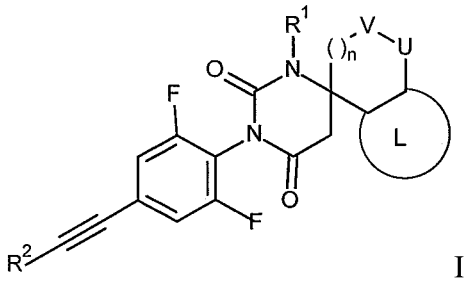
In addition, mGluR4 modulators were also shown to be involved in glucagon secretion inhibition (*Diabetes, 53(4), 998-1006, 2004)*. Therefore, orthosteric or positive allosteric modulators of mGluR4 have potential for the treatment of type 2 diabetes through its hypoglycemic effect.

Moreover, mGluR4 was shown to be expressed in prostate cancer cell-line (*Anticancer Res. 29(1), 371-7, 2009)* or colorectal carcinoma (*Cli. Cancer Research, 11(9)3288-95, 2005).* mGluR4 modulators may therefore have also potential role for the treatment of cancers.

Other proposed effects of mGluR4 PAM's can be expected for the treatment of emesis, obsessive compulsive disorder, anorexia and autism.

Compounds of formula I are distinguished by having valuable therapeutic properties. They can be used in the treatment or prevention of disorders, relating to allosteric modulators for the mGluR4 receptor.

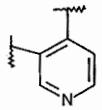
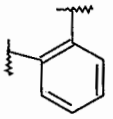
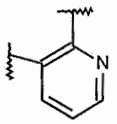
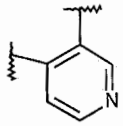
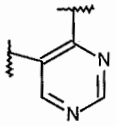
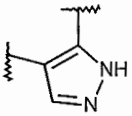
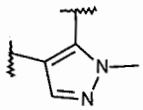
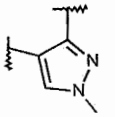
In one aspect, there is provided a compound of formula I



I

wherein

R^1	is lower alkyl;
R^2	is phenyl or pyridinyl, wherein the N atom in the pyridinyl group may be in different positions;
n	is 0, 1 or 2;
V/U	are independently from each other O or CH_2, wherein V and U cannot be simultaneously O;

L is a five or six membered heteroaryl group, selected from , , , , , , , ;

or a pharmaceutically acceptable salt or acid addition salt, a racemic mixture, or its corresponding enantiomer and/or optical isomer and/or stereoisomer thereof.

The most preferred indications for compounds which are allosteric modulators for the mGluR4 receptor are Parkinson's disease, anxiety, emesis, obsessive compulsive disorder, anorexia, autism, neuroprotection, cancer, depression and type 2 diabetes.

The present disclosure relates to compounds of formula I and to their pharmaceutically acceptable salts, to these compounds as pharmaceutically active substances, to the processes for their production as well as to their use in the treatment or prevention of disorders, relating to allosteric modulators for the mGluR4 receptor, such as Parkinson's disease, anxiety, emesis, obsessive compulsive disorder, autism, neuroprotection, cancer, depression and diabetes typ 2 and to pharmaceutical compositions containing the compounds of formula I.

A further object of the embodiments disclosed herein is a method for the treatment or prophylaxis of Parkinson's disease, anxiety, emesis, obsessive compulsive disorder, anorexia, autism, neuroprotection, cancer, depression and type 2 diabetes , which method comprises administering an effective amount of a compound of formula I to a mammal in need.

In another aspect, there is provided a compound of formula I as disclosed herein for use as therapeutically active substances.

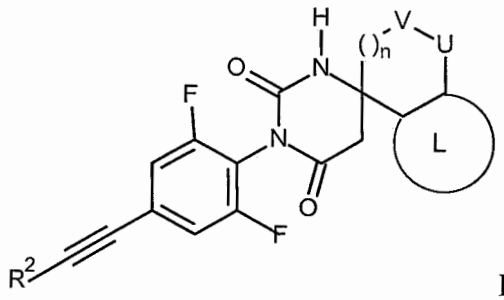
In another aspect, there is provided a compound of formula I as disclosed herein for use in the treatment of Parkinson's disease, anxiety, emesis, obsessive compulsive disorder, autism, neuroprotection, cancer, depression and diabetes type 2.

In another aspect, there is provided a pharmaceutical composition comprising a compound of formula I as disclosed herein and pharmaceutically acceptable excipients.

In another aspect, there is provided use of a compound of formula I as disclosed herein for the preparation of a medicament for the treatment of Parkinson's disease, anxiety, emesis, obsessive compulsive disorder, autism, neuroprotection, cancer, depression and diabetes type 2.

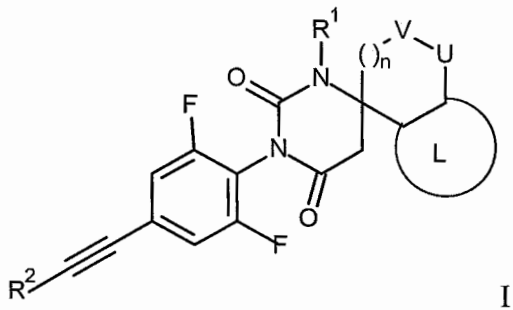
In another aspect, there is provided a process for the manufacture of a compound of formula I as defined herein, which process comprises

a) alkylating a compound of formula



I-1

with R^1-I in the presence of NaH or Cs_2CO_3 in DMF to a compound of formula



I

wherein R^1 is lower alkyl and the remaining substituents are described above, or if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts.

Furthermore, the disclosure includes all racemic mixtures, all their corresponding enantiomers and/or optical isomers, or analogues containing isotopes of hydrogen, fluorine, carbon, oxygen or nitrogen.

The following definitions of the general terms used in the present description apply irrespective of whether the terms in question appear alone or in combination.

16. The use of a compound of formula I according to any one of claims 1 – 11 for the preparation of a medicament for the treatment of Parkinson's disease, anxiety, emesis, obsessive compulsive disorder, autism, neuroprotection, cancer, depression and diabetes type 2.