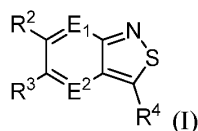


What is Claimed:

1. A compound having a structure of formula (I)



wherein

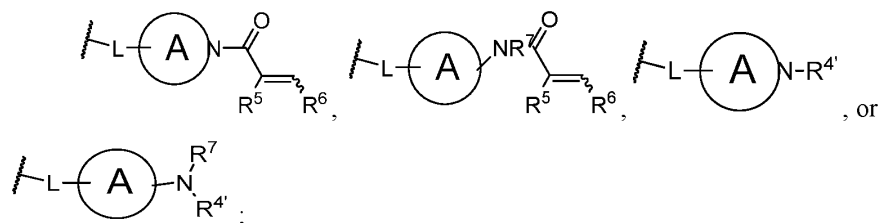
E^1 and E^2 are each independently N or CR^1 ;

R^1 is independently H, hydroxy, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, $NH-C_{1-6}$ alkyl, $N(C_{1-6}alkyl)_2$, cyano, or halo;

R^2 is halo, C_{1-6} alkyl, C_{1-6} haloalkyl, OR^* , $N(R^*)_2$, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{0-3} alkylene- C_{3-14} cycloalkyl, C_{0-3} alkylene- C_{2-14} heterocycloalkyl, aryl, heteroaryl, and each R^* is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-14} cycloalkyl, C_{2-14} heterocycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, or heteroaryl, or two R^* substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

R^3 is halo, C_{1-3} alkyl, C_{1-2} haloalkyl, C_{1-3} alkoxy, C_{3-4} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, or heteroaryl;

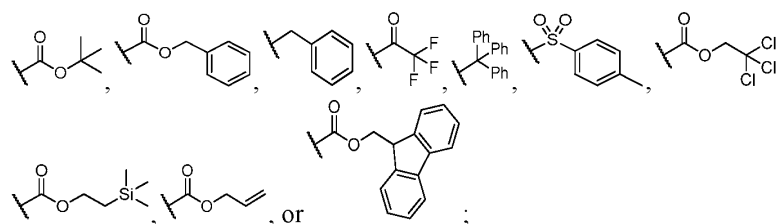
R^4 is



ring A is a monocyclic 4–7 membered ring or a bicyclic, bridged, fused, or spiro 6–11 membered ring;

L is a bond, C_{1-6} alkylene, $-O-C_{0-5}$ alkylene, $-S-C_{0-5}$ alkylene, or $-NH-C_{0-5}$ alkylene, and for C_{2-6} alkylene, $-O-C_{2-5}$ alkylene, $-S-C_{2-5}$ alkylene, and $NH-C_{2-5}$ alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R^4 is H, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkylene- $O-C_{1-4}$ alkyl, C_{1-6} alkylene-OH, C_{1-6} haloalkyl, cycloalkyl, heterocycloalkyl, C_{0-3} alkylene- C_{3-4} cycloalkyl, C_{0-3} alkylene- C_{2-14} heterocycloalkyl, aryl, heteroaryl, C_{0-3} alkylene- C_{6-14} aryl, or selected from

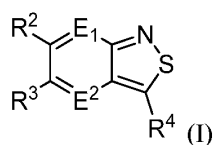


R^5 and R^6 are each independently H, halo, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkylene-O- C_{1-4} alkyl, C_{1-6} alkylene-OH, C_{1-6} haloalkyl, C_{1-6} alkyleneamine, C_{0-6} alkylene-amide, C_{0-3} alkylene-C(O)OH, C_{0-3} alkylene-C(O)OC $_{1-4}$ alkyl, C_{1-6} alkylene-O-aryl, C_{0-3} alkylene-C(O)C $_{1-4}$ alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_{0-3} alkylene-C $_{3-14}$ cycloalkyl, C_{0-3} alkylene-C $_{2-14}$ heterocycloalkyl, C_{0-3} alkylene-C $_{6-14}$ aryl, C_{0-3} alkylene-C $_{2-14}$ heteroaryl, or cyano, or R^5 and R^6 , together with the atoms to which they are attached, form a 4–6 membered ring; and

R^7 is H or C_{1-8} alkyl, or R^7 and R^5 , together with the atoms to which they are attached, form a 4–6 membered ring; or

a pharmaceutically acceptable salt thereof.

2. A compound having a structure of formula (I)



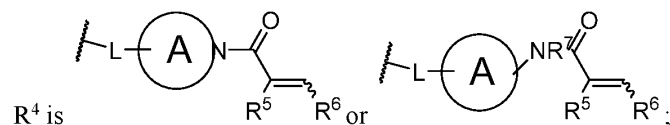
wherein

E^1 and E^2 are each independently N or CR¹;

R^1 is independently H, hydroxy, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, NH- C_{1-6} alkyl, N(C_{1-4} alkyl)₂, cyano, or halo;

R^2 is halo, C_{1-6} alkyl, C_{1-6} haloalkyl, OR', N(R')₂, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{0-3} alkylene-C $_{3-14}$ cycloalkyl, C_{0-3} alkylene-C $_{2-14}$ heterocycloalkyl, aryl, heteroaryl, C_{0-3} alkylene-C $_{6-14}$ aryl, or C_{0-3} alkylene-C $_{2-14}$ heteroaryl, and each R' is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-14} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, or heteroaryl, or two R' substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

R^3 is halo, C_{1-3} alkyl, C_{1-2} haloalkyl, C_{1-3} alkoxy, C_{3-14} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, or heteroaryl;



ring A is a monocyclic 4–7 membered ring or a bicyclic, bridged, fused, or spiro 6–11 membered ring;

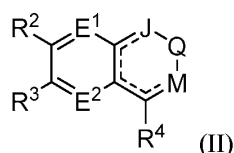
L is a bond, C₁₋₆alkylene, -O-C₀₋₅alkylene, -S-C₀₋₅alkylene, or -NH-C₀₋₅alkylene, and for C₂₋₆alkylene, -O-C₂₋₅alkylene, -S-C₂₋₅alkylene, and NH-C₂₋₅alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R⁵ and R⁶ are each independently H, halo, C₁₋₈alkyl, C₂₋₈alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, C₁₋₆alkyleneamine, C₀₋₆alkylene-amide, C₀₋₃alkylene-C(O)OH, C₀₋₃alkylene-C(O)OC₁₋₄alkyl, C₁₋₆alkylene-O-aryl, C₀₋₃alkylene-C(O)C₁₋₄alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, C₀₋₃alkylene-C₆₋₁₄aryl, C₀₋₃alkylene-C₂₋₁₄heteroaryl, or cyano, or R⁵ and R⁶, together with the atoms to which they are attached, form a 4–6 membered ring; and

R⁷ is H or C₁₋₆alkyl, or R⁷ and R⁵, together with the atoms to which they are attached, form a 4–6 membered ring; or

a pharmaceutically acceptable salt thereof.

3. A compound having a structure of formula (II)



wherein

E¹ and E² are each independently N or CR¹;

J is N, NR¹⁰, or CR¹⁰;

M is N, NR¹³, or CR¹³;

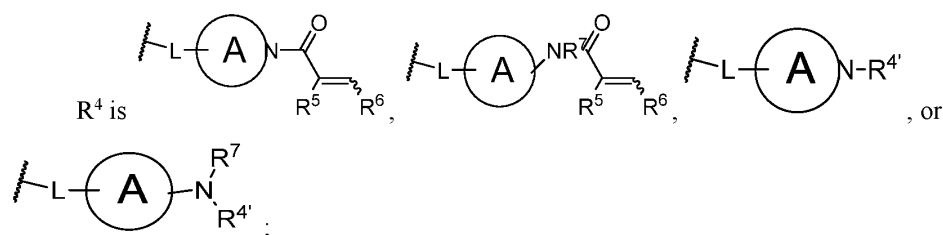
== is a single or double bond as necessary to give every atom its normal valence;

R¹ is independently H, hydroxy, C₁₋₆alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxy, NH-C₁₋₄alkyl, N(C₁₋₄alkyl)₂, cyano, or halo;

R² is halo, C₁₋₆alkyl, C₁₋₆haloalkyl, OR', N(R')₂, C₂₋₃alkenyl, C₂₋₃alkynyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or C₀₋₃alkylene-C₂₋₁₄heteroaryl, and each R' is independently H, C₁₋

6alkyl, C₁₋₆haloalkyl, C₃₋₁₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl, or two R⁷ substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

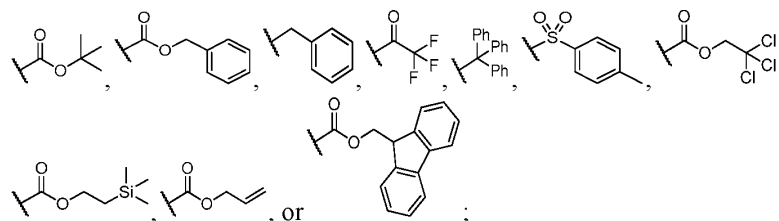
R³ is halo, C₁₋₃alkyl, C₁₋₂haloalkyl, C₁₋₃alkoxy, C₃₋₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl;



ring A is a monocyclic 4–7 membered ring or a bicyclic, bridged, fused, or spiro 6–11 membered ring;

L is a bond, C₁₋₆alkylene, -O-C₀₋₅alkylene, -S-C₀₋₅alkylene, or -NH-C₀₋₅alkylene, and for C₂₋₆alkylene, -O-C₂₋₅alkylene, -S-C₂₋₅alkylene, and NH-C₂₋₅alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R⁴ is H, C₁₋₈alkyl, C₂₋₈alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, cycloalkyl, heterocycloalkyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or selected from



R⁵ and R⁶ are each independently H, halo, C₁₋₆alkyl, C₂₋₆alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, C₁₋₆alkyleneamine, C₀₋₆alkylene-amide, C₀₋₃alkylene-C(O)OH, C₀₋₃alkylene-C(O)OC₁₋₄alkyl, C₁₋₆alkylene-O-aryl, C₀₋₃alkylene-C(O)C₁₋₄alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, C₀₋₃alkylene-C₆₋₁₄aryl, C₀₋₃alkylene-C₂₋₁₄heteroaryl, or cyano, or R⁵ and R⁶, together with the atoms to which they are attached, form a 4–6 membered ring;

R⁷ is H or C₁₋₈alkyl, or R⁷ and R⁵, together with the atoms to which they are attached, form a 4–6 membered ring;

Q is CR⁸R⁹, C=CR⁸R⁹, C=O, C=S, or C=NR⁸;

R^8 and R^9 are each independently H, C_{1-3} alkyl, hydroxy, C_{1-3} alkoxy, cyano, nitro, or C_{3-6} cycloalkyl, or R^8 and R^9 , taken together with the carbon atom to which they are attached, can form a 3–6 membered ring;

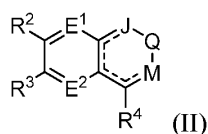
R^{10} is C_{1-8} alkyl, C_{0-3} alkylene- C_{6-14} aryl, C_{0-3} alkylene- C_{3-14} heteroaryl, C_{0-3} alkylene- C_{3-14} cycloalkyl, C_{0-3} alkylene- C_{2-14} heterocycloalkyl, C_{1-6} alkoxy, $O-C_{0-3}$ alkylene- C_{6-14} aryl, $O-C_{0-3}$ alkylene- C_{3-14} heteroaryl, $O-C_{0-3}$ alkylene- C_{3-14} cycloalkyl, $O-C_{0-3}$ alkylene- C_{2-14} heterocycloalkyl, $NH-C_{1-8}$ alkyl, $N(C_{1-8}alkyl)_2$, $NH-C_{0-3}alkylene-C_{6-14}aryl$, $NH-C_{0-3}alkylene-C_{2-14}heteroaryl$, $NH-C_{0-3}alkylene-C_{3-14}cycloalkyl$, $NH-C_{0-3}alkylene-C_{2-14}heterocycloalkyl$, halo, cyano, or C_{1-6} alkylene-amine; and

R^{13} is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkyleneamine, or C_{3-14} cycloalkyl; or a pharmaceutically acceptable salt thereof,

with the proviso that

- (1) when J is NR^{10} , M is N or CR^{13} ;
- (2) when M is NR^{13} , J is N or CR^{10} ;
- (3) when J is CR^{10} , M is N or NR^{13} ; and
- (4) when M is CR^{13} , J is N or NR^{10} .

