February 6, 2025
SymBio Pharmaceuticals Limited
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Representative Director
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(Securities Code: 4582)

SymBio Initiates Phase 1b/2 Clinical Trial of IV Brincidofovir in Patients with Lymphoma in Singapore

TOKYO, Japan, February 6, 2025 – SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") is conducting an international phase 1b/2 clinical trial ("the study", NCT06761677、jRCT2061240096) to evaluate the intravenous formulation of brincidofovir ("IV BCV") for treatment of patients with relapsed or refractory lymphoma (including malignant lymphomas such as NK/T-cell lymphoma[1] and peripheral T-cell lymphoma (PTCL)[2]). Currently, patient enrollment is actively progressing in Japan. SymBio today announced that, in addition to Japan, we have obtained approval of our Clinical Trial Authorization application from the Health Sciences Authority of Singapore and will commence the study in Singapore.

The antitumor effects of IV BCV in malignant lymphomas and brain tumors have already been confirmed in animal studies. Hematology and solid tumors are key therapeutic areas for the expansion of our brincidofovir business, and SymBio aims to establish these areas as the second pillar of our business following post-transplant viral infections. As previously announced, the study commenced in y on August 19, 2024, and the study in Singapore will accelerate our development in the oncology area.

To address the unmet medical needs of patients with diseases lacking effective treatment options, we are committed to expanding the number of regions and sites involved in our clinical trials to accelerate development and deliver new therapies to patients 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 2025.

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Related news release

August 19, 2024: SymBio Initiates Phase 1b Clinical Trial of IV Brincidofovir in Patients with Lymphoma as a First in Human Study for Oncology

Outline of the Study

The study will evaluate the safety, tolerability, pharmacokinetics, and preliminary efficacy of IV BCV in the lymphoma indication of IV BCV in patients with relapsed or refractory lymphoma such as NK/T-cell lymphoma, PTCL and diffuse large B-cell lymphoma (DLBCL) as Phase Ib. In Phase II, we plan to conduct a multicenter international study (clinical trials in Japan, Singapore, and other Asian countries) to evaluate the safety and efficacy of IV BCV in patients with relapsed or refractory NK/T-cell lymphoma using the recommended doses confirmed in Phase Ib. For more information, please refer to the link below.

ClinicalTrials.gov: NCT06761677
Japan Registry of Clinical Trials; jRCT2061240096

Note 1: 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. This disease is characterized by its relatively high prevalence in Southeast Asia, including China.

Note 2: Peripheral T-cell lymphoma (PTCL)

PTCL is a general term for various lymphoid tumors derived from T cells that have differentiated and matured in the thymus and migrated to peripheral tissues. It is a rare cancer classified as a rapidly progressing aggressive lymphoma, angioimmunoblastic T-cell lymphoma, ALK-positive anaplastic large cell lymphoma, and ALK-negative ALCL are the major types. 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 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.

Anti-lymphoma Activity of BCV

- Currently, we are promoting joint research and development with prominent research institutions and actively presenting the results of these collaborative studies at academic conferences. Based on these preclinical study results, the mechanism of the antitumor effect is presumed as follows. During the S phase (DNA replication phase) of the cell cycle, CDV-PP, the active form of BCV, inhibits the DNA replication of tumor cells, causing DNA damage. This induces a DNA damage response. Since the system for repairing this damage is impaired in tumor cells, it leads to cell death. Concurrently, the DNA damage triggers immunogenic cell death through the STING pathway, which induces the secretion of interferons and the expression of PD-L1, creating a state that can activate the immune system. In cases where BCV is used in combination with PD-1 antibodies, more pronounced immune cell infiltration is observed compared to using BCV alone or PD-1 antibodies alone. The gene expression related to chemokines that induce T cells and dendritic cells is also higher in the combination group, suggesting the potential for future combination with immunotherapy.
    - 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.

Ongoing clinical trials of IV BCV

- 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 results were presented at major conferences including ASH 2023, 2024 Tandem Meetings, and ID Week 2024.
- Initiated a Phase 2a clinical trial in patients with CMV infection after Hematopoietic Stem Cell Transplantation in June 2024.

- Initiated a global Phase 1b/2 clinical trial for malignant lymphoma in Japan and Singapore.
- 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.

Related press releases:

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

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

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

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

December 13, 2024: Research Results on the Antitumor Effects of Intravenous Brincidofovir and its Potential Use as a Therapy in Combination with Immune Checkpoint Inhibitors to be Presented at the 66th Annual Meeting of the American Society of Hematology

- 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).

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 BioSolutions Inc.

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.