SHIONOGI & CO., LTD.

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Fiscal 2021 3Q Conference Call

February 1, 2022

Presentation

Kyokawa: Hello. I'm Kyokawa, Vice President, Corporate Communications Department at SHIONOGI & CO., LTD. Thank you very much for taking time out of your busy schedule to join us today.

Now, we start a conference call for FY2022 3Q financial results earning announcement of SHIONOGI.

First of all, I would like to introduce today's speakers.

First of all, this is Takuko Sawada, Director and Executive Vice President and Senior Vice President of Integrated Disease Care Department.

Sawada: I'm Sawada. Thank you.

Kyokawa: Next, this is John Keller, Senior Executive Officer, Senior Vice President of Corporate Strategy Division.

Keller: I am Keller. Thank you.

Kyokawa: Lastly, this is Yuji Hosogai, Vice President, Finance & Accounting Department, Corporate Strategy Division

Hosogai: I am Hosogai. Thank you.

Kyokawa: Today, we will provide an overview of our financial results, and then we will take time for questions and answers. The meeting is scheduled to end at 11:00.

Now, let's begin. Mr. Hosogai, please.

Financial Results (Consolidated)

(Unit: B yen)

	FY2021			FY2020	Y on Y	
	Full year Forecasts (revised on Nov. 1)	Apr.-Dec. results	Achievement (%)	Apr.-Dec. results	Change (%)	Change
Revenue	294.0	**219.6**	**74.7**	224.4	**(2.1)**	**(4.8)**
Operating profit	90.0	**60.4**	**67.1**	105.2	**(42.5)**	**(44.7)**
Core operating profit*	90.0	**61.9**	**68.8**	80.0	**(22.6)**	**(18.1)**
Profit before tax	115.0	**74.8**	**65.0**	119.8	**(37.6)**	**(45.0)**
Profit attributable to owners of parent	100.0	**71.0**	**71.0**	89.0	**(20.3)**	**(18.0)**

- **Revenue and each profit category progressing steadily toward full year forecast**
- **Continued aggressive investment in COVID-19 related projects**
  - R&D expenses: R&D expenses related to COVID-19 include expenses that are the subject of grant negotiations with the Japanese government (Progress against the full year forecast is 86.9%, an increase of 9 B yen year on year)
  - The main reason for the decrease in profits other than the above was the gain on the exchange of the Shionogi Shibuya Building (22.9 B yen) in 3Q FY2020

Exchange Rate (average)	FY2021 forecasts (revised on Nov. 1)	FY2021 Apr.-Dec. results
USD ($) – JPY (¥)	**110**	**111.14**
GBP (£) – JPY (¥)	**150**	**152.76**
EUR (€) – JPY (¥)	**130**	**130.60**

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* Operating profit adjusted for one-time factors (impairment losses, gain on sale of property, plant and equipment, etc.)
Achievement excluding a gain on exchange of Shionogi Shibuya Building (22.9 B yen) is in Appendix p.23

Hosogai: I would like to begin with a summary of the financial results for the third quarter.

Could you please open page four of the document?

Consolidated operating results from April to December. As you can see in the red frame on the left, sales revenue was JPY219.6 billion, which is 74.7% of the full-year forecast. Operating profit was JPY60.4 billion, also 67.1%. Core operating profit is JPY61.9 billion, 68.8%. Profit before tax was JPY74.8 billion, 65%, and Profit attributable to owners of parent was JPY71 billion, 71%.

As you can see in the blue box on the lower left, sales are progressing at the standard rate against the forecast, so we believe that we are making good progress.

As for each profit item, although R&D expenses have made some progress, we have stated that this is within the expected range and that we are making steady progress on a profit basis.

As for the investment in COVID-19 related projects, we have included the governmental grants.

On the other hand, if you look at YoY comparison, sales decreased by 2.1%, JPY4.8 billion, which was not enough to cover the decrease in royalties from Crestor.

As for the operating profit and below, there was a gain of JPY22.9 billion from the exchange of the Shionogi Shibuya Building in the previous year, so considering that, the negative figures look larger.

Statement of Profit or Loss (Consolidated)

(Unit: B yen)

	FY2021			FY2020	Y on Y	
	Full year Forecasts (revised on Nov. 1)	Apr.-Dec. results	Achievement (%)	Apr.-Dec. results	Change (%)	Change
Revenue	294.0	**219.6**	**74.7**	224.4	**(2.1)**	**(4.8)**
Cost of sales	57.0 (19.4)	**39.9** (18.1)	**69.9**	35.9 (16.0)	**10.9**	**3.9**
Gross profit	237.0	**179.8**	**75.9**	188.5	**(4.6)**	**(8.7)**
Selling, general & administrative expenses	89.0 (30.3)	**69.0** (31.4)	**77.6**	68.6 (30.6)	**0.6**	**0.4**
R&D expenses	55.5 (18.9)	**48.2** (22.0)	**86.9**	39.2 (17.5)	**22.9**	**9.0**
Other income & expenses	(2.5)	**(2.1)**	**84.4**	24.6	**(108.6)**	**(26.7)**
Operating profit	90.0 (30.6)	**60.4** (27.5)	**67.1**	105.2 (46.9)	**(42.5)**	**(44.7)**
Core operating profit*	90.0 (30.6)	**61.9** (28.2)	**68.8**	80.0 (35.6)	**(22.6)**	**(18.1)**
Finance income & costs	25.0	**14.4**	**57.4**	14.6	**(1.8)**	**(0.3)**
Profit before tax	115.0 (39.1)	**74.8** (34.1)	**65.0**	119.8 (53.4)	**(37.6)**	**(45.0)**
Profit attributable to owners of parent	100.0	**71.0**	**71.0**	89.0	**(20.3)**	**(18.0)**

Main Variation Factors (Y on Y) ※ Special Notes for 3Q

- **Revenue**
  - Increase: Overseas subsidiaries/export, contract manufacturing
  - Decrease: Royalty income (Crestor®)
- **Cost of sales**
  - Increase: Increase in revenue other than royalty Income (about 7.7 B yen)
    Increase: Product mix due to growth in overseas subsidiaries/export, contract manufacturing
- **Selling, general & administrative expenses**
  - Increase: Launch and sales activity costs of cefiderocol in Europe and the United States
  - Decrease: greater efficiency in domestic sales and in general & administrative expenses
- **R&D expenses**
  - Increase: Concentrated investment in R&D activities related to COVID-19 ※
    ⇒Includes R&D expenses under negotiation with the Japanese government for grants
- **Other income & expenses**
  - Decrease in income: Recognized a gain on the exchange of the Shionogi Shibuya Building in 3Q of the previous year (22.9 B yen) ※

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

Now, I would like to talk about PL in a little more detail on page five.

As for sales revenue, it is as I mentioned earlier. I would like to talk about this breakdown later.

On the other hand, the full-year progress in cost of sales is 69.9%, which is a little positive factor for profit. For this fiscal year, improving the cost of sales is a major theme. The increase in production of Cefiderocol and others as well as the control of expenses at the plants have resulted in this.

As a result of the above, gross profit was 75.9%, which is almost on schedule.

On the other hand, in terms of expenses, the progress of selling, general and administrative expenses was 77.6%. It was almost the same compared to the previous year. However, if we break down the contents of this figure, we can see that overseas expenses related to Cefiderocol have increased significantly, while in Japan, we have been able to control expenses to a large extent, and in a sense, we have changed our resource allocation significantly. Although the progress for the full year has been slightly larger, we recognize that we have been able to make good progress in a sense in that the contents have changed significantly.

