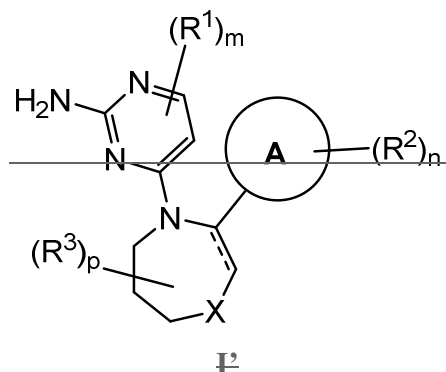


CLAIMS

1. ~~_____~~ A compound of formula **I'**:



or a pharmaceutically acceptable salt thereof, wherein:

Ring A is ring selected from phenyl, a 5-7 membered saturated or partially unsaturated carbocyclic ring, a 8-12 membered saturated or partially unsaturated bicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or an 8-10 membered bicyclic heteroaromatic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R^1 is independently hydrogen, or C_{1-3} -aliphatic optionally substituted by 1-6 halogen; or two R^1 -groups are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused carbocyclic ring;

each of R^2 is independently hydrogen, halogen, CN , NO_2 , $C(O)OR$, $C(O)NR_2$, NR_2 , $NRC(O)R$, $NRC(O)OR$, $NRS(O)_2R$, OR , $P(O)R_2$, SR , $S(O)R$, $S(O)_2R$, $S(O)(NH)R$, $S(O)_2NR_2$, or R ; or

two R^2 -groups are optionally taken together to form $=O$; or

two R^2 -groups are optionally taken together with their intervening atoms to form a 3-8 membered saturated spirocyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R^3 is independently hydrogen, OH , or C_{1-3} -aliphatic; or

two R^3 -groups are optionally taken together to form $=O$; or

two R^3 -groups are optionally taken together to form $=CH_2$; or

~~two R³-groups are optionally taken together with their intervening atoms to form a 3-8 membered saturated spirocyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur; or~~

~~two R³-groups are optionally taken together with their intervening atoms to form a 5-8 membered saturated bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur;~~

~~each R is independently hydrogen or an optionally substituted group selected from C₁₋₆-aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, a 7-10 membered saturated spirobicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 7-10 membered saturated or partially unsaturated fused bicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 4-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or:~~

~~two R-groups on the same nitrogen are optionally taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1-2 oxo-groups;~~

~~----- is a single bond or a double bond;~~

~~X is O, N(R), N(S(O)₂(R)), S, S(O), S(O)₂, CH₂, CH(R³), or C(R³)₂;~~

~~m is 0, 1, or 2;~~

~~n is 0, 1, 2, 3, 4 or 5; and~~

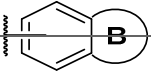
~~p is 0, 1, or 2.~~

~~2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein Ring A is phenyl.~~

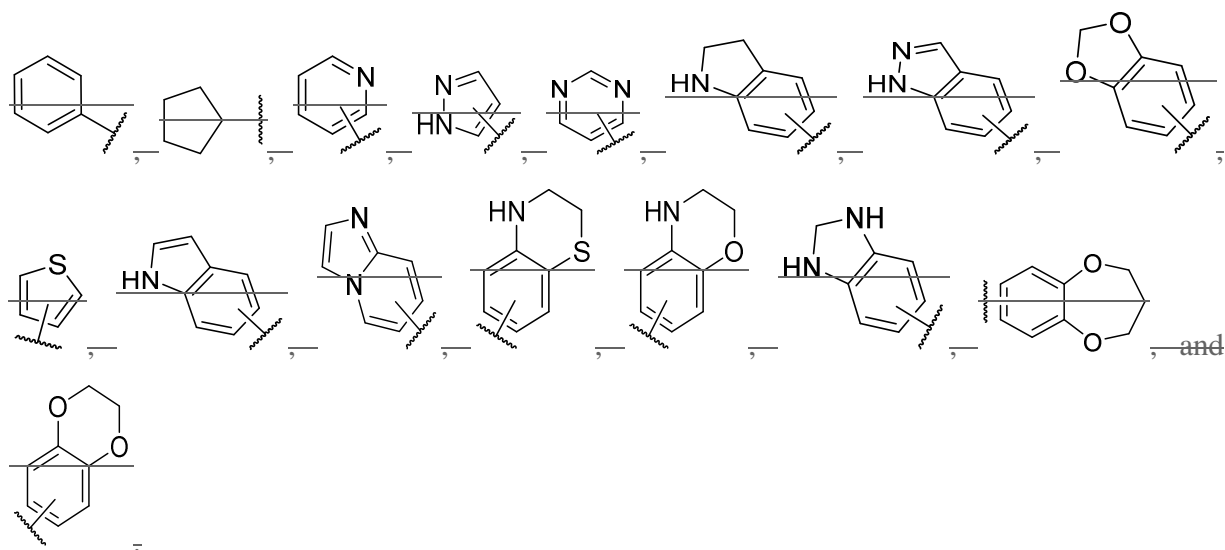
~~3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein Ring A is a 8-12 membered saturated or partially unsaturated bicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur.~~

4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein Ring A is an 8-10 membered bicyclic heteroaromatic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

5. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein Ring A

is , wherein Ring B is 5-7 membered partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or Ring B is 5-6 membered heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein Ring A is selected from:



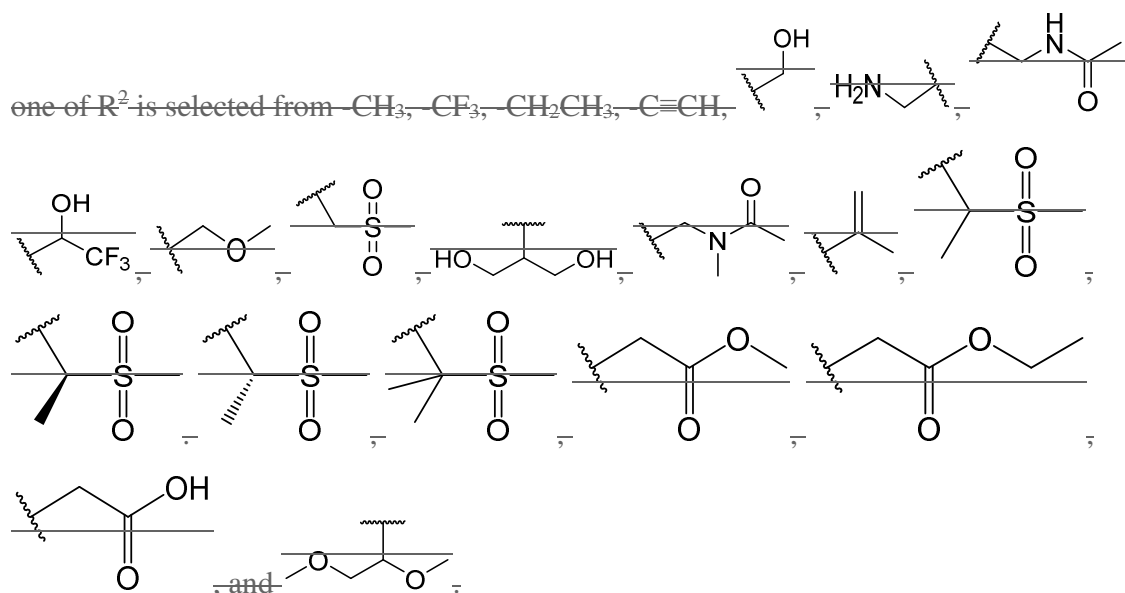
7. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^1 is C_{1-3} -aliphatic.

8. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^1 is CH_3 .

9. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^1 is attached to position 6 of the pyrimidine.

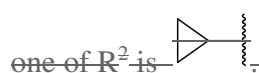
10. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is C_{1-6} aliphatic, optionally substituted 1-4 times by halogen, OH , NH_2 , OCH_3 , $NHC(O)CH_3$, $S(O)_2CH_3$, $COOH$, CO_2CH_3 , $CO_2C_2H_5$, or $N(CH_3)C(O)CH_3$.

11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein at least



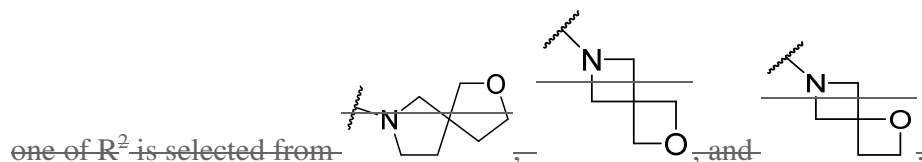
12. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is a 3-6 membered saturated monocyclic carbocyclic ring.

13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein at least



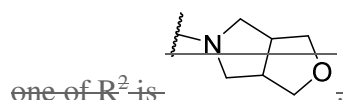
14. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is a 7-10 membered saturated spirobicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen or oxygen.

15. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein at least

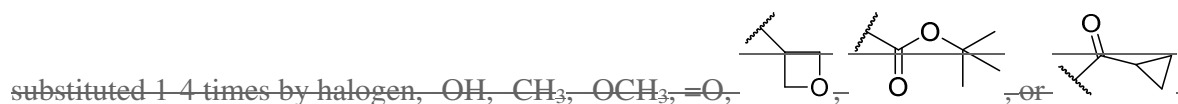


16. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is a 7-10 membered saturated fused bicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen or oxygen.

