GSK plc

GSK plc - Special Call - GSK plc

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Event Participants

Executives 4
David Redfern, Deborah Waterhouse, Nick Stone, Kimberly Smith

Analysts 8
Richard Parkes, Graham Parry, Emmanuel Papadakis, Peter Welford, Kerry Holford, Andrew Baum, James Gordon, Eric Le Berrigaud

David Redfern Executive

Good afternoon, everyone, who's based in the U.K., and good morning to all of those in the U.S. at the start of your day. My name is David Redfern, I'm President of Corporate Development for GSK and the Chairman of ViiV Healthcare. I'm 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.

You should see in the 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 close period, and therefore, we will not be making any comments today on performance matters relating to the current quarter. Those will be covered in the GSK Q3 results reported shortly. I would just refer you to Slide 2, which contains our cautionary and forward-looking statements. Moving on to Slide 3, which is a summary of what we should cover today.

I'm 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 90 minutes will be divided into 2 parts. For the first 45 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 available after the event. We are now on Slide 4. ViiV Healthcare is a joint venture between GSK, Pfizer and Shionogi and is 100% 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 35 years now. 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 discovery, developing and commercializing medicines to treat and prevent HIV worldwide. We are proud of our deep and authentic partnerships with grassroots community organizations who are leading HIV response globally and often in challenging environments where discrimination and stigma remain highly pervasive. Our flagship positive action team has recently celebrated 30 years of supporting the HIV community, and we dedicate significant efforts to ensuring our recruitment programs 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. 4 years ago, we again transformed the treatment paradigm by launching Dovato, the leading oral 2-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 long -- 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, CEO, ViiV Healthcare.

Deborah Waterhouse Executive

Thanks, David. We are on Slide 5. I'm not going to provide an overview of how we are reshaping the HIV treatment and prevention marketing. I want to add how proud we are to be featuring authentic voices throughout the presentation as people living with HIV, all who could benefit from PrEP. So let's hear from Jason, a U.S.

military veteran living with HIV and currently taking Cabenuva. [Presentation]

Deborah Waterhouse Executive

Jason'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 7, 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 in our ambition to remain innovation leaders in HIV delivering progressive acceleration of growth and achieving 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 significant acceleration, and the uptake of our long-acting regimens with cabotegravir replacing dolutegravir as the foundational medicine in our portfolio.

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

Please turn to the slide 8. Today, I am delighted to confirm that as a result of our strong and competitive execution and innovation leadership, we're in a position to upgrade our 2021 to

'26 sales CAGR from mid-single digits to a higher range of between 6% to 8%. This upgrade includes the impact of U.S. Inflation Reduction Act of upto 1 percentage point of [indiscernible]. In our November 2021 update, we committed to delivering every 3 monthly dosing in treatment and prevention, I'm delighted to share that we expect to exceed that ambition, and we are now fully focused on delivering every 4 monthly injectable regimens.

This is significant as it enables us to double the dosing interval of what we have in our hands today with Cabenuva and Apretude and meaningfully increase the benefit of long-action regimens to patients and healthcare professionals. For prevention, we will file a launch in 2026 and for the treatment in 2027 enabling clinic visits to be [halved] to just 3 per year. This [does] in strong 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 to on our roadmap to further extend that dosing interval of our long-acting regimen in treatment and prevention to enable every 6 monthly dosing towards the end of the decade. This would result in patients only needing visiting clinics 2 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 our strong commercial execution is driving growth on slide 9. Please move to Slide 10. Strong commercial execution drives from 2021 to 2026 CAGR to a higher range of between 6% to 8% at constant exchange rate.

With forecasted total sales now exceeding -- now increasing from GBP 6 billion to GBP 7 billion in 2026. Starting on the left of the slide, growth drives 2021 to 2026, market performance firmly reflects prescriber belief in Dovato, which today is our #1 selling HIV medicine. Our long-acting portfolio Cabenuva and Apretude is ahead of expectations and on track to deliver more than GBP 2 billion of sales in 2026, representing around 1/3 of our total HIV sales. Cabenuva is the world's first and only complete, long-acting regimen for treatment of HIV. Cabenuva continues to be supported by strong label evolution and data, which underpins confidence.

Patience awareness of Cabenuva is high and at 70% and more than 50% of switches are coming from Biktarvy. Apretude is the world's first and only long-acting injectable for the prevention of HIV dosed every 2 months. It was launched in the U.S. in January 2022, and we've had high levels of ambition for this medicine. Our Phase III data for Apretude demonstrated superiority in both pivotal men and women studies, which was stopped early to 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 3 target product profiles, ultra-long-acting for treatment and prevention with dosing intervals of 4 months or longer and the world's first self-administered long-acting regimen for treatments. Please move to Slide 11. ViiV Healthcare is

the fastest-growing company in HIV, growing at 12% in Q2 and 14% in the first half of 2023 at constant exchange rates. In the last year, we've increased our global market share by 2 percentage points.

