Supplementary Figure Legends

Supplementary Figure 1
Analysis of the viable tumour volume at the first endpoint of the HCT116 and HT29 xenograft and spheroid experiments revealed that the CAIX expressors had increased viable tissue in HCT116 (A) xenografts (40% more viable tissue at day 14, ***p<0.01, n=10) and (B) spheroids (16% more viable tissue at day 13, **p<0.01, n=5) and HT29 (C) xenografts (34% more viable tissue at day 20, p<0.05, n=5) and (D) spheroids (45% more viable tissue at day 16, *p<0.01, n=5).

Supplementary Figure 2
Analysis of CA9 RNA expression in U87 xenografts untreated and with chronic Bevacizumab treatment. Bevacizumab treatment increased CA9 expression (***p<0.001, n=5).

Supplementary Figure 3
Bar chart of scoring of immunohistochemistry and representative immunohistochemistry images of HT29 shCA9 and EV xenografts with and without Bevacizumab treatment. CAIX expression (**p<0.01 ***p<0.001, n=5), proportion of necrosis (*p<0.05, n=5) and cleaved caspase 3 expression (*p<0.05, n=5) were significantly different between EV and shCA9. CAIX expression (EV ***p<0.001, n=5), HIF1 (shCA9 *p<0.05, n=5, EV**p<0.01, n=5), cleaved caspase 3 expression (shCA9 **p<0.01, n=5, EV *p<0.05, n=5) and CD34 (shCA9 *p<0.05, n=5, EV *p<0.05, n=5) expression were significantly different between Bevacizumab treated and untreated xenografts. CAIX, HIF1, cleaved caspase 3, KI67 and CD34 expression staining is dark brown. H&E, dark pink denotes viable tissue, light pink denotes necrosis. N denotes areas of necrosis. Arrows point to positive staining. Scale bars represent 200μm on 5x images and 100μm on 20x images.

Supplementary Figure 4
Bar chart of scoring of immunohistochemistry and representative immunohistochemistry images of HT29 xenografts with and without acetazolomide and/or Bevacizumab treatment. CAIX expression (vehicle (DMSO) *p<0.05, n=5;
ATZ **p<0.01, n=5) and CD31 (vehicle (DMSO) *p<0.05, n=5; ATZ **p<0.01, n=5) were significantly different between PBS and Bevacizumab treated xenografts. The amount of necrosis was significantly different between vehicle and ATZ treated xenografts (**P<0.001, n=5). CAIX, and CD31 expression staining is dark brown. H&E, dark pink denotes viable tissue, light pink denotes necrosis. N denotes areas of necrosis. Arrows point to positive staining. Scale bars represent 200μm on 5x images and 100μm on 20x images.