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FDA Approves Pfizer's IBRANCE Regimen for HR+, HER2+ Metastatic Breast Cancer Frontline Maintenance

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- *First and only CDK4/6 inhibitor approved for HR+ metastatic disease regardless of HER2 status*
- *Approval based on data from the collaborative Phase 3 PATINA trial, which showed a 24% risk reduction in disease progression for IBRANCE added to anti-HER2 and endocrine therapies*
- *Continues decade-long legacy of IBRANCE helping transform the treatment for HR+ metastatic breast cancer*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced the U.S. Food and Drug Administration (FDA) approved IBRANCE® (palbociclib) in combination with trastuzumab, with or without pertuzumab, and endocrine therapy for the maintenance treatment of adult patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-positive (HER2+) locally advanced or metastatic breast cancer (MBC) following induction treatment. The approval is based on positive results from the Alliance Foundation Trials, LLC (AFT)-sponsored Phase 3 PATINA trial.

"Over the past decade, IBRANCE has helped transform metastatic breast cancer treatment, establishing CDK4/6 inhibition as a cornerstone of care," said Aamir Malik, Chief U.S. Commercial Officer and Executive Vice President, Pfizer. "With today's FDA approval, IBRANCE becomes the first and only CDK4/6 inhibitor indicated for patients with HR+ metastatic breast cancer regardless of HER2 status, extending its impact to patients who continue to face challenges with treatment resistance. This milestone strengthens confidence in IBRANCE as a CDK4/6 inhibitor backbone across combination regimens, reflecting Pfizer's ongoing leadership in delivering meaningful advances for people with breast cancer."

The PATINA trial demonstrated a 24% reduction in the risk of progression or death following induction treatment with the addition of IBRANCE to anti-HER2 (trastuzumab or trastuzumab plus pertuzumab) and endocrine therapies compared to anti-HER2 and endocrine therapies alone (HR: 0.76 [95% CI, 0.59, 0.97]; one-sided p=0.0134). The safety and tolerability of IBRANCE in PATINA were consistent with its known safety profile. The most commonly reported adverse events with IBRANCE were hematologic toxicities, such as white blood cell decreased and neutrophil count decreased. Non-hematologic adverse events included diarrhea, infections, stomatitis, and fatigue, which were generally mild to moderate in severity. Results from the trial were previously published by AFT in the *New England Journal of Medicine* and presented at the 2024 San Antonio Breast Cancer Symposium.

"Resistance to dual anti-HER2 and endocrine therapy remains a central clinical challenge for patients with HR+, HER2+ metastatic breast cancer – even after an excellent response to initial treatment," said Otto Metzger, M.D., principal investigator of the trial for Alliance Foundation Trials and Medical Oncologist at the Dana-Farber Cancer Institute. "Based on the results from the PATINA study, the addition of IBRANCE in the maintenance phase can meaningfully extend the time patients go without their disease progressing. This approval gives

oncologists a new, evidence-based option to optimize maintenance therapy for their patients with HR+, HER2+ disease."

Approximately 10% of all breast cancers are HR+, HER2+,[i] which is sometimes referred to as double-positive or triple-positive breast cancer. Historically, there has been limited research specifically focused on the HR+, HER2+ subtype in MBC, and PATINA is the first registrational study to explore the potential of CDK4/6 inhibition in this subtype.

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 prescribed to more than 900,000 patients and approved in more than 100 countries.

About the PATINA Trial

PATINA (AFT-38) was a randomized, open-label global 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 treatment) for patients with HR+, HER2+ MBC. While Pfizer provided funding support for the trial, PATINA was also supported by an academic collaboration led by Alliance Foundation Trials, LLC (AFT) as the global sponsor in partnership with six international cancer research groups in the U.S.(PrECOG), France (French Breast Cancer Intergroup Unicancer), Germany (GBG), Italy (Fondazione Michelangelo), Portugal and Spain (SOLTI), and Australia and New Zealand (Breast Cancer Trials).

Study participants who received a median of 6 cycles of induction treatment 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 was progression-free survival (PFS) as assessed by the investigator. Overall survival is a secondary endpoint and is not yet mature.

About IBRANCE® (palbociclib)

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; or with fulvestrant in patients with disease progression following endocrine therapy. IBRANCE is indicated in combination with inavolisib and fulvestrant for the treatment of adult patients with endocrine-resistant, PIK3CA-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy. IBRANCE is also indicated in combination with trastuzumab, with or without pertuzumab, and endocrine therapy for the maintenance treatment of adult patients with HR-positive, HER2-positive locally advanced or metastatic breast cancer following induction treatment.

