Supporting Information

Flexible use of commercial rhenium disulfide for various theranostics applications

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Experimental Section

Characterization

The Scanning electron microscope (SEM) image of ReS_2 powder and ALG-Ca^{2+}-ReS_2 hydrogel was obtained by field emission SEM (FEI, America). X-ray diffraction (XRD) pattern was measured on a D/max-2500 diffractometer (Rigaku) using Cu Kα radiation (λ = 1.5418 Å). The acceptable activity was measured by standard Methyl Thiazolyl Tetrazolium (MTT) assay, and absorbance was measured by a microplate reader (bio-tek, USA Park, CA). The 1064-nm laser is produced by Changchun New Industry Optoelectronics Co., LTD. Infrared calorific value images were taken with FLIR E50 infrared camera (FLIR, USA).

Syringe ability of sodium alginate (ALG)-Ca^{2+}-ReS_2 hydrogel

To study the syringe ability of ALG-Ca^{2+}-ReS_2 hydrogel, a certain volume of the proposed ALG-Ca^{2+}-ReS_2 hydrogel (20 mg ReS_2 mL^{-1}) was extruded using a 1 mL syringe respectively to study the feasibility of their syringe ability. The specific pattern (TIJMU) by the extruded ALG-Ca^{2+}-ReS_2 hydrogel was also carried out to explore its excellent syringe ability.

Stability in digestive juice of ultraviolet-cured resin (UCR)-ReS_2 capsule

For the stability of the UCR-ReS_2 capsule in digestive juice. The UCR-ReS_2 capsules were placed in gastric acid and small intestinal fluid at 37 °C. Took photos of them at different time points to observe the shape of the capsules.

Colloidal stability assessment of ALG-Ca^{2+}-ReS_2 hydrogel

To investigate the colloidal stability assessment of ALG-Ca^{2+}-ReS_2 hydrogel, ReS_2 powder (20 mg/mL) was dispersed in water compared with ALG-Ca^{2+}-ReS_2 hydrogel. In addition, pure ALG-Ca^{2+} hydrogel served as a control group. The photos of ReS_2 powders solution and ALG-Ca^{2+}-ReS_2 hydrogel were recorded at different time points (0, 1 d, 7 d and 15 d).

Photothermal performance of ALG-Ca^{2+}-ReS_2 hydrogel

We then investigated the photothermal therapy (PTT) capability of ALG-Ca^{2+}-ReS_2 hydrogel. A 1064-nm laser was used to irradiate ALG-Ca^{2+} hydrogel (1 mL), ultrapure water (1 mL) and ALG-Ca^{2+}-ReS_2 hydrogel (1 mg/mL, 2 mg/mL, 5 mg/mL respectively, 1 mL). Lasers with different power densities (0.5 W/cm^2, 1.0 W/cm^2 and 2.0 W/cm^2) were continuously irradiated for 5 min. The temperature change is recorded every 30 s during laser irradiation. At the same time, an infrared camera was used to capture the thermal image of each sample.

Cytotoxicity of ALG-Ca^{2+}-ReS_2 hydrogel and XG-ReS_2 suspension

The standard MTT method was used to investigate the toxicity of ALG-Ca^{2+}-ReS_2 hydrogel to 4T1 cells (mouse breast cancer cells) and XG-ReS_2 suspension to NCM460 cells (normal colonic epithelial cell line) and CT26 cells (invasive murine colon cancer cell line). For 4T1 cells and NCM460 cells, the cell culture medium consists of Dulbecco's Modified Eagle Medium (DMEM) containing 10% foetal bovine serum (FBS) and 1% streptomycin-penicillin. For CT26 cells, the cell culture medium consists of Roswell Park Memorial Institute (RPMI) 1640 containing 10% FBS and 1% streptomycin-penicillin. For ALG-Ca^{2+}-ReS_2 hydrogel, inoculate 4T1 in a 96-well plate at a

density of 1 × 10^4 cells/well. For XG-ReS_2 suspension, inoculate NCM460 cells or CT26 cells in a 24-well Transwell® plate at a density of 1.5 × 10^4 cells/well because the XG can be miscible with the DMEM or RPMI 1640. After incubating in an incubator containing 5% CO_2 at 37 °C for 24 h. Then add different ReS_2 concentrations of ALG-Ca^{2+}-ReS_2 hydrogel and XG-ReS_2 suspension respectively (ALG-Ca^{2+}-ReS_2: 0 mg/mL, 0.2 mg/mL, 0.4 mg/mL, 0.6 mg/mL, 0.8 mg/mL, 1.0 mg/mL, 1.5 mg/mL, 2.0 mg/mL, XG-ReS_2: 0 mg/mL, 0.2 mg/mL, 0.4 mg/mL, 0.8 mg/mL, 1.0 mg/mL, 2.0 mg/mL), incubated at constant temperature for 24 h. The following day, the materials and culture medium added to the wells were removed and rinsed carefully twice with phosphate buffered saline (PBS), and then 5% MTT (5 mg/mL) of DMEM or RPMI 1640 was added to each well and incubated with the cells for four hours. Subsequently, the cell culture supernatant containing MTT was discarded, and a certain amount of dimethyl sulfoxide (DMSO) was added to each well to dissolve the purple formazan crystals. After 3 minutes on the low-speed vibrating plate, the absorbance of each well at 490-nm was detected with a microplate reader.

Cellular photothermal therapy of ALG-Ca^{2+}-ReS_2 hydrogel

To investigate the *in vitro* photothermal killing ability of ALG-Ca^{2+}-ReS_2 hydrogel, 4T1 cells were seeded in 96-well plates (density of 1 × 10^4 cells/well) and incubated at 37 °C for 24 h. After adding different concentrations of ALG-Ca^{2+}-ReS_2 hydrogel, the cells were exposed to different power densities of the 1064-nm laser irradiation (1.0, 2.0 and 3.0 W/cm^2, 10 min). After the 1064-nm laser treatment, carefully remove the cell supernatant and material from each well and wash it twice with PBS. Then still use the standard MTT method to treat cells and calculate cell survival rate.

***In vivo* photothermal therapy for tumour of ALG-Ca^{2+}-ReS_2 hydrogel**

All animal procedures in this work were performed in accordance with the Guidelines for Care and Use of Laboratory Animals of Tianjin Medical University General Hospital and approved by the Animal Ethics Committee of Tianjin Medical University General Hospital. The mice and rats were purchased from the SPF Biotechnology Co.Ltd. To investigate the capability of photothermal therapy of ALG-Ca^{2+}-ReS_2 hydrogel. The 4T1 tumour model was established by subcutaneous injection of 4T1 cells on the back of Balb/c mice. The mice were randomly divided into five groups (n = 5) when the tumour size was about 70-100 mm^3. The mice were anesthetized with chloral hydrate (4%), followed by various treatments, including a combined injection of ALG-Ca^{2+}-ReS_2 hydrogel (5 mg ReS_2/mL**,** 5 mL/**k**g) and 1064-nm laser irradiation (1 W/cm^2 for 5 min), PBS injection with 1064-nm laser irradiation (1 W/ cm^2 for 5 min), ALG-Ca^{2+} hydrogel (5 mL/**k**g) alone, ALG-Ca^{2+}-ReS_2 hydrogel (5 mg ReS_2/mL**,** 5 mL/**k**g) alone and PBS injection alone. The temperature changes of tumour sites in mice during laser irradiation were recorded with an infrared camera at different time points. Photos of tumours visualized the tumour changes for 12 days, and the tumour sizes were measured before and after photothermal therapy at different time points using a vernier caliper. The volumes of tumours were calculated as follows: the

volume = (tumour length) × (tumour width)2/2. After that, the tumour or healing tissues were frozen rapidly before H&E staining analysis.

