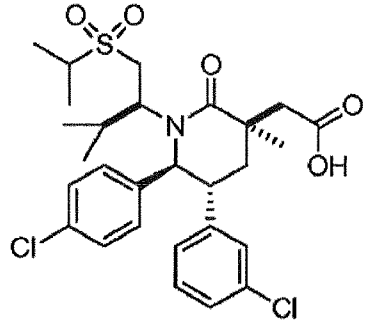
vitro and in vivo. Further, in patients with p53-inactivated tumors, stabilization of wildtype p53 in normal tissues by MDM2 inhibition might allow selective protection of normal tissues from mitotic poisons.

The present invention relates to compounds capable of inhibiting the interaction between p53 and MDM2 and activating p53 downstream effector genes. As such, compounds of the present invention would be useful in the treatment of cancers, bacterial infections, viral infections, ulcers and inflammation. In particular, the compounds of the present invention are useful to treat solid tumors such as: breast, colon, lung and prostate tumors; and liquid tumors such as lymphomas and leukemias. As used herein, MDM2 means a human MDM2 protein and p53 means a human p53 protein. It is noted that human MDM2 can also be referred to as HDM2 or hMDM2.

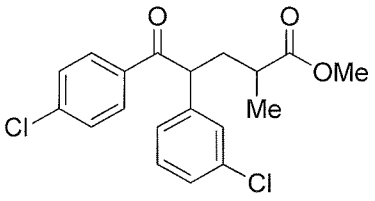
SUMMARY OF THE INVENTION

In one aspect, the present invention refers to the use of a compound of formula

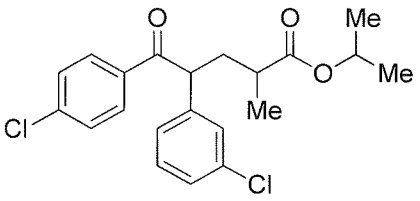


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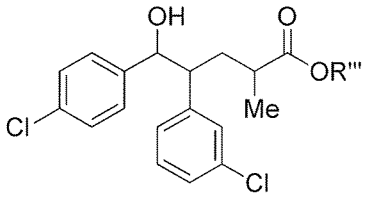
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a subject in need of said treatment. In another aspect, the present invention refers to a compound, wherein the compound is a compound of formula



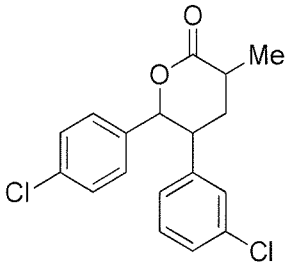
. In another aspect, the present invention refers to a compound, wherein the compound is a compound of formula



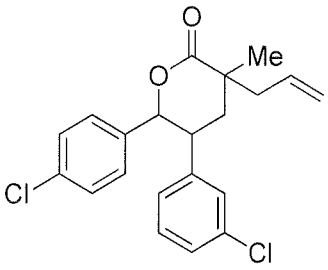
. In still another aspect, the present invention refers to a compound, wherein the compound is a compound of formula



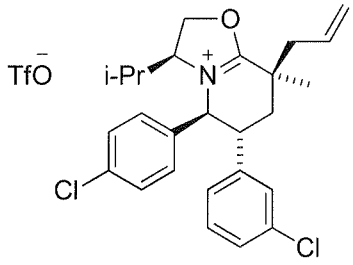
, wherein R''' is hydrogen, methyl, or isopropyl. In another aspect, the present invention refers to a compound, wherein the compound is a compound of formula



. In still another aspect, the present invention refers to a compound, wherein the compound is a compound of formula

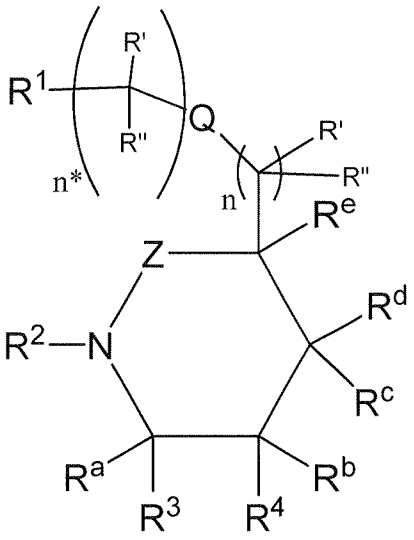


. In another aspect, the present invention refers to a compound, wherein the compound is a compound of formula



.

The present disclosure relates to piperidinone derivatives of Formula I.



I

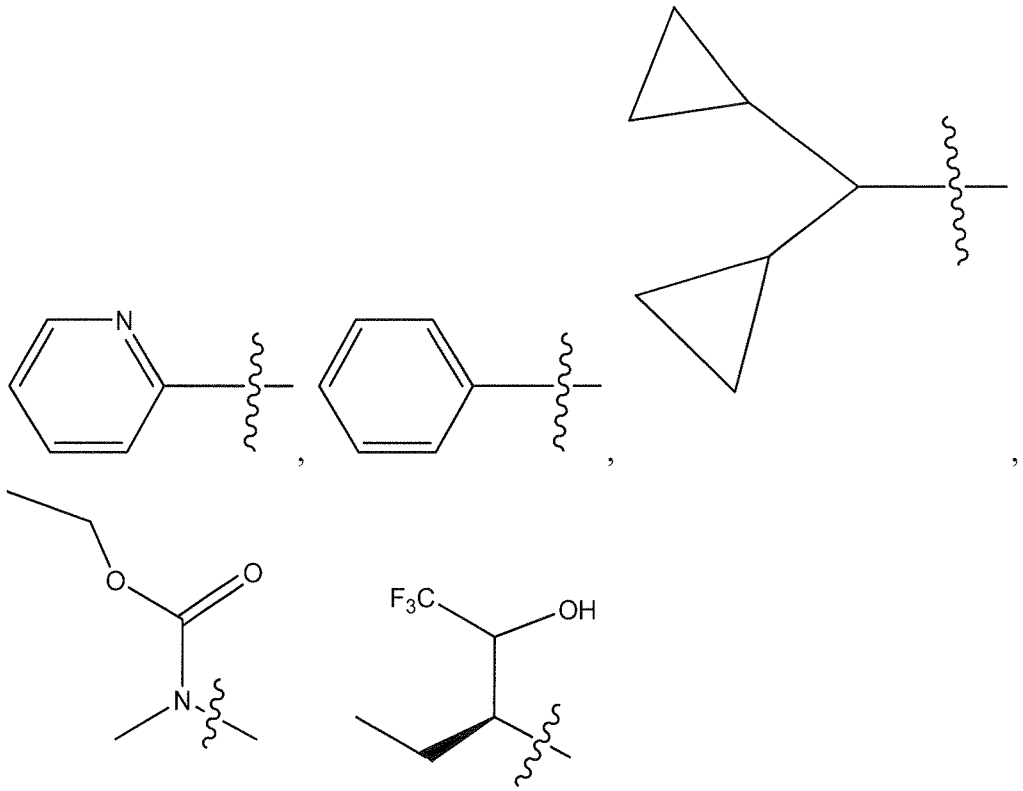
enantiomers, diastereomers and pharmaceutically acceptable salts thereof,

wherein

Q is a bond or optionally can be selected from O, NR^7 and $S(O)_v$, when n* is an integer from 1 to 6,

