October 1, 2019
SymBio Pharmaceuticals Limited
Fuminori Yoshida
Representative Director
President and Chief Executive Officer
(Securities Code: 4582)

SymBio Announces Exclusive Global License Agreement with Chimerix for Antiviral Drug, Brincidofovir

With the development of anti-multiviral agent
SymBio transforms into a global business

TOKYO, Japan, September 30, 2019 -- SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio") announces an exclusive global license agreement with Chimerix Inc. (Headquarters: Durham, NC, "Chimerix") for the antiviral drug, brincidofovir (BCV). Under the terms of the agreement, Chimerix grants SymBio exclusive worldwide rights to develop, manufacture, and commercialize BCV in all human indications, excluding the prevention and treatment of smallpox. With the exclusive worldwide license to BCV, SymBio will transition into a global business, establish an integrated supply system for high-quality pharmaceuticals, and grow as a fully integrated specialty pharma.

Based on BCV's strong data, SymBio will initially target treatment of viral hemorrhagic cystitis (vHC)*1 and HHV-6 encephalitis (HHV-6)*2 after allogeneic hematopoietic stem cell transplantation and kidney transplantation to address critically underserved therapeutic areas. Although other antiviral drugs are currently used for these diseases, there is a long-standing and significant medical need for a treatment that is both effective and safe.

BCV is a lipid conjugate of cidofovir (CDV) *3, which is an antiviral drug already approved and marketed in the United States and the European Union, but unapproved in Japan. As BCV has not only higher anti-viral activity, but also a superior safety profile in comparison with CDV, BCV is expected to be an effective treatment against a wide spectrum of infectious diseases caused by DNA viruses, including herpes viruses (including CMV), adenovirus, BK virus, papilloma virus, and smallpox virus. BCV's innovative mechanism of action*4, which is based on conjugating a lipid chain of specified length to a CDV base, dramatically improves efficiency of uptake into the cells where BCV is converted into a direct-acting agent in the cell, resulting in high anti-viral effect. Furthermore, BCV is easy to use due to its low risk of nephrotoxicity, which is a serious side effect of CDV, making it a novel highly active anti-multiviral drug.

With the acquisition of the exclusive global rights to BCV, Symbio will execute its strategy to build a global presence. The Company will execute a rapid development and commercialization plan in Japan, and proceed with global development in major organ transplant markets, including the United States, Europe, and China. To make BCV available to patients in need as rapidly as possible, and at the same time to maximize the value of BCV business, SymBio will explore partnerships taking into consideration the regional market characteristics of the target diseases to make BCV available to patients worldwide.

Mr. Fuminori Yoshida, President and Chief Executive Officer of SymBio, stated, "Patients with viral hemorrhagic cystitis after hematopoietic stem cell transplantation, which is our initial development target, have extremely poor prognosis and high fatality. Yet, the treatment area remains seriously underserved requiring an effective therapy. There is also significant synergy generated with our core hematology business. We will position BCV as the foundation to build our global presence and transition SymBio into a fully integrated global specialty pharma."

Mr. Mike Sherman, President and Chief Executive Officer of Chimerix, stated, "SymBio's success in transitioning to a commercial-stage biotechnology company, while simultaneously developing a pipeline of novel molecules in oncology and virology, illustrates the strength of their capability and capacity. SymBio is well positioned to explore worldwide development of brincidofovir beyond smallpox and we are excited by the promise of this partnership."

Under the terms of the agreement, SymBio will pay Chimerix an upfront payment, royalties on net sales of brincidofovir worldwide, and potential clinical, regulatory and commercial milestones. Any material impact of the execution of this licensing agreement on Earnings Forecasts for the fiscal year ending December 31, 2019 will be disclosed by the Company in a timely manner.

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(*1) Viral hemorrhagic cystitis

Adenovirus infection accompanied by hemorrhagic cystitis occurs often following hematopoietic stem cell transplantation, and it is generally refractory and shows severe symptoms that afflict patients with such as frequent urination, abdominal pain, and micturition pain. Advanced disease with disseminated infection can be lethal. There are also reported cases where mortality occurs from renal impairment associated with adenovirus infection. Transplantation with unrelated donors including cord blood, of which there is a high proportion in Japan, is a potent risk factor for viral hemorrhagic cystitis. It is often extremely refractory due to the time required to reconstitute the immune system. The only current therapies available to patients, including cidofovir (CDV), are unapproved or off-label.

