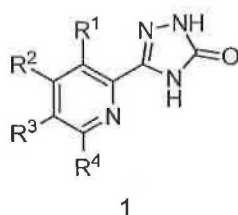


WHAT IS CLAIMED IS:

1. A compound of Formula 1,

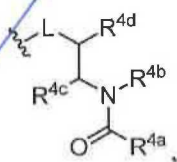


a tautomer thereof or a pharmaceutically acceptable salt of the compound or tautomer,
wherein:

R^1 is selected from hydrogen, halo, -CN, C_{1-4} alkyl, C_{1-4} haloalkyl, and $-OR^{14}$;

R^2 and R^3 are each independently selected from hydrogen, halo, -CN, R^6 , and R^7 , or R^2 and R^3 , together with carbon atoms to which they are attached, form a benzene ring or a pyridine ring in which the benzene ring is optionally substituted with from one to four substituents independently selected from halo, -CN, R^6 , and R^7 , and the pyridine ring is optionally substituted with from one to three substituents independently selected from halo, -CN, R^6 , and R^7 ;

R^4 has the formula



in which $\sim$ indicates a point of attachment;

L is selected from -O-, $-CH_2O-$, and $-N(R^{4c})-$;

R^{4a} is selected from $-CH_2R^5$ and ethenyl optionally substituted with from one to three substituents independently selected from halo, cyano, and R^7 ; and

(a) R^{4c} is hydrogen, R^{4c} is selected from hydrogen and C_{1-4} alkyl when L is $-N(R^{4c})-$, and R^{4b} and R^{4d} , together with a nitrogen atom and carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl; or

(b) R^{4b} is selected from hydrogen and C_{1-4} alkyl, R^{4d} is hydrogen, L is $-N(R^{4c})-$, and R^{4c} and R^{4c} , together with the carbon atoms and a nitrogen atom to which R^{4c} ,

R^{4d} , and R^{4c} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl; or

(c) R^{4d} is hydrogen, R^{4e} is selected from hydrogen and C_{1-4} alkyl when L is $-N(R^{4c})-$, and R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, form pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^5 is selected from hydrogen, halo, and C_{1-4} alkyl;

each R^6 is independently selected from $-OR^8$, $-N(R^8)R^9$, $-NR^8C(O)R^9$, $-NHC(O)NR^8R^9$, $-NR^8C(O)NHR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)N(R^8)R^9$, $-C(O)N(R^8)OR^9$, $-C(O)N(R^8)S(O)_2R^7$, $-N(R^8)S(O)_2R^7$, $-SR^8$, $-S(O)R^7$, $-S(O)_2R^7$, and $-S(O)_2N(R^8)R^9$;

each R^7 is independently selected from

(a) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each optionally substituted with from one to five substituents independently selected from halo, oxo, $-CN$, and R^{10} ; and

(b) C_{3-10} cycloalkyl- $(CH_2)_m-$, C_{6-14} aryl- $(CH_2)_m-$, C_{2-6} heterocyclyl- $(CH_2)_m-$, and C_{1-9} heteroaryl- $(CH_2)_m-$, each optionally substituted with from one to five substituents independently selected from halo, oxo, $-CN$, R^{10} , and C_{1-6} alkyl optionally substituted with from one to five substituents independently selected from halo, oxo, $-CN$, and R^{10} ;

each R^8 and R^9 is independently selected from

(a) hydrogen;

(b) C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each optionally substituted with from one to five substituents independently selected from halo, oxo, $-CN$, and R^{10} ; and

(c) C_{3-10} cycloalkyl- $(CH_2)_m-$, C_{6-14} aryl- $(CH_2)_m-$, C_{2-6} heterocyclyl- $(CH_2)_m-$, and C_{1-9} heteroaryl- $(CH_2)_m-$, each optionally substituted with from one to five substituents independently selected from halo, oxo, $-CN$, R^{10} , and C_{1-6} alkyl optionally substituted with from one to five substituents independently selected from halo, oxo, $-CN$, and R^{10} ;

