Pfizer’s Novel CDK 4/6 Inhibitor Palbociclib plus Letrozole Significantly Prolonged Progression-Free Survival in Patients with Advanced Breast Cancer

Sunday, April 06, 2014 - 06:30am

Final Phase 2 PALOMA-1 Data to Be Presented Today for Potential First-in-Class Palbociclib

Webcast of Conference Call with Securities Analysts to Review Data Scheduled for Today at 1:30 PDT

NEW YORK, N.Y., April 6 – Pfizer Inc. today announced detailed results from the PALOMA-1 study, a randomized Phase 2 study of palbociclib (PD-0332991) in combination with letrozole. PALOMA-1 achieved its primary endpoint by significantly prolonging progression-free survival (PFS) compared with letrozole alone in post-menopausal women with estrogen receptor positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) locally advanced or metastatic breast cancer. For women treated with the combination of palbociclib plus letrozole, the median PFS was 20.2 months, a statistically significant improvement compared to the 10.2 months of PFS in women who received letrozole alone (HR=0.488 [95% CI: 0.319, 0.748]; p=0.0004). These data will be presented today by Dr. Richard S. Finn, associate professor of medicine at University of California, Los Angeles (UCLA) at the American Association of Cancer Research (AACR) Annual Meeting 2014 in San Diego (Abstract #CT101).

"These data demonstrate the potential of palbociclib to be a major advance in the treatment of women with this type of advanced breast cancer," said Dr. Mace Rothenberg, senior vice president of Clinical Development and Medical Affairs and chief medical officer for Pfizer Oncology. "We are proud to be at the forefront of research and development with respect to this promising new class of investigational anticancer agents and have initiated a broad clinical development program for palbociclib that includes breast and non-breast cancers."

Final results for the secondary efficacy endpoints of duration of treatment and clinical benefit rate demonstrated superiority in the palbociclib plus letrozole arm compared to the letrozole-only arm. Per the PALOMA-1 trial protocol, an initial assessment of overall survival (OS), a secondary endpoint, was also performed. Based on the events at the time of the assessment, a median OS of 37.5 months was observed in the combination arm versus 33.3 months for those who received letrozole alone, a difference of 4.2 months (HR = 0.813, 95% CI: 0.492, 1.345). This OS observation at the time of final PFS analysis was not statistically significant. A follow-up OS analysis will be conducted following the accrual of additional events.

The combination of palbociclib and letrozole was generally well-tolerated and the safety profile of the combination was consistent with previously reported data. The most common adverse events in the palbociclib plus letrozole arm were neutropenia (a decrease of the neutrophil count), leukopenia (a decrease in the total white blood cell count), fatigue and anemia. The neutropenia observed with the combination in this study was non-cumulative and clinically manageable. No cases of febrile neutropenia were reported in either arm of the study. Neutropenia is an on-target, anti-proliferative side effect of palbociclib and signifies inhibition of CDK4 and its effect on bone marrow.

Palbociclib received Breakthrough Therapy designation from the United States Food and Drug Administration (FDA) in April 2013, for the initial treatment of women with advanced or metastatic ER+, HER2- breast cancer. This designation was based on interim data from the PALOMA-1 trial. Pfizer continues to work with the FDA and other regulatory authorities to define the appropriate regulatory path forward for palbociclib.

Pfizer invites investors and the general public to view and listen to a webcast of a presentation by Pfizer's Oncology leadership today at 1:30 p.m. Pacific Daylight Time, in connection with the presentation of the final results of PALOMA-1. To view and listen to the webcast, visit our website at www.pfizer.com and click on the "Review of Palbociclib Phase 2 PALOMA-1 Results at AACR Annual Meeting 2014" webcast link in the For Investors section located on the lower right-hand corner of that page.

About PALOMA-1

PALOMA-1 (also known as Study 1003 and TRIO-18) is a Phase 2 trial designed to assess PFS 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). This trial consisted of two parts. Part 1 enrolled 66 patients with ER+, HER2- advanced breast cancer. Part 2 enrolled 99 additional patients whose tumors were selected for presence of biomarkers: cyclin D1 amplification and/or p16 loss. Final results from PALOMA-1 showed that statistically significant improvement in PFS was achieved for the study arm (palbociclib + letrozole) in both Parts 1 and 2. PFS is comprised of time from randomization to time of disease progression or death from any cause.

PALOMA-1 is conducted in collaboration with the Jonsson Cancer Center's Revlon/UCLA Women's Cancer Research Program, led by Dr. Dennis Slamon. PALOMA-1 is a multi-center trial with 101 global sites participating.

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.

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-normal (also known as 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 visit www.clinicaltrials.gov.

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.

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. , CDK 4/6 are key regulators of the cell cycle that trigger cellular progression from growth phase (G1) into phases associated with DNA replication (S). , 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. , Preclinical data suggest that dual inhibition of CDK 4/6 and ER signaling is synergistic and has been shown to stop growth of ER+ BC cell lines in the G1 phase.

Palbociclib is not approved for any indication in any markets.

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.

DISCLOSURE NOTICE: The information contained in this release is as of April 6, 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 that involves substantial risks and uncertainties about palbociclib, an investigational therapy, including with regard to potential indications. Such 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 unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether PALOMA-2 will demonstrate a statistically significant improvement in progression-free survival; 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 jurisdictions for any potential indications for palbociclib; whether and when any such applications may be approved by regulatory authorities, as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of any 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 and Form 8-K.

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