December 22, 2017

ONO Submits Supplemental Application of Opdivo® (Nivolumab) for Indication of Unresectable Advanced or Metastatic Malignant Pleural Mesothelioma in Japan for a Partial Change in Approved Items of Manufacturing and Marketing Approval

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") and Bristol-Myers Squibb Company (NYSE: BMY) announced today that Ono Pharmaceutical Co., Ltd. ("ONO") submitted a supplemental application of Opdivo® Intravenous Infusion 20 mg and 100 mg ("Opdivo"), the human anti-human PD-1 (programmed cell death-1) monoclonal antibody, in Japan for the treatment of unresectable advanced or metastatic malignant pleural mesothelioma for a partial change in the approved items of the manufacturing and marketing approval.

This application is based on the result of a multi-center, open-label, non-comparative Phase II study (ONO-4538-41 study) conducted in patients with unresectable advanced or metastatic malignant pleural mesothelioma in Japan. In this study, 34 patients with malignant pleural mesothelioma were enrolled. The objective response rate (ORR), the primary endpoint, was 29.4% (n=10/34, 95% confidential interval (CI): 16.8 – 46.2). Drug-related adverse event (DRAE) occurred in 23 patients (67.6%). Grade 3/4 DRAEs occurred in 7 patients (20.6%).

The dosage and administration in this application is "Usually, for adults, infuse intravenously at 240 mg of nivolumab every 2 weeks".

Opdivo received orphan drug designation and priority review status for the indication of malignant pleural mesothelioma on December 1, 2017 by the Ministry of Health, Labour and Welfare (MHLW).

Malignant pleural mesothelioma (MPM) is a malignant tumor derived from undifferentiated mesenchymal cells of the mesothelium covering the thoracic surface and its underlying connective tissue. It is estimated that there are about 2,000 patients* affected patients with MPM in Japan. The cause of its occurrence is known to be highly related to asbestos inhaled into the body in occupational or living environment. It develops after a period of about 30 to 50 years following asbestos exposure. The initial drug treatment for MPM is combination therapy of pemetrexed and cisplatin. There is no standard therapy for patients who are resistant or intolerant to the combination therapy of pemetrexed and cisplatin; new treatments are desired and Opdivo is expected to be one of new treatment options.

* : Patient Survey 2014, Statistics and Information Department of the Minister's Secretariat at the Ministry of Health, Labour and Welfare (MHLW)

About Opdivo

Opdivo is a programmed death-1 (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. 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. Opdivo is currently approved in more than 60 countries, including Japan, South Korea, Taiwan, the US and European Union.

Bristol-Myers Squibb (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.

In Japan, ONO and BMS (and BMS Japan subsidiary BMSKK) have formed a strategic partnership that includes co-development, co-commercialization, and co-promotion of multiple immunotherapies for patients with cancer.

About the Ono Pharmaceutical Co., Ltd. and Bristol-Myers Squibb Collaboration

In 2011, through a collaboration agreement with Bristol-Myers Squibb (BMS), Ono Pharmaceutical Co., Ltd. (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.

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