COMPANY RESEARCH AND ANALYSIS REPORT

SymBio Pharmaceuticals Limited

4582

JASDAQ Growth Market

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Index

Summary

2021 is the first year of the “second foundation,” aiming to be a global specialty pharma

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.). On March 24, the Tokyo Stock Exchange (TSE) announced the Company’s shares had entered a grace period based on the standards for delisting from JASDAQ. However, in the new market segments being introduced from April 2022, the standards for results and recording profit* corresponding to the delisting standards were ended, so it will not be delisted due to this reason.

* The standard for results is a negative amount for operating profit and cash flow from operating activities in the most recent fiscal year. The standard for recording profit is a negative amount for operating profit in the fiscal year of the listing application and for operating profit for nine consecutive fiscal years following the listing.

1. Conditions set for profitability in FY12/21

The outlook for FY12/21 is for the Company to become profitable for the first time since its foundation. The three main conditions to achieving profitability are constructing its own sales system for TREAKISYM®, switching from the FD formulation (lyophilized powder formulation) to the high-value-added RTD formulation (liquid type), and expanding the indications of TREAKISYM®. Of these, it completed the construction of its own sales system in June 2020, and started its own sales from December 10, 2020 when the marketing agreement with Eisai Co., Ltd. <4523> ended. For the RTD formulation as well, it acquired marketing approval in September 2020, and began sales on January 12, 2021. Regarding the remaining condition of expanding indications, on March 23, 2021, it acquired marketing approval for BR therapy (bendamustine + rituximab) indicated for relapsed and refractory diffuse large B-cell lymphoma (DLBCL), while Chugai Pharmaceutical Co., Ltd. <4519> acquired marketing approval for P-BR therapy (polatuzumab vedotin + BR therapy), and it can sell it for the same indication from FY12/21 2Q onwards. Therefore, all conditions for profitability are in place. Assuming these conditions are achieved, net sales will increase 206.4% year on year (YoY) to ¥9,151mn and operating profit will be ¥1,361mn (a loss of ¥4,506mn compared to the previous period) for the fiscal year ending December 2021, so the Company is entering a growth stage from its previous development stage.

2. Trends in the other development pipeline

For rigosertib, in order to explore possibilities for combination therapies with existing drugs, including TREAKISYM®, the Company concluded a joint research agreement with The Institute of Medical Science, The University of Tokyo in January 2021, and it intends to decide on a new development strategy during 2021. For BCV (intravenous formulation) as well, from FY12/21 3Q, it plans to start the global joint phase II clinical trial indicated for adenovirus infections (in infants) that develop after hematopoietic stem cell transplantation. If steady progress is made, the outlook is to proceed to the phase III clinical trial in 2023. Within Japan also, it plans to progress development for an indication for viral hemorrhagic cystitis after hematopoietic stem cell transplantation. This is because no treatment for this disease has acquired approval in Japan, so there is strong demand for one from doctors. Moreover, it intends to utilize the features of BCV, which exhibits antiviral activity against a wide range of viruses, and to progress developments in the future for multi-viral infectious diseases after hematopoietic stem cell transplantation and for infections after organ transplants. In addition, it is investigating licensing-in new pipeline drugs to follow-on from BCV.

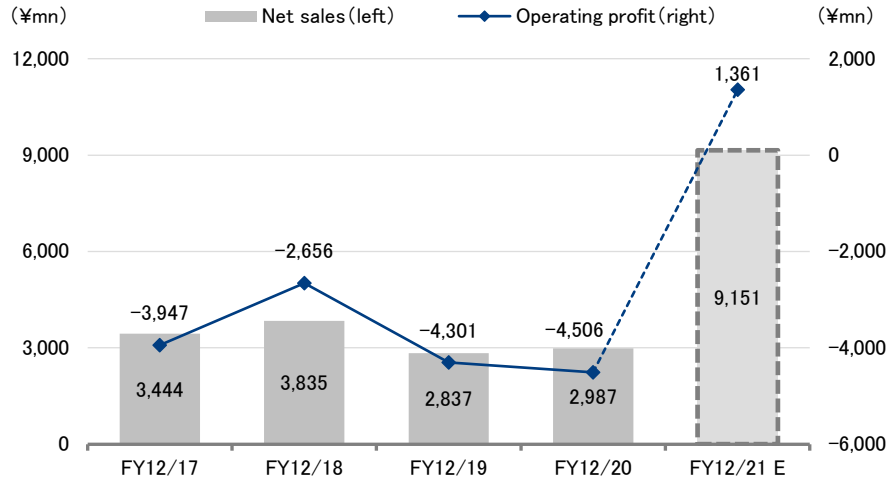
3. Mid-Range Plan

The Company's results targets in the Mid-Range Plan are net sales of ¥12,369mn, operating profit of ¥2,099mn, and EPS of ¥46.5 in FY12/23. Sales are expected to grow from expanded use of TREAKISYM® for relapsed and refractory DLBCL and the start of sales of the RI formulation (reduces the administration period for patients from the previous 60 minutes to 10 minutes) expected in the second half of 2020, use of which is forecast to spread even further due to the implementation of existing multi-drug combination therapies by medical facilities. For profits, R&D expenses are forecast to increase, mainly of BCV development expenses, but this will be absorbed by the rise in gross profit from the Company's own sales and improvement to the gross profit margin from switching to the RTD/RI formulation. The Company has positioned 2021 as the first year of its "second foundation" with the aim of becoming a global specialty pharma, and in addition to realizing sustainable growth, it aims to increase the ratio of overseas sales to 50% by 2030 through the market launch of BCV and to evolve into a global pharmaceutical company.

Key Points

- TREAKISYM® has the growth potential to approximately double sales through starting sales of the RTD formulation and expanding its indications to relapsed and refractory DLBCL
- Global clinical trials for BCV started in 2021 for adenovirus infections after hematopoietic stem cell transplantation
- Operating profit is forecast to grow by more than 20% a year from 2022 onwards due to the increase in sales of TREAKISYM®

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 drug discovery and development for underserved therapeutic areas in which development has not been progressed due to the small numbers of patients. One of its features has 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 relapsed and 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 it concluded licensing agreements for Japan in 2008 and for South Korea and Singapore in 2009*. For Taiwan, in 2012, it concluded a development and marketing agreement with InnoPharmax Inc. (Taiwan) for the FD formulation and it is conducting sales. However, its policy is to end sales in Asia as well of the FD formulation by progressing the switch from the FD formulation to the RTD formulation.

> * 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 is also progressing discussions to terminate the agreements for South Korea and Singapore.

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 relapsed and refractory 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/RI formulation (development codes: SyB L-1701/SyB L-1702)*, acquired marketing approval for the RTD formulation in September 2020 and started sales in January 2021, progressing the switch from the FD formulation. It plans to apply for marketing approval for the RI formulation during 2021.