Our portfolio continues to transform the HIV marketplace, delivering on individualized patient moods. Dovato continues to grow strongly, enabling people that live with HIV to remain virally suppressed with fewer medicines. We are confident that this innovative oral 2-drug regimen is on track to deliver GBP 2 billion 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 GBP 2 billion in 2026.

This is above the expectation we'll set out in the business investor update in 2021. Cabenuva addresses the significant challenges with daily therapy, fear of HIV status disclosure, stress and anxiety about saying adherence and a constant reminder of living with HIV. And as we heard from Jason earlier, long-acting gives people freedom. 23,000 people with HIV are now taking Cabenuva in the U.S. and a further 17,000 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 as is effected as Biktarvy for the treatment of HIV. Importantly, the 12-month findings demonstrated that 9 out of 10 participants who switched from Biktarvy to Cabenuva preferred to 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 is shown by the fact that 96% of Phase III study [patients] chose to transition to Apretude over the daily or standard of care in the open label extension phase of the setting.

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 84% of U.S. health care prescribers, concluding that long-acting regimens will now become a key part of HIV care. We are now on Slide 12. I will now walk you through the expected shape of our HIV business and how a shift in long-acting extended period of exclusivity reduces the impact of the anticipated dolutegravir loss of exclusivity.

The pie line you see on the left, paint a picture of the projected shape of our business in 2027. We expect our business will have moved to a portfolio balance between oral and long-acting regimens with our long-acting portfolio, representing around 40% of our revenue. As we move to the bar chart, I would like to spend a few moments describing our intellectual property, which would help to clarify expectations around the time line of dolutegravir's loss of exclusivity. In Europe, which accounts for around 40% of the dolutegravir-based revenue, the composition of matter patent expires in July 2029. The U.S.

represents around 60% dolutegravir-based revenue. In the U.S., dolutegravir is protected by a composition of matter patent until April 2028, which includes an additional 6 months of exclusivity following the completion of our pediatric studies.

Dovato and Juluca are also protected by formulation and other patents in the U.S., which have expiry date after the composition of matter patent. Therefore, we anticipate a longer exclusivity period in the U.S. for Dovato until December 2029 and Juluca until July 2030, protecting around 35% of dolutegravir-based regimen revenue. Additionally, the current cabotegravir formulation in Cabenuva and Apretude is protected by composition matting patents until February 2031 in the U.S. and April 2031 in the EU, which -- with the potential for an additional 6 month extension for pediatric exclusivity.

There is also potential for patent protection for future long-acting formulations and regimens extending further into the 2030s, depending on the regimen selected for ultra-long-acting treatment and prevention. Please turn to Slide 13, where I will expand on how we intend to reshape the market towards non-GAAP. We are now on Slide 14. Key challenges remain in the treatment and prevention of HIV. The World Health Organization estimates approximately 1.5 million new infections per year globally, with the burn 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 38,000 new infections per year. HIV rates are stubbornly high amidst people of color 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. U.S. patient demand for elongating injectable for precise the stigma around PrEP used and the perceived hassle of daily dosing are current top drivers of discontinuation of PrEP. Prescribers express concern about their lack of ability to observe adherence with current PrEP options and cabotegravir address these concerns in the U.S., less than 25% of those who would benefit from PrEP are currently taking PrEP. And we remain mindful of broader shifts in the reimbursement and payer environment and specifically the introduction of the U.S.

inflation Reduction Act, we are highly conscious of the need to continue to price our medicines responsibly and are proud of our access to medicine 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 15. 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 regimen to a balanced position with long-acting injectable regimen representing around 30% of the market value by 2021. In prevention, we believe that long-acting injectables will grow to around 80% of the value by 2031.

In the U.S., we expect the market to more than double over the next decade to reach GBP 4 billion to GBP 5 billion, supporting the U.S. government's ambitious content HIV epidemic by 2030 and to reduce new infections by 75% by 2025. As stated, our ambition is to remain innovation leaders in HIV with 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 regimes.

Nick Stone Executive

Thank you, Deborah. We are on Slide 16. We'll 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 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 17. 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 multidrug-resistant patients and the development of Triumeq PD the first and only fixed-dose regimen for children living with HIV. The journey map also outlines our innovative oral 2-drug regimens in 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 profile, 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 in being part of getting to the cure for HIV through our own discovery organization and collaborations with academic researchers. Please turn to Slide 18. Our TPPs are driven by patient insights and patient demand and unmet need. Based upon these insights, we are focused on 3 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 25% of the 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. Second TPP is ultra long-acting treatment, which will decrease clinic visits and clinic resource utilization. This will help providers who have told us that they would like more capacity to administer long-acting therapy to more [indiscernible].

