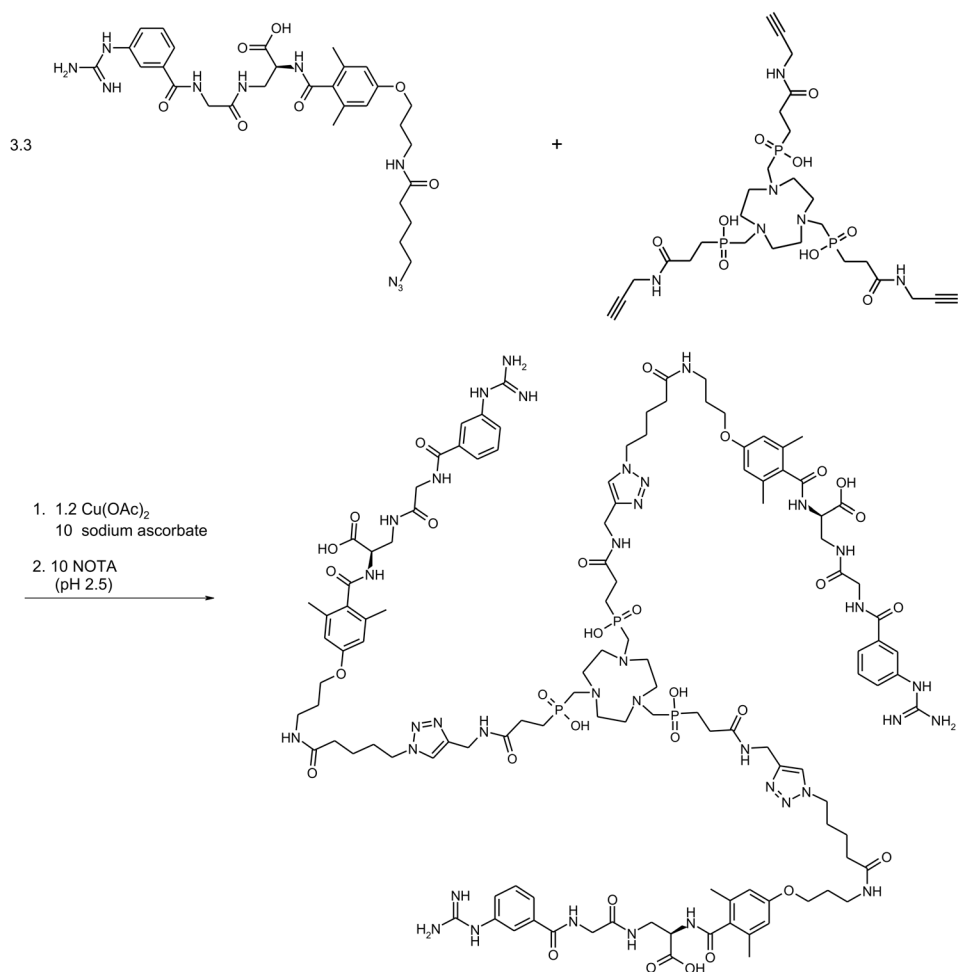
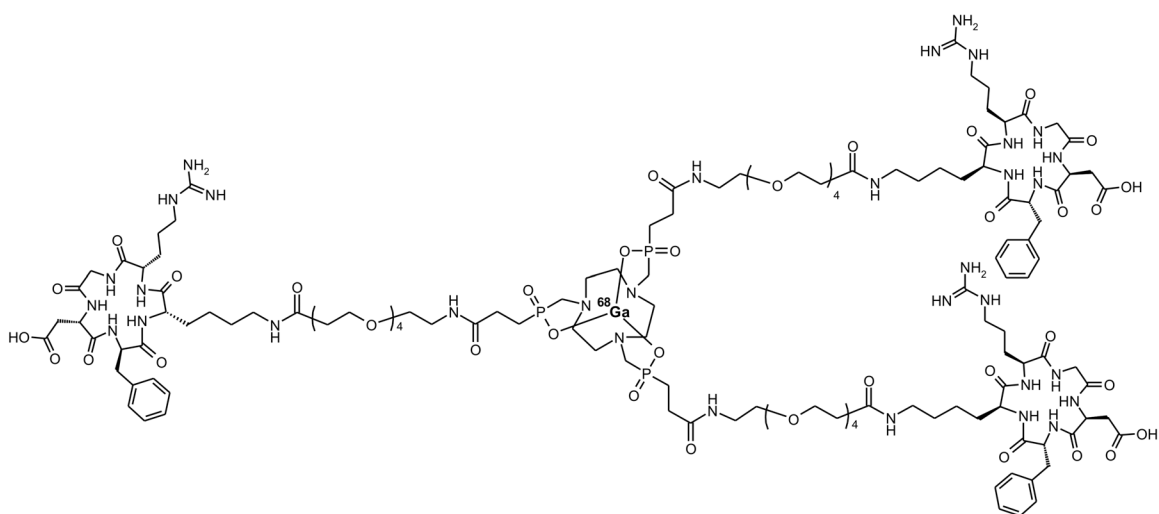


