## Supporting Information

## Linker Modification Strategies to Control the Prostate-specific Membrane Antigen (PSMA)-Targeting and Pharmacokinetic Properties of DOTA-Conjugated PSMA Inhibitors

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## Author Contributions

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Table 1. Cell Surface Binding, and Internalization Determined with LNCaP Cells

| Compound <br> code | Cell surface <br> binding <br> [\%IA/10 cells] | Lysate <br> [\%IA/10 cells] |
| :---: | :---: | :---: |
| $\mathbf{1 1}$ | $24.87 \pm 8.72$ | $2.73 \pm 0.11$ |
| $\mathbf{1 2}$ | $13.56 \pm 0.84$ | $7.00 \pm 2.51$ |
| $\mathbf{1 3}$ | $25.48 \pm 20.19$ | $4.92 \pm 1.32$ |
| $\mathbf{1 4}$ | $\mathbf{2 2 . 6 8} \pm \mathbf{2 . 1 4}$ | $\mathbf{1 3 . 1 1} \pm \mathbf{1 . 9 7}$ |
| $\mathbf{1 5}$ | $34.65 \pm 13.60$ | $7.65 \pm 1.26$ |
| $\mathbf{1 6}$ | $6.58 \pm 2.26$ | $2.22 \pm 1.01$ |
| $\mathbf{1 7}$ | $\mathbf{1 4 . 8 1} \pm \mathbf{8 . 6 7}$ | $\mathbf{1 7 . 5 1} \pm \mathbf{3 . 9 9}$ |
| $\mathbf{1 8}$ | $21.39 \pm 16.57$ | $9.19 \pm 3.31$ |
| $\mathbf{1 9}$ | $7.73 \pm 3.89$ | $0.93 \pm 0.05$ |
| $\mathbf{2 0}$ | $1.18 \pm 0.02$ | $0.21 \pm 0.06$ |
| $\mathbf{2 1}$ | $2.40 \pm 0.62$ | $2.37 \pm 1.86$ |
| $\mathbf{2 2}$ | $\mathbf{1 7 . 2 1} \pm \mathbf{6 . 5 2}$ | $\mathbf{7 . 2 6} \pm \mathbf{2 . 7 6}$ |
| $\mathbf{2 3}$ | $12.42 \pm 11.55$ | $3.12 \pm 1.62$ |
| $\mathbf{2 4}$ | n.d. | n.d |
| $\mathbf{2 5}$ | $5.92 \pm 3.76$ | $1.63 \pm 0.02$ |
| $\mathbf{2 6}$ | $5.10 \pm 6.20$ | $1.50 \pm 0.25$ |
| $\mathbf{2 7}$ | $0.30 \pm 0.29$ | $0.05 \pm 0.05$ |
| $\mathbf{2 8}$ | $\mathbf{4 . 8 4} \pm \mathbf{6 . 0 6}$ | $\mathbf{2 . 7 8} \pm \mathbf{2 . 1 1}$ |

N.b. The values for the most promising compound of each set, including the overall lead candidate, $\mathbf{1 7}$ (also known as PSMA-617), are highlighted in boldface type. ${ }^{a}$ Data are expressed as means $\pm \mathrm{SD}(\mathrm{n}=3)$. n.d. $=$ not determined, $\mathbf{2 4}$ demonstrated instability and degradation at higher temperatures and was thus neither tested in vitro nor in vivo.

## NMR spectra acquired and notes

Spectra referenced to 2.50 ppm (proton) and 39.52 ppm (carbon). When the peaks are broad, the exact chemical shift is uncertain, or the chemical shift was taken from 2D spectra, the number of decimal places is reduced accordingly. Notation: br, broad; d, doublet; ho, higher order; m, multiplet; ol, overlapped; t, triplet; qt, quartet; s, singlet; v, very.


R

Compound 11
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+\mathrm{DEPT}, 400 \mathrm{MHz}, 303 \mathrm{~K}$

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator
No decomposition observed.

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and 19 and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 303 K ): $8.900\left(\mathrm{brt} \mathrm{t}, J_{\mathrm{H} 2^{\prime \prime}}=5.8 \mathrm{~Hz}, \mathrm{H}-1{ }^{\prime \prime}\right), 8.392\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right), 7.798(2 \mathrm{H}$, $\mathrm{AA}^{\prime}$ part of AA'MM' system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-5{ }^{\prime \prime}\right), 7.734\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-8^{\prime \prime}\right), 7.356$ ( $2 \mathrm{H}, \mathrm{MM}^{\prime}$ part of AA'MM' system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-4{ }^{\prime \prime}\right), 6.334\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right)$, $6.298\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.2 \mathrm{~Hz}, \mathrm{H}^{-} 7^{\prime}\right), 4.376\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{H} 1^{\prime \prime}}=5.4 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}\right), 4.089\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{{\mathrm{H} 1 \mathrm{a}^{\prime}}=8.3 \text {, }}\right.$ $\left.J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.030\left(\mathrm{td}, J_{\mathrm{H}^{\prime}}=J_{\mathrm{H5a}^{\prime}}=8.1, J_{\mathrm{H5b}}{ }^{\prime}=5.3 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right), 3.97(2 \mathrm{H}$, v br s, H-2 or $\mathrm{H}-10), 3.92(2 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-2$ or $\mathrm{H}-10), \mathrm{H}-12$ overlapped with $\mathrm{H}_{2} \mathrm{O}$ signal, $3.29(8 \mathrm{H}$, ol m, H-4 and H-5 or H-7 and H-8), $3.224\left(2 \mathrm{H}, \sim \mathrm{qt}, J_{\mathrm{H}-\mathrm{l}^{\prime}}=J_{\mathrm{H}-3^{\prime}}=6.6 \mathrm{~Hz}, \mathrm{H}-2^{\prime}\right), 3.11(8 \mathrm{H}$, v br s, H4 and H-5 or H-7 and H-8), $2.988\left(2 \mathrm{H}, \sim \mathrm{qt}, J_{\mathrm{H}-8^{\prime \prime}}=J_{\mathrm{H}-10^{\prime \prime}}=6.5 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime \prime}\right), 2.26$ (ho m, H-12a'), 2.21 (ho m, H-12b'), 2.039 ( $2 \mathrm{H}, \sim \mathrm{t}, J_{\mathrm{H}-12^{\prime \prime}}=7.4 \mathrm{~Hz}, \mathrm{H}-13{ }^{\prime \prime}$ ), 1.91 (ho m, H-11a'), 1.71 (ol ho m, H-11b'), 1.62 (ol ho m, H-5a'), 1.56-1.45 (5H, m), 1.41-1.32 (2H, m), 1.31-1.21 (4H, m).
${ }^{13} \mathrm{C}$ NMR (303 K): 174.59 (C-15'), 174.21 (C-14'), 173.81 (C-13'), 172.13 (C-14"), 171.53 (br, C-13), 169.27 (v br, C-11), 166.33 (v br, C-1), 165.97 (C-7"), 157.43 (C-8'), 141.56 (C-3"), 133.53 (C-6"), 127.37 (C-5"), 127.27 (C-4"), 54.82 (br, C-2 or C-10), 54.04 (br, C-2 or C-10), 53.05 ( v br, C-12), 52.37 (C-6'), 51.77 (C-10'), 50.63 ( $\mathrm{v} \mathrm{br}, \mathrm{C}-4$ or C-5 or C-7 or C-8), 50.49
(v br, C-4 or C-5 or C-7 or C-8), 48.84 (v br, C-4 or C-5 or C-7 or C-8; 48.84 and 48.64 are C-4 and C-5 or C-7 and C-8), 48.64 (v br, C-4 or C-5 or C-7 or C-8; 48.84 and 48.64 are C-4 and C-5 or C-7 and C-8), 42.15 (C-2"), 39.20 (C-2'), 38.38 (C-9"), 35.46 (C-13"), 31.84 (C$\left.5^{\prime}\right), 29.98$ (C-12'), 28.99 (C-12"), 28.88 (C-3'), 27.58 (C-11'), 26.26 (C-10" or C-11"), 25.25 (C-10" or C-11"), 22.69 (C-4').
${ }^{1}$ H NMR Spectra


${ }^{13}$ C NMR Spectra




Compound 12
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 303 \mathrm{~K}$


6 "
R $\xlongequal[7^{\prime \prime}]{ } 0$
$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 343 \mathrm{~K}$

DEPT, $400 \mathrm{MHz}, 343 \mathrm{~K}$

HSQC, COSY, $400 \mathrm{MHz}, 343 \mathrm{~K}$
${ }^{1} \mathrm{H}$ and ${ }^{1} \mathrm{H}$ with water suppression, $\mathrm{HSQC}, \mathrm{COSY}, \mathrm{HMBC}, 600 \mathrm{MHz}, 303 \mathrm{~K}$

No decomposition observed.

The macrocyclic ring assignments could not be effected with certitude due to dynamic effects causing severe line broadening precluding correlations in the HMBC spectra. All other signals could be fully assigned and the spectra were otherwise fully consistent with the proposed structure.
${ }^{1} \mathrm{H}$ NMR ( $303 \mathrm{~K}, 600 \mathrm{MHz}$ ): $8.872\left(\mathrm{br} \mathrm{t}, J_{\mathrm{H} 2^{\prime \prime}}=5.8 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 8.413\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right)$, $7.795\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-5{ }^{\prime \prime}\right), 7.351\left(2 \mathrm{H}, \mathrm{MM}^{\prime}\right.$ part of $\mathrm{AA}^{\prime} \mathrm{MM}^{\prime}$ system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-4^{\prime \prime}\right), 6.337\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right), 6.316\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=\right.$ $\left.8.2 \mathrm{~Hz}, \mathrm{H}-7^{\prime}\right), 4.371\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{HI}}{ }^{\prime \prime}=5.6 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}\right), 4.088\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{Hlla}^{\prime}}=8.3, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.3 \mathrm{~Hz}\right.$, $\left.\mathrm{H}-10^{\prime}\right), 4.047\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H} 5 \mathrm{a}^{\prime}}=8.1, J_{\mathrm{H} 5 \mathrm{~b}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right), 3.87(2 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-2$ or H-10), 3.86 ( 2 H , v br s, $\mathrm{H}-2$ or $\mathrm{H}-10$ ), 3.63 ( 4 H , v br s, H-12), 3.23 ( 4 H , ol m, H-4 or H-5 or H-7 or H-8), $3.22(2 \mathrm{H}$, ol m, H-2'), 3.21 ( 4 H , ol m, H-4 or H-5 or H-7 or H-8), 3.08 ( 8 H , v br s, H-4 and H5 or H-7 and H-8), 2.25 (ho m, H-12a'), 2.22 (ho m, H-12b'), 1.91 (ho m, H-11a'), 1.70 (ol ho m, H-11b'), 1.67 (ol ho m, H-5a'), 1.54 (ol ho m, H-5b'), 1.51 ( 2 H , ol ho m, H-3'), 1.32 ( 2 H , ol ho m, H-4').
${ }^{13} \mathrm{C}$ NMR (303 K): 174.61 (C-15'), 174.22 (C-14'), 173.83 (C-13'), 171.47 (br, C-13), 169.77 (v br, C-11), 166.68 (v br, C-1), 166.01 (C-7"), 157.44 (C-8'), 141.68 (C-3"), 133.49 (C-6"), 127.38 (C-5"), 127.24 (C-4"), 54.92 (br, C-2 or C-10), 54.13 (br, C-2 or C-10), 53.32 (v br, C12), 52.41 (C-6'), 51.77 (C-10'), 50.68 (v br, C-4 or C-5 or C-7 or C-8), $50.50(\mathrm{vbr}, \mathrm{C}-4$ or C5 or C-7 or C-8), 49.04 ( v br, observed as two signals at $343 \mathrm{~K}, \mathrm{C}-4$ and C-5 or C-7 and C-8), 42.11 (C-2'), 39.16 (C-2'), 31.89 (C-5'), 29.98 (C-12'), 28.89 (C-3'), 27.60 (C-11'), 22.78 (C4').
${ }^{1}$ H NMR Spectra




${ }^{13}$ C NMR Spectra




## COSY




HMBC



$\square$

$\square$



HSQC




## Compound 13

${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 363 \mathrm{~K}$
${ }^{13} \mathrm{C}+\mathrm{DEPT}, 400 \mathrm{MHz}, 363 \mathrm{~K}$

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

No decomposition observed.

