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Pfizer Receives Expanded FDA Approval For IBRANCE (palbociclib) In HR+, HER2- Metastatic Breast Cancer

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First-in-class Therapy Now Approved for Use in a Broader Range of Women New Indication Supported by Results of Phase 3 PALOMA-3 Trial of IBRANCE in Combination with Fulvestrant

“Today's news gives more women with metastatic breast cancer the opportunity to benefit from this first-in-class medicine”

Pfizer Inc. (NYSE:PFE) today announced that the U.S. Food and Drug Administration (FDA) has approved a new indication expanding the use of IBRANCE® (palbociclib) 125mg capsules, Pfizer’s metastatic breast cancer therapy. Now IBRANCE also is approved for the treatment of hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer in combination with fulvestrant in women with disease progression following endocrine therapy.1 Pfizer’s supplemental New Drug Application (sNDA) for IBRANCE was reviewed and approved under the FDA’s Breakthrough Therapy designation and Priority Review programs based on results from the Phase 3 PALOMA-3 trial in pre-, peri- and post-menopausal women with HR+, HER2- metastatic breast cancer whose disease progressed on or after prior endocrine therapy in the adjuvant or metastatic setting.1

IBRANCE first was approved in February 2015 and also is indicated for the treatment of HR+, HER2- advanced or metastatic breast cancer in combination with letrozole as initial endocrine-based therapy in postmenopausal women.1 The indication in combination with letrozole is approved 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.1 The confirmatory Phase 3 trial, PALOMA-2, is fully enrolled.

IBRANCE is the first and only cyclin-dependent kinase 4/6 (CDK 4/6) inhibitor approved by the FDA.

“Today's news gives more women with metastatic breast cancer the opportunity to benefit from this first-in-class medicine," said Liz Barrett, global president and general manager, Pfizer Oncology. “Since IBRANCE was approved just over one year ago, physicians across the U.S. have embraced it as a standard of care in the first-line setting. The expanded approval of IBRANCE is supported by a robust body of evidence and underscores Pfizer's continued commitment to addressing the needs of the metastatic breast cancer community. Pfizer is proud to bring forward innovative therapies like IBRANCE that make a meaningful difference in patients' lives.”

The Phase 3 PALOMA-3 trial enrolled 521 women, regardless of menopausal status, randomized 2:1 to receive IBRANCE plus fulvestrant or placebo plus fulvestrant. This trial demonstrated that IBRANCE in combination with fulvestrant, a standard of care hormonal therapy, prolonged PFS compared with placebo plus fulvestrant in women with HR+, HER2- metastatic breast cancer whose disease progressed on or after prior endocrine therapy.

1 Women in the IBRANCE plus fulvestrant arm had a median PFS of 9.5 months (95% CI: 9.2, 11.0), a substantial improvement compared with 4.6 months (95% CI: 3.5, 5.6) in the group treated with placebo plus fulvestrant [HR 0.461 (95% CI: 0.360, 0.591), p <0.0001].1 Confirmed overall response rate in patients with measurable disease as assessed by the investigator was 24.6% for the IBRANCE plus fulvestrant arm compared to 10.9% for the placebo plus fulvestrant arm.1 Duration of response was 9.3 months in the IBRANCE plus fulvestrant arm compared with 7.6 months in the placebo plus fulvestrant arm.1

The warnings and precautions of IBRANCE include neutropenia, pulmonary embolism and embryo-fetal toxicity.1 Themost common adverse reactions (?10%) of any grade reported in PALOMA-3 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%). For more information, please see Important Safety Information for IBRANCE below.1

“There currently is no cure for metastatic breast cancer, so ongoing treatment is usually needed to control the spread of the disease,” said Marisa Weiss, M.D., chief medical officer and founder, Breastcancer.org. “That's why the availability of a first-of-its-kind treatment option like IBRANCE for women dealing with HR+, HER2- metastatic disease represents a very important advance.”

Both palbociclib (IBRANCE) combination options are recommended by the National Comprehensive Cancer Network.2 Palbociclib plus letrozole is recommended (category 2A) as a first-line treatment for postmenopausal women with HR+, HER2- metastatic breast cancer.2 Palbociclib plus fulvestrant is recommended (category 1) for postmenopausal women with HR+, HER2- metastatic breast cancer who have progressed on endocrine therapy or premenopausal women receiving a luteinizing hormone-releasing hormone (LHRH) agonist.2

Pfizer believes patients should have access to the medications they need, and is committed to ensuring that patients who are prescribed IBRANCE have access to the company’s patient assistance programs. Patients in the U.S. can visit www.PfizerRxPathways.com and www.pfizercopayone.com to learn more.

The full prescribing information for IBRANCE can be found at www.pfizer.com.

Important Safety Information

Neutropenia was the most frequently reported adverse reaction in Study 1 (75%) and Study 2 (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 IBRANCE® (palbociclib) 125mg capsules

IBRANCE is an oral inhibitor of CDKs 4 and 6,1 which are key regulators of the cell cycle that trigger cellular progression.3,4 IBRANCE is indicated 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.1 The indication in combination with letrozole is approved 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.1

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.

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 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 February 19, 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), 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, 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 and when drug applications may be filed with other jurisdictions for potential HR+/HER2- metastatic breast cancer indications for IBRANCE; whether and when any other applications for IBRANCE 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 U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

1IBRANCE® (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: 2016.
2 National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Breast Cancer. Version 1.2016.
3 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.
4 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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