Pfizer’s BRAFTOVI® + MEKTOVI® Shows Long-Term Clinically Meaningful Response in Patients with BRAF V600E-Mutant Metastatic Non-Small Cell Lung Cancer

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BRAFTOVI + MEKTOVI continued to show substantial antitumor activity after a minimum follow up of approximately three years, corresponding to the longest duration of response and progression-free survival in treatment-naïve patients compared to historical outcomesResults support BRAFTOVI + MEKTOVI as a standard of care option for this population

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced longer-term follow-up results from the Phase 2 single-arm PHAROS clinical trial evaluating the efficacy and safety of BRAFTOVI ® (encorafenib) in combination with MEKTOVI ® (binimetinib) for patients with *BRAF* V600E - mutant metastatic non-small cell lung cancer (NSCLC). After an additional 18 months of follow-up, the objective response rate (ORR) and the median duration of response (DoR) as assessed by independent radiology review were 75% and 40 months in treatment-naïve patients and 46% and 16.7 months in previously treated patients, respectively. In addition, after approximately three years of follow-up in treatment-naïve patients, the median progression-free survival (PFS) with BRAFTOVI + MEKTOVI was 30.2 months (95% confidence interval [CI], 15.7-not estimable [NE]), while median overall survival (OS) was not yet reached (95% CI, 31.3-NE). These data will be

presented today during a late-breaking oral session (Abstract LBA56) at the European Society for Medical Oncology (ESMO) Congress 2024 in Barcelona, Spain.

“ *BRAF* V600E-mutant metastatic non-small cell lung cancer tends to be aggressive, and effective targeted first-line treatment options with manageable safety profiles are critical for the thousands of people who are diagnosed globally each year,” 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 longer-term follow-up results from the PHAROS trial represent an important step forward in the treatment of *BRAF* V600E-mutant metastatic NSCLC, especially for treatment-naïve patients. These compelling results support the BRAFTOVI + MEKTOVI combination as a standard of care option for these patients.”

Lung cancer is the number one cause of cancer-related death 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 Understanding the role of the mitogen-activated protein within the pathway including *BRAF* V600E-mutant metastatic NSCLC.

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. Notably, upon longer-term follow-up in previously treated patients, BRAFTOVI + MEKTOVI showed a median PFS of 9.3 months (95% CI, 6.2-24.8) and a median OS of 22.7 months (95% CI, 14.1-32.2), with a safety profile that was consistent with previous findings; no new safety concerns were identified. In this analysis, treatment-related adverse events (AEs) led to dose reduction in 26% of patients, and to permanent discontinuation in 16% of patients. Nausea, diarrhea, and fatigue remained the most common treatment-related AEs.

“These potentially practice-changing results from the PHAROS trial show that the combination of BRAFTOVI + MEKTOVI is providing long-term compelling efficacy for patients, and although no definitive conclusions can be made across trials, the duration of response and progression-free survival in treatment naïve patients appear to be the longest observed for *BRAF* V600E–mutant metastatic NSCLC compared with historical outcomes,” said Roger Dansey, M.D., Chief Development Officer, Oncology, Pfizer. “These latest data reflect our deep understanding of the science behind biomarker-driven cancers and add to our legacy in developing innovative targeted treatments in NSCLC. We are continuing to build upon this strong foundation with a pipeline of targeted medicines and combinations across our tumor areas of focus, including the ongoing investigation of BRAFTOVI in earlier settings of metastatic colorectal cancer, and the

exploration of a next-generation brain-penetrant *BRAF* inhibitor.”

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 ORR (the primary endpoint) and DoR (key secondary endpoint) results from the PHAROS clinical trial.

In addition to PHAROS, safety lead-in data from the ongoing Phase 3 BREAKWATER study investigating BRAFTOVI in combination with cetuximab and FOLFIRI chemotherapy in previously untreated *BRAF* V600E-mutant metastatic colorectal cancer (CRC) will also be presented as a mini-oral session at ESMO (Abstract 515MO). BRAFTOVI in combination with cetuximab and FOLFIRI was found to be generally tolerable in this patient population, with no new safety concerns identified. These findings support the ongoing investigation of this combination regimen as a potential treatment option for *BRAF* V600E-mutant metastatic CRC. The Phase 3 BREAKWATER trial is ongoing, with updated data expected in 2025.

BRAF mutations can occur in a number of tumor types, including metastatic melanoma, metastatic CRC and metastatic NSCLC. Among different types of *BRAF* mutations, the *BRAF* V600E mutation is particularly important as it occurs in approximately half of patients with *BRAF* -mutant metastatic NSCLC. 4 Further, this mutation represents up to 90% of *BRAF* mutations in melanoma 5 and more than doubles the risk of mortality for patients with CRC. 6 In addition to our continued investigation of BRAFTOVI + MEKTOVI for *BRAF*- mutant cancers, Pfizer is also exploring a next-generation *BRAF* inhibitor designed to selectively inhibit mutant *BRAF* monomers and mutant *BRAF*- containing dimers and be brain penetrant. The investigational drug is currently being evaluated in a Phase 1 clinical study.

Pfizer has exclusive rights to BRAFTOVI + 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 Laboratories 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 Laboratories.

INDICATION 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.

BRAFTOVI and 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): serous 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 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 bispecific 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 includes 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 September 14, 2024. 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 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, other potential indications and a next-generation BRAF inhibitor, 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; 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, 2023, 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 2024. 2 American Cancer Society. What is lung cancer? Available at: https://www.cancer.org/cancer/lung-cancer/about/what-is.html . Last accessed: September 2024. 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 2024. 4 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. 5 Cheng L, Lopez-Beltran A, Massari F, *et al* . Molecular testing for BRAF mutations to inform melanoma treatment decisions: a move toward precision medicine. *Mod Pathol* . 2018;31(1):24-38. 6 Safaee Ardekani G, Jafarnejad, SM, Tan, L, *et al* . The prognostic

value of BRAF mutation in colorectal cancer and melanoma: a systematic review and meta-analysis. *PloS ONE* . 2012;7(10):e47054.

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