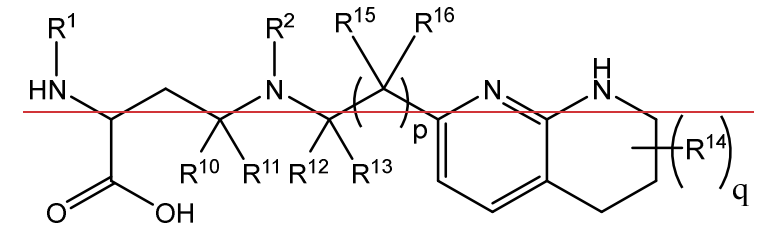
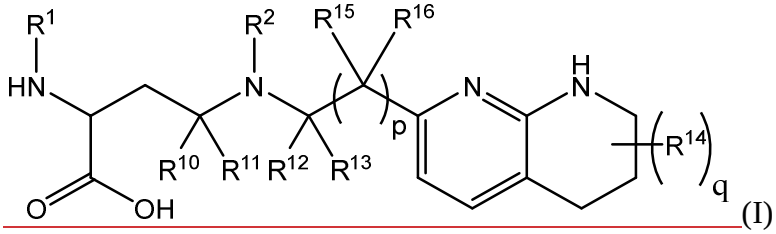
CLAIMS

What is claimed is:

1. ~~A method of treating a condition in an individual in need thereof, comprising: administering to the individual an amount of~~Use of a compound of formula (I) ~~effective to treat the condition~~:





(I)

or a salt thereof, wherein:

R^1 is C_6-C_{14} aryl or 5- to 10-membered heteroaryl wherein the C_6-C_{14} aryl and 5- to 10-membered heteroaryl are optionally substituted by R^{1a};

R^2 is hydrogen; deuterium; C_1-C_6 alkyl optionally substituted by R^{2a}; -O-C_1-C_6 alkyl optionally substituted by R^{2a}; C_3-C_6 cycloalkyl optionally substituted by R^{2b}; -O-C_3-C_6 cycloalkyl optionally substituted by R^{2b}; 3- to 12-membered heterocyclyl optionally substituted by R^{2c}; or -$S(O)_2R^{2d}$; with the proviso that any carbon atom bonded directly to a nitrogen atom is either unsubstituted or substituted with deuterium;

each R^{1a} is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, C_4-C_8 cycloalkenyl, 3- to 12-membered heterocyclyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, deuterium, halogen, -CN, -OR^3, -SR^3, -NR^4R^5, -NO_2, -C=NH(OR^3), -$C(O)R^3$, -$OC(O)R^3$, -$C(O)OR^3$, -$C(O)NR^4R^5$, -$NR^3C(O)R^4$, -$NR^3C(O)OR^4$, -$NR^3C(O)NR^4R^5$, -$S(O)R^3$, -$S(O)_2R^3$, -$NR^3S(O)R^4$, -$NR^3S(O)_2R^4$, -$S(O)NR^4R^5$, -$S(O)_2NR^4R^5$, or -$P(O)(OR^4)(OR^5)$, wherein each R^{1a} is, where possible, independently optionally substituted by deuterium, halogen, oxo, -OR^6, -NR^6R^7, -$C(O)R^6$, -CN, -$S(O)R^6$, -$S(O)_2R^6$, -$P(O)(OR^6)(OR^7)$, C_3-C_8 cycloalkyl, 3- to 12-membered heterocyclyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, or C_1-C_6 alkyl optionally substituted by deuterium, oxo, -OH or halogen;

each R^{2a}, R^{2b}, R^{2c}, R^{2e}, and R^{2f} is independently oxo or R^{1a};

R^{2d} is C_1-C_6 alkyl optionally substituted by R^{2e} or C_3-C_5 cycloalkyl optionally substituted by R^{2f};

R^3 is independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl or 3- to 6-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl and 3- to 6-membered heterocyclyl of R^3 are independently optionally substituted by halogen, deuterium, oxo, -CN, -OR^8, -NR^8R^9, -$P(O)(OR^8)(OR^9)$, or C_1-C_6 alkyl optionally substituted by deuterium, halogen, -OH or oxo;

R^4 and R^5 are each independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl or 3- to 6-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl and 3- to 6-membered heterocyclyl of R^4 and R^5 are independently optionally substituted by deuterium, halogen, oxo, -CN, -OR^8, -NR^8R^9 or C_1-C_6 alkyl optionally substituted by deuterium, halogen, -OH or oxo;

or R^4 and R^5 are taken together with the atom to which they attached to form a 3- to 6-membered heterocyclyl optionally substituted by deuterium, halogen, oxo, -OR^8, -NR^8R^9 or C_1-C_6 alkyl optionally substituted by deuterium, halogen, oxo or -OH;

R^6 and R^7 are each independently hydrogen, deuterium, C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo, C_2-C_6 alkenyl optionally substituted by deuterium, halogen, or oxo, or C_2-C_6 alkynyl optionally substituted by deuterium, halogen, or oxo;

or R^6 and R^7 are taken together with the atom to which they attached to form a 3- to 6-membered heterocyclyl optionally substituted by deuterium, halogen, oxo or C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo;

R^8 and R^9 are each independently hydrogen, deuterium, C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo, C_2-C_6 alkenyl optionally substituted by deuterium, halogen or oxo, or C_2-C_6 alkynyl optionally substituted by deuterium, halogen, or oxo;

or R^8 and R^9 are taken together with the atom to which they attached to form a 3-6 membered heterocyclyl optionally substituted by deuterium, halogen, oxo or C_1-C_6 alkyl optionally substituted by deuterium, oxo, or halogen;

each R^{10}, R^{11}, R^{12} and R^{13} are independently hydrogen or deuterium;

R^{14} is deuterium;

q is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

each R^{15} is independently selected from hydrogen, deuterium, or halogen;

each R^{16} is independently selected from hydrogen, deuterium, or halogen; and

p is 3, 4, 5, 6, 7, 8, or 9;

in the manufacture of a medicament for treating a condition in an individual in need thereof, wherein the medicament comprises an amount of the compound effective to treat the condition,

the condition comprising one or more of: causation by or association with an infectious agent, shock, pancreatitis, or trauma; or

the condition comprising one or more of pulmonary fibrosis associated with rheumatoid arthritis or progressive familial intrahepatic cholestasis (PFIC).

2. The usemethod of claim 1, the condition comprising acute respiratory distress syndrome (ARDS), or a precursor condition to ARDS;

optionally wherein the condition comprises a precursor condition to ARDS, and the use comprises administration of the medicament to the individual effective to mitigate progression from the precursor condition to ARDS in the individual;

or optionally wherein the condition comprises ARDS and the use comprises administration of the medicament to the individual effective to mitigate ARDS.

~~3. The method of claim 2, the condition comprising a precursor condition to ARDS, comprising administering the compound to the individual effective to mitigate progression from the precursor condition to ARDS in the individual.~~

~~4. The method of claim 2, the condition comprising ARDS, comprising administering the compound to the individual effective to mitigate ARDS.~~

~~5.~~3. The usemethod of claim 1, the condition comprising causation by or association with the infectious agent; or the infectious agent causing sepsis in the individual; or the infectious agent causing pneumonia in the individual.

~~6. The method of claim 1, the infectious agent causing sepsis in the individual.~~

~~7. The method of claim 1, the infectious agent causing pneumonia in the individual.~~

~~8.~~4. The use~~method~~ of claim 1, the infectious agent causing pneumonia in the individual, the use comprises administration of the medicament~~comprising administering the compound~~ to the individual effective to mitigate progression from the pneumonia to ARDS in the individual.

~~9.~~5. The use~~method~~ of claim 1, the condition comprising ARDS caused by or associated with the infectious agent.

~~10.~~6. The use~~method~~ of claim 1, the individual being at risk of infection by the infectious agent, the use comprises administration of the medicament~~comprising administering the compound~~ to the individual effective to mitigate the risk of infection.

~~11.~~7. The use~~method~~ of claim 1, the infectious agent comprising one or more of: a bacteria, a virus, a fungus, or a parasite; optionally the infectious agent comprising a virus; or optionally the infectious agent comprising a Coronaviridae virus.

~~12. The method of claim 1, the infectious agent comprising a virus.~~

~~13. The method of claim 1, the infectious agent comprising a Coronaviridae virus.~~

~~14.~~8. The use~~method~~ of claim 7~~13~~, the condition comprising ARDS caused by or associated with the Coronaviridae virus.

~~15.~~9. The use~~method~~ of claim 7~~13~~, the infectious agent comprising a severe acute respiratory syndrome-related coronavirus (SARS-CoV); optionally the infectious agent comprising SARS-CoV or SARS-CoV-2.

~~16. The method of claim 15, the infectious agent comprising SARS-CoV or SARS-CoV-2.~~

~~17.~~10. The use~~method~~ of claim 1, the infectious agent comprising COVID-19.

~~18.~~11. The use~~method~~ of claim 1, the infectious agent comprising an Influenza virus; optionally the condition comprising ARDS caused by or associated with the Influenza virus; optionally the infectious agent comprising an Influenza A virus; or optionally the infectious agent comprising a strain of the Influenza A virus selected from the group consisting of: H1N1, H2N2, H3N2, H3N8, H5N1, H7N7, H1N2, H9N2, H7N2, H7N3, and H10N7.

~~19. The method of claim 18, the condition comprising ARDS caused by or associated with the Influenza virus.~~

~~20. The method of claim 18, the infectious agent comprising an Influenza A virus.~~

~~21. The method of claim 20, the infectious agent comprising a strain of the Influenza A virus selected from the group consisting of: H1N1, H2N2, H3N2, H3N8, H5N1, H7N7, H1N2, H9N2, H7N2, H7N3, and H10N7.~~

~~22. The method of claim 1, the infectious agent comprising influenza.~~

~~23.~~12. The use~~method~~ of claim 1, wherein the condition is caused by or associated with the trauma, optionally wherein the trauma comprises at least one of: mechanical trauma; barotrauma; thermal trauma; electrical trauma; radiation trauma; particulate aspiration; fluid aspiration; increased intracranial pressure; embolism; transfusion-related acute lung injury; pulmonary trauma associated with cardiopulmonary bypass; or chemical trauma other than bleomycin; or optionally wherein the condition is acute respiratory distress syndrome (ARDS) caused by or associated with the trauma.

~~24. The method of claim 23, the trauma comprising at least one of: mechanical trauma; barotrauma; thermal trauma; electrical trauma; radiation trauma; particulate aspiration; fluid aspiration; increased intracranial pressure; embolism; transfusion-related acute lung injury; pulmonary trauma associated with cardiopulmonary bypass; or chemical trauma other than bleomycin.~~

~~25. The method of claim 23, wherein the condition is acute respiratory distress syndrome (ARDS) caused by or associated with the trauma.~~

~~26.~~13. The use~~method~~ of claim 1, wherein the condition comprises over-expression of an α_V integrin in one or more organs; optionally wherein the condition comprises over-expression of an α_V integrin in one or more of: lung, heart, vasculature, brain, kidney, bladder, urethra, testes, ovaries, mucosa, smooth muscle, liver, pancreas, gall bladder, spleen, small intestine, large intestine, or skin.

~~27. The method of claim 1, wherein the condition comprises over-expression of an α_V integrin in one or more of: lung, heart, vasculature, brain, kidney, bladder, urethra, testes, ovaries, mucosa, smooth muscle, liver, pancreas, gall bladder, spleen, small intestine, large intestine, or skin.~~

~~28.~~14. The use~~method~~ of claim 1, the condition being mediated by an α_V integrin; optionally the condition being mediated by an $\alpha_V\beta_6$ integrin.

~~29. The method of claim 1, the condition being mediated by an $\alpha_V\beta_6$ integrin.~~

~~30.~~15. The use~~method~~ of claim 1, the condition comprising pulmonary fibrosis associated with rheumatoid arthritis.

~~31.~~16. The use~~method~~ of claim 1, the condition comprising progressive familial intrahepatic cholestasis (PFIC).

~~32.~~17. The use~~method~~ of claim 1, the condition excluding fibrosis other than pulmonary fibrosis associated with rheumatoid arthritis.

~~33.~~18. The use~~method~~ of claim 1, the condition excluding fibrosis, optionally wherein the condition excludes a fibrotic disease selected from the group consisting of: idiopathic pulmonary

fibrosis (IPF), interstitial lung disease, radiation-induced pulmonary fibrosis, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), alcoholic liver disease induced fibrosis, Alport syndrome, primary sclerosing cholangitis (PSC), primary biliary cholangitis, biliary atresia, systemic sclerosis associated interstitial lung disease, scleroderma, diabetic nephropathy, diabetic kidney disease, focal segmental glomerulosclerosis, chronic kidney disease, and Crohn's Disease.

~~34. The method of claim 1, the condition excluding a fibrotic disease selected from the group consisting of: idiopathic pulmonary fibrosis (IPF), interstitial lung disease, radiation-induced pulmonary fibrosis, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), alcoholic liver disease induced fibrosis, Alport syndrome, primary sclerosing cholangitis (PSC), primary biliary cholangitis, biliary atresia, systemic sclerosis associated interstitial lung disease, scleroderma, diabetic nephropathy, diabetic kidney disease, focal segmental glomerulosclerosis, chronic kidney disease, and Crohn's Disease.~~

~~35.~~19. The use~~method~~ of claim 1, the condition comprising ARDS, the ARDS being caused by or associated with a fibrotic disease selected from the group consisting of: idiopathic pulmonary fibrosis (IPF), interstitial lung disease, radiation-induced pulmonary fibrosis, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), alcoholic liver disease induced fibrosis, Alport syndrome, primary sclerosing cholangitis (PSC), primary biliary cholangitis, biliary atresia, systemic sclerosis associated interstitial lung disease, scleroderma, diabetic nephropathy, diabetic kidney disease, focal segmental glomerulosclerosis, chronic kidney disease, and Crohn's Disease.

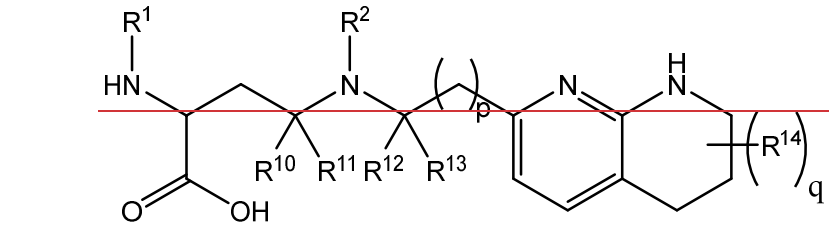
~~36.~~20. The use~~method~~ of claim 1, wherein:

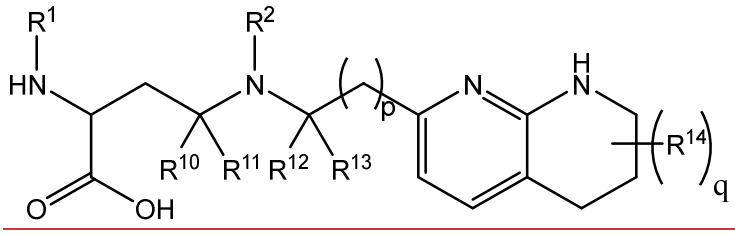
R^2 is C_1-C_6 alkyl optionally substituted by R^{2a}; C_3-C_6 cycloalkyl optionally substituted by R^{2b}; 3- to 12-membered heterocyclyl optionally substituted by R^{2c}; or $-S(O)_2R^{2d}$;

each R^{15} is hydrogen;

each R^{16} is hydrogen;

and the compound is represented by Formula (II):

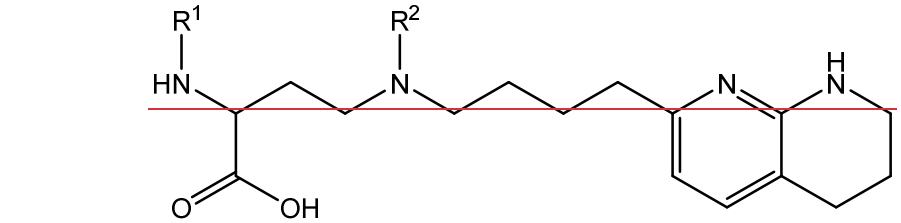


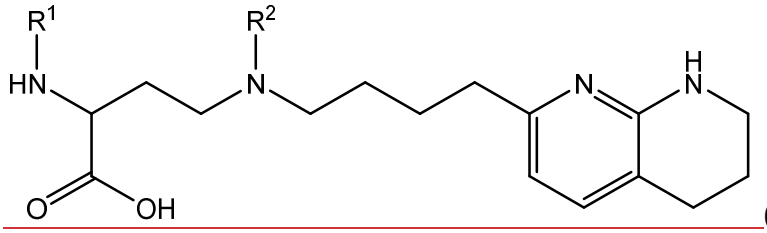


(II); or a salt thereof.

