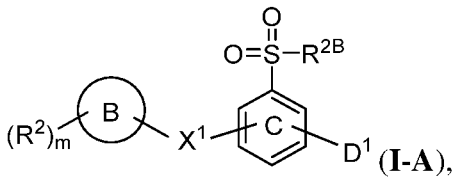
CLAIMS

What is claimed is:

1. A compound of Formula (**I-A**):



(**I-A**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof, wherein:

Ring B is cyclohexyl or phenyl;

R^2 is halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN,

wherein R^{c1} is hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom;

wherein each instance of R^{c2} is independently hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group; or optionally two instances of R^{c2} are taken together with their intervening atoms to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring;

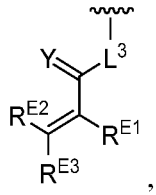
R^{2B} is $–N(R^{c2})_2$, $-OR^{c1}$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

X^1 is –O-, -O(alkylene)-, alkylene, -S-, $–SCH_2–$, $–N(R^{da})–$, or $–N(R^{da})CH_2–$;

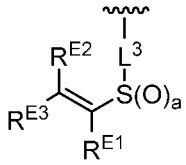
R^{da} is hydrogen, optionally substituted $C_{1–6}$ alkyl, optionally substituted acyl, or a nitrogen protecting group;

m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

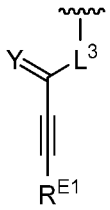
D^1 is a warhead of any one of Formulae (**i-1**) to (**i-23**), (**i-26**) to (**i-31**), (**i-34**) to (**i-40**), (**i-42**), or (**i-43**):



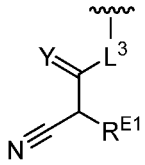
(**i-1**)



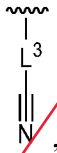
(**i-2**)



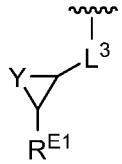
(**i-3**)



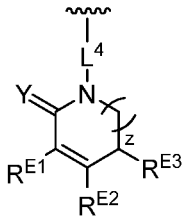
(**i-4**)



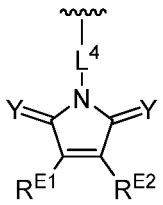
(**i-5**)



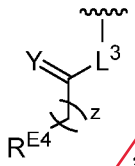
(**i-6**)



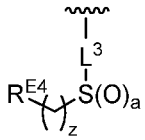
(**i-7**)



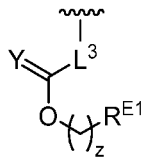
(**i-8**)



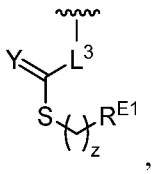
(**i-9**)



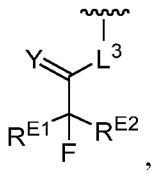
(**i-10**)



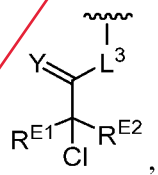
(**i-11**)



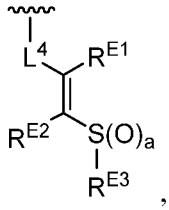
(**i-12**)



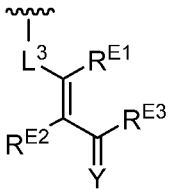
(**i-13**)



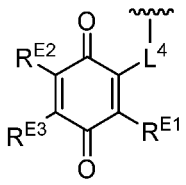
(**i-14**)



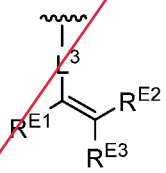
(**i-15**)



(**i-16**)



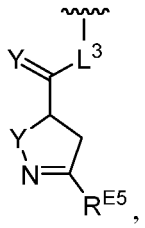
(**i-17**)



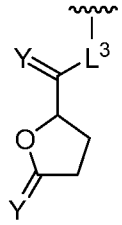
(**i-18**)



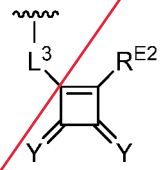
(**i-19**)



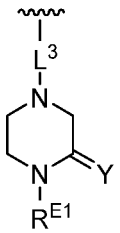
(**i-20**)



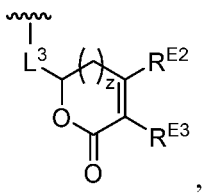
(**i-21**)



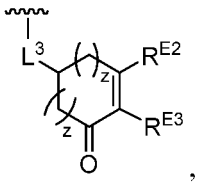
(**i-22**)



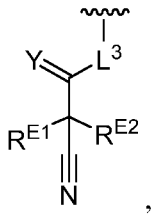
(**i-23**)


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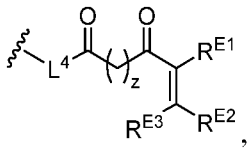
(i-26)


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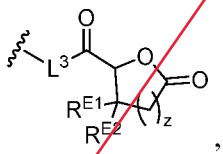
(i-27)


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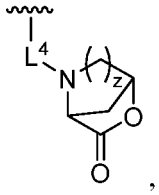
(i-28)


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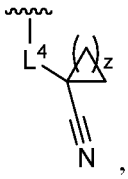
(i-29)


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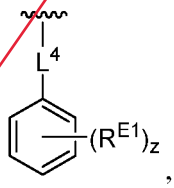
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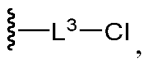
(i-31)


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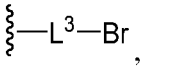
(i-34)


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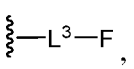
(i-35)


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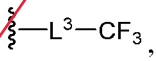
(i-36)


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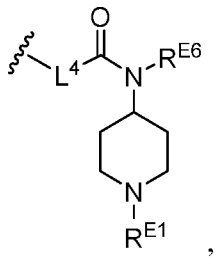
(i-37)


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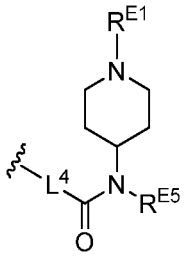
(i-38)


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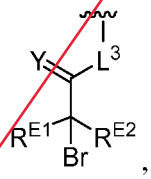
(i-39)


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(i-40)



(i-42); or


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(i-43)

wherein:

L^3 is a bond or an optionally substituted C_{1-4} hydrocarbon chain, optionally wherein one or more carbon units of the hydrocarbon chain are independently replaced with –C=O–, –O–, –S–, $–NR^{L3a}–$, $–NR^{L3a}C(=O)–$, $–C(=O)NR^{L3a}–$, –SC(=O)–, –C(=O)S–, –OC(=O)–, –C(=O)O–, $–NR^{L3a}C(=S)–$, $–C(=S)NR^{L3a}–$, *trans*–$CR^{L3b}=CR^{L3b}–$, *cis*–$CR^{L3b}=CR^{L3b}–$, –C≡C–, –S(=O)–, –S(=O)O–, –OS(=O)–, $–S(=O)NR^{L3a}–$, $–NR^{L3a}S(=O)–$, $–S(=O)_2–$, $–S(=O)_2O–$, $–OS(=O)_2–$, $–S(=O)_2NR^{L3a}–$, or $–NR^{L3a}S(=O)_2–$, wherein R^{L3a} is hydrogen, substituted or unsubstituted C_{1-6} alkyl, or a nitrogen protecting group, and wherein each occurrence of R^{L3b} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally

substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{L3b} groups are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

L^4 is a bond or an optionally substituted, branched or unbranched $C_{1–6}$ hydrocarbon chain;

each of R^{E1}, R^{E2}, and R^{E3} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, –CN, $–CH_2OR^{EE}$, $–CH_2N(R^{EE})_2$, $–CH_2SR^{EE}$, $–OR^{EE}$, $–N(R^{EE})_2$, $–Si(R^{EE})_3$, or $–SR^{EE}$, wherein each instance of R^{EE} is independently hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{EE} groups are joined to form an optionally substituted heterocyclic ring; or R^{E1} and R^{E3}, or R^{E2} and R^{E3}, or R^{E1} and R^{E2} are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

R^{E4} is a leaving group;

R^{E5} is halogen;

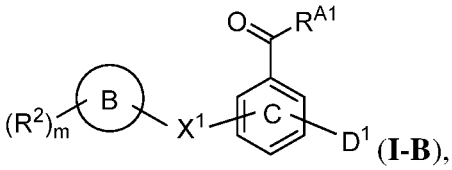
R^{E6} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

each instance of Y is independently O, S, or NR^{E7}, wherein R^{E7} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

a is 1 or 2; and

each instance of z is independently 0, 1, 2, 3, 4, 5, or 6, as valency permits.

2. A compound of Formula (**I-B**):



(**I-B**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof, wherein:

R^{A1} is $–O(R^{a2})$ or $-N(R^{a3})_2$;

R^{a2} is hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or an oxygen protecting group; and

each instance of R^{a3} is independently hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-SO_2(R^{a4})$, or a nitrogen protecting group, or optionally two instances of R^{a3} are taken together with their intervening atoms to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring; and

R^{a4} is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

Ring B is cyclohexyl or phenyl;

R^2 is halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN,

wherein R^{c1} is hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom;

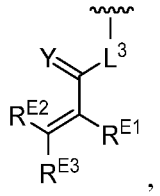
wherein each instance of R^{c2} is independently hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group; or optionally two instances of R^{c2} are taken together with their intervening atoms to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring;

X^1 is –O-, -O(alkylene)-, alkylene, -S-, $–SCH_2–$, $–N(R^{da})–$, or $–N(R^{da})CH_2–$;

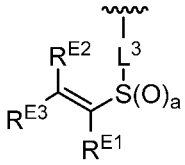
R^{da} is hydrogen, optionally substituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

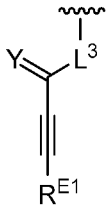
D^1 is a warhead of any one of Formulae (**i-1**) to (**i-23**), (**i-26**) to (**i-31**), (**i-34**) to (**i-40**), (**i-42**), or (**i-43**):



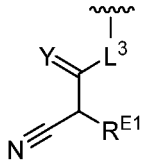
(i-1)



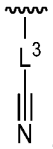
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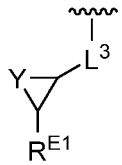
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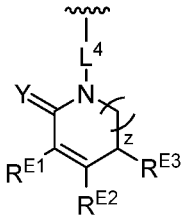
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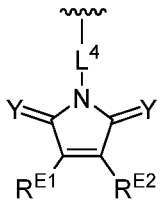
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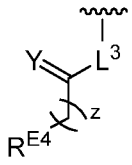
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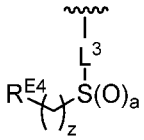
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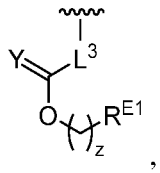
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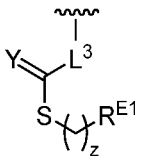
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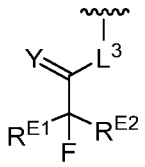
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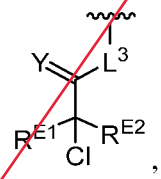
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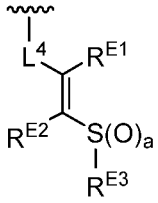
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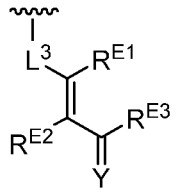
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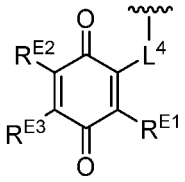
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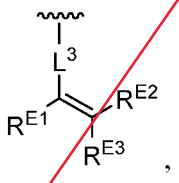
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(i-16)



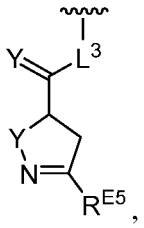
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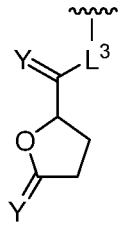
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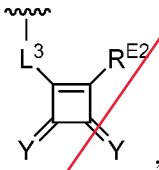
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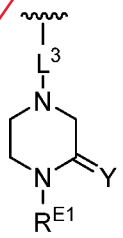
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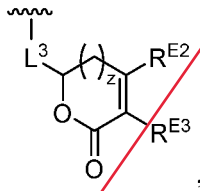
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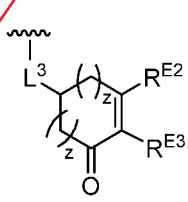
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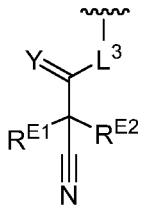
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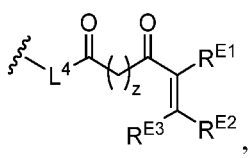
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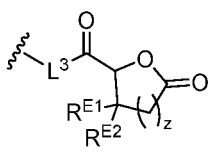
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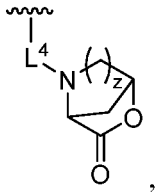
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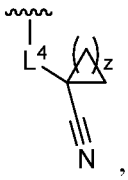
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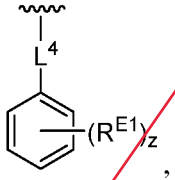
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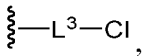
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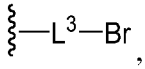
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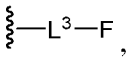
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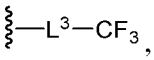
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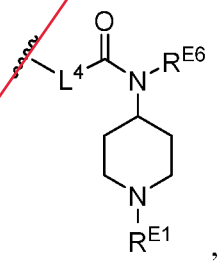
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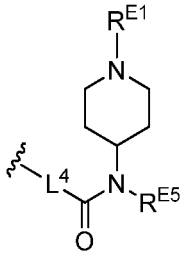
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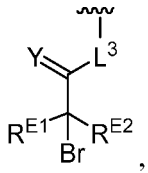
(i-39),



(i-40),



(i-42); or



(i-43)

wherein:

L^3 is a bond or an optionally substituted C_{1-4} hydrocarbon chain, optionally wherein one or more carbon units of the hydrocarbon chain are independently replaced with –C=O–, –O–, –S–, –NR^{L3a}–, –NR^{L3a}C(=O)–, –C(=O)NR^{L3a}–, –SC(=O)–, –C(=O)S–, –OC(=O)–, –C(=O)O–, –NR^{L3a}C(=S)–, –C(=S)NR^{L3a}–, *trans*–CR^{L3b}=CR^{L3b}–, *cis*–CR^{L3b}=CR^{L3b}–, –C≡C–, –S(=O)–, –S(=O)O–, –OS(=O)–, –S(=O)NR^{L3a}–, –NR^{L3a}S(=O)–, –$S(=O)_2$–, –$S(=O)_2$O–, –$OS(=O)_2$–, –$S(=O)_2NR^{L3a}$–, or –$NR^{L3a}S(=O)_2$–, wherein R^{L3a} is hydrogen, substituted or unsubstituted C_{1-6} alkyl, or a nitrogen protecting group, and wherein each occurrence of R^{L3b} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{L3b} groups are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

L^4 is a bond or an optionally substituted, branched or unbranched C_{1-6} hydrocarbon chain;

each of R^{E1}, R^{E2}, and R^{E3} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, –CN, $–CH_2OR^{EE}$, $–CH_2N(R^{EE})_2$, $–CH_2SR^{EE}$, $–OR^{EE}$, $–N(R^{EE})_2$, $–Si(R^{EE})_3$, or $–SR^{EE}$, wherein each instance of R^{EE} is independently hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{EE} groups are joined to form an optionally substituted heterocyclic ring; or R^{E1} and R^{E3}, or R^{E2} and R^{E3}, or R^{E1} and R^{E2} are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

R^{E4} is a leaving group;

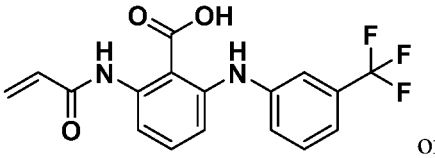
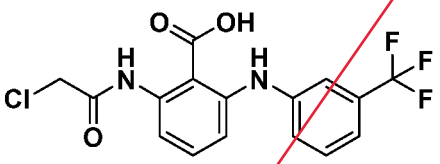
R^{E5} is halogen;

R^{E6} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

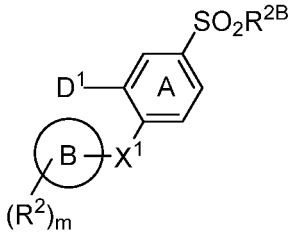
each instance of Y is independently O, S, or NR^{E7}, wherein R^{E7} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

a is 1 or 2; and

each instance of z is independently 0, 1, 2, 3, 4, 5, or 6, as valency permits;

provided that the compound is not of formula:  or .

