COMPANY RESEARCH AND ANALYSIS REPORT

SymBio Pharmaceuticals Limited

4582

Tokyo Stock Exchange Growth Market

24-May-2022

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Summary

The field of development for BCV expanded from viral infection to brain tumors and cranial nerve disease, and its growth potential substantially improved

SymBio Pharmaceuticals Limited <4582> (hereafter, also "the Company") is a bio-venture progressing developments from the clinical trial stage, targeting indications for oncology, hematology, and rare diseases for which there are few patients but medical needs are high. The main development pipeline includes TREAKISYM®, for which it is expanding indications as a treatment for malignant lymphoma; rigosertib, which it in-licensed from Onconova Therapeutics, Inc. <ONTX> (hereafter, Onconova) (U.S.); and the antiviral drug brincidofovir (BCV) in-licensed from Chimerix Inc. <CMRX> (U.S.).

1. Result trend of FY12/21

In the FY12/21 results, net sales increased 176.4% year-on-year (YoY) to ¥8,256mn and operating profit was ¥1,016mn (compared to a loss of ¥4,506mn in the same period in the previous fiscal year). This was due to the shift to the in-house sales structure for TREAKISYM® from December 2020 and then in March 2021, it expanded the indication areas for TREAKISYM® by obtaining approval for the manufacturing and marketing authorization, allowing the product to be used in the bendamustine-rituximab (BR) therapy and in the polatuzumab vedotin plus bendamustine-rituximab (P+BR) therapy to treat recurrent/refractory diffuse large B-cell lymphoma (hereafter, r/r DLBCL). Also, in addition to the shift to the in-house sales structure, it made progress in switching to the RTD formulation (liquid type) from FD formulation (lyophilized powder intravenous type), causing the gross profit margin to greatly increase, rising from 29.0% in the same period in the previous fiscal year to 70.2%, which was a major factor behind the Company becoming profitable.

2. Trends in the development pipeline

In February 2022, the Company received marketing approval for TREAKISYM® Liquid Formulation Rapid Infusion (RI) administration (which reduces the infusion time from the original 60 minutes to 10 minutes). It is expected that RI administration will significantly reduce the burden on healthcare professionals and patients, and also lead to further sales increases. The Company is also working to maximize product value by, for instance, launching joint research with academia to explore the possibility of expanding to new applications through combination therapy with rigosertib and with existing drugs. It also announced in February 2022 that four pharmaceutical companies had received manufacturing and marketing approval for generic versions of RTD formulation products. The Company consulted with U.S. company Eagle Pharmaceuticals, Inc. <EGRX> ("Eagle"), the license holder, and declared its intention to take legal action in the event that patent infringement was discovered. It is FISCO's view that because of the Company's shift in sales to RI administration, even if sales of generic products were launched, the impact would be limited.

Summary

As for BCV (intravenous formulation), the Company began phase II of global joint clinical trials indicated for adenovirus infections after hematopoietic stem cell transplantation in 3Q FY12/21 and may possibly advance to phase III in 2023 if these trials proceed smoothly. It also plans to begin global joint clinical trials indicated for BK virus (BKV) infections after kidney transplantation in the second half of FY12/22. Additionally, it was discovered through academic research papers that BCV could be expected to help treat glioblastoma or multiple sclerosis stemming from cytomegalovirus (CMV) infection, and the Company has unveiled a policy of advancing development in these fields going forward. Because these are refractory diseases, there are still no effective treatments. Therefore, if the Company succeeds at development, future development trends will be given attention all the more because the market value of BCV may surpass ¥100bn.

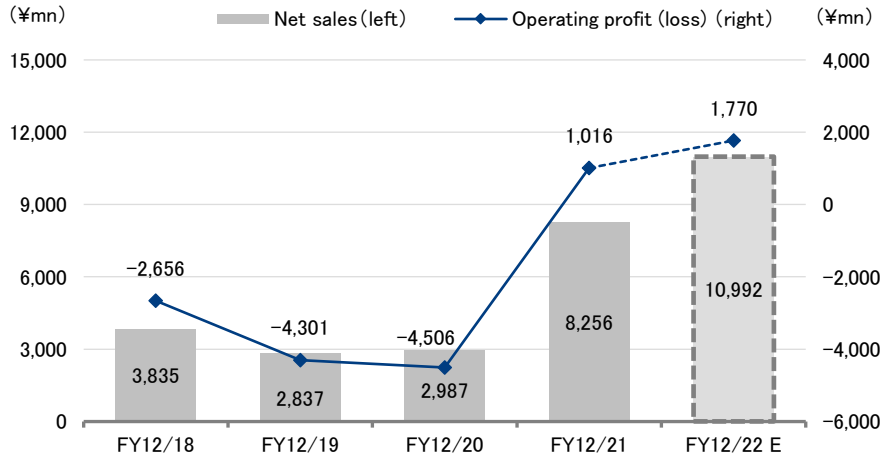
3. Outlook for FY12/22

In FY12/22 results, the Company's forecast calls for net sales to increase 33.1% YoY to ¥10,992mn and for operating profit to increase 74.2% to ¥1,770mn. The increase in net sales will largely result from the full-year contribution from net sales of TREAKISYM® for r/r DLBCL. Furthermore, all sales have been switched to RTD formulation/RI administration since the start of the fiscal year, and the gross profit margin is projected to rise even further to 80.0%. SG&A expenses are projected to increase 46.9% YoY to ¥7,026mn. Among these, R&D expenses are projected to increase 76.0% to ¥3,056mn, mainly centered on expenses for BCV clinical trials. In 1Q, net sales are likely to fall slightly short of the target due to the impact of the novel coronavirus (COVID-19), but will be viewed as having proceeded according to the target from the perspective of profit. Since the Company is enhancing its human resource systems through a U.S. subsidiary that will serve as an integrated base for global clinical trials, it plans to transition to consolidated financial statements beginning in FY12/22.

Key Points

- TREAKISYM® will expand indications to r/r DLBCL and sales are forecast to continue growing through receiving approval for RI administration
- BCV expanded target treatment fields as a unique drug combining both antiviral and anti-cancer activity
- In FY12/22 results, continued increase of sales and profit projected through increased sales of products for r/r DLBCL and an increase in the gross profit margin

Results trends



Source: Prepared by FISCO from the Company's financial results

Company profile

A bio-venture that conducts developments from the clinical trial stage, targeting the fields of oncology, hematology, and rare diseases

SymBio Pharmaceuticals is a bio-venture founded by the current Representative Director and President Chief Executive Officer Fuminori Yoshida in March 2005. For its business strategy, its basic policy is to conduct development and provision of new drugs for underserved therapeutic areas in which development has not been progressed due to the small numbers of patients. One of its features is a business model that aims to achieve highly efficient and rapid drug discovery within the areas targeting oncology, hematology, and rare diseases, which are fields with high medical needs, by in-licensing development candidates for which POC* for humans has been obtained, and conducting development from the clinical trial stage.

* POC (proof of concept): when the usefulness and efficacy of a new drug candidate compound is recognized following its administration to animals or humans during research and development

The first development candidate to be in-licensed was the anticancer agent bendamustine hydrochloride (hereafter, bendamustine hydrochloride; product name in Japan: TREAKISYM®) indicated for malignant lymphoma that was developed by Astellas Pharma GmbH (Germany), for which the Company concluded an exclusive development and marketing rights agreement for Japan in December 2005. With the development code SyB L-0501 (FD formulation), the Company began the phase I clinical trial in 2006 for indications for recurrent/refractory low-grade non-Hodgkin's lymphoma (NHL) and mantle cell lymphoma (MCL), and in 2010, it acquired manufacturing and marketing approval. It progressed licensing activities during this time, and in 2007, it expanded the target areas for the exclusive development and marketing rights in China, South Korea, Taiwan, and Singapore. Then with Eisai Co., Ltd. <4523> it concluded licensing agreements for Japan in 2008 and for South Korea and Singapore in 2009. Due to changes in Eisai's business strategy, the domestic licensing agreement was terminated on the deadline of December 9, 2020, and the Company transitioned to its own sales system. It has also terminated the agreements for South Korea and Singapore during FY12/21. In addition, with the progress made in the switch from the FD formulation to the RTD formulation, the Company terminated the marketing agreements for China and Taiwan during FY12/21.

TREAKISYM® was launched in the Japanese market in December 2010, and since then, the Company has progressed its development to expand its indications. In 2016, it acquired marketing approval for chronic lymphocytic leukemia (CLL) and untreated (first line of treatment) low-grade NHL/MCL, and then in March 2021, it acquired approval for r/r DLBCL, so sales are expected to increase from the rise in the number of patients for which it is indicated. Also, in 2017, it concluded an exclusive development and marketing rights agreement for Japan with Eagle Pharmaceuticals, Inc. <EGRX> (U.S.) for the TREAKISYM® liquid type RTD formulation/RI administration (development codes: SyB L-1701/SyB L-1702)*.

