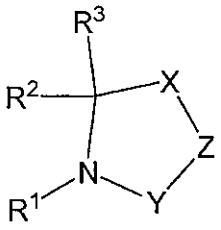
Claims

1. A radiolabelled glutaminyl cyclase (QC) inhibitor for use as an imaging agent.

2. The inhibitor of claim 1, which is a compound of formula (I):



(I)

or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof wherein:

R^1 represents heteroaryl, -carbocyclyl-heteroaryl, -C_{2-6}alkenylheteroaryl, -C_{1-6}alkylheteroaryl, or $(CH_2)_aCR^5R^6(CH_2)_b$heteroaryl wherein a and b independently represent integers 0-5 provided that a + b = 0-5 and R^5 and R^6 are alkylene which together with the carbon to which they are attached form a C_3-C_5 cycloalkyl group;

in which any of aforesaid heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -C(O)C_{1-6}alkyl, -C(O)OC_{1-6}alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, -NH_2, -NHC_{1-4}alkyl, -N(C_{1-4}alkyl)(C_{1-4}alkyl), -C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl), -C(O)NH_2, -C(O)NH(C_{1-4}alkyl) and -C(O)NH(C_{3-10}cycloalkyl);

and in which any of aforesaid carbocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen and C_{1-4}alkoxy;

R^2 represents H, C_{1-8}alkyl, aryl, heteroaryl, carbocyclyl, heterocyclyl, -C_{1-4}alkylaryl, -C_{1-4}alkylheteroaryl, -C_{1-4}alkylcarbocyclyl or -C_{1-4}alkylheterocyclyl;

in which any of aforesaid aryl and heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -C(O)C_{1-6}alkyl, -C(O)OC_{1-6}alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, C_{1-6}alkoxy-C_{1-6}alkoxy-, nitro, halogen, haloC_{1-6}alkyl, haloC_{1-6}alkoxy, cyano, hydroxyl, -C(O)OH, -NH_2, -NHC_{1-4}alkyl, -N(C_{1-4}alkyl)(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl)-N(C_{1-4}alkyl)(C_{1-4}alkyl), -C_{1-4}alkyl-N(C_{1-4}alkyl)(C_{1-4}alkyl), -C_{1-4}alkoxy-N(C_{1-4}alkyl)(C_{1-4}alkyl), -N(C_{3-8}cycloalkyll)(C_{3-8}cycloalkyl), -N(-C_{1-6}alkyl-C_{1-}

$_{6}$alkoxy)(-C_{1-6}alkyl-C_{1-6}alkoxy), -C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl), -$C(O)NH_2$, -C(O)NH(C_{1-4}alkyl) and -C(O)NH(C_{3-10}cycloalkyl);

and in which any of aforesaid carbocyclyl and heterocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen, -C(O)C_{1-4}alkyl and C_{1-4}alkoxy;

or R^2 represents phenyl substituted by phenyl, phenyl substituted by a monocyclic heteroaryl group, phenyl substituted by phenoxy, phenyl substituted by heterocyclyl, phenyl substituted by heterocyclyl wherein said heterocyclyl is substituted by phenyl, phenyl substituted by –O-C_{1-4}alkyl-heterocyclyl, phenyl substituted by benzyloxy, phenyl substituted by carbocyclyl, phenyl substituted by carbocyclyl wherein said carbocyclyl is substituted by heterocyclyl, phenyl substituted by –O-carbocyclyl, heterocyclyl substituted by phenyl, carbocyclyl substituted by phenyl, phenyl fused to carbocyclyl, phenyl fused to heterocyclyl, -C_{1-4}alkyl(phenyl substituted by phenyl), -C_{1-4}alkyl(phenyl substituted by a monocyclic heteroaryl group), -C_{1-4}alkyl(phenyl substituted by a monocyclic heterocyclyl group), -C_{1-4}alkyl(phenyl substituted by an –O-carbocyclyl group), -C_{1-4}alkyl(phenyl substituted by benzyloxy), -C_{1-4}alkyl(optionally substituted phenyl fused to optionally substituted carbocyclyl or -C_{1-4}alkyl(optionally substituted phenyl fused to optionally substituted heterocyclyl);

in which any of aforesaid phenyl, benzyloxy and heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy,

and in which any of aforesaid carbocyclyl and heterocyclyl groups may optionally be substituted by one or more groups selected from methyl, phenyl, oxo, halogen, hydroxyl and C_{1-4}alkoxy;

