Protocol Title: Phase I / II Dose Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics and Clinical Activity of GSK525762 in Combination with Fulvestrant in Subjects with ER+ Breast Cancer

Target Population: Females, ages 18 and older with Estrogen Receptor Positive Breast Cancer

Summary: This is a combination Phase I and II study, with an aim to evaluate the combination of GSK525762 and fulvestrant in women with advanced or metastatic ER+ breast cancer, who has disease that has progressed after prior treatment with at least one line of endocrine therapy.

Key Inclusion Criteria:
- Females 18 years old and greater with histologically or cytologically confirmed diagnosis of advanced or metastatic adenocarcinoma of the breast.
- History of prior therapy that satisfies one of the following criteria:
  - Disease that progressed during treatment or within 12 months of completion of adjuvant therapy with tamoxifen and/or an aromatase inhibitor (AI).
  - Disease that progressed during treatment or within 1 month after the end of treatment with prior tamoxifen, AI, or CDK 4/6 inhibitor plus letrozole, for advanced/metastatic disease.
- Documentation of ER-positive and/or PR-positive tumor.
- Documentation of HER2-negative tumor.
- Measurable disease as per Response Evaluation Criteria in Solid Tumors (RECIST).
- Adequate organ function as per pre-defined hematologic, hepatic, renal, and cardiac criteria.

Key Exclusion Criteria:
- Prior therapy with more than one line of cytotoxic chemotherapy following diagnosis of advanced/metastatic disease, or disease which has progressed despite prior fulvestrant therapy.
- Concomitant active malignancy other than ER+ breast cancer.
- Therapeutic-dose anticoagulation must be continued and coagulation parameters must be normalized prior to the first dose of GSK525762 and fulvestrant.
- Evidence of severe or uncontrolled systemic disease.
- Subjects with advanced/metastatic, symptomatic, visceral spread, that are at risk of life-threatening complications in the short term including subjects with massive uncontrolled effusions, pulmonary lymphangitis, and over 50% of liver involvement in metastases.
- Symptomatic or untreated leptomeningeal or brain metastases or spinal cord compression.
- Cardiac abnormalities.

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For additional information: https://www.clinicaltrials.gov/ct2/show/study/NCT02964507

IRB# 2017.257.A