EDISON

SymBio Pharmaceuticals

Clinical update

Top-line data from registrational DLBCL study

Pharma & biotech

SymBio will be presenting data at the European Society of Hematology (EHA) meeting from its pivotal study in Japan of Treakisym (bendamustine) in combination with rituximab for the treatment of diffuse large B-cell lymphoma (DLBCL). The 38-patient, single-arm study showed a 76% overall response rate (ORR), with 47% of patients achieving a complete response (CR). This gives us a high degree of confidence in the label expansion for this population submitted in May 2020.

Year end	Revenue (¥m)	PBT* (¥m)	EPS* (¥)	DPS (¥)	P/E (x)	Yield (%)
12/18	3,836	(2,749)	(166)	0	N/A	N/A
12/19	2,838	(4,377)	(189)	0	N/A	N/A
12/20e	2,608	(5,256)	(181)	0	N/A	N/A
12/21e	9,228	1,090	19	0	24.8	N/A

Note: *PBT and EPS are adjusted, excluding D&A and exceptional items.

No surprises in safety profile

The EHA abstract includes a report on the safety profile of the combination, which is in line with expectations. Grade 3 and higher events were limited to hematologic adverse events (AE), which is consistent with the profile of this treatment and other reported results. The regimen is positioned as a more tolerable treatment than other second-line therapies, so consistency in the AE profile is important. These results were to be expected but we are pleased to see that no surprises were encountered that could potentially endanger the recent submission of the combination for a label expansion of Treakisym.

Results in line with or better than similar studies

The combination of bendamustine and rituximab (BR therapy) has previously been studied in unaffiliated non-registrational studies in DLBCL patients and other aggressive lymphomas. The results in the current study replicate and/or surpass these historical benchmarks. In particular, the median progression-free survival (PFS) seen in the study of 11.9 months is superior to other reports in this patient population. Median overall survival was not reached during the study period.

Confirmed activity in difficult to treat populations

The results presented in the abstract also included a subgroup analysis based on cancer subtype and patient age. The drug combination showed activity across subgroups, including more difficult to treat non-germinal center B-cell (non-GBC) disease and patients over 75. This supports the use of the regimen in its historical role for these higher-risk groups that are often unfit for other treatments.

Valuation: Unchanged at ¥39.0bn or ¥1,144

Our valuation remains unchanged at ¥39.0bn ($354m), or ¥1,144 ($10.40) per share as we had previously upgraded our valuation for the DLBCL program upon the initial announcement of positive results in November 2019, and we remain confident in its approval (90% probability of success).

26 May 2020

Price	**¥472**
Market cap	**¥16.1bn**
	¥110/US$
Net cash (¥m) at 31 March 2020 + subsequent exercises	5,584
Shares in issue	34.1m
Free float	92.5
Code	4582
Primary exchange	TYO
Secondary exchange	OTC US

Share price performance

%	1m	3m	12m
Abs	45.2	(15.9)	(33.0)
Rel (local)	37.4	(9.4)	(31.2)
52-week high/low		¥791	¥264

Business description

SymBio Pharmaceuticals is a Japanese specialty pharma company with a focus on oncology and hematology. The Treakisym powder formulation was in-licensed from Astellas in 2005; liquid Treakisym was in-licensed from Eagle Pharmaceuticals in 2017. Rigosertib was in-licensed from Onconova. And brincidofovir was licensed from Chimerix in 2019.

Next events

Rigosertib Phase III results	H220
Treakisym RTD approval decision	October 2020

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Edison profile page

Data supports label expansion

SymBio previously completed a Phase III study in Japan to support a label expansion of Treakisym (in combination with rituximab) to relapsed and refractory DLBCL in November 2019 and reported that it received positive results. The company will be presenting the detailed results from this study at the upcoming EHA virtual meeting in June 2020. The study enrolled 40 patients of whom 38 were evaluated for safety and efficacy.

