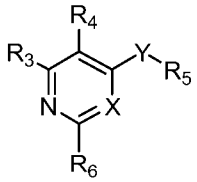
What is claimed is:

1. A compound of structural Formula XI:



(XI)

or a salt thereof, wherein:

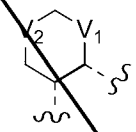
Y is CH_2;

X is chosen from CH and N;

R_3 is chosen from methyl, ethyl, trifluoromethyl, and cyclopropyl;

R_4 is chosen from hydrogen and ethyl;

or R_3 and R_4, together with the atoms to which they are attached, join to form a 5 to 6 membered cycloalkyl or heterocycloalkyl of the form:



V_1 is chosen from CH_2, N, O, SO_2, and S;

V_2 is chosen from a bond, N, O and CH_2;

R_5 is either benzoxaborole, or is chosen from phenyl and pyridinyl, either of which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13};

R_8 is chosen from a bond and lower alkyl;

R_9 is chosen from halogen, lower alkyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy, lower haloalkoxy, cyano, -C(O)N-, $S(O)_2$-, $B(OH)_2$, 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl;

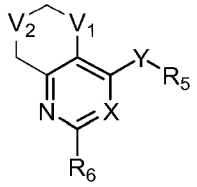
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

2. The compound as recited in claim 1, of structural Formula XII:



(XII)

or a salt thereof, wherein:

Y is CH_2;

X is chosen from CH and N;

V_1 is chosen from CH_2, N, O, SO_2, and S;

V_2 is chosen from a bond, N, O and CH_2;

R_5 is either benzoxaborole, or is chosen from phenyl and pyridinyl, either of which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13};

R_8 is chosen from a bond and lower alkyl;

R_9 is chosen from halogen, lower alkyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy, lower haloalkoxy, cyano, -C(O)N-, $S(O)_2$-, $B(OH)_2$, 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl;

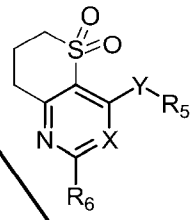
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

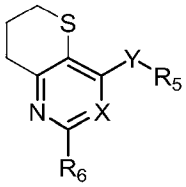
R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

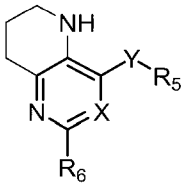
R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

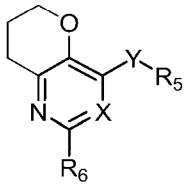
each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

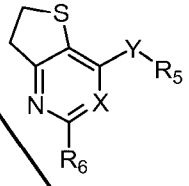
3. The compound as recited in claim 2, having any one of Formulas XIIa, XIIb, XIIc, XIId, XIIe, and XIIf :


(XIIa)

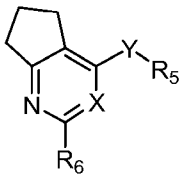

(XIIb)


(XIIc)


(XIId)


(XIIe)

, and


(XIIf)

or a salt thereof, wherein:

Y is CH_2;

X is chosen from CH and N;

R_5 is either benzoxaborole, or is chosen from phenyl and pyridinyl, either of which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13};

R_8 is chosen from a bond and lower alkyl;

R_9 is chosen from halogen, lower alkyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy, lower haloalkoxy, cyano, -C(O)N-, $S(O)_2$-, $B(OH)_2$, 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl;

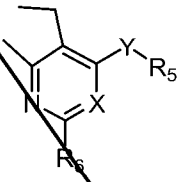
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

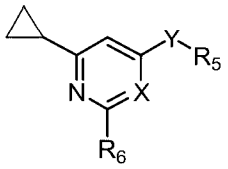
R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

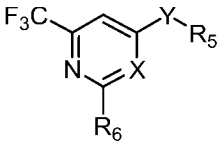
R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

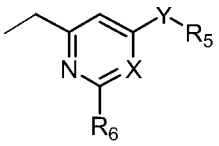
4. The compound as recited in claim 1, having any one of structural Formulas XIII, XIV, XV, and XVI:


(XIII)


(XIV)


(XV)

, and


(XVI)

or a salt thereof, wherein:

Y is CH_2;

X is chosen from CH and N;

R_5 is either benzoxaborole, or is chosen from phenyl and pyridinyl, either of which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13};

R_8 is chosen from a bond and lower alkyl;

R_9 is chosen from halogen, lower alkyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy, lower haloalkoxy, cyano, -C(O)N-, $S(O)_2$-, $B(OH)_2$, 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl;

$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

5. The compound as recited in claim 4, wherein R_5 is either benzoxaborole, or is phenyl which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13}.

6. The compound as recited in claim 5, wherein R_5 is phenyl which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$.

7. The compound as recited in claim 6, wherein

   R_9 is -C(O)N-;

   R_{10a} is lower hydroxyalkyl or hydrogen; and

   R_{10b} is hydrogen.

8. The compound as recited in claim 6, wherein

   R_9 is lower alkyl;

   R_{10a} is C(O)OH; and

   R_{10b} is null.

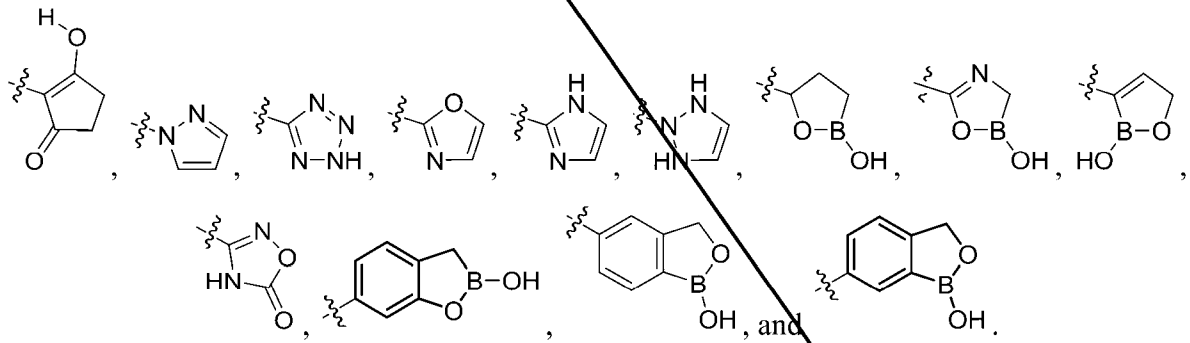
9. The compound as recited in claim6, wherein R_9 is lower hydroxyalkyl.

