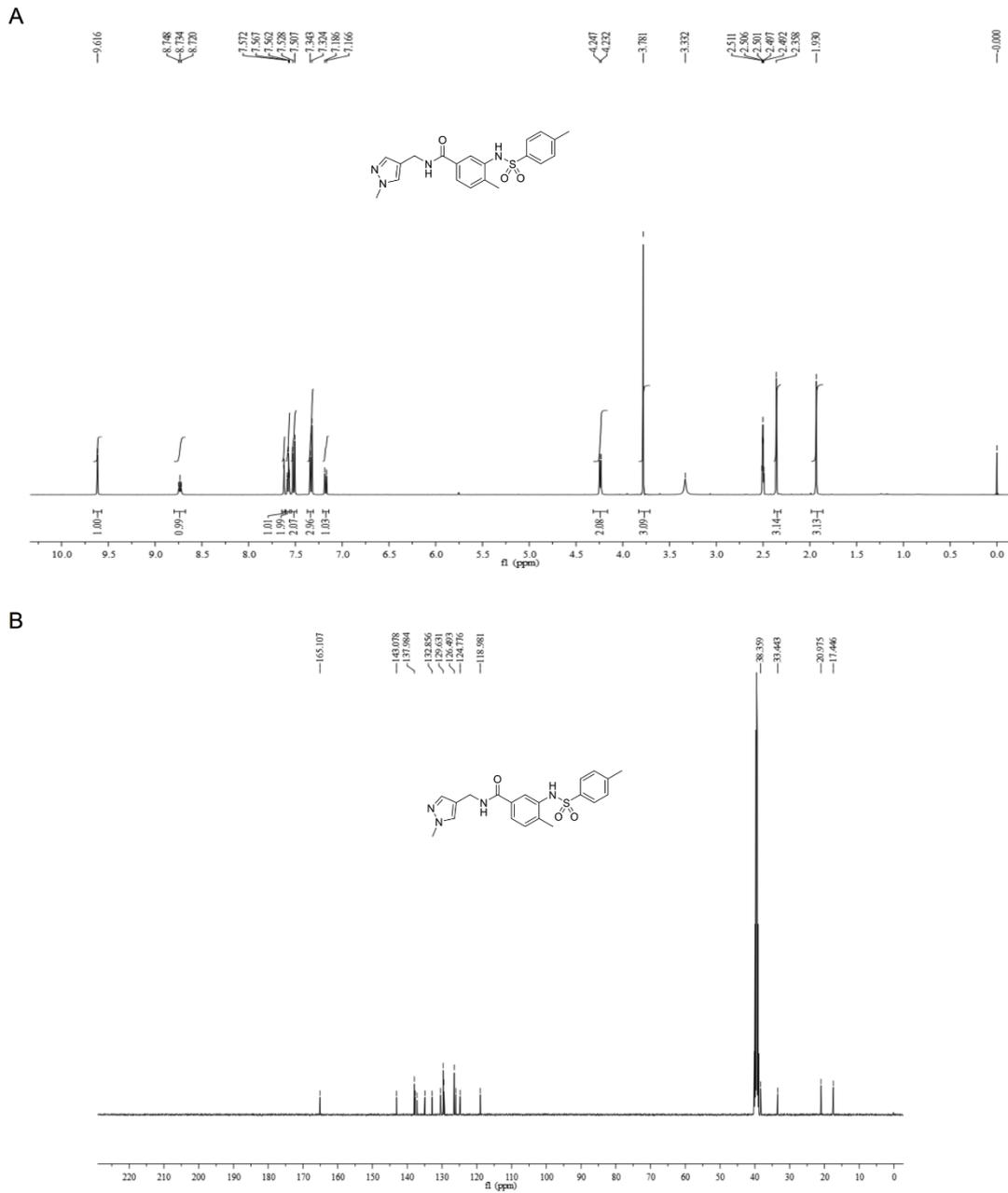
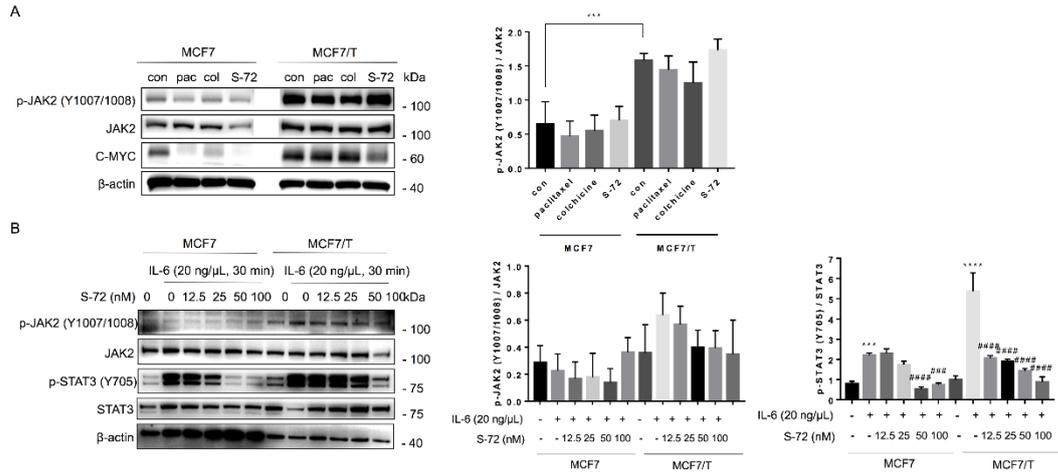


