Supplementary Information

Supramolecularly self-assembled nano-twin drug to reverse the multidrug resistance

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Supplementary Figures



Figure S1. Hydrodynamic size of free DOX (0.5 mg/mL in aqueous solution) and

free SAHA (2 mg/mL in aqueous solution).



Figure S2. Stability of the DOX-SAHA nano-twin drug. Size variation of the DOX-

SAHA nano-twin drug after storage for 12 days in PBS solution at 25 $^{\circ}$ C.



Figure S3. (A) ¹H-NMR NH chemical shift of the DOX-SAHA nano-twin drug as a function of temperature in DMSO-d₆. (B) Variable temperature FTIR spectra of DOX-SAHA nano-twin drug. Samples were allowed to equilibrate for 10 min at each temperature.



Figure S4. Hydrodynamic size of the DOX and lysine mixed solution measured by dynamic light scattering.



Figure S5. Hydrodynamic diameters of the DOX-SAHA nano-twin drug as a function of NaCl concentration in the aqueous solution.



Figure S6. The standard curves of DOX (A) and SAHA (B) that used for determination of drug release profile from the DOX-SAHA nano-twin drug.



Figure S7. The cellular uptake of DOX-SAHA nano-twin drug by MCF-7/ADR cells. Fluorescence of the intracellular DOX was used to quantify the internalization efficiency of DOX-SAHA nano-twin drug as determined by flow cytometry.



Figure S8. Time-dependent DOX accumulation in MCF-7/ADR cells after treatment with free DOX. (A) Confocal microscope images of MCF-7/ADR cells incubated with free DOX for 1 h, 2 h, 4 h, and 6 h. The nucleus stained with DAPI is shown in blue, DOX is displayed in red. Scale bar: 50 μ m. (B) Flow cytometry analysis of MCF-7/ADR cells incubated with free DOX for 1 h, 2 h, 4 h, and 6 h.



Figure S9. Histological analysis of major organs (heart, liver, spleen, lung, kidneys) from the tumor-bearing mice treated with PBS, DOX, SAHA, DOX/SAHA mixture, and the DOX-SAHA nano-twin drug. All scale bars: 100 µm.