***In vitro* computerized tomography (CT) imaging and spectral CT imaging CT of XG-ReS_2 suspension**

To study the CT and spectral CT imaging properties of XG-ReS_2 suspension *in vitro*, XG-ReS_2 suspension and iohexol solutions with equivalent element (Re or I) concentrations (0, 20, 40, 60. 80, 100, 120, 140, 160 mM) were added in 1.5 mL centrifuge tubes, respectively. Then CT scanning was performed on a 2 × 192 slice dual-source CT system (Somatom Force, Siemens Healthineers, Erlangen, Germany) with the following parameters: tube voltage 120 kV, adaptive tube current, slice thickness 0.5 mm, the field of view 80 × 80 mm. The CT images and CT values were analyzed with *syngo.via*. The spectral CT images were recorded on the same CT system with the following parameters: rotation time = 250 ms; adaptive tube current; tube voltage 90/150Sn. We reconstructed spectral CT images (0.5 mm slice thickness and 0.25 mm increment) with Advanced Modeled Iterative Reconstruction (ADMIRE) strength of 4. Virtual monochromatic images were reconstructed at the photon energies range of 40-140 keV with a 10-keV increment. The CT images and CT values in Spectral CT were analyzed by syngo.via.

***In vivo* CT imaging and spectral CT imaging CT of XG-ReS_2 suspension.**

For the gastrointestinal (GI) Tract, Kunming mice were fasted for 12 hours before imaging to clear GI tract contents. Before CT & spectral CT imaging, mice were anesthetized with 4% chloral hydrate. Then the mice were orally administrated with XG solution (2 mg/mL, 20 mL/**k**g), XG-ReS_2 suspension (20 mg ReS_2/mL**,** 20 mL/**k**g) and iohexol (80 mM I, 20 mL/**k**g). The mice without drug administration were regarded as control group. Then GI tract CT imaging and spectral CT imaging were carried out on SIEMENS dual-source CT system respectively with the same imaging sequence as those for *in vitro* CT and spectral CT imaging.

***In vitro* spectral CT imaging of UCR-ReS_2 capsule**

Based on the excellent results of XG-ReS_2 suspension. We further explore the spectral CT capability of the UCR-ReS_2 capsule. We compared UCR-ReS_2 (40 mg/mL, suspension and capsule products) with commonly used X-ray-sensitive contrast agents ($BaSO_4$ and iohexol, the same element concentration of Ba & Re & I) in spectral CT imaging. Because $BaSO_4$ is insoluble in water, we prepared it into ALG-Ca^{2+}-$BaSO_4$ hydrogel and UCR-$BaSO_4$ suspension for comparison to eliminate the interference of ALG-Ca^{2+} hydrogel and UCR suspension. Then spectral CT imaging was carried out on SIEMENS dual-source CT system respectively with the same imaging sequence as those for *in vitro* spectral CT imaging of XG-ReS_2 suspension. Virtual monochromatic images were reconstructed at the photon energies range of 40-160 keV with a 20-keV increment.

***In vivo* spectral CT imaging and GI transit score of UCR-ReS_2 capsule**

For GI transit imaging, fifteen SD rats (250 g ~ 270 g, male) were divided into three groups: intraperitoneal injection (ip.) of vincristine (VCR) as the experiment group, the treatment group injected with AM251 (a cannabinoid receptor inhibitor) after VCR, and the intraperitoneal

injection of normal saline (NS) as the control group. These rats will be administered orally with UCR-ReS_2 capsules (3 pieces, 40 mg/mL ReS_2) with a gastric gavage device and scanned in a SIEMENS CT imaging system at different time points for a total of 8 hours of observation (**Fig. S12**). We use different pre-processing methods for different groups. To display the outline of the GI tract well, the rats treated with an oral iohexol solution 2 hours after the oral capsules should be noted.

According to the results of spectral CT, we assign the position of the material in the GI tract at different time points. Use the scoring method of **Table S1** and calculate the total score by adding the scores of each capsule.

***In vivo* toxicity**

Kunming mice (18-20 g) were randomly divided into four groups (n = 3 in each group). The experimental and control groups of mice were treated with ALG-Ca^{2+}-ReS_2 hydrogel by subcutaneous injection (100 μL, 5 mg/mL), XG-ReS_2 suspension by oral administration (400 μL, 20 mg/mL), PBS by subcutaneous injection (100 μL, pH 7.4, 10 mM) and oral administration (400 μL, pH 7.4, 10 mM), respectively. The mice's body weight and survival state were monitored every other day. On the 15th day, all the mice were sacrificed, and the main organs (including heart, liver, spleen, lung, kidney and digestive tract of the oral group) were collected. After that, the tissues were fixed in a 4% formaldehyde solution before hematoxylin-eosin (H&E) staining analysis. The blood samples were centrifugated at 3000 rpm for 10 min to separate and collect the supernatant serum. Then, the blood biochemistry biomarkers were analyzed, which included aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total protein (TP) and albumin (ALB) for liver function assessment, and blood urea nitrogen (BUN) for kidney function evaluation.

SD rats (190 g) were randomly divided into two groups (n = 3 in each group). The experimental and control groups of mice were treated with UCR-ReS_2 capsules by oral administration (3 pieces, 40 mg/mL ReS_2) and empty capsules by oral administration (3 pieces), respectively. The rat's body weight and survival state were monitored every other day. On the 15th day, all the rats were sacrificed, and the main organs (including heart, liver, spleen, lung, kidney and digestive tract) were collected. After that, the tissues were fixed in a 4% formaldehyde solution before H&E staining analysis. The blood samples were centrifugated at 3000 rpm for 10 min to separate and collect the supernatant serum. Then, the blood biochemistry biomarkers were analyzed, which included AST, ALT, ALP, TP and ALB for liver function assessment, and BUN for kidney function evaluation.

Statistical analysis

All statistical data were recorded as indicated as mean ± standard deviation (SD). Statistical differences were compared with a two-tailed t-test and analysis of variance (ANOVA), and $p < 0.05$ is considered statistically significant.