each R^{10} is independently selected from $-OR^{11}$, $-N(R^{11})R^{12}$, $-N(R^{11})C(O)R^{12}$, $-NHC(O)NR^{11}R^{12}$, $-NR^{11}C(O)NHR^{12}$, $-C(O)R^{11}$, $-C(O)OR^{11}$, $-C(O)N(R^{11})R^{12}$, $-C(O)N(R^{11})OR^{12}$, $-C(O)N(R^{11})S(O)_2R^{13}$, $-NR^{11}S(O)_2R^{13}$, $-SR^{11}$, $-S(O)R^{13}$, $-S(O)_2R^{13}$, and $-S(O)_2N(R^{11})R^{12}$;

each R¹¹ and R¹² is independently selected from

- (a) hydrogen; and
- (b) C₁₋₆ alkyl and C₃₋₁₀ cycloalkyl-(CH₂)_m-, each optionally substituted with from one to five substituents independently selected from halo, oxo, -CN, -OH, and -NH₂;

each R¹³ is independently selected from C₁₋₆ alkyl and C₃₋₁₀ cycloalkyl-(CH₂)_m-, each optionally substituted with from one to five substituents independently selected from halo, oxo, -CN, -OH, and -NH₂;

each R¹⁴ is independently selected from hydrogen, C₁₋₄ alkyl, and C₁₋₄ haloalkyl; and

each m is independently selected from 0, 1, 2, 3, and 4;

wherein each heteroaryl and heterocyclyl of R⁷, R⁸, and R⁹ independently has one to four heteroatoms, each of the heteroatoms independently selected from N, O, and S.

2. A compound, tautomer or pharmaceutically acceptable salt according to claim 1, wherein R¹ is hydrogen.
3. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 and 2, wherein R² and R³ are each independently selected from hydrogen, fluoro, chloro, and methyl.
4. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 and 2, wherein R² and R³, together with the carbon atoms to which they are attached, form a benzene ring or a pyridine ring in which the benzene ring is optionally substituted with from one to four substituents independently selected from halo, -CN, R⁶, and R⁷, and the pyridine ring is optionally substituted with from one to three substituents independently selected from halo, -CN, R⁶, and R⁷.
5. A compound, tautomer or pharmaceutically acceptable salt according to claim 4, wherein the benzene ring or the pyridine ring is optionally substituted with one or two substituents independently selected fluoro, chloro, and methyl.
6. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 4 and 5, wherein R² and R³, together with the carbon atoms to which they are attached, form a benzene ring which is optionally substituted.

7. A compound, tautomer or pharmaceutically acceptable salt according to any one of the preceding claims, wherein R^{4a} is ethenyl optionally substituted with from one to three methyl groups.
8. A compound, tautomer or pharmaceutically acceptable salt according to claim 7, wherein R^{4a} is unsubstituted ethenyl.
9. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein R^{4a} is $-CH_2R^5$ and R^5 is halo.
10. A compound, tautomer or pharmaceutically acceptable salt according to any one of the preceding claims, wherein R^{4c} is hydrogen, R^{4e} is selected from hydrogen and C_{1-4} alkyl when L is $-N(R^{4e})-$, and R^{4b} and R^{4d} , together with the nitrogen atom and the carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.
11. A compound, tautomer or pharmaceutically acceptable salt according to claim 10, wherein R^{4b} and R^{4d} , together with the nitrogen atom and the carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, form a pyrrolidine ring which is optionally substituted with from one to four substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.
12. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1-9, wherein R^{4c} is hydrogen, R^{4e} is hydrogen when L is $-N(R^{4e})-$, and R^{4b} and R^{4d} , together with the nitrogen atom and the carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to four substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.
13. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 10-12, wherein the ring formed by R^{4b} and R^{4d} , together with the nitrogen atom and the carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, is unsubstituted.
14. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1-9, wherein R^{4b} is selected from hydrogen and C_{1-4} alkyl, R^{4d} is hydrogen, L is $-N(R^{4e})-$, and R^{4c} and R^{4e} , together with the carbon atoms and the nitrogen atom to which R^{4c} ,

R^{4d} , and R^{4e} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

15. A compound, tautomer or pharmaceutically acceptable salt according to claim 14, wherein R^{4c} and R^{4e} , together with the carbon atoms and the nitrogen atom to which R^{4c} , R^{4d} , and R^{4e} are respectively attached, form a pyrrolidine ring which is optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

16. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1-9, wherein R^{4b} is hydrogen, R^{4d} is hydrogen, L is $-N(R^{4c})-$, and R^{4c} and R^{4e} , together with the carbon atoms and the nitrogen atom to which R^{4c} , R^{4d} , and R^{4e} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to four substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

17. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 14-16, wherein the ring formed by R^{4c} and R^{4e} , together with the carbon atoms and the nitrogen atom to which R^{4c} , R^{4d} , and R^{4e} are respectively attached, is unsubstituted.

18. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1-9, wherein R^{4d} is hydrogen, R^{4e} is selected from hydrogen and C_{1-4} alkyl when L is $-N(R^{4c})-$, and R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

19. A compound, tautomer or pharmaceutically acceptable salt according to claim 18, wherein R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, form a pyrrolidine ring which is optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

20. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1-9, wherein R^{4d} is hydrogen, R^{4e} is hydrogen when L is $-N(R^{4c})-$, and R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached,

form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to four substituents independently selected from halo, C₁₋₄ alkyl, and C₁₋₄ haloalkyl.

21. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 18-20, wherein the ring formed by R^{4b} and R^{4c}, together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, is unsubstituted.

22. A compound, tautomer or pharmaceutically acceptable salt according to any one of the preceding claims, wherein L is -N(R^{4e})-.

23. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1-13 and 18-21, wherein L is selected from -O- and -CH₂O-.

24. A compound, tautomer or pharmaceutically acceptable salt according to claim 23, wherein L is -O-.

25. A compound according to claim 1, which is selected from the following compounds:

(*R*)-3-(1-((1-methacryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-

5(4*H*)-one;

(*R*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-

one;

(*R,E*)-3-(1-((1-(but-2-enoyl)pyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-

5(4*H*)-one;

N-(1-(3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)isoquinolin-1-yl)pyrrolidin-3-

yl)acrylamide;

(*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-

one;

(*S*)-3-(1-(((1-acryloylpyrrolidin-2-yl)methyl)amino)isoquinolin-3-yl)-1*H*-1,2,4-

triazol-5(4*H*)-one;

(*S*)-3-(1-((1-acryloylpyrrolidin-2-yl)methoxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-

5(4*H*)-one;

(*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-

one;

(*R*)-3-(1-((1-acryloylpyrrolidin-2-yl)methoxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-

5(4*H*)-one;

- (*S*)-3-(1-((1-methacryloylpyrrolidin-3-yl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)(methyl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(1-((1-methacryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(1-(((1-acryloylpyrrolidin-3-yl)oxy)methyl)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S,E*)-5-(1-((1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
- (*S,E*)-3-(1-((1-(but-2-enoyl)pyrrolidin-3-yl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(8-((1-acryloylpyrrolidin-3-yl)oxy)-1,7-naphthyridin-6-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(8-((1-acryloylpyrrolidin-3-yl)amino)-1,7-naphthyridin-6-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-7-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- 3-(1-((*trans*-1-acryloyl-4-methylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- 3-(1-(((3*R*,4*S*)-1-acryloyl-4-methylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- 3-(1-(((3*S*,4*R*)-1-acryloyl-4-methylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-8-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-8-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-7-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-7-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;

- (S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-7-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (S)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-8-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-8-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-8-methoxyisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (S)-3-(6-((1-acryloylpyrrolidin-3-yl)oxy)-4-methylpyridin-2-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (S)-3-(6-((1-acryloylpyrrolidin-3-yl)oxy)pyridin-2-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (S)-3-(6-((1-acryloylpyrrolidin-3-yl)oxy)-5-methylpyridin-2-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
- (S)-5-(1-((1-(2-chloroacetyl)pyrrolidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
- (S)-5-(1-((1-(2-chloroacetyl)pyrrolidin-3-yl)amino)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
- (S)-5-(1-((1-acryloylpiperidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
- (S)-5-(1-((1-acetylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
- (S)-5-(1-((1-propionylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
- a tautomer of any one of the aforementioned compounds;
- a stereoisomer of any one of the aforementioned compounds or tautomers; and
- a pharmaceutically acceptable salt of any one of the aforementioned compounds, tautomers or stereoisomers.

26. A pharmaceutical composition comprising:
- a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1-25; and
- a pharmaceutically acceptable excipient.

~~27. A compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1-25, for use as a medicament.~~

28. Use of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1-25 in the manufacture of a medicament for inhibiting BTK in a subject.

