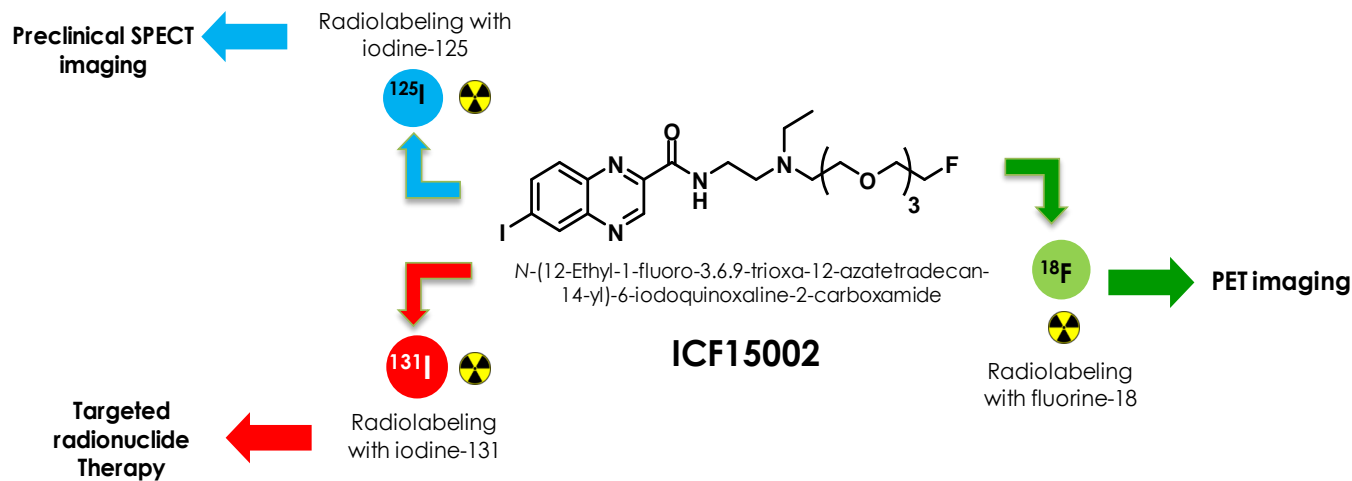


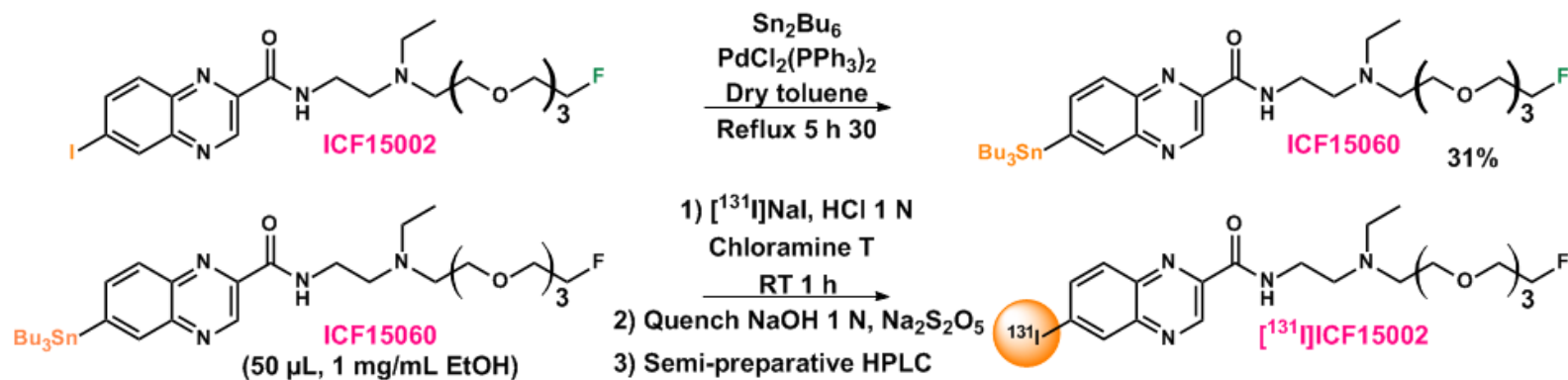
Supplementary figures

Figure 1: (A) Bimodal Concept (Imaging/Therapy). (B) Radiosynthesis of [¹³¹I]ICF15002. (C) Chromatogram of [¹³¹I]ICF15002.

