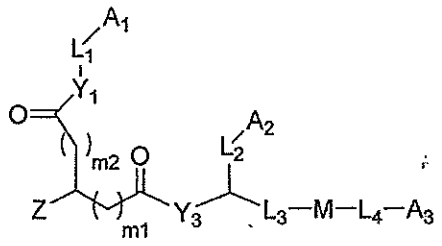
Claims

1. Compounds of formula I,



I

wherein

Z is a pteroate or derivative thereof,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR′, NHR′, CO_2R' or NO_2, wherein R′ represents H or C(1-8)alkyl,

L_2 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR′, NHR′, or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR′-,-NR′-CO-,-CO-NR′, wherein R′ represents H or C(1-8)alkyl,

L_3 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR′, NHR′, CO_2R' or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR′-,-NR′-CO-,-CO-NR′-,-NR′-CO-O-,-O-CO-NR′-,-NR′-CO-NR′-,-CH=CH-,-C≡C-,-O-CO-O-,

-S-R'-, -SO_3R'-, and a five-membered azaheterocycle, wherein R' represents H or C(1-8)alkyl,

Y_1,Y_3 are independently of each other O, N or S,

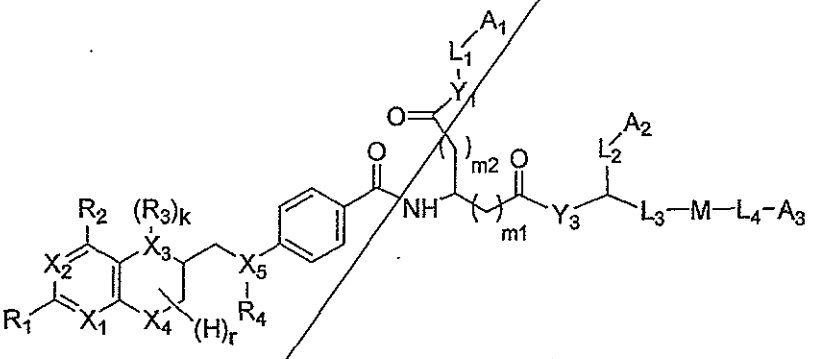
A_1,A_2,A_3 are independently of each other H, a capping group, or an albumin binder,

M is a radionuclide-based therapeutic or diagnostic moiety,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

with the proviso that at least one, preferably one, of A_1, A_2 and A_3 is an albumin binder.

2. Compound according to claim 1 having formula II



II

wherein

X_1 to X_5 are independently of each other C, N or O, preferably N or O,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR_5, -COR_5, -$COOR_5$, -NHR_5, -$CONHR_5$, -$CONHR_5$, wherein R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR', wherein R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR', wherein R' represents H or C(1-8)alkyl,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, wherein R' represents H or C(1-8)alkyl,

L_2 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

L_3 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, $-SO_3R'-$, and a five-membered azaheterocycle, wherein R' represents H or C(1-8)alkyl,

Y_1, Y_3 are independently of each other O, N or S,

A_1, A_2, A_3 are independently of each other H, a capping group, or an albumin binder,

M is a radionuclide-based therapeutic or diagnostic moiety, preferably an imaging moiety M_1 or M_2, wherein M_1 is a chelated metal radionuclide, and M_2 is a gamma- or positron-emitting non-metal radionuclide optionally in combination with a prosthetic group,

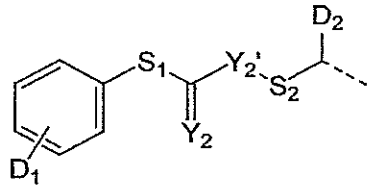
m_1, m_2 are independently of each other 0, 1, 2 or 3,

k is 0 or 1,

r has a value of 1 to 7.

with the proviso that at least one, preferably one, of A_1, A_2 and A_3 is an albumin binder.

3. Compound according to claims 1 or 2 wherein the albumin binder is a linear or branched lipophilic group having 12-40 carbon atoms and a distal acidic group, such as a compound of formula III



III

wherein

$Y_2, Y_{2'}$ are independently of each other N, O or S,

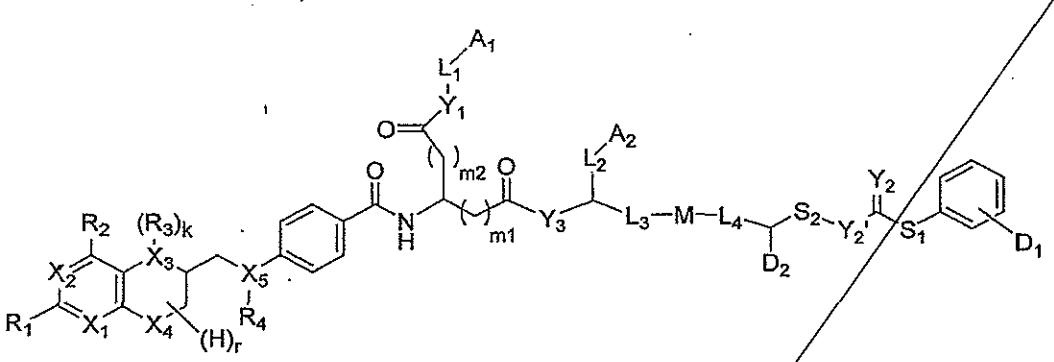
S_1, S_2 are independently of each other a single bond or a spacer selected from a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, $-SO_3R'$-, wherein R' represents H or C(1-8)alkyl,

D_1 is a group selected from H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

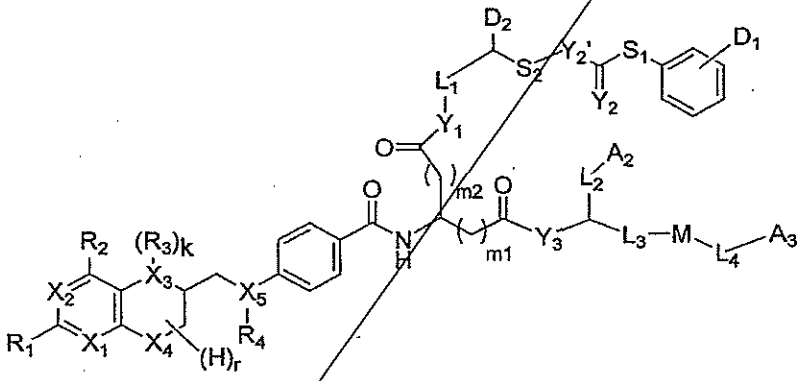
D_2 is an acidic group,

and the broken line represents the linkage to L_1, L_2 or L_4.

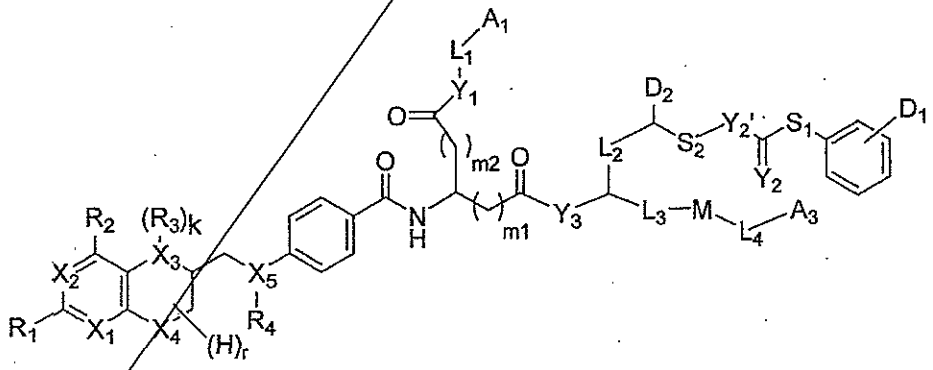
4. A compound according to any preceding claim, having formula IVa, IVb and IVc



IVa



IVb



IVc

wherein

X_1 to X_5 are independently of each other C, N or O, preferably N or O,

Y_1, Y_3 are independently of each other N, O or S,

$Y_2, Y_{2'}$ are independently of each other N, O or S,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR', wherein R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR', wherein R' represents H or C(1-8)alkyl,

A_1 is H or a capping group,

A_2 is H or a capping group,

A_3 is H or a capping group,

M is a radionuclide-based therapeutic or diagnostic moiety, preferably an imaging moiety M_1 or M_2, wherein M_1 is a chelated metal radionuclide, and M_2 is a gamma- or positron-emitting non-metal radionuclide optionally in combination with a prosthetic group,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, wherein R' represents H or C(1-8)alkyl,

L_2 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may indépendently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

L_3 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or

substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-,-S-R'-, $-SO_3R'-$, and a five-membered azaheterocycle, wherein R' represents H or C(1-8)alkyl,

S_1, S_2 are independently of each other a single bond or a spacer selected from a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, $-SO_3R'-$, wherein R' represents H or C(1-8)alkyl,

D_1 is a group selected from H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

D_2 is an acidic group,

k is 0 or 1,

r has a value of 1 to 7.

5. A compound according to claim 4, wherein the acidic group is a group capable of ionizing to donate a hydrogen ion to a base to form a salt, preferably selected from the group consisting of $-COOH$, $-SO_3H$, $-SO_2H$, $-NR'SO_3H$, $-P(O)(OH)_2$, wherein R' represents H or C(1-8)alkyl.

6. A compound according to claim.., wherein S_1 and S_2 are independently of each other a single bond or a spacer

selected from a straight-chain or branched C(1-8)alkyl, wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -COO-, -NR'-, -NR'-CO-, -CO-NR'-, -CH=CH-, wherein R' represents H or C(1-8)alkyl.

7. A compound according to any preceding claim, wherein m_1 is 2 and m_2 is 0 or wherein m_1 is 0 and m_2 is 2.

8. A compound according to any preceding claim, wherein M is a radionuclide-based therapeutic or diagnostic moiety M_1 or M_2, wherein M_1 is a chelated metal radionuclide, and M_2 is a gamma- or positron-emitting non-metal radionuclide optionally in combination with a prosthetic group.

9. A compound according to any preceding claim, with the proviso that when A_2 is an albumin binder, M is a chelated metal radionuclide M_1.

10. A compound according to any preceding claim, wherein the imaging moiety M is a chelated metal radionuclide M_1 comprising a metal radionuclide and a metal chelator.

