

GLAXOSMITHKLINE

VIIV HEALTHCARE MEET THE MANAGEMENT

TUESDAY, 10 DECEMBER 2018

ViiV Healthcare Meet the Management

David Redfern (Chairman): Good afternoon, everyone. It is great to have you all here for the ViiV Healthcare Meet the Management event. I am David Redfern, and I am the Chairman of the Healthcare, and I am really delighted to welcome you on behalf of the entire ViiV executive team, who are all sitting here, looking very professional and handsome in the front row for this event at Deutsche Bank, and we are very grateful to Deutsche Bank for their hospitality.

I would also like to welcome all those people who are participating online, wherever you are in the world. This event is designed to provide you with an opportunity to do a deep dive into our HIV business, which of course is a critical part of GSK and of GSK's investment case, and it is really a chance to hear specifically from members of the ViiV management team, as I say, all of whom are here in person.

The plan is for the first hour we will have a presentation covering key aspects of the business led by Deborah Waterhouse, the Chief Executive, and other members of the ViiV leadership team, and then after that we will spend up to an hour doing Q&A, and these will be the presenters in the first part (refers to slide).

Cautionary statement regarding forward-looking statements

I will start, as always, with the cautionary statement.

30 years and counting – our fight against HIV

GSK has a long and very proud heritage in the fight against HIV, that really goes back over 30 years. Those of you who are based here in Britain will remember this iconic public health campaign of the 1980s 'Don't die of ignorance' – sombre and sobering and, for some, frightening, and hard to believe that people diagnosed just 35 years ago had a life expectancy of around 18 months and, in fact, it was GSK scientists, then of course working for Wellcome, who led the development efforts to bring forward the first approved medicine to treat HIV 30 years ago; AZT in 1987 and, of course, it is amazing to think how the treatment of the disease has advanced so much in what is really a relatively short period of time and, in fact, many of the scientists working on those early treatments or helping to care for patients are working still today for ViiV.

Dr John Pottage, the Chief Scientific Officer at ViiV, who will speak a bit later about the future direction of our research efforts worked with some of the very first people diagnosed with HIV. Also Dr Kim Smith, who joined us five years ago, a distinguished physician and clinical researcher and previously treated HIV patients based out of Chicago, and Dr Harmony Garges, who is Head of our Global Medical Affairs, and who will join us for the Q&A section, is a specialist in working with children, and children and research for children remains a very important part of our efforts.

Our portfolio today is now comprehensive with options right across the treatment spectrum for people living with HIV with 13 approved antiretrovirals on the market, and of course hopefully several more to come soon.

Our unique model

I do want to touch briefly upon the model of ViiV Healthcare, which is a model that I think has very much driven the success of the company. ViiV is now about to celebrate its 10th anniversary. We formed ViiV in 2009, initially as a joint venture between GSK, who of course are the majority shareholder, and Pfizer, and then a few years later we added our Japanese partner, Shionogi.

Throughout the last decade there have been some very important aspects that have always been critical to ViiV, and I have no doubt have contributed to the significant growth that we have seen ViiV achieve. Firstly, we are totally focused on HIV and, as such, aim to build very deep relationships and understanding, understanding of all the stakeholders involved in the fight against HIV, be they people living with the disease, physicians, activists, NGOs or governments, and our relationships with all of those groups run very deeply.

Secondly, it has always been our philosophy to invest very significantly in HIV research and development to precisely identify, and then address the unmet medical need. That R&D for us started with AZT, has progressed through all the very significant and highly positive data we have generated for dolutegravir, and continues today with our two-drug regimens, including long acting formulations and a number of novel, new mechanisms of actions and approaches that we will talk about during the course of this afternoon.

Thirdly, we have invested significantly in building some key capabilities in the business. That includes our global commercial presence, but also, importantly, it also includes our outstanding medical affairs and clinical teams. We have a significant number of highly respected physicians and key opinion leaders in our ranks, and that undoubtedly differentiates our engagement with prescribers and patients.

Finally, culture is also critical and, from day one, we have tried to develop a culture that is very much what we call a challenger mindset; nimble, agile and disruptive, but always 100% dedicated to HIV, challenging the competition, undoubtedly challenging the access agenda but, most importantly of all, challenging the disease itself with the science and, ultimately, the new medicines we can bring.

With that, I am going to hand over to the Chief Executive of ViiV, Deborah Waterhouse.

Deborah Waterhouse (CEO): Thank you very much, David, and welcome everybody. Thank you for coming today. My name is Deborah Waterhouse, and I am the CEO of ViiV Healthcare. Let me take just a couple of minutes to introduce myself given that this afternoon's session is called 'Meet the Management'.

I have been with GSK for about 20 years, and then for the last two years I have been with ViiV Healthcare. During that time with the company, I have spent time in the respiratory business, in the vaccines business, and actually quite a considerable number of years working in the HIV space. In the early 2000s I led the UK HIV business, and then I went on to lead the European HIV business for a number of years, just up until the point at which ViiV was formed.

I have worked in the Asia Pacific region, heading up our Australia and New Zealand GSK organisation. I have spent a number of years working in both Eastern and Western Europe, and then before I was appointed CEO of ViiV, I spent a number of years heading up the vaccines business in the US, and then primary care in the US, so the US is a place where I am very familiar with the healthcare system and the business that we have there.

Last year I was appointed on 1 January CEO Designate, and then as of 1 April became the CEO for ViiV Healthcare, so I am delighted to be here with you today.

To leave no person living with HIV behind

The reason HIV is a special therapy area is because really it signifies a time when the healthcare professionals, the pharmaceutical industry, and also patients, and those that advocate for them, come together to really put the patient at the centre of everything that we do, and our mission as ViiV Healthcare is to leave no person living with HIV behind, and this is really at the core of how we run our business.

The shape of our business

Let me tell you a little bit about our business model before talking more deeply about the way we operate. Our business is in three ways; first of all, in developing countries we offer voluntary free licences, so that generic manufacturers can actually make our medicines and allow access in those developing countries.

In middle income countries, we have high volume lower cost tenders, and then in the developed world we actually sell our medicines to payers and governments across the world. So that is how we make sure that we really are offering all of our medicines to all people living with HIV across the world, and we actually have a very balanced business, and I thought I would start the presentation today by talking a little bit about how our business is constructed.

The US is 64% of our revenue, Europe is 25%, and the international region is 11% of our business, and each of those regions actually offers significant growth opportunity. Let me talk about where we are up until the end of September 2017, and then I will also talk a little bit about why we think we have such significant opportunities across all of those regions.

In terms of the US, the US is currently growing at 13% up until the end of Q3, and our share in the US is about 27.4% of the STR and core agent market.

If I then move onto Europe, Europe is growing by about 6% and, again, we hold about 27% share of the STR and core agent market.

Then if I move over into our international region, the international region is growing at about 24% and the share there is more difficult to calculate because it is such a broad set of markets, but I will pick our biggest market, Japan, where we actually hold 47.2% share of that very important market. So, as you can see, we have a significant business across all three regions, and we believe that there are growth opportunities across those regions as well.

If you think about the US, there are 38,000 new diagnoses a year in the US. In Europe you probably have about the same number of diagnoses and then when you think about the international region, particularly in the middle income countries, where we actually have the significant tenders, you have countries like Brazil where you have 1 million people living with HIV, Russia about the same size, and China about the same size, all of them working out how they are going to tackle the epidemic, as well of course as more developed countries, such as Australia and Japan, all offering great opportunities there, so hopefully you can see that there is still a significant opportunity across the world.

Our strategy

If I think about our strategy, there are three pillars to it; Innovation, Performance, and Trust, and I hope this afternoon as we take you through each of those pillars, you will see that it is our confidence in our innovation that actually leads us to have confidence in our future from a performance perspective and, of course, with our mission of leaving no patient behind guiding us, we also believe that we will have a very strong offering in the trust part of our strategy as well, but let's talk a little bit about innovation.

We have a very strong pipeline, and that pipeline contains assets which are targeting prevention, treatment, remission and cure. We currently have eight Phase III clinical studies ongoing, which are supporting our 2 DR portfolio, and we will have three medicines that we hope to gain approval for and to launch in the next 18 months and, in addition to that, as we look a bit further into the future, we actually have a very strong discovery pipeline, as Dr John Pottage is going to talk us through a little bit later.

Our performance

In terms of performance, we have 600,000 people across the world living with HIV on dolutegravir and it is the number one core agent, and our current business is to the end of Q3 at constant exchange rate growing at 12%, and actually if you were to step back and take a global perspective on our business, so not just looking at the core agent and STR market, but looking at the whole £22 billion HIV market at a global level, our share has actually increased by one percentage point from 22% to 23% over the last 12 months.

The last thing I would like to talk about is trust because given the way this therapy area works, trust is absolutely crucial, so a couple of examples of where we are in our trust agenda; the patient view corporate reputation study, which is basically 1,300 patient groups across 95 countries are surveyed each year, 46 pharmaceutical companies are reviewed against 12 criteria, and actually for the last four years, ViiV Healthcare has been number one in that survey.

We also make a significant contribution to GSK's position in the Access to Medicines Index and, again, for the sixth time in a row GSK has actually been in the number one position.

We run a programme called Positive Action, so if I move beyond the medicine, as it were, we run a programme which is 300 community based initiatives which support education, testing and making sure that people are able to access appropriate treatment across the world, and then we have a significant programme supporting paediatrics, and we hope from 2020 dolutegravir will actually be available and licenced for children 3kg and

above, so that means across the whole lifespan of the human being, dolutegravir is an appropriate medicine for people who are living with HIV.