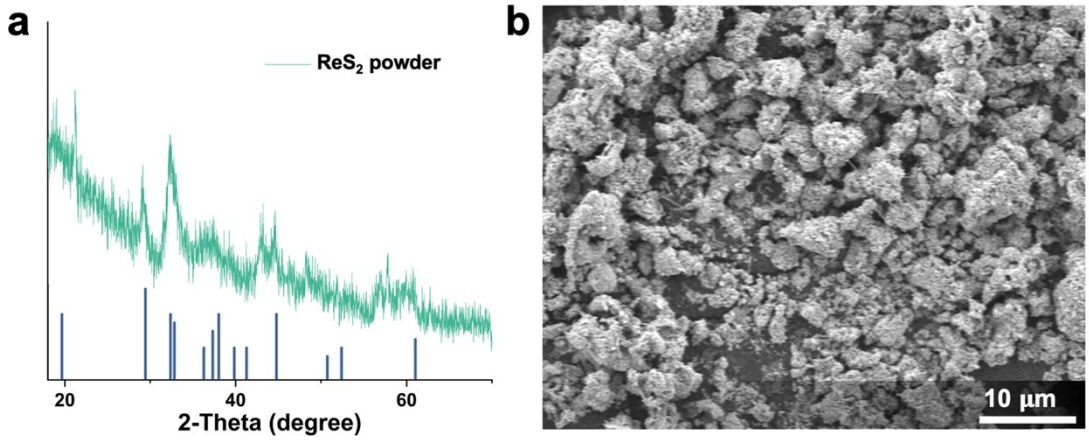

Fig. S1. Characterization of ReS_2 powder. **a.** XRD pattern of ReS_2 powder. **b.** SEM image of ReS_2 powder.

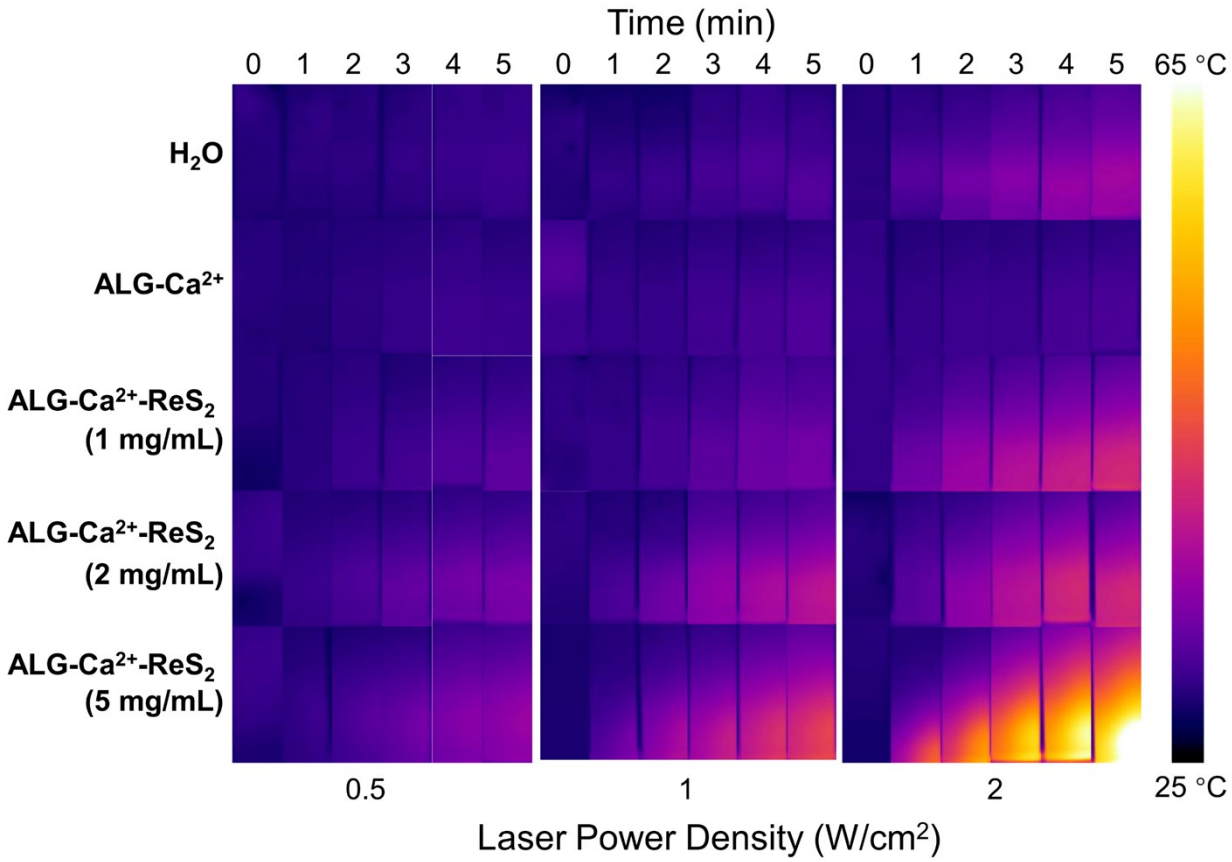

Fig. S2. Infrared images of ultrapure water, ALG-Ca^{2+} hydrogel and ALG-Ca^{2+}-ReS_2 hydrogel with concentrations of ReS_2 powder of 1, 2 and 5 mg/mL under a 1064 nm laser irradiation (0.5 W/cm^2, 1.0 W/cm^2, 2.0 W/cm^2) at room temperature.

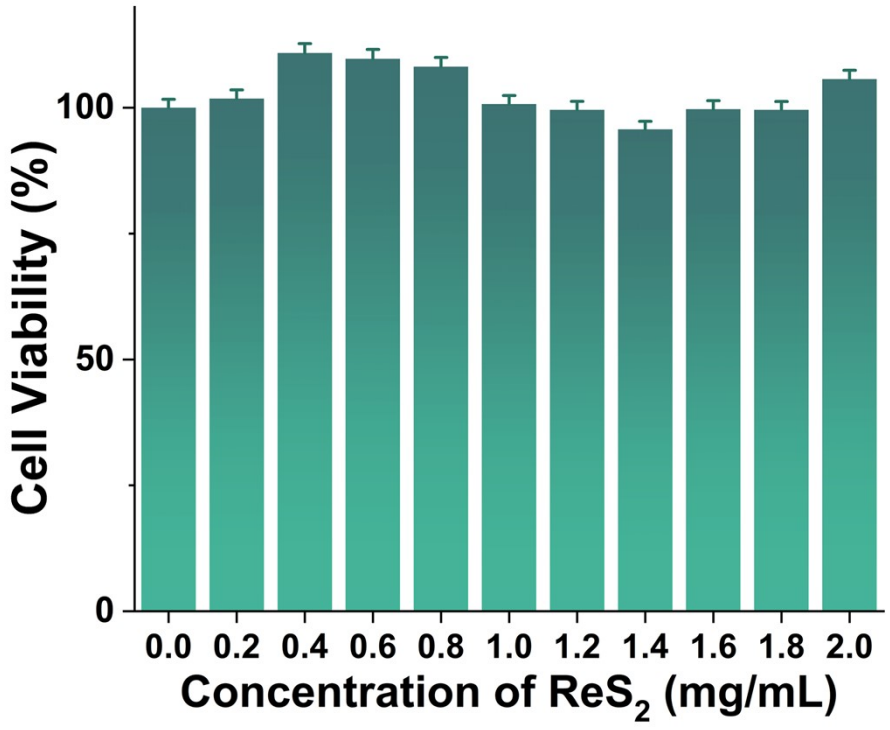

Fig. S3. Cell viability of 4T1 cells treated with ALG-Ca^{2+}-ReS_2 hydrogel after 24 h with different concentrations of ReS_2 powder (n = 5).

