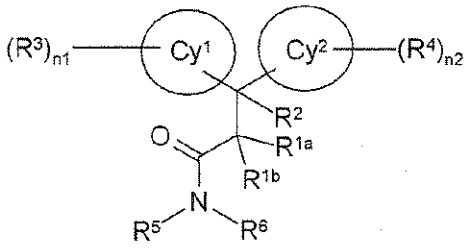
WHAT IS CLAIMED IS:

1. A method for preventing, treating or ameliorating in a mammal a disease or condition that is causally related to RORγt activity in vivo, which comprises administering to the mammal an effective disease-treating or condition-treating amount of a compound according to formula I:



I

or a pharmaceutically acceptable salt, solvate or prodrug thereof;
or stereoisomers, isotopic variants and tautomers thereof;
wherein
each Cy^1 and Cy^2 is independently selected from substituted or unsubstituted aryl and heteroaryl;
each n1 and n2 is independently 1, 2, 3, 4 or 5;
each R^{1a} and R^{1b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, or CN; or R^{1a} and R^{1b} joined together to form cycloalkyl ring;
R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;
or one of R^{1a} and R^{1b} is joined to the C of CR^2 to form a cyclopropyl ring; or R^2 is joined to the C of $CR^{1a}R^{1b}$ to form a cyclopropyl ring;
each R^3 and R^4 is independently selected from H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or

unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thiol; or any two adjacent R^3 groups, or any two adjacent R^4 groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring;

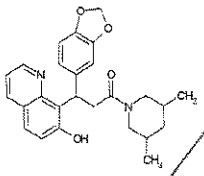
each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl; or

R^5 and R^6, together with the N they are attached to, form a 4-12 membered substituted or unsubstituted heterocycloalkyl;

provided that

i) at least one of Cy^1 and Cy^2 is heteroaryl; and

ii) when the compound is



;

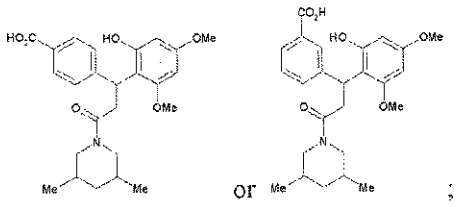
then the compound is in the form of an acid addition salt;

or

provided that

i) when each of Cy^1 and Cy^2 is phenyl; then at least one R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; and wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

ii) when the compound is



or

;

then the compound is in the form of a sodium, potassium, calcium, or ammonium salt; and

iii) the compound is other than the compounds listed in Table 1, wherein compound ID is 83, 84, 95, 100, 111, or 139.

2. The method according to claim 1, wherein each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted and unsubstituted cycloalkyl, and substituted and unsubstituted phenyl.

3. The method according to claim 1, wherein one of R^5 and R^6 is H or Me; and the other is independently selected from H, substituted or unsubstituted alkyl, substituted and unsubstituted cycloalkyl, and substituted and unsubstituted phenyl.

4. The method according to claim 1, wherein each R^5 and R^6 is independently selected from substituted or unsubstituted alkyl.

5. The method according to claim 1, wherein each R^5 and R^6 is independently selected from unsubstituted alkyl.

6. The method according to claim 1, wherein each R^5 and R^6 is independently selected from H, Me, Et, n-Pr, i-Pr, n-Bu, and t-Bu.

7. The method according to claim 1, wherein each R^5 and R^6 is independently selected from H, and alkyl substituted with hydroxyl, amino, alkylamino, dialkylamino, cylcloalkyl, heterocycloalkyl, aryl, and heteroaryl.

8. The method according to claim 1, wherein each R^5 and R^6 is independently selected from H, Me, Et, hydroxyethyl, hydroxypropyl, aminoethyl, aminopropyl, dimethylaminoethyl, dimethylaminopropyl, piperidinoethyl, morpholinoethyl, cyclopropylmethyl, benzyl, phenethyl, and furanylmethyl.

9. The method according to claim 1, wherein each R^5 and R^6 is independently selected from H, and cycloalkyl.

10. The method according to claim 1, wherein each R^5 and R^6 is independently selected from H, and cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

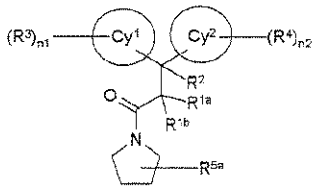
11. The method according to claim 1, wherein R^5 is H; and R^6 is selected from hydroxyethyl, hydroxypropyl, aminoethyl, aminopropyl, dimethylaminoethyl, dimethylaminopropyl, piperidinoethyl, morpholinoethyl, cyclopropylmethyl, cyclohexyl, benzyl, phenethyl, and furanylmethyl.

12. The method according to claim 1, wherein R^5 and R^6 are joined together to form a 4-12 membered substituted or unsubstituted heterocycloalkyl.

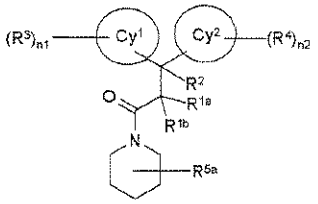
13. The method according to Claim 13, wherein R^5 and R^6 are joined together to form azetidinyl, pyrrolidinyl, piperidinyl, piperizinyl, morpholinyl, tetrahydroquinolinyl,

indolinyl, or azepinyl, unsubstituted or substituted with one or more alkyl, substituted alkyl, haloalkyl, alkoxyalkyl, hydroxyalkyl,alkoxy, hydroxyl, CN, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, amido, acyl, aroyl, or –CO-alkoxy.

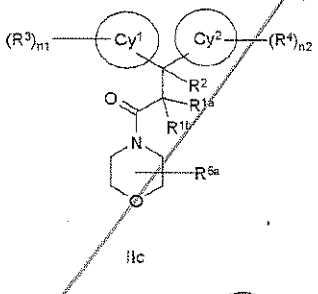
14. The method according to Claim 1, wherein the compound is according to formula IIa, IIb, IIc, IId, IIe, or IIf:



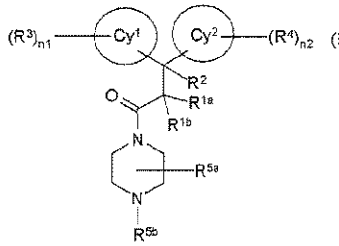
IIa



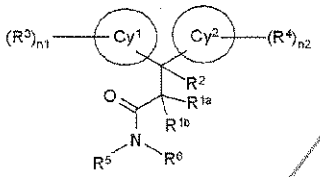
IIb



IIc

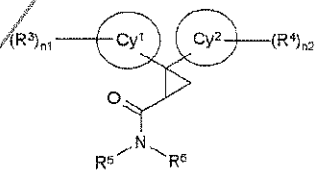


IId



IIe

or



IIf

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

and wherein Cy1, Cy2, n1, n2, R^{1a}, R^{1b}, R^2, R^3, R^4, R^5, and R^6 are as in claim 1; and each R^{5a} and R^{5b} is independently H, alkyl, substituted alkyl, haloalkyl, alkoxyalkyl, hydroxyalkyl,alkoxy, hydroxyl, CN, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, amido, acyl, aroyl, or –CO-alkoxy.

15. The method according to any one of claims 1-14, wherein each of Cy^1 and Cy^2 is phenyl.

16. The method according to any one of claims 1-14, wherein one of Cy^1 and Cy^2 is heteroaryl; and the other is phenyl.

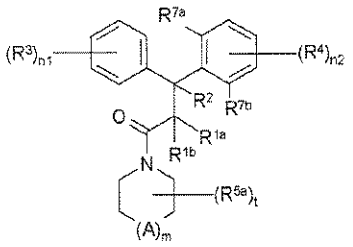
17. The method according to any one of claims 1-14, wherein each of Cy^1 and Cy^2 is heteroaryl.

18. The method according to any one of claims 1-17, wherein n2 is 1, 2, or 3.

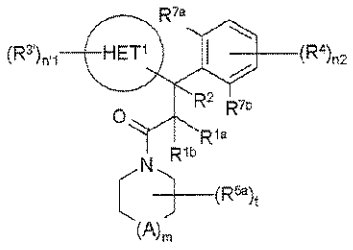
19. The method according to any one of claims 1-17, wherein n2 is 1, 2, or 3; and each R^4 is independenly selected from halo, C_1-C_6 alkyl, CN, OH, and C_1-C_6 alkoxy.

20. The method according to any one of claims 1-17, wherein n2 is 1, 2, or 3; and each R^4 is independenly selected from Cl, Me, OH, and C_1-C_6 alkoxy.

21. The method according to Claim 1, wherein the compound is according to formula IIIa, IIIb, or IIIc:

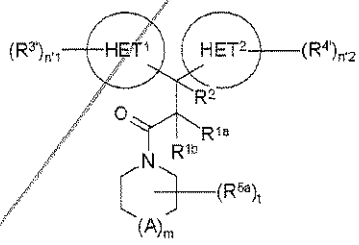


IIIa



IIIb

or



IIIc

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

wherein

n1, R^{1a}, R^{1b}, R^2, R^3, and R^4 are as in claim 1; n2 is 1, 2, or 3;

each HET^1 and HET^2 is independently selected from heteroaryl;

$R^{3'}$ is R^3; $R^{4'}$ is R^4; n'1 is n1; n'2 is n2;

A is $CR^{8a}R^{8b}$, NR^{8a}, O, or S; m is 0 or 1;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3;

R^{7a} is H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkylthio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted

arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thio;

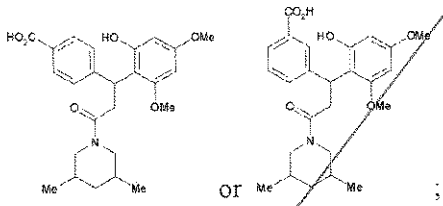
R^{7b} is R^4; or any two adjacent R^4 and R^{7b} groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring; and

each R^{8a} and R^{8b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

provided that

i) when the compound is according to formula IIIa, then at least one R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; and wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

ii) when the compound is



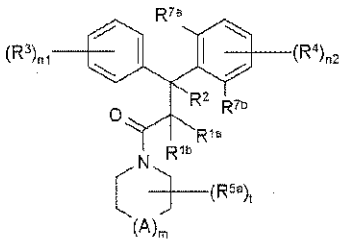
or

;

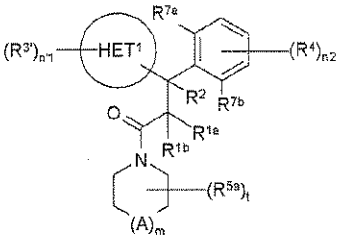
then the compound is in the form of a sodium, potassium, calcium, or ammonium salt; and

iii) the compound is other than the compounds listed in Table 1, wherein compound ID is 83, 84, 95, 100, 111, and 139.

