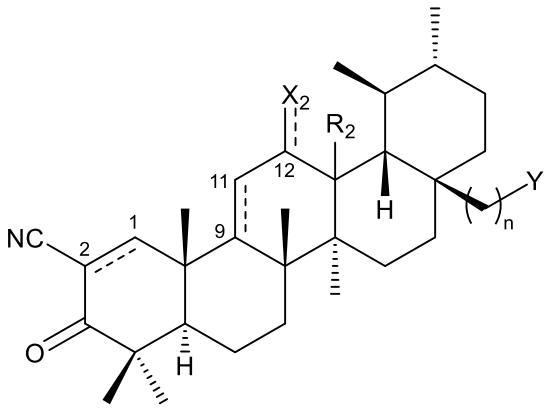
SUMMARY ~~OF THE INVENTION~~

The present disclosure provides novel synthetic triterpenoid derivatives with anti-inflammatory and/or antioxidant properties, pharmaceutical compositions, and methods for their manufacture, and methods for their use.

In one aspect, there are provided compounds of the formula:



(I-A),

wherein:

the bond between atom 1 and atom 2 is a single bond, a double bond, or an epoxidized double bond;

the bond between atom 9 and atom 11 is a single bond or a double bond;

the bond between atom 12 and X_2 is a single bond or a double bond;

n is 0–6;

X_2 is oxo, or X_2 is taken together with Y as defined below, provided that when X_2 is oxo, then the bond between atom 12 and X_2 is a double bond, and when X_2 is taken together with Y as defined below, that the bond between atom 12 and X_2 is a single bond;

R_2 is hydrogen or hydroxy; or R_2 is taken together with Y as defined below; and

Y is hydrogen, hydroxy, halo, or amino; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-arenediyl_{(C\leq12)}-R_3$, substituted $-arenediyl_{(C\leq12)}-R_3$, $-heteroarenediyl_{(C\leq12)}-R_3$, or substituted $-heteroarenediyl_{(C\leq12)}-R_3$, wherein:

R_3 is $alkyl_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

Y is taken together with R_2 and is $-(CH_2)_mX_1-$, wherein:

m is 0–6; and

X_1 is $-O-$; or

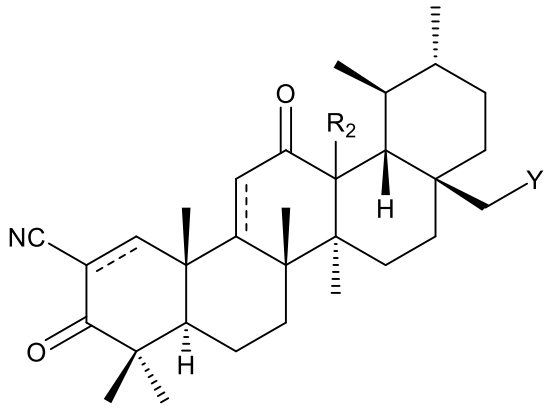
Y is taken together with X_2 and is $-(CH_2)_oC(O)-$, wherein:

o is 0-6; and

X_2 is $-O-$;

or a pharmaceutically acceptable salt thereof.

In some ~~embodiment~~examples, the compound is further defined as:



(I),

wherein:

the bond between atom 1 and atom 2 is a single bond, a double bond, or an epoxidized double bond;

the bond between atom 9 and atom 11 is a single bond or a double bond;

n is 0–6;

R_2 is hydrogen or hydroxy; or R_2 is taken together with Y as defined below; and

Y is hydrogen, hydroxy, halo, or amino; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-arenediyl_{(C\leq12)}-R_3$, substituted $-arenediyl_{(C\leq12)}-R_3$, $-heteroarenediyl_{(C\leq12)}-R_3$, or substituted $-heteroarenediyl_{(C\leq12)}-R_3$, wherein:

R_3 is $alkyl_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-alkanediyl_{(C\leq12)}-R_4$ or substituted $-alkanediyl_{(C\leq12)}-R_4$, wherein:

R_4 is $alkoxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, or a substituted version of any of these groups; or

−alkanediyl$_{(C\leq12)}$C(O)−R_5 or substituted −alkanediyl$_{(C\leq12)}$−C(O)R_5, wherein:

R_5 is hydroxy or amino; or

alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, cycloalkoxy$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−C(O)R_7, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, substituted heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, substituted cycloalkylamino$_{(C\leq12)}$, -NHC(NH)-alkyl$_{(C\leq12)}$, or -NHOR_{13}, wherein:

R_{13} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; or

−NR_8R_9, wherein:

R_8 is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; and

R_9 is acyl$_{(C\leq12)}$, substituted acyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, substituted cycloalkylsulfonyl$_{(C\leq12)}$, or

−CO_2R_{10}, wherein:

R_{10} is hydrogen, alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−C(O)R_{12}, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−CH=NOR_{11}, wherein:

R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; or

Y is taken together with R_2 and is −$(CH_2)_mX_1$−, wherein:

m is 0–6; and

X_1 is −O−;

or a pharmaceutically acceptable salt thereof.

In further ~~embodiment~~examples, the compound is further defined as:

R_8 is hydrogen, $alkyl_{(C\leq12)}$, or substituted $alkyl_{(C\leq12)}$; and

R_9 is $acyl_{(C\leq12)}$, substituted $acyl_{(C\leq12)}$, $alkylsulfonyl_{(C\leq12)}$, substituted $alkylsulfonyl_{(C\leq12)}$, $cycloalkylsulfonyl_{(C\leq12)}$, substituted $cycloalkylsulfonyl_{(C\leq12)}$, or

$-CO_2R_{10}$, wherein:

R_{10} is hydrogen, $alkyl_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-C(O)R_{12}$, wherein:

R_{12} is hydrogen, amino, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $cycloalkylamino_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-CH=NOR_{11}$, wherein:

R_{11} is hydrogen, $alkyl_{(C\leq12)}$, or substituted $alkyl_{(C\leq12)}$; or

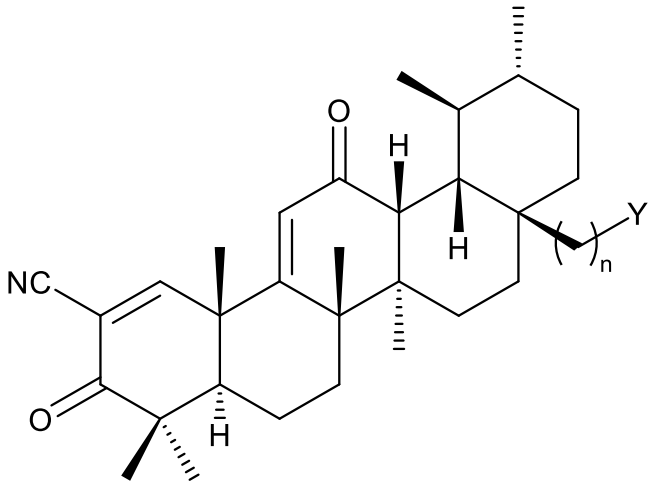
Y is taken together with R_2 and is $-(CH_2)_mX_1-$, wherein:

m is 0–6;

X_1 is $-O-$;

or a pharmaceutically acceptable salt thereof.

In still further ~~embodiment~~examples, the compound is further defined as:



(III),

wherein:

n is 0–6;

Y is hydrogen, hydroxy, halo, or amino; or

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-CH=NOR_{11}$, wherein:

R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$;

or a pharmaceutically acceptable salt thereof. In some ~~embodiment~~examples, the bond between atom 1 and atom 2 is a double bond or an epoxidized double bond. In some ~~embodiment~~examples, the bond between atom 1 and atom 2 is a double bond. In other ~~embodiment~~examples, the bond between atom 1 and atom 2 is an epoxidized double bond. In some ~~embodiment~~examples, the bond between atom 9 and atom 11 is a single bond. In other ~~embodiment~~examples, the bond between atom 9 and atom 11 is a double bond. In some ~~embodiment~~examples, X_2 is oxo. In some ~~embodiment~~examples, n is 0, 1, or 2. In some ~~embodiment~~examples, n is 0. In other ~~embodiment~~examples, n is 1. In still other ~~embodiment~~examples, n is 2.

In some ~~embodiment~~examples, Y is hydrogen, hydroxy, halo, or amino; or

alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-$arenediyl$_{(C\leq12)}-R_3$, substituted $-$arenediyl$_{(C\leq12)}-R_3$, $-$heteroarenediyl$_{(C\leq12)}-R_3$, or substituted $-$heteroarenediyl$_{(C\leq12)}-R_3$, wherein:

R_3 is alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-$alkanediyl$_{(C\leq12)}-R_4$ or substituted $-$alkanediyl$_{(C\leq12)}-R_4$, wherein:

R_4 is alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-$alkanediyl$_{(C\leq12)}$C(O)$-R_5$ or substituted $-$alkanediyl$_{(C\leq12)}-R_5$, wherein:

R_5 is hydroxy or amino; or

alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups.

In some ~~embodiment~~examples, Y is amino; or

alkyl$_{(C\leq12)}$, amido$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-$heteroarenediyl$_{(C\leq12)}-R_3$ or substituted $-$heteroarenediyl$_{(C\leq12)}-R_3$, wherein:

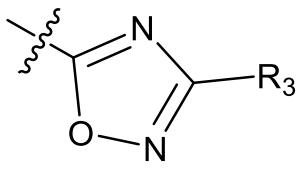
R_3 is alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups); or

−alkanediyl$_{(C\leq12)}$−R_4 or substituted −alkanediyl$_{(C\leq12)}$−R_4, wherein:

R_4 is alkoxy$_{(C\leq12)}$ or substituted alkoxy$_{(C\leq12)}$.

In some ~~embodiment~~examples, Y is amino. In other ~~embodiment~~examples, Y is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, Y is substituted alkyl$_{(C\leq12)}$, such as hydroxymethyl or methylaminomethyl. In still other ~~embodiment~~examples, Y is amido$_{(C\leq12)}$ or substituted amido$_{(C\leq12)}$. In further ~~embodiment~~examples, Y is amido$_{(C\leq12)}$, such as acetamido or propionamido. In other ~~embodiment~~examples, Y is substituted amido$_{(C\leq12)}$, such as 2,2-difluoropropionamido or 2,2-difluoroacetamido. In yet other ~~embodiment~~examples, Y is heterocycloalkyl$_{(C\leq12)}$ or substituted heterocycloalkyl$_{(C\leq12)}$. In some ~~embodiment~~examples, Y is heterocycloalkyl$_{(C\leq12)}$, such as oxazolidin-3-ylmethyl or azetidin-1-yl. In other ~~embodiment~~examples, Y is substituted heterocycloalkyl$_{(C\leq12)}$, such as 2-oxooxazolidin-3-yl, 3-methyl-2-oxoimidazolidin-1-yl, 2-oxoimidazolidin-1-yl, 2,5-dioxopyrrolidin-1-yl, methyl 3-oxopyrazolidine-1-carboxylate, 5-oxopyrazolidin-1-yl, 2-oxoazetidin-1-yl and 2-oxopyrrolidin-1-yl. In other ~~embodiment~~examples, Y is heteroaryl$_{(C\leq12)}$ or substituted heteroaryl$_{(C\leq12)}$. In further ~~embodiment~~examples, Y is heteroaryl$_{(C\leq12)}$, such as 3-methyl-1,2,4-oxadiazol-5-yl, 3-ethyl-1,2,4-oxadiazol-5-yl, 1H-pyrazol-1-yl, 1H-1,2,4-triazol-1-yl, 4-methyl-1H-1,2,3-triazol-1-yl, 1H-tetrazol-1-yl, 1H-1,2,3-triazol-1-yl, 1H-imidazol-1-yl, 5-methyl-1,3,4-oxadiazol-2-yl, or 5-methyl-1,2,4-oxadiazol-3-yl. In other ~~embodiment~~examples, Y is substituted heteroaryl$_{(C\leq12)}$, such as 4-bromo-1H-pyrazol-1-yl, 3-(2-methoxyethyl)-1,2,4-oxadiazol-5-yl, 3-(methoxymethyl)-1,2,4-oxadiazol-5-yl, 3-(2-hydroxyethyl)-1,2,4-oxadiazol-5-yl, 3-(hydroxymethyl)-1,2,4-oxadiazol-5-yl, 3-((dimethylamino)methyl)-1,2,4-oxadiazol-5-yl, 3-(1-methoxyethyl)-1,2,4-oxadiazol-5-yl, or 3-(fluoromethyl)-1,2,4-oxadiazol-5-yl..

In still other ~~embodiment~~examples, Y is −heteroarenediyl$_{(C\leq12)}$−R_3 or substituted −heteroarenediyl$_{(C\leq12)}$−R_3. In further ~~embodiment~~examples, Y is −heteroarenediyl$_{(C\leq12)}$−R_3. In still further ~~embodiment~~examples, Y is a group of the formula:



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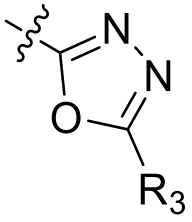
In other ~~embodiment~~examples, Y is a group of the formula:



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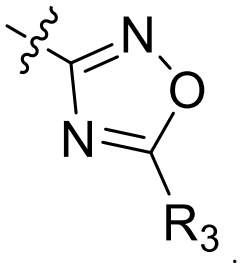
In still other ~~embodiment~~examples, Y is a group of the formula:



In some ~~embodiment~~examples, R_3 is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_3 is alkyl$_{(C\leq12)}$, such as methyl or ethyl. In other ~~embodiment~~examples, R_3 is substituted alkyl$_{(C\leq12)}$, such as 2-methoxyethyl, methoxymethyl, 2-hydroxyethyl, hydroxymethyl, (dimethylamino)methyl, 1-methoxyethyl, or fluoromethyl. In some ~~embodiment~~examples, R_3 is polar-substituted alkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_3 is monopolar-substituted alkyl$_{(C\leq12)}$. In still further ~~embodiment~~examples, monoaminoalkyl$_{(C\leq12)}$, monofluoroalkyl$_{(C\leq12)}$, or monohydroxyalkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_3 is monofluoroalkyl$_{(C\leq12)}$ or monohydroxyalkyl$_{(C\leq12)}$. In still further ~~embodiment~~examples, R_3 is monohydroxyalkyl$_{(C\leq12)}$, such as 2-hydroxyethyl or hydroxymethyl. In other ~~embodiment~~examples, R_3 is monofluoroalkyl$_{(C\leq12)}$, such as fluoromethyl. In other ~~embodiment~~examples, R_3 is cycloalkyl$_{(C\leq12)}$ or substituted cycloalkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_3 is cycloalkyl$_{(C\leq12)}$, such as cyclopropyl. In still other ~~embodiment~~examples, R_3 is −alkanediyl$_{(C\leq12)}$−R_4 or substituted −alkanediyl$_{(C\leq12)}$−R_4. In further ~~embodiment~~examples, R_3 is −methanediyl−R_4. In some ~~embodiment~~examples, R_4 is alkoxy$_{(C\leq12)}$, such as *t*-butoxy.

