ONO PHARMACEUTICAL CO.,LTD.

May 31, 2023

ONO Submits Supplemental Applications for Approval of BRAFTOVI® Capsule and MEKTOVI® Tablet in Japan for the Treatment of Radically Unresectable BRAF-Mutant Thyroid Cancer

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President and CEO: Gyo Sagara; "ONO") today announced that it has submitted supplemental applications for approval of BRAFTOVI® (generic name: encorafenib) Capsule ("BRAFTOVI"), a BRAF inhibitor, and MEKTOVI® (generic name: binimetinib) Tablet ("MEKTOVI"), a MEK inhibitor, in Japan for the treatment of radically unresectable BRAF-mutant thyroid cancer, in doublet combination therapy with BRAFTOVI and MEKTOVI, for a partial change in approved items of the manufacturing and marketing approval.

These applications are based on the results of a Phase 2 study (ONO-7702/7703-03), conducted in Japan, in patients with radically unresectable $BRAF^{V600}$-mutant thyroid cancer.

About Phase 2 study (ONO-7702/7703-03)

This study is a multi-centre, open-label, uncontrolled Phase 2 study (ONO-7702/7703-03), conducted in Japan, evaluating the efficacy and safety of the combination therapy of BRAFTOVI and MEKTOVI in patients with radically unresectable $BRAF^{V600}$-mutant thyroid cancer. Patients received the doublet combination therapy with BRAFTOVI 450 mg once daily, and MEKTOVI 45 mg twice daily, until it was determined that treatment could not be given due to disease progression or safety reasons. The primary endpoint of the study was objective response rate (ORR) as assessed by an imaging central review. Secondary endpoints included ORR as assessed by physician of each medical institution), disease control rate (DCR), overall survival (OS) and progression-free survival (PFS).

About Thyroid Cancer

Thyroid cancer (TC) is a malignant tumor that develops in the thyroid tissue located around the trachea or in front of the neck. Histologically, it is roughly divided into differentiated carcinoma (approximately 97% of TC), undifferentiated carcinoma (1 - 2%), and medullary carcinoma (1 - 2%). It is estimated that approximately 18,600 new cases are diagnosed with TC per year with approximately 1,900 deaths per year in Japan resulting from the disease in 2022*. BRAF-mutation is observed in 37 - 68% of TC patients.

As there are no approved drugs for the treatment of radically unresectable BRAF-mutant TC, new treatment options are needed.

*: Cancer Statics in Japan, 2023, The Editorial Board of Cancer Statistics, Foundation for Promotion of Cancer Research (FPCR), March 2023

About BRAFTOVI and MEKTOVI

BRAFTOVI is a small molecule BRAF kinase inhibitor and MEKTOVI is a small molecule MEK inhibitor. BRAF and MEK are important protein kinases in the MAPK signalling pathway (RAS-RAF-MEK-ERK), which regulates several key cellular activities including proliferation, differentiation, survival and angiogenesis. Inappropriate activation of proteins in this pathway has been shown to occur in many types of cancers including melanoma, colorectal cancer and thyroid cancer. Both BRAFTOVI and MEKTOVI target key enzymes in this pathway.

In Japan, ONO received a manufacturing and marketing approval of BRAFTOVI and MEKTOVI for the treatment of unresectable melanoma with a BRAF mutation in combination therapy with the products in January 2019 and launched them in February 2019. Thereafter, ONO received additional approval in November 2020 for the treatment of unresectable advanced or recurrent BRAF-mutant colorectal cancer that has progressed following chemotherapy, in triplet combination treatment of BRAFTOVI, MEKTOVI and cetuximab, an anti-human EGFR monoclonal antibody, as well as in doublet combination treatment of BRAFTOVI and cetuximab.

Abroad, Array BioPharma Inc. (a wholly owned subsidiary of Pfizer Inc.) and its collaboration partner, Pierre Fabre, received an approval of BRAFTOVI and MEKTOVI for the treatment of unresectable or metastatic $BRAF^{V600}$-mutant melanoma and launched them in 2018 in the US and EU, respectively. Furthermore, the companies received supplemental approval of BRAFTOVI in combination with cetuximab for the treatment of metastatic $BRAF^{V600E}$ -mutant colorectal cancer after prior therapy in the US and EU in 2020.

About the Ono Pharmaceutical Co., Ltd. and Pfizer Inc. Collaboration

In May 2017, ONO entered into the license agreement with Array BioPharma Inc. (became a subsidiary of Pfizer Inc. as of July 30, 2019) regarding BRAFTOVI (encorafenib), a BRAF inhibitor and MEKTOVI (binimetinib), a MEK inhibitor and received rights to develop and commercialize both products in Japan and South Korea.

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