ONO PHARMACEUTICAL CO.,LTD.

February 26, 2021

Opdivo® (Nivolumab) Intravenous Infusion Approved for First–Line Treatment of Advanced or Recurrent Non-Small Cell Lung Cancer in Combination Therapy 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 approval of Opdivo® (nivolumab) Intravenous Infusion 20 mg, 100 mg Inj. ("Opdivo"), a human anti-human PD-1 monoclonal antibody, on February 25, from the Taiwan Food and Drug Administration (TFDA) in Taiwan for additional indication of the first-line treatment of advanced or recurrent non-small cell lung cancer with no EGFR or ALK genomic tumor aberrations, in the following combination therapies:

1) Combination therapy with Opdivo and Yervoy* (tumors express PD-L1 ≧1%)
2) Combination therapy with Opdivo, Yervoy plus 2 cycles platinum-based chemotherapy

* : YERVOY® (generic name: ipilimumab) Injection is a human monoclonal antibody against cytotoxic T-lymphocyte-associated antigen 4（CTLA-4）

These approvals are based on the results from the following clinical studies conducted by ONO and Bristol Myers Squibb (NYSE: BMY; "BMS"):

Above 1): CheckMate -227 Study (Part 1a): a global, multi-center, multi-part, randomized, open-label Phase III study evaluating Opdivo, or Opdivo plus Yervoy compared to platinum-doublet chemotherapy in patients, whose tumors express PD-L1 ≧1%, with previously untreated unresectable advanced or recurrent non-small cell lung cancer (NSCLC)

Above 2): CheckMate -9LA Study: a global, multi-center, randomized, open-label Phase III study evaluating Opdivo plus Yervoy in combination with platinum-doublet chemotherapy (two cycles) compared to platinum-doublet chemotherapy alone in patients with previously untreated unresectable advanced or recurrent NSCLC

About CheckMate -227 study

This study is a global, multi-center, multi-part, randomized, open-label Phase III clinical study, evaluating Opdivo, or Opdivo plus Yervoy, or Opdivo plus platinum-doublet chemotherapy compared to platinum-doublet chemotherapy in patients with previously untreated unresectable advanced or recurrent NSCLC. This study consists of the following three Parts:

1) Part 1a: Evaluating the efficacy and safety of Opdivo, or Opdivo plus Yervoy in patients whose tumors express PD-L1 ≧1%
2) Part 1b: Evaluating the efficacy and safety of Opdivo plus Yervoy, or Opdivo plus platinum-doublet chemotherapy in patients whose tumors express PD-L1 <1%
3) Part 2: Evaluating the efficacy and safety of Opdivo plus platinum-doublet chemotherapy, regardless of PD-L1 expression level

In the Opdivo and Yervoy combination therapy arm of Part 1, patients received Opdivo 3 mg/kg every 2 weeks plus Yervoy 1 mg/kg every 6 weeks for up to 24 months, until disease progression or

onset of unacceptable toxicity is observed. In Part 1a, one of the primary endpoints was overall survival (OS) in patients whose tumors expressed PD-L1 ≧1%.

About CheckMate -9LA study

CheckMate -9LA study is a global, multi-center, randomized, open-label Phase III clinical study evaluating Opdivo (360 mg Q3W) plus Yervoy (1 mg/kg Q6W) in combination with platinum-doublet chemotherapy (two cycles Q3W) compared to platinum-doublet chemotherapy alone in patients with previously untreated unresectable advanced or recurrent NSCLC, regardless of PD-L1 expression and histology. Patients in the combination treatment arm were treated for up to 24 months with Opdivo and Yervoy or until disease progression or unacceptable toxicity. Patients in the control arm were treated with up to four cycles of chemotherapy and optional pemetrexed maintenance (if eligible) until disease progression or toxicity. The primary endpoint of the study was OS in the intent to treat (ITT) population. Secondary endpoints were progression-free survival (PFS), overall response rate (ORR), and efficacy measures according to biomarkers.

About Lung Cancer

Lung cancer is considered to be a form of malignant tumor that arises from cells in the trachea, bronchi and alveoli. Lung cancer is divided into two types, small cell lung cancer and non-small cell lung cancer (NSCLC), depending on the broad histological subtypes. NSCLC is one of the most common types of lung cancer, accounting for about 80-85% of lung cancer [1)]. NSCLC is further classified into adenocarcinoma (about 40% of lung cancer), squamous cell carcinoma (about 25%) and large cell carcinoma (about 10%) [2)]. About 16,000 new cases of lung cancer are diagnosed per year in Taiwan [3)]. It is estimated that approximately 9,000 deaths result from the disease per year in Taiwan [3)], making lung cancer the first leading cause of cancer-related deaths. Survival rates vary depending on the stage and type of the cancer when diagnosed. For patients diagnosed with metastatic lung cancer, the five-year survival rate is about 5%.

