SHIONOGI & CO., LTD.

HIV Business Meeting

March 30, 2023

Presentation

Kyokawa: Thank you very much for joining us today. Shionogi & Co., Ltd. will now hold an HIV business information session.

First, let me introduce today's speakers. First, Isao Teshirogi, CEO.

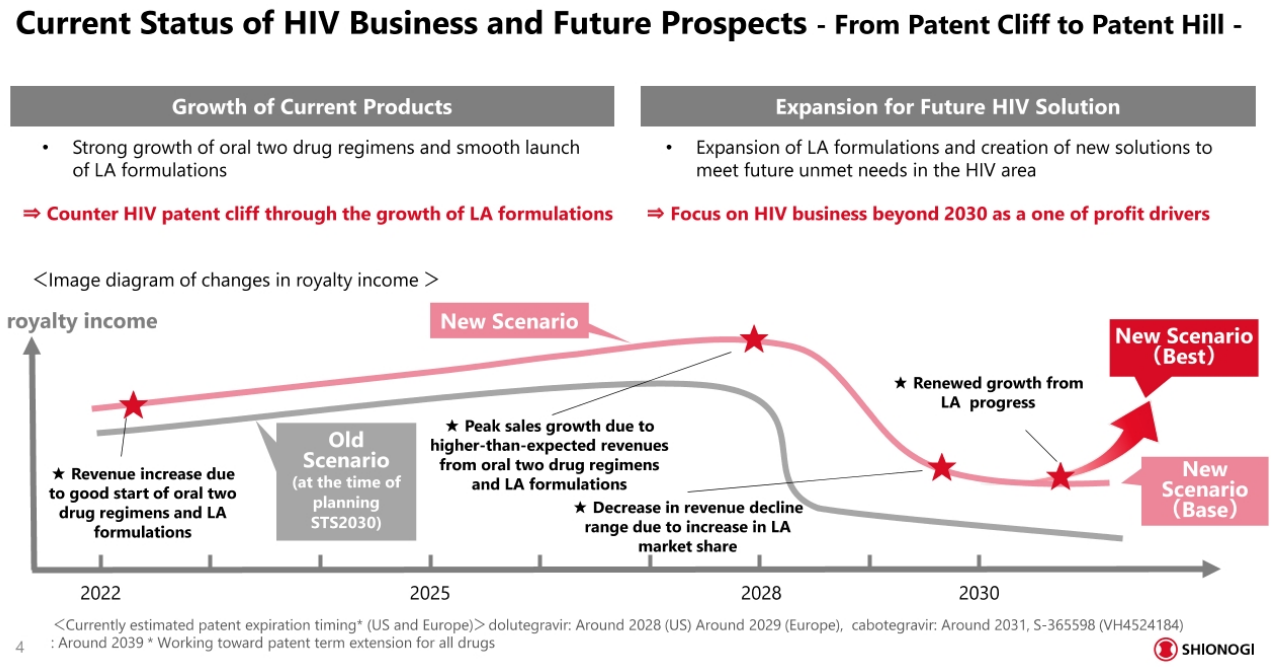
Teshirogi: Teshirogi here. Thank you.

Kyokawa: John Keller, Senior Executive Officer in charge of R&D.

Keller: Keller here. Thank you.

Kyokawa: First, Dr. Teshirogi will give an overview of the current status and future prospects of the HIV business. Next, Dr. Keller will give a presentation on the ViiV/Shionogi HIV business strategy.

We will now get started. Dr. Teshirogi, over to you.



Teshirogi: Hello again. Thank you.

Starting from page four, I would like to give a brief overview of the circumstances that led to the current situation.

Actually, our company and ViiV have had a lot of discussions about dolutegravir. One of the major turning points was when ViiV announced that they were going to launch combination drug with rilpivirine called Juluca. At the time, a three-drug regimen was the norm.

Historically, when two drugs were used, resistance to both drugs occurred, and this was a very bad thing. We were concerned that by trying this, something bad might happen to dolutegravir, but the experts at ViiV were

very confident. They asked us to let them go ahead with this two-drug combination, and started the development of Juluca.

We think that the world as a whole still had a certain skeptical attitude toward two-drug combinations. Accordingly, they started with a fairly high NNRTI and tolerance hurdle. That went quite well, so they said next time it would be with 3TC.

Dovato, as we know it today, was the first drug to be approved, and of course it is extremely safe, but we wondered if it is really possible to treat patients normally with these two drugs without inducing resistance. However, they said they were confident that they would be able to provide us with foundational data, so we were on board.

At the same time, they thought that once-a-day oral administration might be limited. We think that people were thinking about it, maybe vaguely, and in fact we think that it will become a reality when the patent cliff for dolutegravir comes in 2028. We wonder how much the HIV market will change at that time. We think everyone will still be processing that.

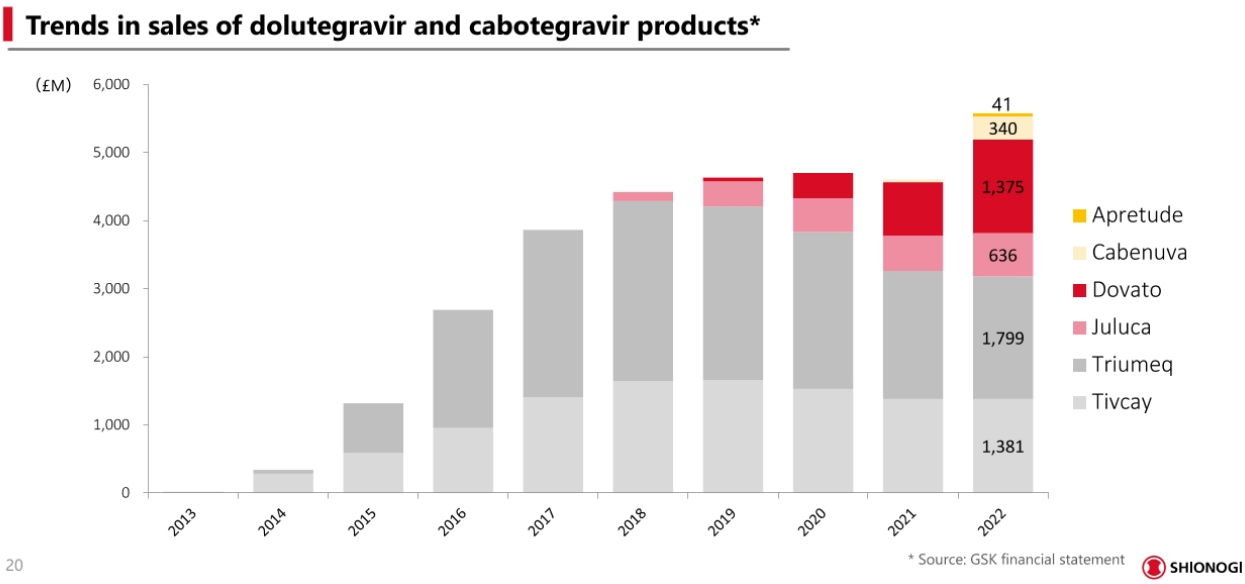
Dovato and Cabenuva also took time to become established. If we can do it orally and accumulate patient data, and then do it with two drugs. We can have an integrase inhibitor like dolutegravir that is really strong even with two drugs and has a high tolerance hurdle, it would be a huge blessing in terms of the burden on patients.

In the case of three-drug regimens, each drug has its own side effects, and the side effects of these drugs can have a multiplicative effect on each other. Therefore, 2 drugs are more beneficial for patients than 3 drugs. We believe that together with ViiV, we are in the process of establishing this 2-drug combination regimen.

