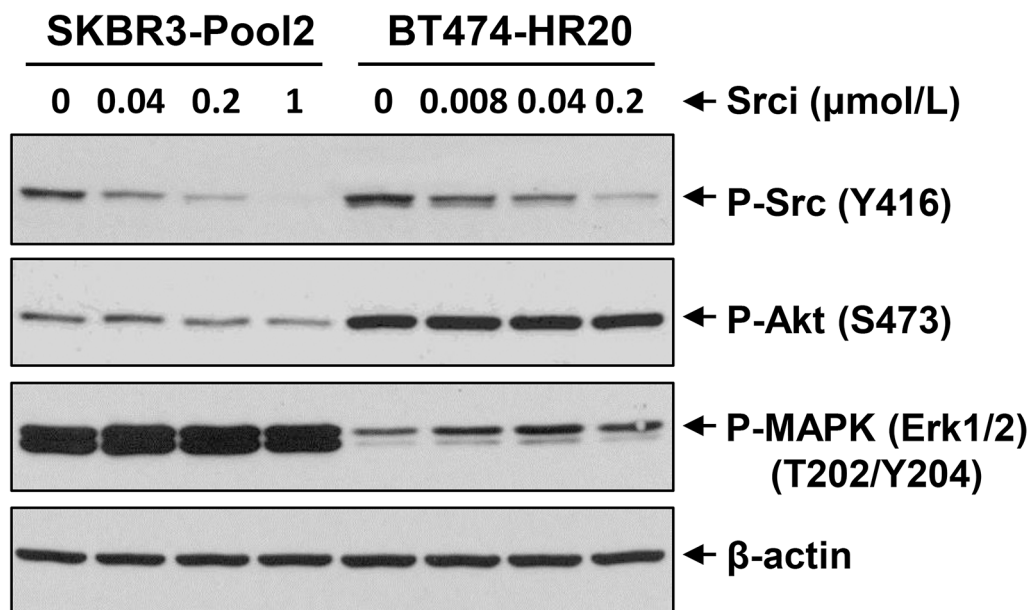
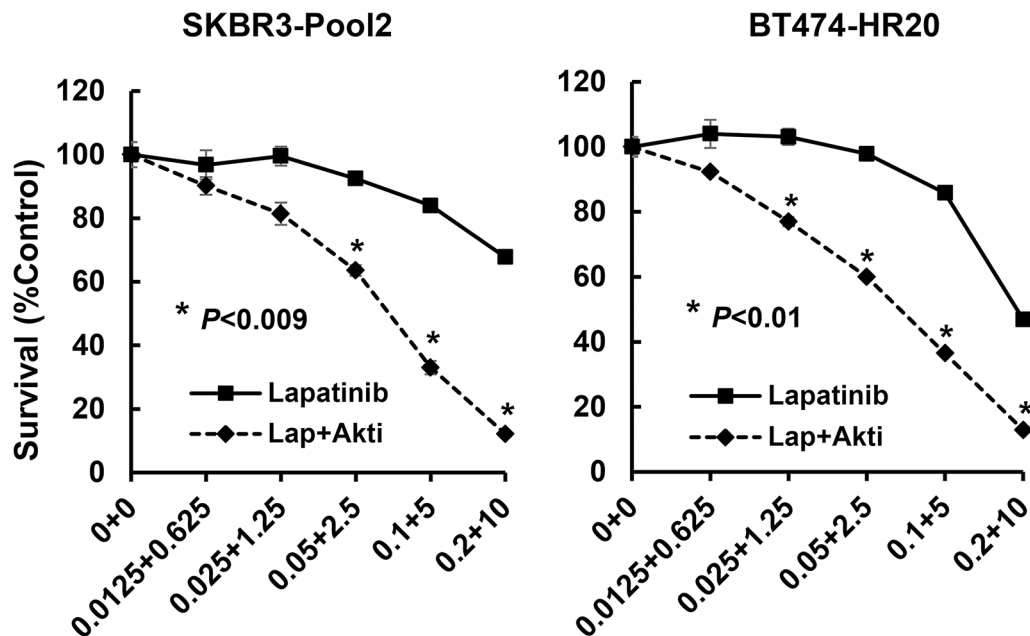


