Proof-of-concept study of the NOTI chelating platform:

Preclinical evaluation of ^{64}Cu-labeled mono- and trimeric

c(RGDfK) conjugates

SUPPORTING INFORMATION

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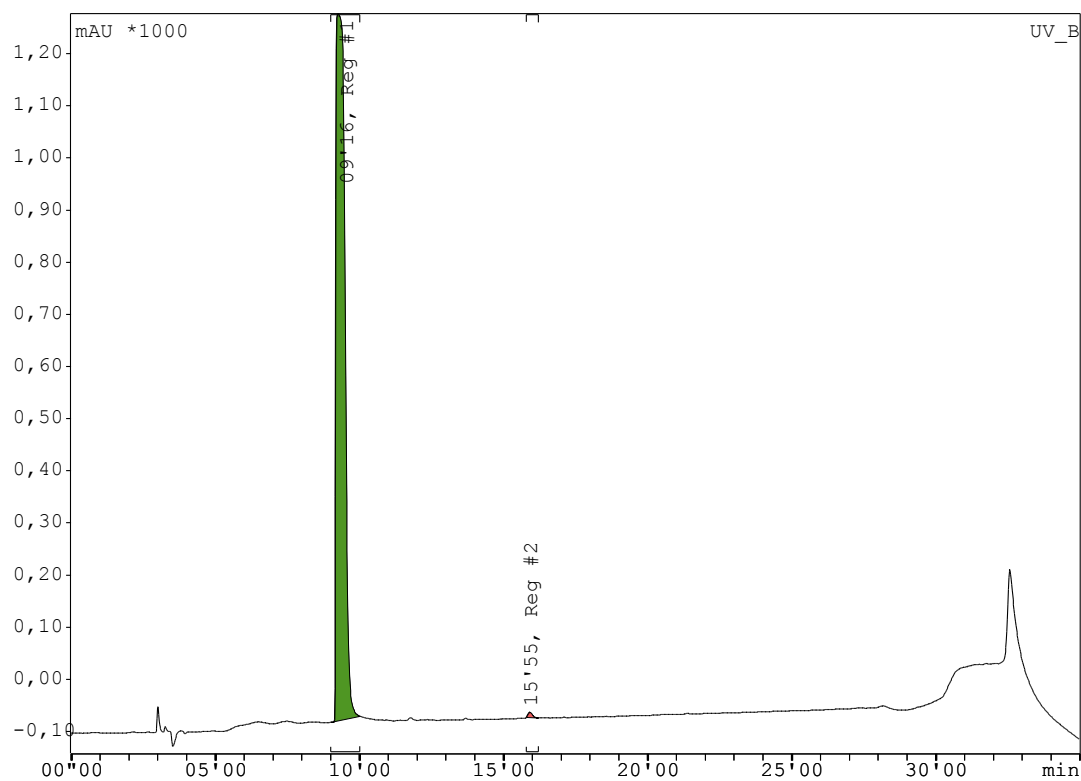
Characterization data compound 4