We believe that this is the ability to think strategically about how to develop things. A strong rival company that has been making things has the ability to really develop things. However, we believe that ViiV, SHIONOGI, and GSK are in a leading position in terms of combining what we have to create a business that meets the needs of patients.

In future, we envision a focus on long-acting formulations. Today, we would like to discuss how our royalty and HIV businesses, including ViiV and the relationship between ViiV and Shionogi, will evolve over the next 10 years or so. The purpose of this meeting is to have a frank discussion with you about the impact of this on Shionogi, including financials.

ViiV's Growth History



As you can see from ViiV's sales forecast on page 20, the first point is that in 2022, sales have begun to grow, partly due to coronavirus pandemic recovery.

The gray curve on page four, which you saw earlier, is the curve we were thinking about when we wondered how far Cabenuva would grow, and how far sales of the long-acting agent would grow, but we thought it might be a little more gradual. However, it is starting to appear that sales will be stronger than expected.

Especially in this area, Dr. Keller will be presenting, injections in two places once every two months, even in a situation where it is quite painful, most patients say that they should not go back to once-a-day orals, so there is still an unmet need for HIV patients.

Major Anti-HIV Drug Development Status including Competitors* (1)

* Source _2022 4Q financial results

	Compounds	Mechanism of action		Phase 1	Phase 2	Phase 3
ViiV	VH3640254	Maturation inhibitor	Self injection			
	VH3810109 (N6LS)	Broadly neutralizing antibody	Every 3 months more / Self-injection			
	VH3739937	Maturation inhibitor	Self injection			
	Cabotegravir 400mg/ml	Integrase strand transfer inhibitor	Every 3 months or more/ Self injection			
	VH4004280	Capsid inhibitor	Every 3 months or more / Self-injection			
	VH4011499	Capsid inhibitor	Every 3 months or more / Self-injection			
	S-365598 (VH4524184)	Integrase strand transfer inhibitor	Every 6 months or more			
Merck	MK-8591A (Islatravir+doravirine)*1	NRTTI*3/NNRTI	Daily Oral			
	MK-8591B (Islatravir+MK-8507)*2	NRTTI/NNRTI	Weekly Oral			
	MK-8591D (Islatravir+lenacapavir)*1	NRTTI/Capsid inhibitor	Weekly Oral			
	MK-8527	NRTTI	PrEP			

17 *1 On FDA partial clinical hold for higher doses than those used in current clinical trials *2 On FDA clinical hold *3 Nucleoside reverse transcriptase translocation inhibitor SHIONOGI

Major Anti-HIV Drug Development Status including Competitors* (2)

* Source _2022 4Q financial results

	Compounds	Mechanism of action		Phase 1	Phase 2	Phase 3
Gilead	Lenacapavir	Capsid inhibitor	Every 6 months subcutaneous PrEP			
	Lenacapavir/bictegravir oral combination	Capsid inhibitor/Integrase strand transfer inhibitor	Daily oral Treatment experienced			
	Lenacapavir	Capsid inhibitor	Every 6 months subcutaneous			
	Lenacapavir/islatravir oral combination	Capsid inhibitor/NRTTI*2	Weekly oral			
	bNAb combination (GS-5423, GS-2872) *1	Broadly neutralizing antibody	Every 6 months subcutaneous Cure			
	Lefitolimod*1	Toll like Receptor9 (TLR9) agonist	Cure			
	Vesatolimod	Toll like Receptor7 (TLR7) agonist	Cure			
	HIV bispecific T-cell engager (GS-8588)	Bispecific T-cell engager	Cure			
	Lenacapavir/bNAb combination	Capsid inhibitor/broadly neutralizing antibody	Every 6 months subcutaneous			
	HIV long-acting injectable INSTI (GS-6212)	Integrase strand transfer inhibitor	Every 3 months subcutaneously			
	HIV long-acting oral NNRTI (GS-5894)	NNRTI*3	Weekly oral			
	HIV long-acting oral INSTI (GS-1720)	Integrase strand transfer inhibitor	Weekly oral			

18 *1 Non-Gilead sponsored trial(s) ongoing *2 Nucleoside reverse transcriptase inhibitor *3 Non-nucleoside reverse transcriptase inhibitor SHIONOGI

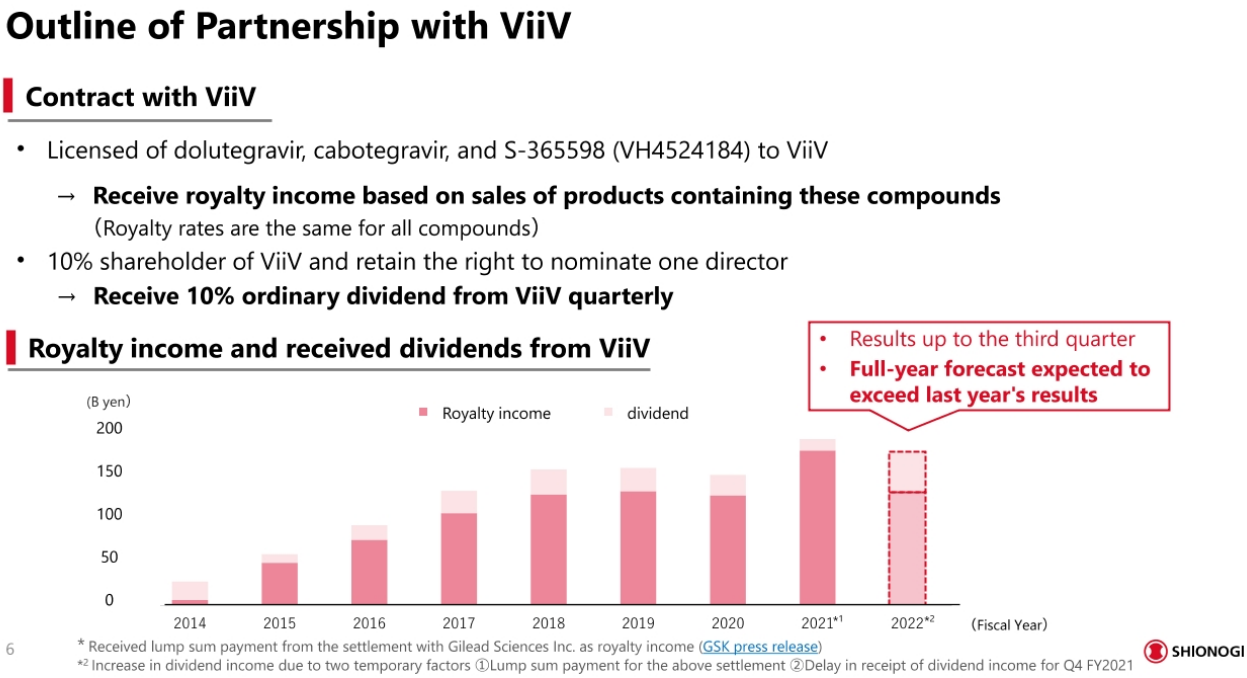
In response to this, for example, on pages 17 and 18, I have shown the pipelines of three companies, including our so-called rivals. None of them is working on a development pipeline that would replace integrase with a so-called once-daily oral formulation. There are still oral once-weekly formulations under development, but you can see that most of the rest of the R&D has shifted to cures and long-acting formulations.

We are truly proud to say that it was ViiV, Shionogi, and GSK that initiated this and created the impetus for it. In this respect, I believe we have a head start.

