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SymBio Pharmaceuticals

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Executive summary

SymBio in-licenses drugs for development and sale

SymBio Pharmaceuticals Ltd. is a specialty pharmaceutical company that acquires development and marketing rights to drug candidates for rare diseases. The main target areas are cancer, blood disorders, and multiple viral infections. The company primarily acquires rights from European and US biotech and pharmaceutical companies. Once the company secures these rights, it conducts clinical trials to obtain manufacturing and sales rights, aiming to generate revenues from product sales.

The company does not conduct basic research but instead focuses on developing novel drug candidates that have already undergone basic research in humans and have established proof of concept (POC). In addition to sourcing potential drug candidates through independent information gathering conducted by internal experts, the company holds a Scientific Advisory Board (SAB) meeting three times a year to evaluate and select candidates with a high probability of approval. The company is also pursuing a lab-less strategy to increase cost efficiency, focusing on unmet medical needs to increase profitability, and seeking to expand revenue opportunities through a global expansion strategy.

Normally, drug development takes 10–17 years from basic research to manufacturing and approval for sale. However, the company obtained domestic manufacturing and sales approval for its first development product, Treakisym®, within five years of in-licensing, and gained a market share of over 50% three years after its launch.

The company had obtained approval for and launched Treakisym® (anticancer agent for hematologic malignancies) for the indications of relapsed or refractory low-grade non-Hodgkin's lymphoma (NHL) and mantle cell lymphoma (MCL), untreated (first-line treatment) low-grade NHL and MCL, chronic lymphocytic leukemia (CLL), and relapsed or refractory diffuse large B-cell lymphoma (DLBCL). Treakisym® is listed in the Practical Guidelines for Hematological Malignancies 2018 edited and published by Japanese Society of Hematology as the standard treatment for relapsed or refractory low-grade B-cell NHL, MCL, and CLL, and as first-line treatment for low-grade NHL.

The company obtained manufacturing and marketing approval for the ready-to-dilute (RTD) liquid formulation of Treakisym® in September 2020 and began sales in January 2021. Unlike the lyophilized (freeze-dried [FD]) powder formulation of Treakisym®, the RTD formulation eliminates the need for troublesome manual dissolution, thereby reducing burdens placed on medical personnel. In February 2022, the company received approval for Treakisym® rapid infusion (RI) formulation. The RI formulation reduces the administration time to just 10 minutes, versus 60 minutes for the lyophilized injection and RTD formulation. This reduces the burden on patients and healthcare professionals.

The re-examination term for the lyophilized formulation of Treakisym® ended in 2020, but by launching and switching to the RTD formulation and RI formulation to which SymBio has exclusive rights, the company believed it could extend the product life cycle of Treakisym® until 2031. However, the situation changed significantly in 2022 when two companies ignored the patent infringement warnings and commercialized generic Treakisym®. The patent infringement litigation related to this matter has been settled with the two companies.

Drugs in the development pipeline includes antiviral drug brincidofovir (BCV). All planned development for Treakisym® has been completed and management is shifting development resources to BCV, which has potential to treat various diseases. In May 2023, the company successfully established the human proof of concept (POC) in the Phase II clinical trial of BCV targeting adenovirus (AdV) infections. In May 2024, a Phase IIa clinical trial post-hematopoietic stem cell cytomegalovirus infection was initiated in the US. In August 2024, the company initiated an international Phase Ib clinical trial of IV brincidofovir in patients with malignant lymphomas. This marks the first clinical trial in the oncology field for BCV.

Earnings

In FY12/24, SymBio reported sales of JPY2.5bn (-56.1% YoY), an operating loss of JPY3.9bn (compared to an operating loss of JPY812mn in FY12/23), a recurring loss of JPY3.7bn (compared to a recurring loss of JPY736mn), and a net loss attributable to owners of the parent of JPY3.8bn (compared to a net loss of JPY2.0bn). As the impact of generic sales of Treakisym® (bendamustine) became apparent, the spread of COVID-19, influenza, and other infectious diseases continued to affect oncology treatment settings, leading to reduced overall use of bendamustine, including its generics.

The revised FY12/25 forecast announced in June 2025 calls for sales of JPY1.4bn (vs. JPY1.9bn in previous forecast), operating loss of JPY4.3bn (vs. loss of JPY4.3bn), recurring loss of JPY4.5bn (loss of JPY4.3bn), and net loss attributable to owners of the parent of JPY4.6bn (vs. loss of JPY4.5bn). The company projects net loss per share of JPY95.95 (vs. loss of

JPY80.45). This downward revision reflects a shift at medical institutions from Treakisym® to generics and an expansion of treatment options following the introduction of new therapies, resulting in fewer prescriptions of the drug. The company expects a decline in total SG&A expenses and anticipates operating loss to remain roughly in line with the previous forecast by cutting non-R&D costs. However, it expects recurring and net losses to widen, reflecting forex losses under the stronger yen assumption and increased bond issuance costs.

The medium-term plan unveiled in February 2020 forecasted FY12/23 sales to reach JPY12.4bn. However, actual results did not meet these projections, primarily due to the commercialization of generic Treakisym® by two companies, which occurred despite SymBio's patent infringement warnings. As of February 2025, the company has yet to announce a new medium-term management plan.

Strengths and weaknesses

Shared Research thinks SymBio's strengths include its unique drug candidate selection process, strong product development team, and business strategy focusing on niche markets. Weaknesses of the company include its dependence on a single individual and product (see Strengths and weaknesses).

Key financial data

(JPYmn)	FY12/15 Parent	FY12/16 Parent	FY12/17 Parent	FY12/18 Parent	FY12/19 Parent	FY12/20 Parent	FY12/21 Parent	FY12/22 Cons.	FY12/23 Cons.	FY12/24 Cons.	FY12/25 Consolidated forecast
Sales	**1,933**	**2,368**	**3,444**	**3,836**	**2,838**	**2,987**	**8,257**	**10,008**	**5,590**	**2,453**	**1,400**
YoY	-1.1%	22.5%	45.4%	11.4%	-26.0%	5.3%	176.4%	21.2%	-44.1%	-56.1%	-42.9%
Gross profit	**583**	**904**	**1,031**	**1,173**	**865**	**867**	**5,800**	**7,600**	**4,411**	**1,873**	
YoY	10.7%	55.1%	14.1%	13.7%	-26.3%	0.2%	569.1%	31.0%	-42.0%	-57.5%	
Gross profit margin	30.2%	38.2%	29.9%	30.6%	30.5%	29.0%	70.2%	75.9%	78.9%	76.4%	
Operating profit	**-2,552**	**-2,127**	**-3,947**	**-2,656**	**-4,302**	**-4,506**	**1,016**	**1,964**	**-812**	**-3,877**	**-4,262**
YoY	-	-	-	-	-	-	-	93.3%	-	-	-
Operating profit margin	-	-	-	-	-	-	12.3%	19.6%	-	-	-
Recurring profit	**-2,630**	**-2,317**	**-3,977**	**-2,749**	**-4,377**	**-4,616**	**1,001**	**2,000**	**-736**	**-3,689**	**-4,467**
YoY	-	-	-	-	-	-	-	99.8%	-	-	-
Recurring profit margin	-	-	-	-	-	-	12.1%	20.0%	-	-	-
Net income	**-2,632**	**-2,313**	**-3,978**	**-2,753**	**-4,376**	**-4,090**	**2,032**	**1,179**	**-1,963**	**-3,833**	**-4,592**
YoY	-	-	-	-	-	-	-	-42.0%	-	-	-
Net margin	-	-	-	-	-	-	24.6%	11.8%	-	-	-
Per-share data (split-adjusted; JPY)											
Shares issued at year-end (000 shares)	32,391	46,531	54,049	20,560	26,438	38,203	38,457	39,604	42,278	45,929	
EPS (JPY)	-325.0	-235.3	-319.1	-165.5	-189.0	-124.1	53.0	30.2	-49.2	-85.0	-96.0
EPS (fully diluted)	-	-	-	-	-	-	52.3	29.8	-	-	
Dividend per share (JPY)	-	-	-	-	-	-	-	-	-	-	
Book value per share (JPY)	510.2	434.4	200.0	212.2	143.1	105.8	162.3	204.8	164.3	84.7	
Balance sheet (JPYmn)											
Cash and cash equivalents	4,261	5,719	2,947	4,821	3,911	3,849	3,860	6,283	6,517	3,964	
Total current assets	**4,827**	**6,685**	**4,037**	**6,038**	**4,887**	**5,815**	**6,748**	**9,313**	**8,083**	**4,924**	
Tangible fixed assets	53	75	47	57	75	77	84	69	-	-	
Investments and other assets	53	77	100	73	70	81	1,362	829	88	44	
Intangible assets	52	42	69	71	241	302	259	222	-	-	
Total assets	**4,984**	**6,878**	**4,252**	**6,239**	**5,274**	**6,275**	**8,453**	**10,433**	**8,170**	**4,968**	
Accounts payable	320	322	604	726	121	665	70	47	-	-	
Short-term debt	-	-	-	-	-	-	-	-	-	-	
Total current liabilities	**551**	**942**	**1,011**	**1,336**	**872**	**1,615**	**1,518**	**1,924**	**957**	**766**	
Long-term debt	-	-	-	-	-	-	-	-	-	-	
Total fixed liabilities	**2**	**451**	**1**	**1**	**2**	**2**	**189**	**3**	**4**	**5**	
Total liabilities	**552**	**1,394**	**1,013**	**1,338**	**874**	**1,617**	**1,707**	**1,927**	**960**	**771**	
Net assets	**4,432**	**5,485**	**3,239**	**4,902**	**4,400**	**4,657**	**6,746**	**8,506**	**7,210**	**4,198**	
Total interest-bearing debt	-	-	-	-	-	-	-	-	-	-	
Cash flow statement(JPYmn)											
Cash flows from operating activities	-2,272	-1,960	-3,817	-2,325	-4,351	-4,122	140	1,614	-195	-3,417	
Cash flows from investing activities	1,489	-44	-78	-26	-216	-160	-71	-47	-377	-4	
Cash flows from financing activities	-3	3,658	1,164	4,272	3,740	4,222	-72	628	680	708	
Financial ratios											
ROA (RP-based)	-42.3%	-39.1%	-71.5%	-52.4%	-76.0%	-79.9%	13.6%	21.2%	-7.9%	-56.2%	
ROE	-48.3%	-50.4%	-102.6%	-77.8%	-107.4%	-104.7%	39.6%	16.5%	-26.1%	-70.9%	
Equity ratio	88.9%	79.7%	76.2%	78.6%	83.4%	74.2%	79.8%	81.5%	88.2%	84.5%	

Source: Shared Research based on company data

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

Note: The company conducted a four-to-one reverse stock split in July 2019. Earnings per share in the FY12/19 earnings forecast reflects the effect of the reverse stock split.

Note: The company moved to consolidated reporting from FY12/22 as SymBio Pharma USA, Inc. started operations. Figures for FY12/22 are consolidated, and YoY figures are provided for reference purposes only.

Recent updates

Research on malignant brain tumors (glioblastoma) accepted for presentation at US Society for Neuro-Oncology

2025-08-12

SymBio Pharmaceuticals Limited announced its research on BCV for malignant brain tumors (glioblastoma) has been accepted for presentation at the US Society for Neuro-Oncology.

The company's research on BCV for malignant brain tumors (glioblastoma) has been accepted for presentation at the 30th Annual Meeting of the Society for Neuro-Oncology (SNO) to be held in Honolulu, Hawaii, US from November 19 to 23, 2025. For grade 4 glioblastoma, the most aggressive form of the disease, median survival after diagnosis is only two to 18 months, and the five-year survival rate is below 5%. Around half of patients show resistance to standard therapy (radiation and temozolomide), underscoring the need for new drug development.

SymBio to present preclinical BCV data in head and neck cancer at ESMO Congress 2025

2025-07-28

SymBio Pharmaceuticals Ltd. announced that its research findings on BCV for head and neck cancer have been accepted for presentation at a European academic conference.

The company conducted preclinical studies to explore the potential of brincidofovir (BCV) as a treatment for solid tumors and obtained promising results in head and neck cancer. These findings have been accepted for presentation at the European Society for Medical Oncology (ESMO Congress 2025), scheduled to take place in Berlin, Germany, in October 2025.

Regarding the issuance of the 65th to 67th series of stock acquisition rights with adjustable exercise prices through a third-party allotment

2025-07-22

SymBio Pharmaceuticals Limited announced the issuance of its 65th to 67th series of stock acquisition rights with adjustable exercise prices through a third-party allotment.

The company resolved to issue its 65th to 67th series of stock acquisition rights with adjustable exercise prices through a third-party allotment, as well as its 1st series of unsecured straight bonds.

Details of the issuance of the 65th to 67th series of stock acquisition rights with adjustable exercise prices through a third-party allotment

If all of the convertible bonds with stock acquisition rights are converted, the number of shares to be issued will be 50mn (500,000 voting rights), resulting in a dilution rate of 102.40% based on the company's total outstanding shares of 48,829,000 as of end-June 2025 (103.33% on a voting rights basis).

Amount of funds raised

- Total proceeds from payment: JPY8.4bn
- Estimated issuance costs: JPY50mn
- Estimated net proceeds: JPY8.4bn

Specific uses of funds to be raised

The company plans to allocate the JPY8.4bn in net proceeds from the issuance of the convertible bonds with stock acquisition rights as follows.

- Redemption of unsecured straight bonds: JPY1.3bn (Aug 2025–Dec 2025)
- Direct development costs for brincidofovir: JPY5.4bn (Mar 2026–Mar 2028)
- Indirect development costs for brincidofovir: JPY1.6bn (Mar 2026–Mar 2028)
- Total: JPY8.4bn

Details of the offering

Allotment date	August 12, 2025
Total number of stock acquisition rights	500,000 (Series 65: 200,000; Series 66: 200,000; Series 67: 100,000)
Issue amount	JPY3.3mn (JPY8 per right for Series 65, JPY7 for Series 66, JPY3 for Series 67)
Number of potential shares from the issuance	50mn (Series 65: 20mn; Series 66: 20mn; Series 67: 10mn)
Amount of funds to be raised	JPY8.4bn
Offering method	Third-party allotment
Allottee	EVO FUND
Exercise period	August 13, 2025–May 15, 2028

Source: Shared Research based on company data

Details of the issuance of the 1st series of unsecured straight bonds

The company will issue JPY1.3bn in unsecured straight bonds to the planned allottee, EVO FUND, and repay them using proceeds from the abovementioned convertible bonds with stock acquisition rights.

Specific uses of funds to be raised

- Direct development costs for brincidofovir: JPY1.0bn (Nov 2025–Mar 2026)
- Indirect development costs for brincidofovir: JPY300mn (Nov 2025–Mar 2026)
- Total: JPY1.3bn

Details of the bonds

Details of the 1st series of unsecured straight bonds

Total amount	Up to JPY1.3bn, less a portion expected to be funded through the exercise of the stock acquisition rights
Payment date	August 26, 2025
Maturity date	October 26, 2026
Interest rate	0.0% per annum
Redemption method	Lump-sum payment at maturity

Source: Shared Research based on company data

SymBio completes clinical trial application for global Phase III study of BCV targeting post-transplant adenovirus infection

2025-06-30

SymBio Pharmaceuticals Limited announced it has completed the clinical trial application to initiate a global Phase III study of brincidofovir (BCV).

The company submitted a clinical trial application to the European Medicines Agency on June 27, 2025, to initiate a Phase III study of BCV for adenovirus (AdV) infections following hematopoietic stem cell transplantation. It plans to enroll 180 patients across 80 sites in four regions—Europe, the US, the UK, and Japan—with the goal of submitting a new drug application in Europe in the second half of 2028.

- The primary endpoint of the trial is the proportion of patients whose blood adenovirus levels become undetectable four weeks after treatment initiation.
- The key secondary endpoint is a composite measure that combines viral clearance with improvement in related clinical symptoms.

SymBio revises its full-year earnings forecast

2025-06-10

SymBio Pharmaceuticals Limited announced a revision to its full-year earnings forecast.

Revision to full-year forecast for FY12/25

- Sales: JPY1.4bn (JPY1.9bn in previous forecast)
- Operating loss: JPY4.3bn (loss of JPY4.3bn)
- Recurring loss: JPY4.5bn (loss of JPY4.3bn)
- Net income attributable to owners of the parent: JPY4.6bn (loss of JPY4.5bn)
- Net loss per share: JPY95.95 (loss of JPY80.45)

Reasons for the revision

The company lowered its FY12/25 sales forecast by JPY458mn to JPY1.4bn (previously JPY1.9bn). This downward revision reflects a shift at medical institutions from Treakisym® to generics and an expansion of treatment options with the introduction of new therapies, resulting in fewer prescriptions of the drug. As a result, the company determined that recovering the sales shortfall in 2H would be difficult.

The company expects SG&A expenses to total JPY5.3bn, down JPY290mn from the previous forecast, by cutting non-R&D costs. As a result, it projects an operating loss of JPY4.3bn, roughly unchanged from the previous estimate, rising just JPY1mn.

The company now assumes a stronger yen of JPY142.0/USD (vs. JPY150.0 in the previous forecast), which—along with higher bond issuance costs—will result in a recurring loss of JPY4.5bn, an improvement of JPY120mn. It also projects a net loss attributable to owners of the parent of JPY4.6bn, an improvement of JPY124mn.

SymBio completes FPI in the global Phase Ib/II clinical trial of BCV for malignant lymphoma

2025-06-10

SymBio Pharmaceuticals Limited announced progress on its global Phase Ib/II clinical trial for malignant lymphoma.

In June 2025, the company completed first patient enrollment (FPI) in Japan for its global Phase Ib/II clinical trial of BCV targeting malignant lymphoma. This multi-center international study has begun enrolling patients in Japan, Hong Kong, and Singapore, with a target of registering 15 patients by end-2025.

Trends and outlook

Quarterly trends and results

Earnings (cumulative)	FY12/24				FY12/25				FY12/25	
(JPYmn)	Q1	Q1-Q2	Q1-Q3	Q1-Q4	Q1	Q1-Q2	Q1-Q3	Q1-Q4	% of forecast	FY forecast
Sales	598	1,284	1,898	2,453	264	647			46.2%	1,400
YoY	-61.3%	-59.6%	-57.1%	-56.1%	-55.8%	-49.7%				-42.9%
Gross profit	471	996	1,444	1,873	202	494				
YoY	-62.1%	-59.7%	-58.5%	-57.5%	-57.0%	-50.5%				
Gross profit margin	78.8%	77.6%	76.1%	76.4%	76.7%	76.3%				
SG&A expenses	1,278	2,716	4,235	5,750	1,372	2,648				
YoY	7.2%	7.6%	12.7%	10.1%	7.3%	-2.5%				
SG&A ratio	213.7%	211.4%	223.1%	234.4%	519.5%	409.4%				
Operating profit	-807	-1,719	-2,791	-3,877	-1,169	-2,154			-	-4,262
YoY	-	-	-	-	-	-				-
Operating profit margin	-	-	-	-	-	-				-
Recurring profit	-727	-1,481	-2,760	-3,689	-1,288	-2,341			-	-4,467
YoY	-	-	-	-	-	-				-
Recurring profit margin	-	-	-	-	-	-				-
Net income	-777	-1,541	-2,845	-3,833	-1,321	-2,369			-	-4,592
YoY	-	-	-	-	-	-				-
Net margin	-	-	-	-	-	-				-

Earnings (quarterly)	FY12/24				FY12/25			
(JPYmn)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Sales	598	687	614	555	264	383		
YoY	-61.3%	-58.0%	-50.6%	-52.5%	-55.8%	-44.3%		
Gross profit	471	525	448	429	202	291		
YoY	-62.1%	-57.3%	-55.3%	-54.1%	-57.0%	-44.6%		
Gross profit margin	78.8%	76.5%	73.0%	77.3%	76.7%	76.1%		
SG&A expenses	1,278	1,438	1,520	1,515	1,372	1,276		
YoY	7.2%	8.0%	22.9%	3.5%	7.3%	-11.3%		
SG&A ratio	213.7%	209.4%	247.5%	273.2%	519.5%	333.5%		
Operating profit	-807	-913	-1,072	-1,086	-1,169	-985		
YoY	-	-	-	-	-	-		
Operating profit margin	-	-	-	-	-	-		
Recurring profit	-727	-754	-1,278	-930	-1,288	-1,053		
YoY	-	-	-	-	-	-		
Recurring profit margin	-	-	-	-	-	-		
Net income	-777	-764	-1,304	-988	-1,321	-1,048		
YoY	-	-	-	-	-	-		
Net margin	-	-	-	-	-	-		

Source: Shared Research based on company data

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

Note: "- "denotes YoY change of over 1,000%.

Note: Starting from FY12/22, the company switched to preparing consolidated financial statements in connection with the commencement of full- fledged operations at SymBio Pharma USA. As data for FY12/22 are on a consolidated basis, YoY comparisons are for reference only.

Breakdown of SG&A expenses

Earnings (cumulative)	FY12/24				FY12/25			
(JPYmn)	Q1	Q1-Q2	Q1-Q3	Q1-Q4	Q1	Q1-Q2	Q1-Q3	Q1-Q4
SG&A expenses	1,278	2,716	4,235	5,750	1,372	2,648		
YoY	7.2%	7.6%	12.7%	10.1%	7.3%	-2.5%		
R&D expenses	691	1,532	2,493	3,379	819	1,582		
YoY	25.7%	27.2%	36.7%	28.1%	18.5%	3.3%		
SG&A expenses excl. R&D	586	1,184	1,743	2,371	552	1,066		
YoY	-8.7%	-10.2%	-10.0%	-8.3%	-5.8%	-10.0%		

Earnings (quarterly)	FY12/24				FY12/25			
(JPYmn)	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
SG&A expenses	1,278	1,438	1,520	1,515	1,372	1,276		
YoY	7.2%	8.0%	22.9%	3.5%	7.3%	-11.3%		
R&D expenses	691	840	961	887	819	763		
YoY	25.7%	28.5%	55.1%	8.9%	18.5%	-9.3%		
SG&A expenses excl. R&D	586	598	559	628	552	514		
YoY	-8.7%	-11.7%	-9.4%	-3.2%	-5.8%	-14.1%		

Source: Shared Research based on company data

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

1H FY12/25 results (out July 31, 2025)

- Sales: JPY647mn (-49.7% YoY)
- Operating loss: JPY2.2bn (versus loss of JPY1.7bn in 1H FY12/24)
- Recurring loss: JPY2.3bn (versus loss of JPY1.5bn in 1H FY12/24)
- Net loss attributable to owners of the parent: JPY2.4bn (versus loss of JPY1.5bn in 1H FY12/24)

Sales of the ready-to-dilute (RTD) intravenous formulation of Treakisym® 100mg/4mL, launched in January 2021, were sluggish in 1H. In Q1, sales to wholesalers were weak due to a combination of factors: inventory stocktaking by wholesalers, inventory adjustments by medical institutions ahead of the April 2025 drug price revision, and prior clearing of wholesaler

inventories. In addition, as the shift to generics continues and treatment options expand with the introduction of new therapies, prescription opportunities are declining, contributing to the overall drop in sales.

- As of February 2025, the company estimates generics have captured roughly 70% of the market for Treakisym® ready-to-dilute (RTD) liquid formulation and expects their share to rise to around 78–80% by end-FY12/25.

Sales dropped 49.7% YoY to JPY647mn, reflecting the impact of generic competition and inventory adjustments ahead of the drug price revision in Q1. Gross profit declined 50.5% YoY to JPY494mn, with a gross profit margin of 76.3%, down 1.3pp YoY. SG&A expenses declined 2.5% YoY to JPY2.6bn, including R&D expenses of JPY1.6bn, up 3.3% YoY. As a result, the company posted an operating loss of JPY2.2bn (versus a loss of JPY1.7bn in 1H FY12/24).

1H progress against full-year company forecast for FY12/25

In June 2025, SymBio revised its full-year forecast (see "Full-year company forecast" for details). As of 1H, sales progress toward the revised FY12/25 forecast was 46.2%, while no progress rates were disclosed for profit figures, as they remain negative. The company posted an operating loss of JPY2.2bn (vs. a full-year forecast loss of JPY4.3bn), a recurring loss of JPY2.3bn (vs. a forecast loss of JPY4.5bn), and a net loss attributable to owners of the parent of JPY2.4bn (vs. a forecast loss of JPY4.6bn).

As of 1H, the company maintained its full-year forecast revised in June 2025.

Business progress

The following is an overview of progress in key businesses since January 2025.

- In July 2025, research results for BCV for head and neck cancer were accepted for presentation at a European conference.
- In July 2025, the company announced the issuance of the 65th–67th series of stock acquisition rights with exercise price adjustment clauses through third-party allotment, as well as the issuance of its first unsecured straight bonds.
- On June 27, 2025, the company submitted a clinical trial application to the European Medicines Agency to initiate a Phase III study of BCV for adenovirus (AdV) infections following hematopoietic stem cell transplantation.
- In June 2025, the company announced a revision to its full-year earnings forecast.
- In May 2025, the company announced the confirmation of the efficacy of brincidofovir (BCV) for malignant brain tumors and the identification of biomarker genes (predictive factors of efficacy).
- In March 2025, Dr. Edwin Rock, who has experience as a Medical Officer at the FDA, was appointed Senior Vice President (Head of R&D) at the company's US subsidiary SPU.
- In February 2025, the company expanded its global phase Ib/II clinical trial of BCV in patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma, to Singapore.
- In January 2025, the company appointed Mr. Masaru Taguchi as CEO and President of its wholly owned subsidiary SymBio Pharma USA, Inc. (SPU).

