ONO PHARMACEUTICAL CO.,LTD.

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Ono and Takeda Initiate Clinical Collaboration on Combination Therapy of Opdivo® (Nivolumab) and Cabozantinib in Japan

- Participate in Phase 3 clinical study evaluating the efficacy and safety in combination therapy of Opdivo and cabozantinib for the treatment of renal cell carcinoma in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") and Takeda Pharmaceutical Co., Ltd. (Osaka, Japan; President and CEO, Christophe Weber; "Takeda") announced today that the companies have collaborated to conduct clinical development for the treatment of renal cell carcinoma (RCC) in Japan in the combination therapy of ONO's Opdivo® (nivolumab, "Opdivo"), a human anti-human PD-1 (programmed cell death-1) monoclonal antibody, and Takeda's cabozantinib, a multi-kinase inhibitor, which Takeda has licensed from Exelixis, Inc. (Alameda, California., "Exelixis") to obtain development and exclusive commercial rights in Japan.

In accordance with this collaboration, ONO and Takeda will join, in Japan, in the ongoing Phase 3 clinical study evaluating the efficacy and safety in the combination therapy of Opdivo and cabozantinib in patients with previously untreated advanced or metastatic RCC, which has been currently conducted outside of Japan under the collaboration among Bristol-Myers Squibb ("BMS"), Exelixis and their other partner, Ipsen Pharma SAS.

Kidney cancer is a malignant tumor arising from the renal parenchyma and is the most common cancer among renal malignant tumor. Globally, about 270,000 cases of kidney cancer are diagnosed yearly and 116,000 people die from the disease[1]. Among kidney cancer, RCC constitutes 90% of all patients[1].

ONO received an approval for Opdivo for supplemental indication of unresectable or metastatic RCC in Japan in August 2016. In addition, a supplemental application for Opdivo was approved in combination therapy with Yervoy® (ipilimumab) for the same indication on August 21, 2018.

Takeda has licensed cabozantinib from Exelixis to collaborate on development and obtain exclusive commercial rights for the product in Japan. Takeda has been currently conducting Phase 2 clinical study in patients with RCC in Japan.

[1] : The epidemiology of renal cell carcinoma. Euro Urol. 2011;60;615-621.

About Opdivo

Opdivo is a PD-1 immune checkpoint inhibitor that is designed to uniquely harness the body's own immune system to help restore anti-tumor immune response by blocking the interaction between PD-1 and its ligands.

In Japan, ONO launched Opdivo for the treatment of unresectable melanoma in September 2014. Thereafter, 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, recurrent or metastatic head and neck cancer in March 2017 and unresectable advanced or recurrent gastric cancer which has progressed after chemotherapy in September 2017, unresectable advanced or recurrent malignant pleural mesothelioma which has progressed after chemotherapy and adjuvant treatment of melanoma, etc. in August 2018. In addition, ONO is conducting clinical development program including esophageal cancer, esophago-gastric junction cancer, small cell lung cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, ovarian cancer, biliary tract cancer, etc.

In abroad, BMS has a robust clinical development program for Opdivo monotherapy and in combination with other Immuno-Oncology and non-Immuno-Oncology therapies across more than 350 clinical trials. BMS is studying Opdivo in approximately 50 types of cancer, across solid tumors and hematologic malignancies, and is utilizing its translational medicine capabilities to tailor approaches with the goal of providing maximal benefit for individual patients.

Opdivo is currently approved in more than 60 countries, including Japan, South Korea, Taiwan, the US and European Union.

About the ONO and Bristol-Myers Squibb Collaboration

In 2011, through a collaboration agreement made between ONO and Bristol-Myers Squibb (BMS), ONO granted BMS its territorial rights to develop and commercialize Opdivo globally except in Japan, South Korea and Taiwan, where ONO had retained all rights to Opdivo except the US at the time. In July 2014, ONO and BMS further expanded their strategic collaboration agreement to jointly develop and commercialize multiple immunotherapies – as single agent and combination regimens – for patients with cancer in Japan, South Korea and Taiwan.

About Cabozantinib

CABOMETYX tablets are approved in the United States for the treatment of patients with advanced RCC. CABOMETYX tablets are also approved in the European Union, Norway, Iceland, Australia, Switzerland and South Korea for the treatment of advanced RCC in adults who have received prior VEGF-targeted therapy, and in the European Union for previously untreated intermediate- or poor-risk advanced RCC.

About the Takeda and Exelixis Collaboration

In January 2017, Takeda entered into a licensing agreement with Exelixis that provides for collaboration on development and exclusive rights to commercialize cabozantinib in Japan.

Exelixis retains exclusive rights to develop and commercialize cabozantinib in the United States and has licensed exclusive rights to commercialize cabozantinib outside of the US and Japan to Ipsen Pharma SAS.

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