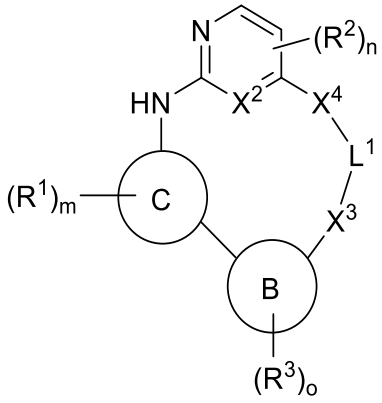
can lead to clinical responses; however, mutations in EGFR can also confer resistance to such therapies.

[0006] New therapeutic methods therefore remain necessary for treating cancers associated with defective signal transduction pathways, including EGFR-driven cancers.

SUMMARY

[0006a] In a first aspect of the present disclosure, there is provided a compound of Formula I:



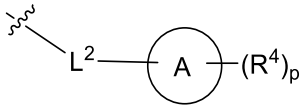
(I),

or a pharmaceutically acceptable salt thereof, wherein

X² is independently N or CR^5;

each of **X³** and **X⁴** is independently a covalent bond, O, S, NR^6, $C(O)NR^6$, $NR^6C(O)$, $NR^6C(O)NR^6$, or $(C(R^7)_2)_q$;

L¹ is independently a covalent bond, C_{1-6} heteroalkylene, C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-6} cycloalkylene, 3- to 10-membered heterocyclylene, phenylene, or 5- to 10-membered heteroarylene;

each **R¹** and **R²** is independently 

(**Substructure A**), OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or $(CH_2)_rR^{12}$, or two **R¹** or two **R²**, together to which the atoms they are attached form a 5- to 10-membered ring;

L² is independently a covalent bond, O, NR^L, C(O), $C(O)NR^L$, $NR^LC(O)$, CR^L_2;

R^L is independently H or C_{1-6} alkyl;

A is independently phenyl, naphthyl, 5- to 13-membered heteroaryl, C_3-C_{10} cycloaliphatic, or 3- to 10-membered heterocyclyl;

B is independently phenyl, naphthyl, 5- to 13-membered heteroaryl, C_3-C_{10} cycloaliphatic, or 3- to 10-membered heterocyclyl;

C is independently 5- or 6-membered heteroaryl;

each $\mathbf{R^3}$ is independently OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or $(CH_2)_rR^{12}$;

each $\mathbf{R^4}$ is independently H, OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, $NR^{11}(CH_2)_sNR^8R^9$, $(CH_2)_tNR^8R^9$, $(CH_2)_tOH$, $(CH_2)_tOCH_3$, $O(CH_2)_tOH$, $O(CH_2)_tOCH_3$, $O(CH_2)_rR^{12}$, or $(CH_2)_rR^{12}$; or $\mathbf{R^4}$ and $\mathbf{R^6}$ or $\mathbf{R^4}$ and $\mathbf{R^7}$, together with the atoms to which they are attached, form a 5- to 6-membered ring;

each $\mathbf{R^5}$ is independently H, OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or $(CH_2)_rR^{12}$;

each $\mathbf{R^6}$ is independently H, a N-protecting group, or C_{1-6} alkyl; or $\mathbf{R^6}$ and $\mathbf{R^4}$, together with the atoms to which they are attached, form a 5- to 6-membered ring;

each $\mathbf{R^7}$ is independently H or C_{1-6} alkyl; or two $\mathbf{R^7}$ on the same carbon combine to from an oxo (=O) group; or $\mathbf{R^7}$ and $\mathbf{R^4}$, together with the atoms to which they are attached, form a 5- to 6-membered ring;

each $\mathbf{R^8}$, $\mathbf{R^9}$, and $\mathbf{R^{11}}$ is independently H or C_{1-6} alkyl; or $\mathbf{R^8}$ and $\mathbf{R^9}$, together with the nitrogen atom to which they are attached, form a 3- to 10-membered heterocyclyl, or $\mathbf{R^8}$ and $\mathbf{R^{11}}$, together with the atoms to which they are attached, form a 3- to 10-membered heterocyclyl;

each $\mathbf{R^{10}}$ is independently C_{1-6} aliphatic, C_3-C_{10} cycloaliphatic, 3- to 10-membered heterocyclyl, phenyl, naphthyl, or a 5- to 12-membered heteroaryl, or $\mathbf{R^{10}}$ and $\mathbf{R^{11}}$, together with the atoms to which they are attached, form a 3- to 10-membered heterocyclyl;

each $\mathbf{R^{12}}$ is independently C_3-C_{10} cycloaliphatic, 3- to 10-membered heterocyclyl, phenyl, naphthyl, or a 5- to 12-membered heteroaryl;

each **m**, **n**, and **o**, is independently 0, 1, or 2;

each **p** is independently 0, 1, 2; 3, or 4;

each **q** is independently 1 or 2;

each **r** is independently an integer of 0-4;

each **s** is independently an integer of 2-6; and

each **t** is independently an integer of 1-6.

[0006b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound as disclosed herein, or a pharmaceutically acceptable salt thereof.

[0006c] In yet another aspect of the present disclosure, there is provided a use of a compound, or a pharmaceutically acceptable salt thereof, as disclosed herein, or a pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating cancer,

optionally wherein said cancer is:

(a) a lung cancer; and/or

(b) non-small cell lung cancer; and/or

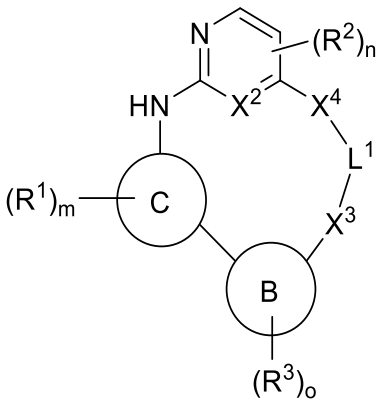
(c) an EGFR-driven cancer; and/or

(d) characterized by an EGFR mutation.

[0006d] In a further aspect of the present disclosure, there is provided a compound, or a pharmaceutically acceptable salt thereof, as disclosed herein, or a pharmaceutical composition as disclosed herein, for use in therapy.

[0007] Described herein are new compounds that can be effective inhibitors of EGFR. Such compounds can be useful for treating various diseases and disorders, including EGFR-driven cancers such as non-small cell lung cancer (NSCLC) characterized by mutant EGFR.

[0008] A first example of the present disclosure relates to compounds of Formula (I):



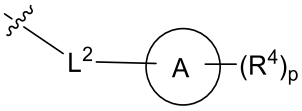
(I),

or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{X^2}$ is independently N or CR^5;

each of $\mathbf{X^3}$ and $\mathbf{X^4}$ is independently a covalent bond, O, S, NR^6, $C(O)NR^6$, $NR^6C(O)$, $NR^6C(O)NR^6$, or $(C(R^7)_2)_q$;

$\mathbf{L^1}$ is independently a covalent bond, C_{1-6} heteroalkylene, C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene, C_{3-6} cycloalkylene, 3- to 10-membered heterocyclylene, phenylene, naphthylene, or 5- to 10- membered heteroarylene;

each $\mathbf{R^1}$ and $\mathbf{R^2}$ is independently  (**Substructure A**), OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or $(CH_2)_rR^{12}$; or two $\mathbf{R^1}$ or two $\mathbf{R^2}$, together to which the atoms they are attached form a 5- to 10-membered ring.

each **r** is independently an integer of 0-4;

each **s** is independently an integer of 2-6; and

each **t** is independently an integer of 1-6.

[0009] In examples, each $\mathbf{R^4}$ is independently H, OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, $NR^{11}(CH_2)_sNR^8R^9$, $(CH_2)_tNR^8R^9$, or $(CH_2)_rR^{12}$; or $\mathbf{R^4}$ and $\mathbf{R^6}$, or $\mathbf{R^4}$ and $\mathbf{R^7}$, together with the atoms to which they are attached, form a 5- to 6-membered ring.

[0010] In examples, each **m**, **n**, **o**, and **p** is independently 0, 1, or 2.

[0011] In examples, at least one **m** or **n** is not 0.

[0012] In examples, one of $\mathbf{R^1}$ and $\mathbf{R^2}$ is present and is **Substructure A** or halogen.

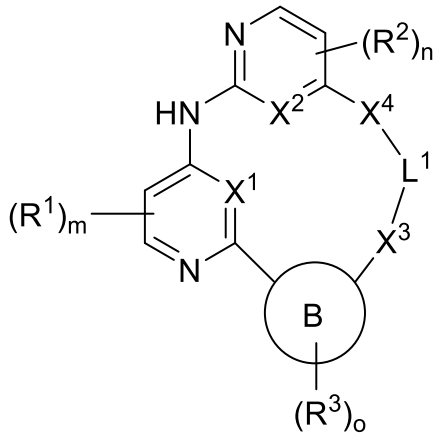
[0013] In examples, one of $\mathbf{R^1}$ and $\mathbf{R^2}$ is present and is **Substructure A**.

[0014] In examples, no more than one **Substructure A** is present.

[0015] In examples, **C** is 5- or 6-membered N-containing heteroaryl.

[0016] In examples, **C** is pyridyl, pyrimidyl, pyrazolyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl.

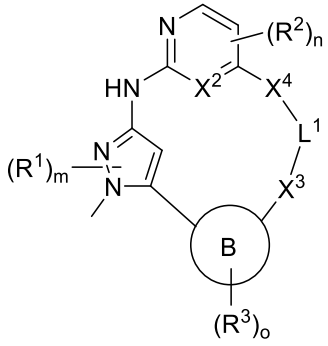
[0017] In examples, a compound has a structure according to Formula (I-A)



(I-A),

or a pharmaceutically acceptable salt thereof, wherein $\mathbf{X^1}$ is N or CR^5.

[0018] In examples, a compound has a structure according to Formula (I-B)

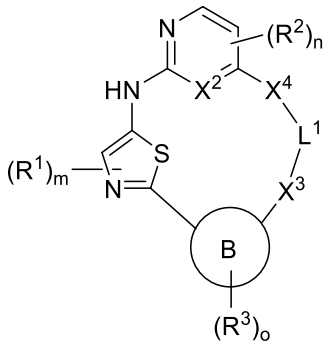


(I-B)

or a pharmaceutically acceptable salt thereof, wherein

m is 0 or 1.

[0019] In examples, a compound has a structure according to Formula (I-C)

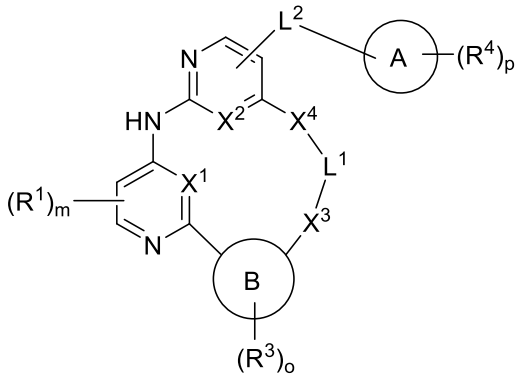


(I-C)

or a pharmaceutically acceptable salt thereof, wherein

m is 0 or 1.

