ONO PHARMACEUTICAL CO.,LTD.

February 28, 2023

ONO Submits Supplemental Application for Approval of Opdivo® in Japan to Expand its Use for the Treatment of Malignant Mesothelioma (Excluding Malignant Pleural Mesothelioma)

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President and CEO, Gyo Sagara; "ONO") today announced that it has submitted a supplemental application of Opdivo® (generic name: nivolumab) Intravenous Infusion ("Opdivo"), a human anti-human PD-1 monoclonal antibody in Japan, to expand its use for the treatment of malignant mesothelioma (excluding malignant pleural mesothelioma), for a partial change in approved items of the manufacturing and marketing approval.

This application is based on the result from the investigator-initiated Phase 2 clinical trial (VIOLA trial: HCM-002), conducted under the leadership of the Hyogo Medical University Hospital, in patients with malignant mesothelioma (excluding malignant pleural mesothelioma).

Among malignant mesothelioma, Opdivo monotherapy and Opdivo combination therapy with Yervoy® (generic name: ipilimumab) were approved in Japan for the treatment of malignant pleural mesothelioma in August 2018 and in May 2021, respectively. On the other hand, there are no drugs approved in Japan or overseas for the treatment of malignant mesothelioma other than malignant pleural mesothelioma. As no standard treatment has not yet been established, a drug development is eagerly desired.

Opdivo was designated as an orphan drug for the indication of malignant mesothelioma (excluding malignant pleural mesothelioma) on February 22, 2023, and accepted for priority review by the Ministry of Health, Labor and Welfare (MHLW).

About VIOLA Trial

VIOLA trial is an investigator-initiated, multi-center, unblinded, non-comparative Phase 2 trial evaluating the efficacy and safety of Opdivo in naïve or previously chemotherapy-treated patients with malignant mesothelioma (excluding malignant pleural mesothelioma). Patients received Opdivo at 240 mg every two weeks. The primary endpoint of the trial is objective response rate (Central Judgment). Secondary endpoints include objective response rate (Physician Judgment by Medical Institution), disease control rate (DCR), overall survival (OS) and progression-free survival (PFS).

About Malignant Mesothelioma

Malignant mesothelioma is a malignant tumor derived from undifferentiated mesenchymal cells of the mesothelium covering the surface of the body cavity and the underlying connective tissue in the thoracic cavity, pericardial cavity, abdominal cavity and tunica vaginalis testis cavity, and is classified into malignant pleural mesothelioma, malignant pericardial mesothelioma, malignant peritoneal mesothelioma, and malignant mesothelioma of the tunica vaginalis testis depending on the occurrence site.

It is estimated that there are 2,283 patients with malignant mesothelioma per year[1)] in Japan. It is reported that 1,605 deaths per year result from the disease in Japan[2)] in 2020. The proportion of patients with malignant mesothelioma by site is reported to be 85.5% for malignant pleural mesothelioma, 13.2% for malignant peritoneal mesothelioma, 0.8% for malignant pericardial mesothelioma, and 0.5% for malignant mesothelioma of the tunica vaginalis testis[3)].

Malignant mesothelioma is a disease with poor prognosis with median and average overall survival being reported to be 7.7 months[4] and 8.6 months[5], respectively, and the 3-year and 5-year survival rates to be 18.6% and 9.9%[6], respectively.

1) Globocan 2020: Japan, World Health Organization. Available at: https://gco.iarc.fr/today/data/factsheets/populations/392-japan-fact-sheets.pdf
2) Annual changes in the number of deaths due to mesothelioma by prefecture (1995-2020), Vital Statistics Annual Report (Fixed Number), Ministry of Health, Labour and Welfare
3) Gemba K, et al. Cancer Science, 2012;103(3):483-90.
4) Gemba K, et al. Acta Oncologica. 2013;52:803-8.
5) Solomons K. S Afr Med J. 1984;66:407-12.
6) Cancer Survival Rates at Japanese Association of Clinical Cancer Centers (November 2021) http://www.zengankyo.ncc.go.jp/etc/index.html.

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, 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, and adjuvant treatment of urothelial carcinoma in March 2022.

In addition, ONO is conducting clinical development program including hepatocellular carcinoma, ovarian cancer, prostate cancer, etc.

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.

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