11. A compound according to claim 9, wherein the metal radionuclide is selected from ^{99}Tc, ^{51}Cr, ^{67}Ga, ^{68}Ga, ^{47}Sc, ^{51}Cr, ^{167}Tm, ^{141}Ce, ^{111}In, ^{168}Yb, ^{175}Yb, ^{140}La, ^{90}Y, ^{88}Y, ^{153}Sm, ^{166}Ho, ^{165}Dy, ^{166}Dy, ^{62}Cu, ^{64}Cu, ^{67}Cu, ^{97}Ru, ^{103}Ru, ^{186}Re, ^{188}Re, ^{203}Pb, ^{211}Bi, ^{212}Bi, ^{213}Bi, ^{214}Bi, ^{105}Rh, ^{109}Pd, ^{117}mSn, ^{149}Pm, ^{161}Tb, ^{177}Lu, ^{198}Au and ^{199}Au.

12. A compound according to claim 9, wherein the metal

chelator is selected from a bidentate, tridentate, or tetradentate, linear, tripodal or macrocyclic ligand, preferably a linear or macrocyclic polyaminocarboxylate chelator, such as DTPA, DOTA, DO3A, HP-DO3A, EDTA, TETA, EHPG, HBED, NOTA, DOTMA, TETMA, PDTA, TTHA, LICAM, MECAM, more preferably a macrocyclic polyaminocarboxylate.

13. A compound according to any preceding claim, wherein the imaging moiety M is a gamma- or positron-emitting non-metal radionuclide M_2 selected from ^{11}C, ^{13}N, ^{15}O, ^{17}F, ^{18}F, ^{75}Br, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I, ^{131}I, optionally in combination with a prosthetic group.

14. Compound according to any preceding claim, wherein L_1 is a covalent bond or straight-chain or branched C(1-6)alkyl.

15. Compound according to any one of claims 4 to 14, wherein L_2 is a covalent bond or straight-chain or branched C(1-6)alkyl.

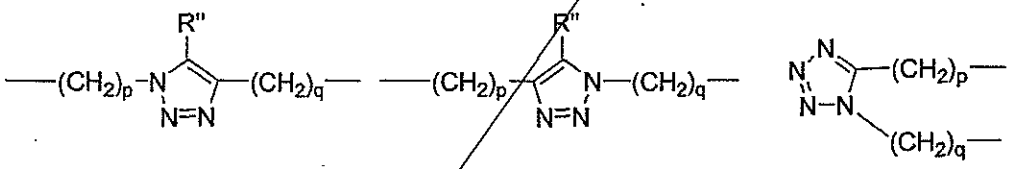
16. Compound according to any one of claims 3 to 14, wherein Y_2 is O and/or $Y_{2'}$ is N.

17. Compound according to any preceding claim, wherein Y_1 is O or N and/or Y_3 is N.

18. Compound according to any preceding claim, wherein L_3 is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a

group selected from -O-, -CO-, -CO-O-,-NR'-,-NR'-CO-, and a five-membered azaheterocycle selected from a triazolyl or tetrazolyl group wherein R' represents H or C(1-8)alkyl.

19. A compound according to any preceding claim, wherein L_3 is a group $L_{3'}$, which is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-NR'-,-NR'-CO-, or L_3 is a group of formulae (a), (b), or (c)

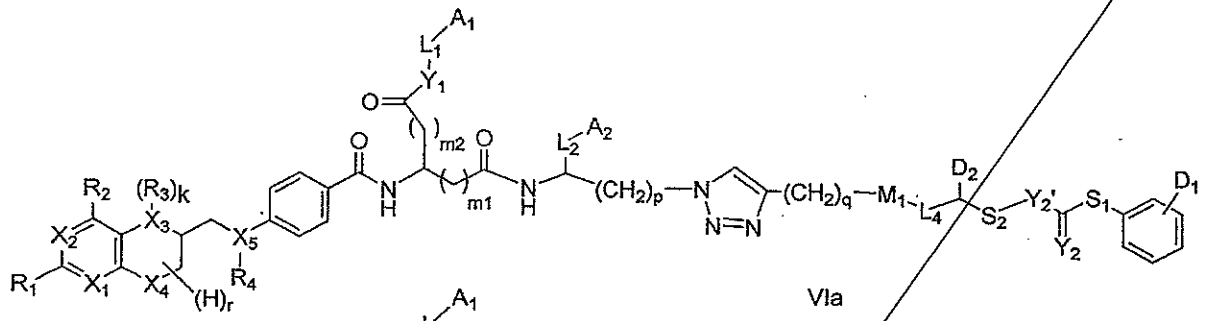


wherein

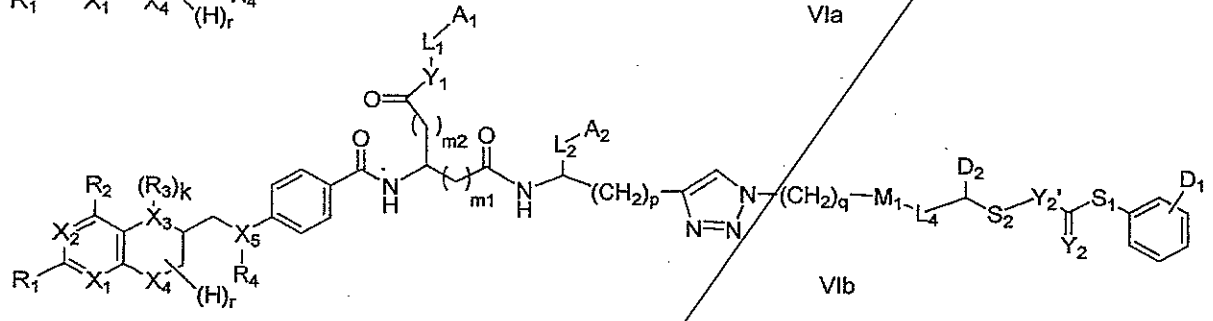
R'' is H or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2,

p,q are independently of each other 0, 1, 2, 3, 4, 5 or 6.

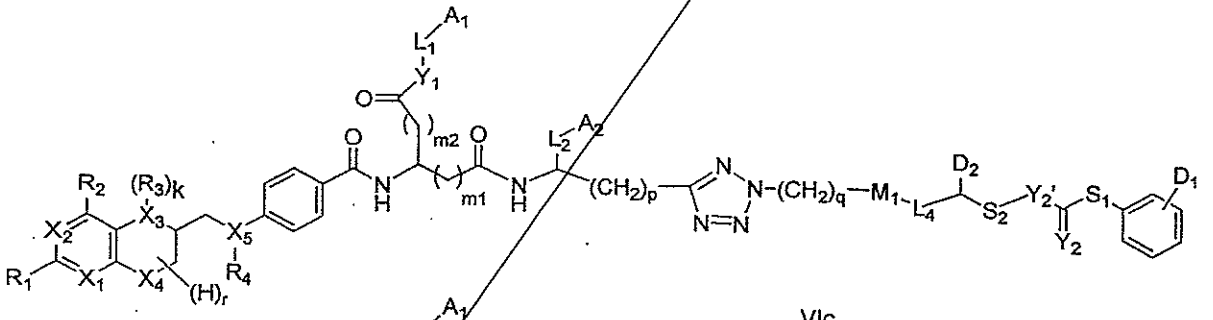
20. A compound according to any preceding claim having formulae VI a-e



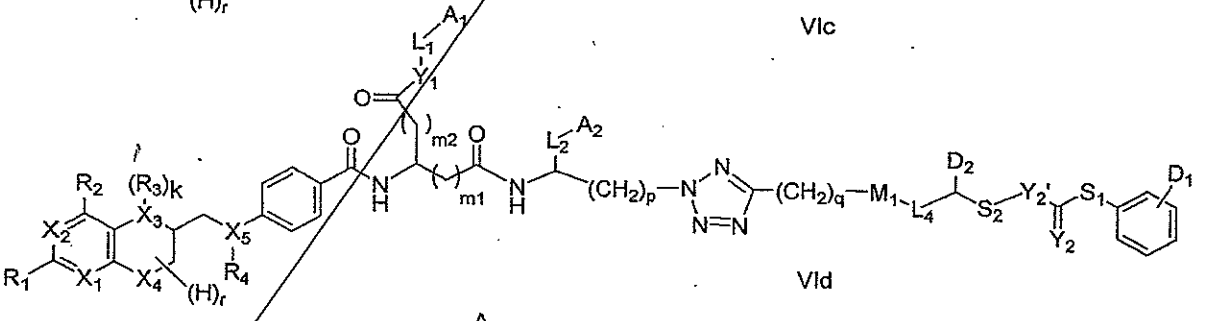
VIa



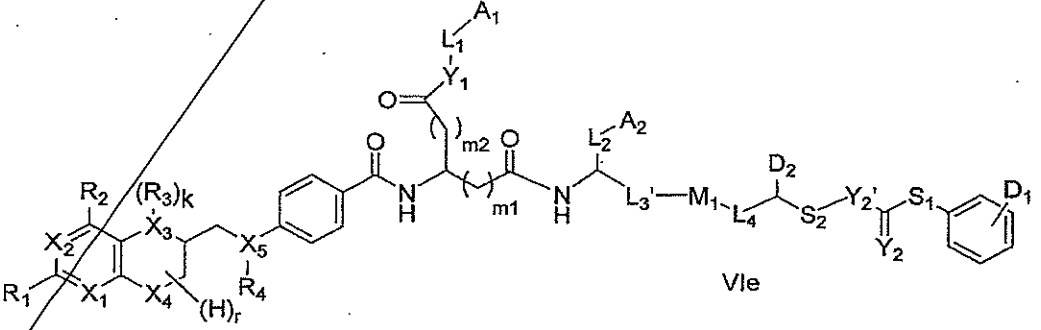
VIb



VIc



VId



VIe

wherein

X_1 to X_5 are independently of each other C, N or O, preferably N or O,

$Y_1, Y_2, Y_{2'}$ are independently of each other N, O or S,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR', wherein R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR', wherein R' represents H or C(1-8)alkyl,

R_5 is H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

A_1 is H or a capping group,

A_2 is H or a capping group,

M_1 is a linear or macrocyclic polyaminocarboxylate, such as DTPA, DOTA, DO3A, HP-DO3A, EDTA, TETA, NOTA, DOTMA, complexed with a radioimaging metal ion,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, wherein R' represents H or C(1-8)alkyl,

L_2 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

S_1, S_2 are independently of each other a single bond or a spacer selected from a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN,

Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C□C-,-O-CO-O-, -S-R'-, $-SO_3R'-$, wherein R' represents H or C(1-8)alkyl

