COMPANY RESEARCH AND ANALYSIS REPORT

SymBio Pharmaceuticals Limited

4582

Tokyo Stock Exchange Growth Market

25-Jun.-2024

FISCO Ltd. Analyst
Yuzuru Sato

FISCO Ltd.
https://www.fisco.co.jp

SymBio Pharmaceuticals Limited
4582 Tokyo Stock Exchange Growth Market
25-Jun.-2024
https://www.symbiopharma.com/en/index2.html

Index

Summary

To begin multiple clinical trials in 2025 to accelerate development after establishing POC of BCV

SymBio Pharmaceuticals Limited <4582> (hereafter, also "the Company") is a bio-venture progressing developments from the clinical trial stage, targeting areas with high unmet medical needs*1 such as oncology, hematology, and viral infections. Through a "no lab or fab" strategy, the Company is promoting efficient business operations. The pipeline includes TREAKISYM®, which has already been commercialized as a treatment for malignant lymphoma, along with the antiviral drug brincidofovir (BCV) in-licensed from Chimerix Inc. <CMRX> (hereafter, Chimerix) (U.S.) and rigosertib, which it in-licensed from Onconova Therapeutics, Inc. <ONTX> (hereafter, Onconova) (U.S.)*2.

*1 Diseases for which there are no effective drugs or other treatments despite a strong need among patients and doctors
*2 As of April 2, 2024, Onconova merged with Trawsfynydd Therapeutics, Inc., a privately-held bio-venture developing next-generation antiviral drugs for influenza and other infectious diseases. The combined company has been renamed Traws Pharma, Inc.

1. Development trends of brincidofovir (BCV)

Research has established that BCV (intravenous formulation) has highly effective antiviral activity against a wide range of DNA viruses as well as anti-tumor activity. Research and development are underway in multiple disease areas with substantial unmet medical needs, such as viral infectious diseases, cancers, and neurodegenerative diseases. In 2023, the Company announced that it had established POC* in a phase II global joint clinical trial indicated for adenovirus (AdV) infections that develop after hematopoietic stem-cell transplantation. The Company plans to begin phase III global joint clinical trials, and sees potential to obtain marketing approval in the second half of 2028 if progress is as expected. Further, in May 2024, the Company announced that it had started phase II clinical trials in the U.S. indicated for cytomegalovirus (CMV) infections, with plans to conduct clinical trials indicated for glioblastoma stemming from CMV infection and NK/T-cell lymphoma in 2025 onward. The Company is also likely to begin clinical trials indicated for multiple sclerosis caused by EBV infection if positive results are obtained for animal studies conducted by the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health (NIH) in the U.S. Its development strategy is to conclude partner agreements with global pharmaceutical companies for each project to reduce its financial burden, with the goal of obtaining approval for at least two indications by 2030. Progress of these development projects (including partner agreement negotiations) will be closely watched, because BCV's business value could exceed ¥100.0bn if they are successful.

* 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.

2. FY12/23 results and outlook for FY12/24

In the FY12/23 results, consolidated net sales declined 44.1% year on year (YoY) to ¥5,589mn and the operating loss was ¥811mn (operating profit of ¥1,963mn in FY12/22). The main reason for the decline in net sales and operating profit was that a generic version of TREAKISYM® went on sale in June 2022. The resulting loss of market share and drug price cut were negative factors for earnings. TREAKISYM®'s estimated average market share in FY12/23 was in the 70% range, and had dropped to around 60% at the end of FY12/23. For FY12/24 results, the Company is forecasting a 53.1% YoY decline in net sales to ¥2,623mn and an operating loss of ¥3,702mn. A continuing double-digit decline in net sales is forecast due to the dug price cut and impact of the spread of generic drugs. The Company also expects a ¥770mn increase in R&D expenses to ¥3,409mn. Given that BCV is still under development, it is pushing ahead with new in-licensing talks for the domestic market to find an earnings source other than TREAKISYM®, aiming to conclude an agreement around fall 2024.

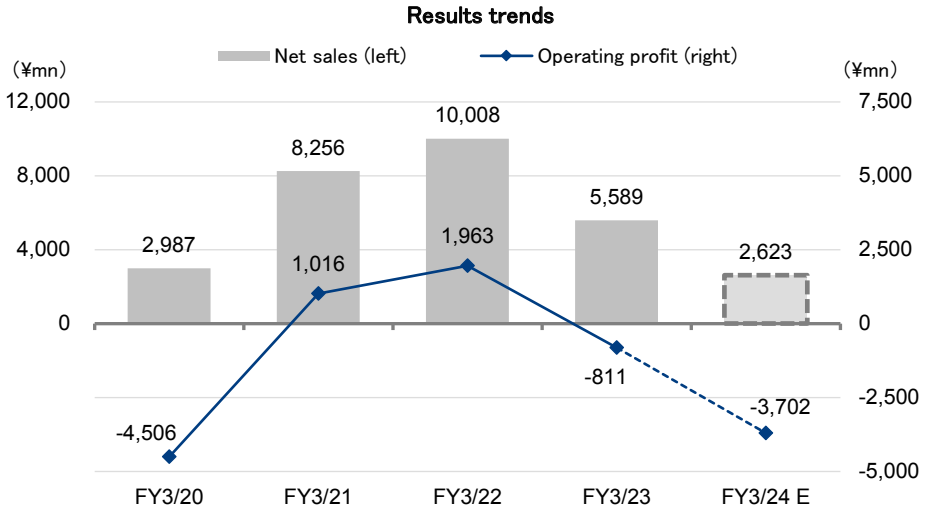
3. Growth strategy through 2030

The Company's strategy through 2030 is to develop a platform for BCV (i.e., develop BCV drugs for multiple indications) to maximize the compound's business value while earning a certain level of revenue from TREAKISYM® and drugs it plans to in-license in Japan. Having established POC for AdV infections and confirmed the optimal dosage and formulation, the Company believes it has reduced development risk for other indications and sees potential for a far shorter development period. Its priority target is to obtain approval for at least two indications by 2030, aiming to turn profitable by obtaining approval and putting BCV drugs on the market and earning partnering revenue, thereby increasing its corporate value in the medium- to long-term as a global pharmaceutical company. With regard to its policy for raising funds, the Company is exploring global partnership revenue and procuring funds from institutional investors to maintain cash on hand of ¥5.5bn to ¥6.5bn.

