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

Presentation of the Results of Biomarker Research Predicting the Antitumor Effects of Brincidofovir at the 17th ICML.

TOKYO, Japan, June 12, 2023 -- SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") today announced that results of its research collaboration with the National Cancer Centre of Singapore ("NCCS") on brincidofovir ("BCV") will be presented by Dr. Jason Yongsheng Chan at the 17th International Conference on Malignant Lymphoma ("ICML") in Lugano, Switzerland, to be held from June 13 to 17, 2023.

The highlights of the presentation will include:
- In testing NK/T-cell lymphoma cell-lines with both high sensitivity and low sensitivity to BCV, the cell-lines with high sensitivity to BCV correlated well with low expression of TLE1, which acts as a tumor suppressor.
- Low expression of TLE1 was also highly correlated with poorer prognosis (PFS: progression-free survival) in NK/T-lymphoma patients.
- Low expression of TLE1 was found to be highly correlated with increased expression of MYC and other genes known as oncogenes.

Statement from Dr. Jason Yongsheng Chan, Principal Investigator of the study, Consultant in the Division of Medical Oncology, NCCS, and Clinical Assistant Professor at Duke-NUS Medical School: "In this joint research, biomarkers were found in NK/T-cell lymphoma cell-lines that could predict the anti-tumor effect of BCV and are also associated with poor prognosis in patients, which will be very useful in the development of a new treatment option. The validation of these findings is expected to lead to significant advances in the treatment of hematologic and other malignancies."

Statement from Mr. Fuminori Yoshida, President and CEO: "The findings of the collaborative study with NCCS about high correlation between TLE1 and NK/T-cell lymphoma with poor prognosis suggest that the efficacy of BCV as a new treatment for not only hematologic malignancies but other malignancies with poor prognosis can be predicted in advance."

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International Conference on Malignant Lymphoma (ICML)

The International Conference on Malignant Lymphoma (ICML) is a key event for the scientific community engaged in the study and treatment of lymphoid neoplasms. Organized by the Foundation for the Institute of Oncology Research (IOR), in cooperation with the American Association for Cancer Research (AACR) and in collaboration with the European School of Oncology (ESO), the ICML is held in Lugano (Switzerland) every two years and brings together up to 3,500 physicians and scientists from all over the world.

National Cancer Centre Singapore (NCCS)

The National Cancer Centre Singapore (NCCS) is a leading national and regional tertiary cancer centre with specialists who are experts in treating cancer. NCCS attends to the majority of cancer cases in Singapore's public healthcare sector.

For further information, please visit NCCS's website: https://www.nccs.com.sg/

NK/T-Cell Lymphoma

A type of malignant lymphoma that originates from NK or T cells. NK/T-cell lymphomas are classified as low grade (progressing yearly), intermediate grade (progressing monthly), or high grade (progressing weekly), and mainly present as extranodal NK/T-cell lymphomas in the perinasal space or on the skin. This disease is characterized by its relatively high prevalence in Southeast Asia, including China.

MYC

Also known as c-Myc, is one of the oldest oncogenes, and abnormalities of this family of genes have been found in a wide range of cancer types, including translocations, mutations, and amplifications in hematopoietic tumors. It functions as a nuclear transcriptional regulator and is known to be a very important factor in controlling the balance of proliferation and differentiation of hematopoietic cells by regulating the expression of dominant genes.

TLE1

TLE1 is a transcriptional repressor known for its ability to suppress cancer, including hematopoietic tumors, by regulating gene expression; low expression of TLE1 has been reported to be associated with poor prognosis in several cancer types. TLE1 has also been reported to suppress Myc expression and other cancer-promoting signaling pathways.

Biomarker

A biomarker is a substance in a body, such as a protein or gene that can be used as an indicator of changes in a disease state or the effectiveness of treatment. Biomarkers are used to investigate the nature of cancer in advance, predict the effectiveness of treatment, and formulate a treatment plan. (Source: Cancer Information Service, National Cancer Center Japan)

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 major R&D collaborations with prominent research institutions are underway as follows:

- 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 Phase II clinical trial in patients with BK virus infection after renal transplantation (May 2022).
- 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).
- With regard to multiple sclerosis, an intractable disease that has recently been proven to be associated with the EB virus, the National Institute of Neurological Disorders and Stroke (NINDS), affiliated with the National Institutes of Health (NIH), will examine BCV's efficacy against the EB virus in the

treatment of multiple sclerosis, and to obtain information needed to conduct future clinical trials (March 2023).

- 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., 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.