

Symbio Pharmaceuticals Ltd.

(4582 JASDAQ)

Issue date: November 8, 2018

Firm decision made to set up its direct sales structure

Company announces plan to market Treakisym® itself

On October 16, 2018 Symbio announced it was preparing to set up an in-house structure for the marketing of its main earnings driver, Treakisym®, from 2021. The company had received approaches from a number of companies offering advantageous terms in the form of sales tie-ups but has made a firm decision to go it alone. The reasons behind this decision are threefold:

- ① By having its own group of medical representatives (MR's) the company can acquire a clearer insight into market demand and react more quickly to that demand.
- ② While building and maintaining the sales structure will entail costs those costs will be less than the outflow of value to a partner, thus allowing the company to capture the maximum value from Treakisym®.
- ③ Treakisym® is indicated for one type of blood cancer. The same group of specialised blood cancer MR's can be used for handling rigosertib (currently under development for the treatment of another kind of cancer, myelodysplastic syndrome, MDS).

The business value (pre-tax) of Symbio's pipeline: JPY41.2 – 44.8 billion

If the company brings sales in-house, we posit a pre-tax business value for Treakisym® of JPY30.2 billion on the assumption that trials targeting recurrent/intractable medium/high grade non-Hodgkin's lymphoma (r/r DLBCL) yield an 80% probability of success. At 100% probability this business value rises to JPY34 billion. However, if the company retains its current sales structure, we estimate its business value would not exceed JPY14.3 – 15.2 billion, which brings into sharp relief the impact of having its own direct marketing structure. The development of rigosertib is also going well, with a pre-tax business value we posit at JPY10.8 billion. These two products together come to JPY41.2 – 44.8 billion (pre-tax). After tax and after adjusting for full-company costs, including new drug discovery costs, and adding in cash on the balance sheet, we arrive at an estimated business value of JPY23.5 – 26.7 billion. However, note should be taken of the fact that fund raising from the exercise of options on the 2018 series has already been completed, and there is approximately JPY7 billion in prospect for the 2019 and 2020 options series.

Profits to trend further upward after turning positive in 2021

In its 4-year medium term management plan, released in February 2018, Symbio's figures were based on the premise that its direct marketing would begin in the period ending December 2021. The company averred that there was no change in its outlook at the present time and that earnings would likely turn positive in 2021. Fair Research Inc. also comes to the same conclusion, positing revenues in 2021 of JPY10.4 billion and operating profits turning positive at JPY1.2 billion (assuming treatment of r/r DLBCL using Treakisym® has a 100% probability of success, the rigosertib injection formulation 50% and the rigosertib oral formulation 30%). Subsequently, in 2022 the rigosertib injection formulation comes to the market and we posit revenues of JPY12.8 billion and operating profits of JPY2.6 billion, with these figures rising in 2023 to JPY15.9 billion and JPY4.9 billion, respectively. The launch of the rigosertib oral formulation in 2024 would then boost revenues above JPY20 billion and operating profits to as much as JPY7.4 billion. However, it should be borne in mind that Symbio is keen on drug development and that the possible introduction and development of new drug candidates leaves a question mark over the Fair Research profit forecasts beyond 2022.

Follow-up Report

Fair Research Inc.

Tsuyoshi Suzuki

Company Outline

Location	Tokyo, Japan
President	Fuminori Yoshida
Established	March 2005
Capital	JPY11,834 million
Listed	October 2011
URL	www.symbiopharma.com
Industry	Pharmaceuticals
Employees	82 (consol. basis)

Key Indicators (at Nov. 7, 2018)

Stock Price	218
Year High	268
Year Low	116
Shares Issued	76,662 thousand
Trading Unit	100 shares
Market Cap	16,712 mil. JPY
Dividend (est)	0
EPS (est)	-50.62 JPY
PER (est)	na
BPS (actual)	46.22 JPY
PBR (actual)	4.72X

