IBRANCE® (palbociclib) Receives Approval in European Union for the Treatment of Women with HR+/HER2- Metastatic Breast Cancer

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IBRANCE is the first and only CDK 4/6 inhibitor, a new class of anti-cancer treatments, to be approved in Europe

Pfizer Inc. (NYSE:PFE) today announced that the European Commission (EC) has approved IBRANCE® (palbociclib) 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 approval is for IBRANCE to be used in combination with an aromatase inhibitor. The approval also covers the use of IBRANCE in combination with fulvestrant in women who have received prior endocrine therapy.

IBRANCE is the first medicine to be approved in Europe that works by inhibiting cyclin-dependent kinases 4 and 6 (CDK 4/6). It also is the first new medicine approved for the treatment of women with this type of metastatic breast cancer in the first-line setting in nearly 10 years. Women with HR+/HER2- metastatic breast cancer represent about 60 percent of all metastatic breast cancer cases.1

“Today’s approval of IBRANCE in the European Union (EU) brings an innovative and much-needed new treatment option to tens of thousands of women with HR+/HER2- metastatic breast cancer,” said Andreas Penk, M.D., regional president, International Developed Markets, Pfizer Oncology. “With strong and consistent data in three pivotal clinical studies and rapid adoption as a standard of care in the U.S., IBRANCE represents a potential new benchmark for the treatment of HR+/HER2- metastatic breast cancer in Europe.”

The EC approval is based on a robust submission package including results from the Phase 2 PALOMA-1 trial in postmenopausal women with estrogen receptor-positive (ER+)/HER2- metastatic breast cancer who had not received prior systemic therapy for their advanced disease, the Phase 3 PALOMA-2 trial in the same population and the Phase 3 PALOMA-3 trial in women with HR+/HER2- metastatic breast cancer who had progressed on prior endocrine therapy. All three randomized trials demonstrated that IBRANCE in combination with an endocrine therapy significantly prolonged progression-free survival (PFS) compared to endocrine therapy alone or endocrine therapy with placebo.

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.2 Up to 30 percent of women diagnosed with and treated for early breast cancer will go on to develop metastatic breast cancer,3,4 which occurs when the cancer spreads beyond the breast to other parts of the body.5 There is no cure for metastatic breast cancer,6 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.3,5

“Palbociclib is an exciting advance in the management of women with hormone receptor-positive breast cancer. Patients with this type of breast cancer are usually treated with hormone therapy but many will progress or relapse – and as a result require chemotherapy, which often comes with life-limiting side-effects,” said Nicholas Turner, M.D., Ph.D., team leader at The Institute of Cancer Research, London, and consultant medical oncologist at The Royal Marsden NHS Foundation Trust, as well as principal investigator of the PALOMA-3 trial. “Palbociclib, when used in combination with standard hormone therapy, increases the duration of tumor control and is well tolerated by most women – and could delay the need for women with this type of advanced breast cancer to start chemotherapy.”

“Metastatic breast cancer patients in Europe need new treatment options available to them,” said Kathi Apostolidis, two-time breast cancer survivor and vice president of the European Cancer Patient Coalition. “Metastatic breast cancer places a heavy burden on cancer patients and their families, but patients hope that novel treatments may have the potential to provide better quality of life and outcomes.”

About the IBRANCE Pivotal Trials

PALOMA-1

The Phase 2 PALOMA-1 trial evaluated IBRANCE in combination with letrozole compared with letrozole alone as a first-line, or initial, therapy in 165 postmenopausal women with ER+/HER2- advanced breast cancer who had not received previous systemic treatment for their advanced disease. The combination of IBRANCE plus letrozole significantly prolonged PFS compared to letrozole alone (HR=0.488 [95% CI: 0.319–0.748]), with the median PFS of 20.2 months (95% CI: 13.8–27.5) in the IBRANCE arm compared to 10.2 months (95% CI: 5.7–12.6) in women who received letrozole alone. The most common adverse events (≥20%) of any grade reported in patients treated with IBRANCE plus letrozole versus 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%) and diarrhea (21% vs 10%).7

PALOMA-2

The Phase 3 PALOMA-2 trial evaluated IBRANCE in combination with letrozole compared with letrozole plus placebo as a first-line treatment in 666 postmenopausal women with ER+/HER2- metastatic breast cancer, the same patient population as PALOMA-1. The combination of IBRANCE plus letrozole resulted in a statistically significant improvement in PFS (HR=0.58 [95% CI: 0.46–0.72], P<0.000001), with a median PFS of 24.8 months compared to 14.5 months for those who were treated with letrozole plus placebo. The most common adverse events (≥20%) of any grade reported in patients treated with IBRANCE plus letrozole versus letrozole plus placebo included neutropenia (79.5% vs 6.3%), fatigue (37.4% vs 27.5%), nausea (35.1% vs 26.1%), arthralgia (33.3% vs 33.8%) and alopecia (32.9% vs 15.8%).8

PALOMA-3

The Phase 3 PALOMA-3 trial evaluated IBRANCE in combination with fulvestrant compared with placebo plus fulvestrant in 521 women with HR+/HER2- metastatic breast cancer, regardless of menopausal status, whose disease progressed on or after prior endocrine therapy. The combination of IBRANCE plus fulvestrant substantially improved PFS compared to fulvestrant plus placebo (HR=0.461 [95% CI: 0.360–0.591), P<0.0001), with a median PFS of 9.5 months (95% CI: 9.2–11.0) in the IBRANCE arm compared to 4.6 months (95% CI: 3.5–5.6) in women who received placebo plus fulvestrant. The most common adverse events (≥20%) of any grade reported in PALOMA-3 of IBRANCE plus fulvestrant versus placebo plus fulvestrant 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%) and constipation (20% vs 16%).7

About IBRANCE® (palbociclib)

IBRANCE is an oral inhibitor of cyclin-dependent kinases 4 and 6,7 which are key regulators of the cell cycle that trigger cellular progression.9,10 With this latest regulatory milestone, IBRANCE now is approved in more than 50 countries.

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

IBRANCE is indicated in the U.S. 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. The indication in combination with letrozole is approved under accelerated approval based on PFS. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Neutropenia was the most frequently reported adverse reaction in PALOMA-1 (75%) and PALOMA-3 (83%). In PALOMA-1, Grade 3 (57%) or 4 (5%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. In PALOMA-3, 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 PALOMA-3. 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 PALOMA-1 (5%) and in patients treated with IBRANCE plus fulvestrant in PALOMA-3 (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 PALOMA-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 PALOMA-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 PALOMA-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 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%).

Grade 3/4 adverse reactions (≥10%) in PALOMA-3 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 PALOMA-3 (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.

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 @Pfizerand @PfizerNews, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of November 10, 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 an approval in the EU for the treatment of women with 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 any such 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 and www.pfizer.com.

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