In light of this, we believe that the HIV field has the potential to be a growing market in the future. Research is ongoing in a once per six months formulation. Our code number is S-365598. ViiV's code number is VH4524184. We will complete Phase 1 of the oral formulation and in calendar year 2023, we are going to start Phase 1 of the injectable formulation to see how long acting it is.

We at Shionogi would like to continue to contribute to this market. In the course of our work on infectious diseases, including influenza, COVID-19, and RSV, we are of course still continuing our research into HIV. The purpose of today's meeting is to reiterate our commitment to this market.

Since Dr. Keller is also on the Board of ViiV and has overall responsibility for R&D, I would like to ask Dr. Keller to talk about what we are doing today, and what we have done to date. I would also like to invite your questions and comments.



Keller: Thank you very much. Thank you for joining us today.

First, I would like to talk about our partnership. Integrase inhibitors are the backbone of current oral therapies. Cabotegravir enables long-term action. In future, we anticipate that S-365598 will allow for activity over a very long time period. All of this is included in the terms of the agreement with ViiV.

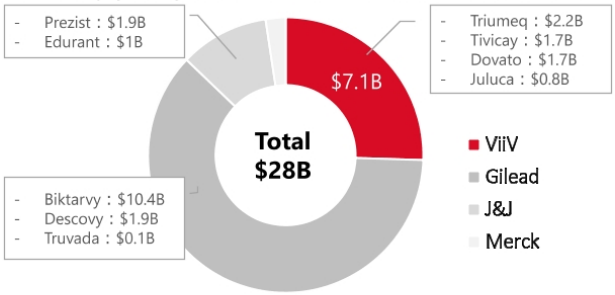
Royalty income is earned on these products. All royalties are set at the same level. In addition, we have an equity stake of 10% in ViiV. And we hold the right to nominate directors.

Royalty income is linked to sales. Dividends vary from year to year depending on cash levels, but the trend is the same. And this is how the number is increasing, we see that the initial stages of the coronavirus pandemic were an exception to that trend, however, we expect this growth to continue.

Current HIV Market Status

Anti-HIV drug market（Treatment＋PrEP）

- The top three companies account for about 98% of the market share in this huge market
- US market is about 65% of value share
- ViiV steadily gaining market share (2015: 16.7%⇒2022: 25.5%)



PrEP market

- Currently only three drugs (Descovy, Truvada, Apretude) are indicated for PrEP
- Among the 1.2 million potential candidates in US, only 25% of them actually use PrEP*3
- The market size is expected to more than double by 2030*4
  - US government support to reduce new infection

The current anti-HIV drug market is about $28 billion*1, and the number of infections has been increasing by about 30,000 people / year in US, a major region*2

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*1 Calculated based on financial statement, 2022 4Q of major pharmaceutical companies selling anti-HIV drugs
*2 US HIV statistics
*3 N Engl J Med 2023; 388:769-771 DOI: 10.1056/NEJMp2216100 *4 US National HIV/AIDS Strategy

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Here is the overall HIV market situation. As for market share, we have about 65% of market share in the US market. For ViiV, the figure is 25.5%, and this is growing all the time. Overall, the HIV market is worth USD28 billion, and the number of infected people in the US is increasing by 30,000 each year.

HIV can be considered an epidemic in both developing and developed countries. We are increasingly focusing on providing patients with a variety of options. We want to provide products that are easier to use, and fit into each individual's life.

With regard to prophylactic drugs, current options are Apretude, which is our product, as well as Descovy and Truvada. There are 1.2 million people who could potentially benefit from these drugs, being sexually active and potentially at risk of contracting HIV. About 25% of these use prophylactics. A factor in the low proportion of potential patients taking prophylaxis is related to insurance reimbursement.

The US government's coverage is not consistent for now, but we believe that the US government's policies and environment will change in the future. And when it comes to injectables, we believe that prophylaxis will be more widely accepted. The market size of PrEP will grow significantly, more than doubling by 2030. We believe it will be USD2.5 billion.

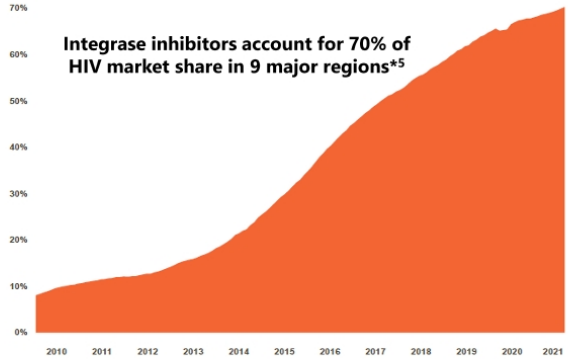
Integrase Inhibitor “Backbone” Leads HIV Market

Basic design of highly active anti-HIV therapy*1

- Efficiently suppress HIV replication by combining multiple anti-HIV drugs with different mechanism of action
- Anti-HIV drugs require long-term clinical evidence due to lifelong administration

Characteristics of integrase inhibitor regimens

- Highly ranked global guidelines*2-4
- Extensive clinical and real-world evidence supporting long-term efficacy, safety and high genetic barrier



*1 Anti-HIV care guidelines (Health and Labor Administration Promotion Survey Project Grant: AIDS Countermeasure Policy Research Project) *2 European AIDS Clinical Society
*3 Panel on Antiretroviral Guidelines for Adults and Adolescents (Create by the US Department of Health and Human Services)
*4 Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring (Created by WHO)
*5 Meet GSK Management Getting ahead of HIV (Nov. 2021)

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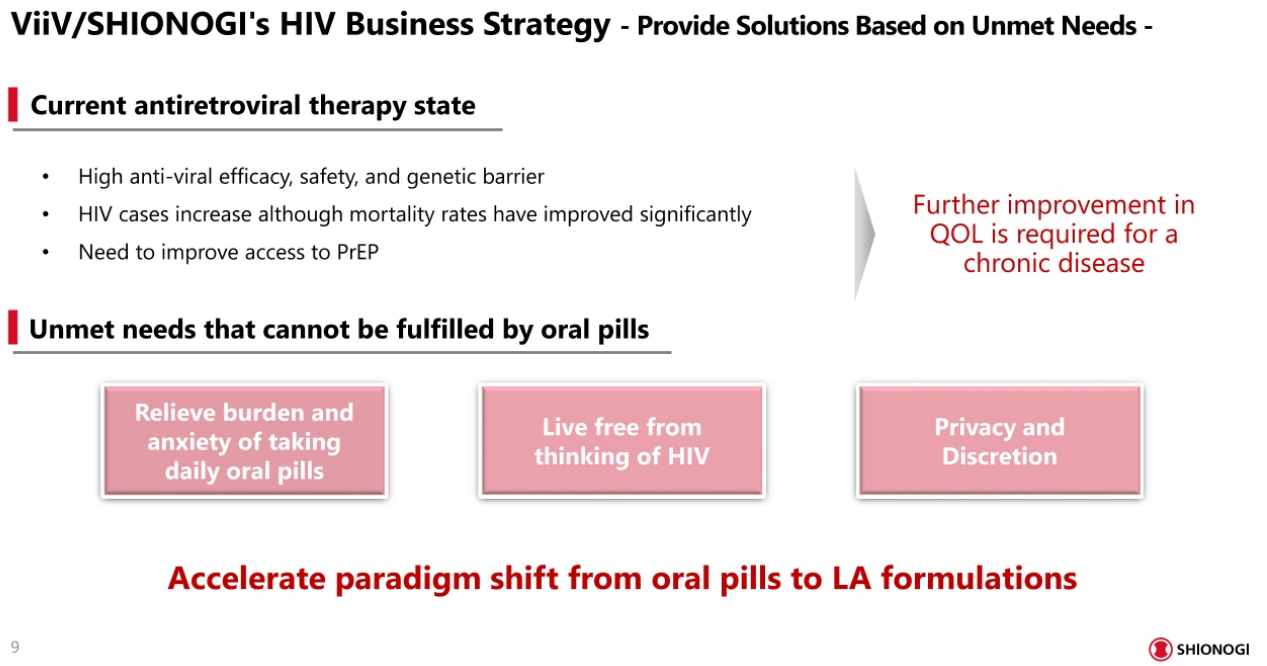
Integrase inhibitors are the backbone of these regimens, both in combination regimens and in the injectable form. These have a very significant antiviral effect, a high barrier to resistance and evidence for good long-term safety and tolerability. This is what we can expect from a fundamental HIV regimen.