IMPORTANT SAFETY 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. In PATINA, neutropenia was the most frequently reported adverse reaction with an incidence of 78%, and Grade ?3 neutropenia was reported in 61% of patients receiving IBRANCE in combination with trastuzumab, with or without pertuzumab, and endocrine therapy. Based on laboratory findings, 93% had a decrease in neutrophil counts including 47% with Grade 3 and 3.1%

with Grade 4. 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. Febrile neutropenia has been reported in 0.8% of patients exposed to IBRANCE in the PATINA study. 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% of IBRANCE-treated patients had ILD/pneumonitis of any grade, 0.1% had Grade 3 or 4, and no fatal cases were reported. In PATINA, 1% of IBRANCE-treated patients had ILD/pneumonitis of any grade and no Grade 3, 4, or 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%), increased blood creatinine (96% vs 91%), decreased neutrophils (95% vs 20%), decreased hemoglobin (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%), increased blood creatinine (95% vs 82%), decreased hemoglobin (78% vs 40%), decreased platelets (62% vs 10%), increased aspartate aminotransferase (43% vs 48%), and increased alanine aminotransferase (36% vs 34%).

Serious adverse reactions occurred in 24% of patients in **INAVO120** who received IBRANCE plus inavolisib and fulvestrant. Serious adverse reactions occurring in ?1% of patients receiving IBRANCE plus inavolisib and fulvestrant included anemia (1.9%), diarrhea (1.2%), and urinary tract infection (1.2%).

Fatal adverse reactions occurred in 3.7% of patients in **INAVO120** who received IBRANCE plus inavolisib and fulvestrant, including (0.6% each) acute coronary syndrome, cerebral hemorrhage, cerebrovascular accident, COVID-19 infection, and gastrointestinal hemorrhage.

The **most (?20%) common adverse reactions** occurring in **INAVO120, including laboratory abnormalities**, for IBRANCE plus inavolisib and fulvestrant vs IBRANCE plus placebo and fulvestrant were decreased neutrophils (95% vs 97%), decreased hemoglobin (88% vs 85%), increased fasting glucose (85% vs 43%), decreased platelets (84% vs 71%), decreased lymphocytes (72% vs 68%), stomatitis (51% vs 27%), diarrhea (48% vs 16%), decreased calcium (42% vs 32%), fatigue (38% vs 25%), decreased potassium (38% vs 21%), increased creatinine (38% vs 30%), increased alanine aminotransferase (34% vs 29%), alkaline phosphatase increased (31% vs 23%), nausea (28% vs 17%), decreased sodium (28% vs 19%), decreased magnesium (27% vs 21%), rash (26% vs 19%), decreased appetite (24% vs 9%), COVID-19 infection (23% vs 10%), and headache (22% vs 14%).

Serious adverse reactions occurred in 25% of patients in **PATINA** who received IBRANCE in combination with trastuzumab, with or without pertuzumab, and endocrine therapy. Serious adverse reactions in ?1% of patients receiving IBRANCE in combination with trastuzumab, with or without pertuzumab, and endocrine therapy included infections (8%), headache and pyrexia (1.5% each), and femur fracture (1.2%).

Fatal adverse reactions occurred in 1.2% of patients in **PATINA** who received IBRANCE in combination with trastuzumab, with or without pertuzumab, and endocrine therapy including (0.4% each) death, hepatic hemorrhage, and sepsis.

The **most common adverse reactions (?20%)** occurring in **PATINA, including laboratory abnormalities,** for IBRANCE in combination with trastuzumab, with or without pertuzumab, and endocrine therapy vs trastuzumab, with or without pertuzumab, and endocrine therapy were white blood cell decreased (94% vs 25%), neutrophil count decreased (93% vs 19%), creatinine increased (92% vs 87%), hemoglobin decreased (81% vs 47%), diarrhea (70% vs 37%), infections (64% vs 43%), platelet count decreased (59% vs 6%), stomatitis (44% vs 11%), aspartate aminotransferase increased (39% vs 25%), decreased calcium (39% vs 30%), alanine aminotransferase increased (38% vs 28%), decreased potassium (33% vs 17%), fatigue (32% vs 21%), alkaline phosphatase increased (31% vs 23%), nausea (30% vs 15%), asthenia (27% vs 21%), headache (26% vs 18%), rash (22% vs 17%), pruritus (21% vs 17%), and muscle spasms (20% vs 11%).

Other Clinical Trials Experience: venous thromboembolism has been reported as an adverse reaction following administration of IBRANCE.

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**.

The full U.S. Prescribing Information for the IBRANCE tablets and the IBRANCE capsules can be found here and here. There may be a delay as the document is updated with the latest information. It will be available as soon as possible. Please check back for the updated full information shortly.

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 multispecific 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, gastrointestinal cancers, genitourinary cancers, 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 more than 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.

Disclosure Notice

The information contained in this release is as of June 24, 2026. 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, IBRANCE® (palbociclib) and an approval in the U.S. for a new indication for IBRANCE in combination with trastuzumab, with or without pertuzumab, and endocrine therapy for the maintenance treatment of adult patients with HR+, HER2+ locally advanced or metastatic breast cancer following induction treatment, including their 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 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 particular 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; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; 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, 2025, 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.

References

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