3. The compound of claim 1, wherein the compound is of formula:



,

or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

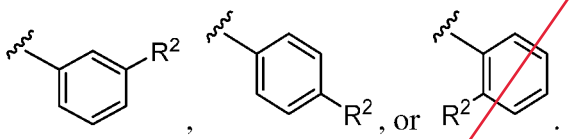
4. The compound of any one of claims 1-3, wherein Ring B is cyclohexyl.

5. The compound of any one of claims 1-3, wherein Ring B is phenyl.

6. The compound of any one of claims 1-5, wherein m is 0.

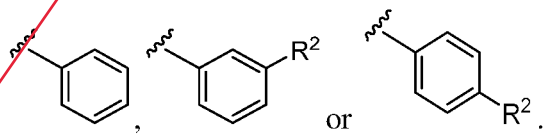
7. The compound of any one of claims 1-5, wherein m is 1.

8. The compound of any one of claims 1-7, wherein Ring B is of formula:



, , or .

9. The compound of any one of claims 1-8, wherein Ring B is of formula:

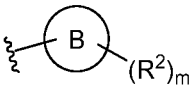
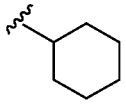


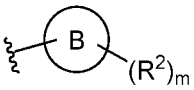
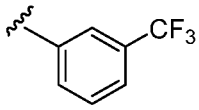
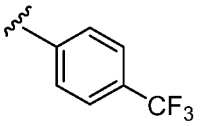
, or .

10. The compound of any one of claims 1-9, wherein at least one instance of R^2 is optionally substituted alkyl.

11. The compound of claim 10, wherein at least one instance of R^2 is optionally substituted C_{1-6} alkyl.

12. The compound of claim 10, wherein at least one instance of R^2 is $-CF_3$.

13. The compound of any one of claims 1-4, 6, 7, or 10-12, wherein the moiety  is of formula: .

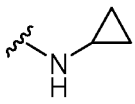
14. The compound of any one of claims 1-3, 5, or 7-12, wherein the moiety  is of formula:  or .

15. The compound of any one of claims 1 or 3-14, wherein R^{2B} is $-N(R^{c2})_2$, and each instance of R^{c2} is independently hydrogen, optionally substituted alkyl, or optionally substituted carbocyclyl.

16. The compound of claim 15, wherein R^{2B} is $-N(R^{c2})_2$, and at least one instance of R^{c2} is hydrogen.

17. The compound of claim 15 or 16, wherein R^{2B} is $-NH(R^{c2})$, wherein R^{c2} is optionally substituted C_{1-6} alkyl or optionally substituted C_{3-10} carbocyclyl.

18. The compound of any one of claims 1 or 3-16, wherein R^{2B} is –NHMe

or .

19. The compound of compound of any one of claims 1 or 3-16, wherein R^{2B} is optionally substituted alkyl.

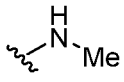
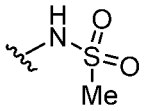
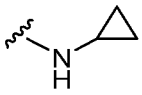
20. The compound of compound of claim 19, wherein R^{2B} is optionally substituted methyl.

21. The compound of claim 2, wherein R^{A1} is $-OR^{a2}$, and R^{a2} is hydrogen or optionally substituted alkyl.

22. The compound of claim 2 or 21, wherein R^{A1} is –OH.

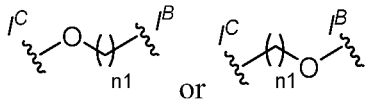
23. The compound of claim 2, wherein R^{A1} is $–N(R^{a3})_2$, wherein at least one instance of R^{a3} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-10} carbocyclyl, or $-SO_2(R^{a4})$, and R^{a4} is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, or optionally substituted carbocyclyl.

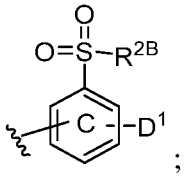
24. The compound of claim 2 or 23, wherein R^{A1} is $–NH(R^{a3})$.

25. The compound of any one of claims 2, 23, or 24, wherein R^{A1} is , , , or $–NMe_2$.

26. The compound of any one of claims 1-25, wherein X^1 is –O-.

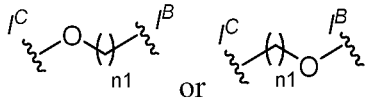
27. The compound of any one of claims 1-25, wherein X^1 is $–O(CR^d)_{1–6}–$, and R^d is hydrogen, halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN.

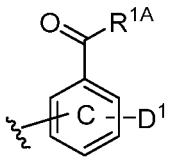
28. The compound of claim 27, wherein X^1 is of formula:  or ;

l^C indicates the point of attachment to the moiety of formula: ;

and l^B indicates the point of attachment to Ring B; and

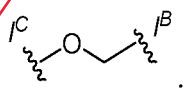
n1 is 1, 2, 3, 4, 5, or 6.

29. The compound of claim 27, wherein X^1 is of formula:  or ;

l^C indicates the point of attachment to the moiety of formula:  ;

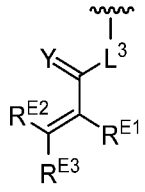
and l^B indicates the point of attachment to Ring B; and

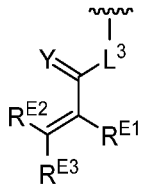
n1 is 1, 2, 3, 4, 5, or 6.

30. The compound of any one of claims 27-29, wherein X^1 is of formula:  .

31. The compound of any one of claims 1-25, wherein X^1 is $-N(R^{da})-$, and R^{da} is hydrogen or optionally substituted C_{1-6} alkyl.

32. The compound of claim 30, wherein X^1 is –NH–.

33. The compound of any one of claims 1-32, wherein D^1 is of formula:  (**i-1**).

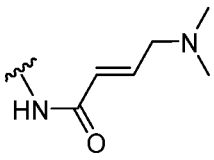
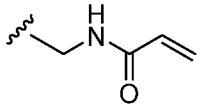
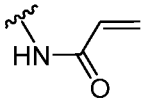
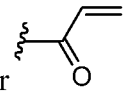
34. The compound of any one of claims 1-32, wherein D^1 is of formula  (**i-1**), wherein:

L^3 is a bond or optionally substituted C_{1-4} alkyl, and optionally wherein 1 to 2 carbon units of the C_{1-4} alkyl are replaced with $-C(=O)-$, $-NR^{L3a}-$, or $-NR^{L3a}C(=O)-$;

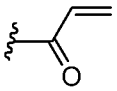
R^{L3a} is hydrogen, substituted or unsubstituted C_{1-6} alkyl, or a nitrogen protecting group; Y is O; and

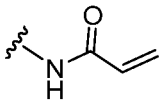
each of R^{E1}, R^{E2}, and R^{E3} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, or optionally substituted alkynyl.

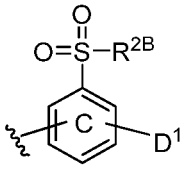
35. The compound of any one of claims 1-34, wherein D^1 is of formula:

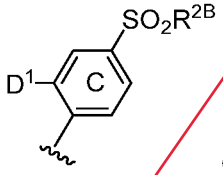
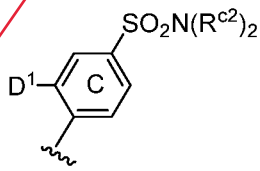

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, or

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36. The compound of any one of claims 1-35, wherein D^1 is of formula:

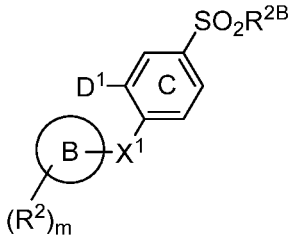

.

37. The compound of any one of claims 1-35, wherein D^1 is of formula:

.

38. The compound of any one of claims 1, 3-20, 26-28, or 30-37, wherein the moiety of formula:

is of formula:


or

.

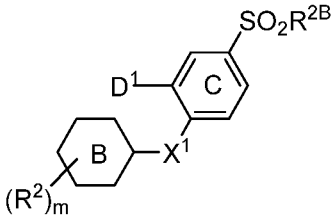
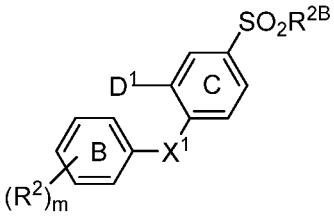
39. The compound of any one of claims 1, 3-20, 26-28, or 30-38, wherein the compound is of formula:


,

or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

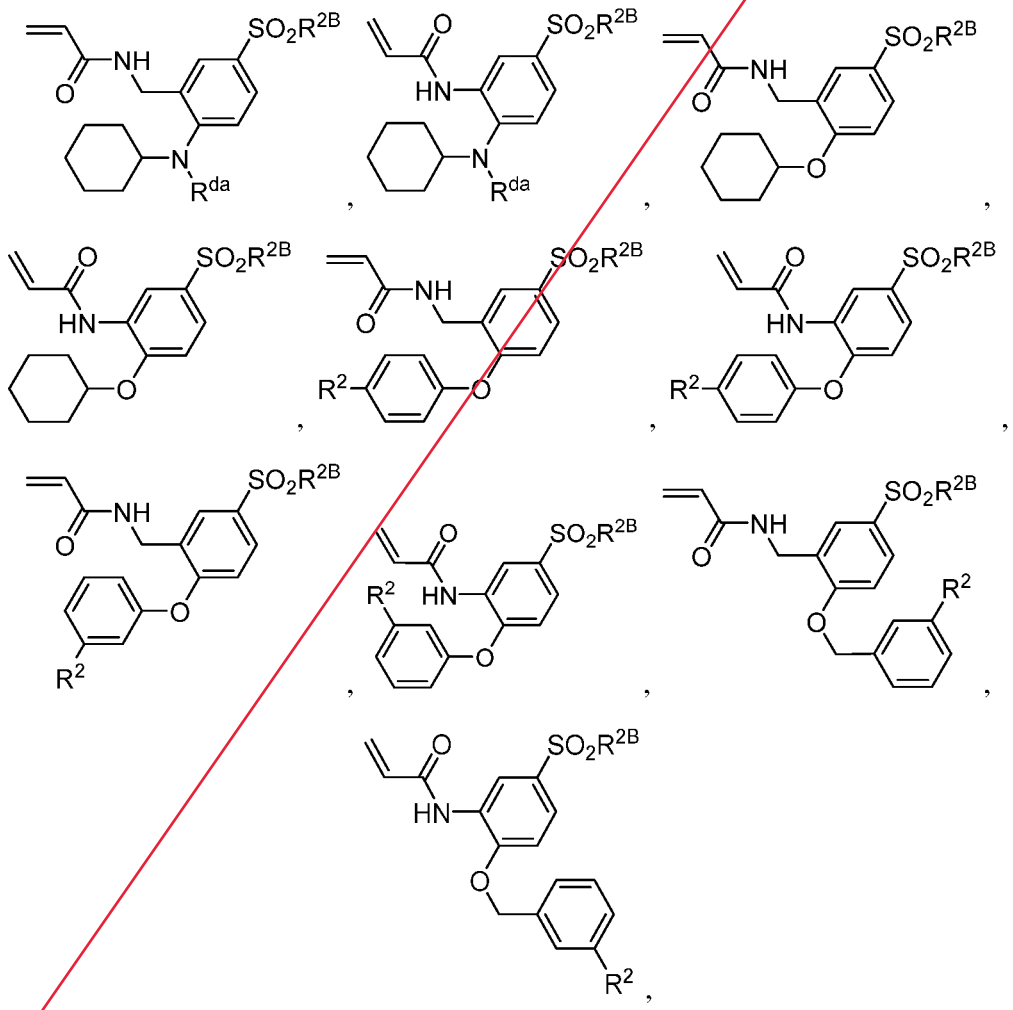
40. The compound of any one of claims 1, 3-20, 26-28, or 30-39, wherein the compound

is of formula:

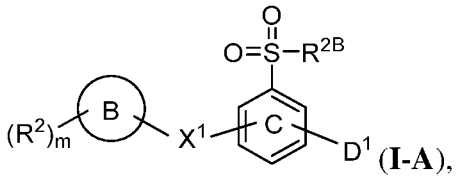
or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

41. The compound of any one of claims 1, 3-20, 26-28, or 30-40, wherein the compound is of formula:



or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

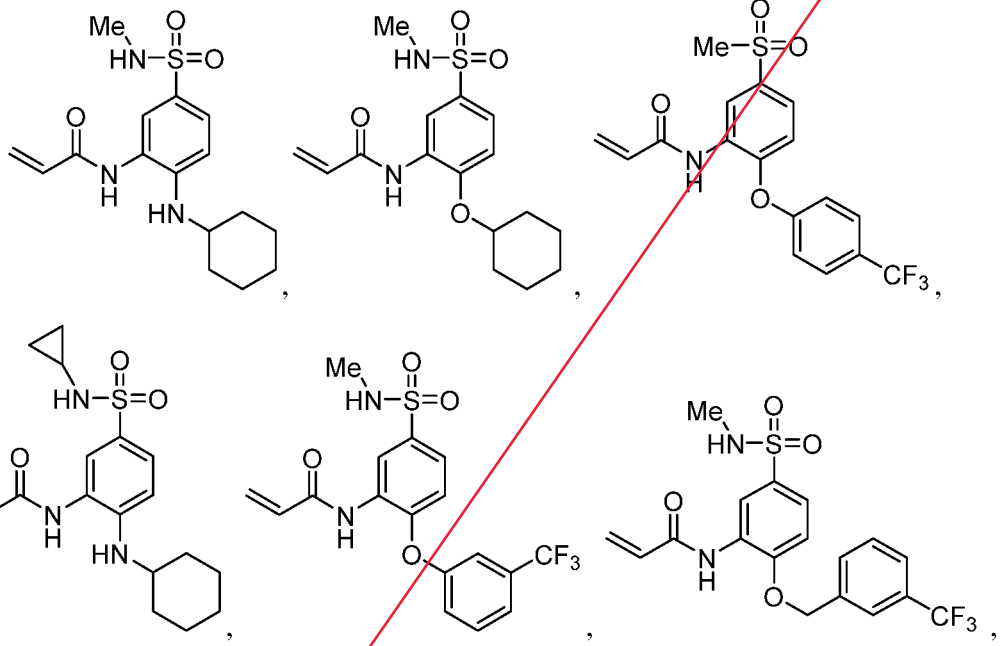
42. The compound of claim 1, wherein the compound is of formula:



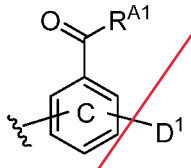
(I-A),

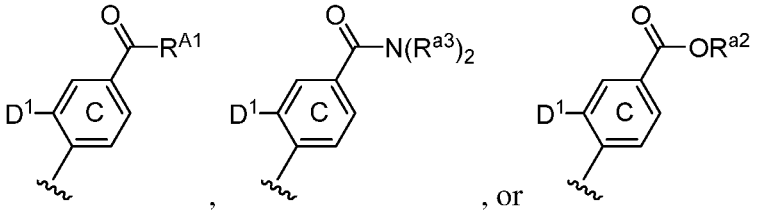
or a pharmaceutically acceptable salt thereof.

