

May 09, 2019
Ohara Pharmaceutical Co., Ltd.

Patent Assignment Agreement on Novel Sarcoma Treatment

Ohara Pharmaceutical Co., Ltd. (Head office: Shiga, Japan; CEO: Seiji Ohara; hereinafter, "Ohara") has entered into a patent assignment agreement concerning the novel compound ZSTK474 (Development No. OP-11) with Zenyaku Kogyo Co., Ltd. (Head office: Tokyo, Japan; CEO: Koichi Hashimoto; hereinafter, "Zenyaku") dated April 19, 2019.

In this agreement, Ohara has acquired the worldwide patent of ZSTK474 and will inherit the development from Zenyaku. Ohara will make an upfront payment and milestone payment to Zenyaku.

ZSTK474 (Development No.: OP-11) is a novel anticancer compound synthesized by Zenyaku. At the Cancer Chemotherapy Center, Japanese Foundation for Cancer Research (Tokyo, Japan; hereinafter, "JFCR"), it has been shown to be a potent inhibitor of phosphatidylinositol-3 kinase (PI3 kinase, PI3K), an intracellular signaling factor that plays a central role in cancer growth and survival.(1)

Phase I clinical trials were conducted in Japan and the United States. Two of four sarcoma patients achieved stable disease in a clinical trial in the US, so the effect on sarcoma has attracted attention.(2) In addition, in reverse translational research at JFCR, in vitro tests and in vivo tests were performed using various sarcoma cells. As a result, ZSTK 474 has shown antitumor activity on sarcomas, in particular Ewing's sarcoma, alveolar rhabdomyosarcoma, and synovial sarcoma cell lines, which are positive for a chromosomal translocation.(3)

Most of these sarcomas occur at a young age. Chemotherapy is the main treatment for metastasis, advanced cancer, and recurrent cancer, but the available anticancer drugs are limited, and the development of new sarcoma therapeutics is of high interest.

Ohara will advance the clinical development so that ZSTK474 (Development No. OP-11) can be delivered as a new treatment option to meet the unmet medical needs of sarcoma patients.

1. Yaguchi S, Fukui Y, Koshimizu I, Yoshimi H, Matsuno T, Gouda H, Hirono S, Yamazaki K, Yamori T. Antitumor activity of ZSTK474, a new phosphatidylinositol 3-kinase inhibitor. J Natl Cancer Inst. 2006; 98: 545-56. doi: 10.1093/jnci/djj133.
2. Lockhart AC, Olszanski AJ, Allgren RL, Yaguchi S, Cohen SJ, Hilton JF, Wang-Gillam A, Shapiro GI. Abstract B271: A first-in-human Phase I study of ZSTK474, an oral pan-PI3K inhibitor, in patients with advanced solid malignancies. Molecular Cancer Therapeutics. 2013; 12: B271-B. doi: 10.1158/1535-7163.targ-13-b271.
3. Namatame N, Tamaki N, Yoshizawa Y, Okamura M, Nishimura Y, Yamazaki K, Tanaka M, Nakamura T, Semba K, Yamori T, Yaguchi S, Dan S. Antitumor profile of the PI3K inhibitor ZSTK474 in human sarcoma cell lines. Oncotarget 2018; 9(80):35141-35161. doi: 10.18632/oncotarget.26216.

[About Ohara Pharmaceutical Co., Ltd.]

Ohara Pharmaceutical Co., Ltd. engages both in orphan drug and generic drug business so that we can contribute to the creation of a society where everyone's wishes are realized. Its 3-year "Challenge 2020" business plan commenced in fiscal 2018, and one key objective of this plan is to challenge and address unmet medical needs. The company develops and markets orphan drugs mainly in the field of pediatric oncology and also operates an innovative generic drug business paying particular attention to prevent medical accidents. Ohara Pharmaceutical Co., Ltd. plans to further expand these businesses into emerging countries, primarily in the Asian region. Currently, the environment for healthcare treatment options and treatment results are improving. In this regard, at Ohara, we are aiming to provide not only treatment options for patients, but also aiming to identify and develop innovative tools to improve the quality of diagnosis, prevention and after care in an effort to become a Total Healthcare Solution company for patients.

[About Zenyaku Kogyo Co., Ltd.]

Since its foundation, Zenyaku Kogyo Co., Ltd. has made constant efforts to develop original medicines based on the drug discovery philosophy of "Zenyaku does not imitate, but creates a drug that is one step ahead, we create efficacy, and serve with efficacy." Layering in the field of OTC pharmaceuticals, on which we have focused since our foundation, we have made efforts to create pharmaceuticals that have both superior efficacy and high safety as our first mission, taking advantage of the technologies developed over many years. Furthermore, in the skin care and health food fields, we apply our drug development capabilities to provide products that meet the various needs of our



customers. In the field of medical pharmaceuticals, we are working on the development of innovative new drugs for cancer and intractable diseases, using the latest technology. Zenyaku will continue to contribute to society by combining support for people's health promotion with OTC drugs and producing results that contribute to advanced medical care.

Contact details for inquiries regarding this issue:
Takahiro Iyo, Representative Executive Director and CFO
Yutaka Hayakawa, D.V.M, Ph.D., R&D Division Director
Ohara Pharmaceutical Co., Ltd.
Tel: 03-6740-7701 FAX: 03-6740-7702

