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On **November 8, 2019**, SymBio Pharmaceuticals Ltd. announced earnings results for Q3 FY12/19.

Cumulative	FY12/18				FY12/19				FY12/19	
(JPYmn)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	% of FY	FY Est.
Sales	888	1,928	3,032	3,836	1,611	2,005	2,008		64.9%	3,092
YoY	2.1%	8.0%	25.5%	11.4%	81.4%	4.0%	-33.8%			-19.4%
Gross profit	250	573	924	1,173	609	529	563			
YoY	4.4%	12.4%	37.0%	13.7%	144.0%	-7.7%	-39.1%			
GPM	28.1%	29.7%	30.5%	30.6%	37.8%	26.4%	28.0%			
SG&A expenses	964	1,898	2,832	3,829	1,205	2,545	4,099			
YoY	26.1%	8.7%	-32.3%	-23.1%	25.0%	34.1%	44.8%			
SG&A ratio	108.5%	98.4%	93.4%	99.8%	74.8%	126.9%	204.1%			
Operating profit	-715	-1,325	-1,908	-2,656	-596	-2,015	-3,536		-	-3,780
YoY	-	-	-	-	-	-	-			-
OPM	-	-	-	-	-	-	-			-
Recurring profit	-749	-1,378	-1,938	-2,749	-616	-2,069	-3,642		-	-3,856
YoY	-	-	-	-	-	-	-			-
RPM	-	-	-	-	-	-	-			-
Net income	-760	-1,389	-1,941	-2,753	-617	-2,070	-3,641		-	-3,859
YoY	-	-	-	-	-	-	-			-
Net margin	-	-	-	-	-	-	-			-

Quarterly	FY12/18				FY12/19			
(JPYmn)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Sales	888	1,040	1,104	803	1,611	394	3	
YoY	2.1%	13.5%	75.1%	-21.8%	81.4%	-62.2%	-99.7%	
Gross profit	250	324	351	249	609	-79	33	
YoY	4.4%	19.5%	113.0%	-30.3%	144.0%	-	-90.5%	
GPM	28.1%	31.1%	31.8%	31.0%	37.8%	-	-	
SG&A expenses	964	934	934	997	1,205	1,340	1,555	
YoY	26.1%	-4.9%	-61.7%	25.4%	25.0%	43.4%	66.5%	
SG&A ratio	108.5%	89.8%	84.6%	124.2%	74.8%	340.4%	-	
Operating profit	-715	-610	-583	-749	-596	-1,419	-1,521	
YoY	-	-	-	-	-	-	-	
OPM	-	-	-	-	-	-	-	
Recurring profit	-749	-629	-560	-811	-616	-1,453	-1,573	
YoY	-	-	-	-	-	-	-	
RPM	-	-	-	-	-	-	-	
Net income	-760	-629	-552	-812	-617	-1,453	-1,571	
YoY	-	-	-	-	-	-	-	
Net margin	-	-	-	-	-	-	-	

Source: Shared Research based on company data
Note: Figures may differ from company materials due to differences in rounding methods.

Breakdown of SG&A expenses

Cumulative	FY12/18				FY12/19			
(JPYmn)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
SG&A expenses	964	1,898	2,832	3,829	1,205	2,545	4,099	
YoY	26.1%	8.7%	-32.3%	-23.1%	25.0%	34.1%	44.8%	
R&D expenses	416	839	1,293	1,833	472	963	1,972	
YoY	5.3%	-0.1%	-52.3%	-39.3%	13.4%	14.8%	52.5%	
SG&A expenses excl. R&D	548	1,059	1,539	1,996	733	1,582	2,127	
YoY	48.5%	16.9%	4.6%	1.8%	33.8%	49.3%	38.3%	

Quarterly	FY12/18				FY12/19			
(JPYmn)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
SG&A expenses	964	934	934	997	1,205	1,340	1,555	
YoY	26.1%	-4.9%	-61.7%	25.4%	25.0%	43.4%	66.5%	
R&D expenses	416	423	454	540	472	491	1,009	
YoY	5.3%	-4.9%	-75.7%	76.0%	13.4%	16.2%	122.1%	
SG&A expenses excl. R&D	548	511	479	458	733	849	546	
YoY	48.5%	-4.8%	-15.2%	-6.4%	33.8%	66.0%	13.8%	

Source: Shared Research based on company data
Note: Figures may differ from company materials due to differences in rounding methods.

