provided that when X6 is N, then R^5 and R^6 are not hydrogen.

[0005a] In one aspect, provided herein is a pharmaceutical composition comprising a compound of Formula (II) or as disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0005b] In another aspect, provided herein is the compound of Formula (II) or as disclosed herein or a pharmaceutical composition as disclosed herein for use as a medicament.

[0005c] In another aspect, provided herein is use of the compound of Formula (II) or as disclosed herein or a pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating cancer.

[0006] One embodiment provides a pharmaceutical composition comprising a compound of Formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient. One embodiment provides a pharmaceutical composition comprising a compound of Formula (II), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0007] One embodiment provides a method of treating cancer in a patient in need thereof, comprising administering to the patient a compound of Formula (I), or a pharmaceutically acceptable salt thereof. One embodiment provides a method of treating cancer in a patient in need thereof, comprising administering to the patient a compound of Formula (II), or a pharmaceutically acceptable salt thereof.

INCORPORATION BY REFERENCE

[0008] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

DETAILED DESCRIPTION OF THE INVENTION

[0009] As used herein and in the appended claims, the singular forms "a," "and," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an agent" includes a plurality of such agents, and reference to "the cell" includes reference to one or more cells (or to a plurality of cells) and equivalents thereof known to those skilled in the art, and so forth. When ranges are used herein for physical properties, such as molecular weight, or chemical properties, such as chemical formulae, all combinations and subcombinations of ranges and specific embodiments therein are intended to be included. The term "about" when referring to a number or a

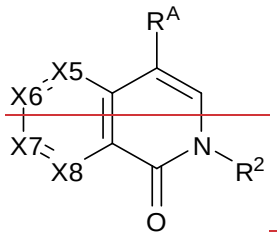
numerical range means that the number or numerical range referred to is an approximation within experimental variability (or within statistical experimental error), and thus the number or numerical range may vary between 1% and 15% of the stated number or numerical range. The term "comprising" (and related terms such as "comprise" or "comprises" or "having" or "including") is not intended to exclude that in other certain embodiments, for example, an embodiment of any composition of matter, composition, method, or process, or the like, described herein, may "consist of" or "consist essentially of" the described features.

Definitions

CLAIMS

We Claim:

1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof,



Formula (I)

wherein,

R^2 is selected from CH_3, CH_2CH_3, CH_2CF_3, CH_2F, CHF_2, CF_3, CH_2D, CHD_2, or CD_3;

X5 is C-R^5 or N;

X6 is C-R^6 or N;

X7 is C-R^7 or N;

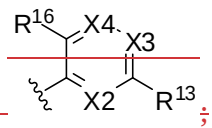
X8 is C-R^8 or N; wherein no more than two of X5, X6, X7, or X8 may be N;

R^5 is hydrogen, halogen, -OH, -CN, -OR^{61}, -NHR^{61}, -$N(R^{61})_2$, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, wherein each R^{61} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

R^6 is hydrogen, halogen, -OH, -CN, -OR^{61}, -NHR^{61}, -$N(R^{61})_2$, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, wherein each R^{61} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

R^7 is hydrogen, halogen, -OH, -CN, -OR^{61}, -NHR^{61}, -$N(R^{61})_2$, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, wherein each R^{61} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

R^8 is hydrogen, halogen, or alkyl;

R^A is ;

X2 is N or C-R^{12}, wherein R^{12} is hydrogen, halogen, alkyl, or alkoxy;

R^{13} is -Y-Z;

Y is selected from a bond, $-CH_2-$, or $-CH(C_1-C_4\text{ alkyl})-$;

Z is selected from $-SO_2R^{21}$, $-N(R^{22})SO_2R^{21}$, $-SO_2N(R^{22})_2$, $-N(R^{22})SO_2N(R^{22})_2$, $-CON(R^{22})_2$, $-N(R^{22})CO_2R^{21}$, $-N(R^{22})CON(R^{22})_2$, $-N(R^{22})COR^{21}$, $-COR^{21}$, $-OC(O)N(R^{22})_2$, $-OSO_2N(R^{22})_2$, or $-N(R^{22})SO_3R^{21}$;

X3 is N or C-R^{14}, wherein R^{14} is hydrogen, halogen, -CN, alkyl, cycloalkyl, or alkoxy;

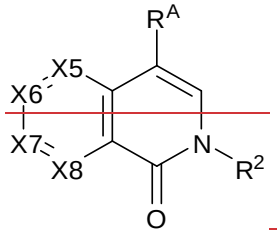
X4 is N or C-R^{15}, wherein R^{15} is hydrogen, halogen, alkyl, -CN, or alkoxy;

R^{16} is hydrogen, halogen, -N(H)COX, or -W-X, wherein W is a bond, -O-, -S-, or -NH-, and X is selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, alkynyl, cycloalkylalkynyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

each R^{21} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; and

each R^{22} is independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl.

2. The compound, or a pharmaceutically acceptable salt thereof, of claim 1, having the structure of Formula (Ib),



Formula (Ib)

wherein,

R^2 is selected from CH_3;

X5 is C-H;

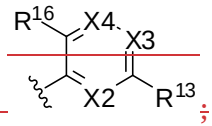
X6 is C-R^6;

X7 is C-R^7;

X8 is C-H;

R^6 is hydrogen, or halogen;

R^7 is hydrogen, or halogen;

R^A is 

;

X2 is C-H;

R^{13} is -Y-Z;

Y is selected from a bond, or $-CH_2-$;

Z is selected from -SO_2R^{21}, -$N(R^{22})SO_2R^{21}$, -$SO_2N(R^{22})_2$, -$N(R^{22})SO_2N(R^{22})_2$, -$CON(R^{22})_2$, -$N(R^{22})CO_2R^{21}$, -$N(R^{22})CON(R^{22})_2$, -$N(R^{22})COR^{21}$, -$OC(O)N(R^{22})_2$, -$OSO_2N(R^{22})_2$, or -$N(R^{22})SO_3R^{21}$;

X3 is C-R^{14}, wherein R^{14} is hydrogen, halogen, C_1-C_3 alkyl, or C_1-C_3 alkoxy;

X4 is C-R^{15}, wherein R^{15} is hydrogen, or halogen;

R^{16} is -W-X, wherein W is a bond, -O-, -S-, or -NH-, and X is selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

each R^{21} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; and

each R^{22} is independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl.

3. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein R^6 is halogen, and R^7 is hydrogen.

4. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein R^6 is hydrogen, and R^7 is halogen.

5. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein R^6 is hydrogen, and R^7 is hydrogen.

6. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein Y is -CH_2-.

7. The compound, or a pharmaceutically acceptable salt thereof, of claim 6, wherein Z is -SO_2R^{21}, or -$N(R^{22})SO_2R^{21}$.

8. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein Y is a bond.

9. The compound, or a pharmaceutically acceptable salt thereof, of claim 8, wherein Z is -$N(R^{22})SO_2R^{21}$, or -$N(R^{22})SO_2N(R^{22})_2$.

10. The compound, or a pharmaceutically acceptable salt thereof, of claim 8, wherein Z is -SO_2R^{21}.

11. The compound, or a pharmaceutically acceptable salt thereof, of claim 8, wherein Z is -$SO_2N(R^{22})_2$.

12. The compound, or a pharmaceutically acceptable salt thereof, of claim 10, wherein R^{21} is heterocyclyl, or heterocyclylalkyl.

13. The compound, or a pharmaceutically acceptable salt thereof, of claim 9, wherein R^{22} is hydrogen or methyl.

14. The compound, or a pharmaceutically acceptable salt thereof, of claim 11, wherein at least one R^{22} is alkyl, cycloalkyl, or aralkyl.

15. The compound, or a pharmaceutically acceptable salt thereof, of claim 10, wherein R^{21} is alkyl, cycloalkyl, or cycloalkylalkyl.

16. The compound, or a pharmaceutically acceptable salt thereof, of claim 15, wherein the alkyl is a C_1-C_4 alkyl.

17. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein R^{14} is hydrogen, and R^{15} is hydrogen.

18. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein W is a bond or –NH–.

19. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein W is –O–.

20. The compound, or a pharmaceutically acceptable salt thereof, of claim 18, wherein X is alkyl.

21. The compound, or a pharmaceutically acceptable salt thereof, of claim 19, wherein X is alkyl.

22. The compound, or a pharmaceutically acceptable salt thereof, of claim 18, wherein X is cycloalkylalkyl.

23. The compound, or a pharmaceutically acceptable salt thereof, of claim 19, wherein X is cycloalkylalkyl.

24. The compound, or a pharmaceutically acceptable salt thereof, of claim 18, wherein X is aryl.

25. The compound, or a pharmaceutically acceptable salt thereof, of claim 19, wherein X is aryl.

26. The compound, or a pharmaceutically acceptable salt thereof, of claim 16, wherein the C_1-C_4 alkyl is a C_1 alkyl.

27. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein Y is a bond, Z is $-SO_2R^{21}$, W is –O–, and X is aryl or cycloalkylalkyl.

28. A compound, or a pharmaceutically acceptable salt thereof, selected from:

N-[4-methyl-3-(2-methyl-1-oxoisoquinolin-4-yl)phenyl]methanesulfonamide;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-6-fluoro-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-7-fluoro-2-methylisoquinolin-1-one;

4-[2-(2,4-difluorophenoxy)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

N-[4-(2,4-difluorophenoxy)-3-(2-methyl-1-oxoisoquinolin-4-yl)phenyl]ethanesulfonamide;

4-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-6-fluoro-2-methylisoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxolan-3-yloxy)phenyl]isoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxan-4-yloxy)phenyl]isoquinolin-1-one;

4-(2-ethoxy-5-methylsulfonylphenyl)-2-methylisoquinolin-1-one;

2-methyl-4-(5-methylsulfonyl-2-propoxyphenyl)isoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxan-3-yloxy)phenyl]isoquinolin-1-one;

4-[2-(trans-4-hydroxycyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[5-ethylsulfonyl-2-(trans-4-hydroxycyclohexyl)oxyphenyl]-2-methylisoquinolin-1-one;

4-[2-(trans-4-aminocyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cis-4-aminocyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-(2-but-2-ynoxy-5-methylsulfonylphenyl)-2-methylisoquinolin-1-one;

4-(2-but-2-ynoxy-5-ethylsulfonylphenyl)-2-methylisoquinolin-1-one;

6-fluoro-4-[2-(trans-4-hydroxycyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

7-fluoro-4-[2-(trans-4-hydroxycyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[5-ethylsulfonyl-2-(trans-4-hydroxycyclohexyl)oxyphenyl]-6-fluoro-2-methylisoquinolin-1-one;

4-[5-ethylsulfonyl-2-(trans-4-hydroxycyclohexyl)oxyphenyl]-7-fluoro-2-methylisoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxolan-3-ylamino)phenyl]isoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxan-4-ylamino)phenyl]isoquinolin-1-one;

4-[2-[(trans-4-hydroxycyclohexyl)amino]-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-7-fluoro-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-7-fluoro-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-2-methyl-6-(trifluoromethyl)isoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-6-methoxy-2-methylisoquinolin-1-one;

[4-(cyclopropylmethoxy)-3-(2-methyl-1-oxoisoquinolin-4-yl)phenyl] sulfamate;

N-[2-(2-methyl-1-oxoisoquinolin-4-yl)-4-methylsulfonylphenyl]-cyclopropanecarboxamide;

N-[2-(2-methyl-1-oxoisoquinolin-4-yl)-4-methylsulfonylphenyl]propanamide;

N-[2-(2-methyl-1-oxoisoquinolin-4-yl)-4-methylsulfonylphenyl]acetamide;

2-methyl-4-(5-methylsulfonyl-2-propylphenyl)isoquinolin-1-one;

4-(2-ethyl-5-methylsulfonylphenyl)-2-methylisoquinolin-1-one;

4-(2-butyl-5-methylsulfonylphenyl)-2-methylisoquinolin-1-one;

4-[2-(2-cyclopropylethyl)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-propan-2-ylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-propan-2-ylsulfonylphenyl]-6-methoxy-2-methylisoquinolin-1-one;

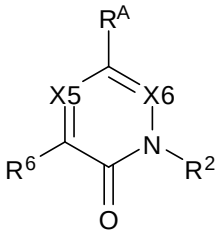
4-[5-(ethylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]-2-methylisoquinolin-1-one; and

2-methyl-4-[5-(methylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]isoquinolin-1-one.

