, think about it as 'what do we do'. We develop new drugs. But, drugs for the treatment of infectious diseases, but actually very specifically for HIV, are used in combination. So, they are part of regimens. So, when we develop medicines, we are always thinking about how do they work with other medicines along that way. And, so, we are thinking about the regimen and we are also talking about or thinking about treatment strategies. Where would this medicine fit in? Is it part of prevention? It is part of cure? Is it part of treatment? Is it all of those? So all these things are going into how we think we will use the drug. And, the

central question that we always answer when we are bringing forward the drug developing it is answering the question the physician who is writing the prescription will ask is: 'why am I writing it? – what is the medical added value we're bringing?' And, so, Dominique showed you the huge amount of information we provided for dolutegravir. The bar is very high now. There have been many medicines that have been developed and the treatment of HIV has turned this disease, fortunately, into a chronic disease. But, it is such that you have to take medicines for your whole life and often that can be 40-50 years. So, we always have to think about the long game of treatments.

And so, since the bar is so high, we put together all those different studies comparing against other drugs with different mechanisms of actions and really showed how special, how unique dolutegravir was. Because really having that data is, I know it is a bold statement, but it is kind of unprecedented. You never really saw that kind of data. But I think the proof that statement is really the movement in the guidelines to where really the integrase inhibitors and really that was driven by dolutegravir with that data. But as we develop that, we have this large amount of data, in terms of studies, so we don't do kind of a short shrift version of that.

So we do that and we think about how do we fit it into the regimens. And actually one of the things is that when ViiV Healthcare was first formed people talked a lot about that we would be dealing with fixed dose combinations. And so we are always thinking as I said about the regimen and how they fit together, but we also try to fit them together into a single pill and you will see that called single tablet regimens. And really, *Triumeq* was the first fixed dose combination that we came forward with as we move across the arrow here.

But then, actually due to characteristics of other drugs coming through our partnership with Shionogi and the integrase category, we have cabotegravir where this has a very long half-life and allows itself to be given parentally or through an injection. And so we started thinking about long acting treatment regimens and when you have long acting the definition there is giving the

drug as little as once a month. So people talk about, well I would like to give a medicine once a year, or once every three months, but if you go in the jargon of the HIV world, it is greater than once a month. And, so looking at this drug, we looked around for other drugs to combine it with and rilpivirine is also a long acting regimen. And, so it is really a two-drug regimen and going forward is a long-acting regimen. And so it is really the two-drug regimen that really we are very excited about now and really over the next several years, and I'll show a few slides on the data being generated for this, it is really the key for us as we think we really answer the medical needs and really answering what physicians need to take care of their patients. And we really are thinking about dolutegravir because it has those characteristics. Do you really need to have three drugs or four drug regimens? We think about the characteristics there that allow us to think about what is the best drug to combine with it. One way to kind of think about it is if HIV appeared today and we had all the medicines already made, what would be the medicines we choose to put together. All the regimens are really historic as the new drugs came out one by one, they kept being added together putting together in different combinations, but what if you had the situation where you could put them all together or how many would you need to use. And we really maintain because of the characteristics of dolutegravir it really forms the central part of that regimen and adding one drug is probably sufficient and I'll go over some more rationale of the two-drug regimen in a second.

But really, moving forward, that is just one step in the way and as I said, we think about different treatment strategies. So prevention – can we use these medicines – and the long-acting version of cabotegravir is being studied for that. So that would be where people worried about being infected with HIV could come in for maybe an injection once every two or three months and not have to worry about taking a daily pill along the line. And, as also was mentioned, we have a number of new medicines, again that are answering the medical needs caused by this virus of different mechanisms of action and much of this comes from the discovery unit in GSK as well as from BMS as we brought those in – and I'll go through those in a second. But really, this slide just gives you a feel for how we think about the long-term strategy of treating patients and it really

is that long-term strategy that is very important that we think about. These are medicines that people will need for many, many years going forward.

Our belief in the market evolution

So one of the ways to also think about this and just here again, this is more of the lexicon, and it is really historic in nature. And, so if you look at the left side, that is the traditional way and that came up historically. Really before the mid-1990s, we had one medicine or two medicines and so people on those were nucleosides because those were the first medicines developed, and we called it a backbone. Some people put together three nucleosides together, and so that is how the term backbone came. Then when the protease inhibitors and the non-nucleoside reverse transcriptase inhibitors came about, that is how they called them the third agent. So they are adding them on top and so that is kind of the traditional way in which we maintain. I think, it is kind of an old or archaic way of determining this, but you will hear the language of a two nuke or two NRTI backbone plus the third agent.

Really we want to move to the middle, and I think that is what we are doing and dolutegravir allows us to do that. We call it the core agent. I always maintain we should call it the first agent. If you go that historic agent going forward. But really, it forms the core of therapy. It is the one you start with and then add to it and we've reversed it so that actually, you are starting with the core agent and then adding a two nuke backbone, or other drugs as you go to the end of the slide where you look at a core agent plus one partner agent. There are going to be patients who need two, but we really think that you don't need those because of the characteristics of dolutegravir. So the language is an evolving point and I think that you always have to be careful the way people refer to these different regimes for patients but they all say the same thing. They all are combinations of medicines for treatments of the patients.

Why can 2-drug regimens (2DR) succeed?