[0020] In examples, a compound has a structure according to Formula (II),

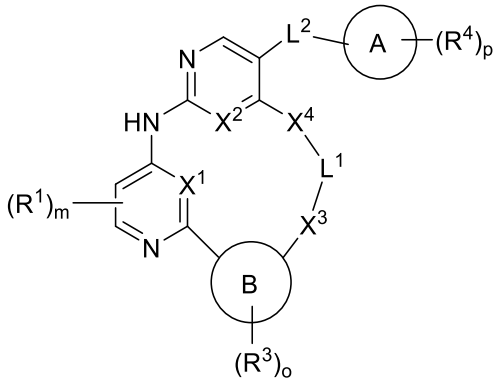


(II),

or a pharmaceutically acceptable salt thereof, wherein

each $\mathbf{R^1}$ is independently OH, CN, halogen, $C_{1\text{-}6}$ aliphatic, $C_{1\text{-}6}$ alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or R^{12}.

[0021] In examples, a compound has a structure according to Formula (II-A),

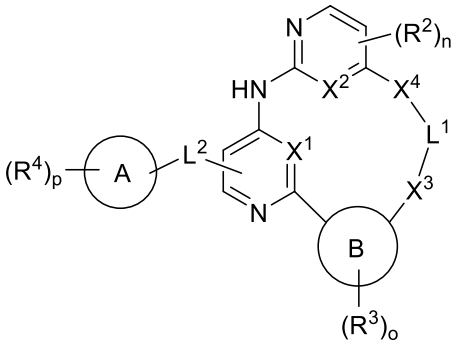


(II-A),

or a pharmaceutically acceptable salt thereof.

[0022] In examples, **m** is 0.

[0023] In examples, a compound has a structure according to Formula (III),

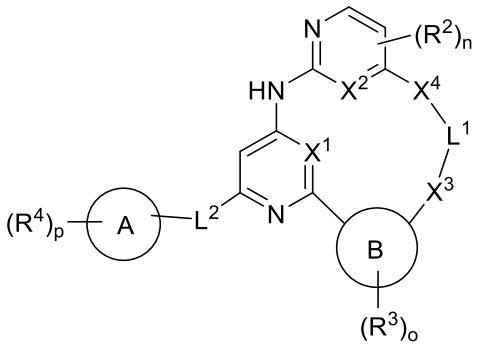


(III),

or a pharmaceutically acceptable salt thereof, wherein

each $\mathbf{R^2}$ is independently OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or R^{12}.

[0024] In examples, a compound has a structure according to Formula (III-A),



(III-A),

or a pharmaceutically acceptable salt thereof.

[0025] In examples, **n** is 0.

[0026] In examples, each of $\mathbf{X^1}$ and $\mathbf{X^2}$ is independently N or CH.

[0027] In examples, $\mathbf{X^1}$ is N.

[0028] In examples, $\mathbf{X^2}$ is CH.

[0029] In examples, $\mathbf{X^3}$ is O.

[0030] In examples, $\mathbf{X^4}$ is O.

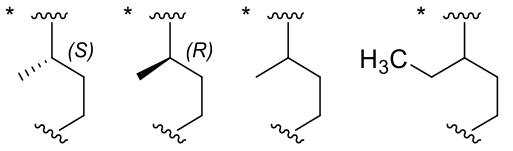
[0031] In examples, each $\mathbf{X^3}$ and $\mathbf{X^4}$ is independently a covalent bond, O, S, NR^6, C(O), CH_2, $CHCH_3$, or $C(CH_3)_2$.

[0032] In examples, $\mathbf{X^2}$ is CH, $\mathbf{X^3}$ is O, and $\mathbf{X^4}$ is O. In examples, $\mathbf{X^1}$ is N.

[0033] In examples, $\mathbf{L^1}$ is unsubstituted $C_{1\text{-}6}$ alkylene or $C_{1\text{-}6}$ alkylene comprising 1 or 2 oxo (=O) substituents.

[0034] In examples, $\mathbf{L^1}$ is unsubstituted $C_{1\text{-}6}$ heteroalkylene or $C_{1\text{-}6}$ heteroalkylene comprising 1 or 2 oxo (=O) substituents.

[0035] In examples, $\mathbf{L^1}$ is an unsubstituted linear $C_{4\text{-}6}$ alkylene or an unsubstituted branched $C_{4\text{-}6}$ alkylene.

[0036] In examples, $\mathbf{L^1}$ is 

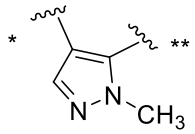
, where * denotes the point of covalent attachment to $\mathbf{X^4}$, and ** denotes the point of covalent attachment to $\mathbf{X^3}$.

[0037] In examples, a $C_{1\text{-}6}$ heteroalkylene comprises 1, 2, or 3 heteroatoms that are independently oxygen or nitrogen.

[0038] In examples, a $C_{1\text{-}6}$ heteroalkylene is $-O(CH_2)_u-$, $-(CH_2)_uO-$, $-O(CH_2)_uO-$, $-OCH_2OCH_2CH_2OCH_2-$, $-CH_2OCH_2CH_2O-$, $-OCH_2CH_2.OCH_2-$, $-NH(CH_2)_u-$, $-(CH_2)_uNH-$, or $-NH(CH_2)_uNH-$, and wherein u is an integer of 1-4.

[0039] In examples, **B** is phenyl or 5- to 6-membered heteroaryl.

[0040] In examples, **B** is phenyl, pyridyl, pyrimidyl, pyrazolyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl.

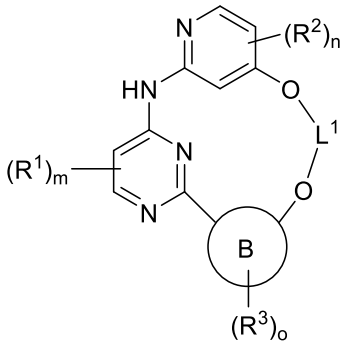
[0041] In examples, **B** is , where * denotes the point of covalent attachment to **C**, and ** denotes the point of covalent attachment to $\mathbf{X^3}$.

[0042] In examples, $\mathbf{R^3}$ is methyl, halogen, or CN, and **o** is 0 or 1.

[0043] In examples, **A** is phenyl or 5- to 6-membered heteroaryl.

[0044] In examples, **A** is phenyl, pyridyl, pyrimidyl, pyrazolyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl.

[0045] In examples, a compound has a structure according to Formula (IV),


(IV),

or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{L^1}$ is unsubstituted linear or branched C_{2-6} alkylene;

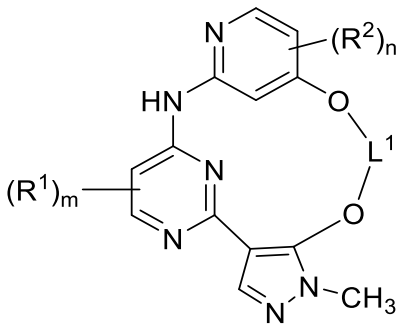
B is phenyl or 5- to 6-membered heteroaryl;

$\mathbf{R^3}$ is methyl, halogen, or CN;

o is 0 or 1; and

one of $\mathbf{R^1}$ and $\mathbf{R^2}$ is present as **Substructure A** .

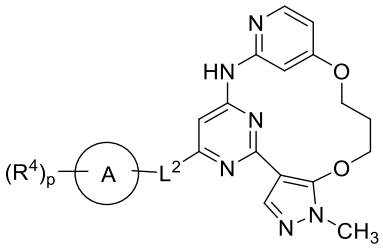
[0046] In examples, a compound has a structure according to Formula (V),

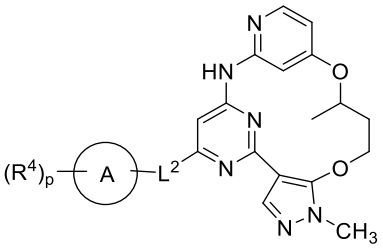

(V),

or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{L^1}$ is $-(CH_2)_3-$ or $-CH(CH_3)CH_2CH_2-$.

[0047] In examples, a compound has a structure according to Formula (VI-1) or Formula (VI-2),

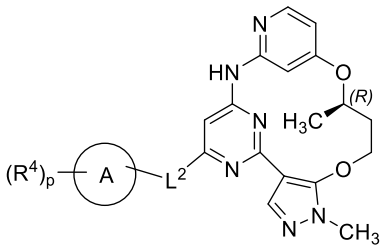


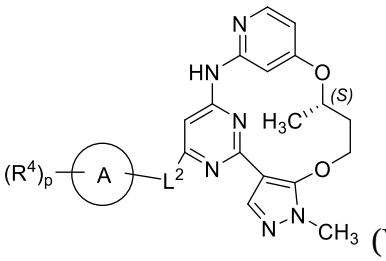
(VI-1) or


(VI-2),

or a pharmaceutically acceptable salt thereof.

[0048] In examples, a compound has a structure according to Formula (VI-3) or Formula (VI-4),

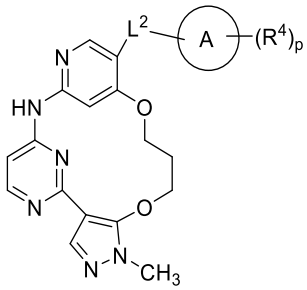


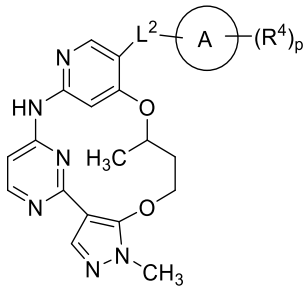
(VI-3) or


(VI-4),

or a pharmaceutically acceptable salt thereof.

[0049] In examples, a compound has a structure according to Formula (VII-1) or Formula (VII-2),

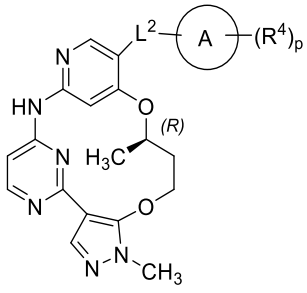


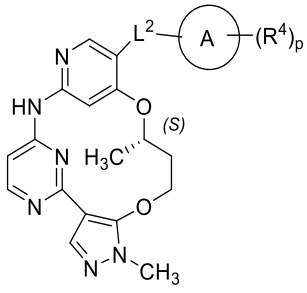
(VII-1) or


(VII-2),

or a pharmaceutically acceptable salt thereof.

