

**Meet GSK Management**  
**Getting Ahead of HIV**  
**Monday, 29 November 2021**

**David Redfern:** Good afternoon, everyone. I am David Redfern; I am the Chairman of ViiV Healthcare and Chief Strategy Officer for GSK.

I am delighted to welcome you to our Meet the Management event – Getting Ahead of HIV, for analysts and investors.

As usual, the presentation materials are available on [gsk.com](http://gsk.com) and were sent to people on our distribution list earlier today.

**Cautionary statement regarding forward-looking statements**

I will just refer you to slide 2, which contains our cautionary and forward-looking statements.

**Agenda**

Moving on to slide 3, which provides a summary of what we shall cover today.

I am delighted to be joined by Deborah Waterhouse, the CEO of ViiV Healthcare, and Dr Kimberly Smith, Head of R&D for ViiV.

The following 90 minutes will be divided into two parts. For the first 45 minutes we will walk you through the shape of our HIV business, the growth drivers, our continued innovation leadership and our pipeline.

Following that, we will have plenty of time for Q&A. As a reminder, questions can be asked via the telephone keypad using \*1. I would also like to remind you that this call is being recorded and that a replay will be available after the event.

**Global specialist HIV company, focused on ending HIV/AIDS**  
**How we meet the challenge**

ViiV Healthcare is a joint venture between GSK, Pfizer and Shionogi, and is 100% focused on combating, preventing and ultimately curing HIV and AIDS. GSK and its predecessor companies have been at the forefront of HIV innovation over the last 35 years.

GSK was proud to develop the world's first medicine (AZT) to treat HIV infection in 1987, followed by the first fixed-dose combination, *Combivir*, in 1997.

ViiV Healthcare was created in 2009 and is responsible and accountable for end-to-end commercial and scientific functions, with now over 1,400 talented people dedicated every day to discovering, developing and commercialising medicines to treat and prevent HIV worldwide.

ViiV also successfully leverages and is heavily reliant on GSK's infrastructure and platforms in areas such as clinical operations, manufacturing, and back office.

In 2013, ViiV launched dolutegravir, which transformed the treatment of HIV by becoming the world-leading integrase inhibitor, and continues to be at the forefront of our innovative portfolio today.

Two years ago we again transformed the treatment paradigm by launching *Dovato*, a two-drug regimen powered by dolutegravir at the core.

And within the last few months we have launched *Cabenuva*, the world's first long-acting injectable for the treatment of HIV.

So we have a long, a proud, and a continuing history and dedication of leading innovation in HIV in pursuit of our mission to leave no person living with HIV behind.

And with that, I will now hand over to Deborah Waterhouse, the CEO of ViiV Healthcare.

## **Reshaping and delivering HIV treatment and prevention**

**Deborah Waterhouse:** Thanks, David.

I am now going to provide an overview of the shape of our business and the scale of the HIV challenge worldwide.

I want to add how proud we are to be using positive and authentic imagery throughout this presentation of people living with HIV. Ale, whom you can see here, is living with HIV in Uruguay, and features as part of a campaign we are leading to transform perceptions and address inequalities and stigma which remain so pervasive.

## **Leading in HIV Progress in 2021 and beyond**

ViiV Healthcare continues to lead in HIV. We are a significant contributor to GSK sales and a driver of growth, reporting global sales of almost £5 billion last year, and £3.5 billion to the end of Q3, representing a 4% increase at constant exchange rates.

We continue to transform the HIV marketplace. Our broad portfolio consists of 16 antiretroviral medicines, offering a wide range of therapeutic options for people living with

HIV. Our strategy is to remain innovation leaders in HIV, achieve a mid-single-digit CAGR to 2026, and absorb the loss of exclusivity of dolutegravir in the latter part of the decade through the changing mix of our portfolio and the success of our pipeline.

We have changed the approach to HIV treatment with the launch of our two-drug regimens, *Juluca* and *Dovato*, and we are now bringing to market the first long-acting injectables for the treatment, and shortly, for the prevention of HIV. We believe *Dovato*, *Cabenuva* and cabotegravir for PrEP will each deliver significant benefits in the treatment and prevention of HIV, and will make a multi-billion-pound sales contribution.

As we move into the second half of the decade, we anticipate seeing continued growth in our long-acting regimens, with cabotegravir replacing dolutegravir as the foundational medicine in our portfolio, and we are excited by our early-stage pipeline, which we believe offers potential for revenue renewal from 2026 onwards.

This pipeline has recently been further strengthened by our exciting new collaborations with Halozyme and Shionogi, and the new partnership we are working on with our existing partners, Janssen, for an ultra-long-acting version of *Cabenuva*, which Kim will talk more about later.

And, finally, we remain motivated by the ultimate goal – a cure – which will one day result in a future free of HIV and AIDS.

### **The shape of our HIV business** **38 million people globally are living with HIV**

HIV remains a global health challenge with significant unmet needs, and our mission to leave no person living with HIV behind is a commitment to access. Across the commercial markets of North America, Western Europe and International, we have a clear and differentiated strategy that we are confident will grow sales, share and profit over the next five years.

We will continue to partner with middle-income tender markets to ensure a consistent supply of our dolutegravir portfolio. In 2020, lower and upper-middle-income countries accounted for around 45% of our volume. For those living in the least developed countries, we provide royalty-free licences to generics manufacturers. We have a wonderful group of partners who ensure treatment reaches those who need it. As a result of our access strategy, of the 28 million people currently taking antiretroviral therapy, more than 18 million are on a dolutegravir-based regimen.

We are also delighted to have developed and are now distributing through partners the world's first dispersible formulation of dolutegravir for children living with HIV, most of whom are living in resource-poor settings.

### **Key trends shaping the £26 bn HIV treatment and prevention market Delivering on significant unmet needs in HIV**

Key challenges remain in the treatment and prevention market, currently valued at around £26 billion. Despite heightened awareness, the WHO estimates approximately 1.5 million new infections per year globally, with the burden remaining greatest in Sub-Saharan Africa.

COVID continues to impact people living with HIV disproportionately. Over the past 18 months we witnessed a significant reduction in the number of people being tested worldwide for HIV.

The dynamic market has also been suppressed by the COVID pandemic. In the US, for example, we have seen that the naïve market has been suppressed by about 10%, and switch by around 40%.

Across America it is estimated that only around half of people living with HIV are virally suppressed, and there are still 38,000 new infections per year. HIV rates are stubbornly high amongst people of colour, and men who have sex with men. As such, there remains a pressing need for new approaches to treatment and prevention.

The HIV population is ageing. Due to advances in treatment and increased life expectancy, it is now estimated that three-quarters of people living with HIV globally are expected to be over 50 by 2030.

Unfortunately, the quality of life for people living with HIV remains lower than the general population, and levels of stigma and inequality persist.

### **Our Business Today**

We are now on slide 9, which depicts Yulia, who is living positively with HIV in Russia.

I am now going to walk through the commercial dynamics which drive our business today.

## **Delivering our pioneering portfolio**

### **Competitive commercial and medical execution**

We have continued to focus on excellent execution and building capabilities to ensure we successfully drive the uptake of our pioneering portfolio. We have done this through disciplined and rigorous investment allocation, and we have increased our levels of spending to drive customer-facing launch activities.

We have focused on enhancing our sales force effectiveness, with the result that our good selling outcomes are now consistently above the industry average. Our sales representative call activity is broadly back to pre-COVID levels, and the chart on right side of this slide demonstrates a leading share of voice, which is above 50% versus the competition in six markets, a statistic which we believe underpins our strong momentum and share progress.

We have transformed our digital, data and analytics capabilities. Just one example of the impact this has created is around our digital share of voice at medical congresses, which is now double that of our closest competitor.

We also have industry-leading US payor capabilities, creating rapid patient access across launch brands – achieving 98% patient access for *Dovato*, and 80% for *Cabenuva*, just ten months post-launch.

We also have an industry-leading medical team building awareness and confidence with HIV physicians, evidenced by the fact that the volume and length of calls with customers actually increased during the pandemic, and we have also seen the rapid inclusion of all our launch medicines into major global guidelines.

