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Pfizer’s IBRANCE® in Combination with Standard-of-Care Therapies Extends Median Progression-Free Survival by Over 15 Months in Phase 3 PATINA Study in Patients with HR+, HER2+ Metastatic Breast Cancer

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IBRANCE is the first CDK4/6 inhibitor to show benefit in a large Phase 3 trial in first-line HR+, HER2+ metastatic breast cancer, in combination with anti-HER2 and endocrine therapy

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE:PFE) and Alliance Foundation Trials, LLC (AFT) today announced results from the Phase 3 PATINA trial demonstrating that the addition of IBRANCE® (palbociclib) to current standard-of-care first-line maintenance therapy (following induction chemotherapy) resulted in statistically significant and clinically meaningful improvement in progression-free survival (PFS) by investigator assessment in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (MBC). In the study, which is sponsored by AFT, median PFS was 44.3 months (95% CI: 32.4-60.9) for patients treated with IBRANCE in combination with anti-HER2 therapy (trastuzumab or trastuzumab plus pertuzumab) and endocrine therapy, and 29.1 months (95% CI: 23.3-38.6) for patients treated with anti-HER2 therapy and endocrine therapy alone [HR: 0.74 (95% CI, 0.58-0.94); unstratified 1-sided p= 0.0074]. This represents an extension in median PFS of over 15 months. Overall survival, a secondary endpoint, was not yet mature at the time of the analysis. These results are being presented during a late-breaking oral session (Abstract GS2-12) and highlighted in the press program at the 47th San Antonio Breast Cancer Symposium (SABCS) in San Antonio, Texas.

“PATINA is the first large Phase 3 study to show the benefit of CDK4/6 inhibition in HR-positive, HER2-positive metastatic breast cancer,” said Otto Metzger, M.D., principal investigator of the trial for Alliance Foundation Trials and Medical Oncologist at the Dana-Farber Cancer Institute. “These results support the potential of this maintenance treatment to slow disease progression and improve clinical outcomes in this patient population.”

Approximately 10% of all breast cancers are HR+, HER2+[i] , which is sometimes referred to as double-positive or triple-positive breast cancer. Despite advances in treatment, the development of resistance to anti-HER2 and endocrine therapy is a challenge, and novel therapeutic approaches are needed for HR+, HER2+ MBC.[ii] IBRANCE is not currently indicated for HR+, HER2+ MBC.

“IBRANCE, the first CDK4/6 inhibitor, revolutionized the treatment of HR-positive, HER2-negative metastatic breast cancer, and has been prescribed to over 773,000 patients since its initial approval in 2015,” said Roger Dansey, M.D., Chief Development Officer, Oncology, Pfizer. “These results demonstrate that the addition of

IBRANCE to standard of care shows promise as maintenance therapy in HR-positive, HER2-positive disease. PATINA underscores Pfizer's ongoing commitment to addressing the unmet needs of people with breast cancer, and we look forward to discussing the results with regulatory authorities."

The safety and tolerability of IBRANCE in the PATINA study was consistent with its known safety profile in HR+, human epidermal growth factor receptor 2-negative (HER2-) MBC, and no new safety signals were identified. The most common adverse events observed with IBRANCE were hematologic toxicities, such as neutropenia and leukopenia. Non-hematologic adverse events included fatigue, stomatitis and diarrhea, which were generally mild to moderate in severity.

Since its initial regulatory approval in 2015, IBRANCE continues to be a standard-of-care first-line treatment for HR+, HER2- MBC and has been approved in more than 108 countries. Pfizer plans to share the results from PATINA with regulatory authorities.

About the PATINA Trial
PATINA (AFT-38) is a randomized, open-label Phase 3 study to evaluate the efficacy and safety of IBRANCE® (palbociclib) in combination with anti-HER2 therapy (trastuzumab or trastuzumab plus pertuzumab) and endocrine therapy compared to anti-HER2 therapy and endocrine therapy alone as a first-line maintenance therapy (following induction chemotherapy treatment) for patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (MBC). While Pfizer is providing funding support for the trial, PATINA is sponsored by Alliance Foundation Trials, LLC (AFT) in collaboration with six international cancer research groups in the U.S., France, Germany, Italy, Spain, Australia, and New Zealand.

Study participants who were previously treated with anti-HER2 therapy were randomized to receive IBRANCE, in addition to anti-HER2 therapy and endocrine therapy (n=261), or anti-HER2 therapy and endocrine therapy alone (n=257). The primary endpoint is progression-free survival (PFS) as assessed by the investigator. Overall survival is a secondary endpoint.

About IBRANCE® (palbociclib)
IBRANCE is an oral inhibitor of CDKs 4 and 6,[iii] which are key regulators of the cell cycle that trigger cellular progression.[iv,v] 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 Alliance Foundation Trials (AFT)
Alliance Foundation Trials, LLC (AFT) is a research organization that develops and conducts cancer clinical trials, working closely with the Alliance for Clinical Trials in Oncology (Alliance) scientific investigators, and its institutional member network, research collaborators, and non-NCI funding sources. AFT seeks to fulfill a shared vision with Alliance to reduce the impact of cancer on people by uniting a broad community of scientists and clinicians from many disciplines committed to discovering, validating and disseminating effective strategies for the prevention and treatment of cancer. Current AFT studies are funded by industry collaborators and the Patient-Centered Outcomes Research Institute (PCORI). For more information about AFT, please visit www.AllianceFoundationTrials.org.

About Pfizer Oncology
At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes three core mechanisms of action to attack cancer from multiple angles, including small molecules, antibody-drug conjugates (ADCs), and bispecific antibodies, including other immune-oncology biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer, hematology-oncology, and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to help people with cancer live better and longer lives.

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 175 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 X at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice
The information contained in this release is as of December 12, 2024. 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 Pfizer Oncology and IBRANCE® (palbociclib), including its potential benefits and results from the Phase 3 PATINA trial in patients with HR+, HER2+ metastatic breast cancer, 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 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; whether the PATINA trial will meet the secondary endpoint for overall survival; 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 any drug applications may be filed in any jurisdictions for IBRANCE for HR+, HER2+ metastatic breast cancer or any other potential indications; whether and when any such applications may be approved by regulatory authorities, which will depend on a 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 impact of COVID-19 on Pfizer's 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, 2023, 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] National Cancer Institute. Cancer Stat Facts: Female Breast Cancer Subtypes. https://seer.cancer.gov/statfacts/html/breast-subtypes.html#:~:text=Percent%20of%20Female,Unknown%20(6%25). Accessed December 2024.
[ii] Nature. Estrogen/HER2 receptor crosstalk in breast cancer: combination therapies to improve outcomes for patients with hormone receptor-positive/HER2-positive breast cancer
[iii] IBRANCE (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: 2023.
[iv] 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.
[v] 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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