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Eisai Co., Ltd.

PRELIMINARY PHASE IB CLINICAL STUDY RESULTS FOR LENVATINIB IN COMBINATION WITH PEMBROLIZUMAB IN SELECTED SOLID TUMORS PRESENTED AT ESMO 2016

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that a presentation on the results of a Phase Ib clinical study of its in-house developed multiple receptor tyrosine kinase inhibitor lenvatinib mesylate (lenvatinib) in combination with the anti-PD-1 antibody pembrolizumab developed by Merck & Co., Inc. (Kenilworth, New Jersey, U.S.A.), known as MSD outside the United States and Canada, in patients with selected solid tumors was given at the European Society for Medical Oncology (ESMO) Congress held from October 7 to 11. Development of this combination regimen is being conducted jointly under the cooperation of both companies.

This investigational study is a multicenter, open-label Phase Ib/II clinical study to evaluate the efficacy and safety of lenvatinib in combination with pembrolizumab. In the Phase Ib part of the study, which was conducted to determine and confirm the maximum tolerated dose (MTD), 13 patients with selected solid tumors (8 patients with renal cell carcinoma, 2 patients with endometrial cancer, 2 patients with non-small cell lung cancer and 1 patient with melanoma) that had progressed after treatment with approved therapies or for which there are no standard effective therapies available were administered lenvatinib (either 24 mg or 20 mg daily) and pembrolizumab (200 mg intravenously every three weeks).

According to the latest results of the Phase Ib part of the study as of August 2016, dose-limiting toxicities (DLTs) were reported in 2 of 3 patients in the lenvatinib 24 mg / pembrolizumab 200 mg group. No DLTs were reported in the lenvatinib 20 mg / pembrolizumab 200 mg group (10 patients), and the MTD was confirmed as 20 mg of lenvatinib per day / 200 mg of pembrolizumab every three weeks. The objective response rate, one of the study's secondary endpoints, was 69.2% (9 of 13 patients). Grade 3 or higher Treatment-Emergent Adverse Events (TEAEs) were observed in 69.2% of patients, and no patients had discontinued treatment due to TEAEs. The three most frequently observed adverse events were decreased appetite, diarrhea and fatigue.

Takashi Owa, Ph.D, Chief Medicine Creation Officer of Eisai's Oncology Business Group, commented "From the results of this study for patients who had progressed after treatment with approved therapies or for which there are no standard effective therapies available, we are encouraged to further explore the combination of lenvatinib and pembrolizumab in the next stage of clinical development."
Currently, the Phase II part of the study is underway in the United States, while preparations to initiate a Phase Ib clinical study in Japan are also underway.

Eisai regards oncology as a key therapeutic area and is aiming to discover revolutionary new medicines with the potential to cure cancer. Eisai remains committed to providing further clinical evidence for lenvatinib aimed at maximizing value of the drug as it seeks to contribute further to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer, their families, and healthcare providers.

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[Notes to editors]

1. About lenvatinib mesylate ("lenvatinib", generic name, product names: Lenvima®, Kisplyx®)

Discovered and developed in-house, lenvatinib is an orally administered multiple receptor tyrosine kinase (RTK) inhibitor with a novel binding mode that selectively inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors (VEGFR1, VEGFR2 and VEGFR3) and fibroblast growth factor (FGF) receptors (FGFR1, FGFR2, FGFR3 and FGFR4) in addition to other proangiogenic and oncogenic pathway-related RTKs (including the platelet-derived growth factor (PDGF) receptor PDGFRα; KIT; and RET) involved in tumor proliferation.

Currently, Eisai has obtained approval for lenvatinib as a treatment for refractory thyroid cancer in over 45 countries including in the United States, Japan, in Europe, Korea, Canada, and Mexico, and is undergoing regulatory review in countries throughout the world including South Africa and Malaysia. Specifically, Eisai has obtained approval for the agent indicated in the United States for the treatment of locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer, in Japan for the treatment of unresectable thyroid cancer, and in Europe for the treatment of adult patients with progressive, locally advanced or metastatic differentiated (papillary, follicular, Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine, respectively.

Lenvatinib was also approved in the United States in May 2016 for an additional indication in combination with everolimus for the treatment of patients with advanced renal cell carcinoma following one prior anti-angiogenic therapy. Furthermore, lenvatinib was approved in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF) targeted therapy in Europe in August 2016. Lenvatinib has been launched in Europe under the brand name Kisplyx® for this indication.

Meanwhile, Eisai is conducting clinical studies of lenvatinib in several other tumor types such as hepatocellular carcinoma (Phase III), endometrial carcinoma (Phase II), biliary tract cancer (Phase II), and in combination with pembrolizumab for various types of cancer (Phase Ib/II). In addition, Eisai has initiated a Phase III clinical study of lenvatinib in combination with pembrolizumab and everolimus in renal cell carcinoma (first-line therapy).

2. About the Phase Ib/II Clinical Study (Study 111)

Study 111 is a multicenter, open-label Phase Ib/II clinical study to evaluate the efficacy and safety of lenvatinib in combination with pembrolizumab. In the Phase Ib part of the study, which was to determine and confirm the maximum tolerated dose (MTD), 13 patients with selected solid tumors (8 patients with renal cell carcinoma, 2 patients with endometrial cancer, 2 patients with non-small cell lung cancer and 1 patient with melanoma) who had progressed after treatment with approved therapies or for which there are no standard effective therapies available were administered 24 mg (3 patients) or 20 mg (10 patients) of lenvatinib orally daily as well as 200 mg of pembrolizumab intravenously every three weeks. Objective response rate, overall survival and progression-free survival are also assessed as secondary endpoints. Currently, the Phase II part of the clinical study is underway in the United States.