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Pfizer Provides Update on Phase 3 PALLAS Trial of IBRANCE® (palbociclib) Plus Endocrine Therapy in HR+, HER2- Early Breast Cancer

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NEW YORK--(BUSINESS WIRE)-- As announced today by the Austrian Breast & Colorectal Cancer Study Group and the Alliance Foundation Trials, LLC, Pfizer Inc. (NYSE: PFE) reports that following a preplanned efficacy and futility analysis, the independent Data Monitoring Committee (DMC) of the collaborative Phase 3 early breast cancer **PAL**bociclib Co**L**laborative **A**djuvant **S**tudy (PALLAS) determined that the trial is unlikely to show a statistically significant improvement in the primary endpoint of invasive disease-free survival (iDFS). Patients currently receiving palbociclib in the study will be advised about next steps by their physicians and long-term follow up of all patients will proceed as planned. No unexpected new safety signals were observed in patients receiving palbociclib.

The PALLAS trial compares palbociclib plus standard adjuvant endocrine therapy to standard adjuvant endocrine therapy alone in women and men with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) early (stage 2 and 3) breast cancer and is an academically-led global collaboration, involving more than 400 centers in 21 countries around the globe.

“We are disappointed in this outcome. Breast cancer is a leading cause of death around the world and delaying or preventing the development of metastatic disease is a significant unmet need. PALLAS is a large study with many subgroups and we are actively collaborating to determine if there are patients who may benefit from adjuvant treatment with the palbociclib combination," said Chris Boshoff, M.D., Ph.D., Chief Development Officer, Oncology, Pfizer Global Product Development. “Since its initial approval in 2015, IBRANCE has helped change the treatment landscape for people with HR+, HER2- metastatic breast cancer. We are grateful to all patients, health care providers and our academic partners who have devoted so much to make this important study possible.”

“This result is not what we hoped for, but we are steadfast in our commitment to advancing the science and care for people living with breast cancer,” said Albert Bourla, Pfizer Chairman and CEO. “Given the continued breadth of our marketed portfolio and strength of our pipeline, our growth projections are not reliant upon any individual marketed medicine or pipeline opportunity. Consequently, we remain highly confident in our ability to deliver, following the closing of the proposed combination of Upjohn with Mylan N.V., a compound annual growth rate for revenues of at least 6% through 2025.”

Health authorities and trial investigators have been notified of this decision. When available, the full results from the PALLAS study will be shared with the scientific community at a later date.

Palbociclib is also being studied in patients with high-risk early breast cancer and results from the collaborative PENELOPE-B trial are expected later this year.

In the U.S., IBRANCE is approved for the treatment of adult patients with HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men; or with fulvestrant in patients with disease progression following endocrine therapy. IBRANCE is not indicated in early breast cancer. The collaborative Phase 3 PENELOPE-B study (NCT01864746) continues to explore the potential of IBRANCE in patients with early breast cancer at high risk of recurrence who have residual disease after neoadjuvant chemotherapy.

About the PALLAS Trial

PALLAS is a randomized (1:1), prospective, international, multicenter, open-label Phase 3 study comparing the combination of palbociclib and standard adjuvant endocrine therapy for two years followed by continuing standard adjuvant therapy to complete five years versus at least five years of standard adjuvant endocrine therapy for pre- and postmenopausal women or men with HR+, HER2- early invasive (Stage 2 and Stage 3) breast cancer, including those at moderate to high risk of recurrence. The trial is co-sponsored by the Austrian Breast & Colorectal Cancer Study Group and the Alliance Foundation Trials as part of a clinical research collaboration with Pfizer and other study groups, including PrECOG, LLC; NSABP Foundation Inc; and the Breast International Group (BIG).

About IBRANCE® (palbociclib) 125 mg tablets and capsules

IBRANCE is an oral inhibitor of CDKs 4 and 6,[1] which are key regulators of the cell cycle that trigger cellular progression.[2,3] In the U.S., IBRANCE is indicated for the treatment of adult patients with HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine based therapy in postmenopausal women or in men; or with fulvestrant in patients with disease progression following endocrine therapy.

IBRANCE currently is approved in more than 95 countries and has been prescribed to more than 300,000 patients globally.

The full U.S. Prescribing Information for the IBRANCE tablets and the IBRANCE capsules can be found here and here.

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

Neutropenia was the most frequently reported adverse reaction in PALOMA-2 (80%) and PALOMA-3 (83%). In PALOMA-2, Grade 3 (56%) or 4 (10%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. In PALOMA-3, Grade 3 (55%) or Grade 4 (11%) decreased neutrophil counts were reported in patients receiving IBRANCE plus fulvestrant. Febrile neutropenia has been reported in 1.8% of patients exposed to IBRANCE across PALOMA-2 and PALOMA-3. 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 15 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.

