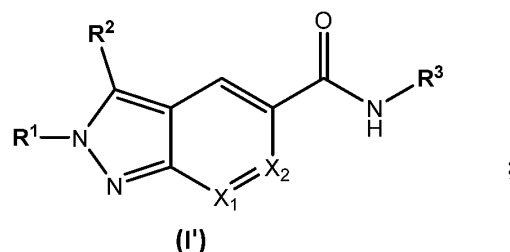


CLAIMS

1. A compound of formula (I'):



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from the group consisting of C_{1-5} alkyl, C_{3-6} cycloalkyl, $-C_{1-2}$ alkyl- C_{3-6} cycloalkyl, a fully saturated 4 to 7 membered heterocycle containing 1 to 2 heteroatoms independently selected from nitrogen, sulfur and oxygen, $-C_{1-2}$ alkyl- C_{4-7} heterocycle, wherein the C_{4-7} heterocycle may be fully or partially saturated and contains 1 to 2 heteroatoms independently selected from nitrogen, sulfur and oxygen, $-C_{1-4}$ alkyl-O- C_{1-2} alkyl, a fully saturated 5 to 8 membered bridged-carbocyclic ring, a fully saturated 5 to 8 membered bridged-heterocyclic ring system having 1 to 2 heteroatoms independently selected from nitrogen and oxygen, a 5 to 10 membered fused heterobicyclic ring system having 1 to 2 heteroatoms independently selected from nitrogen and oxygen and a 5 to 10 membered spiro heterobicyclic ring system having 1 to 2 heteroatoms independently selected from nitrogen and oxygen, wherein R^1 may be optionally substituted with 1, 2 or 3 substituents which are independently selected from halo, nitrile, oxo, halo-substituted C_{1-4} alkyl, hydroxy-substituted C_{1-4} alkyl, C_{1-4} alkyl, C_{4-7} heterocycle containing 1 to 2 heteroatoms independently selected from nitrogen and oxygen, a fully saturated 5 to 8 membered bridged-heterocyclic ring system having 1 to 2 heteroatoms independently selected from nitrogen and oxygen, C_{1-4} alkyl-O- C_{1-2} alkyl, hydroxyl and C_{1-4} alkoxy;

R^2 is hydrogen, C_{1-4} alkyl or halogen;

R^3 is selected from the group consisting of

- i. a 5 or 6 membered heteroaryl having 1 to 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, said heteroaryl is optionally substituted with 1 to 3 R^4 ;
- ii. Phenyl optionally substituted with 1 to 3 R^4 ,

- iii. a 5-6 membered partially or fully saturated heterocycle having 1 to 2 heteroatoms independently selected from oxygen and nitrogen, said heterocycle may be optionally substituted with 1 to 3 R⁴;
- iv. a partially or fully saturated C₃₋₆ cycloalkyl which may be optionally substituted with 1 to 3 R⁴;
- v. a 7 to 10 membered fused heterobicyclic ring system having 1, 2 or 3 heteroatoms independently selected from nitrogen and oxygen, said ring system is optionally substituted with 1 to 3 R⁴; and
- vi. a 7 to 10 membered fused bicyclic ring system optionally having 1, 2 or 3 heteroatoms independently selected from nitrogen and oxygen, said ring system is optionally substituted with 1 to 3 R⁴;

X₁ and X₂ are independently selected from N, CH and CR⁵, wherein only one of X₁ or X₂ may be N;

R⁵ is selected from halogen, C₁₋₄alkyl, nitrile and -OR⁶;

R⁶ is hydrogen, a C₁₋₅alkyl, a C₃₋₆cycloalkyl or a fully saturated 4 to 7 membered heterocycle containing 1 or 2 heteroatoms selected from nitrogen and oxygen, wherein the C₁₋₅alkyl represented by R⁶ is optionally substituted with 1 to 3 substituents R^{6a} independently selected from halogen, hydroxyl, C₁₋₄alkoxy, C₃₋₆cycloalkyl, phenyl and a 4 to 7 membered partially or fully saturated heterocycle containing 1 or 2 heteroatoms selected from nitrogen and oxygen, the C₃₋₆cycloalkyl represented by R⁶ is optionally substituted with 1-3 substituent R^{6b} independently selected from halogen, C₁₋₄alkyl, halo-substitutedC₁₋₄alkyl and C₁₋₄alkoxy; wherein said C₃₋₆cycloalkyl and phenyl represented by R^{6a} may be optionally substituted with 1 to 3 R⁷;

each R⁷ is independently selected from oxo, halo, halo-substitutedC₁₋₄ alkyl and C₁₋₄ alkyl;