Our innovative and competitive pipeline

Let me just delve a little bit more into our performance. We have talked about the number of patients who are currently taking dolutegravir and we have talked about the fact that we have five superiority studies and therefore dolutegravir is the leading core agent. In terms of where we are at the moment, we are in a very competitive marketplace and we are very happy to report that our dolutegravir share in the US is holding firm, despite the launch of Biktarvy this year.

In terms of where we are with *Juluca*, we are really happy with that product launch. *Juluca* in the US is currently being prescribed, or has been prescribed, by about 1500 physicians and we are currently generating about 1600 prescriptions per week. We are now seeing *Juluca* launched in Europe and parts of the international region as well.

We have filed for dolutegravir/3TC fixed dose combination. We filed in September in Europe and in October in the US, and that was a little later because we have a priority review voucher which accompanies our US file. Then we have the positive results from the ATLAS and FLAIR studies, which are the two pivotal cabotegravir/rilpivirine studies: again, that will give us the opportunity to file with regulators in Q2/Q3 2019.

We are projecting that we will grow our global sales, share and profits over the next five-year period, based upon that innovation, and based upon the excellence of our commercial execution. I will let Kim Smith now come to the stage to talk a little about the next phase of our journey, which is really into the two-drug regimen era. Kim, over to you.

Kim Smith (Global Research and Medical Strategy): Thank you, Deborah. Good afternoon. I am Kimberly Smith and, as David mentioned, I joined ViiV about five years ago, after roughly 20 years of being an HIV treater and researcher in Chicago. I joined ViiV because it was a unique company. I have spent most of my career focused on HIV both, again, taking care of patients and doing research. ViiV offered the opportunity to expand the impact that I could have on patients beyond the individual that was in front of me, to a global impact.

From evolution to revolution: entering the 2DR era

It is my job today to talk to you a little more about our 2DR journey. If you look here at our journey map, our strategy map, you can see 2DR right in the middle. There are the 2DR regimens that you are already familiar with – *Juluca*, dolutegravir/rilpivirine, and

dolutegravir/lamivudine which is attracting a good deal of attention right now. I will also talk to you about our long-acting 2DR regimen of cabotegravir/rilpivirine.

The impact of a 2DR on a lifetime of HIV treatment

So, why would we be interested in two-drug regimens? People living with HIV are living a lifespan that is similar to individuals who don't have HIV, because of treatment. Given that individuals are diagnosed in their twenties and thirties, they are on medications for decades and so here, you can see the accumulation of treatment over time. If you start here, with a boosted triple-drug regimen that includes actually four drugs in it, every year, a person takes roughly 1,460 doses and, over 39 years, that is over 57,000 doses. If you look at an unboosted triple therapy, individuals take about 1,100 doses a year, leading to over 42,000 doses over a 39-year period. On our two-drug regimen they take 730 doses a year and 28,000 doses over a 39-year period and so, as you can see, our two-drug regimen reduces the exposure – in comparison to a boosted regimen – by roughly half and, to a typical three-drug regimen, by roughly one-third. Over a lifetime, that is a significant impact, potentially, to the patient.

Complexity of HIV treatment in an ageing HIV population

As I have mentioned, individuals with HIV are living for a long period of time and this means that they are ageing, like the rest of us. That is good news, but the challenge, as with the rest of us, is that as individuals grow older, they have more co-morbid conditions. They start to take medications to treat those co-morbid conditions and that can lead to more drug interactions and, potentially, more complications associated with HIV. By reducing drug exposures, hopefully we could limit that.

In some clinics, even now, the average age of individuals is more than 50 years old and it is predicted – models show – that by 2030, more than 70% of people living with HIV will be over the age of 50.

PLHIV have concerns about long-term effects of medicines

What do patients think about treatment and about the long-term impact of treatment? When you ask them, the things that they describe as being most important are reducing the long-term effects of HIV medicines on their body. There is also a great deal of interest in the possibility of less frequent dosing and so the offer that we have for long-acting falls right in line with the most important interest for individuals.

You can also see that they are interested in having fewer side effects. They love the idea that you can take less medicine and get the same benefit: of course, who wouldn't want that?

Some of the things they see as being less important are pill size, and whether or not you need to have food restrictions. It is important here, however, to emphasise the fact that this is the interests of patients and this is not something that we are driving to patients: this is something that patients are clamouring for.

Why are we confident in 2DR? DTG most potent ARV to date

Why are we confident in 2DR? This graphic shows you drugs in all of the classes – you can see lots of different drugs – but it shows you the 10-day monotherapy data from these particular drugs. This indicates to you the potency of the medication so that when you give it as one drug, you can see how much the virus is driven down in that short period of time. You can see very clearly here that dolutegravir is the most potent medicine on this list but, importantly, dolutegravir is the most potent HIV medicine that has ever been approved. That potency allows us to do things that are different. We don't necessarily need to combine dolutegravir with two other drugs, which is the standard, but maybe we could combine it with one other drug and be able to achieve the same type of efficacy.

DTG-based 2DR inhibit viral life cycle at 2 separate sites as 3DR does

The other thing that makes us confident is that, when you think about the HIV life cycle – so that, in order for HIV to replicate itself, there are multiple steps – three-drug regimens attack HIV typically at two of those steps. Our two-drug regimens also block HIV at two of those steps and so you can see the reverse transcriptase, which is where lamivudine acts: then when you combine dolutegravir with lamivudine, you are attacking the reverse transcriptase and the viral integrase. With rilpivirine, it also attacks the reverse transcriptase and so either the dolutegravir/rilpivirine regimen, or the dolutegravir/lamivudine regimen – both, again, are impacting at two targets. When you are using a three-drug regimen, you typically are using two drugs to attack the reverse transcriptase and so, whether or not that additional drug is of value is the question that comes to mind.

DTG-based 2DR demonstrates potency equal to 3DR in patients with high and low viral loads

We have confidence not just because of the theoretical benefit of two drugs but we now have confidence because of real data that has shown us that two drugs can be just as good as three drugs.

What you see here is data from our GEMINI study. On this, you can see the reduction in viral load over the first 48 weeks of treatment. The red graphic shows dolutegravir+3TC, the two-drug regimen, and the blue line is dolutegravir+tenofovir FTC. What you can see, looking at the left-hand side of this slide, is that the reduction is completely overlapping – the

blue and red lines are completely overlapping, so there is no difference when you look at the population as a whole. Then, on the right-hand side of the slide, you see individuals who had high viral loads from the beginning and you can see, again, there are overlapping graphics. So even in individuals who were the toughest to treat, with high viral loads, there was no difference between the two-drug regimen and the three-drug regimen in their potency in this population.

ViiV Healthcare's 2DR portfolio

To walk you stepwise through our two-drug portfolio, again we started out with *Juluca*. We had the SWORD study which showed that you could take a two-drug regimen and use it to continue to maintain viral suppression in individuals who were on a variety of different regimens. That was the first step – but maybe that is the easy step, right, because individuals are already suppressed and so two drugs can maintain suppression. As Deborah has already mentioned, this was approved in the US at the end of last year and was approved in different parts of the world throughout the year last year. It was approved on the basis of the SWORD study, which showed 95% success in the dolutegravir/rilpivirine arm in comparison to 95% success in continuing other regimens at week 48. We have also shown data out to week 100 now, which has shown that roughly 90% of the population is maintaining that suppression out to two years. We have therefore demonstrated that a two-drug regimen can effectively maintain suppression.

The next step is dolutegravir plus 3TC. Here, we are asking whether we can use a two-drug regimen in individuals who are viraemic, who have virus running around in their system, to get their virus load all the way down to undetectable. What our GEMINI study has actually shown quite effectively is that we absolutely could, as I showed you in the previous slide, and so what dolutegravir 3TC offers is the next step – not just maintenance of suppression, but actually getting individuals who are treatment-naive down to suppressed. This will offer the option for naive or switch patients.

The next step in that journey is not only to reduce the number of exposures to medications that individuals have, but to reduce the number of times they need to dose. Our long-acting regimen, which we refer to as 'CARLA', which is a nice name combining 'CA' from cabotegravir, plus 'Rilpivirine Long Acting'. This is dosing cabotegravir with rilpivirine as an injectable, once a month and, potentially, once every two months: instead of individuals taking a medication every day, and dosing every day, they are actually not dosing 365 days a year, but they are dosing 12 times a year – a significant reduction. I will talk to you a little more about the FLAIR, ATLAS and ATLAS2M studies in just a moment.

DTG and 3TC milestones

I will talk to you a little more about some of the milestones for dolutegravir plus 3TC. In July of this year we presented the GEMINI 1 and 2 studies, which are two identical studies again comparing dolutegravir plus 3TC, to dolutegravir plus Truvada. The week 48 data was presented at the International AIDS Conference, to a lot of excitement. As Deborah mentioned, we have subsequently filed in the EU and the US – in the EU in September and in the US in October, using a priority review voucher.

Also of note, just last month we received the EU type-2 variation, meaning that we added the GEMINI data to the dolutegravir or the *Tivicay* label. Why is that important? It is important because it actually supports the promotion of the two drug separates in the combination for treatment, well ahead of when the fixed-dose tablet for dolutegravir/rilpivirine would be approved, later next year.

Moving along this line, we expect the fixed dosed tablet, dolutegravir/3TC, to be approved in the US in Q2 of 2019. We will present GEMINI 1 and 2 data, hopefully, at the International Aids Conference next year in Q3, July of 2019. We then anticipate that the approval of the fixed-dose tablet, dolutegravir/3TC, in Europe will occur also in the third quarter of next year. So, as you can see, next year will be a very busy year for dolutegravir 3TC.

What to HIV clinicians say about 2DR?

