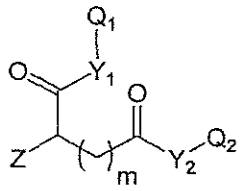
Claims

1. Compounds of formula I,



I

wherein

Z is a pteroate or derivative thereof,

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

m is 1, 2 or 3, and

Q_1, Q_2 are independently of each other H, a protecting group or a group of formula

$$-L-A-L'-{}^{18}F,$$

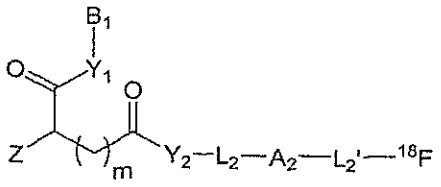
wherein

L,L' are independently of each other a linking group, such as a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, CO_2H, 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'-, $-SO_3R'-$, or a five- or six-membered heterocycle, wherein R' represents H or C(1-8)alkyl, and

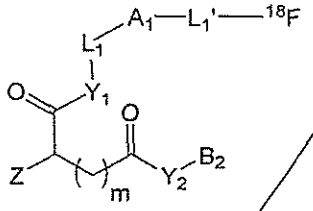
A is a saccharide group,

with the proviso that at least one of Q_1 and Q_2 is a group of formula $-L-A-L'-{}^{18}F$.

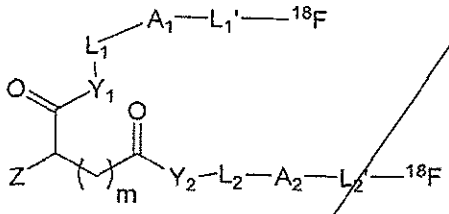
2. Compounds according to claim 1 having formula Ia, Ib, Ic,



Ia



Ib



Ic

wherein

Z is a pteroate or derivative thereof,

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

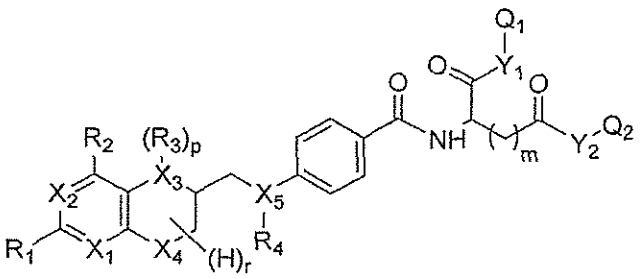
m is 1, 2 or 3,

L_1, L_1', L_2, L_2' are independently of each other a linking group, such as a covalent bond or a straight-chain or branched C(1-50)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, CO_2H, 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'-, $-SO_3R'-$, or a five- or six-membered heterocycle, wherein R' represents H or C(1-8)alkyl,

A_1, A_2 are independently of each other a saccharide group, and

B_1, B_2 are independently of each other H, or a protecting group.

3. 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,

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

m is 1, 2 or 3,

r has a value of 1 to 7,

p is 0 or 1,

Q_1, Q_2 are independently of each other H, protecting group or a group of formula

$$-L-A-L'-{}^{18}F,$$

wherein

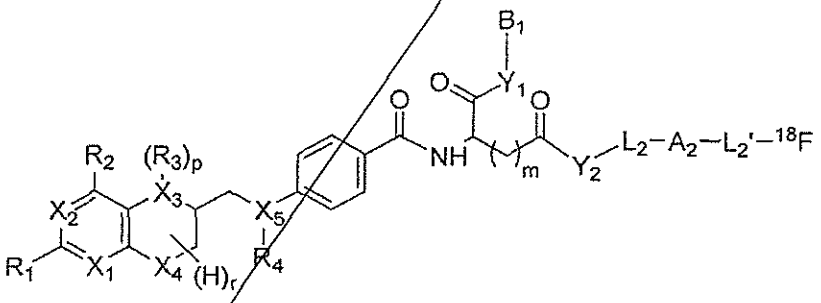
L,L' are independently of each other a linking group, such as a covalent bond or a straight-chain or branched C(1-50)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, CO_2H, NO_2, and wherein one or

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'-, $-SO_3R'-$, or a five- or six-membered heterocycle, wherein R' represents H or C(1-8)alkyl, and

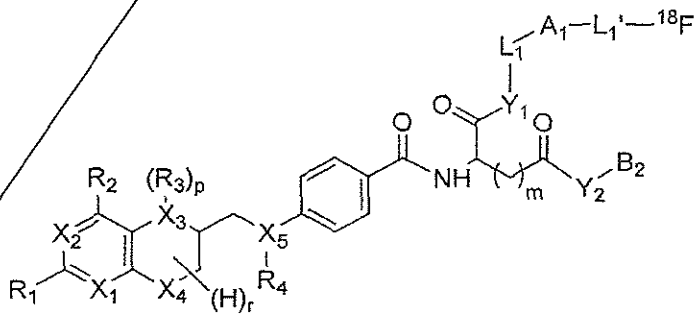
A is a saccharide group,

with the proviso that at least one of Q_1 and Q_2 is a group of formula $-L-A-L'-{}^{18}F$.

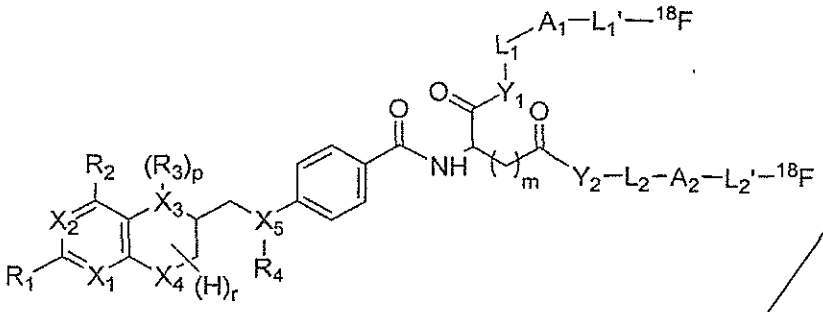
4. Compound according to any preceding claim having formulae IIa, IIb, IIc