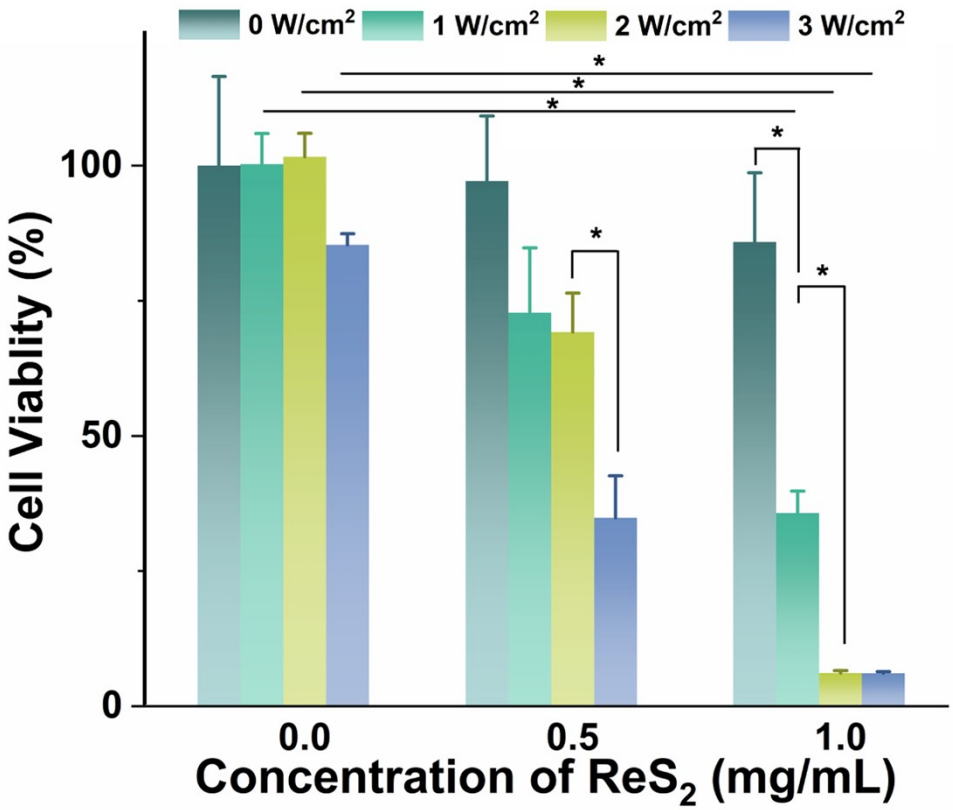

Fig. S4. Viabilities of 4T1 cells after incubation with ALG-Ca^{2+}-ReS_2 hydrogel (0.5 and 1 mg/mL) under a 1064 nm laser exposure at different power densities (1.0, 2.0 and 3.0 W/cm^2) or not for 10 min (n = 3). Cells without any treatment were regarded as the control.

