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Fiscal 2021 1Q Conference Call

August 2, 2021

Kyokawa: Hello. I'm Kyokawa, Director of the Corporate Communications Department at SHIONOGI & CO., LTD. I apologize for the slight delay. Thank you very much for taking time out of your busy schedules to join us today.

I am pleased to announce that SHIONOGI will hold a conference call to discuss financial results for the first quarter of the fiscal year ending March 31, 2022.

First of all, I would like to introduce today's speakers. Takuko Sawada, Executive Vice President and General Manager of the Integrated Disease Care Department.

Sawada: My name is Sawada. Thank you.

Kyokawa: Next, I would like to introduce John Keller, Senior Vice President and General Manager of the Corporate Strategy Division.

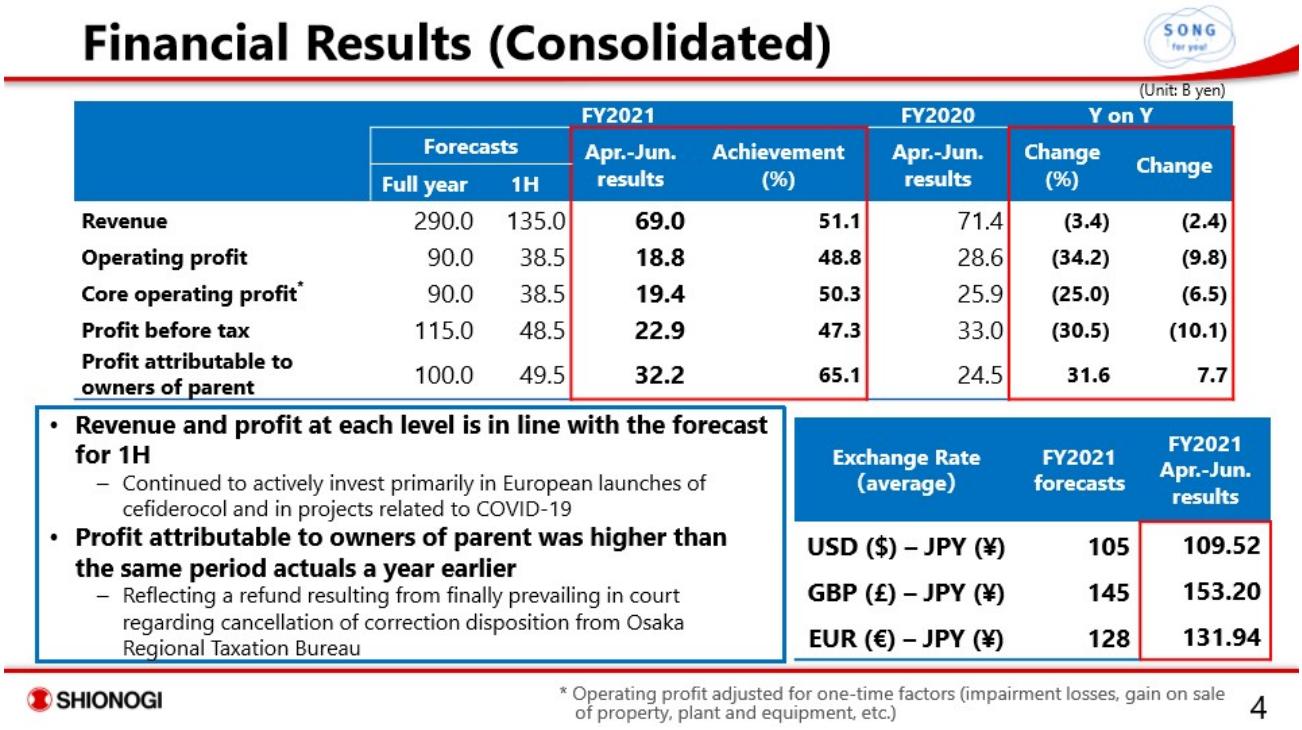
Keller: This is Keller. Thank you.

Kyokawa: Lastly, Yuji Hosogai, Vice President and General Manager of the Finance & Accounting Department.

Hosogai: I am Hosogai. Thank you.

Kyokawa: Today, I will provide an overview of our financial results, and then we will take your questions. The session is scheduled to end at 17:45, but may be extended until around 18:00, depending on the status of the Q&A session.

We will now make a start. Mr. Hosogai, please go ahead.



Hosogai: I would like to begin by presenting an overview of the first-quarter results.

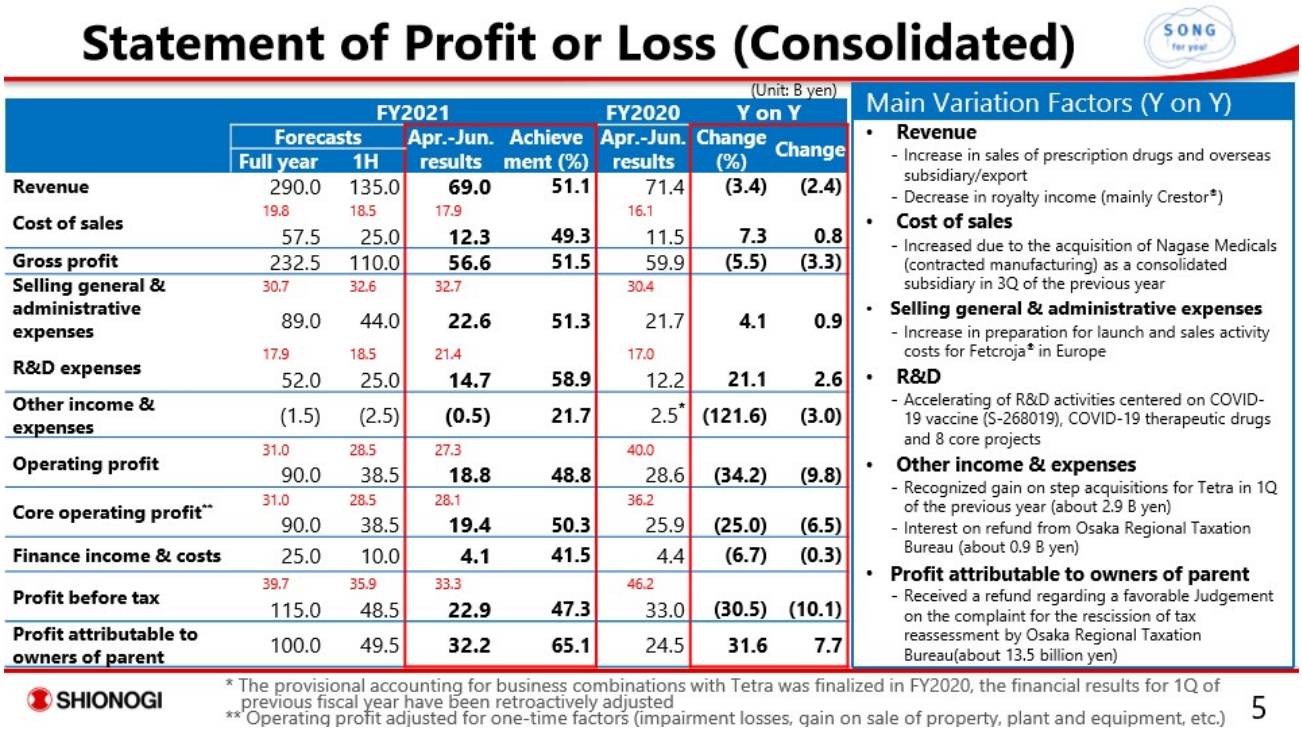
I would like to turn to page 4. The consolidated operating results are shown here.

The results for April to June in the red frame in the middle represent the results for the first quarter. Net sales were JPY69 billion, a 3.4% decrease from the previous year. Operating profit, on the other hand, was JPY18.8 billion, a 34.2% decrease from the previous year. Core operating profit was JPY19.4 billion, down 25% from the previous year. Profit before tax was JPY22.9 billion, a decrease of 30.5%. Profit attributable to owners of parent was JPY32.2 billion, up 31.6% from the previous year.

As you can see in the summary in the blue frame on the lower left, we recognize that sales revenue and each profit item are progressing well against the forecast announced for the first half of the fiscal year.

This includes the overseas progress of cefiderocol and projects related to the coronavirus pandemic, which are continuing to progress smoothly.

Regarding profit attributable to owners of parent, this is due to a tax refund from the Osaka Regional Taxation Bureau. This was about JPY13.5 billion, so there was a large increase in profit. As for the exchange rate on the right, the yen weakened slightly during the April–June period.



