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VIZIMPRO® (dacomitinib) Receives Marketing Authorization in European Union (EU) for the First-Line Treatment of Adult Patients with EGFR-Mutated Non-Small Cell Lung Cancer

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Pfizer Inc. (NYSE: PFE) today announced that the European Commission has approved VIZIMPRO® (dacomitinib), a tyrosine kinase inhibitor (TKI), as monotherapy for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations.

“Lung cancer remains the leading cause of cancer-related death worldwide and despite advances in biomarker-driven therapies, overcoming resistance continues to be crucial in treating EGFR-mutated non-small cell lung cancer,” said Andreas Penk, M.D., regional president, Oncology International Developed Markets at Pfizer. “The marketing authorization of VIZIMPRO, which has shown a more than five-month improvement in progression-free survival over an existing therapy in a Phase 3 clinical trial, provides a new option for patients with EGFR-mutated non-small cell lung cancer and reinforces Pfizer’s ongoing commitment to addressing the remaining needs of the thousands of EU patients with this disease.”

The European Commission’s approval of VIZIMPRO was supported by data from ARCHER 1050, a randomized, multicenter, multinational, open-label, Phase 3 study conducted in patients with unresectable, metastatic or recurrent NSCLC harboring EGFR exon 19 deletion or exon 21 L858R substitution mutations. A total of 452 patients were randomized 1:1 to VIZIMPRO 45 mg (n=227) or gefitinib 250 mg (n=225). The primary endpoint was progression-free survival (PFS) as determined by blinded Independent Radiologic Central (IRC) review. Key secondary endpoints included PFS assessed by the investigator, objective response rate (ORR), duration of response (DoR) and overall survival (OS).

A statistically significant improvement in PFS as determined by the IRC was demonstrated for patients randomized to VIZIMPRO compared with gefitinib (HR = 0.59 [95% CI: 0.47, 0.74], p <0.0001). Median PFS in the VIZIMPRO group was 14.7 months (95% CI: 11.1, 16.6) compared with 9.2 months (95% CI: 9.1, 11.0) in the gefitinib arm.

“Over the last two decades, biomarker-driven therapies have become standard-of-care for patients with EGFR-mutated non-small cell lung cancer,” said Dr. Federico Cappuzzo, Director of Oncology and Hematology Department AUSL della Romagna-Ravenna. “The improvement in progression-free survival for VIZIMPRO over a first-generation standard-of-care therapy in the ARCHER 1050 study is impressive, and I’m pleased it will be available for appropriate patients with non-small cell lung cancer in the EU.”

OS results from the final analysis (data cut-off date of 17-Feb-2017) performed when 48.7 percent of events had occurred, showed a gain of 7.3 months in median OS for patients treated with VIZIMPRO compared to those treated with gefitinib (34.1 months vs. 26.8 months; HR: 0.760 [95% CI: 0.582, 0.993]). However, the statistical significance of the OS improvement could not formally be assessed, as the secondary endpoints from the study were tested in descending order of perceived importance and stopped when no additional statistical significance of ORR was reached.

Among 227 patients with EGFR-mutated metastatic NSCLC who received VIZIMPRO in ARCHER 1050, the most common (? 20%) adverse reactions were diarrhea (87%), rash (77%), stomatitis (70%), nail disorder (66%), decreased appetite (31%), dry skin (30%), weight decreased (26%), transaminases increased (24%), conjunctivitis (23%), alopecia (23%), and pruritus (20%). Serious adverse reactions occurred in 6.2 percent of patients treated with VIZIMPRO. The most common (? 1%) serious adverse reactions reported were diarrhea (2.2%) and interstitial lung disease (1.3%).[1,2]

About VIZIMPRO® (dacomitinib), 45 mg, 30 mg and 15 mg tablets

VIZIMPRO is an oral, once-daily, irreversible pan-human epidermal growth factor receptor kinase inhibitor. VIZIMPRO is approved in the EU for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations.

VIZIMPRO is also approved in the United States for the first-line treatment of patients with metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test. Additionally, VIZIMPRO is approved in Japan for EGFR gene mutation-positive, inoperable or recurrent NSCLC, and in Canada for the first-line treatment of adult patients with unresectable locally advanced or metastatic NSCLC with confirmed EGFR exon 19 deletion or exon 21 L858R substitution mutations. The applications in the US and Japan were reviewed and approved under the Priority Review program.

