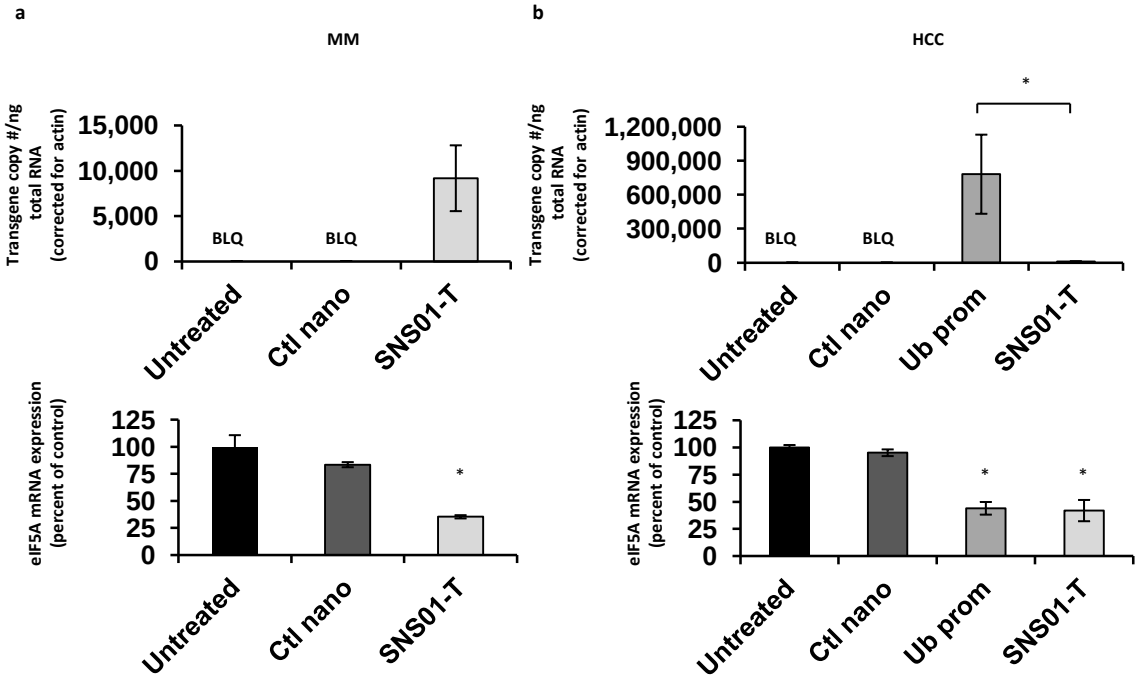
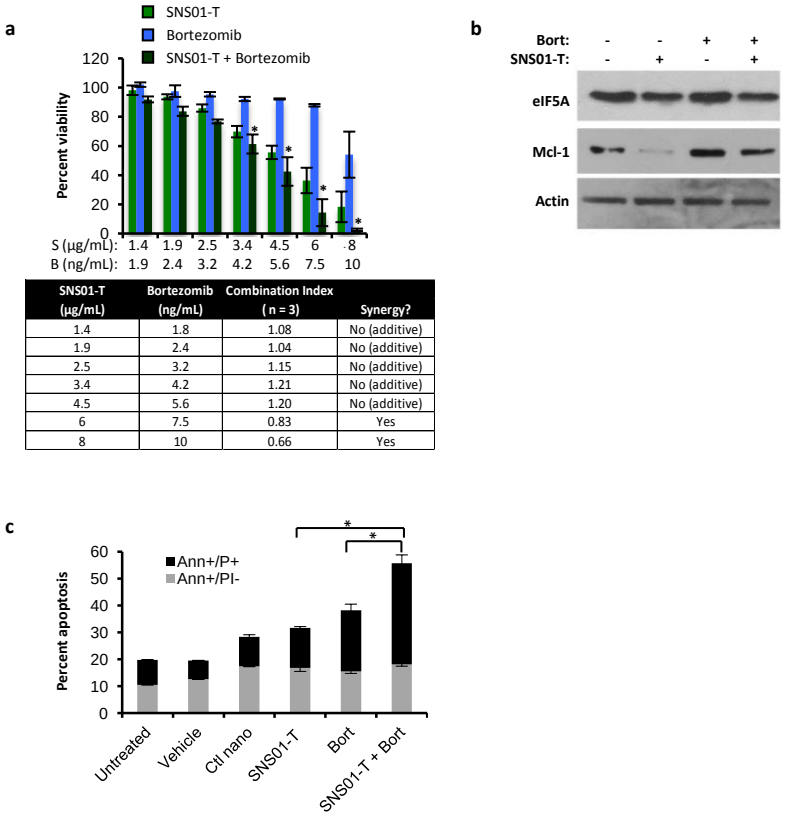
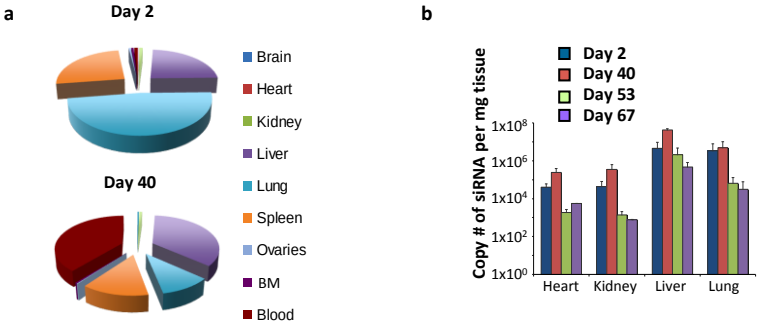