(Note: EPS, PER, BPS, PBR are on the basis of shares outstanding, excl. treasury shares)

Results	Revenues JPY mil	YOY %	OP Income JPY mil	YOY %	RP JPY mil	YOY %	Net Income JPY mil	YOY %	EPS JPY	Share Price	
										High	Low
2015/12 Actual	1,933	-1.1	-2,551	NA	-2,630	NA	-2,632	NA	-81.3	383	177
2016/12 Actual	2,368	22.5	-2,127	NA	-2,316	NA	-2,313	NA	-58.82	509	173
2017/12 Actual	3,444	45.4	-3,947	NA	-3,976	NA	-3,977	NA	-79.78	311	200
2017/12 2Q Actual	1,786	47.5	-1,235	NA	-1,268	NA	-1,266	NA	-26.09	311	200
2018/12 2Q Actual	1,928	8.0	-1,324	NA	-1,377	NA	-1,388	NA	-23.79	247	144
2018/12 Forecast	4,201	22.0	-2,981	NA	-3,044	NA	-3,056	NA	-50.62		

Company outline and philosophy

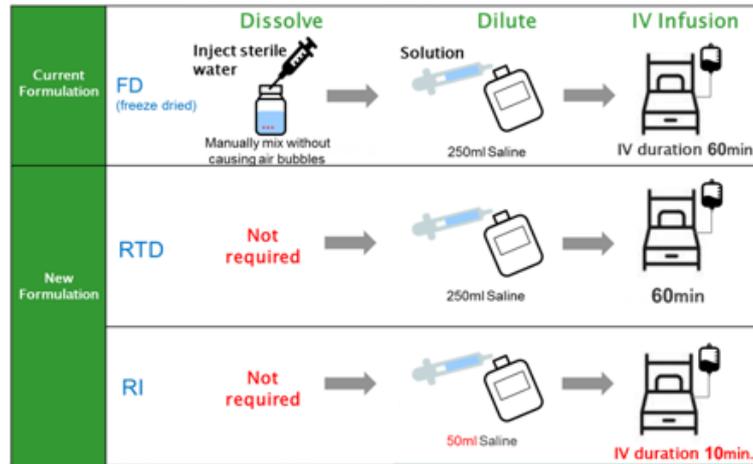
<p>Business Model</p> <p>Requiring neither labs nor factories SymBio is a pharmaceuticals venture with none of the risks normally assumed by drug discovery firms, operating a niche strategy focusing on maximising profits</p>	<p>SymBio Pharmaceuticals Ltd. seen as a bio-venture but has the following distinguishing characteristics:</p> <p>① Controls risk and maximises earnings with a “labless” and “fabless” strategy. In terms of business model, the company does not itself conduct basic research on new drugs. Rather, it seeks out and carefully investigates new drug candidates developed by drug discovery ventures and pharmaceutical companies around the world. A new drug selected as a result of this process would typically be the subject of a licensing agreement and, following development in Japan, would either be licensed out to another company for commercialization or commercialized by SymBio itself.</p> <p>(Since the company itself conducts drug development in Japan it is not simply a technology trader, and when it develops its own sales structure it will become, in name and in fact, a fully-fledged pharmaceutical company).</p> <p>② Targets large market share and high earnings using a niche strategy. The company focuses its development efforts on drugs for relatively rare conditions in, for example, oncology, hematology and pain management which, despite strong medical needs, the major pharmaceutical companies have mostly avoided. It seeks to maximize market share and profits using this niche strategy.</p> <p>③ Post-POC (proof of concept) strategy In most cases proof of concept has already been established. By insisting on prior evidence of efficacy and safety in human subjects, the company reduces the development risks of new drug candidates.</p>
<p>The determinants of commercial success are interactions with a network of drug discovery companies and the ability to discern and evaluate</p>	<p>The above characteristics of the company’s business model allow it to avoid most of the risks confronting drug discovery companies, while at the same time maximising earnings potential.</p> <p>The success or failure of this business model is dependent on having a network of drug discovery companies worldwide and a keenly discerning eye.</p>
<p>The company is a bio-venture in the rare position of having a product which was approved and brought to market within five years of being adopted</p>	<p>Evidence of this ability is provided by the company’s track record. Normally, it takes some 10-20 years to bring a drug from basic research to the market. In terms of the probability of success, some estimates suggest that, counting from the chemical compound stage, it is less than 1/30,000, and even from the POC stage, around 7-8%. But SymBio managed to get its first product, Treakisym®, from adoption to manufacturing and commercial approval in around five years, and in the three years following launch captured 57% of the market. In the eleven or so years since founding, the company has screened 1,500 drug candidates, of which over 600 have been formally investigated in-house. And of these, five products have been adopted and two are currently under development.</p>
<p>Company structure and staff quality are key</p>	<p>We believe this track record has been made possible by the expertise of the company’s staff and by the way the company is organized. SymBio has a staff of 82, of whom more than 40 are involved in research and development. The drug search function is supported by a Scientific Advisory Board (SAB) of specialists (including Nobel Prize candidates) who support drug search activities. Needless to say, the presence of the company’s founder and CEO, Fuminori Yoshida, is of great value in terms of both the experience he brings and his extensive personal network</p>

