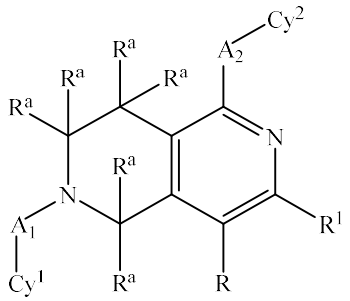
Claims

1. A compound of formula **(A)**



(A)

or a tautomer thereof, isotope thereof, prodrug thereof, N-oxide thereof, a pharmaceutically acceptable ester thereof, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof, wherein

A_1 is absent or is independently selected from substituted or unsubstituted C_{1-4} alkyl, substituted or unsubstituted C_{2-4} alkenyl, substituted or unsubstituted C_{2-4} alkynyl, substituted or unsubstituted C_{3-10} cycloalkyl, substituted or unsubstituted C_{3-10} heterocycloalkyl, -$(CR^bR^c)_p$-, -O-, - S-, -$S(=O)_p$-, -C(=O)- ,-NR^x- , -CO-NR^x- and -NR^x-CO-.

A_2 is absent or is independently selected from substituted or unsubstituted C_{1-4} alkyl, substituted or unsubstituted C_{2-4} alkenyl, substituted or unsubstituted C_{2-4} alkynyl, substituted or unsubstituted C_{3-10} cycloalkyl, substituted or unsubstituted C_{3-10} heterocycloalkyl, -$(CR^bR^c)_p$-, -O-, -S-, -$S(=O)_p$-, -C(=O)- ,-NR^x- , -CO-NR^x- and -NR^x-CO-.

Cy^1 is selected form a cyclic group selected from substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl.

Cy^2 is selected from cyclic group selected from substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl which is optionally substituted by E.

E is a group capable of forming a covalent bond or an “Electrophile” or “electrophilic moiety capable of forming a covalent bond.

R at each occurrence is independently selected from CN (Cyano), COOH, $CONH_2$, SO_3H, $C(=O)OR^b$, $-C(=O)R^b$, $-C(=S)R^b$, $-C(=O)NR^bR^c$, $-C(=O)ONR^bR^c$, $-NR^bR^c$,-$NR^bC(=O)NR^bR^c$, $-NR^bS(=O)R^c$, $-NR^bS(=O)_2R^c$, $-NR^b$-OR^c, =N-NR^bR^c, $-NR^bC(=O)OR^c$, -$NR^bC(=O)R^c$, $-NR^bC(=S)R^c$,–$NR^bC(=S)NR^bR^c$, $-SONR^bR^c$, $-SO_2NR^bR^c$, $-OR^b$, -$OR^bC(=O)NR^bR^c$, $-OR^bC(=O)OR^c$, $-OC(=O)R^b$, $-OC(=O)NR^bR^c$, $-R^bNR^cC(=O)R^b$, $-R^bOR^c$, -$R^bC(=O)OR^c$, $-R^bC(=O)NR^bR^c$, $-R^bC(=O)R^c$, $-R^bOC(=O)R^c$, $-SR^b$, $-SOR^c$, $-SO_2R^b$, -$CR^bR^cC(=O)R^b$ or $-CR^bR^cC(=S)R^z$.

R^1 at each occurrence is independently selected from hydrogen, hydroxy, halogen, substituted or unsubstituted amino, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, $C(=O)OR^b$, $-C(=O)R^b$, $-C(=S)R^b$, -$C(=O)NR^bR^c$, $-C(=O)ONR^bR^c$, $-NR^bR^c$,-$NR^bC(=O)NR^bR^c$, $-NR^bS(=O)R^c$, $-NR^bS(=O)_2R^c$, -NR^b-OR^c, =N-NR^bR^c, $-NR^bC(=O)OR^c$, $-NR^bC(=O)R^c$, $-NR^bC(=S)R^c$,–$NR^bC(=S)NR^bR^c$, -$SONR^bR^c$, $-SO_2NR^bR^c$, $-OR^b$, $-OR^bC(=O)NR^bR^c$, $-OR^bC(=O)OR^c$, $-OC(=O)R^b$, -$OC(=O)NR^bR^c$, $-R^bNR^cC(=O)R^b$, $-R^bOR^c$, $-R^bC(=O)OR^c$, $-R^bC(=O)NR^bR^c$, $-R^bC(=O)R^c$, -$R^bOC(=O)R^c$, $-SR^b$, $-SOR^c$, $-SO_2R^b$, $-CR^bR^cC(=O)R^b$ or $-CR^bR^cC(=S)R^z$.

R^a at each occurrence is independently selected from hydrogen, hydroxy, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, $-C(=O)OR^b$, -$C(=O)R^b$, $-C(=S)R^b$, $-C(=O)NR^bR^c$, $-C(=O)ONR^bR^c$, $-NR^bR^c$, $-NR^b$-OR^c , $-NR^bC(=O)NR^bR^c$, $-NR^bS(=O)R^c$, $-NR^bS(=O)_2R^c$, $-NR^b$-OR^c, =N-NR^bR^c, $-NR^bC(=O)OR^c$, $-NR^bC(=O)R^c$, -$NR^bC(=S)R^c$,–$NR^bC(=S)NR^bR^c$, $-SONR^bR^c$, $-SO_2NR^bR^c$, $-OR^b$, $-OR^bC(=O)NR^bR^c$, -$OR^bC(=O)OR^c$, $-OC(=O)R^b$, $-OC(=O)NR^bR^c$, $-R^bNR^cC(=O)R^b$, $-R^bOR^c$, $-R^bC(=O)OR^c$, -$R^bC(=O)NR^bR^c$, $-R^bC(=O)R^c$, $-R^bOC(=O)R^c$, $-SR^b$, $-SOR^c$, $-SO_2R^b$, $-CR^bR^cC(=O)R^b$ or -$CR^bR^cC(=S)R^z$ or any two R^a may be joined to a form a substituted or unsubstituted saturated or unsaturated 3-6 member ring, which may optionally include heteroatoms which may be same or different and are selected from O, NRa or S or ; any two R^a attached to the same carbon atom may be joined to a form a Oxo (C=O), Imino (=NR^b) , $C=S(O)_p$, or substituted or

unsubstituted saturated or unsaturated 3-6 member ring, which may optionally include heteroatoms which may be same or different and are selected from O, NR^x or S;

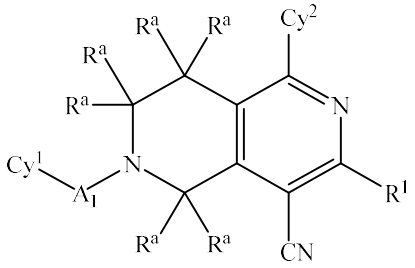
each occurrence of R^b and R^c is independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted heterocyclic ring, substituted heterocyclylalkyl ring, or substituted or unsubstituted amino, or any two of R^x and R^y when bound to a common atom may be joined to form (i) a substituted or unsubstituted saturated or unsaturated 3-14 membered ring, which may optionally include one or more heteroatoms which may be the same or different and are selected from O, NR^x or S, or (ii)an oxo (=O), thio(=S) or imino(=NR^x) group;

each occurrence of R^x and R^z are independently selected from hydrogen, hydroxy, cyano, halogen, -OR^a, -$COOR^a$, -S(=O)q-R^a, -NR^aR^b, -C(=Z)-R^a, substituted or unsubstituted alkyl group, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted Cycloalkyl;

Z is selected from O or S; and

each occurrence of p is independently 0,1 or 2.

