

X is N or C optionally substituted by $-\text{CN}$, $-\text{CF}_3$, $-\text{C}_{1-3}$ alkyl- $\text{NH}-\text{C}(\text{O})-\text{C}_{1-3}$ alkyl,

$-\text{C}(\text{O})-\text{NH}_2$, $-\text{C}(\text{O})-\text{NH}-\text{C}_{1-3}$ alkyl, $-\text{C}(\text{O})-\text{N}(\text{dialkyl})$ or $-\text{CH}_2-\text{NH}-\text{C}(\text{O})-\text{CH}_3$;

R_1 is F or Cl;

R_2 and R_4 are each selected from H, halogen, CN, CF_3 , -O-alkyl or NH_2 ;

R_3 is F, Cl, CN, CF_3 , $-\text{C}_{1-3}$ alkyl, -O-alkyl, carboxylic ester or carboxylic amide

R_5 is Br, CN, CH_3 , CH_2OH , $\text{C}(\text{O})\text{NH}_2$, NH_2 or H;

R_6 is C_{1-8} alkyl substituted by carboxylic acid;

or is C_{3-8} cycloalkyl substituted by carboxylic acid, $-\text{N}-\text{C}_{1-3}$ alkylsulfone,

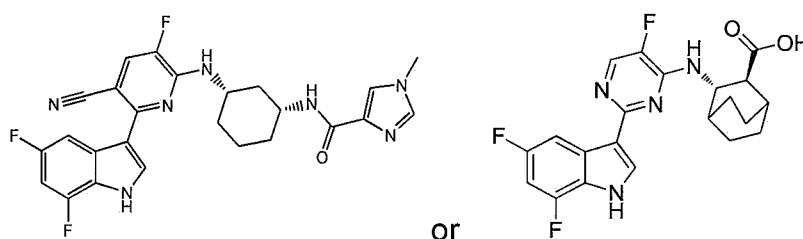
or $-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}$ heterocycle optionally substituted by C_{1-6} alkyl;

or is C_{3-6} heterocycle substituted by $-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}$ heterocycle;

or is C_{3-6} heterocycle substituted by COOH .

Preferably the compound according to the disclosure is the compound according to formula (I) wherein R_1 and R_3 are both F.

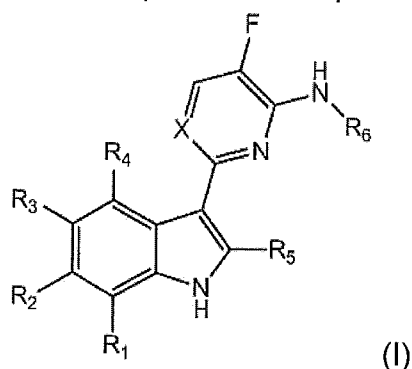
Preferred compounds according to the current disclosure have the structural formula:



Part of the disclosure, in another aspect, is also a pharmaceutical composition comprising a compound of formula (I) or a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph thereof together with one or more pharmaceutically acceptable excipients, diluents or carriers.

The pharmaceutical composition may also include additional therapeutic agents like another antiviral agent or an influenza vaccine, or both.

In another aspect, there is provided a compound of formula (I)



wherein

X is N or C optionally substituted by $-\text{CN}$, $-\text{CF}_3$, $-\text{C}_{1-3}$ alkyl- $\text{NH}-\text{C}(\text{O})-\text{C}_{1-3}$ alkyl, $-\text{C}(\text{O})-\text{NH}_2$, $-\text{C}(\text{O})-\text{NH}-\text{C}_{1-3}$ alkyl, $-\text{C}(\text{O})-\text{N}-(\text{dialkyl})$ or $-\text{CH}_2-\text{NH}-\text{C}(\text{O})-\text{CH}_3$;

R_1 is F or Cl;

R_2 and R_4 are each selected from H, halogen, CN, CF_3 , $-\text{O}-\text{alkyl}$ or NH_2 ;

