

English translation

March 26, 2020

## **Annual Report** (January 1, 2019 through December 31, 2019)

### **1. Business Performance of SymBio Pharmaceuticals Limited**

#### **(1) Business conditions and operating results**

Progress in the Company's business for the fiscal year under review is as follows.

##### **(i) Domestic**

[Issues concerning product defects]

As stated in the reasons for revisions to our earnings forecasts released on August 7, 2019, foreign matter contamination and appearance defects were discovered in lyophilized injection agents imported from Astellas Deutschland GmbH, a subsidiary of Astellas Pharma Inc. Hence, shipments of TREAKISYM® 100 mg vials to the Company's distributor in Japan, Eisai Co., Ltd., faced further delays than originally anticipated. As a result, net sales totaled 2,837,753 thousand yen for the fiscal year ended December 31, 2019, was down 36.4% compared to our initial forecast. Operating loss was 4,301,615 thousand yen (versus our initial forecast of loss of 3,587 million yen).

To prevent similar quality issues from recurring, the Company have filed complaints with Astellas Deutschland GmbH and requested the manufacture and prompt shipment of replacement product batches. Although the Company received the replacement batches, the inventory levels for TREAKISYM® remain low due to unreliable delivery dates and continuing high defect rates for a portion of replacement batches. The Company continues to request that Astellas Deutschland GmbH to fulfill its obligations as our supplier. SymBio will continue to negotiate and demand improvements from Astellas Deutschland GmbH to ensure a stable supply of high-quality pharmaceutical products. Astellas Deutschland GmbH has established the corrective and preventive action program (CAPA), but its effectiveness has not yet been confirmed.

[Establishment of the Company's own salesforce]

In October 2018, the Company began preparations to establish its own salesforce for the sale of TREAKISYM® after the expiration of a business partnership agreement with Eisai

Co., Ltd. (Eisai) in December 2020. The Company's top management objectives are to attain profitability in the fiscal year ending December 31, 2021 and to achieve sustainable growth thereafter. By transitioning to its own salesforce, the Company plans to solidify its future business development.

During the fiscal year under review, the Company continued to expand and train its team of TREAKISYM<sup>®</sup> sales representatives, who will be the core of the Company's own salesforce. Upon completion of their training, sales representatives began conducting regionally focused activities to provide information on July 1, 2019, and the Company made steady progress toward establishing a nationwide salesforce by 1H FY 2022. During the final three months of the fiscal year under review, the Company made significant progress in recruiting the additional regional sales managers and TREAKISYM<sup>®</sup> sales representatives necessary for a nationwide salesforce and our goal of improving our distribution and logistics capabilities. This achievement is in part due to the formation of business alliances with pharmaceutical wholesalers and division of our logistics center into eastern Japan and western Japan. The Company is also establishing an enterprise resource planning (ERP) system. Through these efforts, the Company made steady progress toward establishing a high-performance and high-productivity salesforce.

[Anticancer agents: SyB L-0501 (lyophilized powder formulation), SyB L-1701 (ready-to-dilute ("RTD") formulation), SyB L-1702 (rapid infusion ("RI") formulation) (generic name: bendamustine hydrochloride; trade name: TREAKISYM<sup>®</sup>)]

The Company currently sells TREAKISYM<sup>®</sup>, a drug widely used in the field of malignant lymphoma, in Japan through its business partner, Eisai. The Company obtained manufacturing and marketing approval for first-line treatment of low-grade non-Hodgkin's lymphoma (low-grade NHL) <sup>(Note 1)</sup> and mantle cell lymphoma (MCL) in December 2016, for recurrent/refractory low-grade NHL and MCL in October 2010, and for chronic lymphocytic leukemia (CLL) in August 2016. Further, the combination treatment (BR therapy) of TREAKISYM<sup>®</sup> and rituximab was added to the Guidelines for Tumors of Hematopoietic and Lymphoid Tissues 2018 published by the Japanese Society of Hematology in July 2018, recommending TREAKISYM<sup>®</sup> as one of standard treatments for all previously approved indications. As a result, TREAKISYM<sup>®</sup> gained its foothold as the standard treatment for malignant lymphoma. By switching to a highly specialized internal salesforce, the Company aims to achieve a market share that is on par with our market shares in the U.S. and Europe.

In addition to the approved indications, the Company is conducting a Phase III clinical trial for TREAKISYM<sup>®</sup> targeting recurrent/refractory diffuse large B-cell lymphoma (r/r DLBCL). In November 2019, the Company announced the achievement of a favorable

response rate that exceeded expected levels, which represents a primary endpoint. Currently, the Company is preparing to apply for approval for this indication, targeting the second quarter of FY 2020. The above trial is in response to the serious need at clinics and hospitals as there is currently no reliable standard treatment. Patient groups and relevant academic societies have petitioned to the regulatory authorities for the approval of BR therapy.

The Company entered into an exclusive license agreement (in Japan) for TREAKISYM<sup>®</sup> liquid formulation (RTD and RI liquid formulations) <sup>(Note 2)</sup> with Eagle Pharmaceuticals, Inc. (head office: New Jersey, U.S.) in September 2017. Following consultations with the Pharmaceutical and Medical Devices Agency concerning RTD liquid formulation products, the Company completed an application for approval in September 2019 and forecasts a launch in Q1 FY 2021. A clinical trial for RI liquid formulations began in November 2018 primarily to confirm safety. The Company is steadily recruiting patients since the enrollment of the first patient in April 2019. As of January 31, 2020, 31 patients were enrolled. The Company aims to launch these RI liquid formulations in the first half of FY 2022 following a prompt application for approval after the clinical trial. RI liquid formulations significantly reduce the time required for administration to 10 minutes, down from the 60 minutes required by the currently available freeze-dried (“FD”) powder and ready-to-dilute (RTD) formulations. This will greatly lessen the burdens placed on patients and healthcare providers, enabling the Company to add significant value. Furthermore, the liquid formulations are protected by multiple patents that will make it possible to extend the life of this product until 2031, increasing business value.

Further, as a result of the approval obtained in July 2018 of a partial change application to the Company’s TREAKISYM<sup>®</sup> marketing authorization, TREAKISYM<sup>®</sup> can now be used in combination with not only rituximab but also other new anti-CD20 antibodies for the treatment of CD20 positive follicular lymphoma (FL), a common histologic type of low-grade NHL. As a new treatment option, it is offered to patients in combination with obinutuzumab <sup>(Note 3)</sup>, which was launched in August 2018. In March 2019, the Company received approval for changes to a portion of its application concerning the use of TREAKISYM<sup>®</sup> as a pretreatment agent for tumor-specific T-cell infusion therapy <sup>(Note 4)</sup>. This will allow TREAKISYM<sup>®</sup> to be used as a pretreatment for Kymriah<sup>®</sup> intravenous infusion <sup>(Note 5)</sup>, which was approved as the first chimeric antigen receptor T-cell (CAR-T) therapy <sup>(Note 6)</sup> in Japan and included in the NHI price listings in May 2019. The status of TREAKISYM<sup>®</sup> as a standard treatment for malignant lymphoma is becoming stronger as its use as a pretreatment for regenerative medicine and other products continues to expand.

Two trials aimed at exploring further possibilities for TREAKISYM<sup>®</sup>, a Phase I clinical trial examining TREAKISYM<sup>®</sup> as a treatment for progressive solid tumors and a pre-

clinical trial aimed at verifying the therapeutic effects of TREAKISYM<sup>®</sup> on systemic lupus erythematosus (SLE), were concluded and achieved the initial objectives. However, the Company suspended further development of TREAKISYM<sup>®</sup> in these areas. In order to best utilize limited management resources, the Company made the strategic decision to prioritize the domestic and overseas development of brincidofovir (mentioned below), an antiviral drug for the treatment of infectious disease, for which the Company have newly acquired a license.

- (Note 1) Non-Hodgkin's lymphoma (NHL) refers to malignant lymphoma other than Hodgkin's lymphoma. Malignant lymphoma is a cancer of the lymphatic system in which lymphocytes develop malignant growths. The majority of Japanese malignant lymphoma patients are suffering from NHL.
- (Note 2) RTD and RI are pre-dissolved liquid formulations that differ from currently available freeze-dried ("FD") powder injection. RTD (ready-to-dilute) will significantly reduce the preparation time and labor cost for healthcare providers, and RI (rapid infusion) will reduce infusion duration to 10 minutes from the current 60 minutes, providing significant benefit and value to both patients and healthcare providers.
- (Note 3) Obinutuzumab (Gazyva<sup>®</sup>, marketed by Chugai Pharmaceutical Co., Ltd.): Like rituximab recommended by treatment guidelines for non-Hodgkin's lymphoma in Japan and overseas, obinutuzumab is a glycoengineered type II anti-20 monoclonal antibody that directly binds to CD20 (a protein expressed on B-cells other than stem cells or plasma cells) on target B-cells to attack and destroy them along with the body's immune system.
- (Note 4) Tumor-specific T-cell infusion therapy is a treatment method in which tumor-specific T-cells (T-cells that specifically recognize cancer cells) taken from cancer patients are artificially bestowed with cancer specificity extracorporeally, amplified and then administered to the patient.
- (Note 5) Kymriah<sup>®</sup> intravenous infusion (generic name: tisagenlecleucel; marketed by Novartis Pharma K.K.): Kymriah<sup>®</sup> intravenous infusion is the first chimeric antigen receptor T-cell (CAR-T) therapy approved within Japan. The Company received manufacturing and marketing approval for Kymriah<sup>®</sup> for use in the treatment of CD19 positive recurrent/refractory B-cell acute lymphoblastic leukemia (B-ALL) and CD19 positive recurrent/refractory diffuse large B-cell lymphoma (DLBCL) in March 2019. Kymriah<sup>®</sup> intravenous infusion was included in NHI price listings in May 2019.
- (Note 6) Chimeric antigen receptor T-cell (CAR-T) therapy is a type of tumor-specific T-cell infusion therapy that introduces genes that code chimeric antigen receptors (CARs) into T-cells, amplifies these cells and then infuses them. These chimeric antigen receptors are produced by combining the intracellular domains of T-cell receptors with the antigen binding sites of antibodies capable of recognizing membrane antigens attached to tumor

cells. In clinical trials using CARs to target CD19 that expresses on B-cells, CD19-targeting CARs were introduced into T-cells that were later administered to patients with B-cell tumors. These modified cells produced clear clinical effects.