Clearly, there is no substitute for integrase inhibitors. We believe that dolutegravir has had a similarly crucial role in HIV treatment since its launch.

There has been a transformation in HIV treatment. We decided to start with the best oral form, then two drugs, and then a long-acting form. We would like to consider what the future long-acting form will look like and what the competitive environment will be like. That is critical to the success of the long-acting type.

Currently, 70% of the HIV market share in nine major regions is accounted for by integrase inhibitors.



Looking at strategy, together with ViiV, we are looking at how we can bring more options to our patients in situation that excellent oral agents that have very high antiviral efficacy and the high resistance barrier and tolerability have already been developed.

Furthermore, improvements are needed in prophylaxis. This is because the number of new infections is only increasing. With regard to new infections, many are individuals whose lifestyles are unstable, or whose dwellings are unstable. These people may not be able to easily receive insurance reimbursement. Therefore, providing a long-acting formulation can have a significant impact.

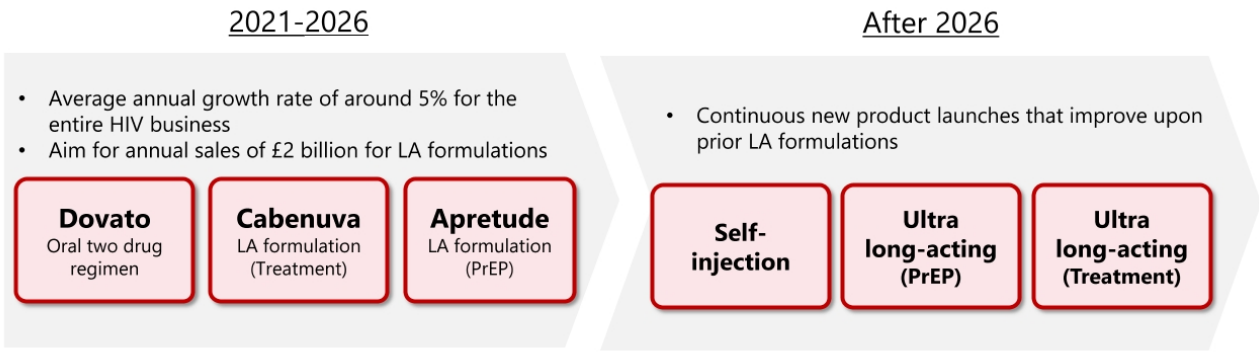
From the perspective of unmet needs, there are clearly unmet needs that cannot be met by oral formulations, and we believe that long-acting injections can be used for both treatment and prevention.

For example, having to take medication every day reminds the individual that he or she has HIV every day. This can place a mental health burden on the individual. They are forced to regularly acknowledge their infection status in their lives. The lack of privacy, the fact that someone could find out from seeing the medications in someone's luggage or bathroom cabinet that they have HIV, for example, could be very unsettling for these individuals.

By giving long-acting injectable drugs instead of oral drugs, we can enable individuals a degree of freedom from their HIV infection. When we talked to patients about this, we got very positive feedback. Patients were very excited and pleased when we told them that a long-acting form would be created.

Medium-to Long-Term Growth Drivers

Innovative products that meet unmet needs



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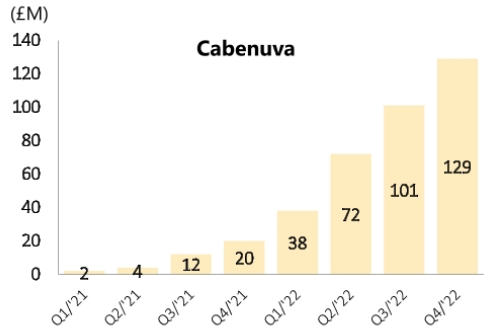
In this early period, from 2021 to 2026, with two drugs and a long-acting form coming out, the average annual growth rate will be 5%. This is anticipated to continue. And we are targeting annual sales of GBP2 billion for long-acting forms. With Cabenuva and Apretude, it will be possible.

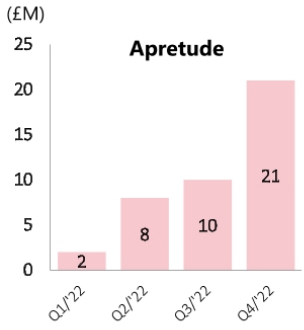
After 2026, we will develop a more user-friendly formulation. One option is self-administered formulations. Patients will appreciate not having to come to the hospital. This may not be the case for patients without privacy, but it is possible to use the system in a way that suits individual conditions.

In addition, ultra-long-acting injectable drugs will be available not only for two months, but also for three months and six months. This is true for both prevention and treatment.

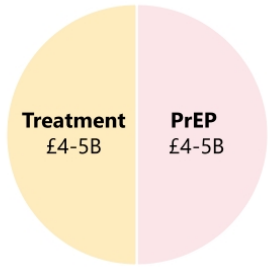
Business Trend of LA Formulations and Market Projections

ViiV sales trend of LA formulations*1





LA market projections*2 (Up to 2030)



Significant lead-time versus competitors in the rapidly growing LA market

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*1 Source: GSK financial statement
*2 Meet GSK Management Getting ahead of HIV (Nov. 2021)

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Cabenuva is growing very steadily.

Injections at the hospital presented a few challenges. But since then, it has grown significantly as insurance reimbursements have worked out and as the pandemic waned. There is no sign of a slowing in sales now. Apretude is a prophylactic drug and is expected to grow more and more significantly in the future.

As for the future of Apretude, we believe that it will continue to grow, but if this is to change significantly, a very big turning point will be what happens with regard to insurance reimbursement and preventive drugs by the US government. CMS in the US has already begun evaluation. This process has begun sooner than we thought. We are currently proceeding faster than we had expected.

As this market becomes more established, we have yet to see competitors, especially for therapeutics.

Characteristics of ViiV's LA Formulations

Cabenuva (cabotegravir + rilpivirine)

- Indication: Treatment of HIV-1 infection
- Dosage: intramuscular injection, once every 2 months
- Release Date: Feb 2021 (US)
- Country of Sale: US, Europe, Japan, others

Apretude (cabotegravir)

- Indication: PrEP of HIV-1 infection
- Dosage: intramuscular injection, once every 2 months
- Release Date: Jan 2022 (US)
- Country of Sale: US, others

The world's first and only LA formulations for HIV, based on integrase inhibitor backbone

About 90% of clinical trial participants*1 prefer Cabenuva therapy over daily oral pills

66% of those who have used daily oral prophylaxis or discontinued it are highly interested in LA formulation*2

*1 FLAIR study: NCT02938520, ATLAS study: NCT02951052, ATLAS-2M study: NCT03299049, SOLAR study: NCT04542070
*2 Meet GSK Management Getting ahead of HIV (Nov. 2021)

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Two drugs are introduced here.