1. Reactions and Structures

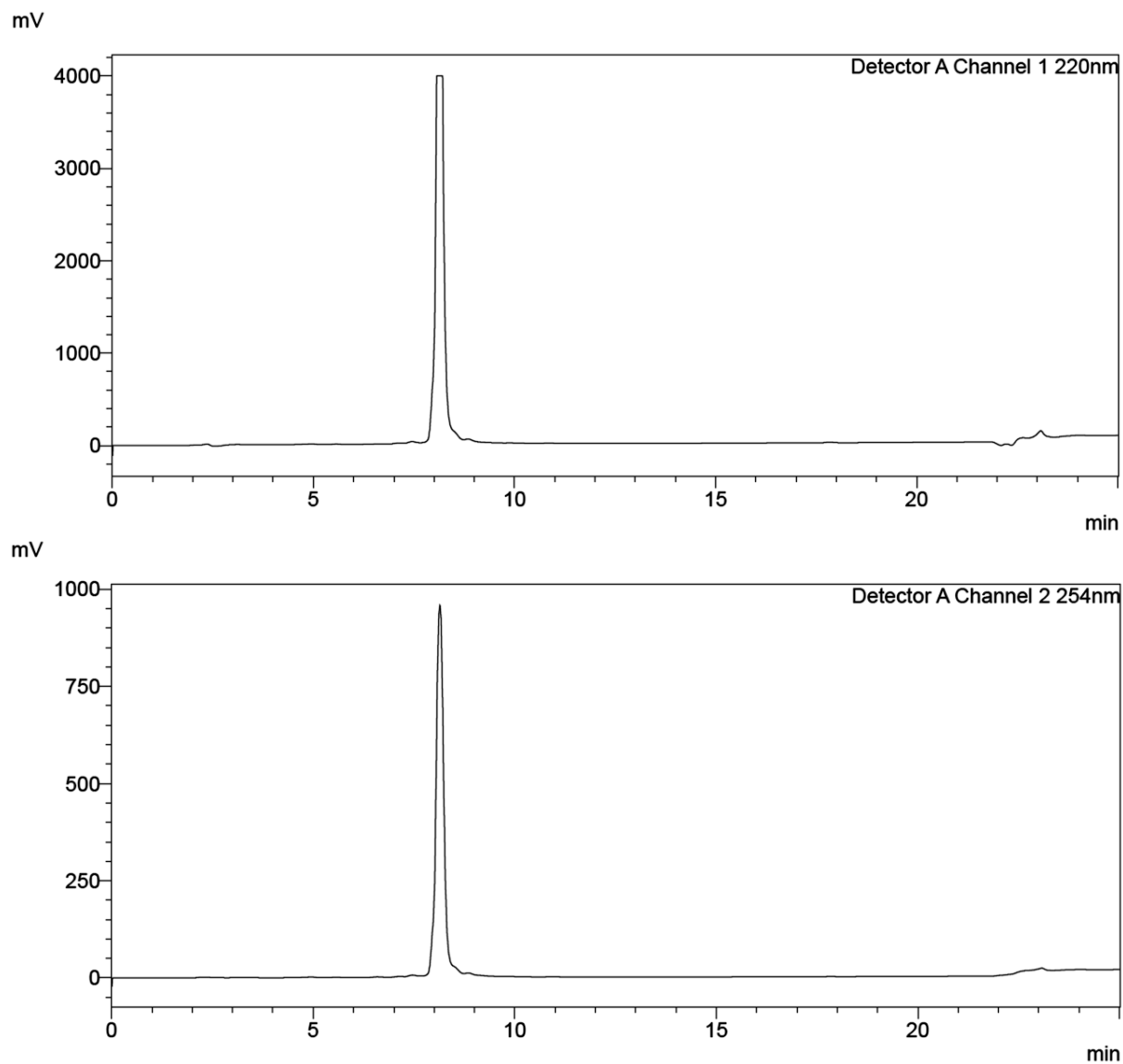


Supplemental Scheme 1: Synthesis of Aquibeptrin from TRAP(alkyne)₃ and an azide-functionalized $\alpha_5\beta_1$ -integrin binding pseudopeptide.

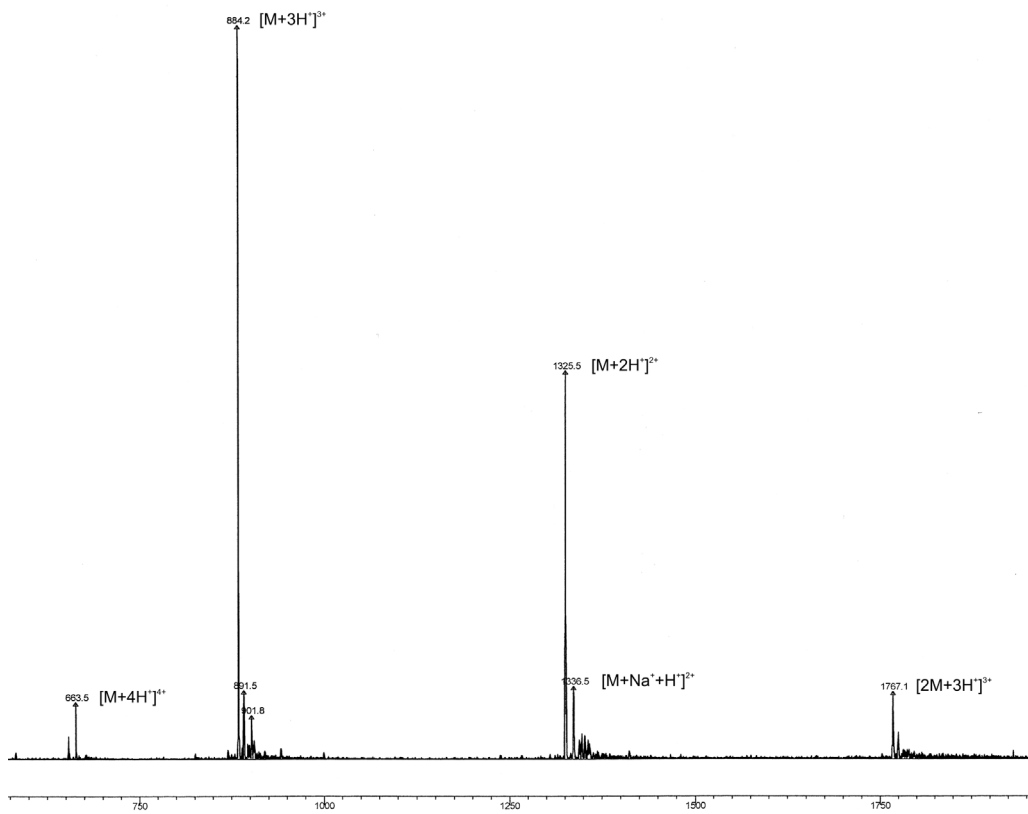


Supplemental Scheme 2: Structure of ⁶⁸Ga-Avebetrin.

