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.\(^1\)

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.\(^2\)

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.

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.

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.\(^3\)

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.\(^4\)

DECEMBER: The Phase 2 portion of PALOMA-1 is initiated.\(^4\)

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

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.\(^4\)

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

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