The trial compound is Cabenuva, and this is an intramuscular injection once every two months. It is already available in the US, Europe, and Japan. Apretude is a prophylactic drug, but its launch in the US has been completed and will be considered in other countries in the future.

Very importantly, those who started and stopped taking oral prophylaxis, two-thirds, have a very great interest in injectables. It's not just the SOLAR study, but every time we do an injectable study, more than 90% of patients say they want to continue with injectables after the study is over.

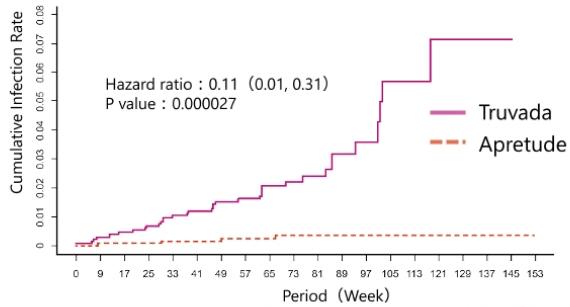
Major Clinical Studies of Cabotegravir Products

Cabenuva (cabotegravir + rilpivirine)

- **FLAIR study*1**
  - Verified non-inferiority of efficacy and safety after 124 weeks in untreated patients
- **ATLAS study, ATLAS-2M study*2**
  - Comparison to daily oral treatment verifying non-inferiority of efficacy at 152 weeks in treatment experienced patients
- **SOLAR study*3**
  - Verified non-inferiority of efficacy and safety in direct comparison with Biktarvy
  - Therapy satisfaction rate statistically superior to Biktarvy

Apretude (cabotegravir)

- **HPTN083 study*4**
  - 66% greater prevention efficacy than Truvada in men or transgender women at high risk of HIV infection
- **HPTN084 study*5**
  - 89% greater prevention efficacy than Truvada in women at high risk of HIV infection



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*1 FLAIR study: NCT02938520 *2 ATLAS study: NCT02951052, ATLAS-2M study: NCT03299049 *3 SOLAR study: NCT04542070
*4 HPTN083 study: NCT04692077 *4 HPTN084 study: NCT04824131

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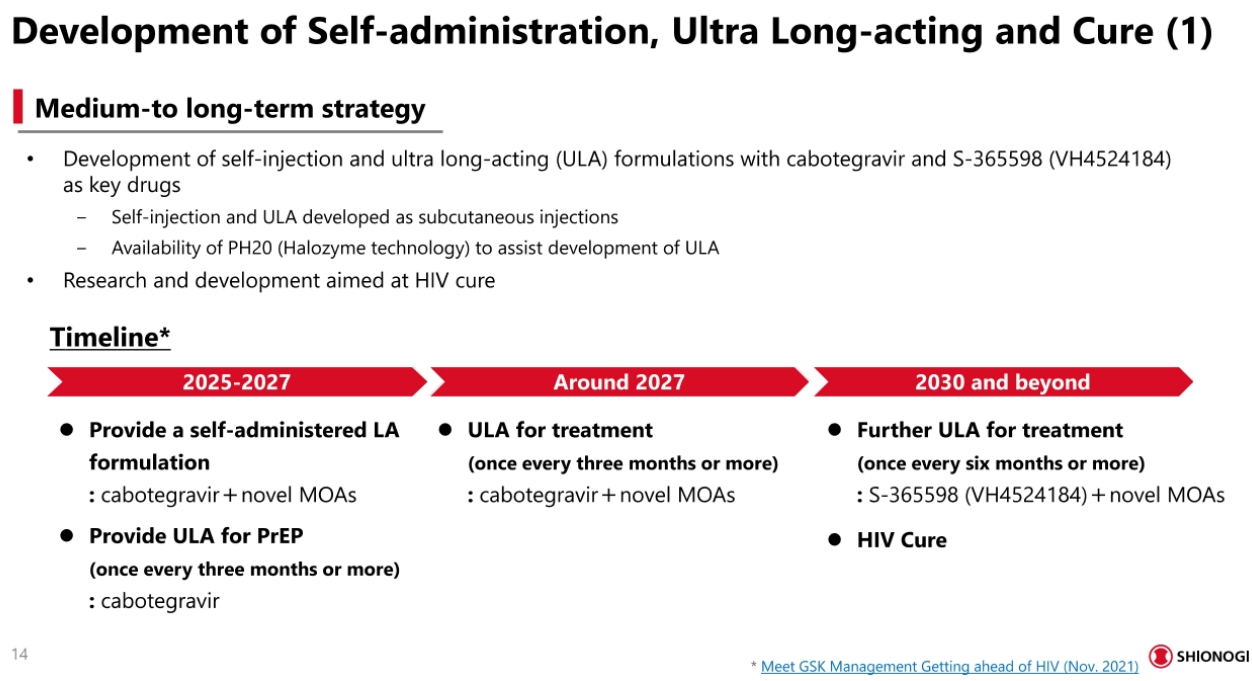
Now we will say a few words about the study data. Some key studies are summarized here.

First, the FLAIR study. Here, the treatment group was untreated patients, with non-inferiority in efficacy and safety at 124 weeks. There was a group that switched to oral or injectable drugs. Long-term efficacy, safety, and high barrier to resistance have been confirmed.

Next is ATLAS study, which is a study for previously treated patients. This also had an oral and injectable group. We changed it to a one-month formulation, and then once every two weeks. This is another study we conducted.

The most recent study is the SOLAR study. This is a head-to-head study with Biktarvy. The results confirmed non-inferiority and safety. We also found a statistically significant increase in treatment satisfaction.

Next is Apretude, a prophylactic drug, which was tested on men and transgender women and found to be very effective in preventing the disease, exceeding Truvada by 66%. Also we confirmed 89% prevention efficacy than Truvada in women at high risk of HIV infection.



Now, let's talk about future prospects. As I mentioned earlier, patients will have more treatment options in the future and will be able to use it in a way that suits their individual conditions. The burden in patients' lives becomes smaller and smaller. This is true for prevention as well as for treatment.

Also, long-acting self-administered drugs, once every three months, will also come in 2025 to 2027. Around 2027, we are aiming to launch an ultra-long-acting treatment, which is administered once every three months, or at an even greater interval. It is also possible that cabotegravir could reach 3-monthly administration.

Next, in 2030 and beyond, there will be S-365598, and then new mechanisms. We anticipate that compounds with an action of greater than six months will require a new mechanism of action. We will need something more than cabotegravir.

This is our vision of the future. We will continue to focus on very interesting and exploratory areas of HIV.

From the patient's point of view, if we can achieve 6-monthly treatment, what do words like "cure" and "treatment" mean at that point? If viral testing can be stopped altogether, and if the frequency of injections can be reduced, the burden on the patient can be greatly reduced.

Development of Self-administration, Ultra Long-acting and Cure (2)

Actions towards 2030 and beyond

- **Application of PH20*1 （Halozyme Thrapeutics, Inc）**
  - Increase subcutaneous administration volume for longer effect time
  - Phase 1 trial combined with cabotegravir ongoing
- **Development of S-365598 (VH4524184)**
  - Created and licensed by SHIONOGI*2
  - Higher genetic barrier than existing integrase inhibitors
  - May enable ≥ 6m dose interval
  - Phase 1 trial on going
- **Development of combination candidates**
  - Candidates from a wide range of mechanisms of action, including broadly neutralizing antibodies*3, capsid inhibitor, maturation inhibitors
  - Phase 2b trial of cabotegravir in combination with broadly neutralizing antibody N6LS*3 to be initiated in 2023
  - Aiming for combination selection by 2024

*1 VIIV press release: license agreement for ENHANZE® drug delivery technology *2 SHIONOGI press release: out-licensing S-365598 (VH4524184), third-generation HIV integrase inhibitor
*3 For details about the development status of concomitant drug, refer to Appendix P.19

Now, we show here what tools are available to achieve these visions.