Key Points

- BCV is a potential game changer, expected to have therapeutic effects on multiple diseases such as viral infectious diseases following transplants, refractory tumors, and neurodegenerative diseases.
- Having established POC in humans, the development risk for BCV has been reduced and the development period likely to be shortened. The Company aims to obtain approval for two indications by 2030
- In FY12/24, the Company will push ahead with new in-licensed products and BCV partner agreement talks amid the ongoing decline in revenue from TREAKISYM®
- Aims for growth as global specialty pharmaceutical company by developing BCV platform

Summary



Note: Figures for FY12/21 and prior fiscal years represent non-consolidated results.
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 viral infections

The Company 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 viral infections, 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.

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 clinical trials in 2006 for indications for recurrent/refractory low-grade non-Hodgkin's lymphoma (NHL) and mantle cell lymphoma (MCL). It concluded a licensing agreement in 2008 with Eisai Co., Ltd. <4523> for a joint development and marketing license for Japan, acquired manufacturing and marketing approval in 2010, and began sales in December 2010. The Company continued development of TREAKISYM® to add new indications, obtaining marketing approval for chronic lymphocytic leukemia (CLL) and untreated (first line of treatment) low-grade NHL/MCL in 2016. Then in March 2021, it acquired approval for recurrent/refractory diffuse large B-cell lymphoma (r/r DLBCL), increasing the number of patients for which TREAKISYM® is indicated. In 2017, the Company concluded an exclusive development and marketing rights agreement for Japan with Eagle Pharmaceuticals, Inc. <EGRX> (U.S.) for the liquid type RTD formulation/RI administration with the development codes SyB L-1701/SyB L-1702*, and obtained marketing authorization for the RTD formulation in September 2020. It has been working to switch from the FD formulation to the RTD formulation since 2021. Following the receipt of authorization for RI administration in February 2022, 90% had switched to RI administration as of the end of December 2023. The domestic licensing agreement with Eisai was terminated on December 9, 2020, and the Company transitioned to its own sales system.

> * 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 three hours, including the adjustment time). But this work is not required with the RTD 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, which also has the benefit of 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 and orthopoxviruses such as monkeypox. BCV is a promising drug with high antiviral activity against a wide range of DNA viruses, with the potential for effective treatment of multiple diseases. The Company is engaged in joint research with overseas academic institutions. In May 2023, the Company announced that it had established POC* in a phase II global joint clinical trial indicated for adenovirus (AdV) infections that develop after hematopoietic stem-cell transplantation. Development by the Company going forward will likely be centered on BCV. It established a subsidiary in the U.S. to formulate and promote its global development strategy as well as a subsidiary in Ireland in January 2024.

> * 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.

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

Company profile

Date	Summary
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®
June 2022	Submitted a clinical trial plan notification to the PDMA for a phase II global joint clinical trial of BCV indicated for patients with BKV infection after kidney transplantation (also submitted to the TGA of Australia in August 2022)
September 2022	All rights and obligations under a licensing agreement with Chimerix, Inc. (U.S.) regarding BCV transferred to Emergent BioSolutions Inc. (U.S.)
March 2023	Concluded cooperative research and development agreement (CRADA) with the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health (NIH) in the U.S.
April 2023	Concluded CRADA with National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH) in the U.S.
May 2023	Obtained POC for humans in phase II clinical trial for BCV indicated for adenovirus (AdV) infections that develop after hematopoietic stem-cell transplantation
January 2024	Obtained use patent in Japan for BCV intravenous formulation indicated for AdV infections and other infections
January 2024	SymBio Pharma Ireland Ltd. established in Ireland
March 2024	BCV intravenous formulation obtains orphan drug designation for the treatment of AdV infection and prevention of CMV infection in immunodeficient patients

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

Development strategy for brincidofovir (BCV)

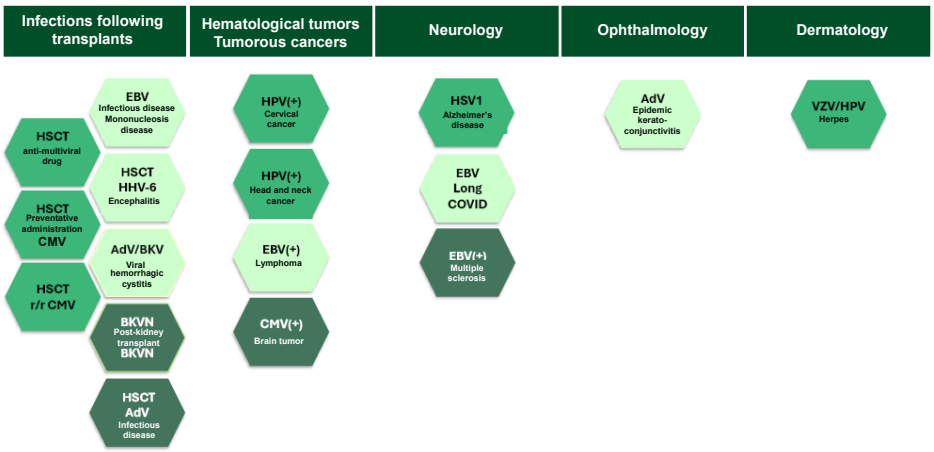
BCV is a potential game changer, expected to have therapeutic effects against multiple diseases such as viral infectious diseases following organ transplants, refractory tumors, and neurodegenerative diseases

1. Features and licensing agreement of BCV

(1) Features of BCV

BCV exhibits strong antiviral activity against a wide range of DNA viruses. Moreover, academic research has uncovered that BCV has high anti-tumor activity, not just following organ transplants, and it is attracting attention as a drug for underserved therapeutic areas where effective treatments have not yet been established, such as various complications caused by viral infections (such as hematological tumors, glioblastoma, and multiple sclerosis).

BCV is a potential game changer



Source: Reprinted from the Company's results briefing materials

Based on IC50, one of the indicators of the strength of antiviral activity, BCV has demonstrated high antiviral activity against a wide range of viruses including AdV and CMV compared to other drugs. This suggests that BCV could have therapeutic effects against many viral diseases and complications. It is rare that a single compound can treat a wide range of diseases, highlighting the potential of BCV.