### ***Dovato* driving growth**

#### **Innovation sales now 27% of the portfolio**

Strong commercial execution is driving the performance of our innovation portfolio. This chart shows that our innovation sales are tracking towards £1 billion year-to-date at the end of Q3, representing nearly 30% of our portfolio, and significantly higher than last year. This is an important milestone, and a proof point of success of our strategy to shift the market from three-drug regimens to two-drug regimens.

*Dovato* continues to grow strongly, building on the positive momentum since launch. We are driving strong growth in the US and Europe, particularly in the switch market. *Dovato* is currently number one or two in switch in key markets, and this is despite the suppression of the overall market due to COVID.

We are particularly pleased by the rapid uptake of *Dovato* in Europe, with the share of switch currently around 28%. *Dovato* delivered sales of £533 million in the year-to-date to the end of Q3, and is on track to deliver more than £1 billion of revenue in 2022, with further potential beyond that.

We see the opportunity for *Dovato* as being balanced globally, with around 50% of the potential sales in the US, and the remainder split between Europe and International. *Dovato* is patent protected until at least 2028 in the US and 2029 in Europe.

### ***Dovato*: best-in-class two-drug regimen**

As Kim will reinforce shortly, HIV physicians are guided by data and guidelines, and we could not be more proud of our robust and industry-leading studies.

The ground-breaking GEMINI trials demonstrated the viability and potency of dolutegravir plus lamivudine as a two-drug regimen for naïve patients.

SALSA and TANGO swiftly followed, demonstrating high levels of efficacy and safety for people living with HIV wanting to switch regimens.

Since then, our comprehensive clinical programme for our two-drug regimen portfolio has continued to demonstrate that *Dovato* is the best version of a dolutegravir-based regimen, with fewer drug-drug interactions and reduced exposure to ARVs.

We now have more than three years of efficacy and safety data for *Dovato*, which sets a very high bar for oral treatment regimens. The US and European Treatment Guidelines include *Dovato* as recommended for most adults living with HIV in both naïve and switch. Physicians report similar levels of confidence in their real-world experience. We have almost 90 investigator-sponsored or real-world studies underway with *Dovato*.

To date, clinical data has been presented on more than 7,000 people living with HIV taking *Dovato* in naïve or switch.

As many of our physicians now say, a person living with HIV will be on treatment for the remainder of their life. Why should they be exposed to three drugs when two is all they need?

### **Shifting the paradigm towards LA treatment LA injectable treatment market c.£4-5bn by 2030**

*Cabenuva*, the world's first and only long-acting injectable treatment for HIV, received FDA approval in January this year. It is also approved in Europe under the brand name *Vocabria/Rekambys*, with dosing every two months.

*Cabenuva* reduces dosing days from 365 to six. It is powered by an integrase inhibitor and has non-inferior efficacy, and comparable safety to daily oral three-drug regimens.

In our pivotal trials, nine out of ten participants preferred *Cabenuva* over daily orals, and the reasons behind this are clear. There are significant challenges with daily therapy – fear of HIV status disclosure, stress and anxiety about staying adherent, and the daily reminder of living with HIV. Long-acting gives people freedom from the burden of daily oral therapy, and globally, more than 5,000 people living with HIV are now taking *Cabenuva*.

We have launched in 11 markets which account for 70% of peak sales, with a further ten markets launching in 2022. We are seeing momentum accelerating in the US with over 80% payor coverage, including a J-CODE in place from 1 October 2021, enabling a smoother, more automated reimbursement process. The prescriber base is increasing week on week.

We initiated DTC TV advertising in October, which we believe will further stimulate patient demand. As with any new class of medicine, *Cabenuva* will take time to build, and the COVID environment continues to constrain switch activity, particularly where a patient needs to visit a physician's office. Despite this constraint, we are particularly pleased with recent progress as enrolments to the *Cabenuva* hub programme have doubled since the beginning of September. We anticipate two positive label updates in the US, one for every two-month dosing expected in December, and one for optional oral lead-in, expected next year. Both updates will simplify the patient and physician experience.

In Europe we are also making positive progress, having recently received an optional oral lead-in label update from the European Commission.

Next year at AIDS 2022, we expect to present data from the SOLAR trial – a Phase 3b head-to-head efficacy trial comparing *Cabenuva* and *Biktarvy*. We believe long-acting regimens are the future of HIV, and with at least a five-year head start versus the competition, we expect to remain leaders in this space.

### **Shifting the paradigm towards LA for pre-exposure prophylaxis (PrEP) Cabotegravir: 1<sup>st</sup> LA regimen for HIV prevention**

Let's switch now to a strategic priority for our HIV business – the prevention of HIV infection, commonly known as PrEP. Cabotegravir for PrEP is a new long-acting injectable, dosed every two months for the prevention of HIV, and offers the potential to transform the

shape of the HIV epidemic. The FDA has given it breakthrough designation with a PDUFA date of 23 January 2022.

US patient demand for a long-acting injectable for PrEP is high. The stigma around PrEP use and the perceived hassle of daily dosing are currently top drivers of discontinuation of PrEP.

Prescribers express concern around their lack of ability to observe adherence with current PrEP options, and cabotegravir addresses these concerns.

In the US, less than 25% of those who could benefit are currently taking PrEP. This is despite research currently published by the CDC, which shows that many people are routinely engaged in behaviour that could make them vulnerable to HIV, such as not using condoms, having sex with multiple partners, or being treated for sexually transmitted infections.

We believe the US PrEP market is strong and viable – approximately £1.5 billion in value today. We expect this to more than double over the next decade to reach £4-5 billion.

The US market is expected to grow further because there is significant motivation for prescribers and health systems to increase PrEP among people vulnerable to HIV, and the US government continues to focus on the goal to end the HIV epidemic by 2030, with an ambitious target to reduce new infections by 75% by 2025.

If approved, we believe cabotegravir will present a new and persuasive option in the PrEP market – dosed every two months, with superior efficacy to the current standard of care.

**LA pipeline with opportunity for revenue renewal post dolutegravir LoE  
Portfolio transition through decade with LA regimens c.£2 bn in sales by 2026**

I will now walk you through the expected shape of the HIV business through the decade, and our ambition to retain our leadership position as innovators in HIV. Between 2021 and 2026 our HIV business is expected to grow mid-single-digit CAGR driven by *Dovato*, *Cabenuva* and Cab PrEP. By 2026 we estimate long-acting regimens will generate around £2 billion of our sales.

We are excited by our early-stage development pipeline, which we believe offers potential for revenue renewal from 2026 onwards. By 2031, we estimate 90% of our business will be in long-acting regimens, delivering significant value to patients, and enabling our HIV business to deliver attractive growth.



I will now hand over to Dr Kimberly Smith to take you through the transition to long-acting regimens and our pipeline.

### **Innovators and disruptors**

**Kimberly Smith:** Thank you, Deborah, and hello, everyone. We are now on slide 16 and this fantastic image of Warren, who is living with HIV in Alabama.

It is great to have another opportunity to talk to you about our exciting year, and our continued role as innovators and disruptors in HIV.

It is an appropriate time for reflection. This year we observed the 40<sup>th</sup> anniversary of the first cases of AIDS. I began my career early in the epidemic, and I look back at that time as the 'bad old days'. Young, mostly gay men were dying, and there were no treatments available.

It was just over 30 years ago when the first antiretroviral for HIV, developed by then Burroughs Wellcome, was introduced. From then on, steady improvements in research have brought us new classes of treatment, and today, modern antiretrovirals have transformed the nature of the disease, changing it from a death sentence to a manageable chronic condition.

Because of the significant progress in better treatments for HIV, people living with HIV are thankfully living long lives, but now they are facing new and evolving sets of challenges, mostly associated with the cumulative effects of ageing combined with being on antiretroviral therapy treatment for life.

These challenges can include issues with tolerability, safety, resistance, dosing schedules, drug interactions and convenience. Over the years, patients have consistently asked us to find medicines that will give them options they need to overcome those challenges, and ViiV has led a paradigm shift with the change to two-drug regimens and long-acting regimens.

At ViiV we aim to take a deeper and broader interest in HIV and AIDS than any company has done before. That entails stepping beyond the development of innovative medicines and care for people living with HIV, to research to better understand the barriers that stand in the way of getting to the end of the epidemic.

