# Pfizer Receives Positive CHMP Opinion For IBRANCE® (palbociclib) In Combination With Endocrine Therapy For The Treatment Of HR+/HER2- Metastatic Breast Cancer In Europe

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**"We look forward to working with the EC as they conduct their review, with the goal of bringing this first-in-class medicine to appropriate patients across the EU."**

Pfizer Inc. (NYSE:PFE) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending that IBRANCE® (palbociclib) be granted marketing authorization in the European Union (EU) for the treatment of women with hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+/HER2-) locally advanced or metastatic breast cancer. The CHMP's positive opinion is for IBRANCE to be used in combination with an aromatase inhibitor, as well as in combination with fulvestrant in women who have received prior endocrine therapy. The CHMP's opinion will now be reviewed by the European Commission (EC).

If approved, IBRANCE would be the first medicine in a new class of anti-cancer treatments, cyclin-dependent kinase 4/6 (CDK 4/6) inhibitors, to be approved by the EC.

"Today's opinion by the CHMP to recommend marketing authorization of IBRANCE in the EU is an important step toward expanding treatment options for women in Europe with HR+/HER2- metastatic breast cancer, and a step toward a potential new standard of care for this cancer," said Mace Rothenberg, M.D., chief development officer, Pfizer Oncology.

“The opinion is supported by robust data with consistent results observed across three separate randomized trials in which the addition of IBRANCE to standard endocrine therapy resulted in significant prolongation of progression-free survival compared to endocrine therapy alone.”

“There have been only modest improvements in the prognosis of patients with metastatic breast cancer in Europe over the past three decades, underscoring the need for new treatment advances,” said Andreas Penk, M.D., regional president, International Developed Markets, Pfizer Oncology. “We look forward to working with the EC as they conduct their review, with the goal of bringing this first-in-class medicine to appropriate patients across the EU.”

Breast cancer is the most common invasive cancer among women in Europe, with more than 464,200 new cases and 131,260 deaths per year.1 Up to 30 percent of women diagnosed with and treated for early breast cancer will go on to develop metastatic breast cancer,2,3 which occurs when the cancer spreads beyond the breast to other parts of the body.4 There is no cure for metastatic breast cancer,5 and patients are in need of new treatment options that help keep their cancer from worsening, manage symptoms and help them maintain quality of life for as long as possible.2,4

Pfizer announced last year that the EMA validated for review the Marketing Authorization Application (MAA) for IBRANCE, which was submitted based on final results from the Phase 2 PALOMA-1 and Phase 3 PALOMA-3 trials. These studies demonstrated that IBRANCE in combination with an endocrine therapy improved progression-free survival (PFS) compared to the endocrine therapy alone or with placebo in certain patients with HR+/HER2- metastatic breast cancer. Results from a separate Phase 3 trial, PALOMA-2, conducted in the same patient population as the Phase 2 PALOMA-1 trial, also demonstrated an improvement in PFS and were added during the MAA review.

About IBRANCE® (palbociclib)

IBRANCE is an oral inhibitor of cyclin dependent kinases (CDKs) 4 and 6,6 which are key regulators of the cell cycle that trigger cellular progression.7,8

In the European Union, IBRANCE is an investigational agent and has not been approved.

IBRANCE is approved by the U.S. Food and Drug Administration (FDA) for the treatment of HR+/HER2- advanced or metastatic breast cancer in combination with letrozole as initial endocrine based therapy in postmenopausal women, or fulvestrant in women with disease progression following endocrine therapy.6 The indication in combination with

letrozole is approved in the U.S. under accelerated approval based on progression-free survival (PFS). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.6 Outside of the U.S., IBRANCE has received regulatory approval in 19 countries to date.

IMPORTANT IBRANCE (palbociclib) SAFETY INFORMATION FROM THE U.S. PRESCRIBING INFORMATION

Neutropenia was the most frequently reported adverse reaction in Study 1 (PALOMA-1) (75%) and Study 2 (PALOMA-3) (83%). In Study 1, Grade 3 (57%) or 4 (5%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. In Study 2, Grade 3 (56%) or Grade 4 (11%) decreased neutrophil counts were reported in patients receiving IBRANCE plus fulvestrant. Febrile neutropenia has been reported in about 1% of patients exposed to IBRANCE. One death due to neutropenic sepsis was observed in Study 2. Inform patients to promptly report any fever.

Monitor complete blood count prior to starting IBRANCE, at the beginning of each cycle, on Day 14 of first 2 cycles, and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Pulmonary embolism (PE) has been reported at a higher rate in patients treated with IBRANCE plus letrozole in Study 1 (5%) and in patients treated with IBRANCE plus fulvestrant in Study 2 (1%) compared with no cases in patients treated either with letrozole alone or fulvestrant plus placebo. Monitor for signs and symptoms of PE and treat as medically appropriate.

Based on the mechanism of action, IBRANCE can cause fetal harm. Advise females of reproductive potential to use effective contraception during IBRANCE treatment and for at least 3 weeks after the last dose. IBRANCE may impair fertility in males and has the potential to cause genotoxicity. Advise male patients with female partners of reproductive potential to use effective contraception during IBRANCE treatment and for 3 months after the last dose. Advise females to inform their healthcare provider of a known or suspected pregnancy. Advise women not to breastfeed during IBRANCE treatment and for 3 weeks after the last dose because of the potential for serious adverse reactions in nursing infants.

