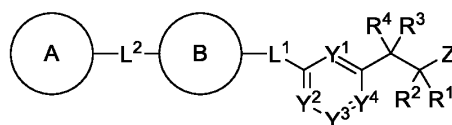


CLAIMS

We Claim:

1. A compound of Formula (I):



Formula (I)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

Z is $-\text{P}(=\text{O})(\text{H})\text{OR}^6$, $-\text{P}(=\text{O})(\text{R}^5)\text{OR}^6$, $-\text{P}(=\text{O})(\text{OR}^6)_2$, $-\text{S}(=\text{O})(\text{OR}^6)$, $-\text{SO}_2\text{OR}^6$, $-$

$\text{C}(=\text{O})\text{NHSO}_2\text{R}^5$, $-\text{C}(=\text{O})\text{NHSO}_2\text{N}(\text{R}^6)_2$, $-\text{N}(\text{R}^6)\text{SO}_2\text{N}(\text{R}^6)_2$, $-$

$\text{N}(\text{R}^6)\text{C}(=\text{O})\text{NHSO}_2(\text{R}^5)$, $-\text{N}(\text{R}^6)\text{C}(=\text{O})\text{NHSO}_2\text{N}(\text{R}^6)_2$, $-\text{N}(\text{R}^6)\text{C}(=\text{NH})\text{NH}_2$, $-$

$\text{C}(=\text{O})\text{NHNHC}(=\text{O})\text{N}(\text{R}^6)_2$, or $-\text{B}(\text{OR}^6)_2$;

R^5 is C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, phenyl, or $-(\text{C}_1$ - C_6 alkyl)-phenyl; wherein each alkyl, cycloalkyl, and phenyl is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, $-\text{CN}$, $-\text{OH}$, $-\text{O}-(\text{C}_1$ - C_6 alkyl), C_1 - C_6 alkyl, C_1 - C_6 fluoroalkyl, C_1 - C_6 hydroxyalkyl, $-\text{O}-(\text{C}_1$ - C_6 fluoroalkyl), C_3 - C_6 cycloalkyl, and 3- to 6-membered heterocycloalkyl;

each R^6 is independently hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, phenyl, or $-(\text{C}_1$ - C_6 alkyl)-phenyl; wherein each alkyl, cycloalkyl, and phenyl is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, $-\text{CN}$, $-\text{OH}$, $-\text{O}-(\text{C}_1$ - C_6 alkyl), C_1 - C_6 alkyl, C_1 - C_6 fluoroalkyl, C_1 - C_6 hydroxyalkyl, $-\text{O}-(\text{C}_1$ - C_6 fluoroalkyl), C_3 - C_6 cycloalkyl, and 3- to 6-membered heterocycloalkyl;

R^1 , R^2 , and R^3 are each independently hydrogen, halogen, $-\text{OH}$, $-\text{O}-(\text{C}_1$ - C_6 alkyl), C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, or 3- to 6-membered heterocycloalkyl; wherein each alkyl, cycloalkyl, and heterocycloalkyl is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, $-\text{CN}$, $-\text{OH}$, $-\text{O}-(\text{C}_1$ - C_6 alkyl), and C_1 - C_6 alkyl;

R^4 is C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, or 3- to 6-membered heterocycloalkyl; wherein each alkyl, cycloalkyl, and heterocycloalkyl is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, $-\text{CN}$, $-\text{OH}$, $-\text{O}-(\text{C}_1$ - C_6 alkyl), and C_1 - C_6 alkyl;

Y^1 , Y^2 , Y^3 , and Y^4 are each independently N, CH, or $\text{C}-\text{R}^Y$;

each R^Y is independently halogen, $-\text{CN}$, $-\text{OH}$, $-\text{O}-(\text{C}_1$ - C_6 alkyl), $-\text{NH}_2$, $-\text{NH}-(\text{C}_1$ - C_6 alkyl), $-\text{N}(\text{C}_1$ - C_6 alkyl) $_2$, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, or 3- to 6-membered

heterocycloalkyl; wherein each alkyl, cycloalkyl, and heterocycloalkyl is independently unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, -CN, -OH, -O-(C₁-C₆ alkyl), and C₁-C₆ alkyl;