IIa



IIb



IIc

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,

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

m is 1, 2 or 3,

r has a value of 1 to 7,

p is 0 or 1,

L_1, L_1', L_2, L_2' are independently of each other a linking group, such as a covalent bond or a straight-chain or branched C(1-50)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, CO_2H, 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'-, $-SO_3R'-$, or a five- or six-membered heterocycle, wherein R' represents H or C(1-8)alkyl,

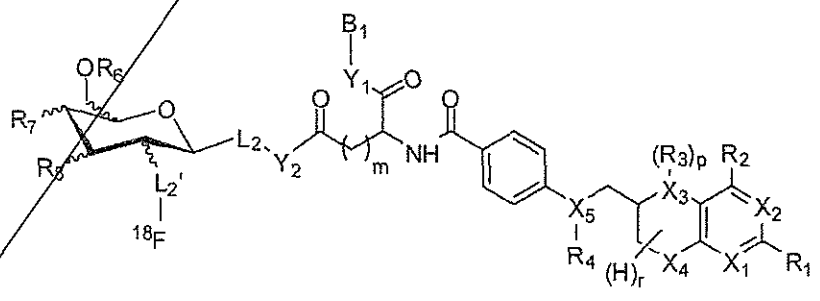
A_1, A_2 are independently of each other a saccharide group, and

B_1, B_2 are independently of each other H, or a protecting group.

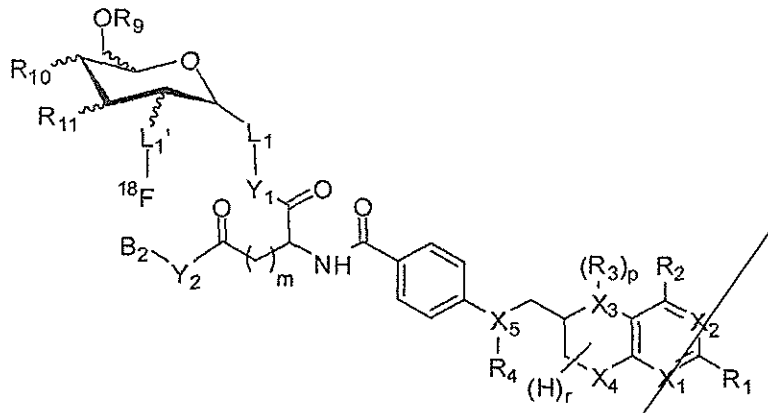
5. A compound according to any preceding claim, wherein the saccharide group is a cyclic monosaccharide or a cyclic oligosaccharide based on a pyranoside, preferably selected from allose, altrose, glucose, mannose, gulose, idose, galactose and talose, or a furanoside, preferably selected from ribose, arabinose, xylose, and lyxose.

6. A compound according to any preceding claim, wherein the saccharide group is a cyclic monosaccharide selected from glucose and galactose.

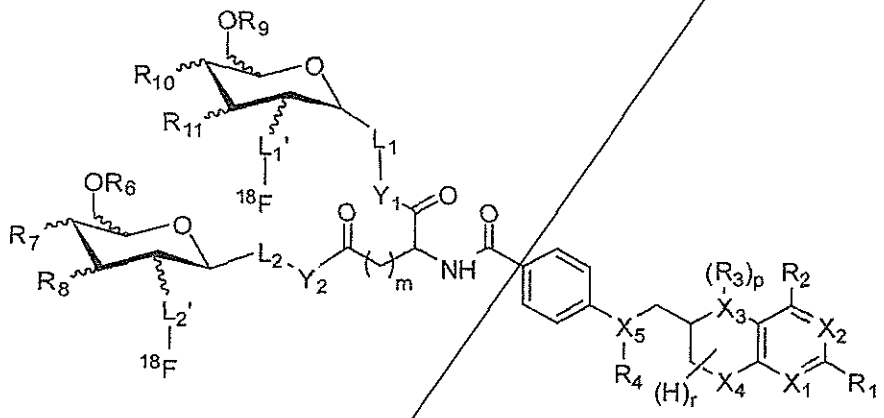
7. A compound according to any preceding claim, having formulae IIIa, IIIb, IIIc,



IIIa



IIIb



IIIc

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,

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

m is 1, 2 or 3,

r has a value of 1 to 7,

p is 0 or 1,

L_1, L_1', L_2, L_2' are independently of each other a linking group, such as a covalent bond or a straight-chain or branched C(1-8)alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, CO_2H, 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'-, $-SO_3R'-$, or a five- or six-membered heterocycle, wherein R' represents H or C(1-8)alkyl,

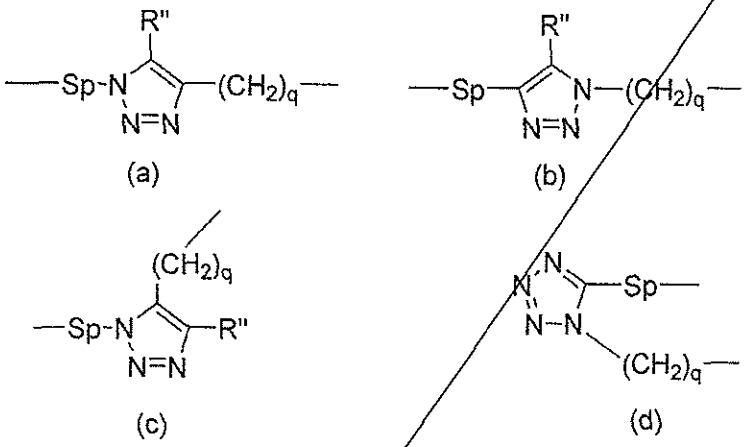
B_1, B_2 are independently of each other H, or a protecting group,

R_6, R_9 is H or C(1-8)alkyl, and

R_7, R_8, R_{10}, R_{11} are independently of each other H, -OH, or -OC(1-8)alkyl.

