

# Pfizer Announces FDA Acceptance of IBRANCE® (palbociclib) Supplemental New Drug Application with Priority Review in HR+, HER2- Metastatic Breast Cancer

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sNDA seeks new indication to expand approved use of IBRANCE based on data from Phase 3 PALOMA-3 trial

Pfizer Inc. (NYSE:PFE) today announced that the U.S. Food and Drug Administration (FDA) has accepted for filing and granted Priority Review for a supplemental New Drug Application (sNDA) for Pfizer's breast cancer medication, IBRANCE® (palbociclib). If approved, the sNDA would expand the approved use of IBRANCE to reflect findings from the Phase 3 PALOMA-3 trial, which evaluated IBRANCE in combination with fulvestrant versus fulvestrant plus placebo in women with hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+, HER2-) metastatic breast cancer, regardless of menopausal status, whose disease progressed after endocrine therapy, including those with and without prior treatment for their metastatic disease. The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA is April 2016.

"We look forward to continuing to work with the FDA to add the robust Phase 3 data set from the PALOMA-3 trial to the available data in the IBRANCE label," said Liz Barrett, global president and general manager, Pfizer Oncology. "Since FDA approval in February, more than 18,000 women have been treated with IBRANCE by approximately 5,000 prescribers in the U.S. With approval of this indication, we hope to expand the role of IBRANCE in combination with endocrine therapy for the treatment of HR+, HER2- metastatic breast cancer and to serve even more patients with this first-in-class medicine."

If Pfizer's sNDA is approved, the updated IBRANCE label would comprise results from two metastatic breast cancer trials in which IBRANCE in combination with an endocrine therapy improved progression-free survival (PFS) compared to endocrine therapy alone, PALOMA-1 and PALOMA-3.

Based on the results of the PALOMA-1 trial, IBRANCE was approved by the FDA in February 2015 for use in combination with letrozole as a treatment for postmenopausal women with estrogen receptor-positive (ER+), HER2- advanced breast cancer as initial endocrine-based therapy for their metastatic disease.<sup>1</sup> This indication is approved under accelerated approval based on PFS. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the ongoing confirmatory trial, PALOMA-2. The most frequently reported adverse event for IBRANCE plus letrozole in PALOMA-1 was neutropenia. For more information on the serious and most common side effects of IBRANCE plus letrozole, please see Important IBRANCE Safety Information at the end of this release.

The sNDA seeks to expand approved use of IBRANCE based on the PALOMA-3 trial results. PALOMA-3 enrolled 521 patients, 350 of whom received the combination of IBRANCE plus fulvestrant. Pfizer announced in April 2015 that the trial was stopped early due to efficacy based on an assessment by an independent Data

Monitoring Committee (DMC). The results were presented as a late-breaker at the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO) and were published in *The New England Journal of Medicine* in June 2015. The adverse events observed with IBRANCE in combination with fulvestrant in PALOMA-3 were generally consistent with their respective known adverse event profiles.

In November 2015, the combination of IBRANCE plus fulvestrant was added to the National Comprehensive Cancer Network Guidelines as a Category 1 recommendation for the treatment of women with HR+, HER2-metastatic breast cancer who have progressed on endocrine therapy or premenopausal women receiving ovarian suppression with a luteinizing hormone-releasing hormone (LHRH) agonist.

### **About IBRANCE® (palbociclib)**

IBRANCE is an oral, first-in-class inhibitor of cyclin-dependent kinases (CDKs) 4 and 6. CDKs 4 and 6 are key regulators of the cell cycle that trigger cellular progression.<sup>1,2</sup>

IBRANCE is approved by the FDA for use in combination with letrozole as a treatment for postmenopausal women with ER+, HER2- advanced breast cancer as initial endocrine-based therapy for their metastatic disease. <sup>1</sup> The effectiveness of IBRANCE in these patients is based on a study that measured PFS.<sup>1</sup> Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. The confirmatory Phase 3 trial, PALOMA-2, is fully enrolled. IBRANCE has also received regulatory approval in Albania, Chile and Macau. In the European Union, the Marketing Authorization Application for IBRANCE, which is based on results from the PALOMA-1 and PALOMA-3 trials, is currently under review with the European Marketing Agency.

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

**Neutropenia:** Neutropenia is frequently reported with IBRANCE therapy. In the randomized phase II study, Grade 3 (57%) or 4 (5%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. Febrile neutropenia can occur.