[Anticancer agents: SyB L-1101 (intravenous formulation) and SyB C-1101 (oral formulation) (generic name: rigosertib sodium)]

U.S. licensor Onconova Therapeutics, Inc. (head office: Pennsylvania, U.S.) (“Onconova”) is conducting a global Phase III clinical trial (with trial sites in more than 20 countries) of the intravenous formulation of rigosertib for higher-risk myelodysplastic syndromes (HR-MDS) in patients who do not respond to the current standard treatment with hypomethylating agents relapse after treatment under the current standard of care, or are intolerant to hypomethylating agents. The Company is responsible for clinical development in Japan and began the trial in December 2015. Forty-eight patients were enrolled as of December 31, 2019, and patient enrollment is in progress. According to an October 2019 announcement from Onconova, global patient enrollment (final target of 360 patients) was more than 90% complete as of November 2019, and top-line results (primary endpoints) are expected to be released in 1H FY 2020. Based on the results of the trial, the Company is planning to apply for approval in Japan at the same time as in the U.S. and Europe.

As for the oral formulation of rigosertib, Onconova completed Phase I/II clinical trials in the U.S. for the target indication of first-line HR-MDS (in combination with azacitidine (Note 7)), and results suggested that the oral formulation of rigosertib and azacitidine were safe and effective when combined. The Company started a Phase I clinical trial in Japan in June 2017 to confirm the tolerability and safety of the oral formulation of rigosertib for Japanese patients. We began patient enrollment with the first patient enrolled in October 2017 and completed the enrollment process in June 2019. After completion of this trial, the Company plans to promptly conduct a Phase I clinical trial for combination therapy with azacitidine. Further, to apply for approval of the oral formulation of rigosertib in Japan no later than in the U.S. and Europe, the Company plans to take part in a global trial for combination therapy with azacitidine for the first-line treatment of patients with higher-risk MDS, which Onconova is currently considering conducting. Data from the global trial was announced at the 61st American Society of Hematology (ASH) Annual Meeting and Exposition in December 2019. Based on this data, Onconova announced that it is discussing the design of a Phase II/III adaptive clinical trial testing this combination therapy as a first-line treatment for HR-MDS during the same month.

(Note 7) Azacitidine (Vidaza<sup>®</sup>, marketed by Nippon Shinyaku Co., Ltd.): This hypomethylating agent (for injection) was approved in 2011 upon successful confirmation of extended

overall survival for the first time in the Phase III clinical trial for the indication of MDS, and is currently used as a first-line drug for MDS patients who have difficulties in hematopoietic stem cell transplantation. MDS is a pre-leukemia, and decreased expression in tumor suppressor gene due to excessive methylation of DNA is thought to be related to the disease. Hypomethylating agents such as azacitidine are thought to suppress progress to leukemia by restoring tumor suppressor gene with a deterrent effect against methylation of DNA.

[Antiviral drug for the treatment of infectious diseases: SyB V-1901 (generic name: brincidofovir)]

On September 30, 2019, the Company entered into an exclusive global licensing agreement for intravenous and oral formulation of brincidofovir<sup>(Note 8)</sup>, an antiviral drug for the treatment of infectious diseases (SyB V-1901; “BCV IV” and “BCV Oral,” respectively) with Chimerix Inc. (head office: North Carolina, U.S.; “Chimerix”). Under this agreement, the Company acquired the exclusive rights for the worldwide development, marketing, and manufacture of BCV for all human indications, excluding smallpox. With the global rights to BCV, the Company aims to transition into a global specialty pharmaceutical company with an integrated system for supplying high-quality pharmaceutical products.

The Company will first develop BCV IV for the treatment of viral hemorrhagic cystitis<sup>(Note 9)</sup> (vHC) that often occurs after hematopoietic stem cell transplantation, which are a niche market with high unmet medical needs. To deliver brincidofovir to patients who urgently need this treatment, we will conduct clinical development in Japan ahead of the rest of the world, aiming to secure approval for the drug. At the same time, we will conduct global clinical trials of BCV IV that extend to Europe and the U.S targeting a global rollout of the drug. Inspired by its potential wide use throughout the field of surgical transplantation including hematopoietic stem cell transplantation and other organ transplantation, the Company is currently planning clinical development of BCV IV as a treatment for viral infections occurring after kidney transplantation. The Company is currently looking to expand our business in Europe, the U.S. and Asia (including China), where the organ transplant market is larger than Japan. Also, the Company is considering forming partnerships that reflect the regional characteristics of target diseases. We will explore all possible means of maximizing our business value through a variety of measures, including strategically utilizing our wholly owned subsidiary, SymBio Pharma USA, Inc. (head office: Menlo Park, California, U.S.; established May 2016). As for BCV Oral, we will discuss a development plan going forward including efforts to improve its formulation. At present, we are discussing future global development for BCV IV and BCV Oral with prominent overseas researchers in a variety of specialized fields. These formulations have

already been found to have highly active antiviral effects, as well as a wide treatment spectrum, through clinical trials conducted by Chimerix, Inc. in the U.S. and Europe. Based on these findings, the Company will discuss the design of global clinical trials.

(Note 8) Brincidofovir (BCV) has a structure in which cidofovir (an antiviral drug for the treatment of infectious disease that is already approved and marketed in the U.S. and Europe, but unapproved in Japan; “CDV”) is bound to a lipid chain (hexadecyloxypropyl; “HDP”). It is quickly absorbed into the lipid bilayer membrane and efficiently transfers into cells, and then the bound lipid chain is metabolized and separated from the structure by intracellular phospholipases. This process generates an activator (CDV-PP; CDV diphosphate) that is retained in the cells for a long period of time, dramatically raising the compound’s antiviral activity. Furthermore, BCV avoids nephrotoxicity, a fundamental issue plaguing CDV, since HDP conjugation prevents the accumulation of the compound in renal tubular epithelial cells through organic anion transporter 1 (OAT1) and CDV is released at low levels in the bloodstream.

(Note 9) Viral hemorrhagic cystitis (vHC): Among viral infections that frequently occur following hematopoietic stem cell transplantation, hemorrhagic cystitis caused by the BK virus or the adenovirus accompanies particularly severe symptoms, including frequent urination, abdominal pain and pain experienced during urination. This type of hemorrhagic cystitis is especially likely to occur in transplantation between unrelated donors and in umbilical cord blood transplantations, which are relatively common in Japan. Its extreme refractory nature is further complicated by the length of time required for reconstruction of the immune system, which hinders treatment in many cases. In severe cases, it can cause disseminated infection and become fatal. There have also been reports of fatal kidney failure cases caused by these viral infections. Drugs currently used in treatment, including cidofovir (CDV), are either unapproved or off-label.

[Patient-controlled pain management drug: SyB P-1501]

In October 2015, the Company entered into an agreement with Incline Therapeutics, Inc., a wholly owned subsidiary of US-based The Medicines Company (head office: New Jersey, U.S.) for an exclusive license to develop and commercialize SyB P-1501 in Japan. The Company, acting in the best interests of patients, temporarily suspended new patient enrollment for SyB P-1501 from April 21, 2017 due to the concern of the continuity of The Medicines Company’s business regarding the product.

The Company initiated arbitration against The Medicines Company on October 11, 2017 under the rules of the International Chamber of Commerce, seeking damages of 82 million U.S. dollar (approximately 9.0 billion yen) arising from The Medicines Company’s repudiation of the license agreement.

Arbitration proceedings against The Medicines Company are ongoing. Novartis International AG (head office: Switzerland) announced on January 6, 2020 that it had completed the acquisition of The Medicines Company.

(ii) Business outside Japan

SyB L-0501 is also marketed in South Korea, Taiwan, and Singapore, and sales of SyB L-0501 in these countries progressed favorably at a level exceeding the Company's forecasts.

(iii) Licensing of new drug candidates

The Company conducts ongoing search and evaluation of multiple new drug candidates for potential in-licensing to expand our research and development ("R&D") pipeline. Our aim is to create long-term business value as a profitable biopharmaceutical company with growth potential.