10. The compound as recited in claim 9, wherein R_9 is chosen from methanol, ethanol, isopropanol, *N*-propanol, and *t*-butanol.

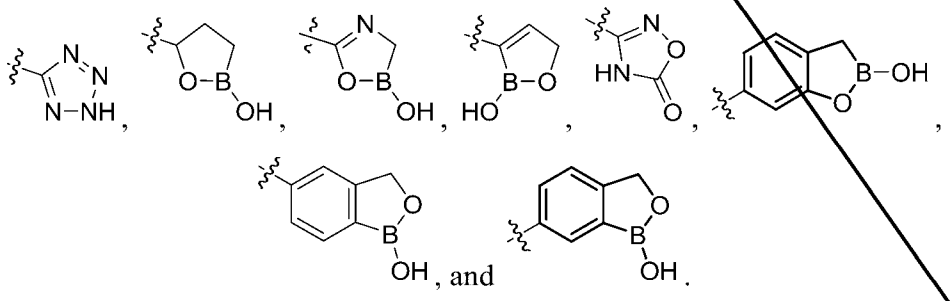
11. The compound as recited in claim 13, wherein R_9 is chosen from ethanol and *N*-propanol.

12. The compound as recited in claim6, wherein R_9 is chosen from 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl.

13. The compound as recited in claim12, wherein -R_9-$(R_{10})_a(R_{10})_b$ is chosen from:



14. The compound as recited in claim 13, wherein -R_9-$(R_{10})_a(R_{10})_b$ is chosen from:



15. The compound as recited in claim 6, wherein R_8 is a bond.

16. The compound as recited in claim6, wherein R_8 is lower alkyl.

17. The compound as recited in claim 19, wherein R_8 is methyl.

18. The compound as recited in claim 5, wherein R_5 is benzoxaborole.

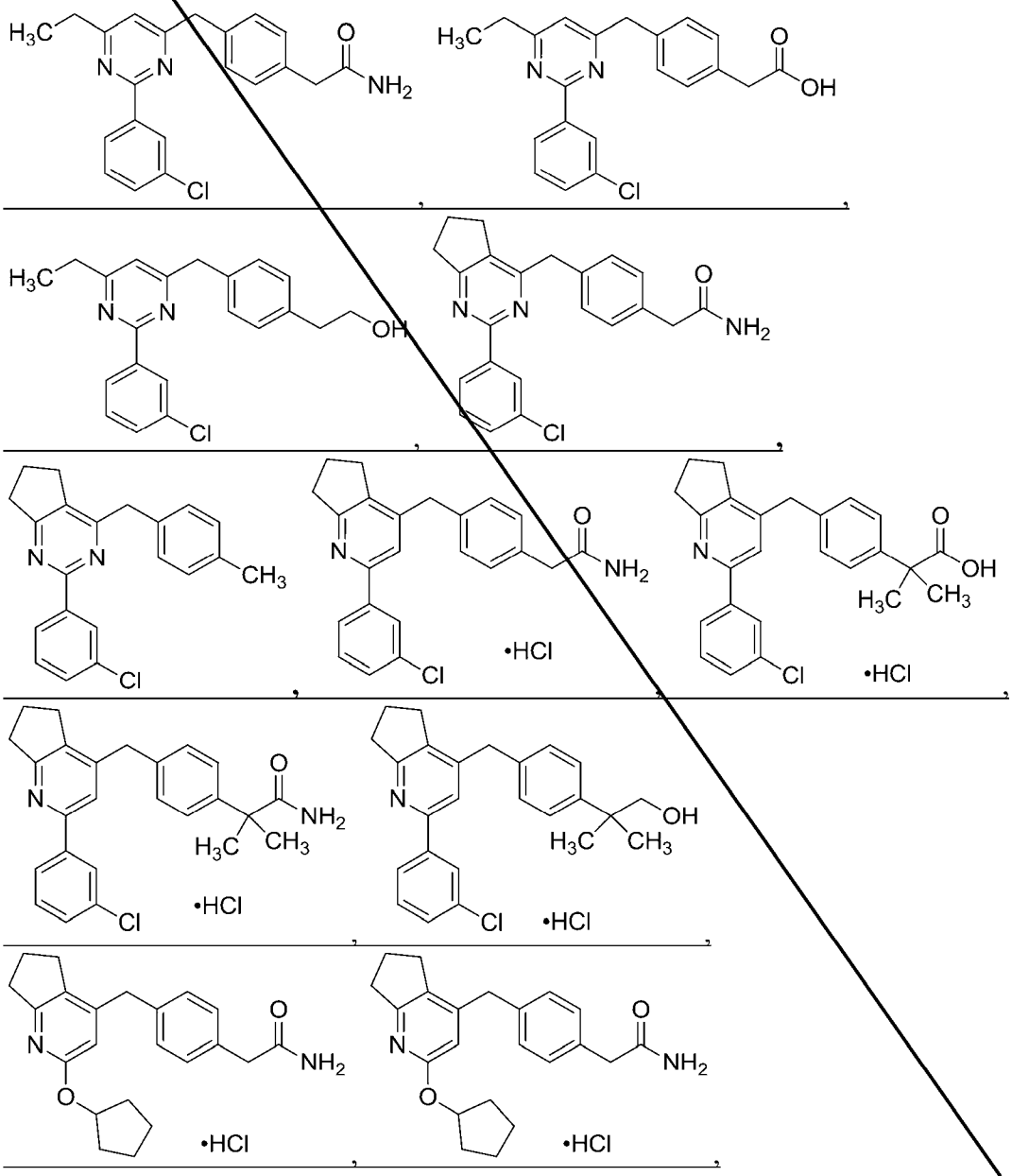
19. The compound as recited in claim 16, wherein X is N.

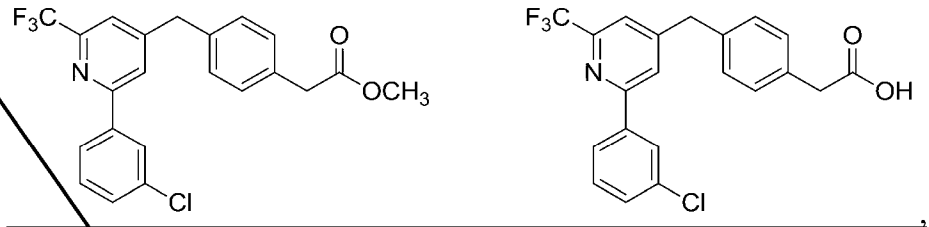
20. The compound as recited in claim 15, wherein X is CH.