## **Most innovative pipeline in the industry**

HIV has evolved, and as you can see with this slide, ViiV is leading that evolution. Let me walk you through our journey and our industry-leading pipeline, which is setting the pace for progress.

It begins with our gold standard dolutegravir-based regimens, which have given rise to the innovative, paradigm-changing two-drug dolutegravir-based regimens.

We are also the first company to deliver long-acting therapy, and with the first approved long-acting two-drug regimen.

But our focus isn't just on the broad population of individuals who are living with HIV; we focus on all patients. Our mission is to leave no person living with HIV behind.

Our attachment inhibitor, *Rukobia*, is a perfect example of that. This is the drug that will impact a much smaller number of lives, but it impacts individuals who have few or no treatment options left, and it has been incredible for us to experience the impact that *Rukobia* has had on individuals, literally saving their lives.

So, what's next? We will continue to evolve long-acting regimens, and we believe there is a lot of room for even better regimens. We want to offer a self-administered regimen, as well as ultra-long regimens that will take us past dosing every two months to intervals of every three months or longer, and we will do that with assets with new mechanisms of action, which I'll describe in more detail.

We have also entered the prevention space, and just like we have with HIV treatment, we are transforming prevention, and we are hoping in January to launch the first long-acting PrEP, but, ultimately, we want to be a part of curing HIV. Yes, it is incredible to see HIV move to being a chronic, manageable disease, but we won't stop until we see the end of the epidemic.

## **Industry-leading innovation creating new options for people living with HIV**

ViiV has been at the cutting edge of developing new options for patients.

These are not accomplishments that have happened overnight. We've been out in front of HIV since our company was created, and since that time we have achieved a remarkable lists of 'firsts':

- The first second generation integrase inhibitor;
- The first approved two-drug regimen;

- The first attachment inhibitor for highly treatment-experienced people living with HIV;
- The first approved long-acting injectable regimen for HIV;
- The first long-acting injectable for PrEP, and we have taken that first long-acting injectable for PrEP into the first head-to-head study of PrEP agents, and showed superiority of long-acting cabotegravir over daily oral pills.

There are many reasons why we are first. We have built a company of people who are passionate about HIV. Remember, we are the only company that's 100% focused on HIV, and so if that's your passion in drug development and education, then ViiV is where you want to be, and that has fuelled our culture with a united focus to deliver for people living with HIV.

Our legacy in HIV is long. Our experience has allowed us to be efficient at moving products forward, and we've had multiple assets to choose from.

We have also been willing to take risks, and it has paid off.

### **The future of HIV treatment is LA**

I would like to underscore what Deborah said earlier. We are now, and expect to continue to be the leaders in long-acting therapies for HIV. We know this is the future because we have heard it directly from patients.

Seven out of ten people living with HIV told us that they are interested in a long-acting regimen because of the challenges that exist with taking daily pills.

We've also heard from patients who are on long-acting as part of our clinical trials. In our pivotal trials, nine out of ten people preferred a long-acting regimen to daily orals, and the reasons behind this are clear. There are significant challenges with daily therapy, with fear of HIV status disclosure, stress and anxiety about staying adherent, and the daily reminder of living with HIV, which is highly stigmatised. These are the unmet needs that we are trying to address.

What made me most proud was to hear from patients in our clinical trials that our long-acting therapy gave them freedom and liberated them from some of the anxieties that I have mentioned. It's been thrilling to be a part of that.

## **The future of HIV treatment is ULA**

We pride ourselves on our strong relationships with patients, providers and the HIV community. What makes ViiV unique is the way we seek patient and provider insights and use them in our pipeline and portfolio strategies.

Our confidence in the future of long-acting is based upon those insights, and I want to highlight a couple of people who have impacted our work.

The first is Patricia, who is in her 50s and lives in Germany. Patricia was diagnosed with HIV in 2005, so she has been living with HIV for almost two decades and she is tired of taking pills every day. She doesn't want people to know she has HIV, so she keeps her medicine cabinet at home locked.

What she wants to do is take her medicine as infrequently as possible. She wants to go to the clinic, get her treatment, and then forget about it.

For Patricia, an HCP-administered ultra-long-acting regimen could provide an even better patient experience with less frequent visits.

## **The future of HIV treatment is self-administered**

Next we have Eric. For Eric, the future of HIV could be a self-administered regimen. Eric is 39, he lives in New York. He is not concerned about people finding out about his HIV status because he is 'out' to his family and friends, so he doesn't mind having medicines in his home.

Eric wants to control where and when he takes his meds, and he prefers not to come into the clinic every two months for a self-administered injection, so for someone like Eric, a monthly, self-administered injection could be a regimen of choice, and that was reinforced with our market research, where we heard that monthly self-administered injections were preferred over taking a pill every day or every week, and they were preferred over clinic visits every two months.

Eric doesn't want to be tied down. He wants to have the flexibility that a self-administered regimen would bring.

These two patient profiles are of real people, and they are just a sample of those who have expressed their desire to have ultra-long-acting regimens, which we define as every three months or longer, and self-administered regimens, which could be given every month or longer.

These two regimens, along with the long-acting regimen that we already have on the market, *Cabenuva*, which is administered every two months, would offer a comprehensive set of long-acting options for people living with HIV.

### **The power of the integrase inhibitor ViiV continues to lead the industry**

So when we build the next generation of long-acting therapies, how will we do it? We'll start with the foundation of an integrase inhibitor, and here is why.

Integrase inhibitors have proven themselves to be the unquestioned gold standard antiretroviral agents because of their potency, tolerability, and high barriers to resistance.

INSTIs are now part of a preferred or recommended antiretroviral regimen in HIV treatment guidelines throughout the world.

When we developed dolutegravir, we compared it to each of the third agents that were guideline-recommended at the time. That list included non-nucleosides, reverse transcriptase inhibitors, boosted protease inhibitors, and first-generation integrase inhibitors, and in each circumstance, dolutegravir demonstrated superiority.

The use of integrase inhibitors has grown on the back of that incredible demonstration of efficacy, long-term tolerability, potency and high barriers to resistance. So the use of integrase inhibitors has grown dramatically, as you can see on the chart on the right. From 2010 to 2021 the integrase inhibitor class has claimed 70% share across the top nine markets. I want to point out the dramatic trajectory that began in 2013 when dolutegravir was approved.

Integrase inhibitors are now the gold standard. As a clinician, you want that trusted foundation when you are building a regimen. The field trusts integrase inhibitors and will not be quick to move away from them as an anchor for future regimens.

The future of long-acting medicines is based with integrase inhibitors, which is why we are building our next wave of medicines with our integrase inhibitor - cabotegravir.

### **Novel MoAs offer multiple options for development of new LA regimens**

So we'll start with an integrase and what will we do next? We will add a second agent. *Cabenuva* is cabotegravir plus rilpivirine. It's potent, it's effective but for some individuals who have previously failed a non-nucleoside reverse transcriptase inhibitor, *Cabenuva* is not a treatment option for them. So we do need to have other agents with novel mechanisms of action to allow more people to take advantage of long-acting regimens.

We have a very diverse portfolio of agents with novel mechanisms of action to combine with cabotegravir to create the next generation of long-acting medicines. We won't be taking all of these assets to late-stage but it is incredible to have this many to work with and, ultimately, to choose from.

The graphic describes the steps in the HIV life-cycle. We have a number of agents with novel mechanisms of action to attack many of these steps and I will walk you through them.

Let's start on the left side of the slide with broadly neutralising antibodies or bNAbs. They are antibodies that are identified in a rare proportion of the population who generate them naturally in response to the virus. These individuals generate antibodies that have the ability to neutralise not just their own virus but to neutralise a broad range of viruses.

We have in-licensed N6LS from the NIH Vaccine Research Center. We chose this particular bNAb because of its great potency and breadth, covering 97% of a broad range of viruses it was tested against and, among the bNAbs that bind to the CD4 binding site on gp120, N6LS was among the most potent.

We have brought N6LS into ViiV and we are currently in Phase 2a, our proof-of-concept study, and are really excited about the antiviral activity we are seeing in the preliminary data which we will be sharing in mid-2022. We hope to get the N6LS and cabotegravir combination into the clinic in 2023.