2. The compound of claim 1, having a compound of formula **(A-I)**



(A-I)

or a tautomer thereof, isotope thereof, prodrug thereof, N-oxide thereof, a pharmaceutically acceptable ester thereof, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof, wherein

A_1 is absent or is independently selected from substituted or unsubstituted C_{1-4} alkyl, substituted or unsubstituted C_{2-4} alkenyl, substituted or unsubstituted C_{2-4} alkynyl, substituted or unsubstituted C_{3-10} cycloalkyl , substituted or unsubstituted C_{3-10} heterocycloalkyl, -$(CR^bR^c)_p$-, -O-,- S-, -$S(=O)_p$-, -C(=O)- ,-NR^x- , -CO-NR^x- and -NR^x-CO-.

Cy^1 is selected form a cyclic group selected from substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl.

Cy^2 is selected from cyclic group selected from substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl which is optionally substituted by E.

E is a group capable of forming a covalent bond or an “Electrophile” or “electrophilic moiety capable of forming a covalent bond.

R^1 at each occurrence is independently selected from hydrogen, hydroxy, halogen, substituted or unsubstituted amino, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, $C(=O)OR^b$, $-C(=O)R^b$, $-C(=S)R^b$, $-C(=O)NR^bR^c$, $-C(=O)ONR^bR^c$, $-NR^bR^c$,$-NR^bC(=O)NR^bR^c$, $-NR^bS(=O)R^c$, $-NR^bS(=O)_2R^c$, $-NR^b$-OR^c, $=N-NR^bR^c$, $-NR^bC(=O)OR^c$, $-NR^bC(=O)R^c$, $-NR^bC(=S)R^c$,$–NR^bC(=S)NR^bR^c$, $-SONR^bR^c$, $-SO_2NR^bR^c$, $-OR^b$, $-OR^bC(=O)NR^bR^c$, $-OR^bC(=O)OR^c$, $-OC(=O)R^b$, $-OC(=O)NR^bR^c$, $-R^bNR^cC(=O)R^b$, $-R^bOR^c$, $-R^bC(=O)OR^c$, $-R^bC(=O)NR^bR^c$, $-R^bC(=O)R^c$, $-R^bOC(=O)R^c$, $-SR^b$, $-SOR^c$, $-SO_2R^b$, $-CR^bR^cC(=O)R^b$ or $-CR^bR^cC(=S)R^z$.

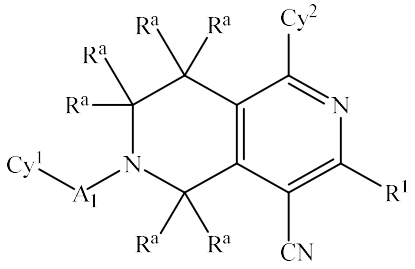
R^a at each occurrence is independently selected from hydrogen, hydroxy, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, $-C(=O)OR^b$, $-C(=O)R^b$, $-C(=S)R^b$, $-C(=O)NR^bR^c$, $-C(=O)ONR^bR^c$, $-NR^bR^c$, $-NR^b$-OR^c , $-NR^bC(=O)NR^bR^c$, $-NR^bS(=O)R^c$, $-NR^bS(=O)_2R^c$, $-NR^b$-OR^c, $=N-NR^bR^c$, $-NR^bC(=O)OR^c$, $-NR^bC(=O)R^c$, $-NR^bC(=S)R^c$,$–NR^bC(=S)NR^bR^c$, $-SONR^bR^c$, $-SO_2NR^bR^c$, $-OR^b$, $-OR^bC(=O)NR^bR^c$, $-OR^bC(=O)OR^c$, $-OC(=O)R^b$, $-OC(=O)NR^bR^c$, $-R^bNR^cC(=O)R^b$, $-R^bOR^c$, $-R^bC(=O)OR^c$, $-R^bC(=O)NR^bR^c$, $-R^bC(=O)R^c$, $-R^bOC(=O)R^c$, $-SR^b$, $-SOR^c$, $-SO_2R^b$, $-CR^bR^cC(=O)R^b$ or -

$CR^bR^cC(=S)R^z$ or any two R^a may be joined to a form a substituted or unsubstituted saturated or unsaturated 3-6 member ring, which may optionally include heteroatoms which may be same or different and are selected from O, NR^a or S or ; any two R^a attached to the same carbon atom may be joined to a form a Oxo (C=O), Imino ($=NR^b$) , $C=S(O)_p$, or substituted or unsubstituted saturated or unsaturated 3-6 member ring, which may optionally include heteroatoms which may be same or different and are selected from O, NR^x or S.

each occurrence of R^b and R^c is independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted heterocyclic ring, substituted heterocyclylalkyl ring, or substituted or unsubstituted amino, or any two of R^x and $R^y$when bound to a common atom may be joined to form (i) a substituted or unsubstituted saturated or unsaturated 3-14 membered ring, which may optionally include one or more heteroatoms which may be the same or different and are selected from O, NR^x or S, or (ii)an oxo (=O), thio(=S) or imino($=NR^x$) group; and

each occurrence of p is independently 0,1 or 2.

3. The compound of claim 1, having a compound of formula **(A-II)**



(A-II)

or a tautomer thereof, isotope thereof, prodrug thereof, N-oxide thereof, a pharmaceutically acceptable ester thereof, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof, wherein

A_1 is absent or is independently selected from substituted or unsubstituted C_{1-4} alkyl, substituted or unsubstituted C_{2-4} alkenyl, substituted or unsubstituted C_{2-4} alkynyl, substituted or unsubstituted C_{3-10} cycloalkyl , substituted or unsubstituted C_{3-10} heterocycloalkyl, $-(CR^bR^c)_p-$, -O-,- S-, $-S(=O)_p-$, -C(=O)- ,$-NR^x-$, -CO-NR^x- and -NR^x-CO-.