Figure S1. Representative analytical HPLC chromatogram of **4** (UV/vis trace).
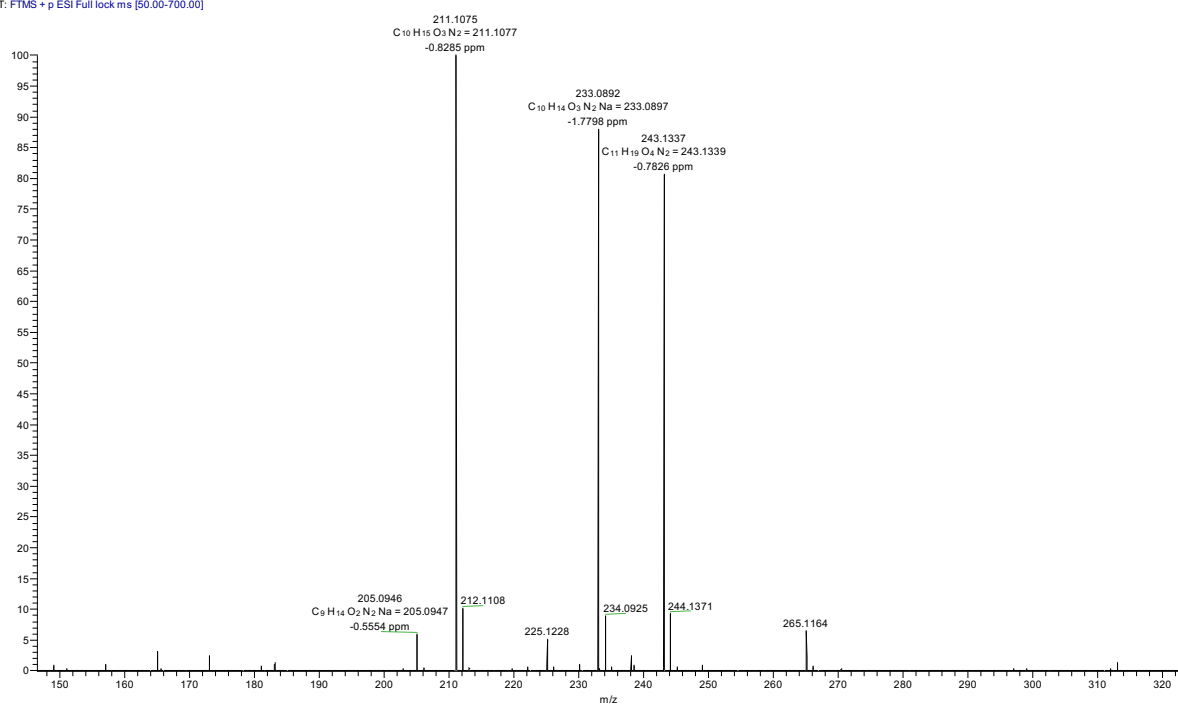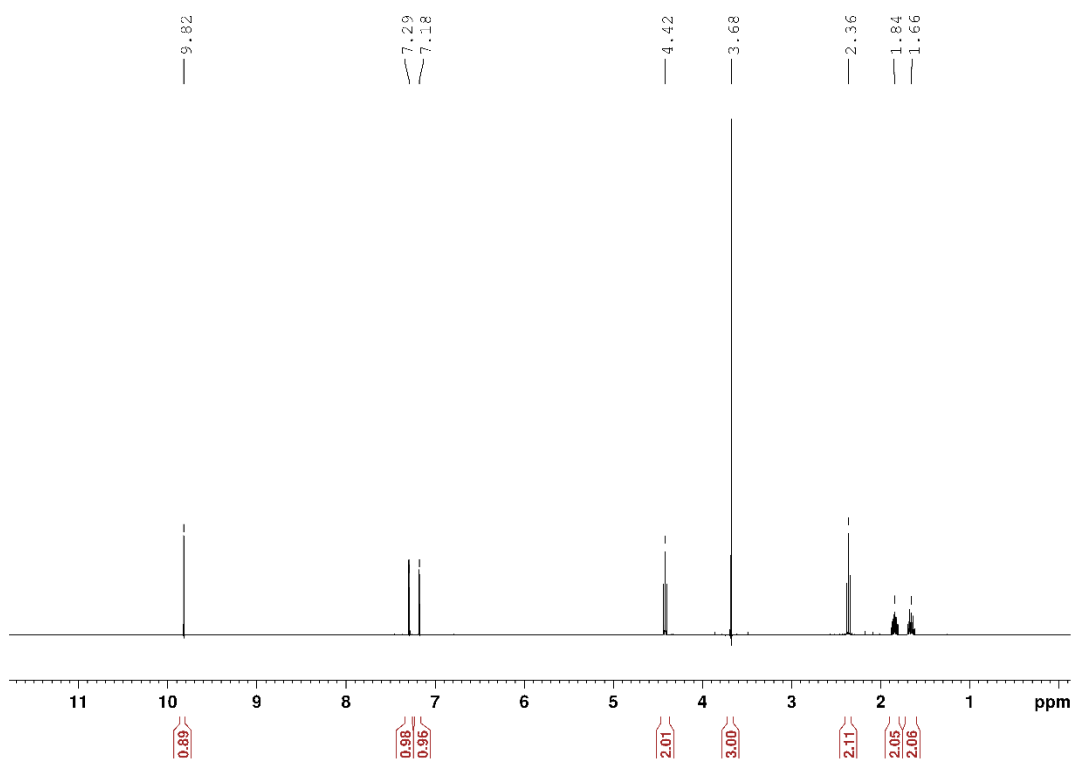

Figure S2. HR-ESI(+) spectrum of **4**.