R&D activities

Antiviral drug SyB V-1901 (generic name: brincidofovir [BCV])

The company in-licensed the antiviral drug BCV from Chimerix Inc. (headquartered in North Carolina, US) in 2019 and is currently working to maximize the business value of its intravenous formulation (SyB V-1901, IVBCV) through global development. Focusing on three therapeutic areas—viral infections following hematopoietic stem cell transplantation, hematologic and solid tumors, and neurodegenerative diseases—the company is advancing clinical development by leveraging BCV's broad-spectrum activity against double-stranded DNA (dsDNA) viruses. In addition to ongoing clinical trials, the company is also conducting joint research with leading domestic and international institutions specializing in these areas. Based on the outcomes of these studies, it plans to pursue global clinical trials.

Earlier clinical trials in the US and Europe conducted by US-based Chimerix Inc. have demonstrated that BCV Oral has broad-spectrum antiviral effects against a variety of dsDNA viruses. BCV IV is expected to be effective and safe for the prevention and treatment of many dsDNA virus infections, including adenovirus (AdV) infections after hematopoietic stem cell transplantation. In June 2021, Chimerix announced that the US FDA had granted BCV Oral approval for the treatment of smallpox.

Post-transplant infectious diseases

Based on a global advisory board review held in February 2020, the company has decided to prioritize the global development of BCV IV primarily in Japan, the US, and Europe, targeting disseminated AdV infections occurring after hematopoietic stem cell transplantation, a niche area with a high unmet medical need.

Adenovirus infection: In March 2021, the company filed an IND application with the US Food and Drug Administration (FDA) to conduct a Phase II clinical trial primarily in pediatric patients suffering from AdV infections (also including adults). This development program was granted fast-track designation by the FDA in April 2021, and the investigational drug was administered to the first patient in August 2021. In May 2023, BCV has demonstrated proof of concept in humans in the same study, and the Phase IIa clinical study was completed in the first half of 2024. In June 2025, the company submitted a clinical trial application to the European Medicines Agency to initiate a Phase III clinical trial. It plans to enroll 180 patients across 80 sites in four regions—Europe, the US, the UK, and Japan—with the goal of submitting a new drug application in Europe in the second half of 2028. A use patent for BCV related to the treatment of AdV infections and infectious diseases was established and registered in Japan in January 2024.

- Phase III clinical trial: The company plans to initiate a Phase III clinical trial in Europe before it does so in other regions in Q3 FY12/25, with the aim of filing for approval in Q4 FY12/28.
- Estimated patient numbers in 2022: 1,300 in Europe, 1,000 in the US, and 400 in Japan
- Current treatments: There is currently no standard treatment. Cidofovir (unapproved) is sometimes used, but it is associated with adverse effects such as renal impairment and myelosuppression.

Cytomegalovirus (CMV) infections: In May 2024, a Phase IIa clinical trial post-hematopoietic stem cell cytomegalovirus (CMV) infection was initiated in the US. In June 2024, the first patient was enrolled, and the trial is currently ongoing. As of end-April 2025, a total of 19 patients had been enrolled.

- The larger patient population for CMV infections compared to adenovirus (AdV) infections has contributed to steady patient enrollment in the trial. At the FY12/25 interim results briefing, the company reported a total of 19 enrolled patients. Dose escalation is underway through cohorts A, B, and subsequent groups, while analyses are underway to determine the optimal dose and identify characteristics of patients who respond to treatment.
    - Cohort A: Nine patients (two PE*, seven R/R**); Cohort B: 10 patients (three PE, seven R/R)
        - *PE: Patients in preemptive therapy who continued treatment despite experiencing adverse effects
        - **R/R: Patients in refractory/relapsed treatment who developed drug resistance
- The competitor drug maribarivir (brand name: LIVTENCITY) from Takeda Pharmaceutical generated sales of JPY33.0bn in FY03/25 (versus JPY19.1bn in FY03/24). The number of transplant recipients treated for CMV is exceptionally high for a rare disease (25,000, of which 10,000 are resistant or refractory). One reason megapharma Takeda decided to develop the competitor drug maribarivir independently was likely its large potential patient base, which made it appear more lucrative. The company noted the large patient base made patient enrollment for clinical trials much easier.

BK virus infections: The development of a treatment for BK virus infection following kidney transplantation is currently under protocol revision. In August 2022, the first patient was dosed (FPD) in an international Phase II clinical trial in Australia; however, patient enrollment has been slower than anticipated.

Hematologic and solid tumors

In addition to its antiviral activity, brincidofovir has shown antitumor effects. The company is exploring new indications in hematologic and solid tumors through joint research with institutions in various countries.

- Since BCV does not exhibit bone marrow suppression as a side effect, the company expects it can selectively target and destroy cancer cells without affecting normal cells.

- In February 2025, the company expanded its global phase Ib/II clinical trial of BCV in patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma, to Singapore.

Malignant lymphoma: In August 2024, the company initiated an international Phase Ib clinical trial of BCV targeting patients with malignant lymphoma as a First in Human (FIH) trial in the oncology field in Japan. The trial is now also underway in Singapore and Hong Kong. Through this trial, it aims to establish human proof of concept (POC) for BCV in cancer treatment.

- This trial is the third clinical trial of BCV, following those for AdV and CMV infections, and it is the first BCV trial in the oncology field.

- NK/T-cell lymphoma Phase Ib trial: Patient enrollment is expected to be completed in Q4 FY12/25. The company intends to initiate a Phase II trial in Q2 FY12/26, with the aim of filing for approval in Japan in Q2 FY12/28.

- In Japan, the company plans to file for approval without conducting a Phase III trial, which it believes could enable earlier approval than for adenovirus (AdV) and cytomegalovirus (CMV) indications. Phase III trials, however, are planned in other regions.

The company is conducting joint research with the National Cancer Centre Singapore to investigate the antitumor effects and mechanisms of BCV against EB virus-positive lymphoma. Between 2022 and 2024, the results of this collaboration were presented at international conferences in the US and Europe on five occasions. These included findings on BCV's efficacy in NK/T-cell lymphoma, B-cell lymphoma, and peripheral T-cell lymphoma (PTCL), as well as research on biomarkers that may predict BCV's antitumor activity.

- In May 2025, the company announced the confirmation of the efficacy of brincidofovir (BCV) for malignant brain tumors and the identification of biomarker genes (predictive factors of efficacy).

Brain tumors: Since 2021, SymBio has been conducting a joint study with the University of California San Francisco Brain Tumor Center on the antitumor effects of brincidofovir (BCV) in brain tumors. In April 2025, the company presented the results at the Annual Meeting of the American Association for Cancer Research (AACR) in Chicago. The presentation highlighted the confirmed efficacy of BCV in malignant brain tumors and the identification of biomarker genes predictive of its effectiveness.

- The company believes BCV's high blood–brain barrier (BBB) permeability could make it effective in treating brain cancers, including brain tumors.

Epstein-Barr Virus-Associated Lymphoproliferative Disorder (EBV-LPD): In April 2023, SymBio also signed a CRADA with the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, to evaluate the efficacy of BCV in EB virus-related lymphoproliferative disorders.

Neurodegenerative diseases

Multiple Sclerosis: Multiple sclerosis (MS), a designated intractable disease, has recently been linked to Epstein-Barr virus (EBV). Given BCV's potent antiviral activity against EBV relative to other agents, SymBio entered into a Cooperative Research and Development Agreement (CRADA) with the National Institute of Neurological Disorders and Stroke (NINDS), part of the US National Institutes of Health (NIH), in March 2023 to pursue joint research on a novel EBV-targeted therapy for MS. In October 2023, the joint research team presented findings at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS 2023, Italy), showing that BCV selectively inhibits EBV activity in cells derived from MS patients. These results underscore the potential of BCV as a therapeutic agent for MS. The company is currently conducting animal studies in marmosets (non-human primates) with a view to future clinical trials.

Alzheimer's disease: Among double-stranded DNA (dsDNA) viruses, certain neurotropic viruses such as herpes simplex virus type 1 (HSV-1) and varicella-zoster virus (VZV) have an affinity for neural tissue. Recent studies suggest that the reactivation of these latent viruses may be involved in the onset of various neurological diseases, including Alzheimer's disease, and research in this field is advancing. In December 2022, the company entered into a Sponsored Research Agreement with Tufts University (US) to evaluate the effects of BCV on dementia-related biomarkers using a three-dimensional HSV infection/reactivation model developed with brain-like tissue derived from human neural stem cells. This collaborative research is currently underway.

Polyomavirus infections: Polyomaviruses, particularly JC virus (JCV), are known to cause severe brain diseases among dsDNA viruses, and the development of effective treatments is highly anticipated. In November 2022, the company concluded a material transfer agreement (MTA) with US-based Penn State College of Medicine, and initiated a non-clinical study evaluating the efficacy of BCV in a mouse model of polyomavirus infection. In July 2024, the first report of these research findings, which included new insights, was published in the journal mBio.

- Progressive multifocal leukoencephalopathy (PML) is a brain disease caused by JC virus (JCV).
- At the FY12/25 interim results briefing, the company noted that the US National Institutes of Health (NIH) may initiate a clinical trial of BCV in progressive multifocal leukoencephalopathy (PML).

Rights

In September 2022, Chimerix announced that it had completed procedures to transfer the rights to brincidofovir to Emergent BioSolutions Inc. (headquarters: Maryland, US). The agreement, however, has no impact on the company's exclusive rights to develop, manufacture, and sell brincidofovir globally for all indications except orthopoxvirus diseases including smallpox and Mpox.

In March 2024, the EU orphan drug designation for BCV, for the prevention of adenovirus and cytomegalovirus infections in immunocompromised patients, was transferred from Emergent BioSolutions to a subsidiary of SymBio.

Anticancer agent SyB L-0501 (FD formulation)/SyB L-1701 (RTD formulation)/SyB L-1702 (RI administration); generic name: bendamustine hydrochloride hydrate, product name: Treakisym®

The company has actively conducted joint research on Treakisym® with institutions such as the University of Tokyo and Kyoto University, but it has since shifted part of its research resources toward BCV.

Anticancer agent SyB L-1101 (IV)/SyB C-1101 (oral); generic name: rigosertib sodium

In April 2025, the company terminated its licensing agreement for rigosertib, which it had in-licensed from Onconova (now Traws Pharma).

Overseas business (SymBio Pharma USA)

In January 2025, the company appointed Mr. Masaru Taguchi as CEO and President of its wholly-owned subsidiary SymBio Pharma USA, Inc. (SPU). In April 2025, Mr. Taguchi also assumed the role of Executive Vice President and COO of the parent company. SPU will serve as a strategic hub to drive the global business for the antiviral drug BCV, accelerating its development across the US, Europe, Japan, and the UK.

In-licensing of drug candidates

The company is currently focusing on unrolling global development plans for the antiviral drug BCV it in-licensed in September 2019, but also constantly looking into multiple licensing deals and looking for and evaluating promising new in-licensing drug candidates. Through the introduction of external products, it aims to create medium- to long-term business value.

Highlights

Possibility of initiating a clinical trial for progressive multifocal leukoencephalopathy (PML)

At the FY12/25 interim results briefing, the company noted that the US National Institutes of Health (NIH) may initiate a clinical trial of BCV in progressive multifocal leukoencephalopathy (PML), with a potential start scheduled in 2026.

- Progressive multifocal leukoencephalopathy (PML) is a brain disease caused by JC virus (JCV).
- In July 2024, results from a non-clinical study of BCV using a mouse model infected with polyomaviruses, including JC virus (JCV), were published in *mBio*.

Fundraising

In July 2025, the company announced the issuance of the 65th–67th series of stock acquisition rights with price adjustment clauses through third-party allotment to EVO FUND, as well as the issuance of its first unsecured straight bonds. The company raised approximately JPY8.4bn in net proceeds to advance its development programs, including the Phase III trial of BCV for adenovirus (AdV) infection.

Key business development goals for FY12/25

At its FY12/24 full-year earnings briefing in February 2025, SymBio outlined the following key business development goals for FY12/25. Among these, the highest priority is the initiation of the Phase 3 trial for post-transplant adenovirus (AdV) infection.

- Q4 target: Initiate a Phase III trial for post-transplant adenovirus (AdV) infection
- Q3 target: Establish proof of concept (POC) in the Phase II trial for post-transplant cytomegalovirus (CMV) infection
  - The company noted that patient enrollment for the second dosage level has been completed as CMV has a relatively large patient population.
- Q4 target: Establish POC in the Phase Ib trial for NK/T-cell lymphoma
  - Given the rarity of the disease, the company believes that in Japan, it can seek regulatory approval after completing a Phase II trial, following the completion of the Phase Ib trial
- Q4 target: Begin reviews toward commencing a Phase Ib trial for glioblastoma (GBM)
- Q4 target: If animal POC for multiple sclerosis is confirmed (expected in Q2), initiate discussions with the NIH on the clinical trial design for a first-in-human (FIH) study
- Q4 target: Finalize a global partnership for BCV. (The company aims to collaborate with a developer of immune checkpoint inhibitors (ICIs), as it envisions BCV's use in combination with ICIs.)
- Q3 target: Work to in-license new products for the domestic market

Full-year company forecast

Full-year company forecast for FY12/25 (revised in June 2025)

	FY12/23			FY12/24			FY12/25	
(JPYmn)	1H results	2H results	FY results	1H results	2H results	FY results	FY forecast	YoY
Sales	3,179	2,411	5,590	1,284	1,168	2,453	1,400	-42.9%
Gross profit	2,473	1,938	4,411	996	877	1,873	1,068	-43.0%
Gross profit margin	77.8%	80.4%	78.9%	77.6%	75.0%	76.4%	76.3%	
SG&A expenses	2,523	2,700	5,223	2,716	3,034	5,750	5,330	-7.3%
SG&A ratio	79.4%	112.0%	93.4%	211.4%	259.7%	234.4%	380.7%	
Operating profit	-50	-762	-812	-1,719	-2,157	-3,877	-4,262	-
Operating profit margin	-	-	-	-	-	-	-	
Recurring profit	67	-803	-736	-1,481	-2,208	-3,689	-4,467	-
Recurring profit margin	2.1%	-	-	-	-	-	-	
Net income	-80	-1,883	-1,963	-1,541	-2,292	-3,833	-4,592	-
Net margin	-	-	-	-	-	-	-	

Source: Shared Research based on company data.
Note: Figures may differ from company materials due to differences in rounding methods.

Revised full-year forecast for FY12/25 (as of June 10, 2025)

In June 2025, the company announced a revision to its full-year forecast for FY12/25.

- Sales: JPY1.4bn (JPY1.9bn in previous forecast)
- Operating loss: JPY4.3bn (loss of JPY4.3bn)
- Recurring loss: JPY4.5bn (loss of JPY4.3bn)
- Net income attributable to owners of the parent: JPY4.6bn (loss of JPY4.5bn)
- Net loss per share: JPY95.95 (loss of JPY80.45)

Reasons for the revision

The company lowered its FY12/25 sales forecast by JPY458mn to JPY1.4bn (previously JPY1.9bn). This downward revision reflects a shift at medical institutions from Treakisym® toward generics and an expansion of treatment options with the introduction of new therapies, reducing prescriptions for the drug. As a result, the company determined that recovering the sales shortfall in 2H would be difficult.

The company expects SG&A expenses to total JPY5.3bn, down JPY290mn from the previous forecast, by cutting non-R&D costs. As a result, it projects an operating loss of JPY4.3bn, roughly unchanged from the previous estimate, rising just JPY1mn.

The company now assumes a stronger yen of JPY142.0/USD (vs. JPY150.0 in the previous forecast), which—along with higher bond issuance costs—results in a recurring loss of JPY4.5bn, an improvement of JPY120mn, and a net loss attributable to owners of the parent of JPY4.6bn, an improvement of JPY124mn.

FY12/25 company forecast (announced on February 6, 2025)

The company's initial full-year forecast for FY12/25 was as follows.

- Sales: JPY1.9bn (-24.3% YoY)
- Operating loss: JPY4.3bn (compared to an operating loss of JPY3.9bn in FY12/24)
- Recurring loss: JPY4.3bn (compared to a recurring loss of JPY3.7bn in FY12/24)
- Net loss: JPY4.5bn (compared to a net loss of JPY3.8bn in FY12/24)

For FY12/25, the company expects the market environment for Treakisym® to remain challenging, with continued penetration of generics, the impact of drug price reductions, and lingering effects of infectious diseases.

- The company projects sales of JPY1.9bn (-24.3% YoY), reflecting the impact of drug price reductions, continued penetration of generics, and lingering effects of infectious diseases.

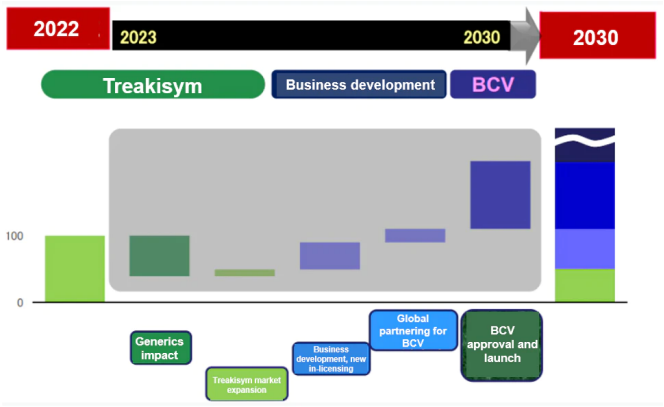
- Gross profit is projected at JPY1.4bn (-27.6% YoY), affected by the decline in sales and the drop in drug prices. GPM is expected to decrease 3.3pp YoY to 73.0%.

The company expects R&D expenses to continue increasing significantly, following the trend from FY12/24. It plans to allocate JPY3.7bn (+8.3% YoY) to advance the global development of treatments for adenovirus and cytomegalovirus infections, as well as NK/T-cell lymphoma, which began in 2024. Additionally, the company will pursue new indication development through academic collaborations and explore the introduction of new drug candidates to enhance long-term corporate value. Meanwhile, SG&A expenses excluding R&D are projected at JPY2.0bn (-17.4% YoY), bringing total SG&A expenses to JPY5.6bn (-2.3% YoY).

The company expects operating loss to expand to JPY4.3bn (versus a loss of JPY3.9bn in FY12/24).

Long-term outlook

Sales projections from 2023 to 2030 (announced February 2023)



Source: Shared Research based on company information.
*Company projections as of the FY12/22 earnings results briefing (February 2023)
**Unit value for figures in the vertical axis is JPY100mn

In the medium-term plan to FY12/23 (announced February 2020), SymBio forecasted Treakisym® sales would continue to grow YoY in FY12/23. This was based on the expectations that although the re-examination period for Treakisym® would end in 2020, SymBio could potentially extend the product life to 2031 through commercialization and switching to Treakisym® RTD and Treakisym® RI, formulations for which SymBio retains exclusive marketing rights. However, following the launch of generic Treakisym® by two companies in June 2022 and December 2022, the company revised its medium-term plan forecasts and now expects FY12/23 Treakisym® sales to decline 30.1% YoY.

At the FY12/22 earnings results briefing held in February 2023, the company explained the rationale for the revised medium-term plan forecasts and presented an overall image of sales from 2023 through 2030. As of February 2023, SymBio has not yet issued a new medium-term plan, including new earnings forecasts.

Treakisym® sales projection in 2030

The reason for management's revision of the medium-term guidance is that the MHLW approved generic Treakisym® and two companies commercialized their versions despite SymBio's patent infringement warnings. Management noted that market share erosion to generic competition in public and quasi-public medical institutions is inevitable given government policies promoting the use of generic drugs. Accordingly, SymBio has reduced its 2030 forecast for Treakisym® to half of the estimated peak sales level of JPY10bn (i.e., approximately JPY5bn). This halving of the Treakisym® sales forecast still accounts for market expansion due to the aging population and the increasing share of Treakisym®. The company still expects Treakisym® to have a 50% share of the prescription market in 2030.

Business development and new in-licensing opportunities

The company is considering multiple licensing opportunities and conducting exploratory assessments to acquire licensing rights to new development candidates. Management indicated that sales contributions from these new acquisitions could generate sales of JPY3bn by 2030.

Business development and BCV global partnering

The company has decided against independent large-scale development of BCV in areas such as multiple sclerosis and Alzheimer's disease, but is considering transfer of rights, including joint development with a large pharmaceutical company capable of global development (i.e., global partnering). Compensation for the transfer of rights for the last five years to 2030 is expected to reach JPY10bn, or an average of JPY2bn per year during this period.

Development of BCV

The company aims to obtain approval for two to three indications for BCV currently under development and generate JPY10.0bn in sales from BCV by 2030, equivalent to the peak annual sales of Treakisym®.

R&D outlook from 2023 to 2030 (as of February 2023)

Management provided a rough roadmap of its R&D plan through 2030 at the FY12/22 earnings results briefing held in February 2023. Development of Treakisym® has been completed and development from 2023 will focus on BCV. As BCV has potential in multiple therapeutic categories, prioritization of development will be important. The development of BCV will focus on three therapeutic categories: hematopoietic stem cell and organ transplantation, hematological malignancies/oncology, and neurodegenerative diseases (NDD). Management explained the development prioritization and the timeline of the development plan, noting that clinical development for hematopoietic stem cell and organ transplantation will be prioritized as approval is the most likely.

- Hematopoietic stem cell and organ transplantation
  - Adenovirus trials, BKVN trials, CMV trials
- Hematological malignancies and oncology
  - CMV (+) brain tumor, NK/T lymphoma
- Neurodegenerative diseases
  - EBV multiple sclerosis, HSV-1 Alzheimer's type dementia

Initial clinical development for hematopoietic stem cell and organ transplantation

Initial clinical development in hematopoietic stem cell and organ transplantation will focus on two indications: adenovirus infection and BK virus infection. In the development plan to 2030, management believes that approval for these indications is most likely.

- Adenovirus trial (post-hematopoietic stem cell transplantation adenovirus infection)
  Phase IIa escalating-dose confirmatory study on safety and tolerability underway. Slated for completion in Q4 2023
- BKVN trial (post-kidney transplantation BK viral infection)
  Phase II underway. Slated for completion in Q2 2025

Announces full-scale development of CMV therapeutics in the transplantation field

- CMV trial (post-hematopoietic stem cell cytomegalovirus infection)
  Preparation for Phase Ib (Slated to start in Q4 2023 and be completed in Q1 2025)

At the FY12/22 earnings results information briefing held in February 2023, management explained the company's policy for full-scale development of BCV for cytomegalovirus (CMV) infection in transplant recipients and its significance. Although CMV is a strong development candidate, SymBio had put development in this indication on hold pending clarification of the therapeutic effect of Takeda's competitor maribavir (approved in November 2021).

After evaluating the therapeutic efficacy of maribavir, management identified an unmet therapeutic need for CMV in the transplantation field and announced the full-scale development of BCV for this indication. SymBio's determination that there is an unmet therapeutic need, even after maribavir has been marketed, is based on the following three points.

- Resistance to maribavir is 44.3% and no effective therapy is available for these resistant patients
- Even after the virus is no longer detectable following maribavir treatment, relapse and resistance occurred in 23% of patients at six weeks and 30% at 12 weeks.
- Maribavir failed to demonstrate equivalence to the original drug (valganciclovir) in a non-inferiority trial

The number of transplant recipients treated for CMV is exceptionally high for a rare disease (25,000, of which 10,000 are resistant or refractory). One reason that megapharma Takeda decided to develop maribarivir independently was likely that the large potential patient base made it look more lucrative. The company noted that the large patient base made patient

enrollment for clinical trials much easier. The Phase Ib clinical trial is being prepared to start with dose selection. The trial is expected to begin in Q4 2023 and be completed by Q1 2025.

Hematological malignancies and oncology

- CMV (+) brain tumors (collaboration with Brown University in the US; glioblastoma [GBM])
  Phase I clinical trial / Slated to start in Q2 FY12/24 and be completed in 1Q FY12/26

The only pipeline in the hematological malignancies and oncology field for which a development timeline has been proposed is glioblastoma, a type of CMV (+) brain tumor. In March 2022, the company launched a joint non-clinical study with Brown University of the US to investigate the antitumor effect on cytomegalovirus positive infection and glioblastoma (GBM). This non-clinical study is expected to be completed in Q3 2023 with the goal of establishing PoC in animals. The Phase I clinical trial is expected to begin in Q2 2024 and be completed in Q1 2026.

- NK/T lymphoma (joint research with National Cancer Centre Singapore)

BCV demonstrated anticancer activity against NK/T cell lymphoma in the non-clinical study regardless of EB viral infection. No clinical trial timeline was disclosed for NK/T lymphoma.

Neurodegenerative diseases (NDD)

SymBio announced that it will not independently develop BVC for neurodegenerative diseases (NDD) such as multiple sclerosis and Alzheimer's disease. Rather, SymBio seeks to partner with a large pharmaceutical company capable of global development (global partnering) and receive compensation through the transfer of rights. The company aims to establish early proof-of-concept in animals through collaborations with world-renowned academic institutions. For the multiple sclerosis indication, SymBio is advancing a Phase I study with the US NIH. For the Alzheimer's disease indication, management is planning a co-development with a partner starting with Phase I.

- EBV multiple sclerosis (joint research with US NIH)
  Basic study (NIH/SymBio) started from Q3 2022
  Animal model (NIH/SymBio) plans to start from Q3 2023
  Phase I clinical trial (NIH/SymBio) plans to start from Q2 2024 with completion projected for Q2 2025

- HSV-1 Alzheimer's type dementia (under joint research with Tufts University of the US)
  3-D brain modeling (Tufts University) started from Q4 2022
  Animal modeling (SymBio) plans to start from Q4 2023
  Phase I clinical trial (partner/SymBio) plans to start from Q1 2025 with completion projected after end-2026

Therapeutic categories under consideration for development

Not specified, but the following therapeutic categories are potentially under consideration for development (as of February 2023).

- Post-transplantation infection
  - Post-hematopoietic stem cell transplantation adenovirus/BK viral hemorrhagic cystitis (VHC) and HHV-6 encephalitis, EBV infectious mononucleosis
- Hematological malignancies/oncology
  - EBV (+) lymphoma
- Neurological
  - EBV sequelae
- Ophthalmological
  - Adenovirus epidemic keratoconjunctivitis

Unexplored development possibilities

Additional potential therapeutic categories that have not been explored for development are listed below (as of February 2023).

