COMPANY RESEARCH AND ANALYSIS REPORT

SymBio Pharmaceuticals Limited

4582

JASDAQ Growth Market

5-Apr.-2019

FISCO Ltd. Analyst
Yuzuru Sato

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

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Summary

Aiming to become profitable in FY12/21 from the expansion of indications of TREAKISYM® as the standard treatment for malignant lymphoma

SymBio Pharmaceuticals Limited <4582> (hereafter, also "the Company") is a bio-venture that is advancing developments in the fields of oncology, hematology, and rare diseases where there are few patients, but high medical needs. The two main drugs in the development pipeline are TREAKISYM®, whose indications as a treatment for malignant lymphoma are expanding, and rigosertib, which is being developed for myelodysplastic syndrome (MDS). Of these two, TREAKISYM® was granted marketing approval for indications for relapsed and refractory low-grade non-Hodgkin's lymphoma (NHL)/mantle cell lymphoma (MCL) in 2010, and for chronic lymphocytic leukemia (CLL) and untreated low-grade NHL/MCL in 2016, and it is being sold by the Company's partner, Eisai Co., Ltd. <4523>. The marketing agreement with Eisai finishes at the end of 2020, so currently the Company is currently working to secure human resources toward constructing its own sales system, and the system construction is scheduled to be completed by June 2020.

1. Highly likely to become profitable in FY12/21

The Company announced a Mid-Range Plan in February 2019, and within it, it sets the targets to become profitable in FY12/21, with net sales of ¥9,132mn and operating profit of ¥1,225mn. The measures to become profitable include increasing sales through building its own sales system, expanding indications of TREAKISYM®, and the approval of and switching to its liquid formulation. Currently, steady progress is being made for each of these measures, and at FISCO, we think it is highly likely that these targets will be achieved. From 2022 onwards also, results may trend upward and continue to grow. This is because TREAKISYM® is currently being developed for diffuse large B-cell lymphoma (DLBCL), which is one type of relapsed and refractory, middle- to high-grade NHL, and if receives marketing approval for it, the number of potential patients in Japan will instantly double, from approximately 17,000 in 2018 to around 35,000. For rigosertib also, the developer Onconova Therapeutics, Inc. <ONTX> (U.S.) (hereafter, Onconova) has announced that it obtained excellent results for the remission rate in the phase II clinical trial for untreated high-risk MDS (in combination with azacitidine), and that in plans to conduct an international, joint phase III clinical trial in 2019. The Company is also planning to participate in this, and if its development is successful, it is expected to contribute to sales in a few years (azacitidine's domestic market scale is approximately ¥15bn). If all of these developments are successful, it is calculated that the sales growth potential will grow from ¥8.5bn in 2018 to around ¥40bn on a drug-price basis.

2. Outlook for FY12/19

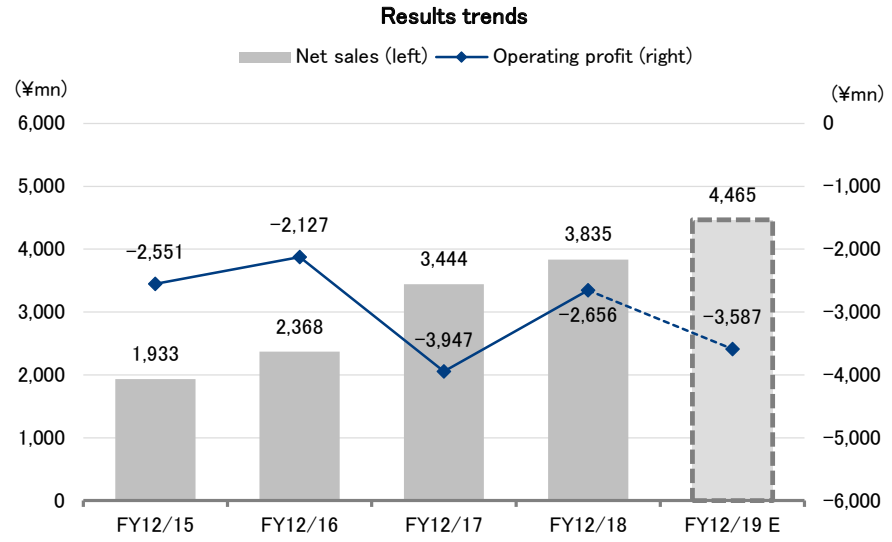
The outlook for the FY12/19 results is for net sales to increase 16.4% year-on-year (YoY) to ¥4,465mn and an operating loss of ¥3,587mn (compared to a loss of ¥2,656mn in the previous fiscal year). The main factors behind the increase in sales include the recommendation of TREAKISYM® (bendamustine) and Rituximab® combination therapy (BR therapy) following its inclusion in the treatment guidelines of the Japan Society of Hematology in July 2018 as the standard treatment for malignant lymphoma, and also as its use for untreated, low-grade NHL is progressing. The market penetration rate of BR therapy increased from 30% in Q3 FY12/17 to 56% in Q3 FY12/18, and the penetration rate is expected to further increase in 2019. On the other hand, expenses are projected to increase for R&D expenses and expenses relating to the in-house sales system construction, which is the main reason why the operating loss will grow.

3. Financial Strategy

The Company issued the 45th through the 47th Stock Acquisition Rights (with Exercise Price Revision Clauses) from an allocation to EVO FUND in April 2018 in order to stably raise funds for business activities in the future. The number of common stocks corresponding to stock acquisition rights is 50 million stocks in total, and the dilution rate is 92.5%. The 45th tranche (20 million stocks) has already been exercised, and the rest are scheduled to be exercised in 2019 and 2020. At the end of FY12/18, cash and deposits were approximately ¥4.8bn, and assuming the Company's results forecasts, in total, cash out of ¥8.8bn will be generated from 2019 to 2020. Therefore, in order to fund business activities up to 2020, it will require at least ¥4bn. But if all of the remaining rights are exercised at the current stock-price level (¥229 on March 14, 2019), it would raise ¥6.8bn, so it can be said that it will be able to sufficiently cover this amount. In addition, the Company is targeting net profit of ¥1,736 to ¥2,060mn in FY12/22, which is the final fiscal year of the Mid-Range Plan, while the earnings per share (EPS), calculated based on if all of the stock acquisition rights up to the 47th tranche are exercised, will be at ¥16.7 to ¥19.8.

