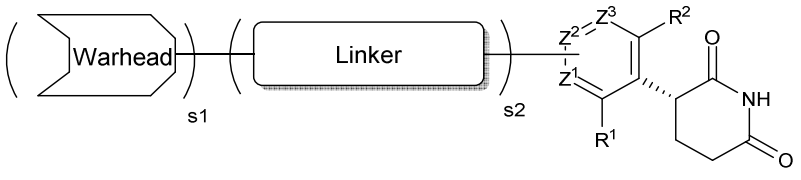
CLAIMS

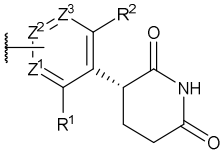
1. A compound of Formula (I):



(I);

or a pharmaceutically acceptable salt, deuterated analog, or a prodrug thereof, wherein:

Warhead is a targeting moiety that binds to a target protein; wherein the target protein is a mediator of a disease in a subject;



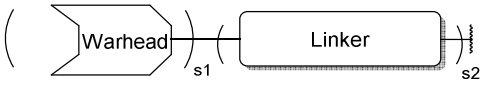
Linker is a divalent chemical group that connects the Warhead moiety and the moiety;

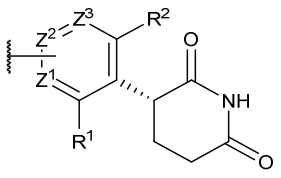
s1 is 0 or 1;

s2 is 0 or 1;

Z^1, Z^2 and Z^3 are each independently N or CR^z, provided that Z^1, Z^2 and Z^3 are not N at the same time;

R^z, at each occurrence, is independentlyhydrogen, halogen, -C_{1-8}alkyl, -$NR^{Za}R^{Zb}$, -OR^{Za}, -SR^{Za}, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl or CN; each of -C_{1-8}alkyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl is optionally substituted with at least one R^{Zc};

the 

moiety is linked to the 

moiety via any one of Z^1, Z^2 or Z^3 which is CR^z and R^z is hydrogen;

R^{Za} and R^{Zb} are each independently hydrogen, -C_1-C_8alkyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl, each of said -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{Zd};

R^{Zc} and R^{Zd} are each independently halogen, hydroxy, -C_1-C_8alkyl, C_3-C_8cycloalkyl, -C_{1-8}alkoxy, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl;

R^1 and R^2 are each independently halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_{1-8}alkoxy, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl, 5- to 12-membered heteroaryl, -CN, -SO_2R^{1a}, -$SO_2NR^{1a}R^{1b}$, -COR^{1a}, -CO_2R^{1a}, -$CONR^{1a}R^{1b}$, -$NR^{1a}R^{1b}$, -$NR^{1a}COR^{1b}$, -$NR^{1a}CO_2R^{1b}$, or –$NR^{1a}SO_2R^{1b}$; each of -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_{1-8}alkoxy, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, 5- to 12-membered heteroaryl, oxo, -CN, -OR^{1c}, -SO_2R^{1c}, -$SO_2NR^{1c}R^{1d}$, -COR^{1c}, -CO_2R^{1c}, -$CONR^{1c}R^{1d}$, -$NR^{1c}R^{1d}$, -$NR^{1c}COR^{1d}$, -$NR^{1c}CO_2R^{1d}$, or –$NR^{1c}SO_2R^{1d}$; and

R^{1a}, R^{1b}, R^{1c} and R^{1d} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl.

2. The compound of claim 1, wherein at most one of Z^1, Z^2 and Z^3 is N.

3. The compound of claim 2, wherein Z^1, Z^2 and Z^3 are each independently CR^z.

4. The compound of claims 1, wherein R^Z, at each occurrence, is independently hydrogen, -F, -Cl, -Br, -I, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, -$NR^{Za}R^{Zb}$, -OR^{Za}, -SR^{Za}, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, 3- to 8-membered heterocyclyl, or CN; each of methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, or 3- to 8-membered heterocyclyl is optionally substituted with at least one R^{Zc};

R^{Za} and R^{Zb} are each independently hydrogen, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, 3- to 8-membered heterocyclyl, phenyl or 5- to 12-membered heteroaryl, each of said hydrogen, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, 3- to 8-membered heterocyclyl, phenyl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{Zd}; and

R^{Zc} and R^{Zd} are each independently -F, -Cl, -Br, -I, hydroxy, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, 3- to 8-membered heterocyclyl, phenyl, or 5- to 12-membered heteroaryl.

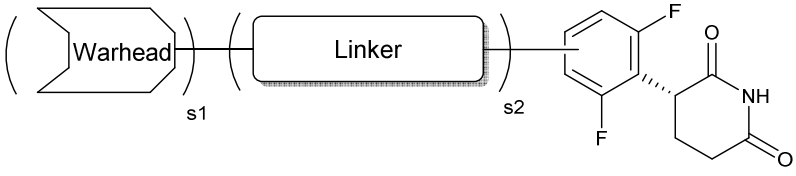
5. The compound of claim 4, wherein R^z is H, -CH_3, -C_2H_5, F, -CH_2F, -CHF_2, -CF_3, -OCH_3, -OC_2H_5, -C_3H_7, -OCH_2F, -$OCHF_2$, -OCH_2CF_3, -OCF_3, -SCF_3, -CF_3 or -$CH(OH)CH_3$.

6. The compound of claim 1, wherein R^1 and R^2 are each independently F, Cl, Br, I, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, methoxy, ethoxy, propoxy, butoxy, pentoxy, hexoxy, heptoxy, octoxy, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl, 5- to 12-membered heteroaryl, -CN, -SO_2R^{1a}, -$SO_2NR^{1a}R^{1b}$, -COR^{1a}, -CO_2R^{1a}, -$CONR^{1a}R^{1b}$, -$NR^{1a}R^{1b}$, -$NR^{1a}COR^{1b}$, -$NR^{1a}CO_2R^{1b}$, or –$NR^{1a}SO_2R^{1b}$; each of methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, methoxy, ethoxy, propoxy, butoxy, pentoxy, hexoxy, heptoxy, octoxy, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl, 5- to 12-membered heteroaryl is optionally substituted with F, Cl, Br, I, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, methoxy, ethoxy, propoxy, butoxy, pentoxy, hexoxy, heptoxy, octoxy, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl, 5- to 12-membered heteroaryl, oxo, -CN, -OR^{1c}, -SO_2R^{1c}, -$SO_2NR^{1c}R^{1d}$, -COR^{1c}, -CO_2R^{1c}, -$CONR^{1c}R^{1d}$, -$NR^{1c}R^{1d}$, -$NR^{1c}COR^{1d}$, -$NR^{1c}CO_2R^{1d}$, or –$NR^{1c}SO_2R^{1d}$; and

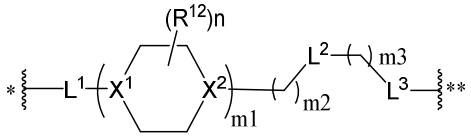
R^{1a}, R^{1b}, R^{1c} and R^{1d} are each independently hydrogen, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, octoxy, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl, or 5- to 12-membered heteroaryl.

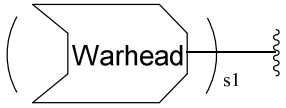
7. The compound of claim 6, wherein R^1 and R^2 are each independently F, Cl, Br, I, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, methoxy, ethoxy, propoxy, butoxy, pentoxy, hexoxy, heptoxy, octoxy, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, -CN, -CH_2F, -CHF_2, -CF_3, -OCH_2F, -$OCHF_2$, -OCH_2CF_3, -OCF_3, or phenyl.

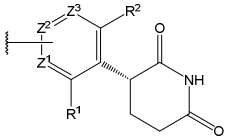
8. The compound of claim 1, wherein the compound is of Formula (II)



(II).

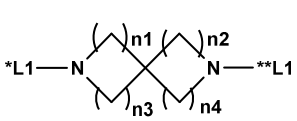
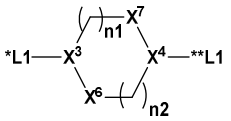
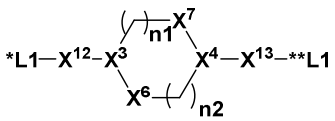
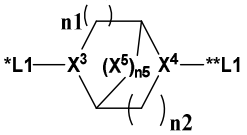
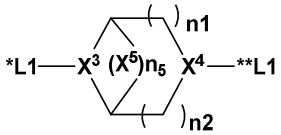
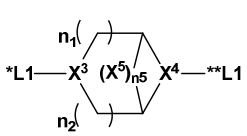
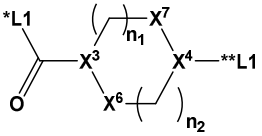
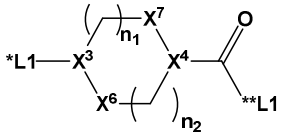
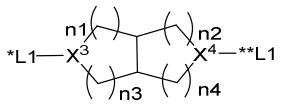
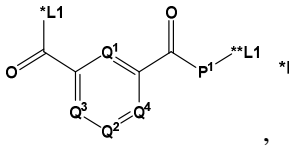
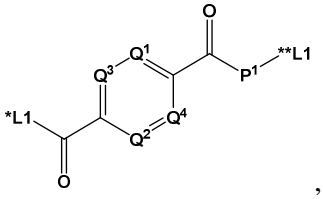
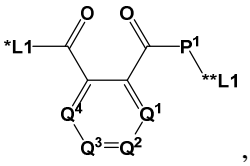
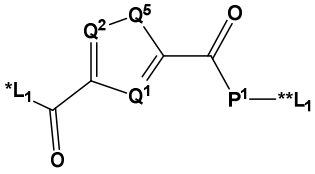
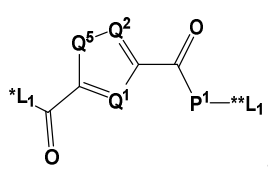
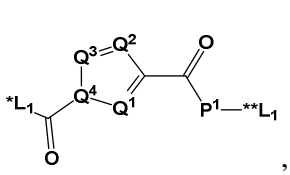
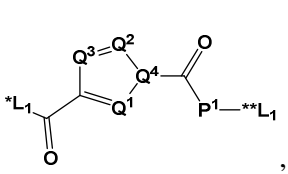
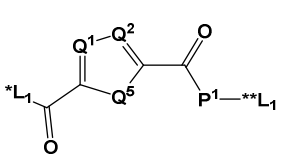
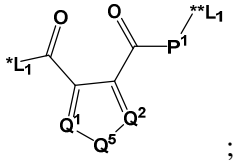
9. The compound of claim 1, wherein Linker is 

, wherein * refers to the position attached to the 

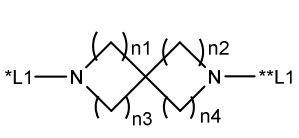
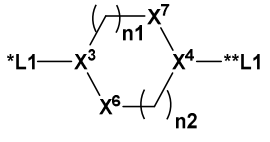
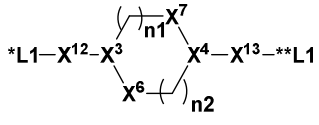
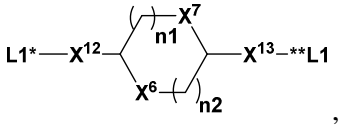
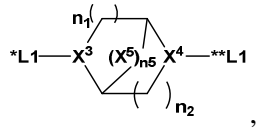
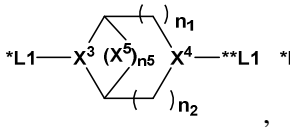
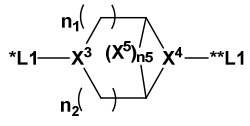
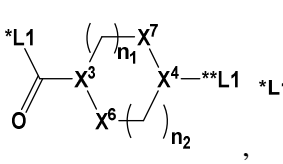
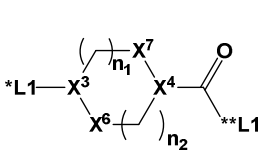
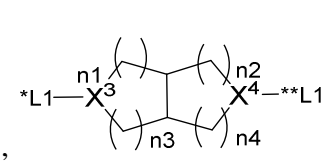
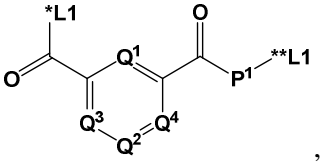
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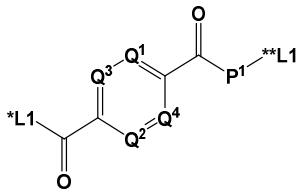
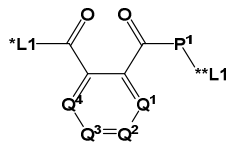
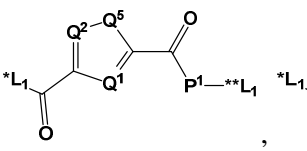
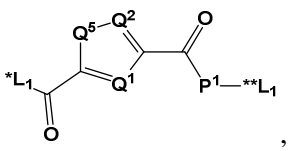
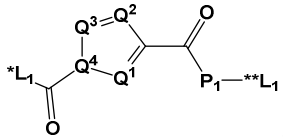
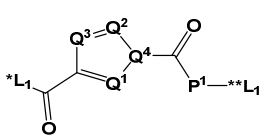
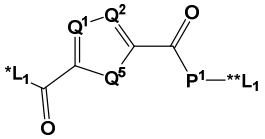
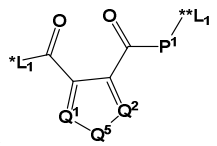
moiety;