- Post-transplantation infections
  - Prevention of post-hematopoietic stem cell transplantation CMV infection, multiviral agent for post-hematopoietic stem cell transplantation use
- Hematological malignancies/oncology
  - HPV (+) head and neck cancer, HPV (+) endometrial cancer
- Dermatological
  - Varicella-zoster virus (VZV)/Herpes virus (HPV)

Business

Business description

SymBio obtains rights to develop and market new drug candidates from biotech companies in the US and EU

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)

- **Post 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.

- Niche market: 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—including oncology, hematology, and rare diseases—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.

- **Global expansion**: The company identifies and capitalizes on opportunities to grow sales by acquiring the right to develop drug candidates in Japan and other international markets.

The company have in-licensed new drug candidates after rigorously evaluating them.

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. Within three years of launch, the product captured over 50% market share.

Products under development: Treakisym® (RTD formulation and RI formulation), brincidofovir, and rigosertib (injection and oral)

Additional indications for Treakisym®

For patients that have developed resistance to other drugs, Treakisym® is safer and more efficacious than existing treatments. As outlined below, the company has gained approval in Japan for the indications of refractory or relapsed low-grade non-Hodgkin's lymphoma and mantle cell lymphoma, chronic lymphocytic leukemia, and first-line treatment of low-grade non-Hodgkin's lymphoma, mantle cell lymphoma, and relapsed or refractory diffuse large B-cell lymphoma (DLBCL).

- Refractory or relapsed low-grade non-Hodgkin's lymphoma and mantle cell lymphoma: After designation as an orphan drug (drug for the treatment of rare diseases), Treakisym® won marketing approval for this indication in October 2010.

- Chronic lymphocytic leukemia: SymBio received approval for this to be added as indication for Treakisym® in August 2016.

- First-line treatment of untreated low-grade non-Hodgkin's lymphoma and mantle cell lymphoma: The company gained approval for this to be added as indication for Treakisym® in December 2016.

- Relapsed or refractory diffuse large B-cell lymphoma (DLBCL): Approved as additional indication in March 2021.

Treakisym® (RTD formulation and RI formulation)

In September 2017, Eagle Pharmaceuticals and SymBio concluded a license agreement that licenses to SymBio rights to develop, market, and sell Eagle's bendamustine hydrochloride ready-to-dilute (RTD) formulation and rapid infusion (RI) administration products in Japan. Securing products to replace freeze-dried (FD) product (whose exclusive sales rights in Japan expired in 2H 2020) had been a priority for the company. SymBio obtained approval for the RTD formulation in September 2020, and launched the product in January 2021. The company obtained approval for the RI formulation in February 2022.

With this, it aims to promote a switch in clinical settings from lyophilized powder formulation to RTD and RI formulations that lighten the workload for medical professionals, at the same time curtailing uptake of Treakisym® generics. The company had expected to extend the product lifecycle of Treakisym® RTD and RI formulations until 2031 through the exclusive license agreement. However, the situation changed significantly in 2022 when two companies launched generic versions of Treakisym® in response to the company's patent infringement warnings. The company reached a settlement in its patent infringement lawsuits with these two companies, but the two companies have continued selling generic versions of the product.

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 of rigosertib (injection) in patients with relapsed or refractory MDS in Europe, and its efficacy was proven in subgroup analysis. SymBio also completed patient registration for Phase I domestic clinical trials in January 2015.

In August 2015, Onconova initiated global Phase III clinical trials for patients with higher-risk MDS who had failed to respond to the standard therapy with hypomethylating agents (HMAs) or relapsed in more than 20 countries, and announced in August 2020 that they had failed to meet the primary endpoints in comparison with physician's choice. In Japan, the company began conducting joint global Phase III clinical trials in cooperation with Onconova in December 2015. SymBio says it will utilize the knowledge obtained from additional analysis of the global Phase III clinical trials in future development of rigosertib.

For the oral form of the drug, Onconova completed Phase I/II clinical trials targeting first-line treatment of higher-risk MDS, which suggested efficacy and safety of rigosertib-azacitidine combination therapy. SymBio initiated the Phase I clinical trial of rigosertib monotherapy for higher-risk MDS in Japan in June 2017 and completed patient enrollments in June 2019.

Brincidofovir

Brincidofovir is an antiviral drug formed by conjugating a lipid chain (hexadecyloxypropyl, or HDP) of specified length to cidofovir (an antiviral drug already approved and marketed in the EU and the US, but not approved in Japan). It has a novel mechanism of action, which is attributed to its being a lipid conjugate, and can be taken up into cells with enhanced efficiency compared to cidofovir (i.e., brincidofovir has higher cell membrane permeability). Once inside a cell, brincidofovir transforms into a direct-acting agent and inhibits viral replication, demonstrating high antiviral effect. It is also easy to use as it has a low risk of nephrotoxicity, which is a side effect of cidofovir, hence making brincidofovir a novel, highly active anti-multiviral drug. It is expected to become an effective treatment for a wide spectrum of infectious diseases caused by DNA viruses, including cytomegalovirus (CMV) and other herpes viruses, adenoviruses, BK virus, papillomaviruses, and smallpox virus.

In September 2019, SymBio entered an exclusive global license agreement with Chimerix Inc. for brincidofovir. As a result, the company acquired exclusive worldwide rights to develop, market, and manufacture brincidofovir for all indications except smallpox. In August 2021, the company launched Phase II clinical trials in the US targeting adenovirus infection in children. In May 2023, the company successfully established proof of concept (POC) for brincidofovir in human patients.

Revenue source: Treakisym® sales

Revenue mainly comes from product sales of Treakisym®. Operating losses had persisted since the company's founding with the exception of FY12/08 when the company booked operating profit due to a one-time contract payment from Eisai for an exclusive domestic right to sell Treakisym®.

In FY12/21, the company turned profitable from the operating profit line down. SymBio began in-house sales of Treakisym® in December 2020 and sales of the RTD formulation in January 2021, and in March 2021 it obtained approval for the additional indication of relapsed or refractory DLBCL in FY12/21, which all contributed to sales growth and GPM improvement.

Since FY12/23, Treakisym® sales have declined sharply due to market erosion by generics

The company's sales of Treakisym® peaked in FY12/22, reaching JPY10.0bn, generating operating profit of JPY2.0bn. However, following the launch of generics, sales began to decline sharply from FY12/23. At the same time, increased R&D expenses to advance the global development of the antiviral drug BCV have resulted in continued operating losses.

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. It can obtain approval 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.

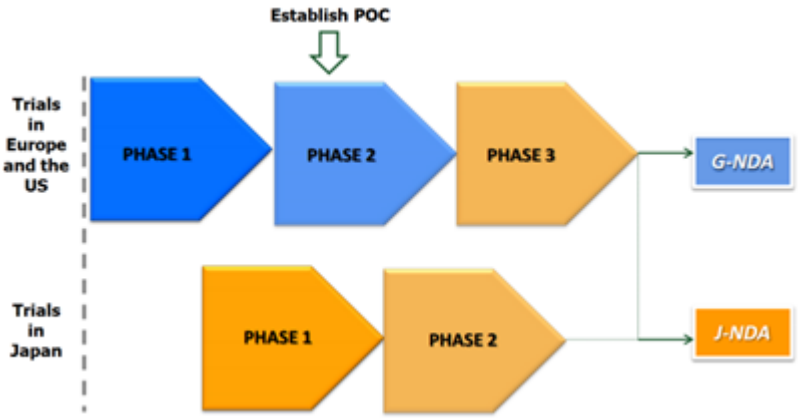
The overall aim is to reduce development risk, streamline expenses, and expand revenue opportunities. This hinges on the following five strategies, namely post proof-of-concept, screening, fabless, niche market, and global expansion.

Post-POC strategy: 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 (confirming efficacy and safety of a new drug candidate through administration to animals or humans) 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: Shared Research based on company data

Screening strategy: independent search network plus evaluation experience

Identify candidate drugs by utilizing independent search network and 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 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.

Evaluation by a panel of pharmaceutical experts

The final in-licensing candidate will be determined by the Scientific Advisory Board after rigorous evaluation by external experts involved in therapeutic research in related fields.

Only a few new drug candidates have met the company's stringent criteria since its foundation

The company has in-licensed only a few new drug candidates that have met its stringent criteria. The first was Treakisym®, which the company currently sells in Japan (as of February 2022). The company is also developing intravenous and oral formulations of rigosertib and antiviral drug brincidofovir.

Scientific Advisory Board

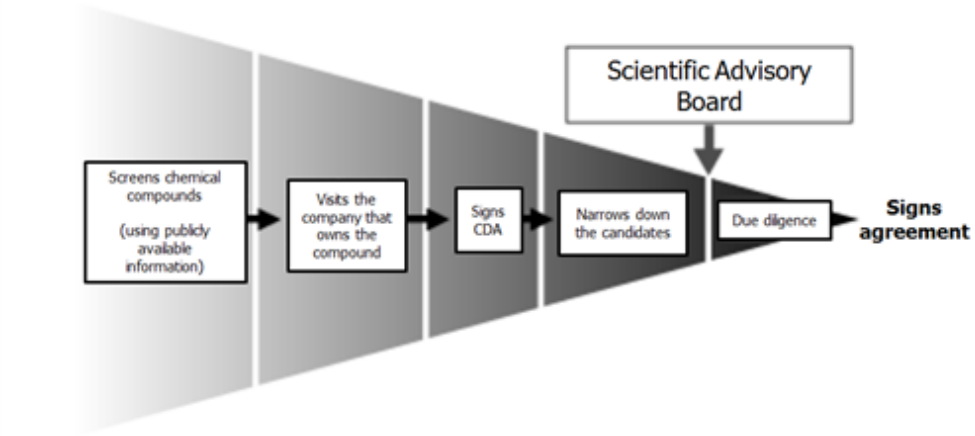
The Scientific Advisory Board is comprised of former directors of pharmaceutical companies, researchers, and doctors, and meets three times a year. Typically, the SAB panel evaluates two to three drug candidates that have been selected via the company's in-house screening process. This in-house screening 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.

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
Tomomitsu Hotta, M.D.	Honorary President, National Cancer Center Honorary Director, Nagoya Medical Center
Makoto Ogawa, M.D., Ph.D.	Honorary President, Aichi Cancer Center
Tatsutoshi Nakahata, M.D., Ph.D.	Professor Emeritus at Kyoto University; Director, Central Institute for Experimental Animals (Public Interest Incorporated Foundation)
Toshio Suda, M.D., Ph.D.	Distinguished Professor, International Research Center for Medical Sciences, Kumamoto University Professor, Cancer Science Institute of Singapore, National University of Singapore
Tsutomu Takeuchi, M.D., Ph.D.	Professor Emeritus at Keio University; President of Saitama Medical University
Toshio Hiratsuka, M.D., Ph.D.	Professor Emeritus at Kyoto University; Director of Hyogo Prefectural Amagasaki General Medical Center
Koichi Takahashi, M.D.	Assistant Professor, Department of Leukemia, Division of Cancer Medicine, MD Anderson Cancer Center, The University of Texas

Source: Shared Research based on company data
In addition to the SAB members listed above, Dr. Mathias J. Rummel serves as Senior Advisor. Dr. Rummel is the Head of the Department of Hematology and Medical Oncology Outpatient Clinic, Justus Liebig University, *Germany*.

Drug candidate selection process



Source: Shared Research based on company data
CDA = confidential disclosure agreement

Fabless strategy with a lean management team

SymBio aims to reduce costs and improve profitability through partnership-based operations with external partners. The company does not own research or manufacturing facilities. After identifying and in-licensing drug candidates, it focuses on strategic development planning while outsourcing routine development activities and manufacturing to contain drug development and manufacturing costs.

Specifically, the company takes the lead in designing clinical trials, coordinating overseas trials, and engaging with medical experts. Routine development activities are outsourced. For manufacturing, it outsources production to the licensor or to

domestic and international pharmaceutical companies. Regarding sales, Eisai Co., Ltd. handled domestic sales of Treakisym® until December 9, 2020, after which the company began direct sales.

Niche markets: oncology, hematology, and rare 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. Specifically, the company specializes in therapeutic areas with high barriers to entry, such as oncology, hematology, and rare diseases.

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. The company can also increase value added of niche disease areas by additional indications and putting new products on the market. For example, its first in-house proprietary drug Treakisym® has gained over 50% market share three years after going on sale. In July 2018, Treakisym® was newly included as a standard option for first-line treatment of low-grade NHL and mantle cell lymphoma in the Guidelines for Hematological Malignancies 2018 issued by the Japan Society of Hematology in July 2018.

Strategy for global expansion

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. Also, it acquired exclusive worldwide rights to develop, manufacture, and market brincidofovir.

Pipeline

パイプライン

Name/ Development number	Indications	Development status
Brincidofovir (BCV injection) SyB V-1901	Adenovirus infection after hematopoietic stem cell transplantation	Completed Phase II clinical trial (POC established in May 2023)
	Cytomegalovirus (CMV) after hematopoietic stem cell transplantation (CMV)	In May 2024, initiated Phase IIa clinical trial in the US
	BK virus infection after kidney transplantation	In August 2023, announced changes to the clinical development plan (consideration of protocol amendments)
	NK/Malignant lymphomas such as T-cell lymphoma	In August 2024, launched an international Phase 1b clinical trial in Japan; in February 2025, expanded an international Phase 1b/2 clinical trial to Singapore
Non-clinical trials of BCV	EB virus / multiple sclerosis	National Institute of Neurological Disorders and Stroke (NINDS)
	Herpes simplex virus / Alzheimer's disease	Tufts University, US
	Cytomegalovirus (CMV) Infectious diseases / glioblastoma (GBM)	Brown University, US
Treakisym®	TBD	Will explore new development possibilities through joint research with institutions such as the University of Tokyo and Kyoto University.
Rigosertib and Treakisym®	TBD	Aims to discover new benefits of both compounds or their combination with existing drugs while exploring new indications through joint research with the University of Tokyo and the establishment of a social collaboration course

Source: Sheard Research based on company materials, website

As of end-FY12/24, the status of the company's main development pipeline is as follows.

- Treakisym®: All development plans have been concluded, so the drug has been removed from the pipeline. However, since its development history represents a success story of the company's business model, a summary of its indication expansions and approval timeline is provided later under SyB L-0501 (generic name: bendamustine hydrochloride, brand name: Treakisym®).
  - SymBio will continue to explore new potential applications of Treakisym®, including via joint research with the University of Tokyo and Kyoto University.
- Rigosertib (injection and oral): SymBio announced in August 2020 that the primary endpoints were not met in the joint global Phase III clinical trials (INSPIRE study), and no further progress has been disclosed.
  - For rigosertib and Treakisym®, the company is searching for new indications as well as new applications for the drugs used in combination with each other or with other existing drugs, through joint research and the offering of academia-industry collaborative courses with the University of Tokyo. In April 2024, the drug's licensor Onconova changed its name to Traws Pharma Inc., headquartered in Pennsylvania, US.
- Antiviral drug brincidofovir (BCV): Under development for multiple indications. Refer to "R&D outlook from 2023 to 2030" for details. As of FY12/24, the development status of major indications is as follows.
  - Adenovirus (AdV) infections: In May 2023, human proof of concept was established in a Phase II clinical trial. A use patent was granted in January 2024.
  - BK virus infections after kidney transplantation: Due to delays in case enrollment, SymBio announced a change to its clinical development plan in August 2023, stating that it will consider a protocol amendment.

- Cytomegalovirus (CMV) infections following hematopoietic stem cell transplantation: In May 2024, a Phase IIa clinical trial post-hematopoietic stem cell cytomegalovirus infection was initiated in the US. In June 2024, the first patient was enrolled, and the trial is currently ongoing.

- In August 2024, the company launched an international Phase 1b/2 clinical trial of BCV in Japan in patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma. In February 2025, the trial was expanded to Singapore.

- Other indications: Collaborative research with multiple academic institution is underway (non-clinical trials in progress).

SyB V-1901 (antiviral drug, brincidofovir [BCV])

In September 2019, SymBio concluded an exclusive global license agreement with Chimerix Inc. for the antiviral drug brincidofovir (SyB V-1901; BCV). The company acquired exclusive global rights to develop, manufacture, and market brincidofovir for all diseases except smallpox. Under the terms of the agreement, the company will pay Chimerix an upfront payment of USD5mn, milestone payments on future developments of USD180mn, and royalties on the product sales. Brincidofovir differs from other candidates in SymBio's pipeline in that it targets the global market and that the company had acquired not only development and marketing rights but also manufacturing rights to the drug.

In June 2021, Chimerix received FDA approval for the use of the oral BCV formulation as a medical defense against smallpox.

According to the company, Chimerix had been developing oral formulation of brincidofovir, but suspended development due to the failure of the Phase III clinical trial. SymBio determined that the failure of the oral formulation was due to its low intestinal absorption rate and side effects arising from toxicity, and thought that it could circumvent such problems if it worked on developing brincidofovir as an intravenous formulation. The company commented that one of the reasons it entered the license agreement with Chimerix was the latter's policy of focusing on cancer.

Mechanism of action and target indications of brincidofovir (BCV)

Brincidofovir is an antiviral drug formed by conjugating a lipid chain (hexadecyloxypropyl, or HDP) of specified length to cidofovir (antiviral drug already approved and marketed in the EU and the US, but not approved in Japan). As a lipid conjugate, it has a novel mechanism of action and can be taken up by cells at enhanced efficiency compared to cidofovir (i.e., brincidofovir has higher cell membrane permeability).

Once inside a cell, brincidofovir transforms into a direct-acting agent and inhibits viral replication, demonstrating high antiviral efficacy. It is also easy to use as it has a low risk of nephrotoxicity, which is a side effect of cidofovir, hence making it a novel, highly active anti-multiviral drug. It is expected to become an effective treatment against a wide array of infectious diseases caused by DNA viruses, including cytomegalovirus (CMV) and other herpes viruses, adenoviruses, BK virus, papillomaviruses, and smallpox virus.

Cidofovir (CDV): Approved by FDA in 1996 for the treatment of cytomegalovirus retinitis in AIDS patients. It inhibits replication of multiple families of DNA viruses other than herpes viruses, including adenoviruses, papillomaviruses, and polyomaviruses.

CDV is taken up by renal tubular epithelial cells through organic anion transporter 1 (OAT1), and its accumulation in the cells cause nephrotoxicity. brincidofovir is expected to have a low risk of nephrotoxicity as its lipid chain prevents it from being taken up by OAT1 and accumulating in renal tubular epithelial cells.

Comparison of brincidofovir (BCV) antiviral activity versus other agents

Viral Family	Virus	BCV	Cidofovir	Maribavir	Letermovir	Ganciclovir*	Foscarnet	Acyclovir
Herpes	Cytomegalovirus	0.001	0.4	0.31	0.005	3.8	50-800	>200
	Epstein-Barr Virus	0.03	65.6	0.63	>10	0.9	<500	6.2
	Human Herpesvirus 6	0.003	2.7	Inactive	>10	5.8	16	10
	Human Herpesvirus 8	0.02	2.6	Inactive	—	8.9	177	>100
	Herpes Simplex Virus 1	0.01	3.0	Inactive	>10	0.7	92-95	3.8
	Herpes Simplex Virus 2	0.02	6.5	Inactive	>10	2.5	91-96	4.4
	Varicella Zoster Virus	0.0004	0.5	Inactive	>10	1.3	39.8	3.6
Adenovirus	Adenovirus (AdV-B7)	0.02	1.3	—	>10	4.5-33	Inactive	>100
Polyoma	BK Virus (BKV)	0.13	115	—	—	>200	Inactive	>200
	JC Virus (JCV)	0.045	>0.1	—	—	—	Inactive	—
Papilloma	Human Papillomavirus	17	716	—	—	Inactive	—	Inactive
Pox	Variola	0.1	27	—	—	—	—	—
	Vaccinia	0.8	46	—	—	>392	Inactive	>144

Source: Company data

Note: Table shows IC50 (μM) values (concentration at which 50% of viruses targeted by pharmaceutical agent can be inhibited). The lower the IC50 value, the greater the antiviral activity.

Note: Cidofovir, Maribavir, Letemovir, Ganciclovir, Foscarnet, and Acyclovir are antiviral agents.

Development status of IV formulation of brincidofovir (BCV)

The US-based Phase I clinical trial of intravenous formulation of brincidofovir was completed. No serious side effects were observed in the study.

Phase II clinical trials targeting adenovirus diseases in children

In March 2021, the company filed an indicative new drug (IND) application with the US FDA, so it could start a Phase II clinical trial for the indication of adenovirus diseases in children (including adults). The development program received fast-track designation from the FDA in April 2021, and the investigational drug was administered to the first patient enrolled in the clinical trial in August 2021. In January 2022, the company submitted a Clinical Trial Application (CTA) to the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK, which was accepted.

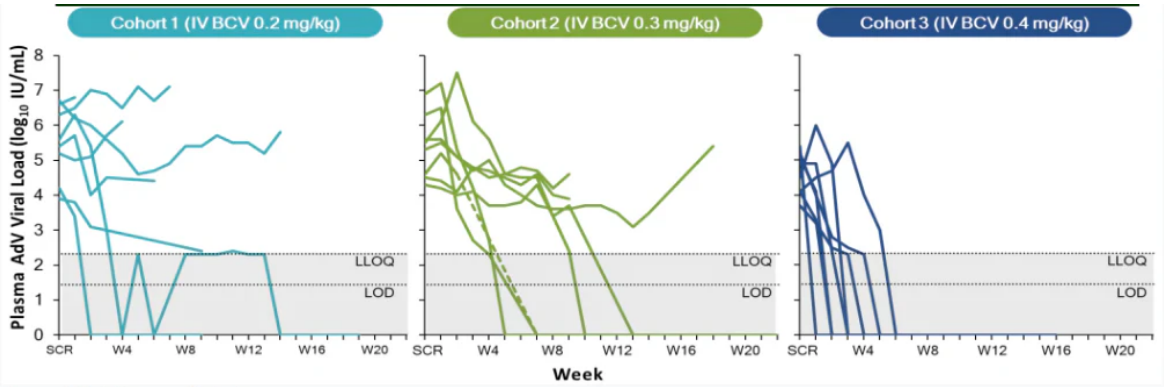
Human POC for BCV established in May 2023

The Phase II clinical trial of BCV targeting adenovirus (AdV) infections demonstrated proof of concept (POC) in human patients in May 2023. POC refers to the demonstration that a drug candidate under research and development is useful and effective when administered to humans. Less than two years after the first patient was dosed (FPI) in August 2021, the efficacy and safety of the BCV injection for AdV were confirmed in humans.

- The Data Safety Monitoring Board (DSMB) and the FDA confirmed the POC in terms of both safety and efficacy. While the POC has been confirmed in trials up to cohort 3.

- For cohorts 1 to 3, BCV was administered twice weekly, at doses of 0.2mg/kg for cohort 1, 0.3mg/kg for cohort 2, and 0.4mg/kg for cohort 3. In cohort 3 (0.4mg/kg, twice weekly via IV), the disappearance of AdV in the blood was confirmed in 100% of patients (n=10). Of these, 90% of patients (n=9) achieved viral clearance within four weeks of treatment.

Excerpt from oral presentation at the American Society of Hematology (ASH) in December 2023



Source: Shared Research based on company data.
Notes: The vertical axis indicates the amount of AdV in the blood, and the closer to zero, the higher the efficacy.
In cohort 3 (0.4 mg/kg IV twice weekly), the disappearance of AdV in the blood was confirmed in 100% of patients (n=10).

Results from the Phase II clinical trial of BCV targeting AdV infections have been presented (or are scheduled to be presented) at the following academic conferences:

- The 65th American Society of Hematology Annual Meeting (ASH) in December 2023, oral presentation
- The 2024 Tandem Meetings in the US in February 2024, selected as a presentation topic for the Pediatric Best Abstracts session
- The 50th European Society for Blood and Marrow Transplantation in April 2024, accepted for oral presentation

Establishment of POC for BCV injectable proves SymBio's business hypothesis

Chimerix had been developing oral formulation of brincidofovir (BCV), but suspended development due to the failure of the Phase III clinical trial. SymBio determined that the failure of the oral formulation was due to its low intestinal absorption rate and side effects arising from toxicity, and thought that it could circumvent such problems if it worked on developing BCV as an intravenous formulation. The company commented that one of the reasons it entered the license agreement with Chimerix was the latter's policy of focusing on cancer.

The company has grown increasingly confident after establishing a human POC for the BCV injection in May 2023, demonstrating its business hypothesis that developing BCV as an injectable could circumvent the issues encountered with the failure of the Phase III clinical trial of the oral formulation of BCV.

In addition to the BCV injection, the company is considering or preparing for development in the areas of transplantation, cancer, and neuroinfectious diseases. SymBio believes that the establishment of the human POC for the BCV injection targeting AdV has enhanced the possibility of commercialization in these multiple therapeutic areas.

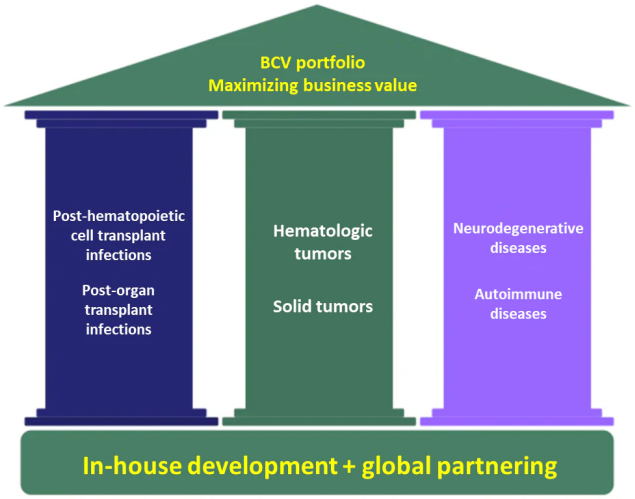
Use patent granted, valid until 2043

Based on the Phase II trial data that established the human POC for BCV in May 2023, the company filed for accelerated review of the use patent for BCV in the treatment of adenovirus infections in September 2023. The patent was granted in January 2024 and will be valid until 2043.

