# PALOMA-2 Phase 3 Study Published In The New England Journal Of Medicine Demonstrates Clinical Benefit Of Pfizer's IBRANCE® (palbociclib) In First-Line ER+, HER2- Metastatic Breast Cancer

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First-in-class IBRANCE in Combination with Letrozole Exceeded 2 Years in Median PFS

Pfizer Inc. (NYSE:PFE) today announced that detailed results from the Phase 3 PALOMA-2 trial were published in The New England Journal of Medicine. These data, presented at the 52nd American Society of Clinical Oncology (ASCO) Annual Meeting in June, further demonstrate the clinical benefit of IBRANCE® (palbociclib) as initial therapy for postmenopausal women with estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+, HER2-) metastatic breast cancer. The PALOMA-2 study showed the combination of IBRANCE and letrozole extended progression-free survival (PFS), or the amount of time before tumor growth, by more than 10 months compared with letrozole plus placebo. Further, the study demonstrated that the median PFS of the IBRANCE and letrozole combination exceeded two years – making it the first and only treatment for this population of women to do so in a randomized Phase 3 study.1

"The median PFS of more than two years observed in this study is unprecedented for this patient population," said Veronique Dieras, M.D., medical oncologist and head of clinical

research, Clinical Investigational Unit Chef de Service Recherche Clinique, Unité d'Investigation Clinique Department of Medical Oncology, Institut Curie, Paris, France. “Building on the Phase 2 PALOMA-1 data, the results of PALOMA-2 provide additional evidence that the combination of IBRANCE and letrozole is a meaningful advancement for these women.”

“Since its accelerated approval in 2015, IBRANCE in combination with letrozole has become a standard of care for the treatment of post-menopausal women with ER+, HER2- advanced or metastatic breast cancer,” said Hope Rugo, M.D., professor of medicine and director of breast oncology and clinical trials education at the University of California San Francisco Helen Diller Family Comprehensive Cancer Center. “We now have seen consistent results across three randomized trials in which the addition of IBRANCE to an endocrine therapy significantly prolonged PFS compared to the endocrine therapy alone.”

In the trial, median PFS for women treated with IBRANCE plus letrozole was 24.8 months (95% CI, 22.1-not estimable) compared with 14.5 months (95% CI, 12.9-17.1) for women treated with letrozole plus placebo (HR=0.58 [95% CI, 0.46-0.72], p<0.001), a 42% reduction in the risk of disease progression.

“IBRANCE has raised the bar for new treatments in hormone-receptor positive advanced breast cancer. The results of this Phase 3 trial add to the growing body of clinical data in support of IBRANCE and translates into hope for patients,” said Mace Rothenberg, M.D., chief development officer, Oncology, Pfizer Global Product Development. “We look forward to sharing the full PALOMA-2 data with global regulatory authorities with the goal of making IBRANCE available to more women around the world. Pfizer is proud of being a leader in the development of innovative therapies like IBRANCE that make a meaningful difference in patients' lives.”

Safety results were consistent with PALOMA-1 and no major unexpected safety findings were observed. The most common grade 3/4 adverse events with IBRANCE plus letrozole versus placebo plus letrozole were neutropenia (66.4% vs 1.4%), leukopenia (24.8% vs 0%), infections (6.5% vs 3.2%) and anemia (5.4% vs 1.8%). Febrile neutropenia was reported in 1.8% of patients in the IBRANCE plus letrozole group and none of the patients in the placebo plus letrozole group. For more information, please see Important Safety Information for IBRANCE below.2

IBRANCE first was approved by the U.S. Food and Drug Administration (FDA) in February 2015 and is indicated for the treatment of hormone receptor positive (HR+), HER2-

advanced or metastatic breast cancer in combination with letrozole as initial endocrine-based therapy in postmenopausal women.2 The indication in combination with letrozole was approved under accelerated approval based on PFS results from the Phase 2 PALOMA-1 study. As stated at the time of the approval, continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial, the double-blind, Phase 3 PALOMA-2 study.2 A supplemental New Drug Application to support the conversion of the accelerated approval to regular approval based on the results of PALOMA-2 has been submitted to the FDA.

IBRANCE also is approved in the U.S. for the treatment of HR+, HER2-advanced or metastatic breast cancer in combination with fulvestrant in women with disease progression following endocrine therapy based on results from the Phase 3 PALOMA-3 study.2

Since the initial approval in February 2015, more than 40,000 women have been prescribed IBRANCE by more than 8,500 prescribers in the U.S.

As previously disclosed, the European Commission has approved IBRANCE for the treatment of women with 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. In total, IBRANCE is approved in more than 50 countries.

About PALOMA-2

PALOMA-2 is a randomized (2:1), multicenter, multinational, double-blind Phase 3 study designed to assess the PFS of IBRANCE (125 mg orally once daily for three out of four weeks in repeated cycles) in combination with letrozole (2.5 mg once daily continuously) versus letrozole plus placebo as a first-line treatment for postmenopausal women with ER+, HER2- metastatic breast cancer. PALOMA-2 evaluated a total of 666 women from 186 global sites in 17 countries.

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

About IBRANCE® (palbociclib) 125 mg capsules

IBRANCE is the first and only FDA approved oral inhibitor of CDKs 4 and 6,2 which are key regulators of the cell cycle that trigger cellular progression.3,4 In the U.S., 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.2 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, PALOMA-2.2

Important IBRANCE (palbociclib) Safety Information from the U.S. Prescribing Information

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.

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 November 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), 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 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 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 and www.pfizer.com.

1 Based on a MEDLINE® literature review for Phase 3 trials in HR+/HER2- MBC treatment as of August 2016. 2 IBRANCE® (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: 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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