	(for CV's of the SAB members and of Fuminori Yoshida see our previous report released on February 19, 2018).																																
Company preparing to market Treakisym® in-house	Preparations underway for its direct marketing structure for Treakisym® On October 16, the company announced that it had started preparations for a switch to its direct marketing structure for domestic sales of its key product, Treakisym®, starting in 2021. At present SymBio markets Treakisym® through Eisai Co., Ltd. but the agreement governing that tie-up is due to expire in December 2020. The company has therefore been looking at all options on how to handle marketing after that date, including switching to its direct structure or arranging a sales tie-up with a major pharmaceuticals company.																																
Three advantages to the direct sales option	The company appears to have received a number of attractive offers from companies looking to take over sales but has now firmly decided to develop its own direct sales structure, a decision which should be regarded positively. There are three main reasons for this:																																
Firstly, accurate grasp of market demand	① By having its own group of medical representatives (MR's) the company can acquire a clearer insight into market demand and react more quickly to that demand.																																
Secondly, big increase in business value	② While developing and maintaining its own sales structure will entail costs, those costs will be less than the outflow of value to a sales partner, thus allowing the company to capture the maximum value from Treakisym®.																																
Having its own sales structure will boost the business value of Treakisym® to above JPY30 billion	If we re-model the business value of Treakisym® (assuming an 80% success probability in trials targeting recurrent/intractable medium/high-grade non-Hodgkin's lymphoma: r/r DLBCL), in the event the company introduces its own marketing structure from 2021, the business value (discounted present value) of Treakisym® rises to JPY30.2 billion, which compares very favourably with the JPY14.3 billion we calculate under the current marketing tie-up arrangement. Modeling the business value of Treakisym® (revised) (JPY 100 mil)																																
	<table border="1"> <thead> <tr> <th rowspan="2">Discount Rate</th> <th colspan="2">Direct Sales</th> <th colspan="2">Current Sales Channel</th> </tr> <tr> <th>r/rDLBCL Success Probability</th> <th>80%</th> <th>100%</th> <th>r/rDLBCL Success Probability</th> <th>80%</th> <th>100%</th> </tr> </thead> <tbody> <tr> <td>10%</td> <td>302.2</td> <td>340.0</td> <td>143.1</td> <td>152.0</td> <td></td> <td></td> </tr> <tr> <td>(Ref.)</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>8%</td> <td>349.7</td> <td>393.5</td> <td>159.4</td> <td>169.6</td> <td></td> <td></td> </tr> </tbody> </table>	Discount Rate	Direct Sales		Current Sales Channel		r/rDLBCL Success Probability	80%	100%	r/rDLBCL Success Probability	80%	100%	10%	302.2	340.0	143.1	152.0			(Ref.)							8%	349.7	393.5	159.4	169.6		
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	Source: Calculated by Fair Research Inc. Note: See end of report for assumptions about market size																																
Its direct marketing group would consist of approximately 40 medical representatives	The above figures assume a staff of around 40 MR's for the direct marketing group. The reasoning behind this number is that Japan has some 1100-1200 clinics and hospitals with hematology departments. Some 800-900 of those are hospitals. Symbio could cover the main ones, i.e. one-third of the total or around 320-360 hospitals. At the most, an individual MR could cover 10 facilities, bringing the total requirement to around 40. The company plans to recruit 10 or so product managers by the end of this year and a further 30 staff later on. The cost of hiring MR's (totaling around JPY1 billion) and the cost of promotional activities (around JPY500 million) comes to an annual JPY1.5 billion, meaning																																