Cy^1 is selected form a cyclic group selected from substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl.

Cy^2 is substituted or unsubstituted heterocyclyl, which is optionally substituted by E.

E is a group capable of forming a covalent bond or an "Electrophile" or "electrophilic moiety capable of forming a covalent bond.

R^1 at each occurrence is independently selected from hydrogen, hydroxy, halogen, substituted or unsubstituted amino, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, $C(=O)OR^b$, $-C(=O)R^b$, $-C(=S)R^b$, $-C(=O)NR^bR^c$, $-C(=O)ONR^bR^c$, $-NR^bR^c$,$-NR^bC(=O)NR^bR^c$, $-NR^bS(=O)R^c$, $-NR^bS(=O)_2R^c$, $-NR^b$-OR^c, $=N$-NR^bR^c, $-NR^bC(=O)OR^c$, $-NR^bC(=O)R^c$, $-NR^bC(=S)R^c$,$–NR^bC(=S)NR^bR^c$, $-SONR^bR^c$, $-SO_2NR^bR^c$, $-OR^b$, $-OR^bC(=O)NR^bR^c$, $-OR^bC(=O)OR^c$, $-OC(=O)R^b$, $-OC(=O)NR^bR^c$, $-R^bNR^cC(=O)R^b$, $-R^bOR^c$, $-R^bC(=O)OR^c$, $-R^bC(=O)NR^bR^c$, $-R^bC(=O)R^c$, $-R^bOC(=O)R^c$, $-SR^b$, $-SOR^c$, $-SO_2R^b$, $-CR^bR^cC(=O)R^b$ or $-CR^bR^cC(=S)R^z$.

R^a at each occurrence is independently selected from hydrogen, hydroxy, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, $-C(=O)OR^b$, $-C(=O)R^b$, $-C(=S)R^b$, $-C(=O)NR^bR^c$, $-C(=O)ONR^bR^c$, $-NR^bR^c$, $-NR^b$-OR^c , $-NR^bC(=O)NR^bR^c$, $-NR^bS(=O)R^c$, $-NR^bS(=O)_2R^c$, $-NR^b$-OR^c, $=N$-NR^bR^c, $-NR^bC(=O)OR^c$, $-NR^bC(=O)R^c$, $-NR^bC(=S)R^c$,$–NR^bC(=S)NR^bR^c$, $-SONR^bR^c$, $-SO_2NR^bR^c$, $-OR^b$, $-OR^bC(=O)NR^bR^c$, $-OR^bC(=O)OR^c$, $-OC(=O)R^b$, $-OC(=O)NR^bR^c$, $-R^bNR^cC(=O)R^b$, $-R^bOR^c$, $-R^bC(=O)OR^c$, $-R^bC(=O)NR^bR^c$, $-R^bC(=O)R^c$, $-R^bOC(=O)R^c$, $-SR^b$, $-SOR^c$, $-SO_2R^b$, $-CR^bR^cC(=O)R^b$ or $-CR^bR^cC(=S)R^z$ or any two R^a may be joined to a form a substituted or unsubstituted saturated or unsaturated 3-6 member ring, which may optionally include heteroatoms which may be same or different and are selected from O, NR^a or S or ; any two R^a attached to the same carbon atom may be joined to a form a Oxo (C=O), Imino ($=NR^b$) , $C=S(O)_p$, or substituted or

unsubstituted saturated or unsaturated 3-6 member ring, which may optionally include heteroatoms which may be same or different and are selected from O, NR^x or S.

each occurrence of R^b and R^c is independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted heterocyclic ring, substituted heterocyclylalkyl ring, or substituted or unsubstituted amino, or any two of R^x and $R^y$when bound to a common atom may be joined to form (i) a substituted or unsubstituted saturated or unsaturated 3-14 membered ring, which may optionally include one or more heteroatoms which may be the same or different and are selected from O, NR^x or S, or (ii)an oxo (=O), thio(=S) or imino(=NR^x) group; and

each occurrence of p is independently 0,1 or 2.

4. The compound of anyone of claims 1-3, wherein

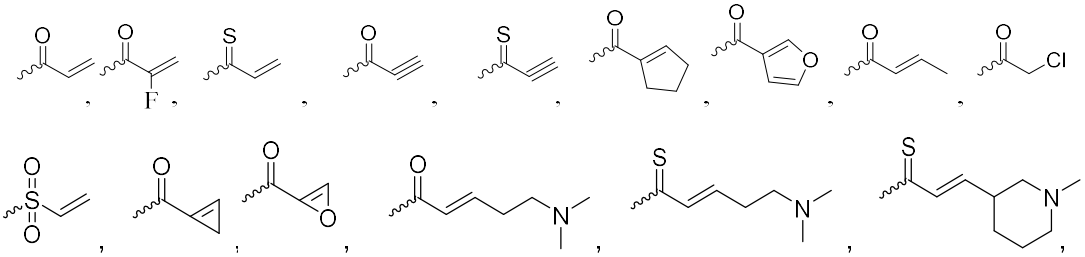
A_1 is absent or is -CR^bR^c-; wherein each of R^b and R^c is independently selected from hydrogen or substituted or unsubstituted alkyl;

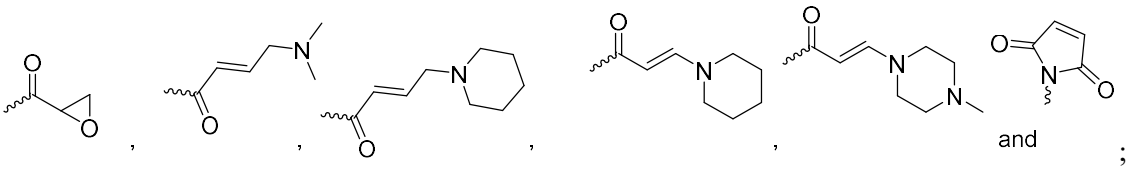
A_2 is absent or is -CR^bR^c-; wherein each of R^b and R^c is independently selected from hydrogen, substituted or unsubstituted alkyl

Cy^1 is selected form a cyclic group selected from substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl;

Cy^2 is selected from cyclic group selected from substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclyl and substituted or unsubstituted heterocyclylalkyl; wherein each group is optionally further substituted with group E;

E is selected from





R is Cyano (CN);

R^1 is selected from

(i) hydrogen, halogen, OR^b, S-R^b, -S(=O)pR^b-, -C(=O)-R^b ,-NR^bR^c, -CO-NR^bR^c- and -NR^b-CO-R^c; or

(ii) -O-R^b

(iii) -NR^bR^c or

(iv) is independently selected from, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted heterocyclyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl; and

R^a is selected from

(i) Hydrogen or substituted or unsubstituted alkyl or

(ii) two R^a attached to same carbon atom form a C=O (Oxo) group.