R_3 is F, Cl, CN, CF_3 , or $-\text{C}_{1-3}$ alkyl;

R_5 is Br, CN, CH_3 , CH_2OH , $\text{C}(\text{O})\text{NH}_2$, NH_2 or H;

R_6 is C_{1-8} alkyl substituted by carboxylic acid;

or is C_{3-8} cycloalkyl substituted by carboxylic acid, $-\text{N}-\text{C}_{1-3}\text{alkylsulfone}$, or

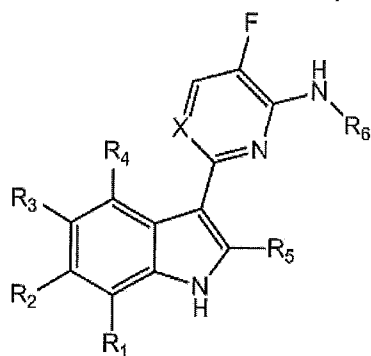
$-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}\text{heterocycle}$ optionally substituted by C_{1-6} alkyl;

or is C_{3-6} heterocycle substituted by $-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}$ heterocycle;

or is C_{3-6} heterocycle substituted by COOH ,

or a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph thereof, or a pharmaceutical composition comprising the compound of formula (I) or a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph thereof together with one or more pharmaceutically acceptable excipients, diluents or carriers, for use as a medicament.

In another aspect, there is provided a compound of formula (I)



(I)

wherein

X is N or C optionally substituted by $-\text{CN}$, $-\text{CF}_3$, $-\text{C}_{1-3}$ alkyl- $\text{NH}-\text{C}(\text{O})-\text{C}_{1-3}$ alkyl, $-\text{C}(\text{O})-\text{NH}_2$, $-\text{C}(\text{O})-\text{NH}-\text{C}_{1-3}$ alkyl, $-\text{C}(\text{O})-\text{N}-(\text{dialkyl})$ or $-\text{CH}_2-\text{NH}-\text{C}(\text{O})-\text{CH}_3$;

R_1 is F or Cl;

R_2 and R_4 are each selected from H, halogen, CN, CF_3 , $-\text{O}-\text{alkyl}$ or NH_2 ;

R_3 is F, Cl, CN, CF_3 , or $-\text{C}_{1-3}$ alkyl;

R_5 is Br, CN, CH_3 , CH_2OH , $\text{C}(\text{O})\text{NH}_2$, NH_2 or H;

R_6 is C_{1-8} alkyl substituted by carboxylic acid;

or is C_{3-8} cycloalkyl substituted by carboxylic acid, $-\text{N}-\text{C}_{1-3}$ alkylsulfone, or

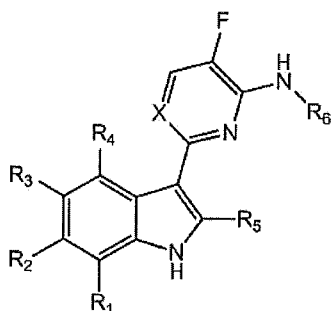
$-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}$ heterocycle optionally substituted by C_{1-6} alkyl;

or is C_{3-6} heterocycle substituted by $-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}$ heterocycle;

or is C_{3-6} heterocycle substituted by COOH ,

or a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph thereof, or a pharmaceutical composition comprising the compound of formula (I) or a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph thereof together with one or more pharmaceutically acceptable excipients, diluents or carriers, for use in the treatment of influenza.

