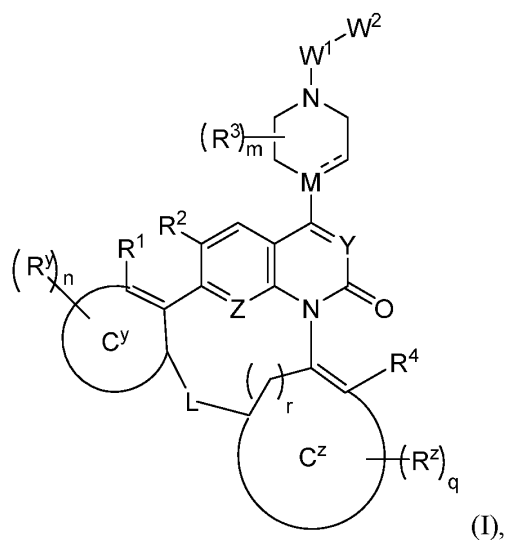


CLAIMS

We claim:

1. A compound of Formula (I)



wherein:

Y is N or C(H);

Z is N or C(R⁵);

M is C or N;

the dashed line in the illustrated ring containing M indicates an optional double bond;

L is C₁-C₇ alkylene or C₁-C₇ heteroalkylene,

wherein said alkylene or heteroalkylene is unsubstituted or substituted by 1 to 5

substituents which are independently selected from oxo, fluoro, C₁-C₃ alkyl, C₁-C₃ fluoroalkyl, amino, and hydroxy;

or alternatively, two geminal, vicinal or hominal substitutions of said alkylene or heteroalkylene can, together with the carbon atoms to which they are attached, form a ring C^L, wherein said ring C^L is C₃-C₆ cycloalkyl, and wherein said ring C^L is unsubstituted or substituted by 1 to 3 fluoro;

R¹ is halo, H, C₁-C₄ alkyl, C₁-C₄ fluoroalkyl, or C₁-C₄ hydroxyalkyl;

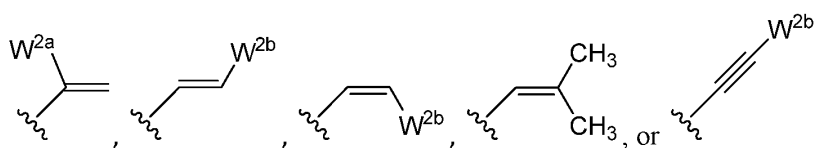
R² is H, CH₃, or halo;

each R³ is independently:

- (a) C₁-C₄ alkyl, C₁-C₄ cyanoalkyl, C₁-C₄ fluoroalkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ alkylphenyl, oxo, or carboxy;
- (b) or, alternatively, two R³ substituents, together with the carbon atoms to which they are attached, can form a 3- to 6-membered bicyclo- or spirocyclic ring system with the illustrated ring containing M;

W¹ is -C(O)- or -S(O)₂-;

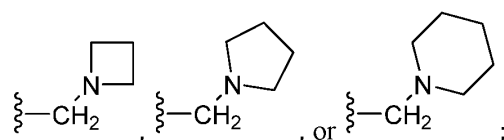
W² is a group of the formula:



wherein

W^{2a} is H, CH₃, F, cyano, CH₂OH, CH₂CH₂OH, or CH₂Br;

W^{2b} is CH₃, CH₂NH₂, CH₂N(H)CH₃, CH₂N(CH₃)₂, CH₂-NH-cyclopropyl,



R⁴ is H, C₁-C₄ alkyl, or C₃-C₅ cycloalkyl;

R⁵ is H or halo;

ring CY is:

- (a) phenyl,
- (b) a 5- to 6-membered monocyclic heteroaryl containing one to three heteroatoms selected from N, O, and S; or
- (c) a 9- to 10-membered bicyclic heteroaryl containing one to four heteroatoms selected from N, O, and S;

each R^Y is independently halo, hydroxy, C₁-C₃ alkyl, C₁-C₃ fluoroalkyl, C₁-C₃ alkoxy, cyano, hydroxy, or C₁-C₃ hydroxyalkyl;