What do clinicians say? You have heard what we think about it, but what do clinicians think? We are giving you here [*on slide*] a few quotes. The first one is from Dr Paul Sax, who is the head of the HIV programme at the Brigham and Women's Hospital at Harvard University. What Dr Sax says, regarding the GEMINI data, is that

“These results are very encouraging, showing that a two-drug initial regimen of dolutegravir and lamivudine is plausible and very effective. It also has major advantages in terms of drug exposure.”

Dr Babafemi Taiwo, who is the head of Infectious Disease at Northwestern in Chicago says here,

“It seems likely that in the near future, almost every patient may be eligible for dual-therapy ART at some point in their long-term continuum of HIV care and that the current paradigm of 3 ARV agents for every patient may soon shift.”

Finally, Dr Pedro Cahn MD from Argentina makes the point that

“This is a new option for treatment. The main reason for doing this is to reduce the amount of drug burden when patients are on lifelong treatment.”

So, providers are excited about the possibility of two-drug regimens.

DTG based 2DR data has accelerated use of 2DR regimens

That is reflected here on this graphic, too, where you can see a significant uptick in the volume of patients in the US who are on two-drug regimens. That uptick has occurred as we have shown more and more data on two-drug regimens. Now, people are seeing four fully-powered study that have shown the efficacy of two-drug regimens that are led by dolutegravir.

CARLA milestones

Let me now talk a little about CARLA. I mentioned CARLA to you, our cabotegravir/rilpivirine long-acting regimen. In August of this year, we had a press release saying that the ATLAS study, which was the first study comparing cabotegravir/rilpivirine long-acting versus continuing on a typical oral regimen had met its primary endpoint. In October, we released also that the FLAIR study – a similar study, but which starts with treatment-naïve patient and then switches them after they are suppressed – had met its primary endpoint. We expect to be able to share this data in detail in Q1 of 2019 at the CROI conference, and we will plan to submit in the EU and in the US in Q2 and Q3 of 2019.

I haven't talked much yet about ATLAS2M, but it is also very exciting, so ATLAS2M is ATLAS two-monthly. This is the opportunity to dose individuals not every month but every two months. Here you go from 365 doses a year to now six doses a year, which is a significant improvement for patients. We expect to see the read-out for that data in Q2 2019 and the US approval of the monthly dosing of the CARLA regimen we expect in Q1 2020.

What do PLHIV say about long-acting injectables? (CARLA)

What do patients say about CARLA? These are some quotes from individuals who have been a part of our Phase III studies for CARLA. You can see one patient here at the top who says:

"It's less and less stigmatised with the injection because I don't feel like I'm reminding myself of HIV ... with the injection you go through days and weeks ... two months not having to worry about that".

You can see here on the right that this individual says:

"In reality, taking the pill every day keeps HIV present ... and the shot is just once a month ... you remember it when you come in and the rest of the time you can basically forget it".

Then you can see what stands out to me really is that this person says:

"If you go on a trip, you don't have to bring your pills or take anything at all along. You follow your normal life."

Normal life really stands out when you think about individuals living with HIV: a normal life is something that is very, very valuable.

Lastly, you see this person saying:

"I love it because I don't have to take a daily medication, so that's just one less thing on my plate that I have to worry about ...".

It is the idea that you can reduce the worry of people living with HIV.

Continuing to disrupt and innovate

My last slide puts all of those deliveries on one slide starting with July of this past year, all the way up to the beginning of 2020. It says that we continue to disrupt the field. It is disruptive to go from a three-drug regimen, changing the paradigm from three to two drugs and to offer the long-acting possibility. That is our plan and that is where we continue to innovate and to disrupt. With that, I'll pass it on to my partner here, Eric Dube.

Eric Dube (Head of North America): Thank you, Kim, and good afternoon and good morning everyone. As Kim mentioned, I lead our North America Commercial region and I joined ViiV Healthcare about a year ago and was really eager to work on the game-changing innovation in our pipeline some of which Dr Smith just shared. Before that, I was with GSK for about 18 years and, most recently, I was based here in London leading our Global Respiratory business. Before that, I was in Japan leading our Respiratory business there. Most of my career has been in the US where I have had the opportunity to lead our Oncology business, as well as a number of other functions including our contracting with national payers. I am very excited to share with you our overview of the US business.

Significant opportunity for improved treatment and growth in US HIV market

I would like to start with a snapshot of the US business, because there are differences in the prevalence rates and the suppression rates across different regions. Here you can see the treatment cascade and, over the last few years, as Deborah mentioned, we saw about a 3% annual growth rate. Much of that is based on the 38,000 new transmissions that have occurred in the US. Importantly, there are 1.3 million people living with HIV in the US and over one third of them are not on treatment. Overall, 50% are virally suppressed, meaning one in two patients living with HIV in the US do not have their HIV virus

suppressed. That is in contrast to here in the UK where over 85% of patients are virally suppressed due to high treatment rates and very effective engagement in therapy.

Unfortunately, in the US last year 7,000 people lost their lives due to AIDS and there are significant unmet needs, as Kim mentioned. What we hear from physicians and patients is that the treatment needs to be taken for decades, so for many patients taking even one pill once a day can often be a burden. We see that the innovation that our colleagues in R&D are working on to help address these gaps can contribute not just to continued growth in the US marketplace but to changing the lives of those who have not been able to achieve viral suppression.

US payer channel distribution for HIV market

Recently, there has been a lot of focus in the US on the payer model. Shown here is the distribution of lives in HIV based on their primary payer type. For example, about 40% of people living with HIV have their health coverage through a commercial or private payer, and 40% are on government-funded programmes with a mandated rebate, and 20% of people living with HIV get their care through Medicare Part D.

It has been well recognised that access and adherence to HIV treatment is essential to controlling the virus and, as a result, most patients pay a low out-of-pocket cost and thus affordability has not been, and should not be, a key barrier to future growth.

Many payers are looking to manage better their HIV budget given the recent launches and market growth. One example is the United Healthcare programme to offer some patients an incentive to switch to preferred medicines. United Healthcare made this decision on their own in a way to more actively to manage their HIV formulary in their commercial space and, importantly, the clinical data are quite robust for our dolutegravir portfolio, and we see continued broad access for our brand at United. More broadly, we expect to have the same very high coverage in 2019 across these three payer channels just as we have today.

Strong data and commercial execution results in maintained DTG market share

Over the last year, we have seen an unprecedented number of launches in the antiretroviral market with eight thus far. Despite the increased competition, we have been able to maintain our share this year. In fact, we have grown our overall market share by over 0.5% this year. While some of this is based on the uptake of *Juluca*, we have seen that physicians still see the difference in dolutegravir, but our share performance is also about competing well.

Customers continue strong support for DTG-based regimens

Throughout this year, ViiV maintained the top share of voice among HIV companies and we expect to do so moving forward. As Kim outlined, we have a series of important studies reporting out over the next couple of years. These data support the paradigm shift towards two-drug regimen. I believe that our recent policy change supporting the use of external speakers will be critical in this paradigm shift. Such important changes in clinical practice have often been seen supporting not just new launches but also, and importantly, a review of clinical evidence. Also, external experts want and need to share their clinical experience with the new treatment and that is even more important when we look at paradigm shifts.

As with any launch, the speed and broad reach of these peer to peer discussions is crucial to the uptake of the medicine, and we are pleased to see that across the globe hundreds of physicians have agreed to speak on our behalf, motivated by the innovation that we have in our pipeline.

The overall dolutegravir business performance remains robust and we continue to receive strong customer support for our brands. In the last year, we have been able to maintain around 800 naïve patient starts per week. The volume of switches is more variable with the new launches in this marketplace and this is a pattern that we have seen in prior HIV launches.

There has been some switching, some of which has gone to competitors and some to *Juluca* and, importantly, we have seen a stable volume of switch business to dolutegravir brands with over 600 per week over the last two quarters. *Juluca* has had a positive impact and we see 1,600 total prescriptions per week with now over 1,700 physicians having prescribed this medicine. We see that our future growth will continue to be the momentum that builds behind two-drug regimen.

As Kim mentioned, the approved treatment options may not be enough given the need for decades-long treatment. Our focus during the two-drug regimens must be on achieving the rate of viral suppression and the high barrier to resistance with dolutegravir-based regimens. The SWORD and GEMINI studies have demonstrated a high efficacy comparable to established three-drug regimen standards of care. HIV remains a therapy area that is driven by clinical practice, clinical data and the DHHS treatment guidelines in the US. In the most recent DHHS guideline updates, we are pleased to see that *Juluca* is well-positioned and, in fact, before approval dolutegravir +3TC is already mentioned in the treatment guidelines. This mention should help once we have FDA approval and the ability to promote.

On track with 3 pillars for driving oral 2DR paradigm shift

Our goal is to ensure that HCPs see strong clinical results in their own practice and we believe that experience and an understanding of the clinical data is critical to building their confidence in two-drug regimens. Feedback over the last year has been very positive and consistently so when physicians have used *Juluca*. We also know that many people living with HIV are becoming even more engaged in their healthcare and wanting to understand their treatment. We see that they also want to understand the long-term consequences of their treatment, as Kim has mentioned.

We believe that raising the awareness of different treatment options, including two-drug regimen, will be critical for this ongoing paradigm shift and execution is essential across this entire set of promotion. In fact, our field-based teams had the 100-week *Juluca* data from the SWORD study within four days of it being presented at a major congress. We were very excited to see that we were able to address the No.1 question that physicians have about two-drug regimen, which is the durability of response. We have been pleased thus far with the uptake of *Juluca*.

