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

Collaborative research with Kyoto University on mechanism of response of bendamustine for diffuse large B-cell lymphoma

TOKYO, Japan, August 2, 2021 -- SymBio Pharmaceuticals Limited (Headquarters: Tokyo, "SymBio") announced today that it has concluded a joint research agreement with Kyoto University on the mechanism of response of bendamustine in diffuse large B-cell lymphoma (DLBCL).

Under the agreement, SymBio will conduct a collaborative study with the Department of Hematology and Oncology, Graduate School of Medicine, Kyoto University (Professor Akifumi Takaori), Dr. Momoko Nishikori (Lymphoma Research Group) to analyze the response mechanism of bendamustine to B-cell lymphoma including activated B-cell ABC-DLBCL.

Traditionally, bendamustine is not cross-resistant to other alkylating agents and clinically has unique efficacy, suggesting that its therapeutic effects on lymphoma may also involve effects that differ from those of other alkylating agents. On the other hand, in the more refractory ABC-DLBCL, the involvement of NF- κ B and the linear ubiquitin chain-generating enzymatic complex (LUBAC) that regulates it has been suggested. In this collaborative study, we analyze the mechanisms of response of bendamustine itself and in combination with other B-cell lymphoma drugs by analyzing the effects associated with LUBAC.

Dr. Nishikori's research group has established outstanding research work in a variety of lymphoma and lymphoproliferative disorders. Recently, the studies first elucidated the mechanisms by which LUBAC activation promotes the development of lymphoma-like ABC-DLBCL and increases the accumulation of other genetic mutations, and addressed the possibility that LUBAC may provide clues for the development of new therapeutic agents.

To improve our understanding of bendamustine's response data to DLBCL, SymBio will work with Kyoto University to analyze the mechanisms of response of bendamustine itself and in combination with other B-cell lymphoma drugs.

Statement of Fuminori Yoshida, President and Chief Executive Officer of SymBio: "TREAKISYM[®] showed superior response rates to refractory ABC-DLBCL in the Phase 3 trial, suggesting the involvement of NF- κ B activation which is regulated by LUBAC. The joint research with Kyoto University, by furthering our understanding of the mechanism of action of bendamustine, will potentially help us to develop new therapies."

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About TREAKISYM®

TREAKISYM® (non-proprietary name: bendamustine hydrochloride), a cytocide anti-cancer drug first used in Germany in the 1970s, is now widely used in more than 50 countries with indications for low-grade non-Hodgkin's lymphoma, mantle cell lymphoma, and chronic lymphocytic leukemia.

- TREAKISYM® Intravenous Infusion 100 mg was approved in October 2010 for manufacturing and marketing for the indication of relapsed/refractory low-grade B-cell non-Hodgkin's lymphoma and mantle cell lymphoma in Japan.
- TREAKISYM® was approved for the additional indication of chronic lymphocytic leukemia in Japan in August 2016.
- TREAKISYM® was approved for the additional indications of first-line treatment of low-grade B-cell non-Hodgkin's lymphoma and mantle cell lymphoma in Japan in December 2016.
- SymBio achieved the primary endpoint (overall response rate) in Phase 3 study of TREAKISYM® in combination with rituximab as treatment for r/r DLBCL and obtained approval of a partial change application with respect to its marketing approval in March 2021.
- TREAKISYM® ready-to-dilute ("RTD") liquid formulation was approved in Japan in September 2020.

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., 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.