Shared Research Report
2014/12/1

SymBio Pharmaceuticals (4582)

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Executive summary

SymBio in-licenses drugs for development and sale in Japan and Asia

SymBio is a specialty pharmaceutical company that buys the right to develop and commercialize drug candidates in order to address the underserved medical needs of patients in Japan and the rest of Asia. With its main focus on the oncology, hematology and autoimmune space, the company typically seeks in-licensing opportunities for niche markets from pharmaceutical and biotech companies based in the US or EU.

Notably, the company does not conduct basic research and outsources preclinical/clinical development, employing a fabless in-licensing approach. Using its proprietary in-house "search engine," the company identifies, assesses and in-licenses only quality drug candidates having proof-of-concept established in human subjects. The company first screens third-party drug candidates being tested in clinical trials, then presents the in-licensing opportunities to its Scientific Advisory Board for further assessment of the science behind each molecule, preclinical/clinical data, target market, and the feasibility of receiving marketing approval from Japanese regulatory authorities.

According to the company, the typical development timeline of an oncology drug in Japan from preclinical studies to marketing approval is about 10 to 17 years. However, the company secured marketing approval for its first oncology drug under development in Japan, Treakisym, in only four years after the first clinical trial was initiated, with product launch only two years after US marketing approval and around the same time that approval was granted in Europe. Within three years of its launch, Treakisym had captured more than 50% of the non-Hodgkin's lymphoma (NHL) and mantle cell lymphoma (MCL) market in Japan.

As of July, 2014, the company's pipeline consisted of two main assets under development: Treakisym (anticancer agent for hematologic malignancies) and rigosertib (anticancer agent for myelodysplastic syndromes).

Earnings

In its mid-term plan, SymBio projects sales of JPY2.2bn-JPY4.2bn and a net loss of JPY1.8bn-JPY2.5bn in FY12/16. The company will seek regulatory approval to market Treakisym as first-line treatment for low-grade NHL and MCL, and chronic lymphocytic leukemia (CLL) during FY12/16. This will result in milestone payments and higher sales. The company expects R&D expenses to fall for Treakisym, but to rise for rigosertib and new drug candidates that it acquires, resulting in higher overall SG&A expenses.

The company expects to achieve profitability in FY12/19-FY12/20, looking for an operating profit of anywhere between JPY900mn and JPY2.6bn in FY12/20. This assumes that products under clinical development in July 2014 receive regulatory approval and generate sales as planned.

Strengths and weaknesses

Shared Research thinks SymBio's strengths include its unique candidate selection process, strong product development team, and business strategy focusing on niche markets. Weaknesses include the lack of its own sales force and funding needs (see Strengths and weaknesses).

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Key financial data

Income Statement (JPYmn)	FY12/09 Par.	FY12/10 Par.	FY12/11 Par.	FY12/12 Par.	FY12/13 Par.	FY12/14 Est.
Sales	**1,191**	**1,450**	**1,883**	**1,955**	**1,532**	**1,990**
YoY	-26.9%	21.7%	29.8%	3.9%	-21.6%	29.9%
Gross Profit	**1,191**	**1,212**	**658**	**593**	**318**	
YoY	-26.9%	1.7%	-45.7%	-9.9%	-46.4%	
GPM	100.0%	83.6%	35.0%	30.3%	20.8%	
Operating Profit	**-208**	**-613**	**-2,067**	**-1,700**	**-1,681**	**-1,311**
YoY	-	-	-	-	-	-
OPM	-	-	-	-	-	-
Recurring Profit	**-214**	**-638**	**-2,095**	**-1,729**	**-1,601**	**-1,308**
YoY	-	-	-	-	-	-
RPM	-	-	-	-	-	-
Net Income	**-218**	**-642**	**-2,105**	**-1,733**	**-1,605**	**-1,311**
YoY	-	-	-	-	-	-
Net Margin	-	-	-	-	-	-
Per Share Data						
Number of Shares ('000)	101	112	19,131	19,131	30,634	
EPS	-32.5	-59.3	-143.6	-90.6	-69.3	-39.5
EPS (Fully Diluted)	-	-	-	-	-	
Dividend Per Share	-	-	-	-	-	
Book Value Per Share	402.8	365.4	345.3	254.7	239.5	
Balance Sheet (JPYmn)						
Cash and Equivalents	4,121	4,016	6,511	4,840	7,264	
Total Current Assets	**4,218**	**4,213**	**7,178**	**5,421**	**7,634**	
Tangible Fixed Assets, net	13	22	17	14	9	
Other Fixed Assets	27	27	48	57	37	
Intangible Assets	2	1	13	11	8	
Total Assets	**4,261**	**4,263**	**7,256**	**5,502**	**7,687**	
Accounts Payable	-	1	309	330	-	
Short-Term Debt	-	-	-	-	-	
Total Current Liabilities	**205**	**178**	**646**	**599**	**251**	
Long-Term Debt	-	-	-	-	-	
Total Fixed Liabilities	**2**	**2**	**5**	**4**	**3**	
Total Liabilities	**207**	**180**	**651**	**602**	**254**	
Net Assets	**4,054**	**4,083**	**6,606**	**4,900**	**7,433**	
Interest-Bearing Debt	-	-	-	-	-	
Cash Flow Statement (JPYmn)						
Operating Cash Flow	-211	-754	-2,074	-1,659	-1,677	
Investment Cash Flow	-4	-116	-117	-411	-1,332	
Financing Cash Flow	2,963	663	4,611	-1	4,057	
Financial Ratios						
ROA	-7.6%	-15.1%	-36.5%	-27.2%	-24.3%	
ROE	-8.1%	-15.8%	-39.4%	-30.1%	-26.0%	
Equity Ratio	95.1%	95.8%	91.0%	89.1%	96.7%	

Figures may differ from company materials due to differences in rounding methods

Source: Company data

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Recent updates

Highlights

On **December 1, 2014**, Shared Research initiated coverage of SymBio Pharmaceuticals.

On **November 13, 2014**, SymBio Pharmaceuticals announced the issue of second series unsecured convertible bonds with subscription rights to new shares, and series 34 subscription rights to new shares by third-party allotment.

The company expects to receive total funds of about JPY1.5bn, net of expenses. The company plans to use the funds for expenses related to the development of new drug candidates between FY12/14 and FY12/16. As of November 13, 2014, SymBio was negotiating license agreements for two to three new drug candidates with pharmaceutical companies in the US and EU. It has based the amount of funding required on the expected cost of in-licensing these drug candidates.

Overview of the offering

Second series unsecured convertible bonds with subscription rights to new shares

- Payment date: December 1, 2014
- Number of stock subscription rights: 25 units
- Issue price of bonds: JPY20mn (JPY100 per JPY100 par value)
- Issue price of stock subscription rights: Gratis
- Number of potential shares: 1.7mn
- Total funding amount: JPY500mn
- Conversion price: JPY300
- Subscription and allocation method: Issued to Oak Capital Corporation via third-party allotment.

Series 34 subscription rights to new shares

- Allotment date: December 1, 2014
- Number of stock subscription rights: 30,304 units
- Issue price: JPY10.4mn (JPY342 per unit)
- Number of potential shares: 3.0mn
- Total funding amount: JPY1.0bn (JPY10.4bn from the issue of subscription rights to new shares; JPY1.0bn from the exercise of subscription rights)
- Exercise price: JPY330
- Subscription and allocation method: Issued to Oak Capital Corporation via third-party allotment.

On **the same day**, the company announced its revised full-year earnings forecast for FY12/14.

Revisions to the full-year earnings forecast for FY12/14 (previous forecast in parentheses)

- Sales: JPY2.0bn (JPY1.8bn)
- Operating loss: JPY1.3bn (operating loss of JPY1.7bn)
- Recurring loss: JPY1.3bn (recurring loss of JPY1.7bn)
- Net loss: JPY1.3bn (net loss of JPY1.7bn).

Reasons for the revisions

The company expects sales to outperform the initial forecast by JPY205mn, mainly due to an increase in overseas product sales of Treakisym. SG&A expenses are also expected to be lower than in the initial forecast owing to a revision of development costs for clinical trials.

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On **November 7, 2014**, the company announced earnings results for Q3 FY12/14 (see the results section for details).

On **November 5, 2014**, the company announced the completion of patient enrollment for the domestic phase II clinical trial of its anticancer agent Treakisym (development code: SyB L-0501; generic: bendamustine hydrochloride) in CLL patients. The company is developing Treakisym in conjunction with partner Eisai Co., Ltd. ("Eisai"). The Ministry of Health, Labour and Welfare (MHLW) has designated Treakisym as a prioritized unapproved drug having high potential to address the lack of an effective therapy in CLL—Treakisym was designated as an orphan drug for the CLL indication in June 2012.

In October 2010, the company received domestic regulatory approval of Treakisym for the indications of relapsed or refractory NHL and MCL. Since December 2010, Eisai, has been selling the drug in Japan under the product name "Treakisym® 100mg for IV Use."

For corporate releases and developments more than three months old, see the News and topics section.

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Trends and outlook

Quarterly trends and results

Quarterly Performance	FY12/13				FY12/14				FY12/14	
(JPYmn)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	% of FY	FY Est.
Sales	489	322	513	209	174	802	373		67.7%	1,990
YoY	-15.8%	-32.0%	10.5%	-52.3%	-64.5%	149.1%	-27.3%			29.9%
GP	151	33	89	45	32	215	106			
YoY	17.6%	-75.7%	-59.5%	-58.5%	-78.6%	543.6%	19.8%			
GPM	30.9%	10.4%	17.3%	21.5%	18.6%	26.8%	28.5%			
SG&A	492	500	475	532	448	445	427			
YoY	-19.2%	-5.9%	-18.7%	-6.5%	-9.0%	-10.8%	-10.1%			
SG&A / Sales	100.6%	155.2%	92.6%	255.3%	257.9%	55.6%	114.5%			
OP	-341	-466	-386	-488	-416	-231	-320			-1,311
YoY	-	-	-	-	-	-	-			-
OPM	-	-	-	-	-	-	-			-
RP	-352	-460	-376	-414	-454	-259	-228			-1,308
YoY	-	-	-	-	-	-	-			-
RPM	-	-	-	-	-	-	-			-
NI	-353	-461	-377	-414	-455	-261	-228			-1,311
YoY	-	-	-	-	-	-	-			-
NPM	-	-	-	-	-	-	-			-

Figures may differ from company materials due to differences in rounding methods
Source: Company data

Q3 FY12/14 results

In Q3 FY12/14, sales increased 1.9% YoY to JPY1.3bn, due to domestic and overseas sales of Treakisym.

Treakisym product sales totaled JPY1.3bn (+9.0% YoY). Net domestic sales of Treakisym were up 0.4%; net overseas sales were up 2.3x.

Milestone payments were JPY15mn (-85.0% YoY), upon the approval of bendamustine hydrochloride ("bendamustine"; product name: Symbenda) for the indication of relapsed or refractory low-grade NHL in South Korea.

SG&A expenses totaled JPY1.3bn (-10.0% YoY). R&D costs were down 33.2%, at JPY545mn. The company incurred costs related to the clinical trials of Treakisym and rigosertib (intravenous and oral forms), but overall R&D costs fell year-on-year as R&D spending on Treakisym winds down. Other SG&A expenses were up 19.1% at JPY775mn.

Overall, SymBio booked an operating loss of JPY967mn (operating loss of JPY1.2bn in Q3 FY12/13). Recurring loss was JPY941mn (recurring loss of JPY1.2bn in Q3 FY12/13). The net loss was JPY944mn (net loss of JPY1.2bn in Q3 FY12/13).

Domestic
Treakisym
In March 2013, patient enrollment was completed for the phase II clinical trial of Treakisym in the first-line treatment of low-grade NHL and MCL. The company is analyzing and evaluating data from the trial as it prepares to file a supplemental new drug application (sNDA) for marketing approval. Astellas

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Pharma GmbH ("Astellas"; European subsidiary of Astellas Pharma Inc.; TSE1: 4503) has already applied for approval of first-line low-grade NHL for bendamustine in Europe; the application is currently under review in Germany by the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte: BfArM).

A phase II clinical trial for the indication of CLL was initiated by the company in May 2013, with the completion of patient enrollment in November 2014.

Rigosertib
The company is conducting a domestic phase I clinical trial for the intravenous (IV) form of rigosertib in relapsed or refractory higher-risk myelodysplastic syndromes (MDS). In February 2014, licensor Onconova Therapeutics, Inc. ("Onconova"; Nasdaq: ONTX) announced the results of its phase III ONTIME clinical trial in patients with higher-risk MDS who had progressed, failed or relapsed after prior therapy with hypomethylating agents (HMAs); 299 MDS patients were enrolled at 89 sites in the US and Europe. Compared with best supportive care (BSC), the clinical trial did not show a statistically significant improvement in the overall survival period (primary outcome measures). However, group analysis showed a statistically significant difference in the survival period for patients whose condition had deteriorated or not responded to previous treatment using HMAs. At the time of writing this report, Onconova was in discussions with regulatory agencies in the US and Europe regarding the future development of intravenous rigosertib. Post phase I development in Japan will depend on the outcome of these discussions.

A domestic phase I clinical trial using the oral form of rigosertib is also underway in Japan for the treatment of lower-risk transfusion-dependent MDS patients as first-line treatment.

Q2 FY12/14 results

In 1H FY12/14, sales increased 20.3% YoY to JPY975mn, due to domestic and overseas sales of bendamustine.

