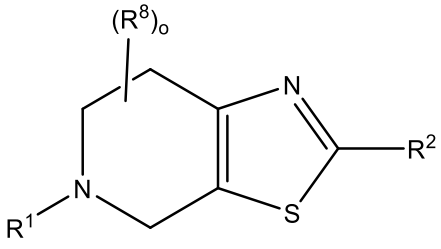
circumvent problems associated with targeting the highly conserved orthosteric ACh binding site, it is believed that developing compounds that act at allosteric sites on mAChRs that are removed from the orthosteric site and are less highly conserved. This approach is proving to be highly successful in developing selective ligands for multiple GPCR subtypes. In the case of mAChRs, a major goal has been to develop allosteric ligands that selectively increase activity of mAChR M_4 or other mAChR subtypes. Allosteric activators can include allosteric agonists, that act at a site removed from the orthosteric site to directly activate the receptor in the absence of ACh as well as positive allosteric modulators (PAMs), which do not activate the receptor directly but potentiate activation of the receptor by the endogenous orthosteric agonist ACh. Also, it is possible for a single molecule to have both allosteric potentiator and allosteric agonist activity.

[0008] More recently, muscarinic agonists including xanomeline have been shown to be active in animal models with similar profiles to known antipsychotic drugs, but without causing catalepsy (Bymaster *et al.*, *Eur. J. Pharmacol.* 1998, 356, 109, Bymaster *et al.*, *Life Sci.* 1999, 64, 527; Shannon *et al.*, *J. Pharmacol. Exp. Ther.* 1999, 290, 901; Shannon *et al.*, *Schizophrenia Res.* 2000, 42, 249). Further, xanomeline was shown to reduce psychotic behavioral symptoms such as delusions, suspiciousness, vocal outbursts, and hallucinations in Alzheimer's disease patients (Bodick *et al.*, *Arch. Neurol.* 1997, 54, 465), however treatment induced side effects, e.g., gastrointestinal effects, have severely limited the clinical utility of this compound.

[0009] Despite advances in muscarinic acetylcholine receptor research, there is still a scarcity of compounds that are potent, efficacious, and selective activators of the M_4 mAChR and also effective in the treatment of neurological and psychiatric disorders associated with cholinergic activity and diseases in which the muscarinic M_4 receptor is involved.

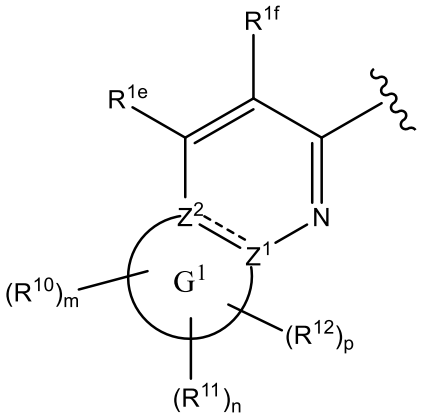
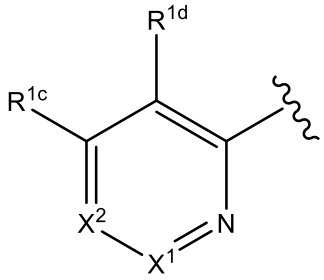
SUMMARY

[0009a] In an aspect, there is provided a compound of formula (I), or a pharmaceutically acceptable salt thereof,



(I)

wherein:

R^1 is  or ;

G^1 is a 5- to 6-membered partially unsaturated or aromatic heterocyclic ring system containing 1-3 nitrogen atoms, wherein Z^1 is C or N, Z^2 is N or C, and Z^1 and Z^2 are not both N;

R^{10} is selected from the group consisting of C_{1-4}alkyl, C_{1-4}fluoroalkyl, halogen, C_{3-4}cycloalkyl, C_{1-2}alkylene-C_{3-4}cycloalkyl, –C(O)OC_{1-4}alkyl, and –C(O)NR^aR^b;

R^{11}, at each occurrence, is independently selected from the group consisting of C_{1-6}alkyl, C_{1-6}fluoroalkyl, halogen, –C_{1-6}alkylene–R^y, –C_{1-6}fluoroalkylene–R^y, G^{11}, or –C_{1-3}alkylene–G^{11};

R^{12} is oxo;

m is 0 or 1;

n is 1, 0, or 2;

p is 1 or 0;

R^a is hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-4}cycloalkyl, or –C_{1-3}alkylene–C_{3-4}cycloalkyl;

R^b is hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, G^{10}, or –C_{1-3}alkylene–G^{10};

wherein alternatively, R^a and R^b, together with the nitrogen to which they attach, form a 4- to 10-membered heterocyclic ring containing the nitrogen attached to R^a and R^b and optionally 1-2 additional heteroatoms that are independently O, N, or S, the heterocyclic ring being optionally substituted with a first substituent selected from the group consisting of halogen, cyano, C_{1-4}alkyl, C_{1-4}fluoroalkyl, oxo, –OR^{50}, –$N(R^{50})_2$, G^{10a}, and –C_{1-3}alkylene–G^{10a}; and optionally further substituted with 1-3 substituents that are independently halogen or C_{1-4}alkyl;

G^{10} is a phenyl, a 5- to 6-membered heteroaryl containing 1-3 heteroatoms, a 4- to 8-

membered heterocyclyl containing 1-2 heteroatoms, or a C_{3-6}cycloalkyl, wherein the heteroatoms are independently selected from the group consisting of O, N, and S, and G^{10} is optionally substituted with a first substituent selected from the group consisting of halogen, cyano, C_{1-4}alkyl, C_{1-4}fluoroalkyl, oxo, $–OR^{50}$, $–N(R^{50})_2$, G^{10a}, and $–C_{1-3}$alkylene$–G^{10a}$ and optionally further substituted with 1-3 substituents that are independently halogen or C_{1-4}alkyl;

G^{10a} is a phenyl, a 5- to 6-membered heteroaryl containing 1-3 heteroatoms, a 4- to 8-membered heterocyclyl containing 1-2 heteroatoms, or a 3- to 8-membered carbocyclyl, wherein the heteroatoms are independently selected from the group consisting of O, N, and S, and G^{10a} is optionally substituted with 1-5 substituents independently selected from the group consisting of halogen, cyano, C_{1-4}alkyl, C_{1-4}fluoroalkyl, oxo, OH, $–OC_{1-4}$alkyl, $–OC_{1-4}$fluoroalkyl, C_{3-4}cycloalkyl, and $–C_{1-3}$alkylene$–C_{3-4}$cycloalkyl;

R^{50}, at each occurrence, is independently hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-6}cycloalkyl, or $–C_{1-3}$alkylene$–C_{3-6}$cycloalkyl, wherein each cycloalkyl is optionally substituted with 1-4 substituents independently selected from the group consisting of halogen, C_{1-4}alkyl, and C_{1-4}fluoroalkyl;

R^y is $–OR^c$, $–N(R^c)_2$, $–C(O)R^c$, $–C(O)OR^c$, or $–C(O)N(R^c)_2$;

R^c, at each occurrence, is independently hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-4}cycloalkyl, or $–C_{1-3}$alkylene$–C_{3-4}$cycloalkyl, wherein alternatively, two R^c, together with the nitrogen to which they attach form a 4- to 8-membered heterocyclic ring containing the nitrogen attached to R^c and optionally 1 additional heteroatom that is O, N, or S, the heterocyclic ring being optionally substituted with 1-4 substituents independently selected from the group consisting of halogen, C_{1-2}alkyl, and C_{1-2}fluoroalkyl;

G^{11} is phenyl, a 4- to 8-membered heterocyclyl containing 1-2 heteroatoms, a 5- to 6-membered heteroaryl containing 1-4 heteroatoms, or a C_{3-6}cycloalkyl, wherein the heteroatoms are independently selected from the group consisting of O, N, and S and G^{11} is optionally substituted with 1-4 substituents independently selected from the group consisting of C_{1-4}alkyl, halogen, cyano, oxo, $–OC_{1-4}$alkyl, C_{1-4}fluoroalkyl, C_{3-4}cycloalkyl, and $–C_{1-2}$alkylene-C_{3-4}cycloalkyl;