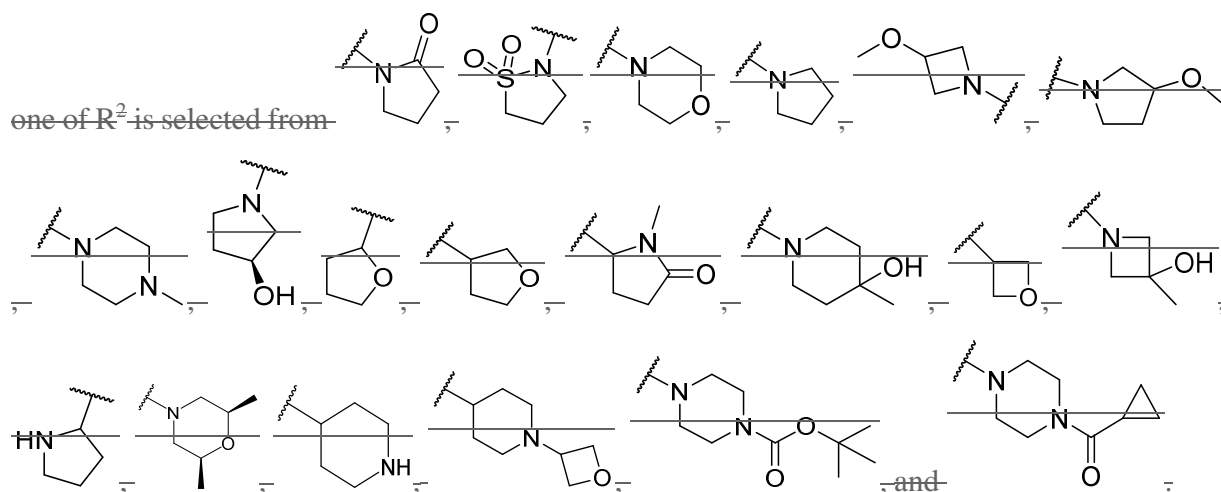
17. The compound of claim 16, or a pharmaceutically acceptable salt thereof, wherein at least



18. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is a 4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, optionally

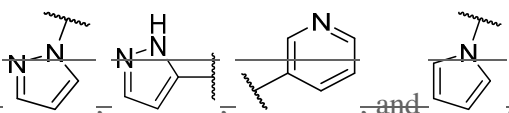


19. The compound of claim 18, or a pharmaceutically acceptable salt thereof, wherein at least



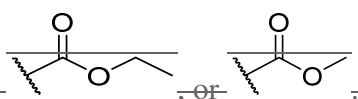
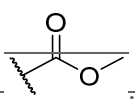
20. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is a 5-6 membered monocyclic heteroaromatic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

21. — The compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein at least

one of R^2 is selected from .

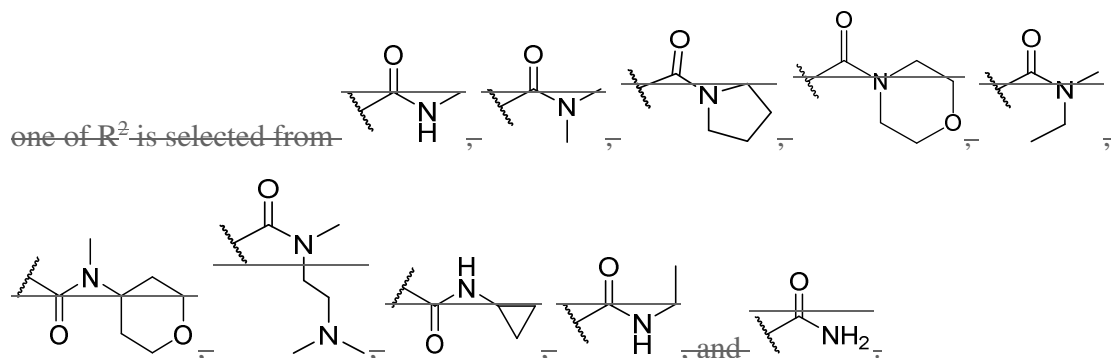
22. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $C(O)OR$, wherein R is hydrogen or C_{1-6} aliphatic.

23. — The compound of claim 22, or a pharmaceutically acceptable salt thereof, wherein at least

one of R^2 is $C(O)OH$, , or .

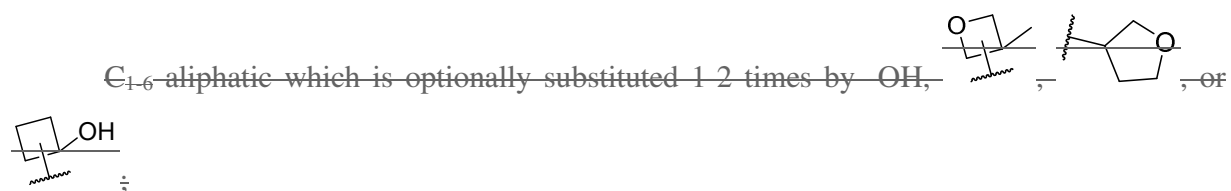
24. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $C(O)NR_2$, wherein each of R is independently hydrogen, C_{1-6} aliphatic which is optionally substituted by a $N(CH_3)_2$, unsubstituted 3-6 membered saturated monocyclic carbocyclic ring, or unsubstituted 4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen or oxygen, or two R taken together with their intervening atoms to form a 4-7 membered saturated and unsubstituted ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen and sulfur.

25. The compound of claim 24, or a pharmaceutically acceptable salt thereof, wherein at least



26. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is NR_2 , wherein each of R is independently:

hydrogen;

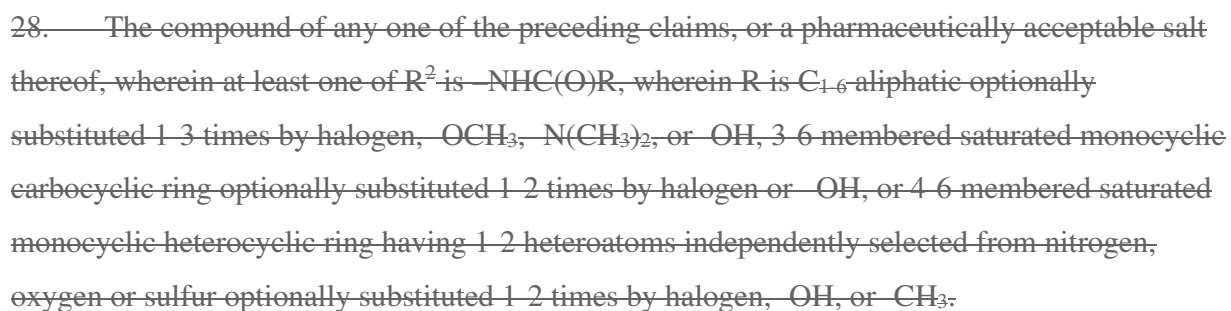


unsubstituted 3-6 membered saturated monocyclic carbocyclic ring;

4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen or oxygen, which is optionally substituted 1-2 times by CH_3 , OH, $C(O)OC(CH_3)_3$, or $C(O)CH_3$; or

6 membered monocyclic heteroaromatic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur which is optionally substituted 1-2 times by CH_3 or NH_2 .

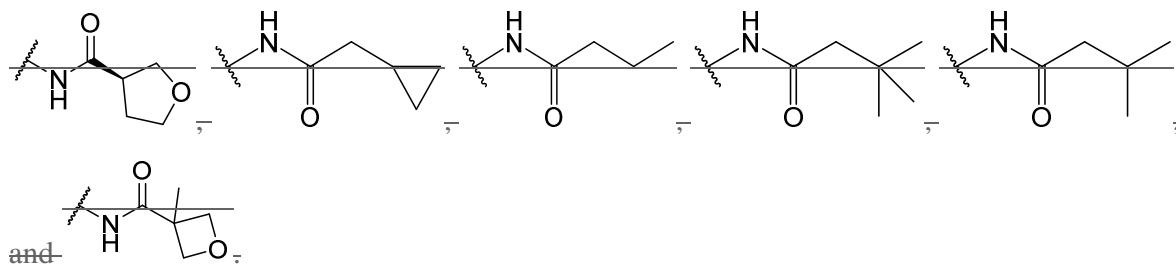
27. The compound of claim 26, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is selected from:



one of R^2 is selected from—

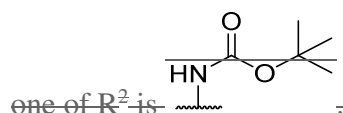
The structures shown are:

- Row 1:
 - NH-C(=O)-CH_3
 - $\text{NH-C(=O)-CH}_2\text{-O-CH}_3$
 - NH-C(=O)-C(F)(F)F
 - $\text{NH-C(=O)-CH}_2\text{-N(CH}_3)_2$
- Row 2:
 - $\text{NH-C(=O)-CH}_2\text{-CH}_2\text{-OH}$
 - $\text{NH-C(=O)-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O}$
 - $\text{NH-C(=O)-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O}$
 - $\text{NH-C(=O)-CH}_2\text{-CH}_2\text{-OH}$
 - $\text{NH-C(=O)-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O}$
 - $\text{NH-C(=O)-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O}$
- Row 3:
 - NH-C(=O)-C(F)(F)F
 - NH-C(=O)-C(F)(F)F
 - $\text{NH-C(=O)-C(CH}_3)_3$
 - $\text{NH-C(=O)-C(CH}_3)_3$
 - NH-C(=O)-C(F)(F)F
 - $\text{NH-C(=O)-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O}$



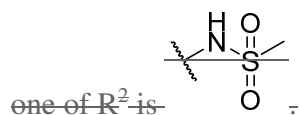
30. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is NHC(O)OR , wherein R is unsubstituted C_{1-6} aliphatic.

