

medical need for therapeutics for the prevention or treatment of viral infections in animals, more in particular in humans and especially for viral infections caused by flaviviruses, more in particular Dengue virus. Compounds with good anti-viral potency, no or low levels of side-effects, a broad spectrum activity against multiple
5 Dengue virus serotypes, a low toxicity and/or good pharmacokinetic or -dynamic properties are highly needed.

WO-2010/021878 discloses 2-phenylpyrrolidine and indoline derivatives as cold menthol receptor antagonists for treatment of inflammatory and central diseases.

10 WO-2013/045516 discloses indole and indoline derivatives for use in the treatment of dengue viral infections.

The present invention now provides compounds, substituted indoline derivatives, which show high potent activity against all four (4) serotypes of the Dengue virus.

15 SUMMARY

The present disclosure is based on the unexpected finding that at least one of the above-mentioned problems can be solved by the current compounds of the disclosure.

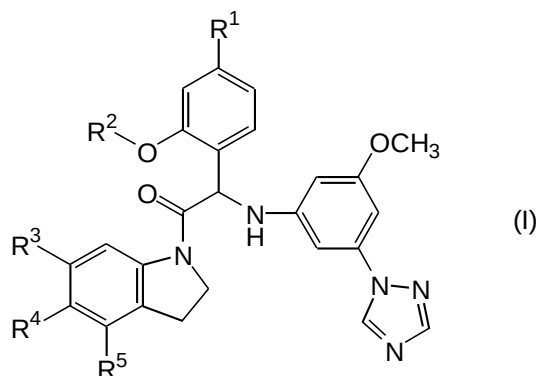
20 The present disclosure provides compounds which have been shown to possess potent antiviral activity against all four (4) serotypes currently known. The present disclosure furthermore demonstrates that these compounds efficiently inhibit proliferation of Dengue virus (DENV). Therefore, these compounds constitute a
25 useful class of potent compounds that can be used in the treatment and/or prevention of viral infections in animals, mammals and humans, more specifically for the treatment and/or prevention of infections with Dengue viruses.

30 The present disclosure furthermore relates to the use of such compounds as medicines and to their use for the manufacture of medicaments for treating and/or preventing viral infections, in particular with viruses belonging to the family of the Dengue viruses in animals or mammals, more in particular in humans. The disclosure also relates to methods for the preparation of all such compounds and to pharmaceutical compositions comprising them in an effective amount.

35 The present disclosure also relates to a method of treatment or prevention of dengue viral infections in humans by the administration an effective amount of one or more such compounds, or a pharmaceutically acceptable salt thereof optionally

in combination with one or more other medicines, like another antiviral agent, to a patient in need thereof.

One aspect of the disclosure is the provision of compounds of formula (I),
5 including any stereochemically isomeric form thereof:



wherein

10 R¹ is chloro or fluoro,

R² is -CH₂CH₂OH, or C₃₋₅alkylCOOH;

R³ is trifluoromethyl, or trifluoromethoxy;

R⁴ is hydrogen, fluoro, or methoxy; and

R⁵ is hydrogen or methyl;

15 or a pharmaceutically acceptable salt, solvate or polymorph thereof.

Another aspect of the disclosure is the provision of a pharmaceutical composition comprising a compound of the disclosure together with one or more pharmaceutically acceptable excipients, diluents or carriers.

20 Another aspect of the disclosure is the provision of a compound of formula (I) of the disclosure for use as a medicine.

Another aspect of the disclosure is the provision of a compound of formula (I) of
25 the disclosure for use in the treatment of Dengue infection and for the prevention or treatment of disease associated with Dengue infection.

The term "C₃₋₅alkyl" as used herein defines straight and branched chain saturated hydrocarbon radicals having from 3 to 5 carbon atoms such as, for example,
30 propyl, butyl, pentyl, 1,1-dimethylpropyl, 2-methylpropyl, 2-methylbutyl and the like.

Specifically above mentioned compounds are selected from the group comprising :