So why would we want to look at this? Why do we think it will succeed? So it is actually as I said there is no magic to three drugs. Clinical investigators for HIV have always been looking at one drug, two drug, three drugs, four drugs. Really going forward, it was this historic kind of centering of adding the third agent those two nucleosides that got people to the third drug and that has worked very well. But we've been looking at different ways of putting together the medicines and what really drives that again is the unmet medical need. It is really needing these medicines over the long term. And so if you can give less medicines that means less side effects, less drug interactions. People are getting older; they have other co-morbidities where they need medicines that often do have drug interactions. And so really if we can reduce the drug burden over time it is a way of really thinking about your patient long term along that line. So in that sense, it does preserve options. Because every time you use a medicine, the patient may fail and it will develop resistance and they lose that option. So why do I want to expend all the medicines upfront, if I don't have to? So I think that that is an important thing, and so I think really that is what drives people mostly as the firm foundation going forward and as I said, there is a persistent interest. There are more and more clinical studies going on among a number of investigators looking at it [2DR], and I think that again the medical need and the market are receptive to advances in the treatment, moving it forward, and so I think the two-drug regimen does have this ability to challenge the three-drug model as people think about it.

ViiV Healthcare integrase inhibitors at the forefront of the 2DR paradigm shift

So again, putting *Tivicay* at the core here. And so we have done that. We have done *Tivicay*, *Triumeq* is that fixed dose combination of three drugs put together with a two nucleoside backbone. So that is kind of our little checkmark. One thing to think about with the treatment strategies is that you have to do this in a very safe and responsible manner going forward. This virus replicates very quickly. It forms resistance very quickly and if you do not have the right regimen and enough potency on board, you will develop resistance to those medicines and you will lose the ability to use them in the future. So many of the studies, particularly when we look at the dolutegravir + rilpivirine and the cabotegravir + rilpivirine, those are centred on patients who

are fully suppressed already. So they are treated with a three-drug regimen and then switched over to a new regimen, but it is more of a switching of people who have already been controlled. As we develop the data for that and I will show one piece of data that really shows great support for that, and there is other data points for that. We think about, well, do we need to do that. Can we just go in and treat a person? Someone who has a circulating virus that is not under control and those are the treatment naïve patients, and that is the approach we are taking with dolutegravir + 3TC. So one of the things when you look at all the different trials. You have to check what they are studying. Whether it is a switch of people fully controlled or is it treatment naïve patients and really this is an effort to again give patients multiple options. So, again we are always going to that long term treatment with that.

Cabotegravir LATTE and LATTE-2 studies

This is a key study for us so this was the LATTE study. This was the study giving proof of concept of a two drug regimen of cabotegravir which is a very close relative of dolutegravir but it has characteristics that allow it to be given as a long-acting injectable. But this study, the LATTE, was actually the oral version. And we looked at three different doses of it, combined with nucleosides versus efavirenz which was the standard of care there. And you can see that the data shows that cabotegravir plus the nucleosides is actually, all three of them are above the purple there which is the efavirenz arm so they are non-inferior or better than what you see with a standard three drug regimen in terms of virologic control. If you look at the far left-hand side there in the dark or the faded part, that is where everyone was treated with three drugs and then the dotted line is when they switched over to the two drug regimen which is the green blue and red lines and then the three drug continued in the purple. And so you see these are the supressed patients mover to a two drug regimen. The same can be said, and we have recently presented the LATTE 2 study. Now the difference there is the same principle, we have treated patients, we have reduced their viral load to undetectable and then given them a two drug regimen. But this is a long acting injectable. So it is not oral therapy. And you can see the data there. Again, the cabotegravir in the purple is the oral version. So that is given with three drugs

versus the two drug injectables which is the green and then the hash line there. And so you see the great data here which really shows a firm support for a two drug strategy. Now this is of a supressed patient population switching over with this regimen. And so it is one of a number going forward.

Investigator initiated 2DR studies

I'm not going to go through all these studies. We can in the Q&A if we want to talk about them. But it really shows the wide breadth of studies going on by various investigators around the world. I think the one I would point out is the GARDEL study that was done by Pedro Cahn looking at lopinavir, ritonavir, which is Kaletra, plus 3TC, a two-drug regimen, which actually did better than a three drug regimen. So that formed a good basis again for two drug regimens going forward for treatment naïve types of patients. The PADDLE study in the middle – that is a small study of dolutegravir + 3TC again in a treatment naïve situation so they are not suppressed and that has been reported out to 48-week data where the regimen looks quite good. A number of these studies are different drugs, but you can see several of them are dolutegravir plus protease inhibitors with darunavir, with atazanavir. And so I think that this is just to really provoke that there is a lot of data going on there.

DTG+RPV

Now in terms of our data going forward. This again is data that should read out at the very end of this year. It is our SWORD study, and so this is the same approach as what we saw with the LATTE study, but now we are using oral drugs dolutegravir plus oral rilpivirine, and I know it is – you kind of bounce back and forth of the different regimens, and so this is two studies. They are exactly the same studies done around the world. It is over 1,000 patients, and we are looking at patients who were suppressed, switched to a two-drug regimen and the read out as I said will be at the end of this year. We hope to then file in the first half of 2017 with this form of therapy. So it mimics what is going on with the cabotegravir + rilpivirine, although this is oral and it is also

dolutegravir rather than cabotegravir. This is a very exciting study for us, and again is a very key one to validating this approach.

DTG+3TC

The dolutegravir + 3TC studies have just recently started and these are termed the GEMINI studies. And so this is over 1,400 patients. The two studies combined, and again, this is in patients who are treatment naïve. So they have elevated viral loads. These are not suppressed patients and so we are looking for this to just get started now, so it will be a bit before we see the readout in early 2018 and this follows the launch of the dolutegravir + rilpivirine by about a year. But this is again a very exciting program going forward.

