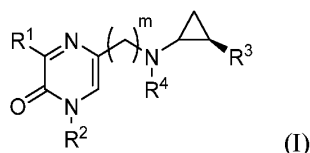


CLAIMS

What is claimed is:

1. A compound of structural Formula I:



or a salt or ester thereof, wherein:

m is chosen from 0, 1, 2, 3, and 4;

R^1 is a nitrogen-containing heterocycloalkyl or heteroaryl, either of which is optionally substituted with 1, 2, or 3 R^5 groups;

R^2 is H, or is chosen from alkyl, cycloalkyl, haloalkyl, heterocycloalkyl, aryl, and heteroaryl, any of which is optionally substituted with 1, 2, or 3 R^6 groups;

R^3 is chosen from aryl and heteroaryl, either of which is optionally substituted with 1, 2, or 3 R^7 groups;

each R^4 is independently chosen from hydrogen, alkyl, alkenyl, alkynyl, and cycloalkyl;

each R^5 is independently chosen from halogen, alkyl, alkenyl, alkynyl, hydroxy, amino, oxo, cyano, COR^8 , $CONR^8R^9$, $COOR^8$, $NHCOR^8$, $NHCONR^8R^9$, SOR^8 , SO_2R^8 , $NHSO_2R^8$, and $SO_2NR^8R^9$;

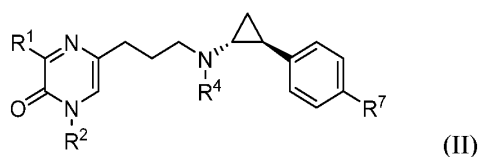
each R^6 is independently chosen from hydrogen, halogen, alkyl, alkylsulfonyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, haloalkoxy, haloaryl, alkoxyaryl, aryl, aryloxy, aralkyl, heterocycloalkyl, heteroaryl, alkylheteroaryl, heteroarylalkyl, cyano, alkoxy, alkoxyaryl, amino, alkylamino, dialkylamino, oxo, COR^8 , SO_2R^8 , $NHSO_2R^8$, $NHSO_2NHR^8$, $SO_2NR^8R^9$, $NHCOR^8$, $NHCONHR^8$, $CONHR^8$, and $CONR^8R^9$;

each R^7 is independently chosen from alkyl, amino, cyano, halo, and hydroxy; and

each R^8 and R^9 is independently chosen from hydrogen, aryl, and lower alkyl; or R^8 and R^9 may be taken together to form a nitrogen-containing heterocycloalkyl or heteroaryl ring, which is optionally substituted with lower alkyl.

2. The compound as recited in claim 1, wherein each R^4 is independently chosen from alkyl, cycloalkyl, and hydrogen.
3. The compound as recited in claim 2, wherein R^3 is aryl, and is optionally substituted with 1, 2, or 3 R^7 groups.

4. The compound as recited in claim 3, wherein R^3 is phenyl, and is optionally substituted with 1 or 2 R^7 groups.
5. The compound as recited in claim 4, wherein each R^7 is independently chosen from hydrogen and fluorine.
6. The compound as recited in claim 5, wherein R^7 is hydrogen.
7. The compound as recited in claim 5, wherein R^7 is fluorine.
8. The compound as recited in claim 1, having structural Formula II:



or a salt or ester thereof, wherein:

R^1 is a nitrogen-containing heterocycloalkyl or heteroaryl, either of which is optionally substituted with 1, 2, or 3 R^5 groups;

R^2 is H, or is chosen from alkyl, cycloalkyl, haloalkyl, heterocycloalkyl, aryl, and heteroaryl, any of which is optionally substituted with 1, 2, or 3 R^6 groups;

each R^4 is independently chosen from hydrogen, alkyl, alkenyl, alkynyl, and cycloalkyl;

each R^5 is independently chosen from halogen, alkyl, alkenyl, alkynyl, hydroxy, amino, oxo, cyano, COR^8 , $CONR^8R^9$, $COOR^8$, $NHCOR^8$, $NHCONR^8R^9$, SOR^8 , SO_2R^8 , $NHSO_2R^8$, and $SO_2NR^8R^9$;