Additionally, the Company will proceed with the transformation into a global specialty pharmaceutical company with the capacity to develop and commercialize new drugs in the U.S., Japan, Europe, and other major global markets by actively acquiring rights to new drug candidates using wholly owned subsidiary SymBio Pharma USA, Inc. as a global business base.

(iv) Business results

Net sales totaled 2,837,753 thousand yen for the fiscal year ended December 31, 2019, primarily reflecting product sales of TREAKISYM<sup>®</sup>, and overall net sales fell 26.0% year on year.

Selling, general and administrative expenses totaled 5,166,366 thousand yen (+34.9% year on year), including R&D expenses of 2,441,552 thousand yen (+33.2% year on year) primarily due to upfront payments for the licensing agreement of brincidofovir, an antiviral drug for the treatment of infectious disease and a new product under development, and expenses associated with clinical trials for the intravenous formulations of TREAKISYM<sup>®</sup> and the intravenous and oral formulations of rigosertib, as well as other selling, general and administrative expenses of 2,724,814 thousand yen (+36.5% year on year).

As a result, an operating loss of 4,301,615 thousand yen was recognized for the fiscal year ended December 31, 2019 (an operating loss of 2,656,072 thousand yen for the previous fiscal year). In addition, non-operating income was 4,331 thousand yen, primarily consisting of insurance claim income of 2,736 thousand yen. Meanwhile, non-operating expenses were 79,372 thousand yen and primarily comprised foreign exchange losses of 54,755 thousand yen, share issuance cost of 13,932 thousand yen, and commission expenses of 10,457 thousand yen. Consequently, ordinary loss totaled 4,376,655 thousand yen (compared to an ordinary loss of 2,748,730 thousand yen in the same period of the previous



fiscal year) and bottom-line loss in the fiscal year ended December 31, 2019 totaled 4,376,258 thousand yen (compared to a loss of 2,752,533 thousand yen for the same period of the previous fiscal year).

Segment information is omitted since the Company operates within a single segment, which includes the R&D, manufacturing, and marketing of pharmaceutical drugs and other related activities.

(v) Capital investment

The total amount of capital expenditures during the fiscal year under review was 225,773 thousand yen, mainly consisting of office investments and the purchase of appliances, network devices and business software.

**(2) Status of fund procurement**

The company procured 3,771,425 thousand yen as a result of the exercise of share acquisition rights associated with the 46th and 47th warrants (with Exercise Price Revision Clauses) in the fiscal year under review.

**(3) Status of assets and profit and loss**

(Unit: thousands of yen)

Fiscal year Classification	FY 2016 The 12th Term	FY 2017 The 13th Term	FY 2018 The 14th Term	FY 2019 The 15th Term (current)
Net sales	2,368,112	3,444,206	3,835,530	2,837,753
Operating profit (loss)	(2,127,049)	(3,947,061)	(2,656,072)	(4,301,615)
Ordinary profit (loss)	(2,316,806)	(3,976,784)	(2,748,730)	(4,376,655)
Profit (loss)	(2,313,233)	(3,977,862)	(2,752,533)	(4,376,258)
Loss per share (yen)	(58.82)	(79.78)	(165.54)	(189.03)
Total assets	6,878,384	4,252,284	6,239,423	5,273,955
Net assets	5,484,870	3,239,402	4,901,799	4,400,116
Net assets per share (yen)	108.61	50.00	212.23	143.07

(Note) The Company conducted a 1-for-4 consolidation of common shares on July 1, 2019. Loss per share and net assets per share and have been calculated based on the assumption that this consolidation was conducted at the beginning of FY 2018.

**(4) Issues to be addressed by the Company**

The Company is committed to focusing on the following key management objectives.

(i) Further expansion of the pipeline

In order to enhance the enterprise value as a specialty pharmaceutical company, we need to expand the pipeline through ongoing in-licensing of new drug candidates for

development.

The Company is conducting or planning development of the following anticancer agents: SyB L-0501, SyB L-1101, SyB C-1101, SyB L-1701, SyB L-1702, and SyB V-1901, an antiviral drug for the treatment of infectious disease. Currently we are in discussion with counterparties regarding the in-licensing of several new drug candidates, and will continue with active efforts to in-license new drug candidates for development in order to further expand our pipeline.

(ii) Life cycle management of products in the existing pipeline

Promoting product life cycle management is also important to enhance enterprise value. The Company will continue to aim to maximize returns from each drug under development through indication expansion after the in-licensed drugs' initial approval.

TREAKISYM<sup>®</sup> is approved for manufacturing and marketing in Japan for the indications of recurrent/refractory low-grade non-Hodgkin's lymphoma and mantle cell lymphoma, chronic lymphocytic leukemia, and first-line treatment of low-grade non-Hodgkin's lymphoma and mantle cell lymphoma. TREAKISYM<sup>®</sup> also achieved primary endpoints in its Phase III clinical trial for the indication of recurrent/refractory diffuse large B-cell lymphoma (r/r DLBCL), and the Company is currently preparing to apply for its approval. In addition, the Company intends to maximize the business value of TREAKISYM<sup>®</sup> by promoting the product life cycle management of the product and is developing the TREAKISYM<sup>®</sup> liquid formulation (RTD and RI liquid formulations) in-licensed from Eagle Pharmaceuticals, Inc. (head office: New Jersey, U.S.).

The development of intravenous and oral formulations of rigosertib for the indication of myelodysplastic syndromes (MDS) is currently progressing. Few useful therapeutic agents are currently available for MDS, so it is an area with very high unmet medical need. With respect to the global Phase III clinical trial of the intravenous formulation for the target indication of recurrent/refractory higher-risk MDS conducted by Onconova, the Company is conducting its clinical trial in Japan. As for the oral formulation, the Company has completed a domestic Phase I clinical trial as a monotherapy for the target indication of lower-risk MDS, and is currently conducting a domestic Phase I clinical trial to confirm the safety of high-dose monotherapy for the target indication of first-line higher-risk MDS. The Company is considering participating in global clinical trials after completing the Phase I clinical trial. The development for the target indication of transfusion-dependent lower-risk MDS will be considered based on the status of development by Onconova.

The Company is focused on maximizing the business value of TREAKISYM<sup>®</sup> and rigosertib by promoting product life cycle management through further indication expansion. Furthermore, we will aim to maximize earnings by pursuing life cycle

management related to brincidofovir, an antiviral drug for the treatment of infectious disease, while transforming into a specialty pharmaceutical company with the capacity to expand into global markets.

(iii) Preparation for the establishment of the Company's own salesforce

Domestic sales of TREAKISYM<sup>®</sup> are currently handled through Eisai, in accordance with the business partnership agreement the Company concluded in August 2008. This agreement is set to expire in December 2020 and, looking ahead to the fiscal year ending December 31, 2021, the Company is planning to transition to its own salesforce.

Providing specialized medical drugs information will enable the Company to more accurately understand the needs of the market and respond more swiftly, allowing it to contribute to the benefit of patients while aiming to maximize the business value of TREAKISYM<sup>®</sup>. Furthermore, the Company strives to build a consistent salesforce with a high level of specialization in the field of hematological diseases. Through this effort, the Company aims to achieve high business efficiency, ensure sustainable earnings growth, and maximize shareholder value once the intravenous and oral formulations of rigosertib, which are currently under development to treat myelodysplastic syndromes (MDS), join TREAKISYM<sup>®</sup> in the product lineup.

With regard to brincidofovir, an antiviral drug for the treatment of infectious disease, we will not only pursue domestic sales, but also consider global business development in all parts of the world, including Europe and the United States.

(iv) Global expansion for further growth

In addition to Japan, the Company identifies China, Hong Kong, South Korea, Taiwan, and Singapore as strategic regions in Asia to move forward with business development.

However, with expanding medical expenditures due to the aging population in Japan, and the advent of the "era of generic drugs comprising 80% of all drugs dispensed" as a governmental policy of Japan, the business environment for innovative drug developers is expected to remain extremely challenging. Such a policy may also be implemented by other Asian countries.

Under these circumstances, the Company will promote global expansion aiming for further growth. Utilizing its experience fostered through its business in Asia, the Company will search, evaluate, and negotiate concerning new drug candidates that can follow brincidofovir, an antiviral drug for the treatment of infectious disease, in order to acquire their rights on a global scale.

(v) Securing personnel

The Company places the highest priority on personnel as the Company's principal management resource. Without talent, we would be unable to make superior achievements in terms of exploring, developing, and providing information concerning new drugs, and unable to develop and commercialize these new drugs on a global scale. We continually recruiting talented people; especially after being listed, we have recruited the best and brightest people in order to strengthen the management organization. Going forward, we plan to continue to further strengthen our human resources by providing on-the-job training and employee development programs.

(vi) Financial

It is necessary for the Company to raise funds required for business activities such as R&D expenditures as pipeline development and global business expansion progress and as drug candidates increase in number.

Therefore, we make every effort to further strengthen the financial base by continually diversifying the method of fund raising and curtailing costs through tight budget control.

**(5) Major business activities** (as of December 31, 2019)

The Company regards underserved therapeutic areas that lack the development of new drugs, despite significant unmet medical needs, as business opportunities. We engage in the development of new drugs with a primary focus on the treatment of rare diseases, mainly in the areas of oncology and hematology; search and evaluation, development and manufacturing to sales are the main activities of our business.