43. The compound of any one of claims 1, 3-20, 28, or 30-42, wherein the compound is of formula:



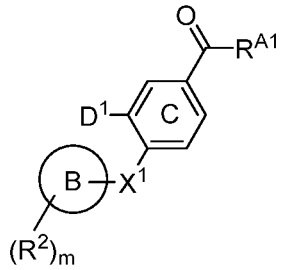
or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof.

44. The compound of any one of claims 2-14, 20-27, or 29-37, wherein the moiety of formula:  is of formula:



, or .

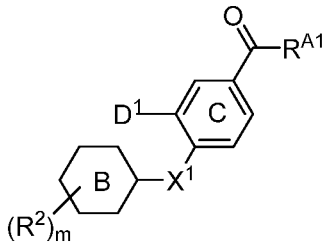
45. The compound of any one of claims 2-14, 20-27, 29-37, or 44, wherein the compound is of formula:

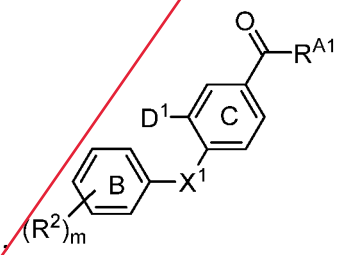


,

or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

46. The compound of any one of claims 2-14, 20-27, 29-37, or 42-45, wherein the compound is of formula:

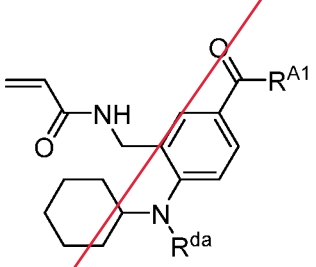


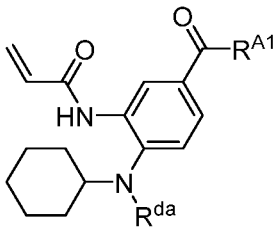
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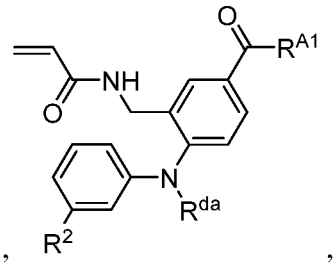
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or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

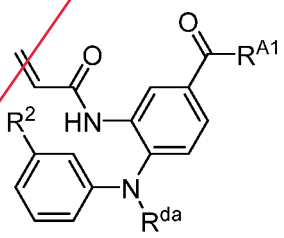
47. The compound of any one of claims 2-14, 20-27, 29-37, or 42-46, wherein the compound is of formula:

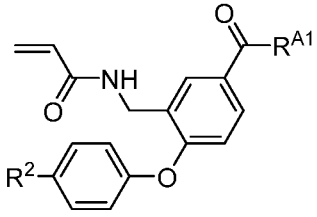


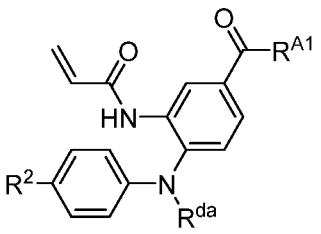
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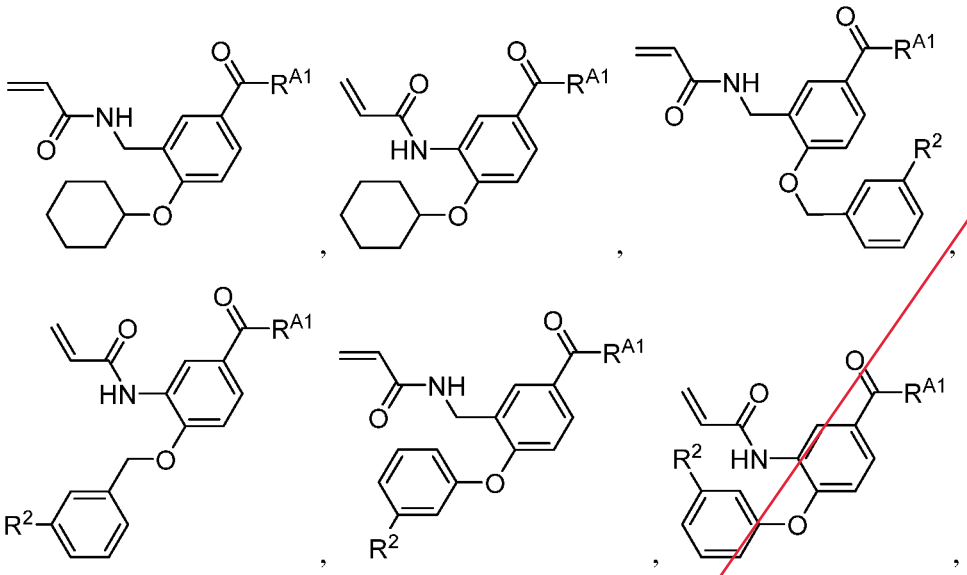
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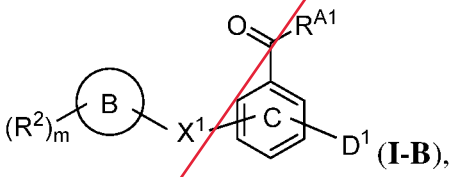
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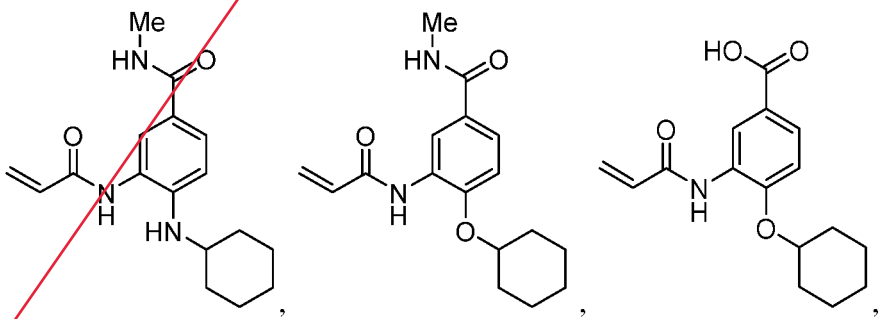
or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

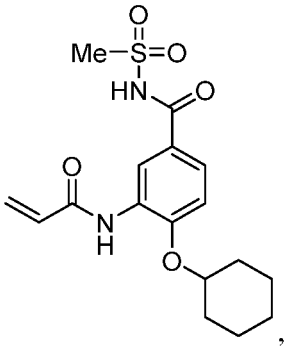
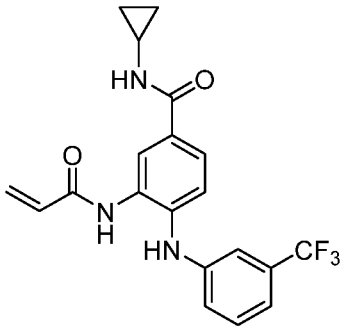
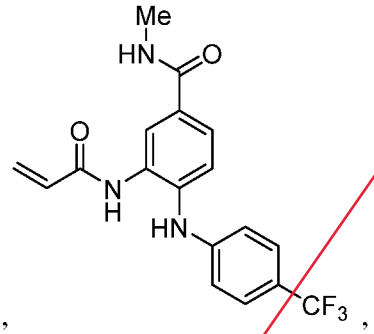
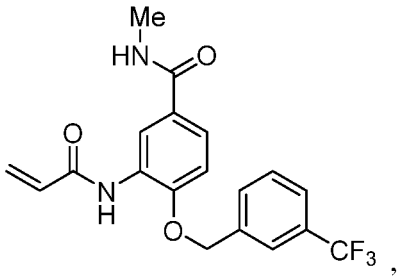
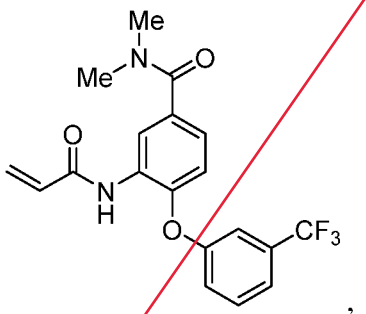
48. The compound of claim 2, wherein the compound is of formula:



or a pharmaceutically acceptable salt thereof.

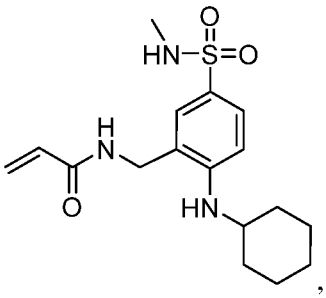
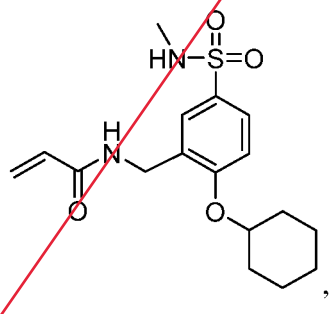
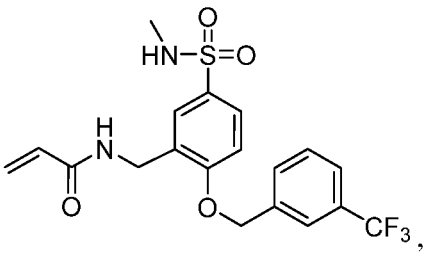
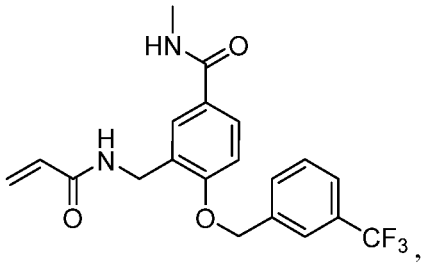
49. The compound of any one of claims 2-14, 20-27, 29-37, or 42-48, wherein the compound is of formula:




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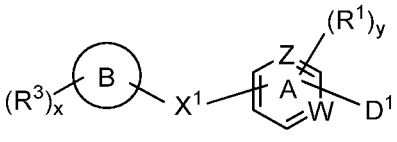
or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof.

50. The compound of any one of claims 1-49, wherein the compound is of formula:


,

,

,

,

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof.

51. A compound of Formula (**II**):



(**II**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof, wherein:

Ring B is cyclohexyl or phenyl;

W is $–C(R^a)=$ or –N=, as valency permits; and R^a is hydrogen, halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN;

Z is $–C(R^b)=$ or –N=, as valency permits; and R^b is hydrogen, halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN;

provided at least one instance of W and Z is $–C(R^a)=$ or $–C(R^b)=$;

each instance of R^1 is independently halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN;

each instance of R^3 is independently halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN;

wherein R^{c1} is hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom;

wherein each instance of R^{c2} is independently hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group; or optionally two instances of R^{c2} are taken together with their intervening atoms to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring;

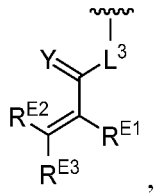
X^1 is –O-, -O(alkylene)-, alkylene, -S-, $–SCH_2–$, $–N(R^{da})–$, or $–N(R^{da})CH_2–$;

R^{da} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted acyl, or a nitrogen protecting group;

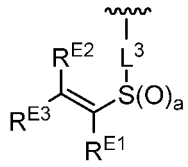
x is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

y is 0, 1, 2, 3, or 4;

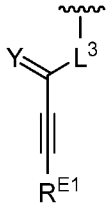
D^1 is a warhead of any one of Formulae (**i-1**) to (**i-23**), (**i-26**) to (**i-31**), (**i-34**) to (**i-40**), (**i-42**), or (**i-43**):



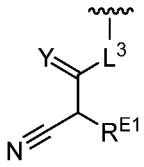
(**i-1**)



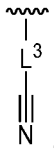
(**i-2**)



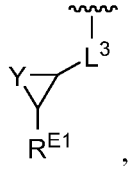
(**i-3**)



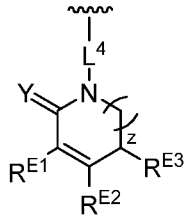
(**i-4**)



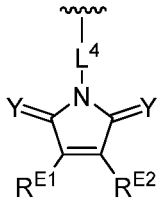
(**i-5**)



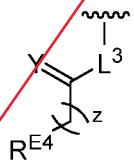
(**i-6**)



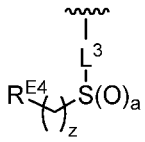
(**i-7**)



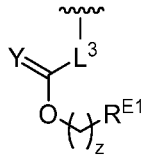
(**i-8**)



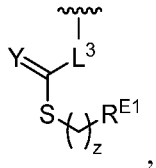
(**i-9**)



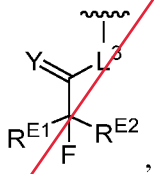
(**i-10**)



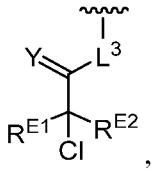
(**i-11**)



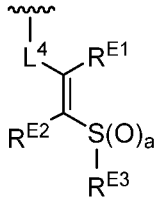
(**i-12**)



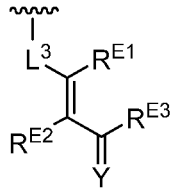
(**i-13**)



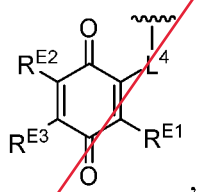
(**i-14**)



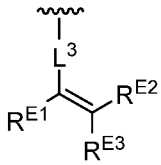
(**i-15**)



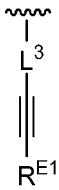
(**i-16**)



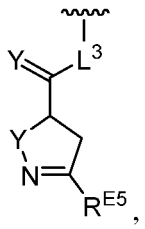
(**i-17**)



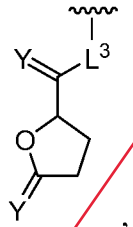
(**i-18**)



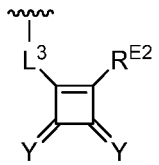
(**i-19**)



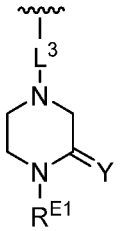
(**i-20**)



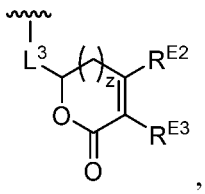
(**i-21**)