In some ~~embodiment~~examples, Y is −alkanediyl$_{(C\leq12)}$−C(O)R_5 or substituted −alkanediyl$_{(C\leq12)}$−C(O)R_5, wherein:

R_5 is hydroxy or amino; or

alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, cycloalkoxy$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups.

In some ~~embodiment~~examples, R_5 is hydroxy. In other ~~embodiment~~examples, R_5 is amino. In still other ~~embodiment~~examples, R_5 is alkoxy$_{(C\leq12)}$, such as methoxy. In some ~~embodiment~~examples, R_5 is alkylamino$_{(C\leq12)}$, such as methylamino or ethylamino. In other ~~embodiment~~examples, R_5 is substituted alkylamino$_{(C\leq12)}$, such as 2,2-difluoroethan-1-amino. In some ~~embodiment~~examples, R_5 is cycloalkyl$_{(C\leq12)}$ or substituted cycloalkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_5 is cycloalkyl$_{(C\leq12)}$, such as cyclopropyl. In some ~~embodiment~~examples, R_5 is cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$. In further ~~embodiment~~examples,

R_5 is cycloalkylamino$_{(C\leq12)}$, such as cyclopropylamino. In some ~~embodiment~~examples, R_5 is heterocycloalkyl$_{(C\leq12)}$ or substituted heterocycloalkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_5 is heterocycloalkyl$_{(C\leq12)}$, such as azetidine or pyrrolidine.

In some ~~embodiment~~examples, Y is

−C(O)R_7, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$, -NHC(NH)-alkyl$_{(C\leq12)}$, or -NHOR$_{13(C\leq12)}$, wherein:

R_{13} is hydrogen, alkyl, or substituted alkyl; or

−NR_8R_9, wherein:

R_8 is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; and

R_9 is acyl$_{(C\leq12)}$, substituted acyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, substituted cycloalkylsulfonyl$_{(C\leq12)}$, or

−CO_2R_{10}, wherein:

R_{10} is hydrogen, alkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−C(O)R_{12}, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$ or a substituted version of any of these groups; or

−CH=NOR_{11}, wherein:

R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$.

In further ~~embodiment~~examples, Y is −C(O)R_7, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$, -NHC(NH)-alkyl$_{(C\leq12)}$, or -NHOR$_{13(C\leq12)}$, wherein:

R_{13} is hydrogen, alkyl, or substituted alkyl.

In some ~~embodiment~~examples, R_7 is hydrogen. In other ~~embodiment~~examples, R_7 is cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$. In further ~~embodiment~~examples, R_7 is cycloalkylamino$_{(C\leq12)}$, such as cyclopropylamino. In some ~~embodiment~~examples, R_7 is heterocycloalkyl$_{(C\leq12)}$ or substituted heterocycloalkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_7 is heterocycloalkyl$_{(C\leq12)}$, such as azetidine or

pyrrolidine. In some ~~embodiment~~examples, R_7 is -NHC(NH)-alkyl$_{(C\leq12)}$, such as -NHC(NH)CH_3. In some ~~embodiment~~examples, R_7 is -NHOR$_{13(C\leq12)}$, wherein:

R_{13} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$.

In some ~~embodiment~~examples, R_{13} is hydrogen. In other ~~embodiment~~examples, R_{13} is alkyl$_{(C\leq12)}$, such as methyl.

In some ~~embodiment~~examples, Y is$-NR_8R_9$, wherein:

R_8 is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; and

R_9 is acyl$_{(C\leq12)}$, substituted acyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, substituted cycloalkylsulfonyl$_{(C\leq12)}$; or

$-CO_2R_{10}$, wherein

R_{10} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-C(O)R_{12}$, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups.

In some ~~embodiment~~examples, R_8 is hydrogen. In other ~~embodiment~~examples, R_8 is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_8 is alkyl$_{(C\leq12)}$, such as methyl. In some ~~embodiment~~examples, R_9 is acyl$_{(C\leq12)}$ or substituted acyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_9 is acyl$_{(C\leq12)}$, such as acetyl, methylacetyl, cyclopropylcarboxyl, or cyclobutylcarboxyl. In other ~~embodiment~~examples, R_9 is substituted acyl$_{(C\leq12)}$, such as methylaminocarbonyl, difluoroacetyl, or difluoromethylacetyl. In some ~~embodiment~~examples, R_9 is alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, or substituted cycloalkylsulfonyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_9 is alkylsulfonyl$_{(C\leq12)}$, such as is methylsulfonyl or ethylsulfonyl. In some ~~embodiment~~examples, R_9 is cycloalkylsulfonyl$_{(C\leq12)}$, such as cyclopropylsulfonyl$_{(C\leq12)}$.

In some ~~embodiment~~examples, R_9 is $-CO_2R_{10}$, wherein R_{10} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$, or a substituted version of any of these groups. In some ~~embodiment~~examples, R_{10} is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_{10} is

alkyl$_{(C\leq12)}$, such as methyl or *t*-butyl. In other ~~embodiment~~examples, R_9 is $-C(O)R_{12}$, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups.

In some ~~embodiment~~examples, R_{12} is hydrogen. In other ~~embodiment~~examples, R_{12} is amino. In still other ~~embodiment~~examples, R_{12} is alkylamino$_{(C\leq12)}$ or substituted alkylamino$_{(C\leq12)}$. In further ~~embodiment~~examples, R_{12} is alkylamino$_{(C\leq12)}$, such as methylamino or ethylamino. In some ~~embodiment~~examples, R_{12} is dialkylamino$_{(C\leq12)}$ or substituted dialkylamino$_{(C\leq12)}$. In other ~~embodiment~~examples, R_{12} is cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$. In further ~~embodiment~~examples, R_{12} is cycloalkylamino$_{(C\leq12)}$, such as cyclopropylamino. In some ~~embodiment~~examples, R_{12} is heterocycloalkyl$_{(C\leq12)}$ or substituted heterocycloalkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_{12} is heterocycloalkyl$_{(C\leq12)}$, such as azetidine.

In some ~~embodiment~~examples, Y is: $-CH=NOR_{11}$, wherein:

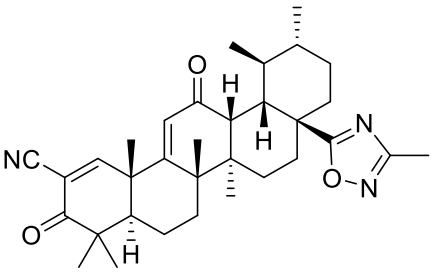
R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$.

In some ~~embodiment~~examples, R_{11} is hydrogen. In other ~~embodiment~~examples, R_{11} is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$. In further ~~embodiment~~examples, R_{11} is alkyl$_{(C\leq12)}$, such as methyl.

In some ~~embodiment~~examples, Y is taken together with R_2 and is $-(CH_2)_mX_1-$, wherein: m is 0–6 and X_1 is $-O-$. In some ~~embodiment~~examples, m is 1. In other ~~embodiment~~examples, m is 2.

In some ~~embodiment~~examples, Y is taken together with X_2 and is $-(CH_2)_oC(O)-$, wherein: o is 0–6. In further ~~embodiment~~examples, o is 1.

In some ~~embodiment~~examples, the compound is further defined as


NC
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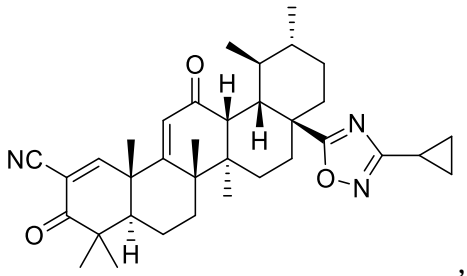
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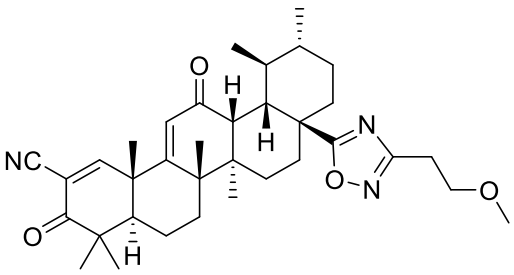
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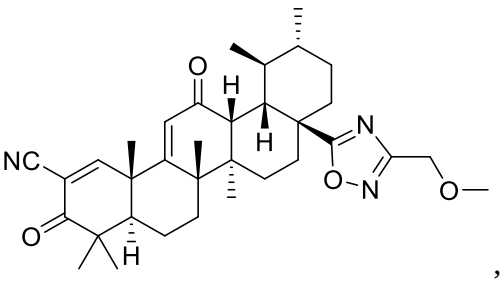
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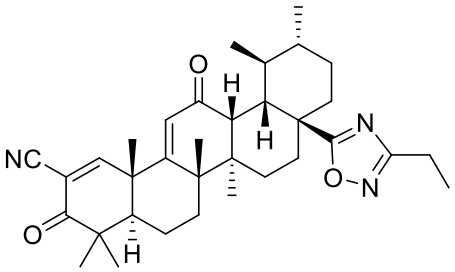
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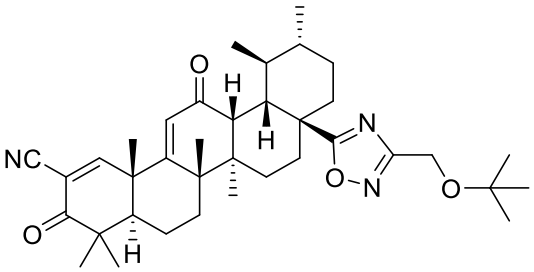
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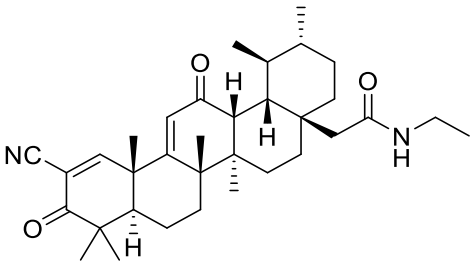
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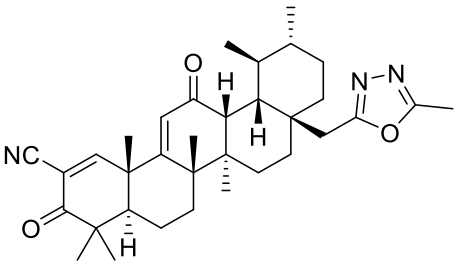
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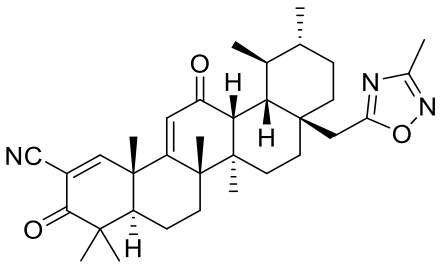
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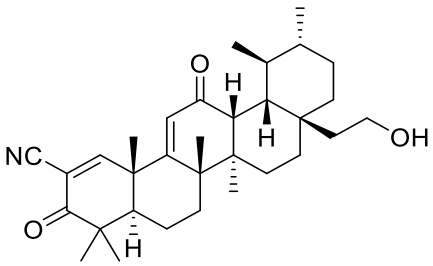
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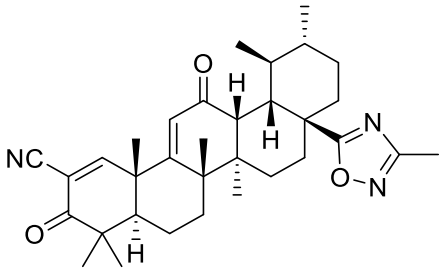
or a pharmaceutically acceptable salt thereof.