29. A pharmaceutical composition comprising a compound of Formula (I) as described in claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

30. A pharmaceutical composition comprising a compound of claim 28, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

31. A compound of Formula (II), or a pharmaceutically acceptable salt thereof,



Formula (II)

wherein:,

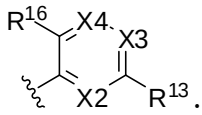
R^2 is alkyl, cycloalkyl, cycloalkylalkyl, heterocyclylalkyl, aralkyl, or heteroarylalkyl;

X6 is C-H or N;

X5 is C-R^5 or N; provided that if X6 is N, then X5 is C-R^5, and if X5 is N, then X6 is CH;

R^5 is hydrogen, halogen, -OH, -CN, -OR^{61}, -NHR^{61}, -$N(R^{61})_2$, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, wherein each R^{61} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

R^6 is hydrogen, halogen, -OH, -CN, alkyl, cycloalkyl, cycloalkylalkyl, amino, alkylamino, dialkylamino, cycloalkylalkylamino, alkoxy, -S-alkyl, cycloalkylalkoxy, heterocyclyl, aralkoxy, heteroaryloxy, aryloxy, alkynyloxy, or –N(H)COalkyl;

R^A is 

;

X2 is N or C-R^{12}, wherein R^{12} is hydrogen, halogen, alkyl, or alkoxy;

R^{13} is –Y-Z;

Y is selected from a bond, -CH_2-, or –CH(C_1-C_4alkyl)-;

Z is selected from -SO_2R^{21}, -$N(R^{22})SO_2R^{21}$, -$SO_2N(R^{22})_2$, –$N(R^{22})SO_2N(R^{22})_2$, -$CON(R^{22})_2$, -$N(R^{22})CO_2R^{21}$, -$N(R^{22})CON(R^{22})_2$, -$N(R^{22})COR^{21}$, -COR^{21}, -$OC(O)N(R^{22})_2$, -$OSO_2N(R^{22})_2$, or -$N(R^{22})SO_3R^{21}$;

X3 is N or C-R^{14}, wherein R^{14} is hydrogen, halogen, -CN, alkyl, cycloalkyl, or alkoxy;

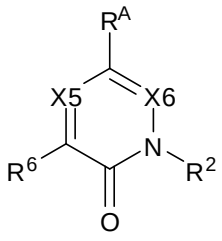
X4 is N or C-R^{15}, wherein R^{15} is hydrogen, halogen, -CN, alkyl, alkoxy, aryloxy, aralkyloxy, cycloalkylalkyloxy, heterocyclyloxy, heteroarylalkyloxy, or alkynyloxy;

R^{16} is hydrogen, halogen, -N(H)COX, or –W-X, wherein W is a bond, –O-, -S-, or –NH-, and X is selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, alkynyl, cycloalkylalkynyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

each R^{21} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; and

each R^{22} is independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; and provided that when X6 is N, then R^5 and R^6 are not hydrogen.

~~3~~2. The compound of claim ~~3~~1, or a pharmaceutically acceptable salt thereof, as represented by Formula (IIa)



Formula (IIa)

wherein~~:~~,

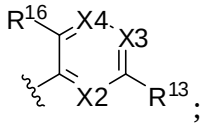
R^2 is CH_3, CH_2CH_3, CH_2CF_3, CH_2F, CHF_2, CF_3, CH_2D, CHD_2, or CD_3;

X6 is C-H or N;

X5 is C-R^5 or N; provided that if X6 is N, then X5 is C-R^5, and if X5 is N, then X6 is CH;

R^5 is hydrogen, halogen, -OH,-CN, -OR^{61}, -NHR^{61}, -$N(R^{61})_2$, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, wherein each R^{61} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

R^6 is hydrogen, halogen, -OH, -CN, alkyl, cycloalkyl, cycloalkylalkyl, amino, alkylamino, dialkylamino, cycloalkylalkylamino, alkoxy, or cycloalkylalkoxy;

R^A is 

;

X2 is N or C-R^{12}, wherein R^{12} is hydrogen, halogen, alkyl, or alkoxy;

R^{13} is –Y-Z;

Y is selected from a bond, or -CH_2-;

Z is selected from -SO_2R^{21}, -$N(R^{22})SO_2R^{21}$, -$SO_2N(R^{22})_2$, –$N(R^{22})SO_2N(R^{22})_2$, -$CON(R^{22})_2$, -$N(R^{22})CO_2R^{21}$, -$N(R^{22})CON(R^{22})_2$, -$N(R^{22})COR^{21}$, -$OC(O)N(R^{22})_2$, -$OSO_2N(R^{22})_2$, or -$N(R^{22})SO_3R^{21}$;

X3 is N or C-R^{14}, wherein R^{14} is hydrogen, halogen, -CN, alkyl, cycloalkyl, or alkoxy;

X4 is N or C-R^{15}, wherein R^{15} is hydrogen, halogen, -CN, alkyl, or alkoxy;

R^{16} is hydrogen, halogen, or –W-X, wherein W is a bond, –O-, -S-, or –NH-, and X is selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

each R^{21} is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; and

each R^{22} is independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; and

provided that when X6 is N, then R^5 and R^6 are not hydrogen.

