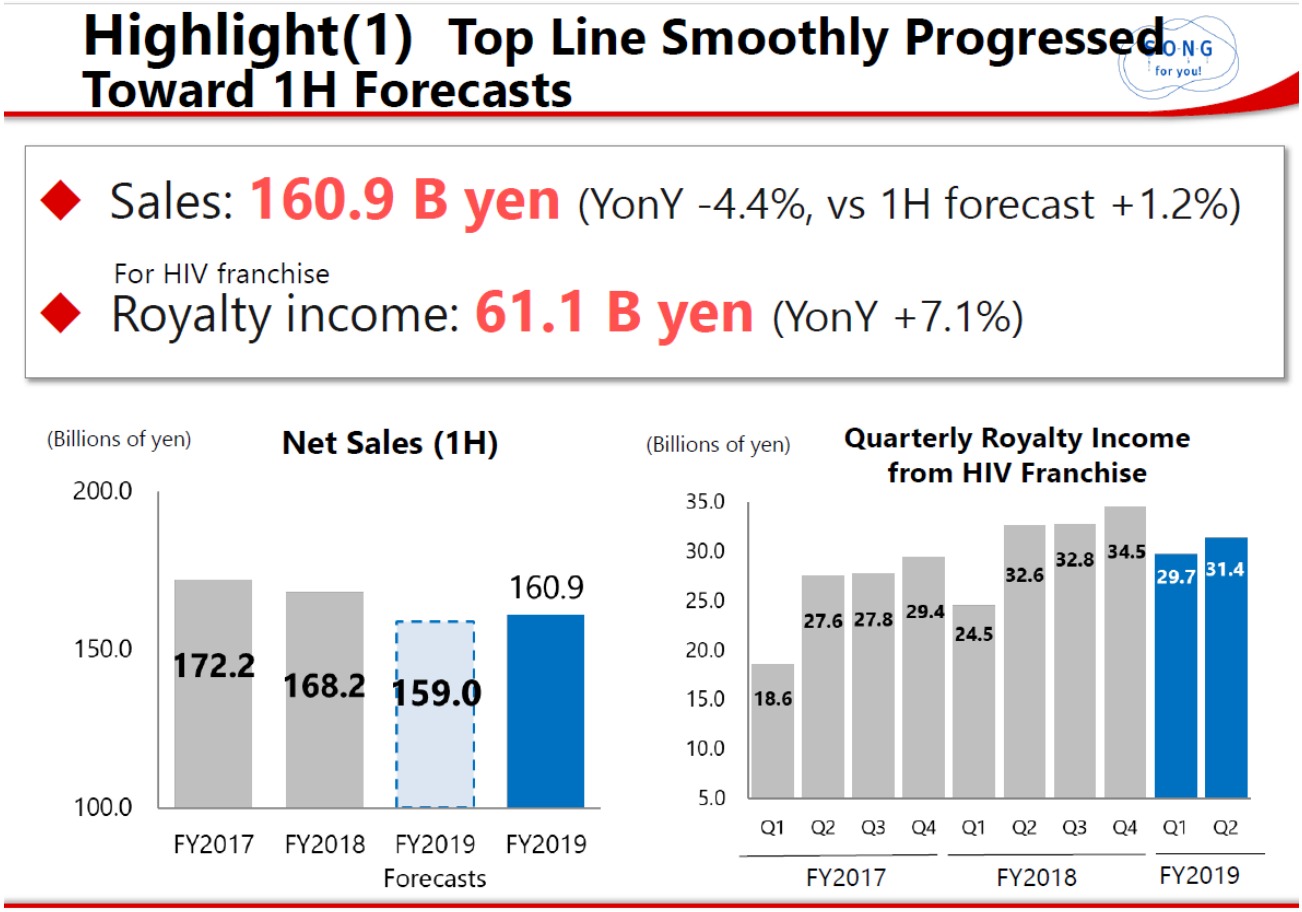
Presentation

Teshirogi: Good morning, ladies and gentlemen.

First of all, today I asked Ms. Sawada to join us in preparation for possible questions associated with infectious diseases. She has been engaging mainly in Xofluza and cefiderocol for the past six months to one year. I will also answer your questions as much as possible, but two of us will explain the details of this matter. Your understanding would be appreciated.

Now, we would like to explain the overview of the financial results for the first half of the fiscal year under review, and your questions are welcome after the presentation.



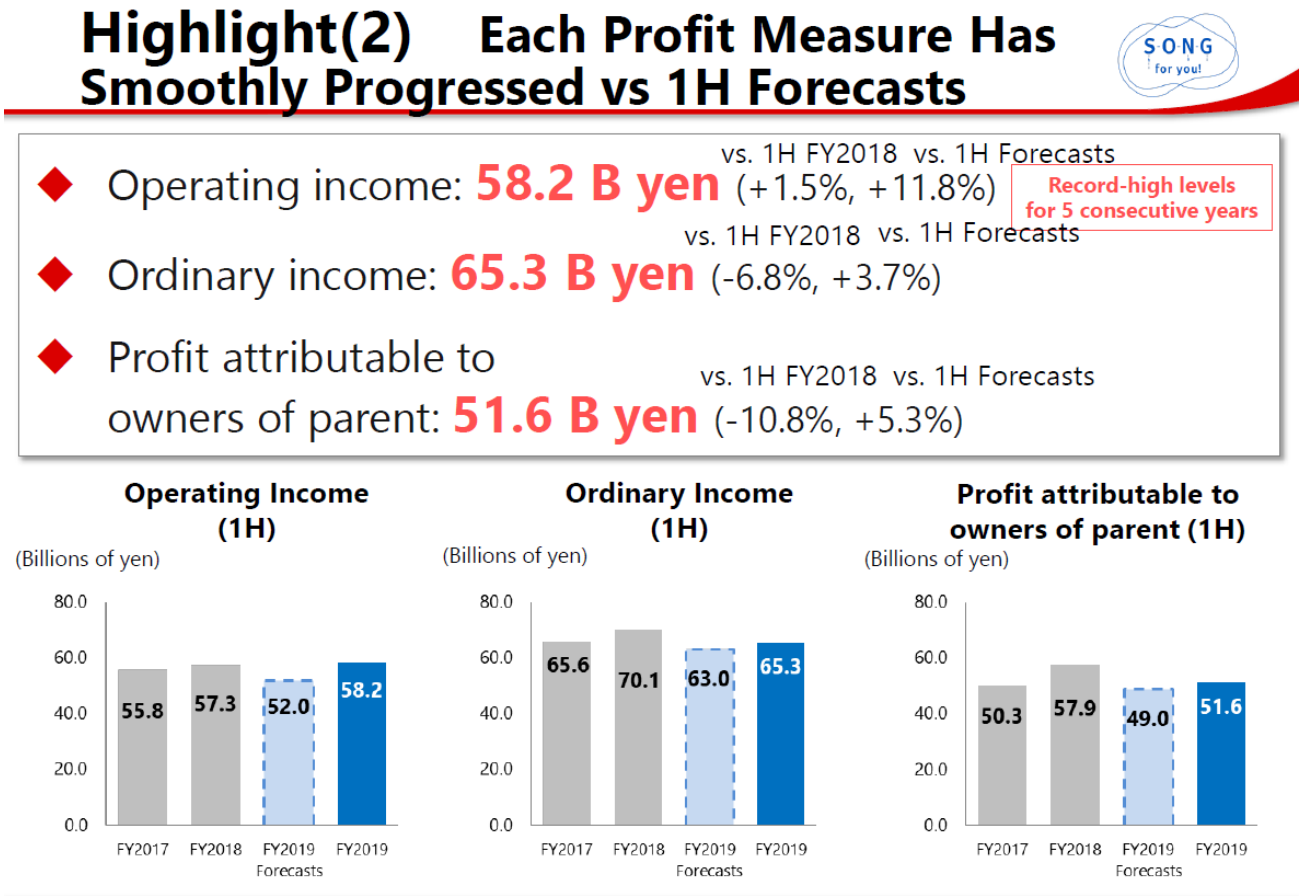
The highlight of the financial result include sales of 160.9 billion yen, which is a 4.4% decline on a year-on-year basis, but this figure represents a 1.2% increase compared with the forecast for the first half period which we announced in May this year. I will explain in detail afterwards, but this was attributable to a reaction against a significant amount of milestone income of about 21 billion yen associated with Xofluza which we received from Roche in the first half of the previous fiscal year. We could hardly make up for the year-on-year gap.

With respect to royalty income, especially that relating to HIV, I suppose there might be some questions concerning this point afterwards. Biktarvy of Giliad, our competitor, will present a full-scale contribution this year. With regard to our 3-drug combination Triumeq and Tivicay plus Descovy regimen which recorded modest sales from last year, some analysts had concerns that these products might show very sluggish sales in

Fiscal 2019. However, the actual results indicated that the loyalties we received in the first half period under review increased 7.1%, which is equivalent to slightly more than 10% increase in local currencies, 10.1%. This means that ViiV contributed relatively strongly in the first half period.

In particular, for the July-December period in the second half, although we anticipate that competitions are likely to become fiercer, I expect we will be able to record an increase of 3% to 5% as the performance of the ViiV franchise. As the results of the 96-week GEMINI test and then the 48-week TANGO test which were reported at the International AIDS Society Conference on HIV Science (IAS 2019) in July, as I may have mentioned before, the market will shift to Dovato and Juluca gradually.

Furthermore, the PDUFA (Prescription Drug User Fee Act) dates are coming closer for our injection form of 2-drug regimen in December. Considering that a full-fledged paradigm shift to 2-drug regimen for HIV treatment will be realized next year and thereafter, the year 2019 may be the toughest year for us. We feel secure to see the year-on-year increase in sales even in such a tough year.



As to profits, operating income was 58.2 billion yen, securing profits albeit slightly. The increase was 1.5% year on year in contrast to 11.8% compared with the forecast for the first half. I will explain more in detail later, but this result is basically attributable to our successful cost control in addition to robust sales. More-than-expected cost of sales was a little bit unexpected for us, but including that, we could manage to secure an increase in operating income. This is our record high operating income for the consecutive five years, in terms of the first half of fiscal year.

Meanwhile, as to ordinary income, almost the total difference from operating income represents the dividend-related income received from ViiV. Following the change in the threshold in the first quarter of Fiscal 2018, we received a special dividend of 20 million pounds sterling. In the current fiscal year, we will receive no such dividend. Even if the amount of dividend received had remained the same in pounds sterling, the stronger yen would have pushed down the converted yen amount to a significant range.

As I mentioned this in the past, a significant part of loyalties were hedged because a certain range of sales can be forecasted. However, it is difficult for us to hedge dividends which is subject to the dividend policy of ViiV. Therefore, the currency risk of dividend remained unhedged and we were directly affected by the currency trend.

Consequently, operating income decreased by 6.8% year on year in contrast to an increase of 3.7% compared with the first half forecast in which we had estimated that the environment would be significantly tough.

Profit attributable to owners of parent reflects a decrease in ordinary income in addition to an increase in R&D expenses as a strategic investment framework applying the milestone income of 21 billion yen that we had expected to receive from Roche in the previous fiscal year. Specifically, we spent more than 13 billion yen for strategic investment, which was recorded as an increase in experimental research costs for the tax purposes, leading to a significant amount of tax deduction. In the current fiscal year, we had no such benefits, resulting in more decrease in profit attributable to owners of parent than the previous fiscal year. The decrease reached 10.8% year on year. I would like to emphasize, however, that we had anticipated this matter appropriately, and the decrease was 5.3% compared with the first half forecasts. Therefore, compared with the forecast, we consider that the result was not so bad.

Financial Results (Consolidated)

(Unit: B yen)

	FY2019				FY2018	Y on Y	
	Forecasts*		1H results	Progress vs. forecasts	1H results	Change (%)	Change (B yen)
	Full year	1H					
Sales	365.5	159.0	**160.9**	101.2%	168.2	(4.4%)	(7.3)
Operating income	147.0	52.0	**58.2**	111.8%	57.3	1.5%	9.0
Ordinary income	170.5	63.0	**65.3**	103.7%	70.1	(6.8%)	(4.8)
Profit attributable to owners of parent	133.0	49.0	**51.6**	105.3%	57.9	(10.8%)	(6.3)

- Sales and each profit measure exceeded the 1H forecasts
- Operating income was higher than the levels achieved in prior fiscal years for 5 consecutive years

Exchange Rate (average)	FY2019 forecasts	FY2019 1H results
USD ($) – JPY (¥)	110.0	108.61
GBP (£) – JPY (¥)	145.0	136.65
EUR (€) – JPY (¥)	130.0	121.41

* Forecasts announced on May 9, 2019 (Revision was announced on October 30, 2019)

This slide shows the mixed results on the right hand on an absolute value basis. As I mentioned earlier, and I will explain in detail later, but this slide indicates that we earned about 14 billion yen in various fields against the milestone income from Roche, but failed to compensate the gap. I mean we could not make up for the gap of 7 billion yen.

As to foreign exchange, with the exchange rate being shifting slightly to the stronger yen, we have hedged almost 80% of the amounts at more than 140 yen against the US dollar throughout the year. Other than those mentioned above, and foreign currency-denominated assets, etc. recorded losses due to yen appreciation.

Statement of Income

SONG for you!

(Unit: B yen)

	FY2019				FY2018	Y on Y	
	Forecasts*		1H results	Achievement (%)	1H results	Change (%)	Change (B yen)
	Full year	1H					
Sales	**365.5**	**159.0**	**160.9**	101.2	168.2	(4.4)	(7.3)
	14.6	16.0	17.3		14.7		
Cost of sales	**53.5**	**25.5**	**27.9**	109.4	24.7	12.8	3.2
Gross profit	**312.0**	**133.5**	**133.0**	99.6	143.5	(7.3)	(10.5)
	45.1	51.3	46.5		51.2		
SG&A expenses	**165.0**	**81.5**	**74.8**	91.8	86.2	(13.2)	(11.4)
	31.6	35.5	32.2		28.3		
Selling & administrative expenses	**115.5**	**56.4**	**51.8**	91.9	47.5	9.1	4.3
	13.5	15.8	14.3		23.0		
R&D expenses	**49.5**	**25.1**	**23.0**	91.5	38.6	(40.6)	(15.7)
Ordinary R&D expenses**	**49.5**	**25.1**	**23.0**	91.5	25.6	(10.2)	(2.6)
Strategic investment	**-**	**-**	**-**	-	13.1	-	(13.1)
	40.2	32.7	36.2		34.1		
Operating income	**147.0**	**52.0**	**58.2**	111.8	57.3	1.5	0.9
Non-operating income & expenses	**23.5**	**11.0**	**7.1**	64.9	12.8	(44.1)	(5.6)
	46.6	39.6	40.6		41.7		
Ordinary income	**170.5**	**63.0**	**65.3**	103.7	70.1	(6.8)	(4.8)
Profit attributable to owners of parent	**133.0**	**49.0**	**51.6**	105.3	57.9	(10.8)	(6.3)

* Forecasts announced on May 9, 2019 (Revision was announced on October 30, 2019)
** Ordinary R&D expenses: Total R&D expenses excluding strategic investment

Here we have the Statement of Income. On page 8, I have described the causes of increases and decreases in profits with some remarks on the right column. We internally value operating income in particular, expecting to maintain the highest operating income in the industry. This is what we stick to earnestly.

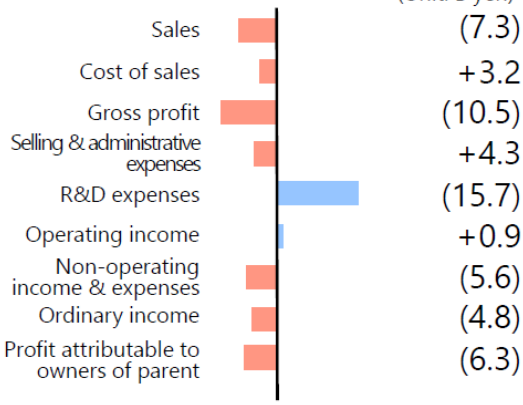
Operating income exceeded 36% in the first half, and with the goal of achieving over 40% on a full-year basis for the first time, we consider that our efforts including cost control are going steadily.

