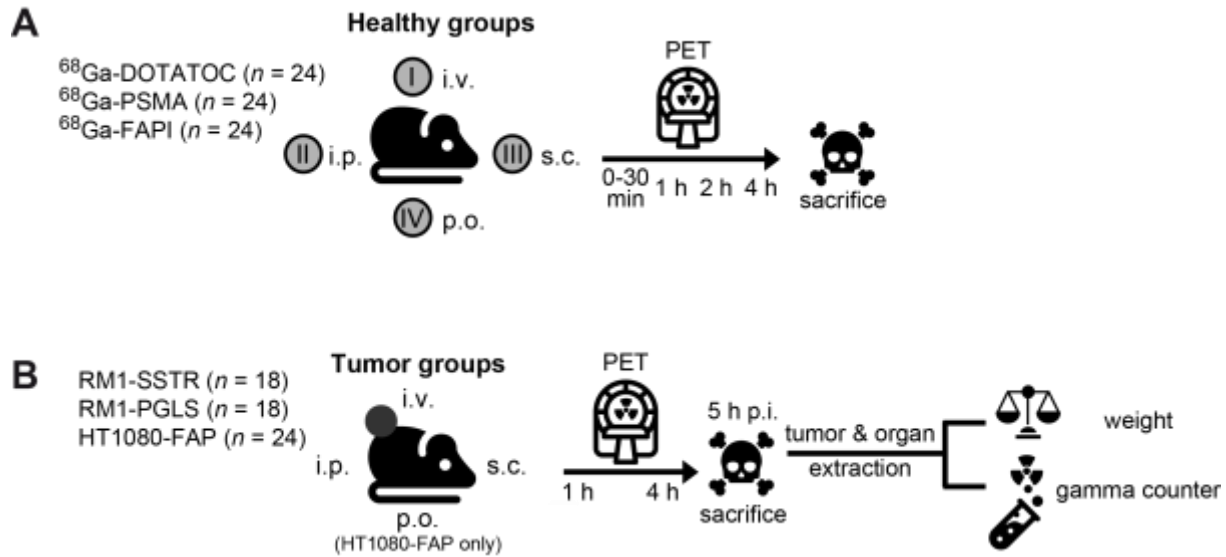


1 **Supplemental Table 1. I.v., i.p., and s.c. injection led to near equivalent organ**
 2 **biodistribution of radioligands in healthy mice.** Healthy mice were injected with
 3 ^{68}Ga -DOTATOC, ^{68}Ga -PSMA11, or ^{68}Ga -FAPI46, respectively. Absolute organ uptake is given as
 4 %IA/g at 1h and 4h p.i. (*in vivo* PET), and 5h p.i. (*ex vivo* gamma counter). Data represent mean
 5 %IA/g \pm SEM of $n=6$ mice/group. * $p<0.05$; ** $p<0.01$.

^{68}Ga -DOTATOC					
	i.v.	i.p.	s.c.	p-value i.v. vs. i.p.	p-value i.v. vs. s.c.
blood 1h	1.3 \pm 0.3	1.0 \pm 0.1	1.1 \pm 0.1	0.7589	0.8431
blood 4h	0.3 \pm 0.1	0.2 \pm 0.02	0.2 \pm 0.04	0.5639	0.8229
kidneys 1h	6.0 \pm 1.0	6.2 \pm 0.4	5.6 \pm 0.5	0.9965	0.9837
kidneys 4h	3.9 \pm 0.7	4.3 \pm 0.2	5.9 \pm 0.5	0.9393	0.1658
^{68}Ga -PSMA11					
	i.v.	i.p.	s.c.	p-value i.v. vs. i.p.	p-value i.v. vs. s.c.
blood 1h	1.6 \pm 0.1	1.0 \pm 0.1	1.1 \pm 0.1	$p=0.0226^*$	$p=0.0880^*$
blood 4h	0.9 \pm 0.1	0.5 \pm 0.1	0.3 \pm 0.04	$p=0.0394^*$	$p=0.0065^{**}$
kidneys 1h	22.4 \pm 3.2	24.4 \pm 0.9	19.7 \pm 2.0	$p=0.9279$	$p=0.8773$
kidneys 4h	14.9 \pm 1.4	20.8 \pm 2.8	16.1 \pm 1.5	$p=0.3040$	$p=0.9251$
^{68}Ga -FAPI46					
	i.v.	i.p.	s.c.	p-value i.v. vs. i.p.	p-value i.v. vs. s.c.
blood 1h	1.2 \pm 0.6	0.8 \pm 0.4	0.8 \pm 0.3	$p=0.9505$	$p=0.9345$
blood 4h	0.2 \pm 0.02	0.02 \pm 0.01	0.1 \pm 0.03	$p=0.0036^{**}$	$p=0.5326$
kidneys 1h	4.9 \pm 1.6	8.7 \pm 1.7	3.1 \pm 1.2	$p=0.5065$	$p=0.8014$
kidneys 4h	1.1 \pm 0.2	3.8 \pm 2.3	1.3 \pm 0.2	$p=0.6694$	$p=0.9513$

