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ONO and BMSKK Submit Supplemental Application for Opdivo® (Nivolumab) and Yervoy® (Ipilimumab) Combination Therapy for Unresctable Melanoma in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") and Bristol-Myers Squibb K.K. (Shinjuku, Tokyo; President, Davide Piras: "BMSKK") announced today that they have submitted a supplemental application for combination therapy of ONO's Opdivo® Intravenous Infusion 20 mg and 100 mg ("Opdivo"), a human anti-human PD-1 (programmed cell death-1) monoclonal antibody, and BMSKK's Yervoy® Injection 50 mg ("Yervoy") , a human monoclonal antibody against the cytotoxic T-lymphocyte antigen-4 (CTLA-4) for the treatment of unresectable melanoma in Japan.

This regulatory application is aiming to seek for potential use for the combination therapy of Opdivo and Yervoy in patients with unresectable melanoma previously untreated with chemotherapy. It is based on the results of a multi-center, open-label, non-comparative Phase II study in patients with previously untreated unresectable or recurrent advanced melanoma (ONO-4538-17 study) conducted in Japan and a double-blind, randomized Phase III study in patients with previously untreated advanced melanoma (CheckMate -067) conducted abroad. This application is intended for additional dosage and administration in the combination treatment with both products, in addition to the currently approved one for each product. The dosage and administration used in the ONO-4538-17 study is "Opdivo 1 mg/kg (body weight) plus Yervoy 3 mg/kg (body weight) every 3 weeks for four doses, followed by Opdivo 3 mg/kg (body weight) every two weeks".

Melanoma is a form of skin cancer characterized by the uncontrolled growth of pigment-producing cells (melanocytes) which are related deeply with the skin color, and said to be the most metastatic and deadliest form of the disease. It is reported that the number of melanoma patients is about 4,000 patients [*1] with about 700 deaths [*2] per year in Japan.

*1: CANCER STATISTICS IN JAPAN 2013, Patient Survey (Basic Disease Classification), Ministry of Health, Labour and Welfare 2011

*2: Vital Statistics, Ministry of Health, Labour and Welfare 2012

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, 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 Japan, South Korea, Taiwan, the US and European Union.

About Yervoy

Yervoy, which is a recombinant, human monoclonal antibody, binds to the cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4). CTLA-4 is a negative regulator of T-cell activation. Yervoy binds to CTLA-4 and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation, including the activation and proliferation of tumor infiltrating T-effector cells. Inhibition of CTLA-4 signaling can also reduce T-regulatory cell function, which may contribute to a general increase in T-cell responsiveness, including the anti-tumor immune response. On March 25, 2011, the U.S. Food and Drug Administration (FDA) approved Yervoy 3 mg/kg monotherapy for patients with unresectable or metastatic melanoma. Yervoy is now approved in more than 50 countries. There is a broad, ongoing development program in place for Yervoy spanning multiple tumor types. In Japan, BMSKK received a manufacturing and marketing approval of Yervoy for the treatment of unresectable melanoma in July 2015.

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.

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