**(6) Main office and employees**

(i) Main office (as of December 31, 2019)

Name	Location
Main office	Minato-ku, Tokyo

(ii) Employees (as of December 31, 2019)

Classification	Number of employees	Increase or decrease from previous fiscal year end	Average age (years)	Average number of years of service
Male	80	15 (increase)	50.3	3.4
Female	27	2 (increase)	46.4	4.4
Total or average	107	17 (increase)	49.3	3.6

(Notes) 1. Number of employees refers to full time employees.

2. The above number of employees does not include 21 temporary staff.

**(7) Status of parent company and significant subsidiaries**

Not applicable.

**(8) Status of main lenders** (as of December 31, 2019)

Not applicable.

## 2. Matters Related to Stock (as of December 31, 2019)

### (1) Total number of authorized shares

Common stock: 41,750,000 shares

### (2) Total number of shares outstanding

Common stock: 26,415,088 shares (excluding 22,593 shares of treasury stock)

### (3) Number of shareholders

32,754

### (4) Major shareholders (10 largest)

Name of shareholder	Number of shares held	Shareholding ratio
Fuminori Yoshida	862,750	3.3%
Cephalon, Inc.	647,250	2.5%
SMBC Nikko Securities Inc.	538,300	2.0%
Daiwa Securities Co. Ltd.	293,350	1.1%
Eisai Co., Ltd.	208,350	0.8%
Matsui Securities Co., Ltd.	189,300	0.7%
Goldman Sachs International	185,075	0.7%
Japan Securities Finance Co., Ltd.	183,900	0.7%
Kazuyuki Ota	157,700	0.6%
Nomura Securities Co., Ltd.	155,622	0.6%

- (Notes) 1. By resolution of the 14th Ordinary General Meeting of Shareholders held on March 28, 2019, the Company conducted a 1-for-4 consolidation of common shares on July 1, 2019. As a result, the total number of authorized shares decreased by 125,250,000 shares and the total number of shares outstanding decreased by 73,088,043 shares.
2. Shareholding ratio (%) indicates the percentage of shares outstanding held. Shares outstanding is equal to the number of shares issued minus treasury shares.
3. After the end of FY 2019, all of the 47th warrants have been exercised by February 12, 2020. As a result, the total number of shares outstanding has increased by 1,675,000 shares.

### 3. Matters Related to Share Acquisition Rights

#### (1) Share acquisition rights held by the Company's Officers that were issued as compensation for services (as of December 31, 2019)

	The 20th warrant by resolution of the Ordinary General Meeting of Shareholders on March 30, 2010	The 24th warrant by resolution of the Ordinary General Meeting of Shareholders on March 30, 2011	The 26th warrant by resolution of the Ordinary General Meeting of Shareholders on April 17, 2012
Number of share acquisition rights	3,445 units	1,920 units	3,625 units
Number of shares to be issued upon the exercise of share acquisition rights <sup>(Note 4)</sup>	86,125 shares	48,000 shares	90,625 shares
Amount paid for share acquisition rights	None	None	None
Value of property to be contributed upon the exercise of each share acquisition right <sup>(Note 1)</sup> <sup>(Note 4)</sup>	2,340 yen per share	2,728 yen per share	2,220 yen per share
Period in which exercise of share acquisition rights is possible	From: April 1, 2012 To: March 31, 2020	From: March 31, 2013 To: March 30, 2021	From: April 18, 2014 To: April 17, 2022
Status of possession by Directors (excluding Outside Directors) <sup>(Note 4)</sup>	1,800 units (1 holder) 45,000 shares	1,200 units (1 holder) 30,000 shares	2,600 units (1 holder) 65,000 shares
Status of possession by Outside Directors	—	—	—

	The 30th warrant by resolution of the Board of Directors meeting on May 14, 2013	The 37th warrant by resolution of the Board of Directors meeting on March 30, 2016	The 40nd warrant by resolution of the Board of Directors meeting on March 29, 2017
Number of share acquisition rights	1,160 units	2,200 units	2,800 units
Number of shares to be issued upon the exercise of share acquisition rights <sup>(Note 4)</sup>	29,000 shares	55,000 shares	70,000 shares
Amount paid for share acquisition rights	None	27,200 yen per unit <sup>(Note 2) (Note 4)</sup>	20,300 yen per unit <sup>(Note 2) (Note 4)</sup>
Value of property to be contributed upon the exercise of each share acquisition right <sup>(Note 1)</sup>	3,196 yen per share <sup>(Note 4)</sup>	1 yen per share	1 yen per share
Period in which exercise of share acquisition rights is possible	From: May 15, 2015 To: May 14, 2023	From: March 31, 2019 To: March 30, 2026	From: March 30, 2020 To: March 29, 2027
Status of possession by Directors (excluding Outside Directors) <sup>(Note 4)</sup>	645 units (1 holder) 16,125 shares	1,490 units (1 holder) 37,250 shares	1,450 units (1 holder) 36,250 shares
Status of possession by Outside Directors	—	—	—



	The 43th warrant by resolution of the Board of Directors meeting on March 29, 2018	The 48th warrant by resolution of the Board of Directors meeting on March 28, 2019
Number of share acquisition rights	3,050 units	2,950 units
Number of shares to be issued upon the exercise of share acquisition rights <sup>(Note 4)</sup>	76,250 shares	73,750 shares
Amount paid for share acquisition rights <sup>(Note 2)</sup> <sup>(Note 4)</sup>	19,800 yen per unit	19,400 yen per unit
Value of property to be contributed upon the exercise of each share acquisition right <sup>(Note 1)</sup>	1 yen per share	1 yen per share
Period in which exercise of share acquisition rights is possible	From: March 30, 2021 To: March 29, 2028	From: March 30, 2022 To: March 29, 2029
Status of possession by Directors (excluding Outside Directors) <sup>(Note 4)</sup>	1,450 units (1 holder) 36,250 shares	2,200 units (2 holder) 55,000 shares
Status of possession by Outside Directors <sup>(Note 4)</sup>	250 units (1 holders) 6,250 shares	750 units (3 holders) 18,750 shares

- (Notes) 1. New shares were issued through the public offering on December 4, 2013, and third-party allotment on December 25, 2013, at the paid-in amount less than the value of property to be contributed upon the exercise of each share acquisition right. Therefore, the stated value of property to be contributed upon the exercise of each share acquisition right excluding those issued for the 32nd warrant and thereafter is adjusted in accordance with the adjustment provision.
2. The person who receives the allotment of share acquisition rights shall offset the amount to be paid for the relevant share acquisition rights against cash compensation equivalent to the amount.
3. There are no share acquisition rights held by Audit & Supervisory Board Members.
4. The Company conducted a 1-for-4 consolidation of common shares on July 1, 2019. Number of shares to be issued upon the exercise of share acquisition rights and exercise price have been adjusted accordingly.

**(2) Share acquisition rights distributed to the Company's employees as compensation for services during the fiscal year under review (as of December 31, 2019)**

	The 49th warrant by resolution of the Board of Directors meeting on March 28, 2019
Number of share acquisition rights	7,165 units
Number of shares to be issued upon the exercise of share acquisition rights <sup>(Note 3)</sup>	179,125 shares
Amount paid for share acquisition rights <sup>(Note 2) (Note 3)</sup>	19,400 yen per unit <sup>(Note 2)</sup>
Value of property to be contributed upon the exercise of each share acquisition right	1 yen per share
Period in which exercise of share acquisition rights is possible	From: March 30, 2022 To: March 29, 2029
Status of allotment to the Company's employees <sup>(Note 1) (Note 3)</sup>	6,185 units (82 holders) 154,625 shares

- (Notes) 1. Of the share acquisition rights mentioned above, 980 units (24,500 shares) have been forfeited due to the retirement of employees.
2. The person who receives the allotment of share acquisition rights shall offset the amount to be paid for the relevant share acquisition rights against cash compensation equivalent to the amount.
3. The Company conducted a 1-for-4 consolidation of common shares on July 1, 2019. Number of shares to be issued upon the exercise of share acquisition rights and exercise price have been adjusted accordingly.

**(3) Other important matters concerning share acquisition rights**

Not applicable.

#### 4. The Company's Officers (as of December 31, 2019)

##### (1) Names of Directors and Audit & Supervisory Board Members

Company position	Name	Responsibility and significant concurrent position
Representative Director	Fuminori Yoshida	Chief Executive Officer
Director	Kenji Murata	Chief Financial Officer
Director	Shigetoshi Matsumoto	
Director	Bruce David Cheson	Scientific Advisory Board, Lymphoma Research Foundation Outside Director, MorphoSys
Director	Rockford Douglas Norby	Outside Director, Krystal Biotech Inc.
Full-time Audit & Supervisory Board Member	Kiyoshi Watanabe	
Audit & Supervisory Board Member	Kesao Endo	Representative, Endo C.P.A Firm Outside Director, Careerlink Co., Ltd. Representative Partner, ABS Audit Corp.
Audit & Supervisory Board Member	Eiji Ebinuma	Partner, Tanabe & Partners Law Firm Outside Director, Mirait Holdings Corp. Outside Director, Rakuten Bank, Ltd. Audit & Supervisory Board Member, Toko Electrical Construction Co., Ltd.