5. The compound of anyone of claims 1-4, wherein

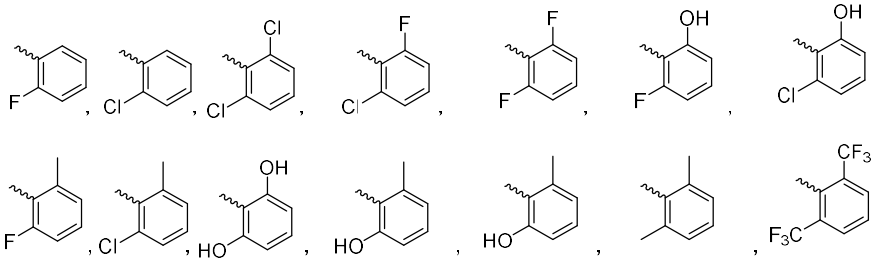
A_1 is absent or is selected from

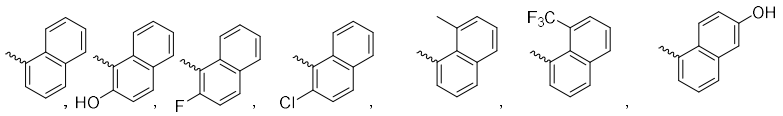
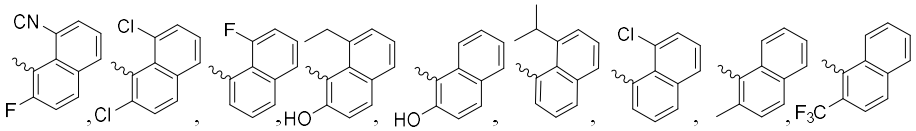
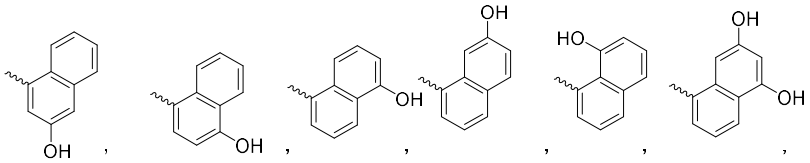
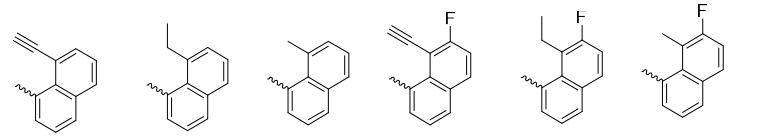
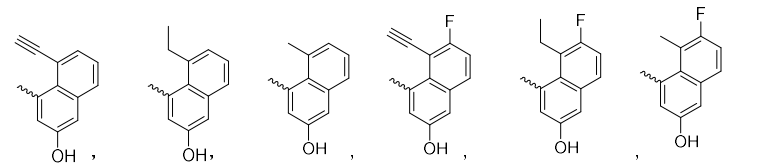
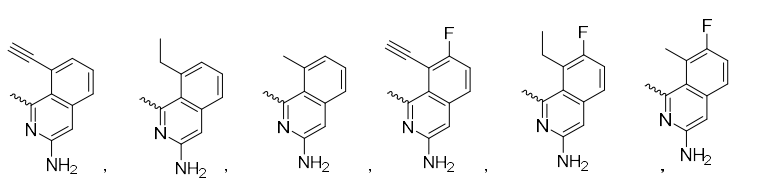
(i) -CR^bR^c-; wherein R^b is hydrogen and R^c is hydrogen or

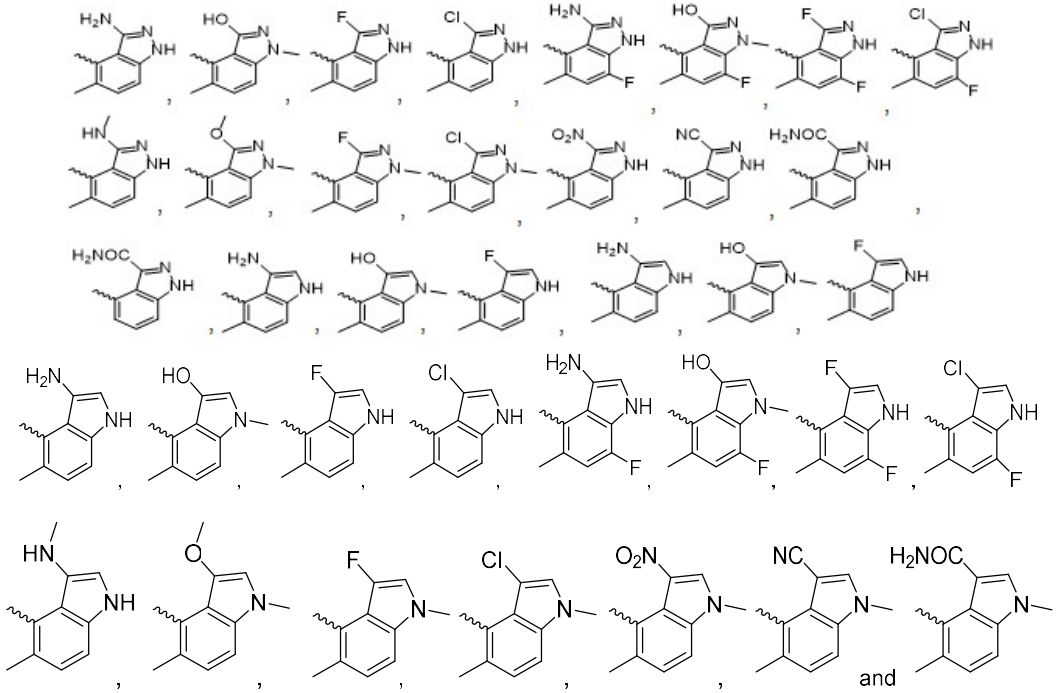
(ii) -CH_2 or -(C=O);

A_2 is absent;