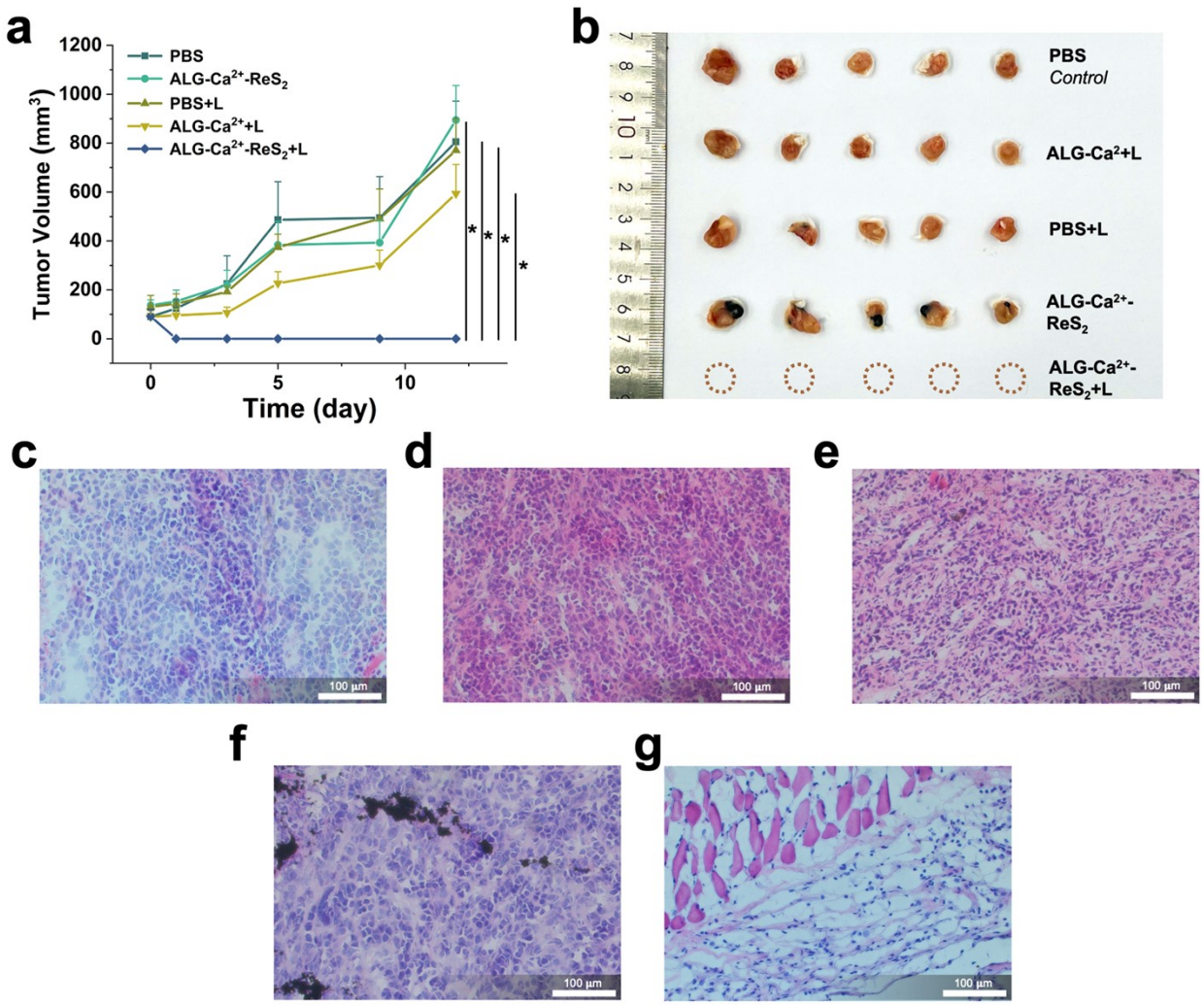

Fig. S5. Photothermal therapy of tumours using ALG-Ca^{2+}-ReS_2 hydrogel. **a.** The relative volume curves of tumours with various treatments: PBS, ALG-Ca^{2+}-ReS_2 hydrogel, PBS + laser irradiation (1064 nm, 1 W/cm^2, 5 min), ALG-Ca^{2+} hydrogel + laser irradiation (1064 nm, 1 W/cm^2, 5 min), ALG-Ca^{2+}-ReS_2 hydrogel + laser irradiation (1064 nm, 1 W/cm^2, 5 min) (n = 5). *$p < 0.05$. **b.** Photo of tumour masses exfoliated from tumour-bearing mice after different treatments (PBS, ALG-Ca^{2+}-ReS_2 hydrogel, PBS + laser irradiation, ALG-Ca^{2+} hydrogel + laser irradiation and ALG-Ca^{2+}-ReS_2 hydrogel + laser irradiation). **c-g.** The H&E staining images of the tumour site with various treatments: **(c)** PBS only, **(d)** ALG-Ca^{2+} hydrogel + laser irradiation (1064 nm, 1 W/cm^2, 5 min), **(e)** PBS + laser irradiation (1064 nm, 1 W/cm^2, 5 min), **(f)** ALG-Ca^{2+}-ReS_2 hydrogel, **(g)** ALG-Ca^{2+}-ReS_2 hydrogel + laser irradiation (1064 nm, 1 W/cm^2, 5 min).

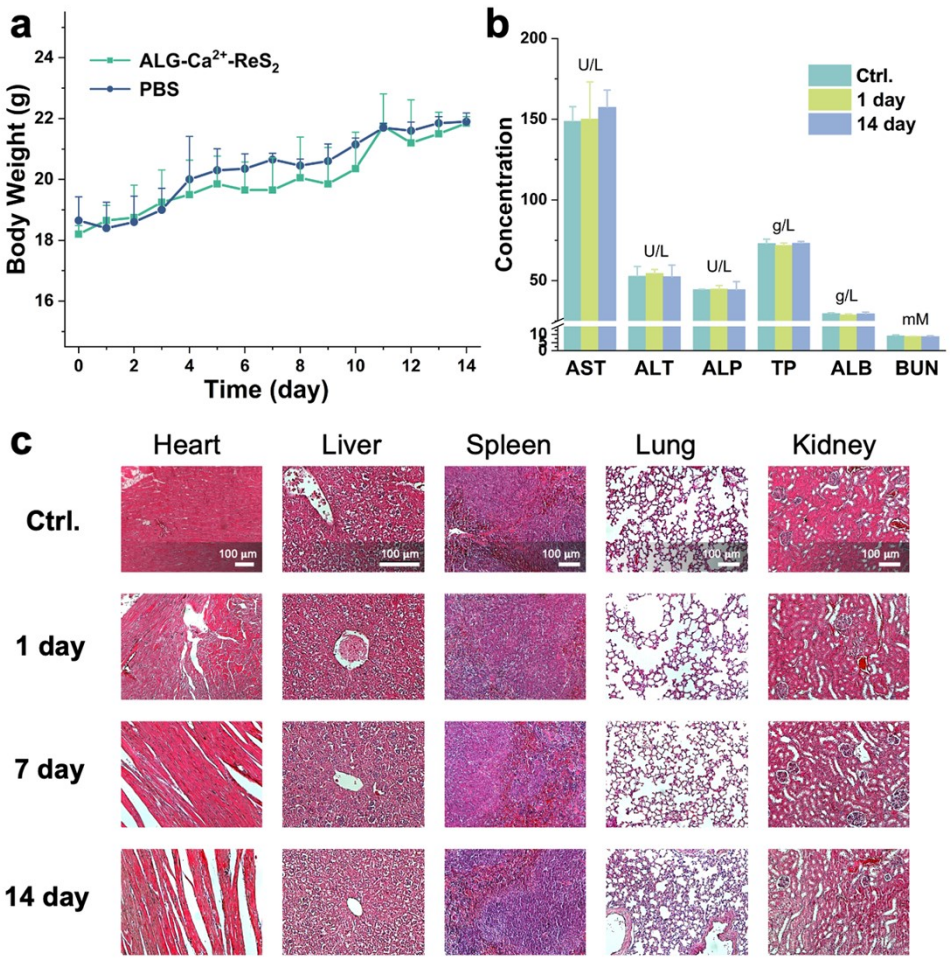

Fig. S6. Toxicity of ALG-Ca^{2+}-ReS_2 hydrogel *in vivo*. **a.** Body weight changes of Kunming mice after subcutaneous injection of ALG-Ca^{2+}-ReS_2 hydrogel. PBS-treated mice were set as control (n = 3). **b.** The blood biochemistry analysis of Kunming mice after subcutaneous injection of ALG-Ca^{2+}-ReS_2 hydrogel (n = 3). **c.** H&E staining of vital organs (heart, liver, spleen, lung and kidney) after administration of ALG-Ca^{2+}-ReS_2 hydrogel.

