ONO PHARMACEUTICAL CO.,LTD.

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ONO Submits Supplemental Application for Approval for Opdivo® (Nivolumab) to Expand the Use for Treatment of Unresectable Advanced or Recurrent Gastric Cancer in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced today that ONO has newly submitted a supplemental application for Opdivo® (generic name: nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human programmed death-1 (PD-1) monoclonal antibody in Japan, to expand the use for the treatment of unresectable advanced or recurrent gastric cancer, for a partial change in approved items of the manufacturing and marketing approval.

This application has been filed based on the data from the following 2 clinical studies:

1) CheckMate -649 study (ONO-4538-44): A global multi-center, randomized, open-label Phase 3 clinical study, conducted by ONO and Bristol Myers Squibb (NYSE: BMY; "BMS") on a world-wide basis including Japan, South Korea and Taiwan
2) ATTRACTION-4 study (ONO-4538-37): A multi-center, randomized Phase 2 / 3 clinical study, conducted in Japan, South Korea and Taiwan

About CheckMate -649 study (ONO-4538-44)

Checkmate -649 is a randomized, multi-center, open-label Phase 3 clinical study evaluating Opdivo plus chemotherapy or the Opdivo plus Yervoy (ipilimumab) combination compared to chemotherapy alone in patients with previously untreated, non-human epidermal growth factor receptor 2 (HER2) positive, advanced or metastatic gastric cancer, gastroesophageal junction (GEJ) cancer or esophageal adenocarcinoma. Patients in the Opdivo plus chemotherapy arm received Opdivo 360 mg plus capecitabine and oxaliplatin (CapeOX) every three weeks or Opdivo 240 mg plus 5-fluorouracil, leucovorin and oxaliplatin (FOLFOX) every two weeks. Patients in the Opdivo plus Yervoy arm received Opdivo 1 mg/kg plus Yervoy 3 mg/kg every three weeks for four cycles followed by Opdivo 240 mg every two weeks. Patients in the chemotherapy arm received FOLFOX or CapeOX every two or three weeks, respectively. All patients continued treatment for two years or until disease progression, unacceptable toxicity or withdrawal of consent. The primary endpoints of the study are overall survival (OS) in PD-L1 positive patients with a combined positive score (CPS) ≥ 5 treated with Opdivo plus chemotherapy and progression-free survival (PFS) in CPS ≥ 5 patients treated with Opdivo plus chemotherapy compared to chemotherapy alone. Key secondary endpoints include OS in CPS ≥ 1 and all-randomized patients treated with Opdivo plus chemotherapy as well as OS and time to symptom deterioration (TTSD) in patients treated with Opdivo plus Yervoy compared to chemotherapy alone.

About ATTRACTION-4 study (ONO-4538-37)

ATTRACTION-4 study is a multi-center, randomized Phase 2 / 3 clinical study evaluating Opdivo in combination with chemotherapy (oxaliplatin + S-1 or capecitabine) compared to placebo in combination with chemotherapy in patients with HER2 negative previously untreated unresectable advanced or recurrent gastric cancer (including esophago-gastric junction cancer). Patients received Opdivo 360 mg or placebo every 3 weeks until disease progression or unacceptable toxicity is observed. The primary endpoints of this study are PFS and OS. The secondary endpoint is overall response rate (ORR).

About Gastruc cancer

It is estimated that about 115,000 new cases are diagnosed with gastric cancer per year in Japan (about 1,033,000 cases worldwide) and approximately 48,000 deaths (about 782,000 worldwide) per year resulting from this disease[1)], which is the 2nd most common type of cancer after lung cancer in Japan. As there has been little progression in the standard of care of first-line chemotherapy for the HER2 negative unresectable, advanced, recurrent gastric cancer in the past decade in Japan, an innovative treatment option is needed in this patient population.

1) Globocan 2018: Stomach Cancer: Estimated cancer incidence, mortality and prevalence worldwide. World Health Organization. Available from: https://gco.iarc.fr/today/fact-sheets-populations

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. By harnessing the body's own immune system to fight cancer, Opdivo has become an important treatment option across multiple cancers since the approval for the treatment of melanoma in Japan in July 2014. Opdivo is currently approved in more than 65 countries, including Japan, South Korea, Taiwan, China, the US and European Union.

In Japan, ONO launched Opdivo for the treatment of unresectable melanoma in September 2014. Thereafter, Opdivo received an approval for additional indications of unresectable, advanced or recurrent non-small cell lung cancer in December 2015, unresectable or metastatic renal cell carcinoma 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, unresectable advanced or recurrent malignant pleural mesothelioma which has progressed after chemotherapy and adjuvant treatment of melanoma in August 2018, and microsatellite instability high (MSI-High) unresectable advanced or recurrent colorectal cancer that has progressed following chemotherapy and unresectable advanced or recurrent esophageal cancer that has progressed following chemotherapy in February 2020.

In addition, ONO is conducting clinical development program including esophago-gastric junction cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, ovarian cancer, bladder cancer, pancreatic cancer, biliary tract cancer, prostate cancer, etc.

About the ONO and Bristol-Myers Squibb Collaboration

In 2011, through a collaboration agreement with 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 the companies' 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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