



Getting ahead of HIV with ViiV Healthcare management  
Thursday, 28 September 2023

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David Redfern | President Corporate Development, GSK and Chairman, ViiV Healthcare

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Good afternoon to UK based investors / good morning to the US at the start of your day. My name is David Redfern; I am the President of Corporate Development for GSK and the Chairman of ViiV Healthcare. I am delighted to host this meet-the-management event focused on our HIV business for analysts and investors. As usual, the materials presented today are available on [gsk.com](https://www.gsk.com).

You should see in front of you now the title-slide of this presentation – Getting Ahead of HIV Together. I should just say that we are now in the closed period and therefore we will not be making any comment today on performance matters relating to the current quarter – those will be covered in the GSK Q3 results reported shortly.

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

Moving on to slide three, which is a summary of what we shall cover today. I am delighted to be joined by Deborah Waterhouse, the CEO of ViiV Healthcare and President of GSK Global Health, and Dr Kimberly Smith, Head of R&D for ViiV.

The following ninety minutes will be divided into two parts. For the first forty-five minutes we will walk you through how we are reshaping the HIV treatment and prevention market; the shape of our HIV business with a specific focus on consolidating our leadership position in long-acting; and our continued innovation leadership and our pipeline.

Following that, we will have plenty of time for Q&A. I would also like to remind you that this call is being recorded and that will be made available after the event.

We are now on slide four.

ViiV Healthcare is a joint venture between GSK, Pfizer and Shionogi, and is one hundred per cent focused on treating, preventing and ultimately curing HIV and AIDS. GSK and its predecessor companies have been at the forefront of HIV innovation for more than thirty-five 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 dedicated to discovering, developing and commercialising medicines to treat and prevent HIV worldwide. We are proud of our deep and authentic partnerships with grassroots community organisations who are leading the HIV response globally and often in challenging environments where discrimination and stigma remain highly pervasive. Our flagship Positive Action team has recently celebrated thirty years of supporting the HIV community and we dedicate significant efforts to ensuring our recruitment programmes bring diversity and inclusion across our teams, reflect the communities we serve and amplify the voice of people living with HIV in everything we do.

In 2013, ViiV launched dolutegravir, which transformed the treatment of HIV by becoming the world's-leading integrase inhibitor, and continues to be at the forefront of our innovative portfolio today. Four years ago, we again transformed the treatment paradigm by launching *Dovato*, the leading oral two-drug regimen powered by dolutegravir at the core.

And within the last few years we have launched *Cabenuva*, the world's first and only complete long-acting injectable regimen for the treatment of HIV and *Apretude*, the world's first and only long-acting injectable for the prevention of HIV.

So we have a long and very proud history 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, the CEO of ViiV Healthcare.

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**Deborah Waterhouse | CEO, ViiV Healthcare and President Global Health, GSK**

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Thanks David. We are on slide five.

I am now going to provide an overview of how we are reshaping the HIV treatment and prevention market. I want to add how proud we are to be featuring authentic voices throughout this presentation of people living with HIV or could benefit from PrEP. So let's hear from Jayson, a US military veteran, living with HIV and currently taking *Cabenuva*.

Jayson's story is one that we hear time and time again – people not just living with HIV – but now thriving due to the innovation of our long-acting injectable *Cabenuva*.

We are now on slide seven, which provides a summary of the key commitments we made at the ViiV investor update which was held in November 2021. As a reminder, we outlined an ambition to remain innovation leaders in HIV; delivering progressive acceleration of growth and achieving a mid-single digit CAGR to 2026.

Through competitive execution we have driven above expectation growth for *Dovato* and our long-acting portfolio, *Cabenuva* and *Apretude*.

As we move into the second half of the decade, we are confident we will see a significant acceleration in the uptake of our long-acting regimens with cabotegravir replacing dolutegravir as the foundational medicine in our portfolio.

And we are excited about our pipeline progress which Kim will cover, which has the potential to significantly replace the revenue from dolutegravir post loss of exclusivity.

Please turn to slide eight.

Today I am delighted to confirm that as a result of our strong and competitive execution and innovation leadership – we are in a position to upgrade our 2021 to 2026 sales CAGR from mid-single-digits to a higher range of between six to eight per cent. This upgrade includes the impact of the US Inflation Reduction Act of up to one percentage point of growth.



In our November 2021 update we committed to delivering every three-monthly dosing in treatment and prevention. I am delighted to share that we expect to exceed that ambition and we are now fully focused on delivering an every four-monthly injectable regimen. This is significant as it enables us to double the dosing intervals of what we have in our hands today with *Cabenuva* and *Apretude*, and meaningfully increases the benefit of long-acting regimens for patients and healthcare professionals. For prevention, we will file and launch in 2026 and for treatment in 2027, enabling clinic visits to be halved to just three per year. This stands in stark contrast to those patients currently taking daily oral therapy who have to remember to take their tablets 365 times every year.

Through the acceleration of our research efforts, we are now able to provide greater clarity on our roadmap to further extend the dosing interval of our long-acting regimens in treatment and prevention to enable every-six monthly dosing towards the end of the decade. This would result in patients only needing to visit the clinic two times a year.

And finally, we will demonstrate our confidence in our ability to navigate through the revenue impact associated with the loss of exclusivity of dolutegravir. This will be delivered through increased momentum in the growth of our long-acting portfolio and clear demonstration that the intellectual property for *Dovato* and *Juluca* has potential to extend through the end of the decade.

I will now share how our strong commercial execution is driving growth.

Please move to slide ten. Strong competitive execution drives our 2021 to 2026 CAGR to a higher range of between six to eight per cent at constant exchange rates, with forecasted total sales now increasing from six billion pounds to seven billion pounds in 2026.

Starting on the left of the slide – Growth Drivers 2021 to 2026. Market performance firmly reflects prescriber belief in *Dovato*, which today is our number one selling HIV medicine.