IP strategy for BCV ("pipeline within a molecule")

With the human POC established for BCV and the use patent granted, SymBio aims to maximize the business value of BCV. The company plans to do this by evaluating the drug's efficacy in dsDNA virus infections, expanding the target indications to include multiviral infections, and striving to address the unmet medical needs for treatments of viral diseases and their accompanying complications.

The company is advancing its IP strategy for BCV under the concept of a "pipeline within a molecule," considering BCV as a compound that can be commercialized as a treatment for many diseases.



Source: Shared Research based on company data

The company's goal for BCV development through 2030 is to have the drug approved and launched for two to three indications. SymBio believes that the indications most likely to receive approval are various viral infections occurring after hematopoietic stem cell transplantation and organ transplantation. These are also areas where clinical development is more advanced.

As BCV has the potential to be commercialized for a wide range of indications, the company seeks to expand the business value of BCV by combining in-house development with partnerships with other companies. For more details, refer to the "Long-term outlook" section.

Transplants

Proceeding with development targeting AdV infections following hematopoietic stem cell transplants

After a review at the global advisory board held in February 2020, the company concluded that it would prioritize global development of brincidofovir (mainly in Japan, the US, and Europe) to treat adenovirus (AdV) infections in patients receiving hematopoietic stem cell transplantation to address an unmet medical need. In Q1 FY12/22, the company started the global Phase II study targeting ADV infections following hematopoietic stem cell transplants and completion was projected for Q4 FY12/23. Based on safety and efficacy data acquired from its study, the company plans to review the drug's efficacy against dsDNA viral infections in patients receiving hematopoietic stem cell transplantation and extend its target indications to include multiviral infections.

Clinical trials by Chimerix have demonstrated superior, broad-spectrum antivirus activity of the oral formulation of brincidofovir, raising expectations for the potential of the liquid formulation as a safe and effective therapy to prevent and treat a range of viral infections in patients receiving hematopoietic stem cell transplantation.

Hematopoietic stem cell transplantation is one of the therapies aimed at completely curing diseases such as blood cancer and immunodeficiency disorders that are difficult to treat with conventional chemotherapy. In Japan, there are about 4,000 patients who have undergone allogeneic hematopoietic stem cell transplantation, and about 60% of them have contacted viral hemorrhagic cystitis (VHC) or HHV-6 encephalitis. For vHC, cidofovir is used as first-line treatment in the EU and US. For encephalitis, foscavir and denocin are designated as the first-line drugs, and cidofovir as the second-line drug.

Expanding target disease areas to cover organ transplants (BK virus infection after kidney transplantation)

In a bid to grow the market for brincidofovir and maximize its business value, the company is exploring the potential for expanding target disease areas to viral infections related to kidney and other organ transplants, in addition to ADV infections following hematopoietic stem cell transplants. In Q3 FY12/22, the company initiated a Phase III clinical trial targeting BK virus infections following kidney transplant. It initially planned to complete the trial in Q2 FY12/25, but this plan was not realized.

The development of a treatment for BK virus infection following kidney transplantation is currently under protocol revision. In August 2022, the first patient was dosed (FPD) in an international Phase II clinical trial in Australia; however, patient

enrollment has been slower than anticipated.

BCV clinical development for cytomegalovirus (CMV) infections following hematopoietic stem cell transplantation

At the FY12/22 earnings results information briefing held in February 2023, management explained the company's policy for full-scale development of BCV for cytomegalovirus (CMV) infection in transplant recipients and its significance. Although CMV is a strong development candidate, SymBio had put development in this indication on hold pending clarification of the therapeutic effect of Takeda's competitor maribavir (approved in November 2021).

After evaluating the therapeutic efficacy of maribavir, management identified an unmet therapeutic need for CMV in the transplantation field and announced the full-scale development of BCV for this indication. SymBio's determination that there is an unmet therapeutic need, even after maribavir has been marketed, is based on the following three points.

- Resistance to maribavir is 44.3% and no effective therapy is available for these resistant patients
- Even after the virus is no longer detectable following maribavir treatment, relapse and resistance occurred in 23% of patients at six weeks and 30% at 12 weeks.
- Maribavir failed to demonstrate equivalence to the original drug (valganciclovir) in a non-inferiority trial

In May 2024, a Phase IIa clinical trial post-hematopoietic stem cell cytomegalovirus infection was initiated in the US. In June 2024, the first patient was enrolled, and the trial is currently ongoing.

- The larger patient population for CMV infections compared to adenovirus (AdV) infections has contributed to steady patient enrollment in the trial.

- The competitor drug maribarivir (brand name: LIVTENCITY) from Takeda Pharmaceutical generated sales of JPY19.1bn in FY03/24. The number of transplant recipients treated for CMV is exceptionally high for a rare disease (25,000, of which 10,000 are resistant or refractory). One reason megapharma Takeda decided to develop competitor maribarivir independently was likely the drug's large potential patient base, which made it appear more lucrative. The company noted the large patient base made patient enrollment for clinical trials much easier.

dsDNA viruses: Includes families of herpesviridae, adenoviridae, polyomaviridae, papillomaviridae, and poxviridae, such as cytomegaloviruses (CMV), adenoviruses (AdV), human herpesvirus 6 (HHV-6), BK virus, herpes simplex virus HSV-1 and -2, varicella-zoster virus (VZV), human papillovirus (HPV), JC virus (JCV), and smallpox (variola virus).

Viral hemorrhagic cystitis (VHC): Among viral infections that frequently occur following hematopoietic stem cell transplantation, adenovirus infections causing hemorrhagic cystitis are particularly refractory. When severe, they can cause disseminated infection and become fatal. Cases of adenovirus spreading to the kidney and causing kidney failure and ultimately death have been reported. These infections are especially likely to occur after unrelated donor and umbilical cord blood transplants, which are relatively common in Japan. The infections are likely to be refractory, as they are further complicated by the length of time required for reconstruction of the immune system. Drugs currently used in treatment, including cidofovir (CDV), are either unapproved or off-label in Japan.

HHV-6 encephalitis: HHV-6 (Human Herpesvirus 6) is the sixth human herpesvirus to be discovered. It reactivates in 30–70% of patients after allogenic hematopoietic stem cell transplantation and can cause HHV-6 encephalitis. Most cases of HHV-6 encephalitis develop within 2–6 weeks of transplantation, most frequently in the third week. It is characterized by the three major symptoms of impaired memory, disordered consciousness, and convulsions, which in typical cases gradually appear in the same order (convulsions occur in 30–70% of patients). In rapidly progressing cases, which are common, neurological symptoms worsen by the hour, often requiring ventilator management for repeated convulsions and respiratory depression.

The condition of HHV-6 encephalitis patients frequently deteriorates rapidly, making early treatment important. According to guidelines from the Japan Society for Hematopoietic Cell Transplantation (February 2018), the first-line drugs are foscarnet (FOS) or ganciclovir (GCV), followed by the second-line drug cidofovir (CDV). CDV is not the preferred first-line drug due to nephrotoxicity and because it transfers poorly into cerebrospinal fluid (CSF). All three drugs have been found to be effective in vitro, but no trials have been conducted yet to confirm their clinical efficacy in patients with HHV-6 encephalitis.

Cancer

In addition to antiviral activity, the company thinks BCV may have antitumor effects. Through joint research with the National Cancer Centre Singapore and University of California San Francisco Brain Tumor Center, SymBio is investigating new indications for BCV in oncology, including refractory brain tumors and EB virus-positive lymphoma.

As of February 2023, the company was conducting a nonclinical study targeting glioblastoma multiforme (GBM), brain tumors associated with cytomegalovirus infection. According to the company, roughly 50% of GBM patients have cytomegalovirus infections, and it is possible that cytomegalovirus promotes tumorigenesis. Further, while many GBM therapies are being developed, none of them target cytomegalovirus and GBM (other than brincidofovir). In March 2022, the company launched a joint nonclinical study with Brown University of the US to investigate the antitumor effect of BCV IV on brain tumors associated with cytomegalovirus infection.

Glioblastoma multiforme: A malignant brain tumor of the glial cells that support the brain's nerve cells. Survival is 15–20 months, with a five-year survival rate of under 5%.

Clinical development of BCV (application in hematologic malignancies and oncology)

In August 2024, the company initiated an international Phase Ib clinical trial of BCV targeting patients with malignant lymphoma as a First in Human (FIH) trial in the oncology field. Through this trial, it aims to establish human proof of concept (POC) for BCV in cancer treatment.

- This trial is the third clinical trial of BCV, following those for AdV and CMV infections, and it is the first BCV trial in the oncology field.
- In February 2025, the company expanded its global phase Ib/II clinical trial of BCV for patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma, to Singapore.

Neuro-infectious diseases and other areas

According to Science magazine (January 2022), a Harvard University team found that Epstein-Barr virus (EBV) infections are a major pathogenic factor in multiple sclerosis (MS). Analysis of a sample of over 10mn US military personnel showed that a history of EBV infection increased the risk of MS by 32 times. A January 2022 story in Nature magazine said that a research team from Stanford University elucidated the mechanism of action whereby the EBV causes MS. The magazine says that this suggests eradication of the EBV from the body after the onset of MS could hinder its progression.

BCV has strong antiviral activity on the EBV, so the company plans to investigate whether it could be an effective treatment for MS.

Multiple sclerosis (MS): A disease in which lesions form throughout the brain, spinal cord, and optic nerves, causing a variety of symptoms. MS often features repeated relapses of symptoms and remissions (symptoms subside). Symptoms vary widely depending on the location of the lesions, and include loss of vision, double vision, and motor paralysis. There are roughly 3mn MS patients worldwide, and treatment sales were over JPY1.5tn (2020).

BCV non-clinical studies: EB virus, multiple sclerosis, lymphoproliferative disorders

SymBio has been preparing for clinical development of brincidofovir for multiple sclerosis, a rare disease related to EB virus. In August 2022, the company signed a collaboration agreement for the transfer of human materials with the National Institute of Neurological Disorders and Stroke (NINDS) of the US National Institute of Health (NIH). In March 2023, SymBio signed a cooperative research and development agreement (CRADA) with NINDS to obtain information necessary to conduct future clinical trials. In October 2023, the results of the research were presented at the 9th Joint ECTRIMS-ACTRIMS Meeting in Milan, Italy.

CRADA: Refers to a contract on collaborative R&D between a US government organization and entities such as a private-sector company. The private-sector company may be able to obtain licensing of patent rights regarding inventions developed under the CRADA. Because a company may receive patent rights from a project using government funds, the barriers to being selected for a CRADA are significant (SymBio is the second Japanese company to be selected).

In April 2023, SymBio also signed a CRADA with the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, to evaluate the efficacy of BCV in EB virus-related lymphoproliferative disorders.

*Refers to a wide range of diseases related to the EB virus: Cancers such as T-cell lymphoma, Burkitt lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, NK T-cell lymphoma, and post-transplant lymphoproliferative disease, X-linked lymphoproliferative syndrome, and AIDS-related lymphoproliferative disease. (Source: Materials for company's 18th ordinary general meeting of shareholders.)

BCV non-clinical joint research: herpes simplex virus, Alzheimer's type dementia

In December 2022, the company concluded a sponsored research agreement with US-based Tufts University, and began a joint research study evaluating the efficacy of BCV in a herpes simplex virus infection model. This study aims to explore BCV's potential to treat neurological diseases, including Alzheimer's disease.

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

Treakisym development: SymBio's success story

Treakisym®: All development plans have been concluded, so the product has been removed from the pipeline. However, since its development history represents a success story of the company's business model, a summary of its indication expansions and approval timeline is provided below.

Treakisym® indications and approval timeline

Product name / development number	Indications	Development status
Treakisym® SyB L-0501 FD lyophilized formulation	Relapsed/refractory low-grade NHL / MCL	Approval obtained in October 2010
	Chronic Lymphatic Leukemia	Approval obtained in August 2016
	Untreated low-grade NHL / MCL	Approval obtained in December 2016
	Relapsed/refractory multiple myeloma	Approval obtained in March 2021
Treakisym® SyB L-1701 RTD formulation	All Indications (excluding relapsed/refractory DLBCL)	Approval obtained in September 2020
	Relapsed/refractory DLBCL	Approval obtained in April 2021
Treakisym® SyB L-1702 RI administration	All indications	Approval obtained in February 2022

Source: Shared Research based on the company's website
NHL: Non-Hodgkin's Lymphoma
MCL: Mantle Cell Lymphoma
DLBCL: Diffuse Large B-Cell Lymphoma (a type of NHL and the most common subtype)

Development history

SyB L-0501 (Treakisym®) or bendamustine hydrochloride is an anticancer agent. Developed in Germany in 1971, 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 (resistance to drugs with a similar structure or action as the study drug) has been shown for this drug, which means it is safer and more efficacious 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 has been selling the drug since its launch in December 2010. The company received permission to add CLL as an indication for Treakisym® in August 2016, and first-line treatment of low-grade NHL and MCL in December 2016. In March 2021, the company gained approval of Treakisym® for the additional indication of relapsed or refractory DLBCL (aggressive NHL).

Obtained approval in September 2020 for RTD formulation and RI formulation in February 2022

The company obtained approval for the bendamustine hydrochloride RTD formulation in September 2020 and rapid infusion (RI) administration in February 2022.

Treakisym® in-licensed from Astellas; developed jointly with Eisai in Japan; sold in-house from December 2020

In December 2005, SymBio signed a license agreement for the exclusive right to bendamustine in Japan with Astellas Deutschland GmbH, a subsidiary of Astellas Pharma Inc (TSE Prime: 4503). The company entered into a second license agreement with Astellas in April 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. 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 the Earnings structure section). The marketing agreement with Eisai expired in December 2020, after which SymBio began to independently market Treakisym® in Japan.

Concluded license agreement for RTD and RI formulations of bendamustine hydrochloride (marketed as Treakisym® in Japan) in September 2017

In September 2017, Eagle Pharmaceuticals and SymBio concluded a license agreement that licenses to SymBio rights to develop, market, and sell Eagle Pharmaceuticals' bendamustine hydrochloride ready-to-dilute (RTD) and rapid infusion (RI) formulations (marketed in the US by Teva Pharmaceutical Industries as BENDEKA®) in Japan. Under the terms of this agreement, SymBio will pay Eagle Pharmaceuticals a USD12.5mn upfront payment and a milestone payment upon approval. The company will also pay additional milestone payments on the achievement of cumulative sales thresholds and royalties on future sales of licensed bendamustine products.

RTD and RI products do not require reconstitution; RI formulation can be administered in one sixth of the time as FD product

The FD powder injection product currently available must be reconstituted manually before administration by intravenous infusion. Since RTD and RI products are already liquidized, they do not require the time-consuming process of reconstitution and reduce the workload of healthcare professionals. RI formulation also does not require reconstitution and can be administered by intravenous infusion in 10 minutes instead of 60 minutes for FD powder injection and RTD products, which

reduces stress on patients. The volume of diluted saline solution is one-fifth that of the RTD formulation, with the lower salt content making it suitable for elderly patients.

Scenario of extending life cycle of Treakisym® until 2031

The re-examination period for the FD formulation of Treakisym® ended in 2020, allowing generics to enter the market. SymBio believed that by promoting the RTD and RI formulations—which reduce healthcare professionals' workload and patient burden—it could extend its exclusive sales period until 2031, provided they gained market penetration. The company aimed to extend Treakisym®'s life cycle and limit the spread of generics.

> Profits of a company that develops a brand-name product are protected by patents and re-examination. After a drug is developed, other companies cannot manufacture products using the same active ingredient until the patent expires (usually 20 years, up to a maximum of 25 years). Brand-name products have a re-examination period, usually of six years up to a maximum of 10 years, and during this period, even if the patent has expired, other companies cannot apply to manufacture generic versions of the drug.

Bendamustine hydrochloride RTD and RI injection products are marketed in the US by Eagle Pharmaceuticals as BENDEKA®, which captured a 97% share of the US bendamustine market within two years after its launch. According to the company, some companies in the US have attempted to launch generic versions of Treakisym® liquid formulations, but they all infringed on Eagle Pharmaceuticals' patents, and Eagle prevailed in lawsuits. The company did not think generic versions of Treakisym® liquid formulations would be marketed in Japan.

However, the situation changed with the commercialization of generic Treakisym by Towa Pharmaceutical in June 2022, followed by Pfizer Japan in December 2022. SymBio filed patent infringement lawsuits against both companies in December 2022, but the two companies have continued sales of the generics.

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

- Rigosertib (injection and oral): SymBio announced in August 2020 that the primary endpoints were not met in the joint global Phase III clinical trials (INSPIRE study), and no further progress has been disclosed.

FY12/24 status

For rigosertib and Treakisym®, the company is searching for new indications as well as new applications for the drugs used in combination with each other or with other existing drugs, through joint research and the offering of academia-industry collaborative courses with the University of Tokyo. In April 2024, the drug's licensor Onconova changed its name to Traws Pharma Inc., headquartered in Pennsylvania, US.

Discontinuation of development program (announced in May 2025)

In April 2025, the company terminated its licensing agreement for rigosertib, originally in-licensed from Onconova (now Traws Pharma), and officially discontinued the project.

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

In July 2011 SymBio bought exclusive rights to develop and sell the intravenous (IV) and oral forms of rigosertib in Japan and Korea following completion of Onconova's Phase II US clinical trial for the IV form (upfront payment of JPY800mn, Shared Research estimate).

In September 2012, Baxter International Inc. acquired exclusive rights to develop and sell rigosertib in Europe. It paid an upfront payment of USD50mn, for a total licensing fee including milestone payments of USD565mn.

Development history of rigosertib

Licensor Onconova conducted joint global Phase III clinical trials in over 20 countries starting in August 2015 for the intravenous form of rigosertib in higher-risk MDS patients who had failed to respond to or relapsed after therapy with hypomethylating agents (HMAs). In the Japanese market, the company conducted joint global Phase III clinical trials starting in December 2015. As a result, in August 2020, Onconova announced that the global Phase III trial of rigosertib (IV) failed to meet its primary endpoints. Onconova is performing additional analysis of the results. The company commented that it is looking to apply the knowledge gleaned from additional analysis of the study to rigosertib development going forward.

Onconova completed Phase I/II clinical trials in the US for the oral form of rigosertib as first-line treatment for higher-risk MDS (in combination with azacitidine), which demonstrated safety and efficacy of the combination therapy. SymBio restarted Phase I clinical trials of the oral formulation of rigosertib monotherapy in Japan in June 2017 and completed patient enrollment in June 2019, to verify the tolerability and safety of the study drug in Japanese patients.

Exploring new indications

In January 2021, the company entered into a joint research agreement with the Institute of Medical Science, the University of Tokyo (IMSUT) to explore potential new indications for bendamustine and rigosertib.

Under this agreement, SymBio will undertake joint research with Professor Toshio Kitamura, from the Division of Cellular Therapy within IMSUT's Advanced Clinical Research Center, using bendamustine and rigosertib in combination or with other approved drugs to explore efficacy and new indications. The joint research will analyze the epigenetic control of various tumor cells to explore as-yet-unknown pharmacological effects of bendamustine and rigosertib, analyzing their effects when used in combination and with other approved drugs.

Professor Kitamura is an accomplished researcher and has a large network of researchers and physicians in the areas of hematopoietic stem cell differentiation and hematopoietic tumors such as leukemia.

He is also studying molecular mechanisms in the development of hematopoietic tumors caused by epigenetic abnormalities, looking to develop novel therapies using hematopoietic tumor models. SymBio will leverage its experience in winning early approval for proprietary anticancer drugs in collaborating with IMSUT to search for new indications for bendamustine and rigosertib.

Earnings structure

(JPYmn)	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
Sales	1,933	2,368	3,444	3,836	2,838	2,987	8,257	10,008	5,590	2,453
YoY	-1.1%	22.5%	45.4%	11.4%	-26.0%	5.3%	176.4%	21.2%	-44.1%	-56.1%
Product sales	1,933	2,137	3,444	3,810	2,811	2,977	8,257	10,008	5,590	2,453
YoY	-0.3%	10.6%	61.1%	10.6%	-26.2%	5.9%	177.4%	21.2%	-44.1%	-56.1%
Treakisym sales (NHI price basis; reference)	4,760	4,720	7,600	8,500	-	-	-	-	-	-
Product sales/Sales (NHI price basis)	40.6%	45.3%	45.3%	44.8%	-	-	-	-	-	-
Royalty revenue	-	231	-	26	26	10	-	-	-	-
Sales to Eisai	1,852	2,265	3,382	3,648	2,831	2,546	-	-	-	-
YoY	-2.9%	22.3%	49.4%	7.9%	-22.4%	-10.1%	-	-	-	-
Sales to other partners	81	104	62	187	6	441	8,257	10,008	5,590	2,453
CoGS	1,350	1,464	2,413	2,663	1,973	2,120	2,452	2,408	1,179	580
COGS / Product sales	69.8%	68.5%	70.1%	69.9%	70.2%	71.2%	29.7%	24.1%	21.1%	23.6%
Cost ratio (CoGS/Sales [NHI price basis])	28.4%	31.0%	31.7%	31.3%	-	-	-	-	-	-
Product procurement	1,242	1,606	2,589	2,969	1,684	3,163	2,145			
Gross profit	583	904	1,031	1,173	865	867	5,800	7,600	4,411	1,873
Product gross profit	583	673	1,031	1,147	838	857	5,800	7,600	4,411	1,873
Gross profit margin	30.2%	31.5%	29.9%	30.1%	29.8%	28.8%	70.2%	75.9%	78.9%	76.4%
Royalty revenue	-	231	-	26	26	10	-	-	-	-
SG&A expenses	3,135	3,031	4,978	3,829	5,166	5,373	4,784	5,636	5,223	5,750
Personnel expenses	488	541	554	504	506	530	574	-	-	-
R&D expenses	2,035	1,667	3,018	1,833	2,442	2,267	1,736	2,555	2,638	3,379
Other	612	823	1,406	1,492	2,219	2,576	2,474	-	-	-
Operating profit	-2,552	-2,127	-3,947	-2,656	-4,302	-4,506	1,016	1,964	-812	-3,877

Source: Shared Research based on company data

*SymBio Pharma USA, Inc was consolidated from FY12/22 in line with the start of operation. Note that FY12/22 results are consolidated figures and the year-on-year changes are for reference.

Sales

The company's sales are made up of product sales and royalty revenue. Per the above table, most of the sales through FY12/19 have originated from Eisai. The company began own sales of Treakisym® from December 10, 2020 and recorded

sales to non-Eisai partners (i.e., wholesalers) of JPY441mn in FY12/20. From FY12/21, all sales were to non-Eisai partners.

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 anticancer agent in December 2010. Through FY12/16, the company booked sales of Treakisym® indicated for relapsed or refractory low-grade NHL and MCL.

In FY12/17, the company booked sales of additional indications of untreated low-grade NHL and MCL, resulting in sales growth YoY.

FY12/19 product sales declined YoY. A lyophilized injection formulation of Treakisym® imported from Astellas Deutschland GmbH, a consolidated subsidiary of Astellas Pharma, was found to contain impurities and appearance defects, and as a result, shipments of Treakisym® 100mg to Japan distributor Eisai were postponed. Consequently, booking of some product sales was delayed until the following fiscal year, resulting in a YoY decline in sales.

Sales increased YoY in FY12/21, largely due to the transfer of sales from Eisai to the company's own sales force. The business alliance agreement with Eisai for Treakisym® expired on December 9, 2020, and SymBio began independently marketing Treakisym® in Japan on December 10. This enabled the company to earn not only its previous gross profit (sales to Eisai minus cost of sales), but also the gross profit earned by Eisai through December 9, 2020 (the difference between the shipment price from Eisai to pharmaceutical wholesalers and the price Eisai paid SymBio to supply Treakisym®).

Since FY12/23, Treakisym®'s sales have declined sharply as generics have taken over the market.

Royalty revenue

Royalty revenue includes one-time contract payments and milestone payments.

CoGS

CoGS refers to procurement costs for drugs. SymBio purchases lyophilized Treakisym® from Astellas Deutschland GmbH. Before December 2019, Astellas supplied Treakisym® to the company for about 70% of SymBio's wholesale price to Eisai. As noted above, the company began own sales of Treakisym® on December 10, 2020. This allowed the company to receive not only the gross profit it received previously, but also the gross profit earned by Eisai through December 9, 2020 (i.e., the difference between the shipment price from Eisai to pharmaceutical wholesalers and the price Eisai paid the company to source the product), boosting GPM.

SymBio sources the liquid (RTD and RI) formulations of Treakisym® from US company Eagle Pharmaceuticals. According to the company, its GPM on the liquid formulations is higher than for lyophilized Treakisym®.

SG&A expenses

Personnel and R&D are the main SG&A expenses.

Personnel expenses

Personnel expenses consist of directors' remuneration as well as expenses for personnel involved in such tasks as marketing, searching for in-licensing candidates and general administration. Personnel expenses have been trending upward in line with additions to the pipeline and business expansion. However, following the launch of generic versions of Treakisym® by two companies in 2022—despite the company's warnings about patent infringement—personnel expenses have declined since FY12/22.

R&D expenses

R&D expenses include personnel expenses for R&D staff as well as clinical trial outsourcing expenses and upfront payments accompanying product in-licensing. 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.

Eisai paid half of the development costs for the Treakisym® freeze-dried (FD) formulation in Japan.

As of FY12/24, the company's pipeline under development consists of the antiviral drug brincidofovir (BCV). With all planned development for Treakisym® completed, the company has reallocated its development resources to BCV, which has potential as a treatment for various diseases.

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.

Strong share in niche markets: SymBio focuses on niche markets for rare oncologic, hematologic, and multiviral infectious diseases and rare 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

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.