L¹ is -O-, -NR⁷-, *-O-CH₂-, *-CH₂-O-, *-NR⁷-CH₂-, *-CH₂-NR⁷-, *-NR⁷-C(O)-, *-C(O)-NR⁷-, or *-C(O)-CH₂-; wherein * represents the connection to Ring B;

R⁷ is hydrogen, C₁-C₆ alkyl, or C₃-C₆ cycloalkyl;

Ring B is cycloalkylene or heterocycloalkylene; wherein the cycloalkylene or heterocycloalkylene is unsubstituted or substituted with 1, 2, 3, or 4 R^B substituents;

Ring A is carbocycle or heterocycle; wherein the carbocycle or heterocycle is unsubstituted or substituted with 1, 2, 3, 4, or 5 R^A substituents;

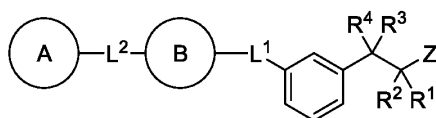
L² is a bond, C₁-C₆ alkylene, or -(C₁-C₆ alkylene)-O-; wherein the alkylene is unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, -CN, -OH, C₁-C₆ alkyl, and -O-(C₁-C₆ alkyl);

each R^A is independently halogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₁-C₁₀ fluoroalkyl, -L^A-CN, -L^A-OH, -L^A-OR¹⁰, -L^A-NR¹¹R¹¹, -L^A-C(=O)R¹⁰, -L^A-C(=O)OR¹¹, -L^A-OC(=O)R¹¹, -L^A-C(=O)NR¹¹R¹¹, -L^A-NR¹¹C(=O)R¹¹, -L^A-NR¹¹C(=O)NR¹¹R¹¹, -L^A-OC(=O)NR¹¹R¹¹, -L^A-NR¹¹C(=O)OR¹⁰, -L^A-OC(=O)OR¹⁰, -L^A-aryl, -L^A-heteroaryl, -L^A-(C₃-C₁₀ cycloalkyl), or -L^A-(3- to 10-membered heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, fluoroalkyl, aryl, heteroaryl, cycloalkyl, and heterocycloalkyl is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen, -CN, -OH, C₁-C₆ alkyl, C₁-C₆ fluoroalkyl, C₁-C₆ hydroxyalkyl, -O-(C₁-C₆ alkyl), and -O-(C₁-C₆ fluoroalkyl);

each R^B is independently halogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₁-C₁₀ fluoroalkyl, -L^B-CN, -L^B-OH, -L^B-OR¹⁰, -L^B-NR¹¹R¹¹, -L^B-C(=O)R¹⁰, -L^B-C(=O)OR¹¹, -L^B-OC(=O)R¹¹, -L^B-C(=O)NR¹¹R¹¹, -L^B-NR¹¹C(=O)R¹¹, -L^B-NR¹¹C(=O)NR¹¹R¹¹, -L^B-OC(=O)NR¹¹R¹¹, -L^B-NR¹¹C(=O)OR¹⁰, -L^B-OC(=O)OR¹⁰, -L^B-aryl, -L^B-heteroaryl, -L^B-(C₃-C₁₀ cycloalkyl), or -L^B-(3- to 10-membered heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, fluoroalkyl, aryl, heteroaryl, cycloalkyl, and heterocycloalkyl is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen, -CN, -OH, C₁-C₆ alkyl, C₁-C₆ fluoroalkyl, C₁-C₆ hydroxyalkyl, -O-(C₁-C₆ alkyl), and -O-(C₁-C₆ fluoroalkyl);