37.21. The usemethod of claim 1 or claim 2036, wherein at least one of R^{1a}, R^{2a}, R^{2b}, R^{2c}, R^{2e}, R^{2f}, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, or R^{13}, ~~or R^{14}~~ is deuterium.

38.22. The usemethod of claim 1 or claim 2036, wherein R^{10}, R^{11}, R^{12}, and R^{13}, ~~and R^{14}~~ are hydrogen; p is 3; q is 0; and the compound is represented by formula (III):





(III), or a salt thereof.

39.23. The usemethod of any one of claims 1 or 20-2236-38, wherein

(i) R^1 is 5- to 10-membered heteroaryl optionally substituted by R^{1a}.; or wherein

(ii) R^1 is pyrimidinyl, quinazolinyl, pyrazolopyrimidinyl, pyrazinyl, quinolinyl, pyridopyrimidinyl, thienopyrimidinyl, pyridinyl, pyrrolopyrimidinyl, quinoxalinyl, indazolyl, benzothiazolyl, naphthalenyl, purinyl, or isoquinolinyl;

each of which is optionally substituted by deuterium, hydroxy, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 perhaloalkyl, C_1-C_6 alkoxyl, C_3-C_8 cycloalkyl, C_3-C_8 halocycloalkyl, C_3-C_8

cycloalkoxyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, cyano, amino, alkylamino, or dialkylamino; or wherein

(iii) R^1 is pyrimidin-2-yl, pyrimidin-4-yl, quinazolin-4-yl, 1H-pyrazolo[3,4-d]pyrimidin-4-yl, 1H-pyrazolo[4,3-d]pyrimidin-7-yl, pyrazin-2-yl, quinolin-4-yl, pyrido[2,3-d]pyrimidin-4-yl, pyrido[3,2-d]pyrimidin-4-yl, pyrido[3,4-d]pyrimidin-4-yl, thieno[2,3-d]pyrimidin-4-yl, thieno[3,2-d]pyrimidin-4-yl, thienopyrimidin-4-yl, pyridin-2-yl, pyridin-3-yl, 7H-pyrrolo[2,3-d]pyrimidin-4-yl, quinoxalin-2-yl, 1H-indazol-3-yl, benzo[d]thiazol-2-yl, naphthalen-1-yl, 9H-purin-6-yl, or isoquinolin-1-yl;

each of which is optionally substituted by: one or more deuterium; methyl; cyclopropyl; fluoro; chloro; bromo; difluoromethyl; trifluoromethyl; methyl and fluoro; methyl and trifluoromethyl; methoxy; cyano; dimethylamino; phenyl; pyridin-3-yl; and pyridin-4-yl; or wherein

(iv) R^1 is pyrimidin-4-yl optionally substituted by R^{1a}; or wherein

(v) R^1 is pyrimidin-4-yl optionally substituted by R^{1a} wherein R^{1a} is 5- to 10-membered heteroaryl or C_1-C_6 alkyl optionally substituted by halogen; or wherein

(vi) R^1 is pyrimidin-4-yl optionally substituted by pyrazolyl, methyl, difluoromethyl, or trifluoromethyl; or wherein

(vii) R^1 is pyrimidin-4-yl substituted by both methyl and trifluoromethyl; or wherein

(viii) R^1 is quinazolin-4-yl optionally substituted by R^{1a}; or wherein

(ix) R^1 is quinazolin-4-yl optionally substituted by halogen, C_1-C_6 alkyl optionally substituted by halogen, or C_1-C_6 alkoxy; or wherein

(x) R^1 is quinazolin-4-yl optionally substituted by fluoro, chloro, methyl, trifluoromethyl or methoxy.

~~40. The method of any one of claims 1 or 36-38, wherein R^1 is:~~

~~pyrimidinyl, quinazolinyl, pyrazolopyrimidinyl, pyrazinyl, quinolinyl, pyridopyrimidinyl, thienopyrimidinyl, pyridinyl, pyrrolopyrimidinyl, quinoxalinyl, indazolyl, benzothiazolyl, naphthalenyl, purinyl, or isoquinolinyl;~~

~~each of which is optionally substituted by deuterium, hydroxy, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 perhaloalkyl, C_1-C_6 alkoxyl, C_3-C_8 cycloalkyl, C_3-C_8 halocycloalkyl, C_3-C_8~~

cycloalkoxyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, cyano, amino, alkylamino, or dialkylamino.

41. The method of any one of claims 1 or 36-38, wherein R^1 is:

pyrimidin-2-yl, pyrimidin-4-yl, quinazolin-4-yl, 1H-pyrazolo[3,4-d]pyrimidine-4-yl, 1H-pyrazolo[4,3-d]pyrimidine-7-yl, pyrazin-2-yl, quinoline-4-yl, pyrido[2,3-d]pyrimidin-4-yl, pyrido[3,2-d]pyrimidin-4-yl, pyrido[3,4-d]pyrimidin-4-yl, thieno[2,3-d]pyrimidin-4-yl, thieno[3,2-d]pyrimidin-4-yl, thienopyrimidin-4-yl, pyridine-2-yl, pyridine-3-yl, 7H-pyrrolo[2,3-d]pyrimidin-4-yl, quinoxaline-2-yl, 1H-indazol-3-yl, benzo[d]thiazol-2-yl, naphthalen-1-yl, 9H-purin-6-yl, or isoquinolin-1-yl;

each of which is optionally substituted by: one or more deuterium; methyl; cyclopropyl; fluoro; chloro; bromo; difluoromethyl; trifluoromethyl; methyl and fluoro; methyl and trifluoromethyl; methoxy; cyano; dimethylamino; phenyl; pyridine-3-yl; and pyridine-4-yl.

42. The method of any one of claims 1 or 36-38, wherein R^1 is pyrimidin-4-yl optionally substituted by R^{1a}.

43. The method of claim any one of claims 1 or 36-38, wherein R^1 is pyrimidin-4-yl optionally substituted by R^{1a} wherein R^{1a} is 5- to 10-membered heteroaryl or C_1-C_6 alkyl optionally substituted by halogen.

44. The method of any one of claims 1 or 36-38, wherein R^1 is pyrimidin-4-yl optionally substituted by pyrazolyl, methyl, difluoromethyl, or trifluoromethyl.

45. The method of any one of claims 1 or 36-38, wherein R^1 is pyrimidin-4-yl substituted by both methyl and trifluoromethyl.

46. The method of any one of claims 1 or 36-38, wherein R^1 is quinazolin-4-yl optionally substituted by R^{1a}.

47. The method of any one of claims 1 or 36-38, wherein R^1 is quinazolin-4-yl optionally substituted by halogen, C_1-C_6 alkyl optionally substituted by halogen, or C_1-C_6 alkoxy.

~~48. The method of any one of claims 1 or 36-38, wherein R^1 is quinazolin-4-yl optionally substituted by fluoro, chloro, methyl, trifluoromethyl or methoxy.~~

~~49.~~24. The use~~method~~ of any one of claims 1 or 20-23~~36-48~~, wherein R^2 is:

(i) hydrogen;

(ii) deuterium;

(iii) hydroxy; ~~or~~

(iv) C_1-C_6 alkyl or C_1-C_6 alkoxyl optionally substituted with: deuterium, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxyl, C_3-C_8 cycloalkyl, C_3-C_8 halocycloalkyl, C_3-C_8 cycloalkoxyl, C_6-C_{14} aryl, C_6-C_{14} aryloxy, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryloxy, 3- to 12-membered heterocyclyl optionally substituted with oxo, $-C(O)NR^4R^5$, $-NR^3C(O)R^4$, or $-S(O)_2R^3$~~.~~;

(v) methyl, methoxy, ethyl, ethoxy, propyl, cyclopropyl, or cyclobutyl;

each of which is optionally substituted with one or more of: hydroxy, methoxy, ethoxy, acetamide, fluoro, fluoroalkyl, phenoxy, dimethylamide, methylsulfonyl, cyclopropoxyl, pyridin-2-yloxy, optionally methylated or fluorinated pyridine-3-yloxy, N-morpholino, N-pyrrolidin-2-one, dimethylpyrazol-1-yl, dioxiran-2-yl, morpholin-2-yl, oxetan-3-yl, phenyl, tetrahydrofuran-2-yl, thiazol-2-yl;

each of which is substituted with 0, 1, 2, or 3 of deuterium, hydroxy, methyl, fluoro, cyano, or oxo;

(vi) C_1-C_6 alkyl optionally substituted by R^{2a}, optionally wherein R^{2a} is: halogen; C_3-C_8 cycloalkyl optionally substituted by halogen; 5- to 10-membered heteroaryl optionally substituted by C_1-C_6 alkyl; $-NR^4R^5$; $-NR^3C(O)R^4$; $-S(O)_2R^3$; or oxo; or optionally wherein R^{2a} is: fluoro; cyclobutyl substituted by fluoro; pyrazolyl substituted by methyl; or $-S(O)_2CH_3$;

(vii) C_1-C_6 alkyl optionally substituted by $-OR^3$, optionally wherein R^3 is hydrogen; C_1-C_6 alkyl optionally substituted by halogen; C_3-C_6 cycloalkyl optionally substituted by halogen; C_6-C_{14} aryl optionally substituted by halogen; or 5- to 6-membered heteroaryl optionally substituted by halogen or C_1-C_6 alkyl; or optionally wherein R^3 is hydrogen; methyl; ethyl; difluoromethyl; $-CH_2CHF_2$; $-CH_2CF_3$; cyclopropyl substituted by fluoro; phenyl optionally substituted by fluoro; or pyridinyl optionally substituted by fluoro or methyl;

(viii) $-CH_2CH_2OCH_3$;

(ix) C_1-C_6 alkyl substituted by both halogen and OR^3, wherein R^3 is C_1-C_6 alkyl;

(x) C_3-C_6 cycloalkyl optionally substituted by R^{2b}; or

(xi) cyclopropyl.

~~50. The method of any one of claims 1 or 36-48, wherein R^2 is:~~

~~methyl, methoxy, ethyl, ethoxy, propyl, cyclopropyl, or cyclobutyl;~~

~~each of which is optionally substituted with one or more of: hydroxy, methoxy, ethoxy, acetamide, fluoro, fluoroalkyl, phenoxy, dimethylamide, methylsulfonyl, cyclopropoxyl, pyridine-2-yloxy, optionally methylated or fluorinated pyridine-3-yloxy, N-morpholino, N-pyrrolidin-2-one, dimethylpyrazol-1-yl, dioxirane-2-yl, morpholin-2-yl, oxetan-3-yl, phenyl, tetrahydrofuran-2-yl, thiazol-2-yl;~~

~~each of which is substituted with 0, 1, 2, or 3 of deuterium, hydroxy, methyl, fluoro, cyano, or oxo.~~

~~51. The method of any one of claims 1 or 36-48, wherein R^2 is C_1-C_6 alkyl optionally substituted by R^{2a}.~~

~~52. The method of any one of claims 1 or 36-48, wherein R^2 is C_1-C_6 alkyl optionally substituted by R^{2a} wherein R^{2a} is: halogen; C_3-C_8 cycloalkyl optionally substituted by halogen; 5- to 10-membered heteroaryl optionally substituted by C_1-C_6 alkyl; $-NR^4R^5$; $-NR^3C(O)R^4$; $-S(O)_2R^3$; or oxo.~~

~~53. The method of any one of claims 1 or 36-48, wherein R^2 is C_1-C_6 alkyl optionally substituted by R^{2a} wherein R^{2a} is: fluoro; cyclobutyl substituted by fluoro; pyrazolyl substituted by methyl; or $-S(O)_2CH_3$.~~

~~54. The method of any one of claims 1 or 36-48, wherein R^2 is C_1-C_6 alkyl optionally substituted by $-OR^3$.~~

~~55. The method of any one of claims 1 or 36-48, wherein R^2 is C_1-C_6 alkyl optionally substituted by -OR^3, and R^3 is: hydrogen; C_1-C_6 alkyl optionally substituted by halogen; C_3-C_6 cycloalkyl optionally substituted by halogen; C_6-C_{14} aryl optionally substituted by halogen; or 5- to 6-membered heteroaryl optionally substituted by halogen or C_1-C_6 alkyl.~~

~~56. The method of any one of claims 1 or 36-48, wherein R^2 is C_1-C_6 alkyl optionally substituted by -OR^3, and R^3 is: hydrogen; methyl; ethyl; difluoromethyl; -CH_2CHF_2; -CH_2CF_3; cyclopropyl substituted by fluoro; phenyl optionally substituted by fluoro; or pyridinyl optionally substituted by fluoro or methyl.~~

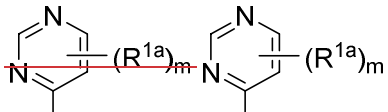
~~57. The method of any one of claims 1 or 36-48, wherein R^2 is -$CH_2CH_2OCH_3$.~~

~~58. The method of any one of claims 1 or 36-48, wherein R^2 is C_1-C_6 alkyl substituted by both halogen and OR^3, wherein R^3 is C_1-C_6 alkyl.~~

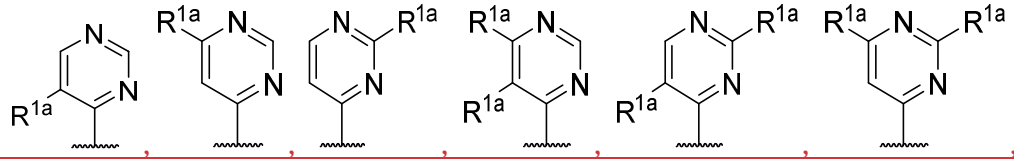
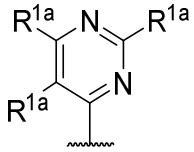
~~59. The method of any one of claims 1 or 36-48, wherein R^2 is C_3-C_6 cycloalkyl optionally substituted by R^{2b}.~~

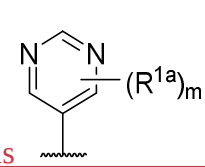
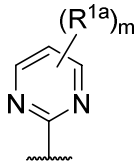
~~60. The method of any one of claims 1 or 36-48, wherein R^2 is cyclopropyl.~~

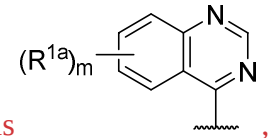
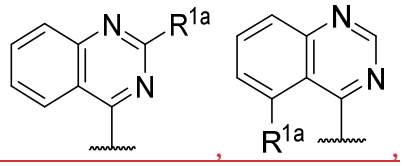
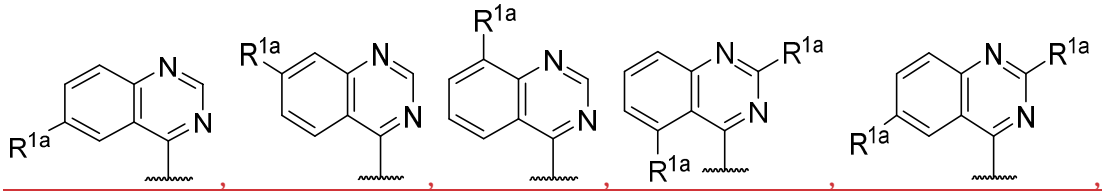
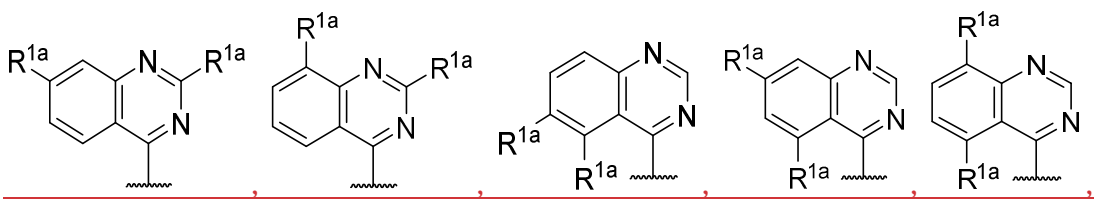
~~61.~~25. The use~~method~~ of any one of claims 1 or 20-22~~36-38~~, wherein