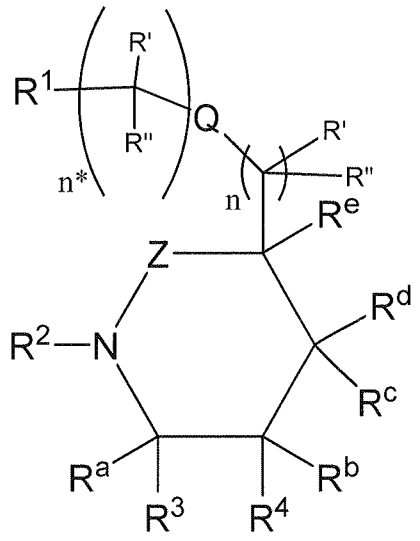
Z is C=O or $S(=O)_2$

R^a is at each occurrence independently selected from H, $(C_1\text{-}C_3)$alkyl, (halo)$(C_1\text{-}C_3)$alkyl, (hydroxy)$(C_1\text{-}C_3)$alkyl, (alkoxy)$(C_1\text{-}C_3)$alkyl, or cyano;



, and any of which may be optionally substituted with one or more R^x groups as allowed by valence.

In another example, example A, the present disclosure provides compounds of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

R* is H, haloalkyl, haloalkoxy, C_{1-6}-alkyl, C_{2-6}alkenyl, C_{2-6}-alkynyl, C_{3-8}-cycloalkyl, C_{4-8}-cycloalkenyl, aryl, heteroaryl, or heterocyclo;

R^+ and R^{++} are independently H, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclo, arylalkyl, heteroarylalkyl, heterocycloalkyl, or cycloalkylalkyl, or R^+ and R^{++} bound to the same nitrogen atom may optionally combine to form a heterocyclo ring system;

m is 1, 2 or 3;

n and n* are each independently selected from 0 or an integer from 1 to 6;

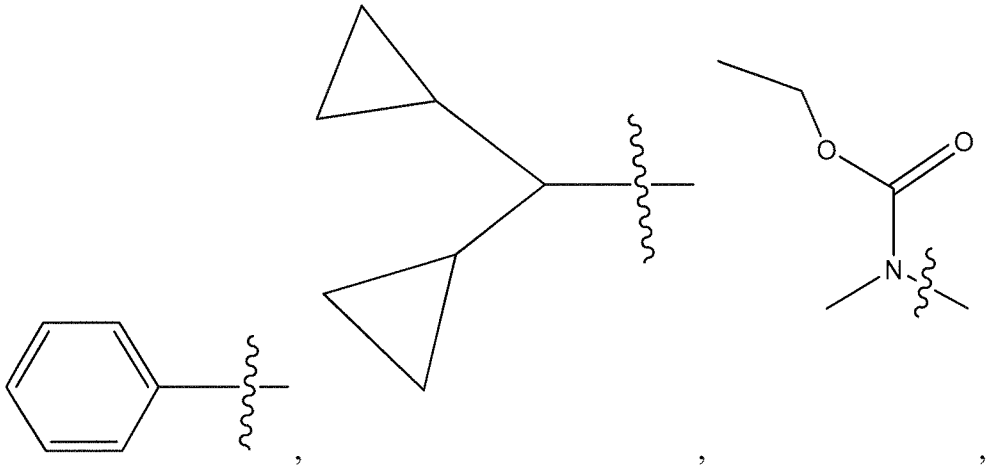
p is 0, 1, 2 or 3;

t at each occurrence is independently 0 or an integer from 1 to 6; and

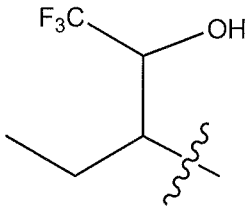
v at each occurrence is independently 0, 1 or 2.

In another example of the compounds of Example A or AA, or the pharmaceutically acceptable salts thereof, R^2 is $-C(H)R^5R^6$, $-NR^7R^8$, phenyl or pyridine, wherein the phenyl or the pyridyl may be optionally substituted with one or more R^x as allowed by valence.

In another example of the compounds of Example A or AA, or the pharmaceutically acceptable salts thereof, R^2 is selected from

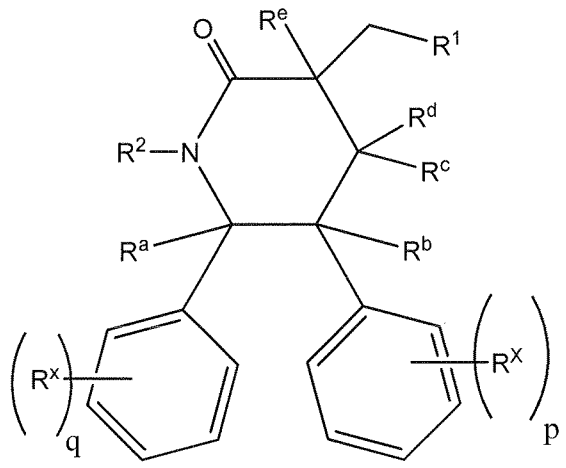


, , , or



, any of which may be optionally substituted with one or more R^x groups as allowed by valence.

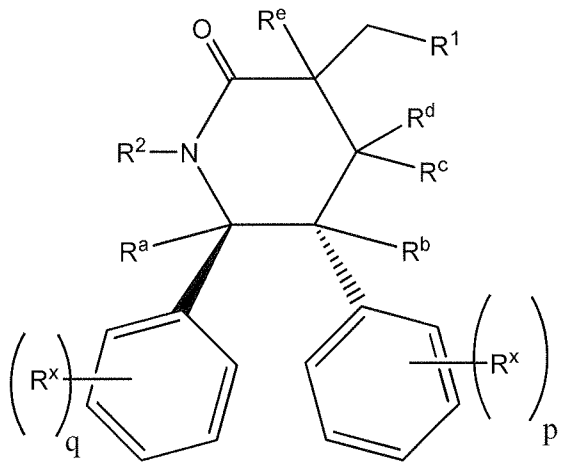
In another example, the compounds of Example A or AA have the structure of Formula IA



IA

or the pharmaceutically acceptable salts thereof, wherein q and p are each independently 0, 1, 2 or 3.

