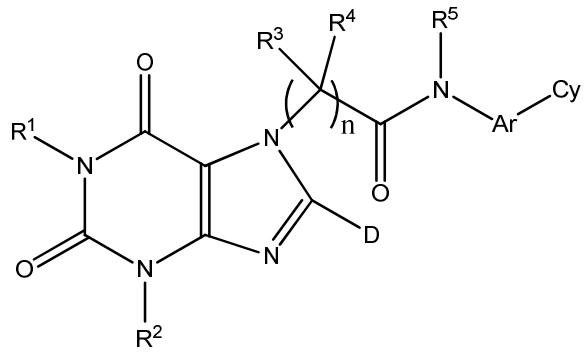
CLAIMS

1. A compound having structure (I)



(I)

wherein:

R^1, R^2, R^3, R^4 and R^5 are each, independently, H or an alkyl group;

D is selected from the group consisting of H, halogen, alkyl, cycloalkyl, aryl, and dialkylamino, each, other than H and halogen, being optionally substituted;

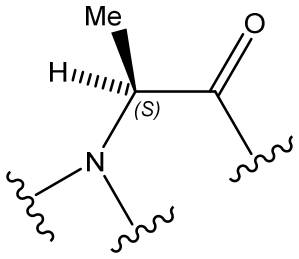
Ar is a 6-membered heteroaryl ring having 1 or 2 nitrogen atoms having no substituents other than Cy and the amide nitrogen atom, these being in a 1,4-relationship on said ring; and

Cy is an aryl, heteroaryl or a saturated ring containing at least one heteroatom, each being optionally substituted; and

n is an integer from 1 to 2,

or an enantiomer, diastereomer or salt thereof.

2. The compound of claim 1, wherein, if n=1 and one of R^3 and R^4 is methyl and the other is H, the stereochemistry of the compound is as shown in partial structure (II):



(II).

3. The compound of claim 1 wherein R^1 and R^2 are the same.

4. The compound of any one of claims 1 to 3 wherein R^1 and R^2 are both methyl.

5. The compound of any one of claims 1 to 3 wherein R^1 and R^2 are both ethyl.

6. The compound of any one of claims 1 to 5 wherein Cy is a 5 or 6 membered aromatic ring having between 0 and 2 nitrogen atoms, 0 or 1 sulfur atoms and 0 or 1 oxygen atoms.

7. The compound of any one of claims 1 to 6 wherein Cy is piperazine, substituted on both nitrogen atoms.

8. The compound of any one of claims 1 to 7 wherein n is 1.

9. The compound of any one of claims 1 to 8 wherein D is H.

10. The compound of any one of claims 1 to 9 wherein R^1 and R^2 are both methyl, R^3, R^4, R^5 and D are all H and n is 1.

11. The compound of any one of claims 1 to 8 in which D is methyl, cyclopropyl, trifluoromethyl, phenyl, dimethylamino, morpholin-N-yl, thiophene-3-yl or bromo.