R^3 represents H, -C_{1-4}alkyl or aryl;

in which aforesaid aryl may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -C(O)C_{1-6}alkyl, -C(O)OC_{1-6}alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, $-NH_2$, -NHC_{1-4}alkyl, -N(C_{1-4}alkyl)(C_{1-4}alkyl), -C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl), $-C(O)NH_2$, -C(O)NH(C_{1-4}alkyl) and, -C(O)NH(C_{3-10}cycloalkyl);

or R^2 and R^3 are joined to form a carbocyclyl ring which is optionally substituted by one or more C_{1-2}alkyl groups;

or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to phenyl, wherein aforesaid carbocyclyl and/or phenyl may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy;

or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to monocyclic heteroaryl, wherein aforesaid carbocyclyl and/or heteroaryl may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy;

X represents C=O, O, S, CR^7R^8, -O-CH_2- or –CH_2-CH_2-;

Y represents CHR^9, C=O or C=S;

Z represents –N-R^4, O or CHR^{10}, such that when X represents O or S, Z must represent CHR^{10};

or X and Z represent two adjacent carbon atoms of a phenyl ring which is fused in that position and which is optionally substituted by one or more halogen or C_{1-2}alkyl groups;

R^4 represents H, -C_{1-8}alkyl, -C(O)C_{1-6}alkyl or –NH_2;

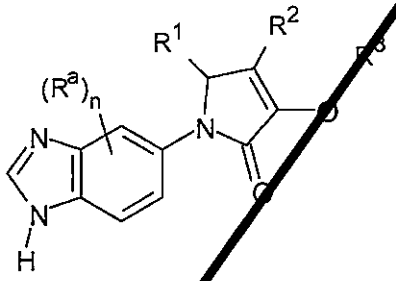
R^7 and R^8 independently represent H, -C_{1-4} alkyl or aryl;

in which said aforesaid aryl may be optionally substituted by C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -C(O)C_{1-6}alkyl, -C(O)OC_{1-6}alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, -NH_2, -NHC_{1-4}alkyl, -N(C_{1-4}alkyl)(C_{1-4}alkyl), -C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl), -C(O)NH_2, -C(O)NH(C_{1-4}alkyl) and, -C(O)NH(C_{3-10}cycloalkyl);

R^9 and R^{10} independently represent H or methyl;

provided that the moiety –Y-Z-X- represents a moiety other than –C(=O)-N(-R^4)-C(=O)- or -C(=S)-N(-R^4)-C(=O)-;

or a compound of formula (II):



(II)

or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof wherein:

R^1 represents -C_{1-6}alkyl, -aryl, -C_{1-6}alkylaryl, -cycloalkyl, -C_{1-6}alkylcycloalkyl, -heteroaryl, -C_{1-6}alkylheteroaryl, -heterocyclyl, -C_{1-6}alkylheterocyclyl, -cycloalkyl substituted by phenyl, -cycloalkyl substituted by phenoxy, -phenyl substituted by cycloalkyl, -phenyl substituted by phenoxy, -phenyl substituted by phenyl, heterocyclyl substituted by phenyl, heteroaryl substituted by phenyl, phenyl substituted by heterocyclyl, phenyl substituted by heteroaryl, phenyl substituted by –O-cycloalkyl or phenyl substituted by –cycloalkyl-heterocyclyl;

and in which any of aforesaid aryl, cycloalkyl, heterocyclyl, heteroaryl, phenyl or phenoxy groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, $-NH_2$, -NHC_{1-4}alkyl, -$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)NH_2$, -$C(O)NH(C_{1-4}alkyl)$ and -$C(O)NH(C_{3-10}cycloalkyl)$;

R^2 represents -C_{1-6}alkyl, C_{1-6}haloalkyl, -aryl, -C_{1-6}alkylaryl, -cycloalkyl, -C_{1-6}alkylcycloalkyl, -heteroaryl, -C_{1-6}alkylheteroaryl, -heterocyclyl or -C_{1-6}alkylheterocyclyl;