Figure S3. Proton NMR of **4**.

Characterization data compound 5

Figure S4. Representative analytical HPLC chromatogram of **5** (UV/vis trace).

Figure S5. HR-ESI(+) spectrum of **5**.

Figure S6. Proton NMR of **5**.

Characterization data compound 6

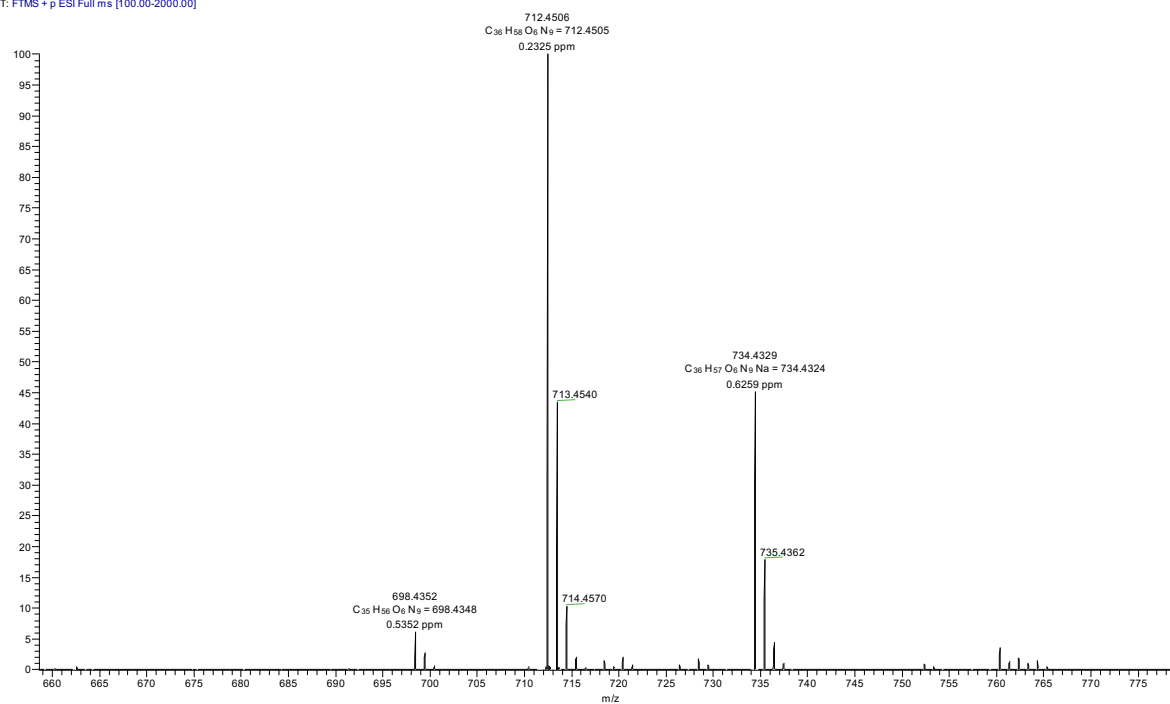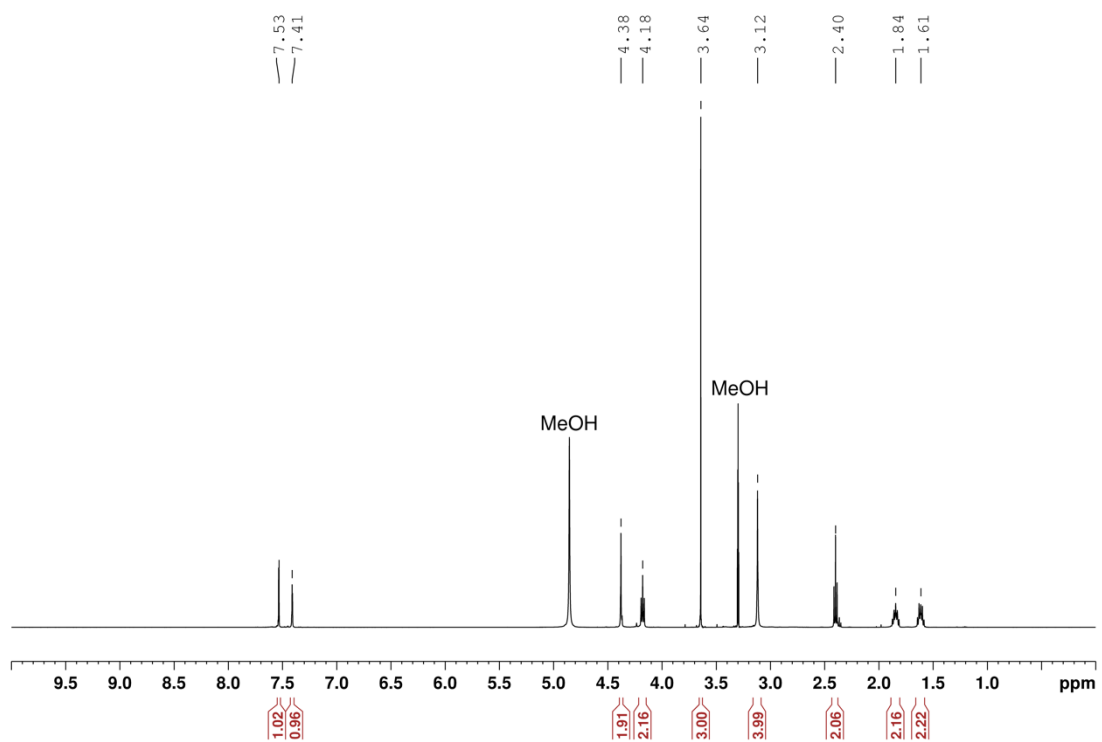Figure S7. Representative analytical HPLC chromatogram of **6** (UV/vis trace).