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and 19 and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 303 K ): 9.056 ( $\mathrm{t}, J_{\mathrm{H} 9{ }^{\prime \prime}}=6.0 \mathrm{~Hz}, \mathrm{H}-8{ }^{\prime \prime}$ ), $8.910\left(\mathrm{br} \mathrm{t}, J_{\mathrm{H} 2^{\prime \prime}}=5.7 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 8.391\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}\right.$ $\left.=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right), 7.865\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}}=8.3 \mathrm{~Hz}, \mathrm{H}-5$ " or H-12"), $7.778\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}}=8.3 \mathrm{~Hz}, \mathrm{H}-5$ " or H-12"), $7.387\left(2 \mathrm{H}, \mathrm{MM}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{Am}}+J_{\mathrm{AM}^{\prime}}=8.8 \mathrm{~Hz}, \mathrm{H}-4$ " or $\mathrm{H}-11$ "), $7.365\left(2 \mathrm{H}, \mathrm{MM}^{\prime}\right.$ part of $\mathrm{AA}^{\prime} \mathrm{MM}^{\prime}$ system, $J_{\mathrm{AM}}+J_{\mathrm{AM}}{ }^{\prime}=8.6 \mathrm{~Hz}, \mathrm{H}-4$ " or H-11"), $6.331\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime}\right), 6.304$
$\left(\mathrm{d}, J_{\mathrm{H} 6^{\prime}}=8.4 \mathrm{~Hz}, \mathrm{H}-7^{\prime}\right), 4.508\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{H} 8^{\prime \prime}}=5.7 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime \prime}\right), 4.389\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{H1}}=5.3 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}\right)$, $4.087\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H11a}^{\prime}}=8.2, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.047\left(\mathrm{td}, J_{\mathrm{H}^{\prime}}=J_{\mathrm{H}^{\prime} \mathrm{a}^{\prime}}=7.9, J_{\mathrm{H} 5 \mathrm{~b}^{\prime}}=5.4 \mathrm{~Hz}\right.$, H-6'), 3.96 ( 2 H , v br s, H-2 or H-10), 3.91 ( 2 H , v br s, H-2 or H-10), H-12 overlapped with $\mathrm{H}_{2} \mathrm{O}$ signal, $3.28\left(8 \mathrm{H}\right.$, ol m, H-4 and H-5 or H-7 and H-8), $3.221\left(2 \mathrm{H}, \sim \mathrm{qt}, J_{\mathrm{H}-\mathrm{l}^{\prime}}=J_{\mathrm{H}-3^{\prime}}=6.7\right.$ Hz, H-2'), 3.11 ( 8 H, v br s, H-4 and H-5 or H-7 and H-8), 2.26 (ho m, H-12a'), 2.21 (ho m, H$12 b^{\prime}$ ), 1.91 (ho m, H-11a'), 1.71 (ol ho m, H-11b'), 1.66 (ol ho m, H-5a'), 1.55 (ol ho m, H$\left.5 b^{\prime}\right), 1.50(2 \mathrm{H}$, ol ho m, H-3'), 1.32 ( 2 H , ol ho m, $\mathrm{H}-4$ ').
${ }^{13} \mathrm{C}$ NMR (303 K): 174.59 (C-15'), 174.22 (C-14'), 173.82 (C-13'), 171.52 (br, C-13, 170.67 at 363 K ), 169.35 ( v br, C-11, 170.09 at 363 K ), 166.32 ( v br, C-1, 167.17 at 363 K ), 166.19 (C$7^{\prime \prime}$ or C-14"), 166.08 (C-7" or C-14"), 157.42 (C-8'), 142.85 (C-3" or C-10"), 141.96 (C-3" or C-10"), 133.27 (C-6" or C-13"), 133.07 (C-6" or C-13"), 127.51 (C-4" or C-5" or C-11" or C12 "), $127.38\left(\mathrm{C}-4^{\prime \prime}\right.$ or $\mathrm{C}-5^{\prime \prime}$ or $\mathrm{C}-11^{\prime \prime}$ or $\left.\mathrm{C}-12^{\prime \prime}\right), 127.27$ (C-4" or C-5" or $\mathrm{C}-11^{\prime \prime}$ or $\left.\mathrm{C}-12^{\prime \prime}\right)$, 127.02 (C-4" or C-5" or C-11" or C-12"), 54.84 (br, C-2 or C-10), 54.04 (br, C-2 or C-10), 53.08 (v br, C-12), 52.40 (C-6'), 51.76 (C-10'), 50.64 (v br, C-4 or C-5 or C-7 or C-8), 50.48 (v br, C-4 or C-5 or C-7 or C-8), 48.87 (v br, C-4 or C-5 or C-7 or C-8; 48.87 and 48.68 are C4 and C-5 or C-7 and C-8), 48.68 (v br, C-4 or C-5 or C-7 or C-8; 48.87 and 48.68 are C-4 and C-5 or C-7 and C-8), 42.48 (C-9"), 42.15 (C-2"), 39.13 (C-2'), 31.88 (C-5'), 29.98 (C-12'), 28.90 (C-3'), 27.59 (C-11'), 22.75 (C-4').
${ }^{1}$ H NMR Spectra



${ }^{13}$ C NMR Spectra




Compound 14
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 363 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 363 \mathrm{~K}$
${ }^{1} \mathrm{H}$ and ${ }^{1} \mathrm{H}$ with water suppression, $600 \mathrm{MHz}, 303 \mathrm{~K}$

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

HSQC, COSY, HMBC, $600 \mathrm{MHz}, 303 \mathrm{~K}$

No decomposition observed.

The macrocyclic ring assignments could not be effected with certitude due to dynamic effects causing severe line broadening precluding correlations in the HMBC spectra. All other signals could be fully assigned and the spectra were otherwise fully consistent with the proposed structure.
${ }^{1} \mathrm{H}$ NMR ( $303 \mathrm{~K}, 600 \mathrm{MHz}$ ): 9.079 (t, $J_{\mathrm{H} 9}=6.0 \mathrm{~Hz}, \mathrm{H}-8$ "), 9.049 (t, $\left.J_{\mathrm{H} 16^{\prime \prime}}=6.1 \mathrm{~Hz}, \mathrm{H}-15^{\prime \prime}\right)$, $8.925\left(\mathrm{brt}, J_{\mathrm{H} 2^{\prime \prime}}=5.7 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 8.394\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right), 7.870\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-55^{\prime \prime}\right), 7.848\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.3$ $\mathrm{Hz}, \mathrm{H}-12$ " $), 7.771\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-19$ " $), 7.398(2 \mathrm{H}$, MM' $^{\prime}$ part of AA'MM' system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.4 \mathrm{~Hz}, \mathrm{H}-11^{\prime \prime}\right), 7.392\left(2 \mathrm{H}, \mathrm{MM}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}}=8.3 \mathrm{~Hz}, \mathrm{H}-4$ " $), 7.359\left(2 \mathrm{H}, \mathrm{MM}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.4$ $\left.\mathrm{Hz}, \mathrm{H}-18{ }^{\prime \prime}\right), 6.333$ (d, $\left.J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right), 6.304\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.2 \mathrm{~Hz}, \mathrm{H}-7{ }^{\prime}\right), 4.521\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{H} 8^{\prime \prime}}=\right.$ $\left.5.9 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime \prime}\right), 4.503\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{H} 15^{\prime \prime}}=5.9 \mathrm{~Hz}, \mathrm{H}-16{ }^{\prime \prime}\right), 4.391\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{Hl}}=5.6 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}\right), 4.085$ $\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H} 11 \mathrm{a}^{\prime}}=8.3, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.046\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H} 5 \mathrm{a}^{\prime}}=8.0, J_{\mathrm{H5b}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right)$, 3.98 ( 2 H , v br s, $\mathrm{H}-2$ or $\mathrm{H}-10$ ), 3.93 ( 2 H , v br s, $\mathrm{H}-2$ or $\mathrm{H}-10$ ), 3.63 ( 4 H , v br s, $\mathrm{H}-12$ ), 3.29 (4H, ol v br s, H-4 or H-5 or H-7 or H-8), $3.28(4 \mathrm{H}$, ol v br s, $\mathrm{H}-4$ or $\mathrm{H}-5$ or $\mathrm{H}-7$ or $\mathrm{H}-8)$, $3.217(2 \mathrm{H}$, ho m, H-2'), $3.11(8 \mathrm{H}$, v br s, $\mathrm{H}-4$ and $\mathrm{H}-5$ or $\mathrm{H}-7$ and $\mathrm{H}-8$ ), 2.25 (ho m, H-12a'), 2.22 (ho m, H-12b'), 1.91 (ho m, H-11a'), 1.70 (ol ho m, H-11b'), 1.67 (ol ho m, H-5a'), 1.54 (ol ho m, H-5b'), 1.50 ( 2 H , ol ho m, H-3'), 1.31 ( 2 H , ol ho m, H-4').
${ }^{13} \mathrm{C}$ NMR (303 K): 174.59 (C-15'), 174.22 (C-14'), 173.82 (C-13'), 171.52 (br, C-13, 170.67 at 363 K ), 169.28 ( v br, C-11, 170.07 at 363 K ), $\sim 166.3$ ( v br, C-1, 167.16 at 363 K ), 166.27 (C14 "), 166.20 (C-7"), 166.09 (C-21"), 157.42 (C-8'), 143.23 (C-10"), 142.88 (C-17"), 141.95 (C-3"), 133.26 (C-20"), 133.06 (C-6"), 132.83 (C-13"), 127.51 (C-5"), 127.40 (C-12" or C-4"), 127.39 (C-12" or C-4"), 127.26 (C-19"), 127.15 (C-11"), 126.98 (C-18"), 54.82 (br, C-2 or C10), 54.02 (br, C-2 or C-10), 53.03 (v br, C-12), 52.40 (C-6'), 51.76 (C-10'), 50.62 (v br, C-4 or C-5 or C-7 or C-8), 50.47 (v br, C-4 or C-5 or C-7 or C-8), 48.83 (v br, C-4 or C-5 or C-7 or C-8; 48.83 and 48.61 are C-4 and C-5 or C-7 and C-8), 48.61 (v br, C-4 or C-5 or C-7 or C8; 48.83 and 48.61 are C-4 and C-5 or C-7 and C-8), 42.49 (C-9"), 42.46 (C-16"), 42.15 (C$\left.2^{\prime \prime}\right), 39.13$ (C-2'), 31.87 (C-5'), 29.98 (C-12'), 28.90 (C-3'), 27.59 (C-11'), 22.74 (C-4').
${ }^{1}$ H NMR Spectra



${ }^{13}$ C NMR Spectra




COSY




HMBC

$\square$

$\square$



$\square$




HSQC




Compound 15
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 363 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 363 \mathrm{~K}$

Approximately 10\% decomposition observed.