- (Notes) 1. Of the Directors, Shigetoshi Matsumoto, Bruce David Cheson, and Rockford Douglas Norby are Outside Directors.
2. Kiyoshi Watanabe, Kesao Endo, and Eiji Ebinuma are outside members of the Audit & Supervisory Board.
3. Shigetoshi Matsumoto, Kiyoshi Watanabe, and Kesao Endo have been designated as independent officers pursuant to the provisions of the Tokyo Stock Exchange and registered as such with the Tokyo Stock Exchange.
4. Kesao Endo possesses deep insight in finance and accounting, which he gained through his profession as a certified public accountant.
5. Eiji Ebinuma is an attorney with specialized knowledge and extensive experience in law.
6. Changes in Directors and Audit & Supervisory Board Members during the fiscal year under review are as follows:
- Directors George Morstyn, Milton Grannatt, and Robin Campbell resigned upon expiration of their terms of office at the closing of the 14th Ordinary General Meeting of Shareholders held on March 28, 2019.
  - Audit & Supervisory Board Member Saneaki Ichijo resigned upon expiration of his term of office at the closing of the 14th Ordinary General Meeting of Shareholders held on March 28, 2019.
  - Kenji Murata was newly appointed as Director at the 14th Ordinary General Meeting of Shareholders held on March 28, 2019.
  - Eiji Ebinuma was newly appointed as an Audit & Supervisory Board Member at the 14th Ordinary General Meeting of Shareholders held on March 28, 2019.

- Representative Director Kazuo Asakawa resigned on June 30, 2019. During his term, he also held the positions of Corporate Officer, Executive Vice President, and Chief Commercial Officer.
- 7. The Company has adopted the Corporate Officer System. The Corporate Officers who do not hold concurrent positions as Directors are as follows:
 

Managing Executive Officer	Shigeo Kimura
Corporate Officer	Nobuo Ishida

**(2) Summary of the contents of the liability limitation agreement**

The Company has executed an agreement with each Director (excluding those who engage in business execution) and each member of the Audit & Supervisory Board with respect to the liability in Article 423, Paragraph 1 of the Companies Act, setting forth that director liability will be limited to the higher of 1,000,000 yen or the maximum liability amount set forth in laws and regulations in cases where the Director or member of the Audit & Supervisory Board has performed their duties in good faith and without gross negligence.

**(3) Compensation of members of the Board of Directors and the Audit & Supervisory Board**

Company Board	Number of Directors or Audit & Supervisory Board Members Paid	Total Amount of Compensation (thousands of yen)
Board of Directors	9 (Outside: 6)	145,670 (Outside: 38,046)
Audit & Supervisory Board	4 (Outside: 4)	21,163 (Outside: 21,163)
Total	13 (Outside: 10)	166,833 (Outside: 59,210)

- (Notes)
1. Salary in the event of a Director doubling as an employee is not included in the above compensation for Directors.
  2. The maximum amount of compensation for Directors was resolved as an annual amount of 130 million yen at the Extraordinary General Meeting of Shareholders held on August 3, 2005. In addition to the aforementioned compensation, it was resolved that compensation for Directors in the form of share acquisition rights as stock options be granted up to a maximum annual amount of 80 million yen at the 9th Ordinary General Meeting of Shareholders held on March 27, 2014. (Of 80 million yen, 30 million yen was granted for Outside Directors, which was resolved at the 11th Ordinary General Meeting of Shareholders held on March 30, 2016.)
  3. The maximum amount of compensation for Audit & Supervisory Board Members was resolved as an annual amount of 30 million yen at the Extraordinary General Meeting of Shareholders held on June 30, 2011.
  4. The number of Directors or Audit & Supervisory Board Members compensated as stated above includes three (3) Directors and one (1) Audit & Supervisory Board Member who resigned at the closing of the 14th Ordinary General Meeting of Shareholders held on March 28, 2019, and one (1) Director who resigned on June 30, 2019.
  5. The total compensation paid includes expenses (for nine (9) Directors, a total of 67,922 thousand yen) in connection with share acquisition rights as stock options for the fiscal year under review.

**(4) Matters Concerning Outside Directors and outside members of the Audit & Supervisory Board**

Status of main activities during the fiscal year under review

Position	Name	Status of attendance at the Board of Directors meetings	Status of attendance at the Audit & Supervisory Board meetings	Opinions at the Board of Directors meetings and the Audit & Supervisory Board meetings
Director	Shigetoshi Matsumoto	14 out of 14 (100%)	—	Mr. Matsumoto expressed opinions from an objective perspective independent from the Company's management engaged in business operations, leveraging his extensive knowledge and experience with the business practices of companies in the same industry and with auditing work.
Director	Bruce David Cheson	8 out of 10 (80%)	—	Dr. Cheson expressed opinions from an objective perspective independent from the Company's management engaged in business operations, leveraging his extensive knowledge and experience as a physician.
Director	Rockford Douglas Norby	10 out of 10 (100%)	—	Dr. Norby expressed opinions from an objective perspective independent from the Company's management engaged in business operations, leveraging his extensive experience and knowledge regarding healthcare companies.
Full-time Audit & Supervisory Board Member	Kiyoshi Watanabe	14 out of 14 (100%)	14 out of 14 (100%)	Mr. Watanabe actively expressed opinions from an objective and fair perspective based on his extensive experience and knowledge as an audit & supervisory board member at listed companies in order to achieve highly effective managerial surveillance.

Position	Name	Status of attendance at the Board of Directors meetings	Status of attendance at the Audit & Supervisory Board meetings	Opinions at the Board of Directors meetings and the Audit & Supervisory Board meetings
Audit & Supervisory Board Member	Kesao Endo	14 out of 14 (100%)	14 out of 14 (100%)	Mr. Endo actively expressed opinions from a neutral perspective based on the specialized knowledge and extensive experience he accumulated as a certified public accountant in order to achieve highly effective managerial surveillance.
Audit & Supervisory Board Member	Eiji Ebinuma	10 out of 10 (100%)	9 out of 9 (100%)	Mr. Ebinuma actively expressed opinions from a neutral perspective based on the specialized knowledge and extensive experience he accumulated as an attorney in order to achieve highly effective managerial surveillance.

(Note) With regard to Directors Bruce David Cheson and Rockford Douglas Norby and Audit & Supervisory Board Member Eiji Ebinuma, their status of attendance at the meetings is calculated from the Board of Directors meetings and the Audit & Supervisory Board meetings held after their appointments on March 28, 2019.

## 5. Status of Accounting Auditor

### (1) Name of accounting auditor

Ernst & Young ShinNihon LLC

### (2) Summary of the contents of the liability limitation agreement

Not applicable.

### (3) Amount of compensation

	Amount paid
Amount of compensation paid to the accounting auditor concerning the fiscal year under review	20,400 thousand yen
Total amount of monetary and other property benefits to be paid by the Company	20,400 thousand yen

(Notes) 1. Reasons for the Audit & Supervisory Board's approval of the amount of compensation to be paid to the accounting auditor

The Audit & Supervisory Board verified the contents of the audit planning by the accounting auditor, performance of its duties in previous years, and status of planning and actual performance, and as a result of a careful review on the adequacy of the amount of compensation for the fiscal year under review, has approved the amount of compensation to be paid to the accounting auditor, pursuant to the provisions of Article 399, Paragraph 1 of the Companies Act.

2. The amounts of compensation for audits paid in accordance with the Companies Act, and the audits conducted in accordance with the Financial Instruments and Exchange Act, are not distinguished in the contract agreement between the Company and the accounting auditor. It is not possible to distinguish between compensation paid for these two types of audits; therefore the total amount thereof is stated.

### (4) Policies for dismissal or non-reappointment of the accounting auditor

When it is deemed necessary to dismiss (or not reappoint) the accounting auditor for reasons relating to the accounting auditor's execution of duties, the Audit & Supervisory Board shall determine the contents of a proposal to be presented to a General Meeting of Shareholders in respect of the dismissal (or non-reappointment). In addition, when the accounting auditor falls under any of the items of Article 340, Paragraph 1 of the Companies Act, the Audit & Supervisory Board shall dismiss the accounting auditor with the consent of all members of the Audit & Supervisory Board. If this is the case, an Audit & Supervisory Board Member selected by the Audit & Supervisory Board shall report the dismissal of the accounting auditor and the reasons for such dismissal at the first General Meeting of Shareholders convened after the dismissal.

## **6. System to Ensure the Appropriateness of Operations**

### **(1) The corporate system to ensure that Directors, officers, and employees comply with laws and ordinances, as well as the Articles of Incorporation, in the process of performing their duties**

#### **(i) Dissemination and thorough implementation of management philosophy**

In order to implement its management philosophy, the Company has established a Corporate Action Charter and standards of conduct to which all Company members are expected to adhere. The Company informs all executives and staff regarding these policies and asks for each member's understanding regarding the spirit of these regulations and for thorough compliance with the same. All business activities of the Company are based on the premise of compliance with laws and ordinances and the maintenance of corporate ethical standards (below, "compliance").