Concerning R&D expenses, the progression rate was 86.9%, a YoY increase of JPY9 billion. This is because we have been investing intensively in COVID-19 related projects, as I mentioned earlier, and this has been reflected in the increase in R&D expenses. The more than JPY6 billion deviations from the standard can be seen as an increase in COVID-19 related expenses after deducting the grants.

With the above factors, the progression rate of operating profit was 67.1%, and the same is true for the following profits.

Revenue by Segment

(Unit: B yen)

	FY2021			FY2020	Y on Y	
	Full year Forecasts (revised on Nov. 1)	Apr.-Dec. results	Achievement (%)	Apr.-Dec. results	Change (%)	Change
Prescription drugs	94.4	**69.5**	**73.7**	71.8	**(3.2)**	**(2.3)**
Overseas subsidiaries/export	35.0	**26.2**	**74.8**	17.5	**49.7**	**8.7**
Shionogi Inc.	12.7	**11.1**	**87.6**	5.4	**106.2**	**5.7**
Fetroja®	-	**4.7**	-	0.9	**425.1**	**3.8**
Ping An-Shionogi* /C&O	12.3	**7.2**	**58.5**	6.9	**3.8**	**0.3**
SBV(Europe)	5.0	**3.8**	**76.7**	1.3	**195.7**	**2.5**
Contract manufacturing	17.8	**11.8**	**66.3**	10.3	**15.3**	**1.6**
OTC and quasi-drug	13.4	**8.4**	**62.5**	8.8	**(4.5)**	**(0.4)**
Royalty income	132.0	**102.4**	**77.6**	114.8	**(10.8)**	**(12.5)**
HIV franchise	125.2	**96.2**	**76.8**	95.1	**1.2**	**1.1**
Crestor®	0.0	**1.2**	-	16.6	**(93.1)**	**(15.4)**
Others	6.7	**5.0**	**74.8**	3.2	**57.3**	**1.8**
Others	1.4	**1.3**	**93.3**	1.2	**8.7**	**0.1**
Total	294.0	**219.6**	**74.7**	224.4	**(2.1)**	**(4.8)**

Main Variation Factors (Y on Y)

- **Prescription drugs**
  - Decrease: Sales of Cymbalta®
- **Overseas subsidiaries/export**
  - US: Increase: Sales of cefiderocol (Fetroja®)
    Increase: Received a one-time payment for the transfer of FORTAMET® sales rights, etc.
  - Europe: Increase: Sales of cefiderocol (Fetcroja®)
- **Contract manufacturing**
  - Increase: The acquisition of Nagase Medicals as a consolidated subsidiary**, increased supply of dolutegravir API
- **OTC and quasi-drug**
  - Decrease: Sales of ISODINE®
- **Royalty income**
  - HIV franchise: Increase: Sales of Dovato
  - Crestor®: Decrease: Based on the contract
  - Others: Increase: Out-licensing agreement with ViiV for S-365598

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* OTC and quasi-drugs also include in revenue of joint venture
** Made a consolidated subsidiary from 3Q of the previous year

Now, please take a look at the breakdown of sales on page six.

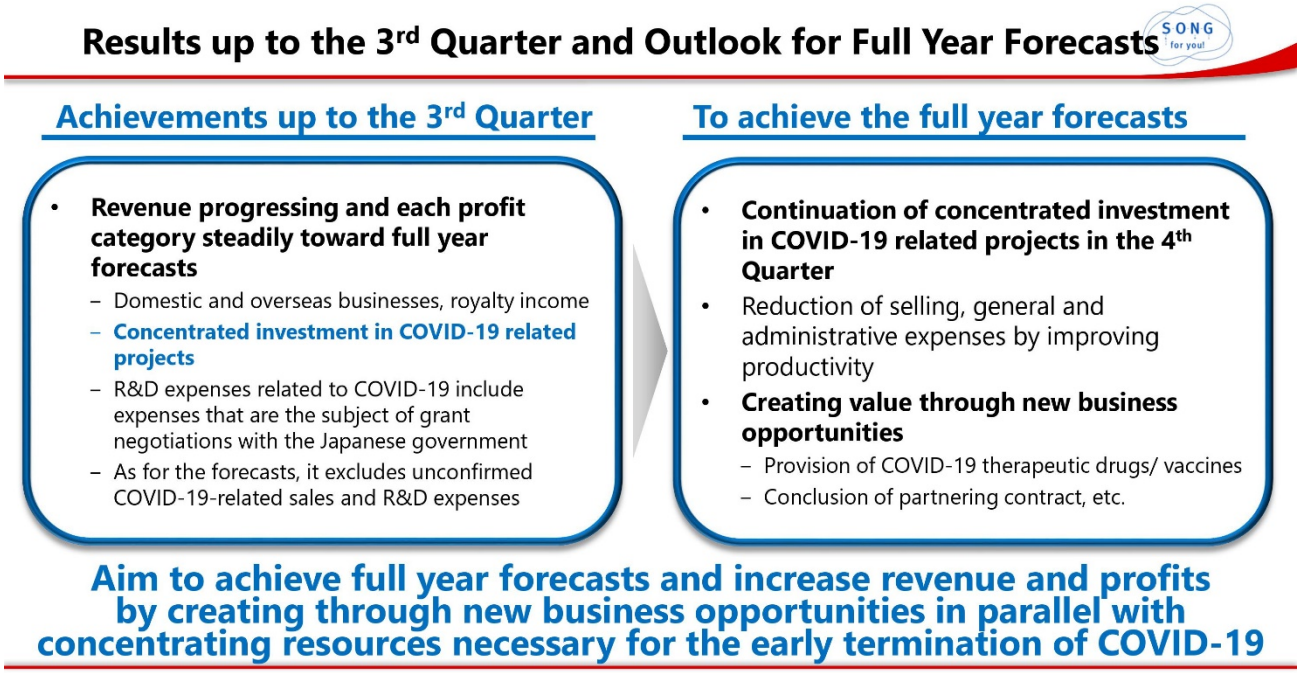
As I mentioned earlier, we have made almost standard progress toward our full-year forecast, but the domestic prescription drugs sales rate of 73.7% is almost within our expectations. Of course, we are aware that the penetration of generics is increasing for Cymbalta, but we believe that this is within our expectation.

On the other hand, as for overseas, Cefiderocol is progressing very well. This is the case in both the US and Europe.

On the other hand, for Ping An-Shionogi, we are still waiting to see how far we can expand the business of the former C&O, but at the moment, the figures are below our target. On the other hand, I would like to say that we are making good progress in research and development.

Also, OTC and quasi-drugs, the progression is a little slow. This is due to the fact that although there was a considerable increase in demand for ISODINE at one time, this has subsided, and demand for cold medicine has remained at a fairly low level this season.

In terms of royalties, I would like to say that things are going well for HIV.



Now, on page seven, I would like to provide a summary and forecast for the full year.

First of all, for the third quarter, as I mentioned, sales and profits were mostly favorable.

On the other hand, some of the expenses related to COVID-19 have been incurred, so it may appear that profit earning is lagging a little behind in terms of numbers. However, we are working on obtaining additional grants. Also, about the progress made in COVID-19 related projects, Sawada will tell you about this later, but I would like to say that things are going very well, including the progress of development.

As for the full year forecasts, I have written three things here: we will continue to invest in the COVID-19 related projects, we will continue to review expenses through productivity improvement, including manufacturing and costs, and contribution to business performance through new business opportunities. As I mentioned earlier, COVID-19 projects are progressing very well, and at the same time, partnering is also progressing well.