D_1 is a group selected from H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

D_2 is an acidic group,

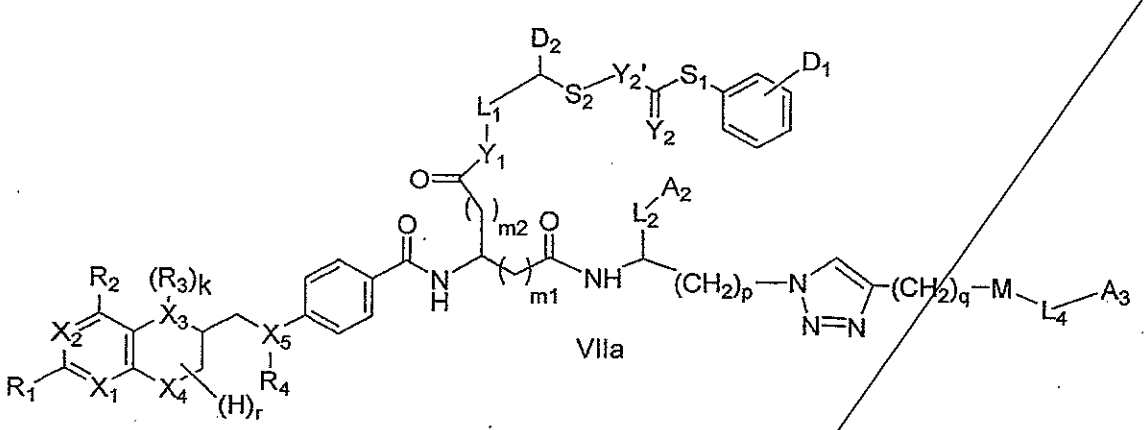
$L_{3'}$ is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-NR'-,-NR'-CO-, wherein R' represents H or C(1-8)alkyl,

p,q are independently of each other 0, 1, 2, 3, 4, 5 or 6,

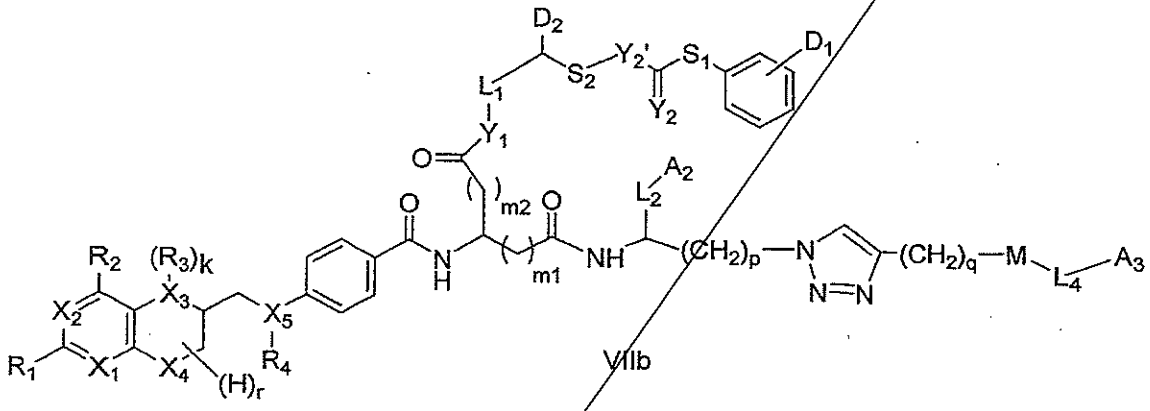
k is 0 or 1,

r has a value of 1 to 7.

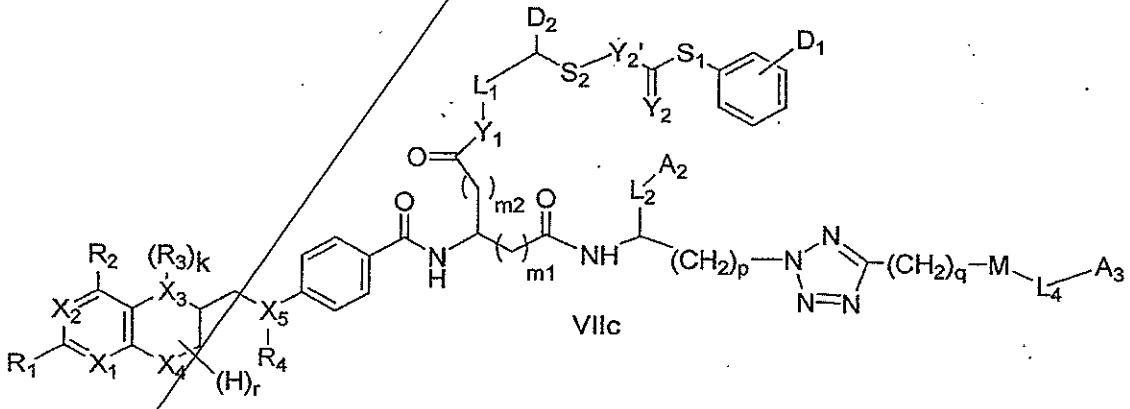
21. A compound according to any preceding claim having formulae VII a-e



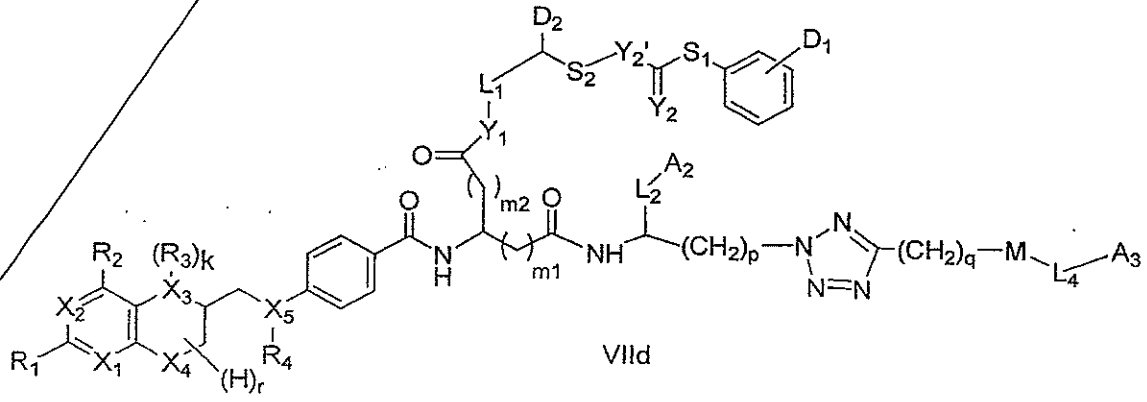
VIIa



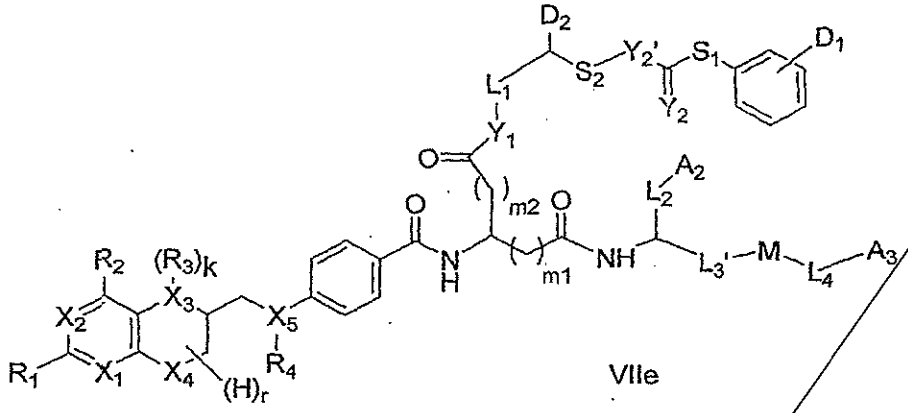
VIIb



VIIc



VIId



VIIe

wherein

X_1 to X_5 are independently of each other C, N or O, preferably N or O,

Y_1, Y_2, Y_2' are independently of each other N, O or S,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR', wherein R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR', wherein R' represents H or C(1-8)alkyl,

A_2 is H or a capping group,

A_3 is H or a capping group,

M is an imaging moiety M_1 or M_2, wherein M_1 is a chelated metal radionuclide selected from a linear or macrocyclic polyaminocarboxylate, such as DTPA, DOTA, DO3A, HP-DO3A, EDTA, TETA, NOTA, DOTMA, complexed with a metal radionuclide ion, and wherein M_2 is a gamma- or positron-emitting non-metal radionuclide, preferably selected from ^{11}C, ^{13}N, ^{15}O, ^{17}F, ^{18}F, ^{75}Br, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I, ^{131}I optionally in combination with a prosthetic group,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, wherein R' represents H or C(1-8)alkyl,

L_2 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

S_1, S_2 are independently of each other a single bond or a spacer selected from a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, $-SO_3R'-$, wherein R' represents H or C(1-8)alkyl,

D_1 is a group selected from H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