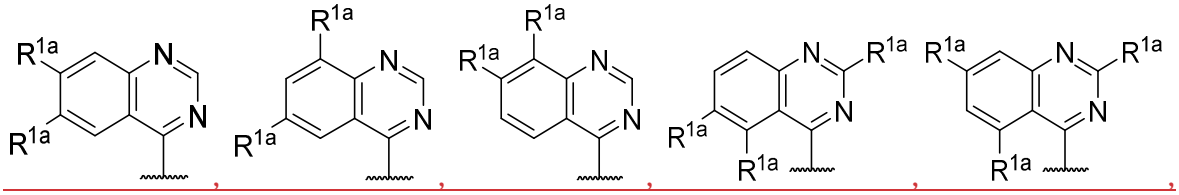
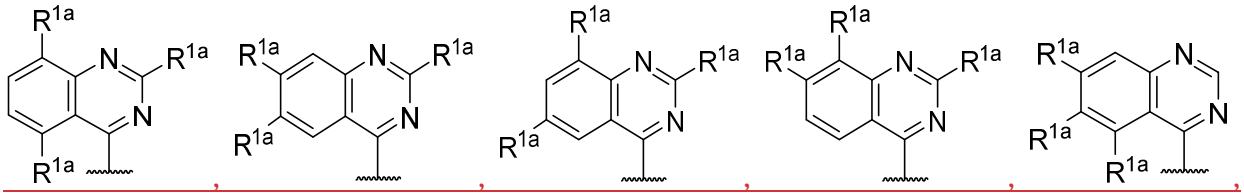
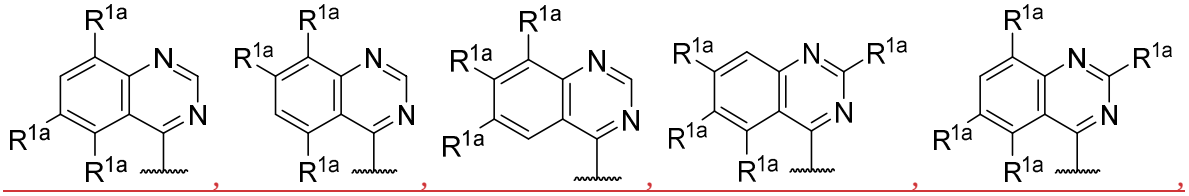
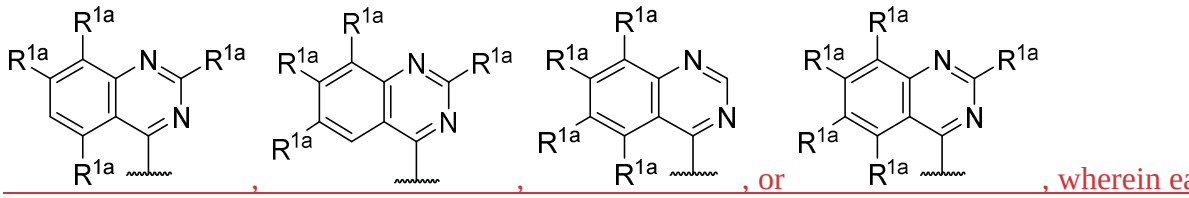


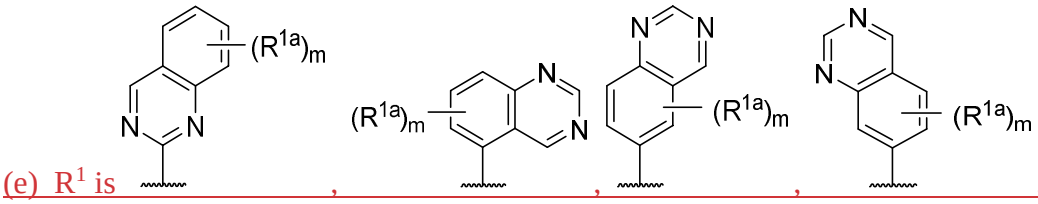
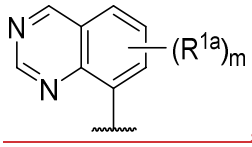
(a) R^1 is _____, wherein m is 0, 1, 2, or 3 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium~~.~~;

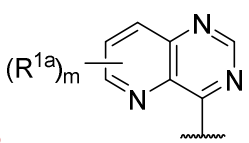
(b) R^1 is  , or  , wherein each R^{1a} is independently deuterium, alkyl, haloalkyl, or heteroaryl;

(c) R^1 is  or  , wherein m is 0, 1, 2, or 3 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium;

(d) R^1 is  , wherein m is 0, 1, 2, 3, 4, or 5 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium; optionally wherein R^1 is  ,  ,  .

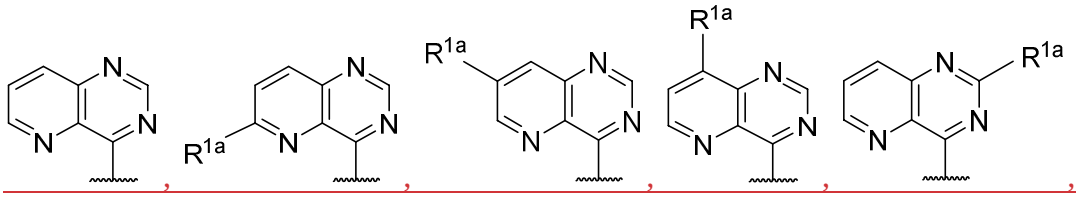
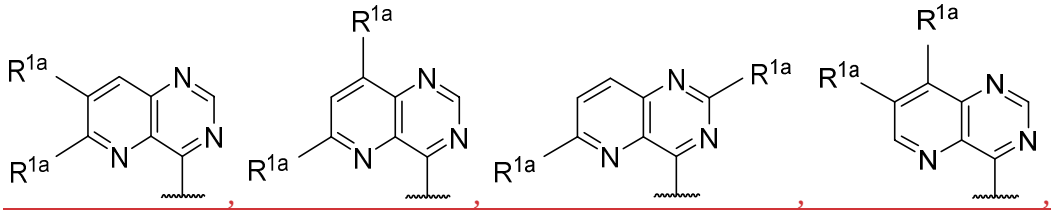
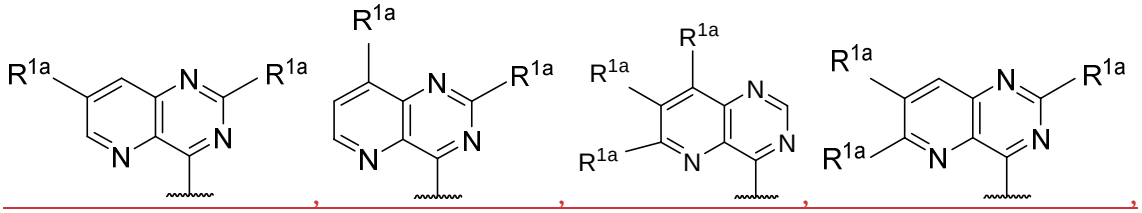




, wherein each R^{1a} is independently deuterium, halogen, alkyl, haloalkyl, or alkoxy;

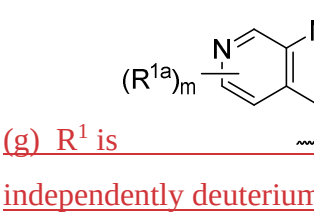
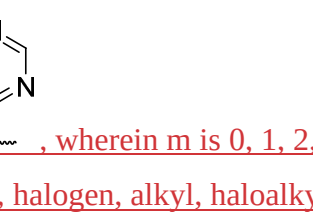
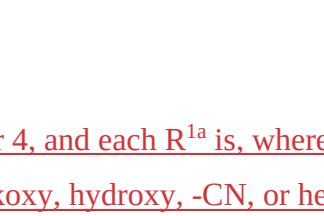
(e) R^1 is 
, or 
, wherein m is 0, 1, 2, 3, 4, or 5 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium;

(f) R^1 is 
, wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl,

wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium;

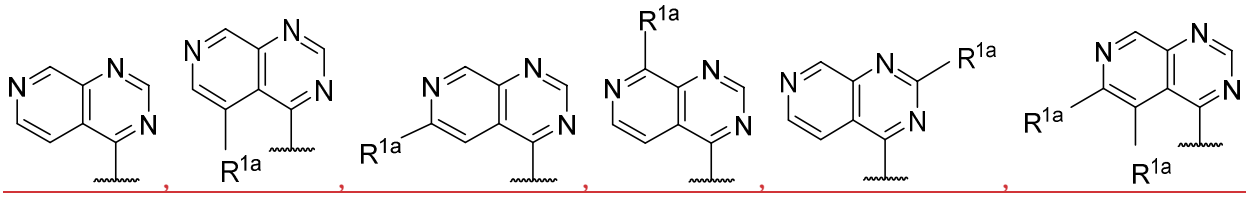
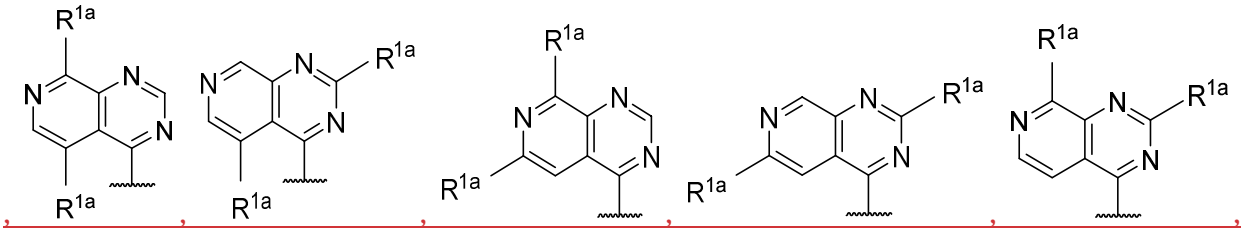
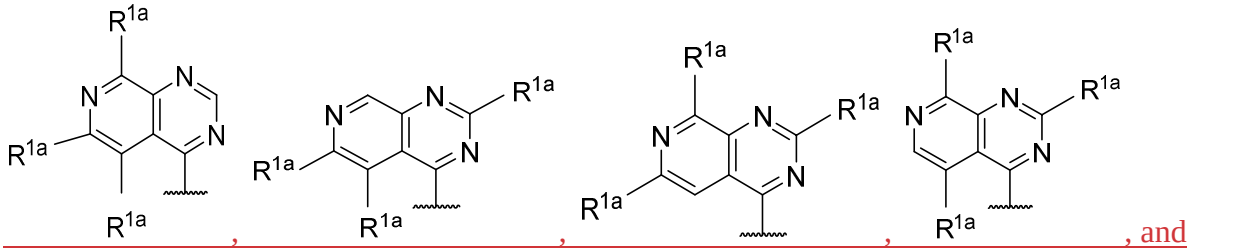
optionally wherein R^1 is selected from the group consisting of

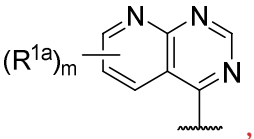




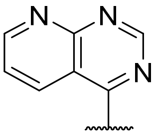
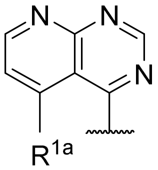
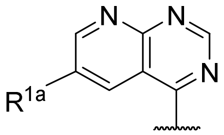
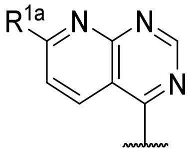
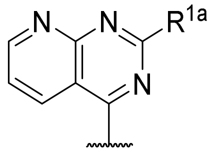
(g) R^1 is , wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium;

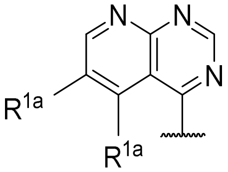
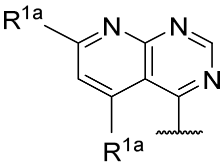
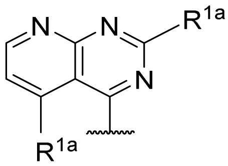
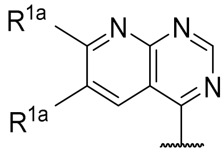
optionally wherein R^1 is selected from the group consisting of

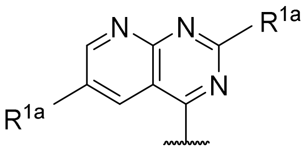
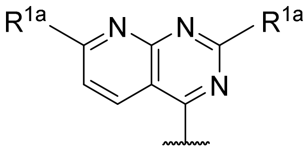
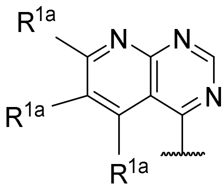
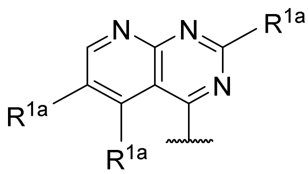




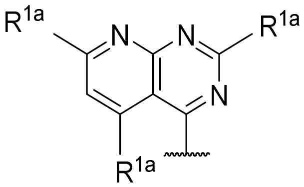
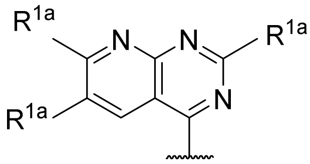
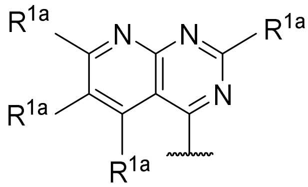

(h) R^1 is  , wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium;

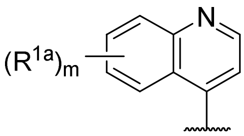
optionally wherein R^1 is selected from the group consisting of

