September 7, 2016

ONO Receives Approval for OPDIVO® (nivolumab) Intravenous Infusion for Treatment of Unresectable or Metastatic Renal Cell Carcinoma in Japan as Part of Partial Change in Approved Items of Manufacturing and Marketing Authorization

ONO PHARMACEUTICAL CO.,LTD. (Osaka, Japan; President, Representative Director and CEO, Gyo Sagara) and Bristol-Myers Squibb Company (NYSE: BMY) announced that ONO PHARMACEUTICAL CO.,LTD. "ONO") received approval for a partial change in approved items of the manufacturing and marketing authorization 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 unresectable or metastatic renal cell carcinoma in Japan on August 26, 2016.

Renal cell carcinoma (RCC) occurs in adult renal parenchyma and is the most common type of kidney cancer, accounting for more than 110,000 deaths worldwide each year*. Therefore, the development of new treatment drugs is expected, at present, for the treatment of unresectable or metastatic RCC patients who have been previously treated.

OPDIVO is an immune checkpoint inhibitor which blocks the interaction of the PD-1 receptor with its ligands and is the first to demonstrate the extension of overall survival (OS) in patients with unresectable or metastatic RCC who have received prior anti-angiogenic therapy in the world. In the interim analysis of CheckMate-025 study, an open-label, randomized Phase 3 clinical trial, which was conducted including Japan, OPDIVO demonstrated a median OS of 25 months (95% CI: 21.7-NE) versus 19.6 months (95% CI: 17.6-23.1) for everolimus, an active comparator (HR: 0.73; [95% CI: 0.60-0.89; p=0.0018])), offering a significant OS extension.

OPDIVO is the first human anti-human PD-1 monoclonal antibody to receive manufacturing and marketing approval for treatment of unresectable melanoma in July 2014 in Japan or anywhere in the world. OPDIVO also received additional approval for the indication of unresectable, advanced or recurrent non-small cell lung cancer in December 2015. Supplemental applications have been submitted for the indications of relapsed or refractory Hodgkin lymphoma and recurrent or metastatic head and neck cancer. Outside of Japan, OPDIVO has regulatory approval in 54 countries as part of the ONO - Bristol-Myers Squibb (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 in Japan.

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.

*: The epidemiology of renal cell carcinoma. Euro Urol. 2011;60:615-621.

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
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 and unresectable or metastatic renal cell carcinoma 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 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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