29. Use of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1-25 in the manufacture of a medicament for treating a disease, disorder or condition associated with BTK in a subject.

30. Use of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1-25 in the manufacture of a medicament for treating a disease, disorder or condition selected from Type I hypersensitivity reactions, autoimmune diseases, inflammatory disorders, cancer, and non-malignant proliferative disorders in a subject.

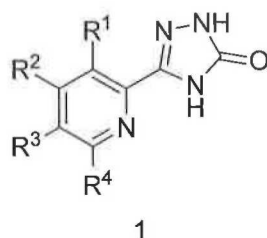
31. Use of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1-25 in the manufacture of a medicament for treating a disease, disorder or condition selected from allergic rhinitis, asthma, atopic dermatitis, rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, lupus nephritis, psoriasis, immune thrombocytopenic purpura, inflammatory bowel disease, chronic obstructive pulmonary disease, Sjögren's syndrome, ankylosing spondylitis, Behcet's disease, graft versus host disease, pemphigus vulgaris, idiopathic plasmacytic lymphadenopathy, atherosclerosis, myocardial infarction, and thrombosis in a subject.

32. Use of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1-25 in the manufacture of a medicament for treating a disease, disorder or condition selected from B-cell lymphoma, chronic lymphocytic leukemia, and multiple myeloma in a subject.

33. A combination of an effective amount of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1-25, and at least one additional pharmacologically active agent.
34. A combination according to claim 33, wherein the additional pharmacologically active agent is a disease modifying antirheumatic drug (DMARD).
35. A combination according to claim 34, wherein the DMARD is methotrexate.

CLAIMS

1. A compound of Formula 1,

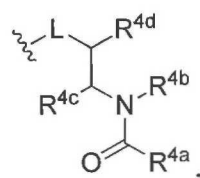


a tautomer thereof or a pharmaceutically acceptable salt of the compound or tautomer,
wherein:

R¹ is selected from hydrogen, halo, and methyl;

R² and R³ are each independently selected from hydrogen, halo, and methyl, or R² and R³, together with carbon atoms to which they are attached, form a benzene ring or a pyridine ring in which the benzene ring is optionally substituted with from one to four substituents independently selected from halo, -CN, -OR⁸, and C₁₋₆ alkyl, and the pyridine ring is optionally substituted with from one to three substituents independently selected from halo, -CN, -OR⁸, and C₁₋₆ alkyl;

R⁴ has the formula



in which $\sim$ indicates a point of attachment;

L is selected from -O-, -CH₂O-, and -N(R^{4e})-;

R^{4a} is selected from -CH₂R⁵ and ethenyl optionally substituted with from one to three substituents independently selected from halo, cyano, and C₁₋₆ alkyl optionally substituted with -N(R¹¹)R¹²; and

(a) R^{4c} is hydrogen, R^{4e} is selected from hydrogen and C₁₋₄ alkyl when L is -N(R^{4e})-, and R^{4b} and R^{4d}, together with a nitrogen atom and carbon atoms to which R^{4b}, R^{4c}, and R^{4d} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C₁₋₄ alkyl, and C₁₋₄ haloalkyl; or

- (b) R^{4b} is selected from hydrogen and C_{1-4} alkyl, R^{4d} is hydrogen, L is $-N(R^{4e})-$, and R^{4c} and R^{4e} , together with the carbon atoms and a nitrogen atom to which R^{4c} , R^{4d} , and R^{4e} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl; or
- (c) R^{4d} is hydrogen, R^{4e} is selected from hydrogen and C_{1-4} alkyl when L is $-N(R^{4e})-$, and R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, form pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^5 is selected from hydrogen, halo, and C_{1-4} alkyl;

each R^8 is independently selected from hydrogen and C_{1-6} alkyl; and

each R^{11} and R^{12} is independently selected from hydrogen and C_{1-6} alkyl.