Statement of Profit or Loss (Consolidated)

(Unit: B yen)

	FY2021 Forecasts Full year	FY2021 Forecasts 1H	FY2021 Apr.-Jun. results	FY2021 Achievement (%)	FY2020 Apr.-Jun. results	Y on Y Change (%)	Y on Y Change
Revenue	290.0	135.0	**69.0**	**51.1**	71.4	**(3.4)**	**(2.4)**
Cost of sales	19.8 57.5	18.5 25.0	17.9 **12.3**	**49.3**	16.1 11.5	**7.3**	**0.8**
Gross profit	232.5	110.0	**56.6**	**51.5**	59.9	**(5.5)**	**(3.3)**
Selling general & administrative expenses	30.7 89.0	32.6 44.0	32.7 **22.6**	**51.3**	30.4 21.7	**4.1**	**0.9**
R&D expenses	17.9 52.0	18.5 25.0	21.4 **14.7**	**58.9**	17.0 12.2	**21.1**	**2.6**
Other income & expenses	(1.5)	(2.5)	**(0.5)**	**21.7**	2.5*	**(121.6)**	**(3.0)**
Operating profit	31.0 90.0	28.5 38.5	27.3 **18.8**	**48.8**	40.0 28.6	**(34.2)**	**(9.8)**
Core operating profit**	31.0 90.0	28.5 38.5	28.1 **19.4**	**50.3**	36.2 25.9	**(25.0)**	**(6.5)**
Finance income & costs	25.0	10.0	**4.1**	**41.5**	4.4	**(6.7)**	**(0.3)**
Profit before tax	39.7 115.0	35.9 48.5	33.3 **22.9**	**47.3**	46.2 33.0	**(30.5)**	**(10.1)**
Profit attributable to owners of parent	100.0	49.5	**32.2**	**65.1**	24.5	**31.6**	**7.7**

Main Variation Factors (Y on Y)

- **Revenue**
  - Increase in sales of prescription drugs and overseas subsidiary/export
  - Decrease in royalty income (mainly Crestor®)
- **Cost of sales**
  - Increased due to the acquisition of Nagase Medicals (contracted manufacturing) as a consolidated subsidiary in 3Q of the previous year
- **Selling general & administrative expenses**
  - Increase in preparation for launch and sales activity costs for Fetcroja® in Europe
- **R&D**
  - Accelerating of R&D activities centered on COVID-19 vaccine (S-268019), COVID-19 therapeutic drugs and 8 core projects
- **Other income & expenses**
  - Recognized gain on step acquisitions for Tetra in 1Q of the previous year (about 2.9 B yen)
  - Interest on refund from Osaka Regional Taxation Bureau (about 0.9 B yen)
- **Profit attributable to owners of parent**
  - Received a refund regarding a favorable Judgement on the complaint for the rescission of tax reassessment by Osaka Regional Taxation Bureau(about 13.5 billion yen)

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* The provisional accounting for business combinations with Tetra was finalized in FY2020, the financial results for 1Q of previous fiscal year have been retroactively adjusted

** Operating profit adjusted for one-time factors (impairment losses, gain on sale of property, plant and equipment, etc.)

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Now, please turn to page 5 for the consolidated statement of income, where I would like to explain mainly the YoY changes.

First of all, although domestic prescription drugs and overseas sales and exports increased, royalty income decreased. This was mainly due to a large decrease in sales of Crestor. Overall, net sales decreased by 3.4%, or JPY2.4 billion.

Cost of sales increased by 7.3% or JPY800 million, but the biggest factor was the increase in cost of sales due to the consolidation of Nagase Medicals, which became a consolidated subsidiary in the third quarter of last year. As a result, gross profit decreased by 5.5%, or JPY3.3 billion.

General and administrative expenses, on the other hand, increased by 4.1%, or JPY900 million. The most significant factor was the increase in pre-launch activities and sales expenses for Fetcroja in Europe.

Research and development expenses increased by 21.1%, or JPY2.6 billion. As well as our research on the COVID-19 vaccines, therapeutic drugs, our 8 core projects are also progressing smoothly.

As for other income/expenses, as explained in the previous year's results, retroactive adjustments were made for the merger of Tetra, and a JPY2.9 billion gain was recorded as a stepped gain. The total of these 2 factors has resulted in a significant decrease from the previous year.

As a result of the above, operating profit decreased by 34.2%, or JPY9.8 billion.

Next is profit attributable to owners of parent. Profit attributable to owners of parent for the quarter increased by 31.6%, or JPY7.7 billion, due to the inclusion of JPY13.5 billion in refunds from the Osaka Regional Taxation Bureau, as I mentioned earlier.

Revenue by Segment

(Unit: B yen)

	FY2021 Forecasts Full year	FY2021 Forecasts 1H	FY2021 Apr.-Jun. results	FY2021 Achievement (%)	FY2020 Apr.-Jun. results	Y on Y Change (%)	Y on Y Change
Prescription drugs	94.4	46.1	**23.5**	**50.9**	22.4	**5.1**	**1.1**
Overseas subsidiaries/export	31.1	12.2	**9.3**	**76.2**	5.5	**70.0**	**3.8**
Shionogi Inc.	8.4	4.2	**4.7**	**111.5**	1.7	**182.7**	**3.0**
Fetroja®	-	-	**1.2**	-	0.1	**835.9**	**1.1**
Ping An-Shionogi* /C&O	14.3	3.9	**2.4**	**60.8**	2.4	**0.2**	**0.0**
SBV(Europe)	3.5	1.4	**0.9**	**63.7**	0.4	**144.1**	**0.5**
Contract manufacturing	17.8	7.4	**3.7**	**50.5**	2.9	**30.2**	**0.9**
OTC and quasi-drug	15.4	6.9	**2.5**	**36.0**	2.3	**9.0**	**0.2**
Royalty income	129.8	61.7	**29.6**	**48.0**	38.0	**(22.1)**	**(8.4)**
HIV franchise	125.2	60.8	**28.8**	**47.5**	31.0	**(6.8)**	**(2.1)**
Crestor®	1.1	-	**-**	**-**	5.6	**-**	**(5.6)**
Others	3.5	0.9	**0.8**	**84.4**	1.5	**(47.4)**	**(0.7)**
Others	1.4	0.7	**0.4**	**51.4**	0.4	**(17.3)**	**(0.1)**
Total	290.0	135.0	69.0	**51.1**	71.4	**(3.4)**	**(2.4)**

Main Variation Factors (Y on Y)

- **Prescription drugs**
  - Increase in sales of Intuniv®
- **Overseas subsidiaries/export**
  - US : Increase in sales of Fetroja®
    : Received a one-time payment for the transfer of FORTAMET® sales rights, etc.
  - EU : Increase in sales of Fetcroja®
- **Contract manufacturing**
  - Revenue on Nagase Medicals consigned manufacturing
- **OTC and quasi-drug**
  - Increase in sales of SEDES® and RINDERON®
    › vs. forecasts for 1H : weak sales trends for ISODINE®
- **Royalty income**
  - Exchange rate impact on royalty income from HIV franchise (£ / $)
  - Decrease in income due to sales trends by country
  - Decrease in royalty income of Crestor® from Jan. 2021 based on the contract

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* OTC and quasi-drugs also include in revenue of joint venture

Now, let's move on to page 6, which shows the breakdown of sales.

Total sales were JPY69 billion, which represents progress of 51.1% toward the full-year forecast. As for the domestic prescription drugs at the top of the list, we made progress of 50.9% in the first half, with an increase of JPY1.1 billion compared to the previous year. The increase in sales of Intuniv is the main reason for the increase in income.

In terms of exports by overseas subsidiaries, Shionogi Inc. has made huge progress with JPY4.7 billion. This is partly due to the progress in sales of Fetroja, but also due to the fact that we have transferred the sales rights of FORTAMET. We have received a one-time payment for this.

In Europe, sales of Fetcroja are also growing significantly, and this is one of the reasons why we are making significant progress in our overseas business.

In addition, in the area of contract manufacturing, we are seeing an increase in orders from Nagase Medicals. As for OTC drugs, sales of SEDES and the newly launched RINDERON contributed to the increase in sales.

In terms of royalties, the foreign currency base for HIV has been almost flat, but the exchange rate has been slightly affected by the appreciation of the pound and the depreciation of the dollar.

In addition, there has been a slight shift in the composition of sales by country. This also had a slight negative impact, resulting in a decrease of JPY2.9 billion YoY.

Crestor, as I mentioned earlier, has been significantly negative.