8. Compound according to anyone of claims 2 to 7, wherein L_1 and L_2 are independently of each other straight-chain or branched C(1-24)alkyl, which is unsubstituted or substituted by at least one group selected from Hal, OH, NHR', 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-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', or a five- or six-membered heterocycle, preferably a five-membered azaheterocycle, wherein R' represents H or C(1-8)alkyl.

9. A compound according to anyone of claims 2 to 8, wherein L_1 and L_2 are independently of each other a group of formulae (a), (b), (c) or (d)



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,

Sp is a spacer (linked to Y1 and/or Y2) such as a straight-chain or branched C(1-8)alkyl, which is unsubstituted or wherein at least one of the $-CH_2-$ groups is substituted with -OH, -NHR', or -COOR', wherein R' represents H or C(1-8)alkyl and,

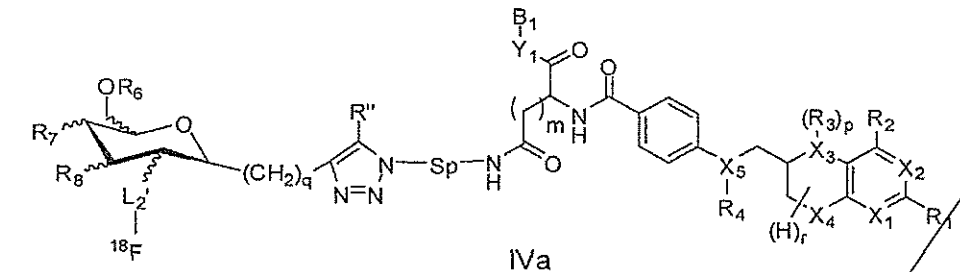
q is 0, 1, 2, 3 or 4.

10. Compound according to anyone of claims 2 to 9, wherein L_1' and L_2' are preferably a covalent bond or a straight-chain or branched C(1-24)alkyl, more preferably C(1-12)alkyl, most preferably C(1-6)alkyl, which is unsubstituted or substituted by at least one group selected from Hal, OH, NHR', CO_2R', and wherein one or

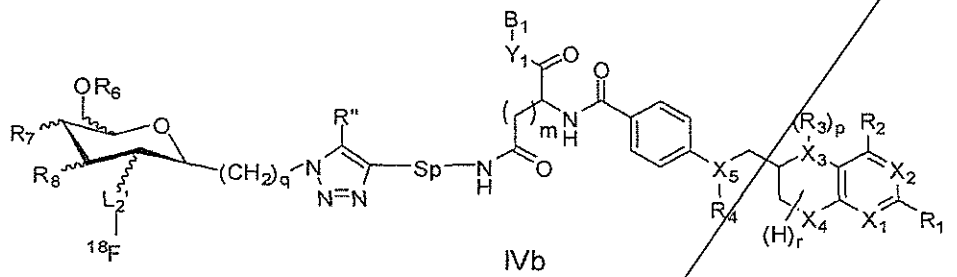
more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl.

11. Compound according to any preceding claim, wherein Y_1 and/or Y_2 is N and B_2 is a carboxamide protecting group.

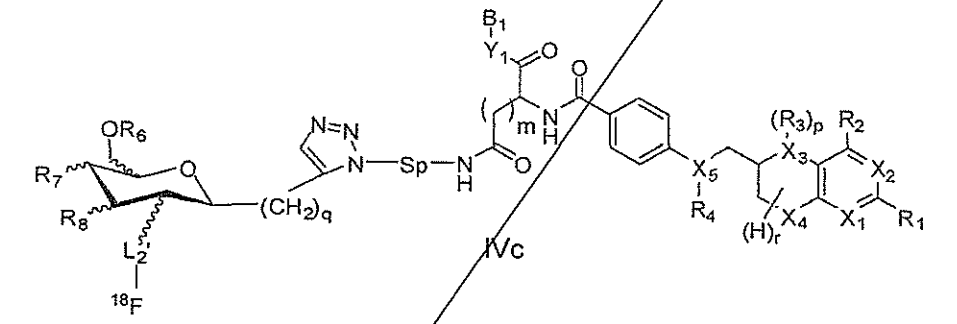
12. A compound according to any preceding claim having formulae IVa, IVb, IVc, IVd



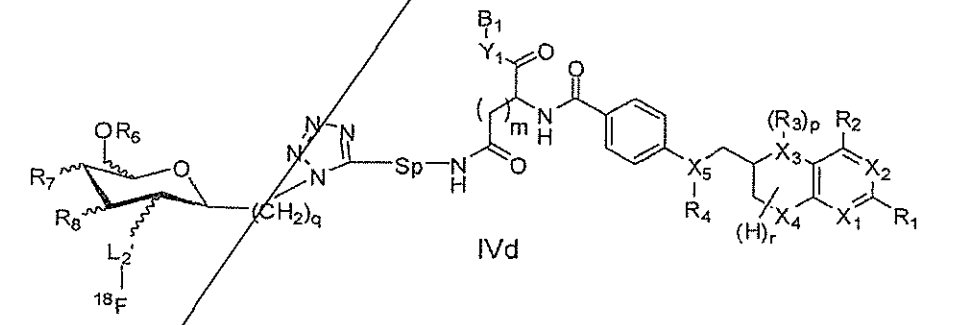
IVa



IVb



IVc



IVd

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, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, 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,

m is 1, 2 or 3,

r has a value of 1 to 7,

p is 0 or 1,

Y_1 is O, N or S,

B_1 is H, or a protecting group,

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,

L_2′ is a covalent bond or a straight-chain or branched C(1-6)alkyl, wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-O-,-O-CO-,-NR′-,-NR′-CO-,-CO-NR′, wherein R′ represents H or C(1-8)alkyl,

