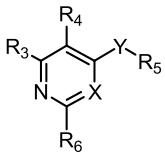
What is claimed is:

1. A compound of structural Formula XI:



(XI)

or a salt thereof, wherein:

Y is ~~chosen from O, NH, NR_2,~~ CH_2~~, $C(R_2)_2$, and $S(O)_n$~~;

X is chosen from CH and N;

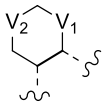
~~n is an integer chosen from 0, 1 or 2;~~

~~each R_2 is independently chosen from hydrogen and lower alkyl;~~

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;

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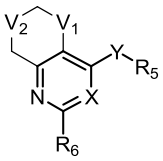
R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

R_6 is chosen from 3-chlorophenyl, ~~5-chloro-2-thienyl,~~ 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 ~~chosen from O, NH, and~~ 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, ~~5-chloro-2-thienyl,~~ cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

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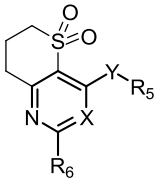
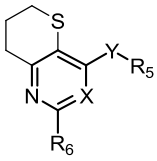
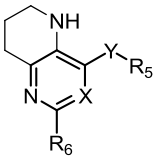
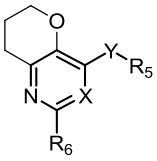
each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

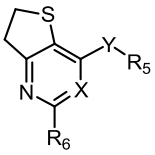
3. The compound as recited in claim 2, having any one of Formulas XIIa, XIIb, XIIc, XIId, XIIe, and XIIf :


(XIIa)

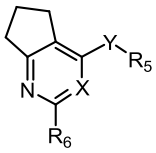

(XIIb)


(XIIc)


(XIId)


(XIIe)

, and


(XIIf)

or a salt thereof, wherein:

Y is ~~chosen from O, NH, and~~ 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, ~~5-chloro-2-thienyl,~~ cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

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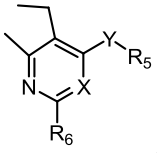
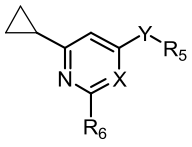
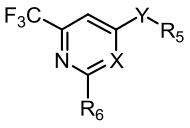
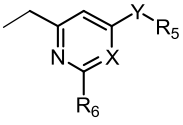
each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

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


(XIII)


(XIV)


(XV)


(XVI)

or a salt thereof, wherein:

Y is ~~chosen from O, NH, and~~ 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, ~~5-chloro-2-thienyl,~~ cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

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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 ~~any preceding~~ 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}.

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~~6. (Cancelled) The compound as recited in any preceding claim, wherein Y is chosen from O, NH, and CH_2.~~

~~7. (Cancelled) The compound as recited in claim 6, wherein Y is NH.~~

~~8. (Cancelled) The compound as recited in claim 6, wherein Y is CH_2.~~

~~9.~~6. The compound as recited in ~~any preceding~~ claim 5, wherein R_5 is phenyl which is *para*-substituted with a substituent of the form R_8-R_9-$(R_{10})_a(R_{10})_b$.

~~10.~~7. The compound as recited in ~~any of claims 1-9~~ claim ~~9~~6, wherein

R_9 is -C(O)N-;

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

R_{10b} is ~~null~~ hydrogen.

~~11.~~8. The compound as recited in ~~any of claims 1-9~~ claim ~~9~~6, wherein

R_9 is ~~C(O)N~~ lower alkyl;

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

R_{10b} is null.

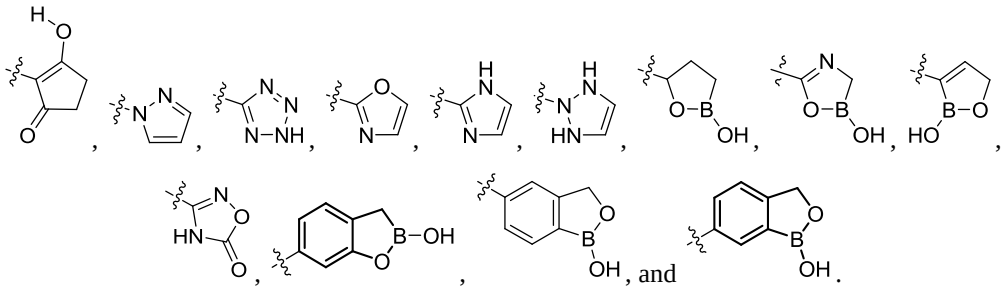
~~12.~~9. The compound as recited in ~~any of claims 1-9~~ claim ~~9~~6, wherein R_9 is lower hydroxyalkyl.

~~13.~~10. The compound as recited in ~~any of claims 1-9~~ claim ~~12~~9, wherein R_9 is chosen from methanol, ethanol, isopropanol, *N*-propanol, and *t*-butanol.

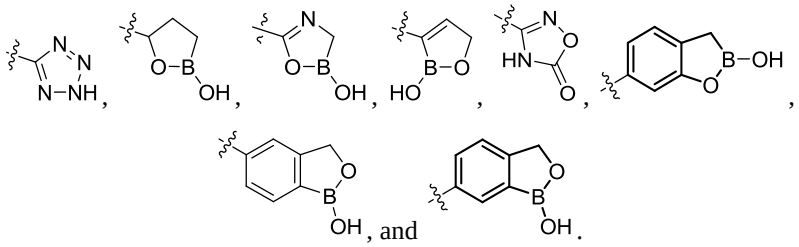
~~14.~~11. The compound as recited in claim 13, wherein R_9 is chosen from ethanol and *N*-propanol.

~~15.~~12. The compound as recited in ~~any of claims 1-9~~ claim ~~9~~6, wherein R_9 is chosen from 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl.

~~16.~~13. The compound as recited in claim ~~15~~12, wherein -R_9-$(R_{10})_a(R_{10})_b$ is chosen from:



~~17.~~14. The compound as recited in claim ~~16~~13, wherein -R_9-$(R_{10})_a(R_{10})_b$ is chosen from:



~~18.~~15. The compound as recited in ~~any preceding~~ claim ~~96~~, wherein R_8 is a bond.

~~19.~~16. The compound as recited in ~~any of claims 1-17~~ claim ~~96~~, wherein R_8 is lower alkyl.

~~20.~~17. The compound as recited in claim 19, wherein R_8 is methyl.

~~21.~~18. The compound as recited in ~~any preceding~~ claim 5, wherein R_5 is benzoxaborole.

~~22.~~19. The compound as recited in ~~any preceding~~ claim ~~19~~16, wherein X is N.

~~23.~~20. The compound as recited in ~~any of claims 1-21~~ claim ~~18~~15, wherein X is CH.

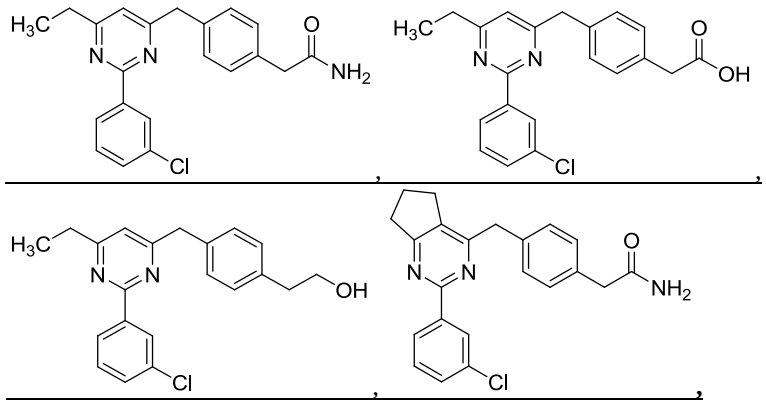
~~24.1. The compound as recited in any preceding claim 23, wherein R_6 is chosen from 3-chlorophenyl and 5-chloro-2-thienyl.~~

~~25.~~21. The compound as recited in claim 24, wherein R_6 is 3-chlorophenyl.

