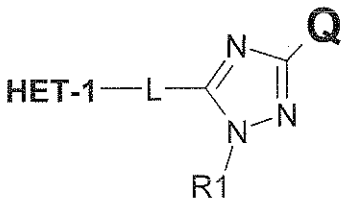
The objective of the present ~~invention~~disclosure is to provide compounds that are selective PDE10A enzyme inhibitors.

A further objective of the present ~~invention~~disclosure is to provide compounds which have such activity, and which have improved solubility, metabolic stability and/or bioavailability compared to prior art compounds.

Another objective of the ~~invention~~disclosure is to provide an effective treatment, in particular long-term treatment, of a human patient, without causing the side effects typically associated with current therapies for neurological and psychiatric disorders.

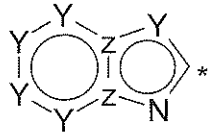
Further objectives of the ~~invention~~disclosure will become apparent upon reading the present specification.

Accordingly, ~~in one aspect~~embodiment of the present ~~invention~~disclosure relates to compounds of formula **I:**



I

wherein **HET-1** is a heteroaromatic group of formula **II** containing from 2 to 4 nitrogen atoms:



II

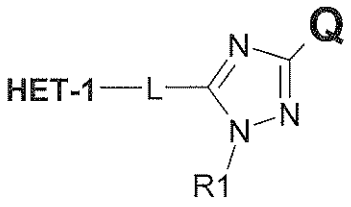
wherein Y can be N or CH, Z can be N or C, and wherein **HET-1** may optionally be substituted with up to three substituents R7, R8 and R9

Wherein R2-R6 are each selected independently from H; C_1-C_6 alkoxy such as methoxy; and halogen such as chlorine or fluorine;

with the proviso that the compound is not 1H-Benzimidazole, 2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; 1H-Benzimidazole, 2-[[[3-(2-pyrazinyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-; 1H-Benzimidazole, 2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)methyl]thio]-; 1H-Benzimidazole, 1-ethyl-5-(1-piperidinylsulfonyl)-2-[[[3-(2-thienyl)-1H-1,2,4-triazol-5-yl]thio]methyl]-; 1H-Benzimidazole, 6-methyl-2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; 1H-Benzimidazole, 2-[[[3-(3-pyridinyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-; Imidazo[1,2-a]pyridine, 8-methyl-2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; Imidazo[1,2-a]pyridine, 6-chloro-2-[[[3-(2-thienyl)-1H-1,2,4-triazol-5-yl]thio]methyl]-; 1H-Benzimidazole, 2-[[[3-(4-pyridinyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-; Imidazo[1,2-a]pyridine, 6-methyl-2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; 1H-Benzimidazole, 2-[[[3-(2-pyridinyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-; Imidazo[1,2-a]pyridine, 6-chloro-2-[[(3-phenyl-1H-1,2,4-triazol-5- yl)thio]methyl]-; 3H-Imidazo[4,5-b]pyridine, 2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; or 1H-Benzimidazole, 2-[[[3-(2-furanyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-;

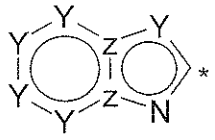
and tautomers and pharmaceutically acceptable salts thereof, and polymorphic forms thereof.

In one aspect of the invention, there is provided a compound having the structure I



I

wherein HET-1 is a heteroaromatic group of formula II containing from 2 to 4 nitrogen atoms:



II

wherein Y can be N or CH, Z can be N or C, and wherein **HET-1** may optionally be substituted with up to three substituents R2-R4 individually selected from hydrogen, C_1-C_6 alkyl; halogen; cyano, halo(C_1-C_6)alkyl; aryl, alkoxy and C_1-C_6 hydroxyalkyl, and wherein * denotes the attachment point,

Q is a is phenyl, optionally substituted with one to five substituents, or a monocyclic 5-membered or 6-membered heteroaromatic group containing 1 or 2 heteroatoms

-L- is a linker selected from -S-CH_2- , -CH_2-S- , -CH_2-CH_2-, -CH=CH-, and $-C\equiv C-$

