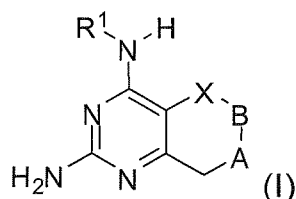


However, there exists a strong need for novel Toll-Like receptor modulators having preferred selectivity, higher potency, higher metabolic stability, and an improved safety profile (for instance a reduced CVS risk) compared to the compounds of the prior art.

- 5 In accordance with the present disclosure, a compound of formula (I) is provided



or a pharmaceutically acceptable salt, tautomer(s), solvate or polymorph thereof, wherein

- 10 A is selected from the group consisting of CH_2 , NCOR^2 , CHR^3 and CR^3R^3 in any stereo chemical configuration,

B is selected from the group consisting of CH_2 , NCOR^4 , CHR^3 and CR^3R^3 in any stereo chemical configuration,

with the proviso that when A is NCOR^2 then B is not NCOR^4 and with the
 15 proviso that A and B are not both selected from CH_2 , CHR^3 or CR^3R^3 ,

X is selected from CH_2 or CHR^5 in any stereo chemical configuration,

R^1 is selected from C_{1-8} alkyl optionally substituted with one or more of the following: C_{1-6} alkyl, C_{3-7} cycloalkyl, hydroxyl, hydroxyalkyl, amino, nitrile, alkoxy, alkoxy(C_{1-4})alkyl, carboxylic acid, carboxylic ester, carbamate or sulfone,

- 20 R^2 is selected from substituted and unsubstituted C_{1-6} alkyl, C_{3-7} cycloalkyl, heterocycle, aryl, heteroaryl, heteroarylalkyl, each of which is optionally substituted by one or more substituents independently selected from halogen, hydroxyl, amino, C_{1-6} alkyl, di-(C_{1-6})alkylamino, C_{1-6} alkylamino, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, carboxylic acid, carboxylic ester, carboxylic amide,
 25 heterocycle, aryl, alkenyl, alkynyl, arylalkyl, heteroaryl, heteroarylalkyl or nitrile,

R^3 is selected from hydrogen, substituted and unsubstituted C_{1-6} alkyl, alkoxy, alkoxy-(C_{1-4})alkyl, C_{3-7} cycloalkyl, C_{4-7} heterocycle, aromatic, bicyclic heterocycle, arylalkyl, heteroaryl, heteroarylalkyl each of which is optionally substituted by one or more substituents independently selected from halogen,

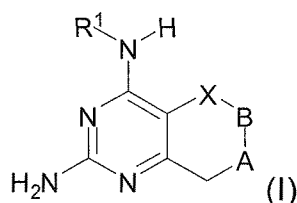
- 30 hydroxyl, amino, C_{1-6} alkyl, di-(C_{1-6})alkylamino, C_{1-6} alkylamino, C_{1-6} alkyl,

C₁₋₆alkoxy, C₃₋₆cycloalkyl, carboxylic acid, carboxylic ester, carboxylic amide, heterocycle, aryl, alkenyl, alkynyl, arylalkyl, heteroaryl, heteroarylalkyl or nitrile,

R⁴ is selected from substituted or unsubstituted C₁₋₇alkyl, alkoxy, alkoxy-(C₁₋₄)alkyl, aryl or C₃₋₇cycloalkyl each of which is optionally substituted by
5 heterocycle, nitrile, heteroarylalkyl or heteroaryl and wherein

R⁵ is selected from aromatic, bicyclic heterocycle, aryl, heteroaryl, each of which is optionally substituted by one or more substituents independently selected from halogen, hydroxyl, amino, C₁₋₆alkyl, di-(C₁₋₆)alkylamino, C₁₋₆alkylamino, C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, carboxylic acid, carboxylic
10 ester, carboxylic amide, heterocycle, aryl, alkenyl, alkynyl, arylalkyl, heteroaryl, heteroarylalkyl or nitrile.

