

English
translation

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SymBio's Long Range Plan: FY2014 to FY2016 (Revised Version)

I. Long Range Plan for the coming three years

(1) Overview of FY 2013 business results as of the date of the Long Range Plan

Progress in the Company's business for FY 2013 (from January 1, 2013 to December 31, 2013) is as follows.

1. Domestic

[SyB L-0501 (the generic name: bendamustine hydrochloride, the trade name: TREAKISYM®)]

Since December 2010, the Company has marketed the anticancer drug SyB L-0501 in Japan through its business partner Eisai Co., Ltd. ("Eisai"), for the indications of refractory/relapsed indolent non-Hodgkin's lymphoma and mantle cell lymphoma.

The Company has also carried out three clinical trials on TREAKISYM® for additional indications.

With respect to the Phase II clinical trial for the indications of previously untreated indolent non-Hodgkin's lymphoma and mantle cell lymphoma, the enrollment for the targeted simple size was completed in March 6, 2013. The application for approval in the EU has already been submitted by Astellas Pharma Europe, and is being reviewed by the European Medicines Agency ("EMA").

The Phase II clinical trial for the indication of chronic lymphocytic leukemia was initiated in May 8, 2013, and favorable progress has been made with enrollment of patients. In this connection, TREAKISYM® was designated an orphan drug (pharmaceutical for treatment of rare diseases) for the indication of chronic lymphocytic leukemia during June 2012.

Discussion about future approaches to development for refractory/relapsed aggressive

non-Hodgkin's lymphoma is currently being continued with the Pharmaceuticals and Medical Devices Agency ("PMDA").

On the other hand, in the Phase II clinical trial on refractory/relapsed multiple myeloma, which was carried out as part of the expansion of indications, although a dose of 90 mg/m² TREAKISYM® was confirmed to be safe for Japanese patients on the basis of interim results, no patients were found to respond to this treatment, and it was judged that it would be very difficult to achieve the target response rate with TREAKISYM® monotherapy, even with inclusion of more patients in the study, so the study was discontinued. In the future, we will not develop this indication but allocate our business resources to other studies with a high probability of approval.

[SyB L-1101 (intravenous formulation) and SyB C-1101 (oral formulation), the generic name: rigosertib]

The Japanese Phase I clinical trial of the anticancer drug SyB L-1101 (intravenous formulation) for the indication of refractory/relapsed myelodysplastic syndrome ("MDS"), a type of blood tumor, has been continued.

With respect to SyB C-1101 (oral formulation), the Japanese Phase I clinical trial for the intended indication of previously untreated MDS was initiated in March 2013.

While presenting study data of several programs currently in development, Onconova Therapeutics, Inc. (USA, "Onconova") has presented favorable data from Phase II trial in transfusion-dependent low risk MDS patients treated with oral formulation on December 10, 2013.

By accelerating development in the Europe and the U.S., it is expected to expand market potential of rigosertib in Japan. Besides, it is also expected to shorten the clinical trial process in Japan through the future utilization of the clinical trial data obtained abroad.

2. Overseas

SyB L-0501 sold largely as planned in South Korea, Taiwan and Singapore. In Singapore and South Korea, we sell the product through Eisai, as we do in Japan, and the sales figures have been going up steadily.

3. Fund procurement

The Company made a resolution on November 19, 2013 regarding the issuance of new shares and secondary offering of shares through a public offering and through a third party allotment. Accordingly, the payments of 2,503,744 thousand yen and 321,118 thousand yen had been completed on December 4, 2013 and December 25, 2013, respectively.

4. Business results

As a result of the above, net sales totaled 1,532,054 thousand yen for the fiscal year ended December 31, 2013, primarily reflecting sales of SyB L-0501 in Japan and the other Asia Pacific territories. The net sales amount was decreased by 21.6% compared to the previous year by following review of the current market inventory level of TREAKISYM®.

