



Figure S3

**Supplemental Figure 3. Unique Enhancer Remodeling and Transcriptional Response Persists Following Chronic Trametinib Treatment.** (A) Motif analysis of H3K27ac peaks significantly upregulated after 14 days treatment in POS cells. (B) Motif analysis of H3K27ac peaks significantly upregulated at D14 in NEG cells in response to chronic trametinib treatment. (C) Row-mean normalized heatmap of dynamic genes in POS cells that change greater than two-fold during chronic treatment. Expression relative to row mean colored from low (white) to high (dark blue). Enrichr GO analysis of the molecular function of gene expression classes shown at right. (D) Row-mean normalized heatmap of dynamic genes in NEG cells that change greater than two-fold during chronic treatment. Expression relative to row mean colored from low (white) to high (maroon). Enrichr GO analysis of the molecular function of gene expression classes shown at right. (E) Row-mean normalized heatmap of PIP3 Binding, row max shown in dark blue, row min shown in white. (F) Row-mean normalized heatmap of PI3K Regulator Activity, row max shown in dark blue, row min shown in white. (G) Row-mean normalized heatmap of PDGF Binding, row max shown in maroon, row min shown in white. (H) Row-mean normalized heatmap of MAPK Y/S/T Phosphatase Activity, row max shown in maroon, row min shown in white. (I) Row-mean normalized heatmap of Integrin Binding, row max shown in maroon, row min shown in white. (J) Row-mean normalized heatmap of Actin Binding, row max shown in maroon, row min shown in white. (K) Venn diagram of the intersection of upregulated genes (left) in POS (blue) and NEG (red) cells. Venn diagram of the intersection of downregulated genes (right) in POS (blue) and NEG (red) cells.