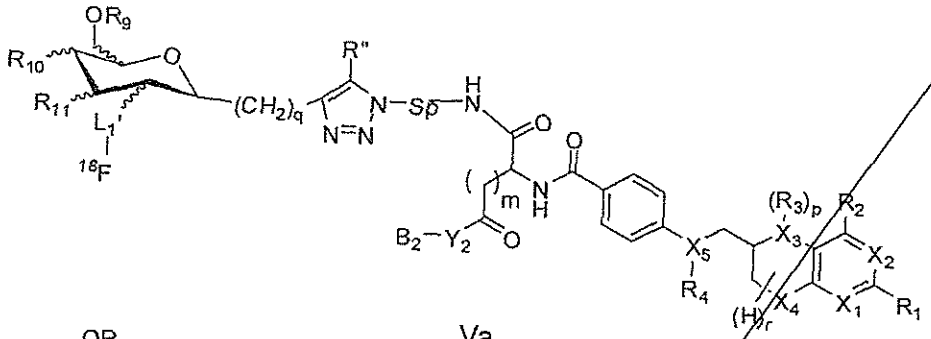
Sp is a spacer such as a straight-chain or branched C(1-8)alkyl, which is unsubstituted or wherein at least one of the $-CH_2-$ groups is substituted with -OH, -NHR′, or -COOR′, wherein R′ represents H or C(1-8)alkyl,

q is 0, 1, 2, 3 or 4,

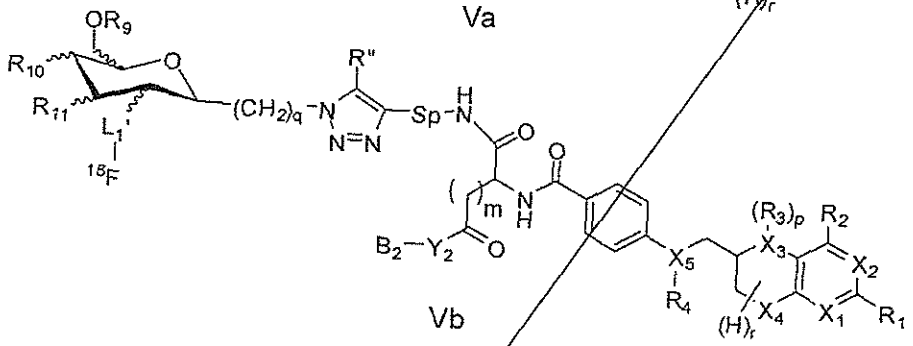
R_6 is H or C(1-8)alkyl, and

R_7,R_8 are independently of each other H, -OH, or -OC(1-8)alkyl.

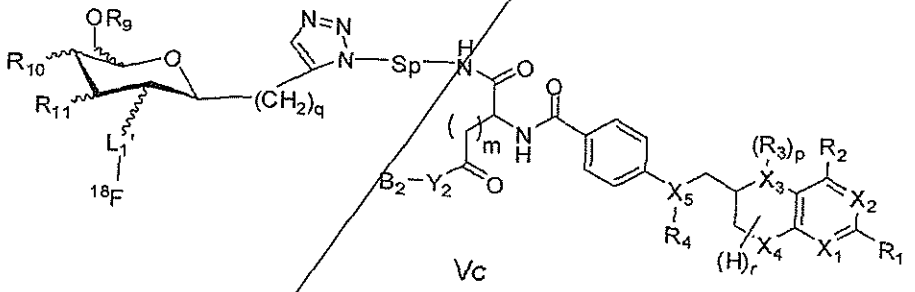
13. A compound according to any preceding claim having formulae Va, Vb, Vc, Vd



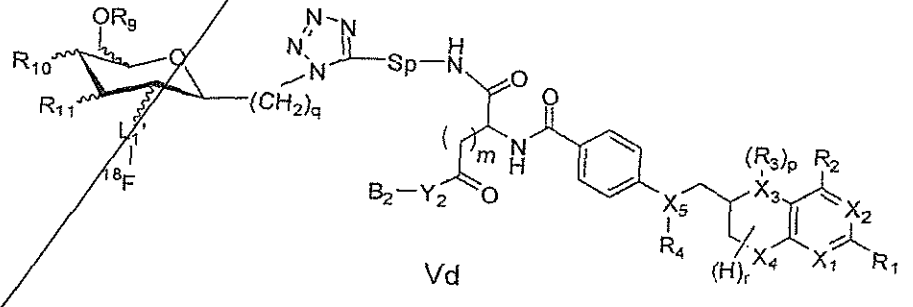
Va



Vb



Vc



Vd

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, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, 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,

m is 1, 2 or 3,

r has a value of 1 to 7,

p is 0 or 1,

Y_2 is O, N or S,

B_2 is H, or a protecting group,

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,

Sp is a spacer such as a straight-chain or branched C(1-8)alkyl, which is unsubstituted or wherein at least one of the $-CH_2-$ groups is substituted with -OH, -NHR', or -COOR', wherein R' represents H or C(1-8)alkyl,

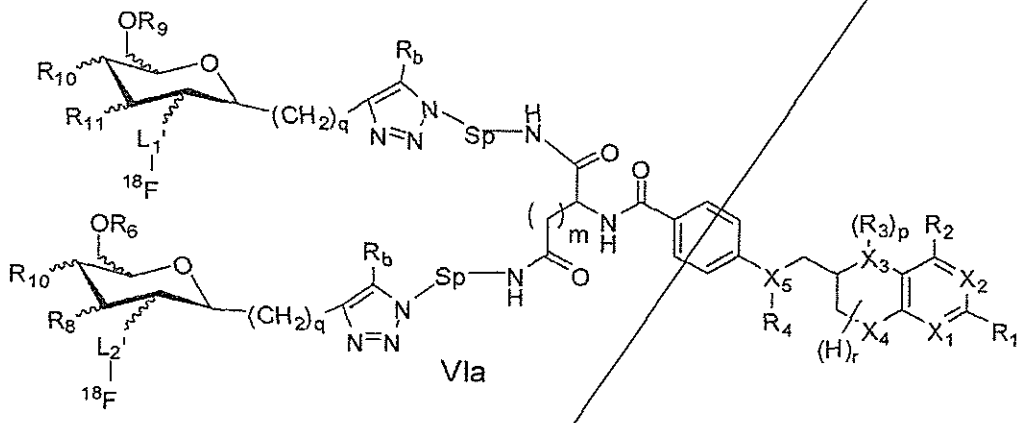
L_1' is a covalent bond or a straight-chain or branched C(1-6)alkyl, wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

