

**Fuelling our future growth
ViiV Healthcare: Update on our pipeline progression**

Tuesday, 30 April 2019

David Redfern: Good afternoon or good morning everyone. Thank you for joining us today to discuss ViiV Healthcare's update on its pipeline progression. I am David Redfern, the Chairman of ViiV and also GSK's Chief Strategy Officer.

The slides for this presentation have hopefully been emailed to some of you but if not, they can be found on the GSK website GSK.com under Investors/Speeches/Presentations. Tomorrow, GSK will announce its Q1 results and this will obviously include the HIV business. We will therefore comment and answer questions tomorrow on Q1 HIV performance. However, it's been a very busy quarter at ViiV with respect to our pipeline.

Our Pipeline

Dovato was approved by the FDA at the beginning of April. Just last Friday we received CHMP positive opinion for *Dovato* in Europe which of course is one of the final steps before a Marketing Authorisation is made by the European Commission, so now we anticipate a final decision being made in Europe in mid-year.

Cabotegravir/rilpivirine was filed with the FDA yesterday, following the fourth publication of the FLAIR and ATLAS pivotal studies at CROI in Seattle a few weeks ago and fostemsavir for heavily treated patients with few remaining options is on track for filing in the US by the end of the year.

These three medicines will drive the majority of the future growth of the HIV business. We know that is an important matter for investors and therefore we thought it would be helpful if we went into more detail on these medicines today than we will have time to cover properly tomorrow, particularly on the clinical data that has so far been generated, also importantly the significant clinical plans going forward and above all how we expect these medicines to influence the treatment of HIV in the future.

Welcome

Moving to Slide 2, I'm joined on the call today by Deborah Waterhouse, the CEO of ViiV and from the US by Dr Kimberly Smith. Kim is currently the head of ViiV Global Research and Medical Strategy, the senior author of the *Dovato* GEMINI studies and until quite recently a practising HIV physician in Chicago.

They will cover a few slides for about 20 minutes and then we will have the opportunity for a Q&A session.

Cautionary Statement Regarding Forward-Looking Statements

Before we begin, please refer to Slide 3 of our presentation for our cautionary statements.

With that, I'll hand over to Deborah.

Deborah Waterhouse: Thanks, David, good afternoon and good morning everyone.

To Leave no Person Living with HIV Behind

We are now on Slide 4. The main purpose of this call is to take you through the details of our pipeline progression and how we continue to develop treatment options for people living with HIV and for their physicians who continue to seek innovative medicines that can improve the lives of their patients.

I will hand over to Dr Kimberly Smith in a moment but by way of introduction, I do want to take just a moment to reinforce our absolute commitment to continuing the work to innovate and bring forward new medicines and treatments. Everyone at ViiV is proud of our ambitious mission to leave no person living with HIV behind.

Our Pipeline

If we move to Slide 5 which is a slide many of you will have seen before, and this is a schematic that depicts our pipeline, whilst there remains a significant unmet medical need in HIV across both the developed and the developing world, we at ViiV Healthcare remain dedicated to continuing to invest in innovation in this space, be it in two-drug regimens, long-acting formulations, our attachment inhibitor, fostemsavir for people who have limited options, antibody approaches or Discovery Research efforts in finding a cure.

This supports our commitment to HIV and our continued growth in the business powered by a broad and innovative pipeline.

But I do want to dwell for a moment on *Dovato*, the first FDA-approved once-daily single tablet two-drug regimen for treatment-naïve adults. The journey to approval for this medicine has been incredible and I am so proud to have been part of it. The FDA approval just a few weeks ago was a proud moment indeed for our company and the HIV community whose response has been fully supportive. Put simply, we believe that *Dovato* is the best version of a dolutegravir-based regimen for treatment-naïve people living with HIV and we

hope and anticipate that very shortly we will have the data to support filing for a switch indication in the US.

Kim will talk in more depth about the treatment journey but it is unbelievable to consider the level of progress that *Dovato* represents for people living with HIV. In the space of David's, Kim's and my lifetime, and if I may be so bold to suggest, probably quite a few of you on the call, the treatment journey for people living with HIV has shifted from a cocktail of 30 or more medicines per day in the late 1980s, through to AZT which was developed by former colleagues at GSK to the standard of care today which is based on three-drug regimens.

But when I meet people living with HIV they consistently tell me they fundamentally want a cure and in the absence of that, fewer drugs and improved tolerability. *Dovato* offers that, powered by dolutegravir at the core and partnered with lamivudine which doctors recognise as a great medicine in its own right, *Dovato* is an opportunity to establish a new normal for people living with HIV.

Dovato is a complete two-drug regimen which, as I stated, is powered by dolutegravir at the core. It offers non-inferior efficacy to a dolutegravir-based three-drug regimen, which is the standard of care, and it reduces exposure to the number of ARVs at the start of treatment.

It is early days, but the reaction from the HIV community has been very encouraging, although as this is a new treatment paradigm, it will take a few quarters to build.

Dovato began shipping from ViiV to wholesalers last week and it is now available in pharmacies.

In the first few weeks of detailing, customers have told us that they feel confident in the efficacy and safety profile of *Dovato*, and that they are keen to begin using the product for appropriate patients.

Early customer response in areas with significant market opportunity, including Texas and Florida have been particularly encouraging, with signs of strong advocacy from HCPs in several high-volume clinics and the first prescriptions being written.