Cy^1 is selected form

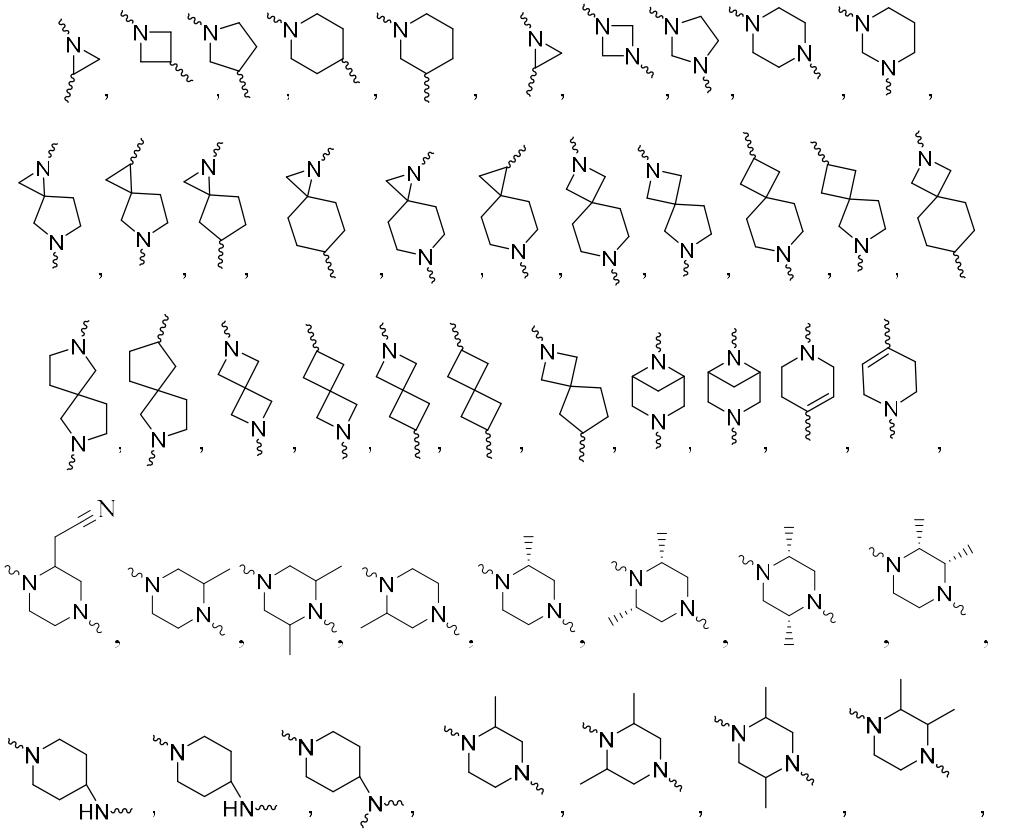


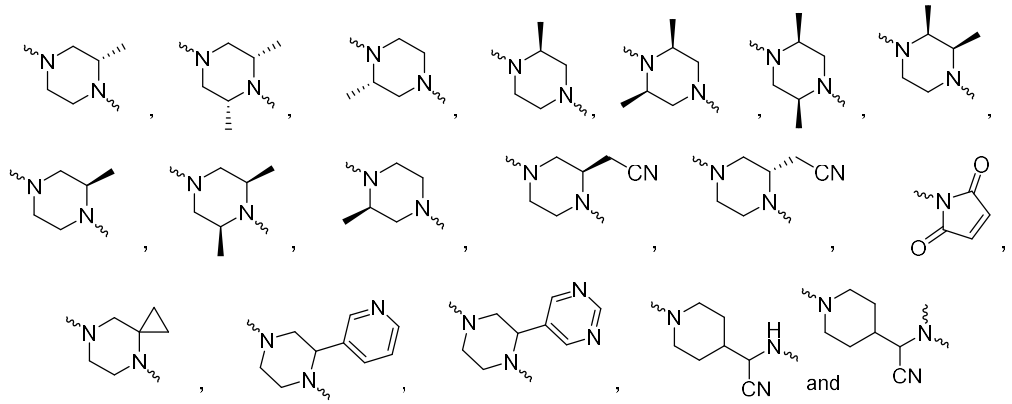









and

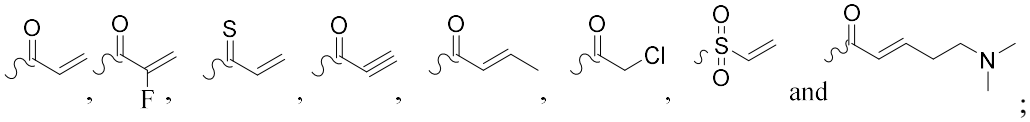
Cy^2 is selected form





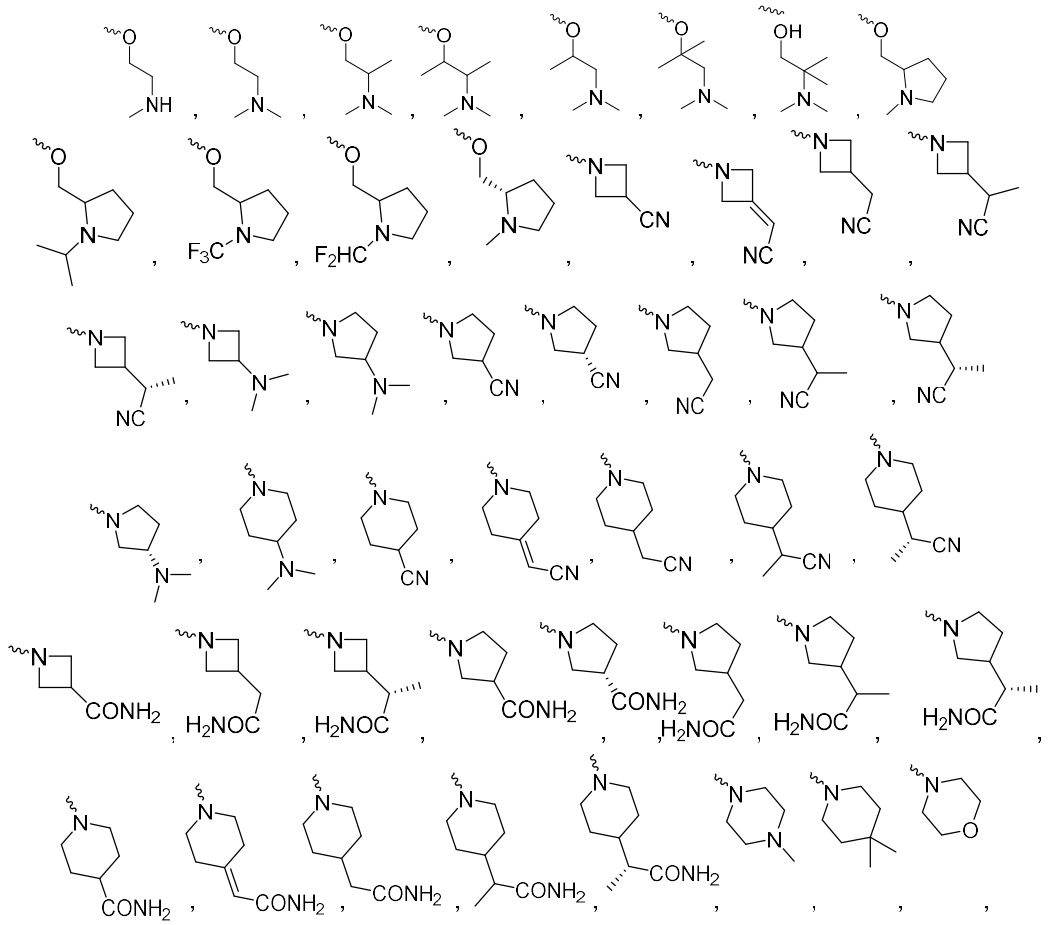
substituted with E a group capable of forming a covalent bond;