In further ~~embodiment~~examples, the compound is further defined as: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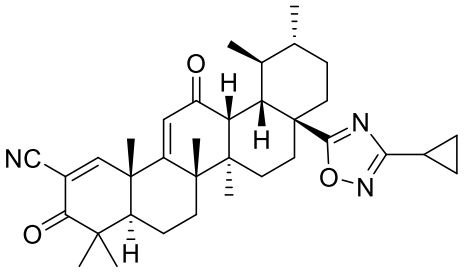
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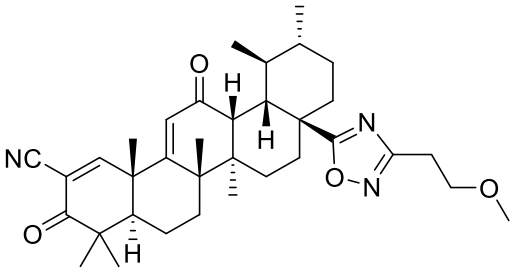
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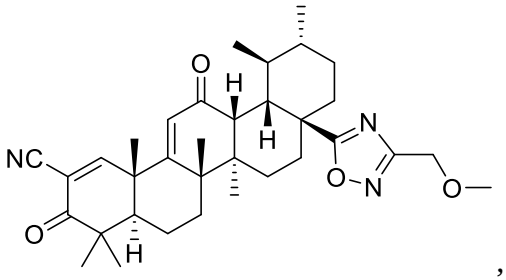
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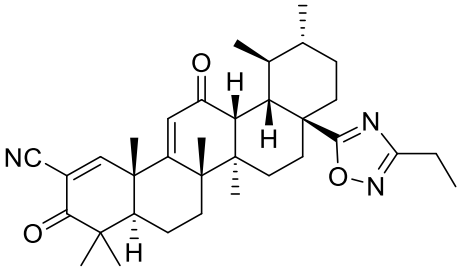
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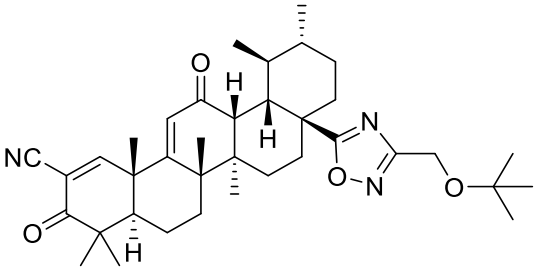
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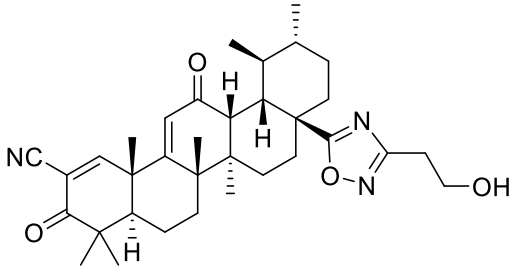
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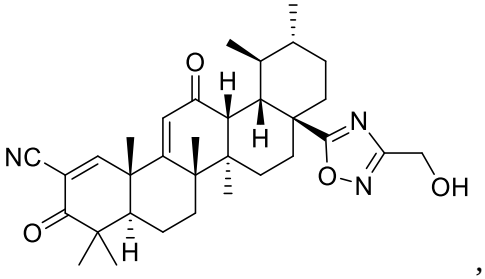
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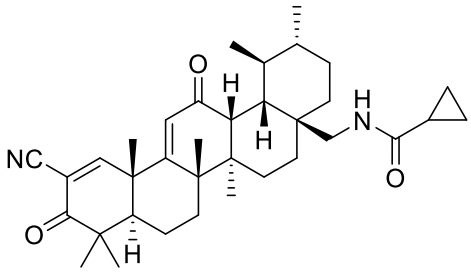
In further ~~embodiment~~examples, the compound is further defined as: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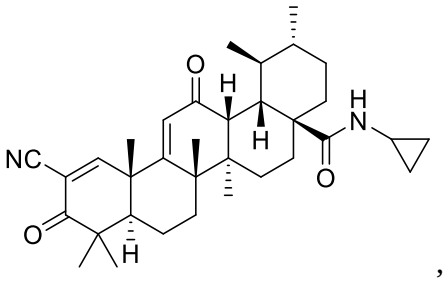
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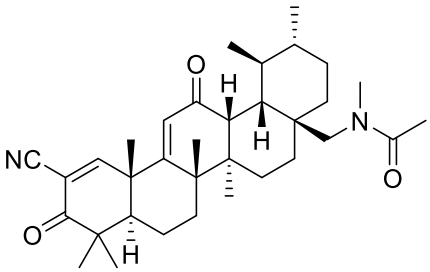
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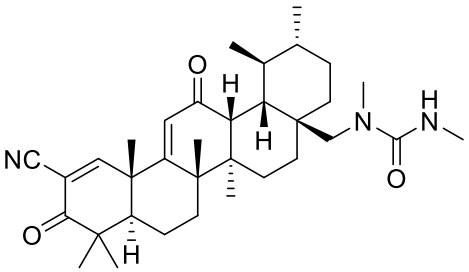
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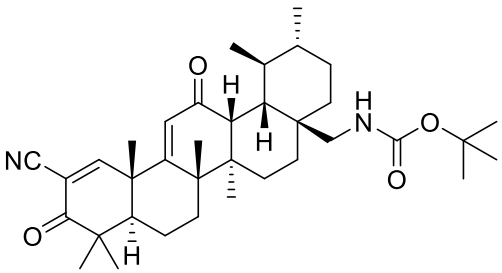
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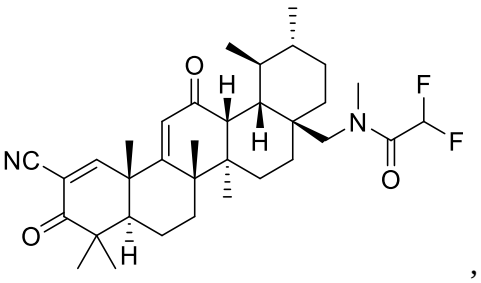
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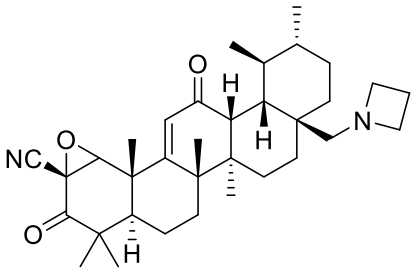
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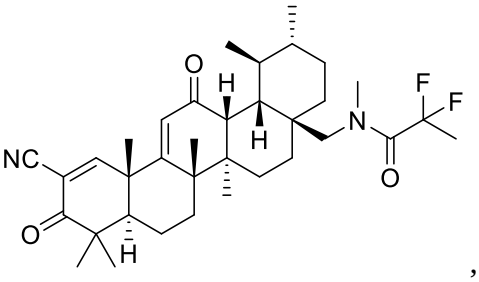
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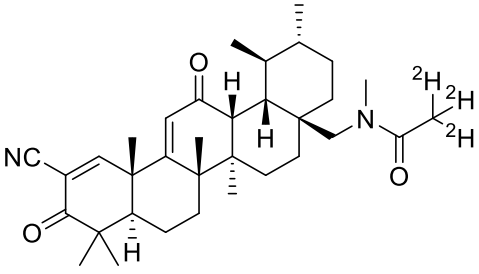
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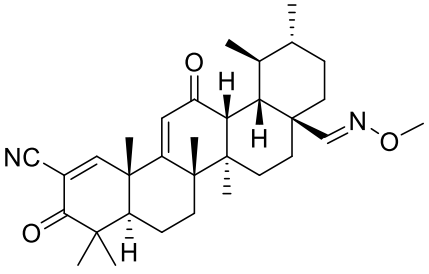

;

or a pharmaceutically acceptable salt thereof.

In some ~~embodiment~~examples, the compound is further defined as:

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-(3-methyl-1,2,4-oxadiazol-5-yl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

2-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-N-ethylacetamide

(4aR,6aS,6bR,8aR,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-((5-methyl-1,3,4-oxadiazol-2-yl)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile

(4aR,6aS,6bR,8aR,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-((3-methyl-1,2,4-oxadiazol-5-yl)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile

(4aR,6aS,6bR,8aR,11R,12S,12aS,12bR,14bS)-8a-(2-hydroxyethyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile

or a pharmaceutically acceptable salt thereof.

or a pharmaceutically acceptable salt thereof.

In some ~~embodiment~~examples, the compound is further defined as:

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-(3-methyl-1,2,4-oxadiazol-5-yl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(2-methoxyethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(methoxymethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

N-((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-2,2-difluoropropanamide;

N-((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)acetamide;

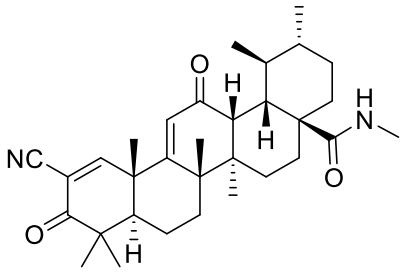
(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(hydroxymethyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((2-oxoazetidin-1-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile; or

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((2-oxopyrrolidin-1-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

or a pharmaceutically acceptable salt thereof.

In one ~~embodiment~~example, the compound is further defined as:



;

or a pharmaceutically acceptable salt thereof.

In a further ~~embodiment~~example, the compound is further defined as:

(1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-N,1,2,6a,6b,9,9,12a-octamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicene-4a(2H)-carboxamide

or a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure provides pharmaceutical compositions comprising:

(A) a compound of the present disclosure; and

(B) an excipient.

In some ~~embodiments~~examples, the pharmaceutical composition is formulated for administration orally, intraadiposally, intraarterially, intraarticularly, intracranially, intradermally, intralesionally, intramuscularly, intranasally, intraocularly, intrapericardially, intraperitoneally, intrapleurally, intraprostatically, intrarectally, intrathecally, intratracheally, intratumorally, intraumbilically, intravaginally, intravenously, intravesicularlly, intravitreally, liposomally, locally, mucosally, parenterally, rectally, subconjunctival, subcutaneously, sublingually, topically, transbuccally, transdermally, vaginally, in crèmes, in lipid compositions, via a catheter, via a lavage, via continuous infusion, via infusion, via inhalation, via injection, via local delivery, or via localized perfusion. In some ~~embodiment~~examples, the pharmaceutical composition is formulated for oral administration. In some ~~embodiment~~examples, the pharmaceutical composition is formulated for administration via injection. In some ~~embodiment~~examples, the pharmaceutical composition is formulated for intraarterial administration, intramuscular administration, intraperitoneal administration, or intravenous administration. In some ~~embodiment~~examples, the pharmaceutical composition is formulated for administration topically. In some ~~embodiment~~examples, the pharmaceutical composition is formulated for topical administration to the skin or to the eye. In some ~~embodiment~~examples, the pharmaceutical composition is formulated as a unit dose.

In still another ~~aspect~~example, the present disclosure provides methods of treating or preventing a disease or disorder in a patient in need thereof comprising administering to the patient a pharmaceutically effective amount of a compound or composition of the present disclosure. In some ~~embodiment~~examples, the patient is a mammal, such as a human. In some ~~embodiment~~examples, the disease or disorder is a condition associated with inflammation and/or oxidative stress. In some ~~embodiment~~examples, the disease or disorder is cancer. In some ~~embodiment~~examples, the disease or disorder is a cardiovascular disease, such as atherosclerosis. In some ~~embodiment~~examples, the disease or disorder is an autoimmune disease, such as Crohn's disease, rheumatoid arthritis, lupus, or psoriasis. In some ~~embodiment~~examples, the disease or disorder is a neurodegenerative disease, such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, or Huntington's disease. In some ~~embodiment~~examples, disease or disorder is chronic kidney disease, diabetes, mucositis, inflammatory bowel disease, dermatitis, sepsis, ischemia-reperfusion injury (including complications from sickle cell anemia), influenza, osteoarthritis, osteoporosis, pancreatitis, asthma, chronic obstructive pulmonary disease, cystic fibrosis, idiopathic pulmonary fibrosis, multiple sclerosis, muscular dystrophy, cachexia, or graft-versus-host disease. In some ~~embodiment~~examples, the disease or disorder is an eye disease, such as uveitis, glaucoma, macular degeneration, or retinopathy. In some ~~embodiment~~examples, the disease or disorder is neuropsychiatric, such as schizophrenia, depression,

bipolar disorder, epilepsy, post-traumatic stress disorder, attention deficit disorder, autism, or anorexia nervosa. In some ~~embodiment~~examples, the disease or disorder is associated with mitochondrial dysfunction, such as Friedreich's ataxia. In some ~~embodiment~~examples, the disease or disorder is chronic pain. In some ~~embodiment~~examples, the disease or disorder is neuropathic pain.

In another example~~aspect~~, the present disclosure provides methods of inhibiting nitric oxide production comprising administering to a patient in need thereof an amount of a compound or composition of the present disclosure sufficient to cause inhibition of IFN-γ-induced nitric oxide production in one or more cells of the patient.

In another aspect, there is provided the compound or pharmaceutical composition as defined above for use in treatment or prevention of a disease or disorder in a patient.

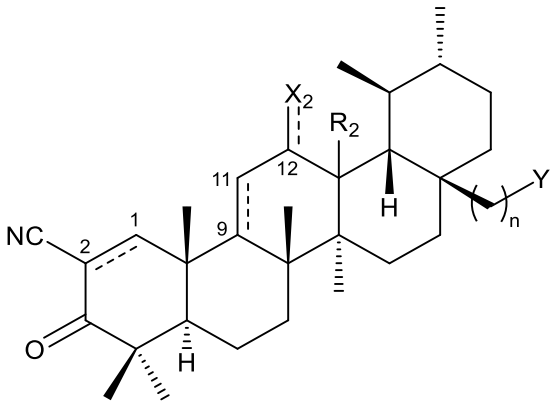
In another aspect, there is provided the use of a compound or pharmaceutical composition as defined above in the manufacture of a medicament for the treatment or prevention of a disease or disorder in a patient.

In another aspect, there is provided the use of the compound or pharmaceutical composition as defined above in the manufacture of a medicament for the inhibition of nitric oxide production in one or more cells of a patient.

Other objects, features and advantages of the present disclosure will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific ~~embodiment~~examples of the disclosure~~invention~~, are given by way of illustration only, since various changes and modifications within the spirit and scope of the ~~invention~~ disclosure will become apparent to those skilled in the art from this detailed description. Note that simply because a particular compound is ascribed to one particular generic formula doesn't mean that it cannot also belong to another generic formula.

WHAT IS CLAIMED IS:

1. A compound of the formula:



(I-A),

wherein:

the bond between atom 1 and atom 2 is a single bond, a double bond, or an epoxidized double bond;

the bond between atom 9 and atom 11 is a single bond or a double bond;

the bond between atom 12 and X_2 is a single bond or a double bond;

n is 0–6;

X_2 is oxo, or X_2 is taken together with Y as defined below, provided that when X_2 is oxo, then the bond between atom 12 and X_2 is a double bond, and when X_2 is taken together with Y as defined below, that the bond between atom 12 and X_2 is a single bond;

R_2 is hydrogen or hydroxy; or R_2 is taken together with Y as defined below; and

Y is hydrogen, hydroxy, halo, or amino; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, or a substituted version of any of these groups;

$-arenediyl_{(C\leq12)}-R_3$, substituted $-arenediyl_{(C\leq12)}-R_3$,

$-heteroarenediyl_{(C\leq12)}-R_3$, or substituted $-heteroarenediyl_{(C\leq12)}-R_3$,

wherein:

R_3 is $alkyl_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-alkanediyl_{(C\leq12)}-R_4$ or substituted $-alkanediyl_{(C\leq12)}-R_4$,

wherein:

R_4 is alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, or a substituted version of any of these groups; or

−alkanediyl$_{(C\leq12)}$−C(O)R_5, or substituted −alkanediyl$_{(C\leq12)}$−C(O)R_5, wherein:

R_5 is hydroxy or amino; or

alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, cycloalkoxy$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups;

−C(O)R_7, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, substituted heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, substituted cycloalkylamino$_{(C\leq12)}$, -NHC(NH)-alkyl$_{(C\leq12)}$, or -NHOR$_{13}$, wherein:

R_{13} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$;

−NR_8R_9, wherein:

R_8 is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; and

R_9 is acyl$_{(C\leq12)}$, substituted acyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, substituted cycloalkylsulfonyl$_{(C\leq12)}$, or

−CO_2R_{10}, wherein:

R_{10} is hydrogen, alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−C(O)R_{12}, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−CH=NOR_{11}, wherein:

R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; or

Y is taken together with R_2 and is −$(CH_2)_mX_1$−, wherein:

m is 0–6; and

X_1 is −O−; or

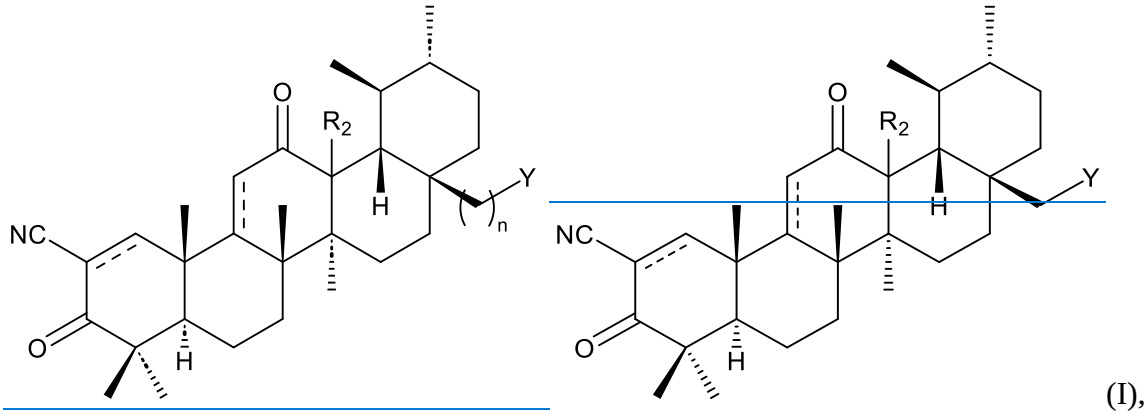
Y is taken together with X_2 and is −$(CH_2)_o$C(O)−, wherein:

o is 0-6; and

X_2 is −O−;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein the compound is further defined as:



(I),

wherein:

the bond between atom 1 and atom 2 is a single bond, a double bond, or an epoxidized double bond;

the bond between atom 9 and atom 11 is a single bond or a double bond;

n is 0–6;