Selling, general and administrative expenses totaled 1,998,522 thousand yen (a year-on-year decrease of 12.9%), including research and development (“R&D”) expenses of 1,052,790 thousand yen (a year-on-year decrease of 26.7%) due to the accrual of expenses associated with the clinical trials for multiple indications for SyB L-0501, clinical trials for SyB L-1101 and SyB C-1101, as well as other selling, general and administrative expenses of 945,732 thousand yen (a year-on-year increase of 10.6 %).

As a result, operating loss of 1,680,528 thousand yen was recognized for the fiscal year ended December 31, 2013 (operating loss of 1,700,273 thousand yen for the previous fiscal year). In addition, recording of amount totaling 35,363 thousand yen as non-operating expenses, primarily comprising commissions and stock-issuance expenses, and amount totaling 114,467 thousand yen as non-operating income, primarily comprising foreign exchange gains, led to ordinary loss of 1,601,424 thousand yen (ordinary loss of 1,729,480 thousand yen for the previous fiscal year) and net loss of 1,605,224 thousand yen (net loss of 1,733,320 thousand yen for the previous fiscal year).

(2) Symbio’s Long Range Plan – Summary and Background

Symbio is the first “specialty pharmaceuticals” in Japan to specialize in the following three areas: oncology, haematology and autoimmune disease. Although there is great medical demand in these areas, development remains challenging due to the need for high degree of specialization. Because major pharmaceutical companies are reluctant to develop these areas for reasons of business productivity, oncology, haematology and autoimmune disease are regarded as the “undeserved therapeutic area” in terms of development in Japan and Asia.

The Company sees business opportunities in these “undeserved therapeutic area” and instead of pursuing the “blockbuster” new drugs (where sales often exceeds 100 billion yen), it focuses on drugs and new drug candidates related to oncology, haematology and autoimmune diseases, even though the markets are relatively small, because the needs are high. Capturing high revenue through development and sales of drugs and new drug candidates in these areas is at the core of the business development of the Company.

The most significant characteristic of Symbio’s business model is one in which the Company does not own research and manufacturing facilities, and instead evaluates new drug candidates that have been tested on humans for efficacy and safety, and brings in

products mainly through pharmaceutical companies and bio venture companies in Europe and the U.S.

By not owning its research and manufacturing facilities, the Company is able to avoid large capital investment and conduct effective business operations with low fixed costs. Also, by concentrating on “late stage” new drug candidates that have been tested for efficacy and safety on humans, the development period is shortened, thus lowering both development cost and risks.

The Company is building a strong pipeline portfolio and aiming for an early return to profitability through these efforts.

SymBio’s Long Range Plan is as follows:

- Maximize the value of our main product of TREAKISYM®, for which manufacturing and marketing approval has been granted in respect of relapsed or refractory indolent non-Hodgkin’s lymphoma, a type of blood cancer, through aggressive promotion of indication expansion (life cycle management).
- Develop SyBL-110 (intravenous formulation)/C-1101 (oral formulation) (the generic name; rigosertib), which was introduced in July 2011, as therapy for MDS, a type of blood cancer. Development decision with regard to solid tumors will be made after considering status and data of development overseas.
- Pro-actively search, evaluate and negotiate with the aim of introducing new drug candidates during the first half of FY2014.
- Pro-actively develop and commercialize drugs for the Asian markets that are expected to grow rapidly (China (including Hong Kong), Taiwan, Korea and Singapore).

