SHIONOGI & CO., LTD.

HIV Follow-up Meeting

October 12, 2023

Question & Answer

Kyokawa : Hello. My name is Kyokawa, Director of Corporate Communications Department at SHIONOGI.

Thank you all for taking time out of your busy schedules to join us today.

We will now begin the HIV follow-up meeting of SHIONOGI & CO., LTD.

There will be two speakers today. First, is Isao Teshirogi, PhD, Chief Executive Officer.

Teshirogi : This is Teshirogi. Thank you for your cooperation.

Kyokawa : And John Keller, PhD, Senior Executive Officer, Senior Vice President, R&D Supervisory Unit.

Keller : This is Keller. Thank you for your cooperation.

Kyokawa : Okay, I will give you a brief explanation of today's flow. Today's session will be a Q&A session on the content of the HIV event organized by GSK on September 28. The session is scheduled to end at 4:45 PM. We would like to facilitate the Q&A session for sell-side analysts. After we have received a set of questions, we will be happy to take questions from the buy-side as time permits, if there is time remaining.

First, we will take questions from the audience, and then we will take questions from those participating via the web.

We will now begin the meeting. If anyone in the audience has any questions, please raise your hand. If you are nominated, we would appreciate your affiliation and name.

Mr. Yamaguchi from Citigroup, please go ahead.

Yamaguchi : My name is Yamaguchi from Citigroup. My first question is a bit vague, but there was some new information at the briefing held for ViiV, such as a slight increase in sales and an explicit date for patent expiry.

I was wondering what the difference is between what ViiV has been saying up to now and what they are saying this time. Also, your company's medium-term plan is already underway, so is everything the same in comparison to that plan, or is there subtle new information in there? I would appreciate it if you could tell me about these two things first, as I was a bit unorganized when I only heard about the content of the briefing.

Teshirogi : John will talk about the GSK side, and I will talk about the relation to our medium-term plan.

Keller : I think the key message was the importance of LA formulation. LA formulation have always been expressed in pounds, but by 2026 it will be around 2 billion pounds. This is exactly one-third of ViiV's total sales in 2026. The total is 7 billion pounds, so that's about one-third.

There is the world they are looking at and the world we are looking at in 2031, and if you look at the total HIV market, 30% of it will be long-term action. And 80%, will be working toward prevention, that is one message.

That means that portfolios are now long-lived. Looking at Dovato and others, the LOE will be in December 2029. It is absolutely possible that the IP of LA formulations will further increase from 2031 by incorporating new combinations.

In addition, ViiV predicts the growth of the HIV market itself. Overall growth of 6 to 8% will come from this sector from 2021 to 2026. I think we are looking at it a little more conservatively this year, but it is all in there. Not so big, maybe not so much, taking inflation into account.

That could be roughly GBP200,000 a year. First, let's put it on that basis: this market for prevention will double. Between GBP4 billion and GBP5 billion, the market for prevention grows at this time of year.

And finally, information on the competition. Although other companies have produced LA products, ours stands out in terms of safety, efficacy, and reliable long-term action. The two key points are that you still have Head Start, and that you maintain it.

Teshirogi : Thank you very much. From our point of view, in the revision of the medium-term management plan issued in June, we presented a schematic chart showing how we expect the figures to move in this way.

But even at that stage, we couldn't give you all the detailed figures, so once the GSK and ViiV figures were available, we explained again what we were saying. I think that when we modelled it in this way, especially the sell-side people understood it. We think it would be the most appropriate way of looking at it if you could endorse what SHIONOGI is trying to say.

There are still some things that we and ViiV share, which of course we cannot tell you. However, we have told you as much as we can in the revision of the medium-term plan, with a certain amount of round numbers. In our perception, there was no excess or deficiency in what we presented in June from the GSK HIV Day material this time.

In this sense, we hope that you will reinterpret the figures we presented as SHIONOGI's own figures in light of the ViiV and GSK announcements, and use them to help you think about our company model.

Kyokawa : Mr. Ueda.

Ueda : My name is Ueda from Goldman Sachs.

Ueda : My first question is about the business environment, including future prices. First, I would like to ask what the current business environment is like, including insurance reimbursement for long-acting formulations, of LA formulations.