D_2 is an acidic group,

L_3, is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a

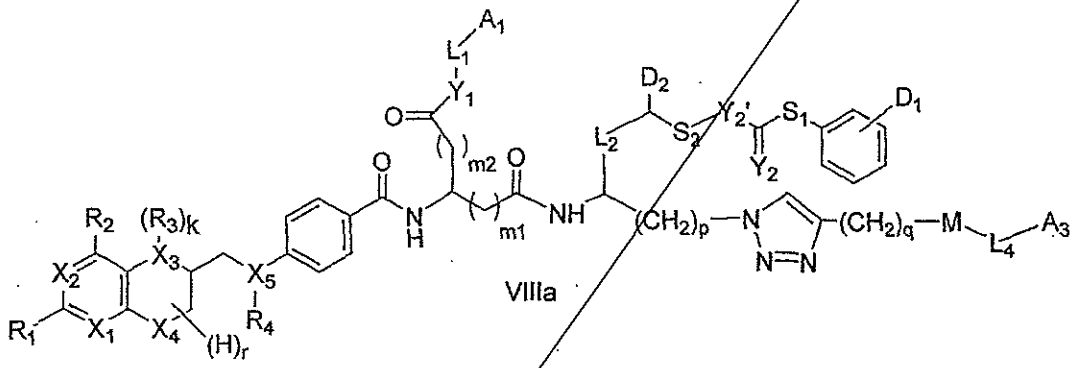
group selected from -O-, -CO-, -CO-O-,-NR'-,-NR'-CO-, wherein R' represents H or C(1-8)alkyl,

p,q are independently of each other 0, 1, 2, 3, 4, 5 or 6,

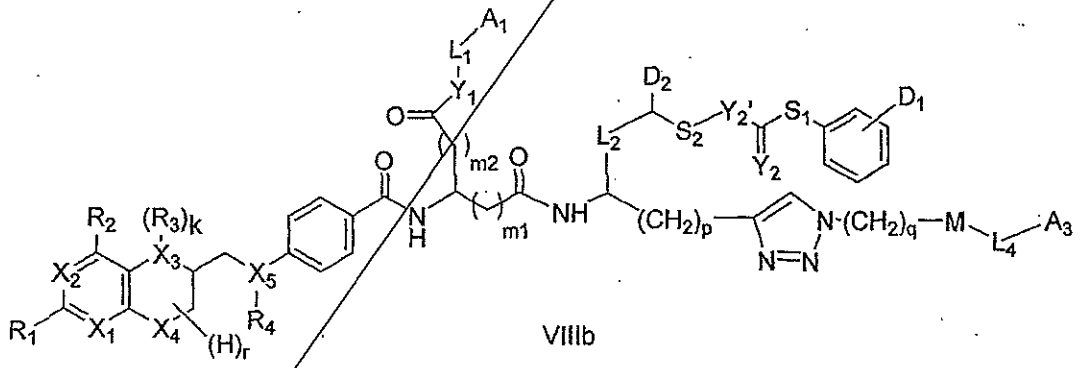
k is 0 or 1,

r has a value of 1 to 7.

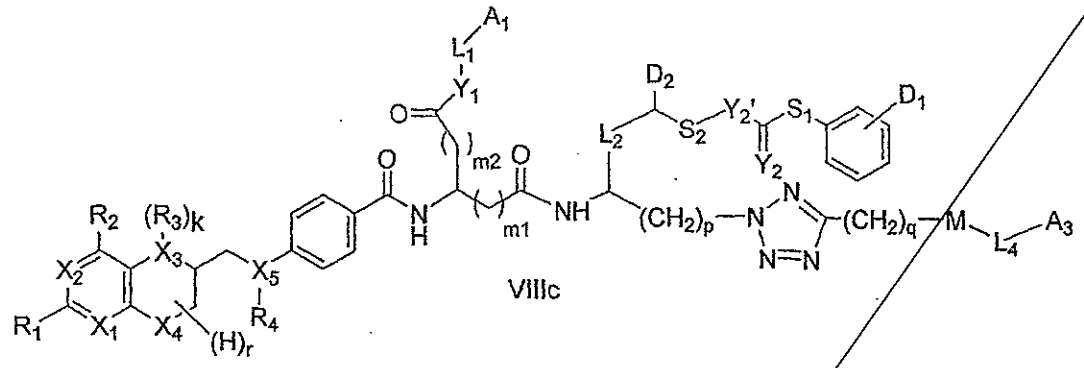
22. A compound according to any preceding claim having formulae VIII a-e



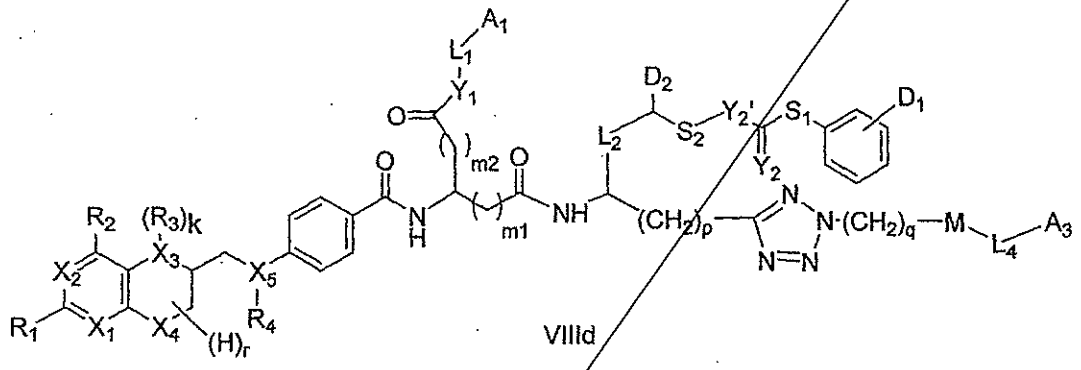
VIIIa



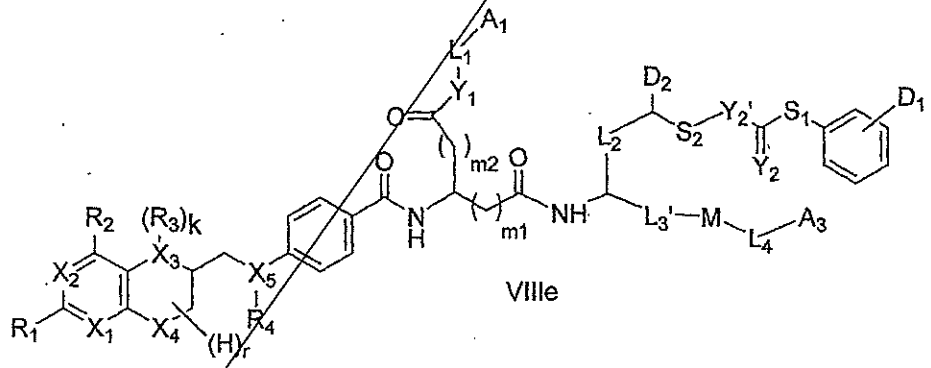
VIIIb



VIIIc



VIIId



VIIIe

wherein

X_1 to X_5 are independently of each other C, N or O, preferably N or O,

$Y_1, Y_2, Y_{2'}$ are independently of each other N, O or S,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR', wherein R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR', wherein R' represents H or C(1-8)alkyl,

A_1 is H or a capping group,

A_3 is H or a capping group,

M is an imaging moiety M_1 or M_2, wherein M_1 is a chelated metal radionuclide selected from a linear or macrocyclic polyaminocarboxylate, such as DTPA, DOTA, DO3A, HP-DO3A, EDTA, TETA, NOTA, DOTMA, complexed with a radioimaging metal ion, and wherein M_2 is a gamma- or positron-emitting non-metal radionuclide, preferably selected from ^{11}C, ^{13}N, ^{15}O, ^{17}F, ^{18}F, ^{75}Br, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I, ^{131}I, optionally in combination with a prosthetic group,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, wherein R' represents H or C(1-8)alkyl,

L_2 is a covalent bond or a linking group, such as straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

S_1, S_2 are independently of each other a single bond or a spacer selected from a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2,

and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, $-SO_3R'-$, wherein R' represents H or C(1-8)alkyl,

D_1 is a group selected from H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, wherein R_5 represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

D_2 is an acidic group,

$L_{3'}$ is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-, -CO-O-,-NR'-,-NR'-CO-, wherein R' represents H or C(1-8)alkyl,

p,q are independently of each other 0, 1, 2, 3, 4, 5 or 6,

k is 0 or 1,

r has a value of 1 to 7.

23. A compound according to any one of claims 2 to 22, wherein R_3 is H, C(1-12)alkyl, or -CO-C(1-8)alkyl.

24. A compound according to any one of claims 2 to 23, wherein R_4 is H, nitroso, -O-C(1-8)alkyl, or -CO-C(1-8)alkyl.

25. A compound according to any one of claims 2 to 24, wherein R_1 and R_2 are independently of each other H, C(1-12)alkyl, $-OR_5$, $-NHR_5$, wherein R_5 is H, C(1-12)alkyl,

C(2-12)alkenyl, or C(2-12)alkynyl.

26. Pharmaceutical composition comprising at least one compound according to any preceding claim.

27. Use of a compound according to any one of claims 1 to 25 for diagnostic imaging of a cell or population of cells expressing a folate-receptor in vitro or in vivo.

28. Use of a compound according to any one of claims 1 to 25 for convenient and effective administration to a subject in need for diagnostic imaging.

29. Method for diagnostic imaging of a cell or population of cells expressing a folate-receptor, said method comprising the steps of administering at least one compound according to any one of claims 1 to 25 in a diagnostic imaging amount, and obtaining a diagnostic image of said cell or population of cells.

30. Method according to claim 29, wherein the diagnostic imaging is performed of a cell or population of cells expressing a folate-receptor in vitro or in vivo.

31. Method for in vitro detection of a cell expressing the folate receptor in a tissue sample which includes contacting said tissue sample with a compound according to any one of claims 1 to 25 in effective amounts and for sufficient time and conditions to allow binding to occur and detecting such binding by PET imaging.

32. Method of diagnostic imaging or monitoring a subject comprising the steps of (i) administering at least one

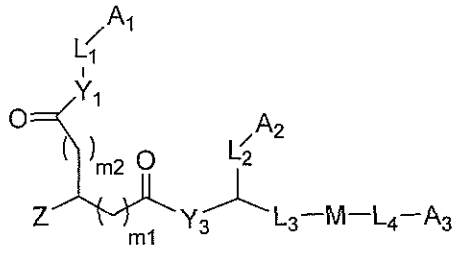
compound according to any one of claims 1 to 25 in a diagnostic imaging amount, and (ii) performing diagnostic imaging using PET by detecting a signal from said at least one compound.

33. Method of monitoring cancer therapy in a subject comprising the steps of (i) administering to a subject in need thereof at least one compound according to any one of claims 1 to 25 in a diagnostic imaging amount in combination with a therapeutically active, and (ii) performing diagnostic imaging using PET by detecting a signal from said at least one compound to follow the course of cancer therapy.

