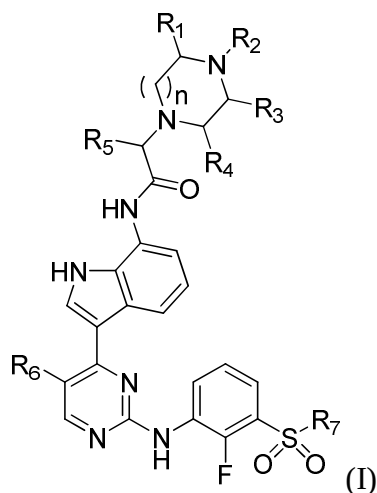


5 Claims

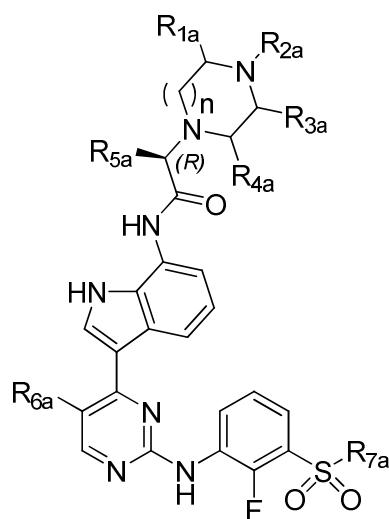
1. A compound of Formula (I):



wherein:

- 10 R₁, R₃, and R₄ are each individually chosen from hydrogen and methyl;
 R₂ is chosen from hydrogen, methyl, and -CH₂CH₂OH;
 n is 1 or 2;
 R₅ is chosen from methyl, ethyl, and -CH₂OR₈;
 R₆ is chosen from methyl, chlorine, and fluorine;
- 15 R₇ is selected from methyl, ethyl, and cyclopropyl; and
 R₈ is selected from methyl, ethyl, and benzyl;
 or a pharmaceutically acceptable salt thereof.
- 20 2. The compound of claim 1, wherein each of R₁-R₄ is chosen independently from
 hydrogen and methyl.
3. The compound of claims 1-2, wherein R₁, R₃, and R₄ are all hydrogen.
4. The compound of claims 1-3, wherein R₂ is methyl.
- 25 5. The compound of claim 1, wherein R₅ is methyl or -CH₂OR₈.
6. The compound of claims 1-5, wherein R₈ is methyl.

- 5 7. The compound of claim 1, wherein R₆ is a methyl or a fluorine atom.
8. The compound of claims 1-7, wherein R₆ is a fluorine atom.
9. The compound of claim 1, wherein R₇ is methyl.
- 10 10. The compound of claim 1, having the structure of formula (Ia):

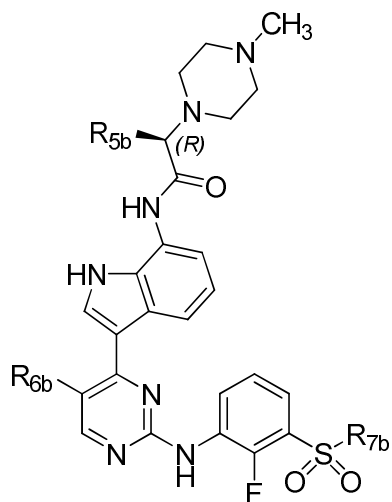


Formula (Ia)

wherein:

- 15 R_{1a}, R_{3a}, and R_{4a} are each individually chosen from hydrogen and methyl;
 R_{2a} is chosen from hydrogen, methyl, and -CH₂CH₂OH;
 n is 1 or 2;
 R_{5a} is chosen from methyl, ethyl, and -CH₂OR_{8a};
 R_{6a} is chosen from methyl, chlorine, and fluorine;
- 20 R_{7a} is selected from methyl, ethyl, and cyclopropyl; and
 R_{8a} is selected from methyl, ethyl and benzyl;
 or a pharmaceutically acceptable salt thereof.

5 11. The compound of claim 1, having the structure of formula (Ib):



Formula (Ib)

wherein:

- 10 R_{5b} is chosen from methyl, ethyl, and -CH₂OR_{8b};
R_{6b} is chosen from methyl, chlorine, and fluorine;
R_{7b} is selected from methyl, ethyl, and cyclopropyl; and
R_{8b} is selected from methyl, ethyl and benzyl;
or a pharmaceutically acceptable salt thereof.

- 5 12. The compound of claim 1, chosen from:
- (R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-(2-hydroxyethyl)piperazin-1-yl)propanamide;
- (R)-N-(3-(2-(2-fluoro-3-(methylsulfonyl)phenylamino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;
- 10 (R)-N-(3-(2-(3-(ethylsulfonyl)-2-fluorophenylamino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;
- (R)-N-(3-(2-(3-(cyclopropylsulfonyl)-2-fluorophenylamino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;
- (R)-N-(3-(5-chloro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;
- 15 (S)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;
- (R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)propanamide;
- 20 (R)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)propanamide;
- (R)-2-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)propanamide;
- 25 (S)-2-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)propanamide;
- (R)-2-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)propanamide;
- 30 (S)-2-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)propanamide;
- (S)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)butanamide;
- (R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)butanamide;
- 35 (S)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methylpiperazin-1-yl)propanamide;

5 (R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methylpiperazin-1-yl)propanamide;

