**Supplemental figure legends**

**SUPPL FIG 1**: **A)** Only yeast transfected with both FAT domain/GAL4DBD +DEPTOR/GAL4 AD show growth on selective media. Yeast transfected w/ either construct alone can not grow. Two separate transformations shown. **B)** Four initial ‘hits’ from drug screen

**SUPPL FIG 2**: **A)** 8226 cells treated with or w/o NSC 126405 for 6 hrs, followed by immunoprecipitation of mTOR (or control IgG). Immunoprecipitates immunoblotted for expression of mTOR and DEPTOR. Input shown for DEPTOR, mTOR and tubulin expression. **B)** 8226 cells treated with DMSO, pp242 or NSC 126405 and then tested for 4E-BP1 phosphorylation by flow cytometry. **C)** Summarized data from all 3 treatment groups

**SUPPL FIG 3**: **A)** Relative DEPTOR expression in MMCLs and hepatocellular carcinoma (HCC) cell lines in a representative experiment (upper panel) and means+/-SD of 3 experiments (lower bar graph); **B)** Relative sensitivity of U266 and FR4 MMCLs vs DEPTOR-expressing JHH7, HUH-1 or HIH7 HCCs; data are means +/- SD (n=3); Asterix demonstrates significant (p<0.05) decreased cell survival in MMCLs vs HCC cells ; **C)** MMCLs or HUH-1 HCC cells following shRNA transfection with control (scramble) or DEPTOR-targeted lentivirus; **D)** Percent apoptosis at 3 or 4 days following DEPTOR silencing in MMCLs or HUH-1 HCC; Data are means +/- SD, n=4 following transfection with control shRNA (scr) or shRNA targeting 2 separate sequences of DEPTOR.

**SUPPL FIG 4**: **A)** 8226 cells treated +/- NSC 126405 for 18 hrs followed by immunoblot assays. Fold BIM increase is determined by densitometry, mean of 3 experiments; **B)** Control (shSCR) or RAPTOR-silenced 8226 cells (shRAPTOR) treated +/- NSC 126405 for 18 hrs followed by immunoblot assays. Fold BIM increase is mean of 3 experiments.

**SUPPL fig 5:** Growth of individual tumors from mice injected with vehicle (control) or drug at 10 or 20 mg/kg

**SUPPL FIG 6**: PBLs obtained from 3 normal individuals and incubated with increasing concentrations of NSC 126405 for 72 hrs. Surviving viable cells enumerated. Data are % of control (no drug B), mean+/-SD, n=3.