22. A compound according to formula IIIa, IIIb, or IIIc:

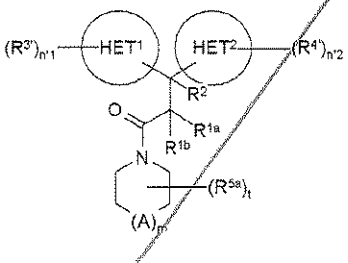


IIIa



IIIb

or



IIIc

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

wherein

n1, R^{1a}, R^{1b}, R^2, R^3, and R^4, are as described for formula I; n2 is 1, 2, or 3;

each HET^1 and HET^2 is independently selected from heteroaryl;

$R^{3'}$ is R^3; $R^{4'}$ is R^4; n'1 is n1; n'2 is n2;

A is $CR^{8a}R^{8b}$, NR^{8a}, O, or S; m is 0 or 1;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3;

R^{7a} is H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thio;

R^{7b} is R^4; or any two adjacent R^4 and R^{7b} groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring; and

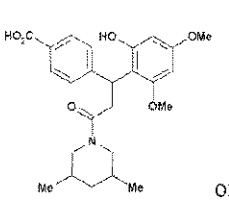
each R^{8a} and R^{8b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

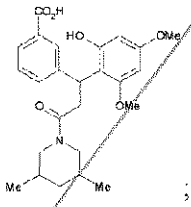
provided that

i) when the compound is according to formula IIIa, then at least one R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; and wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

ii) when the compound is according to formula IIIa, R^3 is $CONR^{3a}R^{3b}$, R^{3a} and R^{3b} joined together to form a morpholino ring, m is 1, and A is O; then R^{7a} is other than H;

iii) when the compound is



or


;

then the compound is in the form of a sodium, potassium, calcium, or ammonium salt;

iv) the compound is other than the compounds listed in Table 1, wherein compound ID is 83, 84, 95, 100, 111, and 139;

v) when the compound is according to formula IIIb; then R^{7a} is other than H;

vi) when the compound is according to formula IIIb, HET^1 is furanyl or quinolin-3-yl, and each of $R^{3'}$ and R^4 is H; then R^{7a} is other than H or methoxy;

vii) when the compound is according to formula IIIb, and HET^1 is pyrrolyl; then R^{7a} is other than H or methyl; and

viii) when the compound is according to formula IIIb; then HET^1 is other than benzopyranyl;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

23. The method or compound according to any one of Claims 21-22, wherein each of R^{7a} and R^{7b} is independently OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thio.

24. The method or compound according to any one of Claims 21-22, wherein each of R^{7a} and R^{7b} is independently OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, CN, halo, amido, or haloalkyl.

25. The method or compound according to any one of Claims 21-22, wherein each of R^{7a} and R^{7b} is independently halo, C_1-C_6 alkyl, CN, OH, or C_1-C_6 alkoxy.

26. The method or compound according to any one of Claims 21-22, wherein each of R^{7a} and R^{7b} is independently Cl, F, Me, CF_3, CN, OH, or OMe.

27. The method or compound according to any one of Claims 21-22, wherein one of R^{7a} and R^{7b} is OH; and the other is alkoxy.

28. The method or compound according to any one of Claims 21-22, wherein each of R^{7a} and R^{7b} is OH or alkoxy.

29. The method or compound according to any one of Claims 21-22, wherein one of R^{7a} and R^{7b} is OH; and the other is OMe.

30. The method or compound according to any one of Claims 1-29, wherein R^{1a} and R^{1b} is independently H, CN, or Me.

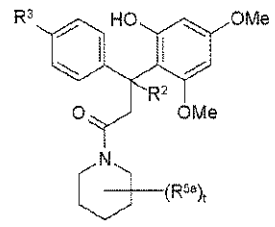
31. The method or compound according to any one of Claims 1-29, wherein each of R^{1a} and R^{1b} is H or Me.

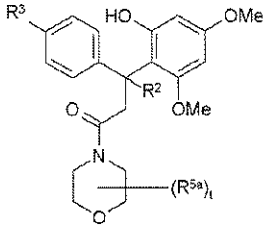
32. The method or compound according to any one of Claims 1-29, wherein one of R^{1a} and R^{1b} is H; and the other is CN.

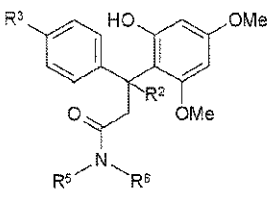
33. The method or compound according to any one of Claims 1-32, wherein m is 0.

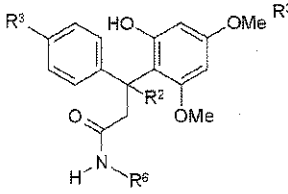
34. The method or compound according to any one of Claims 1-32, wherein m is 1; and A is C or N.

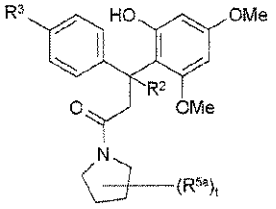
35. The method or compound according to any one of Claims 21-34, wherein HET^1 is selected from pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, triazolyl, oxadiazolyl, and thiadiazolyl.
36. The method or compound according to any one of Claims 21-34, wherein HET^1 is selected from pyridyl, pyrimidyl, and pyrazinyl.
37. The method or compound according to any one of Claims 21-34, wherein HET^1 is selected from indolyl, benzimidazolyl, 2-oxobenzimidazolyl, benzofuranyl, benzothiazolyl, and benzthiophenyl.
38. The method or compound according to any one of Claims 21-34, wherein HET^2 is selected from pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, triazolyl, oxadiazolyl, and thiadiazolyl.
39. The method or compound according to any one of Claims 21-34, wherein HET^2 is selected from pyridyl, pyrimidyl, and pyrazinyl.
40. The method or compound according to any one of Claims 21-34, wherein HET^2 is selected from indolyl, benzimidazolyl, 2-oxobenzimidazolyl, benzofuranyl, benzothiazolyl, and benzthiophenyl.
41. The method or compound according to any one of Claims 1-40, wherein R^4 is H, alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, alkoxyalkyl, amido, hydroxyl, cyano, or alkoxy.
42. The method or compound according to any one of Claims 1-40, wherein R^4 is H, halo, C_1-C_6 alkyl, CN, OH, or C_1-C_6 alkoxy.
43. The method or compound according to any one of Claims 1-40, wherein R^4 is H, Cl, F, Me, CF_3, CN, OH, or OMe.
44. The method or compound according to any one of Claims 1-43, wherein n1 is 1, 2 or 3.
45. The method or compound according to any one of Claims 1-43, wherein n1 is 1.
46. The method or compound according to either of Claims 1 or 22, wherein the compound is according to formula IVa, IVb, IVc, IVd, IVe, or IVf:


IVa

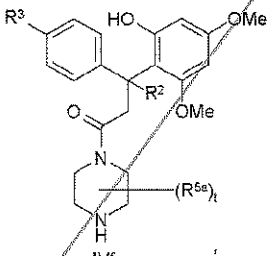

IVb


IVc


IVd


IVe

or


IVf

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

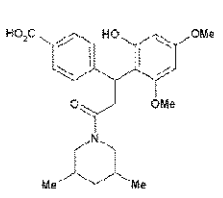
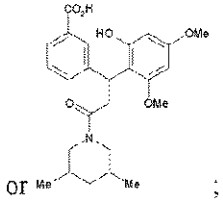
or stereoisomers, isotopic variants and tautomers thereof;

and wherein R^2, R^5, and R^6 are as in claim 1;

R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

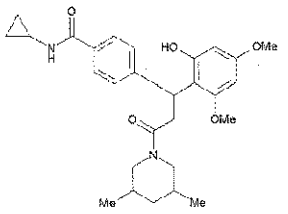
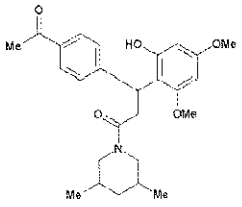
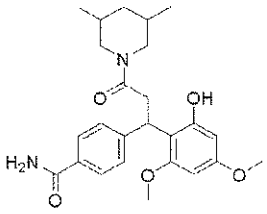
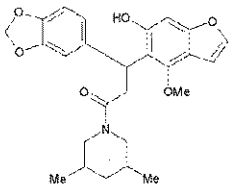
each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; t is 0, 1, 2, or 3; provided that

i) when the compound is



or ;

then the compound is in the form of a sodium, potassium, calcium, or ammonium salt; and

ii) the compound is other than

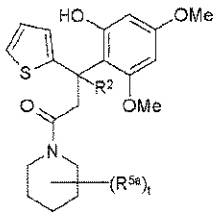





47. The method or compound according to any one of Claims 1-46, wherein R^3 is CO_2H.
48. The method or compound according to any one of Claims 1-46, wherein R^3 is SO_3H.
49. The method or compound according to any one of Claims 1-46, wherein R^3 is CH_2CO_2H.
50. The method or compound according to any one of Claims 1-46, wherein R^3 is heteroaryl.
51. The method or compound according to any one of Claims 1-46, wherein R^3 is pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, triazolyl, oxadiazolyl, thiadiazolyl, and tetrazolyl.
52. The method or compound according to any one of Claims 1-46, wherein R^3 is 1,3,4-triazolyl or tetrazol-5-yl.
53. The method or compound according to any one of Claims 1-46, wherein R^3 is $CONR^{3a}R^{3b}$; wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.
54. The method or compound according to any one of Claims 1-53, wherein R^{3b} is H.
55. The method or compound according to any one of Claims 1-53, wherein R^{3b} is alkyl.
56. The method or compound according to any one of Claims 1-53, wherein R^{3b} is Me, Et, or i-Pr.
57. The method or compound according to any one of Claims 1-46, wherein R^3 is selected from COR^{3a}, SOR^{3a}, and SO_2R^{3a}; wherein R^{3a} is selected from substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.

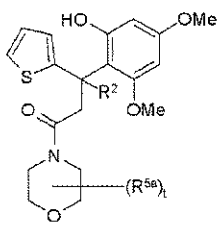
58. The method or compound according to any one of Claims 1-57, wherein R^{3a} is alkyl.