[0050] In examples, a compound has a structure according to Formula (VII-3) or Formula (VII-4),



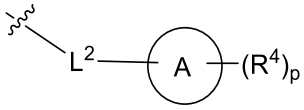
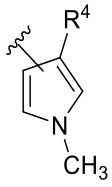
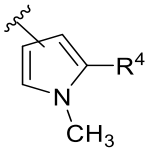
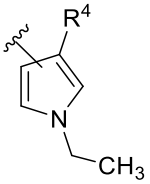
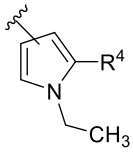
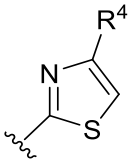
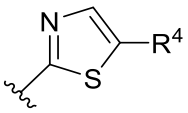
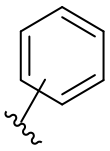
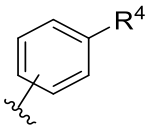
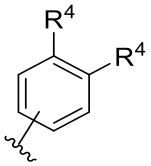
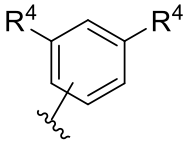
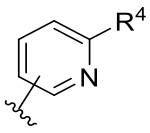
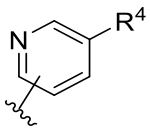
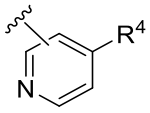
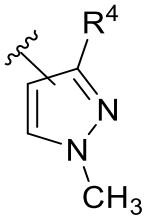
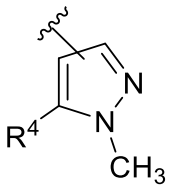
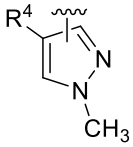
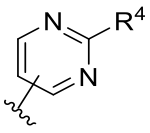
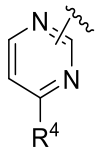
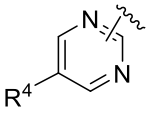
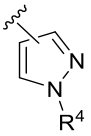
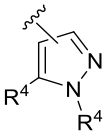
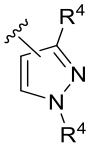
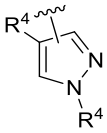
(VII-3) or


(VII-4),

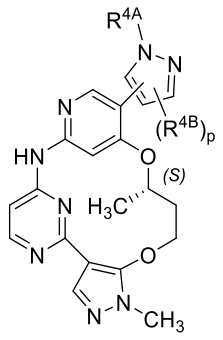
or a pharmaceutically acceptable salt thereof.

[0051] In examples, **A** is phenyl or 5- to 6-membered heteroaryl.

[0052] In examples, $\mathbf{L^2}$ is a covalent bond.

[0053] In examples,  (**Substructure A**) is selected from the group consisting of:  (a1),  (a2),  (a3),  (a4),  (a5),  (a6),  (a7),  (a8),  (a9),  (a10),  (a11),  (a12),  (a13),  (a14),  (a15),  (a16)  (a17),  (a18),  (a19),  (a20),  (a21),  (a22), and  (a23).

[0054] In examples, a compound has a structure according to Formula (VIII),



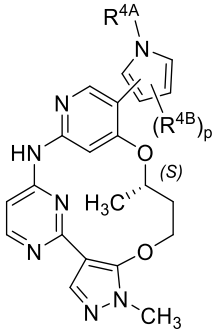
(VIII), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^4** group,

R^{4B} is a second **R^4** group, and

p is 0 or 1.

[0055] In examples, a compound has a structure according to Formula (IX),



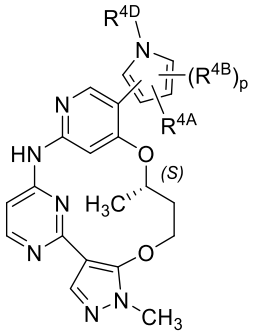
(IX), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^4** group,

R^{4B} is a second **R^4** group, and

p is 0 or 1.

[0056] In examples, a compound has a structure according to Formula (X),



(X), or a pharmaceutically acceptable salt thereof, wherein

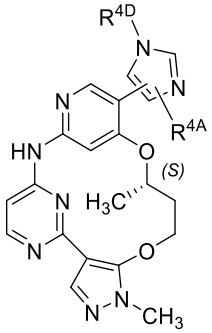
R^{4A} is a first **R^4** group,

R^{4B} is a second **R^4** group,

p is 0 or 1, and

R^{4D} is a **R^4** group that is unsubstituted $C_{1\text{-}6}$ alkyl.

[0057] In examples, a compound has a structure according to Formula (XI),

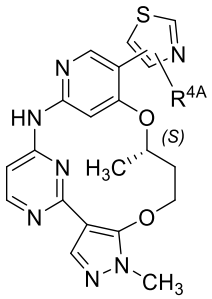


(XI), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group, and

$\mathbf{R^{4D}}$ is a $\mathbf{R^4}$ group that is unsubstituted $C_{1\text{-}6}$ alkyl.

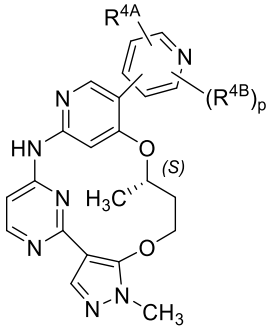
[0058] In examples, a compound has a structure according to Formula (XII),



(XII), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group.

[0059] In examples, a compound has a structure according to Formula (XIII),



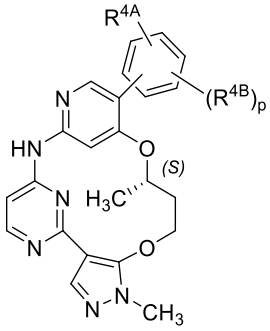
(XIII), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group, and

p is 0 or 1.

[0060] In examples, a compound has a structure according to Formula (XIV),



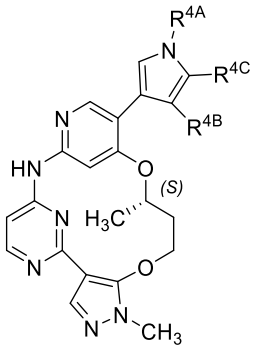
(XIV), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group, and

p is 0 or 1.

[0061] In examples, a compound has a structure according to Formula (XV),



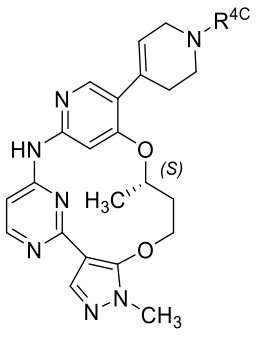
(XV), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group, and

$\mathbf{R^{4C}}$ is a third $\mathbf{R^4}$ group.

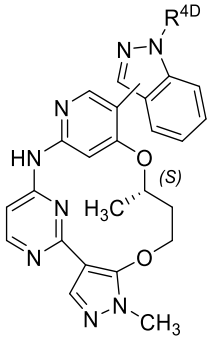
[0062] In examples, a compound has a structure according to Formula (XVI),



(XVI), or a pharmaceutically acceptable salt thereof, wherein

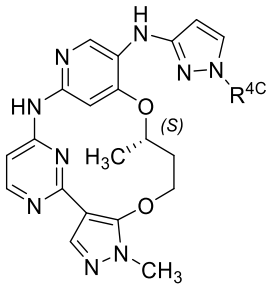
$\mathbf{R^{4C}}$ is a first $\mathbf{R^4}$ group.

[0063] In examples, a compound has a structure according to Formula (XVII),



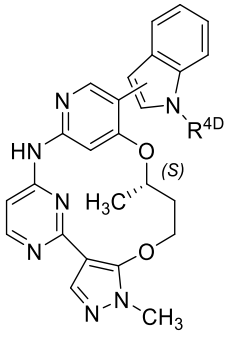
(XVII), or a pharmaceutically acceptable salt thereof, wherein $\mathbf{R^{4D}}$ is a $\mathbf{R^4}$ group that is unsubstituted $C_{1\text{-}6}$ alkyl.

[0064] In examples, a compound has a structure according to Formula (XVIII),



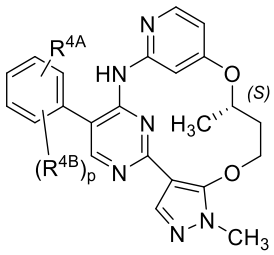
(XVIII), or a pharmaceutically acceptable salt thereof, wherein $\mathbf{R^{4C}}$ is a first $\mathbf{R^4}$ group.

[0065] In examples, a compound has a structure according to Formula (XIX),



(XIX), or a pharmaceutically acceptable salt thereof, wherein $\mathbf{R^{4D}}$ is a $\mathbf{R^4}$ group that is unsubstituted $C_{1\text{-}6}$ alkyl.

[0066] In examples, a compound has a structure according to Formula (XX),



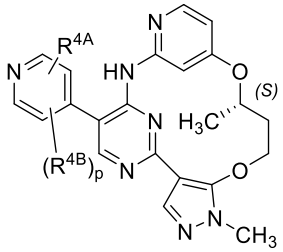
(XX), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group, and

p is 0 or 1.

[0067] In examples, a compound has a structure according to Formula (XXI),



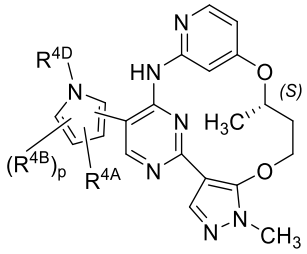
(XXI), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group, and

p is 0 or 1.

[0068] In examples, a compound has a structure according to Formula (XXII),



(XXII), or a pharmaceutically acceptable salt thereof, wherein

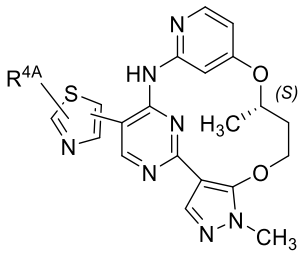
$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group,

p is 0 or 1, and

$\mathbf{R^{4D}}$ is a $\mathbf{R^4}$ group that is unsubstituted $C_{1\text{-}6}$ alkyl.

[0069] In examples, a compound has a structure according to Formula (XXIII),

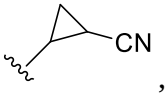
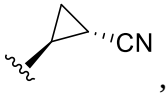
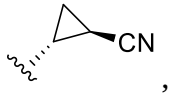
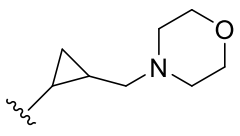
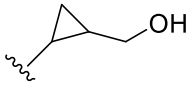


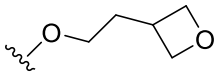
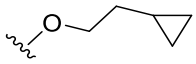
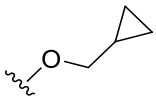
(XXIII), or a pharmaceutically acceptable salt thereof, wherein

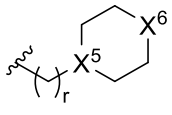
R^{4A} is a first **R^4** group.