X^1 is N or CR^{1a};

R^{1a} is hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, or C_{1-4}fluoroalkyl;

X^2 is N or CR^{1b};

R^{1b} is cyano, halogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, or hydrogen;

R^{1c} and R^{1e} are C_{1-4}alkyl, hydrogen, halogen, C_{1-4}fluoroalkyl, C_{3-6}cycloalkyl, or $–OC_{1-4}$alkyl;

R^{1d} and R^{1f} are C_{1-4}alkyl, hydrogen, halogen, C_{1-4}fluoroalkyl, or C_{3-6}cycloalkyl;

alternatively, either R^{1a} and R^{1b}, together with the atom to which each attaches, or R^{1c} and R^{1d}, together with the atom to which each attaches, form an optionally substituted 6-membered arene, 5- to 6-membered heteroarene containing 1-3 heteroatoms, 5- to 7-membered heterocycle containing 1 heteroatom, or 5- to 7-membered carbocycle, wherein the heteroatoms are independently selected from the group consisting of N, O, and S, wherein the optional substitution is 1-3 optional substituents independently selected from the group consisting of C_{1-4}alkyl, halogen, $–OC_{1-4}$alkyl, C_{1-4}fluoroalkyl, C_{3-4}cycloalkyl, and C_{1-2}alkylene-C_{3-4}cycloalkyl;

R^2 is G^2, $–NR^{2a}R^{2b}$, halogen, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, $–OR^{2a}$, $–NR^{2a}C(O)R^{2b}$, $–C(O)OR^{2a}$, $–C(O)NR^{2a}R^{2b}$, or hydrogen;

R^{2a} and R^{2b} are independently hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, G^2, or $–C_{1-3}$alkylene$–G^2$, provided that R^2 is not $–N(CH_3)_2$;

G^2, at each occurrence, is independently a 3- to 7-membered carbocyclyl, a 5- to 6-membered heteroaryl containing 1-4 heteroatoms, a phenyl, or a 4- to 7-membered heterocyclyl containing 1-2 heteroatoms, wherein the heteroatoms are independently selected from the group consisting of O, N, and S, and G^2 is optionally substituted with a first substituent selected from the group consisting of halogen, cyano, C_{1-4}alkyl, C_{1-4}fluoroalkyl, oxo, $–OR^x$, $–N(R^x)_2$, $–C(O)R^x$, $–C(O)OR^x$, $–C(O)N(R^x)_2$, $–C_{1-6}$alkylene$–OR^x$, $–C_{1-6}$alkylene$–N(R^x)_2$, G^{2a}, and $–C_{1-3}$alkylene$–G^{2a}$ and optionally further substituted with 1-4 substitutents independently selected from the group consisting of halogen, cyano, C_{1-4}alkyl, and C_{1-4}fluoroalkyl;

R^x, at each occurrence, is independently hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-6}cycloalkyl, or $–C_{1-3}$alkylene$–C_{3-6}$cycloalkyl;

G^{2a} is a C_{3-6}cycloalkyl;

R^8, at each occurrence, is independently halogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, or C_{3-4}cycloalkyl; and

o is 0, 1, 2, 3, or 4;

wherein each cycloalkyl at G^{2a} and R^8 is independently unsubstituted or substituted with 1-4 substituents independently selected from C_{1-4}alkyl (e.g., methyl) and halogen (e.g., fluoro);

provided the compound is not:

4,5,6,7-tetrahydro-5-(2-pyridinyl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(4-pyrimidinyl)-thiazolo[5,4-c]pyridin-2-amine;

5-(6-chloro-2-cyclopropyl-5-methyl-4-pyrimidinyl)-4,5,6,7-tetrahydro-2-methyl-thiazolo[5,4-c]pyridine;

2-[2-(4-ethyl-piperazin-1-yl)-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl]-quinoline;

4,5,6,7-tetrahydro-5-[5-(trifluoromethyl)-thiazolo[5,4-c]pyridin-2-amine;

N-(2-aminophenyl)-4,5,6,7-tetrahydro-5-[5-(trifluoromethyl)-2-pyridinyl]-thiazolo[5,4-c]pyridine-2-carboxamide;

5-(2,5-dimethyloxazolo[5,4-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-(2-cyclopentyl-6,7-dihydro-5H-pyrrolo[3,4-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-(5,6-dimethylthieno[2,3-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-thieno[2,3-d]pyrimidin-4-yl-thiazolo[5,4-c]pyridin-2-amine;

5-[2,6-bis(1,1-dimethylethyl)-4-pyrimidinyl]-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

7-(6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2-(trifluoromethyl)-thiazolo[5,4-d]pyrimidine;

4,5,6,7-tetrahydro-5-(2-pyridinyl)-thiazolo[5,4-c]pyridine-2-carboxylic acid, or a salt thereof;

4-(6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-[1,2,5]thiadiazolo[3,4-c]pyridine;

4,5,6,7-tetrahydro-5-[6-methyl-2-(1-methylpropyl)-4-pyrimidinyl]-thiazolo[5,4-c]pyridin-2-amine;

5-(4-chloro-2-pyridinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

5-[2-(1,1-dimethylethyl)-4-pyrimidinyl]-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-[6-(1,1-dimethylethyl)-1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-(2-ethyl-7-methylthieno[3,2-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-(2-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridin-2-amine;

5-(6-cyclopentyl-1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-

c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-[3-(trifluoromethyl)-1,2,4-triazolo[4,3-b]pyridazin-6-yl]-thiazolo[5,4-c]pyridin-2-amine;

6-(6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2-(trifluoromethyl)-9H-purine;

5-(2,6-dicyclopropyl-4-pyrimidinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(5-iodo-2-pyridinyl)-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-(7-methylthieno[3,2-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(2-methyl-4-pyrimidinyl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(4-quinazolinyl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-(3-pyridazinyl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-[6-methyl-2-(1-methylethyl)-4-pyrimidinyl]-thiazolo[5,4-c]pyridin-2-amine;

5-(6-ethyl-5-fluoro-4-pyrimidinyl)-4,5,6,7-thiazolo[5,4-c]pyridin-2-amine;

5-(7-chloro-4-quinazolinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-(5-bromo-2-pyridinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-(2-methylthieno[3,2-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(1H-pyrrolo[2,3-b]pyridin-6-yl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(2-methyl-6-propyl-4-pyrimidinyl)-thiazolo[5,4-c]pyridin-2-amine;

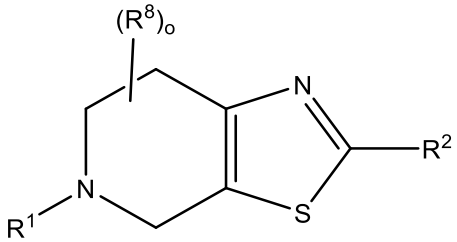
4,5,6,7-tetrahydro-5-(5-methylthieno[2,3-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridin-2-amine;

5-(6-cyclohexyl-4-pyrimidinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-[6-methyl-2-(1-methylpropyl)-4-pyrimidinyl]-thiazolo[5,4-c]pyridine; or

5-(6-bromo-4-quinazolinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine.