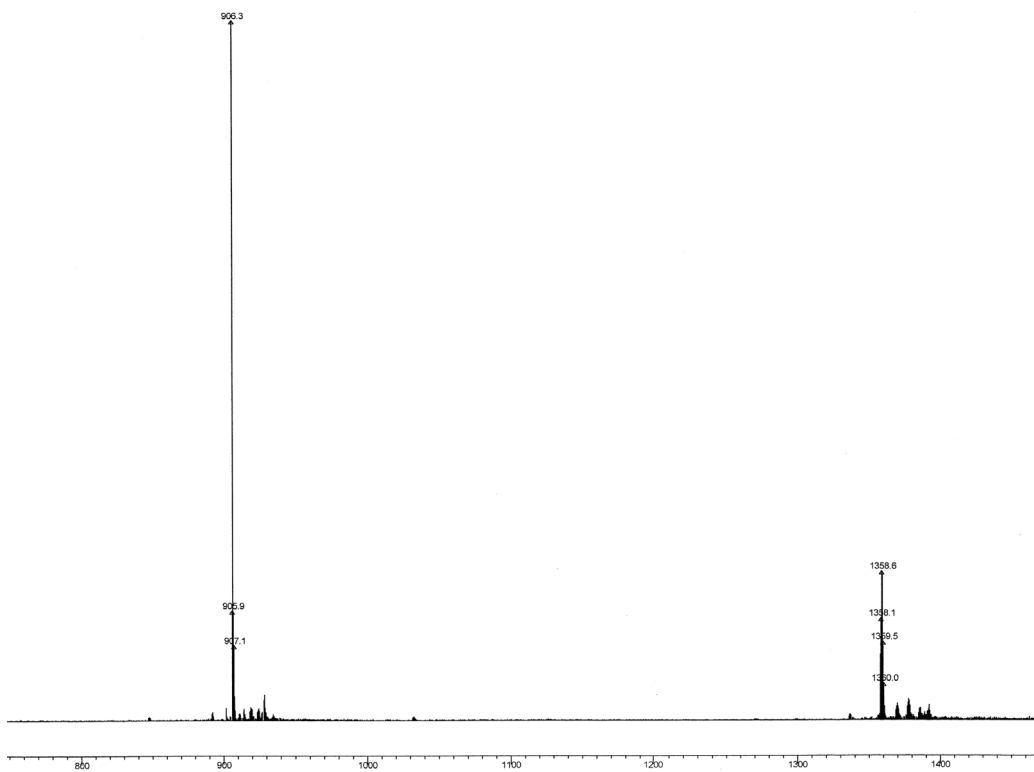
2. Analytical and in-vivo data for Aquibepirin and $^{nat}\text{Ga}/^{68}\text{Ga}$ -Aquibepirin



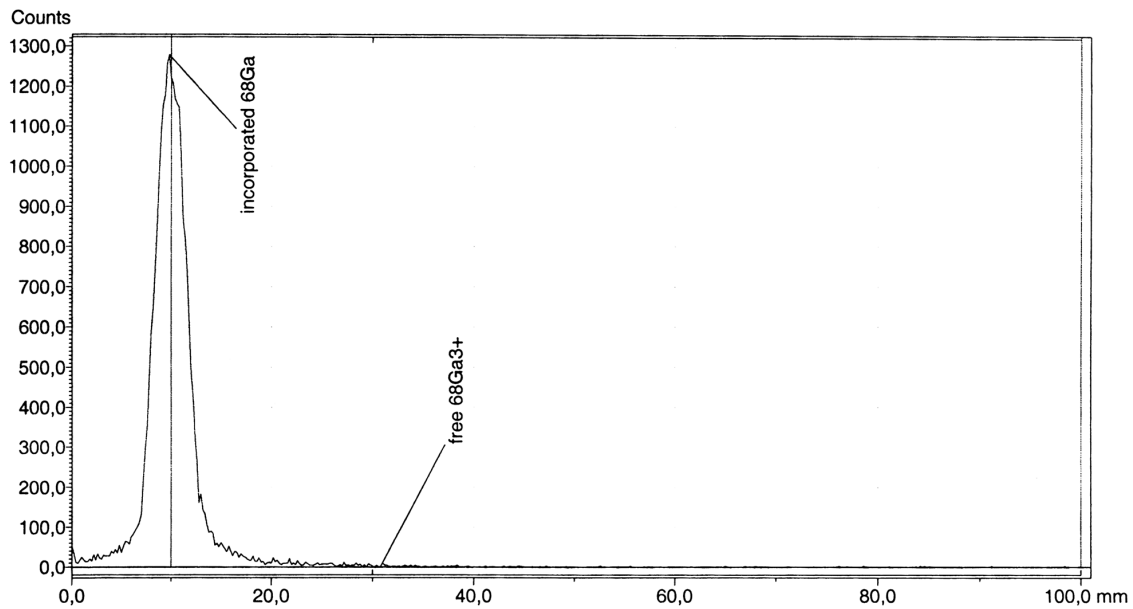
Supplemental Figure 1: HPLC chromatograms for Aquibepirin. Shimadzu HPLC system, column: Nucleosil 100, 5 μm , RP-C18, 125 \times 4.6 mm; flow rate: 1 mL min $^{-1}$; gradient: 15–65 % MeCN in H $_2$ O (both containing 0.1 % trifluoroacetic acid) in 20 min.