#### **(ii) Establishment of internal control committee**

The Company develops internal control systems and employs other measures to support thorough compliance, appropriate risk management, and proper financial reporting. In addition, an internal control committee has been established to ensure complete observance of laws and ordinances, the Articles of Incorporation, and other internal regulations through exhaustive surveillance.

#### **(iii) Establishment of internal audit office**

The Company has established an internal audit office as an independent organizational unit which conducts regular audits and acts under the direct authority of the Representative Director and President. Through such audits, objective assessments are made as to the effectiveness and efficiency of business, the reliability of various financial reports, safeguarding of assets, compliance status of operations, and the appropriateness and effectiveness of corporate risk management policies. When necessary, the Company ensures the efficacy of internal controls by accepting advice and proposals concerning recommended improvements to the maintenance and operation of systems.

#### **(iv) Establishment of compliance reporting and consultation hot-lines**

The Company has established compliance reporting and consultation hot-lines both internal to and outside the Company, and has designated compliance liaisons to respond to reports and requests for consultation from employees and aim to identify and resolve any compliance issues at the earliest stage possible.

#### **(v) Systems for securing reliable financial reporting**

The Company establishes internal control systems and oversees their appropriate operation in order to ensure reliable financial reporting.



**(2) Corporate system for maintenance and control of information regarding the performance of duties by Directors**

The Company appoints an individual to be responsible for the general management of corporate documents and to appropriately maintain and otherwise control all important documents containing information as to the performance by Directors of their duties in addition to legally required records of proceedings of Shareholders meetings and Board of Directors meetings, as provided in laws and ordinances as well as in the Company's own "Rules for the Management of Documents."

**(3) Corporate system for control of risk of loss, including in-house rules for such control**

The Company practices risk control under its basic risk control policy and related rules. The Internal Control Committee is responsible for the supervision and promotion of risk management. Additionally, the Company will swiftly respond to emergency situation by establishing an emergency response headquarters managed by the Representative Director and President.

**(4) Corporate system to ensure the efficient performance of duties by Directors**

- (i) Directors, officers, and employees perform their duties in appropriate and efficient accordance with the "Rules for the Board of Directors" and "Rules for the Internal Approvals," as well as other related regulations.
- (ii) The Company regularly holds Executive Management Committee meetings pursuant to the "Rules for the Executive Management Committee" and reviews key proposals for the purpose of supporting precise and timely decision-making from the Representative Director and President.
- (iii) The Company develops mid- to long-term business plans and operates and expands its business in accordance with these plans. In addition, the Company establishes numerical targets within its business plans for each fiscal year and, through monthly closings, manages progress toward these targets while making relevant reports to Directors.

**(5) Basic policy against anti-social forces**

The Company resolutely opposes anti-social forces that pose a threat to the order or safety of society and forbids their participation in any and all business activities.

**(6) Assistant to Audit & Supervisory Board Members**

Audit & Supervisory Board Members may request that the Representative Director and President appoint an employee to act as an assistant to Audit & Supervisory Board Members. Upon receiving such a request, the Representative Director and President shall make an

appropriate appointment.

**(7) Ensuring the independence of assistants to Audit & Supervisory Board Members from Directors and the effectiveness of the Audit & Supervisory Board Members' instructions to employees**

- (i) Assistants to Audit & Supervisory Board Members shall not receive instructions concerning their supporting duties from anyone other than Audit & Supervisory Board Members.
- (ii) Matters such as personnel evaluation and transfer and disciplinary actions concerning employees that assist Audit & Supervisory Board Members shall be subject to the prior consent of the Audit & Supervisory Board.

**(8) Corporate system for Directors and employees to report to the Audit & Supervisory Board; corporate system for other reports to the Audit & Supervisory Board; and corporate system to ensure the efficient performance of audits by the Audit & Supervisory Board**

- (i) Any Director or employee shall promptly inform the Audit & Supervisory Board if and when he/she becomes aware of any circumstance that threatens to cause any significant damage to, or could adversely affect, the Company.
- (ii) Audit & Supervisory Board Members may participate in all matters that they judge to be important in terms of gaining a better understanding of decision-making processes, conditions, and statuses of the Company's businesses. Accordingly, they may attend Board of Directors meetings, Executive Management Committee meetings, and other important meetings and are also permitted to view key decision-making documents related to these meetings.
- (iii) Audit & Supervisory Board Members may individually interview Directors and employees in key positions of responsibility to obtain information regarding the management conditions of the Company's businesses.
- (iv) Audit & Supervisory Board Members will regularly exchange opinions with the Representative Director and President and the accounting auditor.
- (v) The Company will not apply any sort of unfavorable treatment or unjust punishment to individuals who make reports to the Audit & Supervisory Board.

**(9) Matters related to the treatment of expenses or obligations associated with the execution of duties of Audit & Supervisory Board Members, including the procedures for prepayment or reimbursement of such expenses**

- (i) The Company will respond without delay to claims for the prepayment of expenses made by Audit & Supervisory Board Members under Article 388 of the Companies Act,

accepting responsibility for associated expenses and processing related obligations, except in cases in which these have been determined unnecessary for the execution of the duties of Audit & Supervisory Board Members.

- (ii) The Company authorizes and shoulders expenses incurred when Audit & Supervisory Board Members seek opinions or advice from external experts, including attorneys and certified public accountants, if it is found necessary for the execution of their duties.

#### **7. Summary of the Status of System to Ensure the Appropriateness of Operations**

- (1) The Company is striving to instill a culture of compliance across the organization and ensure appropriate operation of internal control systems through its communications with Directors and employees, and through publication of information such as the basic policies regarding internal control systems, corporate compliance conduct principles, basic risk control policies, and the whistleblowing system manual on the Company's intranet bulletin board.
- (2) At the Board of Directors meetings of the Company, Outside Directors participate in resolutions from an independent standpoint and monitor and supervise the management. Each Audit & Supervisory Board Member carries out management audits as well.
- (3) Full-time Audit & Supervisory Board Members attend important meetings such as the Board of Directors meetings as well as Executive Management Committee meetings, and exchange views with representative directors monthly.

## Balance Sheet

(As of December 31, 2019)

(Unit: thousands of yen)

Item	Amount	Item	Amount
(Assets)		(Liabilities)	
<b>Current assets</b>	<b>4,887,491</b>	<b>Current liabilities</b>	<b>872,219</b>
Cash and deposits	3,910,830	Accounts payable–trade	120,913
Accounts receivable–trade	549,275	Accounts payable–other	639,482
Supplies	640	Income taxes payable	87,756
Prepaid expenses	94,002	Other	24,066
Advances paid	41,791	<b>Non-current liabilities</b>	<b>1,619</b>
Consumption taxes receivable	275,324	Provision for retirement benefits	1,619
Other	15,626	<b>Total liabilities</b>	<b>873,838</b>
<b>Non-current assets</b>	<b>386,463</b>	(Net assets)	
Property, plant and equipment	75,491	<b>Shareholders' equity</b>	<b>3,779,202</b>
Buildings	47,486	Capital stock	14,870,639
Tools, furniture and fixtures	66,241	Capital surplus	14,843,137
Construction in progress	21,513	Legal capital surplus	14,840,639
Accumulated depreciation	(59,750)	Other capital surplus	2,498
Intangible assets	240,525	Retained earnings	(25,919,496)
Software	94,974	Other retained earnings	(25,919,496)
Software in progress	145,551	Retained earnings brought forward	(25,919,496)
Investments and other assets	70,446	Treasury shares	(15,077)
Shares of subsidiaries	0	Share acquisition rights	620,913
Lease and guarantee deposits	70,446	<b>Total net assets</b>	<b>4,400,116</b>
<b>Total assets</b>	<b>5,273,955</b>	<b>Total liabilities and net assets</b>	<b>5,273,955</b>

(Note) Amounts of less than one thousand yen are rounded down.

## Statement of Income

( From January 1, 2019  
to December 31, 2019 )

(Unit: thousands of yen)

Item	Amount	
<b>I. Net sales</b>		<b>2,837,753</b>
<b>II. Cost of goods sold</b>		<b>1,973,002</b>
<b>Gross profit</b>		<b>864,751</b>
<b>III. Selling, general and administrative expenses</b>		<b>5,166,366</b>
<b>Operating loss</b>		<b>(4,301,615)</b>
<b>IV. Non-operating income</b>		
Interest income	235	
Insurance claim income	2,736	
Dividend income of insurance	1,282	
Interest on tax refund	76	
Other	0	4,331
<b>V. Non-operating expenses</b>		
Commission fee	10,457	
Share issuance cost	13,932	
Foreign exchange losses	54,755	
Other	227	79,372
<b>Ordinary loss</b>		<b>(4,376,655)</b>
<b>VI. Extraordinary income</b>		
Gain on reversal of share acquisition rights	4,197	4,197
<b>Loss before income taxes</b>		<b>(4,372,458)</b>
Income taxes—current	3,800	3,800
<b>Net loss</b>		<b>(4,376,258)</b>

(Note) Amounts of less than one thousand yen are rounded down.

