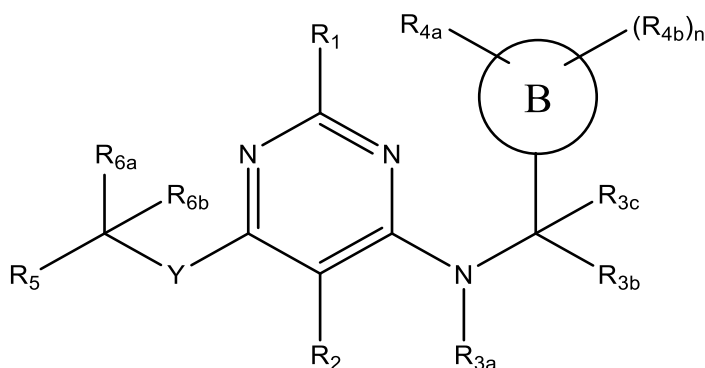


CLAIMS

1. A compound of Formula (I)



Formula (I)

or a pharmaceutically acceptable salt, or stereoisomer thereof, wherein:

Y is NR;

(i) R is selected from the group consisting of hydrogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, and C₁₋₄ hydroxyalkyl; or

R and R₂ in combination with the pyrimidine ring of formula (I) form an unsubstituted pyrrolo[2,3-d]pyrimidine ring or an unsubstituted 6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine ring; or

(ii) R_{3a} is selected from the group consisting of C₁₋₄ alkyl, C₁₋₄ alkylene-C₃₋₆ cycloalkyl, C₁₋₄ alkylene-C₃₋₆ heteroalicycyl, C₃₋₆ cycloalkyl, and C₃₋₅ heteroalicycyl; or

R₂ and R_{3a} in combination with the pyrimidine ring of formula (I) form an unsubstituted pyrrolo[2,3-d]pyrimidine ring or an unsubstituted 6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine ring;

R₁ is selected from the group consisting of hydrogen, halogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, and C₁₋₄ haloalkoxy;

R_{4a} is selected from the group consisting of halogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, and heteroaryl;

R_{4b} is selected from the group consisting of halogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ hydroxyalkyl, C₁₋₄ alkoxy, and C₁₋₄ haloalkoxy;

R₅ is selected from the group consisting of -(CR₈R₉)_pOR₁₂, -(CR₈R₉)_p-CR₁₃R₁₄R₁₅, -(CR₈R₉)_p-C(=O)OR₇, and -(CR₈R₉)_p-C(=O)NR₈R₉;

n and p are integers independently selected from the group consisting of 0, 1, 2, 3 and 4;

R_{6a} is selected from the group consisting of hydrogen, halogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, and aryl;

R_{6b} is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, aryl-C₁₋₆ alkyl, C₂₋₉ heteroalicycyl-C₁₋₆ alkyl, and heteroaryl;

R₇, R₈, R₉, and R₁₂ are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, aryl-C₁₋₆ alkyl, heteroaryl-C₁₋₆ alkyl, and aryl;

R₁₃ is absent, or selected from the group consisting of hydrogen, -CN, -CH₃, fluorine, -OH, -CH₂OH, -OCH₃, -CH₂CH₂OH, -CO₂H, -CO₂-C₁₋₄-alkyl, and -CH₂-SO₂R₂₀ and R₂₀ is C₁₋₆ alkyl;

R₁₄ and R₁₅ are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₃₋₆ cycloalkyl, and C₂₋₉ heteroalicycyl; or

R₁₄ and R₁₅ are combined to form a ring system selected from the group consisting of C₃₋₇ cycloalkyl, C₂₋₆ heteroalicycyl, aryl, and heteroaryl;

B is a ring system selected from the group consisting of aryl and heteroaryl;

R_{3b} is selected from the group consisting of hydrogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkylene-C₃₋₆ cycloalkyl, C₁₋₄ alkylene-C₃₋₆ heteroalicycyl, C₃₋₆ cycloalkyl, and C₃₋₆ heteroalicycyl;

R_{3c} is selected from the group consisting of hydrogen, C₁₋₄ alkyl, and C₃₋₆ cycloalkyl.

2. The compound according to claim 1, wherein R₂ and R_{3a} in combination with the pyrimidine ring of formula (I) form an unsubstituted pyrrolo[2,3-d]pyrimidine or an unsubstituted 6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine.