4. A compound having a structure of formula (II)



wherein

E^1 and E^2 are each independently N or CR^1 ;

J is N, NR^{10} , or CR^{10} ;

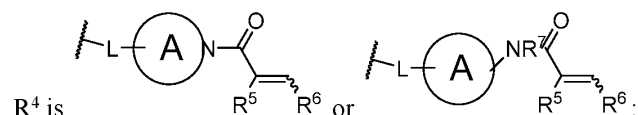
M is N, NR^{13} , or CR^{13} ;

== is a single or double bond as necessary to give every atom its normal valence;

R^1 is independently H, hydroxy, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, $NH-C_{1-4}$ alkyl, $N(C_{1-4}alkyl)_2$, cyano, or halo;

R^2 is halo, C_{1-6} alkyl, C_{1-6} haloalkyl, OR' , $N(R')_2$, $C_{2-3}alkenyl$, $C_{2-3}alkynyl$, $C_{0-3}alkylene-C_{3-14}cycloalkyl$, $C_{0-3}alkylene-C_{2-14}heterocycloalkyl$, aryl, heteroaryl, $C_{0-3}alkylene-C_{6-14}aryl$, or $C_{0-3}alkylene-C_{2-14}heteroaryl$, and each R' is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, $C_{3-14}cycloalkyl$, $C_{2-14}heterocycloalkyl$, $C_{2-3}alkenyl$, $C_{2-3}alkynyl$, aryl, or heteroaryl, or two R' substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

R^3 is halo, C_{1-3} alkyl, C_{1-2} haloalkyl, C_{1-3} alkoxy, C_{3-4} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, or heteroaryl;



ring A is a monocyclic 4–7 membered ring or a bicyclic, bridged, fused, or spiro 6–11 membered ring;

L is a bond, C_{1-6} alkylene, $-O-C_{0-5}$ alkylene, $-S-C_{0-5}$ alkylene, or $-NH-C_{0-5}$ alkylene, and for C_{2-6} alkylene, $-O-C_{2-5}$ alkylene, $-S-C_{2-5}$ alkylene, and $NH-C_{2-5}$ alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R^5 and R^6 are each independently H, halo, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkylene-O- C_{1-4} alkyl, C_{1-6} alkylene-OH, C_{1-6} haloalkyl, C_{1-6} alkyleneamine, C_{0-6} alkylene-amide, C_{0-3} alkylene-C(O)OH, C_{0-3} alkylene-C(O)OC $_{1-4}$ alkyl, C_{1-6} alkylene-O-aryl, C_{0-3} alkylene-C(O) C_{1-4} alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_{0-3} alkylene- C_{3-14} cycloalkyl, C_{0-3} alkylene- C_{2-14} heterocycloalkyl, C_{0-3} alkylene- C_{6-14} aryl, C_{0-3} alkylene- C_{2-14} heteroaryl, or cyano, or R^5 and R^6 , together with the atoms to which they are attached, form a 4–6 membered ring;

R^7 is H or C_{1-8} alkyl, or R^7 and R^5 , together with the atoms to which they are attached, form a 4–6 membered ring;

Q is CR^8R^9 , $C=CR^8R^9$, $C=O$, $C=S$, or $C=NR^8$;

R^8 and R^9 are each independently H, C_{1-3} alkyl, hydroxy, C_{1-3} alkoxy, cyano, nitro, or C_{3-6} cycloalkyl, or R^8 and R^9 , taken together with the carbon atom to which they are attached, can form a 3–6 membered ring;

R^{10} is C_{1-8} alkyl, C_{0-3} alkylene- C_{6-14} aryl, C_{0-3} alkylene- C_{3-14} heteroaryl, C_{0-3} alkylene- C_{3-14} cycloalkyl, C_{0-3} alkylene- C_{2-14} heterocycloalkyl, C_{1-6} alkoxy, $O-C_{0-3}$ alkylene- C_{6-14} aryl, $O-C_{0-3}$ alkylene- C_{3-14} heteroaryl, $O-C_{0-3}$ alkylene- C_{3-14} cycloalkyl, $O-C_{0-3}$ alkylene- C_{2-14} heterocycloalkyl, $NH-C_{1-8}$ alkyl, $N(C_{1-8}alkyl)_2$, $NH-C_{0-3}alkylene-C_{6-14}aryl$, $NH-C_{0-3}alkylene-C_{2-14}heteroaryl$, $NH-C_{0-3}alkylene-C_{3-14}cycloalkyl$, $NH-C_{0-3}alkylene-C_{2-14}heterocycloalkyl$, halo, cyano, or C_{1-6} alkylene-amine; and

R^{13} is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkyleneamine, or C_{3-14} cycloalkyl; or a pharmaceutically acceptable salt thereof,

with the proviso that

- (1) when J is NR^{10} , M is N or CR^{13} ;
- (2) when M is NR^{13} , J is N or CR^{10} ;

(3) when J is CR¹⁰, M is N or NR¹³; and

(4) when M is CR¹³, J is N or NR¹⁰.

5. The compound of claim 3 or 4, wherein when Q is C=O; and E¹ and E² are each CR¹; then either

(1) R¹⁰ is C₁₋₃alkylene-C₆₋₁₄aryl, C₁₋₃alkylene-C₃₋₁₄heteroaryl, C₀₋₃alkylene-C₃₋₈cycloalkyl, C₁₋₃alkylene-C₂₋₇heterocycloalkyl, or halo; or

(2) R¹³ is C₁₋₃haloalkyl or C₃₋₅cycloalkyl.

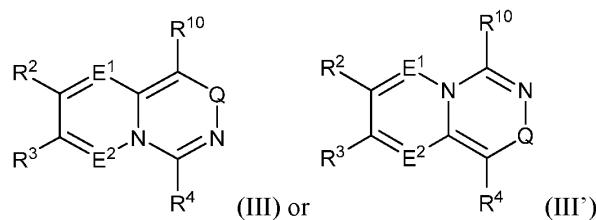
6. The compound of claim 3 or 4, wherein J is NR¹⁰ and M is CR¹³.

7. The compound of claim 3 or 4, wherein J is CR¹⁰ and M is NR¹³.

8. The compound of claim 3 or 4, wherein J is N and M is NR¹³.

9. The compound of claim 3 or 4, wherein J is NR¹⁰ and M is N.

10. A compound having a structure of formula (III) or (III'):



wherein

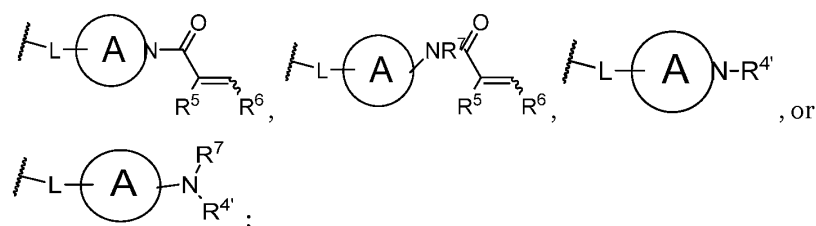
E¹ and E² are each independently N or CR¹;

R¹ is independently H, hydroxy, C₁₋₆alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxy, NH-C₁₋₄alkyl, N(C₁₋₄alkyl)₂, cyano, or halo;

R² is halo, C₁₋₆alkyl, C₁₋₆haloalkyl, OR', N(R')₂, C₂₋₃alkenyl, C₂₋₃alkynyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or C₀₋₃alkylene-C₂₋₁₄heteroaryl, and each R' is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl, or two R' substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

R³ is halo, C₁₋₃alkyl, C₁₋₂haloalkyl, C₁₋₃alkoxy, C₃₋₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl;

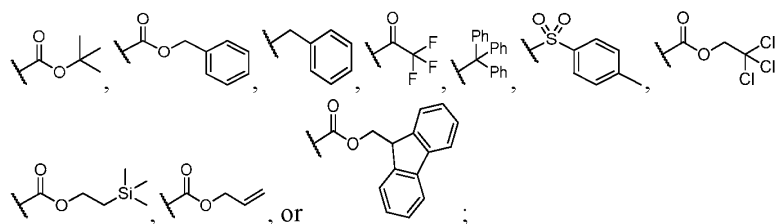
R⁴ is



ring A is a monocyclic 4–7 membered ring or a bicyclic, bridged, fused, or spiro 6–11 membered ring;

L is a bond, C₁₋₆alkylene, -O-C₀₋₅alkylene, -S-C₀₋₅alkylene, or -NH-C₀₋₅alkylene, and for C₂₋₆alkylene, -O-C₂₋₅alkylene, -S-C₂₋₅alkylene, and NH-C₂₋₅alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R^{4'} is H, C₁₋₈alkyl, C₂₋₈alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, cycloalkyl, heterocycloalkyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or selected from



R⁵ and R⁶ are each independently H, halo, C₁₋₆alkyl, C₂₋₆alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, C₁₋₆alkyleneamine, C₀₋₆alkylene-amide, C₀₋₃alkylene-C(O)OH, C₀₋₃alkylene-C(O)OC₁₋₄alkyl, C₁₋₆alkylene-O-aryl, C₀₋₃alkylene-C(O)C₁₋₄alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, C₀₋₃alkylene-C₆₋₁₄aryl, C₀₋₃alkylene-C₂₋₁₄heteroaryl, or cyano, or R⁵ and R⁶, together with the atoms to which they are attached, form a 4–6 membered ring;

R⁷ is H or C₁₋₈alkyl, or R⁷ and R⁵, together with the atoms to which they are attached, form a 4–6 membered ring;

Q is CR⁸R⁹, C=CR⁸R⁹, C=O, C=S, or C=NR⁸;

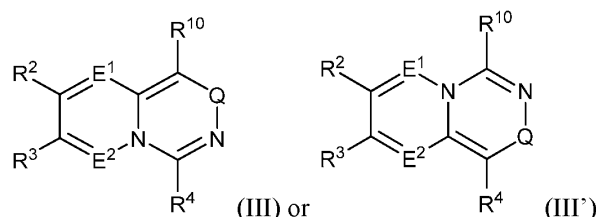
R⁸ and R⁹ are each independently H, C₁₋₆alkyl, hydroxy, C₁₋₆alkoxy, cyano, nitro, or C₃₋₁₄cycloalkyl, or R⁸ and R⁹, taken together with the carbon atom to which they are attached, can form a 3–6 membered ring;

R¹⁰ is C₁₋₈alkyl, C₀₋₃alkylene-C₆₋₁₄aryl, C₀₋₃alkylene-C₃₋₁₄heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, C₁₋₆alkoxy, O-C₀₋₃alkylene-C₆₋₁₄aryl,

O-C₀₋₃alkylene-C₃₋₁₄heteroaryl, O-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, O-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, NH-C₁₋₈alkyl, N(C₁₋₈alkyl)₂, NH-C₀₋₃alkylene-C₆₋₁₄aryl, NH-C₀₋₃alkylene-C₂₋₁₄heteroaryl, NH-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, NH-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, halo, cyano, or C₁₋₆alkylene-amine; or

a pharmaceutically acceptable salt thereof.

11. A compound having a structure of formula (III) or (III'):



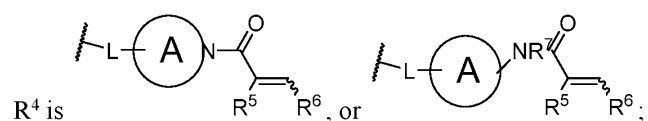
wherein

E¹ and E² are each independently N or CR¹;

R¹ is independently H, hydroxy, C₁₋₆alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxy, NH-C₁₋₄alkyl, N(C₁₋₄alkyl)₂, cyano, or halo;

R² is halo, C₁₋₆alkyl, C₁₋₆haloalkyl, OR', N(R')₂, C₂₋₃alkenyl, C₂₋₃alkynyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or C₀₋₃alkylene-C₂₋₁₄heteroaryl, and each R' is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl, or two R' substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

R³ is halo, C₁₋₃alkyl, C₁₋₂haloalkyl, C₁₋₃alkoxy, C₃₋₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl;



ring A is a monocyclic 4-7 membered ring or a bicyclic, bridged, fused, or spiro 6-11 membered ring;

L is a bond, C₁₋₆alkylene, -O-C₀₋₅alkylene, -S-C₀₋₅alkylene, or -NH-C₀₋₅alkylene, and for C₂₋₆alkylene, -O-C₂₋₅alkylene, -S-C₂₋₅alkylene, and NH-C₂₋₅alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R⁵ and R⁶ are each independently H, halo, C₁₋₆alkyl, C₂₋₆alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, C₁₋₆alkyleneamine, C₀₋₆alkylene-amide, C₀₋

₃alkylene-C(O)OH, C₀₋₃alkylene-C(O)OC₁₋₄alkyl, C₁₋₆alkylene-O-aryl, C₀₋₃alkylene-C(O)C₁₋₄alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, C₀₋₃alkylene-C₆₋₁₄aryl, C₀₋₃alkylene-C₂₋₁₄heteroaryl, or cyano, or R⁵ and R⁶, together with the atoms to which they are attached, form a 4–6 membered ring;

R⁷ is H or C₁₋₈alkyl, or R⁷ and R⁵, together with the atoms to which they are attached, form a 4–6 membered ring;

Q is CR⁸R⁹, C=CR⁸R⁹, C=O, C=S, or C=NR⁸;

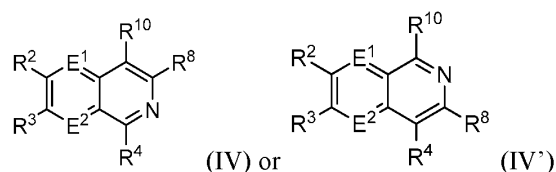
R⁸ and R⁹ are each independently H, C₁₋₆alkyl, hydroxy, C₁₋₆alkoxy, cyano, nitro, or C₃₋₁₄cycloalkyl, or R⁸ and R⁹, taken together with the carbon atom to which they are attached, can form a 3–6 membered ring;

R¹⁰ is C₁₋₈alkyl, C₀₋₃alkylene-C₆₋₁₄aryl, C₀₋₃alkylene-C₃₋₁₄heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, C₁₋₆alkoxy, O-C₀₋₃alkylene-C₆₋₁₄aryl, O-C₀₋₃alkylene-C₃₋₁₄heteroaryl, O-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, O-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, NH-C₁₋₈alkyl, N(C₁₋₈alkyl)₂, NH-C₀₋₃alkylene-C₆₋₁₄aryl, NH-C₀₋₃alkylene-C₂₋₁₄heteroaryl, NH-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, NH-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, halo, cyano, or C₁₋₆alkylene-amine; or

a pharmaceutically acceptable salt thereof.

