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Pfizer Announces Overall Survival Results from Phase 3 PALOMA-2 Trial of IBRANCE® (palbociclib) for the First-Line Treatment of ER+, HER2- Metastatic Breast Cancer

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NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE:PFE) today announced overall survival (OS) results from the Phase 3 PALOMA-2 trial, which evaluated IBRANCE® (palbociclib) in combination with letrozole compared to placebo plus letrozole for the first-line treatment of postmenopausal women with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer (mBC). With a median follow-up of 90 months, patients receiving IBRANCE in combination with letrozole had numerically longer OS compared to placebo plus letrozole (median (95% CI) 53.9 months (49.8–60.8) vs median 51.2 months (43.7–58.9)); the results were not statistically significant (Hazard Ratio (HR)=0.956 [95% CI, 0.777–1.177]). The PALOMA-2 trial was designed for a primary endpoint of progression-free survival (PFS) with OS as one of the secondary endpoints. The results will be presented today as an oral presentation at the American Society of Clinical Oncology (ASCO) 2022 Annual Meeting (LBA 1003).

“IBRANCE continues to provide substantial benefit as a first-line treatment for adults with HR+, HER2- mBC based on strong progression-free survival data, which formed the basis of its worldwide approvals,” said Chris Boshoff, M.D., Ph.D., Chief Development Officer, Oncology, Pfizer Global Product Development. “Interpretation of OS in PALOMA-2 is limited by the large and disproportionate censoring of patients with missing survival data between treatment arms. We remain confident in the compelling benefits that IBRANCE plus endocrine therapy offers to this patient population, which is underscored by data from PALOMA-2 showing delayed time to chemotherapy, maintenance of quality of life and a consistent safety profile. Pfizer continues to invest in expanding the treatment options for people living with metastatic breast cancer.”

“IBRANCE transformed the treatment landscape for patients with HR+, HER2- MBC when it was approved in 2015, representing the first new treatment in this patient population in over a decade,” said Richard Finn, M.D., Professor of Medicine at the UCLA David Geffen School of Medicine and Jonsson Comprehensive Cancer Center. “PALOMA-2 enrolled a diverse patient population including patients whose disease was first diagnosed in the metastatic stage as well as those with Disease Free Interval (DFI) less than 12 months from adjuvant treatment and those with greater than 12 months following adjuvant treatment. The median survival of over 50 months in this population represents a significant improvement in the natural history of HR+ breast cancer.”

PALOMA-2 met its primary endpoint of PFS in 2016 and was published in *The New England Journal of Medicine* in November 2016. The results demonstrated IBRANCE plus letrozole resulted in an improved median PFS of 24.8 months when compared to 14.5 months with placebo plus letrozole (HR=0.580). The PALOMA-2

trial showed that in addition to substantially delaying progressive disease, IBRANCE as first-line treatment, in combination with letrozole, delayed time to chemotherapy (38.1 months vs 29.8 months; HR, 0.73), while maintaining quality of life with no new identified safety issues.

The OS analysis being presented at ASCO included a large proportion of patients with missing survival data (i.e. patients who withdrew consent or were lost to follow-up) and were censored (assumed to be alive) at the time of the analysis: 13% in the treatment arm versus 21% in the control arm. Also of note, 10% of IBRANCE plus letrozole and 2% of placebo plus letrozole patients were still on study treatment at the time of the final analysis. The most common adverse reactions in PALOMA-2 included neutropenia, leukopenia, infections, fatigue and nausea.

IBRANCE continues to be a leader in the CDK4/6 inhibitor class, prescribed to over 450,000 patients across more than 100 countries, and seven out of 10 patients in the U.S. who are prescribed a CDK4/6 inhibitor receiving an IBRANCE prescription.[i]

About the PALOMA-2 Study

PALOMA-2 is a randomized (2:1), multicenter, multinational, double-blind Phase 3 study designed to assess the efficacy (defined by PFS) and safety 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. Patients were to be stratified by site of disease (visceral, non-visceral), by disease-free interval since completion of prior (neo)adjuvant therapy (de novo metastatic, ?12 months, >12 months), and by the nature of prior (neo)adjuvant anti-cancer treatment received (prior hormonal therapy, no prior hormonal therapy). The primary endpoint was progression-free survival, as assessed by the investigators; secondary endpoints were overall survival, objective response, clinical benefit response, patient-reported outcomes, pharmacokinetic effects, and safety.

About the IBRANCE Real-World Evidence Program

The IBRANCE Real-World Evidence (RWE) program is generating data from multiple studies involving more than 8,000 patients around the world. These studies include diverse patient populations treated in everyday clinical practice and are collecting data related to clinical outcomes, translational data and quality of life endpoints, which complement the data generated from the PALOMA randomized clinical trials. Most recently, Pfizer reported results from a retrospective comparative effectiveness study of 2,888 men and postmenopausal women with HR+, HER2- mBC evaluating IBRANCE in the real-world, first-line setting in combination with aromatase inhibitors (AI) compared to AI alone. Pfizer will continue to share new data from these studies with the scientific community as results become available.

About IBRANCE® (palbociclib) 125 mg tablets and capsules

IBRANCE is an oral inhibitor of CDKs 4 and 6,[ii] which are key regulators of the cell cycle that trigger cellular progression.[iii,iv] 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.

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 people living with cancer. Today, we have an industry-leading portfolio of 24 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, genitourinary, colorectal, blood and lung cancers, as well as melanoma.

About Pfizer: 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 170 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 June 4, 2022. 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; uncertainties regarding the commercial impact of the overall survival results of the PALOMA-2 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 biologic license applications may be filed in any jurisdictions for IBRANCE for any additional 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 IBRANCE 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; uncertainties regarding the ability to obtain recommendations from advisory or technical committees and other public health authorities regarding IBRANCE and uncertainties regarding the commercial impact of any such recommendations; the impact of COVID-19 on our business, operations and financial results; 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, 2021 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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[i] Pfizer Data on File – IQVIA February 2021.
[ii] IBRANCE® (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: 2019.
[iii] 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.
[iv] 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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