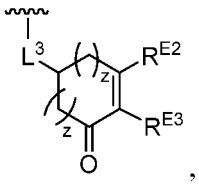
(**i-22**)



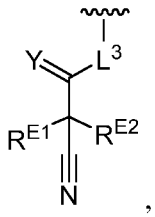
(**i-23**)


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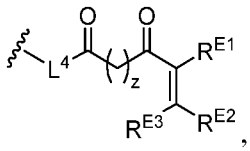
(i-26)


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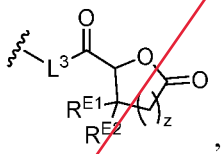
(i-27)


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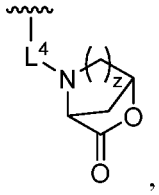
(i-28)


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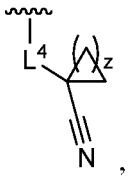
(i-29)


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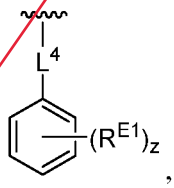
(i-30)


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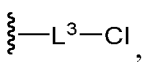
(i-31)

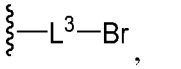

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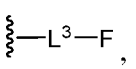
(i-34)

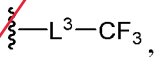

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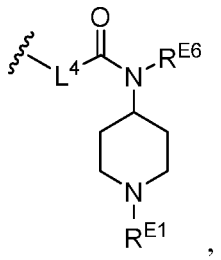
(i-35)


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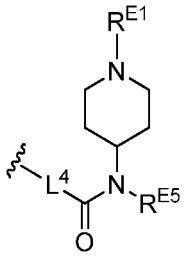

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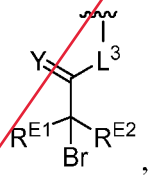

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(i-36) **(i-37)** **(i-38)** **(i-39)** **(i-40)**



(i-42); or


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(i-43)

wherein:

L^3 is a bond or an optionally substituted C_{1-4} hydrocarbon chain, optionally wherein one or more carbon units of the hydrocarbon chain are independently replaced with –C=O–, –O–, –S–, –NR^{L3a}–, –NR^{L3a}C(=O)–, –C(=O)NR^{L3a}–, –SC(=O)–, –C(=O)S–, –OC(=O)–, –C(=O)O–, –NR^{L3a}C(=S)–, –C(=S)NR^{L3a}–, *trans*–CR^{L3b}=CR^{L3b}–, *cis*–CR^{L3b}=CR^{L3b}–, –C≡C–, –S(=O)–, –S(=O)O–, –OS(=O)–, –S(=O)NR^{L3a}–, –NR^{L3a}S(=O)–, –$S(=O)_2$–, –$S(=O)_2$O–, –$OS(=O)_2$–, –$S(=O)_2NR^{L3a}$–, or –$NR^{L3a}S(=O)_2$–, wherein R^{L3a} is hydrogen, substituted or unsubstituted C_{1-6} alkyl, or a nitrogen protecting group, and wherein each occurrence of R^{L3b} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted

alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{L3b} groups are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

L^4 is a bond or an optionally substituted, branched or unbranched $C_{1–6}$ hydrocarbon chain;

each of R^{E1}, R^{E2}, and R^{E3} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, –CN, $–CH_2OR^{EE}$, $–CH_2N(R^{EE})_2$, $–CH_2SR^{EE}$, $–OR^{EE}$, $–N(R^{EE})_2$, $–Si(R^{EE})_3$, or $–SR^{EE}$, wherein each instance of R^{EE} is independently hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{EE} groups are joined to form an optionally substituted heterocyclic ring; or R^{E1} and R^{E3}, or R^{E2} and R^{E3}, or R^{E1} and R^{E2} are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

R^{E4} is a leaving group;

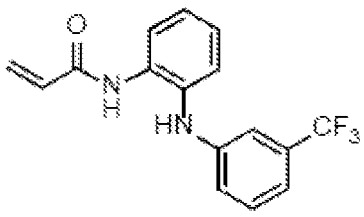
R^{E5} is halogen;

R^{E6} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

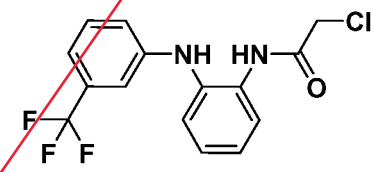
each instance of Y is independently O, S, or NR^{E7}, wherein R^{E7} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

a is 1 or 2; and

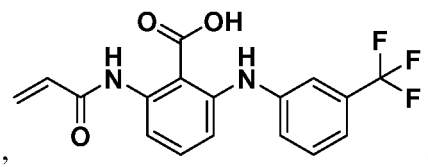
each instance of z is independently 0, 1, 2, 3, 4, 5, or 6, as valency permits;



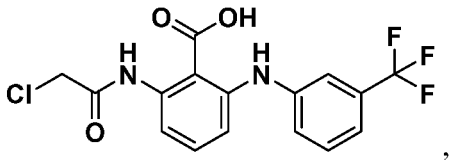
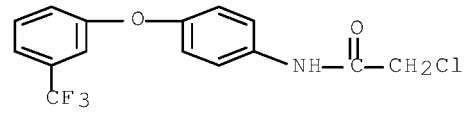
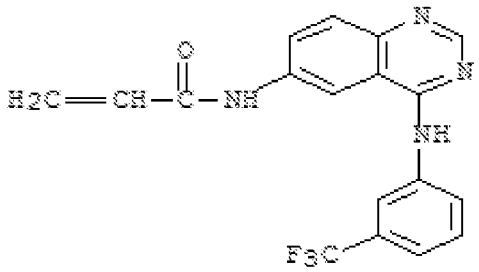
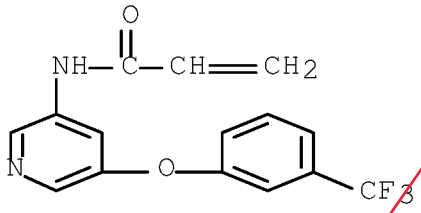
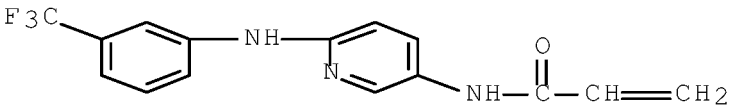
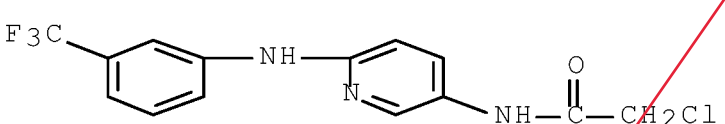
provided that the compound is not of formula:



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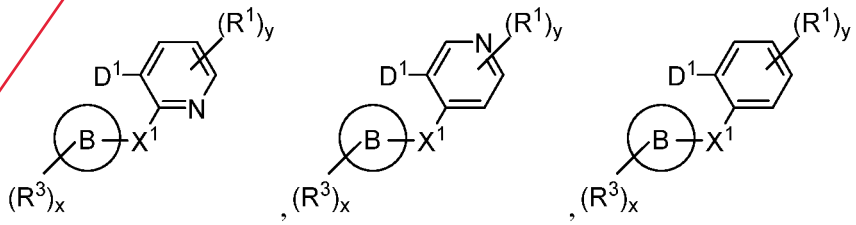
52. The compound of claim 51, wherein Z is –CH=.

53. The compound of claim 51 or 52, wherein W is –CH=.

54. The compound of claim 51 or 53, wherein Z is –N=.

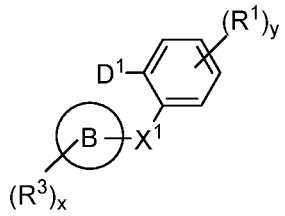
55. The compound of claim 51, 52, or 54, wherein W is –N=.

56. The compound of any one of claims 51-55, wherein Formula (**II**) is of the formula:



or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

57. The compound of any one of claims 51-55, wherein Formula (**II**) is of the formula:



,

or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

58. The compound of any one of claims 51-57, wherein Ring B is cyclohexyl.

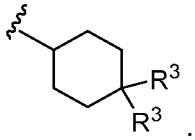
59. The compound of any one of claims 51-57, wherein Ring B is phenyl.

60. The compound of any one of claims 51-59, wherein x is 0.

61. The compound of any one of claims 51-59, wherein x is 1.

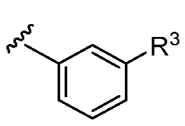
62. The compound of any one of claims 51-59, wherein x is 2.

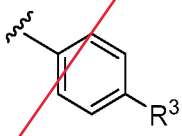
63. The compound of any one of claims 51-62, wherein Ring B is of formula:

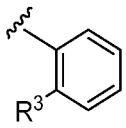


.

64. The compound of any one of claims 51-62, wherein Ring B is of formula:

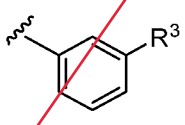


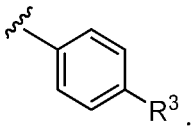
, 

, or 

.

65. The compound of any one of claims 51-63, wherein Ring B is of formula:



or 

.

66. The compound of any one of claims 51-65, wherein at least one instance of R^3 is halogen.

67. The compound of claim 51-66, wherein at least one instance of R^3 is –F.

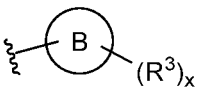
68. The compound of any one of claims 51-65, wherein at least one instance of R^3 is optionally substituted alkyl.

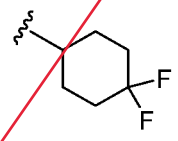
69. The compound of any one of claims 51-65 or 68, wherein at least one instance of R^3 is optionally substituted C_{1-6} alkyl.

70. The compound of claim 51-65, 68, or 69, wherein at least one instance of R^3 is $–CF_3$.

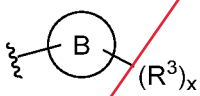
71. The compound of any one of claims 51-65, wherein at least one instance of R^3 is optionally substituted carbocyclyl.

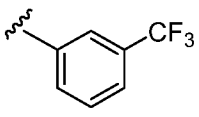
72. The compound of any one of claims 51-65 or 71, wherein at least one instance of R^3 is optionally substituted $C_{3–14}$ carbocyclyl.

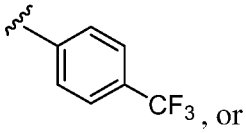
73. The compound of any one of claims 51-58, 60-63, 66, or 67, wherein the moiety 

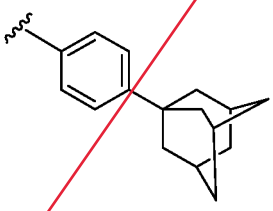
is of formula: 

.

74. The compound of any one of claims 51-57, 59-62, 64, 65, or 68-73, wherein the moiety 

is of formula: 

, 

, or 
.

75. The compound of any one of claims 51-74, wherein y is 0.

76. The compound of any one of claims 51-74, wherein y is 1.

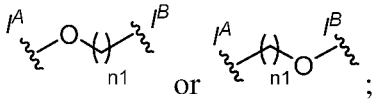
77. The compound of any one of claims 51-76, wherein at least one instance of R^1 is halogen.

78. The compound of any one of claims 51-77, wherein at least one instance of R^1 is –F.

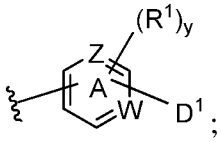
79. The compound of any one of claims 51-78, wherein X^1 is –O-.

80. The compound of any one of claims 51-78, wherein X^1 is $-O(CR^d)_{1-6}-$, and R^d is hydrogen, halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, $-OR^{c1}$, $-NO_2$, $-N(R^{c2})_2$, $-SR^{c1}$, –CN, or -SCN.

81. The compound of any one of claims 51-78 or 80, wherein X^1 is of formula:



;

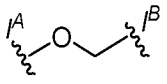
l^A indicates the point of attachment to the moiety of formula: 

;

and l^B indicates the point of attachment to Ring B; and

n1 is 1, 2, 3, 4, 5, or 6.

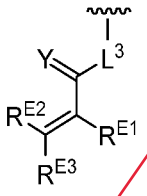
82. The compound of any one of claims 51-78, 80, or 81, wherein X^1 is of formula:



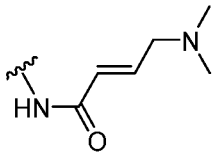
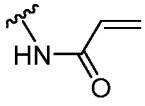
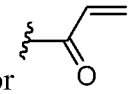
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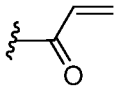
83. The compound of any one of claims 51-78, wherein X^1 is $-N(R^{da})-$, and R^{da} is hydrogen or optionally substituted C_{1-6} alkyl.

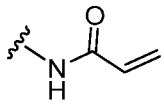
84. The compound of any one of claims 51-78 or 83, wherein X^1 is –NH–.

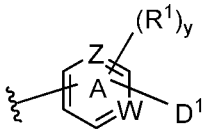
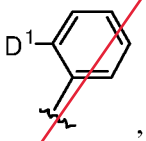
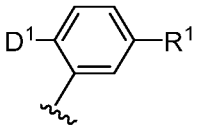
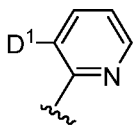
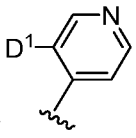
85. The compound of any one of claims 51-84, wherein D^1 is of formula:  (**i-1**).

86. The compound of any one of claims 51-85, wherein D^1 is of formula:

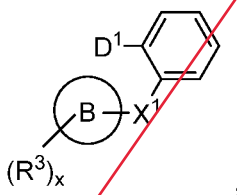
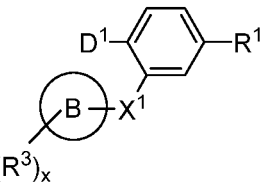
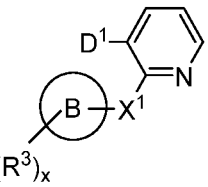
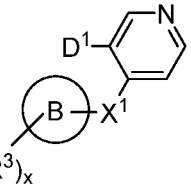
 ,  , or  .

87. The compound of any one of claims 51-86, wherein D^1 is of formula:  .

88. The compound of any one of claims 51-86, wherein D^1 is of formula:  .

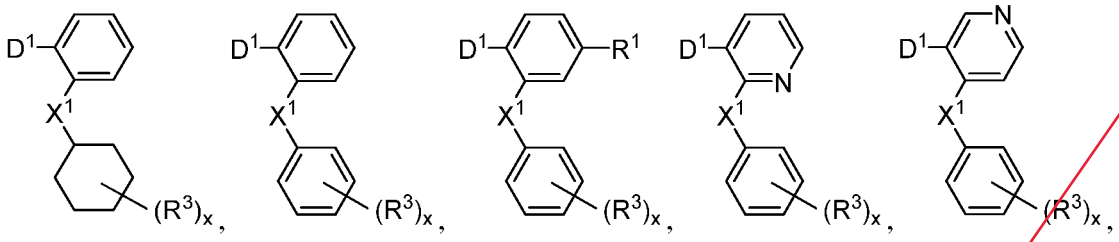
89. The compound of any one of claims 51-88, wherein the moiety of formula:  is of formula:  ,  ,  , or  .

