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

TOKYO, Japan, March 18, 2024 -- Symbio Pharmaceuticals Limited (Headquarters: Tokyo, “Symbio” or the “Company”) today announced that results of its research collaboration with the National Cancer Centre of Singapore (“NCCS”) on brincidofovir (“BCV”) will be presented at the AACR Annual Meeting 2024 in San Diego, California, scheduled to be held from April 5 to April 10, 2024.

Highlights of the presentation will include:

- The anti-tumor effect of BCV was evaluated using 19 B-cell lymphoma cell lines (diffuse large B-cell lymphoma, Burkitt lymphoma and Hodgkin lymphoma) in comparison with NKTCL cell lines. Mouse xenograft models were deployed to assess *in vivo* effects.
- BCV inhibited viability in all B-cell lymphoma cell-lines in a dose-dependent manner. (IC<sub>50</sub> 0.0798~8.414 µg/ml)
- Nine cell lines, including the double-hit DLBCL cell-line, showed marked sensitivity. (IC<sub>50</sub> < 1 µg/ml)
- DLBCL patient samples from two independent datasets showed that TLE1-high tumors conferred worse overall survival. These findings are in stark contrast to NKTCL, in which TLE1 loss confers BCV sensitivity *in vitro* and is associated with poor survival outcomes in patients.
- These results suggest that BCV may be a potential novel therapeutic agent for the treatment of B-cell lymphomas.

Following the ICML conference presentation on biomarkers in NK/T-cell lymphomas in June 2023, we conducted a study on the anti-tumor activity of BCV in B-cell lymphomas, including refractory, double-hit DLBCL, the results of which will be presented at the AACR Annual Meeting 2024.

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(Note)

**Presentation Abstract:**

<https://www.abstractsonline.com/pp8/#!/20272/presentation/8985>

**Double-hit lymphoma** (classified as DLBCL/HGBL with MYC and BCL2 rearrangement in the 5th edition of the WHO classification)

Previously included in high-grade B-cell lymphomas with MYC and BCL2 and/or BCL6 rearrangements, known as lymphomas with very poor prognosis.

**Mouse xenograft model**

Xenograft models using highly immunocompromised mice are used to transplant human cancer cell lines and to evaluate anticancer drugs targeting cancer cells.

**AACR Annual Meeting**

The AACR Annual Meeting is the focal point of the cancer research community, where scientists, clinicians, other health care professionals, survivors, patients, and advocates gather to share the latest advances in cancer science and medicine. From population science and prevention; to cancer biology, translational, and clinical studies; to survivorship and advocacy; the AACR Annual Meeting highlights the work of the best minds in cancer research from institutions all over the world.

**National Cancer Centre Singapore (NCCS)**

The National Cancer Centre Singapore (NCCS) is a leading national and regional tertiary cancer centre with specialists who are experts in treating cancer. NCCS attends to the majority of cancer cases in Singapore's public healthcare sector.

For further information, please visit NCCS's website: <https://www.nccs.com.sg/>

**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, 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). - In recent years, numerous 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: Stephane Berthier).

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.