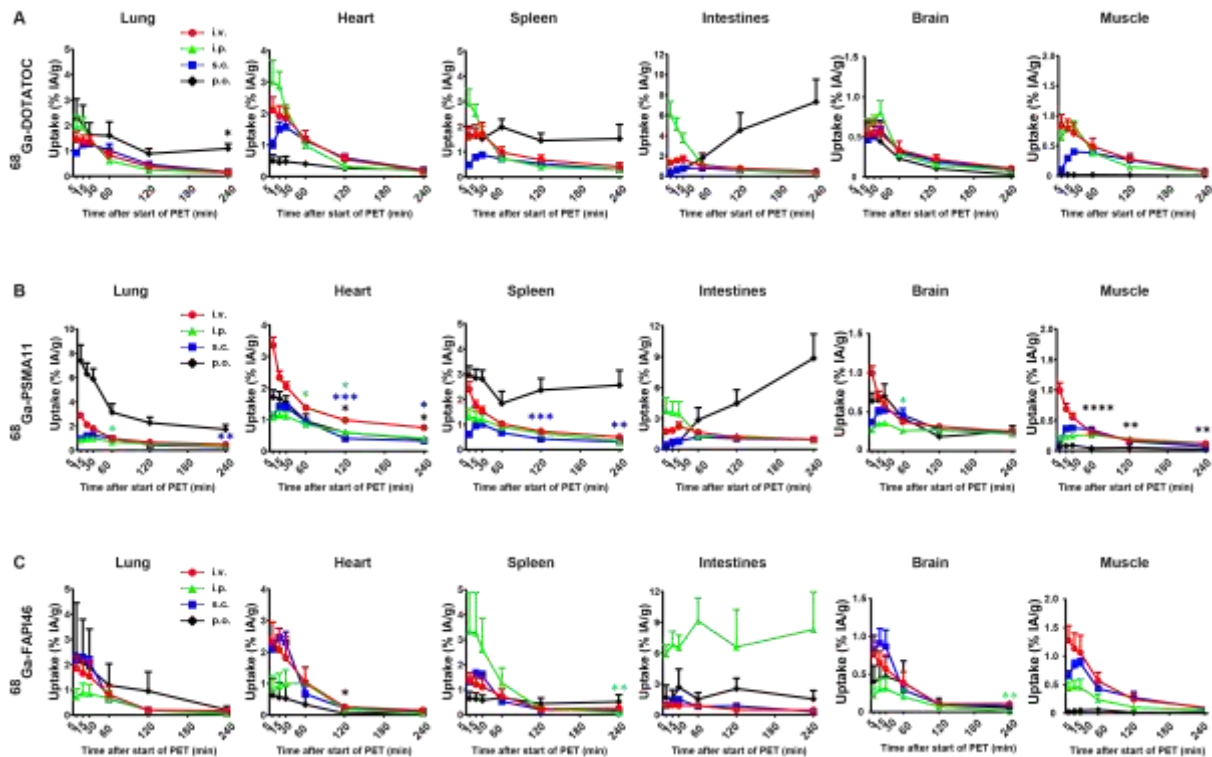
6



8

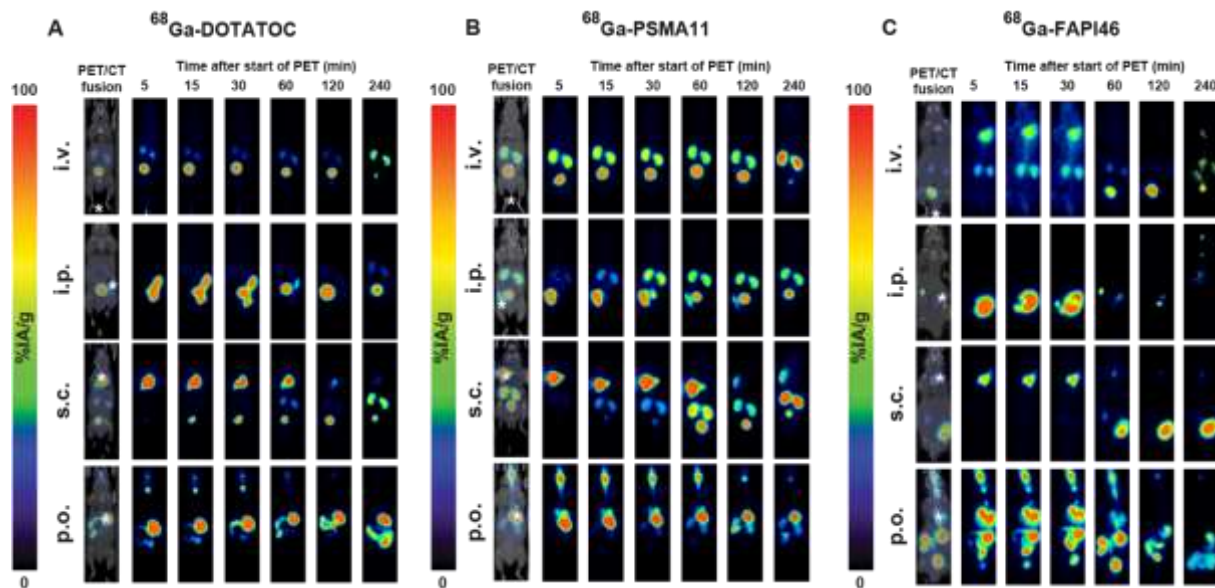
9 **Supplemental Figure 1. Experimental design.** (A) Healthy mice ($n=6/\text{group}$) underwent PET
 10 scans following i.v., i.p., s.c., and p.o. radioligand application, respectively, at minute 0-30 after
 11 start of PET and after 1h, 2h and 4h with subsequent sacrifice of animals. (B) Mice with
 12 subcutaneous RM1-SSTR, RM1-PSMA, or HT1080-FAP tumors ($n=6/\text{group}$) with i.v., i.p. and s.c.
 13 application of ^{68}Ga -DOTATOC, ^{68}Ga -PSMA11, or (C) ^{68}Ga -FAPI46, respectively underwent PET
 14 scans after 1h and 4h, followed by sacrifice (5h) and subsequent assessment of radioactivity in
 15 organs and tumors by gamma counter.

16



17
 18 **Supplemental Figure 2. Near equivalent radioligand organ biodistribution for i.p. and s.c.**
 19 **compared to i.v. injection in healthy mice.** *In vivo* PET biodistribution of ^{68}Ga -ligands in healthy
 20 mice ($n=6/\text{group}$). PET scans with (A) ^{68}Ga -DOTATOC, (B) ^{68}Ga -PSMA11, and (C) ^{68}Ga -FAPI46.
 21 Time-activity curves illustrate radioligand dynamics in selected organ VOIs at indicated time points
 22 for i.v., i.p., s.c., and p.o. application. Data are shown as mean+SEM. %IA/g: percent of the
 23 injected activity per gram. Asterisks indicate significance compared to i.v. application route.
 24 * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.