Revenue of Prescription Drugs in Japan

(Unit: B yen)

	FY2021				FY2020	Y on Y	
	Forecasts		Apr.-Jun. results	Achievement (%)	Apr.-Jun. results	Change (%)	Change
	Full year	1H					
Cymbalta®	15.1	10.0	**6.8**	**68.1**	6.9	**(1.5)**	**(0.1)**
Intuniv®	18.2	8.5	**3.6**	**42.0**	2.6	**37.3**	**1.0**
Vyvanse®	1.0	0.4	**0.1**	**37.3**	0.0	**436.2**	**0.1**
Infectious disease drugs	17.0	4.8	**2.1**	**43.9**	2.1	**(1.6)**	**(0.0)**
Influenza franchise	7.9	0.2	**0.0**	**19.6**	0.0	**290.0**	**0.0**
OxyContin® franchise	5.0	2.6	**1.3**	**48.1**	1.4	**(8.9)**	**(0.1)**
Symproic®	3.1	1.3	**0.6**	**46.1**	0.5	**24.8**	**0.1**
Actair®	0.4	0.2	**0.1**	**58.8**	0.1	**79.1**	**0.0**
Mulpleta®	0.1	0.1	**0.0**	**46.0**	0.0	**18.0**	**0.0**
Pirespa®	3.5	1.8	**1.0**	**54.2**	1.4	**(32.2)**	**(0.5)**
Others	30.9	16.4	**7.9**	**47.8**	7.3	**8.1**	**0.6**
Crestor®	6.5	3.8	**1.4**	**37.8**	1.5	**(7.7)**	**(0.1)**
Irbetan®franchise	3.1	1.7	**0.8**	**47.1**	0.8	**(7.3)**	**(0.1)**
Prescription drugs	94.4	46.1	**23.5**	**50.9**	22.4	**5.1**	**1.1**

<Products included in infectious disease drugs>

- Xofluza®
- Rapiacta®
- Brightpoc®Flu・Neo
- FINIBAX®
- Flumarin®
- Flomox®
- Shiomarin®
- Vancomycin
- Baktar®
- Flagyl®
- Fluconazole
- ISODINE®

SHIONOGI Influenza franchise

Moving on to page 7, I would like to talk about the status of pharmaceuticals in Japan. As mentioned earlier, the result for the April–June period was JPY23.5 billion, an increase of JPY1.1 billion, or 5.1%, from the previous year.

As you can see, the second major factor contributing to the increase in sales is the JPY1 billion increase in Intuniv, which is the second from the top.

Compared to last year's 1Q results, the number of patients has been gradually returning, and the number has started to increase.

Summary of 1st Quarter

Smooth progress in domestic and overseas business

- Growth of Intuniv® and cefiderocol

Making progress in activities for total care of COVID-19

- Vaccines
- Therapeutic drugs
- Sewage epidemiology
- Diagnostic products

Active investment in growth drivers

- COVID-19
- 8 Core projects
- Cefiderocol

On page 8, we can see the main points of the first-quarter results.

As I have just reported, we are making good progress both in Japan and overseas. This is especially true for Intuniv and cefiderocol.

As I mentioned in May, we have already given top priority to COVID-19, and we are making steady progress in the areas of vaccines, therapeutic drugs, sewage epidemiology, and diagnostic products.

We had also been proactively investing in the future, in terms of aggressive investment in the growth drivers on the far right.

1H & FY2021 Earnings Forecasts

Making smooth progress toward achieving the 1H forecast

- **Revenue progressed 51.1% compared to 1H forecast**
  - Favorable progress was made in domestic and overseas business
  - Continuing to implement cost management through cost structure reforms

⇒ **Considered possibility of upward revision based on 1H, but not revising at present**

Making smooth progress toward the realization/expansion of new businesses

- **New business opportunities in FY2021**
  - Providing COVID-19 related products and services
  - Changes in each country's response to prepare for emergencies such as flu and AMR, etc.
  - Product introduction, M&A
  - Aggressive investment for early expansion of new business
  - Maximization of assets and franchises, consideration of partnering

⇒ **The above business opportunities, which are not factored into forecasts, are progressing as planned**

In parallel with focusing resources on providing solutions for COVID-19, achieve growth in revenue and profits by attaining FY2021 earnings forecast through strengthening existing businesses and establishing and growing new businesses

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Moving on to page 9, I would like to explain the forecast for the first half and full year.

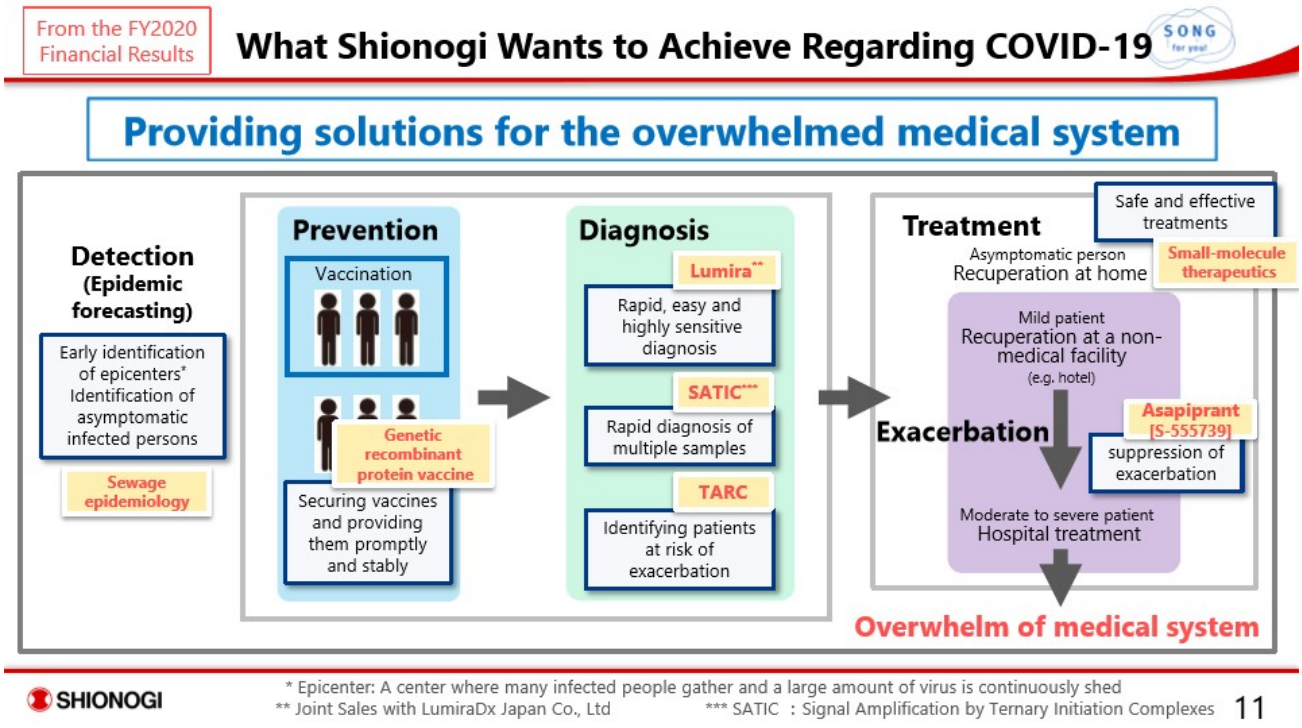
No changes have been made to the external forecast figures for the first half and full year.

However, as you can see on the left side of this page, sales revenue has progressed 51.1% compared to the first-half forecast, and we believe that there is a strong possibility that we will exceed the forecast for the first half. However, we have not made any revisions at this time.

Our current initiatives are written on the right side. We consider these as opportunities for our company. We are making steady progress in various initiatives, including those related to COVID-19, and we will revise our numerical forecasts accordingly when we reach a stage where we can incorporate these initiatives into our figures.

In any case, we are determined to achieve the full year forecast that we announced in May, and to further increase sales and profits in the future.

This concludes my presentation.