Key Points

- A bio-venture that conducts developments from the clinical-trials stage, targeting the fields of oncology, hematology, and rare diseases
- In FY12/19, the Company is progressing clinical trials and working on constructing an in-house sales system
- The sales growth potential is around ¥40bn on a drug-price basis, which is 5 times the 2018 result



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

Company profile

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

1. History

SymBio Pharmaceuticals is a bio-venture founded by the current Representative Director 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 is that it 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 licensing-in development candidates for which *POC for humans has been obtained, and conducting development from the clinical trials 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 development candidate licensed-in first was the anti-cancer agent bendamustine hydrochloride (hereafter, bendamustine) 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 2015. With the development code SyB L-0501, 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 (product name, TREAKISYM®). It progressed licensing activities during this time, and in 2007, it concluded an agreement to widen the target areas for the exclusive development and marketing rights in China, South Korea, Taiwan, and Singapore. Then with Eisai as its marketing partner, it concluded licensing agreements for Japan in 2008 and for South Korea and Singapore in 2009.

* One type of malignant lymphoma.

TREAKISYM®, whose sales were launched in Japan in December 2010, continued to be subsequently developed in order to expand its indications, and in 2016, it acquired approval for indications for chronic lymphocytic leukemia and untreated (first line of treatment) low-grade NHL/MCL, and its sales are growing. Also, in Asia, it sales began in Singapore in 2010, in South Korea in 2011, and in Taiwan in 2012. For Taiwan, in 2008, the Company concluded a licensing agreement with InnoPharmax Inc. (Taiwan), which is conducting sales through the Company.

Also, the second drug licensed-in was rigosertib (development code, SyB L-1101 (intravenous formulation)/SyB C-1101 (oral formulation)), which is a development candidate from Onconova (U.S.) indicated for myelodysplastic syndrome*1 for which the Company concluded an exclusive development and marketing rights agreement in 2011 for Japan and South Korea. Currently also, its development is being progressed. Further, in 2017 it concluded an exclusive development and marketing rights agreement for Japan with Eagle Pharmaceuticals, Inc. <EGRX> (U.S.) for the TREAKISYM® liquid formulation, ready-to-dilute (RTD) formulation / rapid infusion (RI) formulation (development code, SyB L-1701/SyB L-1702)*2, and in the same way, its development is being progressed.

*1 Myelodysplastic syndrome: a disease in which normal blood cells (red blood cells, white blood cells, and platelets) cannot be produced due to abnormalities in the hematopoietic stem cells in the bone marrow. It is known as a disease that has a high incidence in the elderly and that is likely to develop to become acute myeloid leukemia.

*2 Currently, TREAKISYM®, which has been approved in Japan, is a lyophilized powder formulation, which means it must be dissolved at the medical site when it is used. As this task is unnecessary for the liquid formulation, it greatly reduces the workload placed on healthcare workers. 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.

It has been decided that the licensing agreement with Eisai will finish at the end of 2020. Therefore, the Company is currently preparing to construct its own sales system.

Technology licensing-in agreements

Development code name	SyB L-0501 (lyophilized powder formulation) / SyB C-0501 (oral formulation)	SyB L-0501 (lyophilized powder formulation) / SyB C-0501 (oral formulation)	SyB L-1101/C-1101	SyB L-1701 (RTD formulation) / SyB L-1702 (RI formulation)
Licensing-in partner	Astellas Pharma GmbH (Germany)	Astellas Deutschland GmbH (Germany)	Onconova Therapeutics, Inc. (U.S.)	Eagle Pharmaceuticals, Inc. (U.S.)
Date agreement was concluded / agreement period	December 2005 / Whichever is longer; the 10-year period from the first product sales, or the market-exclusive period in Japan	January 2007 / Whichever longer; the 10-year period from the first product sales or the market-exclusive period	July 2011 / Whichever longer; the 10-year period from the first product sales (7 years in South Korea), the market-exclusive period, or the patent-validity period, in each country	September 2017 / Whichever longer; the product-patent period or the market-exclusive period
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 and South Korea	Exclusive development rights and marketing rights in Japan

Technology licensing-out agreements

Development code name	SyB L-0501	SyB L-0501	SyB L-0501	SyB L-0501
Licensing-out partner	InnoPharmax Inc. (Taiwan)	Eisai Co., Ltd. (Japan)	Cephalon, Inc. (U.S.)	Eisai Co., Ltd. (Japan)
Date the agreement was concluded / agreement period	March 2008 / 10 years from the first product sales in Taiwan	August 2008 / 10 years from the first product sales in Japan	March 2009 / 10 years from the first product sales in China	May 2009/ 10 years from the first product sales in South Korea and Singapore
Content of the main agreements	Exclusive development rights and marketing rights in Taiwan	Joint development rights and exclusive marketing rights in Japan	Exclusive development rights and marketing rights in China (including Hong Kong)	Exclusive development rights and marketing rights in South Korea and Singapore

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

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,

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

Use of TREAKISYM® is spreading as the standard treatment for malignant lymphoma

2. Trends in the development pipeline

(1) TREAKISYM® (generic name: bendamustine hydrochloride)

TREAKISYM® is an anti-cancer 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 and organs other than lymph nodes (such as the stomach, intestines, thyroid, spinal cord, lung, liver, skin, and eyes) distributed throughout the body. 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

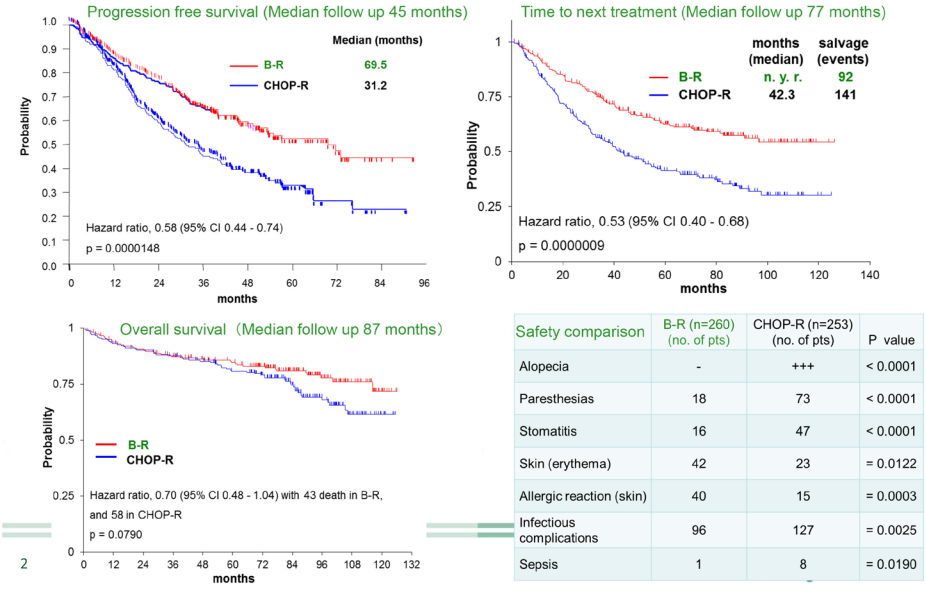
Type according to grade	Non-Hodgkin's lymphoma type (disease type)
Low grade: Indolent lymphoma (progresses yearly)	Follicular lymphoma (grade 1, 2), MALT lymphoma, lymphoplasmacytic lymphoma Mycosis fungoides, Sezary syndrome, chronic lymphocytic leukemia / small lymphocytic lymphoma, etc.
Medium grade: 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 Hospital materials