- each L^A and L^B is independently a bond or C₁-C₆ alkylene; wherein the alkylene is unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of halogen, -CN, -OH, -O-(C₁-C₆ alkyl), and C₁-C₆ alkyl;
- each R^{10} is independently C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, phenyl, or monocyclic heteroaryl; wherein each alkyl, alkenyl, alkynyl, phenyl, heteroaryl, cycloalkyl, and heterocycloalkyl is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen, -CN, -OH, C₁-C₆ alkyl, C₁-C₆ fluoroalkyl, C₁-C₆ hydroxyalkyl, -O-(C₁-C₆ alkyl), and -O-(C₁-C₆ fluoroalkyl); and
- each R^{11} is independently hydrogen, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocycloalkyl, phenyl, or monocyclic heteroaryl; wherein each alkyl, alkenyl, alkynyl, phenyl, heteroaryl, cycloalkyl, and heterocycloalkyl is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen, -CN, -OH, C₁-C₆ alkyl, C₁-C₆ fluoroalkyl, C₁-C₆ hydroxyalkyl, -O-(C₁-C₆ alkyl), and -O-(C₁-C₆ fluoroalkyl);
- or two R^{11} on the same nitrogen atom are taken together with the nitrogen to which they are attached to form a 3- to 10-membered *N*-heterocycloalkyl; wherein the heterocycloalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen, -CN, -OH, C₁-C₆ alkyl, C₁-C₆ fluoroalkyl, C₁-C₆ hydroxyalkyl, -O-(C₁-C₆ alkyl), and -O-(C₁-C₆ fluoroalkyl).

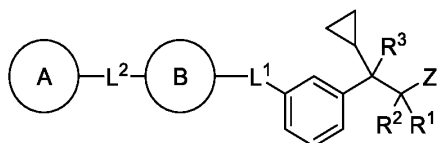
2. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 Y^1 , Y^2 , Y^3 , and Y^4 are each independently N, CH, or C- R^Y ; and
each R^Y is independently F, Cl, Br, -CN, -OH, -O-(C₁-C₆ alkyl), or C₁-C₆ alkyl.
3. The compound of claim 1 or claim 2, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 Y^1 , Y^2 , Y^3 , and Y^4 are each independently N or CH.
4. The compound of any one of claims 1-3, having the structure of Formula (II):



Formula (II)

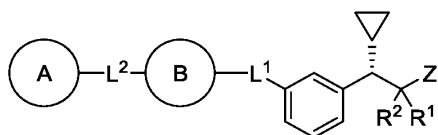
or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 R^1 , R^2 , and R^3 are each independently hydrogen, halogen, or C_1 - C_6 alkyl; and
 R^4 is C_1 - C_6 alkyl or C_3 - C_6 cycloalkyl.
6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 R^1 , R^2 , and R^3 are each independently hydrogen, halogen, or C_1 - C_4 alkyl; and
 R^4 is unsubstituted C_3 - C_6 cycloalkyl.
7. The compound of any one of claims 1-6, having the structure of Formula (III):



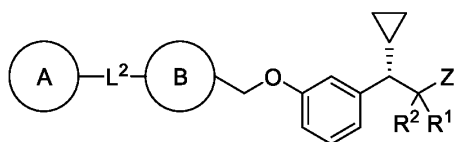
Formula (III)

- or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 R^1 , R^2 , and R^3 are each independently hydrogen, -F, -Cl, or C_1 - C_4 alkyl.
8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 R^1 , R^2 , and R^3 are each independently hydrogen, -F, or methyl.
9. The compound of any one of claims 1-8, having the structure of Formula (IV):

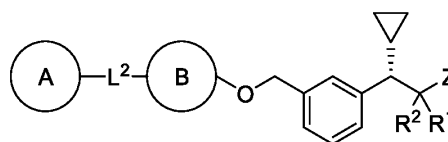


Formula (IV)

- or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 R^1 and R^2 are each independently hydrogen, -F, or methyl.
10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 L^1 is *-O-CH₂-, *-CH₂-O-, *-NR⁷-CH₂-, *-NR⁷-C(O)-, *-C(O)-NR⁷-, or *-C(O)-CH₂-;
 wherein * represents the connection to Ring B.
11. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 L^1 is *-O-CH₂- or *-CH₂-O-; wherein * represents the connection to Ring B.
12. The compound of any one of claims 1-11, having the structure of Formula (IVa) or Formula (IVb):



Formula (IVa)



Formula (IVb)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

13. The compound of any one of claims 1-12, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

Ring B is C_3 - C_{10} cycloalkylene or 3- to 10-membered heterocycloalkylene; wherein the cycloalkylene or heterocycloalkylene is unsubstituted or substituted with 1, 2, 3, or 4 R^B substituents; and

Ring A is aryl, heteroaryl, C_3 - C_{10} cycloalkyl, or 3- to 10-membered heterocycloalkyl; wherein the aryl, heteroaryl, cycloalkyl, or heterocycloalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 R^A substituents.

14. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

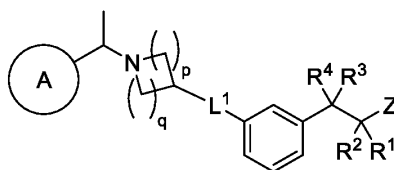
Ring B is 3- to 6-membered heterocycloalkylene; wherein the heterocycloalkylene is unsubstituted or substituted with 1, 2, 3, or 4 R^B substituents;

each R^B is independently halogen, C_1 - C_6 alkyl, or C_1 - C_6 fluoroalkyl;

L^2 is a bond or C_1 - C_6 alkylene; wherein the alkylene is unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of $-OH$, C_1 - C_6 alkyl, and $-O-(C_1-C_6 \text{ alkyl})$; and

Ring A is aryl or heteroaryl; wherein the aryl or heteroaryl is unsubstituted or substituted with 1, 2, or 3 R^A substituents.

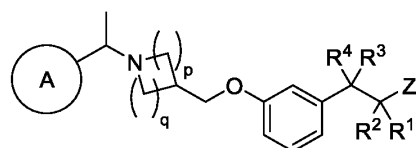
15. The compound of any one of claims 1-9, having the structure of Formula (V):



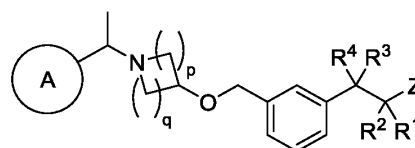
Formula (V)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof; wherein: p and q are each independently 1 or 2.

16. The compound of claim 15, having the structure of Formula (Va) or Formula (Vb):



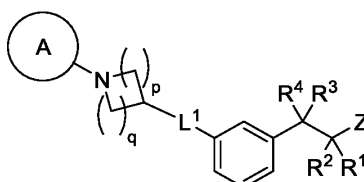
Formula (Va)



Formula (Vb)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

17. The compound of any one of claims 1-9, having the structure of Formula (VI):

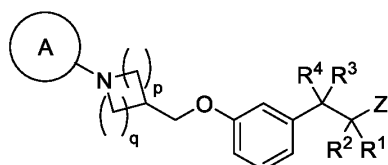


Formula (VI)

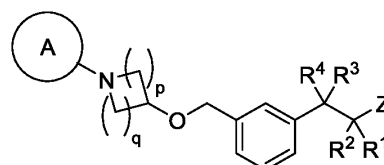
or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof; wherein:

p and q are each independently 1 or 2.

18. The compound of claim 17, having the structure of Formula (VIa) or Formula (VIb):



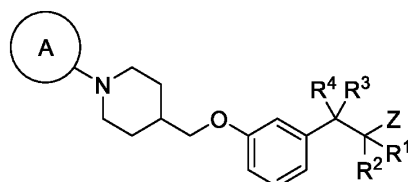
Formula (VIa)



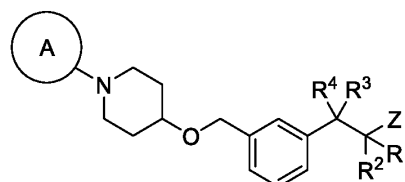
Formula (VIb)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

19. The compound of claim 17 or claim 18, having the structure of Formula (VIa-i) or Formula (VIb-i):



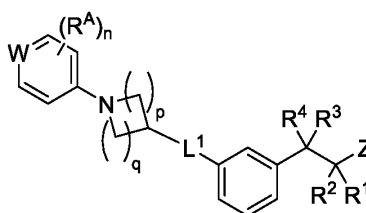
Formula (VIa-i)



Formula (VIb-i)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

20. The compound of claim 17, having the structure of Formula (XV):



Formula (XV)

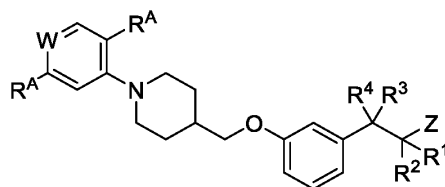
or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof; wherein:

W is N, CH, or CR^A;

each R^A is independently -F, -Cl, C₁-C₇ alkyl, C₁-C₄ fluoroalkyl, -OH, or -OR¹⁰; and

n is 0, 1, or 2.