In another aspect, there is provided use of a compound represented by the following structural formula (I)



(I)

a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein X is N or C optionally substituted by $-\text{CN}$, $-\text{CF}_3$,

-C₁₋₃ alkyl-NH-C(O)-C₁₋₃ alkyl, -C(O)-NH₂, -C(O)-NH-C₁₋₃ alkyl, -C(O)-N-(dialkyl)
or -CH₂-NH-C(O)-CH₃;

R₁ is F or Cl;

R₂ and R₄ are each selected from H, halogen, CN, CF₃, -O-alkyl or NH₂;

5 R₃ is F, Cl, CN, CF₃, or -C₁₋₃ alkyl;

R₅ is Br, CN, CH₃, CH₂OH, C(O)NH₂, NH₂ or H;

R₆ is C₁₋₈ alkyl substituted by carboxylic acid;

or is C₃₋₈ cycloalkyl substituted by carboxylic acid, -N-C₁₋₃alkylsulfone, or

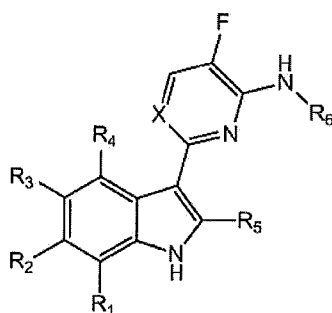
-N-C(O)-C₃₋₆heterocycle optionally substituted by C₁₋₆ alkyl;

10 or is C₃₋₆ heterocycle substituted by -N-C(O)-C₃₋₆ heterocycle;

or is C₃₋₆ heterocycle substituted by COOH

in the manufacture of a medicament for inhibiting the replication of influenza
virus(es) in a patient.

15 In another aspect, there is provided use of a compound represented by the
following structural formula (I)



(I)

a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph
thereof, wherein X is N or C optionally substituted by -CN, -CF₃,

-C₁₋₃ alkyl-NH-C(O)-C₁₋₃ alkyl, -C(O)-NH₂, -C(O)-NH-C₁₋₃ alkyl, -C(O)-N-(dialkyl)

20 or -CH₂-NH-C(O)-CH₃;

R₁ is F or Cl;

R₂ and R₄ are each selected from H, halogen, CN, CF₃, -O-alkyl or NH₂;

R₃ is F, Cl, CN, CF₃, or -C₁₋₃ alkyl;

R₅ is Br, CN, CH₃, CH₂OH, C(O)NH₂, NH₂ or H;

25 R₆ is C₁₋₈ alkyl substituted by carboxylic acid;

or is C₃₋₈ cycloalkyl substituted by carboxylic acid, -N-C₁₋₃alkylsulfone, or

-N-C(O)-C₃₋₆heterocycle optionally substituted by C₁₋₆ alkyl;

or is C₃₋₆ heterocycle substituted by -N-C(O)-C₃₋₆ heterocycle;

or is C₃₋₆ heterocycle substituted by COOH

30 for inhibiting the replication of influenza virus(es) in a biological sample.

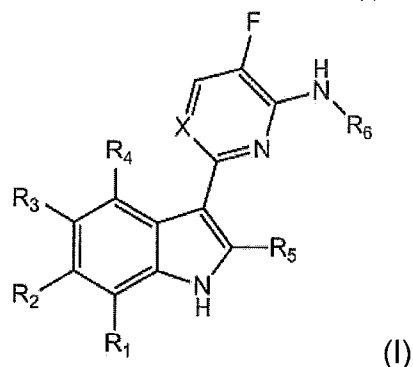
Said use may also comprise the co-administration of an additional therapeutic agent, wherein said additional therapeutic agent is selected from an antiviral agent or influenza vaccine, or both.

- 5 The term “alkyl” refers to a straight-chain or branched-chain saturated aliphatic hydrocarbon containing the specified number of carbon atoms.

The term “halogen” refers to F, Cl, Br or I.

thereof according to claim 1 together with one or more pharmaceutically acceptable excipients, diluents or carriers.

