Supporting Information for

ORIGINAL ARTICLE

Injectable thermo-responsive nano-hydrogel loading triptolide for the anti-breast cancer enhancement *via* localized treatment based on "two strikes" effects

Yaoyao Luo^{a,†}, Jingjing Li^{b,†}, Yichen Hu^c, Fei Gao^a, George Pak-Heng Leung^b, Funeng Geng^{a,d}, Chaomei Fu^{a,*}, Jinming Zhang^{a,*}

^aCollege of Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China

^bDepartment of Pharmacology and Pharmacy, University of Hong Kong, Hong Kong 999077, China

^cCollege of Pharmacy and Biological Engineering, Chengdu University, Chengdu 610100, China

^dSichuan Key Laboratory of Medical American Cockroach, Chengdu 615000, China

*Corresponding authors. Tel.: +86 028 61800231 (Chaomei Fu); +86 13551043885_(Jinming Zhang).

E-mail addresses: <u>chaomeifu@126.com</u> (Chaomei Fu); <u>cdutcmzjm@126.com</u> (Jinming Zhang).

[†]These authors made equal contributions to this work.



Figure S1 GPC analysis result of P(NIPAAm-co-AAc)-g-F68 copolymer.



Figure S2 Cumulative release of TPL from hydrogels at 25 and 37 °C from 0 to 48 h (*n*=3).



Figure S3 Cytotoxicity of blank gel against MDA-MB-231 and MCF-7 cells after treatment for different times (*n*=6).



Figure S4 Effects of TPL@nano-gel on mitochondrial membrane potential (A), apoptosis (B) and cell cycle progression (C) of MCF-7 cells using flow cytometry. MCF-7 cells were treated with or without blank gel (160 μ mg/mL), or free TPL (20 nmol/L) and TPL@nano-gel (20 nmol/L) for 48 h. **P* < 0.05 *versus* the control group. #*P* < 0.05 free TPL *versus* TPL@nano-gel group