A



B



C

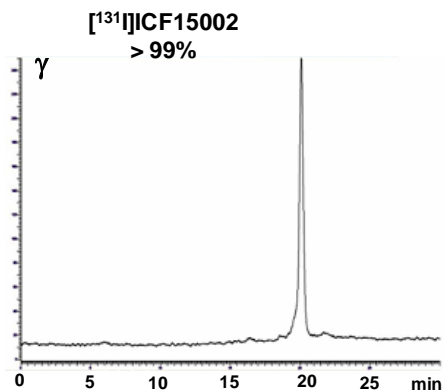


Table 1: *Ex vivo* biodistribution of [¹⁸F]ICF15002 in tumor and tissues of B16BL6 primary melanoma-bearing C57BL/6J mice and human SK-MEL-3 primary melanoma-bearing Swiss nude mice. Data were obtained at 0.5, 1 and 2 h post i.v. injection of the radiotracer. Results were expressed as percentage of injected dose per gram of tissue (%ID/g) after decay correction.

	B16BL6 melanoma-bearing mice			SK-MEL-3 melanoma-bearing mice			A375 melanoma-bearing mice		
	0.5 h p.i.	1 h p.i.	2 h p.i.	0.5 h p.i.	1 h p.i.	2 h p.i.	0.5 h p.i.	1 h p.i.	2 h p.i.
Tumor	11.92±2.12	14.05±1.40	13.07±1.22	4.9± 0.70	7.06 ±1.23	3.42±0.38	2.00±1.01	1.15±1.13	1.23±0.26
Eyes	16.92±2.49	18.36±4.56	18.17±3.15	1.92± 0.43	2.66 ±0.21	2.58±0.80	1.83±0.08	1.65±0.57	2.27±0.50
Muscle	1.88±0.31	1.17± 0.12	0.92±0.15	1.7±0.26	1.7 ±0.18	1.50±0.36	1.67±0.34	1.59±0.61	1.43±0.80
Blood	1.37±0.60	1.42±0.31	1.12±0.24	1.7± 0.29	2.03± 0.28	1.62±0.31	1.93±0.21	1.60±0.37	1.67±0.77
Skin	2.11±0.29	1.44± 0.34	1.51±0.53	2.41± 0.44	2.26 ±0.19	1.78±0.36	2.56±0.47	1.87±0.22	1.61±0.29
Bone	2.67±0.12	1.40±0.15	1.96±0.51	1.8± 0.21	2.03±0.02	2.79±0.67	1.72±0.15	2.18±1.08	2.15±0.42
Stomach	7.55±2.35	4.41±1.34	2.48±0.88	3.33±0.92	3.46±0.43	2.62±0.72	3.43±2.19	4.50±4.03	3.35±2.79
Small intestine	7.93±0.86	7.58±2.08	4.28±1.18	5.51± 1.29	5.35±0.36	3.24±1.03	5.18±0.59	6.77±3.60	4.06±1.82
Colon+Faeces	4.16±0.32	7.17±2.94	6.05±1.72	3.61± 0.62	3.73±0.66	3.40±0.98	3.08±0.19	4.18±0.69	3.83±0.66
Ceacum	3.73±0.22	7.27±0.62	8.94±1.78	3.54± 1.06	5.14±0.53	5.51±1.44	3.62±0.77	5.69±1.99	6.25±0.56
Kidney	7.97±1.78	3.46±0.58	2.18±0.43	5.01± 0.61	2.82±0.08	2.18±0.38	4.74±1.32	3.76±2.07	2.37±0.95
Spleen	7.76±1.24	3.72±1.52	2.88±2.11	4.63± 1.32	2.4±0.24	1.96±0.39	3.72±0.08	2.49±0.82	2.04±1.01
Pancreas	3.34±0.69	2.09±0.51	1.33±0.28	2.36± 0.2	1.64±0.21	1.31±0.41	2.33±0.53	2.86±2.93	1.36±0.67
Liver	3.32±0.26	2.56±0.29	1.88±0.34	2.45± 0.12	2.19±0.15	1.80±0.30	2.58±0.50	2.75±1.42	2.30±1.30
Lung	4.87±0.87	1.86±0.16	1.65±0.11	3.61± 0.16	2.66±0.31	2.31±0.33	3.20±0.58	3.15±1.43	2.42±1.12
Heart	2.94±0.27	2.72±0.22	2.14±0.33	2.31± 0.25	2.26±0.11	2.24±0.43	2.16±0.22	2.55±0.73	2.13±0.93
Brain	1.66±0.10	1.82±0.10	1.39±0.25	1.66± 0.32	1.92±0.15	1.89±0.46	1.49±0.26	2.30±1.03	1.63±0.70
Tumour-to-muscle ratio	6.42±1.033	12.12±1.74	14.46±2.62	2.96±0.80	4.23±1.11	2.36±0.62	1.24± 0.71	0.97±1.23	1.06±0.64
Tumour-to-blood ratio	10.03±5.01	10.241±2.49	12.19±3.32	2.94±0.67	3.56±0.99	2.16±0.44	1.07±0.59	0.79±0.82	0.92±0.66
Tumour-to-bone ratio	4.47±0.81	10.11±1.43	7.13±2.21	2.76±0.59	3.46±0.59	1.27±0.31	1.18±0.62	0.62±0.71	0.59±0.20