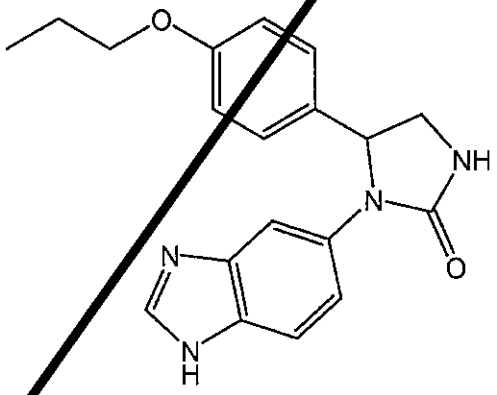
and in which any of aforesaid aryl, heteroaryl or heterocyclyl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, $-NH_2$, -NHC_{1-4}alkyl, -$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)NH_2$, -$C(O)NH(C_{1-4}alkyl)$ and -$C(O)NH(C_{3-10}cycloalkyl)$;

R^3 represents C_{1-6}alkyl or C_{1-6}haloalkyl;

n represents an integer selected from 0 to 3; and

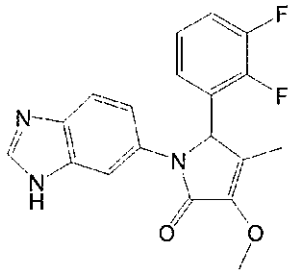
R^a represents C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, $-NH_2$, -NHC_{1-4}alkyl, -$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)NH_2$, -$C(O)NH(C_{1-4}alkyl)$ and -$C(O)NH(C_{3-10}cycloalkyl)$.

3. The inhibitor of claim 2, which is a compound of formula $(I)^a$:



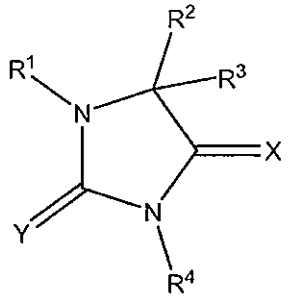
$(I)^a$

4. The inhibitor of claim 2, which is a compound of formula $(II)^a$:



(II)[a]

5. The inhibitor of claim 1, which is a compound of formula (III):



(III)

or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof wherein:

R^1 represents -C_{3-8}carbocyclyl-heteroaryl, -C_{2-6}alkenylheteroaryl, -C_{1-6}alkylheteroaryl, or $(CH_2)_aCR^5R^6(CH_2)_b$heteroaryl wherein a and b independently represent integers 0-5 provided that a + b = 0-5 and R^5 and R^6 are alkylene which, together with the carbon to which they are attached, form a C_3-C_5 cycloalkyl group, or a bicyclic heteroaryl group;

in which any of aforesaid heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, -NH_2, -NHC_{1-4}alkyl, -$N(C_{1-4}$alkyl)(C_{1-4}alkyl), -$C(O)N(C_{1-4}$alkyl)(C_{1-4}alkyl), -$C(O)NH_2$, -$C(O)NH(C_{1-4}$alkyl) and -$C(O)NH(C_{3-10}$cycloalkyl);

and in which any of aforesaid carbocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen and C_{1-4}alkoxy;

R^2 represents C_{1-8}alkyl, aryl, heteroaryl, carbocyclyl, heterocyclyl, -C_{1-4}alkylaryl, -C_{1-4}alkylheteroaryl, -C_{1-4}alkylcarbocyclyl or -C_{1-4}alkylheterocyclyl;

in which any of aforesaid aryl and heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, $-NH_2$, -NHC_{1-4}alkyl, -$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)NH_2$, -$C(O)NH(C_{1-4}alkyl)$ and -$C(O)NH(C_{3-10}cycloalkyl)$;

and in which any of aforesaid carbocyclyl and heterocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen and C_{1-4}alkoxy;

or R^2 represents phenyl substituted by phenyl, phenyl substituted by a monocyclic heteroaryl group, phenyl substituted by benzyloxy, phenyl fused to carbocyclyl, phenyl fused to heterocyclyl, -C_{1-4}alkyl(phenyl substituted by phenyl), -C_{1-4}alkyl(phenyl substituted by a monocyclic heteroaryl group), -C_{1-4}alkyl(phenyl substituted by benzyloxy), -C_{1-4}alkyl(optionally substituted phenyl fused to optionally substituted carbocyclyl or -C_{1-4}alkyl(optionally substituted phenyl fused to optionally substituted heterocyclyl);

in which any of aforesaid phenyl, benzyloxy and heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy,

and in which any of aforesaid carbocyclyl and heterocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen and C_{1-4}alkoxy;