External expert promotional programmes for *Dovato* began in mid-April, and are generating significant interest. These will be ramping up considerably through quarter 2.

Managed care coverage is tracking above our expectations for this point in the launch. For example, for Medicare Part D, Humana, which is a top four Medicare Part D account, covering over 25,000 lives has already started unrestricted coverage to *Dovato*, all of which gives us confidence that *Dovato* will be successful as we build confidence with

prescribers and continue to deliver comprehensive data to alleviate any residual concerns about durability and the resistance barrier.

Having said all of that, I am now going to hand over to Dr Kimberly Smith.

Power Reimagined

Kimberly Smith: Thank you, Deborah. We are now on slide six.

As David stated, we started Q2 by reaching a significant milestone - the FDA approval of *Dovato*, which is a first fixed-dose combination of dolutegravir and lamivudine, the first complete once-daily single tablet, two-drug regimen approved for treatment of previously untreated HIV infected individuals.

The superior efficacy of dolutegravir made it the clear choice to investigate as the core agent in our two-drug regimen programme.

Dovato reduces the exposure to the number of antiretrovirals at the start of treatment and aims to reduce the potential for associated toxicities, while maintaining efficacy in the high barrier to resistance of traditional dolutegravir-based three-drug regimens.

It is important to note that we don't have any label restrictions in terms of viral load, and I will come back to that point in a few minutes.

No-one should take more medicines than they need

Moving on to slide seven.

We are excited about *Dovato* because it supports our belief that no patient living with HIV should take more medications than they need.

People living with HIV say that the number of medications they are exposed to over their lifetimes have become a greater concern for them, and a survey we conducted, reducing the long-term effect of HIV medication on the body ranked as the most important improvement that could be made for a patient.

Nearly three-quarters of those surveyed said that they worried about the long-term effect of treatment, and more than half said that they would consider reducing the number of medications they take to a minimum.

To put this in context, estimates have been done for the number of drugs a person living with HIV will take over the course of their life. It is estimated that the duration of lifetime treatment for a person living with HIV is 39 years. A person on a boosted three-drug regimen would take more than 57,000 doses of medicine in their lifetime.

A non-boosted two-drug regimen, such as *Dovato* could cut that number in half.

The argument about reducing drug exposure has been compelling, and it has been recognised by the FDA.

Dr Deborah Birnkrant, the Director of the FDA's Division of Antiviral Products, referred to *Dovato* approval as an opportunity for naïve patients to have the option of taking a two-regimen in a single pill, while eliminating additional toxicity and reducing drug interactions from the third drug.

The Fair Pricing Coalition also heralded *Dovato* as good news for patients and providers, and issued a press release about the approval of *Dovato*.

GEMINI 1&2 PHASE III Studies: Pivotal 48-week data for approval and launch

Moving onto slide eight. The GEMINI 1 and 2 studies powered the file of *Dovato*.

We demonstrated non-inferior efficacy with dolutegravir plus lamivudine, versus a three-drug regimen of dolutegravir plus a fixed-dosed combination of tenofovir FTC at week 48.

Both of these regimens had low rates of virologic failure, and importantly, there were no individuals that failed with resistance in these studies.

Overall, the safety and tolerability was comparable between the two regimens, but there were fewer drug-related side effects in the two-drug regimen.

We also looked at a number of important biomarkers, specifically those measuring potential renal and bone toxicities, and we showed the likelihood of these biomarkers moving in a negative direction was better for our two-drug regimen.

In addition to the data that we showed in Amsterdam, we subsequently shared more detailed data on baseline viral load above and below 100,000. This data, which was included in the US Regulatory package demonstrates that *Dovato* was equally potent in the individuals with viral load above and below 100,000.

But in addition, in the greater than 100,000 baseline group, we broke that group down into categories as you see in the graphic on this slide. Most notably, there was no difference in any of these groups, even in the group of individuals who had baseline viral loads that were greater than 500,000.

This was particularly compelling, and it was compelling enough for the FDA to decide that there was no need to limit patients on the basis of baseline viral load in our label. We felt this was particularly impactful, and when we showed this data to providers, they described it as remarkable, compelling and reassuring.

Dovato: Evidence Generation Continues

Moving on to slide 9: the week 48 GEMINI data is extremely positive, but we know that in order to change the treatment paradigm we must provide additional studies and longer-term data. Our next major milestone is the presentation of the GEMINI week 96 data, which we hope to present at the International AIDS Conference in Mexico City. There's a lot of anticipation for this data and we expect to be able to demonstrate *Dovato's* continued safety and long-term efficacy.

In addition to presenting the GEMINI week 96 data in Q3, we also expect to be presenting data from the TANGO study, which is the first switch study for *Dovato*. The TANGO study takes individuals who are on TAF-based regimens and randomises them to staying on that regimen or switching to *Dovato*.

A third significant study for us this year is SALSA, which we're planning to start in November. This is the second switch study of *Dovato* and it will take all comers. The objective is to demonstrate non-inferiority of switching to *Dovato* for individuals who are on regimens other than task-based regimens.

These three studies together are very important, they will give providers and patients the varied and longer-term data they are looking for in support of two-drug regimens.