Our long-acting portfolio, *Cabenuva* and *Apretude*, is ahead of expectation and on track to deliver more than two billion pounds of sales in 2026, representing around one third of our HIV total sales. *Cabenuva*, is the world's first and only complete long-acting regimen for the treatment of HIV. *Cabenuva* continues to be supported by strong label evolution and data which underpins confidence. Patient awareness of *Cabenuva* is high at over seventy per cent and more than fifty per cent of switches are coming from *Biktarvy*.

*Apretude* is the world's first and only long-acting injectable for the prevention of HIV, dosed every two months. It was launched in the US in January 2022 and we have high levels of ambition for this medicine. Our phase three data for *Apretude* demonstrated superiority in both the pivotal men and women's studies which were stopped early for superior efficacy versus standard of care and HCP confidence in the potential of this medicine is very high.

As we move to the right of the slide, 2026 to 2031, our ambition is to remain innovation leaders in HIV and cabotegravir will replace dolutegravir as the foundational medicine in our portfolio. Our pipeline is focused on three target product profiles: ultra-long-acting for treatment and prevention with dosing intervals of four months or longer. And the world's first self-administered long-acting regimen for treatment.

Please move to slide eleven.

ViiV Healthcare is the fastest growing company in HIV, growing at twelve per cent in Q2 and fourteen per cent in the first half of 2023 at constant exchange rates. In the last year we have increased our global market share by two percentage points. Our portfolio continues to transform the HIV marketplace, delivering on individualised patient needs.

*Dovato* continues to grow strongly enabling people living with HIV to remain virally suppressed with fewer medicines. We are confident that this innovative oral two-drug regimen is on track to deliver two billion pounds in sales in 2024.

Our long-acting injectable portfolio consisting of *Cabenuva* and *Apretude* continues to transform the paradigm in HIV treatment and prevention. Long-acting portfolio sales are on track to more than double in 2023 and we expect sales to now exceed two billion pounds in 2026. This is above the expectation that we set out at the business investor update in 2021.

*Cabenuva* addresses the significant challenges with daily therapy – fear of HIV status disclosure, stress and anxiety about staying adherent, and the constant reminder of living with HIV. As we heard earlier from Jayson, long-acting gives people freedom. Twenty-three thousand people living with HIV are now taking *Cabenuva* in the US and a further seventeen thousand across Europe.

HIV physicians are guided by data and guidelines, and we could not be more proud of our robust and industry-leading studies. Earlier this year we were delighted by the response to the presentation at CROI of our SOLAR data which demonstrates that *Cabenuva* is as effective as *Biktarvy* for the treatment of HIV. Importantly, the twelve-month findings demonstrated that nine out of ten participants who switched from *Biktarvy* to *Cabenuva* preferred the complete long-acting regimen to daily oral pills.

*Apretude* has the potential to transform the PrEP landscape and play a role in ending the HIV epidemic. Patients tell us that *Apretude* gives them freedom as shown by the fact that ninety-six per cent of phase three study participants chose to transition to *Apretude* over the daily oral standard of care, in the open label extension phase of the study. This, alongside a desire by prescribers, payers and Governments for a new solution to help end the HIV epidemic gives confidence that the PrEP market will continue to grow strongly.

Compelling data for our long-acting injectable portfolio has resulted in eighty-four per cent of US healthcare prescribers concluding that long-acting regimens will now become a key part of HIV care.

We are now on slide twelve.

I will now walk you through the expected shape of our HIV business and how the shift to long-acting and extended period of exclusivity reduces the impact of the anticipated dolutegravir LOE.

The pie-chart you see on the left paints a picture of the projected shape of our business in 2027. We expect our business will have moved to a portfolio balanced between orals and long-acting regimens with our long-acting portfolio representing around forty per cent of our revenue.

As we move to the bar-chart, I would like to spend a few moments describing our intellectual property which should help to clarify expectations around the timeline of dolutegravir's loss of

exclusivity. In Europe, which accounts for around forty per cent of the dolutegravir-based revenue, the composition of matter patent expires in July 2029.

The US represents around sixty per cent of our dolutegravir-based revenue. In the US, dolutegravir is protected by a composition of matter patent until April 2028, which includes an additional six months of exclusivity following the completion of our paediatric studies. *Dovato* and *Juluca* are also protected by formulation and other patents in the US which have expiry dates after the composition of matter patent.

Therefore, we anticipate a longer exclusivity period in the US for *Dovato* until December 2029 and *Juluca* until July 2030, protecting around thirty-five per cent of our dolutegravir-based regimen revenue.

Additionally, the current cabotegravir formulation in *Cabenuva* and *Apretude* is protected by composition of matter patents until February 2031 in the US and April 2031 in the EU, with the potential for an additional six-month extension for paediatric exclusivity. There is also potential for patent protection for future long-acting formulations and regimens extending further into the 2030s depending on the regimens selected for ultra-long-acting treatment and prevention.

Please turn to slide thirteen where I will further expand on how we intend to reshape the market towards long-acting.

We are on slide fourteen.

Key challenges remain in the treatment and prevention of HIV. The World Health Organization estimates approximately one point five million new infections per year globally, with the burden remaining greatest in Sub-Saharan Africa. Across America it is estimated that around half of people living with HIV are virally suppressed, and there are still thirty-eight thousand 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.

Industry pipelines are dominated by long-acting regimens. 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 twenty-five per cent of those who could benefit are currently taking PrEP.

And we remain mindful of broader shifts in the reimbursement and payer environment and specifically the introduction in the US of the Inflation Reduction Act. We are highly conscious of the need to continue to price our medicines responsibly and are proud of our access to medicines efforts which are focused on enabling our medicines to reach those who need them irrespective of location or ability to pay.

Please turn to slide fifteen.

As we move through the decade, we anticipate driving a fundamental shift in the HIV market towards long-acting injectables. In treatment, we envisage the market will move from being dominated by oral regimens to a more balanced position with long-acting injectable regimens representing around thirty per cent of the market value by 2031.