Among these, currently the Company has acquired marketing approval for indications for relapsed and refractory low-grade non-Hodgkin's lymphoma (NHL), mantle cell lymphoma (MCL), chronic lymphocytic leukemia (CLL), and untreated (first line of treatment) low-grade NHL/MCL. In particular, in 2016 its use in this field started to spread following the acquisition of marketing approval for untreated low-grade NHL/MCL, and then in July 2018, in its treatment guidelines, the Japan Society of Hematology recommended TREAKISYM® and Rituximab® combination therapy (BR therapy) as the standard treatment, and it is becoming established as the standard treatment in both name and reality. In the field of untreated low-grade NHL, previously the standard treatment was R-CHOP therapy*, but on looking at the market penetration rates, in Q4 FY12/17 (October to December 2017), BR therapy had overtaken it, and as of Q3 FY12/18 (July to September 2018), BR therapy had a 56% share of the market as a whole. As the efficacy of BR therapy greatly exceeds that of R-CHOP therapy, the Company considers that it will be able to increase the market penetration rate to at least 75% in the untreated area.

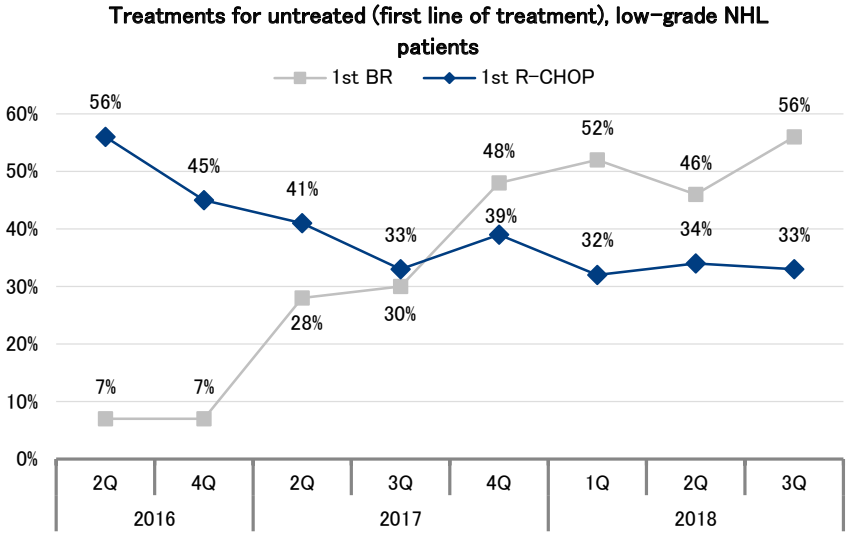
* R-CHOP therapy: a multi-drug combination therapy combining Rituximab® and 4 other drugs

BR therapy It is superior to R-CHOP for both efficacy and safety



Safety comparison	B-R (n=260) (no. of pts)	CHOP-R (n=253) (no. of pts)	P value
Alopecia	-	+++	< 0.0001
Paresthesias	18	73	< 0.0001
Stomatitis	16	47	< 0.0001
Skin (erythema)	42	23	= 0.0122
Allergic reaction (skin)	40	15	= 0.0003
Infectious complications	96	127	= 0.0025
Sepsis	1	8	= 0.0190

Source: From the Company's results briefing material



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

The Company is currently progressing five drugs in the development pipeline. Of these, the phase III clinical trial for the expansion of the indication of the existing lyophilized powder formulation TREAKISYM® for an indication for diffuse large B-cell lymphoma (DLBCL), the registration of subjects for 35 of the 60 planned cases has been completed (as of February 2019). If steady progress is made, the Company should complete the registration for all of the cases by the fall of 2019 and the submit application for manufacturing and marketing approval in 2020, with the aim of launching the sales in the second half of 2021. As DLBCL has the largest number of cases among the malignant lymphomas, if its approved, it will contribute significantly to the increased sales of TREAKISYM®.

Relapsed and refractory DLBCL phase III clinical trial

Indications	Relapsed and refractory diffuse large B-cell lymphoma (r/r DLBCL)
Dose	Rituximab: 375 mg / m2 (Day 1) SyB L-0501: 120 mg / m2 (Day 2 + 3) 6 cycles
Endpoints	Principal evaluation: Anti-tumor effect Secondary evaluation: complete remission rate, duration of remission, overall survival, safety
Number of patients to be registered	60 cases
Implementing facilities	33 facilities
Status of registrations	35 cases (as of February 6, 2019)

