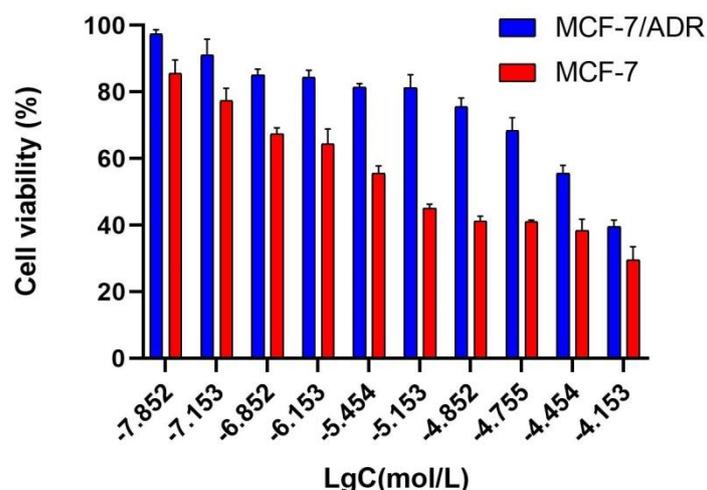


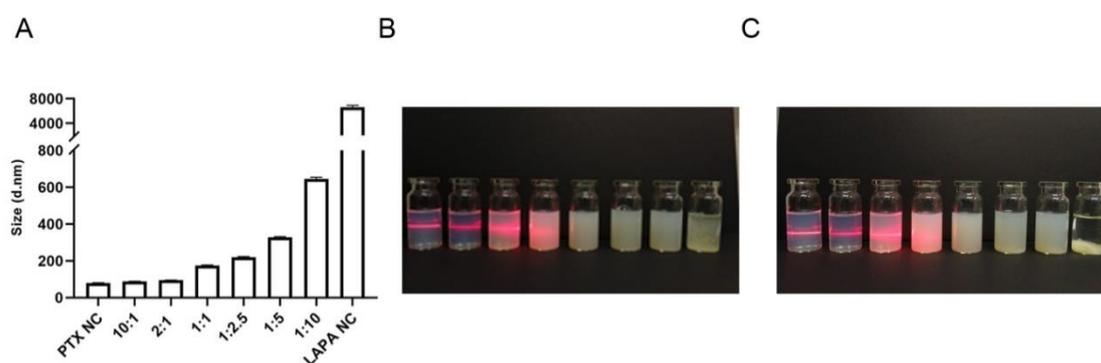
**Supplementary Information:** Considering the results of preparation, when PTX was used alone to form PTX NC, the particle size was  $79.6 \pm 1.6$  nm, PDI was  $0.14 \pm 0.01$ . When LAPA were added to form P:L=10:1, the particle size was  $87.7 \pm 1.5$  nm, PDI was  $0.12 \pm 0.01$ . With the increase of the concentration of LAPA, the particle size and PDI increased. When LAPA increased to form P:L=1:1, the particle size was  $175.3 \pm 2.5$ , PDI was larger than 0.2. When there was LAPA only, the particle size was  $6610.7 \pm 332.9$  nm, and the PDI was  $0.89 \pm 0.16$  (Table S1). The results showed that the particle size increased with the increase of LAPA. The results of the Tyndall effect showed that the beam passed through PTX NC, P:L=10:1 and 2:1, and the scattering occurred in P:L=1:1, which might be precipitation (Figure S2B). After 5min placement, the beam still passed through PTX NC, P:L=10:1 and 2:1, while more obvious than the fresh one in P:L=1:1, which might be the precipitation fell to the bottom of the bottle. P:L=1:5, 1:10 and LAPA NC produced more precipitation (Figure S2C). Combined with the above results, we chose P:L=2:1.



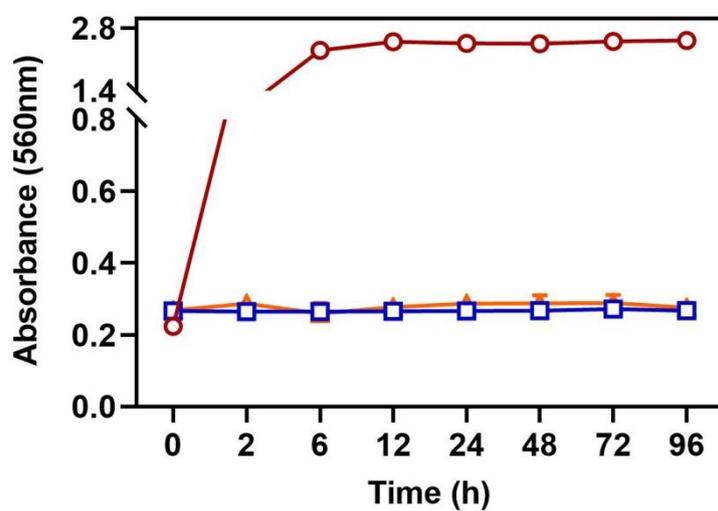
**Figure S1.** Cytotoxicity of free PTX incubated with MCF-7 or MCF-7/ADR for 24 h. RI=  $IC_{50}$  drug resistant cell/ $IC_{50}$  pre-induction cell. (n = 3, mean  $\pm$  SD).