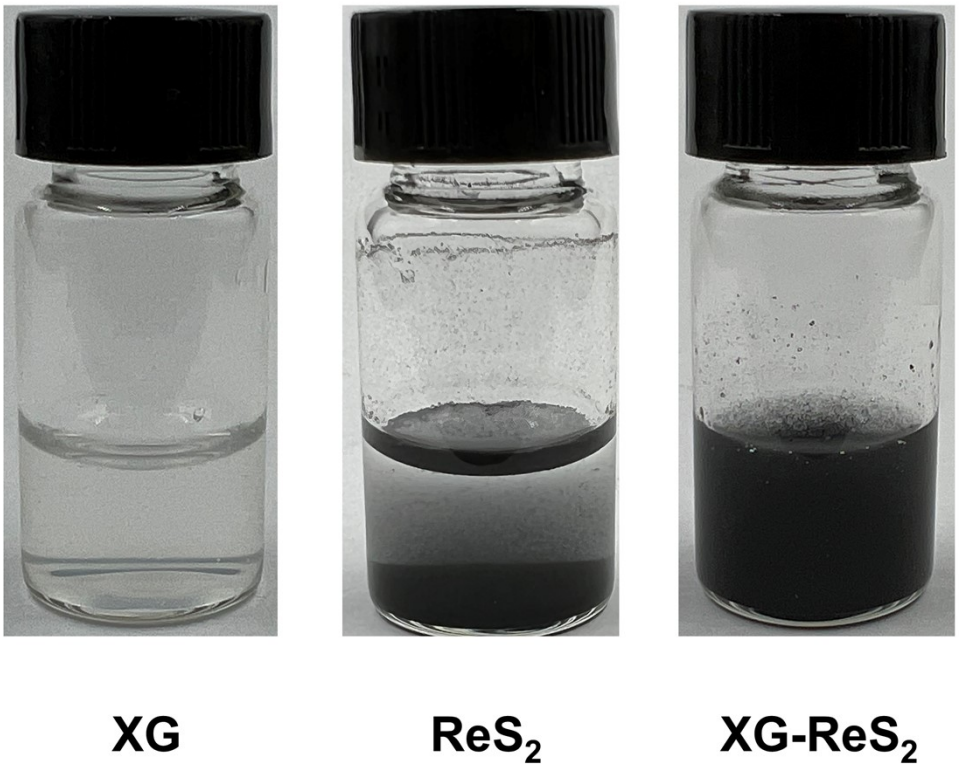

Fig. S7. Photos of XG solution, ReS_2 powders dissolved in water, and XG-ReS_2 suspension.

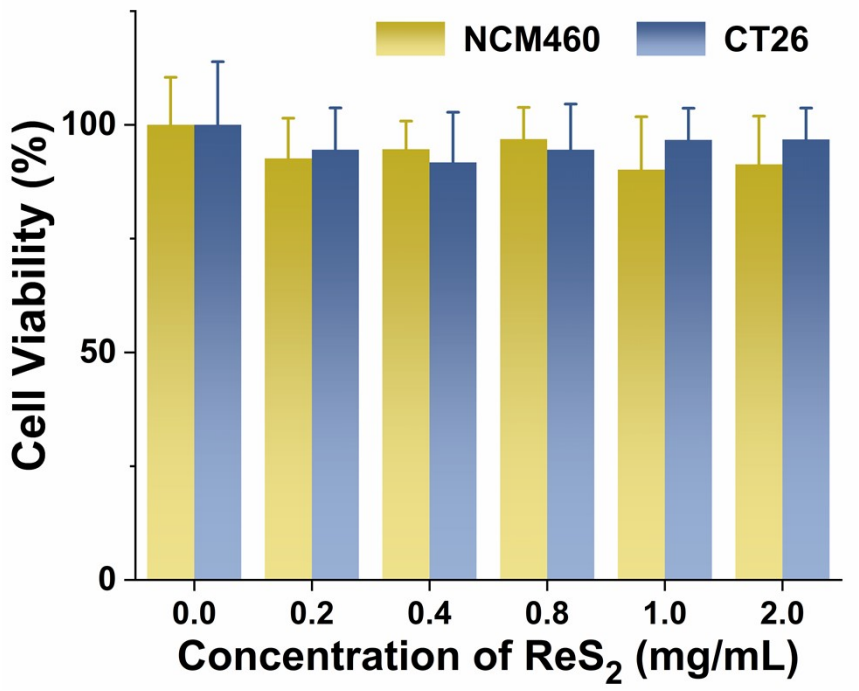

Fig. S8. Cell viability of NCM460 cells and CT26 cells after 24 h incubation with XG-ReS_2 suspension (n = 3).

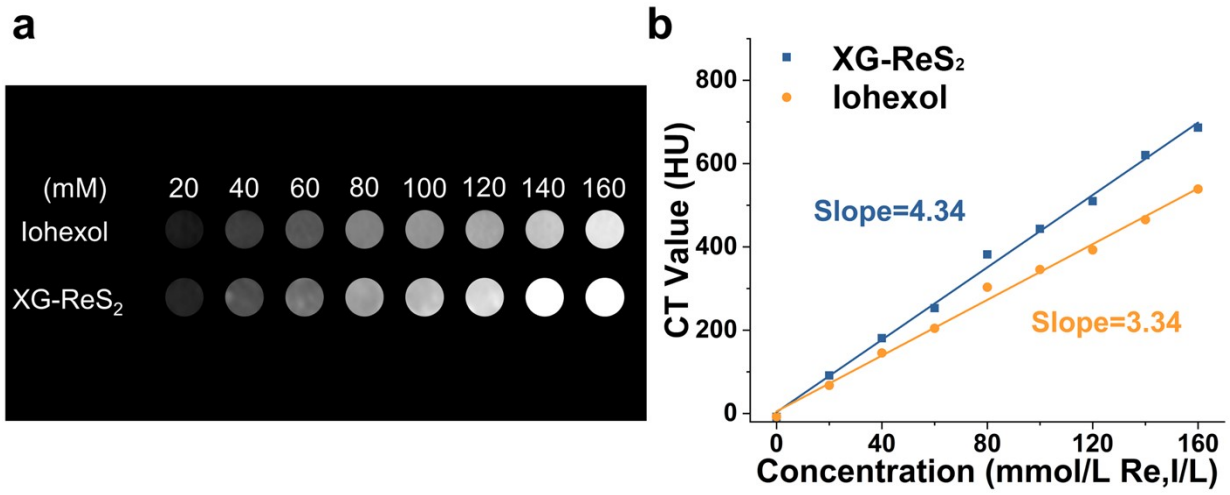

Fig. S9. CT imaging and Hounsfield unit (HU) curves of XG-ReS_2 suspension. CT images **(a)** and HU curves **(b)** of different concentrations (20-160 mM Re or I) of XG-ReS_2 suspension and iohexol.