First, on the right side, the development of new combination drugs. This includes broadly neutralizing antibodies, as well as capsid inhibitors and maturation inhibitors. We are also investigating candidate drugs with new mechanisms of action.

And as for formulation, there is, for example, Halozyme's PH20. This allows for an increased dosage per dose. Also, there is further development of S-365598(VH4524184). If this could be developed, it would achieve a higher resistance barrier than existing integrase inhibitors.

We would also like to continue to discuss combination candidates and S-365598, both internally and in collaboration with ViiV.

This concludes my presentation.

Question & Answer

Kyokawa : We will now move on to the question-and-answer session. Mr. Sakai of Credit Suisse.

Sakai : My name is Sakai from Credit Suisse. I have two questions for Dr. Keller.

I would like to ask about the market for this prophylactic. You said there are 1.2 million potential target patients in the United States, but Only 25% of them actually use prophylaxis. What kind of patients are you targeting? For example, what kind of lifestyle do you have? This is going to be a basic question, but can I ask it?

Keller : This is an important question. Basically, we would like to double this figure. At present, individuals in the US receiving prophylaxis are relatively affluent. Even if an individual belongs to a certain group, it is not guaranteed they will be eligible for reimbursement. Government insurance becomes very important if it is not covered by company insurance.

However, in order to cover a wider range of people, solid insurance reimbursement, Medicare, and especially Medicaid are very important. The current system is a patchwork. Even if you have Medicaid coverage, you may or may not be reimbursed.

There appears to be a trend to incorporate it into the budget in some way in the future, but the legislation has not yet been passed. The CMS process is currently in the process of considering this as Medicare, Part B. This is being done now, and I don't know when, but access should improve if this passes.

Even with improved access, 44% of newly infected people are African Americans. Many newly infected African Americans are in difficult socioeconomic situations. This is especially true of those who live in the southern part of the United States. There are structural and social barriers for these people.

With regard to prophylaxis, there are several programs that are currently in place to provide support and awareness. We are doing things to increase prophylactic use among these people as well, but it will take more time.

Sakai : I think that the more prophylactic drugs are available, the fewer patients there will be. Is that understanding of the cycle correct?

Keller : Yes, that is correct. Unfortunately, the majority of newly infected patients are young. There are potential issues of compliance with prophylaxis among younger patients. Compliance may not be good in younger patients.

Older people are not taking full responsibility for recommending such preventive medicines. But I think we need to take on those responsibilities. As you say, the number of patients will decrease as more prophylactic drugs are available.

Sakai : What are your thoughts on cure?

Keller : I think we are still a long way off. I think 2030 is a very optimistic number. When I said after 2030, I think the real cure will be much later than that.

The patient experience is important. Until now, "cure" has been explored as a research subject by various people. One area of particular interest has been activating viral reservoirs. However, it does not work well. And there are risks. Fever also occurs. There are good arguments for not administering this treatment.

On the other hand, we have compounds with very few side effects, that can be administered three-monthly or six-monthly. Patients are likely to resist a move back to daily oral therapy after receiving this type of treatment.

Therefore, we think that the development of an attractive cure profile will become a major issue as therapeutic agents become easier to use.

Kyokawa : Okay, Mr. Kohtani from Nomura Securities.

Kohtani : I have two questions.

Investors are wondering whether the portfolio can replace Tivcay and Triumeq with cabotegravir by 2028..

I see on page four that royalties are forecast to decrease, but I was a little disappointed because it seemed that royalties would decrease in the future. SOLAR study was the first head-to-head comparison of Cabenuva and Biktarvy. I think the data was clear, but the percentage of patients showing viral suppression seemed was somewhat small, 93% vs. 90%. However I don't think there's much reason not to switch to Cabenuva.

Also, the SOLAR study showed an advantage for QOL, as we found out clearly at the time of the press release. And after completing the survey, 90% of subjects wanted to continue with injectables.

Recently, GSK said that Cabenuva would come from other competitors. The data is there, including the head-to-head data, but isn't it a question not only of replacing Biktarvy, but other regimens as well? But in spite of that, why are royalties forecast to decrease? How big is the impact of SOLAR study? What is the impact of the SOLAR study with respect to penetration? Given the results of the SOLAR study, wouldn't we expect a better outlook for the future?

Keller : This could be seen as being somewhat conservative. We are looking at the overall HIV market, including the potential of long-acting agents and things like that.

And from those, we will also take market share in the future, and I think we will see more and more patients who are using injectable, long-acting formulations as a result of the SOLAR study. New formulations come out.

At first, Gilead said that it was very complicated. They talked about oral lead-in and about pain. However, the truth is that it isn't complicated. Also, the insurance issue is heads up, and then the injections, which are now once every two months, will decrease to once every three months, so the burden is decreasing more and more.

So we are in a very good situation, especially with the support of the data from SOLAR study. In that sense, I think this forecast is conservative.

Kohtani : I think it would be better not to list the date of the patent for the substance. I think it creates misunderstanding.

What I think is no longer true is that I see a patent on the substance. This is especially true with regard to Cabenuva. It is a very complex regimen. And I think that is innovation. Accordingly, I think you should list the patents for the injection regimen.

Keller : I think you are right. I think the general development pathway for generics is not clear.

Kohtani : And as to your second question, the big threat to cabotegravir is the Gilead capsid inhibitor. It is a six-monthly injection. I believe the Phase Ib data has recently come out. It is a broad neutralizing antibody for HIV, but it was able to maintain 95% of the viral response at 6 months, which means that it lost 5% of viral response. Is there a need for this once every six months despite the 5% rebound?

And even with respect to once every two months or once every three months, what about rebound? This is an injectable drug, so I think it will cost more than $40,000 a year. Is the need really there? Is someone really demanding something like this once every six months?

I would like to ask you one more question. With regard to the long-acting S-365598, you are insisting on two drugs instead of three, by putting two antibodies in one drug, and I would like to know what you think. I would like to ask if something like six-monthly administration is really necessary.

Keller : I think you mean the integrase inhibitor backbone. Gilead is pursuing that combination because they do not have a long-acting integrase inhibitor. The mechanisms, including those we list here as combinations, all have high tolerance barriers.

If the first drug is an integrase inhibitor, the second drug can be handled a bit weaker. The data show that using too many capsid inhibitors or too many broadly neutralizing antibodies can be a problem. Long-acting means that it is dependent on a long-acting integrase inhibitor.

As for broadly neutralizing antibodies, we are talking about a regimen of two drugs, and we chose this broadly neutralizing antibody with a coverage range of 95%.

Kyokawa : Next question, Mr. Ueda from Goldman Sachs.

Ueda : This is Ueda from Goldman Sachs.

In the explanation at the beginning of your presentation, Dr. Teshirogi said that your company has been producing a variety of products, and that ViiV's knowledge is very useful in the process of creating business. Could you please explain the strengths of your company and ViiV, and what strengths can be expected in the future by working together?

Teshirogi : Also from Dr. Keller, we have actually had Board meetings and things like that, and we have talked to people on the science side, and we have talked to people on the commercial side, so I will add that again.

