



**Supplementary Figure 4: Combination of MEK inhibitor with venetoclax is synergistic across RAS pathway mutant acute leukemia cell lines.** Synergy was assessed by Chou-Talalay combination index (CI) across the indicated cell lines. Normalized isobolograms depict CI scores over a range of concentrations. The coordinates of the CI scores are  $d_1/Dx_1$  and  $d_2/Dx_2$ , where  $Dx_1$  is the concentration of drug 1 (trametinib) that alone produces the fractional inhibition effect  $x$ , and  $Dx_2$  is the concentration of drug 2 (venetoclax) that alone produces the fractional inhibition effect  $x$ . The red line displayed is the line of additivity. Points below the line are synergistic and above the line are antagonistic. Cell viability was measured at 3 days of combination treatment using an ATP-based assay.