The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and 19 and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 363 K ): 8.77-8.70 (3H, ol t, H-8", H-15", and H-22"), 8.535 (t, $J_{\mathrm{H} 2}=5.7 \mathrm{~Hz}, \mathrm{H}-1$ "), $8.066\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.5 \mathrm{~Hz}, \mathrm{H}-11^{\prime}\right), 7.87-7.81(6 \mathrm{H}$, ol m, H-5" \&/or H-12" \&/or H-19", \&/or H-26"), $7.767\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-5$ " or $\mathrm{H}-12$ " or $\mathrm{H}-19{ }^{\prime \prime}$ or $\mathrm{H}-$ 26"), 7.43-7.35 (8H, ol m, H-4", H-11", H-18", and H-25"), 6.27-6.14 (2H, ol, H-7' and H-9'), 4.56-4.50 ( 6 H , ol, H-9", H-16", and H-23"), $4.392\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{H} 1}=5.7 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}\right), 4.18-4.07$ (2H, ol, H-6' and H-10'), 3.68 ( $2 \mathrm{H}, \mathrm{v}$ br m, H-2 or H-10), 3.63 ( $2 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-2$ or $\mathrm{H}-10$ ), $\mathrm{H}-12$ overlapped with $\mathrm{H}_{2} \mathrm{O}$ signal, 3.11 ( $2 \mathrm{H}, \mathrm{m}, \mathrm{H}-2$ '), $3.07-2.99$ ( 16 H , ol m, H-4, H-5, H-7, and H8), 2.28 (ho m, H-12a'), 2.24 (ho m, H-12b'), 1.96 (ho m, H-11a'), 1.78 (ol ho m, H-11b'), 1.72 (ol ho m, H-5a'), 1.59 (ol ho m, H-5b'), 1.55 ( 2 H , ol ho m, H-3'), 1.37 ( 2 H , ol ho m, H-4').
${ }^{13} \mathrm{C}$ NMR (363 K): 173.78 (C-15'), 173.39 (C-14'), 173.11 (C-13'), 170.68 (C-13), 170.38 (br, C-11), 167.45 (br, C-1), 166.05 ( $\times 2$, C-7" \&/or C-14" \&/or C-21", \&/or C-28"), 165.98 (C-7" or C-14" or C-21" or C-28"), 165.90 (C-7" or C-14" or C-21" or C-28"), 157.06 (C-8'), 142.70 (C-3" or C-10" or C-17" or C-24"), 142.69 (C-3" or C-10" or C-17" or C-24"), 142.32 (C-3" or C-10" or C-17" or C-24"), 141.73 (C-3" or C-10" or C-17" or C-24"), 133.22 (C-6" or C-13" or C-20" or C-27"), 132.96 (C-6" or C-13" or C-20" or C-27"), 132.77 ( $\times 2, \mathrm{C}-6^{\prime \prime}$ \&/or C-13" S40
\&/or C-20", \&/or C-27"), 127.02 (C-4" or C-5" or C-11" or C-12" or C-18" or C-19" or C-25" or C-26"), 126.91 (C-4" or C-5" or C-11" or C-12" or C-18" or C-19" or C-25" or C-26"), 126.90 (C-4" or C-5" or C-11" or C-12" or C-18" or C-19" or C-25" or C-26"), 126.84 (C-4" or C-5" or C-11" or C-12" or C-18" or C-19" or C-25" or C-26"), 126.77 ( $\times 2, \mathrm{C}-4^{\prime \prime} \& /$ or C-5" \&/or C-11" \&/or C-12" \&/or C-18" \&/or C-19", \&/or C-25", \&/or C-26"), 126.73 (C-4" or C$5^{\prime \prime}$ or $\mathrm{C}-11^{\prime \prime}$ or $\mathrm{C}-12^{\prime \prime}$ or $\mathrm{C}-18^{\prime \prime}$ or $\mathrm{C}-19^{\prime \prime}$ or $\mathrm{C}-25$ " or $\left.\mathrm{C}-2^{\prime \prime}\right), 126.62$ (C-4" or C-5" or C-11" or C-12" or C-18" or C-19" or C-25" or C-26"), 55.28 (br, C-2 or C-10), 54.19 (br, C-2 or C-10), 54.09 (C-12), 52.24 (C-6'), 51.68 (C-10'), 51.05 (C-4 or C-5 or C-7 or C-8), 50.63 (C-4 or C-5 or C-7 or C-8), 50.10 (C-4 or C-5 or C-7 or C-8; 50.10 and 49.81 are $\mathrm{C}-4$ and $\mathrm{C}-5$ or $\mathrm{C}-7$ and C-8), 49.81 ( v br, C-4 or C-5 or C-7 or C-8; 50.10 and 49.81 are C-4 and C-5 or C-7 and C-8), 42.29 ( $\times 3, \mathrm{C}-2^{\prime \prime} \& /$ or C-9" \&/or C-16", \&/or C-23"), 41.82 (C-2" or C-9" or C-16" or C-23"), 38.82 (C-2'), 31.63 (C-5'), 29.74 (C-12'), 28.49 (C-3'), 27.40 (C-11'), 22.34 (C-4').
${ }^{1}$ H NMR Spectra



${ }^{13}$ C NMR Spectra




Compound 16
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 363 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 363 \mathrm{~K}$

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

Approximately 16\% decomposition observed.

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $12,14,17$, and 19 and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 363 K ): 8.281 (d, $\left.J_{\mathrm{H} 2^{\prime \prime}}=8.4 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 7.827\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.5 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right), 7.622$ ( 2 H , ho m, H-6"'), $7.555\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}}=8.3 \mathrm{~Hz}, \mathrm{H}-2{ }^{\prime \prime}$ ' or H-3"'), 7.446 ( 2 H , ho m, H-7"'), 7.36-7.31 (1H, ol ho m, H-8'"), 7.323 ( $2 \mathrm{H}, \mathrm{MM}^{\prime}$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}}{ }^{\prime}=8.3 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}$ or H-3"'), 6.28-6.15 $\left(2 \mathrm{H}, \mathrm{v}\right.$ br ol m, H-7' and H-9'), $4.652\left(\mathrm{td}, J_{\mathrm{HI}}{ }^{\prime \prime}\right.$ $\left.=J_{\mathrm{H} 3^{\prime \prime}}=8.7, J_{\mathrm{H} 3}=5.3 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}\right), 4.159\left(\mathrm{v}\right.$ br t, $\left.J \sim 7.3 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.105(\mathrm{v}$ br t, $J \sim 6.7 \mathrm{~Hz}, \mathrm{H}-$ $\left.6^{\prime}\right), 3.725\left(\mathrm{~d}_{\mathrm{AB}}, J_{\mathrm{H} 2 \mathrm{~b}}=-15.6 \mathrm{~Hz}, \mathrm{H}-2 \mathrm{a}\right), 3.665(2 \mathrm{H}, \mathrm{s}, \mathrm{H}-10), 3.631\left(\mathrm{~d}_{\mathrm{AB}}, J_{\mathrm{H} 2 \mathrm{a}}=-15.7 \mathrm{~Hz}, \mathrm{H}-\right.$ 2b), 3.558 ( $4 \mathrm{H}, \mathrm{s}, \mathrm{H}-12$ ), 3.17-2.84 (20H, ol m, H-4, H-5, H-7, H-8, H-2', and H-3"), 2.29 (ho
m, H-12a'), 2.25 (ho m, H-12b'), 1.97 (ho m, H-11a'), 1.79 (ol ho m, H-11b'), 1.68 (ol ho m, H-5a'), 1.55 (ol ho m, H-5b'), 1.43 ( 2 H , ol ho m, H-3'), 1.34 ( 2 H, ol ho m, $\mathrm{H}-4^{\prime}$ ).
${ }^{13} \mathrm{C}$ NMR (363 K): 173.67 (C-15'), 173.27 (C-14'), 172.96 (C-13'), 170.71 (C-13), 170.14 (br, C-11), 169.75 (C-1), 166.27 (br, C-4"), 156.93 (C-8'), 139.62 (C-5"'), 137.97 (C-4"'), 136.44 (C-1"'), 129.33 (C-2"' or C-7"'), 128.35 (C-2"' or C-7"'), 126.70 (C-8"'), 125.99 (C-3"' or C$\left.6^{\prime \prime \prime}\right), 125.85$ (C-3"' or C-6"'), 54.54 (br, C-2 or C-10), 54.00 (C-2 or C-10), 53.93 (C-12), 53.48 (br, C-2"), $52.10\left(\mathrm{C}-6^{\prime}\right), 51.59\left(\mathrm{C}-10^{\prime}\right), 50.84$ (C-4 or C-5 or C-7 or C-8), 50.73 (C-4 or C-5 or C-7 or C-8), 49.69 (br, C-4 or C-5 or C-7 or C-8; 49.69 and 49.32 are C-4 and C-5 or C-7 and C-8), 49.32 (br, C-4 or C-5 or C-7 or C-8; 49.69 and 49.32 are C-4 and C-5 or C-7 and C-8), 38.23 (C-2'), 37.42 (C-3'), 31.54 (C-5'), 29.65 (C-12'), 28.24 (C-3'), 27.37 (C-11'), 22.23 (C4').

## ${ }^{1}$ H NMR Spectra




${ }^{13}$ C NMR Spectra



## Compound 17

${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{1} \mathrm{H}$ and ${ }^{1} \mathrm{H}$ with water suppression,

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator
$600 \mathrm{MHz}, 303 \mathrm{~K}$

HSQC, COSY, HMBC, $600 \mathrm{MHz}, 303 \mathrm{~K}$

No decomposition observed.

The macrocyclic ring assignments could not be effected with certitude due to dynamic effects causing severe line broadening precluding correlations in the HMBC spectra. All other signals could be fully assigned and the spectra were otherwise fully consistent with the proposed structure.
${ }^{1} \mathrm{H}$ NMR ( $303 \mathrm{~K}, 600 \mathrm{MHz}$ ): 8.409 (br t, $\left.J_{\mathrm{H} 2}=6.0 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 7.955\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right)$, $7.908\left(\mathrm{~d}, J_{\mathrm{H} 9}=8.5 \mathrm{~Hz}, \mathrm{H}-8{ }^{\prime \prime}\right), 7.843\left(\sim \mathrm{~d}, J_{\mathrm{H} 6 " '}=7.7 \mathrm{~Hz}, \mathrm{H}-5{ }^{\prime \prime}\right)$ ), $7.787\left(\mathrm{~d}, J_{\mathrm{H} 3}{ }^{\prime \prime}=8.2 \mathrm{~Hz}, \mathrm{H}-\right.$ 4"'), 7.777 ( $\sim$ d, $J_{\mathrm{H7} 7}=8.1 \mathrm{~Hz}, \mathrm{H}-8^{\prime \prime \prime}$ ), 7.678 (br s, H-1"'), 7.463 (ho m, H-7"'), 7.437 (ho m, H$\left.6^{\prime \prime \prime}\right), 7.390\left(\mathrm{dd}, J_{\mathrm{H} 4{ }^{\prime \prime}}=8.5, J_{\mathrm{H} 1{ }^{\prime \prime}}=1.5 \mathrm{~Hz}, \mathrm{H}-3^{\prime \prime \prime}\right), 6.336\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9 '\right), 6.296\left(\mathrm{~d}, J_{\mathrm{H} 6}\right.$ $\left.=8.2 \mathrm{~Hz}, \mathrm{H}-7^{\prime}\right), 4.523\left(\mathrm{td}, J_{\mathrm{H} 8^{\prime \prime}}=J_{\mathrm{H10b}}=8.9, J_{\mathrm{H10a}}{ }^{\prime \prime}=5.3 \mathrm{~Hz}, \mathrm{H}-9 "\right), 4.094\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H} 11 \mathrm{a}^{\prime}}=\right.$ $\left.8.3, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.009\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H5a}}{ }^{\prime}=8.1, J_{\mathrm{H} 5 b^{\prime}}=5.2 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right), 4.01(2 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-2$ or $\mathrm{H}-10), 3.86(2 \mathrm{H}, \mathrm{v}$ br s, H-2 or H-10), $3.55(4 \mathrm{H}$, v br s, $\mathrm{H}-12), 3.31(4 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-4$ or $\mathrm{H}-5$ or H-7 or H-8), 3.27 ( 4 H , v br s, H-4 or H-5 or H-7 or H-8), 3.102 (dd, $J_{\mathrm{H} 10 \mathrm{~b}^{\prime \prime}}=-14.0$, $\left.J_{\mathrm{H} 9}=5.1 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{a} "\right), 3.07(4 \mathrm{H}, \mathrm{v}$ br s, H-4 or H-5 or H-7 or H-8; 3.07 and 3.06 are $\mathrm{H}-4$ and $\mathrm{H}-5$ or $\mathrm{H}-7$ and $\mathrm{H}-8), 3.06(4 \mathrm{H}$, v br s, $\mathrm{H}-4$ or $\mathrm{H}-5$ or $\mathrm{H}-7$ or $\mathrm{H}-8 ; 3.07$ and 3.06 are $\mathrm{H}-4$ and H-5 or H-7 and H-8), 3.04 (ol m, H-2a'), 2.97 (ol m, H-2b'), 2.93 (ol m, H-10b"), 2.92 ( 2 H , ol m, H-2"), 2.26 (ho m, H-12a'), 2.22 (ho m, H-12b'), 2.070 (ho m but $\sim \mathrm{t}, J_{\mathrm{H} 5 \text { axax }}=J_{\mathrm{H} 5 \text { bax" }}=12.0$ Hz, H-6"), 1.914 (ho m, H-11a'), 1.71 (ol ho m, H-11b'), 1.69 (ol m, H-4aeq", attached to C4a"), 1.66 (ol m, H-5a", attached to C-5b"), 1.62 (ol m, H-4beq", attached to C-4b"), 1.59 (ol ho m, H-5a'), 1.49 (ol m, H-5b", attached to C-5a"), 1.45 (ol ho m, H-5b'), 1.32 ( 2 H , ol ho m, H-3'), 1.28 (ol m, H-3"), 1.22 ( 2 H , ol ho m, H-4'), 1.22 (ol m, H-5c", attached to C-5b"), 1.061 (ho m, H-5d", attached to C-5a"), 0.83 (ol m, H-4cax", attached to C-4a"), 0.81 (ol m, H4dax", attached to C-4b").
${ }^{13} \mathrm{C}$ NMR (303 K): 175.03 (C-7"), 174.59 (C-15'), 174.20 (C-14'), 173.80 (C-13'), 171.76 (br, C-13), 171.11 (C-11"), 168.93 (v br, C-11), 165.53 (v br, C-1), 157.41 (C-8'), 135.76 (C-2"'), 132.95 (C-8a'"), 131.84 (C-4a"'), 127.95 (C-3'"), 127.52 (C-5"'), 127.48 (C-1"'), 127.37 (C4"'), 127.33 (C-8"'), 125.99 (C-7"'), 125.42 (C-6"'), 54.92 (br, C-2 or C-10), 54.11 (br, C-2 or C-10), 53.75 (C-9"), 52.80 (v br, C-12), 52.36 (C-6'), 51.76 (C-10'), 50.84 (v br, C-4 or C-5 or C-7 or C-8), 50.69 (v br, C-4 or C-5 or C-7 or C-8), 48.56 (v br, C-4 or C-5 or C-7 or C-8; 48.56 and 48.31 are $\mathrm{C}-4$ and $\mathrm{C}-5$ or $\mathrm{C}-7$ and C-8), 48.31 ( v br, C-4 or C-5 or C-7 or C-8; 48.56 and 48.31 are C-4 and C-5 or C-7 and C-8), 45.09 (br, C-2"), 43.66 (C-6"), 38.43 (C-2'), 38.22 (br, C-10"), 36.77 (C-3"), 31.74 (C-5'), 29.97 (C-12'), 29.60 (br, C-4a"), 29.46 (br, C4b"), 28.73 (C-3'), 28.70 (br, C-5a", adjacent to C-4b"), 28.33 (br, C-5b", adjacent to C-4a"), 27.59 (C-11'), 22.61 (C-4').
${ }^{1}$ H NMR Spectra







${ }^{13}$ C NMR Spectra








COSY



HMBC








## Compound 18

${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$

$$
{ }^{13} \mathrm{C}+\text { DEPT, } 400 \mathrm{MHz}, 303 \mathrm{~K}
$$

No decomposition observed.

