ONO PHARMACEUTICAL CO.,LTD.

March 28, 2019

**ONO Submits Supplemental Application of Opdivo® (Nivolumab) for Indication of MSI-H Unresectable Advanced or Recurrent Colorectal Cancer That Has Progressed Following Chemotherapy, for a Partial Change in Approved Items of Manufacturing and Marketing Approval in Japan**

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced today that ONO submitted a supplemental application of Opdivo® Intravenous Infusion 20mg, 100mg and 240mg ("Opdivo"), the human anti-human PD-1 monoclonal antibody, in Japan for additional indication of microsatellite instability high (MSI-H) unresectable advanced or recurrent colorectal cancer (CRC) that has progressed following chemotherapy for a partial change in the approved items of the manufacturing and marketing approval.

This application is mainly based on the result from Opdivo monotherapy cohort of a multi-center, open-label Phase II study (CheckMate-142) conducted by Bristol-Myers Squibb (NYSE: BMY, "BMS") evaluating Opdivo in patients with MSI-H or mismatch repair deficient (dMMR) recurrent or metastatic CRC that has progressed on or after, or been intolerant of, at least one previous line of treatment with chemotherapy including fluoropyrimidine anticancer drugs.

Colorectal cancer (CRC) is the third most common type of cancer with an estimated about 1.8 million new diagnoses and about 861,000 deaths per year worldwide. In Japan alone, CRC is the most common type of cancer, and it is reported that there are about 146,000 new cases and about 57,000 deaths per year[*1]. Approximately 5% of unresectable CRC patients have MSI-H tumors. There is a tendency of poor prognosis in this patient population compared with those having non MSI-H tumors. [*2] As it is reported that the efficacy of current chemotherapy including the standard therapy with fluoropyrimidine anticancer drugs is poor[*2], an innovative drug is expected to be developed as a treatment option in this patient population.

[*1]: Globocan 2018. Available at: http://globocan.iarc.fr/

[*2]: Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2019 for the treatment of colorectal cancer

**About CheckMate-142 study**

This study is a multi-center, open-label, Phase II study (CheckMate-142) evaluating Opdivo in patients with MSI-H or dMMR recurrent or metastatic CRC that has progressed on or after, or been intolerant of prior treatment with chemotherapy including fluoropyrimidine anticancer drugs. Opdivo was continuously administered every 2 weeks until disease progression, or onset of unacceptable toxicity is observed.

**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, unresectable advanced or recurrent gastric cancer which has progressed after chemotherapy in September 2017, and 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, bladder cancer, glioblastoma, urothelial cancer, ovarian cancer, biliary tract cancer, etc.

Opdivo is currently approved in more than 65 countries, including Japan, South Korea, Taiwan, China, the US and European Union.

**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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