***Juluca* new patient volume & number of prescribers continues to grow nearly 1-year post launch**

Here you can see the NBRx data since launch and the NBRx uptake after the 100-week data presentation. One of the key questions again has been: how long is the durability and the efficacy for 2DR? Since then we have seen that growth is continuing after the launch and the announcement of the 100-week data and it is coming from more consistent prescribing from our physician base.

In the 11 weeks before the 100-week data was presented, we have seen that about 150 physicians prescribed the medicine per week. In the 11 weeks after we announced those data, that has grown to over 180 physicians per week, which is really important to see one year after the launch of a medicine where often you begin to see that plateau. All of this supports our plan for a strong ongoing launch of *Juluca* but also the foundation for ongoing launches of 2DR.

Actively addressing trends influencing US marketplace

My team and I are focused on how do we continue to address not just the paradigm shift of 2DR but the key marketplace challenges or trends that we see within the US. These are three to which we are paying particular attention. First, as previously mentioned, the US marketplace has seen new competitor launches and the potential for payer reform. When we launched *Triumeq*, there were only about two or three single tablet regimens on the

marketplace. Now there are about 10 and payers see the opportunity to be more active in identifying which ones should be preferred based on clinical data and the support of guidelines.

Payers have become more focused on utilisation management and our strategy remains the same: we shall continue to differentiate our dolutegravir-based regimens based on the strength of the clinical data and our responsible pricing. We believe that we shall continue to stay agile as the policy and the payer landscape continues to evolve and, importantly, for 2019 we do not expect any significant changes in our payer coverage for our dolutegravir brands.

Secondly, the HIV demographics are evolving. As Kim mentioned, we continue to see that, based on the effectiveness of treatment, patients are getting older and, as a result, their needs continue to evolve, and we need to stay on top of the evolving needs of the ageing HIV patient.

We also see that where the new transmissions occur is very different than where the epidemic has been in the past. Most of this is within the US southeast and in communities of colour where we often see challenges in healthcare disparities, and we have to continue to evolve our offerings and our engagement as a result.

However, it is not just our patients who are changing. We know that the healthcare providers are continuing to change and those who were attracted to the space of infectious disease and HIV in the 1980s and 1990s are getting older and are retiring. We are also seeing that not as many young physicians are attracted to infectious disease, so now and in the future, we are seeing many more nurse practitioners and physicians' assistants helping to care for people living with HIV. We continue to evolve our promotion and our education to ensure that we can address their needs and those of the patients whom they serve.

Finally, patient engagement continues to grow. As treatment options have increased and improved, patients are now even more invested in their lifelong choice of treatment medication, more so than a few years ago, and, in fact, they are seeking information not just from their healthcare providers, but also from us, and we are very proud to say that we have a number of offerings to help engage physicians and patients through social media and various patient programmes.

This last year ViiV Healthcare innovated as well in launching the first direct-to-consumer TV campaign in HIV with *Triumeq*, and as a reminder, in the US it is a bit of a unique marketplace, where we are able to promote directly to consumers.

That campaign was successful. We saw great results, and it further supports that the voice of the patient is only going to become even more important in the treatment choice that physicians make.

Going forward, our portfolio, our pipeline, our online presence and our offerings that are affordable and have access, we believe, will strongly position us to continue to compete and grow within the US marketplace.

Now, I would like to hand it over to Dr John Pottage.

Dr John Pottage (Chief Scientific and Medical Officer): Thanks, Eric. I also want to extend my welcome to everyone here, so welcome!

Just a brief introduction of myself. I am a trained infectious disease physician, and as was mentioned, I spent 20 years in academic medicine, teaching, doing clinical research, taking care of patients. I was a director of our outpatient HIV clinic, and actually started doing this before we had any effective treatments for HIV.

I have also spent about 20 years in the industry, and most recently I have been with ViiV Healthcare, actually, from the very beginning, from the set-up of the company.

I think, when I am thinking about the talk I am about to give here, it really does always give me a little bit of pause of really thinking about those patients that I took care of early in my career, when we really had no medicines for them, and it is amazing the progress that we have made.

However, clearly, as we look to the future, there is really much more still to be done.

HIV patient pool continues to increase

Therefore, to really set the stage for discussion of that, I went to the numbers, and so every World AIDS Day, UNAIDS comes out with the latest figures for HIV, and so I picked out a few statistics here, and, again, these are global numbers. Eric gave to you numbers from the United States, but you can see that over 37 million people are estimated to be infected with HIV, yet 9.4 million don't know their status.

The second thing that is important is that 21.7 million people living with HIV are on therapy. That means a significant proportion of patients are not, and what these two statistics really tell you is that there are many millions of people who are transmitting the disease, and so, obviously, much more needs to be done, and you see that we have 1.8 million new infections in 2017.

Therefore, again, it really lays out the need, the medical need for really moving forward with better therapies, more effective therapies, and really keeping in mind that patients will need treatments throughout their lifespan going forward.

Our innovative approach to discovery and development

This is actually, I promise, the last time you get to see our swoosh. I am concentrating on the far-right side of it, looking at the pipeline strategy, and so when we think about a number of initiatives starting with prevention, development and discovery of some new anti-virals, so really moving into more of the search for remission and cure I am really talking about the next five to ten years as we go forward.

ViiV pipeline strategy

If you think about the pipeline strategy, I think one thing is to keep these three threads in mind as you go forward, because they all intersect, overlap each other, but as we think about it, you can really categorise all our therapies amongst these overriding principles.

Starting on the left is the treatment cascade, moving from prevention, treatment, and ultimately getting to remission and cure.

What are the types of medicines? We are obviously developing medicines with new mechanisms of action, attacking different parts of the viral replication cycle, but, really, we are moving into the field of more immunologic types of therapy as we try to kick the virus out of its latent stage in infected CD4 cells, and so immunologics is the future of much of the work we will be doing in the pipeline for treatment of HIV.

Then, how are they given? Clearly, we are expert of fixed-dose combinations. Everything now is done as a fixed-dose combination, so it is essentially one pill, once a day, but the movement into injectables Kim reviewed with you, a lot of information on the first real acceptable injectable, but also the fact that it is long acting. We have had injectables in the past, but they are very short acting, and they have to be given quite frequently. Therefore, really combining it along that line.

As we think about the different approaches to care, the different medicines that we are developing, it is really these threads that will all link together.

However, if you think about what will be happening five, ten years plus, it is really the bottom line. Most of what we will be doing is work on remission or cure, with immunologics or immuno-inflammation types of therapies, and all being semi-long acting, whether they are pills or through injectables, but that is the direction of travel as we see it over the next five to ten years.

Cabotegravir long acting for prevention (PrEP)

Just giving a quick survey of some of the more near-term deliverables that we are bringing forward, and we have talked about cabotegravir, but we are also advancing it for PrEP, or prevention of disease, and we look at it as another important option for patients. Therefore, we think about right now we have *Truvada* for PrEP. It is a pill you have to take once a day. Here is an approach where one would receive an injection once every two months, and not need to take pills on a regular basis, and we have two very large studies up and running at this time, being done in conjunction with the NIH HPTN network.

We have the 083 study, which is a prevention trial in men. Presently it is about 66% enrolled. 4,500 patients are being studied here, and it is a comparison of cabotegravir with oral therapy of *Truvada*, and so here we look to finish enrolment in 2019, and it is an event-driven type of study. Therefore, all the prevention studies generally are there. You wait until you get a certain number of the events. If you have a lot of them in the study, it will be done earlier. If you don't get very many it will take a longer period of time, but we look to have data in the 2020/2021 timeframe for that.

We also have a similar study being done in women. It is a little bit further out. It is a study that, again, we hope to get full enrolment by the end of 2019 going forward, and, again, expect to see the data going forward.

With both these studies these will really provide the data we need to go to regulatory agencies to get licensure for cabotegravir for prevention, and we really believe it is an important option for patients for preventing disease.

Exploring novel delivery technologies for cabotegravir

The next wave going forward, if we talk about the way we give cabotegravir, it is through an injection, and it's an intramuscular injection, but, really, we have a lot of work going on going forward, and we look at newer delivery technologies for cabotegravir, but, actually, for all the drugs that we are developing, so we are looking to develop under what we call ultra long acting, and the definition there is greater than three months, so we would like to actually get it to even longer, but ultimately get into long-acting self-administered therapies. Whether it is through a subcutaneous injection, or a device, or some kind of an approach such as that, so we actually have a very strong effort going forward to really improve the patient experience receiving this, and the area we look to is the field of contraceptives.

If you look at all the different approaches in contraceptives, different types of injectables, we can adapt somewhat our model as we go forward, and when you think about

an injection, particularly in women you look at this type of an approach with cabotegravir being given with a contraceptive.

Fostemsavir: a life-saving investigational medicine for patients with few or no treatment options left

Then we have several new drugs that are a little more advanced, and the most advanced is fostemsavir. This is a drug that came over when the BMS purchase occurred three years ago. We are in the finishing touches of the phase three programme. This is a first-in-class attachment inhibitor, so it blocks early stages of virus replication.

It does have a good resistance profile and provides a very good treatment for patients with limited options, and so this is really being brought forward for patients who are highly treatment experienced, or HTEs, as we sometimes call them.

It does have FDA breakthrough status, so they have been working very much closely with us as we bring it forward to a filing planned in the second half of 2019.

We did just present some 48-week data recently in Glasgow in October, which did show excellent data for these types of patients. 54% of the patients had virologic suppression at 48 weeks.

We are also about to be looking at 96-week data, and we will be filing with the 96-week data, going forward with that.

Therefore, a lot of work going on with it to go on top of the activities that you heard from Kim with the filings coming forward with CARLA.