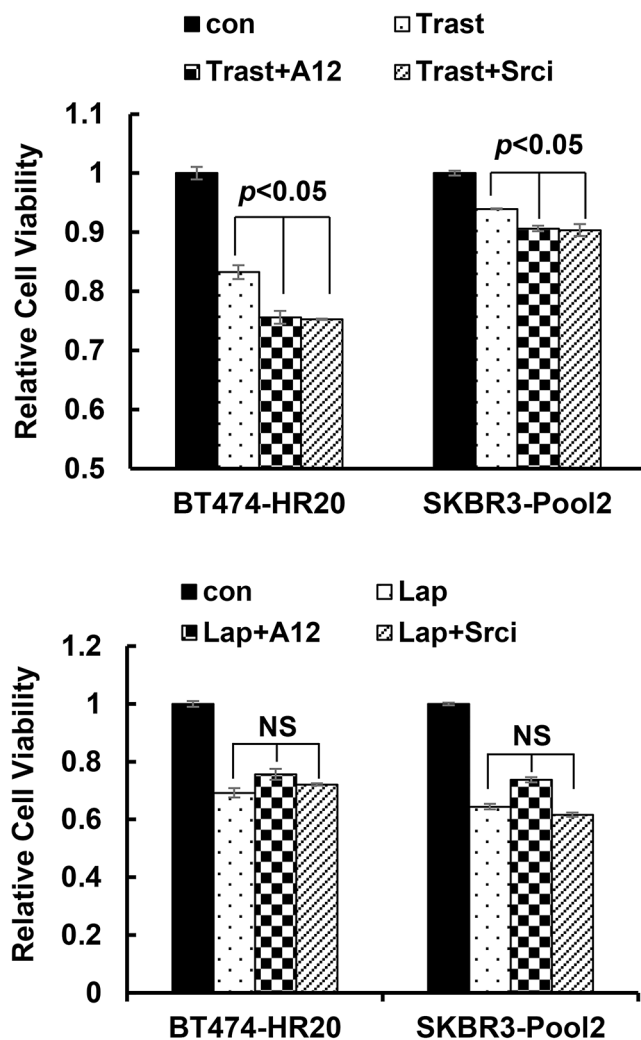
## SUPPLEMENTARY FIGURES



**Supplementary Figure S1: The specific inhibitor of Src reduces P-Src levels of trastuzumab-resistant breast cancer cells in a dose-dependent manner.** SKBR3-Pool2 and BT474-HR20 cells untreated or treated with indicated concentrations of the Src inhibitor (Srci) Saracatinib for 24 hr were collected and subjected to western blot analyses of P-Src (Y416), P-Akt (S473), P-MAPK (Erk1/2) (T202/Y204), or  $\beta$ -actin.



**Supplementary Figure S2: The Akt inhibitor in combination with lapatinib shows a concentration dependent additional inhibitory effect on trastuzumab-resistant breast cancer cells.** SKBR3-Pool2 and BT474-HR20 cells were plated onto 96-well plates. After 24 hr, the culture medium was replaced with 0.1 ml fresh medium containing 0.5% FBS or the same medium containing a series of doses of lapatinib (0.0125, 0.025, 0.05, 0.1, 0.2  $\mu\text{mol/L}$ ) in combination with the indicated concentrations of Akti (0.625, 1.25, 2.5, 5, 10  $\mu\text{mol/L}$ ) for another 72 hr. The percentages of surviving cells from each cell line relative to controls, defined as 100% survival, were determined by reduction of MTS. Bars, SD. Data show a representative of three independent experiments.



**Supplementary Figure S3: Both the anti-IGF-1R Ab A12 and Src inhibitor significantly enhances trastuzumab-, but not lapatinib-mediated growth inhibition in trastuzumab-resistant breast cancer cells.** SKBR3-Pool2 and BT474-HR20 cells were plated onto 96-well plates. After 24 hr, the culture medium was replaced with 0.1 ml fresh medium containing 0.5% FBS or the same medium containing trastuzumab (20  $\mu\text{g/ml}$ )/lapatinib (0.1  $\mu\text{mol/L}$ ), trastuzumab/lapatinib combined with the anti-IGF-1R Ab (Trast/Lap+A12, 10  $\mu\text{g/ml}$ ), trastuzumab/lapatinib combined with Src inhibitor (Trast/Lap+Srci, 0.2  $\mu\text{mol/L}$ ) for another 72 hr. The viability of cells from each cell line relative to controls, defined as 1, were determined by reduction of MTS. Bars, SD. Data show a representative of three independent experiments.