[0010] In one example, disclosed are compounds of formula (I), or a pharmaceutically acceptable salt thereof,



(I)

4,5,6,7-tetrahydro-5-(5-iodo-2-pyridinyl)-thiazolo[5,4-*c*]pyridine;
4,5,6,7-tetrahydro-5-(7-methylthieno[3,2-*d*]pyrimidin-4-yl)-thiazolo[5,4-*c*]pyridin-2-amine;
4,5,6,7-tetrahydro-5-(2-methyl-4-pyrimidinyl)-thiazolo[5,4-*c*]pyridin-2-amine;
4,5,6,7-tetrahydro-5-(4-quinazolinyl)-thiazolo[5,4-*c*]pyridin-2-amine;
4,5,6,7-tetrahydro-5-(7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl)-thiazolo[5,4-*c*]pyridine;
4,5,6,7-tetrahydro-5-(3-pyridazinyl)-thiazolo[5,4-*c*]pyridin-2-amine;
4,5,6,7-tetrahydro-5-[6-methyl-2-(1-methylethyl)-4-pyrimidinyl]-thiazolo[5,4-*c*]pyridin-2-amine;
5-(6-ethyl-5-fluoro-4-pyrimidinyl)-4,5,6,7-thiazolo[5,4-*c*]pyridin-2-amine;
5-(7-chloro-4-quinazolinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-*c*]pyridin-2-amine;
5-(5-bromo-2-pyridinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-*c*]pyridine;
4,5,6,7-tetrahydro-5-(2-methylthieno[3,2-*d*]pyrimidin-4-yl)-thiazolo[5,4-*c*]pyridin-2-amine;
4,5,6,7-tetrahydro-5-(1*H*-pyrrolo[2,3-*b*]pyridin-6-yl)-thiazolo[5,4-*c*]pyridin-2-amine;
4,5,6,7-tetrahydro-5-(2-methyl-6-propyl-4-pyrimidinyl)-thiazolo[5,4-*c*]pyridin-2-amine;
4,5,6,7-tetrahydro-5-(5-methylthieno[2,3-*d*]pyrimidin-4-yl)-thiazolo[5,4-*c*]pyridin-2-amine;
5-(6-cyclohexyl-4-pyrimidinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-*c*]pyridine;
4,5,6,7-tetrahydro-5-[6-methyl-2-(1-methylpropyl)-4-pyrimidinyl]-thiazolo[5,4-*c*]pyridine; or
5-(6-bromo-4-quinazolinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-*c*]pyridin-2-amine.

[0010a] In another aspect, there is provided a pharmaceutical composition comprising the compound as defined above, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

[0011] In another example, the disclosure provides a pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

[0011a] In another aspect, there is provided a use of a compound as defined above, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition as defined above, in the manufacture of a medicament for the treatment of a neurological and/or psychiatric disorder, wherein the disorder is selected from Alzheimer's disease, schizophrenia, a sleep disorder, a pain disorder, and a cognitive disorder.

[0011b] In another aspect, there is provided a compound as defined above, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition as defined above for use in therapy.

[0012] Another example provides a method of treating a neurological and/or psychiatric disorder associated with muscarinic acetylcholine receptor dysfuncti
on in a mammal, comprising administering to the mammal a therapeutically effective amount of the compound of formula (I), or pharmaceutically acceptable salt or composition thereof.

[0013] Another example provides a compound of formula (I), or a pharmaceutically acceptable salt or composition thereof, for use in the treatment of a neurological and/or psychiatric disorder associated with muscarinic acetylcholine receptor dysfunction in a mammal.

[0014] Another example provides use of a compound of formula (I), or a pharmaceutically acceptable salt or composition thereof, for the preparation of a medicament for the treatment of a neurological and/or psychiatric disorder associated with muscarinic acetylcholine receptor dysfunction in a mammal.

[0015] In another example, the disclosure provides kits comprising a compound of formula (I), or a pharmaceutically acceptable salt or composition thereof, and instructions for use.

Brief Description of the Drawing

[0016] The FIGURE shows the effects of Compound 70 in an amphetamine-induced hyperlocomotion assay.

Detailed Description

[0017] Disclosed herein are positive allosteric modulators (i.e. potentiators) of the muscarinic acetylcholine receptor M_4 (mAChR M_4), methods of making same, pharmaceutical compositions comprising same, and methods of treating neurological and psychiatric disorders associated with muscarinic acetylcholine receptor dysfunction using same. The compounds include naphthyridine-substituted pyridazine compounds.

[0018] The human muscarinic acetylcholine receptor M_4 (mAChR M_4) is a protein of 479 amino acids encoded by the CHRM4 gene. The molecular weight of the unglycosylated protein is about 54 kDa and it is a transmembrane GPCR. As described above, the mAChR M_4 is a member of the GPCR Class A family, or the rhodopsin-like GPCRs, which are characterized by structural features similar to rhodopsin such as seven transmembrane segments. The muscarinic acetylcholine receptors have the N-terminus oriented to the extracellular face of the membrane and the C-terminus located on the cytoplasmic face.

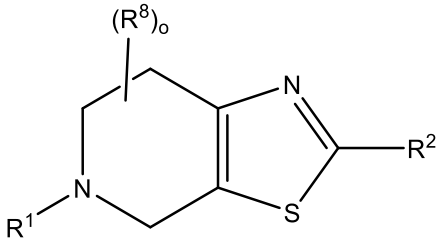
[0019] Previous attempts to develop agonists that are highly selective for individual mAChR subtypes have failed because of the high conservation of the orthosteric ACh binding site. To circumvent problems associated with targeting the highly conserved orthosteric ACh binding site, it is believed that developing compounds that act at allosteric sites on mAChRs that are removed from the orthosteric site and are less highly-conserved. Without wishing to be bound by a particular theory, the disclosed compounds and products of the disclosed methods are believed to bind to an allosteric site distinct from the orthosteric binding site.

1. Definitions

[0020] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art. In case of conflict, the present document, including definitions, will control. Preferred methods and materials are

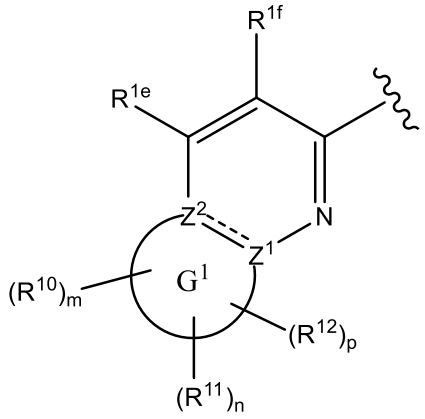
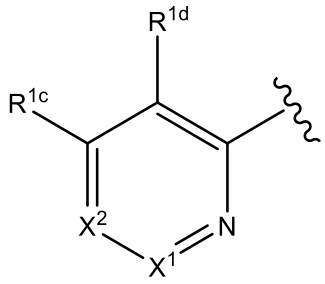
CLAIMS

1. A compound of formula (I), or a pharmaceutically acceptable salt thereof,



(I)

wherein:

R^1 is  or ;

G^1 is a 5- to 6-membered partially unsaturated or aromatic heterocyclic ring system containing 1-3 nitrogen atoms, wherein Z^1 is C or N, Z^2 is N or C, and Z^1 and Z^2 are not both N;

R^{10} is selected from the group consisting of C_{1-4}alkyl, C_{1-4}fluoroalkyl, halogen, C_{3-4}cycloalkyl, C_{1-2}alkylene-C_{3-4}cycloalkyl, –C(O)OC_{1-4}alkyl, and –C(O)NR^aR^b;

R^{11}, at each occurrence, is independently selected from the group consisting of C_{1-6}alkyl, C_{1-6}fluoroalkyl, halogen, –C_{1-6}alkylene–R^y, –C_{1-6}fluoroalkylene–R^y, G^{11}, or –C_{1-3}alkylene–G^{11};

R^{12} is oxo;

m is 0 or 1;

n is 1, 0, or 2;

p is 1 or 0;

R^a is hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-4}cycloalkyl, or –C_{1-3}alkylene–C_{3-4}cycloalkyl;

R^b is hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, G^{10}, or –C_{1-3}alkylene–G^{10};

wherein alternatively, R^a and R^b, together with the nitrogen to which they attach, form a 4- to 10-membered heterocyclic ring containing the nitrogen attached to R^a and R^b and optionally 1-2 additional heteroatoms that are independently O, N, or S, the heterocyclic ring being optionally substituted with a first substituent selected from the group consisting of halogen, cyano, C_{1-4}alkyl, C_{1-4}fluoroalkyl, oxo, $–OR^{50}$, $–N(R^{50})_2$, G^{10a}, and $–C_{1-3}$alkylene$–G^{10a}$; and optionally further substituted with 1-3 substituents that are independently halogen or C_{1-4}alkyl;