~~26.21. The compound as recited in claim 24, wherein R_6 is 5-chloro-2-thienyl.~~

~~27.~~22. The compound as recited in ~~any of claims 1-23~~ claim ~~23~~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}.

~~28.~~23. A compound chosen from ~~Examples 1-41 and 43-317~~:



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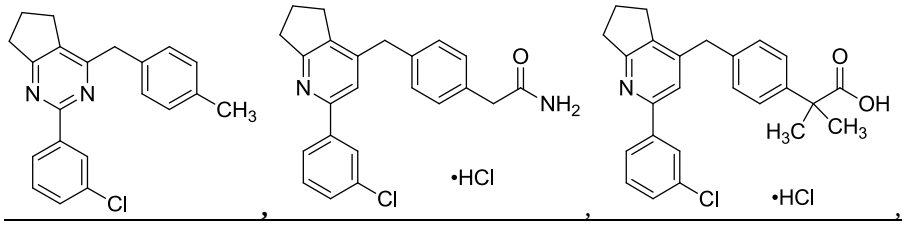

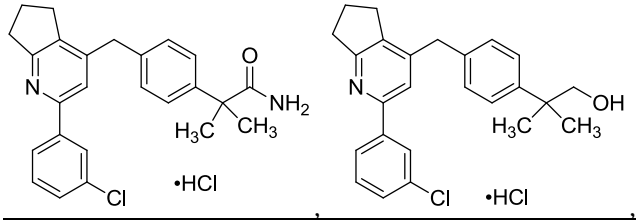

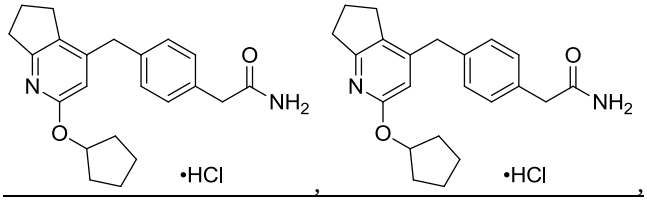

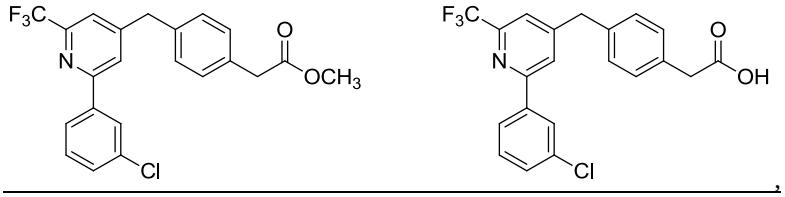

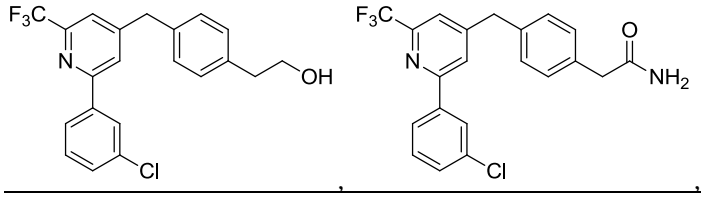

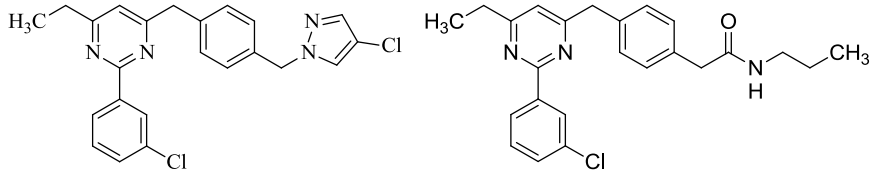

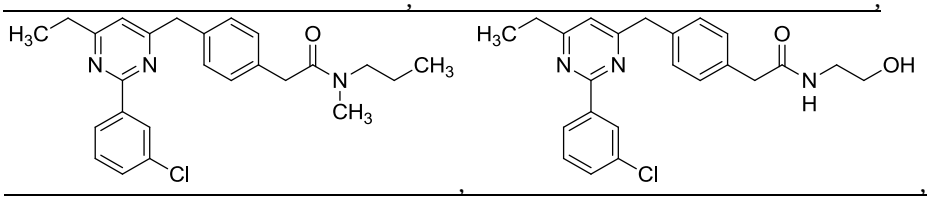

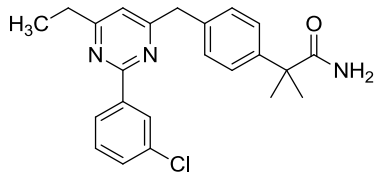
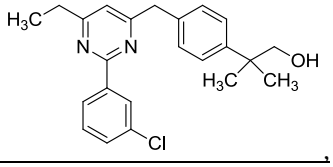
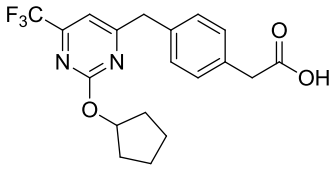
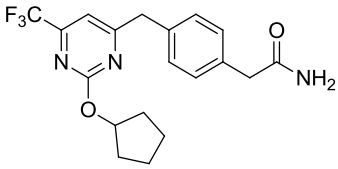
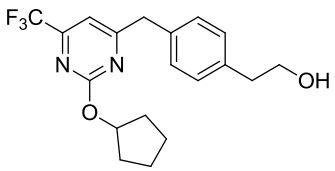
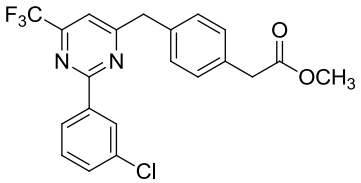
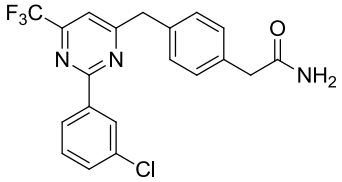
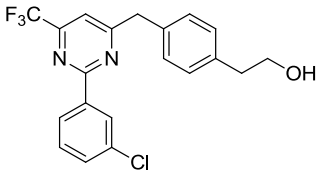
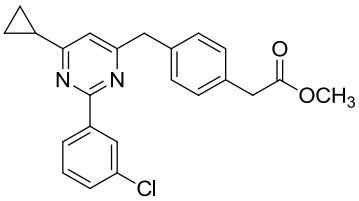
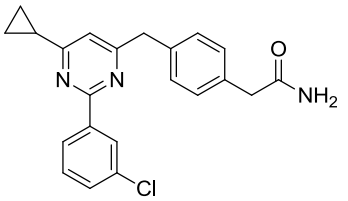
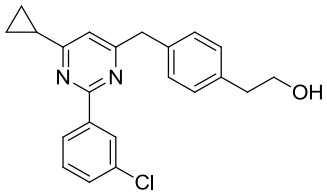
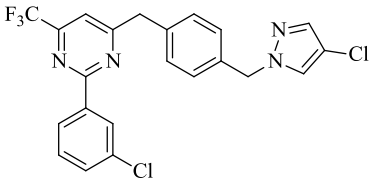
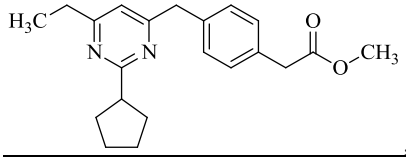
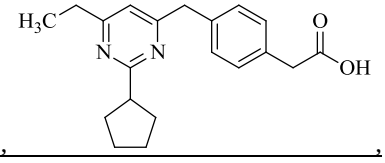