Development strategy for brincidofovir (BCV)

Comparison of antiviral activity (IC50) values

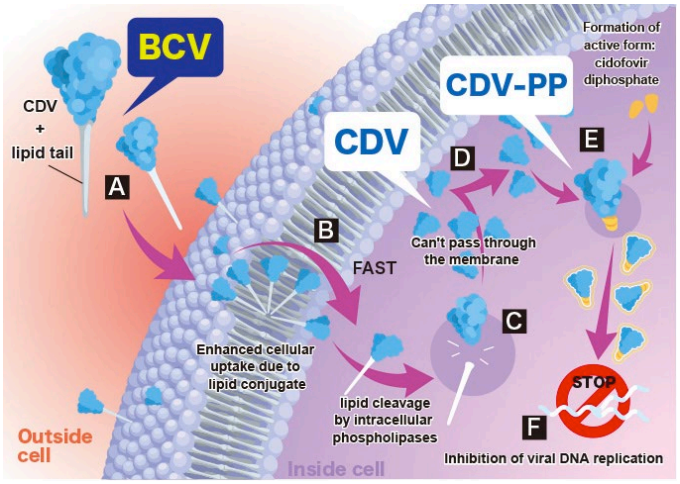
(Unit: μ M)

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
CMV	0.001	0.4	0.31	0.005	3.8	50-800	>200
EBV	0.03	65.6	0.63	>10	0.9	<500	6.2
HPV	17	716	-	-	Inactive	-	Inactive

Note: IC50 is the concentration of an antiviral that inhibits virus replication by 50%. The smaller the value, the more effective the antiviral. BCV shows high antiviral activity against a wide range of viruses.
Source: Prepared by FISCO from the Company's results briefing materials

One of the reasons for BCV's high antiviral activity is its molecular structure. BCV is a lipid conjugate of cidofovir (CDV), known as a treatment of cytomegalovirus (CMV) retinitis. Having a lipid chain attached to CDV dramatically increases the cellular uptake of BCV. Once inside target cells, the lipid chain is cleaved to release CDV, which is then phosphorylated to produce cidofovir diphosphate (CDV-PP). CDV-PP inhibits the replication of DNA viruses (i.e., has high antiviral activity). In terms of safety, Chimerix obtained U.S. Food and Drug Administration (FDA) approval of BCV oral formulation as a treatment for smallpox in 2021, confirming that the risk of severe side effects is low.

How BCV works



Source: Reprinted from the Company's website

The Company concluded a licensing agreement with Chimerix for BCV in 2019 as follows. 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. The Company approached Chimerix to discuss a licensing agreement, because it saw potential for successfully developing BCV. The key point for the 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 hematological tumor area targeted by TREAKISYM®, so it judged that synergies for sales would be easier to obtain.

Development strategy for brincidofovir (BCV)

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. The agreement covers not only an intravenous formulation, but also an oral formulation, allowing for the possibility of developing an oral formulation in the future. 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.

(2) Licensing agreement

The licensing agreement for BCV 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. BCV has been granted fast-track designation by the FDA for the treatment of AdV infections following hematopoietic stem cell transplantation. The Company also announced in March 2024 that in Europe, the EMA has granted orphan drug designation* to BCV for the treatment of AdV and prevention of CMV infections in immunodeficient patients. Orphan drug designation means that the Company is granted exclusive sales rights in the EU for 10 years after BCV goes on sale.

* In the EU, orphan drug designation is granted for treatments of serious, life-threatening diseases with a patient population under 5 per 10,000 people.

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. In September 2022, Chimerix announced that it had completed the transfer of the BCV license to Emergent BioSolutions Inc. <EBS>, but this does not affect the Company's exclusive global rights to development, manufacture, and sales of BCV.

Having established POC in humans, the development risk for BCV has been reduced and the development period likely to be shortened; target is to obtain approval for at least two indications by 2030

2. Development pipeline

BCV is currently under development for multiple indications, such as AdV infection after hematopoietic stem-cell transplantation, brain tumor, hematological tumors, and neurodegenerative diseases, including joint research with academia. Of these, the Company announced in May 2023 that it had established POC* in a phase II global joint clinical trial indicated for AdV infections that develop after hematopoietic stem-cell transplantation. Having established POC, the Company believes it has reduced development risk for other indications and sees potential for a far shorter development period. The Company expects this will facilitate partner agreement talks going forward in the process of developing a platform for BCV to maximize its business value.

Development strategy for brincidofovir (BCV)

Status of BCV development and schedule going forward

Indications	Progress	Future development plans
AdV infection in immunodeficient patients (including after hematopoietic stem-cell transplantation)	Phase II global joint clinical trial being conducted (U.S. and U.K.); POC established	Phase III clinical trial to begin in 4Q 2024
BK virus (BKV) infections after kidney transplantation	Phase II global joint clinical trial being conducted (Japan, Australia)	To review order of priority for development
Cytomegalovirus (CMV) infections after hematopoietic stem-cell transplantation	Phase II clinical trial being conducted	Phase II clinical trial to start in 2Q 2024
NK/T-cell lymphoma	Pre-clinical study being conducted in collaboration with National Cancer Centre Singapore (NCCS)	To report research results in 3Q 2024 To complete pre-clinical study in 4Q 2024 To begin global joint clinical trial in or after 1Q 2025
Glioblastoma (GBM) stemming from CMV infection	Pre-clinical study being conducted in collaboration with University of California, San Francisco	To complete pre-clinical study in 4Q 2024 To begin clinical trial in 2Q 2025
Multiple sclerosis caused by EBV infection	Pre-clinical study being conducted in collaboration with NIH/NINDS	To report results of animal studies in 3Q 2024 To complete pre-clinical study in 4Q 2024 To begin clinical trial in 4Q 2025
Herpes simplex virus (HSV) 1 Alzheimer's disease	Pre-clinical study being conducted in collaboration with Tufts University in the U.S.	To report on collaborative research results in 4Q 2024
EBV-related lymphoproliferative disease	Pre-clinical study being conducted in collaboration with NIH/NIAID	-
Polyomavirus infections	Pre-clinical study being conducted at Penn State College of Medicine in the U.S.	-

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

(1) AdV infection after hematopoietic stem-cell transplantation

For the initial development target of BCV (formulation), the Company initiated a phase IIa global joint clinical trial in August 2021 indicated for infants (but including adults) with adenovirus infections (AdV) after hematopoietic stem cell transplantation in the U.S. AdV 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 effective 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.