Y on Y Comparison and Main Variation Factors (Statements of Income)

SONG for you!

- **Y on Y comparison**

(Unit: B yen)



- **Progress vs 1H Forecasts**

(Unit: B yen)

Main Variation Factors (Y on Y)

- **Sales**
  - FY2018: Income from Roche for Xofluza® *
- **Cost of sales**
  - Increase in export of dolutegravir and Xofluza®, Sales increase of Flumarin®
- **SG & A expenses**
  - **Selling & administrative expenses**
    - › Increased in alignment with sales growth
  - **R&D expenses**
    - › FY2018: Strategic investment (13.1 B yen)
- **Non-operating income & expenses**
  - FY2018: One-time dividend from ViiV
  - Exchange-rate fluctuations

Main Variation Factors (vs 1H Forecasts)

- **Cost of sales**
  - Product mix
  - Increase in exports of dolutegravir and Xofluza®
- **SG & A expenses**
  - **Selling & administrative expenses**
    - › Controlled in preparation for 2H FY2019 activities
  - **R&D expenses**
    - › Change of development plan of S-812217
- **Non-operating income & expenses**
  - Exchange-rate fluctuations

SHIONOGI

* Royalty income from Roche as milestones of R&D achievement

The breakdown is shown here. First, on a year-on-year basis, sales decreased by 7.3 billion yen. This is attributable to the absence of the milestone income for Xofluza equivalent to 21 billion yen. The increase of 3.2 billion yen in cost of sales was far beyond our expectation, although we had anticipated a slight increase. This is what we must admit frankly.

In April 2019, we split our business to Shionogi Pharma Co., Ltd., a wholly-owned subsidiary, for the purpose of further improving cost control. In particular, while we had planned to cut personnel expenses compared with last year, but this may sound as an excuse, there was a shortage problem of antibiotics products in the domestic market, and beta-lactam antibiotics including Flumarin sold much more than we had expected. We were forced to increase production, which was attributable to higher cost of sales.

Exports increased due to the advancement of Xofluza for this winter to Roche and doltegravir API on request from GSK. Bulk products increased in cost of sales due to their inherently high costs.

Meanwhile, in the past six months, we became aware of several facts which we had not anticipated in terms of operations but emerged after the company split. We have realized that such matters are attributable to a little higher cost of sales.

Therefore, we now believe that in the second half of the current fiscal year, we will be able to control costs at a conventional level or to a certain range over such a level anyhow.

With respect to selling, general and administrative (SG&A) expenses, although sales are indicated here, the impact of shifting to the Two Invoices System in China is significant, as may be the same with other pharmaceutical companies. Under such system, as sales grow, the SG&A expenses will also increase. As a result, the increase in SG&A expenses is mostly attributable to such system.

Other than the above, we also spent appropriate SG&A expenses for domestic prescription drugs including Cymbalta, Intuniv and Xofluza, and such measures had impacts on the increase of overall SG&A expenses.

However, I would like to point out that R&D expenses decreased significantly due to the absence of the strategic investments of 13.1 billion yen.

As to non-operating income & expenses, as I explained earlier, the result is attributable to the dividends from ViiV.

As to the comparison with the forecast for the first half, we implemented a certain range of control on SG&A expenses, etc. in an effort to increase operating income, considering that cost of sales rose to a significantly higher level than we had anticipated.

Sales by Segment

(Unit: B yen)

	FY2019				FY2018	Y on Y	
	Forecasts*		1H results	Achievement (%)	1H results	Change (%)	Change (B yen)
	Full year	1H					
Prescription drugs	**144.1**	**53.7**	**52.4**	97.6	50.0	4.9	2.5
Overseas subsidiaries/export	**31.4**	**16.0**	**17.5**	109.2	15.4	13.9	2.1
Shionogi Inc.	**9.9**	**6.3**	**6.8**	108.0	7.4	(8.0)	(0.6)
Mulpleta®	**1.0**	**0.25**	**0.34**	134.8	-**	-	0.3
C&O	**14.6**	**6.8**	**7.2**	104.9	5.0	42.7	2.1
Contract manufacturing	**14.3**	**9.1**	**10.1**	111.0	5.7	75.7	4.3
OTC and quasi-drug	**9.7**	**4.6**	**4.7**	102.3	3.8	25.1	1.0
Royalty income	**163.6**	**74.3**	**75.0**	100.9	92.2	(18.7)	(17.2)
HIV franchise	**126.5**	**61.3**	**61.1**	99.7	57.1	7.1	4.0
Crestor®	**22.0**	**11.0**	**11.1**	100.5	10.9	1.5	0.2
Others	**15.1**	**2.1**	**2.8**	135.6	24.2	(88.4)	(21.4)
Others	**2.4**	**1.2**	**1.1**	94.7	1.1	0.3	(0.0)
Total	**365.5**	**159.0**	**160.9**	**101.2**	168.2	**(4.4)**	**(7.3)**

SHIONOGI

* Forecasts announced on May 9, 2019 (Revision was announced on October 30, 2019)
** The full-scale promotion was initiated in Dec. 2018.

9

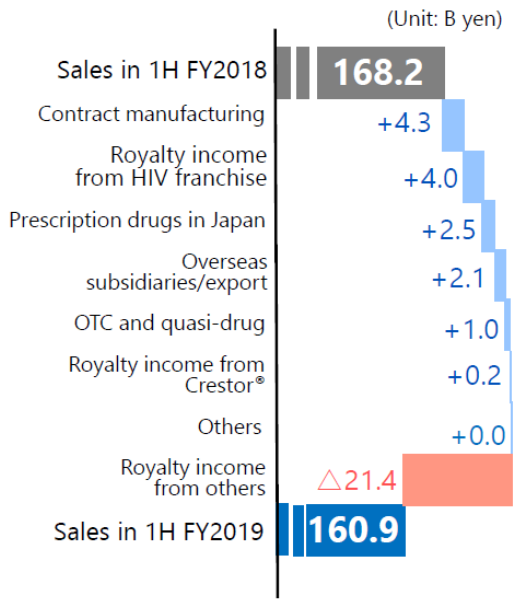
In the right column of the table, the year-on-year changes in sales of each business are indicated as I mentioned earlier. Sales in the domestic prescription drugs segment increased by 2.5 billion yen, overseas subsidiaries and export increased by 2.1 billion yen, contract manufacturing sales rose 4.3 billion yen, OTC and quasi-drug increased by 1.0 billion yen, and loyalty for HIV franchise grew 4.0 billion yen. This table shows the results of various items, and clarifies that those increases failed to make up for the negative figure shown in the bottom line equivalent to approximately 21 billion yen.

As to the achievement rate against the forecast for the first half, the domestic prescription drugs segment shows the lowest figure of 97.6%. I will explain in detail later, but I must point out the results of Crestor, Irbetan and OxyContin. We had expected higher sales, but these products have been under the pressure of generic drugs far more than expected. Sales of these three products combined were 1.4 billion yen short of our forecast. The gap of 1.3 billion yen in the domestic prescription drugs represents a little shortfall from our sales forecasts.

Y on Y Comparison and Main Variation Factors (Sales by Segment)

SONG for you!

- **Y on Y comparison**



Main Variation Factors (Y on Y)

- **Royalty income**

(Increase factor)
  - Sales growth and termination of the threshold period of HIV franchise

(Decrease factor)
  - FY2018: Income from Roche for Xofluza® *

- **Contract manufacturing**
  - Increase in export of dolutegravir and Xofluza®

- **Prescription drugs**
  - Sales Increase of Cymbalta® and Intuniv®

- **Overseas subsidiaries/export**
  - C&O: Sales increase of rabeprazole
  - Shionogi Inc.
    - > FY2018: One-time payment from Purdue
    - > FY2019: One-time payment from BDSI**

* Royalty income from Roche as milestones of R&D achievement
** BioDelivery Sciences International Inc.

Page 10 shows a schematic chart to describe the aforementioned shortfall. As I explained repeatedly, many items recorded year-on-year increases but failed to make up for the negative 21.4 billion yen.

Sales of Prescription Drugs in Japan

(Unit: B yen)

	FY2019				FY2018	Y on Y	
	Forecasts*		1H results	Achievement (%)	1H results	Change (%)	Change (B yen)
	Full year	1H					
Cymbalta®	29.3	13.0	12.9	98.8	11.9	7.8	0.9
Intuniv®	13.6	4.6	4.5	96.6	2.4	86.7	2.1
Xofluza®	28.0	0.28	0.00	0.5	0.46	(99.7)	(0.5)
Rapiacta®	2.6	0.05	0.01	21.8	0.01	77.8	0.0
Brightpoc® Flu	1.8	0.18	0.31	169.0	0.23	32.3	0.1
Total of strategic products	75.7	18.2	17.7	96.9	15.0	17.4	2.6
OxyContin® franchise	6.7	3.6	3.2	87.9	3.8	(16.6)	(0.6)
Symproic®	2.3	1.1	1.1	99.9	0.72	51.6	0.4
Actair®	0.27	0.12	0.12	95.6	0.09	39.8	0.0
Mulpleta®	0.33	0.17	0.07	40.1	0.08	(19.1)	(0.0)
Pirespa®	6.9	3.5	3.4	99.5	2.9	20.2	0.6
Total of new products	92.2	26.7	25.6	95.8	22.6	13.1	3.0
Crestor®	10.0	5.2	4.6	88.0	5.2	(11.5)	(0.6)
Irbetan® franchise	4.9	2.6	2.2	85.5	3.1	(26.6)	(0.8)
Others	36.9	19.2	20.1	104.4	19.1	4.8	0.9
Prescription drugs	144.1	53.7	52.4	97.6	50.0	4.9	2.5

* Forecasts announced on May 9, 2019 (Revision was announced on October 30, 2019)

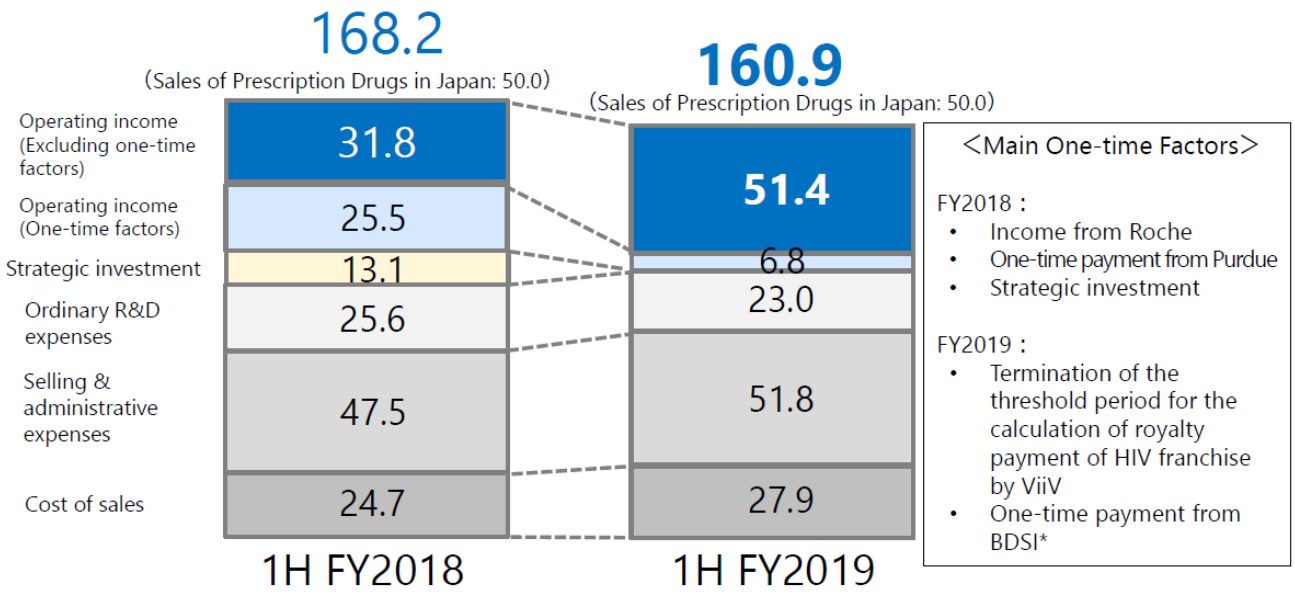
Page 11 shows that sales of Cymbalta and Intuniv fell short of the forecast for the first half by 0.1 billion yen, respectively. We consider that sales of these two products were relatively steady in line with our plan. Particularly, sales of Intuniv have shown robust growth since we obtained the approval for adult patients, reaching 1.8 folds from the previous fiscal year. We consider that the second-half period started with relatively strong sales. We focus on the second half period for sales in terms of influenza.

As I mentioned earlier, sales of OxyContin franchise fell short of 0.4 billion yen compared with the forecast for the first half, or 0.6 billion yen short on a year-on-year basis. These figures are weaker than we expected.

Year-On-Year Comparisons (One-time Factors)

SONG for you!

Sales (Unit: B yen)



Our business is progressing steadily including the sales of new products

* BioDelivery Sciences International Inc.

In the previous fiscal year, we had a lot of one-time factors. We summarized them in this chart to clarify the situations in the real business.

In the first half of FY 2018, sales were 168.2 billion yen while operating income was 57.3 billion yen, to which one-time factors reaching 25.5 billion yen contributed significantly, particularly consisting of the milestone income for Xofluza received from Roche, and a refund for Symproic from Purdue. This amount shrank extremely to 6.8 billion yen in the first half of FY 2019. This means that operating income in a real sense was 31.8 billion yen in the first half of FY 2018 whereas it exceeded 50 billion yen in the first half of FY 2019. It might seem that our basic business still lacks strength, but we believe that we are looking ahead to make steady progress.

Basic Strategy and Progress of 1st Half in FY2019

Driving for sustainable growth beyond 2020, while demonstrating our own earning power created during SGS2020

1. Sales

Increasing sales and profits, demonstrating own earning power by expanding sales of new products and further increasing management efficiency

- **Sales increase of Cymbalta® and Intuniv®**

2. Investment

- Progression of pipeline products as growth drivers beyond 2020
- Establish a global presence in priority regions

- **Further selection and concentration on high-priority projects**
- **Novel HIV drug: Initiation of a clinical trial**
- **Progress in the development of Cefiderocol and Xofluza®**

It is our view that the results for the first half of the current fiscal year were steady to a certain degree although as I mentioned earlier several times, we must accelerate the speed of growth in Cymbalta and Intuniv in the second half.

Furthermore, now I will explain about our investments. Our priority goes to research of novel products such as S-600918, S-812217 or S-637880 while suspending investments in what should be stopped. We commenced the Phase I study of this compounds under new HIV mechanisms. As the speed of study is the most essential factor in the competition, we must examine as quickly as possible the degree of reduction of virus to seek possible combinations with Tivicay or dolutegravir in the future before planning the development matters.

With respect to cefiderocol, we managed to pass the review by the FDA's Advisory Committee (Adcom). And as to Xofluza, we, as the entire company of Shionogi, communicated what we have learned in the previous fiscal year. That is what we consider as our achievements during the first half period of the current fiscal year.