q is 0, 1, 2, 3 or 4,

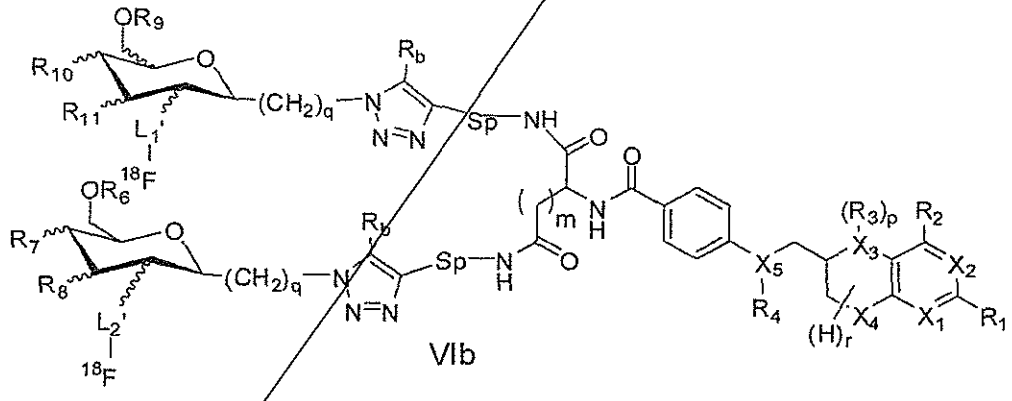
R_9 is H or C(1-8)alkyl, and

R_{10},R_{11} are independently of each other H, -OH, or -OC(1-8)alkyl.

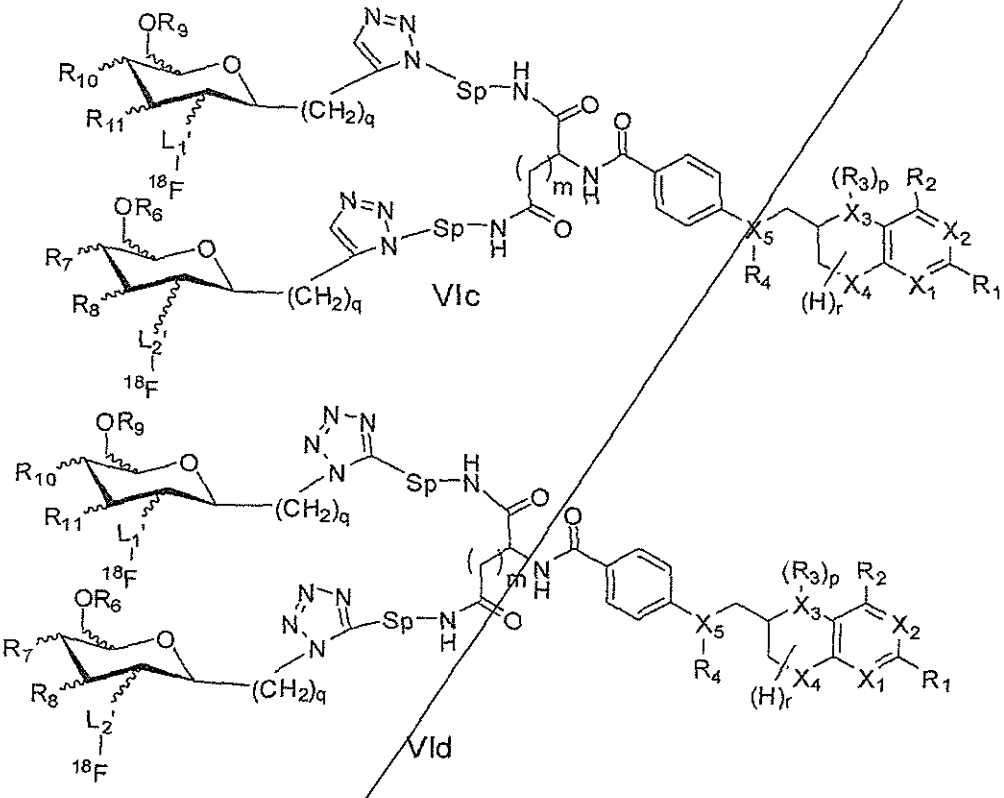
14. A compound according to any preceding claim having formulae VIa, VIb, VIc, VId



VIa



VIb



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, $-OR_5$, $-COR_5$, $-COOR_5$, $-NHR_5$, $-CONHR_5$, 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,

m is 1, 2 or 3,

r has a value of 1 to 7,

p is 0 or 1,

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,

Sp is a spacer such as a straight-chain or branched C(1-8)alkyl, which is unsubstituted or wherein at least one of the $-CH_2-$ groups is substituted with -OH, -NHR', or -COOR', wherein R' represents H or C(1-8)alkyl,

L_1',L_2' are independently of each other a covalent bond or a straight-chain or branched C(1-6)alkyl, wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

q is 0, 1, 2, 3 or 4

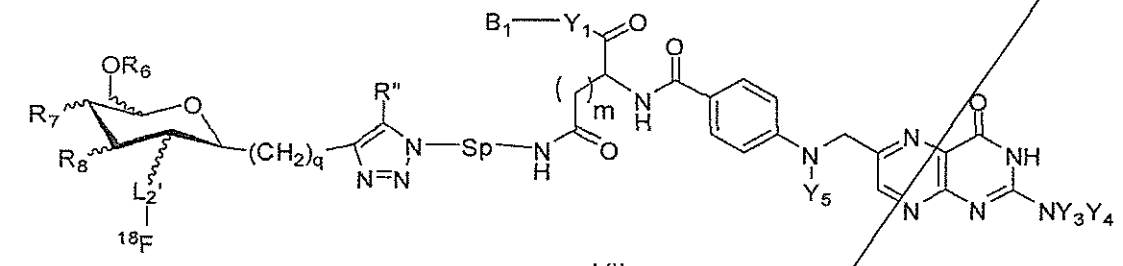
R_6,R_9 is H or C(1-8)alkyl, and

R_7,R_8,R_{10},R_{11} are independently of each other H, -OH, or -OC(1-8)alkyl.