Domestic sales of Treakisym to end users were JPY2.1bn (+2.0% YoY). Product sales were up 35.1%, to JPY960mn. Domestic sales of Treakisym rose 21.1%, as Eisai completed distribution inventory adjustments. Overseas product sales were up about 3.5x.

Milestone payments totaled JPY15mn (-85.0% YoY). The company received these payments upon marketing approval of Symbenda for the additional indication of relapsed or refractory low-grade NHL in South Korea.

SG&A expenses totaled JPY893mn (-9.9% YoY). R&D costs were down 33.5%, at JPY370mn. The company incurred costs related to the clinical trials of Treakisym and rigosertib (intravenous and oral), but overall R&D costs fell year-on-year as R&D spending on Treakisym winds down. Other SG&A expenses were up 20.3% at JPY523mn, due to higher promotional expenses and changes to the categorization of some R&D costs.

Overall, SymBio booked an operating loss of JPY646mn (operating loss of JPY807mn in Q2 FY12/13). The company also booked non-operating expenses of JPY79mn, mainly due to foreign exchange losses. As a result, recurring loss was JPY713mn (recurring loss of JPY812mn in Q2 FY12/13). The net loss was JPY715mn (net loss of JPY814mn in Q2 FY12/13).

Asia Pacific partners
SymBio expects overseas markets to expand, and forecasts about 10% growth in sales in FY12/14. In

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June 2014, Eisai's subsidiary, Eisai Korea Inc. (EKI) received approval in South Korea for the additional indication of relapsed or refractory low-grade NHL for bendamustine (product name: Symbenda). EKI sells the drug for two other indications—CLL and multiple myeloma (MM). A second Eisai subsidiary, Eisai (Singapore) Pte. Ltd., markets bendamustine in Singapore (product name: Symbenda). In Taiwan, the drug is being marketed by InnoPharmax Inc. for relapsed or refractory low-grade NHL and CLL (product name: Innomustine).

For details on previous quarterly and annual results, please refer to the Historical performance section.

Full-year (FY12/14) outlook

FY12/14 Forecasts (JPYmn)	FY12/13 1H Act.	FY12/13 2H Act.	FY12/13 FY Act.	FY12/14 FY Est.
Sales	**811**	**721**	**1,532**	**1,990**
CoGS	626	588	1,214	
Gross Profit	184	134	318	
GPM	22.7%	18.5%	20.8%	
SG&A	992	1,007	1,999	
SG&A / Sales	122.3%	139.7%	130.5%	
R&D expenses	557	496	1,053	
Operating Profit	**-807**	**-873**	**-1,680**	**-1,331**
OPM	-	-	-	-
Recurring Profit	**-812**	**-789**	**-1,601**	**-1,308**
RPM	-	-	-	-
Net Income	**-814**	**-791**	**-1,605**	**-1,311**
Net Margin	-	-	-	-

Figures may differ from company materials due to differences in rounding methods
Source: Company data

FY12/14 Forecasts (sales breakdown) (JPYmn)	FY12/12 FY Act.	FY12/13 FY Act.	FY12/14 FY Est.	YoY
Sales	**1,955**	**1,532**	**1,990**	**29.9%**
Product Sales	1,955	1,432	1,975	37.9%
Domestic	1,861	1,300	1,468	12.9%
Overseas	94	132	507	284.1%
Taiwan	26	46	47	2.2%
Korea	55	58	412	610.3%
Singapore	13	28	48	71.4%
Royalty Revenue	-	100	15	-85.0%

Figures may differ from company materials due to differences in rounding methods
Source: Company data

Earnings outlook

Sales

SymBio forecasts sales of JPY2.0bn (+29.9% YoY) in FY12/14, as Treakisym's market share grows and Eisai Co., Ltd. completes distribution and inventory adjustments (Eisai markets Treakisym under a co-development and commercialization license agreement with SymBio). The company expects product sales of JPY1.5bn (+12.9% YoY).

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Overseas sales may reach JPY507mn (+248.1% YoY). The company announced in June 2014 that Eisai Korea obtained approval from the Ministry of Food and Drug Safety (MFDS) in South Korea for the additional bendamustine indication of relapsed or refractory low-grade NHL. As a result of this approval, the company expects sales in South Korea to increase by 610.3%, in addition to milestone payments from Eisai totaling JPY15mn.

SG&A
The company anticipates SG&A expenses of JPY1.9bn (-6.7% YoY) in FY12/14, and expects R&D costs to fall as it approaches the end of development for Treakisym and it revises overall costs for clinical trial development.

Pipeline

Treakisym
Astellas Pharma Inc. is seeking approval in the EU for the use of bendamustine as first-line treatment for low-grade NHL. Following approval, SymBio plans to file a sNDA in Japan.

The company plans to file a second sNDA for the domestic phase II clinical trial of Treakisym in CLL patients in 1H FY12/16.

Rigosertib
The IV formulation of rigosertib has been in phase I development in Japan to treat second-line higher-risk myelodysplastic syndromes (MDS), a type of hematological malignancy, since June 2012.

Following consultations with the US Food and Drug Administration (FDA) regarding the possibility of filing a marketing application for intravenous rigosertib using results from the phase III 'ONTIME' clinical trial, Onconova has confirmed that an underserved medical need exists for patients who did not respond to standard first-line treatment using hypomethylating agents (HMAs). Onconova plans to continue to focus on this subgroup of patients as it moves forward with rigosertib development.

The company's domestic phase I clinical trial for the oral formulation of rigosertib to treat first-line transfusion-dependent lower-risk MDS has been underway since March 2013.

In-licensing of new drug candidates
SymBio plans to expand its product pipeline by in-licensing additional drug candidates.

Long-term outlook

When it released its FY12/13 results, SymBio also announced a mid-term plan for FY12/14 through FY12/16.

Midterm Plan (JPYmn)	FY12/13 Act.	FY12/14 Est.	FY12/15 Target	FY12/16 Target
Sales	1,532	1,785	2,110	2,162 ~ 4,225
Operating Profit	-1,681	-1,654	-2,355	-2,455 ~ -1,757
Recurring Profit	-1,601	-1,650	-2,351	-2,451 ~ -1,753
Net Income	-1,605	-1,654	-2,355	-2,454 ~ -1,757

Source: Company data

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Main Pipeline Schedule	FY12/14	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20
Treakisym (initial treatment of lower-grade NHL and MCL)		Apply for approval	Obtain approval Start sales				
Treakisym (CLL)			Apply for approval Obtain approval Start sales				
Rigosertib (for injections) (relapsed and refractory higher-risk MDS)					Apply for approval	Obtain approval Start sales	
Rigosertib (for oral use) (blood transfusion-dependent lower-risk MDS)					Apply for approval	Obtain approval Start sales	
Rigosertib (for oral use) (frontline treatment of higher risk MDS)							Apply for approval

Source: Shared Research (includes Shared Research estimates for applications)

Earnings targets

Sales

The company's mid-term plan calls for an increase in Treakisym sales growth by securing a larger share of the relapsed or refractory low-grade NHL and MCL market. The company plans to hold seminars for doctors in Japan to promote Treakisym as an efficacious and safe alternative treatment to existing drug therapies. Such efforts may also lead to an increase in per-patient sales as patients complete additional treatment cycles.

SymBio is targeting sales of JPY2.2bn-JPY4.2bn for FY12/16, the period when the company expects to receive marketing approval in Japan to use Treakisym in the treatment of first-line low-grade NHL and MCL, and CLL. The company expects to see an increase in sales once these additional indications are approved.

SG&A

SG&A expenses, excluding R&D, may remain at about JPY1bn even though personnel costs could increase in line with the mid-term plan. R&D expenses fell in FY12/13, and the company plans for this trend to continue in FY12/14 with the winding down of Treakisym development. R&D expenses will likely rise from FY12/15 onwards due to development costs for rigosertib and additional in-licensed products. These expenses may total between JPY1bn and JPY1.5bn during the period of the plan.

Operating loss

Operating loss may narrow in FY12/14, before widening in FY12/15 on higher R&D expenses for rigosertib and new drug candidates. For FY12/16, operating loss may total between JPY1.8bn and JPY2.5bn, depending on whether the company secures marketing approval to use Treakisym as first-line treatment for low-grade NHL and MCL, and for the treatment of CLL.

Issues in the mid-term plan

Buying new drug candidates

The company aims to in-license two new drug candidates during the period of the mid-term plan. (FY12/14-FY12/16). Shared Research expects the company to spend between JPY500mn and JPY1bn in

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one-time payments and R&D expenses per new drug candidate. These costs are not included in the plan.

Reorganization of sales force ahead of rigosertib sales
The company will consider reorganizing its sales force in preparation for the launch of rigosertib.

In August 2008, the company established an exclusive partnership with Eisai for Treakisym. Eisai agreed to cover one-time payments, milestone payments in accordance with clinical trial stage, and half of R&D expenses, as well as 100% of sales and marketing costs. Shared Research estimates that Eisai takes a margin of about 50% on domestic Treakisym sales at the National Health Insurance (NHI) drug price - SymBio's margin is just over 10%. The company also expects its margin to improve as procurement costs fall in line with higher sales.

> **National Health Insurance (NHI) drug price**: The Ministry of Health, Labour and Welfare sets the prices of drugs that medical institutions can be reimbursed for under national health insurance.

As of July 2014, SymBio had not entered into an exclusive domestic sales agreement for rigosertib with any company, and the creation of its own domestic sales force for the launch of rigosertib in Japan is being considered. Following conversations with the company, Shared Research estimates that Eisai has 120-130 specialist medical representatives focusing on oncologic conditions. Labor costs would increase if SymBio were to create its own sales force of 30-40 medical representatives to sell rigosertib, but the company could realize a significantly higher profit margin on rigosertib sales than with Treakisym.

SymBio could turn profitable in FY12/19-FY12/20 if existing products are approved

The plan does not call for the company to post a profit, but states that it could carve out an operating profit in FY12/20 if products in the current pipeline receive marketing approval as planned.

FY12/20 sales may reach JPY10bn-JPY12bn for Treakisym, and JPY5bn-JPY6bn for rigosertib
Sales may increase if the company receives approval to use Treakisym as first-line treatment for low-grade NHL and MCL, and for the treatment of CLL, in FY12/16.

The number of patients using Treakisym for relapsed or refractory low-grade NHL and MCL is estimated at 4,700, implying potential sales of JPY4.5bn-JPY5bn (company data). However, according to the company, as of July 2014, about 7,100 patients were undergoing first-line treatment for low-grade NHL or MCL, and about 700 patients were being treated for CLL —none of these patients currently use Treakisym. As the population ages, so will the potential patient population. Following discussions with management, Treakisym sales could increase by about JPY6bn-JPY6.5bn if the drug is approved for use in these additional indications.

Rigosertib: the company plans to market the IV and oral form in FY12/19. Shared Research projects that rigosertib sales in both formulations may touch JPY5bn-JPY6bn in FY12/20. All in, sales may reach JPY15bn-JPY18bn in FY12/20—if the indications of the company's current products are approved as planned.

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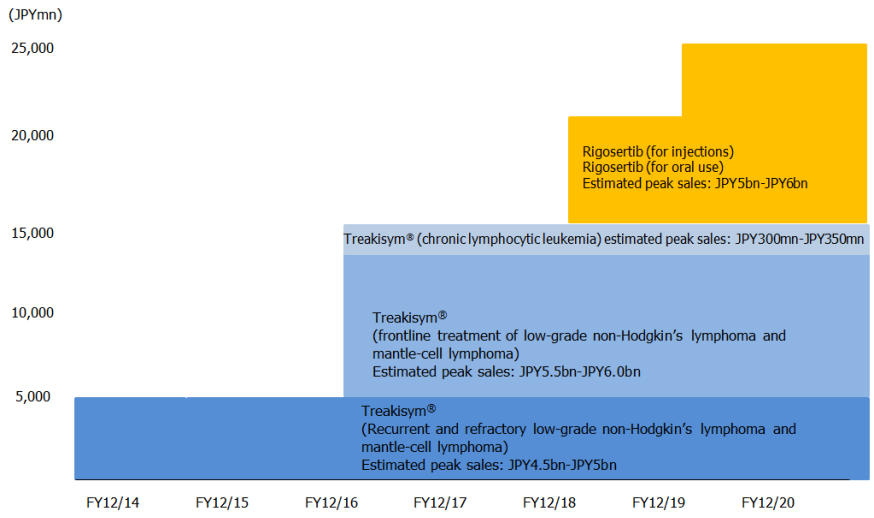
Medium-term sales (NHI prices)



Source: Company materials

Gross profit may reach JPY3.9bn-JPY5.1bn in FY12/20

SymBio's own product sales are about 40% of Treakisym's overall sales. Cost of goods sold is approximately 75% (see Earnings structure section). If Treakisym sales increase to JPY11.5bn, the company's own product sales may reach JPY4.6bn—implying JPY1.2bn in gross profit.

If the company builds its own sales network for rigosertib, sales at wholesale prices will be booked as product sales. Shared Research assumes wholesale prices of about 80-90% of NHI price and CoGS at approximately 25%. Therefore, if SymBio's product sales hit JPY4bn-JPY5.5bn, this would contribute about JPY2.7bn-JPY3.9bn to gross profit.

Following discussions with management, Shared Research thinks that if the current products in the company's development pipeline and their target indications receive marketing approval as planned, gross profit could reach JPY3.9bn-JPY5.1bn in FY12/20, with sales of JPY8.5bn-JPY10.0bn.