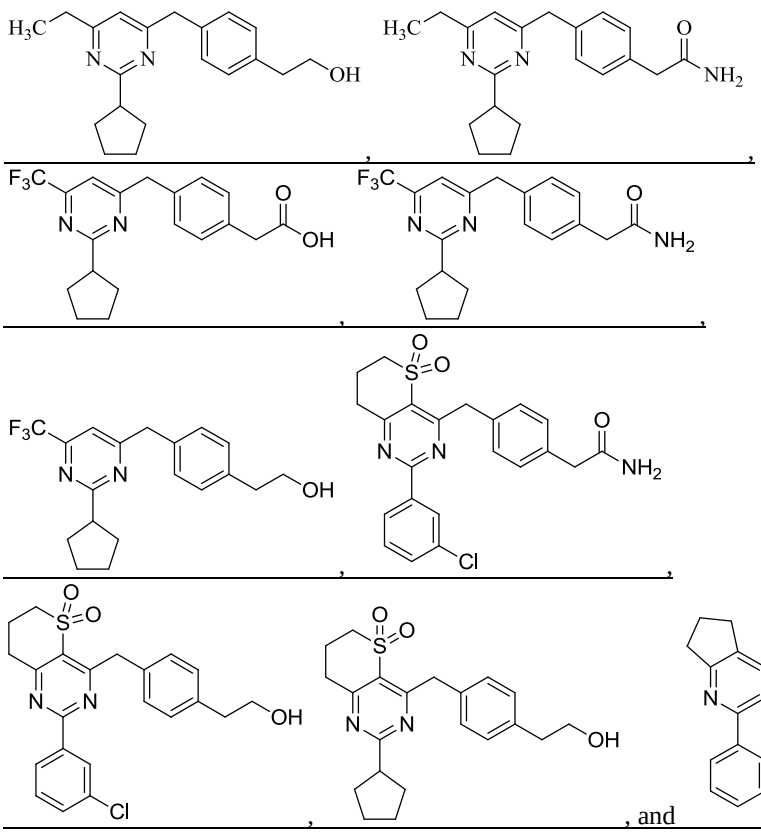

, and .

~~29.~~24. A compound as recited in ~~any of claims 1-28~~ claim 1 for use in the manufacture of a medicament for the treatment of a PDE4-mediated disease.

~~30.~~25. The compound as recited in claim ~~29~~ 264 wherein the PDE4 is PDE4B.

~~31.~~26. The compound as recited in claim ~~30~~ 275 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.

~~32.~~27. The compound as recited in claim ~~29~~ 264 wherein the PDE4 is PDE4D.

~~33.~~28. A compound as recited in claim 1 ~~any of claims 1-28~~ 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.

~~34.~~29. The use of a compound as recited in claim 1 in the manufacture of a medicament ~~any of claims 1-28~~ for the treatment of a PDE4-mediated disease.

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~~35.~~30. The use as recited in claim ~~34~~ ~~31~~29 wherein the PDE4 is PDE4B.

~~36.~~31. The use as recited in claim ~~35~~ ~~32~~30 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.

~~37.~~32. The use as recited in claim ~~34~~ ~~31~~29 wherein the PDE4 is PDE4D.

~~38.~~33. The use of a compound as recited in ~~any of claims 1-26~~ claim 1 in the manufacture of a medicament for the ~~modulation~~ treatment of ~~a~~ a patient in need of cognitive enhancement.

~~PDE4-mediated function, wherein:~~

~~the PDE4 is PDE4D;~~

~~the modulation is enhancement; and~~

~~the function is cognition.~~

~~39. The use of a compound as recited in any of claims 1-28~~ claim 1 ~~as a medicament for the treatment of a PDE4-mediated disease.~~

~~40.~~34. A pharmaceutical composition comprising a compound as recited in ~~any of claims 1-28~~ claim 1, together with a pharmaceutically acceptable carrier.

~~41.~~35. The pharmaceutical composition as recited in claim ~~40~~ ~~36~~34, additionally comprising another therapeutic agent.

~~42.~~36. The pharmaceutical composition as recited in claim ~~41~~ ~~37~~35, where in the additional therapeutic agent is an antidepressant.

~~43.~~37. The pharmaceutical composition as recited in claim ~~40~~ ~~36~~34, formulated as a tablet or capsule.

~~44.~~38. ~~A method of treatment of a~~The use of a compound as recited in claims 1-~~25~~23 in the manufacture of a medicament for the treatment of a PDE4-mediated disease. ~~in a subject comprising the administration of a therapeutically effective amount of a compound as recited in any of claims 1-28.~~

~~45.~~39. The ~~method~~ use as recited in claim ~~44~~ ~~40~~38 wherein the PDE4 is PDE4B.

~~46.~~40. The ~~method~~ use as recited in claim ~~45~~ ~~41~~39 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.

~~47.~~41. The ~~method~~ use as recited in claim ~~44~~ ~~40~~38 wherein the PDE4 is PDE4D.

~~48.~~42. ~~A method of modulation of a~~The use of a compounded as recited in claims 1-~~25~~23 in the manufacture of a medicament for the treatment of a patient in need of cognition

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enhancement. ~~PDE4 mediated function in a subject comprising the administration of a therapeutically effective amount of a compound as recited in any of claims 1-28, wherein:~~

~~the PDE4 is PDE4D;~~

~~the modulation is enhancement; and~~

~~the function is cognition.~~

~~49. A method for achieving an effect in a patient comprising the administration of a therapeutically effective amount of a compound as recited in any of claims 1-28 to a patient, wherein the effect is cognition enhancement.~~

~~50.~~43. ~~A method of inhibiting PDE4 comprising contacting PDE4 with a compound~~The use as recited in any of claims ~~1-28~~40~~38-44~~42 wherein the compound inhibits PDE4 by contact.

~~51.~~44. The compound as recited in any of claims ~~18~~15-~~272~~422, wherein

R_9 is lower alkyl;

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

R_{10b} is null.

~~52.~~45. The compound as recited in any of claims ~~18~~15-~~272~~422, wherein

R_9 is -C(O)N-;

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

R_{10b} is hydrogen.

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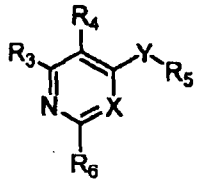
Attorney Docket No. TDP0001-401-PC

REPLACEMENT SHEET

AMENDED CLAIMS – CHANGES SHOWN

What is claimed is:

1. A compound of structural Formula XI:



(XI)

or a salt thereof, wherein:

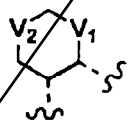
Y is CH_2;

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;

AMENDED SHEET (ART. 34)

Attorney Docket No. TDP0001-401-PC

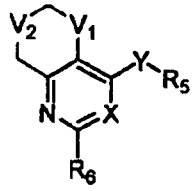
REPLACEMENT SHEET

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

R_6 is chosen from 3-chlorophenyl, 5-chloro-2-thienyl, 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;

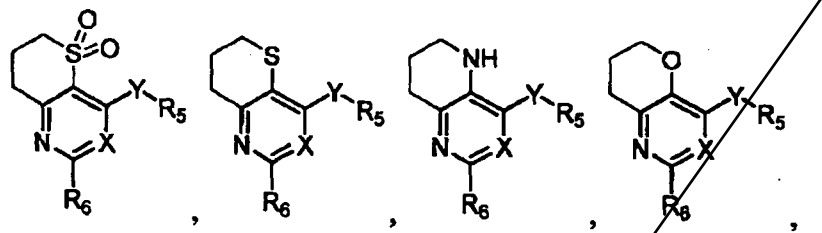
R_6 is chosen from 3-chlorophenyl, 5-chloro-2-thienyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

AMENDED SHEET(ART. 34)

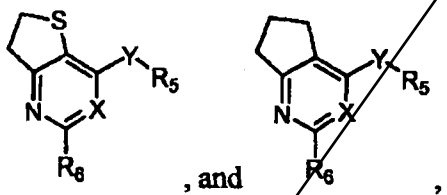
Attorney Docket No. TDP0001-401-PC
REPLACEMENT SHEET

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, 5-chloro-2-thienyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

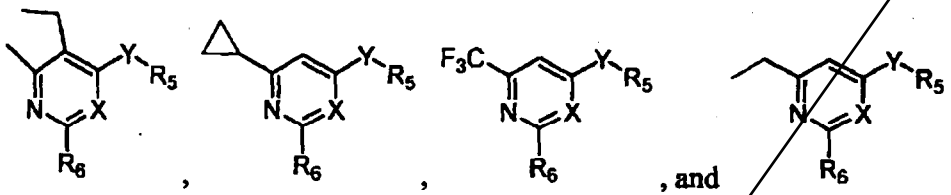
AMENDED SHEET(ART. 34)