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



or a pharmaceutically acceptable salt, tautomer(s), solvate or polymorph
15 thereof, wherein

A is selected from the group consisting of CH₂, and NCOR² in any stereo chemical configuration,

B is selected from the group consisting of CH₂, and NCOR⁴ in any stereo chemical configuration,

20 with the proviso that when A is NCOR² then B is not NCOR⁴,

X is selected from CH₂ in any stereo chemical configuration,

R¹ is selected from C₄₋₈alkyl optionally substituted with hydroxyl,

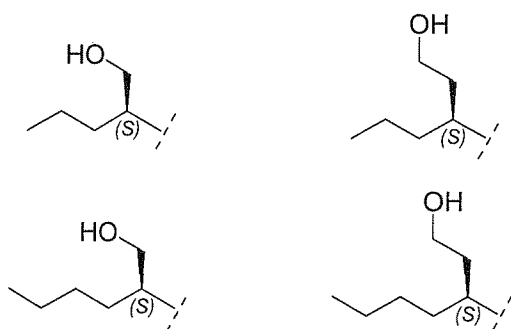
R² is selected from substituted and unsubstituted C₁₋₆alkyl, C₃₋₇cycloalkyl, heterocycle, aryl, heteroaryl, heteroarylalkyl, each of which is optionally
25 substituted by one or more substituents independently selected from halogen, C₁₋₆alkyl, or nitrile,

R⁴ is selected from substituted or unsubstituted C₁₋₇alkyl, alkoxy-(C₁₋₄)alkyl, aryl or C₃₋₇cycloalkyl each of which is optionally substituted by nitrile.

In a first embodiment the present disclosure provides compounds of formula (I) wherein R¹ is butyl and wherein A, B, and X are as specified above.

- 5 In a further embodiment the disclosure concerns compounds of formula (I) wherein R¹ is C₄₋₈alkyl substituted with hydroxyl, and wherein A, B, and X are as specified above.

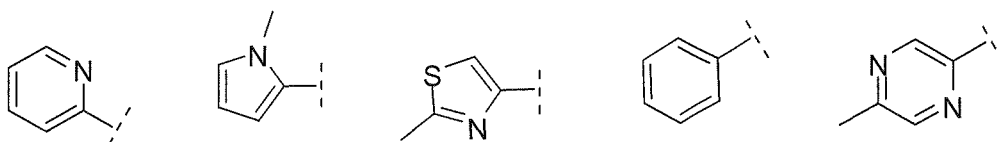
Another embodiment relates to compounds of formula I wherein R¹, being C₄₋₈alkyl substituted with hydroxyl, is one of the following



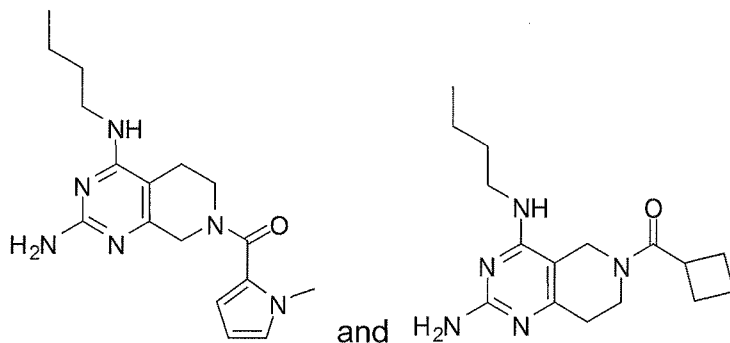
- 10 Furthermore, the present disclosure also provides compounds of formula (I) wherein X is CH₂ and wherein A, and B are as specified above.

In another embodiment the present disclosure provides compounds of formula (I) wherein X is CH₂ and wherein A is CH₂ and B are as specified above.