Ultra long-acting treatment will build on the game-changing impact of Cabenuva. The third TPP is well enacting 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 19. Our current marketed products and our future pipeline are built on the foundation integrase inhibitors. Integrase inhibitors are the gold standard anchor agents that are trusted by health care providers worldwide due to their superior potency, efficacy, long-term tolerability and high barrier to resistance.

Nearly 23 million of 28 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 20. Long-acting cabotegravir is transformative, an opinion shared by patients, health care providers and community members.

This quote is from Dr. Gary Blick, a long-time HIV treater and researcher who tells the story

that patients are enjoying long-acting treatment, and they want more. On the right side of the slide is a photo of a word cloud that I took when I was in a room with 35 U.S. health care providers. 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 more normal and improve their quality of life. Now let's hear more from HIV experts and health care providers. [Presentation]

Nick Stone Executive

Please turn to Slide 21. Data on cabotegravir long-acting has dominated scientific meetings for the last several years. key studies for treatment presented in '22 and '23 are the SOLAR study, the first head-to-head study comparing Cabenuva to Biktarvy, demonstrating noninferior efficacy, improved treatment satisfaction and a strong preference for Cabenuva with 9 of 10 individuals on Cabanuva, preferring it to Biktarvy. The CARLOS study is a real-world evidence study. They've reinforced the preference for long-acting cabotegravir plus rilpivirine with 99% referring it to daily oral.

And the Ward 86 study, where individuals who struggle with adherence and consistent engagement in HIV care and whose virus was not controlled were successfully treated with Cabenuva. Now please note, the Cabenuva is not 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, 95% for cabotegravir long-acting over daily oral in randomized trials and in real-world evidence. Please move to Slide 22.

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, 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 6 times a year to 3 times a year with a new formulation of cabotegravir. We've 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 has doubled the half-life, which allows it to be dosed every 4 months with the potential for every 6-month dosing. We've 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 2 months to every 4 months, which means cutting clinic visits in half. This will allow more patients to access long-acting cabotegravir for PrEP as soon as

2026. In treatment, we will provide -- we will combine ultra long-acting cabotegravir with either rilpivirine or our broadly neutralizing antibody N6LS to deliver ultra long-acting option as soon as 2027. Now let's talk more about these 2 options. Please move to Slide 23.

Looking at Option 1, cabotegravir plus rilpivirine. Our intention is to expand on the use of Cabenuva to deliver an 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're working with our partner, Janssen, to explore alternative doses and formulations. Please move to Slide 24. Option 2 looks at partnering CAB 400 with N6LS.

N6LS is a broadly neutralizing antibody or bNAbs, that targets the CD4 binding site. It's one of the broadest bNAbs discovered to date, covering up to 98% of viruses tested in vitro. It's also one of the most potent bNAbs currently in development. Our proof-of-concept study demonstrated viral reductions up to 2.8 logs following a single injection. Importantly, we have the opportunity to progress N6LS as part of our collaboration with Halozyme using their recombinant hyaluronidase, or PH20 technology, which allows us to deliver 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 4 months. The U.S. Vaccine Research Center did a similar study and add similar findings. They presented that data at CROI 2023. We presented our proof-of-concept data on N6LS at the HIV Glasgow Conference 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 II study in N6LS plus 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 25. This slide describes the HIV replication cycle and our pipeline assets by target. Broadly neutralizing antibodies target binding infusion.

Now I've just talked about N6LS or VH109. In addition to that, we have a new bNAb, a bispecific bNAb. which means it hits 2 targets with 1 antibody. In vitro, it covers 100% of viruses tested across multiple subtypes, and we expect that it 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 2 capsid inhibitors in our pipeline, and then they are currently in Phase II trials. In the middle of the slide are integrase inhibitors, the foundation of our regimens. In addition to CAB 400, we have 2 other integrase inhibitors. VH184, a third-generation integrase inhibitor with ultra long-acting potential and broad coverage of integrase mutations. And a new integrates VH310, which has a half-life at least 4x longer than the current formulation of cabotegravir.

VH184 is in Phase I clinical trials, and VH310 is expected to enter clinical trials in 2024. Finally, we have a maturation inhibitor, VH937. Maturation inhibitors act late in the replication cycle, similar to [protein] inhibitors. We've investigated other maturation inhibitors, but VH937 is a maturation inhibitor with long-acting potential. It's currently in Phase I, and we expect it to enter Phase II by the end of this year.

Please move to Slide 26. This slide provides more detail on our assets and the candidates for each target product profile. Here, we're showing that most of our assets have the potential to contribute to ultra-long acting or self-administered target product profiles. Starting with our entities listed in gray. For example, you can see that CAB 400 is included as a potential option across all TPPs.