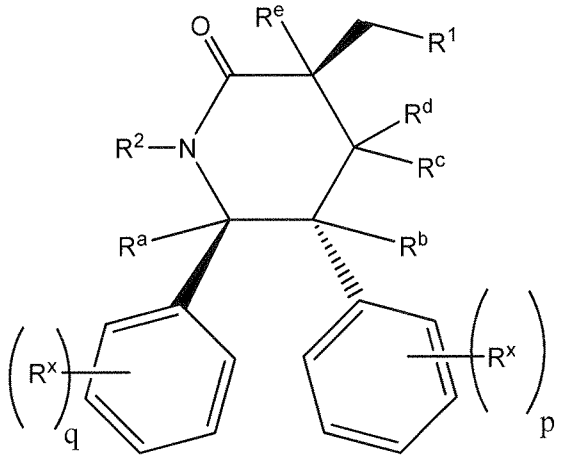
In another example, the compounds of Example A or AA have the structure of Formula IB



IB

or the pharmaceutically acceptable salts thereof, wherein q and p are each independently 0, 1, 2 or 3.

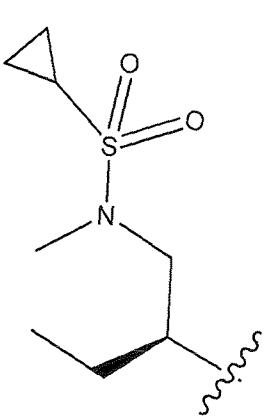
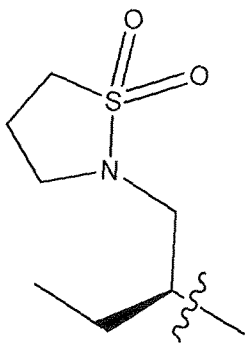
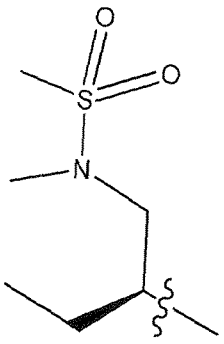
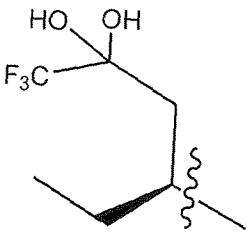
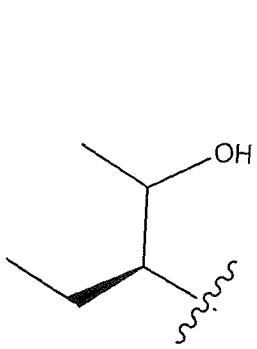
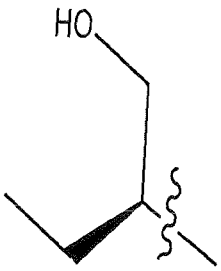
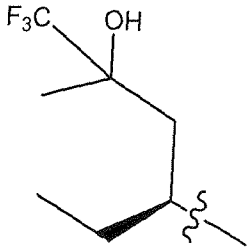
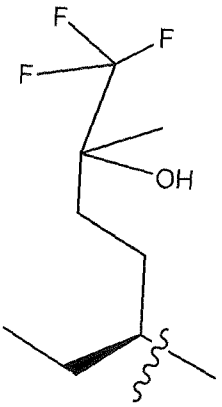
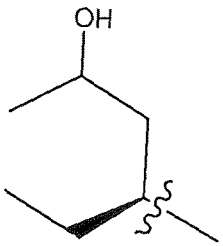
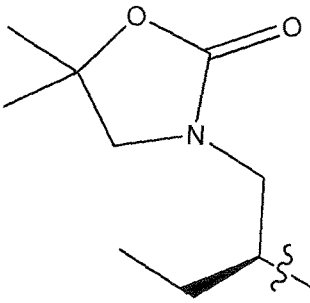
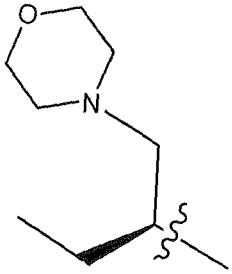
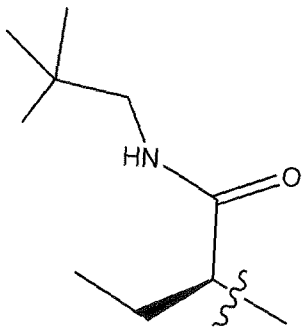
In another example, the compounds of Example A or AA have the structure of Formula IC



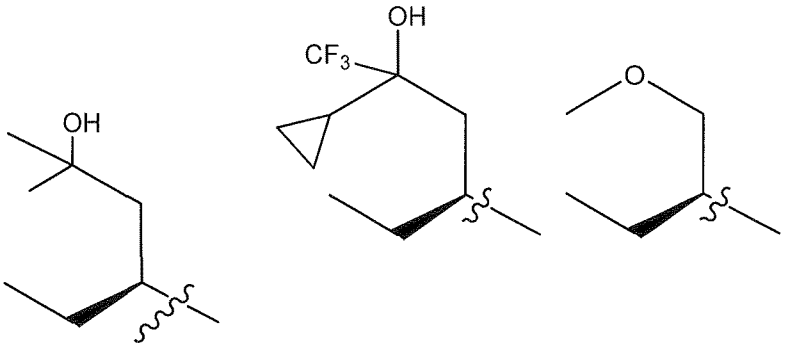
IC

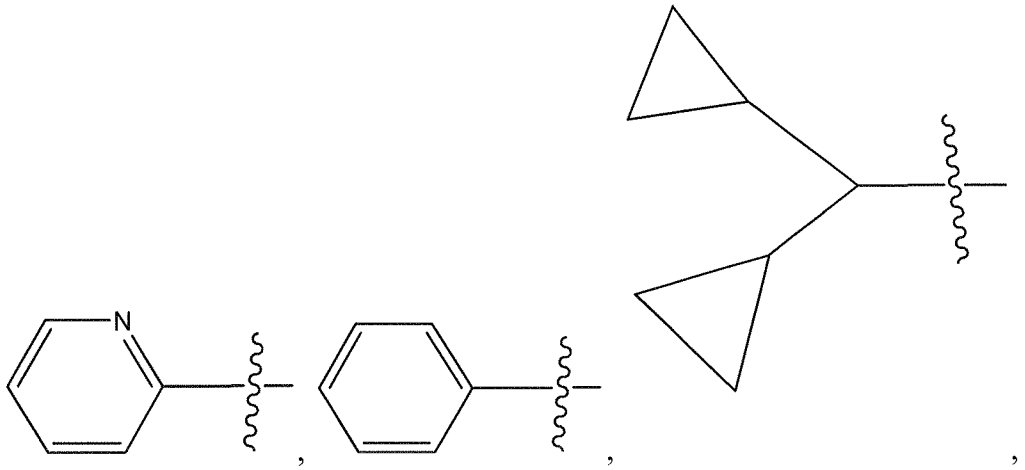
or the pharmaceutically acceptable salts thereof, wherein q and p are each independently 0, 1, 2 or 3.