R_2 is hydrogen or hydroxy; or R_2 is taken together with Y as defined below; and

Y is hydrogen, hydroxy, halo, or amino; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, or a substituted version of any of these groups;

$-arenediyl_{(C\leq12)}-R_3$, substituted $-arenediyl_{(C\leq12)}-R_3$, $-heteroarenediyl_{(C\leq12)}-R_3$, or substituted $-heteroarenediyl_{(C\leq12)}-R_3$, wherein:

R_3 is $alkyl_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-alkanediyl_{(C\leq12)}-R_4$ or substituted $-alkanediyl_{(C\leq12)}-R_4$, wherein:

R_4 is $alkoxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, or a substituted version of any of these groups; or

$-alkanediyl_{(C\leq12)}-C(O)R_5$ or substituted $-alkanediyl_{(C\leq12)}-C(O)R_5$, wherein:

R_5 is hydroxy or amino; or

alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, cycloalkoxy$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-C(O)R_7$, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, substituted heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, substituted cycloalkylamino$_{(C\leq12)}$, $-NHC(NH)$-alkyl$_{(C\leq12)}$, or $-NHOR_{13}$, wherein:

R_{13} is hydrogen, alkyl, or substituted alkyl;

$-NR_8R_9$, wherein:

R_8 is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; and

R_9 is acyl$_{(C\leq12)}$, substituted acyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, substituted cycloalkylsulfonyl$_{(C\leq12)}$,

$-CO_2R_{10}$, wherein:

R_{10} is hydrogen, alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-C(O)R_{12}$, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$ or a substituted version of any of these groups;

$-CH=NOR_{11}$, wherein:

R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; or

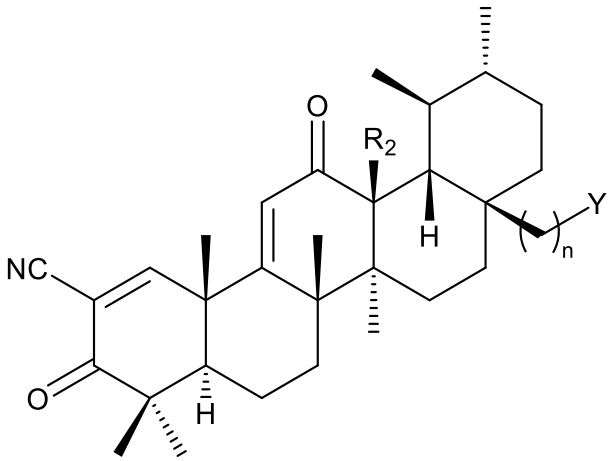
Y is taken together with R_2 and is $-(CH_2)_mX_1-$, wherein:

m is 0–6; and

X_1 is $-O-$;

or a pharmaceutically acceptable salt thereof.

3. The compound of either claim 1 or claim 2, wherein the compound is further defined as:



(II),

wherein:

n is 0–6;

R_2 is hydrogen or hydroxy~~,~~; or R_2 is taken together with Y as defined below; and

Y is hydrogen, hydroxy, halo, or amino; or

alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−arenediyl$_{(C\leq12)}$−R_3, substituted −arenediyl$_{(C\leq12)}$−R_3,

−heteroarenediyl$_{(C\leq12)}$−R_3, or substituted −heteroarenediyl$_{(C\leq12)}$−R_3,

wherein:

R_3 is alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−alkanediyl$_{(C\leq12)}$−R_4 or substituted −alkanediyl$_{(C\leq12)}$−R_4,

wherein:

R_4 is alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, or a substituted version of any of these groups; or

−alkanediyl$_{(C\leq12)}$−C(O)R_5 or substituted −alkanediyl$_{(C\leq12)}$−C(O)R_5,

wherein:

R_5 is hydroxy or amino; or

alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, cycloalkoxy$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−C(O)R_7, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, substituted heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, substituted cycloalkylamino$_{(C\leq12)}$, -NHC(NH)-alkyl$_{(C\leq12)}$, or -NHOR$_{13}$, wherein:

R_{13} is hydrogen, alkyl, or substituted alkyl;

−NR_8R_9, wherein:

R_8 is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; and

R_9 is acyl$_{(C\leq12)}$, substituted acyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, substituted cycloalkylsulfonyl$_{(C\leq12)}$,

−CO_2R_{10}, wherein:

R_{10} is hydrogen, alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−C(O)R_{12}, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$ or a substituted version of any of these groups;

−CH=NOR$_{11}$, wherein:

R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; or

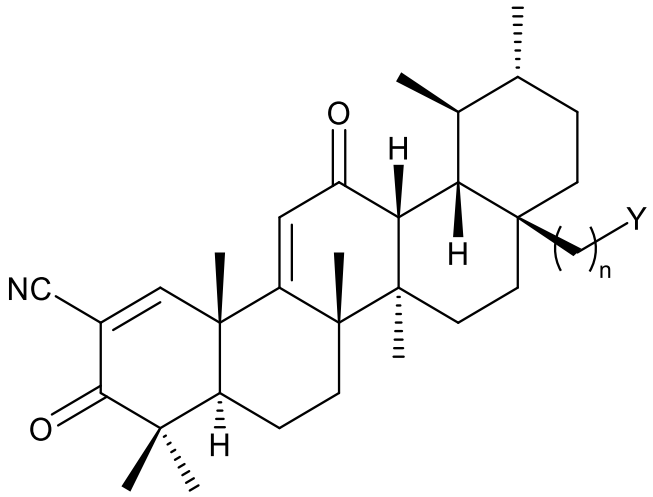
Y is taken together with R_2 and is −$(CH_2)_mX_1$−, wherein:

m is 0–6; and

X_1 is −O−;

or a pharmaceutically acceptable salt thereof.

4. The compound according to any one of claims 1-3, wherein the compound is further defined as:



(III),

wherein:

n is 0–6;

Y is hydrogen, hydroxy, halo, or amino; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-arenediyl_{(C\leq12)}-R_3$, substituted $-arenediyl_{(C\leq12)}-R_3$, $-heteroarenediyl_{(C\leq12)}-R_3$, or substituted $-heteroarenediyl_{(C\leq12)}-R_3$, wherein:

R_3 is $alkyl_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

$-alkanediyl_{(C\leq12)}-R_4$ or substituted $-alkanediyl_{(C\leq12)}-R_4$, wherein:

R_4 is $alkoxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, or a substituted version of any of these groups; or

$-alkanediyl_{(C\leq12)}-C(O)R_5$ or substituted $-alkanediyl_{(C\leq12)}-C(O)R_5$, wherein:

R_5 is hydroxy or amino; or

$alkoxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $cycloalkyl_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups; or

−C(O)R_7, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, substituted heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, substituted cycloalkylamino$_{(C\leq12)}$, −NHC(NH) −alkyl$_{(C\leq12)}$, or −NHOR_{13}, wherein:

R_{13} is hydrogen, alkyl, or substituted alkyl;

−NR_8R_9, wherein:

R_8 is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; and

R_9 is acyl$_{(C\leq12)}$, substituted acyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, substituted cycloalkylsulfonyl$_{(C\leq12)}$,

−CO_2R_{10}, wherein:

R_{10} is hydrogen, alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

−C(O)R_{12}, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$ or a substituted version of any of these groups;

−CH=NOR_{11}, wherein:

R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$;

or a pharmaceutically acceptable salt thereof.

~~5. The compound of claim 1 or claim 2, wherein the bond between atom 1 and atom 2 is a double bond or an epoxidized double bond.~~

~~6. The compound of either claim 1, claim 2, or claim 5, wherein the bond between atom 1 and atom 2 is a double bond.~~

~~7. The compound of either claim 1, claim 2, or claim 5, wherein the bond between atom 1 and atom 2 is an epoxidized double bond.~~

~~8. The compound according to either claim 1 or claim 2, wherein the bond between atom 9 and atom 11 is a single bond..~~

~~9. The compound according to either claim 1 or claim 2, wherein the bond between atom 9 and atom 11 is a double bond.~~

~~10. The compound according to any one of claims 1 or 5-11 wherein X_2 is oxo.~~

~~11~~5. The compound according to any one of claims 1-~~10~~4, wherein n is 0, 1, or 2.

~~12~~6. The compound according to any one of claims 1-~~11~~5, wherein n is 0.

~~13~~7. The compound according to any one of claims 1-~~11~~5, wherein n is 1.

~~14~~8. The compound according to any one of claims 1-~~11~~5, wherein n is 2.

~~15~~9. The compound according to any one of claims 1-8, wherein Y is hydroxy, halo, or amino.

~~The compound according to any one of claims 1-14, wherein Y is hydrogen, hydroxy, halo, or amino; or~~

~~alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or~~

~~=arenediyl$_{(C\leq12)}$-R_3, substituted =arenediyl$_{(C\leq12)}$-R_3, =heteroarenediyl$_{(C\leq12)}$-R_3, or substituted =heteroarenediyl$_{(C\leq12)}$-R_3, wherein:~~

~~R_3 is alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or~~

~~=alkanediyl$_{(C\leq12)}$-R_4 or substituted =alkanediyl$_{(C\leq12)}$-R_4, wherein:~~

~~R_4 is alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, or a substituted version of any of these groups; or~~

~~=alkanediyl$_{(C\leq12)}$C(O)-R_5 or substituted =alkanediyl$_{(C\leq12)}$-C(O)R_5, wherein:~~

~~R_5 is hydroxy or amino; or~~

~~alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, cycloalkoxy$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups.~~

~~16. The compound according to any one of claims 1-15, wherein Y is amino; or~~

~~alkyl$_{(C\leq12)}$, amido$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, or a substituted version of any of these groups; or~~

~~=heteroarenediyl$_{(C\leq12)}$-R_3 or substituted =heteroarenediyl$_{(C\leq12)}$-R_3, wherein:~~

~~R_3 is alkyl$_{(C\leq12)}$, substituted alkyl$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, or substituted cycloalkyl$_{(C\leq12)}$; or~~

~~=alkanediyl$_{(C\leq12)}$-R_4 or substituted =alkanediyl$_{(C\leq12)}$-R_4, wherein:~~

~~R_4 is alkoxy$_{(C\leq12)}$ or substituted alkoxy$_{(C\leq12)}$.~~

~~17. The compound according to any one of claims 1-16, wherein Y is amino.~~

~~18~~10. The compound according to any one of claims 1-~~16~~8, wherein Y is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$.

~~19~~11. The compound according to any one of claims 1-~~16~~ 8 and ~~18~~10, wherein Y is substituted alkyl$_{(C\leq12)}$.

~~20~~12. The compound according to any one of claims 1-~~16~~8, ~~18~~10, and ~~19~~11, wherein Y is hydroxymethyl~~,~~ or methylaminomethyl.

~~21. The compound according to any one of claims 1-16, wherein Y is amido$_{(C\leq12)}$ or substituted amido$_{(C\leq12)}$.~~

~~22. The compound according to any one of claims 1-16 and 21, wherein Y is amido$_{(C\leq12)}$.~~

~~23. The compound according to any one of claims 1-16, 21, and 22, wherein Y is acetamido or propionamido.~~

~~24. The compound according to any one of claims 1-16 and 21, wherein Y is substituted amido$_{(C\leq12)}$.~~

~~25. The compound according to any one of claims 1-16, 21, and 24, wherein Y is 2,2-difluoropropionamido.~~

~~26~~13. The compound according to any one of claims 1-~~16~~8, wherein Y is heterocycloalkyl$_{(C\leq12)}$ or substituted heterocycloalkyl$_{(C\leq12)}$.

~~27. The compound according to any one of claims 1-16 and 26, wherein Y is heterocycloalkyl$_{(C\leq12)}$.~~

~~28. The compound according to any one of claims 1-16, 26, and 27, wherein Y is oxazolidin-3-yl or azetidin-1-yl.~~

~~29~~14. The compound according to any one of claims 1-~~16~~ 8 and ~~26~~13, wherein Y is substituted heterocycloalkyl$_{(C\leq12)}$.

~~30~~15. The compound according to any one of claims 1-~~16~~8, ~~26~~13, and ~~29~~14, wherein Y is selected from the group of: 2-oxooxazolidin-3-yl, 3-methyl-2-oxoimidazolidin-1-yl, 2-

oxoimidazolidin-1-yl, 2,5-dioxopyrrolidin-1-yl, methyl 3-oxopyrazolidine-1-carboxylate, 5-oxopyrazolidin-1-yl, 2-oxoazetidin-1-yl and 2-oxopyrrolidin-1-yl.

~~31~~16. The compound according to any one of claims 1-~~16~~8, wherein Y is heteroaryl$_{(C\leq12)}$ or substituted heteroaryl$_{(C\leq12)}$.

~~32~~17. The compound according to any one of claims 1-~~16~~ 8 and ~~31~~16, wherein Y is heteroaryl$_{(C\leq12)}$.

~~33~~18. The compound according to any one of claims 1-~~16~~8, ~~31~~16, and ~~32~~17, wherein Y is 3-methyl-1,2,4-oxadiazol-5-yl, 3-ethyl-1,2,4-oxadiazol-5-yl, 1H-pyrazol-1-yl, 1H-1,2,4-triazol-1-yl, 4-methyl-1H-1,2,3-triazol-1-yl, 1H-tetrazol-1-yl, 1H-1,2,3-triazol-1-yl, 1H-imidazol-1-yl, 5-methyl-1,3,4-oxadiazol-2-yl, or 5-methyl-1,2,4-oxadiazol-3-yl.

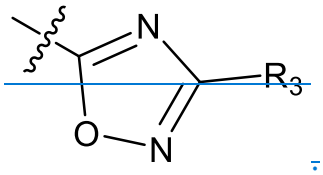
~~34~~19. The compound according to any one of claims 1-~~16~~ 8 and ~~31~~16, wherein Y is substituted heteroaryl$_{(C\leq12)}$.

~~35~~20. The compound according to any one of claims 1-~~16~~8, ~~31~~16, and ~~34~~19, wherein Y is 4-bromo-1H-pyrazol-1-yl, 3-(2-methoxyethyl)-1,2,4-oxadiazol-5-yl, 3-(methoxymethyl)-1,2,4-oxadiazol-5-yl, 3-(2-hydroxyethyl)-1,2,4-oxadiazol-5-yl, 3-(hydroxymethyl)-1,2,4-oxadiazol-5-yl, 3-((dimethylamino)methyl)-1,2,4-oxadiazol-5-yl, 3-(1-methoxyethyl)-1,2,4-oxadiazol-5-yl, or 3-(fluoromethyl)-1,2,4-oxadiazol-5-yl.