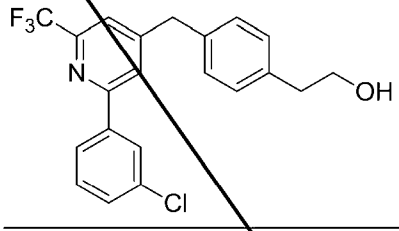
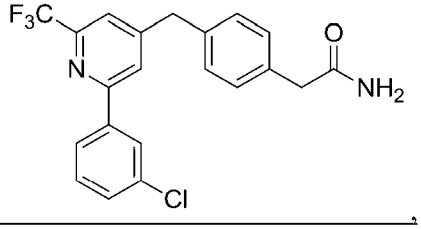
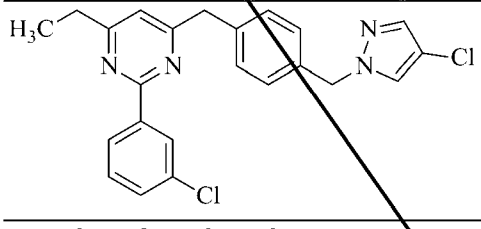
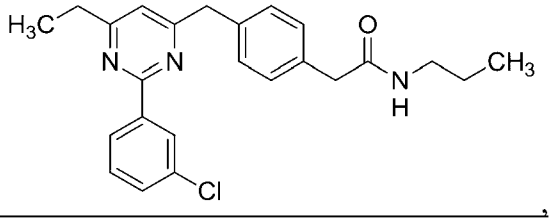
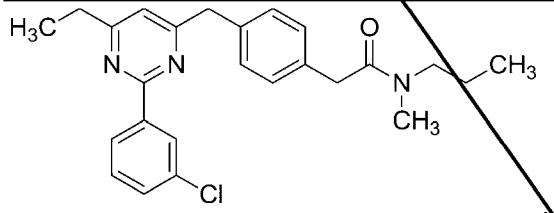
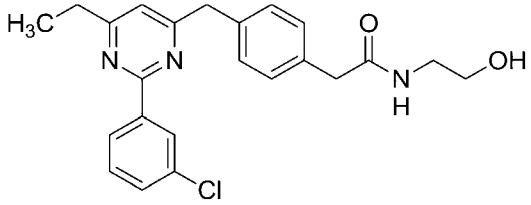
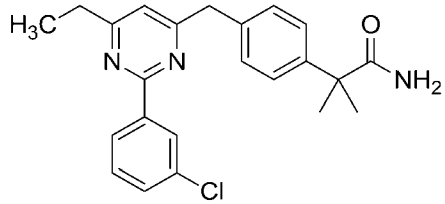
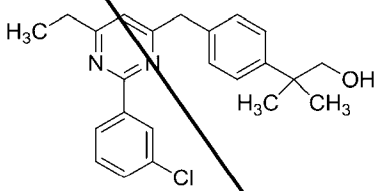
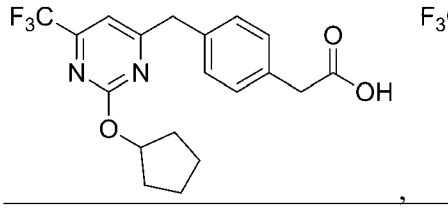
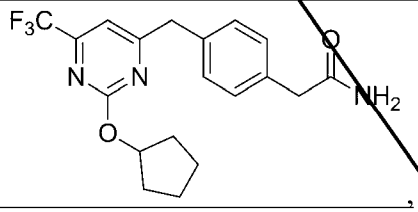
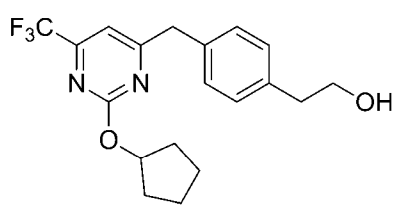
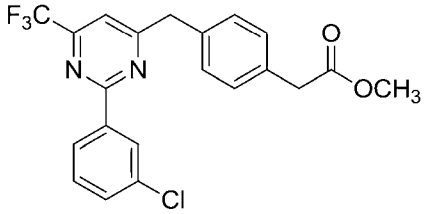
21. The compound as recited in claim 24, wherein R_6 is 3-chlorophenyl.

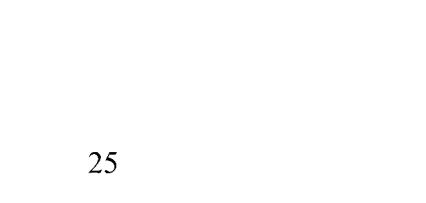
22. The compound as recited in claim 20, wherein R_6 is chosen from cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}.