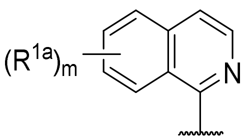
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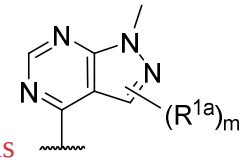
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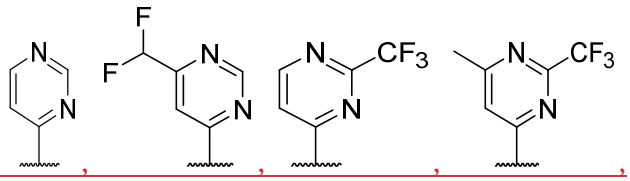
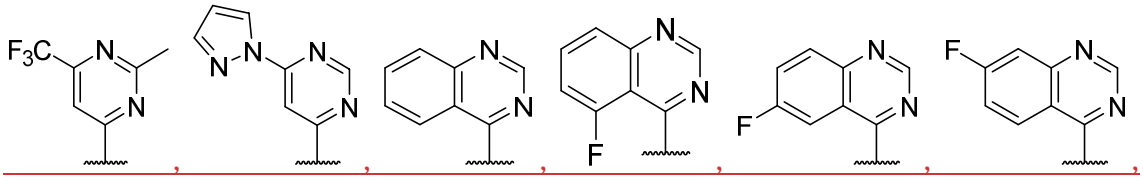
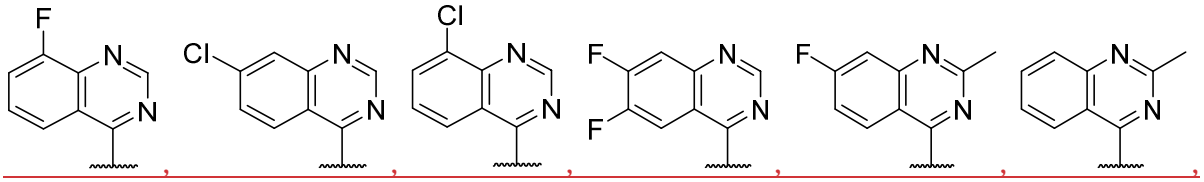
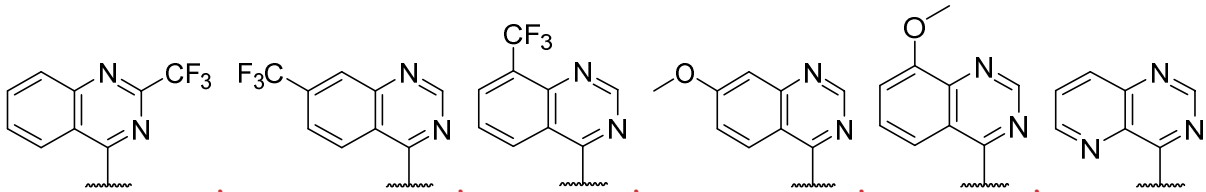
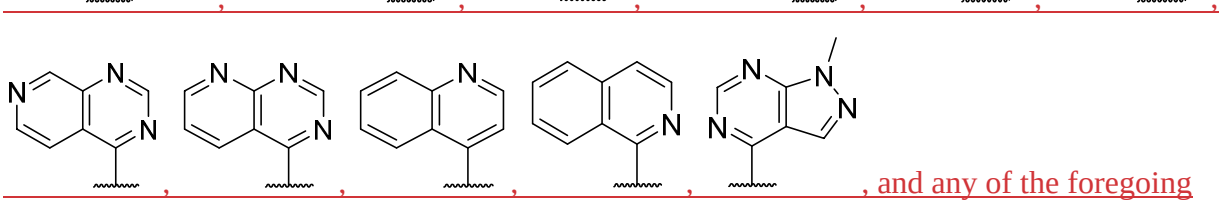
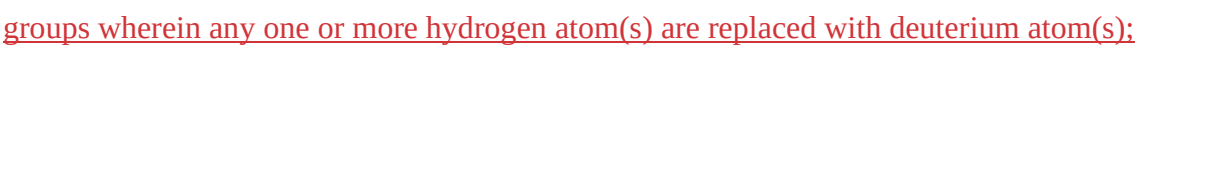
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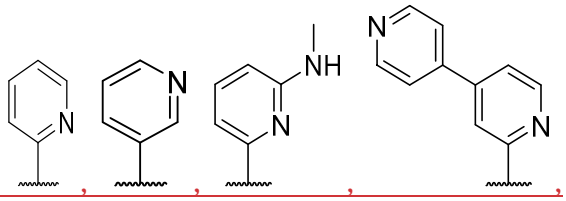
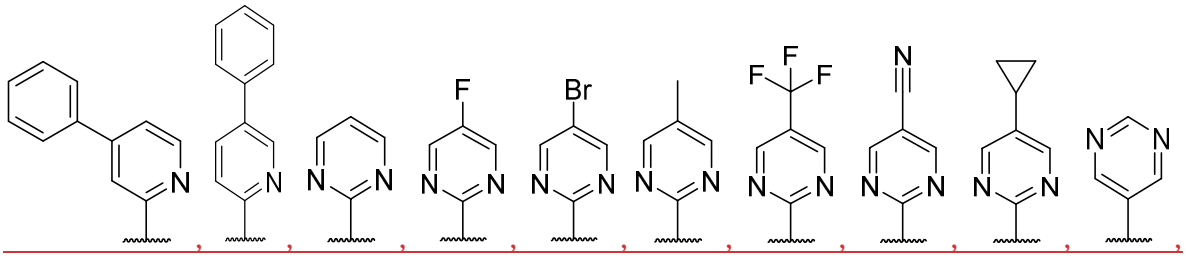
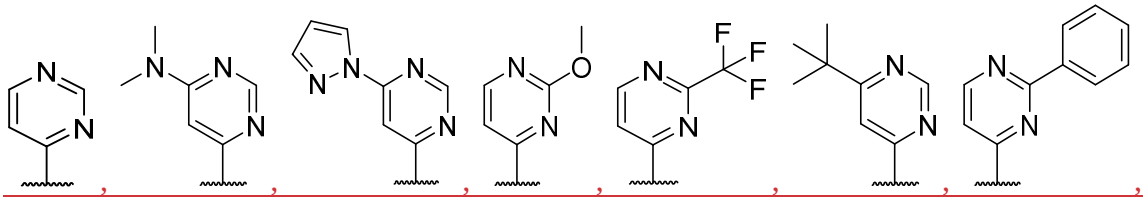
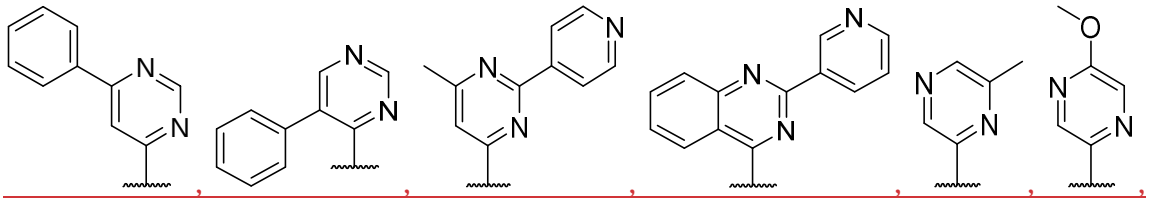
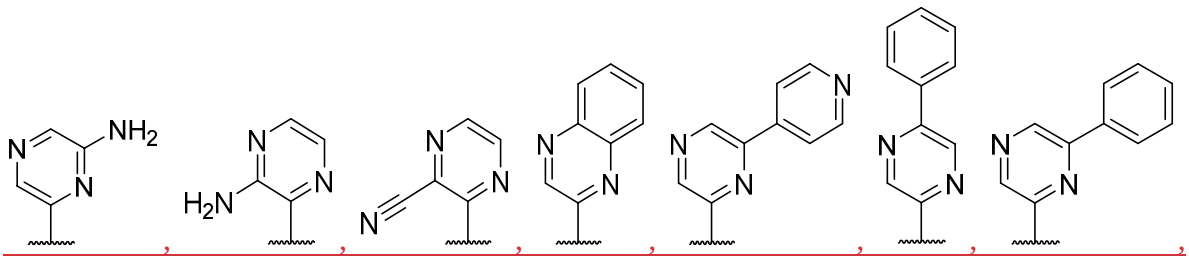
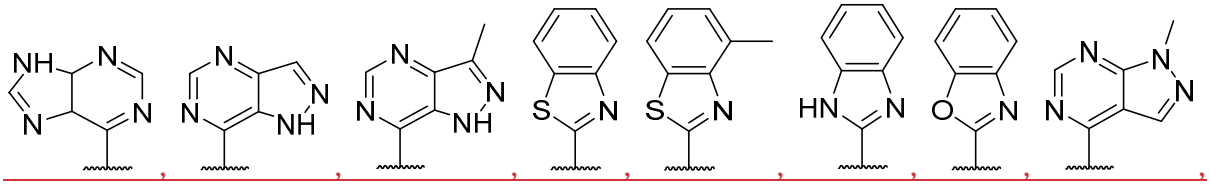
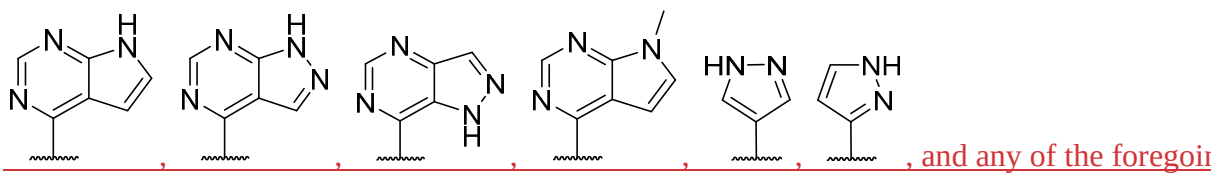
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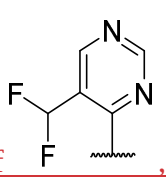
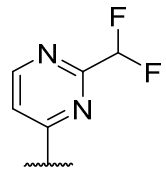
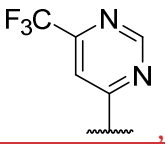
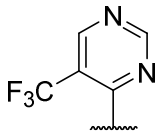
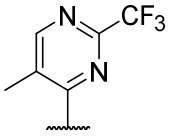
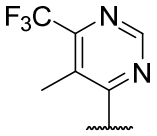
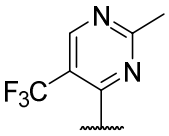
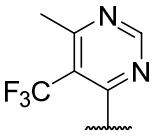
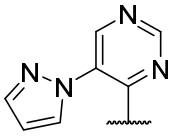
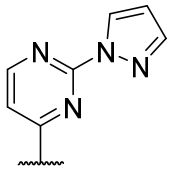
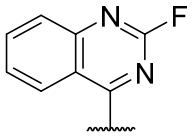
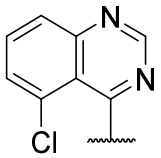
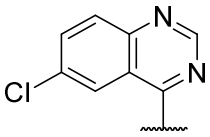
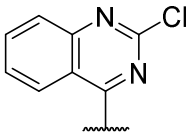
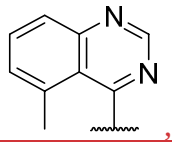
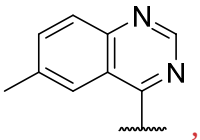
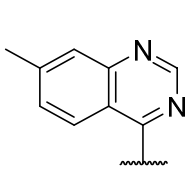
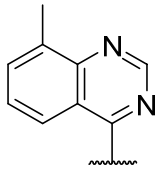
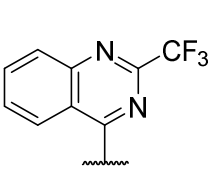
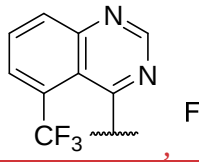
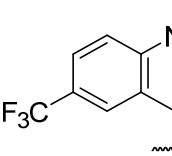
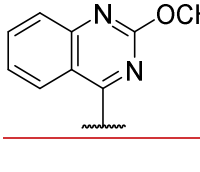
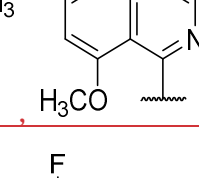
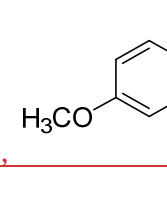
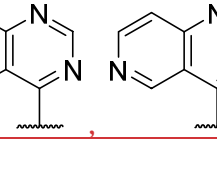
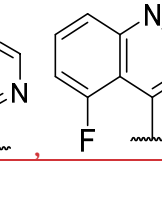
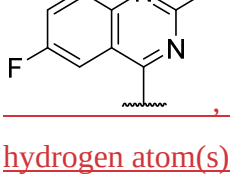
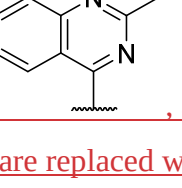
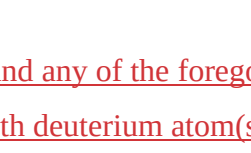
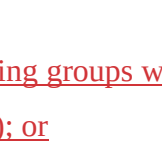
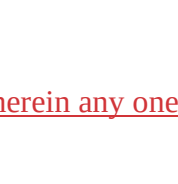
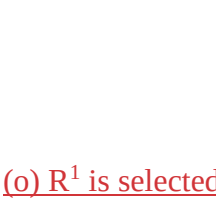
(i) R^1 is  , wherein m is 0, 1, 2, 3, 4, 5, or 6 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium;

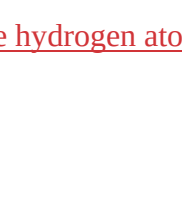
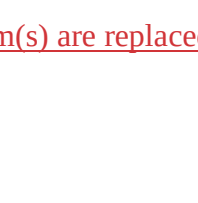
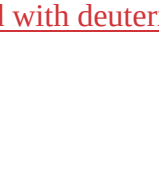
(j) R^1 is  , wherein m is 0, 1, 2, 3, 4, 5, or 6 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium;

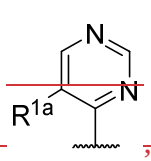
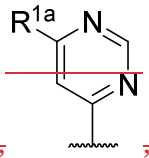
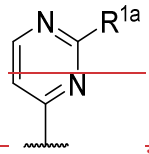
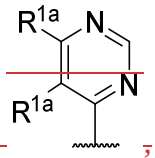
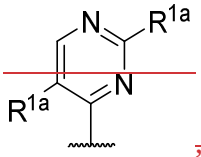
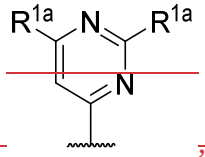
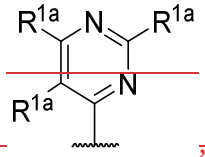
(k) R^1 is  , wherein m is 0, 1, or 2 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium;

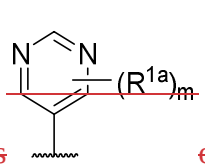
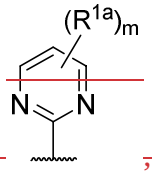
(l) R^1 is selected from the group consisting of  ,  ,  ,  ,  ,  , , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s);

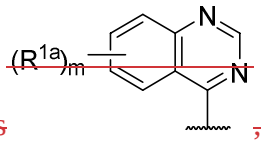
(m) R^1 is selected from the group consisting of  ,  ,  ,  ,  ,  ,  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s);

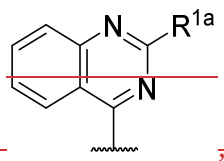
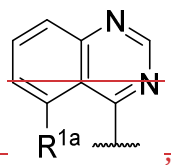
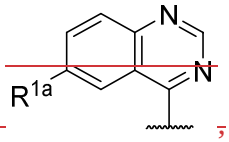
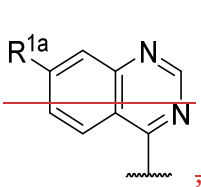
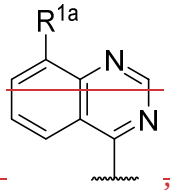
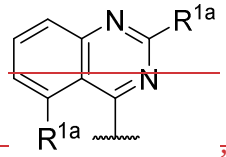
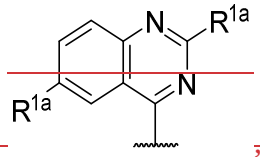
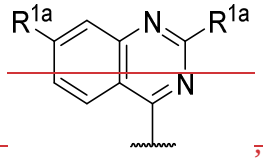
(n) R^1 is selected from the group consisting of  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s); or

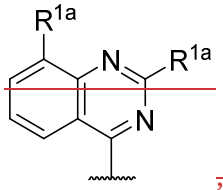
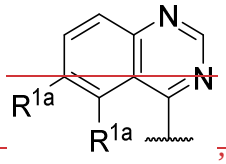
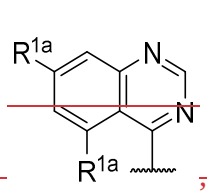
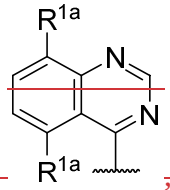
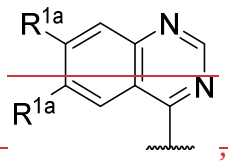
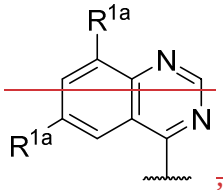
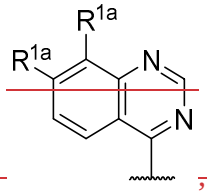
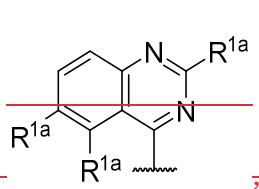
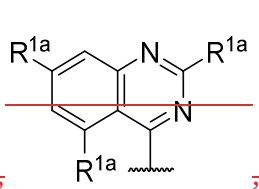
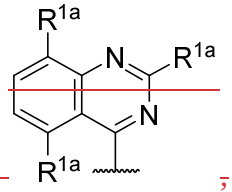
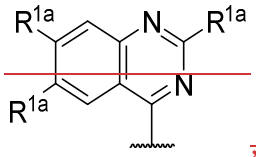
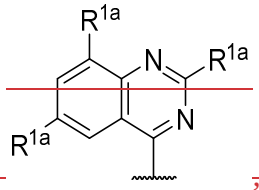
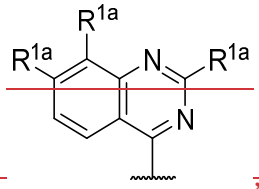
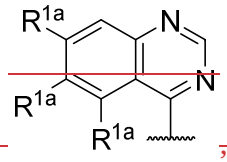
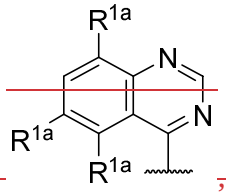
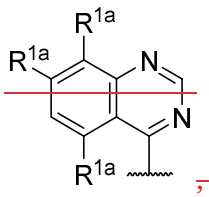
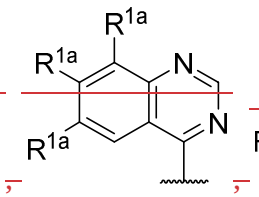
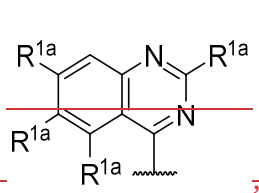
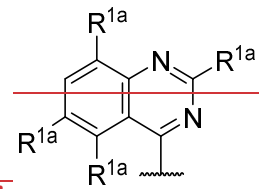
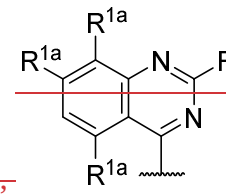
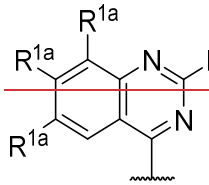
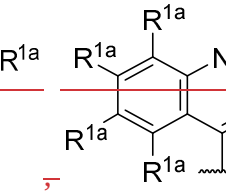
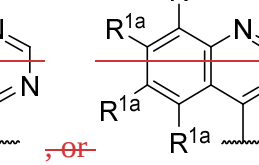
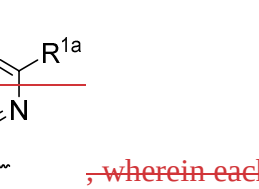
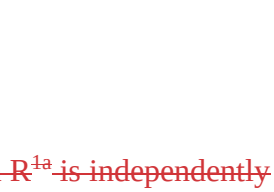
(o) R^1 is selected from the group consisting of  ,  ,  , , , , , , , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

62. The method of claim 60, wherein R^1 is  ,  ,  ,  ,  ,  , or  , wherein each R^{1a} is independently deuterium, alkyl, haloalkyl, or heteroaryl.