A growing body of evidence to support 2DR

This slide just shows again starting at the very start of 2017, you will be seeing a lot of these studies coming forward. And there is a lot of big groups that were doing this. The AIDS Clinical Trials Group, the ANRS… A lot of activity in the treatment investigators going forward. So again, these are things you will be seeing in a very regular basis as we bring forward this approach. Because it is really on us to show that this works. It is really on us again you have this evolution of treatment of patients, but it really is data driven and this is what will support it going forward. And we feel very good with the Latte study that we have there.

Why innovation should remain a priority in HIV

The final thing I will just mention and again this is the viral life cycle of HIV. This is something it completes in one to two days, depending on the conditions that you deal with. It mutates all the time and so really looking at all the specific areas of inhibiting its life cycle that is distinct from the human, or the mammalian cell. And so we have a huge program looking at attachment inhibitors. We are looking at a different part of the integrase inhibitors, so the dolutegravir blocks strand transfers of the DNA, but we also have an inhibitor of the enzyme itself. So that is an allosteric integrase inhibitor. And then the maturation inhibitors which are also at the later stage of the

cycle. So if we look at all these together, we do think about them in combination. Can we mix these with dolutegravir, can we create other ways of treating patients as we go forward with that ultimate idea of needing medicines – new medicines. We certainly do not want to get into the situation that we see with bacteria, where we run out of choices with antibiotics. And so again, a very active program going forward.

So that was a very quick overview of our R&D Program. But again, trying to emphasize the rationale, the basis of the two drug regimen and again, we can dig a little more into it in the Q&A. So with that, I'd like to turn it over back to Dominique for concluding remarks.

Concluding remarks

Our strategic priorities to ensure near and long term success

Dominique Limet: Thank you John. So, you have certainly some questions for the Q&A, but you have the key lines of our strategy for the future. So just to conclude on that slide what are the key objective and strategic priorities that we have. One is clearly to drive the share growth of our traditional three drug regimen based on dolutegravir. We still have a lot to grow. We only have 20% of the patients treated in the US. We also want, as we said, to really move into the two drug regimen, and we have a huge number of clinical trials and we are very excited about that because it can be really transformational for not only the physicians, but potentially for the patients one day. So it is a really, really bold move, but it is also very attractive for the future. And we believe that it will add to what we would create and generate with the first bullet point.

Third point is to move from the current daily pill, to a long-acting therapy. You did not mention the prevention, but it is part or so of the long-term prospective that we have these long-acting injectable forms and that is something which is very exciting. And, finally, we want to maintain this huge weight on our innovativeness because as you said, the virus mutates and we see in some countries that they are already a high level of resistance in kids. That means almost newborns who are born with resistance to viruses. There are growing needs and we want to

cover them as much as we can by developing new breakthrough products. So with that, I think we conclude our presentation, and we open up the floor for your questions. Thank you for listening to us.

Q&A

Question: Question on the competitive landscape in the integrase inhibitor class please. There has been focus on the Gilead compound. They seem kind of excited. They seem to have a lower resistance profile. It looks like it does not need a booster – data coming out in mid-2017 – how does that impact dolutegravir and its various combinations you are working on? Thank you.

John Pottage: I think that one of the issues with this drug is that we have not seen a lot of data with it. And the most important piece of data that was shown this summer was the comparative data in treatment naïve patients, it was done as monotherapy. So, 10 days of monotherapy and you look at the potency of the drug. And so when you look at the data that they presented and you go back and compare it to what we saw with dolutegravir in a similar study, you see that actually, it is not as potent as dolutegravir. And so essentially, 100 milligrams of 9883 comes similar to what you see with dolutegravir at 50 milligrams. And the other issue with the study is that they used about half the number of patients in it, so when you look at the dolutegravir 10-day monotherapy study as Dominique mentioned, actually, 70% of the patients were fully undetectable after that time period and we didn't really see that with the bictegravir study.

So why is that important? So, number one it appears the drug is not quite as potent, and so when we think about moving into different regimens of things going forward like a two-drug regimen, you do need a potent drug with it. We have drugs that have failed two drug regimens because there is not that potency. So, the advantage we think going forward for us is that we believe dolutegravir is more potent. In terms of the resistance profile, I think all that has been presented is some in vitro studies and those again need to be seen in patients. One of the things we did in terms of the dolutegravir program were two studies – the Viking studies, Viking 3 and 4, which were in patients who had very limited options. And actually evidence of integrase resistance, to raltegravir or elvitegravir. And really our drug actually performed quite well. Interestingly when I look at the new clinical studies coming forward from Gilead, they're not

looking at that. So really there is your real test of seeing how well the drug does in terms of a resistance profile. So again, we'll have to wait and see how that goes forward.

The final thing I would just mention is that dolutegravir has been studied for close to nine, ten years, so we have a huge accumulating body of evidence. So we know what the safety profile is. We know what it is in all these different clinical situations. And actually when you look at their clinical program, they don't duplicate the breadth and depth of our studies.

And so again, one can see that. So that's kind of a deep dive on different, specific, aspects of that program. But we'll have to see it going forward. But we think we're kind of ahead of the game, we're reading into more innovative types of approaches, as I said, we're thinking how best to use the medicines and we do think the two drugs in the view of long-term treatment, long-term increased aging of patients really bodes well for dolutegravir going forward. Maybe Kim you can fill in.

Kim Smith: Yeah. I guess I'll add to that and just say that, I mean they have speculated that they think they will have a better resistance profile. However, as John and Dominique pointed out, in our treatment naïve patients, we've done multiple studies. You saw four different studies and in none of those studies have there been any patients who failed dolutegravir with resistance. And so it's hard to get better than none. And so there's no way you can improve on that.