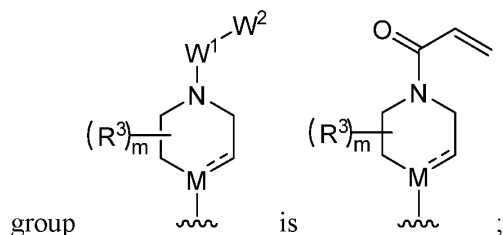
ring CZ is:

- (a) phenyl, or
- (b) a 5- to 6-membered heteroaryl containing one to three heteroatoms selected from N, O, and S;

each R^Z is independently halo, hydroxy, C₁-C₃ alkyl, C₁-C₃ fluoroalkyl, C₁-C₃ alkoxy, cyano, or C₁-C₃ hydroxyalkyl;

the subscript m is 0, 1, 2, or 3;
 the subscript n is 0, 1, 2, 3, or 4;
 the subscript q is 0, 1, 2, 3, or 4; and
 the subscript r is 0 or 1;
 or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 or the pharmaceutically acceptable salt thereof, wherein the



each R³ is independently:

- (a) C₁-C₄ alkyl, C₁-C₄ cyanoalkyl, C₁-C₄ fluoroalkyl, C₁-C₄ hydroxyalkyl, C₁-C₄ alkylphenyl, oxo, or carboxy;
- (b) or, alternatively, two R³ substituents, together with the carbon atoms to which they are attached, can form a 3- to 6-membered bicyclo- or spirocyclic ring system with the illustrated ring containing M; and

each R^y is independently halo, hydroxy, C₁-C₃ alkyl, C₁-C₃ fluoroalkyl, C₁-C₃ alkoxy, cyano, hydroxy, or C₁-C₃ hydroxyalkyl.

3. The compound of claim 1 or 2 or the pharmaceutically acceptable salt thereof, wherein L is a group -X¹-X²-X⁵-X⁴-X³-, wherein:

X¹ and X³ are independently -CH₂-, -O-, -S-, -C(O)-, -C(H)(CH₃)-, or -N(H)-;

X² is -CH₂-, -CF₂-, -C(H)(F)-, -C(H)(OH)-, -C(H)(CH₃)-, -O-, -S-, -N(H)-, or -C(O)-;

X⁴ is absent, -CF₂-, -C(H)(F)-, -C(H)(OH)-, -C(H)(CH₃)-, -CH₂-, -O-, -S-, -N(H)-, or -C(O)-;

X⁵ is absent, -CH₂-, -CF₂-, -C(H)(F)-, -O-, -S-, -N(H)-, -CH₂CH₂-, -CH₂CH₂CH₂-, -O-CH₂-, -CH₂-O-;

wherein:

when X¹ is -O-, -S-, or -N(H)-, then X² is -CH₂- or -C(O)-;

when X² is -O-, -S-, or -N(H)-, then X¹ is -CH₂- or -C(O)- and X⁵, if present, is -CH₂-, -CF₂-, -CH₂CH₂-, or -CH₂CH₂CH₂-;

when X³ is -O-, -S-, or -N(H)-, then X⁴ is -CH₂- or -C(O)-;

when X⁴ is -O-, -S-, or -N(H)- then X³ is -CH₂- and X⁵, if present, is -CH₂-, -CH₂CH₂-,
 , or -CH₂CH₂CH₂-; and

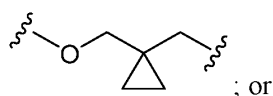
when X⁵ is -O-, -S-, or -N(H)-, then X² and X⁴ are both -CH₂-.