In prevention, we believe that long-acting injectables will grow to around eighty per cent of the value by 2031. In the US, we expect the market to more than double over the next decade to reach between four and five billion pounds, supporting the US Government's ambitious goal to end the HIV epidemic by 2030 and to reduce new infections by seventy-five per cent by 2025.

As stated, our ambition is to remain innovation leaders in HIV and through the changing mix of our portfolio towards long-acting and the success of our pipeline, we have the potential to significantly replace the revenue from dolutegravir post loss of exclusivity.

I will now hand over to Kim to walk you through our pipeline focused on the next wave of innovative long-acting regimens.

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**Dr Kimberly Smith | Head of Research and Development, ViiV Healthcare**

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Thank you Deborah. We are now on slide sixteen.

We will be updating you on the future pipeline, looking ahead to 2027 and beyond. We continue to be the leaders in long-acting therapies for HIV. Long-acting is the future and we have collected a large body of data directly from patients, who are telling us about their experience with the first and only long-acting regimens for HIV treatment and prevention.

In 2021 we made commitments for our next wave of long-acting regimens and our early pipeline is progressing well.

Please turn to slide seventeen.

Our journey map shows the history of our products and pipeline. It outlines our commitment to leaving no person living with HIV behind and is best illustrated by our development of *Rukobia* for multi-drug-resistant patients, and our development of *Triumeq PD*, the first and only fixed-dose regimen for children living with HIV.

The journey map also outlines our innovative oral two-drug regimens and the first and only long-acting regimen for HIV treatment and HIV prevention, which have changed the HIV therapeutic landscape. We will highlight our future Target Product Profiles, or TPPs, and our portfolio of assets in current and new mechanisms of action.

Finally, at the peak of our journey map is HIV cure and remission. We remain invested and committed to being a part of getting to a cure for HIV through our own discovery organisation and collaborations with academic researchers.

Please turn to slide eighteen.

Our TPPs are driven by patient insights, patient demand and unmet need. Based upon these insights, we are focused on three TPPs: ultra-long-acting prevention, ultra-long-acting treatment and long-acting self-administration.

The first TPP is ultra-long-acting prevention. In the United States, only twenty-five percent of people who could benefit from HIV prevention are currently receiving PrEP. We believe *Apretude* today and in the future, ultra-long-acting PrEP, will substantially improve on that statistic.

The second TPP is ultra-long-acting treatment, which will decrease clinic visits and clinic resource utilisation. This will help providers, who have told us that they would like more capacity to administer long-acting therapies. Ultra-long-acting treatment will build on the game-changing impact of *Cabenuva*.

The third TPP is long-acting self-administration, which is for individuals who want more control, who are open about their status and who want more freedom from clinic visits.

Please move to slide nineteen.

Our current marketed products and our future pipeline are built on the foundation of integrase inhibitors. Integrase inhibitors are the gold standard, anchor agents that are trusted by healthcare providers worldwide due to their superior potency, efficacy, long-term tolerability and high barrier to resistance.

Nearly twenty-three of twenty-eight million people living with HIV who are on treatment around the world are on a dolutegravir-based regimen, millions more are on other integrase inhibitors.

Cabotegravir is the world's first and only approved long-acting integrase inhibitor and it is changing the treatment and prevention landscape. Now, let's talk more about cabotegravir.

Please go to slide twenty.

Long-acting cabotegravir is transformative, an opinion shared by patients, healthcare providers and community members. This quote is from Dr. Gary Blick, a long-time HIV treater and researcher, he tells the story that patients enjoy long-acting treatment and they want more.

On the right side of the slide is a word cloud. This is a photo of a word cloud that I took when I was in a room with thirty-five US HCPs. The word cloud was created in response to the question, "what do your patients tell you about their experience with *Cabenuva*?" Their responses articulate exactly what we hoped we could do, which is change people's lives for the better, give patients more freedom, reduce stigma, make them feel "normal" and improve their quality of life.

Now let's hear more directly from HIV experts and HCPs.

Please turn to slide twenty-one.

Data on cabotegravir long-acting has dominated scientific meetings for the last several years. Key studies for treatment presented in 2022 and 2023 include:

- SOLAR, the first head-to-head study comparing *Cabenuva* to *Biktarvy*, demonstrating non-inferior efficacy, improved treatment satisfaction and a strong preference for *Cabenuva* with nine out of ten individuals on *Cabenuva* preferring it to *Biktarvy*.
- CARLOS, a real-world evidence study that reinforces the preference for long-acting cabotegravir + rilpivirine with ninety-nine per cent preferring it to daily oral.

- Ward 86 study, where individuals who struggle with adherence and consistent engagement with HIV care, and whose virus was not controlled, were successfully treated with *Cabenuva*. Please note that *Cabenuva* isn't currently indicated in individuals who are not virologically suppressed. We are currently engaging with the FDA to determine how we can expand our label to include this population.

There have also been a number of important studies of cabotegravir for PrEP, showing an overwhelming patient preference, ninety-five per cent, for cabotegravir long-acting over daily oral in randomised trials and in real-world evidence.

Please move to slide twenty-two.

Through our innovative science, we've demonstrated our leadership in HIV drug development by launching the world's first long-acting portfolio, powered by cabotegravir.

Long-acting cabotegravir has had tremendous impact on HIV treatment and PrEP.

I've shown you and you've heard from providers that cabotegravir is innovative, game changing and transformative. But we are not satisfied with that.

Our goal has been to improve on that and deliver more for patients. So, how do we improve on something so significant?

We intend to improve on the first and only long-acting regimens by doubling the benefits that cabotegravir brings, by doubling the interval between doses and cutting in half the number of clinic visits from six times per year to three times per year with a new formulation of cabotegravir.

We have undertaken creative and intensive formulation work on cabotegravir and have developed a new formulation called CAB 400. CAB 400 is double the concentration of the current formulation and it has double the half-life, which allows it to be dosed every-four-months with the potential for every-six-months dosing.