I would like to know how we should consider the price impact of LA formulations as oral drugs are going generic in the future.

I wonder if there is a bit of risk in taking 30% of the treatment in this 2031, especially if the price difference is significant, so can you tell us about your thoughts on this area?

Keller : I would like to answer. The situation is that access to treatment in the United States is very good. The drug is doing well with great commercials and government insurance coverage.

However, the reason we were not able to be so aggressive was that there were still oral drugs in particular, and although this was the case with therapeutic drugs, the situation with preventive drugs was still very challenging. CMS and Medicare recommend that all oral and injectable medications be covered. It absolutely has to be done though.

This is about Medicare.

As for Medicaid, Medicaid affects the poor more, but the national level insurance, they have a stronger message. Now that the Biden administration is trying to cut costs as much as possible, nothing is immune to its influence. However, this treatment is the largest, and reimbursement for it can be expected, but Europe depends on the country.

For example, depending on each country, it works well in France, but it remains difficult to access in other countries. Such things are different in Europe, though. On balance, I would say that, as a whole, as you know, we, ViiV, have the largest market share in Europe. So, the US has the strongest portfolio for this injectable drug. And each of these countries, as well as the country of Japan, are aware of this benefit.

Teshirogi : I think this is a very important point, Mr. Ueda. At present, the cost of one year of treatment is USD38,000 or USD40,000, which I think that Biktarvy is the highest. The current situation is that we are pricing close to this level. ViiV is not set higher than the best of oral just because it is injectable, so it is set at a similar level.

For us, the most important point is that 95% to 97% of the people in our comparison study with Biktarvy commented that they would never want to go back to oral again. So, for example, if a generic product is released and the insurance holder says that they want the patient to go back to the cheaper orals, the question is whether they can force the patient to go back to orals while they can only take injectables once every two months, once every three months, or for a little longer, and they can have a very good quality of life. Our focus is on whether we can force people who have a fatal disease such as HIV but whose quality of life is so different that they don't want to go back to oral drugs just because they are cheaper. I was wondering if that would be quite a difficult negotiation for the insurance holder.

We are not saying that the entire HIV market will become injectable, but our hypothesis is that patients who are unwilling to take this option because of their own lifestyle may not be able to return to oral therapy simply because of the price difference.

Therefore, we will have to consider at that time whether or not there will be negotiations to adjust the price a little, but I do not think it will be a case of adjusting the injectables to the price of the generics. Rather, it is more of a premium brand, so the 30% or 40% there can continue to be treated very close to the current one-year price. Our current thinking is that this can be justified from the viewpoint of quality of life.

Ueda : Thank you very much. Another thing I would like to know is Gilead's competition in this long-acting market. As you just explained, we also think that cabotegravir is better in terms of data and timing of its launch. I think that Gilead's sales force has been, to a certain extent, turned upside down, and ViiV has had a more difficult time than Gilead. Can you give us some background on your thoughts on whether ViiV can take the lead in long acting?

Keller : Integrase inhibitors are not ultra-long-acting, clinical trials are currently underway. Gilead was launched for salvage patients. So clinical trials are taking place, but if you go in as a single agent, this is thought to be at the end of 2025.

This is a subcutaneous injection. Six-month dosing. In terms of safety, there have been problems with the long-acting type of injection in Gilead. The most important thing is that the injectable drug has no side effects. We will have to see what happens in 6 months. We have to look at the profile and see how the long-acting type works.

Our cabotegravir is an integrase inhibitor, it has been shown to have a very long-term safety profile and efficacy. For our part, we are carefully watching what our competitors are doing. And we are looking at the safety of integrase inhibitors at the molecular level.

Muscular injection, but this is also easier for patients to self-inject. There are various formats and various dosage forms, but I am still trying to figure out what is needed for self-injection. The patients themselves seem to be very satisfied with the intramuscular injection.

Teshirogi : I think that is also a very valid question that we always think about. For example, if a new concept emerged in which two-drug combinations such as capsid inhibitor plus NNRTI, which is not often considered, were to be used for treatment, but we believe that the current treatment paradigm, including doctors and patients, has already established integrase as the backbone and what to put on it as the treatment paradigm.