31. — The compound of claim 30, or a pharmaceutically acceptable salt thereof, wherein at least



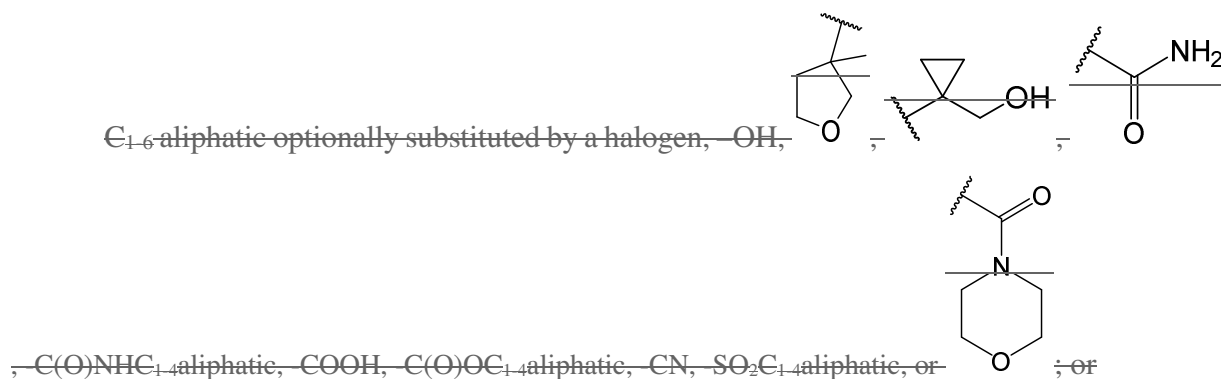
32. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $\text{NHS(O)}_2\text{R}$, wherein R is unsubstituted C_{1-6} aliphatic.

33. — The compound of claim 32, or a pharmaceutically acceptable salt thereof, wherein at least



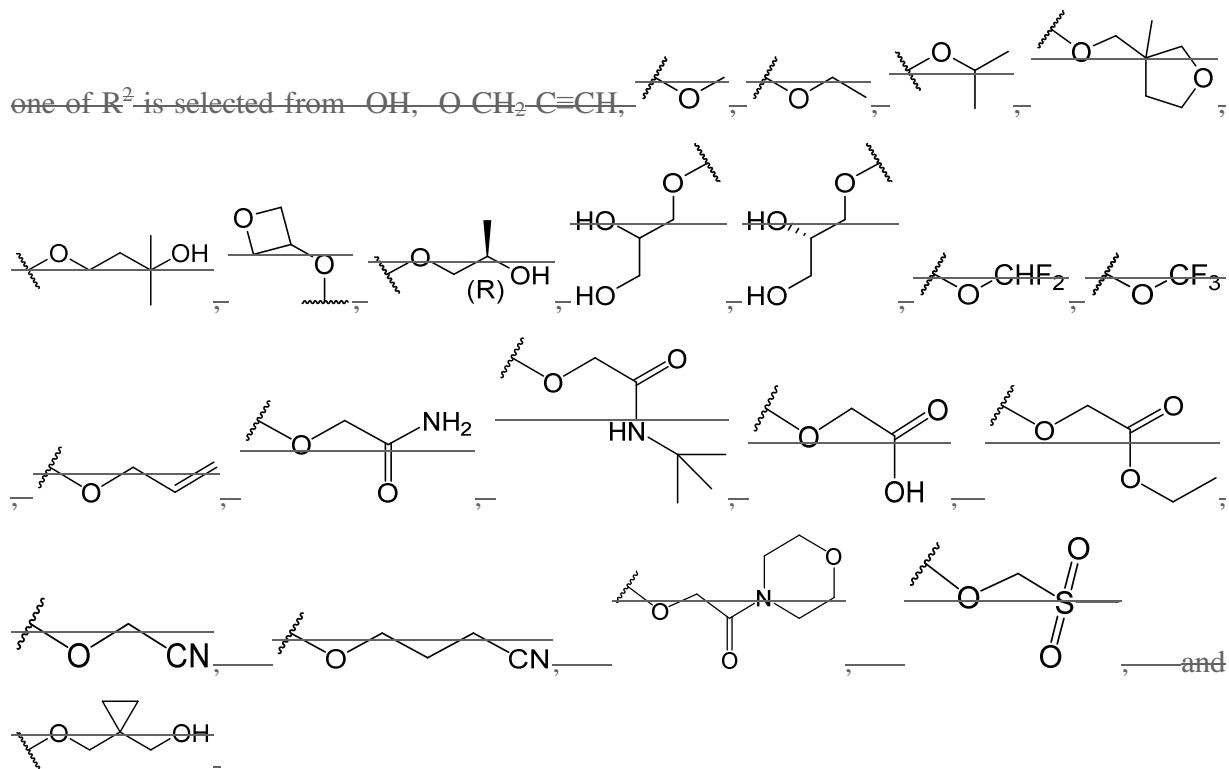
34. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is OR , wherein R is:

hydrogen;



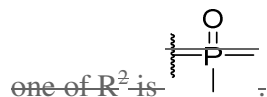
~~4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen or oxygen.~~

35. ~~The compound of claim 34, or a pharmaceutically acceptable salt thereof, wherein at least~~



36. ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R² is P(O)R₂, wherein each of R is independently unsubstituted C₁₋₆-aliphatic.~~

37. ~~The compound of claim 36, or a pharmaceutically acceptable salt thereof, wherein at least~~



38. ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R² is SR, wherein R is unsubstituted C₁₋₆-aliphatic.~~

39. — The compound of claim 38, or a pharmaceutically acceptable salt thereof, wherein at least

one of R^2 is .

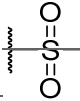
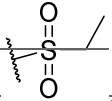
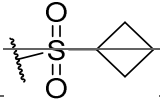
40. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $S(O)R$, wherein R is unsubstituted C_{1-6} aliphatic.

41. — The compound of claim 39, or a pharmaceutically acceptable salt thereof, wherein at least

one of R^2 is .

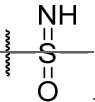
42. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $S(O)_2R$, where R is unsubstituted C_{1-6} aliphatic or 3-6 membered saturated monocyclic carbocyclic ring.

43. — The compound of claim 42, or a pharmaceutically acceptable salt thereof, wherein at least

one of R^2 is selected from , , and .

44. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $S(O)(NH)R$, wherein R is unsubstituted C_{1-6} aliphatic.

45. — The compound of claim 44, or a pharmaceutically acceptable salt thereof, wherein at least

one of R^2 is .

46. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $S(O)_2NR_2$.

47. — The compound of claim 46, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $S(O)_2NH_2$.

48. — ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^3 is C_{1-3} -aliphatic.~~

49. — ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein X is —O—.~~

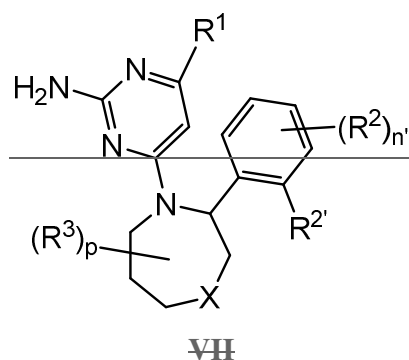
50. — ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein m is 1.~~

51. — ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein p is 0.~~

52. — ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein n is 1, 2, 3, 4, or 5.~~

53. — ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein ~~-----~~ is a single bond.~~

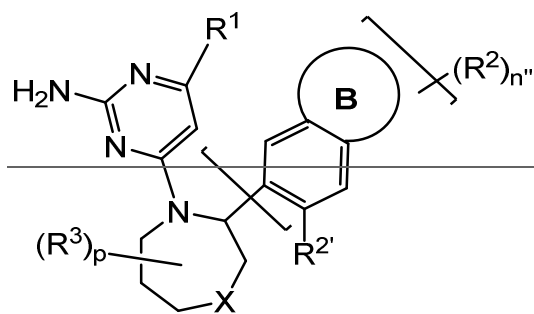
54. — ~~The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula VII~~



~~or a pharmaceutically acceptable salt thereof, wherein:~~
 ~~n' is 1 or 2; and~~

$R^{2'}$ is halogen or OC_{1-3} -aliphatic.