2. A compound, tautomer or pharmaceutically acceptable salt according to claim 1, wherein R^1 is hydrogen.
3. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 and 2, wherein R^2 and R^3 are each independently selected from hydrogen, fluoro, chloro, and methyl.
4. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 and 2, wherein R^2 and R^3 , together with the carbon atoms to which they are attached, form a benzene ring or a pyridine ring in which the benzene ring is optionally substituted with from one to four substituents independently selected from halo, $-CN$, $-OR^8$, and C_{1-6} alkyl, and the pyridine ring is optionally substituted with from one to three substituents independently selected from halo, $-CN$, $-OR^8$, and C_{1-6} alkyl.
5. A compound, tautomer or pharmaceutically acceptable salt according to claim 4, wherein the benzene ring or the pyridine ring is optionally substituted with one or two substituents independently selected from fluoro, chloro, and methyl.
6. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 4 and 5, wherein R^2 and R^3 , together with the carbon atoms to which they are attached,

form a benzene ring which is optionally substituted with one or two substituents independently selected from fluoro, chloro, and methyl.

7. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein R^{4a} is ethenyl optionally substituted with from one to three methyl groups.
8. A compound, tautomer or pharmaceutically acceptable salt according to claim 7, wherein R^{4a} is unsubstituted ethenyl.
9. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 6, wherein R^{4a} is $-\text{CH}_2\text{R}^5$ and R^5 is halo.
10. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 9, wherein R^{4c} is hydrogen, R^{4e} is selected from hydrogen and C_{1-4} alkyl when L is $-\text{N}(\text{R}^{4e})-$, and R^{4b} and R^{4d} , together with the nitrogen atom and the carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.
11. A compound, tautomer or pharmaceutically acceptable salt according to claim 10, wherein R^{4b} and R^{4d} , together with the nitrogen atom and the carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, form a pyrrolidine ring which is optionally substituted with from one to four substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.
12. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 9, wherein R^{4c} is hydrogen, R^{4e} is hydrogen when L is $-\text{N}(\text{R}^{4e})-$, and R^{4b} and R^{4d} , together with the nitrogen atom and the carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to four substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.
13. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 10 to 12, wherein the ring formed by R^{4b} and R^{4d} , together with the nitrogen atom and the carbon atoms to which R^{4b} , R^{4c} , and R^{4d} are respectively attached, is unsubstituted.

14. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 9, wherein R^{4b} is selected from hydrogen and C_{1-4} alkyl, R^{4d} is hydrogen, L is $-N(R^{4c})-$, and R^{4c} and R^{4e} , together with the carbon atoms and the nitrogen atom to which R^{4c} , R^{4d} , and R^{4e} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

15. A compound, tautomer or pharmaceutically acceptable salt according to claim 14, wherein R^{4c} and R^{4e} , together with the carbon atoms and the nitrogen atom to which R^{4c} , R^{4d} , and R^{4e} are respectively attached, form a pyrrolidine ring which is optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

16. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 9, wherein R^{4b} is hydrogen, R^{4d} is hydrogen, L is $-N(R^{4e})-$, and R^{4c} and R^{4e} , together with the carbon atoms and the nitrogen atom to which R^{4c} , R^{4d} , and R^{4e} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to four substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

17. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 14 to 16, wherein the ring formed by R^{4c} and R^{4e} , together with the carbon atoms and the nitrogen atom to which R^{4c} , R^{4d} , and R^{4e} are respectively attached, is unsubstituted.

18. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 9, wherein R^{4d} is hydrogen, R^{4c} is selected from hydrogen and C_{1-4} alkyl when L is $-N(R^{4e})-$, and R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

19. A compound, tautomer or pharmaceutically acceptable salt according to claim 18, wherein R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, form a pyrrolidine ring which is optionally substituted with from one to six substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.

20. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 9, wherein R^{4d} is hydrogen, R^{4c} is hydrogen when L is $-N(R^{4e})-$, and R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, form a pyrrolidine ring or a piperidine ring, each ring optionally substituted with from one to four substituents independently selected from halo, C_{1-4} alkyl, and C_{1-4} haloalkyl.
21. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 18 to 20, wherein the ring formed by R^{4b} and R^{4c} , together with the nitrogen and carbon atoms to which R^{4b} and R^{4c} are respectively attached, is unsubstituted.
22. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 21, wherein L is $-N(R^{4e})-$.
23. A compound, tautomer or pharmaceutically acceptable salt according to any one of claims 1 to 13 and 18 to 21, wherein L is selected from $-O-$ and $-CH_2O-$.
24. A compound, tautomer or pharmaceutically acceptable salt according to claim 23, wherein L is $-O-$.
25. A compound according to claim 1, which is selected from the following compounds:
(R)-3-(1-((1-methacryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
(R)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
(R,E)-3-(1-((1-(but-2-enoyl)pyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
N-(1-(3-(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)isoquinolin-1-yl)pyrrolidin-3-yl)acrylamide;
(S)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
(S)-3-(1-(((1-acryloylpyrrolidin-2-yl)methyl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
(S)-3-(1-((1-acryloylpyrrolidin-2-yl)methoxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;