3. The compound according to claim 1 and 2, wherein R₂ and R_{3a} in combination with the pyrimidine ring of formula (I) form an unsubstituted pyrrolo[2,3-d]pyrimidine.

4. The compound according to any one of claims 1 to 3 wherein R_{3b} is hydrogen.

5. The compound according to any one of claims 1 to 4 wherein R_{3c} is hydrogen.

6. The compound according to any one of claims 1 to 3, wherein R_{3b} is hydrogen, and R_{3c} is selected from the group consisting of hydrogen, methyl, cyclopropyl and cyclobutyl.

7. The compound according to any one of claims 1 to 6, wherein R₅ is -(CR₈R₉)_p-C(=O)OR₇, or -(CR₈R₉)_p-C(=O)NR₈R₉.

8. The compound according to any one of claims 1 to 6, wherein R_5 is $-(CR_8R_9)_pOR_{12}$.
9. The compound according to any one of claims 1 to 6, wherein R_5 is $-(CR_8R_9)_p-
CR_{13}R_{14}R_{15}$.
10. The compound according to claim 9, wherein R_{14} and R_{15} are combined to form a ring system selected from the group consisting of C_{4-7} cycloalkyl, C_{6-12} membered aryl, 4-membered heteroalicycyl, 5-membered heteroaryl, 5-membered heteroalicycyl, 6-membered heteroaryl, 6-membered heteroalicycyl, 7-membered heteroaryl, and 7-membered heteroalicycyl.
11. The compound according to any one of claims 9 to 10, wherein R_{14} and R_{15} are combined to form a ring system selected from the group consisting of phenyl, naphthyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, azetidiny, thietanyl, pyrrolyl, pyrazolyl, imidazolyl, pyrrolidinyl, imidazoliny, pyrazolidiny, thiazolidiny, isothiazolidiny, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, oxathianyl, 1,4-oxathianyl, 4,4-dioxide, thiazolyl, isothiazolyl, pyridiny, pyridaziny, pyraziny, pyrimidinyl, triazinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, dioxolanyl, dioxanyl, furyl, dihydrofuranyl, furazanyl, tetrahydrofuryl, pyranyl, tetrahydropyranyl, tetrahydrothiopyranyl, dithiolanyl, dithianyl, thiopyranyl, thianyl, thianyl-1,1-dioxide, thienyl, oxetanyl, quinolyl, isoquinolyl, indolyl, iso-indolyl, and tetrahydrothienyl.
12. The compounds according to claim 11, wherein the ring system is selected from the group consisting of cycloheptyl, cyclohexyl, cyclopentyl, dioxanyl, furyl, imidazolyl, isothiazolyl, isoxazolyl, morpholinyl, oxazolyl, oxetanyl, oxathianyl, phenyl, piperidinyl, pyranyl, pyrazolidiny, pyrazolyl, pyridyl, pyrimidyl, pyrrolidinyl, pyrrolyl, tetrahydrofuryl, tetrahydropyranyl, tetrazolyl, thianyl, thiazolyl, thienyl, thiomorpholinyl, thiopyryl, and triazolyl.
13. The compound according to claim 12 wherein the ring system is phenyl or oxetanyl.
14. The compound according to claim 13 wherein the ring system is phenyl.
15. The compound according to any one of claims 9 to 14, wherein the ring system formed by the combination of R_{14} and R_{15} is substituted with one or more $-(CH_2)_q(R_{5a})$ wherein R_{5a} is independently selected from the group consisting of $-CH_2COOR_{20}$, $-CH_2CONR_{21}R_{22}$, oxo, -CN, $-CH_2-CN$, C_{1-6} alkyl, $-CH_2-imidazolyl$, $-CH_2-SO_2R_{20}$, $-CH_2C(CH_3)_2(OR_{20})$, $-OR_{20}$, $-CH_2-triazolyl$, $-CF_3$, dimethyl substituted-imidazolyl-2,4-dione, $-CH_2-SO_2NR_{21}R_{22}$, morpholinyl, $-C(=O)-morpholinyl$, piperidyl- CH_2OR_{20} , $-OCH_2-tetrahydrofuryl$, piperazinonyl, piperidinyl- $CONR_{21}R_{22}$, $-OH$, $-COR_{20}$, $-CONR_{21}R_{22}$, $-CH(OR_{20})CH_3$, $-COOR_{20}$, $-CH_2-pyrrolidyl$, C_{1-6} alkylene-

OH, cyclopentyl, pyrrolidonyl, tetrazolyl, -CH₂-tetrazolyl, -CH₂OR₂₀, acyl, -SOR₂₀, -SO₂R₂₀, -SO₂NR₂₁R₂₂, -NR₂₁SO₂R₂₀, and halogen;

R₂₀, R₂₁, and R₂₂ are independently of each other selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, -CN, C₃₋₆ cycloalkyl, and C₂₋₆ heteroalicyclic, or R₂₁ and R₂₂ are combined to form a C₃₋₆ cycloalkyl; and

q is an integer selected from 0, 1 or 2.

