August 14, 2023
SymBio Pharmaceuticals Limited
Fuminori Yoshida
Representative Director
President and Chief Executive Officer
(Securities Code: 4582)

Revision to Development Plan for IV Brincidofovir for BK virus

TOKYO, Japan, August 14, 2023 -- SymBio Pharmaceuticals Limited (Headquarters: Tokyo, Japan; "SymBio") announced that the board of directors, at a meeting held today, approved a revision to the development plan for the Phase II clinical trial of the intravenous formulation of brincidofovir ("IV BCV") for BK virus ("BKV") infection after renal transplantation. The phase II clinical trial was expected to end in 2025. Due to delays in enrollment, protocol modifications will be discussed with the investigators.

The Company plans to initiate two clinical trials for IV BCV in the next fiscal year, a Phase Ib study for cytomegalovirus ("CMV") infection after hematopoietic stem cell transplantation, and a Phase Ib study for brain tumors. We have decided to prioritize these trials within our business strategy.

While there are approved drugs for CMV infection after hematopoietic stem cell transplantation, as they have side effects and many patients show tolerance or resistance, there is a need for development of more effective treatments. Therefore, we have raised the priority of development for CMV and started preparations for the clinical trial.

Regarding the Phase Ib study for the indication of brain tumors, a joint study with the University of California, San Francisco, using an animal model, has shown that BCV extended survival when added to the current standard therapy, and preparations are underway to initiate the clinical trial.

Statement from Mr. Fuminori Yoshida: "As the number of clinical trials will increase in the coming fiscal year, we have reviewed our pipeline strategy and decided to prioritize development for cytomegalovirus infection after hematopoietic stem cell transplantation and brain tumor indications for which there are currently no effective treatments."

The Company does not anticipate the information presented herein to have any material impact on its

financial outlook for the fiscal year ending December 2023.

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About Renal transplantation and infection

Renal transplantation is a procedure in which a new kidney is surgically transplanted to restore kidney function for patients suffer from decreased renal function. However, the immune system of the transplant recipient may recognize the transplanted organ as a foreign body and attempt to destroy it (organ rejection). Fever, malaise, irritation of the peritoneum, and pain in the wound may cause damage to the transplanted kidney and may destroy the transplanted organ within approximately a week. Immunosuppressants are used before surgery to reduce organ rejection and protect the transplanted kidney.

Immune recovery after transplantation takes time. However, because immunity is severely compromised, especially immediately after transplantation, the transplant recipient becomes susceptible to various infectious diseases against which it is important to take effective measures early. The prognosis of transplanted kidneys with BK virus nephropathy is poor, and about half are said to move toward loss of the transplanted kidney (graft loss).

There is no established effective therapy for the various infections after renal transplantation, and healthcare providers have long sought an effective and safe treatment.

About CMV infection after hematopoietic stem cell transplantation

Patients receiving hematopoietic stem cell transplants continue to be at increased risk of various infections, including viruses, until the transplanted hematopoietic stem cells rebuild the immune system. Cytomegalovirus is a virus that many people become infected with during childhood and remains in a latent state in the body, but reactivates and causes serious conditions when immunity is severely compromised, such as after transplantation. Cytomegalovirus infection after hematopoietic stem cell transplantation is considered a viral infection requiring special attention because it causes serious and sometimes fatal infections in various organs. Although several drugs with anti-cytomegalovirus activity have been approved, they all have strong side effects such as bone marrow suppression and renal dysfunction, and the emergence of antiviral drugs that can provide safer and more effective treatment has long been desired. Although drugs to prevent viral reactivation are now available, reactivation and infection still occur at a certain rate, so the need for more effective and safer anti-cytomegalovirus drugs is still high.

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, smallpox virus and monkeypox virus, 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 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, SymBio has entered into an Cooperative Research and Development Agreement

(CRADA) with the National Institute of Neurological Disorders and Stroke (NINDS), affiliated with the National Institutes of Health (NIH), to 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., 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.