As far as HIV is concerned, we are still not sure if it is realistic to build global sales strength in HIV, but we will leave this to ViiV. We are planning to provide HIV treatment to low- and middle-income countries, including MPP, and we are planning to do it by ourselves for other drugs.

What I think is very strong is that they are very good at picking up unmet medical needs from the patient base.

At first, we thought that patients are satisfied with such a good profile and the combination with 3TC once a day is really safe and sufficient for them. They are striving for more.

I believe that in ViiV, the ability to discover the needs of people who are suffering from invisible stigma or who are having a hard time to survive, and to think of solutions to those needs, is very strong. I think they are very strong in this area.

We, on the technical side, make sustained-release injectables, for example. They have Halozyme, but we have our own long-acting injectable technology, and in the case of small molecules, we have design capabilities. Not many companies would have the ability to design a small molecular integrase inhibitor like S-365598 that

would last at least three months and preferably six months. We are aware that our rivals are also having a very difficult time in this area, so we are looking for a combination of the two.

When they ask us if we can do something like this, we can make a proposal with our technology, and I think we are doing a great job of combining the two.

I think the source of the combination is the continuous and very serious attendance at Board meetings, and the constant dialogue with the various medical officers and chief commercial officers before and after Board meetings to find out what the needs are in each market. I think this is a strength of our partnership.

The management of GSK, whether David Redfern or Emma Walmsley, thinks we are very important. Our companies are in constant, sustained contact. We feel we are very active in contributing to this partnership. I think that the two companies supporting ViiV have a very strong combination of capabilities.

Keller : In addition to having that great relationship, ViiV is the only company dedicated entirely to HIV. The Company thinks about HIV morning and night.

And we think in terms of patent cliffs too. At ViiV too, we wondered if we should continue to be a company that specializes in HIV. And the answer was yes. So, while there are issues such as patent cliffs, the development of long-acting formulations continues.

If we think of HIV as a business, we might think that we should look at other businesses because of this patent cliff, but if we think that HIV is our mission that we have to devote ourselves to what's best for patients, then we will still conclude that we have to devote ourselves to HIV. I think that is our mission.

Ueda : Thank you very much. Second, I would like to ask you about the future of the market for long-acting formulations, including with respect to your company. First of all, I would like to know if your company is considering shifting from cabotegravir to, for example, S-365598.

You showed us the pipeline including other companies earlier, but in the future, for example, Biktarvy looks to be a very big player, and I wonder if that in itself carries an advantage. Can you also tell us your thoughts on whether the market will become a little more segmented, so that patients can use the best of the various items in the pipeline that you just gave us?

Keller : I think the key to all of these regimens is long-acting integrase. No other long-acting integrase is available. This is true whether it is three months or six months.

And I believe that we can achieve six months with S-365598. The results of a long-term study would be revealing. The formulation technology also makes it possible to achieve a six-month timeframe.

If you look at the other mechanisms, I don't think any of them have that ability. There was a lot of excitement about Merck's NRTTI, but toxicity issues have emerged. Toxicity can be a particular issue in HIV therapy. Therefore, for now, I believe it is a tailwind for us.

Kyokawa : Mr. Hashiguchi from Daiwa Securities.

Hashiguchi : I am Hashiguchi from Daiwa Securities. Thank you very much.

I think a lot of what you said today was about how much fruit Shionogi can reap from the results it has achieved so far, but what I want to ask is the level of resources Shionogi will devote to HIV in the future.

Of course, I think it is important to invest in areas where the Company has strengths and where investment efficiency is higher, but at the same time, the price pressure is likely to intensify in the future, and the hurdle for creating products that exceed these strengths will continue to rise.

In this context, Shionogi's role in the relationship with ViiV may be to search for promising targets, synthesize promising compounds, or perhaps even to improve existing formulations. What level of resources will be allocated to such efforts, in terms of head count for example? What are your thoughts on the future?

Teshirogi : Thank you very much. For example, our integrase inhibitor S-365598 may be quite hidden, but if the integrase inhibitor is applied to the virus under extremely high pressure, resistance can be created if one wants to create it. The original motivation for S-365598 was to create an integrase inhibitor with a particularly strong tolerance profile.

The number of deaths attributable to HIV has been very low, as you can see in the chart here. The reason why we are seeing more infections among young people is that their recognition of the disease has dropped tremendously. The unfortunate reality is that it has spread very widely again to a group of people who are hardly aware of it.

This is not to say that COVID-19, influenza, and RSV are not also fatal. The onset of AIDS is associated with a significant mortality rate, so there is no doubt that it is a horrific infection.

The resistance barrier of integrase inhibitor is also very high, and people may mistakenly think that this disease has already disappeared.

As Mr. Kohtani mentioned with regard to neutralizing antibodies in particular, although there is coverage, leakage still occurs. I believe that we must continue our research and development based on the recognition that the disease is not easy to treat, including this leakage issue. We are proud to be a Company whose strength lies in infectious diseases.

In this context, we have certain accumulated strengths in antivirals, so the background of S-365598 was not that almost all the people were on S-365598, but that within the same infectious disease team, there is a HIV team, RSV team, and influenza team. The influenza team have recently been focused on COVID-19, and this is changing once again. Our teams have this sort of flexibility.

We will continue to consider what we need to create in the future, but we are not talking about increasing the number of infectious disease teams by a factor of five or anything like that. Of course, within the scope of our activities, we will talk with ViiV, for example, and with the people in charge of COVID-19 or influenza, and we will think about what we need to do.

We have been considering allotment of our resources with respect to our current prioritization.

What you just said, Mr. Kohtani, is very important. This model is really more like an outline. We should have been working with ViiV on a very detailed calculation of how much the price of the injectable regimen would be in the US, how much it would be in Europe, how much it would be in other regions, how many patients it would be sold to, and the level of royalties would be returned to our company. Unfortunately, we are not currently able to perform exact calculations to estimate this. I apologize for that.

We are actually in the same boat as you, and this was also the case with Crestor, but we are also beginning to talk that royalty income may fall significantly. However, the question is whether it was a good idea to present this information this time, but we believe that the amount of money will not decline, and in fact, there may be a possibility of growth.

We are not at liberty to say anything that is not in ViiV's own materials. Based on GSK's materials during this period, we have taken the appropriate steps where we can, but we would like to take the next step of putting out what we think will happen to the royalty stream in our own way in the future.

Hashiguchi : Thank you very much.

Kyokawa : Mr. Yamaguchi of Citi Securities, please go ahead.

Yamaguchi : Thank you very much. Two, briefly, please.

First, I would like to ask about the chart on page 11 that shows the market for prophylactic drugs. The first question is how to eventually calculate the ratio or rather the percentage that will eventually be replaced by LA from existing orals at the time of treatment.

Also, I believe that your products are highly competitive in treatment and prevention, but I would like to ask these two questions first: Is your market share likely to increase considerably from the current market share?

Keller : Thank you for your question. As for Apretude and prophylactics, we have shown clinical superiority, and I believe we have a good chance of capturing more than half of the market share.

The growth of the preventive drug market depends on the extent to which US government insurance will cover it. We think it will depend, in particular, on the increasing speed of the US government's support process. The center of the prophylactic drug market is still the US market. We are preparing for this in Europe, but the US market is bigger.

Gilead has been very successful in switching Truvada and Descovy to prophylaxis. European insurers are trying to get them to move toward generics as much as possible. The approach of the US government will be key here.

As for treatment, we intend to maintain a high level of competitiveness and continue to evolve into a better form.

Teshirogi : Mr. Yamaguchi, the other day, Dr. Keller said that he is talking with ViiV about that. In the past, Biktarvy and our brand still had a lot of oral drugs, but we thought that about 15% to 20% of the HIV market might go to injectable drugs. At this point, we are thinking that if the interval is three or six months, about 30% of patients will go for injectable drugs or LA.

