October 23, 2024
SymBio Pharmaceuticals Limited
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SymBio presents data from Phase IIa clinical trial showing clinical efficacy of IV BCV in treating symptoms of adenovirus infection

TOKYO, Japan, October 23, 2024 – SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio" or the "Company") announced today that data from its Phase IIa clinical trial (hereinafter the "Study") of the intravenous formulation of brincidofovir ("IV BCV") for the treatment of adenovirus (AdV) infection*in severely immunocompromised patients, including patients who have undergone hematopoietic stem cell transplantation (HSCT), showing a correlation between the elimination of AdV from blood and improvement of clinical symptoms was presented on October 17, 2024 (Pacific Standard Time) at ID Week 2024 October 16-19, 2024, in California, USA.

The POC (Proof of Concept) of IV BCV's anti-AdV effect was established in the Study in May 2023, and the clinical data has been presented at major conferences in Europe and the US. Of the 31 patients in the Study, 19 (95%) of the 20 patients who achieved clearance of adenoviremia from the blood reported favorable clinical outcomes, including resolution or improvement of AdV infection, according to the clinical investigators. In Cohort 3 (IV BCV 0.4 mg/kg), 9 cases (100%) showed not only elimination of AdV from blood, but also disappearance or improvement of AdV infection (see table below).

	Cohort 1 n=8	Cohort 2 n=9	Cohort 3 n=10	Cohort 4 n=7	Total
Patients with AdV disease, n	8	8	9	6	31
Viremia clearance by W5D1, n (%)	1 (12.5)	1 (12.5)	8 (88.9)	3 (50.0)	13 (41.9)
Viremia clearance by end of study, n (%)	2 (25.0)	5(62.5)	9 (100.0)	4 (66.7)	20 (64.5)
Resolved/improved disease, n (%)	2 (100.0)	4 (80.0)	9 (100.0)	4 (100.0)	19 (95.0)
Resolved disease, n	2	3	6	4	15
Improved disease, n	0	1	3	0	4
No viremia clearance byend of study, n (%)	6 (75.0)	3 (37.5)	0 (0.0)	2 (33.3)	11 (35.4)
Resolved/improved disease, n (%)	2 (33.3)	0	0	0	2 (6.4%)
Resolved disease, n	1	0*	0	0*	1
Improved disease, n	1	0	0	0	1

Dosing of IV BCV
Cohort 1: 0.2 mg/kg or 10 mg/dose BIW
Cohort 2: 0.3 mg/kg or 15 mg/dose BIW
Cohort 3: 0.4 mg/kg or 20 mg/dose BIW
Cohort 4:.0.4 mg/kg or 20 mg/dose QW

The results of the Study suggest that IV BCV is an effective treatment for adenovirus infection with an ameliorating effect on clinical symptoms. As there are currently no antiviral drugs approved for AdV and no safe and effective treatment options are available, IV BCV is expected to be a potential new treatment option.

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1. Related news releases:

13 February 2024: Preliminary Results of Phase 2a Clinical Trial of Intravenous Brincidofovir (IV BCV) in Immunocompromised Patients with Adenovirus Infection Selected for Oral Presentation at 50th Annual Meeting of the EBMT in Glasgow

23 January 2024: 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

11 December 2023: SymBio Presents New Positive Data from Ongoing Phase 2a Study of IV Brincidofovir in Adenovirus Infection in Oral Presentation at the 65th American Society of Hematology (ASH) Annual Meeting

29 May 2023: IV Brincidofovir in Adenovirus Infection achieved POC in Phase 2 Clinical Trial

2. Summary of the presentation

Title: Adenoviremia Clearance Following Treatment with Intravenous (IV) Brincidofovir (BCV) in Immunocompromised Patients is Associated with Positive Clinical Disease Response: Preliminary Outcomes from the ATHENA Phase IIa Study

Reference translation: Blood adenovirus disappearance after treatment with IV BCV in immunocompromised patients is associated with favorable clinical disease response: preliminary results of the ATHENA Phase IIa Study

Abstract No.: P-103

Date & Time: Thursday, October 17, 2024, 12:15 PM - 1:30 PM (U.S. Pacific Standard Time)

3. Adenovirus infection

AdV infection occurs in approximately 30% of pediatric recipients of hematopoietic stem cell transplantation (HSCT) and 6% of adult HSCT recipients. Disseminated AdV disease is associated with a high mortality rate, especially when it is associated with pneumonia. Adenoviremia is known to be risky and fatal in immunocompromised patients, especially at high viral doses, but there is no approved effective treatment and it is an underserved therapeutic area that is in need of a cure.

4. ID Week

ID Week is the joint annual meeting of the Infectious Diseases Society of America, the American Society for Medical Epidemiology, the American HIV Medicine Association, the Pediatric Infectious Diseases Society of America, and the Infectious Diseases Pharmacists Association.

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

- 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.
- - Initiated a Phase 2a clinical trial in patients with CMV infection after Hematopoietic Stem Cell Transplantation in June 2024.
- 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 for the exclusive worldwide rights to develop, market, and manufacture BCV for all diseases except orthopoxviruses (such as smallpox and mpox). 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.

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.