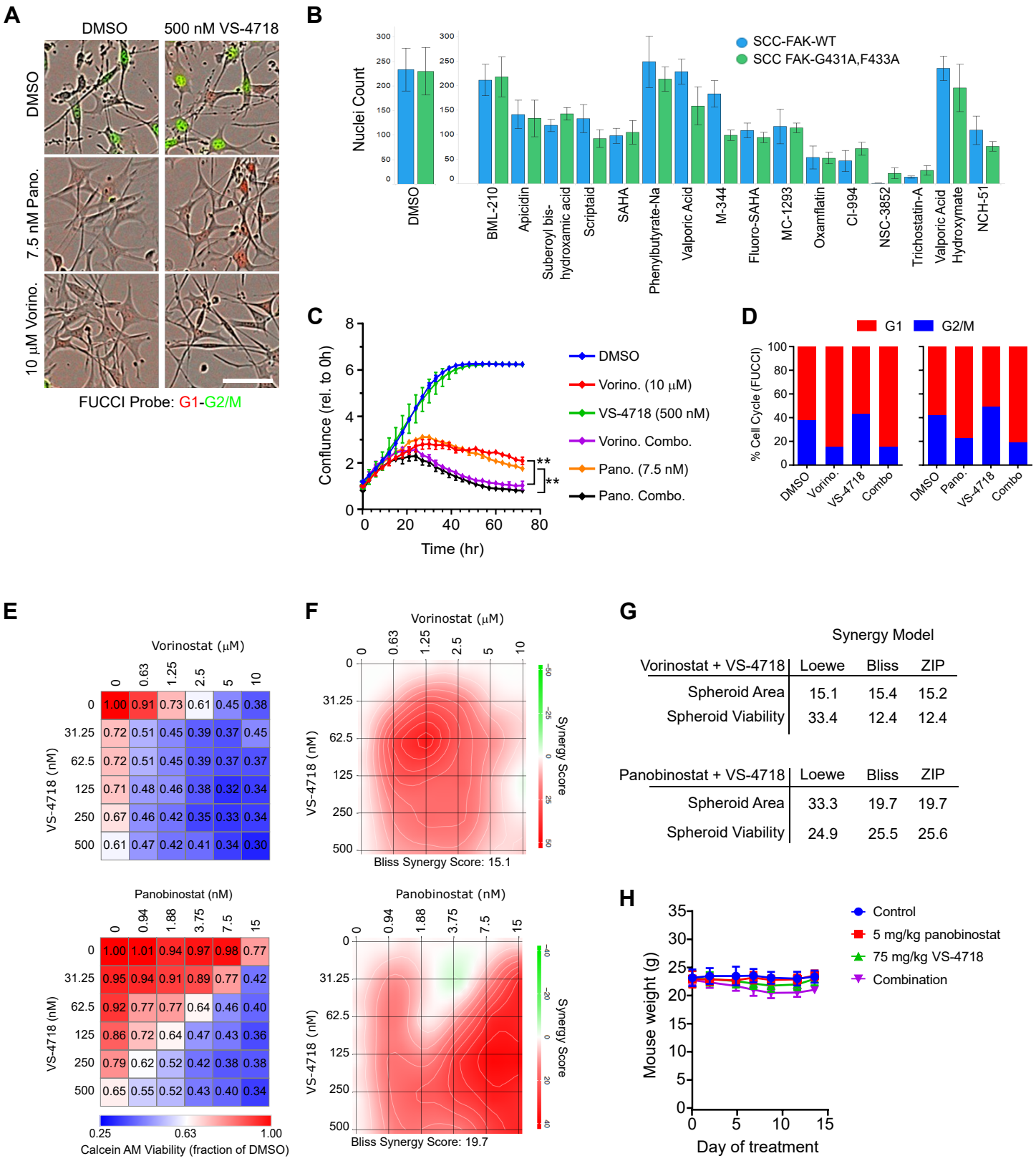

Vorinostat + VS-4718	Loewe	Bliss	ZIP
Spheroid Area	15.1	15.4	15.2
Spheroid Viability	33.4	12.4	12.4

Panobinostat + VS-4718	Loewe	Bliss	ZIP
Spheroid Area	33.3	19.7	19.7
Spheroid Viability	24.9	25.5	25.6

Supplementary Figure S2. Analysis of HDAC and FAK inhibition in SCC cells. **A**, SCC FAK-WT FUCCI cells treated with the indicated drugs for 24 hours. Red cells are in the G1 and green are G2/M phases of the cell cycle, respectively. Scale bar is 50 mm. **B**, Quantification of nuclei counts from compound screen. Mean ± SD is shown (n = 6 images). **C**, SCC FAK-WT cell confluence quantified using the Incucyte Zoom microscope. Mean cell confluence is displayed ± SEM (n = 2 independent experiments). NS, not significant. Stastical significance after 72 hours drug treatment was determined by one-way ANOVA followed by a Tukey's multiple comparison test. **, P<0.01. **D**, Quantification of cell cycle stage from FUCCI reporter at 24 hours post drug treatment. Mean population percentages of the cell cycle stage are shown (n = 2 independent experiments). **E**, Drug treated SCC FAK-WT spheroid viability (Calcein AM) following vorinostat (top) or panobinostat (bottom) treatment in combination with VS-4718 for 7 days. (n = 3 independent experiments) **F**, Example Bliss synergy map for SCC FAK-WT spheroid area and treated with vorinostat (top) and panobinostat (bottom) in combination with VS-4718. Calculated from mean spheroid area values shown in Fig. 2E. **G**, Summary table of synergy scores for Bliss, Loewe and ZIP models for HDAC and FAK inhibitor combinations. **H**, Mouse body weight following compound treatment from day 0. Mean ± SD (n = 5 mice per group). For **C, D, E** and **F**, data are normalized to DMSO.