Camacho *et al*, Fig. S1

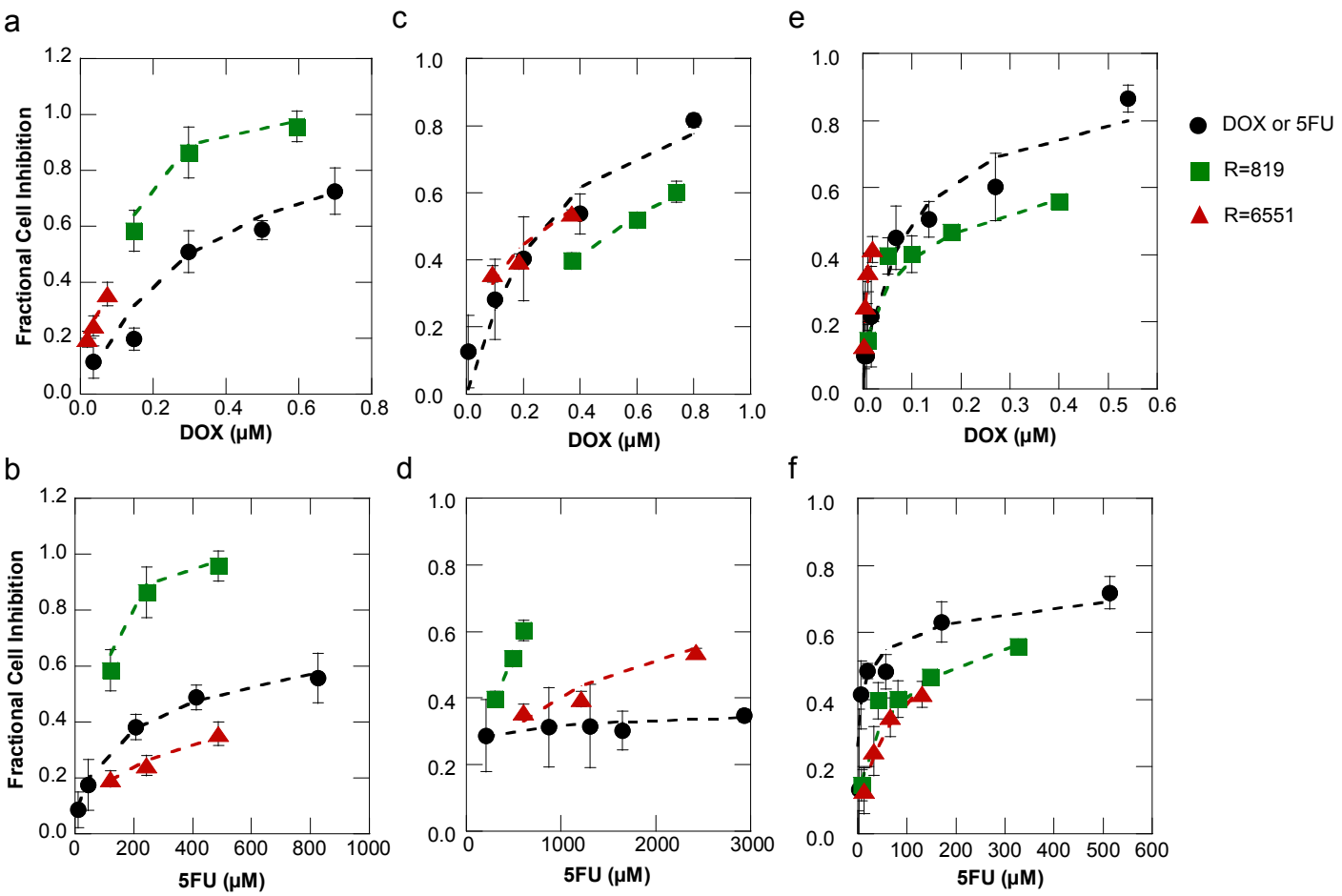

Fig. S1. 5FU+DOX in the synergistic ratio R=819 ± 64 (green squares) or antagonistic ratio R = 6551 ± 170 (red triangles) were exposed to (a)-(b) BT-474 human breast cancer cells, (c)-(d) bEnd.3 mouse brain endothelial cells, or (e)-(f) MCF 10A human breast epithelial cells, and cell growth inhibition was evaluated via MTT cytotoxicity assays. Single drug treatments of DOX (top, black circles) and 5FU (bottom, black circles) are shown for comparison. Dashed lines represent fits to the ME model. Data expressed as mean ± SD (N ≥ 6).

