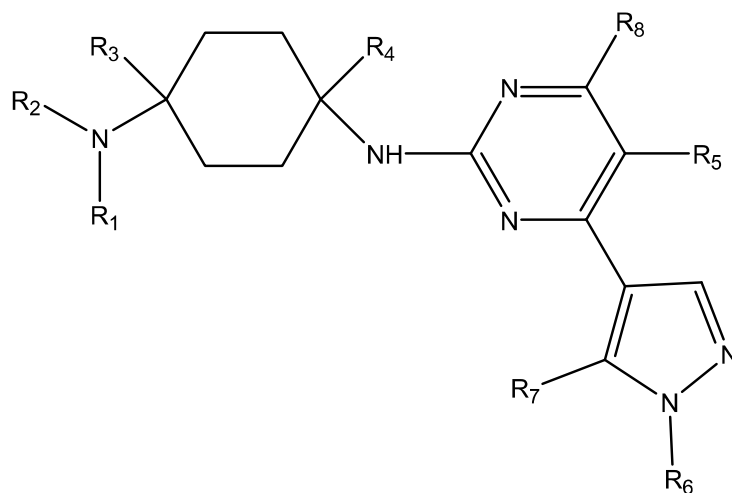


Claims

1. A compound having formula (I), or a stereoisomer or salt thereof:



(I)

wherein:

R₁ and R₂ are each independently selected from H; and straight and branched C₁ – C₈ alkyl, straight and branched C₁ – C₅ alkoxy, straight and branched C₁ – C₅ acyl, C₅ – C₁₅ aryl, and C₃ – C₇ heteroaryl, each optionally substituted by at least one of halide, hydroxyl, ester, ether, C₅ – C₁₅ aryl, C₃ – C₇ heteroaryl, and amide; or

R₁ and R₂ together with the nitrogen atom they are connected to form a 4 – 7 membered saturated, unsaturated, or aromatic ring that may optionally include at least one of N, O, NH, C=N, C=O, and SO₂, and can optionally be substituted with at least one of straight or branched C₁ – C₅ alkyl, C₅ – C₁₅ aryl, C₃ – C₇ heteroaryl, hydroxyl, halide, and cyano;

R₃ and R₄ are each independently selected from H, and straight and branched C₁ – C₈ alkyl optionally substituted by at least one of halide, hydroxyl, alkoxy, C₅ – C₁₅ aryl, C₃ – C₇ heteroaryl, ester, and amide; or

R₁ or R₂ together with R₃ and the carbon and nitrogen atoms they are each connected to form a 4 – 7 membered saturated, unsaturated, or aromatic ring that may optionally include at least one of N, NH, O, C=N, C=O, and SO₂, and can optionally be substituted with at least one of straight or branched C₁ – C₅ alkyl, C₅ – C₁₅ aryl, C₃ – C₇ heteroaryl, hydroxyl, carbonyl, and halide;

R₅ and R₈ are each independently selected from H and halide; and straight and branched C₁ – C₈ alkyl, straight and branched C₂ – C₈ alkenyl, straight and branched C₂ – C₈ alkynyl, each optionally substituted by at least one halide;

R₆ is selected from straight and branched C₁ – C₈ alkyl, straight and branched C₂ – C₈ alkenyl, straight and branched C₂ – C₈ alkynyl, C₅ – C₁₀ cycloalkyl, and saturated and unsaturated 4 – 6 membered heterocycle, each optionally substituted by at least one of straight or branched C₁ – C₈ alkyl, C₃ – C₇ cycloalkyl, 4 – 6 membered heterocycle, C₅ – C₁₅ aryl, C₃ – C₇ heteroaryl, halide, hydroxyl, and C₁ – C₅ alkyl halide;

R₇ is selected from straight and branched C₁ – C₈ alkyl, straight and branched C₂ – C₈ alkenyl, and straight and branched C₂ – C₈ alkynyl, each substituted by at least one C₃ – C₇ cycloalkyl, 4 – 6 membered heterocycle, C₅ – C₁₅ aryl, C₃ – C₇ heteroaryl, halide, hydroxyl, and C₁ – C₅ alkyl halide.

