January 20, 2017

Data with OPDIVO® (nivolumab) Intravenous Infusion in Gastric Cancer from Phase III Clinical Study (ONO-4538-12) Presented at 2017 Gastrointestinal Cancer Symposium (ASCO GI 2017)

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") and Bristol-Myers Squibb Company (NYSE: BMY) announced today that the clinical results of ONO-4538-12, a randomized, double-blind Phase III clinical study conducted by ONO with Opdivo® Intravenous Infusion ("Opdivo"), the human anti-human PD-1 (programmed cell death-1) monoclonal antibody, in patients with unresectable advanced or recurrent gastric cancer refractory to or intolerant of standard therapy were presented at the 2017 Gastrointestinal Cancer Symposium (ASCO GI 2017).

In the final analysis of this study, Opdivo demonstrated a significant extension in overall survival (OS), the primary endpoint, and significantly reduced the risk of death by 37% versus placebo (hazard ratio [HR], 0.63; 95% confidence interval [CI]: 0.50 - 0.78; p<0.0001). In the data as of 5.6 months after the last patient was randomized lastly, median OS was 5.32 months for patients treated with Opdivo versus 4.14 months for those treated with placebo. OS rates at 12 months were 26.6% in the Opdivo group versus 10.9% in the placebo group, and OS rates at 6 months were 46.4% in the Opdivo group versus 34.7% in the placebo group. Grade 3 or more drug-related adverse events (AEs) occurred in 11.5% of patients treated with Opdivo and 5.5% of those treated with placebo; 2.7% of Opdivo treated patients and 2.5% of placebo treated patients discontinued the study treatment due to drug-related AEs (any grade).

The results from this study were presented on Thursday, January 19, 2017 at the 2017 Gastrointestinal Cancer Symposium (ASCO GI 2017) being held in San Francisco, CA, USA.

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. Opdivo is the first Immuno-Oncology therapy to demonstrate extension of OS in patients with unresectable advanced or recurrent gastric cancer in a randomized clinical trial in the world.

Gastric cancer is the fifth most common malignancy in the world with about 950,000 patients diagnosed annually and the third leading cause of cancer death with about 720,000 deaths reported worldwide every year*. Although recent advances in chemotherapy have achieved considerable tumor regression in many cases of unresectable/recurrent gastric cancer, these responses have not ultimately led to complete cure. The current goal of chemotherapy therefore is to delay the manifestation of disease-related symptoms and/or to prolong survival **. Under such condition, novel therapeutic drugs in this patient population are highly expected.

In Japan, ONO launched Opdivo for the treatment of unresectable melanoma in September 2014. 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 and relapsed or refractory classical Hodgkin lymphoma in December 2016. In addition, ONO has submitted supplemental applications for additional indications of head and neck cancer and gastric cancer, and is conducting clinical development program including esophageal cancer, gastro-esophageal junction cancer and esophageal cancer, small cell lung cancer, hepatocellular carcinoma, glioblastoma, urothelial cancer, malignant pleural mesothelioma, ovarian cancer, biliary tract cancer, etc.

Bristol-Myers Squibb (BMS) has a robust clinical development program in Opdivo monotherapy and in combination with other therapies in a variety of tumor types overseas. Opdivo has regulatory approval in more than 60 countries as part of the ONO - BMS collaboration.

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.

* : Globocan 2012. Available at: http://globocan.iarc.fr/ Accessed March 31, 2014.

** : Japanese gastric cancer treatment guidelines 2014 (ver. 4), Japanese Gastric Cancer Association

About ONO-4538-12 Study

This study is a multicenter, double-blind, randomized, placebo-controlled Phase III clinical study conducted in Japan, South Korea and Taiwan aiming to evaluate the efficacy and safety of ONO-4538 (Opdivo; nivolumab) in patients with unresectable advanced or recurrent gastric cancer (including gastroesophageal junction cancer) refractory to or intolerant of standard therapy. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), overall response rate (ORR), and safety.

In this study, 493 patients aged more than 20 years with ECOG PS 0-1 and unresectable advanced or recurrent gastric cancer including gastroesophageal junction cancer who had failed two or more previous chemotherapy regimens were randomized in a 2:1 ratio to receive 3 mg/kg ONO-4538 (N=330) or placebo (N=163) every 2 weeks until disease progression or severe adverse events (AEs) occurred.

In the final analysis of this study, Opdivo demonstrated a significant extension in OS, the primary endpoint, and significantly reduced the risk of death by 37% versus placebo (hazard ratio [HR], 0.63; 95% confidence interval [CI]: 0.50 - 0.78; p<0.0001). In the data as of 5.6 months after the last patient was randomized lastly, median OS was 5.32 months for patients treated with Opdivo versus 4.14 months for those treated with placebo. OS rates at 12 months were 26.6% in the Opdivo group versus 10.9% in the placebo group, and OS rates at 6 months were 46.4% in the Opdivo group versus 34.7% in the placebo group. For the secondary endpoints, the ORR was 11.2% (95% CI: 7.7 - 15.6) in the Opdivo group versus 0% (95% CI: 0.0 - 2.8) in the placebo group (p<0.0001). Median PFS was 1.61 months patients treated with Opdivo versus 1.45 months those treated with placebo

(HR: 0.60; 95% CI: 0.49 - 0.75; p<0.0001). Grade 3 or more drug-related AEs occurred in 11.5% of Opdivo and 5.5% of placebo; 2.7% of Opdivo and 2.5% of placebo discontinued the study treatment due to drug-related AEs (any grade).

About the ONO and Bristol-Myers Squibb Collaboration

In 2011, through a collaboration agreement with Bristol-Myers Squibb, 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 the compound 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 agents and combination regimens – for patients with cancer in Japan, South Korea and Taiwan.

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