



February 8, 2016 SymBio Pharmaceuticals Limited Fuminori Yoshida Representative Director, President and Chief Executive Officer

SymBio and Teikyo Heisei University enter into a Joint Research and Development Agreement for an Anti-cancer Drug using the TTR1 Nano-agonist Molecule

SymBio Pharmaceuticals Limited (head office: Tokyo, "SymBio") announced today that it entered into an agreement with Teikyo Heisei University ("the Agreement") to collaborate on the research and development of an innovative anti-cancer drug which uses the TTR1 nano-agonist molecule¹.

Under the Agreement's terms, SymBio will provide its resources to implement preclinical and IND-enabling studies in collaboration with Teikyo Heisei University. SymBio also secures an option to enter into an exclusive license agreement with Teikyo Heisei University to globally develop and commercialize this innovative drug globally.

The team led by Dr. Isao Ishida, Professor of the Faculty of Pharmaceutical Sciences, Teikyo Heisei University, discovered an antibody against TRAIL-R1 that is expressed on the surface of cancer cells or cancer stem cells, and modified its form to impart more efficient anti-cancer activity (TTR1 nano-agonist). A drug delivery technique using an expression system in *Bifidobacterium*² was developed which enables the TTR1 nano-agonist to act selectively on hypoxic cancer tissue, with confirmation of the anti-cancer activity and safety of this new anti-cancer drug in animal models.

"The research being done by Professor Ishida and his team is a very innovative therapeutic approach for cancer that combines several proprietary techniques, *Bifidobacterium* and the TTR1 nano-agonist molecule utilizing the nature of cancer and cancer stem cells that are preferentially living under hypoxic condition. We look forward to the start of collaboration with Professor Ishida to deliver this first-in-class anti-cancer drug to patients in need on a global basis," said Fuminori Yoshida, Representative Director, President and CEO of SymBio.

By leveraging our extensive experience in compressing development timelines and securing early drug approvals, bringing this innovative TTR1 therapeutic anti-cancer drug to patients is a reflection of our mission to address unmet medical needs as we continue our transformation to a global biopharmaceutical company.

Conclusion of this collaboration agreement with Teikyo Heisei University will have no significant impact on the Company's earnings forecast for fiscal year ended December 31, 2016.





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Note: For an explanation of technical terms used in this press release and additional information on Teikyo Heisei University or SymBio, please refer to the following.

TTR1 nano-agonist¹ TRAIL is a member of the tumor necrosis factor (TNF) family that exerts its apoptotic activity in human cells when it trimerizes by binding to its transmembrane receptors, TRAIL-R1 and TRAIL-R2. It is difficult to form a trimeric structure using conventional anti-TRAIL-R1 antibodies, and thus apoptosis-inducing ability is typically weak. Camelids (e.g. camels, alpacas, llamas) produce functional antibodies devoid of light chains of which the single N-terminal domain is fully capable of antigen binding. These single-domain antibody fragments (VHHs or sdAb) have several advantages for biotechnological applications: they are well expressed in microorganisms, have a high stability and solubility, and can penetrate tissues relatively easily. Trivalent anti-TRAIL-R1 single-domain antibodies (TTR1: an abbreviation for <u>T</u>rivalent anti-<u>T</u>RAIL-<u>R1</u>) used in our collaboration have agonistic activities and induce apoptosis, thus we call them TTR1 nano-agonist(s).

Bifidobacterium² Bifidobacterium is a genus of Gram-positive bacteria, and are one of the major genera of bacteria that make up the colon flora in mammals, with probiotic activity limited to anaerobic environments. *Bifidobacterium* strains are important probiotics and widely used in the food industry (e.g. yogurt). As many types of cancer (specifically solid tumors such as pancreatic cancer) grow in a hypoxic environment, intravenously administered Bifidobacterium expressing the TTR1 nano-agonist molecule will selectively live in cancer tissue and effectively kill cancer cells via TTR1 nano-agonist molecule expression.







About Teikyo Heisei University

Teikyo Heisei University is an incorporated educational institution established in 1987 (with its name changed from Teikyo University of Technology in 1995). The university's motto is "to develop very creative, powerful human resources full of human love through acquisition of extensive knowledge and practical abilities in a special field based on the spirit of practical science" in the Faculties of Pharmaceutical Science, Modern Life, Health Care, Health and Medical Science, and Community Health Care, and the Graduate Schools of Pharmaceutical Science, Environmental Information, Health Science, and Clinical Psychology. As an urban-type university, campuses are in Ikebukuro, Nakano, Chiba, Chiharadai and Makuhari.

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 specialty biopharmaceutical company dedicated to addressing underserved medical needs with main therapeutic focus in oncology, hematology and pain management.