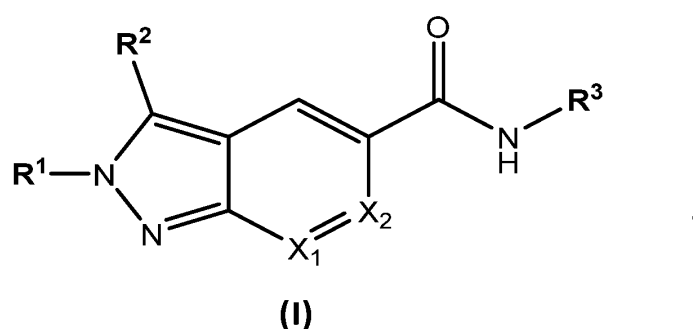
R⁴ for each occurrence, is independently selected from CN, hydroxyl, C₁₋₄ alkyl, CN-substitutedC₁₋₄ alkyl, oxo, halo, halo-substitutedC₁₋₄alkyl, -NR⁸R⁹, C₁₋₄ alkoxy, C₁₋₄ alkoxy-C₁₋₄ alkoxy, hydroxy-substituted C₁₋₄ alkyl, halo-substitutedC₁₋₄ alkoxy, C₃₋₆cycloalkyl, C(O)NR¹⁰R¹¹ and a 5 or 6 membered heteroaryl having 1 to 2 heteroatoms independently selected from nitrogen, oxygen and sulfur, said C₃₋₆cycloalkyl and heteroaryl may be optionally substituted with 1 to 2 substituents independently selected from the group consisting of C₁₋₄ alkyl, hydroxyl and halogen; or two R⁴ groups on the same atom may form a C₃₋₆cycloalkyl, or two R⁴ groups on adjacent ring atoms may form phenyl, C₄₋₆ carbocycle, C₄₋₆ heterocycle, or a 7 membered bridged ring system optionally having 1 heteroatom

selected from nitrogen and oxygen, wherein said phenyl, C₃₋₆cycloalkyl C₄₋₆ carbocycle and C₄₋₆ heterocycle may be optionally substituted with 1 to 2 C₁₋₄ alkyl, halo or halo-substituted C₁₋₄alkyl;

R⁸ and R⁹ are each independently selected from hydrogen, -C(O)C₁₋₄ alkyl and C₁₋₄ alkyl; or R⁸ and R⁹ may combine to form a 4 to 6 membered saturated ring optionally containing one additional heteroatom selected from nitrogen or oxygen wherein said additional nitrogen may be optionally substituted with C₁₋₄ alkyl; and

R¹⁰ and R¹¹ are each independently selected from hydrogen and C₁₋₄ alkyl.

2. The compound of claim 1, wherein the compound is of formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from the group consisting of C₁₋₅ alkyl, C₃₋₆cycloalkyl, -C₁₋₂ alkyl-C₃₋₆cycloalkyl, a fully saturated 4 to 7 membered heterocycle containing 1 to 2 heteroatoms independently selected from nitrogen, sulfur and oxygen, -C₁₋₂ alkyl-C₄₋₇ heterocycle, wherein the C₄₋₇ heterocycle may be fully or partially saturated and contains 1 to 2 heteroatoms independently selected from nitrogen, sulfur and oxygen, -C₁₋₄ alkyl-O-C₁₋₂ alkyl, a fully saturated 5 to 8 membered bridged-carbocyclic ring, a fully saturated 5 to 8 membered bridged-heterocyclic ring system having 1 to 2 heteroatoms independently selected from nitrogen and oxygen, a 5 to 10 membered fused heterobicyclic ring system having 1 to 2 heteroatoms independently selected from nitrogen and oxygen and a 5 to 10 membered spiro heterobicyclic ring system having 1 to 2 heteroatoms independently selected from nitrogen and oxygen, wherein R¹ may be optionally substituted with 1, 2 or 3 substituents which are independently selected from halo, nitrile, oxo, halo-substituted C₁₋₄ alkyl, hydroxy-substituted C₁₋₄ alkyl, C₁₋₄ alkyl, C₄₋₇ heterocycle containing 1 to 2 heteroatoms independently selected from nitrogen and oxygen, C₁₋₄ alkyl-O-C₁₋₂ alkyl, hydroxyl and C₁₋₄ alkoxy;

R² is hydrogen, C₁₋₄ alkyl or halogen;

R^3 is selected from the group consisting of

- i. a 5 or 6 membered heteroaryl having 1 to 2 heteroatoms independently selected from nitrogen, oxygen and sulfur, said heteroaryl is optionally substituted with 1 to 3 R^4 ;
- ii. Phenyl optionally substituted with 1 to 3 R^4 ,
- iii. a 5-6 membered partially or fully saturated heterocycle having 1 to 2 heteroatoms independently selected from oxygen and nitrogen, said heterocycle may be optionally substituted with 1 to 3 R^4 ;
- iv. a partially or fully saturated C_{3-6} cycloalkyl which may be optionally substituted with 1 to 3 R^4 ;
- v. a 7 to 10 membered fused heterobicyclic ring system having 1, 2 or 3 heteroatoms independently selected from nitrogen and oxygen, said ring system is optionally substituted with 1 to 3 R^4 ; and
- vi. a 7 to 10 membered fused bicyclic ring system optionally having 1, 2 or 3 heteroatoms independently selected from nitrogen and oxygen, said ring system is optionally substituted with 1 to 3 R^4 ;