4. The compound of claim 3 or the pharmaceutically acceptable salt thereof, wherein the group -X¹-X²-X⁵-X⁴-X³- is:

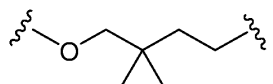
-O-CH₂CH₂CH₂-O-;
 -CH₂CH₂CH₂-O-;
 -O-CH₂CH₂CH₂-;
 -O-C(H)(CH₃)CH₂CH₂-;
 -O-CH₂CH₂CH₂CH₂-;
 -O-CH₂CF₂CH₂CH₂-;
 -CH₂CH₂CH₂CH₂-O-;
 -CH₂CH₂CH₂CH₂-;
 -CH₂CH₂CH₂-;
 -CH₂CH₂C(H)(OH)CH₂-;
 -CH₂C(H)(OH)CH₂CH₂-;
 -O-CH₂CH₂-;
 -CH₂CH₂-O-;
 -O-CH₂CH₂-O-;
 -O-CH₂C(H)(CH₃)-O-;
 -O-C(H)(CH₃)CH₂-O-;
 -O-CH₂CF₂CH₂-O-;
 -CH₂CH₂-O-CH₂CH₂-;
 -O-CH₂CH₂-O-CH₂CH₂-O-;
 -CH₂-O-CH₂CH₂-;
 -CH₂CH₂-O-CH₂-;
 -N(H)-CH₂CH₂CH₂-;
 -O-CH₂CH₂-O-CH₂-;
 -C(O)-N(H)-CH₂CH₂CH₂-;

-CH₂CH₂CH₂-N(H)-C(O)-;

-N(H)-CH₂CH₂-O-CH₂-;



; or



5. The compound of claim 4 or the pharmaceutically acceptable salt thereof, wherein the group -X¹-X²-X⁵-X⁴-X³- is:

-O-CH₂CH₂CH₂-O-;

-CH₂CH₂CH₂-O-;

-O-CH₂CH₂CH₂-;

-O-CH₂CH₂CH₂CH₂-;

-CH₂CH₂CH₂CH₂-;

-O-CH₂CH₂-;

-O-CH₂CH₂-O-;

-O-CH₂CF₂CH₂-O-;

-CH₂CH₂-O-CH₂CH₂-;

-C(O)-N(H)-CH₂CH₂CH₂-; or

-CH₂-O-CH₂CH₂-.

6. The compound of claim 4 or the pharmaceutically acceptable salt thereof, wherein the group -X¹-X²-X⁵-X⁴-X³- is:

-O-CH₂CH₂CH₂-;

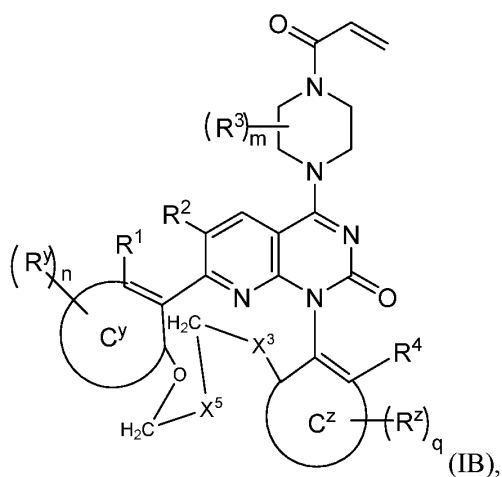
-O-CH₂CH₂CH₂CH₂-;

-O-CH₂CH₂-O-; or

-O-CH₂CF₂CH₂CH₂-.

7. The compound of any one of claims 1-6 or the pharmaceutically acceptable salt thereof, wherein R¹ is fluoro.

8. The compound of any one of claims 1-7 or the pharmaceutically acceptable salt thereof, wherein R² is fluoro or chloro.
9. The compound of any one of claims 1-8 or the pharmaceutically acceptable salt thereof, wherein R⁴ is H or isopropyl.
10. The compound of any one of claims 1-9 or the pharmaceutically acceptable salt thereof, wherein the subscript m is 1 or 2, and R³ is methyl or -CH₂-CN.
11. The compound of any one of claims 1-10 or the pharmaceutically salt thereof, wherein M is N.
12. The compound of any one of claims 1-11 or the pharmaceutically acceptable salt thereof, wherein CY is phenyl.
13. The compound of any one of claims 1-12 or the pharmaceutically acceptable salt thereof, wherein CZ is phenyl or pyridine.
14. The compound of any one of claims 1-13 or the pharmaceutically acceptable salt thereof, wherein Y is N.
15. The compound of any one of claims 1-14 or the pharmaceutically acceptable salt thereof, wherein Z is N.
16. The compound of any one of claims 1-15 or the pharmaceutically acceptable salt thereof, wherein the subscript r is 0.
17. The compound of claim 1 or the pharmaceutically acceptable salt thereof, wherein the compound of Formula (I) has Formula (IB)



wherein:

Cy is phenyl;

Cz is pyridyl;

X³ is -CH₂- or -O-;

X⁵ is absent, -CH₂-, -CF₂-, or -C(H)(F)-;

R¹ is fluoro or chloro;

R² is fluoro or chloro; and

R⁴ is C₁-C₄ alkyl.