~~3~~3. The compound of claim ~~3~~1 or ~~3~~2, wherein R^2 is CH_3 and/or ~~.~~

~~34. The compound of any one of claims 31-33,~~ wherein X6 is C-H~~.~~ or

~~35. The compound of any one of claims 31-33,~~ wherein X6 is N.

4~~36~~. The compound of any one of claims ~~3~~1-3~~5~~, wherein X5 is C-R^5.

5~~37~~. The compound of any one of claims ~~3~~1-3~~5~~, wherein X5 is N.

6~~38~~. The compound of any one of claims ~~3~~1-4~~36~~, wherein R^5 is hydrogen, halogen, or alkyl~~.~~ or

~~39. The compound of any one of claims 31-38,~~ wherein R^6 is hydrogen, halogen, alkyl, or alkoxy~~.~~ or wherein R^5 is hydrogen, halogen, or alkyl and R^6 is hydrogen, halogen, alkyl, or alkoxy.

7~~40~~. The compound of any one of claims ~~3~~1-6~~39~~, wherein Y is a bond~~.~~ or

~~41. The compound of any one of claims 31-39,~~ wherein Y is a $–CH_2-$.

8~~42~~. The compound of any one of claims ~~3~~1-7~~41~~, wherein Z is selected from the group consisting of $-SO_2R^{21}$~~,~~.

~~43. The compound of any one of claims 31-41, wherein Z is~~ $-N(R^{22})SO_2R^{21}$~~,~~.

~~44. The compound of any one of claims 31-41, wherein Z is~~ $-SO_2N(R^{22})_2$~~,~~.

~~45. The compound of any one of claims 31-41, wherein Z is~~ $–N(R^{22})SO_2N(R^{22})_2$~~,~~.

~~46. The compound of any one of claims 31-41, wherein Z is~~ $-CON(R^{22})_2$~~,~~.

~~47. The compound of any one of claims 31-41, wherein Z is~~ $-N(R^{22})CO_2R^{21}$ and~~.~~

~~48. The compound of any one of claims 31-41, wherein Z is~~ $-N(R^{22})CON(R^{22})_2$.

4~~9~~. The compound of any one of claims ~~3~~1-4~~8~~, wherein R^{21} is alkyl, cycloalkyl, or cycloalkylalkyl.

~~50. The compound of any one of claims 31-49, wherein R^{21} is alkyl.~~

5~~1~~0. The compound of any one of claims ~~3~~1-9~~50~~, wherein R^{14} is hydrogen, halogen, or alkyl.

11~~52~~. The compound of any one of claims ~~3~~1-5~~1~~0, wherein X4 is C-R^{15}.

12~~53~~. The compound of any one of claims ~~3~~1-9~~50~~, or 11~~52~~, wherein X3 is N.

1354. The compound of any one of claims 31-1253, wherein X2 is N.

1455. The compound of any one of claims 31-950, wherein X2 and X3 are N, and X4 is C-H or wherein R^{21} is alkyl and X2 and X3 are N, and X4 is C-H.

156. The compound of any one of claims 31-1455, wherein W is –O-, or

57. The compound of any one of claims 31-55, wherein W is –NH-, or

58. The compound of any one of claims 31-55, wherein W is a bond, or.

59. The compound of any one of claims 31-58, wherein X is alkyl.

60. The compound of any one of claims 31-58, wherein X is aryl.

61. The compound of any one of claims 31-58, wherein X is cycloalkylalkyl.

62. The compound of any one of claims 31-55, wherein W is –O- and X is alkyl, or.

63. The compound of any one of claims 31-55, wherein W is –O- and X is aryl, or.

64. The compound of any one of claims 31-55, wherein W is –O- and X is cycloalkylalkyl, or.

65. The compound of any one of claims 31-55, wherein W is a bond and X is alkyl, or.

66. The compound of any one of claims 31-55, wherein W is a bond and X is aryl, or

67. The compound of any one of claims 31-55, wherein W is a bond and X is cycloalkylalkyl.

16. The compound of any one of claims 1-15, wherein X is selected from the group consisting of alkyl, aryl and cycloalkylalkyl.

1768. The compound of any one of claims 31-167, wherein the R^6 is CD_3.

1869. A compound of claim 1 or pharmaceutical acceptable salt thereof, selected from:

N-[3-(1-methyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

N-[3-(1,4-dimethyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

N-[3-(1,4,5-trimethyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1-methylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-(1-methyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(1-methyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(1,4-dimethyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(1,4,5-trimethyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

3-amino-1-methyl-5-(3-methylsulfonylphenyl)pyrazin-2-one;

3-amino-5-(3-ethylsulfonylphenyl)-1-methylpyrazin-2-one;

N-[5-(6-amino-4-methyl-5-oxopyrazin-2-yl)-2-methoxyphenyl]methanesulfonamide;

3-amino-1-methyl-5-(3-methylsulfonylphenyl)pyridin-2-one;

3-amino-5-(3-ethylsulfonylphenyl)-1-methylpyridin-2-one;

N-[5-(5-amino-1-methyl-6-oxopyridin-3-yl)-2-methoxyphenyl]methanesulfonamide;

N-[2-methoxy-5-[1-methyl-5-(methylamino)-6-oxopyridin-3-yl]phenyl]methanesulfonamide;

N-[5-[5-(ethylamino)-1-methyl-6-oxopyridin-3-yl]-2-methoxyphenyl]methanesulfonamide;

N-[5-[5-(cyclopropylmethylamino)-1-methyl-6-oxopyridin-3-yl]-2-methoxyphenyl]methanesulfonamide;

N-[5-[5-(dimethylamino)-1-methyl-6-oxopyridin-3-yl]-2-methoxyphenyl]methanesulfonamide;