X_1 and X_2 are independently selected from N, CH and CR^5 , wherein only one of X_1 or X_2 may be N;

R^5 is selected from halogen, C_{1-4} alkyl, nitrile and $-OR^6$;

R^6 is hydrogen or an optionally substituted C_{1-5} alkyl having 1 to 3 substituents independently selected from halogen, hydroxyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, phenyl and a 4 to 7 membered partially or fully saturated heterocycle containing 1 or 2 heteroatoms selected from nitrogen and oxygen, wherein said C_{3-6} cycloalkyl and phenyl may be optionally substituted with 1 to 3 R^7 ;

each R^7 is independently selected from oxo, halo, halo-substituted C_{1-4} alkyl and C_{1-4} alkyl;

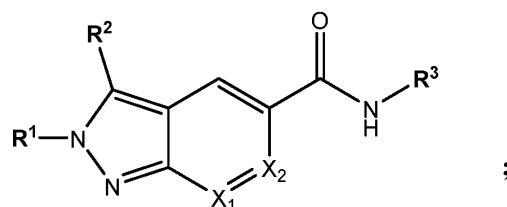
R^4 for each occurrence, is independently selected from CN, hydroxyl, C_{1-4} alkyl, CN-substituted C_{1-4} alkyl, oxo, halo, halo-substituted C_{1-4} alkyl, $-NR^8R^9$, C_{1-4} alkoxy, C_{1-4} alkoxy- C_{1-4} alkoxy, hydroxy-substituted C_{1-4} alkyl, halo-substituted C_{1-4} alkoxy, C_{3-6} cycloalkyl, $C(O)NR^{10}R^{11}$ and a 5 or 6 membered heteroaryl having 1 to 2 heteroatoms independently selected from nitrogen, oxygen and sulfur, said C_{3-6} cycloalkyl and heteroaryl may be optionally substituted with 1 to 2 substituents independently selected from the group consisting of C_{1-4} alkyl, hydroxyl and halogen; or two R^4 groups on the same atom may form a C_{3-6} cycloalkyl, or two R^4 groups on adjacent ring atoms may form phenyl, C_{4-6} carbocycle,

C₄₋₆ heterocycle, or a 7 membered bridged ring system optionally having 1 heteroatom selected from nitrogen and oxygen, wherein said phenyl, C₃₋₆cycloalkyl C₄₋₆ carbocycle and C₄₋₆ heterocycle may be optionally substituted with 1 to 2 C₁₋₄ alkyl, halo or halo-substituted C₁₋₄alkyl;

R⁸ and R⁹ are each independently selected from hydrogen, -C(O)C₁₋₄ alkyl and C₁₋₄ alkyl; or R⁸ and R⁹ may combine to form a 4 to 6 membered saturated ring optionally containing one additional heteroatom selected from nitrogen or oxygen wherein said additional nitrogen may be optionally substituted with C₁₋₄ alkyl; and

R¹⁰ and R¹¹ are each independently selected from hydrogen and C₁₋₄ alkyl.

3. The compound of claim 1 or 2 of formula (I):



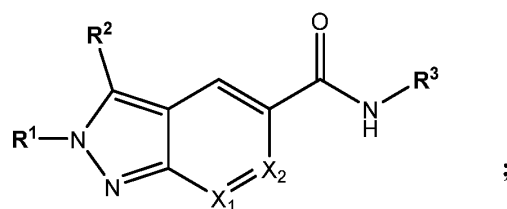
(I)

or a pharmaceutically acceptable salt thereof, wherein:

R² is H; and

X₁ is N or CH; and X₂ is CR⁵.

4. The compound of claim 1 or 2 of formula (I):



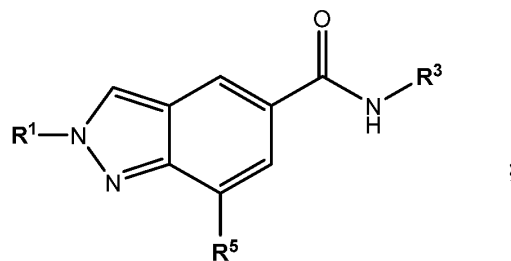
(I)

or a pharmaceutically acceptable salt thereof, wherein:

R^2 is H; and

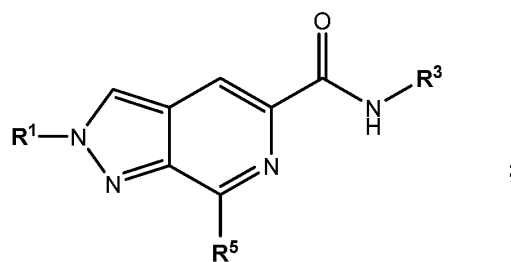
X_1 is CR^5 and X_2 is N or CH.