We have submitted this data for presentation at a conference in early 2024. This new formulation allows us to pursue ultra-long-acting cabotegravir for PrEP, increasing dosing intervals from every two months to every four months, which means cutting clinic visits in half. This will allow more individuals to access long-acting cabotegravir for PrEP as soon as 2026.

In treatment, we will combine ultra-long-acting cabotegravir with either rilpivirine or our broadly neutralising antibody, N6LS, to deliver an ultra-long-acting option as soon as 2027.

Let's talk more about these two options.

Please move to slide twenty-three.

Looking at option one, CAB 400 + rilpivirine, our intention is to expand the use of *Cabenuva* to deliver ultra-long-acting treatment, building on HCP and patient confidence and familiarity and improving the overall patient experience.



Rilpivirine has a half-life of around 200 days and we are working with our partner, Janssen to explore alternative doses and formulations.

We are now on slide twenty-four.

Option two looks at partnering CAB 400 with N6LS. N6LS is a broadly neutralising antibody (or bNAb) that targets the CD4 binding site. It is one of the broadest bNAbs discovered to date, covering up to ninety-eight per cent of viruses tested in vitro. It is also one of the most potent bNAbs currently in development. Our proof-of-concept study demonstrated viral load reductions of up to 2.8 logs following a single injection.

Importantly, we have the opportunity to progress N6LS as a part of our collaboration with Halozyme, using their recombinant hyaluronidase (or PH20) technology, which allows delivery of a larger volume of drug via subcutaneous dosing.

Our studies of N6LS plus PH20, demonstrated we can deliver a single subcutaneous dose that is well-tolerated and can last up to four months. The US Vaccine Research Center did a similar study and had similar findings. They presented that data at CROI 2023. We presented our proof-of-concept data at HIV Glasgow last year.

The ability to deliver this bNAb subcutaneously with PH20 allows for an improved patient experience where individuals do not need to have an IV and receive a long infusion, as is the case with other bNAbs currently under investigation.

Our phase 2 study of N6LS + cabotegravir long-acting, called the EMBRACE study, is currently enrolling and we expect to have data on this combination in 2024.

Please move to slide twenty-five.

This slide describes the HIV replication cycle and our pipeline assets by target.

Broadly neutralising antibodies target binding and fusion. I have just talked about N6LS (or VH109). In addition, we have a new bNAb, a bi-specific bNAb, that hits two targets with one antibody. In vitro it covers 100% of viruses tested across multiple subtypes and will enter clinical trials in 2024.

Capsid inhibitors target multiple steps in the HIV life cycle, nuclear entry and uncoating and assembly and budding. We have two capsid inhibitors in our pipeline and they are currently in phase two trials.

In the middle of the slide are integrase inhibitors, the foundation for our regimens. In addition to CAB 400 we have two other INSTIs: VH184, a 3rd generation INSTI with ultra-long-acting potential and broad coverage of INSTI mutations and a new INSTI, VH310A, which has a half-life at least four times longer than the current formulation of cabotegravir. VH184 is in phase one clinical trials and VH310A is expected to enter clinical trials in 2024.

Finally, we have the maturation inhibitor, VH937. Maturation inhibitors act late in the replication cycle, similar to protease inhibitors. We have investigated other maturation inhibitors but VH937 is a MI with long-acting potential. It is currently in phase one clinical trials and we expect it will enter phase two by the end of this year.

We are now on slide twenty-six.

This slide provides more detail on our assets and the candidates for each TPP. Here, we are showing that most of our assets have the capability to contribute to ULA or SA TPPs.

Starting with our INSTIs; for example, you can see that CAB 400 is included as a potential option across all TPPs.

Looking partner options for treatment, our bNAb, N6LS is included in all of the options as well. However, our maturation inhibitor is a partner agent that would likely only meet the TPP for self-administration.

Please move to slide twenty-seven.

By the end of this year, we will select the dose of CAB 400 that will be studied in 2024 for every-four-month dosing as part of our ultra-long-acting treatment and prevention strategy.

For ultra-long-acting PrEP, the registrational study for cabotegravir every-four-month dosing is expected to start in 2024, with file and launch expected in 2026; our wide array of INSTIs provide the path to every six-month PrEP but timing will depend on the asset we select.

For ultra-long-acting treatment, we expect to deliver a cabotegravir every-four-month regimen with registrational study start in 2025 followed by file and launch in 2027.

Subsequently we intend to partner either VH184 or VH310A with a new mechanism of action agent to deliver an every-six-month dosing regimen by the end of the decade.

For long-acting self-administration we are targeting two-to-three-month dosing. We have set the bar high – seeking a positive patient experience with efficacy and tolerability at least is good as *Cabenuva* but with the benefit of being able to self-administer at home.

Of note, we explored the possibility of switching *Cabenuva* from intramuscular dosing to subcutaneous dosing in a cohort of roughly ninety individuals and we found that two out three preferred IM dosing when administered by a healthcare professional. This gave us several important insights.

Firstly, the current form of *Cabenuva* dosed intramuscularly is very well tolerated. And secondly, sub-cutaneous dosing is not necessarily better tolerated than IM dosing when delivered monthly. Given that we plan to have the option of clinic administered ultra-long-acting treatment with only two to three clinic visits per year, self-administered must deliver a uniquely valuable patient experience when compared to in-clinic treatment. Again, a high bar, but we are up to that task. We will select the regimen next year, this will enable device setup followed by the start of a registrational study in 2026, with file and launch by the end of the decade.

Please move to slide twenty-eight.

We've taken patient insights and turned them into Target Product Profiles and described how we plan to get there, providing patients with the desired flexibility to enable them to live their best lives. Our ambition is driven by people living with HIV and those who would benefit from PrEP. Last

summer we travelled to Cape Town, South Africa to meet and thank the young people who participated in our pivotal trials for *Apretude*. Here is a small part of our conversation.

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**Deborah Waterhouse | CEO, ViiV Healthcare and President Global Health, GSK**

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Thanks Kim, we are on slide twenty-nine.