Dependence on a single product: As of FY12/24, Treakisym® accounted for all product sales of the company. SymBio is a biotech startup whose strength lies in having brought a pharmaceutical product to market, but its dependence on a single product raises the risk of earnings volatility. Sales and gross profit declined in FY12/19 and FY12/20 due to contamination and irregular appearance of lyophilized Treakisym® imported from Astellas Deutschland GmbH, which led to a temporary slump in product sales. Since FY12/23, the company has posted an operating loss due to penetration of generics and other factors.

Market overview

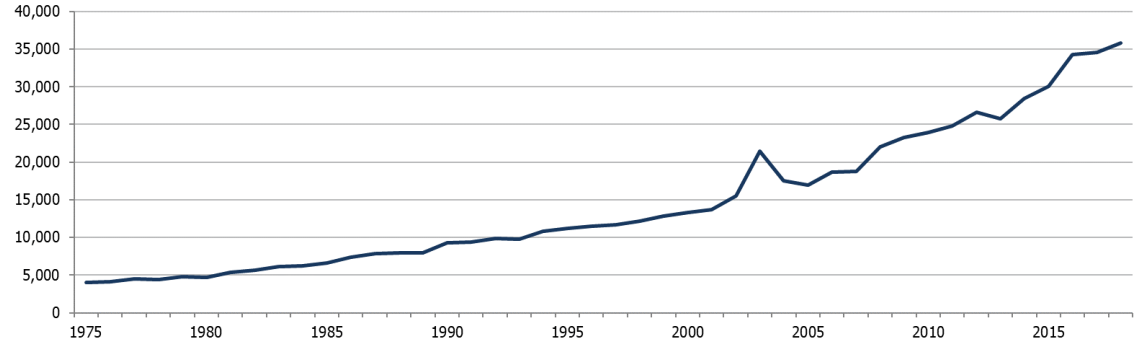
Lymphatic cancer: patient population, market size, treatment drugs

Morbidity of lymphatic cancer

In 2018, the number of people diagnosed with lymphatic cancer in Japan was 35,782 (+3.5% YoY; average annual increase in past 10 years is 4.9%), according to "Cancer statistics and cancer registration in Japan" complied by the Center for Cancer Control and Information Services. Of these, 29,156 (+4.6% YoY), or 81.5% (80.7% in the previous year), were 60 years or older.

Of the 980,856 (+0.4% YoY) people diagnosed with cancer, those diagnosed with lymphatic cancer accounted for only 3.6% (3.5% in the previous year), but their number increased 62.1% between 2008 and 2018, versus a 30.8% increase in the number of people newly diagnosed with cancer.

Morbidity of lymphatic malignancy



	1,975	1,980	1,985	1,990	1,995	2,000	2,005	2,010	2,015
Number of patients	4,013	4,741	6,635	9,297	11,195	13,307	16,991	23,919	30,103
Incidence rate (per 100,000)	3.6	4.1	5.5	7.5	8.9	10.5	13.3	18.7	23.7

Source: Shared Research based on data from Center for Cancer Control and Information Services, National Cancer Center

Treakisym® market potential and patient population

The company estimates that the number of patients being treated for relapsed or refractory low-grade NHL and MCL in Japan is 9,336 and the number of patients with untreated low-grade NHL and MCL is 6,967. On an NHI drug reimbursement price basis, Treakisym® sales reached JPY8.5bn in FY12/18 (JPY7.6bn in FY12/17).

The company estimates that the number of Japanese patients with relapsed or refractory DLBCL is 18,672.

Treakisym® indications and number of patients

Indications	Patients	Progress	Notes
Relapsed or refractory low-grade NHL and relapsed or refractory MCL	9,336	Approved	Sales: JPY8.5bn (FY12/18)
Untreated low-grade NHL, and untreated MCL	6,967	Approved	
CLL	656	Approved	
Relapsed or refractory NHL	18,672	Clinical trials underway	

Drugs competing with Treakisym®

Drugs that compete with Treakisym® include rituximab and ibritumomab tiuxetan. SymBio has successfully pursued a development policy aimed at demonstrating that the co-administration of Treakisym® improves the efficacy of these drugs.

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.

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 Toyama Chemical Co., Ltd., a subsidiary of Fujifilm Holdings Corporation (TSE Prime: 4901).

Patient population, treatment drugs for MDS

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 efficacious treatment available.

Rigosertib indications and number of patients

Condition	Number of patients
Low-risk MDS	7,800
High-risk MDS	3,200

Source: Shared Research based on company data

Historical performance

Q1 FY12/25 results (out May 8, 2025)

- Sales: JPY264mn (-55.8% YoY)
- Operating loss: JPY1.2bn (versus loss of JPY807mn in Q1 FY12/24)
- Recurring loss: JPY1.3bn (versus loss of JPY727mn in Q1 FY12/24)
- Net loss attributable to owners of the parent: JPY1.3bn (versus loss of JPY777mn in Q1 FY12/24)

Sales of the ready-to-dilute (RTD) intravenous formulation of Treakisym® 100mg/4ml, launched in January 2021, were sluggish in Q1. This was due to inventory stocktaking by wholesalers, inventory adjustments by medical institutions ahead of the April 2025 drug price revision, and prior clearing of wholesaler inventories. The company expects sales to continue declining as the shift to generics gradually progresses.

- As of February 2025, the company estimates approximately 70% of the market for Treakisym® ready-to-dilute (RTD) liquid formulation has been eroded by generics.

- Since NHI excluded Treakisym® RTD formulation from the list of drugs eligible for the premium for newly discovered drugs in its April 2024 price revisions, the drug price was reduced by 18.6%. In the interim drug price revision of April 2025, no special price reduction was applied, and the price was lowered by 4.7%.

The company noted the market entry of new therapies has had only a limited impact on sales and remains within expectations. Meanwhile, it expects the current reluctance to prescribe bendamustine*—due to concerns over prolonged or severe COVID-19 infections during or after treatment—to gradually ease. (*Includes both Treakisym and its generics.)

- As of February 2025, the company has reached a settlement in the patent infringement lawsuits with Pfizer Japan Inc. and Towa Pharmaceutical Co., Ltd. (For details, please refer to the Highlights section below).

Sales dropped 55.8% YoY to JPY264mn, reflecting the impact of generic competition and inventory adjustments ahead of the drug price revision. Gross profit declined 57.0% YoY to JPY202mn, with a gross margin of 76.7%, down 2.1pp YoY. SG&A expenses rose 7.3% YoY to JPY1.4bn, including R&D expenses of JPY819mn, up 18.5% YoY. As a result, the company posted an operating loss of JPY1.2bn (versus a loss of JPY807mn in Q1 FY12/24).

Q1 progress against full-year company forecast for FY12/25

Q1 progress against the full-year company forecast for FY12/25 stood at 14.2% for sales. Progress rates for profit metrics are not provided due to negative figures. The company posted an operating loss of JPY1.2bn (full-year forecast: loss of JPY4.3bn), a recurring loss of JPY1.3bn (forecast: loss of JPY4.3bn), and a net loss attributable to owners of the parent of JPY1.3bn (forecast: loss of JPY4.5bn).

As of end-Q1 FY12/25, the company has maintained its initial full-year forecast.

Business progress

The following is an overview of progress in key businesses since January 2025.

- In May 2025, the company announced the confirmation of the efficacy of brincidofovir (BCV) for malignant brain tumors and the identification of biomarker genes (predictive factors of efficacy).

- In March 2025, Dr. Edwin Rock, who has experience as a Medical Officer at the FDA, was appointed Senior Vice President (Head of R&D) at the company's US subsidiary SPU.

- In February 2025, the company expanded its global phase Ib/II clinical trial of BCV in patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma, to Singapore.

- In January 2025, the company appointed Mr. Masaru Taguchi as CEO and President of its wholly owned subsidiary SymBio Pharma USA, Inc. (SPU).

R&D activities

Key developments in Q1 included the launch of an international Phase Ib clinical trial for malignant lymphoma patients in Singapore and Hong Kong, following Japan. This marks the first oncology trial for BCV. Patient enrollment for the cytomegalovirus (CMV) infection program also progressed steadily.

Antiviral drug SyB V-1901 (generic name: brincidofovir)

In development of the intravenous and oral formulations of the antiviral drug brincidofovir (SyB V-1901; BCV IV and BCV Oral), the company is conducting joint research with top research institutions specialized in each field in Japan and overseas in light of the broad spectrum of the drug's effectiveness against dsDNA virus infections. It will consider conducting additional global clinical trials based on the scientific findings of the research.

Earlier clinical trials in the US and Europe conducted by US-based Chimerix Inc. have demonstrated that BCV Oral has broad-spectrum antiviral effects against a variety of dsDNA viruses. BCV IV is expected to be effective and safe for the prevention and treatment of many dsDNA virus infections, including adenovirus (AdV) infections after hematopoietic stem cell transplantation. In June 2021, Chimerix announced that the US FDA had granted BCV Oral approval for the treatment of smallpox.

Post-transplant infectious diseases

BCV clinical development: disseminated AdV infections following hematopoietic stem cell transplantation

Based on a global advisory board review held in February 2020, the company has decided to prioritize the global development of BCV IV primarily in Japan, the US, and Europe, targeting disseminated AdV infections occurring after hematopoietic stem cell transplantation, a niche area with a high unmet medical need. In March 2021, the company filed an IND application with the US Food and Drug Administration (FDA) to conduct a Phase II clinical trial primarily in pediatric patients suffering from AdV infections (also including adults). This development program was granted fast-track designation by the FDA in April 2021, and the investigational drug was administered to the first patient in August 2021. In May 2023, BCV has demonstrated proof of concept in humans in the same study, and the Phase IIa clinical study was completed in the first half of 2024. The company is currently in discussions with regulatory authorities in relevant countries to initiate a global Phase III trial, while also building the framework for conducting the international joint study. In addition, a use patent for BCV related to the treatment of AdV infections and infectious diseases was established and registered in Japan in January 2024.

✓ The Data Safety Monitoring Board (DSMB) and the FDA confirmed the POC in terms of both safety and efficacy. While the POC has been confirmed in trials up to cohort 3.
✓ For cohorts 1 to 3, BCV was administered twice weekly, at doses of 0.2mg/kg for cohort 1, 0.3mg/kg for cohort 2, and 0.4mg/kg for cohort 3. In cohort 3 (0.4mg/kg, twice weekly via IV), the disappearance of AdV in the blood was confirmed in 100% of patients (n=10). Of these, 90% of patients (n=9) achieved viral clearance within four weeks of treatment.

BCV clinical development for cytomegalovirus (CMV) infections following hematopoietic stem cell transplantation

In May 2024, a Phase IIa clinical trial post-hematopoietic stem cell cytomegalovirus (CMV) infection was initiated in the US. In June 2024, the first patient was enrolled, and the trial is currently ongoing. As of end-April 2025, a total of 19 patients had been enrolled.

- The larger patient population for CMV infections compared to adenovirus (AdV) infections has contributed to steady patient enrollment in the trial.

- The competitor drug maribarivir (brand name: LIVTENCITY) from Takeda Pharmaceutical generated sales of JPY33.0bn in FY03/25 (versus JPY19.1bn in FY03/24). The number of transplant recipients treated for CMV is exceptionally high for a rare disease (25,000, of which 10,000 are resistant or refractory). One reason megapharma Takeda decided to develop the competitor drug maribarivir independently was likely its large potential patient base, which made it appear more lucrative. The company noted the large patient base made patient enrollment for clinical trials much easier.

BCV clinical development: BK virus infection following kidney transplantation

The development of a treatment for BK virus infection following kidney transplantation is currently under protocol revision. In August 2022, the first patient was dosed (FPD) in an international Phase II clinical trial in Australia; however, patient enrollment has been slower than anticipated.

BCV non-clinical study: polyomavirus infection

Polyomaviruses, particularly JC virus (JCV), are known to cause severe brain diseases among dsDNA viruses, and the development of effective treatments is highly anticipated. In November 2022, the company concluded a material transfer agreement (MTA) with US-based Penn State College of Medicine, and initiated a non-clinical study evaluating the efficacy of BCV in a mouse model of polyomavirus infection. In July 2024, the first report of these research findings, which included new insights, was published in the journal mBio.

Hematological malignancies

BCV non-clinical joint research: applications for hematological malignancies/oncology

In addition to its antiviral activity, brincidofovir has shown antitumor effects. The company is exploring new indications in hematologic and solid tumors through joint research with institutions in various countries. Target areas include EB virus-positive lymphoma and refractory brain tumors. In March 2022, the company commenced joint research with Brown University of the US to investigate the antitumor effects of brincidofovir on glioblastoma (GBM) caused by cytomegalovirus (CMV) infection.

The company is conducting joint research with the National Cancer Centre Singapore to investigate the antitumor effects and mechanisms of BCV against EB virus-positive lymphoma. Between 2022 and 2024, the results of this collaboration were presented at international conferences in the US and Europe on five occasions. These included findings on BCV's efficacy in NK/T-cell lymphoma, B-cell lymphoma, and peripheral T-cell lymphoma (PTCL), as well as research on biomarkers that may predict BCV's antitumor activity.

- Since BCV does not exhibit bone marrow suppression as a side effect, the company expects it can selectively target and destroy cancer cells without affecting normal cells.

Clinical development of BCV (application in hematologic malignancies and oncology)

In August 2024, the company initiated an international Phase Ib clinical trial of BCV targeting patients with malignant lymphoma as a First in Human (FIH) trial in the oncology field in Japan. The trial is now also underway in Singapore and Hong Kong. Through this trial, it aims to establish human proof of concept (POC) for BCV in cancer treatment.

- This trial is the third clinical trial of BCV, following those for AdV and CMV infections, and it is the first BCV trial in the oncology field.
- In February 2025, the company expanded its global phase Ib/II clinical trial of BCV in patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma, to Singapore.
- In May 2025, the company announced the confirmation of the efficacy of brincidofovir (BCV) for malignant brain tumors and the identification of biomarker genes (predictive factors of efficacy).

Other areas (neurodegenerative diseases)

BCV non-clinical studies: EB virus, multiple sclerosis, lymphoproliferative disorders

SymBio has been preparing for clinical development of brincidofovir for multiple sclerosis, a rare disease related to EB virus. In August 2022, the company signed a collaboration agreement for the transfer of human materials with the National Institute of Neurological Disorders and Stroke (NINDS) of the US National Institute of Health (NIH). In March 2023, SymBio signed a cooperative research and development agreement (CRADA) with NINDS to obtain information necessary to conduct future clinical trials. In October 2023, the results of the research were presented at the 9th Joint ECTRIMS-ACTRIMS Meeting in Milan, Italy. Currently, the company is conducting trials using marmosets (non-human primates) as part of this joint research.

CRADA: Refers to a contract on collaborative R&D between a US government organization and entities such as a private-sector company. The private-sector company may be able to obtain licensing of patent rights regarding inventions developed under the CRADA. Because a company may receive patent rights from a project using government funds, the barriers to being selected for a CRADA are significant (SymBio is the second Japanese company to be selected).

In April 2023, SymBio also signed a CRADA with the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, to evaluate the efficacy of BCV in EB virus-related lymphoproliferative disorders.

BCV non-clinical joint research: herpes simplex virus, Alzheimer's type dementia

In December 2022, the company concluded a sponsored research agreement with US-based Tufts University, and began a joint research study evaluating the efficacy of BCV in a herpes simplex virus infection model. This study aims to explore BCV's potential to treat neurological diseases, including Alzheimer's disease.

Rights

In September 2022, Chimerix announced that it had completed procedures to transfer the rights to brincidofovir to Emergent BioSolutions Inc. (headquarters: Maryland, US). The agreement, however, has no impact on the company's exclusive rights to develop, manufacture, and sell brincidofovir globally for all indications except orthopoxvirus diseases including smallpox and Mpox.

Orphan drug designation for BCV

In March 2024, the EU orphan drug designation for BCV, for the prevention of adenovirus and cytomegalovirus infections in immunocompromised patients, was transferred from Emergent BioSolutions to a subsidiary of SymBio.

BCV's use patent and IP strategy ("pipeline within a molecule")

At the earnings presentation for 1H FY12/24, the company discussed the grant of a use patent for BCV and its future intellectual property (IP) strategy.

- In May 2023, BCV demonstrated a proof of concept (POC) in human patients, and based on this data, the company filed for a use patent.
- The use patent for BCV in the treatment of AdV infections was filed for accelerated review in September 2023. The patent was granted in January 2024 and will be valid until 2043.
- SymBio aims to maximize the business value of BCV by examining the efficacy of the drug in dsDNA virus infections, expanding target indications to include multiviral infections, and striving to meet the underserved medical needs for treatments of viral diseases and accompanying complications.
- The company is advancing its IP strategy for BCV under the concept of "pipeline within a molecule," considering BCV as a compound that can be commercialized as a treatment for many diseases.

SymBio aims for approval and commercialization of two or three indications for BCV by 2030. The indication with the highest potential for approval is viral infection following hematopoietic stem cell and kidney transplantation, two areas of clinical development prioritization.

Anticancer agent SyB L-0501 (FD formulation)/SyB L-1701 (RTD formulation)/SyB L-1702 (RI administration); generic name: bendamustine hydrochloride or bendamustine hydrochloride hydrate, product name: Treakisym®

The company has actively conducted joint research on Treakisym® with institutions such as the University of Tokyo and Kyoto University, but it has since shifted part of its research resources toward BCV.

Anticancer agent SyB L-1101 (IV)/SyB C-1101 (oral); generic name: rigosertib sodium

In April 2025, the company terminated its licensing agreement for rigosertib, originally in-licensed from Onconova (now Traws Pharma), and officially discontinued the project.

Overseas business (SymBio Pharma USA)

In January 2025, the company appointed Mr. Masaru Taguchi as CEO and President of its wholly-owned subsidiary SymBio Pharma USA, Inc. (SPU). In April 2025, Mr. Taguchi also assumed the role of Executive Vice President and COO of the parent company, while continuing to serve as CEO and President of SPU. SPU will serve as a strategic hub to drive the global business for the antiviral drug BCV, accelerating its development across the US, Europe, Japan, and the UK.

- In March 2025, Dr. Edwin Rock, who has experience as a Medical Officer at the FDA, was appointed Senior Vice President (Head of R&D) at the company's US subsidiary SPU. The company has high expectations for his role in leading negotiations with the FDA, including pre-IND meetings.

In-licensing of drug candidates

The company is currently focusing on unrolling global development plans for the antiviral drug BCV it in-licensed in September 2019, but also constantly looking into multiple licensing deals and looking for and evaluating promising new in-licensing drug candidates. Through the introduction of external products, it aims to create medium- to long-term business value.

Highlights

SymBio identifies potential biomarker genes for predicting effectiveness for malignant brain tumors

In May 2025, SymBio announced the confirmation of the efficacy of brincidofovir (BCV) for malignant brain tumors and the identification of biomarker genes (predictive factors of efficacy). The company views the identification of biomarker genes (predictive factors of efficacy) as a key milestone, recognizing that it could significantly increase the likelihood of success in clinical trials. While malignant brain tumors are typically difficult to treat, the biomarker may help narrow down the responder population—patients likely to benefit from BCV treatment.

Key business development goals for FY12/25

At its FY12/24 full-year earnings briefing in February 2025, SymBio outlined the following key business development goals for FY12/25. Among these, the highest priority is the initiation of the Phase 3 trial for post-transplant adenovirus (AdV) infection.

- Q4 target: Initiate a Phase III trial for post-transplant adenovirus (AdV) infection
- Q3 target: Establish proof of concept (POC) in the Phase II trial for post-transplant cytomegalovirus (CMV) infection
  - The company noted that patient enrollment for the second dosage level has been completed as CMV has a relatively large patient population.
- Q4 target: Establish POC in the Phase Ib trial for NK/T-cell lymphoma
  - Given the rarity of the disease, the company believes that in Japan, it can seek regulatory approval after completing a Phase II trial, following the completion of the Phase Ib trial
- Q4 target: Begin reviews toward commencing a Phase Ib trial for glioblastoma (GBM)
- Q4 target: If animal POC for multiple sclerosis is confirmed (expected in Q2), initiate discussions with the NIH on the clinical trial design for a first-in-human (FIH) study
- Q4 target: Finalize a global partnership for BCV. (The company aims to collaborate with a developer of immune checkpoint inhibitors (ICIs), as it envisions BCV's use in combination with ICIs.)
- Q3 target: Work to in-license new products for the domestic market

Full-year FY12/24 results (out February 6, 2025)

- Sales: JPY2.5bn (-56.1% YoY)

- Operating loss: JPY3.9bn (versus loss of JPY812mn in FY12/23)
- Recurring loss: JPY3.7bn (versus loss of JPY736mn in FY12/23)
- Net loss attributable to owners of the parent: JPY3.8bn (versus loss of JPY2.0bn in FY12/23)

In February 2022, SymBio obtained approval for a partial change to the marketing authorization for the ready-to-dilute (RTD) intravenous formulation of Treakisym® 100mg/4ml, which was launched in January 2021, to add rapid infusion (RI) administration. Compared to the freeze-dried (FD) formulation, the RTD formulation reduces the time required for the complicated dissolution process.

- As of February 2025, the company has reached a settlement in the patent infringement lawsuits with Pfizer Japan Inc. and Towa Pharmaceutical Co., Ltd., but the two companies have continued selling generic versions of the product.

Sales decreased by 56.1% YoY to JPY2.5bn. The penetration of generics has gradually progressed, affecting the results. Concerns over the increased risk of infection for patients with blood cancers, especially those with malignant lymphoma, and the potential for prolonged or severe infections during or after treatment with bendamustine have led to decreased prescriptions of bendamustine, including its generics. The spread of COVID-19 and influenza also had a significant impact on prescription volume declines, particularly in 2H FY12/24.

- According to the company's estimates, approximately 70% of the market for Treakisym® ready-to-dilute (RTD) liquid formulation has been eroded by generics.

- Since NHI excluded Treakisym® RTD formulation from the list of drugs eligible for the premium for newly discovered drugs in its April 2024 price revisions, the drug price was reduced by 18.6%. In the interim drug price revision scheduled for April 2025, no special price reduction is expected, and the price adjustment is likely to follow the standard revision rate.

Gross profit was JPY1.9bn (-57.5% YoY), and the gross profit margin reached 76.4% (-2.5pp YoY). SG&A expenses were JPY5.8bn (+10.1% YoY), of which R&D expenses amounted to JPY3.4bn (+28.1% YoY). As a result, the operating loss was JPY3.9bn (compared to a loss of JPY812mn in FY12/23).

Achievement rates against full-year company forecast for FY12/24

In May 2024, the company announced a downward revision of its full-year earnings forecast for FY12/24 (see "Full-year company forecast" below for details). The achievement rate for FY12/24 against the revised full-year forecast (May 2024 revision) was 93.5% for sales, while there is no progress rate for profit items due to negative figures. The operating loss was JPY3.9bn (full-year forecast: JPY3.7bn loss), the recurring loss was JPY3.7bn (full-year forecast: JPY3.5bn loss), and the net loss attributable to owners of the parent was JPY3.8bn (full-year forecast: JPY3.6bn loss).

In Q4, while the spread of COVID-19 and influenza had a negative impact on earnings, the company believes that, apart from these factors, performance was generally in line with the revised company forecast.

Business progress

Progress in the company's key businesses through February 2025 was as follows.

- In February 2025, the company expanded its global phase Ib/II clinical trial of BCV in patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma, to Singapore.

- In January 2025, the company appointed Mr. Masaru Taguchi as CEO and President of its wholly owned subsidiary SymBio Pharma USA, Inc. (SPU).

- In December 2024, the company resolved to enter into an agreement with Cantor Fitzgerald Europe to establish a bond issuance program with stock acquisition rights and to issue the 4th unsecured convertible bonds with stock acquisition rights through a third-party allotment.

- In December 2024, the company gave a presentation on the combination therapy of BCV and immune checkpoint inhibitors for malignant lymphoma at the 66th Annual Meeting of the American Society of Hematology.

- In November 2024, the company appointed a new Executive Vice President and Global Chief Medical Officer (CMO), who also assumed the role of Senior Vice President at its US subsidiary, SymBio Pharma USA (SPU).

- In October 2024, at ID Week 2024 (Infectious Diseases Society of America Annual Meeting), additional data from the Phase IIa clinical trial of BCV for adenovirus (AdV) infections was presented, highlighting the correlation between AdV clearance from the bloodstream and improvements in clinical symptoms.
- In September 2024, the company settled a patent infringement lawsuit it had filed against Towa Pharmaceutical Co., Ltd. (For details, please refer to the Highlights section below).
- In August 2024, the company initiated an international Phase Ib/II clinical trial of BCV targeting patients with relapsed or refractory lymphoma (malignant lymphomas such as NK/T-cell lymphoma) in Japan.
- In July 2024, the company announced that BCV has inhibited the production of infectious polyomaviruses. The US-based Penn State College of Medicine evaluated the efficacy of BCV in a mouse model of polyomavirus infection and published the results in a scientific journal.
- In June 2024, the anti-tumor effects of BCV on peripheral T-cell lymphoma (PTCL) have been confirmed through a mouse model, and the research findings were presented at the 29th European Hematology Association (EHA2024 Hybrid Congress).
- In June 2024, the company has completed the enrollment of the first patient (FPI) for the Phase IIa clinical trial of BCV targeting CMV infection following hematopoietic stem cell transplantation.
- In May 2024, SymBio initiated a Phase IIa clinical trial of BCV for CMV infection after hematopoietic stem cell transplantation. CMV infection is the second indication for BCV after adenovirus (AdV) infection.
- In April 2024, Onconova, rigosertib's licensor (originator), established a new company, Traws Pharma, Inc., through a business merger.
- In April 2024, the CEO and president of the US subsidiary (Symbio Pharma USA, Inc.) was changed from Mr. Stephane Berthier to Mr. John Houghton.
- In April 2024, the anti-tumor effects of BCV for B-cell lymphoma found through joint research between Symbio and the National Cancer Centre Singapore (NCCS) were presented at the American Association for Cancer Research (AACR) Annual Meeting 2024.
- In March 2024, BCV received an orphan drug (a drug for treating rare diseases) designation in the EU.
- In February 2024, an abstract demonstrating the anti-adenovirus (AdV) effects of brincidofovir (BCV) was selected for an oral session at the Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT).
- In February 2024, BCV was selected as a presentation topic for the Pediatric Best Abstracts session at the 2024 Tandem Meetings in the US. The presentation introduced new findings on BCV's effectiveness against AdV in stool samples.
- In January 2024, SymBio obtained a patent in Japan covering the use of BCV injection as a treatment for AdV infections.