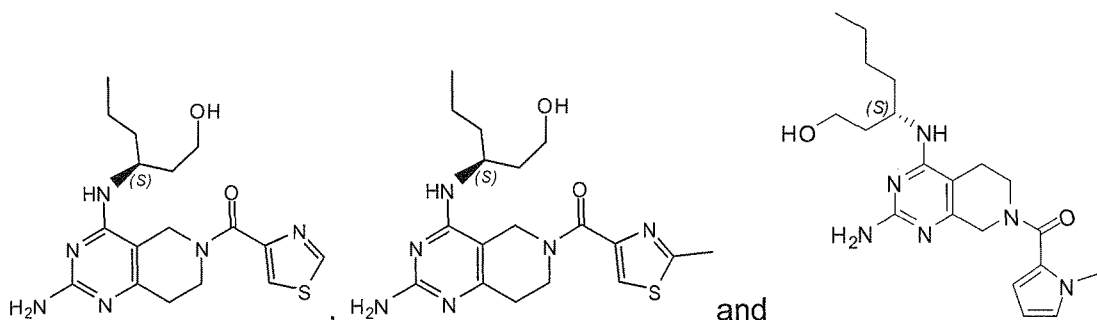
- 15 Furthermore, the disclosure relates to compounds of formula (I) wherein R² is one of the following examples that can be further substituted with C₁₋₃alkyl, hydroxyl, alkoxy, nitrile, heterocycle, carboxylic ester, or carboxylic amide:



Preferred compounds are compound numbers 3 and 1 having the following chemical structures respectively:



- 5 Other preferred compounds according to the disclosure are the compounds having the following chemical structures:



- 10 The compounds of formula (I) and their pharmaceutically acceptable salt, tautomer(s), solvate or polymorph thereof have activity as pharmaceuticals, in particular as modulators of Toll-Like Receptors (especially TLR7 and/or TLR8) activity.

- 15 The present disclosure also provides a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt, tautomer, solvate or polymorph thereof together with one or more pharmaceutically acceptable excipients, diluents or carriers. In another aspect, there is provided a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof as defined herein together with one or more pharmaceutically acceptable excipients, diluents or carriers.

Further, a compound of formula (I) or a pharmaceutically acceptable salt, tautomer, solvate or polymorph thereof according to the current disclosure, or a pharmaceutical composition comprising said compound of formula (I) or a pharmaceutically acceptable salt, tautomer, solvate or polymorph thereof can
5 be used as a medicament. In another aspect, there is provided a compound of formula (I) or a pharmaceutically acceptable salt thereof as defined herein, or a pharmaceutical composition as defined herein for use as a medicament.

Further, a compound of formula (I) or a pharmaceutically acceptable salt, tautomer, solvate or polymorph thereof, or said pharmaceutical composition comprising said compound of formula (I) or a pharmaceutically acceptable salt, tautomer, solvate or polymorph thereof can be used accordingly in the treatment of a disorder in which the modulation of TLR7 and /or TLR8 is involved. In another aspect, there is provided a compound of formula (I) or a pharmaceutically acceptable salt thereof as defined herein, or a pharmaceutical composition as defined herein for use in the treatment of a disorder in which the modulation of TLR7 and /or TLR8 is involved.

10 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 fluorine, chlorine, bromine or iodine.

The term “alkenyl” refers to an alkyl as defined above consisting of at least two carbon atoms and at least one carbon-carbon double bond.

15 The term “alkynyl” refers to an alkyl as defined above consisting of at least two carbon atoms and at least one carbon-carbon triple bond.

The term “cycloalkyl” refers to a carbocyclic ring containing the specified number of carbon atoms.

20 The term “heteroaryl” means an aromatic ring structure as defined for the term “aryl” comprising at least 1 heteroatom selected from N, O and S, in particular from N and O.

The term “aryl” means an aromatic ring structure. Said aromatic ring structure may have 4, 5, 6 or 7 ring atoms. In particular, said aromatic ring structure may have 5 or 6 ring atoms.