The abstract for the presentation reported an ORR in 29 out of 38 patients (76%), of whom 18 of 38 (47%) showed a CR, with a median PFS of 11.9 months. These results are superior on a numerical basis to other reported studies of this combination. For instance, an Italian retrospective study reported a 50% ORR, 28% CR and a PFS of 8.8 months.[1] Other studies have reported lower response rates.[2] The safely profile presented in the abstract was also consistent with other results and predominantly showed hematologic AEs. A majority of patients saw grade 3 or higher drops in lymphocyte counts (90%), neutropenia (74%) or reduction in CD4 lymphocytes (66%). This is to be expected for most drugs targeting hematologic malignancies and is indicative of the drugs' activity.

This combination has been previously studied in a number of different trials across the globe, and is among the arsenal of treatment regimens available to doctors despite not being formally approved. The BR treatment regimen (as it is typically called) has historically been used as a salvage treatment in patients following failure of first-line chemotherapy as an alternative to more aggressive chemotherapy salvage or autologous stem cell transplant. The BR regimen has a generally more tolerable profile than these other treatments. Because of this there have also been attempts to investigate it as an alternative treatment in the first-line in frail patients.[3] However, a limitation to evaluating the data on the BR combination is that there is a lack of placebo controlled studies, although this has not limited other similar approvals. Bendamustine was approved in the US for the treatment of indolent non-Hodgkin lymphoma (NHL) in patients who have failed rituximab treatment, based on a single-arm study.

The company also provided a breakdown of response rates based on patient subgroups. Response rates were provided on the basis of whether patients had germinal center B-cell type (GCB) DLBCL or the generally more aggressive non-GCB subtype of the disease, as well response rates by age (Exhibit 1). These results showed strong activity across subgroups, including the more difficult to treat non-GCB patients and those over 75. These results are relevant because they continue to support the use of Treakisym in harder to treat populations.

Exhibit 1: Patient subgroup analysis

		ORR	CR
Cancer subtype	GCB	83%	67%
	non-GCB	78%	39%
Patient age	Under 65	86%	71%
	65 to 74	75%	45%
	75 or older	73%	36%

Source: SymBio Pharmaceuticals

1 Arcari A. et al. (2016) Safety and efficacy of rituximab plus bendamustine in relapsed or refractory diffuse large B-cell lymphoma patients: an Italian retrospective multicenter study. *Leuk Lymph* 57, 1823-1830.

2 Vacirca JL, et al. (2014) Bendamustine combined with rituximab for patients with relapsed or refractory diffuse large B cell lymphoma *Ann Hematol* 93, 403-409.

3 Storti S, et al. (2018) Rituximab Plus Bendamustine As Front-Line Treatment In Frail Elderly (>70 Years) Patients With Diffuse Large B-Cell Non-Hodgkin Lymphoma: A Phase II Multicenter Study Of The Fondazione Italiana Linfomi. *Haematologica* 103, 1345-1350.

The label expansion to DLBCL is an important aspect of the company's strategy to expand its sales of Treakisym. We estimate that it will expand the target market for the drug to 11,200 second-line DLBCL patients in Japan, approximately double the current market for the drug. Moreover, this is concurrent with the company's pipeline management efforts to seek approval for new formulations of the product: the ready to dilute (RTD) formulation, which was submitted for approval in September 2019, and the rapid infusion (RI) formulation, for which it was recently announced in March 2020 that the ongoing safety confirmation study was fully enrolled.

Valuation

Our valuation remains unchanged at ¥39.0bn ($354m) or ¥1,144 ($10.40). We previously upgraded the probability of success for the Treakisym DLBCL program to 90% from 60% following the initial announcement that the study met its endpoints in November 2019, and the current more granular data does not change our already positive expectations.