R&D activities

A key milestone in FY12/24 was the initiation of an international Phase Ib clinical trial in August 2024, targeting patients with malignant lymphoma. This marks the first clinical trial for BCV in the oncology field (in the post-transplant infection field, the first patient was dosed in August 2021).

Antiviral drug SyB V-1901 (generic name: brincidofovir [BCV])

In development of the intravenous and oral formulations of the antiviral drug brincidofovir (SyB V-1901; BCV IV and BCV Oral), the company is conducting joint research with top research institutions specialized in each field in Japan and overseas in light of the broad spectrum of the drug's effectiveness against dsDNA virus infections. It will consider conducting additional global clinical trials based on the scientific findings of the research.

Earlier clinical trials in the US and Europe conducted by US-based Chimerix Inc. have demonstrated that BCV Oral has broad-spectrum antiviral effects against a variety of dsDNA viruses. BCV IV is expected to be effective and safe for the prevention and treatment of many dsDNA virus infections, including adenovirus (AdV) infections after hematopoietic stem

cell transplantation. In June 2021, Chimerix announced that the US FDA had granted BCV Oral approval for the treatment of smallpox.

Post-transplant infectious diseases

BCV clinical development: disseminated AdV infections following hematopoietic stem cell transplantation

Based on a global advisory board review held in February 2020, the company has decided to prioritize the global development of BCV IV primarily in Japan, the US, and Europe, targeting disseminated AdV infections occurring after hematopoietic stem cell transplantation, a niche area with a high unmet medical need. In March 2021, the company filed an IND application with the US Food and Drug Administration (FDA) to conduct a Phase II clinical trial primarily in pediatric patients suffering from AdV infections (also including adults). This development program was granted fast-track designation by the FDA in April 2021, and the investigational drug was administered to the first patient in August 2021. In May 2023, BCV has demonstrated proof of concept in humans in the same study. Positive data demonstrating efficacy from the study were presented orally at the 65th Annual Meeting of the American Society of Hematology in December 2023. Similar presentations were made at other major academic conferences, including the 2024 Tandem Meetings in the US in February 2024, the 50th Annual Meeting of the EBMT in April 2024, and ID Week 2024 (Infectious Diseases Society of America). In addition, a use patent for BCV related to the treatment of AdV infections and infectious diseases was established and registered in Japan in January 2024.

✓ The Data Safety Monitoring Board (DSMB) and the FDA confirmed the POC in terms of both safety and efficacy. While the POC has been confirmed in trials up to cohort 3.
✓ For cohorts 1 to 3, BCV was administered twice weekly, at doses of 0.2mg/kg for cohort 1, 0.3mg/kg for cohort 2, and 0.4mg/kg for cohort 3. In cohort 3 (0.4mg/kg, twice weekly via IV), the disappearance of AdV in the blood was confirmed in 100% of patients (n=10). Of these, 90% of patients (n=9) achieved viral clearance within four weeks of treatment.

BCV clinical development for cytomegalovirus (CMV) infections following hematopoietic stem cell transplantation

In May 2024, a Phase IIa clinical trial post-hematopoietic stem cell cytomegalovirus infection was initiated in the US. In June 2024, the first patient was enrolled, and the trial is currently ongoing.

- The larger patient population for CMV infections compared to adenovirus (AdV) infections has contributed to steady patient enrollment in the trial.

- The competitor drug maribarivir (brand name: LIVTENCITY) from Takeda Pharmaceutical generated sales of JPY19.1bn in FY03/24. The number of transplant recipients treated for CMV is exceptionally high for a rare disease (25,000, of which 10,000 are resistant or refractory). One reason megapharma Takeda decided to develop competitor maribarivir independently was likely the drug's large potential patient base, which made it appear more lucrative. The company noted the large patient base made patient enrollment for clinical trials much easier.

BCV clinical development: BK virus infection following kidney transplantation

The development of a treatment for BK virus infection following kidney transplantation is currently under protocol revision. In August 2022, the first patient was dosed (FPD) in an international Phase II clinical trial in Australia; however, patient enrollment has been slower than anticipated.

BCV non-clinical study: polyomavirus infection

Polyomaviruses, particularly JC virus (JCV), are known to cause severe brain diseases among dsDNA viruses, and the development of effective treatments is highly anticipated. In November 2022, the company concluded a material transfer agreement (MTA) with US-based Penn State College of Medicine, and initiated a non-clinical study evaluating the efficacy of BCV in a mouse model of polyomavirus infection. In July 2024, the first report of these research findings, which included new insights, was published in the journal mBio.

Hematological malignancies

BCV non-clinical joint research: applications for hematological malignancies/oncology

In addition to antiviral activity, the company expects brincidofovir to have antitumor effects. Through joint research with the National Cancer Centre Singapore and University of California San Francisco Brain Tumor Center, SymBio is investigating new indications for the drug in oncology, including rare brain tumors and EB virus-positive lymphoma. In March 2022, the company commenced joint research with Brown University of the US to investigate the antitumor effects of brincidofovir on glioblastoma (GBM) caused by cytomegalovirus (CMV) infection.

In December 2022, the results of collaborative research with the National Cancer Centre Singapore (NCCS) on the therapeutic efficacy of BCV in the treatment of rapidly progressing NK/T-cell lymphoma were presented at the 64th American Society of Hematology (ASH) Annual Meeting.

- Since BCV does not exhibit bone marrow suppression as a side effect, the company expects it can selectively target and destroy cancer cells without affecting normal cells.

At the 17th International Conference on Malignant Lymphoma (ICML) in June 2023, research into biomarkers that predict the anti-tumor effect of BCV was presented. In April 2024, the anti-tumor effects of BCV for B-cell lymphoma was presented as a poster at the American Association for Cancer Research Annual Meeting. In June 2024, the anti-tumor effects of BCV on peripheral T-cell lymphoma (PTCL) was presented as a poster at the European Hematology Association (EHA2024 Hybrid Congress).

*The use of biomarkers allows for the selection of patients who are likely to respond well to treatment, which increases the probability of successful clinical (POC) trials.

Clinical development of BCV (application in hematologic malignancies and oncology)

In August 2024, the company initiated an international Phase Ib clinical trial of BCV targeting patients with malignant lymphoma as a First in Human (FIH) trial in the oncology field. Through this trial, it aims to establish human proof of concept (POC) for BCV in cancer treatment.

- This trial is the third clinical trial of BCV, following those for AdV and CMV infections, and it is the first BCV trial in the oncology field.

- In February 2025, the company expanded its global phase Ib/II clinical trial of BCV in patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma, to Singapore.

Other

BCV non-clinical studies: EB virus, multiple sclerosis, lymphoproliferative disorders

SymBio has been preparing for clinical development of brincidofovir for multiple sclerosis, a rare disease related to EB virus. In August 2022, the company signed a collaboration agreement for the transfer of human materials with the National Institute of Neurological Disorders and Stroke (NINDS) of the US National Institute of Health (NIH). In March 2023, SymBio signed a cooperative research and development agreement (CRADA) with NINDS to obtain information necessary to conduct future clinical trials. In October 2023, the results of the research were presented at the 9th Joint ECTRIMS-ACTRIMS Meeting in Milan, Italy.

CRADA: Refers to a contract on collaborative R&D between a US government organization and entities such as a private-sector company. The private-sector company may be able to obtain licensing of patent rights regarding inventions developed under the CRADA. Because a company may receive patent rights from a project using government funds, the barriers to being selected for a CRADA are significant (SymBio is the second Japanese company to be selected).

In April 2023, SymBio also signed a CRADA with the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, to evaluate the efficacy of BCV in EB virus-related lymphoproliferative disorders.

*Refers to a wide range of diseases related to the EB virus: Cancers such as T-cell lymphoma, Burkitt lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, NK T-cell lymphoma, and post-transplant lymphoproliferative disease, X-linked lymphoproliferative syndrome, and AIDS-related lymphoproliferative disease. (Source: Materials for company's 18th ordinary general meeting of shareholders.)

BCV non-clinical joint research: herpes simplex virus, Alzheimer's type dementia

In December 2022, the company concluded a sponsored research agreement with US-based Tufts University, and began a joint research study evaluating the efficacy of BCV in a herpes simplex virus infection model. This study aims to explore BCV's potential to treat neurological diseases, including Alzheimer's disease.

Rights

In September 2022, Chimerix announced that it had completed procedures to transfer the rights to brincidofovir to Emergent BioSolutions Inc. (headquarters: Maryland, US). The agreement, however, has no impact on the company's exclusive rights to develop, manufacture, and sell brincidofovir globally for all indications except orthopoxvirus diseases including smallpox and Mpox.

Orphan drug designation for BCV

In March 2024, the EU orphan drug designation for BCV, for the prevention of adenovirus and cytomegalovirus infections in immunocompromised patients, was transferred from Emergent BioSolutions to a subsidiary of SymBio.

BCV's use patent and IP strategy ("pipeline within a molecule")

At the earnings presentation for 1H FY12/24, the company discussed the grant of a use patent for BCV and its future intellectual property (IP) strategy.

- In May 2023, BCV demonstrated a proof of concept (POC) in human patients, and based on this data, the company filed for a use patent.
- The use patent for BCV in the treatment of AdV infections was filed for accelerated review in September 2023. The patent was granted in January 2024 and will be valid until 2043.
- SymBio aims to maximize the business value of BCV by examining the efficacy of the drug in dsDNA virus infections, expanding target indications to include multiviral infections, and striving to meet the underserved medical needs for treatments of viral diseases and accompanying complications.
- The company is advancing its IP strategy for BCV under the concept of "pipeline within a molecule," considering BCV as a compound that can be commercialized as a treatment for many diseases.

SymBio aims for approval and commercialization of two or three indications for BCV by 2030. The indication with the highest potential for approval is viral infection following hematopoietic stem cell and kidney transplantation, two areas of clinical development prioritization.

Anticancer agent SyB L-0501 (FD formulation)/SyB L-1701 (RTD formulation)/SyB L-1702 (RI administration); generic name: bendamustine hydrochloride or bendamustine hydrochloride hydrate, product name: Treakisym®

SymBio will continue to explore new potential applications of Treakisym®, including via joint research with the University of Tokyo and Kyoto University.

Anticancer agent SyB L-1101 (IV)/SyB C-1101 (oral); generic name: rigosertib sodium

For rigosertib and Treakisym®, the company is searching for new indications as well as new applications for the drugs used in combination with each other or with other existing drugs, through joint research and the offering of academia-industry collaborative courses with the University of Tokyo. In April 2024, the drug's licensor Onconova changed its name to Traws Pharma Inc., headquartered in Pennsylvania, US.

Overseas business (SymBio Pharma USA)

In January 2025, the company appointed Mr. Masaru Taguchi (who also serves as the company's Executive Officer and Senior Assistant to the President) as CEO and President of its wholly-owned subsidiary SymBio Pharma USA, Inc. (SPU). SPU will serve as a strategic hub to drive the global business for the antiviral drug BCV, accelerating its development across the US, Europe, Japan, and the UK.

In-licensing of drug candidates

The company is currently focusing on unrolling global development plans for the antiviral drug BCV it in-licensed in September 2019, but also constantly looking into multiple licensing deals and looking for and evaluating promising new in-licensing drug candidates. Through the introduction of external products, it aims to create medium- to long-term business value.

Highlights

At its FY12/24 full-year earnings briefing in February 2025, SymBio outlined the following key business development goals for FY12/25.

- Q4 target: Initiate a Phase III trial for post-transplant adenovirus (AdV) infection
- Q3 target: Establish proof of concept (POC) in the Phase II trial for post-transplant cytomegalovirus (CMV) infection
  - The company noted that patient enrollment for the second dosage level has been completed as CMV has a relatively large patient population.
- Q4 target: Establish POC in the Phase Ib trial for NK/T-cell lymphoma
  - Given the rarity of the disease, the company believes that in Japan, it can seek regulatory approval after completing a Phase II trial, following the completion of the Phase Ib trial
- Q4 target: Begin reviews toward commencing a Phase Ib trial for glioblastoma (GBM)
- Q4 target: If animal POC for multiple sclerosis is confirmed (expected in Q2), initiate discussions with the NIH on the clinical trial design for a first-in-human (FIH) study
- Q4 target: Finalize a global partnership for BCV. (The company aims to collaborate with a developer of immune checkpoint inhibitors (ICIs), as it envisions BCV's use in combination with ICIs.)
- Q3 target: Work to in-license new products for the domestic market

Cumulative Q3 FY12/24 results (out October 31, 2024)

- Sales: JPY1.9bn (-57.1% YoY)
  - R&D expenses: JPY2.5bn (+36.7% YoY)
- Operating loss: JPY2.8bn (versus loss of JPY283mn in cumulative Q3 FY12/23)
- Recurring loss: JPY2.8bn (versus loss of JPY156mn in cumulative Q3 FY12/23)
- Net loss attributable to owners of the parent: JPY2.8bn (versus loss of JPY789mn in cumulative Q3 FY12/23)

In February 2022, SymBio obtained approval for a partial change to the marketing authorization for the ready-to-dilute (RTD) intravenous formulation of Treakisym® 100mg/4ml, which was launched in January 2021, to add rapid infusion (RI) administration. Compared to the freeze-dried (FD) formulation, the RTD formulation reduces the time required for the complicated dissolution process. RI administration further benefits both patients and healthcare providers by reducing the infusion time from the 60 minutes required by the RTD formulation. In addition, the RI administration uses less saline solution and accordingly less salt (sodium chloride).

The switch from the FD to RTD formulation is almost complete. With over 90% of medical institutions administering the RI formulation to patients as of end-September 2024, progress was made in the switch to the RI formulation.

Sales decreased by 57.1% YoY to JPY1.9bn. The penetration of generics has gradually progressed, affecting the results. Meanwhile, the ongoing decline in usage of Treakisym® (bendamustine) per patient due to the COVID-19 pandemic has gradually eased. Concerns over the increased risk of infection for patients with blood cancers, especially those with malignant lymphoma, and the potential for prolonged or severe infections during or after treatment with bendamustine have led to decreased prescriptions of bendamustine, including its generics.

- Since NHI excluded Treakisym® RTD formulation from the list of drugs eligible for the premium for newly discovered drugs in its April 2024 price revisions, the drug price was reduced by 18.6%. As NHI announces the price revision range in advance, both medical institutions and pharmaceutical wholesalers actively adjusted their inventories during Q1 (January–March 2024), aiming to use up the stock of the higher-priced Treakisym® RTD and purchase the same product at the new, lower price. Since Q2, the inventory adjustment has run its cource and sales of Treakisym® RTD formulation recovered QoQ.

- In September 2024, the company settled a patent infringement lawsuit it had filed against Towa Pharmaceutical Co., Ltd. (For details, please refer to the Highlights section below).

Gross profit was JPY1.4bn (-58.5% YoY), and the gross profit margin reached 76.1% (-2.5pp YoY). SG&A expenses were JPY4.2bn (+12.7% YoY), of which R&D expenses amounted to JPY2.5bn (+36.7% YoY). As a result, the operating loss was JPY2.8bn (compared to a loss of JPY283mn in cumulative Q3 FY12/23).

Progress rates against full-year company forecast for FY12/24

In May 2024, the company announced a downward revision of its full-year earnings forecast for FY12/24 (see "Full-year company forecast" below for details). The progress rate for cumulative Q3 against the revised full-year forecast is 72.4% for sales, while there is no progress rate for profit items due to negative figures. The operating loss was JPY2.8bn (full-year forecast: JPY3.7bn loss), the recurring loss was JPY2.8bn (full-year forecast: JPY3.5bn loss), and the net loss attributable to owners of the parent was JPY2.8bn (full-year forecast: JPY3.6bn loss).

The company believes that it is on track against the revised forecast and has maintained its full-year forecast.

Business progress

Progress in the company's key businesses through November 2024 was as follows.

- In November 2024, the company appointed a new Executive Vice President and Global Chief Medical Officer (CMO), who also assumed the role of Senior Vice President at its US subsidiary, SymBio Pharma USA (SPU).

- In October 2024, at ID Week 2024 (Infectious Diseases Society of America Annual Meeting), additional data from the Phase IIa clinical trial of BCV for adenovirus (AdV) infections was presented, highlighting the correlation between AdV clearance from the bloodstream and improvements in clinical symptoms.

- In September 2024, the company settled a patent infringement lawsuit it had filed against Towa Pharmaceutical Co., Ltd. (For details, please refer to the Highlights section below).

- In August 2024, the company initiated an international Phase Ib/II clinical trial of BCV targeting patients with relapsed or refractory lymphoma (malignant lymphomas such as NK/T-cell lymphoma).

- In July 2024, the company announced that BCV has inhibited the production of infectious polyomaviruses. The US-based Penn State College of Medicine evaluated the efficacy of BCV in a mouse model of polyomavirus infection and published the results in a scientific journal.

- In June 2024, the anti-tumor effects of BCV on peripheral T-cell lymphoma (PTCL) have been confirmed through a mouse model, and the research findings were presented at the 29th European Hematology Association (EHA2024 Hybrid Congress).

- In June 2024, the company has completed the enrollment of the first patient (FPI) for the Phase IIa clinical trial of BCV targeting CMV infection following hematopoietic stem cell transplantation.

- In May 2024, SymBio initiated a Phase IIa clinical trial of BCV for CMV infection after hematopoietic stem cell transplantation. CMV infection is the second indication for BCV after adenovirus (AdV) infection.

- In April 2024, Onconova, rigosertib's licensor (originator), established a new company, Traws Pharma, Inc., through a business merger.
- In April 2024, the CEO and president of the US subsidiary (Symbio Pharma USA, Inc.) was changed from Mr. Stephane Berthier to Mr. John Houghton.
- In April 2024, the anti-tumor effects of BCV for B-cell lymphoma found through joint research between Symbio and the National Cancer Centre Singapore (NCCS) were presented at the American Association for Cancer Research (AACR) Annual Meeting 2024.
- In March 2024, BCV received an orphan drug (a drug for treating rare diseases) designation in the EU.
- In February 2024, an abstract demonstrating the anti-adenovirus (AdV) effects of brincidofovir (BCV) was selected for an oral session at the Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT).
- In February 2024, BCV was selected as a presentation topic for the Pediatric Best Abstracts session at the 2024 Tandem Meetings in the US. The presentation introduced new findings on BCV's effectiveness against AdV in stool samples.
- In January 2024, SymBio obtained a patent in Japan covering the use of BCV injection as a treatment for AdV infections.

R&D activities

A key milestone in Q3 was the initiation of an international Phase Ib clinical trial in August 2024, targeting patients with malignant lymphoma. This marks the first clinical trial for BCV in the oncology field (in the post-transplant infection field, the first patient was dosed in August 2021).

Antiviral drug SyB V-1901 (generic name: brincidofovir)

In development of the intravenous and oral formulations of the antiviral drug brincidofovir (SyB V-1901; BCV IV and BCV Oral), the company is conducting joint research with top research institutions specialized in each field in Japan and overseas in light of the broad spectrum of the drug's effectiveness against dsDNA virus infections. It will consider conducting additional global clinical trials based on the scientific findings of the research.

Earlier clinical trials in the US and Europe conducted by US-based Chimerix Inc. have demonstrated that BCV Oral has broad-spectrum antiviral effects against a variety of dsDNA viruses. BCV IV is expected to be effective and safe for the prevention and treatment of many dsDNA virus infections, including adenovirus (AdV) infections after hematopoietic stem cell transplantation. In June 2021, Chimerix announced that the US FDA had granted BCV Oral approval for the treatment of smallpox.

Post-transplant infectious diseases

BCV clinical development: disseminated AdV infections following hematopoietic stem cell transplantation

Based on a global advisory board review held in February 2020, the company has decided to prioritize the global development of BCV IV primarily in Japan, the US, and Europe, targeting disseminated AdV infections occurring after hematopoietic stem cell transplantation, a niche area with a high unmet medical need. In March 2021, the company filed an IND application with the US Food and Drug Administration (FDA) to conduct a Phase II clinical trial primarily in pediatric patients suffering from AdV infections (also including adults). This development program was granted fast-track designation by the FDA in April 2021, and the investigational drug was administered to the first patient in August 2021. In May 2023, BCV has demonstrated proof of concept in humans in the same study. Positive data demonstrating efficacy from the study were presented orally at the 65th Annual Meeting of the American Society of Hematology in December 2023. Similar presentations were made at other major academic conferences, including the 2024 Tandem Meetings in the US in February 2024, the 50th Annual Meeting of the EBMT in April 2024, and ID Week 2024 (Infectious Diseases Society of America). In addition, a use patent for BCV related to the treatment of AdV infections and infectious diseases was established and registered in Japan in January 2024.

✓ The Data Safety Monitoring Board (DSMB) and the FDA confirmed the POC in terms of both safety and efficacy. While the POC has been confirmed in trials up to cohort 3.
✓ For cohorts 1 to 3, BCV was administered twice weekly, at doses of 0.2mg/kg for cohort 1, 0.3mg/kg for cohort 2, and 0.4mg/kg for cohort 3. In cohort 3 (0.4mg/kg, twice weekly via IV), the disappearance of AdV in the blood was confirmed in 100% of patients (n=10). Of these, 90% of patients (n=9) achieved viral clearance within four weeks of treatment.

BCV clinical development for cytomegalovirus (CMV) infections following hematopoietic stem cell transplantation

In May 2024, a Phase IIa clinical trial post-hematopoietic stem cell CMV infection was initiated in the US. In June 2024, the first patient was enrolled, and the trial is currently ongoing.

- The larger patient population for CMV infections compared to adenovirus (AdV) infections has contributed to steady patient enrollment in the trial.

- The competitor drug maribarivir (brand name: LIVTENCITY) from Takeda Pharmaceutical generated sales of JPY19.1bn in FY03/24. The number of transplant recipients treated for CMV is exceptionally high for a rare disease (25,000, of which 10,000 are resistant or refractory). One reason megapharma Takeda decided to develop competitor maribarivir independently was likely the drug's large potential patient base, which made it appear more lucrative. The company noted the large patient base made patient enrollment for clinical trials much easier.

BCV clinical development: BK virus infection following kidney transplantation

The development of a treatment for BK virus infection following kidney transplantation is currently under protocol revision. In August 2022, the first patient was dosed (FPD) in an international Phase II clinical trial in Australia; however, patient enrollment has been slower than anticipated.

BCV non-clinical study: polyomavirus infection

Polyomaviruses, particularly JC virus (JCV), are known to cause severe brain diseases among dsDNA viruses, and the development of effective treatments is highly anticipated. In November 2022, the company concluded a material transfer agreement (MTA) with US-based Penn State College of Medicine, and initiated a non-clinical study evaluating the efficacy of BCV in a mouse model of polyomavirus infection. In July 2024, the first report of these research findings, which included new insights, was published in the journal mBio.

Hematological malignancies

BCV non-clinical joint research: applications for hematological malignancies/oncology

In addition to antiviral activity, the company expects brincidofovir to have antitumor effects. Through joint research with the National Cancer Centre Singapore and University of California San Francisco Brain Tumor Center, SymBio is investigating new indications for the drug in oncology, including rare brain tumors and EB virus-positive lymphoma. In March 2022, the company commenced joint research with Brown University of the US to investigate the antitumor effects of brincidofovir on glioblastoma (GBM) caused by cytomegalovirus (CMV) infection.

In December 2022, the results of collaborative research with the National Cancer Centre Singapore (NCCS) on the therapeutic efficacy of BCV in the treatment of rapidly progressing NK/T-cell lymphoma were presented at the 64th American Society of Hematology (ASH) Annual Meeting.

- Since BCV does not exhibit bone marrow suppression as a side effect, the company expects it can selectively target and destroy cancer cells without affecting normal cells.

At the 17th International Conference on Malignant Lymphoma (ICML) in June 2023, research into biomarkers* that predict the anti-tumor effect of BCV was presented. In April 2024, the anti-tumor effects of BCV for B-cell lymphoma was presented as a poster at the American Association for Cancer Research Annual Meeting. In June 2024, the anti-tumor effects of BCV on peripheral T-cell lymphoma (PTCL) was presented as a poster at the European Hematology Association (EHA2024 Hybrid Congress).

*The use of biomarkers allows for the selection of patients who are likely to respond well to treatment, which increases the probability of successful clinical (POC) trials.

Clinical development of BCV (application in hematologic malignancies and oncology)

In August 2024, the company initiated an international Phase Ib clinical trial of BCV targeting patients with malignant lymphoma as a First in Human (FIH) trial in the oncology field. Through this trial, it aims to establish human proof of concept (POC) for BCV in cancer treatment.

- This trial is the third clinical trial of BCV, following those for AdV and CMV infections, and it is the first BCV trial in the oncology field.

Other

BCV non-clinical studies: EB virus, multiple sclerosis, lymphoproliferative disorders

SymBio has been preparing for clinical development of brincidofovir for multiple sclerosis, a rare disease related to EB virus. In August 2022, the company signed a collaboration agreement for the transfer of human materials with the National Institute of Neurological Disorders and Stroke (NINDS) of the US National Institute of Health (NIH). In March 2023, SymBio signed a cooperative research and development agreement (CRADA) with NINDS to obtain information necessary to conduct future clinical trials. In October 2023, the results of the research were presented at the 9th Joint ECTRIMS-ACTRIMS Meeting in Milan, Italy.

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In December 2022, the company concluded a sponsored research agreement with US-based Tufts University, and began a joint research study evaluating the efficacy of BCV in a herpes simplex virus infection model. This study aims to explore BCV's potential to treat neurological diseases, including Alzheimer's disease.