* The FD formulation, which the Company has purchased from Astellas Pharma up to the present time, has to be dissolved at a medical site at the time of use (which requires about 3 hours, including the adjustment time). But this work is not required with the liquid formulation, so it has the advantage of greatly reducing the burden placed on medical practitioners. Also, the only difference between the RTD formulation and the RI administration is the volume of diluted physiological saline, which is diluted to 250ml in the RTD formulation and to 50ml in the RI administration. Therefore, for the intravenous injection time, the RTD formulation takes the same time as the FD formulation, which is 60 minutes, but the RI administration reduces this to only 10 minutes, greatly reducing the burden on the patient.

Also, as the second in-licensed product, the Company concluded an exclusive development and marketing rights agreement in 2011 for Japan and South Korea with Onconova for rigosertib (development codes: SyB L-1101 (intravenous formulation) / SyB C-1101 (oral formulation)) as a development candidate indicated for myelodysplastic syndrome (MDS)*. Moreover, in September 2019, it concluded an exclusive global development, manufacturing, marketing, and licensing agreement with Chimerix for BCV for all viral diseases excluding smallpox. The features of BCV are that compared to cidofovir (CDV; unapproved in Japan), it has high antiviral efficacy and safety and is effective against multiple DNA viruses.

* MDS is a disease in which the patient cannot produce normal blood cells due to abnormalities in the hematopoietic stem cells in their bone marrow, causing a decrease in normal blood cells and symptoms such as anemia, infection, and hemorrhage. It is also an intractable disease that is highly likely to transition to acute myeloid leukemia, and frequently occurs in the elderly.

Technology in-licensing agreements

Name	TREAKISYM®	Rigosertib sodium	Brincidofovir
Development codes	SyB L-1701 (RTD formulation)/ SyB L-1702 (RI administration)	SyB L-1101(Intravenous formulation)/ C-1101(Oral formulation)	SyB V-1901(Intravenous formulation)
In-licensing partner	Eagle Pharmaceuticals (U.S.)	Onconova Therapeutics (U.S.)	Chimerix (U.S.)
Date agreement was concluded / agreement period	September 2017 / Product patent period or the market-exclusive period, whichever is longer	July 2011 / 10-year period from the first product sales (7 years in South Korea), the market-exclusive period, or the patent validity period, whichever is longest, in each country	September 2019 / Each royalty period is 10 years from the start of sales, the patent period, or the market-exclusive period, whichever is longest, for each product's indication and for each country. The agreement deadline is when the final royalty period expires
Content of the main agreements	Exclusive development and marketing rights in Japan	Exclusive development rights and marketing rights in Japan and South Korea	Exclusive global license agreement concerning the rights to develop, manufacture, and commercialize BCV in all DNA virus indications excluding smallpox

Source: Prepared by FISCO from the Company's securities report and news release

History

Date	Summary
March 2005	Established SymBio Pharmaceuticals Limited at Minato-ku, Tokyo
December 2005	Concluded a license agreement with Astellas Pharma GmbH (Germany) to acquire exclusive development and marketing rights in Japan for anti-cancer agent Bendamustine Hydrochloride
March 2006	Obtained manufacturer's license (packaging, labeling and storage) from Tokyo Metropolitan Government
March 2007	Concluded a license agreement with Astellas Deutschland GmbH (Germany) to acquire development and marketing rights in China, Taiwan, South Korea and Singapore for anti-cancer agent SyB L-0501
August 2008	Concluded a license agreement with Eisai Co., Ltd. to grant co-development and marketing rights in Japan for anti-cancer agent SyB L-0501
March 2009	Concluded sublicense agreement with Cephalon, Inc. (U.S.) to grant development and marketing rights in China for anti-cancer agent SyB L-0501
May 2009	Concluded a license agreement with Eisai to grant co-development and marketing rights in South Korea and Singapore for anticancer agent SyB L-0501
September 2010	Launched SYMBENDA® (generic name: bendamustine hydrochloride) in Singapore for the treatment of low-grade non-Hodgkin's lymphoma and chronic lymphocytic leukemia
October 2010	Acquired manufacturing and marketing approval of anti-cancer agent for malignant lymphoma TREAKISYM® in Japan (launched in December 2010)
July 2011	Concluded a license agreement with Onconova Therapeutics, Inc. for anti-cancer agents SyB L-1101/SyB C-1101
October 2011	Launched SYMBENDA® (generic name: bendamustine hydrochloride) in South Korea for the treatment of chronic lymphocytic leukemia and multiple myeloma
October 2011	Listed on Osaka Securities Exchange JASDAQ Growth Market
February 2012	Launched INNOMUSTINE® in Taiwan for the treatment of low-grade non-Hodgkin's lymphoma and chronic lymphocytic leukemia
October 2015	Concluded a licensing agreement with The Medicines Company (U.S.) to acquire exclusive development and marketing rights in Japan for post-operative, self-administered pain-management medication, SyB P-1501 (the agreement ended in November 2017)
May 2016	Established SymBio Pharma USA, Inc. at Menlo Park, California, USA
August 2016	Acquired manufacturing and marketing approval of anti-cancer agent for malignant lymphoma TREAKISYM® in Japan for the additional indication of chronic lymphocytic leukemia
December 2016	Acquired manufacturing and marketing approval of anti-cancer agent for malignant lymphoma TREAKISYM® in Japan for the additional indication of first-line treatment of low-grade non-Hodgkin's lymphoma and mantle cell lymphoma
September 2017	Concluded a license agreement with Eagle Pharmaceuticals, Inc. to acquire development and marketing rights in Japan for bendamustine liquid formulations (RTD formulation and RI administration) *RTD: Ready-to-dilute, RI: Rapid Infusion
October 2017	Filed for arbitration for damages against The Medicines Company (U.S.) due to the non-fulfillment of the licensing agreement
July 2018	TREAKISYM® was newly listed as the standard treatment for malignant lymphoma in the 2018 edition of the Japan Society of Hematology's Guidelines for the Treatment of Hematopoietic Tumors,
September 2019	Concluded an exclusive global license agreement with Chimerix Inc. (U.S.) concerning the rights to develop, manufacture, and commercialize the antiviral drug, brincidofovir (excluding smallpox)
September 2020	In the final arbitration ruling for the claim for damages filed against The Medicines Company (U.S.) due to the non-fulfillment of a licensing agreement, the Company will receive from the Medicines Company 50% of its expenses relating to the arbitration proceedings, including attorneys' fees.
December 2020	Start of own sales of TREAKISYM®
January 2021	Concluded a joint research agreement with The Institute of Medical Science, The University of Tokyo to search for new indications for bendamustine and rigosertib
March 2021	Submitted an IND application to the FDA in the U.S. for a global joint clinical trial indicated for adenovirus infections (in infants) after hematopoietic stem cell transplantation
March 2021	Acquired marketing approval for a TREAKISYM® and rituximab combination therapy (BR therapy) and TREAKISYM®, rituximab, and polatuzumab vedotin combination therapy (P-BR therapy) indicated for r/r DLBCL
April 2021	Obtained marketing approval of the RTD formulation of TREAKISYM® for its use in BR and P+BR therapy for the treatment of r/r DLBCL
August 2021	Reached First Patient In (FPI) in a phase II global joint clinical trial of BCV indicated for adenovirus infections after hematopoietic stem cell transplantation
February 2022	Obtained approval for a partial change to the manufacturing and marketing approval for the RI administration of TREAKISYM®

Source: Prepared by FISCO from the Company's securities report and website

Trends in the development pipeline

TREAKISYM® will expand indications to r/r DLBCL and sales are forecast to continue growing through receiving approval for RI administration

1. TREAKISYM® (generic name: bendamustine hydrochloride)

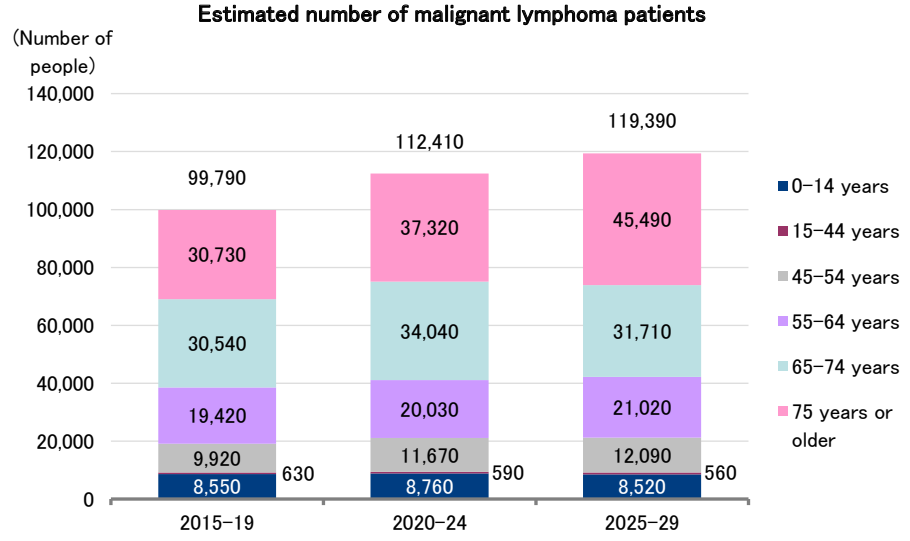
TREAKISYM® is an anticancer agent for malignant lymphoma. Malignant lymphoma is a disease in which lymphocytes, which are a type of white blood cell, undergo canceration (tumorification) and lumps (masses) can grow in lymph nodes distributed throughout the body and organs other than lymph nodes (such as the stomach, intestines, thyroid, spinal cord, lung, liver, skin, and eyes). It is the most frequent disease among blood cancers, with patients in Japan surpassing 30,000 annually, and the number of patients requiring treatment is predicted to increase gradually going forward as the elderly population grows. Malignant lymphoma is mainly divided into Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL), with about 90% of cases in Japan being NHL. It is classified into low-grade, medium-grade, and high-grade according to the progression rate of the symptoms, and there are various disease types.