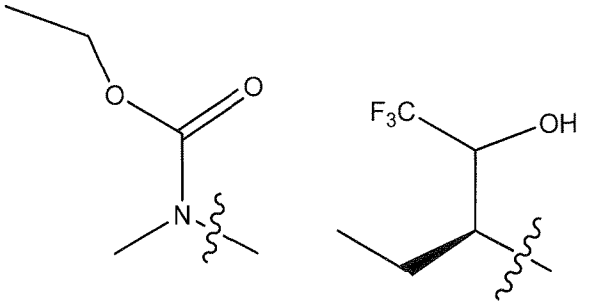
In another example, R^2 is selected from

5



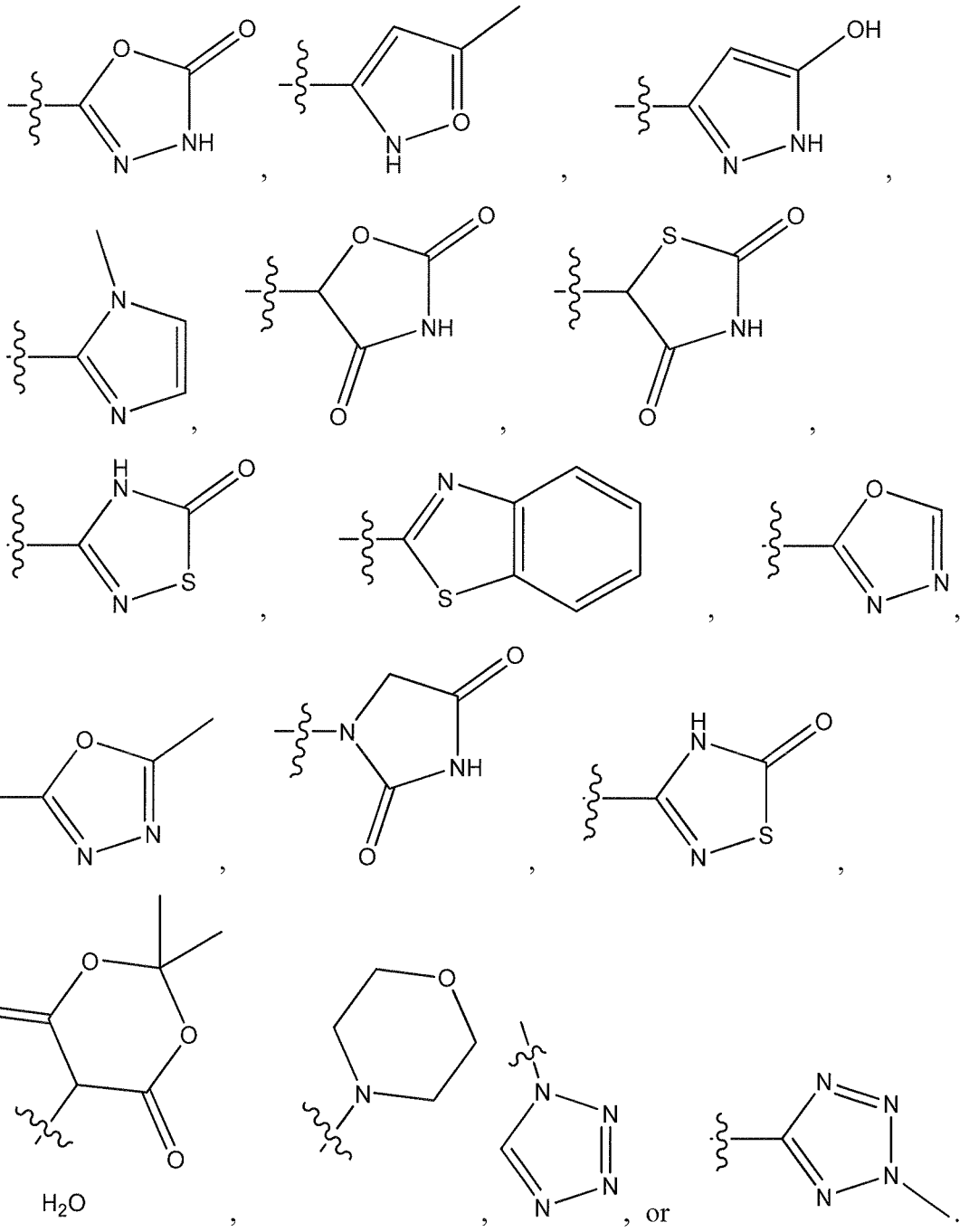




, or , any of which may be optionally substituted with one or more R^x groups as allowed by valence.