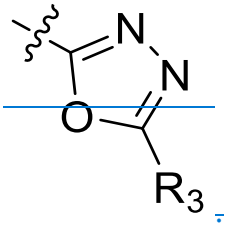
~~36. The compound according to any one of claims 1-16, wherein Y is =heteroarenediyl$_{(C\leq12)}$=R_3 or substituted =heteroarenediyl$_{(C\leq12)}$=R_3.~~

~~37. The compound according to any one of claims 1-16 and 36, wherein Y is =heteroarenediyl$_{(C\leq12)}$=R_3.~~

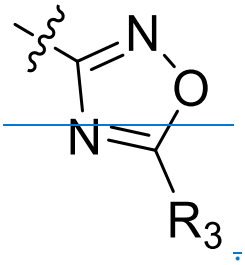
~~38. The compound according to any one of claims 1-16, 36, and 37, wherein Y is a group of the formula:~~



~~39. The compound according to any one of claims 1-16, 36, and 37, wherein Y is a group of the formula:~~



40. The compound according to any one of claims 1-16, 36, and 37, wherein Y is a group of the formula:



41. The compound according to any one of claims 1-16 and 36-40, wherein R_3 is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$.

42. The compound according to any one of claims 1-16 and 36-41, wherein R_3 is alkyl$_{(C\leq12)}$.

43. The compound according to any one of claims 1-16 and 36-42, wherein R_3 is methyl or ethyl.

44. The compound according to any one of claims 1-16 and 36-41, wherein R_3 is substituted alkyl$_{(C\leq12)}$.

45. The compound according to any one of claims 1-16, 36-41, and 44, wherein R_3 is 2-methoxyethyl, methoxymethyl, 2-hydroxyethyl, hydroxymethyl, (dimethylamino)methyl, 1-methoxyethyl, or fluoromethyl.

46. The compound according to any one of claims 1-16, 41, and 44, wherein R_3 is polar-substituted alkyl$_{(C\leq12)}$.

47. The compound according to any one of claims 1-16, 41, 44, and 46, wherein R_3 is monopolar-substituted alkyl$_{(C\leq12)}$.

48. The compound according to any one of claims 1-16, 41, 46, and 47-44, wherein R_3 is monoaminoalkyl$_{(C\leq12)}$, monofluoroalkyl$_{(C\leq12)}$, or monohydroxyalkyl$_{(C\leq12)}$.

~~49. The compound according to any one of claims 1-16, 41, 44, and 46-48,, wherein R_3 is monofluoroalkyl$_{(C\leq12)}$ or monohydroxyalkyl$_{(C\leq12)}$.~~

~~50. The compound according to any one of claims 1-16, 41, 44, and 46-49, wherein R_3 is monohydroxyalkyl$_{(C\leq12)}$.~~

~~51. The compound according to any one of claims 1-16, 41, 44, and 46-50, wherein R_3 is 2-hydroxyethyl or hydroxymethyl.~~

~~52. The compound according to any one of claims 1-16, 41, 44, and 46-49, wherein R_3 is monofluoroalkyl$_{(C\leq12)}$.~~

~~53. The compound according to any one of claims 1-16, 41, 44, and 46-50, wherein R_3 is fluoromethyl.~~

~~54. The compound according to any one of claims 1-16 and 36-40, wherein R_3 is cycloalkyl$_{(C\leq12)}$ or substituted cycloalkyl$_{(C\leq12)}$.~~

~~55. The compound according to any one of claims 1-16 and 36-40, and 54, wherein R_3 is cycloalkyl$_{(C\leq12)}$.~~

~~56. The compound according to any one of claims 1-16 and 36-40, 54, and 55, wherein R_3 is cyclopropyl.~~

~~57. The compound according to any one of claims 1-16 and 36-40, wherein R_3 is =alkanediyl$_{(C\leq12)}$=R_4 or substituted =alkanediyl$_{(C\leq12)}$=R_4.~~

~~58. The compound according to any one of claims 1-16 and 36-40, and 57, wherein R_3 is =methanediyl=R_4.~~

~~59. The compound according to any one of claims 1-16 and 36-40, 57, and 58, wherein R_4 is alkoxy$_{(C\leq12)}$.~~

~~60. The compound according to any one of claims 1-16 and 36-40, and 57-59, wherein R_4 is *t*-butoxy.~~

~~61~~21. The compound according to any one of claims 1-~~15~~8, wherein Y is −alkanediyl$_{(C\leq12)}$−C(O)R_5 or substituted −alkanediyl$_{(C\leq12)}$−C(O)R_5, wherein:

R_5 is hydroxy or amino; or

alkoxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkyl$_{(C\leq12)}$, cycloalkoxy$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups.

~~62~~22. The compound according to any one of claims 1-~~15~~ 8 and ~~61~~21, wherein R_5 is hydroxy.

~~63~~23. The compound according to any one of claims 1-~~15~~ 8 and ~~61~~21, wherein R_5 is amino.

~~64. The compound according to any one of claims 1-15 and 61, wherein R_5 is alkoxy$_{(C\leq12)}$.~~

~~65. The compound according to any one of claims 1-15, 57, or 64, wherein R_5 is methoxy.~~

~~66~~24. The compound according to any one of claims 1-~~15~~ 8 and ~~61~~21, wherein R_5 is alkylamino$_{(C\leq12)}$.

~~67~~25. The compound according to any one of claims 1-~~15~~8, ~~61~~21, ~~or~~ and ~~66~~24, wherein R_5 is methylamino or ethylamino.

~~68. The compound according to any one of claims 1-15, and 61, wherein R_5 is substituted alkylamino$_{(C\leq12)}$.~~

~~69. The compound according to any one of claims 1-15, 61, and 68, wherein R_5 is 2,2-difluoroethan-1-amino.~~

~~70. The compound according to any one of claims 1-15 and 61, wherein R_5 is cycloalkyl.$_{(C\leq12)}$ or substituted cycloalkyl$_{(C\leq12)}$~~

~~71. The compound according to any one of claims 1-15, 61, and 70, wherein R_5 is cycloalkyl$_{(C\leq12)}$.~~

~~72. The compound according to any one of claims 1-15, 61, 70, and 71, wherein R_5 is cyclopropyl$_{(C\leq12)}$.~~

~~73~~26. The compound according to any one of claims 1-~~15~~ 8 and ~~61~~21, wherein R_5 is cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$.

~~74~~27. The compound according to any one of claims 1-~~15~~8, ~~61~~21, and ~~73~~26, wherein R_5 is cycloalkylamino$_{(C\leq12)}$.

~~75~~28. The compound according to any one of claims 1-~~15~~8, ~~61~~21, ~~73~~26, and ~~74~~27, wherein R_5 is cyclopropylamino.

~~76~~29. The compound according to any one of claims 1-~~15~~ 8 and ~~61~~21, wherein R_5 is heterocycloalkyl$_{(C\leq12)}$ or substituted heterocycloalkyl$_{(C\leq12)}$.

~~77~~30. The compound according to any one of claims 1-~~15~~8, ~~61~~21, and ~~76~~29, wherein R_5 is heterocycloalkyl$_{(C\leq12)}$.

~~78~~31. The compound according to any one of claims 1-~~15~~8, ~~61~~21, ~~76~~29, and ~~77~~30, wherein R_5 is azetidine or pyrrolidine.

~~79~~32. The compound according to any one of claims 1-~~14~~8, wherein Y is:

$-C(O)R_7$, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$, $-NHC(NH)-alkyl_{(C\leq12)}$, or $-NHOR_{13}$, wherein:

R_{13} is hydrogen, alkyl, or substituted alkyl;

$-NR_8R_9$, wherein:

R_8 is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$; and

R_9 is acyl$_{(C\leq12)}$, substituted acyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, substituted cycloalkylsulfonyl$_{(C\leq12)}$, or

$-CO_2R_{10}$, wherein:

R_{10} is hydrogen, alkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-C(O)R_{12}$, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

$-CH=NOR_{11}$, wherein:

R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$.

~~80~~33. The compound according to any one of claims 1-~~14~~ 8 and ~~79~~32, wherein Y is:

$-C(O)R_7$, wherein:

R_7 is hydrogen, heterocycloalkyl$_{(C\leq12)}$, substituted heterocycloalkyl$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$, $-NHC(NH)-alkyl_{(C\leq12)}$, or $-NHOR_{13(C\leq12)}$, wherein:

R_{13} is hydrogen, alkyl, or substituted alkyl.

8134. The compound according to any one of claims 1-148, 7932, and 8033, wherein R_7 is hydrogen.

8235. The compound according to any one of claims 1-148, 7932, and 8033, wherein R_7 is cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$.

8336. The compound according to any one of claims 1-148, 7932, 8033, and 8235, wherein R_7 is cycloalkylamino$_{(C\leq12).}$

8437. The compound according to any one of claims 1-148, 7932, 8033, 8235, and 8336, wherein R_7 is cyclopropylamino.

8538. The compound according to any one of claims 1-148, 7932, and 8033, wherein R_7 is heterocycloalkyl$_{(C\leq12)}$ or substituted heterocycloalkyl$_{(C\leq12)}$.

8639. The compound according to any one of claims 1-148, 7932, 8033, and 8538, wherein R_7 is heterocycloalkyl$_{(C\leq12).}$

8740. The compound according to any one of claims 1-148, 7932, 8033, 8538, and 8639, wherein R_7 is azetidine or pyrrolidine.

88. The compound according to any one of claims 1-14, 79, and 80, wherein R_7 is -NHC(NH)-alkyl$_{(C\leq12)}$;

89. The compound according to any one of claims 1-14, 79, 80, and 88, wherein R_7 is -NHC(NH)CH_3.

90. The compound according to any one of claims 1-14, 79, and 80, wherein R_7 is -NHOR$_{13(C\leq12)}$, wherein:

R_{13} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$.

91. The compound according to any one of claims 1-14, 79, 80, and 90, wherein R_{13} is hydrogen.

92. The compound according to any one of claims 1-14, 79, 80, and 90, wherein R_{13} is alkyl$_{(C\leq12)}$.

93 The compound according to any one of claims 1-14, 79, 80, 90, and 92, wherein R_{13} is methyl.

9441. The compound according to any one of claims 1-14 8 and 7932, wherein Y is:

$-NR_8R_9$, wherein:

R_8 is hydrogen, $alkyl_{(C\leq12)}$, or substituted $alkyl_{(C\leq12)}$; and

R_9 is $acyl_{(C\leq12)}$, substituted $acyl_{(C\leq12)}$, $alkylsulfonyl_{(C\leq12)}$, substituted $alkylsulfonyl_{(C\leq12)}$, $cycloalkylsulfonyl_{(C\leq12)}$, substituted $cycloalkylsulfonyl_{(C\leq12)}$; or $-CO_2R_{10}$, wherein R_{10} is hydrogen, $alkyl_{(C\leq12)}$, or substituted $alkyl_{(C\leq12)}$, or a substituted version of any of these groups; or $-C(O)R_{12}$, wherein:

R_{12} is hydrogen, amino, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $cycloalkylamino_{(C\leq12)}$, $heterocycloalkyl_{(C\leq12)}$, or a substituted version of any of these groups.

9542. The compound according to any one of claims 1-148, 7932, and 9441, wherein R_8 is hydrogen.

9643. The compound according to any one of claims 1-148, 7932, and 9441, wherein R_8 is $alkyl_{(C\leq12)}$ or substituted $alkyl_{(C\leq12)}$.

9744. The compound according to any one of claims 1-148, 7932, 9441, and 9643, wherein R_8 is $alkyl_{(C\leq12)}$.

9845. The compound according to any one of claims 1-148, 7932, 9441, 9643, and 9744, wherein R_8 is methyl.

9946. The compound according to any one of claims 1-148, 7932, and 9441-9845, wherein R_9 is $acyl_{(C\leq12)}$ or substituted $acyl_{(C\leq12)}$.

10047. The compound according to any one of claims 1-148, 7932, and 9441-9946, wherein R_9 is $acyl_{(C\leq12)}$.

10148. The compound according to any one of claims 1-148, 7932, and 9441-10047, wherein R_9 is acetyl, methylacetyl, cyclopropanelcarboxyl, or cyclobutanecarboxyl.

49. The compound of claim 48, wherein R_9 is acetyl, further wherein the acetyl is substantially $-C(O)CD_3$.

10250. The compound according to any one of claims 1-148, 7932, and 9441-9946, wherein R_9 is substituted $acyl_{(C\leq12)}$.

~~103~~51. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~99~~46, and ~~102~~50,~~,~~ wherein R_9 is methylaminocarbonyl, difluoroacetyl, or difluoromethylacetyl.

~~104~~52. The compound according to any one of claims 1-~~14~~8, ~~79~~32, and ~~94~~41-~~98~~45, wherein R_9 is alkylsulfonyl$_{(C\leq12)}$, substituted alkylsulfonyl$_{(C\leq12)}$, cycloalkylsulfonyl$_{(C\leq12)}$, or substituted cycloalkylsulfonyl$_{(C\leq12)}$.

~~105~~53. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, and ~~104~~52, wherein R_9 is alkylsulfonyl$_{(C\leq12)}$.

~~106~~54. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, ~~104~~49, and ~~105~~53, wherein R_9 is methylsulfonyl or ethylsulfonyl.

~~107~~55. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, and ~~104~~52, wherein R_9 is cycloalkylsulfonyl$_{(C\leq12)}$.

~~108~~56. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, ~~104~~52, and ~~107~~55, wherein R_9 is cyclopropylsulfonyl$_{(C\leq12)}$.

~~109~~57. The compound according to any one of claims 1-~~14~~8, ~~79~~32, and ~~94~~41-~~98~~45, wherein R_9 is $-CO_2R_{10}$, wherein R_{10} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$, or a substituted version of any of these groups.

~~110~~58. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, and ~~109~~57, wherein R_{10} is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$.

~~111~~59. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, ~~109~~57, and ~~110~~58, wherein R_{10} is alkyl$_{(C\leq12)}$.

~~112~~60. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, and ~~109~~57-~~111~~59, wherein R_{10} is methyl or *t*-butyl.

~~113~~61. The compound according to any one of claims 1-~~14~~8, ~~79~~32, and ~~94~~41-~~98~~45, wherein R_9 is $-C(O)R_{12}$, wherein:

R_{12} is hydrogen, amino, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, cycloalkylamino$_{(C\leq12)}$, heterocycloalkyl$_{(C\leq12)}$, or a substituted version of any of these groups.

~~114. The compound according to any one of claims 1-14, 79, 94-98, and 113, wherein R_{12} is hydrogen.~~

~~115. The compound according to any one of claims 1-14, 79, 94-98, and 113, wherein R_{12} is amino.~~

~~116~~62. The compound according to any one of claims 1-~~14~~ 8, ~~79~~32, ~~94~~41-~~98~~45, and ~~113~~61, wherein R_{12} is alkylamino$_{(C\leq12)}$ or substituted alkylamino$_{(C\leq12)}$.

~~117~~63. The compound according to any one of claims 1-~~14~~ 8, ~~79~~32, ~~94~~41-~~98~~45, ~~113~~61, and ~~116~~62, wherein R_{12} is alkylamino$_{(C\leq12)}$.

~~118~~64. The compound according to any one of claims 1-~~14~~ 8, ~~79~~32, ~~94~~41-~~98~~45, ~~113, 116, and 117~~and 61-63, wherein R_{12} is methylamino or ethylamino.