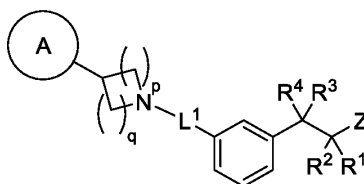
21. The compound of claim 20, having the structure of Formula (XVa-i)



Formula (XVa-i)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

22. The compound of any one of claims 1-9, having the structure of Formula (VII):

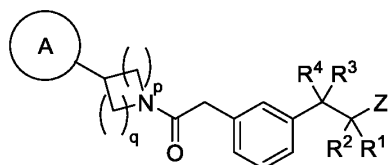


Formula (VII)

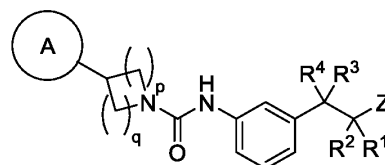
or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof; wherein:

p and q are each independently 1 or 2.

23. The compound of claim 22, having the structure of Formula (VIIa) or Formula (VIIb):



Formula (VIIa)



Formula (VIIb)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

24. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

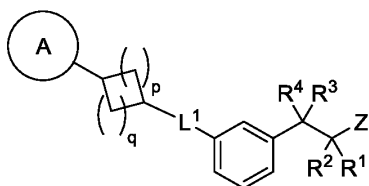
Ring B is C₃-C₆ cycloalkylene; wherein the cycloalkylene is unsubstituted or substituted with 1, 2, 3, or 4 R^B substituents;

each R^B is independently halogen, C₁-C₆ alkyl, or C₁-C₆ fluoroalkyl;

L² is a bond or C₁-C₆ alkylene; wherein the alkylene is unsubstituted or substituted with 1, 2, or 3 substituents selected from the group consisting of -OH, C₁-C₆ alkyl, and -O-(C₁-C₆ alkyl); and

Ring A is aryl or heteroaryl; wherein the aryl or heteroaryl is unsubstituted or substituted with 1, 2, or 3 R^A substituents.

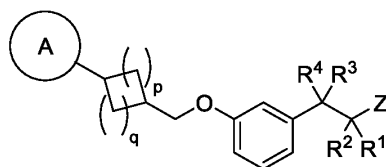
25. The compound of any one of claims 1-9, having the structure of Formula (VIII):



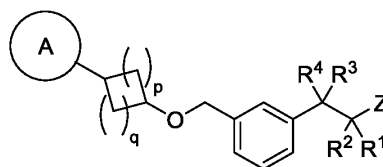
Formula (VIII)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof; wherein: p and q are each independently 1 or 2.

26. The compound of claim 25, having the structure of Formula (VIIIa) or Formula (VIIIb):



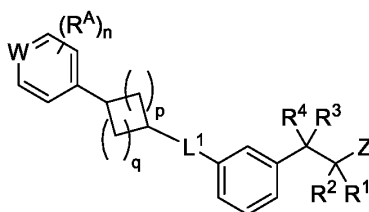
Formula (VIIIa)



Formula (VIIIb)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

27. The compound of claim 25, having the structure of Formula (XIV)



Formula (XIV)

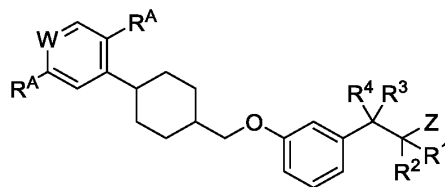
or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof; wherein:

W is N, CH, or CR^A ;

each R^A is independently -F, -Cl, C_1 - C_7 alkyl, C_1 - C_4 fluoroalkyl, -OH, or -OR¹⁰; and

n is 0, 1, or 2.