Maturation inhibitors

Maturation inhibitors – there have been a number of these through the years. I think we are at the point now where we have a drug where we think it has a much better toxicity profile, but also a very strong, good virologic profile, where we don't run into issues of some of the isolates not being covered with it, and so the drug we have going forward is a drug - 254 is the number. It is about to begin proof-of-concept testing in the first part of 2019.

This has been developed as an oral agent, and it is also being developed as a possible combination, fixed-dose combination product with dolutegravir, but also, as we go forward we are also looking at long-acting versions of it with a different molecule than this, but we look forward to seeing how this drug works in the proof-of-concept study, and, again, taking it forward following that data, which we will have at the end of 2019.

Vision for Biologics

Moving a little further out, we have some of the biologic approaches, and a lot of these generally indicate that these are injectable types of approaches.

One is *Combinectin*. This is a long polypeptide strand, which actually has three different mechanisms built into it, so it affects early stages of the viral replication steps, but the important thing here is that it is a once-monthly complete regimen, and it is also subcutaneous, so someone could give the shot themselves. It doesn't require an IM shot, so, again, the ability to treat with an entire regimen with a single shot, once monthly going forward is the desired characteristic for this product.

We are going in first into man in 2019 with this going forward.

The second is in the area of broadly neutralising antibodies. We have a collaboration going on with the NIH in the United States, and so we have one bNAb going forward right now, which is in first in man testing being done by the NIH, but, again, these are products that are both anti-virals, so it neutralises circulating virus, but it also has activities that one could say are more immunologically-related, and perhaps could be helpful in the area of remission and cure.

Again, these are injectables. These are longer acting, and so these are products that could be combined with cabotegravir or long-acting maturation inhibitors, so it gives us, again, a whole panoply of approaches going forward as we get down to...

UNC-CH HIV Cure Centre and QURA:

A unique model for high-risk research

The final slide I just want to mention is really getting into the area of remission and cure.

This is obviously more on the far end of the scale that I talked about, the five to ten, maybe more than that, but I think what we have set up here really is reflective of the approach as we go forward: the culture of the company, really thinking about best ways to work in collaborative ways, and so here we have set up a joint venture with a group at the University of North Carolina in the United States, centred on finding a cure or a long-term remission for HIV.

Clearly, the most important, or the most difficult aspects of cure is what do you do with the latent virus? How can you kick it out and kill it? That is the kick-and-kill approach, or you could lock and block it - that's another way. Put it in there where it never comes out, but the approaches being looked at here are really focused on that aspect of trying to inhibit

or bring out the virus so that we can treat it going forward, and so this is a good collaborative effort going forward, and it is really, again, exemplary of the way we are going forward.

We don't look at this as the only way going forward, so we do look at other approaches going forward.

However, I think what you can see from my very quick discussion here about the future, I think that we have a lot of things on the table. I think that we do have a very challenging attitude, and we really always, though, come back to this statement.

To leave no person living with HIV behind

All the work we do here is really reflecting on the patients, and really leaving no one with HIV behind.

With that, I will thank you and turn it back to David.

Questions and Answers

David Redfern: Okay, thanks, John. Thanks to all the presenters. We are now going to turn it over to Q&A, so I would like the four presenters: Deborah, Kim, Eric and John to come up and take a seat, and also to be joined by Tim Tordoff, who is Head of ViiV in Europe, Craig Williams, who is Head of ViiV in the International Business, Dr Harmony Garges, who is our Global Head of Medical Affairs, and Jill Anderson, who is the Chief Financial Officer of ViiV.

We have a little bit of time, so we will take some questions in the room, and we also have, I think, the opportunity to take some questions from people online, but we will probably start with the room.

I should say just while you are thinking, of course, as always, we will put all the slides and the presentation from today on the GSK Investor Relations website, so, obviously, that will be available to you.

Jo Walton (Credit Suisse): A couple of questions, please. Firstly, from the US side, and I am sure you are expecting more pricing questions – you pointed to United's new method of trying to get people to adopt formularies by giving them rebates back for their medical expenses. I wonder if you could tell us a little bit about how you think the uptake of that programme has gone, and whether you think other payers will start to use the same sort of thing next year?

I wonder if we could go back to slide 29, which you had, which was the channel mix for payers, and I wondered if you could tell us a little bit about how your market share was in each of those so that we could get a sense – I don't know if you could help us with in a few years' time how you think that mix might be, and whether you are particularly strong in the Medicare Part D, or particularly strong in the Commercial? If you could talk to your positioning by that type of payer, please?

David Redfern: Okay, thanks, Jo. Before we go to Eric, who can certainly get into the detail on the channels and the market shares, and, obviously, comment, I might just ask Deborah to give you an overview of how we see US pricing generally, maybe by channel, because obviously there is quite a lot of noise around this, and I think it is quite important to distil out some of the trends in the private insurance market versus the more government mandated.

Deborah is one of probably the few people that has actually read the most recent CMS stuff that has come out, so why don't you comment first of all?

Deborah Waterhouse: Sure, I will certainly start, and then I am going to hand over to Eric.

This graph is a really important one, because it helps you all understand the different channels in the US market, and what we have found in a number of the investor sessions recently was that people were talking about the protected classes change, and then the United Healthcare change, and, actually, it became rather blurred as to which of those initiatives applied to which channel.

Therefore, Jo, the comment that you have just referred to in terms of the United Healthcare payer activity is very much in that private payer, the employer/private section, which is 38% of the market, and, basically, what United have done, as you say, is offered a \$500 incentive in the form of a card that can be used against medical incentives if patients are willing to change from the therapy that they are on to Cimduo, which is a generic of *Truvada* plus *Tivicay*.

That is a carrot approach to getting patients to change their behaviour, and then in April next year they are going to block Atripla, and, then those Atripla patients have to make another choice, and obviously the \$500 incentive applies to them as well so that will people choose to go to the generic plus *Tivicay*, or will they decide to actually upgrade from Atripla to a newer therapy? That remains to be seen, and Eric can talk a bit about that in a moment.

Therefore, there are some things that are happening in the employer/private part of the market, and the United Healthcare approach is what's happening there.

In the Part D part of the market, so Medicare Part D, that is where you saw about ten days ago CMS come out with a proposal, and this proposal does not take away protected class status, and let me just tell you, if you are in a therapy area with protected class status, which is where HIV sits, it means that the people who have those plans, so the payers that put those plans forward, have to list all medications that the FDA approves. Therefore, automatically, new medicines go onto that Part D formulary. They are not allowed to exclude anybody.

That protected class status has not gone away. Therefore, that is very much still in place in that CMS proposal, but what CMS are trying to do is to give the plan's sponsors, so the Aetna's and the United's of this world the opportunity to control cost a bit in the Medicare space, and the two things that they gave the opportunity for those payers to do is if there are above CPI price increases over a set period, then the products that have gone up by more than that acceptable amount can be excluded from the formulary.

The second thing that they also said was that within those plans, the plan for the first time could add in prior authorisations or step edits, which basically means that if you want to prescribe something, and a payer wants to make it more difficult, they can basically make you get a prior authorisation before the script is fulfilled, or they can make you go through a step of one product before you get to the one that you ultimately may want to prescribe.

Now, we are very much in favour of supporting and protecting access all over the world, including the US, so we are not obviously encouraging that approach. We are going to be writing our responses over the next few weeks, but basically, if you think about the population in the Medicare Part D space for us, they are 65 plus, you are not talking about newly-infected people, you are talking about people who will be living with HIV for many years, they will be resistant to certain medications. HIV is a very individualised therapy area, and so the sort of step edits in HIV probably isn't going to work anyway, because if somebody is resistant to a medicine you can't make them take that before they can get to the medicine that they may want to get to. So, I think that piece in HIV isn't going to be quite as applicable, but certainly the CMS proposal around price capping, if you like, may have an impact.

That's at a macro level, the two newest pieces of information we have. One is in that Medicare Part D and the other is in the employee and private, and I just encourage you when you are thinking about the HIV market to very much separate those two out.

The third class, which is the government-mandated, is a set algorithm that the government applies to ADAP to Medicaid, so that's kind of a given and there's no proposed change at the moment in that space. So, the two places for you to focus would be employer and private, and Medicare Part D, but separate them out because they are very different. Eric?

Eric Dube: Thank you for the question. I think first with regard to United, the simple answer is, it's too early to tell. What I can share with you is the range of anecdotal feedback that we hear from physicians and from community advocates and I think the number one concern is that we're limiting access to medications. However, this is a bit of a different approach to utilisation management, where they're incentivising the patient, and for some physicians they are happy to help their patients, because oftentimes patients have very limited money for other healthcare services. So, I think there may be some uptake, but we have to keep in context that of all of the commercial business, United Healthcare in commercial represents about 4% of the market, so we think that it's going to be relatively small.

With regard to the potential spill-over to other payers or PBMs, again, it's a bit too early. I think if there is very broad uptake then it may be that other PBMs will become increasingly emboldened. However, I would not underestimate the importance of the voice of the patient community, and physician community, because as Deborah mentioned, limiting access to treatments where there may not be other options based on resistance profiles is going to be an ongoing and incredibly important way that HIV is treated.

Now, to your second question around the shares across these different segments: we don't see a significant difference in the shares, we've got over 90% access to our dolutegravir brands across these three segments. We expect that that will continue, and we've been competitive in each of those three, and we don't believe that the mix, as Deborah mentioned, will change in terms of these segments over time.

Richard Parkes (Deutsche Bank): I just have a couple of questions as well. There was a comment made that being able to engage with KOLs would help a lot with the messaging around the dual - could you talk about what it is around the dual messaging that needs help with communicating? It seems like quite a simple message: 2 drugs instead of 3, fewer side effects, same efficacy, so if you could help us understand that a little bit. Then, when we survey physicians around their thoughts about the dual strategy, one of the pushbacks is, well, it's okay in a clinical study to have great efficacy and low resistance, but when you go into the real world, when patients are maybe missing doses, etc., and not being

as compliant, that's when you might start to see differences between the treatments. How can you address that upfront, does that just take time to generate real world data and longer-term follow-up from the clinical studies? Thanks.