The additional benefit of the bNAb is that it could be a dual-threat. It not only has direct antiviral activity but it has the potential to enhance the host immune response to the virus. The antibody attaches and identifies to the immune system this is the cell you want to destroy, and that could help control HIV and potentially lead to reduction in the latent viral reservoir, which is part of our work in the HIV cure space.

We are excited about N6LS as a therapeutic agent but also as part of the overall cure strategy.

Next we have to agents that are NRTTI. NRTTIs have a two-prong mechanism of action, inhibiting translocation and acting as chain terminators, similar to other nukes.

Next is the capsid inhibitor. This is an important agent because it blocks the ability of the virus to make and break down the capsule that protects the blueprint of the virus as it transitions from the cytoplasm into the nucleus of the cell.

Next our integrase inhibitors, which block the virus's ability to integrate viral DNA into host DNA. You will see VH184 on this chart, which we believe will be our third-generation INSTI and I will tell you more about that in a moment.

In addition, we have two formulations of cabotegravir. The current formulation is CAB200 and we have a more concentrated version CAB400. We believe that CAB400 may be amenable for self-administration and allow us to use more product with lower volume.

Finally, we have the maturation inhibitor, which works late in the HIV replication cycle, blocking one of the last steps in protein processing, the gag cleavage step, which is necessary for the creation of a mature virus.

It's incredible to have this diverse group of agents to choose from and, potentially, to combine with cabotegravir.

### **The future of LA is in our innovative pipeline Multiple pathways to self-administration and ULA therapies**

We have mapped out the future of long-acting in our pipeline. For now, it's cabotegravir combined with this broad range of agents with novel mechanisms of action. And importantly, what this slide shows you is that many of these assets have the potential to be either self-administered or ultra long-acting. They will allow us to have choices to find the best self-administered regimen and the best ultra long-acting regimen. To be clear, we do not intend to develop all of these agents with cabotegravir. We intend to choose the best combination, led by the science, and having multiple options to study is an enviable position to be in.

### **Our strategic collaborations**

A lot of our success has come from our strategic partnerships. We have selected excellent partners and we think of ourselves as the partner of choice. We have had a long-term partnership with Janssen to develop *Cabenuva*. We are now exploring the possibility of expanding that partnership to evolve *Cabenuva* to an ultra long-acting regimen, expanding from dosing every two months to dosing every three months or longer.

Just this past June, we made an exciting announcement about a partnership with a life sciences company called Halozyme and I will explain on the next slide how that impacts our portfolio.

By now, most of you will be familiar with Shionogi, one of our shareholder companies. We have partnered with them on our successful integrase inhibitors,

dolutegravir and cabotegravir. They will, once again, play a major role in the development of our third-generation integrase inhibitor, which I shall talk more about in a minute.

One of our other exciting partnerships is the unique industry academic partnership we have with the University of North Carolina at Chapel Hill and the creation of a biotech called QURA. Our scientists work side by side with UNC scientists at the HIV Cure Center in the same lab, combining their early science expertise with our drug development expertise to find a cure for HIV. We hope that our work with them will bring a latency-reversing agent into Phase 1 studies in 2022.

### **Expanding our portfolio of LA therapies with Halozyme**

I want to talk to you a little bit more about the deal with Halozyme, and why I am so excited about it and what it brings to our portfolio. Halozyme makes a unique product that we refer to as PH20. When PH20 is injected subcutaneously, it creates a temporary expansion under the skin, allowing increased volumes of medicine to be delivered subcutaneously without added discomfort to the patient.

How does this translate to our long-acting pipeline? With the ability to give a larger dose, we will be able to expand the interval between doses. The perfect example is cabotegravir. With *Cabenuva*, when we increase the volume of the injection by 50%, we double the interval between doses. It is a 2ML dose of cabotegravir for a monthly interval, and a 3ML dose for a two-monthly interval, but that is the maximum dose we can give without PH20.

We believe that PH20 will allow us to give larger doses and with cabotegravir's long half-life, dosing regimens could be extended to intervals well beyond two months. That is the potential of PH20. This expands the opportunity for ultra long-acting regimens combining cabotegravir with our pipeline products for treatment and for PrEP. We are looking to expand the dosing interval for Cab for PrEP beyond every two months to at least every three months in combination with PH20. The exclusive collaboration covers targets for nearly all of the assets in our pipeline.

We are extremely excited that, over the course of the next year, we will start to see Phase 1 studies for each of these assets in combination with PH20.

**20 years of integrase inhibitor success with Shionogi  
Exclusive collaboration on 3<sup>rd</sup> generation INSTI inhibitor has potential for ULA regimens**



Now let me share a few more details about our recent announcement with Shionogi with whom we have established a 20-year heritage of developing integrase inhibitors for HIV. Our most recent collaboration with Shionogi is for a very exciting third-generation integrase inhibitor called VH184.

The preclinical data has shown that VH184 has a high genetic barrier and a resistance profile that is distinct from dolutegravir and cabotegravir. Its long half-life may support its development as an ultra long-acting medicine that could be delivered with infrequent dosing up to every six months. We believe VH184 could anchor the future pipeline of innovative, long-acting therapies for HIV beyond 2030, with an expected loss of exclusivity beyond 2039. This will be combined with our agents with novel mechanisms of action that I described to you previously.

Our preclinical studies for this asset are under way. We intend to initiate the first time in human studies with VH184 by 2023, and we hope to have the next generation of integrase inhibitors to continue our pioneering leadership in this space.

### **The future of HIV prevention is LA The PrEP landscape and unmet need**

Let's shift gears now and move from long-acting treatment to long-acting prevention for HIV.

Deborah has described the expected increases in the size of the PrEP market and, importantly, the PrEP landscape has a significant amount of unmet need.

Globally, more than 50% of people say they feel burdened by the idea of having to remember to take their medicine every day to prevent HIV and, importantly, PrEP has not penetrated the communities who need it most. Sixty-nine percent of PrEP users are white, just 13% are Latinx and 11% black. Yet black American and Latinx people represent nearly 70% of new cases in the US. We also know that, while daily PrEP is effective, it is limited by inconsistent adherence.

We know there is interest in long-acting PrEP. Our research shows us that those who are currently taking daily oral PrEP, or those who have tried it and stopped taking it, are still interested in long-acting cabotegravir. The majority of people who have never been on PrEP have also expressed interest in a long-acting regimen. The presence of long-acting PrEP will allow us to reach more significant proportions of the individuals who could benefit from it.

## **Major opportunities in PrEP**

### **Cabotegravir for PrEP: offers potential to transform the shape of the epidemic**

People have said they want long-acting PrEP for convenience and, while we can tick the box for convenience, what we can show most convincingly is the superior efficacy of long-acting PrEP over daily pills. You are aware of the data we have shared this past year from the HPTN 083 and 084 studies, comparing long-acting cabotegravir to oral daily Truvada in men who have sex with men, and transgender women on 083 and cisgender women in 084.

The data are outstanding and, as you can see from this graph from the 084 study in women, the rising solid purple line represents increasing new cases on the Truvada arm, while the red dotted line across the bottom of the graph shows a much lower number of cases in the Cab arm; HPTN 083 had similar results.

These pivotal studies demonstrated superior efficacy in men and women, three times to nine times better than oral Truvada, and both studies were stopped early for efficacy with all participants being offered the opportunity to switch to cabotegravir. This is unprecedented in HIV prevention.

These remarkable data form the basis for our file with the FDA which we completed in July. We have received both Breakthrough Therapy status and Priority Review status, and expect a regulatory decision on 23 January 2022. If approved, we believe cabotegravir will represent a new and persuasive option in the PrEP market, dosed every two months, with efficacy that is superior to the current standard of care.

### **The future of HIV prevention is LA**

Those data are really good news for people like Harvey, who is our third patient profile. Harvey is a 31-year old who lives in Florida, he is aware that he might be vulnerable to HIV and wants to protect himself. He tried oral PrEP a year ago and had a hard time taking it every day and experienced some GI side-effects. Harvey wants PrEP without the side-effects he experienced with oral PrEP. He wants something that is low hassle and is an easy fit with his busy professional and social life.

We believe that a clinic-administered injectable, dosed every two months, could offer certainty, discretion and long-term protection, characteristics that are often appealing to dissatisfied oral PrEP users.