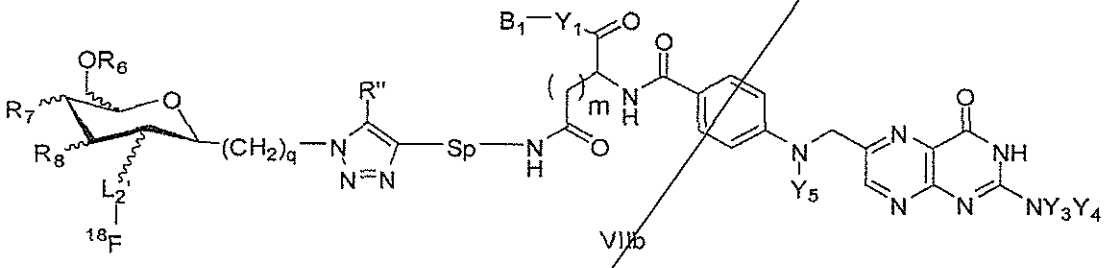
15. A compound according to any preceding claim wherein m is 2.

16. A compound according to anyone of claims 9 to 15, wherein q is 0.

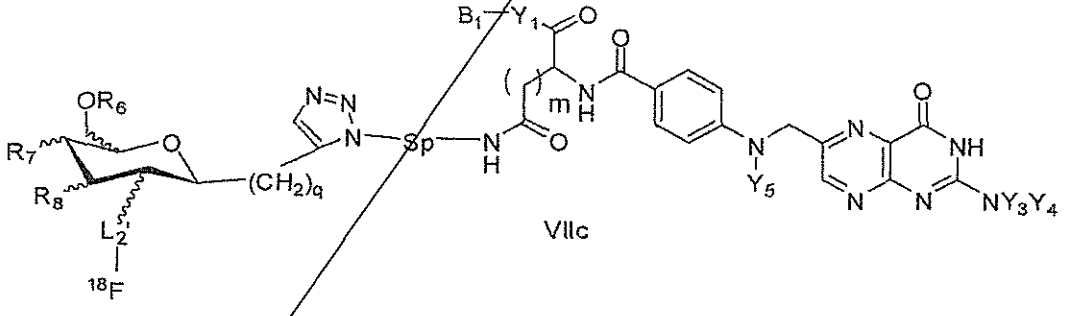
17. A compound according to any preceding claim having formulae VIIa, VIIb, VIIc, VIId



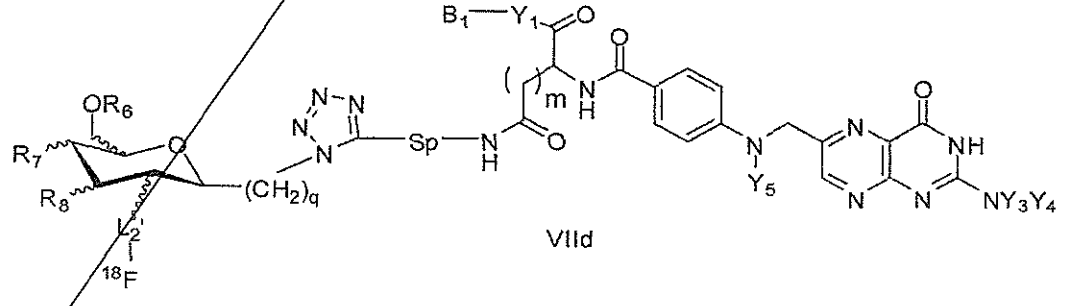
VIIa



VIIb



VIIc



VIId

wherein

Y_3, Y_4 are independently of each other selected from H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', and -NHR', wherein R' is H or C(1-8)alkyl,

Y_5 is selected from H, nitroso, C(1-12)alkyl, -OR', -COR',

and halosubstituted -COR', wherein R' is H or C(1-12)alkyl,

m is 1, 2 or 3,

Y_1 is O, N or S,

B_1 is H, or a protecting group,

Sp is a spacer such as a straight-chain or branched C(1-8)alkyl, which is unsubstituted or wherein at least one of the $-CH_2-$ groups is substituted with -OH, -NHR', or -COOR', wherein R' represents H or C(1-8)alkyl,

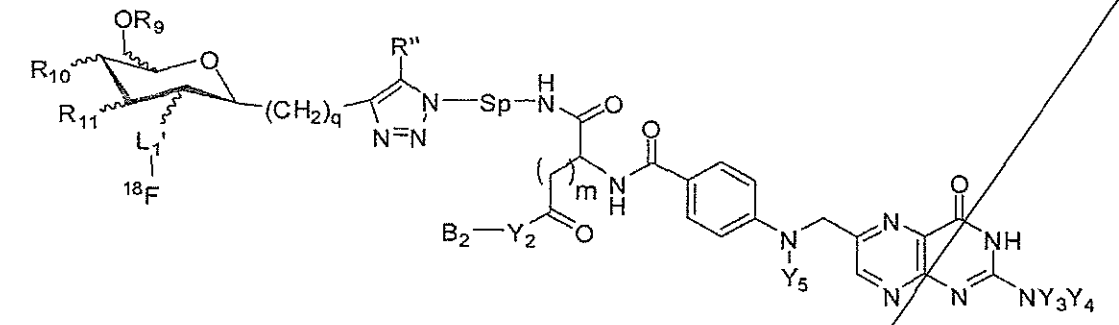
L_2' is a covalent bond or a straight-chain or branched C(1-6)alkyl, wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