Types of non-Hodgkin's lymphoma

Type according to grade	Non-Hodgkin's lymphoma type (disease type)
Low grade: Indolent lymphoma (progresses yearly)	Follicular lymphoma (grade 1, 2), MALT lymphoma, lymphoplasmacytic lymphoma Mycosis fungoides, Sezary syndrome, chronic lymphocytic leukemia / small lymphocytic lymphoma, etc.
Medium grade: Aggressive lymphoma (progresses monthly)	Follicular lymphoma (grade 3), mantle cell lymphoma, diffuse large B-cell lymphoma Peripheral T cell lymphoma, extranodal NK / T cell lymphoma, adult T cell leukemia / lymphoma (chronic type), etc.
High grade: Highly aggressive lymphoma (progresses weekly)	Burkitt's lymphoma, acute lymphocytic leukemia / lymphoblastic lymphoma Adult T-cell leukemia / lymphoma (acute type, lymphoma type), etc.

Source: Prepared by FISCO from National Cancer Center Japan materials

Estimated number of malignant lymphoma patients



Note: Number of patients who required treatment during these periods
Source: Estimations by the Company based on cancer information service data from the National Cancer Center Japan

(1) Expansion of indications

As its sales strategy for TREAKISYM®, the Company has been working to sequentially expand its indications. It acquired marketing approval for recurrent/refractory low-grade non-Hodgkin's lymphoma (NHL) and mantle cell lymphoma (MCL) in October 2010, chronic lymphocytic leukemia (CLL) in August 2016 and untreated (first line of treatment) low-grade NHL/MCL in December 2016. Also, in July 2018, TREAKISYM® and rituximab combination therapy (BR therapy) was newly listed in the Japan Society of Hematology's Guidelines for the Treatment of Hematopoietic Tumors, and it has come to be recommended as the standard treatment option for all indications for which it has been approved. So TREAKISYM® has come to be positioned as the standard treatment for malignant lymphoma in both name and reality.

Other than the above, for CD20-positive follicular lymphoma (FL), which is a typical type of low-grade NHL, the Company acquired approval in July 2018 for partial changes relating to combination use with a new anti-CD20 antibody formulation, in addition to rituximab, and combination therapy with obinutuzumab*1 was added as a therapy option. Furthermore, in March 2019, it acquired approval for partial changes relating to pre-treatment with tumor-specific T-cell infusion therapy*2, and for the first time in Japan, TREAKISYM® can be used as a pre-treatment for the CAR T-cell therapy*3 Kymriah® intravenous drip*4.

*1 Obinutuzumab (GAZYVA®; sold by Chugai Pharmaceutical Co., Ltd.): similar to rituximab, which is recommended in the treatment guidelines domestically and overseas as a therapeutic drug for NHL, it is a glycosylated modified type II anti-CD20 monoclonal antibody that binds to CD20, a protein that expresses on B cells other than stem cells and plasma cells, and it directly attacks and destroys the B cells it targets together with the body's immune system.

*2 Tumor-specific T-cell infusion therapy: a therapy administered to patients after artificially applying and multiplying cancer specificity outside the body to the cancer patient's own T cells (a type of lymphocyte).

*3 CAR T-cell therapy (chimeric antigen receptor T-cell therapy): among tumor-specific T-cell infusion therapies, this is a therapy to introduce, amplify, and infuse into the gene-coding T cells the chimeric antigen receptors (CAR) that combine the antigen-binding site of the antibody that recognizes the membrane antigen on the tumor cell and the T-cell receptor's intracellular domain.

*4 Kymriah® intravenous drip (generic name: tisagenlecleucel; sold by Novartis Pharma KK as the first CAR-T therapy approved in Japan. In March 2019, it acquired manufacturing and marketing approval indicated for recurrent/refractory CD19-positive B cell acute lymphoblastic leukemia (B-ALL) and recurrent/refractory CD19 positive DLBCL.

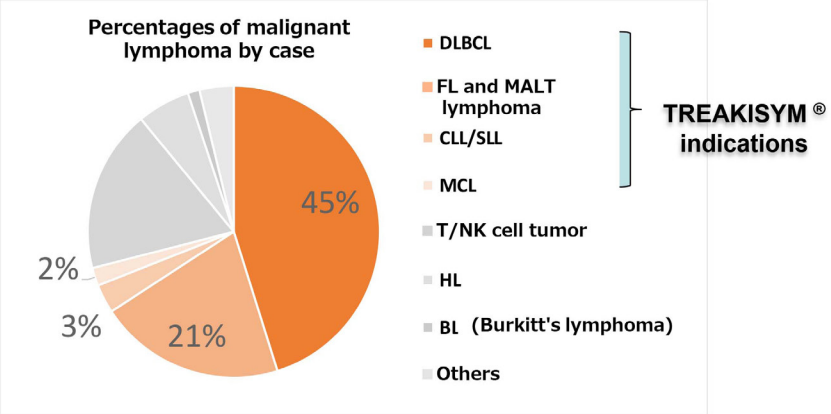
Then in March 2021, it announced the acquisition of marketing approval for r/r DLBCL *1. In addition to the combination therapy (BR therapy) with rituximab developed by the Company, the combination therapy with polatuzumab vedotin (P-BR therapy)*2 developed by Chugai Pharmaceutical Co., Ltd. <4519> was also approved. Through these marketing approvals, the number of patients TREAKISYM® is indicated for has greatly expanded (actual sales started from 2Q FY12/21).

*1 The standard treatment for untreated DLBCL is to provide a combination therapy of rituximab and chemotherapy, but recurrence is seen in approximately 40% of patients. Also, autologous stem cell transplantation (ASCT) is recommended as one treatment for r/r DLBCL, but for approximately half of patients, the relief chemotherapy provided prior to ASCT is not successful and ASCT cannot be provided. Moreover, there are many patients for whom ASCT is not suitable as a treatment, such as due to their age or complications, and it has yet to be established as the standard treatment.

*2 Polatuzumab vedotin: an anti-CD79b antibody drug compound developed by Roche <ROG>using the antibody drug conjugate technologies of Seattle Genetics Inc. (U.S.), in which humanized anti-CD79b monoclonal antibodies and tubulin polymerization inhibitors are combined with a linker. CD79b proteins are expressed specifically on many B cells, and this is a promising target in terms of developing new therapies. It is considered that polatuzumab vedotin binds with CD79b while suppressing the effects on normal cells and destroys B cells through the delivered chemotherapy agent.

Trends in the development pipeline

Details of malignant lymphomas



Source: Prepared by SymBio Pharmaceuticals based on Chihara D, et al. Br J Haematol 164:536-545,2014

Source: Reprinted from the business plan and items relating to growth potential

The results of the phase III clinical trial for BR combination therapy indicated for r/r DLBCL announced by the Company were excellent, with a complete response rate of 47.4% and an overall response rate of 76.3%. In particular, it seems that medical specialists were surprised by the level of the complete response rate for persons aged 76 years and older, which was 36.4%. There was no effective treatment for r/r DLBCL until now, and a multi-drug combination therapy that combines multiple anticancer agents (3 to 6 types) was administered as relief chemotherapy. However, it had strong side effects and little effectiveness. For these reasons, it is highly likely that the use of BR therapy and P-BR therapy, which have few side effects and high effectiveness, will spread as the standard therapies and sales of TREAKISYM® are forecast to further increase. The choice of whether to use BR therapy or P-BR therapy depends on the doctor's decision, based on factors such as the patient's symptoms and gene type*.

* In BR therapy, TREAKISYM® 120mg/m^2 (body surface area) is administered once a day for 2 consecutive days, and then not administered for 19 days. This constitutes one cycle, and it is administered for a maximum of six cycles while observing the patient's condition. In P-BR therapy, the dosage is 90mg/m^2.

(2) RTD formulation /RI administration

Sales of the RTD formulation, which is the TREAKISYM® liquid type, began in January 2021, and the full switch from the FD formulation was completed in December of the same year. The switching rate increased from approximately 20% in March 2021 to slightly less than 50% by June, and increased to slightly less than 60% as of September. Sales were started initially for existing indications except for r/r DLBCL, but it acquired marketing approval for r/r DLBCL in April 2021 and it is currently being sold for all existing indications.