Possible operating profit of JPY900mn to JPY2.6bn in FY12/20

SG&A, excluding R&D, may remain at about JPY1bn. Despite the approaching end of development for rigosertib, R&D spending may increase by JPY1bn-JPY1.5bn if the company acquires new drug candidates. The establishment of the company's own sales network for rigosertib may also drive up labor costs by about JPY500mn (assuming the company employs 40 medical representatives). Shared Research thinks SG&A expenses (excluding R&D expenses) may increase by JPY1.5bn.

Operating profit may be between JPY900mn and JPY2.6bn in FY12/20, in line with expected gross profit.

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Business

Business description

SymBio licenses drugs for development and sale in Japan and Asia Pacific

President and CEO, Fuminori Yoshida, established SymBio in March 2005 to address underserved medical needs in Japan and the Asia Pacific region, with main focus on oncologic, hematologic and autoimmune diseases. The company aspires to be a leading specialty pharmaceutical company in the Asia Pacific region. Its strategic approach to drug development negates the need for costly and time-consuming investment in earlier-stage R&D activities with an in-house search and evaluation team to identify and assess only quality drug candidates having proof-of-concept established in human subjects.

Strategy Overview (details to follow)

- **Proof-of-concept**: The company reduces product development risk by focusing on drug candidates undergoing clinical development with preclinical/clinical data establishing safety and efficacy in human subjects.
- **Screening**: The company uses an in-house search and evaluation team to screen and evaluate drug candidates having a high unmet medical in Japan and other Asia Pacific markets with the potential to secure marketing approval in a shorter clinical development period. A select number of drug candidates will then undergo rigorous review by the company's Scientific Advisory Board (SAB).
- **Fabless**: The company outsources preclinical/clinical studies and manufacturing to reduce fixed costs.
- **New areas:** The company targets drugs with the potential to receive orphan drug designation and thus, secure a longer marketing exclusivity period due to high unmet medical needs and smaller patient populations. Larger pharmaceutical companies may be reluctant to develop drugs in niche markets due to limited sales potential—SymBio sees an opportunity to avoid intense competition in the marketplace by focusing on the development of orphan or 'orphan-like' drugs.
- **Asia expansion strategy**: The company identifies and capitalizes on opportunities to grow sales by acquiring the right to drug candidates, mainly from US or EU pharmaceutical and biotech companies, for clinical development and commercialization in Japan and other key Asia Pacific markets.

> **Proof-of-concept**: Per company materials, "confirming the efficacy and safety of a new drug candidate in human subjects through clinical trials…"

As of September 2014, the company had evaluated over 395 drug candidates from 315 companies since its establishment in March 2005, signing on three deals.

According to the company, the development of a drug—from preclinical studies to approval—usually takes 10 to 17 years. A newly developed chemical compound has a 1/100,000 chance of securing regulatory approval. By contrast, the company's first product, Treakisym, received approval for domestic production only five years after signature of the License Agreement. The company achieved sales of JPY4.2bn in Japan in the third year after launch (FY12/13), equivalent to a market share of over 50%.

An example of the company's ability to identify and pursue quality in-licensing opportunities with proof-of-concept established is the license agreement signed for the development and commercialization right to rigosertib—currently in phase I clinical trials in Japan. In July 2011, once phase II clinical trials in the US established the drug's proof-of-concept, SymBio secured an exclusive right to all indications for rigosertib in Japan and South Korea from Onconova within seven months from the initial meeting between

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the two companies. The following year, Baxter International Inc. entered into an agreement with Onconova for the commercialization rights to rigosertib in Europe with a USD50mn upfront payment and USD337.5mn in pre-commercial milestones tied to MDS and pancreatic cancer indications (in addition to an existing equity investment with Onconova of USD55mn), a market that is approximately twice the size of Japan.

Products under development: Treakisym and rigosertib (IV and oral)

Treakisym

For patients that have developed resistance to other drugs, Treakisym is safer and more effective than existing treatments. In October 2010, SymBio received approval to use the drug in Japan for relapsed or refractory low-grade NHL and MCL, having previously received orphan drug designation and priority review for these two indications.

Refractory conditions are difficult to treat, or do not respond to treatment.

A pivotal phase II clinical trial for Treakisym in first-line low-grade NHL and MCL has been completed in Japan, with completion of patient enrollment for the pivotal phase II clinical trial in CLL in November 2014. The company plans to file for marketing approval of first-line low-grade NHL and MCL in FY12/15, and file the sNDA for CLL in 1H FY12/16.

Rigosertib

Rigosertib is a treatment for myelodysplastic syndromes (MDS). According to the company, rigosertib may be used alone or—due to its safety—in combination with other anticancer drugs. The drug is being developed in both intravenous (IV) and oral forms.

In February 2014, Onconova completed phase III clinical trials for the IV form of rigosertib in patients with higher-risk MDS who had progressed on, failed or relapsed after prior therapy with hypomethylating agents (HMAs). For the oral form of the drug, Onconova is conducting a phase II clinical trial in the US for the first-line treatment of transfusion-dependent lower-risk MDS. In Japan, SymBio has been conducting a phase I clinical trial for the oral formulation in lower-risk MDS patients since 2013. The company expects to submit an application in CY2018 and receive marketing approval for the oral form in 2019.

Revenue: milestone payments and Treakisym; profitability target: FY12/19-FY12/20

Revenue comes from milestone payments and product sales. Operating losses have persisted since the company's foundation with the exception of FY12/08 when the company booked an operating profit due to a one-time contract payment from Eisai for an exclusive domestic right to sell Treakisym (see Historical performance). For FY12/14, the company expects an operating loss and net loss of JPY1.7bn each. Per the mid-term plan, the company expects to post annual operating losses of JPY1.5bn to JPY2.5bn through FY12/16.

SymBio seeks to post a profit in FY12/19-FY12/20 after receiving marketing approval for indications now under development. In light of conversations with management, Shared Research thinks the company may post sales of JPY8.5bn and JPY10.0bn and operating profit of between JPY900mn and JPY2.6bn in FY12/20. Caveat: this assumes that indications for bendamustine and rigosertib receive regulatory approval as planned (see Long-term outlook).

SymBio expects operating losses to total JPY5.8bn-JPY6.5bn through FY12/16. To achieve growth in the mid-term, the company needs to in-license new drug candidates for development and commercialization.

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In FY12/13, the company had cash and deposits plus securities of about JPY7.3bn. More cash may be necessary to continue bankrolling growth.

Business strategy

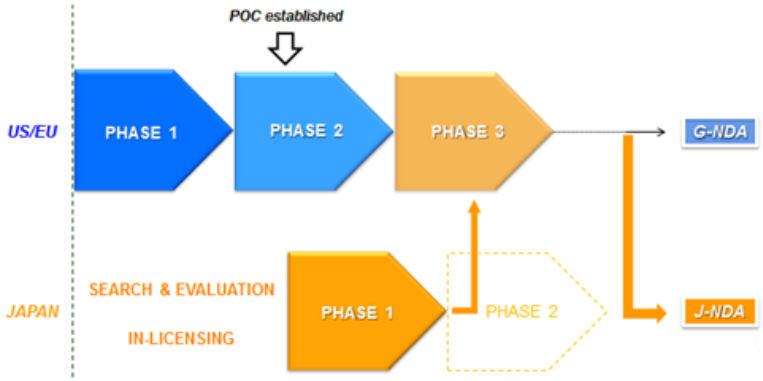
Unlike conventional pharmaceutical companies, SymBio does not conduct basic research or develop its own drug candidates in labs or clinics. Rather, it in-licenses drug candidates from pharmaceutical and biotech companies based in the US or EU.

The company focuses on developing drugs that have strong safety and efficacy data in clinical trials, providing an opportunity to develop new drugs more likely to succeed and secure regulatory approval with the use of bridging data whenever possible to shorten development timelines. Because the company does not conduct basic research, the company can file an NDA and start selling a drug within five to six years of securing the development and commercialization right. The company increases the chance that drug candidates it in-licenses will be approved in the future through an effective in-house screening process and rigorous evaluation by the company's Scientific Advisory Board. The overall aim is to reduce development risk by reducing development costs and shortening approval timelines, lifting earnings.

SymBio targets compounds with an established proof-of-concept

The pharmaceutical business requires substantial financial commitment in terms of upfront investment, not to mention the number of years of development required in order to realize a return on the investment and the high risk of failure in clinical studies from Phase I through III. According to the company, the probability of a chemical compound having a signal with pharmacological activity in a particular disease being approved as a drug is 1/20,000 to 1/25,000, and only 15-20% of drugs that manage to enter the marketplace achieve profitability for the sponsor. Given the high rate of attrition of drug candidates in clinical development, SymBio reduces development risk by only targeting quality drug candidates undergoing clinical development with proof-of-concept established in human subjects and/or market sales. NDA filings that use clinical data generated overseas can expedite product development in Japan and other parts of Asia, slashing development costs and improving the overall success rate.

Post-proof-of-concept strategy



Source: Company data

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It may be possible for the company to file NDAs in Japan by bridging Japanese Phase I clinical trials with foreign data through its participation in global Phase III studies, thereby avoiding the need to complete domestic Phase II and/or Phase III studies for marketing approval.

Screening: independent search network plus evaluation experience

The company identifies quality chemical compounds owned by pharmaceutical and biotech companies in the US or EU using a proprietary "search engine" and rigorous evaluation process. These candidates are first screened in-house by the search and evaluation team, whose members have extensive product development experience working at various pharmaceutical and biotech companies.

Onsite due diligence
After a select team, including the President and CEO, visits the potential licensor to conduct due diligence, a decision is made regarding whether to pursue the in-licensing opportunity based on the results of onsite due diligence and input from the company's SAB members.

Only four drugs out of 395 have met the company's stringent criteria since its foundation
As of September 2014, the company had screened 395 products under development or marketed by over 315 companies. It acquired four. The first was Treakisym, which Eisai Co., Ltd. (TSE1: 4523) sells in Japan. Clinical trials for additional Treakisym indications were underway as of July 2014. A second drug candidate, an antiemetic transdermal patch, was in-licensed from Abeille Pharmaceuticals, Inc. in March 2007, but the program was discontinued in 2013 when the phase II trial failed to show statistically significant efficacy versus placebo in reducing radiation-induced nausea and vomiting (RINV) in 189 patients. In addition to Treakisym, the company is also developing both the IV and oral formulations of rigosertib, the third and fourth drugs.

Scientific Advisory Board
The Scientific Advisory Board is comprised of former directors of pharmaceutical companies, researchers, and doctors, and meets three times a year. Typically, the SAB panel evaluates two to three drug candidates that have been selected via the company's in-house screening process. This in-house screening of only those drug candidates having proof-of-concept established in human subjects with supportive efficacy and safety data followed by SAB assessment enables the company to reduce development risk and to pursue only those opportunities having the best chance of reaching the marketplace.

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Scientific Advisory Board members

Name	Profile
George Morstyn, M.D., Ph.D.	Presently Chairman GBS Venture Capital firm, Deputy Chairman Victorian Comprehensive Cancer Centre, Director of Co-operative Research Centre for Cancer Therapeutics and Proacta. Former Senior Vice-President of Development and CMO at Amgen Inc..
Robert Lewis, M.D., Ph.D.	Former Senior Vice-President of US R&D, Aventis Pharmaceuticals; Chief Scientific Officer, Cell Therapeutics; Head of Discovery Research, Syntex Pharmaceuticals; Associate Professor, Harvard Medical School Currently serves as consultant in Immunology/Inflammation, Roche Palo Alto; Adjunct Faculty Member, Rockefeller University, New York
Makoto Ogawa, M.D., Ph.D.	Honorary President, Aichi Cancer Center
Tatsutoshi Nakahata, M.D., Ph.D.	Deputy Director and Professor of Center for iPS Cell Research and Application (CiRA), Institute for Integrated Cell-Material Sciences, Kyoto University Honorary member, The Japanese Society of Hematology
Toshio Suda, M.D., Ph.D.	Professor, Keio University School of Medicine (Chair in Developmental and Differential Biology) Guest Professor, Institute of Molecular Embryology and Genetics, Kumamoto University Vice President, The Japanese Society of Hematology in 2012
Tsutomu Takeuchi, M.D., Ph.D.	Professor of Medicine, Keio University, School of Medicine (Division of Rheumatology, Clinical Immunology, Department of Internal Medicine)
Kenzaburo Tani, M.D., Ph.D.	Director, Medical Institute of Bioregulation, Kyushu University Professor, Kyushu University Hospital (Department of Advanced Molecular and Cell Therapy) Vice-Chairman, The Japan Society of Gene Therapy in 2011 and 2012
Shinji Nakao, M.D., Ph.D.	Professor, Kanazawa University College of Medical, Pharmaceutical and Health Sciences, Division of Cancer Medicine Cellular Transplantation Biology (Hematology/Respirology) Executive Director, The Japanese Society of Hematology in 2012
Toshio Heike, M.D., Ph.D.	Professor, Kyoto University Graduate School of Pharmaceutical Sciences (Developmental Medicine, Pediatrics) Director, Clinical Genetics Unit, Kyoto University Hospital Director, Division for iPS Cell Application Development, Kyoto University Hospital

Source: Company website

A fabless strategy with a lean management team

SymBio seeks to reduce costs and raise profits by finding the right partner(s) to develop and commercialize drugs nimbly and efficiently through flawless execution.