Japanese Business - Cymbalta®, ADHD family -

Cymbalta®

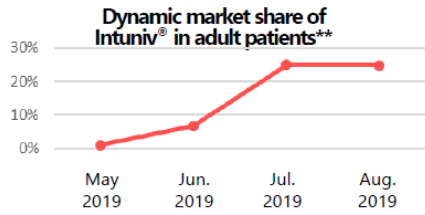
- **Improving awareness of the mechanism of Cymbalta® supported by guideline recommendations and clinical evidence**
- **Improving awareness of the direct analgesic effects of Cymbalta®, rather than through the mediation of its antidepressant effects**

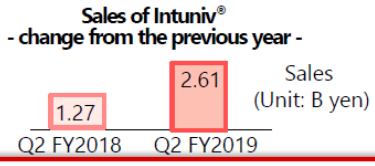
⇒ The proportion of patients prescribed Cymbalta® with chronic low back pain increased by about 10% from Feb 2019 to Sep. 2019*

(naïve patients：Feb. 12.8%→Sep. 23.8%, all patients：Feb. 14.3%→Sep. 23.6%)

ADHD family（Intuniv®, Vyvanse®）

- **Intuniv® : Share capture in adult market**
  - **Adult :**
    - > **Sales increased about 2 times after approval for the treatment of adult patients(Y on Y, from Jul. 2019 to Sep. 2019)**
  - **Pediatric :**
    - > Seeking to expand share in naïve patient market by making the mechanism and efficacy fully understood
- **Vyvanse®: Preparation for proper use after launch**
  - Promoting understanding of the efficacy and safety profile and establishing distribution management system





SHIONOGI

* Company data

Speaking of Cymbalta, to be frank, I have an impression that this product is still far from being strong, but we are stepping forward little by little with the development of this product especially in the field of pain. We concentrated our efforts to ensure that medical doctors know that Cymbalta was recommended in the Guidelines. I think that the degree of recognition remains low. Therefore, we think we need to continue our efforts.

Furthermore, I will explain about Intuniv of the ADHD family. We recorded significant growth in the treatment for adult patients. As to the pediatric patients market, Concerta, as a stimulant, maintains a top share in naïve pediatric patients by a narrow margin whereas in the non-stimulant domain we have had a top share for a long time. Therefore, we will exert further efforts to grow in this domain.

As to Vyvanse, we actually had long discussions with the Ministry of Health, Labour and Welfare about how this product should be distributed. After collecting opinions of general public through the public comment procedures, we have finally come to the current situation.

We worked to establish environment where ADHD patients in Japan can use the second stimulant and Concerta by free choice. For such purpose, the first step we made was to enable the patients to use distribution systems, etc. under relevant regulations as is the case for Concerta. Now finally, we are pleased to see the appropriate environment established for providing both stimulants and non-stimulants of ADHD.

研究開発_優先8プロジェクトの進捗

		パイプライン	上期の進捗
感染症	自社	**S-648414**（HIV）	米国Phase I試験開始
		S-004992（結核）	非臨床試験結果より、塩野義での研究開発は中止し開発権をC&Oに返還（後述）
疼痛／神経	自社	**S-600918** （難治性・原因不明慢性咳嗽）	Phase IIa試験完了（国内）、欧州呼吸器学会にて結果発表 Phase IIb試験開始（グローバル）
		S-637880 （神経障害性疼痛）	Phase I反復投与試験（日本）、Phase II試験開始（グローバル）に向けた準備
	共同	**S-812217 [一般名Zuranolone]** （うつ病・うつ状態）	Phase I試験 症例集積完了（日本） Phase II試験開始に向けた準備（日本）
その他	自社	**S-540956**（核酸アジュバント）	2020年度の臨床入りに向け、非臨床試験を遂行
		S-770108 （特発性肺線維症）	肺沈着試験開始に向けた準備（英国）
	共同	**ペプチド医薬品**	2020年度前臨床開発入りに向け、PDPS創薬技術を活用したプログラムの遂行

パイプラインの価値を速やかに見極め、
次世代成長ドライバーへの効率的な投資を実施

The notable points in the R&D activities are indicated in red and blue. I explained the blue parts earlier. I mean, the Phase I test of HIV, then the congress presentation on clinical study of S-600918 for the treatment of chronic cough, and the commencement of Phase IIb study. Then, about S-812217, I will explain this later. This is about the commencement of the Phase II study in Japan.

R&D_Efforts for Elimination of Tuberculosis

SONG for you!

Changes in environment in the 1st half FY2019

- FDA has approved a combination therapy using Pretomanid, Bedaquiline, and Linezolid as a treatment for drug-resistant tuberculosis
- Obtained new non-clinical data on S-004992

Have ceased research & development of S-004992 at Shionogi and returned development rights to C&O given differentiation and pricing challenges

License agreement and research collaboration with Hsiri regarding the research and development of drugs to treat mycobacterial* diseases

- In May 2018, executed a contract for collaborative research on a candidate on a mycobacterial disease drug with a new mechanism
- In October 2019, executed another contract to pursue collaborative research on another mycobacterial disease drug with another new mechanism

Continue to pursue elimination of tuberculosis by pursuing research on mycobacterial* disease drugs with novel mechanisms and the potential for a superior profile

SHIONOGI * Diseases caused by infection of mycobacteria (tuberculosis, non-tuberculous mycobacteria)

As to S-004992 which is described in the second paragraph from above, as shown on page 17, our further investigation revealed that Pretomanid had, in fact, the similar mechanisms to Delamanid of Otsuka Pharmaceutical. Our chemical compound also has the similar mechanisms.

In terms of effectiveness and safety, we believe our product is competitive enough, but considering that Pretomanid has already preceded to such an extent in the market, the question was whether it was right for us to jump into the full-scale competitions in the global markets including the United States and Europe with the similar product as the existing ones. Then, we came to a conclusion that it would be appropriate to conduct clinical tests and development in China because the drug had been created in China. Subsequently, we began to negotiate this matter with a Chinese company through C&O Pharmaceutical Technology by returning the development to C&O. Therefore, this means that Shionogi has ceased the development of this drug.

On the other hand, for the treatment of so-called mycobacterium infections including tuberculosis, we have changed directions of development considering that we should discover and develop novel mechanisms which are different from Delamanid or Pretomanid in the future. Traditionally, we had been working on non-tuberculous mycobacterial (NTM) diseases in cooperation with Hsiri Therapeutics, but we decided to develop chemical compounds for the treatment of general mycobacterium infections, tuberculosis and NTM .

Global Development

Progress in the Development of Cefiderocol

- **Development progress in the U.S.**
  - Submitted a New Drug Application to FDA* for the "treatment of complicated urinary tract infections, including pyelonephritis**."
    →On October 16, 2019, the Advisory Committee voted to recommend approval (14:2)

* Patients with limited or no alternative treatment options
** Based on the data from the complicated urinary tract infection study

- **Progress in clinical studies**
  - **Phase III clinical study in patients with infections caused by CR Gram-negative pathogens (CREDIBLE-CR) completed**
    - ✓ Cefiderocol showed similar clinical and microbiological outcomes as those of the best available therapy (primary endpoint).
    - ✓ The rate of all-cause mortality (secondary endpoint) was higher in the cefiderocol arm. However, patients enrolled in the study had various underlying critical illnesses. It was concluded by investigators, a data safety monitoring board, and an independent blinded adjudication committee that there was no association between the treatment with cefiderocol and the higher rate of all-cause mortality. The cause of the mortality difference is unknown and could be due to chance.
  - **Phase III clinical study in patients with nosocomial pneumonia (APEKS-NP) completed**
    - ✓ Efficacy: Cefiderocol met the primary endpoint of non-inferiority compared to high-dose meropenem in all-cause mortality at 14 days after the end of treatment. Cefiderocol also showed clinical and microbiological outcomes similar to high-dose meropenem.
    - ✓ Safety: The incidence of treatment-emergent adverse events was similar to high-dose meropenem.

* Patients with limited or no alternative treatment options
** Based on the data from the complicated urinary tract infection study

As for the details of page 18, Sawada knows better than anyone. So if you have any questions, please ask her later. We initially submitted this to FDA for UTI. But since this is originally for a multidrug-resistant gram-negative bacteria drug, rather than for UTI, we had always thought that we should pay attention to the results of carbapenem-resistant tests, in other words, bacteria-focused tests.

We dealt with UTI and RTI because FDA insisted that we should do on an indication basis. Now with data accumulated, it seems that we succeeded in having the full set at least examined by the ADCOM this time. For RTI, however, we barely had the top line included.

In CR study, for carbapenem resistance, after examining the very details, most ADCOM members are said to have judged that it would be OK to approve this drug. We are therefore planning to have final negotiations with FDA on labeling and then make preparations for the commercial launch.

Global Development

Expansion of Xofluza® (baloxavir marboxil)

- **Pursued new indications to expand share in the U.S. (collaboration with the Roche Group)**
  - **On October 16, 2019, Received approval for additional indication for "the treatment of acute, uncomplicated influenza in people 12 years of age and older who are at high risk of developing influenza-related complications"**
    - ✓ Xofluza® is the first medicine indicated specifically for the treatment of influenza in high-risk patients*.
  - **Positive results from the Global Pediatric Phase III study (MINISTONE-2)**
- **August 28, 2019, Received approval in Taiwan of indication for the treatment of acute influenza Types A and B in patients 12 years of age and older**
- **October 16, 2019, Submitted the Supplemental New Drug Application of XOFLUZA® in Japan for Post-Exposure Prophylaxis of Influenza Virus Infection**

*High-risk patients: Patients at high risk for influenza-related complications

Now about Xofluza, everything is as written here. So I would like to give more explanation in response to your questions later on in the Q&A session. At least in the United States, CDC also recommends the use of Xofluza as equivalent as other drugs. In this sense, having obtained approval for indication for the high-risk, the Roche side is very excited about the deal. Therefore we continue to have a good prospect for the current fiscal year.

As for the global pediatric study, as Sawada mentioned yesterday, it is quite difficult to bring the results to Japan because of the difference in dosage. However, at least on MINISTONE-2 for Europe and the US, we have obtained highly favorable results about Xofluza. We will continue to make efforts to build evidence from both aspects of efficacy and safety, taking into consideration the situations in Japan, so that it will be used propely.

In addition, on October 16 we announced only the top line data on the post-exposure prophylaxis, which we consider as our advantage. We have already commenced the transmission study, which will be explained later. Honestly, I do not think there are no other firms that do such a variety of things for anti-influenza and anti-virus drugs.

Through these studies, as an expert, we will accumulate data on how the anti-influenza drugs, including currently prevailing Neuraminidase inhibitors, should be properly used.

About Xofluza®

Statement/Guidelines for the use of Xofluza® in Japan

Statement of the Japanese Association for Infectious Diseases (JAID) regarding the use of Xofluza® (Announced on October, 2019)

1. ≥12 to 19 years of age and adults: No decision on a recommendation for Xofluza® use has been made at present due to limited clinical data.
2. Children <12 years of age: Careful consideration of the use of Xofluza®, taking into account the high rates of emergence of variant viruses with reduced susceptibility to Xofluza® in children observed in clinical studies to date.
3. Immunocompromised and severe influenza patients: No recommendation on active use of Xofluza® as monotherapy.*

Upon careful analysis of the available clinical data for Xofluza®, JAID has decided not to provide a definitive recommendation for Xofluza® use at present, but has confirmed multiple seasons of data are normally required before a recommendation for Xofluza® can be issued.

Guidelines of the Japanese Pediatric Society (JPS) regarding the use of Xofluza® for the 2019-2020 season (Announced on October, 2019)

1. The committee does not actively recommend the use of Xofluza® in pediatric patients <12 years of age, as the reports of the clinical experience of Xofluza® in this population are currently limited and the emergence of resistant viruses has been observed.
2. While the use of Xofluza® is not to be restricted for the time being, the emergence and potential transmission of resistant viruses needs to be carefully monitored.
3. For the treatment of immunocompromised patients, Xofluza® should not be used as monotherapy as the shedding of resistant viruses may be prolonged. In the case of severe influenza or influenza complicated with pneumonia, combination therapy with Xofluza® and other anti-flu drug(s) could be considered, although the committee views that the current level of clinical evidence is insufficient and are in the process of collecting and assessing such data.*

*Please note the potential usage of XOFLUZA in this patient population(s) is not approved by the PMDA

Page 20 is as written here. I heard there were many discussions. We think these are the most appropriate settlement for now, though limited in Japan. To be honest, sufficient data have not been accumulated yet as we actually experienced only one winter. So it naturally seems too early to say something definite, whether positive or negative. We will continue to work hard to accumulate data and provide you with them in a timely manner.

About Xofluza®

About PA/I38X-substituted viruses

Data from clinical studies announced to date

- **Incidence of PA/I38X-substituted viruses**
  - The incidence was high in younger pediatric patients
  - The incidence was higher in adults, adolescent and pediatric patients infected with A/H3N2
- **Association between the incidence of PA/I38X-substituted viruses and clinical symptoms**
  - **Adult and adolescent patients** See appendices for details
    There was no clear association between the incidence of PA/I38X-substituted viruses and the median time to alleviation or improvement. These data suggest clinical benefit of Xofluza in these populations irrespective of the substitution.
  - **Pediatric patients**
    It is important to continue to obtain additional data about PA/I38X-substituted viruses because the available analysis data are limited as of this moment especially in pediatric patients.

Shionogi will continue to proactively monitor and characterize PA/I38X-substituted viruses, and will communicate findings to medical institutions and academic conferences

For the issue of I38, since the data is mostly made open, we show here only the top line information. As for the incidence of substitution, although we specified the group aged 12 or younger in Japan because no relevant paper has been published yet, our data actually show the incidence is particularly high in younger pediatric patients.

This tendency is strong for patients who have not yet established immunity or who have no history of influenza, which may be the case for any virus. Therefore the incidence of H3 among the strain A-type is particularly high in younger pediatric patients. The incidence of H1 and B is not high. Especially for B, almost no incidence has been reported. However, all these are based on as far as we know so far, and we must gather more data on them.

As you know, the H1 strain that prevailed in the season from 2008 to 2009 came from Norway, which I learned from Sawada. Norway is a country where Tamiflu had never been used, but all the strains there were Tamiflu-resistant. I wonder why this happened. Anyway the Tamiflu-resistant strains prevailed through the winter. At that time, there were no H3 nor B. We had only the Tamiflu-resistant strains during that year, which caused a shock to us. But the next year, no such strains appeared at all.

How influenza viruses appear and how they disappear are not exactly known yet. So it is necessary to take some time, like three years or five years, to see how they change or not change with the use of the drug. Otherwise we cannot say anything definite. Based on this standpoint, we will continue to proactively gather data.

Revision of Forecasts (Announced on Oct 30, 2019)

(Unit: B yen)

	FY2019 Forecasts			FY2018	Y on Y	
	Original (May 9)	Revised (Oct 30)	Change (B yen)	Results	Change (%)	Change (B yen)
Sales	365.5	367.0	1.5	363.7	0.9	3.3
Operating income	147.0	150.0	3.0	138.5	8.3	11.5
Ordinary income	170.5	171.5	1.0	166.6	3.0	4.9
Profit attributable to owners of parent	133.0	135.0	2.0	132.8	1.7	2.2

Exchange rate (average)	FY2019 forecasts (May 9)	FY2019 forecasts (Revised on Oct 30)	1H FY2019 Results
USD ($) – JPY (¥)	110.0	107.0	108.61
GBP (£) – JPY (¥)	145.0	133.0	136.65
EUR (€) – JPY(¥)	130.0	120.0	121.41

This shows the revised forecasts based on the results of the first half. The revision is for very small amounts. However, as we explained earlier today, we have kept the stance of settling at a little better than forecasts since 2011 and therefore we decided that we would be able to keep this stance with these revisions.

Sales will be 367.0 billion, an increase of 1.5 billion from the original forecast. Forecast for operating income is 150.0 billion, a 3.0 billion upward revision, marking the first time for us to reach 150 billion. Ordinary income will be 171.5 billion, a 1.0 billion upward revision. Profit attributable to owners of parent will be 135.0 billion, 2.0 billion upward revision. As shown on the very right, our determination is to renew the highest profit, and we are making company-wide efforts to this end.

