FOR IMMEDIATE RELEASE
September 8, 2017

Eisai Co., Ltd.
Ono Pharmaceutical Co., Ltd.

CONCLUSION OF DEVELOPMENT COLLABORATION AGREEMENT FOR LENVIMA® (LENVATINIB MESYLATE) AND OPDIVO® (NIVOLUMAB) COMBINATION THERAPY FOR TREATMENT OF HEPATOCELLULAR CARCINOMA

Eisai Co., Ltd. (Headquarters: Bunkyo-ku, Tokyo, CEO: Haruo Naito, "Eisai") and Ono Pharmaceutical Co., Ltd. (Headquarters: Chuo-ku, Osaka, Representative Director and President: Gyo Sagara, "Ono") have announced that they have entered into a collaboration agreement to jointly develop the combination therapy of Eisai's multi-kinase inhibitor, Lenvima® (lenvatinib mesylate) and Ono's human anti-human PD-1 (programmed cell death-1) monoclonal antibody, Opdivo® (nivolumab) for the treatment of hepatocellular carcinoma (HCC) .

Based on this agreement, Eisai and Ono will swiftly implement a Phase Ib clinical trial in Japan to investigate the safety, tolerability, and efficacy of the combination of Lenvima and Opdivo in patients with HCC. Details relating to the financial and other conditions of this agreement are confidential.

Liver cancer is the second most common cause of cancer related deaths, with an estimated 750,000 deaths per year globally.[1] Additionally, 780,000 cases are newly diagnosed each year, about 80% of which occur in Asian regions, including Japan and China.[1] HCC accounts for approximately 85% to 90% of liver cancer cases. It is estimated that there are approximately 42,000 HCC patients in Japan,[2] with 26,000 deaths per year.[3] Treatment options for unresectable HCC are limited and the prognosis is very poor, so this remains an area with high unmet medical needs.
Eisai submitted an application for an additional indication of Lenvima for the treatment of HCC in Japan in June 2017. Ono is currently conducting a Phase III clinical trial of Opdivo for the treatment of HCC in Japan.

Dr. Takashi Owa, Vice President, Chief Medicine Creation Officer, Oncology Business Group, Eisai, commented, "Our non-clinical research has demonstrated synergistic antitumor activities in the Lenvima and anti-PD1 antibody combination, which are considered to be a result of an immunostimulatory response through a reduction in immunosuppressive tumor-associated macrophages and an increase in cytotoxic T lymphocytes by Lenvima. Through the development of a combination therapy that has the potential to produce synergistic effects between Lenvima and nivolumab, both drugs of Japanese origin, we anticipate being able to further contribute to addressing the high unmet medical needs of HCC patients and their families and improving their benefits."

Hiroshi Awata, Vice President Executive Officer / Executive Director, Clinical Development, Ono, commented, "We have been actively engaged in the development of Opdivo not only in monotherapy, but combination therapies with other agents. As we believe that the combination therapy may exert more excellent therapeutic efficacy compared to the monotherapy, we are very pleased to pursue the potential for developing the combination therapy of Opdivo with lenvatinib. We expect that the combination therapy with Opdivo and lenvatinib will be a new treatment option for the patients with hepatocellular carcinoma."

About Lenvima (lenvatinib mesylate)

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 50 countries, including the United States, Japan, and in Europe. Additionally, Eisai has obtained approval for the agent in combination with everolimus as a treatment for renal cell carcinoma (second-line) in over 35 countries, including the United States and in Europe. In Europe, the agent was launched under the brand name Kisplyx® for renal cell carcinoma.

The submission of applications in Japan (June 2017), the United States and Europe (July 2017), Eisai also plans to submit an application for lenvatinib for the treatment of HCC in China within the latter half of fiscal 2017.

Furthermore, a Phase III study of lenvatinib in separate combinations with everolimus and pembrolizumab in renal cell carcinoma (first-line) was initiated and is underway. A Phase Ib/II study to investigate the agent in combination with pembrolizumab in select solid tumors (non-small cell lung cancer, renal cell carcinoma, endometrial cancer, urothelial cancer, head and neck cancer, and melanoma) and a Phase Ib study in HCC are also underway.

About Opdivo (nivolumab)

Opdivo is a PD-1 immune checkpoint inhibitor that uses the body's immune system to help restore antitumor immune response. In Japan, Ono launched Opdivo for the treatment of unresectable melanoma in September 2014. Ono received an approval for additional indication of unresectable, advanced or recurrent non-small cell lung cancer in December 2015, unresectable or metastatic renal cell cancer in August 2016, relapsed or refractory classical Hodgkin lymphoma in December 2016 and recurrent or metastatic head and neck cancer in March 2017. In addition, ONO has submitted supplemental application for additional indication of gastric cancer, and is conducting clinical development program including esophageal cancer, gastro-esophageal junction cancer, small cell lung cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, malignant pleural mesothelioma, ovarian cancer, biliary tract cancer, etc. Opdivo is currently approved in more than 60 countries, including the US, Europe, South Korea and Taiwan.

[1] GLOBOCAN2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. http://globocan.iarc.fr/

[2] Ministry of Health, Labour and Welfare, 2014 Patient Survey

[3] Ministry of Health, Labour and Welfare, 2014 Population Trends Survey

About Eisai Co., Ltd.

Eisai Co., Ltd. defines its corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care* (*hhc*) philosophy. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products to address unmet medical needs, with a particular focus in our strategic areas of Oncology and Neurology. Furthermore we invest and participate in several partnership-based initiatives to improve access to medicines in developing and emerging countries.
For more information about Eisai Co., Ltd., please visit www.eisai.com.

About Ono Pharmaceutical Co., Ltd.

Ono Pharmaceutical Co., Ltd., headquartered in Osaka, is an R&D-oriented pharmaceutical company committed to creating innovative medicines in specific fields. It focuses especially on oncology and diabetes. For further information., please visit the company's website at http://www.ono.co.jp/eng/.

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