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U.S. FDA Approves Pfizer's BRAFTOVI® + MEKTOVI® for BRAF V600E-Mutant Metastatic Non-Small Cell Lung Cancer

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BRAFTOVI + MEKTOVI now gives adult patients with BRAF V600E-mutant metastatic non-small cell lung cancer a new personalized treatment option

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) announced today that the U.S. Food and Drug Administration (FDA) has approved BRAFTOVI® (encorafenib) + MEKTOVI® (binimetinib) for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with a *BRAF* V600E mutation, as detected by an FDA-approved test.[1] *BRAF* V600Emutations can be assessed from either plasma or tumor tissue using the FoundationOne Liquid CDx or the FoundationOne CDx FDA-approved companion diagnostic tests, respectively.

"Today's approval builds on our long-standing commitment to deliver innovative, personalized medicines to patients with lung cancer. By pursuing precision medicines that target a patient's specific type of cancer, we are leveraging our deep understanding of tumor biology to help address the underlying cause of disease," said Chris Boshoff, M.D., Ph.D., Chief Oncology Research and Development Officer and Executive Vice President at Pfizer. "Since its initial FDA approval in 2018, BRAFTOVI + MEKTOVI combination therapy has helped thousands of people living with *BRAF* V600E- or V600K-mutant unresectable or metastatic melanoma.[2] We look forward to helping even more patients with our BRAFTOVI + MEKTOVI targeted combination therapy."

The FDA's approval is based on data from the ongoing Phase 2 PHAROS clinical trial (NCT03915951), an open-label, multicenter, single?arm study examining BRAFTOVI + MEKTOVI combination therapy in both treatment-naïve and previously treated patients with *BRAF* V600E-mutant metastatic NSCLC.

"*BRAF* V600E mutations identify a unique subtype of metastatic non-small cell lung cancer that presents an actionable biomarker that precision medicines like BRAFTOVI + MEKTOVI combination therapy can help address," said Gregory Riely, M.D., Ph.D., Vice Chair, Clinical Research in the Department of Medicine at Memorial Sloan Kettering Cancer Center (MSK) and PHAROS investigator. "The PHAROS trial demonstrated that these patients could benefit from BRAFTOVI + MEKTOVI targeted therapy regardless of their prior treatment history. Given the specific efficacy and safety profile, patients and providers now have another option to help personalize treatment plans based on individual risk factors and preferences."

The PHAROS study met its major efficacy outcome measures of objective response rate (ORR), as assessed by independent review committee (IRC), and duration of response (DOR) in both treatment groups. For treatment-naïve patients (n=59), ORR was 75% (95% CI: 62, 85), and 59% of the patients responded for at least 12 months. Median DOR was not estimable (NE) for this group at the time of data cutoff. For previously treated

patients (n=39), ORR was 46% (95% CI: 30, 63), and 33% of the patients responded for at least 12 months. Median DOR was 16.7 months (95% CI: 7.4, NE). These data were presented earlier this year at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published in the Journal of Clinical Oncology (JCO).[3]

The most common (?25%) all-causality adverse reactions observed in the PHAROS trial were fatigue, nausea, diarrhea, musculoskeletal pain, vomiting, abdominal pain, visual impairment, constipation, dyspnea, rash, and cough. A total of 17% of patients experienced an adverse reaction that resulted in permanent discontinuation of MEKTOVI and 16% experienced an adverse event that resulted in permanent discontinuation of BRAFTOVI. Serious adverse reactions occurred in 38% of patients. Serious adverse reactions occurring in ?2% of patients included hemorrhage (6%), diarrhea (4.1%), anemia, dyspnea, pneumonia (3.1% each), arrhythmia, device-related infection, edema, myocardial infarction, and pleural effusion (2% each). Fatal adverse reactions occurred in 2% of patients, including intracranial hemorrhage and myocardial infarction (1% each).

BRAFTOVI + MEKTOVI is also FDA-approved for the treatment of patients with unresectable or metastatic melanoma with a *BRAF* V600E or V600K mutation, as detected by an FDA-approved test. BRAFTOVI is FDA-approved, in combination with cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a *BRAF* V600E mutation, as detected by an FDA-approved test, after prior therapy.