David Redfern: That seems like both questions are probably for the physicians, so Kim, why don't you start and maybe Harmony, you might want to comment as well.

Kim Smith: I could start with the second one, and Harmony can address the first question. So, with regard to the comparison of what you see in the clinical trials versus the real world, our trials are pretty close to real world, these are global trials where we enrol treatment-naïve patients, so we don't cherry-pick for patients who are going to be adherent to their medications. It's a good cross-section of naïve patients that are coming into clinics and obviously we won't see very much real-world data for a couple of years, but clearly the graphic that I showed you shows that providers are using a lot more 2-drug regimens. If they weren't having success with those regimens, you certainly wouldn't see that uptake continue. I think the fact that we have now 100-week data from SWORD that has shown really durable success and we will soon have 96-week data from the GEMINI studies, and again, individuals that failed in that GEMINI study, there were no individuals on the 2-drug regimen or the 3-drug regimen that developed resistance, so it really demonstrated itself to have potency even in the high viral load population. So, we have a tremendous amount of confidence, and that's backed up by the data.

Harmony Garges: If I can just build on that, back to the real-world evidence piece, we are doing additional studies once medicines are in the real world, trying to gather that data we know clinicians want, so we have very robust plans in place to get that information.

Then related to HCP speakers, and how we can now compensate them, we're quite excited about this opportunity, given that we are a specialty area. What we're hearing from the external healthcare providers is, they do want to hear from their external peers what this data means to them, so taking the clinical trial data and putting some clinical context around it, and part of why we evolved our policy was based on the feedback we had from external healthcare providers around that, but again, they really do want to hear from external peers about what this means for them.

Kerry Holford (Exane BNP Paribas): Thank you, a couple of questions. Firstly, on the outlook, you mentioned earlier about sales and profit growth over the next five years, being confident in that, I wonder if you can talk about the phasing of that – is that

something that you foresee every year here on for the next five years, or something that's perhaps weighed to future years? And in conjunction with that, how confident are you, or comfortable are you, with the consensus view that sales will grow around 7% next year for ViiV?

Secondly, on cabo/rilpivirine, I wonder if you can talk about who the target patient population would be for that product. Is that something that you would envisage compliant patients using, or non-compliant patients? Some of the physicians we have spoken to have suggested actually it would be less useful for the non-compliant patients, because they may feel more confident and less likely to go back?

Then lastly, previously you've talked about the expansion within integrase inhibitors more broadly, could you just update us on what proportion of HIV patients are now taking an integrase inhibitor, and whether you see further growth there.

David Redfern: Okay, let me have a go on the outlook, and then I'll pass it over to Kim. As Deborah said, we expect ViiV to be a growing business going forward, including in 2019. That growth will come from the international business and the European businesses continuing to grow and continuing to gain market share, and in the US, where clearly our TRx, as Eric showed, is relatively stable right now, we expect the growth next year really to come pretty much entirely from 2-drug regimes, so the ongoing second year, or first full year, of *Juluca*, and then importantly, dolutegravir / lamivudine, when we are able to launch that, hopefully in Q2.

We do expect the growth to continue, I'm not going to go into more detail than that. We don't, obviously it's a bigger business now, so we don't expect growth rates to be quite what they have been in the past, but we do expect this to be sustainably growing business and how much over the next few years will depend in part on how much the two-drug regimens penetrate the market, but we feel we are in a good place.

Kim, do you want to discuss cabo?

Kim Smith: I think the question of who is cabotegravir/rilpivirine long-acting for, when we've surveyed patients, more than 50% of patients have said that they would like to switch to a long-acting regimen. There is a lot of demand, a lot of interest in a long-acting regimen, for all the reasons that I mentioned, that patients don't like to be reminded of living with HIV and don't like taking a pill every day.

Will it be for compliant patients or non-compliant patients? Our studies and our indication will be in individuals who have a suppressed virus, so they need to be able to be compliant enough to get their virus suppressed, and then be able to switch over to the long-

acting regimen. I think that definitely physicians are interested in the possibility that for patients that really have a tough time taking medicines every day, that this could be potentially an option, so in addition to the Phase 3 studies that we have described, we actually have a study that we are doing with the NIH that specifically is targeting individuals that have had trouble taking their medicines in the past.

So ultimately, we expect that CARLA will be an option for individuals who maybe have had problems with adhering in the past, but mostly who want to take the daily pill out of their lives.

Deborah Waterhouse: Just on the integrase question, Kerry, currently about 55-57% of patients in the developed world are currently taking an integrase. If you look at the US number, from an NBRx perspective that is currently sitting at about 70%, so you have two things going on. You have more patients moving onto integrase at a macro level, and then within the integrase class you actually have people switching from the first generation to the second generation integrases within that, either through moving from one fixed dose regimen to another, or people mix and matching regimens such as *Tivicay*, Descovy or whatever, so there is integrase within the class and then the class will ultimately, I think, end up at about 70% of the total core agent market.

Emmanuel Papadakis (Barclays): Maybe just a couple. David, you talked about prescriptions being broadly flattish for the DTG-based regimens in the US, and most of the growth coming from the two-drug regimens, should we assume that embeds a net flat pricing assumption for DTG regimens in the US next year? That was the first question. Then maybe if you talk about net pricing expectations more broadly, that would be very helpful.

Then just a couple for John. You didn't give any timelines on the broadly neutralising antibodies, I would be very interested to hear those, if you can talk about how quickly you might see something clinical. Then one notable omission from your admittedly brief presentation was vaccines, so do you think that's no longer relevant in this space, do you not have anything you're investing in right now and is also available? Thank you.

David Redfern: On pricing, I think you should expect some small, modest price rises on the innovative part of the portfolio, but obviously we will keep those at the reasonable end. I think we continue to innovate, we continue to generate more data, so that will probably be reflected in some modest price rises, but beyond that, I don't know. Deborah, do you want to comment any more?

Deborah Waterhouse: The only thing I think we need to think about as you look at the whole portfolio for ViiV, which probably puts us in a slightly different position to our competitors, is that we will have the broadest portfolio to offer the market, so I think we have *Tivicay* as a standalone, integrase inhibitor second generation, so the other second generation integrase, which is Bictegravir, isn't available as a standalone, it's only available as part of a triple, so if people want to have a backbone and mix and match it with a dolutegravir-based regimen they can do that. We have the duals – we will have three that we've talked about today: cabotegravir/rilpivirine, *Juluca* and dolutegravir 3TC, then you will have *Triumeq* as a triple, then we've got the highly treatment-experienced end of the market covered with fostemsavir.

If you think about the short term, we're going to have a broader portfolio, but actually that will be at a mix of price points, and I think David's absolutely right in terms of what he says about the overall opportunity to put in price increases in the US moving forward, but the other thing it would be worth considering would be the different elements of our portfolio, the different price points, and how that will play out in terms of the overall revenue and profitability of the company.

John Pottage: Just a couple of comments on antibodies. As I mentioned our collaboration with the NIH is the N6LS antibody, and at the moment is the first-in-man study, so we should have data from that, and then if all looks well, potentially we could get into a PoC type study next year, so that would be late 2019 or 2020 going forward.

With that whole field, every time you think you have one, new ones appear, and so we are always getting better and better, and with all the different players coming forward, including the NIH, that seems to be operative. In our collaboration we have the ability to look at others going forward, but if you think about a timeframe, it really is in the three-to-five-year period where you are going to be able to lock onto something as a true clinical candidate going forward.

We will also have a PoC study going forward with VRC01 with cabotegravir with the ACTG, so we are combining with cabotegravir. There are different approaches, whether it is an all antibody approach, a mix with long-acting antivirals with the antibodies, or can it be used in prevention, and so, again, it will be a very exciting time over the next two or three years, and then after that time period, you will see more discrete approaches as we head into getting approval from regulatory authorities.

In terms of vaccine use, perhaps I will flip it back to David here; originally the business model of ViiV is that vaccines were excluded from our scope. Going forward, I do

think there are a number of therapeutic vaccines being brought forward, which might be useful in the area of remission or cure, and so we are anxious to look at them. However, at the moment, our scope of business is somewhat limited in that approach, so I will throw it back to you, David.

David Redfern: If there was an opportunity for a vaccine, we would definitely be open to it. I have to say I don't think there is anything even on the near or medium, or even long-term horizon. Our own vaccine group in GSK has had, and continues to have some HIV programmes, but they are a very very long way back and, at this point, there are a many hurdles they would have to overcome, so certainly not ruling it out, but it is not something we are in a position to talk about today, although of course, with long acting prophylactics for use in a wide variety of potential patients, which John talked about in those big studies of 4,500 patients, whilst not technically a vaccine, it is obviously moving towards the vaccine space, and operates in a similar way.

Tim Anderson (Wolfe Research): A couple of questions; the storyline behind the two-drug regimen is that three or more drugs over the long-term is not great for the patient. Yet, you guys have a very large three-drug regimen in the form of *Triumeq*, which is about £2.5 billion so, commercially, how do you segment the market such that you don't cannibalise because your pricing on a two-drug, you have already shown with *Juluca*, is going to be less than pricing with a three-drug, and you have said that would be the same with dolutegravir plus 3TC, so how do you prevent that negative economic mixture from occurring? That is the first question.