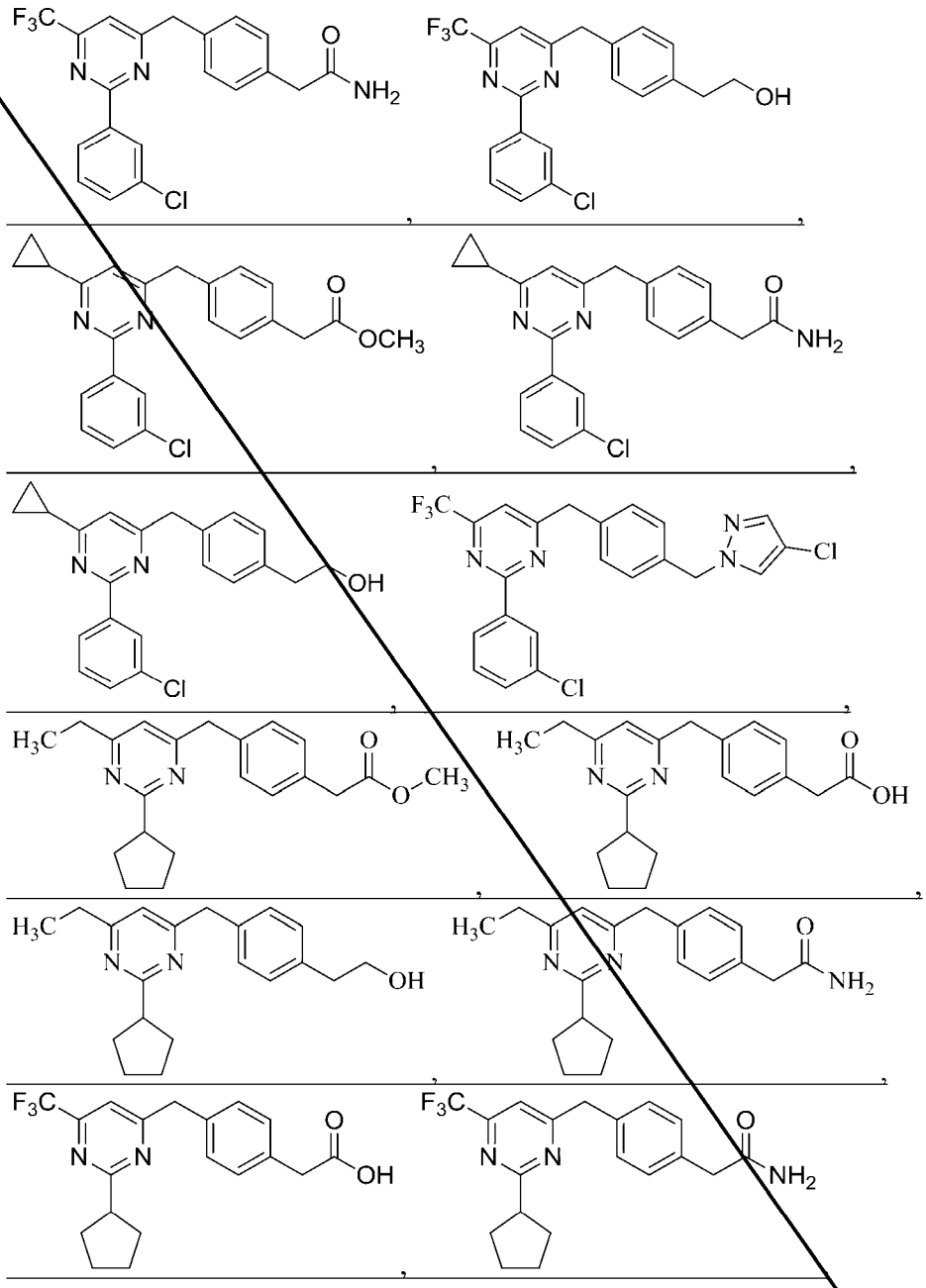
23. A compound chosen from:

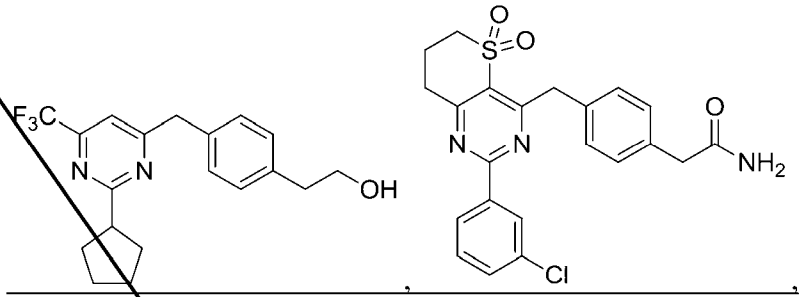


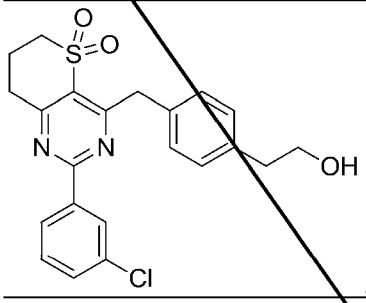
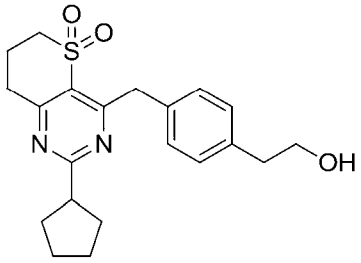
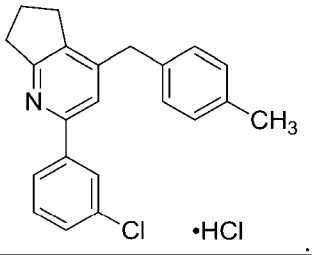








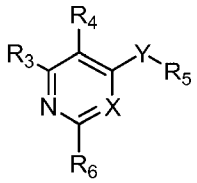




24. A compound as recited in claim 1 for use in the manufacture of a medicament for the treatment of a PDE4-mediated disease.
25. The compound as recited in claim 24 wherein the PDE4 is PDE4B.
26. The compound as recited in claim 25 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.
27. The compound as recited in claim 24 wherein the PDE4 is PDE4D.
28. A compound as recited in claim 1 for use in the manufacture of a medicament for the modulation of a PDE4-mediated function, wherein:
    the PDE4 is PDE4D;
    the modulation is enhancement; and
    the function is cognition.
29. The use of a compound as recited in claim 1 in the manufacture of a medicament for the treatment of a PDE4-mediated disease.
30. The use as recited in claim 29 wherein the PDE4 is PDE4B.
31. The use as recited in claim 30 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.
32. The use as recited in claim 29 wherein the PDE4 is PDE4D.
33. The use of a compound as recited in claim 1 in the manufacture of a medicament for the treatment of a patient in need of cognitive enhancement.

34. A pharmaceutical composition comprising a compound as recited in claim 1, together with a pharmaceutically acceptable carrier.
35. The pharmaceutical composition as recited in claim 34, additionally comprising another therapeutic agent.
36. The pharmaceutical composition as recited in claim 35, where in the additional therapeutic agent is an antidepressant.
37. The pharmaceutical composition as recited in claim 34, formulated as a tablet or capsule.
38. The use of a compound as recited in claims 1-23 in the manufacture of a medicament for the treatment of a PDE4-mediated disease.
39. The use as recited in claim 38 wherein the PDE4 is PDE4B.
40. The use as recited in claim 39 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.
41. The use as recited in claim 38 wherein the PDE4 is PDE4D.
42. The use of a compounded as recited in claims 1-23 in the manufacture of a medicament for the treatment of a patient in need of cognition enhancement.
43. The use as recited in any of claims 38-42 wherein the compound inhibits PDE4 by contact.
44. The compound as recited in any of claims 15-22, wherein
    R_9 is lower alkyl;
    R_{10a} is C(O)OH; and
    R_{10b} is null.
45. The compound as recited in any of claims 15-22, wherein
    R_9 is -C(O)N-;
    R_{10a} is lower hydroxyalkyl or hydrogen; and
    R_{10b} is hydrogen.