(*2) HHV-6 encephalitis

HHV-6 (Human herpesvirus 6) is the sixth human herpes virus. The reactivation of HHV-6 occurs in 30-70 % of allogeneic hematopoietic stem cell transplantation, and can cause HHV-6 encephalitis. HHV-6 encephalitis typically develops within 2 to 6 weeks, and most frequently occurs in the 3rd week after transplantation. Typically, symptoms gradually progress from memory impairment to consciousness disorder and convulsions, which are the three major symptoms. The incidence ratio of convulsions has been reported to be 30% to 70%. In rapidly progressing cases, neurological symptoms worsen with time, and many cases require respirator management for repeated convulsions and respiratory depression. Early treatment is very important for patients with HHV-6 encephalitis, as the patient's condition often worsens rapidly in a short time. According to clinical guidelines*, the first-line drug is foscarnet (FOS) or ganciclovir (GCV), and the second-line drug is cidofovir (CDV). CDV is defined as the second-line drug due to its strong nephrotoxicity and poor delivery of the drug into the cerebrospinal fluid (CSF). However, no studies have been conducted to confirm the clinical effects of these drugs that have been shown to be effective on HHV-6 infection in vitro.

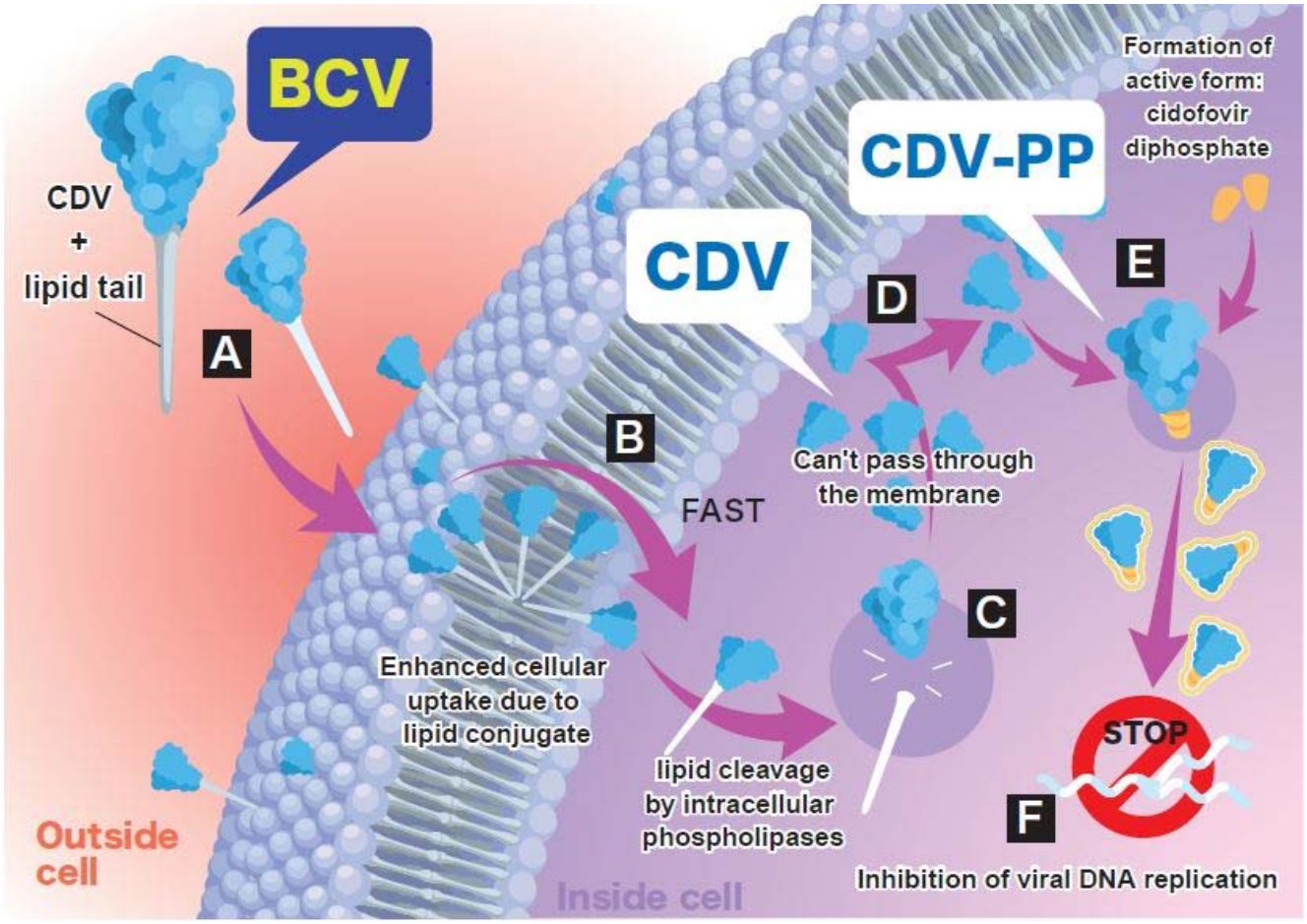
* Guidelines for hematopoietic cell transplantation: Prevention and treatment of viral infections HHV-6 (The Japan Society for Hematopoietic Cell Transplantation, February 2018 edition)