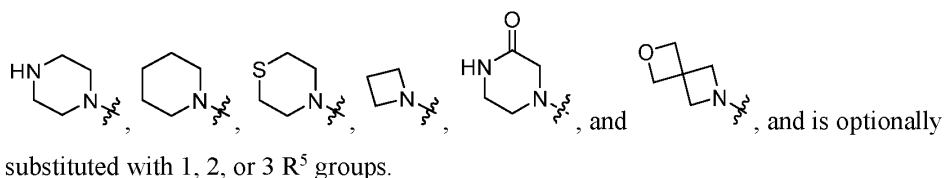
each R^6 is independently chosen from hydrogen, halogen, alkyl, alkylsulfonyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, haloalkoxy, haloaryl, alkoxyaryl, aryl, aryloxy, aralkyl, heterocycloalkyl, heteroaryl, alkylheteroaryl, heteroarylalkyl, cyano, alkoxy, alkoxyaryl, amino, alkylamino, dialkylamino, oxo, COR^8 , SO_2R^8 , $NHSO_2R^8$, $NHSO_2NHR^8$, $SO_2NR^8R^9$, $NHCOR^8$, $NHCONHR^8$, $CONHR^8$, and $CONR^8R^9$;

each R^7 is independently chosen from hydrogen, alkyl, amino, cyano, halo, and hydroxy; and

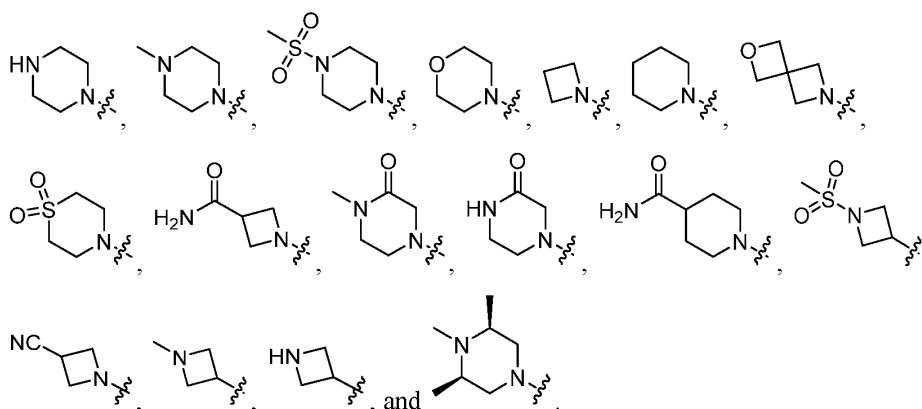
each R^8 and R^9 is independently chosen from hydrogen, aryl, and lower alkyl; or R^8 and R^9 may be taken together to form a nitrogen-containing heterocycloalkyl or heteroaryl ring, which is optionally substituted with lower alkyl.

9. The compound as recited in any one of claims 1 – 8, wherein each R^4 is independently chosen from methyl and hydrogen.
10. The compound as recited in claim 9, wherein R^4 is hydrogen.

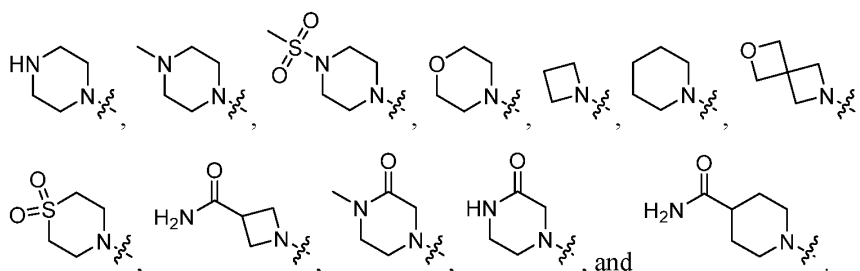
11. The compound as recited in claim 10, wherein R¹ is a nitrogen-containing heterocycloalkyl, which is optionally substituted with 1, 2, or 3 R⁵ groups.
12. The compound as recited in claim 11, wherein R¹ is chosen from:



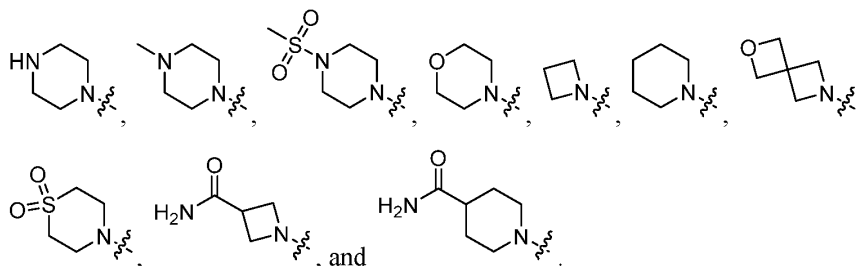
13. The compound as recited in claim 12, wherein each R⁵ is independently chosen from halogen, alkyl, hydroxy, amino, oxo, cyano, COR⁸, CONR⁸R⁹, COOR⁸, NHCOR⁸, NHCONR⁸R⁹, SOR⁸, SO₂R⁸, NHSO₂R⁸, and SO₂NR⁸R⁹.
14. The compound as recited in claim 13, wherein each R⁵ is independently chosen from alkyl, oxo, CONR⁸R⁹, COOR⁸, SOR⁸, and SO₂R⁸.
15. The compound as recited in claim 11, wherein R¹, with substitution R⁵ where appropriate, and further with substitutions R⁸ and R⁹ where appropriate, is chosen from:



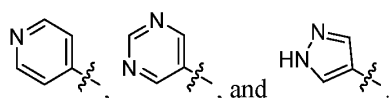
16. The compound as recited in claim 11, wherein R¹, with substitution R⁵ where appropriate, and further with substitutions R⁸ and R⁹ where appropriate, is chosen from:



17. The compound as recited in claim 11, wherein R¹, with substitution R_s where appropriate, and further with substitutions R⁸ and R⁹ where appropriate, is chosen from:

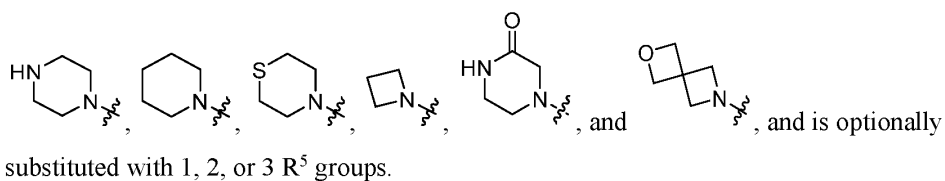


18. The compound as recited in claim 10, wherein R^1 is a nitrogen-containing heteroaryl, which is optionally substituted with 1, 2, or 3 R^5 groups.
19. The compound as recited in claim 18, wherein R^1 is chosen from:

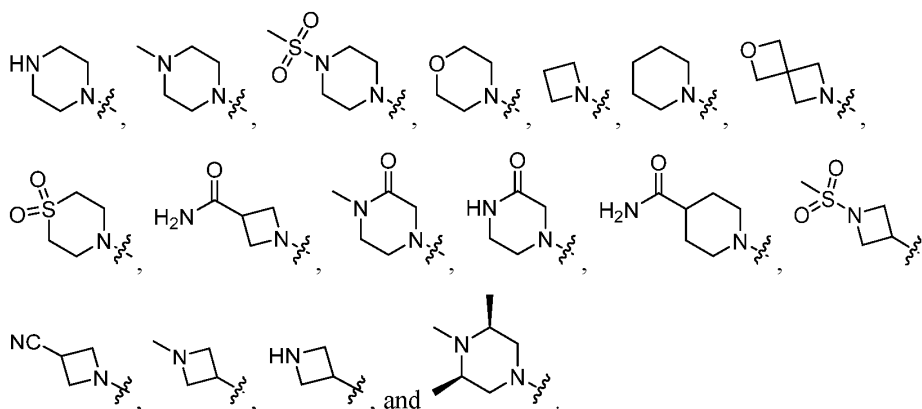


20. The compound as recited in claim 10, wherein R^2 is H.
21. The compound as recited in claim 10, wherein R^2 is chosen from aryl and heteroaryl, either of which is optionally substituted with 1 or 2 R^6 groups.
22. The compound as recited in claim 21, wherein each R^6 is independently chosen from halogen, alkyl, cycloalkyl, heterocycloalkyl, heteroaryl, alkylheteroaryl, heteroarylalkyl, cyano, COR^8 , SO_2R^8 , $NHSO_2R^8$, $NHSO_2NHR^8$, $SO_2NR^8R^9$, $NHCOR^8$, and $NHCONHR^8$.
23. The compound as recited in claim 22, wherein each R^6 is independently chosen from halogen, heteroaryl, alkylheteroaryl, SO_2R^8 , $NHSO_2R^8$, $NHSO_2NHR^8$, $SO_2NR^8R^9$, $NHCOR^8$, and $NHCONHR^8$.
24. The compound as recited in claim 23, wherein R^2 is chosen from phenyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, triazolyl, thiazolyl, pyridinyl, pyrazinyl, pyridazinyl, and pyrimidinyl, any of which is optionally substituted with 1 or 2 R^6 groups.
25. The compound as recited in claim 24, wherein R^2 is chosen from phenyl, pyridinyl, and pyrimidinyl, any of which is optionally substituted with 1 or 2 R^6 groups.
26. The compound as recited in claim 25, wherein:
- R^2 is phenyl substituted with one R^6 group; and
 - R^6 is chosen from heteroaryl and dimethylsulfonamido.
27. The compound as recited in claim 21, wherein R^6 is a heteroaryl chosen from triazolyl, pyrimidinyl, and pyridazinyl.
28. The compound as recited in claim 21, wherein each R^6 is independently chosen from halogen, cyano, alkoxy, alkoxyaryl, amino, alkylamino, and dialkylamino.