CLAIMS

1. A compound of structural Formula XI:



(XI)

or a salt thereof, wherein:

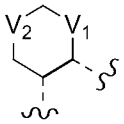
Y is CH_2;

X is chosen from CH and N;

R_3 is chosen from methyl, ethyl, trifluoromethyl, and cyclopropyl;

R_4 is chosen from hydrogen and ethyl;

or R_3 and R_4, together with the atoms to which they are attached, join to form a 5 to 6 membered cycloalkyl or heterocycloalkyl of the form:



V_1 is chosen from CH_2, N, O, SO_2, and S;

V_2 is chosen from a bond, N, O and CH_2;

R_5 is either benzoxaborole, or is chosen from phenyl and pyridinyl, either of which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13};

R_8 is chosen from a bond and lower alkyl;

R_9 is chosen from halogen, lower alkyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy, lower haloalkoxy, cyano, -C(O)N-, $S(O)_2$-, $B(OH)_2$, 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl;

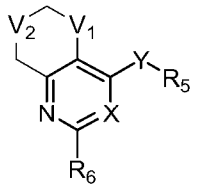
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

2. The compound as recited in claim 1, of structural Formula XII:



(XII)

or a salt thereof, wherein:

Y is CH_2;

X is chosen from CH and N;

V_1 is chosen from CH_2, N, O, SO_2, and S;

V_2 is chosen from a bond, N, O and CH_2;

R_5 is either benzoxaborole, or is chosen from phenyl and pyridinyl, either of which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13};

R_8 is chosen from a bond and lower alkyl;

R_9 is chosen from halogen, lower alkyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy, lower haloalkoxy, cyano, -C(O)N-, $S(O)_2$-, $B(OH)_2$, 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl;

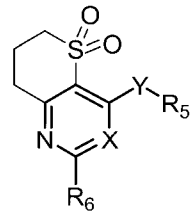
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

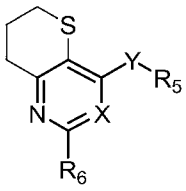
R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

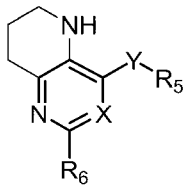
R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

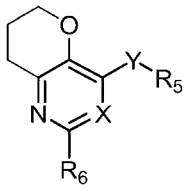
each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

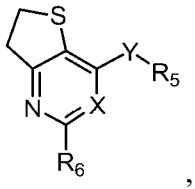
3. The compound as recited in claim 2, having any one of Formulas XIIa, XIIb, XIIc, XIId, XIIe, and XIIf:


(XIIa)

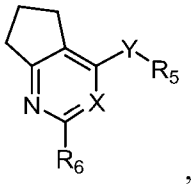

(XIIb)


(XIIc)


(XIId)


(XIIe)

, and


(XIIf)

or a salt thereof, wherein:

Y is CH_2;

X is chosen from CH and N;

R_5 is either benzoxaborole, or is chosen from phenyl and pyridinyl, either of which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13};

R_8 is chosen from a bond and lower alkyl;

R_9 is chosen from halogen, lower alkyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy, lower haloalkoxy, cyano, -C(O)N-, $S(O)_2$-, $B(OH)_2$, 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl;

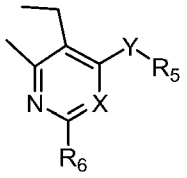
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

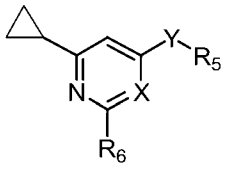
R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

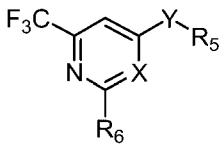
R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

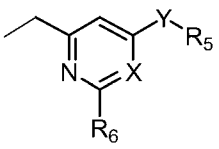
4. The compound as recited in claim 1, having any one of structural Formulas XIII, XIV, XV, and XVI:


(XIII)


(XIV)


(XV)

, and


(XVI)

or a salt thereof, wherein:

Y is CH_2;

X is chosen from CH and N;

R_5 is either benzoxaborole, or is chosen from phenyl and pyridinyl, either of which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13};

R_8 is chosen from a bond and lower alkyl;

R_9 is chosen from halogen, lower alkyl, lower haloalkyl, lower hydroxyalkyl, lower alkoxy, lower haloalkoxy, cyano, -C(O)N-, $S(O)_2$-, $B(OH)_2$, 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl;

$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

5. The compound as recited in claim 4, wherein R_5 is either benzoxaborole, or is phenyl which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$, and is optionally substituted with a substituent R_{13}.

6. The compound as recited in claim 5, wherein R_5 is phenyl which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$.

7. The compound as recited in claim 6, wherein

   R_9 is -C(O)N-;

   R_{10a} is lower hydroxyalkyl or hydrogen; and

   R_{10b} is hydrogen.

8. The compound as recited in claim 6, wherein

   R_9 is lower alkyl;

   R_{10a} is C(O)OH; and

   R_{10b} is null.

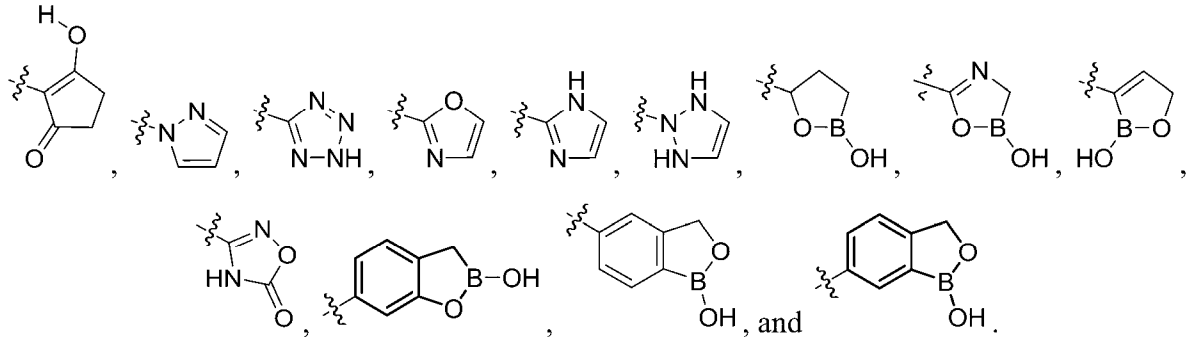
9. The compound as recited in claim6, wherein R_9 is lower hydroxyalkyl.

