ONO PHARMA

Press Release

Opdivo® Intravenous Infusion Approved in Taiwan in Combination with Yervoy® for the First-Line Treatment of Adult Patients with Unresectable or Metastatic Hepatocellular Carcinoma

Osaka, Japan, July 28, 2025 - Ono Pharmaceutical Co., Ltd. (Headquarters: Osaka, Japan; President and COO: Toichi Takino; "Ono") today announced that Ono Pharma Taiwan Co., Ltd., a Taiwanese subsidiary of Ono, received the additional approval of Opdivo® (nivolumab) Intravenous Infusion ("Opdivo"), an anti-PD-1 antibody, on July 25 from the Taiwan Food and Drug Administration (TFDA) in Taiwan, in combination with ipilimumab, for the first-line treatment of adult patients with unresectable or metastatic hepatocellular carcinoma.

This approval is based on the results from the CheckMate -9DW study, a global multi-center Phase 3 clinical study (CA209-9DW: ONO-4538-92), evaluating Opdivo plus Yervoy compared to investigator's choice of lenvatinib or sorafenib monotherapy for patients with unresectable HCC who have not received prior systemic anti-cancer therapy. In this study, in which 85% of patients in the comparator arm were treated with lenvatinib and 15% were treated with sorafenib, Opdivo plus Yervoy met its primary endpoint of overall survival (OS), demonstrating a statistically significant and clinically meaningful improvement in OS compared to lenvatinib or sorafenib monotherapy. The median OS with Opdivo plus Yervoy (n=335) was 23.7 months (95% CI: 18.8-29.4) vs. 20.6 months (95% CI: 17.5-22.5) with lenvatinib or sorafenib (n=333; HR=0.79; 95% CI: 0.65-0.96 P=0.018), reducing the risk of death by 21%.[1)] The safety profile of Opdivo plus Yervoy was consistent with previously reported data, with no new safety signals identified.

About CheckMate -9DW Study (CA209-9DW: ONO-4538-92)

CheckMate -9DW study is a global multicenter randomized open-label Phase 3 study evaluating the combination of Opdivo plus Yervoy compared to investigator's choice of lenvatinib or sorafenib monotherapy in patients with advanced hepatocellular carcinoma who have not received prior systemic anti-cancer therapy.
668 patients were randomized to receive Opdivo plus Yervoy (Opdivo 1 mg/kg plus Yervoy 3 mg/kg Q3W for up to four doses, followed by Opdivo monotherapy 480 mg Q4W) infusion, or single agent lenvatinib or sorafenib as oral capsules in the control arm (335 patients in the Opdivo and Yervoy combination therapy arm, 333 patients in the control arm). The primary endpoint of the study is OS and key secondary endpoints include objective response rate (ORR), duration of response (DOR) and time to symptom deterioration (TTSD).

About Hepatocellular Carcinoma

Liver cancer is the third most frequent cause of cancer death worldwide. It is estimated that there were approximately 866,000 new cases of liver cancer worldwide in 2022, with an estimated approximately 758,000 deaths.[2)] In Taiwan, it is estimated that there were approximately 9,000 new cases of liver cancer in 2022, with an estimated approximately 8,000 deaths.[3)] Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and accounts for 90% of all liver cancers.[4)] In the past, many cases of HCC developed caused by viral liver disease, such as infection with the hepatitis B virus (HBV) or hepatitis C virus (HCV), but in recent years, the number of cases caused by non-viral liver diseases has been increasing.[5)] With the rise in non-viral liver cancer, HCC is often diagnosed in an advanced stage, where effective treatment options are limited and are

usually associated with poor outcomes.
Up to 70% of patients experience recurrence within five years, particularly those still considered to be at high risk after surgery or ablation.[6)]

References:

1): Opdivo Prescribing Information. Opdivo U.S. Product Information. Last updated: April 2025. Princeton, NJ: Bristol Myers Squibb Company.
2): Globocan 2022: Available at: https://gco.iarc.fr/today/en/fact-sheets-populations#countries
3)：CANCER REGISTRY ANNUAL REPORT, 2022 TAIWAN
4): Kim E, Viatour P. Hepatocellular carcinoma: old friends and new tricks. Exp Mol Med. 2020; 52: 1898–07.
5): The Japan Society of Hepatology, Liver Cancer White Paper 2022
6): Forner A, Reig M, Bruix J. Hepatocellular carcinoma. Lancet. 2018; 391: 1301–14.

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, 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, 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, cancer of unknown primary in December 2021, adjuvant treatment of urothelial carcinoma in March 2022, malignant mesothelioma (excluding malignant pleural mesothelioma) in November 2023, unresectable advanced or recurrent malignant epithelial tumors in February 2024, unresectable urothelial carcinoma in December 2024, and unresectable hepatocellular carcinoma in June 2025.

About Yervoy

Yervoy is a recombinant, human monoclonal antibody, and binds to the cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4). CTLA-4 is a negative regulator of T-cell activation. Yervoy binds to CTLA-4, and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation, including the activation and proliferation of tumor infiltrating T-effector cells. Inhibition of CTLA-4 signaling can also reduce T-regulatory cell function, which may contribute to a general increase in T-cell responsiveness, including anti-tumor immune response. On March 25, 2011, the U.S. Food and Drug Administration (FDA) approved Yervoy 3 mg/kg monotherapy for patients with unresectable or metastatic

melanoma. Yervoy is now approved in more than 50 countries. There is a broad, ongoing development program in place for Yervoy spanning multiple tumor types. In Japan, Yervoy was approved for the indication of unresectable malignant melanoma in July 2015.

About the 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 the companies' 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.

About Ono Pharma Taiwan Co., Ltd.

Ono Pharma Taiwan Co., Ltd. (Taipei, Taiwan, "OPTW") is an ONO's wholly-owned subsidiary established in in December 2014. OPTW has marketed Opdivo, an anti-PD-1 antibody/anti-neoplastic drug in Taiwan since 2016. OPTW is committed to bringing more innovative new products to meet unmet medical needs to patients in Taiwan as soon as possible.

Contact:
Ono Pharmaceutical Co., Ltd.
Corporate Communications
public_relations@ono-pharma.com