34. Method of claims 32 or 33 used in combination with any other methods of cancer diagnosis or therapy.

Claims

1. A compound of formula I,



I

wherein

Z is a pteroate or derivative thereof,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2,

R' represents H or C(1-8)alkyl,

L_2 is a covalent bond or a linking group, which is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-, or -CO-NR',

L_3 is a covalent bond or a linking group, which is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by a group selected from -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, $-SO_3R'-$, and a five-membered azaheterocycle,

Y_1, Y_3 are independently of each other O, N or S,

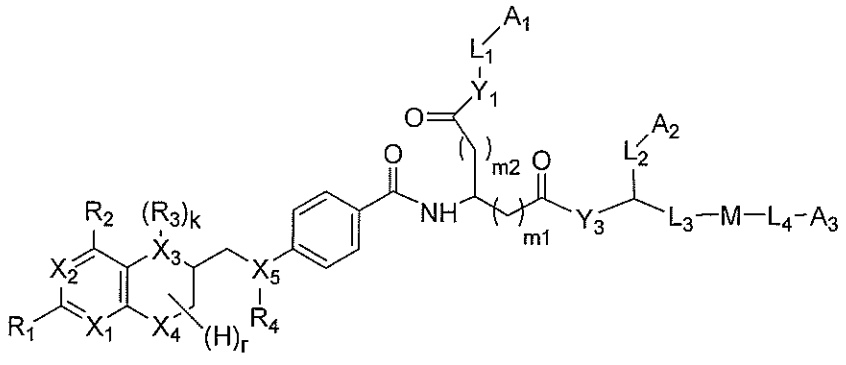
A_1, A_2, A_3 are independently of each other H, a capping group, or an albumin binder,

M is a radionuclide-based therapeutic or diagnostic moiety,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

with the proviso that at least one, of A_1, A_2 and A_3 is an albumin binder.

2. The compound according to claim 1 having formula II



II

wherein

X_1 to X_5 are independently of each other C, N or O,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, $-CONHR_5$,

R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR',

R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR',

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal,

OR′, NHR′, CO_2R' or NO_2,

L_2 is a covalent bond or a linking group, which is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR′, NHR′, or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR′-,-NR′-CO-, or -CO-NR′,

L_3 is a covalent bond or a linking group, which is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR′, NHR′, CO_2R' or NO_2, and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by a group selected from the group consisting of -O-, -CO-, -CO-O-,-O-CO-,-NR′-,-NR′-CO-,-CO-NR′-,-NR′-CO-O-,-O-CO-NR′-,-NR′-CO-NR′-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R′-, $-SO_3R'-$, and a five-membered azaheterocycle, wherein R′ represents H or C(1-8)alkyl,

Y_1, Y_3 are independently of each other O, N or S,

A_1, A_2, A_3 are independently of each other H, a capping group, or an albumin binder,

M is a radionuclide-based therapeutic or diagnostic moiety,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

k is 0 or 1,

r has a value of 1 to 7.

with the proviso that at least one of A_1, A_2 and A_3 is an albumin binder.

3. The compound according to claim 2, wherein R_3 is H, C(1-12)alkyl, or -CO-C(1-8)alkyl.

4. The compound according to claim 2, wherein R_4 is H, nitroso, -O-C(1-8)alkyl, or -CO-C(1-8)alkyl.

5. The compound according to claim 2, wherein R_1 and R_2 are independently of each other H, C(1-12)alkyl, $-OR_5$, $-NHR_5$, wherein R_5 is H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl.

6. The compound according to claim 2,

wherein

X_1 to X_5 are independently of each other N or O,

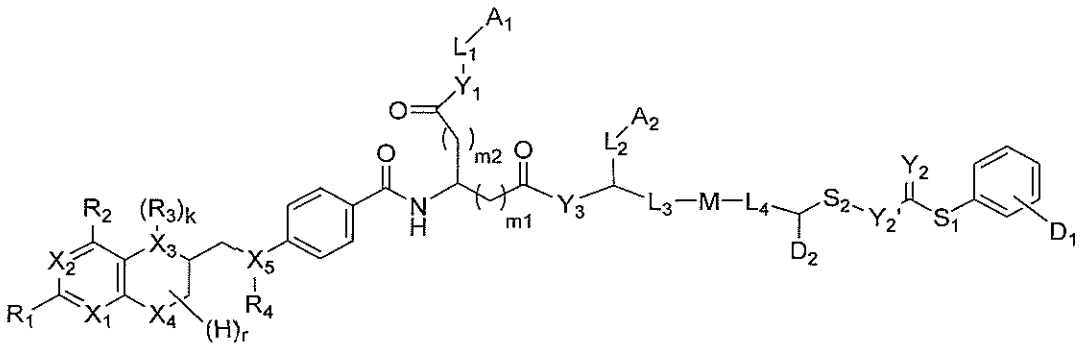
M is a imaging moiety M_1 or M_2,

M_1 is a chelated metal radionuclide, and

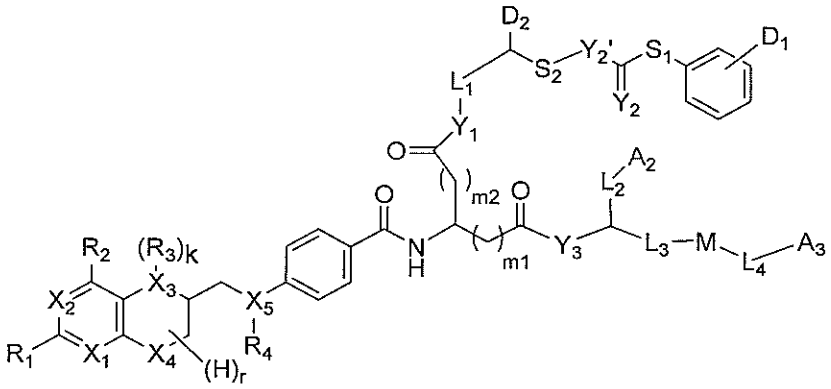
M_2 is a gamma- or positron-emitting non-metal radionuclide optionally in combination with a prosthetic group.

7. The compound according to claim 1 wherein the albumin binder is a linear or branched lipophilic group having 12-40 carbon atoms and a distal acidic group.

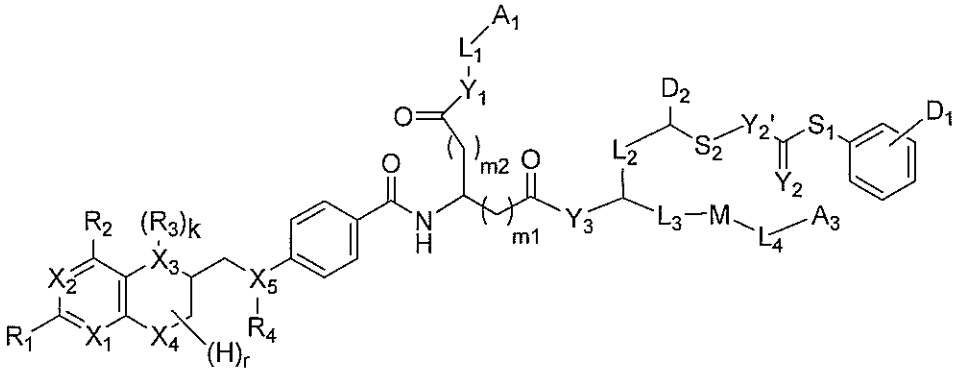
8. The compound according to claim 1, having formula IVa, IVb and IVc



IVa



IVb



IVc

wherein

X_1 to X_5 are independently of each other C, N or O,

Y_1,Y_3 are independently of each other N, O or S,

Y_2,$Y_{2'}$ are independently of each other N, O or S,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$,

R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR',

R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR',

A_1 is H or a capping group,

A_2 is H or a capping group,

A_3 is H or a capping group,

M is a radionuclide-based therapeutic or diagnostic moiety,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2,

L_2 is a covalent bond or a linking group, which is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR',

L_3 is a covalent bond or a linking group, which is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2, and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by a group selected from the group consisting of -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, $-SO_3R'-$, and a five-membered azaheterocycle,

S_1, S_2 are independently of each other a single bond or a spacer which is straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-

NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, -SO_3R'-,

D_1 is H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR_{5*}, -COR_{5*}, -$COOR_{5*}$, -NHR_{5*}, or -$CONHR_{5*}$,

R_{5*} represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

D_2 is an acidic group,

k is 0 or 1,

r has a value of 1 to 7.

9. A compound according to claim 8, wherein the acidic group is a group capable of ionizing to donate a hydrogen ion to a base to form a salt, which is —COOH, —SO_3H, —SO_2H, —NR'SO_3H, —P(O)$(OH)_2$, wherein R' represents H or C(1-8)alkyl.

10. The compound according to claim 8, wherein L_2 is a covalent bond or straight-chain or branched C(1-6)alkyl.

11. The compound according to claim 8,

wherein

X_1 to X_5 are independently of each other N or O,

M is a imaging moiety M_1 or M_2,

M_1 is a chelated metal radionuclide, and

M_2 is a gamma- or positron-emitting non-metal radionuclide optionally in combination with a prosthetic group.

12. The compound according to claim 1, wherein m_1 is 2 and m_2 is 0 or wherein m_1 is 0 and m_2 is 2.

13. The compound according to claim 1, wherein

M is a radionuclide-based therapeutic or diagnostic moiety M_1 or M_2, wherein

M_1 is a chelated metal radionuclide, and

M_2 is a gamma- or positron-emitting non-metal radionuclide optionally in combination with a prosthetic group.

14. The compound according to claim 1, with the proviso that when A_2 is an albumin binder, M is a chelated metal radionuclide M_1.

15. The compound according to claim 14, wherein the metal radionuclide is selected from the group consisting of ^{99}Tc, ^{51}Cr, ^{67}Ga, ^{68}Ga, ^{47}Sc, ^{51}Cr, ^{167}Tm, ^{141}Ce, ^{111}In, ^{168}Yb, ^{175}Yb, ^{140}La, ^{90}Y, ^{88}Y, ^{153}Sm, ^{166}Ho, ^{165}Dy, ^{166}Dy, ^{62}Cu, ^{64}Cu, ^{67}Cu, ^{97}Ru, ^{103}Ru, ^{186}Re, ^{188}Re, ^{203}Pb, ^{211}Bi, ^{213}Bi, ^{214}Bi, ^{105}Rh, ^{109}Pd, ^{117}mSn, ^{149}Pm, ^{161}Tb, ^{177}Lu, ^{198}Au and ^{199}Au.

16. The compound according to claim 14, wherein the metal chelator is a bidentate, tridentate, or tetradentate, linear, tripodal or macrocyclic ligand.

17. The compound according to claim 14, wherein the metal chelator is a linear or macrocyclic polyaminocarboxylate chelator.

18. The compound according to claim 14, wherein the metal chelator is DTPA, DOTA, DO3A, HP-DO3A, EDTA, TETA, EHPG, HBED, NOTA, DOTMA, TETMA, PDTA, TTHA, LICAM, or MECAM.

19. The compound according to claim 1, wherein the imaging moiety M is a chelated metal radionuclide M_1 comprising a metal radionuclide and a metal chelator.