55. — The compound of any one of the claims 1-53, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula VIII



or a pharmaceutically acceptable salt thereof, wherein:

Ring B is 5-7 membered partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or Ring B is 5-6 membered heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

n'' is 0, 1, 2, 3, or 4; and

$R^{2'}$ is halogen or OC_{1-3} -aliphatic.

56. — The compound of claims 54 or 55, or a pharmaceutically acceptable salt thereof, wherein $R^{2'}$ is halogen or OC_{1-3} -aliphatic.

57. — The compound of any one of claims 54-56, or a pharmaceutically acceptable salt thereof, wherein $R^{2'}$ is Cl.

58. — The compound of any one of claims 54-56, or a pharmaceutically acceptable salt thereof, wherein $R^{2'}$ is OCH_3 .

59. — The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the compounds depicted in Tables 1, 2, and 2A.

60. — ~~A pharmaceutical composition comprising a compound according to any one of claims 1 to 59, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.~~

61. — ~~A method for treating a cellular proliferative disorder in a patient comprising administering to said patient a compound according to any one of claims 1 to 59, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof.~~

62. — ~~The method of claim 61, further comprising determining the Wolframin (WFS1) expression level.~~

63. — ~~The method of claims 61 or 62, wherein the cellular proliferative disorder is cancer.~~

64. — ~~The method of any one of claims 61–63, wherein the cellular proliferative disorder is selected from non-small cell lung cancer (NSCLC), myeloma, hepatocellular carcinoma (HCC), breast cancer, colorectal cancer, endometrial cancer, cancer of the esophagus, pancreatic cancer, renal cell carcinoma, and melanoma.~~

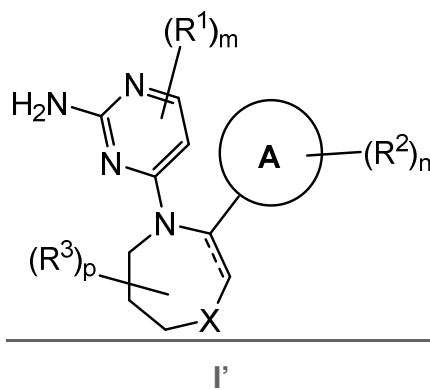
65. — ~~A method for inducing ER stress in a patient in need thereof, comprising administering to said patient a compound according to any one of claims 1 to 59, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof.~~

66. — ~~A method for inducing the unfolded protein response (UPR) in a patient in need thereof, comprising administering to said patient a compound according to any one of claims 1 to 59, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof.~~

67. — ~~A method for causing calcium release from the endoplasmic reticulum (ER) via a putative Ca^{2+} channel known as Wolframin (WFS1) in a patient in need thereof, comprising administering to said patient a compound according to any one of claims 1 to 59, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof.~~

68. ~~The compound according to any one of claims 1 to 59, or a pharmaceutically acceptable salt thereof, for use in the treatment of a cellular proliferative disorder.~~

1. A compound of formula I':



or a pharmaceutically acceptable salt thereof, wherein:

Ring A is ring selected from phenyl, a 5-7 membered saturated or partially unsaturated carbocyclic ring, a 8-12 membered saturated or partially unsaturated bicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 5-6 membered heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or an 8-10 membered bicyclic heteroaromatic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each R¹ is independently hydrogen, or C₁₋₃ aliphatic optionally substituted by 1-6 halogen; or

two R¹ groups are optionally taken together with their intervening atoms to form a 5-8 membered partially unsaturated fused carbocyclic ring;

each of R² is independently hydrogen, halogen, -CN, -NO₂, -C(O)OR, -C(O)NR₂, -NR₂, -NRC(O)R, -NRC(O)OR, -NRS(O)₂R, -OR, -P(O)R₂, -SR, -S(O)R, -S(O)₂R, -S(O)(NH)R, -S(O)₂NR₂, or R; or

two R² groups are optionally taken together to form =O; or

two R² groups are optionally taken together with their intervening atoms to form a 3-8 membered saturated spirocyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R³ is independently hydrogen, -OH, or C₁₋₃ aliphatic; or

two R³ groups are optionally taken together to form =O; or

two R³ groups are optionally taken together to form =CH₂; or

two R³ groups are optionally taken together with their intervening atoms to form a 3-8 membered saturated spirocyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur; or

two R³ groups are optionally taken together with their intervening atoms to form a 5-8 membered saturated bridged bicyclic ring having 0-2 heteroatoms independently selected from nitrogen, oxygen or sulfur;

each R is independently hydrogen or an optionally substituted group selected from C₁₋₆ aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, a 7-10 membered saturated spirobicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 7-10 membered saturated or partially unsaturated fused bicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 4-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered monocyclic heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or:

two R groups on the same nitrogen are optionally taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or heteroaryl ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1-2 oxo groups;

----- is a single bond or a double bond;

X is -O-, -N(R)-, -N(S(O)₂(R))-, -S-, -S(O)-, -S(O)₂-, -CH₂-, -CH(R³)-, or -C(R³)₂-

:

m is 0, 1, or 2;

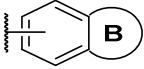
n is 0, 1, 2, 3, 4 or 5; and

p is 0, 1, or 2.

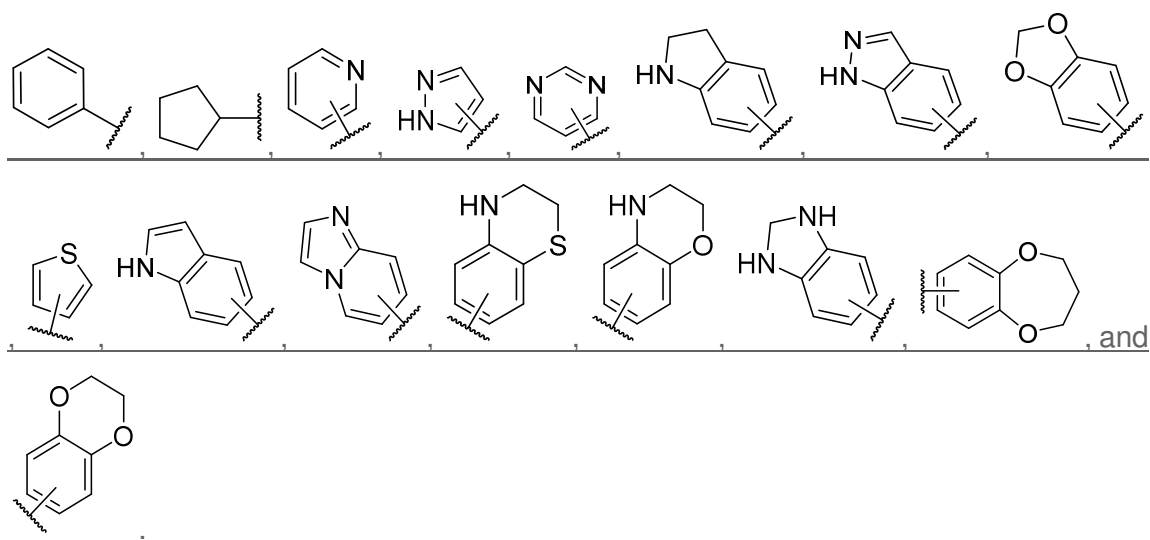
2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein Ring A is phenyl; or:

wherein Ring A is a 8-12 membered saturated or partially unsaturated bicyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or:

wherein Ring A is an 8-10 membered bicyclic heteroaromatic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or:

wherein Ring A is , wherein Ring B is 5-7 membered partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or Ring B is 5-6 membered heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or:

wherein Ring A is selected from:



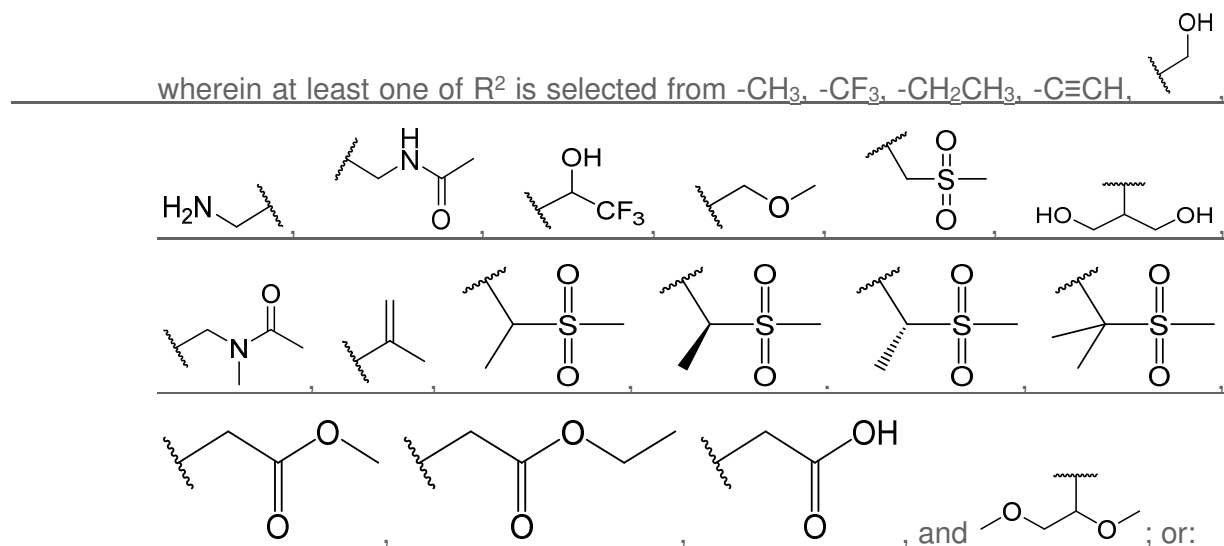
3. The compound of claim 1 or claim 2, or a pharmaceutically acceptable salt thereof, wherein at least one of R¹ is C₁₋₃ aliphatic; or:

wherein at least one of R¹ is -CH₃; and/or:

wherein at least one of R¹ is attached to position 6 of the pyrimidine.

4. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R² is C₁₋₆ aliphatic, optionally substituted 1-4 times

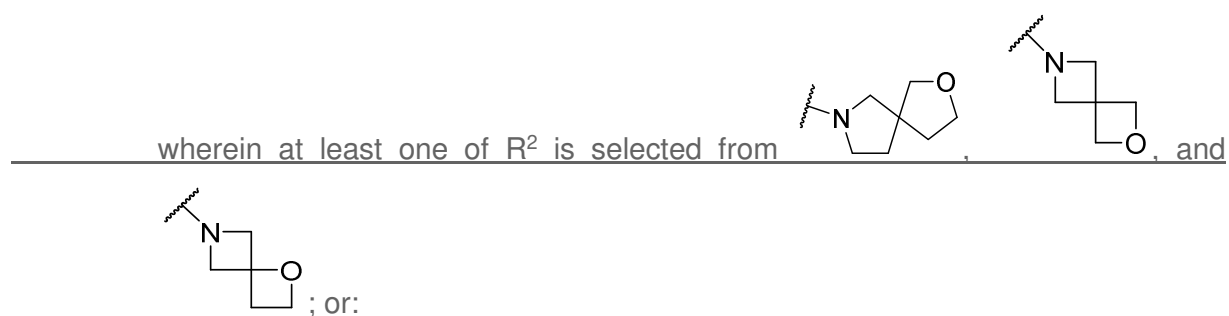
by halogen, -OH, NH₂, -OCH₃, -NHC(O)CH₃, -S(O)₂CH₃, -COOH, -CO₂CH₃, -CO₂C₂H₅,
or -N(CH₃)C(O)CH₃; optionally:



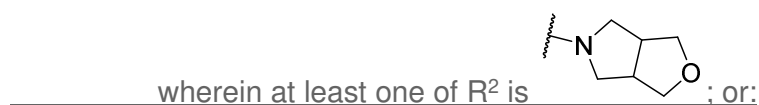
wherein at least one of R² is a 3-6 membered saturated monocyclic carbocyclic ring;
optionally:



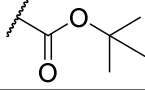
wherein at least one of R² is a 7-10 membered saturated spirobicyclic heterocyclic ring
having 1-2 heteroatoms independently selected from nitrogen or oxygen; optionally:

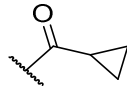


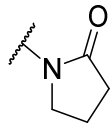
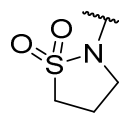
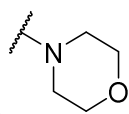
wherein at least one of R² is a 7-10 membered saturated fused bicyclic heterocyclic ring
having 1-2 heteroatoms independently selected from nitrogen or oxygen; optionally:

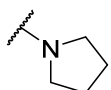
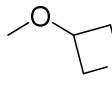
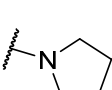
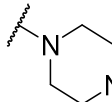
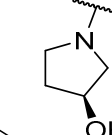
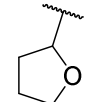
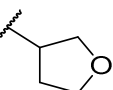


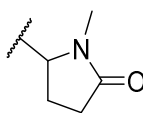
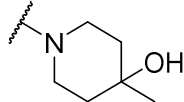
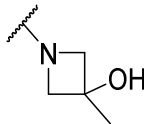
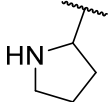
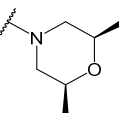
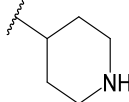
wherein at least one of R² is a 4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur,

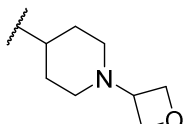
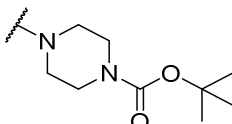
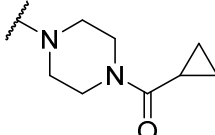
optionally substituted 1-4 times by halogen, -OH, -CH₃, -OCH₃, =O, , ,

, or ; optionally:

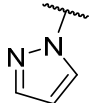
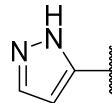
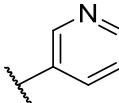
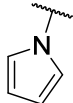
wherein at least one of R² is selected from , , ,

, , , , , , ,

, , , , , , ,

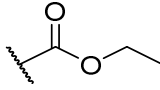
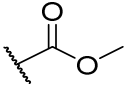
, , and ; or:

wherein at least one of R² is a 5-6 membered monocyclic heteroaromatic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur; optionally:

wherein at least one of R² is selected from , , , and ,

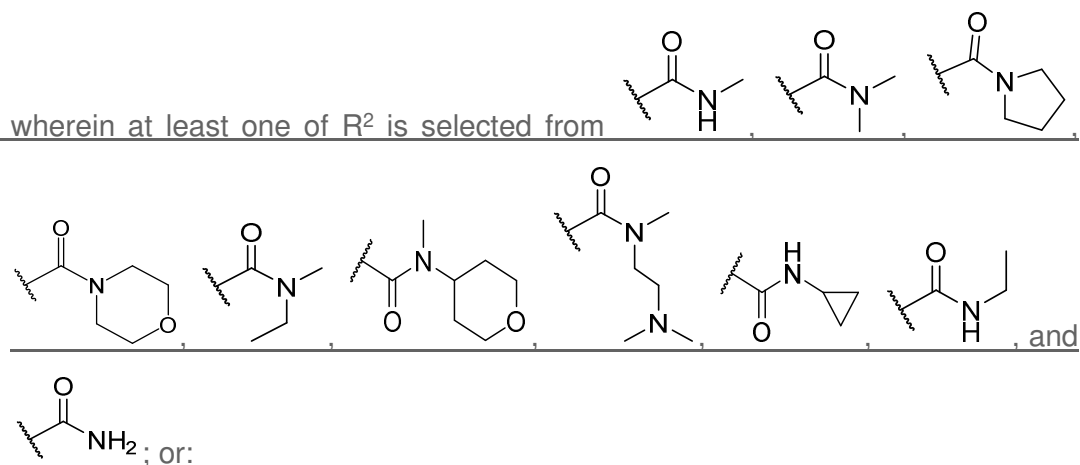
; or:

wherein at least one of R² is -C(O)OR, wherein R is hydrogen or C₁₋₆ aliphatic; optionally:

wherein at least one of R² is -C(O)OH, , or ; or:

wherein at least one of R² is -C(O)NR₂, wherein each of R is independently hydrogen, C₁₋₆ aliphatic which is optionally substituted by a -N(CH₃)₂, unsubstituted 3-6 membered

saturated monocyclic carbocyclic ring, or unsubstituted 4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen or oxygen, or two R taken together with their intervening atoms to form a 4-7 membered saturated and unsubstituted ring having 0-3 heteroatoms, in addition to the nitrogen, independently selected from nitrogen, oxygen and sulfur; optionally:



wherein at least one of R² is -NR₂, wherein each of R is independently:

hydrogen;

C₁₋₆ aliphatic which is optionally substituted 1-2 times by -OH,



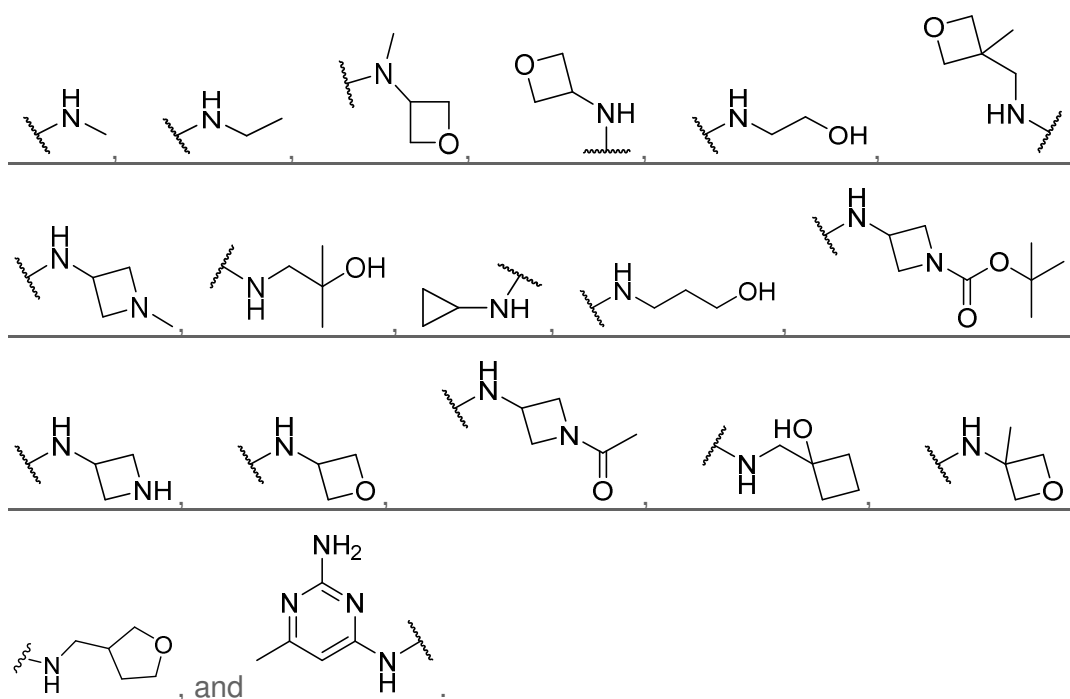
or

unsubstituted 3-6 membered saturated monocyclic carbocyclic ring;