Pfizer has exclusive rights to BRAFTOVI and MEKTOVI in the U.S., Canada, and all countries in Latin America, Africa, and the Middle East. 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 has exclusive rights in all other countries, including Europe and Asia-Pacific (excluding Japan and South Korea).

The PHAROS trial is conducted with support from Pierre Fabre.

About *BRAF* V600E-mutant Non-Small Cell Lung Cancer (NSCLC)

Lung cancer is the second most common type of cancer and the number one cause of cancer-related death around the world.[4] NSCLC accounts for approximately 80-85% of all lung cancers.[5]

Certain lung cancers are linked to acquired genetic abnormalities like a *BRAF* V600E mutation. By using biomarkers to identify a person's particular tumor type, treatment can become more personalized and effective, since the molecular makeup of a person's cancer often determines how they respond to different therapies.

A *BRAF* V600E mutation occurs in approximately 2% of NSCLC cases.[6] It stimulates tumor cell growth and proliferation by altering the MAP kinase (MAPK) signaling pathway. Targeting components of this pathway could potentially help inhibit tumor growth and proliferation caused by *BRAF* mutations.[7]

Precision medicine is increasingly being developed for NSCLC patients with genetic changes, such as *BRAF* mutations, that can be detected using biomarker tests.[8,9] In recent years, more widespread use of biomarker testing and targeted therapies have been associated with improvements in population-level NSCLC mortality.[10]

INDICATIONS AND USAGE

BRAFTOVI® (encorafenib) and MEKTOVI® (binimetinib) are kinase inhibitors indicated for use in combination for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test.

BRAFTOVI is indicated, in combination with cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy.

BRAFTOVIand MEKTOVI are kinase inhibitors indicated for use in combination for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, as detected by an FDA-approved test.

Limitations of Use: BRAFTOVI is not indicated for treatment of patients with wild-type BRAF melanoma, wild-type BRAF CRC, or wild-type BRAF NSCLC.

IMPORTANT SAFETY INFORMATION

This information applies to the safety of BRAFTOVI when used in combination with either MEKTOVI or cetuximab.

WARNINGS AND PRECAUTIONS

New Primary Malignancies: New primary malignancies, cutaneous and non-cutaneous, can occur. BRAFTOVI may promote malignancies associated with activation of RAS through mutation or other mechanisms. Perform dermatopathologic 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. 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.

- **BRAF-mutant type (BRAF-mt) metastatic melanoma (COLUMBUS study):** Cutaneous squamous cell carcinoma (cuSCC), including keratoacanthoma (KA), occurred in 2.6% and basal cell carcinoma occurred in 1.6% of patients receiving BRAFTOVI with MEKTOVI. Median time to first occurrence of cuSCC/KA was 5.8 months.
- **BRAF-mt metastatic CRC (BEACON CRC study):** cuSCC, including KA, occurred in 1.4% of patients with CRC, and a new primary melanoma occurred in 1.4% of patients who received BRAFTOVI with cetuximab.
- **BRAF-mt metastatic NSCLC (PHAROS study):** cuSCC and skin papilloma (SP), each occurred in 2% of patients.

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. Patients with cardiovascular risk factors should be monitored closely. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

- 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).
- **BRAF-mt metastatic melanoma (COLUMBUS study):** Evidence of cardiomyopathy occurred in 7% and Grade 3 left ventricular dysfunction occurred in 1.6% of patients receiving BRAFTOVI with MEKTOVI. The median time to first occurrence of left ventricular dysfunction (any grade) was 3.6 months. Cardiomyopathy resolved in 87% of patients.
- **BRAF-mt metastatic NSCLC (PHAROS study):** Evidence of cardiomyopathy occurred in 11% and Grade 3 left ventricular dysfunction occurred in 1% of patients. Cardiomyopathy resolved in 82% of patients.