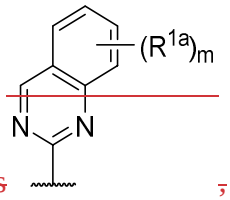
63. The method of any one of claims 1 or 36-38, wherein R^1 is  or  , wherein m is 0, 1, 2, or 3 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

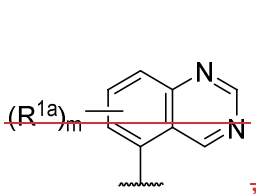
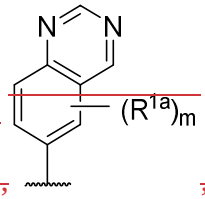
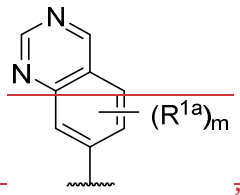
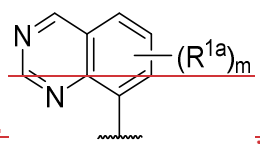
64. The method of any one of claims 1 or 36-38, wherein R^1 is  , wherein m is 0, 1, 2, 3, 4, or 5 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

65. The method of claim 64, wherein R^1 is  ,  ,  ,  ,  ,  ,  ,  .

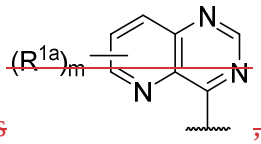


























, or , wherein each R^{1a} is independently deuterium, halogen, alkyl, haloalkyl, or alkoxy.

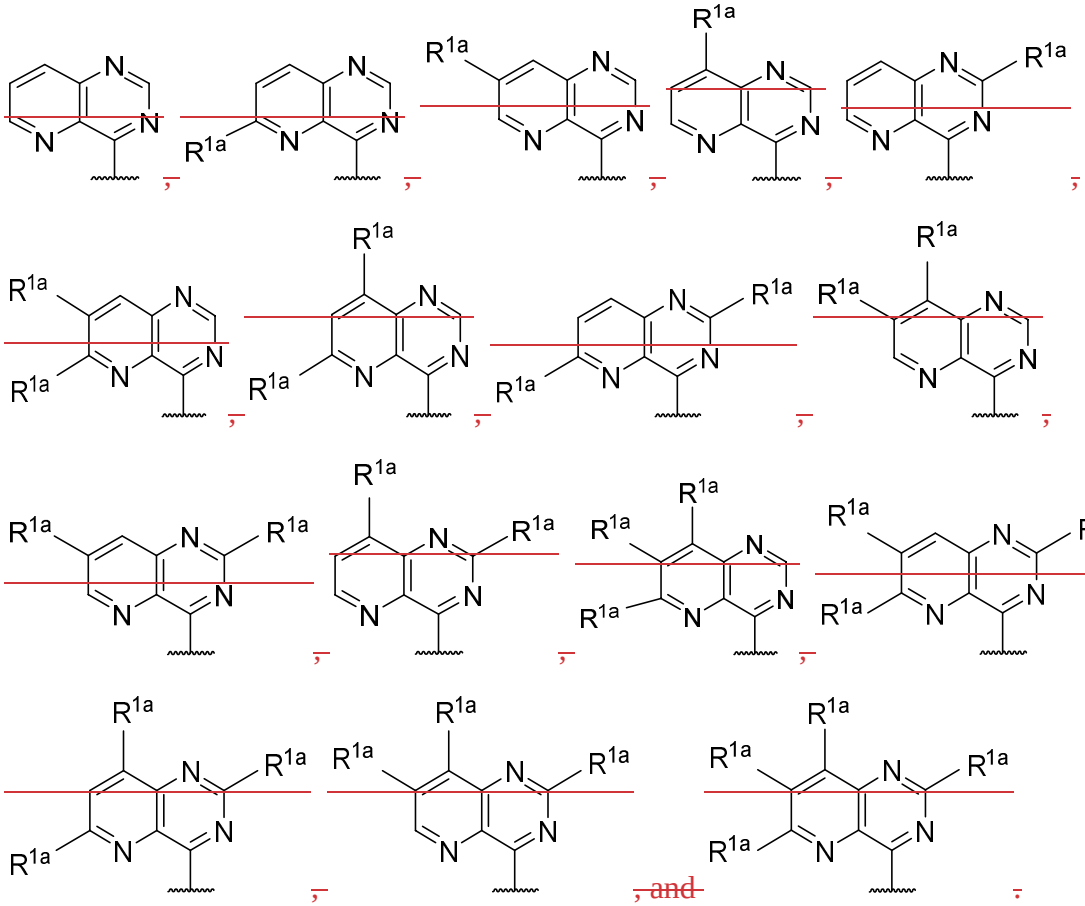
66. The method of any one of claims 1 or 36-38, wherein R^1 is  ,

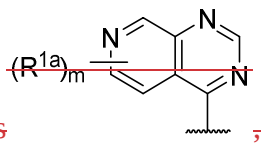





, wherein m is 0, 1, 2, 3, 4, or 5 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

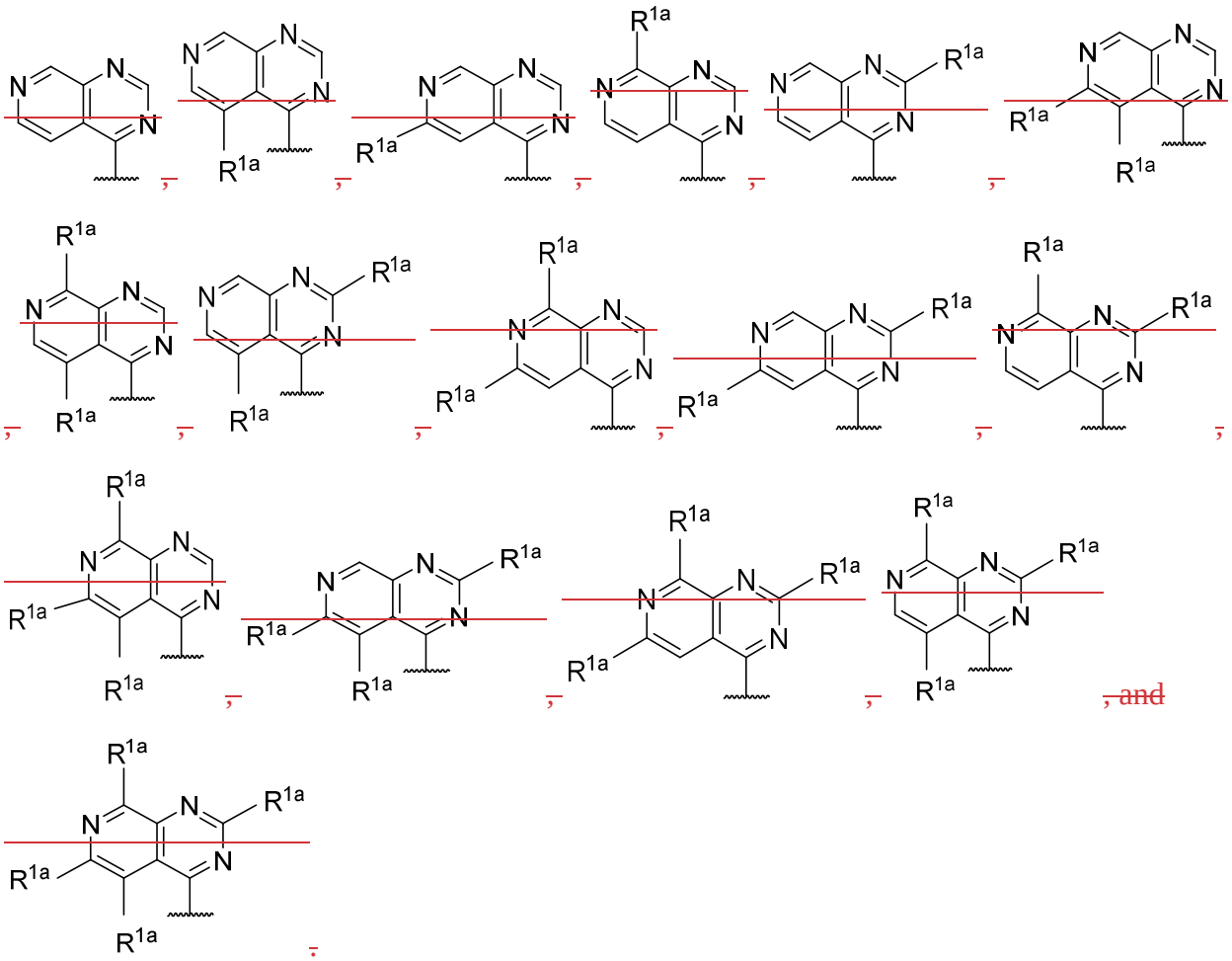
67. The method of any one of claims 1 or 36-38, wherein R^1 is  , wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

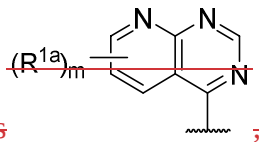
68. The method of claim 67, wherein R^1 is selected from the group consisting of



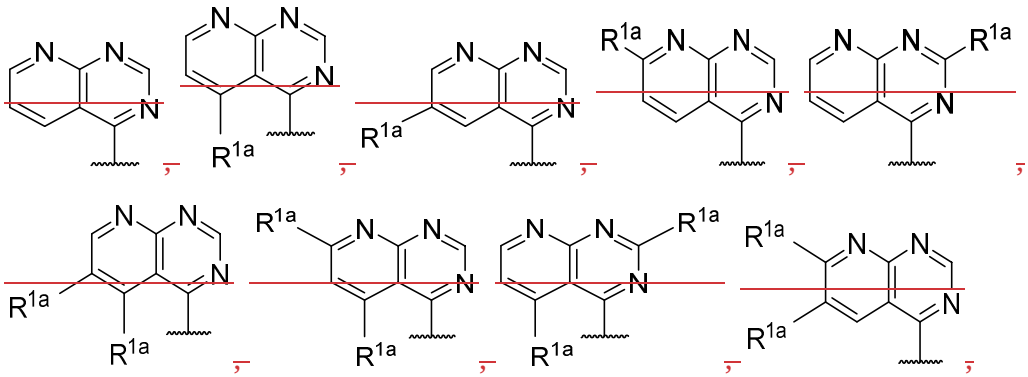
69. The method of any one of claims 1 or 36-38, wherein R^1 is  , wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

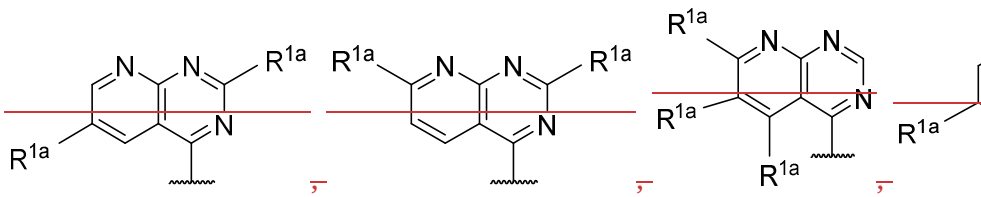
70. The method of claim 69, wherein R^1 is selected from the group consisting of

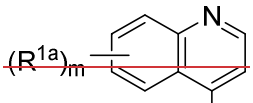


71. The method of any one of claims 1 or 36-38, wherein R^1 is  , wherein m is 0, 1, 2, 3, or 4, and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

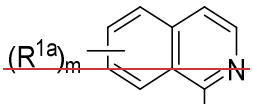
72. The method of claim 71, wherein R^1 is selected from the group consisting of



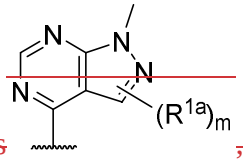


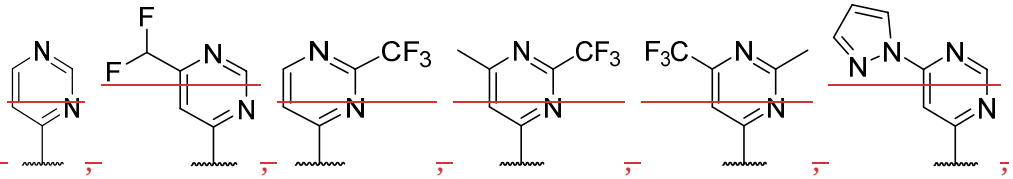
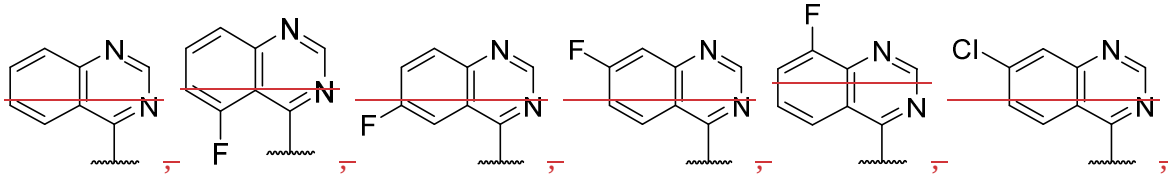
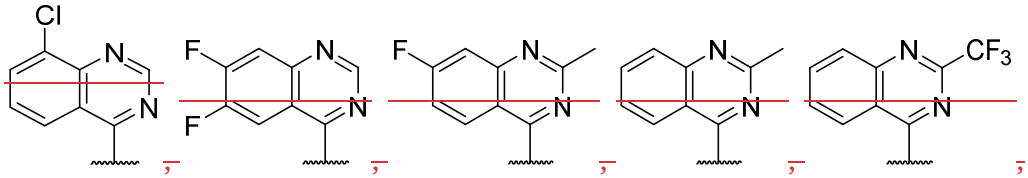
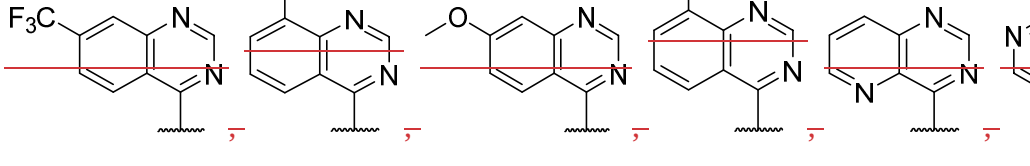
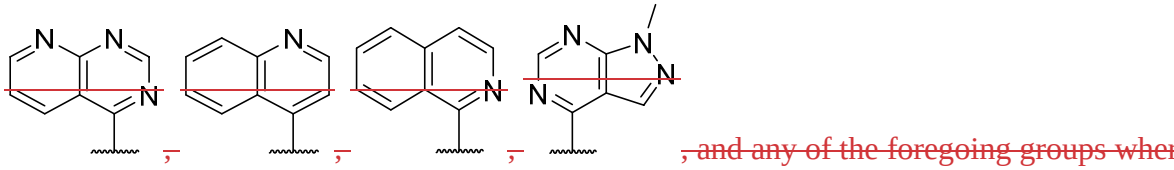
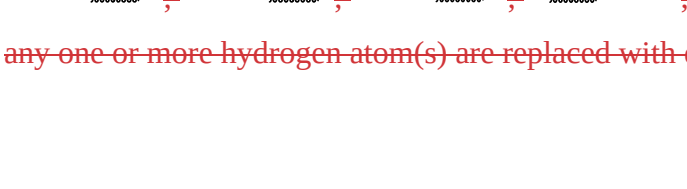


