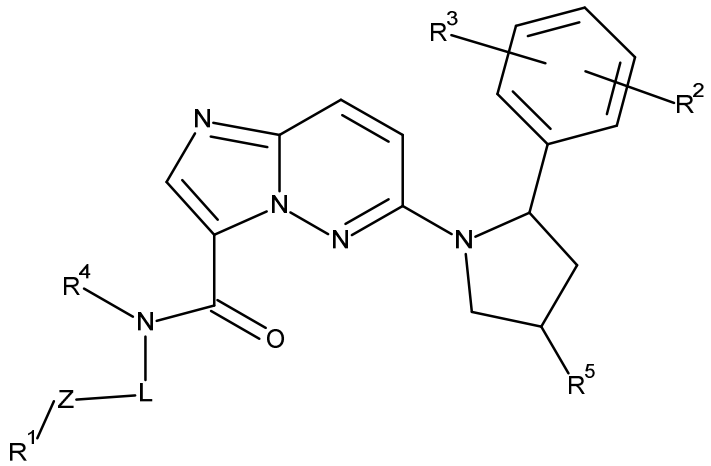
CLAIMS

1. A compound of Formula (I):



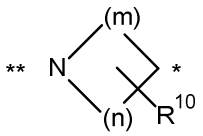
(I)

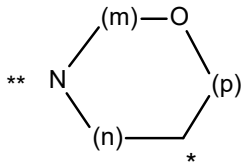
or a pharmaceutically acceptable salt or solvate thereof;

wherein:

L is $(CR^6R^7)_r$;

Z is absent or selected from:

i)  ; and

ii)  ;

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

m is 1 or 2;

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 $–XR^9$;

X is selected from $–CH_2$-, -C(O)-, and $–S(O_2)$-;

R^2 is selected from H and $–SR^8$;

R^3 is selected from H and halo;
R^4 is selected from H and $(C_1\text{-}C_3)$alkyl;
R^5 is selected from H, hydroxyl and halo;
R^6 and R^7 are each independently selected from H and $(C_1\text{-}C_3)$alkyl;
R^8 is methyl;
R^9 is phenyl substituted by a group selected from hydroxy , -OC(O)$(C_1\text{-}C_6)$alkyl, C(O)OH and -C(O)O$(C_1\text{-}C_6)$alkyl, wherein the phenyl ring is optionally further substituted by halo;
R^{10} is selected from H and $(C_1\text{-}C_3)$alkoxy.

2. A compound according to claim 1 wherein R^1 is $–CH_2R^9$.

3. A compound according to any preceding claim wherein R^2 is $–SR^8$.

4. A compound according to any preceding claim wherein R^3 is H or fluoro.

5. A compound according to any preceding claim wherein R^4 is H.

6. A compound according to any preceding claim wherein R^5 is H or fluoro.

7. A compound according to any preceding claim wherein R^6 is H.

8. A compound according to any preceding claim wherein R^7 is H.

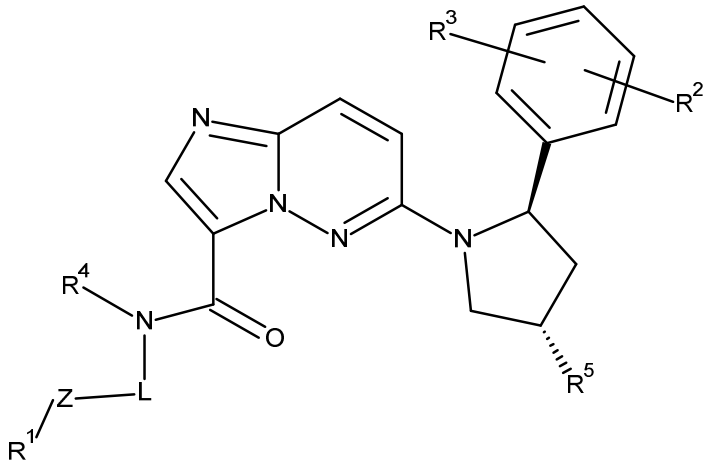
9. A compound according to any preceding claim wherein R^9 is phenyl substituted by hydroxy wherein the hydroxyphenyl is optionally further substituted by fluoro.