They speculated that they may be better for treatment experienced patients who have failed integrated inhibitors, that's the speculation. However,as John said they have no plans to study that population of patients. And so I think that it's a lot of speculation about what they think they may have. What we know is that what we have is really data that we can demonstrate the resistance profile, which is a very high barrier to resistance and that we are very effective, demonstrated to be effective in treatment experienced patients.

Greg Reinaud: If I can maybe just add to that. I think you have a very good answer I think from the R&D side, in terms of the value of dolutegravir. I think from the commercial side the value from a Gilead perspective is to combine it with F/TAF, and have a single pill. And that's really what their selling point will be. So I think you know, there's no doubt that they will put a huge amount of effort behind it. Providing their clinical trials do read out as they expect. And I think then it will be a choice for the marketplace, for the patients, in terms of do they want to stay with a more traditional three drug regiment? Or do they believe in the two drug regiments going forward?

So there's no doubt that you know, again you can look at it just from a pure clinical perspective. And I don't think we see much that so far and again there's really limited data available. They just don't have the same quantity of data and so on. From the commercial perspective, yes. I mean it will be a threat, I think we feel confident in the two drug regimens should over time prove a very compelling proposition for physicians and patients.

Question: I just wanted to ask two quick questions, one around, raltegravir which still sells obviously a significant amount. And I understand that a fair portion comes from post-exposure prophylaxis, and I was just wondering whether you're looking at that. And then second, I was just curious in terms of – can you talk about payer mix? Obviously there's significant Medicaid and Medicare exposure to the revenue base, so I'm just curious. How much is commercial and how do you think that might evolve given all the increasing metrics around pricing and reimbursement in the U.S.?

John Pottage: Kim do you want to talk about post-exposure process?

Kim Smith: Yes, the post-exposure prophylaxis just to describe it for those who aren't familiar is a setting with someone who may be exposed to HIV, either in an occupational setting or they're a nurse or a physician, and they're drawing blood and they get stuck with a needle from someone who has HIV. Or in a sexual exposure, so a person who finds out at hopefully after the fact, that

they had the unprotected sex with a person who is HIV infected. And so that is one of the uses of anti-retroviral therapy that has been shown to be effective. And so raltegravir is getting quite a bit of use in that area, mostly because it's very well tolerated.

So we have supported a number of investigator-initiated studies, basically just to demonstrate that dolutegravir can be similarly effective in that environment. But it's mostly that you're looking at how well it's tolerated, because you don't have comparative studies which would need to be compared to not giving anything. And so what we're doing is generating similar types of data that show dolutegravircould be a reasonable option in that environment.

John Pottage: So it helped them move to that point, but I think again that's a drug that's preceded us. And I think people are comfortable with it and we will as the data develops move forward with that.

Dominique Limet: And your other question, you know, that in the US HIV treatments are mostly prescribed through public part of the payers and the commercial segment of the total of the HIV market is much more limited than in the rest of GSK, for instance. And it is clear that, you know, there are plenty of unknowns in the US with Obamacare, with the elections and so forth. We know that there is price pressure everywhere, but for the time being I must say that on the whole the price pressure has been limited. And we've been able to manage it pretty well.

Question: The guidelines have been very supportive so far where it's kind of enhancing the existing treatment paradigm. You maybe talk about how important patient pool will be and do you really think they'll see a difference between a single tablet regiment of three drugs or two? And also, how important doctor acceptance is within all this and how long it will take to generate that doctor acceptance? And what key side effects or drug drug interactions you would focus on in the over 50-year-old population that would drive this? And then a follow-up question just on the size of the

market going forward as we come towards genericisation of some of the legacy triple combinations. Can you maybe talk about your expectations for the overall market size; you flagged a slide showing temps and CAGR between 2013 and 2015? Going forward from here on the next five years with genericisation, do you – and the market being able to maintain its existing dollar size with the share? Do you think you can grow it or it will deflate?

Dominique Limet: So I'll start with the second. You know, that the 10% CAGR is actually a blend of three different dimensions. One is a real patient volume increase, which was from the 5-6% in the early stage. So we have ~3% more patient numbers. And then 5% of price increase, and 5% of mixed effect. Mixed because actually due to the fact that we're more integrated, which are more recent products, the net price is slightly ahead of the others. And that's why the combination of the three, and certainly this 13% for the last year.

John Pottage: Right, it varies a little bit. But it's about a third, a third, a third, between increase in volume, increase in price of existing medication and shifts from older medications to new more expensive medication.

Dominique Limet: It is clear that we might see some price erosion here and there, but the two other elements carry on growing. Because most of the value is in the third agent and the new ones, and that's something specific to HIV because of the side effects of the old drugs and the resistance threat of old drugs. Actually we see that the generics have had very little inroads into the HIV market. Because actually they're not old, they're old and obsolete most of them. And that's why they are not so much used. So we do not see a major impact. In Europe there will be a price impact because it's more or less mandatory. But it will be slow in the US.

Greg Reinaud: That's actually a very dynamic market compared to perhaps what you see from the outside. I mean every time there's a new product, beforehand the physicians or the patients might say, 'It's fine, our unmet medical needs are fine, we won't need to do anything until there is

a cure. But when you look at the product launch over the last five years, they've gone from zero to fifty per cent today, of prescriptions. They are really the ones that are providing the growth in the market. We do expect new products to rejuvenate the market.