The second question is on GEMINI and the GEMINI trial design; I imagine that Gilead would try to take the air out of those results by saying that, when you guys chose Truvada as the comparator, that is a TDF-based regimen and not a TAF-based regimen like Descovy, and we know that the efficacy is not different between Truvada and Descovy, but you do have better renal and bone health with Descovy, so how are you going to answer that question when physicians pose that, or if Gilead raises that as the counter message to GEMINI?

David Redfern: Why don't we do them the other way around? Kim, I know you have thought about that second question, and we get it quite a bit and, of course, that is probably one of the things that Gilead will say, but I think we have a very robust view on that. Why don't you comment on that?

Kim Smith: Your point about TDF and TAF not having difference in efficacy is a really important one. There is repeatedly data that shows there is no added benefit from

an efficacy standpoint of TAF. The question is, is there added benefit for renal and bone, and so in the short-term they have been able to demonstrate that, but there has actually been more recently some data, and in particular meta-analysis, done by Andrew Hill that looked at when you use TAF with integrase inhibitors versus TDF with integrase inhibitors, there is really no difference between them, and so there was no real added benefit to TAF. For us, we wanted to get the study done as soon as we possibly could, which is why we used TDF, and really the main point of this study was to demonstrate that a two-drug regimen could be as effective as a three-drug regimen, so there is not necessarily a need to use TAF.

We are actually quite confident in the data, and even though TAF in those Gilead studies showed a short-term benefit in bone and renal, really the question is whether or not there will be a long-term benefit, and it will take a while for us to understand that fully.

David Redfern: I will answer your first question. The short answer is we really expect two-drug regimes now given the comprehensive data we have, firstly, with the switch patients with *Juluca*, but now, importantly, with the naïve patients with the GEMINI studies. We have the opportunity to have two-drug regimes that could cover very large parts of the market, so we see, as I said, a major part of our future growth coming from two-drug regimes, and we hope that with dolutegravir/lamivudine we can penetrate into the naïve market share, and hopefully we will also pick up some switch patients as well.

One of the interesting things this year has been that *Juluca* has cannibalised existing dolutegravir regimes about 40%, so about 60% of prescriptions of *Juluca* are coming from regimes that don't contain dolutegravir, and that is quite a big contrast from Biktarvy where we think about 70% or so, and I think Gilead almost would say the same thing, is coming from existing Gilead combinations, and about 30% or so from other combinations, some of which is *Triumeq* but only round the edges.

There has been, and there probably will be, some cannibalisation as we go forward, but we do think the two-drug regimes have the opportunity to penetrate right across the market. It is always amazing in this marketplace, and these guys can comment more, just how many patients are still on the old regimes; how many are on Atripla, how many are still taking efavirenz in one shape or form, so there is obviously a real opportunity there, and if you pull all that together, we can grow quite strongly. Deborah, do you want to add anything to that?

Deborah Waterhouse: That is a great way to think about. As I said before, we have a portfolio of medicines that we are offering, and this is a very individualised therapeutic area where each patient has many years to live with the virus. The way I think

about it is along that journey there is an option for the patient, whether it is two-drug regimen to begin with, whether you then decide that the long-acting injectable is the right medicine for you, whether you end up highly treatment experienced, and on fostemsavir, along with dolutegravir, or whatever it is you end up taking alongside it, or whether you take, in Europe perhaps, *Tivicay*, plus a generic backbone of some description.

I guess what I would say is that portfolio, we believe, will lead us to have a higher market share than we have today, and the mix of those products will lead us to be able to grow our business, and that is the way we are looking at. You have many different options to have an individualised lifetime worth of treatment, of which our portfolio plays all the way through that journey.

David Redfern: Great. We have a question on the phone.

Steve Scala (Cowen): Thank you. I have a few questions. First, fostemsavir has been in development for a long time between GSK and Bristol, when does the patent expire in major markets? That is the first question.

Secondly, Merck is particularly excited about MK-8591 a NNRTI in Phase 2. What competitive intelligence do you have on this agent?

Lastly, the advantages of two-drug versus three-drug regimens makes sense, but is there any data showing that patients that have been on three-drug regimens for decades now have specific medical problems because of that? Thank you.

David Redfern: Thanks, Steve. Great to hear from you as always. Why don't we comment a little bit on what is going on with fostemsavir? We are excited about the data. We have some CMC work, which is really on the critical path. Why don't you comment on that first, John?

John Pottage: Some of the issues arose when fostemsavir moved from BMS to GSK in terms of manufacturing issues and sorting through them, and we have finally done that, and that has led to a little bit of a slowdown as we have gone forward. The upside of that is actually it has allowed us to advance the clinical programme out to 96 weeks, and so when we apply for approval we will be doing so with 96-week data. We are planning to do that, as we mentioned, in 2019 so, again, all the issues with CMC have been sorted out. Manufacturing is all set to proceed as we need to go forward with that.

David Redfern: Filing in the second half of next year, and it is just worth saying there is still about 5% of the population that progresses to virtually full-blown HIV

AIDS. We met a patient the other day with a CD4 count of 0, had completely run out of options, and was basically saying you need to get us fostemsavir –

John Pottage: And actually, the study has really shown good tolerability and good safety profile going forward, so we really look at that as the real advantage to patients.

Deborah Waterhouse: The patent goes out to 2030

David Redfern: John, do you want to talk about Merck?

John Pottage: It is interesting the approach there with looking at long-acting drugs so, again, the approach is similar to our thought going forward, and then the different combinations going forward including two-drug regimens. I cannot really comment too much specifically about their programmes, but the high-level approach, again, is similar as we look to bring forward more long-acting types of approaches, injectable approaches, and even two-drug regimens as they come forward.

David Redfern: I guess it is all in the pivotal data, and it is still early days on that and, Kim, three drugs, are they safe in the long-term?

Kim Smith: There are a couple of points. Probably the best example of a drug with long term toxicity issues is TDF or tenofovir disoproxil fumarate, and so that drug we know over the long-term has been shown clearly to be associated with renal problems as well as loss of bone mineral density. However, that was not seen in the first few years. It took a long time for that to be understood, and that is the case with many HIV medicines; in the first few years, after they launch, you may not see some of the long-term side effects, but actually they develop later.

Stavudine is another example of that. It was seen to be a wonderful drug when it first came out, and we saw the long-term effects of it after years, so clearly when individuals are going to need to be on these medicines for decades, any way that you can minimise the kind of exposures that they may have the better. When you talk about a combination like dolutegravir and 3TC, clearly, 3TC has been around for 25 years, it has a legacy, it is the drug that has stood up in the guidelines for the longest period of time and has probably the best safety profile of any of the antiretroviral therapies.

Obviously dolutegravir, as the second generation integrase inhibitor offer, has a very strong tolerability profile, so when you combine two drugs like that with great tolerability profile we do expect over the long-term there to be a benefit to patients, and so we have made our studies go out for a longer period of time, not just one year or two years, but actually three years in order to be able to distinguish between what you can get from a two-drug as far as long-term side effects versus a three-drug regimen.

Will Hamlyn (ManuLife Asset Management): The first question is on the *Tivicay* label in Europe. To what extent, if *Tivicay* is being used as part of a two-drug regimen alongside 3TC, does that limit the ability to get pricing in European markets once the single tablet is out?

The second one is on the long-acting. To what extent is the ambition of making the long-acting two months and longer just a drug delivery problem, or is it limited by the rilpivirine. My understanding was rilpivirine is the constraining factor on taking long-acting out further and you will need other products there. If you could just confirm that, thanks.

David Redfern: Thanks, Will. Tim, do you want to comment on Europe and the *Tivicay* dynamics now we've had the Type 2 variation, and how you see that playing through?

Tim Tordoff: From a European point of view, getting the type 2 variation allows physicians to be using that before the fixed dose combination is available which we think is really important for patients as John and Kim have said; that's core to our mission. But also, it allows the movement from three drugs to two, so we believe that has actually encouraged that. We see it's early days obviously, but we have seen some upswing particularly in Spain, Italy and France already in the two-drug regimens moving on.

In terms of price, clearly, we have to price in Europe in a number of countries. There is mechanistic pricing and we will go through that, and we don't see the type two variation as a negative to that, we only see it as a positive in moving towards the two-drug regimen era. From our point of view, in a business point of view, it's very positive and we believe it is very positive from a patient point of view as well.

David Redfern: I think it's important to state, we have pretty much consistently said that in the United States, the primary driver for prescribing two-drug regimes will always be the medical data, the translation of that medical data into the guidelines which are a critical component, and then the persuasion of the physician and increasingly the patient community to take the best medicines which we believe are the two-drug regimes. The pricing dynamic in that is probably really not a major constituent of the prescribing decision, it's all about data and the guidelines.

I think in Europe the dynamics are quite different. It is a much more price-sensitive market. Two-drug regimes will, on the whole, be priced less than three-drug regimes, and we have already seen that play through as an added incentive. Of course, the medical data will obviously be critical in Europe as well, but in Italy, irrespective of not having the data, we

have seen quite a lot of use of two-drug regimes in their individual components. It is just worth having in mind the dynamics of the marketplaces are quite different and pricing will play much more in Europe.

Long-acting two months? We are pretty excited about that prospect.

Kim Smith: We are. We have a lot of confidence in those two-monthly dosing on the basis of the data that we have presented from the LATTE-2 study, where just a couple of months ago we presented the 160-week data from LATTE-2, showing that the two-drug long-acting regimen can work either both monthly or every two-monthly, very effectively, out to three years. But you are correct in that we don't really believe that rilpivirine can be stretched beyond two months, and so that is part of why when John talked about other partners for cabotegravir, we are looking at other products. It might be able to go for a longer period of time, because we do think there is a potential for cabotegravir potentially to be longer than two months.