R^3 represents H, -C_{1-4}alkyl or aryl;

in which aforesaid aryl may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, -C_{1-6}thioalkyl, -SOC_{1-4}alkyl, -SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, -O-C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, -SO_2C_{3-8}cycloalkyl, -SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, -$C(O)C_{1-6}$alkyl, -$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, -C(O)OH, $-NH_2$, -NHC_{1-4}alkyl, -$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, -$C(O)NH_2$, -$C(O)NH(C_{1-4}alkyl)$ and, -$C(O)NH(C_{3-10}cycloalkyl)$;

or R^2 and R^3 are joined to form a carbocyclyl ring which is optionally substituted by one or more C_{1-2}alkyl groups;

or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to phenyl, wherein aforesaid carbocyclyl and/or phenyl may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy;

or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to monocyclic heteroaryl, wherein aforesaid carbocyclyl and/or heteroaryl may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy;

R^4 represents H, -C_{1-8}alkyl, -$C(O)C_{1-6}$alkyl or $-NH_2$;

X represents O or S; and

Y represents O or S.

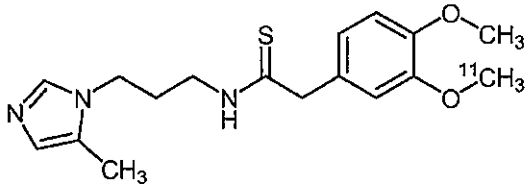
6. The inhibitor of any of claims 1 to 5, which comprises a single radiolabel.

7. The inhibitor of any of claims 1 to 6, wherein the radiolabel is selected from the group consisting of ^{2}H (D or deuterium), ^{3}H (T or tritium), ^{11}C, ^{13}C, ^{14}C, ^{13}N, ^{15}N, ^{15}O, ^{17}O, ^{18}O, ^{18}F, ^{35}S, ^{36}Cl, ^{82}Br, ^{75}Br, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I, ^{125}I and ^{131}I.

8. The inhibitor of any of claims 1 to 6, wherein the radiolabel is selected from the group consisting of ^{11}C, ^{13}C, ^{18}F, ^{19}F, ^{120}I, ^{123}I, ^{131}I, ^{75}Br and ^{76}Br.

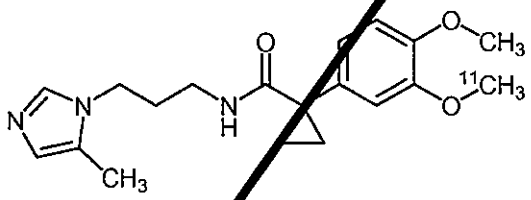
9. The inhibitor of claim 8, wherein the radiolabel is ^{11}C.

10. The inhibitor of claim 9, wherein the radiolabelled compound is a compound of formula (IV):



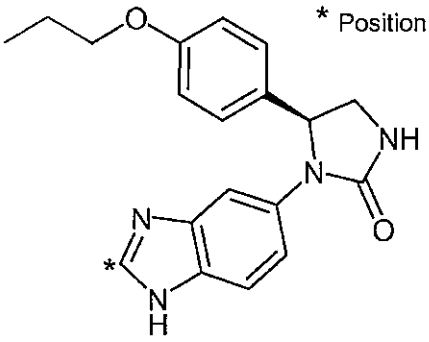
(IV)

11. The inhibitor of claim 9, wherein the radiolabelled compound is a compound of formula (V):



(V)

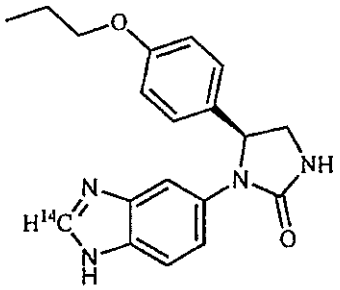
12. The inhibitor of claim 9, wherein the radiolabelled compound is a compound of formula (VI):



(I)[d]

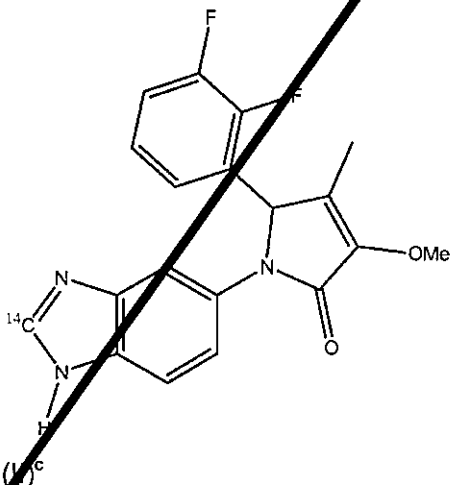
13. The inhibitor of claim 7, wherein the radiolabel is ^{14}C.