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator
The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and $19 \mathrm{and} /$ or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR (303 K): $8.386\left(\mathrm{br} \mathrm{t}, J_{\mathrm{H} 2}=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 7.941\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.7 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right), 7.880(\mathrm{~d}$, $J_{\mathrm{H} 9}=8.6 \mathrm{~Hz}, \mathrm{H}-8$ "), 7.846 (ho m, H-5"'), $7.790\left(\sim \mathrm{~d}, J_{\mathrm{H} 7{ }^{\prime \prime}}=8.7 \mathrm{~Hz}, \mathrm{H}-8^{\prime \prime \prime}\right.$ ), 7.781 (ho m, H$4^{\prime \prime \prime}$ ), 7.680 (br s, H-1"'), 7.46 (ho m, H-7"'), 7.44 (ho m, H-6"'), 7.392 (dd, $J_{\mathrm{H} 4{ }^{\prime \prime}}=8.5, J_{\mathrm{H} 1{ }^{\prime \prime}}=$ $\left.1.7 \mathrm{~Hz}, \mathrm{H}-3^{\prime \prime \prime}\right), 6.326\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right), 6.284\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.2 \mathrm{~Hz}, \mathrm{H}-7{ }^{\prime}\right), 4.534\left(\mathrm{td}, J_{\mathrm{H} 8^{\prime \prime}}=\right.$ $\left.J_{\mathrm{H} 10 b^{\prime \prime}}=8.9, J_{\mathrm{H} 10 \mathrm{a}^{\prime \prime}}=5.2 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime \prime}\right), 4.104\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H1la}^{\prime}}=8.3, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.2 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.017$ $\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H5a}}{ }^{\prime}=8.0, J_{\mathrm{H5b}}{ }^{\prime}=5.4 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right), 4.02(2 \mathrm{H}, \mathrm{v}$ br s, H-2 or H-10$), 3.87(2 \mathrm{H}, \mathrm{v}$ br s, H2 or $\mathrm{H}-10), 3.55(4 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-12), 3.32(4 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-4$ or $\mathrm{H}-5$ or $\mathrm{H}-7$ or $\mathrm{H}-8), 3.27(4 \mathrm{H}, \mathrm{v}$ br s, H-4 or H-5 or H-7 or H-8), $3.107\left(\mathrm{dd}, J_{\mathrm{H} 10 b^{\prime \prime}}=-13.9, J_{\mathrm{H} 9}=5.0 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{a}\right.$ " $), 3.11-2.89$ (13H, v br s and ol m, H-4, H-5, H-7, H-8, H-2a', H-2b', H-10b", and H-2"), 2.27 (ho m, H$12 \mathrm{a}^{\prime}$ ), 2.22 (ho m, H-12b'), 2.074 (ho m but $\sim \mathrm{t}, J_{\text {H5ax" }}=J_{\text {H5bax" }}=11.9 \mathrm{~Hz}, \mathrm{H}-6^{\prime \prime}$ ), 1.923 (ho m, H-11a'), 1.77-1.55 (5H, ol m, H-11b', $2 \times$ H-4eq", H-5a", and H-5a'), 1.54-1.41 ( 2 H , ol m, H$5 b^{\prime \prime}$ and $\left.\mathrm{H}-5 b^{\prime}\right), 1.39-1.16$ ( 6 H , ol m, H-3', H-3", H-4', and H-5c"), 1.068 (ho m, H-5d"), 0.90$0.76(2 \mathrm{H}$, ol m, $2 \times \mathrm{H}-4 \mathrm{ax}$ " $)$.
${ }^{13} \mathrm{C}$ NMR (303 K): 174.77 (C-7"), 174.49 (C-15'), 174.11 (C-14'), 173.67 (C-13'), 171.71 (br, C-13), 170.95 (C-11"), 168.80 (v br, C-11), 165.40 (v br, C-1), 157.26 (C-8'), 135.73 (C-2'"), 132.86 (C-8a'"), 131.74 (C-4a"'), 127.88 (C-3"'), 127.42 (C-5"' or C-1"' or C-4"' or C-8"'), 127.38 (C-5"' or C-1"' or C-4"' or C-8"'), $127.24\left(\times 2, \mathrm{C}-5{ }^{\prime \prime}\right.$ or C-1"' or C-4"' or C-8"'), 125.87 (C-7"'), 125.30 (C-6"'), 54.82 (br, C-2 or C-10), 54.01 (br, C-2 or C-10), 53.61 (C-9"), 52.67 (v br, C-12), 52.25 (C-6'), 51.66 (C-10'), 50.75 (v br, C-4 or C-5 or C-7 or C-8), 50.60 (v br, C-4 or C-5 or C-7 or C-8), 48.42 (v br, C-4 or C-5 or C-7 or C-8; 48.42 and 48.13 are C-4 and C-5 or C-7 and C-8), 48.13 (v br, C-4 or C-5 or C-7 or C-8; 48.42 and 48.13 are C-4 and C-5 or C-7 and C-8), 45.02 (br, C-2"), 43.55 (C-6"), 38.39 (C-2'), 38.19 (br, C-10"), 36.70 (C-3"), 31.72 (C-5'), 29.88 (C-12'), 29.54 (br, C-4a"), 29.39 (br, C-4b"), 28.68 (C-3'), 28.61 (br, C$5 \mathrm{a}^{\prime \prime}$, adjacent to $\mathrm{C}-4 \mathrm{~b}^{\prime \prime}$ ), 28.26 (br, C-5b", adjacent to C-4a"), 27.52 (C-11'), 22.55 (C-4').
${ }^{1}$ H NMR Spectra




${ }^{13}$ C NMR Spectra




Compound 19
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT + UDEFT, $400 \mathrm{MHz}, 303 \mathrm{~K}$

HSQC, COSY, HMBC, $400 \mathrm{MHz}, 303 \mathrm{~K}$


$R=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

No decomposition observed.

The macrocyclic ring assignments could not be effected with certitude due to dynamic effects causing severe line broadening precluding correlations in the HMBC spectra. All other signals could be fully assigned and the spectra were otherwise fully consistent with the proposed structure.
${ }^{1} \mathrm{H}$ NMR ( 303 K ): $8.310\left(\mathrm{v}\right.$ br s, H-1"), 8.211 (br d, $J_{\mathrm{H} 7{ }^{\prime \prime \prime}}=8.4 \mathrm{~Hz}, \mathrm{H}-8{ }^{\prime \prime}$ ), $7.918\left(\mathrm{br} \mathrm{d}, J_{\mathrm{H} 9}=\right.$ $\left.8.5 \mathrm{~Hz}, \mathrm{H}-8{ }^{\prime \prime}\right), 7.892$ (dd, $\left.J_{\mathrm{H} 6^{\prime \prime}}=8.5, J_{\mathrm{H} 7{ }^{\prime \prime}}=1.5 \mathrm{~Hz}, \mathrm{H}-55^{\prime \prime}\right), 7.873\left(\mathrm{br} \mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.8 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right)$, $7.764\left(\mathrm{dd}, J_{\mathrm{H} 3^{\prime \prime \prime}}=7.9, J_{\mathrm{H} 22^{\prime \prime}}=1.3 \mathrm{~Hz}, \mathrm{H}-4{ }^{\prime \prime \prime}\right), 7.548\left(\mathrm{ddd}, J_{\mathrm{H} 8^{\prime \prime}}=8.3, J_{\mathrm{H} 6 " '}=6.8, J_{\mathrm{H} 5^{\prime \prime}}=1.6 \mathrm{~Hz}\right.$, $\left.\mathrm{H}-7{ }^{\prime \prime \prime}\right), 7.504\left(\mathrm{ddd}, J_{\mathrm{H} 5 " '}=8.0, J_{\mathrm{H} 7{ }^{\prime \prime}}=6.8, J_{\mathrm{H} 8 " '}=1.2 \mathrm{~Hz}, \mathrm{H}-6{ }^{\prime \prime \prime}\right), 7.370\left(\mathrm{dd}, J_{\mathrm{H} 4{ }^{\prime \prime}}=7.7, J_{\mathrm{H} 2 " '}=\right.$ $\left.7.0 \mathrm{~Hz}, \mathrm{H}-3^{\prime \prime \prime}\right), 7.345\left(\mathrm{dd}, J_{\mathrm{H} 3^{\prime \prime \prime}}=7.2, J_{\mathrm{H} 4{ }^{4}}=1.7 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime \prime}\right), 6.3186\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.2 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right)$,
$6.284\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-7^{\prime}\right), 4.555\left(\mathrm{td}, J_{\mathrm{H} 8 "}=J_{\mathrm{H} 10 \mathrm{~b}^{\prime \prime}}=8.4, J_{\mathrm{H1Oa}}{ }^{\prime \prime}=5.9 \mathrm{~Hz}, \mathrm{H}-9 "\right), 4.098(\mathrm{td}$, $\left.J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H11a}}{ }^{\prime}=8.3, J_{\mathrm{H11b}}{ }^{\prime}=5.2 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.012\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H} 5 \mathrm{a}^{\prime}}=8.1, J_{\mathrm{H5b}}{ }^{\prime}=5.2 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right)$, 3.85 ( 2 H , v br s, $\mathrm{H}-2$ or $\mathrm{H}-10$ ), 3.77 ( 2 H , v br s, $\mathrm{H}-2$ or $\mathrm{H}-10$ ), 3.57 ( 4 H , v br s, $\mathrm{H}-12$ ), 3.439 (dd, $\left.J_{\mathrm{H} 10 \mathrm{~b}^{\prime \prime}}=-13.5, J_{\mathrm{H} 9}=5.5 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{a} "\right), 3.19(4 \mathrm{H}, \mathrm{v}$ br s, H-4 or H-5 or H-7 or H-8), 3.186 (dd, $\left.J_{\mathrm{H} 10 \mathrm{a}^{\prime \prime}}=-13.8, J_{\mathrm{H} 9}=8.6 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{~b}{ }^{\prime \prime}\right), 3.16(4 \mathrm{H}, \mathrm{v}$ br s, H-4 or H-5 or H-7 or H-8), 3.02 ( 8 H , v br s, H-4 and H-5 or H-7 and H-8), 3.01 (ol m, H-2a'), 2.94 (ol m, H-2b'), 2.93 ( 2 H , ol m, H-2"), 2.26 (ho m, H-12a'), 2.22 (ho m, H-12b'), 2.079 (ho mbut $\sim$, $J_{\mathrm{HSaax}}=J_{\mathrm{H} 5 \mathrm{bax}}=11.8$ Hz, H-6'), 1.917 (ho m, H-11a'), 1.70 (ol ho m, H-11b'), 1.69 (ol m, H-4aeq", attached to C4b"), 1.66 (ol m, H-5a", attached to C-5b"), 1.66 (ol m, H-4beq", attached to C-4a"), 1.60 (ol ho m, H-5a'), 1.51 (ol m, H-5b", attached to C-5a"), 1.47 (ol ho m, $\mathrm{H}-5 \mathrm{~b}^{\prime}$ ), 1.29 ( 2 H , ol ho m, H-3'), 1.29 (ol m, H-3"), 1.22 (ol m, H-5c", attached to C-5b"), 1.19 ( 2 H , ol ho m, H-4'), 1.072 (ho m, H-5d", attached to C-5a"), 0.84 (ol m, H-4cax", attached to C-4b"), 0.82 (ol m, H4dax", attached to C-4a").
${ }^{13} \mathrm{C}$ NMR (303 K): 175.01 (C-7"), 174.57 (C-15'), 174.16 (C-14'), 173.74 (C-13'), 171.64 (br, C-13), 170.90 (C-11"), 169.84 (v br, C-11), 166.14 (v br, C-1), 157.34 (C-8'), 133.83 (C-1'"), 133.37 (C-4a"'), 131.73 (C-8a"'), 128.52 (C-5"'), 127.47 (C-2"'), 126.98 (C-4"'), 126.01 (C7"'), 125.52 (C-6"'), 125.20 (C-3"'), 123.91 (C-8"'), 54.97 (br, C-2 or C-10), 54.21 (br, C-2 or C-10), 53.27 (v br, C-12), 53.25 (C-9"), 52.33 (C-6'), 51.71 (C-10'), 50.94 (v br, C-4 or C-5 or C-7 or C-8), 50.67 ( v br, C-4 or C-5 or C-7 or C-8), 48.84 ( $\mathrm{v} \mathrm{br}, \mathrm{C}-4$ and C-5 or C-7 and C-8), 44.95 (br, C-2"), 43.60 (C-6"), 38.45 (C-2'), 36.81 (C-3"), 35.24 (br, C-10"), 31.75 (C-5'), 29.93 (C-12'), 29.61 (br, C-4a"), 29.45 (br, C-4b"), 28.66 (C-3'), 28.70 (br, C-5a", adjacent to C-4b"), 28.28 (br, C-5b", adjacent to C-4a"), 27.57 (C-11'), 22.60 (C-4').