10. The compound as recited in claim 9, wherein R_9 is chosen from methanol, ethanol, isopropanol, *N*-propanol, and *t*-butanol.

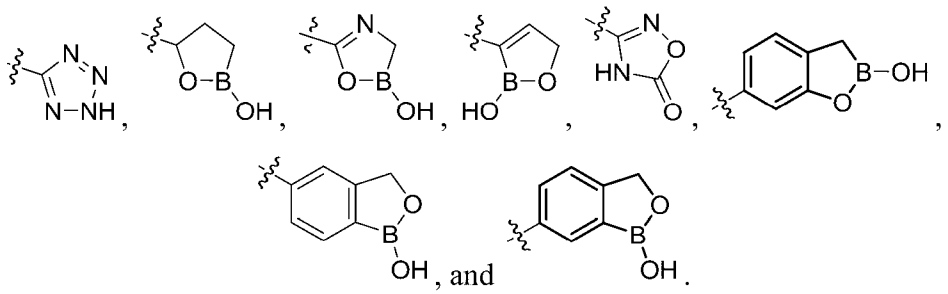
11. The compound as recited in claim 13, wherein R_9 is chosen from ethanol and *N*-propanol.

12. The compound as recited in claim6, wherein R_9 is chosen from 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl.

13. The compound as recited in claim12, wherein $-R_9-(R_{10})_a(R_{10})_b$ is chosen from:



14. The compound as recited in claim 13, wherein $-R_9-(R_{10})_a(R_{10})_b$ is chosen from:



15. The compound as recited in claim 6, wherein R_8 is a bond.

16. The compound as recited in claim6, wherein R_8 is lower alkyl.

17. The compound as recited in claim 19, wherein R_8 is methyl.

18. The compound as recited in claim 5, wherein R_5 is benzoxaborole.

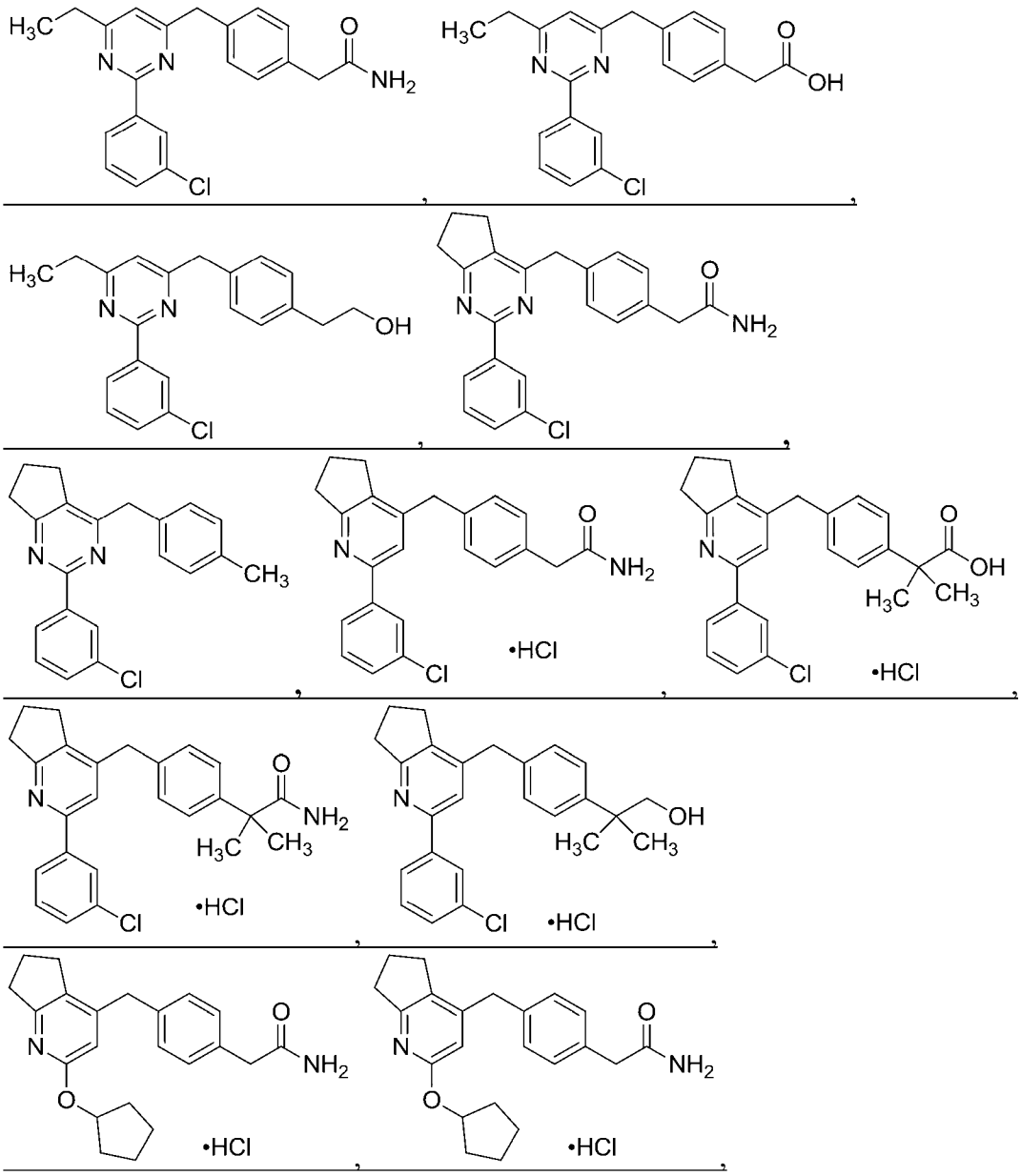
19. The compound as recited in claim 16, wherein X is N.

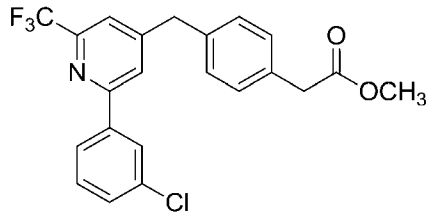
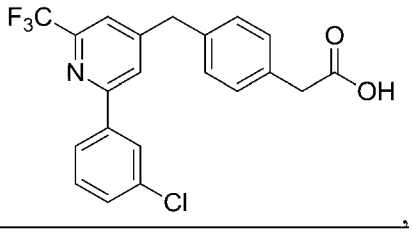
20. The compound as recited in claim 15, wherein X is CH.

