December 2, 2016

OPDIVO® (nivolumab) Intravenous Injection Receives Approval for Supplemental Indication of Relapsed or Refractory Classical Hodgkin Lymphoma in Japan

ONO PHARMACEUTICAL CO., LTD. (Osaka, Japan; President, Representative Director and CEO, Gyo Sagara; "ONO") and Bristol-Myers Squibb Company (NYSE: BMY) announced today that ONO has received the approval for additional indication of OPDIVO® Intravenous Infusion 20 mg and 100 mg ("Opdivo"), the human anti-human PD-1 (programmed cell death-1) monoclonal antibody, for the treatment of relapsed or refractory classical Hodgkin lymphoma in Japan.

In Phase II clinical study (ONO-4538-15) conducted in Japan in patients with relapsed or refractory classical Hodgkin lymphoma, the objective response rate by the Central Review was 75.0% (95% CI: 47.6 – 92.7). Opdivo was designated to be an orphan drug for the indication of Hodgkin lymphoma on March 16, 2016 by the Ministry of Health, Labour and Welfare (MHLW). Opdivo is the first immune checkpoint inhibitor approved in Japan in hematological cancer.

Hodgkin lymphoma is a localized or diffuse malignant cell cancer derived from the lymphatic system. It is estimated that there are about 2,000 patients* with Hodgkin lymphoma annually in Japan. The disease is initially treated with chemotherapy and radiation therapy. When patients relapse or are treatment-resistant, the treatment will be shifted to chemotherapy or autologous hematopoietic stem cell transplantation. As patients with recurrent or refractory Hodgkin lymphoma have a poor prognosis, the development of new treatment drugs is expected.

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. In Japan, ONO launched Opdivo for the treatment of unresectable melanoma in September 2014. Thereafter, it was approved for additional indication of unresectable, advanced or recurrent non-small cell lung cancer in December 2015 and then unresectable or metastatic renal cell cancer in August 2016. In addition, ONO has submitted supplemental application for the indication of head and neck cancer, and is conducting clinical development programs including gastric cancer, 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 57 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.

ONO considers it to be important to accumulate further clinical data in order to ensure that Opdivo can be used more properly and effectively. In accordance with the conditional approval, ONO is committed to taking actions necessary for the proper use of Opdivo by implementing a post-marketing use-results survey (all-case surveillance) and collecting clinical data on the safety and efficacy of Opdivo.

*: Patient Survey, 2014 (Disease and Injury), Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare).

Overview of OPDIVO® Intravenous Infusion 20 mg and 100 mg

Product name	OPDIVO® Intravenous Infusion 20 mg and 100 mg
Generic name (JAN)	Nivolumab (recombinant)
Indication	• Unresectable melanoma • Unresectable, advanced or recurrent non-small cell lung cancer • Unresectable or metastatic renal cell carcinoma • Relapsed or refractory classical Hodgkin lymphoma
Dosage and administration	1. Unresectable melanoma Chemotherapy-naive patients: Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks. Chemotherapy-treated patients: Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks or 2 mg/kg (body weight) of nivolumab every 3 weeks. 2. Unresectable, advanced or recurrent non-small cell lung cancer, unresectable or metastatic renal cell carcinoma, and relapsed or refractory classical Hodgkin lymphoma Usually, for adults, infuse intravenously at 3 mg/kg (body weight) of nivolumab every 2 weeks.
Manufacturer/distributor	Ono Pharmaceutical Co., Ltd.
Co-promotion	Bristol-Myers Squibb KK
Conditions for approval	1. Risk Management Plan should be designed and appropriately implemented. 2. Because of the very limited number of patients treated with Opdivo in Japanese clinical trials, a post-marketing use-results survey covering all cases should be performed until data on a certain minimum number of patients have been accumulated. Through these activities, actions necessary to ensure the proper use of Opdivo should be taken by identifying the characteristics of patients to be treated with Opdivo and collecting safety and efficacy data as soon as possible.

* Underlined parts show the revised ones due to the approval for the partial change in approved items of the manufacturing and marketing authorization.

About ONO-4538-15 Study

This study is a multicenter, open-label, non-comparative Phase II clinical study to evaluate the efficacy of ONO-4538 (Opdivo; nivolumab) on objective response rate (ORR) by the Central Review as the primary endpoint, safety and pharamacokinetic in patients with relapsed or refractory classical Hodgkin lymphoma. In this study, ONO-4538 was administered intravenously at 3 mg/kg (body weight) every 2 weeks.

About the ONO and Bristol-Myers Squibb (BMS) Collaboration

In 2011, through a collaboration agreement with 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 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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