20. The compound according to claim 1, wherein the imaging moiety M is a gamma- or positron-emitting non-metal radionuclide M_2 selected from ^{11}C, ^{13}N, ^{15}O, ^{17}F, ^{18}F, ^{75}Br, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I, and ^{131}I, optionally in combination with a prosthetic group.

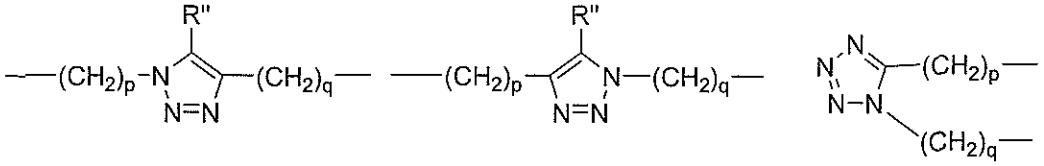
21. The compound according to claim 1, wherein L_1 is a covalent bond or straight-chain or branched C(1-6)alkyl.

22. The compound according to claim 1, wherein Y_1 is O or N and/or Y_3 is N.

23. The compound according to claim 1, wherein L_3 is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by a group selected from the group consisting of -O-, -CO-, -CO-O-,-NR'-,-NR'-CO-, and a five-membered azaheterocycle, which is a triazolyl or tetrazolyl group, and wherein R' represents H or C(1-8)alkyl.

24. The compound according to claim 1, wherein L_3 is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently

replaced by -O-, -CO-, -CO-O-,-NR'-,-NR'-CO-, or L_3 is a group of formulae (a), (b), or (c)



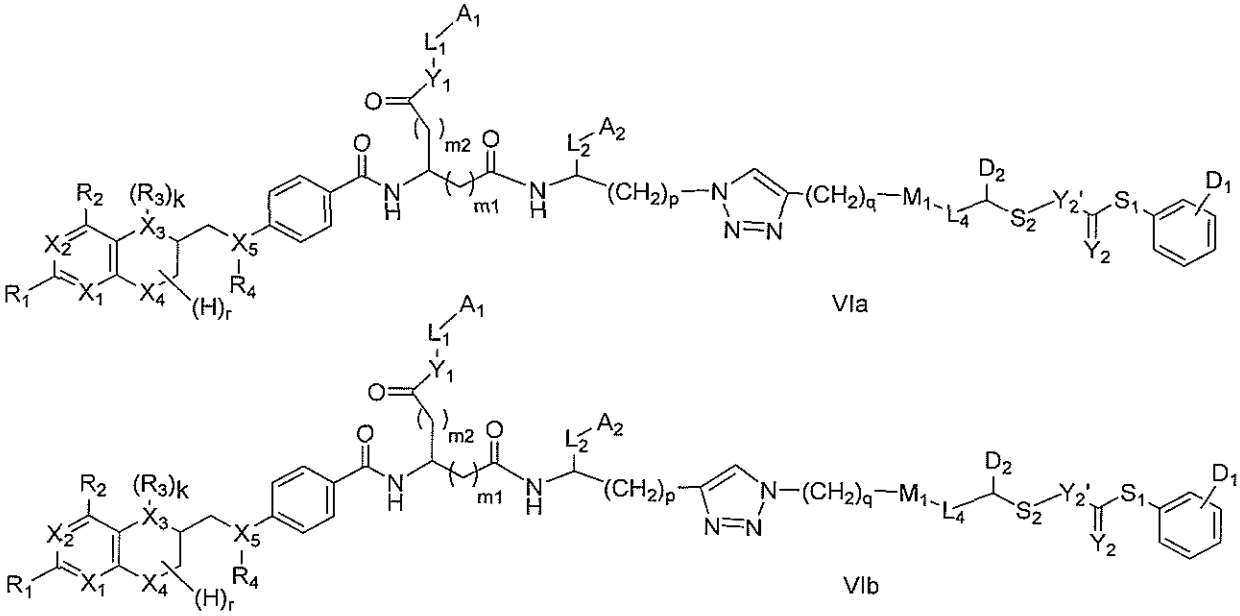
(a) (b) (c)

wherein

R'' is H or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2,

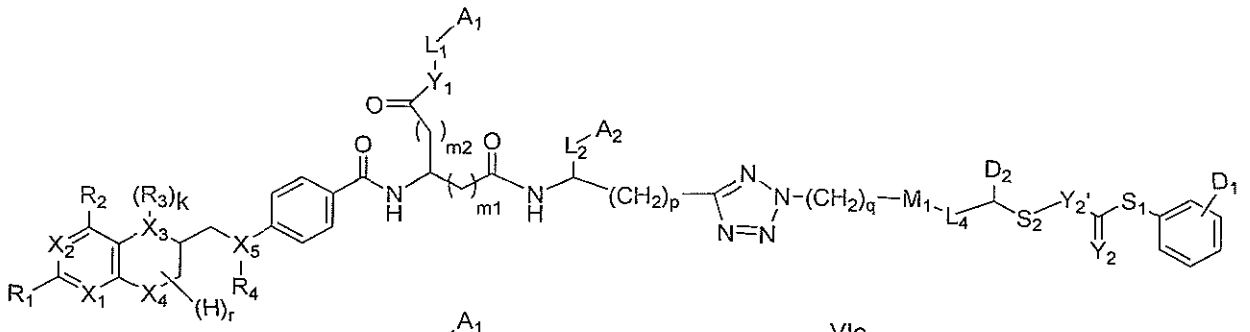
p,q are independently of each other 0, 1, 2, 3, 4, 5 or 6.

25. The compound according to claim 1 having formulae VI a-e

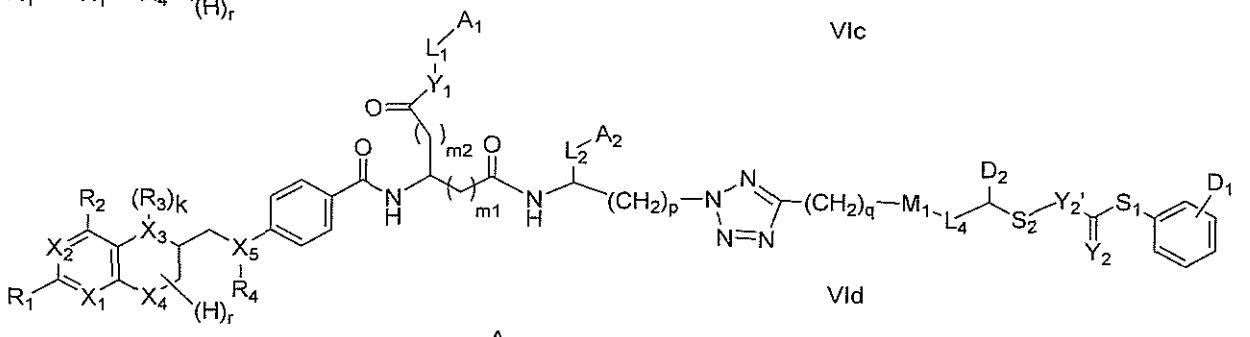


VIa

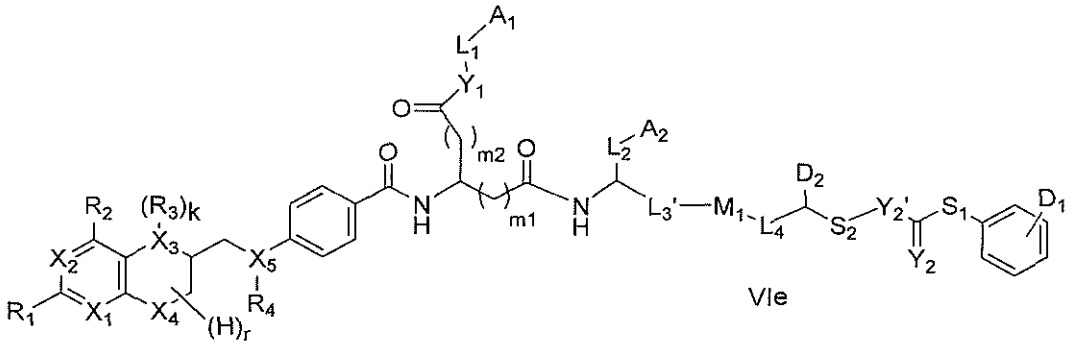
VIb



VIc



VId



VIe

wherein

X_1 to X_5 are independently of each other C, N or O,

Y_1, Y_2, Y_2' are independently of each other N, O or S,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$,

R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR',

R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR',

A_1 is H or a capping group,

A_2 is H or a capping group,

M_1 is a linear or macrocyclic polyaminocarboxylate, complexed with a radioimaging metal ion,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2,

L_2 is a covalent bond or a linking group, which is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR',

S_1, S_2 are independently of each other a single bond or a spacer which is a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, -SO_3R'-,

D_1 is H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR_{5*}, -COR_{5*}, -$COOR_{5*}$, -NHR_{5*}, or -$CONHR_{5*}$,

R_{5*} represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

D_2 is an acidic group,

L_3, is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently

replaced by -O-, -CO-, -CO-O-,-NR'-, or -NR'-CO-,

p,q are independently of each other 0, 1, 2, 3, 4, 5 or 6,

k is 0 or 1,

r has a value of 1 to 7.