Rights

In September 2022, Chimerix announced that it had completed procedures to transfer the rights to brincidofovir to Emergent BioSolutions Inc. (headquarters: Maryland, US). The agreement, however, has no impact on the company's exclusive rights to develop, manufacture, and sell brincidofovir globally for all indications except orthopoxvirus diseases including smallpox and Mpox (monkeypox).

Orphan drug designation for BCV

In March 2024, the EU orphan drug designation for BCV, for the prevention of adenovirus and cytomegalovirus infections in immunocompromised patients, was transferred from Emergent BioSolutions to a subsidiary of SymBio.

BCV's use patent and IP strategy ("pipeline within a molecule")

At the earnings presentation for 1H FY12/24, the company discussed the grant of a use patent for BCV and its future intellectual property (IP) strategy.

- In May 2023, BCV demonstrated a proof of concept (POC) in human patients, and based on this data, the company filed for a use patent.

- The use patent for BCV in the treatment of AdV infections was filed for accelerated review in September 2023. The patent was granted in January 2024 and will be valid until 2043.

- SymBio aims to maximize the business value of BCV by examining the efficacy of the drug in dsDNA virus infections, expanding target indications to include multiviral infections, and striving to meet the underserved medical needs for treatments of viral diseases and accompanying complications.

- The company is advancing its IP strategy for BCV under the concept of "pipeline within a molecule," considering BCV as a compound that can be commercialized as a treatment for many diseases.

SymBio aims for approval and commercialization of two or three indications for BCV by 2030. The indication with the highest potential for approval is viral infection following hematopoietic stem cell and kidney transplantation, two areas of clinical development prioritization.

Anticancer agent SyB L-0501 (FD formulation)/SyB L-1701 (RTD formulation)/SyB L-1702 (RI administration); generic name: bendamustine hydrochloride or bendamustine hydrochloride hydrate, product name: Treakisym®

SymBio will continue to explore new potential applications of Treakisym®, including via joint research with the University of Tokyo and Kyoto University.

Anticancer agent SyB L-1101 (IV)/SyB C-1101 (oral); generic name: rigosertib sodium

For rigosertib and Treakisym®, the company is searching for new indications as well as new applications for the drugs used in combination with each other or with other existing drugs, through joint research and the offering of academia-industry collaborative courses with the University of Tokyo. In April 2024, the drug's licensor Onconova changed its name to Traws Pharma Inc., headquartered in Pennsylvania, US.

Overseas business (SymBio Pharma USA)

The company's wholly-owned subsidiary SymBio Pharma USA, Inc. (SPU) will serve as a strategic hub to drive the global business for the antiviral drug BCV, accelerating its development across the US, Europe, Japan, and the UK.

- In November 2024, the company appointed Dr. Jay Marshall Feingold as Executive Vice President and Global CMO. He will also serve as Senior Vice President at SPU.

In-licensing of drug candidates

The company is currently focusing on unrolling global development plans for the antiviral drug BCV it in-licensed in September 2019, but also constantly looking into multiple licensing deals and looking for and evaluating promising new in-licensing drug candidates. Through the introduction of external products, it aims to create medium- to long-term business value.

- The company mentioned the possibility of new in-licensing agreements for development candidates for the Japanese market during Q3 FY12/24; however, no announcement was made within the period.

Highlights

In September 2024, the company settled a patent infringement lawsuit, which it had filed against Towa Pharmaceutical Co., Ltd. The details are as follows.

- In February 2022, four companies obtained approval for the manufacture and sale of generic versions of the company's product Treakisym® RTD, an original brand drug. Of these, two companies began selling the generic product in 2022. Subsequently, two companies received approval for the rapid intravenous (RI) formulation and commenced sales.
- In December 2022, the company, together with its licensor Eagle Pharmaceuticals, jointly filed a lawsuit against Pfizer Japan Inc. and Towa Pharmaceutical Co., Ltd., seeking an injunction to halt the manufacture and sale of generic drugs based on patent infringement, along with claims for damages.
- The lawsuit against Towa Pharmaceutical was settled in September 2024, while the lawsuit against Pfizer Japan is ongoing. As of October 2024, three companies are selling generic versions of the drug.

- According to Towa Pharmaceutical's release, it will continue selling the generic version of Treakisym® RTD even after the settlement, which will have minimal impact on SymBio's earnings.

1H FY12/24 results (out August 1, 2024)

- Sales: JPY1.3bn (-59.6% YoY)
- R&D expenses: JPY1.5bn (+27.2% YoY)
- Operating loss: JPY1.7bn (versus loss of JPY50mn in 1H FY12/23)
- Recurring loss: JPY1.5bn (versus profit of JPY67mn in 1H FY12/23)
- Net loss attributable to owners of the parent: JPY1.5bn (versus loss of JPY80mn in 1H FY12/23)

In February 2022, SymBio obtained approval for a partial change to the marketing authorization for the ready-to-dilute (RTD) intravenous formulation of Treakisym® 100mg/4ml, which was launched in January 2021, to add rapid infusion (RI) administration. Compared to the freeze-dried (FD) formulation, the RTD formulation reduces the time required for the complicated dissolution process. RI administration further benefits both patients and healthcare providers by reducing the infusion time from the 60 minutes required by the RTD formulation. In addition, the RI administration uses less saline solution and accordingly less salt (sodium chloride).

The switch from the FD to RTD formulation is almost complete. With over 90% of medical institutions administering the RI formulation to patients as of end-June 2024, progress was made in the switch to the RI formulation.

Sales decreased by 59.6% YoY to JPY1.3bn. The ongoing decline in usage of Treakisym® (bendamustine) per patient due to the COVID-19 pandemic has gradually eased. Concerns over the increased risk of infection for patients with blood cancers, especially those with malignant lymphoma, and the potential for prolonged or severe infections during or after treatment with bendamustine have led to decreased prescriptions of bendamustine, including its generics. Meanwhile, the penetration of generics has gradually progressed, affecting the results.

- Since NHI excluded Treakisym® RTD formulation from the list of drugs eligible for the premium for newly discovered drugs in its April 2024 price revisions, the drug price was reduced by 18.6%. As NHI announces the price revision range in advance, both medical institutions and pharmaceutical wholesalers actively adjusted their inventories during Q1 (January–March 2024), aiming to use up the stock of the higher-priced Treakisym® RTD and purchase the same product at the new, lower price. In Q2, the inventory adjustment ended and sales of Treakisym® RTD formulation recovered QoQ.

- The company estimates that the switch to generics of Treakisym® RTD formulation reached just under 60% as of end-1H FY12/24. Meanwhile, the overall bendamustine market, including both Treakisym® and its generics, appears to have bottomed out from a shrinking trend.

- The patent infringement litigation related to Treakisym® RTD formulation is ongoing, and the company expects it to conclude within 2024.

Gross profit was JPY996mn (-59.7% YoY), and the gross profit margin reached 77.6% (-0.2pp YoY). SG&A expenses were JPY2.7bn (+7.6% YoY), of which R&D expenses amounted to JPY1.5bn (+27.2% YoY). As a result, the operating loss was JPY1.7bn (compared to a loss of JPY50mn in 1H FY12/23).

- SG&A expenses, excluding R&D expenses, were JPY1.2bn (-10.2% YoY). As of end-December 2023, the employee count dropped by 13 YoY. The associated reduction in personnel costs also contributed to the lower SG&A expenses.

- The 27.2% YoY increase in R&D expenses was due to the steady progress of the company's clinical trials and higher overseas clinical trial costs in yen terms due to the yen's depreciation.

Progress rates against full-year company forecast for FY12/24

In May 2024, the company announced a downward revision of its full-year earnings forecast for FY12/24 (see "Full-year company forecast" below for details). The progress rate for 1H against the revised full-year forecast is 49.0% for sales, while there is no progress rate for profit items due to negative figures. The operating loss was JPY1.7bn (full-year forecast: JPY3.7bn loss), the recurring loss was JPY1.5bn (full-year forecast: JPY3.5bn loss), and the net loss attributable to owners of the parent was JPY1.5bn (full-year forecast: JPY3.6bn loss).

The company believes that it is on track against the revised forecast and has maintained its full-year forecast.

Business progress

Progress in the company's key businesses through August 2024 was as follows.

- In July 2024, the company announced that BCV has inhibited the production of infectious polyomaviruses. The US-based Penn State College of Medicine evaluated the efficacy of BCV in a mouse model of polyomavirus infection and published the results in a scientific journal.
- In June 2024, the anti-tumor effects of BCV on peripheral T-cell lymphoma (PTCL) have been confirmed through a mouse model, and the research findings were presented at the 29th European Hematology Association (EHA2024 Hybrid Congress).
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- In April 2024, Onconova, rigosertib's licensor (originator), established a new company, Traws Pharma, Inc., through a business merger.
- In April 2024, the CEO and president of the US subsidiary (Symbio Pharma USA, Inc.) was changed from Mr. Stephane Berthier to Mr. John Houghton.
- In April 2024, the anti-tumor effects of BCV for B-cell lymphoma found through joint research between Symbio and the National Cancer Centre Singapore (NCCS) were presented at the American Association for Cancer Research (AACR) Annual Meeting 2024.
- In March 2024, BCV received an orphan drug (a drug for treating rare diseases) designation in the EU.
- In February 2024, an abstract demonstrating the anti-adenovirus (AdV) effects of brincidofovir (BCV) was selected for an oral session at the Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT).
- In February 2024, BCV was selected as a presentation topic for the Pediatric Best Abstracts session at the 2024 Tandem Meetings in the US. The presentation introduced new findings on BCV's effectiveness against AdV in stool samples.
- In January 2024, SymBio obtained a patent in Japan covering the use of BCV injection as a treatment for AdV infections.

R&D activities

Please refer to "Business progress" from April onward for progress of research and development since Q2 FY12/24 (April–June). Among these developments, the most significant achievement was the initiation of a Phase IIa clinical trial for BCV targeting CMV infection post-hematopoietic stem cell transplantation in May 2024, with the first patient enrollment (FPI) completed in June 2024.

Antiviral drug SyB V-1901 (generic name: brincidofovir)

In development of the intravenous and oral formulations of the antiviral drug brincidofovir (SyB V-1901; BCV IV and BCV Oral), the company is conducting joint research with top research institutions specialized in each field in Japan and overseas in light of the broad spectrum of the drug's effectiveness against dsDNA virus infections. It will consider conducting additional global clinical trials based on the scientific findings of the research.

Earlier clinical trials in the US and Europe conducted by US-based Chimerix Inc. have demonstrated that BCV Oral has broad-spectrum antiviral effects against a variety of dsDNA viruses. BCV IV is expected to be effective and safe for the prevention and treatment of many dsDNA virus infections, including adenovirus (AdV) infections after hematopoietic stem cell transplantation. In June 2021, Chimerix announced that the US FDA had granted BCV Oral approval for the treatment of smallpox.

Post-transplant infectious diseases

BCV clinical development: disseminated AdV infections following hematopoietic stem cell transplantation

Based on a global advisory board review held in February 2020, the company has decided to prioritize the global development of BCV IV primarily in Japan, the US, and Europe, targeting disseminated AdV infections occurring after hematopoietic stem cell transplantation, a niche area with a high unmet medical need. In March 2021, the company filed an IND application with the US Food and Drug Administration (FDA) to conduct a Phase II clinical trial primarily in pediatric patients suffering from AdV infections (also including adults). This development program was granted fast-track designation by the FDA in April 2021, and the investigational drug was administered to the first patient in August 2021. In May 2023, BCV has demonstrated proof of concept in humans in the same study. Positive data demonstrating efficacy from the study were presented orally at the 65th Annual Meeting of the American Society of Hematology in December 2023. Similar presentations were made at other major academic conferences, including the 2024 Tandem Meetings in the US in February 2024 and the 50th Annual Meeting of the EBMT in April 2024. In addition, a use patent for BCV related to the treatment of AdV infections and infectious diseases was established and registered in Japan in January 2024.

- The Data Safety Monitoring Board (DSMB) and the FDA confirmed the POC in terms of both safety and efficacy. While the POC has been confirmed in trials up to cohort 3.

- For cohorts 1 to 3, BCV was administered twice weekly, at doses of 0.2mg/kg for cohort 1, 0.3mg/kg for cohort 2, and 0.4mg/kg for cohort 3. In cohort 3 (0.4mg/kg, twice weekly via IV), the disappearance of AdV in the blood was confirmed in 100% of patients (n=10). Of these, 90% of patients (n=9) achieved viral clearance within four weeks of treatment.

- The company positions the year 2023, when BCV's proof of concept (POC) was established, as a turning point in its business. While the sales of Treakisym® FD formulation declined, the company believes that the future value of BCV has risen discontinuously in a stepwise manner.

BCV clinical development for Cytomegalovirus (CMV) infections following hematopoietic stem cell transplantation

In May 2024, a Phase IIa clinical trial post-hematopoietic stem cell cytomegalovirus infection was initiated in the US. In June 2024, the first patient was enrolled, and the trial is currently ongoing.

- The progress of this clinical development was the company's most significant achievement in Q2 FY12/24 (April–June 2024).

- The competitor drug maribarivir (brand name: LIVTENCITY) from Takeda Pharmaceutical generated sales of JPY19.1bn in FY03/24. The number of transplant recipients treated for CMV is exceptionally high for a rare disease (25,000, of which 10,000 are resistant or refractory). One reason megapharma Takeda decided to develop competitor maribarivir independently was likely the drug's large potential patient base, which made it appear more lucrative. The company noted the large patient base made patient enrollment for clinical trials much easier.

BCV clinical development: BK virus infection following kidney transplantation

BK virus nephropathy after kidney transplantation is considered a disease with serious consequences for the recipient, the donor, the medical practitioner, and society, as it may result in serious conditions such as decreased renal function and graft loss. In order to find an early solution to this problem, SymBio submitted a clinical trial notification for a global Phase II study in patients infected with BK virus after receiving kidney transplant to the Pharmaceuticals and Medical Devices Agency (PMDA) of Japan in May 2022 and to the Therapeutic Goods Administration (TGA) of Australia in August 2022. The investigational drug was administered to the first patient in Australia in August 2022. While the trial was initially planned for completion in 2025, delays in the accumulation of cases have led to a review of the protocol.

BCV non-clinical study: polyomavirus infection

Polyomaviruses, particularly JC virus (JCV), are known to cause severe brain diseases among dsDNA viruses, and the development of effective treatments is highly anticipated. In November 2022, the company concluded a material transfer agreement (MTA) with US-based Penn State College of Medicine, and initiated a non-clinical study evaluating the efficacy of BCV in a mouse model of polyomavirus infection. In July 2024, the first report of these research findings, which included new insights, was published in the journal mBio.

Hematological malignancies

BCV non-clinical joint research: applications for hematological malignancies/oncology

In addition to antiviral activity, the company expects brincidofovir to have antitumor effects. Through joint research with the National Cancer Centre Singapore and University of California San Francisco Brain Tumor Center, SymBio is investigating new indications for the drug in oncology, including rare brain tumors and EB virus-positive lymphoma. In March 2022, the company commenced joint research with Brown University of the US to investigate the antitumor effects of brincidofovir on glioblastoma (GBM) caused by cytomegalovirus (CMV) infection.

In December 2022, the results of collaborative research with the National Cancer Centre Singapore (NCCS) on the therapeutic efficacy of BCV in the treatment of rapidly progressing NK/T-cell lymphoma were presented at the 64th American Society of Hematology (ASH) Annual Meeting.

- At the earnings presentation for 1H FY12/24, Symbio mentioned the possibility of initiating a Phase Ib clinical trial for NK/T-cell lymphoma in Japan, with the company taking the lead.
- Since BCV does not exhibit bone marrow suppression as a side effect, the company expects it can selectively target and destroy cancer cells without affecting normal cells.

At the 17th International Conference on Malignant Lymphoma (ICML) in June 2023, research into biomarkers* that predict the anti-tumor effect of BCV was presented. In April 2024, the anti-tumor effects of BCV for B-cell lymphoma was presented as a poster at the American Association for Cancer Research Annual Meeting. In June 2024, the anti-tumor effects of BCV on peripheral T-cell lymphoma (PTCL) was presented as a poster at the European Hematology Association (EHA2024 Hybrid Congress).

*The use of biomarkers allows for the selection of patients who are likely to respond well to treatment, which increases the probability of successful clinical (POC) trials.

Other

BCV non-clinical studies: EB virus, multiple sclerosis, lymphoproliferative disorders

SymBio has been preparing for clinical development of brincidofovir for multiple sclerosis, a rare disease related to EB virus. In August 2022, the company signed a collaboration agreement for the transfer of human materials with the National Institute of Neurological Disorders and Stroke (NINDS) of the US National Institute of Health (NIH). In March 2023, SymBio signed a cooperative research and development agreement (CRADA) with NINDS to obtain information necessary to conduct future clinical trials. In October 2023, the results of the research were presented at the 9th Joint ECTRIMS-ACTRIMS Meeting in Milan, Italy.

CRADA: Refers to a contract on collaborative R&D between a US government organization and entities such as a private-sector company. The private-sector company may be able to obtain licensing of patent rights regarding inventions developed under the CRADA. Because a company may receive patent rights from a project using government funds, the barriers to being selected for a CRADA are significant (SymBio is the second Japanese company to be selected).

In April 2023, SymBio also signed a CRADA with the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, to evaluate the efficacy of BCV in EB virus-related lymphoproliferative disorders.

*Refers to a wide range of diseases related to the EB virus: Cancers such as T-cell lymphoma, Burkitt lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, NK T-cell lymphoma, and post-transplant lymphoproliferative disease, X-linked lymphoproliferative syndrome, and AIDS-related lymphoproliferative disease. (Source: Materials for company's 18th ordinary general meeting of shareholders.)

BCV non-clinical joint research: herpes simplex virus, Alzheimer's type dementia

In December 2022, the company concluded a sponsored research agreement with US-based Tufts University, and began a joint research study evaluating the efficacy of BCV in a herpes simplex virus infection model. This study aims to explore

BCV's potential to treat neurological diseases, including Alzheimer's disease.

Rights

In September 2022, Chimerix announced that it had completed procedures to transfer the rights to brincidofovir to Emergent BioSolutions Inc. (headquarters: Maryland, US). The agreement, however, has no impact on the company's exclusive rights to develop, manufacture, and sell brincidofovir globally for all indications except orthopoxvirus diseases including smallpox and monkeypox.

Orphan drug designation for BCV

In March 2024, the EU orphan drug designation for BCV, for the prevention of adenovirus and cytomegalovirus infections in immunocompromised patients, was transferred from Emergent BioSolutions to a subsidiary of SymBio.

BCV's use patent and IP strategy ("pipeline within a molecule")

At the earnings presentation for 1H FY12/24, the company discussed the grant of a use patent for BCV and its future intellectual property (IP) strategy.

- In May 2023, BCV demonstrated a proof of concept (POC) in human patients, and based on this data, the company filed for a use patent.
- The use patent for BCV in the treatment of AdV infections was filed for accelerated review in September 2023. The patent was granted in January 2024 and will be valid until 2043.
- SymBio aims to maximize the business value of BCV by examining the efficacy of the drug in dsDNA virus infections, expanding target indications to include multiviral infections, and striving to meet the underserved medical needs for treatments of viral diseases and accompanying complications.
- The company is advancing its IP strategy for BCV under the concept of "pipeline within a molecule," considering BCV as a compound that can be commercialized as a treatment for many diseases.

SymBio aims for approval and commercialization of two or three indications for BCV by 2030. The indication with the highest potential for approval is viral infection following hematopoietic stem cell and kidney transplantation, two areas of clinical development prioritization.

Anticancer agent SyB L-0501 (FD formulation)/SyB L-1701 (RTD formulation)/SyB L-1702 (RI administration); generic name: bendamustine hydrochloride or bendamustine hydrochloride hydrate, product name: Treakisym®

SymBio will continue to explore new potential applications of Treakisym®, including via joint research with the University of Tokyo and Kyoto University.

Anticancer agent SyB L-1101 (IV)/SyB C-1101 (oral); generic name: rigosertib sodium

For rigosertib and Treakisym®, the company is searching for new indications as well as new applications for the drugs used in combination with each other or with other existing drugs, through joint research and the offering of academia-industry collaborative courses with the University of Tokyo. In April 2024, the drug's licensor Onconova changed its name to Traws Pharma Inc., headquartered in Pennsylvania, US.

Overseas business (SymBio Pharma USA)

In April 2024, the company appointed Mr. John Houghton as CEO and President of its wholly-owned subsidiary SymBio Pharma USA, Inc. SymBio Pharma USA is leading the global development of the antiviral drug brincidofovir.

In-licensing of drug candidates

The company is currently focusing on unrolling global development plans for the antiviral drug brincidofovir it in-licensed in September 2019, but also constantly looking into multiple licensing deals and looking for and evaluating promising new in-licensing drug candidates.

- Please refer to "Topic 2: key milestones expected for FY12/24." The company mentioned the possibility of new in-licensing agreements for development candidates for the Japanese market during Q3 FY12/24.

Topic 1: possibility of initiating a Phase Ib clinical trial for BCV in the oncology field

At the earnings presentation for 1H FY12/24, Symbio mentioned the possibility of initiating a Phase Ib clinical trial for NK/T-cell lymphoma in Japan, with the company taking the lead.

Symbio is currently conducting clinical trials for BCV in two areas: Adenovirus (AdV) infections and CMV infections following hematopoietic stem cell transplantation. If the clinical trial for NK/T-cell lymphoma is initiated, it will be the company's first venture into clinical development of BCV in the oncology field.

Topic 2: key milestones expected for FY12/24

During its full-year earnings presentation for FY12/23, Symbio outlined its development objectives for BCV in FY12/24. Regarding cytomegalovirus (CMV) infection, the company initiated Phase II clinical trials in May 2024 as planned (see Topic 1 above).

- Q2: Initiation of a Phase II study for cytomegalovirus infections
- Q4: Start of a global Phase III study for AdV infections

In terms of business development, the company indicated the possibility of progress in Q3 concerning new in-licensing opportunities or partnership negotiations:

- Q3: Potential for new in-licensing agreements for development candidates for the Japanese market
- Q3: Possibility of starting partnership negotiations for BCV development

For collaborative research on non-clinical studies, the company suggested the possibility of progress in the latter half of FY12/24. The company hopes to initiate clinical trials for some of these projects during FY12/25:

- Q3: Potential for the National Cancer Centre Singapore to report research findings
- Q3: Potential for NIH/NINDS to report findings from experiments on multiple sclerosis animal models
- Q4: Potential for Tufts University to report on collaborative development results

Income statement

Income statement	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
(JPYmn)	Parent	Parent	Parent	Parent	Parent	Parent	Parent	Cons.	Cons.	Cons.
Sales	**1,933**	**2,368**	**3,444**	**3,836**	**2,838**	**2,987**	**8,257**	**10,008**	**5,590**	**2,453**
YoY	-1.1%	22.5%	45.4%	11.4%	-26.0%	5.3%	176.4%	21.2%	-44.1%	-56.1%
CoGS	1,350	1,464	2,413	2,663	1,973	2,120	2,452	2,408	1,179	580
Gross profit	**583**	**904**	**1,031**	**1,173**	**865**	**867**	**5,800**	**7,600**	**4,411**	**1,873**
Gross profit margin	30.2%	38.2%	29.9%	30.6%	30.5%	29.0%	70.2%	75.9%	78.9%	76.4%
SG&A expenses	3,135	3,031	4,978	3,829	5,166	5,373	4,784	5,636	5,223	5,750
SG&A ratio	162.1%	128.0%	144.5%	99.8%	182.1%	179.9%	57.9%	56.3%	93.4%	234.4%
Operating profit	**-2,552**	**-2,127**	**-3,947**	**-2,656**	**-4,302**	**-4,506**	**1,016**	**1,964**	**-812**	**-3,877**
YoY	-	-	-	-	-	-	-	93.3%	-	-
Operating profit margin	-	-	-	-	-	-	12.3%	19.6%	-	-
Non-operating income	17	7	5	2	4	3	17	139	133	225
Non-operating expenses	96	196	34	95	79	112	32	103	57	37
Recurring profit	**-2,630**	**-2,317**	**-3,977**	**-2,749**	**-4,377**	**-4,616**	**1,001**	**2,000**	**-736**	**-3,689**
YoY	-	-	-	-	-	-	-	99.8%	-	-
Recurring profit margin	-	-	-	-	-	-	12.1%	20.0%	-	-
Extraordinary gains	3	9	17	10	4	529	0	106	101	14
Extraordinary losses	1	1	15	10	-	-	-	-	561	132
Income taxes	4	4	4	4	4	4	-1,031	927	767	27
Implied tax rate	-	-	-	-	-	-	-	-	-	-
Net income	**-2,632**	**-2,313**	**-3,978**	**-2,753**	**-4,376**	**-4,090**	**2,032**	**1,179**	**-1,963**	**-3,833**
YoY	-	-	-	-	-	-	-	-42.0%	-	-
Net margin	-	-	-	-	-	-	24.6%	11.8%	-	-

Source: Shared Research based on company data
Note: Figures may differ from company materials due to differences in rounding methods.

See the Earnings Structure section for more information about specific items (from total sales to recurring profit) on the company's income statement. Regarding non-operating profit/loss, extraordinary gain/loss, corporate income tax, etc., extraordinary gain of JPY529mn in FY12/20 mainly comes from the booking of JPY525mn in settlement payment. Income taxes of -JPY1.0bn in FY12/21 were due to the booking of JPY1.3bn in deferred tax assets. The extraordinary loss of JPY561mn in FY12/23 was due to impairment losses and other factors based on an assessment of recoverability under the Accounting Standard for Impairment of Fixed Assets.