[0070] In examples, a compound described herein comprises one or more **R^4** groups selected from: -C≡N; -C≡CH; a saturated linear or branched C_{1-6} aliphatic or C_1-$_6$ alkoxy comprising 0-4 fluoro substituents; $NR^{11}(CH_2)_sNR^8R^9$; $(CH_2)_tNR^8R^9$; $O(CH_2)_tOCH_3$; $O(CH_2)_rR^{12}$; and $(CH_2)_rR^{12}$. In examples, **R^{12}** is selected from the group consisting of: a C_{3-6} cycloalkyl; a 3-9 membered heterocyclyl comprising 1-3 heteroatoms selected from O, N, and S; and 5- to 6-membered heteroaryl. In examples, **R^{12}** is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, oxetanyl, tetrahydrofuryl, tetrahydropyanyl, azetidine, pyrroldinyl, piperidinyl, piperazinyl, and morpholino. In examples, **R^{12}** is substituted with 0-4 **R^{14}**, wherein each **R^{14}** is independently selected from –CN, oxo (=O), halogen, -OH, $-NH_2$, monoalkylamino, dialkylamino, unsubstituted C_{3-6} cycloalkyl, or unsubstituted 3- to 4-membered heterocyclyl. In examples, each **R^{14}** is independently selected from –CN,–F, -OH, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-NHCH_2CH_3$, $-N(CH_2CH_3)_2$, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_3$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2F$, $-CH_2CH_2CHF_2$, $-CH_2CH_2CF_3$, $-CH_2CH_2OCH_3$, $-COCH_3$, $-COCH_2CH_3$, $-CH_2COCH_3$, $-CH_2COCH_2CH_3$, cyclopropyl, cyclobutyl, oxetanyl, and azetidinyl.

[0071] In examples, a compound described herein comprises:

an **R^4** group selected from: -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_3$, $-CH_2CFH_2$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH(CH_3)_2$, $-C(CH_3)_3$, -C≡CH, , , , , , , ,

$CH_2CH(CH_3)_2$, $-OCH_2CH_2OCH_3$, , , , $-CO_2CH_3$, and CH_3.

[0072] In examples, $\mathbf{R^4}$ is selected from unsubstituted C_{1-6} alkyl, CO_2(unsubstituted C_{1-6} alkyl), O-(unsubstituted C_{1-6} alkyl), O-(C_{1-6} haloalkyl), $NH(CH_2)_sNMe_2$, $(CH_2)_tNMe_2$, or , wherein

$\mathbf{X^5}$ is independently CH or N;

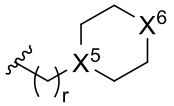
$\mathbf{X^6}$ is independently O, CHR^{13}, or NR^{13};

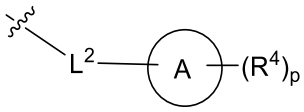
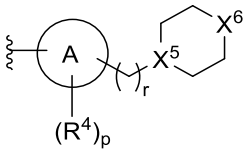
$\mathbf{R^{13}}$ is independently H, C_{1-6} alkyl, or C_{3-6} cycloalkyl;

r is 0 or 1;

s is an integer of 2-4; and

t is an integer of 1-6.

[0073] In examples, one $\mathbf{R^4}$ is , and, if present, a second $\mathbf{R^4}$ is selected from unsubstituted C_{1-6} alkyl, CO_2(unsubstituted C_{1-6} alkyl), O-(unsubstituted C_{1-6} alkyl), O-(C_{1-6} haloalkyl), $NH(CH_2)_sNMe_2$, and $(CH_2)_tNMe_2$.

[0074] In examples,  (**Substructure A**) is , wherein

A is phenyl or 5- to 6-membered heteroaryl.

$\mathbf{X^5}$ is independently CH or N;

$\mathbf{X^6}$ is independently O, CHR^{13}, or NR^{13};

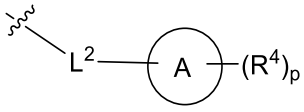
$\mathbf{R^{13}}$ is independently H, unsubstituted C_{1-6} alkyl, or unsubstituted C_{3-6} cycloalkyl;

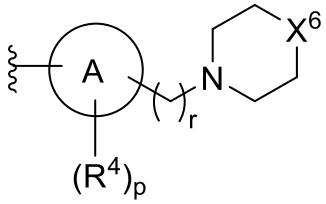
r is 0 or 1;

$\mathbf{R^4}$ is selected from unsubstituted C_{1-6} alkyl, CO_2(unsubstituted C_{1-6} alkyl), O-(unsubstituted C_{1-6} alkyl), O-(C_{1-6} haloalkyl), or $NH(CH_2)_sNMe_2$;

p is 0 or 1; and

s is an integer of 2-6.

[0075] In examples,  (**Substructure A**) is

 , wherein $\mathbf{X^6}$ is O, NCH_3, or N(cyclopropyl).

[0076] In examples, **r** is 0.

[0077] In examples, **r** is 1.

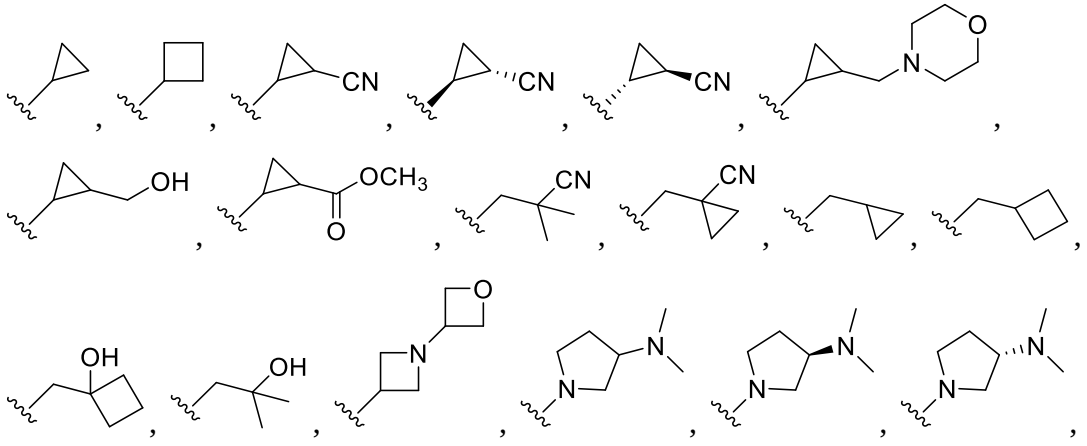
[0078] In examples, a compound comprises a $\mathbf{R^4}$ group that is $-CO_2CH_3$, $-OCH_2CF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, $-OCH_2CH_3$, $-NHCH_2CH_2N(CH_3)_2$, or $-CH_2N(CH_3)_2$.

[0079] In examples, **A** is phenyl, pyridyl, pyrimidyl, pyrazolyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl.

[0080] In examples, each $\mathbf{R^{4A}}$, $\mathbf{R^{4B}}$, and $\mathbf{R^{4C}}$, when present, is independently selected from: -C≡N; -C≡CH; a saturated linear or branched $C_{1\text{-}6}$ aliphatic or $C_{1\text{-}6}$ alkoxy comprising 0-4 fluoro substituents; $NR^{11}(CH_2)_sNR^8R^9$; $(CH_2)_tNR^8R^9$; $O(CH_2)_tOCH_3$; $O(CH_2)_rR^{12}$; and $(CH_2)_rR^{12}$.

[0081] In examples,

an $\mathbf{R^{4A}}$ and/or a $\mathbf{R^{4C}}$ group, when present, is selected from: -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_3$, $-CH_2CFH_2$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH(CH_3)_2$, $-C(CH_3)_3$, -C≡CH,



[0082] In examples, a compound is any exemplary compound described herein, including any compound described in **Table A** (e.g., any one of Compounds (1)-(169)), or a pharmaceutically acceptable salt thereof.

[0083] In another example, the present disclosure features a pharmaceutical composition comprising any compound described herein, or a pharmaceutically acceptable salt thereof.

[0084] In another example, the present disclosure features a method of treating cancer comprising administering to a human in need thereof an effective amount of any compound described herein, or a pharmaceutically acceptable salt thereof, in a pharmaceutical composition.

[0085] In examples, a cancer is a lung cancer.

[0086] In examples, a cancer is non-small cell lung cancer.

[0087] In examples, a cancer (e.g., a lung cancer such as non-small cell lung cancer) is an EGFR-driven cancer.

[0088] In examples, a cancer (e.g., a lung cancer such as non-small cell lung cancer) is characterized by an EGFR mutation.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

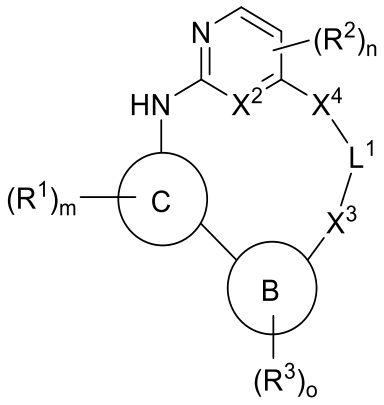
[0089] In order for the present invention to be more readily understood, certain terms are first defined below. Additional definitions for the following terms and other terms are set forth throughout the specification. The publications and other reference materials referenced herein to describe the background of the invention and to provide additional detail regarding its practice are hereby incorporated by reference.

[0090] *Animal:* As used herein, the term "animal" refers to any member of the animal kingdom. In some embodiments, "animal" refers to humans, at any stage of development. In some embodiments, "animal" refers to non-human animals, at any stage of development. In certain embodiments, the non-human animal is a mammal (*e.g.*, a rodent, a mouse, a rat, a rabbit, a monkey, a dog, a cat, a sheep, a bovine, a primate, and/or a pig). In some embodiments, animals include, but are not limited to, mammals, birds, reptiles, amphibians, fish, insects, and/or worms. In some embodiments, an animal may be a transgenic animal, genetically-engineered animal, and/or a clone.

CLAIMS

What is claimed is:

1. A compound of Formula I:



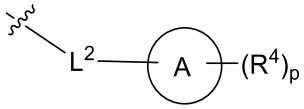
(I),

or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{X^2}$ is independently N or CR^5;

each of $\mathbf{X^3}$ and $\mathbf{X^4}$ is independently a covalent bond, O, S, NR^6, $C(O)NR^6$, $NR^6C(O)$, $NR^6C(O)NR^6$, or $(C(R^7)_2)_q$;

$\mathbf{L^1}$ is independently a covalent bond, $C_{1\text{-}6}$ heteroalkylene, $C_{1\text{-}6}$ alkylene, $C_{2\text{-}6}$ alkenylene, $C_{2\text{-}6}$ alkynylene, $C_{3\text{-}6}$ cycloalkylene, 3- to 10-membered heterocyclylene, phenylene, or 5- to 10-membered heteroarylene;

each $\mathbf{R^1}$ and $\mathbf{R^2}$ is independently  (**Substructure A**), OH, CN, halogen, $C_{1\text{-}6}$ aliphatic, $C_{1\text{-}6}$ alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or $(CH_2)_rR^{12}$, or two $\mathbf{R^1}$ or two $\mathbf{R^2}$, together to which the atoms they are attached form a 5- to 10-membered ring;

$\mathbf{L^2}$ is independently a covalent bond, O, NR^L, C(O), $C(O)NR^L$, $NR^LC(O)$, CR^L_2;

$\mathbf{R^L}$ is independently H or $C_{1\text{-}6}$ alkyl;

A is independently phenyl, naphthyl, 5- to 13-membered heteroaryl, C_3-C_{10} cycloaliphatic, or 3- to 10-membered heterocyclyl;

B is independently phenyl, naphthyl, 5- to 13-membered heteroaryl, C_3-C_{10} cycloaliphatic, or 3- to 10-membered heterocyclyl;