The expansion in gross margin will more than compensate for the higher cost of sales

that cost of sales will be JPY1.3 - 1.4 billion higher than the current level (including costs associated with future changes in product formulation for life-cycle management). Further, it is estimated that the gross margin rises from around 14% of the current official drug price to some 50% in its direct marketing context. Hence, any increase in cost of sales will be more than compensated for by a rise in business value.

< Reference: Changes in formulation >



Source: SymBio IR meeting materials

Note: The target date for approval of the RTD formulation is 2021, and for the RI formulation 2022. In the US, there has already been a 97% switch to the RI formulation.

As noted in our previous follow-up report released on August 21, 2018, SymBio commissioned an external entity to survey, as of March, internal medicine practitioners specializing in blood conditions and found that the use of Treakisym® in combination with rituximab (B-R therapy) for the treatment of untreated low-grade non-Hodgkin’s lymphoma had exceeded 50%, well above that for the conventional R-CHOP therapy. Further, in the 2018 edition of Guidelines for Clinical Practice in Hematopoietic Tumors, published by the Japan Society of Hematology on July 20, Treakisym® was newly selected as a standard treatment option for all approved indications.

Comparison of market penetration of B-R therapy and R-CHOP therapy



Note: Target indication: Untreated low-grade non-Hodgkin’s lymphoma

Source: SymBio IR meeting materials

The third advantage of its direct marketing capability is that the same sales force can be used for rigosertib

As a result of the change in the expected launch date we now posit rigosertib's business value at JPY10.8 billion

This development means that Treakisym® has now established itself as a standard therapy in the field of malignant lymphoma. If the anticipated probability of success in current Phase 3 clinical trials targeting recurrent/intractable medium to high-grade non-Hodgkin's lymphoma (r/r DLBCL) is 100%, we would model a business value of JPY34 billion (for reference, assuming a discount rate of 8% yields a business value of JPY39.3 billion).

③ Treakisym® is indicated for one type of blood cancer. The same group of specialised blood cancer MR's can be used for rigosertib, currently under development for the treatment of high-risk myelodysplastic syndrome (MDS), another kind of blood cancer.

In this report, we have revised the dates for application and product launch used in our modelling of rigosertib's business value. Specifically, for the injection formulation, now undergoing global Phase 3 clinical trials (INSPIRE study), we have brought forward by one year both the application for approval (to 2021) and the market launch (to 2022). This reflects the fact that good progress has been made in the development process, such that at the end of July 2018, 36 cases had been registered for Japanese domestic trials, and registration of the targeted 40 cases should be achieved shortly. The launch date for the oral formulation is now likely in 2024, also one year earlier than anticipated.

If we assume the probability of successful development at 50% for the injection formulation (now in Phase 3), and 30% for the oral formulation (now in Phase 1), we can posit a business value for rigosertib of JPY10.8 billion. It should be noted that the estimated values above are predicated on a sales infrastructure, including MR's, which is shared in common with Treakisym® (see end of report for market size considerations).

