KEY MILESTONES IN THE HISTORY & DEVELOPMENT OF PALBOCICLIB IN BREAST CANCER

1990

EARLY 1990s

Cyclin-dependent kinases (CDKs) are identified as key regulators of cell growth and division, a significant scientific discovery.[1] Cancer researchers begin exploring the treatment potential of CDK inhibition, but note the toxicity of pan-CDK inhibitors in the clinic.[1]

1995-2001

2000

Pfizer researchers in Ann Arbor, Michigan, discover the compound palbociclib, a selective inhibitor of CDKs 4 and 6, as part of a multi-year research collaboration with Onyx Pharmaceuticals (now a subsidiary of Amgen).

2001

Three UK researchers – Sir Paul Nurse, Tim Hunt and Leland Hartwell – are awarded the Nobel Prize for their work uncovering the role of CDKs on the cell cycle.[2]

2002

Pfizer's Oncology Research Unit selects palbociclib as its lead CDK inhibitor because of its ability to selectively target CDKs 4 and 6, key regulators of the cell cycle that trigger cellular progression.

2004

Palbociclib enters Phase 1 clinical trials and the first patient is treated.

2004-2007

Multiple clinical studies are conducted to investigate the safety and anti-tumor activity of palbociclib. While these studies add to the scientific understanding of the compound, they do not demonstrate a strong clinical signal of efficacy for palbociclib in unselected patient populations.

2007

Pfizer researchers in La Jolla, California, begin collaborating with translational oncology scientists at UCLA's Jonsson Comprehensive Cancer Center, including pioneer breast cancer researcher Dr. Dennis Slamon, and clear signals of differentiated activity in pre-clinical models of estrogen receptor positive (ER+) breast cancer are identified.[3]

2008

SEPTEMBER: The first patient is dosed in the Phase 1 portion of PALOMA-1, the Phase 1/2 study evaluating palbociclib in combination with letrozole in ER+, human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer.[4]

2009

DECEMBER: The Phase 2 portion of PALOMA-1 is initiated.[4]

2010

2012

MARCH: Pfizer demonstrates proof of concept for palbociclib, showing that the compound is active in patients with ER+, HER2- breast cancer.

DECEMBER: PALOMA-1 lead investigator Dr. Richard Finn presents interim results from the study at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium (SABCS). The interim results show a statistically significant improvement in progression-free survival (PFS) for palbociclib in combination with letrozole compared to letrozole alone in postmenopausal women with ER+, HER2- locally advanced or metastatic breast cancer.[6]

2013

FEBRUARY: Pfizer initiates PALOMA-2, a global Phase 3 trial in the same population of women as PALOMA-1.[5]

APRIL: Palbociclib is granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA).

SEPTEMBER: Pfizer initiates PALOMA-3, a global Phase 3 trial evaluating palbociclib in combination with fulvestrant for the treatment of women with hormone receptor positive (HR+), HER2- metastatic breast cancer whose disease has progressed after prior endocrine therapy.[7]

NOVEMBER: An additional global Phase 3 trial, PENELOPE-B, evaluating palbociclib in HR+, HER2- early breast cancer is initiated, led by the German Breast Group (GBG).[8]

2014

FEBRUARY: Pfizer announces positive top-line results from PALOMA-1, which demonstrate that adding palbociclib to letrozole significantly prolongs PFS over letrozole alone.

APRIL: Dr. Richard Finn presents detailed results from PALOMA-1 at the American Association of Cancer Research (AACR) Annual Meeting 2014 in San Diego.

AUGUST: Pfizer announces it has completed the submission of a New Drug Application (NDA) to the FDA for palbociclib.

OCTOBER: On October 13, which is Metastatic Breast Cancer Awareness Day, Pfizer announces that its NDA for palbociclib has been accepted for filing and granted Priority Review by the FDA.

DECEMBER: Results from PALOMA-1 are published online ahead of print in *The Lancet Oncology.*

Pfizer Oncology

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[4] Clinicaltrials.gov. Study Of Letrozole With Or Without Palbociclib (PD-0332991) For The First-Line Treatment Of Hormone-Receptor Positive Advanced Breast Cancer. Available at: https://www.clinicaltrials.gov/ct2/show/NCT00721409?term=PD+0332991&rank=10. Accessed on December 22, 2014.

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