16. The compound according to any one of claims 9 to 15 wherein the ring system formed by the combination of R₁₄ and R₁₅ is substituted with one -CH₂CONH₂.

17. The compound according to any one of claims 9 to 16 wherein R₁₃ is absent or -CH₂OH.

18. The compound according to claim 17 wherein R₁₃ is absent.

19. The compound according to any one of claims 1 to 18, wherein R is hydrogen.

20. The compound according to any one of claims 1 to 19, wherein R₁ is selected from the group consisting of hydrogen, halogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, and C₁₋₄ hydroxyalkyl.

21. The compound according to any one of claims 1 to 20, wherein R₁ is hydrogen or -CF₃.

22. The compound according to any one of claims 1 to 21 wherein R₁ is hydrogen.

23. The compound according to any one of claims 1 to 22, wherein R_{4a} is selected from the group consisting of halogen, C₁₋₄ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, and heteroaryl.

24. The compound according to any one of claims 1 to 23, wherein R_{4a} is selected from the group consisting of methyl, ethyl, propyl, iso-propyl, *tert*-butyl, chlorine, fluorine, methoxy, ethoxy, C₁₋₂ haloalkyl, C₁₋₂ haloalkoxy, and triazolyl.

25. The compound according to any one of claims 1 to 24, wherein R_{4a} is selected from the group consisting of -CF₃, -CHF₂, -OCF₃, and -OCHF₂.

26. The compound according to any one of claims 1 to 25 wherein R_{4a} is -CF₃.

27. The compound according to any one of claims 1 to 26, wherein R_{4b} is selected from the group consisting of methyl, ethyl, propyl, iso-propyl, *tert*-butyl, chlorine, fluorine, methoxy, ethoxy, -OH, C₁₋₂ haloalkyl, and C₁₋₂ haloalkoxy.

28. The compound according to any one of claims 1 to 27, wherein R_{4b} is selected from the group consisting of $-CF_3$, $-CF_2CF_3$, $-CHF_2$, $-OCF_3$, $-OCF_2CF_3$, and $-OCHF_2$.

29. The compound according to any one of claims 1 to 28 wherein R_{4b} is $-CF_3$.

30. The compound according to any one of claims 1 to 29, wherein R_{6a} is selected from the group consisting of hydrogen, halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, and aryl.

31. The compound according to claim 30, wherein R_{6a} is hydrogen.

32. The compound according to any one of claims 1 to 31, wherein R_{6b} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, and C_{1-6} -alkoxy- C_{1-6} -alkyl,

or R_{6b} is selected from the group consisting of $-(CH_2)_q-C_{3-6}$ cycloalkyl, $-(CH_2)_q$ -aryl, $-(CH_2)_q-C_{2-9}$ heteroalicycyl, $-(CH_2)_q$ -heteroaryl, which may be substituted by one or more substituent selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{3-5} cycloalkyl, $-(CH_2)_q-CONR_{23}R_{24}$, $-(CH_2)_q-SO_2R_{23}$, $-(CH_2)_q-NR_{23}SO_2R_{24}$ and $-(CH_2)_q-SO_2NR_{23}$,

R_{23} , and R_{24} are independently of each other selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-CN$, C_{3-6} cycloalkyl, and C_{2-6} heteroalicycyl; and

q is an integer selected from 0, or 1.

