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Pfizer’s BRAFTOVI® + MEKTOVI® Shows Sustained Long-Term Survival in Patients with Advanced Lung Cancer

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- *BRAFTOVI + MEKTOVI continued to show a substantial median overall survival benefit of 47.6 months in treatment-naïve patients with BRAF V600E-mutant metastatic non-small cell lung cancer after approximately four years*
- *Results from the Phase 2 PHAROS trial potentially establish new benchmark with targeted combination therapies for this patient population*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced updated follow-up results from the single-arm Phase 2 PHAROS trial evaluating BRAFTOVI® (encorafenib) + MEKTOVI® (binimetinib) for the treatment of adults with metastatic non-small cell lung cancer (mNSCLC) with a *BRAF V600E* mutation. In treatment-naïve patients, the median overall survival (OS) was 47.6 months (95% confidence interval [CI], 31.3, not estimable) after a median follow-up of 52.3 months. In previously treated patients, the median OS was 22.7 months (95% CI, 14.1, 32.6), after a median follow-up of 48.2 months. The four-year OS rates were 49% (95% CI, 35, 62) and 31% (95% CI, 16, 47) for treatment-naïve and previously treated patients, respectively. These data, from pre-specified secondary trial endpoints, will be presented today in an oral presentation (1849MO) at the 2025 European Society for Medical Oncology (ESMO) Congress in Berlin, Germany, and have been simultaneously published in the *Journal of Clinical Oncology*.

"The PHAROS trial results set a new standard for NSCLC patients with the *BRAF V600E* mutation, with survival outcomes nearing four years—the longest survival we've seen in people with treatment-naïve metastatic NSCLC who harbor a *BRAF V600E* mutation," said Melissa Johnson, M.D., Director of Lung Cancer Research at Sarah Cannon Research Institute and PHAROS investigator. "These findings, which highlight the potential impact of encorafenib and binimetinib for newly diagnosed metastatic NSCLC patients with *BRAF V600E*, offer renewed optimism for their prognosis and treatment goals."

Lung cancer is the number one cause of cancer-related deaths around the world.[1] NSCLC accounts for approximately 80-85% of lung cancers,[2] with *BRAF V600E* mutations occurring in about 2% of patients with NSCLC.[3] Prior to the development of targeted treatments, patients with *BRAF V600E*-mutant metastatic NSCLC had poor outcomes with standard chemotherapy.[4]

At the time of this analysis, the safety profile of BRAFTOVI + MEKTOVI was consistent with previous findings. The most common (?30%) treatment-related adverse events were nausea (52%), diarrhea (44%), fatigue (33%), and vomiting (30%).

"These long-term survival results reinforce Pfizer's unwavering commitment to improving outcomes in lung cancer," said Jeff Legos, Chief Oncology Officer, Pfizer. "The findings provide hope for treatment-naïve *BRAF V600E* mNSCLC patients and their families and underscore the importance of advancing therapies that can provide a sustained impact for patients."

The Phase 2 PHAROS trial (NCT03915951) is an open-label, multicenter, single-arm study examining BRAFTOVI + MEKTOVI combination therapy in treatment-naïve and previously treated patients with *BRAF V600E*-mutant metastatic NSCLC. BRAFTOVI + MEKTOVI was approved by the U.S. Food and Drug Administration (FDA) in October 2023, and by the European Commission in August 2024, for the treatment of *BRAF V600E*-mutant metastatic NSCLC based on the initial objective response rate (ORR; the primary endpoint) and duration of response (secondary endpoint) results from the PHAROS trial. The ORR was 75% (95% CI: 62, 85) for treatment-naïve patients (n=59) and 46% (95% CI: 30, 63) for previously treated patients (n=39).

Pfizer is continuing its commitment to help non-scientists understand the latest findings with the development of abstract plain language summaries (APLS) for company-sponsored research being presented, which are written in non-technical language. Those interested in learning more can visit www.Pfizer.com/apls to access the summaries.

