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ASAHI KOGYOSHA CO.,LTD.

Press Release

Astellas, the Institute of Medical Science of the University of Tokyo, Chiba University, and Asahi Kogyosha Enter into Collaborative Research Agreement on Rice-based Oral Vaccine “MucoRice”

Tokyo, December 6, 2017 - Astellas Pharma Inc. (Tokyo, President and CEO: Yoshihiko Hatanaka, “Astellas”), the Institute of Medical Science, the University of Tokyo (Tokyo, Dean: Yoshinori Murakami, “IMSUT”), Chiba University (Chiba, President: Takeshi Tokuhisa, “Chiba University”), and ASAHI KOGYOSHA CO.,LTD. (Tokyo, CEO: Yasutomo Takasu, “Asahi Kogyosha”) today announced that they have signed a collaborative research agreement aiming at the practical application of the rice-based oral vaccine “MucoRice-CTB” (“MucoRice”). This research program has been designated as a project under Cyclic Innovation for Clinical Empowerment (CiCLE)¹ and will be supported by the Japan Agency for Medical Research and Development (“AMED”).

MucoRice is a rice-based oral vaccine genetically engineered to express vaccine antigens and suppress the endogenous rice storage protein, which was developed by Prof. Hiroshi Kiyono, Project Researcher Yoshikazu Yuki and their colleagues at International Research and Development Center for Mucosal Vaccines in IMSUT. MucoRice does not require the strict temperature management that is usual for the storage of biopharmaceuticals and can be stored at room temperature. The establishment of the cultivation techniques that enable efficient production should help reduce medical expenses for the vaccine.

Under the agreement, Astellas will take charge of examining the conditions for MucoRice production and formulation of the vaccine while IMSUT, Chiba University, and Asahi Kogyosha will develop the production system.

IMSUT and Astellas have been engaged in a project for collaborative research on vaccines against cholera² and enterotoxigenic *Escherichia coli*³ utilizing MucoRice system since 2016, and the scope of the research was expanded to viral gastroenteritis diarrhea⁴ (including norovirus⁵ infection) in 2017.

Through this collaborative research program, Astellas, IMSUT, Chiba University, and Asahi Kogyosha will promote research and development of vaccines and therapeutic

drugs against infectious diseases that seriously affect social life. We hope that our efforts to establish a robust MucoRice production system will facilitate the further utilization of genetically engineered crops for the production of pharmaceuticals that fulfill unmet medical needs.

(1) CiCLE (Cyclic Innovation for Clinical Empowerment): CiCLE is aiming to promote medical research and development to respond to medical needs, the establishment of infrastructure (including human resource) for accelerating the practical use of drug discovery and the creation of an environment for open innovation and venture development based on industry-academia-government collaboration.

(2) Cholera: Cholera is an acute gastroenteritis by *Vibrio cholerae* which produce cholera toxin causing severe diarrhea. It is spread through contaminated food or water, therefore it is more common in developing countries.

(3) Enterotoxigenic *Escherichia coli*: Enterotoxigenic *E coli* produces a toxin that causes diarrhea and abdominal pain in humans. Severe diarrhea is caused by ingesting food or water contaminated by it. It is common in areas that lacks an adequate environmental sanitation, responsible for diarrhea in infants, and is also known to be a major cause of diarrhea in tourists who visit these areas.

(4) Viral gastroenteritis diarrhea: Viral gastroenteritis diarrhea is an acute diarrhea which is caused not by bacteria such as Cholera but by rotavirus and norovirus.

(5) Norovirus: Norovirus is one of the viruses that can cause infectious gastroenteritis and food poisoning. The virus, which enters the body through the mouth, proliferates in the intestinal tract and causes the symptoms of retching, vomiting, diarrhea and abdominal pain. Generally, the symptoms of viral infection are mild in people not having poor health. However, small infants and elderly people with less physical strength occasionally experience exacerbation of infection or are at the risk of choking on vomit and dying.

About Astellas

Astellas Pharma Inc., based in Tokyo, Japan, is a company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. We focus on Urology, Oncology, Immunology, Nephrology and Neuroscience as prioritized therapeutic areas while advancing new therapeutic areas and discovery research leveraging new technologies/modalities. We are also creating new value by combining internal capabilities and external expertise in the medical/healthcare business. Astellas is on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at <https://www.astellas.com/en>.

About the Institute of Medical Science, the University of Tokyo

The Institute of Medical science, the University of Tokyo (IMSUT) was founded by Prof. Shibasaburo Kitasato in 1892 as "The Institute of Infectious Disease". IMSUT with its own affiliated hospital is Japan's foremost university-associated research institute for medical and life science. Focusing on infectious disease, cancer and immunological diseases, our mission is to translate basic research findings directly to novel drug, vaccine and medical therapies. Thus, research environment of IMSUT is represented by the "bed to bench and bench to bed" inheriting the Kitasato's DNA of "Wisdom and Practice" for medical science leading to the next generation of Genome-based medicine, Antibody-drugs, Mucosal Vaccines, Gene-therapy and Regenerative medicine.

About Faculty of Horticulture, Chiba University

Faculty of Horticulture, it is known as only faculty of horticulture among Japanese national universities , has 100 years history and tradition and has many achievement and intellectual resources related "Food, Horticulture and Landscape".Also, as a unique faculty different from Faculty of Science, Technology and General agriculture, we expand the area to the life sciences and environmental sciences in addition to the traditional domains related to horticulture and landscape and conduct education and research on a wide range of fields including people's health and living space science in order to respond accurately to the needs of local communities and international society.

About Asahi Kogyosha

Asahi Kogyosha Co., Ltd. is a company which has developed businesses in installation work and the manufacture and sale of equipment for the mission "To create optimal spatial environments through sophisticated technology based on the sciences of air, water and heat." as stated in our Corporate Philosophy. Since founded in 1925, we have consistently strived "to create comfortable environments and optimal spaces that contribute to people's good lives and the progress of society". We will steadily push forward these efforts to contribute to the realization of a low-carbon society through the proposal and construction of environment-friendly facilities and energy-saving systems and the manufacture and sale of energy-saving equipment.

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