Supplementary Figure 1: GDC-0941 inhibits hypoxic signaling in drug sensitive U87 tumors. Western blot data for expression of HIF-1 and CA-IX in U87 (A) and HCT116 (B) tumors, with densitometric analysis in C and D respectively (Average ± SEM, *p<0.01). Data are representative of 4 independent mice dosed with vehicle or 50 mg/kg GDC-0941 twice daily for 8 days. β-actin was used as the loading control.

Supplementary Figure 2: Acute dosing with GDC-0941 leads to an increase in apoptotic signaling in in sensitive tumors. **A**, Western blot data for expression of c-PARP in U87 tumors. Each lane represents a tumor dosed with vehicle or 50 mg/kg GDC-0941 for 18 hours. β-actin was used as the loading control. **B,** Western blot data for expression of c-PARP in HCT116 tumors. Each lane represents a tumor dosed with vehicle or 50 mg/kg GDC-0941 for 18 hours. β-actin was used as the loading control.

Supplementary Figure 3: Uptake of [^{18}F]-FDG decreases significantly after ~18h of GDC-0941 treatment in U87, but not HCT116, tumors. **A**, Average maximum normalized uptake time activity curves for treated (closed symbol) and untreated (open symbol) U87 tumors,*p<0.05. **B**, maximum intensity projections of data from 70-75 minutes after injection of [^{18}F]-FDG showing treated and untreated U87 xenografts, with tumor indicated by dotted circle. **C**, Average maximum normalized uptake time activity curves for treated (closed symbol) and untreated (open symbol) HCT116 tumors. **D**, maximum intensity projections of data from 70-75 minutes after injection of [^{18}F]-FDG showing treated and untreated HCT116 xenografts, with tumor indicated by dotted circle. **E**, Average tumor volume of U87 xenografts treated with 50mg/kg GDC-0941(n=4) or vehicle control (n=4) for 8 days,*p<0.01. **F,** Average tumor volume of HCT116 xenografts treated with 50mg/kg GDC-0941 (n=2) or vehicle control (n=4) for 8 days,*p<0.01. Data represent average tumor volume ± SEM.

Supplementary Figure 4: Chronic dosing with GDC-0941 leads to an increase in MAP-kinase pathway signaling in sensitive tumors. A, Western blot data for expression of p-ERK in U87 tumors. Data are representative of 4 independent mice dosed with vehicle or 50 mg/kg GDC-0941 twice daily for 8 days. β-actin was used as the loading control.