And looking at partner options for treatment in orange, our bNAb and N6LS is included in all the options as well. However, the maturation inhibitor is a partner agent that would likely only meet the TPP for self-administration. Please move to Slide 27. By the end of this year, we will select the dose of CAB 400 to be studied in 2024 for every 4-month dosing as a part of our ultra long-acting treatment and prevention strategy. For ultra long-acting PrEP, the registrational study for cabotegravir every 4-month dosing is expected to start in 2024 with a file and launch expected in 2026.

Our wide array of entities provide a path to every 6-month PrEP but timing will depend on the asset that we select. For ultra long-acting treatment, we expect to deliver the cabotegravir every 4-month regimen with the registrational study start in 2025, followed by filing launch in 2027. Subsequently, we intend to partner either VH184 or VH310 with a new mechanism of action agent to deliver an every 6-month dosing regimen by the end of the decade. For long-acting self-administration, we are targeting every 2- to 3-month dosing. We've set the bar high seeking a positive patient experience with efficacy and tolerability that is at least as good as Cabanuva, but with the benefit of being able to administer at home.

Of note, we explored the possibility of switching Cabenuva from intramuscular dosing to subcutaneous dosing in a cohort of roughly 90 individuals, and we found out that 2 out of 3 individuals prefer intramuscular dosing to subcutaneous dosing when administered by a health care professional. This gave us several important insights. Firstly, the current form of Cabenuva dosed intramuscular is very well tolerated. And secondly, subcutaneous dosing is not necessarily better tolerated than intramuscular dosing when delivered monthly. Given that we plan to have an option for clinic-administered ultra long-acting treatment with only 2 to 3 clinic visits per year, a self-administered regimen must deliver a uniquely valuable patient experience when compared to in-clinic treatment.

Again, a high bar, but we are up to the task. We plan to select regimen next year, which will enable device setup followed by a registrational study starting in 2026 with a target to file and launch by the end of the decade. Please move to Slide 28. We've taken patient insights and turn them in the target product profiles and describe 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 could benefit from PrEP.

Last summer, we traveled 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 that conversation. [Presentation]

Deborah Waterhouse Executive

We are on Slide 29. Please turn to Slide 30, where I'll summarize our updated commitments. We've 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 digits to a higher range of between 6% to 8%, which includes the estimated impact from the U.S. inflation Reduction Act of up to 1 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 would each deliver more than GBP 2 billion 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 expected to deliver a new long-acting formulation of cabotegravir, which has the potential to double the dosing interval in prevention to every 4 months in 2026 and in treatment in 2027, enabling people to reduce clinic visits to just 3 a year for the treatment and prevention of HIV. We have also outlined a clear road map to further extend the dosing interval of our long-acting regimens in treatment and prevention to enable every 6 months dosing towards the end of the decade. This would result in people only needing to visit the clinic 2 times year.

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

Nick Stone Executive

So, with that, we will take our first question from Richard Parkes at Exanes. So Richard, over to you please.

Richard Parkes Analyst

Thanks, Nick. Yes, suppose. So sticking to the 1 question. Could you just tell us a little bit more in terms of CAB 400 around the number of injections and the needle gauge and the device. And then maybe what you need to achieve to transition that to every 6 months would be very helpful.

David Redfern Executive

Great. Thanks, Richard. I think we'll go straight to Kim.

Kimberly Smith Executive

Thank you for the question. So I won't get into the details of the needle gauge because we are still finalizing the dose, but I expect it will be similar to the needle that we use for Cabenuva now. So I don't expect be a larger needer. And again, with that needle, we have very good tolerability. So 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 the ideal volume the ideal tolerability and the ideal device. And so we're pulling all of those things together as we gain more data on each of the products.

Richard Parkes Analyst

And the number of injections for CAB 400, is that 2 separate injections every 4 months?

Kimberly Smith Executive

No, 1 injection.

Richard Parkes Analyst

1 injection.

Nick Stone Executive

Graham Parry, can we come to you, please?

Graham Parry Analyst

Actually, one about the IP protection. So you've sort of formally said you think you could get Juluca, Dovato protection it's 2030. I think the patents expect to protect out to their combination of formulation patents and those have I guess, traditionally provided a fairly weak protection to combination products. So what gives you the confidence to say you could get -- you think you will be now 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, perhaps just give us a bit more around the legal strategy there.

David Redfern Executive

Okay. Thanks, Graham. We actually set December 29 for Dovato and July 2030 for Juluca, but we have reasonable visibility. But Deborah, do you want to elaborate?

Deborah Waterhouse Executive

Yes. Thanks. So just to kind of reiterate. So the dolutegravir composition of master patent in the U.S. is April 2028 in Europe, it's July 2029.

We then have formulation patents for Dovato and Juluca. Dovato December 2029, and Juluca 2030, and that's July 2030. And actually, we had a number of generic submissions. We've [indiscernible] and we feel confident that those formulation patents will hold and give us that coverage to the dates that we've mentioned.

