Pfizer Announces FDA Acceptance Of Palbociclib New Drug Application With Priority Review

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NDA Requests Approval of Palbociclib as a First-Line Therapy in Combination with Letrozole for ER+, HER2- Advanced Breast Cancer

Pfizer Inc. today announced the New Drug Application (NDA) for palbociclib has been accepted for filing and granted Priority Review by the United States Food and Drug Administration (FDA). This NDA requests FDA approval of palbociclib, in combination with letrozole, as a first-line treatment for postmenopausal women with estrogen receptor positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer who have not received previous systemic treatment for their advanced disease. The submission is based on the final results of PALOMA-1, a randomized, Phase 2 trial comparing palbociclib plus letrozole versus letrozole alone in this population of patients.

The FDA’s Priority Review status accelerates the review time from 10 months to a goal of six months from the day of acceptance of filing and is given to drugs that may offer major advances in treatment or may provide a treatment where no adequate therapy exists. The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA is April 13, 2015.

Palbociclib received Breakthrough Therapy designation from the FDA in April 2013, for the first-line systemic treatment of women with advanced or metastatic ER+, HER2- breast cancer.

“If approved as a first-line therapy in combination with letrozole, palbociclib will be an important new option for the thousands of women in the U.S. who are living with metastatic breast cancer,” said Garry Nicholson, president, Pfizer Oncology. “We look forward to continuing to work closely with the FDA through the review process.”

Pfizer recently announced the initiation of a multi-center, open-label expanded access program (EAP) in the United States for palbociclib. Through the program, palbociclib is available to post-menopausal women with hormone receptor-positive (HR+), HER2- advanced breast cancer who are eligible for letrozole therapy and for whom enrolling in other palbociclib clinical trials is not an option. Healthcare professionals and patients can learn more about the palbociclib EAP by visiting www.clinicaltrials.gov (trial number: NCT02142868).

About Palbociclib

Palbociclib is an investigational oral targeted agent that selectively inhibits cyclin-dependent kinases (CDKs) 4 and 6 to regain cell cycle control and block tumor cell proliferation.1

Loss of cell cycle control is a hallmark of cancer and CDK 4/6 are overactivated in numerous cancers, leading to loss of proliferative control.2,3CDK 4/6 are key regulators of the cell cycle that trigger cellular progression from growth phase (G1) into phases associated with DNA replication (S).4,5 CDK 4/6, whose increased activity is frequent in estrogen receptor-positive (ER+) breast cancer (BC), are key downstream targets of ER signaling in ER+ BC.6,7 Preclinical data suggest that dual inhibition of CDK 4/6 and ER signaling is synergistic, and it has been shown to stop growth of ER+ BC cell lines in the G1 phase.

Palbociclib is not approved for any indication in any market.

About PALOMA-1

PALOMA-1 (also known as Study 1003 and TRIO-18) is a Phase 2 trial designed to assess progression-free survival in post-menopausal women with ER+, HER2- advanced breast cancer receiving palbociclib (125 mg once daily for three out of four weeks in repeated cycles) in combination with letrozole versus letrozole alone (2.5 mg once daily on a continuous regimen). Final results from PALOMA-1 were presented at the American Association for Cancer Research (AACR) Annual Meeting 2014. PALOMA-1 was conducted in collaboration with the Jonsson Cancer Center’s Revlon/UCLA Women’s Cancer Research

Program, led by Dr. Dennis Slamon.

Palbociclib Development Program in ER+, HER2- Breast Cancer

Pfizer has worked closely with investigators and international breast cancer experts to establish a robust development program for palbociclib in ER+, HER2- breast cancer across stages and treatment settings.

Pfizer has initiated two Phase 3 studies of palbociclib in advanced/metastatic breast cancer. PALOMA-2 (also known as Study 1008) is a randomized (2:1), multi-center, double blind Phase 3 study that evaluates palbociclib in combination with letrozole versus letrozole plus placebo as a first-line treatment for post-menopausal patients with ER+, HER2- advanced breast cancer. PALOMA-3 (also known as Study 1023) is a randomized (2:1), multi-center, double blind Phase 3 study that evaluates palbociclib in combination with fulvestrant versus fulvestrant plus placebo in women with hormone receptor-positive (HR+), HER2- metastatic breast cancer whose disease has progressed after prior endocrine therapy. PALOMA-2 and PALOMA-3 have recently completed enrollment.