Attorney Docket No. TDP0001-401-PC

REPLACEMENT SHEET

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) (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, 5-chloro-2-thienyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

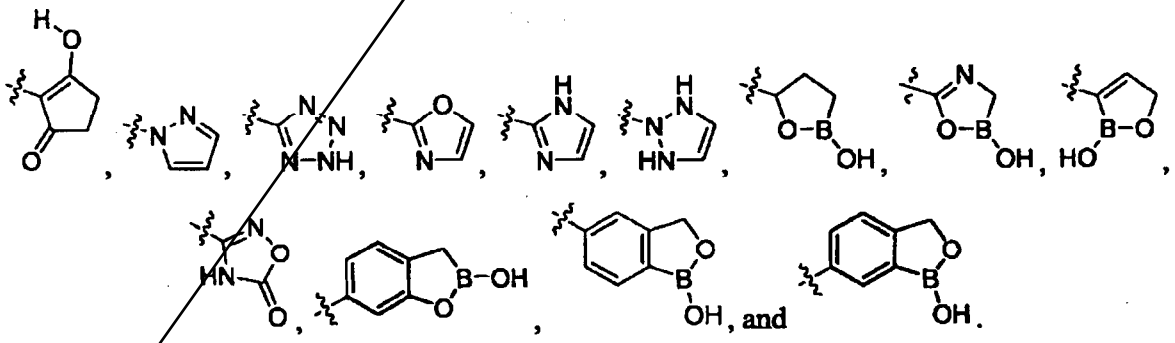
each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

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}.

AMENDED SHEET (ART. 34)

Attorney Docket No. TDP0001-401-PC
REPLACEMENT SHEET

6. (Cancelled)
7. (Cancelled)
8. (Cancelled)
9. 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-$(R_{10})_a(R_{10})_b$.
10. The compound as recited in claim 9, wherein
    R_9 is -C(O)N-;
    R_{10a} is lower hydroxyalkyl or hydrogen; and
    R_{10b} is hydrogen.
11. The compound as recited in claim 9, wherein
    R_9 is lower alkyl;
    R_{10a} is C(O)OH; and
    R_{10b} is null.
12. The compound as recited in claim 9, wherein R_9 is lower hydroxyalkyl.
13. The compound as recited in claim 12, wherein R_9 is chosen from methanol, ethanol, isopropanol, *N*-propanol, and *t*-butanol.
14. The compound as recited in claim 13, wherein R_9 is chosen from ethanol and *N*-propanol.
15. The compound as recited in claim 9, wherein R_9 is chosen from 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl.
16. The compound as recited in claim 15, wherein -R_9-$(R_{10})_a(R_{10})_b$ is chosen from:

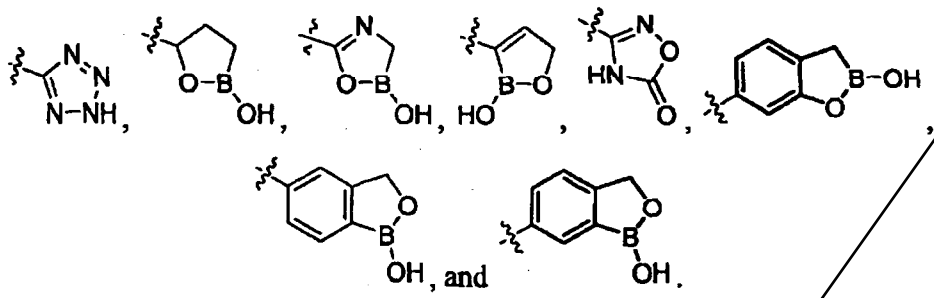


17. The compound as recited in claim 16, wherein -R_9-$(R_{10})_a(R_{10})_b$ is chosen from:

AMENDED SHEET (ART. 34)

Attorney Docket No. TDP0001-401-PC

REPLACEMENT SHEET



18. The compound as recited in claim 9, wherein R_8 is a bond.

19. The compound as recited in claim 9, wherein R_8 is lower alkyl.

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

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

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

23. The compound as recited in claim 18, wherein X is CH.

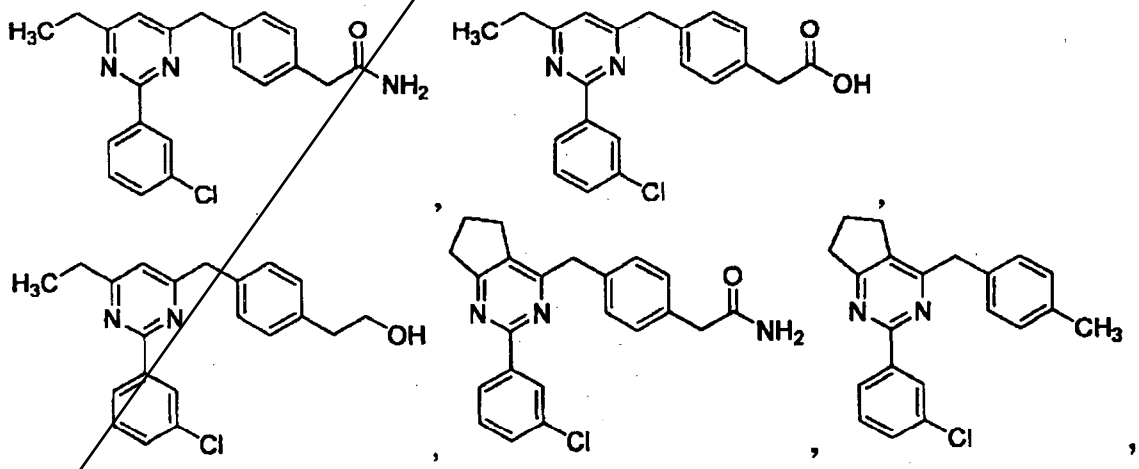
24. The compound as recited in claim 23, wherein R_6 is chosen from 3-chlorophenyl and 5-chloro-2-thienyl.

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

26. The compound as recited in claim 24, wherein R_6 is 5-chloro-2-thienyl.

27. The compound as recited in claim 23, 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}.

28. A compound chosen from:



AMENDED SHEET(ART. 34)