As for the full year forecasts, we have left the November figures unchanged, but for this fiscal year, we did not include the sales and expenses related to COVID-19 in the initial forecast. We have released the minimum figures that must be achieved.

At this point in time, expenses, especially R&D expenses, have been recorded as actual results, so profits may appear to be a little behind schedule, but this is because we are making steady progress while also making contributions from new business opportunities. I hope you will understand that we have left these figures unchanged.

These are the minimum figures, and I hope you will see that we have not changed our original goal of increase revenue and profits.

That concludes my explanation.

Sawada: Now, I would like to explain the second item, the achievements in the third quarter and our activities for future growth.

I know that there is a strong interest in oral therapeutic drugs and vaccines against COVID-19, so I would like to focus on them in my presentation.

Actions for COVID-19: S-217622

Development of oral therapeutic drug (S-217622)

- Nonclinical efficacy: activity against omicron variant

In vitro assay using VeroE6T cells

SARS-CoV-2 variant	EC_{50} (μM)	Major mutation site	
		Spike-protein	3CL-protease
WK-521 strain	**0.37**	-	-
α variant (QHN001/QHN002/QK002)	**0.31/0.46/0.33**	N501Y, D614G	-
β variant (TY8-612)	**0.40**	K417N, E484K, N501Y, D614G	K90R*
Γ variant (TY7-501/TY7-503)	**0.50/0.43**	K417T, E484K, N501Y, D614G	-
δ variant (TY11-927-P1)	**0.41**	L452R, T478K, D614G	-
ο variant (TY38-873)	**0.29**	K417N, K440K, G446S, S477N, T478K, E484A, Q493K, G496S, Q498R, N501Y, Y505H	P132H

Antiviral activity retained across various strains, including the current globally problematic omicron variant

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* Inhibitory assessment using K90R enzyme confirmed no effect on drug efficacy

Now let's refer to page nine.

There have been various variants including the Delta variant, but the Omicron variant is now almost dominant. Concerning our oral therapeutic drug, we have examined the antiviral activity also against the Omicron variant in vitro.

As you can see, the effect is comparable to that for other variants, and the results are similar to those obtained in vitro using other variants. It does not target S protein. Therefore, we believe that it is unlikely to be affected by mutations in the normal S protein.

Actions for COVID-19: S-217622

Development of oral therapeutic drug (S-217622)

The 10th page shows the current development schedule.

We have just completed Phase 2a part of Phase 2/3 trials, and we are now entering the next phase, and we hope to start the global Phase 3 trials in February.

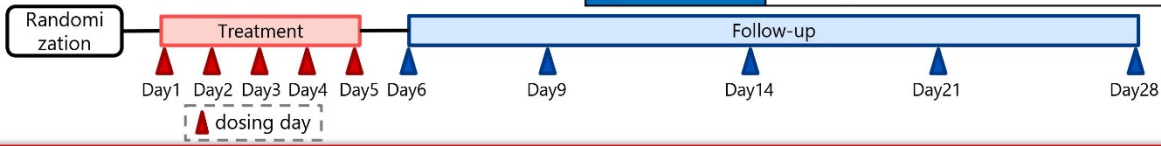
We have already started commercial production, and the first lot has been completed, and we are preparing to secure enough for one million people by the end of March and for 10 million people/year from April.

Actions for COVID-19: S-217622
- Design of Phase 2a part of Phase 2/3 trial -

Development of oral therapeutic drug (S-217622)

- Outline of Phase 2a part
  - **Purpose**
    - > Antiviral effect of repeated administration of S-217622 for 5 days to mild/moderate and asymptomatic SARS-CoV-2 infected patients
  - **Measurement of antiviral effect**
    - > **Viral titer**
      - = Amount of infectious virus (living virus) contained in the sample
    - > **Viral RNA**
      - = Amount of viral RNA (including fragments of the dead virus genome) contained in the sample

Subjects	Asymptomatic or mild/moderate COVID-19 patients
Clinical trial design	Multicenter, randomized, double-blind, placebo-controlled study
Endpoints	Efficacy, Safety
Primary endpoint	Change from baseline in SARS-CoV-2 viral titer at each time point
Secondary endpoint	• Change from baseline in amount of SARS CoV-2 viral RNA at each time point • Proportion of participants with positive SARS-CoV-2 viral titer at each time point • Change from baseline in total score of COVID 19 symptoms at each time point, etc.
Age	12 to 70 years old



Next, see page 11. In terms of our COVID-19 related projects, we have summarized the trial plan for Phase 2a part here.

In this trial, we are measuring viral titers and amount of viral RNA in mild/moderate and asymptomatic infected patients by examining the antiviral effects after repeated administration five-day treatment.

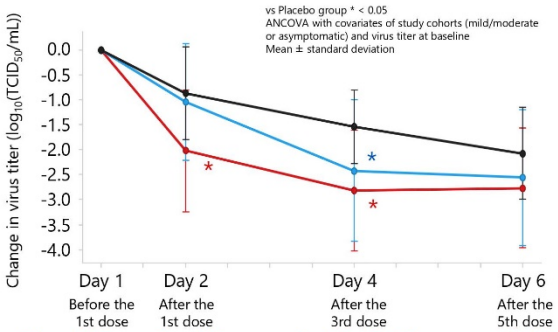
Actions for COVID-19: S-217622
- Antiviral effect: Phase 2a part of Phase 2/3 trial -

SONG for you!

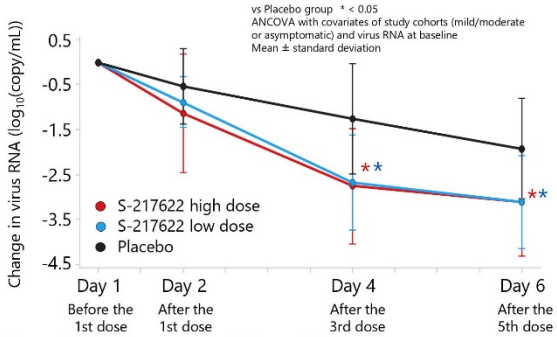
Development of oral therapeutic drug (S-217622)

- Antiviral effect

Mean change from baseline in **viral titer**



Mean change from baseline in amount of **viral RNA**



Rapid reduction of viral titer and RNA load compared to placebo group

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As shown on page 12, there was a significant difference in the amount of change from baseline in titer, which can be thought of as viral activity, on day four in both dose groups.

Significant decrease can be seen also in the placebo group on day six. Unfortunately, the difference is not significant, but the trend is still going on.

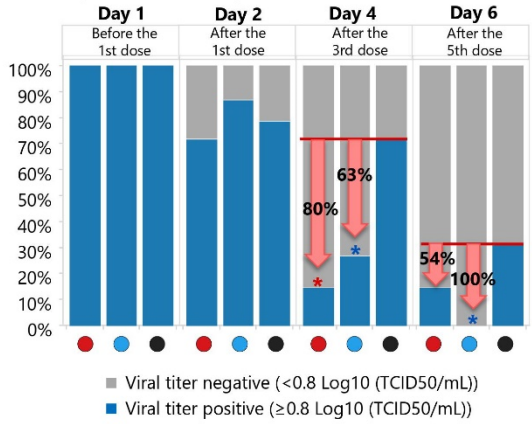
Although the amount of viral RNA is the result of PCR measurement, other companies' data usually show drug efficacy in terms of changes in the amount of viral RNA, so please read this data when making comparisons as a reference.

A difference of about one log was observed on day four, and significant differences were observed on day four, day six, the morning of the fourth day after the third administration, and the morning of the sixth day after the fifth administration. We think this is the strongest result in terms of numbers when we compare to the antiviral effect obtained before. Of course, we can't make a direct comparison.