Finally on our *Dovato* milestone list for 2019, we are excited to have received, as David mentioned, the CHMP positive opinion for *Dovato* last week. Note, this was ahead of schedule, and we are expecting the EU approval of *Dovato* in late Q2 or early Q3 of this year.

Lastly on this slide, I want to remind you that the GEMINI 1 and 2 studies go on for 148 weeks, allowing us to demonstrate durability of this two-drug regimen.

Giving Treatment a shot: cabotegravir + rilpivirine long acting injectable (investigational)

Moving on to slide 10, giving treatment a shot. I'd like to talk about another exciting treatment in our portfolio: as many of you know, in March we presented Phase III data on the new HIV treatment, the first ever monthly injectable two-drug regimen of cabotegravir + rilpivirine. This innovative treatment regimen offered as a co-pack in the US and Canada will be given intramuscularly once a month.

With this long-acting injectable we're reducing ARV dosing from 365 days a year to just 12. People living with HIV have told us that not taking a daily pill means they get to live a more normal life, and one that is less stigmatised. For nearly a month they can avoid the daily reminder of living with HIV.

In addition to developing CAB + Rilpivirine for treatment we are also developing cabotegravir as a single therapy for HIV prevention. In this case, it is dosed once every two

months. There are two ongoing Phase II studies in collaboration with the HPTN or the HIV Prevention Trials Network.

There is an important invisibility factor of long-acting technologies: they are more discreet to the user, and this can reduce stigma and the relief from the need for a daily pill.

ATLAS/FLAIR meet primary endpoints: Cabotegravir and Rilpivirine monthly injectable demonstrates non-inferiority to oral three-drug regimen

Moving on to slide 11, the two Phase III studies supporting the monthly long-acting injectable are called ATLAS and FLAIR. As I mentioned, these were presented at CROI in March. The ATLAS study was designed to assess the treatment approach for individuals already on treatment and controlling their disease, to see if they could get the same level of control by switching from a daily oral regimen to a monthly injectable regimen.

The FLAIR study evaluated treatment-naïve patients who were started on *Triumeq*, and after 20 weeks, once their virus was suppressed, they were randomised to either staying on *Triumeq* or moving to the long-acting cabotegravir + rilpivirine. The graphs here show that both studies met their primary endpoint and showed that the monthly two-drug injectable combination of cabotegravir and rilpivirine was as effective as a daily oral three-drug regimen.

Virologic failure was rare, it occurred in 7 individuals – approximately 1% of the study population – across both studies. Notably, the seven virologic failures were all in participants from Russia, and six of seven of these had a particular HIV sub-type which is seen frequently in Russia, Eastern Europe and Eastern Africa, however is seen infrequently in other parts of the world, and is extremely rare in the US. We are doing more investigation to better understand this finding.

Strong patient preference for monthly injectable over daily oral regimen

Moving on to slide 12.

In addition to the remarkable efficacy of this regimen, we were very excited to see the patient reaction to therapy. It is important to let you know that it is not just ViiV that thinks that long-acting therapies are a good idea. Both providers and patients have been asking us for them. We didn't realise just how much demand there was until we heard from one of principal investigators on ATLAS and FLAIR that so many people in one of the ATLAS sites lined up to be in the study that they had to hold a lottery in order to select individuals who could screen for this study.

In FLAIR, one of the London clinics reported that they had patients literally lined up down the sidewalk for screening. Not only were patients excited by the idea of long-acting therapy, what we found in the study is that they actually preferred it. After about 10 months on treatment, we asked individuals in ATLAS and FLAIR a single question survey: which

treatment they preferred, the long-acting injectable or their previous oral therapy taken every day.

You can see the results here on this slide. In ATLAS, 97% preferred a long-acting regimen over previous oral therapy, and in FLAIR, 99% preferred monthly therapy over previous oral therapy. We were extremely excited and reassured by this response from study participants.

Reaction to ATLAS/FLAIR

Moving on to Slide 13, following our presentation at CROI in Seattle in March, reaction to the ATLAS and FLAIR studies was immediate and widespread. This slide shows examples of some of the global media coverage we saw following the presentation, and while we are always excited to get the attention of scientific and financial outlets, I have to admit our teams were most excited by the coverage in *Rolling Stone*. It reflects that this treatment was of interest, not just to scientists and the business community, but to the community at large because of the remarkable shift this could represent in HIV treatment options. The media coverage showed us that there are high expectations for this new treatment option by both physicians and people living with HIV.

Cabotegravir: Evidence generation and milestones

Moving on to Slide 14, this slide describes the ongoing data generation for cabotegravir and rilpivirine long-acting. As you know – and David again mentioned – yesterday we filed for US FDA approval for this two-drug regimen, and next in Q3, we will file a regulatory submission in the EU. Later this year, we will present another study, the ATLAS 2M study which is looking at the use of cabotegravir plus rilpivirine dosed every two months. At the beginning of 2020, we expect approval in the US and later in the year in Europe for the once-a-month regimen. As I have mentioned, we are also studying cabotegravir monotherapy for prevention, and we expect the HPTN studies, 083 and 084, to read out in 2021 and 2022.

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

Moving on to Slide 15, before I finish, I would like to remind you of another new important drug in our pipeline. We are extremely proud of fostemsavir, an oral medicine for heavily treatment-experienced individuals, those who have failed all or most treatment regimens. There is a continued need for new anti-retroviral regimens with novel mechanisms of action to address the needs of those who are running out of treatment options, a group that accounts for about 5% of all HIV infected individuals.