Figure S8. HR-ESI(+) spectrum of **6**.

Figure S9. Proton NMR of **6**.

Characterization data of Cu-8/[⁶⁴Cu]Cu-8

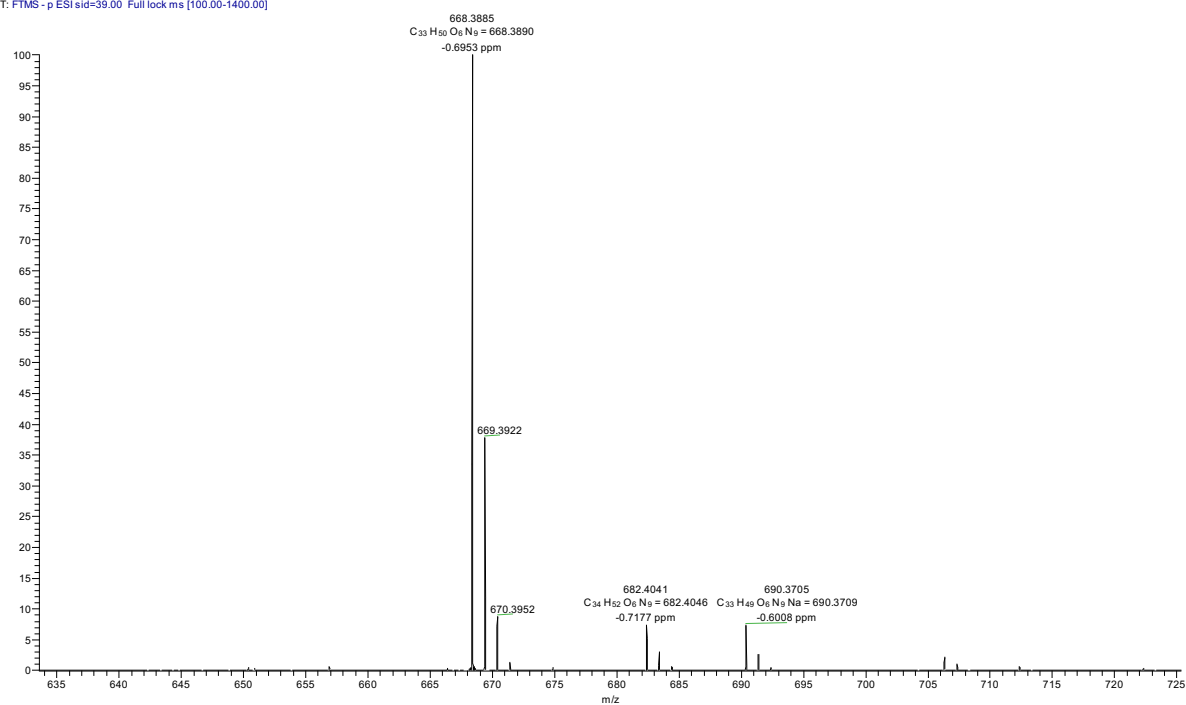