Hepatotoxicity: Hepatotoxicity can occur. Monitor liver laboratory tests before initiation, monthly during treatment, and as clinically indicated. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

- **BRAF-mt metastatic melanoma (COLUMBUS study):** The incidence of Grade 3 or 4 increases in liver function laboratory tests in patients receiving MEKTOVI with BRAFTOVI was 6% for alanine aminotransferase (ALT), 2.6% for aspartate aminotransferase (AST), and 0.5% for alkaline phosphatase.
- **BRAF-mt metastatic NSCLC (PHAROS study):** The incidence of Grade 3 or 4 increases in liver function laboratory tests was 10% for AST, 9% for ALT, and 3.2% for alkaline phosphatase.

Hemorrhage: Hemorrhage can occur when BRAFTOVI is administered in combination with MEKTOVI or cetuximab. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

- **BRAF-mt metastatic melanoma (COLUMBUS study):** Hemorrhage occurred in 19% of patients receiving BRAFTOVI with MEKTOVI and Grade 3 or higher hemorrhage occurred in 3.2% of patients. The most frequent hemorrhagic events were gastrointestinal, including rectal hemorrhage (4.2%), hematochezia (3.1%), and hemorrhoidal hemorrhage (1%). Fatal intracranial hemorrhage in the setting of new or progressive brain metastases occurred in 1.6% of patients.
- **BRAF-mt metastatic CRC (BEACON CRC study):** Hemorrhage occurred in 19% of patients receiving BRAFTOVI with cetuximab; Grade 3 or higher hemorrhage occurred in 1.9% of patients, including fatal gastrointestinal hemorrhage in 0.5% of patients. The most frequent hemorrhagic events were epistaxis (6.9%), hematochezia (2.3%), and rectal hemorrhage (2.3%).
- **BRAF-mt metastatic NSCLC (PHAROS study):** 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).

Uveitis: Uveitis, including iritis and iridocyclitis, has been reported in patients treated with BRAFTOVI with MEKTOVI. 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.

- **BRAF-mt metastatic melanoma (COLUMBUS study):** The incidence of uveitis among patients treated with BRAFTOVI with MEKTOVI was 4%.
- **BRAF-mt metastatic NSCLC (PHAROS study):** The incidence of uveitis among patients treated with BRAFTOVI with MEKTOVI was 1%.

QT Prolongation: BRAFTOVI is associated with dose-dependent QTc interval prolongation in some patients. 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.

- **BRAF-mt metastatic melanoma (COLUMBUS study):** An increase in QTcF to >500 ms was measured in 0.5% (1/192) of patients who received BRAFTOVI with MEKTOVI.
- **BRAF-mt metastatic NSCLC (PHAROS study):** An increase in QTcF to >500 ms was measured in 2.1% (2/95) of patients who received BRAFTOVI with MEKTOVI.

Embryo-Fetal Toxicity: Both BRAFTOVI and MEKTOVI can cause fetal harm when administered to a pregnant woman. BRAFTOVI can render hormonal contraceptives ineffective.

- **BRAF-mt metastatic melanoma (COLUMBUS study) and BRAF-mt metastatic NSCLC (PHAROS study):** 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.
- **BRAF-mt metastatic CRC (BEACON CRC study):** Advise females of reproductive potential to use effective nonhormonal contraception during treatment with BRAFTOVI and for 2 weeks after the final dose.

BRAFTOVI as a Single Agent is associated with increased risk of certain adverse reactions compared to when BRAFTOVI is used with MEKTOVI.

- **BRAF-mt metastatic melanoma (COLUMBUS study):** Grades 3 or 4 dermatologic reactions occurred in 21% of patients receiving BRAFTOVI as a single agent compared to 2% in patients receiving the combination of BRAFTOVI with MEKTOVI.
- If MEKTOVI is temporarily interrupted or permanently discontinued, reduce the dose of BRAFTOVI as recommended.