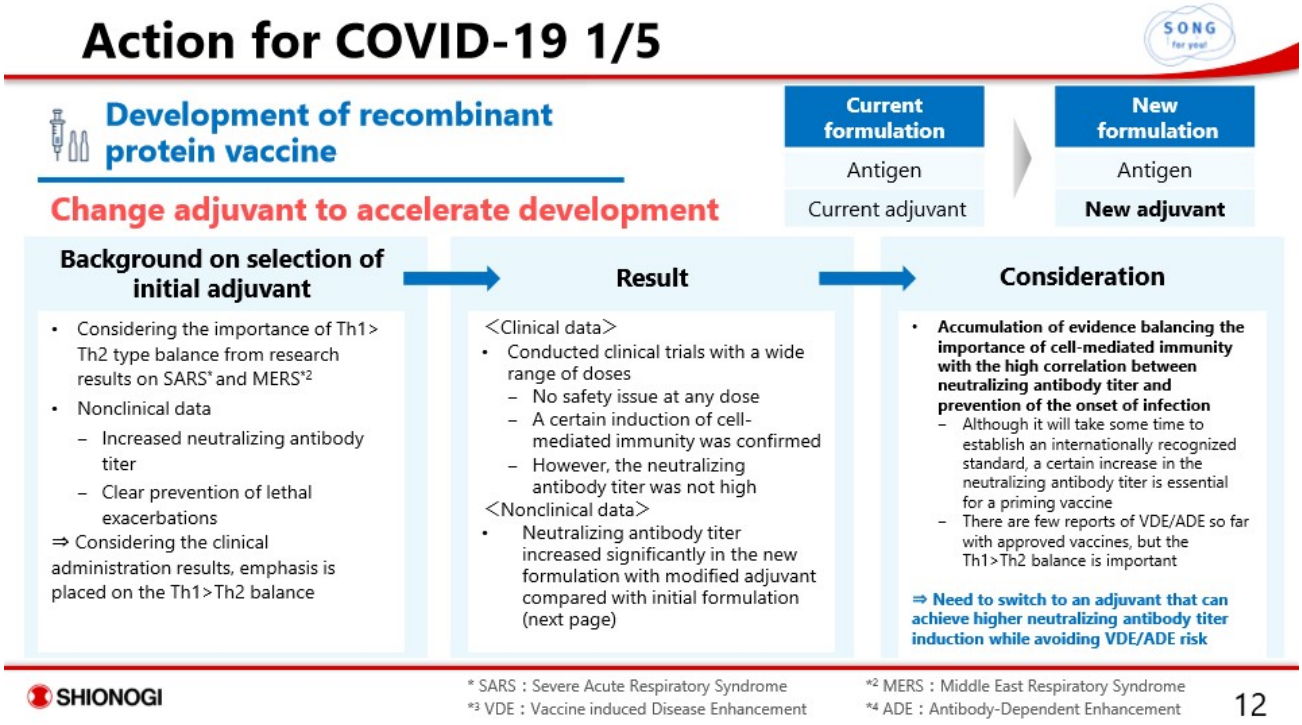


Sawada: As for the main initiatives and achievements in the first quarter, as Mr. Hosogai mentioned on page 8, I think the most important point in the first quarter is the progress of the COVID-19 total care initiative, so I would like to focus on that.

Lastly, on the subject of HIV, I would like to introduce John, who has just been appointed as the General Manager of the Corporate Strategy Division after having worked as the general manager of the overseas business division.

Please turn to page 11.

With regard to COVID-19, SHIONOGI hopes to provide not only therapeutic drugs for infectious diseases from conventional diagnosis, but also detection, prevention, diagnosis, treatment, and suppression of exacerbation. We are aiming to provide the pipeline described here.



Next, on page 12, I would like to talk about vaccines and therapeutic drugs, which are the most important topics here.

We would like to make some changes in the vaccine development policy. This is a recombinant protein vaccine adjuvant that we have been developing. We selected adjuvants with enhanced cellular immunity for development, partly because we feared that serious events such as VDE/ADE as seen in SARS and MERS might occur in the future.

However, the formulation was put into clinical use after the increase in neutralizing antibody titer in mice was confirmed, as well as observing a clear effect in preventing severe disease.

In the clinical trials, a wide range of antigens, adjuvants, and combinations of antigens were tested, and we were able to confirm high safety and a certain level of induction of cellular immunity. However, unfortunately, the high neutralizing antibody titer that has been confirmed for mRNA vaccines was not achieved in this clinical trial.

In parallel, we have been investigating the induction of neutralizing antibody titer and cellular immunity using one combination of monkeys with different adjuvants, which is more extrapolatable to humans.

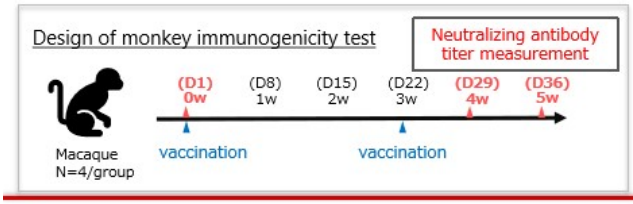
As a result, as you can see in the consideration on the right, we have reached the point where we can switch to an adjuvant that can avoid the risk of VDE/ADE, induce higher neutralizing antibody titers, and also provide cellular immunity.

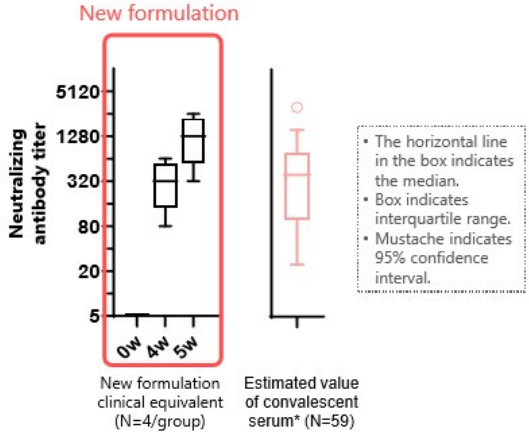
Action for COVID-19 2/5

Development of recombinant protein vaccine

Reexamine with a combination of various adjuvants

- Monkey immunogenicity test
  - 2 vaccinations (3 weeks intervals)
  - Measure neutralizing antibody titers 29 and 36 days after vaccination
  - Very high correlation with clinical data accumulated so far





Confirmed higher neutralizing antibody titer compared to the prior formulation (Similar to recovered patient serum)

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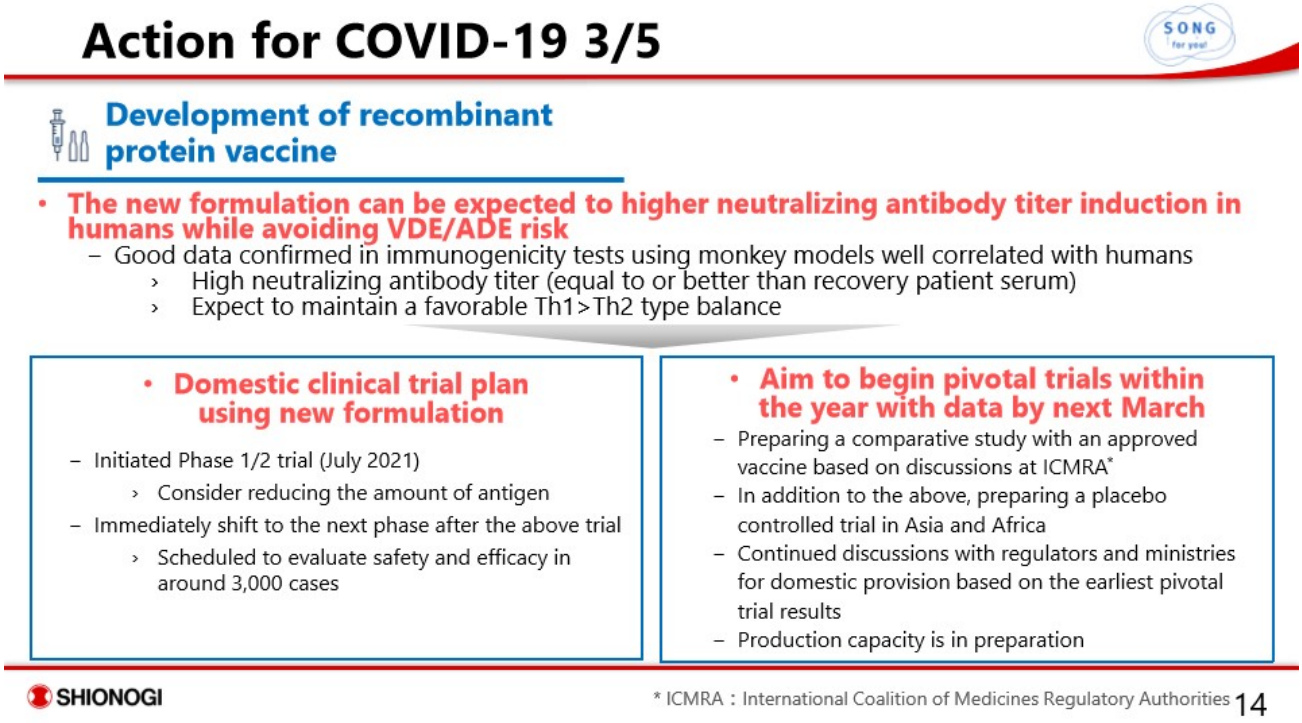
* Estimate from measurements in another test

Page 13 shows the data for monkeys.