**Figure S1.** Plasma concentration-time curves of S-72. ICR mice were orally administered 5 mg/kg S-72 or intravenous injected 1 mg/kg S-72. Plasma concentrations of S-72 were analyzed by a LC-MS/MS method.

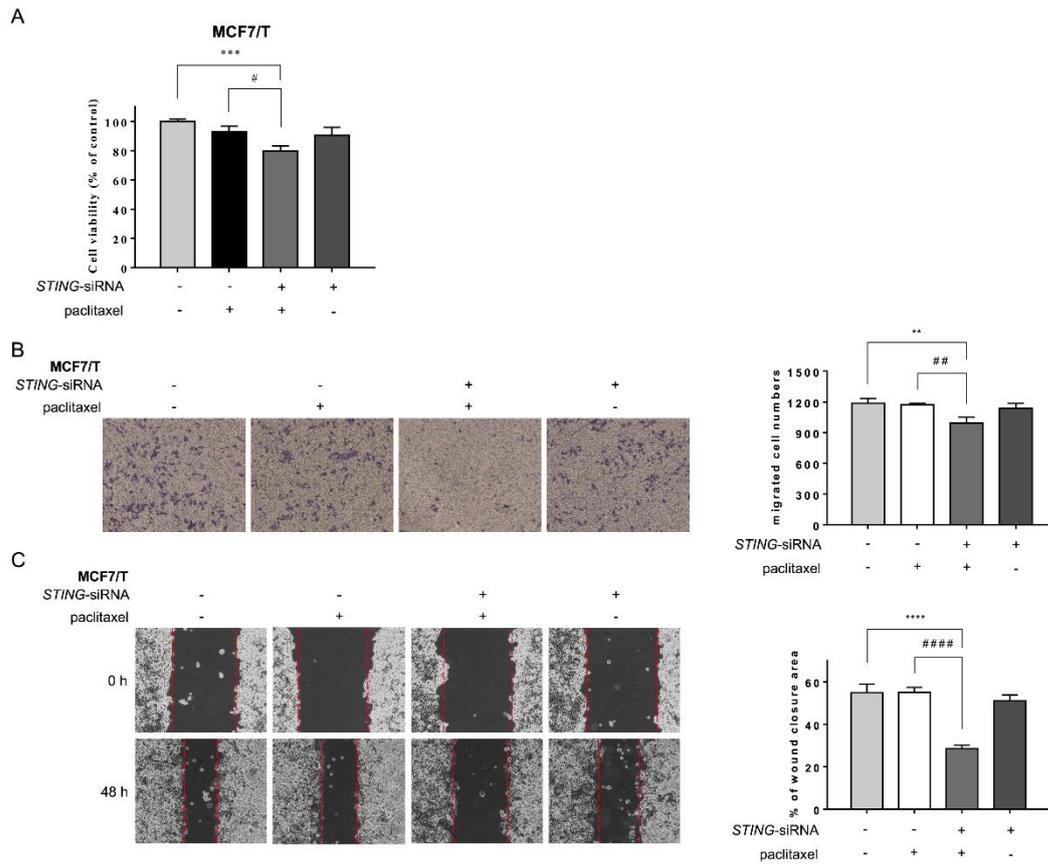


**Figure S2.** (A) <sup>1</sup>H NMR and (B) <sup>13</sup>C NMR spectrum of S-72.

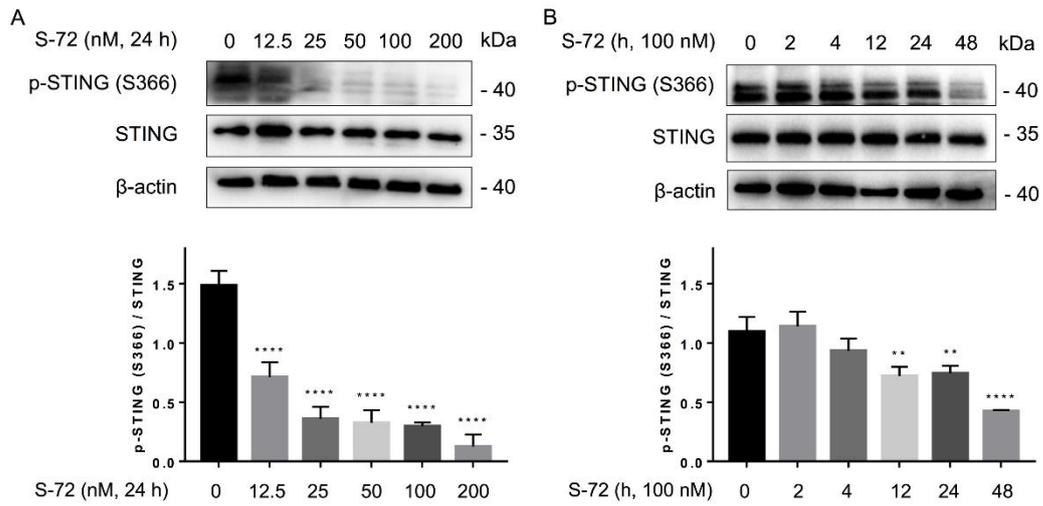


**Figure S3.** S-72 inhibits STAT3 activation in both MCF7 and MCF7/T cells. (A) Protein levels of p-JAK2 (Y1007/1008), JAK2 and C-MYC were identified by western blot after treatment with 100 nM paclitaxel, 100 nM colchicine or 100 nM S-72 for 24 h. (B) S-72 concentration-dependently inhibited STAT3 phosphorylation at Tyr705 induced by IL-6 in MCF7 and MCF7/T cells.  $N = 3$ ,  $*p < 0.05$ ,  $**p < 0.01$ ,  $***p < 0.001$ ,  $****p < 0.0001$  versus con and  $\#p < 0.05$ ,  $\##p < 0.01$ ,  $\###p < 0.001$ ,  $\####p < 0.0001$  versus the IL-6 group.





**Figure S5.** Knockdown of STING restores sensitivity to paclitaxel in MCF7/T cells. (A) Cell viability determined by CCK8 assay. (B-C) Effects of STING knockdown on paclitaxel sensitivity evaluated by (B) transwell migration assay and (C) wound healing assay.  $N = 3$ ,  $*p < 0.05$ ,  $**p < 0.01$ ,  $***p < 0.001$ ,  $****p < 0.0001$  versus the control group and  $\#p < 0.05$ ,  $\#\#p < 0.01$ ,  $\#\#\#p < 0.001$ ,  $\#\#\#\#p < 0.0001$  versus the paclitaxel-treated group.



**Figure S6.** Changes in protein levels of p-STING (Ser366) after S-72 treatment. (A) Dose course study on the effect of S-72 treatment on p-STING (Ser366) expressions in MCF7/T cells. Cells were treated with gradient concentrations of S-72 for 24 h. (B) Time course study on the effect of S-72 treatment on p-STING (Ser366) expressions in MCF7/T cells. Cells were treated with 100 nM S-72 for various time periods. Protein levels were detected by western blot analysis.  $N = 3$ ,  $*p < 0.05$ ,  $**p < 0.01$ ,  $***p < 0.001$ ,  $****p < 0.0001$  versus con.

**Table S1.** Pharmacokinetic parameters of S-72.

Parameters	Units	po. (5 mg/kg)	iv. (1 mg/kg)
$t_{1/2\beta}$	h	4.07	0.38
$T_{\max}$	h	0.083	0.03
$C_{\max}$	ng/ml	1436	1192
$AUC_{(0-t)}$	h*ng/ml	1740	469
$AUC_{(0-\infty)}$	h*ng/ml	1962	480
$MRT_{(0-t)}$	h	3.26	0.42
$MRT_{(0-\infty)}$	h	4.92	0.46
$V_z$	ml/kg	-	1155
CL	ml/h/kg	-	2084
F%	-	74.1	-