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SymBio Pharmaceuticals Limited
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Representative Director
President and Chief Executive Officer
(Securities Code: 4582)

The Results of CRADA Study on Brincidofovir in Multiple Sclerosis Presented at the 9th Joint ECTRIMS-ACTRIMS Meeting

TOKYO, Japan, October 12, 2023 -- SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") is currently collaborating with the National Institute of Neurological Disorders and Stroke ("NINDS"), part of the National Institutes of Health ("NIH") in the United States for the treatment of multiple sclerosis ("MS"). SymBio today announced that the research results regarding brincidofovir ("BCV") were presented by Dr. Maria Chiara Monaco (of NINDS) at the 9th Joint ECTRIMS-ACTRIMS Meeting in Milan, Italy, held from October 11 to 13, 2023.

The highlights of the presentation include:
- BCV inhibited viral replication in a dose dependent manner in lymphoblastoid cells immortalized by endogenous EBV (EBV positive B cell lines) derived from both MS patients and healthy controls.
- In the EBV negative B cell line, no BCV activity was observed including growth inhibition.
- These preliminary data suggest the potential use of BCV as an anti-EBV therapeutic in patients with MS.

In recent years, an increasing number of studies have demonstrated that EBV is a risk factor for MS. SymBio entered into a Cooperative Research and Development Agreement ("CRADA") with the NINDS in March 2023 to establish a new treatment method for MS with BCV, and has been conducting collaborative research towards a clinical trial. The presentation at the 9th joint ECTRIMS-ACTRIMS meeting was the first report of the CRADA study.

Statement from Mr. Fuminori Yoshida, President and CEO: "We are very excited at the findings, which suggest that directly targeting Epstein Bar virus could provide a new treatment option for patients suffering from multiple sclerosis. We look forward to the next step of our collaboration with the NINDS team towards a clinical study."

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(Note)

National Institute of Neurological Disorders and Stroke (NINDS)

The NINDS is one of the 27 institutes and centers that make up the NIH, whose mission is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease for all people. The NINDS' FY 2023 budget is $2.8 billion. Its major research areas include basic biology of the brain and nervous system, genetics, neuro degeneration, learning and memory, motor control, brain repair, and synapses, and also funds clinical research on diseases and disorders of the brain and nervous system, including AIDS, Alzheimer's disease, epilepsy, muscular dystrophy, multiple sclerosis, Parkinson's disease, spinal cord injury, stroke, and traumatic brain injury. The NINDS also funds clinical research on brain and nervous system diseases and disorders, including Alzheimer's disease, epilepsy, multiple sclerosis, spinal cord injury, stroke, and traumatic brain injury.

National Institutes of Health (NIH)

NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases.

9th Joint ECTRIMS-ACTRIMS Meeting (MSMilan2023)

MSMilan2023 – to be held 11-13 October in Milan, Italy – offers participants a full range of opportunities to participate onsite and online, with a diverse program aimed at connecting colleagues from across multiple disciplines, institutes, and countries.

Lymphoblastoid cell lines (LCLs)

LCLs are EBV-transformed lymphoblastoid B-cell lines, which can be easily established by EBV infection or derived spontaneously from peripheral blood B lymphocytes.

Cooperative Research and Development Agreement (CRADA)

A Cooperative Research and Development Agreement (CRADA) is a formal agreement that facilitates research and development collaborations between federal laboratories at a government agency and a non-federal partner such as a private company or university, to jointly pursue common research goals. The purpose of the CRADA is to make available government facilities, intellectual property, and expertise for collaborative interactions that lead to the development of useful, marketable products that benefit public health. Under the CRADA, the Collaborator is granted the first option to take a license, for any inventions that are made jointly by NIH inventors/researchers and the Collaborator's inventors/researchers during the research program or by NIH inventors/researchers alone.

About the anti-viral drug Brincidofovir

Brincidofovir (BCV) has a new mechanism of action as 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. BCV is expected to be an effective treatment against a wide spectrum of dsDNA virus infections (cytomegalovirus, adenovirus, Epstein-Barr virus, herpes virus, BK virus, papillomavirus and smallpox virus including monkeypox, etc.), with superior features such as high activity antiviral effect in comparison with CDV and other antiviral drugs.

Due to the breakthrough nature of the BCV molecule, in which a specific length of lipid chain is attached to the CDV, BCV is converted into a molecule that acts directly within the cell, thereby dramatically increasing the efficiency of cellular uptake and showing a high antiviral activity.

In September 2019, SymBio entered into a license agreement with Chimerix for the exclusive worldwide rights to develop, market, and manufacture BCV for all diseases except orthopoxviruses (such as smallpox and monkeypox).

The tablets and oral suspension (oral formulation) were approved on June 4, 2021, for the treatment of smallpox in adults and pediatric patients, including neonates.

In addition to its high antiviral activity, BCV is also expected to have anti-tumor effects. We are currently conducting collaborative studies with the National Cancer Center of Singapore, the University of California, San Francisco, and other institutions to confirm its anti-cancer activity and to identify synergistic effects when combined with its antiviral activity.

Clinical trials and important R&D collaborations with prominent research institutions include:

- Initiated a Phase II clinical trial in patients with adenovirus infection after hematopoietic stem cell transplantation (March 2021) and received Fast Track designation from the FDA (April 2021). Proof of Concept (POC) of antiviral efficacy established based on data up to cohort 3 (May 2023).
- Initiated a non-clinical trial at the University of California, San Francisco Neurosurgery Brain Tumor Center to evaluate the anti-tumor effect of BCV on refractory brain tumors (September 2021).
- In recent years, large numbers of studies have demonstrated that EBV is a risk factor for MS. SymBio entered into CRADA with the NINDS in March 2023 to establish a new antiviral treatment method for MS, and has been conducting collaborative research to develop a clinical trial.
- CRADA with the National Institute of Allergy and Infectious Diseases (NIAID), affiliated with the NIH, to evaluate the efficacy of BCV for EB virus-associated lymphoproliferative diseases (April 2023).
- Research on the involvement of infection by reactivation of latent viruses in various neurological severity diseases of the brain, including Alzheimer's disease, has been ongoing for the past several years, and a simple three-dimensional mimicry of human neural stem cell cultures and brain tissue established by Tufts University in the United States, the A Sponsored Research Agreement was signed (December 2022) to examine the effect of BCV on HSV infection using a herpes simplex virus (HSV) infection/reactivation model established by Tufts University in the U.S., which uses human neural stem

cells cultured to mimic brain tissue in three dimensions.

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., called SymBio Pharma USA, Inc. (Headquarters: Durham, North Carolina, representative: Stephane Berthier). 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.