The Company also received marketing approval for the RI formulation in February 2022. As of March 2022, it had obtained informal consent to switch to RI administration from approximately 90% of the medical institutions with which it conducts business, and projects that the switch to RI administration will proceed smoothly going forward. RI administration reduces the infusion time from the original 60 minutes to 10 minutes, thereby making it possible to significantly reduce the burden on healthcare professionals and patients. In particular, reducing the administration time is a major advantage for outpatients. Therefore, at FISCO we think that it is highly likely that the use of the RI formulation will spread even more at medical facilities conducting multi-drug combination therapy.

Sales progress of TREAKISYM®

Drug	Indication	Progress
SyB L-0501 (FD lyophilized powder formulation)	r/r low-grade NHL/MCL CLL First-line low-grade NHL/MCL r/r DLBCL	Approved for sale in October 2010 Approved for sale in August 2016 Approved for sale in December 2016 Approved for sale in March 2021
SyB L-1701 (RTD liquid formulation)	Already approved indications	Marketing approval in September 2020 (Marketing approval for relapsed and refractory DLBCL in April 2021)
SyB L-1702 (RI liquid formulation)	Already approved indications	Applied for marketing approval in May 2021

Source: Prepared by FISCO from the Company's results briefing materials and website

(3) Impact of generic drugs

In February 2022, it was announced that four companies (Pfizer Inc., Meiji Seika Pharma Co., Ltd., KOA ISEI CO., LTD., and TOWA PHARMACEUTICAL CO., LTD. <4553>) had received marketing approval for generic drugs using RTD formulation as a brand-name drug. There are two indications, which are low-grade NHL/MCL and pre-treatment with tumor-specific T-cell infusion therapy. Recurrent/refractory DLBCL, for which are there many patients, will not be included this time. That being said, more than 30% of the target fields will impacted by generic drugs, and there is a possibility that NHI price listings will be given and that sales will begin roughly in June 2022. However, Eagle has obtained a formulation patent and several use patents related to RI administration. The Company, which holds exclusivity rights for these patents domestically, has sent a written notification to the four companies regarding its concerns over patent infringement, and requested an appropriate response. It has also declared its intention to take legal action in cooperation with Eagle in the event that patent infringement is discovered.

The formulation patent for RTD formulation determines the density of components (bendamustine, glycol, and antioxidants) and the component ratio, among other things. Although the components of the generic drugs made by the four companies differ from what is listed in the patent, it is not necessarily the case that this difference alone clears them of patent infringement, and it appears that judgement will be made based on a comprehensive view including use patents. In fact, in the U.S., Mylan <MYL> and three other companies had tried to sell generic drugs for RTD formulation, but at a trial held in August 2021, the court ruled in favor of Eagle and declared that its patent was valid until 2031. However, it cannot be denied that a different ruling may possibly be made in Japan, so the Company must be mindful of business risks. Although RTD formulation/RI administration are products subject to price maintenance premiums*, and the prices are being maintained, if sales of generic drugs are launched, it is possible that they will no longer be applicable starting from the year when prices are revised, and that the price of the drugs will fall more than 10%.

> * Price maintenance premiums (premium to promote the development of new drugs and eliminate off-label use) are premiums applied to new drugs that meet certain criteria during the period of drug price revisions. This is a system in which drug prices are maintained or made difficult to lower until the patents expire in an aim to promote the creation of innovative new drugs and the development of unauthorized or off-label drugs.

Based on factors including the fact that indications of generic drugs make up only a little more than 30% of TREAKISYM® and that the Company's product competitiveness will substantially increase by switching to RI administration, which enables rapid infusion, FISCO believes that even if sales of generic drugs are launched, the impact on FY12/22 results will be limited. Furthermore, it appears that the Company's future policies and the impact on results will become clear in the second half of 2022.

(4) Future development plans

For TREAKISYM®, going forward, the Company will progress joint research with academia to search for new indications, and its policy is to work to further increase business value. Specifically, in January 2021 it concluded a joint research agreement with The Institute of Medical Science, The University of Tokyo, and they are conducting research into new treatments through possible developments not only for blood cancer, but also for solid cancers and other types of cancer, and also through combinations with other drugs, while utilizing AI technologies. In addition, in August of the same year it concluded a joint research agreement with Kyoto University, and they are progressing research into its inhibitory effect on LUBAC, which it has been suggested is involved in refractory activated B cell type (ABC) DLBCL.

In January 2022, the Company concluded a joint research agreement with the University of Tokyo to establish a social collaboration course entitled "Molecular Oncology" and also initiated an investigator-led phase II clinical trial indicated for autologous hematopoietic stem cell transplantation in patients with r/r DLBCL through BR therapy, pursuant to an agreement between SymBio and Saitama Medical University.

BCV expanded target treatment fields as a unique drug combining both antiviral and anti-cancer activity

2. Brincidofovir (BCV) (intravenous formulation/oral formulation)

(1) Overview and licensing agreement

BCV is a lipid conjugate of cidofovir (CDV), which is known as a treatment of cytomegalovirus (CMV) retinitis. BCV is an antiviral drug candidate whose features are that it has higher antiviral activity, exhibits antiviral activity against a wider range of viruses. In addition, academic research has recently uncovered that BCV has high anti-cancer activity, and it is gaining attention as a development candidate to enhance a niche area with high unmet medical needs where treatments have not yet been established.

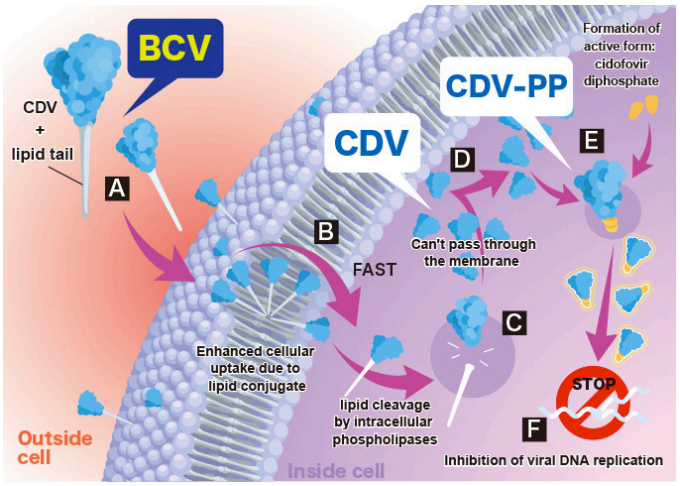
Comparison of antiviral activity (EC50)

Virus	BCV	CDV	Maribavir	Letermovir	Ganciclovir	Foscarnet	Acyclovir
ADV	0.02	1.3	-	>10	4.5-33	Inactive	>100
BKV	0.13	115	-	-	>200	Inactive	>200
EBV	0.03	65.6	0.63	>10	0.9	<500	6.2
CMV	0.001	0.4	0.31	0.005	3.8	50-800	>200

Note: EC50 (the concentration at which a drug or antibody shows a 50% maximum response from the lowest value) indicates that the lower the value, the higher the activity. BCV possesses high antiviral activity for all viruses.
Source: Prepared by FISCO from the Company's results briefing materials

BCV has a structure that conjugates a lipid chain into CDV, which allows for more efficient uptake of BCV into cells than CDV alone. Once inside target cells, the lipid chain is cleaved, releasing CDV, which is then converted to its active form of cidofovir diphosphate (CDV-PP), which fulfills the role of inhibiting viral DNA replication. Data obtained from in vivo tests and other studies shows that BCV has a much higher antiviral replication effect than CDV and other antiviral drugs through these action mechanisms. In terms of the safety profile, CDV has risks for side effects such as strong nephrotoxicity, including renal dysfunction caused by the accumulation of CDV in renal tubular epithelial cells. However, because the lipid conjugation of BCV brings no accumulation of CDV in renal tubular epithelial cells, BCV has the outstanding feature of reducing the risk of nephrotoxicity associated with CDV. CDV has been granted fast-track designation by the FDA for the prevention of cytomegalovirus and the treatment of adenovirus, while in Europe, the EMA has granted orphan drug designation for the same viruses.

How BCV works



Source: Reprinted from the Company's website

Chimerix had been developing an oral formulation of BCV, but it discontinued development because it did not obtain statistically significant results in the phase III clinical trials, and as there were some side effects, including diarrhea. Subsequently, Chimerix was looking for a partner to whom it could out-license BCV to concentrate its management resources in the anticancer agent field, and in September 2019, the Company and Chimerix concluded a licensing agreement for the global manufacture, marketing and development (excluding smallpox) of BCV. The key point for the Company's decision to in-license BCV was that it has excellent safety and functionality (high antiviral activity against a wide range of viruses), and it judged that its development was highly likely to be a success. Also, its target diseases are "rare diseases," and "niche areas with high unmet medical needs," are not only consistent with the Company's development targets, but are also the same blood disease areas targeted by TREAKISYM®, so it judged that synergies for sales would be great.