**Figure S1. SNS01-T plasmid activity is specific to B-cells.** (**a**) KAS-6/1 cells were transfected with control nanoparticles (Ctl nano), SNS01-T, or were left untreated and (**b**), Hep3B-βhCG-C4 cells were transfected with a control nanoparticle, a nanoparticle containing an $eIF5A_{K50R}$ plasmid driven by the ubiquitous EF-1 promoter (Ub prom), SNS01-T, or were left untreated for 24 hours. Biological activity was assessed by RT-qPCR. Transgene copy number reflects plasmid activity while suppression of eIF5A mRNA expression reflects siRNA activity. The data indicate the mean +/- s.e.m.; asterisks indicate statistically significant differences (Student's *t*-test; n=3, *P* value < 0.05). MM, multiple myeloma, HCC, hepatocellular carcinoma, BLQ, below limit of quantification.




| SNS01-T (µg/mL) | Bortezomib (ng/mL) | Combination Index ( n = 3) | Synergy? |
|---|---|---|---|
| 1.4 | 1.8 | 1.08 | No (additive) |
| 1.9 | 2.4 | 1.04 | No (additive) |
| 2.5 | 3.2 | 1.15 | No (additive) |
| 3.4 | 4.2 | 1.21 | No (additive) |
| 4.5 | 5.6 | 1.20 | No (additive) |
| 6 | 7.5 | 0.83 | Yes |
| 8 | 10 | 0.66 | Yes |

**Figure S2. SNS01-T and bortezomib synergize in KAS-6/1 cells.** (**a**) KAS-6/1 cells were treated with increasing doses of SNS01-T and bortezomib at a constant ratio of 1:1.25 for 48 hours. Cytotoxicity was measured by XTT, and synergy was determined using ComboSyn software. Mean +/- s.e.m. is shown (n=3); single asterisk indicates *P* values < 0.05 (One way ANOVA, Bonferroni post-test) compared to bortezomib. S, SNS01-T; B, bortezomib. (**b**) Western blot analysis of KAS-6/1 cells after treatment with either vehicle, SNS01-T (2 µg/mL), bortezomib (2.5 ng/mL), or a combination of SNS01-T and bortezomib for 48 hours. (**c**) Percentage of KAS-6/1 cells undergoing apoptosis after treatment with controls, SNS01-T (1.25 µg/mL), bortezomib (1.56 ng/mL), or a combination of the two at a ratio of 1:1.25 for 48 hours. Mean values (n=2) are shown and are representative of two trials; asterisk indicates a *P* value < 0.05.