q is 0, 1, 2, 3 or 4,

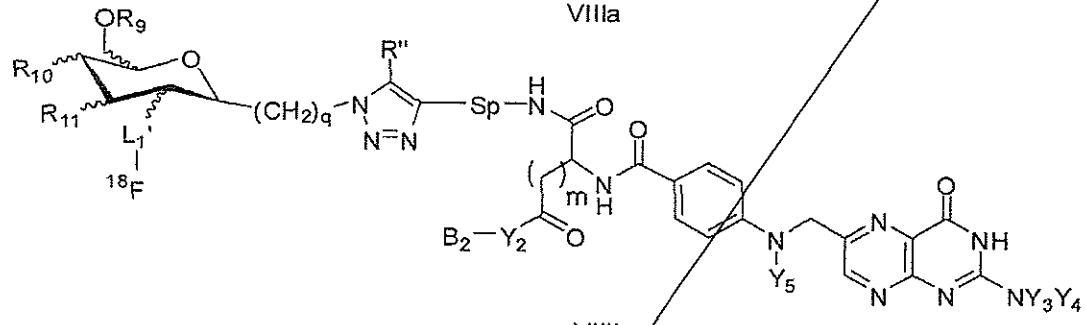
R_6 is H or C(1-8)alkyl, and

R_7,R_8 are independently of each other H, -OH, or -OC(1-8)alkyl.

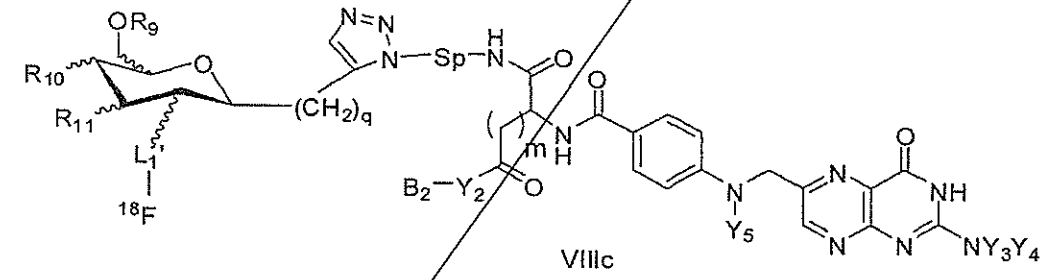
18. A compound according to any preceding claim having formulae VIIIa, VIIIb, VIIIc, VIIId



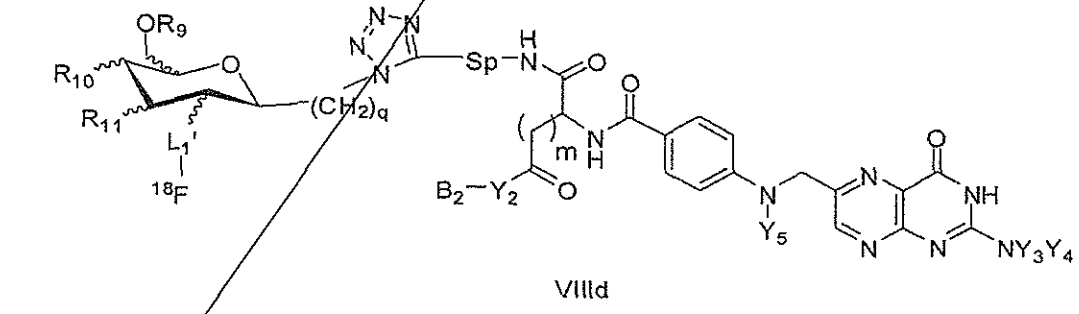
VIIIa



VIIIb



VIIIc



VIIId

wherein

Y_3, Y_4 are independently of each other selected from H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', and -NHR', wherein R' is H or C(1-8)alkyl,

Y_5 is selected from H, nitroso, C(1-12)alkyl, -OR', -COR', and halosubstituted -COR', wherein R' is H or C(1-

12)alkyl,

m is 1, 2 or 3,

Y_2 is O, N or S,

B_2 is H, or a protecting group,

Sp is a spacer such as a straight-chain or branched C(1-8)alkyl, which is unsubstituted or wherein at least one of the $-CH_2-$ groups is substituted with -OH, -NHR', or -COOR', wherein R' represents H or C(1-8)alkyl,

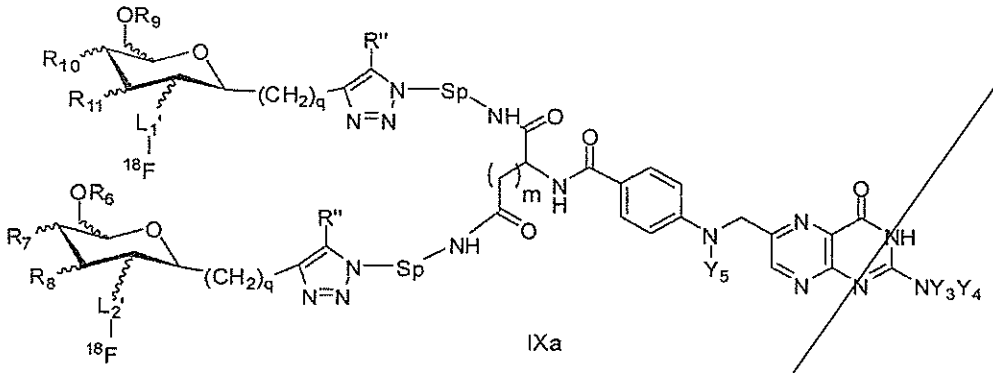
L_1' is a covalent bond or a straight-chain or branched C(1-6)alkyl, wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