G^{10} is a phenyl, a 5- to 6-membered heteroaryl containing 1-3 heteroatoms, a 4- to 8-membered heterocyclyl containing 1-2 heteroatoms, or a C_{3-6}cycloalkyl, wherein the heteroatoms are independently selected from the group consisting of O, N, and S, and G^{10} is optionally substituted with a first substituent selected from the group consisting of halogen, cyano, C_{1-4}alkyl, C_{1-4}fluoroalkyl, oxo, $–OR^{50}$, $–N(R^{50})_2$, G^{10a}, and $–C_{1-3}$alkylene$–G^{10a}$ and optionally further substituted with 1-3 substituents that are independently halogen or C_{1-4}alkyl;

G^{10a} is a phenyl, a 5- to 6-membered heteroaryl containing 1-3 heteroatoms, a 4- to 8-membered heterocyclyl containing 1-2 heteroatoms, or a 3- to 8-membered carbocyclyl, wherein the heteroatoms are independently selected from the group consisting of O, N, and S, and G^{10a} is optionally substituted with 1-5 substituents independently selected from the group consisting of halogen, cyano, C_{1-4}alkyl, C_{1-4}fluoroalkyl, oxo, OH, $–OC_{1-4}$alkyl, $–OC_{1-4}$fluoroalkyl, C_{3-4}cycloalkyl, and $–C_{1-3}$alkylene$–C_{3-4}$cycloalkyl;

R^{50}, at each occurrence, is independently hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-6}cycloalkyl, or $–C_{1-3}$alkylene$–C_{3-6}$cycloalkyl, wherein each cycloalkyl is optionally substituted with 1-4 substituents independently selected from the group consisting of halogen, C_{1-4}alkyl, and C_{1-4}fluoroalkyl;

R^y is $–OR^c$, $–N(R^c)_2$, $–C(O)R^c$, $–C(O)OR^c$, or $–C(O)N(R^c)_2$;

R^c, at each occurrence, is independently hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-4}cycloalkyl, or $–C_{1-3}$alkylene$–C_{3-4}$cycloalkyl, wherein alternatively, two R^c, together with the nitrogen to which they attach form a 4- to 8-membered heterocyclic ring containing the nitrogen attached to R^c and optionally 1 additional heteroatom that is O, N, or S, the heterocyclic ring being optionally substituted with 1-4 substituents independently selected from the group consisting

of halogen, C_{1-2}alkyl, and C_{1-2}fluoroalkyl;

G^{11} is phenyl, a 4- to 8-membered heterocyclyl containing 1-2 heteroatoms, a 5- to 6-membered heteroaryl containing 1-4 heteroatoms, or a C_{3-6}cycloalkyl, wherein the heteroatoms are independently selected from the group consisting of O, N, and S and G^{11} is optionally substituted with 1-4 substituents independently selected from the group consisting of C_{1-4}alkyl, halogen, cyano, oxo, –OC_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-4}cycloalkyl, and –C_{1-2}alkylene-C_{3-4}cycloalkyl;

X^1 is N or CR^{1a};

R^{1a} is hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, or C_{1-4}fluoroalkyl;

X^2 is N or CR^{1b};

R^{1b} is cyano, halogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, or hydrogen;

R^{1c} and R^{1e} are C_{1-4}alkyl, hydrogen, halogen, C_{1-4}fluoroalkyl, C_{3-6}cycloalkyl, or –OC_{1-4}alkyl;

R^{1d} and R^{1f} are C_{1-4}alkyl, hydrogen, halogen, C_{1-4}fluoroalkyl, or C_{3-6}cycloalkyl;

alternatively, either R^{1a} and R^{1b}, together with the atom to which each attaches, or R^{1c} and R^{1d}, together with the atom to which each attaches, form an optionally substituted 6-membered arene, 5- to 6-membered heteroarene containing 1-3 heteroatoms, 5- to 7-membered heterocycle containing 1 heteroatom, or 5- to 7-membered carbocycle, wherein the heteroatoms are independently selected from the group consisting of N, O, and S, wherein the optional substitution is 1-3 optional substituents independently selected from the group consisting of C_{1-4}alkyl, halogen, –OC_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-4}cycloalkyl, and C_{1-2}alkylene-C_{3-4}cycloalkyl;

R^2 is G^2, –$NR^{2a}R^{2b}$, halogen, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, –OR^{2a}, –$NR^{2a}C(O)R^{2b}$, –$C(O)OR^{2a}$, –$C(O)NR^{2a}R^{2b}$, or hydrogen;

R^{2a} and R^{2b} are independently hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, G^2, or –C_{1-3}alkylene–G^2, provided that R^2 is not –$N(CH_3)_2$;

G^2, at each occurrence, is independently a 3- to 7-membered carbocyclyl, a 5- to 6-membered heteroaryl containing 1-4 heteroatoms, a phenyl, or a 4- to 7-membered heterocyclyl containing 1-2 heteroatoms, wherein the heteroatoms are independently selected from the group consisting of O, N, and S, and G^2 is optionally substituted with a first substituent selected from the group consisting of halogen, cyano, C_{1-4}alkyl, C_{1-4}fluoroalkyl, oxo, –OR^x, –$N(R^x)_2$, –$C(O)R^x$, –$C(O)OR^x$, –$C(O)N(R^x)_2$, –C_{1-6}alkylene–OR^x, –C_{1-6}alkylene–$N(R^x)_2$,

G^{2a}, and –C_{1-3}alkylene–G^{2a} and optionally further substituted with 1-4 substitutents independently selected from the group consisting of halogen, cyano, C_{1-4}alkyl, and C_{1-4}fluoroalkyl;

R^x, at each occurrence, is independently hydrogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, C_{3-6}cycloalkyl, or –C_{1-3}alkylene–C_{3-6}cycloalkyl;

G^{2a} is a C_{3-6}cycloalkyl;

R^8, at each occurrence, is independently halogen, C_{1-4}alkyl, C_{1-4}fluoroalkyl, or C_{3-4}cycloalkyl; and

o is 0, 1, 2, 3, or 4;

wherein each cycloalkyl at G^{2a} and R^8 is independently unsubstituted or substituted with 1-4 substituents independently selected from C_{1-4}alkyl (e.g., methyl) and halogen (e.g., fluoro);

provided the compound is not:

4,5,6,7-tetrahydro-5-(2-pyridinyl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(4-pyrimidinyl)-thiazolo[5,4-c]pyridin-2-amine;

5-(6-chloro-2-cyclopropyl-5-methyl-4-pyrimidinyl)-4,5,6,7-tetrahydro-2-methyl-thiazolo[5,4-c]pyridine;

2-[2-(4-ethyl-piperazin-1-yl)-6,7-dihydro-4H-thiazolo[5,4-c]pyridin-5-yl]-quinoline;

4,5,6,7-tetrahydro-5-[5-(trifluoromethyl)-thiazolo[5,4-c]pyridin-2-amine;

N-(2-aminophenyl)-4,5,6,7-tetrahydro-5-[5-(trifluoromethyl)-2-pyridinyl]-thiazolo[5,4-c]pyridine-2-carboxamide;

5-(2,5-dimethyloxazolo[5,4-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-(2-cyclopentyl-6,7-dihydro-5H-pyrrolo[3,4-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-(5,6-dimethylthieno[2,3-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-thieno[2,3-d]pyrimidin-4-yl-thiazolo[5,4-c]pyridin-2-amine;

5-[2,6-bis(1,1-dimethylethyl)-4-pyrimidinyl]-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

7-(6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2-(trifluoromethyl)-thiazolo[5,4-d]pyrimidine;

4,5,6,7-tetrahydro-5-(2-pyridinyl)-thiazolo[5,4-c]pyridine-2-carboxylic acid, or a salt thereof;

4-(6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-[1,2,5]thiadiazolo[3,4-c]pyridine;

4,5,6,7-tetrahydro-5-[6-methyl-2-(1-methylpropyl)-4-pyrimidinyl]-thiazolo[5,4-c]pyridin-2-amine;

5-(4-chloro-2-pyridinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

5-[2-(1,1-dimethylethyl)-4-pyrimidinyl]-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-[6-(1,1-dimethylethyl)-1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-(2-ethyl-7-methylthieno[3,2-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-(2-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridin-2-amine;

5-(6-cyclopentyl-1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-[3-(trifluoromethyl)-1,2,4-triazolo[4,3-b]pyridazin-6-yl]-thiazolo[5,4-c]pyridin-2-amine;

