Supplemental Figure 1. Cytokine profile of siNTC and siSV1 treated mice. To determine whether there was a non-specific, siRNA-mediated pro-inflammatory effect in mice we analyzed serum from mice treated with 6 doses of siSV1 (3mg/kg) and assayed for IFNγ, TNFα or interleukins 1b, 2, 4-6, 10 and 12 (SearchLight Cytokine Array; ThermoFisher). No significant differences between treated and untreated animals was detected.

Supplemental Figure 2. siSV1 uptake in ovarian intraperitoneal nodules. After implantation of SKOV3 cells and confirmation of tumor nodules using WBLI, we administered two doses of Cy3-labeled siSV1 *Accell*^{TM} molecules (10 mg/kg) via the intraperitoneal route. Mice were sacrificed within 4 hours following administration of the final dose. All disseminated tumors within the three test mice, showed strong uptake of siSV1-Cy3.

Supplemental Figure 3. The effects of siSV1 and cisplatin treatment in combination. Isobologram analysis of siSV1 and cisplatin was performed using normalized IC_{50} equivalents of single agents. The experimental data are best fit to the line of additivity (black diagonal line).

Supplemental Figure 4. a. Targeted inhibition of KLF6-SV1 induces apoptosis in a number of different cancer cell lines, 53S (ovarian), HCT116 (colon), and MDA-435 (breast). **b.** KLF6-SV1 inhibition upregulates NOXA *in vivo*. Western blot analysis of NOXA in tumors from mice that were systemically treated with either siNTC or siSV1.

Supplemental Figure 5. siSV1 induced apoptosis is independent of p53. Isogenic ovarian cancer cell lines A2780 (p53 wildtype) or A2780CP20 (p53 mutant) were treated with siSV1. Apoptosis was induced in both cell lines and NOXA upregulation was present regardless of p53 status.

Supplemental Figure 6. Targeted inhibition of KLF6-SV1 results in a reduction of Mcl-1 protein levels.

Supplemental Figure 7. a. HDM2 overexpression leads to the reduction KLF6-SV1 protein levels and this effect is abrogated with the addition of MG132. **b.** HDM2 mediates the degradation of KLF6-SV1 in HELA cells. Cells were treated with either increasing amounts of a synthetic inhibitor of MDM2 (EMD, cat # 444145) for 6 hours and cell lysates were immunoblotted KLF6-SV1, NOXA and actin.