28. The compound of claim 27, having the structure of Formula (XIVa-i)

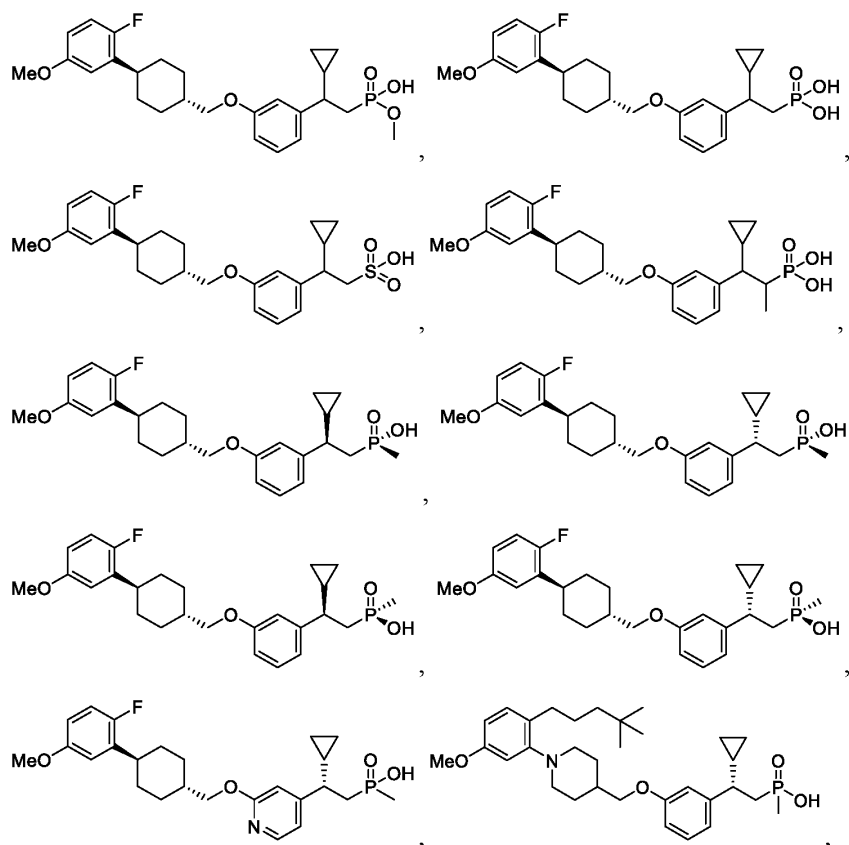


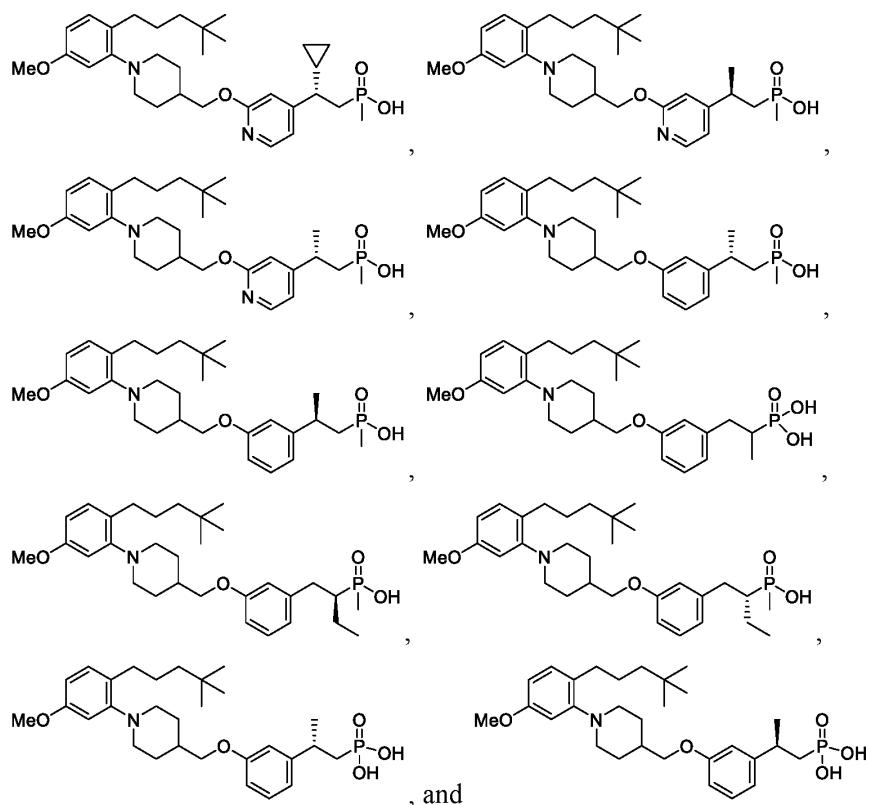
Formula (XIVa-i)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