Camacho *et al*, Fig. S2

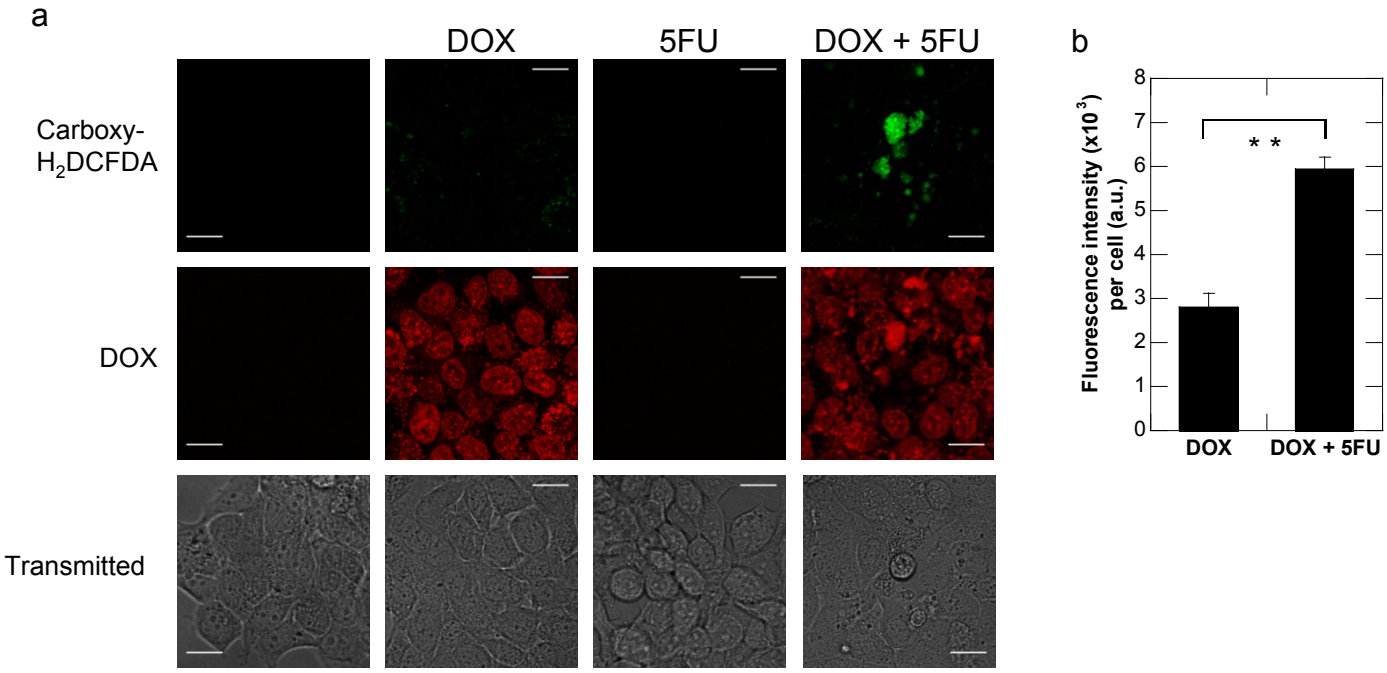

Fig. S2. (a) Production of reactive oxygen species (ROS) in BT-474 cells exposed to no drug (top), 0.6 μM DOX (second from top), 487 μM 5FU (second from bottom), 0.6 μM DOX in combination with 5FU in a molar ratio of 819:1 5FU:DOX (bottom). Cells were exposed to free drug solutions for 24 hrs, incubated with 10 μM carboxy-H_2DCFDA (green) for 30 minutes, washed and imaged live immediately via confocal microscopy. (b) Carboxy-H_2DCFDA fluorescence intensity is reported as mean ± SD (N=3). Representative images are shown as an average of 10 μm z-stacks. Scale bar=20 μm. **, $P < 0.01$ performed by two-tailed Student's *t*-test.