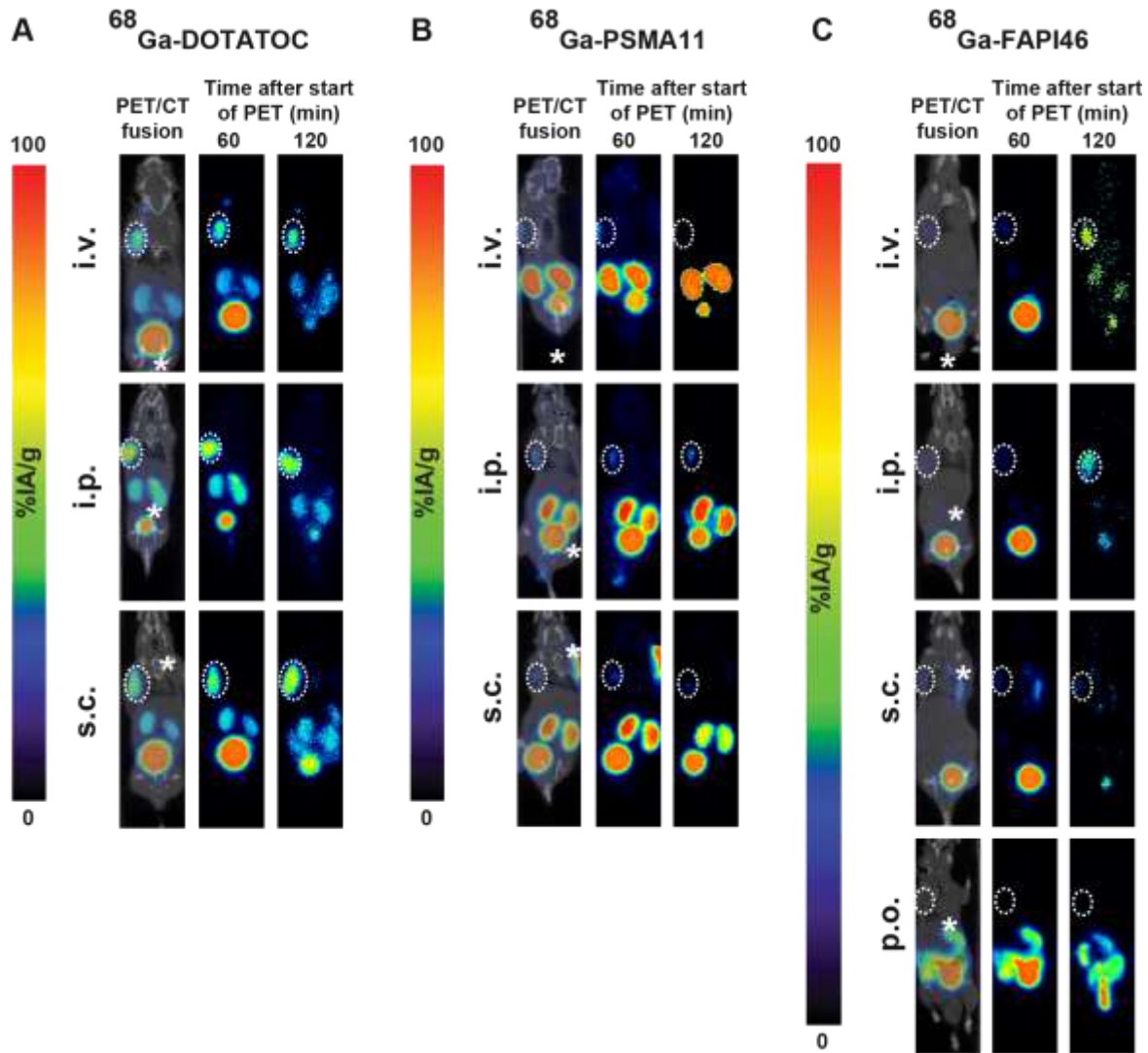
25
 26



27
 28 **Supplemental Figure 3. PET biodistribution of ^{68}Ga -ligands in healthy mice.** Whole body
 29 maximum intensity projections of one representative mouse out of $n=6/\text{group}$ for each application
 30 route after injection of ^{68}Ga -labelled ligands. (A) ^{68}Ga -DOTATOC, (B) ^{68}Ga -PSMA11, and
 31 (C) ^{68}Ga -FAPI46 after i.v., i.p., s.c., and p.o. application in healthy mice. Asterisks indicate the
 32 injection site.