Exhibit 2: Valuation of SymBio

Product	Indication	Launch	Peak sales (¥m)	NPV (¥m)	Probability	rNPV (¥m)	rNPV/share (¥/share)
Treakisym	Low grade NHL/MCL (r/r and 1st line); CLL	2010	8,600	19,571	100–95%	18,724	549.8
Treakisym (DLCBL)	r/r DLBCL	2021	9,600	13,383	90%	11,975	351.6
Rigosertib (IV)	r/r HR-MDS	2023	3,800	2,909	50%	1,365	40.1
Rigosertib (oral)	LR-MDS (mono) or First-line HR-MDS (combo)	2025	7,500	4,302	15%	436	12.8
Brincidofovir	vHC	2025	4,200	3,383	30%	882	25.9
Net cash (March 2020 + subsequent exercises)				5,584	100%	5,584	164.0
Valuation				49,132		38,967	1,144.2

Source: SymBio Pharmaceuticals reports, Edison Investment Research

Financials

Our financial forecasts remain unchanged at this time.

Exhibit 3: Financial summary

Accounts: JPN GAAP; year-end 31 December; ¥m	2016	2017	2018	2019	2020e	2021e	2022e	2023e	2024e	2025e
Total revenues	2,368	3,444	3,836	2,838	2,608	9,228	11,484	12,769	14,048	15,395
Cost of sales	(1,464)	(2,413)	(2,663)	(1,973)	(1,956)	(1,619)	(2,261)	(1,904)	(2,097)	(2,299)
Gross profit	904	1,031	1,173	865	652	7,609	9,223	10,864	11,951	13,096
SG&A (expenses)	(1,364)	(1,961)	(1,996)	(2,725)	(3,325)	(5,772)	(6,397)	(7,542)	(7,440)	(8,005)
R&D costs	(1,667)	(3,018)	(1,833)	(2,442)	(2,603)	(765)	(1,040)	(1,815)	(1,547)	(866)
Other income/(expense) included in adjusted	0	0	0	0	0	0	0	0	0	0
Other income/(expense) excluded from adjusted	0	0	0	0	0	0	0	0	0	0
Reported EBIT	(2,127)	(3,947)	(2,656)	(4,302)	(5,276)	1,072	1,786	1,507	2,964	4,226
Finance income/(expense)	5	3	1	0	20	19	28	57	96	177
Other income/(expense) included in adjusted	7	3	(0)	4	0	0	0	0	0	0
Other income/(expense) excluded from adjusted	(195)	(33)	(93)	(75)	0	0	0	0	0	0
Reported PBT	(2,309)	(3,974)	(2,749)	(4,372)	(5,256)	1,090	1,814	1,564	3,061	4,403
Income tax expense	(4)	(4)	(4)	(4)	(4)	(437)	(571)	(555)	(801)	(1,024)
Reported net income	(2,313)	(3,978)	(2,753)	(4,376)	(5,260)	653	1,243	1,008	2,259	3,379
Average number of shares - basic (m)	9.8	12.5	16.6	23.2	29.0	34.1	34.1	34.1	34.1	34.1
Basic EPS (¥)	(235.27)	(319.14)	(165.54)	(189.03)	(181.42)	19.17	36.47	29.59	66.30	99.16
Adjusted EBITDA	(2,101)	(3,917)	(2,621)	(4,264)	(5,179)	1,165	1,883	1,613	3,081	4,356
Adjusted EBIT	(2,127)	(3,947)	(2,656)	(4,302)	(5,276)	1,072	1,786	1,507	2,964	4,226
Adjusted PBT	(2,317)	(3,977)	(2,749)	(4,377)	(5,256)	1,090	1,814	1,564	3,061	4,403
Adjusted EPS (¥)	(236.02)	(319.35)	(165.54)	(189.22)	(181.42)	19.17	36.47	29.59	66.30	99.16
Adjusted diluted EPS (¥)	(236.02)	(319.35)	(165.54)	(189.22)	(181.42)	18.94	36.03	29.23	65.50	97.96
BALANCE SHEET										
Property, plant and equipment	75	47	57	75	80	136	201	263	323	380
Goodwill	0	0	0	0	0	0	0	0	0	0
Intangible assets	42	69	71	241	211	191	178	169	163	159
Other non-current assets	77	100	73	70	70	70	70	70	70	70