Therefore, I think the first thing to do is to see if Gilead can make an integrase inhibitor once every two months, once every three months, or in some cases once every six months, is the square number one.

As was the case with Biktarvy, which is a late comer, dolutegravir had a lot more safety and efficacy data than Biktarvy, but the fact that Biktarvy was able to beat dolutegravir by so much is due in part to its sales force. I don't think dolutegravir is inferior to bictegravir in terms of efficacy and safety at all, but I think Gilead was very strong there.

If, at the time of this injectable, Gilead were to start from scratch to produce an injection for dose of every two or three months, similar to cabotegravir, and the efficacy and safety of the integrase inhibitor were to be proven in, say, 2026 to 2028, would the market be so comfortable at that time? The question arises whether the market will be comfortable at that time. Also, the efficacy, safety and resistance profile of integrase inhibitors used for the first time will inevitably take several years. After all, HIV is a fatal disease at the end of the day, so it is not easy to do treatment failures.

In this light, the database of the efficacy and safety of cabotegravir that has been accumulated up to now should provide users with tremendous peace of mind, even if a new integrase inhibitor is released by Gilead.

Even if, for example, a very good integrase inhibitor, combined with capsid or with a new NNRTI, were to emerge, it is unlikely that the market would be turned over as early as 2026 to 2028. If you think about it that way, our point is that we think our advantage is considerable.

It is still a medicine, so it can only be used if it is safe, effective, and has a resistance profile; all three of which are required. Considering how easy it would be to prove that with an integrase inhibitor that you are now creating from scratch, I think it is reasonable to assume that there is at least a four to five year, or seven to eight year advantage.

If the question is whether the injectable market will expand or not, then the argument is how will it expand? And if the question is whether the injectables market will expand, I think it is a very reasonable prospect for us to say that the main player is ViiV.

Ueda : Thank you very much. That is all.

Kyokawa : Mr. Sakai.

Sakai : This is Sakai from UBS. As an extension of what you just said, I would like to ask you about ViiV presentation 22, 23, and CAB 400, the data of which will be available in 2024. I think this will be one of the keys to the success of the CAB 400, as you said, in terms of prevention. I think that the advantage or effectiveness of this is one of the keys, but I would like to ask whether this is the correct understanding.

Also, option one and option two are shown here. What is this to be brought in combination with? This may or may not have an economic impact for your company, whichever ViiV chooses to do.

Also, it comes up here, but it's self-injection. As Mr. Keller just mentioned, though, I am told that muscle injection is better. I think that when it comes to self-injection, we are inevitably talking about subcutaneous injection. How should we think about those points? There are several points, but please tell me about this.

Keller : Thank you. Cabotegravir is used both, prevention and treatment, and we have considerable experience. If we could match PK for the new formulation of every four months or so, the advantage is that we can keep the same profile for this long period of time with safety and efficacy secured.

That should also help from a regulatory perspective. We have to talk to the regulatory authorities, but regulatory efforts would be accelerated as the basic PK profile has already been identified. The pharmaceutical process is a very long process basically.

Next, regarding options for injectable partners, injectables every four months are important. At the moment, doctor conduct testing for the virus every three months, but in the future they may change every four months. There are two potential combination drug options: rilpivirine and neutralizing antibodies. Both options have been very successful. Working with J&J, rilpivirine is doing well.

And the advantage of this is familiarity, being the same kind of combination agent that we have had and used before. We had been using drugs with same efficacy and performance for some time, so there is a possibility that development can proceed relatively smoothly.

If you are talking about self-injection at home, this is what about half of the patients will do. Privacy is important to some people, so they don't want it to appear that they have HIV medicine in their home. However, some people believe that fewer injections are better. It is desirable to be able to choose the most convenient format for this purpose.

Before the once every four months came out, we first tried intramuscular injections once every two months and once every three months, so there was a need for the device to be simple and comfortable. So, this bar for self-injection is a bit of a technical high point.

That's why this self-injection timeline longer. The reason we have a timeframe for about to 2028 is that we still need a long timeline for long-acting injectable drugs and their self-injection.