## Statement of Changes in Equity

( From January 1, 2019  
to December 31, 2019 )

(Unit: thousands of yen)

	Shareholders' equity				
	Capital stock	Capital surplus			Retained earnings
		Legal capital surplus	Other capital surplus	Total capital surplus	Other retained earnings Retained earnings brought forward
Balance as of January 1, 2019	12,972,579	12,942,579	—	12,942,579	△21,543,238
Changes of items during period					
Issuance of new shares (exercise of share acquisition rights)	1,898,059	1,898,059		1,898,059	
Net loss					△4,376,258
Purchase of treasury shares					
Disposal of treasury shares			2,498	2,498	
Net changes of items other than shareholders' equity					
Total changes of items during period	1,898,059	1,898,059	2,498	1,900,558	△4,376,258
Balance as of December 31, 2019	14,870,639	14,840,639	2,498	14,843,137	△25,919,496

	Shareholders' equity		Share Acquisition rights	Total net assets
	Treasury shares	Total shareholders' equity		
Balance as of January 1, 2019	△17	4,371,902	529,897	4,901,799
Changes of items during period				
Issuance of new shares (exercise of share acquisition rights)		3,796,119		3,796,119
Net loss		△4,376,258		△4,376,258
Purchase of treasury shares	△20,871	△20,871		△20,871
Disposal of treasury shares	5,811	8,310		8,310
Net changes of items other than shareholders' equity			91,016	91,016
Total changes of items during period	△15,059	△592,699	91,016	△501,663
Balance as of December 31, 2019	△15,077	3,779,202	620,913	4,400,116

(Note) Amounts of less than one thousand yen are rounded down.

## Notes to Non-Consolidated Financial Statements

### (Significant accounting policies)

#### (1) Valuation basis and method of marketable and investment securities

##### Marketable and investment securities

Shares of subsidiaries and affiliates	Shares of subsidiaries are stated at cost determined by the moving-average method.
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##### Other marketable and investment securities

Available-for-sale securities with determinable market value	Available-for-sale securities with a determinable market value are stated at fair value based on marketable value on the closing date and other premises. Any valuation differences are included directly in shareholders' equity. Cost of securities sold is calculated by the moving-average method.
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Available-for-sale securities without determinable market value	Available-for-sale securities without determinable market value are stated at cost determined by the moving-average method.
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Derivative transactions	Derivative financial instruments are stated at fair value.
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Inventories	Inventories are stated at cost determined by the weighted-average method. The amount on the balance sheet is calculated by reducing book value when the contribution of inventories to profitability declines.
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#### (2) Depreciation and amortization of non-current assets

Property, plant and equipment (excluding lease assets)	Depreciation of property, plant and equipment is computed by the straight-line method. The useful lives of major property, plant and equipment are summarized as follows:
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Buildings	3 to 18 years
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Tools, furniture and fixtures	4 to 20 years
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Intangible assets (excluding lease assets)	Amortization of intangible assets is computed by the straight-line method.
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Capitalized software costs are being amortized over the period of the internal use of five years.

Lease assets	Depreciation of lease assets is computed by the straight-line method over the lease term with no residual value.
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(3) Deferred assets

Share issuance costs and bond issuance costs	Share issuance costs and bond issuance costs are recorded as expenses in full at the time of expenditure.
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(4) Basis for translating assets and liabilities denominated in foreign currencies into Japanese yen

Monetary assets and liabilities denominated in foreign currencies are translated into Japanese yen at the spot exchange rates prevailing on the closing date, and resulting gains or losses are credited or charged to income.

(5) Basis for reserves and provisions

Allowance for doubtful accounts	The allowance for doubtful accounts is provided at an amount determined based on the historical experience of bad debt with respect to ordinary receivables and an estimate of uncollectible amounts determined by reference to specific doubtful receivables from customers which are experiencing financial difficulties.
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For the fiscal year under review, no allowance for doubtful accounts is provided due to no historical experience of bad debt and no receivable balances that are deemed uncollectible.

Provision for retirement benefits	The provision for retirement benefits is provided based on an estimated amount for retirement benefit obligations at the end of fiscal year under review.
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The Company applies the simplified method to calculate amounts of provision for retirement benefits and retirement benefit expenses. That is, the amount of retirement benefit obligations are the payments required for voluntary retirement as of each fiscal year end.

(6) Accounting for consumption tax

Transactions are recorded at amounts exclusive of consumption tax.

**(Balance sheet)**

Monetary assets receivable from subsidiaries are as follows.

Short-term monetary assets receivable: 1,540 thousand yen

**(Statement of income)**

(1) Inventories at fiscal year-end are stated after writing down based on the decrease in profitability. The following amount is included within cost of sales as loss on valuation of inventories.

Cost of sales: 187,840 thousand yen

A certain batch of TREAKISYM® 100mg was determined to be unsalable due to its poor quality, which resulted in an inventory valuation loss.

(2) R&D costs included in general and administrative expenses: 2,441,552 thousand yen

**(Statement of changes in equity)**

(1) Type and number of shares issued and treasury shares

(Unit: number of shares)

		At beginning of current period	Increase	Decrease	At end of current period
Common stock	Shares outstanding	82,398,924	17,126,800	73,088,043	26,437,681
	Treasury shares	75	31,050	8,532	22,593

(Notes) 1. Increase of 17,126,800 shares issued in common stock is due to the exercise of share acquisition rights.

2. Decrease of 73,088,043 shares issued in common stock is due to the 1-for-4 consolidation of common shares conducted on July 1, 2019.

3. Increase of 31,050 treasury shares in common stock is due to the purchase of shares less than one unit.

4. Of the decrease of 8,532 treasury shares in common stock, the decrease of 57 shares is due to the 1-for-4 consolidation of common shares conducted on July 1, 2019, 6,775 shares to the exercise of share acquisition rights, and 1,700 shares to the sale of shares less than one unit.

(2) Number of shares to be issued upon exercise of share acquisition rights issued at the end of the fiscal year under review

Common stock 2,265,950 shares

(Note) Excludes share acquisition rights for which the commencement date of the exercise period has not yet arrived.

**(Deferred tax accounting)**

Significant components of deferred tax assets and liabilities

Deferred tax assets:	(Unit: thousands of yen)
Excess depreciation for lump-sum depreciable assets	3,404
Excess amortization for deferred assets	669,030
Research and development expenses disallowed	2,033,400
Accounts payable—other disallowed	4,385
Provision for retirement benefits disallowed	495
Enterprise tax payable disallowed	27,509
Asset retirement obligations disallowed	1,458
Share-based compensation expenses disallowed	162,750
Loss carried forward	4,063,034
Subtotal of deferred tax assets	6,965,465
Valuation allowances for loss carried forward	(4,063,034)
Valuation allowances for deductible temporary differences	(2,902,431)
Subtotal of valuation allowances	(6,965,465)
Total deferred tax assets	—

**(Financial instruments)**

(1) Financial instruments

(i) Policies for financial instruments

The Company procures the funds necessary in light of the pipeline development plan (primarily by third-party allotment and offering by new share issuance). A temporary surplus fund is invested in financial instruments which are highly safe and liquid.

As a principle, the Company does not enter into derivative transactions for speculative trading purposes but uses them within the scope prescribed in the Company's internal rules.

(ii) Types of financial instruments and related risks

Operating receivables such as accounts receivable-trade and advances paid in connection with joint development are exposed to the credit risk of customers and joint development partners. Operating receivables denominated in foreign currencies are exposed to foreign exchange fluctuation risk.

The Company intends to invest in marketable and investment securities which have a relatively low risk of falling below initial investments, however, it might entail a finite risk.

Operating payables such as accounts payable-trade and accounts payable-other are mostly due within 75 days. Operating payables denominated in foreign currencies are exposed to foreign exchange fluctuation risk.

The Company uses derivative transactions to avoid foreign exchange fluctuation risks and enters into forward exchange contracts within the scope prescribed in the internal rules based on balances of receivables and payables denominated in foreign currencies as well as the actual volume of export and import transactions denominated in foreign currencies.

Lease and guarantee deposits are mostly security deposits related to leased office premises and their refunds are subject to the credit risk of the lessor.

(iii) Risk management for financial instruments

1. Monitoring of credit risks (the risk that customers or counterparties may default on obligations)

In accordance with the Company's internal credit policies for managing credit risk arising from operating receivables, the Company's marketing department periodically monitors the creditworthiness of major customers and monitors due dates and outstanding balances by individual customers. In addition, the Company is making efforts to promptly identify and mitigate risks of bad debts from customers who are having financial difficulties.

The Company enters into derivative transactions only with financial institutions which have a sound credit profile in order to mitigate the counterparty risk.

2. Monitoring of market risk (the risk arising from fluctuations in foreign exchange rates, interest rates, and others)

The Company deposits cash primarily with financial institutions with high credit ratings.

For marketable and investment securities, the Company intends to avoid risks of falling below initial investments by investing in securities with a satisfactory credit rating and investment period in accordance with the Company's internal investment policies.

The Company enters into forward exchange contracts in order to avoid foreign exchange fluctuation risks in connection with receivables and payables denominated in foreign currencies.

Followed by appropriate authorization procedures prescribed in the Company's internal rules, the Finance & Accounting department executes and monitors derivative transactions. Monthly transaction performances are reported to the Executive Management Committee.

3. Monitoring of liquidity risks (the risk that the Company may not be able to meet its obligations on the scheduled due date)

Based on the report from each department, the responsible department of the Company prepares and updates its cash flow plans on a timely basis and ensures to maintain the liquidity on hand to manage liquidity risk.

