**Supplemental Figure 1:** Co-genomic alterations occurring in the 47 patients treated with binimetinib.

**Supplemental Figure 2:** (A) Kaplan-Meier estimates of OS; (B) PFS in all 47 patients treated with binimetinib.

**Supplemental Figure 3:** Kaplan-Meier estimates of PFS comparing patients with binimetinib-treated colorectal and non-colorectal cancer.

**Supplemental Figure 4:** Kaplan-Meier estimates of PFS comparing patients with binimetinib-treated colorectal, cholangiocarcinoma, and non-colorectal/cholangiocarcinoma cancer.

**Supplemental Figure 5:** Computed tomography (CT) scans of a codon 61 *NRAS*-mutated colorectal cancer patient at baseline and after 4 cycles of binimetinib treatment.

**Supplemental Figure 6:** (A) Kaplan-Meier estimates of OS; (B) PFS comparing binimetinib-treated patients with tumors harboring codon 61 *NRAS* mutations to binimetinib-treated patients harboring codon 12 or 13 *NRAS* mutations.

**Supplemental Figure 7:** (A) Kaplan-Meier estimates of OS; (B) PFS comparing binimetinib-treated patients with non-colorectal cancer with tumors harboring codon 61 *NRAS* mutations to patients with non-colorectal cancer harboring codon 12 or 13 *NRAS* mutations.

**Supplemental Figure 8**: Kaplan-Meier estimates of OS comparing colorectal cancer patients in the TCGA database harboring codon 61 *NRAS*-mutations compared to colorectal cancers patients harboring codon 12 or 13 *NRAS*-mutations.

**Supplemental Figure 9:** Comparison of MEK inhibitor sensitivity between codon 61 *NRAS*-mutated cell lines and codon 12/13 *NRAS*-mutated cell lines in the Cancer Cell Line Encyclopedia. MEK inhibitors evaluated include Trametinib (A), Selumetinib (B), and PD318088 (C). Drug sensitivity was measured by analyzing the area under the fitted dose response curve (AUC) and significance was determined using two-tailed Welch’s t-test.