C is independently 5- or 6-membered heteroaryl;

each $\mathbf{R^3}$ is independently OH, CN, halogen, $C_{1\text{-}6}$ aliphatic, $C_{1\text{-}6}$ alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or $(CH_2)_rR^{12}$;

each **R[4]** is independently H, OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, $NR^{11}(CH_2)_sNR^8R^9$, $(CH_2)_tNR^8R^9$, $(CH_2)_tOH$, $(CH_2)_tOCH_3$, $O(CH_2)_tOH$, $O(CH_2)_tOCH_3$, $O(CH_2)_rR^{12}$, or $(CH_2)_rR^{12}$; or **R[4]** and **R[6]** or **R[4]** and **R[7]**, together with the atoms to which they are attached, form a 5- to 6-membered ring;

each **R[5]** is independently H, OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or $(CH_2)_rR^{12}$;

each **R[6]** is independently H, a N-protecting group, or C_{1-6} alkyl; or **R[6]** and **R[4]**, together with the atoms to which they are attached, form a 5- to 6-membered ring;

each **R[7]** is independently H or C_{1-6} alkyl; or two **R[7]** on the same carbon combine to from an oxo (=O) group; or **R[7]** and **R[4]**, together with the atoms to which they are attached, form a 5- to 6-membered ring;

each **R[8]**, **R[9]**, and **R[11]** is independently H or C_{1-6} alkyl; or **R[8]** and **R[9]**, together with the nitrogen atom to which they are attached, form a 3- to 10-membered heterocyclyl, or **R[8]** and **R[11]**, together with the atoms to which they are attached, form a 3- to 10-membered heterocyclyl;

each **R[10]** is independently C_{1-6} aliphatic, C_3-C_{10} cycloaliphatic, 3- to 10-membered heterocyclyl, phenyl, naphthyl, or a 5- to 12-membered heteroaryl, or **R[10]** and **R[11]**, together with the atoms to which they are attached, form a 3- to 10-membered heterocyclyl;

each **R[12]** is independently C_3-C_{10} cycloaliphatic, 3- to 10-membered heterocyclyl, phenyl, naphthyl, or a 5- to 12-membered heteroaryl;

each **m**, **n**, and **o**, is independently 0, 1, or 2;

each **p** is independently 0, 1, 2; 3, or 4;

each **q** is independently 1 or 2;

each **r** is independently an integer of 0-4;

each **s** is independently an integer of 2-6; and

each **t** is independently an integer of 1-6.

2. The compound of claim 1, wherein

(a) at least one **m** or **n** is not 0; and/or

(b) one of **R[1]** and **R[2]** is present and is **Substructure A** or halogen; and/or

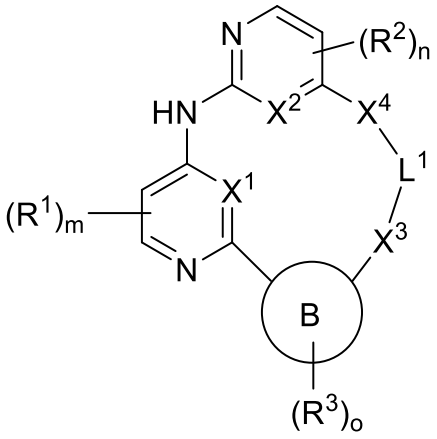
(c) one of **R[1]** and **R[2]** is present and is **Substructure A**; and/or

(d) no more than one **Substructure A** is present; and/or

(e) **C** is 5- or 6-membered N-containing heteroaryl, optionally wherein **C** is pyridyl, pyrimidyl, pyrazolyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl.

3. The compound of claim 1 or 2, having a structure according to

(a) Formula (I-A),

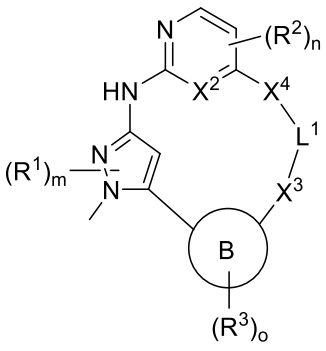


(I-A),

or a pharmaceutically acceptable salt thereof, wherein

X¹ is N or CR^5; or

(b) Formula (I-B),

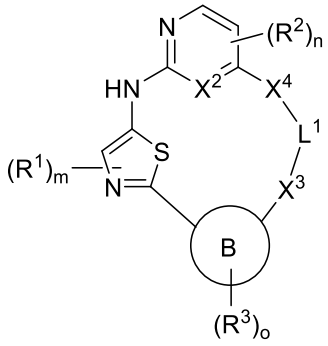


(I-B),

or a pharmaceutically acceptable salt thereof, wherein

m is 0 or 1; or

(c) Formula (I-C),

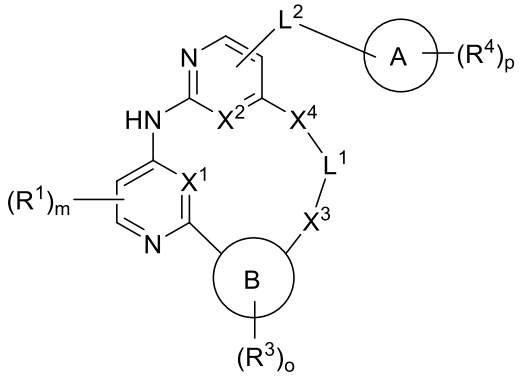


(I-C),

or a pharmaceutically acceptable salt thereof, wherein

m is 0 or 1; or

(d) Formula (II),

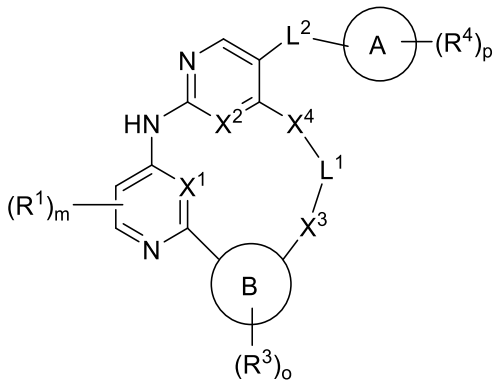


(II),

or a pharmaceutically acceptable salt thereof, wherein

each **R1** is independently OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or R^{12}, optionally

(i) wherein the compound has a structure according to Formula (II-A),

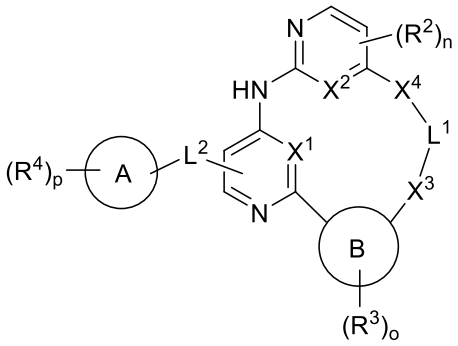


(II-A),

or a pharmaceutically acceptable salt thereof; and/or

(ii) wherein **m** is 0; or

(e) Formula (III),

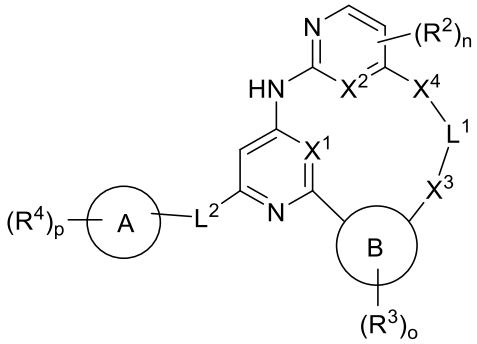


(III),

or a pharmaceutically acceptable salt thereof, wherein

each **R^2** is independently OH, CN, halogen, C_{1-6} aliphatic, C_{1-6} alkoxy, NR^8R^9, $C(O)R^{10}$, CO_2R^{10}, $C(O)NR^8R^9$, $NR^{11}C(O)R^{10}$, $NR^{11}CO_2R^{10}$, $NR^{11}C(O)NR^8R^9$, or R^{12}, optionally

(i) wherein the compound has a structure according to Formula (III-A),



(III-A),

or a pharmaceutically acceptable salt thereof; and/or

(ii) wherein **n** is 0.

4. The compound of claim 3, wherein

(a) each of **X^1** and **X^2** is independently N or CH; and/or

(b) **X^1** is N.

5. The compound of any one of claims 1-4, wherein

(a) **X^2** is CH; and/or

(b) **X^3** is O.

6. The compound of any one of claims 1-3(e)(i) and 4-5, wherein $\mathbf{X^4}$ is NR^6, $\mathbf{R^2}$ is **Substructure A**, and wherein

$\mathbf{R^4}$ and $\mathbf{R^6}$, together with the atoms to which they are attached, form a 5 membered ring.

7. The compound of any one of claims 1-5, wherein $\mathbf{X^4}$ is O.

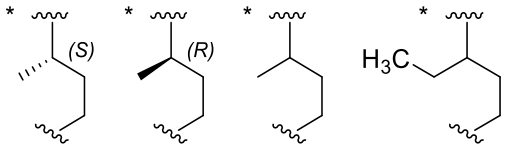
8. The compound of any one of claims 1-5(a), wherein each $\mathbf{X^3}$ and $\mathbf{X^4}$ is independently a covalent bond, O, S, NR^6, C(O), CH_2, $CHCH_3$, or $C(CH_3)_2$.

9. The compound of any one of claims 1-8, wherein

(a) $\mathbf{X^2}$ is CH, $\mathbf{X^3}$ is O, and $\mathbf{X^4}$ is O, optionally wherein $\mathbf{X^1}$ is N; and/or

(b) $\mathbf{L^1}$ is unsubstituted C_{1-6} alkylene or C_{1-6} alkylene comprising 1 or 2 oxo (=O) substituents, optionally wherein

(i) $\mathbf{L^1}$ is an unsubstituted linear C_{4-6} alkylene or an unsubstituted branched C_{4-6} alkylene; and/or

(ii) $\mathbf{L^1}$ is 

, wherein * denotes the point of covalent attachment to $\mathbf{X^4}$, and ** denotes the point of covalent attachment to $\mathbf{X^3}$; or

(c) $\mathbf{L^1}$ is unsubstituted C_{1-6} heteroalkylene or C_{1-6} heteroalkylene comprising 1 or 2 oxo (=O) substituents, optionally wherein

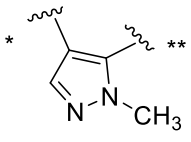
(i) the C_{1-6} heteroalkylene comprises 1, 2, or 3 heteroatoms that are independently oxygen or nitrogen; and/or

(ii) the C_{1-6} heteroalkylene is $-O(CH_2)_u-$, $-(CH_2)_uO-$, $-O(CH_2)_uO-$, $-OCH_2OCH_2CH_2OCH_2-$, $-CH_2OCH_2CH_2O-$, $-OCH_2CH_2OCH_2-$, $-NH(CH_2)_u-$, $-(CH_2)_uNH-$, or $-NH(CH_2)_uNH-$, and wherein u is an integer of 1-4; and/or

(d) **B** is phenyl or 5- to 6-membered heteroaryl, optionally wherein

(i) **B** is phenyl, pyridyl, pyrimidyl, pyrazolyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl; and/or

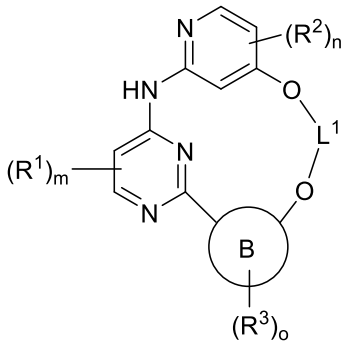
(ii) $\mathbf{R^3}$ is methyl, halogen, or CN, and **o** is 0 or 1; and/or

(iii) **B** is 

, wherein * denotes the point of covalent attachment to **C**, and ** denotes the point of covalent attachment to $\mathbf{X^3}$; and/or

(e) **A** is phenyl or 5- to 6-membered heteroaryl, optionally wherein **A** is phenyl, pyridyl, pyrimidyl, pyrazolyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl.

