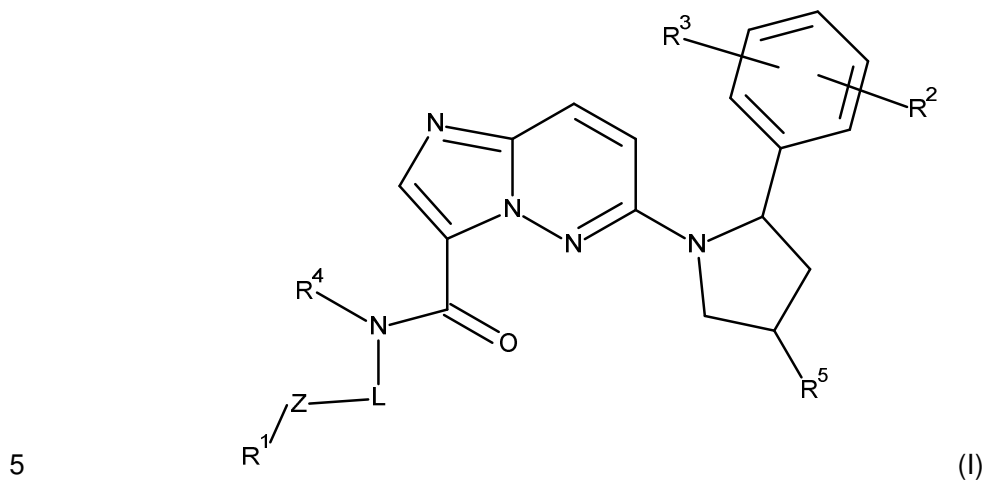


CLAIMS

1. A compound of Formula (I):

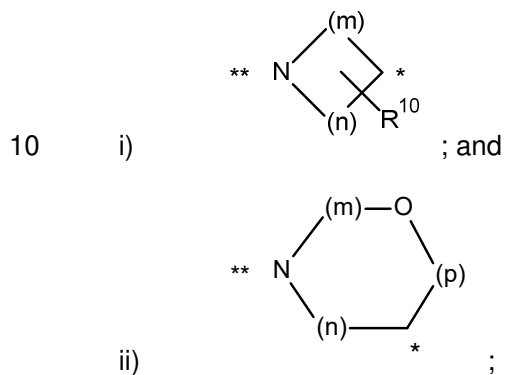


or a pharmaceutically acceptable salt or solvate thereof;

wherein:

L is $(\text{CR}^6\text{R}^7)_r$;

Z is absent or selected from:



wherein * denotes the point of attachment to L and ** denotes the point of attachment to R^1 ;

m is 1 or 2;

15 n is 1 or 2;

p is 0 or 1;

provided that the sum of m, n and p is in the range of 2 to 4;

r is 0 or 1;

R^1 is $-\text{XR}^9$;

20 X is selected from $-\text{CH}_2-$, $-\text{C}(\text{O})-$, and $-\text{S}(\text{O}_2)-$;

R^2 is selected from H and $-\text{SR}^8$;

R³ is selected from H and halo;

R⁴ is selected from H and (C₁-C₃)alkyl;

R⁵ is selected from H, hydroxyl and halo;

R⁶ and R⁷ are each independently selected from H and (C₁-C₃)alkyl;

5 R⁸ is methyl;

R⁹ is phenyl substituted by a group selected from hydroxy, -OC(O)(C₁-C₆)alkyl, C(O)OH and -C(O)O(C₁-C₆)alkyl, wherein the phenyl ring is optionally further substituted by halo;

R¹⁰ is selected from H and (C₁-C₃)alkoxy.

10 2. A compound according to claim 1 wherein R¹ is -CH₂R⁹.

3. A compound according to any preceding claim wherein R² is -SR⁸.

4. A compound according to any preceding claim wherein R³ is H or fluoro.

15

5. A compound according to any preceding claim wherein R⁴ is H.

6. A compound according to any preceding claim wherein R⁵ is H or fluoro.

20 7. A compound according to any preceding claim wherein R⁶ is H.

8. A compound according to any preceding claim wherein R⁷ is H.

9. A compound according to any preceding claim wherein R⁹ is phenyl substituted
25 by hydroxy wherein the hydroxyphenyl is optionally further substituted by fluoro.

