



Supplementary information, Fig. S8. Pharmacokinetic (PK) parameters of NAT used in the *in vivo* studies.

a Plasma concentration-time profiles of NAT via IV, IP, or PO in male CD-1 mice. $n = 3$ biological replicates. **b** The plasma concentration of NAT after an IV dose of 1 mg/kg. **c** The plasma concentration of NAT after an IP dose of 30 mg/kg. **d** The plasma concentration of NAT after a PO dose of 30 mg/kg. $T_{1/2}$, elimination half-life; T_{max} , time to reach peak plasma concentration following drug administration; C_{max} , peak plasma drug concentration; AUC_{last} area under the curve from the time zero to the time of the last measurable (positive) concentration; AUC_{INF} , area under the plasma concentration-time curve from time zero to infinity; V_{ss} , the volume of distribution at steady-state; CL, total plasma clearance; F%, bioavailability. **e** NAT does not affect PTX-mediated cytotoxicity. U2OS cells were treated with PTX in the absence or presence of 3 μ M NAT for 48 h. Cell viability was measured by the CellTiter-Glo assay. Data are presented as mean \pm SEM. $n = 3$ biological replicates. **f** The body weight of NATs-treated mice compared to that of vehicle-treated controls. Means \pm SEM. Mice were treated with vehicle, 30 mg/kg NAT or NAT-5r for 14 days ($n=5$ per group). **g** NAT or NAT-5r does not induce liver toxicity in mice after 14 days of treatment. Blood samples were taken on the last day of treatment from the eye vein. Tests for the levels of alanine transaminase (ALT, in U/L) and aspartate aminotransferase (AST, in U/L) were used to monitor liver toxicity in response to drug treatment. Data are presented as mean \pm SEM, $n = 5$ biological replicates.