(S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (R)-3-(1-((1-acryloylpyrrolidin-2-yl)methoxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-methacryloylpyrrolidin-3-yl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)(methyl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-methacryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-(((1-acryloylpyrrolidin-3-yl)oxy)methyl)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S,*E*)-5-(1-((1-(4-(dimethylamino)but-2-enoyl)pyrrolidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
 (S,*E*)-3-(1-((1-(but-2-enoyl)pyrrolidin-3-yl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(8-((1-acryloylpyrrolidin-3-yl)oxy)-1,7-naphthyridin-6-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(8-((1-acryloylpyrrolidin-3-yl)amino)-1,7-naphthyridin-6-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-7-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 3-(1-((*trans*-1-acryloyl-4-methylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 3-(1-(((3*R*,4*S*)-1-acryloyl-4-methylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 3-(1-(((3*S*,4*R*)-1-acryloyl-4-methylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-8-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-8-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;

(S)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-7-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-7-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-7-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-8-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-8-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-8-methoxyisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(6-((1-acryloylpyrrolidin-3-yl)oxy)-4-methylpyridin-2-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(6-((1-acryloylpyrrolidin-3-yl)oxy)pyridin-2-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-3-(6-((1-acryloylpyrrolidin-3-yl)oxy)-5-methylpyridin-2-yl)-1*H*-1,2,4-triazol-5(4*H*)-one;
 (S)-5-(1-((1-(2-chloroacetyl)pyrrolidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
 (S)-5-(1-((1-(2-chloroacetyl)pyrrolidin-3-yl)amino)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
 (S)-5-(1-((1-acryloylpiperidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
 (S)-5-(1-((1-acetylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
 (S)-5-(1-((1-propionylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one;
 a tautomer of any one of the aforementioned compounds;
 a stereoisomer of any one of the aforementioned compounds or tautomers; and
 a pharmaceutically acceptable salt of any one of the aforementioned compounds, tautomers or stereoisomers.

26. A compound according to claim 1, which is (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
27. A compound according to claim 1, which is (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)isoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
28. A compound according to claim 1, which is (*S*)-3-(8-((1-acryloylpyrrolidin-3-yl)oxy)-1,7-naphthyridin-6-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
29. A compound according to claim 1, which is (*S*)-3-(8-((1-acryloylpyrrolidin-3-yl)amino)-1,7-naphthyridin-6-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
30. A compound according to claim 1, which is (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-8-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
31. A compound according to claim 1, which is (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-8-fluoroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
32. A compound according to claim 1, which is (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-7-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
33. A compound according to claim 1, which is (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-7-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
34. A compound according to claim 1, which is (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)oxy)-8-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.

35. A compound according to claim 1, which is (*S*)-3-(1-((1-acryloylpyrrolidin-3-yl)amino)-8-chloroisoquinolin-3-yl)-1*H*-1,2,4-triazol-5(4*H*)-one, a tautomer thereof, or a pharmaceutically acceptable salt of the compound or tautomer.
36. A pharmaceutical composition comprising:
a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1 to 35; and
a pharmaceutically acceptable excipient.
37. A compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1 to 35, for use as a medicament.
38. Use of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1 to 35 in the manufacture of a medicament for treating a disease, disorder or condition selected from allergic rhinitis, asthma, atopic dermatitis, rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, lupus nephritis, inflammatory bowel disease, and Sjögren's syndrome in a subject.
39. Use of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1 to 35 in the manufacture of a medicament for treating a disease, disorder or condition is selected from B-cell lymphoma, chronic lymphocytic leukemia, and multiple myeloma in a subject.
40. A combination of an effective amount of a compound, tautomer or pharmaceutically acceptable salt as defined in any one of claims 1 to 35, and at least one additional pharmacologically active agent.
41. A combination according to claim 40, wherein the additional pharmacologically active agent is a disease modifying antirheumatic drug (DMARD).
42. A combination according to claim 41, wherein the DMARD is methotrexate.