12. The compound of claim 10 or 11, having a structure of formula (III).
13. The compound of claim 10 or 11, having a structure of formula (III').
14. The compound of any one of claims 3 to 12, wherein Q is C=O.
15. The compound of any one of claims 3 to 12, wherein Q is C=S.
16. The compound of any one of claims 3 to 12, wherein Q is C=NR⁸.
17. The compound of claim 16, wherein R⁸ is C₁₋₂alkyl.
18. The compound of any one of claims 3 to 12, wherein Q is CR⁸R⁹.
19. The compound of any one of claims 3 to 12, wherein Q is C=CR⁸R⁹.
20. The compound of claim 18 or 19, wherein R⁸ and R⁹, taken together with the carbon atom to which they are attached, form a 3–4 membered ring.
21. The compound of claim 18 or 19, wherein R⁸ is C₁₋₂alkyl, and R⁹ is H.

22. A compound having a structure of formula (IV) or (IV'):



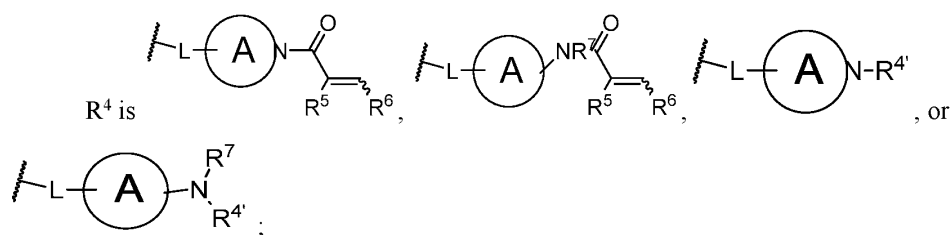
wherein

E¹ and E² are each independently CR¹ or N;

R¹ is independently H, hydroxy, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy, NH-C₁₋₆alkyl, N(C₁₋₆alkyl)₂, cyano, or halo;

R² is halo, C₁₋₆alkyl, C₁₋₆haloalkyl, OR', N(R')₂, C₂₋₃alkenyl, C₂₋₃alkynyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or C₀₋₃alkylene-C₂₋₁₄heteroaryl, and each R' is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl, or two R' substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

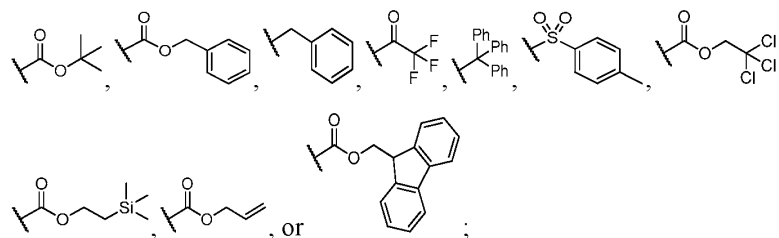
R³ is halo, C₁₋₂haloalkyl, C₁₋₃alkoxy, C₃₋₄cycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl;



ring A is a monocyclic 4-7 membered ring or a bicyclic, bridged, fused, or spiro 6-11 membered ring;

L is a bond, C₁₋₆alkylene, -O-C₀₋₅alkylene, -S-C₀₋₅alkylene, or -NH-C₀₋₅alkylene, and for C₂₋₆alkylene, -O-C₂₋₅alkylene, -S-C₂₋₅alkylene, and NH-C₂₋₅alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R⁴ is H, C₁₋₈alkyl, C₂₋₈alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, cycloalkyl, heterocycloalkyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or selected from



R^5 and R^6 are each independently H, halo, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkylene-O- C_{1-4} alkyl, C_{1-6} alkylene-OH, C_{1-6} haloalkyl, C_{1-6} alkyleneamine, C_{0-6} alkylene-amide, C_{0-3} alkylene-C(O)OH, C_{0-3} alkylene-C(O)OC $_{1-4}$ alkyl, C_{1-6} alkylene-O-aryl, C_{0-3} alkylene-C(O)C $_{1-4}$ alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_{0-3} alkylene-C $_{3-14}$ cycloalkyl, C_{0-3} alkylene-C $_{2-14}$ heterocycloalkyl, C_{0-3} alkylene-C $_{6-14}$ aryl, C_{0-3} alkylene-C $_{2-14}$ heteroaryl, or cyano, or R^5 and R^6 , together with the atoms to which they are attached, form a 4–6 membered ring;

R^7 is H or C_{1-8} alkyl, or R^7 and R^5 , together with the atoms to which they are attached, form a 4–6 membered ring;

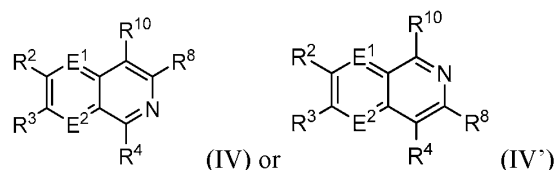
R^8 is H, C_{1-3} alkyl, hydroxy, C_{1-3} alkoxy, halo, cyano, nitro, C_{3-14} cycloalkyl, or $NR^{11}R^{12}$;

R^{11} and R^{12} are each independently H, C_{1-8} alkyl, or C_{3-14} cycloalkyl; and

R^{10} is C_{1-8} alkyl, C_{0-3} alkylene-C $_{6-14}$ aryl, C_{0-3} alkylene-C $_{2-14}$ heteroaryl, C_{0-3} alkylene-C $_{3-14}$ cycloalkyl, C_{0-3} alkylene-C $_{2-14}$ heterocycloalkyl, C_{1-6} alkoxy, O- C_{0-3} alkylene-C $_{6-14}$ aryl, O- C_{0-3} alkylene-C $_{2-14}$ heteroaryl, O- C_{0-3} alkylene-C $_{3-14}$ cycloalkyl, O- C_{0-3} alkylene-C $_{2-14}$ heterocycloalkyl, NH- C_{1-8} alkyl, N(C_{1-8} alkyl) $_2$, NH- C_{0-3} alkylene-C $_{6-14}$ aryl, NH- C_{0-3} alkylene-C $_{2-14}$ heteroaryl, N- C_{0-3} alkylene-C $_{3-14}$ cycloalkyl, N- C_{0-3} alkylene-C $_{2-14}$ heterocycloalkyl, halo, cyano, or C_{1-6} alkylene-amine; or

a pharmaceutically acceptable salt thereof.

23. A compound having a structure of formula (IV) or (IV'):



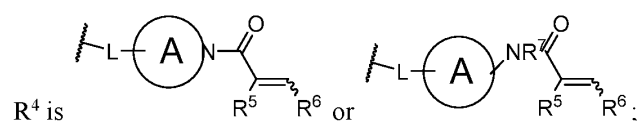
wherein

E^1 and E^2 are each independently CR^1 or N;

R^1 is independently H, hydroxy, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, NH- C_{1-6} alkyl, N(C_{1-6} alkyl) $_2$, cyano, or halo;

R^2 is halo, C_{1-6} alkyl, C_{1-6} haloalkyl, OR' , $N(R')_2$, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{0-3} alkylene- C_{3-14} cycloalkyl, C_{0-3} alkylene- C_{2-14} heterocycloalkyl, aryl, heteroaryl, C_{0-3} alkylene- C_{6-14} aryl, or C_{0-3} alkylene- C_{2-14} heteroaryl, and each R' is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-14} cycloalkyl, C_{2-14} heterocycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, or heteroaryl, or two R' substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

R^3 is halo, C_{1-2} haloalkyl, C_{1-3} alkoxy, C_{3-14} cycloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, or heteroaryl;



ring A is a monocyclic 4-7 membered ring or a bicyclic, bridged, fused, or spiro 6-11 membered ring;

L is a bond, C_{1-6} alkylene, $-O-C_{0-5}$ alkylene, $-S-C_{0-5}$ alkylene, or $-NH-C_{0-5}$ alkylene, and for C_{2-6} alkylene, $-O-C_{2-5}$ alkylene, $-S-C_{2-5}$ alkylene, and $NH-C_{2-5}$ alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R^5 and R^6 are each independently H, halo, C_{1-6} alkyl, C_{2-6} alkynyl, C_{1-6} alkylene- $O-C_{1-4}$ alkyl, C_{1-6} alkylene-OH, C_{1-6} haloalkyl, C_{1-6} alkyleneamine, C_{0-6} alkylene-amide, C_{0-3} alkylene- $C(O)OH$, C_{0-3} alkylene- $C(O)OC_{1-4}$ alkyl, C_{1-6} alkylene- O -aryl, C_{0-3} alkylene- $C(O)C_{1-4}$ alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_{0-3} alkylene- C_{3-14} cycloalkyl, C_{0-3} alkylene- C_{2-14} heterocycloalkyl, C_{0-3} alkylene- C_{6-14} aryl, C_{0-3} alkylene- C_{2-14} heteroaryl, or cyano, or R^5 and R^6 , together with the atoms to which they are attached, form a 4-6 membered ring;

R^7 is H or C_{1-8} alkyl, or R^7 and R^5 , together with the atoms to which they are attached, form a 4-6 membered ring;

R^8 is H, C_{1-3} alkyl, hydroxy, C_{1-3} alkoxy, halo, cyano, nitro, C_{3-14} cycloalkyl, or $NR^{11}R^{12}$;

R^{11} and R^{12} are each independently H, C_{1-8} alkyl, or C_{3-15} cycloalkyl; and

R^{10} is C_{1-8} alkyl, C_{0-3} alkylene- C_{6-14} aryl, C_{0-3} alkylene- C_{3-14} heteroaryl, C_{0-3} alkylene- C_{3-14} cycloalkyl, C_{0-3} alkylene- C_{2-14} heterocycloalkyl, C_{1-6} alkoxy, $O-C_{0-3}$ alkylene- C_{6-14} aryl, $O-C_{0-3}$ alkylene- C_{3-14} heteroaryl, $O-C_{0-3}$ alkylene- C_{3-14} cycloalkyl, $O-C_{0-3}$ alkylene- C_{2-14} heterocycloalkyl, $NH-C_{1-8}$ alkyl, $N(C_{1-8}alkyl)_2$, $NH-C_{0-3}alkylene-C_{6-14}aryl$, $NH-C_{0-3}alkylene-$

C₂₋₁₄heteroaryl, NH-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, NH-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, halo, cyano, or C₁₋₆alkylene-amine; or

a pharmaceutically acceptable salt thereof.

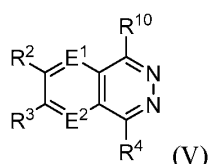
24. The compound of claim 22 or 23, having a structure of formula (IV).

25. The compound of claim 22 or 23, having a structure of formula (IV').

26. The compound of any one of claims 22 to 25, wherein E¹ and E² are each CR¹, and R⁸ is hydroxy, halo, nitro, or C₃₋₆cycloalkyl.

