Supplementary Figure 1. Extended data related to Figure 1.

A, Violin plot depicting EZH2 mRNA levels in CRC tumors separated by mutant KRAS allele status and matched normal colonic tissue. Others include other mutant KRAS alleles (G12A, G12R, G12S, A59, A146).

B, Schematic depicting for treatment timeline for all in vitro experiments. C, Proliferation assays in the indicated cells conducted via CellTiter-Glo (LOVO, SW620, SW1116) or manual cell counting (SK-CO1, LS513) after treatment with DMSO or 5 μM tazemetostat and increasing concentrations of trametinib. Graphs depict log2 fold change in viability or cell number after 5 days of treatment. D, Synergy plot depicting Gaddum’s non-interaction model (HSA) for SW403 cells treated with EZH2i and/or MEKi. E, Graph depicting normalized counts of EZH2 mRNA in CRC cell lines from CCLE RNA-seq gene expression data. F, Proliferation assay in HIEC6 (human intestinal epithelial cells) treated with the indicated compounds for 5 days. P value = ns, as determined by unpaired t test. G, percentage of caspase 3/7+ SW403 cells after treatment with the indicated treatments over time as measured by Incucyte live cell imaging. 4 images were taken per technical replicate. P value determined by two-way ANOVA between MEKi, and combo treated cells. H, (Left) Proliferation assay in LOVO cells after treatment with the indicated compounds, trametinib or binimetinib as an alternate MEK inhibitor for 5 days. (Right) Immunoblot from LOVO protein lysates treated with the indicated treatments. I, (Left) Proliferation assay in LOVO cells after treatment with the indicated compounds (EZH2i = tazemetostat or EEDi = MAK683) for 5 days. (Right) Immunoblot from LOVO protein lysates treated with the indicated treatments. J, Proliferation assay in HT29 cells (harboring BRAFV600E mutations) after treatment with EZH2i, and/or trametinib (MEKi), encorafenib (BRAFi) and/or cetuximab at the indicated concentrations for 5 days. Note that data from DMSO, EZH2i, and one concentration of MEKi is also represented in Fig. 1I. K, Proliferation assay in SW48 cells harboring non-oncogenic KRAS or BRAF mutations after treatment with the trametinib (MEKi) at the indicated concentrations for 5 days. Note that data from DMSO, EZH2i, and one concentration of MEki is also represented in Fig. 1J. Unless otherwise indicated, for all subfigures bars represent mean ± SD, p value measured by unpaired T-test and P values are indicated with *, **, ***, and **** to represent values of <0.05, <0.01, <0.001, and <0.0001 respectively.