Risks Associated with Combination Treatment

- In **BRAF-mt metastatic melanoma (COLUMBUS study)**, BRAFTOVI is used in combination with MEKTOVI so refer to the prescribing information for MEKTOVI for additional risk information.
- In **BRAF-mt metastatic CRC (BEACON CRC study)**, BRAFTOVI is used in combination with cetuximab so refer to the prescribing information for cetuximab for additional risk information.
- In **BRAF-mt metastatic NSCLC (PHAROS study)**, BRAFTOVI is indicated for use as part of a regimen in combination with MEKTOVI, so refer to the prescribing information for MEKTOVI for additional risk information.

Additional WARNINGS AND PRECAUTIONS for MEKTOVI When Used With BRAFTOVI

Venous Thromboembolism (VTE): VTE occurred in 6% of patients with **BRAF-mt metastatic melanoma (COLUMBUS study)**, including 3.1% of patients who developed pulmonary embolism. VTE occurred in 7% of patients with **BRAF-mt metastatic NSCLC (PHAROS study)**, including 1% of patients who developed pulmonary embolism. Withhold, reduce dose, or permanently discontinue based on severity of adverse reaction.

Other Ocular Toxicities

- **Serous retinopathy**
    - Assess for visual symptoms at each visit. Perform an ophthalmologic examination at regular intervals, 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.

    - **BRAF-mt metastatic melanoma (COLUMBUS study):** serious retinopathy occurred in 20% of patients receiving MEKTOVI with BRAFTOVI; 8% were retinal detachment and 6% were macular edema. Symptomatic serous retinopathy occurred in 8% of patients with no cases of blindness. The median time to onset of the first event of serous retinopathy (all grades) was 1.2 months.
    - **BRAF-mt metastatic NSCLC (PHAROS study):** 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 receiving MEKTOVI with BRAFTOVI. In **BRAF-mt metastatic melanoma (COLUMBUS study)**, 1 patient experienced RVO (0.1%) in the MEKTOVI with BRAFTOVI group (n=690).
    - 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.

Interstitial Lung Disease (ILD): ILD, including pneumonitis, occurred in 0.3% (2 of 690 patients) with **BRAF-mt metastatic melanoma (COLUMBUS study)** receiving MEKTOVI with BRAFTOVI. One patient (1%) with **BRAF-mt metastatic NSCLC (PHAROS study)** 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.

Rhabdomyolysis: Rhabdomyolysis can occur when MEKTOVI is taken with BRAFTOVI. Monitor creatine phosphokinase (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.

- **BRAF-mt metastatic melanoma (COLUMBUS study):** Elevation of laboratory values of serum CPK occurred in 58% of patients receiving MEKTOVI with BRAFTOVI. Rhabdomyolysis was reported in 0.1% (1 of 690 patients) with BRAF mutation-positive melanoma receiving MEKTOVI with BRAFTOVI.
- **BRAF-mt metastatic NSCLC (PHAROS study):** Elevation of laboratory values of serum creatine kinase (CK) occurred in 41% of patients. No patient experienced rhabdomyolysis.

ADVERSE REACTIONS

BRAF-mt Metastatic Melanoma (COLUMBUS study)

- **Most common adverse reactions** (?20%, all grades) for patients receiving BRAFTOVI with MEKTOVI compared to vemurafenib were fatigue (43% vs 46%), nausea (41% vs 34%), diarrhea (36% vs 34%), vomiting (30% vs 16%), abdominal pain (28% vs 16%), arthralgia (26% vs 46%), myopathy (23% vs 22%), hyperkeratosis (23% vs 49%), rash (22% vs 53%), headache (22% vs 20%), constipation (22% vs 6%), visual impairment (20% vs 4%), serous retinopathy/RPED (20% vs 2%).
- **Other clinically important adverse reactions** occurring in <10% of patients who received BRAFTOVI with MEKTOVI were facial paresis, pancreatitis, panniculitis, drug hypersensitivity, and colitis
- **Most common laboratory abnormalities** (?20%, all grades) for BRAFTOVI with MEKTOVI compared to vemurafenib included increased creatinine (93% vs 92%), increased CPK (58% vs 3.8%), increased gamma glutamyl transferase (GGT) (45% vs 34%), anemia (36% vs 34%), increased ALT (29% vs 27%), hyperglycemia (28% vs 20%), increased AST (27% vs 24%), and increased alkaline phosphatase (21% vs 35%).