Dominique Limet: It's not always easy to convince physicians to move their patients, especially when patients look relatively well treated by their treatments. We have seen in the past and it's also possible because the voice of competitors is really high, a lot of physicians were relatively happy minimising the side effect profile of the drug they used. By coming with new products we have revealed unmet medical needs and silent sufferers. And over time thanks to dolutegravir we were able to increase the dynamism of that market because we will meet some of the unmet needs. Having said that, it's tough, it takes time. The patients need time to see their physicians and it takes us time to install a new territory area, a new territory regimen. And we know that it will take time to convince people to abandon their old beliefs and move into a new drug regimen That's why we need a very solid advantage to convince them. When I saw the announcement of the iPhone 7 the other day, I think the third NRTI that we could get rid of, it is a bit like the jack plug of the iPhone. People are uncomfortable with newness, but if we have the demonstration that it brings value to the patients, if it brings value to the payers, if it brings value to the community in general then we are convinced that we will be able to do it. Because we have already done it once. We were able to move the market with dolutegravir; we can do it another time.

Question: In five years could we see an increase in the market?

Greg Reinaud: I would expect something relatively similar to today. What's going to change is a shift within the composition of that market. As was pointed out, it's roughly fifty/fifty today, between the third agents and the NRTIs. If we are successful with the two drug regimen strategy, if that works, you should see a reduction in the size of the NRTI backbone market. And you should see

an increase in the size of the third agent market. There is a relatively stable market, different forces at play, but if you've got the right product and approach there is room for growth.

John Pottage: Do you want to talk about aging?

Kim Smith: Well I was actually going to talk about the patient, and I can address aging too. So why would a patient want a two-drug over a three-drug regimen. I think Dominique started making this point regarding the silent suffers. The long and short of it is, if you can get the same potency and efficacy with two drugs then you were getting with three drugs, it's kind of a no brainer. You reduce the number of side effects that patients experience. Patients are very much driven by what their doctors recommend. If the doctors believe and they get less side effects, then they will believe. So why would the doctors believe? Well, we are doing studies against three-drug regimens and are expecting to show we have a similar amount of efficacy, and as good or better tolerability. Part of it is because dolutegravir is a unique drug. Part of the reason we have three drugs in a regimen is that you need those three drugs to get the amount of potency to get the virus all the way down and keep the virus from mutating. We've shown that dolutegravir has unprecedented potency and a very high barrier to resistance. That's what allows us to use one drug then add one drug to it and get to the same effectiveness. As far as aging, it comes back to the side effect profile. As people get older they have more challenges, one of them is fragile bones, renal toxicities, and those are some of the side effects you avoid by using the two-drug regimens that we're proposing. So, older patients may get that benefit from fewer side effects, and as Dominique mentioned earlier fewer drug side effects from drug to drug interactions. So if you need to take a drug for hypertension or heart disease you're less likely to have an interaction with dolutegravir than with some of the other drugs.

John Pottage: It's simpler so you don't have to make a lot of drug adjustments. Everything to me is very data driven speaking to the physicians, and we've initiated a number of studies in aging patients. So we have a big study going on with the NEAT network, which is a European clinical trial group

with dolutegravir, switching to dolutegravir in patients who are older. So there are a number of proposals looking at that, and actually in our GEMINI studies we are looking to enhance the number of older patients to have that data. We also have a large effort in health outcomes and a lot of other patient outcome parameters that are related to aging, or people being older with this disease. It's our job to convince while keeping in the mind the physician, and educating the patient, this is a long term proposition. We are putting in place the data to drive that to find where we get to.

Question: So silent suffers at the moment versus those that are looking to avoid the side effects several years out?

John Pottage: I think the answer right away was those who took efavirenz. There are a lot of issues where people have what are called neuropsychiatric effects. These include people not feeling well, having abnormal dreams, and just feel off. As they are treated with dolutegravir, you saw it in one of our studies one of our pivotal studies of dolutegravir against efavirenz, the SINGLE study, and the reason dolutegravir was better was because there were less of these types of side effects. The overall data with efavirenz was great. So physicians taking it, yeah this is great. Though the patients are having this underlying problem to it, there weren't alternatives. So we went out there and showed that there was an alternative. It's not like we make a new medicine and just say take it, we show why it is better. Really putting in place the study were we can show that superiority. I think with these changes and the guidelines it's amazing how quick this happened. End of game, this is done, we don't need to do anything more with HIV. Then all of a sudden, it's off the guidelines as treatment of choice.

Kim Smith: I'll make two more quick points. John made the point about our studies, in the SWORD study, which is dolutegravir with rilpivirine we made a point of having twenty-five per cent of the population in the study over fifty, we met that. And then the second point of physician interest. When they showed you the list of studies, they are all investigator initiated studies, these are

investigators wanting to study our drug in combination with one other drugs. It really demonstrates the demand, the pull for that from clinicians.

Dominique Limet: Possibly the last point about the rate of adoption. We see that it varies from country to country. We couldn't give you more of a unique answer. For instance, we know that in Europe we see a not-insignificant amount of physicians using a two-drug regimen. And actually if you reference the clinical trial publications you would see more and more of these core studies, observational studies in the months of come. We already have a number of physicians who have tested those regimens.

Question: You said initially you were interested in having a good reputation concerning fair pricing. With *Epzicom* going off patent, will the *Triumeq* price stay the same or go down? If it goes down do you think it will help you to gain share, or do you think that Gilead will just match?

Dominique Limet: In the US we have no intent to reduce the price of *Triumeq*.

Question: Might that be different for Europe? Will you be forced to think about pricing from a government or reimbursement perspective?

Dominique Limet: So it's different from the US. The US pricing environment is more about discount where the European is more about price decay or price declines. So there are numerous countries in Europe where automatically you have price cuts, which have been included in our forecasts. That's something that will impact the value of *Triumeq*. That is also why we are so keen to make sure the main value driver is dolutegravir.