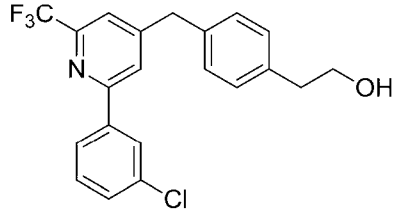
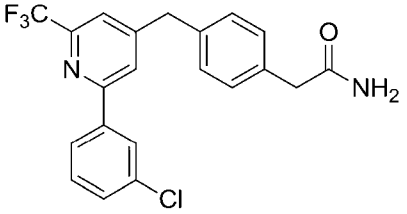
21. The compound as recited in claim 24, wherein R_6 is 3-chlorophenyl.

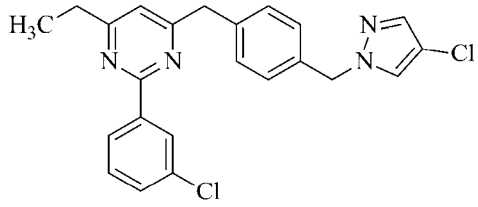
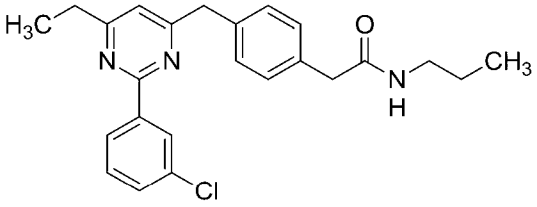
22. The compound as recited in claim 20, wherein R_6 is chosen from cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}.

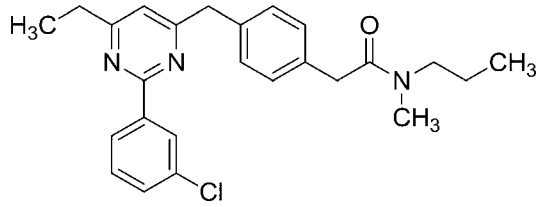
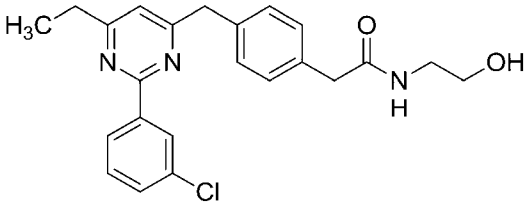
23. A compound chosen from:

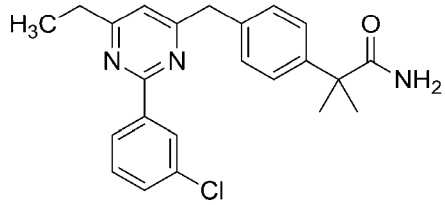
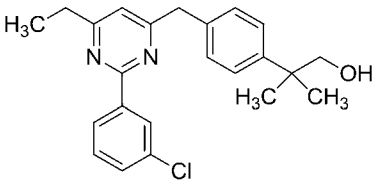


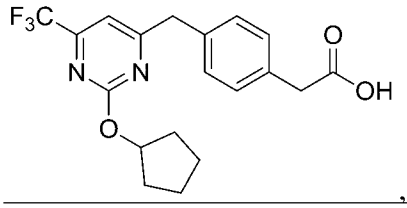
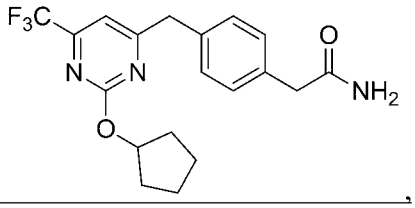



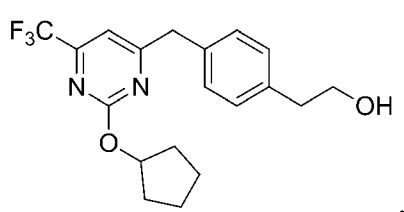
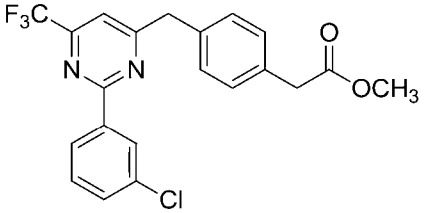



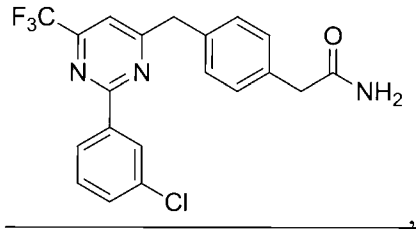
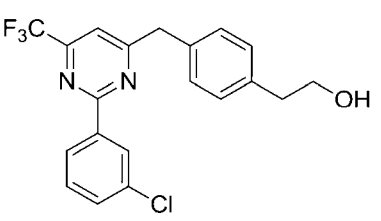
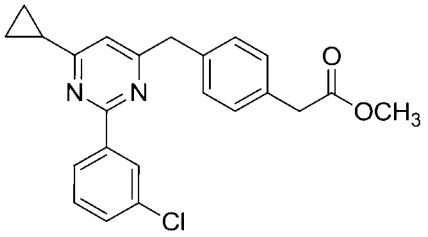
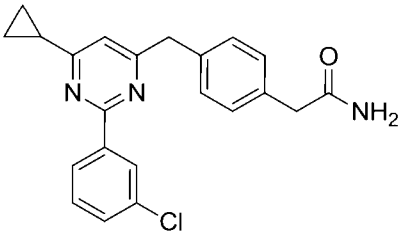
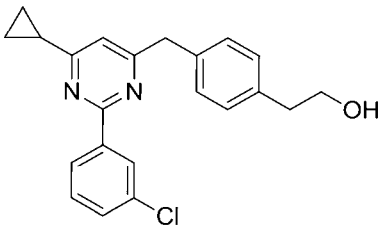
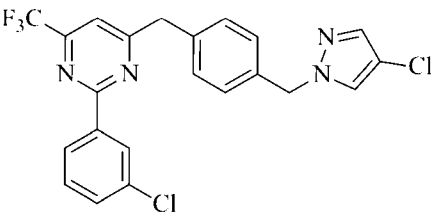
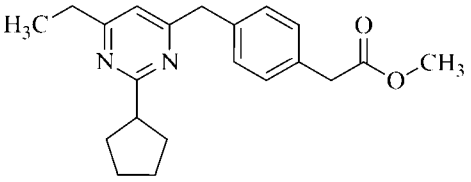
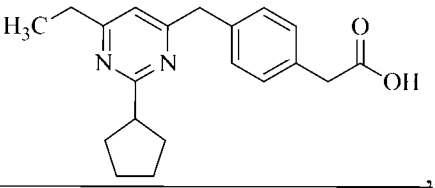
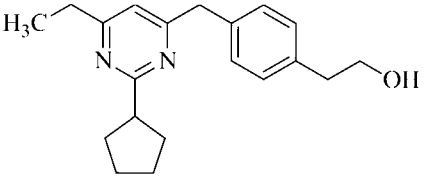
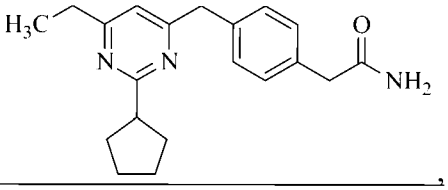
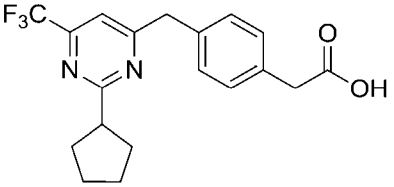
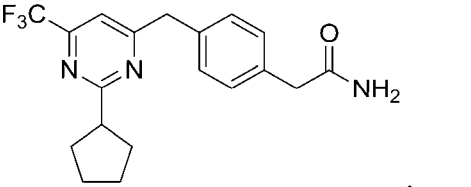