R_1 is selected from H, C_1-C_6 alkyl; C_1-C_6 alkyl(C_3-C_8)cycloalkyl; C_1-C_6 hydroxyalkyl, CH_2CN, $CH_2C(O)NH_2$, C_1-C_6 arylalkyl, and C_1-C_6 alkyl-heterocycloalkyl,

with the proviso that the compound is not 1H-Benzimidazole, 2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; 1H-Benzimidazole, 2-[[[3-(2-pyrazinyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-; 1H-Benzimidazole, 2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)methyl]thio]-; 1H-Benzimidazole, 1-ethyl-5-(1-piperidinylsulfonyl)-2-[[[3-(2-thienyl)-1H-1,2,4-triazol-5-yl]thio]methyl]-; 1H-Benzimidazole, 6-methyl-2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; 1H-Benzimidazole, 2-[[[3-(3-pyridinyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-; Imidazo[1,2-a]pyridine, 8-methyl-2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; Imidazo[1,2-a]pyridine, 6-chloro-2-[[[3-(2-thienyl)-1H-1,2,4-triazol-5-yl]thio]methyl]-; 1H-Benzimidazole, 2-[[[3-(4-pyridinyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-; Imidazo[1,2-a]pyridine, 6-methyl-2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; 1H-Benzimidazole, 2-[[[3-(2-pyridinyl)-1H-

1,2,4-triazol-5-yl]methyl]thio]-; Imidazo[1,2-a]pyridine, 6-chloro-2-[[(3-phenyl-1H-1,2,4-triazol-5- yl)thio]methyl]-; 3H-Imidazo[4,5-b]pyridine, 2-[[(3-phenyl-1H-1,2,4-triazol-5-yl)thio]methyl]-; or 1H-Benzimidazole, 2-[[[3-(2-furanyl)-1H-1,2,4-triazol-5-yl]methyl]thio]-;

and tautomers and pharmaceutically acceptable salts thereof, and polymorphic forms thereof, with the proviso that when the linker (L) is -CH_2-S- then HET-1 is neither imidazo[1,2-a]pyridine nor imidazo[1,2-a]pyrimidine.

In separate embodiments ~~of the invention~~, the compound of formula I is selected among the specific compounds disclosed in the Experimental Section herein.

The ~~invention~~disclosure further provides a compound of formula I, or a pharmaceutically acceptable salt thereof, for use as a medicament.

In another aspect, there is provided a compound as defined above, but without proviso, for use as a medicament.

In another aspect, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound of formula I as disclosed herein and a pharmaceutically acceptable carrier, diluent or excipient.

The ~~invention~~disclosure further provides the use of a compound of formula I, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment of a neurodegenerative or psychiatric disorder.

In one aspect, there is provided the use of a compound as defined above but without proviso, alone or in combination with one or more neuroleptic agents such as sertindole, olanzapine, risperidone, quetiapine, aripiprazole, haloperidol, clozapine, ziprasidone and osanetant, in the manufacture of a medicament for the treatment of a neurodegenerative or psychiatric disorder, wherein the neurodegenerative disorder is selected from the group consisting of Alzheimer's disease, multi-infarct dementia, alcoholic dementia or other drug-related dementia, dementia associated with intracranial tumors or cerebral trauma, dementia associated with Huntington's disease or Parkinson's disease, or AIDS-related dementia; delirium; amnestic disorder; post-traumatic stress disorder; mental retardation; a learning disorder, for example reading disorder, mathematics disorder, or a disorder of written expression; attention-deficit/hyperactivity disorder; and age-related cognitive decline, and the psychiatric disorder is selected from the group consisting of schizophrenia, for example of the paranoid, disorganized, catatonic, undifferentiated, or residual type; schizophreniform disorder; schizoaffective disorder, for example of the delusional type or the depressive type; delusional disorder; substance-induced psychotic disorder, for example psychosis induced by alcohol, amphetamine, cannabis, cocaine, hallucinogens, inhalants, opioids, or phencyclidine; personality disorder of the paranoid type; and personality disorder of the schizoid type.