59. The method or compound according to any one of Claims 1-57, wherein R^{3a} is Me, Et, or i-Pr.

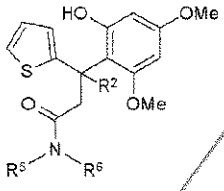
60. The method or compound according to either of Claims 1 or 22, wherein the compound is according to formula Va, Vb, Vc, Vd, Ve, or Vf:



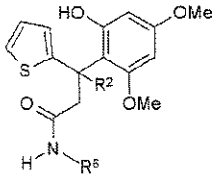
Va



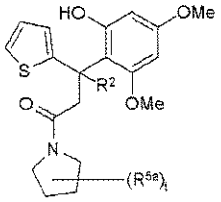
Vb



Vc

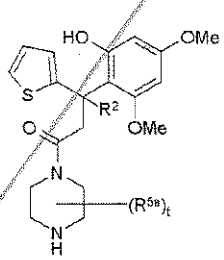


Vd



Ve

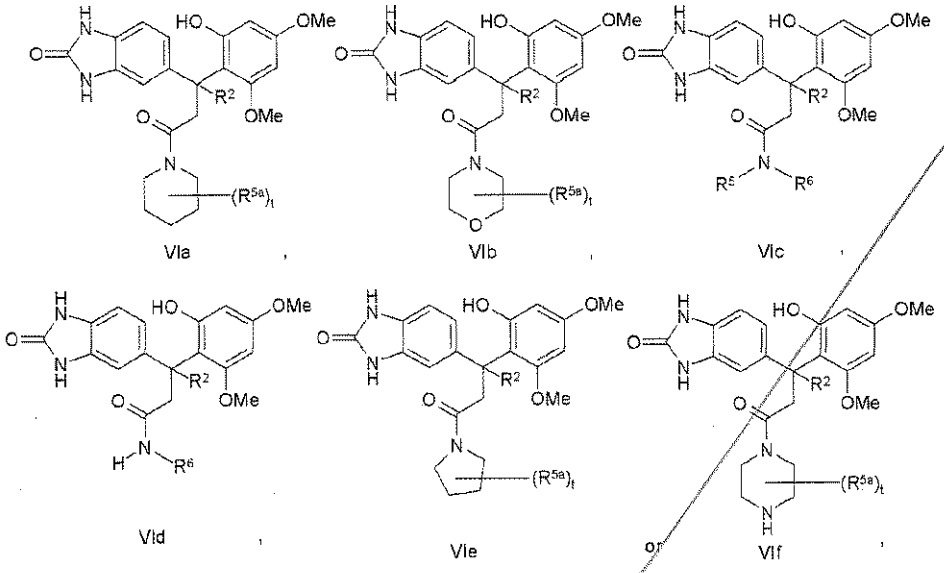
or



Vf

or a pharmaceutically acceptable salt, solvate or prodrug thereof;
or stereoisomers, isotopic variants and tautomers thereof;
and wherein R^2, R^5, and R^6 are as in claim 1; each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; t is 0, 1, 2, or 3.

61. The method or compound according to either of Claims 1 or 22, wherein the compound is according to formula VIa, VIb, VIc, VId, VIe, or VIf:



or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

and wherein R^2, R^5, and R^6 are as in claim 1; each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3.

62. The method or compound according to any one of Claims 1-61, wherein R^2 is OH.

63. The method or compound according to any one of Claims 1-61, wherein R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or substituted or unsubstituted phenyl.

64. The method or compound according to any one of Claims 1-61, wherein R^2 is H, Me, or Ph.

65. The method or compound according to any one of Claims 1-61, wherein R^2 is H.

66. The method or compound according to any one of Claims 21-65, wherein t is 0.

67. The method or compound according to any one of Claims 21-65, wherein t is 1 or 2; and each R^{5a} is independently OH, Ph, benzyl, or Me.

68. The method or compound according to any one of Claims 21-65, wherein t is 1; and R^{5a} is Me, Et, n-Pr, or n-Bu.

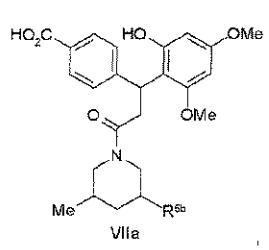
69. The method or compound according to any one of Claims 21-65, wherein t is 1; and R^{5a} is 3-Me, 3-Et, 3-n-Pr, or 3-n-Bu.

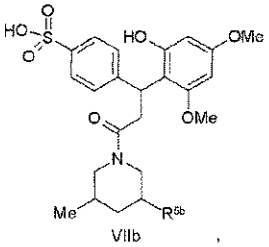
70. The method or compound according to any one of Claims 21-65, wherein t is 2; and one R^{5a} is 3-Me and the other is 5-Me.

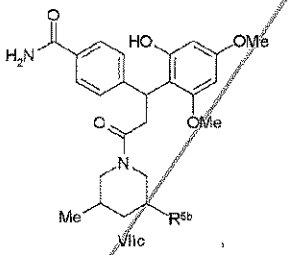
71. The method according to any one of Claims 21-61, wherein R^5 is Me, or Et.

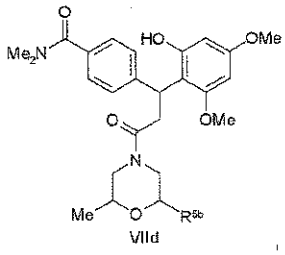
72. The method according to any one of Claims 21-61, wherein R^6 is Me, Et, n-Pr, n-Bu, n-pentyl, n-hexyl, or n-heptyl.

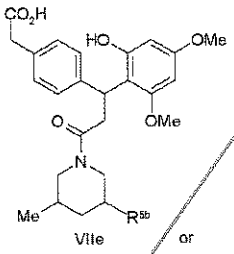
73. The method according to claim 1 or the compound according to Claim 22, wherein the compound is according to formula VIIa, VIIb, VIIc, VIId, VIIe, or VIIf:


VIIa

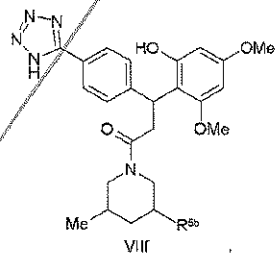

VIIb


VIIc


VIId


VIIe

or

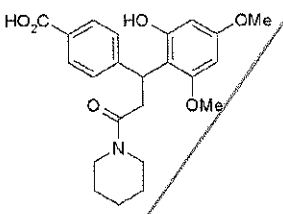

VIIf

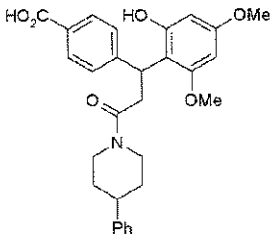
and wherein R^{5b} is H or Me;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

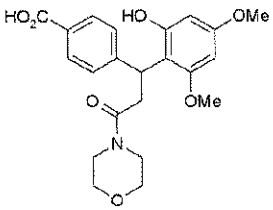
or stereoisomers, isotopic variants and tautomers thereof.

74. The method according to claim 1 or the compound according to Claim 22, wherein the compound is according to formula VIIIa, VIIIb, or VIIIc:


VIIIa


VIIIb

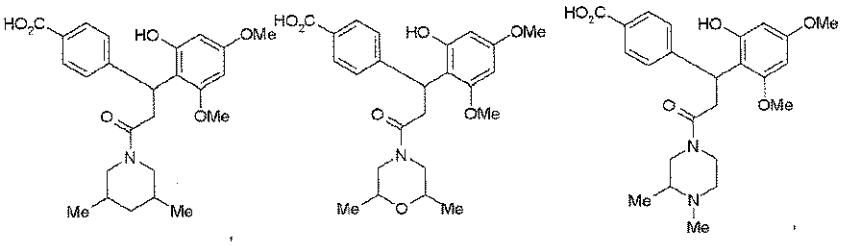
or


VIIIc

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

75. The method according to claim 1 or the compound according to Claim 22, wherein the compound is according to formula IXa, IXb, or IXc:

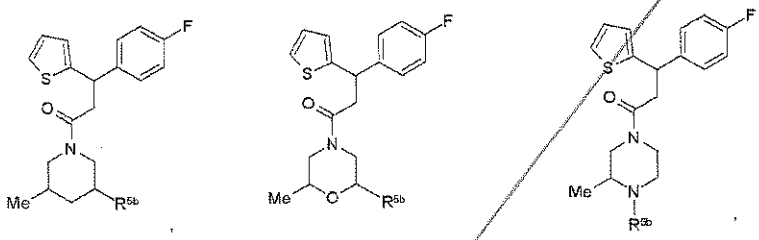


IXa IXb or IXc

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

76. The method according to claim 1 or the compound according to Claim 22, wherein the compound is according to formula Xa, Xb, or Xc:



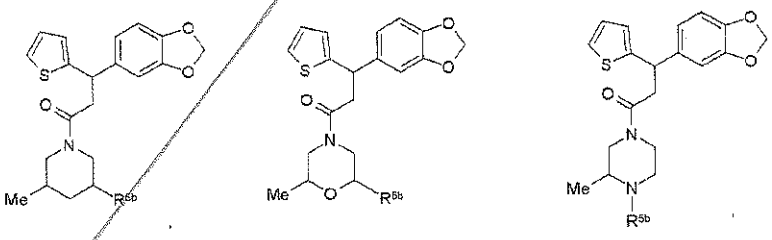
Xa Xb or Xc

and wherein R^{5b} is H or Me;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

77. The method according to claim 1 or the compound according to Claim 22, wherein the compound is according to formula XIa, XIb, or XIc:



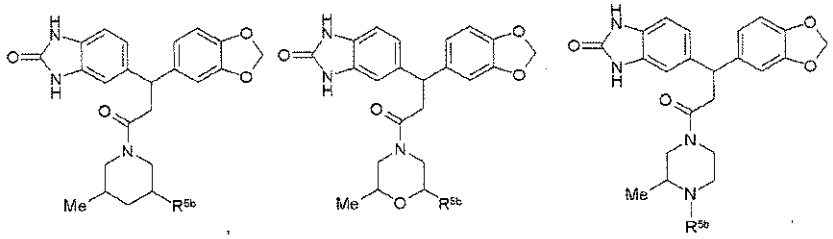
XIa XIb or XIc

and wherein R^{5b} is H or Me;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

78. The method according to claim 1 or the compound according to Claim 22, wherein the compound is according to formula XIIa, XIIb, or XIIc:



XIIa XIIb or XIIc

and wherein R^{5b} is H or Me;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

79. A compound according to formula Xa, Xb, Xc, XIa, XIb, XIc, XIIa, XIIb, or XIIc.

80. The method according to claim 1, wherein the compound is a compound with Compound ID 99 or 101; or a pharmaceutically acceptable salt, solvate or prodrug thereof; or stereoisomers, isotopic variants and tautomers thereof.

81. The method according to claim 1, wherein the compound is Compound with Compound ID 95, 100, 111, or 139; or a pharmaceutically acceptable salt, solvate or prodrug thereof; or stereoisomers, isotopic variants and tautomers thereof.

82. A compound selected from compounds with compound IDs 99 and 101; or a pharmaceutically acceptable salt, solvate or prodrug thereof; or stereoisomers, isotopic variants and tautomers thereof.

83. A compound selected from compounds with Compound ID 95, 100, 111, and 139 or a pharmaceutically acceptable salt, solvate or prodrug thereof; or stereoisomers, isotopic variants and tautomers thereof.

84. The method according to claim 1 or the compound according to Claim 22, wherein the compound is any one of compounds listed in Table 1.

85. The method according to claim 1 or the compound according to Claim 22, wherein the compound is selected from compounds listed in Table 1; and wherein the Compound ID is 70, 79 106-108, or 142.

86. The method according to claim 1 or the compound according to Claim 22, wherein the compound is selected from compounds listed in Table 1A.