Actions for COVID-19: S-217622
- Antiviral effect: Phase 2a part of Phase 2/3 trial -

Development of oral therapeutic drug (S-217622)

- Proportion of patients** with viral titer positivity



vs Placebo group *< 0.05
Mantel-Haenszel test stratified by study cohorts (mild/moderate or asymptomatic)

- S-217622 high dose
- S-217622 low dose
- Placebo

- **Decrease in proportion of patients with viral titer positivity in the active group compared to the placebo**

S-217622 rapidly reduces the number of patients shedding infectious virus

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** Patients with a virus detected in the nasopharyngeal swab

Page 13 shows the percentage of patients with positive viral titers.

On day four, the number of negative patients in both dose groups increased by 63% to 80% compared to the placebo group. On day six, there were no positive patients in the low-dose group. Therefore, we believe that if this drug is administered, the number of patients who shed the virus can be rapidly reduced, and the isolation period for infected patients can be shortened.

Actions for COVID-19: S-217622

Development of oral therapeutic drug (S-217622)

- **Phase 2/3 trial**
  - Phase 2a part, interim evaluation
    - > Confirmed prompt antiviral effect
    - > No major safety concerns, and no serious adverse events have been observed
  - Phase 2b/3 part in progress
    - > Patients enrollment goes smoothly in January 2022 with increased COVID-19 positive cases
    - > Site activation completed in global countries to accelerate patients enrollment
- **Global Phase 3 trial**
  - Under discussion with FDA and EMA to initiate trial
- **Commercial production**
  - Completed commercial production of the first lot in December 2021
- **Partnering**
  - Under discussion with candidate companies

Documents necessary for application are continuously submitted to the authorities, aiming for the fastest domestic provision

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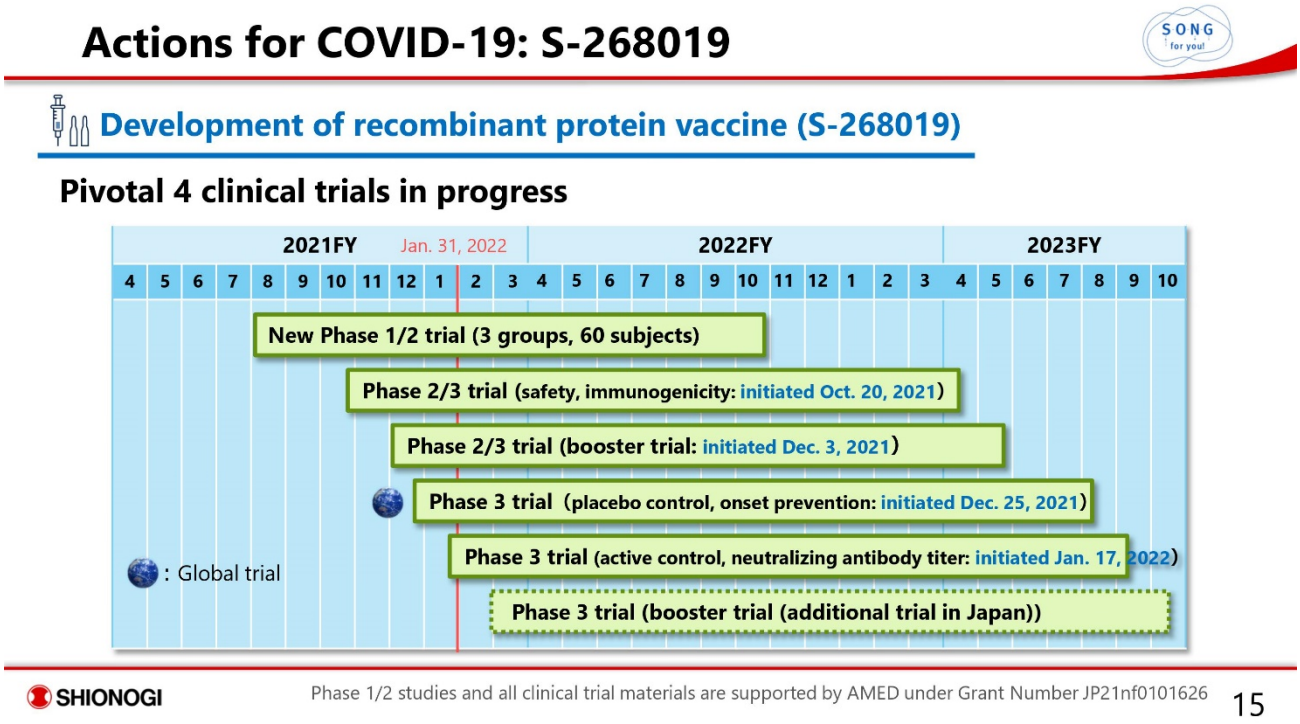
We present a summary of our efforts regarding this COVID-19 therapeutic drug on page 14.

In the Phase 2/3 trial, as I have indicated, we are currently conducting further analysis of Phase 2a part, and we have confirmed the rapid antiviral effect, and we have also seen that there were no major problems with tolerability. We hope to present the results of the detailed analysis on the February 7h.

We are currently on Phase 2b/3 part. Since January, the number of patients has increased considerably, and the accumulation of cases has been progressing steadily compared to December, but we are still diligently continuing to enroll patients. Also, the establishment of overseas facility has been completed.

We are currently in discussions with FDA and EMA to start the global Phase 3 trial, which I mentioned in the previous figure that we hope to start in February.

As for partnering, we are continuing discussions with candidate companies, and we are submitting the necessary materials to the authorities as needed to ensure the fastest possible delivery in Japan.



On page 15, We would like to explain our vaccine from here.

As you can see on page 15, we are currently conducting four clinical trials for the vaccine and are currently compiling the data.

Actions for COVID-19: S-268019

Development of recombinant protein vaccine (S-268019)

Pivotal 4 clinical trials in progress

- **Phase 2/3 trial**
  - Completed the 2nd inoculation of all subjects
  - Completed observation through Day 57 with no major safety concerns
  - Topline results including GMT of neutralizing antibody will be presented at Annual Meeting of Japanese Association for Infectious Diseases in April 2022
- **Active control, neutralizing antibody titer trial**
  - Superiority trial to compare GMT of neutralizing antibody to a licensed vaccine (Bakiszebria intramuscular injection)
  - Completed the 1st inoculation of all subjects
- **Booster trial**
  - Non-inferiority trial with COMIRNATY intramuscular injection with booster immunization after priming of COMIRNATY intramuscular injection
  - Completed observation through Day 29 with no major safety concerns
  - Topline results will be announced early March 2022
- **Placebo control, onset prevention trial**
  - Initiated in Vietnam from December 2021
  - Subject registration is progressing smoothly

All trials are progressing steadily,
aiming for initiation of prior consultation in February and early commercialization

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All clinical trial materials are supported by AMED under Grant Number JP21nf0101626

The contents of each of these trials are briefly summarized on page 16.

The Phase 2/3 trial was an open trial, but after completing the second vaccination of all subjects and the day 57 observation, there were no major safety concerns. The main purpose of this trial was to see the safety and the transition of neutralizing antibody titer, so we would like to present this preliminary report at Annual Meeting of Japanese Association for infectious Diseases in April.

The following three trials are all comparative studies, and the neutralizing antibody titer comparison study is a study to verify the superiority to Vaxzevria intramuscular injection for naïve patients, and all cases have been completed, so the first round of vaccination has been completed.