> * The FD formulation, which it had 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 type, so it has the advantage of greatly reducing the work burden placed on medical practitioners. Also, the difference between the RTD formulation and the RI formulation is the intravenous injection time. The RTD formulation takes the same time, 60 minutes, as existing products, but the time for the RI formulation is as short as 10 minutes, so the burden on the patient is greatly reduced.

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 brincidofovir (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 also has a high likelihood of transitioning into intractable diseases and often occurs in elderly people. There are approximately 11,000 patients in Japan. The only treatment of the root cause is hematopoietic stem cell transplantation. In chemical therapy, azacitidine is used as the drug of first choice. In Japan, Vidaza® of Nippon Shinyaku Co., Ltd <4516> is on the market, and it has annual sales on a scale of ¥15bn to ¥16bn on a drug price basis.

Technology in-licensing agreements

Name		TREAKISYM®		Rigosertib sodium	Brincidofovir
Development codes	SyB L-0501 (Lyophilized powder formulation) / SyB C-0501 (Oral formulation)	SyB L-0501 (Lyophilized powder formulation) / SyB C-0501 (Oral formulation)	SyB L-1701 (RTD formulation) / SyB L-1702 (RI formulation)	SyB L-1101 (Intravenous formulation) / C-1101 (Oral formulation)	SyB V-1901 (Intravenous formulation)
In-licensing partner	Astellas Pharma (Germany)	Astellas Deutschland (Germany)	Eagle Pharmaceuticals (U.S.)	Onconova (U.S.)	Chimerix (U.S.)
Date agreement was concluded / agreement period	December 2005 / 10-year period from the first product sales or the market-exclusive period in Japan, whichever is longer	March 2007 / 10-year period from the first product sales or the market-exclusive period, whichever is longer	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 China (including Hong Kong), Taiwan, South Korea, and Singapore	Exclusive development rights 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 anti-cancer 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 formulation) *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,

Date	Summary
September 2019	Concluded an exclusive global license agreement with Chimerix (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 and TREAKISYM®, rituximab, and polatuzumab vedotin combination therapy indicated for relapsed and refractory diffuse large B-cell lymphoma

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

Trends in the development pipeline

The sales growth potential of TREAKISYM® will approximately double by expanding its indications to relapsed and refractory DLBCL

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 said to be the most common of the blood cancers, with approximately 10 out of every 100,000 people contracting it each year in Japan. 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

(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 relapsed and 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. In such ways, its position as the standard therapy for malignant lymphoma is being further solidified.

*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 non-Hodgkin's lymphoma, 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.

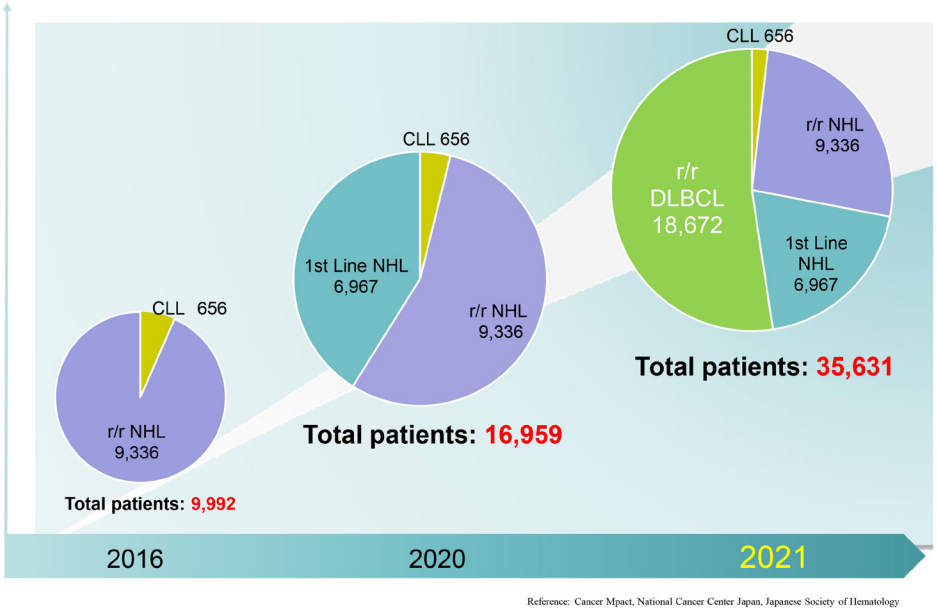
*4 Kymriah® intravenous drip (generic name: tisagenlecleucel; sold by Novartis Pharma K.K.): as the first CAR T-cell therapy approved in Japan, in March 2019, it acquired manufacturing and marketing approval indicated for relapsed and refractory CD19-positive B-cell acute lymphoblastic leukemia (B-ALL) and relapsed and refractory CD19-positive DLBCL. Then on March 23, 2021, it was announced that it had acquired marketing approval for relapsed and refractory DLBCL, which is of the same scale in terms of the number of targeted patients as its existing indications*5. In addition to the combination therapy with rituximab (BR therapy) that was developed by the Company, BR therapy combination therapy with polatuzumab vedotin*6 (P-BR therapy), which was developed by Chugai Pharmaceutical, was also approved. Through this marketing approval, the number of patients it is indicated for has doubled compared to previously, so the market value of TREAKISYM® has risen significantly.

*5 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 relapsed and refractory 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.

*6 Polatuzumab vedotin: an anti-CD79b antibody drug compound developed by Roche using the antibody drug conjugate technologies of Seattle Genetics Inc., 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

The number of patients indicated has approximately doubled
from the additional indication for r/r DLBCL



Source: From the Company's results briefing materials

The results of the phase III clinical trials announced by the Company were excellent, noting a complete response rate of 47.4% and an overall response rate of 76.3%. In particular, it seems that the medical specialists were surprised by the level of the complete response rate for persons aged 76 years and older, which was 36.4%. Also, it seems that the follow-up study (on the total survival period) that is currently being conducted is obtaining excellent data that is better than expected, and the details are scheduled to be announced during the first half of 2021.