Specifically, the company designs clinical trial protocols and whenever possible, will participate in global phase III studies being conducted by its partner(s) overseas with the aim of shortening development timelines in Japan. It may be possible to file NDAs in Japan using foreign data to support or "bridge" data generated in Japanese clinical trials, thereby avoiding the need to complete domestic Phase II and/or Phase III studies for marketing approval. The company uses its well established network for bendamustine to coordinate with medical professionals, outsourcing routine development duties. Production is also outsourced either to the company that originally granted the product license, or to other domestic or foreign manufacturer(s).

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Focusing on rare oncologic, hematologic, and autoimmune diseases

SymBio focuses on drugs for underserved medical needs—even when the market may be as small as JPY10bn—rather than focusing on blockbuster drugs with sales in the hundreds of billions of yen. It aims to take advantage of therapeutic areas that tend to be overlooked in the pharmaceutical industry and thus, lack effective drugs.

According to the company, globally Japan has the third largest oncology market after the US and EU, and the market is expected to continue to expand due to Japan's aging population. However, regarding the type of tumors that anticancer drugs can effectively treat, there is a considerable range of indications with a limited number of patients who will benefit from approved cancer treatments, particularly in the elderly population where the occurrence of serious adverse events can be prohibitive. As a result, barriers to entry are high—developing cancer drugs for niche markets is especially difficult and requires a high level of expertise. Concerns about having sufficient profit margins from marketed drugs to fund large operations means that major pharmaceutical companies may be reluctant to target indications with limited patient numbers for development, presenting an opportunity with fewer competitors in the marketplace for smaller and more specialized pharmaceutical companies such as SymBio.

Strategy for expansion in Asia

Demand for medical services is expected to rise in Asia as economies continue to grow. Yet—as in Japan—there remains a lack of effective treatments for rare oncologic, hematologic, and autoimmune diseases. The company is seeking to develop new drugs that are complementary to Treakisym and rigosertib to sell in China/Hong Kong, Taiwan, South Korea, and Singapore, as well as in Japan.

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Pipeline

Name/Code	Category	Licensed Country	Indications	Development Stage	Partner
Treakisym SyB L-0501	Anti-cancer agent	Japan	Refractory/relapsed low-grade NHL	Market approval (2010/10/27)	Eisai Co., Ltd. (co-developed; exclusive sales rights granted to Eisai)
			Refractory/relapsed mantle cell lymphoma	Market approval (2010/10/27)	
			Refractory/relapsed intermediate/high-grade NHL	PII (completed)	
			Initial low-grade NHL	PII (completed)	
			Initial mantle cell lymphoma	PII (completed)	
			CLL	PII (underway)	
		Singapore	low-grade NHL, CLL	Market approval (2010/1/20)	Eisai Co., Ltd. (exclusive development and sales rights granted to Eisai)
		Korea	CLL, MM	Market approval (2011/5/31)	Eisai Co., Ltd. (exclusive development and sales rights granted to Eisai)
			Refractory/relapsed low-grade NHL	Market approval (2014/6/16)	
		China	low-grade NHL	PIII (underway)	Teva Pharmaceutical Industries Ltd. (China) (exclusive development and sales rights granted to Teva)
		Hong Kong	low-grade NHL, CLL	Market approval (2009/12/30)	
		Taiwan	low-grade NHL, CLL	Market approval (2011/10/18)	Innopharmax, Inc. (Taiwan) (exclusive development and sales rights granted to Innopharmax)
Rigosertib (intravenous) SyB L-1101	Anti-cancer agent (intravenous)	Japan	Refractory/relapsed high-risk MDS	PI (underway)	—
		Korea		—	—
Rigosertib (oral) SyB C-1101	Anti-cancer agent (oral)	Japan	Blood transfusion-dependent, low-risk MDS	PI (underway)	—
			Initial treament of intermediate- and high-risk MDS (together with Azacitidine)	PI (underway)	—
		Korea	—	—	—

Source: Company website

SyB L-0501 (generic: bendamustine HCl; product name: Treakisym)

SyB L-0501 (Treakisym) or bendamustine hydrochloride is an anticancer agent. It is used as a treatment for low-grade NHL, MCL, MM and CLL.

> *Bendamustine was developed in 1971 by Jenapharm in former East Germany, where it was approved as a first-line treatment for low-grade NHL, MM, and CLL. After the unification of Germany in 1990, bendamustine was again evaluated for its effectiveness against these indications. In 2005, Germany approved the use of the drug for untreated low-grade NHL, MM and CLL. The drug was also approved in several other European countries in 2007. In the US, Treanda (bendamustine) was approved in March 2008 for relapsed or refractory NHL and CLL, with sales in October the same year. A separate application was filed in the US (2008) for the additional indication of previously untreated CLL.

According to the company, no cross-resistance has been shown for this drug, which means it is safer and more effective than existing treatments for target indications. In October 2010, SymBio received regulatory approval in Japan to market the drug for relapsed or refractory low-grade NHL and MCL. Eisai covers 100% of the marketing and sales costs, and has been selling the drug since its launch in December 2010 (see Earnings structure).

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The company has completed phase II clinical trials for Treakisym in the first-line treatment of low-grade NHL and MCL. Patient enrollment in a phase II trial for CLL was completed in November 2014. The company aims to secure approval to market Treakisym for these indications in FY12/16.

Lymphatic cancer

Lymphatic cancer is a malignant growth of lymphatic corpuscles in white blood cells. It causes inflammation of the lymphatic nodes. Lymphatic cancer is divided into Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL). Among the Japanese population, only 4% of lymphatic malignancies are HL. About 70-80% of NHL cases affect B-cells; the remaining 20-30% affect T/NK cells. Physicians examine tissue and determine the method of treatment depending on the type of cancerous cells observed: they look at the grade (high, intermediate, or low, depending on the aggressiveness of the disease) and clinical staging, which shows to what extent the cancer has spread.

Lymphatic malignancy: frequency by type

Category	Frequency
Non-Hodgkin's lymphoma	94%
B lymphocytes	69%
T/NK lymphocytes	25%
Hodgkin's lymphoma	4%
Other	2%

Source: Japanese Society for Lymphoreticular Tissue Research (JSLTR)

Treakisym in-licensed from Astellas; Eisai handles sales

In December 2005, SymBio signed a license agreement for the exclusive right to bendamustine in Japan with Astellas Deutschland GmbH ("Astellas"), a subsidiary of Astellas Pharma Inc. The company entered into a second license agreement with Astellas in March 2007 to extend its exclusive development and commercialization right for bendamustine to China/Hong Kong, Taiwan, South Korea, and Singapore.

In August 2008, SymBio granted Eisai Co., Ltd. ("Eisai") the co-development and exclusive marketing right for Treakisym in Japan. Under the agreement, SymBio receives one-time payments from Eisai as well as milestone payments based on the clinical trial stage for a particular indication, plus revenues after supplying Treakisym to Eisai. Eisai shoulders half of the development costs for Treakisym, including labor costs for researchers and outsourcing costs for clinical trials (see Earnings structure).

Approval for relapsed or refractory low-grade NHL, MCL

In October 2010, five years after acquiring the right to Treakisym, SymBio received marketing approval in Japan for relapsed or refractory low-grade NHL and MCL. In FY12/13—three years after the Japan launch of the drug in December 2010—Treakisym sales reached JPY4.2bn. According to company estimates, the drug has achieved a market share of more than 50%.

According to the company, Japan has about 4,700 patients who suffer from relapsed or refractory NHL and MCL. SymBio thinks annual Treakisym sales could reach JPY4.5bn-JPY5.0bn.

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Treakisym: adding more indications

As of July 2014, Treakisym was under phase II development by the company for the first-line treatment of low-grade NHL /MCL, and CLL as part of its plans for label expansion.

Market for Treakisym® and number of patients

	Non-Hodgkin's Lymphoma		Chronic Lymphatic Leukemia
	Low-grade B-cell	High and intermediate grade	
Initial treatment	Number of patients: 7,100 Obtain approval in FY12/15 (planned) Phase III trials complete in Europe Phase II trials complete in Japan		Number of patients: 700 Obtain approval in FY12/16 (planned) Approval obtained in Europe and the US Phase II trials underway
Relapsed and refractory conditions	Number of patients: 4,700 Approval obtained Approval obtained in Japan in Oct. 2010 Sales launched in Japan in Dec. 2010	Number of patients: 6,700 Consultation on application underway Phase II trials complete in Japan	

Source: Company data

First-line treatment of low-grade NHL and MCL

In Japan, R-CHOP therapy—a combination of rituximab with CHOP chemotherapy drugs (cyclophosphamide, doxorubicin, vincristine, and prednisolone)—is standard first-line treatment for low-grade NHL and MCL despite the frequent occurrence of adverse events due to toxicity. Researchers have yet to establish the most appropriate method of treatment using rituximab in combination with chemotherapy.

Phase III clinical trials conducted overseas have demonstrated that rituximab in combination with bendamustine (R-B therapy) was safer and more efficacious than standard R-CHOP therapy for previously untreated low-grade B-cell NHL. Based on these results, the National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) guidelines recommend the use of R-B therapy as first-line therapy for patients with untreated low-grade NHL. The efficacy and safety of R-B therapy demonstrated during clinical trials for previously untreated low-grade NHL led to recommendations as first-line treatment for this indication.

Development status: Astellas seeking approval in Europe
A randomized phase III trial completed in March 2011 by Dr. M. J. Rummel and researchers affiliated with Study Group Indolent Lymphomas (StiL) in Germany investigating efficacy and safety of bendamustine + rituximab (B-R) vs R-CHOP in first-line low-grade NHL and MCL is encouraging. The phase III clinical trial was conducted at 81 facilities in Germany, treating patients who were newly diagnosed between September 2003 and August 2008 with stage III or IV low-grade NHL or MCL. The trials involved a comparison between R-CHOP and the bendamustine-rituximab (B-R) regimen (bendamustine is marketed as Levact®, Ribomustin®, or Ribovact® in Europe). A total of 275 patients underwent R-CHOP therapy, while 274 were administered the B-R combination. The median follow-up period was 45 months. Clinical results showed that the median progression-free survival period was 69.5 months for the bendamustine

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hydrochloride-rituximab group while that for the R-CHOP group was 31.2 months (p<0.0001), demonstrating the superiority of the B-R therapy.

Results from the BRIGHT study, reported at the 2012 American Society of Hematology (ASH) Annual Meeting, combined with long-term safety data from other studies, suggest that the combination of bendamustine and rituximab may be an important alternative treatment option for the initial therapy of patients with low-grade NHL and MCL (Flinn et al reported in *Blood*). This randomized, noninferiority, phase III study evaluated the efficacy and safety of B-R vs a standard R-CHOP regimen or R-CVP (rituximab plus cyclophosphamide, vincristine, and prednisone) for treatment-naive patients with indolent NHL or MCL. The B-R combination was found to be noninferior to commonly used chemotherapy with R-CHOP/R-CVP in terms of complete response rate. Assessed by the primary endpoint of complete response rate, B-R was noninferior to R-CHOP/R-CVP (31% vs 25%, *P* = .0225 for noninferiority). The complete response rate for B-R was greater than the 22% threshold for noniferiority, an 88% margin.

sNDA filing in Japan for 1st-line low-grade NML and MCL in FY12/15
Astellas has filed a marketing application for the approval of bendamustine in first-line low-grade NHL in Europe which includes the StiL and BRIGHT study data, and data generated from SymBio's phase II study for first-line low-grade NHL in Japan. As of July 2014, the application was being reviewed by Germany's Federal Institute for Drugs and Medical Devices (BfArM) under the Decentralised Procedure. Astellas may be able to obtain approval for this indication in Europe in Q4 FY12/14 or Q1 FY12/15 (with eventual approval in 24 European countries—the 23 Concerned Member States plus Germany). After Astellas receives approval in Europe for first-line low-grade NHL, SymBio plans to use data both from its domestic phase II clinical trial and the data package in Europe when it files its sNDA in Japan. The company expects to receive marketing approval in Japan in FY12/16.

Patient population
SymBio estimates that there are 7,100 first-line low-grade NHL and MCL patients in Japan—1.5 times the number of patients with relapsed or refractory low-grade NHL and MCL. Treakisym sales could reach JPY5.5bn-JPY6bn as the Japanese population continues to age.

Targets chronic lymphocytic leukemia (CLL)

Astellas' European subsidiary has obtained approval in the US and the EU to market bendamustine for the indication of untreated CLL. In Japan, Treakisym was designated as an orphan drug (drug for the treatment of rare diseases) in June 2012 by the Review Committee on Unapproved or Off-Label Drugs with High Medical Needs after it was determined that this drug met critical demand for new therapies to treat CLL.

R&D status: application to be submitted in 1H FY12/16
The use of Treakisym to treat CLL has already been approved in the US and Europe. In May 2013, SymBio initiated a pivotal phase II trial for Treakisym in CLL as a joint project with Eisai. With patient enrollment completed in November 2014, the company plans to submit an application to market the drug in 1H FY12/16.

Potential patient population, expected sales
SymBio estimates that there are about 700 CLL patients in Japan. Shared Research estimates that sales could reach JPY300mn-JPY350mn. This estimate is based on Treakisym sales per patient with relapsed or refractory low-grade NHL or MCL.

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Relapsed or refractory DLBCL (aggressive NHL)

Diffuse large B-cell lymphoma (DLBCL), or aggressive NHL, progresses rapidly but recovery may be expected in patients for whom anti-cancer drugs are effective. R-CHOP is the standard initial therapy for DLBCL, the most common type of NHL.