29. The compound of any one of claims 1-28, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 Z is $-\text{P}(=\text{O})(\text{H})\text{OR}^6$, $-\text{P}(=\text{O})(\text{R}^5)\text{OR}^6$, $-\text{P}(=\text{O})(\text{OR}^6)_2$, $-\text{S}(=\text{O})(\text{OR}^6)$, $-\text{SO}_2\text{OR}^6$, $-\text{C}(=\text{O})\text{NHSO}_2\text{R}^5$;
 R^5 is C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, phenyl, or $-(\text{C}_1$ - C_6 alkyl)-phenyl; wherein each alkyl, cycloalkyl, and phenyl is independently unsubstituted or substituted with one, two, or three substituents selected from $-\text{F}$, $-\text{Cl}$, $-\text{OH}$, $-\text{O}-(\text{C}_1$ - C_6 alkyl), C_1 - C_6 alkyl, and C_1 - C_6 hydroxyalkyl; and
 each R^6 is independently hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, phenyl, or $-(\text{C}_1$ - C_6 alkyl)-phenyl; wherein each alkyl, cycloalkyl, and phenyl is independently unsubstituted or substituted with one, two, or three substituents selected from $-\text{F}$, $-\text{Cl}$, $-\text{OH}$, $-\text{O}-(\text{C}_1$ - C_6 alkyl), C_1 - C_6 alkyl, and C_1 - C_6 hydroxyalkyl.
30. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 Z is $-\text{P}(=\text{O})(\text{H})\text{OR}^6$, $-\text{P}(=\text{O})(\text{R}^5)\text{OR}^6$, $-\text{P}(=\text{O})(\text{OR}^6)_2$, $-\text{S}(=\text{O})(\text{OR}^6)$, or $-\text{SO}_2\text{OR}^6$;
 R^5 is C_1 - C_6 alkyl; and
 each R^6 is independently hydrogen or C_1 - C_6 alkyl.
31. The compound of any one of claims 1-30, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 Z is $-\text{P}(=\text{O})(\text{H})\text{OR}^6$, $-\text{P}(=\text{O})(\text{R}^5)\text{OR}^6$, $-\text{P}(=\text{O})(\text{OR}^6)_2$, or $-\text{SO}_2\text{OR}^6$;
 R^5 is $-\text{CH}_3$, $-\text{CH}_2\text{CH}_3$, $-\text{CH}_2\text{CH}_2\text{CH}_3$, $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $-\text{CH}_2\text{CH}(\text{CH}_3)_2$, or $-\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$; and
 each R^6 is independently hydrogen, $-\text{CH}_3$, $-\text{CH}_2\text{CH}_3$, $-\text{CH}_2\text{CH}_2\text{CH}_3$, $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $-\text{CH}_2\text{CH}(\text{CH}_3)_2$, or $-\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$.
32. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 Z is $-\text{P}(=\text{O})(\text{H})\text{OH}$, $-\text{P}(=\text{O})(\text{CH}_3)\text{OH}$, $-\text{P}(=\text{O})(\text{CH}_2\text{CH}_3)\text{OH}$, $-\text{PO}_3\text{H}_2$, $-\text{P}(=\text{O})(\text{OCH}_3)(\text{OH})$, $-\text{S}(=\text{O})\text{OH}$, $-\text{SO}_2\text{OH}$, or $-\text{C}(=\text{O})\text{NHSO}_2\text{CH}_3$.
33. The compound of any one of claims 1-32, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 Z is $-\text{P}(=\text{O})(\text{CH}_3)\text{OH}$, or $-\text{SO}_2\text{OH}$.
34. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
 Z is $-\text{P}(=\text{O})(\text{CH}_3)\text{OH}$.