6-(6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2-(trifluoromethyl)-9H-purine;

5-(2,6-dicyclopropyl-4-pyrimidinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(5-iodo-2-pyridinyl)-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-(7-methylthieno[3,2-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(2-methyl-4-pyrimidinyl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(4-quinazolinyl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-(3-pyridazinyl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-[6-methyl-2-(1-methylethyl)-4-pyrimidinyl]-thiazolo[5,4-c]pyridin-2-amine;

5-(6-ethyl-5-fluoro-4-pyrimidinyl)-4,5,6,7-thiazolo[5,4-c]pyridin-2-amine;

5-(7-chloro-4-quinazolinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine;

5-(5-bromo-2-pyridinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-(2-methylthieno[3,2-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(1H-pyrrolo[2,3-b]pyridin-6-yl)-thiazolo[5,4-c]pyridin-2-amine;

4,5,6,7-tetrahydro-5-(2-methyl-6-propyl-4-pyrimidinyl)-thiazolo[5,4-c]pyridin-2-amine;

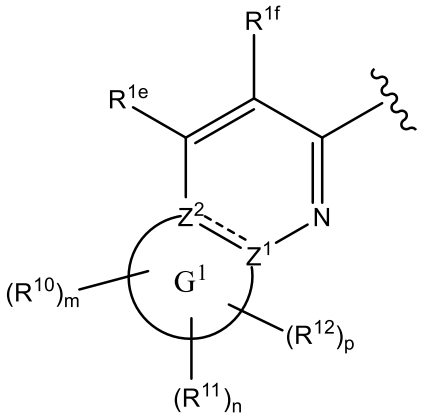
4,5,6,7-tetrahydro-5-(5-methylthieno[2,3-d]pyrimidin-4-yl)-thiazolo[5,4-c]pyridin-2-amine;

5-(6-cyclohexyl-4-pyrimidinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine;

4,5,6,7-tetrahydro-5-[6-methyl-2-(1-methylpropyl)-4-pyrimidinyl]-thiazolo[5,4-c]pyridine; or

5-(6-bromo-4-quinazolinyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridin-2-amine.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is



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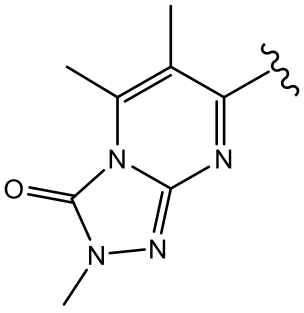
3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein

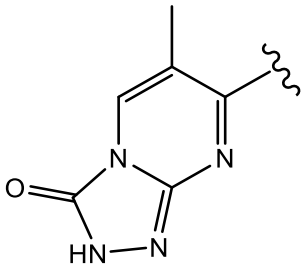
a) Z^1 is C and Z^2 is N; or Z^1 is N and Z^2 is C; or Z^1 is C and Z^2 is C; and / or

b) wherein G^1 is the 5-membered partially unsaturated heterocyclic ring system; or G^1 is the 6-membered partially unsaturated heterocyclic ring system; or G^1 is the 5-membered aromatic heterocyclic ring system; or G^1 is the 6-membered aromatic heterocyclic ring system; and / or