The FDA has designated fostemsavir as a break-through therapy, and we have previously shared the results of the BRIGHT study which examined the use of fostemsavir in highly treatment-experienced individuals. Importantly, the individuals in the BRIGHT study not only had limited treatment options with more than 60% of them having less than one anti-retroviral agent available, but they also had very advanced disease with 72% of the population having CD4 cell counts below 200, and 27% having CD4 cell counts below 20.

The data from the BRIGHT study showed that fostemsavir demonstrated 54% virologic suppression at 48 weeks and had significant improvements in CD4 cells. This is a remarkable accomplishment for patients with such advanced disease and so many limited treatment options.

We believe this is a perfect example of our mission to leave no patient living with HIV behind, and we plan to file for US regulatory approval for fostemsavir in the second half of this year.

Continuing to disrupt and innovate

Moving on to Slide 16, I will close today's presentation by taking you back to our pipeline journey map that Deborah showed you earlier. What you see here illustrates our strategic mission to develop novel treatments for people living with HIV. Although very effective and potent medications for HIV treatment are now available, there is still significant unmet medical need for new treatments and better options for people living with HIV. We intend to continue to address that need, to disrupt and to innovate with new modes of treatment and new mechanisms of action, and ultimately, we are seeking to be a part of the development of a cure for HIV.

With that, I hand it back over to David and Deborah.

David Redfern: Thank you, Kim. Now we would like to open up the line for Q&A.

Question & Answer Session

Jo Walton (Credit Suisse): Thank you. I just have a few, please. When you compare your dual with a TDF backbone, is that really the best way of comparing it now that we have TAF backbones instead and TAF has a superior adverse event profile, so presumably it's a relatively easy score to look at it relative to TDF I wonder if you could tell

us about any head-to-heads that you are doing that show your superiority to a TAF backbone.

My second question would be about the long-acting injectable and just how you are looking at mitigating the injection site reaction and pain that we've seen with IM injections. Is there something that you can do to make this available to be administered subcutaneously at home?

And finally because you are talking about the pipeline here, I wonder if you could tell us are you doing anything about a functional cure? Gilead is talking about Phase I data that they have with functional cures; can you tell us a little bit about your work in that area? Thank you.

David Redfern: Thanks, Jo. We are doing lots of work on a functional cure actually predominantly based in North Carolina but we will come to that in a minute. I will ask Kim to respond to you on the TDF backbone as a comparator and long-acting reaction sites. Kim.

Kimberly Smith: Sure. On the question of TDF versus TAF, I think that it's a really good question. I think it's important to recognise that in the studies comparing TDF and TAF there was never any evidence of there being an efficacy advantage to TAF. As you have mentioned, there has been demonstrated a short-term benefit with regard to some of the toxicities, however it's important to recognise that TAF continues to be tenofovir and so it's just less tenofovir in the plasma and more in the cell. And so only time will tell whether or not the improved side effect profile that has been seen in early studies will bear out in the long-term.

We mostly wanted to get our study started as soon as possible and again because there was no efficacy difference between TDF and TAF, we really wanted to demonstrate mostly the potency of the two-drug regimen in comparison to a three-drug dolutegravir-based regimen and we think we demonstrated that quite clearly.

With regard to your second question, the injection site reactions, as you may recall from the presentation in Seattle, injection site reactions were quite common. However, the study participants very, very rarely discontinued as a result of injection site reactions and what we saw was a pattern where individuals had injection site reactions most commonly in the beginning and the most common symptom was pain that lasted for on average three days and then over time the frequency of injection site reactions improved. That may be that patients got used to it or the individuals that were delivering the injections improved their technique, so we overall have been actually quite impressed at how well patients have

tolerated the injections. And again, a low rate of discontinuation as a result of injection site reactions.

With regard to your question about subcutaneous at home, when we did initially study [cabotegravir] as a subcutaneous medication it wasn't tolerated as well as the IM and so we continued to look at different ways that we may be able to deliver cabotegravir. For the time being, the intramuscular injection is the way that we will continue to progress for the time being.

David already addressed the question around cure and we are working, as he mentioned, with colleagues at the University of North Carolina in a number of cure initiatives.

David Redfern: Yes, and we don't have time to go into that now, Jo but at CROI we did have a poster from the cure initiative on a STING agonist that got some attention. Obviously it's pretty early days on that, but as Kim said we have a lot of work going on and hope we can make some progress.

Next question.

Graham Parry (Bank of America Merrill Lynch): Thanks for taking my question. Firstly, a lot of physicians have expressed caution around using a two-drug med in newly diagnosed patients because of the risk of resistance development in poorly compliant patients based on the non-GSK trials that did show some resistance with dual or even monotherapy dolutegravir. Essentially what is your marketing message to those physicians?

Secondly, Deborah's comments highlighted that physicians are keen to use in appropriate patients, so is there a way to determine the likely compliance of a patient before they start therapy and how important are the TANGO and SALSA data in being able to address a number of these concerns and perhaps target a more appropriate patient population who are more compliant in the switch setting and how long before you can get that data on the label?