## **Maintaining HIV leadership beyond dolutegravir INSTI-based LA regimens anchor current and future pipeline**

I want to finish by talking to you about the timeline for the delivery of our pipeline over the next decade, which illustrates the strength and breadth of our innovation.

In the near term, in 2022 through 2023, we will have a significant amount of data from our early pipeline. In 2022, you will see Phase 1 data on CAB400, Cab in combination with PH20, proof-of-concept data showing the antiviral potency of N6LS and Phase 1 data for N6LS in combination with PH20.

In 2023, we will see data delivery for our other agents with the unique mechanism of action we have talked about. We will deliver Phase 2B data for the maturation inhibitor 254 programme and, in addition, we will see data for the NRTTI and the capsid inhibitor in combination with PH20. We will also see proof-of-concept data for those assets. We also expect new data from Janssen on rilpivirine.

Our expectation is that we shall be able to initiate our Phase 2b study of cabotegravir in combination with N6LS in 2023.

By 2024, all of the data that we have gathered between now and the end of 2023 will enable us to make our partner selection so that we can initiate late-stage studies in the 2024 timeframe. That will allow us in 2025-27 to deliver the first self-administered, long-acting regimen for treatment and also we hope to launch an extended interval cabotegravir for prevention.

From 2027, we expect to see a launch of our first long-acting regimen with dosing of at least every three months, anchored by cabotegravir with one of the agents with a novel mechanism of action.

Post-2030, we are looking to have the next generation of ultra long-acting with dosing every six months, anchored by our new third-generation integrase inhibitor VH184, combined with an agent with a novel mechanism of action.

Our ultimate goal is always a cure of HIV. It is certainly my hope, and that of my team members, that we will contribute to getting there by 2030 if not sooner.

Today, we have shared our rationale for, and our belief in, our long-acting regimens as the future of HIV treatment and prevention. I have shown you what is in the industry's most robust and innovative pipeline based upon years of success, experience and patient

insights. I have shared with you the exclusive partnerships that are going to help us build the next generation of long-acting regimens and I have shown you that we are in the enviable position of having multiple assets to choose from to partner with cabotegravir, which will take place over the next couple of years and will take us to the next decade and beyond.

Our strategic mission is to develop novel therapies for people living with HIV. Our company mission is to leave no person living with HIV behind and our presentation today demonstrates our commitment to that mission. With that, I will turn it back to Deborah.

**Deborah Waterhouse:** Thanks, Kim.

### **Getting ahead of HIV**

Our ambition is to get ahead of HIV, driving towards the ultimate goal of a cure. We shall do this by continuing to reshape the HIV treatment and prevention landscape, maintaining innovation leadership in the long-acting space. Through strong commercial execution, we expect to deliver mid-single-digit sales growth over the next five years. We will consolidate our multi-year head start in long-acting injectables for treatment and prevention with cabotegravir becoming the foundational medicine.

Our exciting long-acting pipeline provides the opportunity for revenue renewal post the dolutegravir loss of exclusivity and it offers people living with HIV freedom from daily oral medication and governments the ability to transform the shape of prevention efforts. With that, I will hand it back to David to open up for Q&A.

### **Question & Answer Session**

**David Redfern:** Thanks, Deborah. As Deborah said, we are now happy to open it up to Q&A so I will hand you back to the operator. [*instructions given*]

**Andrew Baum (Citi):** A couple of topics please. First, on R&D, I wonder if you can comment on whether you are seeing or are concerned about dose-dependent mitochondrial toxicity with either of your NRTTIs in light of the lymphocyte reductions seen with Merck's islatravir?

Secondly, on the commercial topic, when I talk to infectious disease physicians they cite the burden they have for frequent administration of IM injections in the clinic, so could

you update us on how you are thinking about how you would seek to implement the use of alternate injection sites for pharmacy use in order to alleviate the burden?

Separately, when you talk about self-administered injections, my understanding is that *Cabenuva* requires refrigeration. Given this patient population and the cost of these drugs, that doesn't seem to be desperately practical for many of the patients infected with HIV, so how can you seek to resolve that? Many thanks.

**David Redfern:** Thanks, Andrew. Let's start with your important question with Kim on the mitochondrial lymphocyte issue that Merck have potentially seen and how that might translate across. Kim, why don't you start?

**Kimberly Smith:** Thanks, Andrew, for the question. With regard to the limited amount of information that we have seen on this lymphocyte reduction, it is hard to draw definitive conclusions without seeing a full illustration of the data; we have basically just seen a hint of it. That said, though, clearly lymphocyte increases are the hallmark of HIV successful treatment, particularly elevations in CD4 cell count, so blunted recovery or declines in CD4 are certainly very concerning.

I am certain that Merck is working hard now to try to get to the mechanism of action, and you mentioned mitochondrial toxicity. That is probably in the differential of things that could potentially be causing this toxicity but we have to wait to see what they find.

Clearly, as you saw, we have two NRTTIs in our pipeline, so we shall be watching with great interest as we understand exactly what the mechanism is and whether or not this particular toxicity is present with our agent. However, at this point, I believe it is a little early to be able to draw conclusions.

**Deborah Waterhouse:** There are two questions that came for me, Andrew. First of all, there are a couple of label changes that will be made in the US and have already taken place in Europe. The oral lead-in will become optional, so you will be able to go direct to inject which is taking away a little of the complexity that is there at the moment. Secondly, we will be seeking a licence in the US as we have done in Europe for the injection of *Cabenuva* to take place every two months, which again takes away some of the burden, because in the US it is an every month injection at the moment.

We are moving towards alternative sites of care. Many physicians, particularly in the bigger institutions, are quite happy to undertake the injections of *Cabenuva*, which is a source of revenue for them. However, in places where they are not happy to do so, we do have local alternative sites of care which are available.

As far as pharmacy, we are exploring the opportunity to have *Cabenuva* administered in pharmacies but we have not progressed that at the moment, because we are still working our way through getting the processes established within the large sites of care and getting alternative sites of care set up.

To the third part of the question on refrigeration, it hasn't been an issue in clinics and healthcare settings. We did go out and asked the question of patients: would you be happy to have a box - and we know roughly how big it would be - in your fridge? It would need to be refrigerated between the time you pick it up from the pharmacy and the time you take it, and that did not appear in our research to be a barrier. The people who will be appropriate and keen to adopt this medicine are people who are out with their family and friends and who are not worried about anybody seeing it in the fridge for the period that it would be sitting there. We don't expect it to be that long, because you would normally pick it up, bring it home and administer within a short period of time.

**David Redfern:** All I would add, Andrew, is that it has definitely required some set-up of the practices to run injectables and run the clinics up front but now we are seeing that multiple clinics have these protocols and processes in place. As time goes on, I believe that the whole administration is less and less of an issue.

**Kimberly Smith:** Could I add something there, David? I want to add a quick comment in response to that question about alternative sites, because we do have an implementation study that is currently under way looking at alternative sites. Therefore, we will have some data to help inform how we can operationalise that in the most effective way.

As far as the issue around self-administration and refrigeration, I really want to underscore the point that Deborah made. There is a unique population of individuals who want self-administered. These are people who are more likely not to be hiding their HIV, they are more out about it. Whereas the individuals who are seeking long-acting *Cabenuva*, for example, want the privacy, so there are different sets of individuals who are more ideal either for a self-administered product or an ultra long-acting product.

**Graham Parry (Bank of America):** Thanks for taking my questions. First, on slide 31, you say that by 2024 you will have done partner selection for the self-administered regimen and ultra long-acting regimens to progress to Phase 2B and 3. Can you just run us through what the options are that you are testing or deciding upon here? For

self-administered, is that CAB400 plus novel MoAs, and for ULA is that Cab or CAB400 that is going into the Halozyme technology?

Can I just confirm that the maturation inhibitor is not part of the ULA collaboration with Halozyme and why not?

Secondly, when do you expect to have first Phase 3 ultra long-acting combo data published to the market?

My third and final question is a big picture: when you think through the long-term strategy in HIV beyond dolutegravir patent expiry, do you envisage that the long-acting portfolio that you have will see HIV sales materially above the 2027 level in 2030 and beyond? Thank you.