5. A compound of formula (I)



wherein

X is N or C optionally substituted by $-\text{CN}$, $-\text{CF}_3$, $-\text{C}_{1-3}$ alkyl- $\text{NH}-\text{C}(\text{O})-\text{C}_{1-3}$ alkyl, $-\text{C}(\text{O})-\text{NH}_2$, $-\text{C}(\text{O})-\text{NH}-\text{C}_{1-3}$ alkyl, $-\text{C}(\text{O})-\text{N}(\text{dialkyl})$ or $-\text{CH}_2-\text{NH}-\text{C}(\text{O})-\text{CH}_3$;

R_1 is F or Cl;

10 R_2 and R_4 are each selected from H, halogen, CN, CF_3 , -O-alkyl or NH_2 ;

R_3 is F, Cl, CN, CF_3 , or $-\text{C}_{1-3}$ alkyl;

R_5 is Br, CN, CH_3 , CH_2OH , $\text{C}(\text{O})\text{NH}_2$, NH_2 or H;

R_6 is C_{1-8} alkyl substituted by carboxylic acid;

or is C_{3-8} cycloalkyl substituted by carboxylic acid, $-\text{N}-\text{C}_{1-3}$ alkylsulfone, or

15 $-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}$ heterocycle optionally substituted by C_{1-6} alkyl;

or is C_{3-6} heterocycle substituted by $-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}$ heterocycle;

or is C_{3-6} heterocycle substituted by COOH ,

or a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or

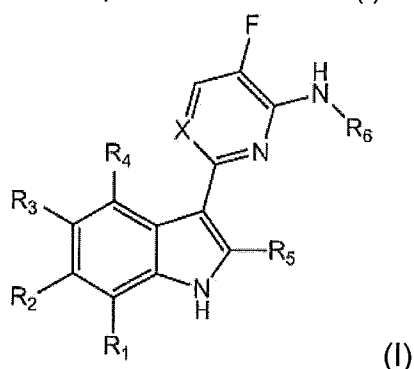
polymorph thereof, or a pharmaceutical composition comprising the compound

20 of formula (I) or a stereo- isomeric form, a pharmaceutically acceptable salt,

solvate or polymorph thereof together with one or more pharmaceutically

acceptable excipients, diluents or carriers, for use as a medicament.

6. A compound of formula (I)



wherein

X is N or C optionally substituted by -CN, -CF₃, -C₁₋₃ alkyl-NH-C(O)-C₁₋₃ alkyl,
-C(O)-NH₂, -C(O)-NH-C₁₋₃ alkyl, -C(O)-N-(dialkyl) or -CH₂-NH-C(O)-CH₃;

R₁ is F or Cl;

R₂ and R₄ are each selected from H, halogen, CN, CF₃, -O-alkyl or NH₂;

R₃ is F, Cl, CN, CF₃, or -C₁₋₃ alkyl;

R₅ is Br, CN, CH₃, CH₂OH, C(O)NH₂, NH₂ or H;

R₆ is C₁₋₈ alkyl substituted by carboxylic acid;

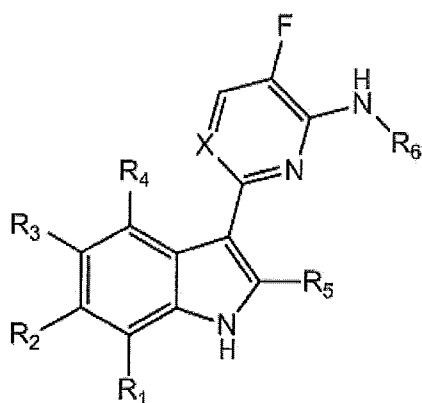
or is C₃₋₈ cycloalkyl substituted by carboxylic acid, -N-C₁₋₃alkylsulfone, or
-N-C(O)-C₃₋₆heterocycle optionally substituted by C₁₋₆ alkyl;

or is C₃₋₆ heterocycle substituted by -N-C(O)-C₃₋₆ heterocycle;

or is C₃₋₆ heterocycle substituted by COOH,

or a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or
polymorph thereof, or a pharmaceutical composition comprising the compound
of formula (I) or a stereo- isomeric form, a pharmaceutically acceptable salt,
solvate or polymorph thereof together with one or more pharmaceutically
acceptable excipients, diluents or carriers, for use in the treatment of influenza.