Historical forecast accuracy

Results vs. initial forecast	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
(JPYmn)	Parent	Parent	Parent	Parent	Parent	Parent	Parent	Cons.	Cons.	Cons.
Sales (initial forecast)	1,785	2,339	2,903	4,201	4,465	3,404	9,151	10,992	7,000	3,641
Sales (Results)	1,933	2,368	3,444	3,836	2,838	2,987	8,257	10,008	5,590	2,453
Results vs. initial forecast	**8.3%**	**1.2%**	**18.6%**	**-8.7%**	**-36.4%**	**-12.2%**	**-9.8%**	**-8.9%**	**-20.1%**	**-32.6%**
Operating profit (initial forecast)	-1,654	-2,778	-3,238	-2,981	-3,587	-5,090	1,361	1,770	-331	-2,837
Operating profit (Results)	-2,552	-2,127	-3,947	-2,656	-4,302	-4,506	1,016	1,964	-812	-3,877
Results vs. initial forecast	**-**	**-**	**-**	**-**	**-**	**-**	**-25.3%**	**10.9%**	**-**	**-**
Recurring profit (initial forecast)	-1,650	-2,811	-3,303	-3,044	-3,612	-5,134	1,350	1,750	-351	-2,867
Recurring profit (Results)	-2,630	-2,317	-3,977	-2,749	-4,377	-4,616	1,001	2,000	-736	-3,689
Results vs. initial forecast	**-**	**-**	**-**	**-**	**-**	**-**	**-25.8%**	**14.3%**	**-**	**-**
Net income (initial forecast)	-1,654	-2,815	-3,306	-3,056	-3,612	-4,803	1,149	1,480	-370	-2,870
Net income (Results)	-2,632	-2,313	-3,978	-2,753	-4,376	-4,090	2,032	1,179	-1,963	-3,833
Results vs. initial forecast	**-**	**-**	**-**	**-**	**-**	**-**	**76.9%**	**-20.3%**	**-**	**-**

Source: Shared Research based on company data

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

Balance sheet

Balance sheet (JPYmn)	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
	Parent	Parent	Parent	Parent	Parent	Parent	Parent	Cons.	Cons.	Cons.
Assets										
Cash and deposits	4,261	5,719	2,947	4,821	3,911	3,849	3,860	6,283	6,517	3,964
Marketable securities	-	-	-	-	-	-	-	-	-	-
Accounts receivable	301	487	490	412	549	407	2,148	2,085	913	423
Inventories	133	273	363	534	1	945	386	469	232	239
Other current assets	131	205	237	271	427	615	355	476	420	299
Total current assets	**4,827**	**6,685**	**4,037**	**6,038**	**4,887**	**5,815**	**6,748**	**9,313**	**8,083**	**4,924**
Buildings (net)	22	31	28	37	47	43	45	41	-	-
Tools, furniture, and fixtures (net)	31	43	18	20	19	34	39	28	-	-
Total tangible assets	**53**	**75**	**47**	**57**	**75**	**77**	**84**	**69**	**-**	**-**
Investments and other assets	**53**	**77**	**100**	**73**	**70**	**81**	**1,362**	**829**	**88**	**44**
Software	51	42	66	51	95	296	255	222	-	-
Other	1	-	3	20	146	6	4	-	-	-
Total intangible assets	**52**	**42**	**69**	**71**	**241**	**302**	**259**	**222**	**-**	**-**
Total fixed assets	**158**	**193**	**216**	**201**	**386**	**459**	**1,705**	**1,121**	**88**	**44**
Total assets	**4,984**	**6,878**	**4,252**	**6,239**	**5,274**	**6,275**	**8,453**	**10,433**	**8,170**	**4,968**
Liabilities										
Accounts payable	320	322	604	726	121	665	70	47	-	-
Unearned revenue	-	-	-	-	-	193	-	-	-	-
Accounts payable–other	184	553	331	504	639	646	515	1,164	854	636
Short-term debt	-	-	-	-	-	-	-	-	-	-
Other	47	68	76	107	112	111	933	697	103	130
Total current liabilities	**551**	**942**	**1,011**	**1,336**	**872**	**1,615**	**1,518**	**1,924**	**957**	**766**
Long-term debt	-	-	-	-	-	-	-	-		-
Corporate bonds	-	450	-	-	-	-	-	-		-
Other fixed liabilities	2	1	1	1	2	2	189	20	4	5
Total fixed liabilities	**2**	**451**	**1**	**1**	**2**	**2**	**189**	**3**	**4**	**5**
Total interest-bearing debt	-	-	-	-	-	-	-	-	-	-
Total liabilities	**552**	**1,394**	**1,013**	**1,338**	**874**	**1,617**	**1,707**	**1,927**	**960**	**771**
Net assets										
Capital stock	8,331	9,948	10,762	12,973	14,871	17,045	17,158	17,548	17,953	18,337
Capital surplus	8,301	9,918	10,732	12,943	14,841	17,019	17,133	17,523	17,928	18,312
Retained earnings	-12,500	-14,813	-18,791	-21,543	-25,919	-30,010	-27,978	-26,889	-28,852	-32,686
Treasury stock	-0	-0	-0	-0	-15	-18	-86	-88	-89	-90
Share subscription rights	300	431	537	530	621	620	519	412	277	317
Net assets	**4,432**	**5,485**	**3,239**	**4,902**	**4,400**	**4,657**	**6,746**	**8,506**	**7,210**	**4,198**
Working capital	114	439	249	220	429	686	2,464	2,508	1,145	662
Total interest-bearing debt	-	-	-	-	-	-	-	-	-	-
Net debt	-4,261	-5,719	-2,947	-4,821	-3,911	-3,849	-3,860	-6,283	-6,517	-3,964

Source: Shared Research based on company data

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

Assets

SymBio outsources manufacturing and clinical development. Therefore, most of the company's assets are cash and deposits.

Within current assets, inventory assets consist mostly of Treakisym® merchandise inventory. Since FY12/23, the company has not recorded tangible fixed assets due to the application of impairment accounting.

Liabilities

As of FY12/24, the company had no interest-bearing debt. Recorded liabilities are and accrued expenses and others.

Net assets

Capital stock and capital surplus are increasing as a result of fundraising efforts. However, there is a deficit in retained earnings as the company continued to post losses.

Cash flow statement

Cash flow statement	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
(JPYmn)	Parent	Parent	Parent	Parent	Parent	Parent	Parent	Cons.	Cons.	Cons.
Cash flows from operating activities (1)	-2,272	-1,960	-3,817	-2,325	-4,351	-4,122	140	1,614	-195	-3,417
Cash flows from investing activities (2)	1,489	-44	-78	-26	-216	-160	-71	-47	-377	-4
Free cash flow (1+2)	-783	-2,004	-3,894	-2,351	-4,567	-4,283	69	1,567	-571	-3,420
Cash flows from financing activities	-3	3,658	1,164	4,272	3,740	4,222	-72	628	680	708
Depreciation and good will amortization (A)	24	26	30	35	38	64	94	98	96	-
Capital expenditures (B)	-24	-28	-57	-40	-217	-149	-64	-52	-233	-47
Change in working capital (C)	-98	325	-190	-29	209	257	1,777	44	-1,363	-483
Simple FCF (NI + A + B - C)	-2,534	-2,640	-3,815	-2,729	-4,764	-4,433	285	1,182	-737	-3,397
Cash and cash equivalents (year-end)	4,261	5,719	2,947	4,821	3,911	3,849	3,860	6,283	6,517	3,964

Source: Shared Research based on company data
Note: Figures may differ from company materials due to differences in rounding methods.

Cash flows from operating activities

Cash flows from operating activities almost matches the company's net income before income tax.
In FY12/21, accounts receivable increased as the company started in-house sales, giving rise to a gap between cash flows from operating activities and net income before income tax.

Cash flows from investing activities

Outlays on the purchase of tangible fixed assets and intangible assets are limited as SymBio outsources clinical trials and manufacturing. But investment in time deposits and securities meant outflow from investing activities widened in FY12/12 and FY12/13. SymBio booked an inflow of JPY1.5bn in FY12/15 due to payments from time deposits and the redemption of securities.

Cash flows from financing activities

The company has historically often reported inflows from financing activities.

Major fundraising activities

年月日	Total shares issued	Total shares issued	Capital stock and capital surplus	Capital stock and capital surplus	
	Total change in issued shares	Total outstanding balance	Increase amount		
	(shares)	(shares)	(JPYmn)	(JPYmn)	
Dec 2014	1,756,666	32,390,923	544	16,632	Exercise of stock acquisition rights attached to unsecured convertible bondst and other stock acquisition rights
Jan–Dec 2016	14,139,901	46,530,824	3,235	19,867	Exercise of stock acquisition rights attached to unsecured convertible bonds and other stock acquisition rights
Jan-Dec 2017	7,518,400	54,049,224	1,627	21,493	Exercise of stock acquisition rights attached to unsecured convertible bondst and other stock acquisition rights
Apr–Dec 2018	28,349,700	82,398,924	4,422	25,915	Exercise of stock acquisition rights
Jan–Dec 2019	1,726,800	26,437,681	3,796	29,711	Exercise of stock acquisition rights
Jan–Dec 2020	11,765,275	38,202,956	4,349	34,064	Exercise of stock acquisition rights
Jan–Dec 2021	254,250	38,457,206	221	34,285	Exercise of stock acquisition rights
Jan–Dec 2022	1,146,400	39,603,606	787	35,072	Exercise of stock acquisition rights
Jan—Dec 2023	2,674,475	42,278,081	808	35,880	Issuance of new shares through third-party allotment and exercise of stock options
Jan–Dec 2024	3,650,775	45,928,856	768	36,649	Resolved to raise new funds through the exercise of stock options (December 2024)

Source: Shared Research based on company materials
In July 2019, the company conducted a 4-to-1 reverse stock split, reducing the number of issued shares by 73,088,043.

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.; TSE Prime: 4568), Medical & Biological Laboratories Co., Ltd., EPS Corporation, and SBI Holdings, Inc. (TSE Prime: 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 more than 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).

SymBio obtained Japanese marketing and manufacture approval for Treakisym® in October 2010 and began domestic sales in December of that year.

Treakisym® for relapsed or refractory low-grade NHL and MCL is the company's mainstay product. Clinical trials are also in preparation or under way toward attaining domestic approval for additional Treakisym® indications, RI formulation of Treakisym®, and anticancer drug rigosertib for myelodysplastic syndromes.

In addition, after acquiring exclusive worldwide rights from Chimerix in September 2019 to develop, manufacture, and market brincidofovir for all indications except smallpox, SymBio looks to commercialize it by the mid-2020s.

Date	Summary
Mar 2005	SymBio Pharmaceuticals Limited established with JPY30mn in capital.
Dec 2005	License Agreement finalized with Astellas Pharma GmbH for SyB L-0501 (bendamustine) development and commercialization rights in Japan.
Mar 2006	Manufacturer's License (packaging, labeling and storage) obtained from Tokyo Metropolitan Government (License #13AZ200010).
Mar 2007	License Agreement finalized with Astellas Deutschland GmbH for SyB L-0501 (bendamustine) development & commercialization rights in China (HK), Taiwan, South Korea and Singapore.
Aug 2008	License Agreement finalized with Eisai Co., Ltd. for co-development and commercialization rights of SyB L-0501 (bendamustine) in Japan.
Mar 2009	SymBio Pharmaceuticals concluded 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 South Korea and Singapore.
Sep 2010	SymBio Pharmaceuticals and Eisai launch SYMBENDA® (bendamustine) in Singapore for the treatment of Low-grade Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia.
Oct 2010	Announced NDA Approval of Treakisym® (bendamustine) in Japan.
Dec 2010	Launched Treakisym® in Japan.
Jul 2011	Onconova and SymBio Pharmaceuticals concluded License Agreement for SyB L-1101/SyB C-1101 (rigosertib, a Phase III stage multi-kinase inhibitor for Myelodysplastic Syndromes).
Oct 2011	Launched Symbenda® (bendamustine hydrochloride) in South Korea for the treatment of Chronic Lymphocytic Leukemia and multiple myeloma.
Oct 2011	Listed on Osaka Securities Exchange JASDAQ Growth Market.
Feb 2012	Launched Innomustine® (bendamustine hydrochloride) in Taiwan for the treatment of Low-grade Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia.
Aug 2016	Received approval for the additional indication of chronic lymphocytic leukemia for Treakisym®.
Dec 2016	Obtained approval for the additional indication of untreated low-grade non-Hodgkin's lymphoma and mantle cell lymphoma for the anticancer drug Treakisym®
Sep 2017	Concluded an exclusive license agreement with Eagle Pharmaceuticals, Inc. (US) on rights to develop, market, and sell Eagle's bendamustine hydrochloride RTD and RI formulations in Japan.
Sep 2019	Concluded an exclusive global license agreement with Chimerix Inc. (US) on rights to develop, manufacture, and market antiviral brincidofovir for all indications except smallpox.
Dec 2020	Began in-house sales of anticancer drug Treakisym®
Jan 2021	Launched Treakisym® liquid formulation (RTD)
Mar 2021	Obtained approval for use of Treakisym® in bendamustine-rituximab combination therapy to treat r/r DLBCL
Feb 2022	Received approval for Treakisym® rapid infusion (RI) administration

Source: Shared Research based on company data

Major shareholders

Top shareholders	Shares held (shares)	Shareholding ratio
Fuminori Yoshida	1,684,200	3.46%
MSIP CLIENT SECURITIES	1,118,572	2.30%
Sukenori Ito	430,000	0.88%
Rakuten Securities, Inc.	392,500	0.81%
Matsui Securities Co., Ltd.	341,400	0.70%
SBI Securities Co., Ltd.	225,480	0.46%
Norio Osakabe	201,100	0.41%
Monex, Inc.	196,904	0.40%
Nomura Securities Co., Ltd.	196,656	0.40%
MACQUARIE BANK LIMITED DBU AC	189,100	0.39%
Total	4,975,912	10.21%

Source: Shared Research based on company data
As of June 30, 2025
Note: Shareholding ratio calculated excluding treasury shares from shares issued.

Top management

President and CEO Fuminori Yoshida

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

As of end-FY12/24, the company had 108 employees (-1 YoY). Since reaching a peak of 141 employees at end-FY12/21, the company has reduced its headcount by 33 over three fiscal years.

Number of employees	FY12/15	FY12/16	FY12/17	FY12/18	FY12/19	FY12/20	FY12/21	FY12/22	FY12/23	FY12/24
	Parent	Parent	Parent	Parent	Parent	Parent	Parent	Cons.	Cons.	Cons.
Number of employees	74	77	78	90	107	127	141	122	109	108
Change	5	3	1	12	17	20	14	-19	-13	-1

Source: Shared Research based on company data

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: Shared Research based on 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 2008 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%, and 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 acceptable if a bridging study demonstrates that such data can be used for Japanese people.

Glossary

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.

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.

Medical Representative (MR)

A medical information specialist is responsible for providing, collecting, and transmitting information on the quality, efficacy, safety, and other aspects of pharmaceuticals by visiting medical institutions and holding discussions with healthcare professionals. The specialist is an expert on the company's pharmaceutical products.

Overall Survival (OS)

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

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.

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.

Myelodysplastic Syndromes

Myelodysplastic Syndrome 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 infection or bleeding due to the reduction in blood cells. The disease is most common among the elderly. 10 to 20% of MDS patients progress to acute leukemia.

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.

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.

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.

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.

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).

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.

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.

Chronic Lymphocytic Leukemia (CLL)

CLL is a type of cancer in which lymphocytes—a type of white blood cell—become cancerous and proliferate excessively in the bone marrow. It is the most common form of leukemia in Western countries, accounting for approximately 30% of all leukemia cases. In Japan, however, it is a rare disease, with an estimated patient population of around 2,000 and an incidence rate of roughly 0.3 per 100,000 people.

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.

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.

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.

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.

News and topics

SymBio confirms efficacy of BCV in malignant brain tumors and identifies potential biomarker genes for predicting effectiveness

2025-05-12

SymBio Pharmaceuticals Limited announced the confirmation of the efficacy of brincidofovir (BCV) for malignant brain tumors and the identification of biomarker genes (predictive factors of efficacy).

In a joint study with the University of California San Francisco Brain Tumor Center, the company confirmed the antitumor effects of BCV on glioblastoma in preclinical trials. In April 2025, it presented these findings at the annual meeting of the American Association for Cancer Research (AACR) in Chicago. The company also reported on the efficacy of BCV in malignant brain tumors and the identification of potential biomarker genes predictive of its effectiveness. The main points of the presentation are as follows.

- Confirmation of efficacy in malignant brain tumors: BCV monotherapy showed dose-dependent efficacy starting from low concentrations. The drug also demonstrated antitumor activity in malignant brain tumor cells resistant to the current standard therapy, temozolomide.
- Biomarker identification: Two genetic biomarkers that may predict BCV's therapeutic effect were identified, raising expectations for patient-specific treatment prediction.
- Antitumor effect in an intracranial mouse model: In an animal model, BCV suppressed tumor growth and significantly extended survival time.

Conclusion of agreement to establish a bond issuance program with stock acquisition rights and the issuance of the 7th unsecured convertible bonds with stock acquisition rights through third-party allotment

2025-03-25

SymBio Pharmaceuticals Limited announced the conclusion of an agreement to establish a bond issuance program with stock acquisition rights and the issuance of its 7th series of unsecured convertible bonds with stock acquisition rights through a third-party allotment.

In December 2024, the company entered into an agreement with Cantor Fitzgerald Europe to establish a bond issuance program with stock acquisition rights.

Under the program, SymBio initially planned for four allocations, from the 4th through the 7th tranches. However, it canceled the sixth tranche in February 2025. In March 2025, the company approved the seventh tranche.

Following the resolution to proceed with the seventh tranche, SymBio revised the total maximum payment amount for bonds with stock acquisition rights to be issued under the program from JPY2.4bn to JPY1.8bn. It also revised the maximum number of shares to be issued upon full conversion of the bonds from 11,300,000 shares (representing 113,000 voting rights) to 10,602,000 shares (106,023 voting rights). As a result, the company revised the initially projected dilution of up to 24.61% (24.86% in terms of voting rights), relative to its 45,916,000 outstanding shares (454,609 voting rights), to a maximum of 23.09% (23.32% in terms of voting rights).

Amount to be raised

- Total payment amount: JPY1.8bn (revised from the initially planned JPY2.4bn)
- Approximate amount of various issuance-related expenses: JPY100mn (unchanged)
- Estimated net proceeds: JPY1.7bn (revised from the initially estimated JPY2.3bn)

Use of net proceeds

The proceeds of JPY1.7bn from the third-party allotments are planned to be used as follows (excerpt from the February 20, 2025 release).

- Development funds for antiviral drug brincidofovir (direct expenses): JPY960mn (revised from the initially planned JPY1.3bn; scheduled for expenditure from January 2025 to October 2025)

- Development funds for antiviral drug brincidofovir (indirect expenses): JPY740mn (revised from the initially planned JPY1.0bn; scheduled for expenditure from January 2025 to October 2025)

SymBio expands global phase Ib/II clinical trial of BCV for malignant lymphoma patients to Singapore

2025-02-06

SymBio Pharmaceuticals Limited announced the launch of a clinical trial for BCV in the oncology field in Singapore.

The company will expand its global phase Ib/II clinical trial of BCV for patients with relapsed or refractory lymphoma, including NK/T-cell lymphoma, to Singapore. This trial initially began in Japan in August 2024 and is now being extended to Singapore.

Symbio appoints CEO and president of its US subsidiary, SPU.

2024-12-27

SymBio Pharmaceuticals Limited announced the appointment of the CEO and president of its US subsidiary, SPU.

The company appointed Masaru Taguchi as CEO and president of its US subsidiary, SPU, effective January 2025. Mr. Taguchi has led overseas subsidiary launches and global business expansion at Otsuka Pharmaceutical Co., Ltd. and Philips Japan, Ltd.

Conclusion of agreement to establish a bond issuance program with stock acquisition rights and the issuance of the 4th unsecured convertible bonds with stock acquisition rights through third-party allotment

2024-12-25

SymBio Pharmaceuticals Limited announced the conclusion of agreement to establish a bond issuance program with stock acquisition rights and the issuance of the 4th unsecured convertible bonds with stock acquisition rights through a third-party allotment.

The company resolved to enter into an agreement with Cantor Fitzgerald Europe to establish a bond issuance program with stock acquisition rights and to issue the 4th unsecured convertible bonds with stock acquisition rights through a third-party allotment.

The convertible bonds with stock acquisition rights will be issued across four tranches: the 4th, 5th, 6th, and 7th third-party allotments. The total payment amount for bonds issued under the program will be JPY2.4bn. If all the bonds are converted, the maximum number of shares to be issued will be 11,300,000 shares (representing 113,000 voting rights). This corresponds to a maximum dilution of 24.61% (24.86% in terms of voting rights) relative to the company's total number of issued shares of 45,916,000 shares (454,609 voting rights) as of September 30, 2024.

Amount to be raised

- Total payment amount: JPY2.4bn
- Approximate amount of various issuance-related expenses: JPY100mn
- Estimated net proceeds: JPY2.3bn

Use of net proceeds

The proceeds from the third-party allotments are planned to be used as follows.

- Development funds for antiviral drug brincidofovir (direct expenses): JPY1.3bn (scheduled for expenditure from January 2025 to October 2025)

- Development funds for antiviral drug brincidofovir (indirect expenses): JPY1.0bn (scheduled for expenditure from January 2025 to October 2025)

Overview of the offering

Overview of the issuance of 4th, 5th, 6th, 7th convertible bonds with stock acquisition rights

Payment dates	December 25, 2024, January 20, 2025, February 21, 2025, March 26, 2025 (four installments in total)
Issuance price of bonds with stock acquisition rights	JPY2.4bn (maximum)
Offering method	Third-party allotment
Allottee	Cantor Fitzgerald Europe

Source: Shared Research based on company data

SymBio presents at a US conference on the potential therapeutic use of BCV in combination with immune checkpoint inhibitors

2024-12-13

SymBio Pharmaceuticals Limited presented at a US conference on the potential therapeutic use of intravenous brincidofovir (BCV) in combination with immune checkpoint inhibitors.

The company presented research findings from a study jointly conducted with the National Cancer Centre Singapore on the potential use of BCV in combination with immune checkpoint inhibitors at the 66th Annual Meeting of the American Society of Hematology. The study showed that this drug combination significantly enhances immune cell infiltration into tumors.

Symbio to give a presentation on the combination therapy of BCV and immune checkpoint inhibitors at a medical conference

2024-11-20

SymBio Pharmaceuticals Ltd. announced that it will give a presentation on the combination therapy of brincidofovir (BCV) and immune checkpoint inhibitors for malignant lymphoma at a medical conference.

The company will give a presentation on the combination therapy of BCV and immune checkpoint inhibitors for malignant lymphoma at the 66th Annual Meeting of the American Society of Hematology (ASH). This presentation highlights the results of joint research conducted with the National Cancer Centre Singapore.

- The abstract for this presentation is available on the ASH website at the link below:
https://ash.confex.com/ash/2024/webprogram/Paper202761.html

Symbio appoints Executive Vice President and CMO

2024-11-05

SymBio Pharmaceuticals Limited announced the appointment of an Executive Vice President and Global Chief Medical Officer (CMO).

The company appointed Dr. Jay Marshall Feingold as Executive Vice President and Global Chief Medical Officer (CMO). He will also serve as Senior Vice President at the company's US subsidiary, SymBio Pharma USA (SPU).

Dr. Feingold previously held key positions at Wyeth (acquired by Pfizer in 2009) and Daiichi Sankyo Co., Ltd.

Publication of detailed data from BCV's phase IIa clinical trial for adenovirus infection

2024-10-23

SymBio Pharmaceuticals Ltd. announced the presentation of detailed data from the Phase IIa clinical trial of brincidofovir (BCV) for adenovirus (AdV) infection at a conference.

Detailed data from a Phase IIa clinical trial of BCV in patients with AdV infection was presented at ID Week 2024 (Infectious Diseases Society of America). The Proof of Concept (POC) for the trial was established in May 2023 and has already been presented at several major conferences in Europe and the US. This latest presentation highlighted the additional findings on the correlation between AdV clearance from the bloodstream and improvements in clinical symptoms.

- In Cohort 3 (0.4 mg/kg, twice-weekly dosing group), AdV was cleared from the bloodstream in all nine patients (100%). Additionally, AdV-related clinical symptoms were resolved in six patients, while three patients showed improvement.
- Out of a total of 31 cases in Cohorts 1 to 4, AdV was cleared from the bloodstream in 20 patients. Of these 20, 19 (95%) experienced either resolution of AdV-related clinical symptoms (15 patients) or symptom improvement (four patients).

SymBio settles a patent infringement lawsuit concerning Treakisym®

2024-09-30

SymBio Pharmaceuticals Co., Ltd. announced that it has reached a settlement in the patent infringement lawsuit concerning Treakisym®.

On September 30, 2024, the company settled a patent infringement lawsuit, which it had jointly filed with US-based Eagle Pharmaceuticals, Inc. against Towa Pharmaceutical Co., Ltd. The lawsuit pertained to a generic version of SymBio's product, Treakisym® Intravenous Infusion 100mg/4mL.

The terms of the settlement are confidential, and the impact on the company's performance for FY12/24 is expected to be minimal.

Initiation of an international Phase Ib clinical trial of BCV targeting patients with malignant lymphoma

2024-08-19

SymBio Pharmaceuticals Limited announced the initiation of clinical trials for BCV in the oncology field.

The company has initiated an international Phase Ib/II clinical trial of BCV targeting patients with relapsed or refractory lymphoma (malignant lymphomas such as NK/T-cell lymphoma). This advancement to a First in Human (FIH) trial in the oncology field is based on the results of a collaborative non-clinical study on BCV with the National Cancer Centre Singapore.

This is the third clinical trial for BCV, following trials for Adenovirus (AdV) infections after hematopoietic stem cell transplantation and Cytomegalovirus infections after hematopoietic stem cell transplantation. It marks the first clinical trial for BCV in the oncology field.

Profile

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Exchange Listing

2011-10-20

Fiscal Year-End

Dec

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