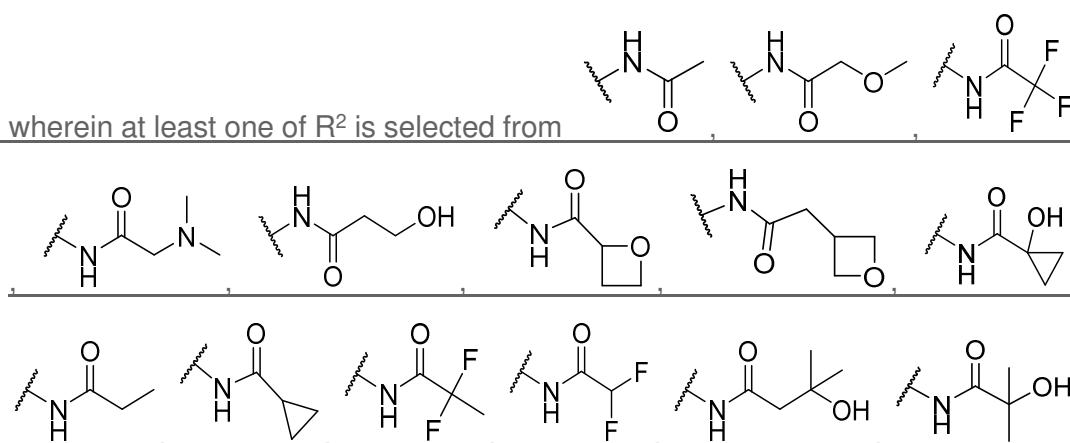
4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen or oxygen, which is optionally substituted 1-2 times by CH₃, -OH, -C(O)OC(CH₃)₃, or -C(O)CH₃; or

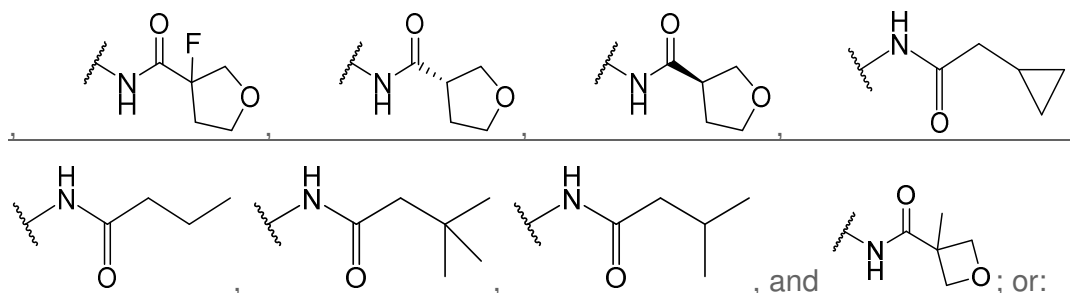
6 membered monocyclic heteroaromatic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur which is optionally substituted 1-2 times by -CH₃ or -NH₂; optionally:

wherein at least one of R² is selected from:

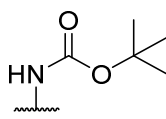


5. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^2 is $-NHC(O)R$, wherein R is C_{1-6} aliphatic optionally substituted 1-3 times by halogen, $-OCH_3$, $-N(CH_3)_2$, or $-OH$, 3-6 membered saturated monocyclic carbocyclic ring optionally substituted 1-2 times by halogen or $-OH$, or 4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen or sulfur optionally substituted 1-2 times by halogen, $-OH$, or $-CH_3$; optionally:



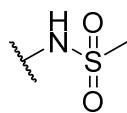


wherein at least one of R^2 is $-NHC(O)OR$, wherein R is unsubstituted C_{1-6} aliphatic; optionally:



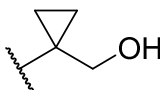
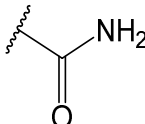
wherein at least one of R^2 is ; or:

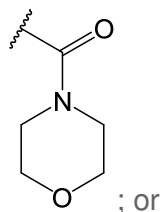
wherein at least one of R^2 is $-NHS(O)_2R$, wherein R is unsubstituted C_{1-6} aliphatic; optionally:



wherein at least one of R^2 is ; or:

wherein at least one of R^2 is $-OR$, wherein R is: hydrogen;

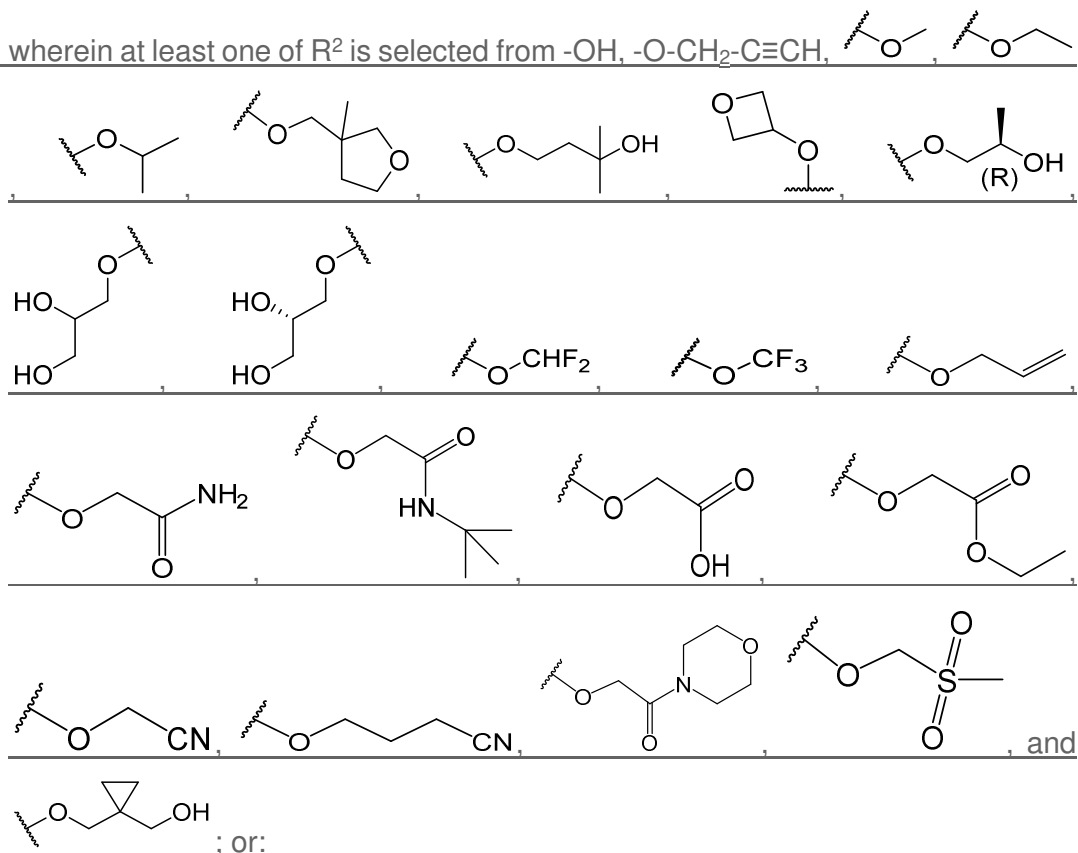
C_{1-6} aliphatic optionally substituted by a halogen, $-OH$, , , , $-C(O)NHC_{1-4}$ aliphatic, $-COOH$, $-C(O)OC_{1-4}$ aliphatic, $-CN$, $-SO_2C_{1-4}$ aliphatic, or



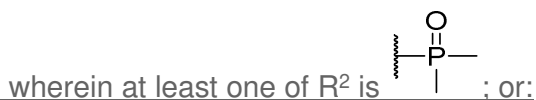
; or

4-6 membered saturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen or oxygen; optionally:

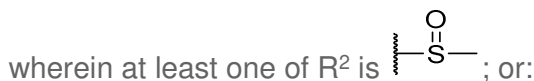
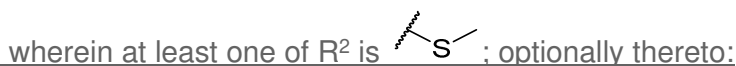
wherein at least one of R² is selected from -OH, -O-CH₂-C≡CH,



wherein at least one of R² is -P(O)R₂, wherein each of R is independently unsubstituted C₁₋₆ aliphatic; optionally:

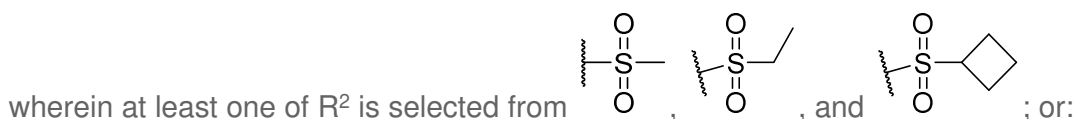


wherein at least one of R² is -SR, wherein R is unsubstituted C₁₋₆ aliphatic; optionally:

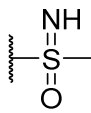


wherein at least one of R² is -S(O)R, wherein R is unsubstituted C₁₋₆ aliphatic; or:

wherein at least one of R² is -S(O)₂R, where R is unsubstituted C₁₋₆ aliphatic or 3-6 membered saturated monocyclic carbocyclic ring; optionally:



wherein at least one of R^2 is $-S(O)(NH)R$, wherein R is unsubstituted C_{1-6} aliphatic; optionally:



wherein at least one of R^2 is $-S(O)_2NR_2$; or:

wherein at least one of R^2 is $-S(O)_2NR_2$; optionally:

wherein at least one of R^2 is $-S(O)_2NH_2$.

6. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein at least one of R^3 is C_{1-3} aliphatic; and/or:

wherein X is $-O-$; and/or:

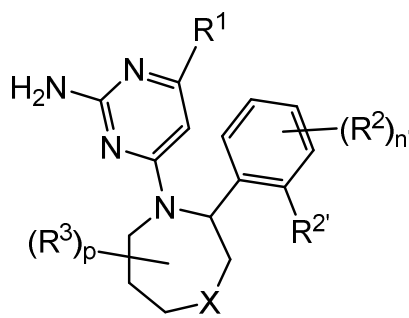
wherein m is 1; and/or:

wherein p is 0; and/or:

wherein n is 1, 2, 3, 4, or 5; and/or:

wherein $-----$ is a single bond.

7. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula VII



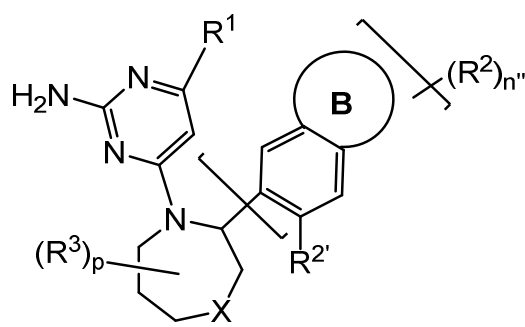
VII

or a pharmaceutically acceptable salt thereof, wherein:

n' is 1 or 2; and

$R^{2'}$ is halogen or $-OC_{1-3}$ aliphatic; or:

wherein the compound is of Formula VIII



VIII

or a pharmaceutically acceptable salt thereof, wherein:

Ring B is 5-7 membered partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or Ring B is 5-6 membered heteroaromatic ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

n'' is 0, 1, 2, 3, or 4; and

R^{2'} is halogen or -OC₁₋₃ aliphatic.

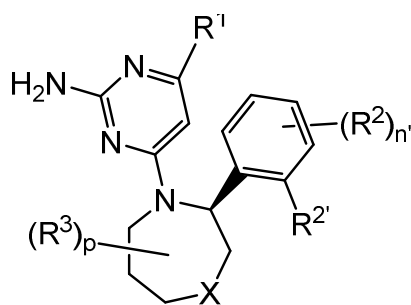
8. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^{2'} is halogen or -OC₁₋₃ aliphatic; or:

wherein R^{2'} is Cl; or:

wherein R^{2'} is -OCH₃.

