**The BEACON Study (BrEaSt Cancer Outcomes With NKTR-102): A Phase 3 Open-Label, Randomized, Multicenter Study of Eliotinotecan Pegol (NKTR-102) Versus Treatment of Physician’s Choice (TPC) in Patients With Locally Metastatic Breast Cancer Previously Treated With Anthracycline, a Taxane, and Capecitabine**

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**Background**
- Nektar Therapeutics is a biopharmaceutical company developing a pipeline of drug candidates that utilizes its advanced polymer conjugation technology to improve the benefits of drugs for patients.

- Eliotinotecan pegol (NKTR-102) is in clinical trials for patients with solid tumors, including breast, ovarian, cervical, and colorectal cancers.

- Eliotinotecan is a next-generation topoisomerase I inhibitor with a unique pharmacokinetic (PK) profile that provides a continuous concentration of active drug with reduced peak concentrations (Figure 1).

- Studies have shown etirinotecan pegol to have a markedly reduced (SN-38 peak concentration) that improves tolerability and a continuous exposure to SN-38 compared to irinotecan.

**Introduction**
- There are currently no topoisomerase I inhibitors approved by the FDA to treat breast cancer. Nektar is currently evaluating the potential of etirinotecan pegol as a treatment option in breast cancer.

- Eliotinotecan pegol is a large molecule, and is believed to penetrate the leaky vasculature within the tumor environment more readily than normal vasculature, increasing exposure of tumor cells to the active anti-tumor agent SN-38 (Figure 3).

- The BEACON study will randomize approximately 840 patients using a 1:1 randomization ratio to receive either single agent etirinotecan pegol (Q3W) 145 mg/m² or TPC.

**The BEACON Study**
- A previous phase 2 study evaluated etirinotecan pegol in two irinotecan schedules (150 mg/m² and 175 mg/m²) for patients with Metastatic Breast Cancer (MBC) against an anthracycline, a taxane or both.

- Approximately 840 patients (420 patients per treatment group) will be required to test the hypothesis that etirinotecan pegol, administered Q3W 145 mg/m² will be non-inferior to TPC in terms of OS and PFS and that the BEACON study design will be used to replicate future studies.

- The BEACON study design is based on a previous phase 2 study performed by Perez et al. that evaluated etirinotecan pegol at 175 mg/m² Q3W and arm A: single agent etirinotecan pegol vs. arm B: TPC in patients with Metastatic Breast Cancer (MBC). The study met the non-inferiority endpoint for OS with a hazard ratio of 0.90 (p=0.035).

**Key Patient Entry Criteria**
- Adult females with histologically or cytologically confirmed carcinoma of the breast.
- Patients meeting the non-inferiority or inferiority criteria for OS and PFS.
- Patients must have received a minimum of 2 and a maximum of 5 prior chemotherapy regimens for the treatment of breast cancer.
- Patients with brain metastases may be eligible, provided local therapy was completed and use of corticosteroids for this indication discontinued for at least 3 weeks prior to randomization.

**Statistical Plan and Methods**
- Based on better tolerability, OS and PFS, the q3w 145 mg/m² schedule showed similar ORR.

**Protocol Procedures**
- Investigator determination of response and progression by RECIST v1.1.

**Accrual**
- BEACON is open for enrollment and enrollment is expected to be completed by December 2013.

**Regions**
- Approximately 190 sites in North America, Europe and Asia.

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**References**