invention, which are structurally unrelated to any of the known PDE10 inhibitors (Kehler, J. *et al. Expert Opin. Ther. Patents* **2007**, *17*, 147-158).

The compound of the invention is for the first time disclosed in WO09/152825 from which application priority is claimed. The compound of the invention proves to be an efficient PDE10A enzyme inhibitor and an in vivo active compound that reverses the PCP induced hyperactivity by 99% and may thus offer alternatives to current marketed treatments for neurodegenerative and/or psychiatric disorders, which are not efficacious in all patients. Hence, there remains a need for alternative methods of treatment.

Summary of the Invention

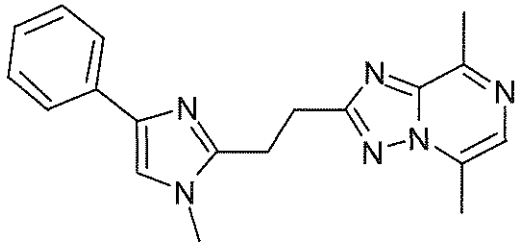
The objective of the ~~invention~~disclosure is to provide a compound that is a selective PDE10A enzyme inhibitor.

A further objective of the ~~invention~~disclosure is to provide a compound that has such activity, and has good, preferably 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~~ will become apparent upon reading the specification.

Accordingly, in one aspect, there is provided~~the invention relates to~~ the compound 5,8-Dimethyl-2-[2-(1-methyl-4-phenyl-1H-imidazol-2-yl)-ethyl]-[1,2,4]triazolo[1,5-a]pyrazine of formula **I**:



Formula I – compound of the invention

In the context of the present application the term "compound of the invention" includes 5,8-Dimethyl-2-[2-(1-methyl-4-phenyl-1H-imidazol-2-yl)-ethyl]-[1,2,4]triazolo[1,5-a]pyrazine of formula I and pharmaceutically acceptable acid addition salts thereof.

Another aspect~~The invention~~ further provides the compound of the invention, or a pharmaceutically acceptable acid addition salt thereof, for use as a medicament.

In another aspect, there is~~ invention~~ provides~~d~~ a pharmaceutical composition comprising the compound of the invention and a pharmaceutically acceptable carrier, diluent or excipient.

The ~~invention~~disclosure further provides the use of the compound of the invention for the preparation of a medicament for the treatment of a neurodegenerative or psychiatric disorder.

The ~~invention~~disclosure further provides the compound of the invention for use as a medicament.

The ~~invention~~disclosure further provides the compound of the invention for the treatment of a psychiatric disorder 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; bipolar disorder, for example bipolar I disorder, bipolar II disorder, and cyclothymic 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.

Furthermore the ~~invention~~disclosure provides a method of treating a patient suffering from a neurodegenerative disorder, comprising administering to the patient the compound of the invention. In a still further aspect, the invention provides a method of treating a patient suffering from a psychiatric disorder, comprising administering to the patient the compound of the invention. In another embodiment, the invention provides a method of treating a patient suffering from a drug addiction, such as an alcohol, amphetamine,

cocaine, or opiate addiction comprising administering to the patient the compound of the invention.

In another aspect, there is provided the use of the compound as defined above for the preparation 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; bipolar disorder, for example bipolar I disorder, bipolar II disorder, and cyclothymic 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 yet another aspect, there is provided the use of the compound as defined above and a further compound selected from the group consisting of sertindole, olanzapine, risperidone, quetiapine, aripiprazole, haloperidol, clozapine, ziprasidone and osanetant for the preparation 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; bipolar disorder, for example bipolar I disorder, bipolar II disorder, and cyclothymic 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.

Detailed Description of the Invention

Throughout this application the terms PDE 10, PDE 10A and PDE 10A enzyme are used interchangeably.

The compound of the invention has, when tested as described in the section PDE10A enzyme inhibition assay, an IC_{50} value of about 2.2 nM which makes it a useful compound for inhibition of PDE 10A enzyme activity.

Further, the compound has been tested for its ability to reverse phencyclidine (PCP) induced hyperactivity. The reversal of the PCP effect is measured as described in the section "Phencyclidine (PCP) induced hyperactivity". The experiment shows that the compound of the invention is an in vivo active compound that reverses the PCP induced hyperactivity by 99 %.

Pharmaceutically Acceptable Salts

The invention also comprises salts of the compound the invention, typically, pharmaceutically acceptable salts. Such salts include pharmaceutically acceptable acid addition salts. Acid addition salts include salts of inorganic acids as well as organic acids.

Representative examples of suitable inorganic acids include hydrochloric, hydrobromic, hydroiodic, phosphoric, sulfuric, sulfamic, nitric acids and the like. Representative examples of suitable organic acids include formic, acetic, trichloroacetic, trifluoroacetic, propionic, benzoic, cinnamic, citric, fumaric, glycolic, itaconic, lactic, methanesulfonic, maleic, malic, malonic, mandelic, oxalic, picric, pyruvic, salicylic, succinic, methane sulfonic, ethanesulfonic, tartaric, ascorbic, pamoic, bismethylene salicylic, ethanedisulfonic, gluconic, citraconic, aspartic, stearic, palmitic, EDTA, glycolic, p-aminobenzoic, glutamic, benzenesulfonic, p-toluenesulfonic acids, theophylline acetic acids, as well as the 8-halotheophyllines, for example 8-bromotheophylline and the like. Further examples of pharmaceutically acceptable inorganic or organic acid addition

cannabis, cocaine, hallucinogens, inhalants, opioids, or phencyclidine; personality disorder of the paranoid type; and personality disorder of the schizoid type.

4. Use of the compound of claim 1 for the preparation 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; bipolar disorder, for example bipolar I disorder, bipolar II disorder, and cyclothymic 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.

~~5. A method of treating a patient suffering from 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; bipolar disorder, for example bipolar I disorder, bipolar II disorder, and cyclothymic 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; which method comprises administering an effective amount of a compound of claim 1 to a patient, alone or in combination with one or more neuroleptic agents selected from sertindole, olanzapine, risperidone, quetiapine, aripiprazole, haloperidol, clozapine, ziprasidone and osanetant.~~

5~~6~~. A pharmaceutical composition comprising the compound of claim 1, and one or more pharmaceutically acceptable carriers, diluents and excipients.

6~~7~~. Use of the compound of claim 1 and a further compound selected from the group consisting of sertindole, olanzapine, risperidone, quetiapine, aripiprazole, haloperidol, clozapine, ziprasidone and osanetant for the preparation 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; bipolar disorder, for example bipolar I disorder, bipolar II disorder, and cyclothymic 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.

7~~8~~. The compound of claim 1 or 2 and a further compound selected from the group consisting of sertindole, olanzapine, risperidone, quetiapine, aripiprazole, haloperidol, clozapine, ziprasidone and osanetant as a combined preparation for simultaneous, separate or sequential use in 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; bipolar disorder, for example bipolar I disorder, bipolar II disorder, and cyclothymic 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.

8~~9~~. The compound of claim 1 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