In terms of the reason why Chimerix failed to develop an oral formulation, the Company thinks that as the drug absorption rate from the digestive organs was low, it was necessary to administer a large dosage. The Company believes that an intravenous formulation could have the same effect as an oral formulation at just 10% of the dosage, so it thinks there is a lower risk of side effects and a higher probability of success. This agreement covers both the intravenous formulation and the oral formulation, as the Company believes that going forward, there is a possibility that it can resolve these issues through new improvements to the drug. Of the viral infectious diseases, the reason why smallpox alone is excluded from the agreement is that the U.S. government needs to maintain its ability to manufacture and stockpile a smallpox treatment independently within the country as a measure to counter bioterrorism*.

* In June 2021, Chimerix announced that the U.S. FDA approved its New Drug Application (NDA) for BCV Oral as a medical countermeasure for smallpox.

This licensing agreement is noted for being a global licensing agreement and for covering manufacturing rights. The use of a licensing agreement covering manufacturing rights stems from a TREAKISYM® quality defect issue that occurred in 2019. The Company understands that controlling manufacturing rights on its own and constructing systems to limit business risks to the best of its ability benefit all stakeholders, including patients, and is critical in order to aim for growth as a global specialty pharmaceutical company.

Target indications of these developments include viral infections after hematopoietic stem cell transplantation or organ transplantation, in addition to brain tumors, which the results of university research show are derived from cytomegalovirus infection, and the Company indicates its intention to advance development through antibodies for multiple sclerosis which has been revealed to largely be caused by the EV virus. In October 2021, the Company commenced operations of SymBio Pharma USA, which will serve as an integrated development base in the U.S. (the company was established in 2016, but had been in a dormant state). The Company hired a talented individual with the expertise and experience to smoothly advance clinical trials on a global scale as the vice president. It plans to increase the number of personnel from 3 in March 2022 to 10 by around 2025, and enhance its development systems.

Furthermore, in relation to the BCV licensing agreement, the Company paid a lump-sum contract payment of $5 million USD (approx. ¥540mn) to Chimerix, the original developer, in FY12/19. According to the agreement, as a future milestone, the Company will pay a maximum of $180 million USD (approx. ¥19.4bn) as a two-digit royalty payment corresponding to net sales of goods.

(2) Development plans

a) Adenovirus infections after hematopoietic stem cell transplantation

For the initial development target of BCV (formulation), the Company initiated a phase II global joint clinical trial in August 2021 indicated for infants (but including adults) with adenovirus infections after hematopoietic stem cell transplantation (scheduled number of patients: 24 cases) in the US. Adenovirus is a naturally existing virus that causes infectious diseases such as pharyngitis, tonsilitis, conjunctivitis, gastroenteritis, and hemorrhagic cystitis through the infection of areas including the respiratory organs, eyes, intestines, and urinary organs. Although cases of able-bodied individuals developing serious complications after being infected are rare, there is a high risk of serious complications when patients' immunity is lowered after hematopoietic stem cell transplantation, and there are still no treatments, so there is a strong desire for the development of treatments or preventative drugs. Every year, there are 35,000 cases of hematopoietic stem cell transplantation around the world, among which there are approximately 2,000 patients infected with adenovirus (Source: Bone Marrow Transplantation 2016, Bone Marrow Transplantation 2019).

In the phase II trial, drug dosage is divided into four groups, and aspects such as safety, tolerability, and efficacy are evaluated and the recommended dosage for the next trial is determined. As of March 2022, the trial has advanced to Group II. Going forward, the Company will strive to increase the pace through measures such as additional trial facilities in the U.S. and launching trials in the UK, and aims to complete phase II within the year. At the current stage, there are no reports of adverse events occurring, and if the trial progresses smoothly, it is predicted that the Company will progress to the phase III clinical trial in 2023. It is also possible that the Company will conclude a partner agreement and advance to the phase III clinical trial depending on the results of phase II.

b) BKV virus infections after kidney transplantation

As the second pipeline, the Company is moving ahead with preparations in order to begin phase II global joint clinical trials indicated for BK virus infections after kidney transplantation in the second half of 2022. Although trial protocols and number of patients have not yet been determined, it is assumed that they will be similar to the clinical trial for adenovirus infections after hematopoietic stem cell transplantation. The initial plan was to advance trials in Japan and Australia, but trials may be conducted in other countries as well depending on the situation.

Kidney transplantation is the only definitive treatment for end-stage renal disease. It is FISCO's view that the number of patients worldwide who require transplantation surgery is approximately 100,000. Because immunity is lowered following kidney transplantation, cases of infection are frequent; the incidence rate is less than 15% for BKV, less than 20% for CMV, and less than 10% for the varicella-zoster virus. For BKV, nearly 100% of even able-bodied individuals are infected during infancy, and although there are no issues as long as the individual is in healthy condition, in a state where immunity is lowered after organ transplantation, the virus becomes active, causing illnesses such as hemorrhagic cystitis and interstitial nephritis. Furthermore, there are even cases in which failure of the newly transplanted kidney occurs if symptoms worsen. There are 8,000 patients with BKV infections every year (Source: International Report on Organ Donation and Transplantation Activities Executive Summary 2019, April 2021 & Transplantation 2012). Currently, immunosuppressive drugs and CMV anti-infective agents are prescribed as symptomatic therapy, but the results are limited, so BKV infection is a disease with a high level of unmet medical needs for which treatment has yet to be established.

Potential needs for kidney and liver transplantation

(Unit: people)

	U.S.	EU	Japan	Other countries	Total
Kidney transplantation	39,515	28,053	1,827	30,702	100,097
Liver transplantation	13,070	10,754	395	11,565	35,784

Source: Prepared by FISCO from the Company's results briefing materials

c) CMV infection in brain tumors (GBM)

In other news, research related to antitumor efficacy is progressing in overseas academia. Specifically, it entered into a collaborative research agreement with the National Cancer Centre Singapore (NCCS) to explore anti-tumor efficacy and mechanisms in EB virus (EBN)* positive lymphoma in September 2021. Also in September of that year, a non-clinical study was initiated to investigate anti-tumor efficacy against brain tumors at the Brain Tumor Center within the Department of Neurological Surgery at the University of California, San Francisco. Additionally, in March 2022, the Company has also announced the initiation of a non-clinical study to investigate anti-tumor efficacy against brain tumors associated with CMV infections in collaboration with Brown University in the U.S.

* EBV is known for infecting roughly 50% of five-year-olds and nearly 95% of adults. Nearly all EBV infections are asymptomatic, while some result in hematological cancer or auto-immune diseases. EBV typically infects B lymphocytes and lies hidden within the cell, inactive, but becomes active due to some sort of environmental change.

CMV infections are discovered in nearly half the cases of GBM (glioblastoma) which has a particularly high degree of malignancy among brain tumors. The reactivation of CMV causes inflammation in cells, and creates a hypoxic state, thereby increasing the VEGF which is a growth factor related to the formation of new blood vessels, and it has been indicated that this may accelerate the multiplication of cancer cells. The standard treatments for GBM are surgical operations, radiation therapy, and chemotherapy, but the average life expectancy is between 15 to 20 months, and the survival rate after five years is extremely low at under 5%, so it is becoming a field where there is a strong desire for the development of effective treatments. Although there are currently many GBM treatments in development, there are none which target both CMV and brain tumors, so if BCV is proven to be effective, it is predicted that its market value will increase significantly. It is thought that the number of GBM patients around the world is approximately 30,000*.

* Company estimates based on GlobalData: Forecast of incident cases of GBM in US, 5EU, China and Japan (2027)

The Company is currently examining the results of two non-clinical studies underway at U.S. universities and working to determine whether or not will it will progress to clinical trials. The results of the non-clinical studies are projected to be confirmed in 2022, and it is predicted that the Company will initiate phase II trials in 2023 if things go smoothly.

d) Multiple sclerosis

The possibility is emerging that BCV will be developed as a treatment for multiple sclerosis. This is because it has been discovered that EBV is associated as being one cause behind the onset of multiple sclerosis. Multiple sclerosis is one type of neurological disease that causes functional impairments in areas such as the brain, spinal cord, and optic nerve due to inflammation of the central nervous system or optic nerve for some reason or another. As resurgence and remission occur over and over in repeated cycles, vision, limb functions, and cognitive abilities will decline if symptoms develop further. There are many patients in North America and Europe, with approximately 3 million people around the world and approximately 18,000 in Japan.

Multiple items are being sold as treatments, including Ocrevus which is an anti-CD20 antibody, and the scope of scales surpasses a total of ¥1.5tn. However, because the cause of onset had been unclear, there are only symptomatic treatments to hold back the progression of the disease, and root treatments have not yet been developed, so even now many companies are advancing development.