18. The compound of claim 17 or the pharmaceutically acceptable salt thereof, wherein the group -O-CH₂-X⁵-CH₂-X³- is:

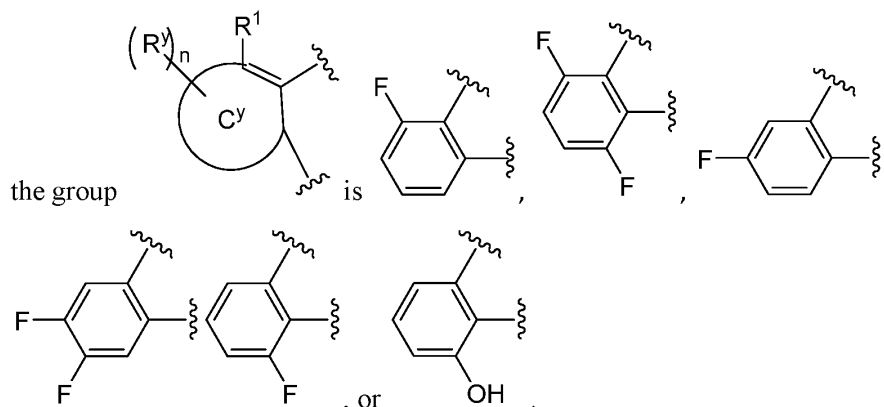
-O-CH₂CH₂CH₂-;

-O-CH₂CH₂CH₂CH₂-;

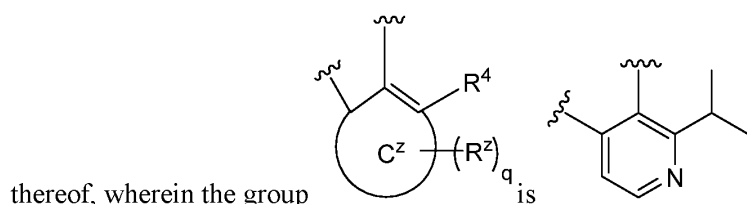
-O-CH₂CH₂-O-; or

-O-CH₂CF₂CH₂CH₂-.

19. The compound of claim 17 or 18 or the pharmaceutically acceptable salt thereof, wherein



20. The compound of any one of claims 17-19 or the pharmaceutically acceptable salt thereof, wherein the group



21. The compound of claim 1, wherein the compound is:

18,21-difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-12,13-dihydro-4*H*,11*H*-1,19-ethenopyrido[4,3-*f*]pyrimido[1,6-*h*][1,5,8,10]benzodioxadiazacyclotridecin-4-one;

21-fluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-12,13-dihydro-4*H*,11*H*-1,19-(ethanediyliidene)dipyrido[4,3-*b*:3',2'-*h*]pyrimido[1,6-*d*][1,10,4,6]dioxadiazacyclotridecin-4-one;

22-fluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-12,13-dihydro-4*H*,11*H*-1,20-ethenopyrido[4',3':2,3]pyrimido[1',6':4,5][1,4,6,10]oxatriazacyclotridecino[8,9,10-*hi*]indazol-4-one;

18,21-difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-ethenopyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

20-fluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,18-(ethanediyliidene)pyrazolo[5,1-*e*]pyrido[4,3-*k*]pyrimido[1,6-*α*][1,3,6]triazacyclododecin-4-one;

22-fluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,20-

(ethanediylidene)pyrido[4',3':12,13]pyrimido[1',6':1,2][1,3,7]triazacyclotridecino[5,6,7-*hi*]indazol-4-one;

2-[(3*R*,5*S*)-3,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-18,21-difluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-ethenopyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-18,21-difluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-ethenopyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