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

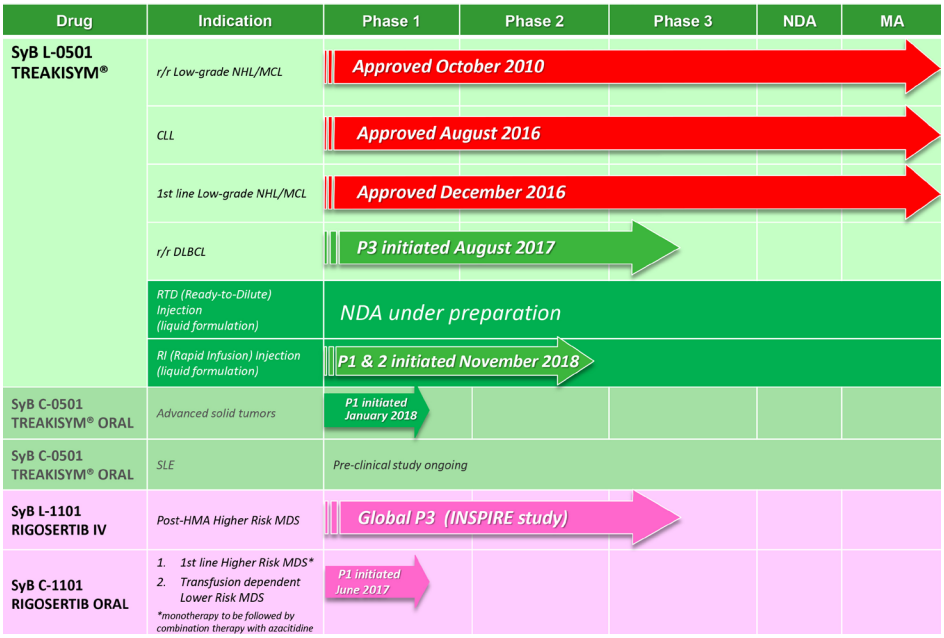
The Company is currently preparing to apply for marketing approval for RTD, which is the TREAKISYM® liquid formulation, and the plan is to apply for approval by Q3 FY12/19, to acquire approval in Q3 FY12/20, and to launch sales in Q1 FY12/21. In addition, the clinical trials of the RI formulation started in November 2018, with the main aim of confirming its safety (planned number of cases, 36), and if its safety is confirmed, the Company can apply for marketing approval and it is aiming to acquire the approval and to launch sales in 2022. The indications include all those for which TREAKISYM® has already been approved, and also for relapsed and refractory DLBCL. Teva Pharmaceutical Industries Ltd. (U.S.) and BENDEKA® are already on the U.S. market as RTD/RI formulations, and most patients have already switched to the liquid formulation. For example, as of 2017, they had acquired a 97% share of the bendamustine market. In addition to eliminating the need for dissolving work, the administration time is short for the RI formulation, so the burden on patients is greatly reduced. Therefore, there are strong calls for its early marketing approval.

As the exclusive sales period for the existing, lyophilized powder formulation type ends in 2020 in Japan, generics may be developed for it. But if the RTD/RI formulations are launched, there will be major differences in terms of their functions, so this would effectively extend the exclusive marketing period until 2031. If the RTD/RI formulations are launched, the drug prices will be the same level as the previous products, but the supplier will be changed to Eagle Pharmaceuticals so at FISCO, we think that it is highly likely that the profit margin will improve compared to the existing products.

In addition, the phase I clinical trial of the TREAKISYM® oral formulation (development code: SyB C-0501), indication for advanced solid tumors, began in January 2018. Also, the pre-clinical trial for an indication for systemic lupus erythematosus (SLE)* began in July 2018.

* An autoimmune disease in which the patient's own immune system mistakenly attacks normal cells. It is designated as an intractable disease because it causes inflammation and tissue damage in various organs throughout the body. There are approximately 60,000 to 100,000 patients in Japan.

Steady progress in the FY18 highlights (III) development pipeline



Source: From the Company's results briefing material

(2) Rigosertib (intravenous formulation/oral formulation)

Rigosertib is an anti-cancer agent that has a 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 development is being progressed indicated for high-risk myelodysplastic syndrome (MDS)*.

* MDS is a disease in which the patient cannot produce normal blood cells due to abnormalities in the hematopoietic stem cells in the bone marrow, causing a decrease in normal blood cells and symptoms such as anemia, infection and hemorrhage. It is also known to transition to become acute myeloid leukemia. The condition of the bone marrow is examined, the leukemia transition period is determined, and it is classified into four stages, such as according to the length of the period. The high-risk type has a 25% leukemia transition period of 0.2 of year, and the 50% survival period median value is 0.4 of a year. There are approximately 11,000 patients in Japan.

MDS treatments include support therapy*, immunosuppression therapy, chemical therapy, and hematopoietic stem cell transplants, while 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, Nippon Shinyaku Co., Ltd.'s Vidaza® is on the market, and it has annual sales on a scale of ¥15 to ¥16bn on a drug-price basis.

* A treatment that compensates for the lack of blood cells through blood transfusions and medication.

For the current development situation, an international joint phase III clinical trial is being progressed by Onconova for the intravenous formulation indicated for relapsed and refractory high-risk MDS (target number of cases, 360). In Japan, the Company has completed the registration of subjects for 40 of the 50 cases (as of February 6, 2019), and it plans to complete all of the registrations during 2019.

For the oral formulation also, the phase I clinical trial is being progressed for the single drug indicated for relapsed and refractory high-risk MDS, while in the future, the plan is to switch to development for its joint use with azacitidine. This is because in 2018, the American Society of Hematology announced the results of the Onconova phase II clinical trial for its combination therapy with azacitidine, and these results showed good tolerability, an excellent overall remission rate and complete remission* for untreated high-risk MDS. Complete remission was achieved in 10 of the 29 cases (34%), compared to a 15% level with azacitidine as a single-drug therapy, indicating that it is more than twice as effective.

* Indicates that all lesions (cancers) have disappeared and that no new cancers have appeared.

HMA refractory high-risk MDS international joint phase III clinical trial (intravenous formulation)
Results of the HMA untreated, relapsed and refractory myelogenesis syndrome phase II clinical trial
Rigosertib (oral formulation) + azacitidine combination therapy

Remission rate (2006 IWG standard)	Hypomethylated drug untreated cases (1st line, 29 cases)	Hypomethylated drug refractory cases (2nd line, 26 cases)
Overall remission rate	26 cases (90%)	14 cases (54%)
Complete remission (CR)	10 cases (34%)	1 case (4%)
Partial remission (PR)	0 cases (0%)	1 case (4%)

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

Based on these results, Onconova filed on application for an SPA* with the FDA in December 2018. It plans to conduct an international joint phase III clinical trial for combination use with azacitidine for untreated high-risk MDS following the consultations with the FDA during the first half of 2019. The main endpoints are expected to be the overall remission rates (the rates of total remissions and partial remissions to the total number of cases). If the levels are similar to or close to those seen in the phase II clinical trial, it seems extremely highly likely that it will be approved. Therefore, the Company also plans to take part in the international joint clinical trial after the FDA approves the SPA. The trial may begin as early as the second half of 2019, and if the development is a success, sales on the same scale as Vidaza® can be expected.

* SPA (Special Protocol Assessment): a system in which, after the phase II clinical trial, for the phase III clinical trial, agreement is obtained in advance from the FDA for aspects such as the indicated disease, purpose, study design, endpoints (primary and secondary evaluation items), and analysis method, and after the trial has been completed, it is recognized as meeting the approval requirements in the approval review as it is, without changing the contents of the agreement. By using this system, if the endpoints are achieved for the evaluation and review of the trial results, it increases the likelihood of approval with shorter review process and time.