(iv) Supplementary explanation of the estimated fair value of financial instruments

The fair value of financial instruments is based on their quoted market price, if available. When there is no quoted market price available, fair value is reasonably estimated. Since various assumptions and factors are reflected in estimating the fair value, different assumptions and factors could result in different fair value.

(v) Concentration of credit risk

As of the end of fiscal year under review, all operating receivables are from one particular major customer.

(2) Fair value of financial instruments

The carrying value on the balance sheet, fair values, and their differences are as follows.

(Unit: thousands of yen)

	Carrying value on the balance sheet	Fair value	Difference
(1) Cash and deposits	3,910,830	3,910,830	—
(2) Accounts receivable—trade	549,275	549,275	—
(3) Advances paid	41,791	41,791	—
(4) Consumption taxes receivable	275,324	275,324	—
Assets, total	4,777,222	4,777,222	—
(1) Accounts payable—trade	120,913	120,913	—
(2) Accounts payable—other	639,482	639,482	—
(3) Income taxes payable	87,756	87,756	—
Liabilities, total	848,153	848,153	—
Derivative transactions, total (*)	—	—	—

(\*) Receivables and liabilities arising from derivative transactions are presented on a net basis and net liabilities are shown in parentheses.

(Note) 1. Fair value measurement of financial instruments and other matters related to securities and derivative transactions

Assets

(1) Cash and deposits, (2) Accounts receivable—trade, (3) Advances paid, and (4) Consumption taxes receivable

The carrying value is deemed as the fair value since these are scheduled to be settled in a short period of time.

Liabilities

(1) Accounts payable—trade, (2) Accounts payable—other, and (3) Income taxes payable

The carrying value is deemed as the fair value since these are scheduled to be settled in a short period of time.

Derivative transactions

Forward exchange contracts

The fair value of forward exchange contracts is measured based on market quotes obtained from financial institutions.

(Note) 2. Financial instruments whose fair value is extremely difficult to determine

Lease and guarantee deposits (carrying value of 70,446 thousand yen) are not included in the above table since no market quote is available and their fair value is extremely difficult to determine.

(Note) 3. The redemption schedule for monetary assets and securities with maturities after the closing date

(Unit: thousands of yen)

	Due in one year or less	Due after one year through five years	Due after five years through ten years	Due after ten years
Deposits	3,910,739	—	—	—
Accounts receivable-trade	549,275	—	—	—
Advances paid	41,791	—	—	—
Consumption taxes receivable	275,324	—	—	—
Total	4,777,131	—	—	—

**(Transactions with affiliated parties)**

None to be reported.

**(Per-share information)**

(1) Net assets per share 143.07 yen

(2) Net loss per share (189.03) yen

Average number of shares outstanding during the year 23,150,655 shares

(Note) The Company conducted a 1-for-4 consolidation of common shares on July 1, 2019. Loss per share has been calculated based on the assumption that this consolidation was conducted at the beginning of FY 2019.

**(Other notes)**

The Company has overdraft and commitment line contracts with three banks in a business relationship to efficiently procure working capital. The status of the bank overdraft and loan commitments based on these contracts at the end of the fiscal year under review is as follows:

(Unit: thousands of yen)

Total amounts of bank overdraft limit and loan commitment line	1,350,000
Balance of borrowing outstanding	—
Unused balance	1,350,000

**(Significant subsequent events)**

None to be reported.

## Independent Auditor's Report

February 18, 2020  
The Board of Directors  
SymBio Pharmaceuticals Limited

Ernst & Young ShinNihon LLC

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Hironao Yazaki  
Certified Public Accountant  
Designated and Engagement Partner

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Koichiro Kitaike  
Certified Public Accountant  
Designated and Engagement Partner

Pursuant to Article 436, Section 2, Paragraph 1 of the Companies Act, we have audited the accompanying financial statements, which comprise the balance sheet, the statement of income, the statement of changes in equity, the notes to non-consolidated financial statements and the related supplementary schedules of SymBio Pharmaceuticals Limited (the "Company") applicable to the 15th fiscal year from January 1, 2019 through December 31, 2019.

*Management's Responsibility for the Financial Statements and the Related Supplementary Schedules*

Management is responsible for the preparation and fair presentation of these financial statements and the related supplementary schedules in accordance with accounting principles generally accepted in Japan, and for designing and operating such internal control as management determines is necessary to enable the preparation and fair presentation of the financial statements and the related supplementary schedules that are free from material misstatement, whether due to fraud or error.



#### *Auditor's Responsibility*

Our responsibility is to express an opinion on these financial statements and the related supplementary schedules based on our audit. We conducted our audit in accordance with auditing standards generally accepted in Japan. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements and the related supplementary schedules are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements and the related supplementary schedules. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements and the related supplementary schedules, whether due to fraud or error. The purpose of an audit of the financial statements is not to express an opinion on the effectiveness of the entity's internal control, but in making these risk assessments the auditor considers internal controls relevant to the entity's preparation and fair presentation of the financial statements and the related supplementary schedules in order to design audit procedures that are appropriate in the circumstances. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by management, as well as evaluating the overall presentation of the financial statements and the related supplementary schedules.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

#### *Opinion*

In our opinion, the financial statements and the related supplementary schedules referred to above present fairly, in all material respects, the financial position and results of operations of SymBio Pharmaceuticals Limited applicable to the 15th fiscal year ended December 31, 2019 in conformity with accounting principles generally accepted in Japan.

#### *Conflicts of Interest*

We have no interest in the Company which should be disclosed in compliance with the Certified Public Accountants Act.

## **Report of the Audit & Supervisory Board**

We, Audit & Supervisory Board Members, prepare this report of audit with regard to the execution of Directors' duties during the 15th Term of the Company from January 1, 2019 to December 31, 2019, as the unanimous opinion of all the Audit & Supervisory Board Members after careful discussion based on the audit reports prepared by respective Audit & Supervisory Board Members, and report as follows.

### **1. Method and Contents of the Audit by the Audit & Supervisory Board Members and the Audit & Supervisory Board**

The Audit & Supervisory Board formulated the audit policy and plan for the Term reported, and received reports from the respective Audit & Supervisory Board Members with regard to the state of implementation and results of audits as well as received the reporting from Directors and the accounting auditor with regard to the state of execution of their duties, and requested additional explanations as deemed necessary.

The respective Audit & Supervisory Board Members, in conformity with the standards for audits by Audit & Supervisory Board Members that the Audit & Supervisory Board set forth and in accordance with the audit policy and plan for the Term, strove to collect information and improve audit environments by communicating with Directors, the internal audit section, and other employees. We also attended Board of Directors meetings and other important meetings, received the reporting from Directors and employees with regard to the state of execution of their duties, requesting additional explanations as deemed necessary, reviewed documents for important settlements, and researched the situation of operations and assets. Moreover, with regard to the system to ensure that the execution of Directors' duties described in the business report was compliant with laws and ordinances and the Company's Articles of Incorporation and other systems required to secure the appropriateness of operations as a stock company maintained based on the contents of resolution by the Board of Directors with regard to the maintenance of systems stipulated by the Ordinance for Enforcement of Article 100, Paragraph 1 and 3 of the Companies Act (hereinafter the "Internal Control System"), we received reporting on the status of their establishment and operation from Directors and employees, requested additional explanation as deemed necessary, and expressed our opinion. Based on the method described above, we reviewed the business report and supplementary schedules with regard to the Term reported.

In addition, we monitored and inspected the independent position of the accounting auditor and the execution of appropriate audits by the accounting auditor, and also received the reporting from the accounting auditor with regard to the state of execution of its duties, requesting additional explanation as deemed necessary. Furthermore, we received the notification from the accounting auditor that “the system to ensure that its duties are executed as appropriate (the items listed by the respective paragraphs of Article 131 of the Ordinance on the Accounting of Companies)” is maintained in accordance with “the standards for quality control of audits (Business Accounting Council, October 28, 2005),” requesting additional explanation as deemed necessary. Based on the method described above, we reviewed the financial report (including balance sheet, statement of income, statement of changes in equity, and notes to non-consolidated financial statements) and related supplementary schedules for the Term reported.

## 2. Results of audit

### (1) Results of the audit of the business report

- a. The business report and supplementary schedules fairly present the Company’s situation in accordance with laws and ordinances and the Company’s Articles of Incorporation.
- b. No misconduct in the execution of Directors’ duties or any material facts in violation of laws or ordinances or the Company’s Articles of Incorporation was observed.
- c. The contents of resolution by the Board of Directors with regard to the Internal Control System are appropriate. Also, there is no matter to be noted as for the descriptions in the business report regarding such Internal Control System and the execution of Directors’ duties.

### (2) Results of the audit of the financial statements and related supplementary schedules

Both the method used for and the result of the audit conducted by the accounting auditor, Ernst & Young ShinNihon LLC, are appropriate.

February 18, 2020

Audit & Supervisory Board,  
SymBio Pharmaceuticals Limited

Kiyoshi Watanabe, (seal)  
Full-time Audit & Supervisory Board Member (Outside)

Kesao Endo, (seal)  
Audit & Supervisory Board Member (Outside)

Eiji Ebinuma, (seal)  
Audit & Supervisory Board Member (Outside)

End of Report

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