~~119. The compound according to any one of claims 1-14, 79, 94-98, and 113, wherein R_{12} is dialkylamino$_{(C\leq12)}$ or substituted dialkylamino$_{(C\leq12)}$.~~

~~120~~65. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, and ~~113~~61, wherein R_{12} is cycloalkylamino$_{(C\leq12)}$ or substituted cycloalkylamino$_{(C\leq12)}$.

~~121~~66. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, ~~113~~61, and ~~120~~65, wherein R_{12} is cycloalkylamino$_{(C\leq12)}$

~~122~~67. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, ~~113~~61, ~~120~~65, and ~~121~~66, wherein R_{12} is cyclopropylamino.

~~123~~68. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, and ~~113~~61, wherein R_{12} is heterocycloalkyl$_{(C\leq12)}$ or substituted heterocycloalkyl$_{(C\leq12)}$.

~~124~~69. The compound according to any one of claims 1-~~14~~8, ~~79~~32, ~~94~~41-~~98~~45, ~~113~~61, and ~~123~~68, wherein R_{12} is heterocycloalkyl$_{(C\leq12)}$.

~~125~~70. The compound according to any one of claims 1-~~14~~8, ~~79~~32, 41~~94~~-~~98~~45, ~~113~~61, ~~123~~ 68 and ~~124~~69, wherein R_{12} is azetidine.

~~126. The compound according to any one of claims 1-14 and 79, wherein Y is: =CH-NOR$_{11}$, wherein:~~

~~R_{11} is hydrogen, alkyl$_{(C\leq12)}$, or substituted alkyl$_{(C\leq12)}$.~~

~~127. The compound according to any one of claims 1-14, 79, and 126, wherein R_{11} is hydrogen,~~

~~128. The compound according to any one of claims 1-14 79, and 126 wherein R_{11} is alkyl$_{(C\leq12)}$ or substituted alkyl$_{(C\leq12)}$.~~

~~129. The compound of claim 128, wherein R_{11} is alkyl$_{(C\leq12)}$.~~

~~130. The compound of claim 129, wherein R_{11} is methyl.~~

~~131. The compound according to any one of claims 1-3 and 5-14, wherein Y is taken together with R_2 and is $=(CH_2)_mX_1=$, wherein:~~

~~m is 0-6; and~~

~~X_1 is $=O=$.~~

~~132. The compound of claim 94, wherein Y is taken together with R_2 and is $=(CH_2)_mX_1=$, wherein:~~

~~m is 1 and~~

~~X_1 is $=O=$.~~

~~133. The compound of claim 94, wherein Y is taken together with R_2 and is $=(CH_2)_mX_1=$, wherein:~~

~~m is 2.~~

~~X_1 is $=O=$.~~

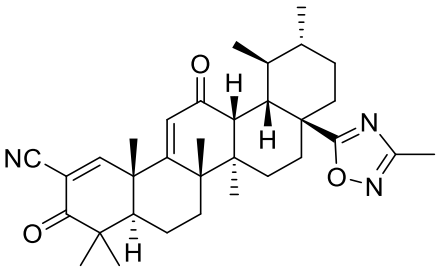
~~134. The compound according to any one of claims 1 and 5-14, wherein Y is taken together with X_2 and is $=(CH_2)_oC(O)-$, wherein:~~

~~o is 0-6.~~

~~135. The compound according to any one of claims 1 and 5-14, wherein Y is taken together with X_2 and is $=(CH_2)_oC(O)-$, wherein:~~

~~o is 1.~~

136~~71~~. The compound according to any one of claims 1-135~~70~~, wherein the compound is further defined as: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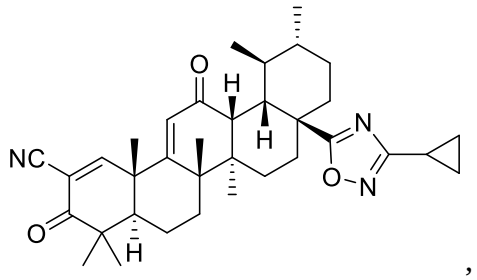
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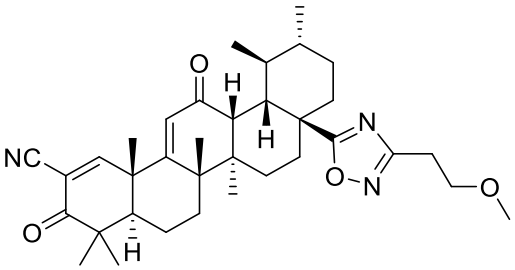
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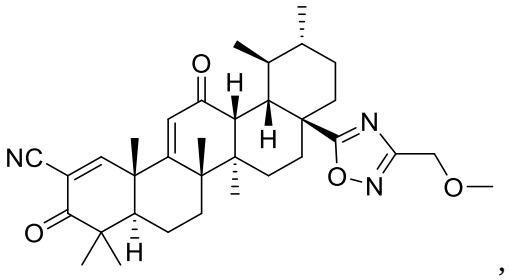
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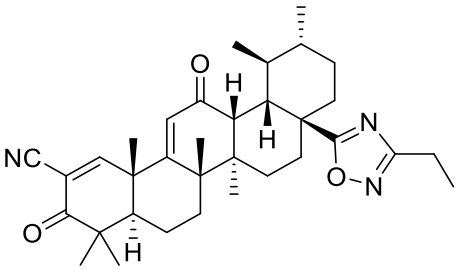
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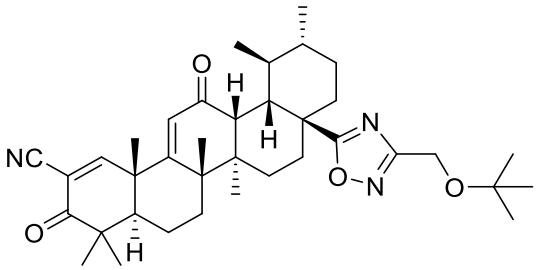
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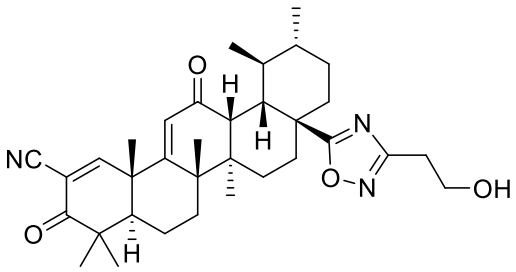
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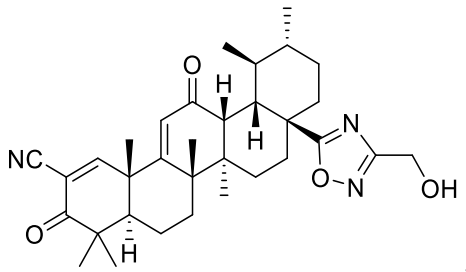
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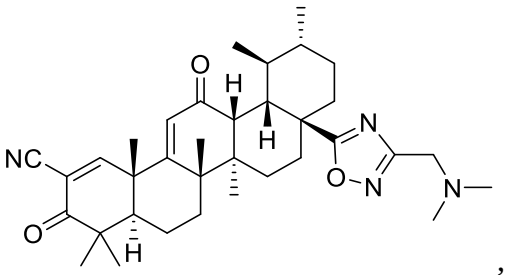
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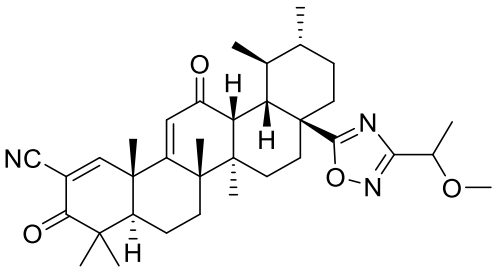
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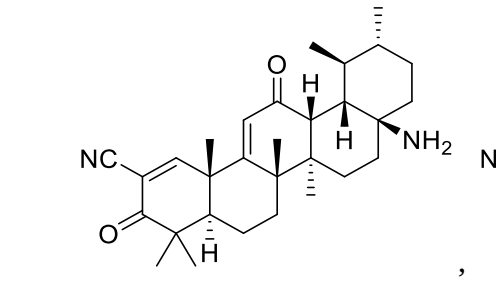
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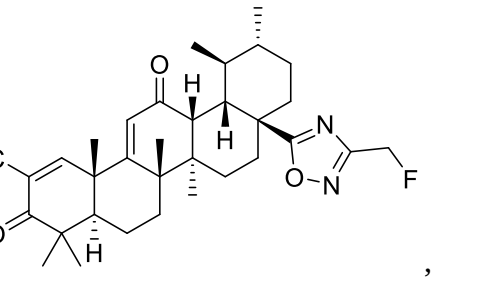
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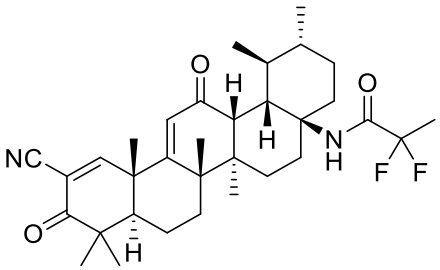
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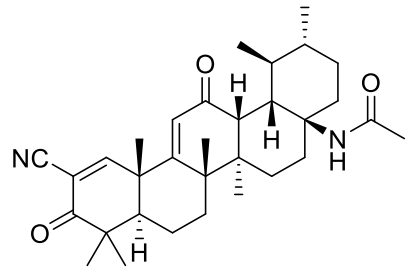
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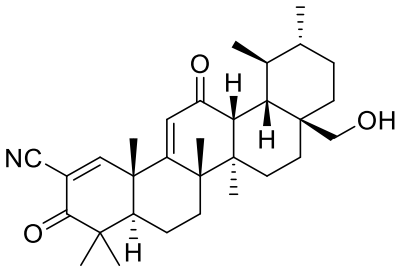
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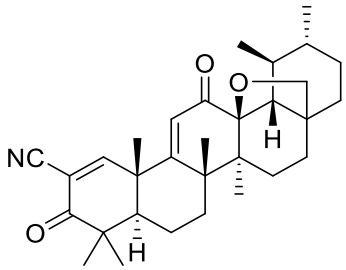
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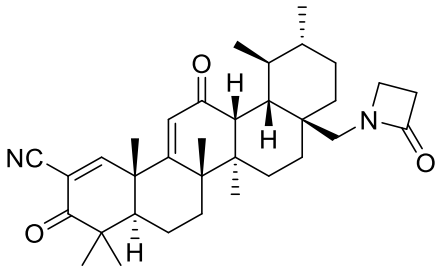
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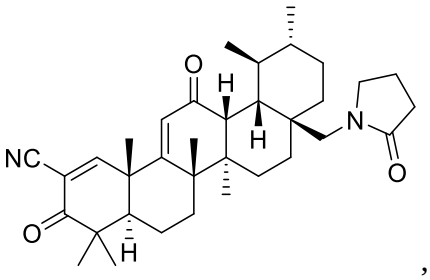
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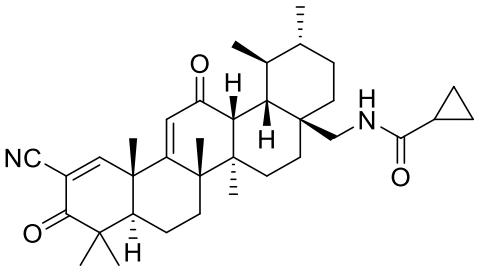
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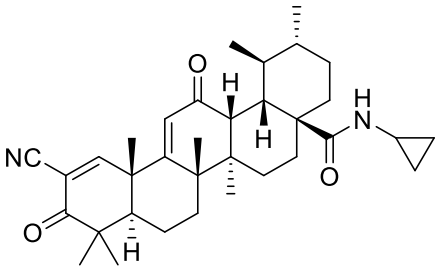
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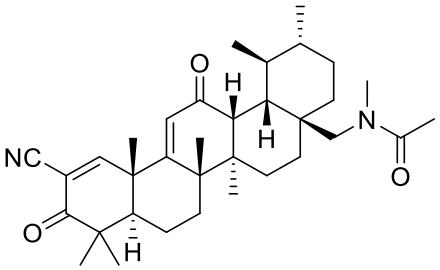
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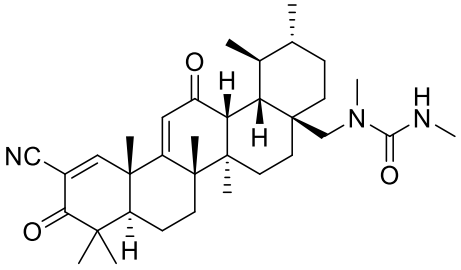
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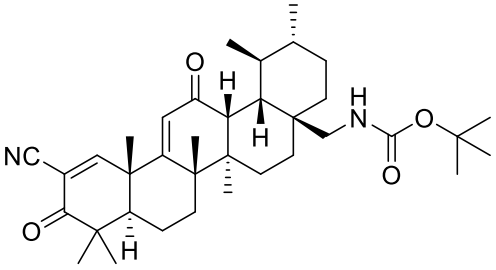
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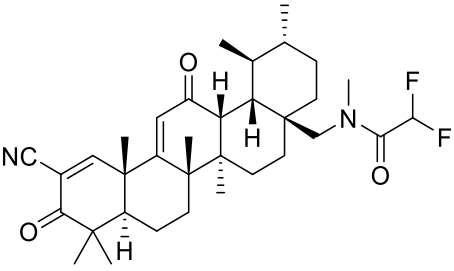
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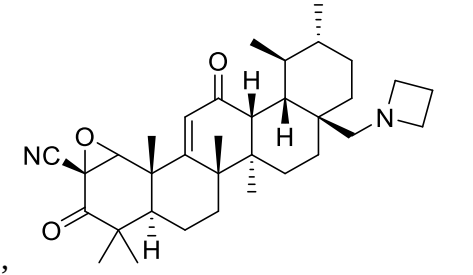
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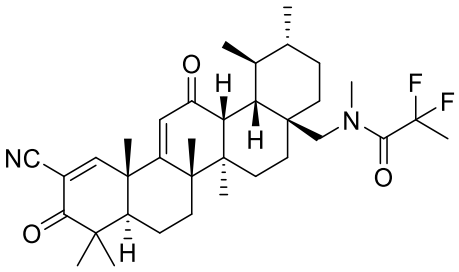
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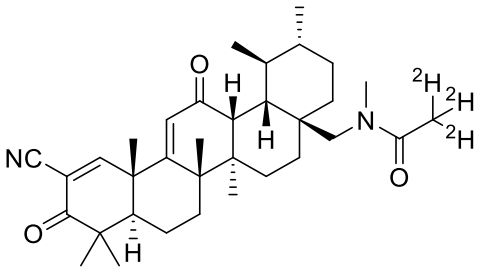
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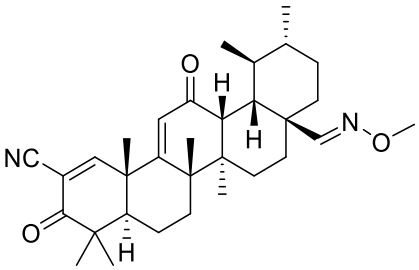
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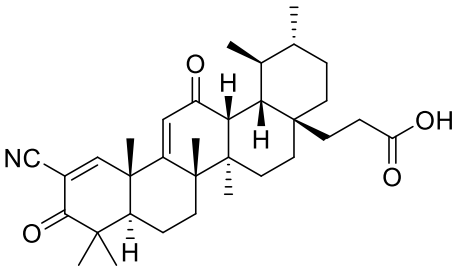
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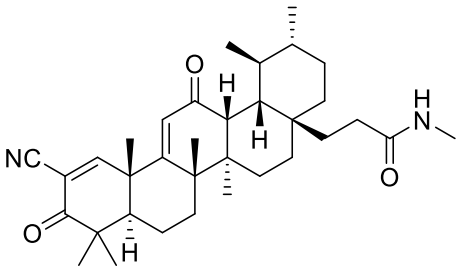
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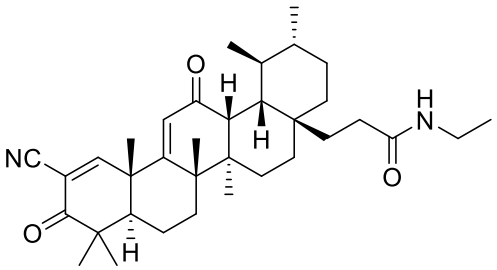
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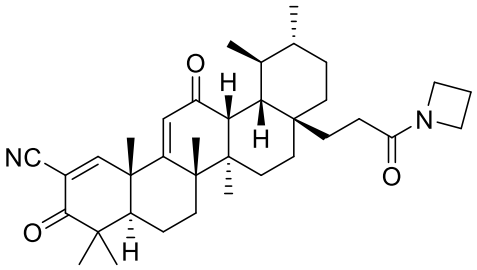
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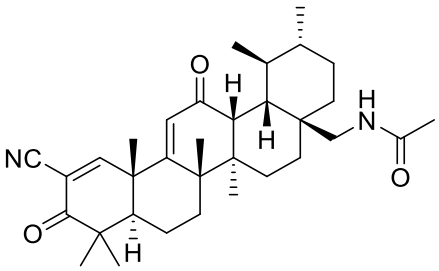
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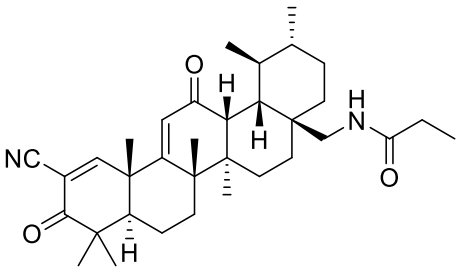
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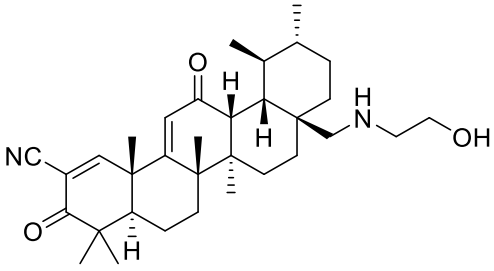
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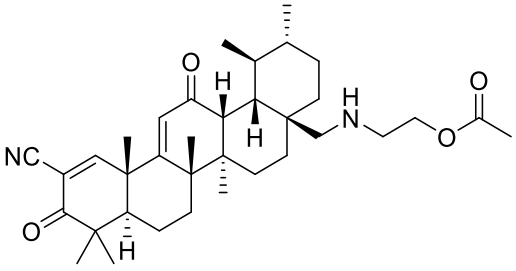
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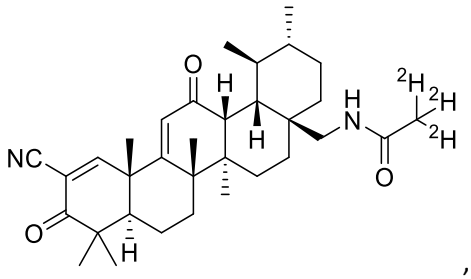
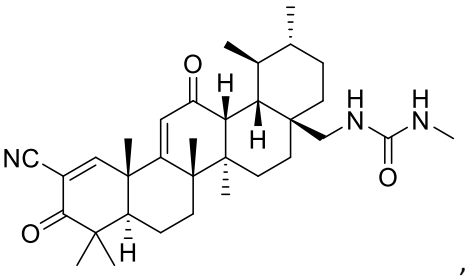
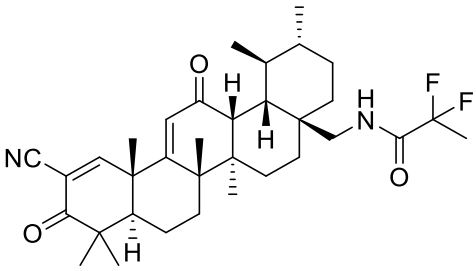
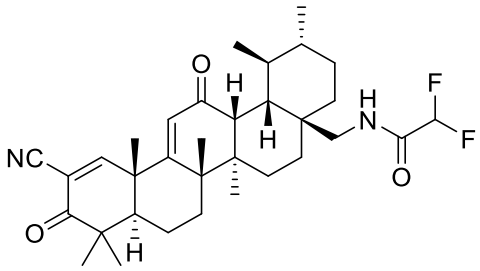
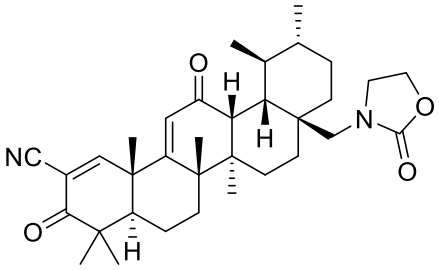
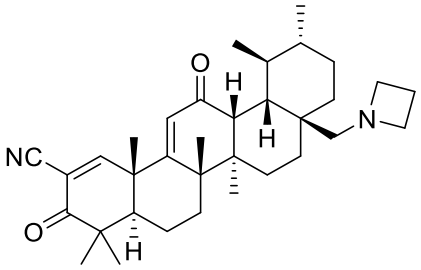
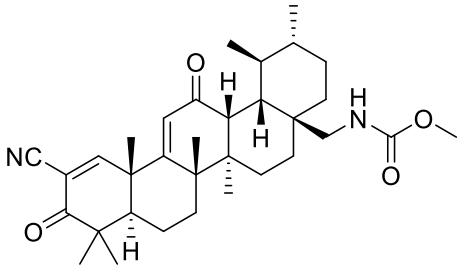
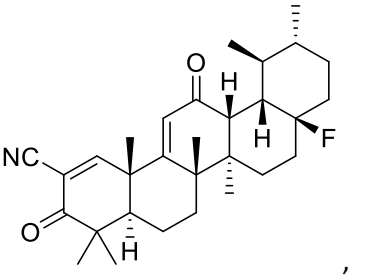
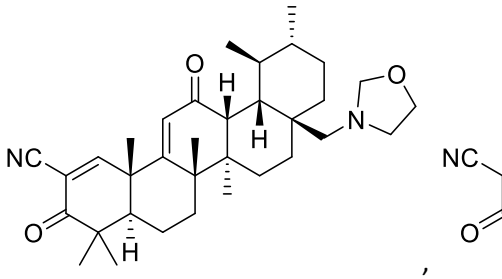
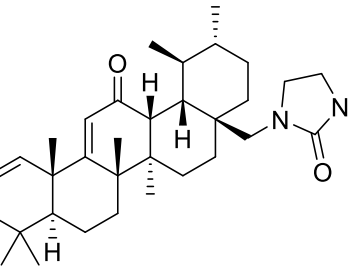
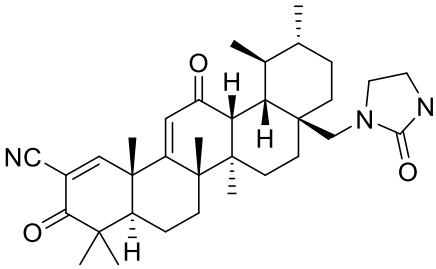
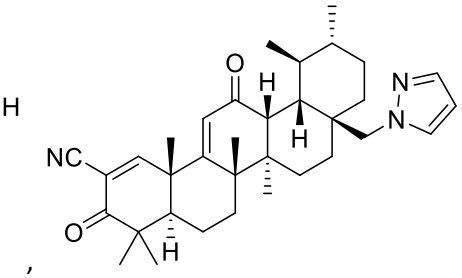