90. The compound of any one of claims 51-89, wherein the compound is of formula:

 ,  ,  ,  ,

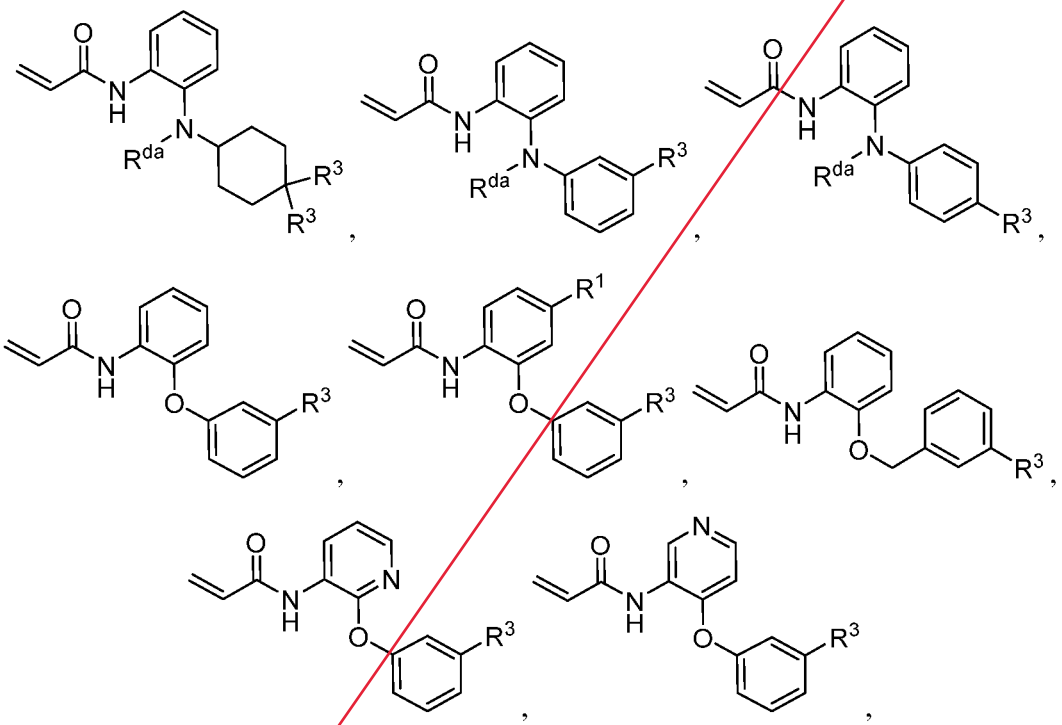
or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

91. The compound of any one of claims 51-90, wherein the compound is of formula:



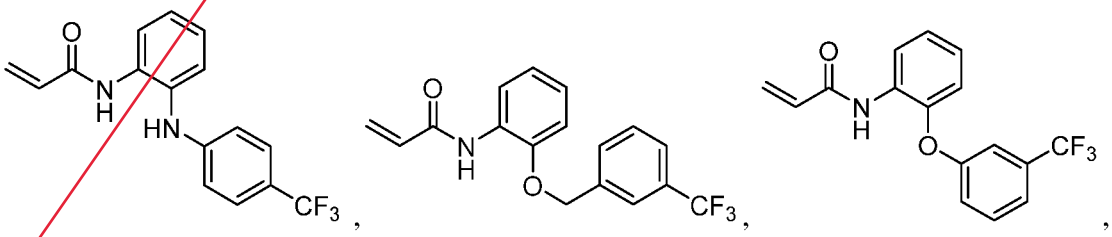
or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

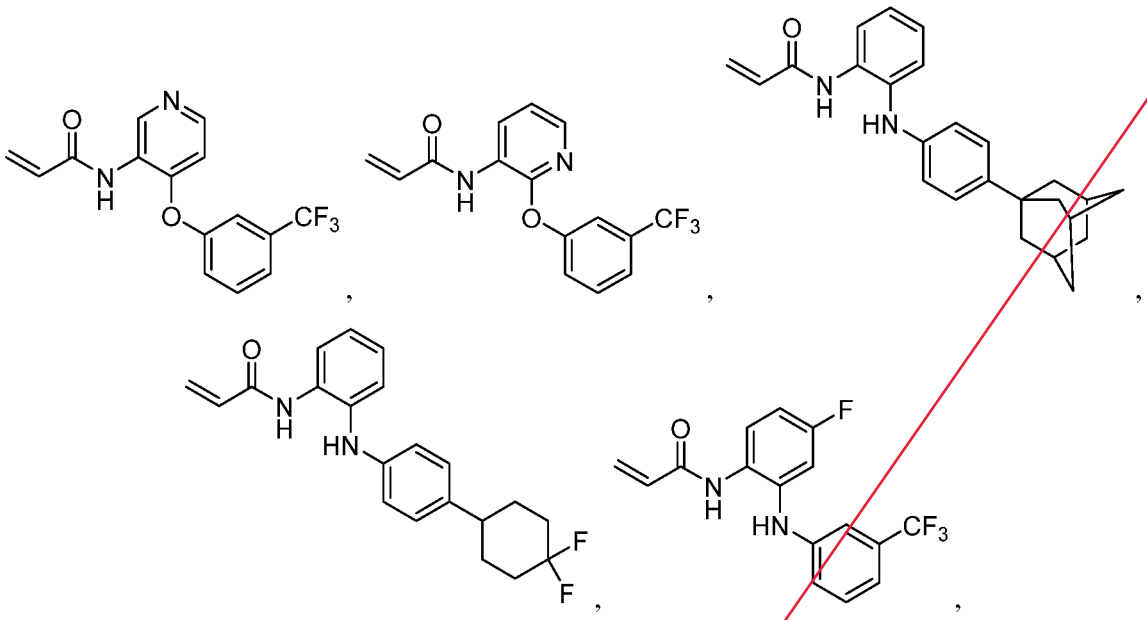
92. The compound of any one of claims 51-91, wherein the compound is of formula:



or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

93. The compound of any one of claims 51-92, wherein the compound is of formula:





or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof.

94. A pharmaceutical composition comprising a compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, and optionally a pharmaceutically acceptable excipient.

95. The pharmaceutical composition of claim 94, wherein the pharmaceutical composition comprises a therapeutically effective amount of the compound for use in treating a proliferative disease in a subject in need thereof.

96. A method of treating a proliferative disease in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 94 or 95.

97. The method of claim 96, wherein the proliferative disease is cancer.

98. The method of claim 97, wherein the cancer is a sarcoma.

99. The method of claim 98, wherein the sarcoma is Kaposi's sarcoma.

100. The method of claim 97, wherein the cancer is lung cancer.

101. The method of claim 100, wherein the lung cancer is non-small cell lung cancer.

102. The method of claim 100, wherein the lung cancer is mesothelioma.

103. The method of claim 97, wherein the cancer is a thyroid cancer.

104. The method of claim 97, wherein the cancer is breast cancer.

105. The method of claim 97, wherein the cancer is liver cancer.

106. The method of claim 97, wherein the cancer is prostate cancer.

107. The method of claim 97, wherein the cancer is pancreatic cancer.

108. The method of claim 97, wherein the cancer is colorectal cancer.

109. The method of claim 97, wherein the cancer is ovarian cancer.

110. The method of claim 97, wherein the cancer is skin cancer.

111. The method of claim 97, wherein the cancer is esophageal cancer.

112. The method of claim 97, wherein the cancer is a carcinoma.

113. The method of claim 97, wherein the cancer is fallopian tube carcinoma.

114. The method of claim 97, wherein the cancer is resistant to inhibitors of EGFR or MEK.

115. The method of claim 96, wherein the proliferative disease is an inflammatory disease.

116. The method of claim 115, wherein the inflammatory disease is fibrosis.

117. The method of claim 96, wherein the proliferative disease is an autoimmune disease.

118. The method of claim 117, wherein the autoimmune disease is sclerosis.

119. A method of inhibiting a transcription factor in a subject in need thereof, the method comprising:

administering to the subject a therapeutically effective amount of a compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 94 or 95.

120. A method of inhibiting a transcription factor in a biological sample, the method comprising:

contacting the biological sample with an effective amount of a compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 94 or 95.

121. A method of inhibiting the transcription of a gene in a subject in need thereof, the method comprising:

administering to the subject a therapeutically effective amount of a compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 94 or 95.

122. A method of inhibiting the transcription of a gene in a biological sample, the method comprising:

contacting the biological sample with an effective amount of a compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 94 or 95.

123. The method of claim 121 or 122, wherein the gene is controlled or regulated by a transcription factor.

124. The method of any one of claims 119, 120, or 123, wherein the transcription factor is TEAD1, TEAD2, TEAD3, or TEAD4.

125. The method of claim 124, wherein the transcription factor is TEAD1.

126. The method of claim 124, wherein the transcription factor is TEAD2.

127. The method of claim 126, wherein the compound is capable of covalently binding TEAD2.

128. The method of claim 126 or 127, wherein the compound is capable of covalently binding a cysteine residue of TEAD2.

129. The method of claim 124, wherein the transcription factor is TEAD4.

130. The method of any one of claims 119-122, wherein the compound is capable of binding the YAP/TAZ domain of a TEAD family transcription factor.

131. The method of claim 120 or 122, wherein the biological sample is a tissue or cell.

132. Use of a compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 94 or 95, for treating a disease in a subject in need thereof.

133. A compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 94 or 95, for use in treating a disease in a subject in need thereof.

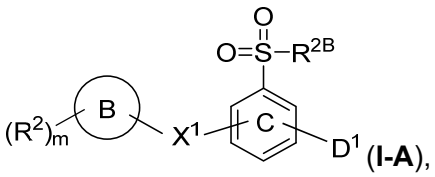
134. A kit comprising: a compound of any one of claims 1-93, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 94 or 95; and

instructions for administering to a subject or contacting a biological sample with the compound, or the pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or the pharmaceutical composition.

CLAIMS

What is claimed is:

1. A compound of Formula (**I-A**):



(**I-A**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof, wherein:

Ring B is cyclohexyl or phenyl;

R^2 is halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN,

wherein R^{c1} is hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom;

wherein each instance of R^{c2} is independently hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group; or optionally two instances of R^{c2} are taken together with their intervening atoms to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring;

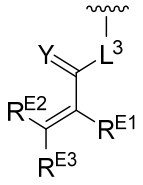
R^{2B} is $–N(R^{c2})_2$, $-OR^{c1}$, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

X^1 is –O-, -O(alkylene)-, alkylene, -S-, $–SCH_2–$, $–N(R^{da})–$, or $–N(R^{da})CH_2–$;

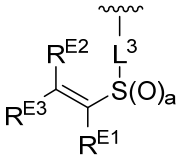
R^{da} is hydrogen, optionally substituted $C_{1–6}$ alkyl, optionally substituted acyl, or a nitrogen protecting group;

m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

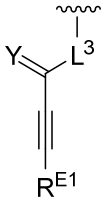
D^1 is a warhead of any one of Formulae (**i-1**) to (**i-23**), (**i-26**) to (**i-31**), (**i-34**) to (**i-40**), (**i-42**), or (**i-43**):



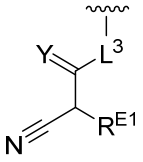
(i-1)



(i-2)



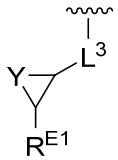
(i-3)



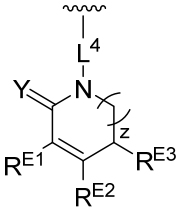
(i-4)



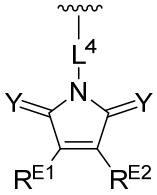
(i-5)



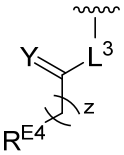
(i-6)



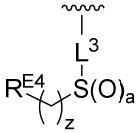
(i-7)



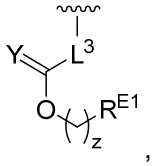
(i-8)



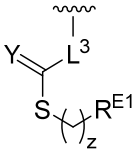
(i-9)



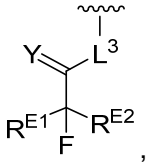
(i-10)



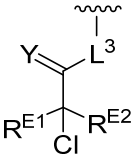
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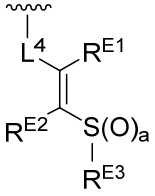
(i-12)



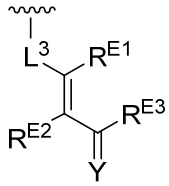
(i-13)



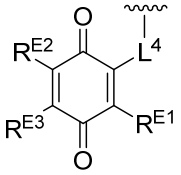
(i-14)



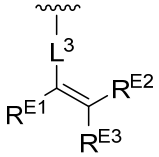
(i-15)



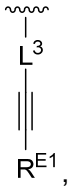
(i-16)



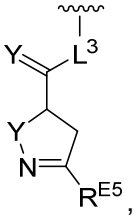
(i-17)



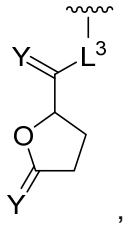
(i-18)



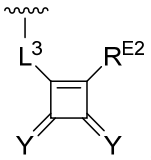
(i-19)



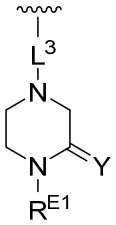
(i-20)



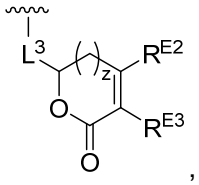
(i-21)



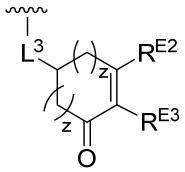
(i-22)



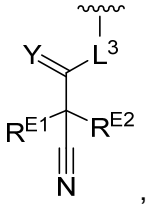
(i-23)



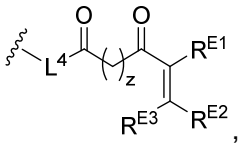
(i-26)



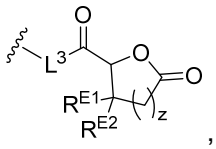
(i-27)



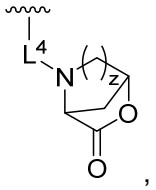
(i-28)



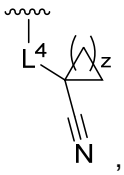
(i-29)



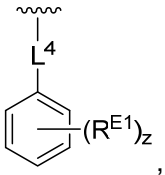
(i-30)



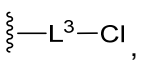
(i-31)



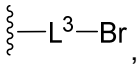
(i-34)



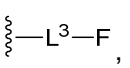
(i-35)



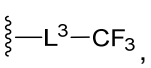
(i-36)



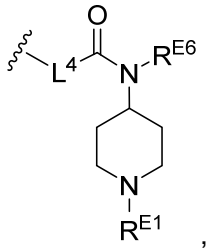
(i-37)



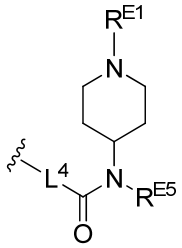
(i-38)



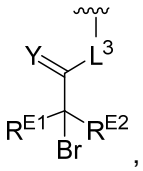
(i-39)



(i-40)



(i-42); or



(i-43)

wherein:

L^3 is a bond or an optionally substituted $C_{1–4}$ hydrocarbon chain, optionally wherein one or more carbon units of the hydrocarbon chain are independently replaced with –C=O–, –O–, –S–, –NR^{L3a}–, –NR^{L3a}C(=O)–, –C(=O)NR^{L3a}–, –SC(=O)–, –C(=O)S–, –OC(=O)–, –C(=O)O–, –NR^{L3a}C(=S)–, –C(=S)NR^{L3a}–, *trans*–CR^{L3b}=CR^{L3b}–, *cis*–CR^{L3b}=CR^{L3b}–, –C≡C–, –S(=O)–, –S(=O)O–, –OS(=O)–, –S(=O)NR^{L3a}–, –NR^{L3a}S(=O)–, –$S(=O)_2$–, –$S(=O)_2$O–, –$OS(=O)_2$–, –$S(=O)_2NR^{L3a}$–, or –$NR^{L3a}S(=O)_2$–, wherein R^{L3a} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group, and wherein each occurrence of R^{L3b} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl,

optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{L3b} groups are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

L^4 is a bond or an optionally substituted, branched or unbranched $C_{1–6}$ hydrocarbon chain;

each of R^{E1}, R^{E2}, and R^{E3} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, –CN, $–CH_2OR^{EE}$, $–CH_2N(R^{EE})_2$, $–CH_2SR^{EE}$, $–OR^{EE}$, $–N(R^{EE})_2$, $–Si(R^{EE})_3$, or $–SR^{EE}$, wherein each instance of R^{EE} is independently hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{EE} groups are joined to form an optionally substituted heterocyclic ring; or R^{E1} and R^{E3}, or R^{E2} and R^{E3}, or R^{E1} and R^{E2} are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

R^{E4} is a leaving group;

R^{E5} is halogen;

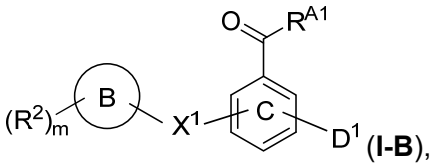
R^{E6} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

each instance of Y is independently O, S, or NR^{E7}, wherein R^{E7} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

a is 1 or 2; and

each instance of z is independently 0, 1, 2, 3, 4, 5, or 6, as valency permits.