Nick Stone Executive

Can we take the next question from Emmanuel Papadakis, please, at Deutsche Bank.

Emmanuel Papadakis Analyst

Maybe a question on the Q4M treatment options. It looks like -- correct me if I'm wrong, but only option 2 is subcutaneous. So the question, you seem to be alluding to 98% coverage, but I think some of the data we saw presented earlier at the year it might be somewhat less than that. So just your confidence on the breadth of coverage and the need for testing to

assess which patients might be suitable for treatment with that single bNAb.

David Redfern Executive

Thanks, Emmanuel. Kim?

Kimberly Smith Executive

Sure. So you're referring to the N6LS. And so yes, the 98% that I was referring to is in vitro. And so that's based upon the panels that all of the broadly neutralizing antibodies are tested against. And so that is -- that's one of the highest breath of all of the bNAb that have been -- that have been tested using that testing.

Now in vivo, those -- we expect those numbers to be lower. And I can't tell you exactly where we will land there. But so there will be a need for a test to make sure that individuals are sensitive to the broadly neutralizing antibody before individuals receive it. And so that is the plan for N6LS.

Deborah Waterhouse Executive

Just confirming the administration of the 2 options that we've got because I think Emmanuel referred to how IM versus subcutaneous. Is it worth just clarifying the 2 options, how they're administered.

Kimberly Smith Executive

Sure. So for broadly neutralizing antibodies, again, what I mentioned was that we can use it in combination with hyaluronidase, Halozyme's hyaluronidase or PH20, and that allows you to give a subcutaneous injection instead of having to get an IV infusion, which is the case with other broadly neutralizing antibodies that are being studied. And so 1 subcutaneous injection lasting for 4 months. So with cabotegravir, our intention is that we will be dosing every 4 months with an intramuscular injection because we have found that to be actually extremely well tolerated.

David Redfern Executive

And just worth emphasizing also Emmanuel, remember that N6LS is 1 of 2 options we have to partner with CAB 400, the other being rilpivirine, and we'll make a decision on that next year.

Nick Stone Executive

Peter Welford, come to you next, please.

Peter Welford Analyst

I just want to come back to actually the every 4-month dosing. Just so I understand then, if you pursued option 1, am I right in saying that, that will still be 2, as it currently is 2, if you like, IM injections, one of CAB 400 and one of the rilpivirine which it sounds as though you're also going to try and reformulate. And I guess I'm curious to know how -- is that the similar sort of idea to CAB 400 then the second IM presumably injection. And am I right in saying the second option would be an IM CAB 400 every 4 months, but then with a subcut VH109 together with

the Halozyme technology. So again, 2 injections with that, I mean 1 IM and 1 subcut.

Is that the right way of thinking about it?

And I guess are option 1 and 2, both on the table? Or will only one of those go into a registrational trial, just to be clear.

Kimberly Smith Executive

Great question, Peter. Yes, we do have [indiscernible]. So our intention is that we would have a regimen that's very similar to current Cabenuva, except that they would come in 3 times a year and for option 1, would come in 3 times a year instead of 6 times a year. And so yes, with 2 injections. That is the intention.

And again, as I mentioned, we're working with our partners at Janssen for getting to that right correct dosing interval with rilpivirine. As I mentioned, rilpivirine already inherently has 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 think, was regarding the combination with N6LS. And yes, you're right, it would be IM cabotegravir along with the subcutaneous N6LS.

And so our intention is not that we would launch both. We will make a decision about which of those 2 has the best profile next year and move that into late-stage registrational studies following that.

Nick Stone Executive

Could we take the next question from Kerry Holford, please at Berenberg. Over to you, Kerry.

Kerry Holford Analyst

My question is on the guidance. Today, you've upgraded that 2021-2026 outlook. The footnote there states that you included an estimated GBP 200 million of annual impact on 2025 related to IRA. I just wondering if you can walk us through how you get to that figure what your assumptions are behind that GBP 200 million headwind in 2025?

David Redfern Executive

Thanks, Kerry. Deborah?

Deborah Waterhouse Executive

Yes. Thanks for the question, Kerry. So in terms of the Medicare Part D redesign, we are assuming that Medicare Part D products, which are our oral 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. So you have kind of a whole year's coverage. In the first section, you kind of 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 GBP 200 million. We haven't factored any other elements in because. They're not really relevant to our medicines. There is a small impact on Part B, which is

Cabenuva and Apretude, but it's really small.

The main area where we've got impact through to the catastrophic -- due to catastrophic coverage is on our orals.

Nick Stone Executive

Thanks, Deborah. We're going to take our next question from Andrew Baum at Citi.