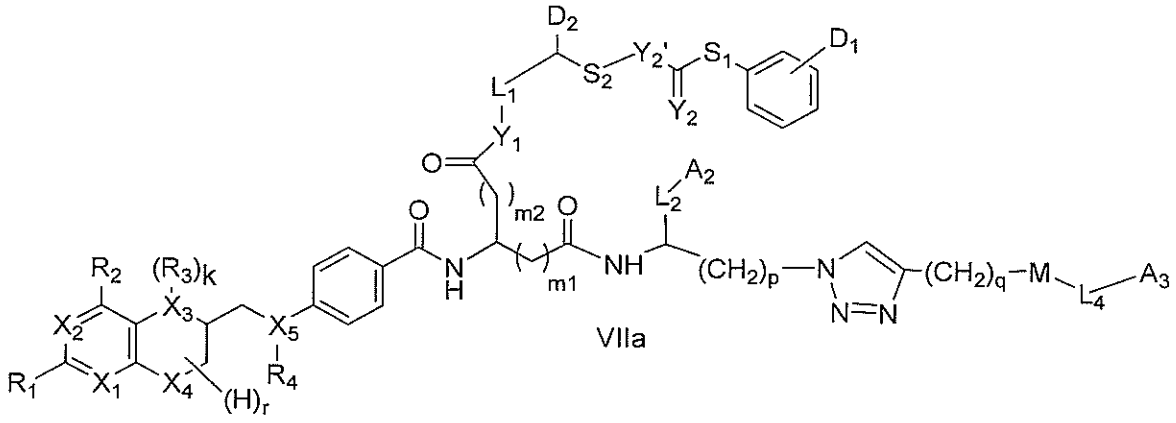
26. The compound according to claim 25,

wherein

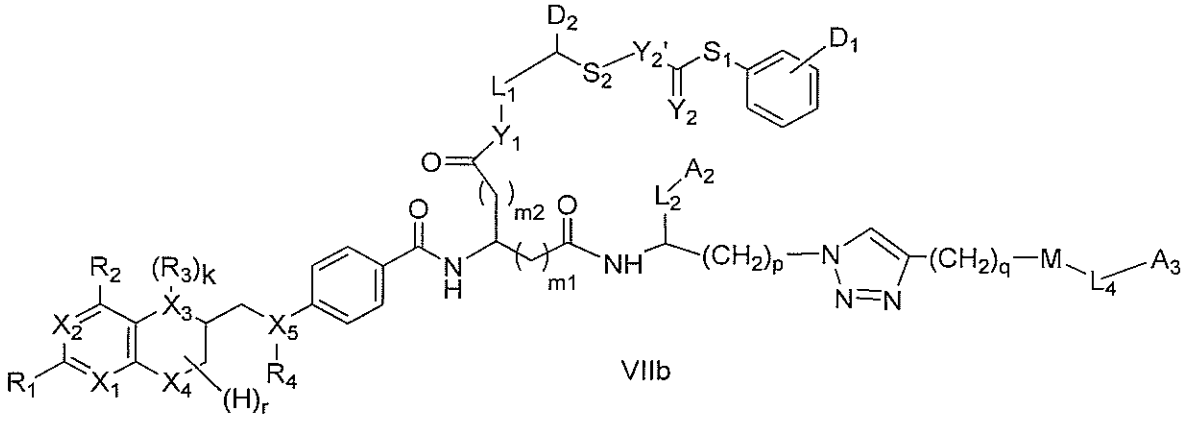
X_1 to X_5 are independently of each other N or O, and

M_1 is DPTA, DOTA, DO3A, HP-DO3A, EDTA, TETA, NOTA, or DOTMA complexed with a radioimaging metal ion.

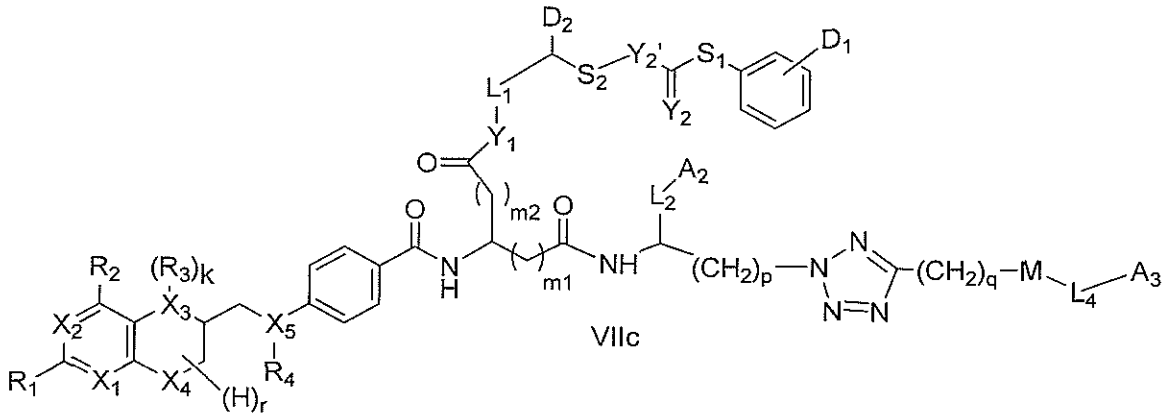
27. The compound according to claim 1 having formulae VII a-e



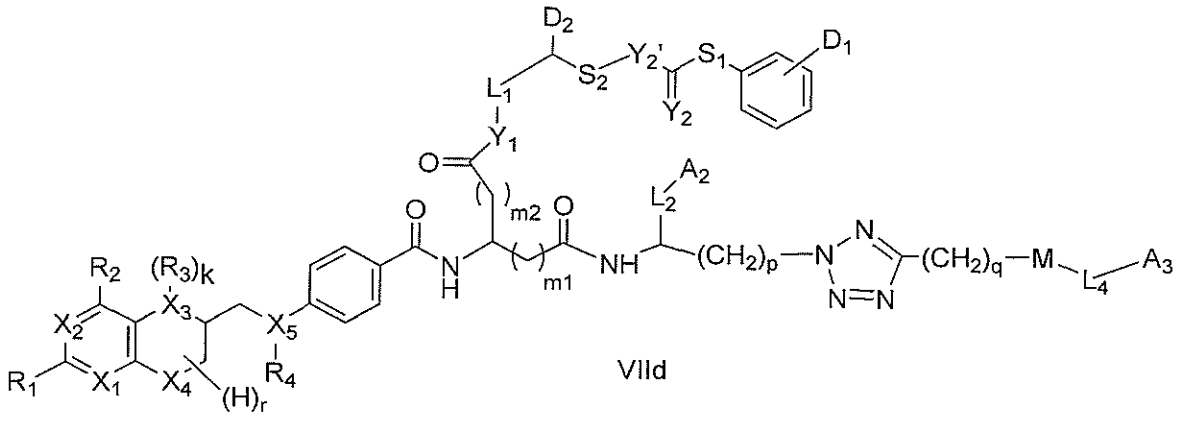
VIIa



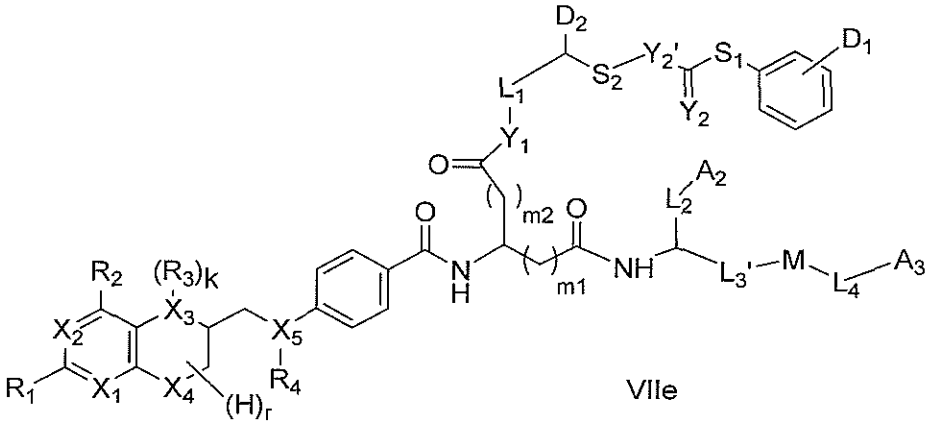
VIIb



VIIc



VIId



VIIe

wherein

X_1 to X_5 are independently of each other C, N or O,

Y_1, Y_2, Y_2' are independently of each other N, O or S,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$,

R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR',

R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR',

A_2 is H or a capping group,

A_3 is H or a capping group,

M is an imaging moiety M_1 or M_2,

M_1 is a chelated metal radionuclide which is a linear or macrocyclic polyaminocarboxylate, complexed with a metal radionuclide ion,

M_2 is a gamma- or positron-emitting non-metal radionuclide, optionally in combination with a prosthetic group,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2,

L_2 is a covalent bond or a linking group, which is a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR',

S_1, S_2 are independently of each other a single bond or a spacer which is a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, or $-SO_3R'-$,

D_1 is H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_{5*}$, $-COR_{5*}$, $-COOR_{5*}$, $-NHR_{5*}$, or $-CONHR_{5*}$,

R_{5*} represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

D_2 is an acidic group,

$L_{3'}$ is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-, -NR'-, -NR'-CO-,

p,q are independently of each other 0, 1, 2, 3, 4, 5 or 6,

k is 0 or 1,

r has a value of 1 to 7.

28. The compound according to claim 27,

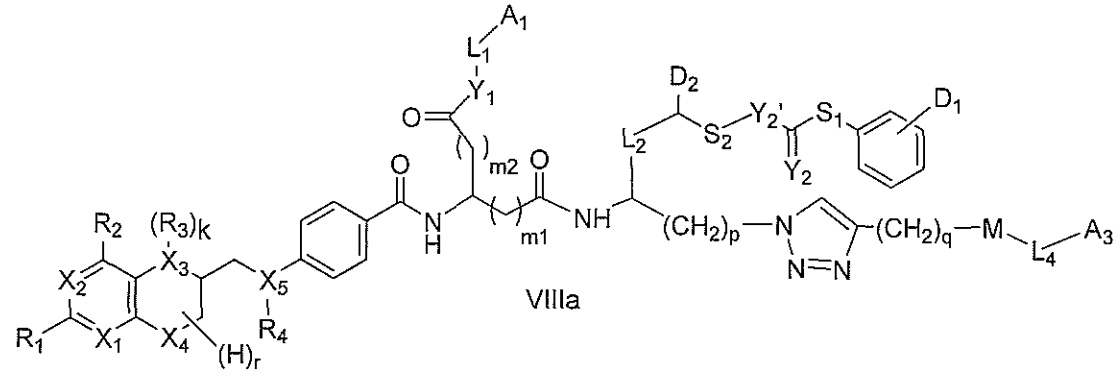
wherein

X_1 to X_5 are independently of each other N or O,

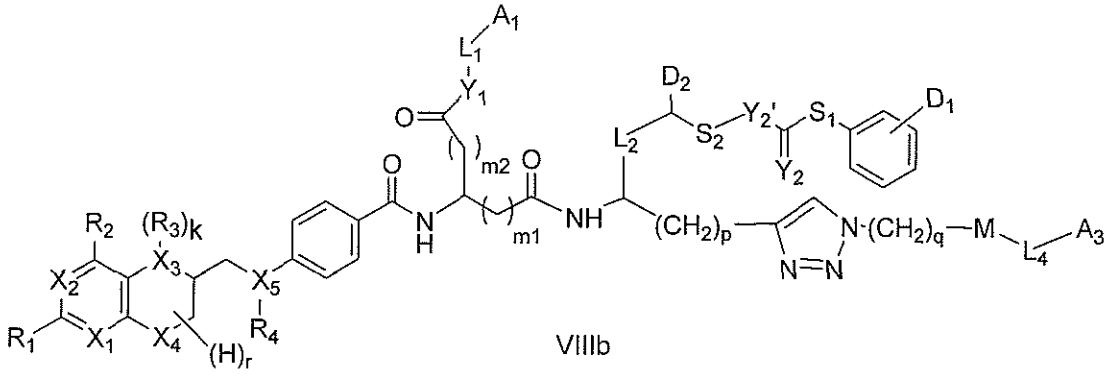
M_1 is a chelated metal radionuclide which is DPTA, DOTA, DO3A, HP-DO3A, EDTA, TETA, NOTA, or DOTMA complexed with a metal radionuclide ion, and

M_2 is a gamma- or positron-emitting non-metal radionuclide, which is ^{11}C, ^{13}N, ^{15}O, ^{17}F, ^{18}F, ^{75}Br, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I, and ^{131}I, optionally in combination with a prosthetic group.