Question: Just to follow up on the two-drug regimen concept. What are the key guideline changes, the bodies involved, and what are the steps? What should we be looking for in terms of milestones that could give us some comfort that there is acceptance of a two-drug regimen. For

years it's been hard, it's always been three drugs. How many years of patient data do you need before you can prove that there is no resistance that could emerge? Where do you draw that comfort?

John Pottage: In terms of the guidelines there are independent bodies. There are four important guidelines around the world. They all have different approaches. Starting in the United States there are two sets in the US, one is the Department of Health of Human Services (DHHS) guidelines, that's an evergreen type of rolling change as the data comes out. They have a large number of clinicians both in the United States and internationally; it's an independent body, with some of the members being investigators on studies including ours. As data is presented they concentrate on presentations and publications to evaluate where the drug fits in to the treatment guidelines, so they come fairly quickly.

There is a second group in the US the International Aids Society, I get a little tripped up with the different societies. But it is a group that actually meets every two years, until you see new guidelines coming from it. The most recent one you saw was a couple of months so, so the next set for that typically would be in 2018, which doesn't move as quickly. These smaller groups are more US-centric and are patient oriented. What I mean by that is that they give guidelines with no sense of price, although they are starting to comment amount that. So it's what is the best data, which gives you the best patient outcome for that particular patient. So if you're a patient you look at those. There is no, we'll do the best for the least amount of money that you see in some of the other guidelines.

The third set that you look for are the European guidelines, which come out on a yearly basis. They incorporate all the multiple European countries so you'll see a wider display of recommendations. There are some countries where some of the medicines are not available. It is more of a public health approach, more so than what you see in the US oriented studies. Their guidelines come out now, or late September/October. They will sometimes come out more often.

The final group is the penultimate World Health Organization (WHO) guidelines, those are very public health-driven. You've seen changes with them in the past, they didn't come out very often. They seem to be moving them more frequently then they did before, concentrating on the most good for the most people with the least amount of money or expense. So they're driven from more of a public health approach than the US gaudiness. So you look at all four of those and you'll see them all moving, and they did more very quickly with the integrase inhibitors and dolutegravir then they've done in the past. So those would be signals for you to look at. Again, those all independent bodies, we provide the data and they are all very data-driven in their deliberation.

Greg Reinauld: You've also got two established products were there are a lot of information on them. Whether it's dolutegravir or efavirenz. You've also got new products that come out. How quickly do those make it on the guidelines? We don't have an answer for you, but it's an interesting parallel in terms of what's the more risky. Is it the combination of two established products or is it a new entity for which you don't have long-term data?

Question: How many years of patient data do you need to prove you don't have an issue or risk criteria?

Kim Smith: I think you'll get an indication from the initial phase three studies. Because what you typically would see is within the first year if people fail, do they develop resistance? So where we've distinguished ourselves is that people fail and they don't. As it comes into the market, more time passes and you use it in the real world. And the question is in the real world, do you develop resistance? So what we've established with dolutegravir is not only established in the trials but in the real world. The trials will be the first sign and then over the years you will start to see what happens in the real world setting.

John Pottage: I think there will be a demand for longer term data with two-drug regimens than three-drug regimens. So, what we are putting in place is not just twenty-four week or forty-eight week or one-year data, we really carry them out to two years and beyond. So some physicians would be more conservative, ok, two drug regimen, I still have some concern on a potency issue, I want to see what's the durability. So they'll say I'm not going to do anything until I see two years. So I think two years versus what you might see from a three-drug regimen is enough. I think as Kim said, it's really in the first twenty-four-week period where the dye is cast, you really see it. It's really just having a better feel of that durability, and actually now having treated very long-term coming up to five years in some patients with dolutegravir, we haven't seen the emergence of resistance. The durability is there, whether you can do that in the two-drug, the bar will be higher. We're aware of that and that's why we'll produce the data for that.

Greg Reinauld: One more point on that, with the two-drug regimens there is almost a different bar when you're talking about naive patients and suppressed patients. I think there is less concern around suppressed patients then naive patients. So you may see, back to you question on guidelines, you may see a different amount of data required.

Question: How will you think about pricing the dual regimen?

Dominique Limet: Most products will be clearly priced already. There will be an added value to the product because of its price. Partially in some markets. But it's clearly and option that will attract the attention of some payers.

Question: This will be the first kind of data we will get to see. Can you speak to how the patients in the study compare to real world samples and developed markets? Can you speak of recruitment and anything we should be aware of from that trail that may not be represented in the real world?

Kim Smith: So, the population really is the real world in developed markets. So, as I mentioned, we did set the bar to make sure that we had representation of over 50, and it was an easy bar to cover in the study, because that's who's in the clinic. And so this was basically individuals who were in the clinic who were interested in an alternative regimen. And so it enrolled really actually very rapidly. We also really set the bar – we wanted to make sure that we had a good number of women in the study. And so we have – we met the bar for women as well. And so it's really quite representative of the patients that are in developed country clinics really – mostly the US, Canada, Western Europe.

Question: Have you got that data in house at the moment and you're cleaning it up?

Kim Smith: We do not. It will come at the end of the year.

Dominique Limet: We expect as John said to release the data by first half of next year.

Question: You'll get it in house, clean it up and then headline it? Or you'll wait for a congress?

Dominique Limet: We have it at the congress first. [nb: We will consider having a press release for topline results.]

Question: What are you aiming for?

John Pottage: What congress? We're aiming for CROI.

Question: 2017?

John Pottage: In Seattle.

Kim Smith: It'll be in February.

Question: Can I get some thoughts on your next generation integrase inhibitor, cabotegravir, and that as an injection once every two months. How does it sort of shape up potentially as a profile from a patient dynamic point of view, treatment point of view? How does it change things, given that we're sort of used to a pill?