## ${ }^{1}$ H NMR Spectra








${ }^{13}$ C NMR Spectra



 COSY




HMBC






HSQC







Compound 20
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}, 400 \mathrm{MHz}, 303 \mathrm{~K}$

No decomposition observed.

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and $\mathbf{1 9}$ and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 303 K ): 8.820 (v br d, $\left.J_{\mathrm{H} 9}=7.7 \mathrm{~Hz}, \mathrm{H}-88^{\prime \prime}\right), 8.171$ (br t, $\left.J_{\mathrm{H} 2}=5.7 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 7.88-$ $7.80\left(3 \mathrm{H}\right.$, ol ho m, H-5'", H-8'", and H-4'"), 7.710 (br s, H-1'"), 7.598 (t, $J_{\mathrm{H} 2}=5.6 \mathrm{~Hz}, \mathrm{H}-1$ '), 7.51-7.42 (3H, ol ho m, H-7"', H-6"', and H-3"'), 6.327 (d, $\left.J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime}\right), 6.296\left(\mathrm{~d}, J_{\mathrm{H} 6}\right.$ $\left.=8.2 \mathrm{~Hz}, \mathrm{H}-7^{\prime}\right), 4.722\left(\mathrm{td}, J_{\mathrm{H} 8}=J_{\mathrm{H10b}}=8.8, J_{\mathrm{H10a}}{ }^{\prime \prime}=5.8 \mathrm{~Hz}, \mathrm{H}-9 "\right), 4.097\left(\mathrm{td}, J_{\mathrm{H} 9}=J_{\mathrm{H} 11 \mathrm{a}^{\prime}}=\right.$ $\left.8.3, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.038\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H5a}}{ }^{\prime}=8.0, J_{\mathrm{Hbb}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right), 3.97(2 \mathrm{H}, \mathrm{v}$ br s, H-2 or H-10), 3.94 ( $2 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-2$ or $\mathrm{H}-10$ ), , $\mathrm{H}-12, \mathrm{H}-4, \mathrm{H}-5, \mathrm{H}-7$, and $\mathrm{H}-8$ overlapped with $\mathrm{H}_{2} \mathrm{O}, 3.188\left(\mathrm{dd}, J_{\mathrm{H} 10 \mathrm{~b}^{\prime \prime}}=-13.4 J_{\mathrm{H} 9}=5.4 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{a} "\right), 3.07-2.89$ and $2.85-2.77(13 \mathrm{H}, \mathrm{v}$ br s and ol m, H-4, H-5, H-7, H-8, H-2a', H-2b', H-10b", and H-2"), 2.26 (ho m, H-12a'), 2.22 (ho m, H-12b'), 1.98-1.87 (2H, ho m, H-6" and H-11a'), 1.77-1.13 (12H, ol m, H-11b', $2 \times \mathrm{H}-$ $4 e q ", 4 \times \mathrm{H}-5{ }^{\prime \prime}, 2 \times \mathrm{H}-5^{\prime}, \mathrm{H}-3^{\prime}, \mathrm{H}-3^{\prime \prime}$, and H-4'), 0.85-0.71 ( 2 H, ol m, $2 \times \mathrm{H}-4 \mathrm{ax}{ }^{\prime \prime}$ ). N.b. For convenience, the numbering used for the linker is as per $\mathbf{1 7}$.
${ }^{13} \mathrm{C}$ NMR (303 K): 174.84 (C-7"), 174.49 (C-15'), 174.09 (C-14'), 173.67 (C-13'), 171.73 (br, C-13), 169.98 (C-11"), 168.75 (v br, C-11), 164.91 (v br, C-1), 157.27 (C-8'), 135.10 (C-2'"), 132.82 (C-8a'"), 131.77 (C-4a"'), 127.83 (C-3"' or C-5"' or C-1"' or C-4"' or C-8"'), 127.68 (C$3{ }^{\prime \prime \prime}$ or C-5"' or C-1"' or C-4"' or C-8"'), 127.56 (C-3"' or C-5"' or C-1"' or C-4"' or C-8"'), 127.46 (C-3"' or C-5"' or C-1"' or C-4"' or C-8"'), 127.38 (C-3"' or C-5"' or C-1"' or C-4"' or C-

8"'), 126.04 (C-7"'), 125.52 (C-6"'), 54.62 (br, C-2 or C-10), 54.24 (br, C-2 or C-10), 53.96 (C9'), 52.66 (v br, C-12), 52.26 (C-6'), 51.65 (C-10'), 50.59 (v br, C-4 or C-5 or C-7 or C-8), 50.23 (v br, C-4 or C-5 or C-7 or C-8), 48.24 (v br, C-4, C-5, C-7, and C-8), 44.88 (C-2"), 43.97 (C-6"), 38.11 (br, C-10"), 36.76 (C-3"), 31.80 (C-5'), 29.88 (C-12'), 29.58 ( $\times 2$, br, $2 \times$ C-4'), 28.83 (br, C-3' or $1 \times$ C-5"), $28.66\left(\times 2, \mathrm{C}-3^{\prime}\right.$ and $1 \times \mathrm{C}-5{ }^{\prime \prime}$ or $\left.2 \times \mathrm{C}-5{ }^{\prime \prime}\right), 27.53\left(\mathrm{C}-11^{\prime}\right)$, 22.55 (C-4'), C-2' ol with solvent. N.b. For convenience, the numbering used for the linker is as per 17.
${ }^{1}$ H NMR Spectra




${ }^{13}$ C NMR Spectra





Compound 21
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 303 \mathrm{~K}$

No decomposition observed.

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and $\mathbf{1 9}$ and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 303 K ): 8.781 (br d, $\left.J_{\mathrm{H} 2^{\prime \prime}}=7.0 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 8.214\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right), 7.88-7.80$ (3H, ol m, H-5'", H-8'", and H-4"'), 7.703 (br s, H-1'"), 7.51-7.42 (3H, ol m, H-7"', H-6'", and $\left.\mathrm{H}-3^{\prime \prime}\right), 6.338\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.2 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right), 6.300\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-7{ }^{\prime}\right), 4.676\left(\mathrm{td}, J_{\mathrm{H} 1 "}=J_{\mathrm{H} 3 \mathrm{~b}^{\prime \prime}}=\right.$ $\left.9.0, J_{\mathrm{H3a}}{ }^{\prime}=5.2 \mathrm{~Hz}, \mathrm{H}-22^{\prime \prime}\right), 4.103\left(\mathrm{td}, J_{\mathrm{H}^{\prime}}=J_{\mathrm{H} 11 \mathrm{a}^{\prime}}=8.2, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.2 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.030\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=\right.$ $\left.J_{\mathrm{Ha}^{\prime}}=8.1, J_{\mathrm{H} 5 b^{\prime}}=5.4 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right), 3.91(2 \mathrm{H}, \mathrm{v}$ br s, H-2 or H-10$), \mathrm{H}-2, \mathrm{H}-10, \mathrm{H}-12, \mathrm{H}-4, \mathrm{H}-5$, H-7, and H-8 all overlapped, $3.195\left(\mathrm{dd}, J_{\mathrm{H} 3 \mathrm{~b} "}=-13.5, J_{\mathrm{H} 2}=5.0 \mathrm{~Hz}, \mathrm{H}-3 \mathrm{a} "\right), 3.14-2.86(11 \mathrm{H}$,
v br s and ol m, H-4, H-5, H-7, H-8, H-2a', H-2b', and H-3b"), 2.26 (ho m, H-12a'), 2.22 (ho m, H-12b'), 1.924 (ho m, H-11a'), 1.77-1.68 (ho m, H-11b'), 1.67-1.56 (ho m, H-5a'), 1.531.42 (ho m, H-5b'), $1.40-1.31$ ( 2 H, ol m, H-3'), $1.30-1.20$ ( 2 H, ol m, H-4').
${ }^{13} \mathrm{C}$ NMR (303 K): 174.51 (C-15'), 174.10 (C-14'), 173.68 (C-13'), 171.67 (br, C-13), 169.95 (C-4"), 169.11 (v br, C-11), 165.16 (v br, C-1), 157.28 (C-8'), 135.20 (C-2"'), 132.80 (C-8a"'), 131.76 (C-4a'"), 127.84 (C-1"' or C-3"' or C-4'" or C-5'" or C-8"'), 127.68 (C-1"' or C-3"' or C$4 "$ or C-5"' or C-8"'), $127.55(\mathrm{C}-1 " '$ or C-3"' or C-4"' or C-5"' or C-8"'), 127.46 (C-1'" or C-3'" or C-4"' or C-5"' or C-8"'), 127.37 (C-1"' or C-3"' or C-4"' or C-5"' or C-8"'), 126.04 (C-7"'), 125.52 (C-6"'), 54.57 (br, C-2 or C-10), 54.17 (br, C-2"), 53.98 (br, C-2 or C-10), 52.81 (v br, C-12), 52.25 (C-6'), 51.66 (C-10'), 50.58 (v br, C-4 or C-5 or C-7 or C-8), 50.24 (v br, C-4 or C-5 or C-7 or C-8), 48.36 (v br, C-4 and C-5 or C-7 and C-8), 38.74 (C-3"), 38.52 (C-2'), 31.77 (C-5'), 29.88 (C-12'), 28.64 (C-3'), 27.54 (C-11'), 22.65 (C-4').
${ }^{1}$ H NMR Spectra



${ }^{13}$ C NMR Spectra




## Compound 22

${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 303 \mathrm{~K}$

No decomposition observed.