Please turn to slide thirty where I will summarise our updated commitments.

We have confirmed that as a result of our strong and competitive execution and innovation leadership – we will upgrade our 2021 to 2026 sales CAGR from mid-single-digit to a higher range of between six to eight per cent which includes the estimated impact from the US Inflation Reduction Act of up to one percentage point of growth.

*Dovato*, *Cabenuva* and *Apretude* will each deliver significant benefits for people living with HIV or those who could benefit from PrEP. We are confident that *Dovato* and our long-acting injectable portfolio will each deliver more than two billion pounds of revenue.

As we move into the second half of the decade, cabotegravir will replace dolutegravir as our foundational medicine. We expect to see a significant acceleration in the uptake of our long-acting injectables, which allows us to be confident in our ability to navigate through the revenue impact associated with the loss of exclusivity of dolutegravir.

As a result of strong pipeline progress, we expect to deliver a new long-acting formulation of cabotegravir which has the potential to double the dosing interval in prevention to every four months in 2026, and in treatment in 2027, enabling people to reduce clinic visits to just three a year for the treatment and prevention of HIV. We have also outlined a clear roadmap to further extend the dosing interval of our long-acting regimens in treatment and prevention to enable every-six-month dosing towards the end of the decade. This would result in people only needing to visit the clinic two times a year.

Finally, we are confident that we will consolidate our position as innovation leaders and deliver further growth in our long-acting portfolio into the next decade and we remain fully committed to our mission to leave no person living with HIV behind.

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## Q&A

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**Nick Stone (SVP, Head of Investor Relations, GSK):** With that we will take the first question from Richard Parkes at Exane. Richard, over to you please.

**Richard Parkes (PNB Paribas Exane):** Sticking to the one question, could you just tell us a little bit more in terms of CAB 400 around the number of injections, the needle gauge and the device? And then what you need to achieve to transition that to every six months would be very helpful, thank you.

**David Redfern:** Great, thanks, Richard. We will go straight to Kim.

**Kimberly Smith:** Thank you for the question. I won't get into the detail of the needle gauge because we are still finalising the dose, but I expect it will be similar to the needle that we use for *Cabenuva* now, so don't expect it to be a larger needle. Again, with that needle we have very good tolerability.

With regard to self-administration, it may be that we use CAB 400 but, as I mentioned, the other integrase inhibitors are possibilities for self-administration as well. You have to get to the ideal volume, the ideal tolerability and the ideal device and so we are pulling all of those things together as we gain more data on each of the products.

**Richard Parkes:** And the number of injections for CAB 400 – is that two separate injections every four months?

**Kimberly Smith:** No – one injection.

**Richard Parkes:** One injection – okay, thank you.

**Graham Parry (Bank of America):** Thanks for taking my question. It is one about the IP protection. You have formerly said that you think you could get *Juluca/Dovato* protection near to 2030. I think the patents protect out – they are combination or formulation patents and those I guess traditionally provided fairly weak protection to combination products. What gives you the confidence to say that you think you will now be protected to 2030? For example, can you see all filers – have you settled with all filers? Is there something which blocks others from the market through first-to-file, having been settled with, for example? Could you just give us a little more around the legal strategy there? Thank you.

**David Redfern:** Thanks, Graham. We actually said December 29 for *Dovato* and July 2030 for *Juluca*, but we have reasonable visibility. Deborah, would you like to elaborate?

**Deborah Waterhouse:** Yes, thanks. Just to reiterate, the dolutegravir composition of matter patent in the US is April 2028; in Europe it is July 2029. We then have formulation patents for *Dovato* and *Juluca* – *Dovato* in December 2029, and *Juluca* 2030, and that is July 2030. Actually, we have had a number of generic submissions. We have settled the ANDAs and we feel confident that those formulation patents will hold and give us that coverage until the dates that we have mentioned.

**Emmanuel Papadakis (Deutsche Bank):** Maybe a question on the q4m treatment options. It looks like – correct me if I am wrong – only option 2 is subcutaneous. The question is that you seem to be alluding to 98% of coverage but I think some of the data we saw presented earlier this year suggested it might be somewhat less than that. Does your confidence on the breadth of played coverage and the need for testing to assess which patients might be suitable for treatment with that single bNAb? Thank you.

**Kimberly Smith:** You are referring to the N6LS. So yes, the 98% that I was referring to was *in vitro*, so that is based upon the panels that all of the broadly neutralising antibodies are tested against. That is one of the highest breadths of all of the bNAbs that have been tested using that testing.

*In vivo*, we expect those numbers to be lower and I can't tell you exactly where we will land there, but there will be a need for a test to make sure that individuals are sensitive to the broadly neutralising antibody before individuals receive it, so that is the plan for N6LS.

**Deborah Waterhouse:** Is it worth confirming the administration of the two options that we have got, because I think Emmanuel referred to IM versus subcutaneous. It is worth just clarifying for the two options how they are administered?

**Kimberly Smith:** Sure. For broadly neutralising antibodies, again what I mentioned was that we can use it in combination with hyaluronidase but Halozyme's hyaluronidase are PH20, and that allows you to give a subcutaneous injection instead of having to give an IV infusion which is the case with other broadly neutralising antibodies that are being studied, so one subcutaneous injection lasting for four months. With cabotegravir our intention is that we will be dosing every four months with an intramuscular injection, because we have found that to be extremely well tolerated.

**David Redfern:** It is also worth emphasising, Emanuel, that N6LS is one of two options we have to partner with CAB 400, the other being rilpivirine and we shall make a decision on that next year.

**Peter Welford (Jefferies):** I want to come back to the every four month dosing. Just so I understand then, if you pursue option 1, am I right in saying that will still be two - as it currently is - IM injections, one of CAB 400 and one of the rilpivirine, which it sounds as though you are going to try to reformulate, and I am curious to know if that is a similar idea to CAB 400 presumably for the second IM injection. Am I right in saying that the second option would be an IM CAB 400 every four months but with a subcut VH109 together with the Halozyme technology? Again, two injections with one IM and one subcut. Is that the right way of thinking about it and are options 1 and 2 both on the table, or will only one of those go into a registrational trial, just to be clear? Thank you.