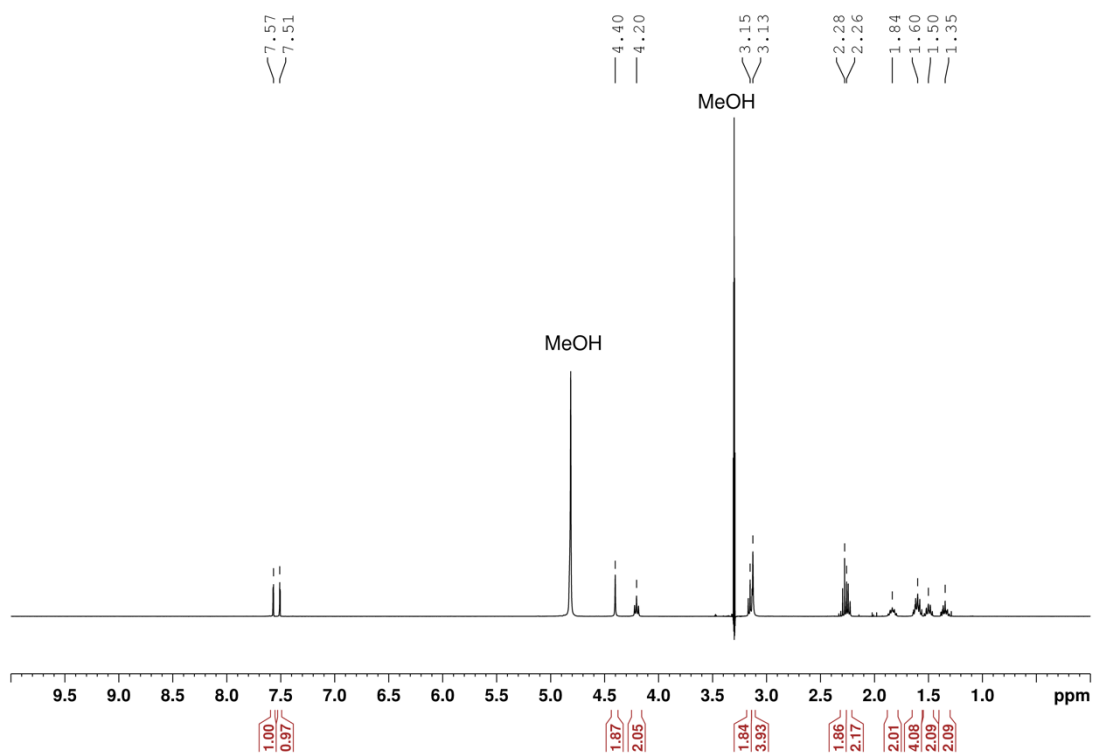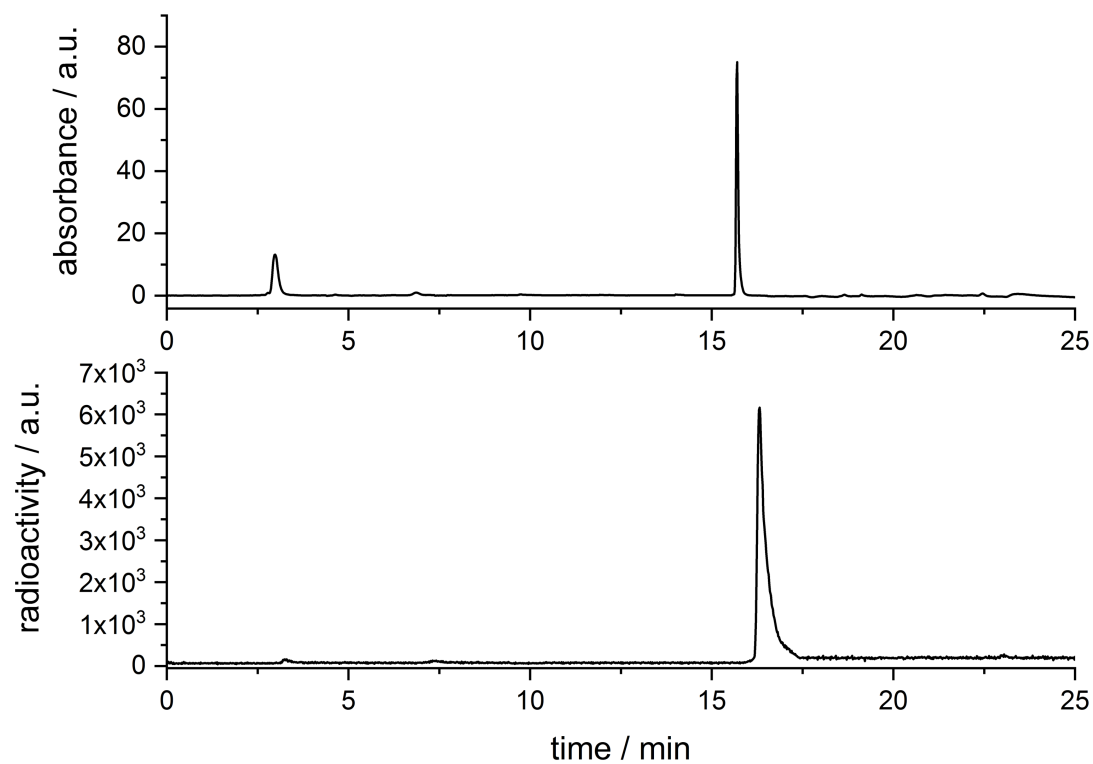Figure S10. Representative analytical HPLC chromatograms of