Companies with highest ranking net sales for multiple sclerosis treatments

Mechanism	Name	Sales company	Global net sales (¥bn)
Anti-CD20 antibodies	Ocrevus	Biogen/Roche/Genentech	492.2
Immunoregulation	Tecfidera	Biogen	422.2
Sphingosine 1-phosphate receptor activation	GILENYA/ IMUSERA	Mitsubishi Tanabe Pharma Corporation/ Novartis	324.6
Inhibition of dihydroorotate dehydrogenase	AUBAGIO	Sanofi	249.1
Anti-α4 Integrin antibody	TYSABRI	Biogen/ Biogen Japan	207.8

Source: Prepared by FISCO from the Company's results briefing materials

A paper published by a research team from the U.S.'s Harvard University in January 2022, which was based on an analysis of data from 1,000 patients with multiple sclerosis among the more than 10 million currently enlisted U.S. soldiers, revealed that the risk of onset is substantially higher for patients with a history of EBV infection, and that EBV is the main cause of onset for multiple sclerosis. Furthermore, according to a research paper published by a research team from the U.S.'s Stanford University in January of this year, the nuclear antigen of EBV resembles the antigen of glia cells, which proves that EBV is the mechanism which triggers multiple sclerosis through B-cells that have multiplied after EBV infection. This shows that the development of symptoms after the onset of multiple sclerosis can be prevented through treatment by quickly eliminating EBV.

The Company has declared a policy of advancing developments indicated for multiple sclerosis based on these academic research findings, and intends to formulate a development strategy in 2022. It is already in the process of advancing talks with renowned medical institutions in the same field about joint research. There are a large number of multiple sclerosis patients and the scale of clinical trials will be large, so it is thought that in the event the Company advances development, it will do so by concluding a partner agreement at a relatively early stage. With no other companies working to develop antiviral treatments, this may gain attention as a new approach.

Progress status of BCV clinical trials

Drug	Indication	Progress
SyB V-1901 (Intravenous formulation)	Adenovirus infections in patients with immunodeficiency after hematopoietic stem cell transplantation (infants and adults)	Global joint clinical phase II trial being conducted (U.S. and UK)
	BKV infection after kidney transplantation	Plans to initiate phase II clinical trial in second half of 2022 (Japan and Australia)
	GBM from CMV infections	Non-clinical studies in progress

Source: Prepared by FISCO from the Company's results briefing materials and website

e) Results of joint research with the National Institute of Infectious Diseases

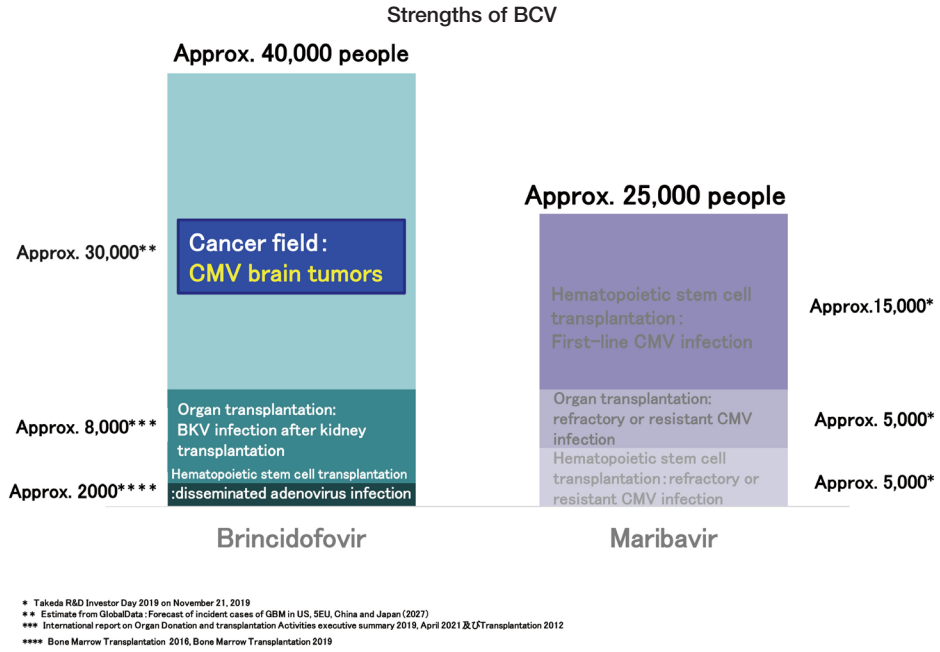
On February 24, 2022, the Company published the results of joint research with the National Institute of Infectious Diseases on BCV. In summary, based on the results of verifying the antiviral activity of BCV against 17 different serotypes of adenoviruses of previously unknown responsiveness, they were able to confirm approximately 200-fold antiviral activity in all cases compared to CDV. The research showed BCV to exhibit a high level of antiviral activity, particularly against D54 or B11, which are known in Japan to cause hemorrhagic cystitis after epidemic keratoconjunctivitis or hematopoietic stem-cell transplantation. Because there are no drugs approved as treatments for adenovirus, there is an emerging possibility that the Company will advance developments indicated for these diseases.

f) Underlying market value of BCV

In terms of antiviral treatments, maribavir (LIVTENCITY) from Takeda Pharmaceutical Company Limited <4502> received U.S. marketing approval in November 2021 as a treatment for refractory or resistant CMV infection* after organ or hematopoietic stem-cell transplantation. According to estimates by Takeda Pharmaceutical Company Limited, every year approximately 200,000 adults around the world undergo transplantation surgery, and it is understood that roughly 25% of these people face the risk of CMV infection. With the number of indicated patients, including those with first-line CMV infections after hematopoietic stem-cell transplantation, at 25,000, Takeda Pharmaceutical Company Limited projects net sales to reach between $700 and 800mn USD during the peak of maribavir. The number of patients indicated for BCV, which this company develops, is approximately 40,000 when including patients with brain tumors from CMV infections, and if patients with multiple sclerosis are also included, the potential market value of BCV will surpass ¥100bn, and attention will be given to development trends going forward.

* Four types of antiviral treatments (ganciclovir, valganciclovir, foscarnet, and cidofovir) are indicated for refractory or resistant CMV infections

Trends in the development pipeline



* Takeda R&D Investor Day 2019 on November 21, 2019
** Estimate from GlobalData:Forecast of incident cases of GBM in US, 5EU, China and Japan (2027)
*** International report on Organ Donation and transplantation Activities executive summary 2019, April 2021 及びTransplantation 2012
**** Bone Marrow Transplantation 2016, Bone Marrow Transplantation 2019

Source: From the Company's results briefing materials

Is exploring the possibilities of developing rigosertib through combinations with other drugs, including TREAKISYM®

3. Rigosertib (intravenous formulation/oral formulation)

Rigosertib is an anticancer agent candidate that has unique multi-kinase inhibitory action (which causes cancer cells to die by inhibiting the multiple kinases involved in cancer cell proliferation, invasion, and metastasis). Its licensor, Onconova, has conducted the global joint phase III clinical trials (INSPIRE trial) with the overall survival period as the primary endpoint for high-risk myelodysplastic syndrome (MDS) recurring after treatment, for which sufficient treatment efficacy cannot be obtained through the current standard treatment of hypomethylating drugs as it shows resistance to such drugs. In August 2020, it was announced that the primary endpoint had not been achieved in comparison to the doctor-selected therapy.

The Company is responsible for clinical development in Japan, and its policy is to search for new disease targets, including from the findings obtained from the INSPIRE trial's additional analysis. Specifically, through the joint research agreements concluded with the Institute of Medical Science, The University of Tokyo, and Gunma University, they are creating new treatments through combination therapies for bendamustine and rigosertib and their combined use with other existing drugs, and searching for new disease targets, including in treatment areas other than the oncology area, while utilizing AI technologies. The Company intends to formulate a new rigosertib development plan in 2022.

Also, for the development of the rigosertib oral formulation, in September 2021 Onconova announced the interim results for the doctor-led phase 1/2a clinical trial (combined used with immune checkpoint inhibitors) for progressive KRAS* mutated NSCLC (non-small cell lung cancer, stage IV). Positive results were obtained showing antitumor activity in the combination therapy, which suggest the possibility that the effectiveness of immune checkpoint inhibitors is increased by their combination use with the rigosertib oral formulation, and development trends from now on will be closely watched. The Company has completed the phase I clinical trial in Japan in 2019 to confirm the safety of a high dosage of a single drug and its tolerability among Japanese people.

* KRAS is a cancer gene. The KRAS gene usually inhibits the replication of cells, but when a mutation of the KRAS gene occurs, a signal for cells to replicate is continually sent out, which causes cancerous cells to actively replicate. Patients with mutated KRAS genes have been identified in a certain percentage of patients with certain forms of cancer, including colorectal cancer and lung cancer.