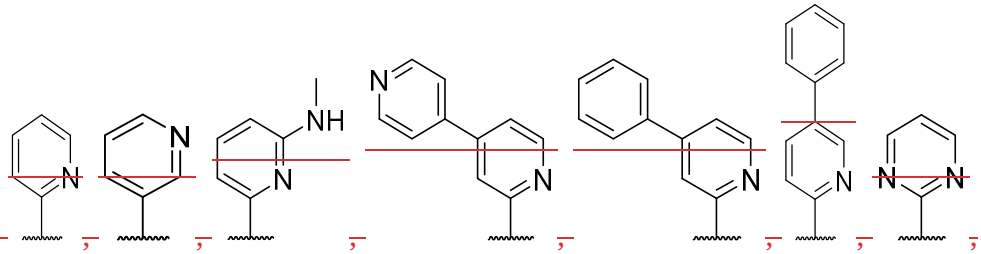
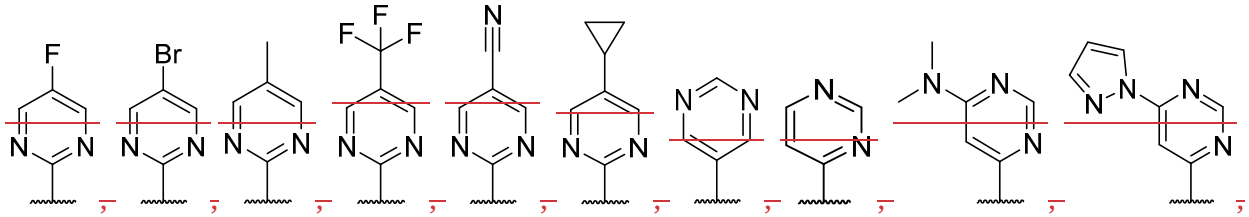
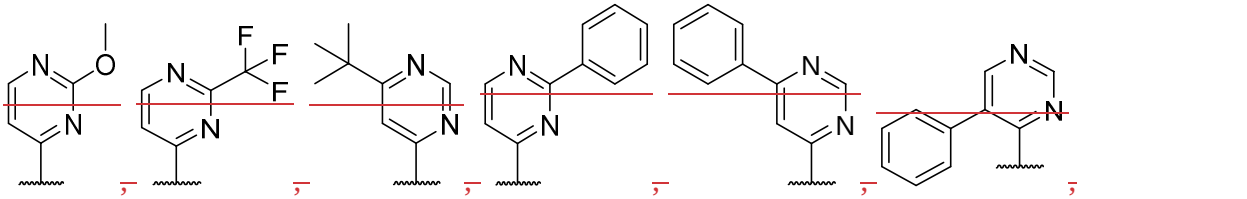
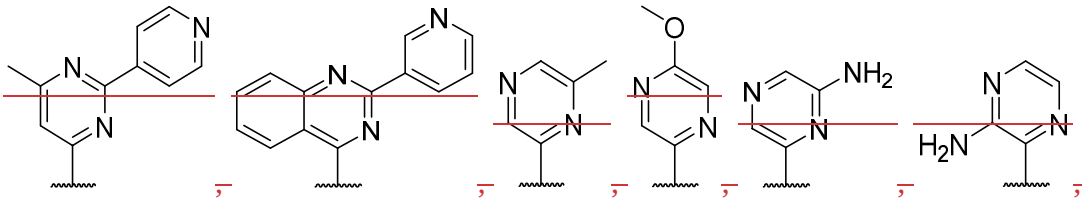
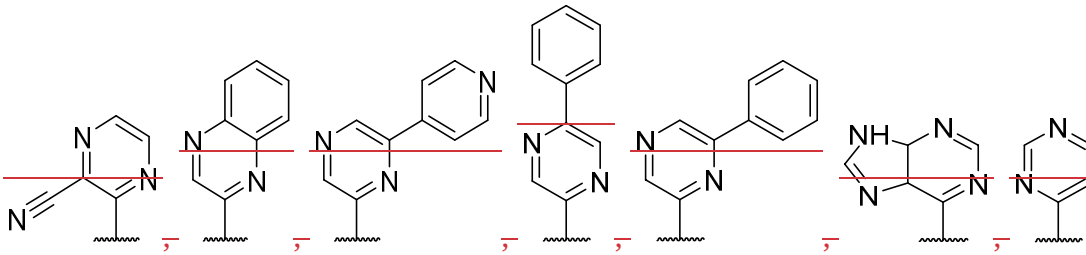
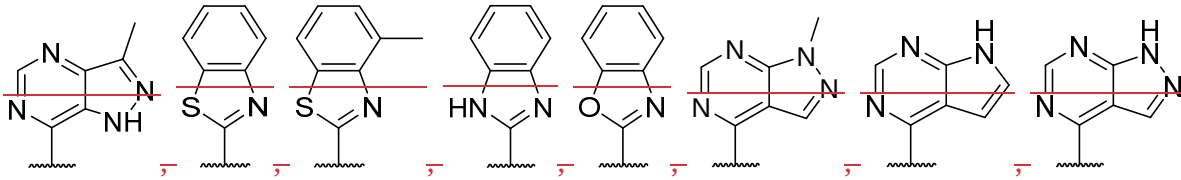
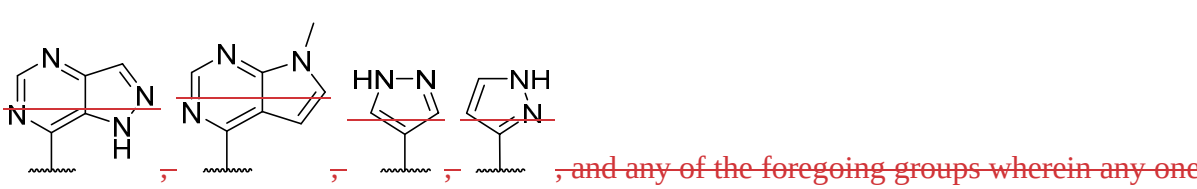
~~73. The method of any one of claims 1 or 36-38, wherein R^1 is , wherein m is 0, 1, 2, 3, 4, 5, or 6 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.~~

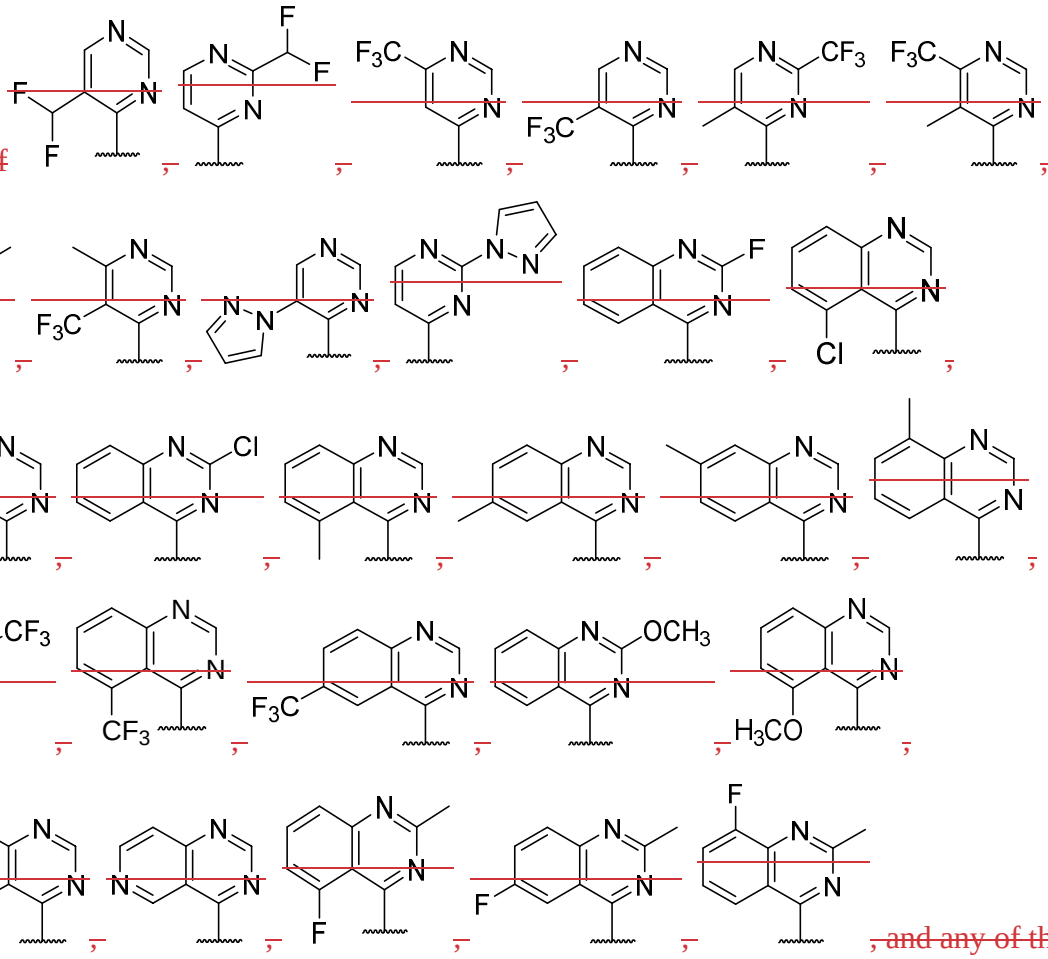


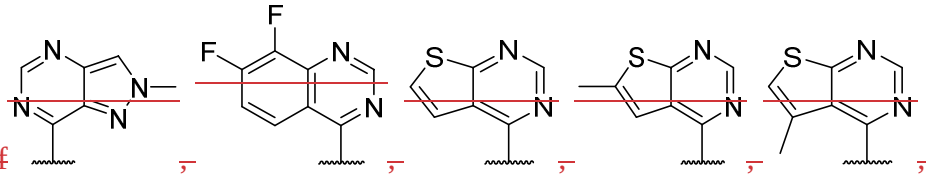
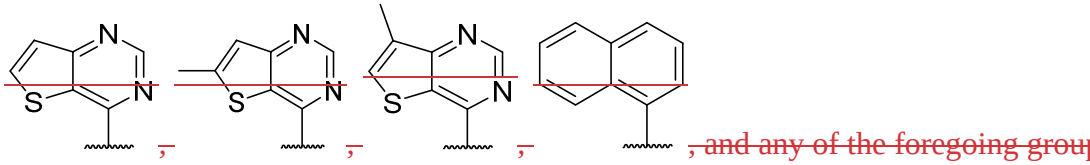
~~74. The method of any one of claims 1 or 36-38, wherein R^1 is , wherein m is 0, 1, 2, 3, 4, 5, or 6 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.~~

75. The method of any one of claims 1 or 36-38, wherein R^1 is  , wherein m is 0, 1, or 2 and each R^{1a} is, where applicable, independently deuterium, halogen, alkyl, haloalkyl, alkoxy, hydroxy, -CN, or heteroaryl, wherein the alkyl, haloalkyl, alkoxy, hydroxy, and heteroaryl of R^{1a} are independently optionally substituted by deuterium.

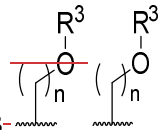
76. The method of any one of claims 1 or 36-38, wherein R^1 is selected from the group consisting of  ,  ,  ,  ,  ,  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

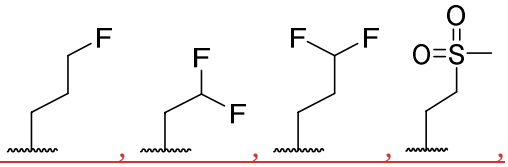
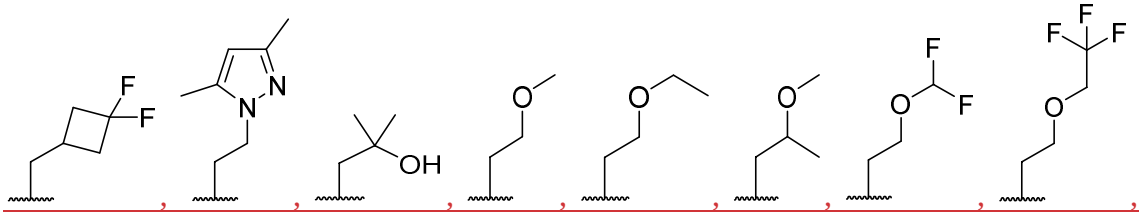
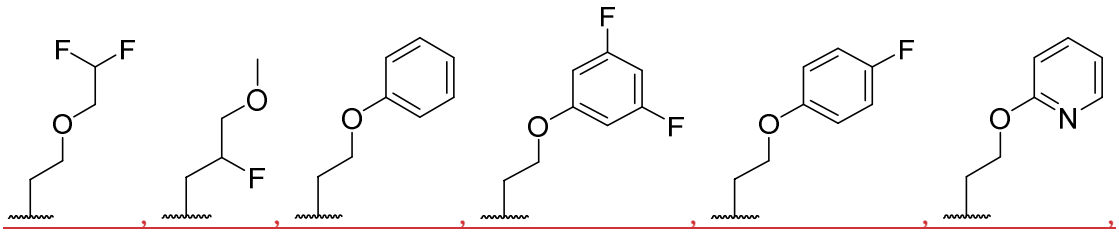
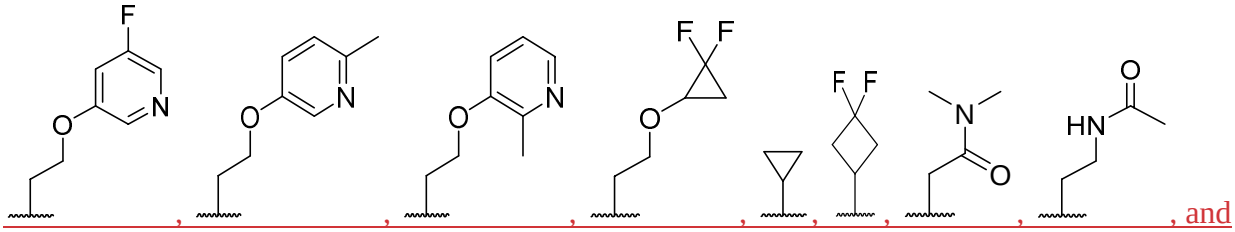
77. The method of any one of claims 1 or 36-38, wherein R^1 is selected from the group consisting of  ,  ,  ,  ,  ,  ,  , , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

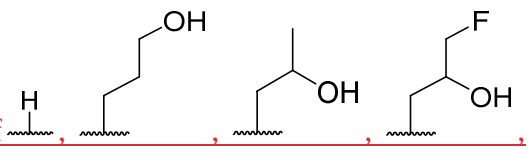
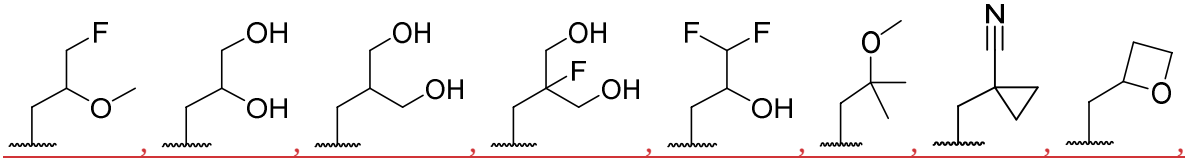
~~78. The method of any one of claims 1 or 36-38, wherein R^1 is selected from the group consisting of~~  , , , , , , , ~~and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).~~