The additional immunization comparison study is a non-inferiority trial of additional immunization after two doses of COMIRNATY intramuscular injection. Day 29 observations have been completed, and there are no major safety concerns, so the release of the preliminary report is scheduled for early-March.

In addition, a placebo-controlled comparative study on the prevention of the onset of illness started in Vietnam in December last year and has already resulted in more than 5,000 cases.

Each trial is progressing smoothly, and we will start preliminary evaluation consultations in February, aiming for early commercialization.

R&D Progress: 8 Core Projects

	Pipeline	Indication	Status
Infectious disease	**S-540956**	Infectious disease, cancer	Preparing for Phase 1 trial
Psycho-neurological diseases	**S-600918 [sivopixant]**	①Refractory chronic cough ②Sleep apnea syndrome	**①Preparing for Phase 3 trial** **②Closed**
	S-637880	Neuropathic low back pain	Phase 2a trial in progress
	S-812217 [zuranolone]	Depression	**Phase 3 trial in progress**
	BPN14770 [zatolmilast]	①Alzheimer's disease ②Fragile X syndrome	①Phase 2 trial in progress ②Phase 2b trial in progress, Preparing for Phase 2b/3 trial
	S-874713	Psycho-neurological diseases	Preparing for Phase 1 trial
New growth areas	**S-531011**	Solid tumor	Phase 1b/2 trial in progress
	S-005151 [redasemtide]	①Epidermolysis bullosa ②Acute ischemic stroke ③Knee osteoarthritis ④Chronic liver disease ⑤Cardiomyopathy	**①Preparing for additional clinical trial** **②Preparing for Phase 3 trial** ③④Investigator initiated clinical trial (Phase 2 trial) in progress ⑤Preparing for Investigator initiated clinical trial

Steady progress of 8 core projects in parallel with COVID-19 projects

Page 17 shows the progress of the other eight core projects.

The blue texts are for this term. In particular, we have started Phase 3 trial for S-812217, Zuranolone.

R&D Progress: 8 Core Projects

Steady progress in development of projects for medium to long term growth

Zuranolone
-Efficacy that changes existing concepts of depression treatment-

- **Phase 3 trial in Japan in progress**
  - Development as an acute therapeutic drug characterized by rapid onset based on the favorable results of the Phase 2 trial in Japan and the global Phase 3 trial
    - > New positioning that can differentiate from existing antidepressants
- **Smooth progress in overseas (Sage/ Biogen) development**
  - **Preparing for NDA submission to FDA**
    - > Early 2022: Rolling submission scheduled to start

Redasemtide
-Changing the regenerative medicine paradigm-

- **Acute ischemic stroke**
  - **Preparing for the global Phase 3 trial**
    - > **Achieved primary endpoint* in Phase 2 trial**
    - > The implementation rate of revascularization therapy** is low in various countries around the world, and unmet medical needs are large
- **Epidermolysis bullosa**: Preparing for additional clinical trial
- **Knee osteoarthritis**: Completion of recruitment of Investigator initiated clinical trial (Phase 2 trial)
- **Chronic liver disease**: Recruitment of Investigator initiated clinical trial (Phase 2 trial) in progress
- **Cardiomyopathy**: Preparing for Investigator initiated clinical trial

* To evaluate the efficacy compared to placebo in patients with acute ischemic stroke with respect to modified Rankin Scale (mRS : A scale commonly used to measure the degree of disability or dependence in the daily activities of people suffering from stroke or other causes of neuropathy) 90 days after the first dose
** Thrombolytic therapy or mechanical thrombectomy

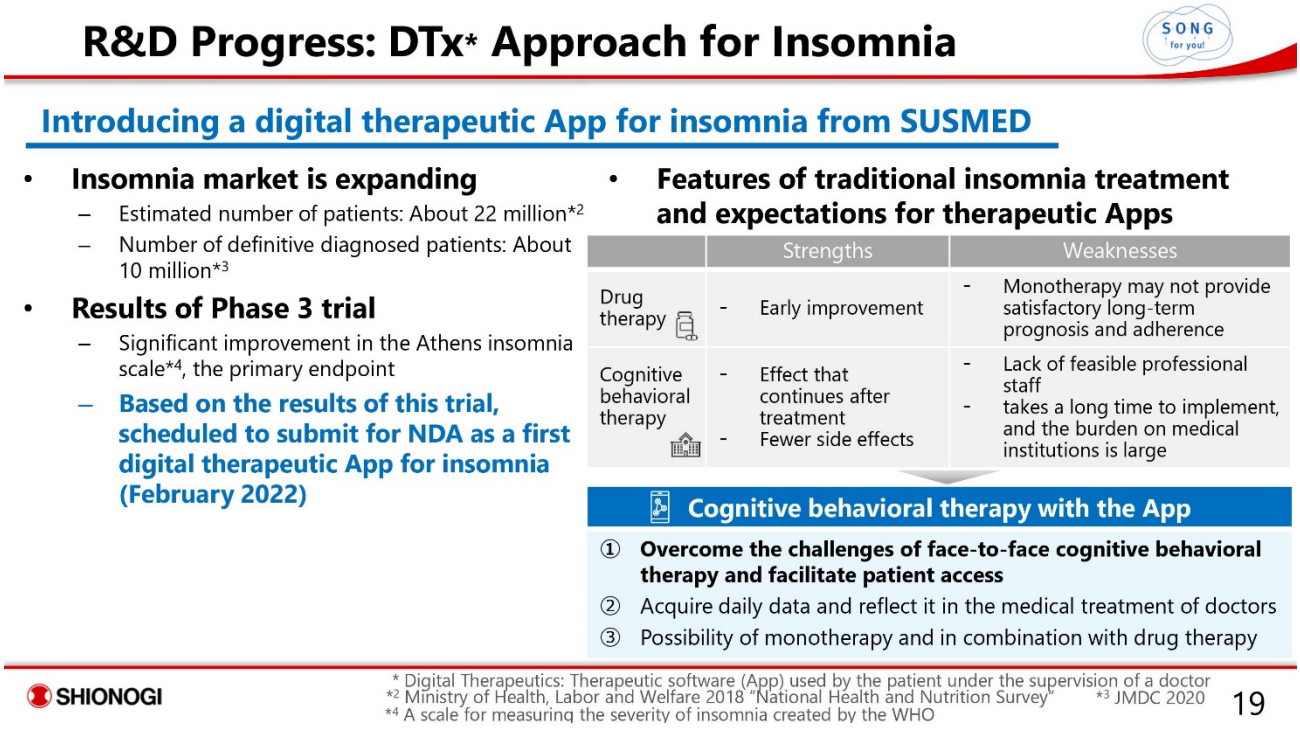
On page 18, among the eight core projects, we would like to focus on Zuranolone and Redasemtide.

As for Zuranolone, we have already started Phase 3 trial, and we believe that there is a need for a drug that can immediately demonstrate its efficacy for patients suffering from depression, and we will be able to provide it to the market in a way that differentiates it from other drugs.

Overseas, Sage and Biogen are making good progress, and are currently preparing for filing.

Unlike so-called cell-based regenerative medicine, Redasemtide is a drug that is based on the concept of regenerative therapy through pharmaceutical products, but it has shown very positive results in clinical trials for acute cerebral infarction, and we are now preparing for global Phase 3 trial.

As soon as we have positive data on other diseases, we would like to expand our activities further.



Please see page 19.

Although it was not included in these eight core projects, we have decided to introduce an application for the treatment of insomnia through the partnership with SUSMED, which we announced last year.

We believe that insomnia, especially in Japan, is a condition in which the satisfaction with sleep is so low that there are probably very few people who do not suffer from insomnia. However, there are many people who do not like to take medication, although medical therapies are a shortcut.

