January 23, 2024
SymBio Pharmaceuticals Limited
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Preliminary Results of a Phase 2a Clinical Trial of Intravenous Brincidofovir (IV BCV) in Immunocompromised Patients with Adenovirus Infection Selected for Pediatric Best Abstracts at the 2024 Tandem Meetings of ASTCT and CIBMTR

TOKYO, Japan, January 23, 2024 -- SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") is conducting a Phase 2a clinical trial (NCT04706923) of intravenous brincidofovir ("IV BCV") in immunocompromised patients including recipients of hematopoietic stem cell transplantation with adenovirus ("AdV") viremia or disseminated AdV disease (the "Study"). SymBio today announced that an abstract of the preliminary results of the Study showing the antiviral activity of IV BCV against AdV infection has been selected for the Pediatric Best Abstracts session at the 2024 Tandem Meetings, the combined annual meetings of the American Society for Transplantation and Cell Therapy (ASTCT) and the Center for International Blood and Marrow Transplant Research (CIBMTR), which will be held February 21-24, 2024, in San Antonio, Texas.

The presenter is Michael Grimley, MD, Medical Director, Division of Bone Marrow Transplantation and Immune Deficiency, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio. The POC data showing the antiviral activity of IV BCV against AdV infection, as confirmed by the clearance of AdV from blood, was presented at the 65th Annual Meeting of the American Society of Hematology held in December 2023. The presentation at the Tandem Meetings will include new data on the antiviral effect of IV BCV against AdV infection as shown by clearance of AdV from stool. AdV viremia, especially at higher levels, is known to cause life threatening or fatal infections in immunocompromised patients. In addition, AdV in stool is known to be positive prior to AdV viremia in children and is monitored as an early indicator in standard medical care in Europe and other countries.

Summary of the presentation

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- In this dose-escalation study to evaluate the safety, tolerability, and antiviral efficacy of IV BCV, a total of 27 immunocompromised patients with AdV infection were treated with IV BCV in Cohorts 1 to 3.
- Antiviral activity was dose-dependent. Viral clearance from the blood (viral load below the detection limit in two consecutive PCR tests at least 72 hours apart) was achieved in 100% of patients in Cohort 3, who received the highest dose of IV BCV. For 90% of these patients, AdV viremia clearance was

achieved within 4 weeks of treatment initiation.

- In Cohorts 2 and 3, all patients who achieved AdV viremia clearance maintained undetectable AdV in the blood through the follow-up period.
- Clearance of AdV in stool (below the detection limit by PCR testing) was also observed in a dose-dependent manner.
- BCV IV was highly effective in a dose-dependent manner, led to rapid clearance of AdV from blood and stool within a short treatment period, and provided sustained virologic response.

Presentation Details:

https://tandem.confex.com/tandem/2024/meetingapp.cgi/Session/7839

Title: Preliminary Results of a Phase 2a Clinical Trial to Evaluate Safety, Tolerability and Antiviral Activity of Intravenous Brincidofovir (BCV IV) in Immunocompromised Patients with Adenovirus Infection

Session: PEDS-04 - (PEDS) Pediatric Best Abstracts

Date: Wednesday, February 21, 2024

Time: 3:30 PM - 5:30 PM

Presentation Time: 4:10 PM

Location: Henry B. Gonzalez Convention Center - 221

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(Note)

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 and the European Union, 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, large numbers of 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 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., called 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.