Rigosertib business value (revised)
(JPY100 mil.)

Discount rate	
10%	108.3
(Ref)	
8%	134.8

Source: Calculated by Fair Research Inc.

Medium-term earnings trend

Even with the establishment of its direct sales structure, there is a high probability of the company turning profitable in 2021

Rising earnings trend to be maintained beyond 2022

High probability of the company turning profitable in 2021

In its 4-year medium-term management plan, released in February 2018, SymBio's figures were based on the premise that direct marketing would begin in the period ending December 2021. The company stated that there was no change in its outlook at the present time and that earnings would likely turn positive in 2021. Fair Research also comes to the same conclusion, positing revenues in 2021 of JPY10.4 billion and operating profits turning positive at JPY1.2 billion (assuming treatment of r/r DLBCL using Treakisym® has a 100% probability of success, the rigosertib injection formulation 50% and the rigosertib oral formulation 30%). What investors want to know now is the level of earnings following the company's move into profitability. The answer should come in February of next year when it will issue a new medium-term management plan revealing its expectations for sales and earnings through to 2022.

SymBio's medium-term management plan

Unit: millions of yen

	FY 2018 (forecast)	FY 2019 (target)	FY 2020 (target)	FY 2021 (target)
Net Sales	4,201	4,238	4,413	11,624 ~ 10,325
Operating Income (loss)	(2,981)	(3,786)	(3,709)	1,777 ~ 878
Ordinary Income (loss)	(3,044)	(3,849)	(3,772)	1,724 ~ 825
Net Income (loss)	(3,056)	(3,853)	(3,776)	1,467 ~ 702

Source: SymBio Medium-Term Management Plan released on February 7, 2018

According to our own modelling, in 2022 the rigosertib injection formulation comes to the market and we posit revenues of JPY12.8 billion and operating profits of JPY2.6 billion, with these figures rising in 2023 to JPY15.9 billion and JPY4.9 billion, respectively. The launch of the rigosertib oral formulation in 2024 would then boost revenues above JPY20 billion and operating profits to as much as JPY7.4 billion. However, it should be borne in mind that SymBio is an active drug developer and that the possible introduction and development of new drug candidates leaves a question mark over the Fair Research earnings forecasts beyond 2022.

Fair Research's vision of the medium-term outlook (revised)

		(JPY100 mil.)						
		2018	2019	2020	2021	2022	2023	2024
Sales	Total	41.8	42.1	45.8	104.8	128.6	159.7	202.8
	Treakisym	41.8	42.1	45.8	104.8	118.6	144.7	170.8
	Rigosertib	0.0	0.0	0.0	0.0	10.0	15.0	32.0
OP Income	Total	-29.7	-37.8	-38.9	12.9	26.6	49.0	74.1
	Treakisym	-5.8	-12.6	-11.0	41.0	49.6	60.6	84.1
	Rigosertib	-4.9	-6.2	-8.8	-9.1	-4.0	7.4	9.0
	Total Costs	-19.0	-19.0	-19.0	-19.0	-19.0	-19.0	-19.0
		In Profit						

Source: Calculations by Fair Research Inc.