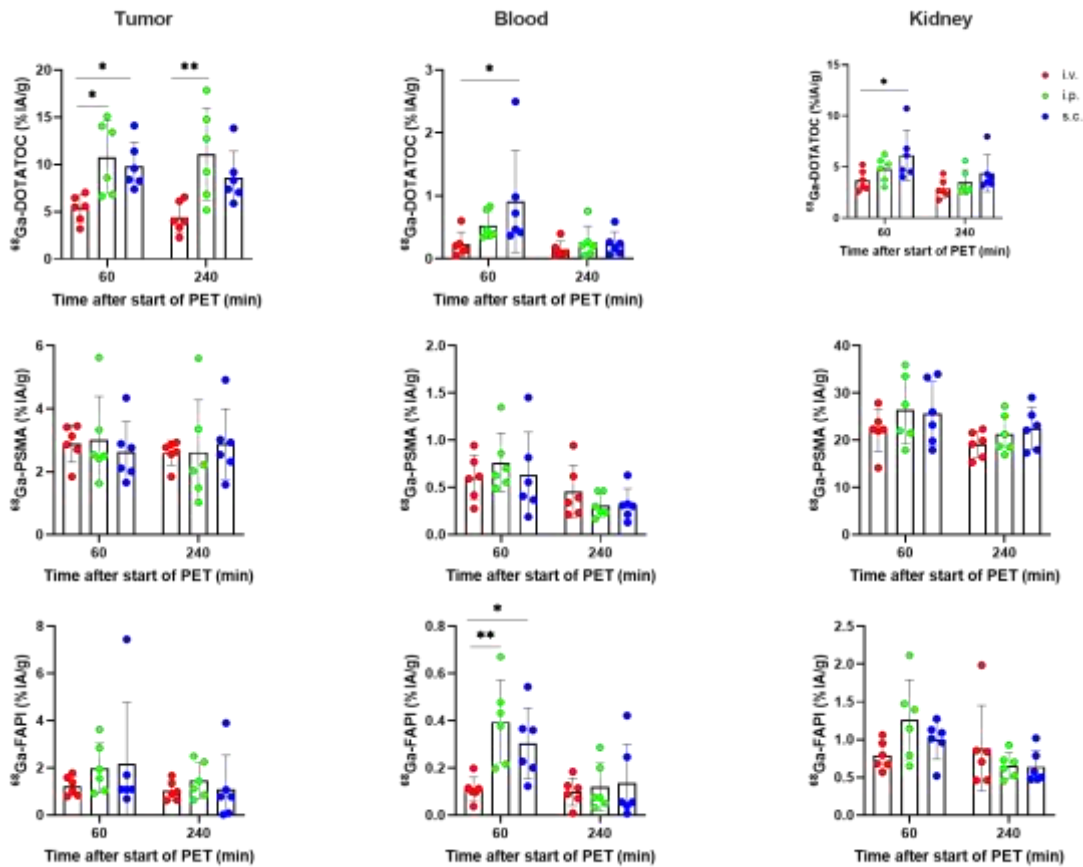
33

34



36
37 **Supplemental Figure 4. PET biodistribution of ^{68}Ga -ligands in tumor-bearing mice.** Whole
38 body maximum intensity projections of one representative mouse out of $n=6$ /group for each
39 application route 1h and 4h after injection of ^{68}Ga -labelled ligands. (A) ^{68}Ga -DOTATOC, (B)
40 ^{68}Ga -PSMA11, and (C) ^{68}Ga -FAPI46 via i.v., i.p., and s.c. application in RM1-SSTR-, RM1-PSMA-
41 , or HT1080-FAP-tumor-bearing mice with additional p.o. application, respectively. Asterisks
42 indicate the injection site; dashed circles indicate subcutaneous tumor in the right shoulder region.