5. The compound of claim 1 or 2 of formula (Ia):



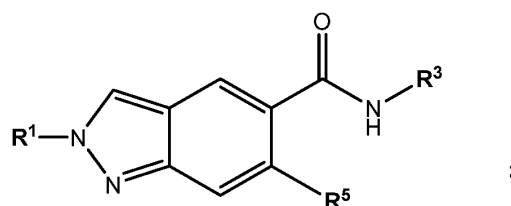
or a pharmaceutically acceptable salt thereof.

6. The compound of claim 1 or 2 of formula (Ib):



or a pharmaceutically acceptable salt thereof.

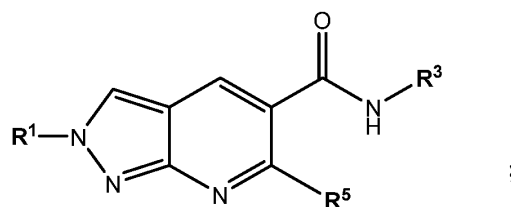
7. The compound of claim 1 or 2 of formula (Ic):



(Ic)

or a pharmaceutically acceptable salt thereof.

8. The compound of claim 1 or 2 of formula (Id):



(Id)

or a pharmaceutically acceptable salt thereof.

9. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein:

R^3 is selected from the group consisting of

- i. a 5 or 6 membered heteroaryl having 1 to 2 heteroatoms independently selected from nitrogen, oxygen and sulfur, said heteroaryl is optionally substituted with 1 to 3 R^4 ;
- ii. Phenyl optionally substituted with 1 to 3 R^4 ;
- iii. a 5-6 membered partially or fully saturated heterocycle having 1 to 2 heteroatoms independently selected from oxygen and nitrogen, said heterocycle may be optionally substituted with 1 to 3 R^4 ;
- iv. a partially or fully saturated C_{3-6} cycloalkyl which may be optionally substituted with 1 to 3 R^4 ;

- v. a 7 to 10 membered fused heterobicyclic ring system having 1, 2 or 3 heteroatoms independently selected from nitrogen and oxygen, said ring system is optionally substituted with 1 to 3 R⁴; and
 - vi. a 7 to 10 membered fused bicyclic ring system optionally having 1, 2 or 3 heteroatoms independently selected from nitrogen and oxygen, said ring system is optionally substituted with 1 to 3 R⁴;
10. The compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein:
R³ is phenyl, a 5 or 6 membered monocyclic heteroaryl having 1 to 2 heteroatoms independently selected from nitrogen and oxygen, pyridinyl-2(1H)-one or a 9 to 10 membered bicyclic heteroaryl having 1 to 3 heteroatoms independently selected from nitrogen and oxygen, wherein the monocyclic heteroaryl, pyridinyl-2(1H)-one or the bicyclic heteroaryl are each optionally substituted with 1 or 2 R⁴.
11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:
R³ is phenyl, a 5 or 6 membered monocyclic heteroaryl having 1 to 2 nitrogen atoms, pyridinyl-2(1H)-one or a 9 to 10 membered bicyclic heteroaryl having 2 to 3 nitrogen atoms, wherein the monocyclic heteroaryl, pyridinyl-2(1H)-one or the bicyclic heteroaryl are each optionally substituted with 1 or 2 R⁴.
12. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein R⁴, for each occurrence, is independently selected from hydroxyl, halo, halo-substitutedC₁₋₄ alkyl, -NR⁸R⁹, and C₁₋₄ alkyl.
13. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein:
R³ is selected from pyridyl, oxazolyl, pyrazinyl, oxadiazoyl, thiophenyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, said R³ is optionally substituted with 1 to 2 substituents independently selected from the group consisting of halo, halo-substitutedC₁₋₄ alkyl, -NR⁸R⁹, and C₁₋₄ alkyl.
14. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof wherein:

R³ is pyridinyl-2(1H)-one optionally substituted with 1 to 2 substituents independently selected from the group consisting of halo, halo-substituted C₁₋₄ alkyl, -NR⁸R⁹, and C₁₋₄ alkyl.

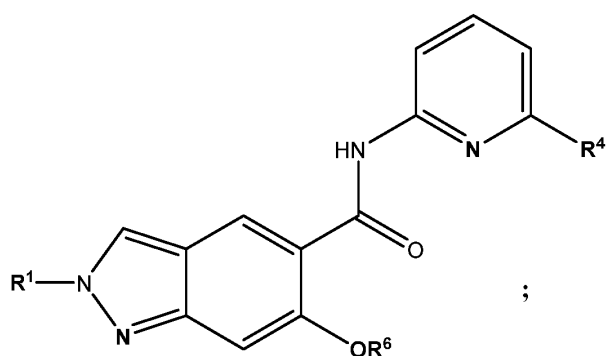
15. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein:

R³ is phenyl, said phenyl is optionally substituted with 1 to 2 substituents independently selected from the group consisting of halo, halo-substituted C₁₋₄ alkyl, -NR⁸R⁹, and C₁₋₄ alkyl.

16. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein:

R³ is selected from the group consisting of 1,3-dihydroisobenzofuran, 2,3-dihydrobenzofuran, 4-oxaspiro[bicyclo[3.2.0]heptane-6,1'-cyclobutane], oxaspiro[bicyclo[3.2.0]heptane-6,1'-cyclobutane], bicyclo[3.1.0]hexane, cyclohexyl, spiro[2.5]octane, 1S,5R)-1-methylbicyclo[3.1.0]hexane, 2,3-dihydro-1H-indene, spiro[2.5]octane, 1,2,3,4-tetrahydronaphthalene, tetrahydrofuran, 2,3-dihydrobenzofuran, 2,3-dihydro-1H-indene, 4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazine, pyrido[3,2-d]pyrimidinyl, 1,2,3,4-tetrahydro-1,4-epoxynaphthalene, 5,6-dihydro-4H-pyrrolo[1,2-b]pyrazole, 6,7-dihydro-5H-cyclopenta[b]pyridine, 1,2,3,4-tetrahydronaphthalene, indolin-2-one, 2,3-dihydrobenzofuran, pyrazolo[1,5-a]pyrimidine, 1-methyl-2-oxo-1,2,3,4-tetrahydroquinoline, 3,4-dihydroquinolin-2(1H)-one, chromane, and isochromane, wherein said R³ is optionally substituted with 1 to 2 substituents independently selected from the group consisting halo, halo-substituted C₁₋₄ alkyl, -NR⁸R⁹, and C₁₋₄ alkyl.

17. The compound of any one of claims 1 to 4 of formula (II):

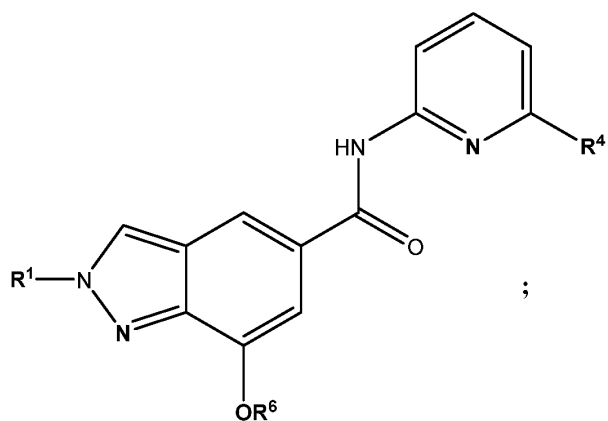


(II)

or a pharmaceutically acceptable salt thereof, wherein:

R^6 is an optionally substituted C_{1-5} alkyl having 1 to 3 substituents independently selected from halogen, hydroxyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, phenyl and a 4 to 7 membered partially or fully saturated heterocycle containing 1 or 2 heteroatoms selected from nitrogen and oxygen, wherein said C_{3-6} cycloalkyl and phenyl may be optionally substituted with 1 to 3 R^7 .

18. The compound of any one of claims 1 to 4 of formula (III):

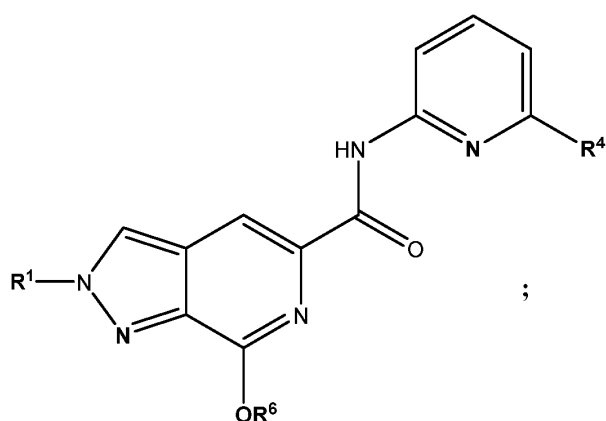


(III)

or a pharmaceutically acceptable salt thereof, wherein:

R⁶ is an optionally substituted C₁₋₅alkyl having 1 to 3 substituents independently selected from halogen, hydroxyl, C₁₋₄alkoxy, C₃₋₆cycloalkyl, phenyl and a 4 to 7 membered partially or fully saturated heterocycle containing 1 or 2 heteroatoms selected from nitrogen and oxygen, wherein said C₃₋₆cycloalkyl and phenyl may be optionally substituted with 1 to 3 R⁷.

19. The compound of any one of claims 1 to 4 of formula (IV):



(IV)

or a pharmaceutically acceptable salt thereof, wherein:

R⁶ is an optionally substituted C₁₋₅alkyl having 1 to 3 substituents independently selected from halogen, hydroxyl, C₁₋₄alkoxy, C₃₋₆cycloalkyl, phenyl and a 4 to 7 membered partially or fully saturated heterocycle containing 1 or 2 heteroatoms selected from nitrogen and oxygen, wherein said C₃₋₆cycloalkyl and phenyl may be optionally substituted with 1 to 3 R⁷.

20. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein:

R¹ is a fully saturated C₄₋₇ heterocycle or a 5 to 8 membered bridged-heterocyclic ring system which contain 1 to 2 heteroatoms independently selected from nitrogen and oxygen, said C₄₋₇ heterocycle or a 5 to 8 membered bridged-heterocyclic ring system may be optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁₋₄alkyl, halogen, halo-substituted C₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy; or R¹ is

a C₁₋₅ alkyl which is optionally substituted with 1 or 3 substituents independently selected from the group consisting of halogen, halo-substitutedC₁₋₄ alkyl, hydroxy-substitutedC₁₋₄ alkyl, hydroxyl, C₁₋₄alkoxy and C₃₋₆cycloalkyl, wherein said C₃₋₆cycloalkyl is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy.

21. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein:

R¹ is a fully saturated C₄₋₇ heterocycle or a 5 to 8 membered bridged-heterocyclic ring system which contain 1 to 2 heteroatoms independently selected from nitrogen and oxygen, said C₄₋₇ heterocycle or a 5 to 8 membered bridged-heterocyclic ring system may be optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁₋₄alkyl, halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy.

22. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein:

R¹ is a C₁₋₅ alkyl which is optionally substituted with 1 or 3 substituents independently selected from the group consisting of halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl, C₁₋₄alkoxy and C₃₋₆cycloalkyl, wherein said C₃₋₆cycloalkyl is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy.

23. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein R¹ is a C₄₋₇ heterocycle, -C₁₋₂alkyl-C₄₋₇ heterocycle or a 5 to 8 membered bridged-heterocyclic ring system containing 1 to 2 heteroatoms independently selected from nitrogen and oxygen, wherein the C₄₋₇ heterocycle is fully saturated and contains 1 to 2 heteroatoms independently selected from nitrogen and oxygen and at least one of the heteroatoms is oxygen and wherein the C₄₋₇ heterocycle or the 5 to 8 membered bridged-heterocyclic ring system is optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁₋₄alkyl, halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy; or R¹ is a C₁₋₅ alkyl which is optionally substituted with 1 or 3 substituents independently selected from the group consisting of halogen, halo-substitutedC₁₋₄ alkyl, hydroxy-substitutedC₁₋₄ alkyl, hydroxyl, C₁₋₄alkoxy and C₃₋₆cycloalkyl, wherein said C₃₋

cycloalkyl is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy.

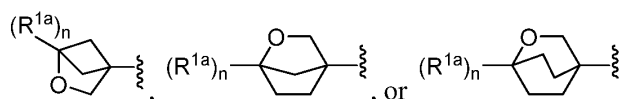
24. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein R¹ is a C₄₋₇ heterocycle, -C₁₋₂alkyl-C₄₋₇ heterocycle or a 5 to 8 membered bridged-heterocyclic ring system containing 1 to 2 heteroatoms independently selected from nitrogen and oxygen, wherein the C₄₋₇ heterocycle is fully saturated and contains 1 to 2 heteroatoms independently selected from nitrogen and oxygen and at least one of heteroatom is oxygen and wherein the C₄₋₇ heterocycle or the 5 to 8 membered bridged-heterocyclic ring system may be optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁₋₄alkyl, halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy.

25. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein R¹ is a C₁₋₅ alkyl substituted with 1 or 3 substituents independently selected from the group consisting of halo-substitutedC₁₋₄ alkyl, hydroxyl, C₁₋₄alkoxy and C₄₋₆cycloalkyl, wherein said C₃₋₆cycloalkyl is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy.

26. The compound of any one of claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein R¹ is a 5 to 8 membered bridged-heterocyclic ring system which contains 1 to 2 heteroatoms independently selected from nitrogen and oxygen, wherein the 5 to 8 membered bridged-heterocyclic ring system is optionally substituted with one or two substituents R^{1a} independently selected from C₁₋₄alkyl, halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy.

27. The compound of claim 26, or a pharmaceutically acceptable salt thereof, wherein R¹ is a 5 to 8 membered bridged-heterocyclic ring system containing one oxygen atom and wherein the 5 to 8 membered bridged-heterocyclic ring is optionally substituted with one or two substituents R^{1a} independently selected from C₁₋₄alkyl, halogen, halo-substitutedC₁₋₄ alkyl, hydroxyl and C₁₋₄alkoxy.

28. The compound of claim 27, or a pharmaceutically acceptable salt thereof, wherein R¹ is a 5 to 8 membered bridged-heterocyclic ring system represented by the following formula:



wherein R^{1a} is C_{1-4} alkyl or halo-substituted C_{1-4} alkyl; and n is 0 or 1.