Figure 2: (A) Effect of [¹³¹I]ICF15002 treatment (2 X 20 MBq) on B16BL6 murine melanoma tumor growth. [¹³¹I]ICF15002 was administered at day-7 and day-11 after inoculation. Arrows indicate treatment days. Tumor growth was evaluated by measuring the tumor volume of each mouse thrice per week during treatment and twice per week thereafter until a volume of 2 cm³ was reached. (B) Effect of [¹³¹I]ICF15002 on human melanoma SK-MEL-3 tumor growth. [¹³¹I]ICF15002 was administered at 25 MBq once weekly for 2 or 3 weeks. Tumor growth was evaluated by measuring the tumor volume of each mouse thrice per week during treatment and twice per week thereafter until a volume of 2 cm³ was reached. Data are expressed as the percentage variation in tumor volume relative to baseline. Data are expressed as the percentage variation in tumor volume relative to baseline.

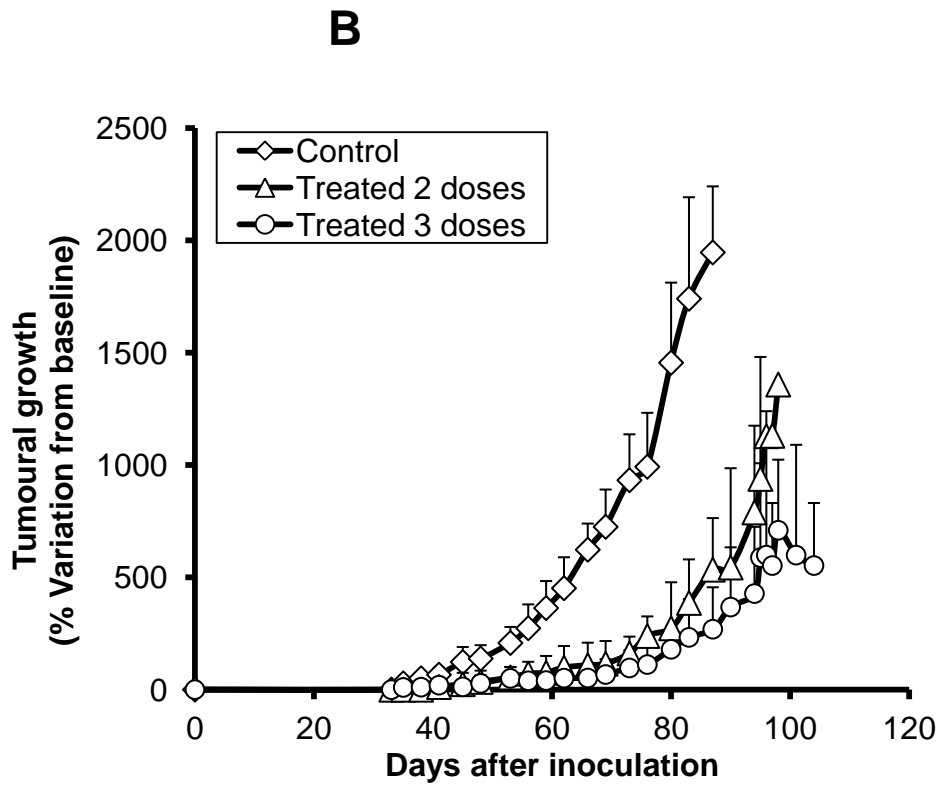
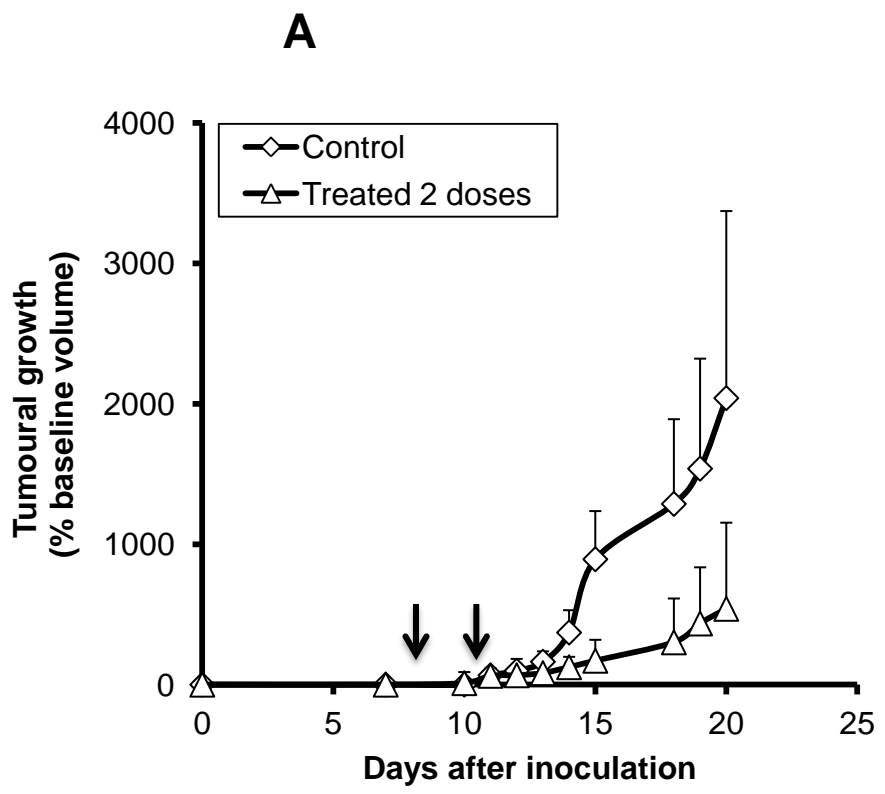