33. The compound according to any one of claims 1 to 32, wherein R_{6b} is selected from the group consisting of hydrogen, $-(CH_2)C(CH_3)_3$, phenyl, phenyl substituted with 1 to 3 halogens, $-CH(CH_3)OC(CH_3)_3$, $-CH_2$ -phenyl- OCH_3 , $-phenyl-OCH_3$, $-CH_2$ -cyclohexyl- CH_2CO_2H , $-CH_2$ -cyclohexyl- CH_2CONH_2 , $-CH_2$ -cyclohexyl- CH_2 -tetrazolyl, $-CH_2$ -cyclohexyl- CH_2OH , $-CH_2$ -cyclohexyl- $NHSO_2CH_3$, $-CH_2$ -cyclohexyl- $NHSO_2CH_2CF_3$, $-CH_2$ -cyclohexyl- CH_2CN , $-CH_2$ -phenyl- CH_2CO_2H , $-CH_2$ -phenyl- CH_2CONH_2 , $-CH_2$ -phenyl- $CH_2CONH_2CH_3$, $-CH_2$ -phenyl- CH_2 -tetrazolyl, $-CH_2$ -phenyl- $CONH_2$, $-CH_2$ -phenyl- SO_2NH -cyclopropyl, $-CH_2$ -phenyl- SO_2CH_3 , $-CH_2$ -phenyl- $NHSO_2CF_3$, $-CH_2$ -phenyl- $NHSO_2CH_3$, $-CH_2$ -phenyl- $NHSO_2CHF_2$, $-CH_2$ -pyridyl- CH_3 , $-CH_2$ -pyridyl- SO_2CH_3 , $-CH_2$ -pyridyl- CH_2CONH_2 , $-CH_2$ -pyrimidyl- $NHSO_2CH_3$, $-CH_2$ -piperidyl- $COCH_3$, $-CH_2$ -piperidyl- SO_2CH_3 , $-CH_2$ -piperidyl- SO_2CF_3 , $-CH_2$ -thienyl- CH_2CO_2H , $-CH_2$ -cyclobutyl- CH_2CO_2H , $-CH_2$ -cyclobutyl- CH_2CONH_2 , $-CH_2$ -cyclobutyl- CO_2H , $-CH_2$ -cyclobutyl- $CONH_2$, $-CH_2$ -tetrahydrothiopyryl, $-CH_2$ -cyclopentyl, $-CH_2$ -cyclohexyl, $-CH_2$ -tetrahydrofuranlyl, $-CH_2$ -tetrahydropyranlyl, $-CH_2$ -oxetanyl, and $-CH_2$ -pyranlyl.

34. The compound according to claim 33, wherein R_{6b} is hydrogen.

35. The compound according to any one of claims 1 to 34, wherein R_7 , R_8 , R_9 , and R_{12} are independently selected of each other from hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, and aryl.

36. The compound according to any one of claims 1 to 35, wherein R_7 , R_8 , R_9 , and R_{12} are independently selected of each other from hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, and C_{1-4} hydroxyalkyl.

37. The compound according to any one of claims 1 to 36, wherein R_7 , R_8 , R_9 , and R_{12} are independently selected of each other from hydrogen, methyl, ethyl and *tert*-butyl.

38. The compound according to any one of claims 1 to 37, wherein ring system B is aryl.

39. The compound according to any one of claims 1 to 38, wherein ring system B is selected from a 6-membered aryl having R_{4a} in the *para*-position or *meta*-position, 6-membered heteroaryl having R_{4a} in the *para*-position or *meta*-position, or 5-membered heteroaryl having R_{4a} in 2- or 3-position.

40. The compound according to any one of claims 1 to 39 wherein ring system B is a 6-membered aryl ring having R_{4a} in the *para*-position or *meta*-position.

41. The compound according to any one of claims 1 to 40, wherein ring system B is selected from the group consisting of phenyl, pyridyl, pyrazolyl, pyridazinyl, pyrimidinyl, naphthyl and furanyl.

42. The compound according to any one of claims 1 to 41 wherein ring system B is a phenyl.

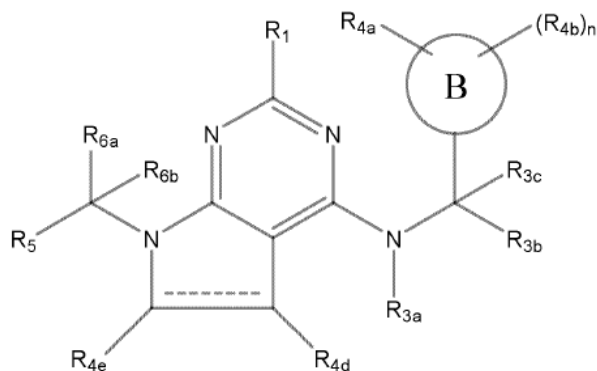
43. The compound according to any one of claims 1 to 42, wherein n is an integer selected from the group consisting of 1, 2, 3 and 4.