In another aspect, there is provided the use of a compound as defined above but without proviso, in the manufacture of the medicament for the treatment of a drug addiction in a mammal, including a human, such as an alcohol, amphetamine, cocaine, or opiate addiction.

Furthermore, in yet another ~~aspect~~embodiment, the present ~~invention~~disclosure provides a method of treating a subject suffering from a neurodegenerative disorder, comprising administering to the subject a therapeutically effective amount of a compound of formula I. In a still further ~~aspect~~embodiment, the present ~~invention~~disclosure provides a method of treating a subject suffering from a psychiatric disorder, comprising administering to the subject a therapeutically effective amount of a compound of formula I. In another embodiment, the present ~~invention~~disclosure provides a method of treating a subject suffering from a drug addiction, such as an alcohol, amphetamine, cocaine, or opiate addiction.

Detailed Description of the Invention

Definition of Substitutents

As used in the context of the present invention, the terms "halo" and "halogen" are used interchangeably and refer to fluorine, chlorine, bromine or iodine.

The term "C_1-C_6 alkyl" refers to a straight-chain or branched saturated hydrocarbon having from one to six carbon atoms, inclusive. Examples of such groups include, but are not limited to, methyl, ethyl, 1-propyl, 2-propyl, 1-butyl, 2-butyl, 2-methyl-2-propyl, 2-methyl-1-butyl, and n-hexyl. The expression "C_1-C_6 hydroxyalkyl" refers to a C_1-C_6 alkyl group as defined above which is substituted with one hydroxy group. The term "halo(C_1-C_6)alkyl" refers to a C_1-C_6 alkyl group as defined above which is substituted with up to three halogen atoms, such as trifluoromethyl.

The expression "C_1-C_6 alkoxy" refers to a straight-chain or branched saturated alkoxy group having from one to six carbon atoms, inclusive, with the open valency on the oxygen. Examples of such groups include, but are not limited to, methoxy, ethoxy, n-butoxy, 2-methyl-pentoxy and n-hexyloxy.

5-phenyl-2H-[1,2,4]triazol-3-yl]-ethyl}-5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyrazine; and 8-Methoxy-2-{2-[2-(2-methoxy-ethyl)-5-phenyl-2H-[1,2,4]triazol-3-yl]-ethyl}-5-methyl-[1,2,4]triazolo[1,5-a]pyridine
and pharmaceutically acceptable salts thereof.

25. A compound of any one of claims 1 to 24, but without proviso, for use as a medicament.

26. Use of a compound of any one of claims 1 to 24 but without proviso, alone or in combination with one or more neuroleptic agents such as sertindole, olanzapine, risperidone, quetiapine, aripiprazole, haloperidol, clozapine, ziprasidone and osanetant, in the manufacture of a medicament for the treatment of a neurodegenerative or psychiatric disorder, wherein the neurodegenerative disorder is selected from the group consisting of Alzheimer's disease, multi-infarct dementia, alcoholic dementia or other drug-related dementia, dementia associated with intracranial tumors or cerebral trauma, dementia associated with Huntington's disease or Parkinson's disease, or AIDS-related dementia; delirium; amnestic disorder; post-traumatic stress disorder; mental retardation; a learning disorder, for example reading disorder, mathematics disorder, or a disorder of written expression; attention-deficit/hyperactivity disorder; and age-related cognitive decline, and the psychiatric disorder is selected from the group consisting of schizophrenia, for example of the paranoid, disorganized, catatonic, undifferentiated, or residual type; schizophreniform disorder; schizoaffective disorder, for example of the delusional type or the depressive type; delusional disorder; substance-induced psychotic disorder, for example psychosis induced by alcohol, amphetamine, cannabis, cocaine, hallucinogens, inhalants, opioids, or phencyclidine; personality disorder of the paranoid type; and personality disorder of the schizoid type.

28. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 24 but without proviso, and one or more pharmaceutically acceptable carriers, diluents and excipients.