June 11, 2024
SymBio Pharmaceuticals Limited
Fuminori Yoshida
Representative Director
President and Chief Executive Officer
(Securities Code: 4582)

# SymBio Announces Enrollment of the First Patient of Phase 2a Clinical Trial of Intravenous Brincidofovir for Treatment of Cytomegalovirus Infection after Hematopoietic Stem Cell Transplantation

TOKYO, Japan, June 11, 2024 – SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") today announced First Patient in its Phase 2 clinical trial of an intravenous formulation of the anti-viral drug brincidofovir ("IV BCV") for treatment of CMV virus infection after Hematopoietic Stem Cell Transplantation (the "Study") on June 10, 2024 (Central time).

This study is a protocol amendment of the ongoing Phase 2a clinical trial for adenovirus infection in immunocompromised patients, which was accepted by the U.S. Food and Drug Administration (FDA) in February 2024, and newly targets CMV infection in addition to adenovirus infection.

CMV infection has the highest incidence among viral infections after hematopoietic stem cell transplantation. Although prophylactic and therapeutic drugs are already available, there are many reactivation and resistant/refractory cases. Earlier clinical trials of oral BCV (conducted by Chimerix Inc.) have shown that BCV is highly effective against CMV infection, and SymBio's Study will use an intravenous formulation of BCV which does not have the GI and hepatic toxicities associated with the oral formulation.

Statement from Fuminori Yoshida, President and CEO: "I am pleased that the Phase IIa clinical trial for CMV infection after hematopoietic stem cell transplantation has started in the United States and that we enrolled the first case in the U.S. We look forward to leveraging BCV's activity against a variety of double-stranded DNA viruses and using POC data to advance clinical trials for other indications as well."

The Company does not expect the information presented herein to have any material impact on its financial outlook for the fiscal year ending December 2024.

**[Contact]**

Investor Relations/Tel: +81 (0)3 5472 1125

(Note)

**Cytomegalovirus infection after hematopoietic stem cell transplantation**

Patients undergoing hematopoietic stem cell transplantation continue to be at increased risk of various infections, including viral infections, 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 of infection in the body. Cytomegalovirus infection, especially after hematopoietic stem cell transplantation, causes serious and sometimes fatal infections in various organs, and is therefore considered a virus infection requiring special attention. 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, 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 (EBV), 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 Centre 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).

- A number of recent 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 3 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, Representative: John Houghton).

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.