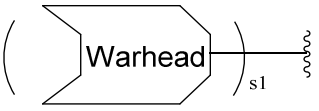
L^1 is a single bond, -O-, -SO_2-, -C(O)-, -NR^{L1a}-, -C_3-C_8cycloalkylene-, *^{L1}-O-C_{1-8}alkylene-**^{L1}, *^{L1}-C_{1-8}alkylene-O-**^{L1}, *^{L1}-SO_2-C_{1-8}alkylene-**^{L1}, *^{L1}-C_{1-8}alkylene-SO_2-**^{L1}, *^{L1}-CO-C_{1-8}alkylene-**^{L1}, *^{L1}-C_{1-8}alkylene-CO-**^{L1}, *^{L1}-NR^{L1a}-C_{1-8}alkylene-**^{L1}, *^{L1}-C_{1-8}alkylene-NR^{L1a}-**^{L1}, *^{L1}-NR^{L1a}C(O)-**^{L1}, *^{L1}-C(O)NR^{L1a}-**^{L1}, -C_{1-8}alkylene-, -C_{2-8}alkenylene-, -C_{2-8}alkynylene-, -[O($CR^{L1a}R^{L1b}$)$_{m4}$]$_{m5}$-,

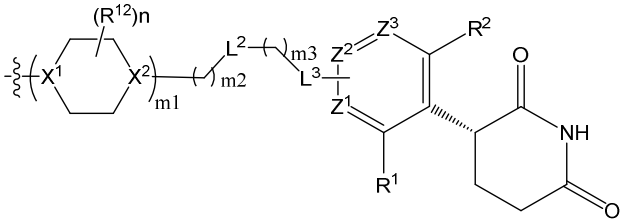

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or

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wherein each of said -C_3-C_8cycloalkylene-, *^{L1}-O-C_{1-8}alkylene-**^{L1}, *^{L1}-C_{1-8}alkylene-O-**^{L1}, *^{L1}-SO_2-C_{1-8}alkylene-**^{L1}, *^{L1}-C_{1-8}alkylene-SO_2-**^{L1}, *^{L1}-CO-C_{1-8}alkylene-**^{L1}, *^{L1}-C_{1-8}alkylene-CO-**^{L1}, *^{L1}-NR^{L1a}-C_{1-8}alkylene-**^{L1}, *^{L1}-C_{1-8}alkylene-NR^{L1a}-**^{L1}, -C_{1-8}alkylene-, -C_{2-8}alkenylene-, -C_{2-8}alkynylene-,


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and is optionally substituted with at least one R^{L1c};

wherein $*^{L1}$ refers to the position attached to the 

moiety, and $**^{L1}$ refers to the position attached to the 

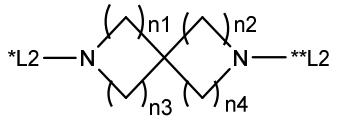
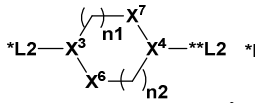
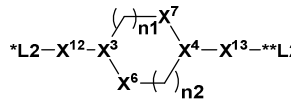
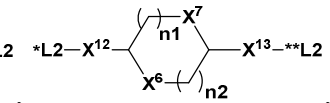
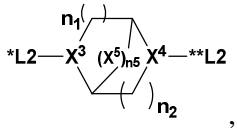
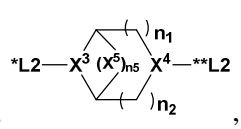
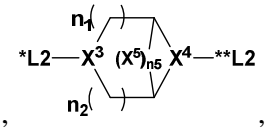
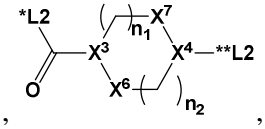
moiety;

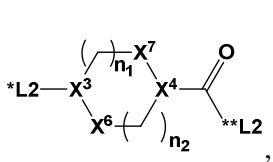
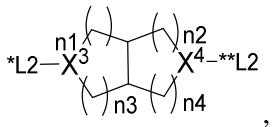
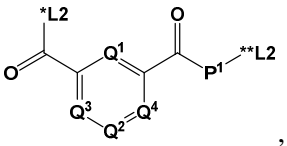
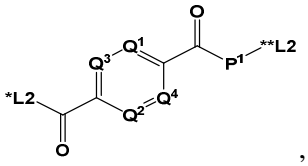
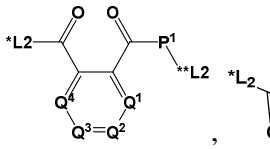
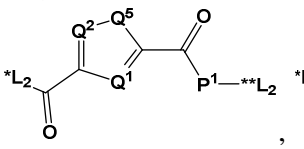
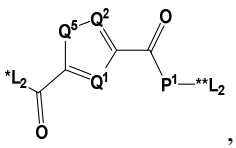
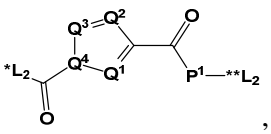
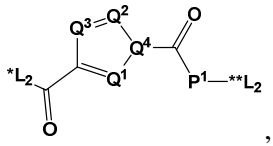
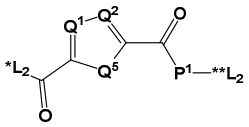
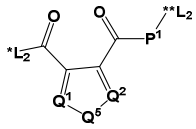
R^{L1a} and R^{L1b} are each independently selected from hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, and 5- to 12-membered heteroaryl, each of said -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{L1d};

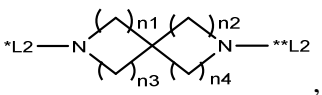
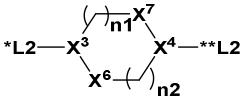
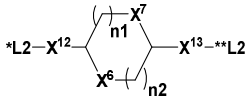
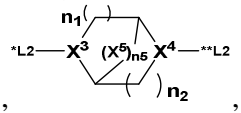
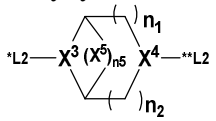
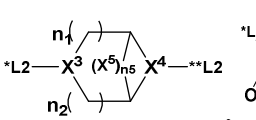
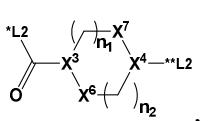
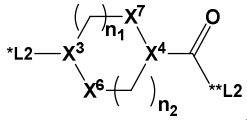
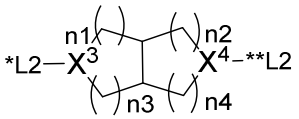
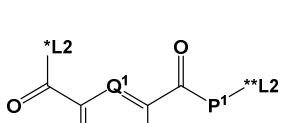
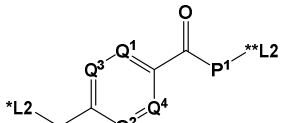
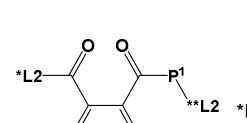
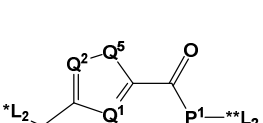
each of said R^{L1c} and R^{L1d} are independently oxo, halogen, hydroxy, -C_{1-8}alkyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl; or

two R^{L1c} together with the atoms to which they are attached, form a 3- to 12-membered ring, said ring comprising 0-3 heteroatoms independently selected from nitrogen, oxygen and sulfur; said ring is optionally substituted with at least one substituent halogen, hydroxy, or -C_{1-8}alkyl;

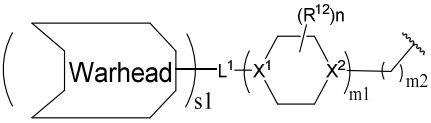
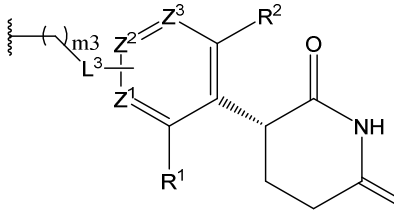
L^2 is a single bond, -O-, -SO_2-, -CO-, -NR^{L2a}-, -C_3-C_8cycloalkylene-, $*^{L2}$-O-C_{1-8}alkylene-$**^{L2}$, $*^{L2}$-C_{1-8}alkylene-O-$**^{L2}$, $*^{L2}$-SO_2-C_{1-8}alkylene-$**^{L2}$, $*^{L2}$-C_{1-8}alkylene-SO_2-$**^{L2}$, $*^{L2}$-CO-C_{1-8}alkylene-$**^{L2}$, $*^{L2}$-C_{1-8}alkylene-CO-$**^{L2}$, $*^{L2}$-NR^{L2a}-C_{1-8}alkylene-$**^{L2}$, $*^{L2}$-C_{1-8}alkylene-NR^{L2a}-$**^{L2}$, $*^{L2}$-NR^{L2a}C(O)-$**^{L2}$, $*^{L2}$-C(O)NR^{L2a}-$**^{L2}$, -C_{1-8}alkylene-, -C_{2-8}alkenylene-, -C_{2-8}alkynylene-, -$[O(CR^{L2a}R^{L2b})_{m4}]_{m5}$-,












or ;

wherein each of said -C_3-C_8cycloalkylene-, *^{L2}-O-C_{1-8}alkylene-**^{L2}, *^{L2}-C_{1-8}alkylene-O-**^{L2}, *^{L2}-SO_2-C_{1-8}alkylene-**^{L2}, *^{L2}-C_{1-8}alkylene-SO_2-**^{L2}, *^{L2}-CO-C_{1-8}alkylene-**^{L2}, *^{L2}-C_{1-8}alkylene-CO-**^{L2}, *^{L2}-NR^{L2a}-C_{1-8}alkylene-**^{L2}, *^{L2}-C_{1-8}alkylene-NR^{L2a}-**^{L2}, -C_{1-8}alkylene-, -C_{2-8}alkenylene-, -C_{2-8}alkynylene-,














and is optionally substituted with at least one substituent R^{L2c};

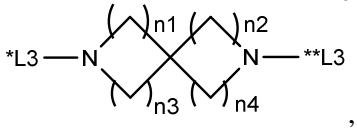
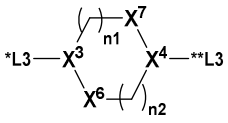
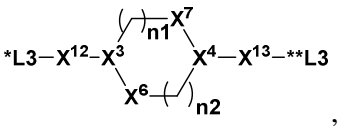
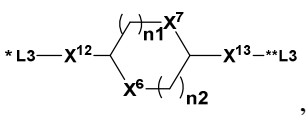
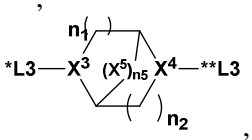
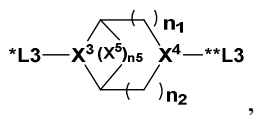
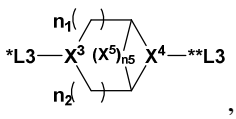
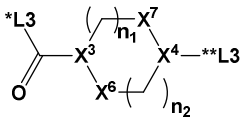
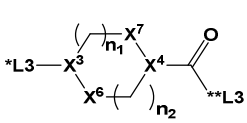
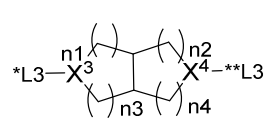
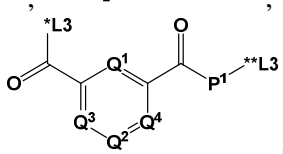
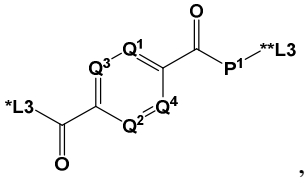
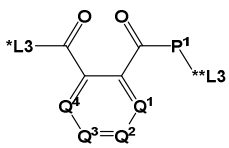
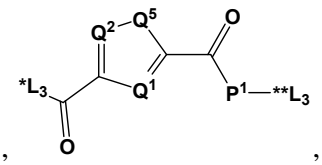
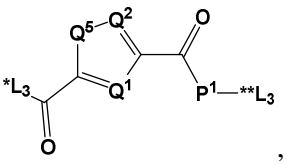
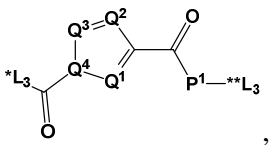
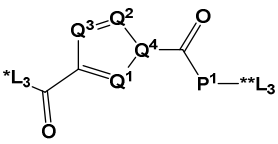
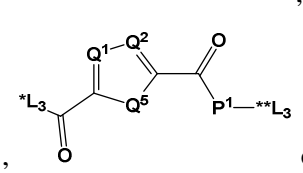
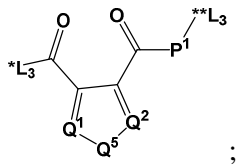
wherein *^{L2} refers to the position attached to  moiety, and **^{L2} refers to the position attached to the  moiety;