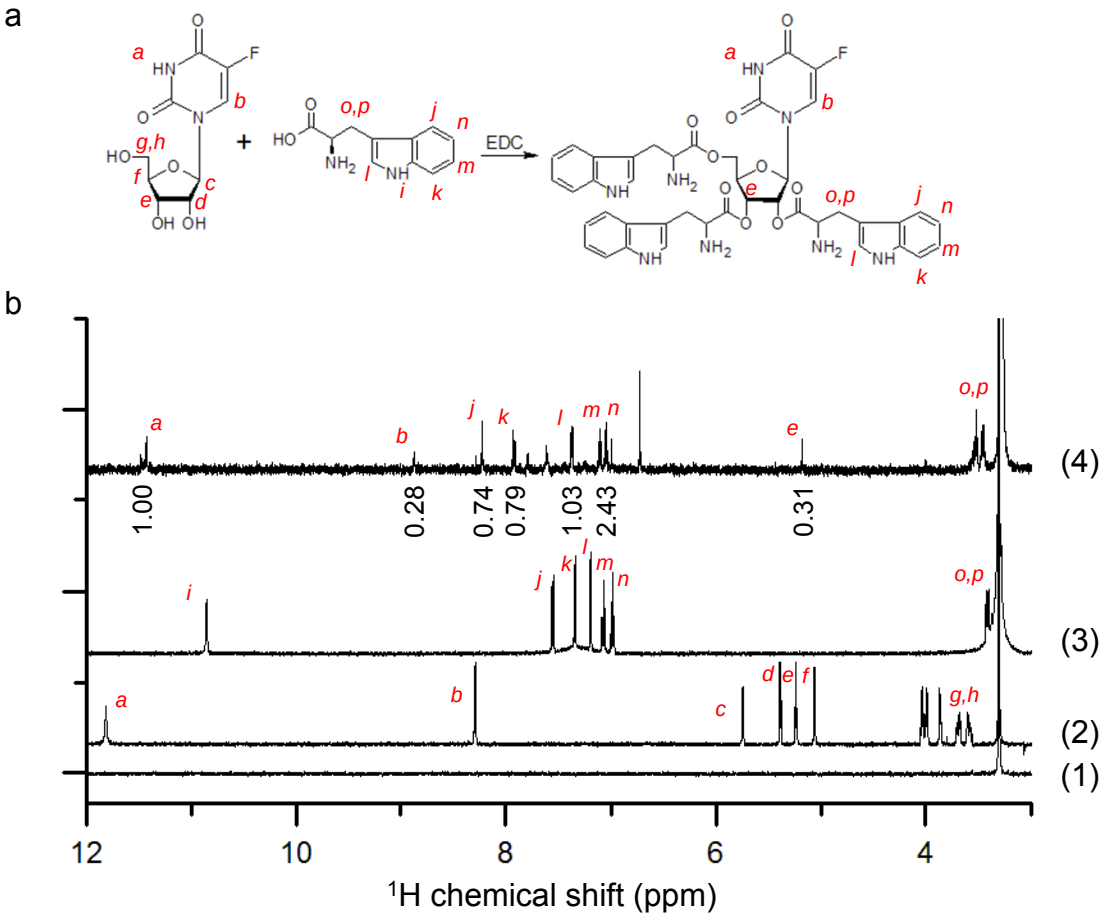

Fig S3. (a) Chemical synthesis of 5FURW by esterification of 5FUR and tryptophan. (b) NMR spectroscopy of reactants and product of (a). Spectra of d_6-DMSO, 5FUR, tryptophan, and 5FURW are designated as (1), (2), (3), and (4), respectively. Characteristic peaks are labelled as a-p, and integrations are provided for the final product 5FURW.

