Protocol Title: A Randomized, Open Label, Phase III Trial to Evaluate the Efficacy and Safety of Palbociclib + Anti-HER2 Therapy + Endocrine Therapy vs. Anti-HER2 Therapy + Endocrine Therapy After Induction Treatment for Hormone Receptor Positive (HR+)/HER2-Positive Metastatic Breast Cancer

Target Population: HER-2 Positive and Estrogen Receptor Positive Breast Cancer

Summary: Subjects will be randomized into one of two treatment arms following minimum of 4 and maximum of 8 cycles of induction treatment with anti-HER2 therapy. Arm A subjects will receive the experimental therapy, Palbociclib, in addition to their current anti-HER2 therapy and endocrine therapy. Arm B subjects will continue to receive the anti-HER2 therapy.

Key Inclusion Criteria:
- Age ≥18 years (or per national guidelines)
- Must have histologically confirmed invasive breast cancer that is metastatic or not amenable for resection or radiation therapy with curative intent
- Must have histologically confirmed HER2+ and (ER+ and/or PR+), metastatic breast cancer
- Must agree to provide a FFPE tumor tissue block preferred from primary breast or metastatic site OR ≥ 15 freshly cut unstained slides from such a block, along with pathology report documenting HER2 & HR positivity
- Should be willing to provide representative tumor specimen from metastatic disease if clinically feasible
- ECOG Performance Status 0-1
- Negative serum or urine pregnancy test within 7 Days of randomization in women of childbearing potential
- Resolution of all acute toxic effects of prior induction anti-HER2-based chemotherapy regimen to ≤ 12 Weeks between last dose of chemotherapy-anti-HER2 therapy and randomization are allowed
- May or may not have received neo/adjuvant therapy, but must have a disease-free interval from completion of anti-HER2 therapy to metastatic diagnosis ≥ 6 Months
- Must have received an acceptable, standard, chemotherapy containing anti-HER2 based induction therapy for the treatment of metastatic breast cancer prior to study enrollment
- Participants with a history of treated CNS metastases are eligible, provided they meet specific criteria
- Adequate bone marrow, renal, and liver function
- LVEF ≥ 50% at baseline as determined by either ECHO or MUGA

Key Exclusion Criteria:
- Concurrent therapy with other Investigational Products
- Prior therapy with any CDK 4/6 Inhibitor
- History of allergic reactions attributed to compounds of chemical or biologic composition similar to Palbociclib
- Receiving any medications or substances that are strong inhibitors or inducers of CYP3A isoenzymes within 7 Days of randomization
- Uncontrolled current illness
- Patients on combination antiretroviral therapy, i.e. those who are HIV-positive, are ineligible because of the potential for pharmacokinetic interactions or increased immunosuppression with Palbociclib
- QTc interval > 480 msec, Brugada Syndrome or known history of QTc prolongation or Torsade de Pointes
- Patients with clinically significant history of liver disease, including viral or other known hepatitis, current alcohol abuse, or cirrhosis

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For additional information: https://clinicaltrials.gov/ct2/show/NCT02947685

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