**Kimberly Smith:** A great question, Peter, and, yes, we do have a commit, so our intention is that we would have a regimen that is very similar to the current *Cabenuva* except that they would come in three times a year for option 1 instead of six times a year, so, yes, with two injections, that is the intention. Again, as I mentioned, we are working with our partners at Janssen for getting to that correct dosing interval with rilpivirine. As I mentioned, rilpivirine already inherently has a 200-day half-life, so it has a very long half-life that certainly makes that a possibility.

The second part of your question I believe is regarding the combination with N6LS and, yes, you are right, it would be IM cabotegravir along with the subcutaneous N6LS. Our intention is not that we would launch both. We will make a decision about which of those two has the best profile next year and move that into late stage registrational studies following that.

**Kerry Holford (Berenberg):** Thank you for taking my question. My question is on the guidance today. You have upgraded the 2021 to 2026 outlook and the footnote states that you include an estimated £200 million of annual impact from 2025 related to IRA. I wonder whether you can walk us through how you get to that figure and what your assumptions are for that £200 million headwind to 2025? Thank you.

**Deborah Waterhouse:** Thanks for the question, Kerry. In terms of the Medicare Part D redesign, we are assuming that our Medicare Part D products, which are our orals - *Tivicay*, *Triumeq*, *Juluca* and *Dovato* - will be impacted by the element of the redesign that holds manufacturers accountable for

20% of the catastrophic phase of the treatment. You have a whole year's coverage, in the first section you have a threshold where you get to about \$6,000 of cost and then after that, the manufacturer becomes responsible for 20% of the cost, so that is where you get to the 200 million. We haven't factored any other elements in because they are not really relevant to our medicines. There is a small impact on Part B which is *Cabenuva* and *Apretude* but it is really small. The main area where we have impact due to the catastrophic coverage is on our orals.

**Andrew Baum (Citi):** I apologise if you addressed this at the beginning of the call but I wasn't on. I am just curious why you are not prosecuting a 12-month formulation of cabotegravir or a pro-drug of that given there clearly are examples of where the pharmacokinetics would lend themselves to this? Is this a life-cycle strategy that you are reserving that for your next generation integrase, or is there some other reason why the 12-month PrEP is unappealing?

**Kimberly Smith:** Thank you for the question, Andrew. We are evaluating and, as I mentioned, we have the VH310 which has four times the half-life of CAB, and we are looking to evaluate that and to get that into patients next year. Once we have data in patients, if we can get to 12 months, we absolutely will pursue that but we are not at this point over committing on the basis of not having seen the results of that product in humans yet and so we certainly wouldn't take it off the table for the future if we deliver that PK in humans, but at this point we haven't started clinical trials on that product yet.

**James Gordon (JP Morgan):** Hello, thanks for taking the question. It was just about lenacapavir from Gilead and how to think about that because their capsid is being developed as a six-month injection both as a prevention and a treatment and also a weekly oral treatment, so just how you would see that comparing with the offerings that it looks like you are likely to go with. And if they do get their six-monthly launched ahead of you, which I think they are already at least for prevention already in Phase III, what would drive patients to then move towards your preferred offering if you subsequently launched them?

**David Redfern:** Thanks, James. We obviously think about that a lot. Kim, do you want to maybe start on prevention?

**Kimberly Smith:** Let me start with the fact that we have a long-acting prevention agent on the market now and so providers and patients are gaining experience and familiarity with *Apretude* today. Our plan is to be able to actually extend that, so that they are coming in instead of six times a year down to three times a year as soon as 2026, and we have an ambition to get to six-month dosing at least in the future by the end of the decade.

I think the comparison to lenacapavir is an interesting one but I would just say first that they have to finish enrolment of their clinical trials which they are currently not completely enrolled and they have to demonstrate efficacy. We have set a very high bar because we have shown efficacy and not just efficacy but superiority in comparison to daily oral, so we have set a very high bar.

The other thing to note about lenacapavir is that it is two subcutaneous injections and in some cases individuals may experience some skin *sequelae* from those subcutaneous injections – bruising, nodules, redness and so the tolerability profile of that product in comparison to our product I think will be very key when they are both on the market. That's assuming that lenacapavir is able again to demonstrate appropriate efficacy.

We are very confident that *Apretude*, because it is really extremely well tolerated and again we are getting to a longer interval which will be very appealing to patients.

**David Redfern:** Do you want to say something about the competitive landscape in treatment as well?

**Kimberly Smith:** In the treatment phase, you are right, there is a study using lenacapavir in combination with islatravir, dosed weekly. Obviously islatravir has to overcome the toxicity challenge that was demonstrated in the past couple of years, where it has shown lymphocyte toxicity. We will see if the lower dose which the dose that they are using now weekly is essentially ten-fold lower than the dose that they were originally planning to use, so does it have the efficacy when it's dosed weekly and does it have the tolerability profile.

That question has to be answered in their clinical trials, but with regard to long-acting therapy, we are already at two months, we are heading towards four months and I expect that we will launch our second generation long-acting injectable regimen before they are able to launch their first one because lenacapavir is at this point looking for a partner agent. We have been the leaders in this space and we are very, very proud of that and we are actually happy that our competitors are following us down this path, but I think it's very clear that we have shown leadership here.

**Eric Le Berrigaud (Stifel):** Thank you. The question is to clarify a couple of things on the guidance please because you are sticking with the 2021/2026 period so into this we have 18 months behind us where you delivered 12% growth and so for the remainder, to reach the 8%, we only need 5% for the next three and a half years.

If we take the £7bn in sales that you expect in '26 and we extrapolate the first half into the full 2023, we may be at £6.4bn at the end of this year and then reaching 7 would mean 3% for the next three years.

The question is why should we think about such a slowdown before the first part of the period and the remaining part of the period? Thank you.