Revision of Statement of Income

(Unit: B yen)

	FY2019 Forecasts			FY2019 2H Forecasts			FY2018	Y on Y	
	Original (May 9)	Revised (Oct 30)	Change	Original (May 9)	Revised (Oct 30)	Change	Results	Change (%)	Change (B yen)
Sales	365.5	**367.0**	**1.5**	206.5	**206.1**	**(0.4)**	363.7	**0.9**	**3.2**
	14.6	15.3		13.6	13.6		15.1		
Cost of sales	53.5	**56.0**	**2.5**	28.0	**28.1**	**0.1**	54.9	**2.0**	**1.1**
Gross profit	312.0	**311.0**	**(1.0)**	178.5	**178.0**	**(0.5)**	308.8	**0.7**	**2.2**
	45.1	43.9		40.4	41.8		46.8		
SG&A expenses	165.0	**161.0**	**(4.0)**	83.5	**86.2**	**2.7**	170.3	**(5.5)**	**(9.3)**
Selling & administrative expenses	31.6 115.5	30.5 **112.0**	**(3.5)**	28.6 59.1	29.2 **60.2**	**1.1**	28.0 102.0	**9.8**	**10.0**
	13.5	13.4		11.8	12.6		18.8		
R&D expenses	49.5	**49.0**	**(0.5)**	24.4	**26.0**	**1.6**	68.3	**(28.3)**	**(19.3)**
Ordinary R&D expenses*	49.5	**49.0**	**(0.5)**	24.4	**26.0**	**1.6**	51.4	**(4.7)**	**(2.4)**
Strategic investment	-	**-**	**-**	-	**-**	**-**	16.9	**-**	**(16.9)**
	40.2	40.9		46.0	44.6		38.1		
Operating income	147.0	**150.0**	**3.0**	95.0	**91.8**	**(3.2)**	138.5	**8.3**	**11.5**
Non-operating income & expenses	23.5	**21.5**	**(2.0)**	12.5	**14.4**	**1.9**	28.0	**(23.3)**	**(6.5)**
	46.6	46.7		52.1	51.5		45.8		
Ordinary income	170.5	**171.5**	**1.0**	107.5	**106.2**	**(1.3)**	166.6	**3.0**	**4.9**
Profit attributable to owners of parent	133.0	**135.0**	**2.0**	84.0	**83.4**	**(0.6)**	132.8	**1.7**	**2.2**

SHIONOGI

* Ordinary R&D expenses: Total R&D expenses excluding strategic investment

On this statement, if you look at cost, in particular the revised amount, you can see an increase in sales by 1.5 billion but also a rise in cost by 2.5 billion. We thought that the amount in excess for the first half would not be easily compensated but would continue to remain in excess in the full-year result. But we expect that the figure for the second half will settle as forecast.

Gross profit is a little less than original forecast. With control on selling & administrative expenses, especially selling expenses, operating income is expected to be a 3.0 billion increase. Foreign exchange rates are also expected to decline. There will be a general election, so there is a slight possibility that the UK may quit Brexit, which may be associated with appreciation of the pound. However, for now we expect the current trends will continue and therefore forecast for profit increase remains to be 1.0 billion.

Revision of Sales by Segment

(Unit: B yen)

	FY2019 Forecasts			FY2019 2H Forecasts			FY2018	Y on Y	
	Original (May 9)	Revised (Oct 30)	Change	Original (May 9)	Revised (Oct 30)	Change	Results	Change (%)	Change (B yen)
Prescription drugs	144.1	144.1	-	90.4	**91.6**	**1.3**	128.7	12.0	15.4
Overseas subsidiaries/export	31.4	**31.3**	**(0.0)**	15.3	**13.8**	**(1.5)**	29.4	**6.5**	**1.9**
Shionogi Inc.	9.9	**10.2**	**0.3**	3.6	**3.4**	**(0.2)**	11.8	**(13.8)**	**(1.6)**
Mulpleta®	1.0	1.0	-	0.75	**0.66**	**(0.1)**	0.08	N/A*	0.9
C&O	14.6	**14.5**	**(0.0)**	7.8	**7.4**	**(0.4)**	11.5	**26.7**	**3.1**
Contracting manufacturing	14.3	**15.4**	**1.0**	5.3	**5.3**	**0.1**	14.8	**4.1**	**0.6**
OTC and quasi-drug	9.7	9.7	-	5.1	**5.0**	**(0.1)**	8.1	19.7	1.6
Royalty income	163.6	**164.2**	**0.6**	89.3	**89.3**	**(0.0)**	180.3	**(8.9)**	**(16.0)**
HIV franchise	126.5	**126.3**	**(0.2)**	65.2	65.2	-	124.4	**1.5**	**1.9**
Crestor®	22.0	**21.8**	**(0.2)**	11.0	**10.8**	**(0.3)**	22.0	**(0.7)**	**(0.1)**
Others	15.1	**16.1**	**1.0**	13.0	**13.3**	**0.2**	33.9	**(52.5)**	**(17.8)**
Others	2.4	**2.2**	**(0.1)**	1.2	**1.1**	**(0.1)**	2.5	**(8.7)**	**(0.2)**
Total	**365.5**	**367.0**	**1.5**	**206.5**	**206.1**	**(0.4)**	**363.7**	**0.9**	**3.3**

SHIONOGI

* N/A: Not applicable because Mulpleta® was sold only for 7 months in FY2018.

On page 25, major revisions are 1.0 billion for contracting manufacturing and an increase of around 1.0 billion for royalty income, etc. as far as we have confirmed. These two are the major factors for the sales increase.

Revision of Sales Forecasts for Prescription Drugs in Japan

(Unit: B yen)

	FY2019 Forecasts			FY2019 2H Forecasts			FY2018	Y on Y	
	Original (May 9)	Revised (Oct 30)	Change	Original (May 9)	Revised (Oct 30)	Change	Results	Change (%)	Change (B yen)
Cymbalta®	29.3	29.3	-	16.2	**16.4**	**0.2**	24.1	21.6	5.2
Intuniv®	13.6	13.6	-	9.0	**9.2**	**0.2**	5.3	157.2	8.3
Vyvanse®	0.38	**0.05**	**△0.3**	0.33	**0.05**	**△0.3**	-*	-*	**0.05**
Xofluza®	28.0	28.0	-	27.7	**28.0**	**0.3**	26.3	6.5	1.7
Rapiacta®	2.6	2.6	-	2.6	**2.6**	**0.0**	2.0	27.7	0.6
Brightpoc® Flu	1.8	**2.2**	**0.3**	1.6	**1.8**	**0.2**	1.2	84.0	1.0
Total of strategic products	75.7	**75.7**	**(0.0)**	57.5	**58.1**	**0.6**	58.9	**28.6**	**16.8**
OxyContin® franchise	6.7	**6.4**	**(0.3)**	3.1	**3.2**	**0.1**	7.3	**(12.1)**	**(0.9)**
Symproic®	2.3	2.3	-	1.2	**1.2**	**0**	1.6	43.8	0.7
Actair®	0.27	**0.26**	**(0.0)**	0.14	0.14	-	0.19	**35.5**	**0.1**
Mulpleta®	0.33	**0.23**	**(0.1)**	0.16	0.16	-	0.15	**50.2**	**0.1**
Pirespa®	6.9	**7.0**	**0.1**	3.4	**3.5**	**0.1**	5.7	**23.0**	**1.3**
Total of new products	92.2	**91.9**	**(0.3)**	65.5	**66.3**	**0.8**	73.8	**24.5**	**18.1**
Crestor®	10.0	**9.5**	**(0.5)**	4.8	**4.9**	**0.1**	9.9	**(4.0)**	**(0.4)**
Irbetan® franchise	4.9	**4.6**	**(0.3)**	2.3	**2.4**	**0.1**	5.4	**(13.5)**	**(0.7)**
Others	36.9	**38.1**	**1.1**	17.7	**18.0**	**0.3**	39.6	**(4.0)**	**(1.6)**
Total	**144.1**	**144.1**	**-**	**90.4**	**91.6**	**1.3**	**128.7**	**12.0**	**15.4**

SHIONOGI

* To be launched in 2H FY2019

26

On page 26, sales in Japan, most of the items in “Others” are antibiotics, in particular Flumarin and the like, which are still taking time to settle, with several requests outstanding. Here, I would like to ask for your understanding and support. A beta-lactam plant is not allowed to produce anything other than beta-lactam under CGMP. Therefore, if requested to produce something else because there is some room at the plant, we cannot do so. If requested to produce more Flumarin, on the other hand, we cannot do that either, because our plants are not designed for such a setup.

Especially for antibiotics, the price of a cefazolin generic is 97 yen for 500 ml, which is cheaper than Evian. This discourages manufacturers to produce them. So I think without any support from all of you for suppliers of some specific antibiotics, , including the specific restrictions on their plants, the entire industry in Japan will face serious difficulties. We will do our best not to cause a shortage in supply. But please understand that we are facing severe conditions, including costs.

Toward Growth Beyond 2020

Progress in achievement of KPIs in the current mid-term business plan (SGS2020)

➢ **Most KPIs have been achieved**

		FY2020 Target	FY2019 Target	FY2018 Results
Growth	Sales of new products*	200.0 billion yen	100.6 billion yen	83.1 billion yen
	Ordinary income	150.0 billion yen	170.5 billion yen	**166.6 billion yen**
Efficacy	ROIC**	13.5% or more	15.0% or more	**16.5%**
	CCC***	Less than 7.0 months	Less than 7.6 months	8.9 months
	Original pipeline ratio	50% or more	50% or more	**69%**
Shareholder Return	ROE	15.0% or more	18.0% or more	**20.9%**
	DOE	4.0% or more	4.3% or more	**4.6%**

Set new targets for further growth and formulate a new mid-term business plan, one year earlier than scheduled, to prepare for the dolutegravir cliff. (release scheduled for the end of April 2020)

Focus on solving pending issues to transit to a new med-term business plan in the second half of FY2019.

SHIONOGI

* New products: See the Appendix
New Products were defined in Updates to SGS2020 issued on October 31, 2016

** Return on invested capital
*** Cash conversion cycle

Toward the growth beyond 2020, as written here and as you noticed, we have achieved most of the targets except for sales of new products. It is not that we do not pursue the target for sales of new products. However, as we move on to the next stage, we are required to determine what to do in preparation for the weakening of HIV franchise, such as dolutegravir, expected in 2028 and subsequent years.

In this sense, we are currently preparing to release our new medium-term business plan at the time of financial settlement next year.

Efforts in 2H FY2019

SONG for you!

1. Sales

Increasing sales and profits, demonstrating own earning power by expanding sales of new products and further increasing management efficiency

- **Evolution of sales activities in Japan**

2. Investment

- Progression of pipeline products as growth drivers beyond 2020
- Establish a global presence in priority regions

- **Progress of R&D for high-priority projects and new candidates**
- **Establish specialized sales base in the U.S. and EU market initiating with Cefiderocol**
- **Continued excellent progress of HIV Franchise**

3. Business innovation

- **Establishment of "Stream-I", M3 and Shionogi Joint Venture**
- **Improve operating processes by introducing international accounting standards (IFRS) and increasing transparency**
- **Promote activities related to ESG* and diversity & inclusion**
- **Advance business of group companies including Shionogi Pharma**

Proceed consistently to sustainable growth after FY2020

* ESG (Environment, Society, Governance) : Non-financial information to evaluate corporate sustainability and risk

Focusing on the second half, a rather short period, it is very important in Japan to properly manage the influenza family, including Xofluza and Rapiacta. On the other hand, with the launch of Vivanse scheduled, we will also focus on the ADHD franchise, and take full advantage of the Cymbalta distributorship, which we will be able to exercise till the end of 2021. We will thus focus efforts on these.

For the second item, investments, look at the second point. As evident from the fact that Achaogen went bankrupt six months after it released Plazomicin, it is now very difficult in the United States to make profits from sales of a multidrug-resistsant antibiotics in a short period of time. Since we are rather more robust than startup ventures, we should make investments to grow such drugs from a medium to long-term perspective.

Fortunately, European countries, though not all, are showing positive attitude in talks with us, including stock pile. Some discussions have reached almost the final stage, and this second half, our focus will be on how we should grow this Cefiderocol in the US and Europe.

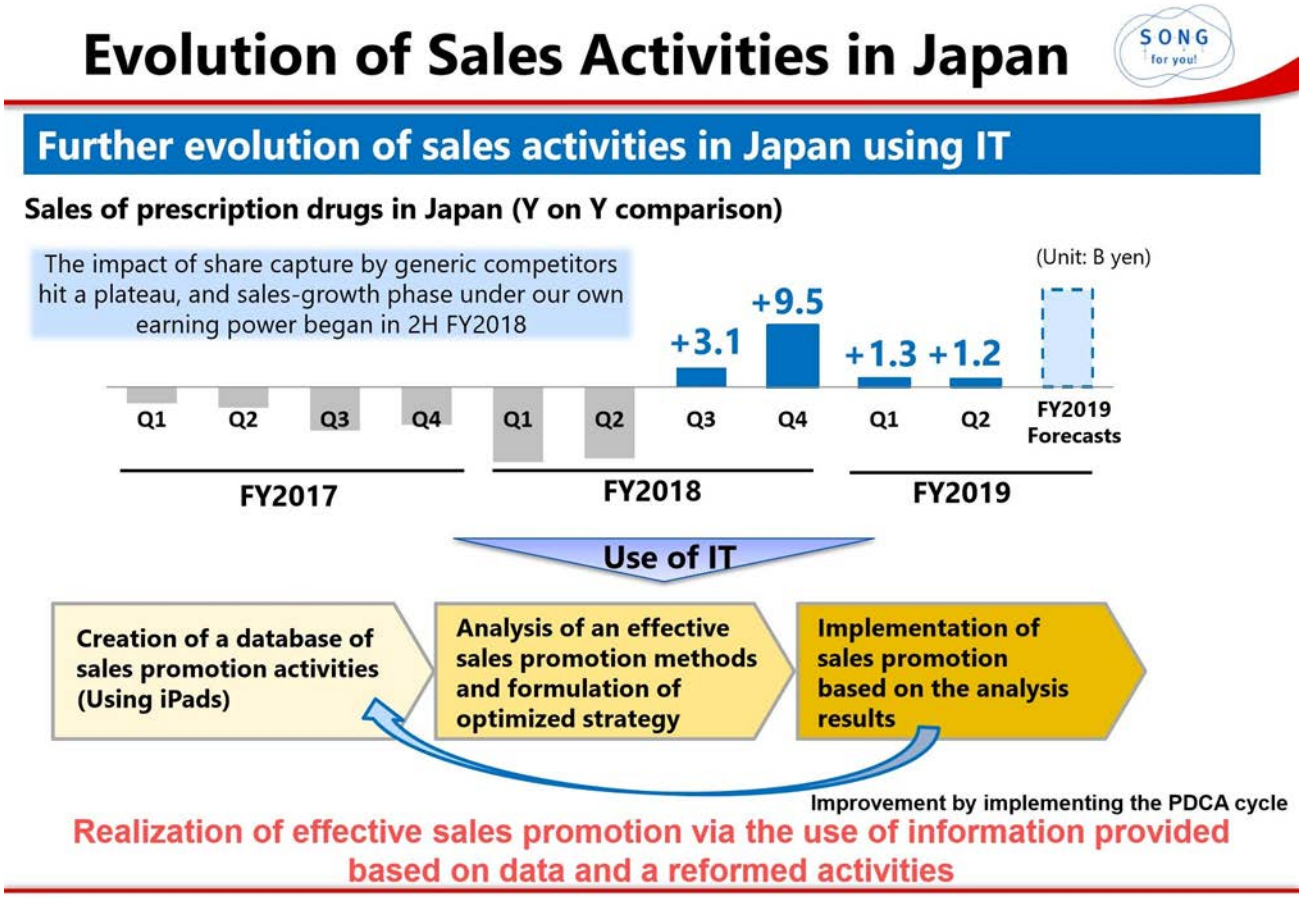
As I said earlier, for S-648414, a new chemical compound, speed is most important. We should increase the speed as much as possible in examining its antiviral effects, and the possibility of combined use with our dolutegravir. We will start with oral regimen and in the medium to long run, will accelerate the work on the possibility to be used for injection.

For the third item, "Stream-I," we do not expect to see the results within this year or the next year. But regarding the issue of how we should offer pharmaceuticals after 2020, when we will have many newcomers entering the health care field from outside of the medical industry, we must think thoroughly about what profit model or what business model we should make up based on IT, and draft several patterns.

As I will explain later, acquisition of UMN demonstrates our view of the vaccine business, the field with no entries of generics, as a firm dealing with vaccines, especially infections. We will start with considering an information delivery model including Stream-I, as to how we will gather information from the public and how we will deliver it, not only through a face-to-face manner by so-called MRs.