19-Chloro-16-fluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-10,11-dihydro-4*H*-1,17-ethenodibenzo[*b,h*]pyrimido[6,1-*f*][1,5,7]oxadiazacycloundecin-4-one;

17,20-difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

[(2*S*)-4-[17,20-difluoro-4-oxo-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-2-yl]-1-(prop-2-enoyl)piperazin-2-yl]acetonitrile;

17,20-difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-12,12,18,21-tetrafluoro-6-(propan-2-yl)-12,13-dihydro-4*H*,11*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,5,8,10]benzodioxadiazacyclotridecin-4-one;

[(2*S*)-4-[17,20-difluoro-4-oxo-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-2-yl]-1-(prop-2-enoyl)piperazin-2-yl]acetonitrile;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

19,22-Difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-7-(propan-2-yl)-11,12,13,14-tetrahydro-4*H*-1,20-(ethanediylidene)-6,10-(metheno)pyrimido[1,6-*k*][1,8,11,13]benzoxatriazacyclohexadecin-4-one;

18,21-Difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,13,14-tetrahydro-4*H*-1,19-ethenopyrido[3,4-*e*]pyrimido[6,1-*c*][9,2,4]benzoxadiazacyclotridecin-4-one;

17,20-difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11-dihydro-1,18-ethenopyrido[3,4-*e*]pyrimido[6,1-*c*][9,2,4]benzoxadiazacyclododecin-4(13*H*)-one;

18,21-Difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-1,19-ethenopyrido[3,4-*e*]pyrimido[6,1-*c*][2,4,10]benzotriazacyclotridecine-4,14-dione;

17,20-Difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-12,13-dihydro-1,18-ethenopyrido[3,4-*e*]pyrimido[6,1-*c*][7,2,4]benzoxadiazacyclododecin-4(11*H*)-one;

(5*aS_a*,17*aR_a*)-20-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

(5*aS_a*,17*aR_a*)-20-Chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17-difluoro-6-(propan-2-yl)-11,12-di[(²H)hydro](11,12-²H₂)-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

(5*aR_a*,18*aR_a*)-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-12,12,18,21-tetrafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

(5*aR_a*,18*aR_a*)-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-12,12,17,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

(5*aR_a*,18*aR_a*)-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-12,12,15,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

(5*aR_a*,18*aR_a*)-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-12,12,16,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

(5*aS_a*,17*aR_a*)-20-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-16,17-difluoro-6-(propan-2-yl)-11,12-di[(²H)hydro](11,12-²H₂)-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-12,12,17,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)dipyrimido[4,5-*f*:1',6'-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

21-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-12,12,18-trifluoro-6-(propan-2-yl)-12,13-dihydro-4*H*,11*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,5,8,10]benzodioxadiazacyclotridecin-4-one;

2'-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-18',21'-difluoro-6'-(propan-2-yl)-10',11'-dihydro-4'*H*,13'*H*-spiro[cyclopropane-1,12'-[14]oxa[3,5,7,20]tetraaza[1,19](ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin]-4'-one;

2'-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-15',18',21'-trifluoro-6'-(propan-2-yl)-10',11'-dihydro-4'*H*,13'*H*-spiro[cyclopropane-1,12'-[14]oxa[3,5,7,20]tetraaza[1,19](ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin]-4'-one;

2'-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17',18',21'-trifluoro-6'-(propan-2-yl)-10',11'-dihydro-4'*H*,13'*H*-spiro[cyclopropane-1,12'-[14]oxa[3,5,7,20]tetraaza[1,19](ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin]-4'-one;

20-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17-fluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-Dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-16,17,20-trifluoro-6-(propan-2-yl)-11,12-di[(²H)hydro](11,12-²H₂)-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

12,12,17,18,21-pentafluoro-6-(propan-2-yl)-2-[4-(prop-2-enoyl)piperazin-1-yl]-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

12,12,17,18,21-pentafluoro-2-[(3*R*)-3-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

2-[(2*S*,5*R*)-2,5-Dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17,20-trifluoro-6-(propan-2-yl)-11,12-di[(²H)hydro](11,12-²H₂)-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-22-fluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,20-(ethanediylidene)pyrido[4',3':12,13]pyrimido[1',6':1,2][1,3,7]triazacyclotridecino[5,6,7-*hi*]indazol-4-one;