2. A compound of Formula (**I-B**):



(**I-B**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof, wherein:

R^{A1} is $–O(R^{a2})$ or $-N(R^{a3})_2$;

R^{a2} is hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or an oxygen protecting group; and

each instance of R^{a3} is independently hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $-SO_2(R^{a4})$, or a nitrogen protecting group, or optionally two instances of R^{a3} are taken together with their intervening atoms to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring; and

R^{a4} is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl;

Ring B is cyclohexyl or phenyl;

R^2 is halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN,

wherein R^{c1} is hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom;

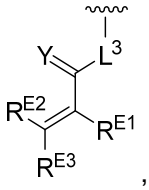
wherein each instance of R^{c2} is independently hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group; or optionally two instances of R^{c2} are taken together with their intervening atoms to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring;

X^1 is –O-, -O(alkylene)-, alkylene, -S-, $–SCH_2–$, $–N(R^{da})–$, or $–N(R^{da})CH_2–$;

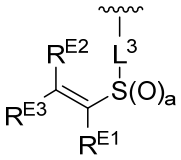
R^{da} is hydrogen, optionally substituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

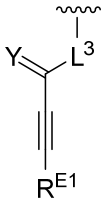
D^1 is a warhead of any one of Formulae (**i-1**) to (**i-23**), (**i-26**) to (**i-31**), (**i-34**) to (**i-40**), (**i-42**), or (**i-43**):



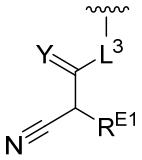
(i-1)



(i-2)



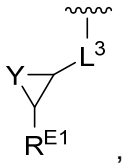
(i-3)



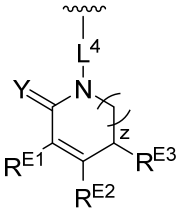
(i-4)



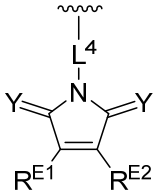
(i-5)



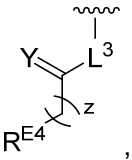
(i-6)



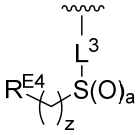
(i-7)



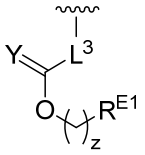
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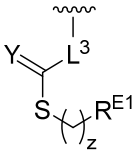
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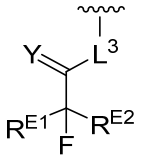
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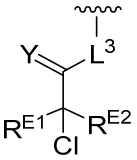
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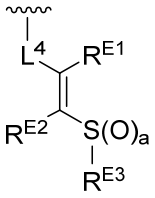
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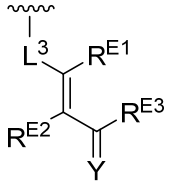
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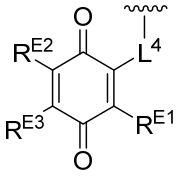
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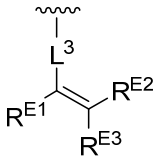
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(i-16)



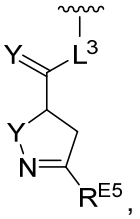
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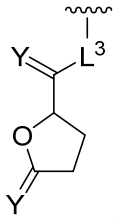
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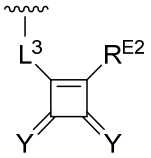
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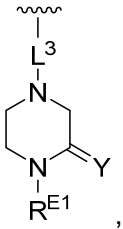
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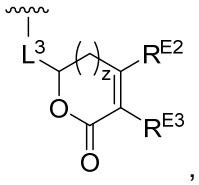
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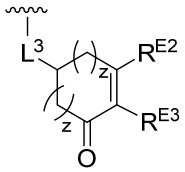
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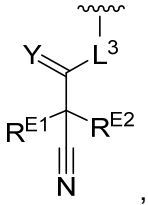
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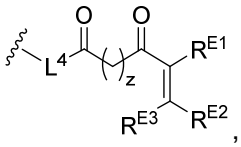
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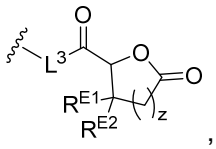
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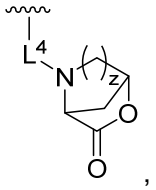
(i-28)



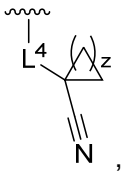
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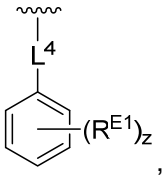
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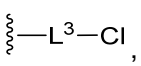
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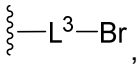
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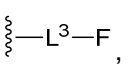
(i-35)



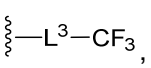
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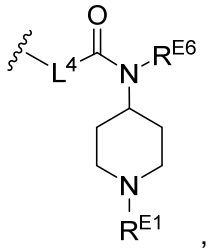
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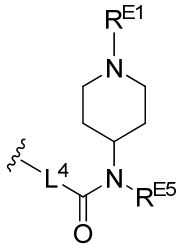
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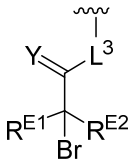
(i-39)



(i-40)



(i-42); or



(i-43)

wherein:

L^3 is a bond or an optionally substituted $C_{1–4}$ hydrocarbon chain, optionally wherein one or more carbon units of the hydrocarbon chain are independently replaced with –C=O–, –O–, –S–, –NR^{L3a}–, –NR^{L3a}C(=O)–, –C(=O)NR^{L3a}–, –SC(=O)–, –C(=O)S–, –OC(=O)–, –C(=O)O–, –NR^{L3a}C(=S)–, –C(=S)NR^{L3a}–, *trans*–CR^{L3b}=CR^{L3b}–, *cis*–CR^{L3b}=CR^{L3b}–, –C≡C–, –S(=O)–, –S(=O)O–, –OS(=O)–, –S(=O)NR^{L3a}–, –NR^{L3a}S(=O)–, –$S(=O)_2$–, –$S(=O)_2$O–, –$OS(=O)_2$–, –$S(=O)_2NR^{L3a}$–, or –$NR^{L3a}S(=O)_2$–, wherein R^{L3a} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group, and wherein each occurrence of R^{L3b} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl,

optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{L3b} groups are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

L^4 is a bond or an optionally substituted, branched or unbranched $C_{1–6}$ hydrocarbon chain;

each of R^{E1}, R^{E2}, and R^{E3} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, –CN, $–CH_2OR^{EE}$, $–CH_2N(R^{EE})_2$, $–CH_2SR^{EE}$, $–OR^{EE}$, $–N(R^{EE})_2$, $–Si(R^{EE})_3$, or $–SR^{EE}$, wherein each instance of R^{EE} is independently hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{EE} groups are joined to form an optionally substituted heterocyclic ring; or R^{E1} and R^{E3}, or R^{E2} and R^{E3}, or R^{E1} and R^{E2} are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

R^{E4} is a leaving group;

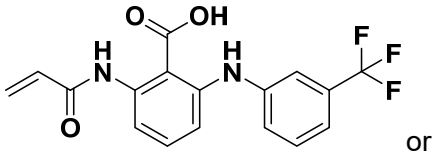
R^{E5} is halogen;

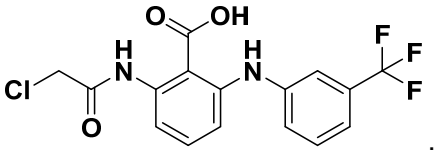
R^{E6} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

each instance of Y is independently O, S, or NR^{E7}, wherein R^{E7} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group;

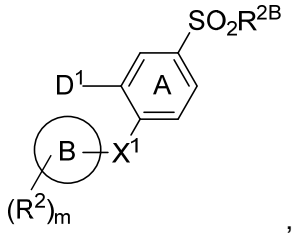
a is 1 or 2; and

each instance of z is independently 0, 1, 2, 3, 4, 5, or 6, as valency permits;

provided that the compound is not of formula:  or

.

3. The compound of claim 1, wherein the compound is of formula:



,

or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

4. The compound of any one of claims 1-3, wherein Ring B is cyclohexyl or phenyl;

m is 0 or 1; and

at least one instance of R^2 is optionally substituted alkyl.

5. The compound of any one of claims 1 or 3-4, wherein R^{2B} is $–N(R^{c2})_2$, and each instance of R^{c2} is independently hydrogen, optionally substituted alkyl, or optionally substituted carbocyclyl;

R^{2B} is $–NH(R^{c2})$, wherein R^{c2} is optionally substituted C_{1-6} alkyl or optionally substituted C_{3-10} carbocyclyl; or

R^{2B} is optionally substituted alkyl.

6. The compound of claim 2, wherein R^{A1} is $–OR^{a2}$, and R^{a2} is hydrogen or optionally substituted alkyl;

R^{A1} is $–N(R^{a3})_2$, wherein at least one instance of R^{a3} is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-10} carbocyclyl, or $-SO_2(R^{a4})$, and R^{a4} is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, or optionally substituted carbocyclyl; or

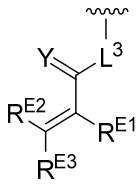
R^{A1} is $–NH(R^{a3})$.

7. The compound of any one of claims 1-6, wherein X^1 is –O-;

$–O(CR^d)_{1–6}–$, and R^d is hydrogen, halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN; or

$–N(R^{da})–$, and R^{da} is hydrogen or optionally substituted $C_{1–6}$ alkyl.

8. The compound of any one of claims 1-7, wherein D^1 is of formula



(**i-1**),

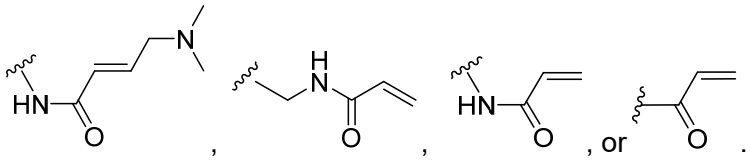
wherein:

L^3 is a bond or optionally substituted C_{1-4} alkyl, and optionally wherein 1 to 2 carbon units of the C_{1-4} alkyl are replaced with –C=O–, $–NR^{L3a}–$, or $–NR^{L3a}C(=O)–$;

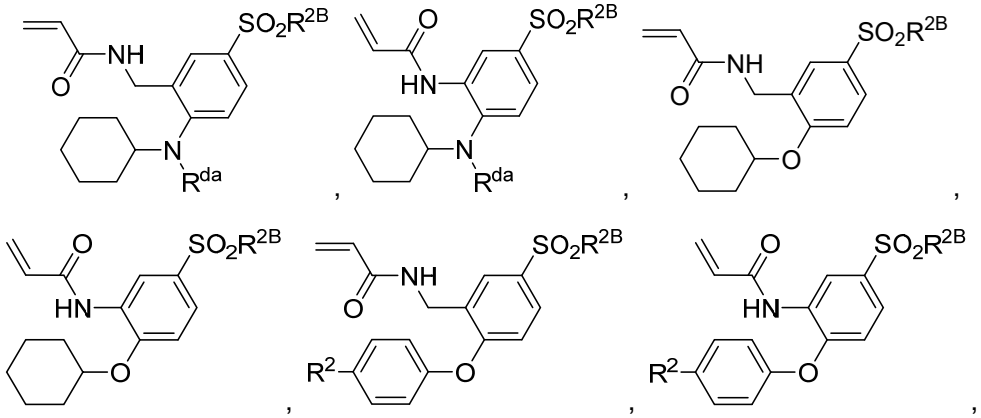
R^{L3a} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group; Y is O; and

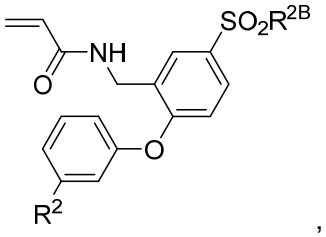
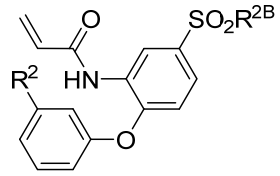
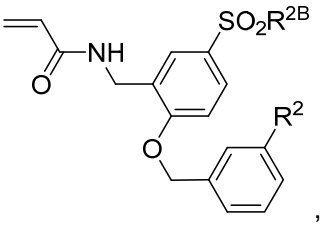
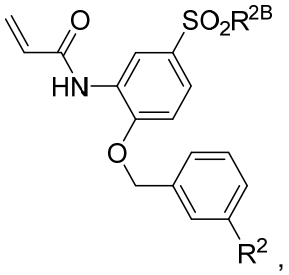
each of R^{E1}, R^{E2}, and R^{E3} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, or optionally substituted alkynyl.

9. The compound of any one of claims 1-8, wherein D^1 is of formula:


, , , or .