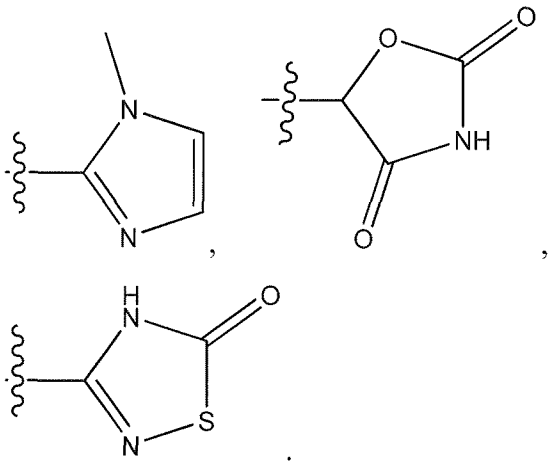
In another example,

R^2 is selected from



In another example,

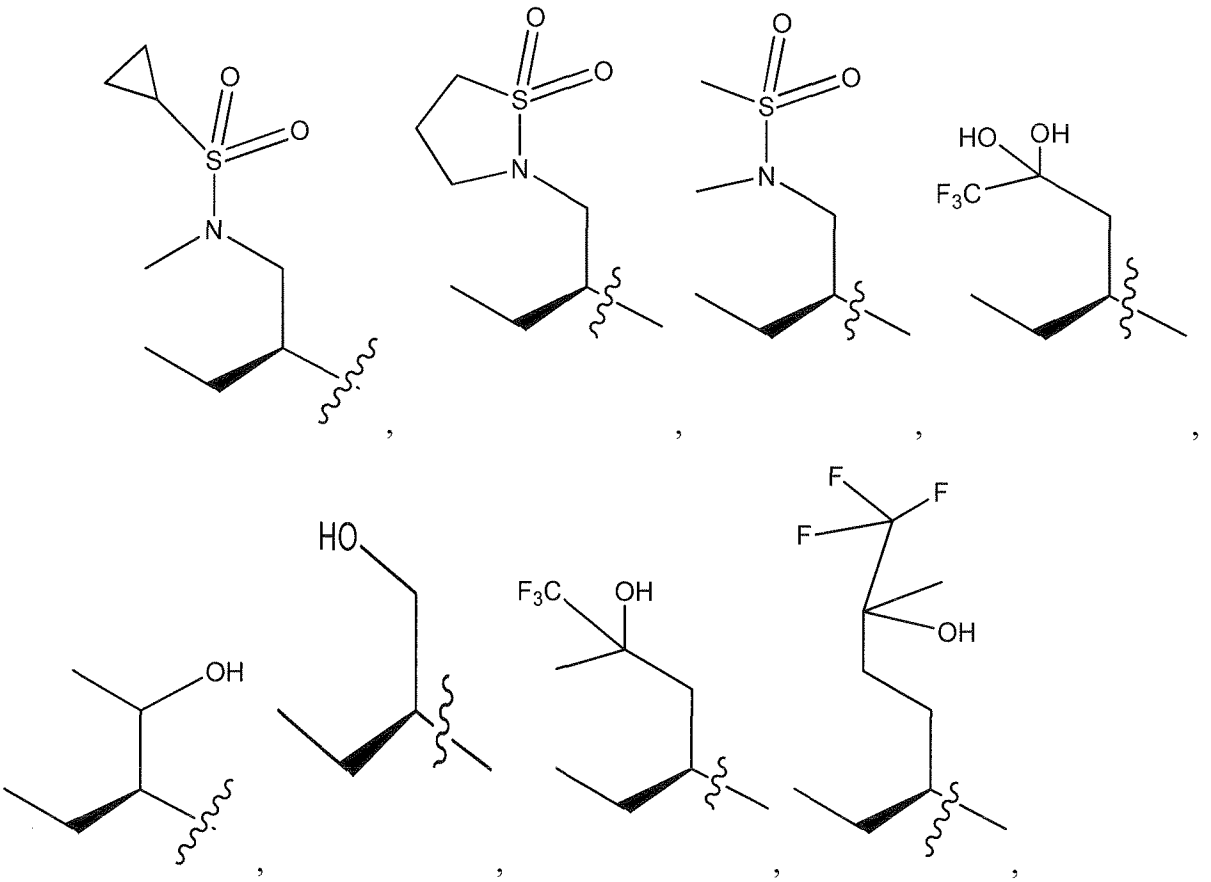
R^2 is selected from



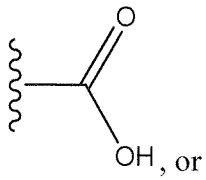
, , , or .

In another example,

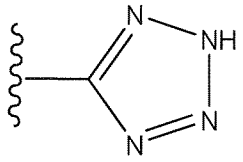
R^2 is selected from



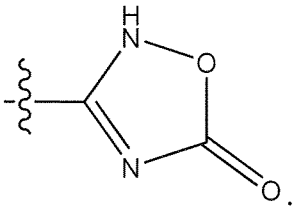
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, or a heteroaryl or heterocycle selected from

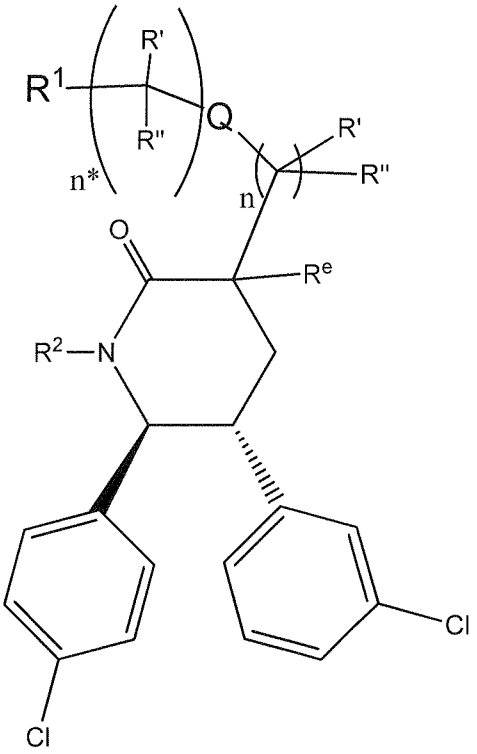


or



.

In another example, the compounds of Example A have the structure of Formula ID

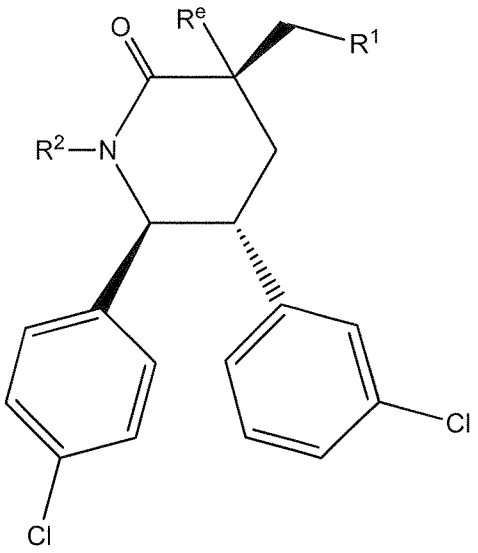


ID

or a pharmaceutically acceptable salt thereof.

In another example, Re is H or methyl or ethyl.

In another example, the compounds of Example A have the structure of Formula IE



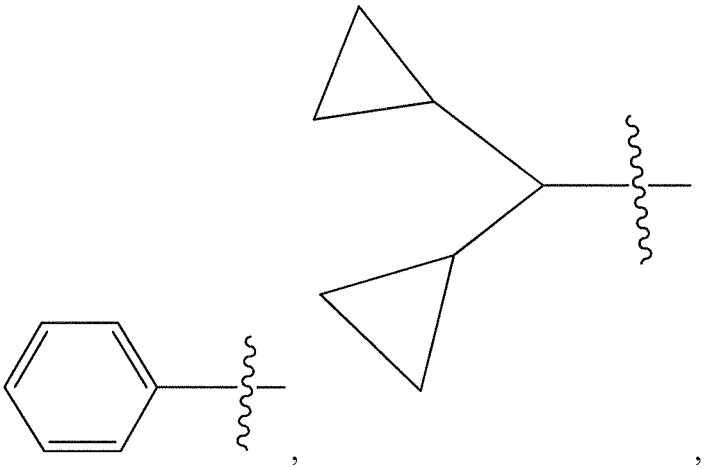
IE

or the pharmaceutically acceptable salts thereof.

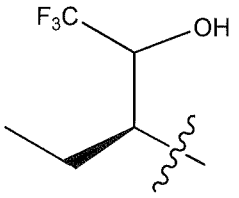
In another example, Re is H or methyl or ethyl.

In another example,

R^2 is selected from

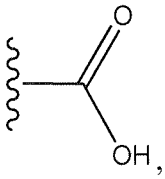


, , , or

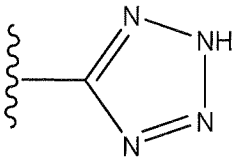


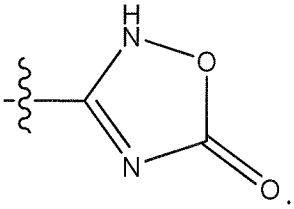
, any of which may be optionally substituted with one or more R^x groups as allowed by valence; and

R^1 is



, or a heteroaryl or heterocycle selected from

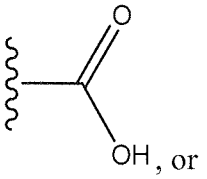


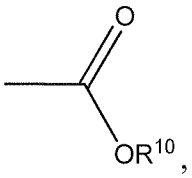
or 

.