87. The method according to claim 1 or the compound according to Claim 22, wherein the compound is selected from compounds listed in Table 1B.

88. The method according to claim 1 or the compound according to Claim 22, wherein the compound is selected from compounds listed in Table 1A; and wherein the Compound ID is 202.

89. The method according to claim 1 or the compound according to Claim 22, wherein the compound is selected from compounds listed in Table 1C.

90. A compound selected from the compounds listed in Table 1.

91. Any one of compounds selected from compounds listed in Table 1; and wherein the Compound ID is 70, 79 106-108, or 142.

92. Any one of compounds selected from compounds listed in Table 1A.

93. Any one of compounds selected from compounds listed in Table 1B.

94. Any one of compounds selected from compounds listed in Table 1C.

95. The method according to claim 1 or the compound according to Claim 22, wherein the compound is a salt of Compound 99, 101, 201 or 202.

96. The method according to claim 1 or the compound according to Claim 22, wherein the compound is a sodium salt of Compound 99, 101, 201 or 202.

97. The method according to claim 1 or the compound according to Claim 22, wherein the compound is a salt of Compound 317-332, 401-405, 407-412, 414, 416, 417, or 418.

98. A pharmaceutical composition of compound according to any one of claims 1-97.

99. The method of Claim 1, wherein the disease or condition is autoimmune disease.

100. The method of Claim 1, wherein the disease or condition is inflammatory disease.

101. The method of Claim 1, wherein the disease or condition is selected from arthritis, diabetes, multiple sclerosis, uveitis, rheumatoid arthritis, psoriasis, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, atherosclerosis, H. pylori infections and ulcers resulting from such infection, and inflammatory bowel diseases.

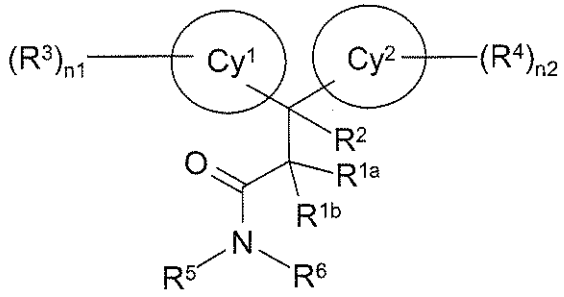
102. The method of Claim 1, wherein the disease or condition is selected from Crohn's disease, ulcerative colitis, sprue and food allergies.

103. The method of Claim 1, wherein the disease or condition is selected from multiple sclerosis and experimental autoimmune encephalomyelitis (EAE).

104. The method of Claim 1, wherein the disease or condition is selected from rheumatoid arthritis or collagen-induced arthritis (CIA).

WHAT IS CLAIMED IS:

1. Use of an effective disease-treating or condition-treating amount of a compound according to formula I:



I

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof in the preparation of a medicament for preventing, treating or ameliorating a disease or condition in a mammal that is causally related to RORγt activity in vivo;

wherein

each Cy^1 and Cy^2 is independently selected from substituted or unsubstituted aryl and heteroaryl;

each n1 and n2 is independently 1, 2, 3, 4 or 5;

each R^{1a} and R^{1b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, or CN; or R^{1a} and R^{1b} joined together to form cycloalkyl ring;

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

or one of R^{1a} and R^{1b} is joined to the C of CR^2 to form a cyclopropyl ring; or R^2 is joined to the C of $CR^{1a}R^{1b}$ to form a cyclopropyl ring;

each R^3 and R^4 is independently selected from H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or

unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thiol; or any two adjacent R^3 groups, or any two adjacent R^4 groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring;

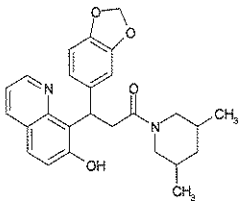
each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl; or

R^5 and R^6, together with the N they are attached to, form a 4-12 membered substituted or unsubstituted heterocycloalkyl;

provided that

i) at least one of Cy^1 and Cy^2 is heteroaryl; and

ii) when the compound is



;

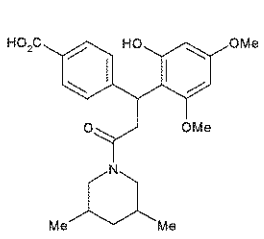
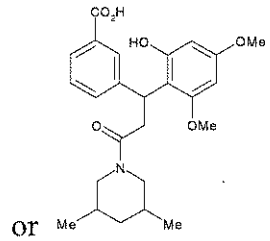
then the compound is in the form of an acid addition salt;

or

provided that

i) when each of Cy^1 and Cy^2 is phenyl; then at least one R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; and wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

ii) when the compound is

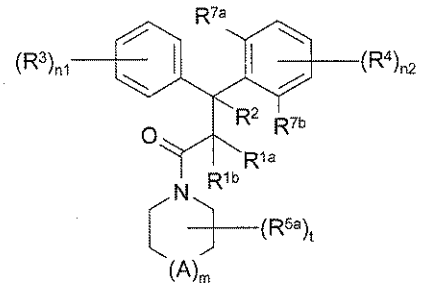



or ;

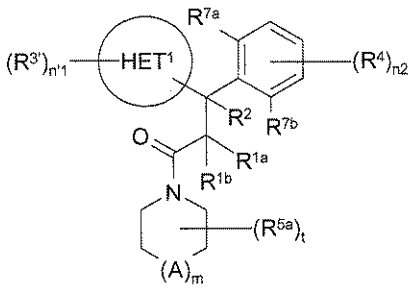
then the compound is in the form of a sodium, potassium, calcium, or ammonium salt; and

iii) the compound is other than the compounds listed in Table 1, wherein compound ID is 83, 84, 95, 100, 111, or 139.

2. A compound according to formula IIIa, IIIb, or IIIc:

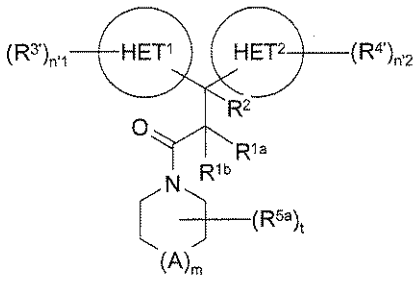


IIIa



IIIb

or



IIIc

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

wherein

each R^{1a} and R^{1b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, or CN; or R^{1a} and R^{1b} joined together to form cycloalkyl ring;

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

or one of R^{1a} and R^{1b} is joined to the C of CR^2 to form a cyclopropyl ring; or R^2 is joined to the C of $CR^{1a}R^{1b}$ to form a cyclopropyl ring;

each R^3 and R^4 is independently selected from H, OH, substituted or unsubstituted alkyl,

substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thiol; or any two adjacent R^3 groups, or any two adjacent R^4 groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring;

n1 is 1, 2, 3, 4 or 5;

n2 is 1, 2, or 3;

each HET^1 and HET^2 is independently selected from heteroaryl;

$R^{3'}$ is R^3; $R^{4'}$ is R^4; n'1 is n1; n'2 is n2;

A is $CR^{8a}R^{8b}$, NR^{8a}, O, or S; m is 0 or 1;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3;

R^{7a} is H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thiol;

R^{7b} is R^4; or any two adjacent R^4 and R^{7b} groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring; and

each R^{8a} and R^{8b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, substituted or

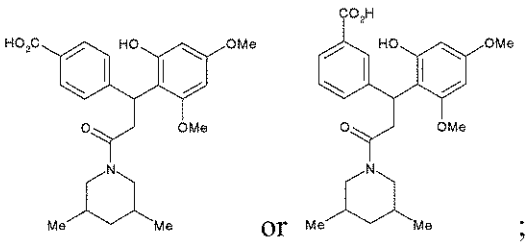
unsubstituted aryl, or substituted or unsubstituted heteroaryl;

provided that

i) when the compound is according to formula IIIa, then at least one R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; and wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

ii) when the compound is according to formula IIIa, R^3 is $CONR^{3a}R^{3b}$, R^{3a} and R^{3b} joined together to form a morpholino ring, m is 1, and A is O; then R^{7a} is other than H;

iii) when the compound is



;

then the compound is in the form of a sodium, potassium, calcium, or ammonium salt;

iv) the compound is other than the compounds listed in Table 1, wherein compound ID is 83, 84, 95, 100, 111, and 139;

v) when the compound is according to formula IIIb; then R^{7a} is other than H;

vi) when the compound is according to formula IIIb, HET^1 is furanyl or quinolin-3-yl, and each of $R^{3'}$ and R^4 is H; then R^{7a} is other than H or methoxy;

vii) when the compound is according to formula IIIb, and HET^1 is pyrrolyl; then R^{7a} is other than H or methyl; and

viii) when the compound is according to formula IIIb; then HET^1 is other than benzopyranyl;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

3. The compound according to Claim 2, wherein

each of R^{7a} and R^{7b} is independently OH, substituted or unsubstituted alkyl, substituted

or unsubstituted alkoxy, CN, halo, amido, or haloalkyl; or

each of R^{7a} and R^{7b} is independently halo, C_1-C_6 alkyl, CN, OH, or C_1-C_6 alkoxy; or

each of R^{7a} and R^{7b} is independently Cl, F, Me, CF_3, CN, OH, or OMe; or

one of R^{7a} and R^{7b} is OH; and the other is alkoxy; or

each of R^{7a} and R^{7b} is OH or alkoxy; or

one of R^{7a} and R^{7b} is OH; and the other is OMe.

4. The compound according to Claim 2, wherein R^{1a} and R^{1b} is independently H, CN, or Me; or

each of R^{1a} and R^{1b} is H or Me; or

one of R^{1a} and R^{1b} is H; and the other is CN.

5. The compound according to Claim 2, wherein HET^1 is selected from pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, triazolyl, oxadiazolyl, and thiadiazolyl; or

HET^1 is selected from pyridyl, pyrimidyl, and pyrazinyl; or

HET^1 is selected from indolyl, benzimidazolyl, 2-oxobenzimidazolyl, benzofuranyl, benzothiazolyl, and benzthiophenyl.

6. The compound according to Claim 2, wherein HET^2 is selected from pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, triazolyl, oxadiazolyl, and thiadiazolyl; or

HET^2 is selected from pyridyl, pyrimidyl, and pyrazinyl; or

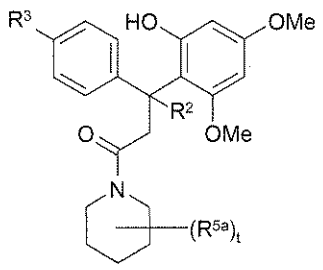
HET^2 is selected from indolyl, benzimidazolyl, 2-oxobenzimidazolyl, benzofuranyl, benzothiazolyl, and benzthiophenyl.