10. A compound according to any preceding claim wherein R^{10} is H.

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

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

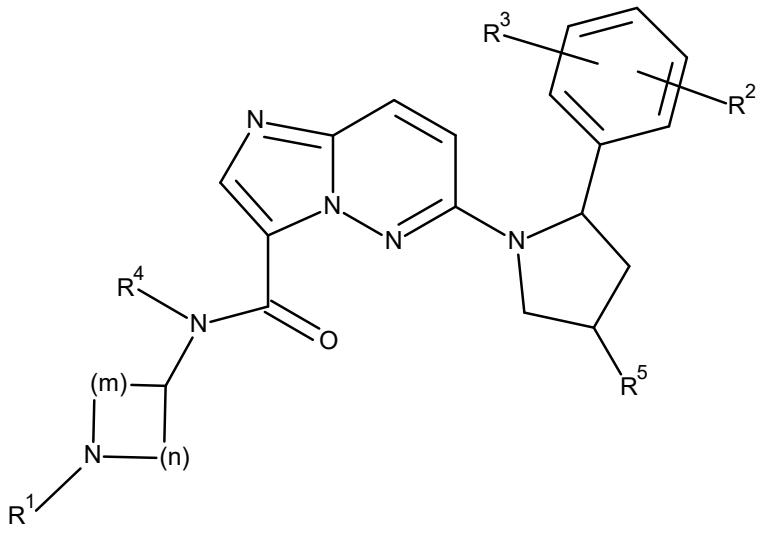
13. A compound of Formula I’



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.

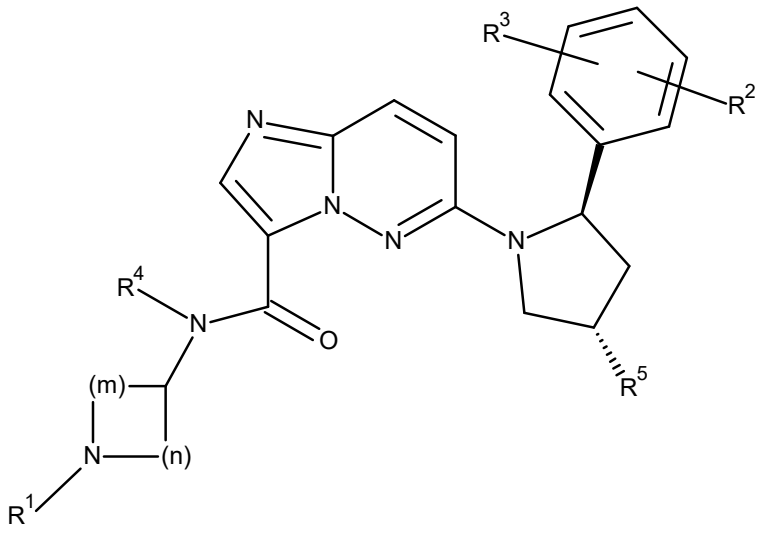
14. A compound of Formula Ia



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.

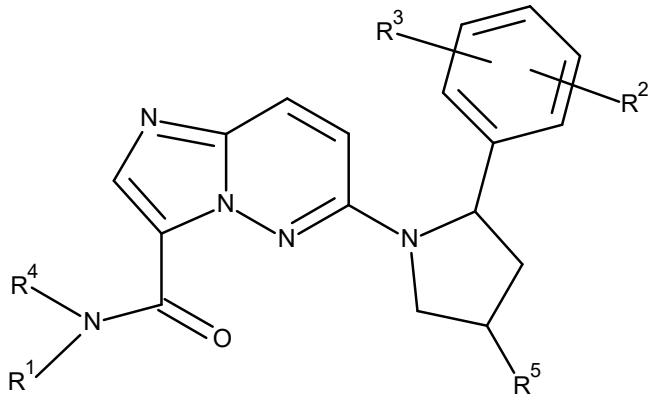
15. A compound of Formula Ia'



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.

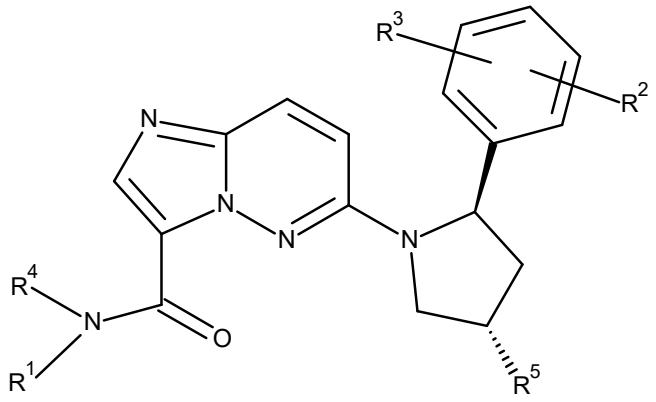
16. A compound of Formula Ib



Ib

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 Ib'



Ib'

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.

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;
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;
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;
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;
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;
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-(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;
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-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-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-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;
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;

or a pharmaceutically acceptable salt or solvate thereof.

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

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;
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;
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-[(3-hydroxyphenyl)methyl]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;
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;
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;

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;
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;
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;
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;
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;
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;
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;

Butyl 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;
5-[(2R,4S)-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;

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.

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.

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.

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

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

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.

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

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

29. A compound 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 administered topically.