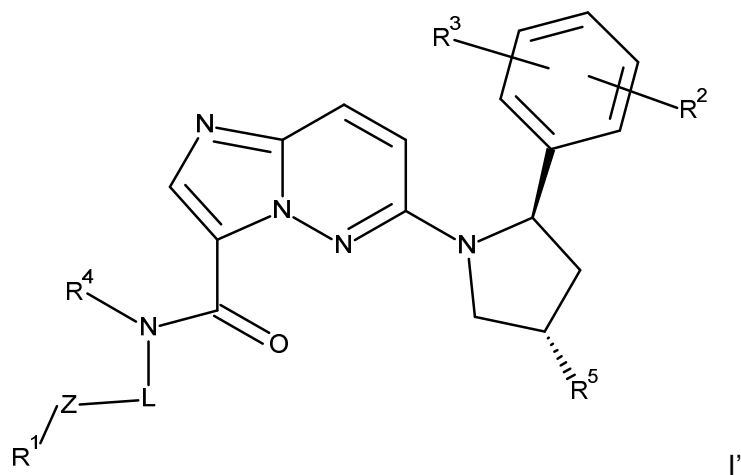
10. A compound according to any preceding claim wherein R¹⁰ is H.

11. A compound according to any preceding claim wherein r is 0.

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12. A compound according to any preceding claim wherein Z is absent.

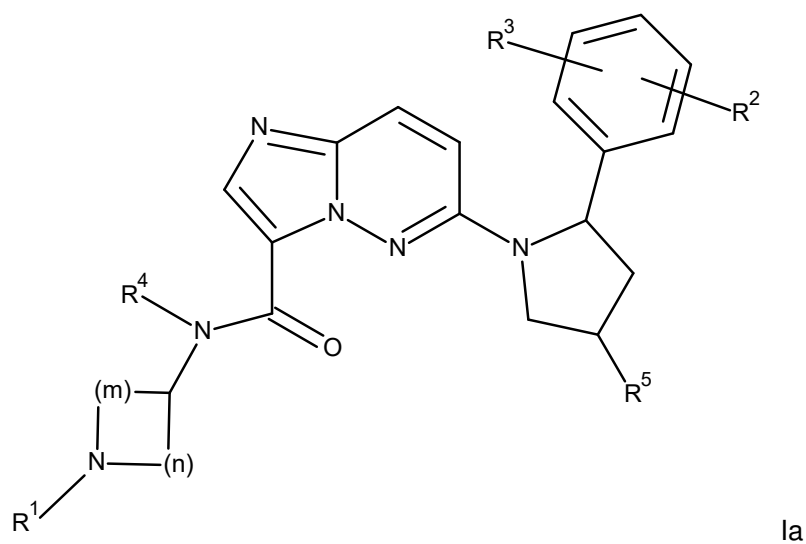
13. A compound of Formula I'



or a pharmaceutically acceptable salt or solvate thereof wherein R^1 , R^2 , R^3 , R^4 , R^5 , L and Z, are as defined in any preceding claim.

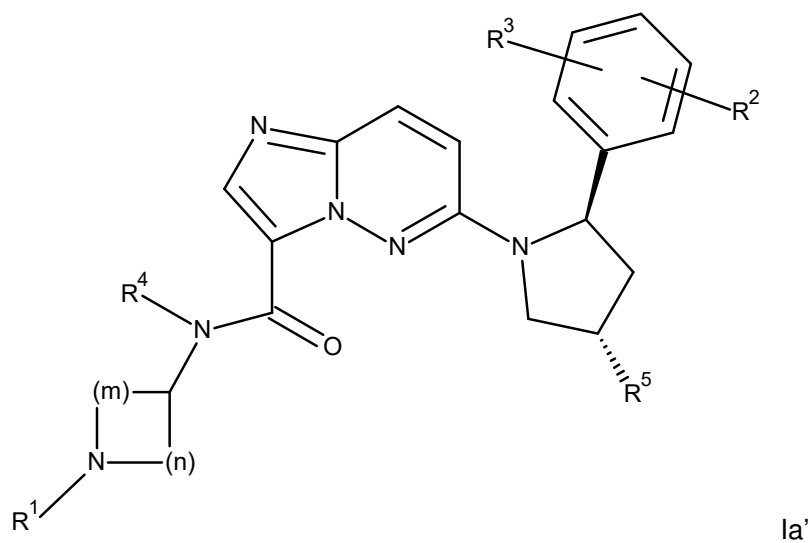
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14. A compound of Formula Ia



10 or a pharmaceutically acceptable salt or solvate thereof wherein R^1 , R^2 , R^3 , R^4 , R^5 , m and n, are as defined in any preceding claim.