N-[5-[5-(diethylamino)-1-methyl-6-oxopyridin-3-yl]-2-methoxyphenyl]methanesulfonamide;

N-[3-(5-amino-1-methyl-6-oxopyridin-3-yl)-4-(2,4-difluorophenoxy)phenyl]ethanesulfonamide;

3-amino-5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1-methylpyridin-2-one;

4-ethoxy-3-(1-methyl-6-oxopyridin-3-yl)benzenesulfonamide;

4-(2,4-difluorophenoxy)-3-(1-methyl-6-oxopyridin-3-yl)benzenesulfonamide;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-3-fluoro-1-methylpyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-methylsulfonylphenyl]-3-fluoro-1-methylpyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-ethylsulfonylphenyl]-3-fluoro-1-methylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-(5-fluoro-1-methyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

N-[3-(5-chloro-1-methyl-6-oxopyridin-3-yl)-4-(2,4-

difluorophenoxy)phenyl]ethanesulfonamide;

6-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-2,4-dimethylpyridazin-3-one;

6-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-2,5-dimethylpyridazin-3-one;

N-[4-(2,4-difluorophenoxy)-3-[1-methyl-6-oxo-5-(trifluoromethyl)pyridin-3-yl]phenyl]ethanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(4-fluoro-1-methyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

N-[3-(5-cyclopropyl-1-methyl-6-oxopyridin-3-yl)-4-(2,4-difluorophenoxy)phenyl]ethanesulfonamide;

N-{4-(2,4-difluorophenoxy)-3-[1-($^{2}H_{3}$)methyl-6-oxopyridin-3-yl]phenyl}ethanesulfonamide;

5-[5-(cyclopropylmethoxy)-2-(methylsulfonylmethyl)pyrimidin-4-yl]-1,3-dimethylpyridin-2-one;

5-[5-(2,4-difluorophenoxy)-2-(methylsulfonylmethyl)pyrimidin-4-yl]-3-methoxy-1-methylpyridin-2-one;

5-[5-(2,4-difluorophenoxy)-2-(methylsulfonylmethyl)pyrimidin-4-yl]-1,3-dimethylpyridin-2-one;

5-[5-(2,4-difluorophenoxy)-2-methylsulfonylpyrimidin-4-yl]-1,3-dimethylpyridin-2-one;

5-[5-(2,4-difluorophenoxy)-2-methylsulfonylpyrimidin-4-yl]-3-methoxy-1-methylpyridin-2-one;

N-[5-(cyclopropylmethoxy)-4-(1,5-dimethyl-6-oxopyridin-3-yl)pyrimidin-2-yl]methanesulfonamide;

N-[5-(cyclopropylmethoxy)-4-(1,5-dimethyl-6-oxopyridin-3-yl)pyrimidin-2-yl]-N-ethylmethanesulfonamide;

N-[5-(2,4-difluorophenoxy)-4-(1,5-dimethyl-6-oxopyridin-3-yl)pyrimidin-2-yl]methanesulfonamide;

N-[5-(2,4-difluorophenoxy)-4-(5-methoxy-1-methyl-6-oxopyridin-3-yl)pyrimidin-2-yl]methanesulfonamide;

N-[5-(2,4-difluorophenoxy)-4-(5-methoxy-1-methyl-6-oxopyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;

N-[5-(2,4-difluorophenoxy)-4-(1,5-dimethyl-6-oxopyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;

[4-(cyclopropylmethoxy)-3-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl] sulfamate;

N-[4-(2,4-difluorophenoxy)-3-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl]-N-methylmethanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl]-N-(oxetan-3-yl)methanesulfonamide;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1-(cyclopropylmethyl)-3-methylpyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-3-methyl-1-(2-methylpropyl)pyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1-(2-methoxyethyl)-3-methylpyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-3-methyl-1-(oxetan-3-ylmethyl)pyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-3-methyl-1-(1,3-oxazol-4-ylmethyl)pyridin-2-one;

N-[3-[1-(cyclopropylmethyl)-5-methyl-6-oxopyridin-3-yl]-4-(2,4-difluorophenoxy)phenyl]ethanesulfonamide;

N-[4-[1-(cyclopropylmethyl)-5-methyl-6-oxopyridin-3-yl]-5-(2,4-difluorophenoxy)pyrimidin-2-yl]methanesulfonamide;

N-[4-[1-(cyclopropylmethyl)-5-methyl-6-oxopyridin-3-yl]-5-(2,4-difluorophenoxy)pyrimidin-2-yl]ethanesulfonamide;

1-(cyclopropylmethyl)-5-[4-(2,4-difluorophenoxy)-1-(methylsulfonylmethyl)-6-oxopyridin-3-yl]-3-methylpyridin-2-one;

1-cyclopropyl-5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-3-methylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-(5-fluoro-1-methyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

3-chloro-5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-1-methylpyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-3-fluoro-1-methylpyridin-2-one;

3-chloro-5-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-1-methylpyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-(methanesulfonylmethyl)phenyl]-3-($^{2}H_{3}$)methyl-1-methyl-1,2-dihydropyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-[5-($^2H_3$)methyl-1-methyl-6-oxo-1,6-dihydropyridin-3-yl]phenyl]methanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-[5-($^2H_3$)methyl-1-methyl-6-oxo-1,6-dihydropyridin-3-yl]phenyl]ethane-1-sulfonamide;

N-[3-(5-cyclopropyl-1-methyl-6-oxopyridin-3-yl)-4-(2,4-difluorophenoxy)phenyl]methanesulfonamide;

3-cyclopropyl-5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-1-methylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-(1-methyl-6-oxo-5-pyrrolidin-1-ylpyridin-3-yl)phenyl]methanesulfonamide;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-1-methyl-3-pyrrolidin-1-ylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-(5-ethynyl-1-methyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-3-ethynyl-1-methylpyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-3-ethynyl-1-methylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-(5-ethynyl-1-methyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-3-(difluoromethoxy)-1-methylpyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-1-methyl-3-(2,2,2-trifluoroethoxy)pyridin-2-one;