Q3 FY12/19 results

- Sales: JPY2.0bn (-33.8% YoY)
- Operating loss: JPY3.5bn (loss of JPY1.9bn in Q3FY12/18)
- Recurring loss: JPY3.6bn (loss of JPY1.9bn in Q3 FY12/18)
- Net loss: JPY3.6bn (loss of JPY1.9bn in Q3 FY12/18)

As the company explained as its reason for earnings forecast revisions announced in August 2019, foreign matter contamination and appearance defects were discovered in lyophilized injection agents imported from Astellas Deutschland GmbH, a subsidiary of Astellas Pharma Inc. The extent of contamination and defects significantly exceeded limits permitted by quality standards stipulated in the supply agreement, and as a result, the shipments of Treakisym® 100mg vials to its domestic distributor Eisai was delayed. Accordingly, sales declined.

SG&A expenses rose 44.8% YoY to JPY4.1bn and R&D expenses increased 52.5% YoY to JPY2.0bn. This included upfront payments for new antiviral drug candidate brincidofovir, and expenses for conducting clinical trials of intravenous and oral formulations of Treakisym® and rigosertib. Excluding R&D expenses, SG&A expenses increased by 38.3% YoY to JPY2.1bn.

As a result, operating loss, recurring loss, and net loss widened YoY.

Introduction of new pipeline candidate

SymBio concluded an exclusive global license agreement with Chimerix Inc. for the antiviral drug brincidofovir (SyB V-1901, hereafter BCV)*[1]. The company acquired exclusive global rights to develop, manufacture, and market BCV for all diseases except smallpox.

The company will initially develop BCV for treatment of viral hemorrhagic cystitis (vHC)*[2] and HHV-6 encephalitis*[3] occurring after hematopoietic stem cell and kidney transplantation, which have high unmet medical demand. The company also looks to expand its business in Europe, the US and Asia (including China), where organ transplant markets are large. It will also consider forming partnerships that take advantage of regional characteristics of these target diseases. The company will explore all options for maximizing business value, including the strategic utilization of wholly-owned subsidiary SymBio Pharma USA, Inc. established in May 2016.

1. Brincidofovir (BCV) has a structure in which cidofovir (CDV, an antiviral drug already approved and marketed in the US and Europe but not approved in Japan) is bound to a lipid chain (hexadecycloxypropyl, HDP). It is absorbed into the lipid bilayer membrane and transferred into cells, where the bound lipid chain (HDP) is metabolized and separated from the structure by intracellular phospholipases. This process generates an activator (CDV diphosphate [CDV-PP]) that is retained in the cells for a long period of time, raising the compound's antiviral activity. Furthermore, BCV avoids nephrotoxicity, a fundamental issue plaguing CDV, since HDP conjugation prevents the accumulation of the compound in renal tubular epithelial cells through organic anion transporter 1 (OAT 1) and CDV is released at low levels into the bloodstream.

2. Viral hemorrhagic cystitis (vHC): Among viral infections that frequently occur following hematopoietic stem cell transplantation, adenovirus infections causing hemorrhagic cystitis are particularly refractory in nature. When severe, they can cause disseminated infection and become fatal. Cases of adenovirus spreading to the kidney and causing kidney failure and ultimately death have been reported. These infections are especially likely to occur in transplantation between unrelated donors and in umbilical cord blood transplantation, which are relatively common in Japan. The infections are likely to be refractory, as they are further complicated by the length of time required for reconstruction of the immune system. Drugs currently used in treatment, including cidofovir (CDV), are either unapproved or off-label in Japan.

3. HHV-6 encephalitis: HHV-6 (Human Herpesvirus 6) is the sixth human herpesvirus to be discovered. It reactivates in 30–70% of patients after allogenic hematopoietic stem cell transplantation and can cause HHV-6 encephalitis. Most cases of HHV-6 encephalitis develop within 2–6 weeks after transplantation, most frequently in the third week after transplantation. It is characterized by the three major symptoms of impaired memory, disordered consciousness, and convulsions, which in typical cases gradually appear in the same order (convulsions occur in 30–70% of patients). In rapidly progressing cases, which are not uncommon, neurological symptoms worsen by the hour, often requiring respirator management for repeated convulsions and respiratory depression. The conditions of HHV-6 encephalitis patients often deteriorate rapidly over a short period of time, making early treatment important. According to guidelines edited and issued by the Japan Society for Hematopoietic Cell Transplantation (February 2018), the first-line drugs are foscarnet (FOS) and ganciclovir (GCV), followed by the second-line drug cidofovir (CDV). CDV is not the preferred first-line drug

due to nephrotoxicity and because it transfers poorly into cerebrospinal fluid (CSF). All three of these drugs have been found to be effective in vitro, but no trials have been conducted yet to confirm their clinical efficacy in patients with HHV-6 encephalitis.