The most common adverse reactions (≥10%) of any grade reported in Study 1 of IBRANCE plus letrozole vs letrozole alone included neutropenia (75% vs 5%), leukopenia (43% vs 3%), fatigue (41% vs 23%), anemia (35% vs 7%), upper respiratory infection

(31% vs 18%), nausea (25% vs 13%), stomatitis (25% vs 7%), alopecia (22% vs 3%), diarrhea (21% vs 10%), thrombocytopenia (17% vs 1%), decreased appetite (16% vs 7%), vomiting (15% vs 4%), asthenia (13% vs 4%), peripheral neuropathy (13% vs 5%), and epistaxis (11% vs 1%).

Grade 3/4 adverse reactions (≥10%) in Study 1 reported at a higher incidence in the IBRANCE plus letrozole group vs the letrozole alone group included neutropenia (54% vs 1%) and leukopenia (19% vs 0%). The most frequently reported serious adverse events in patients receiving IBRANCE plus letrozole were pulmonary embolism (4%) and diarrhea (2%).

Lab abnormalities occurring in Study 1 (all grades, IBRANCE plus letrozole vs letrozole alone) were decreased WBC (95% vs 26%), decreased neutrophils (94% vs 17%), decreased lymphocytes (81% vs 35%), decreased hemoglobin (83% vs 40%), and decreased platelets (61% vs 16%).

The most common adverse reactions (≥10%) of any grade reported in Study 2 of IBRANCE plus fulvestrant vs fulvestrant plus placebo included neutropenia (83% vs 4%), leukopenia (53% vs 5%), infections (47% vs 31%), fatigue (41% vs 29%), nausea (34% vs 28%), anemia (30% vs 13%), stomatitis (28% vs 13%), headache (26% vs 20%), diarrhea (24% vs 19%), thrombocytopenia (23% vs 0%), constipation (20% vs 16%), vomiting (19% vs 15%), alopecia (18% vs 6%), rash (17% vs 6%), decreased appetite (16% vs 8%), and pyrexia (13% vs 5%).

Grade 3/4 adverse reactions (≥10%) in Study 2 reported at a higher incidence in the IBRANCE plus fulvestrant group vs the fulvestrant plus placebo group included neutropenia (66% vs 1%) and leukopenia (31% vs 2%). The most frequently reported serious adverse reactions in patients receiving IBRANCE plus fulvestrant were infections (3%), pyrexia (1%), neutropenia (1%), and pulmonary embolism (1%).

Lab abnormalities occurring in Study 2 (all grades, IBRANCE plus fulvestrant vs fulvestrant plus placebo) were decreased WBC (99% vs 26%), decreased neutrophils (96% vs 14%), anemia (78% vs 40%), and decreased platelets (62% vs 10%).

Avoid concurrent use of strong CYP3A inhibitors. If patients must be administered a strong CYP3A inhibitor, reduce the IBRANCE dose to 75 mg/day. If the strong inhibitor is discontinued, increase the IBRANCE dose (after 3-5 half-lives of the inhibitor) to the dose used prior to the initiation of the strong CYP3A inhibitor. Grapefruit or grapefruit juice may increase plasma concentrations of IBRANCE and should be avoided. Avoid concomitant use of strong CYP3A inducers. The dose of sensitive CYP3A substrates with a

narrow therapeutic index may need to be reduced as IBRANCE may increase their exposure.

IBRANCE has not been studied in patients with moderate to severe hepatic impairment or in patients with severe renal impairment (CrCl <30 mL/min).

About Pfizer Oncology

Pfizer Oncology is committed to pursuing innovative treatments that have a meaningful impact on those living with cancer. As a leader in oncology speeding cures and accessible breakthrough medicines to patients, Pfizer Oncology is helping to redefine life with cancer. Our strong pipeline of biologics, small molecules and immunotherapies, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments and licensing partners, Pfizer Oncology strives to cure or control cancer with its breakthrough medicines. Because Pfizer Oncology knows that success in oncology is not measured solely by the medicines you manufacture, but rather by the meaningful partnerships you make to have a more positive impact on people’s lives.

Pfizer Inc.: Working together for a healthier worldTM

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 healthcare products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer healthcare 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, Pfizer has worked to make a difference for all who rely on us. For more information, please visit us at www.pfizer.com. In addition, to learn more, 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 September 16, 2016. 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 IBRANCE (palbociclib) and the MAA in Europe for a potential indication for the treatment of HR+/HER2- locally advanced or metastatic breast cancer, 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 IBRANCE; the uncertainties inherent in research and development, including further investigation of the clinical benefit of IBRANCE, the ability to meet anticipated clinical trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when the accelerated approval for IBRANCE will be converted to regular approval in the U.S.; whether and when drug applications may be filed in any additional jurisdictions for IBRANCE for potential HR+/HER2- metastatic breast cancer indications or in any jurisdictions for any other potential indications for IBRANCE; whether and when the MAA filed by Pfizer with the EMA for IBRANCE may be approved and whether and when any such other applications may be approved by regulatory authorities, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of IBRANCE; 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, 2015 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 (link is external) and www.pfizer.com.

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