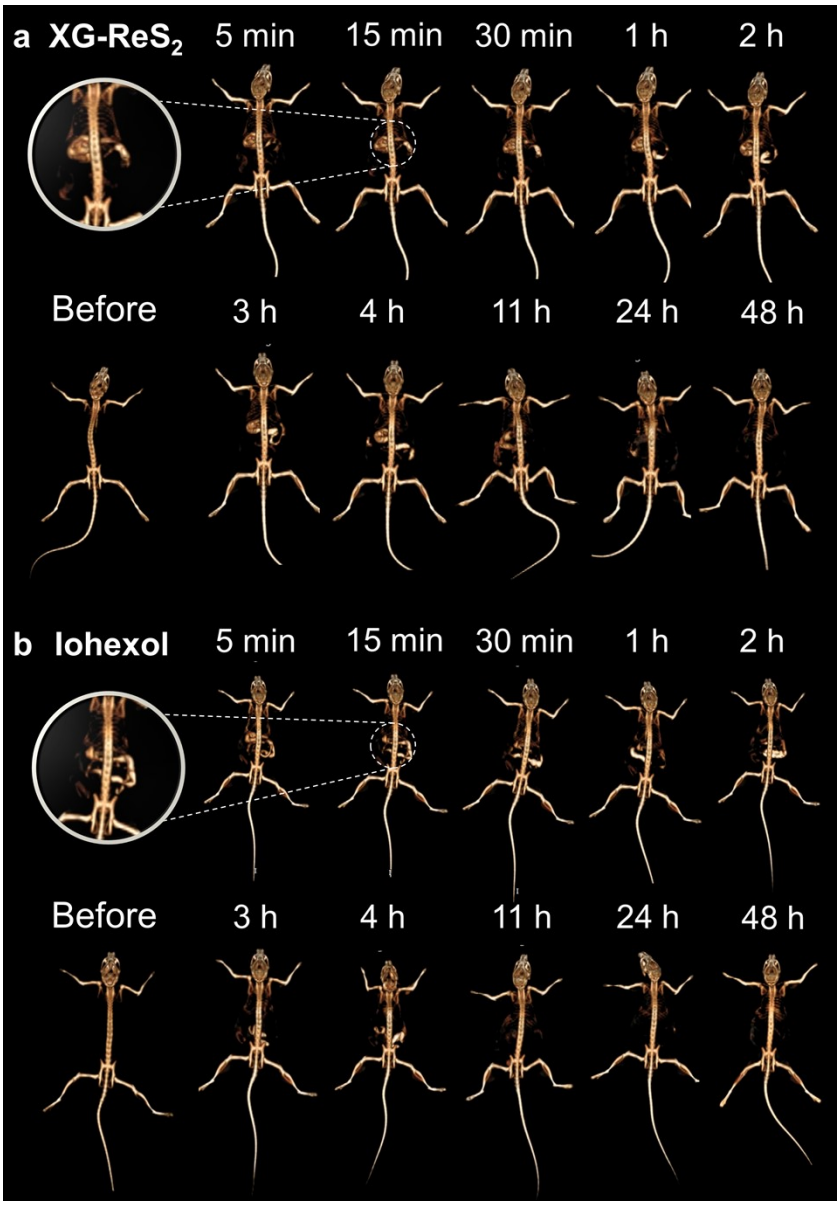

Fig. S10. CT imaging of GI tract using XG-ReS_2 suspension and iohexol *in vivo*. CT images of upper GI tract at various time points after oral administration of **a.** XG-ReS_2 suspension and **b.** iohexol.

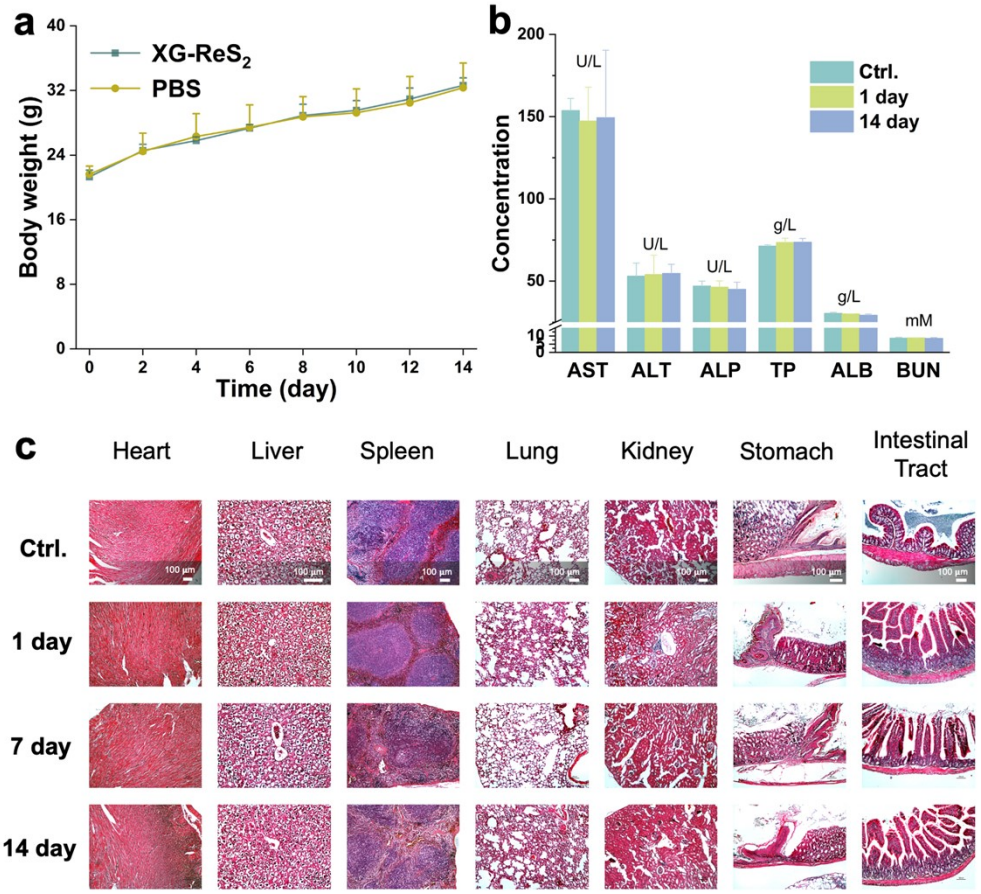

Fig. S11. Toxicity of XG-ReS_2 suspension *in vivo*. **a.** Body weight changes of Kunming mice after oral treatment of XG-ReS_2 suspension. PBS-treated mice were set as control (n = 3). **b.** The blood biochemistry analysis of Kunming mice after oral treatment of XG-ReS_2 suspension (n = 3). **c.** *In vivo* toxicity XG-ReS_2 suspension. H&E staining of vital organs (heart, liver, spleen, lung, kidney, stomach and intestinal tract) after administration of XG-ReS_2 suspension.