Expects to acquire approval for additional indications
for r/r DLBCL (BR120 therapy) in 1H of the current period

◆ **Results of the phase III clinical trial**

Complete response rate(CR) :47.4%、Response rate(ORR):76.3%

Types	(number of cases)	Response rate (%)	Comprehensive effects (%)	Complete response (%)
Total number of cases	38	CR; 47.4 / PR; 28.9	76.3	47.4
Response rate by age				
Under 65 years	7	CR; 71.4 / PR; 14.3	85.7	71.4
65 to 75 years	20	CR; 45.0 / PR; 30.0	75.0	45.0
76 years and older	11	CR; 36.4 / PR; 36.4	72.7	36.4

◆ **Currently implementing the trial's follow-up study (primary endpoint: total survival period)**

→ Plans to announce the data in 1H

Source: From the Company's results briefing materials

Currently, there is no effective treatment for relapsed and refractory DLBCL, and multi-drug combination therapy that combines multiple anticancer agents (3 to 6 types) is administered as relief chemotherapy. However, it has strong side effects, so there are hopes for the development of new highly effective therapeutic drugs and treatments with few side effects. BR therapy and P-BR therapy have been approved, and it is highly likely that the use of these therapies will spread as standard therapies. There have also been request documents submitted by patient groups and related academic societies to be able to use BR therapy at an early stage, so sales of TREAKISYM® are forecast to increase further with the start of sales in FY12/21 2Q. 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 the 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/RI formulation

The Company acquired manufacturing and marketing approval for the RTD formulation, which is the TREAKISYM® liquid type, in September 2020 and started sales on January 12, 2021. The RTD formulation reduces the work burden at medical sites as it does not require dissolving, and it is expected that the switch from the FD formulation to the RTD formulation will be progressed. It is considered that the percentage of sales from the RTD formulation will rise from 20% in FY12/21 1Q to 91% in FY12/21 4Q, the majority of which will be from switching to the RTD formulation. In one year from the start of sales of the RTD formulation, its market penetration rate has reached 97%* in the U.S., so this increase is considered to be feasible. Currently, sales of the RTD formulation have started for existing indications except for relapsed and refractory DLBCL, but the Company applied for approval for relapsed and refractory DLBCL as well on March 25. As the application and approval procedure is simple, the outlook is that approval will be acquired within a few months, and it seems sales could start in the second half of 2021.

* In the U.S., sales of the RTD formulation BENDEKA® began in January 2016, and its market penetration rate had reached 70% by May of the same year and 90% after one year.

For the RI formulation also, the observation period for the clinical trials, which started in November 2018, was completed in September 2020, and the plan is to apply for marketing approval in the first half of 2021. If the investigation proceeds steadily, sales are expected to start in the second half of 2022. The RI formulation reduces the intravenous administration period from 60 minutes to 10 minutes, so it not only helps medical practitioners, it also contributes to improving patients' QOL. Therefore, the replacement of the RTD formulation with the RI formulation will progress from the second half of 2022, and moreover as its advantages are significant, there is a high likelihood it will be introduced at medical facilities that are currently providing multi-drug combination therapies and it is expected to contribute to further sales growth as the market penetration rate rises.

The exclusive market period for the FD formulation in Japan ended in 2020, so generics may be developed. However, due to major differences in terms of functionality compared to the RTD/RI formulation, it is expected that the exclusive marketing period of TREAKISYM® will actually continue until 2031, which is when the RTD/RI formulation patent expires. Also, the price of the FD formulation is forecast to fall slightly with the drug price revisions in April 2021, but the RTD formulation has only just been launched in the market so its drug price is expected to be maintained for the time being. On the other hand, there are differences in contract conditions for purchase prices, and it seems that the prices for the RTD/RI formulation have been set low compared to the FD formulation, so switching from the FD formulation to the RTD/RI formulation will be a factor causing the profit margin to rise.

Alongside the switch from the FD formulation to the RTD formulation, the Company ended purchases of the FD formulation at the end of 2020 (it has already completed purchases for sales of the FD formulation from 2021 onwards), while it has also completed processing all of its debts and credits with Astellas Pharma. Therefore, it also plans to end sales of the FD formulation in Asia, and it is concentrating on sales of TREAKISYM® in Japan.

Sales progress of TREAKISYM®

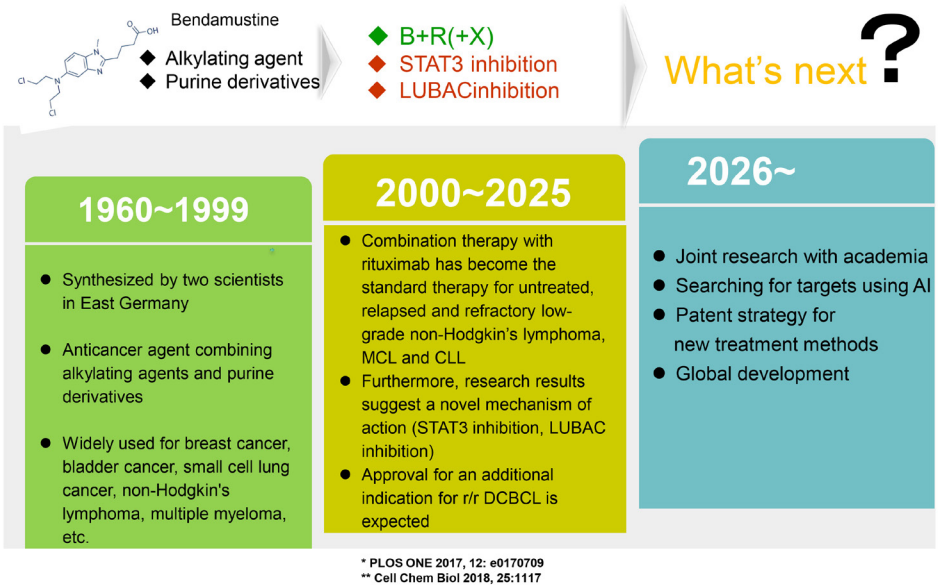
Drug	Indication	Progress
SyB L-0501 (FD lyophilized powder formulation)	r/r low-grade NHL/MCL	Approved for sale in October 2010
	CLL	Approved for sale in August 2016
	First-line low-grade NHL/MCL	Approved for sale in December 2016
	r/r DLBCL	Approved for sale in March 2021
SyB L-1701 (RTD liquid formulation)	Already approved indications (except for r/r DLBCL)	Marketing approval in September 2020 (applied for approval for r/r DLBCL in March 2021 and scheduled to acquire it during 2021)
SyB L-1702 (RI liquid formulation)	Already approved indications	The clinical trial observation period ended in September 2020 and plans to apply for marketing approval in the first half of 2021)

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

(3) Future development plans

The development of TREAKISYM® for malignant lymphoma will complete the current round of expansion of indications, but the Company is progressing 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 plan to progress research, including into possibilities for new treatments through developments not only for blood cancer, but also for solid cancers and other types of cancer, and through combinations with other drugs, while utilizing AI technologies.

