ONO PHARMACEUTICAL CO.,LTD.

December 18, 2023

ONO Submits Supplemental Application of Opdivo® in Japan to Expand its Use for Treatment of Unresectable Urothelial Carcinoma

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 unresectable urothelial carcinoma, for a partial change in approved items of the manufacturing and marketing approval.

This application is based on the results from the sub-study of CheckMate -901 trial, a global, multi-center Phase 3 clinical trial (CA209-901/ONO-4538-56), in patients with untreated unresectable or metastatic urothelial carcinoma. In this study, Opdivo in combination with cisplatin-based chemotherapy followed by Opdivo monotherapy demonstrated statistically significant improvements in the primary efficacy endpoints of overall survival (OS) and progression-free survival (PFS) as assessed by Blinded Independent Central Review (BICR) compared to standard-of-care cisplatin-based chemotherapy alone. The safety profile of Opdivo in combination with cisplatin-based chemotherapy followed by Opdivo monotherapy was consistent with the known safety profiles of the combination regimen. No new safety concerns have been identified.

With respect to the indication of urothelial carcinoma, Opdivo was approved in Japan for the adjuvant treatment of urothelial carcinoma as an Opdivo monotherapy in March 2022.

About CheckMate -901 Trial (CA209-901/ONO-4538-56)

CheckMate -901 trial is a randomized, open-label Phase 3 clinical trial, evaluating Opdivo in combination with Yervoy (primary study) or Opdivo in combination with cisplatin-based chemotherapy followed by Opdivo monotherapy (sub-study) compared to standard-of-care chemotherapy alone, in patients with untreated unresectable or metastatic urothelial carcinoma.

In the sub-study of CheckMate -901, patients eligible for cisplatin-based chemotherapy were randomized 1:1 to receive either Opdivo 360 mg in combination with cisplatin-based chemotherapy every 3 weeks followed by 480 mg/Q4 Opdivo monotherapy or chemotherapy alone. Patients received the treatment until disease progression or death up to a maximum of two years. The primary endpoints of the sub-study are overall survival (OS) and progression-free survival (PFS). The OS and PFS outcomes are based on the final efficacy analyses for these endpoints.

The primary study is ongoing to assess Opdivo plus Yervoy vs. standard-of-care chemotherapy.

About Urothelial Carcinoma

Urothelial carcinoma is a tumor that begins in the renal pelvis, ureter, bladder and urethra, most of which is bladder cancer. Histopathologically, urothelial carcinoma (transitional epithelial cancer) accounts for more than 90% of bladder cancer[1]. It is estimated that about 37,000 new cases[2] of bladder cancer are diagnosed per year in Japan (about 573,000 cases worldwide[3]) and about 11,000 deaths[2] (about 213,000 deaths worldwide[3]) per year result from this disease. Standard treatment for untreated unresectable or metastatic urothelial carcinoma is a cisplatin-based

chemotherapy[4], but the effect on OS prolongation is not sufficient, and new treatment options are needed.

1): Lynch CF, Cohen MB. Urinary System. Cancer. 1995;75:316-29.
2): Globocan 2020: Bladder Cancer, Japan, World Health Organization. Available at: https://gco.iarc.fr/today/data/factsheets/populations/392-japan-fact-sheets.pdf
3): Globocan 2020: Bladder Cancer, World, World Health Organization. Available at: https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf
4): Clinical Practice Guidelines for Bladder Cancer 2019 edition. The Japanese Urological Association

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, and adjuvant treatment of urothelial carcinoma in March 2022.

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

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