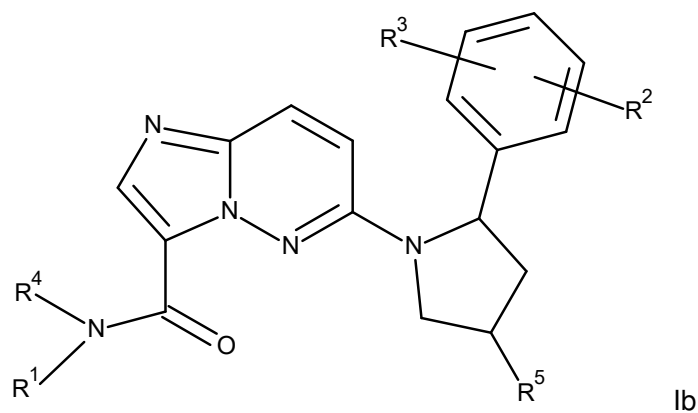
15. A compound of Formula Ia'



or a pharmaceutically acceptable salt or solvate thereof wherein R^1 , R^2 , R^3 , R^4 , R^5 , m and n , are as defined in any preceding claim.

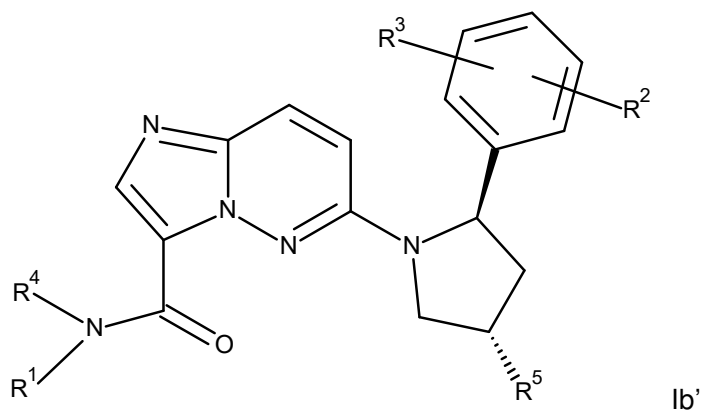
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16. A compound of Formula 1b



10 or a pharmaceutically acceptable salt or solvate thereof wherein R^1 , R^2 , R^3 , R^4 , R^5 , m and n , are as defined in any preceding claim..

17. A compound of Formula 1b'



or a pharmaceutically acceptable salt or solvate thereof wherein R¹, R², R³, R⁴, R⁵, m and n, are as defined in any preceding claim.

5

18. A compound according to claim wherein said compound is selected from:

- 6-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(4-fluoro-3-hydroxyphenyl)methyl]azetidin-3-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
- 10 6-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(4-fluoro-3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
- 6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(3-hydroxyphenyl)methyl]piperidin-4-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
- 6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(4-fluoro-3-hydroxyphenyl)methyl]azetidin-3-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
- 15 6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(3-hydroxyphenyl)methyl]azetidin-3-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
- 6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(4-fluoro-3-hydroxyphenyl)methyl]piperidin-4-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
- 20 6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(3-hydroxyphenyl)methyl]imidazo[1,2-b]pyridazine-3-carboxamide;
- 6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
- 3-[[3-{6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]phenyl pentanoate;
- 25 Methyl 3-[[3-{6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;

- 6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(4-fluoro-3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 Butyl 3-[[3-{6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;
- 5 Ethyl 3-[[3-{6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;
 6-[4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(4-fluoro-3-hydroxyphenyl)methyl]imidazo[1,2-b]pyridazine-3-carboxamide;
 N-[1-[(4-fluoro-3-hydroxyphenyl)methyl]pyrrolidin-3-yl]-6-[2-[3-fluoro-5-
- 10 (methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 Methyl 3-[[3-{6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
- 15 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(4-fluoro-3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(4-fluoro-3-hydroxyphenyl)methyl]azetidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(3-
- 20 hydroxyphenyl)methyl]azetidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(4-fluoro-3-hydroxyphenyl)methyl]piperidin-4-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(3-
- 25 hydroxyphenyl)methyl]piperidin-4-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-[(4-fluoro-3-hydroxyphenyl)methyl]-4-methoxypyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[4-[(4-fluoro-3-
- 30 hydroxyphenyl)methyl]-1,4-oxazepan-6-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(4-fluoro-3-hydroxyphenyl)methyl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[1-(3-
- hydroxybenzoyl)pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 3-[[3-{6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]phenyl acetate;
- 35 3-[[3-{6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoic acid;

Butyl 3-[[3-{6-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;

5-[4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(3-hydroxyphenyl)methyl]piperidin-4-yl}pyrazolo[1,5-a]pyrimidine-3-carboxamide;

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or a pharmaceutically acceptable salt or solvate thereof.

