

## **Description of Additional Supplementary Files**

File Name: Supplementary Data 1

Description: Images and accompanying image cytometry analysis for all tumors analyzed in Figure 1

File Name: Supplementary Data 2

Description: Results from the targeted therapy screen in HCC1143 and SUM149PT cell lines

File Name: Supplementary Data 3

Description: Tables describing the genesets used in the study and all raw GSEA results

File Name: Supplementary Data 4

Description: A zip file containing all raw .vcf files from Mutect analyses and .seg files from LP-WGS copy number alteration analyses

File Name: Supplementary Data 5

Description: VIPER results and pathway ontology analyses

File Name: Supplementary Data 6

Description: SciATAC-seq DNA-binding domain motif enrichment analysis