But according to the company, DLBCL patients relapse or become refractory to R-CHOP used as first-line therapy in about 40% of cases, and only patients who are 65 or younger can undergo chemotherapy at higher doses together with autologous stem cell transplants. Because the majority of relapsed or refractory DLBCL patients are elderly, physicians must consider potential side effects when selecting a suitable treatment. Weaker patients—due to age or other illnesses—have limited choices for treatment, and there is a need for a safer, more effective method of treatment such as Treakisym.

R&D status
In March 2012, the company completed final analysis and evaluation of data from its phase II clinical trial using Treakisym in combination with rituximab for relapsed or refractory DLBCL (aggressive NHL). The trial, with clinical trial sites in both Japan and South Korea, demonstrated an improved prognosis with a median progression free survival (PFS) of 6.7 months as well as clinically manageable side effects in elderly patients.

SymBio had planned to file for marketing approval in Japan following completion of the phase II clinical trial and presentation of the data at the 54th American Society of Hematology (ASH) Annual Meeting in December 2012, however, the company decided to delay submission of the marketing application after subsequent consultations with the Pharmaceuticals and Medical Devices Agency (PMDA).

Potential patient population
According to SymBio, the number of relapsed or refractory DLBCL (aggressive NHL) patients in Japan is approximately 6,700.

SyB L-1101 (intravenous)/SyB C-1101 (oral) (generic name：rigosertib)

Rigosertib is a tumor-specific dual-specificity inhibitor, which inhibits both the PI3K (phosphoinositide 3-kinase) and the PLK (polo-like kinase 1) pathway. It is being developed in the US and EU by Onconova as a treatment for myelodysplastic syndromes (MDS) as well as in other indications such as first-line MDS and AML (in combination with Vidaza), and head and neck cancer (solid tumor).

According to SymBio, rigosertib's high safety profile enables the drug to be used as both a monotherapy and in combination with other anticancer drugs. It is being developed in both intravenous and oral forms.

> **Onconova**: A US biopharmaceutical company. Established in 1998, Onconova focuses on discovering and developing small molecule drug candidates to treat cancer.

Myelodysplastic Syndromes (MDS)

MDS is a refractory disease with a poor prognosis and progression to acute myeloid leukemia (AML) in approximately 30% of cases. It leads to abnormalities in hematopoietic stem cells that produce blood cells, resulting in a lack of blood. Blood cells produced this way are abnormally shaped. This change in the cells is called dysplasia. The disease typically leads to frequent anemia with some patients dying from

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infection or bleeding due to the reduction in blood cells. The average survival period is about three to five years, with some patients surviving 10 years or longer. It is still not clear what environmental or genetic factors are responsible for the occurrence of MDS, although those who have received radiation treatment or taken anti-cancer drugs may have a higher risk of developing the disease (source: Japan Adult Leukemia Study Group: JALSG).

Risk level assigned based on International Prognostic Scoring System
The seriousness of MDS is determined with the use of the International Prognostic Scoring System (IPSS). The IPSS score is calculated based on the ratio of myeloblasts (immature blood cells) in the bone marrow, chromosome analysis, and the results of a general laboratory blood test. The risk level is assessed based on the number of years that the patient is expected to live, disease progression, and the probability that the disease may lead to acute myeloid leukemia. Risk categories: low, intermediate-1, intermediate-2, and high. Lower-risk MDS refers to low and intermediate-1 patients, while higher-risk MDS refers to intermediate-1 and high in the IPSS risk categories.

Acquired rights from Onconova to develop and sell rigosertib in Japan, Korea

In July 2011 SymBio bought the exclusive right to develop and sell the intravenous (IV) and oral forms of rigosertib following completion of Onconova's phase II US clinical trial for the IV form. In September 2012, Baxter International Inc. acquired the exclusive right to develop and sell rigosertib in Europe.

Development status of rigosertib

Onconova has completed its phase III trial for the intravenous form of rigosertib in post-HMA higher-risk MDS patients in the US and Europe. Although there was no statistically significant improvement in survival period in primary outcome measures, the efficacy of the drug was confirmed in a subgroup analysis. In Japan, SymBio is conducting phase I clinical trials for both the IV (started in June 2012) and oral form (started in March 2013), with completion of both trials expected in 1H FY12/15.

Onconova is currently conducting a phase II clinical trial for the oral form of rigosertib in the US as first-line treatment for transfusion-dependent lower-risk MDS. As well as investigating the use of the oral form of rigosertib as a monotherapy, Onconova is conducting a phase II clinical trial combining Vidaza (azacitidine) and the oral form of rigosertib as first-line treatment in patients with MDS and AML, and the use of the agent in solid tumor indications such as head and neck cancer is also being investigated by Onconova in clinical trials.

SymBio plans to begin a phase I clinical trial using this rigosertib-Vidaza combination therapy in Japan in 1H FY12/16.

IV form of Rigosertib for post-HMA higher-risk MDS

Higher-risk MDS is likely to cause a decline in blood cells or lead to leukemia. Treatment may involve stem cell transplants, depending on the patient's age, condition, and the compatibility of the donor. In the US and Europe, Vidaza (azacitidine) and Dacogen (decitabine) are standard drug therapies for this treatment. In Japan, Vidaza (being marketed by Nippon Shinyaku) is also administered in cases where stem cell transplants are not used. (for Vidaza, see Market and value chain)

However, some cases of higher-risk MDS show resistance to standard treatment with hypomethylating agents (HMAs) such as Vidaza and Dacogen, including relapse following treatment. The most advanced

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research being conducted for rigosertib as of July 2014 was for the treatment of patients with higher-risk MDS who had progressed on, failed or relapsed after prior therapy with HMAs. According to the company, no drugs have been approved for the treatment of post-HMA higher-risk MDS patients.

R&D status: phase III clinical trial demonstrates no significant difference
In February 2014, Onconova completed its phase III ONTIME clinical trial for the intravenous form of the drug in MDS patients in the US who showed resistance to standard treatment with HMAs, or who experienced recurrence of the disease after treatment with HMAs.

Of the 299 patients enrolled in the phase III clinical trial, 199 were administered rigosertib and 100 were placed in the control group. The overall survival (OS) period for those who received rigosertib was 8.2 months, while OS for the control group (BSC) was 5.8 months. However, with a p-value of 0.27, there was no statistically significant difference between the two groups.

Among patients whose condition had deteriorated or not responded to previous treatment using hypomethylating agents (184 of 299 people, or 62%), the overall survival period for higher-risk MDS patients who received rigosertib was 8.5 months, while for those in the control group (BSC) it was 4.7 months. The p-value was 0.022, showing a statistically significant difference. The hematological toxicity of the conventional anti-cancer agent was approximately 60%. With rigosertib, toxicity of Grade 3 or above did not exceed 7%, and non-hematological toxicity did not exceed 3%, confirming safety of the drug.

Following consultations with the US Food and Drug Administration (FDA) and European regulatory agencies, Onconova plans to continue development work on rigosertib for the above indication. Onconova plans to announce its development plans for the intravenous form of rigosertib in Q4 FY12/14.

Domestic phase I clinical trials to continue
SymBio initiated its phase I clinical trial for intravenous rigosertib to treat relapsed or refractory higher-risk MDS in June 2012. Both the IV and oral phase I trials are scheduled to be completed in 1H FY12/15. The company stated that it would consider its future development plan in Japan and South Korea based on the outcome of Onconova's discussions with the FDA and European regulatory agencies.

In Japan, the company is considering the submission of a marketing application for both IV and oral rigosertib in FY12/18 with an eye to receiving approval in FY12/19. The plan could be delayed by about a year since Onconova's phase III ONTIME trial failed to meet its primary endpoint, demonstrating a numerical but not significant benefit compared to best supportive care (BSC) in the trial.

Oral form of rigosertib for first-line lower-risk MDS

Lower-risk MDS corresponds to all the low-risk categories and intermediate-1 of the IPSS with a blast-cell ratio (the ratio of blast cells in the marrow and peripheral blood) of less than 5%. It is primarily caused by a decline in blood cells. It poses a low risk of progression to acute leukemia.

Patients who do not suffer a large decline in blood cells and who do not have any subjective symptoms are placed under observation instead of being treated. Those who develop anemia receive an infusion of red blood cells in accordance with their age. Sometimes an immunosuppressant is used to prevent lymphocyte cells from attacking hematopoietic stem cells. Depending on a patient's age and condition, and HLA compatibility with a donor, an allogeneic hematopoietic stem cell transplant is sometimes carried out. Patients who are not suitable candidates for an allogeneic hematopoietic stem cell transplant, but who are in critical condition due to hematopoietic failure, may be given Vidaza.

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R&D status: US phase II clinical trial in first-line lower-risk MDS demonstrates efficacy
Onconova is conducting a phase II clinical trial in the US for the oral form of rigosertib in first-line transfusion-dependent, lower-risk MDS. As of July 2014, the company was in discussions with the FDA regarding design of the phase III clinical trial, which the company expects to start in FY12/15.

Interim results of the ongoing phase II clinical trial in first-line lower-risk MDS were released in December 2013 at the 55th American Society of Hematology (ASH) Annual Meeting. The trial was conducted in first-line transfusion-dependent, lower-risk MDS patients to determine the efficacy and safety of rigosertib. A combined response rate of 53% was observed in 36 evaluable patients receiving the intermittent dosing schedule. Major adverse effects include toxicity in the bladder (such as trouble urinating, frequent urination, and bloody urine). However, no severe cases of bone marrow suppression were observed (adverse events of anti-cancer agents include lower white blood cell, red blood cell, and platelet counts).

In the clinical trial, 36 patients were given rigosertib twice a day for 14 days, and then did not receive the drug for the next seven days. This was repeated for at least eight weeks. In the study, transfusion dependency was resolved for 14 (39%) of these patients. To address urinary adverse events, a modified dosing regimen was tested in a cohort, and of the 13 patients receiving the new regimen only one patient reported a Grade 2+ urinary event (8%). The results were promising. At the same time, a whole genome scan was used to identify a methylation signature in 32 patients, helping to relate transfusion independence with the genomic profile in the 32 patients analyzed—genetic markers that could be associated with the elimination of blood transfusion dependency. An additional cohort of 20 lower-risk MDS patients to confirm genomic signature is now being enrolled.

Combination therapy of rigosertib (oral) and Vidaza (azacitidine)
As well as investigating the use of the oral form of rigosertib as a monotherapy, Onconova is conducting a phase II clinical trial combining Vidaza and the oral form of rigosertib as first-line treatment in patients with MDS or AML. SymBio plans to begin a phase I clinical trial using this rigosertib-Vidaza combination therapy in Japan in 1H FY12/16.

Patient population, estimated sales
According to SymBio estimates, patients with lower-risk MDS in Japan number about 7,800, with 3,200 MDS patients classified as higher-risk.

Nippon Shinyaku Co., Ltd. (TSE1: 4516) has been selling azacitidine in Japan as first-line therapy for MDS under the product name Vidaza since March 2011. According to Nippon Shinyaku, sales of Vidaza were JPY9.7bn for FY03/14 (+38.1% YoY). The company expects to book sales of JPY10.8bn for FY03/15. Shared Research thinks that sales of the intravenous and oral forms of rigosertib could match or exceed sales of Vidaza, used when patients who receive treatment with Vidaza relapse.

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Earnings structure

Earnings structure

(JPYmn)	FY12/08	FY12/09	FY12/10	FY12/11	FY12/12	FY12/13
Sales	1,630	1,191	1,450	1,883	1,955	1,532
Product Sales	-	-	326	1,632	1,955	1,432
Treakisym Sales to End Users (Reference)	-	-	644	3,390	3,940	4,230
Product Sales / Sales to End Users	-	-	50.6%	48.2%	49.6%	33.9%
Royalty Revenue	1,630	1,191	1,124	250	-	100
Sales to Eisai	1600	1,085	1,446	1,872	1,930	1,486
Non-Eisai Sales	30	106	4	10	26	46
CoGS	-	-	238	1,224	1,362	1,214
CoGS / Product Sales	-	-	73.1%	75.0%	69.7%	84.8%
CoGS / Sales to End Users	-	-	-	36.1%	34.6%	28.7%
Product Procurement	-	-	238	1,434	1,322	1,175
Gross Profit	1,630	1,191	1,212	658	593	318
SG&A	1,497	1,399	1,825	2,725	2,293	1,999
Personnel	252	323	343	365	413	441
Research	868	817	1,118	1,945	1,438	1,053
Other	377	259	364	415	442	505
Operating profit	133	-208	-613	-2,067	-1,700	-1,681

Source: Company data

Sales

The company's sales are made up of product sales and royalty revenue. Since FY12/08, per the above table most of the sales have originated from Eisai.

Product sales

Product sales are revenue from selling Treakisym. The company began booking product sales in FY12/10, when it obtained approval for Treakisym and started selling the anti-cancer agent in December 2010. FY12/13, product sales comprise sales of bendamustine to Eisai and InnoPharmax. Bendamustine is supplied wholesale at the NHI price minus a percentage based on past transactions. Shared Research estimates this percentage to be about 40%.

Royalty revenue

Royalty revenue includes one-time contract payments and milestone payments. Since granting the exclusive marketing right for Treakisym to Eisai in August 2008, SymBio books one-time payments and milestone payments in accordance with clinical trial stage.

CoGS

Cost of goods sold refers to procurement costs for drugs. As mentioned earlier, the company's only product on the market as of July 2014 was Treakisym (bendamustine). Astellas supplies bendamustine to

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the company for about 75% of SymBio's wholesale price. Margins may improve as sales increase.