c) wherein R^{1e} is $C_{1\text{-}4}$alkyl or hydrogen; and / or

d) wherein R^{1f} is $C_{1\text{-}4}$alkyl; and / or

e) wherein R^1 is 

, 

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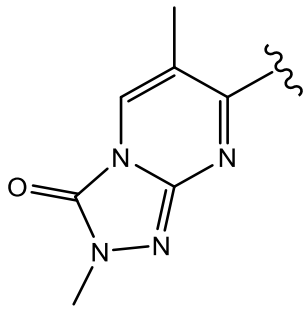
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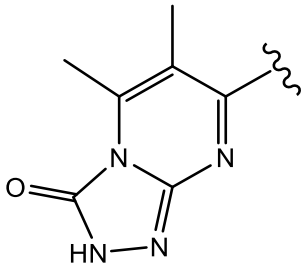
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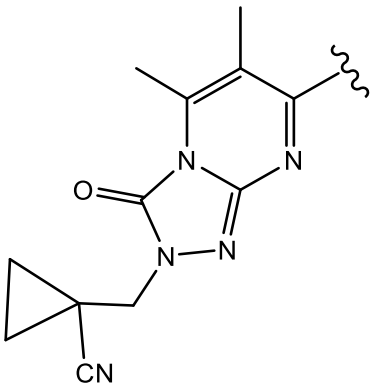
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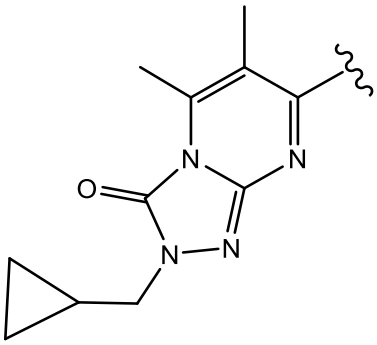
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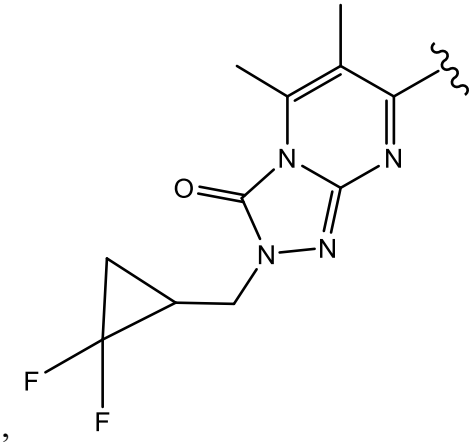
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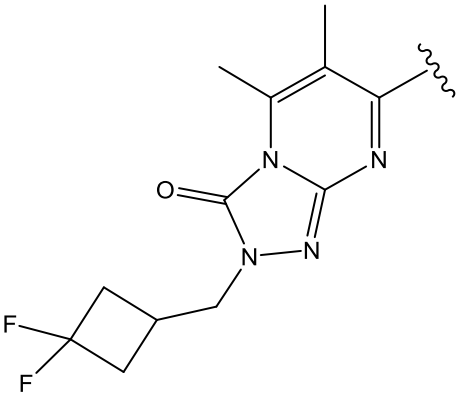
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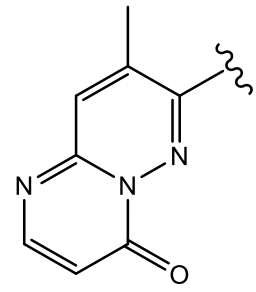
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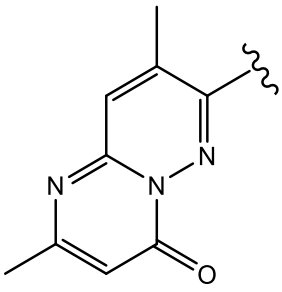
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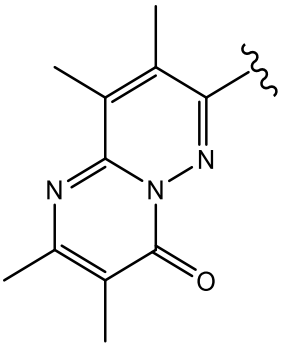
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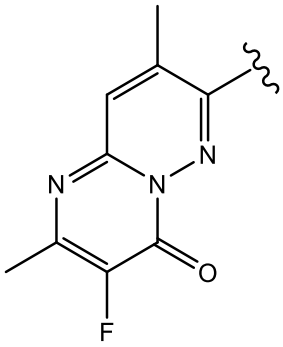
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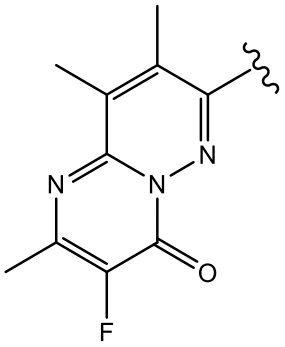
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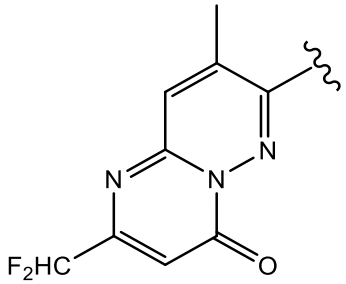
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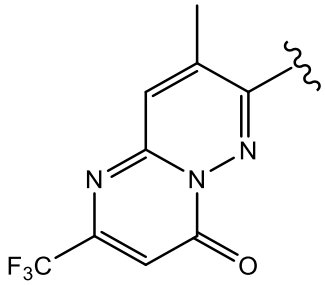
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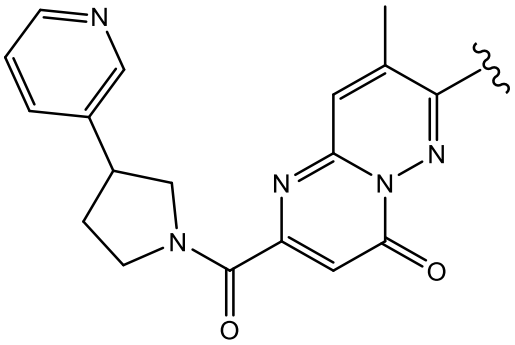
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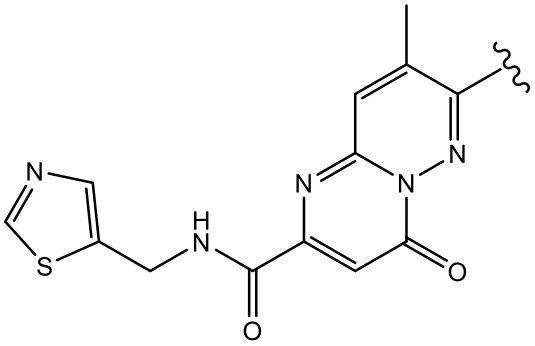
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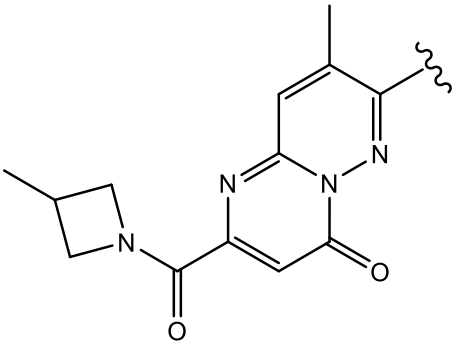
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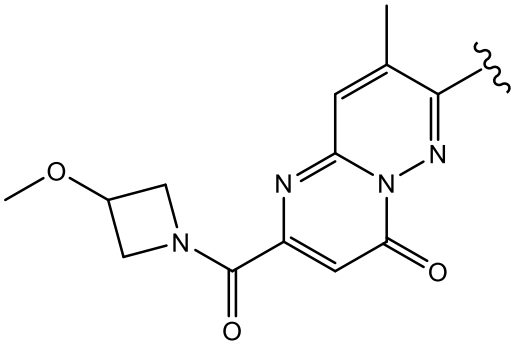
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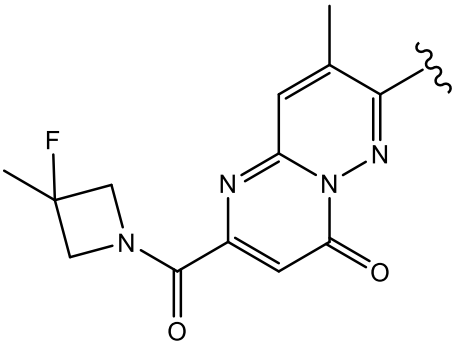
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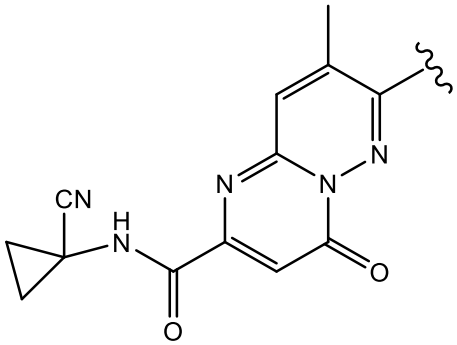
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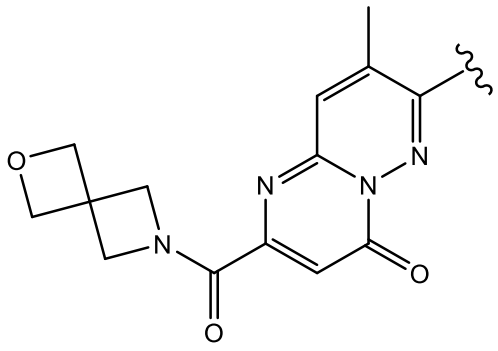
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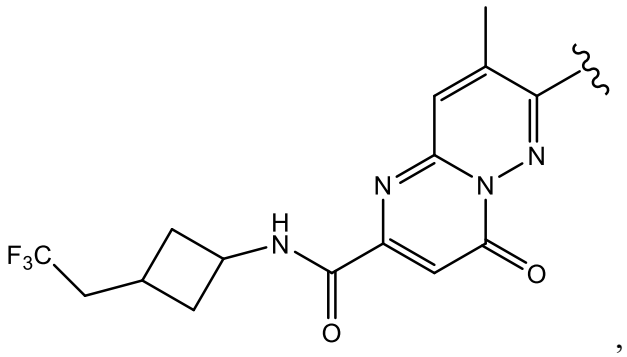
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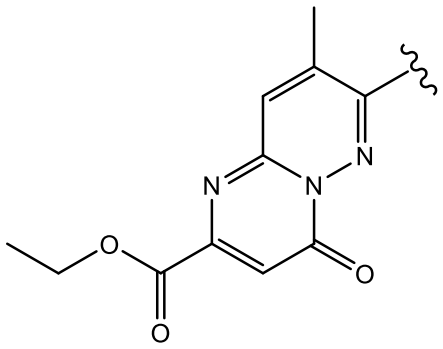
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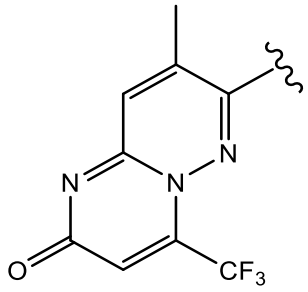
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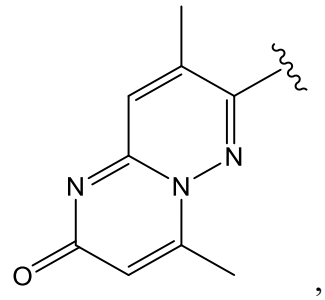
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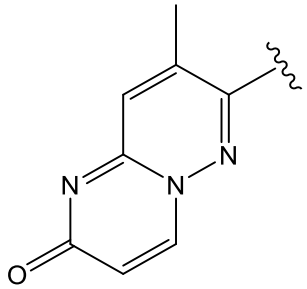
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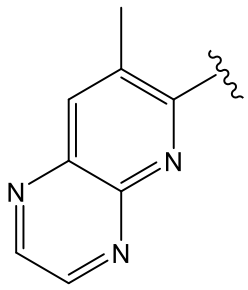
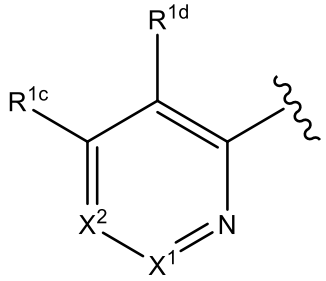

.