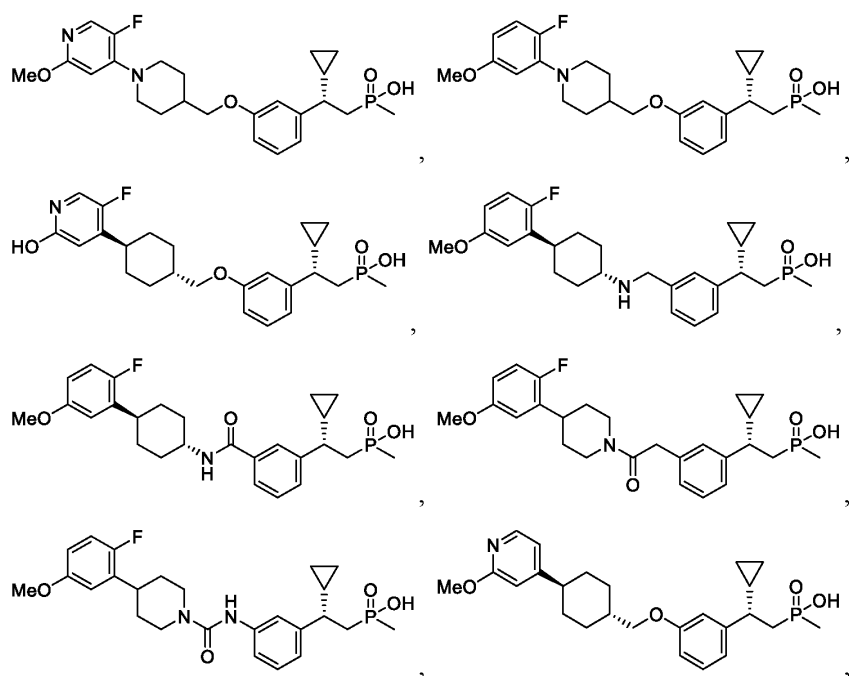
35. The compound of any one of claims 1-34, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:
- each R¹⁰ is independently C₁-C₆ alkyl; wherein each alkyl is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen, -OH, C₁-C₆ alkyl and C₁-C₆ hydroxyalkyl; and
- each R¹¹ is independently hydrogen, C₁-C₆ alkyl, or monocyclic heteroaryl; wherein each alkyl and heteroaryl is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen, -OH, C₁-C₆ alkyl and C₁-C₆ hydroxyalkyl;
- or two R¹¹ on the same nitrogen atom are taken together with the nitrogen to which they are attached to form a 3- to 6-membered *N*-heterocycloalkyl; wherein the heterocycloalkyl is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected from the group consisting of halogen, -OH, C₁-C₆ alkyl, and C₁-C₆ hydroxyalkyl.
36. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, selected from:

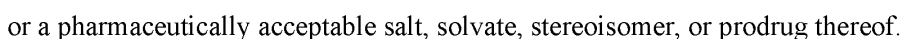




or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

37. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, selected from:





38. A pharmaceutical composition comprising a compound of any one of claims 1-37, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, and at least one pharmaceutically acceptable excipient.
39. A method of treating a condition or disorder involving the gut-brain axis 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 1-37, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.
40. The method of claim 39, wherein the condition or disorder is associated with GPR40 activity.

41. The method of claim 39 or claim 40, wherein the condition or disorder is a metabolic disorder.
42. The method of claim 41, wherein the condition or disorder is type 2 diabetes, hyperglycemia, metabolic syndrome, obesity, hypercholesterolemia, nonalcoholic steatohepatitis, or hypertension.
43. The method of claim 39 or claim 40, wherein the condition or disorder is a nutritional disorder.
44. The method of claim 43, wherein the condition or disorder is short bowel syndrome, intestinal failure, or intestinal insufficiency.
45. The method of any one of claims 39-44, wherein the compound is gut-restricted.
46. The method of claim 45, wherein the compound has low systemic exposure.
47. The method of any one of claims 39-46, further comprising administering one or more additional therapeutic agents to the subject.
48. The method of claim 47, wherein the one or more additional therapeutic agents are selected from a TGR5 agonist, a GPR119 agonist, an SSTR5 antagonist, an SSTR5 inverse agonist, a CCK1 agonist, a PDE4 inhibitor, a DPP-4 inhibitor, a GLP-1 receptor agonist, a GOAT inhibitor, metformin, or combinations thereof.
49. The method of claim 48, wherein the TGR5 agonist, GPR119 agonist, SSTR5 antagonist, SSTR5 inverse agonist or CCK1 agonist is gut-restricted.