not efficacious in all patients. Hence, there remains a need for alternative methods of treatment.

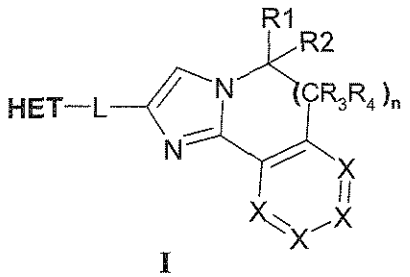
Summary of the Invention

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

Another objective of the invention 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 will become apparent upon reading the present specification.

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



I

wherein

n is 0 or 1,

X is CH;

R1 and R2 are each selected independently from the group consisting of H; C1-C6 alkyl; C1-C6 alkyl(C3-C8)cycloalkyl; C1-C6 hydroxyalkyl; C1-C6 alkoxy; CH2CN; CH2C(O)NH2 ;C1-C6 arylalkyl; and C1-C6 alkyl-heterocycloalkyl; halogen; and hydroxy;

R3 and R4 are each selected independently from the group consisting of H, OH, F, CH3, and OCH3;

L is a linker selected from the group consisting of $-CH_2-CH_2-$, -CH=CH-, $-CH_2-S-$, and $-S-CH_2-$; and

HET is a heteroaromatic group selected from the group consisting of [1,2,4]triazolo[1,5-a]pyrazine, [1,2,4]triazolo[1,5-a] pyridine, and [1,2,4]Triazolo[1,5-a]pyrimidine;

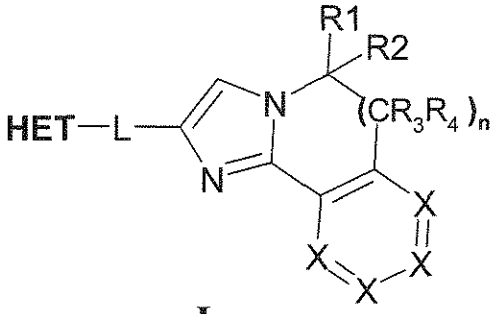
and tautomers and pharmaceutically acceptable acid addition salts thereof, and polymorphic forms thereof.

In another aspect, there is provided a compound as defined above as a medicament.

In another aspect, there is provided the use of a compound as defined above alone or in combination with one or more neuroleptic agents in the manufacture of a medicament for treatment of a neurodegenerative or psychiatric disorder.

In another aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound as defined above, and one or more pharmaceutically acceptable carriers, diluents and excipients.

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



I

wherein

n is 0 or 1

X is selected from the group consisting of CH, CF, COCH3, COH, and N; with the limitation that no more than one X is N;

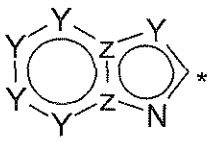
R1 and R2 are each selected independently from the group consisting of H; C1-C6 alkyl such as methyl, ethyl, 1-propyl, 2-propyl, isobutyl; C1-C6 alkyl(C3-C8)cycloalkyl such as cyclopropylmethyl; C1-C6 hydroxyalkyl such as hydroxyethyl; C1-C6 alkoxy such as methoxy and ethoxy; CH2CN; CH2C(O)NH2 ;C1-C6 arylalkyl such as benzyl and 4-chlorobenzyl; and C1-C6

alkyl-heterocycloalkyl such as tetrahydropyran-4-yl-methyl and 2-morpholin-4-yl-ethyl; halogen such as F; and hydroxy;

R3 and R4 are each selected independently from the group consisting of H, OH, F, CH3, and OCH3.

Further, L is a linker selected from the group consisting of -CH=CH-, -CH_2-S-, -CH_2-CH_2- and -S-CH_2-; and

HET 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

HET optionally can be substituted with up to three substituents R5, R6 and R7 individually selected from the group consisting of H; C1-C6 alkyl such as methyl; halogen such as chlorine, flour or bromine; cyano; halo(C1-C6)alkyl such as trifluoromethyl; aryl such as phenyl; alkoxy, preferably C1-C6 alkoxy, such as methoxy, dimethoxy, ethoxy, methoxy-ethoxy and ethoxy-methoxy, and C1-C6 hydroxyalkyl such as CH2CH2OH; and

"*" denotes the attachment point.

In a preferred embodiment~~, of the invention~~ R1 and R2 are independently selected from the group consisting of H, OH, F, CH3, and OCH3.

In another preferred embodiment~~, of the invention~~ R5, R6 and R7 are independently selected from the group consisting of H, CH3, and OCH3.

In another preferred embodiment, R1 and R2 are independently selected from the group consisting of H, OH, F, CH3, and OCH3 while at the same time R5, R6 and R7 are independently selected from the group consisting of H, CH3, and OCH3.

Further, the ~~invention~~disclosure relates to tautomers and pharmaceutically acceptable acid addition salts of a compound of formula I or II, and polymorphic forms thereof.

In a particular embodiment, the ~~invention~~disclosure relates to a compound of formula I in the form of a single tautomer or a polymorph.

In separate embodiments ~~of the invention~~, the compound of formula I is selected among the specific compounds disclosed in the examples of this application.

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

In another ~~aspect~~embodiment, the present ~~invention~~disclosure provides a pharmaceutical composition comprising a therapeutically effective amount of a compound of formula I 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 acid addition salt thereof, for the preparation of a medicament for the treatment of a neurodegenerative or psychiatric disorder.

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