About *BRAF V600E*-mutant non-small cell lung cancer (NSCLC)

NSCLC treatment has dramatically evolved, enabling more individualized treatment options based on molecular profiles and immunologic status. *BRAF* mutations exemplify this precision medicine opportunity—while *BRAF V600E* mutations occur in only about 2% of NSCLC cases,[3] they represent approximately half of all *BRAF*-mutant metastatic NSCLC.[5] Targeting *BRAF* offers potential to inhibit tumor growth and proliferation driven by these specific mutations.[6]

Despite this evolution, unmet needs remain for advanced disease. Approximately one in six patients with advanced NSCLC have no biomarker testing results prior to first-line treatment.[7] Among tested patients, many do not receive targeted therapy or have limited to no options available for targeted therapy.[8-10]

About BRAFTOVI® (encorafenib) + MEKTOVI® (binimetinib)

BRAFTOVI is an oral small molecule kinase inhibitor that targets BRAF V600E, and MEKTOVI is an oral small molecule MEK inhibitor, both of which target key proteins in the MAPK signaling pathway (RAS-RAF-MEK-ERK). Inappropriate activation of proteins in this pathway has been shown to occur in certain cancers, including melanoma, CRC, and NSCLC.

Pfizer has exclusive rights to BRAFTOVI + MEKTOVI in the U.S., Canada, Latin America, Middle East, and Africa. Ono Pharmaceutical Co., Ltd. has exclusive rights to commercialize both products in Japan and South Korea, Medison has exclusive rights in Israel and Pierre Fabre Laboratories has exclusive rights in all other countries, including Europe and Asia (excluding Japan and South Korea). The PHAROS trial is conducted with support from Pierre Fabre.

INDICATION AND USAGE

WARNINGS AND PRECAUTIONS

New Primary Malignancies: New primary malignancies, cutaneous and non-cutaneous, can occur. In the PHAROS trial, cutaneous squamous cell carcinoma (cuSCC) and skin papilloma (SP), each occurred in 2% of

patients. Perform dermatologic evaluations prior to initiating treatment, every 2 months during treatment, and for up to 6 months following discontinuation of treatment. Manage suspicious skin lesions with excision and dermatopathologic evaluation. Dose modification is not recommended for new primary cutaneous malignancies. Based on its mechanism of action, BRAFTOVI may promote malignancies associated with activation of RAS through mutation or other mechanisms. Monitor patients receiving BRAFTOVI for signs and symptoms of non-cutaneous malignancies. Discontinue BRAFTOVI for RAS mutation-positive non-cutaneous malignancies. Monitor patients for new malignancies prior to initiation of treatment, while on treatment, and after discontinuation of treatment.

Tumor Promotion in *BRAF* Wild-Type Tumors: In vitro experiments have demonstrated paradoxical activation of MAP-kinase signaling and increased cell proliferation in *BRAF* wild-type cells exposed to *BRAF* inhibitors. Confirm evidence of *BRAF V600E* or *V600K* mutation using an FDA-approved test prior to initiating BRAFTOVI.

Cardiomyopathy: Cardiomyopathy manifesting as left ventricular dysfunction associated with symptomatic or asymptomatic decreases in ejection fraction, has been reported in patients. In the PHAROS trial, evidence of cardiomyopathy occurred in 11% and Grade 3 left ventricular dysfunction occurred in 1% of patients. Cardiomyopathy resolved in 82% of patients. Assess left ventricular ejection fraction (LVEF) by echocardiogram or multi-gated acquisition (MUGA) scan prior to initiating treatment, 1 month after initiating treatment, and then every 2 to 3 months during treatment. The safety has not been established in patients with a baseline ejection fraction that is either below 50% or below the institutional lower limit of normal (LLN). Patients with cardiovascular risk factors should be monitored closely. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

Hepatotoxicity: Hepatotoxicity can occur when MEKTOVI is administered in combination with BRAFTOVI. In the PHAROS trial, the incidence of Grade 3 or 4 increases in liver function laboratory tests was 10% for aspartate aminotransferase (AST), 9% for alanine aminotransferase (ALT), and 3.2% for alkaline phosphatase. Monitor liver laboratory tests before initiation of BRAFTOVI and MEKTOVI, monthly during treatment, and as clinically indicated. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

Rhabdomyolysis: Rhabdomyolysis can occur when MEKTOVI is administered in combination with BRAFTOVI. In the PHAROS trial, elevation of laboratory values of serum creatine kinase (CK) occurred in 41% of patients. No patient experienced rhabdomyolysis. Monitor CPK and creatinine levels prior to initiating MEKTOVI, periodically during treatment, and as clinically indicated. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

Hemorrhage: Hemorrhage can occur when BRAFTOVI is administered in combination with MEKTOVI. In the PHAROS trial, hemorrhage occurred in 12% of patients, including fatal intracranial hemorrhage (1%); Grade 3 or 4 hemorrhage occurred in 4.1% of patients. The most frequent hemorrhagic events were anal hemorrhage and hemothorax (2% each). Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

Venous Thromboembolism (VTE): In the PHAROS trial, VTE occurred in 7% of patients, including 1% of patients who developed pulmonary embolism. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