N-[3-[5-(difluoromethoxy)-1-methyl-6-oxopyridin-3-yl]-4-(2,4-difluorophenoxy)phenyl]ethanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-[1-methyl-6-oxo-5-(2,2,2-trifluoroethoxy)pyridin-3-yl]phenyl]ethanesulfonamide;

3-(difluoromethoxy)-5-[2-(2,4-difluorophenoxy)-5-(ethylsulfonylmethyl)phenyl]-1-methylpyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-(ethylsulfonylmethyl)phenyl]-1-methyl-3-(2,2,2-trifluoroethoxy)pyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1-methyl-3-(1-methylpyrazol-4-yl)oxypyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1-methyl-3-(1-propan-2-

ylpyrazol-4-yl)oxypyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1-methyl-3-phenoxypyridin-2-one;

N-[4-(1-butyl-5-methyl-6-oxopyridin-3-yl)-5-(2,4-difluorophenoxy)pyrimidin-2-yl]methanesulfonamide;

N-[4-(1-butyl-5-methyl-6-oxopyridin-3-yl)-5-(2,4-difluorophenoxy)pyrimidin-2-yl]ethanesulfonamide;

N-[4-[1-(cyclobutylmethyl)-5-methyl-6-oxopyridin-3-yl]-5-(2,4-difluorophenoxy)pyrimidin-2-yl]methanesulfonamide;

N-[4-[1-(cyclobutylmethyl)-5-methyl-6-oxopyridin-3-yl]-5-(2,4-difluorophenoxy)pyrimidin-2-yl]ethanesulfonamide;

5-(5-ethyl-2-methylsulfonylpyrimidin-4-yl)-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-(2-methylsulfonyl-5-propylpyrimidin-4-yl)pyridin-2-one;

5-(5-butyl-2-methylsulfonylpyrimidin-4-yl)-1,3-dimethylpyridin-2-one;

N-[4-(1,5-dimethyl-6-oxopyridin-3-yl)-5-ethylpyrimidin-2-yl]ethanesulfonamide;

N-[4-(1,5-dimethyl-6-oxopyridin-3-yl)-5-propylpyrimidin-2-yl]ethanesulfonamide;

N-[5-butyl-4-(1,5-dimethyl-6-oxopyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;

5-(2-ethyl-5-methylsulfonylphenyl)-1-methylpyridin-2-one;

1-methyl-5-(5-methylsulfonyl-2-propylphenyl)pyridin-2-one;

5-[2-(2-cyclopropylethyl)-5-methylsulfonylphenyl]-1-methylpyridin-2-one;

5-(2-butyl-5-methylsulfonylphenyl)-1-methylpyridin-2-one;

5-[3-[(4-methoxyphenyl)methoxy]-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-(3-methylsulfonyl-5-phenylmethoxyphenyl)pyridin-2-one;

5-[3-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-[3-methylsulfonyl-5-(2-phenylethoxy)phenyl]pyridin-2-one;

5-[3-(2-cyclopropylethoxy)-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-[3-methylsulfonyl-5-(2,2,2-trifluoroethoxy)phenyl]pyridin-2-one;

1,3-dimethyl-5-[3-[(3-methyloxetan-3-yl)methoxy]-5-methylsulfonylphenyl]pyridin-2-one;

1,3-dimethyl-5-[3-methylsulfonyl-5-(pyridin-2-ylmethoxy)phenyl]pyridin-2-one;

5-[3-[(2,6-dimethylphenyl)methoxy]-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[3-[(2-chlorophenyl)methoxy]-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-

one;

5-[3-[[2-(difluoromethoxy)phenyl]methoxy]-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

2-[[3-(1,5-dimethyl-6-oxopyridin-3-yl)-5-methylsulfonylphenoxy]methyl]benzonitrile;

5-[3-[(2,4-difluorophenyl)methoxy]-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-[3-methylsulfonyl-5-(1-phenylethoxy)phenyl]pyridin-2-one;

5-[3-[(2,3-dichlorophenyl)methoxy]-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-[3-methylsulfonyl-5-(pyridin-3-ylmethoxy)phenyl]pyridin-2-one;

3-[[3-(1,5-dimethyl-6-oxopyridin-3-yl)-5-methylsulfonylphenoxy]methyl]benzonitrile;

5-(3-but-2-ynoxy-5-methylsulfonylphenyl)-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-[3-methylsulfonyl-5-(1-phenylethoxy)phenyl]pyridin-2-one;

N-[3-(2,4-difluorophenoxy)-5-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

4-[3-[(4-methoxyphenyl)methoxy]-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

2-methyl-4-(3-methylsulfonyl-5-phenylmethoxyphenyl)isoquinolin-1-one;

4-[3-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

N-[4-(2,4-difluorophenoxy)-6-(1,5-dimethyl-6-oxopyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;

N-[2-(2,4-difluorophenoxy)-6-(1,5-dimethyl-6-oxopyridin-3-yl)pyrimidin-4-yl]ethanesulfonamide;

1-methyl-5-(2-methylsulfonyl-5-propylpyrimidin-4-yl)pyridin-2-one;

5-(5-butyl-2-methylsulfonylpyrimidin-4-yl)-1-methylpyridin-2-one;

3-chloro-1-methyl-5-(2-methylsulfonyl-5-propylpyrimidin-4-yl)pyridin-2-one;

5-(5-butyl-2-methylsulfonylpyrimidin-4-yl)-3-chloro-1-methylpyridin-2-one;

3-methoxy-1-methyl-5-(2-methylsulfonyl-5-propylpyrimidin-4-yl)pyridin-2-one;

5-(5-butyl-2-methylsulfonylpyrimidin-4-yl)-3-methoxy-1-methylpyridin-2-one;

N-[4-(1-methyl-6-oxopyridin-3-yl)-5-propylpyrimidin-2-yl]ethanesulfonamide;