Andrew Baum Analyst

I apologize if you addressed this at the beginning of the call that I wasn't on. I'm just curious why you're not prosecuting a 12-month formulation of cabotegravir or 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're reserving that for your next-generation integrase? Or is there some other reason why the 12-month PrEP is unappealing?

David Redfern Executive

Thanks, Andrew, Kim?

Kimberly Smith Executive

So thank you for the question, Andrew. We are evaluating, as I mentioned, we have VH310, which has 4x the half-life of CAB, and we are looking to evaluate that and 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're not, at this point, overcommitting 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.

Nick Stone Executive

We're going to take our next question from James Gordon at JPMorgan.

James Gordon Analyst

It was just lenacapavir and Gilead and how to think about that because I think their capsid is being developed as a 6-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're likely to go with? And if they do get their 6 monthly launched ahead of you, which I think they were already at least for prevention already in Phase IIi, what would drive patients to then move towards your preferred offering if you subsequently launch them?

David Redfern Executive

Thanks, James. We obviously think about that a lot. Kim, do you want to maybe start with prevention?

Kimberly Smith Executive

Well, 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 6 times a year, down to 3 times a year as soon as 2026. And we have an ambition to get to 6-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, they have to finish enrollment of their clinical trials, which they're currently not completely enrolled, and they have to demonstrate efficacy.

And we have set a very high bar because we've shown efficacy and not just efficacy but superiority in comparison to daily oral. So we've set a very high bar. The other thing to note about lenacapavir is that it is 2 subcutaneous injections and in some cases individuals may experience some skin sequela from those subcutaneous injections, bruising, nodules, redness. And so the tolerability profile of that product in comparison to our product, I think, would be very key when they are both on the market that's assuming that lenacapavir is able, again, to demonstrate appropriate efficacy. So we're very confident that Apretude because it is really extremely well tolerated.

And again, we're getting to a longer interval, which will be very appealing to patients.

David Redfern Executive

Do you want to a little bit about competitive -- sorry Deborah, competitive landscape in treatment as well.

Kimberly Smith Executive

Yes. I mean in the treatment space, you're 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 is has shown lymphocyte toxicity. We'll see if the lower dose, which the dose that they're using now weekly is essentially tenfold 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.

So I think that question has to be answered in their clinical trials. But with regard to long-acting therapy, so we're heading towards -- we're already at 2 months. We're heading towards 4 months. And I expect that we will launch our second-generation long-acting regimen, injectable regimen before they're able to launch their first one because lenacapavir at this point looking for a partner agent. And so we have been leaders in this space, and we're very, very proud of that.

And we're actually happy that our competitors are following us down this path, but I think it's very clear that we have shown leadership here.

Nick Stone Executive

Thanks, Tim. Okay. We're going to take our next question from Eric Le Berrigaud at Stifel.

Eric Le Berrigaud Analyst

Thank you, Nick. The question is to try to clarify a couple of things on the guidance, please.

Because you're sticking with 2021, 2026 period. And so into this, we have 18 months behind us, where you delivered 12% growth. And so for the reminder, to reach the 8%, we only need 5% for the next 3.5 years.

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

David Redfern Executive

Thanks, Eric. Deborah, can explain that.

Deborah Waterhouse Executive

Yes. So obviously, we have performed extremely well over the last kind of 2.5 years, and we're ambitious for our kind of 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 Russia and Brazil, where we lose the patents of dolutegravir in 2026. So there is some drag on revenue, which leads us to believe that the 6% to 8% CAGR is the sensible upgrading guidance to give. All of that is factored into that guidance.

And obviously, we're 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 Executive

And what's definitely true is we're very pleased about the real momentum 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.

Nick Stone Executive

Thanks, David. [Operator Instructions] With that, we will come back for a second round now. So, Richard Parkes can I come back to you please?

Richard Parkes Analyst

Thanks, Nick. Yes, largely clarifications, actually. Just on the guidance. So can I just clarify that the 6% to 8% [CER] guidance is broadly consistent with where consensus is, which I think is about GBP 7.3 billion in 2026. So despite that pressure from IRA over that period.

Then the second question is on clarification of the self-administered product because I think -- we've now got a kind of a good view of what the treatment kind of product profiles look like. But I'm still a bit confused about what the scenarios are for the self-administered.

David Redfern Executive

Anything to add on guidance, Deborah. I think you're exactly right, Richard.

Deborah Waterhouse Executive

I think Richard is right. I mean, we think that upgraded from GBP 6 billion to GBP 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, that 6% to 8% guidance is positive because it accounts for all the headwinds and at the same time, reflect the opportunity that we see before us. And as you say, consensus is broadly in the same range for '26 in terms of around GBP 7 billion.

So I think we've got very confident in that guidance and happy that we've been able to upgrade it.

David Redfern Executive

Kim do you want to talk about self=medication and.