SymBio receives bendamustine in nude vials from Astellas, carries out the packaging and labelling, and supplies the drug wholesale to Eisai. SymBio pays Astellas in euros, with these transactions usually taking place several months apart. Thus, the company faces the risk that euro-yen forex rates will change during this period. The company hedges this risk with forward foreign-exchange contracts, and by reporting gains and losses on forex as a non-operating profit (or loss).

SG&A

Labor and R&D are the main SG&A expenses. Labor costs have been trending upward in line with business growth. R&D expenses fluctuate depending on the progress of clinical trials and new license agreements from in-licensing activities. According to the company, in-licensing expenses are between JPY500mn and JPY1bn per drug, and domestic clinical trials cost between JPY1bn and JPY2bn. Note: Eisai pays half of the development costs for Treakisym in Japan.

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Strengths and weaknesses

Strengths

- **Unique candidate selection process:** SymBio makes decisions on in-licensing new drug candidates based on an initial assessment and screening process by its in-house search and evaluation team. The final decision is made by the company after evaluation by a team of medical experts—the Scientific Advisory Board (SAB). President Yoshida's extensive range of contacts in the pharmaceutical industry built during his tenure at Amgen Japan and Amgen Inc. is a significant hurdle for competitors attempting to emulate the quality of the company's search and evaluation team, SAB panel and selection process.
- **Strong product development**: Treakisym (bendamustine hydrochloride)—the first drug the company developed—received marketing approval in Japan just five years after the license agreement was signed with Astellas. Treakisym, launched by the company in December 2010, is being used by a number of Japanese physicians and is considered to be an essential drug for the treatment of relapsed or refractory low-grade NHL and MCL. The company's success with Treakisym demonstrates its strong product development capabilities and nimbleness. Three additional indications are now under development by the company for the drug (relapsed or refractory aggressive NHL; first-line low-grade NHL and MCL; and chronic lymphocytic leukemia), which may receive marketing approval in the future.
- **Strong share in niche markets**: SymBio focuses on niche markets for rare oncologic, hematologic, and autoimmune diseases. The company takes advantage of a less competitive environment by developing drugs for indications that serve a limited number of patients and require a high degree of in-house expertise. Thus, the company has succeeded in securing more than 50% of the target market for Treakisym in relapsed or refractory low-grade NHL and MCL in the third year after launch.

Weaknesses

- **Lack of sales force:** The company does not currently have its own sales force, thus Treakisym is being sold through Eisai, an alliance partner. The company is considering the creation of its own sales and marketing organization for rigosertib and other drugs approved beyond rigosertib. Such efforts could drive up costs and impact the company's future profitability.
- **Funding needs**: It takes time and significant investment for pharmaceutical and biotech companies to develop and commercialize drugs, and they must secure funding on a regular basis to cope with the uncertainty of their earnings. For SymBio, cash and equivalents plus short-term investments totalled about JPY7.3bn at the end of FY12/13. But the company expects total losses of JPY5.8bn-JPY6.5bn over the period of its mid-term plan (FY12/14-FY12/16). Losses could be heavier if the company acquires new drug candidates, requiring one-time payments and more R&D spending. The company's operations would be affected if it fails to secure additional funding.
- **Dependence on a single individual**: Founding President and CEO, Fuminori Yoshida, has played a central role in all aspects of SymBio's management since its foundation. If for any reason Mr. Yoshida is unable to perform his duties, this could have an impact on company operations.

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Market and value chain

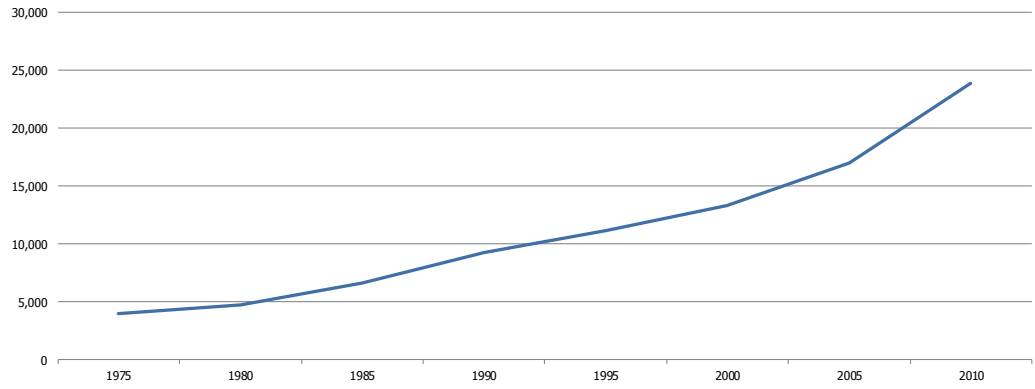
Market strategy

Lymphatic cancer: patient population, market size, drugs

Newly diagnosed patients with lymphatic cancer

In 2010, the number of people newly diagnosed with lymphatic cancer in Japan was 23,919, according to the Center for Cancer Control and Information Services of the National Cancer Center. Of these, 18,240, or 76.3%, were 60 years or older. The number of people newly diagnosed with lymphatic cancer has been rising along with Japan's aging population. This number rose by 80% from 2000 to 2010. Between 2010 and 2014, the total number of people newly diagnosed with lymphatic cancer was 21,100, per National Cancer Center data. This number is expected to rise to 23,000 between 2015 and 2019, and to 24,500 between 2020 and 2024.

Patients newly diagnosed with lymphatic malignancy



Source: Center for Cancer Control and Information Services, National Cancer Center

Patients newly diagnosed with lymphatic malignancy

	1975	1980	1985	1990	1995	2000	2005	2010
Number of patients	4,013	4,741	6,635	9,297	11,195	13,307	16,991	23,919
Incidence rate (per 100,000)	3.6	4.1	5.5	7.5	8.9	10.5	13.3	18.7

Source: Center for Cancer Control and Information Services, National Cancer Center

Market for lymphatic cancer drugs may expand

According to the Fuji Keizai Group, the domestic market potential for anticancer agents was JPY769.1bn in 2012. The market is growing, and is expected to hit JPY1.1tn by 2021—the result of a larger elderly population in Japan and more treatable patients as cancer is discovered at an earlier stage. Within this market, the market for lymphatic cancer drugs is expected to expand to JPY60.2bn in 2021 from JPY38.9bn in 2012.

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Market for drugs for lymphatic malignancy

(JPYbn)	2012	YoY	2021 (Est.)	Growth (2021/2012)
Anticancer agents	769.1	105.0%	1,061.4	138.0%
Breast cancer	119.5	112.4%	199.4	166.9%
Lymphatic malignancy	38.9	111.5%	60.2	154.8%

Source: Fuji Keizai Group

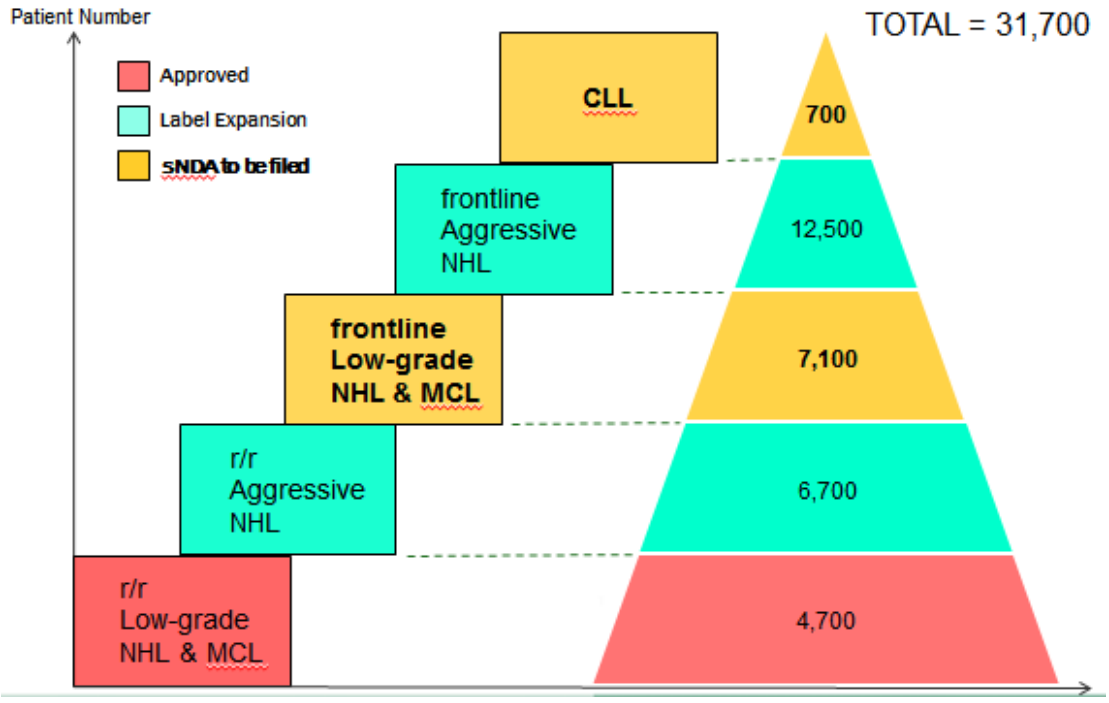
As of July 2014, the first-line drug for lymphatic cancer was rituximab. According to Chugai Pharmaceutical Co., Ltd., Japanese Rituxan sales were JPY22.9bn in 2011, JPY24.7bn in 2012, and JPY26.2bn in 2013.

Treakisym market potential and patient population

The company estimates that the number of patients being treated for relapsed or refractory low-grade NHL in Japan is 4,700. Treakisym sales reached JPY4.2bn in FY12/13.

The company estimates that the number of Japanese patients receiving first-line treatment for low-grade NHL and MCL is about 7,100 (phase II completed); the number of patients with relapsed or refractory aggressive NHL is about 6,700 (phase II completed). Japanese patients with CLL is estimated to be about 700 (phase II ongoing). The estimate for total number of users and potential users of Treakisym: 19,200.

Treakisym® Market Potential in Japan



Drugs competing with Treakisym

These include rituximab and ibritumomab tiuxetan. Immunochemotherapy (the combination of immunotherapy and chemotherapy drugs) is often used to treat B-cell lymphatic malignancies.

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Rituximab (product name: Rituxan)
The drug, co-developed by the US companies IDEC Pharmaceuticals and Genentech, Inc. received US approval in November 1997 as the world's first monoclonal antibody.

Rituxan consists of a portion of both mouse antibody and IgG, a human antibody. It attaches itself to the CD20 antigen that appears on B cells in the body and fights tumors through complement-dependent cytotoxicity and antibody-dependent cell-mediated cytotoxicity effects (source: Chugai, Zenyaku Kogyo). In Japan, Zenyaku Kogyo and Chugai have been jointly selling the drug since September 2001. Chugai's Rituxan sales were JPY26.2bn in 2013.

Ibritumomab tiuxetan (product name: Zevalin)
Like Rituxan, the antibody drug Zevalin targets CD20 antigen on B cells. It combines the antibody with a radioactive substance and attacks B cells with radiation. The treatment is only available at medical institutions authorized to handle radioactive elements.

Zevalin was approved in January 2008 as a treatment for refractory lymphatic cancer (low-grade B-cell NHL). It is sold by Fujifilm RI Pharma Co., Ltd., a subsidiary of Fujifilm Holdings Corporation.

MDS patients, drugs

MDS patient population estimated at 11,000
A high proportion of people aged 60 or older suffer from MDS. The number of patients totaled 9,000 in 2008, with 2,781 deaths from the disease according to Japan's Ministry of Health, Labour and Welfare (MHLW). SymBio estimates that there are currently about 11,000 MDS patients in Japan amid a larger elderly population. Even though the number of patients continues to rise, there is a high unmet medical need in Japan with no effective treatment available.

Rigosertib indications and number of patients

Condition	Patients	Notes
Low-risk MDS	7,800	Domestic Phase I clinical trial in progress
High-risk MDS	3,200	Domestic Phase I clinical trial in progress

Source: Company data

Azacitidine (product name: Vidaza)
Vidaza, developed by Pharmion Corporation (now Celgene Corporation) in the US, is a treatment for first-line intermediate and higher-risk MDS. Nippon Shinyaku Co., Ltd. signed a license agreement with Pharmion in 2006 to sell this drug in Japan, obtaining marketing approval in January 2011 following the completion of domestic clinical trials. Nippon Shinyaku booked Vidaza sales of JPY9.7bn in FY03/14 (+38.1% YoY), according to the company, and expects sales of JPY10.8bn in FY03/15.

In addition to killing cancerous cells, azacitidine inhibits DNA methylation. It becomes effective after use for three to six months, with bone marrow suppression as the main side effect (a decline in white blood cells and platelets). However, while the use of hypomethylating agents such as azacitidine and decitabine (Dacogen) in the treatment of MDS has improved the outcome of patients who tend to have very poor survival, about half of MDS patients do not respond, progress, or relapse at different times after their response on these HMAs, followed by an extremely poor prognosis.

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According to the company, as of July 2014 Vidaza was the only approved drug in Japan for the first-line treatment of higher-risk MDS, with no effective treatment available once patients treated with Vidaza relapse. The company plans to position the IV formulation of rigosertib in the marketplace to treat Japanese patients who have failed or relapsed after azacitidine treatment.

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Historical performance

FY12/13

Treakisym sales in Japan and other parts of Asia were JPY1.5bn (-21.6% YoY) due to adjustments in distribution inventory. Sales to end users were JPY4.2bn (+7.4% YoY). However, Treakisym sales totaled JPY1.4bn (-26.8% YoY) due to adjustments in Treakisym distribution inventory at Eisai.

