Supplemental Figure & Table Legends

Supplemental Figure 1: Lapatinib induces a homologous recombination repair defect in 
HER2+ breast cancer cell. Homologous recombination (HR) repair capacity was measured in 
BT-474 human HER2+ breast cancer cells by assessing radiation-induced rad51 foci, a well 
characterized marker for HR repair. Briefly, cells were treated with 10nM lapatinib or vehicle 
control, and 16 hours later were exposed to mock or 4Gy irradiation and subsequently subjected 
to immunofluorescence staining for rad51 foci. Shown is the representative data of 3 
independent experiments the % of cells (mean +/- SEM) with rad51 foci (**p<0.01 compared to 
vehicle).

Supplemental Figure 2: Homologous recombination repair capacity in MCF7 cells. HR 
repair capacity in MCF7 breast cancer cells was measured by assessing radiation-induced rad51 
foci. Briefly, cells were exposed to mock or 4Gy irradiation (IR) and subsequently subjected to 
immunofluorescence staining for rad51 foci. Shown is the representative data of 2 independent 
experiments performed in triplicate the % of cells (mean +/- SEM) with rad51 foci (**p<0.01 
compared to vehicle).

Supplemental Figure 3: MCF7 HER2 cells but not its isogenic MCF7 NEO controls are 
susceptible to the PARP inhibitors ABT-888 and AZD-2281. Viability of (A) MCF7 HER2 
and (B) MCF7 NEO cells was measured using ATP-Lite assay following 24 hour treatment with 
various doses of ABT-888, AZD-2281, or vehicle control. Shown is the average fold change in 
cell viability (+/- SEM) from at least three independent experiments performed in quadruplicate.
(**p<0.01). (C) Verification of reduced HER2 levels following siRNA transfection. BT-474, MDA-MB-361, and MCF7 HER2 were transfected with either HER2 siRNA (HER2) or scrambled control siRNA (Scr). 24 hours later, HER2 levels were assayed via immunoblotting. Actin was used as a loading control. Shown is a representative western blot of at least 3 independent experiments.

Supplemental Figure 4: ABT-888 reduces levels of the NFκB regulated protein cMyc.
Exponentially growing HER2 overexpressing BT-474 and MDA-MB-361 breast cancer cells were seeded and subjected to either 10μM ABT-888 or vehicle control. Protein lysates were harvested 24 hours following the treatment and levels of the NFκB regulated protein cMyc was detected by immunoblot analysis. Actin was used as a loading control. Shown is a representative western blot.

Supplemental Figure 5: Verification of the expected effects of p65 or IκBα overexpression on NFκB transcriptional activity in breast cancer cells. (A-D) Cells were seeded and co-transfected with p65 DsRed or vector control and the NFκB-driven luciferase plasmid NFκB-MetLuc2 or its vector control MetLuc2. 24 hours following transfection, luciferase activity was assayed in (A) BT-474, (B) MDA-MB-361, (C) MCF7 HER2 and (D) MCF7 NEO cell lines. (E-H) Cells were seeded and co-transfected with IκBα GFP or vector control and the NFκB-driven luciferase plasmid NFκB-MetLuc2 or its vector control MetLuc2. 24 hours following transfection, luciferase activity was assayed in (E) BT-474, (F) MDA-MB-361, (G) MCF7 HER2 and (H) MCF7 NEO cell lines. Shown is the average fold change in reporter activity (+/- SEM) from at least three independent experiments performed in triplicate (**p<0.01).
Supplemental Table 1: Gene cluster, ER, PR and p53 status of the various HER2+ breast cancer cell lines ((3) and COSMIC database).