And then secondly, going back to Jo's question really, the comparator you have used is I guess an easier comparator. Physicians tend to dismiss superiority on bone and renal in AE outcomes, so what data longer term showing better adverse events, outcomes for patients might we expect for two-drug versus three-drug regimens, notwithstanding the bone and renal benefits that you saw in the short-term because of the use of tenofovir as the control arm? Thanks.

David Redfern: Great, thanks Graham. I am going to pass all those over to Kim for lots of reasons but not least that she was until recently a very eminent practising physician and obviously spent a lot of time interfacing with the medical community.

Kimberly Smith: Thank you, David. There were a lot of questions there! I tried to take a couple of notes to capture all of them.

Let's first talk about resistance. Prior to the GEMINI study, there was a suggestion that there was a good amount of resistance seen in previous dual in monotherapy studies. Let me just make it very clear that there is an unquestionable difference between dual therapy and monotherapy, and we have never advocated, nor supported any monotherapy studies of dolutegravir or any other product, for that matter. So with regard to our previous regimens with studies or pilot studies with dolutegravir with lamivudine, there was one individual in the treatment-naïve study who had known very chaotic adherence, so much so that the investigators in that study and the provider in that study recognises this is the type of patient that is likely to develop resistance to any regimen, not to mention a dual regimen. It was very clear that the response of the provider community was that that was one case, and that the GEMINI study was really going to answer this question with regards to the barriers to resistance, and, again, through week 48, has quite clearly demonstrated a very high barrier to resistance.

I think the question around the adherence, there is a suggestion that individuals that in our clinical trials tend to be more adherent, and I think that that's actually quite a bit of a myth. When we talk to our investigators, particularly in the US and parts of Europe as well, because they are seeing fewer and fewer treatment-naïve patients, they are tending to enrol all of their patients, the naïve patients that they see, into the clinical trials. They certainly aren't cherry picking for individuals that they think might be adherent, and if you recall data from the past of studies that have looked at how good doctors do at picking which patients are going to be adherent, show that we are horrible at it, so I think you should think about our studies. Really, if you look at the baseline characteristics of the GEMINI studies, they really look very similar to the general population of treatment-naïve patients, so I think the studies are a good reflection of the real world.

Therefore, with regards to the switch studies, as I mentioned, the TANGO study will compare individuals staying on a TAF-based regimen to going on to D3. So this is a study that will give you a really head-to-head comparison of a TAF-based regimen versus *Dovato*.

That study is actually designed to go out for three years in order to give us time to be able to see differences, but I think that while we will look to demonstrate differences both in bone, renal and other drug interaction side issues and other problems that individuals can

experience with TAF-based regimen, the reality is that providers basically accept the notion that if you reduce a drug that you are going to get a benefit, and so by reducing the amount of tenofovir, there are some benefits.

What we believe is that by actually getting rid of tenofovir altogether, as well as potentially abacavir in the other regimens, that you are basically reducing the number of drugs, and since all drugs have side effects, you are likely to give the patient a benefit.

We will demonstrate in our clinical trials, but, again, this is an idea that is very well accepted by the general treater population.

I think I answered all those questions. Was anything that I missed?

Deborah Waterhouse: There was just one element that I think Graham referred to that talked about appropriate patients for *Dovato*, which I think I said in my opening.

The reason I phrased it like that, Graham, is because obviously at the moment we only have the naïve licence in the US because that was the population we studied, and that's the way FDA therefore gives you the licence.

As you can see, we are studying *Dovato* in switch, and we expect to have a switch and a naïve licence in the US by the middle of next year.

The European licence is going to be a very broad licence, so in that part of the world you will be able to use for switch and naïve from the very beginning.

For us, what we believe is that, actually, *Dovato* has very broad applicability both in naïve and switch, and we will be generating data to demonstrate that, and that this is the best dolutegravir-containing medicine that you can take, regardless of CD4 counts, viral load, whether you are naïve, or whether you are somebody that wishes to switch your regimen.

Graham Parry: Okay, thanks. What sort of timing for getting SALSA data on label, because that would be a fairly obvious patient population, if you have an aging, protease-inhibitor patient with a high kill burden and lots of drugs being taken, particularly one who is well compliant, that would seem like an ideal patient population to switch, so when do you think you can get SALSA on the label?

Deborah Waterhouse: Actually, we believe that by doing TANGO we will get a broad switch label, which will give us permission to actually promote in all patients who should switch or would like to switch their regimen.

SALSA is not necessarily being done for the sake of the label, because we think it will be already broad enough. It is just to keep on building the data and the confidence in the two-drug regimen over time, because we know that is what physicians like.

Graham Parry: TANGO we will have in the second half of this year?

Deborah Waterhouse: We are hoping that TANGO will be presented at the International Aids Conference in Mexico. Obviously, we can't say definitively that will happen because it is up to the conference what data they take in, but we are hoping that both TANGO and GEMINI 96-week will be in Mexico.

David Redfern: Yes, and all I would add, Graham, is just to emphasise what Kim said. Remember, the GEMINI studies are being run for three years. We have obviously had the 48-week one-year data. We should have the two-year data, which I think will be very eagerly anticipated. We certainly saw a kick up in *Juluca* following the two-year data, and, hopefully, obviously that will provide more data, both on safety and the renal and bone biomarkers, and obviously in resistance as well.

Graham Parry: Thank you.