27. The compound of any one of claims 22 to 25, wherein R⁸ is methyl.

28. A compound having a structure of formula (V):



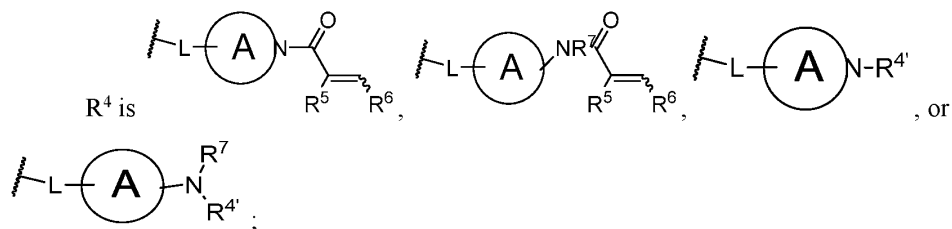
wherein

E¹ and E² are each independently CR¹ or N;

R¹ is independently H, hydroxy, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy, NH-C₁₋₆alkyl, N(C₁₋₆alkyl)₂, cyano, or halo;

R² is halo, C₁₋₆alkyl, C₁₋₆haloalkyl, OR', N(R')₂, C₂₋₃alkenyl, C₂₋₃alkynyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or C₀₋₃alkylene-C₂₋₁₄heteroaryl, and each R' is independently H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₃₋₁₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₂₋₃alkenyl, C₂₋₃alkynyl, aryl, or heteroaryl, or two R' substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

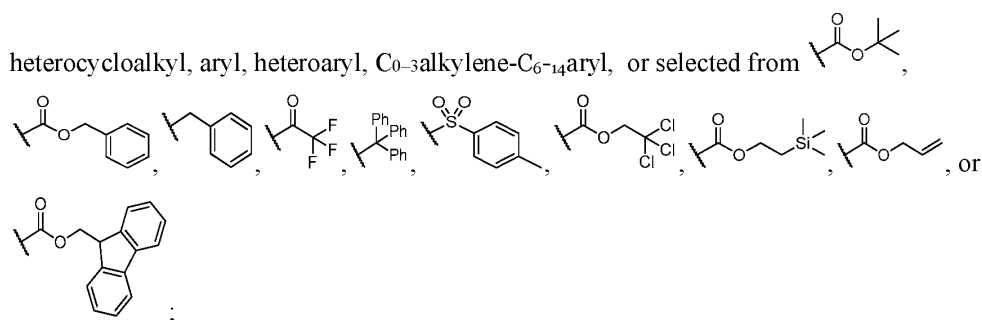
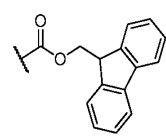
R³ is halo, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆alkoxy, C₃₋₁₄cycloalkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, aryl, or heteroaryl;



ring A is a monocyclic 4-7 membered ring or a bicyclic, bridged, fused, or spiro 6-11 membered ring;

L is a bond, C₁₋₆alkylene, -O-C₀₋₅alkylene, -S-C₀₋₅alkylene, or -NH-C₀₋₅alkylene, and for C₂₋₆alkylene, -O-C₂₋₅alkylene, -S-C₂₋₅alkylene, and NH-C₂₋₅alkylene, one carbon atom of the alkylene group can optionally be replaced with O, S, or NH;

R⁴ is H, C₁₋₈alkyl, C₂₋₈alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, cycloalkyl, heterocycloalkyl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄

heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₆₋₁₄aryl, or selected from , or ;

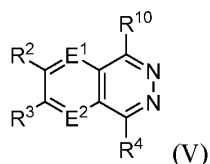
R⁵ and R⁶ are each independently H, halo, C₁₋₆alkyl, C₂₋₆alkynyl, C₁₋₆alkylene-O-C₁₋₄alkyl, C₁₋₆alkylene-OH, C₁₋₆haloalkyl, C₁₋₆alkyleneamine, C₀₋₆alkylene-amide, C₀₋₃alkylene-C(O)OH, C₀₋₃alkylene-C(O)OC₁₋₄alkyl, C₁₋₆alkylene-O-aryl, C₀₋₃alkylene-C(O)C₁₋₄alkylene-OH, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, C₀₋₃alkylene-C₆₋₁₄aryl, C₀₋₃alkylene-C₂₋₁₄heteroaryl, or cyano, or R⁵ and R⁶, together with the atoms to which they are attached, form a 4–6 membered ring;

R⁷ is H or C₁₋₈alkyl, or R⁷ and R⁵, together with the atoms to which they are attached, form a 4–6 membered ring; and

R¹⁰ is C₁₋₈alkyl, C₀₋₃alkylene-C₆₋₁₄aryl, C₀₋₃alkylene-C₃₋₁₄heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, C₁₋₆alkoxy, O-C₀₋₃alkylene-C₆₋₁₄aryl, O-C₀₋₃alkylene-C₃₋₁₄heteroaryl, O-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, O-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, NH-C₁₋₈alkyl, N(C₁₋₈alkyl)₂, NH-C₀₋₃alkylene-C₆₋₁₄aryl, NH-C₀₋₃alkylene-C₂₋₁₄heteroaryl, NH-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, NH-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, halo, cyano, or C₁₋₆alkylene-amine; or

a pharmaceutically acceptable salt thereof.

29. A compound having a structure of formula (V):



₃alkylene-C₂₋₁₄heteroaryl, NH-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, NH-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, halo, cyano, or C₁₋₆alkylene-amine; or

a pharmaceutically acceptable salt thereof.

30. The compound of any one of claims 1 to 29, wherein each of E¹ and E² is CR¹.

31. The compound of any one of claims 1, 2, 3, 4, 6 to 29 wherein E¹ is CR¹ and E² is N.

32. The compound of any one of claims 1, 2, 3, 4, 6 to 29, wherein E¹ is N and E² is CR¹.

33. The compound of any one of claims 1, 2, 3, 4, 6 to 29, wherein each of E¹ and E² is N.

34. The compound of any one of claims 1, 2, 3, 4, 6 to 33, wherein R¹⁰ is C₁₋₆alkyl, aryl, heteroaryl, C₃₋₁₄cycloalkyl, C₂₋₁₄heterocycloalkyl, C₁₋₄alkoxy, O-C₀₋₃alkylene-C₆₋₁₄aryl, O-C₀₋₃alkylene-C₂₋₁₄heteroaryl, O-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, O-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl, NH-C₁₋₈alkyl, N(C₁₋₈alkyl)₂, NH-C₀₋₃alkylene-C₃₋₁₄aryl, NH-C₀₋₃alkylene-C₂₋₁₄heteroaryl, NH-C₀₋₃alkylene-C₃₋₁₄cycloalkyl, or NH-C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl.

35. The compound of claim 28 or 29, wherein E¹ and E² are each CR¹, and R¹⁰ is C₁₋₃alkylene-C₆₋₁₄aryl, C₁₋₃alkylene-C₂₋₁₄heteroaryl, C₀₋₃alkylene-C₃₋₁₄cycloalkyl, C₁₋₃alkylene-C₂₋₁₄heterocycloalkyl, or halo.

36. The compound of any one of claims 3 to 33, wherein R¹⁰ is C₁₋₈alkyl.

37. The compound of any one of claims 3 to 33, wherein R¹⁰ is C₀₋₃alkylene-C₆₋₁₄aryl.

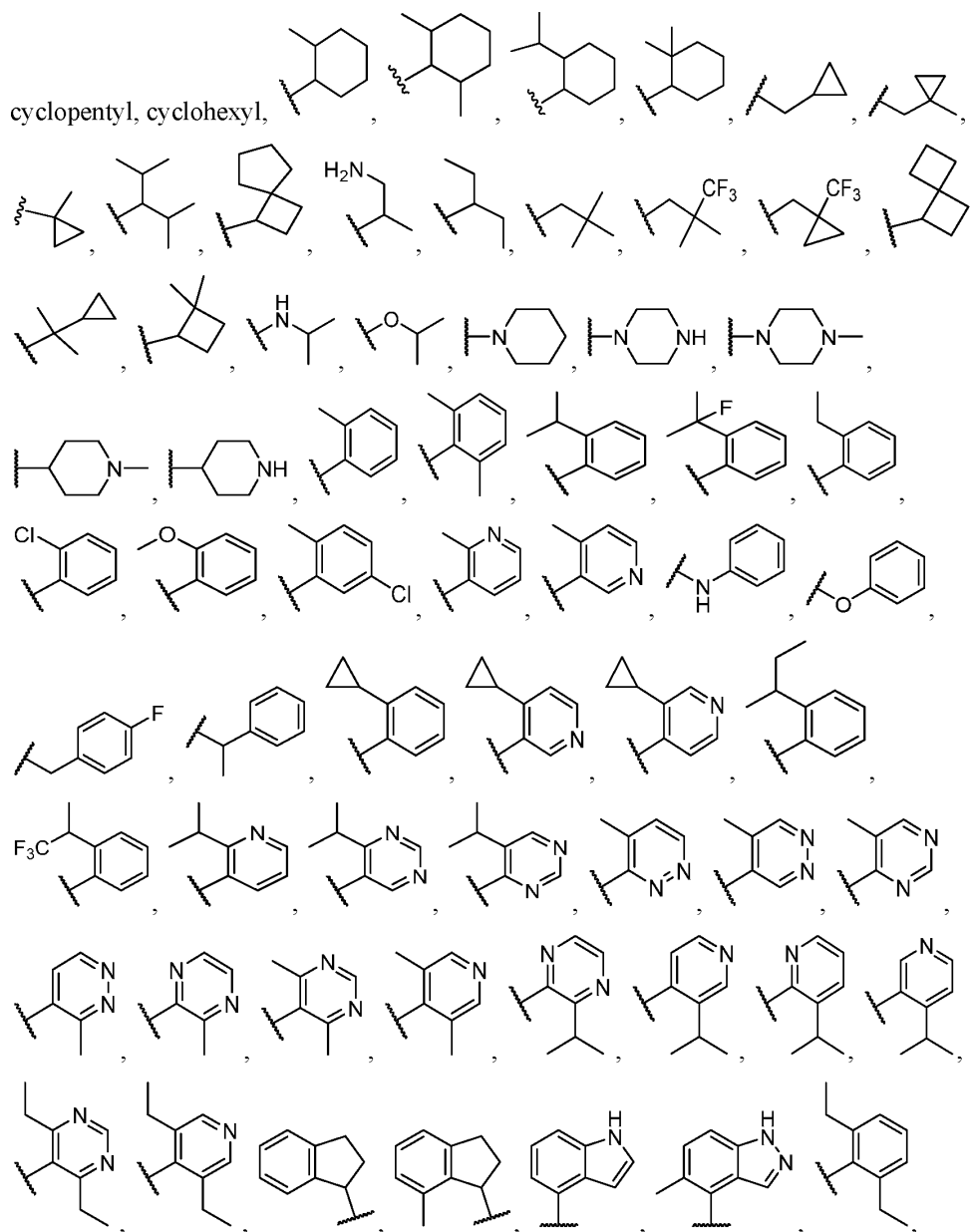
38. The compound of any one of claims 3 to 34, wherein R¹⁰ is C₀₋₃alkylene-C₃₋₁₄heteroaryl.

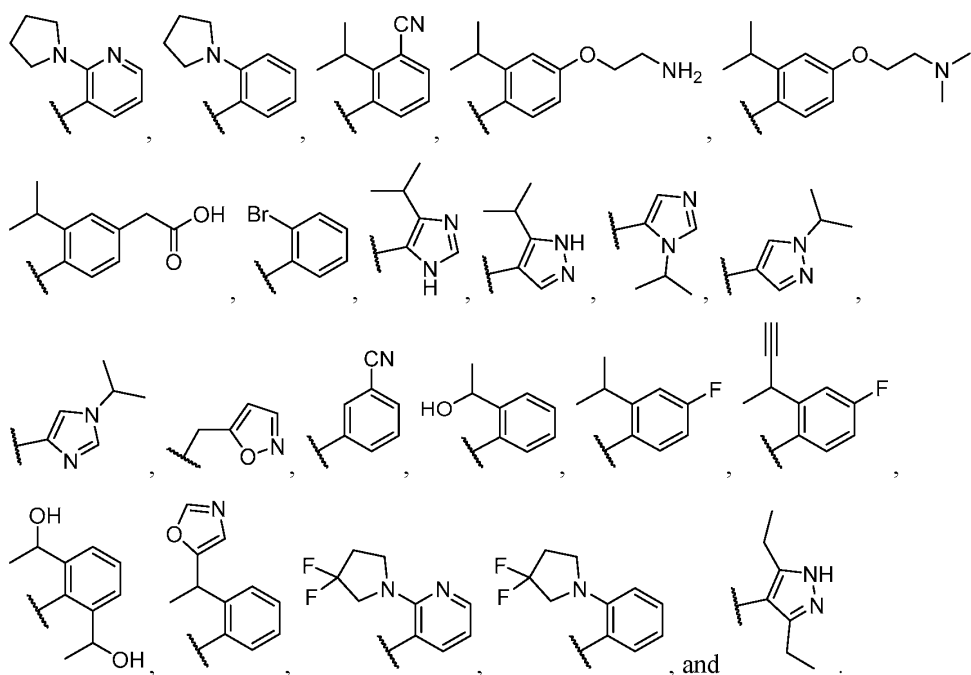
39. The compound of any one of claims 3 to 35, wherein R¹⁰ is C₀₋₃alkylene-C₃₋₁₄cycloalkyl.

40. The compound of any one of claims 3 to 24, 26, 27, and 30 to 33, wherein R¹⁰ is C₀₋₃alkylene-C₂₋₁₄heterocycloalkyl.

41. The compound of any one of claims 3 to 33, wherein R^{10} is C₀₋₆alkylene-amine.

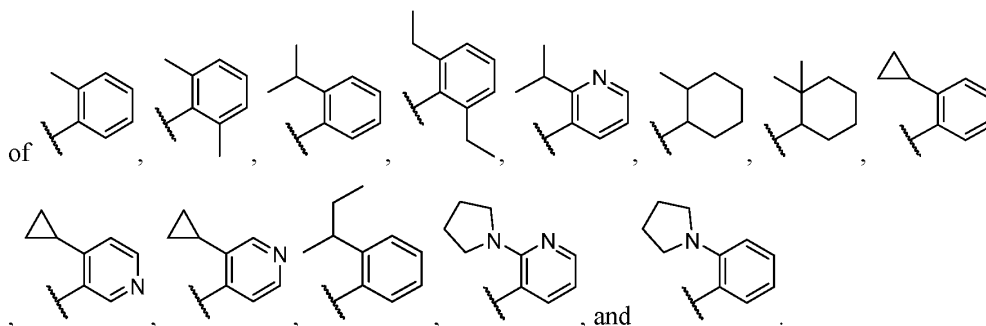
42. The compound of any one of claims 3 to 33, wherein R^{10} is selected from the group consisting of *i*-Pr, *t*-Bu, phenyl, benzyl, OCH₃, Cl, cyclopropyl, cyclobutyl,





43. The compound of any one of claims 3 to 33, wherein R¹⁰ comprises ortho-substituted aryl, ortho-substituted heteroaryl, or 2-substituted cyclohexyl.