Attorney Docket No. TDP0001-401-PC

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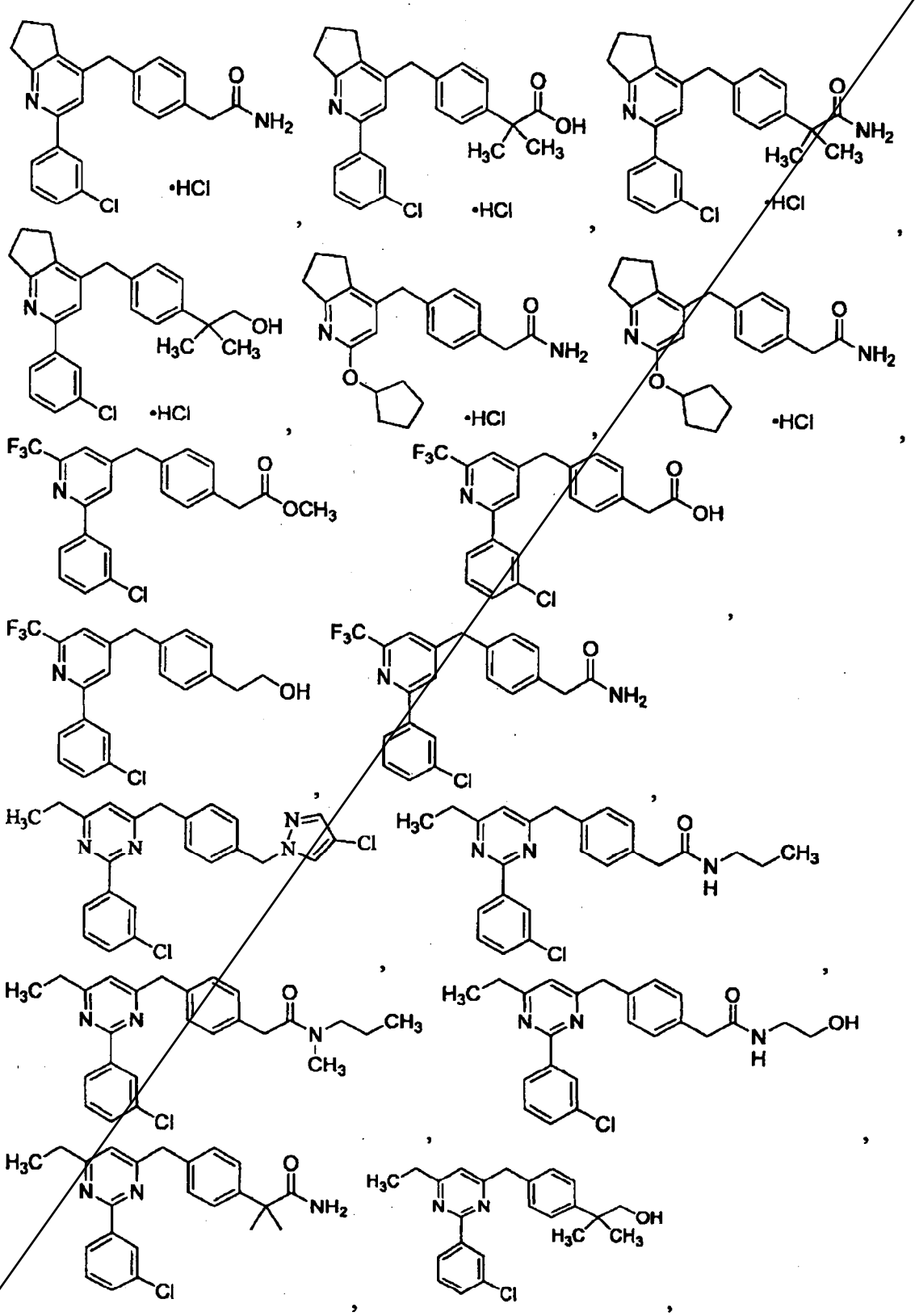

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Attorney Docket No. TDP0001-401-PC

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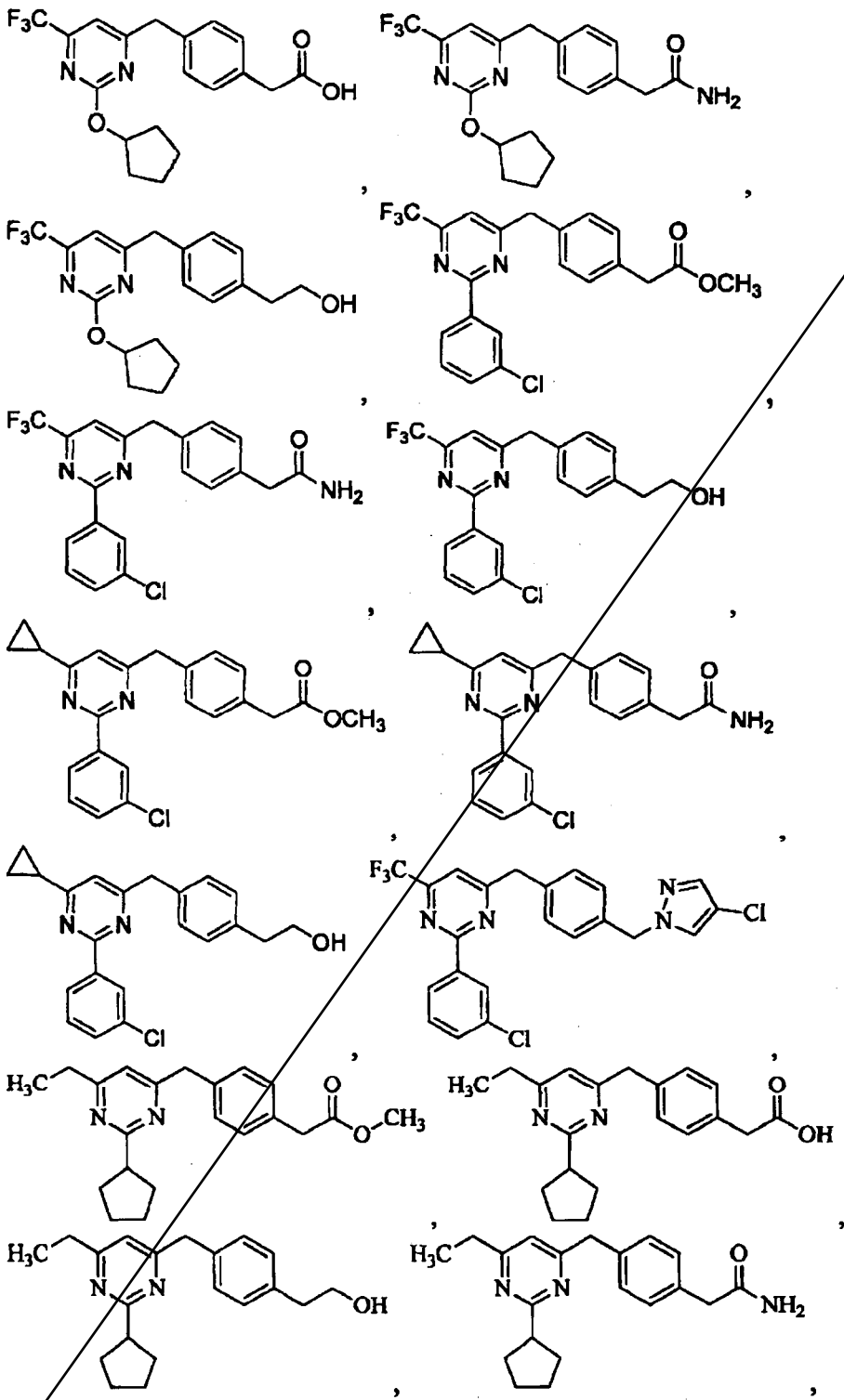

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Attorney Docket No. TDP0001-401-PC

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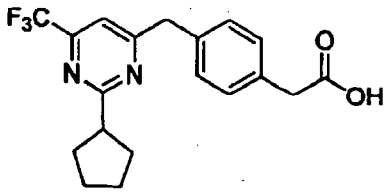
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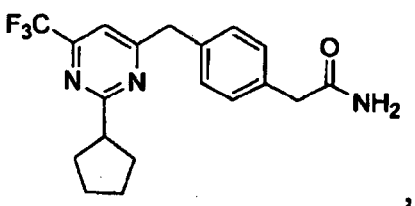
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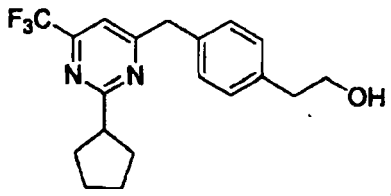
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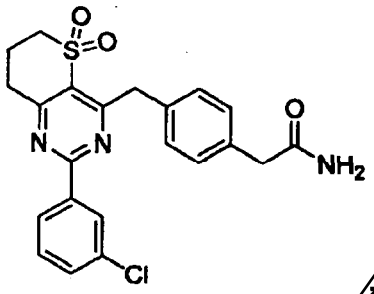
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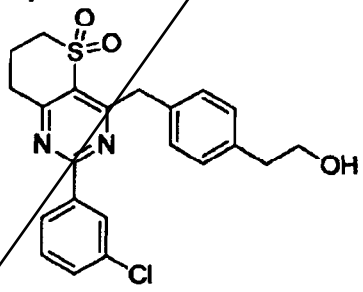
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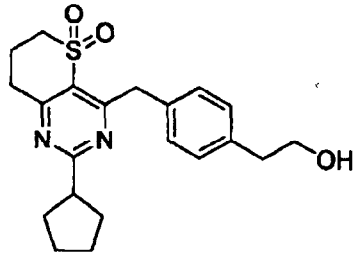
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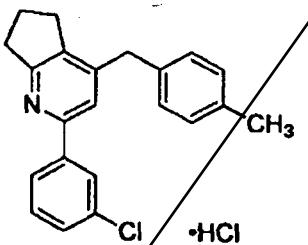

•HCl .