Rigosertib intravenous formulation and oral formulation

Drug	Indication	Phase 1	Phase 2	Phase 3	NDA	MA
Rigosertib intravenous formulation	Relapsed and refractory high-risk MDS	International joint phase III clinical trial Currently registering cases				
Rigosertib oral formulation	Relapsed and refractory high-risk MDS single drug	Currently registering cases				
	Untreated high-risk MDS AZA combination use	Being prepared				
	Untreated high-risk MDS AZA combination use	International joint phase III clinical trial Being prepared				

Source: From the Company's results briefing material

Results trends

FY12/18 was a major turning point toward growth in the future

1. FY12/18 results

It is considered that FY12/18 have been a major turning point for growth in the future. This is because the three business elements that will become the driving forces behind becoming profitable from 2021 onwards were put in place. The first was that the Company decided that the sales of TREAKISYM® would be conducted through its own sales system from 2021, the second was that the Japan Society of Hematology recommended TREAKISYM® as the standard treatment in both name and reality for malignant lymphoma, and the third was that steady progress was made in the development pipeline. The major progress made in the development pipeline was that an agreement was reached with the PMDA to apply for approval for the TREAKISYM® liquid RTD formulation even if clinical trials are not conducted, with a possible date for its sales launch in Q1 FY12/21, while for the liquid RI formulation also, if safety is confirmed in the clinical trial with a small number of cases, of 36, it will be possible to apply for approval, with a possible date for its market launch in 2022. These developments are significant, because as previously explained, they will effectively block the entry of generics for the lyophilized powder formulation.

In this situation, in FY12/18, net sales increased 11.4% YoY to ¥3,835mn, the operating loss was ¥2,656mn (compared to a loss of ¥3,947mn in the previous fiscal year), the ordinary loss was ¥2,748mn (a loss of ¥3,976mn), and the loss was ¥2,752mn (a loss of ¥3,977mn).

Results trends

FY12/18 results

(¥mn)

	FY12/17		FY12/18				
	Results	vs. net sales	Initial forecast	Results	vs. net sales	YoY	vs. plan
Net sales	3,444	-	4,201	3,835	-	11.4%	-8.7%
Product sales	3,444	-	-	3,809	-	10.6%	-
Other sales	-	-	-	25	-	-	-
Gross profit	1,031	29.9%	1,369	1,172	30.6%	13.7%	-14.3%
Selling, general and administrative expenses	4,978	144.5%	4,350	3,828	99.8%	-23.1%	-12.0%
Research and development expenses	3,017	87.6%	2,311	1,832	47.8%	-39.3%	-20.7%
Other selling, general and administrative expenses	1,960	56.9%	2,039	1,996	52.0%	1.8%	-2.1%
Operating profit (loss)	-3,947	-114.6%	-2,981	-2,656	-69.2%	32.7%	-
Ordinary profit (loss)	-3,976	-115.5%	-3,044	-2,748	-71.7%	30.9%	-
Profit (loss)	-3,977	-115.5%	-3,056	-2,752	-71.8%	30.8%	-

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

The main factor behind the higher net sales was that sales of TREAKISYM® grew 10.6% YoY due to the rise in its market penetration rate for untreated low-grade NHL/MC. The result was 8.7% below the initial forecast, but this was because, among the formulations imported from Astellas Deutschland, appearance defects were found in small-volume formulations (25 mg), so imports and shipments were temporarily suspended during the period. It was also because of slower than expected switching pace for untreated low-grade NHL/MCL from R-CHOP therapy was slower than expected. Among the imported products, sales of the 100mg formulation are continuing without any problems. At the present time, sales of the 25mg formulation remain suspended, but switching to the 100 mg formulation will have no impact on users, so this will not affect sales in 2019.

Research and development expenses decreased 39.3% YoY to ¥1,832mn. But this was because 2017 included a one-time payment of ¥1,393mn to Eagle Pharmaceuticals on concluding the licensing agreement, and if this payment is excluded, research and development expenses increased 12.8% alongside the progress made in the clinical trials. This amount was below the initial forecast by ¥2,311mn. It seems this was mainly due to a slightly delay in registered subjects for the phase III clinical trial for relapsed and refractory DLBCL, and that the liquid RTD formulation clinical trials have become unnecessary following the consultations with the PMDA. The increase in other SG&A expenses was kept down to 1.8% YoY from the measures to control costs. As a result of the above, the operating loss was reduced ¥1,290mn YoY.

In FY12/19, the Company is progressing clinical trials and working on constructing an in-house sales system

2. Outlook for FY12/19

The outlook for the FY12/19 results is for net sales to increase 16.4% YoY to ¥4,465mn, an operating loss of ¥3,587mn (compared to a loss of ¥2,656mn in FY12/18), an ordinary loss of ¥3,612mn (a loss of ¥2,748mn), and a loss of ¥3,616mn (a loss of ¥2,752mn).

Outlook for FY12/19

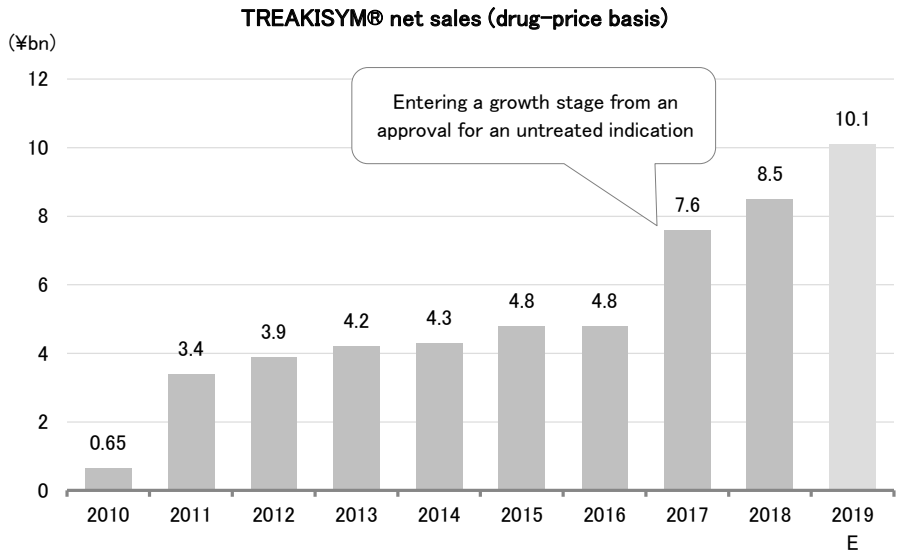
(¥mn)