44. The compound of claim 43, wherein R¹⁰ is selected from the group consisting



45. The compound of any one of claims 1 to 44, wherein R¹ is H.

46. The compound of any one of claims 1 to 44, wherein R¹ is F.

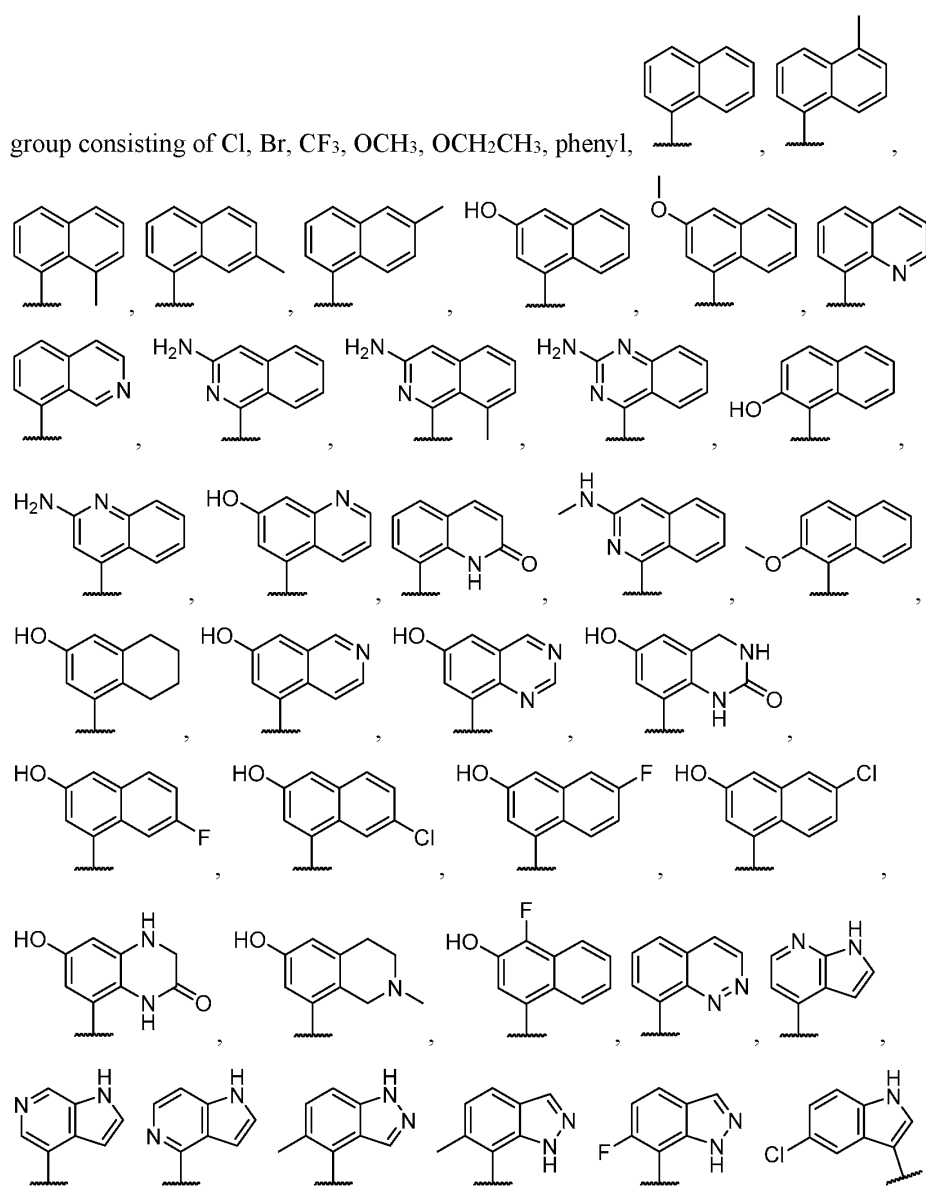
47. The compound of any one of claims 1 to 44, wherein R¹ is methyl.

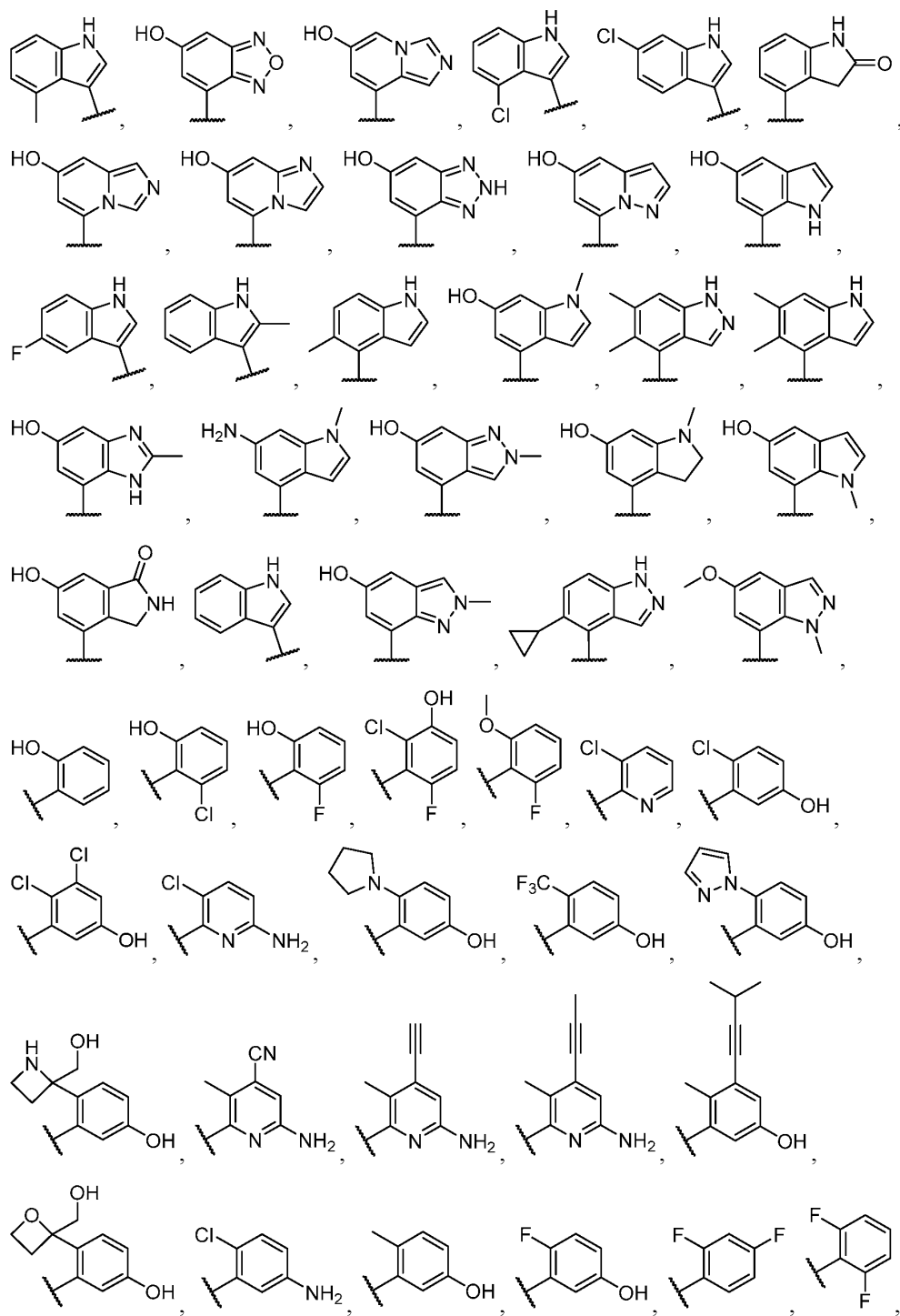
48. The compound of any one of claims 1 to 47, wherein R² is aryl.

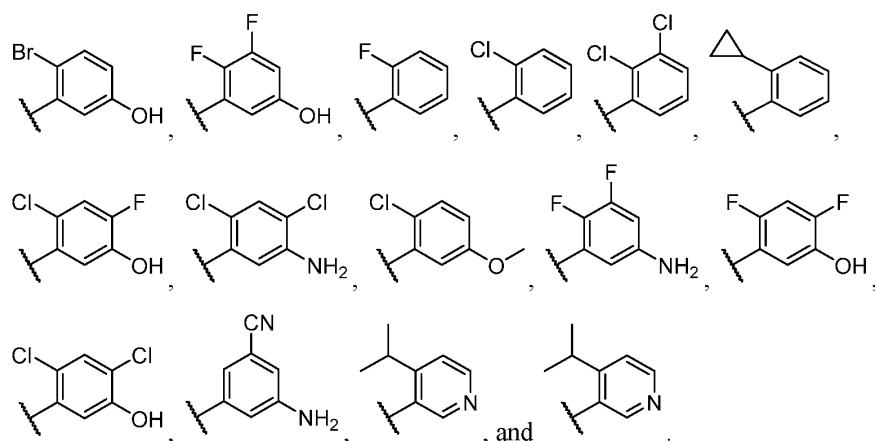
49. The compound of any one of claims 1 to 47, wherein R² is heteroaryl.

50. The compound of any one of claims 1 to 47, wherein R^2 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, piperidine, pyrrolidine, azetidine, phenyl, naphthyl, pyridyl, indazolyl, indolyl, azaindolyl, indolinyl, benzotriazolyl, benzoxadiazolyl, imidazolyl, cinnolinyl, imidazopyridyl, pyrazolopyridyl, quinolinyl, isoquinolinyl, quinazolinyl, quinazolinonyl, indolinonyl, isoindolinonyl, tetrahydronaphthyl, tetrahydroquinolinyl, or tetrahydroisoquinolinyl.

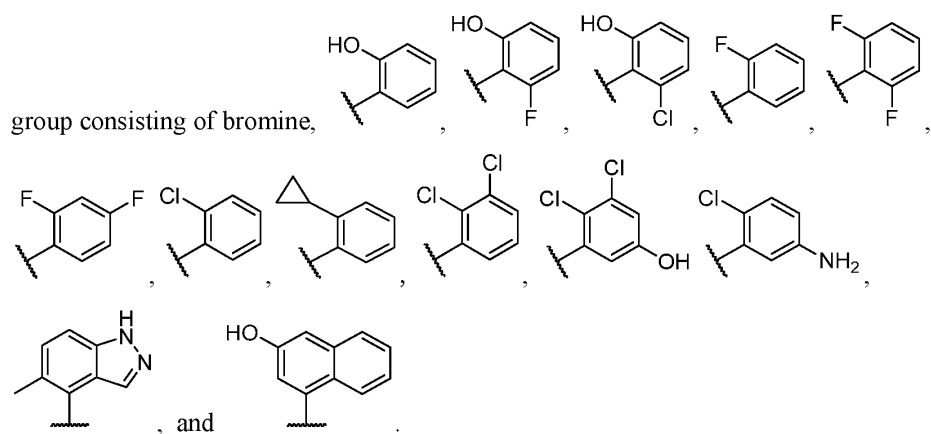
51. The compound of any one of claims 1 to 47, wherein R^2 is selected from the







52. The compound of any one of claims 1 to 47, wherein R² is selected from the



53. The compound of any one of claims 1 to 52, wherein R³ is halo.

54. The compound of claim 53, wherein R³ is Cl.

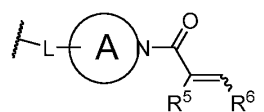
55. The compound of any one of claims 1 to 52, wherein R³ is C₁₋₂alkyl.

56. The compound of claim 55, wherein R³ is methyl.

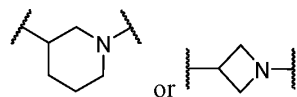
57. The compound of any one of claims 1 to 52, wherein R³ is C₁₋₂haloalkyl.