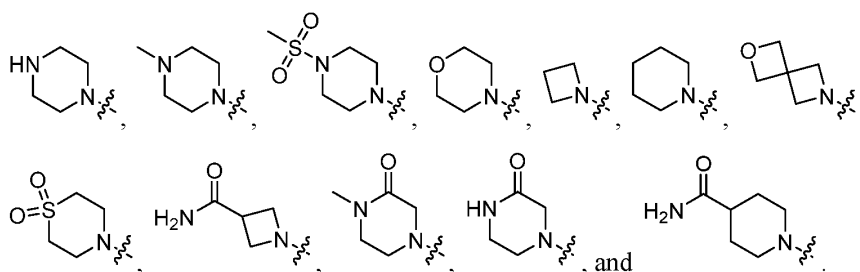
29. The compound as recited in claim 21, wherein R¹ is chosen from piperidine, morpholine, thiomorpholine, piperazine, pyrrolidine, azetidine, 2-azaspiro[3.3]heptane, 2,6-diazaspiro[3.3]heptane, and 2-oxa-6-azaspiro[3.3]heptane, and is optionally substituted with 1, 2, or 3 R⁵ groups.
30. The compound as recited in claim 29, wherein each R⁵ is independently chosen from halogen, alkyl, hydroxy, amino, oxo, cyano, COR⁸, CONR⁸R⁹, COOR⁸, NHCOR⁸, NHCONR⁸R⁹, SOR⁸, SO₂R⁸, NHSO₂R⁸, and SO₂NR⁸R⁹.
31. The compound as recited in claim 30, wherein each R⁵ is independently chosen from alkyl, oxo, CONR⁸R⁹, COOR⁸, SOR⁸, and SO₂R⁸.
32. The compound as recited in claim 31, wherein R₁ is chosen from:



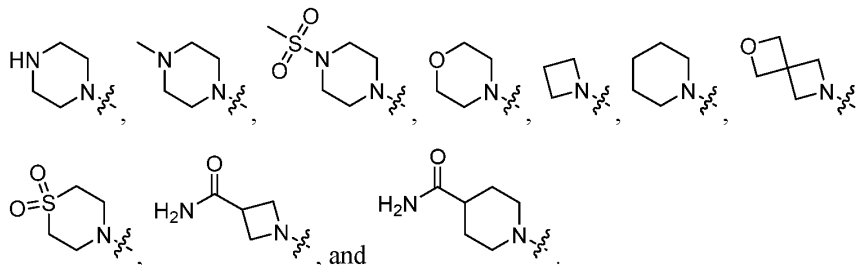
33. The compound as recited in claim 21, wherein R₁, with substitution R₅ where appropriate, and further with substitutions R⁸ and R⁹ where appropriate, is chosen from:



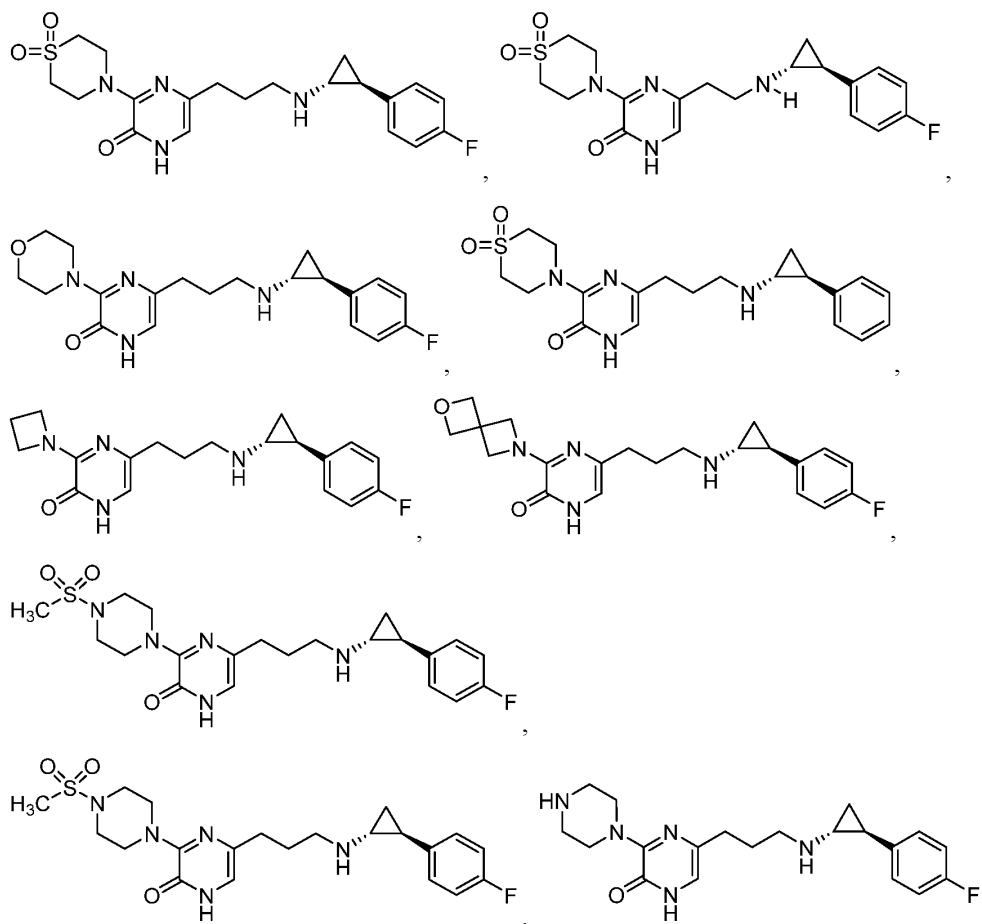
34. The compound as recited in claim 21, wherein R¹, with substitution R₅ where appropriate, and further with substitutions R⁸ and R⁹ where appropriate, is chosen from:

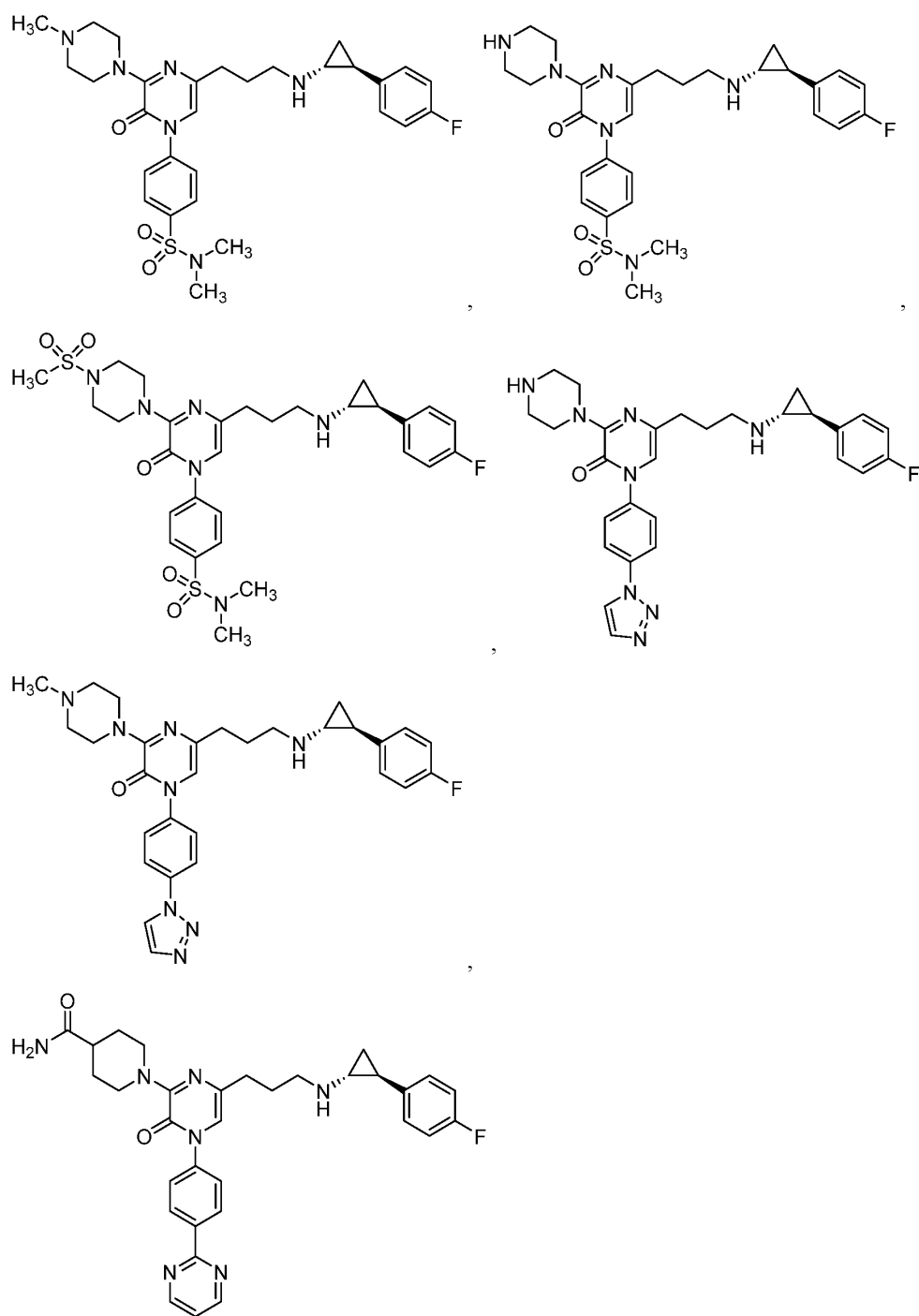


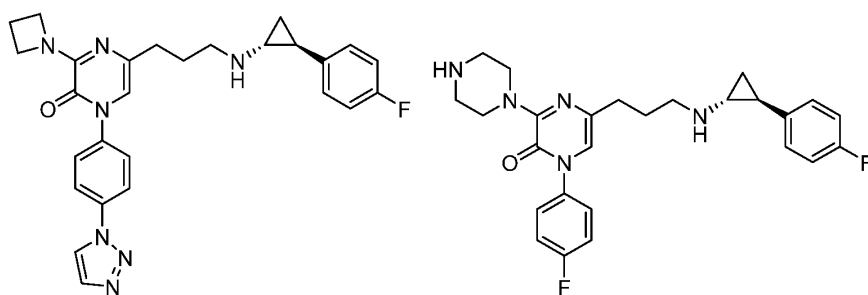
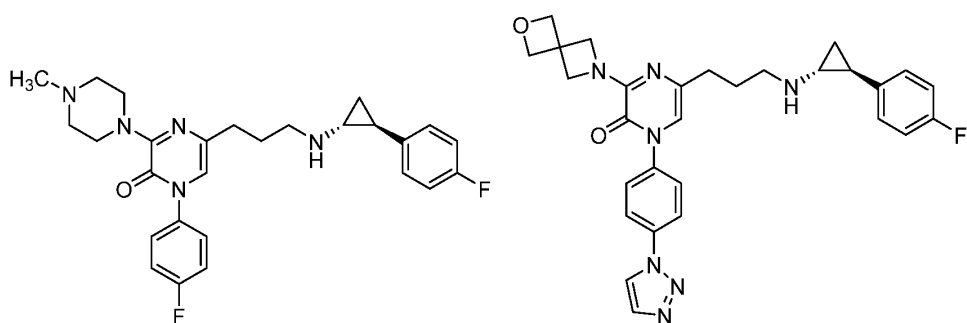
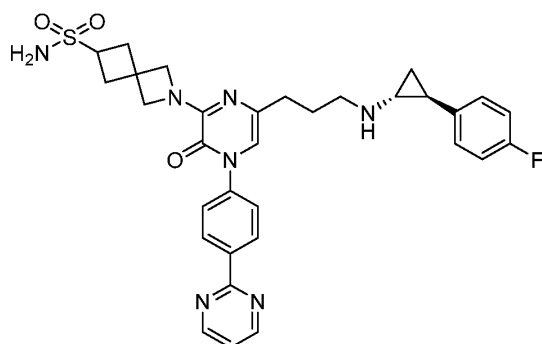
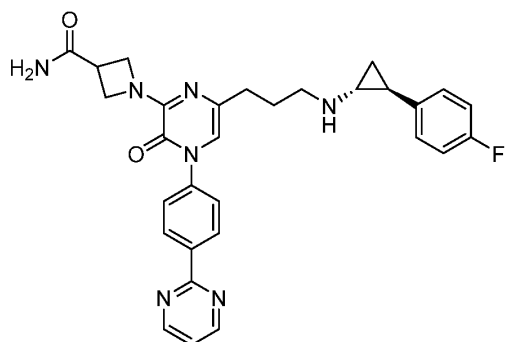
35. The compound as recited in claim 21, wherein R^1 , with substitution R_5 where appropriate, and further with substitutions R^8 and R^9 where appropriate, is chosen from:

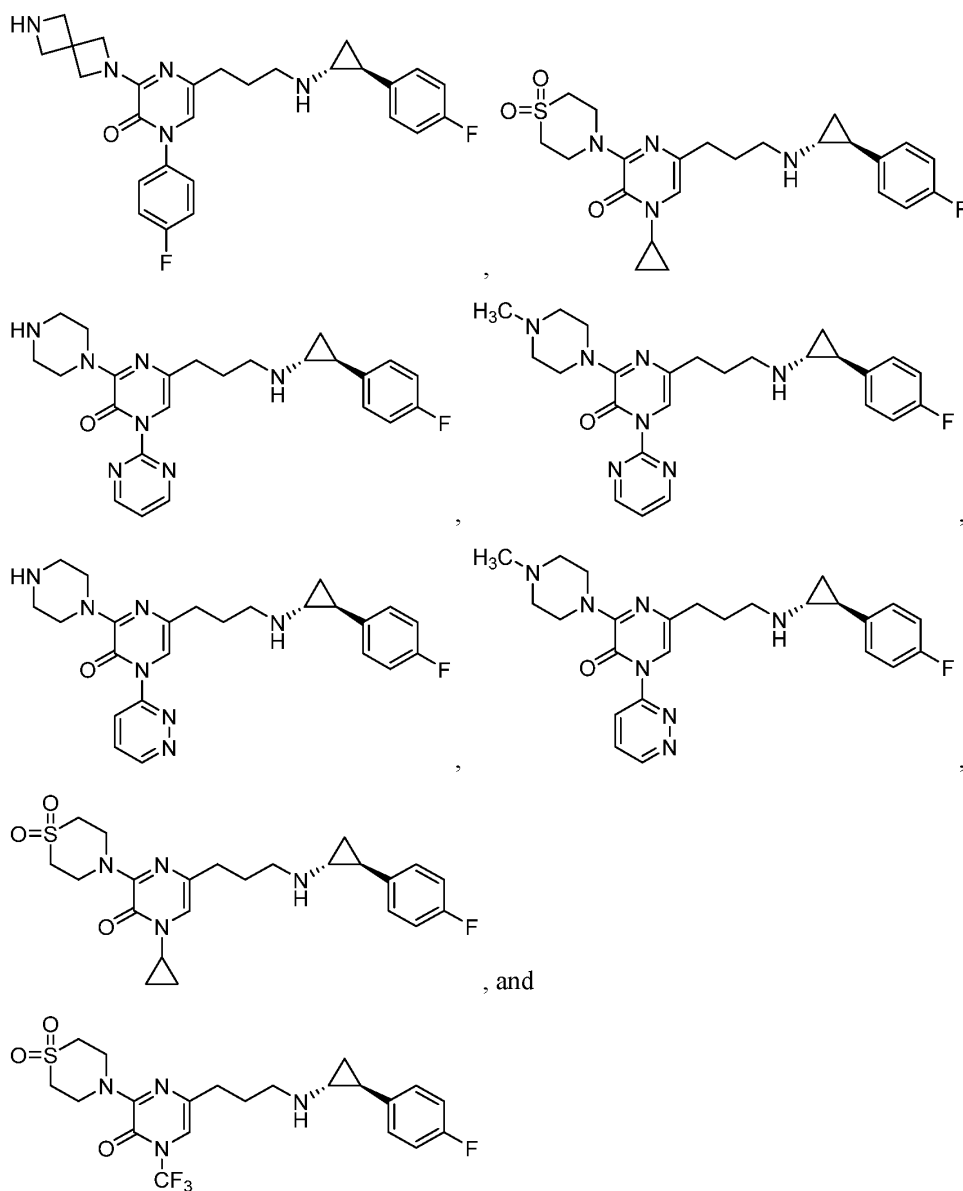


36. The compound as recited in claim 1, wherein the structure is chosen from:









37. A compound as recited in Claim 1 for use as a medicament.
38. A compound as recited in Claim 1 for use in the treatment of a KDM1A-mediated disease.
39. A compound as recited in Claim 1 for use in the manufacture of a medicament for the prevention or treatment of a disease or condition ameliorated by the inhibition of KDM1A.