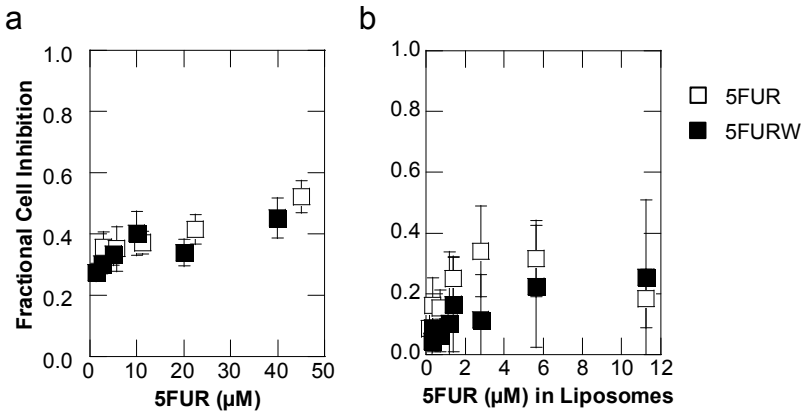

Fig. S4. Comparison of *in vitro* activities of the ribonucleoside analogue of 5FU (5FUR) (open squares) and tryptophan-modified 5FUR (5FURW) (filled squares) in (a) free solution or (b) liposomes. Data shown as average ± SD (N=6).

Camacho *et al*, Fig. S5

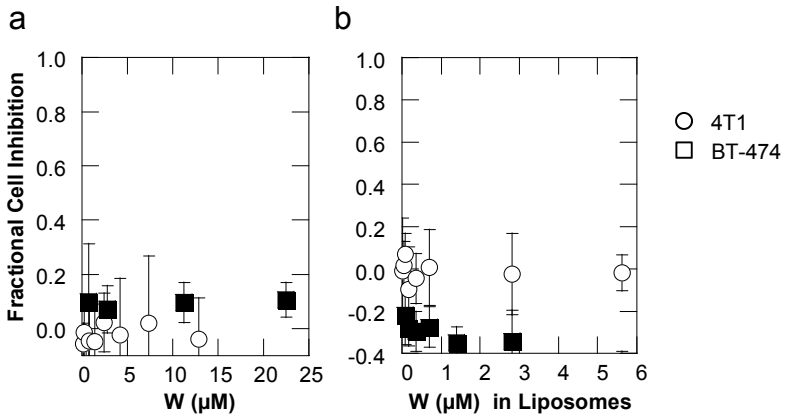

Fig. S5. Toxicity of (a) free tryptophan (W) or (b) liposome-encapsulated W incubated with 4T1 (white circles) or BT-474 (black squares) cells. Cells were incubated with W concentrations expected to be present during 5FURW cytotoxicity assays. Data expressed as mean ± SD (N=6).

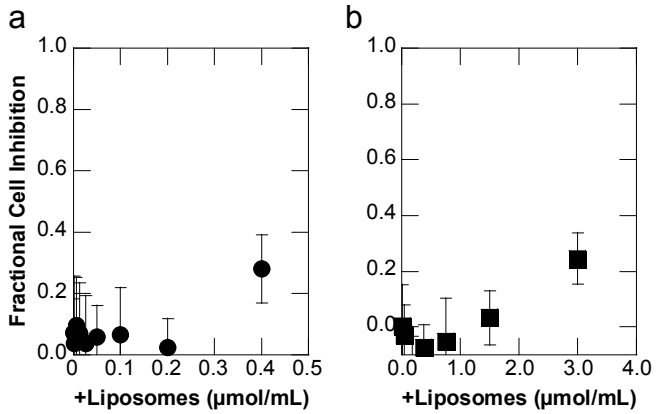

Fig. S6. *In vitro* toxicity of blank cationic liposomes against (a) murine breast carcinoma cell line 4T1 and (b) human breast cancer cell line BT-474. Data expressed as mean ± SD (N=6). For all *in vitro* studies, non-toxic doses of <3 µmol/mL or <0.4 µmol/mL were utilized against BT-474 and 4T1 cell lines, respectively.