29. A compound as recited in claim 1 for use in the manufacture of a medicament for the treatment of a PDE4-mediated disease.
30. The compound as recited in claim 29 wherein the PDE4 is PDE4B.
31. The compound as recited in claim 30 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.
32. The compound as recited in claim 29 wherein the PDE4 is PDE4D.
33. 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.
34. The use of a compound as recited in claim 1 for the treatment of a PDE4-mediated disease.
35. The use as recited in claim 34 wherein the PDE4 is PDE4B.
36. The use as recited in claim 35 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.
37. The use as recited in claim 34 wherein the PDE4 is PDE4D.

AMENDED SHEET(ART. 34)

Attorney Docket No. TDP0001-401-PC

REPLACEMENT SHEET

38. The use of a compound as recited in claim 1 for the modulation of a PDE4-mediated function, wherein:
the PDE4 is PDE4D;
the modulation is enhancement; and
the function is cognition.
39. The use of a compound as recited in claim 1 as a medicament for the treatment of a PDE4-mediated disease.
40. A pharmaceutical composition comprising a compound as recited in claim 1, together with a pharmaceutically acceptable carrier.
41. The pharmaceutical composition as recited in claim 40, additionally comprising another therapeutic agent.
42. The pharmaceutical composition as recited in claim 41, where in the additional therapeutic agent is an antidepressant.
43. The pharmaceutical composition as recited in claim 40, formulated as a tablet or capsule.
44. A method of treatment of a PDE4-mediated disease in a subject comprising the administration of a therapeutically effective amount of a compound as recited in any of claims 1-28.
45. The method as recited in claim 44 wherein the PDE4 is PDE4B.
46. The method as recited in claim 45 wherein the PDE4B-mediated disease is chosen from depression and depression secondary to illness.
47. The method as recited in claim 44 wherein the PDE4 is PDE4D.
48. A method of modulation of a PDE4-mediated function in a subject comprising the administration of a therapeutically effective amount of a compound as recited in any of claims 1-28, wherein:
the PDE4 is PDE4D;
the modulation is enhancement; and
the function is cognition.
49. A method for achieving an effect in a patient comprising the administration of a therapeutically effective amount of a compound as recited in any of claims 1-28 to a patient, wherein the effect is cognition enhancement.

AMENDED SHEET (ART. 34)

Attorney Docket No. TDP0001-401-PC
REPLACEMENT SHEET

50. A method of inhibiting PDE4 comprising contacting PDE4 with a compound as recited in any of claims 1-28.

51. The compound as recited in any of claims 18-27, wherein

R_9 is lower alkyl;

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

R_{10b} is null.

52. The compound as recited in any of claims 18-27, wherein

R_9 is -C(O)N-;

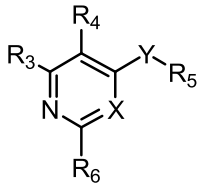
R_{10a} is lower hydroxyalkyl or hydrogen; and

R_{10b} is hydrogen.

AMENDED SHEET (ART. 34)

What is claimed is:

1. A compound of structural Formula XI:



(XI)

or a salt thereof, wherein:

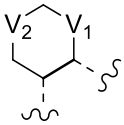
Y is CH_2;

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;

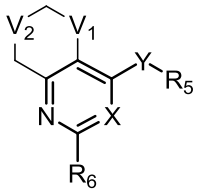
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

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;

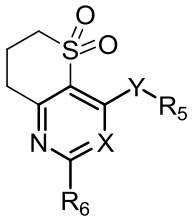
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

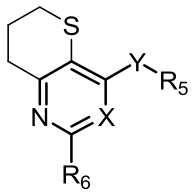
R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

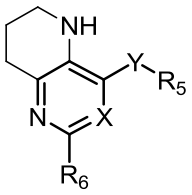
R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

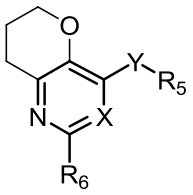
each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

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



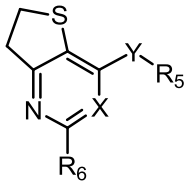
, 

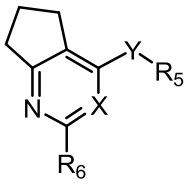
, 

, 

,

(XIIa) (XIIb) (XIIc) (XIId)



, and 

,

(XIIe) (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;

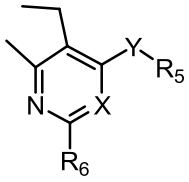
$(R_{10})_a$ and $(R_{10})_b$ are each independently chosen from null, hydrogen, halogen, trifluoromethyl, trifluoromethoxy, hydroxyl, lower hydroxyalkyl, cyano, oxo, lower alkyl, C(O)OH, and C(O)O lower alkyl;

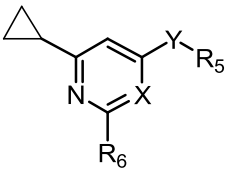
R_{13} is chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano;

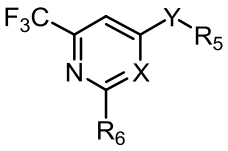
R_6 is chosen from 3-chlorophenyl, cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}; and

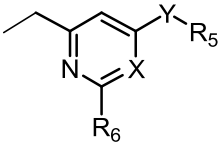
each R_{14} is independently chosen from halogen, hydroxy, lower alkyl, trifluoromethyl, lower alkoxy, trifluoromethoxy, NH_2, and cyano.

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



, 

, 

, and 

(XIII) (XIV) (XV) (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.

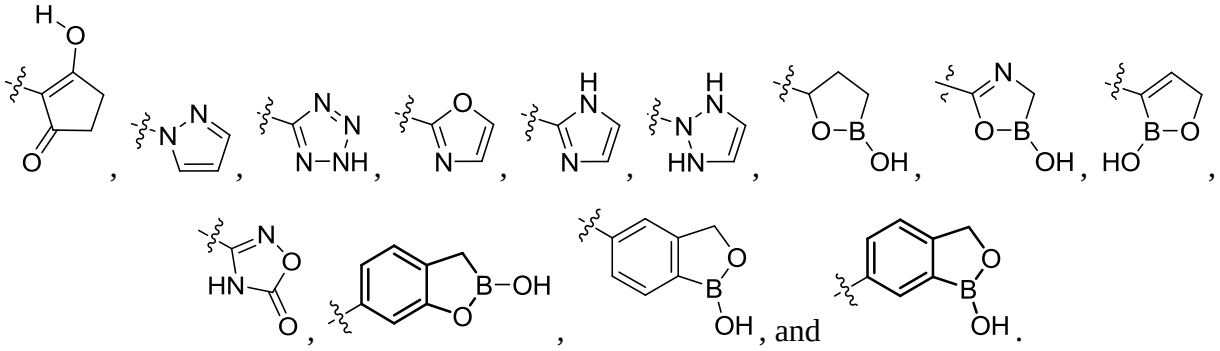
9. The compound as recited in claim6, wherein R_9 is lower hydroxyalkyl.

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.

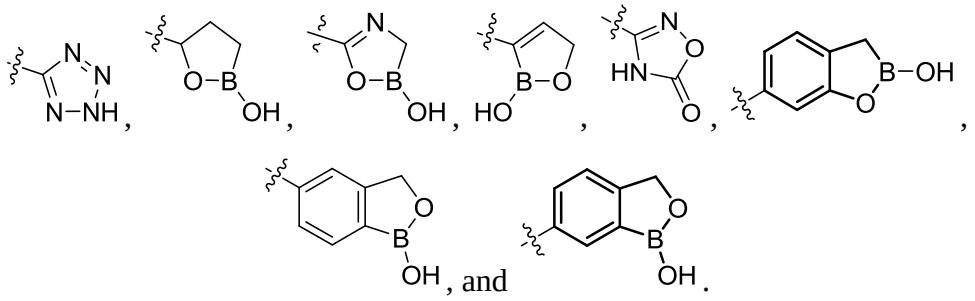
12. The compound as recited in claim6, wherein R_9 is chosen from 5-6 membered monocyclic heterocycloalkyl, and 5-6 membered monocyclic heteroaryl.