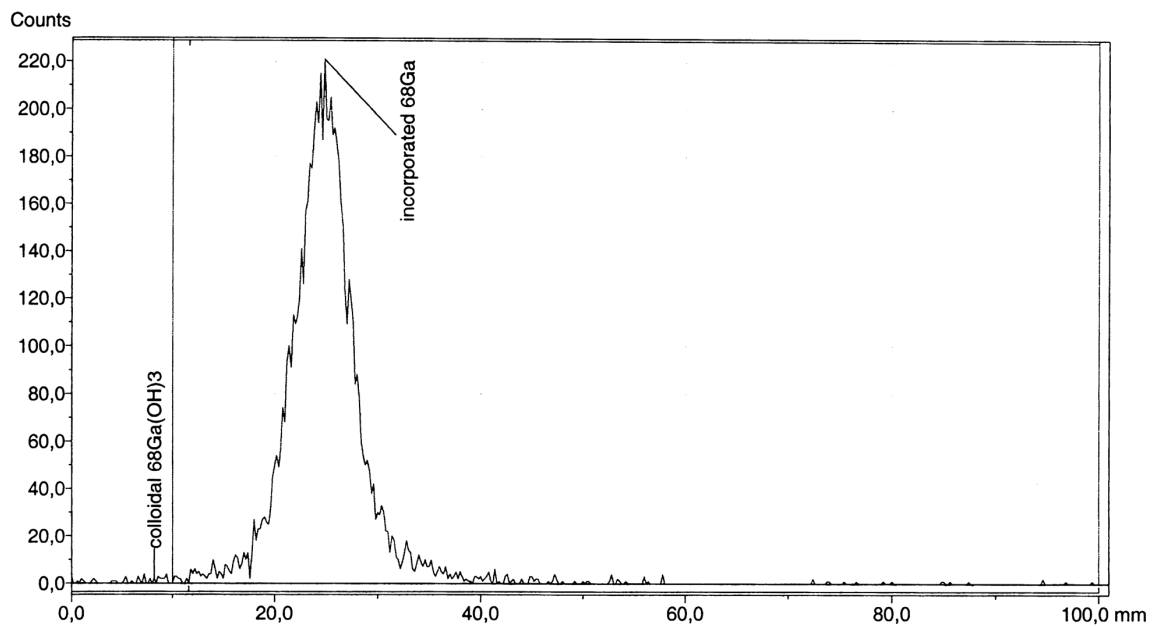
Supplemental Figure 2: MS (ESI, positive mode) for Aquibepirin



Supplemental Figure 3: MS (ESI, positive mode) for ^{nat}Ga -Aquibepirin.