	FY12/18 results	FY12/19 forecast	change	% change
Net sales	3,835	4,465	629	16.4%
Product sales	3,809	4,457	648	17.0%
Other sales	25	7	-18	-72.1%
Gross profit	1,172	1,466	293	25.1%
Selling, general and administrative expenses	3,828	5,053	1,225	32.0%
Research and development expenses	1,832	2,508	676	36.9%
Other selling, general and administrative expenses	1,996	2,545	549	27.5%
Operating profit (loss)	-2,656	-3,587	-931	-
Ordinary profit (loss)	-2,748	-3,612	-864	-
Profit (loss)	-2,752	-3,616	-863	-

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

Sales of TREAKISYM® are expected to continue to increase, up 17.0% YoY, from its growth for untreated low-grade NHL/MCL. In expenses, research and development expenses will rise ¥676mn to ¥2,508mn alongside the progress made in the clinical trials, while other SG&A expenses will also increase ¥550mn to ¥2,545mn, which will be the main reasons for the higher operating loss. Other SG&A expenses will increase mainly for the preparations to construct in-house sales system. Specifically, there will be increases in the number of core human resources who will be responsible for the sales of TREAKISYM® in the future (TREAKISYM managers) from 10 people at the end of 2018 to 20 people, and expenses for sales and marketing activities and for constructing the in-house sales system. In total for these expenses, an increase of ¥550mn is expected. The Company plans to appoint 20 people as TREAKISYM managers by April 2019 and be operative from Q2 FY12/19. Although the Company cannot conduct sales directly yet, it will start marketing activities towards those customers that Eisai was unable to approach, in the form of add-ons to Eisai's MR. In particular, it will work to switch customers from the R-CHOP therapy to the BR therapy for untreated low-grade NHL/MCL, and in 2019, it is aiming to achieve TREAKISYM® net sales of ¥10.1bn on a drug-price basis.

Results trends



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

The Mid-Range Plan

Highly likely to become profitable in FY12/21 and to achieve sustainable growth from 2022 onwards

1. The Mid-Range Plan's results assumptions

In February 2019, the Company announced its four-year Mid-Range Plan, with FY12/22 as its final fiscal year. In this plan, it sets the target of becoming profitable in FY12/21 and moreover, doubling profit growth from FY12/22 onwards.

Mid-Range Plan

(¥mn)

	FY12/19	FY12/20	FY12/21	FY12/22
Net sales	4,465	3,282	9,132	11,282~11,809
Operating profit (loss)	-3,587	-5,180	1,225	2,084~2,464
Ordinary profit (loss)	-3,612	-5,224	1,181	2,040~2,420
Profit (loss)	-3,616	-5,228	1,005	1,736~2,060

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

Looking at the assumptions for the results targets, the outlook for FY12/20 is that net sales will temporarily decline, down 26% YoY to ¥3,282mn. This is because Eisai will be working in 2H to reduce its inventory with the marketing sales agreement finishing at the end of FY12/20. It is assumed that the market penetration rate of BR therapy for untreated low-grade NHL will be at the 70% level at the end of 2020. Expenses will increase, mainly due to higher research and development expenses (a rise in rigosertib oral formulation development expenses and a milestone payment on the approval of the liquid RTD formulation), and also as other SG&A expenses will rise in order to expand the salesforce of 60 people by June 2020, and because sales-preparation activities will become fully fledged. Therefore, the operating loss is forecast to be ¥5,180mn.

In FY12/21, net sales are forecast to rapidly increase to ¥9,132mn, and for this, the effects of switching to in-house sales will be considerable. Looking at net sales on a drug-price basis, compared to the FY12/19 target of ¥10.1bn, in FY12/21 they are expected to increase by 20% to approximately ¥12bn. If provisionally calculated based on the previous sales standard (sales to Eisai), this is a sales scale of around ¥5.4bn. The liquid RTD formulation is expected to be market launched during Q1, and it is estimated that the annual rate of switching to it from the lyophilized powder formulation will be 60%. In addition, sales for relapsed and refractory DLBCL have hardly been included in the sales forecasts because the market launch will be in Q3 or later. In expenses, sales expenses will increase, but this will be due to the higher sales, and in addition, the effects will be significant from the transition to in-house sales and the improvement to the gross profit margin from the switch to the liquid RTD formulation. So for operating profit, the outlook is for the Company to become profitable for the first time since it was listed.

The forecast for net sales in FY12/22 is in the range of ¥11,282mn to ¥11,809mn. The majority of the higher sales will be from the contribution of sales for relapsed and refractory DLBCL, and the extent of the market penetration rate will be maintained. The operating profit margin is expected to rise to a level of around 20%, as it seems that the gross profit margin improvement trend will continue from the progress made in switching to the liquid RTD/RI formulations.

In 2015, the Company concluded a licensing-in agreement with The Medicines Company (U.S.) for the self-administered pain-management medication (SyB P-1501). In October 2017, it filed for arbitration seeking a payment of US$82mn (around ¥9bn) as compensation for damages for the non-fulfillment of the licensing agreement, and this agreement was terminated in November of the same year. This arbitration procedure is still ongoing, but from the viewpoint that reflects the conservative earnings targets in the current Mid-Range Plan, the effects of this have not been included in the targets. The arbitration-procedure period generally lasts 1.5 to 2 years, but it will depend on the other party, so the period remains undetermined.

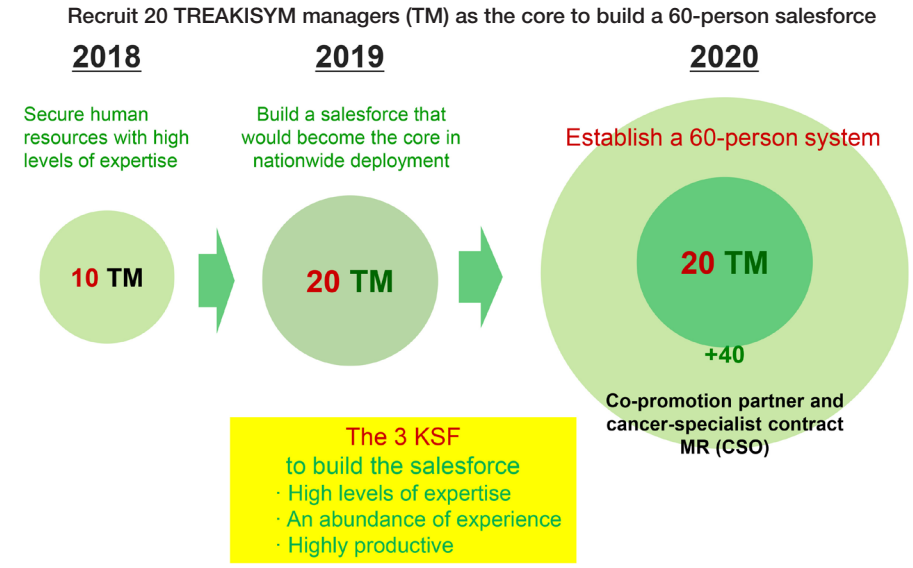
Expectations for TREAKISYM® in a combination therapy with immune checkpoint inhibitors

2. Issues toward achieving the plan's targets

Toward achieving the targets in the Mid-Range Plan, the Company has set the following five KSF (Key Success Factors), and if it achieves them, it can be expected to become profitable in FY12/21 and to secure sustainable growth. But on the other hand, if it cannot clear these issues, they will become risk factors.