Tim Anderson (Wolfe Research): I have a question on commercial dynamics, really related to the protected drug class reform measures in the US. Specifically, whether you think that goes through and if it goes through, what it means for Glaxo. There are three approved integrase inhibitors, you have one of those going generic in a few years, and there are more and more product offerings here. It seems like it is a potential set-up to threaten access restrictions that foster price competition that really has not existed because of that protected drug class designation. Can you comment on what you expect here, and what the impact would be if it goes through as proposed?

Deborah Waterhouse: Thanks for the question, Tim. The proposal that was put forth was not to remove protected class status in total, but it was to allow the introduction of things like prior authorisation, step edits, into the Medicare Part D space which, as you know at the moment, isn't there, and you basically get a licence for the medicine and it pretty quickly goes into the Medicare Part D plan.

What we are not looking at, at the moment, which is our understanding, is the removal of the protected class status, and for those of you who watch this space carefully, you will see, even with the more limited restrictions that have been proposed, there has been huge amount of response from the HIV community where they have written their responses

to the proposal into the health system, and also, there has been a lot of media coverage, adverts taken out, protesting at any limit to access.

The impact of that we will see over the coming months, but we do know that there is a very strong response from the community, and obviously from ourselves, to anything that limits choice and access, because it is a very individualised disease, and therefore, particularly when you're older – because that is what most of the Medicare patients tend to be – you will have resistance, you will have a particular set of co-morbidities, and therefore having the opportunity to really prescribe what's most appropriate for your patient is very important in this group particularly. Of all the responses that I've seen from the advocates and ourselves, those are the points that are made. Keeping these protected classes isn't being taken away in total. There are just some limitations being proposed which are being strongly responded to.

David Redfern: All I would add, Tim, is, remember HIV is one of six protected classes and it may be that in the end they are treated differently. We will see how it goes. Since this proposal has come forth, we have also had the State of the Union address where the President mentioned trying to eliminate the implications of HIV by 2030, and remember, in the United States today, out of about 1.2/1.3 million Americans living with HIV, only about 800,000 are on treatment. There is still a lot of unmet medical need and restricting access through a mechanism like this is probably not going to help towards that.

We will see where it goes, but there has been a very significant backlash against it from the community.

Tim Anderson: Can we just play forward the scenario where reform does happen on this, though? I understand that naturally is going to be rebuffed by patients and by manufacturers, but if this does go through, it seems to me like you could probably expect there to be price competition?

Deborah Waterhouse: I think that is a logical conclusion to draw, but I guess our response to that is we have *Dovato*, for example, which we have priced at \$2295, and that is between \$700 and \$1000 cheaper than the other three-drug regimen competitors, so the response that we've had from payors, both in the Medicare Part D and the broader commercial book of business – and actually ADAP and Medicaid as well – has been extremely positive. You have an efficacious medicine that could deliver side-effect benefits at what is an extremely compelling price point. For us, we think that the pipeline that we are bringing to market and have brought to market with *Dovato* gives us a compelling position. Therefore, we think we have already taken a step forward in managing the exposure.

Tim Anderson: Thank you.

Kerry Holford (Exane Paribas): I wonder if you can first of all give a broader update on the ViiV performance. Since you exited last year, we have clearly seen continued pressure on volumes in Q1. I just wonder if you are able to give us an update on the process so far, just playing out as you have anticipated so far this year?

Secondly, on the rebate environment in HIV, historically it has clearly been low, but I wonder in the context of your commentary around unrestricted access for *Dovato* in Humira's plans, what the cost of achieving that has been? Should we expect rebates in general to continue to rise maybe there within HIV over time?

Then thirdly, on cabotegravir/rilpivirine, every two months dosing, ATLAS 2M, is this just about more convenience for the patients, or are there certain patients that would benefit from less frequent dosing, baseline characteristics and so on?

I also saw you had filed an oral formulation of that combo – could you just explain why? Thank you.

David Redfern: Thanks, Kerry. If you don't mind, I'm going to duck the performance question today because I think that really fits best with our Q1 results tomorrow, and we'll be happy to go into detail then but I don't want to get ahead, so feel free to ask that question again tomorrow. I will ask Deborah to comment on the general contracting environment in the US. It's pretty stable, but you can give a bit more flavour and Kim can comment on cabotegravir.

Deborah Waterhouse: I think 'stable' is the right word. To be honest with you, Kerry, we have brought *Dovato* to market, we priced it very sensibly at \$2295. The response from the community was extremely positive, so the Fair Pricing Coalition came out with a very positive press release, which kind of showed their appreciation for the fact that the cost of treating an HIV patient if they were to be prescribed *Dovato* had been reduced by literally 30-odd percent, so the community received it well. In the conversations we are having with payors, *Dovato* has been really well received. I think the payor environment is relatively stable and I can absolutely confirm to you that the payor conversations with *Dovato* have been extremely positive and that's because we were very sensible about how we priced the medicine.

David Redfern: Yes, it remains very guideline-driven, Kerry, and all the dolutegravir regimes, including *Dovato*, are on the US guidelines and I think there is a very clear principle that the formularies and the insurance companies understand, that HIV

patients want access to the medicines that are on the guidelines. Those guidelines are updated regularly.

Kim, do you want to comment on CAB 2M and also why we have the oral formulation?