As a result of changing the adjuvant, the titer of neutralizing antibodies in the serum of recovered patients was almost even with 1 week post-vaccination after 2-dose vaccination at a 3-week interval. At this point, 2 weeks after the second vaccination, which is the fifth week, higher neutralizing antibody titers can be obtained.

Furthermore, we have found that we can induce cellular immunity at the expected level and, based on this, we would like to further accelerate this development by changing to this formulation.



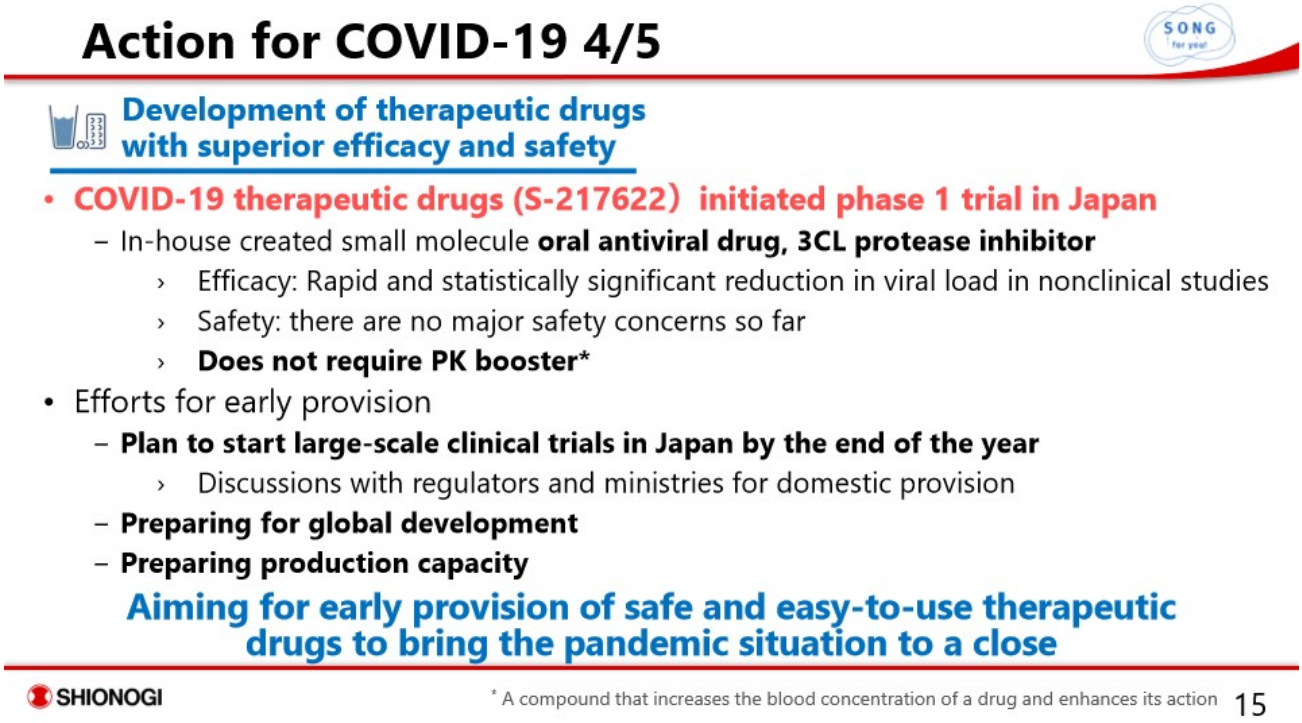
On page 14, you can see the domestic clinical trial plan for the new formulation on the left.

We submitted a notification in July. And by conducting clinical trials and Phase I/II trials, we believe that it may be possible not only to induce neutralizing antibody titers but also to reduce the amount of antigen in some cases. After that, we intend to move to the next phase as soon as possible after determining this capacity.

The ICMRA, a joint meeting of global regulatory authorities, concluded that if the neutralizing antibodies and other values are almost the same as those of existing vaccines, the data from about 3,000 cases would be sufficient for approval.So we have assumed a scale of 3,000 cases.

On the other hand, as you can see on the right, we are also aware of the importance of conducting placebo-controlled trials to see the actual effect of preventing infection and disease onset, so we are preparing for placebo-controlled trials in Asia and Africa, including this possibility.

By taking these measures, we hope to be able to provide the product in Japan by the end of the fiscal year, although this will be subject to consultation with the regulatory authorities.



Next, on page 15, we will talk about therapeutic drugs.

As we have already announced in the press release, we have started domestic Phase I trials, and we are now moving forward with the development of a 3CL protease inhibitor that does not require a PK booster, as described here.

Today, Pfizer announced that they have achieved good results in PK, and although the data for this drug are still from a low dose, I believe that we have already achieved a long enough half-life in PK without a booster.

As for the efficacy of the drug, we have confirmed in non-clinical studies that it rapidly and effectively reduces viral load. We have no major concerns about safety at this time.

With regard to this therapeutic drug, as the delta strain is spreading around the world, incidence of infection in vaccinated individuals has become a considerable problem. Therefore, we are aiming to start large-scale clinical trials in Japan as soon as possible, and at the same time we are preparing for global development.

We would like to build a production system that will enable us to provide our products worldwide as soon as possible.

Vaccines are very important, but considering the containment of the pandemic, we believe that the early provision of safe and simple therapeutic drug is also extremely important. Therefore, we are focusing on this therapeutic drug with the same level of urgency as a vaccine.

Action for COVID-19 5/5

Diagnostic markers that can predict exacerbation

- **HISCL® TARC* reagent**
  - Approved for an additional indication (June 7, 2021) as an auxiliary for detection of COVID-19 aggravation; launched with insurance coverage (June 11, 2021)
  - Conduct clinical research post-marketing to accumulate additional evidence

Rapid and highly sensitive antigen test

- **LumiraDx SARS-CoV-2 Ag Test and LumiraDx Instrument**
  - Launched at the end of May 2021
  - Going forward, planning for the broad application of the same device for the diagnosis and monitoring of other infections and diseases

Establishment of analysis system for SARS-CoV-2 in sewage

- **Initiated sewage epidemiology surveillance service for detecting SARS-CoV-2**
- **Concluded the basic agreement for business partnership to support early implementation**
- **In discussions with several municipalities to expand services**
  - Launched in June 2021

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* TARC (thymus and activation-regulated chemokine)
One of the chemokines driving migration of Th2 cells, a type of lymphocyte, to the site of inflammation

This is page 16. We have already released other COVID-19 initiatives.

As you know, insurance coverage for TARC, a diagnostic marker that predicts the severity of the disease, already started in June, and we are conducting clinical research to build further evidence. In addition, we have started to offer Lumira test strips, which have a sensitivity similar to that of PCR.

In addition, we have already started research services for the SARS-CoV-2 sewage inspection system. In terms of social implementation, we believe that standardization is very important, so we have concluded a basic agreement with Shimadzu Corporation for a business alliance and are moving forward. In addition, we are currently in discussions with several local governments to expand this service.

R&D Progress : 8 Core Projects

	Pipeline	Indication	Status
Infectious disease	**S-540956**	HIV infection, cancer	Preparing Phase 1 study
Psycho-neurological diseases	**S-600918 [sivopixant]**	①Refractory chronic cough ②sleep apnea syndrome	①Phase 2b study in progress ②Phase 2a study in progress
	S-637880	Neuropathic low back pain	Phase 2a study in progress
	S-812217 [zuranolone]	Depression	Phase 2b study in progress
	BPN14770 [zatolmilast]	①Alzheimer's disease ②Fragile X Syndrome	①Phase 2 study in progress ②Preparing Phase 2b and Phase 3 study (US)
	S-874713	Psycho-neurological diseases	Preparing Phase 1 study
New growth areas	**S-531011**	Solid tumor	Preparing Phase 1b/2 study
	S-005151 [redasemtide]	①Epidermolysis bullosa ②Acute stroke ③Osteoarthritis ④Chronic liver disease	①Preparing for application ②Phase 2 study in progress ③④Investigator initiated clinical trial (Phase 2 trial) in progress

Steady progress of 8 core projects and COVID-19 project
(Details to be reported at R&D day on Sep. 29, 2021)

* See appendix p.22-24

As you can see on page 17, some of the 8 R&D focus projects were affected by COVID-19 to some extent, so some of them have been delayed, but I think we are making steady progress in general.