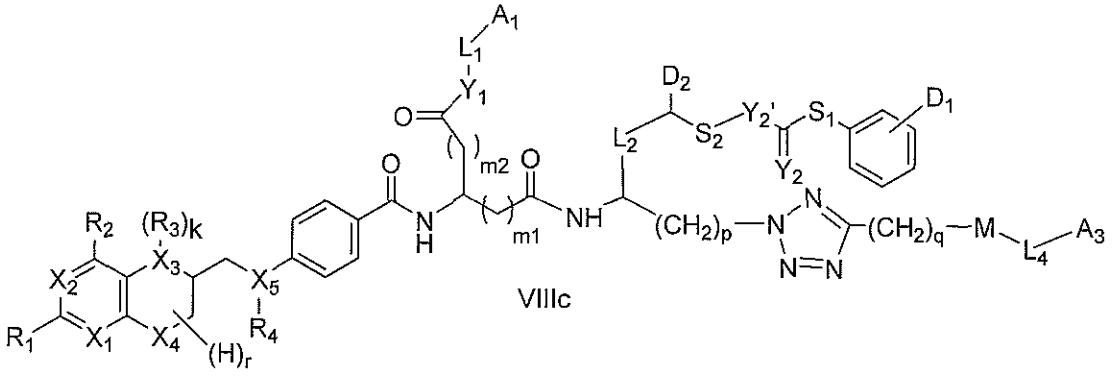
29. The compound according to claim 1 having formulae VIII a-e



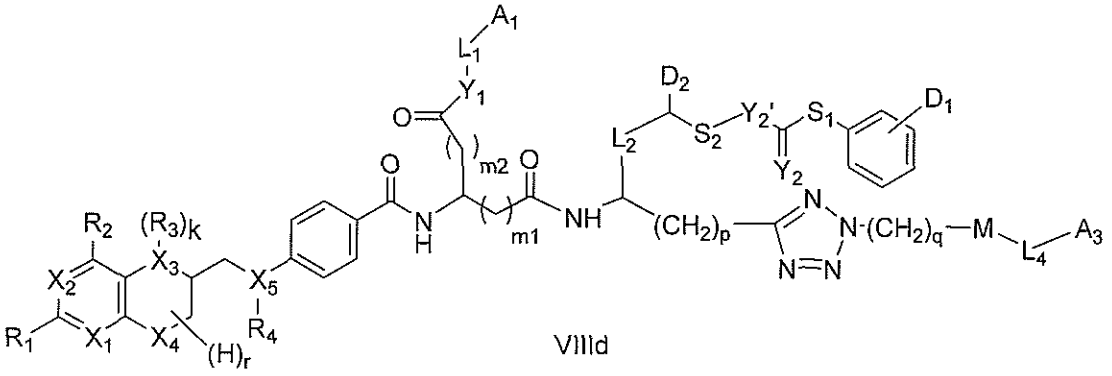
VIIIa



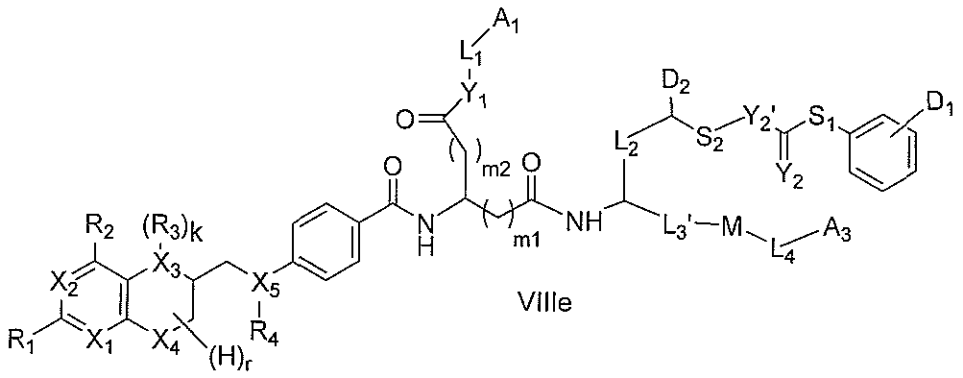
VIIIb



VIIIc



VIIId



VIIIe

wherein

X_1 to X_5 are independently of each other C, N or O,

Y_1, Y_2, Y_2' are independently of each other N, O or S,

R_1, R_2 are independently of each other H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$,

R_5 represents H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', or -NHR',

R' is H or C(1-8)alkyl,

R_3, R_4 are independently of each other H, nitroso, C(1-12)alkyl, -OR', -COR' or halosubstituted -COR',

A_1 is H or a capping group,

A_3 is H or a capping group,

M is an imaging moiety M_1 or M_2,

M_1 is a chelated metal radionuclide which is a linear or macrocyclic polyaminocarboxylate complexed with a radioimaging metal ion,

M_2 is a gamma- or positron-emitting non-metal radionuclide optionally in combination with a prosthetic group,

m_1, m_2 are independently of each other 0, 1, 2 or 3,

L_1, L_4 are independently of each other a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R' or NO_2,

L_2 is a covalent bond or a linking group, which is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-, or -CO-NR',

S_1, S_2 are independently of each other a single bond or a spacer which is a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OR', NHR', CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR'-,-NR'-CO-O-,-O-CO-NR'-,-NR'-CO-NR'-,-CH=CH-,-C≡C-,-O-CO-O-, -S-R'-, or $-SO_3R'-$,

D_1 is H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_{5*}$, $-COR_{5*}$, $-COOR_{5*}$, $-NHR_{5*}$, or $-CONHR_{5*}$,

R_{5*} represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl,

D_2 is an acidic group,

$L_{3'}$ is straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one Hal, OR', NHR', or CO_2R', and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-,-NR'-, or -NR'-CO-,

p,q are independently of each other 0, 1, 2, 3, 4, 5 or 6,

k is 0 or 1,

r has a value of 1 to 7.

30. The compound according to claim 29,

wherein

X_1 to X_5 are independently of each other N or O,

M_1 is a chelated metal radionuclide which is DPTA, DOTA, DO3A, HP-DO3A, EDTA, TETA, NOTA, or DOTMA, complexed with a radioimaging metal ion, and

M_2 is a gamma- or positron-emitting non-metal radionuclide, which is ^{11}C, ^{13}N, ^{15}O, ^{17}F, ^{18}F, ^{75}Br, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I, or ^{131}I, optionally in combination with a prosthetic group.

31. A pharmaceutical composition comprising at least one compound according to claim 1 and one or more pharmaceutically acceptable carriers.

32. A method for diagnostic imaging of a cell or population of cells expressing a folate-receptor, said method comprising administering at least one compound according to claim 1 in a diagnostic imaging amount, performing diagnostic imaging by PET, detecting a signal from said at least one compound, and obtaining a diagnostic image of said cell or population of cells.

33. The method according to claim 32, wherein the diagnostic imaging is performed of a cell or population of cells expressing a folate-receptor in vitro.

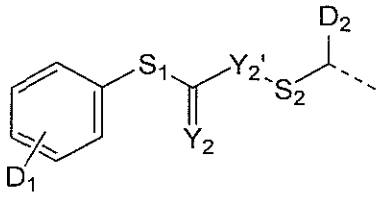
34. The method according to claim 32, wherein the diagnostic imaging is performed of a cell or population of cells expressing a folate-receptor in vivo.

35. A method for in vitro detection of a cell expressing the folate receptor in a tissue sample which includes contacting said tissue sample with a compound according to claim 1 in effective amounts and for sufficient time and conditions to allow binding to occur and detecting such binding by PET imaging.

36. A method of diagnostic imaging or monitoring a subject comprising administering at least one compound according to claim 1 in a diagnostic imaging amount, and performing diagnostic imaging by PET, and detecting a signal from said at least one compound.

37. The compound according to claim 1, wherein only one of A_1, A_2 and A_3 is an albumin binders.

38. The compound according to claim 1, wherein the albumin binder is a compound of formula III



III

wherein

$Y_2, Y_{2'}$ are independently of each other N, O or S,

S_1, S_2 are independently of each other a single bond or a spacer which is a straight-chain or branched C(1-12)alkyl, which is unsubstituted or substituted by at

least one CN, Hal, OR′, NHR′, CO_2R', SH, SO_3H or NO_2, and wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR′-, -NR′-CO-, -CO-NR′-, -NR′-CO-O-, -O-CO-NR′-, -NR′-CO-NR′-, -CH=CH-, -C≡C-, -O-CO-O-, -S-R′-, or $-SO_3R'-$,

R′ represents H or C(1-8)alkyl,

D_1 is H, halogen, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$,

R_5 represents H, C(1-12)alkyl, C(2-12)alkenyl, or C(2-12)alkynyl, and

D_2 is an acidic group,

and the broken line represents the linkage to L_1, L_2 or L_4.

39. The compound according to claim 38, wherein

S_1 and S_2 are independently of each other a single bond or a spacer which is a straight-chain or branched C(1-12)alkyl, wherein one or more of the non-adjacent CH_2 groups are optionally independently replaced by -O-, -CO-, -COO-, -NR′-NR′-CO-, -CO-NR′-, -CH=CH-,

wherein R′ represents H or C(1-8)alkyl,

40. The compound according to claim 38, wherein Y_2 is O and/or Y_2 is N.