Pfizer Presents Overall Survival Data From PALOMA-3 Trial of IBRANCE® (palbociclib) in Patients With HR+, HER2- Metastatic Breast Cancer

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Results Presented at the ESMO 2018 Congress (European Society for Medical Oncology) and Simultaneously Published in The New England Journal of Medicine

NEW YORK--(BUSINESS WIRE)--Pfizer Inc.(NYSE:PFE) today announced detailed overall survival (OS) data from the PALOMA-3 trial, which evaluated IBRANCE® (palbociclib) in combination with fulvestrant compared to placebo plus fulvestrant in women with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer whose disease progressed on or after prior endocrine therapy. In the study, there was a numerical improvement in OS of nearly seven months with IBRANCE plus fulvestrant compared to placebo plus fulvestrant, although this difference did not reach the prespecified threshold for statistical significance (median OS: 34.9 months [95% CI: 28.8, 40.0] versus 28.0 months [95% CI: 23.6, 34.6]; HR=0.81 [95% CI: 0.64, 1.03], 1-sided p=0.0429). These data will be presented as a late-breaking oral abstract during the Presidential Symposium at the ESMO 2018 Congress (European Society for Medical Oncology) in Munich, Germany, and simultaneously published in The New England Journal of Medicine.

The difference in median OS demonstrated in this analysis (6.9 months) is consistent with the improvement previously demonstrated for the primary endpoint of median progression-free survival (mPFS). In the updated PFS analysis for this study (non-

prespecified), the combination of IBRANCE plus fulvestrant showed a statistically significant and clinically meaningful 6.6-month mPFS improvement compared to placebo plus fulvestrant (11.2 vs. 4.6 months; HR=0.50 [95% CI: 0.40-0.62], p<0.000001).1 Overall survival is a secondary endpoint of PALOMA-3, and the trial design was not optimized to detect a statistically significant difference in OS.

“It’s noteworthy that the magnitude of progression-free survival benefit observed in PALOMA-3 has translated to a similar difference of nearly seven months in overall survival, which is clinically meaningful. This is particularly significant given the challenges of demonstrating overall survival in this disease setting, where post-progression therapy is often substantially longer than time on study,” said Massimo Cristofanilli, M.D., associate director for Translational Research at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, as well as senior investigator of the PALOMA-3 trial. “The overall survival data, coupled with the previously demonstrated progression-free survival benefit, are encouraging for patients.”

At the time of this analysis, follow-up was 44.8 months and approximately 60 percent (n=310) of events had occurred in the 521 patients enrolled. Patients on both arms received up to 10 lines (range 1-10) of post-progression treatment.

The trend toward OS favoring the IBRANCE plus fulvestrant arm was observed across most subgroups, with hazard ratios consistent with the overall population. In addition, for the overall population, the difference in OS was associated with prolonged time from randomization to first use of chemotherapy post-progression, an exploratory endpoint (HR=0.58 [95% CI: 0.47, 0.73], 1-sided p<0.000001). Median time to chemotherapy was 17.6 months (95% CI: 15.2, 19.7) for patients who received IBRANCE plus fulvestrant, twice that observed in patients who received placebo plus fulvestrant (8.8 months [95% CI: 7.3, 12.7]).

“Delaying the need for chemotherapy is a central goal of treatment for women with this disease. These new data from PALOMA-3 show that adding IBRANCE to fulvestrant led to a substantial improvement in this important area,” said Nicholas Turner, M.D., Ph.D., professor of molecular oncology at The Institute of Cancer Research, London, and consultant medical oncologist at The Royal Marsden NHS Foundation Trust, as well as principal investigator of the PALOMA-3 trial. “The difference in overall survival and prolonged time to chemotherapy demonstrated in PALOMA-3 further support the role of IBRANCE in combination with endocrine therapy as a standard of care in HR+, HER2- metastatic breast cancer.”

“Looking at the data from the PALOMA-3 trial and across the PALOMA program, IBRANCE has transformed the treatment landscape for this disease,” said Mace Rothenberg, M.D., chief development officer, Oncology, Pfizer Global Product Development. “We are proud of the compelling body of evidence supporting the use of IBRANCE in this setting, and the difference this medicine continues to make in the lives of patients.”

The most common adverse reactions in PALOMA-3 included neutropenia, leukopenia, infections, fatigue and nausea. No new safety signals observed with longer follow-up were identified as part of this final OS analysis.

About IBRANCE® (palbociclib) 125 mg capsules

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

IBRANCE currently is approved in more than 85 countries and has been prescribed to more than 160,000 patients globally.

The full prescribing information for IBRANCE can be found at www.pfizer.com.

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.

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 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 on the lives of patients. Today, Pfizer Oncology has an industry-leading portfolio of 12 approved cancer medicines across 20 indications, including breast, prostate, kidney, lung and hematology. We also have one of the deepest oncology biosimilars pipelines, with two medicines approved globally and several assets in mid to late-stage development for the treatment of cancer or as supportive care. Pfizer Oncology is striving to change the trajectory of cancer.

Working together for a healthier world®

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. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care 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, 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 October 20, 2018. 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 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 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 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, 2017 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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1 Turner NC, André F, Cristofanilli M, et al. Treatment postprogression in women with endocrine-resistant HR+/HER2- advanced breast cancer who received palbociclib plus fulvestrant in PALOMA-3. In: Proceedings of the 2016 San Antonio Breast Cancer Symposium; Dec 6-10, 2016; San Antonio, TX. Abstract P4-22-06.

2 IBRANCE® (palbociclib) Prescribing Information. New York. NY: Pfizer Inc: 2018.

3 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.

4 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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