7. The compound according to Claim 2, wherein R^4 is H, alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, alkoxyalkyl, amido, hydroxyl, cyano, or alkoxy; or

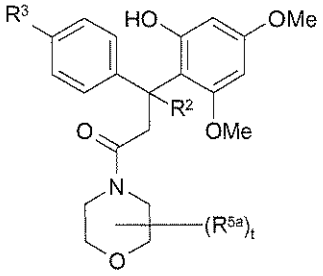
R^4 is H, halo, C_1-C_6 alkyl, CN, OH, or C_1-C_6 alkoxy; or

R^4 is H, Cl, F, Me, CF_3, CN, OH, or OMe.

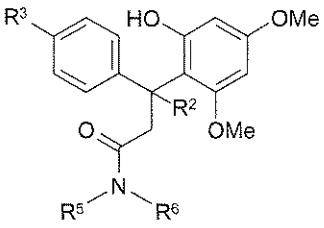
8. A compound according to formula IVa, IVb, IVc, IVd, IVe, or IVf:



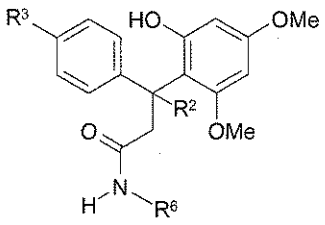
IVa ,



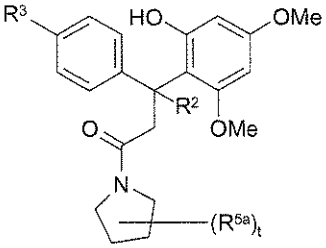
IVb ,



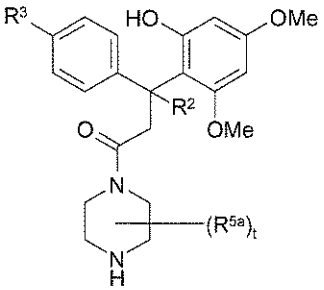
IVc ,



IVd ,



IVe or



IVf ,

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

and wherein

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

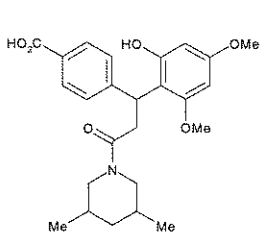
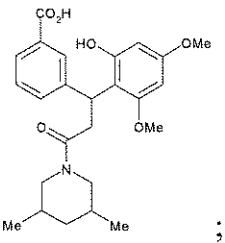
R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; t is 0, 1, 2, or 3;

provided that

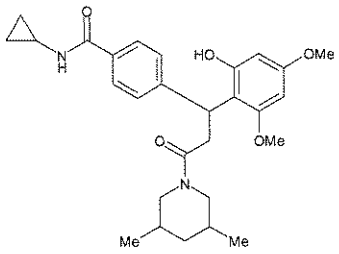
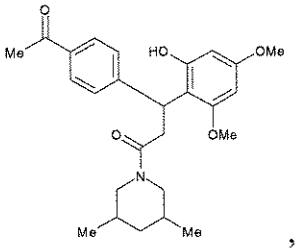
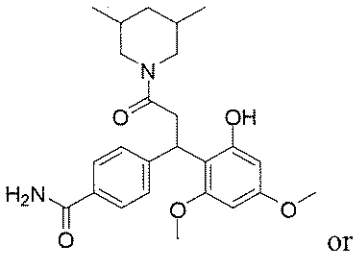
i) when the compound is

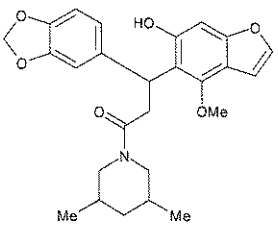
or ;

then the compound is in the form of a sodium, potassium, calcium, or ammonium salt; and

ii) the compound is other than

or



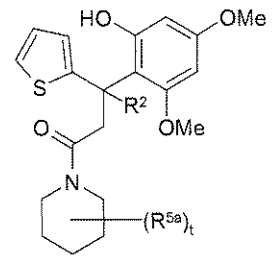
9. The compound according to Claim 2 or claim 8, wherein R^3 is CO_2H, SO_3H, or CH_2CO_2H; or

R^3 is pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, triazolyl, oxadiazolyl, thiadiazolyl, and tetrazolyl; or

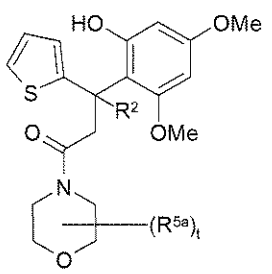
R^3 is 1,3,4-triazolyl or tetrazol-5-yl; or

R^3 is $CONR^{3a}R^{3b}$; wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.

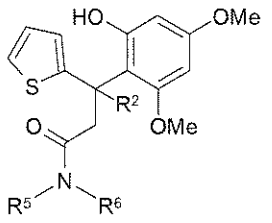
10. A compound according to formula Va, Vb, Vc, Vd, Ve, or Vf:



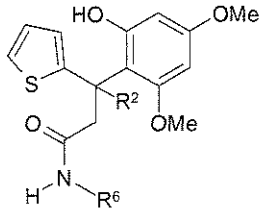
Va ,



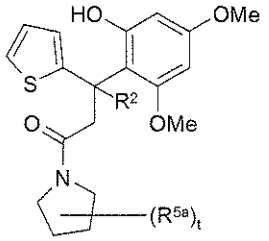
Vb ,



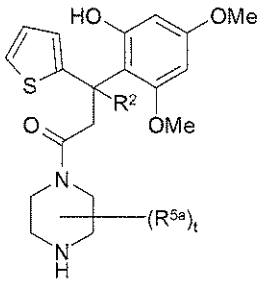
Vc ,



Vd ,



Ve or



Vf ,

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

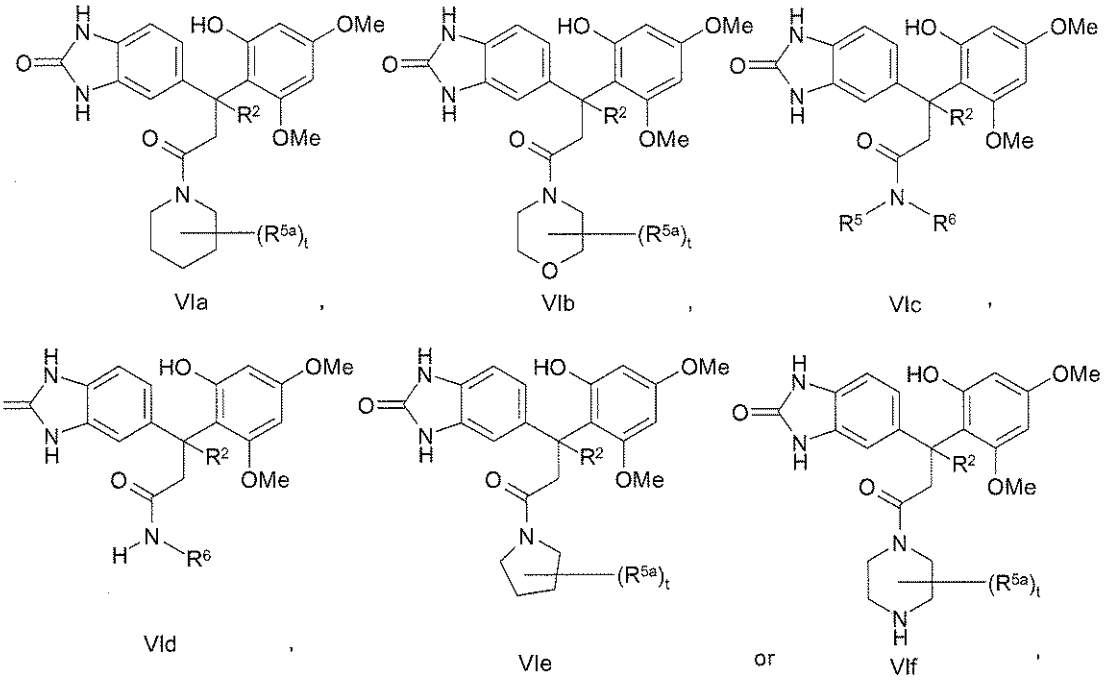
and wherein

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3.

11. A compound according to formula VIa, VIb, VIc, VId, VIe, or VIf:



or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

and wherein

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3.

12. The compound according to any one of Claims 2, 8, 10 or 11, wherein R^2 is H, Me, OH or Ph.

13. The compound according to any one of Claims 2, 8, 10 or 11, wherein t is 0; or

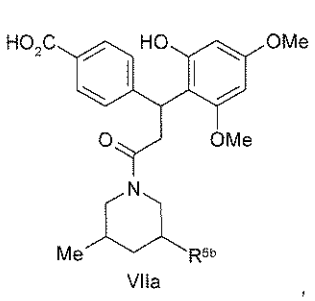
t is 1 or 2; and each R^{5a} is independently OH, Ph, benzyl, or Me; or

t is 1; and R^{5a} is Me, Et, n-Pr, or n-Bu; or

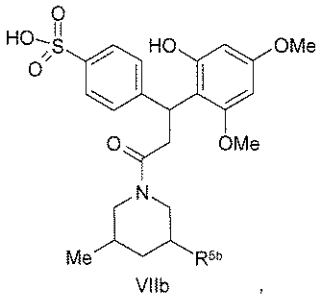
t is 1; and R^{5a} is 3-Me, 3-Et, 3-n-Pr, or 3-n-Bu; or

t is 2; and one R^{5a} is 3-Me and the other is 5-Me.

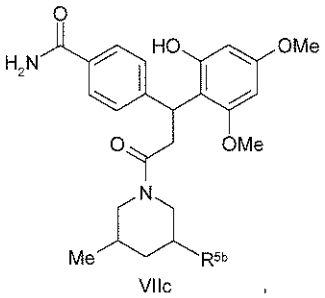
14. The compound according to Claim 2, wherein the compound is according to formula VIIa, VIIb, VIIc, VIId, VIIe, or VIIf:



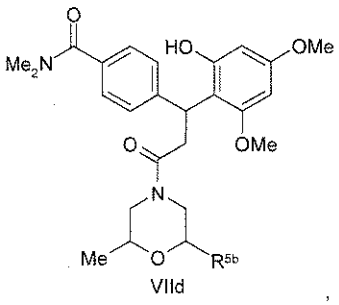
VIIa ,



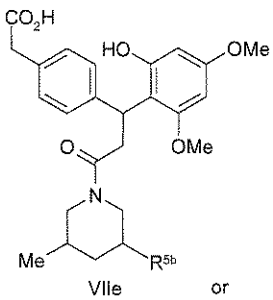
VIIb ,



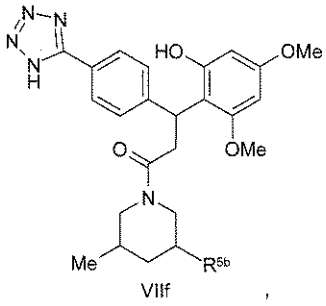
VIIc ,



VIId ,



VIIe or



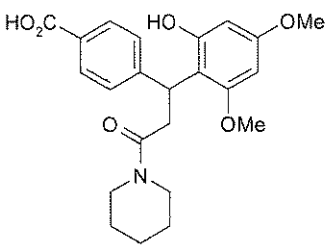
VIIf ,

and wherein R^{5b} is H or Me;