(3) Business Status, Outlook and Other Assumptions

- With regard to TREAKISYM®, from December 2010, domestic sales have commenced through Eisai, our business partner, for relapsed or refractory indolent non-Hodgkin’s lymphoma and mantle cell lymphoma indications. Sales have been increasing steadily and market share has reached a high level.
- Going forward, in order to further increase sales, the Company aims to strengthen the marketing arrangement for TREAKISYM® with Eisai, achieve product differentiation from targeted competing drugs, and endeavors to obtain early approval for additional indications. Among the clinical trials that are being done to expand indication, case registration is complete and data analysis in progress for Phase II clinical trial for indication of untreated indolent non-Hodgkin’s lymphoma, and while taking into account outcome of approval in Europe, the Company will continue to prepare for

regulatory approval. Phase II clinical trial in respect of chronic lymphocytic leukemia is in progress with a view to obtain early approval. With regard to relapsed or refractory aggressive non-Hodgkin's lymphoma, although Phase II clinical trial produced good results, the Company is in further discussion with PMDA regarding plans for additional clinical trials and shall continue to put in best efforts to obtain approval.

With regard to relapsed or refractory multiple myeloma, based on the interim results of the Phase II clinical trial, a determination was made to discontinue development for this indication because, although safety was confirmed for Japanese patients, response was not observed, and even if further patient enrollment is continued, expected response rate as a single drug would be difficult to achieve.

- Anticancer drug SyB L-1101 ((intravenous formulation) /C-1101 (oral formulation) (the generic name: rigosertib), With regard to SyB L-1101 (intravenous formulation), the Company will consider domestic development plans based on results of Phase III clinical trial for refractory or relapsed aggressive MDS by Onconova Therapeutics Inc. ("Onconova"), results of further discussions to take place between Onconova and the US Food and Drug Administration ("FDA") or the European Medicines Agency ("EMA"), and Onconova' development policy taking into the above results. In Japan, the Company plans to continue current Phase I clinical trial. With regard to SyB C-1101 (oral), development will continue for indications of transfusion-dependent low risk MDS and untreated high risk MDS. As for development relating to solid tumor, determination will be made after consideration of overseas development status and data.
- As for transdermal analgesic anti-emetic SyB D-0701, there are no further plans to develop, as other programs are higher priorities.
- With regard to the Asian market, SyB L-0501 has been approved and sold in Singapore, Hong Kong, South Korea and Taiwan, and sales have been progressing at a steady rate. Sales in these markets are done through business alliances and to maximize sales in the Asian market, the Company will work on further strengthening of business alliances. With regard to SyB L-1101/C-1101, the Company owns the rights in South Korea and will continue to develop towards obtaining approval there.

II. Earnings Forecast and Performance Target

(Unit: millions of yen)

Fiscal year	Net sales	Operating income (loss)	Ordinary income (loss)	Net income (loss)
FY 2013 (Actual)	1,532	(1,680)	(1,601)	(1,605)
FY 2014 (Forecast)	1,990	(1,311)	(1,308)	(1,311)
FY 2015 (Target)	2,110	(2,355)	(2,351)	(2,355)
FY 2016 (Target)	4,225 to 2,162	(1,757) to (2,455)	(1,753) to (2,451)	(1,757) to (2,454)

Assumptions and Numerical Bases for Projections and Performance Targets

- With regard to sales, TREAKISYM® makes up the majority of product sales. The performance target for drug sales assume that new drugs (additional indications) are approved as assumed in the business plan, and figures are derived after detailed analysis and discussion about market size projections, competitive positioning vis-à-vis existing therapies, market dominance, and sales performance after commencement of sales. Furthermore, milestone revenue is estimated based on the Company's development plan.
- Cost of sales is estimated based on the provisions of existing licensing agreement.
- Selling and general administrative expenses mainly categorized as research and development ("R&D") expenses or other selling expenses and general administrative expenses.
 - Research and development expenses are estimated based on "III. Other reference information – Status of Development Portfolio and Performance Targets". However, with regard TREAKISYM®, since the business alliance agreement with Eisai provides that R&D expenses be split equally between the two parties, half of estimated expenses are assumed. Milestone payments are estimated in accordance with provisions in the existing contract.
 - Other selling and general administrative expenses mainly consist of expenses incurred from TREAKISYM® marketing, new business development, production & distribution and administrative operations. However, with regard to TREAKISYM®, since the business alliance agreement with Eisai provides that marketing expenses be split equally between the two parties, half of estimated expenses are assumed, similar to the R&D expenses.
- As stated in "III. Other reference information – Status of Development Portfolio and

Performance Targets”, with respect to indication for relapsed or refractory aggressive non-Hodgkin’s lymphoma, as there are no additional clinical trial plans at this point, no sales and expenses are assumed for this indication.