N-[5-butyl-4-(1-methyl-6-oxopyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;

N-[4-(5-chloro-1-methyl-6-oxopyridin-3-yl)-5-propylpyrimidin-2-yl]ethanesulfonamide;

N-[5-butyl-4-(5-chloro-1-methyl-6-oxopyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;

N-[4-(5-methoxy-1-methyl-6-oxopyridin-3-yl)-5-propylpyrimidin-2-yl]ethanesulfonamide;

N-[5-butyl-4-(5-methoxy-1-methyl-6-oxopyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;

N-[5-butyl-4-(1,5-dimethyl-6-oxopyridin-3-yl)pyrimidin-2-yl]methanesulfonamide;

5-(2-but-2-ynoxy-5-methylsulfonylphenyl)-1,3-dimethylpyridin-2-one;

5-(2-but-2-ynoxy-5-ethylsulfonylphenyl)-3-methoxy-1-methylpyridin-2-one;

5-(5-ethylsulfonyl-2-pent-2-ynoxyphenyl)-3-methoxy-1-methylpyridin-2-one;

5-[2-(3-cyclopropylprop-2-ynoxy)-5-ethylsulfonylphenyl]-3-methoxy-1-methylpyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-ethylsulfonylphenyl]-1-methyl-3-(trifluoromethyl)pyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-propan-2-ylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-5-phenylmethoxyphenyl]ethanesulfonamide;

5-[2-(2,4-difluoroanilino)-5-ethylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-[(4,4-difluorocyclohexyl)amino]-5-ethylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-(2,4-difluoroanilino)-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-3-methoxy-1-methylpyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-(methylsulfonylmethyl)phenyl]-3-methoxy-1-methylpyridin-2-one;

5-[2-(4-hydroxycyclohexyl)oxy-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-(1-methyl-5-methylsulfanyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

5-[2-(4-aminocyclohexyl)oxy-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-(4-aminocyclohexyl)oxy-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-[5-methylsulfonyl-2-(3,3,3-trifluoropropoxy)phenyl]pyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-(methylsulfonylmethyl)phenyl]-1-(2-hydroxyethyl)-3-methylpyridin-2-one;

5-[5-(ethylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]-1-(2-hydroxyethyl)-3-methylpyridin-2-one;

5-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-1-methyl-3-(methylamino)pyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-1-methyl-3-(methylamino)pyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-[1-methyl-5-(methylamino)-6-oxopyridin-3-yl]phenyl]ethanesulfonamide;

5-[5-(ethylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]-1,3-dimethylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-[1-methyl-5-(methylamino)-6-oxopyridin-3-yl]phenyl]methanesulfonamide;

5-[2-[(4,4-difluorocyclohexyl)amino]-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-3-methoxy-1-methylpyridin-2-one;

5-[2-(4,4-difluorocyclohexyl)oxy-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-(cyclopentylamino)-5-ethylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-(cyclopentylamino)-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

3-chloro-1-methyl-5-[5-(methylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]pyridin-2-one;

5-(2-cyclopentyloxy-5-methylsulfonylphenyl)-1,3-dimethylpyridin-2-one;

1,3-dimethyl-5-[5-methylsulfonyl-2-(oxan-4-yloxy)phenyl]pyridin-2-one;

3-fluoro-1-methyl-5-[5-(methylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]pyridin-2-one;

5-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-1,4-dimethylpyridin-2-one;

5-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-1,4-dimethylpyridin-2-one;

1,3-dimethyl-5-[5-methylsulfonyl-2-(oxolan-3-ylamino)phenyl]pyridin-2-one;

1,3-dimethyl-5-[5-methylsulfonyl-2-(oxolan-3-yloxy)phenyl]pyridin-2-one;

1,3-dimethyl-5-[5-(methylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]pyridin-2-one;

5-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-1-ethyl-3-methylpyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-(methylsulfonylmethyl)phenyl]-1-ethyl-3-methylpyridin-2-one;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(4-hydroxycyclohexyl)oxyphenyl]ethanesulfonamide;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(4-hydroxycyclohexyl)oxyphenyl]ethanesulfonamide;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(4-hydroxycyclohexyl)oxyphenyl]methanesulfonamide;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(4-hydroxycyclohexyl)oxyphenyl]methanesulfonamide;

1,3-dimethyl-5-[5-methylsulfonyl-2-(oxan-4-ylamino)phenyl]pyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-(methylsulfonylmethyl)phenyl]-3-fluoro-1-methylpyridin-2-one;

5-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-3-(dimethylamino)-1-methylpyridin-2-one;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(oxan-4-yloxy)phenyl]methanesulfonamide;

5-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-3-(dimethylamino)-1-methylpyridin-2-one;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(oxan-4-yloxy)phenyl]ethanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(5-methoxy-1-methyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(5-methoxy-1-methyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(oxolan-3-yloxy)phenyl]methanesulfonamide;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(oxolan-3-yloxy)phenyl]ethanesulfonamide;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(oxan-3-

yloxy)phenyl]methanesulfonamide;

N-[4-(4,4-difluorocyclohexyl)oxy-3-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

N-[3-(1,5-dimethyl-6-oxopyridin-3-yl)-4-(oxan-3-yloxy)phenyl]ethanesulfonamide;

N-[4-(4,4-difluorocyclohexyl)oxy-3-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-(5-hydroxy-1-methyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;

4-(cyclopropylmethylamino)-3-(1,5-dimethyl-6-oxopyridin-3-yl)benzenesulfonamide;

4-(cyclopropylmethylamino)-3-(1-methyl-6-oxopyridin-3-yl)benzenesulfonamide;

5-[2-(2,4-difluorophenoxy)-5-(methylsulfonylmethyl)phenyl]-1,4-dimethylpyridin-2-one;

5-[2-(2,4-difluorophenoxy)-5-(methylsulfonylmethyl)phenyl]-1,3-dimethylpyridin-2-one;