44. The compound according to any one of claims 1 to 42, wherein n is 0.

45. The compound according to any one of claims 1 to 44, wherein p is an integer selected from 0, 1 or 2.

46. The compound according to any one of claims 1 to 45, wherein p is 0.

47. The compound according to claim 1, wherein the compound of formula (I) has the formula (IIa)

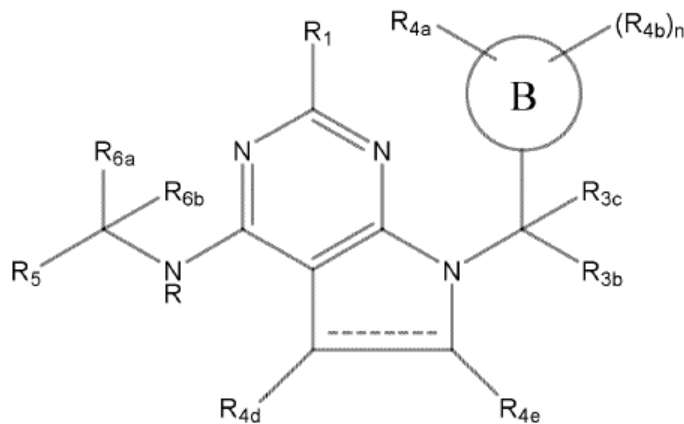


Formula (IIa)

wherein R_{4e} and R_{4d} are independently selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C₁₋₄ alkyl, substituted or unsubstituted C₁₋₄ alkoxy and -OH.

48. The compound according to claim 47, wherein R_{4e} and R_{4d} are independently selected from the group consisting of hydrogen, methyl and fluorine.

49. The compound according to claims 1 to 46, wherein the compound of formula (I) has the formula (IIab)



Formula (IIab)

wherein R_{4e} and R_{4d} are independently selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C₁₋₄ alkyl, substituted or unsubstituted C₁₋₄ alkoxy and -OH.

50. The compound according to claim 49 wherein R_{4e} and R_{4d} are independently selected from the group consisting of hydrogen, methyl and fluorine.

51. The compound according to claim 50 wherein R_{4e} and R_{4d} are independently hydrogen.

52. A pharmaceutical composition comprising a compound according to any one of claims 1 to 51 and at least one pharmaceutical acceptable excipient.

53. A compound according to any one of claims 1-51 or pharmaceutical composition according to claim 52, for use in therapy.

54. A compound according to any one of claims 1-51 or pharmaceutical composition according to claim 52, for use in the treatment and/or prevention of inflammatory, metabolic and autoimmune diseases or disorders.

55. A compound according to any one of claims 1-51 or pharmaceutical composition according to claim 52, for use in the treatment and/or prevention of a disease or disorder selected from the group consisting of asthma, chronic obstructive pulmonary disease (COPD), bronchitis, atherosclerosis, helicobacter pylori infection, allergic diseases including allergic rhinitis, allergic conjunctivitis and uveitis, sprue and food allergy, atopic dermatitis, cystic fibrosis, lung allograft rejection, multiple sclerosis, rheumatoid arthritis, juvenile rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, psoriasis, psoriatic arthritis, steatosis, steatohepatitis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), lupus erythematosus, Hashimoto's disease, pancreatitis, autoimmune diabetes, autoimmune ocular disease, ulcerative colitis, colitis, Crohn's disease, inflammatory bowel disease (IBD), inflammatory bowel syndrome (IBS), Sjögren's syndrome, optic neuritis, type I diabetes, neuromyelitis optica, Myasthenia Gravis, Guillain-Barre syndrome, Graves' disease, scleritis, obesity, obesity-induced insulin resistance and type II diabetes, and cancer.

56. A compound according to any one of claims 1-51 or pharmaceutical composition according to claim 52, for modulating the activity of a retinoic acid receptor-related orphan receptor (ROR).

57. A compound or pharmaceutical composition according to claim 56, wherein the receptor is a ROR γ receptor.

58. A compound or pharmaceutical composition according to claim 56 or claim 57, wherein the receptor is a ROR γ 1 or ROR γ t receptor.

59. A compound or pharmaceutical composition according to claim 56, wherein the compound or pharmaceutical composition modulates the activity of an ROR γ receptor to a larger extent than it modulates the activity of ROR α and/or ROR β receptors.