Palbociclib (PD-0332991) in Breast Cancer

FACT SHEET

Palbociclib (PD-0332991) is an investigational agent and has not been approved for marketing by any regulatory agency at this time.

ABOUT
PALBOCICLIB

Palbociclib (PD-0332991) 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

Palbociclib is a potential first-in-class CDK 4/6 inhibitor. It was discovered and is being developed by Pfizer Inc.

TARGETING CDKs 4 and 6
IN CANCER

CDKs are a family of proteins that serve as key regulators of cell growth and division. Specifically, cyclins pair with CDKs 4 and 6 to take part in a fundamental process in the division of cells, called the cell cycle.2,3 This occurs in both normal and cancer cells and is composed of four phases:2,3

- **G1**: This phase marks the early beginning of the cell, where the raw material is built and prepared for the S phase.2,3
- **S**: DNA, or the vital information instructing the function of the cell, is constructed.4
- **G2**: The cell begins to grow and prepares for mitosis.2
- **M**: The cell cycle is completed and the cell duplicates into two genetically alike daughter cells.3

CDKs 4 and 6 are key regulators of the cell cycle that trigger progression through G1 to the S phase.2,3 In some cancers, including ER+ breast cancer, increased activity of the cyclin D1-CDK 4/6-complex may result in a failure to regulate cell proliferation.2,4,5 Inhibiting CDKs 4 and 6 may help stop cancer cells from dividing in an uncontrolled fashion.3,6

PHASE 2 CLINICAL
STUDY

- PALOMA-1 (also known as Study 1003) is a randomized Phase 2 trial designed to assess progression-free survival in post-menopausal women with ER+, HER2- advanced breast cancer receiving palbociclib in combination with letrozole versus letrozole alone.7
- In February 2014, Pfizer announced that this trial achieved its primary endpoint. Detailed efficacy and safety data from PALOMA-1 were presented at the American Association for Cancer Research (AACR) Annual Meeting 2014.
- In December 2014, Pfizer announced the publication of the detailed results from PALOMA-1 in *The Lancet Oncology*.
- PALOMA-1 was conducted in collaboration with the Jonsson Comprehensive Cancer Center’s Revlon/UCLA Women’s Cancer Research Program. PALOMA-1 is a global, multi-center trial.
- This trial is ongoing but no longer enrolling patients.

PHASE 3 CLINICAL
STUDIES

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

PALOMA-2 (Study 1008)8
- PALOMA-2 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. This trial has completed enrollment.
PALOMA-3 (Study 1023)\(^9\)
- PALOMA-3 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 HR+, HER2- metastatic breast cancer whose disease has progressed after prior endocrine therapy. This trial has completed enrollment.

PENELOPE-B\(^{10}\)
- PENELOPE-B is a randomized (1:1), double blind, placebo-controlled Phase 3 study that compares palbociclib plus standard endocrine therapy to placebo plus standard endocrine therapy in patients with HR+, HER2-normal (also known as HER2-negative) 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).

PEARL\(^{11}\)
- PEARL is a randomized (1:1), multi-center, open-label Phase 3 trial that evaluates palbociclib in combination with exemestane versus capecitabine in post-menopausal women with HR+, HER2- metastatic breast cancer whose disease was refractory to previous non-steroidal aromatase inhibitors (letrozole or anastrozole). This study is 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).

These trials are event-driven. Therefore, timing of data availability will depend on a variety of factors including how quickly the trials enroll and the number and timing of events.

In addition to breast cancer, pre-clinical and early phase clinical studies are underway in other tumor types.

For more information on palbociclib clinical trials, please visit www.clinicaltrials.gov.

REGULATORY MILESTONES

In October 2014, Pfizer announced that the New Drug Application (NDA) for palbociclib had been accepted for filing and granted Priority Review by the U.S. Food and Drug Administration. The NDA requests FDA approval of palbociclib, in combination with letrozole, as a first-line treatment for postmenopausal women with ER+, HER2- advanced breast cancer who have not received previous systemic treatment for their advanced disease.

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.