4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1 is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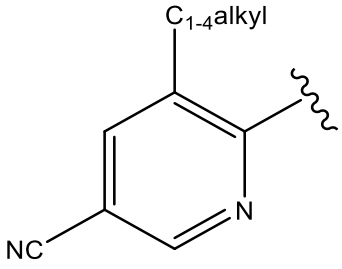
5. The compound of claim 1 or 4, or a pharmaceutically acceptable salt thereof, wherein

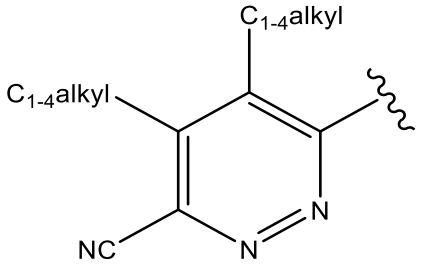
a) X^1 is N; or X^1 is CR^{1a}; and / or

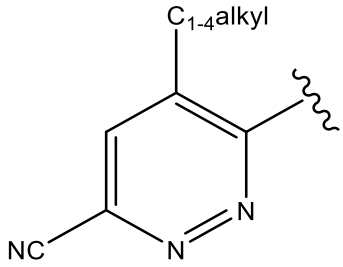
b) X^2 is N or CR^{1b}; and / or

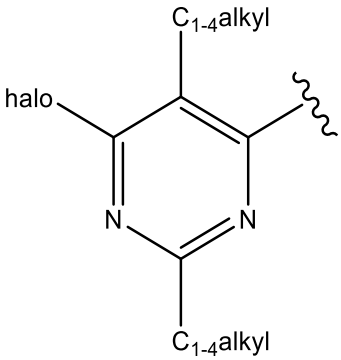
c) R^{1a} is hydrogen or C_{1-4}alkyl; and / or R^{1b} is cyano; or R^{1a} and R^{1b}, together with the atom to which each attaches, form the optionally substituted 6-membered arene, 5- to 6-membered heteroarene containing 1-3 heteroatoms, 5- to 7-membered heterocycle containing 1 heteroatom, or 5- to 7-membered carbocycle; and / or

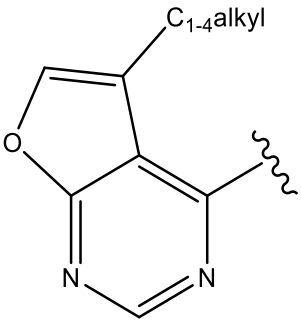
d) R^{1c} is hydrogen, C_{1-4}alkyl, or halogen; and / or R^{1d} is hydrogen or C_{1-4}alkyl; or R^{1c} and R^{1d}, together with the atom to which each attaches, form the optionally substituted 6-membered arene, 5- to 6-membered heteroarene containing 1-3 heteroatoms, 5- to 7-membered heterocycle containing 1 heteroatom, or 5- to 7-membered carbocycle; and / or

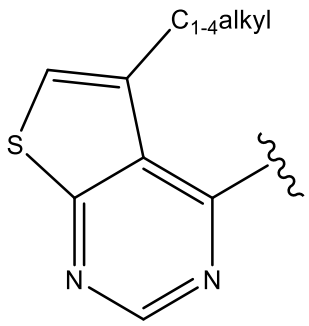
e) wherein R^1 is 

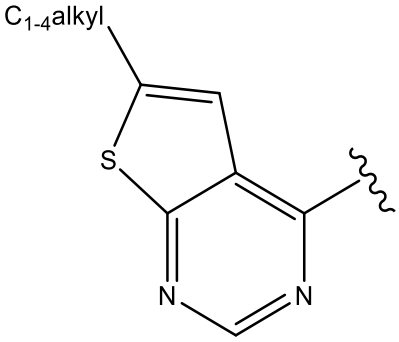
, 

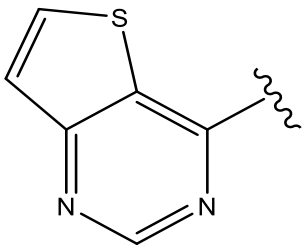
, 

, 

, 

, 

, 

, 

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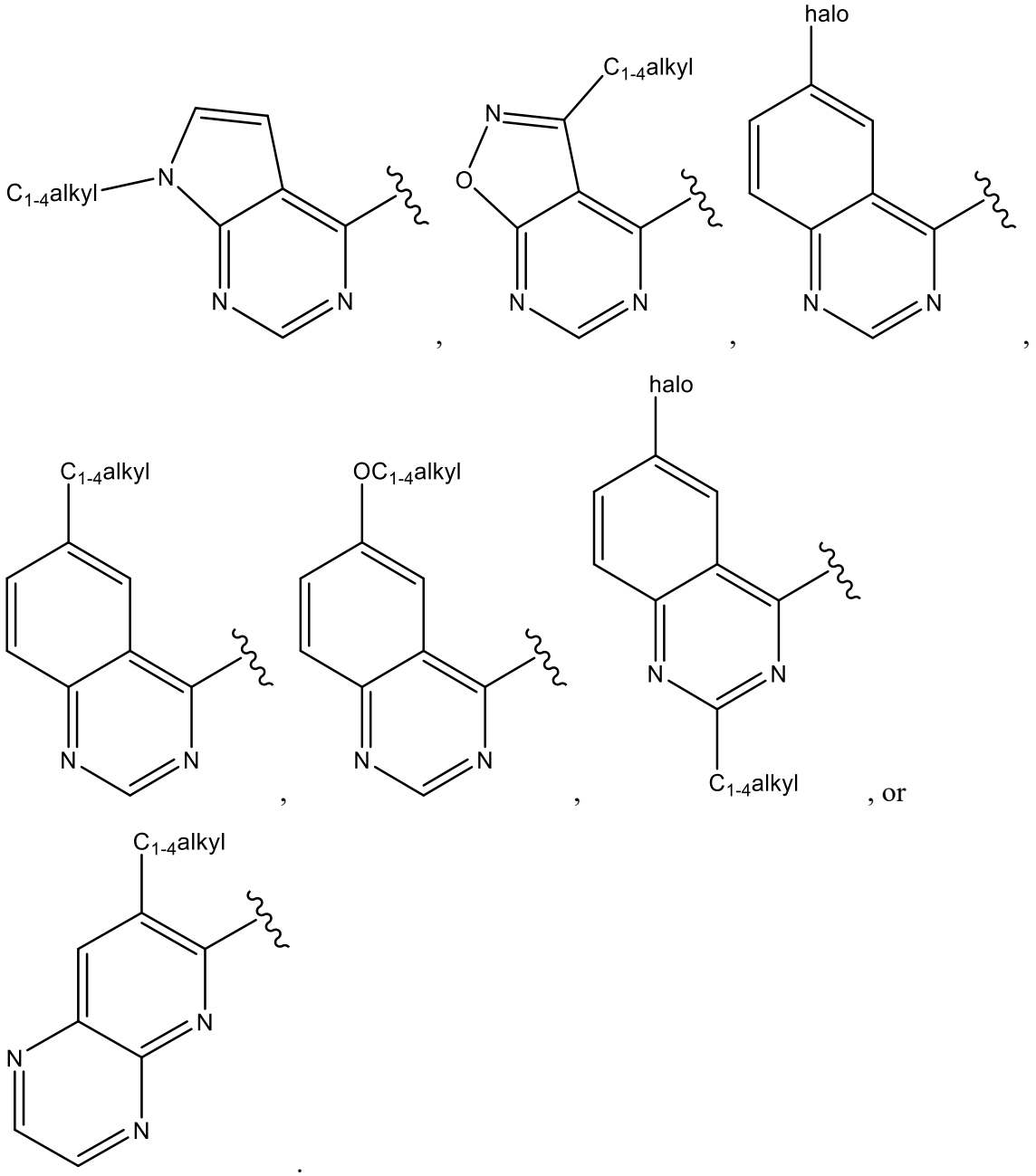
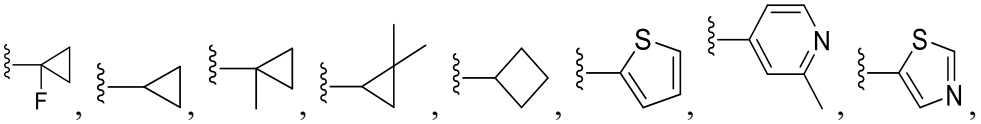
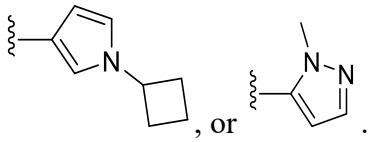


6. The compound of any of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein R^2 is G^2, $–NR^{2a}R^{2b}$, halogen, cyano, C_{1-6}alkyl, C_{1-6}haloalkyl, $–OR^{2a}$, $–C(O)OR^{2a}$, $–C(O)NR^{2a}R^{2b}$, or hydrogen; optionally wherein R^2 is G^2; and optionally wherein G^2 is the optionally substituted 3- to 7-membered carbocyclyl, or optionally wherein G^2 is the optionally substituted 5- to 6-membered heteroaryl, or optionally wherein G^2 is the optionally substituted phenyl.