In another example,

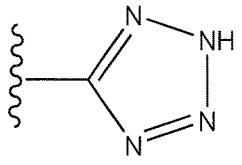
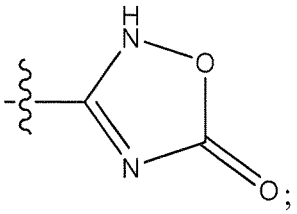
R^1 is



, or 

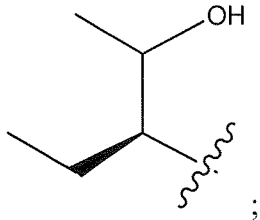
,

or a heteroaryl or heterocycle selected from

or ;

R^2 is

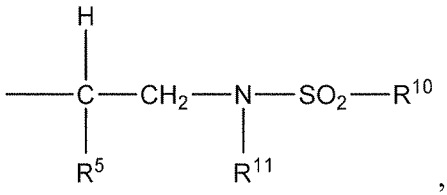
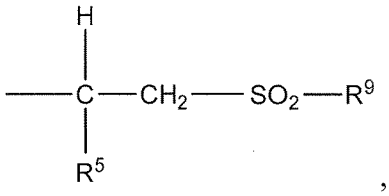
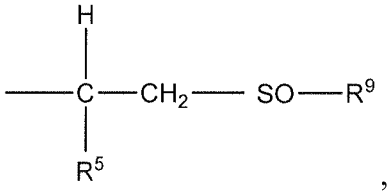
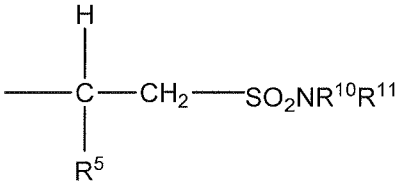
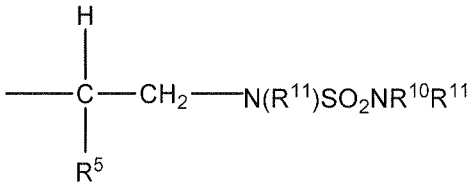


; and

R^e is methyl.

In another example,:

R^2 is


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,

, or

;

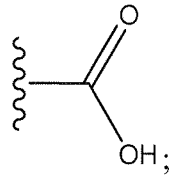
R^5 is cyclopropyl, or $C_{1\text{-}6}$alkyl;

R^9 is haloalkyl, haloalkoxy, $C_{1\text{-}6}$-alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$-alkynyl, $C_{3\text{-}8}$-cycloalkyl, ($C_{3\text{-}8}$-cycloalkyl)($C_{1\text{-}3}$alkyl), $C_{4\text{-}8}$-cycloalkenyl, aryl, heteroaryl, or heterocycloalkyl, or R^9 is haloalkyl, haloalkoxy, $C_{1\text{-}6}$-alkyl, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$-alkynyl, $C_{3\text{-}8}$-cycloalkyl, ($C_{3\text{-}8}$-cycloalkyl)($C_{1\text{-}3}$alkyl), $C_{4\text{-}8}$-cycloalkenyl, aryl, heteroaryl, or heterocyclo, any of which may be optionally independently substituted with one or more R^x groups as allowed by valence; and

R^{10} and R^{11} at each occurrence, respectively, are independently selected from H, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclo, arylalkyl, heteroarylalkyl, heterocycloalkyl, or cycloalkylalkyl, any of which may be optionally substituted as allowed by valence with one or more R^x, or R^{10} and R^{11} may combine to form a heterocyclo ring optionally substituted with one or more R^x.

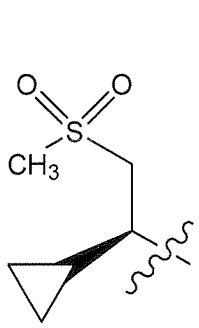
In another example,

R^1 is

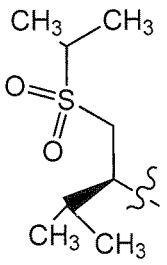


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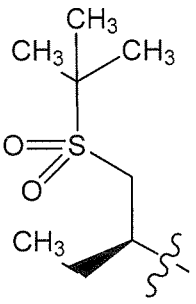
R^2 is



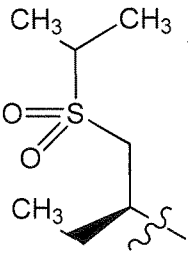
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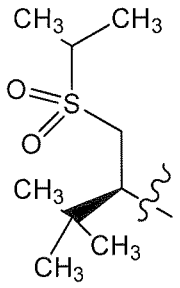
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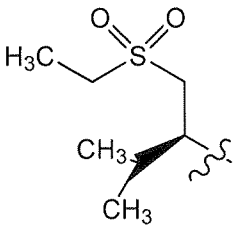
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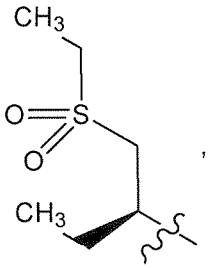
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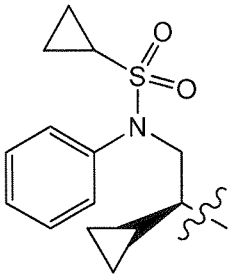
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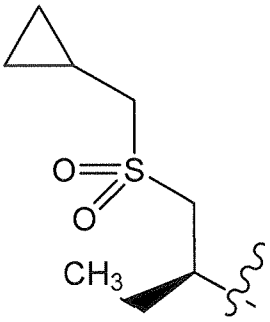
,



,



, or



;

2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-2-oxo-1-(pyrimidin-2-yl)piperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-1-(3-methylpyridin-2-yl)-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-1-(4-methylpyridin-2-yl)-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(dicyclopropylmethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3S, 5R, 6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(dicyclopropylmethyl)-3-methyl-2-oxopiperidin-3-yl) acetic acid;

((3S,4R,6R)-4-(3-chlorophenyl)-3-(4-chlorophenyl)-1,1-dioxido-2-(2-propanyl)-1,2-thiazinan-6-yl)acetic acid;

((3S,4R,6S)-4-(3-chlorophenyl)-3-(4-chlorophenyl)-1,1-dioxido-2-(2-propanyl)-1,2-thiazinan-6-yl)acetic acid;

((3S,4R,6R)-4-(3-chlorophenyl)-3-(4-chlorophenyl)-6-methyl-1,1-dioxido-2-(2-propanyl)-1,2-thiazinan-6-yl)acetic acid;

((3S,4R,6S)-4-(3-chlorophenyl)-3-(4-chlorophenyl)-6-methyl-1,1-dioxido-2-(2-propanyl)-1,2-thiazinan-6-yl)acetic acid;

2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(5-chloropyridin-2-yl)-3-methyl-1-((S)-1-morpholinobutan-2-yl)-2-oxopiperidin-3-yl)acetic acid;

2-((3S,5R,6S)-5-(3-Chlorophenyl)-6-(5-chloropyridin-2-yl)-3-methyl-2-oxo-1-(pentan-3-yl)piperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(5-chloropyridin-2-yl)-3-methyl-2-oxo-1-(pentan-3-yl)piperidin-3-yl)acetic acid;