58. The compound of claim 57, wherein R³ is CF₃.

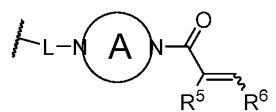
59. The compound of any one of claims 1 to 58, wherein R^4 is



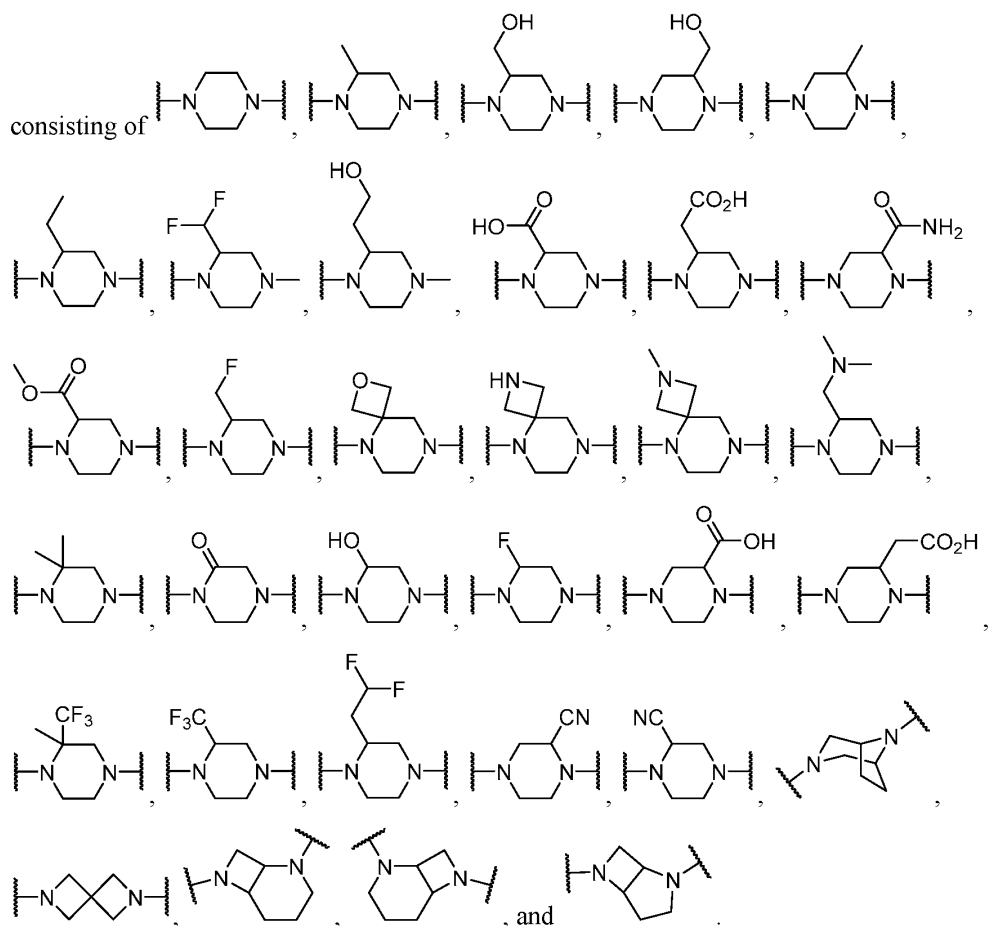
60. The compound of claim 59, wherein ring A is



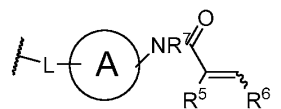
61. The compound of any one of claims 1 to 58, wherein R^4 is



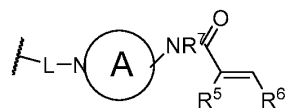
62. The compound of claim 61, wherein ring A is selected from the group



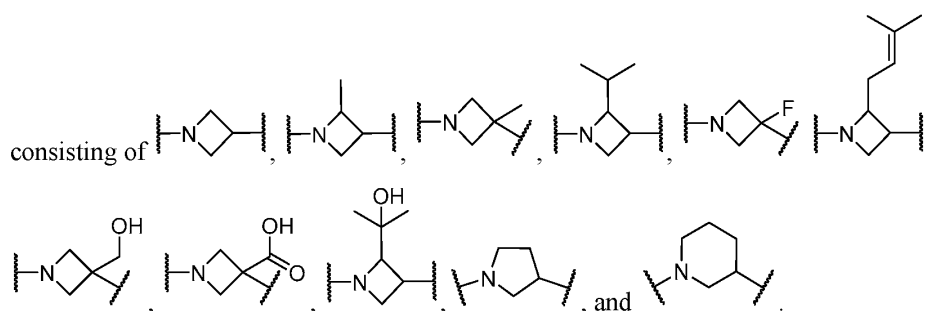
63. The compound of any one of claims 1 to 58, wherein R^4 is



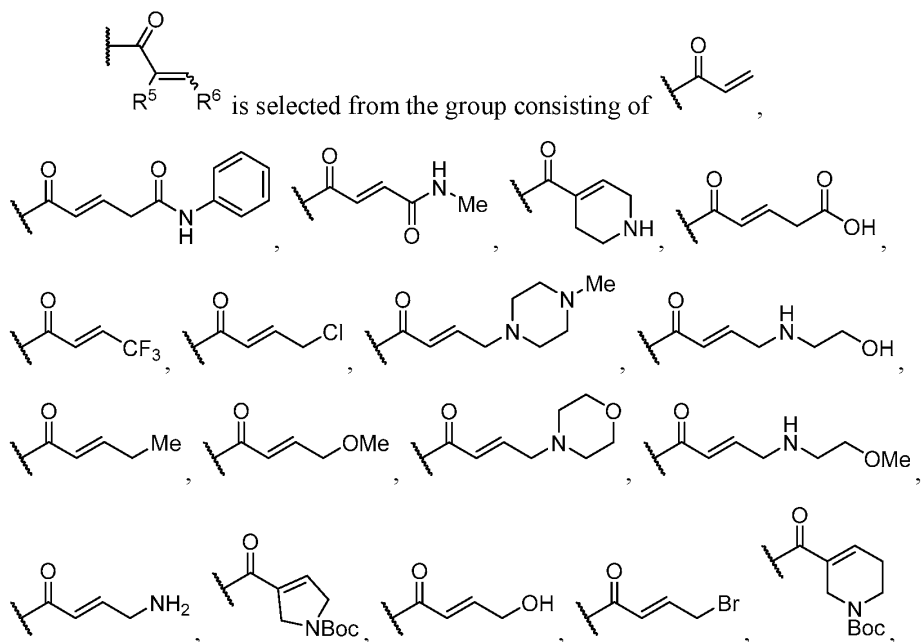
64. The compound of any one of claims 1 to 58, wherein R^4 is

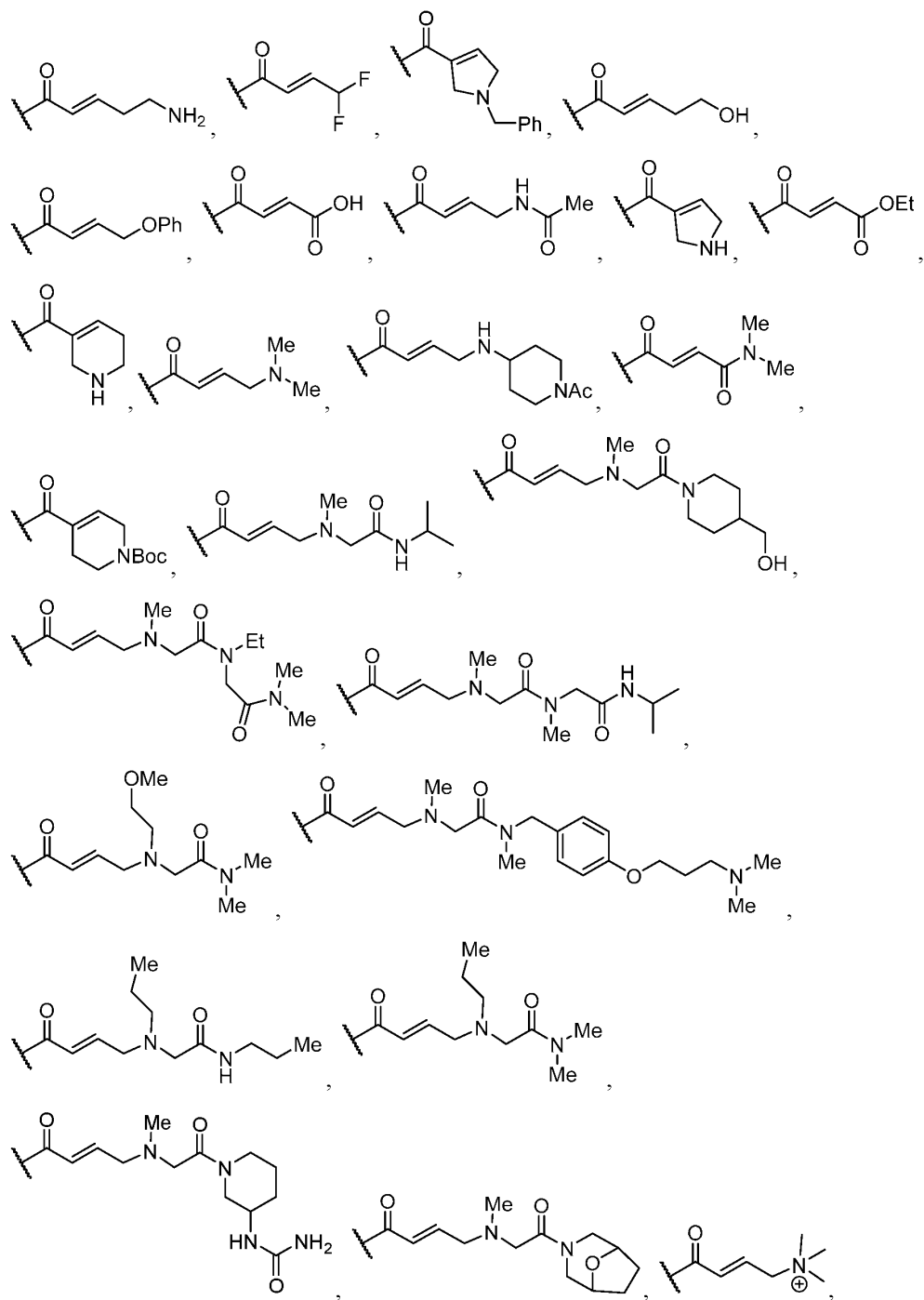


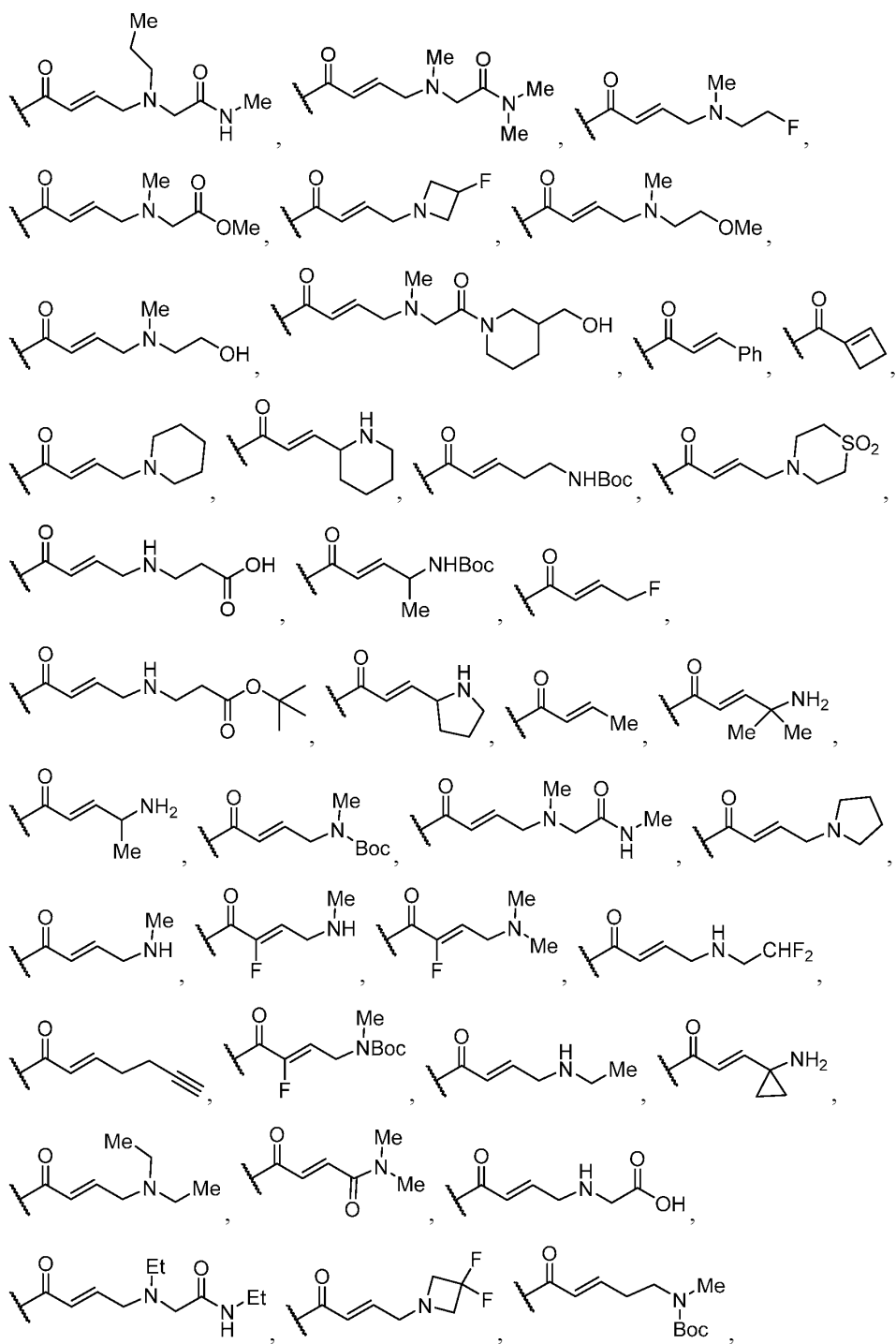
65. The compound of claim 64, wherein ring A is selected from the group