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and $19 \mathrm{and} /$ or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR (303 K): 8.896 (br t, $\left.J_{\mathrm{H} 2}=6.9 \mathrm{~Hz}, \mathrm{H}-1{ }^{\prime \prime}\right), 8.529\left(\mathrm{~d}, J_{\mathrm{H} 9}=8.4 \mathrm{~Hz}, \mathrm{H}-8^{\prime \prime}\right), 8.119(\mathrm{t}$, $\left.J_{\mathrm{H} 2^{\prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right), 7.86-7.75$ ( 6 H , ol m, H-5"', H-8"', H-4'", H-1"', and H-5"), 7.504 (ho m, H-3'"), 7.45 (ho m, H-7'"), 7.43 (ho m, H-6"'), 7.327 ( $2 \mathrm{H}, \mathrm{MM}^{\prime}$ part of AA'MM' system, $J_{\mathrm{AM}}+$ $\left.J_{\mathrm{AM}^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-4^{\prime \prime}\right), 6.336\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}^{\prime} 9^{\prime}\right), 6.303\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-7^{\prime}\right), 4.773(\mathrm{ddd}$, $\left.J_{\mathrm{H10b}}=9.8, J_{\mathrm{H} 8 "}=8.6, J_{\mathrm{H10a}}{ }^{\prime \prime}=4.8 \mathrm{~Hz}, \mathrm{H}-9 "\right), 4.358\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{H1}}=5.5 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}\right), 4.105$ (td, $\left.J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H11a}}{ }^{\prime}=8.3, J_{\mathrm{H11b}}{ }^{\prime}=5.3 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.036\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H5a}}{ }^{\prime}=8.1, J_{\mathrm{H5b}}{ }^{\prime}=5.3 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right)$, 3.93 and $3.88(4 \mathrm{H}, 2 \times \mathrm{v}$ br s, $\mathrm{H}-2$ and $\mathrm{H}-10), 3.62(4 \mathrm{H}, \mathrm{v}$ br s, $\mathrm{H}-12), 3.245\left(\mathrm{br} \mathrm{dd}, J_{\mathrm{H} 10 \mathrm{~b}}{ }^{\prime \prime}=\right.$ $\left.-13.5, J_{\mathrm{H} 9}=4.6 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{a} "\right), 3.154\left(\mathrm{br} \mathrm{dd}, J_{\mathrm{H}_{10 \mathrm{a}}{ }^{\prime \prime}}=-13.6, J_{\mathrm{H} 9}=10.0 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{~b} "\right), 3.32-2.97$ ( 18 H , v br s and ol m, H-4, H-5, H-7, H-8, and H-2'), 2.26 (ho m, H-12a'), 2.22 (ho m, H12b'), 1.922 (ho m, H-11a'), 1.75-1.68 (ho m, H-11b'), 1.68-1.57 (ho m, H-5a'), 1.54-1.44 (ho m, H-5b'), 1.42-1.32 (2H, ol m, H-3'), 1.32-1.21 ( 2 H , ol m, H-4').
${ }^{13} \mathrm{C}$ NMR (303 K): 174.52 (C-15'), 174.13 (C-14'), 173.69 (C-13'), 171.47 (br, C-13), 171.01 (C-11"), 169.43 (v br, C-11), 166.29 (v br, C-1), 165.85 (C-7"), 157.31 (C-8'), 141.81 (C-3"), 136.09 (C-2"'), 132.93 (C-6"), 132.81 (C-8a"'), 131.76 (C-4a"'), 127.86 (C-1"' or C-3"' or C-4'" or C-5"' or C-8"'), 127.54 (C-5"), 127.44 (C-1'" or C-3"' or C-4"' or C-5"' or C-8"'), 127.40 (C1 "' or C-3"' or C-4"' or C-5"' or C-8"'), 127.36 (C-1"' or C-3"' or C-4"' or C-5"' or C-8"'), 127.27 (C-1"' or C-3"' or C-4"' or C-5'" or C-8"'), 127.08 (C-4"), 125.94 (C-7"'), 125.35 (C$6^{\prime \prime \prime}$ ), 54.89 (br, C-9"), 54.73 (br, C-2 or C-10), 53.97 (br, C-2 or C-10), 53.06 (v br, C-12), 52.29 (C-6'), 51.69 (C-10'), 50.57 (v br, C-4 or C-5 or C-7 or C-8), 50.42 (v br, C-4 or C-5 or C-7 or C-8), 48.80 (v br, C-4 and C-5 or C-7 and C-8), 42.01 (C-2"), 38.52 (C-2'), 37.76 (C$\left.10{ }^{\prime \prime}\right), 31.74$ (C-5'), 29.90 (C-12'), 28.74 (C-3'), 27.54 (C-11'), 22.61 (C-4').
${ }^{1}$ H NMR Spectra





${ }^{13}$ C NMR Spectra





## Compound 23

${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 303 \mathrm{~K}$

COSY $400 \mathrm{MHz}, 303 \mathrm{~K}$

$R=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

No decomposition observed.

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and 19 and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR (303 K): 8.326 (br t, $\left.J_{\mathrm{H} 2 "}=5.8 \mathrm{~Hz}, \mathrm{H}-11^{\prime \prime}\right), 8.021\left(\mathrm{~d}, J_{\mathrm{H} 9}=8.5 \mathrm{~Hz}, \mathrm{H}-8{ }^{\prime \prime}\right), 7.972(\mathrm{t}$, $J_{\mathrm{H} 2^{\prime}}=5.7 \mathrm{~Hz}, \mathrm{H}-1^{\prime}$ ), 7.845 (ho m, H-5'"), 7.792 (ho m, H-8'"), 7.797 (d, $J_{\mathrm{H} 3^{\prime \prime}}=8.8 \mathrm{~Hz}, \mathrm{H}-4^{\prime \prime \prime}$ ), 7.693 (br s, H-1"'), 7.46 (ho m, H-7"'), 7.44 (ho m, H-6'"), 7.401 (dd, $J_{\mathrm{H} 3}{ }^{\prime \prime}=8.5, J_{\mathrm{H1}{ }^{\prime \prime}}=1.7 \mathrm{~Hz}$, $\mathrm{H}-3{ }^{\prime \prime}$ ) $, 6.341\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.2 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime}\right), 6.294\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-7{ }^{\prime}\right), 4.555\left(\mathrm{td}, J_{\mathrm{H} 10 \mathrm{~b}^{\prime \prime}}=8.9\right.$, $\left.J_{\mathrm{H} 10 \mathrm{a}^{\prime \prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime \prime}\right), 4.102\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H} 1 \mathrm{a}^{\prime}}=8.3, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.3 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.016\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=\right.$ $\left.J_{\mathrm{HFa}^{\prime}}=8.1, J_{\mathrm{H5b}}{ }^{\prime}=5.3 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right), 3.98(2 \mathrm{H}$, v br s, $\mathrm{H}-2$ or $\mathrm{H}-10), 3.81(2 \mathrm{H}$, v br s, $\mathrm{H}-2$ or $\mathrm{H}-$ 10), $3.57\left(4 \mathrm{H}, \mathrm{v}\right.$ br s, H-12), $3.28\left(8 \mathrm{H}, \mathrm{v}\right.$ br s, $\mathrm{H}-4$ or H-5 or H-7 or H-8), $3.111\left(\mathrm{br} \mathrm{dd}, J_{\mathrm{H} 10 \mathrm{~b}}{ }^{\prime \prime}=\right.$ $\left.-13.8, J_{\mathrm{H} 9}=5.3 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{a} "\right), 2.915\left(\mathrm{br} \mathrm{dd}, J_{\mathrm{H} 10 \mathrm{a}^{\prime \prime}}=-13.6, J_{\mathrm{H9}}=9.4 \mathrm{~Hz}, \mathrm{H}-10 \mathrm{~b} "\right), 3.10-2.91$ ( 12 H , ol m, H-4 or H-5 or H-7 or H-8, H-2' and H-2"), 2.26 (ho m, H-12a'), 2.22 (ho m, H$\left.12 b^{\prime}\right), 2.030\left(\mathrm{t}, J_{\mathrm{H} 5}=7.4 \mathrm{~Hz}, \mathrm{H}-6 "\right.$ ), 1.921 (ho m, H-11a'), 1.76-1.66 (ho m, H-11b'), 1.641.54 (ho m, H-5a'), 1.51-1.41 (ho m, H-5b'), 1.39-1.17 (8H, ol m, H-3', H-4', H-3", and H-5"), 1.11-1.01 (2H, ol m, H-4").
${ }^{13} \mathrm{C}$ NMR (303 K): 174.53 (C-15'), 174.14 (C-14'), 173.71 (C-13'), 172.01 (C-7"), 171.68 (br, C-13), 170.98 (C-11"), 169.15 (v br, C-11), 165.45 (v br, C-1), 157.33 (C-8'), 135.72 (C-2'"), 132.92 (C-8a"'), 131.79 (C-4a"'), 127.83 (C-1"' or C-3"' or C-4"' or C-5"' or C-8"'), 127.45 (C$1{ }^{\prime \prime \prime}$ or C-3"' or C-4"' or C-5"' or C-8"'), 127.43 (C-1"' or C-3"' or C-4"' or C-5"' or C-8"'), 127.35 (C-1"' or C-3"' or C-4"' or C-5"' or C-8"'), 127.31 (C-1"' or C-3"' or C-4"' or C-5"' or C8"'), 125.93 (C-7"'), 125.36 (C-6'"), 54.84 (br, C-2 or C-10), 54.06 (br, C-2 or C-10), 53.93 (C9'), 52.91 ( v br, C-12), 52.30 (C-6'), 51.70 (C-10'), 50.74 ( $\mathrm{v} \mathrm{br}, \mathrm{C}-4$ or C-5 or C-7 or C-8), 50.60 ( $\mathrm{vbr}, \mathrm{C}-4$ or C-5 or C-7 or C-8), 48.57 ( v br, C-4 or C-5 or C-7 or C-8; 48.57 and 48.42 are C-4 and C-5 or C-7 and C-8), 48.42 (v br, C-4 or C-5 or C-7 or C-8; 48.57 and 48.42 are C-4 and C-5 or C-7 and C-8), 38.69 (C-2'), 38.39 (C-2"), 38.25 (C-10"), 35.10 (C-6"), 31.71
(C-5'), 29.92 (C-12'), 28.70 (C-3'), 28.48 (C-5"), 27.55 (C-11'), 25.91 (C-3" or C-4"), 24.83 (C-3" or C-4"), 22.57 (C-4').
${ }^{1}$ H NMR Spectra







${ }^{13}$ C NMR Spectra



 COSY




## Compound 24

${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 363 \mathrm{~K}$

$$
{ }^{13} \mathrm{C}+\text { DEPT, } 400 \mathrm{MHz}, 363 \mathrm{~K}
$$

Approximately 17\% decomposition observed.

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and 19 and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 363 K ): $8.203\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime \prime}}=5.9 \mathrm{~Hz}, \mathrm{H}-1{ }^{\prime \prime}\right.$ or $\mathrm{H}-12^{\prime \prime}$ or $\left.\mathrm{H}-1^{\prime}\right), 8.064\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right.$ or $\mathrm{H}-12^{\prime \prime}$ or $\mathrm{H}-1^{\prime}$ ), 8.034 (t, $J_{\mathrm{H} 2^{\prime}}=5.8 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}$ or $\mathrm{H}-12^{\prime \prime}$ or $\mathrm{H}-1$ '), 7.84 (ho m, $\mathrm{H}-5^{\prime \prime}$ '), $7.80-$ $7.74\left(2 \mathrm{H}\right.$, ol m, H-4"' and H-8"'), $7.710\left(2 \mathrm{H}, \mathrm{AA}^{\prime}\right.$ part of AA'MM' system, $J_{\mathrm{AM}}+J_{\mathrm{AM}}=8.5$ Hz, H-16"'), $\sim 7.69$ (br m, H-1"'), 7.616 (d, $J_{\mathrm{H} 9}=8.3 \mathrm{~Hz}, \mathrm{H}-8{ }^{\prime \prime}$ ), 7.46 (ho m, H-7"'), 7.45 (ho m, H-6'"), 7.386 (dd, $\left.J_{\mathrm{H} 4{ }^{\prime \prime}}=8.4, J_{\mathrm{H1}{ }^{\prime \prime}}=1.8 \mathrm{~Hz}, \mathrm{H}-3^{\prime \prime \prime}\right), 7.234\left(2 \mathrm{H}, \mathrm{MM}^{\prime}\right.$ part of AA'MM' system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}}=8.6 \mathrm{~Hz}, \mathrm{H}-15^{\prime \prime \prime}\right), 6.30-6.15\left(2 \mathrm{H}, \mathrm{v}\right.$ br ol m, H-7' and H-9'), $4.678\left(\mathrm{td}, J_{\mathrm{H} 8}{ }^{\prime \prime}\right.$ $\left.=J_{\mathrm{H} 10 b^{\prime \prime}}=8.4, J_{\mathrm{H} 10 \mathrm{a}^{\prime \prime}}=5.6 \mathrm{~Hz}, \mathrm{H}-9{ }^{\prime \prime}\right), 4.329\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{H} 12}=5.9 \mathrm{~Hz}, \mathrm{H}-13^{\prime \prime}\right), 4.153(\mathrm{v}$ br t, $J \sim 6.5$ Hz, H-10'), 4.120 (v br t, J $\sim 6.4 \mathrm{~Hz}, \mathrm{H}-6$ '), 3.765 ( $2 \mathrm{H}, \mathrm{s}, \mathrm{H}-2$ or $\mathrm{H}-10$ ), 3.709 ( $2 \mathrm{H}, \mathrm{s}, \mathrm{H}-2$ or H10), 3.605 ( $4 \mathrm{H}, \mathrm{s}, \mathrm{H}-12$ ), 3.30-3.00 ( 20 H , ol m, H-4, H-5, H-7, H-8, H-2', and H-10"), 2.969 $\left(2 \mathrm{H}, \mathrm{t}, J_{\mathrm{H} 3^{\prime \prime}}=J_{\mathrm{H} 1^{\prime \prime}}=6.2 \mathrm{~Hz}, \mathrm{H}-22^{\prime \prime}\right), 2.29$ (ho m, H-12a'), 2.25 (ho m, H-12b'), 2.103 (tt, $J_{\mathrm{H} 5 a a x "}$ $\left.=J_{\text {H5bax" }}=12.0, J_{\text {H5aeq" }}=J_{\text {H5beq" }}=3.3 \mathrm{~Hz}, \mathrm{H}-6^{\prime \prime}\right), 1.964$ (ho m, H-11a'), 1.83-1.52 (9H) and 1.43-1.22 (4H) (H-11b', H-4aeq", H-4beq", H-5a-c", H-5', H-3', H-3", and H-4'), 1.172 (ho m, H-5d"), 0.95-0.81 ( 2 H , ol m, H-4cax" and H-4dax").
${ }^{13} \mathrm{C}$ NMR (363 K): 174.48 (C-7"), 173.68 (C-15'), 173.28 (C-14'), 172.97 (C-13'), 170.82 (C11), 170.73 (C-13), 169.86 (br, C-1), 166.29 (br, C-11" or C-18"), 165.66 (br, C-11" or C-18"), 156.94 (C-8'), 141.72 (C-14"), 135.19 (C-2"'), 133.14 (C-17"), 132.64 (C-8a"'), 131.51 (C-