Camacho *et al*, Fig. S7

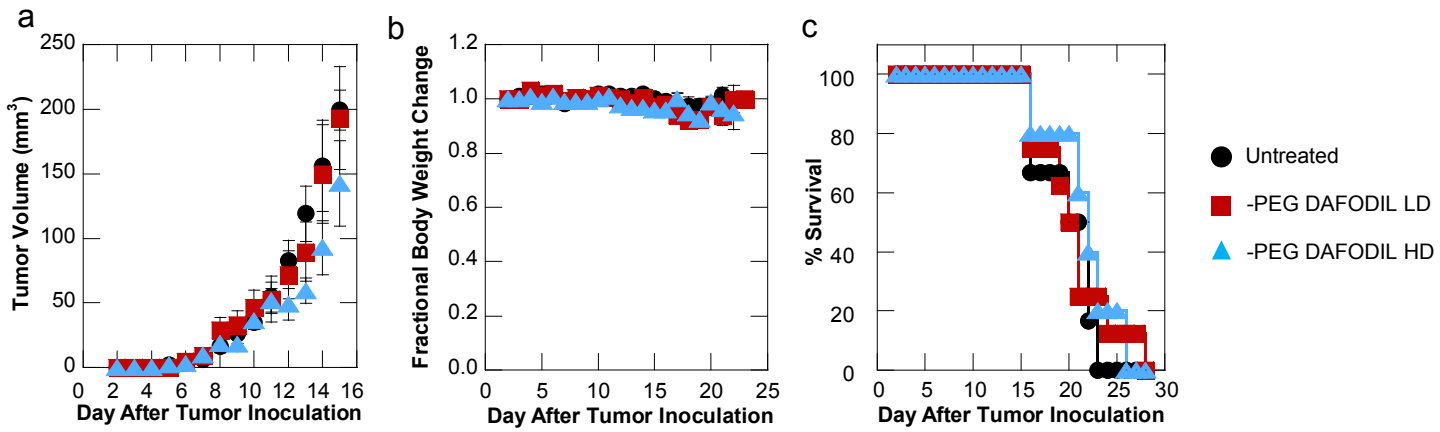

Fig. S7. Tumor growth inhibition of –PEG DAFODIL. (a) Tumor growth of mice bearing 4T1 breast cancer tumors, without treatment (black circles), with i.v. injections of low dose –PEG DAFODIL (red squares), or high dose –PEG DAFODIL (blue triangles) on Days 3, 5, 7, 9, 11, 13 post tumor inoculation. Low dose –PEG DAFODIL treatments consisted of drug-equivalent doses of 1 mg/kg DOX + 0.3 mg/kg 5FURW, while high dose –PEG DAFODIL treatments consisted of 4 mg/kg DOX + 1.1 mg/kg 5FURW. (b) Effect of treatment on body weight fluctuations. Data is reported as mean ± SEM (N≥5). (c) Survival rates for all treatment groups.

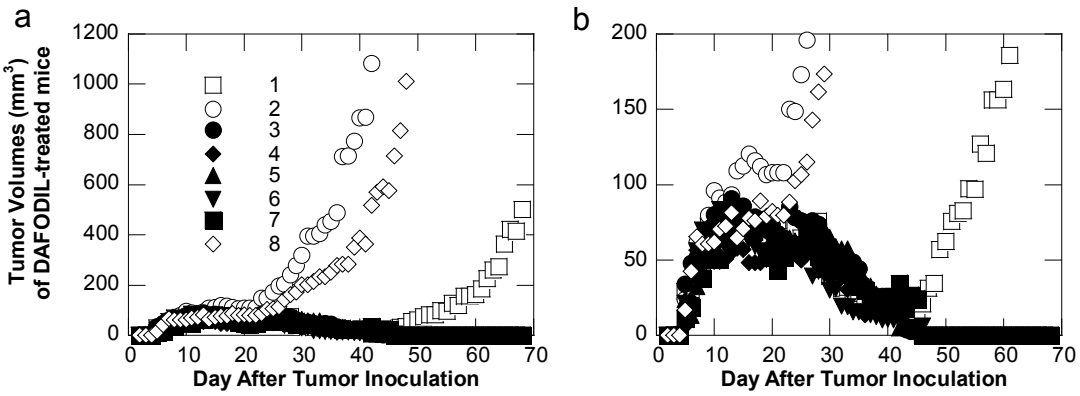

Fig. S8. (a) Individual tumor growth profiles of mice bearing 4T1 breast cancer tumors, treated with 4 i.v. injections of DAFODIL. Mice were administered DAFODIL in drug-equivalent doses of 3 mg/kg DOX + 0.61 mg/kg 5FURW (same as main text Fig. 5). Blank markers represent tumors which eventually grew, whereas filled markers represent eventual no detectable tumors. (b) Smaller scale version of the (a), to provide greater detail.