14. The inhibitor of claim 13, wherein the radiolabelled compound is a compound of formula (I)[c]:



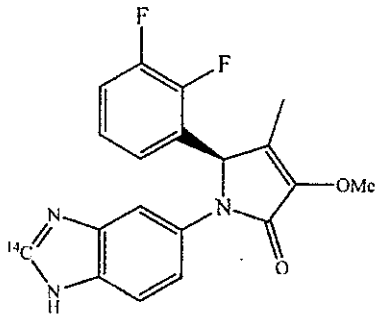
(I)[c]

15. The inhibitor of claim 13, wherein the radiolabelled compound is a compound of formula (II)[c]:



(II)[c]

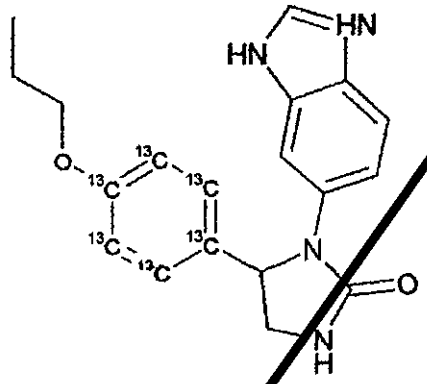
16. The inhibitor of claim 15, wherein the radiolabelled compound is a compound of formula (II)[d]:



(II)[d]

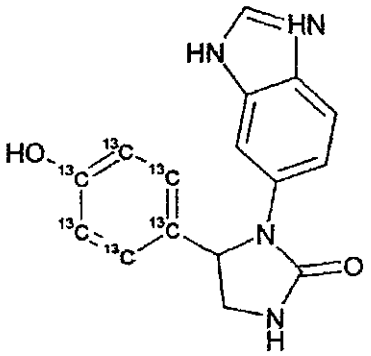
17. The inhibitor of claim 7, wherein the radiolabel is ^{13}C.

18. The inhibitor of claim 17, wherein the radiolabelled compound is a compound of formula (I)[e]:



(I)[e]

19. The inhibitor of claim 17, wherein the radiolabelled compound is a compound of formula (I)[f]:



(I)[f]

20. The inhibitor of any of claims 1 to 19, which is used as an imaging agent in the detection of a neurological disorder.

21. A pharmaceutical composition comprising a radiolabelled compound as defined in any of claims 1 to 19 or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof, in combination with one or more pharmaceutically acceptable excipients.

22. The pharmaceutical composition of claim 21, for use as an imaging agent in the detection of a neurological disorder.

23. The inhibitor or composition of claim 20 or claim 22, wherein the neurological disorder is mild cognitive impairment, Alzheimer's disease, Familial British Dementia, Familial Danish Dementia, neurodegeneration in Down Syndrome and Huntington's disease, such as Alzheimer's disease.

24. The inhibitor or composition of any of claims 20 to 23, for use in the detection of amyloid peptides.

25. The inhibitor or composition of any of claims 20 to 24, for use in the detection of tau proteins of neurofibrillary tangles.

26. A method for imaging and detection of senile plaques and/or neurofibrillary tangles in brain tissue, the method comprising treating the tissue with an inhibitor as defined in any of claims 1 to 19 for detection of neurological disorders.

27. A method according to claim 26 wherein the neurological disorder is detected by measuring the affinity of an inhibitor as defined in any of claims 1 to 19 for senile plaques.

28. A method according to claim 26 wherein the neurological disorder is detected by measuring the affinity of an inhibitor as defined in any of claims 1 to 19 for tau aggregates.

29. A method for *ex vivo* or *in vitro* detection of amyloid deposits in a brain tissue, the method comprising treating the tissue with an inhibitor as defined in any of claims 1 to 19 for detection of the amyloid deposit.