12. The compound of any one of claims 1 to 11 wherein R^3 and R^4 are either both H or both methyl.

13. The compound of any one of claims 1 to 11 wherein one of R^3 and R^4 is H and the other is methyl or ethyl.

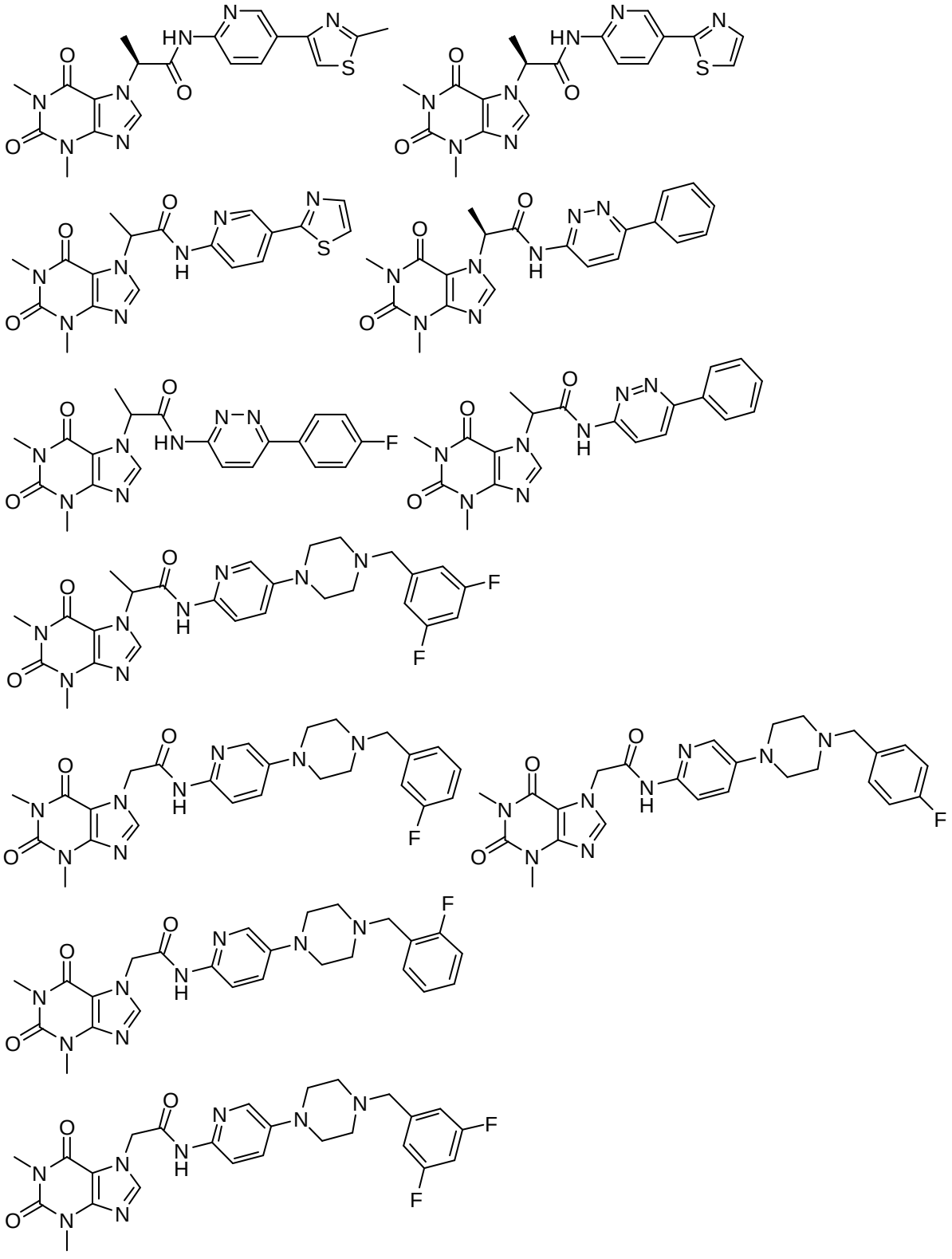
14. The compound of any one of claims 1 to 13 wherein R^5 is H.

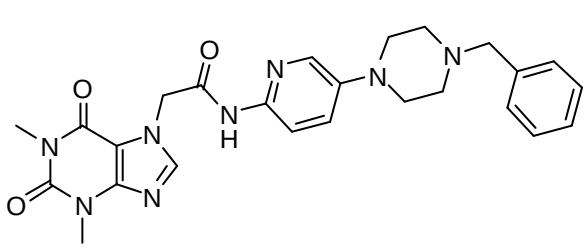
15. The compound of claim 1 in which R^1 and R^2 are both Me, D is H, n is 1 and R^3 and R^4 are both H.

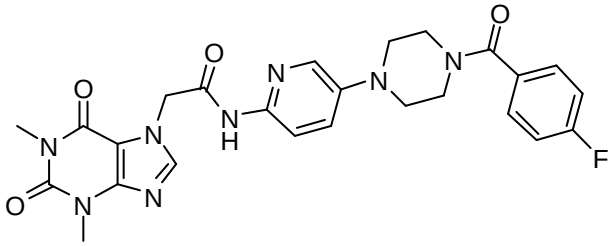
16. The compound of any one of claims 1 to 15 having IC_{50} against STF3A of less than 10 micromolar, optionally less than 5 micromolar.