Searching for the "undiscovered power" of TREAKISYM®



Source: From the Company's results briefing materials

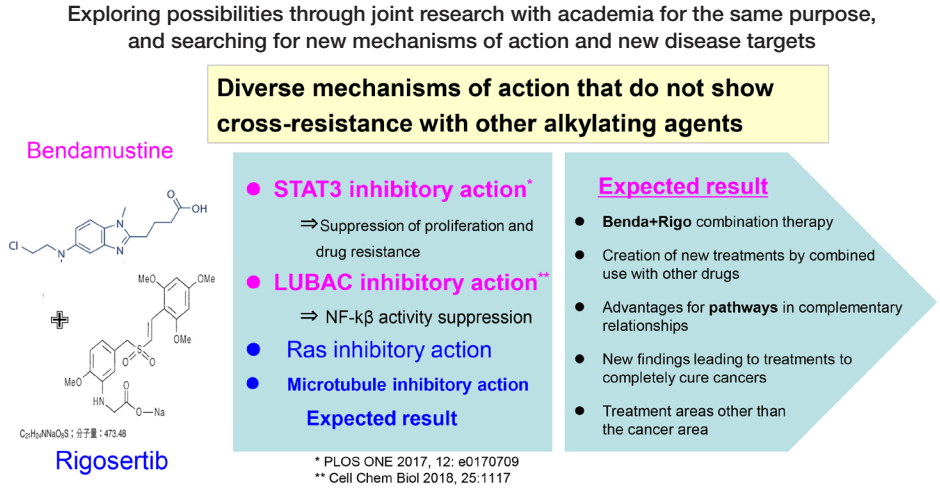
Is exploring the possibilities of developing rigosertib through combinations with other drugs, including TREAKISYM®

2. 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 progressed the global joint phase III clinical trials (INSPIRE trial) with the overall survival period as the primary endpoint for high-risk myelodysplastic syndrome (MDS), for which sufficient treatment efficacy cannot be obtained through the current standard treatment of hypomethylating drugs, which recurs after treatment, and which shows resistance to hypomethylating 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 the 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, in January 2021, it concluded a joint research agreement with The Institute of Medical Science, The University of Tokyo to search for new indications for bendamustine and rigosertib. In the future, they will create new treatments through combination therapies and combined use with existing drugs, and search for new disease targets, including in treatment areas other than the cancer area.

When using a treatment with multiple anticancer drugs, there is the risk that the impact of the side effects will be amplified through drugs that have the same side effects. But the side effects of bendamustine and rigosertib are different, so it seems that their combination therapy is possible. Professor Toshio Kitamura of Advanced Clinical Research Center, The Institute of Medical Science, The University of Tokyo is one of the lead researchers in the field of hematopoietic tumors, and he is using hematopoietic tumor models to search for findings to develop new treatments. Going forward, while performing gene analysis utilizing AI technologies, he will search for the possibilities for new cancer treatments and therapeutic drug candidates for new diseases in areas other than cancer. Based on the joint research, the Company intends to formulate a rigosertib development plan during 2021.



Source: From the Company's results briefing materials

Also, for the development of the rigosertib oral formulation, Onconova is conducting a global joint phase I/II clinical trial (combined use with azacitidine) for untreated high-risk MDS, and the results are suggesting that it is effective and safe. Also, as a new indication, in June 2020, it started a doctor-led phase I/IIa clinical trial (combined use with immune checkpoint inhibitors) for progressive KRAS*-positive NSCLC (non-small cell lung cancer, stage IV), and this development is attracting attention. The Company completed the phase I clinical trial in Japan in 2019 in order to confirm the safety of a high dose 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 considerable percentage of patients with certain forms of cancer, including colorectal cancer and lung cancer.

State of progress of rigosertib's development

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

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

In 2021, started a global trial for brincidofovir for adenovirus infections after hematopoietic stem cell transplantation

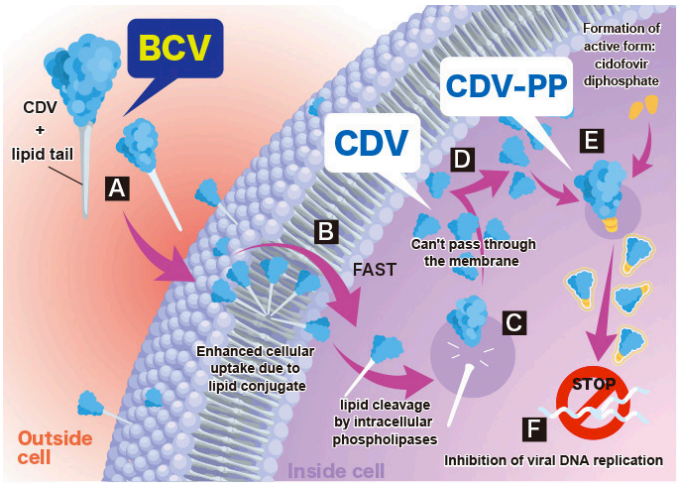
3. Brincidofovir (intravenous formulation/oral formulation)

a) Overview and licensing agreement

Brincidofovir (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, and has a superior safety profile compared to CDV. 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 (the U.S. Food and Drug Administration) for the prevention of cytomegalovirus and the treatment of adenovirus and smallpox, while in Europe, the EMA has granted orphan drug designation for the same viruses.

Trends in the development pipeline

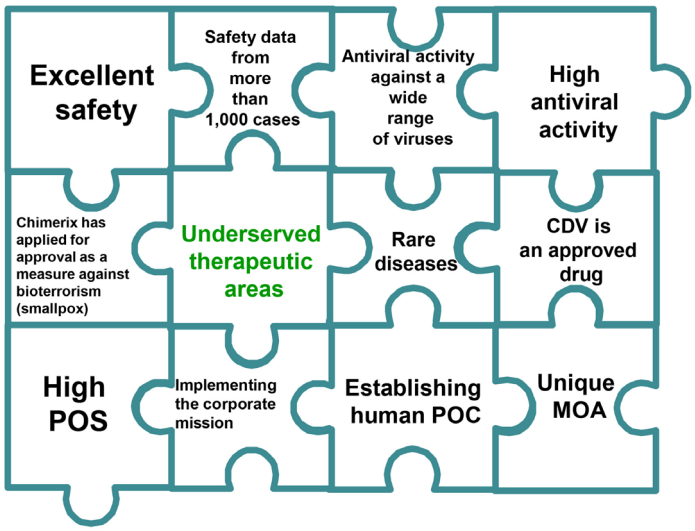
How BCV works



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, while the Company was searching for new drug agents to in-license. The timing was right for both companies, and in September 2019, they 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 "underserved therapeutic areas," which 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.

12 reasons for in-licensing BCV



Source: From the Company's results briefing materials

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 December 2020, Chimerix submitted a new drug application for BCV to the FDA for smallpox, and it announced that the investigation is scheduled to be completed by July 7, 2021. If it is approved, it is anticipated that the market value of BCV and the degree of attention placed on it will increase even more.