Dominique Limet: I stand by something about the environment and, you know, it's patient change. Actually, it's pretty tough to change people to move from one treatment which fit them well. When we started the first trials, we were concerned by the fact that it was an injection – in injectable form. And actually when we discussed with physicians – what, three years ago now? – they were not particularly impressed by that idea. And I can tell you something, is more we go along our trials, more traction we see with both patients and physicians. And actually we have now data which proves that. But I think it's an illustration again, looking at how fast the market can evolve. It's a slow – there is a slow start but then, when they are on the trial, they are being very, very positive. So that means that there is an absolute confidence that the cabotegravir is going to be a long-acting formulation associated with rapid and long acting can really make a great success within the HIV market.

Kim Smith: Yeah, the only thing I would add to that is that if you can measure on the basis of the popularity of the studies, the long-acting study enrolled in really about half the time we anticipated enrolling. So it was extremely competitive and extremely popular. One of the things that we worried about was whether or not patients were going to leave the study because they didn't like the shots, but that was very, very rare. And so, as Dominique said, a number of clinicians said, 'Oh, patients aren't going to want to have to have a shot.' And they have come back to us and said – you know, one investigator in particular said, 'I didn't think patients were going to like it, but one patient essentially came back and said 'You'd have to pull the needle from my cold, dead hand in order to get me to go back to a pill.' And so for some patients, it is the getting away from

the daily reminder of living with HIV, which is still associated with a tremendous amount of stigma. And so the idea that they could just get their shot and go on with their life and not worry about their daily routine is appealing to a number of patients.

Greg Reinauld: If you want to get a better sense of the qualitative side, there was a presentation that was done in Durban at the last IAC meeting just a couple of months ago, which was fantastic, which went alongside the clinical trial results, which was a series of in-depth interviews with both patients and physicians. You might want to take a look through that. It'll basically gave more detail to what we've just been describing.

John Pottage: This needs a healthcare professional to administer it. So it is an intra-muscular shot, so it's not something you can do yourself for this.

Question: Does it fall under path B then? Or how does it play out from a payer perspective? How does it play out from a payer perspective as a path B drug? So…

Greg Reinauld: It's still something we're working through. It could fall in one or the other, and so it's something we're working through. We've got a little while until commercialisation, so we're looking at both options.

Question: I just wanted to follow up around sort of the market outside of the US, cause I'm conscious I think about 70% of your revenues, certainly for *Triumeq*, come from the US. So, in Europe, just how you think about the outlook there in the context of your earlier comments around the market being stable in five years' time, is that driven primarily by US accelerated growth versus Europe continuing to decline?

Greg Reinauld: You are absolutely right. The US represent almost 70% of the total sales today and will remain a very high contributor of the global sales at Viiv Healthcare. We have a limited presence,

actually – we have a big presence in Europe, where we grow also very well, at a different pace because of pricing effect. You know, in Germany, for instance, you have one year, let's say, with no reimbursement discussion, and then the product is discussed, and then the price generally goes down. So we have ups and downs like that, but Europe is still a very significant chunk of our business. We still hope to be able to drive more sales and more growth from the international region, and particularly in Brazil, in China, in Russia, but these are long-term goals because it's pretty complex to get access to these markets and they will represent in any case a much smaller opportunity compared to what we can get in let's say the US or Europe. But we are still betting on a substantial growth in Europe, particularly because the integrase class is not yet as developed as it is in the US and we don't have everywhere the market share that we should have. So altogether being by the evolution of the patient numbers, the evolution of the integrase class, the evolution of our market share in that class, we believe that we still have a significant growth for Europe to come.

Dominique Limet: I would echo that I think. You know, I think before when I was saying stable I think I was probably being a little bit tongue in cheek. I think the market will continue to grow. I think it may slow depending on how the two drug regimen pans out. I think that may put a – it may have an impact on the overall growth. But I think certainly, the way that we've grown so far, the dynamics within Europe are very favourable from our perspective.

Question: It seems as if the clinical trial programme that you've had has created a lot of goodwill and acceptance of the product. How many more big trials can you do from here? Can you maybe talk about kind of evolution of the clinical trial programme for dolutegravir in the two-drug regimen? And why do you think Gilead isn't following you with a broad clinical trial programme? Is it because they haven't got enough data yet and therefore at some point they will press the accelerator? Or have you any other thoughts on that?

Dominique Limet: Before you go into the medical front, because there are plenty of good reasons why they don't do it, I think we have in a way the privilege of being more focused than they are and having more value attached to the third agent segment than they are. And one of their challenges is to defend and protect both segments at the same time, where actually we have – just elaborating on the question you raised earlier, I was very pleased to see the programme of development of these new integrase because that means that really they believe that their current integrate is far from being optimal. That's actually what they have done with their NRTI as well in switching from the old to the new one. Once again, how long will it take to know really if that new backbone is absolutely immune against long-term side-effect profile? The same would apply as you raised earlier on resistance. So we believe that they have a huge amount of sales and profits to preserve, meaning that they are a bit more exposed and not as innovative in terms of treatment regimen, because it might cost them too much.