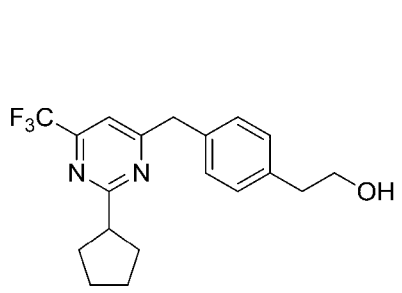
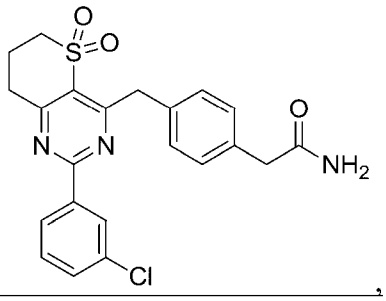
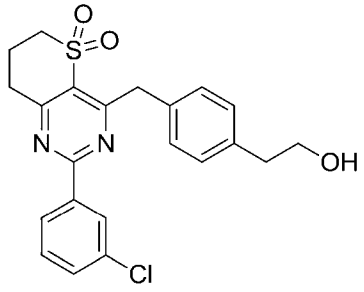
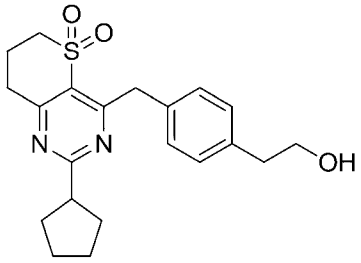
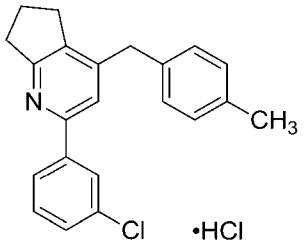



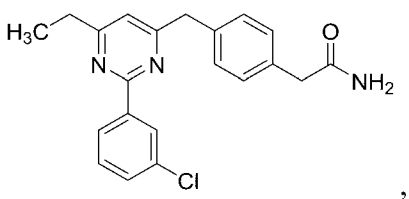
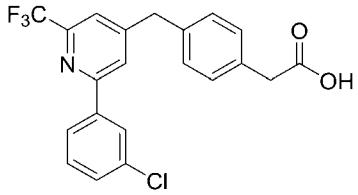
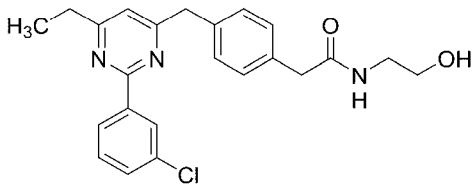



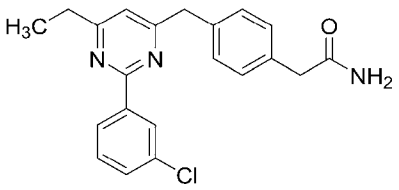













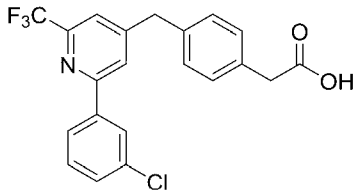
24. Use of a compound as recited in claim 1 in the manufacture of a medicament for the treatment of Alzheimer's disease, age-associated memory impairment, depression, and depression secondary to illness.
25. The use of a compound as recited in claim 24 in the manufacture of a medicament for the treatment of AIDS-related dementia (HIV dementia) and mild cognitive impairment (MCI).
26. The compound as recited in claim 23, wherein the compound is chosen from

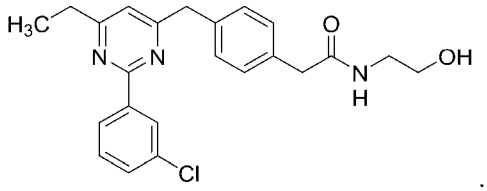
27. The compound as recited in claim 26, wherein the compound is



28. The compound as recited in claim 26, wherein the compound is



29. The compound as recited in claim 26, wherein the compound is



30. A pharmaceutical composition comprising a compound as recited in any of claims 1, 23, and 26-29 together with a pharmaceutically acceptable carrier.

31 . The pharmaceutical composition as recited in claim 30, additionally comprising another therapeutic agent.

32. The pharmaceutical composition as recited in claim 31, where in the additional therapeutic agent is an antidepressant.

33. The pharmaceutical composition as recited in claim 30, formulated as a tablet or capsule.

34. The compound as recited in any of claims 15-22, wherein

R_9 is lower alkyl;

R_{10a} is C(O)OH; and

R_{10b} is null.

35. The compound as recited in any of claims 15-22, wherein

R_9 is -C(O)N-;

R_{10a} is lower hydroxyalkyl or hydrogen; and

R_{10b} is hydrogen.