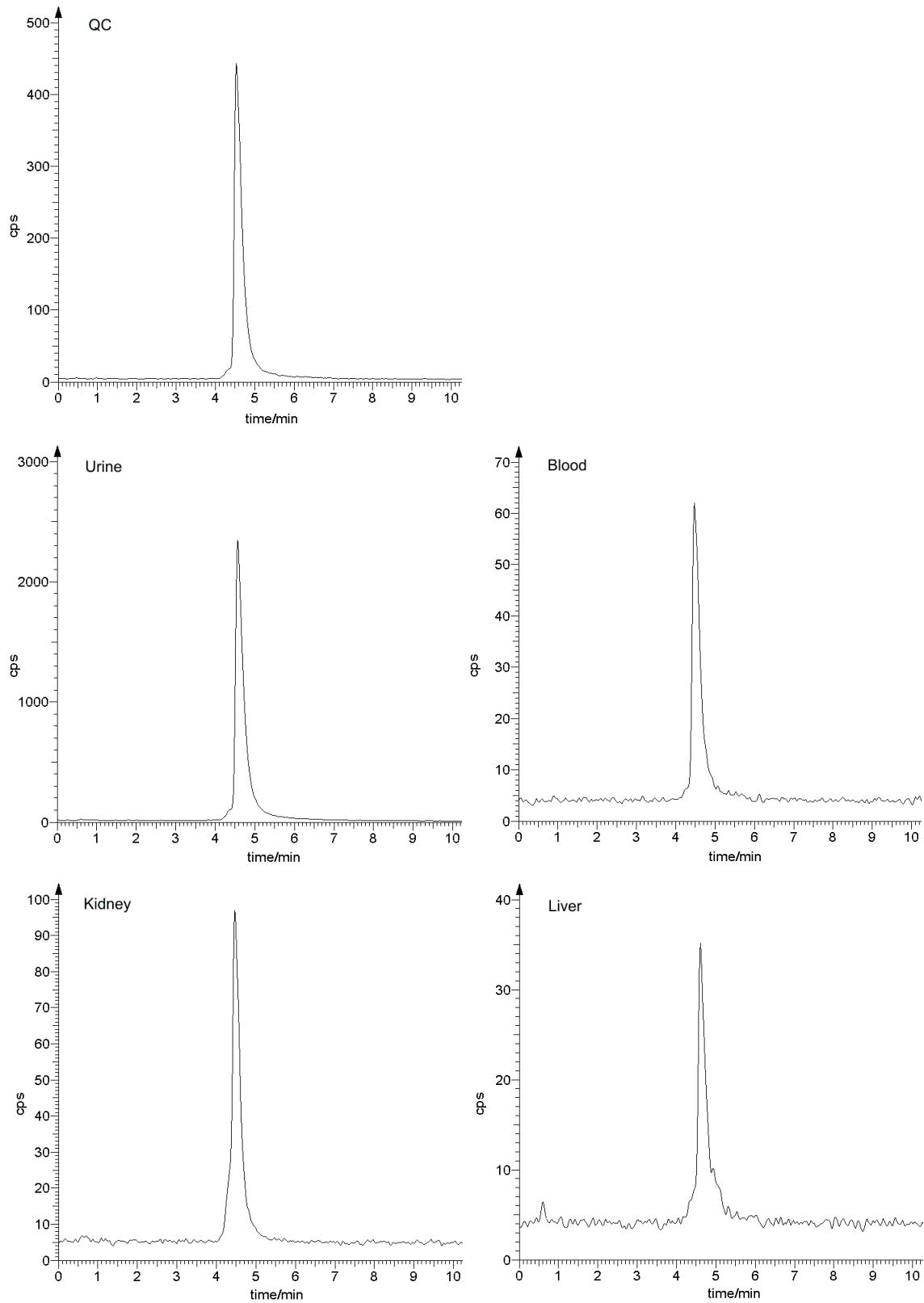


| Name | Start (mm) | End (mm) | Retention (RF) | Height (Counts) | Area (Counts) | %ROI (%) | %Total (%) |
|-------------------|------------|----------|----------------|-----------------|----------------|---------------|---------------|
| incorporated 68Ga | 0,0 | 30,0 | -0,0 | 1278,0 | 26325,0 | 99,32 | 99,32 |
| free 68Ga3+ | 30,0 | 100,0 | 0,2 | 11,0 | 180,0 | 0,68 | 0,68 |
| 2 Peaks | | | | | 26505,0 | 100,00 | 100,00 |



| Name | Start (mm) | End (mm) | Retention (RF) | Height (Counts) | Area (Counts) | %ROI (%) | %Total (%) |
|---------------------|------------|----------|----------------|-----------------|---------------|---------------|---------------|
| colloidal 68Ga(OH)3 | 0,0 | 11,6 | -0,0 | 4,0 | 56,0 | 0,78 | 0,78 |
| incorporated 68Ga | 11,6 | 100,0 | 0,2 | 221,0 | 7121,0 | 99,22 | 99,22 |
| 2 Peaks | | | | | 7177,0 | 100,00 | 100,00 |