Teshirogi : This is a very difficult point, Mr. Sakai, and I don't have a concrete answer for this. Until now, for example, in the case of HIV, the market has been dominated by Triumeq and Biktarvy, with one type of drug covering most patients. I think that when it comes to long acting injectables, perhaps we need to have a large variety of them.

For example, as John just mentioned, most patients visit the doctor for a viral check to see if their HIV is now relapsing, usually every three months, but some patients come to see the doctor every four months or so, because they have stabilized a lot.

If this kind of thing can be made to work, it may be possible to have virus checks only once every six months, so it is highly beneficial for patients to receive injection every time they have a virus check and have the virus check go around. Some people want to check the virus every three months, some want to do it every four months, and some want to do it every six months, so it's not one-size-fits-all, but we need to have several injectables depending on the life cycle of each patient or country. This is what we are discussing now.

And then, I also heard that they don't want to use intramuscular injection, that they don't want to use two doses, and now both rilpivirine and cabotegravir are used twice, so in that sense, I wondered if it would be possible to use only one drug. I think we need to respond to those needs, such as whether it is possible to do

subcutaneous injections at home. I am not saying that there are no technological limits, but I think we are entering an era in which companies will be asked how they respond to such limitations.

Incidentally, as I am sure you can quickly understand, the difference between intramuscular and subcutaneous injections is that, in terms of injection volume, subcutaneous injections need to be smaller, otherwise their skin will be bloated, so I am not sure if it is really correct to put 10 cc or 20 cc in this area to last for six months. When injecting subcutaneously, we still want to lower the injection volume. It goes in during muscle injection, so it means that it can withstand a certain volume to a certain extent.

From the subcutaneous injection side, they have to drop the injection volume. If you want to do self-injection at home in a less conspicuous way, you have to do it once a month or once every three months, but in that case, the volume of subcutaneous injection will be very high. Although, I think we have to prepare several patterns according to such patient attributes, such as whether they are willing to accept it or not.

So, with HIV, I think, as I have said many times, we are moving from a place where we were dealing with all patients with one tablet to a place where we are managing quite a lot of formulations well and providing them according to patient preferences, and there could be a number of options for that.

Of course, there is the problem of what to do if NNRTI causes side effects in partner drugs, or what to do if neutralizing antibody causes resistance, although it is said to be safe so far. I still think we need to have several options for that too, not just one.

However, we have often talked about whether this is a phase in which we will offer products that are considerably more complex than in the past, depending on the business and patient situation, so I think it's probably that way.

Sakai : Thank you.

Kyokawa : Thank you very much. Mr. Muraoka.

Muraoka : My name is Muraoka from Morgan Stanley. I want to talk about the next year or two. I also had a document with a timeline of once every four months and once every six months. Looking at it this way, many studies will start around 2024 and 2025, so I don't think there is any event that we can look at the results of and think this is interesting. But I think there should be a VH184 (S-365598) data readout by now, and if there is an event or data readout that we should expect in a little, one- or two-year time frame, please let me know. That is all.

Keller : Yes, that's right. Certainly, the long term and oral PK results will be available next year. Then, later that year, the actual combination, the long-acting study will start, and the results will be got in 2025. I think you can see the progress with those.

And a number of other studies will be conducted next year. In it, you will find N6LS's, various combinations, and capsids, and many portfolios. That will be the timeline.

Muraoka : Also, sorry. N6LS was listed as option two in Q4M this time. Why didn't the capsid come in like option three, even though there is a capsid in ViiV? Is there any background to that?

Keller : Capsid, this is an inherent long-acting type, but integrase inhibitors also cover the weakness of capsid.

If we can confirm good data with capsid, we may consider self-injection or intramuscular injection. Capsid is unlikely to be an option, but when considering the development of once every 6 months or once every 12 months, we may return to capsid.

Teshirogi : In terms of competing for limited resources, the once-every-three-months or once-every-four-months schedule for cabotegravir and rilpivirine is by far the highest competitions for us. Naturally, we will consider various options, such as neutralizing antibodies, capsids, and maturation, and we will also consider combining them in some way.