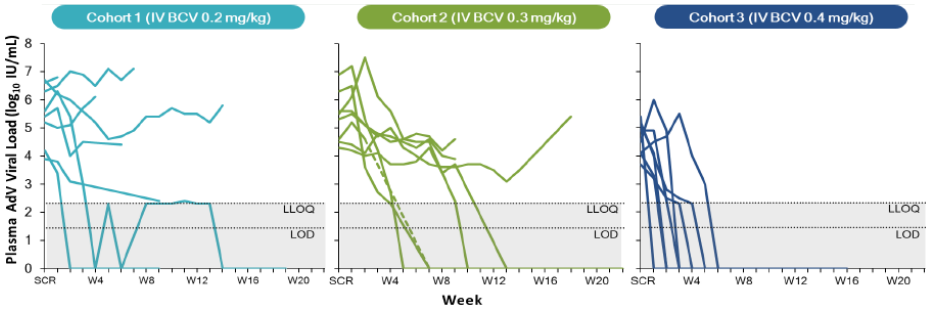
* Source: The business plan and items relating to growth potential

In the phase II clinical trial, aspects such as safety, tolerability, and efficacy (change in blood AdV levels) are evaluated and the recommended dosage for the next trial is determined. Patients were divided into 4 groups, receiving twice-weekly doses of 0.2mg/kg, 0.3mg/kg, and 0.4mg/kg*1, and once weekly dose of 0.4mg/kg. No AdV was detected in the blood of 10 patients in the group receiving 2 doses of 0.4mg/kg per week, and no AdV was detected in the blood of 90% of these patients within 4 weeks of treatment. No serious adverse events related to treatment with the oral formulation (including gastrointestinal toxicity and liver toxicity) were reported in any of the 27 patients enrolled in the study*2, which the Company understands has established POC. The publication of these results at an academic conference was well received, leading to three requests to use BCV from the families and doctors of patients who developed AdV infections after hematopoietic stem-cell transplantation. In response, the Company supplied BCV free of charge for humanitarian reasons. It has since received a report that symptoms improved for one of these patients (a teenager in the U.S.).

*1 For patients with bodyweight over 50kg, the doses were 10mg, 15mg, and 20mg, respectively.
*2 Administration was terminated due to treatment-related adverse events in 6 patients out of 27, including one patient in the group receiving 0.4mg/kg twice weekly, but these symptoms disappeared after treatment ended.

Development strategy for brincidofovir (BCV)

Clinical trial results for BCV intravenous formulation



Source: Reprinted from the Company's results briefing materials

Based on the clinical trial results, the Company applied for a use patent* in Japan, and announced that the application had been fast-tracked and the patent registered in January 2024 after just four months. The Company also plans to obtain a use patent in Europe and North America, pursuing its patent strategy to increase the business value of BCV. Having established POC, the Company thinks that it can develop treatments for other indications with a guideline dosage of 0.4mg/kg twice weekly. This means reduced development risk and much shorter development period for BCV – a significant step forward for the Company's strategy of building a BCV platform.

* Prescribes intravenous administration of a specified quantity of liquid BCV based on patient bodyweight at specified intervals over a specified period of time. Treatment must be suspended in compliance with criteria for terminating treatment.

In terms of future development plans for BCV indicated for AdV infections, the Company intends to hold talks in 1H 2024 with the regulatory authorities of the U.S., E.U., and U.K. to prepare for commencing phase III global joint clinical trials with a view to starting trials in 4Q FY12/24 at the earliest. The Company expects First Patient In (FPI) to be in 1Q FY12/25, and must pay a milestone payment of US$500mn when FPI is confirmed. For this reason, it has not factored this payment into its FY12/24 plan. The Company may obtain approval for BCV in 2H 2028 if development progresses well.

(2) BK virus (BKV) infections after kidney transplantation

The Company was conducting a phase II global joint clinical trial in Australia and Japan starting in December 2022 of BCV indicated for BK virus (BKV)* infections after kidney transplantation as a second pipeline product. However, the Company made this project a lesser priority in August 2023, because it was taking longer than expected to enroll patients and in view of development progress of other pipeline products.

* BKV is a DNA virus that belongs to the polyomavirus family. For BKV, nearly 100% of even able-bodied individuals are infected during infancy, and although there are no notable symptoms as long as the individual is in healthy condition, in a state where immunity is lowered after organ or bone marrow transplantation, the virus becomes active, causing illnesses such as hemorrhagic cystitis and interstitial nephritis. Furthermore, if symptoms worsen, there are even cases in which failure of the newly transplanted kidney occurs and the organ is lost.

Kidney transplantation is the only definitive treatment for end-stage renal disease. The number of patients worldwide who require transplantation surgery is approximately 100,000. Because immunity is lowered following kidney transplantation, there is risk of developing various viral infections, among which BKV infection is estimated to affect approximately 8,000 people* per year. 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 the early development of an effective treatment is desired. Although the Company has made this project a lower priority for development, it plans to resume clinical trials once it is ready to do so.

* Source: The business plan and items relating to growth potential

(3) CMV infections after hematopoietic stem-cell transplantation

In May 2024, the Company announced that it had started a phase II global joint clinical trial in the U.S. of BCV indicated for CMV infections after hematopoietic stem-cell transplantation*1. The number of patients with CMV infections after hematopoietic stem-cell transplantation is estimated at 25,000 worldwide per year*2. Antivirals used to treat CMV infections include Ganciclovir, Foscarnet, and CDV, as well as Livtencity (generic name: Maribavir) from Takeda Pharmaceutical Co. Ltd. <4502>, which was approved in Europe, North America, China, and Australia to treat refractory/resistant CMV infections since 2021 (Takeda applied for approval in Japan in November 2023). In clinical trials, Maribavir was not effective in 44.3% of patients, and some patients in which therapeutic effects were observed suffered a recurrence after developing resistance. Thus, a more effective treatment is being sought.

*1 Symptoms include systemic symptoms such as fever (over 38ºC), lethargy, and joint pain, and localized symptoms depending on the CMV infection site such as pneumonia, gastroenteritis, retinitis, and skin ulcers.
*2 Source: The business plan and items relating to growth potential

Clinical trials previously conducted by Chimerix demonstrated high efficacy of the oral formulation of BCV as a treatment for CMV infections. The Company will now conduct clinical trials of the intravenous formulation, which has demonstrated superior safety, and we at FISCO see a strong possibility of positive results. We think the Company aims to obtain approval by 2030. Takeda Pharmaceutical has estimated peak sales of US$700mn to US$800mn for Maribavir, which suggests a similar level of sales from the successful development of BCV. Future trends will be watched closely.

(4) EB virus (EBV) positive NK/T-cell lymphoma

As the fourth BCV pipeline, the Company aims to begin in or after 1Q 2025 a global joint clinical trial of BCV indicated for NK/T-cell lymphoma*1. Animal studies have been conducted at the National Cancer Centre Singapore (NCCS) for this indication following the conclusion of a collaborative research agreement in September 2021, and the investigator of the study announced at an academic conference in December 2022 research results regarding the anti-tumor effects of BCV, and in June 2023 regarding a Matibiri biomarker that predicts anti-tumor effects (TLE1*2).