4a'"), 127.35 (C-3'"), 126.96 (C-5"'), 126.94 (C-1"'), 126.88 (C-4"'), 126.83 (C-8"'), 126.61 (C15 " or C-16"), 126.38 (C-15" or C-16"), 125.37 (C-7"'), 124.83 (C-6"'), 54.96 (br, C-2 or C10), 54.03 (C-2 or C-10), 53.72 (C-12), 53.46 (br, C-9"), 52.16 (C-6'), 51.59 (C-10'), 51.13 (C-4 or C-5 or C-7 or C-8), 50.68 (C-4 or C-5 or C-7 or C-8), 49.55 (br, C-4 or C-5 or C-7 or C-8; 49.55 and 49.17 are C-4 and C-5 or C-7 and C-8), 49.17 (br, C-4 or C-5 or C-7 or C-8; 49.55 and 49.17 are C-4 and C-5 or C-7 and C-8), 44.56 (C-2"), 43.44 (C-6"), 41.67 (C-13"), 38.74 (C-2'), 37.51 (br, C-10'), 36.44 (C-3'), 31.59 (C-5'), 29.67 (C-12'), 29.24 (C-4a"), 29.15 (C-4b"), 28.45 (C-5a", adjacent to C-4b"), 28.25 (C-3'), 27.98 (C-5b", adjacent to C-4a"), 27.36 (C-11'), 22.29 (C-4').
${ }^{1}$ H NMR Spectra





## ${ }^{13}$ C NMR Spectra





## Compound 25

${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 363 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 363 \mathrm{~K}$

$R=$ glutamate-urea-lysine binding motif and $R^{\prime}=$ DOTA chelator Approximately $12 \%$ decomposition observed.

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and 19 and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR (363 K): $8.037\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime \prime}}=5.5 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right.$ or $\left.\mathrm{H}-1^{\prime}\right), 7.306\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime}}=5.5 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right.$ or H-1'), 6.27-6.13 (2H, v br ol m, H-7' and H-9'), 4.147 (v br t, $J \sim 6.7 \mathrm{~Hz}, \mathrm{H}-10$ '), 4.086 (v br t, $J \sim 6.4$ Hz, H-6'), 3.739 ( $2 \mathrm{H}, \mathrm{s}, \mathrm{H}-2$ or H-10), 3.704 (2H, s, H-2 or H-10), 3.608 (4H, s, H-12), 3.222.96 (20H, ol m, H-4, H-5, H-7, H-8, H-2', and H-10'), 2.28 (ho m, H-12a'), 2.25 (ho m, H12b'), 2.029 (ho m but $\sim \mathrm{t}, J_{\mathrm{H} 5 \text { aax" }}=J_{\text {H5bax" }}=12.1 \mathrm{~Hz}, \mathrm{H}-6^{\prime \prime}$ ), 1.962 (ho m, H-11a'), 1.83-1.71
(5H), 1.67 ( 1 H, ho m), 1.539 ( 1 H , ho m), and 1.47-1.26 (7H) (H-11b', H-4aeq", H-4beq", H$5^{\prime \prime}, \mathrm{H}-5^{\prime}, \mathrm{H}-3^{\prime}, \mathrm{H}-3^{\prime \prime}$, and H-4'), 0.919 ( 2 H , ol m, H-4cax" and H-4axd").
${ }^{13} \mathrm{C}$ NMR (363 K): 174.43 (C-7"), 173.67 (C-15'), 173.27 (C-14'), 172.96 (C-13'), 170.73 (C13), 169.93 (br, C-11), 166.36 (br, C-1), 156.92 (C-8'), 55.00 (br, C-2 or C-10), 54.04 (C-2 or C-10), 53.76 (C-12), 52.12 (C-6'), 51.59 (C-10'), 51.17 (C-4 or C-5 or C-7 or C-8), 50.69 (C-4 or C-5 or C-7 or C-8), 49.61 (br, C-4 or C-5 or C-7 or C-8; 49.61 and 49.19 are C-4 and C-5 or C-7 and C-8), 49.19 (br, C-4 or C-5 or C-7 or C-8; 49.61 and 49.19 are C-4 and C-5 or C-7 and C-8), 44.61 (C-2"), 43.75 (C-6"), 37.88 (C-2'), 36.55 (C-3"), 31.56 (C-5'), 29.66 (C-12'), 29.32 ( $2 \times \mathrm{C}-4$ "), 28.46 (C-5a"), 28.35 (C-3' or C-5b"), 28.33 (C-3' or C-5b"), 27.35 (C-11'), 22.16 (C-4').
${ }^{1}$ H NMR Spectra


${ }^{13}$ C NMR Spectra




## Compound 26

${ }^{1} \mathrm{H}, 600 \mathrm{MHz}, 303 \mathrm{~K}$

$$
{ }^{13} \mathrm{C}+\text { DEPT, } 600 \mathrm{MHz}, 303 \mathrm{~K}
$$

No decomposition observed.

$\mathbf{R}=$ glutamate-urea-lysine binding motif and $\mathbf{R}^{\prime}=$ DOTA chelator

The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and 19 and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 303 K ): 8.413 (br t, $\left.J_{\mathrm{H} 2}=6.1 \mathrm{~Hz}, \mathrm{H}-11^{\prime \prime}\right), 7.634\left(\mathrm{t}, J_{\mathrm{H}^{\prime} / 9^{\prime \prime}}=5.9 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right.$ or H-8"), $7.630\left(\mathrm{t}, J_{\mathrm{H} 2^{\prime} / 9^{\prime \prime}}=5.5 \mathrm{~Hz}, \mathrm{H}-1^{\prime}\right.$ or H-8' $), 6.315\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right), 6.282\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.3 \mathrm{~Hz}\right.$, $\left.\mathrm{H}-7^{\prime}\right), 4.090\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H11a}^{\prime}}=8.3, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=5.2 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.027\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H5a}^{\prime}}=8.0, J_{\mathrm{H5b}}{ }^{\prime}=\right.$ $5.2 \mathrm{~Hz}, \mathrm{H}-6$ '), 4.03 ( v br s, H-2a or H-10a), 3.88 (v br s, H-2b or H-10b), H-2b, H-10b, H-12, and H-4 or H-5 or H-7 or H-8 overlapped with $\mathrm{H}_{2} \mathrm{O}, 3.12-3.03$ (5H, ol m, H-2' or H-2" or H$9^{\prime \prime}$ or H-4 or H-5 or H-7 or H-8), 3.01-2.94 (4H, H-2' or H-2" or H-9"), $2.857\left(\mathrm{t}, J_{\mathrm{H1}} / 88^{\prime \prime}=\right.$ $J_{\mathrm{H} 3^{\prime \prime} / 10^{\prime \prime}}=6.2 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}$ or $\mathrm{H}-9{ }^{\prime \prime}$ ), 2.25 (ho m, H-12a'), 2.25 (ho m, H-12b'), 2.037 (tt, $J_{\text {H5axa"/12aax" }}=J_{\text {H5bax"/12bax" }}=12.0, J_{\text {H5aeq"/12aeq" }}=J_{\text {H5beq"/12beq" }}=3.2 \mathrm{~Hz}, \mathrm{H}-6$ " or H-13"), 1.984 (tt,
$J_{\text {H5aax"/12aax" }}=J_{\text {H5bax"/12bax" }}=12.2, J_{\text {H5aeq"/12aeq" }}=J_{\text {H5beq"/12beq" }}=3.0 \mathrm{~Hz}, \mathrm{H}-6 "$ or H-13"), 1.914 (ho m, H-11a'), 1.76-1.65 (9H), 1.65-1.59 (1H, ho m), 1.53-1.46 (1H), and 1.40-1.21 (10H) (H-11b', H-11aeq", H-11beq", H-4aeq", H-4beq", H-12", H-5', H-5", H-3', H-10", H-3", and H4'), 0.92-0.79 (4H, ol m, H-11cax", H-11dax", H-4cax", and H-4dax").
${ }^{13} \mathrm{C}$ NMR (303 K): 175.15 (C-7" or C-14"), 175.09 (C-7" or C-14"), 174.55 (C-15'), 174.16 (C-14'), 173.77 (C-13'), 171.76 (br, C-13), 168.85 (br, C-11), 165.46 (br, C-1), 157.36 (C-8'), 54.94 (br, C-2 or C-10), 54.07 (br, C-2 or C-10), 52.68 (v br, C-12), 52.33 (C-6'), 51.72 (C$10^{\prime}$ ), 50.81 ( v br, C-4 or C-5 or C-7 or C-8), 50.65 (v br, C-4 or C-5 or C-7 or C-8), 48.48 (br, C-4 or C-5 or C-7 or C-8; 48.48 and 48.14 are C-4 and C-5 or C-7 and C-8), 48.14 (br, C-4 or C-5 or C-7 or C-8; 48.48 and 48.14 are C-4 and C-5 or C-7 and C-8), 45.14 (C-2" or C-9"), 44.55 (C-2" or C-9"), 44.17 (C-6" or C-13"), 44.04 (C-6" or C-13"), 38.19 (C-2'), 37.16 (C-3" or C-10"), 36.87 (C-3" or C-10"), 31.83 (C-5'), 29.94 (C-12'), 29.71 ( $2 \times, \mathrm{C}-4 \mathrm{a}^{\prime \prime}$ or C-4b" or C$11 \mathrm{a}^{\prime \prime}$ or C-11b"), 29.61 ( $2 \times$ C-4a" or C-4b" or C-11a" or C-11b"), 28.86 (C-3'), 28.85 ( $2 \times, \mathrm{C}-$ 5 a " or $\mathrm{C}-5 \mathrm{~b}^{\prime \prime}$ or $\mathrm{C}-12 \mathrm{a}$ " or $\mathrm{C}-12 \mathrm{~b}$ "), 28.83 ( $2 \times, \mathrm{C}-5 \mathrm{a}^{\prime \prime}$ or $\mathrm{C}-5 \mathrm{~b}^{\prime \prime}$ or $\mathrm{C}-12 \mathrm{a}^{\prime \prime}$ or $\mathrm{C}-12 \mathrm{~b}$ "), 27.57 (C-11'), 22.58 (C-4').
${ }^{1}$ H NMR Spectra



${ }^{13}$ C NMR Spectra




Compound 27
${ }^{1} \mathrm{H}, 400 \mathrm{MHz}, 303 \mathrm{~K}$
${ }^{13} \mathrm{C}+$ DEPT, $400 \mathrm{MHz}, 303 \mathrm{~K}$

No decomposition observed.