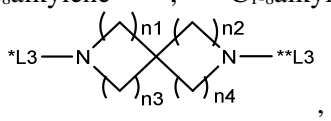
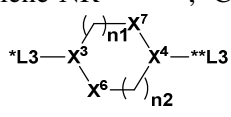
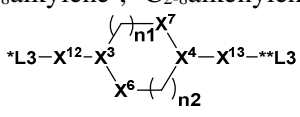
R^{L2a} and R^{L2b} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl, each of said -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{L2d};

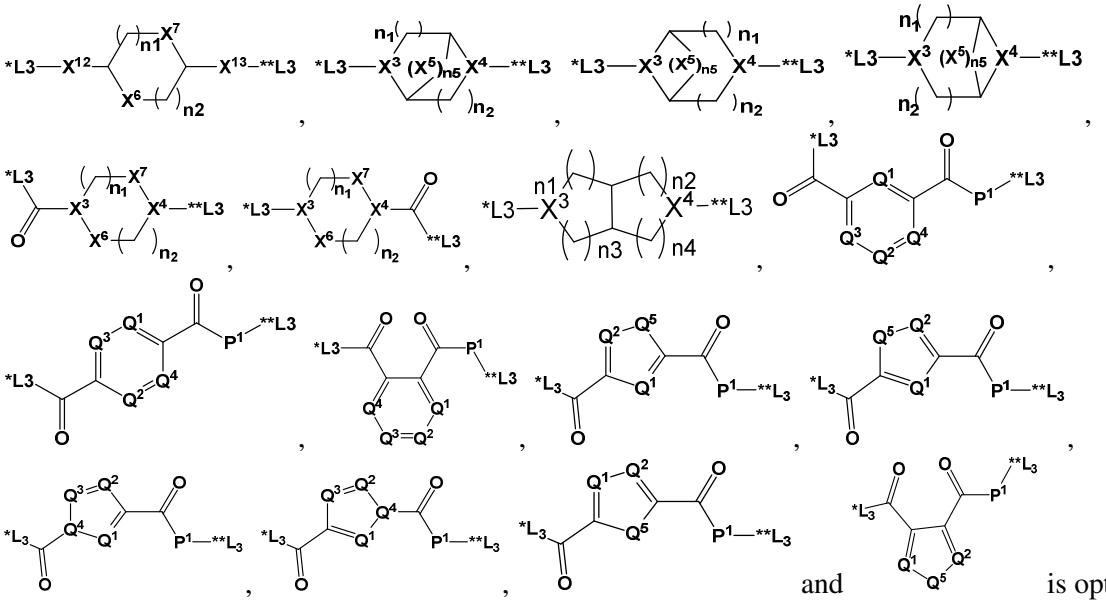
each of said R^{L2c} and R^{L2d} are independently oxo, halogen, hydroxy, -C_{1-8}alkyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl; or

two R^{L2c} together with the atoms to which they are attached, form a 3- to 12-membered ring, said ring comprising 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur; said ring is optionally substituted with at least one substituent halogen, hydroxy, -C_{1-8}alkyl;

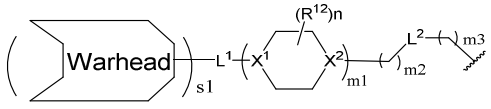
L^3 is a single bond, -O-, -SO_2-, -CO-, -NR^{L3a}-, -C_3-C_8cycloalkylene-, *^{L3}-O-C_{1-8}alkylene-**^{L3}, *^{L3}-C_{1-8}alkylene-O-**^{L3}, *^{L3}-SO_2-C_{1-8}alkylene-**^{L3}, *^{L3}-C_{1-8}alkylene-SO_2-**^{L3}, *^{L3}-CO-C_{1-8}alkylene-**^{L3}, *^{L3}-C_{1-8}alkylene-CO-**^{L3}, *^{L3}-NR^{L3a}-C_{1-8}alkylene-**^{L3}, *^{L3}-C_{1-8}alkylene-NR^{L3a}-**^{L3}, *^{L3}-NR^{L3a}C(O)-**^{L3}, *^{L3}-C(O)NR^{L3a}-**^{L3}, -C_{1-8}alkylene-, -C_{2-8}alkenylene-, -C_{2-8}alkynylene-, -[O($CR^{L3a}R^{L3b}$)$_{m4}$]$_{m5}$-,

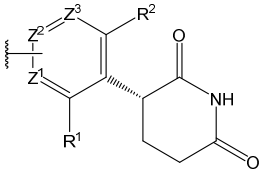

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or

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wherein each of said -C_3-C_8cycloalkylene-, *^{L3}-O-C_{1-8}alkylene-**^{L3}, *^{L3}-C_{1-8}alkylene-O-**^{L3}, *^{L3}-SO_2-C_{1-8}alkylene-**^{L3}, *^{L3}-C_{1-8}alkylene-SO_2-**^{L3}, *^{L3}-CO-C_{1-8}alkylene-**^{L3}, *^{L3}-C_{1-8}alkylene-CO-**^{L3}, *^{L3}-NR^{L3a}-C_{1-8}alkylene-**^{L3}, *^{L3}-C_{1-8}alkylene-NR^{L3a}-**^{L3}, -C_{1-8}alkylene-, -C_{2-8}alkenylene-, -C_{2-8}alkynylene-,

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is optionally substituted with at least one substituent R^{L3c};

wherein $*^{L3}$ refers to the position attached to  moiety, and



$**^{L3}$ refers to the position attached to the moiety;

R^{L3a} and R^{L3b} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl, each of said -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{L3d};

each of said R^{L3c} and R^{L3d} are independently oxo, halogen, hydroxy, -C_{1-8}alkyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl; or

two R^{L3c} together with the atoms to which they are attached, form a 3- to 12-membered ring, said ring comprising 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur; said ring is optionally substituted with at least one substituent halogen, hydroxy, or -C_{1-8}alkyl;

R^{12} is independently hydrogen, halogen, -C_{1-8}alkyl, -$NR^{12a}R^{12b}$, -OR^{12a}, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl, 5- to 12-membered heteroaryl, oxo, or -CN; each of -C_{1-8}alkyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{12c}; or

two R^{12} together with the carbon atoms to which they are attached, form a 3- to 12-membered ring, said ring comprising 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur; said ring is optionally substituted with at least one substituent R^{12c};

R^{12a} and R^{12b} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl or 5- to 12-membered heteroaryl, each of said -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{12d}; or

R^{12c} and R^{12d} are each independently halogen, hydroxy, -C_{1-8}alkyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl or 5- to 12-membered heteroaryl;

X^1, X^2, X^3 and X^4 are each independently -CR^a, or N;

X^5, X^6 and X^7 are each independently selected from -NR^a-, -O-, -S- and -CR^aR^b-;

X^{12} and X^{13} are each independently selected from -C(O)-, -NR^a- and -O-;

Q^1, Q^2, Q^3 and Q^4 are each independently CR^a or N;

Q^5 is each independently -O-, -NR^a-, -CR^aR^b-, -S- or -C(O)-;

P^1 is a single bond, -O-, -NR^a-, -CR^aR^b -, -S-, -SO- or -SO_2-;

at each occurrence, R^a and R^b are each independently hydrogen, hydroxy, halogen, CN, -C_{1-8}alkyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl or 5- to 12-membered heteroaryl, each of said -C_{1-8}alkyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent halogen, hydroxy, halogen, -C_{1-8}alkyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, -C_6-C_{12}aryl or 5- to 12-membered heteroaryl; or

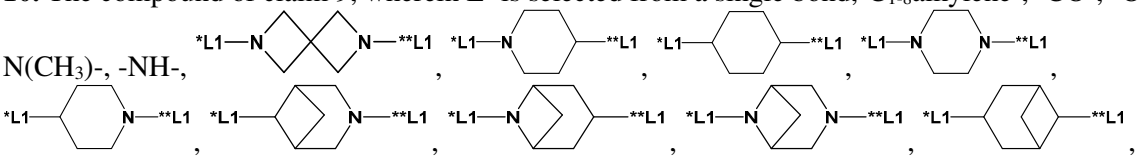
R^a and R^b together with the carbon atoms to which they are attached, form a 3- to 12-membered ring, said ring comprising 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur; said ring is optionally substituted with at least one substituent halogen, hydroxy, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_{1-8}alkoxy, -C_{2-8}alkenyl, -C_{2-8}alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl;

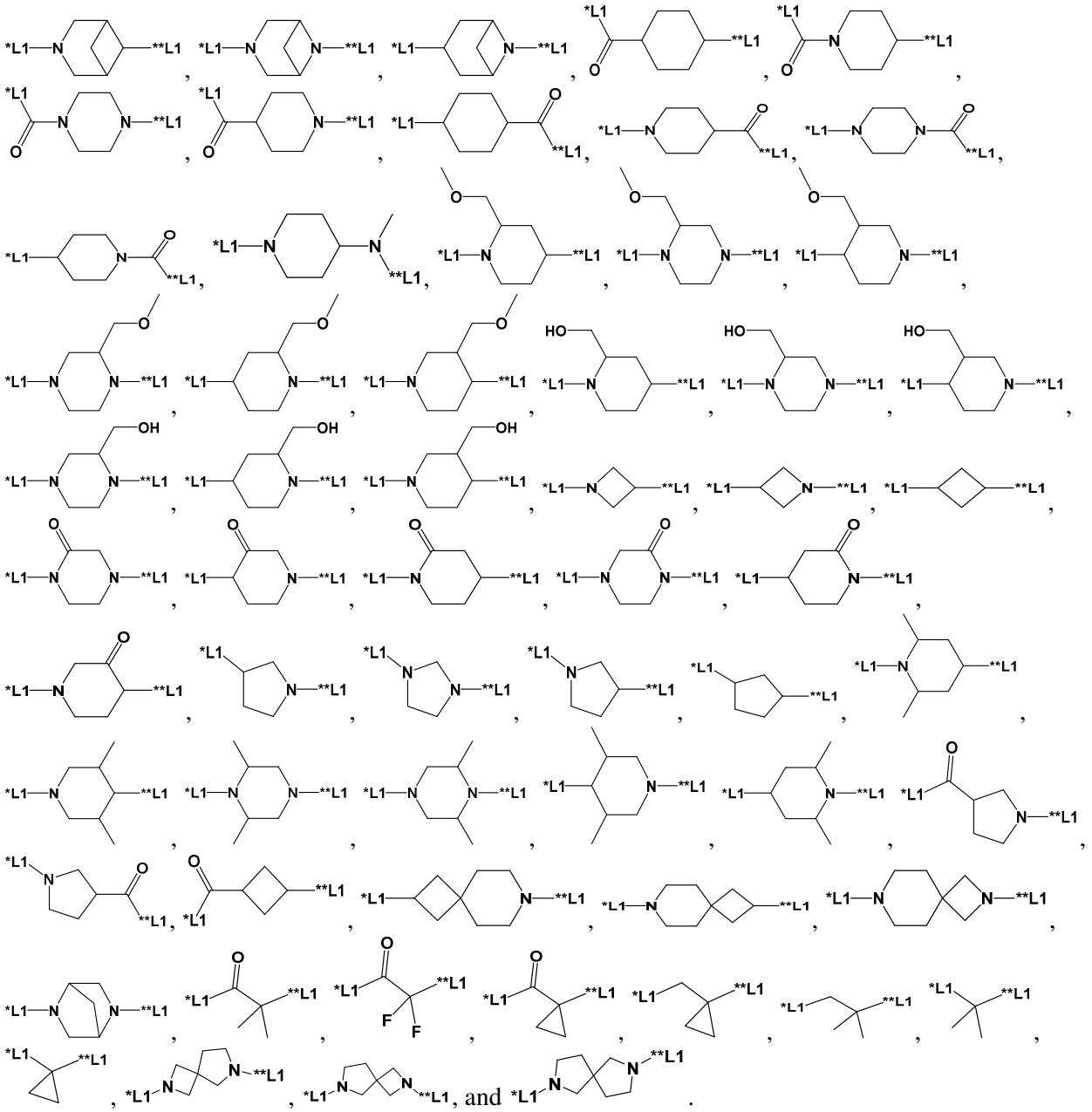
m_1 is 0 or 1;

m_2 and m3 is 0, 1, 2, 3, 4, 5, 6, 7 or 8;

m_4 and m_5 are each independently 0, 1, 2 or 3;

n, n_1, n_2, n_3, n_4 and n_5 are each independently 0, 1, 2 or 3.