I thought that integrase, plus rilpivirine, would be the fastest way to go for now. ViiV does not have such unlimited resources for research and development. In terms of what order we will do it anyway, rilpivirine plus cabotegravir, or a bit longer, the backbone integrase is already crucial, after all. Whatever we combine it with, we will not be able to proceed without Integrase. In that sense, both ViiV and we would like to know whether VH184 (S-365598) can really go to four months or six months. We recognize that what is combined with it is the next phase.

Muraoka : One thing that caught my attention in President Teshirogi's discussion about pricing is that you said that when oral drugs become generic, whether or not they will be asked to lower their prices is another story.

Teshirogi : I don't know if the insurance holder will say anything at all yet.

Muraoka : That's not hypothetical, I just haven't looked into it because I haven't studied it enough, but have there been similar disease profiles in the past, where in similar cases, because the patent for the oral formulation expired, they were asked to reduce the price and they actually reduced the price of the injectable formulation or used it for similar diseases? Have there been any similar disease profiles in the past? If you know anything about this, please give us some hints, so we can easily look it up ourselves later.

Teshirogi : The only similar example we have really heard of is risperidone. Risperidone was not lowered. The injectable form has a huge benefit to patients, so if they were to go to generic oral risperidone once a day or something, that would be that, but in terms of benefits to patients, once-every-three-months risperidone was a whole different world for them, so the price was not lowered at all.

We believe that is true as well. I mentioned a little that since this is a life-threatening matter, the patient is important, but the insurance holder also has an IRA and so on, so I am not sure how they will behave. From our point of view, the benefit to the patient in terms of life, length of treatment, and the length of time that treatment is required are not products that can be priced concessionally from an overall perspective, and we believe that we can maintain that.

In case you are asking me if I am thinking about it at all as a possibility, I think their attitudes will have changed according to the insurance situation in the US in about five or six years from now. By then, the President will have been replaced by someone after Biden, so it's a bit difficult to see what's going to happen. I wonder if this is a story we need to consider as a possibility. That is what I meant.

Muraoka : Thank you very much. Very helpful.

Keller : As an example in the UK, oral combination drugs have a very strong position as compliance is extremely important for both healthcare professionals and patients. I think it's true that combination drugs a very big issue in terms of price.

Muraoka : Thank you very much.

Mamegano : Thank you very much. This is BofA's Mamegano. This time, there was talk of a patent for the oral formulations of Dovato and Julca, which will be extended slightly. Also, the schedule for ultra-long acting was revealed. So, I am just wondering if we can assume that several options for ultra-long acting will be available by the time the patent for the oral formulation expires.

First of all, I think that ultra-long acting will be approved before the patent for the oral formulation expires, because it is 2026 and 2027 for the once-every-four-month formulation and 2028 to 2030 for the once-every-six-month formulation, but let me check that first.

Keller : Yes. Of course, we are very much focused on that, one every four months until 2027, and then one every six months by 2029. We are working to obtain benefits for patients for the long-acting.

Mamegano : Thank you very much. First of all, regarding oral drugs, as mentioned in the Q&A session at the GSK presentation, since the patent for dolutegravir alone is set to expire first, what is your view on whether or not it will ever be used in combination with other generics?

Keller : It's just a matter of what happens to the patents at the moment. We are discussing it now. Protection with respect to the formulation is considered to be extended.

Teshirogi : What Mr. Mamegano is saying is that, as we can see from the example of UK, if a patient who is taking one tablet is forced to take two tablets because it is cheaper, the patient or the doctor will take responsibility if the patient becomes resistant to the drug. The issue is to what extent doctors and patients can take responsibility for the fall in compliance.

It is logical that some people would go for two tablets because they would prefer the cheaper option. In response to the concern that when the patent for dolutegravir expires, all the drugs, including Dovato, will stop being used, I think that HIV patients' lives are at stake and that they are taking things quite seriously, including compliance. In such a situation, I think it is quite impossible whether we can force everyone to go there because it will be cheaper if we split it into two tablets then.

However, there may be a certain drop-off because there may be some patients who do so, but we don't have to think about suddenly jumping 80% or 90% in a year, like with ordinary generics.

Mamegano : The once-every-six-months formulation, I think you are doing two here with VH184 and VH310, is this subcutaneous injection, or is this a self-injection development? Or is it a muscle injection?

