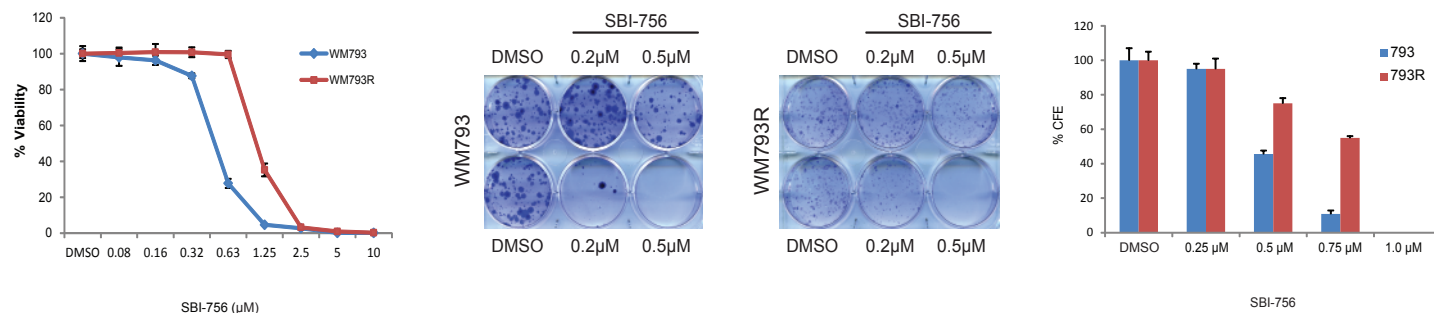
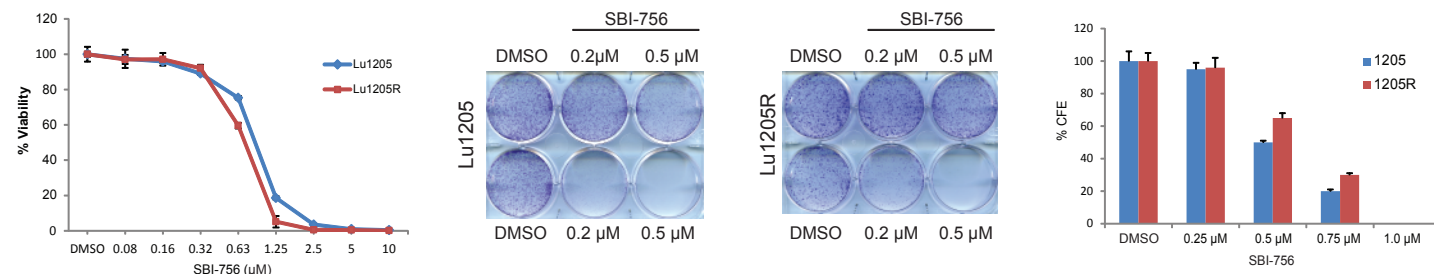


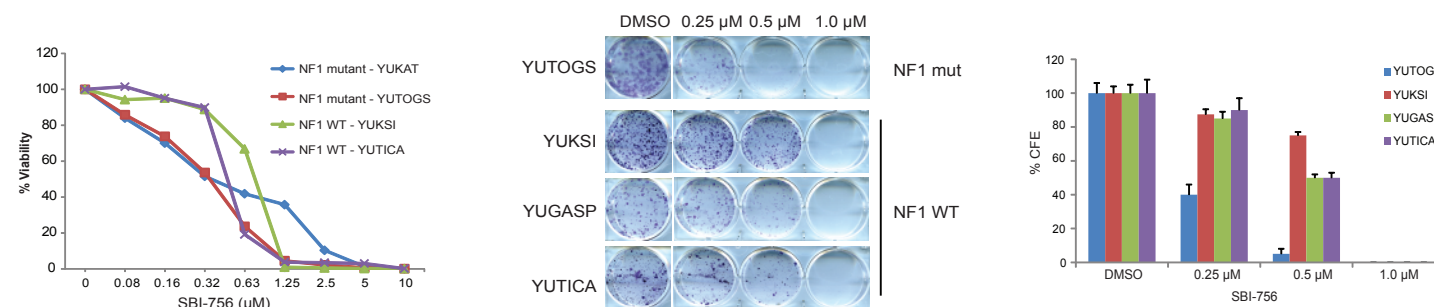
A



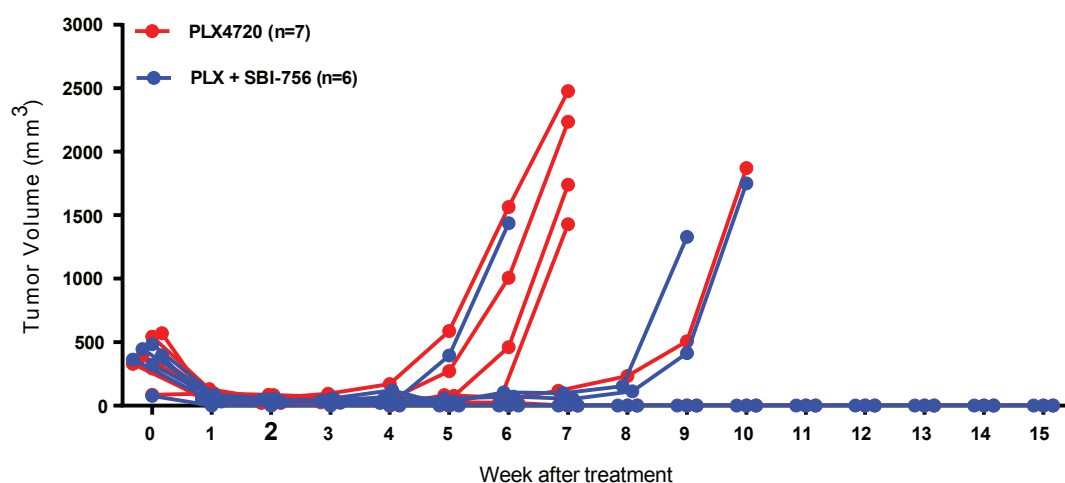
B



C



D



Supplementary Figure 4. SBI-756 inhibits both 3D and *in vivo* growth of NF1-mutant, BRAFi-resistant melanoma. (A,B) SBI-756 effectively overcomes melanoma BRAFi resistance. Indicated parental and BRAFi-resistant melanomas WM793 (A) and LU1205 (B), were monitored for viability (left panel) colony forming efficiency (CFE, middle and quantification on right panels) to SBI-756 at indicated concentrations; Experiments were performed as indicated in Fig. 4A. (C) Experiments performed similar to those outlined in panels A,B, except that cell lines are NF1-mutant or WT primary melanoma cultures. Viability shown on left panel whereas CFE in middle and right (quantification) panels. (D) Combined administration of SBI-756 and a BRAFi delays relapse of BRAFi-resistance melanoma in mice subjected to treatment when tumor size was larger. Analysis was performed as in Fig. 4C, except that drugs were administered once tumors reached ~500 mm<sup>3</sup>.