**David Redfern:** Great, thanks, Graham. Kim, why don't you talk about all the multiple options? You gave an overview but it is probably worth going through it.

**Kimberly Smith:** We are basing our long-acting regimens on cabotegravir. CAB400 may be the best option for self-administered or it may be CAB200, we are testing both. Our main point is that we have multiple formulations to meet the needs, so whichever combination is best tolerated is what we will move forward with.

We have the option as you saw in what we call the triangle slide where many of these novel mechanism of action agents that we are talking about could be combined with Cab in self-administered. Some of them have the ability to be either self-administered or ultra long-acting. As we get more of those Phase 1 data, in particular the Phase 1 data in combination with Halozyme, that is when we will have a better idea about exactly which combinations are best for ultra long-acting and which combinations are best for self-administered.

As you can see, I have mapped out the timeframe of when we are going to see those data, which tells us that we should be able to initiate Phase 2B with Cab and N6LS in 2023. In 2024, we will initiate additional studies. I cannot go into any more detail than that without having data in front of me, which we will have, as you see mapped out here, over the course of the next year.

Regarding the question that you asked about MI and Halozyme, we decided from the beginning that we would not include that in our targets but it is possible that we will expand our partnership with Halozyme to include maturation inhibitor if we find that there is value in looking at that combination.

**David Redfern:** Great, thanks, Kim. Deborah, do you want to talk about the shape of the business and particularly beyond 2027?

**Deborah Waterhouse:** Sure. Graham, let me take us back to the Investor Update that GSK did on 23 June. Emma and Iain presented a picture which by 2031 demonstrated that GSK would be delivering around £33 billion of revenue. The first question I want to answer before I dive into ViiV is that we are very confident that GSK can offset the loss of dolutegravir through the medicines that they have launched today and those that they are launching from the pipeline that they have, so that is very important.

Within that £33 billion, we obviously have Cab for PrEP and *Cabenuva* but the early development pipeline is not part of that; it was separate because it's a little bit early. GSK are in a very positive place and let me just talk about ViiV.

We believe that, if things evolve in the way that Kim has described, so that we have our ideal regimens selected by 2024 and we deliver them within the timelines that you have seen on slide 31, there is a significant amount of revenue renewal that will have taken place by 2031 and beyond. We are obviously able to match cabotegravir up with our new mechanisms of action which have IP out to the end of the 2030s, and then the Shionogi integrase has IP again out to the end of the 2030s.

I won't give you a specific number today, Graham, but what I can say is that there is an opportunity for revenue renewal if what Kim has described today comes to pass. Even if that does not happen, it is really important to know that GSK are confident they can get to that £33 billion number and the company will large successfully moves through the dolutegravir loss of exclusivity.

**Graham Parry:** Thanks and when do you expect to have first Phase 3 ultra long-acting combo data that will be published externally to the market?

**Kimberly Smith:** You will have to follow along with that timeline. If we initiate Phase 3 studies in the 2024 timeframe, then we will have data in the 2024 timeframe then we would have data in late '25/'26 timeframe, depending on the speed and momentum of the trials, so that's when we would expect to have that, based upon the timelines that I've mapped out there.

**Graham Parry:** Thank you.

**David Redfern:** Thanks, Graham. Let's move on to the next question.



**Laura Sutcliffe (UBS):** Hello, thank you. Firstly a high-level question, you have a lot of options in the pipeline, but could you just give us an idea of what you think the ideal long-acting portfolio looks like if all your assets look feasible? Do you want a product in every bracket of dosing frequency to be competitive, or are there a couple of key wins in there, so for example a Q6 months that you see as critical to overall success?

Then on PrEP, it seems like the PrEP market could move to more of an on-demand model, do you think you can stop that, or shape it by offering the right long-acting products? I know you have some great data, but I'm thinking more about how you translate that into uptake and use.

Then lastly, just going back to your event in June, could you talk to the greater than £2 billion that you envisage by mid-decade for long-acting products, and just tell us if you have in mind a split between PrEP and treatment? Thanks.

**David Redfern:** Thanks, Laura. I think Kim can best talk about what our ideal profile is for long-acting. Remember we're trying to ideally create a long-acting self-administered treatment and an ultra-long-acting treatment, as well as a longer-acting PrEP, but Kim, why don't you be a bit more specific on exactly what you're seeking?

**Kimberly Smith:** When you think about what is an ideal self-administered regimen, it's one that actually is extremely well-tolerated by the patient, so one that causes them the least amount of injection site reactions, that's basically easy for them to give to themselves, every month at a minimum, so that's the target profile that we have. Really high tolerability, dosing intervals of a month at least, if not longer, that, in a nutshell, is what we're looking at for self-administered.

For ultra-long-acting, we really want to make a step up from where we are now, which is every two months, so every three months would be an improvement, that means visits four times a year, every four months would be an improvement, meaning visits three times a year, but yes, we would like to get to every six months, that's a high bar.

I think, Laura, it's important to remember how far ahead of the competition we are, so the ambition of our competitors that was articulated previously was to have an injectable regimen in 2027, well, obviously we have a long-acting injectable regimen in the clinic now, by 2027 we'll be bringing more injectable regimens that have improved profiles, and when I say an improved profile from an ultra-long-acting standpoint it means fewer visits a year, longer dosing intervals. Those are the profiles that we're focused on, and again I think what is exciting is we have many choices. Andrew's question around the challenge that the NRTTI

has had, is a perfect illustration of why it's so important to have multiple classes in your pipeline, so that if one particular class runs into unexpected problems, you're not lost, you have many alternatives. That's what's exciting about our portfolio, is all of that diversity.

**David Redfern:** Great, thanks Kim. I think on PrEP, we see huge potential to develop the market, particularly in the US, and a significant opportunity over time.

**Deborah Waterhouse:** Yes, I agree with you. Just to describe the market in a bit more detail, Laura. In the US, where most of the value sits, you have about 1.2 million people who should be taking PrEP to protect themselves from acquiring HIV. That pool is currently about 200-250,000 people are taking PrEP, so clearly there's a significant opportunity to grow that market.

The question you were asking more specifically was, is it an on-demand market, and the answer is yes, you don't stay on PrEP for a lifetime, generally speaking you stay on PrEP for 10-12 months when your lifestyle means that you are at risk, and it would be wise for you to protect yourself. That 1.2 million cohort have people coming in, as their lifestyle at that particular moment means they are part of that pool, and then you have people who are moving out of that pool when their lifestyle changes, so maybe they have only one partner, or they get married, or whatever, and that risk is no longer there for them.

Think of it as a pool that's usually about 1.2 million people, but with those people coming in and out, and people taking treatment on average for about 10-12 months. Our job is to give people the opportunity to switch from the oral that they're on today, onto the long-acting injectable, because we have such great data, but then over time to expand the market, because as I said in my presentation earlier on, some of the places where HIV acquisition is at its highest are hard to reach groups, and we're looking to expand the coverage of PrEP in some of those hard to reach groups, and that's very much supported by the CDC and the NIH, because that's the only way they'll reach those ending the epidemic targets that have been set.

The third thing you asked me was about the split of the £2 billion. At the moment we're not going to split it out, because honestly, Laura, I'd like to tell you that I was really that good at forecasting, but it's really hard for new products that are going into clinics, and new processes and everything to be implemented. We're very confident in the £2 billion, but the exact split I'm not going to share, because I think it's just a bit too early to do that, so as we get closer to '26 we'll definitely be able to be more specific on that and I'll be happy to share it.

**David Redfern:** I think what we can say, though, is both prevention and treatment with cabotegravir make meaningful contributions to it.

**Deborah Waterhouse:** Definitely, and don't forget that the prevention, for the PrEP, is all new revenue, because we're not in PrEP at the moment, whereas with treatment we do take a lot of business from our competitors – I think at the moment 53% of our *Cabenuva* is coming from Gilead, but it is also cannibalising some of our own business, so in PrEP for us it's all new revenue, so it means it's extra-valuable, if I can put it like that.

Thanks, Laura.

**James Quigley (Morgan Stanley):** Hello, thank you for taking my questions. You highlighted the VH184 as a potential backbone for greater than six months' treatment, and I'm just wondering if you could talk through cabotegravir, which was highlighted as a greater than every three months' treatment, from what you've seen so far.