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



, and .

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



, and .

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.

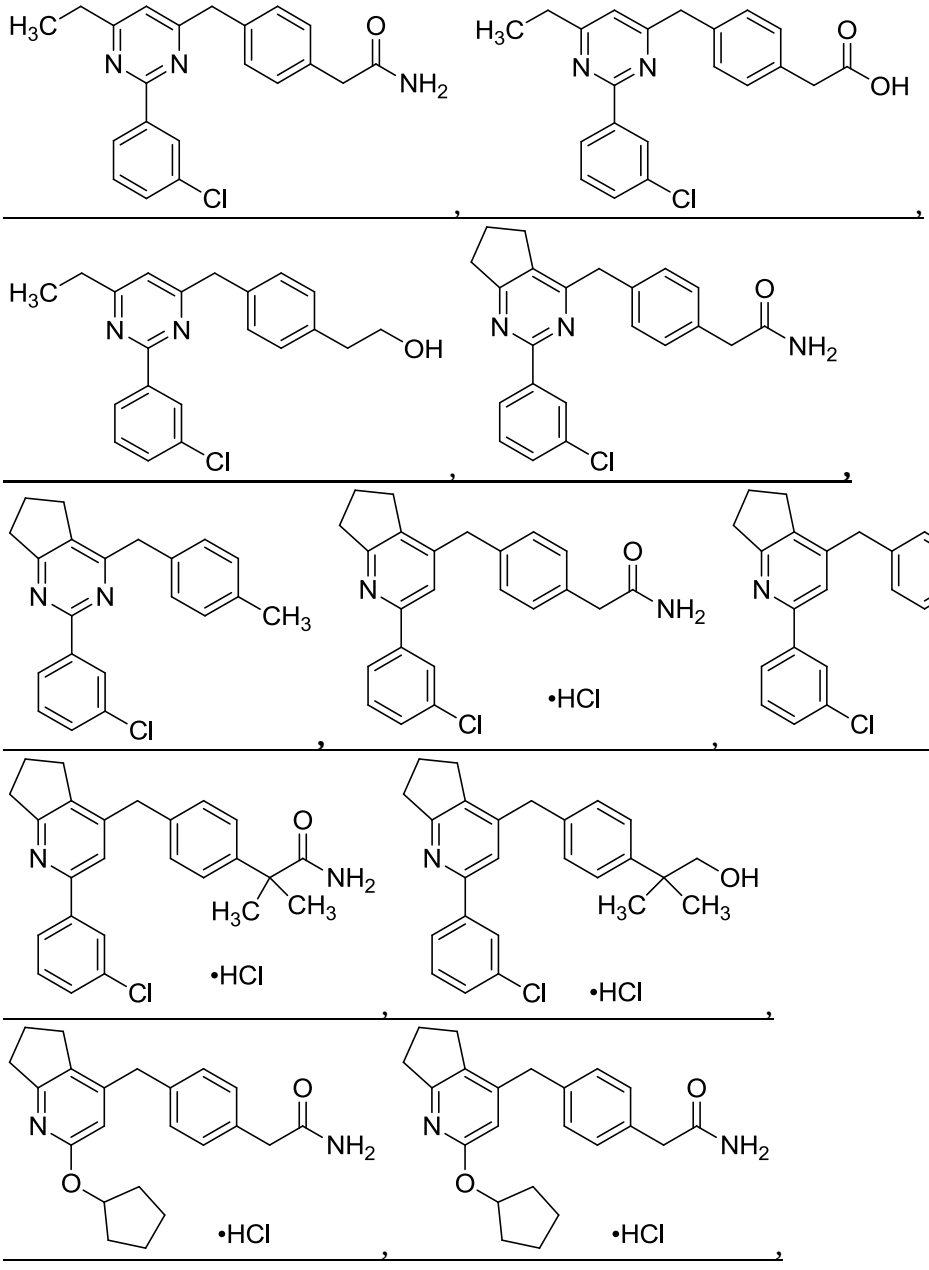
19. The compound as recited in claim 16, wherein X is N.

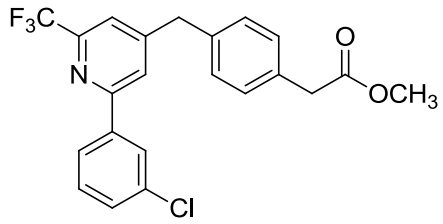
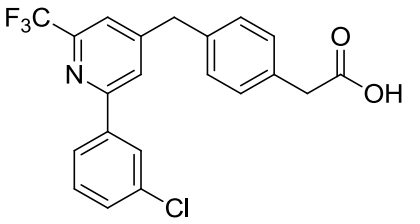
20. The compound as recited in claim 15, wherein X is CH.

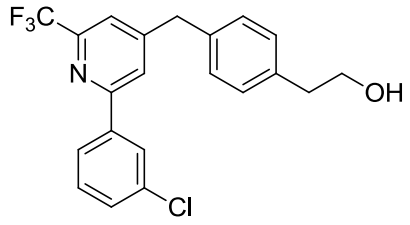
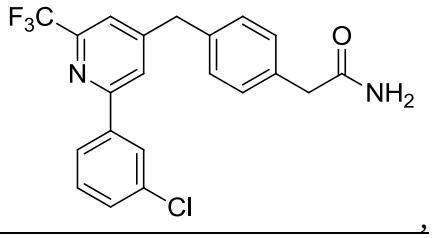
21. The compound as recited in claim 24, wherein R_6 is 3-chlorophenyl.

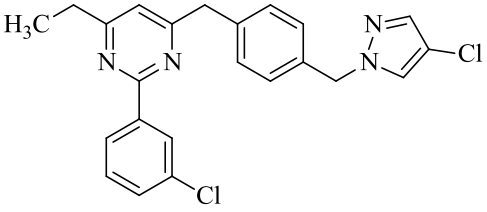
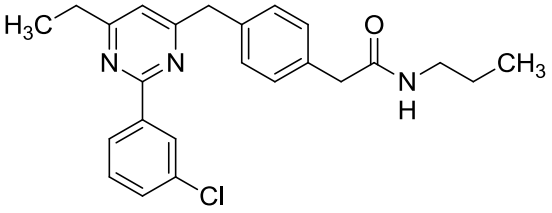
22. The compound as recited in claim 20, wherein R_6 is chosen from cyclopentyl optionally substituted with one or two R_{14}, and cyclopentoxy optionally substituted with one or two R_{14}.