Domestic

Preparations for in-house sales organization begin

The business alliance agreement between SymBio and Eisai Co., Ltd. under which Eisai acts as a sales agent expires in December 2020. SymBio started to build an in-house sales organization for Treakisym® in the domestic market in October 2018. Key management priority is to move into the black in FY12/21 and ongoing profit growth thereafter. The company is therefore laying the groundwork for a shift to an internal sales organization to drive future business development.

The company increased Treakisym® sales representatives and conducted training needed to form the core of its in-house marketing network. Information provision activities were started from July 2019 by the Treakisym® sales representatives dispatched to each region to promote the shift to a nationwide operation with close local ties. The company also made steady progress with preparation of infrastructure such as logistics, distribution, and information systems.

Treakisym® (SyB L-0501[lyophilized injection]/SyB L-1701 [RTD]/SyB L-1702 [RI]/SyB C-0501 [oral]; anticancer agent; generic name: bendamustine hydrochloride)

The company markets the anticancer agent Treakisym® in Japan through its business partner, Eisai Co., Ltd. (TSE1: 4523) for the indications of untreated low-grade non-Hodgkin's lymphoma and mantle cell lymphoma (marketing approval obtained in December 2016), refractory or relapsed low-grade non-Hodgkin's lymphoma and mantle cell lymphoma (October 2010), and chronic lymphocytic leukemia (August 2016).

As a result of additional indications, Treakisym® is steadily increasing its market share in the area of first-line treatment in medical settings by replacing R-CHOP, the conventional standard treatment. The combination therapy of Treakisym® and rituximab (BR therapy) was newly included in the Practical Guidelines for Hematological Malignancies 2018 edited and published by Japanese Society of Hematology as a standard treatment option, which applies to all of the approved indications. This has seen Treakisym® establish its position as a standard treatment for lymphatic cancer. According to the company, market share in the area of first-line treatment increased to 55%.

In addition to the above three approved indications, the company is conducting a phase III clinical trial for the fourth indication of relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL), and the trial is progressing well with an aim to obtain approval. In response to strong medical needs, the company began a phase III clinical trial in August 2017. With the enrollment of the first patient in January 2018, the company made steady progress and completed enrollments in April 2019. The observational period for all patients (Last Patient Last Visit, LPLV) was completed in September 2019. Results of the trial indicated that the primary endpoint of response rate exceeded initial expectations. Going forward, the company will prepare for the approval filing, projected for Q2 2020.

SymBio is targeting a transition to Treakisym® liquid formulation (RTD and RI formulations), for which it concluded an exclusive licensing agreement in Japan with Eagle Pharmaceuticals (based in New Jersey, US) in September 2017. The company has already consulted with PMDA and filed for approval of the RTD formulation in September 2019 with an eye towards commercialization by Q1 2021. SymBio launched clinical trials for the RI formulation in November 2018 primarily to confirm safety, and has made steady progress with patient enrollments since enrolling the first patient in April 2019, having enrolled 26 patients as of end October 2019. Liquid formulations of Treakisym® will offer significant value added (reduced burden) to patients and healthcare professionals, and liquid formula patent protection makes it possible to extend the product life of Treakisym® until 2031.

In July 2018, SymBio obtained approval for the partial revision to the marketing authorization of Treakisym®. As a result, Treakisym® can now be used in combination with not only rituximab but new anti-CD20 antibodies as well. This will allow combination therapy with obinutuzumab (launched in August 2018) for the treatment of CD 20-positive follicular lymphoma (FL), the most common histological type of low-grade NHL, enabling the company to provide patients with a new treatment therapy. In March 2019, the company obtained approval for the partial revision to its application concerning the use of Treakisym® as a

pretreatment agent in tumor-specific T cell infusion therapy. This will allow Treakisym® to be used as a pretreatment agent for Kymriah® intravenous infusion, which was approved as the first chimeric antigen receptor T-cell (CAR-T) therapy in Japan and listed on the NHI drug price list in May 2019.