10. The compound of any one of claims 1-3(a), having a structure according to Formula (IV),



(IV),

or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{L^1}$ is unsubstituted linear or branched $C_{2\text{-}6}$ alkylene;

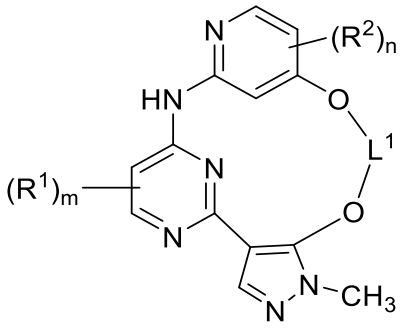
B is phenyl or 5- to 6-membered heteroaryl;

$\mathbf{R^3}$ is methyl, halogen, or CN;

o is 0 or 1; and

one of $\mathbf{R^1}$ and $\mathbf{R^2}$ is present as **Substructure A**,

optionally wherein the compound has a structure according to Formula (V),



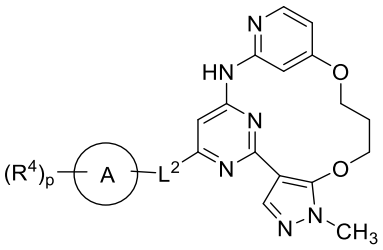
(V),

or a pharmaceutically acceptable salt thereof, wherein

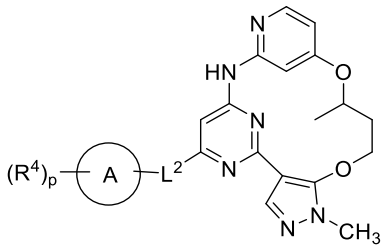
L^1 is -$(CH_2)_3$- or -$CH(CH_3)CH_2CH_2$-,

preferably wherein the compound has a structure according to

(a) Formula (VI-1) or Formula (VI-2),



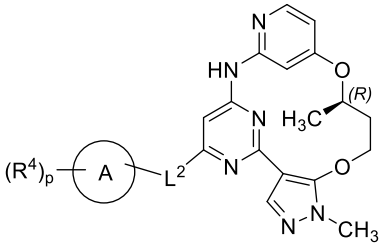
(VI-1) or



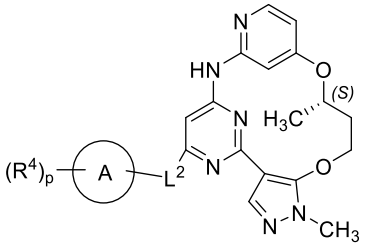
(VI-2),

or a pharmaceutically acceptable salt thereof; or

(b) Formula (VI-3) or Formula (VI-4),



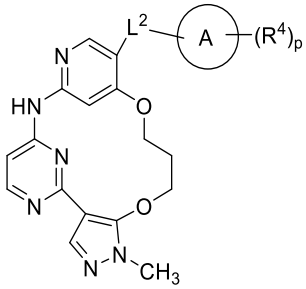
(VI-3) or



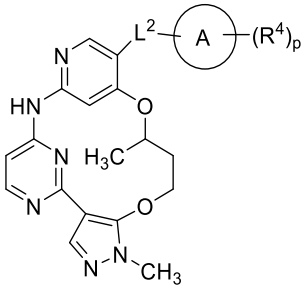
(VI-4),

or a pharmaceutically acceptable salt thereof; or

(c) Formula (VII-1) or Formula (VII-2),



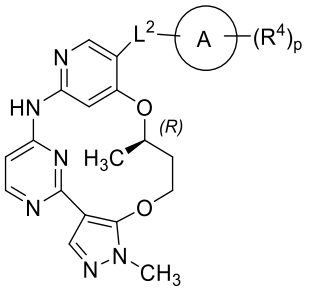
(VII-1) or



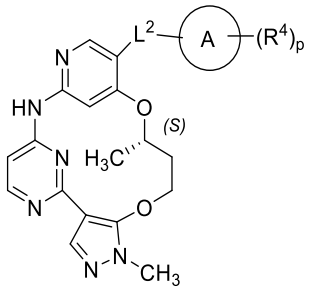
(VII-2),

or a pharmaceutically acceptable salt thereof; or

(d) Formula (VII-3) or Formula (VII-4),



(VII-3) or



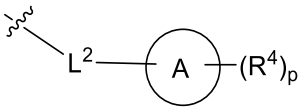
(VII-4),

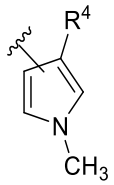
or a pharmaceutically acceptable salt thereof.

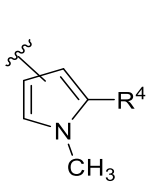
11. The compound of claim 10, wherein **A** is phenyl or 5- to 6-membered heteroaryl.

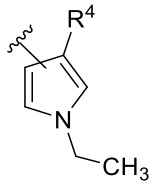
12. The compound of any one of claims 1-11, wherein

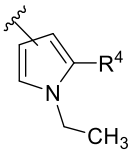
(a) $\mathbf{L^2}$ is a covalent bond; or

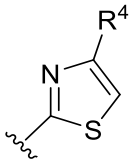
(b) 

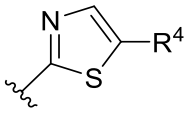
(**Substructure A**) is selected from the group consisting of: 

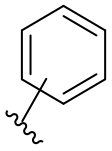
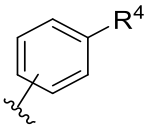
(a1), 

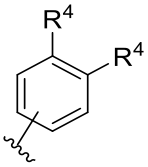
(a2), 

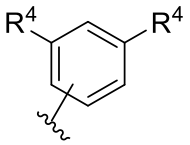
(a3), 

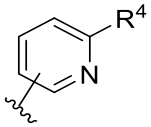
(a4), 

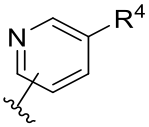
(a5), 

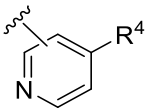
(a6), 
(a7), 

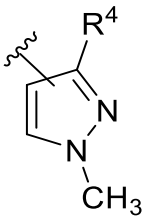
(a8), 

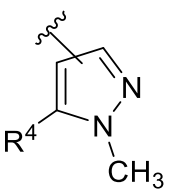
(a9), 

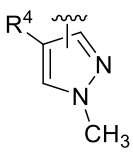
(a10), 

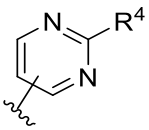
(a11), 

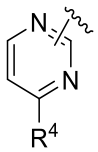
(a12), 

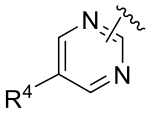
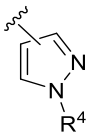
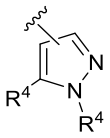
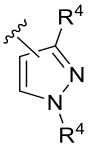
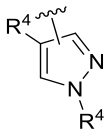
(a13), 

(a14), 

(a15), 

(a16) 

(a17), 

(a18),  (a19), a  (a20),  (a21),  (a22), and  (a23).

13. The compound of any one of claims 1-12, wherein:

(a) the compound comprises one or more **R⁴** groups selected from: -C≡N; -C≡CH; a saturated linear or branched C_{1-6} aliphatic or C_{1-6} alkoxy comprising 0-4 fluoro substituents; $NR^{11}(CH_2)_sNR^8R^9$; $(CH_2)_tNR^8R^9$; $O(CH_2)_tOCH_3$; $O(CH_2)_rR^{12}$; and $(CH_2)_rR^{12}$,

optionally wherein

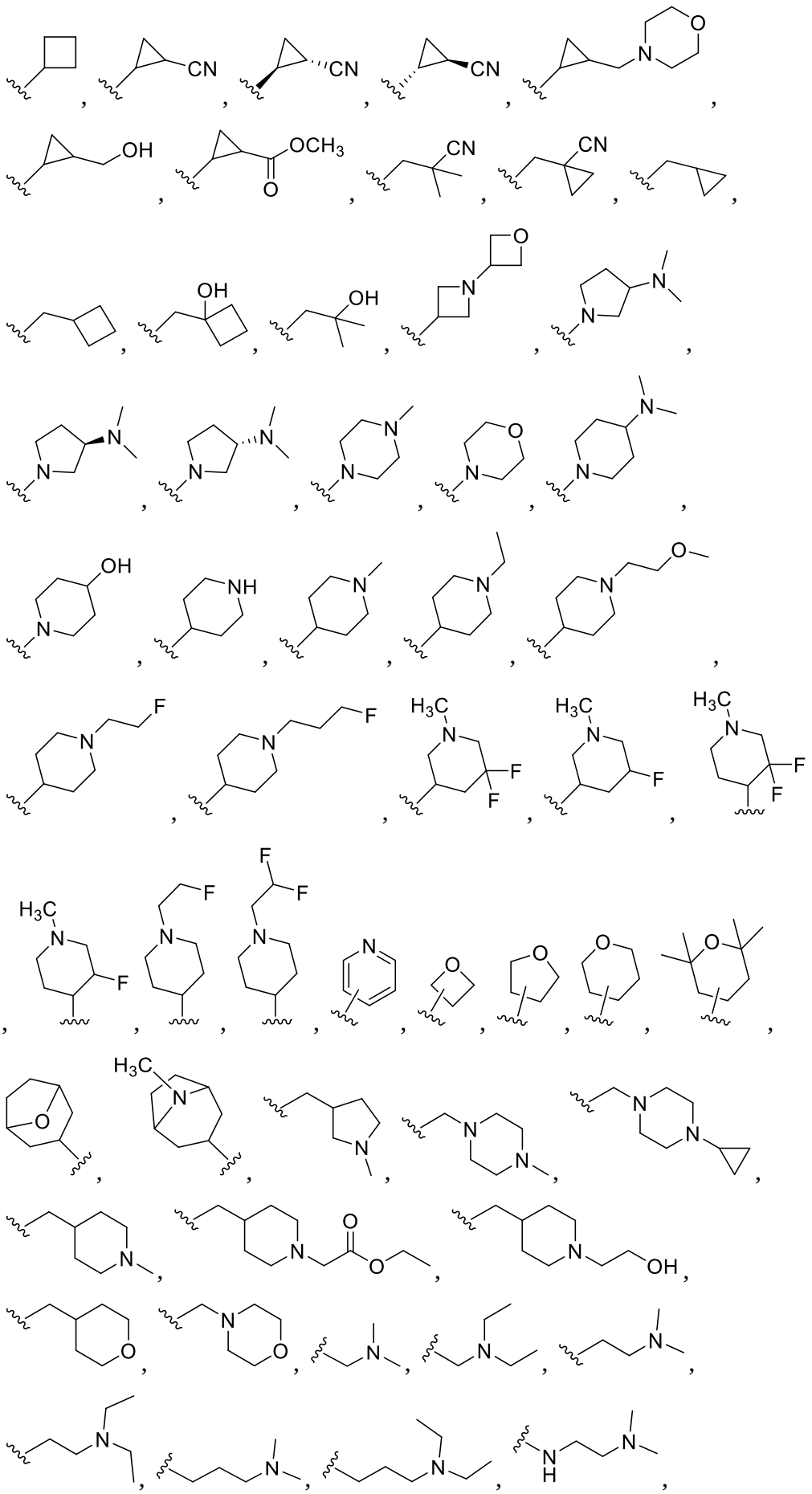
(i) **R¹²** is selected from the group consisting of: a C_{3-6} cycloalkyl; a 3-9 membered heterocyclyl comprising 1-3 heteroatoms selected from O, N, and S; and 5- to 6-membered heteroaryl; and/or