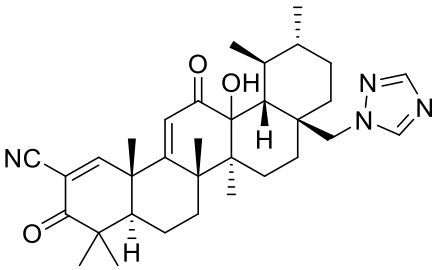
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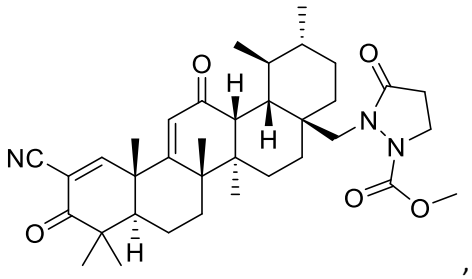
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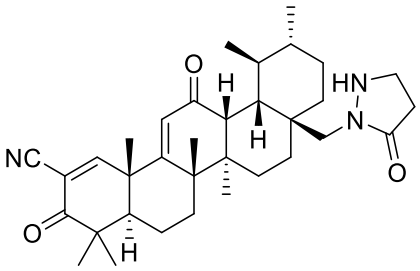
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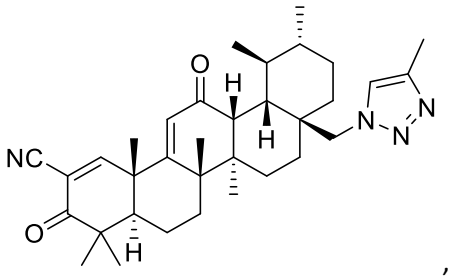
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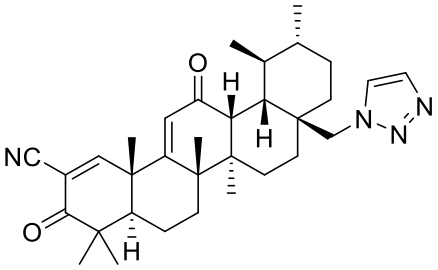
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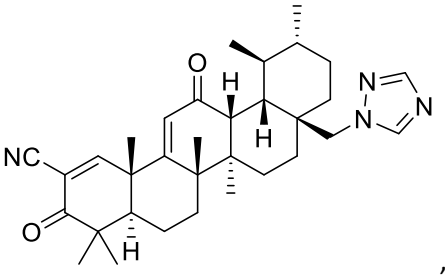
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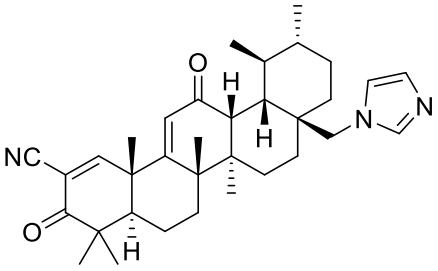
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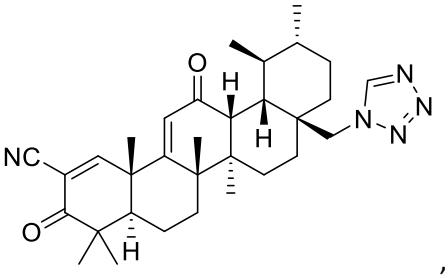
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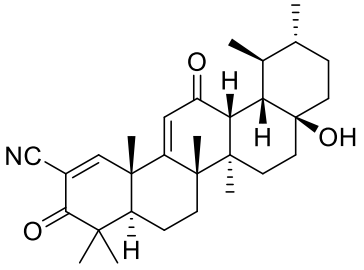
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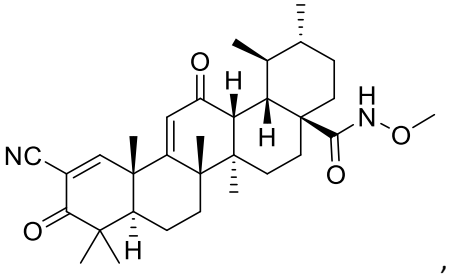
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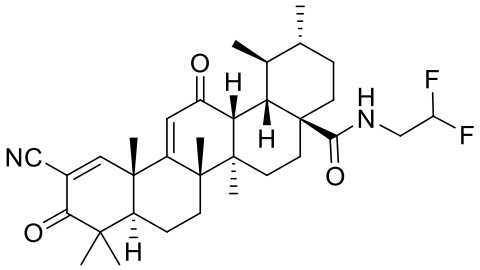
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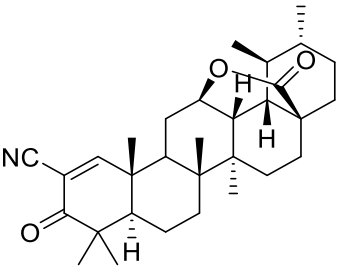
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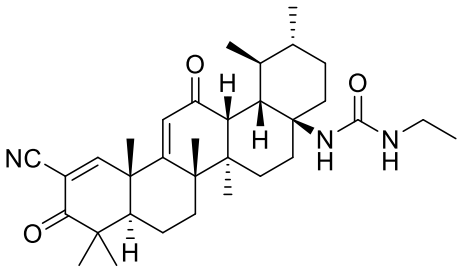
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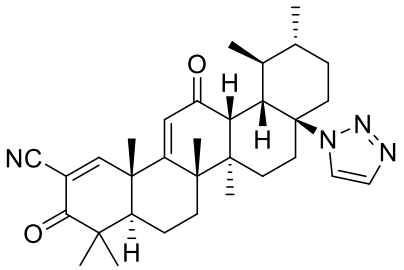
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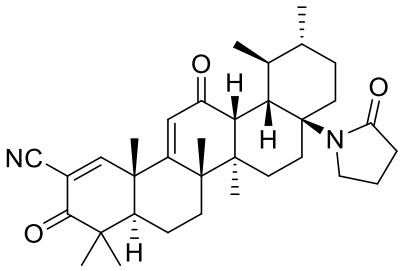
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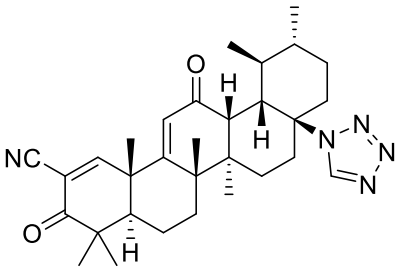
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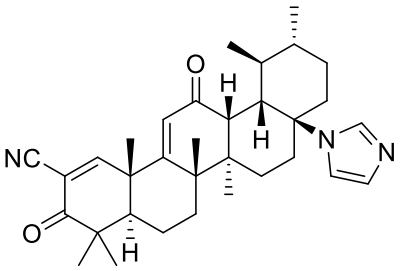
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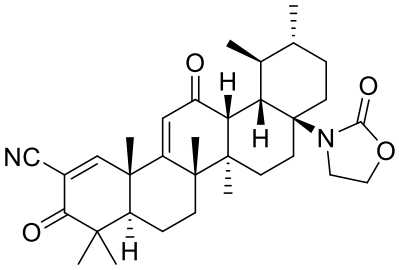
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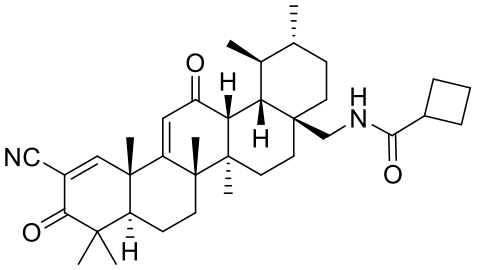
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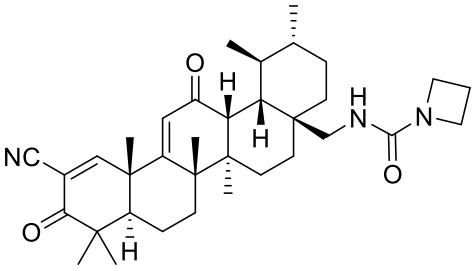
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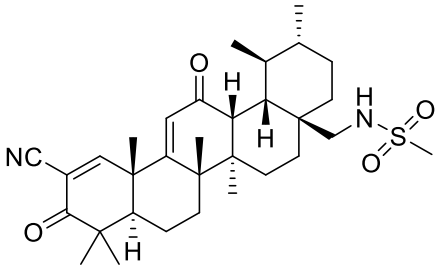
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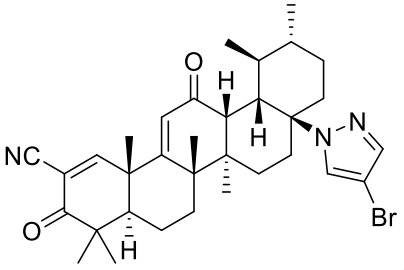
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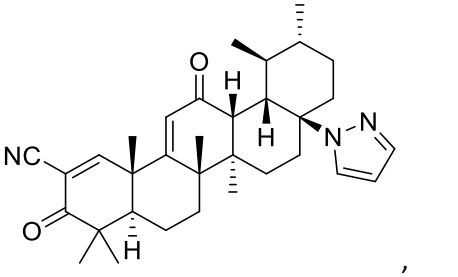
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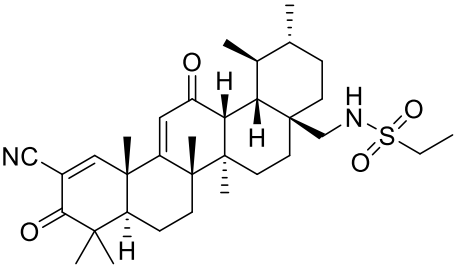
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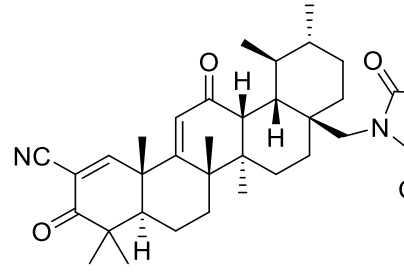
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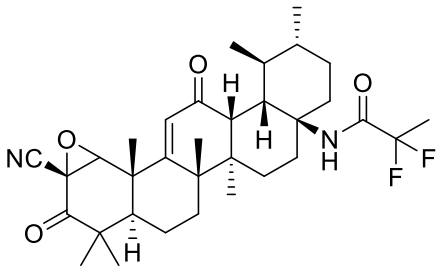
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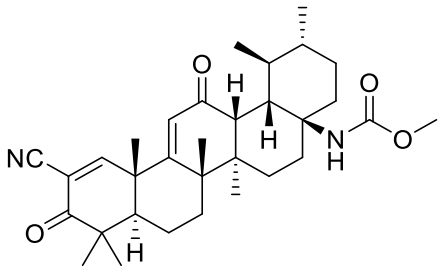
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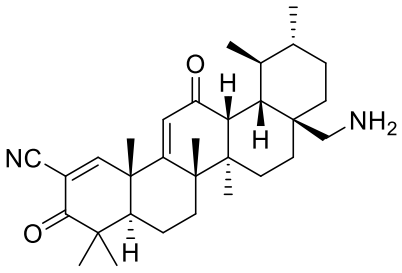
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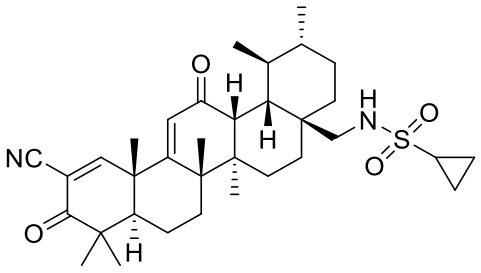
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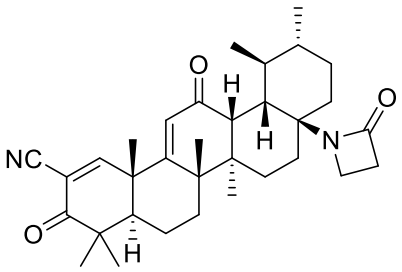
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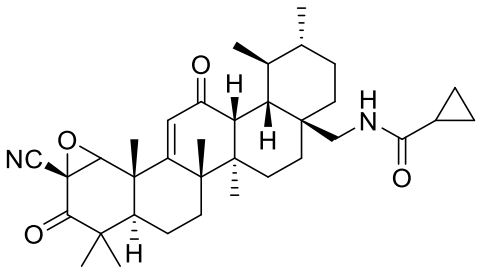
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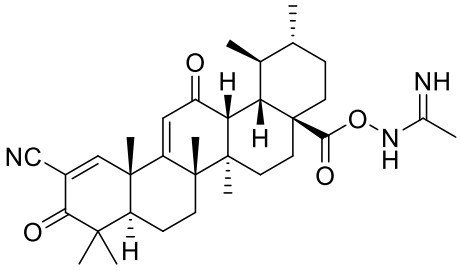
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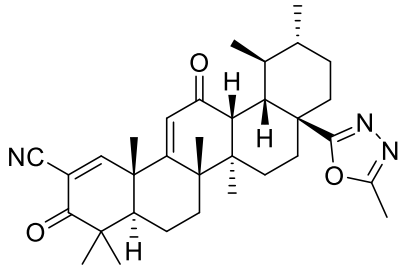
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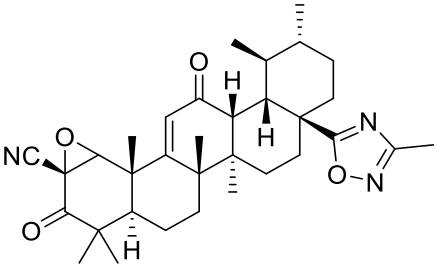
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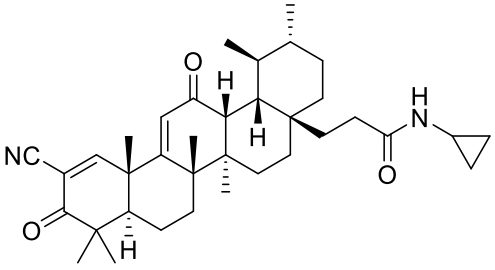
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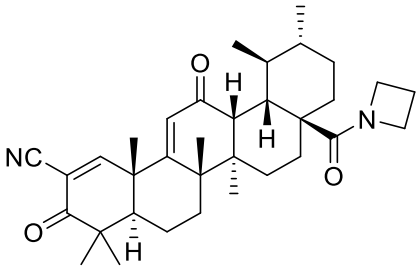
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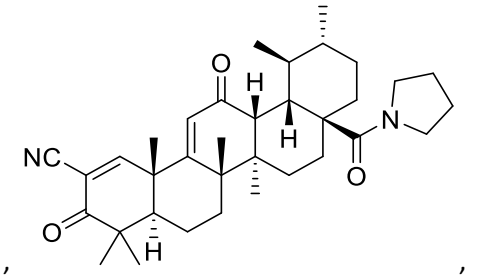
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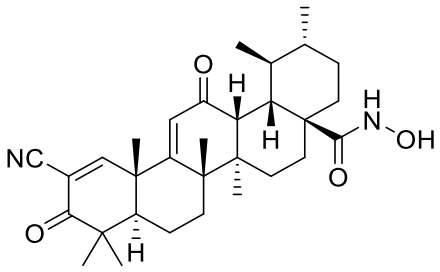
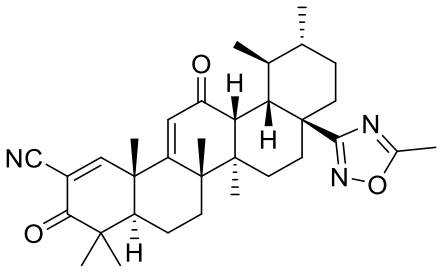
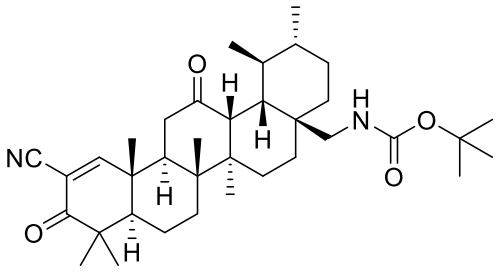
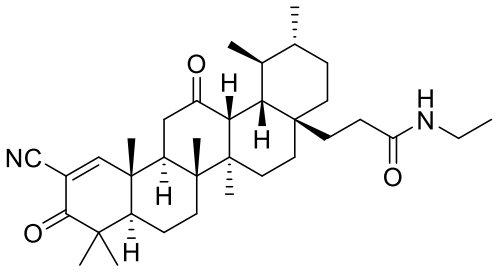
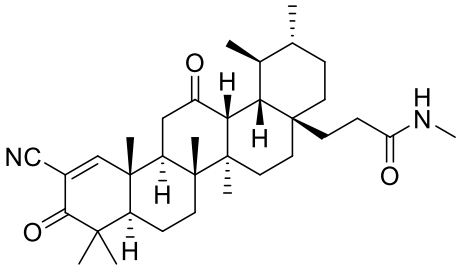
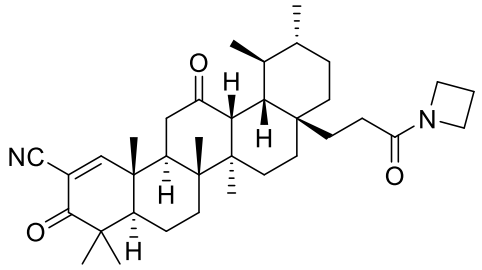
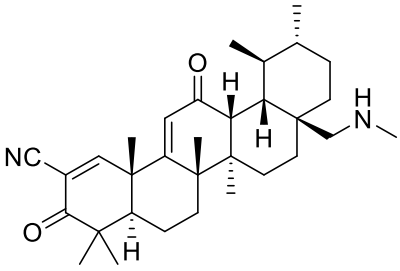
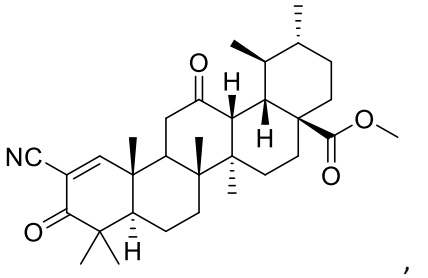
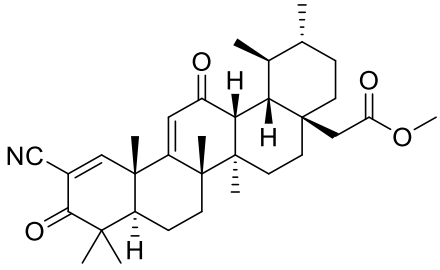
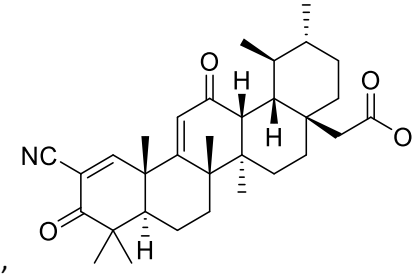
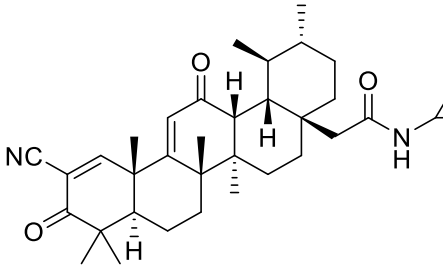
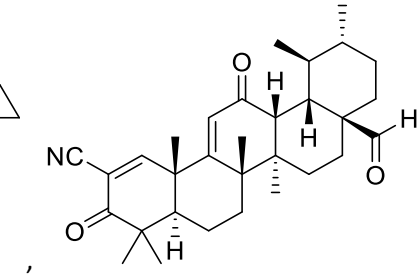