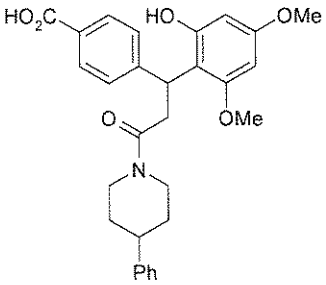
or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

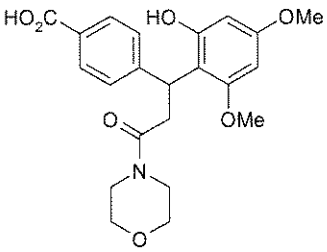
15. The compound according to Claim 2, wherein the compound is according to formula VIIIa, VIIIb, or VIIIc:



VIIIa ,



VIIIb or

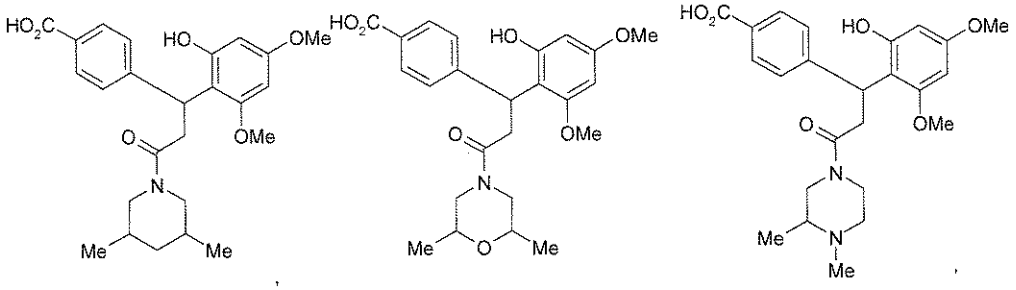


VIIIc

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

16. The compound according to Claim 2, wherein the compound is according to formula IXa, IXb, or IXc:

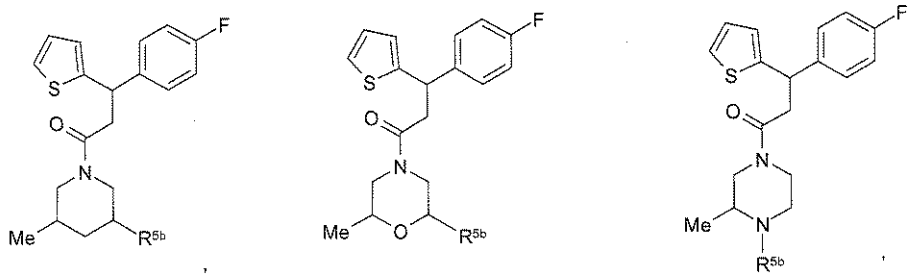


IXa IXb or IXc

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

17. The compound according to Claim 2, wherein the compound is according to formula Xa, Xb, or Xc:



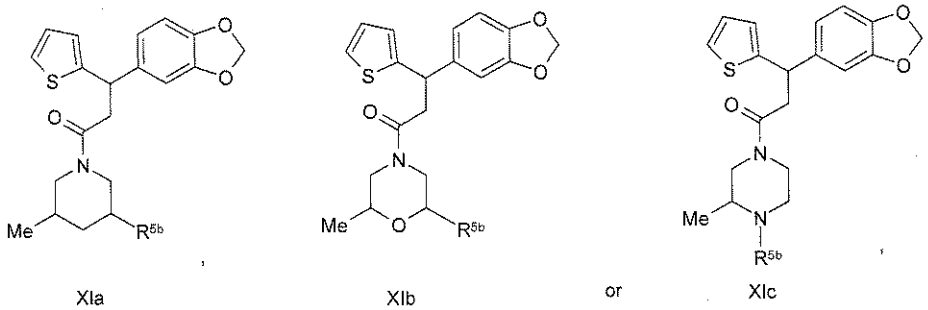
Xa Xb or Xc

and wherein R^{5b} is H or Me;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

18. The compound according to Claim 2, wherein the compound is according to formula XIa, XIb, or XIc:



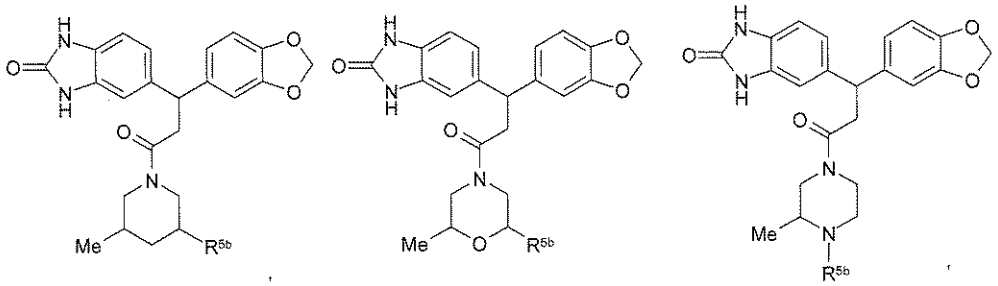
XIa XIb or XIc

and wherein R^{5b} is H or Me;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

19. The compound according to Claim 2, wherein the compound is according to formula XIIa, XIIb, or XIIc:



XIIa XIIb or XIIc

and wherein R^{5b} is H or Me;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

20. The compound according to Claim 2, wherein the compound is according to formula Xa, Xb, Xc, XIa, XIb, XIc, XIIa, XIIb, or XIIc.

21. The compound according to Claim 2, wherein the compound is selected from compounds with Compound ID 95, 99, 100, 101, 111, and 139

or a pharmaceutically acceptable salt, solvate or prodrug thereof; or stereoisomers, isotopic variants and tautomers thereof.

22. The compound according to Claim 2, wherein the compound is any one of compounds listed in Table 1, Table 1A, Table 1B or Table 1C.

23. The compound according to Claim 2, wherein the compound is selected from compounds listed in Table 1; and wherein the Compound ID is 70, 79, 106-108, or 142; or a pharmaceutically acceptable salt, solvate or prodrug thereof; or stereoisomers, isotopic variants and tautomers thereof.

24. A pharmaceutical composition of the compound according to any one of claims 2, 8, 10 or 11.

25. The use according to Claim 1, wherein the disease or condition is an autoimmune disease or inflammatory disease; or

the disease or condition is selected from arthritis, diabetes, multiple sclerosis, uveitis, rheumatoid arthritis, psoriasis, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, atherosclerosis, H. pylori infections and ulcers resulting from such infection, and inflammatory bowel diseases; or

the disease or condition is selected from Crohn's disease, ulcerative colitis, sprue and food allergies; or

the condition is rheumatoid arthritis or collagen-induced arthritis (CIA).

26. The compound of any one of claims 2 to 23, or the pharmaceutical composition of claim 24 for use in preventing, treating or ameliorating a disease or condition that is causally related to RORγt activity in a mammal, wherein the compound or pharmaceutical composition prevents, treats or ameliorates the disease or condition when administered in an effective disease-treating or condition-treating amount.

27. Use of the compound of any one of claims 2 to 23, or the pharmaceutical composition of claim 24 in the preparation of a medicament for preventing, treating or ameliorating a disease or condition in a mammal that is causally related to RORγt activity in vivo.

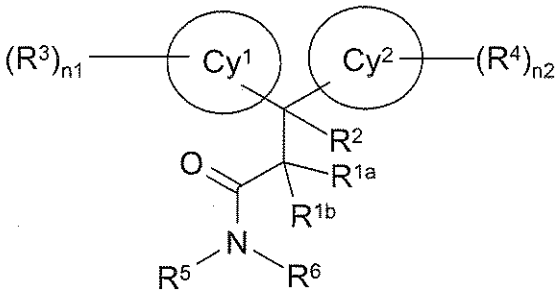
metabolic levels, whose imbalance is linked to obesity and diabetes, modulators of RORγ/γt may also be useful in treating obesity and diabetes through regulation of circadian rhythm.

[0006] WO2011/112263 discloses diphenylsubstituted amido compounds as RORγ/γt modulators. WO2011/112264 discloses a series of compounds as RORγ/γt modulators.

[0007] In view of the above, a need exists for therapeutic agents, and corresponding pharmaceutical compositions and related methods of treatment that address conditions causally related to RORγt activity, and it is toward the fulfillment and satisfaction of that need, that the present invention is directed.

SUMMARY OF THE ~~INVENTION~~

[0008] The present ~~invention~~ disclosure provides a method for preventing, treating or ameliorating in a mammal a disease or condition that is causally related to RORγ or RORγt activity in vivo, which comprises administering to the mammal an effective disease-treating or condition-treating amount of a compound according to formula I:



I

wherein

each Cy^1 and Cy^2 is independently selected from substituted or unsubstituted aryl and heteroaryl;

each n1 and n2 is independently 1, 2, 3, 4 or 5;

each R^{1a} and R^{1b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, or CN; or R^{1a} and R^{1b} joined together to form cycloalkyl ring;

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

or one of R^{1a} and R^{1b} is joined to the C of CR^2 to form a cyclopropyl ring; or R^2 is joined to the C of $CR^{1a}R^{1b}$ to form a cyclopropyl ring;

each R^3 and R^4 is independently selected from H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or

unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thiol; or any two adjacent R^3 groups, or any two adjacent R^4 groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring;

each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl; or

R^5 and R^6, together with the N they are attached to, form a 4-12 membered substituted or unsubstituted heterocycloalkyl;

provided that

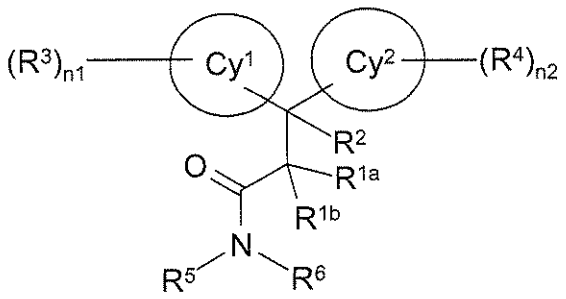
i) at least one of Cy^1 and Cy^2 is heteroaryl; or

ii) when each of Cy^1 and Cy^2 is phenyl; then at least one R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; and wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

[0008A] In one aspect, there is provided use of an effective disease-treating or condition-treating amount of a compound according to formula I:



I

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof in the preparation of a medicament for preventing, treating or ameliorating a disease or condition in a mammal that is causally related to RORγt activity in vivo;

wherein

each Cy^1 and Cy^2 is independently selected from substituted or unsubstituted aryl and heteroaryl;

each n1 and n2 is independently 1, 2, 3, 4 or 5;

each R^{1a} and R^{1b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, or CN; or R^{1a} and R^{1b} joined together to form cycloalkyl ring;