Although cognitive behavioral therapy is normally required before medication, it is difficult to implement because of the lack of specialized staff and the heavy burden on medical institutions due to the considerable time required.

We believe that this application is very important in supporting this process, and since we obtained very good results in Phase 3, we would like to promote it as a cognitive behavioral therapy that is accessible to patients once it is approved, taking into account that a regulatory application as a therapeutic application is scheduled to be filed in February.

Initiatives to Strengthen Domestic and Overseas Businesses

Domestic business

- **ADHD franchise**
  - Continued efforts to increase Intuniv® share of the adult ADHD market
- **Influenza franchise**
  - Flexible efforts according to the influenza epidemic situation

US and Europe business

- **Cefiderocol**
  - Continue efforts to maximize value in the US and Europe
  - Implementing access framework for low- and middle-income countries

China business

- **Ping An-Shionogi**
  - Increase sales via new sales channels, including online medical platforms
  - Focus on activities for early launch of new drugs
  - Expansion of research approaches utilizing AI technology

To achieve full year forecasts,
accelerate the execution of optimal top-line strategies for each region

Page 20 is about domestic/overseas business enhancement. In Japan, the ADHD family is a very important product group under the current circumstances, and we would like to expand the adult market of Intuniv.

On the other hand, the influenza epidemic has not been very prevalent this year, so we would like to change our activity plan for the influenza family flexible depending on the epidemic situation.

On the other hand, in the US and Europe, Cefiderocol is growing very steadily. Looking at the patients who are currently receiving the medication, we believe that it is actually being used by the target patients and is being used appropriately, so we would like to continue our efforts to maximize its value.

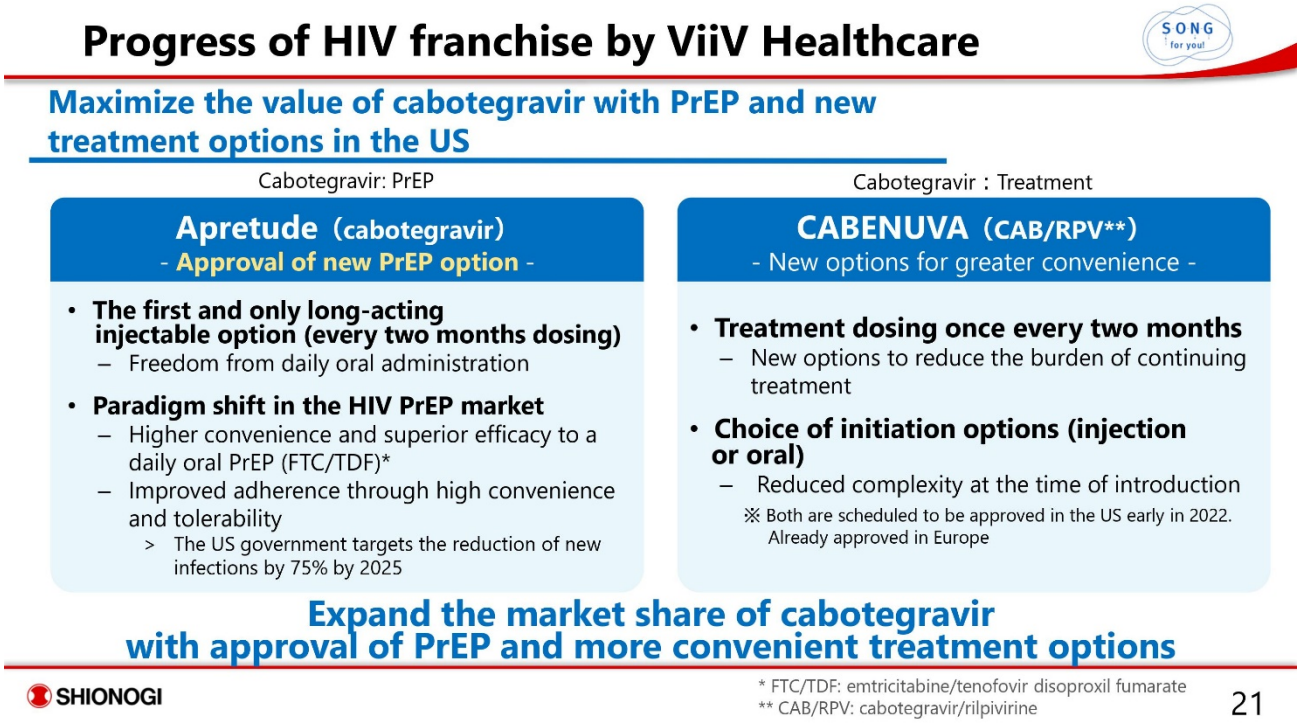
On the other hand, it has been included in the WHO Essential Medicines List, and we believe that we should promote the improvement of access in low- and middle-income countries, so we would like to continue to strengthen our partnership with CHAI and GARDP, which we have already announced.

For the China business, we are expanding our research approach using AI technology. The early phase is progressing quite well, but there is still the issue of pricing policy, and in order to increase sales through new sales channels, including online medical platforms, we believe it is very important to have the right pipeline. We would like to think about expanding this area.

At the same time, we would like to be able to develop our business by promoting activities aimed at the early launch of new drugs that we have.

In this way, we hope further enhancement by accelerating the implementation of the most appropriate top-line strategy for each region.

Next, John will explain the ViiV part.



Keller: We aim to maximize the value of Cabotegravir through prevention and new treatment options in the US.

We are very pleased to announce that cabotegravir obtained approval of new PrEP option. This is the world's first long-acting injectable preventive option, which means that it only needs to be administered once every two months.

This frees people from daily prevention medication. In addition, we have also confirmed a high prevention effect against current PrEP option (FTC / TDF), and we believe this is highly tolerable and will lead to improve adherence. Our efforts are also in line with the USA national policy to reduce the number of new HIV infections and cases to 75% by 2025.

From here, we will talk about CABENUVA. We expect to receive new approval soon, and there are two important points in it.

The first point is that CABENUVA can be administered once every two months in the US. This makes it possible to reduce the burden of continuing treatment. The second point is that patients will be able to choose initiation options. It will be possible to choose to start treatment by oral introduction or by injection. This will eliminate the complexity of introduction.

Both of these points have already been approved in Europe, and we expect them to be approved in the US soon.

We are very happy with the progress of cabotegravir.

That is all from me. Thank you very much.

Question & Answer

Kyokawa : Now, let's move on to the question-and-answer session.

Operator : Our first question comes from Mr. Ueda of Goldman Sachs Japan Co., Ltd. Thank you.

Ueda : I am Ueda from Goldman Sachs.

I would like to ask you first about the therapeutic agent for COVID-19. With the data provided this time, you explained and expected that your drug seemed to be strongest compared to other drugs. However, I think it is difficult to make a direct comparison because the data were originally obtained from different studies and the characteristics of the virus infecting people have changed. Have you ever evaluated and compared these compounds in the same preclinical model?

Sawada : Whether or not this model completely reflects the clinical dose of each compound remains a bit of issues, so even if the results are good, it is not clear whether they will be reflected in clinical setting.

Ueda : Okay, thank you very much.

Sawada : Regarding to the Phase2a trial, because many patients are infected with the Delta variant, probably the data obtained by Pfizer and the target variant are almost the same. As for Merck, I have heard that after the interim analysis, the part that was done in Europe and the USA is also with the Delta variant, so I hope you will consider it as such.

Ueda : I understand. Thank you very much.