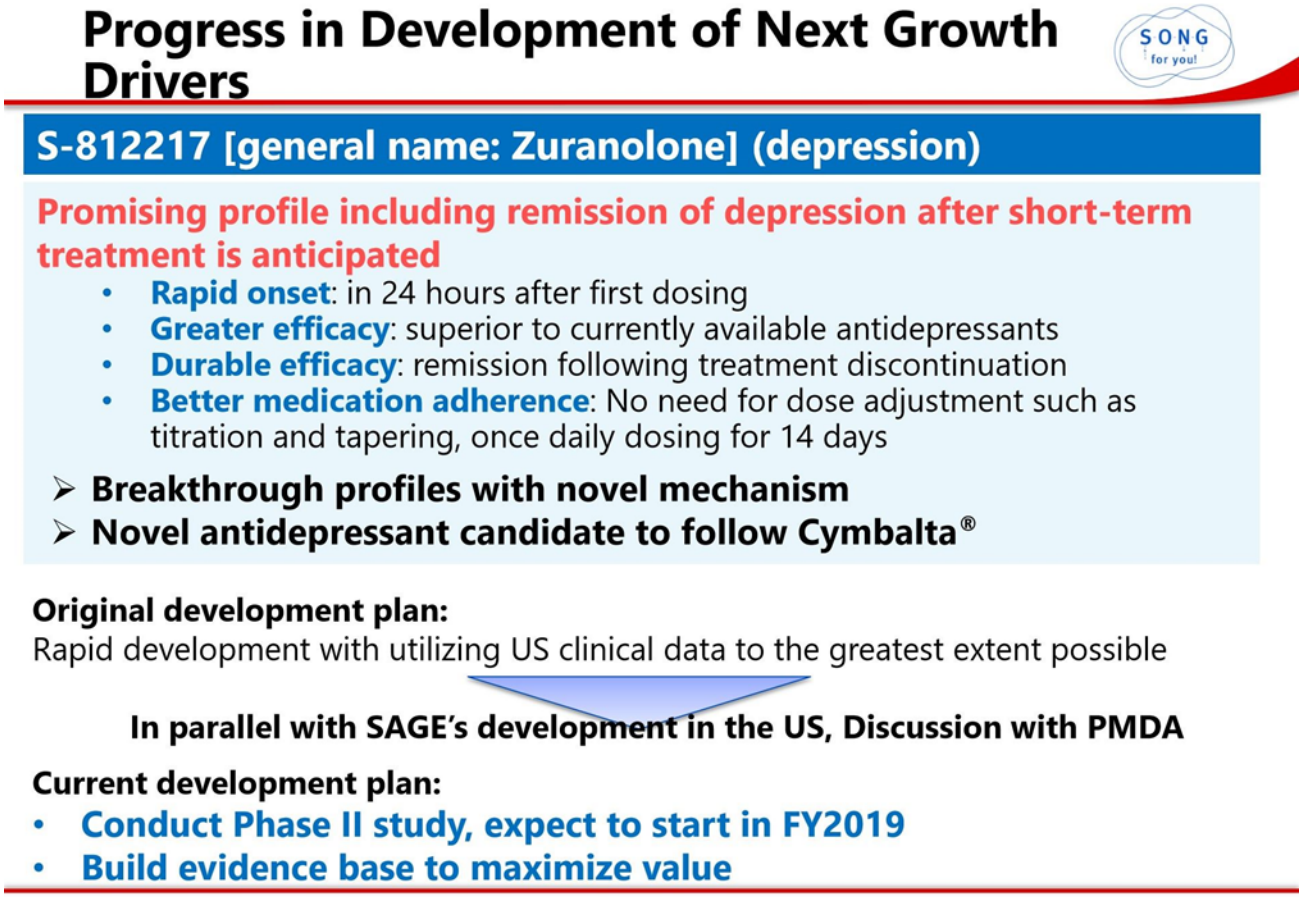
Since this is one of the major projects of the business models for after 2020 I explained earlier, we started this from this year ahead of the plan.

Moreover, in response to many feedbacks from you, we will improve our integrated report, including the ESG part, by listing up what we should do. These initiatives are not directly connected to sales. But we would like to demonstrate that Shionogi is capable of adequately handling all of these matters.



As for sales in Japan, we have marked, though slightly, an year-on-year increase for the fourth consecutive quarter. The remarkable increase for the fourth quarter last year was largely due to Xoflusa. But without that, a slight increase has been achieved, indicating that we have managed to get out of the most difficult time after some mainstem products, such as Crestor and Irbetan, became generics.

We now have to think about how we can continue this increase. At the same time, as I mentioned earlier, we are reducing the number of MRs along with the retirement of baby boomers. Now the number of those who are active has come to slightly less than 1,000. We must also think about how we should further promote this initiative.



For 217, I guess some of you have questions, which I will answer later along with Sawada. For the initial plan, shown a little below the center, Sage has launched phase III in the US and Europe, and advanced talks with FDA. We predicted their intention to a certain degree through communications with Sage at the time of our licensing. But we still think their compound is a little too innovative. FDA have not reached a 100% agreement with Sage on such matters as how safety can be secured and how long-term testing should be conducted in a medium to long run.

About two-thirds of patients have obtained remission in two weeks. This should be an unprecedentedly good news for patients. But what should they do after remission? They can stop taking it forever? Or they can take existing drugs, such as SSRI or SNRI? Or how many times a year can they take it? If asked, we must be able to answer all of these questions.

However, resources are limited, including for Sage, and therefore the truth is that it is difficult to agree with FDA on which tests should be done this time and which tests should be postponed to a later time.

Knowing that it is such an innovative drug, we would strongly like to release it to the public. At the same time, we must consider how we label it. As you know, deciding how to label a drug is equal to deciding what price strategy to take. Considering these, we have decided to change our strategy from completing Phases II and III as quickly as possible using the Phase III results in the US to carefully examining the Phase II results with Japanese patients, including dose findings, as we think it prudent in view of the fact that it deals with central nervous system disorders.

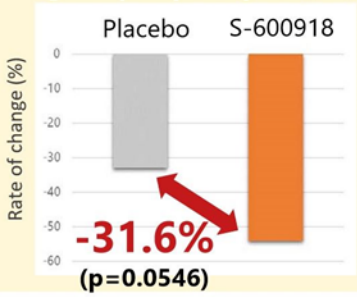
Progress in Development of Our Next Growth Drivers

S-600918 (Refractory/unexpected chronic cough)

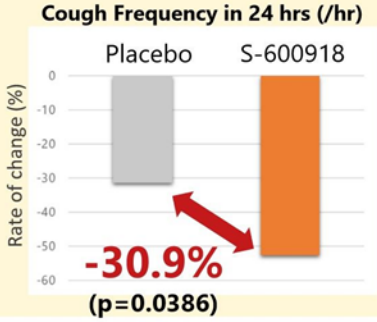
- **Results of Phase IIa study in Japan**[1]
  - Double-blind, cross-over, placebo and S-600918 (150 mg)
  - QD for 2 weeks, N=31

Efficacy

Cough Frequency in Daytime (/hr)



Cough Frequency in 24 hrs (/hr)



Safety

- S-600918 was well-tolerated and showed favorable safety

The incidence of taste disturbance, an adverse event seen at high frequency with similar drugs

Placebo	S-600918
0% (0/31)	6.5% (2/31)

- **Design of global Phase IIb study**
  - Double-blind, placebo-controlled, parallel group
  - S-600918 (50, 150, 300 mg) or Placebo, QD for 4 weeks, N=93/arm

⇒To determine the optimal dose of S-600918

SHIONOGI

1 Akio Niimi et al., ERS2019

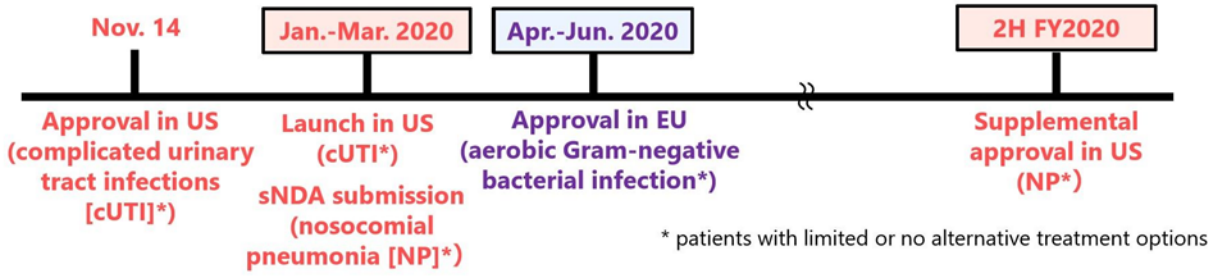
Next is 918. For chronic cough, we believe ours is better than the items of competitors, including at least in safety as provided on the right. So we must go through the Phase IIb at a super-high speed. At present, we aim to obtain this coughing as the indication. Meanwhile, however, other firms are aiming at three or four new indications with this same mechanism.

We believe that it is a P2X3 compound of very high quality and thus we are now working to determine the second and third indications as quite a big project. We hope to start working on the second and third indications as soon as possible.

Establish A Global Presence

Strengthen own sales structure in US/EU by starting with Cefiderocol

Cefiderocol Development Schedule (Planned)



* patients with limited or no alternative treatment options

Future Major Products in US/EU, and Sales Structure

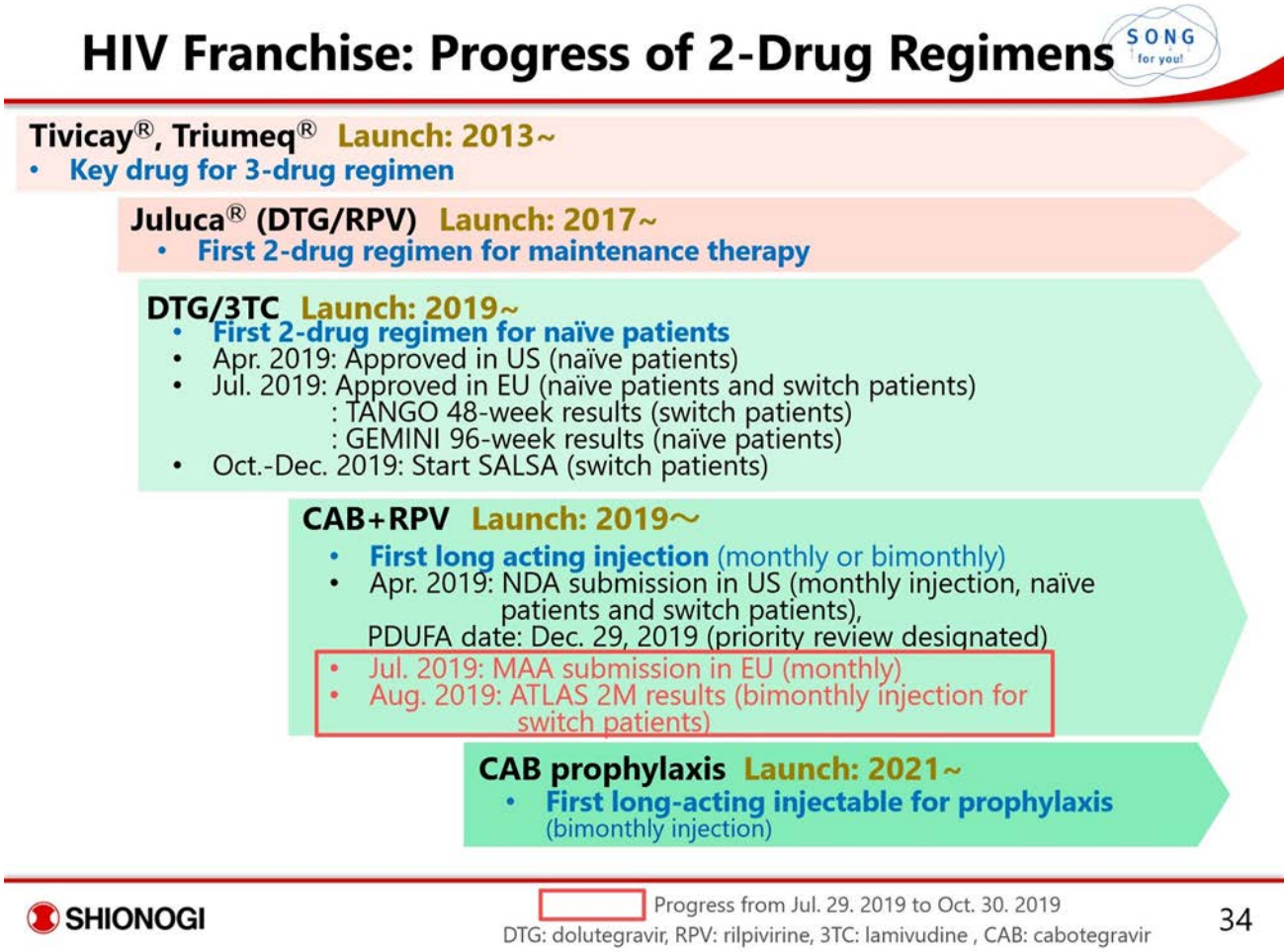
	US	EU
Cefiderocol	Own sales (Planned)	Own sales (Planned)
Lustrombopag (Product name in the US: Mulpleta®)	Own sales	Own sales (Planned)
Naldemedine (Product name in the US: Symproic®, in the EU: Rizmoic®)	Partnering with BDSI* commercialization	Partnering with Sandoz, Molteni, and Ferrer for commercialization

Strengthen own sales structure in HP/specialty market

Page 33 shows the schedule for the launch of cefiderocol. We are planning the launch in the US in the first calendar quarter next year and the launch in Europe in the second calendar quarter next year. At the same time, as we experienced difficulty with Osphena and others in selling a single item for primary care, this time we are considering selling two or three items together mainly for the hospital field and also with a total of less than 100 sales staff members to manage the business in the US.

To this end, if we could add one or two more items to lustrombopag and cefiderocol, we can make the business foundation highly robust. So we are looking for appropriate items.

。



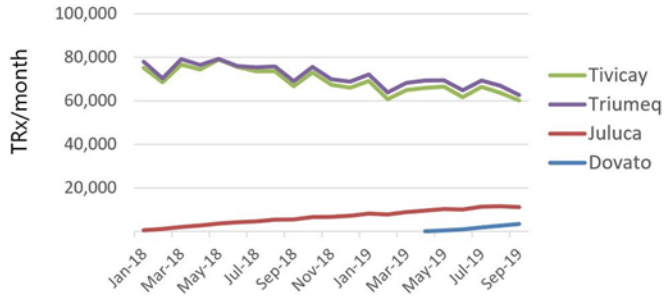
For HIV, I explained earlier. Regarding the red-framed part, for CAB+RPV, we have applied as injection drug in Europe and this time we obtained favorable results with once every two months.

Due to the relationship with rilpivirine, however, an interval longer than once every two months seems difficult for now. I heard that HIV virus check by patients is conducted once every three months as routine. So it would be clinically good if the injection drug for once every three months is made. We think CAB alone is possible with once every three months. So GSK, ViiV, and we have been striving to find appropriate drugs to combine with it, though so far we have proven the possibility of once every two months at the maximum.

Progress of HIV Franchise

Changes in total prescriptions of DTG franchise

Changes in TRx for DTG franchise in the US*



- Growth of our two Drug Regimens is encouraging in that it more than offsets the decline in our 3 Drug Regimen Triumeq® as we transition to the new portfolio.
- Dovato® uptake will take time as access and physician acceptance increases supported by our data and updated treatment guidelines.