BRAF-mt Metastatic CRC (BEACON CRC study)

- **Most common adverse reactions** (?25%, all grades) in patients receiving BRAFTOVI with cetuximab compared to irinotecan with cetuximab or FOLFIRI with cetuximab (control) were fatigue (51% vs 50%), nausea (34% vs 41%), diarrhea (33% vs 48%), dermatitis acneiform (32% vs 43%), abdominal pain (30% vs 32%), decreased appetite (27% vs 27%), arthralgia (27% vs 3%), and rash (26% vs 26%).
- **Other clinically important adverse reactions** occurring in <10% of patients who received BRAFTOVI with cetuximab was pancreatitis.
- **Most common laboratory abnormalities** (?20%, all grades) in the BRAFTOVI with cetuximab arm compared to irinotecan with cetuximab or FOLFIRI with cetuximab (control) were: anemia (34% vs 48%) and lymphopenia (24% vs 35%).

BRAF-mt Metastatic NSCLC (PHAROS study)

- **Most common adverse reactions** (?25%, all grades) in patients receiving 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 occurring in ?2% of patients 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 were peripheral neuropathy, dysgeusia, facial paresis, pancreatitis, hyperkeratosis, erythema, and drug hypersensitivity.
- **Most common laboratory abnormalities** (?20%, all grades) 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 With BRAFTOVI When Used in Combination With Either MEKTOVI or Cetuximab

- Avoid coadministration of BRAFTOVI with strong or moderate CYP3A4 inhibitors (including grapefruit juice) or CYP3A4 inducers and use caution with sensitive CYP3A4 substrates. Avoid coadministration of BRAFTOVI with hormonal contraceptives
- Modify BRAFTOVI dose if coadministration with a strong or moderate CYP3A4 inhibitor cannot be avoided
- Avoid coadministration of BRAFTOVI with drugs known to prolong QT/QTc interval
- Dose reductions of drugs that are substrates of OATP1B1, OATP1B3, or BCRP may be required when used concomitantly with BRAFTOVI

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.

For BRAF-mt metastatic melanoma and for BRAF-mt metastatic NSCLC, see full Prescribing Information and Medication Guide for BRAFTOVI and full Prescribing Information and Medication

Guide for MEKTOVI. See full Prescribing Information for BRAFTOVI and for MEKTOVI for dose modifications for adverse reactions. There may be a delay as the documents are updated with the latest information. They will be available as soon as possible. Please check back for the updated full information shortly.

For BRAF-mt metastatic CRC, see full Prescribing Information and Medication Guide for BRAFTOVI. See full Prescribing Information for BRAFTOVI for dose modifications for adverse reactions. Refer to cetuximab prescribing information for recommended dosing and safety information.

About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of people living with cancer. Today, we have an industry-leading portfolio of 24 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, genitourinary, colorectal, blood and lung cancers, as well as melanoma.

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 more than 170 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 Twitter 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 12, 2023. 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 BRAFTOVI® (encorafenib) + MEKTOVI® (binimetinib) and a new indication in the U.S. for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, as detected by an FDA-approved test, including its 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, 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; whether the final results from the PHAROS study will be consistent with the results discussed in this release; uncertainties regarding the commercial success of BRAFTOVIand MEKTOVI; 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 applications for BRAFTOVI and MEKTOVI may be filed with regulatory authorities in any other jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be pending or filed for BRAFTOVI and MEKTOVI, which will depend on myriad factors, including making a determination as to whether the products' benefits outweigh their known risks and

determination of the products' efficacy and, if approved, whether BRAFTOVIand MEKTOVI will be commercially successful; decisions by regulatory authorities regarding labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of BRAFTOVI and MEKTOVI, including the new indication; 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, 2022 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 .

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Category: Prescription Medicines

[1] BRAFTOVI® (encorafenib) Prescribing Information. Array BioPharma, Inc. (a wholly owned subsidiary of Pfizer Inc.): 2023.

[2] Data on File Pfizer March 2022 (REF-BMK0842 + REF-BMK1009)

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