*1 NK/T-cell lymphoma is a type of malignant lymphoma. NK/T-cell lymphomas are classified as low-grade (progressing yearly), intermediate-grade (progressing monthly), or high-grade (progressing weekly). NK/T cell lymphomas are mostly extranodal NK/T cell lymphomas and mainly present in the perinasal space or on the skin. This disease is characterized by its relatively high prevalence in Southeast Asia, including China.
*2 TLE1 is a transcriptional repressor known to inhibit cancer (including hematopoietic organ tumors) by regulating gene expression. Low TLE1 expression is related to poor treatment outcomes in some types of cancer. It has been reported that TLE1 inhibits the expression of MYC (a type of cancer-causing gene) and other tumor-promoting signaling pathways.

It has been confirmed that in highly malignant NK/T-cell lymphoma, for which no effective treatment has been established, BCV inhibits the expression of MYC (which promotes malignant alteration of tumors) and induces immunogenic cell death known to stimulate cancer immunity. BCV demonstrated a clear tumor growth suppression effect in mouse models transplanted with NK/T-cell lymphoma. Going forward, development of a combination therapy with immunotherapy is likely to be effective, and the final results of animal studies are expected to be released in 4Q FY12/24. The Company expects synergies between BCV and TREAKISYM®, because malignant lymphoma is also a target disease of TREAKISYM®.

(5) Glioblastoma (GBM) stemming from CMV infection

The fifth BCV pipeline is Glioblastoma (GBM) stemming from CMV infection. GBM is one of the most malignant types of brain tumor, with approximately 30,000 newly diagnosed patients per year*, of which about half have CMV infections. It is believed that reactivation of CMV causes cell inflammation resulting in hypoxia, which leads to the increase in VEGF, a growth factor associated with the formation of new blood vessels that may stimulate the multiplication of cancer cells. Standard treatment for GBM is surgery, radiation therapy and chemotherapy, with average survival at 15 months to 20 months and only a 5% five-year survival rate. It is therefore a disease area with a high need for the development of effective drug treatment. While there are many GBM treatment drug candidates under development, none of them target both CMV and brain tumors. Thus, BCV's market value would increase further if its efficacy were confirmed.

* Source: The business plan and items relating to growth potential

With regard to BCV indicated for GBM, the Company has moved forward with research after it concluded a contract research agreement for a pre-clinical study with University of California, San Francisco (UCSF) Brain Tumor Center in December 2022. Using animal models to administer standard therapy in combination with BCV, the research so far has produced data showing longer survival, demonstrating that it was worth progressing to clinical trials. Animal studies are scheduled to be completed in 2024, and assuming progress is on track, the Company plans to begin clinical trials around 2Q FY12/25.

(6) Multiple sclerosis caused by EBV infection

Multiple sclerosis (MS)*1 is an intractable disease. Recent studies have demonstrated a causal relationship between MS and EBV*2. The Company is therefore targeting MS as well in the development of BCV. Many drugs to treat MS (oral and intravenous formulations) have been approved, with the overall market projected to grow from US$29.6bn in 2024 to US$35.1bn in 2029 in terms of sales. However, these treatments can only prevent a recurrence or progression of MS, since the cause of onset is unknown, and no drug has been developed that completely cures it. For this reason, many companies are developing treatments for MS.

*1 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.

*2 EBV is a type of herpes virus. EBV is known for infecting roughly 50% of five-year olds and nearly 95% of adults. In infancy or early childhood, nearly all EBV infections are asymptomatic. EBV infections can cause transitory symptoms such as fever, sore throat, and swollen lymph nodes beginning in adolescence. EBV typically infects B lymphocytes and lies hidden within the cell, inactive, but becomes active due to some sort of environmental change. In addition to MS, it has been found that EBV is linked to the onset of certain cancers, including some lymphomas and nasopharyngeal cancer.

Against this backdrop, in August 2022, the Company entered into a collaboration agreement with the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health (NIH) in the U.S., for the transfer of materials related to BCV. In March 2023, the Company concluded a cooperative research and development agreement (CRADA) with NINDS. A NINDS investigator announced part of the research results at an academic conference in October 2023. The summarized conclusions are as follows. BCV inhibited EBV replication in a dose dependent manner in lymphoblastoid cells immortalized by endogenous EBV (EBV positive B cell lines) derived from both MS patients and healthy controls. In the EBV negative B cell line, no BCV activity was observed including growth inhibition. These preliminary data suggest the potential use of BCV as an anti-EBV therapeutic in patients with MS.

For future development plans, the Company plans to announce results of MS model animal studies in 4Q FY12/24 and aims to begin clinical trials in or after 4Q FY12/25. Although competition is intense in the MS treatment market given its size, progress of the project (including partner agreements) will be closely watched, because no other drug candidates target CMV.

(7) Other development pipelines

In other development pipelines, the Company concluded a Sponsored Research Agreement (SRA) with Tufts University in the U.S. in December 2022 to conduct a non-clinical study that will evaluate the efficacy of BCV in a herpes simplex virus 1 (HSV-1) infection model using a 3D brain model created by culturing human neural stem cells established by the university. Recent research findings suggest that HSV-1 may be involved in the onset of Alzheimer's disease, which means that if BCV can eliminate HSV-1, it could suppress the onset of Alzheimer's disease. Announcement of the results of this collaborative research project expected in 4Q FY12/24 is keenly anticipated.

In April 2023, the Company also concluded a CRADA with the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH) in the U.S., to conduct a pre-clinical study to investigate the efficacy of BCV in the treatment of Epstein-Barr virus (EBV)-related lymphoproliferative diseases. It also entered into a Material Transfer Agreement (MTA) for BCV materials with Penn State College of Medicine, and started a non-clinical study to evaluate the efficacy of BCV in a mouse model of polyomavirus infection*. Polyomaviruses are known to cause serious diseases through their infection. As existing antiviral drugs show little efficacy, the development of an effective treatment is eagerly awaited. The Company will be exploring the potential for development in this disease area.

> * Normally, polyomavirus infections such as BKV and JCV are asymptomatic. However, when the body's immune system is significantly compromised for some reason, these viruses are reactivated and manifest as severe infections in the infected tissues (primarily in the genitourinary system, central nervous system, and hematopoietic cells).