10. The compound of claim 9, wherein L^1 is selected from a single bond,-C_{1-8}alkylene-, -CO-, -O-, -$N(CH_3)$-, -NH-, 

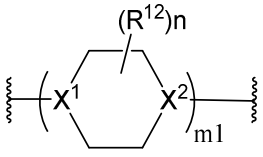
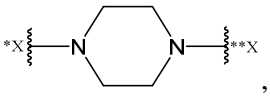
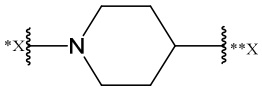
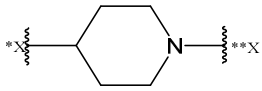
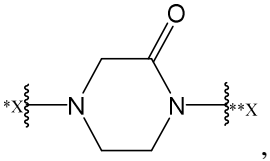
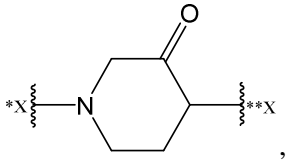
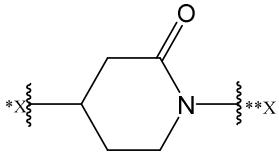
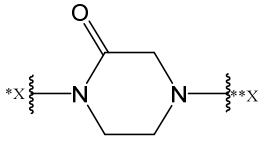
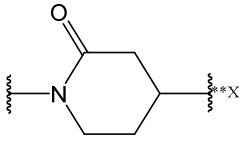
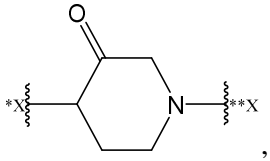
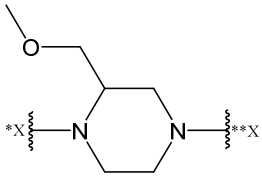
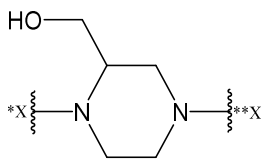
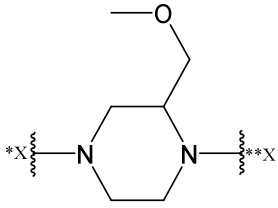
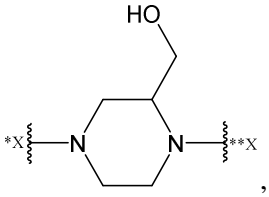
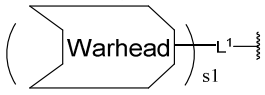
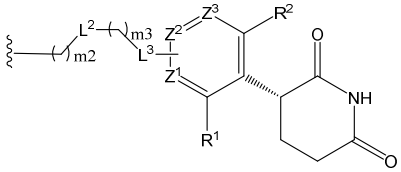


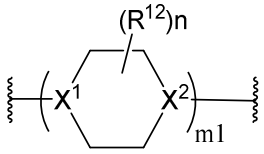
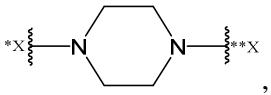
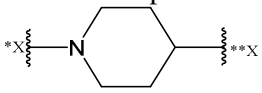
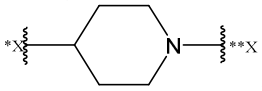
11. The compound of claim 9, wherein X^1 and X^2 are each independently -CR^a or N;

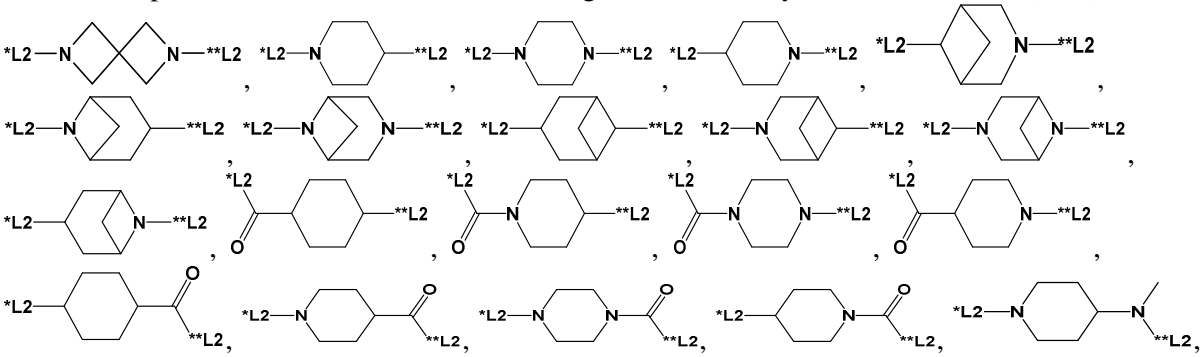
R^a is selected from hydrogen, -F, -Cl, -Br, -I, CN, methyl, ethyl, methoxy, ethoxy, or cyclopropyl, wherein each of said methyl, ethyl, methoxy, ethoxy, and cyclopropyl is optionally substituted with at least one substituent selected from -F, -Cl, -Br, -I, hydroxy, methyl, and ethyl;

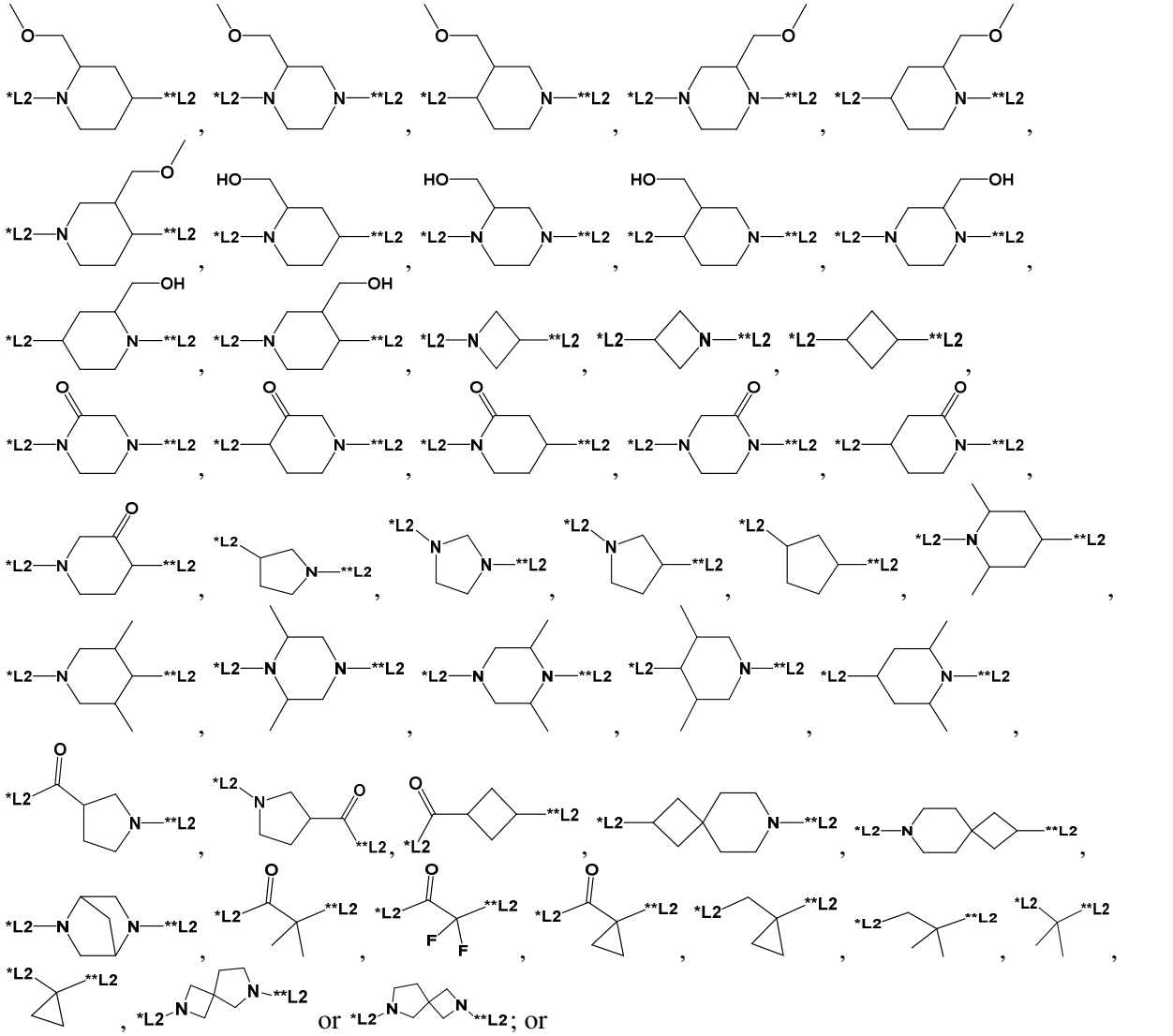
m_1=1 or 0; and

R^{12} is hydrogen, oxo, methoxymethyl, hydroxymethyl, -CN or -CH_3.

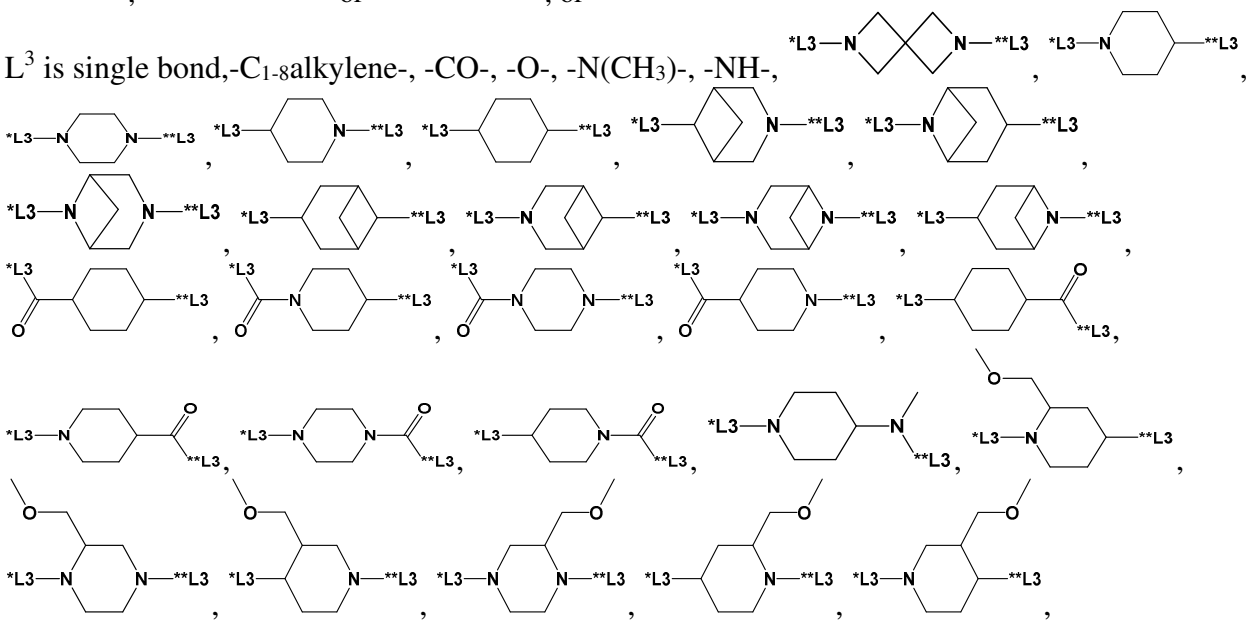
12. The compound of claim 9, wherein m_1 is 1;  moiety is , , , , , , , , , , , ,  or , wherein $*^X$ refers to the position attached to  moiety, and $**^X$ refers to the position attached to the  moiety.