OPTW is 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. have co-promoted the sales of Opdivo, based on the strategic collaboration agreement made between ONO and BMS in July 2014.

1) American Cancer Society; What Is Non-Small Cell Lung Cancer? : https://www.cancer.org/content/cancer/en/cancer/lung-cancer/about/what-is.html
2) Non-Small Cell Lung Cancer Treatment (PDQ®)–Health Professional Version, National Cancer Institute: https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq#_12_toc
3) Cancer Registry Annual Report, 2018 Taiwan

Outline of Opdivo® Intravenous Infusion 20 mg, 100 mg

Product name	Opdivo® Intravenous Infusion 20 mg, 100 mg
Generic name (INN)	Nivolumab
Indication	1. Unresectable or metastatic melanoma Unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab 2. Adjuvant treatment of melanoma Adjuvant treatment of melanoma with involvement of lymph nodes or metastatic disease that has undergone complete resection 3. Non-small cell lung cancer 3.1 In combination with ipilimumab, the first-line treatment of adult patients with metastatic or recurrent non-small cell lung cancer whose tumors express PD-L1 ≥1%, with no EGFR or ALK genomic tumor aberrations 3.2 In combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy, the first-line treatment of adult patients with metastatic or recurrent non-small cell lung cancer, with no EGFR or ALK genomic tumor aberrations 3.3 Advanced non-squamous non-small cell lung cancer with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression after treatment with EGFR or ALK inhibitor 4. Advanced renal cell carcinoma 4.1 Advanced renal cell carcinoma after prior anti-angiogenic therapy 4.2 in combination with ipilimumab, intermediate and poor risk previously untreated advanced renal cell carcinoma 5. 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 6. Classical Hodgkin lymphoma Adult classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or 3 or more lines of systemic therapy that includes autologous HSCT 7. Urothelial carcinoma Locally advanced unresectable or metastatic urothelial carcinoma after failure of prior platinum-containing therapy 8. Unresectable advanced or recurrent gastric cancer Advanced or recurrent gastric or gastroesophageal junction (GEJ) adenocarcinoma after two or more prior chemotherapy regimens 9. Hepatocellular carcinoma Hepatocellular carcinoma (HCC) previously treated with sorafenib 10. Metastatic Colorectal Cancer As a single agent or in combination with ipilimumab, adult microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan 11. Squamous cell carcinoma of esophageal cancer Unresectable advanced or recurrent squamous cell carcinoma of esophageal cancer who are refractory or intolerant to prior fluoropyrimidine- and platinum-based chemotherapy

Dosage and administration	<Monotherapy> **1. Melanoma, non-small cell lung cancer, renal cell carcinoma, squamous cell carcinoma of the head and neck, classical Hodgkin lymphoma, urothelial carcinoma, gastric cancer, hepatocellular carcinoma and colorectal cancer** As a single agent, infuse intravenously at 3 mg/kg of Opdivo every 2 weeks. In case of adjuvant treatment of melanoma, the administration period does not exceed 1 year. **2. Esophageal squamous cell carcinoma** Infuse intravenously at 240 mg of Opdivo every 2 weeks. <Combination therapy> **1. Melanoma** In combination with ipilimumab, infuse intravenously at 1 mg/kg of Opdivo, followed by intravenous infusion of ipilimumab at 3 mg/kg over 90 minutes on the same day, every 3 weeks for 4 doses. Thereafter, infuse intravenously at 3mg/kg (body weight) of Opdivo. **2. Non-small cell lung cancer** In combination with ipilimumab, infuse intravenously at 3 mg/kg of Opdivo every 2 weeks and 1 mg/kg of ipilimumab every 6 weeks. The treatment period is up to 2 years. In combination with ipilimumab and platinum-based chemotherapy, infuse intravenously at 360 mg of Opdivo every 3 weeks, 1 mg/kg of ipilimumab every 6 weeks and 2 cycles of platinum-based chemotherapy every 3 weeks. The treatment period is up to 2 years. **3. Renal cell carcinoma and colorectal cancer** In combination with ipilimumab, infuse intravenously at 3 mg/kg of Opdivo, followed by intravenous infusion at 1 mg/kg of ipilimumab on the same day every 3 weeks for 4 doses. Thereafter, infuse intravenously at 3 mg/kg of Opdivo every 2 weeks. *: Unless otherwise described, Opdivo and ipilimumab should be infused intravenously over 30 minutes.
Approval date	February 25, 2021
Manufacturer	Ono Pharmaceutical Co., Ltd.
Importer/distributor	Ono Pharma Taiwan Co., Ltd.
Distribution collaboration	Bristol Myers Squibb (Taiwan) Ltd.

* Underline shows the revised parts according to this approval

About Ono Pharma Taiwan 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 agent, 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 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 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, urothelial cancer, ovarian cancer, bladder cancer, prostate cancer, pancreatic cancer, biliary tract cancer, etc.

About 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 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.

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