29. The compound of claim 28, or a pharmaceutically acceptable salt thereof, wherein R^{1a} is CH_3 or CH_2F .

30. The compound of any one of claim 1 to 4, or a pharmaceutically acceptable salt thereof, wherein:

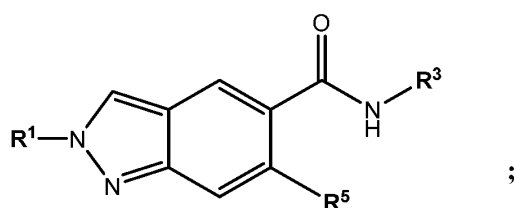
R^1 is a fully saturated C_{4-7} heterocycle or a 5 to 8 membered bridged-heterocyclic ring system which contain 1 to 2 heteroatoms independently selected from nitrogen and oxygen, said C_{4-7} heterocycle or a 5 to 8 membered bridged-heterocyclic ring system may be optionally substituted with 1 or 2 substituents independently selected from the group consisting of C_{1-4} alkyl,

halogen, halo-substituted C_{1-4} alkyl, hydroxyl and C_{1-4} alkoxy; and R^3 is pyridinyl substituted with

1 or 2 substituents independently selected from and C_{1-4} alkyl and halo-substituted C_{1-4} alkyl.

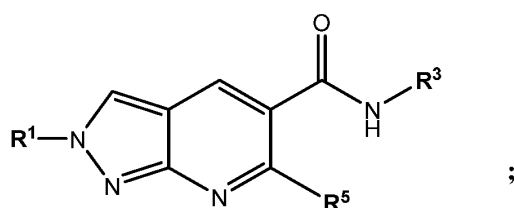
31. The compound of any one of claims 1-16 and 20-30, or a pharmaceutically acceptable salt thereof, wherein R^6 is an optionally substituted C_{1-5} alkyl or an optionally substituted C_3 cycloalkyl, wherein the C_{1-5} alkyl is optionally substituted with 1 to 3 substituents independently selected from halogen, hydroxyl and C_{1-4} alkoxy and the C_3 -cycloalkyl is optionally substituted with 1 to 3 substituents independently selected from halo, C_{1-4} alkyl, halo-substituted C_{1-4} alkyl and C_{1-4} alkoxy.

32. The compound of claim 1, wherein the compound is represented by the following formula:



(Ic)

or



(Id)

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is $-C_{1-2}$ alkyl- C_{4-7} heterocycle or a 5 to 8 membered bridged-heterocyclic ring system containing 1 to 2 heteroatoms independently selected from nitrogen and oxygen, wherein the C_{4-7} heterocycle is fully saturated and contains 1 to 2 heteroatoms independently selected from nitrogen, sulfur and oxygen and wherein the C_{4-7} heterocycle and the 5 to 8 membered bridged-heterocyclic ring system is optionally substituted with one or two substituents R^{1a} ;

R^{1a} , for each occurrence, is independently selected from C_{1-4} alkyl, halogen, halo-substituted C_{1-4} alkyl, hydroxyl and C_{1-4} alkoxy;

R^3 is phenyl, a 5 or 6 membered monocyclic heteroaryl having 1 to 2 heteroatoms independently selected from nitrogen and oxygen, pyridinyl-2(1H)-one or a 8 to 10 membered bicyclic heteroaryl having 1 to 3 heteroatoms independently selected from nitrogen and oxygen, wherein the monocyclic heteroaryl, pyridinyl-2(1H)-one or the bicyclic heteroaryl are each optionally substituted with 1 or 2 R^4 ;

R^4 , for each occurrence, is independently selected from hydroxyl, halo, halo-substituted C_{1-4} alkyl, $-NR^8R^9$, and C_{1-4} alkyl;

R^5 is OR^6 ; and

R^6 is an optionally substituted C_{1-5} alkyl or an optionally substituted C_{3-6} cycloalkyl, wherein the C_{1-5} alkyl is optionally substituted with 1 to 3 substituents independently selected

from halogen, hydroxyl and C₁₋₄alkoxy and the C₃₋₆cycloalkyl is optionally substituted with 1 to 3 substituents independently selected from halo, C₁₋₄alkyl, halo-substitutedC₁₋₄ alkyl and C₁₋₄alkoxy.

33. The compound of claim 32, or a pharmaceutically acceptable salt thereof, wherein R¹ is -C₁₋₂ alkyl-C₄₋₇ heterocycle or a 5 to 8 membered bridged-heterocyclic ring system containing one oxygen atom, wherein the C₄₋₇ heterocycle contains one oxygen atom and wherein the C₄₋₇ heterocycle and the 5 to 8 membered bridged-heterocyclic ring system is optionally substituted with one substituent R^{1a};

R^{1a} is C₁₋₄alkyl or halo-substitutedC₁₋₄ alkyl;