7. The compound of any of claims 1-6, or a pharmaceutically acceptable salt thereof,

wherein G^2 is , , or .

8. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein R^2 is

a) $–NR^{2a}R^{2b}$; or

b) $–C(O)NR^{2a}R^{2b}$; or

c) $–C(O)OR^{2a}$; or

d) $–OR^{2a}$.

9. The compound of any of claims 1-6 or 8, or a pharmaceutically acceptable salt thereof, wherein R^{2b} is hydrogen, $C_{1\text{-}6}$alkyl, $C_{1\text{-}6}$haloalkyl, G^2, or $–C_{1\text{-}3}$alkylene$–G^2$.

10. The compound of any of claims 1-6, 8 or 9, or a pharmaceutically acceptable salt thereof, wherein R^{2a} is hydrogen or $C_{1\text{-}6}$alkyl.

11. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein R^2 is $C_{1\text{-}6}$alkyl; or halogen; or hydrogen; or $C_{1\text{-}6}$haloalkyl; or cyano.

12. The compound of any of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein o is 0.

13. The compound of claim 1 selected from the group consisting of:

7-(2-(1-fluorocyclopropyl)-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-2,5,6-trimethyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one

7-(2-cyclobutyl-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-6-methyl-[1,2,4]triazolo[4,3-a]pyrimidin-3(2H)-one
7-(2-cyclobutyl-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2,6-dimethyl-[1,2,4]triazolo[4,3-a]pyrimidin-3(2H)-one
5,6-dimethyl-7-(2-(1-methylcyclopropyl)-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
7-(2-(1-fluorocyclopropyl)-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-5,6-dimethyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
7-(2-(1-fluorocyclopropyl)-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-5,6-dimethyl-2-(methyl-d_3)-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
7-(2-cyclopropyl-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-5,6-dimethyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
1-((7-(2-cyclopropyl-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-5,6-dimethyl-3-oxo-[1,2,4]triazolo[4,3-*a*]pyrimidin-2(3*H*)-yl)methyl)cyclopropane-1-carbonitrile
7-(2-cyclopropyl-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-2-((2,2-difluorocyclopropyl)methyl)-5,6-dimethyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
7-(2-cyclopropyl-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-2-(cyclopropylmethyl)-5,6-dimethyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
7-(2-cyclopropyl-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-2-((3,3-difluorocyclobutyl)methyl)-5,6-dimethyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
7-(2-cyclopropyl-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-2,5,6-trimethyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
2-(cyclopropylmethyl)-7-(2-(1-fluorocyclopropyl)-6,7-dihydrothiazolo[5,4-*c*]pyridin-5(4*H*)-yl)-5,6-dimethyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-3(2*H*)-one
6-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-5-methylnicotinonitrile
5-methyl-6-(2-(2-methylpyridin-4-yl)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)nicotinonitrile
5-methyl-6-(2-(thiazol-5-yl)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)nicotinonitrile
6-(2-(1-cyclobutyl-1H-pyrazol-4-yl)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-5-methylnicotinonitrile

6-(2-((2-fluorophenyl)amino)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-4,5-dimethylpyridazine-3-carbonitrile
6-(2-((3-fluorophenyl)amino)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-4,5-dimethylpyridazine-3-carbonitrile
6-(2-((4-fluorophenyl)amino)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-4,5-dimethylpyridazine-3-carbonitrile
6-(2-methoxy-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-4,5-dimethylpyridazine-3-carbonitrile
5-(6-chloro-2,5-dimethylpyrimidin-4-yl)-2-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
6-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-4,5-dimethylpyridazine-3-carbonitrile
2-bromo-5-(6-chloro-2,5-dimethylpyrimidin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
6-(2-cyclopropyl-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-4,5-dimethylpyridazine-3-carbonitrile
5-(6-cyano-4,5-dimethylpyridazin-3-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carbonitrile
5-(6-chloro-2,5-dimethylpyrimidin-4-yl)-N-(2-fluorophenyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-amine
5-methyl-6-(2-methyl-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)nicotinonitrile
6-(2-cyclopropyl-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-5-methylnicotinonitrile
6-(6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-5-methylnicotinonitrile
6-(2-((3-fluorobenzyl)amino)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-5-methylnicotinonitrile
6-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-5-methylpyridazine-3-carbonitrile
5-methyl-6-(2-(methyl-d3)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)nicotinonitrile
5-(5-cyano-3-methylpyridin-2-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide

4-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-5-methylfuro[2,3-d]pyrimidine
2-bromo-5-(5-methylthieno[2,3-d]pyrimidin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-bromo-5-(6-methylthieno[2,3-d]pyrimidin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
4-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-3-methylisoxazolo[5,4-d]pyrimidine
2-bromo-5-(thieno[3,2-d]pyrimidin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-bromo-5-(7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-bromo-5-(6-fluoroquinazolin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-bromo-5-(6-chloroquinazolin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-bromo-5-(6-methylquinazolin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-bromo-5-(6-methoxyquinazolin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-bromo-5-(6-chloro-2-methylquinazolin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-bromo-5-(6-fluoro-2-methylquinazolin-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2,8-dimethyl-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-2-(trifluoromethyl)-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-3-fluoro-2,8,9-trimethyl-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2,3,8-trimethyl-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2-(difluoromethyl)-8-methyl-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-3-fluoro-2,8-dimethyl-4H-pyrimido[1,2-b]pyridazin-4-one

7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-2-(3-(pyridin-3-yl)pyrrolidine-1-carbonyl)-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-4-oxo-N-(thiazol-5-ylmethyl)-4H-pyrimido[1,2-b]pyridazine-2-carboxamide
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-2-(3-methylazetidine-1-carbonyl)-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2-(3-methoxyazetidine-1-carbonyl)-8-methyl-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-2-(3-fluoro-3-methylazetidine-1-carbonyl)-8-methyl-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-N-(1-cyanocyclopropyl)-8-methyl-4-oxo-4H-pyrimido[1,2-b]pyridazine-2-carboxamide
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-2-(2-oxa-6-azaspiro[3.3]heptane-6-carbonyl)-4H-pyrimido[1,2-b]pyridazin-4-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-4-oxo-N-(3-(2,2,2-trifluoroethyl)cyclobutyl)-4H-pyrimido[1,2-b]pyridazine-2-carboxamide
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-4-(trifluoromethyl)-2H-pyrimido[1,2-b]pyridazin-2-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-2H-pyrimido[1,2-b]pyridazin-2-one
7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-4,8-dimethyl-2H-pyrimido[1,2-b]pyridazin-2-one
ethyl 7-(2-bromo-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl)-8-methyl-4-oxo-4H-pyrimido[1,2-b]pyridazine-2-carboxylate
5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-cyclopropyl-5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-(1-methylcyclopropyl)-5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine

5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-2-(thiophen-2-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-methyl-5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
ethyl 5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxylate
2-(1-methyl-1H-pyrazol-5-yl)-5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-amine
2-chloro-5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-2-(trifluoromethyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-(2,2-dimethylcyclopropyl)-5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-isopropyl-5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine
2-(tert-butyl)-5-(7-methylpyrido[2,3-b]pyrazin-6-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine

or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising the compound of any of claims 1-13, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

15. Use of a compound of any of claims 1-13, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 14, in the manufacture of a medicament for the treatment of a neurological and/or psychiatric disorder, wherein the disorder is selected from Alzheimer's disease, schizophrenia, a sleep disorder, a pain disorder, and a cognitive disorder.

16. A compound of any of claims 1-13, or a pharmaceutically acceptable salt thereof, or the

pharmaceutical composition of claim 14 for use in therapy.