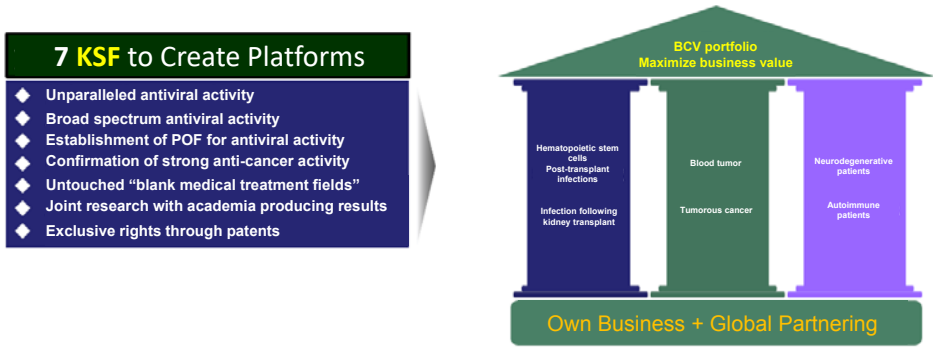
(8) Partnering strategy and BCV's potential business value

It is difficult for a single company to develop so many pipeline products on its own. The Company's strategy is one of concluding partner agreements with major global pharmaceutical companies to reduce the financial burden while progressing development. It plans to begin partner agreement talks in earnest in the latter half of 2024 with a view to progressing talks with the optimal partner for each pipeline. We at FISCO expect talks to progress smoothly, given that the Company has established POC in clinical trials of BCV indicated for AdV infections with clear-cut results (AdV was eliminated in all 10 patients receiving a dose of 0.4mg/kg twice weekly).

Development strategy for brincidofovir (BCV)

A compound that targets multiple diseases is rare. We at FISCO think that BCV is a potential blockbuster drug with a business value far exceeding ¥100.0bn if all pipeline developments succeed. The Company aims to obtain approval for at least two indications by 2030. Although development in the neurodegenerative disease area is likely to take a long time, the Company has the potential for a breakthrough to become a global pharmaceutical company by maximizing the business value of the BCV platform.

Features of BCV



Source: Reprinted from the Company's results briefing materials

Trends of other pipeline products

Gradual market share contraction expected for TREAKISYM® due to generics going on the market

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, intermediate-grade, and high-grade according to the progression rate of the symptoms, and there are various disease types.

Types of non-Hodgkin's lymphoma

Classification by grading	Types of non-Hodgkin's lymphoma (disease type)
Low-grade: Indolent lymphoma (Progressing yearly)	Follicular lymphoma (Grade 1 and 2), MALT lymphoma, lymphoplasmacytic lymphoma Mycosis fungoides, Sezary syndrome, chronic lymphocytic leukemia/small lymphocytic lymphoma, etc.
Intermediate-grade: Aggressive lymphoma (Progressing 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 (Progressing weekly)	Burkitt's lymphoma, acute lymphocytic leukemia/lymphoblastic lymphoma Adult T-cell leukemia/lymphoma (acute and lymphoma types), 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 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 tissue 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. <4519>): 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), 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. Going forward, we think 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. 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.

*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.

The liquid (RTD) formulation of TREAKISYM® went on sale in January 2021 and the switch from the FD formulation to the RTD formulation was completed in December of the same year. The Company obtained marketing approval for RI administration in February 2022 and 90% of the total had switched over to RI administration at the end of December 2023, because it dramatically reduces the burden on healthcare professionals and patients by shortening the infusion time from 60 minutes to 10 minutes.

TREAKISYM®

Drug	Indications	Progress
SyB L-0501 (FD lyophilized powder formulation)	First-line low-grade NHL/MCL	Marketing approval in October 2010
	CLL	Marketing approval in August 2016
	r/r low-grade NHL/MCL	Marketing approval in December 2016
	r/r DLBCL	Marketing approval in March 2021
SyB L-1702 (RI liquid formulation)	Already approved indications	Marketing approval in September 2020
	r/r DLBCL	Marketing approval in April 2021
SyB L-1701 (RTD liquid formulation)	Already approved indications	Marketing approval in February 2022

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

(2) Impact of generic drugs

In February 2022, it was announced that four companies (TOWA PHARMACEUTICAL CO., LTD. <4553>, Pfizer Japan Inc., Meiji Seika Pharma Co., Ltd., and KOA ISEI CO., LTD.) had received marketing approval for generic drugs using the RTD formulation of the brand-name drug. Of these companies, TOWA PHARMACEUTICAL CO., LTD. and Pfizer Japan Inc. have announced that they received marketing approval for RI administration in November 2022. Following on from the launch of sales by TOWA PHARMACEUTICAL CO., LTD. in June 2022, Pfizer Japan Inc. launched sales in December 2022. Although this had minimal impact on sales through 2022, the Company's market share gradually eroded through 2023, contracting from over 90% in January 2023 to around 60% in December. We assume this is because the price of generic drugs was set at approximately 43% of the price of the brand-name drug as well as Pfizer Japan's launch of the generic drug for RI administration. That being said, the rate of market share contraction after generics go on sale is slower than that for other anticancer agents. We think this is due to the Company's efforts to build an extensive network with key opinion leaders and hematology doctors nationwide, providing the latest information in the form of regular seminars, as well as the high safety rating of the brand-name drug. The Company also thinks that another contributing factor is that TREAKISYM®'s price is in the lower range for an anticancer drug, and although the price difference with generics is substantial, the drug price is likely a lower priority for medical institutions when making purchase decisions.

In December 2022, the Company filed a lawsuit in the Tokyo District Court with licensor Eagle against TOWA PHARMACEUTICAL and Pfizer Japan (which had begun advance sales of the generic versions), seeking an injunction against the manufacture and sale of the generic drugs and claiming compensation for damages based on patent infringement. We think it will take some time before a final decision is reached. Until then, we expect the gradual contraction of TREAKISYM®'s market share will continue.

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 conducted the phase III global joint clinical trials (INSPIRE trial) for myelodysplastic syndrome (MDS). In August 2020, it was announced that the primary endpoint had not been achieved in comparison to the doctor-selected therapy. The Company is developing rigosertib indicated for squamous cell carcinoma. In April 2024, Onconova merged with Trawsfynydd Therapeutics, Inc., a privately-held bio-venture company developing next-generation antiviral drugs for infectious diseases such as influenza. The combined company has been renamed Traws Pharma, Inc.

The Company is responsible for clinical development for MDS 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 therapeutic areas other than the oncology area, while utilizing AI technologies.

Results trends

In the FY12/23 results, net sales decreased sharply due to the spread of generics and drug price cuts

1. Summary of FY12/23 results

In the FY12/23 consolidated results, net sales declined for the first time in four years and the Company posted a loss for the first time in three years. Net sales decreased 44.1% YoY to ¥5,589mn, operating loss was ¥811mn (¥1,963mn profit in FY12/22), ordinary loss was ¥736mn (¥1,999mn profit in FY12/22), and loss attributable to owners of parent was ¥1,962mn (¥1,179mn profit in FY12/22).