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

or one of R^{1a} and R^{1b} is joined to the C of CR^2 to form a cyclopropyl ring; or R^2 is joined to the C of $CR^{1a}R^{1b}$ to form a cyclopropyl ring;

each R^3 and R^4 is independently selected from H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thiol; or any two adjacent R^3 groups, or any two adjacent R^4 groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring;

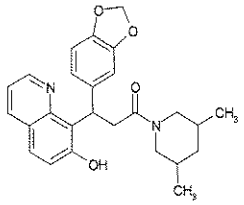
each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl; or

R^5 and R^6, together with the N they are attached to, form a 4-12 membered substituted or unsubstituted heterocycloalkyl;

provided that

i) at least one of Cy^1 and Cy^2 is heteroaryl; and

ii) when the compound is



;

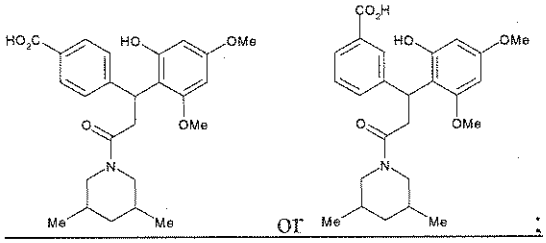
then the compound is in the form of an acid addition salt;

or

provided that

i) when each of Cy^1 and Cy^2 is phenyl; then at least one R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; and wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

ii) when the compound is



;

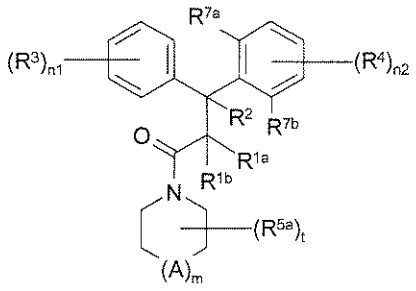
then the compound is in the form of a sodium, potassium, calcium, or ammonium salt; and

iii) the compound is other than the compounds listed in Table 1, wherein compound ID is 83, 84, 95, 100, 111, or 139.

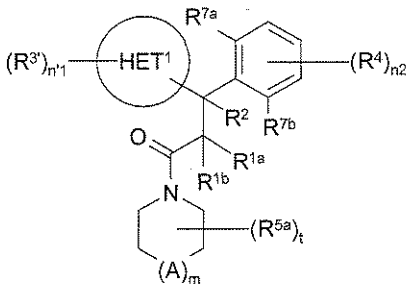
[0009] In one embodiment, with respect to the compounds of formula I, R^5 and R^6 are joined together to form substituted or unsubstituted azetidinyl, pyrrolidinyl, piperidinyl, piperizinyl, morpholinyl, tetrahydroquinolinyl, indolinyl, or azepinyl. In another embodiment, R^5 and R^6 are joined together to form unsubstituted pyrrolidinyl, piperidinyl, piperizinyl, morpholinyl, or azepinyl. In a particular embodiment, R^5 and R^6 are joined together to form piperidinyl or piperizinyl.

[0010] ~~In a further aspect, the present invention provides~~Disclosed is a compound according to formula IIIa-IIIc:

[0010A] In another aspect, there is provided a compound according to formula IIIa, IIIb, or IIIc:

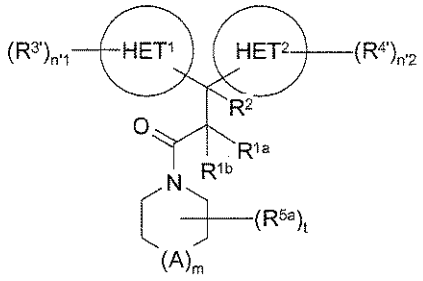


IIIa



IIIb

or



IIIc

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

wherein

each R^{1a} and R^{1b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, or CN; or R^{1a} and R^{1b} joined together to form cycloalkyl ring;

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

or one of R^{1a} and R^{1b} is joined to the C of CR^2 to form a cyclopropyl ring; or R^2 is joined to the C of $CR^{1a}R^{1b}$ to form a cyclopropyl ring;

each R^3 and R^4 is independently selected from H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or

unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thiol; or any two adjacent R^3 groups, or any two adjacent R^4 groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring;

n1 is 1, 2, 3, 4 or 5;

n2 is 1, 2, or 3;

each HET^1 and HET^2 is independently selected from heteroaryl;

$R^{3'}$ is R^3; $R^{4'}$ is R^4; n'1 is n1; n'2 is n2;

A is $CR^{8a}R^{8b}$, NR^{8a}, O, or S; m is 0 or 1;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3;

R^{7a} is H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted acyl, substituted or unsubstituted acylamino, substituted or unsubstituted alkylamino, substituted or unsubstituted alkythio, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkylarylamino, substituted or unsubstituted amino, substituted or unsubstituted arylalkyl, sulfo, substituted sulfo, substituted sulfonyl, substituted sulfinyl, substituted sulfanyl, substituted or unsubstituted aminosulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, azido, substituted or unsubstituted carbamoyl, carboxyl, cyano, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted dialkylamino, halo, nitro, and thiol;

R^{7b} is R^4; or any two adjacent R^4 and R^{7b} groups may join together to form a substituted or unsubstituted carbocyclic or heterocyclic ring; and

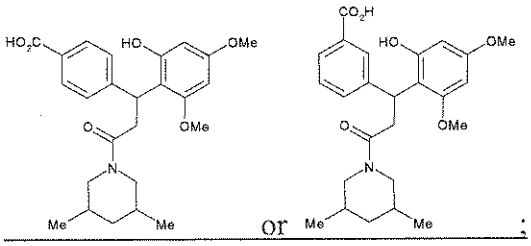
each R^{8a} and R^{8b} is independently H, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

provided that

i) when the compound is according to formula IIIa, then at least one R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; and wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

ii) when the compound is according to formula IIIa, R^3 is $CONR^{3a}R^{3b}$, R^{3a} and R^{3b} joined together to form a morpholino ring, m is 1, and A is O; then R^{7a} is other than H;

iii) when the compound is



;

then the compound is in the form of a sodium, potassium, calcium, or ammonium salt;

iv) the compound is other than the compounds listed in Table 1, wherein compound ID is 83, 84, 95, 100, 111, and 139;

v) when the compound is according to formula IIIb; then R^{7a} is other than H;

vi) when the compound is according to formula IIIb, HET^1 is furanyl or quinolin-3-yl, and each of $R^{3'}$ and R^4 is H; then R^{7a} is other than H or methoxy;

vii) when the compound is according to formula IIIb, and HET^1 is pyrrolyl; then R^{7a} is other than H or methyl; and

viii) when the compound is according to formula IIIb; then HET^1 is other than benzopyranyl;

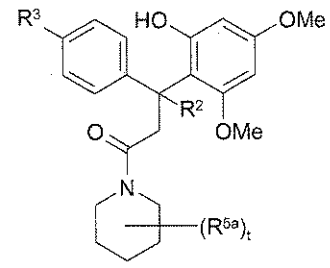
or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof.

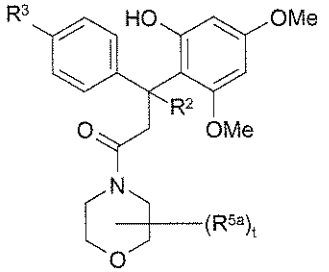
[0011] In one particular embodiment, with respect to the compound of formula IIIa-IIIb, R^{7a} is other than H. In one particular embodiment, with respect to the compound of formula IIIa-IIIb, R^{7b} is other than H.

[0012] In one particular embodiment, with respect to the compound of formula IIIa-IIIc, when m is 1, A is N; then the N can be substitituted or unsubstituted. In one embodiment A is NH. In another embodiment, A is N-R^{5a} and R^{5a} is as described herein.

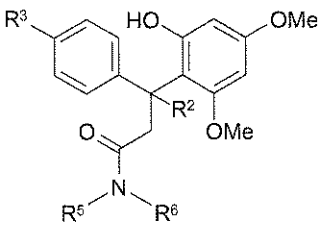
[0012A] In another aspect, there is provided a compound according to formula IVa, IVb, IVc, IVd, IVe, or IVf:



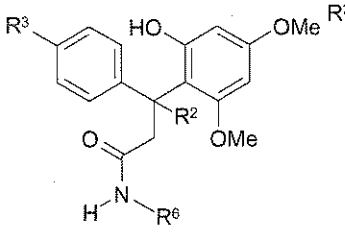
IVa ,



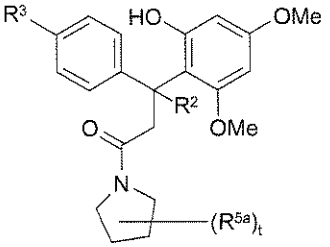
IVb ,



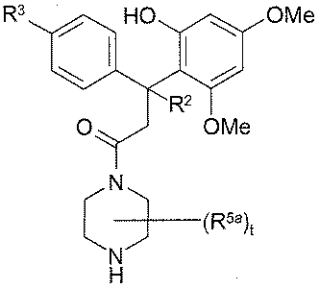
IVc ,



IVd ,



IVe or



IVf ,

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

and wherein

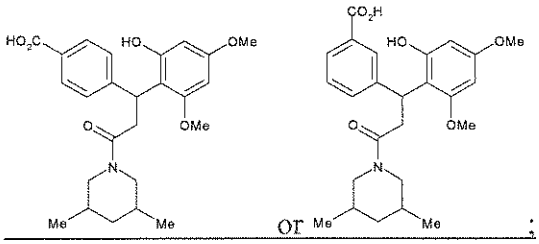
R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

R^3 is selected from CO_2H, CH_2CO_2H, COR^{3a}, $CONR^{3a}R^{3b}$, SO_3H, SOR^{3a}, SO_2R^{3a}, and heteroaryl; wherein each R^{3a} and R^{3b} is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; or R^{3a} and R^{3b} may join together to form a substituted or unsubstituted heterocyclic ring;

each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; t is 0, 1, 2, or 3; provided that