What would be your expectations for VH184 relative to *Cabenuva*? Then on the HIV cure, where are you with candidate selection and could you give us an overview of your approach and mechanisms for latency reversal. You mentioned the broadly-neutralising antibodies could play a role in priming the immune response, but what are your timelines in terms of when we could see the initial proof of concept data from the study? Thank you.

**David Redfern:** Great, thanks James. We're very excited to have licensed the integrase from Shionogi for next generation, I think it does have an important part to play. It's early, but Kim, maybe you want to elaborate a bit more on the reasons for doing the deal, and what it might bring, as well as James' great question about cure, which we're definitely excited about, and there's lots of progress.

**Kimberly Smith:** Thank you, James, for the question. VH184 is a very exciting compound because it has a potency that we expect to be comparable to dolutegravir, and it has a half-life that is longer than cabotegravir, which is why we believe it gives us the opportunity to get to six-month regimens. It also has a unique resistance profile that is distinct from dolutegravir and cabotegravir, and so it potentially could even salvage previous failures of integrase inhibitors, so it is very exciting to see this. Literally, when we look at the profile of this product in comparison to something like dolutegravir and cabotegravir and we see strength above those, it's kind of hard to imagine, but it's very, very exciting.

Our intent, as I said, is that we're going to get this product in the first time in human as soon as possible, by 2023 is the timing that we have in mind, so I can't say much more than that because we don't have clinical data on this product yet, but again, the pre-clinical profile that we've seen is very, very exciting.

In the cure space our work with QURA has identified a candidate, it is QURA 086, it is an IAP inhibitor, and it is a product that we've candidate selected, and hope that by the end of 2022 we'll be able to get that into a first time in human as a latency reversing agent.

For N6LS, we think about that as potentially an agent that helps with clearance, so the concept of basically inducing the virus out of hiding, out of latency, and then finding a way to clear it, N6LS and other bNAbs have a potential to contribute in that space, so that's essentially our approach.

**James Quigley:** Could you follow up on cabotegravir and the potential dosing and given what you've said there with the longer half-life with the third generation integrase inhibitor, are you thinking that CAB400 could potentially go for six months, or are you now focusing more on the six months being the third generation?

**Kimberly Smith:** We'll have data with all of the formulations of cabotegravir in combination with PH20, starting next year we'll see that data, and that will tell us whether or not cabotegravir can give us a six month profile. We are very, very confident that it can give us at least a three months profile, but can it get to six months, we can't know until we have that Phase I data. We will test all the formulations in order to get to the best one, that gives us the profile that we're looking for.

**Peter Welford (Jefferies & Company):** Hi, thanks for taking my questions – just a couple. Firstly, with regard to the DTC, I'm curious what was the trigger to begin the DTC advertising, given some of the comments you made about still decreasing the burden with the oral lead-in becoming optional and also the Q2M. Why start DTC now, and risk potentially a poor patient experience, if you want to call it that, rather than potentially delaying until you have then the option when patients come in to offer them the full package? I'm curious about any comments about that.

Secondly then, just with regard to PH20, again, pardon my ignorance but do we have any long term data on chronic use of PH20? I'm aware it's used in a number of approved drugs, but I just wonder what the longest we have so far, as far as chronic use of that as an agent within a combination that's injected?

Then finally, just with regard to cure again, the idea of an HIV vaccine. Obviously you have GSK's vaccine expertise at hand, I don't think there is a vaccine against HIV and I know it's a torrid history here, but is there any thought about that for ViiV, or is it not an area that you want to be involved in? Thank you.

**David Redfern:** Thanks Peter. Deborah?

**Deborah Waterhouse:** Thanks, Peter. I can answer the first question really quickly, the DTC that we have launched is targeted very specifically to geographical areas where we have the health system up and running, and already prescribing *Cabenuva*, so where we've put the investment in DTC, is in places where we know the patient journey is set up to be successful. You do still have to go through the oral lead-in, but actually the early adopters are willing to do that, and obviously the early adopters are also willing to go for an every month injection, but obviously it is known in the community that it will turn into an every two month injectable if that was what the individual wanted later on. We've been very targeted and very specific, but what is so encouraging is that literally in the last eight weeks we've seen the number of people that are enrolling in our hub, i.e. the physician has taken the person living with HIV through the process and is now ready to initiate, that has doubled in the last eight weeks, so I'm feeling quite encouraged, particularly as we still have the headwind of COVID. That's a great question, thank you for that.

**David Redfern:** Thanks. Kim, do you want to talk about PH20 and what data there is on chronic use, and also our thoughts on the vaccine?

**Kimberly Smith:** Thank you. Probably the best example of long-term use of PH20 is in individuals with primary immunoglobulin deficiencies. Those folks have been using PH20 in combination with supplemental immunoglobulin for years, and in very large volumes, so there is quite a bit of experience with that along with other products; so the best place to see the long-term data for PH20 is actually on the Halozyme website, where it describes all of the collaborations, and there are lots of examples of individuals who have been on it for years.

With regard to the vaccine prospect, we're not currently in the vaccine space, but it's something that we are considering, so it's possible that we could get into the vaccine space, specifically focused on a therapeutic vaccine that could go along with the rest of our cure strategy.

**David Redfern:** Great, thanks Peter, let's move on to the next question.

**Kerry Holford (Berenberg):** Thank you very much, a couple from me, please. Firstly, on the pipeline, clearly you have much to work with, as you show in Slide 24, but I just wonder if you believe you have all the potential combinations that you would like to have for cabotegravir in-house, or are there other assets/mechanisms that you would be interested in in this HIV space that would mean you would consider external partnerships?

Then secondly, for clarification, you mentioned earlier Deborah, the IP for *Dovato* expiring in '28 and '29 in the US and Europe respectively, I wonder if you can just detail when in those years you expect the IP to roll off, whether there is anything different here versus the patent you have with dolutegravir. Thank you.

**David Redfern:** Thanks, Kerry. We certainly have a lot in the pipeline to be working on, but Kim, do you want to say anything else?

**Kimberly Smith:** As you heard, we really have assets in our pipeline that are tackling just about every target that's out there, but we don't stop, our discovery teams are continuing to always look for new potential targets, and new assets within the already identified targets, but we're always open to the possibility of partnership if it can bring about a new regimen that can be helpful for people living with HIV, we are always open to trying to move the field forward, so I would just leave it with that. Deborah, I don't know if you want to add anything to that?

**Deborah Waterhouse:** No, that's spot on.

**David Redfern:** And IP?

**Deborah Waterhouse:** IP. Kerry, the US patent, if we assume we're going to get six months' paediatric exclusivity, the studies are under way, they will report out in '23, so we're confident that we'll get that paediatric exclusivity, it's April '28 in the US then it's July\* '29 in the EU. You asked me a second question, there are additional patents, particularly on the two-drug regimens, and that's why we say at least 2028 and 2029, because obviously we do have additional patents and protection, and we'll just need to see how that unfolds around *Juluca* and *Dovato* towards the end of the decade, but in our modelling we've assumed the patents go April and July\*, '28 and '29 respectively, but we always fight for our IP.

\* corrected, assumes pediatric exclusivity

**David Redfern:** And I think cabotegravir, for modelling, you can add two years to that for both US and Europe.

**Deborah Waterhouse:** Yes, 2031 for Cab, but Cab is different, because obviously we will team Cab up with other mechanisms which have much longer IP out to the 2039, 2040, so that's why cabotegravir will be a little bit more protected, let's say.

**David Redfern:** Great, thanks. Let's move on to the next question.

**Geoffrey Porges (SVB Leerink):** Thank you very much for taking a question, and for all of the information. Maybe just turn a little bit to the US market, very much your comments have focused on the US market and particularly PrEP, and we've been wondering for a while how the payor environment might change in the US. Could you talk a little bit, first of all, about the mix of payors that you have in the US today, and then secondly, how the transition to injectable is going in terms of coverage, and particularly patient out of pocket cost; then what, if any, impact would you expect Build Back Better to have, if indeed it passes in the next couple of weeks, gets through the Senate as is? Thanks.