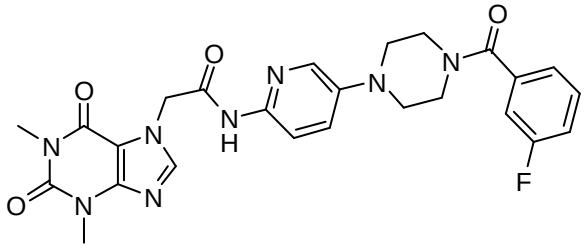
17. The compound of any one of claims 1 to 16 which does not inhibit TRPA1 at an IC_{50} of 10 micromolar, optionally 5 micromolar.

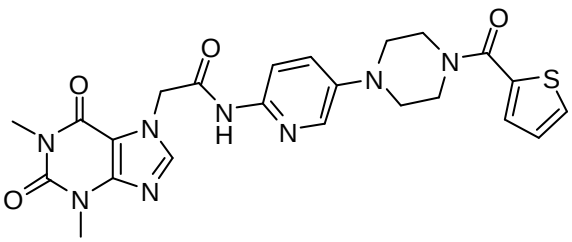
18. The compound of claim 1 which is one of the following:

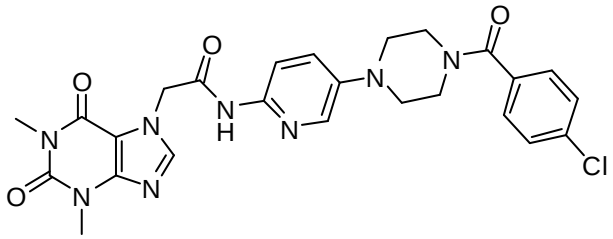


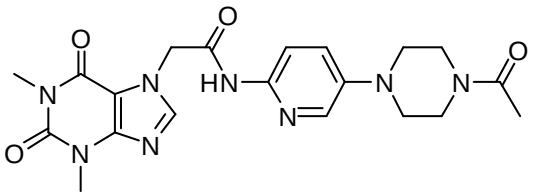


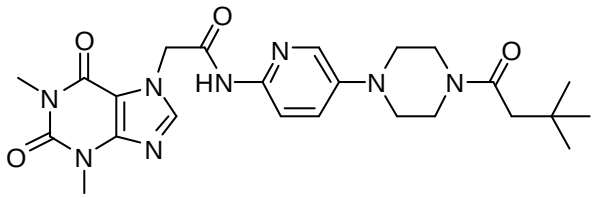


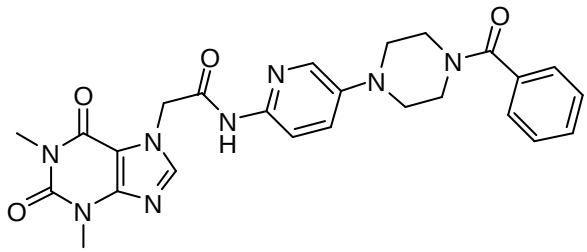


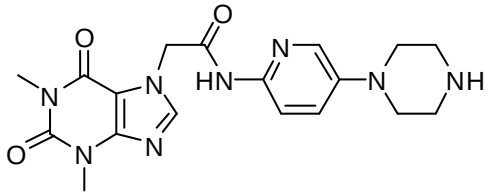


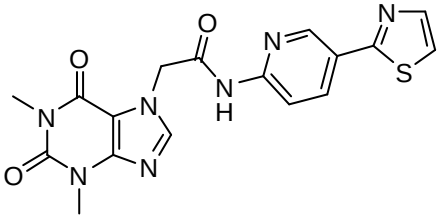