40. A method of treatment of a KDM1A-mediated disease comprising the administration of a therapeutically effective amount of a compound as recited in Claim 1 to a patient in need thereof.
41. The method as recited in claim 40, wherein the disease is cancer.
42. The method as recited in claim 41, wherein the cancer is chosen from Ewing's sarcoma, multiple myeloma, T-cell leukemia, Wilm's tumor, small-cell lung cancer, bladder cancer, prostate cancer, breast cancer, head/ neck cancer, colon cancer, and ovarian cancer.
43. The method as recited in claim 40, wherein the disease is a myeloid disease.
44. The method as recited in claim 43, wherein the myeloid disease is chosen from Myelofibrosis, Polycythemia Vera, Essential Thrombocythemia, Myelodysplastic Syndrome (MDS), Acute Myelogenous Leukemia (AML), and Chronic Myelogenous Leukemia (CML).
45. The method as recited in claim 40, wherein the disease is an inflammatory disease.
46. The method as recited in claim 45, wherein the inflammatory disease is chosen from inflammatory bowel disease, rheumatoid arthritis, or systemic lupus erythematosus.
47. A method of treatment of a KDM1A-mediated disease comprising the administration of:
- a. a therapeutically effective amount of a compound as recited in Claim 1; and
 - b. another therapeutic agent.
48. The method as recited in Claim 47, wherein said disease is cancer.
49. The method as recited in Claim 47, wherein said disease is a myeloid disease.
50. The method as recited in Claim 47, wherein said disease is an inflammatory disease.
51. The method as recited in Claim 47, wherein said other agent is chosen from a DNA methyltransferase inhibitor, a histone deacetylase inhibitor, a histone de-sumoylase inhibitor, a histone de-ubiquitinase inhibitor, a histone phosphatase inhibitor, an antisense RNA that inhibits the expression of other components of the protein complex bound at the DR site in the gamma globin promoter, a Klf1 inhibitor, an agent that inhibits expression of *KLF1*, a Bcl11a inhibitor, an agent that inhibits the expression of *BCL11A*, an agent that inhibits cell cycle progression, and an agent that induce differentiation in leukemic cells.
52. A method of treatment of a globin-mediated disease comprising the administration of a therapeutically effective amount of a compound as recited in claim 1, or a salt, polymorph, or solvate thereof, to a patient in need thereof.

53. A pharmaceutical composition comprising a compound as recited in claim 1, or a salt, polymorph, or solvate thereof, together with a pharmaceutically acceptable carrier.
54. The pharmaceutical composition as recited in claim 53, formulated for oral administration.
55. The pharmaceutical composition as recited in claim 53, additionally comprising another therapeutic agent.
56. A method of inhibition of KDM1A comprising contacting KDM1A with a compound as recited in claim 1, or a salt, polymorph, or solvate thereof.
57. A method for achieving an effect in a patient comprising the administration of a therapeutically effective amount of a compound, or a salt, polymorph, or solvate thereof, as disclosed herein, or a salt thereof, to a patient, wherein the effect is chosen from an elevation of red blood cell count, an elevation of the red blood cell count of red cells containing fetal hemoglobin, an elevation in the total concentration of fetal hemoglobin in red cells, an elevation in the total concentration of fetal hemoglobin in reticulocytes, an increase in the transcription of the gamma globin gene in bone marrow-derived red cell precursors, e.g., pro-erythroblasts, a reduction in the number of sickle cell crises a patient experiences over a unit period of time, a halt to or prevention of tissue damage e.g., in the heart, spleen, brain or kidney caused by sickling cells, a reduction in the proportion of red cells that undergo sickling under physiological conditions of relative hypoxia as measured using patient blood in an in vitro assay, an increase in the amount of histone 3 lysine methylation at lysine position 4 (H3K4me1 and H3K4me2), and/or a decrease in the amount of histone 3 methylation at lysine position 9 (H3K9me1 or H3K4me2) near or at the gamma globin promoter as assayed by ChIP using cells derived from a treated patient.
58. A method of inhibiting at least one KDM1A function comprising the step of contacting KDM1A with a compound as recited in claim 1, or a salt, polymorph, or solvate thereof, wherein the inhibition is measured by phenotype of red cells or their precursors either cultured or in vivo in humans or mouse or transgenic mice containing the human beta globin locus or portions thereof, the ability of cancer cells to proliferate, become differentiated, or induced to undergo apoptosis, the expression of specific genes known to be regulated by KDM1A activity such as gamma globin or HOXA9, a change in the histone methylation states, a change in the methylation state of proteins known to be demethylated by KDM1A such as G9a, p53, DNMT1 or SUV39H1, expression of

KDM1A-regulated genes, or binding of KDM1A with a natural binding partner such as CoREST, NuRD, DNMT1 or HDACs.