(R)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methyl-1,4-diazepan-1-yl)butanamide;

(S)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methyl-1,4-diazepan-1-yl)butanamide;

10 (S)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)butanamide;

(R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)butanamide;

15 (S)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)propanamide;

(R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)propanamide;

(S)-N-(3-(5-fluoro-2-(2-fluoro-3-(methylsulfonyl)phenylamino)pyrimidin-4-yl)-1H-indol-7-yl)-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)butanamide;

20 (R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(piperazin-1-yl)propanamide;

(S)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(piperazin-1-yl)propanamide;

25 (R)-2-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)butanamide;

(S)-2-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)butanamide;

30 (S)-2-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxypropanamide;

(R)-2-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxypropanamide;

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5 (S)-2-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)butanamide;
(R)-2-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)butanamide;
(S)-2-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-3-
10 methoxypropanamide;
(R)-2-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-3-
methoxypropanamide;
15 (S)-N-(3-(5-fluoro-2-(2-fluoro-3-(methylsulfonyl)phenylamino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methylpiperazin-1-yl)propanamide;
(R)-N-(3-(5-fluoro-2-(2-fluoro-3-(methylsulfonyl)phenylamino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methylpiperazin-1-yl)propanamide;
(S)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-
20 indol-7-yl)-2-(4-methyl-1,4-diazepan-1-yl)butanamide;
(R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methyl-1,4-diazepan-1-yl)butanamide;
(R)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)butanamide;
25 (S)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)butanamide;
(S)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)propanamide;
(R)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-
30 indol-7-yl)-3-methoxy-2-((3S,5S)-3,4,5-trimethylpiperazin-1-yl)propanamide;
(R)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methyl-1,4-diazepan-1-yl)propanamide;
(S)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methyl-1,4-diazepan-1-yl)propanamide;
35 (S)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methyl-1,4-diazepan-1-yl)propanamide;

5 (R)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methyl-1,4-diazepan-1-yl)propanamide;
(R)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methyl-1,4-diazepan-1-yl)propanamide;
(S)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-
10 (methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)propanamide;
(R)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)propanamide;
15 (R)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)propanamide;
(S)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)butanamide;
20 (R)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)butanamide;
(S)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)butanamide;
25 (R)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)butanamide;
(S)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxypropanamide;
30 (R)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-3-methoxypropanamide;
(S)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxypropanamide;
35 methoxypropanamide;

5 (R)-2-((R)-2,4-dimethylpiperazin-1-yl)-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxypropanamide;

(R)-2-((S)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)propanamide;

10 (S)-2-((S)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)propanamide;

(R)-2-((S)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)butanamide;

15 (S)-2-((S)-2,4-dimethylpiperazin-1-yl)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)butanamide;

(R)-3-ethoxy-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;

20 (R)-3-ethoxy-N-(3-(5-fluoro-2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)pyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;

(R)-3-(benzyloxy)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;

25 (S)-3-(benzyloxy)-N-(3-(2-((2-fluoro-3-(methylsulfonyl)phenyl)amino)-5-methylpyrimidin-4-yl)-1H-indol-7-yl)-2-(4-methylpiperazin-1-yl)propanamide;

(R)-N-(3-(5-fluoro-2-(2-fluoro-3-(methylsulfonyl)phenylamino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(piperazin-1-yl)propanamide; and

30 (S)-N-(3-(5-fluoro-2-(2-fluoro-3-(methylsulfonyl)phenylamino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(piperazin-1-yl)propanamide;

or a pharmaceutically acceptable salt thereof.

- 5 13. The compound of claim 1, which is (R)-N-(3-(5-fluoro-2-(2-fluoro-3-(methylsulfonyl)phenylamino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methylpiperazin-1-yl)propanamide or a pharmaceutically acceptable salt thereof.
- 10 14. The compound of claim 1, which is (R)-N-(3-(5-fluoro-2-(2-fluoro-3-(methylsulfonyl)phenylamino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methylpiperazin-1-yl)propanamide.
- 15 15. The compound of claim 1, which is a pharmaceutically acceptable salt of (R)-N-(3-(5-fluoro-2-(2-fluoro-3-(methylsulfonyl)phenylamino)pyrimidin-4-yl)-1H-indol-7-yl)-3-methoxy-2-(4-methylpiperazin-1-yl)propanamide.
- 20 16. A pharmaceutical composition comprising a compound according to claims 1-15, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent, excipient, or carrier.
- 25 17. A compound according to claims 1-15, or a pharmaceutically acceptable salt thereof, for use in treating a JAK1-related disorder, wherein the JAK1-related disorder is chosen from Type 1 diabetes, lupus, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, atopic dermatitis, autoimmune thyroid disorders, ulcerative colitis, Crohn's disease, COPD, vitiligo and alopecia areata.
- 30 18. A pharmaceutical composition comprising a compound of any one of claims 1-15, or a pharmaceutically acceptable salt thereof, for use in treating a JAK1-related disorder, wherein the JAK1-related disorder is chosen from Type 1 diabetes, lupus, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, atopic dermatitis, autoimmune thyroid disorders, ulcerative colitis, Crohn's disease, COPD, vitiligo and alopecia areata.
- 35 19. A compound according to claims 1-15, or a pharmaceutically acceptable salt thereof, for use in therapy.