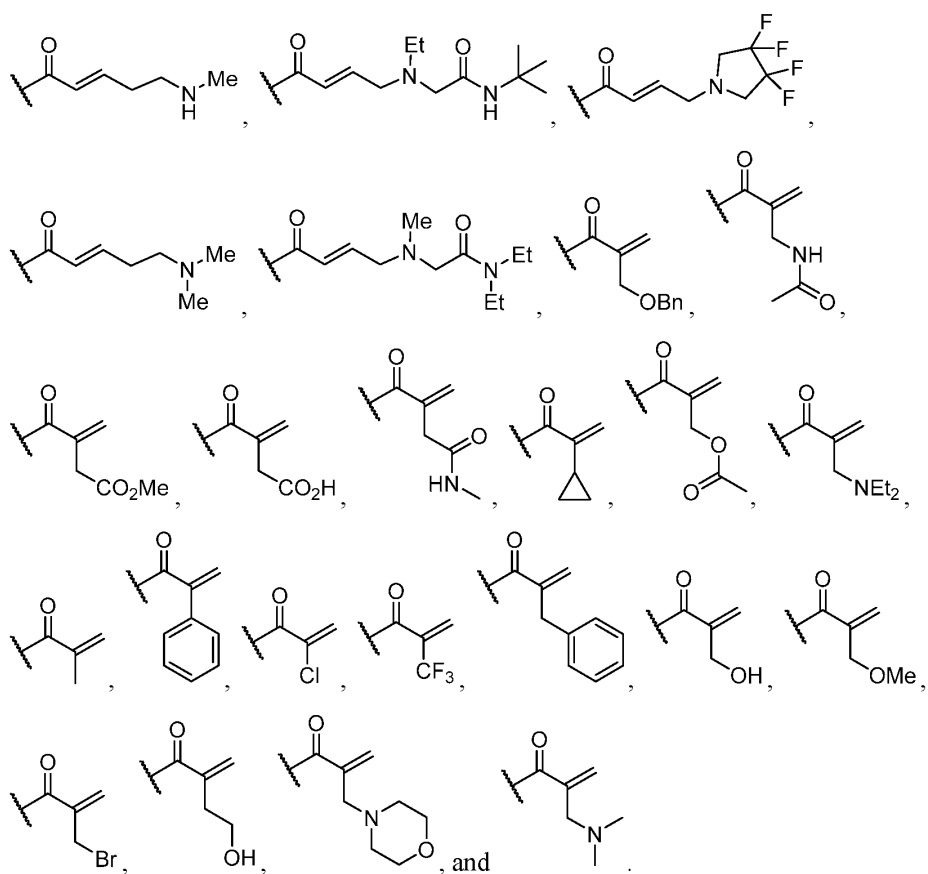


66. The compound of any one of claims 59 to 65, wherein



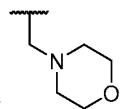






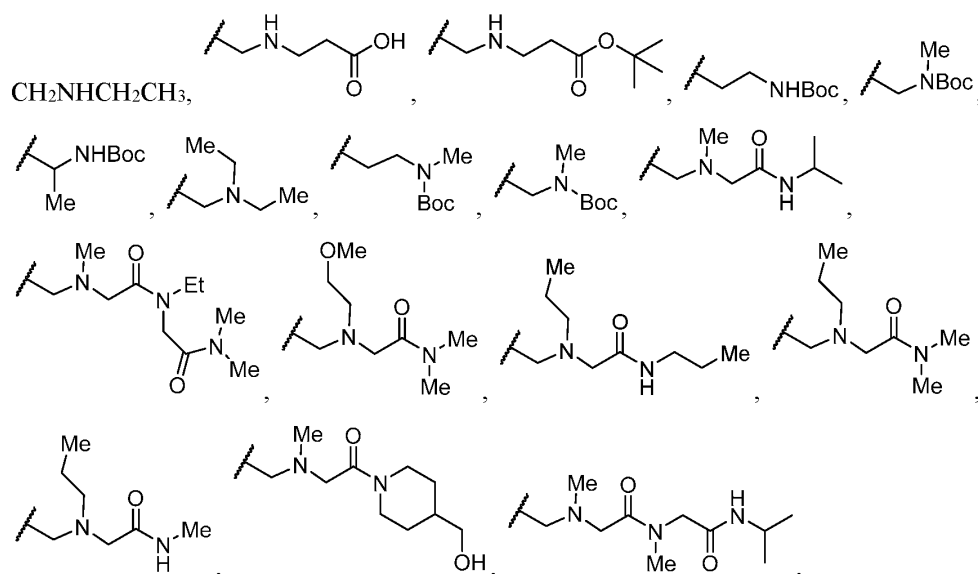
67. The compound of any one of claims 59 to 66, wherein L is a bond.
68. The compound of any one of claims 59 to 66, wherein L is C₁-2alkylene.
69. The compound of claim 59, 60, 62, 63, or 66, wherein L is O.
70. The compound of claim 59, 60, 62, 63, or 66, wherein L is S.
71. The compound of claim 59, 61, 64, 65, or 66, wherein L is NH.
72. The compound of any one of claims 1 to 59, 61, 63, 64 and 66, wherein ring A comprises piperidiny, piperaziny, pyrrolidiny, or azetidiny.
73. The compound of claim 72, wherein ring A comprises piperidiny.
74. The compound of any one of claims 1 to 59, 61, 63, 64 and 65, wherein R⁵ is H or halo.

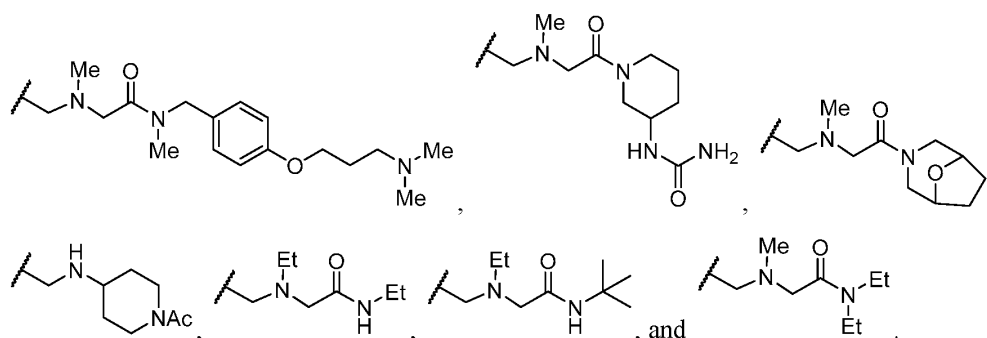
75. The compound of any one of claims 1 to 59, 61, 63, 64 and 65, wherein R⁵ is H, Br, Cl, F, CN, CH₃, CF₃, CH₂Br, CH₂OH, CH₂CH₂OH, CH₂OCH₂phenyl, cyclopropyl, phenyl, CH₂phenyl, CH₂OCH₃, CH₂N(CH₃)₂, CH₂N(CH₂CH₃)₂, CH₂CO₂H, CH₂CO₂CH₃,

 $\text{CH}_2\text{NHC}(\text{O})\text{CH}_3$, $\text{CH}_2\text{C}(\text{O})\text{NHCH}_3$, $\text{CH}_2\text{OC}(\text{O})\text{CH}_3$, or

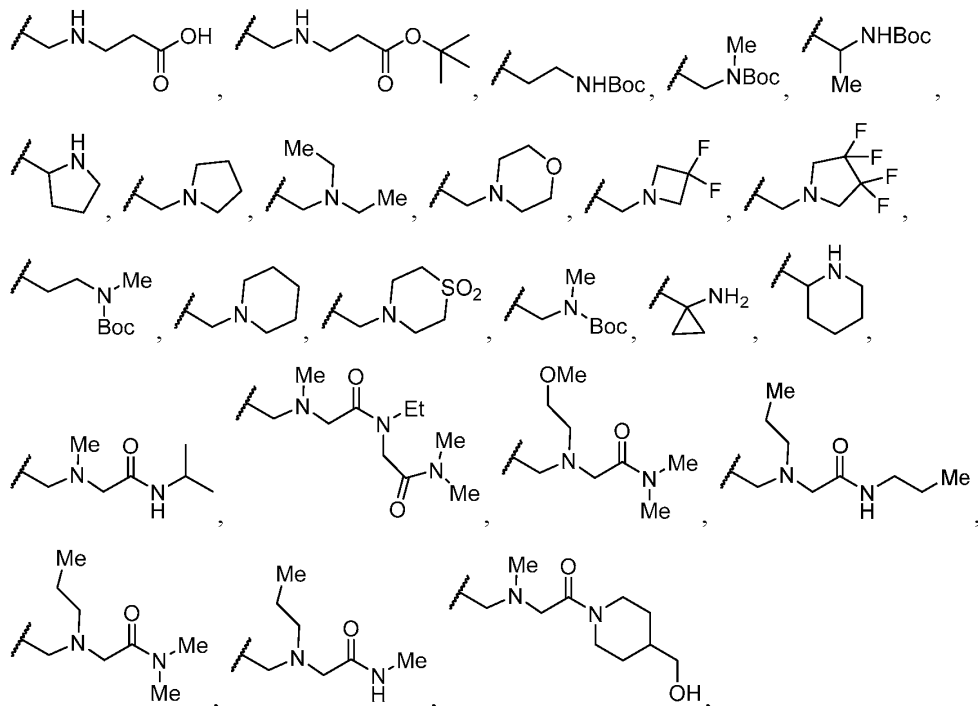
76. The compound of any one of claims 1 to 65 and 67 to 75, wherein R⁶ is H, C₁₋₃alkyl, C₁₋₃alkylene-O-C₁₋₂alkyl, C₁₋₃alkylene-OH, C₁₋₃haloalkyl, C₁₋₃alkylene-amine, C₀₋₃alkylene-amide, C₀₋₁alkylene C(O)OC₁₋₃alkyl, C₀₋₁alkylene-C₂₋₇heterocycloalkyl, C₀₋₁alkylene-C₃₋₈cycloalkyl, or C₀₋₃alkylene-C₆₋₁₄aryl.

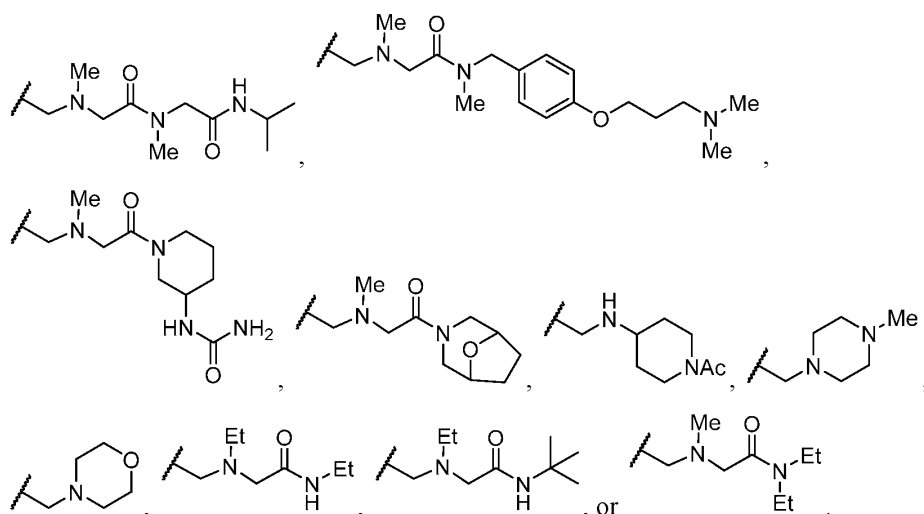
77. The compound of claim 76, wherein R⁶ is C₁₋₃alkylene-amine or C₁₋₃alkylene-amide and is selected from the group consisting of CH₂NH₂, CH(CH₃)NH₂, CH(CH₃)₂NH₂, CH₂CH₂NH₂, CH₂CH₂N(CH₃)₂, CH₂NHCH₃, C(O)NHCH₃, C(O)N(CH₃)₂, CH₂C(O)NHphenyl, CH₂NHC(O)CH₃, CH₂NHCH₂CH₂OH, CH₂NHCH₂CO₂H, CH₂NH(CH₃)CH₂CO₂CH₃, CH₂NHCH₂CH₂OCH₃, CH₂NH(CH₃)CH₂CH₂OCH₃, CH₂NH(CH₃)CH₂C(O)N(CH₃)₂, CH₂NH(CH₃)CH₂C(O)NHCH₃, CH₂NMe₂, CH₂NH(CH₃)CH₂CH₂OH, CH₂NH(CH₃)CH₂CH₂F, CH₂N⁺(CH₃)₃, CH₂NHCH₂CHF₂,