- Application for approval for the indication untreated indolent non-Hodgkin's lymphoma planned in FY 2015 is dependent on the outcome of approval in Europe. Therefore, numerical assumptions were made based on the two scenarios (approval obtained in Europe and approval not obtained in Europe) and presented as maximum and minimum figures.

III. Other Reference Information

Status of Development Portfolio and Performance Targets

Development code Therapeutic category	Indication	Preclinical study	Phase I clinical trial	Phase II clinical trial	Filing application for approval	Approved	
SyB L-0501 Anticancer drug	Refractory/relapsed indolent non-Hodgkin's lymphoma	Approved on October 2010					
	Untreated indolent non-Hodgkin's lymphoma	Completed as of December 31, 2013 (FY 2013)		FY 2014 target	FY 2015 target	FY 2016 target	
	Refractory/relapsed aggressive non-Hodgkin's lymphoma	Completed as of December 31, 2013 (FY 2013)		Under discussion with PMDA			
	Chronic lymphocytic leukemia	Completed as of December 31, 2013 (FY 2013)		FY 2014 target	FY 2015 target	FY 2016 target	
SyB L-1101 Anticancer drug Intravenous formulation	Refractory/relapsed aggressive MDS (myelodysplastic syndrome)	Completed as of December 31, 2013 (FY 2013)		FY 2014 target	Details after Phase I clinical trial are currently under discussion.		
SyB C-1101 Anticancer drug Oral formulation	Untreated medium/high risk MDS (myelodysplastic syndrome)	Completed as of December 31, 2013 (FY 2013)		FY 2015 target	FY 2016 target		
	Untreated transfusion-dependent low risk MDS (myelodysplastic syndrome)	Completed as of December 31, 2013 (FY 2013)		FY 2014 target	FY 2015 target	FY 2016 target	

- Note 1.  : The development plan
 : Completed as of December 31, 2013 (FY 2013)
 : FY 2014 target
 : FY 2015 target
 : FY 2016 target

Portfolio summary and issues for achieving plans are set out below.

○ **SyB L-0501 (the generic name: bendamustine hydrochloride, the trade name: TREAKISYM®)**

Summary:

- The principle component of SyB L-0501, bendamustine hydrochloride (the generic name), was used in Germany for many years as anticancer drug for non-Hodgkin's lymphoma, multiple myeloma and chronic lymphocytic leukemia (the trade name: Ribomustin).
- From 2000, the efficacy and safety of this drug has been re-evaluated and it is now approved and sold in 60 countries around the world. In July 2005, the Company obtained the exclusive rights of development and marketing from the licensor, Astellas Deutschland GmbH, a German subsidiary of Astellas, to develop and sell the drug in Japan, China (including Hong Kong), South Korea, Taiwan and Singapore, and in all regions other than China, has obtained approval. Going forward, the Company will collaborate closely with local business partners and maximize sales.
- In Japan, manufacturing and marketing approval was obtained in October 2010 for indications relapsed or refractory indolent non-Hodgkin's lymphoma and mantle cell lymphoma and sales started through Eisai, a business alliance, in December 2010. After starting its sales, this drug has been administered to over 7000 patients (estimated by the Company) by the end of 2013.
- In order to expand the value of this drug, the Company is working on development for other indications such as untreated indolent non-Hodgkin's lymphoma, mantle cell lymphoma and chronic lymphocytic leukemia. The Company is also continuing discussions with PMDA regarding the indication relapsed or refractory aggressive non-Hodgkin's lymphoma.