Initiatives to Strengthen Domestic and Overseas Businesses

Domestic business

- **2 strategic products contribute to top line growth**
  - **Cymbalta®**
    - Continue to introduce resources to realize sustainable stable supply given the various changes in social conditions
  - **Intuniv®**
    - Growth in the pediatric field
    - Progression of efforts to expand the adult domain
- **Improve productivity by reorganizing domestic operations**
  - Ripple effect to regions and nationwide by strengthening hospital business

Overseas business: Acceleration of US, European and Chinese business

- **Cefiderocol**
  - Strong uptake of cefiderocol in US and Europe
  - Implementing initiatives to improve access to cefiderocol in low- and middle-income countries*
- **Ping An-Shionogi**
  - Expanding product range for sale on online platform "Ping An Good Doctor"
  - Acceleration of data-driven drug discovery and development utilizing Real World Data (RWD) collection and analysis research

* See appendix p.25

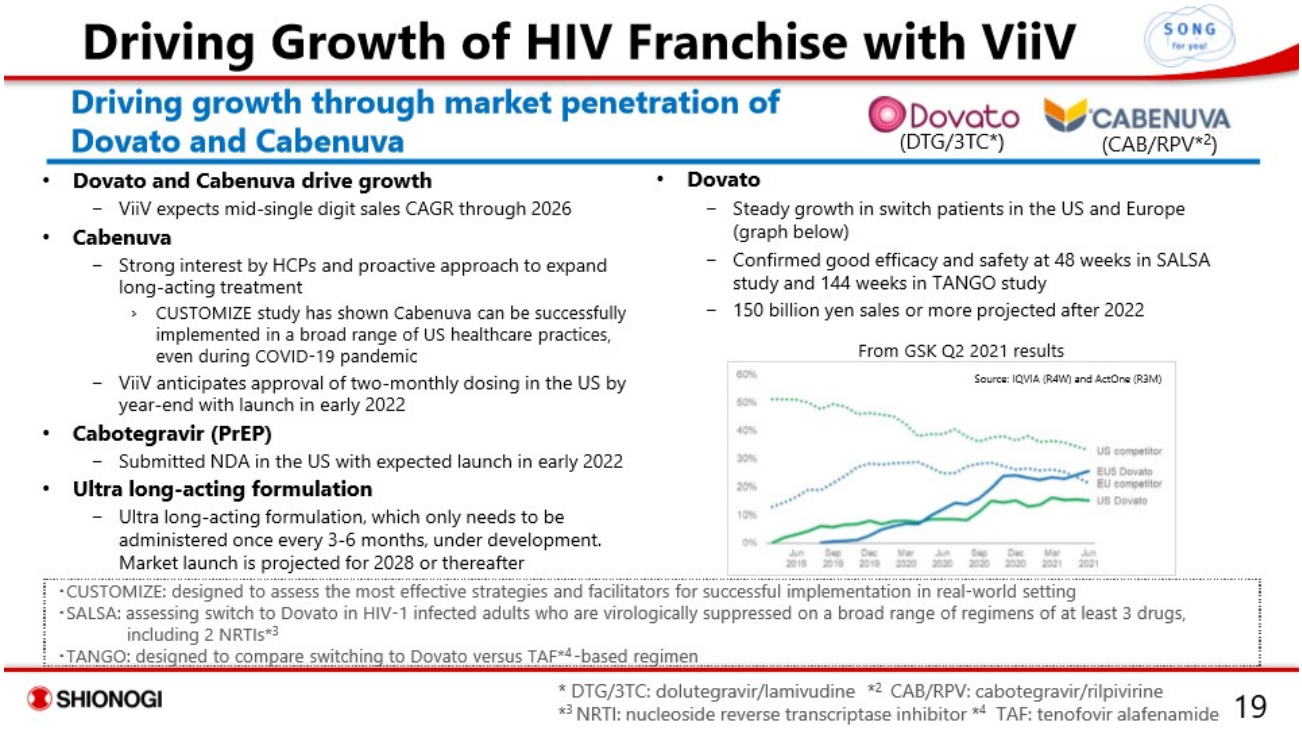
Based on the above, we are working to strengthen our domestic and overseas businesses. In the domestic business, Cymbalta has been affected by shipment adjustments by generic manufacturers, but we believe that sales in the first quarter were quite steady.

In addition, there has been an expansion of the use of Intuniv not only in the pediatric field but also in the adult field, and we are determined to make progress in this area.

By strengthening the hospital field, we aim to promote a ripple effect not only within hospitals but also at a regional level and nationwide. In addition, I expect that this will lead to an improvement in the capabilities of the actual sales force itself.

At the same time, it is important to provide access to low- and middle-income countries, so we have already announced that we have signed MOUs with GARDP and CHAI. We intend to continue our activities at Heian Shionogi with even more vigor than before.

That concludes my presentation.



Keller: This is Keller. Starting from page 19, I will discuss the progress of the HIV franchise.

Dovato's market share in Europe and the US is growing steadily. As was recently announced at an international conference, the SALSA and TANGO studies, which involved switching from other drugs, confirmed favorable efficacy and safety at 48 weeks and 144 weeks, respectively. Based on this evidence, we expect Dovato to continue to drive growth in the future.

As for Cabenuva, active efforts are underway to incorporate treatment with sustained formulations. We have confirmed that health care professionals are still able to see patients during the coronavirus pandemic. There is strong interest in this therapy.

In addition, an application was filed in the US in February of this year for once-every-2-months maintenance therapy, with plans for approval by the end of 2021 and launch in early 2022.

As for the prophylactic administration of cabotegravir, we are steadily preparing for its launch in early 2022. In addition, ViiV is working diligently to develop a new, more convenient, ultra-long-acting formulation. In the HIV area, we continue to expect growth mainly cabotegravir, which contains Cabenuva and Dovato.

This concludes our first-quarter earnings announcement.

Question & Answer

Kyokawa: We will now move on to the Q&A session. Please follow the instructions of the operator.

Operator: If you have any questions, please state your company name and your name when you speak and then ask your question. The first question comes from Mr. Kohtani of Nomura Securities. Please go ahead.

Kohtani: I'm Kohtani from Nomura Securities.

Sawada: Hello.

Kohtani: I'd like to ask you about coronavirus drugs. Could you tell me why development of a 3CL protease inhibitor took place, instead of an RdRp polymerase inhibitor? Many of your past HIV drugs involve bonds with metal ions, so I think the concept behind a polymerase inhibitor is more structurally similar to some of your previous compounds. If this is a complete misunderstanding, please do let me know.

Second, if I quote from the paper, the prodrug, PF-07304814, has a half-life of 0.1 hours, and the activator one has a half-life of 2 hours, and if you look at the AP1 results, it is about 3 hours when combined with CYP3A5 inhibitors. I think the half-life is about 6 to 8 hours max, based on the effects of food, so I think that's why it's twice a day.

To be honest, I think the drug has questionable effectiveness, and a short half-life. Could give us some hints about the PK of your drug? Can you also tell me if there are any other advantages compared to molnupiravir or AT-527? That’s my first question.

Sawada: First of all, regarding the coronavirus drug mechanism, several factors are involved in decisions about development. In this case, we chose the most active compound from the various candidates tested.

With regard to the second issue, PK, as I mentioned earlier, it should be recognized as a drug with a rather long half-life. In that sense, I think our offering is completely different from the 2 existing products.

Kohtani: I understand. The second point is that your company's therapeutic drugs are a little behind Pfizer, Merck, and Roche in terms of development. The Phase I trial will start now, and the Phase III trial in Japan will probably start within this year. I think it will take quite a while to get to global.

In the end, I believe that the best approach is through combination therapy. Given the concerns about mutation, there is a lot of concern about using either of the single agents alone. Whether it is a single agent or a combination, speed of development is important. I think it is important to derive the data as soon as some progress is made and start global testing as soon as possible, rather than waiting until the end of a Phase I trial.

This is because if you look back at the time of Xofluza, Phase I trials were completed in mid-2015, and a global marketing agreement was signed with Roche in February 2016. Do you have any suggestions on how this process can be accelerated, such as reducing the time to the next step to less than 3 months?

Sawada: Whether or not to include the combined use in the package at the time of the initial application is, to be honest, not really mandatory according to the current requirements. We think it is something we need to do, but we don't actually consider it necessary data package for the initial approval.

However, when it comes to the actual development of the product, we think that we can speed up the process by proceeding independently rather than negotiating.