5-(2-ethoxy-5-ethylsulfonylphenyl)-1-($^{2}H_{3}$)methyl-4-methylpyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]- 1-($^{2}H_{3}$)methyl-4-methylpyridin-2-one;

5-(2-ethoxy-5-ethylsulfonylphenyl)-1,4-dimethylpyridin-2-one;

5-[2-(cyclobutylmethoxy)-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-(cyclobutylmethoxy)-5-methylsulfonylphenyl]-1-methylpyridin-2-one;

5-(5-ethylsulfonyl-2-methoxyphenyl)-3-hydroxy-1-methylpyridin-2-one;

5-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

N-[4-(2,4-difluorophenoxy)-3-[5-(dimethylamino)-1-methyl-6-oxopyridin-3-yl]phenyl]methanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-[5-(dimethylamino)-1-methyl-6-oxopyridin-3-yl]phenyl]ethanesulfonamide;

5-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-1,3-dimethylpyridin-2-one;

5-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-1,4-dimethylpyridin-2-one;

N-[3-(5-hydroxy-1-methyl-6-oxopyridin-3-yl)phenyl]methanesulfonamide;

5-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-1-methylpyridin-2-one;
3-(dimethylamino)-5-(2-ethoxy-5-ethylsulfonylphenyl)-1-methylpyridin-2-one;
5-[2-(2,4-difluorophenoxy)-5-(methylsulfonylmethyl)phenyl]-1-methylpyridin-2-one;
N-[3-(1-methyl-6-oxo-5-phenylmethoxypyridin-3-yl)phenyl]methanesulfonamide;
N-[4-(2,4-difluorophenoxy)-3-(1,5-dimethyl-6-oxopyridin-3-yl)phenyl]ethanesulfonamide;
5-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-1-methylpyridin-2-one;
5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-3-(dimethylamino)-1-methylpyridin-2-one;
5-[4-fluoro-2-methoxy-5-(methylsulfonylmethyl)phenyl]-1-methylpyridin-2-one;
5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1,3-dimethylpyridin-2-one;
5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-1,4-dimethylpyridin-2-one;
N-[6-[3-(methanesulfonamido)phenyl]-4-methyl-3-oxopyrazin-2-yl]acetamide;
N-[3-(1,4-dimethyl-6-oxopyridazin-3-yl)phenyl]ethanesulfonamide;
N-[3-(1,5-dimethyl-6-oxopyridazin-3-yl)phenyl]ethanesulfonamide;
N-[5-[3-(methanesulfonamido)phenyl]-1-methyl-2-oxopyridin-3-yl]propanamide;
N-[5-[3-(methanesulfonamido)phenyl]-1-methyl-2-oxopyridin-3-yl]acetamide;
1-cyclobutyl-5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-3-methylpyridin-2-one;
N-[3-(1-cyclobutyl-5-methyl-6-oxopyridin-3-yl)-4-(2,4-difluorophenoxy)phenyl]methanesulfonamide;
1-benzyl-5-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-3-methylpyridin-2-one;
5-(5-butyl-2-methylsulfonylpyrimidin-4-yl)-3-methyl-1-propan-2-ylpyridin-2-one;
N-[5-(2,4-difluorophenoxy)-4-(5-methyl-6-oxo-1-propan-2-ylpyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;
5-[5-(2,4-difluorophenoxy)-2-methylsulfonylpyrimidin-4-yl]-3-methyl-1-propan-2-ylpyridin-2-one;
N-[5-butyl-4-(5-methyl-6-oxo-1-propan-2-ylpyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;
N-[5-butyl-4-(1-methyl-6-oxo-5-propan-2-ylpyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide;

5-(5-butyl-2-methylsulfonylpyrimidin-4-yl)-1-methyl-3-propan-2-ylpyridin-2-one;

N-[5-(2,4-difluorophenoxy)-4-(1-methyl-6-oxo-5-propan-2-ylpyridin-3-yl)pyrimidin-2-yl]ethanesulfonamide; or

5-[5-(2,4-difluorophenoxy)-2-methylsulfonylpyrimidin-4-yl]-1-methyl-3-propan-2-ylpyridin-2-one.

1970. A pharmaceutical composition comprising a compound of Formula (II) or of claim 18, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

20. The compound of Formula (II) or of claim 18 or a pharmaceutical composition according to claim 19 for use as a medicament.

~~71. A method of regulating gene transcription in a cell comprising exposing a bromodomain containing protein to a compound of Formula (II).~~

~~72. A method of inhibiting of bromodomain-mediated recognition of an acetyl lysine region of a protein comprising exposing the bromodomain to a compound of Formula (II).~~

2173. Use of the compound of Formula (II) or of claim 18 or a pharmaceutical composition according to claim 19 in the manufacture of a medicament for ~~A method of~~ treating cancer ~~in a patient in need thereof, comprising administering to the patient a compound of Formula (II), or a pharmaceutically acceptable salt thereof~~.

~~74. A pharmaceutical composition comprising a compound of claim 69, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.~~

~~75. A method of regulating gene transcription in a cell comprising exposing a bromodomain containing protein to a compound of claim 69.~~

~~76. A method of inhibiting of bromodomain-mediated recognition of an acetyl lysine region of a protein comprising exposing the bromodomain to a compound of claim 69.~~

~~77. A method of treating cancer in a patient in need thereof, comprising administering to the patient a compound of claim 69, or a pharmaceutically acceptable salt thereof.~~

~~78. A method of regulating gene transcription in a cell comprising exposing a bromodomain containing protein to a compound of Formula (I).~~

~~79. A method of inhibiting of bromodomain-mediated recognition of an acetyl lysine region of a protein comprising exposing the bromodomain to a compound of Formula (I).~~

~~80. A method of treating cancer in a patient in need thereof, comprising administering to the patient a compound of Formula (I), or a pharmaceutically acceptable salt thereof.~~