**c**

| Organ | Plasmid clearance (% of day 40) | | siRNA clearance (% of day 40) | |
|---|---|---|---|---|
| | Day 53 | Day 67 | Day 53 | Day 67 |
| Brain | 6.3 | 18.4 | n/a | n/a |
| Heart | 1.8 | 5.0 | 0.8 | 2.3 |
| Kidney | 5.4 | 7.6 | 0.4 | 0.2 |
| Liver | 4.1 | 5.0 | 5.0 | 1.1 |
| Lung | 11.7 | 15.7 | 1.3 | 0.6 |
| Spleen | 0.8 | 1.1 | n/a | n/a |
| Tail[1] | 8.1 | 10.1 | n/a | n/a |
| Ovaries | 5.5 | 9.4 | n/a | n/a |
| Bone marrow | 7.2 | 2.1 | n/a | n/a |
| Blood | 0.6 | 1.1 | n/a | n/a |

**Figure S3. Biodistribution of SNS01-T components in healthy female mice.** (**a**) Plasmid biodistribution in female mice after a single dose (day 2) or twelve doses (day 40) of SNS01-T. (**b**) Biodistribution of siRNA in various tissues from female mice after one dose (day 2), twelve doses (day 4), 2 weeks recovery post-treatment (day 53), or 4 weeks recovery post-treatment (day 67). Data indicate the mean +/- s.e.m. (**c**) Plasmid and siRNA clearance as a percentage of the quantity on day 40, based on the data in **b** and **c**. [1], site of injection.

## Supplementary Tables

### Table S1. Comparison of SNS01-T and SNS01-T-fluor.

| | [Nucleic acid], mg/mL | Zeta diameter, nm | Zeta potential, mV | Polydispersity index |
|---|---|---|---|---|
| SNS01-T | 0.075 | 72.84 +/- 1.6 | 36.1 +/- 0.7 | 0.208 +/- 0.008 |
| SNS01-T-fluor | 0.075 | 78.98 +/- 1.0 | 38.3 +/- 0.8 | 0.171 +/- 0.004 |

1 mL batches of SNS01-T and SNS01-T with FITC-conjugated plasmid and DY547-siRNA (SNS01-T-fluor) were compared using dynamic light scattering. Data shown are means +/- one standard deviation.

Supplementary Information

**Table S2. Cytotoxicity of SNS01-T in B cell cancer cell lines.**

| | Multiple Myeloma | | | | | Mantle Cell Lymphoma | | | Diffuse Large B-Cell Lymphoma | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cell Line | KAS-6/1 | U266 | RPMI 8226 | MM.1S | MM.1R | Z138 | JEKO1 | JVM2 | Su-DHL6 | Toledo | Pfeiffer |
| $IC_{50}$, ng/µL | 7.27 | 3.56 | 4.06 | 6.32 | 9.25 | 5.06 | 3.29 | 7.17 | 4.09 | 5.17 | 12.57 |
| 95% CI | 5.56-9.51 | 3.23-3.93 | 3.50-4.71 | 2.48-10.16 | 6.97-11.53 | 3.83-6.66 | 2.48-4.36 | 4.98-10.33 | 3.37-5.00 | 4.03-6.63 | 9.40-16.81 |

Supplementary Information

## Supplementary Materials and Methods

### Flow cytometry

KAS-6/1 cells were treated with controls, SNS01-T (1.25 μg/mL), bortezomib (1.56 ng/mL), or a combination of the two drugs at a ratio of 1:1.25 and incubated for 48 hours. The percentage of cells undergoing apoptosis was determined by staining the cells with Annexin V-FITC and propidium iodide according to the manufacturer's instructions (BD Biosciences). The percentage of annexin-positive and annexin/PI-positive cells was assessed on a FACSCalibur flow cytometer (BD Scientific)