2-((3S,5R,6S)-5-(3-Chlorophenyl)-6-(5-chloropyridin-2-yl)-3-methyl-2-oxo-1-(pentan-3-yl)piperidin-3-yl)acetic acid;

2-((3R,5R,6S)-1-((S)-1-tert-butoxy-1-oxobutan-2-yl)-5-(3-chlorophenyl)-6-(5-chloropyridin-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or

2-((3R,5S,6S)-1-((S)-1-tert-butoxy-1-oxobutan-2-yl)-6-(4-chlorophenyl)-5-(4-chloropyridin-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((1S,2R)-1-cyclopropyl-2-hydroxybutyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(N-methylcyclopropanesulfonamido)ethyl)-3-ethyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-2-(cyclopropanesulfonamido)-1-cyclopropylethyl)-3-ethyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(ethylsulfonamido)ethyl)-3-ethyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(N-methylcyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((1S,2R)-1-cyclopropyl-2-hydroxypropyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((1S,2S)-1-cyclopropyl-2-hydroxypropyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(1-methylethylsulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((R)-1-cyclopropyl-2-(N-methylcyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((2S,3S)-2-hydroxy-4-methylpentan-3-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-cyclopropyl(pyridin-2-yl)methyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((R)-cyclopropyl(pyridin-2-yl)methyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:
2-(1-(1-tert-butoxy-1-oxobutan-2-yl)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-ethoxy-1-oxobutan-2-yl)-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-ethoxy-4-methyl-1-oxopentan-2-yl)-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-1-(4-methylpyridin-2-yl)-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(dicyclopropylmethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

(4-(3-chlorophenyl)-3-(4-chlorophenyl)-1,1-dioxido-2-(2-propanyl)-1,2-thiazinan-6-yl)acetic acid;

(4-(3-chlorophenyl)-3-(4-chlorophenyl)-6-methyl-1,1-dioxido-2-(2-propanyl)-1,2-thiazinan-6-yl)acetic acid;

2-(5-(3-chlorophenyl)-6-(5-chloropyridin-2-yl)-3-methyl-1-(1-morpholinobutan-2-yl)-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(5-chloropyridin-2-yl)-3-methyl-2-oxo-1-(pentan-3-yl)piperidin-3-yl)acetic acid;

2-(1-(1-tert-butoxy-1-oxobutan-2-yl)-5-(3-chlorophenyl)-6-(5-chloropyridin-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or

2-(1-(1-tert-butoxy-1-oxobutan-2-yl)-6-(4-chlorophenyl)-5-(4-chloropyridin-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:

2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(1-(N-methylcyclopropanesulfonamido)butan-2-yl)-2-oxopiperidin-3-yl)acetic acid;

5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(1-(N-methylcyclopropanesulfonamido)butan-2-yl)-2-oxopiperidin-3-yl)propanoic acid;

tert-butyl 2-(3-((1H-tetrazol-5-yl)methyl)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-2-oxopiperidin-1-yl)butanoate;

2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-1-(1-(methylsulfonamido)butan-2-yl)-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-3-methyl-2-oxo-1-(5-oxohexan-3-yl)piperidin-3-yl)acetic acid;

2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(5-hydroxy-5-methylhexan-3-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-2-oxo-1-(6,6,6-trifluoro-5-hydroxy-5-methylhexan-3-yl)piperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-methylcyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(2-hydroxy-4-methylpentan-3-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(cyclopropyl(pyridin-2-yl)methyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:
2-((3S,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(N-methylcyclopropanesulfonamido)butan-2-yl)-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(1,1-dioxidoisothiazolidin-2-yl)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((2S,3S)-2-hydroxypentan-3-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((2R,3S)-2-hydroxypentan-3-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(1,1-dimethylethylsulfonamido)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid
2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(N,2-dimethylpropan-2-ylsulfonamido)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(N,1-dimethylcyclopropanesulfonamido)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(N-methylcyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((1S,2R)-1-cyclopropyl-2-hydroxypropyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((1S,2S)-1-cyclopropyl-2-hydroxypropyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-(N-methylcyclopropanesulfonamido)butan-2-yl)-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-(1,1-dioxidoisothiazolidin-2-yl)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(2-hydroxypentan-3-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(2-hydroxypentan-3-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-(1,1-dimethylethylsulfonamido)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-(N,2-dimethylpropan-2-ylsulfonamido)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-(N,1-dimethylcyclopropanesulfonamido)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-methylcyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-hydroxypropyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(thiophene-2-sulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(N-methylthiophene-2-sulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-2-(5-chlorothiophene-2-sulfonamido)-1-cyclopropylethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-1-((S)-2-(5-Chloro-N-methylthiophene-2-sulfonamido)-1-cyclopropylethyl)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(N-(difluoromethyl)-2-methylpropan-2-ylsulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(N-(difluoromethyl)ethylsulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(N-(difluoromethyl)cyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

(3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(ethylsulfonyl)ethyl)-3-(3-hydroxy-2-oxopropyl)-3-methylpiperidin-2-one;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(diethylamino)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(dimethylamino)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or
(2S,3S,5S,6R,7aR,10aS)-6-(3-chlorophenyl)-5-(4-chlorophenyl)-3-ethyl-2,7a-dimethylhexahydrofuro[2,3-b]oxazolo[3,2-a]pyridin-9(5H)-one.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(thiophene-2-sulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-methylthiophene-2-sulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(2-(5-chlorothiophene-2-sulfonamido)-1-cyclopropylethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(1-(2-(5-Chloro-N-methylthiophene-2-sulfonamido)-1-cyclopropylethyl)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-(difluoromethyl)-2-methylpropan-2-ylsulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-(difluoromethyl)ethylsulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-(difluoromethyl)cyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
1-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(2-(cyclopropanesulfonamido)-1-cyclopropylethyl)-3-methyl-2-oxopiperidin-3-yl)cyclopropanecarboxylic acid;
2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-(2-fluorophenyl)ethylsulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-(2-fluorophenyl)methylsulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(N-phenylcyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-isopropyl-6-methyl-2-oxopiperidin-3-yl)acetic acid;
5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(1-(1,1-dioxidoisothiazolidin-2-yl)butan-2-yl)-3-((6-methoxypyridin-2-yl)methyl)piperidin-2-one;
5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-(1,1-dioxidoisothiazolidin-2-yl)butan-2-yl)-3-((6-hydroxypyridin-2-yl)methyl)piperidin-2-one;
5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-(1,1-dioxidoisothiazolidin-2-yl)butan-2-yl)-3-((6-methoxypyridin-2-yl)methyl)-3-methylpiperidin-2-one;
5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(1-(1,1-dioxidoisothiazolidin-2-yl)butan-2-yl)-3-((6-hydroxypyridin-2-yl)methyl)-3-methylpiperidin-2-one;
(5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(1-cyclopropyl-2-(ethylsulfonyl)ethyl)-3-(3-hydroxy-2-oxopropyl)-3-methylpiperidin-2-one;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(diethylamino)-3-methyl-2-oxopiperidin-3-yl)acetic acid;
2-(5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(dimethylamino)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or
6-(3-chlorophenyl)-5-(4-chlorophenyl)-3-ethyl-2,7a-dimethylhexahydrofuro[2,3-b]oxazolo[3,2-a]pyridin-9(5H)-one.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:
2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(methylsulfonyl)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(isopropylsulfonyl)-3-methylbutan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-1-((S)-1-(tert-butylsulfonyl)butan-2-yl)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(isopropylsulfonyl)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(isopropylsulfonyl)-3,3-dimethylbutan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(ethylsulfonyl)-3-methylbutan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-(ethylsulfonyl)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-((3R,5R,6S)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-cyclopropyl-2-(N-phenylcyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid; or

2-((3R,5R,6S)-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-((S)-1-((cyclopropylmethyl)sulfonyl)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid.