Table 2: *Ex vivo* biodistribution of [¹²⁵I]ICF15002 in tumor and tissues and organs in B16BL6 melanoma C57BL/6J bearing mice at different time points post tracer injection.

B16BL6 melanoma C57BL/6J-bearing mice

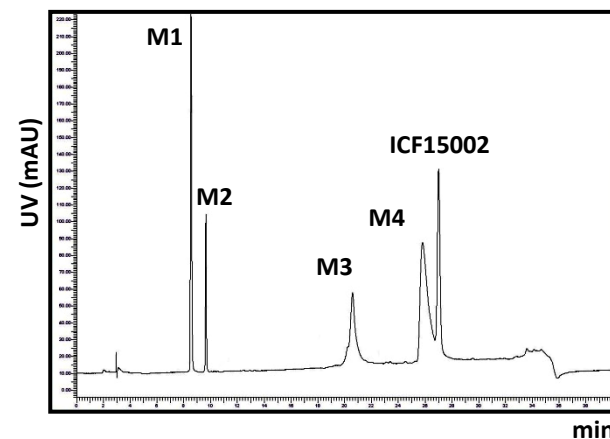
Organs	1 h	3 h	6 h	24 h	72 h	10 d
Blood	0.97±0.07	0.82±0.05	0.62±0.20	0.06±0.01	0.03±0.01	0.00±0.00
Tumor	11.99±3.52	17.69±1.10	12.04±4.39	10.47±3.22	8.74±0.38	1.20±0.54
Eyes	15.01±4.84	15.48±2.57	17.40±2.21	20.30±6.08	14.87±1.18	9.97±2.24
Liver	6.33±1.69	3.37±0.14	2.02±0.64	0.46±0.10	0.08±0.00	0.01±0.00
Kidney	4.75±0.71	3.14±1.27	1.56±0.82	0.15±0.02	0.24±0.04	0.04±0.03
Skin	1.04±0.06	1.34±0.72	0.62±0.31	0.17±0.00	0.50±0.26	0.05±0.06
Adipose	0.61±0.01	0.36±0.05	0.19±0.06	0.028±0.00	0.02±0.00	0.01±0.01
Muscle	0.55±0.16	0.30±0.04	0.17±0.07	0.02±0.00	0.02±0.00	0.01±0.06
Bone	0.79±0.09	0.48±0.03	0.30±0.10	0.03±0.00	0.02±0.01	0.01±0.01
Colon	4.51±4.40	21.19±18.02	15.92±9.97	0.69±0.23	0.25±0.10	0.02±0.01
Ceacum	4.97±3.01	25.73±7.88	23.31±16.47	0.41±0.13	0.33±0.29	0.02±0.02
Small intestine	16.68±10.70	4.16±0.70	2.23±1.35	0.12±0.03	0.07±0.03	0.01±0.00
Stomach	9.2±1.49	4.53±0.94	7.39±4.08	0.54±0.25	0.16±0.05	0.03±0.01
Spleen	2.14±0.20	2.37±2.58	6.45±8.15	0.06±0.01	0.52±0.96	0.23±0.41
Pancreas	2.96±0.15	1.48±0.07	0.65±0.18	0.05±0.01	0.03±0.01	0.02±0.03
Lung	3.12±0.42	2.14±0.27	1.04±0.37	0.08±0.01	0.05±0.01	0.01±0.01
Heart	1.17±0.07	0.77±0.05	0.46±0.17	0.16±0.06	0.08±0.02	0.03±0.01
Brain	0.27±0.03	0.15±0.01	0.08±0.03	0.01±0.01	0.01±0.00	0.00±0.00
Testis	0.68±0.19	0.54±0.03	0.36±0.08	0.03±0.01	0.02±0.00	0.00±0.00
Thyroid	15.33±2.65	46.68±9.65	89.32±13.31	99.51±14.67	62.11±9.42	9.30±1.09