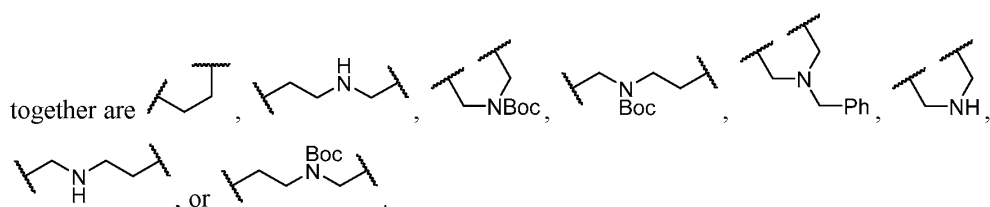


78. The compound of any one of claims 1 to 65 and 67 to 75, wherein R⁶ is phenyl, cyclopropyl, CH₃, CF₃, CH₂CH₃, CH₂NH₂, CH(CH₃)NH₂, CH(CH₃)₂NH₂, CH₂Cl, CH₂Br, CH₂OCH₃, CH₂Ophenyl, CH₂OH, CO₂H, CO₂CH₂CH₃, CH₂CO₂H, CH₂CH₂NH₂, CH₂CH₂OH, CH₂CH₂N(CH₃)₂, CH₂NHCH₃, C(O)NHCH₃, C(O)N(CH₃)₂, CH₂C(O)NHphenyl, CH₂CHF₂, CH₂F, CHF₂, CH₂NHC(O)CH₃, CH₂NHCH₂CH₂OH, CH₂NHCH₂CO₂H, CH₂NH(CH₃)CH₂CO₂CH₃, CH₂NHCH₂CH₂OCH₃, CH₂NH(CH₃)CH₂CH₂OCH₃, CH₂NH(CH₃)CH₂C(O)N(CH₃)₂, CH₂NH(CH₃)CH₂C(O)NHCH₃, CH₂CH₂CCH₃, CH₂NMe₂, CH₂NH(CH₃)CH₂CH₂OH, CH₂NH(CH₃)CH₂CH₂F, CH₂N⁺(CH₃)₃, CH₂NHCH₂CHF₂, CH₂NHCH₂CH₃,





79. The compound of any one of claims 1 to 65 and 67 to 73, wherein R⁵ and R⁶



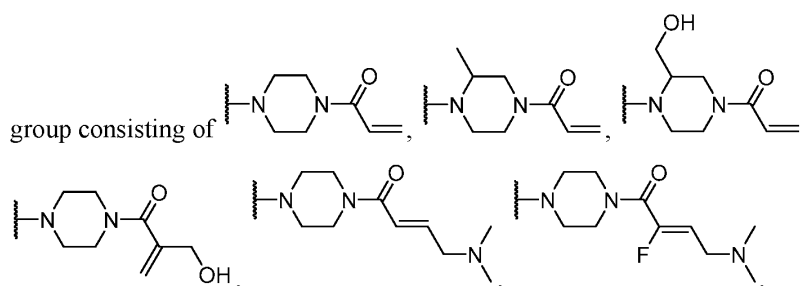
80. The compound of any one of claims 1 to 65 and 67 to 73, wherein each of R⁵ and R⁶ is H.

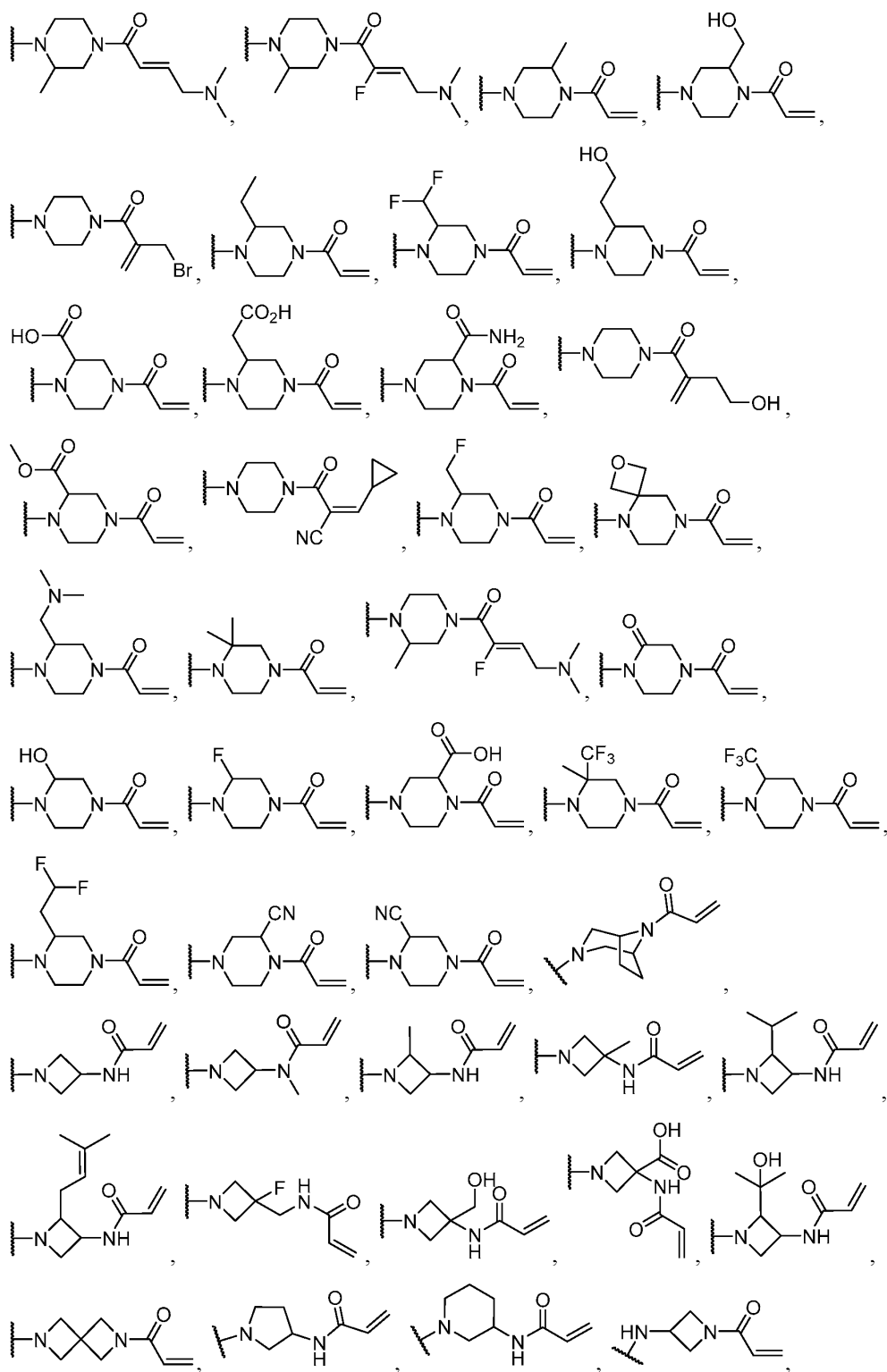
81. The compound of any one of claims 1 to 58 and 63 to 80, wherein R⁷ is H.

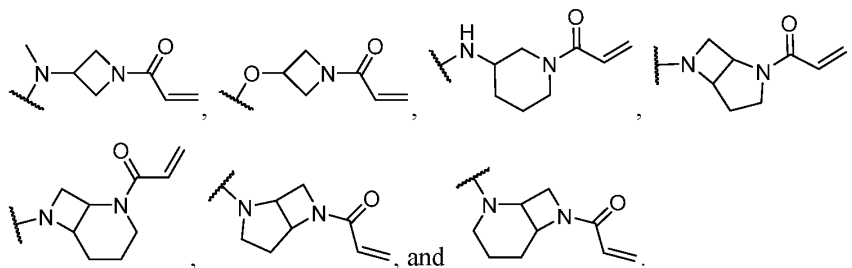
82. The compound of any one of claims 1 to 58 and 63 to 80, wherein R⁷ is methyl.

83. The compound of any one of claims 1 to 58, 63 to 65, 67-73 and 76 to 78, wherein R⁷ and R⁵ together are -CH₂- or -C(O)CH₂-.

84. The compound of any one of claims 1 to 58, wherein R⁴ is selected from the







85. A compound as recited in Table 1.

86. The compound of any one of claims 1 to 85 in the form of a pharmaceutically acceptable salt.

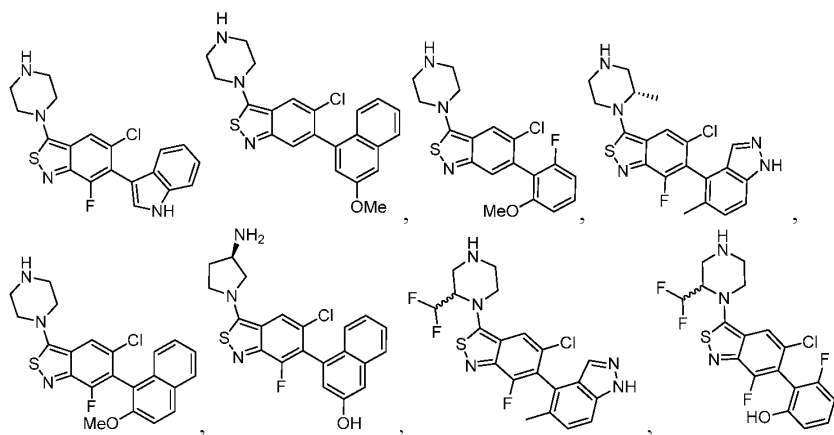
87. A pharmaceutical formulation comprising the compound of any one of claims 1 to 86 and a pharmaceutically acceptable excipient.

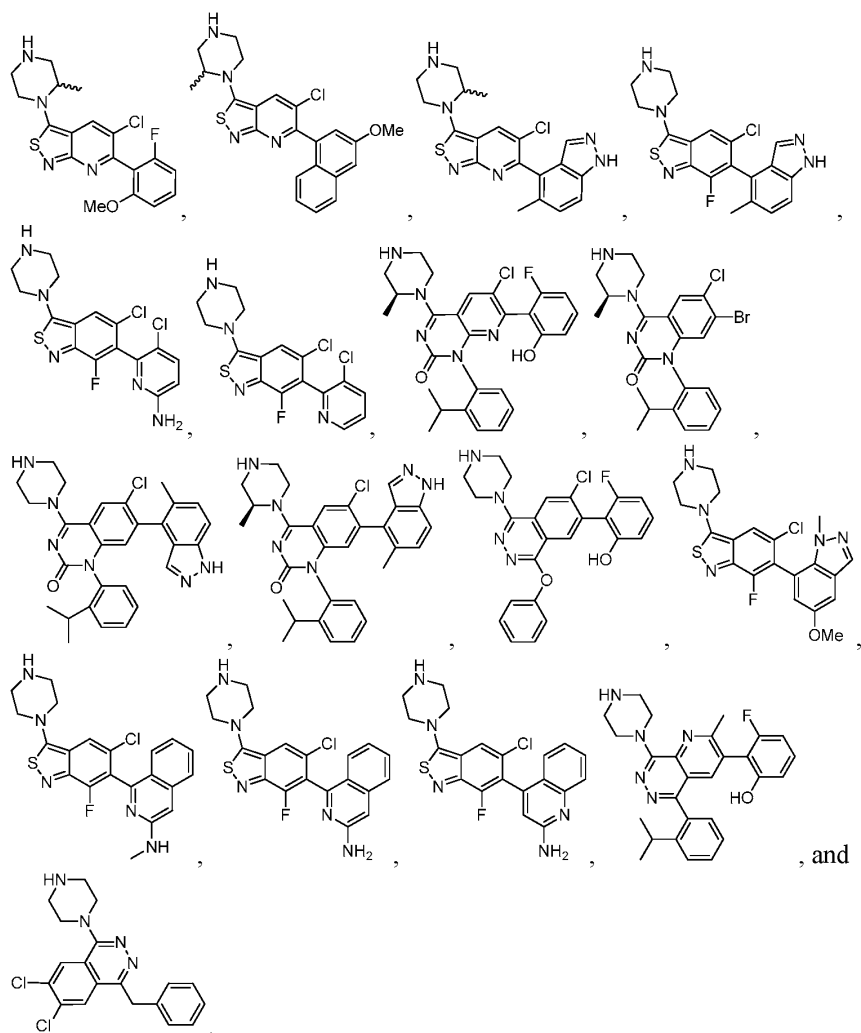
88. A method of inhibiting KRAS G12C in a cell, comprising contacting the cell with the compound of any one of claims 1 to 86 or the composition of claim 87.

89. A method of treating cancer in a subject comprising administering to the subject a therapeutically effective amount of the compound of any one of claims 1 to 86 or the composition of claim 87.

90. The method of claim 89, wherein the cancer is lung cancer, pancreatic cancer, or colorectal cancer.

91. A compound having a structure selected from:





92. The compounds of claim 91 in the form of a pharmaceutically acceptable salt.

93. A pharmaceutical formulation comprising the compounds of claim 91 or 92 and a pharmaceutically acceptable excipient.