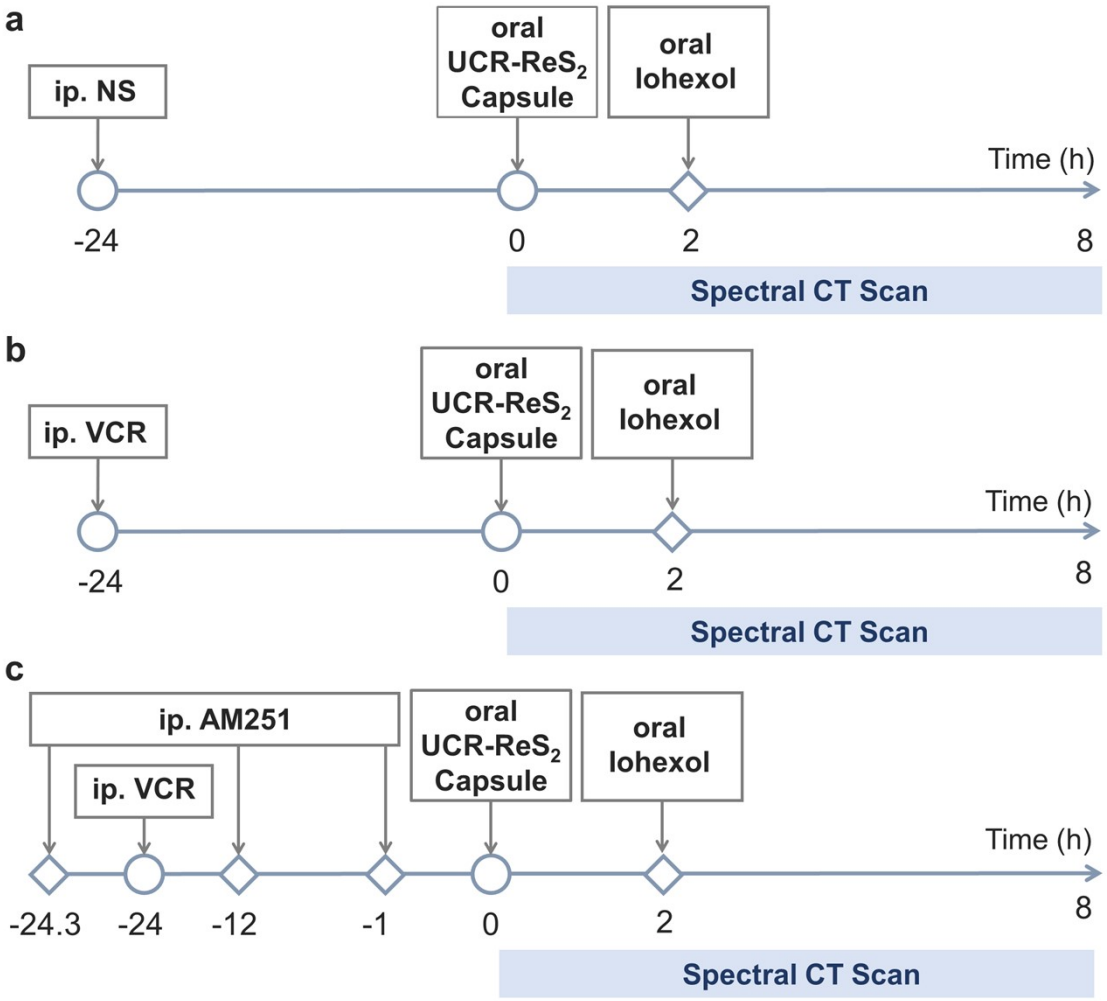

Fig. S12. Schematic diagram of UCR-ReS_2 capsule for spectral CT imaging *in vivo*. **a.** Rats with intraperitoneal (ip.) injection of normal saline (NS) were set as control group. **b.** Rats with intraperitoneal injection of VCR were set as enteroparalysis group. **c.** The treatment group for enteroparalysis with intraperitoneal injection of AM251.

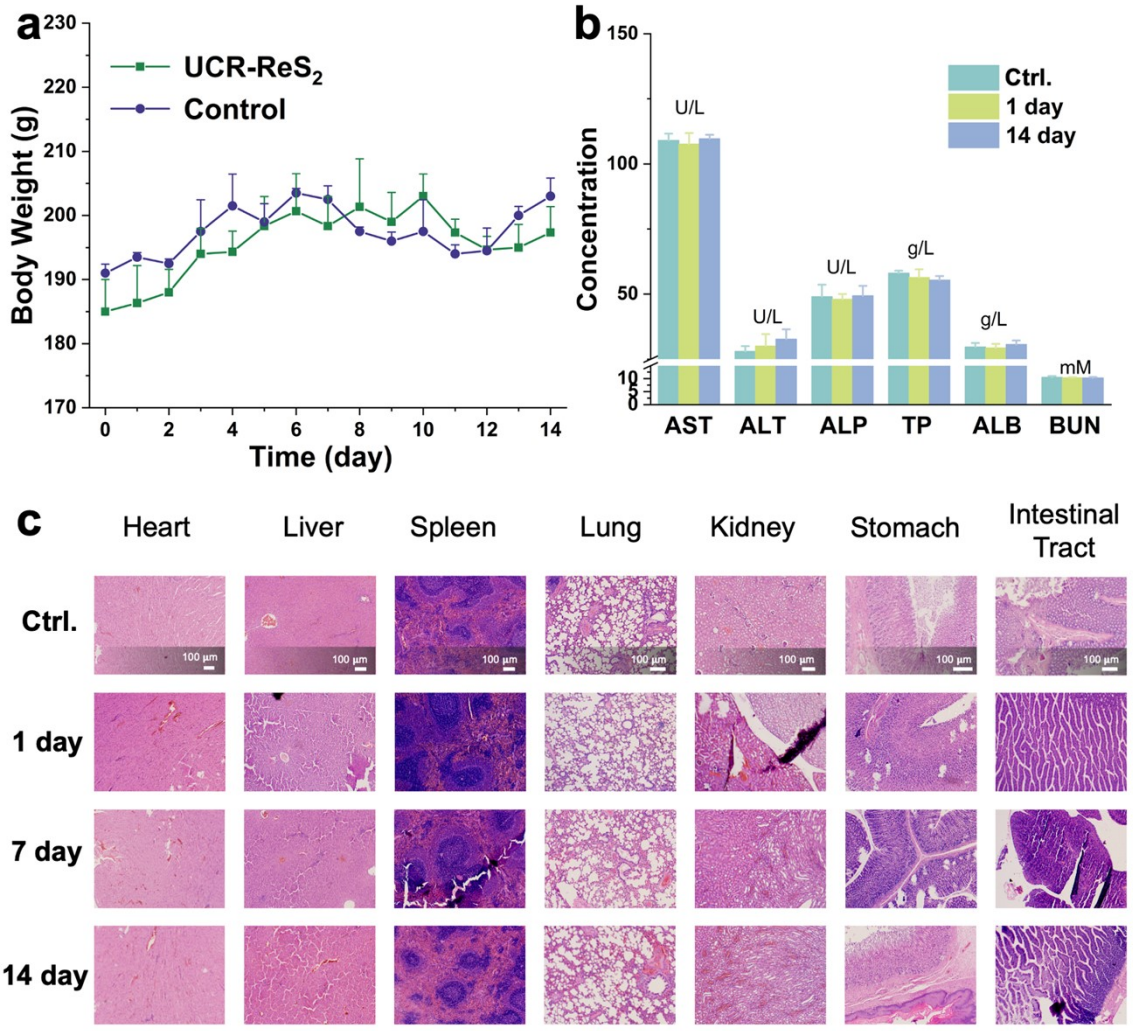

Fig. S13. Toxicity of UCR-ReS_2 capsules *in vivo*. **a.** Body weight changes of SD rats after oral treatment of UCR-ReS_2 capsules. Empty capsule-treated mice were set as control (n = 3). **b.** The blood biochemistry analysis of SD rats after oral treatment of UCR-ReS_2 capsules (n = 3). **c.** H&E staining of vital organs (heart, liver, spleen, lung, kidney, stomach and intestinal tract) after administration of UCR-ReS_2 capsules.

Table S1. Score standards of digestive tract capsule position

Location	Stomach	Proximal Small Bowel	Distal Small Bowel	Caecum	Colon	Eliminate from the Body
Score	**0**	**1**	**2**	**3**	**4**	**5**