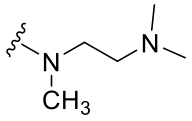
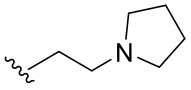
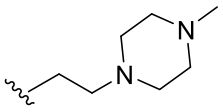
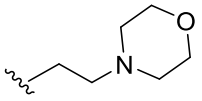
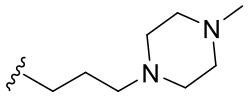
(ii) **R¹²** is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, oxetanyl, tetrahydrofuryl, tetrahydropyanyl, azetidine, pyrroldinyl, piperidinyl, piperazinyl, and morpholino; and/or

(iii) **R¹²** is substituted with 0-4 **R¹⁴**, wherein each **R¹⁴** is independently selected from –CN, oxo (=O), halogen, -OH, $-NH_2$, monoalkylamino, dialkylamino, unsubstituted C_{3-6} cycloalkyl, or unsubstituted 3- to 4-membered heterocyclyl, preferably wherein each **R¹⁴** is independently selected from –CN, –F, -OH, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-NHCH_2CH_3$, $-N(CH_2CH_3)_2$, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_3$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2F$, $-CH_2CH_2CHF_2$, $-CH_2CH_2CF_3$, $-CH_2CH_2OCH_3$, $-COCH_3$, $-COCH_2CH_3$, $-CH_2COCH_3$, $-CH_2COCH_2CH_3$, cyclopropyl, cyclobutyl, oxetanyl, and azetidinyl; or

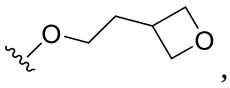
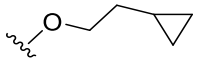
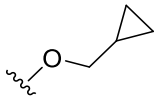
(iv) the compound comprises:
an **R⁴** group selected from: -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_3$,

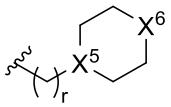
$-CH_2CFH_2$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH(CH_3)_2$, $-C(CH_3)_3$, -C≡CH, ,




, 
, 
, 
, and 
;

and/or

an **R[4]** group selected from -CH_2OCH_3, -OCH_3, -OCH_2F, -$OCHF_2$, -OCF_3, -OCH_2CH_3, -OCH_2CH_2F, -OCH_2CHF_2, -OCH_2CF_3, -$OCH_2CH_2CH_3$, -$OCH_2CH(CH_3)_2$, -$OCH_2CH_2OCH_3$, 
, 
, 
, -CO_2CH_3, and CH_3; or

(b) **R[4]** is selected from unsubstituted C_{1-6} alkyl, CO_2(unsubstituted C_{1-6} alkyl), O-(unsubstituted C_{1-6} alkyl), O-(C_{1-6} haloalkyl), $NH(CH_2)_sNMe_2$, $(CH_2)_tNMe_2$, or 
, wherein

X[5] is independently CH or N;

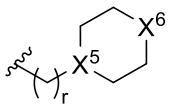
X[6] is independently O, CHR^{13}, or NR^{13};

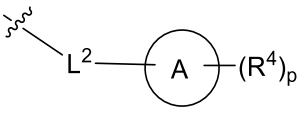
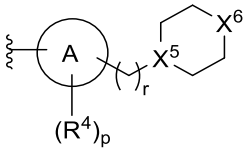
R[13] is independently H, C_{1-6} alkyl, or C_{3-6} cycloalkyl;

r is 0 or 1;

s is an integer of 2-4; and

t is an integer of 1-6,

optionally wherein one **R[4]** is 
, and, if present, a second **R[4]** is selected from unsubstituted C_{1-6} alkyl, CO_2(unsubstituted C_{1-6} alkyl), O-(unsubstituted C_{1-6} alkyl), O-(C_{1-6} haloalkyl), $NH(CH_2)_sNMe_2$, and $(CH_2)_tNMe_2$; or

(c)  (**Substructure A**) is , wherein

A is phenyl or 5- to 6-membered heteroaryl.

X^5 is independently CH or N;

X^6 is independently O, CHR^{13}, or NR^{13};

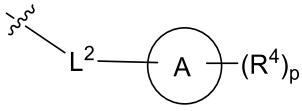
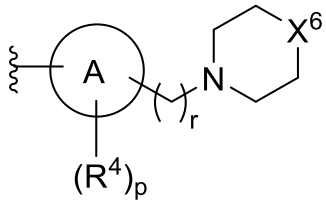
R^{13} is independently H, unsubstituted C_{1-6} alkyl, or unsubstituted C_{3-6} cycloalkyl;

r is 0 or 1;

R^4 is selected from unsubstituted C_{1-6} alkyl, CO_2(unsubstituted C_{1-6} alkyl), O-(unsubstituted C_{1-6} alkyl), O-(C_{1-6} haloalkyl), or $NH(CH_2)_sNMe_2$;

p is 0 or 1; and

s is an integer of 2-6,

optionally wherein  (**Substructure A**) is , wherein **X^6** is O, NCH_3, or N(cyclopropyl).

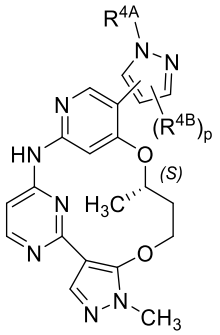
14. The compound of any one of claims 13(b)-(c), wherein **r** is 0 or **r** is 1.

15. The compound of any one of claims 12(b)-14, comprising an **R^4** group that is $-CO_2CH_3$, $-OCH_2CF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, $-OCH_2CH_3$, $-NHCH_2CH_2N(CH_3)_2$, or $-CH_2N(CH_3)_2$.

16. The compound of any one of claims 13(b)-15, wherein **A** is phenyl, pyridyl, pyrimidyl, pyrazolyl, pyrrolyl, thiazolyl, oxazolyl, or imidazolyl.

17. The compound of claim 1, wherein said compound has a structure according to

(a) Formula (VIII),



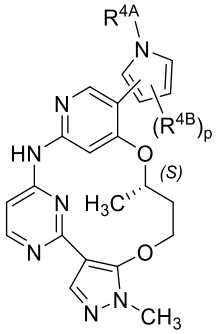
(VIII), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group, and

p is 0 or 1; or

(b) Formula (IX),



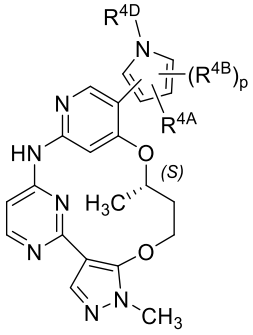
(IX), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group, and

p is 0 or 1; or

(c) Formula (X),



(X), or a pharmaceutically acceptable salt thereof, wherein

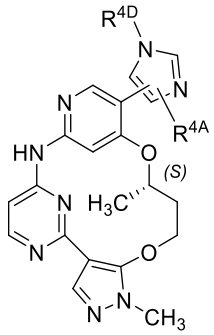
$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

$\mathbf{R^{4B}}$ is a second $\mathbf{R^4}$ group,

p is 0 or 1, and

R^{4D} is a **R^4** group that is unsubstituted C_{1-6} alkyl; or

(d) Formula (XI),

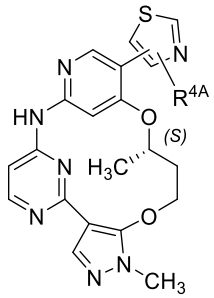


(XI), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^4** group, and

R^{4D} is a **R^4** group that is unsubstituted C_{1-6} alkyl; or

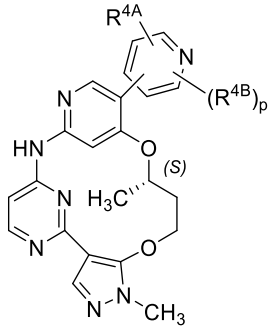
(e) Formula (XII),



(XII), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^4** group; or

(f) Formula (XIII),



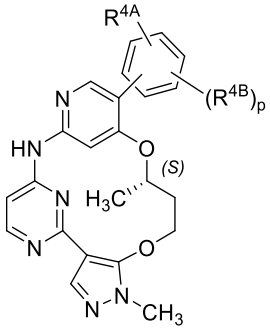
(XIII), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^4** group,

R^{4B} is a second **R^4** group, and

p is 0 or 1; or

(g) Formula (XIV),



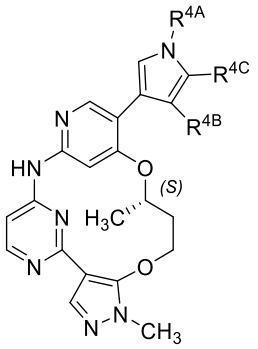
(XIV), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^{4}** group,

R^{4B} is a second **R^{4}** group, and

p is 0 or 1; or

(h) Formula (XV),



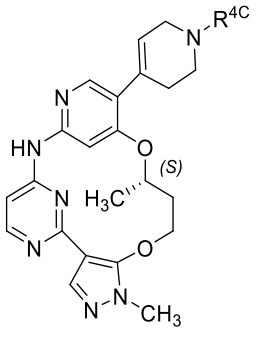
(XV), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^{4}** group,

R^{4B} is a second **R^{4}** group, and

R^{4C} is a third **R^{4}** group; or

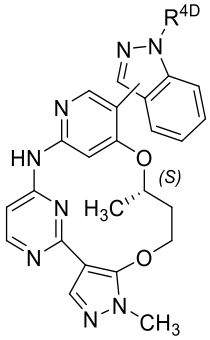
(i) Formula (XVI),



(XVI), or a pharmaceutically acceptable salt thereof, wherein

R^{4C} is a first **R^{4}** group; or

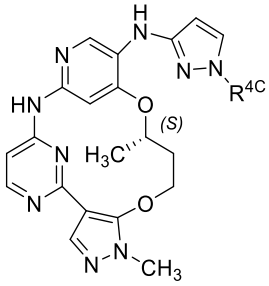
(j) Formula (XVII),



(XVII), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4D}}$ is a $\mathbf{R^4}$ group that is unsubstituted $C_{1\text{-}6}$ alkyl; or