2. The compound according to claim 1, wherein R₁ and R₂ are each independently selected from H and straight or branched C₁ – C₈ alkyl optionally substituted by at least one of halide, C₅ – C₁₅ aryl, C₃ – C₇ heteroaryl, hydroxyl, ester, ether, and amide.

3. The compound according to claim 1, wherein R₁ and R₂ are each independently selected from H and straight or branched C₁ – C₅ alkoxy optionally substituted by at least one of halide, hydroxyl, ester, and amide.

4. The compound according to claim 1, wherein R₁ and R₂ are each independently selected from H and C₁ – C₅ acyl optionally substituted by at least one of halide, hydroxyl, ester, ether, and amide.

5. The compound according to claim 1, wherein R₁ and R₂ are each independently selected from H and C₅ – C₁₅ aryl optionally substituted by at least one of halide, hydroxyl, ester, ether, and amide.

6. The compound according to any one of the preceding claims, wherein R₄ is H.

7. The compound according to any one of the preceding claims, wherein R₃ and R₄ are each H.

8. The compound according to any one of the preceding claims, wherein R₅ is selected from H, Cl, and straight and branched C₁ – C₄ alkyl.

9. The compound according to any one of the preceding claims, wherein R₅ is H.

10. The compound according to any one of the preceding claims, wherein R₈ is selected from H, Cl, and straight and branched C₁ – C₄ alkyl.

11. The compound according to any one of the preceding claims, wherein R₈ is H.

12. The compound according to any one of the preceding claims, wherein one of R₅ and R₈ is H.

13. The compound according to any one of the preceding claims, wherein at least one of R₁ and R₂ is H.

14. The compound according to any one of the preceding claims, wherein R₆ selected from straight and branched C₁ – C₈ alkyl, C₅ – C₁₀ cycloalkyl, and saturated and unsaturated 4 –

6 membered heterocycle; and R₇ is selected from straight and branched C₁ – C₈ alkyl substituted by at least one of C₃ – C₇ cycloalkyl, 4 – 6 membered heterocycle, C₅ – C₁₅ aryl, C₃ – C₇ heteroaryl, halide, hydroxyl, and C₁ – C₅ alkyl halide.

15. The compound according to any one of the preceding claims, wherein R₆ is selected from straight and branched C₁ – C₈ alkyl, C₅ – C₁₀ cycloalkyl, and 4 – 6 membered saturated heterocycle.

16. The compound according to any one of the preceding claims, wherein R₇ is straight or branched C₁ – C₈ alkyl substituted by at least one of C₃ – C₇ cycloalkyl and hydroxyl.

17. The compound according to claim 1, wherein R₆ is selected from straight and branched C₁ – C₈ alkyl, and saturated, unsaturated, and aromatic 4 – 6 membered heterocycle, each optionally substituted by at least one of straight or branched C₁ – C₈ alkyl, C₃ – C₇ cycloalkyl, halide, hydroxyl, and CF₃.

18. The compound according to any one of the preceding claims, wherein R₇ is straight or branched C₁ – C₈ alkyl substituted by at least one C₃ – C₇ cycloalkyl.

19. The compound according to claim 1, wherein R₁ and R₂ together with the nitrogen atom they are connected to form a 4 – 7 membered saturated ring optionally including at least one of N, O, NH, C=N, C=O, and SO₂; and can optionally be substituted with at least one of straight or branched C₁ – C₅ alkyl, hydroxyl, halide, and cyano.

20. The compound according to claim 1, wherein R₁ and R₂ together with the nitrogen atom they are connected to form a 4 – 7 membered saturated ring.