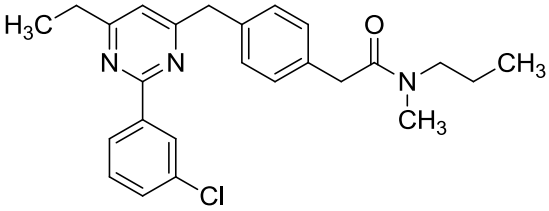
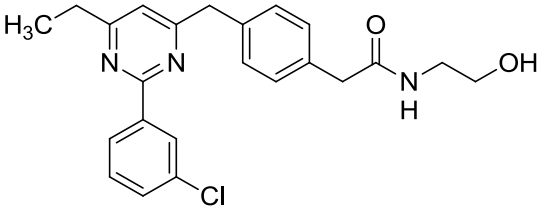
23. A compound chosen from:

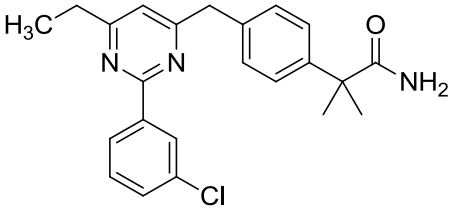
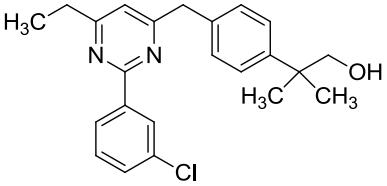


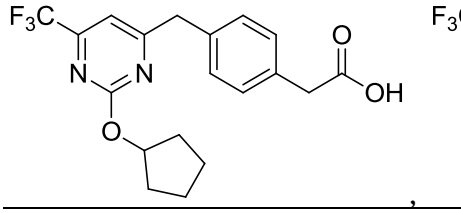
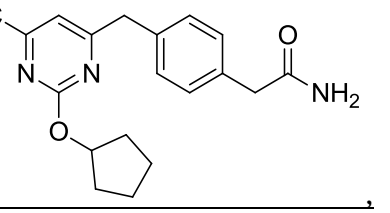



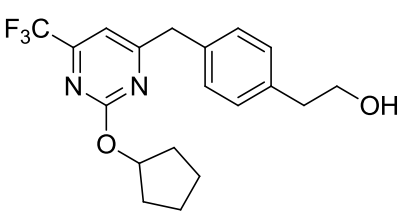
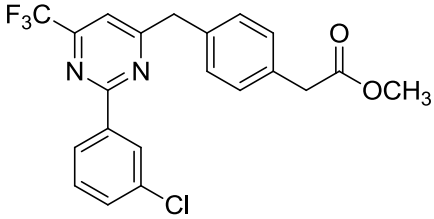



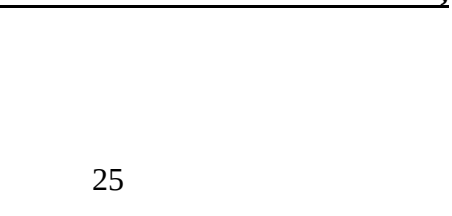



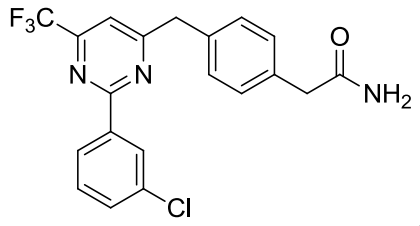



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O
NH2
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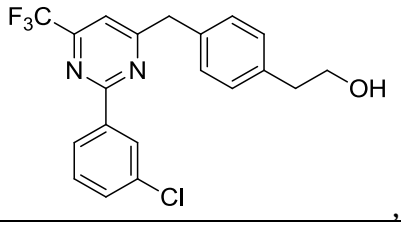
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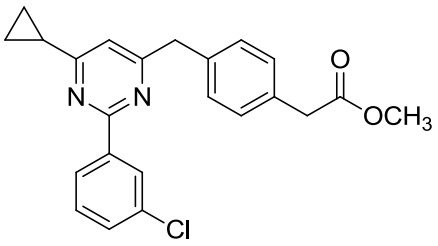
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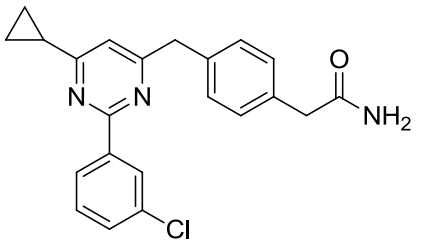
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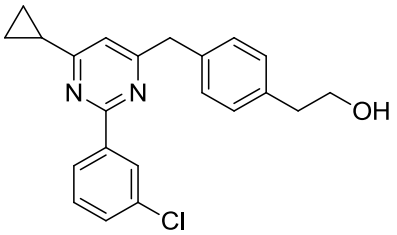
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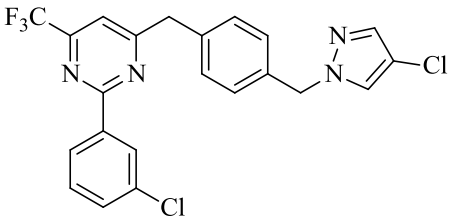
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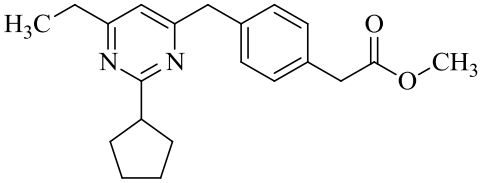
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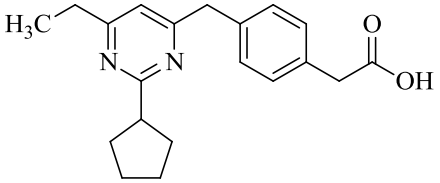
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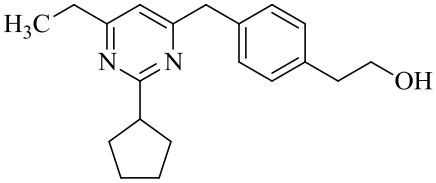
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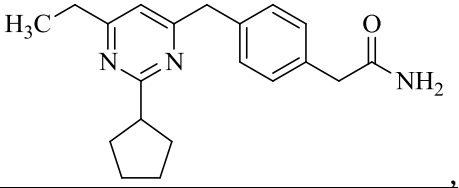
H3C
N
N
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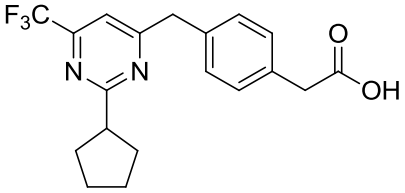
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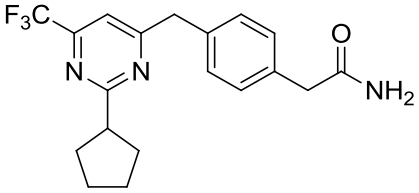
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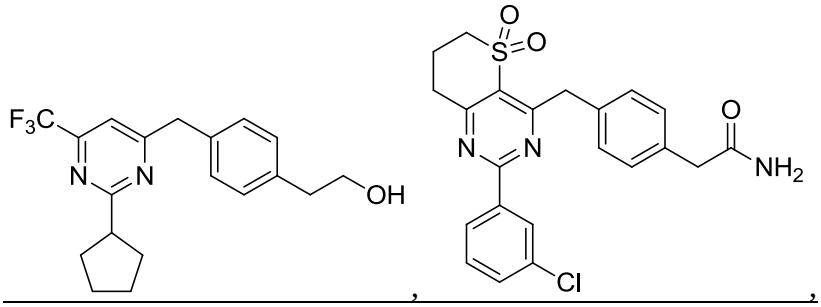

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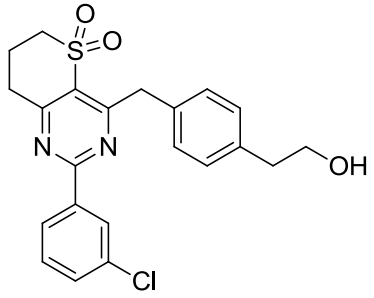

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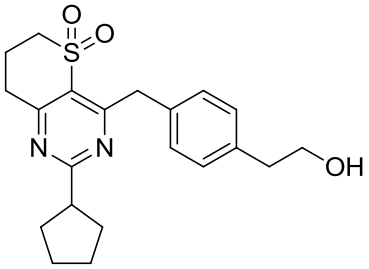

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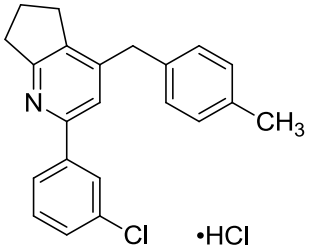

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24. A compound as recited in claim 1 for use in the manufacture of a medicament for the treatment of a PDE4-mediated disease.
25. The compound as recited in claim 24 wherein the PDE4 is PDE4B.
26. The compound as recited in claim 25 wherein the PDE4B-mediated 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.