Kimberly Smith Executive

Sure. Yes, just to be clear, so for self-administration, it will be -- 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 3 options that we have, most likely either cabotegravir VH184 and use that in combination with one of the novel mechanisms of action. And again, we're targeting 2 to 3 monthly dosing, but yes, it will be subcutaneous dosing for self-administered.

For the 4-month dosing and just to make sure that that's clear, for the 4-month dosing, depending on whether we choose the rilpivirine option or the N6LS option, the CAB dosing will be intramuscular. And then recovering is likely would be intramuscular as well. And then the N6LS would be subcutaneous with PH20 as a subcutaneous injection. So I hope that, that's clear.

Nick Stone Executive

Graham Parry we'll come back to you now, please.

Graham Parry Analyst

Yes. So actually, I had a follow-up on the self-admin timelines. I think you originally said 2025 to '27 launch time frame. And I think you said you had a [indiscernible] formulation of cabotegravir that you're pretty comfortable with? So is the issue on the delayed '28, 2030 launch here, the device.

So perhaps you can just give us a little bit more background to which device partners you're working with? And if that's what's holding up and what the issue is there. Secondly, on 6-monthly plus, if that's able to come in the sort of '28 to 2030 timeframe with the VH184, that's only a year or so after your sort of time frames on 4 monthly. So would you launch both and have both in the market at the same time? Or is there a possibility you end up dropping 4-monthly to actually just progress?

And on that, are you in clinic with injectable, VH184 and I think that was due to go in Q4. And then -- sorry, last one is just I think you'd also talked about a weekly oral, VH184, I think that

was also in Phase I. You don't mention weekly orals as an option here. So if you drop that as a strategy now?

Kimberly Smith Executive

Okay. That was a lot. All right. 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 -- we were looking at dosing monthly. And what we ultimately decided was that as we get to longer and longer intervals for ultra-long acting every 4 months, every 6 months, where individuals are only coming into the clinic twice a year or 3 times a year. The proposition, the comparison just 1 month wasn't enough. And so we've raised the bar and said we want to have a self-administered that at least 2 months or 3 months, so that it's more appealing. And so that is a part of what's caused the delay.

And then with regard to the device, it's 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. So it's the combination of really us setting the bar higher and really not being able to move that monthly, just not seeing that monthly as being the right way to go forward that has pushed the time line back. With regard to the next question.

David Redfern Executive

184 first time in humans.

Kimberly Smith Executive

Yes. So 184 first time in human oral is an ongoing study. The injectable formulation of 184 has not entered the clinic yet, but is soon to enter the clinic, and so we'll have some data on that in 2024. And 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's going to enable us to make those regimen selection for the -- to move forward into later-stage studies.

Deborah Waterhouse Executive

I'm sorry, Kim, I thought you finished. I'm going to comment on market after you finished. Sorry.

Kimberly Smith Executive

No, no, no. Go ahead, Deborah.

Deborah Waterhouse Executive

So I'm just going to comment on your -- or answer your question on the market, Graham. So I think it's a really good one. So Kim is setting out lots of options, and we will make choices as we've said previously. The HIV market over the next kind of 5, 6, 7 years is slow growing, and let's say it's relatively fixed at around GBP 20 billion of value. And 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 [indiscernible] and also the

shareholder value it delivers from a return on capital perspective.

So I would think of it as a set tie on what we need to do is every time something gets better, long-acting, intramuscular injections every 4 months to 6 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 because the bar is getting higher all the time in terms of the profile of the medicines you're developing, and that means that the self-admin at 1 month probably isn't good enough.

We now need to be at least every 2 to 3 months, and that's why we've chosen to go for a best-in-class approach because otherwise, the share it would take is less beneficial financially because every 4 months and every 6 months is just so compelling. So I think that's 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 higher bar for the self-admin because we've got so far ahead on the intramuscular. So we may make a choice between the 2 classes or if every 6 months is rapid and compelling, we may not launch every 4 months, but we'll definitely do it through the lens of patient benefit and return on capital invested.

I hope that makes sense, but I think that's an important way to think about the market.

Graham Parry Analyst

That's super clear, Kim and weekly oral is that still an option?

Kimberly Smith Executive

Yes.

Deborah Waterhouse Executive

We're looking at weekly oral -- Kim, do you want to talk about?

Kimberly Smith Executive

Sure. So we're evaluating every one of the products that are in our pipeline for the potential for it to be weekly oral. And if we determined 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 -- we really basically just keeping an eye on the products that we have in the portfolio. And so we will keep you posted if we make a decision to take on that target product profile.

Graham Parry Analyst

Great. And actually, one quick follow-up. You mentioned, obviously, the capsid maturation inhibitors on Slide 25, but they're not in your option 1, option 2. So are those only for combo with the VH184 later? Or are those ones that you might get into cabotegravir combination still?