(1) Establish its own sales system

As previously stated, for its own sales system, the Company intends to establish a system of 20 TREAKISYM managers and to add an additional 40 members by June 2020 in order to establish a network of 400 priority medical facilities that cover the entire country, based on a local community-centered approach. TREAKISYM® is currently sold to approximately 900 facilities, and the priority facilities (400 facilities) covers about 90% of net sales. Normally, the major pharmaceutical companies cover the country with a personnel system of 300 to 400 MR, but the Company plans to expand sales effectively through using a small but highly skilled salesforce. For the remaining 40 people, the Company is currently considering whether to utilize them for sales to pharmaceutical companies in the blood cancer area and to construct a co-promotion partner system, or as cancer-specialist contract MR (CSO), and it plans to have decided this by Q2 FY12/19.



Source: From the Company's results briefing material

(2) Achieve TREAKISYM® annual net sales of ¥10bn (on a drug-price basis)

The Company expects to achieve the annual net sales target of ¥10bn for TREAKISYM® in 2019. As previously explained, the effects of it being listed in the Japan Society of Hematology's treatment guidelines as the standard treatment for malignant lymphoma are considerable. Also, the fact that the BR therapy market penetration rate for untreated areas did not grow as much as expected in 2018 is due to the volume of Eisai's sales activities from April 2018 (such as by the salesforce and the holding of seminars) which fell to around half the volume at its peak, because Eisai diverted resources to its in-house developed products. In 2019, the recruited TREAKISYM managers will carry out sales activities to progress the switch from R-CHOP therapy to BR therapy, raising the market penetration rate to around 60-70%, so it considered that the ¥10bn target can be achieved.

Also, at the current time it is judged that the risk that demand for TREAKISYM® will decline in the future due to the development of new drugs is extremely low. Currently, within the developments of new drugs for malignant lymphoma that are being progressed in the U.S. and Europe, there are close to 100 combination therapies with BR therapy that are being developed, so it is no exaggeration to say that the existence of TREAKISYM® is essential to the development of therapeutic agents for malignant lymphoma. In particular, seven clinical trials are being progressed for its combination therapy with immune checkpoint inhibitors, and developments are expected in this area going forward. Therefore, demand for TREAKISYM® is forecast to trend stably in the future also.

Clinical developments through combination use with immune checkpoint inhibitor

Mechanism of action	Product name	Development stage	Indication	Combination-use regimen	Progress
PD-1 antibody	Opdivo®	1/2	r/r DLCBL	BR therapy + Opdivo + Gemcitabine	Ongoing
		2	HL	B single drug + Opdivo + Adcetris	Being progressed
		1/2	r/r HL	B single drug + Opdivo + Gemcitabine	Being progressed
		1/2	r/r HL	B single drug + Opdivo + Adcetris	Completed
PD-L1 antibody	Tecentriq®	1/2	NHL	B single drug + Tecentriq + Obinutuzumab	Completed
	Bavencio®	3	r/r DLCBL	BR therapy + Bavencio + Utomilumab	Being progressed
	Imfinzi®	1/2	HNHL • CLL	B±R + Imfinzi	Being progressed

Source: Prepared by FISCO from company briefing material

(3) Obtain approval and switch to the TREAKISYM® liquid RTD/RI formulations

At FISCO, we think it is highly likely that the liquid RTD/RI formulations will be approval as planned, because in the U.S., the penetration rate is already closed to 100% and also from the strong calls for them from medical sites. The switch to them from the lyophilized powder formulation is also forecast to proceed quickly due to the major advantages of the liquid formulation.

(4) Expand the indications of TREAKISYM® to relapsed and refractory DLBCL

The clinical trial for relapsed and refractory DLBCL is scheduled to be completed by the end of 2019, and if steady progress is made for the approval, sales can be expected to begin from Q3 FY12/21.

(5) Secure excellent human resources

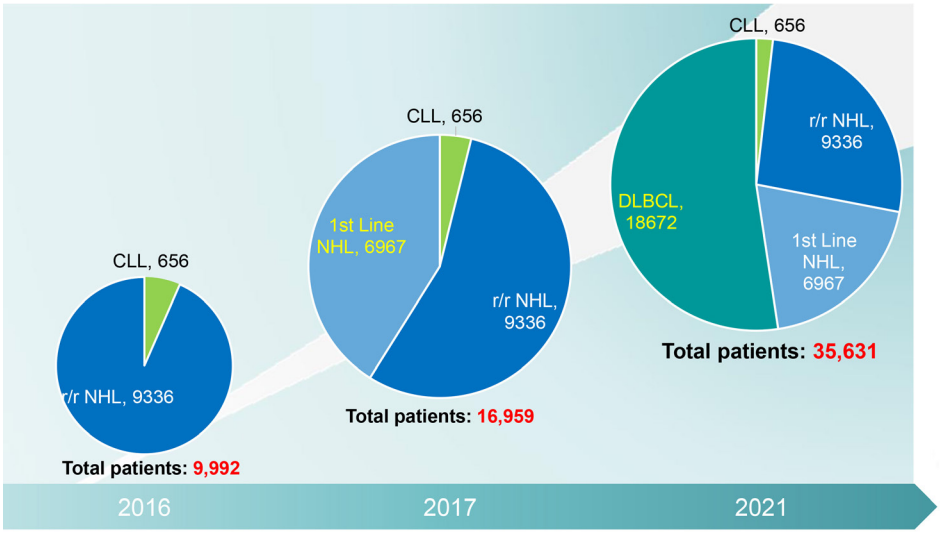
The important point for the transition to the in-house sales system is securing excellent human resources in the salesforce who have high levels of expertise, an abundance of experience, and who are highly productive. For the time being, the Company seems to be working to secure 20 human resources that meet the conditions to be TREAKISYM managers, and their sales activities can be expected to produce results going forward.