In fact, although John did not mention it, 60% of the current Cabenuva patients have switched from non-ViiV regimens, so we are not cannibalizing our own sales, but patients are flowing to long-acting treatment from other sources. We believe that the market for long-acting therapy will grow, and that about 30% of all HIV patients, mostly in the US, will go in that direction.

Our current thinking is that, at least at that stage, we will have a near monopoly. Of course, our rivals may also produce good LA formulations, but from our point of view, when it comes to tolerance hurdles and side-effect profiles, we think it is a very big question whether a truly strong LA market can be created without a long-acting integrase inhibitor.

Our current thinking is that about 30% of the $28 billion shown in the first table will go to LA.

Yamaguchi : Thank you. That is all.

Kyokawa : Thank you very much. Next, Ms. Kumagai from Mitsubishi UFJ Morgan Stanley, please go ahead.

Kumagai : This is Kumagai. Thank you very much. I would like to ask you about Slide 4 which shows the image Dr. Teshirogi mentioned earlier. The drop in 2028 and 2029 is much milder than the previous scenario, but when you look at the contributions here, can you give us some indication of how each component, such as self-injection or three-month preventative cabotegravir, will contribute?

Teshirogi : I'm sorry, but we cannot comment on that. We cannot comment beyond ViiV's development plans. Recently GSK showed that it is stated that the target for cabotegravir once every 3 months is around 2027, so I can only speak within this range, but I believe we will be able to do a little better.

However, we can't say beyond this, as they have provided us with such materials in the first place. At this point, it's cabotegravir every two months, and then how far we can stretch Apretude, which is realistically the launch pad for the rest of the year. This is because it will be the biggest characteristic in setting the starting point of how far that launch pad will go. I believe the trend in this area to about 2025 or 2026 will be very important for subsequent trends.

Kumagai : Understood. I know this is a similar question, but I think GSK had a chart called HIV Portfolio Mix for 2026, which was a mix of one-third each of two oral regimens, other orals, and injections.

What is the breakdown of the HIV portfolio in 2029, and is this also something that is difficult to say because of the ViiV connection? If you have any ideas about this, please let us know.

Teshirogi : This is true not only for us, but also for our competitors, as dolutegravir becomes generic and we have shown that the combination with 3TC can be used once a day. I think that if dolutegravir becomes generic, the oral market will be virtually over. It would be swamped by generics.

Of course, there will be a certain number of people who want to use dolutegravir or Biktarvy brand products, but I think the market will become quite difficult. It may not be possible to sell at the current price.

Therefore, considering lifestyle, efficacy, and safety, I believe that the overall market size will be determined by how many HIV patients will be treated with injectable drugs at the same or higher price, including insurance reimbursement.

At this point, we have no doubt that ViiV's market share will be the largest.

Kumagai : I understand. Thank you very much.

Kyokawa : Mr. Mamegano, BofA, please go ahead.

Mamegano : This is Mamegano from BofA. Thank you very much. I would like to confirm something about the preventive medicine market.

I believe Gilead is developing lenacapavir for prevention right now, and I expect the results of this clinical trial to be available around H1 of next year. I understand that you have a two-month formulation of Apretude, but I would like to know if you have any comments or concerns about the longer dosing period.

Since you mentioned earlier that integrase inhibitors will be the main focus, please tell us first whether you think you can still win against the competition in this area. Thank you.

Keller : Integrase inhibitors are very important with regard to treatment. They are absolutely critical. As for prophylaxis, we have long experience with integrase being effective, but we do not have much experience with capsid inhibitors.

The use of capsid inhibitors in long-acting prophylaxis may work in cases where the capsid is selective, but what is still unknown is the safety and efficacy of capsid inhibitors in long-acting prophylaxis.

We know about integrase, but the long-term safety and efficacy of capsid is not yet known, and I think it is still a bit risky.

Teshirogi : Also, six months is also attractive. As Dr. Keller said, there is a certain validity in covering with one mechanism, at least in terms of prevention rather than treatment. However, we still need to think carefully about how safe it will be over a period of years. We place great importance on this point, because the target population of PrEP is basically able-bodied people. For prevention, the trade-off between effectiveness and side effects of the treatment is important. As these individuals are healthy, the safety profile is extremely important.

That has always been an issue for Truvada and Descovy, and I wondered if we should really continue to allow healthy people to take something that may produce renal bone effects in the long term. I am not saying that it would be good if it were a patient, but I have always wondered about the positioning of the therapeutic drug in the context of how to regulate the virus in order to save lives, and whether it would be a good idea to have totally healthy people take the drug all the time, knowing that there might be renal bone effects in the future. We have been in the integrase inhibitor market for more than 10 years now, and I believe that the safety profile is one of our strengths. This is a benefit even for healthy people.

Mamegano : Thank you for your explanation. Thank you. I would like to ask one more question. On page 11 is the market forecast for LA formulations. The estimate for prophylactic administration of these drugs is GBP4 billion to GBP5 billion, but how much of this is accounted for by integrase inhibitors? I think you mentioned earlier that it is about half, but how much does your company expect? Please let me know if there is anything you can tell us about that area. Thank you.

Keller : I don't have a specific prediction, but, however, given the superiority and the long-acting availability, I think it's about half. Or possibly more.

Teshirogi : Gilead is quite strong commercially. As I mentioned earlier, there are still many unknowns in the area of safety, but when they put forward the idea that it can be done every 6 months or by subcutaneous injection, it was a very positive step forward. However, as I mentioned earlier, there are still many things we don't know about the safety of PrEP. For example, in Europe, as I mentioned earlier, even if the NRTTI regimen has a renal bone effect, the price of oral drugs is probably considerably lower. I think that a part of the PrEP market may go to oral drugs when they become price-dominant. Considering all of these factors, we thought that at least half of individuals would be able to switch to integrase PrEP, which we consider to be the best.

Mamegano : Thank you very much.

Kyokawa : Last question. Mr. Muraoka, go ahead.

Muraoka : This is Muraoka, Morgan Stanley. Thank you. I'm going back to the chart on page four, but in relation to the mid-term plan, which will be reviewed this time, I believe the forecast core operating profit is JPY200 billion in 2030. Looking at it this way, it would appear that core operating income in 2030, even with the HIV factor alone, would it be correct to assume that something like a 50% increase will appear in the space of a few months?

Teshirogi : We will make a full announcement of our new medium-term plan in a few months, so I hope you can wait until then. We are well aware of what you are saying, and we need to come up with a comprehensive report that includes the various pipelines that lead to this point, such as COVID-19 and influenza, which we are currently working on. We will let you know about that at that time.

Muraoka : Thank you very much. One more thing, and this is something I haven't fully digested, but I heard in the US that the IRA law says that the drug prices of top products will drop in 2026 or 2027. I think Biktarvy was one of the candidates on that list. If the price of Biktarvy is reduced suddenly, should we expect that the unit price for LA, injectables, Cabenuva, Tivcay or others will also be affected to some degree?

Keller : I don't know how big the drop will be. With regard to the list itself, there is a lot of HIV activism and lobbying, and Gilead is very powerful. So I do not know how high the number will be. Overall, ViiV is conservative for price. We have not given an aggressive price figure. Therefore, how will the market change? ViiV does not charge a large premium for oral LA preparations. ViiV has aimed to set a price that will please payers, the government, and the community. Thank you very much.

Kyokawa : With that, we will conclude the HIV Business Meeting.

[END]