Monitor complete blood count prior to starting IBRANCE and at the beginning of each cycle, as well as Day 14 of the first two cycles, and as clinically indicated. For patients who experience Grade 3 neutropenia, consider repeating the complete blood count monitoring 1 week later. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

**Infections:** Infections have been reported at a higher rate in patients treated with IBRANCE plus letrozole (55%) compared with letrozole alone (34%). Grade 3 or 4 infections occurred in 5% of patients treated with IBRANCE plus letrozole vs no patients treated with letrozole alone. Monitor patients for signs and symptoms of infection and treat as medically appropriate.

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

**Pregnancy and lactation:** Based on the mechanism of action, IBRANCE can cause fetal harm. Advise females with reproductive potential to use effective contraception during therapy with IBRANCE and for at least 2 weeks after the last dose. Advise females to contact their healthcare provider if they become pregnant or if pregnancy is suspected during treatment with IBRANCE. Advise women not to breastfeed while on IBRANCE therapy because of the potential for serious adverse reactions in nursing infants from IBRANCE.

**Additional hematologic abnormalities:** Decreases in hemoglobin (83% vs 40%), leukocytes (95% vs 26%), lymphocytes (81% vs 35%), and platelets (61% vs 16%) occurred at a higher rate in patients treated with IBRANCE plus letrozole vs letrozole alone.

**Adverse reactions:** The most common all causality adverse reactions (≥10%) of any grade reported in patients treated with IBRANCE plus letrozole vs letrozole alone in the phase II study 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 reported (≥10%) occurring at a higher incidence in the IBRANCE plus letrozole vs letrozole alone group include neutropenia (54% vs 1%) and leukopenia (19% vs 0%). The most frequently reported serious adverse events in patients receiving IBRANCE were pulmonary embolism (4%) and diarrhea (2%).

**General dosing information:** The recommended dose of IBRANCE is 125 mg taken orally once daily for 21 days followed by 7 days off treatment in 28-day cycles. IBRANCE should be taken with food and in combination with letrozole 2.5 mg once daily continuously.

Patients should be encouraged to take their dose at approximately the same time each day.

Capsules should be swallowed whole. No capsule should be ingested if it is broken, cracked, or otherwise not intact. If a patient vomits or misses a dose, an additional dose should not be taken that day. The next prescribed dose should be taken at the usual time.

Management of some adverse reactions may require temporary dose interruption/delay and/or dose reduction, or permanent discontinuation. Dose modification of IBRANCE is recommended based on individual safety and tolerability.

**Drug interactions:** 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 and moderate CYP3A inducers. The dose of the sensitive CYP3A substrates with a narrow therapeutic index may need to be reduced as IBRANCE may increase their exposure.

**Hepatic and renal impairment:** 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 the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide. Our strong pipeline of biologics and small molecules, 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 breakthrough medicines, to deliver the right drug

for each patient at the right time. For more information, please visit [www.Pfizer.com](http://www.Pfizer.com).

**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, Pfizer has worked to make a difference for all who rely on us. To learn more, please visit us at [www.pfizer.com](http://www.pfizer.com).

*DISCLOSURE NOTICE: The information contained in this release is as of December 10, 2015. 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) that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Forward-looking statements include those about IBRANCE's potential benefits and about the sNDA for IBRANCE accepted for filing [and granted Priority Review] by the FDA for a potential indication for the treatment of women with HR+/HER2- advanced or metastatic breast cancer in combination with endocrine therapy. 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 the PALOMA-2 Phase 3 trial of IBRANCE will demonstrate a statistically significant improvement in progression-free survival and whether the other trials of IBRANCE will meet their primary endpoints; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications or supplemental drug applications may be filed with other jurisdictions for potential HR+/HER2- metastatic breast cancer indications for IBRANCE; whether and when the FDA may approve the sNDA and whether and when any other applications may be approved by other 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, 2014 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 SEC and available at [www.sec.gov](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).*

1 Weinberg RA. pRb and Control of the Cell Cycle Clock. In: Weinberg RA, ed. The Biology of Cancer. 2nd ed. New York, NY: Garland Science; 2014:275-329.

2 Sotillo E, Grana X. Escape from Cellular Quiescence. In: Enders GH, ed. Cell Cycle Deregulation in Cancer. New York, NY: Humana Press; 2010:3-22.

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