What is notable in this agreement is that it is a global license, and it also covers manufacturing rights. This drug will be used to treat viral infectious diseases that occur following hematopoietic stem cell transplantation or organ transplants. The organ transplant market in particular is large not only in the U.S. and Europe, but also in Asia, and the potential market scale is significant as well. TREAKISYM® has been marketed in South Korea, Taiwan, and Singapore through sales partners. However, sales volumes were small and there was only a negligible impact on the Company's business performance. If the overseas rollout of BCV is successful, it will expand the scope of overseas sales and enable it to grow as a global specialty pharmaceutical company.

Also, the quality issue for TREAKISYM® that arose in 2019 impacted the decision to have the agreement include manufacturing rights. The Company understands that controlling manufacturing on its own and building a system to suppress business risks to the fullest extent is critical in order to benefit all stakeholders, including patients, and aim for growth. It has already decided on the manufacturing outsourcer, and preparations to manufacture the investigational new drug are being progressed. In conjunction with the conclusion of the BCV licensing agreement, the Company paid developer Chimerix an upfront payment of US$5mn (approximately ¥540mn) in FY12/19 3Q, and it will pay future milestones of up to US$180mn (approximately ¥19.4bn), as well as double-digit royalties on net sales of brincidofovir products.

b) Future development plans

As its development strategy for BCV (intravenous formulation), the Company decided on its future policy during the Global Advisory Board meeting held in February 2020. Specifically, it decided the following three points: progress development utilizing the multi-virus activity of BCV, which is its strength; target multiple viral infections, including adenoviruses for which there are no treatments and medical needs are high; and conduct development as the highest priority for the infant transplant area, for which medical needs are high.

Including due to the strong wishes of board members who are medical experts, it will start the global joint phase II clinical trial for adenovirus infections after hematopoietic stem cell transplantation as the first development target. It will skip safety as it can utilize the data from the clinical trial conducted by Chimerix (cases on more than 1,000 people). Adenoviruses are viruses existing in nature and they cause infections such as pharyngitis, tonsillitis, conjunctivitis, gastroenteritis, and hemorrhagic cystitis by infecting the respiratory organs, eyes, intestine, and urinary organs. Serious cases are rare among infections in healthy people. But the risk of severe complications increases in infections in patients whose immune systems have been weakened after hematopoietic stem cell transplantation and as yet there is no treatment, so there are strong hopes for the development of treatments and prophylactic drugs. While there are few cases, the plan is to first progress development for infants and after that to widen the scope to adults and to other viral infectious diseases.

Trends in the development pipeline

On March 10, 2021, the Company submitted an IND application to the FDA, and if it proceeds smoothly, registrations of the first subjects are expected to start in 3Q of 2021. Regarding the CRO (contract research organization) to which progress of global clinical trials will be outsourced, it concluded an agreement with Syneos Health, Inc. of the U.S. in December 2020. The trial design is an open label trial that will divide the 24 subjects into 4 groups according to dosage to observe safety and tolerability. The trial's primary endpoint is the number of adverse events occurring during the trial period, and the secondary endpoint is the amount of change of the adenovirus in blood plasma in the five weeks from the start of administration. The clinical trial is scheduled to be completed in the second half of 2022, and if it obtains good results, it will progress to the phase III clinical trial in 2023, toward a possible market launch in 2026 at the earliest. It is expected that the costs of the phase III clinical trial will be on a scale of billions of yen.

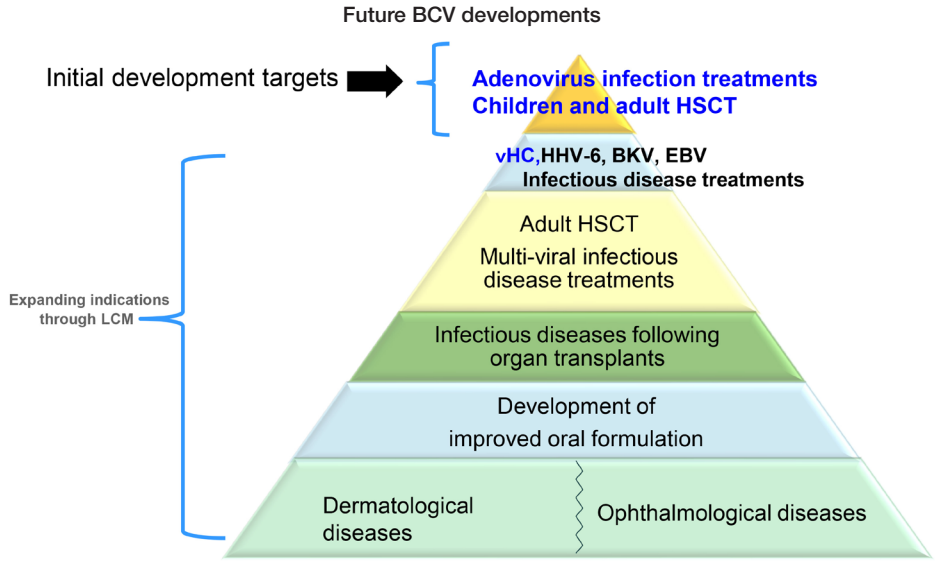
Professor Roy Chemaly of the MD Anderson Cancer Center, which is the largest bone marrow transplantation surgery-related medical facility in the U.S., announced in a paper in March 2020 that "BCV has less nephrotoxicity and bone marrow suppression, which are problems with other drugs, and it can be an excellent treatment option," indicating his support for the Company's development. In such ways, it seems that there are great expectations for BCV.

On the other hand, in Japan, the Company plans to start development for viral hemorrhagic cystitis (vHC)*1 after hematopoietic stem cell transplantation in 2021. This disease is one of the complications after hematopoietic stem cell transplantation, but as yet no therapeutic drugs have been approved for it in Japan, and while bladder perfusion is carried out as a therapy to treat it, there are cases of it being treated using imported CDV at a doctor's discretion. However, as nephrotoxicity is strong, the effects of CDV are limited and there is strong demand for development of a highly effective therapeutic drug with few side effects. Initially, the plan was to progress in advance the global trial for adenovirus infections, but due to the strong wishes, including of the Japanese Society for Transplantation and Cellular Therapy and doctors, it has been decided to progress development for vHC in parallel in Japan. Going forward, discussions will be held with the Pharmaceuticals and Medical Devices Agency to decide on the trial design. Other than for vHC, it is also conducting developments for various viral infectious diseases after hematopoietic stem cell transplantation, including HHV-6 encephalitis*2 and the BK virus, and it plans to progress developments while observing conditions.