Expectations for the growth of HIV franchise by CAB+RPV

- Once approved, it will become the first long-acting regimen for HIV infection.
- According to patient satisfaction assessment in the Phase III studies, 97% (266/273) of patients in ATLAS and 99% (257/259) of patients in FLAIR answered that they preferred long-acting injections of CAB+RPV over their previous oral regimen.**
- Provide patients with a new value proposition that is different from oral medications
  - People who have concerns with disclosure
  - People who struggle to swallow the relatively large pills
  - People who struggle with compliance
  - People who suffer from the psychological burden of being reminded daily of their HIV status

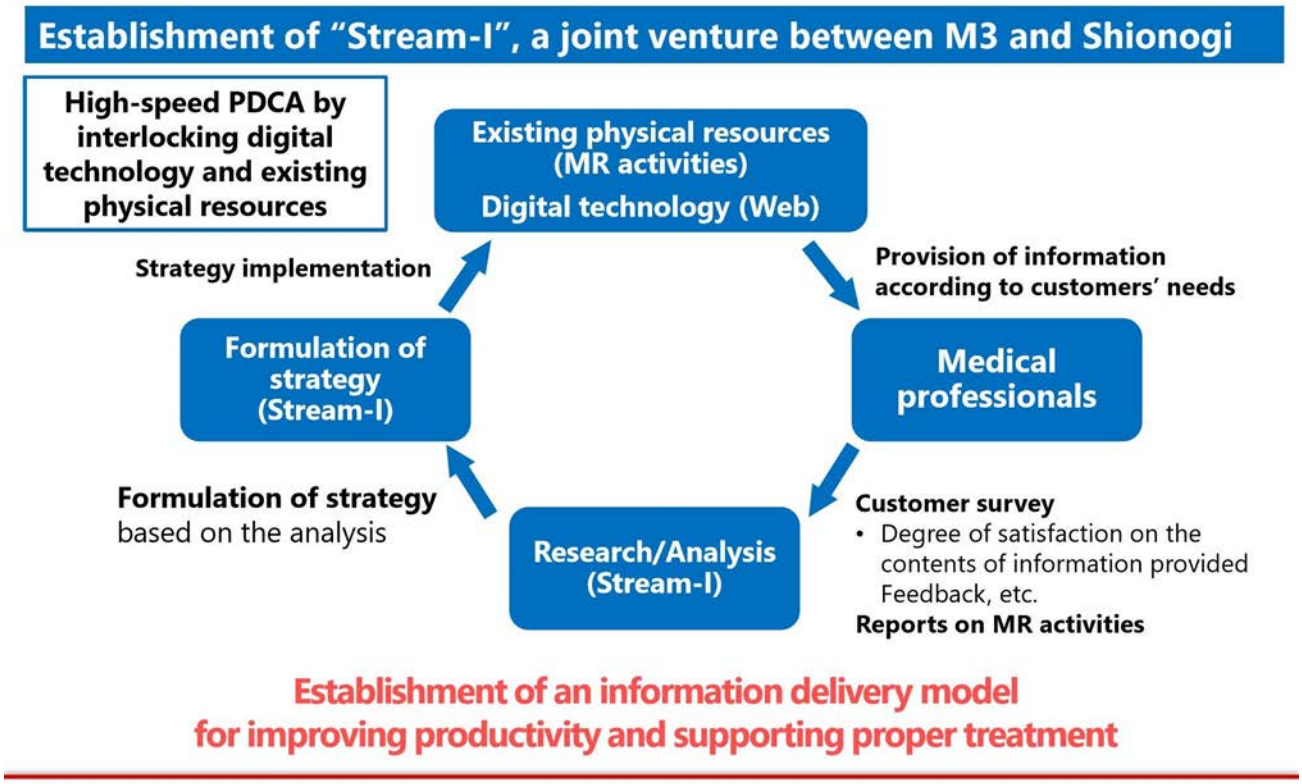
SHIONOGI **April 30, 2019 ViiV Healthcare analyst call https://www.gsk.com/media/5411/fuelling-our-future-growth-slides.pdf 35
DTG: dolutegravir、3TC: lamivudine、CAB: cabotegravir、RPV: rilpivirine

As for the recent progress in oral drugs, the decline in dolutegravir franchise, especially Triumeq and Tivicay alone, seems to have settled. With Dovato and Juluca rising, ViiV has regained the total share up to around 27.5%. The task from now on is to increase these blue and red portions. By growing the blue portion, in particular, we hope to expand the share of ViiV in the entire HIV market.

Regarding to what kind of applicants the injections are applicable, various questionnaire surveys we conducted show that around 15 to 20% of patients, in the United States, are very much interested in injections. At the moment, we would like to target the 15 to 20% of patients as the market, and have them take this CAB+PRV once a month, and later once every two months.

A good news is, as I said several times, that 99% of the patients who have once experienced this injection regimen say that they do not want to return to oral regimen. This indicates how easier the life is with injection once a month instead of oral taking every day. We will therefore accumulate more data related to their daily life, with the aim of promoting the effects.

Business Innovation



Next is about Stream-I. For this fiscal year, we are considering how it should be operated based mainly on the I38, which I explained earlier, and the safety data accumulated over the past year. Ultimately, if a pandemic occurs, should the infected patients be instructed to go to hospital? It would allow them to further spread the disease. Our goal is to prevent such situation by communicating, for example, what kind of information is available on the Internet and what kind of patients are present at what locations, and determining what kind of information should be provided to prevent pandemic.

Establishment of "Stream-I"

Stream-I's contribution to the treatment of influenza

Prevention	• Continuous increase in infection with influenza virus at homes and schools
Diagnosis	• Difficulty in diagnosis in early stages of infection
Treatment	• Existence of patients in serious condition

Potential of Stream-I

- Prompt provision of information on the results of surveillance, promotion of precautionary measures, and proposal of new options
- Development of a new simplified diagnosis method and examination of a new medical treatment model
- Prevention of serious conditions by offering a tool to promote communication between patients and medical staff

Offer a new, optimal option in the treatment of influenza, leading to a disease solution

The influenza diagnosis, which we have been promoting by investing in IRIS, is non-invasive. The goal is to enable diagnosis at home, while making maximum use of our influenza drugs. Eventually we must pay more attention to prevention.

Commencement of Tender Offer for Certificates of Shares, etc. in UMN Pharma Inc.

Purpose and Outline of the Tender Offer (announced on Oct 30, 2019)

【Purpose】

- **Entering the vaccine business by acquiring 100% ownership of UMN Pharma**

【Outline】

- Target for the tender offer : common shares and issued share warrants of UMN Pharma
- Capital relationship : holding 5,500,000 target company shares which represent 31.08% of the total issued through capital and business alliance entered in Oct 2017, as of today
- Number of shares and warrants to be purchased : upper limit; none, lower limit; 6,322,000
- Tender offer period : from Oct 31, 2019 to Dec 12, 2019 (30 business days)
- Tender offer price : 540 yen per share (a premium of 70% on 318 yen, which was the simple average closing price over the six-month period preceding October 29, 2019)
- Total amount of the tender offer* : approx. 6.6 B yen
- Plan to acquire 100% ownership through the prescribed procedures after completion of the tender offer
- The board of directors of UMN Pharm express its support for the tender offer

* Estimated when the company acquires total common shares and issued share warrants of UMN Pharma.

On October 30, 2019, we announced our plans to purchase shares in UMN Pharma Inc. from the open market. This is the content of our plans which I would now like to discuss.

Achievements of the Capital and Business Alliance with UMN Pharma Inc.

Entered into the Capital and Business Alliance Agreement on Oct 31, 2017

- Implementation of planned 1st Phase activities and funding to achieve those goals
- Decide the transition to the 2nd Phase conditional upon an establishment of their own core technologies

1st Phase

Core technology improvement

Establish core technologies for drug discovery, including the discovery of vaccines for the prevention of infectious diseases in humans

Basic research toward 2nd Phase

Conduct basic research on development candidates

Re-establishment of Akita plant

Restructuring of GMP facility

Milestone payment	third-party allotment	Convertible bond
0.3 B yen*	0.178 B yen	1.46 B yen

2nd Phase

Driving development pipelines

Develop promising pipeline(s) selected in the 1st Phase

Achievements in the 1st Phase

- Almost established a technology platform utilizing genetic recombination technology for manufacturing proteins to be drug substances for biopharmaceuticals, including human infectious disease vaccines
- Basic research has been progressed steadily for prioritization of development pipeline(s)

SHIONOGI * Including an upfront fee at the time of execution of agreement 39

In 2017, UMN Pharma, in partnership with Astellas Pharma Inc. and also IHI Corporation, submitted an application to the Ministry of Health, Labour and Welfare (MHLW) for an influenza vaccine. It was at this stage that a paper was released in the US citing “it cannot be denied that there is a possibility of rhabdovirus contamination given UMN and its partners’ use of a genetic recombination technology and BEVS produced baculovirus.” This was very interesting. Despite the fact that this paper was published in the US, the FDA assumed this was fine and approved the flu virus without issue.

However, given that influenza vaccines are plentiful in Japan, it was my recognition that the point of discussion was whether it was necessary to take a risk. Thus, the company withdrew from the submission of this vaccine.

As long as they used the virus and BEVS at that time, the possibility of rhabdovirus contamination could not be denied. We therefore participated on a trial basis given that we did not know at the Phase 1 stage if development of the vaccine could truly be realized. This led to the establishment of a rhabdovirus-free BEVS. We spent two years on this project. Our employees were also fairly committed to the project as we believed it would be interesting if we could somehow complete this vaccine.

At this stage, we were fairly confident, and examined and discussed this with the PMDA. I believe it is okay to say that the BEVS we established is rhabdovirus-free.

At the time, the Akita Plant was nearly in a hopeless position. We made modifications to the inside of the plant. We took two years to bring the plant to a point where it could produce product in line with GMPs.

Addressing the Issues in the Capital and Business Alliance

SONG for you!

Issues with the transition to the 2nd Phase in the business alliance

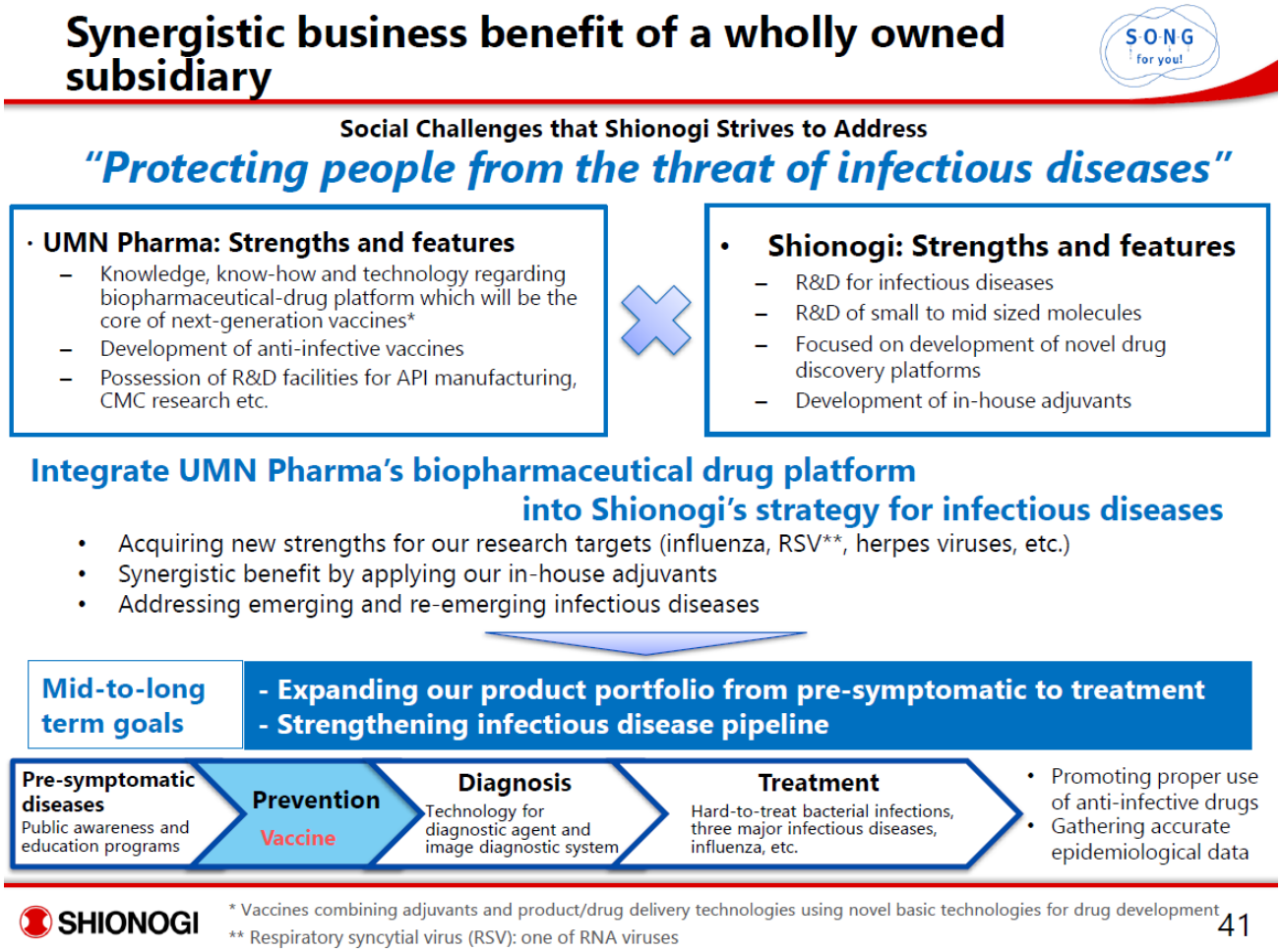
- Need to conclude the license agreement for each development candidate in the current framework
  - Limited benefit in investment of Shionogi's management resources and integration of the strengths of both companies
- Strengthening revenue stream of UMN Pharma
  - Continued payment is necessary for ensuring their sales enough to maintain the listing
  - Necessity of additional capital increases, etc. in order to achieve early approval and launch of development candidates

Framework such as forming a business alliance is not enough to drive forward vaccine business actively, flexibly and globally in drastic changes of external environment surrounding pharmaceutical industry

To invest Shionogi's management resources in the promising vaccine-related assets in UMN Pharma's more actively and flexibly than before,
we consider it is essential to revitalize UMN Pharma's project(s) and improve its efficiency by consolidating R&D, manufacture and marketing systems of both companies

Proposal to UMN Pharma for the Transaction of a wholly owned subsidiary

In particular, UMN Pharma has compound candidates that can be taken to clinical trial in the near future. Rather than wondering whether or not to license these candidates or whether to develop just a few of them, we believe it will be best for both parties to acquire them out right. Through this acquisition, we will secure a vaccine platform. To be straight with you, the first product we plan to develop is the influenza vaccine. Including this, we plan to develop various types of vaccines.



As I mentioned earlier, I am fairly confident about the capability of the technicians at UMN Pharma, as we worked with them for two years. We plan to have our employees team up with these technicians from UMN Pharma to carry out clinical trials. In addition to new viruses, we especially plan to tackle clinical trials for an influenza vaccine as our first development project shown in the middle of the next page.

R&D on drugs for RSV, herpes and the development of our own Adjuvant S-540956 are in a very good status. We believe that by combing the strengths of UMN Pharma in these areas we can come up with vaccines that are slightly different from those developed thus far in terms of the efficacy and safety of gene recombination. We aim to carry out R&D using a method that does not rely on eggs.

