

Supplementary Figure legends

Supplementary Figure S1. BEZ235 inhibits phosphorylation of PI3K/mTOR. Western blot showing phospho-AKT (Ser473) and phospho-S6 (Ser235/236) expression in serum-starved H460 and A549 cells treated with indicated doses of BEZ235 and stimulated with IGF-1 (100 ng/ml).

Supplementary Figure S2. TUNEL assay in H460 and A549 cells after 48 hours treatment. H460 cells irradiated with 20 Gy were used as a positive control.

Supplementary Figure S3. BEZ235 does not induce abnormal mitoses in irradiated H460 and A549 cells. Number of abnormal mitoses at 48 hours following indicated treatment. An average of 70 cells per group was counted to determine mean +/- SEM.

Supplementary Figure S4. IL-8, MIF and PAI-1 levels in supernatant from H460 and A549 cells after 96 hours treatment. Supernatant volumes were normalized to cell number and analyzed using cytokine antibody arrays.

Supplementary Figure S5. Representative immunofluorescence images of γ H2AX (Ser139) foci in H460 and A549 cells at indicated time points after 4 Gy radiation (x 60 magnification). *Green*, γ H2AX foci. *Blue*, DAPI staining. *Below*, Number of γ H2AX foci per cell. Data are mean +/- SEM from three independent experiments. ***, $P < 0.001$ **, $P < 0.01$ *, $P < 0.05$.

Supplementary Figure S6. Representative immunofluorescence images of phospho-ATM (Ser1981) foci in H460 and A549 cells at 30 minutes after 10 Gy dose of radiation (x 60 magnification). *Green*, phospho-ATM foci. *Blue*, DAPI staining.

Supplementary Figure S7. Induction of accelerated senescence by BEZ235 in irradiated cells is p53-dependent. *A*, Representative images of SA- β Gal activity cells at 48 hours after 10 Gy radiation (x 200 magnification). *B*, Western blot showing total p53 and p21 levels in p53-inducible H1299 cells exposed to indicated concentrations ($\mu\text{g/ml}$) of Ponasterone A (PoA) for 48 hours. *C*, Representative images of SA- β Gal activity cells in p53-inducible H1299 cells 48 hours after 10 Gy radiation (x 200 magnification). PoA (0.5 $\mu\text{g/ml}$) was added to growth medium 8 hours prior to irradiation and maintained in growth medium until cells were fixed and stained.

Supplementary Figure S8. Representative immunofluorescence images of phospho-DNA-PKcs (Thr2609) foci in H460 cells at 30 minutes after 10 Gy radiation (x 60 magnification). *Green*, phospho-DNA-PKcs foci. *Blue*, DAPI staining.