**David Redfern:** Thanks, Eric. Deborah can explain that.

**Deborah Waterhouse:** Yes, so obviously we have performed extremely well over the last two and a half years and we are ambitious for our future growth. Towards the end of the period, you have the impact of the Inflation Reduction Act and we also have a few international markets, most notably China and Brazil, where we lose the patent of dolutegravir in 2026, so there is some drag on revenue which leads us to believe that the 6%-8% CAGR is the sensible upgraded guidance to give.

All of that is factored into that guidance and obviously we are giving a sensible range that we believe is achievable but we remain extremely confident in the future trajectory of our business, particularly the rapid growth that we see in the long-acting injectables.

**David Redfern:** And what is definitely true is we are very pleased about the real momentum that is in the business today. As you said, double-digit growth last year and up 14% in the first part of this year, so a lot of momentum in the business.

**Richard Parkes:** Thanks Nick. Largely clarifications actually. Just on the guidance, so can I just clarify that the 6%-8% CER guidance is broadly consistent with where consensus is which is I think is about 7.3 billion in about 2026, so despite that pressure from IRA over that period.

Then the second question is on clarification of the self-administered product. We now have quite a good view of what the treatment PrEP products profiles look like, but I am still a bit confused about what the scenarios are for the self-administered.

**David Redfern:** Anything to add on guidance on Deborah? I think you are exactly right Richard.

**Deborah Waterhouse:** I think Richard is right, we think that an upgrade from 6 billion to 7 billion in 2026 is very positive. It's based on really tremendous performance, a competitive performance from our long-acting injectables and also our oral 2-drug regimens and we think that 6% to 8% guidance is positive, because it accounts for all the headwinds and at the same time reflects the opportunity that we see before us. As you say, consensus is broadly in the same range for 2026 in terms of around the 7 billion, so I think we feel very confident in that guidance and happy that we have been able to upgrade it.

**David Redfern:** Great, Kim do you want to talk about self-medication?

**Kimberly Smith:** Just to be clear, for self-administration it will most likely be subcutaneous dosing using an auto-injector. As you know, most of the auto-injectors dose subcutaneously and so what we are looking to do is use the foundational INSTI, one of the three options that we have, most likely either cabotegravir or VH184 and use that in combination with one of the novel mechanisms of action. Again, we are targeting two- or three- monthly dosing but yes, it will be subcutaneously dosing for a self-administered.

For the four-month dosing and just to make sure that's clear, for the four-month dosing depending on whether we choose the rilpivirine option, or the N6LS option, the CAB dosing will be intermuscular and then rilpivirine likely would be inter-muscular as well and then the N6LS would be subcutaneous with PH20 as a subcutaneous injection. So I hope that's clear.

**Graham Parry:** Thanks, I actually had a follow-up on the self-admin timelines as well. I think you had originally said 2025-2027 launch timeframe and I think you said had a 2ml formulation of cabotegravir that you were pretty comfortable with, so is the issue on the delay to 2028-2030 launch here the device? So perhaps you can just give us a little bit more background to which device partners you are working with and if that is what is holding up and what the issue is there.

Secondly, on six-monthly plus, if that is able to come in the sort of 2028-2030 timeframe with VH184, that is only a year or so after your timeframes on four monthly, so would you launch both and have both in the market at the same time or is there a possibility you will end up dropping four-monthly to actually just progress.

On that, are you in clinic with injectable VH184 and I think that was due to go in Q4?

Then, last one is, I think you had also talked about a weekly oral VH184, I think that was also in Phase I, you don't mention weekly oral as an option here so have you dropped that as a strategy now? Thank you.



**Kimberly Smith:** Okay, that was a lot! Alright let me start with the question around 2025. Yes, we did originally talk about the potential of bringing the self-administered earlier but in that case we were looking at dosing monthly. What we ultimately decided was that as we get to longer and longer intervals for ultra-long acting and every four months and every six months where individuals are only coming into the clinic twice a year, or three times a year, that the proposition that compares in just one month wasn't enough, and so we have raised the bar and said we want to have a self-administered that is at least two months, or three months, so that's it more appealing and so that is part of what's caused the delay.

With regard to the device, it is always important obviously to pick the right device that will allow you to have the volume that you need to get to the intervals that you need. It's the combination of us really us setting the bar higher and not being able to move that monthly – just not seeing monthly as the right way to go forward, that has pushed the timeline back.

With regard to the next question –

**David Redfern:** 184 – first time in humans.

**Kimberly Smith:** Yes, 184, first time in human, oral, is an ongoing study. The injectable formulation of 184 has not entered the clinic yet but it is soon to enter the clinic and so we will have some data on that in 2024. So we expect to get a lot of our first-time-in-human data from the injectable formulations of 184, the capsids, that data is going to come in 2024, which is what will enable us to make those regimen selections to move forward into later stage studies. Go ahead, Deborah.

**Deborah Waterhouse:** I was just going to answer your question on the market, Graham, because I think it is a really good one. Kim is setting out lots of options and we will make choices, as we have said previously.

The HIV market over the next five, six, seven years is slow-growing and it is relatively fixed at around £20 billion of value. Within that market, every time a new competitor or we put forward innovation, we have to decide, is that innovation good enough to launch, both in terms of the patient benefit it brings, and also the shareholder value it delivers from the return on capital perspective. So I would think of it as a set tie and what we need to do is, every time something gets better – long-acting, intramuscular injections, every four months to six months – the bar goes up for the other elements that you could launch into the market, such as the self-administered, or even weekly orals. The bar is getting higher all the time in terms of the profile of the medicines you are developing and that means that the self-admin at one month, probably isn't good enough and we now need to be at least every two to three months. That is why we have chosen to go for a best-in-class approach because otherwise the share it would take is less beneficial financially because every four months and every six months is just so compelling.