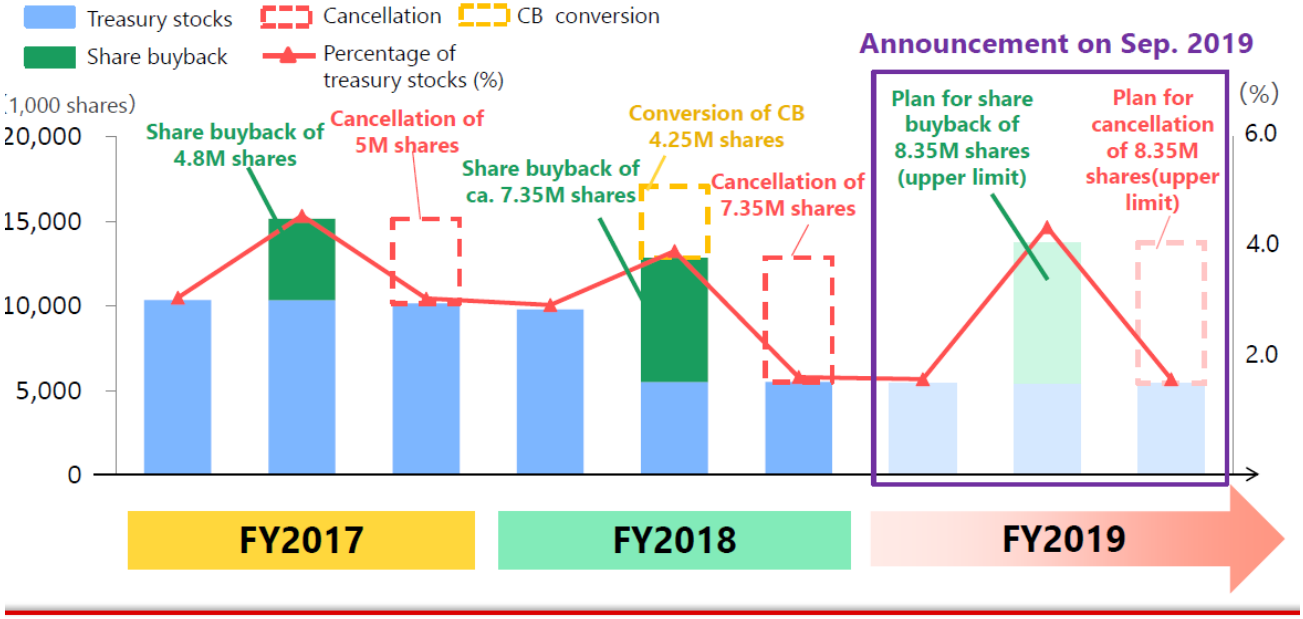
Flexible and Prompt Capital Policy

Share buyback

- Share buyback: 8.35M shares (upper limit)
- Total amount of buyback: 50 B yen (upper limit)
- Period: Oct. 1, 2019~Feb. 28, 2020

Cancellation of treasury shares

- Total shares to be cancelled: 8.35M shares (upper limit)
- Date for cancellation: Mar. 13, 2020

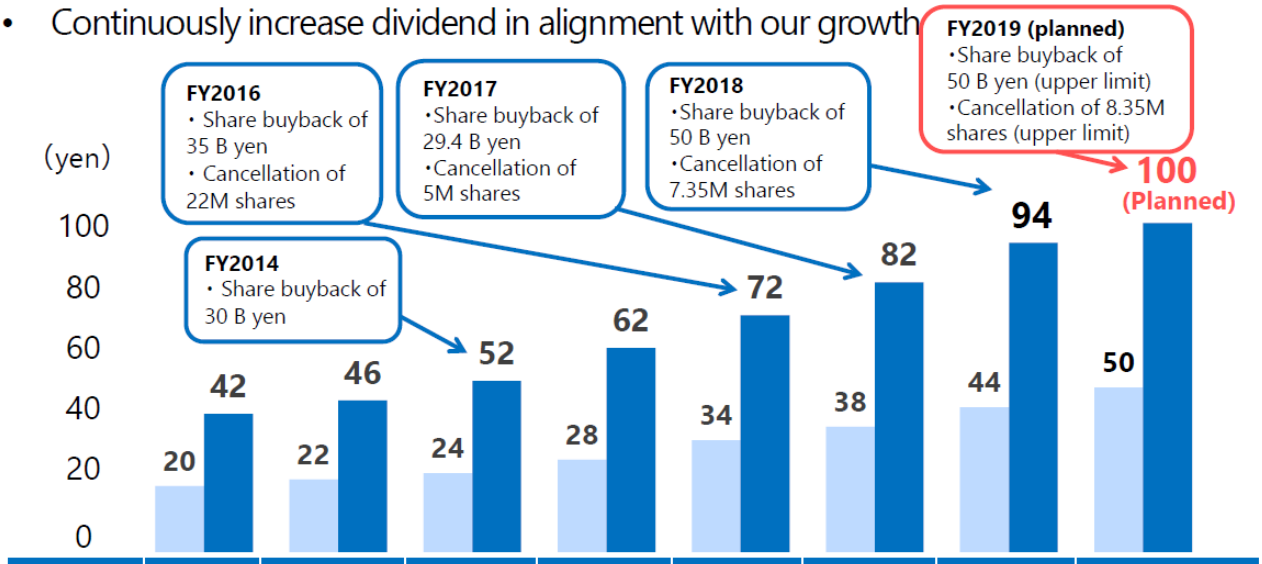


Moving on to shareholder returns, in September of this year, we announced plans for a share buyback of a maximum 8.35 million shares or ¥50 billion. Since we have become close, I hope you will forgive me for being blunt but we received a fair amount of criticism for not announcing the buyback plans in July at the time of our quarterly earnings results presentation. The use of cash is truly an ongoing issue. At that time, we were considering an investment project, among other matters. Given this potential investment, we decided to place priority on using our cash on this project.

It just happened that this project fell through so in September, which is the end of our first half and a time when we were able to get a picture of our earnings results, we decided that given our financial conditions, we would go ahead with a share buyback. This decision reflects our goal to balance returns for all our stakeholders. We plan to take actions such as this going forward.

Shareholder Return Policy Through Which Shareholders Can Feel Our Growth

- Plan to **increase dividend for 8 consecutive years and reach 100 yen in FY2019**
- Continuously increase dividend in alignment with our growth



FY	12	13	14	15	16	17	18	19
DOE	3.7	3.5	3.7	4.1	4.5	4.6	4.6	Over 4.3 (planned)
ROE	17.5	9.2	9.4	13.6	16.3	19.4	20.9	Over 18.0 (planned)

It is our policy to maintain the level of dividend payouts, and do not plan to cut our dividends barring the occurrence of any major events. In light of this, we are basing our interim dividend for the current fiscal year on the year-end dividend of ¥50 per share for the fiscal year ended March 31, 2019. We plan an interim dividend hike of ¥6 per share, in contrast with the interim dividend paid in the previous fiscal year.

This ends my portion of the presentation. Thank you for listening.

Q&A

Emcee: Thank you. In the remaining 40 minutes we will take questions. When I call on you, please start by giving us your name and the name of your company.

Let's start with Yamaguchi-san.

Mr. Yamaguchi: My name is Yamaguchi and I am from Citibank. Thank you for your presentation. This being the first question, forgive me for asking a very basic question. In the section on HIV drugs, you said Shionogi is on schedule. I am unclear on the additional information of S-648414 but are you talking about the future position of your HIV franchise. If you can divulge anything details on the current status of this franchise I would appreciate it.

Teshirogi: As with the development of any type of oral drug, the first step is to see how much of the viral load can be lowered, this is roughly a 1.5 log or 2 log decreases, with the oral drug alone. We first check to see if the oral drug alone has the ability to lower the viral load by approximately this level. In addition, we also check the degree of potential of the medical compound. These are some of the issues we take into consideration. We also see if the oral can be used in combination with a drug delivered by injection. This is our process.

Our first step above all else in Phase I is to confirm safety. We do our best to quickly enroll patients as we want to see the viral load reaction as soon as possible to move on to a regular Phase III trial. In the basic data, we found that the viral load was reduced but there are other factors, including human PK properties.

Mr. Yamaguchi: This style illustrates the introduction of a drug mechanism that has not been used before. In other words, to a certain extent, this drug is completely different from your conventional approach to develop a drug with the same mechanisms, such as a long-acting drug.

Teshirogi: Yes, this is a new drug mechanism.

Mr. Yamaguchi: My second question is, you provided a detailed explanation for cefiderocol but there are two basic things I would like to know.

First, you plan to broaden indications for the drug. However, among these indications, you stated that for some of these indications the market environment is harsh. How do you envisage the scale for each existing and potential markets? I believe you said there are a number of scenarios you are considering, such as whether you would inject another drug in terms of sales based on your market scale projections, and whether you would partner up with another company. Can you give a recap these two measures?

Sawada: The market, even in the US, is a fairly large market worth over ¥10 billion for anti-bacterial drugs that target AMR. From that standpoint, I do not think we are talking about a drug that will become a blockbuster.

Respiratory diseases are a very important area so I would like to add this to our pipeline. The level of demand in US guidelines is very high therefore making additions for other diseases would be somewhat difficult.

However, globally, there is a trend for gaining approval for efficacy drug treatments on a pathogen basis. We are considering following this trend in those regions.

In the case of anti-bacterials, aiming for a single drug with sales of ¥10 billion-plus would be very inefficient, even if there were only a few target hospitals that we try to cover with limited sales resources. In light of this,

it is our goal to quickly get drug candidates to those target hospitals where there is an overlap in target doctors.

Mr. Yamaguchi: So essentially, rather than teaming up with another company, you plan to add drug candidates that meet this criteria to your existing franchise. You said you plan to add 2-3 drug candidates? Do you plan to add two immediately? Or do you plan to add them a little further down the road? Just like for anti-bacterials? Is that correct?

Sawada: Yes.

Mr. Yamaguchi: Did you decide to embark on a share buyback program because you were close to but ultimately did not decide on the BD for this? Is that essentially what you are saying? No necessarily?

Teshirogi: You are close.

Mr. Yamaguchi: Thank you. Lastly, at its presentation, M3 explained a variety of topics related to Stream-I. I think it is an interesting experiment.

What I want to ask you is I felt that in your medium-term business plan, Shionogi plan to step in and take a fairly prominent role in domestic sales from the next fiscal year onward. I also felt that you would be doing this by taking on a new approach. Do you plan to partake in domestic sales with the strategy of increasing sales while simultaneously reducing cost in a specific disease area by employing this approach? Do you plan to accomplish this using this flow?

For example, in the treatment of depression or pain, it can be any area, it is your idea to increase those drugs that perfectly suit Shionogi?

Sawada: Yes, as an overall flow, that is correct.

Mr. Yamaguchi: Thank you.

Emcee: Next we will hear from Hashiguchi-san.

Mr. Hashiguchi: My name is Hashiguchi and I am from Daiwa Securities. Thank you for your presentation. I have three questions.

First, regarding the HIV drug candidate that entered Phase I trials, can you tell us why you started trials from the oral drug? Does this reflect current trends? If Shionogi is trying to differentiate from rivals, it seems to me that it would be more beneficial for Shionogi to successfully develop an injection drug. So I am wondering why you decided to start with an oral drug version.

Teshirogi-san said earlier that in the medium-to-long term, you would develop an injection. So does that mean you will not embark on development of an injection immediately but that this is further down the road? Can you explain the reason for this?

Teshirogi: Actually, at present, in clinical trials, we are giving patients the oral form of cabotegravir for a month. We then confirm the patient is stable, after which we administer an injection. This is because when administering an injection once a month the compound goes into the body and does not leave. We make sure to secure a certain level of safety before administering an injection. I think this process will likely remain the same.

Consequently, the good point of cabotegravir is the same as dolutegravir, it is powerful as an oral drug but also can be administered by injection. This is probably true for Gilead Sciences as well as Shionogi. Among

integrase inhibitors, it is difficult to develop drugs with this character. I believe that at the moment cabotegravir may be the only one.

In the same way, initially an oral version of a compound will have to be tested on patients to evaluate the potential of the drug compound. This is common sense these days. If an injection form of a drug is established from the onset, and we know that we can launch a compound in injection form then it may be fine in that case to develop an injection drug from the start. At present, we believe we need to test both an oral and injection form, otherwise development will be difficult.

Mr. Hashiguchi: In that case, when do you plan to do clinical trials on the injection?

Teshirogi: Before any of that happens, we need to confirm in Phase II that the oral drug lowers the viral load in patients to a certain degree. This is likely to around 2022 therefore we are conducting research with the objective of starting on trials for an injection around that time.

Mr. Hashiguchi: Thank you. My second question is about Sage-217. Earlier you discussed the changes to your development plan. However, hearing what you had to say, I came away with the impression that you basically already know the outcome from the beginning. In your presentation a year ago, you said the PMDA had a very favorable response and that you believed you would be able to quickly develop the drug. You said that after discussions with the PMDA, you stated that development will make it in time for the launch of Cymbalta. However, there appears to be some new information. Can you explain what has happened?

Sawada: I believe this reflects a slight change in development policy at Sage Therapeutics. In light of this, it has become difficult to implement the scenario we drew up. This is the basis for the delay. Sage views this as a drug regimen as a two-week treatment. They plan to promote the drug by doing a close-up on this.

Meanwhile, depression is a chronic illness. So it is important that a treatment keeps the patient in a positive condition. This is a crucial point that we are currently discussing. At present, the Ministry of Health, Labour and Welfare and the PMDA have settled their position on this as a chronic illness. From that standpoint, if you are asking whether we can simply apply overseas data to our findings, I believe that we need to consider providing extra information. Taking this into account, it is my belief that we need to properly clarify the drug profile ourselves.

Mr. Hashiguchi: How has the development policy at Sage Therapeutics changed?

Sawada: Sage planned to highlight the drug as a treatment for an acute phase, versus its previous goal of widely defining depression. On the other hand, unless we view this as a treatment for chronic depression, I think it will be difficult for use to establish a comprehensive treatment plan. This is an area that will need to be discussed at length. I think we need to decide on a plan that is best for the patient. To do so, we require data. We plan to take proper steps to acquiring this data.

Mr. Hashiguchi: Thank you. My final question is about the Zofluza issue. The Ministry of Health, Labour and Welfare may not have solidified its stance but what is your projection for approval of use in Japan on patients under 20 kilos and for the introduction of a granule formulation?

Sawada: I understand the ministry is currently quietly moving forward with deliberations.

Mr. Hashiguchi: So by the next flu season, the drug may be on the market? It is okay to understand that in the not so distant future Zofluza will be approved and the granule formulation will also be on the market sometime in the current fiscal year?

Sawada: There is also the issue of the drug price. We are not look at this flu season, but we expect to have the drug out by the next flu season.

Mr. Hashiguchi: What about the timing for approval?

Sawada: As for approval, data has not yet passed through sectional or other meetings. From that standpoint, guidelines are still up in the air and discussions are likely to be carried out factoring in advice. This is portion of the process is behind schedule but I think that approval itself will sometime during the current fiscal year.

Mr. Hashiguchi: Thank you.

Emcee: Ueda-san.

Mr. Ueda: My name is Ueda and I am from Goldman Sachs. My first question is about Cefiderocol.

In your explanation earlier, I believe you said that in Europe you were negotiating by planning to receive incentives for stockpiling. Can you be more specific?

In the US, you said that given current conditions, there are too many customers to negotiate with so you are at a loss as to what to do. Do you have any thoughts about what is necessary to change the US market?

Sawada: To be honest, I would like you to tell me if you have any good ideas on how to change the market. However, the US is the largest market for pharmaceuticals in general. It is fairly difficult to take those pharmaceuticals that do not generate profit in the US and try to generate profit by selling them in other regions.

When looking at the market from that standpoint, there are several companies that are actually taking into consideration the bankruptcy of Achaogen and ventures in the antibacterial business that are looking to cash out within the next 12 months. This trend is taking place in the US that is why it is being taken more seriously. Given insurance reimbursements, hospitals have to pay out of their own pockets if they use high-price pharmaceutical. The situation has been changed. If the drug for the treatment of AMR is used after AMR is identified, reimbursement is accepted. This is an important point.

Hospitals are not looking to stockpile a massive amount of drugs. In the US, BARDA is currently looking for and considering stockpiling drugs for specific pathogens.

In addition to this, the US is fairly advanced from the standpoint of putting together a budget for fund what needs to be done, including lawmaker legislation, and interviews between companies.

In Europe, the UK, Germany and Sweden have fairly good incentives in place in this area. In the case of Sweden, there are very few AMR patients. If the country aims to stockpile, budget is not earmarked. This likely makes Sweden easy to stockpile.

However, the issue going forward is how to apply this to countries that have many patients suffering from AMR.

Mr. Ueda: In regard to reimbursements in Europe, for example, is the price for stockpiling really high? Or, for instance, will hospitals pay an annual fee for the stock they have?

