May 29, 2023
SymBio Pharmaceuticals Limited
Fuminori Yoshida
Representative Director
President and Chief Executive Officer
(Securities Code: 4582)

IV Brincidofovir in Adenovirus Infection achieved POC in Phase 2 Clinical Trial

TOKYO, Japan, May 29, 2023 -- SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") today announced that the human POC as antiviral drug has been confirmed in the phase 2 clinical trial for its intravenous formulation of brincidofovir (IV BCV) in disseminated adenovirus infection in immunocompromised patients who have had post-hematopoietic stem cell transplantation (the "AdV Study"). The POC was confirmed through the Company's submission to the U.S. Food and Drug Administration (FDA) of combined data from a total of 24 clinical subjects of the study, including 7 subjects from cohort 3, after evaluation by the Independent Data Safety Monitoring Board (DSMB). As a result, Cohort 3 will end and a dosing schedule will be studied in Cohort 4. Simultaneously, the Company will proceed with discussions with the FDA regarding the initiation of a Phase 3 trial.

Oral BCV was approved by the FDA in June 2021 for the treatment of human smallpox disease in adult and pediatric patients. Emergent BioSolutions Inc. (Headquarters: Maryland, U.S.A.) completed its acquisition of brincidofovir business from Chimerix Inc. in 2022. Oral formulation of BCV was developed by Chimerix Inc. as national security countermeasure for smallpox under a collaboration with the Biomedical Advanced Research and Development Authority (BARDA), part of the U.S. Department of Health and Human Services.

In September 2019, SymBio acquired the exclusive worldwide license of BCV from Chimerix, Inc. and began development of BCV in the Company's AdV Study, which is the first study to establish POC of IV BCV. The study was granted the fast-track status by the FDA in April 2021 and is in an area of high medical need.

Statement of Mr. Fuminori Yoshida, President and CEO of SymBio: "The establishment of POC for IV BCV in the Phase II clinical trial currently underway in the U.S. is a milestone for the global expansion of our brincidofovir business and of great significance for our business strategy. Adenovirus infection after hematopoietic stem cell transplantation has a high fatality rate, and currently there is no cure for

this disease and medical needs are extremely high. The FDA has granted fast-track designation to our program and we are diligently preparing to initiate a global Phase III trial."

The Company does not anticipate the information presented herein to have any material impact on its financial outlook for the fiscal year ending December 31, 2023.

[Contact]
Investor Relations
Tel: +81 (0)3 5472 1125

Adenovirus (AdV) infection after hematopoietic stem cell transplantation

Adenovirus infection after hematopoietic stem cell transplantation is a complication with a high mortality rate but no effective and safe treatment. There is an urgent need to develop a new treatment as medical institutions eagerly await an effective and safe treatment option.

Adenovirus Infection After Hematopoietic Stem Cell Transplantation, Phase II Clinical Study: ATHENA Study (NCT 04706923)

Objective: To confirm the safety and tolerability of IV BCV in patients with adenovirus infection
Subjects: Disseminated AdV infection and AdV infection in immunocompromised states
Treatment cohort: All 4 cohorts (dose escalation method)
Number of patients: 6 patients in each cohort
Primary endpoint: Number of subjects with BCV treatment-related adverse events as assessed by the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v5.0 (from the start of BCV administration to 4 weeks)

FDA's Fast Track Designation System

The FDA's Fast Track designation system is designed to facilitate the development and expedited review of drugs for difficult-to-treat diseases that address unmet medical needs. Under the fast-track designation system, closer collaboration with the FDA and sequential review of applications for approval is possible, and if relevant criteria are met, the product will be eligible for priority review.

Human POC (Proof of Concept) in New Drug Development

In the R&D stage of a new drug, the criteria for determining whether or not a new drug candidate compound can treat the target disease are established in advance, and the concept is confirmed by conducting non-clinical and clinical studies to demonstrate the basic concept of the new drug. If the concept is demonstrated through clinical trials, it is called the establishment of a human POC.

BARDA: Biomedical Advanced Research and Development Authority

The Biomedical Advanced Research and Development Authority (BARDA) provides an integrated, systematic approach to the development of the necessary vaccines, drugs, therapies, and diagnostic tools for public health medical emergencies such as chemical, biological, radiological, and nuclear (CBRN) accidents, incidents and attacks; pandemic influenza (PI), and emerging infectious diseases (EID).

About the anti-viral drug Brincidofovir

BCV has a new mechanism of action as a lipid conjugate of cidofovir (CDV, not approved in Japan), which is already approved in the U.S. and Europe, and is expected to be an effective treatment for a wide range of double-stranded DNA 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 compared to CDV and other antiviral drugs.

The fractional nature of the BCV molecule dramatically improves the efficiency of cellular uptake by binding a specific length of fatty chain to CDV, which is converted into a molecule that acts directly within the cell and exerts a high antiviral effect. Furthermore, it is expected to be a new highly active anti-multiviral drug that can avoid nephrotoxicity and myelosuppression, which are serious side effects compared to other antiviral drugs, including CDV.

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 the 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.