Kohtani: In terms of shortening the time to out-licensing, last time it probably took more than 6 months for Xofluza, I'm not sure. Can it be shortened further?

Sawada: The reason it took so long to develop Xofluza was that our development plan was earlier than theirs.

Although we had received offers from several companies, we would rather speed up the development process by doing it on our own than spending time discussing it with them.

Given this, our primary focus is on moving forward with development as quickly as possible, so I'm not saying that we won't negotiate, but rather, negotiations must not have any effect on the development schedule.

Kohtani: I understand. Last, regarding cabotegravir, in GSK's conference call on the 28th, they forecasted the market size of long-acting injectable HIV drugs and HIV prevention drugs for 2030, estimating roughly GBP4 billion to GBP5 billion for each. For prophylactic drugs, I think that competing drugs will probably enter the market, but for therapeutic drugs, it will take about 5 years for injectable drugs to really become competitive.

If that is the case, I think it is possible to get a good portion of the total market of GBP8 billion to GBP10 billion with cabotegravir.

I think that in the past, your company estimated that peak cabotegravir sales were 20% of the market, maybe GBP3 billion. Is there any change in this view? That's my last question.

Keller: I don't think it's a large change. I think when you look at the market overall, you are looking at a 25-30 billion dollars market, and we are always have considered about 20% of the population to be deeply interested in long-acting treatment in that consisting with all market research would done. And so, something on the order of 4-6 billion market is not out of range. Whether we can capture all of that ourselves, our competitor would do their relatively early in development that remains to be seen. However, in terms of long-acting safety in efficacy, it's very hard to imagine anything with evidence based and success of integrase, so we would expect to capture a majority fraction in that market.

Kohtani: Thank you.

Operator: Our next question comes from Mr. Ueda of Goldman Sachs Japan. Please go ahead.

Ueda: I am Ueda from Goldman Sachs. I would like to ask you a few questions about vaccines.

I would first like to know about the neutralizing antibody titer. The old adjuvant did not raise this antibody titer sufficiently. What specific level were you aiming for and, as a result, what level was achieved with that original adjuvant? With this adjuvant, what kind of level can we expect compared to the vaccines from Pfizer or Moderna?

The vaccines from Pfizer and Moderna have a neutralizing antibody titer that is a little higher than that of recovering patients.

Also, since you started clinical trials in July, could you tell us about the efficacy of the new vaccine, for example, whether it is expected to be highly effective against the delta strain of the virus, and how that compares with existing vaccines?

Sawada: It is true that the ability of mRNA vaccines to induce neutralizing antibodies is generally higher than that of other classes of vaccines. However, the reason why it is difficult to make head-to-head comparisons is that the neutralizing antibody titer of the volunteers before vaccination was zero when we conducted the Phase I study.

However, when we look at the data provided by researchers in Japan, there are many people who already have neutralizing antibodies even before vaccination, so we believe that this difference will have a significant impact on the results.

However, even if that were the case, I still wanted it to be at the same level as the serum for the recovery patients, but it didn't reach that level. Or, of course, depending on the combination, some of them did not reach it at all.

Considering this, rather than increasing the amount of antigen, the amount of antigen must eventually cover the number of people, so we would like to keep the amount of antigen low, but still be able to induce neutralizing antibody titers and still expect cellular immunity. This is why we changed the adjuvant this time.

Ueda: What kind of expectations do you have for the delta strain mutation?

Sawada: With regard to the delta strain, the neutralizing activity of neutralizing antibodies themselves has been examined for alpha, beta, gamma, and delta. In fact, there has been almost no decrease in the neutralizing activity against delta, which I think is an interesting point of our antigens.

At this point, we have not created antigens specifically for delta strains, but from the standpoint of neutralizing antibody titers, we believe that the delta strain will not have a significant impact.

Ueda: Thank you very much. The second question is about the adjuvant. Is it a new one or has it been approved before?

According to the PMDA's guidance, when new adjuvants are used in the development of coronavirus vaccines, the emphasis is on safety. In the case of your company, is it correct to understand that the adjuvant has a proven track record of use since there is a plan for provision within the fiscal year?

Sawada: As a class, it is an adjuvant with a proven track record of use.

Ueda: I understand. If so, is it safe to assume that the risk of delays is low?

Sawada: At present, that is not a particular issue in our consultations with PMDA.

Ueda: I understand. Thank you. Last, I would like to know about the design of large-scale clinical trials.

I think you mentioned a little bit about the implementation area, timing, and evaluation items earlier. But globally, there are discussions about using neutralizing antibody titers as surrogate markers. Can you tell us about the fact that discussions are proceeding properly in domestic approval as well?

Sawada: Discussion is also progressing in Japan. However, regarding the press release from a few days ago, the issue of how to obtain this positive control has not been solved yet. We are preparing trials for prevention of infection and symptom development while keeping that point of uncertainty in mind.

Ueda: I understand. That's all. Thank you very much.

Sawada: Thank you very much.

Operator: Our next question comes from Mr. Yamaguchi of Citigroup Global Markets Japan. Please go ahead.

Yamaguchi: This is Yamaguchi from Citi. Thank you. First, in the financial results, you mentioned that the upfront payment for Fortamet was not included in the forecast. Regarding the tax authority issue, I was wondering if is included in the forecast.

Hosogai: It's included. Tax is included.

Yamaguchi: I understand. With regard to whether or not to change the forecast, I believe you said that the progress rate for the first half of the fiscal year was quite good, so you considered changing the forecast, but ultimately didn't. Was that referring to a change in the forecast for the first half of the year, or the full-year forecast?

Hosogai: Initially, for the first half. For the first half of the fiscal year, there is a high possibility of over-achievement at this time. The second half of the fiscal year will be very challenging for us, so we would like to make revisions as soon as the possibility of realization of various items increases.

Yamaguchi: I understand. In terms of the challenges you mentioned, do you mean that the hurdles are higher in the second half of the fiscal year?

Hosogai: If you look at it on a profit basis, the second half of the fiscal year has been quite heavy in terms of the balance between the top and bottom line.

Yamaguchi: I see. I understand. Thank you. Also, I'm sorry, but I have a fairly basic question about coronavirus.

For the products that you have been developing, there has been progress on Phase I/II, and the data have already been obtained internally. With the existing formulation, the neutralizing antibody level did not increase sufficiently, and while it induced a certain level of cellular immunity, but if I may say so without fear of misunderstanding, this was not competitive enough for a vaccine, so the adjuvant was changed and it was reformulated.

Sawada: Yes, that's right. However, it is actually unclear as to what balance between cellular immunity and neutralizing antibody titers would really be effective in preventing the onset of the disease. Overseas, there is also progress in the development of vaccines that use cellular immunity as a major component.

However, at present, there is a movement to put the neutralizing antibody titer in the forefront and to approve even on the basis of a small number of cases. We are considering moving forward in that way, as we think it would be better to proceed with the neutralizing antibody titer, which will increase to a certain extent, so that we can choose both ways later on.

Yamaguchi: I understand. Since the new formulation is to start in July, I believe it was originally at the end of the fiscal year, so how much will this delay the start? Regarding the gap between the scheduling and the original timing of the old formulation, it seemed to be about 3 months, so it seems to me your company can get there in about that time.

Sawada: We are working at full steam to reduce it to less than 3 months.

Yamaguchi: I see, but, in a way, that's how far off the mark it was to start with.

Sawada: Yes, that's right. Considering the fact that we usually have to follow the neutralizing antibody titer for about 2 months. However we will consider accelerating the expansion of our business from the domestic market to overseas as well.

Yamaguchi: Thank you very much. Last, what is the status of production capacity? How many vaccinations does it seem feasible to produce, at present? Is the figure affected by this adjuvant change?

Sawada: Mr. Teshirogi's announcement of doubling the number was partly based on this data with expectations. We are also reviewing the production system itself to see if we can increase the number of lots per year or the number of units per lot.

Yamaguchi: What Mr. Teshirogi was talking about was 30 million, I think. That number is based on this, which means that story and this story are consistent.

Sawada: I think we had some of these data in mind when we decided on 60 million.

Yamaguchi: I understand. Thank you very much.

Operator: Our next question comes from Mr. Sakai of Credit Suisse Securities Japan. Please go ahead.

Sakai: This is Sakai from Credit Suisse. I'm sorry, I just need some basic information on the vaccine part.

I was a little curious about what Ms. Sawada just said. Is it the case that there are many people in Japan who are infected and have neutralizing antibodies? If your company were to set up a clinical trial in Japan with a certain number of patients using placebo and so on, would it be necessary to set up a protocol after confirming whether the patients have neutralizing antibodies or not? I think this is true not only in Japan, but also overseas.