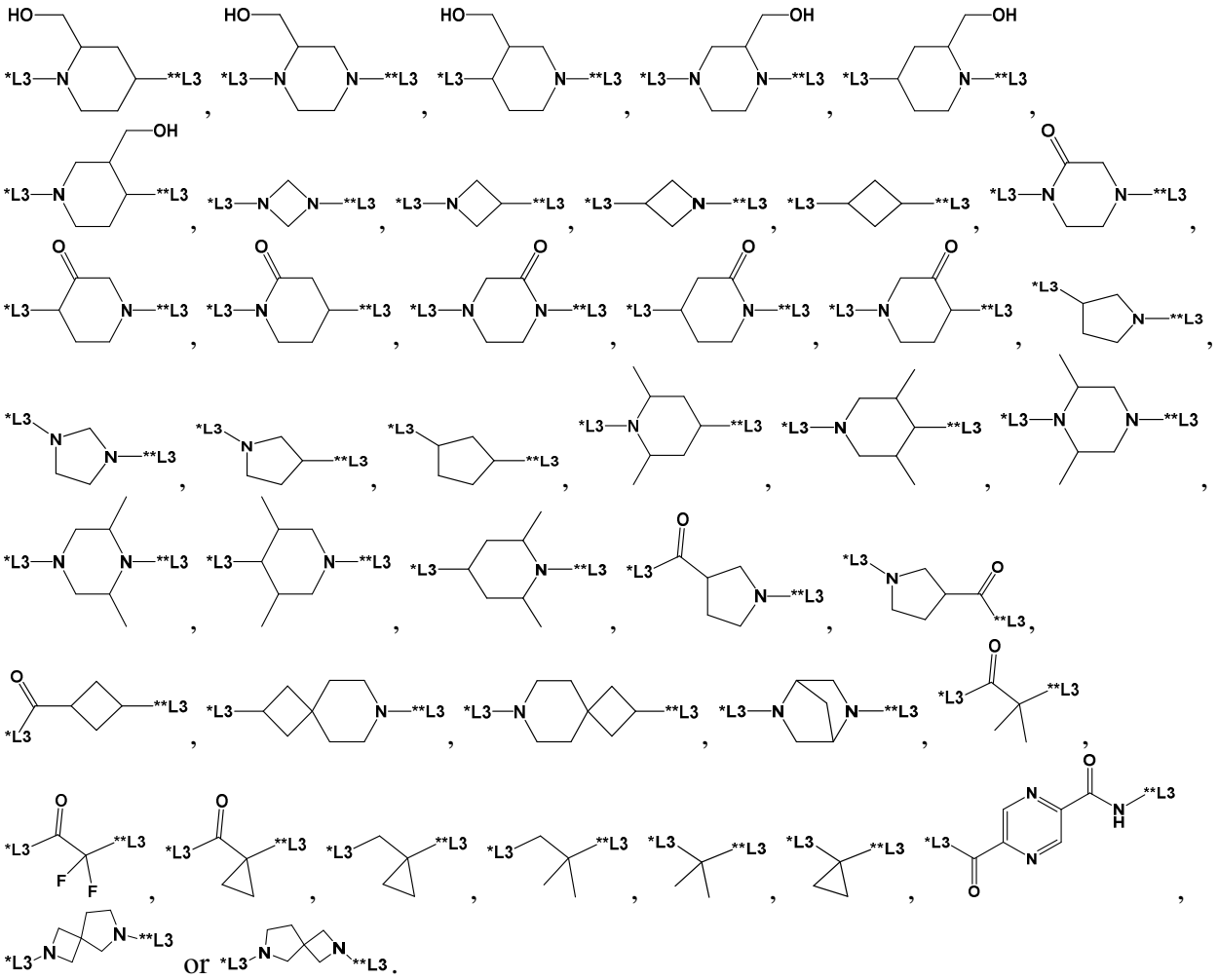
13. The compound of claim 12, wherein m_1 is 1,  moiety is ,  or .

14. The compound of claim 9, wherein L^2 is a single bond,-$C_{1\text{-}8}$alkylene-, -CO-, -O-, -N(CH_3)-, -NH-, 

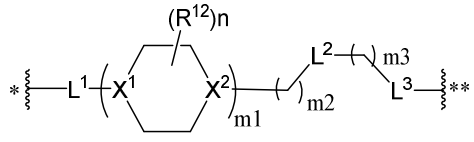


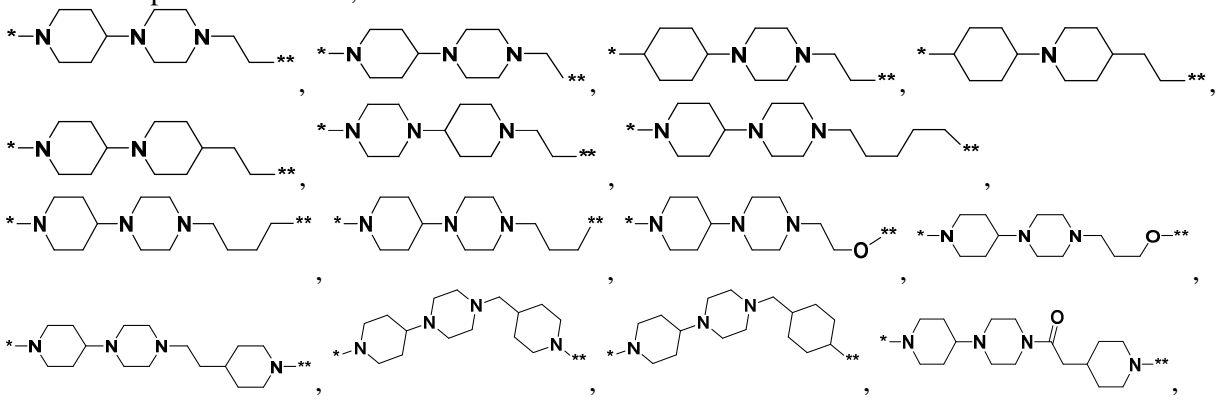
L^3 is single bond,-$C_{1\text{-}8}$alkylene-, -CO-, -O-, -$N(CH_3)$-, -NH-,