Secondly, I would like to know about the current status of your China business. Looking at the YoY comparison, I have the impression that the growth rate is a little low and progress is also low compared to the plan that was revised downward in the second quarter. What is the challenge at the moment and what is required to recover? Also, can you tell us if there is a solution for achieving the mid-term plan?

Sawada : I think it will be the same as I mentioned earlier, but China's medical policy, especially the pricing policy, puts very strong pressure on pharmaceutical companies, and it is recommended to use generics with much lower prices. We need to have some pipeline, including such generics. Otherwise, we think it will be difficult to get into the online system.

I believe that the challenge is how to expand our pipeline, and we would like to take steps to address this issue.

Ueda : If that is the case, is it correct to say that you will first increase your lineup of generics, and then introduce your new drugs?

Sawada : That's right. It would be nice if new drugs could be scaled up, but that would be a matter of consultation with the authorities.

Ueda : I understand. Thank you very much. That concludes my explanation.

Operator : Our next question comes from Mr. Yamaguchi, Citi group Global Markets Japan Inc. Please.

Yamaguchi : I am Yamaguchi from Citi group. Let me ask you three simple questions.

One is about R&D expenses, and I'm not sure I could understand your explanation, but did you mean that you had already included some kind of grants even up to the third quarter, and that you spent JPY20 billion in the third quarter after lowering to the net amount?

Hosogai : The R&D expenses after deducting the subsidies included up to 3Q was reflected in the consolidated income statement.

Yamaguchi : I understand. That includes the part that has not yet been settled, and there is a possibility that other grants will come out for the fourth quarter as well. Thus, R&D expenses may be more than planned, but they will be covered with additional grants. May I understand like this?

Hosogai : We will continue to work on that.

Yamaguchi : Okay, thank you very much.

Also, one simple question about S-217622. I think the easiest way to compare is how much the difference in the amount of viral RNA change from baseline on Day 4 is reduced by log against placebo.

Did you mention about 1 log reduction? Although it is difficult to make a direct comparison between trials, I think Pfizer had about 0.9 log reduction, so did you mention that it was about 1 log reduction when compared to that?

Sawada : That's right.

Yamaguchi : If you look at this figure, if you just look at this point, this is log, so you think it is pretty good.

Sawada : That's right. On the contrary, it is said that Pfizer's one is about 0.9 log reduction, which is the strongest so far, so if you say that. The antibody drugs were about 0.86 log reduction or so.

Yamaguchi : I understand.

There is one more question. I think there was a discussion about whether you can make an application with the data of Phase 2a or with the next Phase 2b/3 trial. Of course, the timing is depending on the authorities, but do you have a vision now? I would like to know the condition regarding the timing of application in Japan.

Sawada : Actually, we are having a discussion with authorities today, so I can't say anything too definite right now, but we are discussing in a certain direction.

Yamaguchi : I understand. So, you have disclosed various information as soon as there was a development in the past, and if you can see the next direction including this data, you can let us know about the release.

Sawada : Yes. Alternatively, I will explain Phase 2a part again on February 7, so it may be possible to do so at that time as well.

Yamaguchi : I see. Are you planning to hold any information sessions on February 7?

Kyokawa : I'm Kyokawa, and we are currently preparing for the information session on the evening of February 7th. I hope you will be able to attend.

Yamaguchi : I understand. What time is it starting in the evening?

Kyokawa : It's going to be around 5:00 PM. It will be separate from the press conference.

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

Operator : The next question comes from Mr. Kohtani of Nomura Securities Co., Ltd. Please.

Kohtani : I'm Kohtani from Nomura Securities. I would like to ask you some more details about slides 13 and 12 for S-217622.

Regarding the slide 13, this is a positive or negative result using your company's detection limit of viral titers, it will be different from the positive in general PCR diagnosis, so I am not sure how to interpret this.

I think I should look at slide 12. As you mentioned, the number of viral RNA copies on the right figure, where Paxlovide and Molnupiravir are also presented, the number of Day 4 is very important here, and Molnupiravir does not give a statistically significant difference even at the maximum dose of 800 mg. I don't know about Pfizer because it doesn't have data, but as far as Day 5, I think it can be said that Pfizer is almost the same.

As you mentioned, the right figure is only looking at amount of viral RNA, so you are also looking at a dead virus. The most important is the viral titer on the left figure. This is a test for infectious viruses. In the high-dose group, there was already a significant difference on day 2, and there was a significant difference in both the low and high dose groups on day 4.

As the number of patients in each group was about 10, I guess we shouldn't take statistical significance too seriously, but at any rate, the efficacy of the drug seems to be higher than that of Molnupiravir and Paxlovid.

The question I would like to ask is how to examine the viral titer, and whether or not this is a reliable examination in general. I think it is the amount of viral RNA that the authorities look at and make some kind of judgment, but can you comment on the examination itself, what cells are used, whether it is reproducible, and whether it is generally credible?

Sawada : It is naturally reproducible and reliable, but viral titer measurement is very expensive, troublesome, and time-consuming, so it is not very general in that sense. I think the PCR method to measure the amount of RNA is generally used. But I don't think this data will be ignored.

However, if you want to compare it with other drugs, other companies do not achieve such a troublesome examination, so I think that there are places where it is difficult to compare unless it is the amount of viral RNA.

Kohtani : But if you stop a infectious virus, it will naturally stop the spread of infection, so in that sense, is it correct to mention that the data are very meaningful for public health?

Sawada : We think that the data on viral activity are more valuable. In fact, when we talk with specialists, there are many doctors who say that data on viral activity are important. In this sense, we believe that the data are valuable.

Kohtani : I would like to know more details. Are these cells from the airway or something else? What kind of cells? I think they are culturing cells to see how much they die.

Sawada :It is taken from the nasopharynx.

Kohtani : I understand.

The second and last point is that despite the recent approval of Molnupiravir and Paxlovid, there have been very few presses on coronavirus drugs, and according to the *New York Times*, they are very difficult to obtain, and doctors are still not prescribing them.

In the media, there is a lot of talk about vaccines, but to be honest, as you mentioned before, vaccines cannot control viral infections, can they? It's to prevent serious illness.

In that case, I believe that coronavirus drugs are the most effective tools of controlling the disease, but has there been any recent changes in your view of this?

Sawada : According to what we hear from the US and other countries, it is currently quite difficult to provide medication within five days, and unless a platform for this purpose is created, it will not be possible to provide medication within five days properly. Also, the supply itself is very limited. I have heard that Pfizer in particular will have a very large supply starting in the second half of this year, but until the first half of this year, I have heard that the supply will be quite difficult.

I recognize that these two are the biggest challenges, and for these reasons, even if we wanted to use it as a treatment, it would be difficult to do so.

Kohtani : As for the importance of coronavirus drugs, it is safe to say that nothing has changed in your view, right?

Sawada : Yes, that’s right.

Kohtani : I understand. Thank you very much.

Operator : The next question comes from Mr. Wakao of J. P. Morgan Securities Japan. Please.

Wakao : I would like to know something about S-217622. Its antivirus effect and change in the amount of virus were well observed. I believe this result was good. On the other hand, in patients with mild symptom, which is the primary endpoint of Phase 2b/3 trial, the time to recovery from symptoms, the rate of symptom onset in asymptomatic patients, and so on. I would like to know if you have any confidence in your company's ability to achieve this endpoint based on the data you have obtained, or what is your current view on this endpoint?

Even if S-217622 could reduce the number of viruses, I wondered if symptoms themselves would continue, and when I looked at the results of Pfizer, I had the impression that it would be quite difficult to improve these symptoms.