Kimberly Smith: Sure, absolutely. The reason for every eight week is really because we believe that these two long-acting agents will support that dosing regimen until we've clearly demonstrated the efficacy of every four weeks or monthly. If we can stretch it out to every two months, again that does reduce even further the number of days that a patient needs to dose. The goal is to improve basically the lifestyles and, as we say, to make HIV a lesser part of people's lives. When patients have been surveyed about long-acting therapy they like it to be at least a month, but longer is better and so if we can have it go longer, that's what we seek. What we are looking at in the rest of our earlier pipeline is the possibility of longer dosing intervals.

With regard to the oral, so the oral really has two purposes. One is that when you are starting a long-acting therapy that's going to stay in a person's system for a prolonged period of time, it is good at least in the beginning to be comfortable that individuals are going to tolerate that medication and so the oral lead-in allows us to demonstrate the safety if a person tolerates cabotegravir and rilpivirine before they start with the long-acting, which again stays in their system for many months.

The other role that the oral plays is actually for bridging, so for example if an individual, let's say that they needed to go out of the country or for some reason they were not going to be available to come into the clinic for their monthly dosing, then we can provide them with an oral combination to actually bridge them until they can get to the next dosing. It allows people to live a normal life. You are not necessarily bound to having to get to the clinic every month if there needs to be a break.

Kerry Holford: And just to clarify; that would be a once-daily oral pill?

Kimberly Smith: That would be one cabotegravir tablet and one rilpivirine tablet, separate tablets.

Deborah Waterhouse: And Kerry, you asked about who the patient kind of was for cabotegravir. There are four characteristics that we think about. One is those people who have a real issue with disclosure, so they do not and have not disclosed to those around them the fact that they are HIV positive. Secondly, those people that really struggle to swallow the relatively large pills that all HIV meds tend to be made up of. The third are those that struggle with compliance and the fourth are those who actually have a real mental

burden by taking a tablet every day and being reminded that they are HIV positive and actually those four groups are a very important population for this medicine. Those are the characteristics of the people who will benefit most.

Kerry Holford: Thank you.

Laura Sutcliffe (UBS): Hello, thanks for taking my questions. Just on cabo/rilpivirine, I know you are pursuing this eight-week programme; is the intent that the eight-week if it is approved will eventually replace the four-week product or will you leave patients with a choice? If and when the eight-week product comes, is it rational to assume that it's going to be twice as expensive as the four-week product?

Then just on manufacturing, where do you stand? Is it you that will be putting together the kit that we can see in the slide deck and are you ready to go at the point of launch? Thank you.

David Redfern: Great, thanks, Laura. It is being manufactured in-house. It's quite technically complicated with things like nano-milling and so forth but it's predominantly going to be done in Singapore. We can give you more details but it's in-house and we have been working on it for many years and are very confident.

Kim, do you want to comment on eight weeks and whether it will replace four weeks?

Kimberly Smith: We expect that both will be approved and so it will be the choice of patients and providers whether they would want to do the every four-week or the every eight-week dosing.

David Redfern: Great. And Deborah, pricing?

Deborah Waterhouse: We are not going to comment on pricing at the moment. We as a company are very open about the fact that we price very sensibly and we are currently looking at where we think we would price the four and the eight-weeks, so we are not in a position to comment on that at the moment, Laura.

Simon Baker (Redburn): Thanks for taking my questions. Just continuing on with Laura's question on cabo/rilpivirine, as the picture shows it's administered as two separate IM injections. Are the two components chemically incompatible? So would it be right to assume that you couldn't have a single formulation of that combination?

Then a more general question. Going back to a point made at the beginning by Deborah, I wondered if there are any regional perception differences on the subject of two-

drug versus three-drug regimen, so I'd be interested to get your perspectives there. Then finally, just revisiting the question on cure: it would be interesting to hear your perspectives on what the case of the London patient tells us, as a means to achieving that goal of curative treatment. Thanks very much.

David Redfern: Thanks Simon, great questions. Kim, do you just want to start on the two injections, why there are two injections?

Kimberly Smith: Each of the agents is 2ml, so to combine them into one syringe would mean a very large injection, which is beyond what you typically would want to give. Typically we don't give IM injections that are more than 3ml, and so that would give them up to 4ml, and that doesn't even include what would happen with the loading dose. We actually don't think that that is the most convenient way for patients to get it. I know it doesn't sound ideal for an individual to have to get two injections, but again, based upon our data so far it has been very well tolerated.

With regard to the question that you asked about regional preference of two or three drugs, the one thing that I can say is that in Europe there has been a very, very strong effort towards two-drug regimens for a long period of time, and many of the early pilot studies of dolutegravir plus lamivudine actually were initiated in Europe - a couple of them in the US, but even more in Europe, so I would say, if I had to say one region versus the other, I would say slightly more enthusiasm in Europe for two-drug regimens than in the US, but the US is catching up.

David Redfern: Great, and the London patient, Kim, do you want to comment on that and its significance – obviously lots of excitement around it.

Kimberly Smith: Sure - lots of excitement, and I think very good for the field. The story with the London patient is very similar to the story with the Berlin patient, Timothy Brown. The only difference is that Timothy Brown is now out many years, and the London patient is just out roughly 18 months, and so I think it's still a situation where time will tell, and we just need to continue to follow that patient to see if they, again, maintain that what appears to be a "cure" like Timothy Brown for the long term.

