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SymBio Pharmaceuticals Limited
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Representative Director
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(Securities Code: 4582)

SymBio enters into Sponsored Research Agreement for non-clinical study to verify the effectiveness of brincidofovir in a virus-infected brain tissue model

TOKYO, Japan, December 19, 2022 -- SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") today announced that the Company has entered into a Sponsored Research Agreement (SRA) with Tufts University ("Tufts University") to conduct joint research on the intravenous formulation of the anti-viral drug brincidofovir*¹ ("BCV IV"). This joint research is a non-clinical study (the "Study") that will evaluate the efficacy of BCV in a herpes simplex virus (HSV) infection model using a 3D (three-dimensional) brain model*² established by Tufts University.

Some double-stranded DNA viruses*³ (dsDNA), such as HSV1, VZV, and HHV6, are directed against cranial nerve tissues and are known to cause serious diseases in various cranial nerve areas due to infection caused by their reactivation. BCV is an antiviral drug effective against a broad spectrum of dsDNA viruses. SymBio is currently conducting global Phase II clinical studies using BCV in patients with adenovirus infection after hematopoietic stem cell transplantation, and in patients with BK virus infection after renal transplantation. The research conducted under the SRA will test the potential utility of BCV against HSV infection and reactivation using human-induced neural stem cells in a three-dimensional bioengineered brain model, which has been established at Tufts University.

Statement from David Kaplan, Chair, Professor of the Department of Biomedical Engineering, Tufts University and lead investigator with Dana Cairns (research associate in the lab) of the Study: "The goal of this study is to provide evidence to support the development of new treatments for neurological diseases for which there is still no fundamental cure."

Statement from Mr. Fuminori Yoshida, President and CEO of SymBio: "In the past few years, Professor Ruth Itzhaki of Oxford University in the UK has shown that the presence of HSV1 in the brain, in combination with a specific gene, APOE4, increases the likelihood of developing Alzheimer's disease, and there is increasing evidence that dsDNA viruses are involved in neurological disorders, including Alzheimer's disease. If we can suppress the onset and progression of these diseases by directly inhibiting the causative virus, we expect to be able to develop therapeutic methods and provide new treatment options."

The Company does not expect the information presented herein to have any material impact on its financial outlook for the fiscal year ending December 2022.

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(Note1) About the Anti-viral Drug Brincidofovir

Brincidofovir (BCV) is a lipid conjugate of cidofovir (CDV). CDV is an antiviral drug already approved and marketed in the United States and the European Union, but unapproved in Japan. As BCV exhibits not only higher anti-viral activity, but also a superior characteristics profile in comparison with CDV and other antiviral drugs, BCV is expected to be an effective treatment against a wide spectrum of dsDNA viruses such as herpesviruses, cytomegalovirus (CMV), adenovirus (AdV), Epstein-Barr virus (EBV), papillomavirus and BK virus. Moreover, BCV is expected to be a highly active anti-multiviral agent that can reduce the risk of nephrotoxicity or myelosuppression, which are serious side effects of other antiviral drugs including CDV. Symbio entered into an exclusive global license agreement with Chimerix Inc. (Headquarters: Durham, NC, "Chimerix") for brincidofovir (BCV) on September 30, 2019. Under the terms of the agreement, Chimerix grants Symbio exclusive worldwide rights to develop, manufacture, and commercialize BCV in all human indications, excluding the prevention and treatment of orthopox infections (which includes smallpox and monkeypox).

The Company aims to expand its business to become a global specialty pharmaceutical company by 2030. To maximize business value, the Company is currently conducting a global Phase II clinical trial mainly in the U.S. for patients with adenovirus infection after hematopoietic stem cell transplantation, and initiated a global Phase II clinical trial mainly in Australia, Japan, and South Korea for patients with BK virus infection after kidney transplantation in June 2022.

In addition to its high antiviral activity, BCV is also expected to have anti-tumor effects, and we are currently conducting joint research with the National Cancer Center of Singapore, the University of California, San Francisco, and Brown University in the U.S. to confirm BCV's anti-cancer activity and synergistic effects when combined with its antiviral activity. Furthermore, the Company has initiated a study to evaluate the potential antiviral activity of BCV against Epstein-Barr virus in collaboration with the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health (NIH) in the U.S.

(Note 2) Herpes simplex virus (HSV) infection model using a 3D (three-dimensional) brain model

Using a porous silk protein sponge with a collagen filler as a substrate, human neural stem cells are cultured in this experimental system where they grow and differentiate into a functional network of neurons and glial cells, which is sensitive to viral infection. The system can be evaluated for

electrophysiological function. amyloid β fiber formation, neuroinflammation, etc. induced by HSV infection under conditions that exclude other factors.

<https://www.science.org/doi/10.1126/sciadv.aay8828>

(Note 3) Double-stranded DNA (dsDNA) viruses

Double-stranded DNA (dsDNA) viruses includes Herpesviridae (e.g., CMV, HHV-6), adenoviridae (AdVs), polyomaviridae (e.g., BK virus and JC virus), papillomaviridae (HPVs), and poxviridae.

About SymBio Pharmaceuticals Limited

SymBio Pharmaceuticals Limited was established in March 2005 by Fuminori Yoshida who previously served concurrently as Corporate VP of Amgen Inc. and founding President of Amgen Japan. In May 2016, the Company incorporated its wholly-owned subsidiary in the U.S., SymBio Pharma USA, Inc. (Headquarters: Durham, North Carolina, President: Carolyn Yanavich).

The Company's underlying corporate mission is to "deliver hope to patients in need" as it aspires to be a leading global specialty biopharmaceutical company dedicated to addressing underserved medical needs.