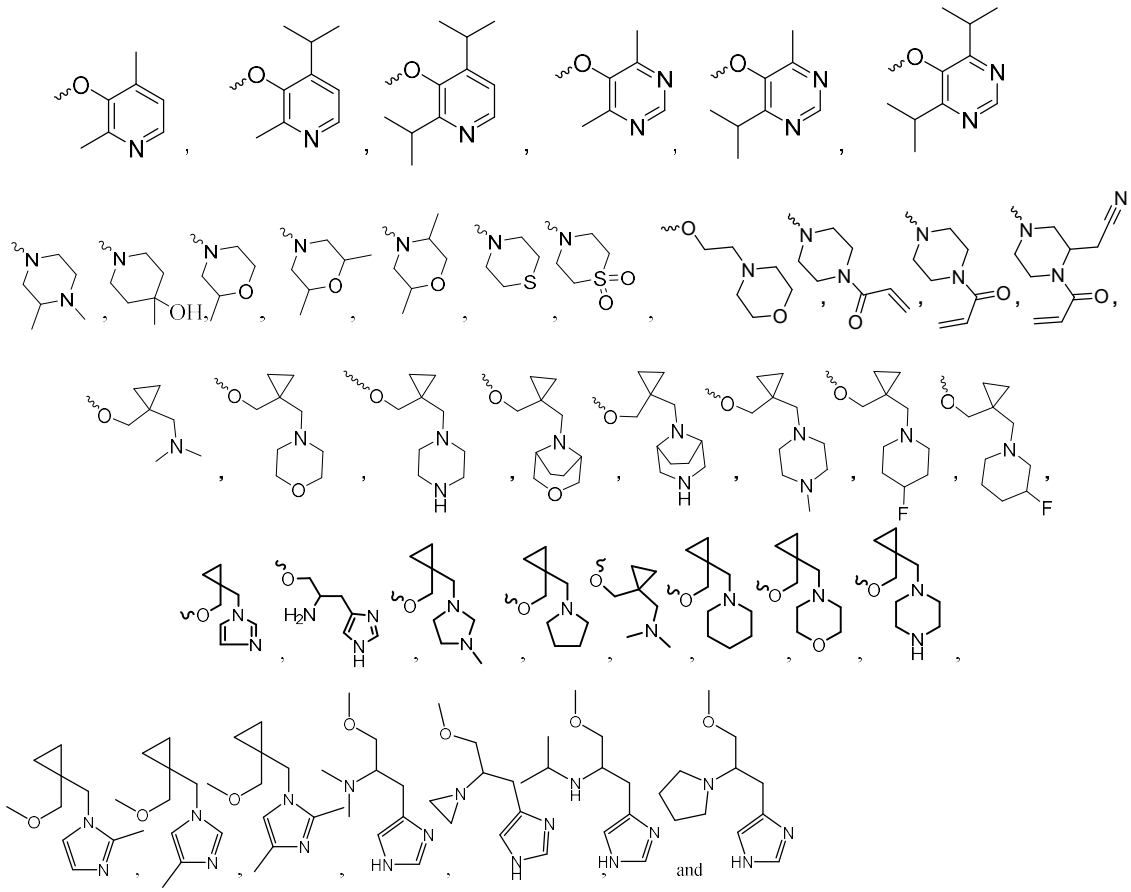
E is selected from



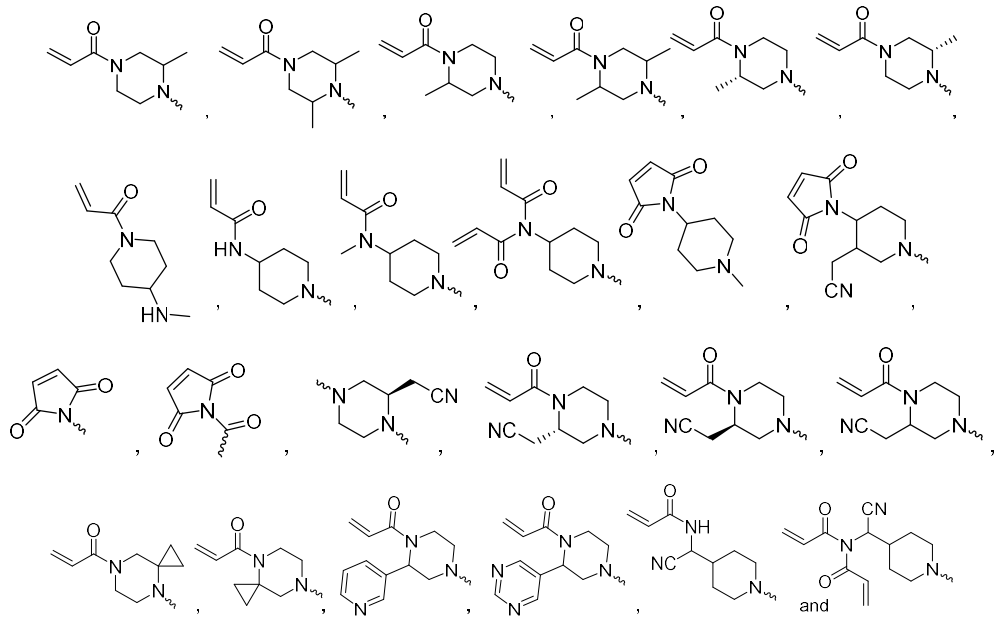
; and

R^1 is independently selected from

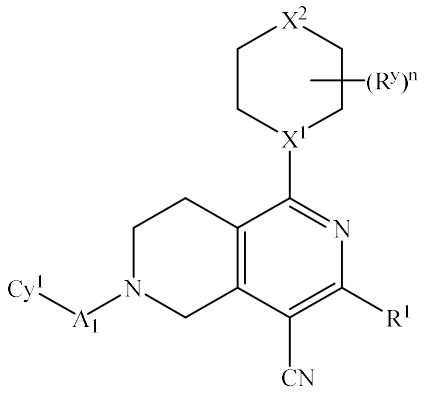




6. The compound of anyone of claims 1-5, wherein A_2-Cy^2-E is selected from



7. A compound of formula **(A-III)**



(A-III)

or a tautomer thereof, isotope thereof, prodrug thereof, N-oxide thereof, a pharmaceutically acceptable ester thereof, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof, wherein

A_1 is absent or substituted or unsubstituted alkyl;

Cy^1 is selected from substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl;

R^1 is selected from hydrogen, halogen, substituted or unsubstituted alkyl, $-NR^bR^c$ or $-OR^b$; each occurrence of R^b and R^c are independently selected from hydrogen, substituted or unsubstituted alkyl, or variables of R^b and R^c together with the nitrogen which they attached can form a substituted or unsubstituted heterocyclic ring;

X^1 is C or N;

X^2 is selected from -N-E or CH_2-E, O or S;

E is a group capable of forming a covalent bond or an "Electrophile" or "electrophilic moiety capable of forming a covalent bond.

