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BrightPath Concludes Agreements with Osaka University, BIKEN Foundation and Teikyo University for Development of TLR9 Agonist Lipid-Nucleic Acid as Immuno-stimulator

Tokyo, December 24, 2019 — BrightPath Biotherapeutics Co., Ltd. (an immuno-oncology company) has concluded the following agreements with Osaka University, the Research Foundation for Microbial Diseases of Osaka University ("BIKEN Foundation") and Teikyo University, aiming at the clinical development of a TLR9 agonist lipid-nucleic acid drug as an immuno-stimulator with anti-tumor effects (the "Drug").

- Joint R&D agreement for development of a process for manufacturing the Drug, between BrightPath and Osaka University
- Agreement for the grant of license for manufacturing the Drug, among BrightPath, BIKEN Foundation, Osaka University and Teikyo University

While using immune checkpoint inhibitors, as typified by PD-1 blockade, is becoming a promising option in cancer treatment, their response rates still remain unsatisfactory, except in cases of specific types of cancer. Immune checkpoint inhibitors are drugs that help "release the brakes" on immune cells capable of attacking cancer cells. However, this function cannot produce sufficient anti-tumor effects by merely releasing the brakes when tumors are immunologically silent ("cold tumors"). The term "cold tumors" refers to a condition where there are no immune cells within the tumor or where immune cells are not ready to attack cancer cells while they exist in the tumor. This is regarded as a major factor for low response rates of immune checkpoint inhibitors. A big challenge in cancer immunotherapies is to make cold tumors hot, i.e., to infiltrate immune cells into tumors and enable them to attack cancer cells. To this end, researchers and pharmaceutical companies around the world are struggling to make progress through various approaches.

TLR9 (toll-like receptor 9) is a receptor protein expressed on endosomes in specific types of cells of the innate immune system, and has the ability to detect viruses and other foreign invaders. In the context of cancer treatment, TLR9 agonists are considered to stimulate immune responses by triggering signaling through cytokines produced from cells of the innate immune system and helping activate T-cells to attack cancer cells (in other words, to convert "cold" tumors into "hot" ones). In the US, TLR9 agonists have already been approved

for use as hepatitis B vaccines. TLR9 agonists as a cancer therapeutic drug are currently under clinical development mostly in the US and are demonstrating certain clinical efficacy in their early phase trials. However, most of those TLR9 agonists are subject to a restriction that requires direct administration into tumor cells, resulting from the nature of their drug formulation. This restriction poses some big challenges. First, TLR9 agonists are applicable and effective only for accessible cancer. Second, TLR9 agonists cannot be directly administered to visually undetectable tumors (for example, small metastases may be overlooked). Third, invasive procedures are required to administer TLR9 agonists into the affected area, which increases the physical burden on the patient (resulting in limitation on the number of administrations).

Dr. Taiki Aoshi (*1), Dr. Takashi Matsuzaki (*2), Dr. Shohei Koyama (*3), Dr. Ryo Suzuki (*4) and others have overcome these challenges and succeeded in developing an intravenously administered drug. With a focus on nucleic acids, which are the active ingredient of TLR9 agonists, they propose to embed those nucleic acids in lipids. This can enhance the stability of TLR9 agonists in the patient's blood and make it unnecessary to limit the number of administrations, unlike the case of direct administration to tumors.

Under circumstances where clinical concepts of TLR9 agonists are to be demonstrated, we believe that a superior format for delivery of TLR9 agonists adopted for the Drug will assuredly bring differentiation to the Drug, even with lower development risks.

BrightPath is committed to pushing this development project forward, aiming to launch a clinical trial for the Drug in fiscal 2021.

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BrightPath

BrightPath is a clinical stage biopharmaceutical company focused on the development of novel cancer immunotherapies able to transform cancer treatment for progressive or refractory cancers that cannot be treated using conventional standard therapies. In addition to its cancer peptide vaccines currently in clinical trials in the United States, BrightPath is actively involved in developing cell therapies, immunomodulatory antibodies and new drugs targeted toward cancer-specific neoantigens.

Inquiries

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