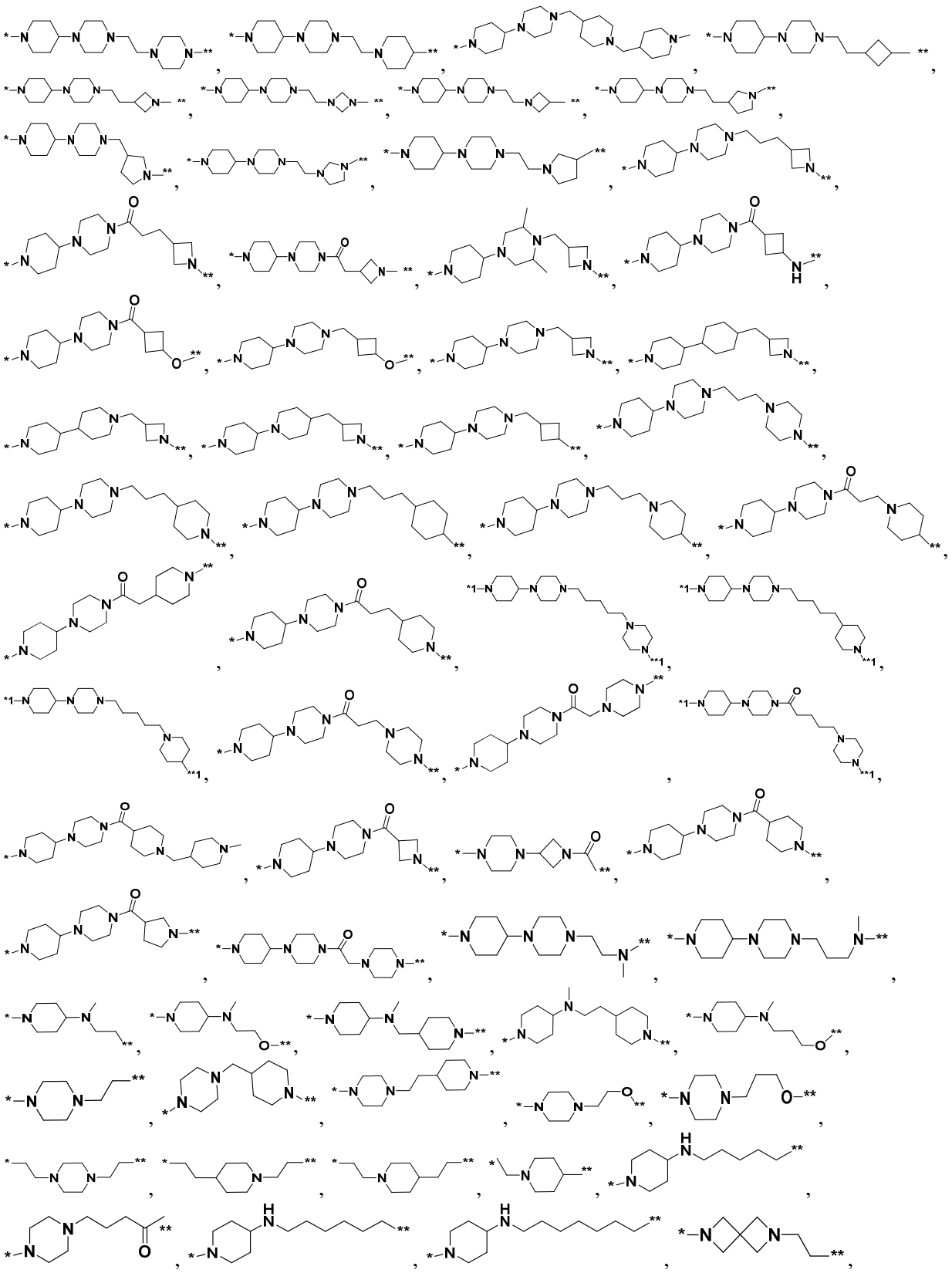


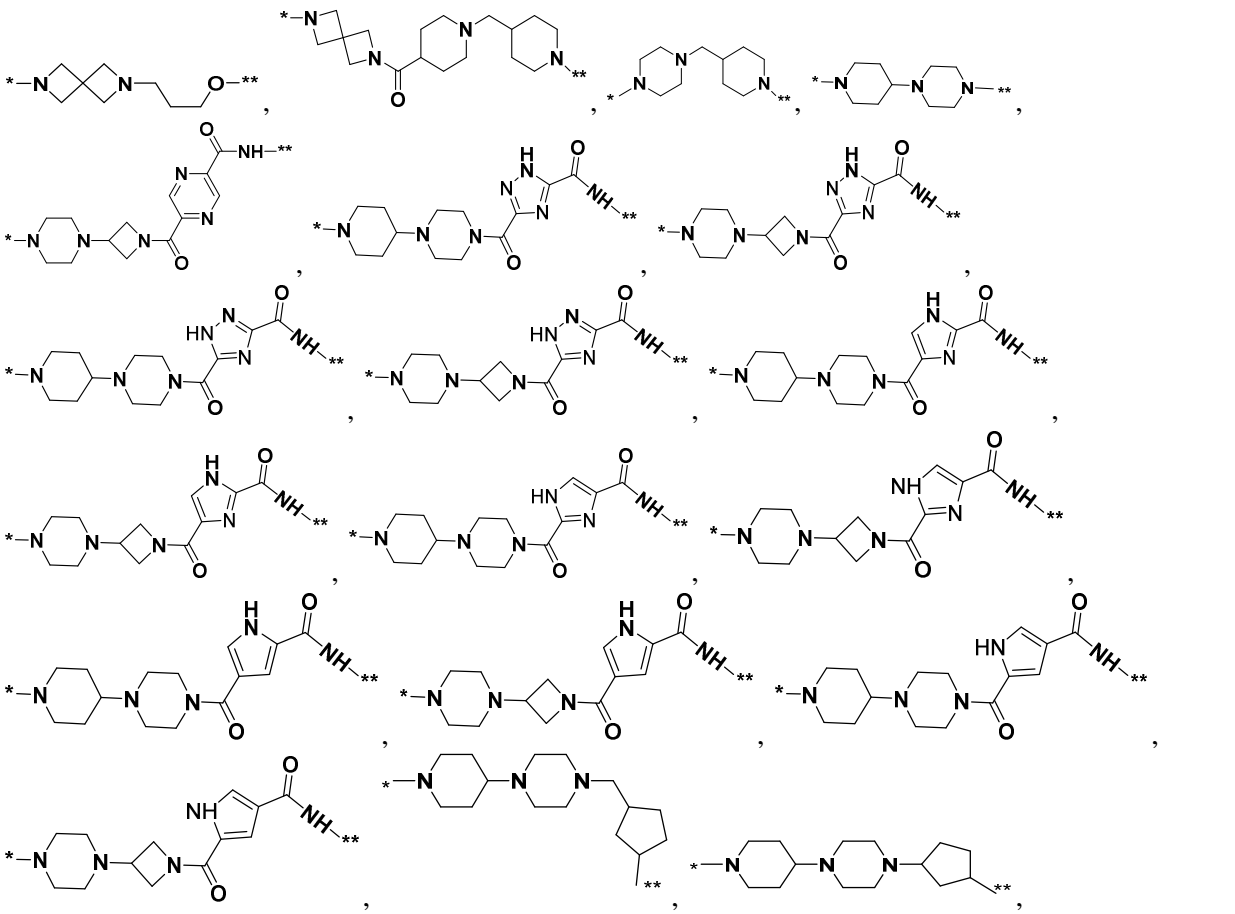


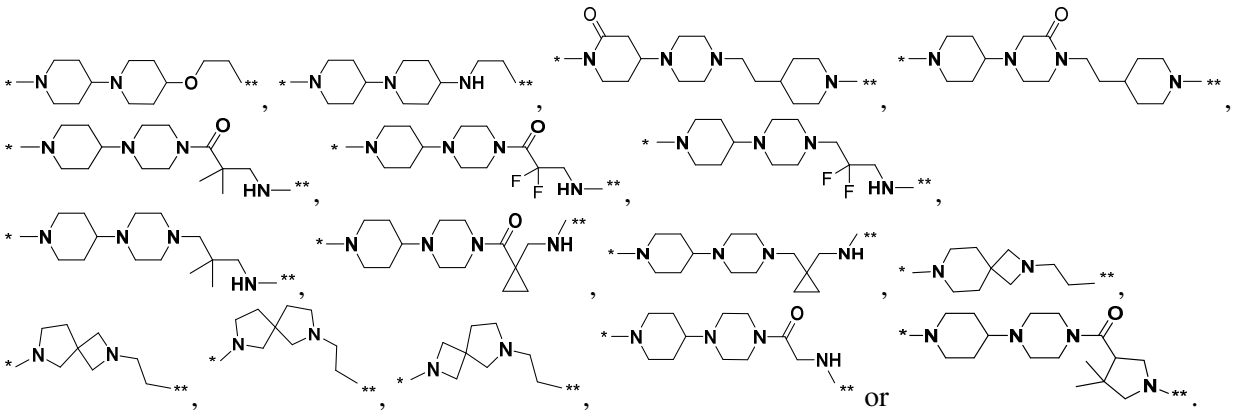
15. The compound of claim 14, wherein L^2 is a single bond; L^3 is a single bond; or L^2 and L^3 are a single bond.

16. The compound of claim 9, wherein  is





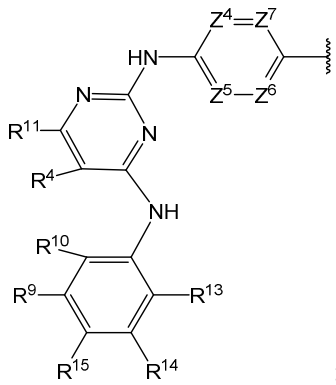




17. The compound of claim 1, wherein Warhead is a moiety which binds to a target protein, wherein said target protein is selected from the group consisting of structural proteins, receptors, enzymes, cell surface proteins, proteins pertinent to the integrated function of a cell, including proteins involved in catalytic activity, aromatase activity, motor activity, helicase activity, metabolic processes (anabolism and catabolism), antioxidant activity, proteolysis, biosynthesis, proteins with kinase activity, oxidoreductase activity, transferase activity, hydrolase activity, lyase activity, isomerase activity, ligase activity, enzyme regulator activity, signal transducer activity, structural molecule activity, binding activity (protein, lipid carbohydrate), receptor activity, cell motility, membrane fusion, cell communication, regulation of biological processes, development, cell differentiation, response to stimulus, behavioral proteins, cell adhesion proteins, proteins involved in cell death, and proteins involved in transport (including protein transporter activity, nuclear transport, ion transporter activity, channel transporter activity, carrier activity, permease activity, secretion activity, electron transporter activity, pathogenesis, chaperone regulator activity, nucleic acid binding activity, transcription regulator activity, extracellular organization and biogenesis activity and translation regulator activity).

18. The compound of claim 1, wherein Warhead is a moiety which binds to a target protein, wherein said target protein is selected from the group consisting of ErbB receptors, B7.1 and B7, TINFR1m, TNFR2, NADPH oxidase, Bcl-Bax and other partners in the apoptosis pathway, C5a receptor, HMG-CoA reductase, PDE V phosphodiesterase type, PDE IV phosphodiesterase type 4, PDE I, PDEII, PDEIII, squalene cyclase inhibitor, CXCR1, CXCR2, nitric oxide synthase, cyclo-oxygenase 1, cyclo-oxygenase 2, 5HT receptors, dopamine receptors, G Proteins, histamine receptors, 5-lipoxygenase, tryptase serine protease, thymidylate synthase, purine nucleoside phosphorylase, trypanosomal GAPDH, glycogen phosphorylase, Carbonic anhydrase, chemokine receptors, JAW STAT, RXR and similar, HIV 1 protease, HIV 1 integrase, influenza, neuraminidase, hepatitis B reverse transcriptase, sodium channel, multi drug resistance (MDR), protein P-glycoprotein (and MRP), tyrosine kinases (including Bruton's Tyrosine Kinase), CD23, CD124, tyrosine kinase p561ck, CD4, CD5, IL-2 receptor, IL-1 receptor, TNF-alphaR, ICAM1, Cat+ channels, VCAM, VLA-4 integrin, selectins, CD40/CD40L, neurokinins and receptors,

inosine monophosphate dehydrogenase, p38 MAP Kinase, RAS-RAF-MEK-ERK pathway, interleukin-1 converting enzyme, caspase, HCV, NS3 protease, HCV NS3 RNA helicase, glycinamide ribonucleotide formyl transferase, rhinovirus 3C protease, herpes simplex virus-1 (HSV-I), protease, cytomegalovirus (CMV) protease, poly (ADP-ribose) polymerase, cyclin dependent kinases, vascular endothelial growth factor, oxytocin receptor, microsomal transfer protein inhibitor, bile acid transport inhibitor, 5 alpha reductase inhibitors, angiotensin 11, glycine receptor, noradrenaline reuptake receptor, endothelin receptors, neuropeptide Y and receptor, adenosine receptors, adenosine kinase and AMP deaminase, purinergic receptors (P2Y1, P2Y2, P2Y4, P2Y6, P2X 1-7), farnesyltransferases, geranylgeranyl transferase, TrkA a receptor for NGF, beta-amyloid, tyrosine kinase Flk-IIKDR, vitronectin receptor, integrin receptor, Her-21 neu, telomerase inhibition, cytosolic phospholipaseA2 and EGF receptor tyrosine kinase, ecdysone 20-monooxygenase, ion channel of the GABA gated chloride channel, acetylcholinesterase, voltage-sensitive sodium channel protein, calcium release channel, chloride channels, Acetyl-CoA carboxylase, adenylosuccinate synthetase, protoporphyrinogen oxidase, L-1 receptor associated kinase-3 (IRAK-3 or IRAK-M) and enolpyruvyl-shikimate-phosphate synthase.

19. The compound of claim 1, wherein Warhead is  ;

wherein R^{13} is $-P(O)R^{13a}R^{13b}$, $-SO_2R^{13a}$, $-SO_2-NR^{13a}R^{13b}$ or $-N(R^{13a})-SO_2R^{13b}$;

R^{13a} and R^{13b} are each independently hydrogen, $-C_1-C_8$alkyl or C_3-C_8cycloalkyl, said $-C_1-C_8$alkyl or C_3-C_8cycloalkyl is optionally substituted with at least one halogen;

R^{14} and R^{15} are each independently hydrogen, halogen, $-C_1-C_8$alkyl, $-C_3-C_8$cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, 5- to 12-membered heteroaryl, -CN, $-OR^{14a}$, $-SO_2R^{14a}$, $-SO_2NR^{14a}R^{14b}$, $-COR^{14a}$, $-CO_2R^{14a}$, $-CONR^{14a}R^{14b}$, $-NR^{14a}R^{14b}$, $-NR^{14a}COR^{14b}$, $-NR^{14a}CO_2R^{14b}$, or $–NR^{14a}SO_2R^{14b}$; each of $-C_1-C_8$alkyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{14d}, or

R^{14} and R^{15} together with the carbon atoms to which they are attached, form a 5 or 6-membered unsaturated or saturated ring, said ring comprising 0-3 heteroatoms independently selected from nitrogen, oxygen and sulfur; said ring is optionally substituted with at least one substituent R^{14e};

R^{14e}, at each occurrence, is independently hydrogen, halogen, $-C_1-C_8$alkyl, $-C_1-C_8$alkoxy, $-C_3-C_8$cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, 5- to 12-membered heteroaryl, oxo (=O), -

OR^{14a}, thioxo (=S), $-SR^{14a}$, -CN, $-SO_2R^{14a}$, $-SO_2NR^{14a}R^{14b}$, $-COR^{14a}$, $-CO_2R^{14a}$, $-CONR^{14a}R^{14b}$, $-NR^{14a}R^{14b}$, $-NR^{14a}COR^{14b}$, $-NR^{14a}CO_2R^{14b}$ or $-NR^{14a}SO_2R^{14b}$; each of $-C_1$-C_8alkyl, $-C_1$-C_8alkoxy, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{14d};

R^{14a} and R^{14b} are each independently hydrogen, $-C_1$-C_8alkyl, $-C_1$-C_8haloalkyl, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, C_1-C_8alkoxy-C_1-C_8alkyl-, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl;

R^{14d}, at each occurrence, is independently halogen, -OH, -CN, oxo, $-C_1$-C_8alkyl, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, $-C_3$-C_8cycloalkyl, 3- to 8-membered heterocyclyl, $-C_6$-C_{12}aryl, or 5- to 12-membered heteroaryl;

R^4 is hydrogen, halogen, $-C_1$-C_8alkyl, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, $-C_1$-C_8alkoxy, $-C_3$-C_8cycloalkyl, 3- to 8-membered heterocyclyl, $-C_6$-C_{12}aryl, 5- to 12-membered heteroaryl, -CN, $-SO_2R^{4a}$, $-SO_2NR^{4a}R^{4b}$, $-COR^{4a}$, $-CO_2R^{4a}$, $-CONR^{4a}R^{4b}$, $-NR^{4a}R^{4b}$, $-NR^{4a}COR^{4b}$, $-NR^{4a}CO_2R^{4b}$ or $-NR^{4a}SO_2R^{4b}$; each of $-C_1$-C_8alkyl, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, $-C_1$-C_8alkoxy, $-C_3$-C_8cycloalkyl, 3- to 8-membered heterocyclyl, $-C_6$-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with halogen, $-C_1$-C_8alkyl, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, $-C_3$-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, 5- to 12-membered heteroaryl, oxo, -CN, $-OR^{4c}$, $-SO_2R^{4c}$, $-SO_2NR^{4c}R^{4d}$, $-COR^{4c}$, $-CO_2R^{4c}$, $-CONR^{4c}R^{4d}$, $-NR^{4c}R^{4d}$, $-NR^{4c}COR^{4d}$, $-NR^{4c}CO_2R^{4d}$ or $-NR^{4c}SO_2R^{4d}$;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently hydrogen, $-C_1$-C_8alkyl, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl;

R^9, R^{10} and R^{11} are each independently hydrogen, halogen, $-C_1$-C_8alkyl, $-NR^{9a}R^{9b}$, $-OR^{9a}$, $-C_3$-C_8cycloalkyl, 3- to 8-membered heterocyclyl, $-C_6$-C_{12}aryl, 5- to 12-membered heteroaryl, oxo or -CN; each of $-C_1$-C_8alkyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{9c};