Sawada: I cannot go into details about this right now. However, the UK has disclosed that it is moving forward with the implementation of a subscription model. I think this is the level of where things are at.

Mr. Ueda: Thank you. My second question is about the HIV franchise. It is in regards to the two-drug regimen. I believe that you are waiting for guidelines to be set forth for Dovato. Data has been released for both GEMINI and TANGO. Has there been some change at clinical sites? Also, can we expect to see an actual expansion in sales after the revision of guidelines? Can you provide some other details as well?

Teshirogi: It was originally found that around 30%-40% of people surveyed said they are okay with a two-drug regimen, another 30%-40% said they would not accept anything less than a 3-drug treatment, and the remaining 30%-40% said it depended on the data. According to the survey by ViiV and a third-party survey

company employed by ViiV after IAS, it was shown that there was a fair amount of the neutral 30-40% has been OK for a two-drug regiment, in particular based on the 96 week findings for GEMINI and 48 week findings for TANGO.

In addition, the guidelines will be revised soon, and furthermore, long-acting injectable cabotegravir will be approved in this year. Considering these situations, we expect a full-fledged pick up in the pace of sales from the next fiscal year onward.

In addition, it's natural that many insurers do not add newly approved drugs to their drug list for 1year. Negotiation with insurers will be carried out in February and March. I believe we are likely to see full-fledged contribution from this.

Mr. Ueda: Thank you. My final question is about Xofluza. Statement/Guidelines were release from JAID and JPS. Can you explain what impact you expect from actual decisions by doctors as to how the drug should be prescribed in a clinical setting in line with these guidelines?

Sawada: To be honest, I do not know. The points that each doctor places emphasis on differ. From our standpoint, there is a fact that these statement or guidelines are released and there are data that actually exist. Taking this into account and factoring in the risk benefit, it is up to the doctor to decide what drugs to prescribe.

Mr. Ueda: Thank you. I have no further questions.

Emcee: Kotani-san, you are next.

Mr. Kotani: My name is Kotani and I am from Nomura Securities. Thank you for your presentation.

My first question is on CREDIBLE-CR. Looking at the data, there is a significant gap in the mortality rate between Cefiderocol arm and BAT (Best Available Therapy) arm. Looking at the data, it simply seems like patients that were administered Cefiderocol did not see any benefit. However, when digging deeper the study design of the trial, there seems to be many factors to be considered. There is a major gap in patients over 65 years of age 63% in Cefiderocol arm and 45% in BAT arm.

There are also various minute issues such as a gap in the creatinine clearance. Remarkably, 83% patients of Cefiderocol arm were treated with monotherapy, while 71% of patients in BAT arm were treated with combination therapy What was this trial conducted in this manner? What do you expect to achieve from this trial? Can you explain this one more time?

This is my own opinion but it likely takes two days to confirm carbapenem resistance by cultivating cultures and determining MIC. I think this was fairly severe, especially for elderly patients. Can you elaborate on this?

Sawada: You are correct. The CR study was a very difficult to design. The population is small, only 150 patients in total. This study was not designed or powered to conduct hypothesis testing in order to compare treatment groups. When trying to assess efficacy and safety, there is no way to make a comparison if there is no control. Therefore, patients were randomized two to one to either Cefiderocol or BAT arm.

This study is different from studies for other AMR treatments. When only targeting carbapenem-resistant *Enterobacteriaceae* (CRE), the bacteria has a high pathogenicity therefore the majority of patients have a certain degree of immunity. When expanding the target to *Acinetobacter*, the patient backgrounds become extremely diverse.

In light of this, for example, if a patient enters the ICU, there are some patients that have suffered a septic shock in the past few days or a month and entering the ICU. From this standpoint, the study is designed in a manner that background of patients cannot be balanced between the two arms given this background.

Furthermore, it would not have been possible to gather this patient population without conducting the study globally. In the global study, it was impossible to set single control drug, and a blind study cannot be conducted. It therefore becomes a comparative, open-label study.

I think results of the vitro and vivo studies for Cefiderocol were too good. There is substantial expectation on the drug. The result has been the use of Cefiderocol as a single treatment although the BAT being a combination treatment. Consequently, from this standpoint, the test was not a fair comparative study, as you stated.

Mr. Kotani: Thank you. My second question is about the HIV franchise. Recently GSK also commented on this but an issue has been an increase in weight. In the ADVANCE trial in South Africa, the use of Dolutegravir and TAF triggered an increase in weight. Furthermore, taking a more detailed look, the weight gain was not simply because the patients were healthier. These findings were published in the NEJM. Moreover, it has been shown that torso fat, which is known to be related with heart disease, is increased.

Recently, findings have also been released from the meta-analysis of eight trials. Looking at these findings, Bictegravir, TAF and Dolutegravir have all been linked to weight gain. How will this play out when the treatment is commercialized?

Also, at CROI, it was said that there were few cases of weight gain when using cabotegravir. Taking this into mind, how will this impact the commercialization of the drug going forward? I believe that GSK hinted that it had the advantage. What is your opinion?

Teshirogi: You incredibly summarized some important points but these are all difficult to answer. As a backbone therapy, I believe that TAF triggers a slight weight gain. More importantly, I think that integrase inhibitors, Dolutegravir, and Bictegravir also trigger weight gain. So if a patient continues to take an oral daily dose, they are likely to suffer a rise in cholesterol, another side-effect of TAF. I think that the accumulation of medium/long-term data is one tasks that needs to be carried out going forward.

Dolutegravir has been on the market for 7 or 8 years. Taking a retrospective look, there has been no fatal side effects. Naturally, it is a fact that weight gain due to an increase in torso fat negatively impacts the cardiovascular system. The view on life of these HIV patients is an issue we need to tackle going forward.

We also need to examine Cabotegravir. Is the weight gain mechanism-driven by the integrase inhibitor? What will happen if a patient continues to take the drug? What will happen if the drug is administered by injection? These are all issues that need to be monitored and studied going forward.

However, weight gain is currently a major issue among HIV treatments. One doctor said this is about the only bad thing he can say about the drug as it successfully maintains viral suppression. The doctor said the side effects need to be closely examined moving forward.

Mr. Kotani: If I were a sales representative with ViiV, I would ask about the potential double weight gain given that TAF triggers a weight gain and Bictegravir also triggers a weight gain. What is your opinion on this?

Teshirogi: I cannot comment on this.

Mr. Kotani: Thank you. Lastly, I would like to ask you about the timeline for the novel HIV drug. I understand you has started a Phase I trial and you will move on to a Phase II trial. Is it correct to assume that in 2021, when the Crestor royalties disappear and the generic-version of Cymbalta is released, you will be handing the drug over to GSK?

Teshirogi: We only recently began to hold discussions with ViiV on S-648414. This is because we plan to implement a combination therapy with Dolutegravir from Phase I. Naturally, we have received consent from ViiV as we will be using this drug. If all goes well, the timing will fall in line with what you just said. We naturally aim to focus on this while conducting negotiations.

However, if it is realized, we don't know whether we can receive milestone income or we can get more shares.

Mr. Kotani: Thank you.

Emcee: Sakai-san.

Mr. Sakai: My name is Sakai. I am from Credit Suisse. Can you sort out the details of the HIV franchise? Looking at GSK's earnings results presentation yesterday, sales of Triumeq are declining. ViiV and GSK have both clearly stated they plan to fortify their two-drug regimens. I think this is a trend that cannot be avoided.

However, previously the president said that Triumeq sales need to be shored up as this will directly hurt Shionogi's royalty income. In other words, even if two-drug regimens are expanded, the total sales will shrink. What are your thoughts on this? That is my first question.

I would also like to discuss injections. Gilead has already embarked on a fairly negative campaign. Putting it extremely, Gilead is saying who would ever use an injection. There are obviously people that entered the clinical trial for Cabotegravir because they want to use an injection, and there are also doctors that want to prescribe the drug. Clearly, even after the survey, there were many patients who want to use the injection. For the treatment of HIV, I think people are very conservative. Some patients still use Isentress, which requires oral dose twice daily. Amid this, what policies will you put in place or have you put in place for your strategy to make a switch to injections and have you reached an agreement with ViiV?

Teshirogi: Triumeq sales are down in the US but we forecast that once sales touch bottom they will rebound. In particular, as you said, there are still patients that use Isentress. It is much the same. There are patients who have a control on their virus level owing to Triumeq. At the very least, ViiV is not carrying out a campaign to aggressively switch Triumeq.

In addition to requesting patients that are having success with their current drug regimen, we also ask those patients that are experiencing unstable effects or want to switch Triumeq to Dovato. For naïve patients, there is naturally a minimum burden and the price setting is also very attractive. I recommend they start from Dovato.

As for our royalty income, Medicare and Medicaid cover 60% of the total prescriptions of Dolutegravir franchise in the US. 6-7 years have passed since launch so the price has risen fairly high. ViiV has to pay rebate to Medicare and Medicaid for the portion of this price hike. Therefore, the net price of Triumeq is almost the same as that of Dovato.

Consequently, on a royalty basis, we would be in trouble if the price of Dovato rose or dropped rapidly. Boosting share at the current $27,000-$28,000 WAC price range would not substantially impact our royalties. We believe if anything, boosting share would be positive for Shionogi.

As for injections, what you said is correct. We also believe that the maximum interest in injections is around 15%-20% of patients. Conversely, 80%-85% of patients are in favor of the oral formulation that is taken once daily.

However, this is likely to become an issue the entire industry must confront. The more this trend progresses, all patients will follow that return by the time the generic version of Dolutegravir comes out in 2028. This actually indicates the disappearance of the HIV drug market itself. In other words, these actions represent a functional cure, something close to being an actual cure. We need to create a trend where, in a paradigm where patients cannot treat themselves using generics, more patients will see this as a benefit.

Based on this, the trend in HIV treatments will shift to focus on better patient convenience. In other words, only having to take an injection once every three months or coming up with a functional cure.

Mr. Sakai: Thank you. I have one additional question. How does Shionogi view the PrEP market?

Teshirogi: Recently, Truvada for PrEP is said to currently be a $1 billion business in the U.S. The portion of Truvada sales that has not dropped is said mainly to be for PrEP. The company naturally wants to replace this with Descovy. As Mr. Kotani posed before, I believe Descovy is better than Truvada but it's not perfect.

Logically speaking, patients that use the drug for PrEP have not been infected with HIV virus. It's not ideal that continuous use of the drug can have some effects on the kidneys or bones even if it's small. Given this, if PrEP can be realized by an integrase inhibitor, it would be best for the patient. On top of this, if it only had to be taken once every two or three months, we believe it would truly be a benefit for patients. We believe the market, mainly in the US, is around $1 billion at lowest.

Mr. Sakai: Are there people taking Truvada and Tivicay for PrEP?

Teshirogi: According to the label, people who take Truvada for PrEP likely only use Truvada.

At IAS the other day, Gilead released data about switching Truvada to Descovy. I think they want to switch as soon as possible. In the US, there is a huge campaign being run using TV commercials. This seems to indicate that Gilead played a fairly large role in creating the HIV PrEP market. The large this market grows, the easier it will be for us to enter so we wish them luck in their endeavors.

Mr. Sakai: Thank you.

Emcee: Next is Arai-san from Merrill Lynch.

Mr. Arai: I have two questions related to HIV franchise.

First, is about drug prices in the US. Not only for HIV drugs, but for drugs overall, I believe there is rising pressure to suppress drug prices, mainly forMedicare. Do you believe that amid this trend HIV treatments will be an easy target? Is this currently being debated within the industry?

Based on what you just said about Triumeq, the net price is almost on a par with Dovato. Is there no need for concern about a non-sequential decline in the price of Triumeq? What are your thoughts at the moment?

Teshirogi: I think this is linked with how well Trump and the Republic Party fares in the next presidential election. Regardless of realistic the Democratic Party is, I believe that this will be quite negative for the pharmaceutical industry overall.

While this is an extension of the Republican Party and Trump, this became a major issue this year and was put on the table for discussion. The discussion revolved around whether HIV drugs should be excluded from the protected classes. Trump was in favor keeping HIV drugs as a protected class drug. Given this huge declaration of keeping people safe from infectious disease including HIV, it is not likely that HIV drugs can easily be removed from this class. This issue is likely to be put on the chopping block once more. However, if a Democratic president is elected, I do not know the situation.

However, the Democratic Party is relatively permissive when it comes to diseases such as HIV which are prevalent among the poor. In light of this, I do not see an immediate major threat to HIV drugs.

Mr. Arai: Thank you. My next question concerns your opinions on launch next year of the long-acting injection formulation of Cabotegravir. Assuming approval is acquired in December in the US, this should become one driver to boost sales of the HIV franchise in 2020. What are your thoughts on the speed of share capture after the launch.

Do you believe that, given the high level of unmet needs, sales will skyrocket in the first year on the market? Or do you think the drug will take off slowly given it uses a new mechanism of drug delivery? Or do you it will become mainstream after taking several years to replace the Dolutegravir franchise? Can you please give your thoughts on this launch?

Teshirogi: As Mr. Sakai said, the market is on the conservative side. Given that a patient's life is at risk they tend to take a reserved position on changing their drugs. Accordingly, I do not foresee patients switch to Cabotegravir rapidly.

On a community basis, the American South is such a region. There are people who will assume that compliance is poor. It is in these places we are likely to see the overall benefit of HIV drugs as people switch from a once a day oral formulation to an injection that only needs to be administered once a month or once every two months.

According to data, in those places, around 40% of patients clearly claim they forget to take their oral medication. If a patient forgets to take their medication once in two days, it is unlikely that it will result in a variant virus or a tremendous deterioration in one's health. However, there are a substantial number of patients that do not take their medication as instructed. It is in a market such as this that the injection is likely to get its start. I do not forecast a rocket start for this drug.

Mr. Arai: I understand. Thank you.

Emcee: Lastly, I would like to call on Wakao-san.

Mr. Wakao: My name is Wakao. I am from Mitsubishi UFJ Morgan Stanley. Could you briefly tell me about the timing of the launch of S-812217. Was it originally scheduled to coincide with the loss of royalty payments for Crestor? You initially said you would like to make it in time to launch the drug in the fiscal year ending March 2022. However, listening to your presentation today, I came away with the impression that you are behind schedule. Can you please tell me what your current target is for your market launch?

Teshirogi: Discussion between Sage Therapeutics and the FDA is ongoing, and this partially depends on the outcome of their discussion. If we go about regularly carrying out Phase II and then Phase III, in the event we need to secure all data in Japan, I think a reasonable launch date would be in 2023 or 2024.

However, based on what we have heard about labeling requirements and approvals by the FDA, I believe that there is an ample possibility that we will also need to make changes. If we move ahead in line with our usual processes, I think that is how long it will take.

Mr. Wakao: Thank you. One more question. Regarding your talk on M&A or the purchase of assets, you said that you did not purchase the asset you first considered. I came away with the impression that this asset was quite large in scale and the assets you are currently considering acquiring are small in scale. Have you changed your direction on the scale of assets you aim to purchase, including M&A?

I think that since Cefiderocol is about to be launched, it is important that you quickly strengthen your operations. If you decide to purchase the asset you discussed, when do you plan to make the purchase?

Teshirogi: To be honest, and I am likely to get yelled at for putting it like this but, the amount has not been finalized. If it is a good asset and one that we truly want we are willing to acquire an asset for ¥100 billion, ¥200 billion, ¥300 billion or even slightly higher, as we have the cash. There are such assets on our radar screen. We did not want to acquire the asset because it was high priced. We wanted it because we really thought it was attractive. However the asset is no longer available. These types of assets do not come along regularly. Currently our focus is not making one large purchase but on acquiring two smaller assets.

However, this could change tomorrow. From that standpoint, we need to fortify our business and optimize Cefiderocol so that we can conduct a large-scale business in the US or Europe or China. This is something I have been looking forward to. This could be tomorrow or it could be three years from now or later. But I am always on the lookout for such an opportunity.

Both I and John are originally from BD so this is all we have been doing. So I have witnessed this quite frequently.

Mr. Wakao: Thank you. I have nothing else.

Emcee: Well our time is up so I will end here. Thank you.

［END］