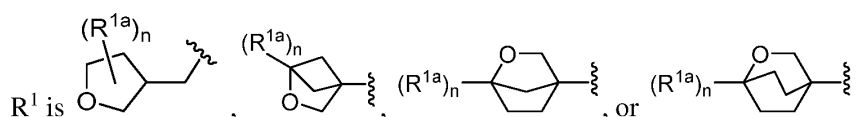
R³ is phenyl, a 5 or 6 membered monocyclic heteroaryl having 1 to 2 nitrogen atoms, pyridinyl-2(1H)-one or a 8 to 10 membered bicyclic heteroaryl having 2 to 3 nitrogen atoms, wherein the monocyclic heteroaryl, pyridinyl-2(1H)-one or the bicyclic heteroaryl are each optionally substituted with 1 or 2 R⁴;

R⁴, for each occurrence, is independently selected from hydroxyl, halo, C₁₋₄alkoxy, halo-substitutedC₁₋₄ alkyl, and C₁₋₄ alkyl;

R⁵ is OR⁶; and

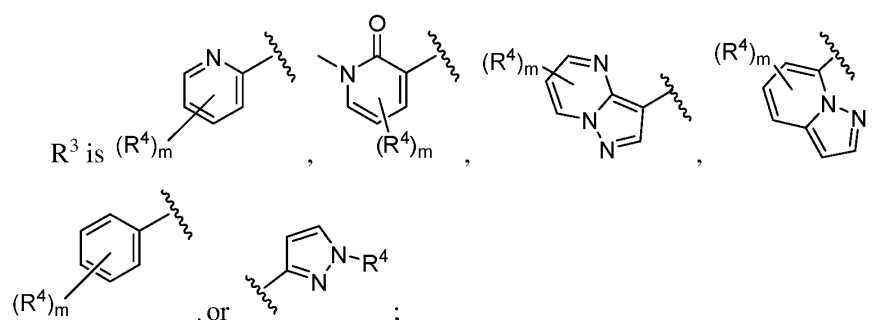
R⁶ is an optionally substituted C₁₋₅alkyl or an optionally substituted C₃₋₆cycloalkyl, wherein the C₁₋₅alkyl is optionally substituted with 1 to 3 substituents independently selected from halogen and the C₃₋₆cycloalkyl is optionally substituted with 1 to 3 substituents independently selected from C₁₋₄alkyl, halo-substitutedC₁₋₄alkyl and halogen..

34. The compound of claim 33, or a pharmaceutically acceptable salt thereof, wherein:



R^{1a} is C₁₋₄ alkyl or halo-substitutedC₁₋₄ alkyl;

n is 0 or 1;



R⁴ is halo, C₁₋₄alkoxy, C₁₋₄ alkyl or halo-substituted C₁₋₄ alkyl;

m is 0 or 1;

R⁵ is OR⁶; and

R⁶ is C₁₋₄alkyl or C₄₋₆cycloalkyl.

35. The compound of claim 34, wherein R^{1a} is CH₃; and R⁴ is CH₃, F, OMe, or CHF₂; and R⁶ is -CH(CH₃)₂, cyclobutyl, or cyclopentyl.
36. The compound of claim 1, selected from any one of the compounds of Examples 1-140 or a pharmaceutically acceptable salt thereof..
37. A pharmaceutical composition comprising a compound of any one of the preceding claims or a pharmaceutically acceptable salt thereof.
38. The pharmaceutical composition of claim 37, further comprising one or more additional pharmaceutical agent(s).
39. A method of treating an IRAK4 mediated disease in a subject comprising administering to the subject a compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 36 or a pharmaceutical composition of any one of claims 37 to 38.
40. The method of claim 39, wherein the IRAK4 mediated disease is selected from the group consisting from Rheumatoid Arthritis, Psoriatic arthritis, Osteoarthritis, Systemic Lupus Erythematosus, Lupus nephritis, Ankylosing Spondylitis, Osteoporosis, Systemic sclerosis, Multiple Sclerosis, Psoriasis, Type I diabetes, Type II diabetes, Inflammatory Bowel Disease, Cronh's Disease, Ulcerative Colitis, Hyperimmunoglobulinemia D, periodic fever syndrome, Cryopyrin-associated periodic syndromes, Schnitzler's syndrome, Systemic

juvenile idiopathic arthritis, Adult's onset Still's disease, Gout, Pseudogout, SAPHO syndrome, Castleman's disease, Sepsis, Stroke, Atherosclerosis, Celiac disease, Deficiency of IL-1 Receptor Antagonist, Alzheimer's disease, Parkinson's disease, Multiple Sclerosis and Cancer.

41. The method of claim 39, wherein the IRAK4 mediated disease is selected from the group consisting from is selected from an autoimmune disease, an inflammatory disease, bone diseases, metabolic diseases, neurological and neurodegenerative diseases and/or disorders, cardiovascular diseases, allergies, asthma, hormone-related diseases, Ischemic stroke, Cerebral Ischemia, hypoxia, Traumatic Brain Injury, Chronic Traumatic Encephalopathy, epilepsy, Parkinson's disease, and Amyotrophic Lateral Sclerosis.