Camacho *et al*, Fig. S8

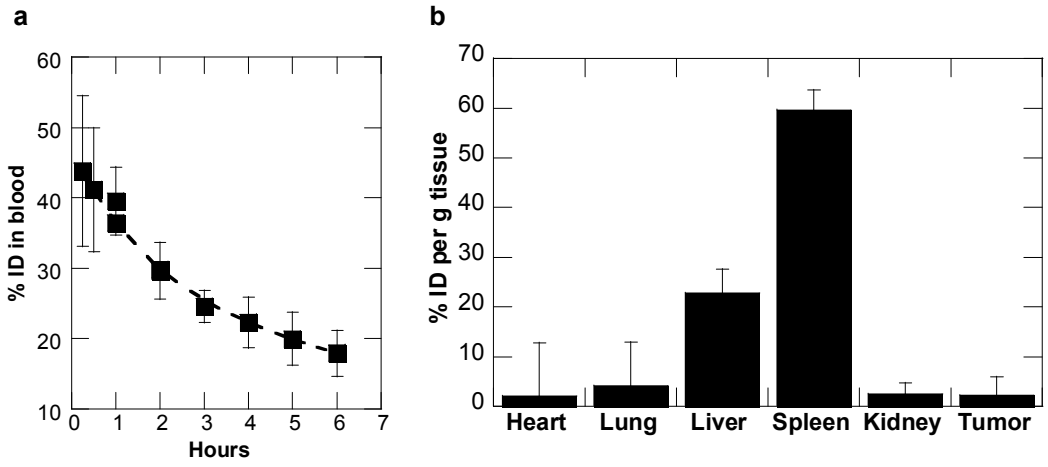

Fig. S9. (a) Pharmacokinetic study of ^{3}H-DAFODIL for 6 hours post i.v. tail injection. Dashed line represents fit to double exponential model, where distribution and elimination half lives were calculated to be 1.1 and 8.3 hrs, respectively. (b) Biodistribution of ^{3}H-DAFODIL after 6 hours post i.v. tail injection. Data expressed as mean ± SEM (N=4).

Camacho *et al*, Fig. S9

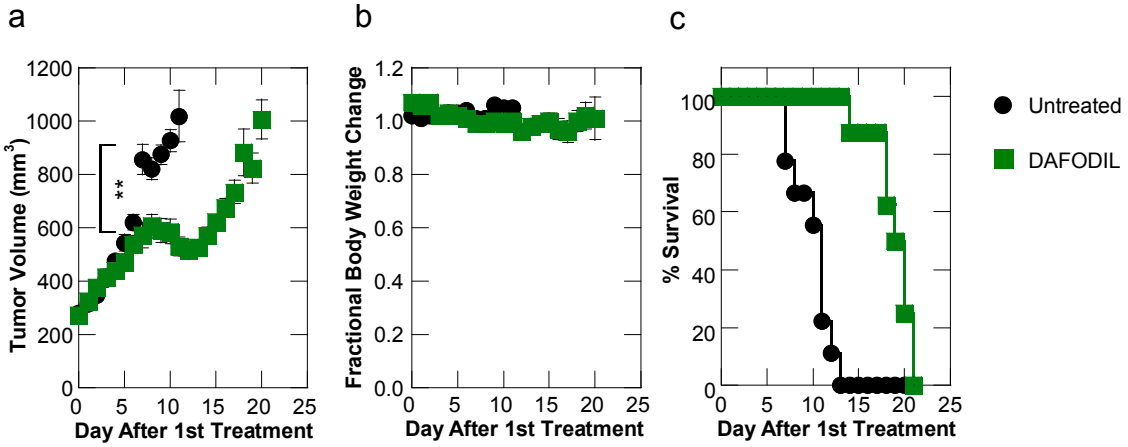

Fig. S10. (a) 4T1 tumor volumes of untreated BALB/c mice (black circles) or mice treated with DAFODIL (green squares) at drug-equivalent doses of 0.61 mg/kg 5FURW and 3 mg/kg DOX (R=0.15) for treatments starting at large (300 mm^3) tumor volumes. Significance is provided for the last day when untreated mice survival > 50%. (b) Corresponding body weight changes of tumor-bearing mice. Data shown as mean ± SEM (Initial N=8, and varies according to survival). (c) Survival rates for all experimental groups.