21. The compound according to claim 1, wherein R₁ and R₂ together with the nitrogen atom they are connected to form a 4 – 7 membered saturated ring including at least one of N and O.

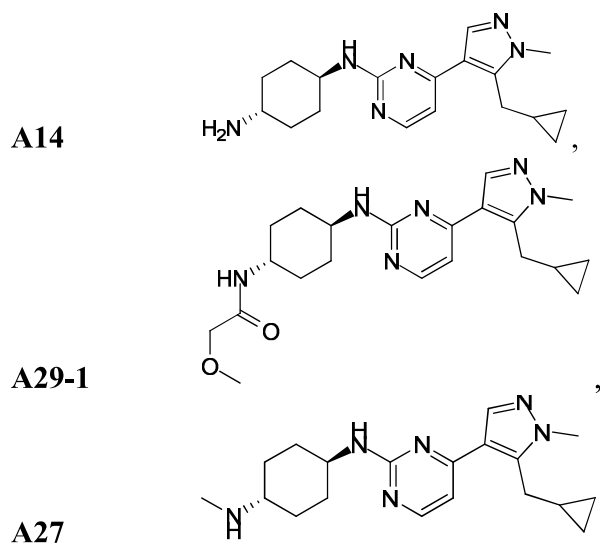
22. The compound according to claim 1, wherein R₁ and R₂ together with the nitrogen atom they are connected to form a 4 – 7 membered aromatic ring optionally including at least one of N and O.

23. The compound according to any one of the preceding claims, wherein R₃ and R₄ are each H.

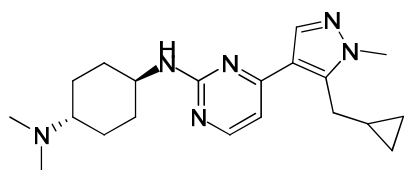
24. The compound according to claim 1, wherein R₁ or R₂ together with R₃ and the carbon and nitrogen atoms they are connected to form a 4 – 7 membered saturated ring that optionally includes at least one of N, NH, O, C=O, and SO₂, and can optionally be substituted with at least one of straight or branched C₁ – C₅ alkyl, hydroxyl, carbonyl, and halide.

25. The compound according to claim 1, wherein R₁ or R₂ together with R₃ and the carbon and nitrogen atoms they are connected to form a 4 – 7 membered saturated ring that includes at least one of NH, O, and C=O.

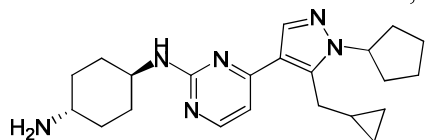
26. The compound according to claim 1, selected from:



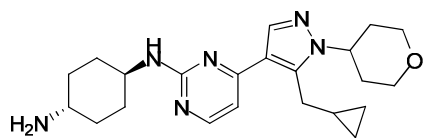
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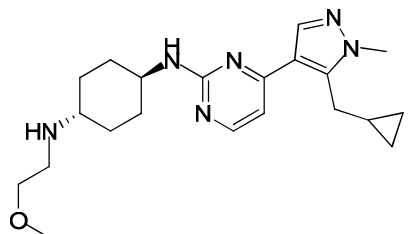
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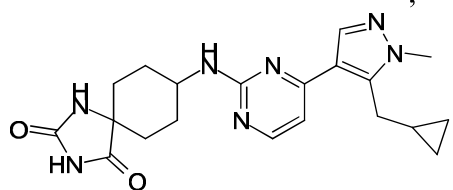
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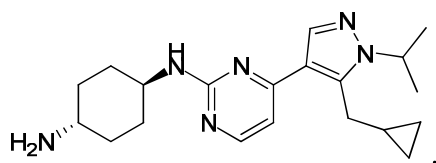
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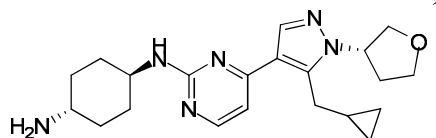
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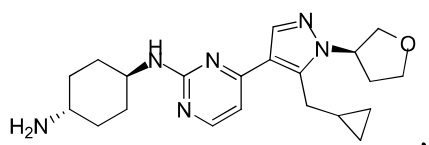
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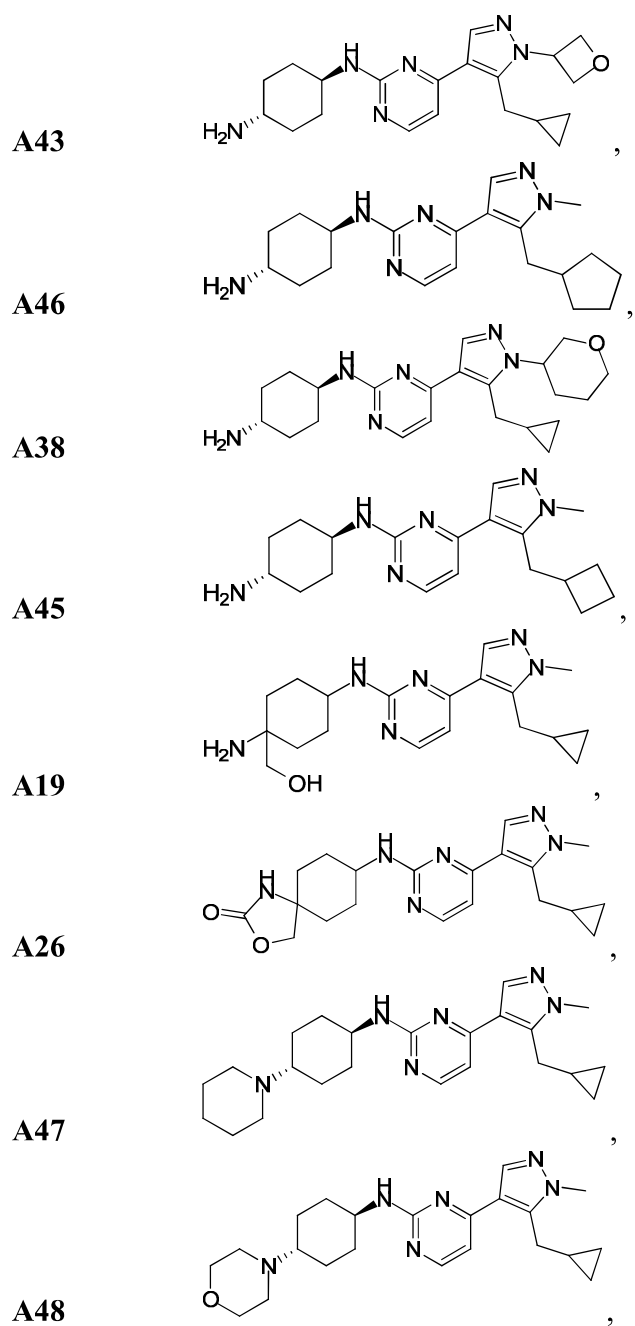


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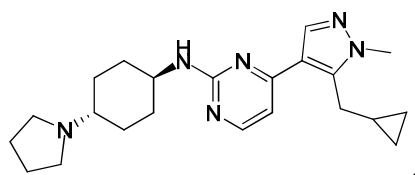


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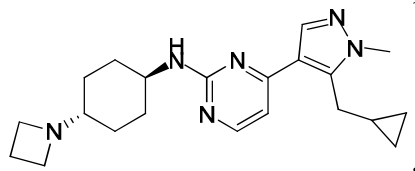