(*3) Cidofovir (CDV)

Cidofovir was approved by the FDA in 1996 for the treatment of cytomegalovirus (CMV) retinitis in AIDS patients. Cidofovir is a cytosine nucleotide derivative that inhibits replication of DNA viruses such as adenovirus, papillomavirus, polyomavirus as well as herpesviruses. Cidofovir is also effective against ganciclovir (GCV) resistance (UL97 gene mutation), and is considered useful in cases where GCV resistance appears and foscarnet (FOS) cannot be used. Cidofovir has not been developed or approved in Japan.

(*4) Brincidofovir (BCV)

Brincidofovir (BCV) is a lipid conjugate of cidofovir (CDV) with hexadecyloxypropyl (HDP), showing a rapid incorporation to the plasma membrane with efficient cellular uptake due to the lipid conjugate. Once uptaken inside target cells, the lipid chain is cleaved by action of intracellular phospholipases releasing CDV, which is then converted to the active form, CDV diphosphate. As a result of CDV diphosphate being retained in the cell for an extended period, the antiviral activity of BCV is dramatically improved compared with CDV. Furthermore, BCV can greatly reduce the risk of nephrotoxicity associated with CDV because HDP conjugation brings no accumulation of CDV in renal tubular epithelial cell through the transporter (OAT-1) and low plasma exposure of CDV.



About Chimerix

Chimerix (NASDAQ:CMRX) is a development-stage biopharmaceutical company dedicated to accelerating the advancement of innovative medicines that make a meaningful impact in the lives of patients living with cancer and other serious diseases. Chimerix has developed two types of nucleotide compounds using its own lipid technology. Chimerix was developing brincidofovir (CMX001) as the world's first drug with strong and broad activity against viral diseases (AdV, BKV, EBV, HHV-6, etc.) for which there is currently no effective treatment. In order to concentrate on businesses centering on the oncology field, Chimerix Co., Ltd. out-licensed a global license excluding smallpox to SymBio Pharmaceuticals in September 2019. In July 2019, "CX-01" was in-licensed from Cantex Pharmaceuticals, Inc., and Phase 3 is in development for acute myeloid leukemia (AML). For more information on Chimerix, please visit its website (https://www.cimerix.com/).

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 SymBio incorporated its wholly-owned subsidiary in the U.S., called SymBio Pharma USA, Inc. (Headquarters: Menlo Park, California, President: Mr. Fuminori Yoshida). SymBio'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 with main therapeutic focus in oncology and hematology.

TREAKISYM® was approved for relapsed/refractory low-grade B-cell non-Hodgkin's lymphoma ("iNHL") and mantle cell lymphoma in Japan in October, 2010, and was subsequently approved for chronic lymphocytic leukemia and first-line iNHL. Symbio Pharmaceuticals currently markets TREAKISYM® in Japan, South Korea, and Singapore through Eisai Co., Ltd., and in Taiwan through InnoPharmax Inc. SymBio recorded net sales of JPY 8.5 billion in Japan for 2018 on an NHI (National Health Insurance) drug price basis. Since July 2018, TREAKISYM has been designated as the standard therapy for the three approved indications under the Guidelines for Hematological Malignancies issued by the Japanese Society of Hematology.