Total non-current assets	193	216	201	386	362	398	449	503	557	609
Cash and equivalents	5,719	2,947	4,821	3,911	1,875	1,855	2,801	3,812	5,824	8,970
Inventories	273	363	534	0	220	182	254	214	236	258
Trade and other receivables	487	490	412	549	286	1,011	1,258	1,399	1,540	1,687
Other current assets	205	237	272	427	427	427	427	427	427	427
Total current assets	6,685	4,037	6,038	4,887	2,808	3,476	4,741	5,852	8,027	11,343
Non-current loans and borrowings	450	0	0	0	0	0	0	0	0	0
Trade and other payables	0	0	0	0	0	0	0	0	0	0
Other non-current liabilities	1	1	1	2	2	2	2	2	2	2
Total non-current liabilities	451	1	1	2	2	2	2	2	2	2
Trade and other payables	322	604	726	121	479	530	603	760	729	718
Current loans and borrowings	0	0	0	0	0	0	0	0	0	0
Other current liabilities	620	407	610	751	751	751	751	751	751	751
Total current liabilities	942	1,011	1,336	872	1,231	1,281	1,355	1,512	1,480	1,470
Equity attributable to company	5,485	3,239	4,902	4,400	1,937	2,591	3,833	4,842	7,101	10,481
Non-controlling interest	0	0	0	0	0	0	0	0	0	0
CASH FLOW STATEMENT										
Profit before tax	(2,309)	(3,974)	(2,749)	(4,372)	(5,256)	1,090	1,814	1,564	3,061	4,403
Depreciation and Amortisation	26	30	35	38	97	93	98	106	117	130
Share based payments	137	121	148	0	0	0	0	0	0	0
Other adjustments	197	42	61	229	(20)	(19)	(28)	(57)	(96)	(177)
Movements in working capital	(13)	(35)	184	(242)	402	(637)	(246)	56	(193)	(181)
Interest paid / received	6	3	1	1	20	19	28	57	96	177
Income taxes paid	(4)	(4)	(4)	(4)	(4)	(437)	(571)	(555)	(801)	(1,024)
Cash from operations (CFO)	(1,960)	(3,817)	(2,325)	(4,351)	(4,761)	110	1,095	1,171	2,183	3,329
Capex	(28)	(57)	(40)	(217)	(72)	(129)	(149)	(160)	(171)	(183)
Acquisitions & disposals net	0	0	0							
Other investing activities	(16)	(20)	14	0	0	0	0	0	0	0
Cash used in investing activities (CFIA)	(44)	(78)	(26)	(216)	(72)	(129)	(149)	(160)	(171)	(183)
Net proceeds from issue of shares	3,226	1,164	4,272	3,738	2,797	0	0	0	0	0
Movements in debt	450	0	0	0	0	0	0	0	0	0
Other financing activities	(18)	0	0	2	0	0	0	0	0	0
Cash from financing activities (CFF)	3,658	1,164	4,272	3,740	2,797	0	0	0	0	0
Currency translation differences and other	(196)	(42)	(47)	(83)	0	0	0	0	0	0
Increase/(decrease) in cash and equivalents	1,458	(2,772)	1,874	(911)	(2,036)	(20)	946	1,011	2,012	3,146
Opening net (debt)/cash	4,261	5,719	2,947	4,821	3,911	1,875	1,855	2,801	3,812	5,824
Cash and equivalents at end of period	5,719	2,947	4,821	3,911	1,875	1,855	2,801	3,812	5,824	8,970
Net (debt)/cash	5,269	2,947	4,821	3,911	1,875	1,855	2,801	3,812	5,824	8,970
Movement in net (debt)/cash over period	1,008	(2,322)	1,874	(911)	(2,036)	(20)	946	1,011	2,012	3,146

Source: SymBio Pharmaceuticals reports, Edison Investment Research

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