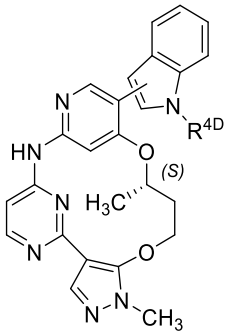
(k) Formula (XVIII),



(XVIII), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4C}}$ is a first $\mathbf{R^4}$ group; or

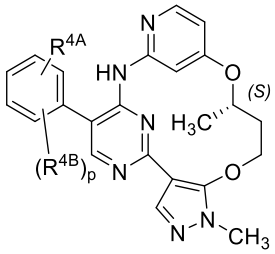
(l) Formula (XIX),



(XIX), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4D}}$ is a $\mathbf{R^4}$ group that is unsubstituted $C_{1\text{-}6}$ alkyl; or

(m) Formula (XX),



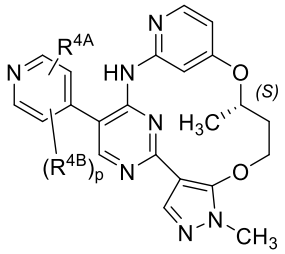
(XX), or a pharmaceutically acceptable salt thereof, wherein

$\mathbf{R^{4A}}$ is a first $\mathbf{R^4}$ group,

R^{4B} is a second **R^4** group, and

p is 0 or 1; or

(n) Formula (XXI),



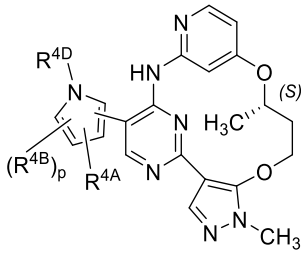
(XXI), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^4** group,

R^{4B} is a second **R^4** group, and

p is 0 or 1; or

(o) Formula (XXII),



(XXII), or a pharmaceutically acceptable salt thereof, wherein

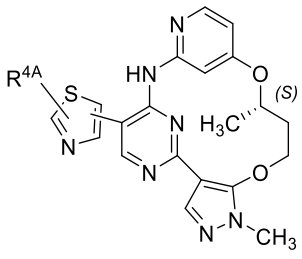
R^{4A} is a first **R^4** group,

R^{4B} is a second **R^4** group,

p is 0 or 1, and

R^{4D} is a **R^4** group that is unsubstituted $C_{1\text{-}6}$ alkyl; or

(p) Formula (XXIII),



(XXIII), or a pharmaceutically acceptable salt thereof, wherein

R^{4A} is a first **R^4** group.

18. The compound of claim 17, wherein

(a) each **R^{4A}**, **R^{4B}**, and **R^{4C}**, when present, is independently a **R^4** group selected from: -C≡N; -C≡CH; a saturated linear or branched C_{1-6} aliphatic or C_{1-6} alkoxy comprising 0-4 fluoro substituents; $NR^{11}(CH_2)_sNR^8R^9$; $(CH_2)_tNR^8R^9$; $O(CH_2)_tOCH_3$; $O(CH_2)_rR^{12}$; and $(CH_2)_rR^{12}$,

optionally wherein

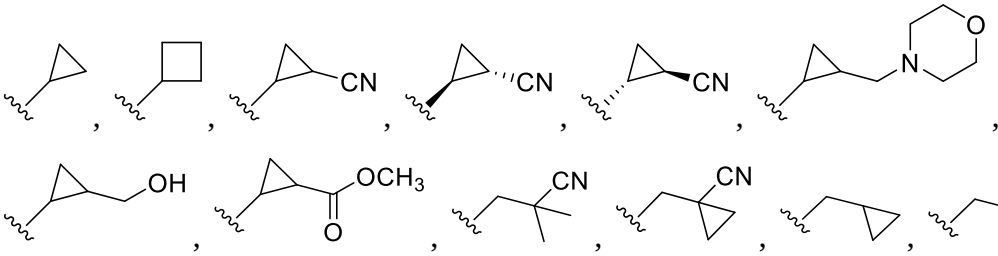
(i) **R^{12}** is selected from the group consisting of: a C_{3-6} cycloalkyl; a 3-9 membered heterocyclyl comprising 1-3 heteroatoms selected from O, N, and S; and 5- to 6-membered heteroaryl; and/or

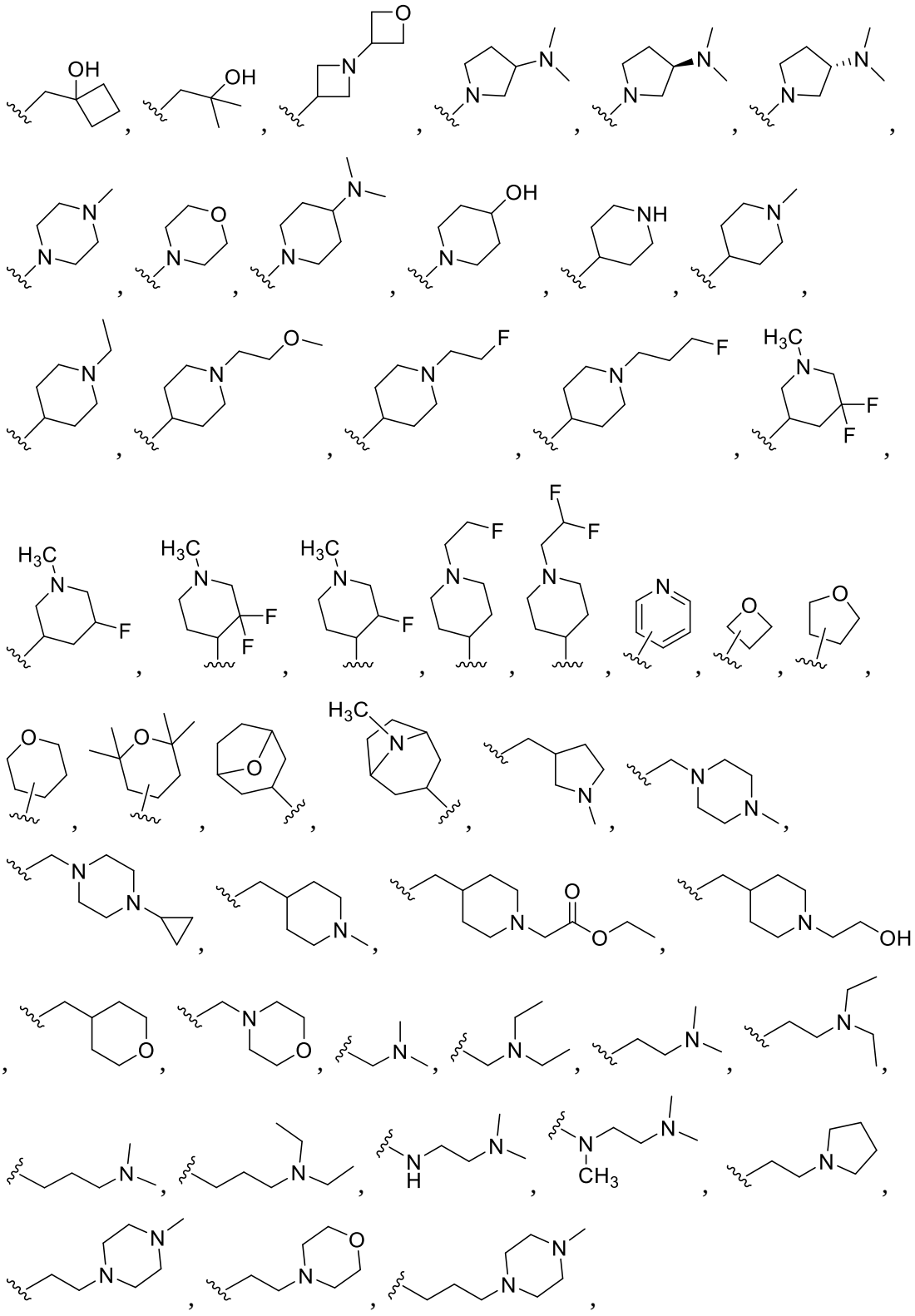
(ii) **R^{12}** is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, oxetanyl, tetrahydrofuryl, tetrahydropyanyl, azetidine, pyrroldinyl, piperidinyl, piperazinyl, and morpholino; and/or

(iii) **R^{12}** is substituted with 0-4 **R^{14}**, wherein each **R^{14}** is independently selected from –CN, oxo (=O), halogen, -OH, $-NH_2$, monoalkylamino, dialkylamino, unsubstituted C_{3-6} cycloalkyl, or unsubstituted 3- to 4-membered heterocyclyl,

preferably wherein each **R^{14}** is independently selected from –CN, –F, -OH, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-NHCH_2CH_3$, $-N(CH_2CH_3)_2$, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_3$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH_2CH_2CH_3$, $-CH_2CH_2CH_2F$, $-CH_2CH_2CHF_2$, $-CH_2CH_2CF_3$, $-CH_2CH_2OCH_3$, $-COCH_3$, $-COCH_2CH_3$, $-CH_2COCH_3$, $-CH_2COCH_2CH_3$, cyclopropyl, cyclobutyl, oxetanyl, and azetidinyl; and/or

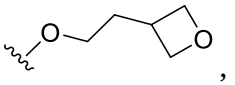
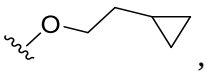
(b) an **R^{4A}** and/or a **R^{4C}** group, when present, is selected from: -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_3$, $-CH_2CFH_2$, $-CH_2CHF_2$, $-CH_2CF_3$, $-CH(CH_3)_2$, $-C(CH_3)_3$, -C≡CH,

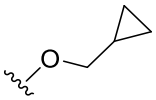




and/or

an $\mathbf{R^{4B}}$ group, when present, is selected from $-CH_2OCH_3$, $-OCH_3$, $-OCH_2F$, $-OCHF_2$, $-OCF_3$, $-OCH_2CH_3$, $-OCH_2CH_2F$, $-OCH_2CHF_2$, $-OCH_2CF_3$, $-OCH_2CH_2CH_3$,

-$OCH_2CH(CH_3)_2$, -$OCH_2CH_2OCH_3$, , ,

, -CO_2CH_3, and CH_3.

19. The compound of claim 1, selected from the group consisting of Compounds (1)-(169), or a pharmaceutically acceptable salt thereof.

20. A pharmaceutical composition comprising a compound according to any one of claims 1-19, or a pharmaceutically acceptable salt thereof.

21. Use of a compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-19, or a pharmaceutical composition of claim 20, in the manufacture of a medicament for treating cancer,

optionally wherein said cancer is:

(a) a lung cancer; and/or

(b) non-small cell lung cancer; and/or

(c) an EGFR-driven cancer; and/or

(d) characterized by an EGFR mutation.

22. A compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-19, or a pharmaceutical composition of claim 20, for use in therapy.