



Supplemental Figure Legends:

Figure S1:

String analysis of synovial sarcoma selective genes identified in our study is shown. Nodes indicate genes, edges indicate connections between the genes as represented by participation in common protein complexes identified in deposited experimental data from other groups.

Figure S2: Correlation matrix of replicates from the *in vitro* and *in vivo* screen is shown. Rep = replicate. Day 0 = start of the assay and D14 is the end of the *in vitro* assay.

Figure S3: Immunoblotting for total SUMO2 in lysates from SYO1 cells treated with TAK-981 compared to DMSO control are shown with vinculin as the loading control.

Figure S4: Fold changes (Y-axis) of SUMO2 transcripts in doxycycline-treated relative to DMSO-treated HS-SY-II cells as measured by quantitative PCR are shown with 5 independent SUMO2-targeting shRNAs is shown (X-axis). Doxycycline was used to induce the shRNA from a tetracycline-responsive promoter.

Figure S5: Immunoblot analysis of whole-cell lysates from 1273/99 cells treated with TAK-981 and probed for the SS18-SSX2 fusion protein are shown. Vinculin is shown as a loading control.

Figure S6: Integrated genome viewer (IGV) tracks for the SS18-SSX fusion and H2AK119ub in DMSO or TAK-981 treated SYO1 cells along with corresponding RNAseq tracks are shown for SOX8, a SS18-SSX target gene

Figure S7: Weights of mice (grams, Y-axis), treated with TAK-981 (scarlet) compared to DMSO (black) lines are shown at various time intervals (days, X-axis).