The company earned JPY100mn in royalty revenue (no such revenue was posted a year earlier). The company received milestone payments associated with the start of the phase II clinical trial for CLL.

The company posted R&D costs of JPY1.1bn (-26.8% YoY) due to clinical trials for additional Treakisym indications, and rigosertib indications. R&D costs declined from a year earlier as development for Treakisym nears completion. With other expenses totaling JPY946mn (+10.6% YoY), total SG&A expenses were JPY2.0bn (-12.9% YoY).

Operating loss was JPY1.7bn (almost unchanged from a year earlier). There were non-operating expenses of JPY35mn associated with payment of fees and stock issuance costs. The company posted a non-operating profit of JPY114mn due to currency gains. Consequently, recurring loss was JPY1.6bn (a loss of JPY1.7bn a year earlier), and net loss was 1.6bn (a loss of JPY1.7bn a year earlier).

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Income statement

Income Statement (JPYmn)	FY12/08 Par.	FY12/09 Par.	FY12/10 Par.	FY12/11 Par.	FY12/12 Par.	FY12/13 Par.
Total Sales	**1,630**	**1,191**	**1,450**	**1,883**	**1,955**	**1,532**
YoY	-	-26.9%	21.7%	29.8%	3.9%	-21.6%
CoGS	-	-	238	1,224	1,362	1,214
Gross Profit	**1,630**	**1,191**	**1,212**	**658**	**593**	**318**
GPM	100.0%	100.0%	83.6%	35.0%	30.3%	20.8%
SG&A	1,497	1,399	1,825	2,725	2,293	1,999
SG&A / Sales	91.8%	117.5%	125.8%	144.8%	117.3%	130.4%
Operating Profit	**133**	**-208**	**-613**	**-2,067**	**-1,700**	**-1,681**
YoY	-	-	-	-	-	-
OPM	8.2%	-	-	-	-	-
Non-Operating Income	6	20	13	56	7	114
Non-Operating Expenses	115	26	38	85	37	35
Recurring Profit	**24**	**-214**	**-638**	**-2,095**	**-1,729**	**-1,601**
YoY	-	-	-	-	-	-
RPM	1.5%	-	-	-	-	-
Extraordinary Gains	-	-	-	-	-	-
Extraordinary Losses	1	-	0	5	0	-
Tax Charges	2	4	4	4	4	4
Implied Tax Rate	-	-	-	-	-	-
Net Income	**21**	**-218**	**-642**	**-2,105**	**-1,733**	**-1,605**
YoY	-	-	-	-	-	-
Net Margin	-	-	-	-	-	-

Figures may differ from company materials due to differences in rounding methods

Source: Company data

FY12/12

Sales were JPY2.0bn (+3.9% YoY). Product sales were JPY2.0bn (+19.8% YoY) due to an increase in Treakisym sales to end users, which totaled JPY3.9bn (+16.2% YoY). The company did not receive any royalty revenue.

SG&A expenses were JPY2.3bn (-15.8% YoY). R&D costs totaled JPY1.4bn (-26.1% YoY), which included the cost of clinical trials for additional Treakisym indications and rigosertib. The company, which made one-time payments for the acquisition of rigosertib a year earlier, did not make such payments, slashing R&D expenses.

FY12/11

Sales were JPY1.9bn (+29.8% YoY). Product sales were JPY1.6bn (+401.3% YoY). Sales of Treakisym to end users were JPY3.4bn (JPY64mn in FY12/10). Royalty revenues were JPY250mn. The company received milestone payments associated with the start of domestic development of first-line low-grade non-Hodgkin's lymphoma and mantle-cell lymphoma, plus the marketing approval of Treakisym in South Korea and Taiwan.

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SG&A expenses were JPY2.7bn (+49.4% YoY). R&D costs were JPY1.9bn (+73.9% YoY). The company conducted clinical trials for additional Treakisym indications and SyB D-0701 (antiemetic transdermal patch for RINV). The company also made one-time payments for the acquisition of rigosertib rights (both IV and oral).

FY12/10

Sales were JPY1.5bn (+21.7% YoY). Product sales were JPY326mn (no product sales a year earlier). The company began to post product sales as it started to sell Treakisym in Japan. Royalty revenue totaled JPY1.1bn. The company received milestone payments from Eisai associated with the marketing approval of Treakisym in Japan, marketing approval of Symbenda in Singapore, and the start of the phase II clinical trial for multiple myeloma in Japan.

SG&A expenses were JPY1.8bn (+30.4% YoY). R&D costs were JPY1.1bn (+36.9% YoY), which included spending for clinical trials, preparation for additional Treakisym indications and the clinical trial for SyB D-0701 (antiemetic transdermal patch for RINV). The company made one-time payments for SyB 0702 (HSP32 inhibitor).

FY12/09

Sales were JPY1.2bn (-26.9% YoY), all from royalty revenues. The pivotal phase II clinical trial for Treakisym targeting low-grade NHL and MCL patients who had received prior treatment was completed in March 2009. The company submitted an application for accelerated marketing approval of Treakisym in October 2009 (receiving orphan drug designation with 10-year marketing exclusivity once approved).

SG&A expenses were JPY1.4bn (-6.5% YoY). R&D costs were JPY817mn (-5.9% YoY). The company sought to develop its product pipeline with emphasis on phase II clinical trials for additional indications of Treakisym, and phase I clinical trial for the combination therapy of Treakisym plus rituximab in first-line low-grade NHL and MCL.

FY12/08

Sales were JPY1.6bn (no sales for FY12/07). All sales were comprised of royalty revenue. In August 2008, the company entered into a license agreement with Eisai for the co-development and exclusive marketing right to Treakisym in Japan. SymBio received one-time payments for the agreement. SG&A expenses: JPY1.5bn. R&D expenses: JPY868mn.

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Historical forecast accuracy

Initial CE vs. results (JPYmn)	FY12/09 Par.	FY12/10 Par.	FY12/11 Par.	FY12/12 Par.	FY12/13 Par.
Sales (Initial CE)	-	-	1,933	2,338	1,927
Sales (Results)	-	-	1,883	1,955	1,532
Initial CE versus Results	**-**	**-**	**-2.6%**	**-16.4%**	**-20.5%**
Operating Profit (Initial CE)	-	-	-2,351	-1,625	-1,889
Operating Profit (Results)	-	-	-2,067	-1,700	-1,681
Initial CE versus Results	**-**	**-**	**-**	**-**	**-**
Recurring Profit (Initial CE)	-	-	-2,398	-1,652	-1,922
Recurring Profit (Results)	-	-	-2,095	-1,729	-1,601
Initial CE versus Results	**-**	**-**	**-**	**-**	**-**
Net Income (Initial CE)	-	-	-2,407	-1,656	-1,926
Net Income (Results)	-	-	-2,105	-1,733	-1,605
Initial CE versus Results	**-**	**-**	**-**	**-**	**-**

Figures may differ from company materials due to differences in rounding methods

Source: Company data

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Balance sheet

Balance Sheet (JPYmn)	FY12/08 Par.	FY12/09 Par.	FY12/10 Par.	FY12/11 Par.	FY12/12 Par.	FY12/13 Par.
Assets						
Cash and Equivalents	1,070	3,902	2,314	4,559	4,540	6,163
Marketable securities	300	219	1,701	1,953	300	1,100
Accounts Receivable	-	-	6	162	148	-
Inventories	-	-	-	207	165	125
Other Current Assets	90	97	191	297	268	245
Total Current Assets	**1,460**	**4,218**	**4,213**	**7,178**	**5,421**	**7,634**
Buildings		7	7	7	8	8
Equipment, Plant		18	31	32	34	34
Acc. Depreciation		-12	-16	-22	-28	-33
Total Tangible Fixed Assets	**13**	**13**	**22**	**17**	**14**	**9**
Total Other Fixed Assets	**25**	**27**	**27**	**48**	**57**	**37**
Software	3	2	1	10	8	6
Other	-	-	-	3	3	2
Total Intangible Assets	**3**	**2**	**1**	**13**	**11**	**8**
Total Fixed Assets	**41**	**42**	**50**	**78**	**82**	**53**
Total Assets	**1,501**	**4,261**	**4,263**	**7,256**	**5,502**	**7,687**
Liabilities						
Accounts Payable	-	-	1	309	330	-
Accrued Amount Payable	111	182	124	278	196	207
Short Term Debt	-	-	-	-	-	-
Other Current Liabilities	82	23	52	59	73	44
Total Current Liabilities	**193**	**205**	**178**	**646**	**599**	**251**
Long Term Debt	-	-	-	-	-	-
Other Fixed Liabilities	1	2	2	5	4	3
Total Long Term Liabilities	**1**	**2**	**2**	**5**	**4**	**3**
Total Interest Bearing Debt	**-**	**-**	**-**	**-**	**-**	**-**
Total Liabilities	**195**	**207**	**180**	**651**	**602**	**254**
Shareholder Equity (Net Assets)	1,307	4,060	4,083	6,606	4,873	7,336
Issued Capital	1,893	3,378	3,711	6,025	6,025	8,059
Reserves	1,863	3,348	3,681	5,995	5,995	8,029
Retained Earnings	-2,448	-2,666	-3,309	-5,413	-7,146	-8,752
Subscription Rights to Shares	-	-	-	-	27	97
Total Shareholder Equity (Net Assets)	**1,307**	**4,054**	**4,083**	**6,606**	**4,900**	**7,433**
Working Capital	-	-	5	61	-17	125
Interest Bearing Debt	-	-	-	-	-	-
Net Debt (Net Cash)	-1,070	-3,902	-2,314	-4,559	-4,540	-6,163

Figures may differ from company materials due to differences in rounding methods.

Source: Company data

Assets

SymBio does not have its own manufacturing facilities, clinical facilities or salesforce: the company

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outsources manufacturing, clinical development, and sales and marketing. Therefore, most of the company's assets are cash, deposits, and negotiable securities.

Within current assets, inventory assets consist of Treakisym merchandise inventory.

Liabilities

The company does not have interest-bearing liabilities such as loans. Booked liabilities are accounts payable and arrears.

Net assets

Capital and capital reserves are increasing as a result of fundraising efforts. However, the deficit in retained earnings is expanding as the company continues to post losses.

Cash flow statement

Cash Flow Statement (JPYmn)	FY12/08 Par.	FY12/09 Par.	FY12/10 Par.	FY12/11 Par.	FY12/12 Par.	FY12/13 Par.
Operating Cash Flow (1)	154	-211	-754	-2,074	-1,659	-1,677
Investment Cash Flow (2)	-13	-4	-116	-117	-411	-1,332
Free Cash Flow (1+2)	141	-215	-870	-2,191	-2,069	-3,010
Financial Cash Flow	554	2,963	663	4,611	-1	4,057
Depreciation & Amortization (A)	4	4	7	8	9	8
Capital Expenditures (B)	-8	-3	-14	-12	-3	-
Working Capital Changes (C)	-	-	5	56	-78	142
Simple FCF (NI + A + B - C)	17	-217	-655	-2,165	-1,650	-1,739
Cash and Equivalents (year-end)	1,370	4,121	3,916	6,311	4,240	5,294

Figures may differ from company materials due to differences in rounding methods.

Source: Company data

Cash flow from operations

Cash flow from operations almost matches the company's current net loss before tax.

Cash flow from investment activities

Purchases of tangible fixed assets and intangible assets are limited as SymBio outsources manufacturing, clinical development, and sales and marketing. But investment in time deposits and securities meant outflow from investment activities widened in FY12/12 and FY12/13.

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Cash flow from financing activities

The company has reported a series of inflows from financing activities. As the table below shows, the company has raised capital on multiple occasions in order to finance its operations in the face of continuous operating losses.

Main sources of funding

Date	Change in shares outstanding	Total shares outstanding	Change in capital/reserves (JPYmn)	Total capital/reserves (JPYmn)	Method
Mar. 2009	7,404	66,017	888	4,643	Paid-in third-party allotment
Nov. 2011	8,334	90,268	500	6,104	Paid-in third-party allotment
Dec. 2009	9,553	100,651	573	6,727	Paid-in third-party allotment
Feb. 2011	11,032	122,769	772	8,164	Paid-in third-party allotment
Feb. 2011	17,368	140,137	1,216	9,380	Paid-in third-party allotment
Oct. 2011	5,100,000	19,130,900	2,628	12,019	Paid-in public offering (price determined by the book building process)
Jan.-Dec. 2013	3,921,257	23,052,157	1,244	13,263	Exercise of stock options attached to convertible corporate bonds and other stock options
Dec. 2013	6,720,200	29,772,357	2,504	15,767	Paid-in public offering (price determined by the book building process)

Source: Company data

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Other information

History

SymBio was established in March 2005 by Fuminori Yoshida, former Corporate Vice President of Amgen Inc., and founding President and CEO of the Japanese subsidiary, Amgen Japan. Mr. Yoshida's desire to address the unmet medical needs of patients in underserved markets often overlooked by the pharmaceutical industry due to limited patient numbers inspired him to create SymBio Pharmaceuticals.

> In 2013, Amgen Inc. was the largest biopharmaceutical company in the world by revenue. It was established in 1980 in Thousand Oaks, California as Applied Molecular Genetics. Mr. Yoshida established Amgen Japan in May 1993, serving as President and CEO for 12 years prior to founding SymBio Pharmaceuticals in March 2005. In February 2008, Takeda Pharmaceutical Co. Ltd. acquired Amgen Japan.