Cu-**8** (UV/vis; top) and [⁶⁴Cu]Cu-**8** (radioactivity; bottom).
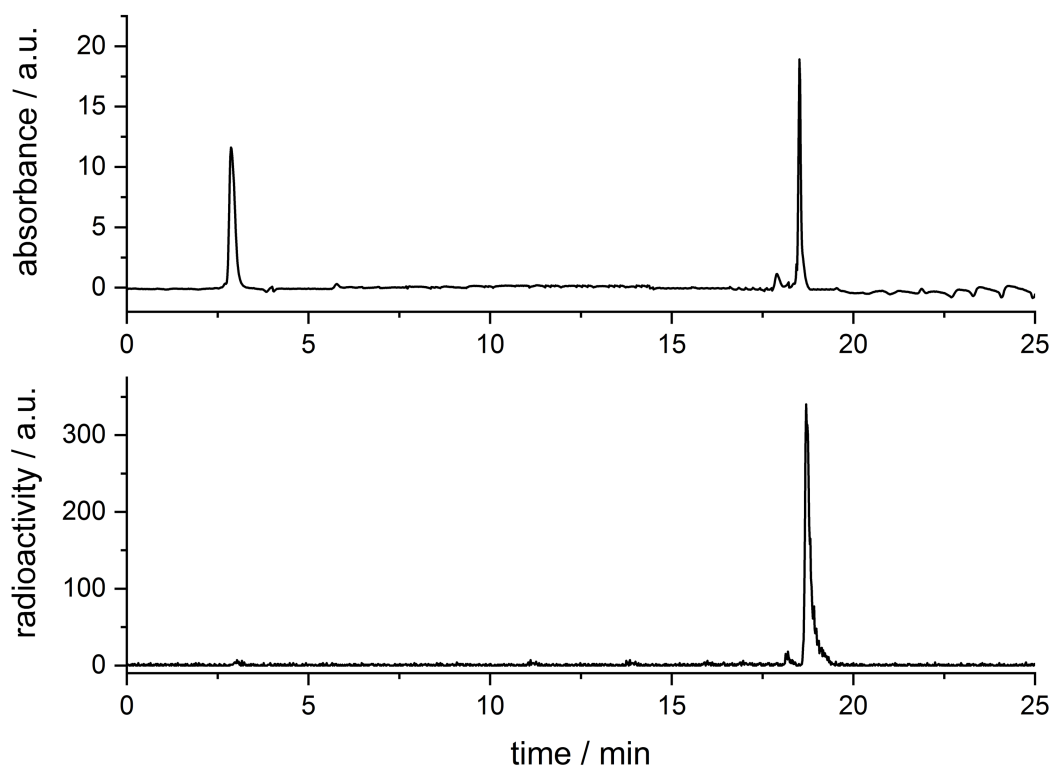
Characterization data of Cu-9/[^{64}Cu]Cu-9