Anything you want to add to that, John? [No]

David Redfern: Great! Anything else? Jo, have another go!

Jo Walton (Credit Suisse): Just two questions. We look at the IQVIA data quite a lot, and of course we look at Biktarvy versus *Triumeq*. We do see Biktarvy seeming to be gaining some share, so could you remind me, if I'm sitting there as a doctor, being busily happy, moving to Biktarvy, how you get me to use more *Triumeq* instead?

From a European perspective, is there more of a use of a generic, if it's available, and now we have more generics becoming available, is it going to be difficult to price a brand in a generic market? I was particularly surprised at your picture which showed that patients didn't seem to care how many pills there were. The fewer pills per day seemed to be remarkably low down on their list, so is it much more common to say 'well, I know there's one single tablet here, but the patient takes three separate ones', and how you see that evolving in Europe and perhaps in the international market as well. We haven't heard from you.

David Redfern: Deborah, do you want to have a go on Bik/*Triumeq* to begin with?

Deborah Waterhouse: Yes, sure. If you look at the charts, and I have spent many hours looking at them and you probably do too, so let's just unpick that a little bit. You have seen the Biktarvy curve is quite steep and significant. What is happening with Biktarvy is their source of business is – as David said – about 70% from their own portfolio, 5 or 6%

from old regimens which do not contain either one of their own medicines or a dolutegravir-based regimen, and about 25% of their business for Biktarvy is coming from a dolutegravir-based regimen.

The reason their curve is so steep is because basically what they are asking doctors to do is, in the main, switch from an existing Gilead medicine to their newest one, and that has been their strategy for a number of years.

When I look at the *Triumeq* and the Biktarvy data, I also have to add *Juluca* in. The way I look at it is single tablet regimens that contain dolutegravir. You basically have *Juluca* and you have *Triumeq*. If you look at those two together, the data has been remarkably robust, both from an NBRx and a TRx perspective, so you have seen a slight downturn in *Triumeq*, and what you've seen is *Juluca* has compensated for that. Therefore, our share of the single tablet regimen part of that class in those graphs is very stable.

For us, we are actually very happy where dolutegravir is positioned, both in terms of physicians' willingness to keep their patients on *Triumeq* because it is a tried and tested medicine with dolutegravir at the core, and to also prescribe *Juluca*, some of which has come from *Triumeq* but a majority of which has come from competitor regimens.

The way we think of it is how is dolutegravir as a core agent faring in a world where you have a bictegravir-powered triple, and the answer is 'actually pretty well'. Physician loyalty to *Triumeq* is still high, which is why you have seen it quite stable, a little bit of downturn on NBRx, but those that would like a change, many of them have been willing to either take the patient from *Triumeq* to *Juluca*, or to take patients off other medicines onto *Juluca*, and therefore that has left us in a good dolutegravir position. But we don't tend to look at it just individual brand by brand because obviously there is a choice of backbone, there is a choice of core agent that's going on within that market at the moment.

David Redfern: I think at the end of the day, during the course of this year, all the feedback we get is that people/patients/physicians at best think that bictegravir is equivalent to dolutegravir, and it still doesn't have anywhere the breadth of the data that we have across the five superiority studies and in all the Phase 3b/4 studies, and now the 600,000 patient real-life database. The desire to keep prescribing dolutegravir underpins pretty much everything else that goes on, and that is the key thing. That's why the *Tivicay* business has really been pretty stable. Of course, there has been some switching around the edges, different physicians prefer different backbones, but the stability of dolutegravir as the core agent has underpinned it all, and obviously that is a good basis to move forward, as Kim outlined, on two-drug regimes.

Tim, do you want to talk about pricing dynamics in Europe, and then I'm going to come to the fastest growing part of the business of all.

Tim Tordoff: To your point, though, in Europe, we know it's a cost-sensitive area, but the good news is, we know that and obviously we've planned for that. In different countries, there's different aspects. For example, in France we have the ASMR high with *Tivicay*, in Germany, we have the benefit of *Triumeq*, so therefore our prices are pretty good in those markets.

But even if you go to a market like the UK here, dolutegravir, even in an incredibly price-constrained market, dolutegravir is still the No. 1 treatment in the UK. Some of those treatments in terms of the 2DR will go in terms of one component is generic, and therefore that could offer some savings as well. As David said, dolutegravir has shown superiority, and it has shown that in France, Germany and even in the UK, and in some circumstances, a two-drug regimen is also going offer very cost-effective treatment in the health system.

We are very confident that with the two-drug regimens we will be able to grow our market share, as we have, even with that genericisation. Of course, when you look at our competitors as they start to get generics, you can see that their market share is dropping, that's why we're confident, not only in the future, but in terms of what's happened over the Kivexa genericisation.

David Redfern: I think the question is where do you see the growth coming from in international markets?

Craig Williams: I think there are two questions, one on bictegravir and one on generics. The way to view the international region is, they have such a wide range of markets, you have Japan and Australia which are quite mature, slower in growth, but quite mature, and that's where we are performing very well. We have 47% market share in Japan, over 40% in Australia, and clearly, we have a pretty solid base on dolutegravir in those countries, and really an advocacy base that is quite strong.

Then you start looking at the big three, Brazil, China and Russia. This is where you have over one million patients, of which we have only started to tap into. Again, we are ahead of Biktarvy in that case as well. In Brazil, we are already first-line, over 175,000 patients on dolutegravir already. You have Russia, where we have just entered the Essential Drug list, and again this is only the beginning but already 13,000 patients in Russia are on dolutegravir and that is increasing rapidly. Then you have China, so to the point on generics, this is where generics do have an impact on access and innovation because in China, you have the case of generic efavirenz being used at a very, very low price, and at

the same time, them wanting to use dolutegravir first-line, and trying to work with the government to, I guess, find that access point is where we are right now.

You have that spectrum in the big three between Brazil, where we are already first-line, and almost 200,000 patients on; to Russia where we're just getting started; to China which is at the very beginning, but clearly, we have a private market opportunity there with over 130,000 patients available on the private market in China.

So, clear commercial opportunity. At the same time, you have 37 million people living with HIV, of which the vast majority of those are in our region, and so the part about generics that is helpful is that we partner with generic companies to make this medicine available, and that is a part of what ViiV does that no other company does, which is to make sure that this innovation is available to people. We are very proud of that as well.

David Redfern: What is very important in International is having a flexible portfolio with single agents, having single agent dolutegravir in *Tivicay*, and single agent lamivudine and so forth, because the use of STRs in the international market is much more limited. You have to be able to mix and match much more, and that is really the success in Brazil, that we got a big government contract for *Tivicay*, and we were able to do that, and then they can combine it with whatever generic backbone they want. Having that flexibility is key.

Craig Williams: I agree. In some cases, STRs are not even on the essential drug list.

Richard Parkes (Deutsche Bank): I wondered if, when you survey physicians, you could talk about the kinds of patients that are going on *Juluca*, what is driving that decision to switch, and how does that inform your strategy of positioning the dolutegravir 3TC regimen?

Expanding on that, what is going to be the strategy there because obviously you have done the studies in treatment-naïve patients, but it might be easier for a dual to be going for patients that aren't tolerating current therapy. How do you go about educating physicians about which is the patients they need to choose for the dual?

Kim Smith: The question about which patients we studied it in, we have studied dolutegravir 3TC in treatment-naïve patients and in switch patients, that's going on now. *Juluca* was studied in individuals who are already suppressed, and so we basically we have the availability of two-drug regimens for really any patient.

How do you go about talking to doctors? Just like we talk to you. Docs certainly get it that patients will be on medicines for the long-term, and they have experience over the years of the long-term side effects of those medications. As much as, when we present it, it sounds like that this is something that we're pushing out, the reality is that this has been a pull. The doctors have been looking for two-drug regimens and effective two-drug regimens that can be combined into a single tablet for years, and it's only now with *Juluca* and dolutegravir 3TC that we can have a regimen that you can prove, that you can put into a fixed dose tablet and that you can show is as effective as a three-drug regimen. There is a lot of interest from physicians to go down a two-drug path. It is almost intuitive from a clinician standpoint: you only want to use as much medicine as you need to in order to keep a patient suppressed; you do not want to go above and beyond that.

Deborah Waterhouse: Just to answer the first part of that question, if you think about the whole market, *Juluca* will ultimately be much more of a niche product and it will be a product where you can use two-drug regimen for patients who after the launch of dolutegravir 3TC really are resistant to NRTIs. So, you have an NNRTI and an integrase within that two-drug regimen, which will be more of a niche proposition and it is in switch only. Dolutegravir 3TC is the big opportunity because you have data in a naïve population and then we have a large Phase 3 study called TANGO which is a switch study, exploring in suppressed patients the performance of dolutegravir 3TC. You have a broad population for dolutegravir 3TC both naïve and switch, and the third category is where does cabotegravir/rilpivirine fit in? That is for people living with HIV who either struggle to comply, who hate taking a tablet every single day and who really find the burden of taking that tablet, being reminded that they have HIV a real psychological challenge.

There is a quite distinct patient segment that fits into that category, so with those three profiles we believe that the two-drug regimen portfolio will be appropriate for a large proportion of those people who are living with HIV where the patient and the physician feels this is the best way forward. That is how we shall divide the patient profiles for those three medicines.

David Redfern: Great! I think that is probably enough, so we shall bring an end to the formal proceedings. We are very grateful for your attention and for your questions. We shall stop now and move next-door for tea and Deutsche Bank mince pies. The whole management team will be there, so if any of you want to have any more interaction on any aspects, that is absolutely fine. Otherwise, if you have any further

questions, as always feel free to follow up through our great Investor Relations team. Thank you all very much for coming or for listening.

[Ends]