Issues and Specific Measures:

- **Promotion of Indication Expansion**
For untreated indolent non-Hodgkin's lymphoma and mantle cell lymphoma, case registration for Phase II clinical trial is complete and observation period has begun. Since approval in Japan is subject to obtaining approval in Europe, as soon as such European approval is confirmed, the Company will proceed with the domestic application process. For relapsed or refractory aggressive non-Hodgkin's lymphoma, Phase II clinical trial is complete but additional clinical trials are required before the application for approval. Sales and expenses relating to this indication are not included in this long range plan, as details of the clinical trial plans are not confirmed

at this point. With regard to chronic lymphocytic leukemia, current Phase II clinical trial is moving forward in order to obtain approval at an early stage.

➤ **Maximizing Sales**

In Japan, our most significant market, sales of the product is through Eisai, with whom we have a business alliance. In order to further promote market penetration, the efficacy and safety of the drug already proven through clinical trials need to be more widely understood so that it is more often prescribed. To that end, the Company will work closely with Eisai and plan strategies vis-à-vis competing therapies, and aggressively develop marketing strategies such as collaboration with academic conferences and study groups.

○ **SyB L-1101 (intravenous formulation) /C-1101 (oral formulation) (the generic name: rigosertib)**

Summary:

- SyB L-1101/C-1101 is an anticancer drug, which operates as a unique multi-kinase inhibitor. Since obtaining exclusive rights to develop and distribute in Japan and South Korea from Onconova in July 2011, the Company has been developing this drug. (The Company has obtained rights for both intravenous and oral formulations.)
- With regard to development of this drug, currently, Onconova is conducting development in the U.S. and Europe for the indications of myelodysplastic syndromes (“MDS”), head and neck cancer, ovarian cancer, etc. With regard to the intravenous formulation for relapsed or refractory MDS, Onconova will consider development policies taking into account results of the Phase III clinical trial and discussions with FDA and EMA. As for the oral formulation, Phase II clinical trial for the indication of transfusion-dependent low risk MDS is complete. For untreated medium/high risk MDS, Phase I clinical trial is in progress.
- Onconova is proceeding with Phase II clinical trial for the indication of head and neck cancer and the Company will await status report, data, etc. from such clinical trial before proceeding domestic development.
- Currently, the Company is conducting Phase I clinical trial of the intravenous formulation for the indication of relapsed or refractory MDS, and of the oral formulation for the indication of untreated MDS.

Issues and Specific Measures:

- **Promotion of Indication Expansion**
With regard to the intravenous formulation, domestic development policy will be determined taking into account the result of Phase II clinical trial by Onconova for

relapsed or refractory high risk MDS, anticipated discussions between Onconova and FDA as well as EMA, and Onconova' development policy resulting from the above. Domestically, the Company plans to continue Phase I clinical trials that are in progress. With regard to the oral formulation, domestic clinical trials will be conducted taking into account the two trials (transfusion-dependent low risk MDS and untreated medium/high risk MDS) currently in progress in Europe and the U.S. With regard to solid tumors (head and neck cancer, etc.), development will be considered upon review of development status/data from overseas.

➤ Use of Overseas Data

In order to cut costs and reduce development time, it is assumed that results of clinical trials conducted overseas will be used as materials for domestic approval applications. Such data will be reviewed in detail by the Company in order to be assured of high quality.

This disclosure document is for the purpose of providing information on the Company's future business strategies to investors, and is not for the purpose of soliciting investments.

The evaluation on the Company's business strategies and investment decisions shall be made by investors themselves based on their own judgment.

The Company does not guarantee, in any sense, the possibility of realizing and achieving any performance target or other matter of our business strategies and does not assume any liability for any such information.

All forward-looking statements (including, but not limited to, the performance targets in our business plan) contained in this document are judgmentally prepared by the Company based on the information available as of the date of this document. Therefore, in the event there are future changes to conditions that make up the assumptions of the business strategy, such as economic conditions, there may be impact on the actual business condition and performance such that the results will be different from statements in this disclosure document.