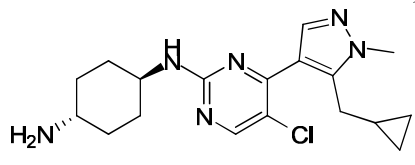
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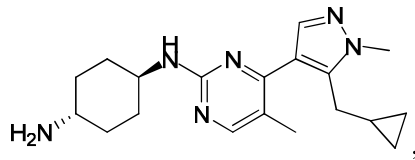
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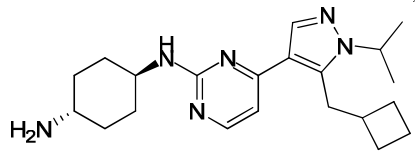
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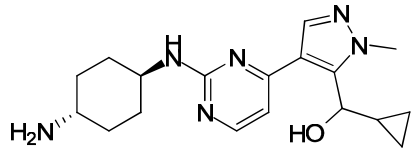
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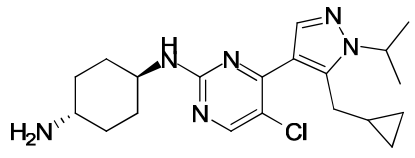
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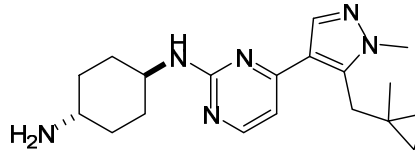
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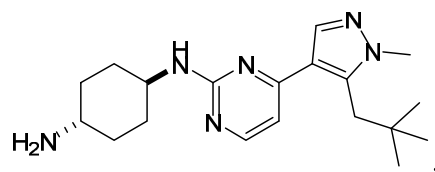
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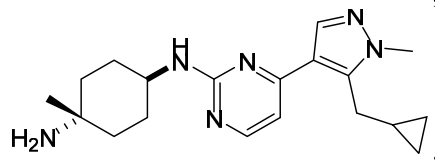