9-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-20-fluoro-6-(propan-2-yl)-17-(trifluoromethyl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

20-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-16,17-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenodipyrimido[4,5-*e*:1',6'-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

17-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-20-fluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,16,17,20-tetrafluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-16,17,20-trifluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

15,18,21-trifluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-15,16,17,20-tetrafluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-12-methyl-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

20-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,16-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

17-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-20-fluoro-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-15,16,20-trifluoro-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

18,21-difluoro-2-[(2*S*)-4-(2-fluoroprop-2-enoyl)-2-methylpiperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-ethenopyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-20-fluoro-6-(propan-2-yl)-16-(trifluoromethyl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

6-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17,20-trifluoro-11,12-dihydro-4*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-19,22-difluoro-24-methyl-7-(propan-2-yl)-11,12,13,14-tetrahydro-4*H*-1,20-etheno-6,10-(metheno)pyrimido[1,6-*k*][1,8,11,13]benzoxatriazacyclohexadecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-16,17,20-trifluoro-10-methyl-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2'-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-16',17',20'-trifluoro-6'-(propan-2-yl)-4'*H*,10'*H*,12'*H*-spiro[cyclopropane-1,11'-[13]oxa[3,5,7,19]tetraaza[1,18]ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin]-4'-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17,20-trifluoro-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7]benzodioxazacyclododecin-4-one;

(11*S*)-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17,20-trifluoro-11-methyl-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17,20-trifluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-16,19-difluoro-6-(propan-2-yl)-10,11-dihydro-4*H*-1,17-ethenopyrido[4,3-*d*]pyrimido[1,6-*f*][1,6,8]benzoxadiazacycloundecin-4-one;

12,12,17,18,21-pentafluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

2-[(2*S*)-2-ethyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[2-(difluoromethyl)-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[2-benzyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

17,20-difluoro-6-(propan-2-yl)-2-[4-(prop-2-enoyl)-2-(2,2,2-trifluoroethyl)piperazin-1-yl]-11,12-dihydro-4*H*,10*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[2,2-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(3*S*)-3-ethyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

18,21-difluoro-6-(propan-2-yl)-2-[(1*S*,4*S*)-5-(prop-2-enoyl)-2,5-diazabicyclo[2.2.1]heptan-2-yl]-10,11,12,13-tetrahydro-4*H*-1,19-ethenopyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;

17,20-difluoro-6-(propan-2-yl)-2-[5-(prop-2-enoyl)-2,5-diazabicyclo[2.2.2]octan-2-yl]-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

17,20-difluoro-4-oxo-6-(propan-2-yl)-2-[5-(prop-2-enoyl)-2,5-diazabicyclo[2.2.2]octan-2-yl]-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-19,22-difluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,20-(ethanediylidene)pyrido[4',3':12,13]pyrimido[1',6':1,2][1,3,7]triazacyclotridecino[5,6,7-*hi*]indazol-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-18,22-difluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,20-(ethanediylidene)pyrido[4',3':12,13]pyrimido[1',6':1,2][1,3,7]triazacyclotridecino[5,6,7-*hi*]indazol-4-one;

20-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17-fluoro-6-(propan-2-yl)-10,11-dihydro-1,18-ethenopyrido[3,4-*e*]pyrimido[6,1-*c*][9,2,4]benzoxadiazacyclododecin-4(13*H*)-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17-difluoro-20-methyl-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

6-cyclopropyl-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17,20-trifluoro-11,12-dihydro-4*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

17,20-difluoro-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzotriazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-20-fluoro-14-hydroxy-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,20-difluoro-6-(propan-2-yl)-11,12-dihydro-4*H*-1,18-(ethanediylidene)pyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-17,20-difluoro-6-(propan-2-yl)-10,11-dihydro-1,18-ethenopyrido[3,4-*e*]pyrimido[6,1-*c*][9,2,4]benzoxadiazacyclododecin-4(13*H*)-one;

2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-20-fluoro-6-(propan-2-yl)-14-(trifluoromethyl)-11,12-dihydro-4*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,4,7,9]benzodioxadiazacyclododecin-4-one;