With the spread of the delta strain and the like, I think it is becoming very difficult to set up this protocol. Please let me know if you have any thoughts on that.

Sawada: I don't necessarily say that we don't measure that, but I honestly don't think it is necessary to include it in the exclusion criteria by measuring it. At present, it is not known what level of neutralizing antibody titer is really effective in preventing the onset of the disease.

So, I think that unnecessarily taking time to exclude on that basis would reduce the viability of the clinical trial.

Of course, we exclude based on past medical history, but I don’t think it is necessary to look specifically at antibodies.

Sakai: I understand. Is that something that has been discussed with the PMDA? As you probably heard yesterday, Daiichi-Sankyo is also talking about the future development of vaccines.

Sawada: At the moment, talk of a scale of 3,000 cases is the main point. In Japan. At present, it is quite difficult to conduct placebo-controlled trials on a scale of tens of thousands of people in Japan.

Sakai: I understand. I'm sorry for the long-winded question. When referring to overseas, I guess that would be Asia and Africa. Is it correct to say that your company is proceeding on the premise that such an exclusion does not need to be provided here?

Sawada: Currently, yes. If the conditions change significantly again after this, there is still the possibility of changing them again. That's how I see it at this point.

Sakai: I understand. Also, excuse me, just 1 thing. This is my last question.

As for the royalties from ViiV, we already know how much ViiV is actually paying because it has already been announced. I think the exchange rate may have had a considerable impact on your company's income this time. Do you have any analysis of the impact of the strong pound, whether it was the pound versus the dollar or the pound versus the yen?

Keller: The pound to the dollar is the most important because majority of the ViiV sales are in dollars because over 75% of the market are to the US. After that, we go to the pound to yen conversion but the impact of that is relatively small, it's really driven by the pound to dollar.

Sawada: The pound sterling is actually not much affected even if it fluctuates a little, because a large part of it has reservations against it.

Hosogai: The pound versus yen has exchange contract against it.

Sakai: Yes. That's the relationship between the pound and the yen. So the numbers that ViiV is disclosing are affected in pound sterling terms, is that correct?

Hosogai: That's right.

Sakai: I understand. Thank you very much.

Operator: The next question comes from Mr. Tanaka, Mizuho Securities. Please go ahead.

Tanaka: Hello. I'd like to know a little more about the vaccine. The trial S-268019 of 300 cases is listed on the clinical trials site. Does this mean that this does not include the new formulation and that another trial started in July?

Sawada: Yes, that's correct.

Tanaka: I see. In that case, it seems difficult for the delay to be less than 3 months. It started in December last year. Is it possible?

Sawada: We have actually done a great many combinations of adjuvants and antigens in conventional formulations, but this time we have a pretty good idea of the ratio of adjuvants and antigens that we can use here, so status is completely different.

Tanaka: I see. I understand. Also, I read an article written by Mr. Teshirogi in a magazine in which he said that the current mRNA vaccine is overdosed, and I think he wrote that it should be about 70% of what it is.

Will that be the same policy for this genetically modified protein vaccine that your company is now working on?

Sawada: At least with our peptide and recombinant protein vaccines, it is not necessarily the case that the induction of cellular immunity is enhanced by increasing the amount of antigen. In that sense, we want to keep it at the optimal doses.

Tanaka: I wonder if we can actually compare the neutralizing antibody titer or cellular immunity, not in terms of the prevention rate, but in terms of these factors with existing mRNA vaccines.

In the case of your product, booster doses are going to be the mainstream, aren't they?

Sawada: In Japan, yes.

Tanaka: Yes, that's right. At that time, I think it will be necessary to properly test the booster, but have you already solved that problem to some extent? How will you do it?

Sawada: We have been discussing boosters separately. We are aware that none of the regulators are currently arguing that it is necessary to include it in the initial application package.

We are aware that it is necessary to consider the actual situation when using it, so we have started such discussions with some researchers.

Tanaka: I understand. Thank you very much.

Operator: The next question comes from Mr. Hashiguchi of Daiwa Securities. Please go ahead.

Hashiguchi: This is Mr. Hashiguchi from Daiwa Securities. Thank you.

Sawada: Thank you very much.

Hashiguchi: Thank you very much. The first question is about vaccines. In the graph on page 13, there are no data for the old formulation, so I am not sure how much of an increase in neutralizing antibodies can be expected in people with the new formulation.

If you look at the history of the old formulation on page 12, you wrote that the increase in neutralizing antibody titer was confirmed in the non-clinical data. Ms. Sawada, I think you said earlier that you expected the antibody titer to rise to the level of the serum of recovered patients.

The result shown in the middle column is that the neutralizing antibody titer did not increase sufficiently. Is it safe to assume that there is a risk that even if the new formulation shows a reasonable increase in antibody titer in non-clinical data, it will not necessarily meet the expectations in clinical trials?

Sawada: As I mentioned earlier, the leftmost non-clinical data are a mouse model, and the one shown on page 13 is a monkey model. Unfortunately, when we looked at the extrapolation to humans, we had to argue that we should have used monkeys instead of mice.

In fact, there were many variations and combinations in the old formulation, so we couldn't include them all here. Unfortunately, the differences are seen to be so great that even the boxes do not overlap at all.

Hashiguchi: Thank you very much. On page 15, you write that you are preparing for the global development of S-217622, a therapeutic drug, but when do you plan to start clinical trials for this?

Sawada: We would like to start discussions with overseas regulatory authorities when we have reached the dose of blood concentration where some efficacy can be expected in Phase I.

I don't know if you're aware of it, but the requirements that BARDA is putting forward for the COVID drug that they're going to end up stockpiling as well, or they're going to buy it, so it’ll be a case of doing the IND by September of this year, with Phase III completion by the end of January of next year, and an emergency use authorization by the end of March. Then it would be a question of providing 500,000 courses within 8 weeks of that, so whether that can be met is.

Hashiguchi: Thank you very much. Lastly, with regard to R&D expenses, the rate of progress in the first quarter has been quite high compared to your plan for the first half.

What do you think now about the possibility of exceeding the forecast for this first half or full year, taking into account the situation of the development of vaccines and therapeutic drugs that you have just mentioned?

Hosogai: Hosogai here. I will answer. At this point, there is a possibility that we may overachieve in the first half of the fiscal year, but on a full-year basis, we are reviewing various expenses, and we are basically trying to keep the full-year forecast of JPY52 billion unchanged.

However, this is based on our goal of eventually achieving the profit base, so if sales are overachieving, we will naturally review our expenses. There is still a good chance that we will increase R&D.

Hashiguchi: Thank you very much. That's all.

Operator: The next question will be the last. BofA Securities Japan, Mr. Arai, thank you very much.

Arai: This is Arai of BofA Securities.

Sawada: Thank you very much.

Arai: Thank you very much. Regarding the vaccine, I'm afraid this is a layman's question, but is there anything that can be suggested from the data at this point in time, such as the side effects, or fever?

The existing Pfizer and Moderna vaccines have issues with fevers, and there are quite a few people around me who are suffering from them. Please let me know if there is anything that you can suggest about the adverse events here, or the profiling of side effects.

Sawada: It is extremely mild. There have been mild adverse events seen in a few cases, and the profile is similar to that of conventional vaccines for other diseases, rather than that of conventional COVID-related vaccines.

Arai: I understand. Thank you. One last thing, I wonder if you are collecting data internally on drugs for the treatment of chronic cough. Please let me know if there is any information you can disclose about this.

Sawada: As you can see on page 17, we will be able to report this at the right time, probably around the R&D briefing in September. I'm sorry, but I hope you can wait until then.

Arai: I understand. Thank you. Sorry, I said last, but I have one more thing to add.

In the end, the idea of ups and downs for the current fiscal year's plan is, of course, that there are various ups and downs that have not been factored into the budget, such as revenue from government stockpiles related to vaccines and support from the government for the R&D budget.

Are there any such factors that could be disclosed in any more detail? Thank you.

Hosogai: Hosogai here. On page 9, you can see the new projects on the right side. I hope you understand that all of these are potentially quantifiable.

However, at this point, the specific amount has not been decided yet, so it has not been factored in.

In addition to this, as you pointed out, we are already working diligently on government subsidies, so I hope you can see that there are also such factors in R&D.

Arai: I understand. Thank you.

Sawada: Thank you very much.

Kyokawa: This concludes the SHIONOGI Q1 earnings conference call for the fiscal year ending March 31, 2022. Thank you very much for taking time out of your busy schedules to join us today.

Sawada: Thank you very much.

[END]