*1 One complication after hematopoietic stem cell transplantation, in which a viral infection causes inflammation of the bladder that results in severe pain, urination disorders and hematuria (blood in the urine). There have been cases of severe complications, including renal failure and viral nephropathy, and research reports state that it occurs in 10% to 30% of cases. The cause of infant viral hemorrhagic cystitis is most often an adenovirus infection.
*2 Encephalitis that develops due to infection with the human herpes virus after hematopoietic stem cell transplantation and organ transplants. The rate of occurrence in Japan is low at 2% to 3%, but if infected, disturbances of consciousness occur and the risk of death increases. In Japan, foscarnet was approved as a therapeutic drug in March 2019, but its nephrotoxicity is high. Also, the trial data has confirmed that BCV's antiviral activity is much higher.

In addition, for viral infectious diseases after organ transplants, the Company's policy is to search for partner companies and to progress developments through collaborations. Looking to the future, it has in its sights a development to improve the oral formulation and developments in the dermatology and ophthalmology areas, and is considered to be aiming to maximize the market value of BCV by expanding indications through LCM (life cycle management). Globally, the number of hematopoietic stem cell transplantations (allogeneic transplantations) is 35,000 cases a year, while the market for organ transplants is more than 110,000 cases. So BCV's growth potential as a viral infection therapeutic drug and prophylactic drug is enormous, and we shall be paying attention to development trends in the future.

Trends in the development pipeline



Source: From the Company's results briefing materials

Results trends

In FY12/20, expenses increased to build the Company's own sales system for TREAKISYM®, so results were basically unchanged YoY

1. Overview of the FY12/20 results

In the FY12/20 results, net sales increased 5.3% YoY to ¥2,987mn, operating loss was ¥4,506mn (compared to a loss of ¥4,301mn in the previous period), ordinary loss was ¥4,615mn (a loss of ¥4,376mn compared to the same period of the previous fiscal year), and loss was ¥4,090mn (a loss of ¥4,376mn compared to the same period of the previous fiscal year), leading to results that were on par with the previous fiscal year.

FY12/20 results

(¥mn)

	FY12/19 Results	FY12/20				
		Initial forecast	Results	YoY	YoY (%)	Vs. forecast
Net sales	2,837	3,404	2,987	+149	5.3%	-416
Product sales	2,811	3,404	2,977	+165	5.9%	-426
Other sales	26	0	10	-16	-62.2%	10
Gross profit	864	1,146	866	+2	0.2%	-279
SG&A expenses	5,166	6,236	5,373	+206	4.0%	-862
R&D expenses	2,441	2,731	2,266	-174	-7.2%	-464
Other SG&A expenses	2,724	3,505	3,106	+381	14.0%	-398
Operating profit (loss)	-4,301	-5,090	-4,506	-204	-	583
Ordinary profit (loss)	-4,376	-5,134	-4,615	-239	-	518
Extraordinary profit (loss)	4	-	529	+525	-	529
Profit (loss)	-4,376	-4,803	-4,090	+286	-	712

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

Due to the prolonged impact of the TREAKISYM® (FD formulation) defective quality issue (contamination and poor external appearance), which had continued since the spring of 2019, net sales were 12% below the initial forecast. But from 2Q onwards, sales volume recovered due to the strengthening of the quality inspection system within Japan and a YoY increase in sales was secured for the full fiscal year. For the products that were determined to be unsellable due to the defective quality, cost of sales of ¥69mn was recorded as an inventory assets valuation loss (recorded ¥187mn in the previous period).

SG&A expenses increased 4.0% YoY to ¥5,373mn. R&D expenses decreased 7.2% to ¥2,266mn due to reductions in development expenses for rigosertib and TREAKISYM®, but construction of the Company's own TREAKISYM® sales system caused other SG&A expenses to increase 14.0% to ¥3,106mn. Expenses related to the construction of its own sales system (sales promotion expenses) rose from ¥733mn in the previous period to ¥1,301mn, and if excluding sales promotion expenses, other SG&A expenses decreased ¥185mn YoY following the introduction of the teleworking system in response to the novel coronavirus pandemic and efforts to reduce expenses. Also, compared to the initial forecasts, both R&D expenses and other SG&A expenses were kept low and total SG&A expenses decreased ¥862mn. R&D expenses included a milestone payment of approximately ¥500mn following the acquisition of marketing approval for the RTD formulation (recorded in 3Q).

In FY12/20, the Company recorded settlement received of ¥525mn as extraordinary profit. In October 2017, it filed a petition* with the International Chamber of Commerce (ICC) against The Medicines Company of the U.S. for damages for the non-fulfillment of a licensing agreement for the post-operative self-administered pain management medication SyB P-1501. The ICC announced its final arbitration ruling on September 1, 2020, which became this settlement received. Specifically, it ruled that The Medicines Company would pay to the Company 50% of the various costs (US$4.95mn) relating to the arbitration proceedings, including attorneys' fees.

> * In October 2015, the Company concluded an in-licensing agreement with The Medicines Company for a self-administered short-term acute pain management medication. The Company, acting in the best interests of patients, temporarily suspended new patient enrollment for the drug from April 2017 due to the concern about the continuity of The Medicines Company's business regarding the product. In October 2017, the Company filed for arbitration with the ICC seeking a payment of US$82mn as compensation for damages for the non-fulfillment of the licensing agreement. In the arbitration, the Company claims that The Medicines Company was not able to provide the Company with adequate assurance of its performance of obligations under the licensing agreement in light of its decision to discontinue commercialization activities regarding the product and withdraw from markets in the U.S. and Europe, and that such failure by The Medicines Company was a material breach of the licensing agreement. The Company then terminated the licensing agreement.

On December 10, 2020, the Company started its own sales of TREAKISYM®. It began preparations to construct its own sales system in 2019 and completed it in June 2020, and subsequently continued to work with Eisai. Regarding sales personnel, it has respectively allocated a total of 57 people, consisting of 51 MR with high levels of expertise in the blood disease area and 6 RSM (regional sales managers), to 6 blocks nationwide. Also, regarding marketing personnel, it has appointed 1 KAM (KOL key account manager) and 4 HE (hematology experts) for a total of 62 personnel (of whom, approximately 60% are contract employees). It has completed the training of the sales personnel so they can respond immediately for the RTD formulation and the expansion of indications to relapsed and refractory DLBCL, and going forward, the 62 personnel will continue to conduct sales activities.

Also, for its distribution system, on September 7, 2020, the Company concluded basic transaction agreements for the buying and selling of pharmaceuticals with Suzuken Co., Ltd. <9987> and TOHO PHARMACEUTICAL CO., LTD. (a consolidated subsidiary of TOHO HOLDINGS CO., LTD. <8129>), and it became a general agent for these two companies. It is also outsourcing logistics to S.D. Collabo Co., Ltd., which is a subsidiary of Suzuken Co., Ltd. (one logistics base in each of eastern and western Japan). For the current sales system, the Company has been highly evaluated for being able to build an organization that is particularly highly specialized even within its industry, and it is expected to contribute to increasing sales and improving the profit margin from 2021 onwards.