Kimberly Smith Executive

Yes. So capsid has the potential to do all of the above. So it could be 6 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's now in Phase II, long-acting version is just entering the clinic. So we'll look to see what that data is. But our expectation is that it could potentially be responsive in all 3 of those target product profiles. The maturation inhibitor, on the other hand, though, we don't believe that it will have the half-life to allow it to get to be every 6 months. And so it would be focused on the self-administered profile.

Nick Stone Executive

Thanks, Kim, and thanks, Graham. We have A question now from Andrew Baum again.

Andrew Baum Analyst

Could you just follow up [indiscernible] bridging where appropriate. I would imagine that when you're injecting in the same compartment, bridging is going to be relatively straightforward from a regulatory point of view. But I can't imagine subcu to IM bridging is going to be allowed or maybe not. If you could share your thoughts, that would be helpful.

Kimberly Smith Executive

So obviously, that's always subject to engagements 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. And so certainly, PK bridging is an important part of that strategy to allow us to get that option to patients as quickly as possible.

Nick Stone Executive

Thanks, Kim. It looks like Kerry Holford has also come back for a second round.

Kerry Holford Analyst

Another more financial question for me. Just thinking about the various combinations, novel molecules you've got coming through. And you talked any potential [indiscernible], you need to consider when we're thinking about modeling these assets in the longer term.

David Redfern Executive

I think it's mainly on rilpivirine, Kerry, but Deborah, do you want to elaborate?

Deborah Waterhouse Executive

Yes, sure. So on the integrases, it's fairly straightforward. It's the [indiscernible] as we've always had. So the payaways are the same as on dolutegravir and on the current version of cabotegravir. And Obviously, we've got there follow-on compound as well.

In terms of the payaways, so yes, there is a payaway to Janssen on rilpivirine. There is a limited payaway on the bNAb to the NIH. And there is, obviously, as we've shared previously, a payaway to Halozyme if we use PH20 but they are obviously at much lower levels. So there are varying amounts of payaway on each of the different molecules. The material difference is whether or not we have rilpivirine or one of our own -- we developed assets as the partner

to cabotegravir or VH184 and that obviously remains to be seen over the clinical data that we generate in the coming months and years.

Kerry Holford Analyst

Can you quantify the level of those payaways on the bNAb [indiscernible].

Deborah Waterhouse Executive

So Nick, have we shared those things? I don't think we've shared them specifically.

Nick Stone Executive

We haven't. But Kerry, we'll do is we'll come back to you offline, if that's okay. And we'll certainly make an addendum just to the transcripts just to help people. So I think that's probably the easiest thing to do. So with that, can I take another question, please, from Richard Parkes.

So Richard, over to you.

Richard Parkes Analyst

Sorry about that. So it's just a follow-up from Graham's question earlier on about the strength of the patents protecting Dovato and Juluca. And it's a slightly different sort of way of thinking about it. I think sometimes we're seeing generics try and get around those kinds of formulation patterns by maybe co-packaging 2 separate pills in order to get around that. I don't know how successful that has been in the past.

So just wonder if that's something that one should consider and what the precedent suggests that in terms of impact that's had on drugs going generic in the past.

Deborah Waterhouse Executive

So thanks, Richard. So you can split as you say, the components of the medications and let's say, 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. But in the UK, for example, there was a very strong push through the NHS and in some parts of the U.K., there was uptake. In the U.S., where that has been proposed, has not been successful because Obviously, we're trying to enhance patient adherence and support viral suppression across the health care system.

At the moment, viral suppression is very poor from a 1990 goal, the U.S.. 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. So I think splitting is unlikely in the U.S., which is where this extension sits. So it's U.S. only because people are trying to drive greater levels of virus suppression, not undermine the kind of the goals that we've currently got or the offerings that we currently got in place today.

So I would say splitting is very unlikely in the U.S. It may happen in Europe that we don't have the additional coverage for Dovato and Juluca in the U.S. So I assume that, that market will just move straight into generics.

Nick Stone Executive

Thanks, Deborah. So at this point in time, we have no further questions. So what I propose is that we just quickly come back to you, Deborah, just to wrap things up, and then we'll close the call.

Deborah Waterhouse Executive

Thanks, Nick. So I hope from the call today that you can feel our confidence in the momentum of our business between -- due to the upgrade from our 2021 to '26 CAGR to 6% to 8%. I hope you're 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 with our pipeline, particularly now with the opportunity of every 4 month and every 6 months in treatment and PrEP and obviously, the progress we're making on self-admin, which will see us through the loss of exclusivity of dolutegravir. So I hope you 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.

Nick Stone Executive

Thanks, Deborah. And with that, we will now end the call. So thanks very much for the attendance. If there's any further questions, don't hesitate to contact the IR team at gsk.com. Thanks very much.