R^y is selected from hydrogen, halogen, substituted or unsubstituted alkyl; and

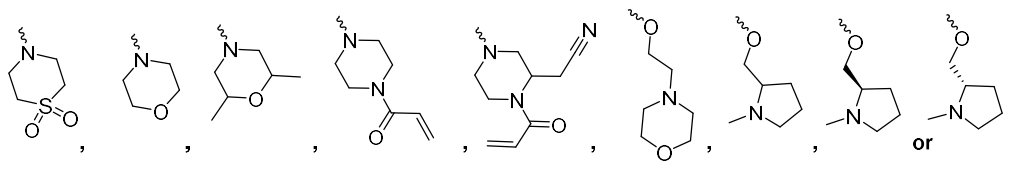
n is 0, 1, 2, 3, 4, 5, 6, 7 or 8.

8. The compound of anyone of claims 1-7, wherein

A_1 is absent or methyl.

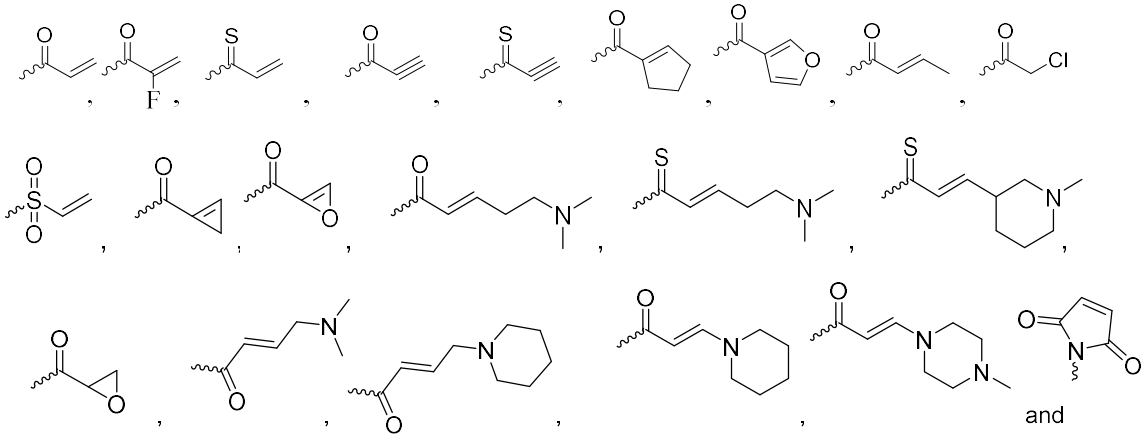
Cy^1 is selected from substituted or unsubstituted aryl;

R^1 is selected from hydrogen, halogen,



X^1 is N

X^2 is selected from -N-E or CH_2-E or O, wherein E is selected from



9. The compound of anyone of claims 1-8, wherein

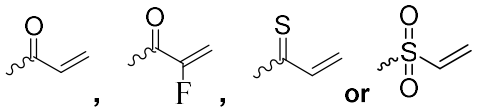
A_1 is absent

Cy^1 is selected from

(i) phenyl or naphthalene, optionally substituted with halogen, hydroxy or substituted or unsubstituted alkyl; or

(ii) quinoline or quinazoline, optionally substituted with halogen, hydroxy or substituted or unsubstituted alkyl;

X^2 is selected from -N-E or CH_2-E or O, wherein E is selected from

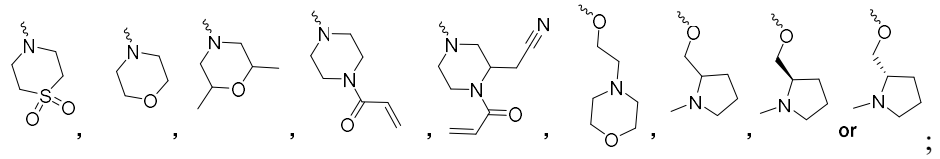


10. The compound of anyone of claims 1-9, wherein

A_1 is absent or methyl;

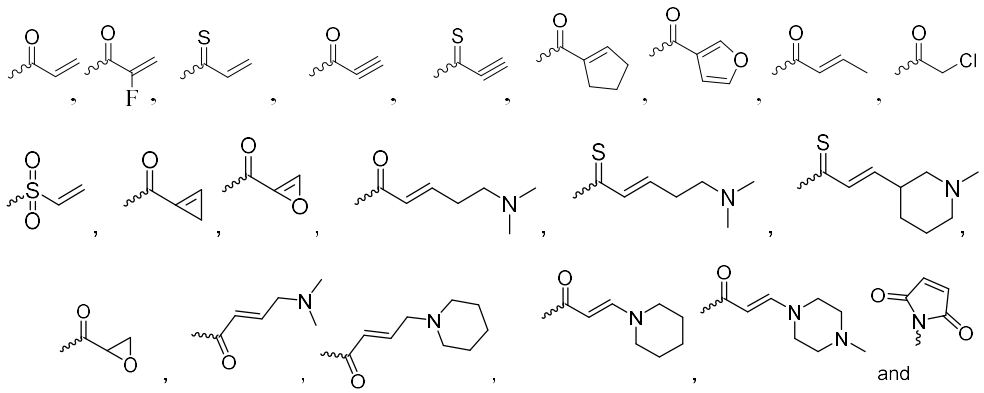
Cy^1 is selected from substituted or unsubstituted aryl;

R^1 is selected from hydrogen, halogen,



X^1 is N; and

X^2 is selected from -N-E or CH_2-E or O, wherein E is selected from



11. The compound of anyone of claims 1-10 is selected from

1-(4-acryloylpiperazin-1-yl)-3-(1,1-dioxidothiomorpholino)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

1-(4-acryloylpiperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-morpholino-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

1-(4-acryloylpiperazin-1-yl)-3-(2-morpholinoethoxy)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

1-(4-acryloylpiperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-(2-orpholinoethoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