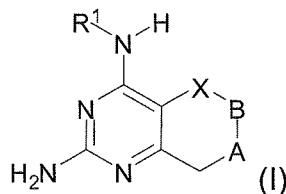
25 The term “bicyclic heterocycle” means an aromatic ring structure, as defined for the term “aryl” comprised of two fused aromatic rings. Each ring is optionally comprised of heteroatoms selected from N, O and S, in particular from N and O.

30 The term “arylalkyl” means an aromatic ring structure as defined for the term “aryl” optionally substituted with an alkyl group.

The term “heteroarylalkyl” means an aromatic ring structure as defined for the term “heteroaryl” optionally substituted by an alkyl group.

Claims

1. A compound of formula (I)



or a pharmaceutically acceptable salt, tautomer(s), solvate or polymorph thereof,
5 wherein

A is selected from the group consisting of CH_2 , and NCOR^2 in any stereo chemical configuration,

B is selected from the group consisting of CH_2 , and NCOR^4 in any stereo chemical configuration,

10 with the proviso that when A is NCOR^2 then B is not NCOR^4 ,

X is selected from CH_2 in any stereo chemical configuration,

R^1 is selected from C_{4-8} alkyl optionally substituted with hydroxyl,

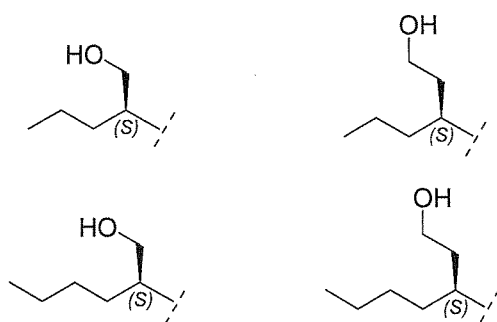
R^2 is selected from substituted and unsubstituted C_{1-6} alkyl, C_{3-7} cycloalkyl, heterocycle, aryl, heteroaryl, heteroarylalkyl, each of which is optionally substituted by one or more
15 substituents independently selected from halogen, C_{1-6} alkyl, or nitrile,

R^4 is selected from substituted or unsubstituted C_{1-7} alkyl, alkoxy- (C_{1-4}) alkyl, aryl or C_{3-7} cycloalkyl each of which is optionally substituted by nitrile.

2. A compound of formula (I) according to claim 1 wherein R^1 is butyl and wherein A, B,
5 and X are as defined in claim 1.

3. A compound of formula (I) according to claim 1 wherein R^1 is C_{4-8} alkyl substituted
with hydroxyl, and wherein A, B, and X are as defined in claim 1.

10 4. A compound of formula (I) according to claim 3 wherein R^1 , being C_{4-8} alkyl
substituted with hydroxyl, is one of the following

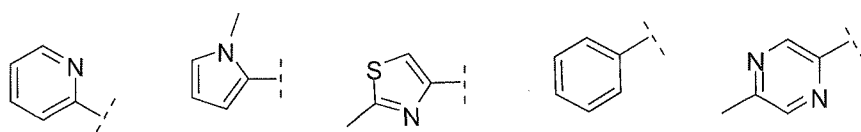


15 5. A compound of formula (I) according to claim 1 wherein X is CH_2 and wherein A, and
B are as defined in claim 1.

6. A compound of formula (I) according to claim 1 wherein X is CH_2 and wherein A is
 CH_2 and B is as defined in claim 1.

20

7. A compound of formula (I) according to claim 1 wherein R^2 is one of the following
examples that can be further substituted with C_{1-3} alkyl or nitrile:



8. A pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof according to one of the claims 1-7 together with one or more pharmaceutically acceptable excipients, diluents or carriers.
9. A compound of formula (I) or a pharmaceutically acceptable salt thereof according to one of the claims 1-7, or a pharmaceutical composition according to claim 8 for use as a medicament.
10. A compound of formula (I) or a pharmaceutically acceptable salt thereof according to one of the claims 1-7, or a pharmaceutical composition according to claim 8 for use in the treatment of a disorder in which the modulation of TLR7 and /or TLR8 is involved.