The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and $\mathbf{1 9}$ and/or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR (303 K): 8.433 (br t, $\left.J_{\mathrm{H} 2}=5.8 \mathrm{~Hz}, \mathrm{H}-1^{\prime \prime}\right), 7.65-7.58(3 \mathrm{H}$, ol m, H-1', H-8", and H$\left.1^{\prime \prime}\right), 6.317\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right), 6.282\left(\mathrm{~d}, J_{\mathrm{H} 6^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-7{ }^{\prime}\right), 4.094\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{{\mathrm{H} 1 \mathrm{a}^{\prime}}=8.3 \text {, }}\right.$ $\left.J_{\mathrm{H11b}}{ }^{\prime}=5.2 \mathrm{~Hz}, \mathrm{H}-10^{\prime}\right), 4.032\left(\mathrm{td}, J_{\mathrm{H} 7^{\prime}}=J_{\mathrm{H5a}}{ }^{\prime}=8.0, J_{\mathrm{H5b}}{ }^{\prime}=5.2 \mathrm{~Hz}, \mathrm{H}-6^{\prime}\right), 4.04(\mathrm{v}$ br s, H-2a or $\mathrm{H}-10 \mathrm{a}$ ), 3.89 (v br s, H-2b or H-10b), H-2b, H-10b, H-12, and H-4 or H-5 or H-7 or H-8 overlapped with $\mathrm{H}_{2} \mathrm{O}, 3.13-3.03\left(7 \mathrm{H}\right.$, ol m, $\mathrm{H}-2^{\prime}$ or $\mathrm{H}-2^{\prime \prime}$ or $\mathrm{H}-9{ }^{\prime \prime}$ or $\mathrm{H}-16^{\prime \prime}$ or $\mathrm{H}-4$ or $\mathrm{H}-5$ or $\mathrm{H}-$

7 or H-8), 3.01-2.94 (4H, H-2' or H-2" or H-9" or H-16"), 3.01-2.94 (4H, H-2' or H-2" or H9" or H-16"), 2.26 (ho m, H-12a'), 2.25 (ho m, H-12b'), 2.09-1.87 (4H, H-6", H-13", H-20", and H-11a'), 1.78-1.58 (14H), 1.55-1.45 (1H, ho m), and 1.42-1.21 (13H) (H-11b', H-11aeq", H-11beq", H-18aeq", H-18beq", H-4aeq", H-4beq", H-12", H-19", H-5', H-5", H-3', H-17", H10", H-3", and H-4'), 0.94-0.77 (4H, ol m, H-18cax", H-18dax", H-11cax", H-11dax", H4cax", and H-4dax").
${ }^{13} \mathrm{C}$ NMR (303 K): 174.97 (C-7" or C-14" or C-21"), 174.92 (C-7" or C-14" or C-21"), 174.87 (C-7" or C-14" or C-21"), 174.46 (C-15'), 174.08 (C-14'), 173.65 (C-13'), 171.72 (br, C-13), 168.84 (br, C-11), 165.46 (br, C-1), 157.24 (C-8'), 54.85 (br, C-2 or C-10), 54.00 (br, C-2 or C-10), 52.64 (v br, C-12), 52.24 (C-6'), 51.63 (C-10'), 50.76 (v br, C-4 or C-5 or C-7 or C-8), 50.60 (v br, C-4 or C-5 or C-7 or C-8), 48.39 (br, C-4 or C-5 or C-7 or C-8; 48.39 and 48.10 are C-4 and C-5 or C-7 and C-8), 48.10 (br, C-4 or C-5 or C-7 or C-8; 48.39 and 48.10 are C4 and C-5 or C-7 and C-8), 45.04 (C-2" or C-9" or C-16"), 44.45 ( $2 \times, \mathrm{C}-2^{\prime \prime}$ or C-9" or C-16"), 44.08 ( $2 \times, \mathrm{C}-6^{\prime \prime}$ or $\mathrm{C}-13^{\prime \prime}$ or $\mathrm{C}-20^{\prime \prime}$ ), 43.94 (C-6" or C-13" or C-20"), 38.10 (C-2'), 37.12 (C-3" or C-10" or C-17"), 37.10 (C-3" or C-10" or C-17"), 36.81 (C-3" or C-10" or C-17"), 31.78 (C$\left.5^{\prime}\right), 29.87$ (C-12'), 29.65 ( $4 \times, \mathrm{C}-4 \mathrm{a}^{\prime \prime}$ or C-4b" or C-11a" or C-11b" or C-18a" or C-18b"), 29.56 ( $2 \times$ C-4a" or C-4b" or C-11a" or C-11b" or C-18a" or C-18b"), $28.89\left(2 \times, \mathrm{C}-5 \mathrm{a}^{\prime \prime}\right.$ or C-5b" or C-12a" or C-12b" or C-19a" or C-19b"), 28.81 (C-3'), 28.77 ( $4 \times, \mathrm{C}-5 \mathrm{a}^{\prime \prime}$ or C-5b" or C-12a" or C-12b" or C-19a" or C-19b"), 27.52 (C-11'), 22.51 (C-4').
${ }^{1}$ H NMR Spectra




${ }^{13}$ C NMR Spectra




Compound 28
${ }^{1} \mathrm{H}, 600 \mathrm{MHz}, 303 \mathrm{~K}$

UDEFT + DEPT, $600 \mathrm{MHz}, 303 \mathrm{~K}$

No decomposition observed.


The compound was deemed to be fully consistent with its assigned structure by NMR in terms of proton count, carbon count, and carbon multiplicities. Partial or tentative assignments based on analogy to $\mathbf{1 2}, \mathbf{1 4}, \mathbf{1 7}$, and $19 \mathrm{and} /$ or by the use of incremental shift calculations.
${ }^{1} \mathrm{H}$ NMR ( 303 K ): 8.858 (br s, H-1"), $8.379\left(\mathrm{t}, J_{\mathrm{H} 2}=5.8 \mathrm{~Hz}, \mathrm{H}-1\right.$ '), 7.808 ( $2 \mathrm{H}, \mathrm{AA}^{\prime}$ part of $\mathrm{AA}^{\prime} \mathrm{MM}^{\prime}$ system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}}{ }^{\prime}=8.4 \mathrm{~Hz}, \mathrm{H}-55^{\prime \prime}\right), 7.649\left(\mathrm{t}, J_{\mathrm{H} 9}=5.7 \mathrm{~Hz}, \mathrm{H}-8{ }^{\prime \prime}\right), 7.354\left(2 \mathrm{H}, \mathrm{MM}^{\prime}\right.$ part of AA'MM' system, $\left.J_{\mathrm{AM}}+J_{\mathrm{AM}^{\prime}}=8.4 \mathrm{~Hz}, \mathrm{H}-4^{\prime \prime}\right), 6.313\left(\mathrm{~d}, J_{\mathrm{H} 10^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-9^{\prime}\right), 6.280(\mathrm{~d}$, $\left.J_{\mathrm{H} 6^{\prime}}=8.3 \mathrm{~Hz}, \mathrm{H}-7^{\prime}\right), 4.376\left(2 \mathrm{H}, \mathrm{d}, J_{\mathrm{HI}}=5.8 \mathrm{~Hz}, \mathrm{H}-2^{\prime \prime}\right), 4.089\left(\mathrm{td}, J_{\mathrm{H} 9^{\prime}}=J_{\mathrm{H} 11 \mathrm{a}^{\prime}}=8.3, J_{\mathrm{H} 11 \mathrm{~b}^{\prime}}=\right.$
 10), $3.63(2 \mathrm{H}$, v br s, $\mathrm{H}-2$ or $\mathrm{H}-10), \mathrm{H}-12$ and $\mathrm{H}-4$ or $\mathrm{H}-5$ or $\mathrm{H}-7$ or $\mathrm{H}-8$ overlapped with $\mathrm{H}_{2} \mathrm{O}$, 3.12-3.04 (9H, ol m, H-2' or H-9" or H-4 or H-5 or H-7 or H-8), 3.02-2.94 (2H, H-2' or H$9^{\prime \prime}$ ), 2.92-2.85 (1H, v br m, H-2' or H-9'), 2.25 (ho m, H-12a'), 2.25 (ho m, H-12b'), 2.016 (tt, $\left.J_{\mathrm{H} 12 \text { aax }}=J_{\mathrm{H} 12 \mathrm{bax}}=12.0, J_{\mathrm{H} 12 \text { aeq" }}=J_{\mathrm{H} 12 \mathrm{beq}}{ }^{\prime \prime}=3.3 \mathrm{~Hz}, \mathrm{H}-13^{\prime \prime}\right), 1.913($ ho m, H-11a'), 1.79-1.67 $(5 \mathrm{H}), 1.66-1.59(1 \mathrm{H}$, ho m$), 1.53-1.45(2 \mathrm{H})$, and $1.40-1.21(6 \mathrm{H})(\mathrm{H}-11 \mathrm{~b}, \mathrm{H}-11 \mathrm{aeq}$ ", $\mathrm{H}-$ 11beq", H-12", H-5', H-3', H-10", and H-4'), $0.915\left(\sim \mathrm{qt}, J_{\mathrm{H} 11 a / b e q " ~}=J_{\mathrm{H} 12 \mathrm{a}-\mathrm{dax}}=J_{\mathrm{H} 10^{\prime \prime}}=12.8 \mathrm{~Hz}\right.$, H-11cax" or H-11dax" $), 0.909\left(\sim \mathrm{qt}, J_{\mathrm{H} 11 \text { a/beq" }}=J_{\mathrm{H} 12 \mathrm{a}-\mathrm{dax}}=J_{\mathrm{H} 10^{\prime \prime}}=12.8 \mathrm{~Hz}, \mathrm{H}-11 \mathrm{cax} "\right.$ or H11dax").
${ }^{13} \mathrm{C}$ NMR (303 K): 175.00 (C-14"), 174.51 (C-15'), 174.13 (C-14'), 173.72 (C-13'), 171.47 (br, C-13), C-11 and C-1 not observed, 166.01 (C-7"), 157.30 (C-8'), 141.61 (C-3"), 133.48 (C$6^{\prime \prime}$ ), 127.35 (C-5"), 127.14 (C-4"), 54.88 (br, C-2 or C-10), 54.05 (br, C-2 or C-10), 53.25 (v br, C-12), 52.28 (C-6'), 51.68 (C-10'), 50.67 (v br, C-4 or C-5 or C-7 or C-8), 50.49 (v br, C-4 or C-5 or C-7 or C-8), 49.01 (v br, C-4 and C-5 or C-7 and C-8), 45.40 (C-9"), 44.14 (C-13"), 42.02 (C-2"), 38.16 (C-2'), 37.13 (C-10"), 31.82 (C-5'), 29.90 (C-12' or C-11a" or C-11b"), $29.86\left(2 \times, \mathrm{C}-12{ }^{\prime}\right.$ or $\mathrm{C}-11 \mathrm{a}^{\prime \prime}$ or $\left.\mathrm{C}-11 \mathrm{~b}^{\prime \prime}\right), 28.85\left(\mathrm{C}-3^{\prime}\right.$ or $\mathrm{C}-12 \mathrm{a}^{\prime \prime}$ or $\left.\mathrm{C}-12 \mathrm{~b}^{\prime \prime}\right), 28.84\left(2 \times, \mathrm{C}-3^{\prime}\right.$ or C-12a" or C-12b"), 27.55 (C-11'), 22.55 (C-4').
${ }^{1}$ H NMR Spectra






${ }^{13}$ C NMR Spectra





Figure 1. Whole-body coronal slices ( 0.8 mm ) derived from $\mu \mathrm{PET}$ imaging of an athymic BALB/c nu/nu mouse with LNCaP tumor (right trunk). Scans were evaluated for 20, 40, 60 and 120 min post-injection with 0.5 nmol of ${ }^{68} \mathrm{Ga}$-labeled $\mathbf{1 1}, \mathbf{1 2}, \mathbf{1 3}, \mathbf{1 4}, 15$ and 16.







Figure 2. Whole-body coronal slices $(0.8 \mathrm{~mm})$ derived from $\mu \mathrm{PET}$ imaging of an athymic $\mathrm{BALB} / \mathrm{c}$ nu/nu mouse with LNCaP tumor (right trunk). Scans were evaluated for $20,40,60$ and 120 min post-injection with 0.5 nmol of ${ }^{68}$ Ga-labeled 17, 18, 19, 20.


Figure 3. Whole-body coronal slices ( 0.8 mm ) derived from $\mu$ PET imaging of an athymic BALB/c nu/nu mouse with LNCaP tumor (right trunk). Scans were evaluated for $20,40,60$ and 120 min post-injection with 0.5 nmol of ${ }^{68}$ Ga-labeled 21, 22 and 23.


Figure 4. Whole-body coronal slices ( 0.8 mm ) derived from $\mu \mathrm{PET}$ imaging of an athymic BALB/c nu/nu mouse with LNCaP tumor (right trunk). Scans were evaluated for $20,40,60$ and 120 min post-injection with 0.5 nmol of ${ }^{68}$ Ga-labeled 25, 26, 27 and 28.


Figure 5. Time-activity curves for tumor and background and for kidneys up to 1 h post injection of 0.5 nmol of ${ }^{68} \mathrm{Ga}$-labeled 11, 12, 13, 14, $\mathbf{1 5}$ and 16. Data are expressed as mean standardized uptake value (SUV).



Figure 6. Time-activity curves for tumor and background and for kidneys up to 1 h post injection of 0.5 nmol of
${ }^{68}$ Ga-labeled 17, 18, 19, 20. Data are expressed as mean standardized uptake value (SUV).



Figure 7. Time-activity curves for tumor and background and for kidneys up to 1 h post injection of 0.5 nmol of ${ }^{68} \mathrm{Ga}$-labeled 21, 22 and 23. Data are expressed as mean standardized uptake value (SUV).


Figure 8. Time-activity curves for tumor and background and for relevant kidneys up to 1 h post injection of 0.5 nmol of ${ }^{68} \mathrm{Ga}$-labeled 25, 26, 27 and 28. Data are expressed as mean standardized uptake value (SUV).