Figure S11. Representative analytical HPLC chromatograms of Cu-**9** (UV/vis; top) and [^{64}Cu]Cu-**9** (radioactivity; bottom).

Table S1. *Ex vivo* biodistribution of [^{64}Cu]Cu-**8** and [^{64}Cu]Cu-**9** in mice bearing $\alpha_v\beta_3$-positive U-87MG tumors at 1 h p.i. along with blocking studies. Data are expressed as %IA g^{-1} and represent mean ± SD (n = 3).

Organ	[^{64}Cu]Cu-**8**			[^{64}Cu]Cu-**9**		
	1 h	1 h blockade	*P* value*	1 h	1 h blockade	*P* value*
Blood	0.16 ± 0.05	0.05 ± 0.02	0.0199	0.34 ± 0.05	0.27 ± 0.09	0.3042
Heart	0.30 ± 0.02	0.06 ± 0.01	0.0001	1.03 ± 0.13	0.52 ± 0.07	0.0037
Lung	0.50 ± 0.34	0.14 ± 0.13	0.1653	2.81 ± 0.53	1.52 ± 0.23	0.0186
Spleen	0.72 ± 0.15	0.16 ± 0.01	0.0026	1.92 ± 0.24	0.65 ± 0.21	0.0011
Liver	2.75 ± 0.05	1.79 ± 0.26	0.0034	5.63 ± 1.61	3.32 ± 0.09	0.0675
Pancreas	0.30 ± 0.20	0.04 ± 0.01	0.0931	0.94 ± 0.37	0.46 ± 0.13	0.1038
Stomach	1.41 ± 0.43	0.13 ± 0.07	0.0068	1.66 ± 1.23	0.66 ± 0.37	0.2493
Intestine	0.73 ± 0.20	0.21 ± 0.05	0.0125	2.11 ± 1.15	1.73 ± 0.65	0.6462
Kidney	2.67 ± 0.33	1.59 ± 0.15	0.0070	7.65 ± 0.52	5.45 ± 0.59	0.0084
Muscle	0.28 ± 0.20	0.03 ± 0.01	0.0923	0.41 ± 0.06	0.29 ± 0.27	0.5046
Bone	0.35 ± 0.08	0.09 ± 0.03	0.0206	0.66 ± 0.23	0.38 ± 0.13	0.1289
Tumor	2.30 ± 0.28	0.26 ± 0.02	0.0002	5.57 ± 0.83	2.24 ± 0.11	0.0024
Tumor-to-blood	14.99 ± 3.05			16.22 ± 0.20		
Tumor-to-kidney	0.86 ± 0.04			0.73 ± 0.11		
Tumor-to-liver	0.83 ± 0.10			1.03 ± 0.26		
Tumor-to-muscle	10.53 ± 4.79			14.08 ± 3.83		

* statistical analysis of normal *vs.* blocking group using unpaired two-tailed t-test.