Table 3: (A) [¹²⁵I]ICF15002 metabolism in different tissues and fluids of B16BL6 primary melanoma-bearing C57BL/6J mice. **(B)** Analytical HPLC chromatogram of ICF15002 and its metabolites. [¹²⁵I]ICF15002, [¹²⁵I]M1, [¹²⁵I]M2, [¹²⁵I]M3, [¹²⁵I]M4 and [¹²⁵I]⁻ were identified by comparison of their retention time with their nonradioactive counterparts

% of radioactivity	1 h p.i.	3 h p.i.	6 h p.i.	24 h p.i.	72 h p.i.	10 d p.i.
Tumor						
[¹²⁵ I]ICF15002	90%	91%	90%	93%	92%	>99%
[¹²⁵ I] ⁻	10%	7%	9%	0%	0%	0%
Eyes						
[¹²⁵ I] ICF15002	91%	95%	96%	90%	97%	>99%
[¹²⁵ I] ⁻	10%	6%	4%	0%	0%	0%
Blood						
[¹²⁵ I] ICF15002	2%	0%	4%	<i>n.d.^a</i>	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I]M1	22%	12%	11%	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I] ⁻	77%	89%	86%	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>
Liver						
[¹²⁵ I] ICF15002	28%	24%	9%	0%	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I]M4	8%	0%	0%	0%	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I]M3	26%	46%	55%	71%	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I] ⁻	20%	22%	30%	30%	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I]X1 ^b	9%	10%	5%	0%	<i>n.d.</i>	<i>n.d.</i>
Kidneys						
[¹²⁵ I] ICF15002	13%	6%	0%	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I]M3	19%	12%	0%	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I]M1	29%	34%	43%	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I] ⁻	21%	37%	57%	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>
[¹²⁵ I]X1	9%	9%	0%	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>
Urine						
[¹²⁵ I] ICF15002	13%	0%	0%	0%	0%	<i>n.d.</i>
[¹²⁵ I]M3	7%	13%	4%	0%	0%	<i>n.d.</i>
[¹²⁵ I]M2	30%	24%	21%	7%	0%	<i>n.d.</i>
[¹²⁵ I]M1	17%	20%	16%	4%	0%	<i>n.d.</i>
[¹²⁵ I] ⁻	26%	31%	51%	85%	99%	<i>n.d.</i>
Faeces						
	0-24 h	24-48 h				
[¹²⁵ I] ICF15002	5%	3%				
[¹²⁵ I]M4	7%	3%				
[¹²⁵ I]M3	16%	14%				
[¹²⁵ I]M1	8%	8%				
[¹²⁵ I] ⁻	8%	27%				
[¹²⁵ I]X2 ^b	10%	8%				
[¹²⁵ I]X3 ^b	39%	31%				
[¹²⁵ I]X4 ^b	8%	5%				

^an.d. non detectable

^bnon identified metabolites



min