In another example, the present disclosure provides a compound, or a pharmaceutically acceptable salt thereof, selected from:

2-(-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(-1-cyclopropyl-2-(methylsulfonyl)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(-1-(isopropylsulfonyl)-3-methylbutan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(-1-(-1-(tert-butylsulfonyl)butan-2-yl)-5-(3-chlorophenyl)-6-(4-chlorophenyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(-1-(isopropylsulfonyl)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(-1-(isopropylsulfonyl)-3,3-dimethylbutan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

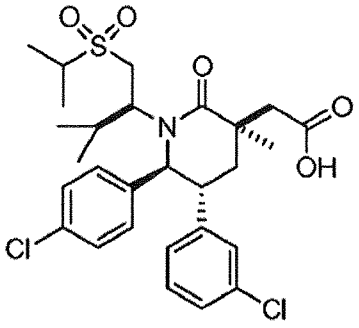
2-(-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(-1-(ethylsulfonyl)-3-methylbutan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(-5-(3-Chlorophenyl)-6-(4-chlorophenyl)-1-(-1-(ethylsulfonyl)butan-2-yl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

2-(-5-(3-chlorophenyl)-6-(4-chlorophenyl)-1-(-1-cyclopropyl-2-(N-phenylcyclopropanesulfonamido)ethyl)-3-methyl-2-oxopiperidin-3-yl)acetic acid;

What is claimed is:

1. Use of a compound of formula



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or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a subject in need of said treatment

2. The use of claim 1, wherein the cancer is selected from

(a) carcinomas, which comprise cancer of the bladder, breast, colon, rectum, kidney, liver, lung, esophagus, gall-bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin;

(b) hematopoietic tumors of lymphoid lineage, which comprise leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell-lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, hairy cell lymphoma and Burkett's lymphoma;

(c) hematopoietic tumors of myeloid lineage, which comprise acute and chronic myelogenous leukemias, myelodysplastic syndrome and promyelocytic leukemia;

(d) tumors of mesenchymal origin, which comprise fibrosarcoma and rhabdomyosarcoma, and other sarcomas, which comprise soft tissue sarcomas and bone sarcomas;

(e) tumors of the central and peripheral nervous system, which comprise astrocytoma, neuroblastoma, glioma and schwannomas;

(f) melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer, Kaposi's sarcoma, endometrial cancer, head and neck cancer, glioblastoma, malignant ascites, or hematopoietic cancers.

3. The use of claim 2, wherein the cancer is a hematopoietic tumor of lymphoid lineage.

4. The use of claim 2, wherein the cancer is soft tissue sarcoma.

5. The use of claim 2, wherein the cancer is breast cancer.

6. The use of claim 2, wherein the cancer is glioblastoma.

7. The use of claim 2, wherein the cancer is acute myeleogenous leukemia (AML).

8. The use of claim 2, wherein the cancer is melanoma.

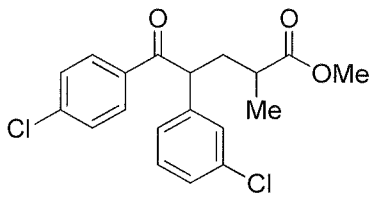
9. The use of claim 2, wherein the cancer is myelodysplastic syndrome.

10. The use of any one of claims 1-9, wherein the cancer is identified as p53wildtype (p53WT).

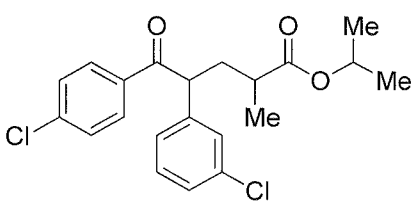
11. The use of any one of claims 1-9, wherein the medicament is to be used in combination with radiation therapy.

12. The use as claimed in claim 10, wherein the medicament is to be used in combination with radiation therapy.

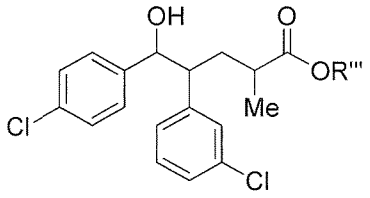
13. A compound, wherein the compound is a compound of formula



14. A compound, wherein the compound is a compound of formula



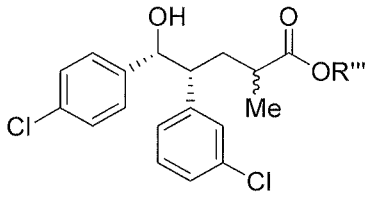
15. A compound, wherein the compound is a compound of formula



, wherein

R''' is hydrogen, methyl, or isopropyl.

16. The compound of claim 15, wherein the compound is a compound of formula



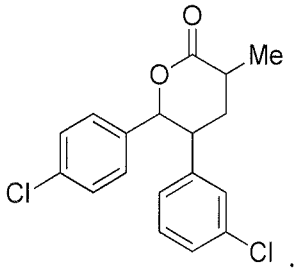
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17. The compound of claim 15 or claim 16, wherein R''' is hydrogen.

18. The compound of claim 15 or claim 16, wherein R''' is methyl.

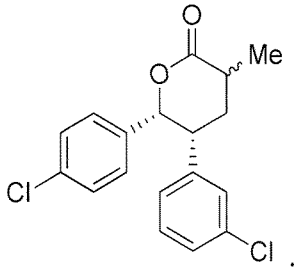
19. The compound of claim 15 or claim 16, wherein R''' is isopropyl.

20. A compound, wherein the compound is a compound of formula



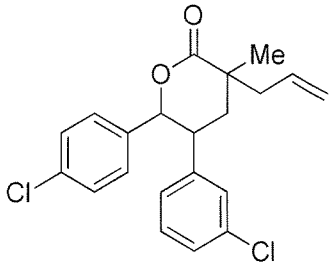
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21. The compound of claim 20, wherein the compound is a compound of formula

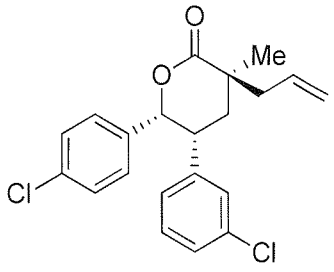


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22. A compound, wherein the compound is a compound of formula



23. The compound of claim 22, wherein the compound is a compound of formula



24. A compound, wherein the compound is a compound of formula