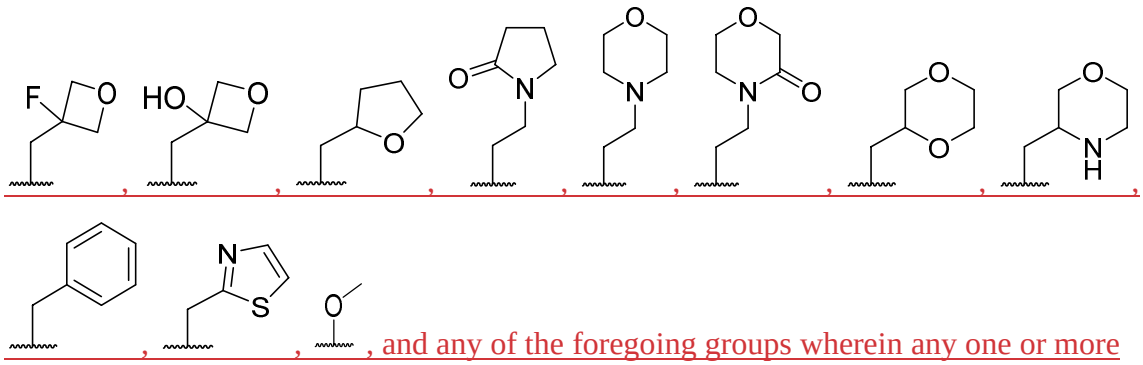
~~79. The method of any one of claims 1 or 36-38, wherein R^1 is selected from the group consisting of~~  ,  , ~~and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).~~

80.26. The use~~method~~ of any one of claims 1 or 20-23~~36-48~~ or 25~~61-79~~, wherein

(i) R^2 is  , wherein n is 1, 2, 3, 4, 5, or 6, and R^3 is C_1-C_2 alkyl optionally substituted by fluoro; phenyl optionally substituted by fluoro; pyridinyl optionally substituted by fluoro or methyl; or cyclopropyl optionally substituted by fluoro;

(ii) R^2 is selected from the group consisting of  ,  ,  ,  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s);

(iii) R^2 is selected from the group consisting of  , 



, and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s);

(iv) R^2 is C_3-C_5 alkyl substituted by both fluorine and -OCH_3;

(v) R^2 is C_1-C_6 alkyl optionally substituted by -OR^3, and R^3 is phenyl optionally substituted by fluorine;

(vi) R^2 is C_1-C_6 alkyl optionally substituted by -OR^3, and R^3 is pyridinyl optionally substituted by fluorine or methyl;

(vii) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is halogen;

(viii) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is deuterium;

(ix) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is 3- to 12-membered heterocyclyl optionally substituted by oxo;

(x) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is 4- to 5-membered heterocyclyl optionally substituted by oxo;

(xi) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is C_6-C_{14} aryl optionally substituted by halogen or –OR^6;

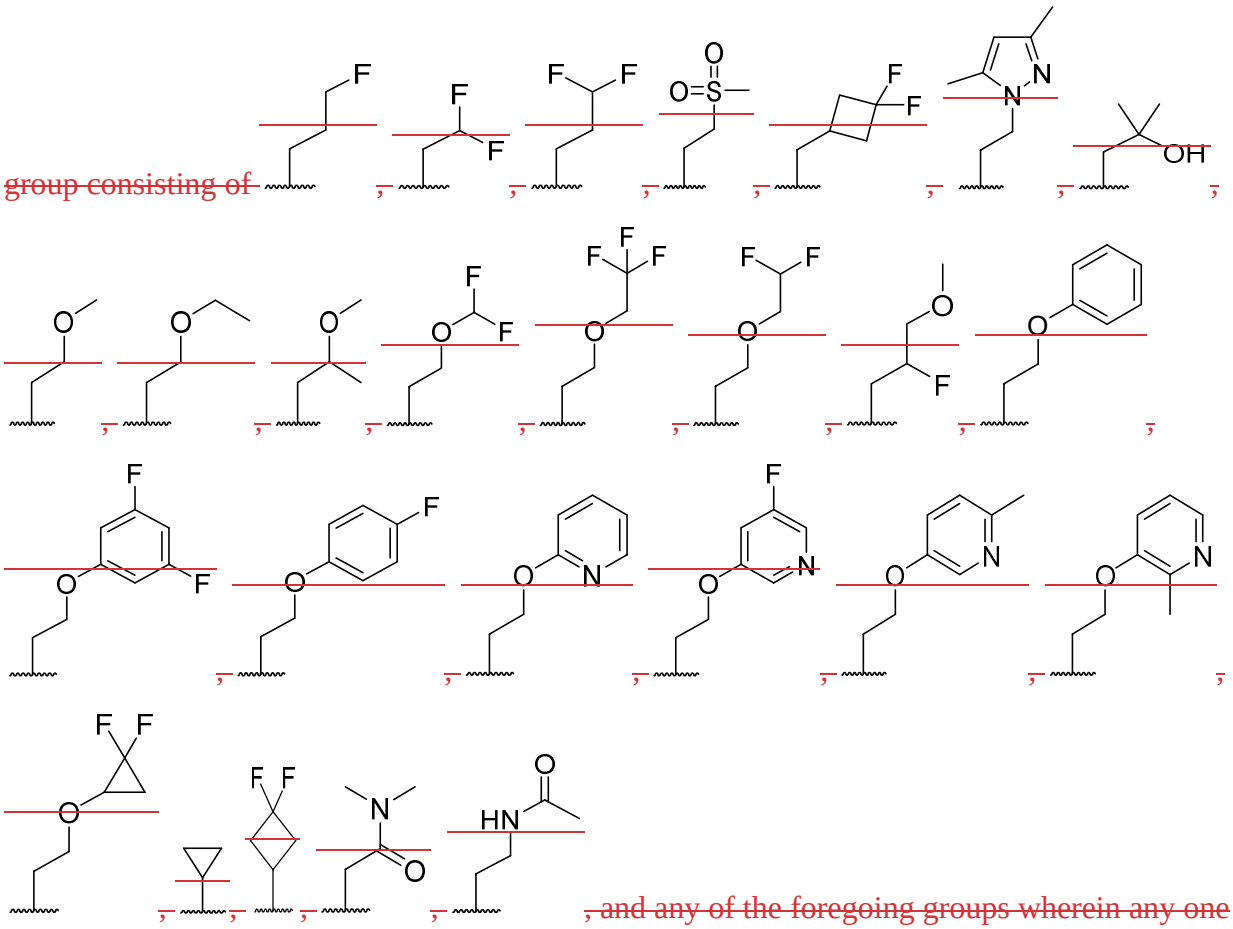
(xii) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is phenyl optionally substituted by halogen or –OR^6;

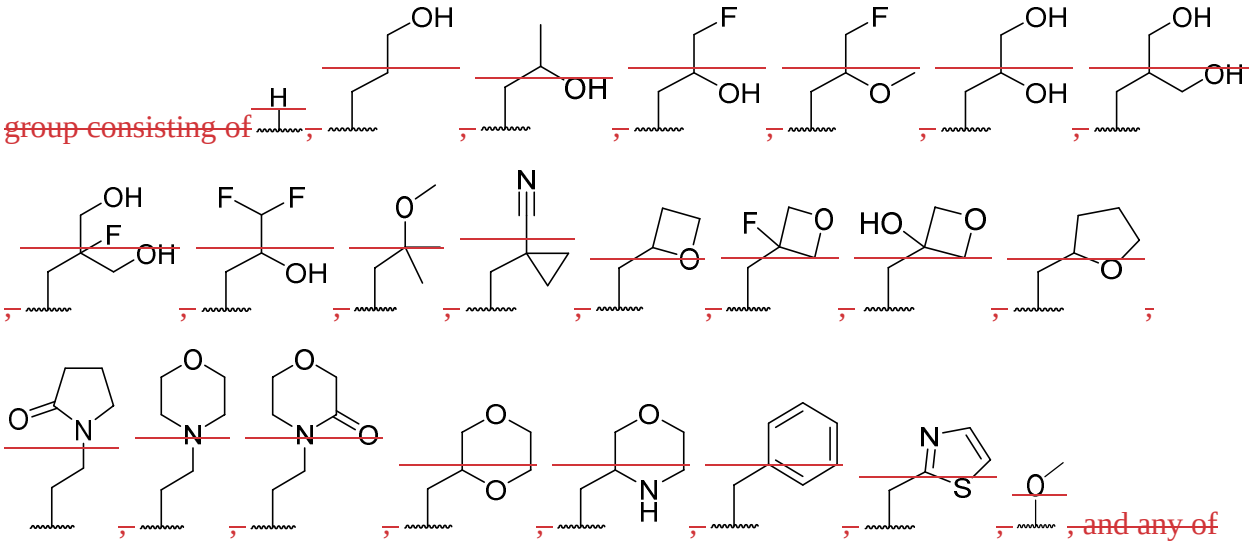
(xiii) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is 5- to 10-membered heteroaryl optionally substituted by C_1-C_6 alkyl;

(xiv) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is pyrazolyl optionally substituted by methyl;

(xv) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is C_3-C_8 cycloalkyl optionally substituted by -CN, halogen, or –OR^6; or

(xvi) R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is -$S(O)_2R^3$.

81. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is selected from the group consisting of  , and any of the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).

82. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is selected from the group consisting of  , and any of

~~the foregoing groups wherein any one or more hydrogen atom(s) are replaced with deuterium atom(s).~~

~~83. The method of any one of claims 1 or 36-45, wherein R^2 is C_3-C_5 alkyl substituted by both fluorine and $-OCH_3$.~~

~~84. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl optionally substituted by $-OR^3$, and R^3 is phenyl optionally substituted by fluorine.~~

~~85. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl optionally substituted by $-OR^3$, and R^3 is pyridinyl optionally substituted by fluorine or methyl.~~

~~86. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is halogen.~~

~~87. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is deuterium.~~

~~88. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is 3- to 12-membered heterocyclyl optionally substituted by oxo.~~

~~89. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is 4- to 5-membered heterocyclyl optionally substituted by oxo.~~

~~90. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is C_6-C_{14} aryl optionally substituted by halogen or $-OR^6$.~~

~~91. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is phenyl optionally substituted by halogen or $-OR^6$.~~

~~92. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is 5- to 10-membered heteroaryl optionally substituted by C_1-C_6 alkyl.~~

~~93. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is pyrazolyl optionally substituted by methyl.~~

~~94. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is C_3-C_8 cycloalkyl optionally substituted by -CN, halogen, or -OR^6.~~

~~95. The method of any one of claims 1 or 36-48 or 61-79, wherein R^2 is C_1-C_6 alkyl substituted by R^{2a} wherein R^{2a} is -$S(O)_2R^3$.~~

~~96.~~27. The use~~method~~ of any one of claims 1 or 20-22~~36-38~~, wherein R^1 is pyridyl optionally substituted by R^{1a}~~.~~; or
wherein R^1 is indazolyl optionally substituted by R^{1a}; or
wherein R^1 is 1*H*-pyrrolopyridyl optionally substituted by R^{1a}; or
wherein R^1 is quinolinyl optionally substituted by R^{1a}; or
wherein R^1 is phenyl optionally substituted by R^{1a} or
wherein R^1 is indanyl optionally substituted by R^{1a}.

~~97. The method of any one of claims 1 or 36-38, wherein R^1 is indazolyl optionally substituted by R^{1a}.~~

~~98. The method of any one of claims 1 or 36-38, wherein R^1 is 1*H*-pyrrolopyridyl optionally substituted by R^{1a}.~~

~~99. The method of any one of claims 1 or 36-38, wherein R^1 is quinolinyl optionally substituted by R^{1a}.~~

~~100. The method of any one of claims 1 or 36-38, wherein R^1 is phenyl optionally substituted by R^{1a}.~~

~~101. The method of any one of claims 1 or 36-38, wherein R^1 is indanyl optionally substituted by R^{1a}.~~

~~102.~~28. The use~~method~~ of claim 1, wherein the compound, or a salt thereof, is selected from Compound Nos. 1-780.

~~103. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-2-((7-fluoro-2-methylquinazolin-4-yl)amino)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a salt thereof.~~

~~104. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-4-((2-hydroxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid, or a salt thereof.~~

~~105.~~29. The use~~method~~ of any one of claims 1, 20~~36~~, or 22~~38~~, wherein the compound is (S)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid, or a salt thereof.

30. The use of claim 29, wherein the compound is (S)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid.

31. The use of claim 30, wherein the condition is ARDS, or a precursor condition to ARDS.

32. The use of claim 29, wherein the compound is a salt of (S)-4-((2-methoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid.

33. The use of claim 32, wherein the condition is ARDS, or a precursor condition to ARDS.

~~106. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-4-((2-(3,5-difluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(quinazolin-4-ylamino)butanoic acid, or a salt thereof.~~

~~107. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-phenylpyrimidin-4-yl)amino)butanoic acid, or a salt thereof.~~

~~108. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((5-phenylpyrimidin-4-yl)amino)butanoic acid, or a salt thereof.~~

~~109. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-2-((6-(1H-pyrazol-1-yl)pyrimidin-4-yl)amino)-4-((3-fluoropropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a salt thereof.~~

~~110. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-4-(((S)-3-fluoro-2-methoxypropyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-(thieno[2,3-d]pyrimidin-4-ylamino)butanoic acid, or a salt thereof.~~

~~111. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl)amino)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a salt thereof.~~

~~112. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((2-phenoxyethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a salt thereof.~~

~~113. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-2-((1H-pyrazolo[3,4-d]pyrimidin-4-yl)amino)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)butanoic acid, or a salt thereof.~~

~~114. The method of any one of claims 1, 36, or 38, wherein the compound is (S)-4-((2-(4-fluorophenoxy)ethyl)(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)amino)-2-((2-methyl-2H-pyrazolo[4,3-d]pyrimidin-7-yl)amino)butanoic acid, or a salt thereof.~~

~~115.~~34.The use~~method~~ of any of claims 1-33~~114~~, wherein the amount of the compound effective to treat the condition in mg is about one of: 10, 15, 20, 30, 40, 50, 75, 80, 100, 120, 160, 240, or 320, or a range between any two of the preceding values; or wherein the amount of the compound effective to treat the condition in mg is about one of: 400, 480, 560, 640, 720, 800, 880, 960, or 1040, or a range between any two of the preceding values.

~~116. The method of any of claims 1-114, wherein wherein the amount of the compound effective to treat the condition in mg is about one of: 400, 480, 560, 640, 720, 800, 880, 960, or 1040, or a range between any two of the preceding values.~~

~~117.~~35.The use~~method~~ of any of claims 1-34~~116~~, wherein the use comprises administration of the medicament ~~comprising administering the compound, or a salt thereof,~~ to the individual effective to provide a plasma-adjusted concentration in the individual with respect to an α_V integrin in the individual of at least about one of IC_{50}, IC_{70}, or IC_{90}, optionally wherein the α_V integrin being $\alpha_V\beta_6$.

~~118. The method of claim 117, the α_V integrin being $\alpha_V\beta_6$.~~

~~119.~~36.The use~~method~~ of claim 1, the individual being warm blooded, or the individual being a mammal; or the individual being a human; or the individual being a rodent, bovid, ovid, ursine, equine, porcine, pinniped, ungulate, canine, feline, bat, or pangolin; or the individual being avian; or the individual being a chicken, duck, goose, swan, or corvid; or the individual being cold-blooded; or the individual being a reptile; or the individual being an amphibian.

~~120. The method of claim 119, the individual being a mammal.~~

~~121. The method of claim 119, the individual being a human.~~

~~122. The method of claim 119, the individual being a rodent, bovid, ovid, ursine, equine, porcine, pinniped, ungulate, canine, feline, bat, or pangolin.~~

~~123. The method of claim 119, the individual being avian.~~

~~124. The method of claim 119, the individual being a chicken, duck, goose, swan, or corvid.~~

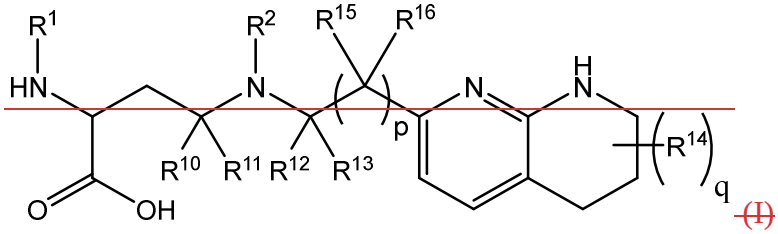
~~125. The method of claim 1, the individual being cold-blooded.~~

~~126. The method of claim 1, the individual being a reptile.~~

~~127. The method of claim 1, the individual being an amphibian.~~

~~128.~~37. The use~~method~~ of claim 1, the infectious agent comprising a human-infectious agent derived from a nonhuman reservoir species, the use comprises administration of the medicament ~~method comprising administering the compound~~ to an individual of the nonhuman reservoir species.