Has entered a phase for achieving profitability in FY12/21, and fundraising is expected to be mainly borrowings from financial institutions

2. Financial condition

Looking at the financial condition at the end of FY12/20, total assets were up ¥1,000mn on the end of the previous fiscal period to ¥6,274mn. In current assets, main factors included that accounts receivable-trade decreased ¥142mn and cash and deposits declined ¥62mn, but merchandise and finished goods increased ¥944mn. Merchandise and finished goods were not previously recorded in assets because the FD formulation purchased in the previous period was only handed over to Eisai, but due to the Company's own inspection work to address the defective quality problem, they were recorded in assets in FY12/20. Also, if the year-end level of inventory is calculated from the sales forecasts for FY12/21, this means that the Company holds approximately 5 months' worth of inventory. Although this level appears somewhat high, it is because the Company completed procurement of the amount of FD formulation it expects to sell in the future by the end of 2020. In non-current assets, main factors included that the total of software and software in progress increased ¥61mn, relating to the construction of the Company's own sales system.

Total liabilities were up ¥743mn on the end of the previous fiscal year to ¥1,617mn. Main factors included that accounts payable-trade increased ¥544mn and that unearned revenue of ¥192mn was recorded. Net assets increased ¥257mn to ¥4,657mn. Retained earnings decreased ¥4,090mn due to the recording of a loss, but the total of share capital and capital surplus increased ¥4,350mn following the exercise of stock acquisition rights. As a result, the equity ratio declined by 7.4 percentage points (pp), from 71.7% to 64.3%.

In December 2020, the Company concluded a commitment line agreement with two banks with an upper limit of ¥3bn. It had previously raised funds for business activities, mainly for R&D expenses, through equity financing by issuing stock acquisition rights. But as it is expected to become profitable from FY12/21, it has become able to borrow from financial institutions. Therefore, its policy going forward is to pay for business activities through fiscal-period earnings and borrowings from financial institutions.

Balance sheet and management indicator

(¥mn)

	FY12/17	FY12/18	FY12/19	FY12/20	Change
Current assets	4,036	6,038	4,887	5,815	927
(Cash and deposits)	2,947	4,821	3,910	3,848	-62
(Merchandise and finished goods)	362	533	-	944	944
Non-current assets	215	200	386	459	72
Total assets	4,252	6,239	5,273	6,274	1,000
Total liabilities	1,012	1,337	873	1,617	743
(Interest-bearing debt)	-	-	-	-	-
Net assets	3,239	4,901	4,400	4,657	257
Management indicator					
Equity ratio	63.6%	70.1%	71.7%	64.3%	-7.4pt

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

Outlook

The outlook for FY12/21 is that the Company will become profitable for the first time since its foundation through its own sales of TREAKISYM®, switching to the RTD formulation, and the expansion of indications

1. Outlook for FY12/21

For the FY12/21 results, the outlook is that the Company will become profitable for the first time since its foundation, with net sales forecast to increase 206.4% YoY to ¥9,151mn, operating profit of ¥1,361mn (a loss of ¥4,506mn in the previous period), ordinary profit of ¥1,350mn (a loss of ¥4,615mn), and profit of ¥1,149mn (a loss of ¥4,090mn). At FISCO, we think that it is highly likely to become profitable as it has previously achieved all of the conditions cited to become profitable; namely, constructing its own sales system, starting sales of the RTD formulation, and acquiring marketing approval for relapsed and refractory DLBCL.

Outlook for FY12/21

(¥mn)

	FY12/20		FY12/21		Change	% change
	Results	vs. net sales	Company forecast	vs. net sales		
Net sales	2,987	-	9,151	-	6,163	206.4%
Gross profit	866	29.0%	6,957	76.0%	6,090	702.6%
SG&A expenses	5,373	179.9%	5,596	61.2%	222	4.1%
R&D expenses	2,266	75.9%	2,019	22.1%	-247	-10.9%
Other SG&A expenses	3,106	104.0%	3,577	39.1%	470	15.1%
Operating profit (loss)	-4,506	-	1,361	14.9%	5,867	-
Ordinary profit (loss)	-4,615	-	1,350	14.8%	5,965	-
Profit (loss)	-4,090	-	1,149	12.6%	5,239	-

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

Net sales are forecast to increase significantly because of the start of the Company's own sales on December 20, 2020, and in addition, the start of sales of the RTD formulation on January 12, 2021, and the start of sales from 2Q for the new indication of relapsed and refractory DLBCL. On a drug-price basis, sales are expected to increase by approximately 40%, from the previous period's result of ¥8.1bn to ¥11.3bn. Breaking down this ¥11.3bn, the forecasts are for untreated low-grade NHL to contribute ¥4.1bn, other existing indications ¥4.6bn, and relapsed and refractory DLBCL ¥2.6bn. The reason for existing indications increasing from ¥8.1bn in the previous period to ¥8.7bn is that sales were restricted in the previous period due to the FD formulation defective quality problem, and as it seems that that BR therapy market penetration rate will further rise due to switching to the RTD formulation.

The rise in the percentage of sales from the RTD formulation is expected to accelerate, from approximately 20% in 1Q to around 91% by December 2021. The Company applied for marketing approval for an indication for relapsed and refractory DLBCL on March 25 and is expected to acquire approval in just a few months as the investigation is simple, so it seems that sales may start in the second half of 2021. In FY12/21, the Company estimates that the percentage of sales from the RTD formulation will reach 65% to 70%. The gross profit margin is forecast to rise rapidly from 29.0% in the previous period to 76.0% (assuming an exchange rate of ¥110 to US$1) from the Company's own sales and the progress made in switching to the highly profitable RTD formulation.

Within SG&A expenses, R&D expenses are forecast to decrease 10.9% YoY to ¥2,019mn. In the previous period, the Company incurred a milestone payment of approximately ¥500mn following the acquisition of approval for the RTD formulation, but no milestone payments are scheduled for FY12/21. Although expenses will actually increase if excluding this factor, the main reason for this increase is the higher expenses due to the start of the BCV clinical trial. Conversely, other SG&A expenses are forecast to increase 15.1% YoY to ¥3,577mn. Following the start of the Company's own sales, operating expenses (including personnel expenses) are expected to increase from ¥1,301mn in the previous period to ¥1,961mn.

Looking at the results outlook on a fiscal quarterly basis, while it will depend on the state of progress made in switching to the highly profitable RTD formulation and the pace of the sales increase for relapsed and refractory DLBCL, at FISCO we think that it is highly likely that the Company will become profitable from 2Q due to the start of sales for relapsed and refractory DLBCL.