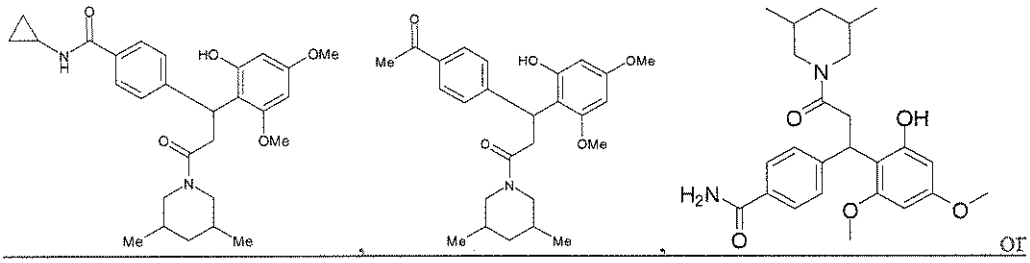
i) when the compound is



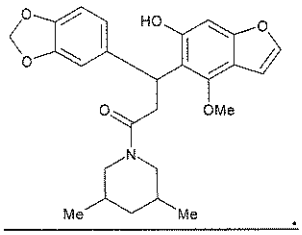
or ;

then the compound is in the form of a sodium, potassium, calcium, or ammonium salt; and

ii) the compound is other than

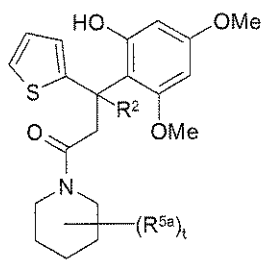


or

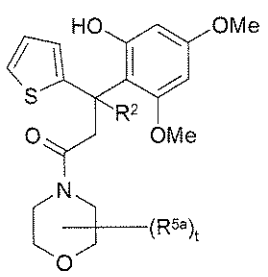


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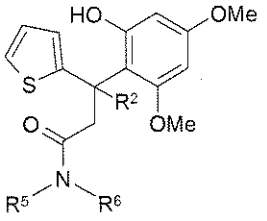
[0012B] In another aspect, there is provided a compound according to formula Va, Vb, Vc, Vd, Ve, or Vf:



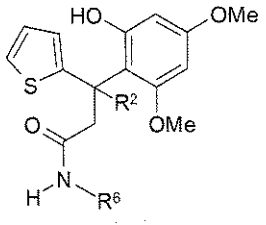
Va ,



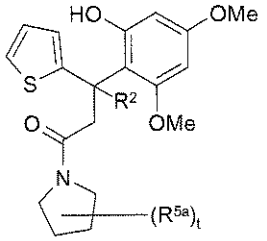
Vb ,



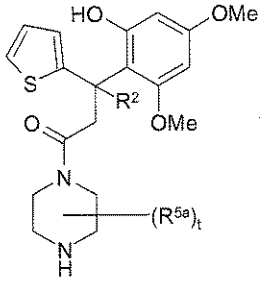
Vc



Vd ,



Ve or



Vf ,

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

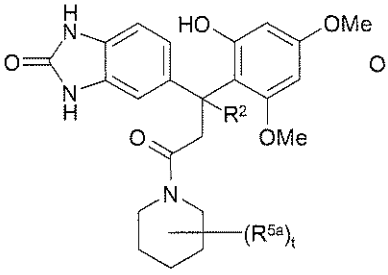
and wherein

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

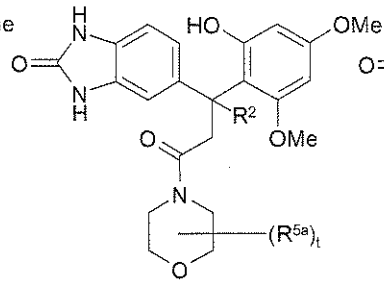
each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3.

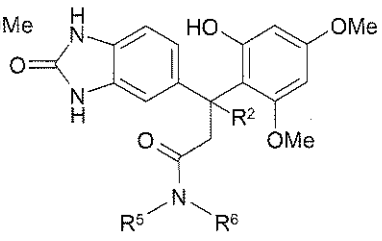
[0012C] In another aspect, there is providedA compound according to formula VIa, VIb, VIc, VId, VIe, or VIf:



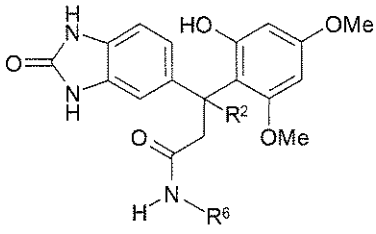
VIa ,



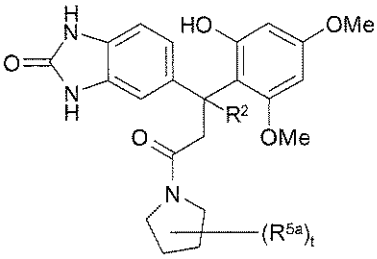
VIb ,



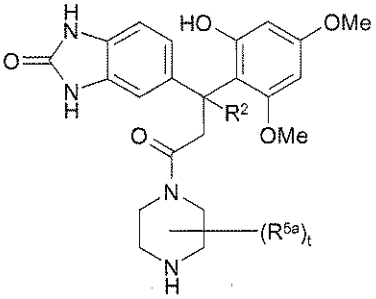
VIc ,



VId ,



VIe or



VIf ,

or a pharmaceutically acceptable salt, solvate or prodrug thereof;

or stereoisomers, isotopic variants and tautomers thereof;

and wherein

R^2 is H, substituted or unsubstituted C_1-C_6 alkyl, or aryl;

each R^5 and R^6 is independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, and substituted or unsubstituted heteroarylalkyl;

each R^{5a} is alkyl, substituted alkyl, halo, haloalkyl, hydroxyalkyl, aryl, heteroaryl, CN, alkoxyalkyl, amido, hydroxyl, alkoxy or substitituted alkoxy; and t is 0, 1, 2, or 3.

[0012D] In another aspect, there is provided a pharmaceutical composition of the compound as defined above.

[0013] ~~In a further aspect, the present invention provides~~Disclosed are pharmaceutical compositions comprising a heterocyclic compound of the ~~invention~~disclosure, and a pharmaceutical carrier, excipient or diluent. In this aspect of the disclosure~~invention~~, the pharmaceutical composition can comprise one or more of the compounds described herein. Moreover, the compounds of the present disclosure~~invention~~ useful in the pharmaceutical compositions and treatment methods disclosed herein, are all pharmaceutically acceptable as prepared and used.

[0013A] In one aspect, there is provided the compound as defined above, or the pharmaceutical composition as defined above for use in preventing, treating or ameliorating a disease or condition that is causally related to RORγt activity in a mammal, wherein the compound or pharmaceutical composition prevents, treats or ameliorates the disease or condition when administered in an effective disease-treating or condition-treating amount.

[0013B] In one aspect, there is provided use of the compound as defined above, or the pharmaceutical composition as defined above in the preparation of a medicament for preventing, treating or ameliorating a disease or condition in a mammal that is causally related to RORγt activity in vivo.

[0014] ~~In a further aspect, this invention provides~~Disclosed is a method of treating a mammal susceptible to or afflicted with a condition from among those listed herein, and particularly, such condition as may be associated with RORγt. Such conditions include, without limitation, multiple sclerosis (and the animal model thereof, EAE), rheumatoid arthritis (and the animal model thereof, CIA), inflammatory bowel disease (IBD), cancer, graft-versus-host disease, asthma, psoriasis, diabetes, uveitis, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, arteriosclerosis, and *H. pylori* infections and ulcers resulting from such infection.

[0015] ~~In a further aspect,~~Also disclosed is an assay for screening to identify modulators of RORγ/γt transcriptional activity is envisioned, the assay comprising a first insect cell line that expresses a fusion protein (SEQ ID NO: 2; encoded by SEQ ID NO: 1) comprising a RORγ/γt sequence, wherein the RORγ/γt sequence does not comprise the DNA binding domain (DBD) of full length RORγ/γt and a yeast GAL4 DBD, wherein expression of the fusion protein is transcriptionally regulated by an inducible promoter, and wherein the first insect cell line further comprises a reporter, whose expression is upregulated in the presence of the fusion protein. Accordingly, the component of the fusion protein representative of RORγ/γt sequences is a DBD-deleted RORγ/γt sequence. The fusion protein is essentially a chimeric protein wherein the RORγ/γt DBD is deleted from the RORγ/γt sequences and replaced with the yeast GAL4 DNA binding domain DBD. In a particular embodiment, the Gal4 DNA binding domain (G4DBD) corresponds to amino acids 1 through 147 of Gal4 protein and the DBD-deleted RORγ/γt sequence is amino acids 79 to the carboxyl terminal end. Accordingly, the G4DBD corresponds to amino acids 1-147 of SEQ ID NO: 2 and the DBD-deleted RORγ/γt sequence corresponds to amino acids 148-564 of SEQ ID NO: 2. In a particular embodiment, the inducible promoter is a copper inducible promoter.

[0016] In an embodiment of the assay, the reporter is transcriptionally regulated by a plurality of copies of the GAL4 binding site enhancer (UAS) operatively linked to nucleic acid sequences encoding the reporter. In a particular embodiment of the assay, the plurality of copies of the GAL4 binding site enhancer (UAS) is between 1 and 5 copies. In a more particular embodiment, the reporter is the firefly luciferase reporter.

[0017] In an ~~aspect~~ embodiment of the assay, the first insect cell line is the S2 cell line. In another ~~aspect~~ embodiment of the assay, the fusion protein is encoded by nucleic acids that are integrated into the genome of the first insect cell line or encoded by extrachromosomal nucleic acids incorporated into the first insect cell line. Accordingly, the assay may relate to stably transfected cell line or a transiently transfected cell line. The choice of stably or transiently transfected cell line depends, in part, on the number of compounds to be tested and availability and cost of assay reagents required.

[0018] As described herein, the assay may further comprise a second insect cell line that expresses a second fusion protein (SEQ ID NO: 4; encoded by SEQ ID NO: 3) comprising a RORα sequence, wherein the RORα sequence does not comprise the DBD of full length RORα sequence and a yeast GAL4 DBD; a third insect cell line that expresses a third fusion protein (SEQ ID NO: 6; encoded by SEQ ID NO: 5) comprising a DHR3 sequence, wherein the DHR3 sequence does not comprise the DNA binding domain (DBD) of full length DHR3 sequence and a yeast GAL4 DBD, and a fourth insect cell line that expresses a fourth fusion protein (SEQ ID NO: 8; encoded by SEQ ID NO: 7) comprising a transcriptionally active domain of general transcriptional activator VP16 and a yeast GAL4 DBD, wherein expression of the second, third and fourth fusion proteins is transcriptionally regulated by inducible promoters. In a particular embodiment, the DBD-deleted mouse RORα sequence is amino acids 142 to the carboxyl terminal end of mouse RORα and the DBD-deleted *Drosophila* DHR3 is amino acids 120 to the carboxyl terminal end of *Drosophila* DHR3. Accordingly, the G4DBD corresponds to amino acids 1-147 of SEQ ID NOs: 4, 6, and 8 and the DBD-deleted RORα sequence corresponds to amino acids 148-529 of SEQ ID NO: 4, the DBD-deleted DHR3 sequence corresponds to amino acids 148-513 of SEQ ID NO: 6, and the VP16 sequence corresponds to amino acids 148-231 of SEQ ID NO: 8. In an embodiment, inducible promoters regulating expression of the first, second, third, and fourth fusion proteins are identical promoters. In yet another embodiment, the inducible promoters regulating expression of the first, second, third, and fourth fusion proteins are copper inducible promoters.

[0019] Methods for using the assay of the ~~invention~~disclosure are also encompassed herein. Such methods include those involving use of the cell-based assay systems described

herein to screen diverse compound libraries, such as those available from research institutions, federal agencies,