John Pottage: I think in terms of the clinical trials, we always say the bar is very high because there is a lot of good therapies out there. And our programme is not really driven by any particular number or anything like that – it really is driven by what is the data we need to answer what a physician needs to prescribe the medicine in answering that. And so when – and right now, we are still doing large clinical trials with dolutegravir. We have two large Phase III trials – one is in second-line therapy in the developing world, and so it's a comparison to Kaletra, which is kind of the standard second-line therapy according to World Health Organization guidelines. And it's fully enrolled and we'll start to see data from that in the coming years. But we are also doing a large study where people are worried about co-infection with tuberculosis. Now that's really more in the developing world, but clearly you do still see unfortunately tuberculosis in North America, in Europe. But how to treat that because of the drug interactions with the treatments of TB with the HIV medicine. So we have a large study there which is about to finish enrolment in the next month. That's called the INSPIRE Trial. The first one I talked about was the Dawning Trial. Now those are the last two very large dolutegravir-specific studies. We've now kicked off – we have the two SWORD studies, we have the two GEMINI studies, we have other studies following

GEMINI, probably looking at different scenarios of switching to that. And then the cabotegravir programme is quite large and so that's kicking off with it. But these are all large because they're centred in specific clinical questions, issues to answer, to drive the data, to help people understand where it's slotted in. Kim?

Kim Smith: Yeah, I think that everything that John – the only thing I'd add to that is that around the two-drug regimens, there is not only the work that we're doing but all of those studies that I mentioned and more that people would like to do. And so there's a huge amount of interest in the two drug regimens for resource limited environments, because of both improved tolerability and potentially cost. And so we have people coming to us – networks coming to us wanting us to work with them to be able to do these types of studies. So we do collaborative studies with some of the big networks like the French network ANRS and the NIH network, AIDS clinical trial group, to do, to answer questions that are not just for the developed world but also for the rest of the world.

Question: Sorry, big picture question just in terms of how ViiV Healthcare fits in the big picture of, within GSK. I'm curious to know if you can remind us of all the various puts and calls that you have amongst the three owners of the organisation. I suspect there is some sort of contractual limitations as well. Could you just address some of that? Because if there is a change in control any of these players, how does it affect ViiV as an entity? Thanks.

Dominique Limet: So, I could have a very simple answer. I am not responding or commenting on a change of ownership. I think the past history of GSK has shown clearly that GSK didn't want to evoke that. The only way that GSK might be interested is to acquire more equity than to sell equity. This is the answer I would give today. There is no change of put options of any form compared to what has been already largely commented by Andrew and David Redfern, the chairman, in the last year or so.

Question: And do you have a call option or do you have a put option that Shionogi, Pfizer have a control? Could you just remind us of who has that?

James Dodwell: Shionogi has an option for that 10% and there's a window that starts in – various windows – the first one is March next year and Pfizer can put their stake to us at any stage, but they've shown no indication of doing that at the moment.

Question: And does GSK have a call option?

James Dodwell: Not to my knowledge.

Question: Before you go, I've got a big picture question. Just on the joint venture, given the fact that you acquired the BMS pipeline and we're no longer seeing the kind of breakout of the profitability of the ViiV Healthcare unit, how much agreement is there between the three part-owners on the spending plans and how that evolves from here?

Dominique Limet: So, the decision – or not the decision, let's say the endorsement of R&D budget is made at the board level, once in a year. And let's say we had identified early enough – John and I – that we needed to invest more, both strategically and also tactically for increasing the sustainability of our business long term, and that was something which was absolutely blessed by the board, we came a number of times but clearly last year we had another call for action. And so when an opportunity has arisen like the BMS one, obviously we were happy because it matches both the strategic element but also the fact that we needed to invest more in R&D. And we are completely backed up by the three – that's a board decision and up to now it was extremely well regarded.

Question: Dominique, can I ask a big picture question, which is you've had a very successful period through inception, especially over the last few years more profoundly. Is there – do you see a

role for ViiV Healthcare to go beyond HIV into other kind of infectious areas? Kind of where do you think the science kind of takes you? Is there any interest at all?

Dominique Limet: Actually, in 2010 we came to the board explaining that we were thinking that having a company dedicated to a broader vision of the HIV patients and particularly at the time we had some interest for the Hepatitis C co-infected patients. So we had some idea there and I think GSK clearly at the time, as well as Pfizer, said 'Ladies and gentlemen, you have not yet proven any success or started delivering on the HIV field, and then we'll see.' And I must say, today we are a very focused organisation and we have learned also about the other areas which are close to our field, because a key question about diversification is what kind of value would we add to other one. And even the Hepatitis C field, for illustration, is relatively different, because we have focused, we have 15 countries that we represent 15 entities that represents almost 90% of our turnover. Hepatitis C indication is a different geography in some form. And the numbers are much bigger in terms of, and so it's a different field. So what would be… The disease itself is different. The mechanism of the virus is different. So there are not obvious synergies in between such an indication and HIV. And so that's why I believe today being part of the GSK organisation too, I would say that what could be copied or mimicked is the spirit that we have developed, the culture that we have, the accountability, autonomy and focus that we have. That's something that could be extrapolated elsewhere. But having additional indication areas within this today, at the time we have so much growth potentially offered to us without distracting the management, distracting the R&D organisation is not in our plan so far. But…

Question: Being owned by GSK, the majority of budget is going [break in audio]. You're allowed to be so focused, cause if you were an independent, would you be comfortable being as focused on HIV as you are if you were an independent listed entity? Assuming that you stayed that way.

Dominique Limet: That's a good question. Honestly, that's a question that we had, because you could have a different view, because it is clear that when you have a multi-therapy area business

like GSK has, you can hedge the different businesses with the others. We can't because we are in HIV. But, may I say that there is a merit of it. We know that our future is in HIV. We know that we have to develop as much as possible our sustainability, to be smart at that, because as a management team we believe that we have a responsibility to do that. And by being focused and possibly more exposed than a big group with a large set of areas, we are hopefully also more effective.

Keyur Parekh: Any other questions on the floor? If not, thank you all very much for your time and your part this morning. I really appreciate it. Thank you all again for joining us.