November 20, 2024
SymBio Pharmaceuticals Limited
Fuminori Yoshida
Representative Director
President and Chief Executive Officer
(Securities Code: 4582)

SymBio Presents Research Results Showing Potential Use of Intravenous Brincidofovir in Combination with Immune Checkpoint Inhibitors as a Therapy for Malignant Lymphoma at the 66th the American Society of Hematology Annual Meeting

TOKYO, Japan, November 20, 2024 – SymBio Pharmaceuticals Limited (Headquarters: Tokyo; hereinafter "SymBio") today announced that the results of its collaborative research with the National Cancer Centre Singapore on the potential use of intravenous brincidofovir in combination with immune checkpoint inhibitors[1] as a therapy for non-Hodgkin lymphoma[2], will be presented on December 9, 2024 (Pacific Standard Time) at the American Society of Hematology (ASH) Annual Meeting to be held December 7-10, 2024, in San Diego, California.

Summary of the presentation

Title: 4172 Therapeutic Repurposing of Brincidofovir in Non-Hodgkin Lymphoma - Potential Synergy with Immune Checkpoint Blockade
Program: Oral and Poster Abstracts
Session: 605. Molecular Pharmacology and Drug Resistance: Lymphoid Neoplasms: Poster III
Hematology Disease Topics & Pathways:
Research, Translational Research
Date: Monday, December 9, 2024, 6:00 PM-8:00 PM

Presentation Abstract: https://ash.confex.com/ash/2024/webprogram/Paper202761.html

[Contact]

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

Note 1: Immune Checkpoint Inhibitors

Immune checkpoint inhibitors are drugs that activate and sustain immune responses against cancer cells by inhibiting immune checkpoints, which are pathways that normally suppress the function of various immune cells.

Note 2: Non-Hodgkin lymphoma

Non-Hodgkin lymphoma is a disease in which lymphocytes undergo malignant transformation. It encompasses B-cell lymphomas, T-cell lymphomas, and NK-cell lymphomas, and accounts for over 90% of all malignant lymphomas.

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 mpox, 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

The Company 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). A use patent that SymBio applied for based on the results of this study has been granted by the Japan Patent Office (January 2024). The preliminary result was presented in major conferences: ASH 2023, 2024 Tandem Meetings, and ID Week 2024.

The Company initiated a Phase 2a clinical trial in patients with CMV infection after Hematopoietic Stem Cell Transplantation in June 2024.

The Company submitted a Clinical Trial Notification in Japan and initiated 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 Inc. for the exclusive worldwide rights to develop, market, and manufacture BCV for all diseases except orthopoxviruses (such as smallpox and mpox). In June 2021, brincidofovir tablets and oral suspension (oral

formulation) were approved in the United States for the treatment of smallpox in adults and pediatric patients, including neonates. In September 2022, Chimerix's brincidofovir business was acquired by Emergent Biodefense Operations Lansing LLC.

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.
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.