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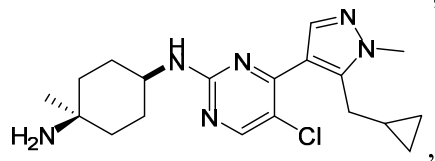
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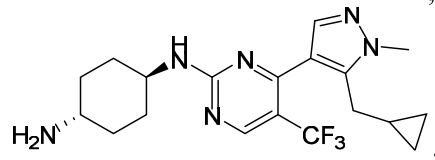
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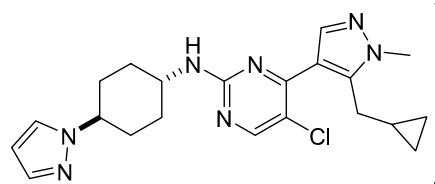
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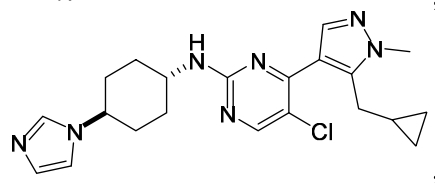
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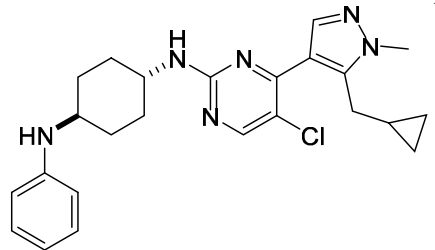
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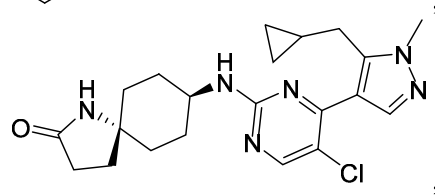
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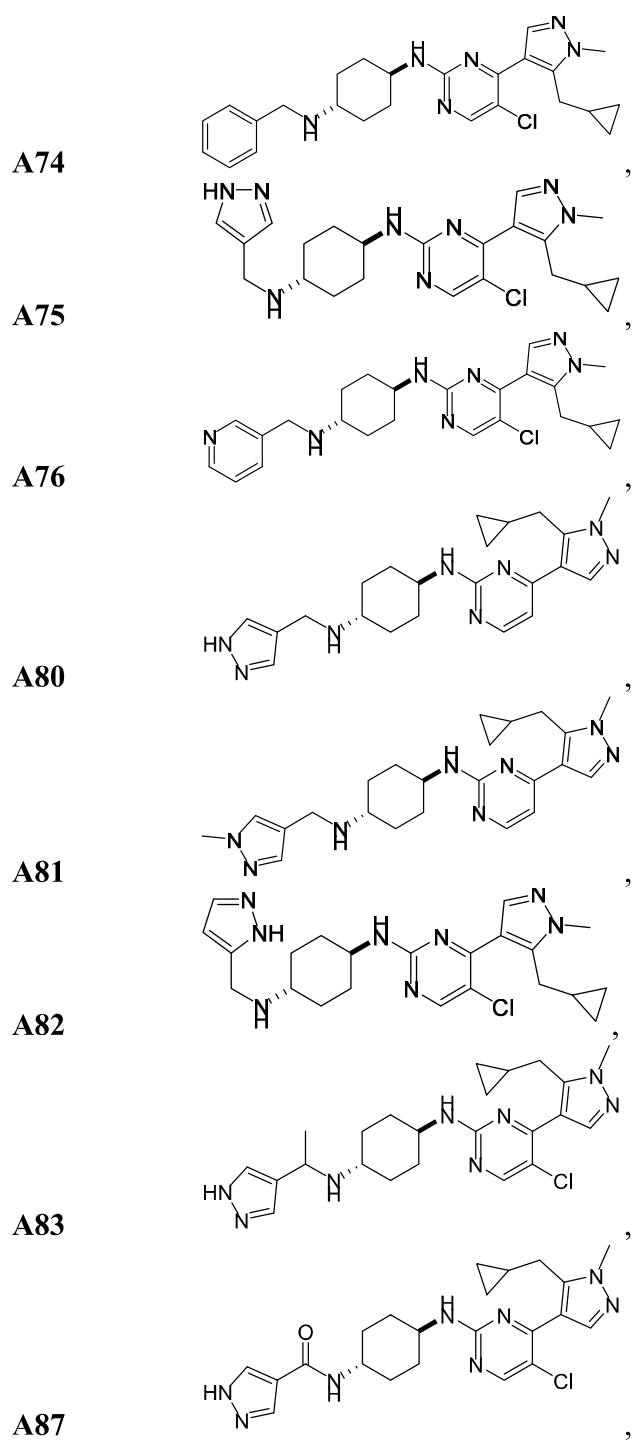


