ONO PHARMACEUTICAL CO.,LTD.

November 2, 2018

Opdivo® (Nivolumab) Intravenous Infusion Approved for Supplemental Indication of Intermediate and Poor Risk Previously Untreated Advanced Renal Cell Carcinoma in Combination Therapy with Ipilimumab in Taiwan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") announced that Ono Pharma Taiwan Co., Ltd. ("OPTW"), a Taiwanese subsidiary of ONO, received the supplemental approval of Opdivo® (nivolumab) Intravenous Infusion 20 mg, 100 mg Inj. ("Opdivo"), a human anti-human PD-1 monoclonal antibody, on October 30 by the Taiwan Food and Drug Administration (TFDA), for the indication of intermediate and poor risk previously untreated advanced renal cell carcinoma in combination therapy with ipilimumab (Product name: Yervoy®) ("Yervoy") in Taiwan.

This approval allows Opdivo to be used for the treatment of intermediate and poor risk previously untreated advanced renal cell carcinoma in combination therapy with Yervoy.

About renal cell carcinoma

Kidney cancer is a malignant tumor arising from the renal parenchyma and is the most common cancer among renal malignant tumor. Globally, about 270,000 cases of kidney cancer are diagnosed yearly and 116,000 people*1 die from the disease. Among kidney cancer, renal cell carcinoma (RCC) constitutes almost 90%*1 of all patients. In Taiwan, it is estimated that there are about 1,330 renal malignant tumor patients (among them, about 1,240 patients with RCC) newly diagnosed yearly and about 520 deaths*2.

*1: The epidemiology of renal cell carcinoma. Euro Urol. 2011;60;615-621.
*2: Cancer Registry Annual Report, 2015 TAIWAN

OPTW has been committed to taking measures necessary for proper use of Opdivo by collecting clinical data on the safety and efficacy of Opdivo. In Taiwan, OPTW and Bristol-Myers Squibb (Taiwan) Ltd. continue to co-promote the sales of Opdivo, based on the strategic collaboration agreement made between ONO and Bristol-Myers Squibb in July 2014.

Outline of Opdivo® Intravenous Infusion 20 mg, 100 mg

Product name	Opdivo® 20 mg, 100 mg Inj.
Generic name (INN)	Nivolumab
Indication	1. Unresectable or metastatic melanoma Unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab 2. Non-small cell carcinoma 2.1 Advanced squamous non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy 2.2 Advanced non-squamous NSCLC with progression on or after platinum-based chemotherapy and with tumors express PD-L1 (IHC PD-L1 expression ≧5%). Patients with EGFR or ALK genomic tumor aberrations should have disease progression after treatment with EGFR or ALK inhibitor 3. Advanced renal cell carcinoma 3.1 Advanced renal cell carcinoma after prior anti-angiogenic therapy 3.2 Intermediate and poor risk previously untreated advanced renal cell carcinoma in combination therapy with ipilimumab 4. Squamous cell carcinoma of the head and neck Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after platinum-based therapy 5. Classical Hodgkin lymphoma As monotherapy, classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin 6. Urothelial carcinoma Locally advanced unresectable or metastatic urothelial carcinoma after failure of prior platinum-containing therapy 7. Unresectable advanced or recurrent gastric cancer Advanced or recurrent gastric or gastroesophageal junction adenocarcinoma after two or more prior chemotherapy regimens 8. Hepatocellular carcinoma Hepatocellular carcinoma (HCC) previously treated with sorafenib
Dosage and administration	1. Melanoma: As monotherapy, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 60 minutes every 2 weeks. In combination with ipilimumab, infuse intravenously at 1 mg/kg (body weight) of nivolumab over 60 minutes, followed by intravenous infusion of ipilimumab at 3 mg/kg on the same day, every 3 weeks for the first 4 doses. Thereafter, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 60 minutes every 2 weeks.

	2. Renal cell carcinoma: As monotherapy, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 60 minutes every 2 weeks. In combination with ipilimumab, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 60 minutes, followed by intravenous infusion of ipilimumab at 1 mg/kg on the same day, every 3 weeks for the first 4 doses. Thereafter, infuse intravenously at 3 mg/kg (body weight) of nivolumab over 60 minutes every 2 weeks. 3. Non-small cell lung cancer, squamous cell carcinoma of the head and neck, classical Hodgkin lymphoma, urothelial carcinoma, gastric cancer and hepatocellular carcinoma: Infuse intravenously at 3 mg/kg (body weight) of nivolumab over 60 minutes every 2 weeks.
Approval date	October 30, 2018
Manufacturer	Ono Pharmaceutical Co., Ltd.
Importer/distributor	Ono Pharma Taiwan Co., Ltd.、
Distribution collaboration	Bristol-Myers Squibb (Taiwan) Ltd.

* Underlined parts show the revised ones due to this approval.

About Ono Pharma Korea Co., Ltd.

Ono Pharma Taiwan Co., Ltd. (OPTW), in Taipei, Taiwan, was established as an ONO's wholly-owned subsidiary in December 2014. OPTW has marketed specialty products such as anti-cancer agents, including Opdivo. OPTW is committed to developing and marketing its products created internally for further penetration into the Taiwanese market

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, 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 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, glioblastoma, urothelial cancer, ovarian cancer, biliary tract cancer, etc.

In abroad, BMS has a robust clinical development program for Opdivo monotherapy and in combination with other Immuno-Oncology and non-Immuno-Oncology therapies across more than

350 clinical trials. BMS is studying Opdivo in approximately 50 types of cancer, across solid tumors and hematologic malignancies, and is utilizing its translational medicine capabilities to tailor approaches with the goal of providing maximal benefit for individual patients.

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

About ONO and BMS Collaboration

In 2011, through a collaboration agreement made between ONO and 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 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.

Contact
ONO PHARMACEUTICAL CO., LTD.
Corporate Communications
public_relations@ono.co.jp