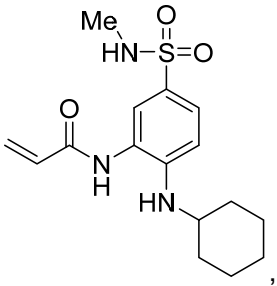
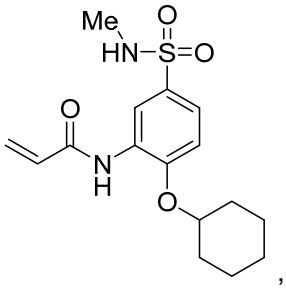
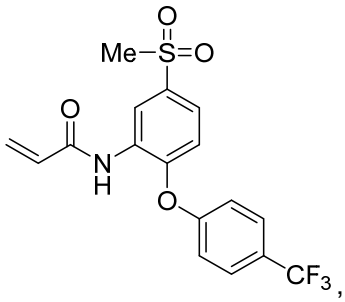
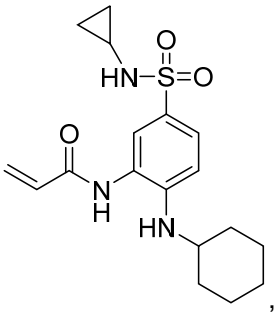
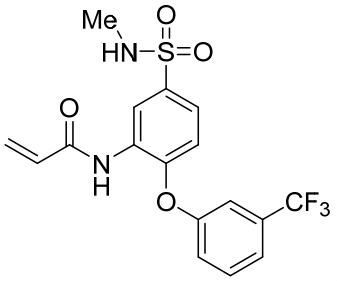
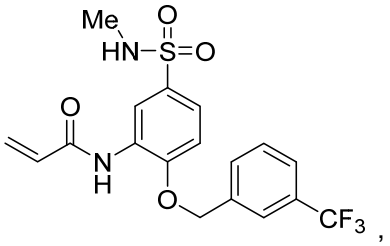
10. The compound of any one of claims 1, 3-5, 7, or 8-9, wherein the compound is of formula:


, , , , , , .

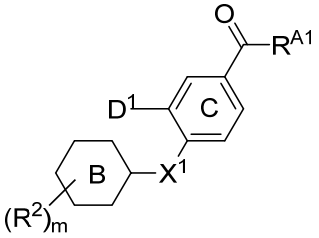
or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

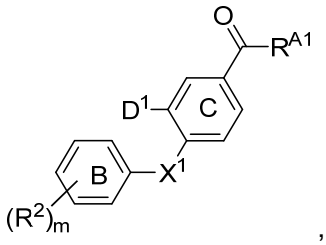
11. The compound of any one of claims 1, 3-5 or 8-10, wherein the compound is of formula:

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof.

12. The compound of any one of claims 2-4, 6-7, 8-9 and 11, wherein the compound is of formula:

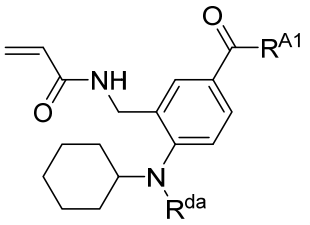


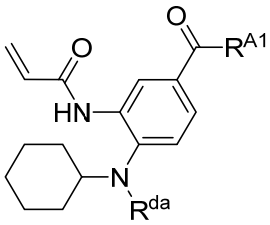
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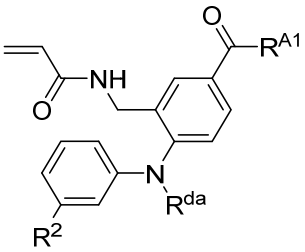
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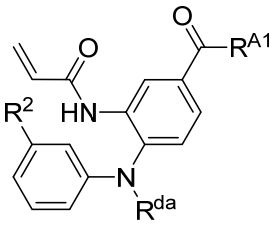
or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

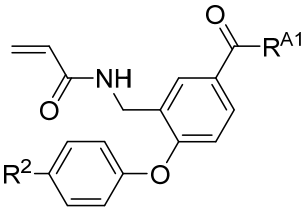
13. The compound of any one of claims 2-4, 6-7, 8-9 and 11-12, wherein the compound is of formula:

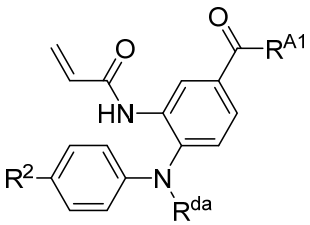


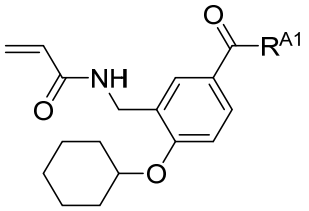
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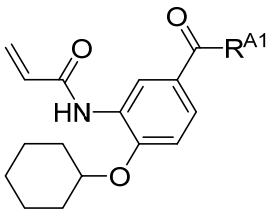
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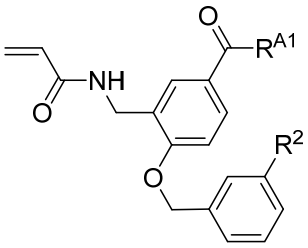
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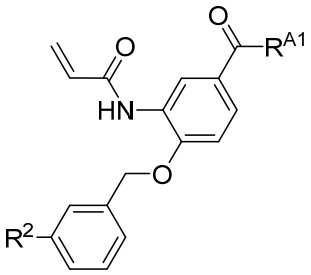
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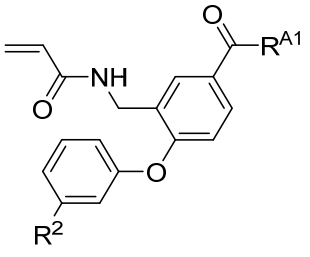
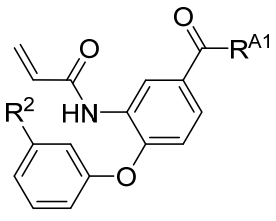
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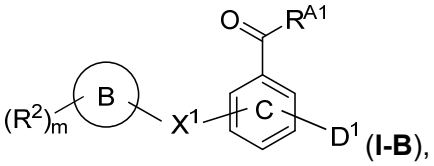
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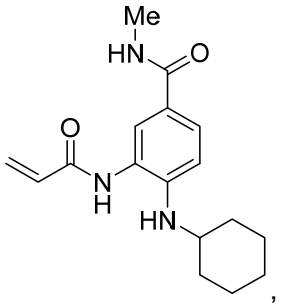
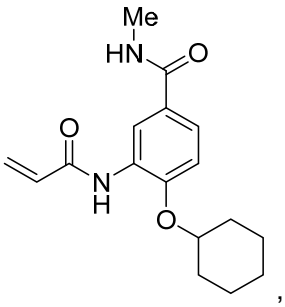
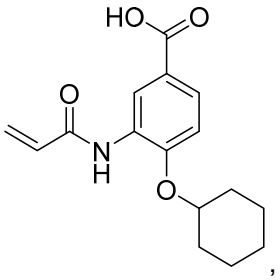
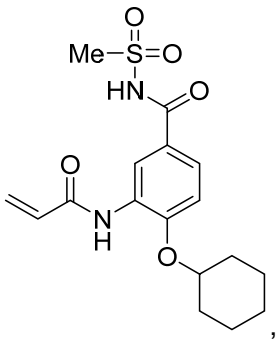
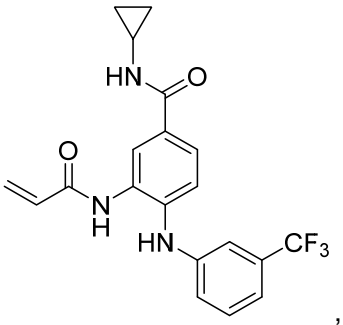
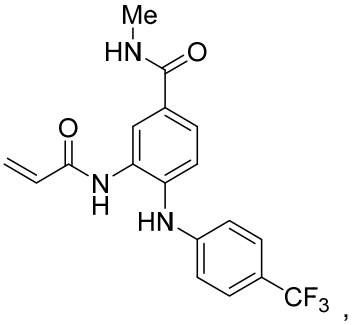
or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

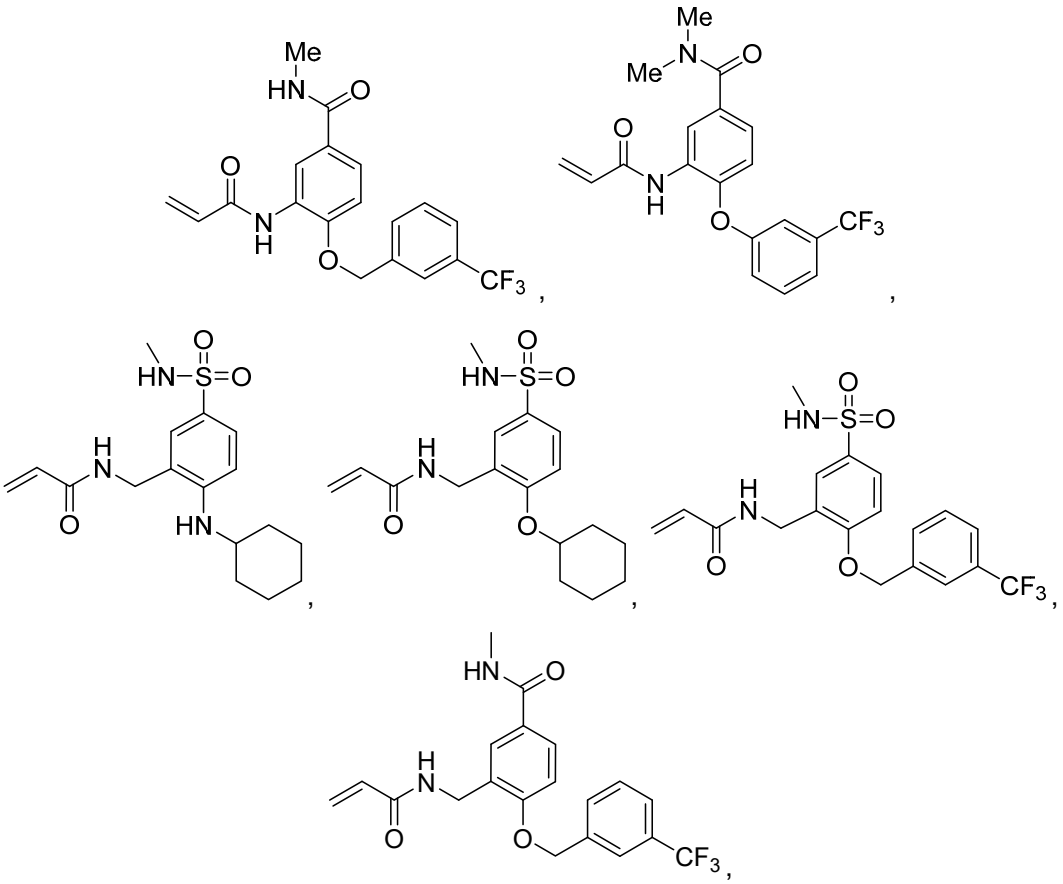
14. The compound of claim 2, wherein the compound is of formula:


(**I-B**),

or a pharmaceutically acceptable salt thereof.

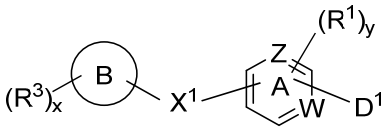
15. The compound of any one of claims 2-4, 6-7, 8-9, and 11-14, wherein the compound is of formula:


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or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof.

16. A compound of Formula (**II**):


(**II**),

or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof, wherein:

Ring B is cyclohexyl or phenyl;

W is $–C(R^a)=$ or –N=, as valency permits; and R^a is hydrogen, halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, $–OR^{c1}$, $–NO_2$, $–N(R^{c2})_2$, $–SR^{c1}$, –CN, or -SCN;

Z is –C(R^b)= or –N=, as valency permits; and R^b is hydrogen, halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, –OR^{c1}, –NO_2, –$N(R^{c2})_2$, –SR^{c1}, –CN, or -SCN;

provided at least one instance of W and Z is –C(R^a)= or –C(R^b)=;

each instance of R^1 is independently halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, –OR^{c1}, –NO_2, –$N(R^{c2})_2$, –SR^{c1}, –CN, or -SCN;

each instance of R^3 is independently halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, –OR^{c1}, –NO_2, –$N(R^{c2})_2$, –SR^{c1}, –CN, or -SCN;

wherein R^{c1} is hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom;

wherein each instance of R^{c2} is independently hydrogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group; or optionally two instances of R^{c2} are taken together with their intervening atoms to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring;

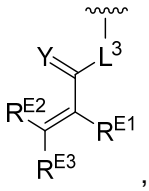
X^1 is –O-, -O(alkylene)-, alkylene, -S-, –SCH_2–, –$N(R^{da})$–, or –$N(R^{da})CH_2$–;

R^{da} is hydrogen, optionally substituted $C_{1–6}$ alkyl, optionally substituted acyl, or a nitrogen protecting group;

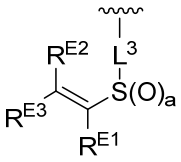
x is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

y is 0, 1, 2, 3, or 4;

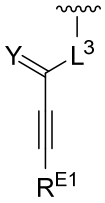
D^1 is a warhead of any one of Formulae (**i-1**) to (**i-23**), (**i-26**) to (**i-31**), (**i-34**) to (**i-40**), (**i-42**), or (**i-43**):



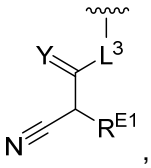
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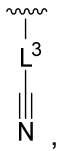
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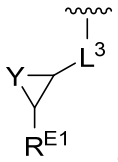


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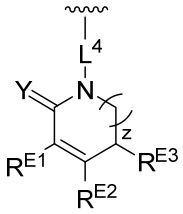


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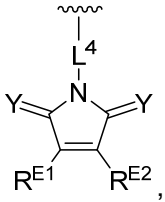
(i-1) **(i-2)** (**i-3**) **(i-4)** **(i-5)**



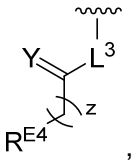
(i-6)



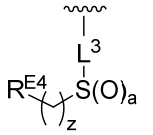
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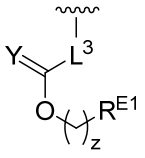
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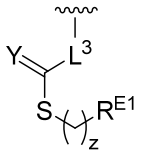
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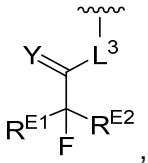
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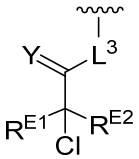
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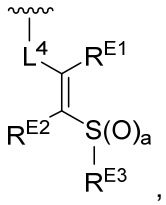
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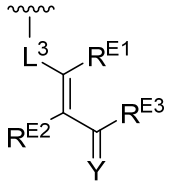
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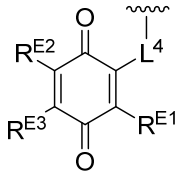
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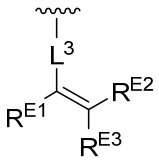
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(i-16)



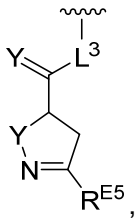
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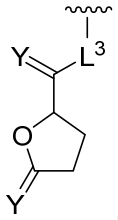
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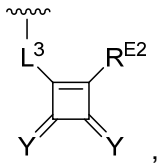
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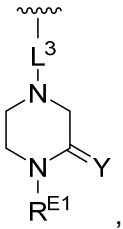
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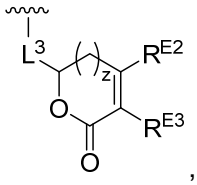
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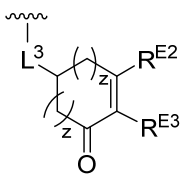
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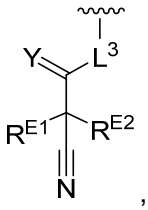
(i-23)