22-fluoro-9-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-13-(propan-2-yl)-18,19-dihydro-11*H*,17*H*-6,8-ethenopyrido[4',3':11,12]pyrimido[1',6':1,2][1,3,7]triazacyclododecino[5,6,7-*hi*]indazol-11-one;
 17,20-difluoro-12-hydroxy-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,18-ethenopyrido[3,4-*e*]pyrimido[6,1-*c*][2,4]benzodiazacyclododecin-4-one;
 17,20-difluoro-11-hydroxy-2-[(2*S*)-2-methyl-4-(prop-2-enoyl)piperazin-1-yl]-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,18-ethenopyrido[3,4-*e*]pyrimido[6,1-*c*][2,4]benzodiazacyclododecin-4-one;
 19-chloro-2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-16-fluoro-6-(propan-2-yl)-10,11-dihydro-4*H*-1,17-ethenopyrido[4,3-*d*]pyrimido[1,6-*f*][1,6,8]benzoxadiazacycloundecin-4-one;
 2-[(2*S*,5*R*)-2,5-dimethyl-4-(prop-2-enoyl)piperazin-1-yl]-14,17-difluoro-20-methyl-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-4-one;
 2-{(2*R*,5*S*)-4-[20-chloro-14,17-difluoro-4-oxo-6-(propan-2-yl)-11,12-dihydro-4*H*,10*H*-1,18-ethenopyrido[4,3-*e*]pyrimido[1,6-*g*][1,7,9]benzoxadiazacyclododecin-2-yl]-2,5-dimethylpiperazine-1-carbonyl}prop-2-enenitrile;
 2-{(2*S*,5*R*)-4-[4-(dimethylamino)but-2-ynoyl]-2,5-dimethylpiperazin-1-yl}-12,12,17,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;
 2-[(2*S*,5*R*)-4-(but-2-ynoyl)-2,5-dimethylpiperazin-1-yl]-12,12,17,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;
 2-[(2*S*,5*R*)-2,5-dimethyl-4-(2-methylprop-2-enoyl)piperazin-1-yl]-12,12,17,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;
 2-{(2*S*,5*R*)-4-[(2*E*)-4-(dimethylamino)but-2-enoyl]-2,5-dimethylpiperazin-1-yl}-12,12,17,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one;
 2-[(2*S*,5*R*)-4-(ethanesulfonyl)-2,5-dimethylpiperazin-1-yl]-12,12,17,18,21-pentafluoro-6-(propan-2-yl)-10,11,12,13-tetrahydro-4*H*-1,19-(ethanediylidene)pyrido[4,3-*f*]pyrimido[1,6-*h*][1,8,10]benzoxadiazacyclotridecin-4-one; or
 a pharmaceutically acceptable salt thereof.

22. A pharmaceutical composition comprising the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
23. A method of inhibiting KRAS G12C protein comprising contacting KRAS G12C protein with the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, to inhibit the activity of the KRAS G12C protein.
24. A method of treating cancer comprising administering a therapeutically effective amount of the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, to a subject in need of such treatment.
25. The method of claim 24, further comprising administering an additional active agent to the subject.
26. The compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, for use in therapy, or use of the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, in therapy.
27. The compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, for use in treating cancer, or use of a compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, for treating cancer.
28. The compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment of cancer, or use of the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment of cancer.
29. The compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, and an additional anti-cancer agent, for use in the treatment of cancer, or use of the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, and the additional anti-cancer agent for treating cancer.

30. The compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, and an additional anti-cancer agent, for the preparation of a medicament for the treatment of cancer, or use of the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, and the additional anti-cancer agent, for the preparation of a medicament for the treatment of cancer.

31. A pharmaceutical composition comprising the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, for use in the treatment of cancer, or use of the pharmaceutical composition comprising the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, for treating cancer.

32. A pharmaceutical composition comprising the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, and an additional anti-cancer agent, for use in the treatment of cancer, or use of the pharmaceutical composition comprising the compound of any one of claims 1-21, or the pharmaceutically acceptable salt thereof, and the additional anti-cancer agent, for treating cancer.