**Table S1.** Optimization of paclitaxel and lapatinib with different ratios (n=3, mean  $\pm$  SD).

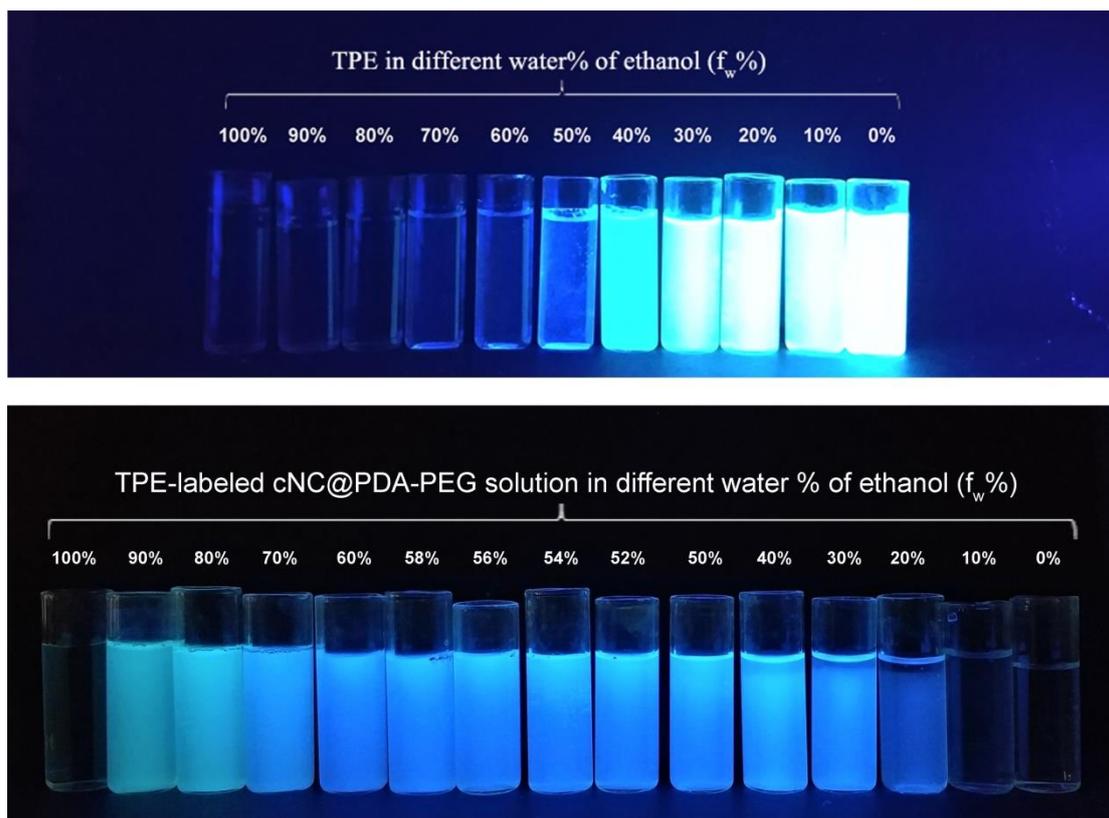
Formulation (P:L)	Size (nm) $\pm$ SD	PDI $\pm$ SD
PTX NC	$79.6 \pm 1.6$	$0.14 \pm 0.01$
10:1	$87.7 \pm 1.5$	$0.12 \pm 0.01$
2:1	$95.1 \pm 1.1$	$0.14 \pm 0.02$
1:1	$175.3 \pm 2.5$	$0.24 \pm 0.03$
1:2.5	$220.4 \pm 3.1$	$0.30 \pm 0.02$
1:5	$327.6 \pm 4.4$	$0.65 \pm 0.14$
1:10	$645.3 \pm 8.9$	$0.66 \pm 0.03$
LAPA NC	$6610.7 \pm 332.9$	$0.89 \pm 0.16$



**Figure S2.** (A) Optimize the size and PDI of the formulation by changing the ratio of paclitaxel to lapatinib ( $n = 3$ , mean  $\pm$  SD). Tyndall effect of freshly prepared nanocrystals (B) and placed for 5 min (C).



**Figure S3.** Size aggregation in PBS measured by absorbance at 560 nm.



**Figure S4.** Glass vials of TPE NC and TPE-labeled cNC@PDA-PEG in water/ethanol mixtures of various v/v ratios under UV illumination.