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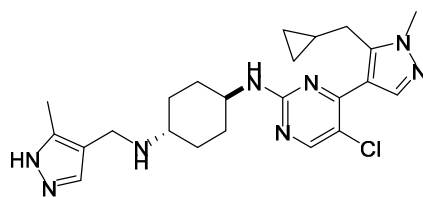


A71

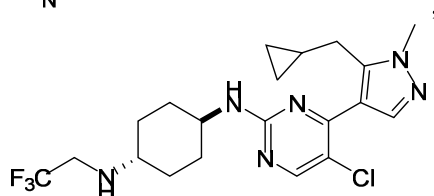




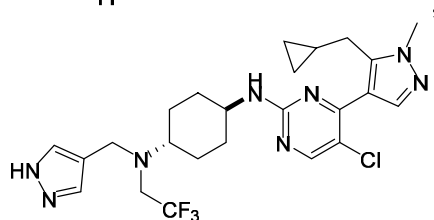
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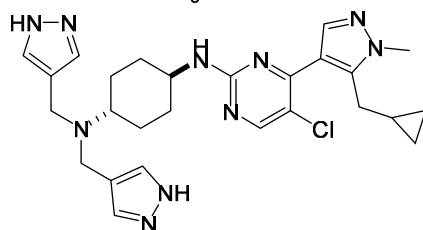
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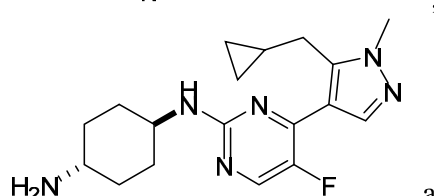
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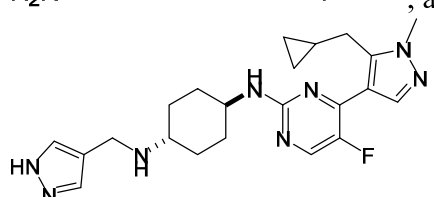
A96



A86



A85



27. A composition comprising the compound according to any one of claims 1 to 26.
28. A compound according to any one of claims 1 to 26 for use in therapy.

29. A compound according to any one of claims 1 to 26 for use in the inhibition of a casein kinase I (CKI) or interleukin-1 receptor-associated kinase 1 (IRAKI).

30. A compound according to any one of claims 1 to 26 for use in the inhibition of a casein kinase I (CKI).

31. A compound according to any one of claims 1 to 26 for use in the inhibition of an interleukin-1 receptor-associated kinase 1 (IRAKI).

32. A compound according to any one of claims 1 to 26 for use in inducing antitumor response.

33. The compound for use according to claim 32, wherein said antitumor response comprises cancer immunotherapy response.

34. A compound according to any one of claims 1 to 26 for use in the treatment of a condition, symptom or disease associated with a malignant condition.

35. The compound for use according claim 34, wherein said malignant condition is cancer.

36. The compound for use according claim 34, wherein said malignant condition is selected from hematological malignancies, multiple myeloma, myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), melanoma, ER-negative breast cancer, diffuse large B cell lymphoma (DLBCL), chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL), and head and neck cancer.

37. The compound for use according claim 35, wherein said cancer has WT p53.

38. A compound according to any one of claims 1 to 26 for use in the treatment of cancer having WT p53, wherein said WT p53 is a biomarker for the said compound efficacy.

39. The compound for use according claim 35, wherein said cancer is selected from multiple myeloma, leukemia, malignant melanoma, breast cancer, prostate cancer, and colorectal cancer.

40. The compound for use according to any one of claims 34 to 39 in further inducing cancer immunotherapy response.

41. A compound according to any one of claims 1 to 26 for use in the treatment of an inflammatory or immune related disorder.

42. Use of the compound according to any one of claims 1 to 26 in the manufacture of a medicament for inhibiting a casein kinase I (CKI) or interleukin-1 receptor-associated kinase 1 (IRAK1).

43. Use of the compound according to any one of claims 1 to 26 in the manufacture of a medicament for inhibiting a casein kinase I (CKI).

44. Use of the compound according to any one of claims 1 to 26 in the manufacture of a medicament for inhibiting an interleukin-1 receptor-associated kinase 1 (IRAK1).

45. Use of the compound according to any one of claims 1 to 26 in the manufacture of a medicament for treating a condition, symptom, or disease associated with a malignant condition.

46. The use according to claim 45, wherein said malignant condition is cancer.

47. The use according to claim 46, wherein said cancer has WT p53.

48. The use according to claim 46, wherein said cancer is selected from leukemia, multiple myeloma, malignant melanoma, breast cancer, prostate cancer, and colorectal cancer.

49. The use according to claim 45, wherein said malignant condition is selected from hematological malignancies, multiple myeloma, myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), melanoma, ER-negative breast cancer, diffuse large B cell lymphoma (DLBCL), chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL), and head and neck cancer.

50. Use of the compound according to any one of claims 1 to 26 in the manufacture of a medicament for inducing an immunotherapy response.

51. Use of the compound according to any one of claims 1 to 26 in the manufacture of a medicament for treating an inflammatory or immune related disorder.