30. A method for *in vivo* detection of amyloid deposits in a patient, the method comprising administering an effective amount of an inhibitor as defined in any of claims 1 to 19 to the patient, and detecting the binding level of the compound to the amyloid deposit to the patient.

31. A method for *ex vivo* or *in vitro* detection of tau proteins in a brain tissue, the method comprising treating the tissue with an inhibitor as defined in any of claims 1 to 19 for detection of the neurofibrillary tangles.

32. A method for *in vivo* detection of neurofibrillary tangles in a patient, the method comprising administering an effective amount of an inhibitor as defined in any of claims 1 to 19 to the patient, and detecting the binding level of the compound to tau proteins.

33. The method of any of claims 26 to 32, wherein the detection is performed using gamma imaging, magnetic resonance imaging, magnetic resonance spectroscopy or fluorescence spectroscopy.

34. The method of claim 33, wherein the detection by gamma imaging is PET or SPECT.

35. A kit for diagnosing a neurological disorder which comprises a pharmaceutical composition as defined in claim 21 and instructions to use said kit in accordance with the methods described in any of claims 26 to 34.

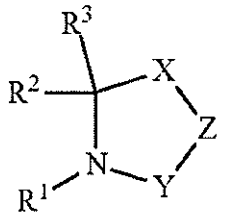
36. The kit of claim 35, wherein the neurological disorder is mild cognitive impairment, Alzheimer's disease, Familial British Dementia, Familial Danish Dementia, neurodegeneration in Down Syndrome and Huntington's disease, such as Alzheimer's disease.

What is claimed is:

1. A radiolabeled glutaminyl cyclase (QC) inhibitor for use as an imaging agent, comprising: a radiolabel selected from the group consisting of ^{2}H (D or deuterium), ^{3}H (T or tritium), ^{11}C, ^{14}C, ^{13}N, ^{15}N, ^{15}O, ^{17}O, ^{18}O, ^{18}F, ^{35}S, ^{36}Cl, ^{82}Br, ^{75}Br, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I, ^{125}I, and ^{131}I: and

a QC inhibitor compound of formula (I),

(I)



or a pharmaceutically acceptable salt, including all tautomers and stereoisomers thereof;

wherein

R^1 represents heteroaryl, -carbocyclyl-heteroaryl, —C_{2-6}alkenylheteroaryl, —C_{1-6}-alkylheteroaryl, or $(CH_2)_aCR^5R^6(CH_2)_b$heteroaryl wherein a and b independently represent integers 0-5 provided that a+b=0-5 and R^5 and R^6 are alkylene which together with the carbon to which they are attached form a C_3-C_5cycloalkyl group;

in which any of aforesaid heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, —C1-6thioalkyl, —SOC_{1-4}alkyl, —SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, —O—C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, —SO_2C_{3-8}cycloalkyl, —SOC_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, —$C(O)C_{1-6}$alkyl, —C(O)OC_{1-6}alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, —C(O)OH, —NH_2, —NHC_{1-4}alkyl, —$N(0_{1-4}$alkyl)(C_{1-4}alkyl), —$C(O)N(C_{1-4}$alkyl)(C_{1-4}alkyl), —$C(O)NH_2$, —$C(O)NH(C_{1-4}$alkyl) and —$C(O)NH(C_{3-10}$cycloalkyl);

and in which any of aforesaid carbocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen and C_{1-4}alkoxy;

R^2 represents H, C_{1-8}alkyl, aryl, heteroaryl, carbocyclyl, heterocyclyl, —C_{1-4} alkylaryl, —C_{1-4}alkyl heteroaryl, —C_{1-4}alkylcarbocyclyl or —C_{1-4}alkyl heterocyclyl;