Ocular Toxicities: In the PHAROS trial, serous retinopathy (retinal detachment) occurred in 2% of patients with no cases of blindness. Retinal vein occlusion (RVO) is a known class-related adverse reaction of MEK inhibitors and may occur in patients treated with MEKTOVI in combination with BRAFTOVI. The safety of MEKTOVI has not been established in patients with a history of RVO or current risk factors for RVO including uncontrolled

glaucoma or a history of hyperviscosity or hypercoagulability syndromes. Perform ophthalmological evaluation for patient-reported acute vision loss or other visual disturbance within 24 hours. Permanently discontinue MEKTOVI in patients with documented RVO. Uveitis, including iritis and iridocyclitis, was reported in patients treated with MEKTOVI in combination with BRAFTOVI. In PHAROS, uveitis occurred in 1% of patients. Assess for visual symptoms at each visit. Perform an ophthalmological evaluation at regular intervals and for new or worsening visual disturbances, and to follow new or persistent ophthalmologic findings. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

QT Prolongation: BRAFTOVI is associated with dose-dependent QTc interval prolongation in some patients. In the PHAROS trial, an increase in QTcF to >500 ms was measured in 2.1% (2/95) of patients who received BRAFTOVI with MEKTOVI. Monitor patients who already have or who are at significant risk of developing QTc prolongation, including patients with known long QT syndromes, clinically significant bradyarrhythmias, severe or uncontrolled heart failure and those taking other medicinal products associated with QT prolongation. Correct hypokalemia and hypomagnesemia prior to and during BRAFTOVI administration. Withhold, reduce dose, or permanently discontinue for QTc >500 ms.

Interstitial Lung Disease (ILD): In the PHAROS trial, 1 patient (1%) receiving MEKTOVI with BRAFTOVI developed pneumonitis. Assess new or progressive unexplained pulmonary symptoms or findings for possible ILD. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

Embryo-Fetal Toxicity: BRAFTOVI and MEKTOVI can cause fetal harm when administered to pregnant women. BRAFTOVI can render hormonal contraceptives ineffective. Effective, non-hormonal contraceptives should be used during treatment and for at least 30 days after the final dose for patients taking BRAFTOVI with MEKTOVI.

Risks Associated with BRAFTOVI as a Single Agent: There is an increased risk of certain adverse reactions compared to when BRAFTOVI is used in combination with MEKTOVI. If MEKTOVI is temporarily interrupted or permanently discontinued, reduce the dose of BRAFTOVI as recommended.

Risks Associated with Combination Treatment: BRAFTOVI is indicated for use as part of a regimen in combination with MEKTOVI. Refer to the prescribing information for BRAFTOVI and MEKTOVI for additional risk information.

Lactation: Advise women not to breastfeed during treatment with BRAFTOVI and MEKTOVI and for 2 weeks after the final dose.

Infertility: Advise males of reproductive potential that BRAFTOVI may impair fertility.

ADVERSE REACTIONS

The most common adverse reactions (?25%, all grades, in the PHAROS trial) for BRAFTOVI with MEKTOVI were: fatigue (61%), nausea (58%), diarrhea (52%), musculoskeletal pain (48%), vomiting (37%), abdominal pain (32%), visual impairment (29%), constipation (27%), dyspnea (27%), rash (27%), and cough (26%).

Serious adverse reactions occurred in 38% of patients receiving BRAFTOVI with MEKTOVI. Serious adverse reactions (?2% of patients in the PHAROS trial) were hemorrhage (6%), diarrhea (4.1%), anemia (3.1%), dyspnea (3.1%), pneumonia (3.1%), arrhythmia (2%), device related infection (2%), edema (2%), myocardial infarction (2%), and pleural effusion (2%). Fatal adverse reactions occurred in 2% of patients, including intracranial hemorrhage (1%) and myocardial infarction (1%).

Other clinically important adverse reactions occurring in <10% of patients who received BRAFTOVI with MEKTOVI in the PHAROS trial were peripheral neuropathy, dysgeusia, facial paresis, pancreatitis, hyperkeratosis, erythema, photosensitivity, and drug hypersensitivity.

In the PHAROS trial, the most common laboratory abnormalities (all grades) (?20%) for BRAFTOVI and MEKTOVI included increased creatinine (91%), hyperglycemia (48%), anemia (47%), increased creatine kinase (41%), lipase increased (40%), increased ALT (34%), hypoalbuminemia (32%), increased alkaline phosphatase (31%), increased AST (31%), hyperkalemia (31%), hyponatremia (26%), lymphopenia (24%), serum amylase increased (22%), and thrombocytopenia (20%).