After its establishment, SymBio obtained financing totaling JPY1bn from Daiichi Pharmaceutical Co., Ltd. (now Daiichi Sankyo, Inc.; TSE1: 4568), Medical & Biological Laboratories Co., Ltd. (JASDAQ: 4557), EPS Corporation (TSE1: 4282), and SBI Holdings, Inc. (TSE1: 8473). The company used the cash raised to in-license its first drug candidate, bendamustine hydrochloride, from Astellas Pharma GmbH in December 2005 with the exclusive right to develop and commercialize the drug in Japan.

After the global financial crisis of September 2008, the company experienced a shortage of capital as Treakisym was advancing in the clinic. Mr. Yoshida visited at least 50 venture capital firms in Japan and elsewhere in December 2008, eventually raising JPY1.5bn in capital from Cephalon, Inc. (acquired by Teva Pharmaceutical Industries Ltd. (NASDAQ: TEVA) in October 2011).

Since obtaining marketing approval for Treakisym in October 2010 for relapsed or refractory low-grade NHL and MCL and the drug's launch onto the Japanese market in December of that year, the company has continued to build a robust pipeline supported by Treakisym cash flow through commercial expansion into other key Asia Pacific markets and the completion of clinical trials in additional indications. Treakisym was granted orphan drug designation and priority review for these two indications in October 2009, with 10-yr market exclusivity through 2020. However, investment in Treakisym development has reached its peak, with the company shifting resources to accelerate rigosertib development.

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Company history

Date	Details
March 2005	SymBio Pharmaceuticals Limited established with JPY30mn in capital.
December 2005	License Agreement finalized with Astellas Pharma GmbH for SyB L-0501 (bendamustine) development and commercialization rights in Japan.
March 2006	Manufacturer's License (packaging, labeling and storage) obtained from Tokyo Metropolitan Government (License #13AZ200010).
March 2007	Abeille Pharmaceuticals licenses SyB D-0701 (granisetron patch) to SymBio Pharmaceuticals for development & commercialization in Japan, China (HK), Taiwan, Korea and Singapore.
March 2007	License Agreement finalized with Astellas Deutschland GmbH for SyB L-0501 (bendamustine) development & commercialization rights in China (HK), Taiwan, Korea and Singapore.
August 2008	License Agreement finalized with Eisai Co., Ltd. for co-development and commercialization rights of SyB L-0501 (bendamustine) in Japan.
March 2009	SymBio Pharmaceuticals concludes Sublicense Agreement with Cephalon, Inc. for development and commercialization rights of bendamustine hydrochloride in China (HK).
May 2009	License Agreement finalized with Eisai Co., Ltd. for co-development and commercialization rights of SyB L-0501 (bendamustine) in Korea and Singapore.
September 2010	SymBio Pharmaceuticals and Eisai launch SYMBENDA® (bendamustine) in Singapore for the treatment of Low-grade Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia.
October 2010	SymBio Pharmaceuticals announces NDA Approval of TREAKISYM® (bendamustine) in Japan.
December 2010	SymBio Pharmaceuticals launches TREAKISYM® in Japan.
July 2011	Onconova and SymBio Pharmaceuticals complete License Agreement for SyB L-1101/SyB C-1101 (rigosertib, a Phase Ⅲ stage multi-kinase inhibitor for Myelodysplastic Syndromes).
October 2011	SymBio Pharmaceuticals launches Symbenda® (bendamustine hydrochloride) in Korea for the treatment of Chronic Lymphocytic Leukemia and multiplemyeloma.
October 2011	Listed on Osaka Securities Exchange JASDAQ Growth Market.
February 2012	SymBio Pharmaceuticals launches Innomustine® (bendamustine hydrochloride) in Taiwan for the treatment of Low-grade Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia.

Source: Company website

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Major shareholders

Top Shareholders	Amount Held
Fuminori Yoshida	10.2%
Teva Pharmaceutical Industries Ltd.	8.4%
JAFCO Co., Ltd.	6.0%
Weru Investment Co., Ltd.	4.4%
Eisai Co., Ltd.	2.7%
Japan Securities Finance Co., Ltd.	1.0%
TNP On The Road Corp.	0.8%
Daiichi Sankyo Co., Ltd.	0.7%

(as of September 30, 2014)

Source: Company data

Top management

Representative Director, President and CEO, Fuminori Yoshida established SymBio Pharmaceuticals Limited, his third company, in March of 2005. As founding president of two other major healthcare companies, Nippon BioRad Laboratories (1980) and Amgen Japan (1993), he has earned high visibility and credibility within Japan's healthcare and academic communities. Following his graduation from Gakushuin University in 1971 with a B.S. in Organic Chemistry, he went on to receive an M.S. in Molecular Biology from MIT (1973) and M.S. in Health Policy and Management from Harvard University Graduate School (1975). He possesses dual experience and expertise in the management of major Japanese and American corporations due to his prior work experience at various companies, including Mitsubishi Corporation and AHS Japan, Syntex Japan (1993) as President and CEO, and Amgen Inc. where he served concurrently as Corporate Vice-President, President and CEO of Amgen Japan, for 12 years.

Employees

SymBio had a total of 72 employees as of September 30, 2014, with about 60% of employees working in the R&D department.

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Other

Overview of clinical trials

Development of a new drug takes between 10 and 17 years

The development process of a new drug follows the four stages described below. It usually takes 10 to 17 years for a new drug to win regulatory approval, according to the company.

Ordinary process and periods of developing new drugs

Process	Period	What is done
Basic research	2-3 years	Creation of new substances and decision on candidates for drugs
Preclinical test	3-5 years	Confirmation of efficacy and safety through experiments on animals
Clinical trials	3-7 years	Phase I: Confirmation of safety and pharmacokinetics with a small number of healthy people
		Phase II: Confirmation of efficacy and safety with a small number of patients
		Phase III: Confirmation of efficacy and safety with many patients in comparison to existing drugs
Application and approval	1-2 years	Examination by the Ministry of Health, Labour and Welfare

Source: Company data

Probability of a compound receiving drug approval is 1/100,000

The probability of a chemical compound receiving regulatory approval is said to be 1/100,000, according to the company.

According to the 2013 edition of the Thomson Reuters Pharmaceutical R&D Factbook, the success rate of pharmaceutical companies around the globe from 2006 to 2009 at various stages in the development process was:

- Preclinical: 67%
- Phase I clinical trials: 46%
- Phase II clinical trials: 19%
- Phase III clinical trials: 77%
- Regulatory approval: 90%.

The success rate of cancer drugs tends to be lower than that of other drugs. The success rate of cancer drugs that went through clinical trials in the US between 2004 and 2011 was only 6.7%, compared with 12.1% for other drugs, according to BIOtechNow. The success rate of cancer drugs that went through Phase III clinical trials was 45%, while other drugs had a 64% success rate.

Ethnic factors in the acceptability of foreign clinical data

Japan's Ministry of Health, Labour, and Welfare (MHLW) in 1998 released a report entitled Ethnic Factors in the Acceptability of Foreign Clinical Data (ICH-E5 Guideline) to spell out the government's stance on the use of data on clinical trials conducted outside Japan. The report discusses whether the use of such extrapolated data is acceptable.

Applications for drug approval in Japan normally require pharmacokinetic data, dose-responsive data, and clinical trial data on efficacy for Japanese people. However, data from overseas clinical trials are

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acceptable if a bridging study demonstrates that such data can be used for Japanese people.

> **Pharmacokinetic data**: Data concerning the fate of substances administered externally to a living organism: absorption, distribution, metabolization, and excretion (ADME).

Glossary

Antigen
Normally, a protein or other substance carrying bacteria and viruses that the body rejects as foreign, causing an antigen-antibody reaction (AAR). When antigens enter the body, they either stimulate the production of antibodies or combine with them.

Bridging Data
Data generated from overseas clinical trials that can be applied to Japanese patients and used in Japan regulatory filings for marketing approval. The goal is to shorten the number of preclinical/clinical studies required for marketing approval in Japan by avoiding the need to repeat the same studies that have already been carried out overseas (e.g., dispense with the need to do a phase II and/or III clinical trial in Japan).

Chronic Lymphocytic Leukemia (CLL)
A disease in which white blood cells, called lymphatic corpuscles, become cancerous.

Contract Research Organization (CRO)
Pharmaceutical companies often outsource some of their work to contract research organizations so they can focus on core operations. Outsourced work may include monitoring of clinical trials to ensure that they are proceeding according to plan, and the management of clinical trial data.

Dose-Responsiveness
Does-responsiveness shows the relationship between the dosage and efficacy of a drug. It is used to determine the method and dosage. Under normal circumstances, the effectiveness of a drug corresponds to its dosage.

First-line Drug
The first drug given to a patient for a disease that is typically part of a standard set of treatments such as surgery followed by chemotherapy and radiation. When used by itself, first-line therapy is the one accepted as the best treatment. If it doesn't cure the disease (the patient has a relapse) or causes severe side effects, other treatments (second-line, third-line etc.) may be added or used instead.

Immunoglobulin G (IgG)
The main antibody isotype found in blood and extracellular fluid which protects the body from infection by binding to many kinds of pathogens such as viruses, bacteria, and fungi —it does this via several immune mechanisms: IgG-mediated binding of pathogens causes their immobilization and binding together.

Key Opinion Leader (KOL)
Key opinion leaders are physicians whose opinions concerning the treatment of certain illnesses have a strong influence on other doctors.

Mantle-Cell Lymphoma (MCL)
A type of fast-growing B-cell non-Hodgkin's lymphoma that normally affects people over a certain age. It is characterized by small and medium-sized cancer cells that appear in lymphatic nodes, the spleen, bone marrow, blood, and the digestive system.

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Monoclonal Antibody
A single antibody molecule taken from a single cell. It is possible to produce large amounts of these special antibodies and use them in the development of antibody drugs.

Multikinase Inhibitor
Multikinase inhibitor blocks tyrosine kinases, which play an important role in transmitting signals involving the multiplication and division of cells. Tyrosine kinases can be energized due to genetic mutations. If this happens, the number of cells rapidly increases, causing cancer or other illnesses.

Non-Hodgkin's Lymphoma (NHL)
A group of ailments associated with all types of malignant tumors other than Hodgkin's lymphoma. In Japan, many of these diseases are diffuse large cell lymphomas.

Overall Survival (OS)
Overall survival refers to the duration between the initiation of treatment and a patient's death.

Progression-Free Survival (PFS)
Progression-free survival refers to the duration between the initiation of treatment, and either death or disease progression.

Proof-of-Concept (POC)
A proof-of-concept, when applied to drug development, is the concept that the efficacy and safety of a new drug candidate must be validated through data generated in clinical trials.

Rare Disorders
Rare disorders are illnesses that affect few people, although they may be serious and/or life-threatening. Drugs designed to treat rare medical conditions are called 'orphan drugs', and pharmaceutical companies often receive government incentives for the development of these drugs.

In Japan, the Ministry of Health, Labour and Welfare seeks to promote the development of orphan drugs by offering subsidies. When a drug is designated as an orphan, it is placed on a fast track for approval (the time between the application and approval is reduced). The period of market exclusivity can also be extended to 10 years, and a system is in place to keep the NHI price of orphan drugs above a certain level.

R-CHOP therapy
A combination of rituximab with chemotherapy drugs cyclophosphamide, doxorubicin (hydroxydaunomycin), vincristine (Oncovin®), and prednisolone. R-CHOP is an acronym derived from the names of the drugs used. It is the standard initial treatment for low-grade non-Hodgkin's lymphoma (NHL) and mantle-cell lymphoma (MCL).

Special Protocol Assessment (SPA)
A system under which the US Food and Drug Administration (FDA) approves the protocol or design of a planned phase III clinical trial, such as target illness, purpose, primary and secondary endpoints, and method of data analysis – the protocol may be revised following FDA consultation prior to the start of the study. The SPA is intended to shorten the review period of new drug applications (NDAs) by the FDA.

Standard Therapy
Standard therapy refers to treatment that is considered to be the best therapy currently available. It is a treatment widely recommended to patients by physicians.

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Company name

SymBio is derived from the words "symbiosis" and "biotechnology." The company's corporate philosophy emphasizes the symbiotic or mutually supportive relationship that exists among major players in the healthcare industry, and is reflected in the company's logo which symbolizes physicians, scientists, regulators, and investors, with patients at its center. The color of the logo represents the evergreen tree—the company's endeavor to create and sustain a life-giving force.

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Company profile

Company Name	Head Office
SymBio Pharmaceuticals Limited	Toranomon 30 Mori Building, 3-2-2 Toranomon Minato-ku, Tokyo, JAPAN 〒105-0001
Phone	**Listed On**
+81-3-5472-1125	TSE JASDAQ Growth
Established	**Exchange Listing**
March 25, 2005	October 20, 2011
Website	**Fiscal Year-End**
http://www.symbiopharma.com/index_e.html	December
IR Contact	**IR Web**
Tsutomu Abe	http://www.symbiopharma.com/ir_e/01.html
IR Mail	**IR Phone**
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Digital Garage Inc.	MAC-HOUSE Co.	3-D Matrix, Ltd.
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Dream Incubator Inc.	Medinet Co., Ltd.	Verite Co., Ltd.
Elecom Co.	MIRAIT Holdings Corp.	WirelessGate, Inc.
EMERGENCY ASSISTANCE JAPAN Co.	NAGASE & CO., LTD	Yellow Hat Ltd.
en-Japan Inc.	NAIGAI TRANS LINE LTD.	Yumeshin Holdings
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Fields Corp.	Nippon Parking Development Co., Ltd.	ZIGExN Co., Ltd.
FreeBit Co., Ltd.	NS Tool Co.	

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