August 19, 2024
SymBio Pharmaceuticals Limited
Fuminori Yoshida
Representative Director
President and Chief Executive Officer
(Securities Code: 4582)

# SymBio Initiates Phase 1b Clinical Trial of IV Brincidofovir in Patients with Lymphoma as a First in Human Study for Oncology

TOKYO, Japan, August 19, 2024 – SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") today announced that SymBio submitted a Clinical Trial Notification to the Pharmaceuticals and Medical Devices Agency (PMDA) regarding the Company's global Phase 1b/2 clinical trial of intravenous formulation of brincidofovir ("IV BCV") for treatment of relapse or refractory lymphoma including NK/T-cell Lymphoma (the "study") on August 5, 2024, and started the study today.

The anti-tumor activity of IV BCV against malignant lymphomas such as NK/T-cell lymphoma and PTCL has been confirmed in SymBio's collaborative research conducted with the National Cancer Centre Singapore. The purpose of the study is to confirm human POC of BCV in the area of oncology.

Statement from Fuminori Yoshida, President and CEO: "NK/T-cell lymphoma and PTCL are intractable diseases, and new drugs for the treatment of these diseases are desperately needed. We expect that the study will serve as a foundation for our IV BCV business in the oncology area."

SymBio will advance development in order to provide new treatment options for patients with NK/T-cell lymphoma and PTCL as soon as possible.

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.

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## 1. Related news releases:

13 December 2022: Presentation on the Anti-lymphoma Activity of Brincidofovir at the 64th ASH Annual Meeting

12 June 2023: Presentation of the Results of Biomarker Research Predicting the Antitumor Effects of Brincidofovir at the 17th ICML

18 March 2024: Research results showing anti-proliferative activity of brincidofovir in B-cell lymphoma to be presented at the AACR Annual Meeting 2024

24 June 2024: Confirmed Antitumor Effects of Brincidofovir in Peripheral T-Cell Lymphoma Suppression of the oncogenic MYC and Induction of Expression of Immunogenic Response Pathways (Presented at EHA2024)

## 2. Summary of the study

Phase Ib will evaluate the safety, tolerability, pharmacokinetics, and preliminary efficacy of IV BCV in patients with relapsed or refractory lymphoma, including NK/T cell lymphoma, peripheral T-cell lymphoma (PTCL), and diffuse large B-cell lymphoma (DLBCL). Subsequently, Phase II will be a multicenter, global study, conducted in Japan and other countries in Asia, to evaluate the safety and efficacy of IV BCV in patients with relapsed or refractory NK/T-cell lymphoma at the recommended dose confirmed in Phase Ib.

## 3. 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. Because this disease is characterized by its relatively high prevalence in Southeast Asia, including China, the development of new therapeutic agents is desired.

## 4. Peripheral T-cell lymphoma, PTCL

PTCL is a general term for a variety of lymphoid tumors derived from T cells that have differentiated and matured in the thymus and migrated to peripheral tissues, and is a rare cancer classified as a rapidly progressing aggressive lymphoma; PTCL-NOS, nTFHcL, and ALCL. Primary treatment involves multidrug chemotherapy and radiation, but they are not always effective enough. Although various therapeutic agents have been clinically used for relapsed or refractory PTCL in recent years, no standard treatment has been established, and the development of new therapeutic agents is desired.

## About 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 (herpesvirus such as cytomegalovirus and Epstein-Barr virus (EBV), adenovirus, 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.

### Clinical trials

- Initiated a Phase 2a 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 Phase 2a clinical trial in patients with CMV infection after Hematopoietic Stem Cell Transplantation in June 2024.
- Clinical Trial Notification submitted in Japan for a global Phase 1b/2 clinical trial for malignant lymphoma in June 2024.

Based on the establishment of POC data, SymBio will continue to build a clinical development platform and move forward with clinical development for other indications.

### Preclinical trials

Collaborations with prominent research institutions include:

- 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.

- 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. Research results were presented in several congresses: ASH in December 2022, ICML in June 2023 and EHA in June 2024.
- 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).
- SymBio entered into a Material Transfer Agreement (MTA) with the School of Medicine at Pennsylvania State University in the U.S. to conduct a preclinical study to verify the antiviral activity of BCV in a mouse model of poliomyelitis virus infection. In November 2022, we concluded Material Transfer Agreement (MTA) with Penn State College of Medicine in the U.S. to conduct a preclinical study to verify the antiviral activity of BCV in a mouse model of poliomavirus infection (November 2022). In July 2024, new findings from the research were published in journal *mBio®*.

**License Agreement**

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.

**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.