DRUG INTERACTIONS

Strong or moderate CYP3A4 inhibitors: Avoid coadministration of BRAFTOVI with strong or moderate CYP3A4 inhibitors, including grapefruit juice. If coadministration is unavoidable, reduce the BRAFTOVI dose.

Strong CYP3A4 inducers: Avoid coadministration of BRAFTOVI with strong CYP3A4 inducers.

Sensitive CYP3A4 substrates: Avoid the coadministration of BRAFTOVI with CYP3A4 substrates (including hormonal contraceptives) for which a decrease in plasma concentration may lead to reduced efficacy of the substrate. If the coadministration cannot be avoided, see the CYP3A4 substrate product labeling for recommendations.

Dose reductions of drugs that are **substrates of OATP1B1, OATP1B3, or BCRP** may be required when used concomitantly with BRAFTOVI.

Avoid coadministration of BRAFTOVI with **drugs known to prolong QT/QTc interval.**

The information above applies to the safety of the combination of BRAFTOVI and MEKTOVI unless otherwise noted. See full Prescribing Information for BRAFTOVI and for MEKTOVI for dose modifications for adverse reactions.

Please see full Prescribing Information for BRAFTOVI and full Prescribing Information for MEKTOVI for additional information.

About Pfizer Oncology

At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes three core mechanisms of action to attack cancer from multiple angles, including small molecules, antibody-drug conjugates (ADCs), and multispecific antibodies, including other immune-oncology biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer, hematology-oncology, and thoracic cancers, which include lung cancer. Driven by science, we are committed to accelerating breakthroughs to help people with cancer live better and longer lives.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety, and value in the discovery, development, and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments, and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's

premier innovative biopharmaceutical companies, we collaborate with health care providers, governments, and local communities to support and expand access to reliable, affordable health care around the world. For 175 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on X at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Disclosure Notice

The information contained in this release is as of October 19, 2025. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer Oncology and the BRAFTOVI ® (encorafenib) and MEKTOVI® (binimetinib) combination for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of BRAFTOVI plus MEKTOVI; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed in any additional jurisdictions for BRAFTOVI plus MEKTOVI for the treatment of patients with metastatic NSCLC with a BRAF V600E mutation or in any jurisdictions for any other potential indications for BRAFTOVI and MEKTOVI or any other product candidates; whether and when any such applications may be approved by regulatory authorities, which will depend on a myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether BRAFTOVI plus MEKTOVI or any such other product candidates will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of BRAFTOVI plus MEKTOVI or any other product candidates; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2024, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

References

[1]World Health Organization. International Agency for Research on Cancer. GLOBOCAN 2022: Global Population Fact sheet. Available at: https://gco.iarc.who.int/media/globocan/factsheets/populations/900-world-fact-sheet.pdf. Last accessed: September 2025.
[2]American Cancer Society. What is lung cancer? Available at: https://www.cancer.org/cancer/lung-cancer/about/what-is.html. Last accessed: September 2025.
[3]American Lung Association. *BRAF* and lung cancer. Available at: https://www.lung.org/lung-health-

diseases/lung-disease-lookup/lung-cancer/symptoms-diagnosis/biomarker-testing/braf. Last accessed: September 2025.
[4]Planchard D, Sanborn RE, Negrao MV, Vaishnavi A, Smit EF. BRAF^{V600E}-mutant metastatic NSCLC: Disease overview and treatment landscape. *NPJ Precis Oncol*. 2024;8(1):90.
[5]Paik PK, Arcila ME, Fara M, et al. Clinical characteristics of patients with lung adenocarcinomas harboring *BRAF* mutations. *J Clin Oncol*. 2011;29(15):2046-51.
[6]Lieu CH, Corcoran RB, Overman MJ. Integrating biomarkers and targeted therapy into colorectal cancer management. *Am Soc Clin Oncol Educ Book*. 2019;39:207-215.
[7]Evangelist MC, et al. Presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL. Abstract 9109.
[8]Hendriks LE, Kerr KM, Menis J, et al. Oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2023 Apr;34(4)339-357.
[9]Non-Small Cell Lung Cancer, Version 3.2025. NCCN Clinical Practice Guidelines in Oncology. Accessed April 17, 2025.
[10]Dennis MJ, et al. Presented at: AACR Annual Meeting; April 5-10, 2024; San Diego, CA. Abstract 2552.?

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