That is how we should think about it. We will make choices, and it will be made according to what the profile of the medicines that we develop look like. If we can't hit a high enough bar for the self-admin, because we have got so far ahead on the intramuscular, we may make a choice between the two classes. Or, if every six months is rapid and compelling, we may not launch every four months, but we will definitely do it through the lens of patient benefit and return on capital invested. I hope that makes sense, but that is an important way to think about the market.

**Graham Parry:** That is super-clear. And weekly oral, is that still an option?

**Deborah Waterhouse:** We are looking at weekly oral, aren't we, Kim. Would you like to talk about that?

**Kimberly Smith:** Sure. We are evaluating every one of the products that are in our pipeline for the potential for it to be weekly oral. If we determine that we have products that look like they meet that profile well, we will consider adding that as a target product profile but, for now, we are just keeping an eye on the products that we have in the portfolio. We will keep you posted if we make a decision to take on that target product profile.

**Graham Parry:** Great. And actually one quick follow-up, you have mentioned obviously, the capsid and maturation inhibitors on slide 25, but then not in your option 1, option 2. Are those only for combo with VHI84 later, or are those ones that you might put into cabotegravir combination still?

**Kimberly Smith:** Capsid has the potential to do all of the above, so it could be six months. It could be - what our expectation is, it's also the long-acting version of it is just entering the clinic as I mentioned it is now in phase II. The long-acting version is just entering the clinic so we will look to see what that data is. Our expectation is that it could potentially be responsive in all three of those target product profiles. The maturation inhibitor, on the other hand - we don't believe that it will have the half-life to allow it to get to be every six months, and so it would be focused on the self-administered profile.

**Graham Parry:** Great, very clear, thanks very much.

**Andrew Baum:** Thank you. Could you just forecast on bridging where appropriate. I would imagine that when you are injecting in the same compartment, bridging is going to be relatively straightforward from a regulatory point of view, but I can't imagine subcut IM bridging is going to be allowed, or maybe not. If you could share your thoughts, that would be helpful.

**Kimberly Smith:** Obviously, that is always subject to engagement and negotiations with regulatory agencies, but it is certainly true that for cabotegravir for PrEP, what we are looking to do is essentially extend the interval, so the same method of delivery with a product that just lasts longer, so certainly PK bridging is an important part of that strategy to allow us to get that option to patients as quickly as possible.

**Kerry Holford:** Another more financial question from me. Just thinking about the various combinations, novel molecules you have coming through, have you talked to any potential meaningful pay-aways that you need to consider when we are thinking about modelling these assets in the longer term? Thank you.

**David Redfern:** I think it is mainly on rilpivirine, Kerry, but Deborah, do you want to elaborate?

**Deborah Waterhouse:** On the integrases, it is fairly straightforward. It is the same deal with Shionogi as we have always had, so the pay-aways are the same as on dolutegravir and the current version of cabotegravir. Obviously, we have their follow-on compound as well.

Regarding the pay-aways, there is a pay-away to Janssen on rilpivirine. There is a limited pay-away on the BNAb to the NIH and there is, as we shared previously, a pay-away to Halozyme if we use PH20 but they are obviously at much lower levels. There are varying amounts of pay-away on

each of the different molecules. The material difference is whether or not we have rilpivirine or one of our own ViiV-developed assets as the partner to cabotegravir or VHI84, and that remains to be seen over the clinical data that we generate in the coming months and years.

**Kerry Holford:** Can you quantify the level of those pay-aways on the BNAbs?

**Deborah Waterhouse:** Nick, have we shared those things? I don't think we have shared them specifically, have we?

**Nick Stone:** We haven't but, Kerry, we will come back to you offline if that is okay and certainly make an addendum to the transcript to help people. That is probably the easiest thing to do.

**Richard Parkes:** It is a follow-up from Graham's question earlier about the strength of the patents protecting *Dovato* and *Juluca*. This is a slightly different way of thinking about it. Sometimes we are seeing generics trying to get around those kind of formulation patents by co-packaging two separate pills in order to get around that. I don't know how successful that has been in the past, so I wonder whether that is something that we should consider and what the precedents suggest as far as the impact that has had on drugs going generic in the past? Thanks very much.

**Deborah Waterhouse:** Thanks, Richard. You can split the components, as you say, of the medication so let us say for *Dovato* you could have dolutegravir and lamivudine, both of which are generic or will become generic, in separate tablets. That has been done in a few parts in Europe and it has been unpopular. In the UK, for example, there was a very strong push through the NHS and in some parts of the UK there was uptake. In the US, where that has been proposed, it has not been successful because obviously we are trying to enhance patient adherence and support viral suppression across the healthcare system. At the moment, viral suppression is very poor. From a 90/90/90 goal, the US, if you look across people who are diagnosed, people who are treated and people who are virally suppressed, you get just over 50% of people who are living with HIV virally suppressed. I think that splitting is unlikely in the US which is where this extension sits, so it is US only because people are trying to drive greater levels of viral suppression, not undermine the goals or the offerings that we currently have in place today. Therefore, I would say that splitting is very unlikely in the US. It may happen in Europe but we do not have the additional coverage for *Dovato* and *Juluca* in the US, so I assume that market will just move straight into generics.

**Richard Parkes:** Perfect, that's very helpful, thank you.

**Nick Stone:** Thanks, Deborah. At this point in time, we have no further questions, so what I propose is that we quickly come back to you, Deborah, to wrap things up and then we'll close the call.

**Deborah Waterhouse:** Thanks, Nick. I hope from the call today that you can feel our confidence in the momentum of our business due to the upgrade from our 2021-2026 CAGR to 6%-8%. I hope you are feeling very positive as we are about the momentum in our long-acting injectable portfolio, which will be 40% of our business in 2027, and we believe that we have a really strong set of offerings in our pipeline, particularly now with the opportunity of every four months and every six months in treatment and PrEP and obviously the progress we are making on self-admin which will see us through the loss of exclusivity of dolutegravir.

I hope you have felt our confidence and our enthusiasm and of course our commitment to leaving no person living with HIV behind, so thank you for your time this afternoon.