**Deborah Waterhouse:** Thanks for the questions. We have found that the data that we have for treatment with *Cabenuva* in the US has been helpful for payors and as a result we have 80% coverage, and that's a mixture of Medicare, Medicaid and the commercial payors, so I think we're in a very good position. In HIV the out of pocket is actually very limited, so that's not going to be a barrier to uptake in the main. Just to remind you, 40% of our patients sit in commercial, 60% sit in ADAP, Medicaid, Medicare, etc.

So far we're in a good position with *Cabenuva*, and Cab for PrEP we believe we have very compelling data, and that we'll also be able to secure good coverage, but we're still in the middle of negotiating, but having superiority data from two studies is obviously very helpful, and given that there is a focus on ending the epidemic, again, that gives us a lot of ambition around what we are able to achieve.

**David Redfern:** On Build Back Better, Geoff, I think it's all going to be in the detail as it goes through the Hill, and both the House and the Senate will probably make changes, so let's see how it comes out and then we can comment more fully.

Let's move on to the next question. We have quite a few more questions in the queue, we will extend by a little bit, but if you could endeavour to keep to one question, that would help enormously.

**Simon Baker (Redburn):** Thanks for taking my question, I will keep it to one. Just continuing with PrEP, as you've highlighted, PrEP is essentially a US opportunity, I was just wondering how much of that potential doubling comes from ex-US, and how sensitive is the ex-US market and payors within that to the duration of therapy? I would have thought that as you increase compliance by moving to long-acting, it makes it a more appealing proposition, but I just wondered what the current perspectives are around the world on that. Thanks very much.

**Deborah Waterhouse:** Thanks for the question. A majority of the value in the market today and in the future will come from the US. The reason that ex-US at the moment the opportunity is limited is that payors are using and buying generic Truvada at about €/\$20-30 a pack; however, what we are doing is talking to each individual country, because there are still significant amounts of new infections across Europe, 22,000 a year. To your point, Simon, what we are doing is sharing with them our data on adherence and obviously the superiority that we saw in 083 and 084, and putting together a case that this would be a good medicine to have available for those who are most at risk, and those dialogues are ongoing at the moment.

Given that you have a price point of generic Truvada that is so low, some countries are not going to be willing to fund Cab for PrEP; others have demonstrated interest and have asked us to go and talk to them, so I think it might be a country by country approach in Europe, but we're still having those dialogues today.

**David Redfern:** And there are still some pretty powerful patient lobbies that may well help.

**Deborah Waterhouse:** But most of the value that I quoted today, £4-5 billion, the vast majority is in the US.

**David Redfern:** Thanks Simon, and particularly for keeping it to one question. Let's move on to the next question.

**Elizabeth Walton (Credit Suisse):** Hi, good afternoon, thank you for taking my question. I'm hoping we can dive a little bit more into your market research around desires for long-acting therapies. I know historically you've talked about it being a niche group of patients that were seeking long-acting therapies, today you've highlighted that 70% of patients are interested in long-acting treatments and 66% interested in PrEP. I'm just curious if you can give us a breakdown of those that would be interested in what's available



today for treatment, so in-office administration versus future self-administered long-acting options, both in treatment and in PrEP. Thank you.

**Deborah Waterhouse:** Thanks for the question. I think when we've talked about this before Elizabeth, actually, we talked about *Cabenuva*, the addressable market for *Cabenuva* being about 15%, because obviously it's two intramuscular shots every couple of months, so that's not going to be for everybody.

What we know from our research is that every time you elongate the gap between administration, or you're able to let people have control by administering at home, the amount of people who would be willing and would be keen to take a long-acting increases, so you get more up to your 30-40% at that point as an addressable market. However, you have to then filter that by what kind of payor coverage is available for those individuals, or whatever the country is that they're living in, whether or not the medicine is available.

The principle is, the more options that you give, particularly the gap between the administration, the bigger the pool that becomes addressable for the medicine goes up - that's treatment. In PrEP there's a much higher willingness to take the injectable. It's one shot, it's every couple of months, and you're only going to be taking it for probably 10, 12 months at a time, it's not a lifetime commitment, so we see the addressable market for long-acting medicines, especially with the superiority data, as really significant. Hopefully that differentiates the two.

Kim, did I miss anything, because I know that this is something that you have a lot of insight and passion about?

**Kimberly Smith:** No, I think you nailed it, Deborah!

**Deborah Waterhouse:** Thank you.

**David Redfern:** Great, thanks. Let's move on to the next question.

**Simon Mather (BNP Paribas):** Afternoon everybody, thanks for taking my question. Just one on the pipeline, actually, looking on your slide, you have two NRTTIs and capsid inhibitor, just wondering why you haven't flagged potential combination, which would obviously mirror the ongoing, albeit paused, efforts with Merck and Gilead with islatravir and lenacapavir. Just a quick follow-on, if I could, obviously your pipeline looks like it's all based on the long-acting, with an integrase as a background, and all these are injectable products. How should we think about GSK/ViiV now, you talk about from an ESG perspective wanting

to help the world, obviously injectables might be potentially a bit more difficult from a logistical perspective for third world countries, just thinking how we should think about future efforts for the wider market. Thank you.

**David Redfern:** Thanks, Simon. Kim, do you want to comment on NRTTI combinations?

**Kimberly Smith:** Yes. I think I've probably emphasised it quite a bit in the presentation, that we think it is critically important to have the foundation of an integrase inhibitor, because the field has accepted integrase inhibitors as the gold standard, for all of the reasons that I articulated, so we see the most likely future being to start with an integrase inhibitor and add a novel mechanism of action. Certainly we have two NRTTIs in our pipeline, one lead and one back-up, similarly we have a lead and a back-up capsid inhibitor. We will see exactly what those profiles are, as I said, to combine those with cabotegravir, and later on potentially with VH184, but again, we think of long-acting regimens really having an INSTI at the core, as the foundation, is really more of an appeal to providers.

Novel mechanisms of action are exciting, but the challenge with them is that you can sometimes have unexpected issues that will come up, and we really like the idea of having something that is established and trusted by providers as the foundation.

**David Redfern:** Thanks, Kim.

**Deborah Waterhouse:** Simon, to your second question, obviously we've been very successful with dolutegravir, we have a policy to offer all of our medicines to generics companies on voluntary licences. You are correct, the generics companies are not as willing or enthusiastic of taking up our offer on the injectables, so I don't think you'll see *Cabenuva*-type products in least developed countries, but there is an enormous interest in PrEP. What we are currently doing is putting together our models to work out if no generic manufacturer steps up to make a cabotegravir PrEP via a voluntary licence, that we would step in, in partnership with PEPFAR, the Gates Foundation, etc., and we would be then the supplier of that preventative agent in the countries where it's most needed.

We are currently talking to many of the supranationals, and the governments in those least developed countries, and we are currently working out what volume would be required to support the effort to end the epidemic in those countries as well.

**David Redfern:** I think we just have time for one more question.

**Seamus Fernadez (Guggenheim):** Thanks. I just want to follow up on the NRTTIs. Can you talk about some of the internal work you're doing to explore the mechanism that we've seen with islatravir; and then how you see the impact of what we've seen with islatravir impacting both the treatment and PrEP markets, if there's any differentiation between the two. Thank you.

**David Redfern:** Thanks. Kim, do you want to comment?

**Kimberly Smith:** This is quite fresh news, this potential toxicity with islatravir, so we have not yet introduced new safety efforts to try to understand the mechanism, but certainly we will be watching very closely as that data is presented. Again, we have only heard a tidbit of the data, so we're looking to see the details and then we will map out our own programme for how we will try to understand the impact of those results.

**David Redfern:** Great, thanks Kim. I think that brings us to almost the end of the call, so I'd just like to thank all of you for your participation. All I'd like to say in closing is, we're incredibly proud of the history of GSK and its predecessor companies over the last 35 years, and what it's done in treating HIV and now turning it into a chronic disease that can be extremely well-managed. We're also equally excited, not just about the past but the future, and I hope today has been helpful in setting out our vision for the future, and particularly our long-acting pipeline, which I think we feel very strongly gives us the strong possibility of revenue renewal through the dolutegravir patent expiry.

We're excited to share that with you, we will obviously update you as we go forward and as the data comes through next year, and into the middle of the decade. Thank you very much for your time, and we appreciate you attending.

[Ends]