R^{9a} and R^{9b} are each independently hydrogen, $-C_1$-C_8alkyl, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, $-C_3$-C_8cycloalkyl, 3- to 8-membered heterocyclyl, $-C_6$-C_{12}aryl or 5- to 12-membered heteroaryl; each of said $-C_1$-C_8alkyl, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{9d}; or

R^{9c} and R^{9d} are each independently halogen, hydroxy, $-C_1$-C_8alkyl, $-C_1$-C_8alkoxy, $-C_2$-C_8alkenyl, $-C_2$-C_8alkynyl, $-C_3$-C_8cycloalkyl, 3- to 8-membered heterocyclyl, $-C_6$-C_{12}aryl or 5- to 12-membered heteroaryl;

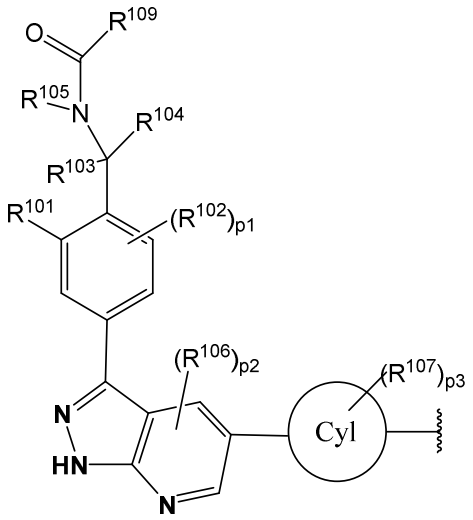
Z^4, Z^5, Z^6 and Z^7 are each independently $-CR^{Z4}$, or N;

R^{Z4}, at each occurrence, is independently hydrogen, halogen, $-C_1$-C_8alkyl, $-NR^{Z4a}R^{Z4b}$, $-OR^{Z4a}$, $-SR^{Z4a}$, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, 5- to 12-membered heteroaryl, or CN; each of $-C_1$-C_8alkyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl is optionally substituted with at least one R^{Z4c};

R^{Z4a} and R^{Z4b} are each independently hydrogen, -C_1-C_8alkyl, -C_2-C_8alkenyl, -C_2-C_8alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl, each of said -C_1-C_8alkyl, -C_2-C_8alkenyl, -C_2-C_8alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl is optionally substituted with at least one substituent R^{Z4d}; and

R^{Z4c} and R^{Z4d} are each independently halogen, hydroxy, -C_1-C_8alkyl, -C_1-C_8alkoxy, -C_2-C_8alkenyl, -C_2-C_8alkynyl, C_3-C_8cycloalkyl, 3- to 8-membered heterocyclyl, C_6-C_{12}aryl, or 5- to 12-membered heteroaryl.

20. The compound of claim 1, wherein Warhead is



wherein  is a 5- or 6- membered aromatic ring comprising 0-3 heteroatoms selected from nitrogen, oxygen and sulfur;

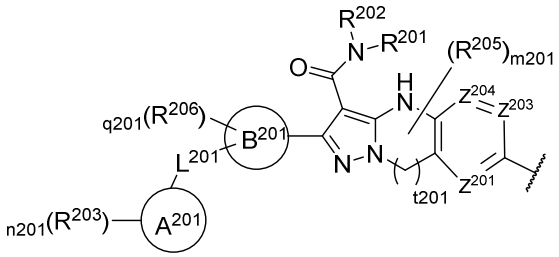
R^{101}, R^{102}, R^{103}, R^{104}, R^{105}, R^{106} and R^{107} are each independently hydrogen, halogen, -C_{1-8}alkyl, -C_{1-8}alkoxy,-C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, -CN, -NO_2, -OR^{10a}, -SO_2R^{10a}, -COR^{10a}, -CO_2R^{10a}, -$CONR^{10a}R^{10b}$, -$C(=NR^{10a})NR^{10b}R^{10c}$, -$NR^{10a}R^{10b}$, -$NR^{10a}COR^{10b}$, -$NR^{10a}CONR^{10b}R^{10c}$, -$NR^{10a}CO_2R^{10b}$, -$NR^{10a}SONR^{10b}R^{10c}$, -$NR^{10a}SO_2NR^{10b}R^{10c}$, or –$NR^{10a}SO_2R^{10b}$, each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with halogen, hydroxy, -haloC_{1-8}alkyl, -C_{1-8}alkyoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

R^{109} is 5- or 6- membered aromatic ring comprising 0-3 heteroatoms selected from nitrogen, oxygen and sulfur; said aromatic ring is optionally substituted with halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_{1-8}alkoxy, cycloalkyl, heterocyclyl, aryl, heteroaryl, -CN, -NO_2, -OR^{10a}, -SO_2R^{10a}, -COR^{10a}, -CO_2R^{10a}, -$CONR^{10a}R^{10b}$, -$C(=NR^{10a})NR^{10b}R^{10c}$, -$NR^{10a}R^{10b}$, -$NR^{10a}COR^{10b}$, -$NR^{10a}CONR^{10b}R^{10c}$, -$NR^{10a}CO_2R^{10b}$, -$NR^{10a}SONR^{10b}R^{10c}$, -$NR^{10a}SO_2NR^{10b}R^{10c}$, or –$NR^{10a}SO_2R^{10b}$, each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with halogen, hydroxy, -haloC_{1-8}alkyl, -C_{1-8}alkyoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

p1, p2 and p3 are each independently 0, 1, 2, 3 or 4; and

R^{10a}, R^{10b} and R^{10c} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl.

21. The compound of claim 1, wherein Warhead is



ring A^{201} and B^{201} are each independently an aromatic ring comprising 0-3 heteroatoms selected from nitrogen, sulfur and oxygen as ring member(s);

Z^{201}, Z^{203} and Z^{204} are each independently N or CR^{20z};

L^{201} is independently a bond, -C_{1-8}alkylene-, -N(R^{204})-, -O-, -S-, ^{*L201}-C_{1-8}alkylene-O-^{**L201}, ^{*L201}-O-C_{1-8}alkylene-^{**L201}, ^{*L201}-N(R^{204})CO-^{**L201}, ^{*L201}-CON(R^{204})-^{**L201}, ^{*L201}-N(R^{204})CO-C_{1-8}alkylene-^{**L201}, ^{*L201}-CON(R^{204})-C_{1-8}alkylene-^{**L201}, ^{*L201}-N(R^{204})-C_{1-8}alkylene-^{**L201}, ^{*L201}-C_{1-8}alkylene-N(R^{204})-^{**L201}, -heterocyclene-, or -heteroarylene-, wherein each of said -C_{1-8}alkylene-, ^{*L201}-C_{1-8}alkylene-O-^{**L201}, ^{*L201}-O-C_{1-8}alkylene-^{**L201}, ^{*L201}-N(R^{204})CO-C_{1-8}alkylene-^{**L201}, ^{*L201}-CON(R^{204})-C_{1-8}alkylene-^{**L201}, ^{*L201}-N(R^{204})-C_{1-8}alkylene-^{**L201}, ^{*L201}-C_{1-8}alkylene-N(R^{204})-^{**L201}, -heterocyclene- and -heteroarylene- is optionally substituted with at least one substituent R^{20L};

wherein ^{*L201} refers to the position attached to ring A, and ^{**L201} refers to the position attached to ring B;

m201, n201 and q201 are each independently 0, 1, 2, 3 or 4;

t201 is 0, 1 or 2;

R^{201}, R^{202}, and R^{204} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each of said -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with halogen, hydroxy, -C_{1-8}alkyoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

R^{20L}, R^{203}, R^{205} and R^{206} are each independently hydrogen, halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, -CN, -NO_2, -OR^{20a}, -SO_2R^{20a}, -COR^{20a}, -CO_2R^{20a}, -$CONR^{20a}R^{20b}$, -C(=NR^{20a})$NR^{20b}R^{20c}$, -$NR^{20a}R^{20b}$, -$NR^{20a}COR^{20b}$, -$NR^{20a}CONR^{20b}R^{20c}$, -$NR^{20a}CO_2R^{20b}$, -$NR^{20a}SONR^{20b}R^{20c}$, -$NR^{20a}SO_2NR^{20b}R^{20c}$, or –$NR^{20a}SO_2R^{20b}$, wherein each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with at least one halogen, hydroxy, -C_{1-8}alkyl, -C_{1-8}alkyoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

R^{20z} is hydrogen, halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, -CN, -NO_2, -OR^{20a}, -SO_2R^{20a}, -COR^{20a}, -CO_2R^{20a}, -$CONR^{20a}R^{20b}$, -$C(=NR^{20a})NR^{20b}R^{20c}$, -$NR^{20a}R^{20b}$, -$NR^{20a}COR^{20b}$, -$NR^{20a}CONR^{20b}R^{20c}$, -$NR^{20a}CO_2R^{20b}$, -$NR^{20a}SONR^{20b}R^{20c}$, -$NR^{20a}SO_2NR^{20b}R^{20c}$, or –$NR^{20a}SO_2R^{20b}$, each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with at least one halogen, hydroxy, -C_{1-8}alkyl, -C_{1-8}alkyoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

R^{20a}, R^{20b}, and R^{20c} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

or two R^{20L}, together with the atom(s) to which they are attached, form a 3- to 12-membered ring, said ring comprising 0, 1 or 2 additional heteroatoms independently selected from nitrogen, oxygen and optionally oxidized sulfur as ring member(s), said ring is optionally substituted with at least one substituent independently selected from halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, oxo, -CN, -NO_2, -OR^{203f}, -SO_2R^{203f}, -$SO_2NR^{203f}R^{203g}$, -COR^{203f}, -CO_2R^{203f}, -$CONR^{203f}R^{203g}$, -$C(=NR^{203f})NR^{203g}R^{203h}$, -$NR^{203f}R^{203g}$, -$NR^{203f}COR^{203g}$, -$NR^{203f}CONR^{203g}R^{203h}$, -$NR^{203f}CO_2R^{203f}$, -$NR^{203f}SONR^{203f}R^{203g}$, -$NR^{203f}SO_2NR^{203g}R^{203h}$, and –$NR^{203f}SO_2R^{203g}$, each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with at least one substituent selected from halogen, -C_{1-8}alkyl, -OR^{203i}, -$NR^{203i}R^{203j}$, cycloalkyl, heterocyclyl, aryl, and heteroaryl;

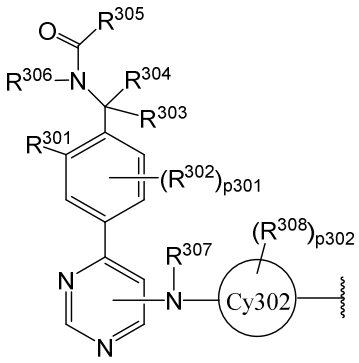
or two R^{203}, together with the atoms to which they are attached, form a 3- to 12-membered ring, said ring comprising 0, 1 or 2 additional heteroatoms independently selected from nitrogen, oxygen and optionally oxidized sulfur as ring member(s), said ring is optionally substituted with at least one substituent independently selected from halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, oxo, -CN, -NO_2, -OR^{203f}, -SO_2R^{203f}, -$SO_2NR^{203f}R^{203g}$, -COR^{203f}, -CO_2R^{203f}, -$CONR^{203f}R^{203g}$, -$C(=NR^{203f})NR^{203g}R^{203h}$, -$NR^{203f}R^{203g}$, -$NR^{203f}COR^{203g}$, -$NR^{203f}CONR^{203g}R^{203h}$, -$NR^{203f}CO_2R^{203f}$, -$NR^{203f}SONR^{203f}R^{203g}$, -$NR^{203f}SO_2NR^{203g}R^{203h}$, and –$NR^{203f}SO_2R^{203g}$, each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with at least one substituent selected from halogen, -C_{1-8}alkyl, -OR^{203i}, -$NR^{203i}R^{203j}$, cycloalkyl, heterocyclyl, aryl, and heteroaryl;

or R^4 and one of R^3, together with the atoms to which they are attached, form a 3- to 12-membered ring, said ring comprising 0, 1 or 2 additional heteroatoms independently selected from nitrogen, oxygen and optionally oxidized sulfur as ring member(s), said ring is optionally substituted with at least one substituent independently selected from halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, oxo, -CN, -NO_2, -OR^{203f}, -SO_2R^{203f}, -$SO_2NR^{203f}R^{203g}$, -COR^{203f}, -CO_2R^{203f}, -$CONR^{203f}R^{203g}$, -$C(=NR^{203f})NR^{203g}R^{203h}$, -$NR^{203f}R^{203g}$, -$NR^{203f}COR^{203g}$, -$NR^{203f}CONR^{203g}R^{203h}$, -$NR^{203f}CO_2R^{203f}$, -$NR^{203f}SONR^{203f}R^{203g}$, -$NR^{203f}SO_2NR^{203g}R^{203h}$, and –$NR^{203f}SO_2R^{203g}$, each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted

with at least one substituent selected from halogen, -C_{1-8}alkyl, -OR^{203i}, -$NR^{203i}R^{203j}$, cycloalkyl, heterocyclyl, aryl, and heteroaryl; and

R^{203f}, R^{203g}, R^{203h}, R^{203i}, and R^{203j} are each independently hydrogen, -C_{1-8}alkyl, C_{1-8}alkoxy-C_{1-8}alkyl-, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl.