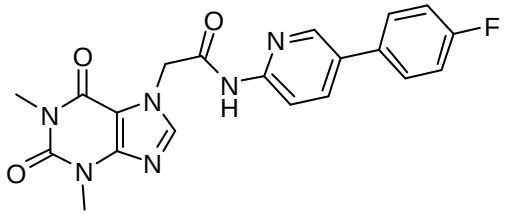


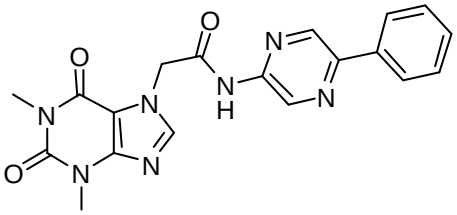


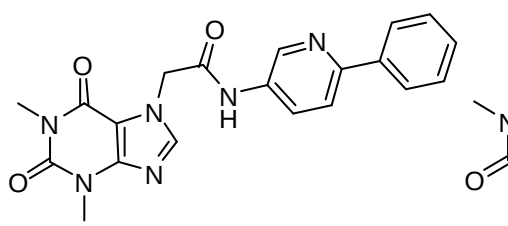


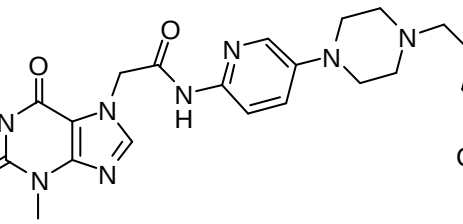


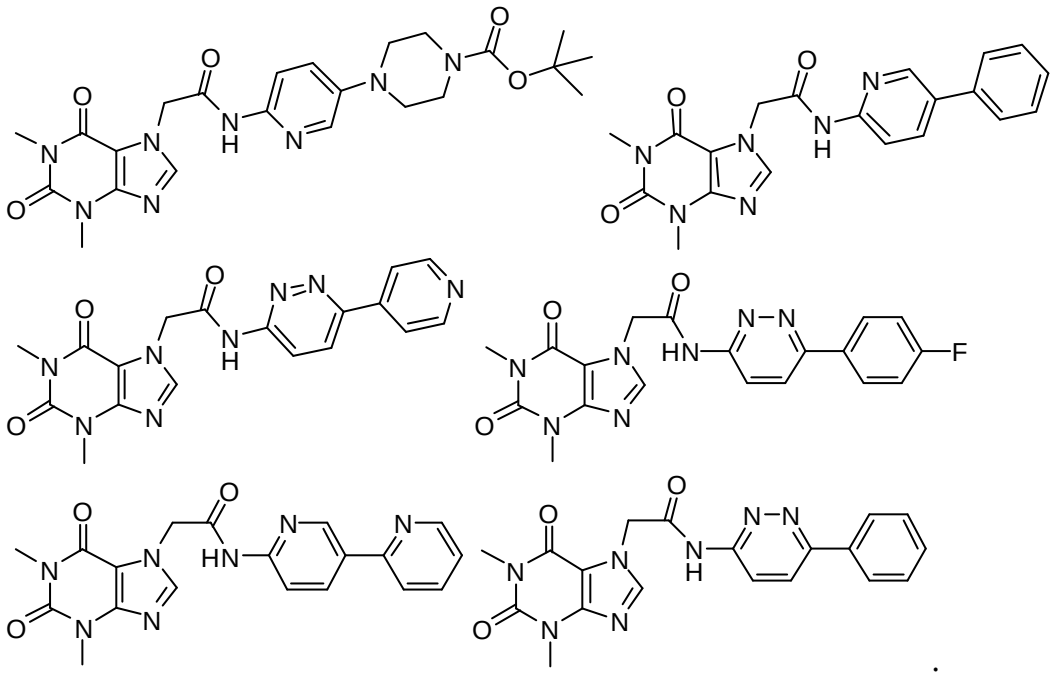






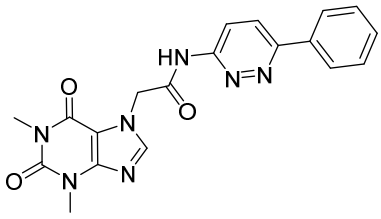






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19. The compound of claim 1 which is:



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20. The compound of any one of claims 1 to 19 for use in the treatment of a disease or condition associated with Wnt pathway activity.