Teshirogi : For now, I think subcutaneous injection of Integrase is quite challenging. For the six months it is. We might be able to go for a shorter one, though. The volume for a six-month subcutaneous injection is a bit large, and we are wondering if it is really a good idea. When the volume increases with subcutaneous injection, it inevitably becomes irritating, so it is difficult to know what to think about that.

The VH184 we are doing is naturally more potent than cabotegravir or dolutegravir. Naturally, the injection volume will decrease. It will be reduced, but I am wondering how far you can go with subcutaneous injection six months at a time, which is quite a lot of volume. We will see if we can do a three-month subcutaneous infusion or a two-month subcutaneous infusion, but I think it may be difficult to suddenly do a six-month subcutaneous infusion.

However, we are currently thinking that we can manage to do this while considering the balance between PK and volume for muscle injection.

Mamegano : Thank you very much.

Kyokawa : Thank you very much. Mr. Akabane of Tokai Tokyo, please.

Akabane : I didn't hear you well on the way, so I'm just confirming. In your explanation earlier, when you said, "by country," you only looked at the US and the rest of the world. You mentioned the importance of Medicaid when moving from oral to long acting injectables, and when you and Mr. Biden talked about France, what did

you say the US and European governments would do in the short and medium term going forward? I am sorry I am having a little trouble hearing you.

Keller : Yes. First of all, regarding this injectable drug, the US is 70% of the global market, but I think it is safe to say that the US is almost entirely responsible for this market. 75% of the preventive market is also in the US. So, in a sense, I think it is safe to assume that the US will take the lead.

In terms of the treatment of injections, we are taking our coverage, i.e., commercial, and the US government's coverage. Vocabria has also shown very good uptake in some countries. The difference is that in some countries it is difficult. But in a way, it depends on each individual.

As for prevention it is. Prevention is a bit of a pain, in Europe. But in the United States, prevention is also progressing. That is what I said. That is why I mentioned the difference between Medicare and Medicaid. Medicaid is important. And prevention has not been covered very well so far. So, treatment is covered. There are some programs that cover treatment. Prevention may be a question of what to do in the future in the United States.

Akabane: In the short to medium term, as SHIONOGI, am I right in thinking that sales in the US will increase quite rapidly?

Keller : Yes. That is correct. However, Dovato is still very strong. Long-term is still the United States. However, we must also remember that this Dovato is still very strong. This is true in Europe and the United States.

Akabane : I understand very well. Thank you very much.

Kyokawa : Thank you very much. Mr. Tsuzuki from Mizuho, please go ahead.

Tsuzuki : My name is Tsuzuki from Mizuho Securities. Thank you very much. I just wanted to confirm one point.

I was wondering if VH310 belongs to your company or not, and if it belongs to another company, I was a little surprised that a company other than yours could produce an integrase inhibitor. We would be interested to hear your response, including your perspective on that.

Keller : Yes. I can't talk about it, but I would like to describe this as a collaboration.

Tsuzuki : So, in terms of collaboration, in that sense, I don't know whether the integrase inhibitor that follows Cabenuva will be S-365598 or VH310, but even if it becomes VH310, is it from the perspective that the economic conditions will not change that much? I wonder if you could answer this question, because I think it will probably be important when we think about 2035 or 2040.

Teshirogi : The answer is yes.

Tsuzuki : I understand. Thank you very much.

Kyokawa : Ms. Haruta.

Haruta : I'm sorry to add this. As was mentioned earlier in the ViiV briefing, among the eligibles in PrEP, the situation is still 25%, and there is still 70% of the market left. Of course, there is also access to insurance to increase penetration, but what measures can be taken to increase penetration? Also, can you tell us again what would increase the penetration rate all at once?

In the PrEP market, LA formulations already have a large share of the market, and I think this is where the market itself will further expand. I also wanted to check if oral medications are being used, so please let me know about that as well.

Keller : There are a couple of important things. First of all, I would like to talk about prevention, and I believe that the long acting formulation will take about 80% of the market. This is because there is a clear superiority. Compared to existing oral drugs, it has been confirmed to be approximately 60% more effective in preventing men and 90% more effective in women. After all, it is about compliance, and it is about consistency.

