

April 25, 2019
Ohara Pharmaceutical Co., Ltd.

License and Joint Development Agreement on Novel Biliary Tract Cancer Treatment

Ohara Pharmaceutical Co., Ltd. (Head office: Shiga, Japan; CEO: Seiji Ohara; hereinafter, "Ohara") has entered into a license and joint development agreement with J-Pharma Co., Ltd, dated April 25, 2019 regarding the novel compound JPH203. (Head office: Kanagawa, Japan; Representative Director and Chairman: Hitoshi Endou, M.D., Ph.D; Representative Director and President: Masuhiro Yoshitake; hereinafter, "J-Pharma").

With the execution of this agreement, Ohara has obtained the exclusive right to research, develop, commercialize and manufacture JPH203 for the treatment of advanced biliary tract cancer in Asia, including Japan and China, as well as Africa. To secure these rights, Ohara will pay J-Pharma development milestone fees and royalty payments. In addition, Ohara will support a capital increase by J-Pharma through participation in a third-party allotment of shares to be issued by J-Pharma.

JPH203 is a novel low-molecular compound that induces apoptosis of tumor cells by selectively inhibiting L-type amino acid transporter-1 (LAT1), which is specifically expressed in tumor cells, and by inhibiting the uptake of amino acids through LAT1. In phase I clinical trial in patients with advanced solid tumors, JPH203 was well-tolerated and demonstrated potential efficacy for biliary tract cancer. A phase II clinical trial for advanced biliary cancer is currently ongoing.

Ohara is actively expanding its development pipeline to address unmet medical needs in Japan, and this strategic alliance with J-Pharma is a part of these initiatives. Ohara will promote the development of JPH203, so that products can be provided to patients suffering from biliary tract cancer as soon as possible.

[About Ohara Pharmaceutical Co., Ltd.]

Ohara Pharmaceutical Co., Ltd. is a pharmaceutical company focusing on the businesses of orphan drugs and generic drugs. Its mid-term 3-year

business plan started in FY2018 under the catchphrase “Challenge 2020,” with the key objective of “addressing unmet medical needs,” to advance management innovations and make the next leap forward. The company focuses on the development and marketing of orphan drugs mainly in the field of pediatric oncology and on the development, manufacture and marketing of generic drugs that give extra consideration to the prevention of medical accidents. Ohara plans to further expand these businesses into emerging countries, primarily in the Asian and African regions.

[About J-Pharma]

J-Pharma is a venture company that aspires to contribute the drug discovery that targets “Transporter” proteins, which mainly exist in cell membrane and have function as transmembrane substance transporters. As there are now only a few drugs that target transporters, the mission of J-Pharma is to focus on drug discovery targeting such transporters, and to establish a robust integrated portfolio of drugs and diagnostics based on pioneering research on transporters. The company currently promotes the development of anticancer drugs JPH203 and OKY-034, which target LAT1, as well as the novel PET diagnostic, NKO-028. For details, please visit: <http://www.j-pharma.com>.

[About the amino acid transporter LAT1]

Amino acid transporters exist in normal cells as nutrition transporters that transport extracellular nutrients into the cell interior. LAT1 is one such amino acid transporter that is selectively and highly expressed in tumor cells, and transports large neutral amino acids, including many essential amino acids. It has been reported that the expression of LAT1 is increased in many forms of cancer, such as cancers of the colon, lung, prostate, stomach, biliary tract, pancreas, kidney, pharynx, esophagus and brain tumors, and that patient groups exhibiting high LAT1 expression have a poor prognosis in biliary tract and pancreatic cancers.

[About biliary tract cancer]

The number of deaths due to biliary tract cancer in Japan is approximately 18,000, and has been increasing in recent years.¹⁾ On the other hand, a second-line chemotherapy that is recommended for patients with biliary tract cancer who have no response to the standard chemotherapy has yet to be established and there is a high, unmet need for a second-line chemotherapy.²⁾

- 1) Vital Statistics (Vital Health and Social Statistics Office to the Counsellor for Vital, Health and Social Statistics to the Director-General for Statistics and Information Policy, Ministry of Health, Labour and Welfare) Cancer Mortality (1958-2016)
- 2) Clinical practice guidelines for management of biliary tract cancers, edited by the Publishing committee of the evidence-based clinical practice guidelines for the management of biliary tract cancers, Japanese Society of Hepato-Biliary-Pancreatic Surgery

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