Supplemental Figure 4: Radio-TLC (Agilent ITLC-SG sheets) for ^{68}Ga -Aquibepirin, using 0.1 M aq. trisodium citrate (top) and an 1:1 (v/v) mixture of 1 M aq. NH_4OAc and MeOH (bottom). The solvent front is at 100 mm.



Supplemental Figure 5: Radio-HPLC (100×4.6 mm Merck Chromolith® column, flow 3 mL/min, 3-95% MeCN in water (both w/ 0.1% TFA) within 10 min) of ^{68}Ga -Avebetrin (QC) as well as samples of body fluids and tissue extracts.

Supplemental Table 1: Biodistribution data (90 min p.i.) for ⁶⁸Ga-Aquibepirin without (n = 5) and with (n = 4) addition of 40 nmol (approx. 100 μg) of Aquibepirin.

| Organ/Tissue | ⁶⁸ Ga-Aquibepirin | | + 40 nmol (100 μg) cold |
|-------------------------|------------------------------|-------------------|-------------------------|
| | %ID/g | tumor/organ ratio | |
| blood | 0.24 ± 0.06 | 10.6 ± 2.5 | 0.10 ± 0.03 |
| heart (myocard) | 0.24 ± 0.05 | 10.6 ± 1.8 | 0.13 ± 0.04 |
| lung | 0.67 ± 0.07 | 3.7 ± 0.5 | 0.36 ± 0.08 |
| liver | 0.48 ± 0.07 | 5.1 ± 0.5 | 0.36 ± 0.04 |
| spleen | 0.29 ± 0.04 | 8.5 ± 0.7 | 0.19 ± 0.03 |
| pancreas | 0.19 ± 0.04 | 13.3 ± 2.2 | 0.07 ± 0.02 |
| stomach (empty) | 0.51 ± 0.12 | 4.9 ± 0.8 | 0.20 ± 0.05 |
| small intestine (empty) | 0.32 ± 0.05 | 7.6 ± 0.7 | 0.22 ± 0.12 |
| large intestine (empty) | 0.60 ± 0.09 | 4.1 ± 0.9 | 0.23 ± 0.05 |
| kidneys | 7.97 ± 1.49 | 0.3 ± 0.0 | 6.04 ± 0.31 |
| muscle | 0.12 ± 0.02 | 20.9 ± 2.4 | 0.04 ± 0.00 |
| tumor M21 | 2.42 ± 0.21 | | 0.92 ± 0.13 |

Supplemental Table 2: Biodistribution data and tumor/organ ratios for ⁶⁸Ga-Avebetrin (90 min p.i., n = 6).

| Organ/Tissue | ⁶⁸ Ga-Avebetrin | |
|-------------------------|----------------------------|-------------------|
| | %ID/g | tumor/organ ratio |
| blood | 0.13 ± 0.04 | 25.4 ± 8.0 |
| heart (myocard) | 0.49 ± 0.08 | 6.2 ± 0.8 |
| lung | 1.28 ± 0.18 | 2.4 ± 0.2 |
| liver | 1.80 ± 0.27 | 1.7 ± 0.2 |
| spleen | 2.12 ± 0.73 | 1.5 ± 0.4 |
| pancreas | 0.32 ± 0.07 | 9.8 ± 1.7 |
| stomach (empty) | 1.66 ± 0.21 | 1.8 ± 0.2 |
| small intestine (empty) | 1.92 ± 0.36 | 1.6 ± 0.4 |
| large intestine (empty) | 1.39 ± 0.29 | 2.2 ± 0.3 |
| kidneys | 3.47 ± 0.58 | 0.8 ± 0.1 |
| muscle | 0.21 ± 0.03 | 14.9 ± 2.0 |
| tumor M21 | 3.02 ± 0.30 | |