Progress on sales of rigosertib

Drug	Indication	Progress
SyB L-1101 (Intravenous formulation)	Recurrent/refractory high-risk MDS single drug	Global joint phase III clinical trial Currently conducting additional analysis
SyB L-1101 (Oral formulation)	Recurrent/refractory high-risk MDS single drug	Completed the phase I clinical trial in Japan
	Untreated high-risk MDS (combined use with AZA)	Completed the global joint phase I/II clinical trial

Source: Prepared by FISCO from the Company's results briefing materials and website

Results trends

In the FY12/21 results, become profitable for the first time through the increase in sales of TREAKISYM®

1. Summary of FY12/21 results

In the FY12/21 results, net sales increased 176.4% YoY to ¥8,256mn, operating profit was ¥1,016mn (compared to a loss of ¥4,506mn), ordinary profit was ¥1,001mn (a loss of ¥4,615mn), and profit was ¥2,032mn (a loss of ¥4,090mn), and the Company become profitable for the first time since its foundation.

FY12/21 results

(¥mn)

	FY12/20		FY12/21					
	Results	vs. net sales	Initial forecast	Results	vs. net sales	YoY Change	YoY % change	vs. plan Change
Net sales	2,987	-	9,151	8,256	-	5,269	176.4%	-894
Gross profit	866	29.0%	6,957	5,800	70.2%	4,933	569.1%	-1,156
SG&A expenses	5,373	179.9%	5,596	4,784	57.9%	-588	-11.0%	-811
R&D expenses	2,266	75.9%	2,019	1,736	21.0%	-530	-23.4%	-282
Other SG&A expenses	3,106	104.0%	3,577	3,047	36.9%	-58	-1.9%	-529
Operating profit (loss)	-4,506	-150.9%	1,361	1,016	12.3%	5,522	-	-344
Ordinary profit (loss)	-4,615	-154.5%	1,350	1,001	12.1%	5,617	-	-348
Extraordinary profit (loss)	529	-	-	0	-	-529	-	0
Profit (loss)	-4,090	-136.9%	1,149	2,032	24.6%	6,122	-	883

Source: Prepared by FISCO from the Company's financial results

Net sales increased significantly, mainly because in December 2020 the Company transitioned to an in-house structure for sales of TREAKISYM®* and as its indications were expanded to r/r DLBCL, for which there are many patients. The gross profit margin also rose greatly, from 29.0% in the same period in the previous fiscal year to 70.2%, including due to the transition to the in-house sales structure and the progress made in switching from the FD formulation to the RTD formulation. As a result, gross profit increased 569.1% YoY to ¥5,800mn. On the other hand, an inventory loss of ¥331mn of the FD formulation was recorded in 4Q primarily as a result of the switch from the FD to RTD formulation.

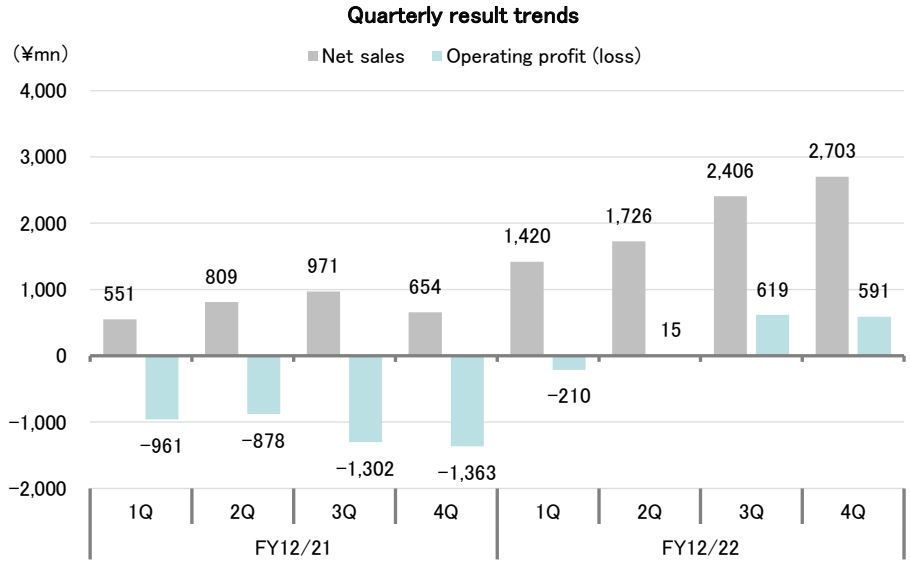
* For its distribution system, in September 2020 the Company concluded agreements with Suzuken Co., Ltd. <9987> and TOHO PHARMACEUTICAL CO., LTD., a consolidated subsidiary of Toho Holdings Co., Ltd. <8129>, and it became their general agent. It is also outsourcing logistics to S.D Collabo Co., Ltd., which is a subsidiary of Suzuken (one logistics base in both eastern and western Japan).

Conversely, SG&A expenses decreased 11.0% YoY to ¥4,784mn, mainly due to the decline in R&D expenses. R&D expenses declined ¥530mn YoY, although within this amount, ¥520mn was due to an absence of the RTD formulation milestone payment recorded in the previous fiscal year, and on excluding this factor, R&D expenses were basically unchanged YoY. Other SG&A expenses decreased ¥58mn due to a curb on other expenses despite the rise in sales costs following the transition to the in-house sales system. As a result of the above, operating profit increased ¥5,522mn YoY.

Looking at how net sales trended on a quarterly basis, although making a full-scale transition to an in-house sales structure from 1Q FY12/21 has caused net sales to increase, net sales from Eisai in 4Q FY12/20 were ¥1.9bn, so sales have in actuality decreased compared to the previous quarter. This decrease was mainly because market inventory of TREAKISYM® was greater than anticipated, and because the number of patients receiving treatment slowed due to the impact of COVID-19. In 2Q, market inventory was depleted, and sales for r/r DLBCL began in earnest in 3Q, which has led net sales to increase further, expanding to ¥2,703mn in 4Q. 4Q operating profit decreased slightly from the previous quarter to ¥591mn, but this was primarily due to the recording of ¥331mn of valuation loss.

Looking at the Company's plan, net sales fell short by ¥894mn. ¥450mn of this amount was due to market inventory being greater than anticipated, and ¥400mn was because the number of patients receiving treatment failed to grow as people refrained from consultations due to COVID-19. Although the Company was able to curb SG&A expenses more than it had been planned, operating profit fell short by ¥344mn due in part to the recording of valuation loss. On the other hand, profit managed to exceed the plan by ¥883mn partially through the recording of ¥1,275mn in deferred tax assets.

Results trends



Source: Prepared by FISCO from the Company's financial results

Has entered a phase for expanding profitability in FY12/22, and fundraising is expected to be mainly borrowings from financial institutions

2. Financial condition

At the of end of FY12/21, total assets were up ¥2,178mn compared to the end of the previous fiscal period to ¥8,452mn. Looking at the main change factors, in current assets, there were increases of accounts receivable-trade of ¥1,740mn and advance payments of ¥149mn, but there were decreases of semi-finished goods of ¥412mn, accrued consumption taxes of ¥314mn, and merchandise and finished goods of ¥146mn. In non-current assets, deferred tax assets increased ¥1,275mn.

Total liabilities were up ¥89mn compared to the end of the previous fiscal period to ¥1,707mn. The main change factors were increases in accrued consumption taxes of ¥516mn, and income taxes payable of ¥301mn, provision for product changeover of ¥186mn, but decreases in accounts payable-trade of ¥595mn, and accounts payable of ¥130mn. Net assets increased ¥2,088mn to ¥6,745mn. This was mainly due to an increase of ¥2,032mn in retained earnings due to the recording of profit and increases in share capital of ¥112mn and capital surplus of ¥113mn following the exercise of stock acquisition rights. As a result, the equity ratio rose 9.3 percentage points, from 64.3% at the end of the previous period to 73.7%.

At the end of March 2022, the Company renewed its syndicate loan (commitment line) agreement with three banks. The upper limit has been set at ¥3.15bn with the commitment period set to last until April 4, 2024.

Balance sheet and management indicator

(¥mn)

	FY12/18	FY12/19	FY12/20	FY12/21	Change
Current assets	6,038	4,887	5,815	6,747	932
(Cash and deposits)	4,821	3,910	3,848	3,860	11
Non-current assets	200	386	459	1,705	1,245
Total assets	6,239	5,273	6,274	8,452	2,178
Total liabilities	1,337	873	1,617	1,707	89
(Interest-bearing debt)	-	-	-	-	-
Net assets	4,901	4,400	4,657	6,745	2,088
Management indicator					
Equity ratio	70.1%	71.7%	64.3%	73.7%	9.3pt

Source: Prepared by FISCO from the Company's financial results

Outlook

In FY12/22 results, continued increase of sales and profit projected through increased sales of products for r/r DLBCL and an increase in the gross profit margin

1. Outlook for FY12/22

In FY12/22 results, the Company's forecast calls for net sales to increase 33.1% YoY to ¥10,992mn, operating profit to increase 74.2% to ¥1,770mn, ordinary profit to increase 74.8% to ¥1,750mn, and profit to decrease 27.2% to ¥1,480mn. Sales and profit are projected to increase mainly through expanded sales of products for r/r DLBCL. It cannot be precisely determined which indications TREAKISYM® is being used for, but by inferring through analogy from sales and outlooks for drugs used in combination, products for r/r DLBCL were launched effectively beginning in 3Q FY12/21, so the Company forecasts approximately ¥4.0bn in FY12/22 which will be a little less than a two-fold increase YoY. In addition, it forecasts sales increases through share expansion in target fields and increases in the number of treatments. The impact of generic drugs has not been incorporated into the plan at this time.