FY12/23 consolidated results

(¥mn)

	FY12/22		FY12/23			YoY		vs plan
	Results	% of sales	Company's forecast*	Results	% of sales	Change	% change	
Net sales	10,008	-	5,603	5,589	-	-4,418	-44.1%	-13
Gross Profit	7,599	75.9%	-	4,411	78.9%	-3,188	-42.0%	-
SG&A expenses	5,636	56.3%	-	5,222	93.4%	-413	-7.3%	-
R&D expenses	2,554	25.5%	-	2,638	47.2%	83	3.3%	-
Other SG&A expenses	3,081	30.8%	-	2,584	46.2%	-497	-16.1%	-
Operating profit	1,963	19.6%	-680	-811	-14.5%	-2,775	-	-131
Ordinary profit	1,999	20.0%	-549	-736	-13.2%	-2,736	-	-187
Extraordinary income (loss)	106	-	-	-459	-	-565	-	-
Profit attributable to owners of parent	1,179	11.8%	-1,291	-1,962	-35.1%	-3,142	-	-671

* Company forecast figures were announced in November 2023
Source: Prepared by FISCO from the Company's financial results

The main reasons for the sharp decline in net sales were the increased infection risk for malignant lymphoma patients amid the spread of COVID-19, a prolonged period of curtailing bendamustine prescriptions due to concerns of the spread of infection and deterioration of patients' condition during or after treatment with the drug, and the contraction of TREAKISYM®'s market share and drug price cut amid the spread of generics.

The gross profit margin increased from 75.9% in FY12/22 to 78.9% in FY12/23. The Company recorded a sales milestone of ¥550mn under cost of sales in FY12/22. Excluding this impact, the gross profit margin would have been approximately 81%, and thus it decreased slightly in real terms. This was mainly due to quality problems with TREAKISYM® occurring in June 2023, which resulted in a one-time spike in expenses. The TREAKISYM® sales milestone has concluded with the FY12/22 payment.

Among SG&A expenses, R&D expenses increased 3.3% YoY to ¥2,638mn due to increased clinical trial and collaborative research costs for BCV. Other SG&A expenses decreased 16.1% to ¥2,584mn, mainly due to a ¥543mn decrease in sales promotion costs related to TREAKISYM® to ¥937mn. The Company recorded as an extraordinary loss impairment losses of ¥560mn mainly on property, plant and equipment and software assets and made a ¥744mn reversal of deferred tax assets, which increased loss attributable to owners of parent.

To maintain cash on hand of ¥5.5bn to ¥6.5bn

2. Financial condition

As of the end of FY12/23, total assets decreased ¥2,263mn compared to the end of the previous fiscal period to ¥8,170mn. Looking at the main change factors, in current assets, cash and deposits increased by ¥234mn, whereas accounts receivable – trade decreased by ¥1,171mn. In non-current assets, there were decreases of ¥69mn in property, plant and equipment and ¥222mn in software due to recording an impairment charge, and a ¥744mn decrease in deferred tax assets.

Total liabilities decreased ¥966mn compared to the end of the previous fiscal period to ¥960mn. The main change factors were decreases of ¥309mn in accounts payable-other and ¥382mn in income taxes payable, and a decrease in other current liabilities. Net assets decreased ¥1,296mn to ¥7,209mn. There were increases of ¥404mn both in share capital and capital surplus following the issuance of new shares, offset against the recording of loss attributable to owners of parent of ¥1,962mn.

Cash and deposits came to ¥6,517mn at the end of FY12/23. The Company aims to maintain cash on hand of ¥5.5bn to ¥6.5bn. It will need to raise funds to invest in the development of BCV for the next few years. The Company will consider raising funds from institutional investors in addition to one-time revenue from partners in BCV development. Having established clear POC with BCV in 2023, the Company is attracting more interest among institutional investors as well as pharmaceutical companies. Although share dilution is a concern, we at FISCO think that the Company is unlikely to run out of cash.

Balance sheet

(¥mn)

	FY12/20	FY12/21	FY12/22	FY12/23	Change
Current assets	5,815	6,747	9,312	8,082	-1,230
(Cash and deposits)	3,848	3,860	6,282	6,517	234
Non-current assets	459	1,705	1,120	87	-1,032
Total assets	6,274	8,452	10,433	8,170	-2,263
Total liabilities	1,617	1,707	1,927	960	-966
(Interest-bearing debt)	-	-	-	-	-
Net assets	4,657	6,745	8,506	7,209	-1,296
Management indicators					
Equity ratio	64.3%	73.7%	77.6%	84.9%	7.3pt
Interest-bearing debt ratio	-	-	-	-	-

Note: Figures for FY12/21 and prior fiscal years are non-consolidated
Source: Prepared by FISCO from the Company's financial results

Outlook

In FY12/24, the Company will push ahead with new in-licensed products and BCV partner agreement talks amid the ongoing decline in revenue from TREAKISYM®

1. Outlook for FY12/24

For FY12/24 results, the Company's forecast announced on May 7, 2024 was a downward revision from the initial plan and calls for net sales to decrease 53.1% YoY to ¥2,623mn, operating loss of ¥3,702mn (¥811mn loss in FY12/23), ordinary loss of ¥3,524mn (¥736mn loss in FY12/23), and loss attributable to owners of parent of ¥3,628mn (¥1,962mn loss in FY12/23).

Outlook

Outlook for FY12/24 results

(¥mn)

	FY12/23		FY12/24			YoY	
	Results	vs. net sales	Initial forecast	Revised forecast	vs. net sales	Change	% change
Net sales	5,589	-	3,641	2,623	-	-2,966	-53.1%
Gross profit	4,411	78.9%	2,787	1,922	73.3%	-2,489	-56.4%
SG&A expenses	5,222	93.4%	5,624	5,624	214.4%	401	7.7%
R&D expenses	2,638	47.2%	3,207	3,409	130.0%	770	29.2%
Other SG&A expense	2,584	46.2%	2,416	2,215	84.4%	-369	-14.3%
Operating profit	-811	-14.5%	-2,837	-3,702	-141.1%	-2,890	-
Ordinary profit	-736	-13.2%	-2,867	-3,524	-134.3%	-2,787	-
Profit attributable to owners of parent	-1,962	-35.1%	-2,870	-3,628	-138.3%	-1,665	-

Note: Revised forecast are figures announced on May 7, 2024
Source: Prepared by FISCO from the Company's results briefing materials

A double-digit decline in net sales was forecast at the beginning of FY12/24 due to drug price cuts and spread of generics. The Company revised downward its initial forecast, because net sales decreased 61.3% YoY in 1Q FY12/24 to ¥597mn due to the impact of inventory adjustment prior to the application of new drug prices. With 1Q net sales falling far short of forecast, the Company concluded that it would be difficult to regain lost ground in 2Q onward given the ongoing impact of drug price cuts and market share contraction. The drug price cut in the April 2024 NHI drug price revision was steep at around 18% YoY because of TREAKISYM® RTD formulation/RI administration being excluded from the price maintenance premium (new drug creation premium)* due to generics going on sale. We think that the drug price cut will be smaller (a few percent per year) from 2025 onward. Since generic drug prices have also been cut by about 15%, the Company assumes that the market share of TREAKISYM® will gradually decrease from around 60% at the end of FY12/23.