3-(4-acryloylpiperazin-1-yl)-1-(2,6-dimethylmorpholino)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

3-(4-acryloylpiperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-1-(2,6-dimethylmorpholino)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

3-(4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-1-(2,6-dimethylmorpholino)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

(S)-1-(4-acryloylpiperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-((1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

(S)-1-(4-acryloylpiperazin-1-yl)-6-(3-hydroxynaphthalen-1-yl)-3-((1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

(S)-1-(4-(2-fluoroacryloyl)piperazin-1-yl)-3-((1-methylpyrrolidin-2-yl)methoxy)-6-(quinazolin-4-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

(S)-6-(8-chloronaphthalen-1-yl)-3-((1-methylpyrrolidin-2-yl)methoxy)-1-(4-(vinylsulfonyl)piperazin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

6-(8-chloronaphthalen-1-yl)-1-(4-(2-fluoroacryloyl)-3-methylpiperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-3-(2,6-dimethylmorpholino)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
1-((S)-4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-3-(2,6-dimethylmorpholino)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
1-((R)-4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-3-(2,6-dimethylmorpholino)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
1-(4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
1-((S)-4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
1-((R)-4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
1-(4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-6-(3-hydroxynaphthalen-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
1-(3-(cyanomethyl)-4-(2-fluoroacryloyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
(S)-1-(4-acryloylpiperazin-1-yl)-6-(isoquinolin-4-yl)-3-((1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
(S)-1-(4-acryloylpiperazin-1-yl)-3-((1-methylpyrrolidin-2-yl)methoxy)-6-(quinolin-8-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
1-(4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile:
1-((R)-4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile ;
1-((S)-4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile ;
6-(8-chloronaphthalen-1-yl)-1-(3-(cyanomethyl)-4-(2-fluoroacryloyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;
6-(8-chloronaphthalen-1-yl)-1-((S)-3-(cyanomethyl)-4-(2-fluoroacryloyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

6-(8-chloronaphthalen-1-yl)-1-((R)-3-(cyanomethyl)-4-(2-fluoroacryloyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

1-(4-acryloylpiperazin-1-yl)-6-benzyl-3-chloro-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

N-(1-(6-benzyl-3-chloro-4-cyano-5,6,7,8-tetrahydro-2,6-naphthyridin-1-yl)piperidin-4-yl)acrylamide;

N-(1-(6-benzyl-4-cyano-5,6,7,8-tetrahydro-2,6-naphthyridin-1-yl)piperidin-4-yl)acrylamide

1,3-bis(4-acryloylpiperazin-1-yl)-6-benzyl-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-6-benzyl-4-cyano-5,6,7,8-tetrahydro-2,6-naphthyridin-3-yl acrylate

1-(4-acryloylpiperazin-1-yl)-6-benzyl-3-morpholino-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-6-benzyl-3-(4-methylpiperazin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-6-benzyl-3-(4-methylpiperazin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

6-(1-naphthoyl)-1-(4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-3-(4-methylpiperazin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

(S)-1-(4-acryloyl-2-methylpiperazin-1-yl)-6-benzyl-3-(4-methylpiperazin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

(R)-1-(4-acryloyl-2-methylpiperazin-1-yl)-6-benzyl-3-(4-methylpiperazin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-6-benzyl-3-hydroxy-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-3-(4-methylpiperazin-1-yl)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

1-(4-acryloylpiperazin-1-yl)-6-benzyl-3-(piperidin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

1-(4-acryloylpiperazin-1-yl)-6-benzyl-3-(2-fluoropyridin-4-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

1-(4-acryloylpiperazin-1-yl)-6-(naphthalen-1-yl)-3-(piperidin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-6-benzyl-3-((1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

1,3-bis(4-acryloylpiperazin-1-yl)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1,3-bis(4-acryloylpiperazin-1-yl)-6-(benzo[b]thiophen-4-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-6-(naphthalen-1-yl)-3-(4-propionylpiperazin-1-yl)-5,6,7,8-etrahydro-2,6-naphthyridine-4-carbonitrile.

3-(4-acryloylpiperazin-1-yl)-6-(naphthalen-1-yl)-1-(4-propionylpiperazin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

1-(4-acryloylpiperazin-1-yl)-3-morpholino-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

3-(4-acetylpiperazin-1-yl)-1-(4-acryloylpiperazin-1-yl)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-3-(2,6-dimethylmorpholino)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-3-(4-(methylsulfonyl)piperazin-1-yl)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-3-(4-ethylpiperazin-1-yl)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

(S)-1-(4-acryloylpiperazin-1-yl)-3-((1-methylpyrrolidin-2-yl)methoxy)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile.

1-(4-acryloylpiperazin-1-yl)-6-(naphthalen-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

1-(4-(2-fluoroacryloyl)piperazin-1-yl)-6-(naphthalen-1-yl)-3-(4-propionylpiperazin-1-yl)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

and pharmaceutically acceptable salts thereof.

12. The compound of anyone of claims 1-11 is selected from

1-(4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile:

1-((R)-4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile ;

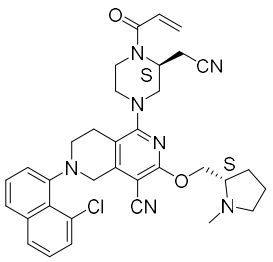
1-((S)-4-acryloyl-3-(cyanomethyl)piperazin-1-yl)-6-(8-chloronaphthalen-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile 6-(8-chloronaphthalen-1-yl)-1-(3-(cyanomethyl)-4-(2-fluoroacryloyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile;

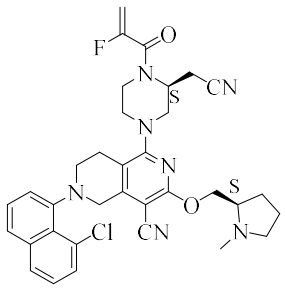
6-(8-chloronaphthalen-1-yl)-1-((S)-3-(cyanomethyl)-4-(2-fluoroacryloyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

6-(8-chloronaphthalen-1-yl)-1-((R)-3-(cyanomethyl)-4-(2-fluoroacryloyl)piperazin-1-yl)-3-(((S)-1-methylpyrrolidin-2-yl)methoxy)-5,6,7,8-tetrahydro-2,6-naphthyridine-4-carbonitrile

and pharmaceutically acceptable salts thereof.

13. The compound of claim 7 selected form



or


a pharmaceutically acceptable salt thereof.

14. A Pharmaceutical composition comprising a compound of claim 1-13, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

15. Use of a compound of claim 1-14, for treating cancer or a RAS-mediated disorder, in particular KRAS G12C mediated cancer or disorder in a subject.