What is your company's thought at this point? If you can get domestic approval with the results of this Phase 2a, I wonder if it would also be a situation that you don't necessarily have to meet the endpoint with the results of Phase 2b/3 trial. Can you tell us about the endpoints of Phase 2b/3 trial, including that?

Sawada : We are currently discussing this issue with PMDA.

Wakao : Does that mean that the endpoints of Phase 2b/3 trial may change?

Sawada : It is possible that they will change.

Wakao : I understand. If that is the case, I think Phase 2b/3 trialwill be conducted until July, but even if the endpoints change, will you continue the trial until then? Even if you get approval with the results of Phase 2a trial early, do you continue it with different endpoints, and submit the final data even though the endpoints may be different to make an application?

Sawada : That is initiated in the discussion.

Wakao : I understand. Thank you very much.

The second question is the global Phase 3 trial. In the past, I think you said that you wanted to complete that trial by the end of March, but this time the trial will start in February and end in the middle of October, so I have the impression that it has been moved back quite a bit.

What is the background to this? And what is the premise for the development plan of Phase 3 trial, which will be after the application is filed in the US? Do you plan to work on your own or with a partner? As you have explained so far, I think the trial design itself will be the same as what Pfizer and Merck have been doing, but I wonder if you could tell us about the trial design as well.

Sawada : The reason why this has been extended to October is that we are planning to collect data including long COVID-19, so if you look at the completion in total, it has been long time, but the data for the acute phase, which is usually done, will come out much earlier than that.

We are still negotiating on partnering, so of course we will be involved with partners in the future, but at the moment we have a system in place that allows us to operate without them.

Wakao : I understand. If so, when would that be in terms of the first data readout and the first application? Will it be in October?

Sawada : It depends on the pandemic, so we would naturally like to do it in the first half of this year.

Wakao : Okay, I am looking forward to it.

Lastly, you just commented on partnering, and you mentioned that you might be able to form a partnership by the end of December, and now that the Phase 2a data has come out, I think it would not be surprising if a partnership were to be formed soon with such good results.

When would be the best time for your company to partner? I was thinking that it would be a large pharmaceutical company, but since contract manufacturing is an important point, I wondered if there was a possibility that the Company would be like a CMO. If you could tell me about that.

Sawada : I think it would be a global company with a high production capacity.

Wakao : How about the timing?

Keller : Thank you for your question. Now that we have very good data, so we believe that we will be able to accelerate partnering negotiation.

We have already started contacting and talking with potential candidates, but the most important thing is to find out how much manufacturing capacity they have, and the capacity will be the key.

And here, if we think about how we can market this as a big package rather than just getting approval, we will have to invest more and look for people who can help us scale it up. So, I would like to say that this may be the direction of large pharmaceutical companies.

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

Operator : The next question comes from Mr. Hashiguchi of Daiwa Securities Co., Ltd. Please.

Hashiguchi : You mentioned that the design of the S-217622 Phase 2/3 trial is currently being reconsidered. If the current design remains the same and there are no major changes in the current COVID-19 pandemic, when do you think the primary endpoint data will be available?

Sawada : Does your question mean when the Phase 3 part is completely finished?

Hashiguchi : No. This is about the expected timing of the topline results of the primary endpoint for the Phase 2b/3 part.

Sawada : In terms of the topline results, the 28-day follow-up should be completed due to the primary endpoints, so in fact we cannot provide a topline report until the trial itself is completed. In that sense, if we continue with the current protocol, we will be able to collect 2,000 cases by the end of March or April.

Hashiguchi : Around the end of March or April.

Sawada : However, we need to hurry up with the cleanup.

Hashiguchi : Thank you very much.

One more point is about the status of S-600918. When you explained at the R&D Day in September, you said that whether or not you would actually enter the Phase 3 trial would depend on the results of consultations with the authorities on dosage settings, etc. Could you tell us what the status of this trial now and what kind of design is likely to enter the Phase 3 trial?

Sawada : Regarding S-600918, as you know, Merck obtained a complete response letter from FDA and received a request for additional efficacy indicators, which I think has been made public. FDA looks for indicators to evaluate additional efficacy, and we are currently discussing this.

Hashiguchi : In that case, you mentioned in today's slide that you are preparing for Phase 3 trial during this fiscal year, but is there a possibility that it will take some time to start?

Sawada : FDA seems to be a little busy at the moment, so some of the discussions are not proceeding on schedule, so there is a possibility that only that part may shift a little.

Hashiguchi : Lastly, is there anything you can comment at this stage regarding your approach to R&D and R&D expenses for the next fiscal year?

Hosogai : This is Hosogai.

There is a possibility that R&D expenses related to COVID-19 may continuously occur in the next fiscal year, so there is a possibility that R&D expenses will increase accordingly. On the other hand, as I mentioned earlier, we will continue to aim to obtain grants, so I would like to mention that we are currently considering a plan that will prevent over R&D expenses. That’s all.

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

Operator : Next question will be the last one. Thank you very much, Mr. Muraoka, Morgan Stanley MUFG Securities Co., Ltd.

Muraoka : I think the additional update for Phase 2a results that will come out next week on February 7 means that we'll get more information about day 28 data, not day 6 this time.

I'm sorry, my imagination may be limited, but if I look at the Day 28 data, I saw that there was not much difference from placebo, and I thought that I would wonder what the data was for. I was wondering if you could tell me how to interpret the data, so that I can prepare for it.

Sawada : Safety data will be added, and changes in clinical symptoms will be included.

Muraoka : So, we will be able to hear information about clinical symptoms, not just the amount of virus, next Monday? I understand. Thank you very much.

Also, with regard to the vaccine S-268019, there was a report that the PMDA had a problem with the fact that vaccines developed by Takeda had not Rhabdo-free, but I understand that your company is fine, but is it natural for such a problem to occur, especially with such an urgent drug? What do you think?

Sawada : Considering that one company actually fell into a management crisis as a result of the last time it became a problem in Japan, I think it is natural that it would become a problem unless the problem is scientifically solved.

Muraoka : I understand. Thank you very much.

Lastly, I would like to ask you a question about the future that I don't understand, but if we assume that the pandemic will gradually approach to the endemic stage, if we compare the demand for this oral drug between 2022 and 2023, will it increase or decrease in 2023 compared to 2022? I can't imagine myself on this at all, but if you could tell me about scenario analysis as well, I would learn a lot.

Sawada : Normally, when proliferative capacity is acquired, the symptoms themselves become rather mild. However, considering that there will always be people who become seriously ill even so, I think it will be handled like a flu. I believe that the number of people who are eligible will increase, although there may be some differences between countries.

It is difficult to say how the number of infected people will change.

Muraoka : Do you imagine that the demand in 2023 as a medicine will increase more than that in 2022?

Sawada : I think that is probably the part that is difficult to read, including how it is covered by insurance. Currently, there is an impression that we want to reduce the number of infected people as much as possible in order to reduce the social public health issues and economic impact.

Considering the fact that some countries are currently providing treatment for influenza and others are not, the policy here will change in each country, and depending on how it works, it could be positive or negative. However, I believe that a certain amount of need will continue to exist.

Muraoka : In terms of business from the perspective of S-217622 global, 2023 is bigger and more important than 2022, isn't it? Maybe in a time frame. Can I have that understanding?

Sawada : So, the time when the business has not yet become a normal business may be larger in the global perspective.

Muraoka : Government stockpile, etc. I understand. It was helpful. Thank you very much. That’s all.

Kyokawa : This concludes the Conference Call for SHIONOGI's financial results for FY2022 3Q.

Thank you for joining us today despite your busy schedule.

Sawada : Thank you very much.

Hosogai : Thank you very much.

[END]