In 2012, Pfizer and SFJ Pharmaceuticals entered into a collaborative development agreement to conduct ARCHER 1050 across multiple sites. SFJ is a global drug development company, which provides a unique and highly customized co-development partnering model for the world’s top pharmaceutical and biotechnology companies. Under the terms of this agreement, SFJ Pharmaceuticals provided the funding and conducted the trial to generate the clinical data used to support this application. Pfizer retains all rights to commercialize VIZIMPRO globally.

About ARCHER 1050

The efficacy of VIZIMPRO was demonstrated in ARCHER 1050, a global Phase 3 head-to-head trial conducted in patients with unresectable, metastatic or recurrent non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations, with no prior therapy for metastatic disease or recurrent disease with a minimum of 12 months disease-free after completion of systemic therapy. A total of 452 patients were randomized 1:1 to VIZIMPRO 45 mg (n=227) or gefitinib 250 mg (n=225). Randomization was stratified by region and EGFR mutation status. The primary endpoint of the study was progression-free survival (PFS) as determined by blinded Independent Radiology Central (IRC) review. Key secondary endpoints included PFS assessed by the investigator, objective response rate (ORR), duration of response (DoR), overall survival (OS), and patient-reported outcomes (PROs).

VIZIMPRO® (dacomitinib) IMPORTANT SAFETY INFORMATION FROM THE U.S. PRESCRIBING INFORMATION

There are no contraindications for VIZIMPRO.

Interstitial Lung Disease (ILD): Severe and fatal ILD/pneumonitis occurred in patients treated with VIZIMPRO and occurred in 0.5% of the 394 VIZIMPRO-treated patients; 0.3% of cases were fatal. Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis. Withhold VIZIMPRO and promptly investigate for ILD in patients who present with worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough, and fever). Permanently discontinue VIZIMPRO if ILD is confirmed.

Diarrhea: Severe and fatal diarrhea occurred in patients treated with VIZIMPRO. Diarrhea occurred in 86% of the 394 VIZIMPRO-treated patients. Grade 3 or 4 diarrhea was reported in 11% of patients and 0.3% of cases were fatal. Withhold VIZIMPRO for Grade 2 or greater diarrhea until recovery to less than or equal to Grade 1 severity, then resume VIZIMPRO at the same or a reduced dose depending on the severity of diarrhea. Promptly initiate anti-diarrheal treatment (loperamide or diphenoxylate hydrochloride with atropine sulfate) for diarrhea.

Dermatologic Adverse Reactions: Rash and exfoliative skin reactions occurred in patients treated with VIZIMPRO. Rash occurred in 78% of the 394 VIZIMPRO-treated patients. Grade 3 or 4 rash was reported in 21% of patients. Exfoliative skin reactions of any severity were reported in 7% of patients. Grade 3 or 4 exfoliative skin reactions were reported in 1.8% of patients. Withhold VIZIMPRO for persistent Grade 2 or any Grade 3 or 4 dermatologic adverse reaction until recovery to less than or equal to Grade 1 severity, then resume VIZIMPRO at the same or a reduced dose depending on the severity of the dermatologic adverse reaction. The incidence and severity of rash and exfoliative skin reactions may increase with sun exposure. At the time of initiation of VIZIMPRO, initiate use of moisturizers and appropriate measures to limit sun exposure. Upon development of Grade 1 rash, initiate treatment with topical antibiotics and topical steroids. Initiate oral antibiotics for Grade 2 or more severe dermatologic adverse reactions.

Embryo-Fetal Toxicity: VIZIMPRO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with VIZIMPRO and for at least 17 days after the final dose.

Adverse Reactions: The most common (>20%) adverse reactions were diarrhea (87%), rash (69%), paronychia (64%), stomatitis (45%), decreased appetite (31%), dry skin (30%), decreased weight (26%), alopecia (23%), cough (21%), and pruritus (21%). The most common (?1%) serious adverse reactions were diarrhea (2.2%) and interstitial lung disease (1.3%).