Additional, investigator-led studies of palbociclib in advanced/metastatic breast cancer and in early breast cancer are open and enrolling patients, including the PEARL and PENELOPE-B studies. PEARL, sponsored by Grupo Español de Investigación en Cáncer de Mama (GEICAM, Spanish Breast Cancer Research Group), with participation from the Central European Cooperative Oncology Group (CECOG), is a randomized (1:1), multi-center, open-label Phase 3 study evaluating palbociclib in combination with exemestane versus capecitabine in post-menopausal women with ER+, HER2- metastatic breast cancer whose disease was refractory to previous non-steroidal aromatase inhibitors (letrozole or anastrozole). PENELOPE-B is a randomized (1:1), double blind, placebo-controlled Phase 3 study comparing palbociclib plus standard endocrine therapy to placebo plus standard endocrine therapy in patients with HR+, HER2- early-stage breast cancer with certain features that suggest an increased risk for recurrence after completing pre-operative chemotherapy followed by surgery. This international study is sponsored by the German Breast Group (GBG).

For more information on these and other ongoing clinical trials of palbociclib in breast cancer and other tumor types, please visitwww.clinicaltrials.gov.

About Pfizer Oncology

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide. Our strong pipeline of biologics and small molecules, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments, and licensing partners, Pfizer Oncology strives to cure or control cancer with breakthrough medicines, to deliver the right drug for each patient at the right time. For more information, please visit www.Pfizer.com.

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DISCLOSURE NOTICE: The information contained in this release is as of October 13, 2014. 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 palbociclib, an investigational therapy, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Forward-looking statements include those about palbociclib’s potential benefits and the potential indication for the treatment of postmenopausal women with ER+, HER2- advanced breast cancer who have not received previous systemic treatment for their advanced disease (the “Potential Indication”). Risks and uncertainties include, among other things, 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 the PALOMA-2 Phase 3 trial of palbociclib for the Potential Indication will demonstrate a statistically significant improvement in progression-free survival and whether the other Phase 3 trials of palbociclib will meet their primary endpoints; 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 other jurisdictions for the Potential Indication or in any jurisdictions for any other potential indications for palbociclib; whether and when the NDA or any such other applications may be approved by the FDA or other 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 the FDA and other regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of the Potential Indication or any other such indications; 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, 2013 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the SEC and available at www.sec.gov and www.pfizer.com.

1 Clinicaltrials.gov. Study of Letrozole with or without PD 0332991 for the first-line treatment of hormone-receptor positive advanced breast cancer. Available here: http://www.clinicaltrials.gov/ct2/show/NCT00721409?term=PD+0332991&rank=10. Accessed April 6, 2014. 2 Shapiro GI. Cyclin-dependent kinase pathways as targets for cancer treatment. J Clin Oncol. 2006;24(11):1770-1783. 3 Weinberg RA. The Biology of Cancer. New York, NY. Garland Science; 2013. 4 Hirama T and H. Phillip Koeffler. Role of the Cyclin-Dependent Kinase Inhibitors in the Development of Cancer. Blood. 1995; 86: 841-854. 5 Fry D et al. Specific Inhibition of cyclin-dependent kinase 4/6 by PD 0332991 and associated antitumor activity in human tumor xenografts.Molecular Cancer Therapeutics. 2004; 3: 1427-1437. 6 Finn RS et al. PD 0332991, a selective cyclin D kinase 4/6 inhibitor, preferentially inhibits proliferation of luminal estrogen receptor-positive human breast cancer cell lines in vitro. Breast Cancer Res. 2009;11(5):R77. 7 Lamb R, Lehn S, Rogerson L, Clarke RB, Landberg G. Cell cycle regulators cyclin D1 and CDK4/6 have estrogen receptor-dependent divergent functions in breast cancer migration and stem cell-like activity. Cell Cycle. 2013;12(15):2384-2394.

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