19. A compound according to claim wherein said compound is selected from:

- 10 6-[(2R)-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(4-fluoro-3-hydroxyphenyl)methyl]azetidin-3-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R)-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(3S)-1-[(4-fluoro-3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(3-hydroxyphenyl)methyl]piperidin-4-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
 15 6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(4-fluoro-3-hydroxyphenyl)methyl]azetidin-3-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(3-hydroxyphenyl)methyl]azetidin-3-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
 20 6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(4-fluoro-3-hydroxyphenyl)methyl]piperidin-4-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(3S)-1-[(3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 25 3-[[[(3S)-3-{6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]phenyl]pentanoate;
 Methyl 3-[[[(3S)-3-{6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;
 30 6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(3S)-1-[(4-fluoro-3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 Butyl 3-[[[(3S)-3-{6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;
 Ethyl 3-[[[(3S)-3-{6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;
 35 ylidimidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;

- 6-[(2R,4S)-4-fluoro-2-[5-fluoro-2-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(4-fluoro-3-hydroxyphenyl)methyl]imidazo[1,2-b]pyridazine-3-carboxamide;
 N-[(3S)-1-[(4-fluoro-3-hydroxyphenyl)methyl]pyrrolidin-3-yl]-6-[(2R)-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
- 5 Methyl 3-[[[(3S)-3-{6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoate;
 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(3S)-1-[(3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(3S)-1-[(4-fluoro-3-hydroxyphenyl)methyl]pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
- 10 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(4-fluoro-3-hydroxyphenyl)methyl]azetidin-3-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(3-hydroxyphenyl)methyl]azetidin-3-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
- 15 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(4-fluoro-3-hydroxyphenyl)methyl]piperidin-4-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-{1-[(3-hydroxyphenyl)methyl]piperidin-4-yl}imidazo[1,2-b]pyridazine-3-carboxamide;
- 20 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(3S,4S)-1-[(4-fluoro-3-hydroxyphenyl)methyl]-4-methoxypyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(6S)-4-[(4-fluoro-3-hydroxyphenyl)methyl]-1,4-oxazepan-6-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
- 25 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(6R)-4-[(4-fluoro-3-hydroxyphenyl)methyl]-1,4-oxazepan-6-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(4-fluoro-3-hydroxyphenyl)methyl]imidazo[1,2-b]pyridazine-3-carboxamide;
- 30 6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]-N-[(3S)-1-(3-hydroxybenzoyl)pyrrolidin-3-yl]imidazo[1,2-b]pyridazine-3-carboxamide;
 3-[[[(3S)-3-{6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]phenyl acetate;
 3-[[[(3S)-3-{6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfanyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl]methyl]benzoic acid;
- 35

Butyl 3-[[[(3S)-3-{6-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfonyl)phenyl]pyrrolidin-1-yl]imidazo[1,2-b]pyridazine-3-amido}pyrrolidin-1-yl)methyl]benzoate;
 5-[(2R,4S)-4-fluoro-2-[3-fluoro-5-(methylsulfonyl)phenyl]pyrrolidin-1-yl]-N-{1-[(3-hydroxyphenyl)methyl]piperidin-4-yl}pyrazolo[1,5-a]pyrimidine-3-carboxamide;

5

or a pharmaceutically acceptable salt or solvate thereof.

20. A pharmaceutical composition comprising a compound according to any of claims 1 to 19 and one or more pharmaceutically acceptable excipients.

10

21. A pharmaceutical composition according to claim 20 in combination with one or more other therapeutic agents.

22. A compound according to any of claims 1 to 19 for use as a pharmaceutical.

15

23. A compound as defined in any of the preceding claims for use in treating or preventing a condition or disorder which is mediated by Trk, wherein the condition or disorder includes diseases of pruritus and itch, autoimmune disease of skin, diseases of skin pain and neuropathy and diseases of dermatitis.

20

24. A compound ~~according to claim 23~~ for use according to claim 23 wherein the condition or disorder is mediated by TrkA, TrkB, and TrkC.

25. A compound ~~according to claim 23 or 24~~ for use according to claim 23 or 24 wherein the condition or disorder is atopic dermatitis.

25

26. Use of a compound as defined in any of claims 1 to 19 in the manufacture of a medicament for treating or preventing a condition or disorder which is mediated by Trk, wherein the condition or disorder includes diseases of pruritus and itch, autoimmune disease of skin, diseases of skin pain and neuropathy and diseases of dermatitis.

30

27. Use according to claim 26 wherein the condition or disorder is mediated by TrkA, TrkB, and TrkC.

35 28. Use according to claim 26 or 27 wherein the condition or disorder is atopic dermatitis.

29. A compound ~~according to any one of claims 23 to 25~~ for use according to any one of claims 23 to 25 wherein the compound is to be administered topically.

30. Use according to any one of claims 26 to 28 wherein the medicament is to be
5 administered topically.