To reinforce the position of Treakisym® at the core of its business to strengthen its business foundation, SymBio is looking at the possibility of developing Treakisym® for other disorders such as solid tumors and autoimmune diseases. The company commenced a phase I clinical trial for progressive solid tumors in January 2018, with the aim of examining the recommended dosage and schedule as well as tolerability and safety of the oral formulation of Treakisym®, and narrowing down the types of potential target tumors. With the enrollment of the first patient in May 2018, the company is currently working on enrolling more patients for the trial. To evaluate the effect of oral administration of Treakisym® on the immune system, the company concluded a joint research agreement with Keio University in May 2018 and performed a preclinical study to verify the efficacy of the oral formulation of Treakisym® in treating systemic lupus erythematosus (SLE), a form of autoimmune disease. The company is currently compiling study results and after evaluating the findings will consider the next stage of this research project (including clinical trials).

Rigosertib Sodium (SyB L-1101 [IV]/SyB C-1101 [oral]; anticancer agent; generic name: Rigosertib Sodium)
Onconova Therapeutics, Inc., the licensor, is currently conducting a global phase III trial and SymBio Pharmaceuticals started the Japan trial in December 2015 (48 patients enrolled as of October 2019). The global phase III trial addresses higher-risk myelodysplastic syndromes (higher-risk MDS), which do not respond to the current standard treatment with hypomethylating agents, which relapse after treatment under the current standard of care, or which are intolerant to hypomethylating agents, and is under way at clinical trial sites in more than 20 countries worldwide. In October 2019, Onconova announced that it had reached 90% of its target of enrolling 360 patients worldwide. The company plans to report top-line (primary endpoint) results in 1H 2020. Based on these trial results, the company plans to apply for approval in Japan at the same time as in the US and Europe.

Regarding the oral formulation of rigosertib, Onconova has completed phase I/II clinical trials for the drug used in combination with azacitidine as first-line treatment for higher-risk MDS and phase II clinical trials for transfusion-dependent lower-risk MDS in the US. To verify the tolerability and safety of the oral formulation of rigosertib among Japanese patients, SymBio began phase I clinical trials in Japan in June 2017, enrolled the first patients in October 2017, and completed patient enrollment in June 2019. After completing the phase I trials, the company will consider phase I clinical trials for rigosertib used in combination with azacitidine, participate in global phase III clinical trials of the drug used in combination with azacitidine as first-line treatment for higher-risk MDS currently planned by Onconova, and apply for approval of the oral formulation of the drug in Japan at the same time as in the US and Europe. In December 2018, Onconova submitted a Special Protocol Assessment (SPA) request to the US Food and Drug Administration (FDA) to speed up the approval review for the global trials. Onconova announced in October 2019 that it was considering a phase II controlled study comparing rigosertib + azacitidine to azacitidine stand-alone therapy for untreated patients with higher-risk MDS. In regards to development of rigosertib for transfusion-dependent lower-risk MDS, the company is considering participating from Japan while monitoring Onconova's development progress.

SyB P-1501, a post-operative patient-controlled analgesia
Regarding SyB P-1501 licensed by The Medicines Company (through its wholly owned subsidiary Incline Therapeutics, Inc.) in October 2015, SymBio learned of an event that raised concerns about the continuity of its business, and in the interests of patient welfare, it suspended further patient enrollment in April 2017.

The company initiated an arbitration against The Medicines Company, under the rules of the International Chamber of Commerce, seeking damages of USD82mn (approximately JPY9.0bn) arising from The Medicines Company's repudiation of the license agreement. SymBio argued that The Medicine Company's failure to provide sufficient assurance to the company regarding the performance of obligations under on the license agreement in light of its decision to suspend and withdraw from business activities relating to SyB P-1501in the European and US markets was a material breach of the license agreement. Arbitration proceedings against The Medicines Company are still ongoing.

Overseas

The company marketed SyB L-0501 in South Korea, Taiwan, and Singapore, and product sales were in line with the company's plans.

This note is the most recent addition to the full report.

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