q is 0, 1, 2, 3 or 4,

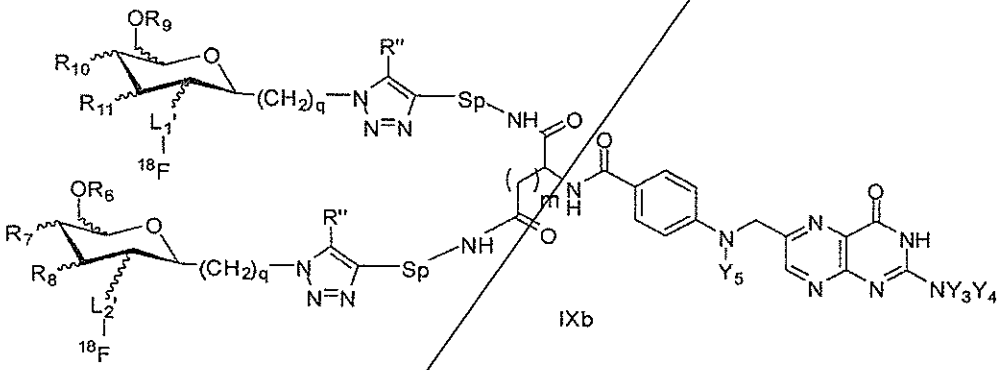
R_9 is H or C(1-8)alkyl, and

R_{10},R_{11} are independently of each other H, -OH, or -OC(1-8)alkyl.

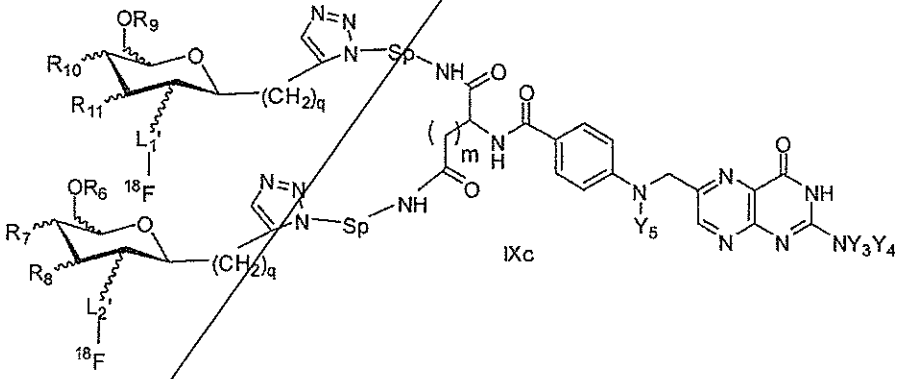
19. A compound according to any preceding claim having formulae IXa, IXb, IXc, IXd



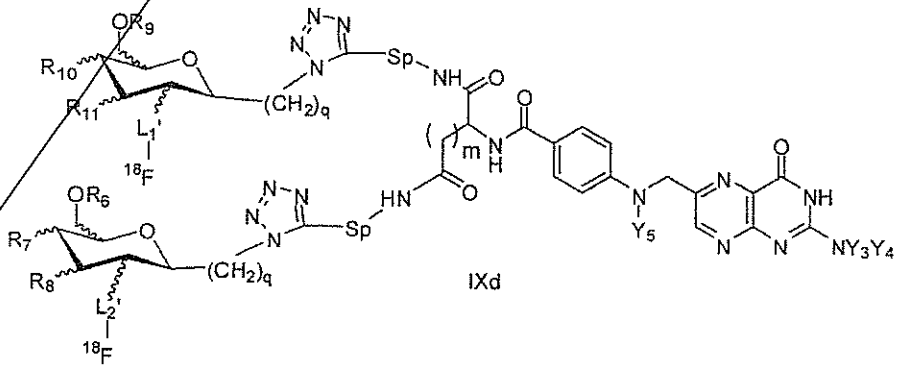
IXa



IXb



IXc



IXd

wherein

Y_3, Y_4 are independently of each other selected from H, halo, C(1-12)alkyl, C(2-12)alkenyl, C(2-12)alkynyl, -OR', -COR', -COOR', and -NHR', wherein R' is H or C(1-8)alkyl,

Y_5 is selected from H, nitroso, C(1-12)alkyl, -OR', -COR', and halosubstituted -COR', wherein R' is H or C(1-12)alkyl,

m is 1, 2 or 3,

Sp are independently of each other a spacer such as a straight-chain or branched C(1-8)alkyl, which is unsubstituted or wherein at least one of the $-CH_2-$ groups is substituted with -OH, -NHR', or -COOR', wherein R' represents H or C(1-8)alkyl,

L_1',L_2' are independently of each other a covalent bond or a straight-chain or branched C(1-6)alkyl, wherein one or more of the non-adjacent CH_2 groups may independently be replaced by a group selected from -O-, -CO-O-,-O-CO-,-NR'-,-NR'-CO-,-CO-NR', wherein R' represents H or C(1-8)alkyl,

q is 0, 1, 2, 3 or 4,

R_6,R_9 are independently of each other H or C(1-8)alkyl, and

R_7,R_8,R_{10},R_{11} are independently of each other H, -OH, or -OC(1-8)alkyl

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

21. Use of a compound according to claims 1 to 19 or a pharmaceutical composition according to claim 20 for diagnostic imaging of a cell or population of cells

expressing a folate-receptor in vitro or in vivo.

22. Use of a compound according to claims 1 to 19 or a pharmaceutical composition according to claim 20 for convenient and effective administration to a subject in need for diagnostic imaging.

23. 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 claims 1 to 19 in a diagnostic imaging amount, and obtaining a diagnostic image of said cell or population of cells.

24. Method according to claim 23, wherein the diagnostic imaging is performed of a cell or population of cells expressing a folate-receptor in vitro or in vivo.

25. 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 claims 1 to 19 in effective amounts and for sufficient time and conditions to allow binding to occur and detecting such binding by PET imaging.

26. Method of diagnostic imaging and/or monitoring a subject comprising the steps of (i) administering at least one compound according to claims 1 to 19 in a diagnostic imaging amount, and (ii) performing diagnostic imaging using PET by detecting a signal from said at least one compound.

27. 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 claims 1 to 19 in a diagnostic imaging amount in combination with a therapeutically active compound of choice, and (ii) performing diagnostic imaging using PET by detecting a signal from said at least one compound to follow the course of cancer therapy.

28. Method of claims 26 or 27 used in combination with any other methods of cancer diagnosis or therapy.

Claims:

1. An invention not claimed in any divisional application.