Outlook for FY12/22

(¥mn)

	FY12/21		FY12/22		Change	% change
	Results	vs. net sales	Company forecast	vs. net sales		
Net sales	8,256	-	10,992	-	2,735	33.1%
Gross profit	5,800	70.2%	8,796	80.0%	2,995	51.7%
SG&A expenses	4,784	57.9%	7,026	63.9%	2,241	46.9%
R&D expenses	1,736	21.0%	3,056	27.8%	1,319	76.0%
[BCV]	408	4.9%	1,269	11.5%	861	211.0%
Other SG&A expenses	3,047	36.9%	3,970	36.1%	922	30.3%
Operating profit	1,016	12.3%	1,770	16.1%	753	74.2%
Ordinary profit	1,001	12.1%	1,750	15.9%	748	74.8%
Profit	2,032	24.6%	1,480	13.5%	-552	-27.2%

Source: Prepared by FISCO from the Company's financial results

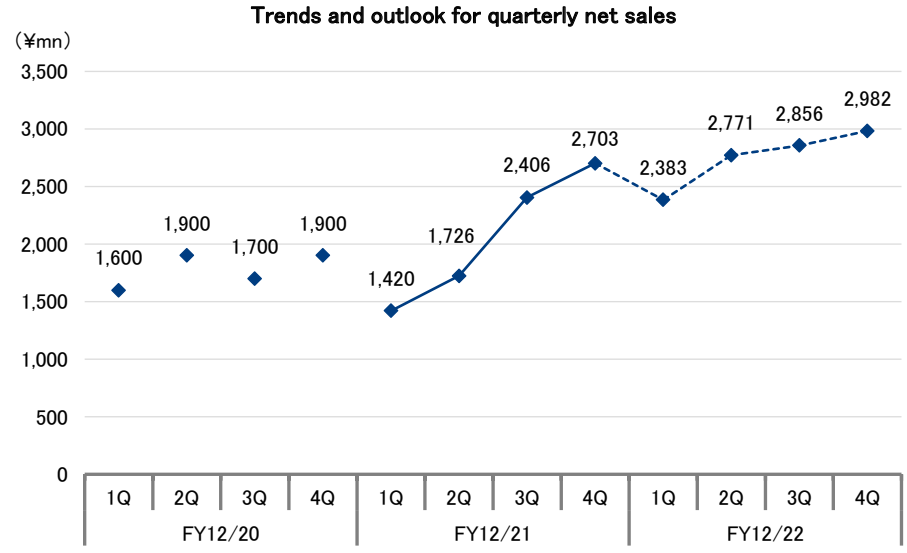
Outlook

The gross profit margin is forecast to rise from 70.2% in the previous period to 80.0% because the switch to RTD formulation/RI administration has been fully completed since the beginning of the period. The exchange rate has been progressing around ¥123 per U.S. dollar, moving toward a weakened yen since the formulation of the plan when it was ¥110 per U.S. dollar. However, purchases from Eagle for the fiscal year under review have mostly already been reserved, so profits will largely be unaffected.

The Company projects SG&A expenses to increase 46.9% YoY to ¥7,026mn. Among these, R&D expenses are projected to increase 76.0% to ¥3,056mn. The main factors behind this increase include expenses for BCV clinical trials in addition to the recording of expenses for the operation of its U.S. company that will serve as an integrated development base, and an increase in fees for joint research with academia. The Company projects that other SG&A expenses will increase 30.3% to ¥3,970mn. This increase is mainly due to the inclusion of a ¥550mn milestone payment to Eagle which will occur once total net sales of RTD formulation have reached a certain level. Additionally, discussions are underway to in-license new development candidates, but these have not been incorporated into the results forecast. With regard to domestic sales and employees whose duties are not directly related to sales, the Company intends to maintain its levels from the end of the previous period. Although there is a possibility that overseas business expenses may increase due to the continually weakening yen, the Company's view is that these expenses are within a range where they can be offset by a curb on expenses.

The main factor behind the decrease in profit is the elimination of the impact of deferred tax assets recorded in the previous period. Its U.S. company will increase from the current structure of 3 to 4 people, and plans to expand its scale up to a dozen or more employees by around 2025 because it will actively promote development overseas going forward.

The Company displays its outlook on a quarterly basis, and forecasts net sales in FY12/22 to increase 67.8% YoY to ¥2,383mn in 1Q. As for the actual status of sales, it is thought that they will fall slightly short of the plan due to the impact of patients refraining from consultations because of COVID-19, but it appears that they will proceed according to plan on a profit basis through a curb on expenses.



Note: Figures up to 4Q FY12/20 are net sales of Eisai
Source: Prepared by FISCO from the Company's results briefing materials

Advance development of BCV and aim for growth as a global specialty pharmaceutical company

2. Future business strategy

In the three-year Mid-Range Plan that the Company announced in February 2021, the numerical results targets for the plan's final fiscal year of FY12/23 were net sales of ¥12,369mn, operating profit of ¥2,099mn, ordinary profit of ¥2,088mn, profit of ¥1,778mn, and earnings per share of ¥46.5. However, because of the expansion of indications of brincidofovir, the Company is in the middle of formulating a new research development plan and has decided not to disclose a plan for FY12/23.

In terms of expenses, R&D expenses are predicted to increase up to the low ¥4.0bn range in FY12/23. This is because although these expenses were set to be roughly ¥3.8bn in the initial plan, there is an emerging possibility that the Company will newly initiate clinical trials indicated for brain tumors (glioblastoma) from CMV infections as a pipeline for BCV development. The Company intends for personnel structures to be maintained in their current state in Japan, while increasing personnel appropriately at its U.S. company.

Mid-Range Plan (announced in February 2021)

(¥mn)

	FY12/21 Plan	FY12/22 Target	FY12/23 Target
Net sales	9,151	10,985	12,369
Operating profit (loss)	1,361	1,738	2,099
Ordinary profit (loss)	1,350	1,727	2,088
Profit (loss)	1,149	1,470	1,778
Earnings per share (¥)	30.1	38.5	46.5

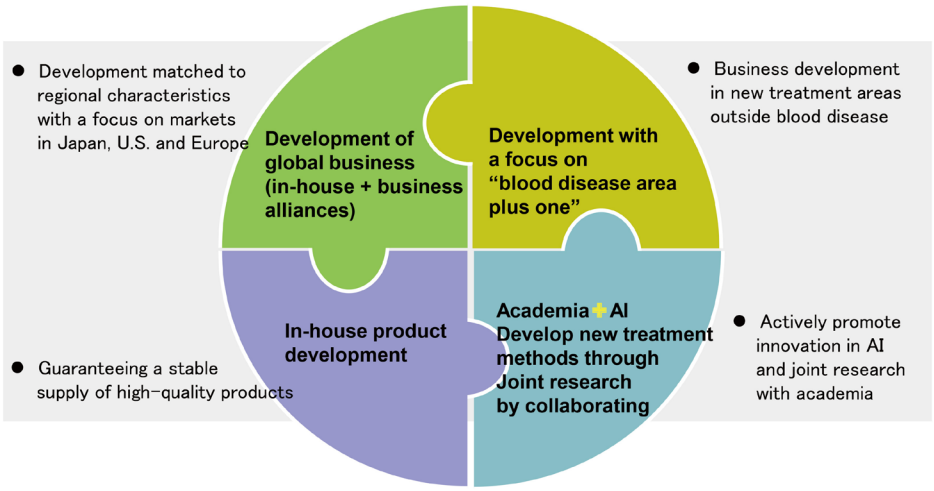
Source: Prepared by FISCO from the Company's announcement material

In the long term, the Company is forming a policy to aim for growth as a global specialty pharmaceutical company. Specifically, in addition to initiatives aimed at expanded sales of TREAKISYM®, the Company's strategy involves establishing POC in four niche areas with high unmet medical needs through BCV, and expanding its overseas business while considering entering partnership agreements. As for BCV, in order to carry out a stable supply of high-quality products, the Company plans to maximize profit by conducting in-house manufacturing (manufacturing consignment) and also uncover fundamental business values contained by each pipeline while advancing joint research with academia and others, and bridging that to maximization of business values, while simultaneously working on in-licensing new development candidates.

The Company has set "Local & Global" and "50 and 50 in 30" as the management keywords. These keywords signify taking a dramatic leap forward as a global pharmaceutical company by successfully guiding the development of BCV with the aim of increasing the percentage of total sales from overseas sales to 50% by 2030. At FISCO, we expect that the Company's corporate value will substantially improve if it succeeds at developing BCV as a treatment for adenovirus infection after hematopoietic stem-cell transplantation or organ transplantation, and as a treatment for brain tumors or cranial nerve disease caused by this virus, and are focused on future development trends.

Outlook

The Company's strategies



Source: From the Company's results briefing materials

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