In addition, as the business plan, the Company will apply for approval for the RI formulation by 2Q, and in 2H, its plans include beginning registrations of subjects for the BCV global joint phase II clinical trial, starting the clinical trial toward acquiring POC in Japan, starting operations at Symbio Pharma USA (it intends to recruit 1 or 2 personnel) and formulating the rigosertib development plan.

From 2022 onwards, operating profit is expected to grow by more than 20% a year from the increase in sales of TREAKISYM®

2. Mid-Range Plan

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 are net sales of ¥12,369mn, operating profit of ¥2,099mn, ordinary profit of ¥2,088mn, and profit of ¥1,778mn. It plans to continuously achieve double digit increases in sales and profits from 2022 onwards.

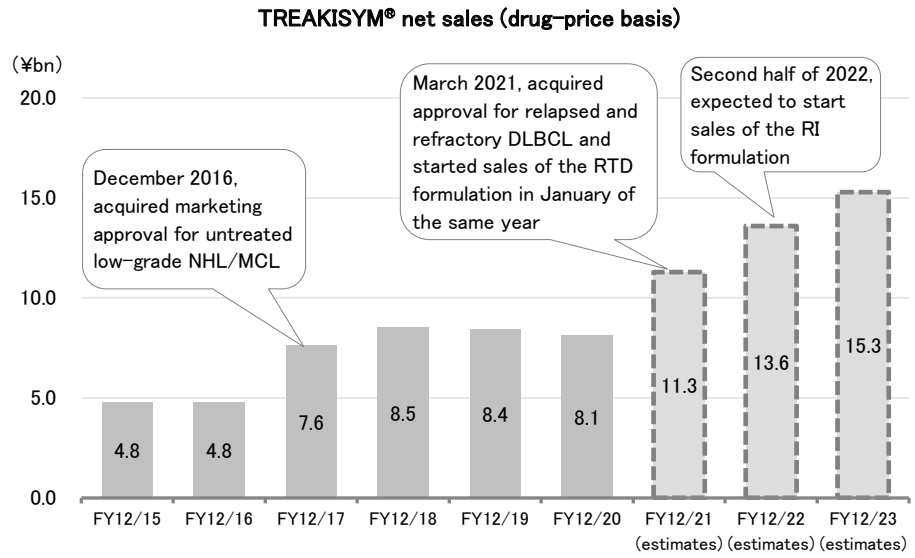
Mid-Range Plan

(¥mn)

	FY12/21 Company forecast	FY12/22 targets	Growth rate	FY12/23 targets	Growth rate
Net sales	9,151	10,985	20.0%	12,369	12.6%
Operating profit (loss)	1,361	1,738	27.7%	2,099	20.8%
Ordinary profit (loss)	1,350	1,727	27.9%	2,088	20.9%
Profit (loss)	1,149	1,470	27.9%	1,778	21.0%
Earnings per share (¥)	30.1	38.5	-	46.5	-

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

For net sales, sales will continue to increase for relapsed and refractory DLBCL, and in addition, sales of the RI formulation will start from the second half of 2022, while it seems the use of TREAKISYM® is progressing in medical facilities using multi-drug combination therapies, which will also lead to higher sales. On a drug-price basis, sales are forecast to increase from ¥8.1bn in FY12/20 to ¥15.3bn in FY12/23. Also, currently multiple pharmaceutical companies are progressing clinical trials for multi-drug combination therapies that include TREAKISYM®. So in the future, it is fully possible that treatments for existing indications and new indications using TREAKISYM® will increase, leading to sales growth from 2024 onwards. Within Japan, the situation in which in actuality the Company has exclusive marketing rights is likely to continue until 2031, which is when the patent expires for the RTD/RI formulation, and TREAKISYM® will be the driver of earnings.



Sources: the results are from interviews with the Company and from the results briefing materials for FY12/21, while the figures for FY12/22 onwards are estimates prepared by FISCO based on the FY12/21 figures

The gross profit margin is forecast to rise from 76.0% in FY12/21 to 79% in FY12/22, and to 80% in FY12/23. The profit margin is expected to increase from the progress made in switching from the FD formulation to the RTD/RI formulation. By the end of 2022, the percentage of sales from the RTD/RI formulation is forecast to be around 95%. This assumes that going forward, some medical facilities will continue to use the FD formulation, but when considering the superiority of its functions, it is anticipated that close to 100% of medical facilities will switch to the RTD/RI formulation.

SG&A expenses are forecast to continue to trend upward, increasing from ¥5,596mn in FY12/21 to ¥6,940mn in FY12/22, and to ¥7,796mn in FY12/23. Within this amount, R&D expenses are expected to increase from ¥2,019mn in FY12/21 to approximately ¥3.1bn in FY12/22 (of which, milestone payments of around ¥500mn), and to approximately ¥3.8bn in FY12/23 (of which, milestone payments of around ¥500mn). After excluding the milestone payments, they will continue to trend upwards, but this is mainly due to the increase in BCV development expenses. Conversely, other SG&A expenses are forecast to increase only slightly, from ¥3,577mn in FY12/21 to approximately ¥3.7bn in FY12/22, and to around ¥3.9bn in FY12/23. In TREAKISYM® operating expenses, logistics expenses will increase somewhat, while the Company plans to maintain the current situation for the personnel system. On the other hand, personnel expenses are forecast to increase toward BCV's global deployment. An important issue for the Company is continuing to grow after 2032, which is when the patent for the RTD/RI formulation expires. So it is searching for new development candidates to follow-on from BCV, but the current results forecasts do not incorporate any one-off payments relating to in-licensing.

With 2021 as the first year of the second foundation, is aiming to be a global specialty pharma

3. Long-term targets

Since it was founded in 2005, the Company has continuously worked to develop TREAKISYM® as a bio-venture, arriving at its current situation in 2021 when it can become profitable for the first time. So in 2021, it is transitioning from a development stage to an earnings-growth stage. Therefore, the Company has positioned 2021 as the first year of its second foundation, and it is aiming to grow as a global specialty pharma by working continuously to increase and to create business value, and at the same time, to progress overseas business development through BCV.

Specifically, the Company is aiming for sustainable earnings growth by maximizing earnings from TREAKISYM®, and in addition, by targeting the market launches of rigosertib and BCV. Moreover, it is finding the fundamental business value in each pipeline while progressing joint research with academia and others, which is leading to the maximization of business value. This also includes activities such as the in-licensing of new pipeline drugs.

The Company has set “Local & Global” and “50 and 50 in 30” as the management keywords. Their meaning is to take 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. As previously explained, BCV is expected to be an effective treatment for various viral infectious diseases after hematopoietic stem cell transplantation, while it also possible that developments will be progressed for viral infectious diseases after organ transplants and for viral infectious diseases in other areas (dermatology and ophthalmology). So it has enormous growth potential, and we shall be paying attention to development trends in the future.

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