43

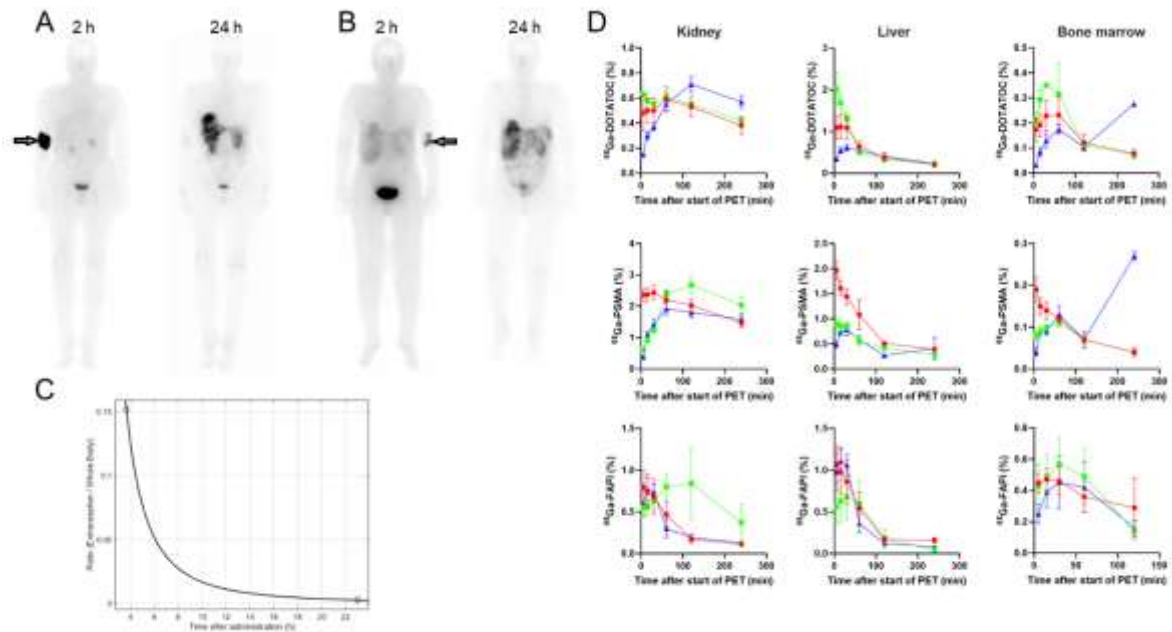


45

46 **Supplemental Figure 5. PET biodistribution of ^{68}Ga -ligands in tumor-bearing mice.** *In vivo*
 47 PET uptake of ^{68}Ga -ligands in tumor-bearing mice ($n=6/\text{group}$). after ^{68}Ga -DOTATOC, ^{68}Ga -
 48 PSMA11, and ^{68}Ga -FAPI46. Bars illustrate radioligand uptake in selected organ VOIs at indicated
 49 time points for i.v., i.p., and s.c. application. Data are shown as mean \pm SD. %IA/g: percent of the
 50 injected activity per gram. Asterisks indicate significance compared to i.v. application route.
 51 * $p < 0.05$; ** $p < 0.01$.

52

53



54

55 **Supplemental Figure 6.** Anterior whole-body planar images of ¹⁷⁷Lu-DOTATOC distribution 2h
56 and 24h after paravenous infusion (arrow) of the radioligand in two patients (A and B). Radioligand
57 absorption in patient A occurs with a half-life of 3.3 hours (C). Extrapolation from mice to humans
58 suggests comparable biodistribution of ⁶⁸Ga-radioligands in healthy organs (D). Data are shown
59 as mean±SEM.