Drug Interactions: Concomitant use with a proton pump inhibitor (PPI) decreases dacomitinib concentrations, which may reduce VIZIMPRO efficacy. Avoid the concomitant use of PPIs with VIZIMPRO. As an alternative to PPIs, use locally-acting antacids or an H2-receptor antagonist. Administer VIZIMPRO at least 6 hours before or 10 hours after taking an H2-receptor antagonist. Concomitant use of VIZIMPRO increases the concentration of drugs that are CYP2D6 substrates which may increase the risk of toxicities of these drugs. Avoid concomitant use of VIZIMPRO with CYP2D6 substrates where minimal increases in concentration of the CYP2D6 substrate may lead to serious or life-threatening toxicities.

Lactation: Because of the potential for serious adverse reactions in breastfed infants from VIZIMPRO, advise women not to breastfeed during treatment with VIZIMPRO and for at least 17 days after the last dose.

Hepatic Impairment: No dose adjustment is recommended in patients with mild or moderate hepatic impairment. The recommended dose of VIZIMPRO has not been established for patients with severe hepatic impairment.

Renal Impairment: No dose adjustment is recommended for patients with mild or moderate renal impairment. The recommended dose of VIZIMPRO has not been established for patients with severe renal impairment.

Please see full prescribing information at Pfizer.com

About Non-Small Cell Lung Cancer

Lung cancer is the most common cancer worldwide, with more than two million new cases diagnosed globally in 2018.[1] About 85 percent of all lung cancers are identified as non-small cell, and approximately 75 percent of these are metastatic, or advanced, at diagnosis.[2]

EGFR is a protein that helps cells grow and divide. When the EGFR gene is mutated it can cause the protein to be overactive resulting in cancer cells to form. EGFR mutations may occur in 10 to 35 percent of NSCLC tumors globally, and the most common activating mutations are deletions in exon 19 and exon 21 L858R substitution, which together account for more than 80 percent of known activating EGFR mutations. The disease is associated with low survival rates and disease progression remains a challenge.[3,4]

About Pfizer in Lung Cancer

Pfizer Oncology is committed to addressing the unmet needs of patients with lung cancer, the leading cause of cancer-related deaths worldwide and a particularly difficult-to-treat disease. Pfizer strives to address the diverse and evolving needs of patients with non-small cell lung cancer (NSCLC) by developing efficacious and tolerable therapies, including biomarker-driven therapies and immuno-oncology (IO) agents and combinations. By combining leading scientific insights with a patient-centric approach, Pfizer is continually advancing its work to match the right patient with the right medicine at the right time. Through our growing research pipeline and collaboration efforts, we are committed to delivering renewed hope to patients living with NSCLC.

About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference on the lives of patients. Today, Pfizer Oncology has an industry-leading portfolio of 18 approved innovative cancer medicines and biosimilars across more than 20 indications, including breast, prostate, kidney, lung and hematology. Pfizer Oncology is striving to change the trajectory of cancer.

Pfizer Inc: Working together for a healthier world®

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. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. 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 150 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 April 3, 2019. 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 VIZIMPRO (dacomitinib), a kinase inhibitor, and an approval by the European Commission, including their potential benefits, that involve 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; 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 applications for VIZIMPRO may be filed in other jurisdictions; whether and when any such other applications for VIZIMPRO that may be pending or filed may be approved by regulatory authorities, which will depend on 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 VIZIMPRO 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 VIZIMPRO; 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, 2018 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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[1] VIZIMPRO® (dacomitinib). Summary of Product Characteristics.]

[2] Pfizer. Data on File.

[3] Lovly CM, Horn L. Molecular profiling of lung cancer. My Cancer Genome; 2016. https://www.mycancergenome.org/content/disease/lung-cancer/. Accessed January 2019.

[4] Pao W, Miller VA. Epidermal growth factor receptor mutations, small-molecule kinase inhibitors, and non-small-cell lung cancer: current knowledge and future directions. J Clin Oncol. 2005;23:2556-2568.

Pfizer Media Contacts: Jessica Smith (U.S.) (212) 733-6213 Jessica.M.Smith@pfizer.com Lisa O'Neill (EU) (44) 7929 339 560 Lisa.O'Neill@pfizer.com Pfizer Investor Contact: Ryan Crowe (212) 733-8160 Ryan.Crowe@pfizer.com