9. The compound of any one of claims 7 or 8, or a pharmaceutically acceptable salt thereof, wherein

the compound is of Formula VII-a



VII-a

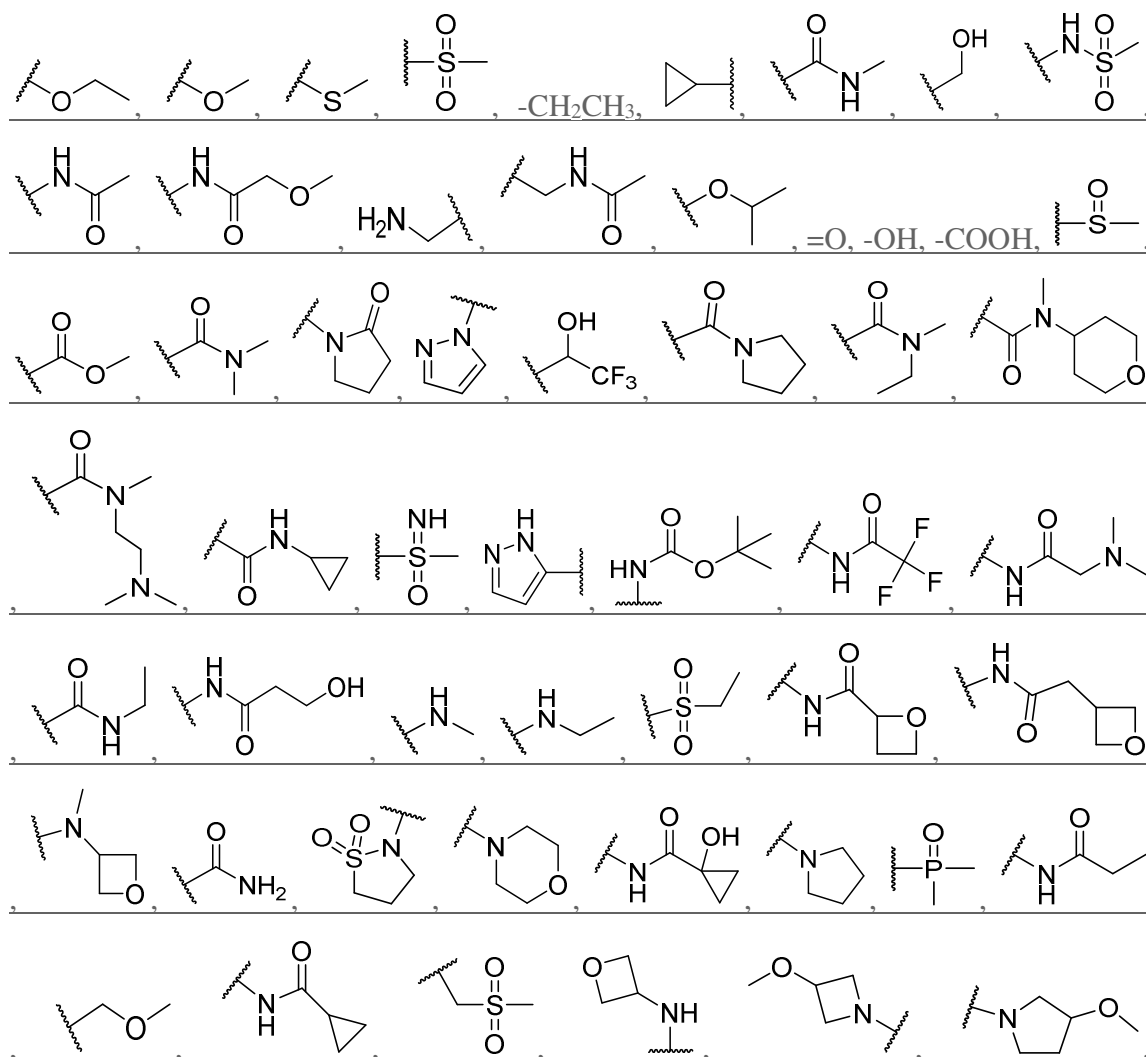
; and

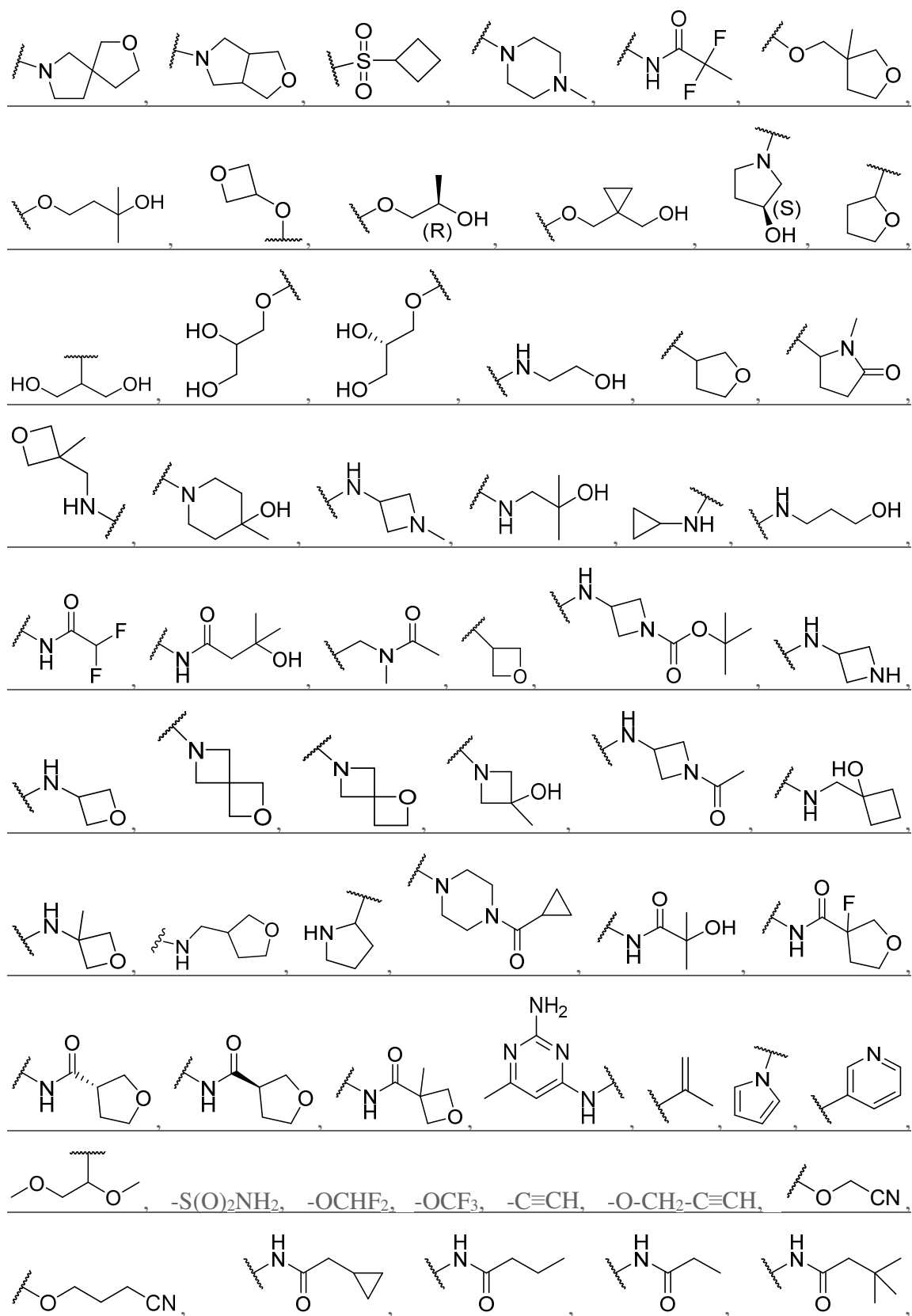
R^{2'} is Cl.

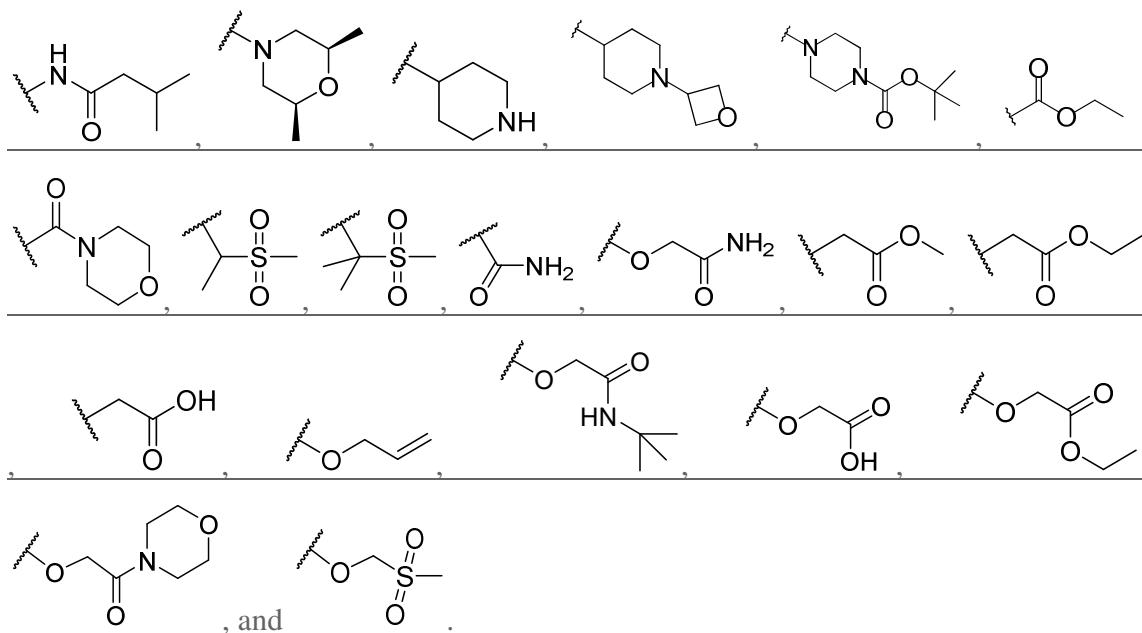
10. The compound of any of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula **XI** or **XI-a**:



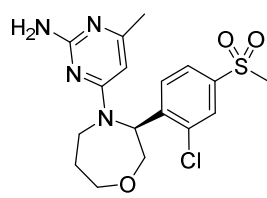
11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein R^2 is Cl and each of R^2 is selected from the group consisting of halogen, $-NH_2$, $-CH_3$, $-CF_3$,



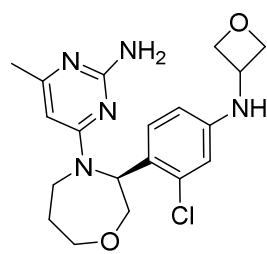




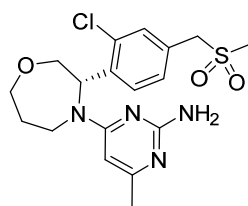
12. The compound of any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the compounds depicted in Tables 1, 2, and 2A.
13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the compounds



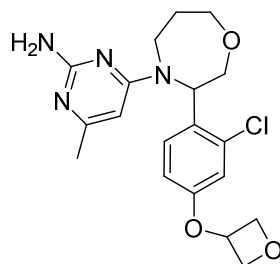
I-68,



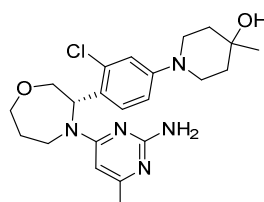
I-215,



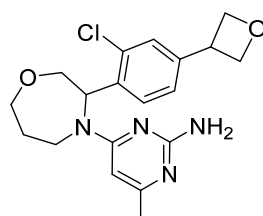
I-224,



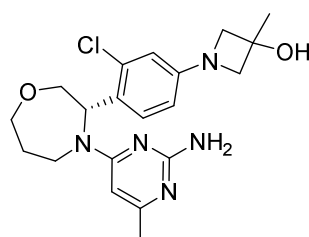
I-231,



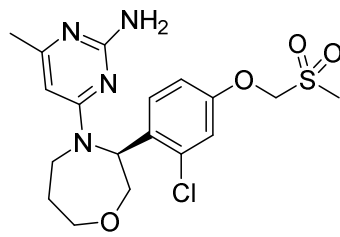
I-242,



I-255,

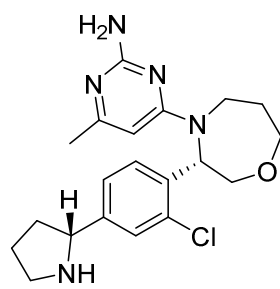


I-261,



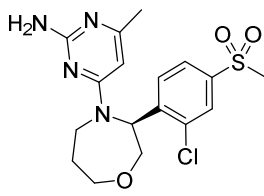
D-1.

and



D-90.

14. The compound of any of claims 12 and 13, or a pharmaceutically acceptable salt thereof, wherein the compound is



I-68.

15. A pharmaceutical composition comprising a compound according to any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.
16. Use of a compound according to any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament or a pharmaceutical composition for treating a cellular proliferative disorder in a patient, wherein said medicament or pharmaceutical composition is to be administered to said patient.

17. The use of claim 16, wherein said treating of a cellular proliferative disorder in a patient further comprises determining the Wolframin (WFS1) expression level.
18. The use of claims 16 or 17, wherein the cellular proliferative disorder is cancer; or: wherein the cellular proliferative disorder is selected from non-small cell lung cancer (NSCLC), myeloma, hepatocellular carcinoma (HCC), breast cancer, colorectal cancer, endometrial cancer, cancer of the esophagus, pancreatic cancer, renal cell carcinoma, and melanoma.
19. Use of a compound according to any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament or a pharmaceutical composition for inducing ER stress in a patient in need thereof, or for inducing the unfolded protein response (UPR) in a patient in need thereof, wherein said medicament or composition is to be administered to said patient.
20. Use of a compound according to any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament or a pharmaceutical composition for causing calcium release from the endoplasmic reticulum (ER) via a putative Ca^{2+} channel known as Wolframin (WFS1) in a patient in need thereof, wherein said medicament or composition is to be administered to said patient.
21. A compound according to any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, for use in therapy.