21. The compound of claim 20 wherein the disease or condition is selected from a cancer, such as cervical, colon, breast, bladder, head and neck, gastric, lung, ovarian, prostate, thyroid, non-small-cell lung, chronic lymphocytic leukemia, mesothelioma, melanoma, pancreatic adenocarcinoma, basal cell carcinoma, osteosarcoma, hepatocellular carcinoma, Wilm's tumor or medulloblastoma; a fibrotic disease, such as pulmonary fibrosis, liver fibrosis, skin fibrosis or renal fibrosis; a degenerative disease; or a metabolic disease such as diabetic retinopathy.

22. Use of a compound according to any one of claims 1 to 19 in the manufacture of a medicament for the treatment of a disease or condition associated with Wnt pathway activity, said disease or condition being selected from the group consisting of cancer, such as

cervical, colon, breast, bladder, head and neck, gastric, lung, ovarian, prostate, thyroid, non-small-cell lung, chronic lymphocytic leukemia, mesothelioma, melanoma, pancreatic adenocarcinoma, basal cell carcinoma, osteosarcoma, hepatocellular carcinoma, Wilm's tumor or medulloblastoma; a fibrotic disease, such as pulmonary fibrosis, liver fibrosis, skin fibrosis or renal fibrosis; a degenerative disease; or a metabolic disease such as diabetic retinopathy.

23. The use of claim 22 wherein the disease or condition is selected from the group consisting of cancer, fibrosis, stem cell and diabetic retinopathy, rheumatoid arthritis, psoriasis and myocardial infarction.

24. The use of claim 22 or claim 23 wherein the cancer is characterised by high Wnt activity or a fibrotic disease or a degenerative disease.

25. A pharmaceutical composition comprising a compound according to any one of claims 1 to 19 together with one or more pharmaceutically acceptable carriers, diluents or adjuvants.

26. An anhydrous form of the free base of 2-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)-N-(6-phenylpyridazin-3-yl)acetamide.

27. The anhydrous form of claim 26 which is a non-hydrated single polymorph.

28. The anhydrous form of claim 26 or claim 27 which is crystalline.

29. The anhydrous form of claim 28 which shows on X-ray diffraction a peak on the 2theta scale at 22.2°±0.5°.

30. The anhydrous form of claim 28 or claim 29 which shows on X-ray diffraction peaks on the 2theta scale at 5.5°±0.5° and 14.2°±0.5°.

31. The anhydrous form of any one of claims 28 to 30 which shows on X-ray diffraction at least four peaks on the 2theta scale selected from the group consisting of 5.5°±0.5° and 12.5°±0.5°, 14.2°±0.5°, 16.7°±0.5°, 17.7°±0.5°, 18.8°±0.5°, 22.4°±0.5°, 24.2°±0.5° and 31.7°±0.5°.

32. The anhydrous form of any one of claims 28 to 31 which shows on X-ray diffraction peaks on the 2theta scale of and 5.5°±0.5° and 12.5°±0.5°, 14.2°±0.5°, 16.7°±0.5°, 17.7°±0.5°, 18.0°±0.5°, 18.8°±0.5°, 19.6°±0.5°, 20.6°±0.5°, 22.4°±0.5°, 24.2°±0.5°, 24.4°±0.5°, 25.0°±0.5°, 27.0°±0.5°, 27.6°±0.5°, 29.8°±0.5°, 31.7°±0.5° and 32.2°±0.5°.

33. A pharmaceutical composition comprising an anhydrous free base according to any one of claims 26 to 32.

34. Use of an anhydrous free base according to any one of claims 26 to 32 in the manufacture of a medicament for the treatment of a proliferative disorder associated with Wnt pathway activity, said disorder selected from cancer, such as cervical, colon, breast, bladder, head and neck, gastric, lung, ovarian, prostate, thyroid, non-small-cell lung, chronic lymphocytic leukemia, mesothelioma, melanoma, pancreatic adenocarcinoma, basal cell carcinoma, osteosarcoma, hepatocellular carcinoma, Wilm’s tumor or medulloblastoma; a fibrotic disease, such as pulmonary fibrosis, liver fibrosis, skin fibrosis or renal fibrosis; a degenerative disease; or a metabolic disease such as diabetic retinopathy.

35. Use according to claim 34 wherein the proliferative disorder is cancer.