in which any of aforesaid aryl and heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, —C_{1-6}thioalkyl, —SOC_{1-4}alkyl, —SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, —O—C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, —SO_2C_{3-8}cycloalkyl, —SOC_{3-6}cycloalkyl, O_{3-6}alkenyloxy-, O_{3-6}alkynyloxy-, —$C(O)C_{1-6}$alkyl, —$C(O)OC_{1-6}$alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, C_{1-6}alkoxy-C_{1-6}alkoxy-, nitro, halogen, haloC_{1-6}alkyl, haloC_{1-6}alkoxy, cyano, hydroxyl, —C(O)OH, —NH_2, —NHC_{1-4}alkyl, —$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, —$N(C_{1-4}alkyl)(C_{1-4}alkyl)$-$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, —$C_{1-4}$alkyl-$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, —$C_{1-4}$alkoxy-$N(C_{1-4}alkyl)(C_{1-4}alkyl)$, —$N(C_{3-8}cycloalkyll)(C_{3-8}cycloalkyl)$, —N(—$C_{1-6}$alkyl-$C_{1-6}$alkoxy)(—$C_{1-6}$alkyl-$C_{1-6}$alkoxy), —$C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl)$, —$C(O)NH_2$, —$C(O)NH(C_{1-4}alkyl)$ and —$C(O)NH(C_{3-10}cycloalkyl)$;

and in which any of aforesaid carbocyclyl and heterocyclyl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, oxo, halogen, —$C(O)C_{1-6}$alkyl and C_{1-4}alkoxy;

or R^2 represents phenyl substituted by phenyl, phenyl substituted by a monocyclic heteroaryl group, phenyl substituted by phenoxy, phenyl substituted by heterocyclyl, phenyl substituted by heterocyclyl wherein said heterocyclyl is substituted by phenyl, phenyl substituted by —O—C_{1-4}alkyl-heterocyclyl, phenyl substituted by benzyloxy, phenyl substituted by carbocyclyl, phenyl substituted by carbocyclyl wherein said carbocyclyl is

substituted by heterocyclyl, phenyl substituted by —O-carbocyclyl, heterocyclyl substituted by phenyl, carbocyclyl substituted by phenyl, phenyl fused to carbocyclyl, phenyl fused to heterocyclyl, —C_{1-4}alkyl(phenyl substituted by phenyl), —C_{1-4}alkyl(phenyl substituted by a monocyclic heteroaryl group), —C_{1-4}alkyl(phenyl substituted by a monocyclic heterocyclyl group), —C_{1-4}alkyl(phenyl substituted by an —O-carbocyclyl group), —C_{1-4}alkyl(phenyl substituted by benzyloxy), —C_{1-4}alkyl(optionally substituted phenyl fused to optionally substituted carbocyclyl or —C_{1-4}alkyl(optionally substituted phenyl fused to optionally substituted heterocyclyl);

in which any of aforesaid phenyl, benzyloxy and heteroaryl groups may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy, and in which any of aforesaid carbocyclyl and heterocyclyl groups may optionally be substituted by one or more groups selected from methyl, phenyl, oxo, halogen, hydroxyl and C_{1-4}alkoxy;

R^3 represents H, —C_{1-4}alkyl or aryl;

in which aforesaid aryl may optionally be substituted by one or more groups selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, —C_{1-6}thioalkyl, —SOC_{1-4}alkyl, —SO_2C_{1-4} alkyl, C_{1-6}alkoxy-, —O—C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, —SO_2C_{3-8}cycloalkyl, —SOC_{3-6} cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, —C(O)C_{1-6}alkyl, —C(O)OC_{1-6}alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, —C(O)OH, —NH_2, —NHC_{1-4}alkyl, —N(C_{1-4} alkyl)(C_{1-4}alkyl), —C(O)N(C_{1-4}alkyl)(C_{1-4}alkyl), —C(O)NH_2, —C(O)NH(C_{1-4}alkyl) and, —C(O)N H(C_{3-10}cycloalkyl);

or R^2 and R^3 are joined to form a carbocyclyl ring which is optionally substituted by one or more C_{1-2}alkyl groups;

or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to phenyl, wherein aforesaid carbocyclyl and/or phenyl may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy;

or R^2 and R^3 are joined to form a carbocyclyl ring which is fused to monocyclic heteroaryl, wherein aforesaid carbocyclyl and/or heteroaryl may optionally be substituted by one or more groups selected from C_{1-4}alkyl, halogen and C_{1-4}alkoxy;

X represents C═O, O, S, CR^7R^8, —O—CH_2— or —CH_2—CH_2—;

Y represents CHR^9, C═O or C═S;

Z represents —N—R^4, O or CHR^{10}, such that when X represents O or S, Z must represent CHR^{10};

or X and Z represent two adjacent carbon atoms of a phenyl ring which is fused in that position and which is optionally substituted by one or more halogen or C_{1-2}alkyl groups;

R^4 represents H, —C_{1-8}alkyl, —C(O)C_{1-6}alkyl or —NH_2;