Teshirogi: It is a little difficult to say, but STDs are spreading at a tremendous rate globally, not just HIV. The younger generation is almost unaware, or not even aware that such a disease exists. I hear that syphilis is now exploding in Osaka.

So, I still think we need to redo education, oddly enough, a bit more globally, including the government, because we have been without an STD thread for too long, and most of your young people have never even heard of the name.

Therefore, it seems that most people do not even know what is happening in the early stages of the disease, so I think that is one of the themes that the society needs to address.

And for oral drugs, some time ago, maybe three or four years ago, we estimated from various data how much of the sales of Truvada were PrEP and how much were treatments, as Truvada was being replaced by Descovy.

At one time, it was said that about USD2 billion of Truvada's sales were probably spent at PrEP. At that stage, the coverage was not that good, the education was not that advanced, and moreover, with Truvada pricing, the market would have been used for PrEP for about USD2 billion.

We believe that the market will become quite large as education progresses and usage advances to a certain degree.

Haruta : Thank you very much.

Kyokawa : Mr. Sakai.

Sakai : I have two weird questions, if I may. One is, I think it was some months ago. There was a news story about a rapid decrease in the rate of infections in Sydney, and that is because the so-called PrEP was used very much in Sydney. I think the reason for this is that the LGBT community is very strong, and the spread has been promoted there, although this may be an afterthought.

In that sense, from the perspective of the current trends, I think one of the first things to do is to expand in LGBT societies. I wouldn't go so far as to say that PrEP is effective or safe or that it contributes to society, but as the President has just said, I think the market for PrEP will expand greatly as awareness of infectious diseases increases. Furthermore, I would like to ask you first of all whether the government's move to provide insurance for PrEP will strengthen in the future.

The other thing is that, although we don't hear it very often these days, until a few years ago, we used to hear people say that if you were treated for HIV for a long time, you would look cosmetically older, so to speak, by about 10 years. This, of course, would probably be the case with any drug. However, integrase and reverse transcriptase inhibitors cause significant cell damage, especially to the skin.

Now, in the process of HIV becoming a normal infection like this, I feel that this cosmetic part is going to be quite a big part of the process, and if it is really a side effect, but a drug effect, I feel that it will be one of the issues that we have to solve. Can you tell us about these two things?

Keller : I think we talk about the LGBT society first. LGBT, I still think that access to this society and support is very important. This is exactly what the Biden administration is doing, which is also increasing around the world today.

One more thing, there are a lot of patients, patients who are treated with PrEP, patients in the US, but there are also a lot of homeless patients and patients who have to move around. Long acting injectables are very important to them. These patients cannot continue to visit clinics with a safe environment. I think there is a market problem, but a clinic in San Francisco, we see a homeless community with chronic HIV, and the reality is that patients are not being treated.

So, doing injectables, they can self-inject themself on a sustained basis. We believe that safety and effectiveness can be assured by this kind of community. We believe that this benefit of the society, this is something that is very much recognized.

Teshirogi : I think John talked about the San Francisco example, too, but I heard that they started working with a clinic in a rather poor community, and the atmosphere of the community itself changed a lot, and the community became a little more uplifting.

As Sakai-san said, we are not talking about that with all governments at the moment, but the US is quite serious about how to stop the diseases that are spreading in the Deep South and poor communities in the US, and the Biden administration is quite serious about that.

For example, in London, the area south of the original Soho area is said to be very bad, so I think the government and the City of London have conducted trials in this area. I am not sure to what extent we will appeal to the public, but I am sure that it will be a positive thing for society.

Keller : Protease inhibitors were said they may make patients look older than in the early days, but with regard to integrase, I don't think it has much of a cosmetic effect. Weight gain may be a possibility, though. I think this is also a protease inhibitor, but it could be.

As for appearance, such cosmetic issues are rather infrequent. There may have been a little problem with weight gain, though.

Sakai : I understand. Thank you very much.

Teshirogi : We are still in the early stages, so based on the product profiles, we will decide which ones will be better for the market in the future. So, it's going to be one of the ones that we have now. We will know about this in the end of next year.

Kyokawa : There are about five minutes left. Any more questions? With that, we would like to conclude the HIV follow-up meeting of SHIONOGI.

Thank you all for your time today.