James Quigley (JP Morgan): Hello, thank you for taking my question – a couple of quick ones from me: on sales force efforts for *Dovato*, you mentioned that it's going to take a while to build, so with that in mind, when do you expect to start DTC campaigns and how will the shift from *Tivicay* and *Triumeq*, or effort on *Tivicay* and *Triumeq*, over to *Dovato*, how will that phasing happen? Will it be before or after the switch data? Then secondly, on the pipeline, we used to hear snippets that it's about broadly neutralising antibodies, is that still happening or is that no longer in the pipeline?

David Redfern: It's definitely happening, James, we'll come back to that, but maybe, Deborah, you can comment on the sales force?

Deborah Waterhouse: Yes. If I look at HIV and what makes a medicine successful, the first thing is that you have strong and compelling data, both at the point of launch, but then you continue to characterise the medicine by continuing to generate strong clinical data, so obviously that's at the heart of what we're expecting to do.

On top of that we have a very strong commercial plan, both in the US, Europe, Australia, Canada, Japan, etc. That means we will have strong sales force, that we will have a strong digital presence, that we will make sure our share of voice is strong and matches our competitors in both of those sales force and digital areas, that we will be doing Direct to Consumer. That doesn't necessarily mean big television ads, actually the Direct to Consumer campaign is a little bit more refined than that. I'm not saying we won't do TV, but it is a mixture of press, banner ads, a lot of digital content and TV may be part of that.

Then in addition we are able now to do - as I'm sure you all know - peer to peer programmes, so we haven't been able to pay healthcare professionals to promote our products for a number of years. We are very happy with the policy change, that happened in October last year, because we know that physicians want to hear the data from us, but they want to hear the clinical experience of their peers. Therefore we are able now to, and have planned a significant number of, peer to peer promotional meetings where we have a ViiV expert partnering with a healthcare professional, and that's working extremely well.

From our perspective, we have a very strong commercial plan, and we are looking to, initially obviously we have the naïve licence in the US and we will be promoting strongly in naïve. We know that physicians make their own choices about where to use medicines and that may or may not be within the label, but clearly we will only be promoting in naïve.

I think you will find that over time you will get broad uses of *Dovato*, and I think we will end up cannibalising *Triumeq*, competitor products and *Tivicay/Descovy* as well most likely, so we are not going after one particular product as a conversion strategy. Once we are able to promote in switch we actually believe that this dolutegravir-based regimen, teamed with lamivudine is the best version of dolutegravir, and is something that physicians should prescribe in both naïve and switch patients, so that is where we see the medicine position very broadly, and taking naïve and other regimens.

David Redfern: Great, thanks. Kim, do you just want to comment very briefly on our broadly neutralising antibody approach that we have in place?

Kimberly Smith: We have collaborations with the NIH in the United States, basically the Vaccine Trials Network where they have a number of broadly neutralising antibodies that we are investigating with them for possible end-licensing.

We also have a proof-of-concept study that we are doing with the HIV AIDS Clinical Trials Group, basically, looking at cabotegravir in combination with a broadly neutralising antibody to really look at the concept of whether or not a small molecule and a broadly neutralising antibody could work well together, and so this is a very exciting area. We are very, very well entrenched in it and we are looking for great opportunities for products to develop, and potentially we think that having cabotegravir already as a long acting, actually potentially gives us an advantage in that area.

David Redfern: Great, thanks. I think we have time for just one more question.

Peter Welford (Jefferies): Hi, that will be great. I have just a couple left. Firstly, on the cabotegravir injection, just with regards to you mentioned in the US and Canada it will be available as a co-pack. Just to be clear, is that also going to be true in the rest of the world or is there something different that will happen in other geographies?

Also, are those efforts underway to potentially develop either new needles and/or perhaps pre-filled formulations of this in the pipeline, rather than requiring the reconstitution steps prior to the injection?

Then, finally, just a quick one on the pipeline. Are the antisense approaches still on going, or have they been discontinued or returned to the inbound? Thank you.

David Redfern: Great, thanks, Peter. Kim, I think they are probably all for you.

Kimberly Smith: I didn't hear the last one, but I will answer the co-pack question.

The co-pack will happen in the US and Canada. However, Europe does not support co-packs. They have tougher rules around co-packs, and so it will not be co-pack there, it will be the separate entities packaged separately.

I didn't hear the second question, though?

Peter Welford: Sorry. Efforts to potentially improve either the fineness of the needle, potentially also, I guess, create pre-filled vials rather than require assembling the injection prior to use?

Kimberly Smith: Yes, we are always working with our device colleagues to try to find ways to make this as convenient as possible, and the co-pack is actually a manifestation of that, where all the pieces are put together, and there is a particular top to

the vial that actually makes it very easy for the sites to actually fill the syringe, and so we are always looking for easier ways to provide the medications to the sites.

David Redfern: Great, and the third question, I think, was do we have any approaches on antisense for cure?

Kimberly Smith: Not that I am aware of. Most of our approaches are working on latency reversing agents.

David Redfern: Yes. Okay, I think we are out of time, so very much appreciate everyone dialling in. For any of you who have more questions or weren't able to ask a question we have the GSK Q1 results tomorrow. Obviously, that's an opportunity to discuss HIV performance, but we are clearly happy to take further questions on the pipeline and the progress we have made, but thank you for your time today.

[Ends]