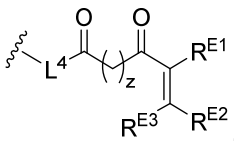
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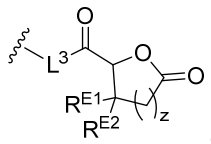
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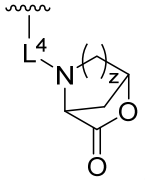
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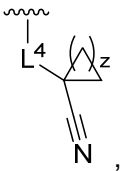
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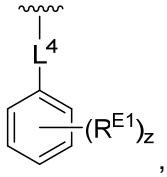
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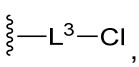
(i-31)



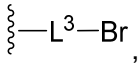
(i-34)



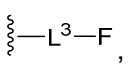
(i-35)



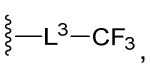
(i-36),



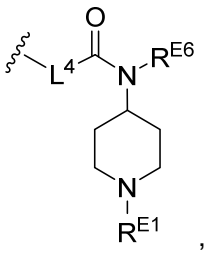
(i-37),



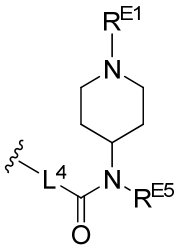
(i-38),



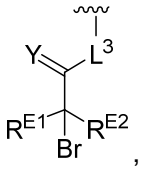
(i-39),



(i-40),



(i-42); or



(i-43),

wherein:

L^3 is a bond or an optionally substituted $C_{1–4}$ hydrocarbon chain, optionally wherein one or more carbon units of the hydrocarbon chain are independently replaced with –C=O–, –O–, –S–, –NR^{L3a}–, –NR^{L3a}C(=O)–, –C(=O)NR^{L3a}–, –SC(=O)–, –C(=O)S–, –OC(=O)–, –C(=O)O–, –NR^{L3a}C(=S)–, –C(=S)NR^{L3a}–, *trans*–CR^{L3b}=CR^{L3b}–, *cis*–CR^{L3b}=CR^{L3b}–, –C≡C–, –S(=O)–, –S(=O)O–, –OS(=O)–, –S(=O)NR^{L3a}–, –NR^{L3a}S(=O)–, –$S(=O)_2$–, –$S(=O)_2$O–, –$OS(=O)_2$–, –$S(=O)_2NR^{L3a}$–, or –$NR^{L3a}S(=O)_2$–, wherein R^{L3a} is hydrogen, substituted or unsubstituted $C_{1–6}$ alkyl, or a nitrogen protecting group, and wherein each occurrence of R^{L3b} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{L3b} groups are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

L^4 is a bond or an optionally substituted, branched or unbranched $C_{1–6}$ hydrocarbon chain;

each of R^{E1}, R^{E2}, and R^{E3} is independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, –CN, –CH_2OR^{EE}, –$CH_2N(R^{EE})_2$, –CH_2SR^{EE}, –OR^{EE}, –$N(R^{EE})_2$, –$Si(R^{EE})_3$, or –SR^{EE}, wherein each instance of R^{EE} is independently hydrogen, optionally substituted alkyl, optionally

substituted alkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{EE} groups are joined to form an optionally substituted heterocyclic ring; or R^{E1} and R^{E3}, or R^{E2} and R^{E3}, or R^{E1} and R^{E2} are joined to form an optionally substituted carbocyclic or optionally substituted heterocyclic ring;

R^{E4} is a leaving group;

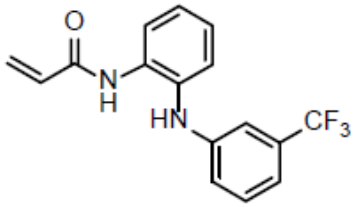
R^{E5} is halogen;

R^{E6} is hydrogen, substituted or unsubstituted C_{1-6} alkyl, or a nitrogen protecting group;

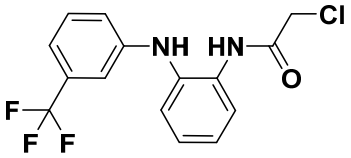
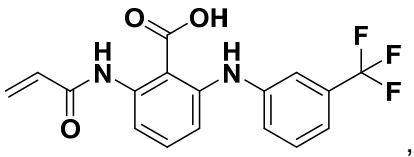
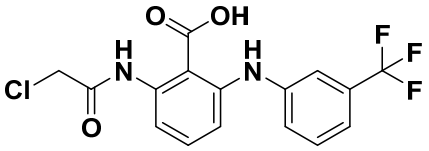
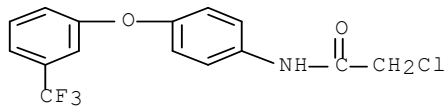
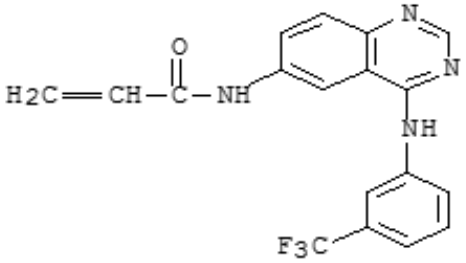
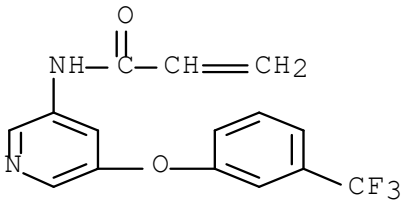
each instance of Y is independently O, S, or NR^{E7}, wherein R^{E7} is hydrogen, substituted or unsubstituted C_{1-6} alkyl, or a nitrogen protecting group;

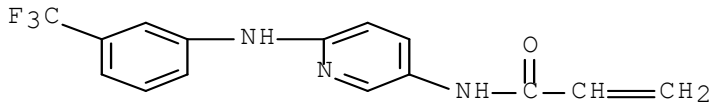
a is 1 or 2; and

each instance of z is independently 0, 1, 2, 3, 4, 5, or 6, as valency permits;

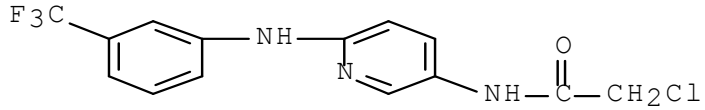


provided that the compound is not of formula:


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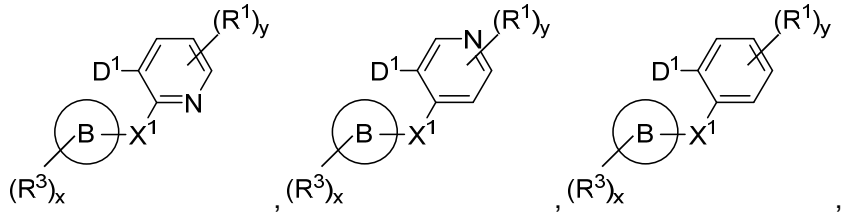


, or



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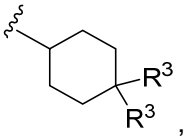
17. The compound of claim 16, wherein Formula (**II**) is of the formula:



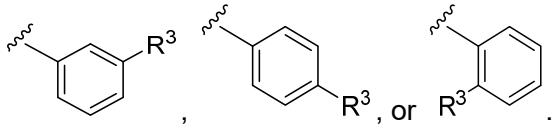
or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

18. The compound of any one of claims 16-17, wherein Ring B is cyclohexyl or phenyl;
x is 0, 1, or 2; and
y is 0 or 1.

19. The compound of any one of claims 16-18, wherein Ring B is of formula:



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20. The compound of any one of claims 16-19, wherein at least one instance of R^3 is halogen, optionally substituted alkyl, or optionally substituted carbocyclyl.

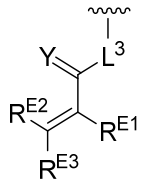
21. The compound of any one of claims 16-20, wherein at least one instance of R^1 is halogen.

22. The compound of any one of claims 16-21, wherein X^1 is –O-;

–O(CR^d)$_{1–6}$–, and R^d is hydrogen, halogen, optionally substituted acyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, –OR^{c1}, –NO_2, –N(R^{c2})$_2$, –SR^{c1}, –CN, or -SCN; or

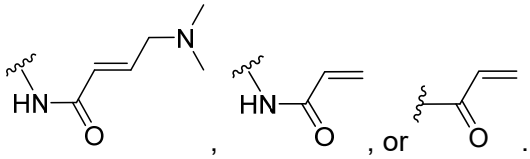
–N(R^{da})–, and R^{da} is hydrogen or optionally substituted $C_{1–6}$ alkyl.

23. The compound of any one of claims 16-22, wherein D^1 is of formula:



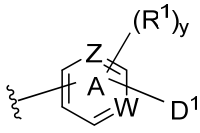
(**i-1**).

24. The compound of any one of claims 16-23, wherein D^1 is of formula:

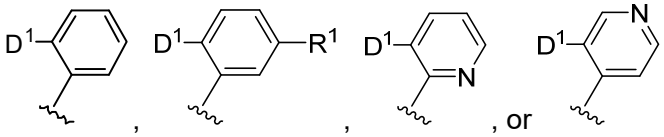


, , , or .

25. The compound of any one of claims 16-24, wherein the moiety of formula:

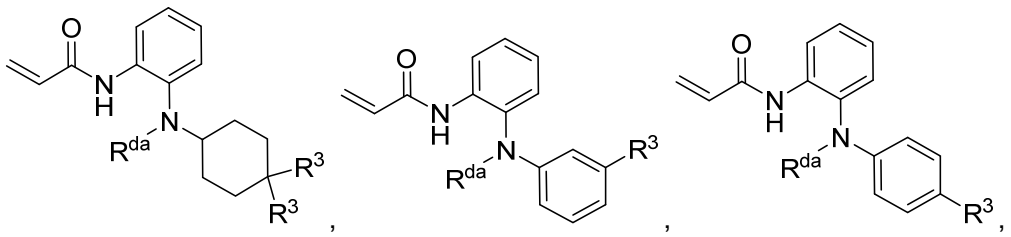


is of formula:

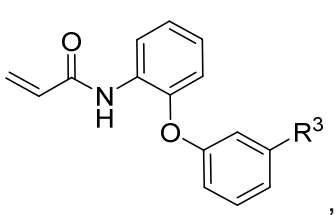
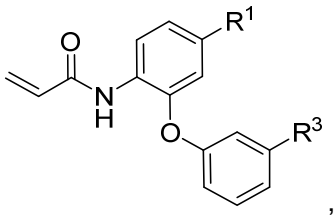
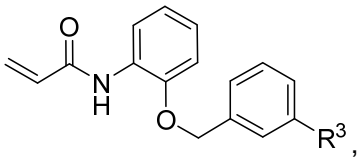
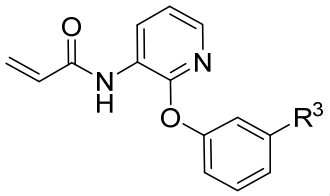
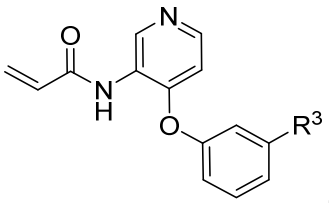


, , , or .

26. The compound of any one of claims 16-25, wherein the compound is of formula:

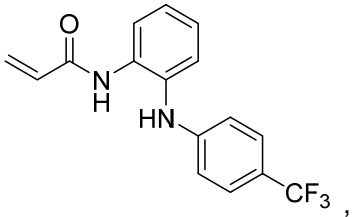
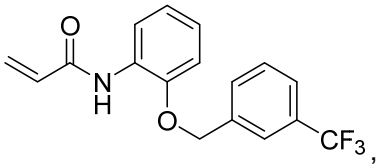
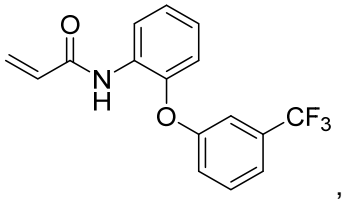
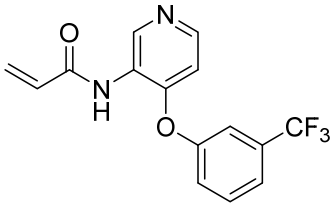
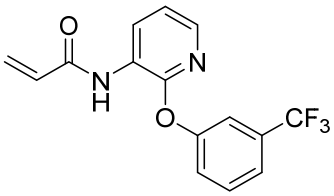
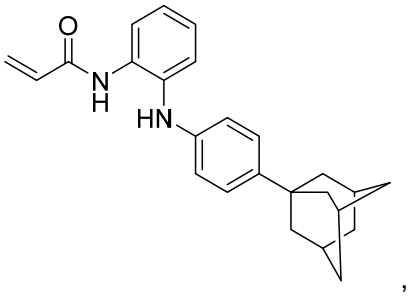
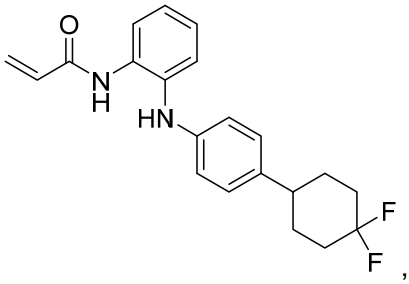
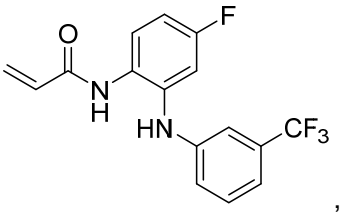


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or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof.

27. The compound of any one of claims 16-26, wherein the compound is of formula:


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or a pharmaceutically acceptable salt, co-crystal, tautomer, stereoisomer, solvate, hydrate, polymorph, isotopically enriched derivative, or prodrug thereof.

28. A pharmaceutical composition comprising a compound of any one of claims 1-27, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, and optionally a pharmaceutically acceptable excipient.

29. Use of a compound of any one of claims 1-27, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 28 in the manufacture of a medicament for treating a proliferative disease in a subject in need thereof, wherein a therapeutically effective amount of the compound, or the pharmaceutical composition is to be administered to the subject.

30. The use of claim 29, wherein the proliferative disease is cancer.

31. The use of claim 30, wherein the cancer is a sarcoma, lung cancer, thyroid cancer, breast cancer, liver cancer, prostate cancer, pancreatic cancer, colorectal cancer, ovarian cancer, skin cancer, esophageal cancer, or a carcinoma.

32. The use of claim 31, wherein the sarcoma is Kaposi’s sarcoma, and the lung cancer is non-small cell lung cancer or mesothelioma.

33. The use of claim 29, wherein the proliferative disease is an inflammatory disease or an autoimmune disease.

34. The use of claim 33, wherein the inflammatory disease is fibrosis, and the autoimmune disease is sclerosis.

35. Use of a compound of any one of claims 1-27, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 28 in the manufacture of a medicament for inhibiting a transcription factor in a subject in need thereof, wherein a therapeutically effective amount of the compound or the pharmaceutical composition is to be administered to the subject.

36. The use of claim 35, wherein the transcription factor is TEAD1, TEAD2, TEAD3, or TEAD4.

37. A compound of any one of claims 1-27, or a pharmaceutically acceptable salt, solvate, hydrate, polymorph, co-crystal, tautomer, stereoisomer, isotopically labeled derivative, or prodrug thereof, or a pharmaceutical composition of claim 28 for use in therapy.