22. The compound of claim 1, wherein Warhead is



wherein:

Cy302 is a 5- or 6- membered saturated ring or unsaturated ring comprising 0-3 heteroatoms selected from nitrogen, oxygen and sulfur as ring member(s);

each of occurrence, R^{301}, R^{302}, R^{303}, R^{304} and R^{308} are each independently hydrogen, halogen, -C_{1-8}alkyl, -C_{1-8}alkoxy,-C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, oxo (=O), -CN, -NO_2, -OR^{30c}, -SO_2R^{30c}, -COR^{30c}, -CO_2R^{30c}, -$CONR^{30c}R^{30d}$, -$C(=NR^{30c})NR^{30d}R^{30e}$, -$NR^{30c}R^{30d}$, -$NR^{30c}COR^{30d}$, -$NR^{30c}CONR^{30d}R^{30e}$, -$NR^{30c}CO_2R^{30d}$, -$NR^{30c}SONR^{30d}R^{30e}$, -$NR^{30c}SO_2NR^{30d}R^{30e}$, or –$NR^{30c}SO_2R^{30d}$, each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with halogen, hydroxy, -haloC_{1-8}alkyl, -C_{1-8}alkyoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

R^{306} and R^{307} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl or heteroaryl, each of said -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with halogen, hydroxy, -haloC_{1-8}alkyl, -C_{1-8}alkyoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

R^{305} is 5- or 6- membered aromatic ring comprising 0-3 heteroatoms selected from nitrogen, oxygen and sulfur as ring member(s); said aromatic ring is optionally substituted with halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, -C_{1-8}alkoxy, cycloalkyl, heterocyclyl, aryl, heteroaryl, -CN, -NO_2, -OR^{30c}, -SO_2R^{30c}, -COR^{30c}, -CO_2R^{30c}, -$CONR^{30c}R^{30d}$, -$C(=NR^{30c})NR^{30d}R^{30e}$, -$NR^{30c}R^{30d}$, -$NR^{30c}COR^{30d}$, -$NR^{30c}CONR^{30d}R^{30e}$, -$NR^{30c}CO_2R^{30d}$, -$NR^{30c}SONR^{30d}R^{30e}$, -$NR^{30c}SO_2NR^{30d}R^{30e}$, or –$NR^{30c}SO_2R^{30d}$, each of said -$C_{1-8}$alkyl, -$C_{2-8}$alkenyl, -$C_{2-8}$alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally

substituted with -C_{1-8}alkyl, halogen, hydroxy, -haloC_{1-8}alkyl, -C_{1-8}alkyoxy, cycloalkyl, heterocyclyl, aryl, or heteroaryl;

p301 and p302 are each independently 0, 1, 2, 3 or 4; and

R^{30c}, R^{30d} and R^{30e} are each independently hydrogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl; or

(R^{30c} and R^{30d}) or (R^{30d} and R^{30e}) together with the atom(s) to which they are attached, form a 3- to 12-membered ring, said ring comprising 0, 1 or 2 additional heteroatoms independently selected from nitrogen, oxygen and optionally oxidized sulfur as ring member(s), said ring is optionally substituted with at least one substituent independently selected from halogen, -C_{1-8}alkyl, -C_{2-8}alkenyl, -C_{2-8}alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, oxo, -CN and -NO_2.

23. A pharmaceutical composition comprising a compound of Claim 1 or a pharmaceutically acceptable salt, tautomer or prodrug thereof, together with a pharmaceutically acceptable excipient.

24. A compound according to Claims 1 or a pharmaceutically acceptable salt thereof including the compound of formula (I), for use in a method of treating a disease in a subject in need thereof by degrading a target protein, the method comprising administering to the subject a therapeutically effective amount of a compound of claim 1, wherein said target protein is selected from the group consisting of structural proteins, receptors, enzymes, cell surface proteins, proteins pertinent to the integrated function of a cell, including proteins involved in catalytic activity, aromatase activity, motor activity, helicase activity, metabolic processes (anabolism and catabolism), antioxidant activity, proteolysis, biosynthesis, proteins with kinase activity, oxidoreductase activity, transferase activity, hydrolase activity, lyase activity, isomerase activity, ligase activity, enzyme regulator activity, signal transducer activity, structural molecule activity, binding activity (protein, lipid carbohydrate), receptor activity, cell motility, membrane fusion, cell communication, regulation of biological processes, development, cell differentiation, response to stimulus, behavioral proteins, cell adhesion proteins, proteins involved in cell death, and proteins involved in transport (including protein transporter activity, nuclear transport, ion transporter activity, channel transporter activity, carrier activity, permease activity, secretion activity, electron transporter activity, pathogenesis, chaperone regulator activity, nucleic acid binding activity, transcription regulator activity, extracellular organization and biogenesis activity and translation regulator activity).

25. The use of claim 24, wherein said target protein bound by is selected from the group consisting of ErbB receptors, B7.1 and B7, TINFR1m, TNFR2, NADPH oxidase, Bcl-Bax and other partners in the apoptosis pathway, C5a receptor, HMG-CoA reductase, PDE V phosphodiesterase type, PDE IV phosphodiesterase type 4, PDE I, PDEII, PDEIII, squalene cyclase inhibitor, CXCR1, CXCR2, nitric oxide synthase, cyclo-oxygenase 1, cyclo-oxygenase 2, 5HT receptors, dopamine receptors, G Proteins,

histamine receptors, 5-lipoxygenase, tryptase serine protease, thymidylate synthase, purine nucleoside phosphorylase, trypanosomal GAPDH, glycogen phosphorylase, Carbonic anhydrase, chemokine receptors, JAW STAT, RXR and similar, HIV 1 protease, HIV 1 integrase, influenza, neuraminidase, hepatitis B reverse transcriptase, sodium channel, multi drug resistance (MDR), protein P-glycoprotein (and MRP), tyrosine kinases (including Bruton's Tyrosine Kinase), CD23, CD124, tyrosine kinase p561ck, CD4, CD5, IL-2 receptor, IL-1 receptor, TNF-alphaR, ICAM1, Cat+ channels, VCAM, VLA-4 integrin, selectins, CD40/CD40L, neurokinins and receptors, inosine monophosphate dehydrogenase, p38 MAP Kinase, RAS-RAF-MEK-ERK pathway, interleukin-1 converting enzyme, caspase, HCV, NS3 protease, HCV NS3 RNA helicase, glycinamide ribonucleotide formyl transferase, rhinovirus 3C protease, herpes simplex virus-1 (HSV-I), protease, cytomegalovirus (CMV) protease, poly (ADP-ribose) polymerase, cyclin dependent kinases, vascular endothelial growth factor, oxytocin receptor, microsomal transfer protein inhibitor, bile acid transport inhibitor, 5 alpha reductase inhibitors, angiotensin 11, glycine receptor, noradrenaline reuptake receptor, endothelin receptors, neuropeptide Y and receptor, adenosine receptors, adenosine kinase and AMP deaminase, purinergic receptors (P2Y1, P2Y2, P2Y4, P2Y6, P2X 1-7), farnesyltransferases, geranylgeranyl transferase, TrkA a receptor for NGF, beta-amyloid, tyrosine kinase Flk-IIKDR, vitronectin receptor, integrin receptor, Her-21 neu, telomerase inhibition, cytosolic phospholipaseA2 and EGF receptor tyrosine kinase, ecdysone 20-monooxygenase, ion channel of the GABA gated chloride channel, acetylcholinesterase, voltage-sensitive sodium channel protein, calcium release channel, chloride channels, Acetyl-CoA carboxylase, adenylosuccinate synthetase, protoporphyrinogen oxidase, L-1 receptor associated kinase-3 (IRAK-3 or IRAK-M) and enolpyruvyl-shikimate-phosphate synthase.

26. The use of claim 24, wherein the disease is cancer.

27. The compound of claim 1, wherein s1 is 0.

28. A compound according to Claims 27 or a pharmaceutically acceptable salt thereof including the compound of formula (I), for use in a method of binding and altering the specificity of cereblon complex to induce the degradation of a complex-associated protein comprising administering a the compound of Claim 27, wherein the protein is selected from ErbB receptors, B7.1 and B7, TINFR1m, TNFR2, NADPH oxidase, Bcl-Bax and other partners in the apoptosis pathway, C5a receptor, HMG-CoA reductase, PDE V phosphodiesterase type, PDE IV phosphodiesterase type 4, PDE I, PDEII, PDEIII, squalene cyclase inhibitor, CXCR1, CXCR2, nitric oxide synthase, cyclo-oxygenase 1, cyclo-oxygenase 2, 5HT receptors, dopamine receptors, G Proteins, histamine receptors, 5-lipoxygenase, tryptase serine protease, thymidylate synthase, purine nucleoside phosphorylase, trypanosomal GAPDH, glycogen phosphorylase, Carbonic anhydrase, chemokine receptors, JAW STAT, RXR and similar, HIV 1 protease, HIV 1 integrase, influenza, neuraminidase, hepatitis B reverse transcriptase, sodium channel, multi drug

resistance (MDR), protein P-glycoprotein (and MRP), tyrosine kinases (including Bruton's Tyrosine Kinase), CD23, CD124, tyrosine kinase p561ck, CD4, CD5, IL-2 receptor, IL-1 receptor, TNF-alphaR, ICAM1, Cat+ channels, VCAM, VLA-4 integrin, selectins, CD40/CD40L, neurokinins and receptors, inosine monophosphate dehydrogenase, p38 MAP Kinase, RAS-RAF-MEK-ERK pathway, interleukin-1 converting enzyme, caspase, HCV, NS3 protease, HCV NS3 RNA helicase, glycinamide ribonucleotide formyl transferase, rhinovirus 3C protease, herpes simplex virus-1 (HSV-I), protease, cytomegalovirus (CMV) protease, poly (ADP-ribose) polymerase, cyclin dependent kinases, vascular endothelial growth factor, oxytocin receptor, microsomal transfer protein inhibitor, bile acid transport inhibitor, 5 alpha reductase inhibitors, angiotensin 11, glycine receptor, noradrenaline reuptake receptor, endothelin receptors, neuropeptide Y and receptor, adenosine receptors, adenosine kinase and AMP deaminase, purinergic receptors (P2Y1, P2Y2, P2Y4, P2Y6, P2X 1-7), farnesyltransferases, geranylgeranyl transferase, TrkA a receptor for NGF, beta-amyloid, tyrosine kinase Flk-IIKDR, vitronectin receptor, integrin receptor, Her-21 neu, telomerase inhibition, cytosolic phospholipaseA2 and EGF receptor tyrosine kinase, ecdysone 20-monooxygenase, ion channel of the GABA gated chloride channel, acetylcholinesterase, voltage-sensitive sodium channel protein, calcium release channel, chloride channels, Acetyl-CoA carboxylase, adenylosuccinate synthetase, protoporphyrinogen oxidase, L-1 receptor associated kinase-3 (IRAK-3 or IRAK-M), enolpyruvyl-shikimate-phosphate synthase and neo-substrates (like IKZF1, IKZF3, and CK1a).

29. A compound according to Claims 1 or a pharmaceutically acceptable salt thereof including the compound of formula (I), for use in a method of treating an CRBN-mediated disorder, disease, or condition in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a compound of claim 1 or the pharmaceutical composition of claim 23.

30. The use of claim 29, wherein the disorder, disease, or condition is selected from proliferative disorders, neurological disorders, and disorders associated with transplantation.