PHASE II STUDY OF PALBOCICLIB (PD-0332991) + LETROZOLE VS LETROZOLE ALONE IN FIRST-LINE ER+/HER2- ADVANCED BREAST CANCER

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Background: Palbociclib (PD-0332991), a selective cyclin-dependent kinase (CDK) 4/6 inhibitor, prevents DNA synthesis by blocking cell cycle progression. Preclinical studies identified the luminal ER+ subtype as being associated with sensitivity to palbociclib (Finn et al. 2009). This randomized phase II study comparing palbociclib plus letrozole (P + L) vs letrozole alone (L) was initiated after determining the recommended phase II combination dose (P 125 mg/day on Schedule 3/1 + L 2.5 mg/day).

Methods: The phase II portion of study had 2 parts: 1) postmenopausal patients (pts) with ER+/HER2- advanced breast cancer (BC); 2) in addition to ER+/HER2- criteria, pts were screened for CCND1 amplification and/or loss of p16 by FISH. In both parts, pts were randomized 1:1 to P + L or L. Pts continued on assigned treatment until disease progression, unacceptable toxicity, or consent withdrawal, and were followed for tumor assessments every 8 weeks. The primary endpoint was PFS.

Results: There were 66 pts randomized in Part 1 and 99 pts in Part 2. Preliminary results previously reported from Part 1 (IMPAKT BC Conference, abstract 292, Finn et al. May 2012) demonstrated a significant improvement in median PFS in the P + L vs L arm (hazard ratio [HR] = 0.35; 95% confidence interval [CI], 0.17-0.72; P = .006). At interim analysis with additional 99 pts in Part 2 (total phase II N = 165), substantially significant improvement in median PFS (26.1 vs 7.5 months, respectively) continues to be observed at second interim analysis (HR = 0.37; 95% CI, 0.21-0.63; P < .001).

Objective response rates were 34% vs 26% for P + L arm (n = 84) vs L arm (n = 81), respectively. Clinical benefit rates were 70% vs 44%, respectively. The most common treatment-related adverse events in the P + L arm were neutropenia, leukopenia, anemia, and fatigue.

Conclusions: P + L was well tolerated and had encouraging clinical benefit in postmenopausal pts with ER+/HER2- advanced BC. Phase III study in this setting will commence in 2013.