The sales growth potential is around ¥40bn on a drug-price basis, which is 5 times the 2018 result

3. Sales growth potential

Results from 2022 onwards may also trend upward and continue to grow. This is because if marketing approval is received for TREAKISYM® that is being developed for relapsed and refractory DLBCL, the number of potential patients within Japan will instantly double, increasing from approximately 17,000 in 2018 to 35,000. According to the Company's materials, as of 2018, the total number of potential patients was 16,959, consisting of 9,336 relapsed and refractory NHL patients, 6,967 untreated NHL patients, 656 CLL patients, and 18,672 relapsed and refractory DLBCL patients. Although the amount will change depending on what percentage is set for the market penetration rate, if excluding DLBCL, potential sales are ¥12bn to ¥13bn on a drug-price basis, and if simply calculated, this amount will approximately double simply by adding relapsed and refractory DLBCL patients.

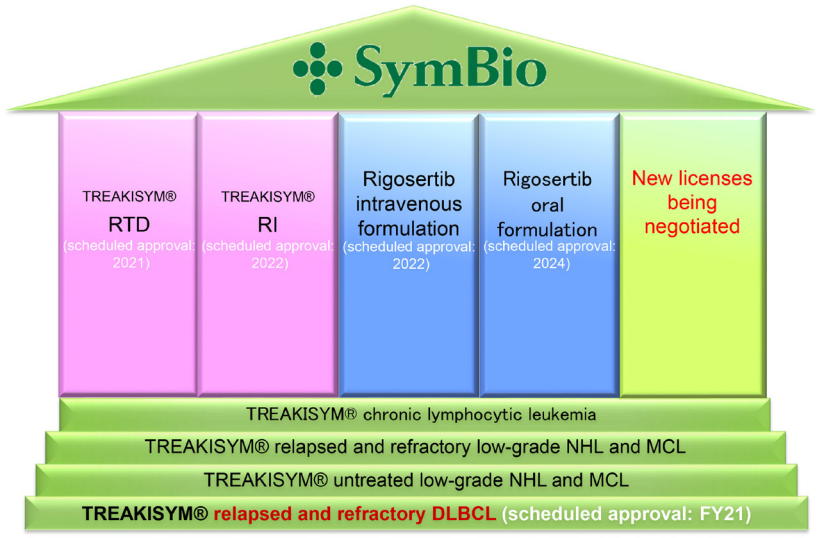
Growth in the potential market scale for TREAKISYM® from its approval for a new indication (r/r DLBCL)



Source: From the Company's results briefing material

Moreover, if rigosertib is approved for a combination therapy with azacitidine for untreated high-risk MDS, it can be expected to achieve sales of around the same scale of azacitidine (approximately ¥15bn). If all of these developments are successful, it is calculated that the sales growth potential will increase from ¥8.5bn in 2018 to approximately ¥40bn on a drug-price basis, while the Company's net sales will become more than ¥30bn. It also seems to be progressing licensing-in negotiations for 2 new proposals, and they may be added to the pipeline before 2022.

Developments in SymBio's pipeline strategy to realize sustainable growth



Source: From the Company's results briefing material

Intends to raise business funds up to FY12/20 through the exercise of stock acquisition rights

4. Financial condition

Looking at the financial condition at the end of FY12/18, total assets were up ¥1,987mn on the end of the previous fiscal year to ¥6,239mn. This was because in current assets, cash and deposits, and merchandise and finished goods increased ¥1,874mn and ¥171mn respectively. Conversely, total liabilities were up ¥324mn on the end of the previous fiscal year to ¥1,337mn, mainly due to increases in accounts payable-other of ¥172mn and accounts payable-trade of ¥121mn.

Also, net assets were up ¥1,662mn on the end of the previous fiscal year to ¥4,901mn, as although retained earnings decreased ¥2,752mn due to the recording of a loss, capital stock and capital surplus both increased ¥2,210mn following the exercise of third-party stock acquisition rights.

The Company issued the 45th through the 47th Stock Acquisition Rights (with Exercise Price Revision Clauses) from an allocation to EVO FUND in April 2018 in order to stably raise funds for business activities in the future. The number of common stocks corresponding to stock acquisition rights is 50 million stocks in total, and the dilution rate is 92.5%. It is a scheme to raise funds stably by exercising stock acquisition rights three times each year. The exercise of the 45th tranche (20 million stocks) has already been completed, raising estimated funds-on-hand of ¥2,579mn, and the rest are scheduled to be exercised in 2019 and 2020. At the end of FY12/18, cash and deposits were approximately ¥4.8bn, and assuming the Company's results forecasts, in total, cash out of ¥8.8bn will be generated from 2019 to 2020. Therefore, in order to fund business activities up to 2020, it will require at least ¥4bn, but if all of the remaining rights are exercised at the current stock-price level (¥229 on March 14, 2019), it would raise ¥6.8bn, so it can be said that it will be able to sufficiently cover this amount. However, it is necessary to be aware that should the stock price decline in the future and trend around the ¥113 level, which is the lower limit of the exercise price, it may have a shortage of funds and require new funding. The Company is targeting net profit of ¥1,736 to ¥2,060mn in FY12/22, which is the final fiscal year of the Mid-Range Plan, and EPS, calculated based on if all of the stock acquisition rights up to the 47th tranche are exercised in the future, will be at ¥16.7 to ¥19.8.

Balance sheet

(¥mn)

	FY12/15	FY12/16	FY12/17	FY12/18	Change
Current assets	4,826	6,685	4,036	6,038	2,001
(Cash and deposits)	4,261	5,719	2,947	4,821	1,874
Non-current assets	157	193	215	200	-14
Total assets	4,984	6,878	4,252	6,239	1,987
Total liabilities	552	1,393	1,012	1,337	324
(Interest-bearing debt)	-	450	-	-	-
Net assets	4,431	5,484	3,239	4,901	1,662

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

Overview on the issuance of acquisition rights by third-party allotment

	45th	46th	47th
Number of stock acquisition rights issued	20,000	15,000	15,000
Exercise period	April 26, 2018 to October 23, 2018	April 26, 2019 to September 17, 2019	April 27, 2018 to September 17, 2018
Exercise status	100%	-	-
Amount funded	2,579	-	-
Minimum exercise price	113	113	113

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

Uses of the funds

	Amount (¥mn)	Expected timing of expenditure
Development of in-licensed drugs	4,700	April 2018 to December 2020
Creation of an independent sales structure	3,300	
Investment in new in-licensing, M&A, and other	2,413	
Total	10,413	

Source: Prepared by FISCO from Company material

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