R^7 and R^8 independently represent H, —C_{1-4} alkyl or aryl;

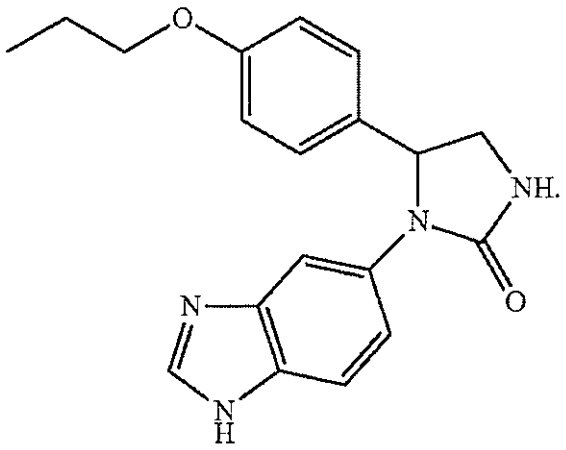
in which said aforesaid aryl may be optionally substituted by C_{1-6}alkyl, C_{2-6} alkenyl, C_{2-6}alkynyl, C_{1-6}haloalkyl, —C_{1-6}thioalkyl, —S O C_{1-4}alkyl, —SO_2C_{1-4}alkyl, C_{1-6}alkoxy-, —O—C_{3-8}cycloalkyl, C_{3-8}cycloalkyl, —SO_2C_{3-8}cycloalkyl, —S O C_{3-6}cycloalkyl, C_{3-6}alkenyloxy-, C_{3-6}alkynyloxy-, —C(O)C_{1-6}alkyl, —C(O)OC_{1-6}alkyl, C_{1-6}alkoxy-C_{1-6}alkyl-, nitro, halogen, cyano, hydroxyl, —C(O)OH, —NH_2, —N H C_{1-4}alkyl, —N(C_{1-4}alkyl)(C_{1-4}alkyl), —C(O)N(C_{1-4} alkyl)(C_{1-4}alkyl), —C(O)NH_2, —C(O)NH(C_{1-4}alkyl) and, —C(O)NH(C_{3-10}cycloalkyl);

R^9 and R^{10} independently represent H or methyl;

provided that the moiety —Y—Z—X— represents a moiety other than —C(═O)—N(—R^4)—C(═O)— or —C(═S)—N(—R^4)—C(═O)—.

2. The radiolabeled QC inhibitor of claim **1**, wherein the QC inhibitor is a compound of formula (I)[a]:

(I)[a]



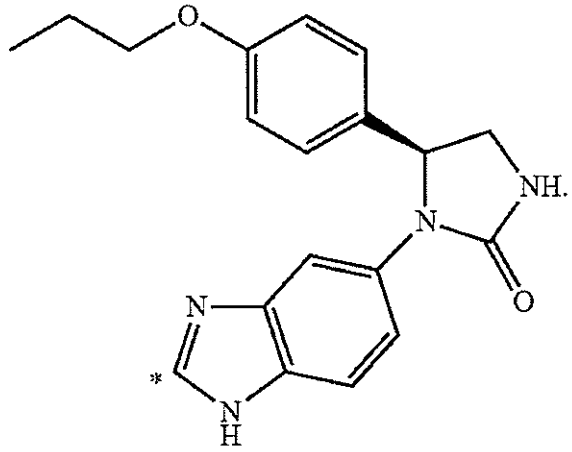
3. The radiolabeled QC inhibitor of claim **1**, comprising a single radiolabel.

4. The radiolabeled QC inhibitor of claim **1**, wherein the radiolabel is selected from the group consisting of ^{11}C, ^{18}F, ^{19}F, ^{120}I, ^{123}I, ^{131}I, ^{75}Br, and ^{76}Br.

5. The radiolabeled QC inhibitor of claim **4**, wherein the radiolabel is ^{11}C.

6. The radiolabeled QC inhibitor of claim **5**, wherein the radiolabel and compound are according to formula (I)[d]:

(I)[d]



* Position ^{11}C-Label

7. The radiolabeled QC inhibitor of claim **1**, wherein the radiolabel is ^{14}C.

8. The radiolabeled QC inhibitor of claim **7**, wherein the radiolabel and compound are according to formula (I)^c:

(I)^c