~~129. Use of a compound represented by formula (I):~~



~~(I)~~

~~or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a condition, the condition comprising one or more of: causation by or association with an infectious agent, shock, pancreatitis, or trauma;~~

~~wherein:~~

~~R^1 is C_6-C_{14} aryl or 5- to 10-membered heteroaryl wherein the C_6-C_{14} aryl and 5- to 10-membered heteroaryl are optionally substituted by R^{1a};~~

~~R^2 is hydrogen; deuterium; C_1-C_6 alkyl optionally substituted by R^{2a}; -O-C_1-C_6 alkyl optionally substituted by R^{2a}; C_3-C_6 cycloalkyl optionally substituted by R^{2b}; -O-C_3-C_6 cycloalkyl optionally substituted by R^{2b}; 3- to 12-membered heterocyclyl optionally substituted by R^{2c}; or -$S(O)_2R^{2d}$; with the proviso that any carbon atom bonded directly to a nitrogen atom is either unsubstituted or substituted with deuterium;~~

~~each R^{1a} is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, C_4-C_8 cycloalkenyl, 3- to 12-membered heterocyclyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, deuterium, halogen, -CN, -OR^3, -SR^3, -NR^4R^5, -NO_2, -C=NH(OR^3), -$C(O)R^3$, -$OC(O)R^3$, -$C(O)OR^3$, -$C(O)NR^4R^5$, -$NR^3C(O)R^4$, -$NR^3C(O)OR^4$, -$NR^3C(O)NR^4R^5$, -$S(O)R^3$, -$S(O)_2R^3$,~~

~~$-NR^3S(O)R^4$, $-NR^3S(O)_2R^4$, $-S(O)NR^4R^5$, $-S(O)_2NR^4R^5$, or $-P(O)(OR^4)(OR^5)$, wherein each R^{1a} is, where possible, independently optionally substituted by deuterium, halogen, oxo, $-OR^6$, $-NR^6R^7$, $-C(O)R^6$, -CN, $-S(O)R^6$, $-S(O)_2R^6$, $-P(O)(OR^6)(OR^7)$, C_3-C_8 cycloalkyl, 3- to 12-membered heterocyclyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, or C_1-C_6 alkyl optionally substituted by deuterium, oxo, -OH or halogen;~~

~~each R^{2a}, R^{2b}, R^{2c}, R^{2e}, and R^{2f} is independently oxo or R^{1a};~~

~~R^{2d} is C_1-C_6 alkyl optionally substituted by R^{2e} or C_3-C_5 cycloalkyl optionally substituted by R^{2f};~~

~~R^3 is independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl or 3- to 6-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl and 3- to 6-membered heterocyclyl of R^3 are independently optionally substituted by halogen, deuterium, oxo, -CN, $-OR^8$, $-NR^8R^9$, $-P(O)(OR^8)(OR^9)$, or C_1-C_6 alkyl optionally substituted by deuterium, halogen, -OH or oxo;~~

~~R^4 and R^5 are each independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl or 3- to 6-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl and 3- to 6-membered heterocyclyl of R^4 and R^5 are independently optionally substituted by deuterium, halogen, oxo, -CN, $-OR^8$, $-NR^8R^9$ or C_1-C_6 alkyl optionally substituted by deuterium, halogen, -OH or oxo;~~

~~or R^4 and R^5 are taken together with the atom to which they attached to form a 3- to 6-membered heterocyclyl optionally substituted by deuterium, halogen, oxo, $-OR^8$, $-NR^8R^9$ or C_1-C_6 alkyl optionally substituted by deuterium, halogen, oxo or -OH;~~

~~R^6 and R^7 are each independently hydrogen, deuterium, C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo, C_2-C_6 alkenyl optionally substituted by deuterium, halogen, or oxo, or C_2-C_6 alkynyl optionally substituted by deuterium, halogen, or oxo;~~

~~or R^6 and R^7 are taken together with the atom to which they attached to form a 3- to 6-membered heterocyclyl optionally substituted by deuterium, halogen, oxo or C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo;~~

~~R^8 and R^9 are each independently hydrogen, deuterium, C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo, C_2-C_6 alkenyl optionally substituted by deuterium, halogen or oxo, or C_2-C_6 alkynyl optionally substituted by deuterium, halogen, or oxo;~~

or R^8 and R^9 are taken together with the atom to which they attached to form a 3-6 membered heterocyclyl optionally substituted by deuterium, halogen, oxo or C_1-C_6 alkyl optionally substituted by deuterium, oxo, or halogen;

each R^{10}, R^{11}, R^{12} and R^{13} are independently hydrogen or deuterium;

R^{14} is deuterium;

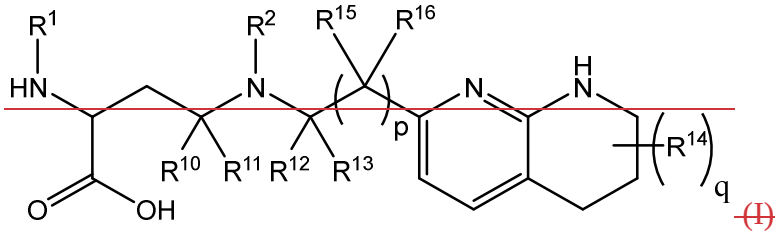
q is 0, 1, 2, 3, 4, 5, 6, 7, or 8;

each R^{15} is independently selected from hydrogen, deuterium, or halogen;

each R^{16} is independently selected from hydrogen, deuterium, or halogen; and

p is 3, 4, 5, 6, 7, 8, or 9.

130. Use of a compound represented by formula (I):



(I)

or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a condition, the condition comprising one or more of pulmonary fibrosis associated with rheumatoid arthritis or progressive familial intrahepatic cholestasis (PFIC);

wherein:

R^1 is C_6-C_{14} aryl or 5- to 10-membered heteroaryl wherein the C_6-C_{14} aryl and 5- to 10-membered heteroaryl are optionally substituted by R^{1a};

R^2 is hydrogen; deuterium; C_1-C_6 alkyl optionally substituted by R^{2a}; -O-C_1-C_6 alkyl optionally substituted by R^{2a}; C_3-C_6 cycloalkyl optionally substituted by R^{2b}; -O-C_3-C_6 cycloalkyl optionally substituted by R^{2b}; 3- to 12-membered heterocyclyl optionally substituted by R^{2c}; or $-S(O)_2R^{2d}$; with the proviso that any carbon atom bonded directly to a nitrogen atom is either unsubstituted or substituted with deuterium;

each R^{1a} is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, C_4-C_8 cycloalkenyl, 3- to 12-membered heterocyclyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, deuterium, halogen, -CN, $-OR^3$, $-SR^3$, $-NR^4R^5$, $-NO_2$, $-C{=}NH(OR^3)$, $-C(O)R^3$, $-OC(O)R^3$, $-C(O)OR^3$, $-C(O)NR^4R^5$, $-NR^3C(O)R^4$, $-NR^3C(O)OR^4$, $-NR^3C(O)NR^4R^5$, $-S(O)R^3$, $-S(O)_2R^3$, $-NR^3S(O)R^4$, $-NR^3S(O)_2R^4$, $-S(O)NR^4R^5$, $-S(O)_2NR^4R^5$, or $-P(O)(OR^4)(OR^5)$, wherein each R^{1a}

is, where possible, independently optionally substituted by deuterium, halogen, oxo, -OR^6, -NR^6R^7, -$C(O)R^6$, -CN, -$S(O)R^6$, -$S(O)_2R^6$, -$P(O)(OR^6)(OR^7)$, C_3-C_8 cycloalkyl, 3- to 12-membered heterocyclyl, 5- to 10-membered heteroaryl, C_6-C_{14} aryl, or C_1-C_6 alkyl optionally substituted by deuterium, oxo, -OH or halogen;

each R^{2a}, R^{2b}, R^{2c}, R^{2e}, and R^{2f} is independently oxo or R^{1a};

R^{2d} is C_1-C_6 alkyl optionally substituted by R^{2e} or C_3-C_5 cycloalkyl optionally substituted by R^{2f};

R^3 is independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl or 3- to 6-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl and 3- to 6-membered heterocyclyl of R^3 are independently optionally substituted by halogen, deuterium, oxo, -CN, -OR^8, -NR^8R^9, -$P(O)(OR^8)(OR^9)$, or C_1-C_6 alkyl optionally substituted by deuterium, halogen, -OH or oxo;

R^4 and R^5 are each independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl or 3- to 6-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, C_6-C_{14} aryl, 5- to 6-membered heteroaryl and 3- to 6-membered heterocyclyl of R^4 and R^5 are independently optionally substituted by deuterium, halogen, oxo, -CN, -OR^8, -NR^8R^9 or C_1-C_6 alkyl optionally substituted by deuterium, halogen, -OH or oxo;

or R^4 and R^5 are taken together with the atom to which they attached to form a 3- to 6-membered heterocyclyl optionally substituted by deuterium, halogen, oxo, -OR^8, -NR^8R^9 or C_1-C_6 alkyl optionally substituted by deuterium, halogen, oxo or -OH;

R^6 and R^7 are each independently hydrogen, deuterium, C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo, C_2-C_6 alkenyl optionally substituted by deuterium, halogen, or oxo, or C_2-C_6 alkynyl optionally substituted by deuterium, halogen, or oxo;

or R^6 and R^7 are taken together with the atom to which they attached to form a 3- to 6-membered heterocyclyl optionally substituted by deuterium, halogen, oxo or C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo;

R^8 and R^9 are each independently hydrogen, deuterium, C_1-C_6 alkyl optionally substituted by deuterium, halogen, or oxo, C_2-C_6 alkenyl optionally substituted by deuterium, halogen or oxo, or C_2-C_6 alkynyl optionally substituted by deuterium, halogen, or oxo;

~~or R^8 and R^9 are taken together with the atom to which they attached to form a 3-6 membered heterocyclyl optionally substituted by deuterium, halogen, oxo or C_1-C_6 alkyl optionally substituted by deuterium, oxo, or halogen;~~

~~each R^{10}, R^{11}, R^{12} and R^{13} are independently hydrogen or deuterium;~~

~~R^{14} is deuterium;~~

~~q is 0, 1, 2, 3, 4, 5, 6, 7, or 8;~~

~~each R^{15} is independently selected from hydrogen, deuterium, or halogen;~~

~~each R^{16} is independently selected from hydrogen, deuterium, or halogen; and~~

~~p is 3, 4, 5, 6, 7, 8, or 9.~~

~~131~~38. The use~~method~~ of any one of claims 1-37~~128 or the use of claim 129 or claim 130~~, wherein the use comprises administration of ~~comprising administering~~ about 1, 2.5, 5, 7.5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, or 125 mg of the medicament~~compound~~, or a range between any two of the preceding values; or

administration of an amount of the medicament in mg of about one of: 1, 2.5, 5, 7.5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 150, 175, 200, 225, or 250, or a range between any two of the preceding values; or

administration of an amount of the medicament in mg of about one of: 1, 2.5, 5, 7.5, 10, 15, 20, or a range between any two of the preceding values; or

administration of an amount of the medicament in mg of about one of: 10, 15, 20, 30, 40, 50, 75, 80, 100, 120, 160, 240, or 320, or a range between any two of the preceding values; or

administration of an amount of the medicament in mg of about one of about: 320, 400, 480, 560, 640, 720, 800, 880, 960, or 1040, or a range between any two of the preceding values; or

administration of an amount of the medicament in mg of a range between about 320 and any one of about 400, 480, 560, 640, 720, 800, 880, 960, or 1040; or

administration of an amount of the medicament in mg of about one of: 400, 480, 560, 640, 720, 800, 880, 960, or 1040, or a range between any two of the preceding values.

~~132. The method of any one of claims 1-128 or the use of claim 129 or claim 130, comprising administering an amount of the compound in mg of about one of: 1, 2.5, 5, 7.5, 10, 15, 20, 25,~~

~~30, 35, 40, 50, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 150, 175, 200, 225, or 250, or a range between any two of the preceding values.~~

~~133. The method of any one of claims 1-128 or the use of claim 129 or claim 130, comprising administering an amount of the compound in mg of about one of: 1, 2.5, 5, 7.5, 10, 15, 20, or a range between any two of the preceding values.~~

~~134. The method of any one of claims 1-128 or the use of claim 129 or claim 130, comprising administering an amount of the compound in mg of about one of: 10, 15, 20, 30, 40, 50, 75, 80, 100, 120, 160, 240, or 320, or a range between any two of the preceding values.~~

~~135. The method of any one of claims 1-128 or the use of claim 129 or claim 130, comprising administering an amount of the compound in mg of about one of about: 320, 400, 480, 560, 640, 720, 800, 880, 960, or 1040, or a range between any two of the preceding values;~~
~~or administering an amount of the compound in mg of a range between about 320 and any one of about 400, 480, 560, 640, 720, 800, 880, 960, or 1040;~~
~~or administering an amount of the compound in mg of about one of: 400, 480, 560, 640, 720, 800, 880, 960, or 1040, or a range between any two of the preceding values.~~

~~136~~39. The use~~method~~ of any one of claims 1-37~~128 or the use of claim 129 or claim 130~~, wherein the use comprises administration of~~comprising administering~~ an amount effective on administration to an individual to produce a C_{max} in plasma of the individual in ng/mL of at least about one of 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, or 1500, or a range between any two of the preceding concentrations; or

administration of the medicament~~comprising administering the compound~~ to an individual in an amount effective to produce a C_{max} in plasma of the individual in ng/mL in a range between of at least about any one of 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, or 1450 as a lower limit and 1500 as an upper limit; or

administration of the medicament to an individual in an amount effective to produce a C_{max} in plasma of the individual in ng/mL of at least about one of: 1500, 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, or 2500, or a range between any two of the preceding concentrations; or

administration of the medicament to an individual in an amount effective to produce a C_{max} in plasma of the individual in ng/mL of at least about one of: 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, or 2500, or a range between any two of the preceding concentrations; or

administration of the medicament to an individual in an amount effective to produce a C_{max} in plasma of the individual in ng/mL in a range between at least 1500 and any one of 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, or 2500; or

administration of the medicament to an individual in an amount effective to produce a C_{max} in ng/mL in plasma of the individual, the C_{max} corresponding to a plasma-adjusted concentration effective to inhibit a percentage of $\alpha_V\beta_6$ or $\alpha_V\beta_1$ in the individual of at least about one of about 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100, or a range between any two of the preceding percentages; or

administration of the medicament to an individual in an amount effective to produce a C_{max} in ng/mL in plasma of the individual, the C_{max} corresponding to a plasma-adjusted concentration effective to inhibit a percentage of $\alpha_V\beta_6$ or $\alpha_V\beta_1$ in the individual of at least about one of about 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 97, 98, 99, or 100, or a range between any two of the preceding percentages.

~~137. The method of any one of claims 1-128 or the use of claim 129 or claim 130, comprising administering the compound to an individual in an amount effective to produce a C_{max} in plasma of the individual in ng/mL of at least about one of: 1500, 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, or 2500, or a range between any two of the preceding concentrations;~~

~~or comprising administering the compound to an individual in an amount effective to produce a C_{max} in plasma of the individual in ng/mL of at least about one of: 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, or 2500, or a range between any two of the preceding concentrations;~~

~~or comprising administering the compound to an individual in an amount effective to produce a C_{max} in plasma of the individual in ng/mL in a range between at least 1500 and any one of 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, or 2500.~~

~~138. The method of any one of claims 1-128 or the use of claim 129 or claim 130, comprising administering the compound to an individual in an amount effective to produce a C_{max} in ng/mL~~

~~in plasma of the individual, the C_{max} corresponding to a plasma-adjusted concentration effective to inhibit a percentage of $\alpha_V\beta_6$ or $\alpha_V\beta_1$ in the individual of at least about one of about 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100, or a range between any two of the preceding percentages;~~

~~or comprising administering the compound to an individual in an amount effective to produce a C_{max} in ng/mL in plasma of the individual, the C_{max} corresponding to a plasma-adjusted concentration effective to inhibit a percentage of $\alpha_V\beta_6$ or $\alpha_V\beta_1$ in the individual of at least about one of about 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 97, 98, 99, or 100, or a range between any two of the preceding percentages.~~