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Pfizer Announces Positive Top-Line Results for Phase 3 PALOMA-2 Clinical Trial of IBRANCE® (palbociclib)

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Phase 3 Trial Provides Confirmatory Evidence for IBRANCE in the First-Line Setting and Will Support Global Regulatory Submissions

“PALOMA-2 represents the third randomized study to demonstrate the benefit of IBRANCE when added to hormonal therapy in the management of women with ER+, HER2- advanced breast cancer. IBRANCE remains the only CDK 4/6 inhibitor with Phase 3 data in this disease”

Pfizer Inc. (NYSE:PFE) today announced positive top-line results from the Phase 3 PALOMA-2 trial for IBRANCE® (palbociclib), an oral, first-in-class inhibitor of cyclin-dependent kinases (CDKs) 4 and 6.1 The study met its primary endpoint by demonstrating an improvement in progression-free survival (PFS) for the combination of IBRANCE plus letrozole compared with letrozole plus placebo in post-menopausal women with estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+, HER2-) advanced or metastatic breast cancer who had not received previous systemic treatment for their advanced disease. The PALOMA-2 trial provides confirmatory evidence for IBRANCE in combination with letrozole in the first-line setting, which was first studied in the Phase 2 PALOMA-1 trial. These data will support additional planned global regulatory submissions and a request for conversion of the accelerated approval for IBRANCE to regular approval in the U.S. Detailed efficacy and safety results from PALOMA-2 will be submitted for presentation at the American Society of Clinical Oncology (ASCO) 2016 Annual Meeting.

“PALOMA-2 represents the third randomized study to demonstrate the benefit of IBRANCE when added to hormonal therapy in the management of women with ER+, HER2- advanced breast cancer. IBRANCE remains the only CDK 4/6 inhibitor with Phase 3 data in this disease,” said Dr. Mace Rothenberg, MD, chief medical officer, Pfizer Oncology & senior vice president, Global Product Development, Oncology. “These results provide confirmatory evidence for PALOMA-1 and will be used to support regulatory submissions around the world, including a request for conversion of IBRANCE from accelerated to full approval in the United States. We look forward to sharing the detailed results of PALOMA-2 with the oncology community and advancing our discussions with regulatory authorities.”

The adverse events observed with IBRANCE in combination with letrozole in PALOMA-2 were generally consistent with the known safety profile for IBRANCE across the different patient populations and lines of therapy in the clinical development program to date. The warnings and precautions of IBRANCE include neutropenia, pulmonary embolism and embryo-fetal toxicity.1 For more information, please see Important Safety Information for IBRANCE below.1

Since its introduction in February 2015, more than 25,000 women have been prescribed IBRANCE by more than 6,000 prescribers in the U.S.

Based on the results of PALOMA-1, IBRANCE first was approved by the U.S. Food and Drug Administration (FDA) in February 2015 for the treatment of postmenopausal women with ER+, HER2- advanced breast cancer in combination with letrozole as initial endocrine-based therapy for their metastatic disease.1 The indication in combination with letrozole was approved under accelerated approval based on PFS. As stated at the time of the approval, continued approval for this indication may be contingent upon verification and description of clinical benefit in PALOMA-2, which the FDA identified as the confirmatory trial.1 Pfizer will work with the FDA to submit the results of PALOMA-2 to support conversion of the accelerated approval for IBRANCE to regular approval in the U.S.

As previously announced in February 2016, IBRANCE also is approved in the U.S. for the treatment of hormone receptor-positive (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.1

IBRANCE also is approved in eight countries outside of the U.S., and Pfizer will work with additional global regulatory authorities to review the PALOMA-2 data. As previously disclosed in August 2015, Pfizer has filed a Marketing Authorization Application (MAA) with the European Medicines Agency (EMA) for IBRANCE in combination with endocrine therapy for the treatment of HR+, HER2- advanced or metastatic breast cancer. The MAA was based on the results from the PALOMA-1 and PALOMA-3 trials. Pfizer will work with the EMA to submit the PALOMA-2 results as additional supporting data for the ongoing review of the MAA.

About the PALOMA Trials

Pfizer has worked closely with investigators and international breast cancer experts to establish a robust development program for IBRANCE in HR+, HER2- breast cancer across stages and treatment settings.

PALOMA-1

- PALOMA-1 is a randomized (1:1), multi-center, multinational, open label Phase 2 trial designed to assess PFS in postmenopausal women with ER+, HER2- advanced breast cancer receiving IBRANCE (125 mg once daily for three out of four weeks in repeated cycles) in combination with letrozole versus letrozole alone (2.5 mg once daily on a continuous regimen) as a first-line treatment. The results from PALOMA-1 were published online by *The Lancet Oncology* in December 2014.

PALOMA-2

- PALOMA-2 is a randomized (2:1), multicenter, multinational, double-blind Phase 3 study designed to assess PFS in postmenopausal women with ER+, HER2- advanced breast cancer receiving 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. PALOMA-2 has more than 200 global sites participating and 666 patients enrolled.

PALOMA-3

- PALOMA-3 is a randomized (2:1), multicenter, multinational, double-blind Phase 3 study designed to assess PFS with IBRANCE (125 mg once daily orally for three out of four weeks in each cycle) in combination with fulvestrant (500 mg intramuscularly on days 1 and 15 of cycle 1, and then on day 1 of

each subsequent 28 day cycle) versus fulvestrant plus placebo in pre/perimenopausal and postmenopausal women with HR+, HER2- metastatic breast cancer whose disease has progressed during or after endocrine therapy. Based on the PALOMA-3 results, a supplemental New Drug Application (sNDA) was reviewed and approved in February 2016 under the FDA's Breakthrough Therapy designation and Priority Review programs to expand the use of IBRANCE to include use in combination with fulvestrant in women with HR+, HER2- advanced or metastatic breast cancer with disease progression following endocrine therapy.1

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 (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 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.

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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 April 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 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 in combination with endocrine therapy for the treatment of HR+, HER2- advanced or metastatic breast cancer 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 and www.pfizer.com.

1 IBRANCE® (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: 2016.

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