* 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. Once a generic drug goes on sale, the drug price falls sharply, because it will be excluded from the premium in the next round of drug price revisions.

The gross profit margin is expected to drop from 78.9% in FY12/23 due to the impact of the drug price cut and unfavorable exchange rate (yen depreciation). The Company revised its forex assumption from ¥141.8 per U.S. dollar to ¥151.4 per U.S. dollar, which will add to purchase costs. Of SG&A expenses, the Company initially forecast R&D expenses of ¥3,207mn, an increase of ¥568mn from FY12/23, but made an upward revision to ¥3,409mn, due in part to yen depreciation. R&D expenses are impacted by yen depreciation, because they mainly comprise clinical trial expenses for BCV and expenses for collaborative research with overseas academia. However, the Company is keeping SG&A expenses overall to ¥5,624mn (just ¥401mn more than the initial forecast) by reviewing other expenses. The Company expects the number of employees to be at a similar level as 109 at the end of FY12/23 (consolidated basis; 103 on a non-consolidated basis).

In-licensing talks between the Company and several other companies are underway for drugs likely to generate revenue relatively quickly to supplement TREAKISYM®, with the goal of concluding agreements around 3Q FY12/24. The Company also plans to begin BCV partner agreement talks in earnest in 3Q onward. With several pipelines proceeding to the clinical trial stage in 2025 onward, the Company may confirm multiple partner agreements in the lead-up to 2025 provided partner agreement talks progress as expected. The outcome of these talks will be keenly anticipated.

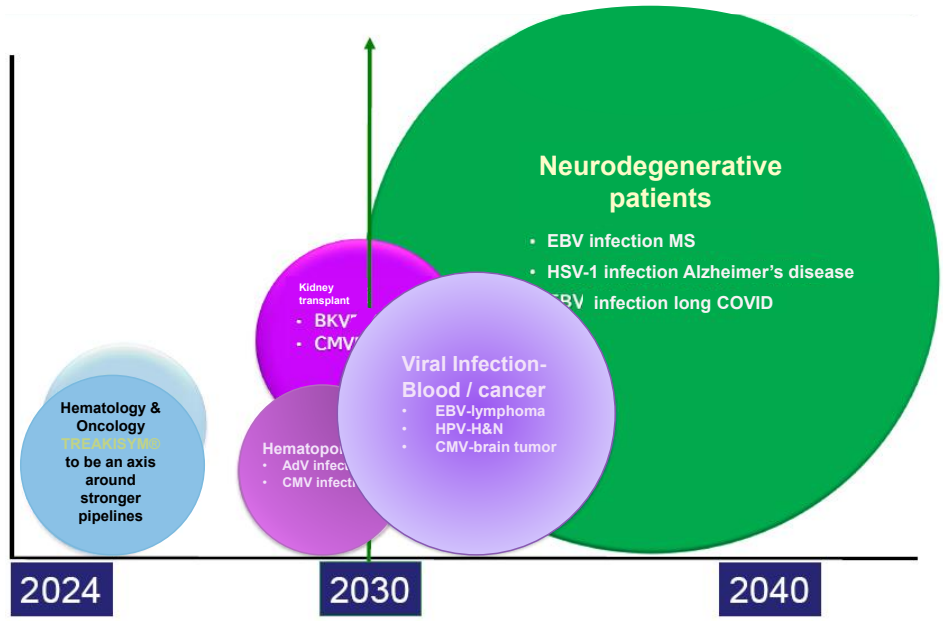
Aim for growth as a global specialty pharmaceutical company by developing the BCV platform

2. Long-term strategy

In the long term, the Company is aiming for growth as a global specialty pharmaceutical company, with the goal of a 50/50 domestic and overseas sales weighting in 2030. In Japan, it plans to increase sales with TREAKISYM®, new products to be in-licensed, and launching BCV. Its overseas strategy is to grow sales by putting at least two BCV products on the market.

In developing the BCV platform, the Company will first focus on development and launch of treatments for viral infections after transplantation and tumors caused by viral infections, but after 2030, the launch of products for the neurodegenerative disease area (a much larger market) will come within range. We at FISCO believe that in progressing the development of BCV, having established POC for AdV infections and confirmed the optimal dosage and formulation will be a big advantage in taking clinical development and partner agreement talks forward. BCV could become a blockbuster drug if clinical development of the pipelines progress smoothly, which will likely increase the Company's corporate value (market capitalization) from the current ¥8.0bn level.

Implementing strategy of multiple therapeutic areas + global business



Source: Reprinted from the Company's results briefing materials

FISCO

Disclaimer

FISCO Ltd. (“FISCO”) offer stock price and index information for use under the approval of the Tokyo Stock Exchange, the Osaka Stock Exchange and Nikkei Inc.

This report is provided solely for the purpose of offering information, and is not a solicitation of investment nor any other act or action.

FISCO prepared and published this report based on information which it considered reliable; however, FISCO does not warrant the accuracy, completeness, fitness nor reliability of the contents of this report or the said information.

The issuers’ securities, currencies, commodities, securities and other financial instruments mentioned in this report may increase or decrease in value or lose their value due to influence from corporate activities, economic policies, world affairs and other factors. This report does not make any promises regarding any future outcomes. If you use this report or any information mentioned herein, regardless of the purpose therefor, such use shall be made based on your judgment and responsibility, and FISCO shall not be liable for any damage incurred by you as a result of such use, irrespective of the reason.

This report has been prepared at the request of the company subject hereto based on the provision of information by such company through telephone interviews and the like. However, the hypotheses, conclusions and all other contents contained herein are based on analysis by FISCO. The contents of this report are as of the time of the preparation hereof, and are subject to change without notice. FISCO is not obligated to update this report.

FISCO and its affiliated companies, as well as the directors, officers and employees thereof, may currently or in the future trade or hold the financial instruments or the securities of issuers that are mentioned in this report.

Please use the information in this report upon accepting the above points.

■ For inquiry, please contact: ■
FISCO Ltd.
5-13-3 Minami Aoyama, Minato-ku, Tokyo, Japan 107-0062
Phone: 03-5774-2443 (IR Consulting Business Division)
Email: support@fisco.co.jp