Note: Sales figures adjusted for probability of success

<p>While the provision of its direct sales capability will involve costs, the decision to go ahead is a shrewd one</p> <p>We model the combined business value of Treakisym® and rigosertib at JPY41.2 - 44.8 billion, and the enterprise value after adjusting for company costs at JPY30.7 - 34.3 billion (before tax). The after-tax figure we estimate at JPY23.5 - 26.7 billion</p>	<p>Conclusions</p> <p>We posit the business value of Treakisym® sold through the company's own sales structure as JPY30.2 billion (pre-tax), assuming an 80% probability of success in trials targeting recurrent/intractable medium-high grade non-Hodgkin's lymphoma. Assuming a 100% probability of success lifts the value to JPY34 billion. On the other hand, assuming continued use of the current sales channel reduces the business value of Treakisym® to JPY14.3 - 15.2 billion, bringing into sharp relief the advantage of having its own sales structure. The wisdom of deciding on its direct sales structure is clear, even given the set-up costs.</p> <p>The rigosertib product development is also proceeding well. As a result of the change in our estimate of its launch date we have revised its business value (pre-tax) to JPY10.8 billion, bringing the combined two-product business value to around JPY41.2 - 44.8 billion. As a result, we posit enterprise value (pre-tax) at JPY 30.7 - 34.3 billion, after adjusting for company costs, including costs associated with new drug development (excluding the two main products) and after adjusting for cash on the balance sheet. Assuming an effective tax rate of 31% we arrive at a post-tax enterprise value of JPY23.5 - 26.7 billion.</p> <p>However, it should be borne in mind that of the multi-year (2018-2020) options to subscribe for new shares announced in April, the 2018 portion of the options has already been fully exercised, thus leaving pending approximately JPY7 billion for the 2019 and 2020 series of the fund raising.</p> <p>Procedures are still ongoing in the arbitration of the company's dispute with The Medicines Company in the US concerning the self-pain management medical product IONSYS (SymBio has requested the International Chamber of Commerce to rule on its claim for compensation in the amount of JPY9 billion from The Medicines Company). Depending on the outcome of this arbitration SymBio's capital raising requirements may change.</p>
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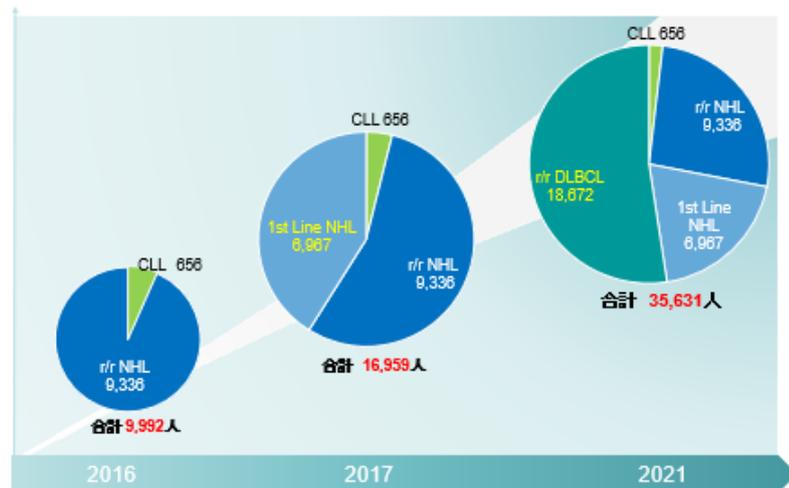
<Reference>

The market size assumptions we have used in modelling business value are JPY20.4 billion for Treakisym® and JPY16.0 billion for rigosertib

<Reference: Market size for Treakisym® and rigosertib>

Details on the market size of Treakisym® and rigosertib were provided in the basic report we issued on February 19, 2018. That estimate is given added credence as a result of the recognition of Treakisym® as a standard treatment. We therefore adhere to our modelling of JPY10.6 billion market size for the three Treakisym® approved indications: 1 Recurrent/intractable low-grade NHL/MCL; 2 Chronic lymphocytic leukemia (CLL); and 3, Untreated low-grade NHL/MCL. We also reiterate our market size estimate of JPY9.8 billion for r/r DLBCL, now at Phase 3.

The Treakisym market



Source: Symbio IR meeting materials

Turning to the potential for rigosertib, since the injection formulation in cases of high-grade MDS is limited to MHA refractory we estimate its market size at JPY4.6 billion. The oral formulation has an estimated potential of JPY11.6 billion, bringing the total to around JPY16 billion (see our basic report released on February 19, 2018).



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