Severe, life-threatening, or fatal **interstitial lung disease (ILD) and/or pneumonitis** can occur in patients treated with CDK4/6 inhibitors, including IBRANCE when taken in combination with endocrine therapy. Across clinical trials (PALOMA-1, PALOMA-2, PALOMA-3), 1.0% of IBRANCE-treated patients had ILD/pneumonitis of any grade, 0.1% had Grade 3 or 4, and no fatal cases were reported. Additional cases of ILD/pneumonitis have been observed in the post-marketing setting, with fatalities reported.

Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis (e.g. hypoxia, cough, dyspnea). In patients who have new or worsening respiratory symptoms and are suspected to have developed pneumonitis, interrupt IBRANCE immediately and evaluate the patient. Permanently discontinue IBRANCE in patients with severe ILD or pneumonitis.

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 to consider sperm preservation before taking IBRANCE. 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-2** for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (80% vs 6%), infections (60% vs 42%), leukopenia (39% vs 2%), fatigue (37% vs 28%), nausea (35% vs 26%), alopecia (33% vs 16%), stomatitis (30% vs 14%), diarrhea (26% vs 19%), anemia (24% vs 9%), rash (18% vs 12%), asthenia (17% vs 12%), thrombocytopenia (16% vs 1%), vomiting (16% vs 17%), decreased appetite (15% vs 9%), dry skin (12% vs 6%), pyrexia (12% vs 9%), and dysgeusia (10% vs 5%).

The **most frequently reported Grade ?3 adverse reactions (?5%)** in **PALOMA-2** for IBRANCE plus letrozole vs placebo plus letrozole were neutropenia (66% vs 2%), leukopenia (25% vs 0%), infections (7% vs 3%), and anemia (5% vs 2%).

Lab abnormalities of any grade occurring in **PALOMA-2** for IBRANCE plus letrozole vs placebo plus letrozole were decreased WBC (97% vs 25%), decreased neutrophils (95% vs 20%), anemia (78% vs 42%), decreased platelets (63% vs 14%), increased aspartate aminotransferase (52% vs 34%), and increased alanine aminotransferase (43% vs 30%).

The **most common adverse reactions (?10%)** of any grade reported in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were 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%), diarrhea (24% vs 19%), thrombocytopenia (23% vs 0%), vomiting (19% vs 15%), alopecia (18% vs 6%), rash (17% vs 6%), decreased appetite (16% vs 8%), and pyrexia (13% vs 5%).

The **most frequently reported Grade ?3 adverse reactions (?5%)** in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were neutropenia (66% vs 1%) and leukopenia (31% vs 2%).

Lab abnormalities of any grade occurring in **PALOMA-3** for IBRANCE plus fulvestrant vs placebo plus fulvestrant were decreased WBC (99% vs 26%), decreased neutrophils (96% vs 14%), anemia (78% vs 40%), decreased platelets (62% vs 10%), increased aspartate aminotransferase (43% vs 48%), and increased alanine aminotransferase (36% vs 34%).

Avoid concurrent use of **strong CYP3A inhibitors**. If patients must be administered a strong CYP3A inhibitor, reduce the IBRANCE dose to 75 mg. 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.

For patients with **severe hepatic impairment** (Child-Pugh class C), the recommended dose of IBRANCE is 75 mg. The pharmacokinetics of IBRANCE **have not been studied** in patients **requiring hemodialysis**.

About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of patients. Today, Pfizer Oncology has an industry-leading portfolio of 22 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, prostate, kidney and lung cancers, as well as leukemia and melanoma.

Pfizer Inc.: Breakthroughs that change patients' lives

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, including innovative medicines and vaccines. 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 @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 May 29, 2020. 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 and the anticipated timing of results from the Phase 3 PENELOPE-B study, and the Company's projected compound annual growth rate for revenues 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; uncertainties regarding the commercial impact of the results of the PALLAS trial; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in any jurisdictions for IBRANCE for the treatment of high-risk early breast cancer 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 myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the

product's efficacy and, if approved, whether such product candidate will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of IBRANCE; the uncertainties inherent in business and financial planning, including, without limitation, risks related to Pfizer's business and prospects, adverse developments in Pfizer's markets, or adverse developments in the U.S. or global capital markets, credit markets, regulatory environment or economies generally; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; risks related to the parties ability to consummate the proposed combination of Upjohn with Mylan N.V.; 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, 2019 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: 2019.
[2] 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.
[3] 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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