7. A use of a compound represented by the following structural formula (I)

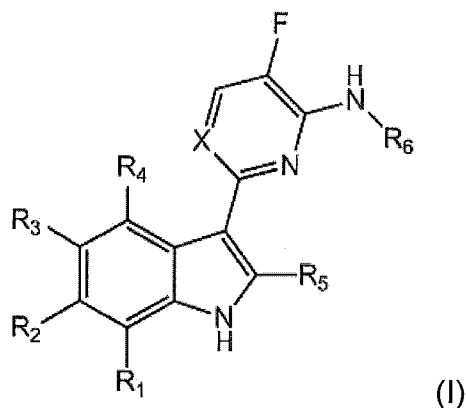


(I)

- 5 a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein
- X is N or C optionally substituted by -CN, -CF₃, -C₁₋₃ alkyl-NH-C(O)-C₁₋₃ alkyl,
- C(O)-NH₂, -C(O)-NH-C₁₋₃ alkyl, -C(O)-N-(dialkyl) or -CH₂-NH-C(O)-CH₃;
- 10 R₁ is F or Cl;
- R₂ and R₄ are each selected from H, halogen, CN, CF₃, -O-alkyl or NH₂;
- R₃ is F, Cl, CN, CF₃, or -C₁₋₃ alkyl
- R₅ is Br, CN, CH₃, CH₂OH, C(O)NH₂, NH₂ or H;
- R₆ is C₁₋₈ alkyl substituted by carboxylic acid;
- 15 or is C₃₋₈ cycloalkyl substituted by carboxylic acid, -N-C₁₋₃alkylsulfone,
- or
- N-C(O)-C₃₋₆heterocycle optionally substituted by C₁₋₆ alkyl;
- or is C₃₋₆ heterocycle substituted by -N-C(O)-C₃₋₆ heterocycle;
- or is C₃₋₆ heterocycle substituted by COOH

in the manufacture of a medicament for inhibiting the replication of influenza virus(es) in a patient.

8. A use of a compound represented by the following structural formula (I)



a stereo- isomeric form, a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein

10 X is N or C optionally substituted by $-\text{CN}$, $-\text{CF}_3$, $-\text{C}_{1-3}$ alkyl- $\text{NH}-\text{C}(\text{O})-\text{C}_{1-3}$ alkyl,

$-\text{C}(\text{O})-\text{NH}_2$, $-\text{C}(\text{O})-\text{NH}-\text{C}_{1-3}$ alkyl, $-\text{C}(\text{O})-\text{N}(\text{dialkyl})$ or $-\text{CH}_2-\text{NH}-\text{C}(\text{O})-\text{CH}_3$;

R_1 is F or Cl;

R_2 and R_4 are each selected from H, halogen, CN, CF_3 , $-\text{O}-\text{alkyl}$ or NH_2 ;

15 R_3 is F, Cl, CN, CF_3 , or $-\text{C}_{1-3}$ alkyl

R_5 is Br, CN, CH_3 , CH_2OH , $\text{C}(\text{O})\text{NH}_2$, NH_2 or H;

R_6 is C_{1-8} alkyl substituted by carboxylic acid;

or is C_{3-8} cycloalkyl substituted by carboxylic acid, $-\text{N}-\text{C}_{1-3}\text{alkylsulfone}$,

or

20 $\text{N}-\text{C}(\text{O})-\text{C}_{3-6}\text{heterocycle}$ optionally substituted by C_{1-6} alkyl;

or is C_{3-6} heterocycle substituted by $-\text{N}-\text{C}(\text{O})-\text{C}_{3-6}$ heterocycle;

or is C_{3-6} heterocycle substituted by COOH

for inhibiting the replication of influenza virus(es) in a biological sample.

25 9. The use of claim 7 or 8 further comprising an additional therapeutic agent.

10. The use of claim 9 wherein the additional therapeutic agent is selected from an antiviral agent or influenza vaccine, or both.