Note: This cover is translated from the Japanese version and used for the JP version in Japanese (not in English).

ONO PHARMA

Press Release

February 4 2025

Pfizer's BRAFTOVI® Combination Regimen Significantly Improved Progression-Free Survival and Overall Survival in Phase 3 BREAKWATER Trial

This document is a Japanese translation of the original English press release issued on February 3, 2025 (US local time) by Pfizer Inc, with whom Ono Pharmaceutical Co., Ltd. has a license agreement on BRAFTOVI®. Please note that the original English text takes precedence over the contents of the Japanese translation. Please see the following link for the original English press release: https://investors.pfizer.com/investor-news/default.aspx.

(1st paragraph of the press release)

New York, February 3, 2025 – Pfizer Inc. (NYSE: PFE) today announced positive topline results from the progression-free survival (PFS) analysis of the Phase 3 BREAKWATER study of BRAFTOVI® (encorafenib) in combination with cetuximab (marketed as ERBITUX®) and mFOLFOX6 (fluorouracil, leucovorin and oxaliplatin) in patients with metastatic colorectal cancer (mCRC) harboring a *BRAF V600E* mutation. The trial showed a statistically significant and clinically meaningful improvement in PFS, one of its dual primary endpoints, as assessed by blinded independent central review (BICR) compared to patients receiving chemotherapy with or without bevacizumab. Further, the BRAFTOVI combination regimen demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS), a key secondary endpoint in the trial.

NOTE:

On December 12, 2024, Ono Pharmaceutical Co., Ltd. submitted a supplemental application for BRAFTOVI® (generic name: encorafenib) Capsule, a BRAF inhibitor, in combination with cetuximab, an anti-human EGFR monoclonal antibody, and chemotherapy in Japan for the indication of "unresectable, advanced or recurrent colorectal cancer with BRAF-mutation".

About the Approval Status of BRAFTOVI® in Japan

In January 2019, Ono Pharmaceutical Co., Ltd. received the manufacturing and marketing approvals for BRAFTOVI® (generic name: encorafenib) Capsule ("Braftovi"), a BRAF inhibitor, in combination with MEKTOVI® (generic name: binimetinib) Tablet ("Mektovi"), a MEK inhibitor, for the indication of unresectable melanoma with a BRAF mutation in Japan and launched them in February 2019. Thereafter, Ono received additional approval in November 2020 for the treatment of unresectable advanced or recurrent colorectal cancer with a BRAF mutation 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. Ono also received additional approval for Braftovi in May 2024 in combination with Mektovi for the indications of unresectable thyroid cancer with a BRAF mutation that has progressed following chemotherapy, and unresectable anaplastic thyroid cancer with a BRAF mutation.

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

In May 2017, Ono Pharmaceutical Co., Ltd. entered into the license agreement with Array BioPharma Inc. (currently, a subsidiary of Pfizer Inc.) regarding BRAFTOVI® (encorafenib), a BRAF inhibitor and MEKTOVI® (binimetinib), a MEK inhibitor to receive rights to develop and commercialize both products in Japan and South Korea.

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