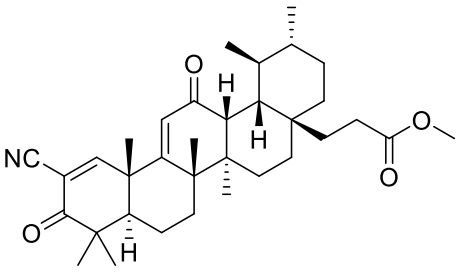

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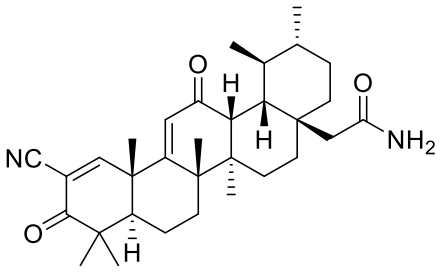

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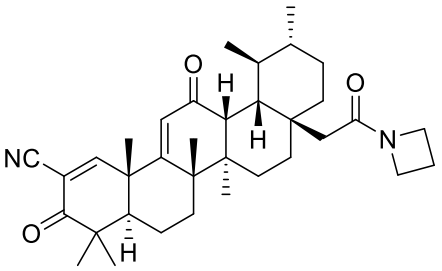

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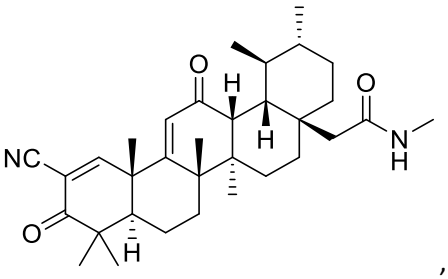

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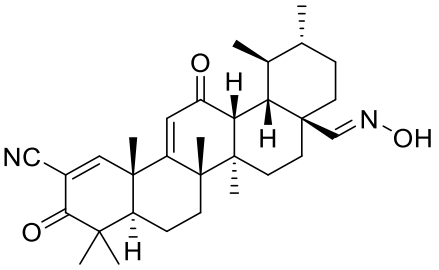

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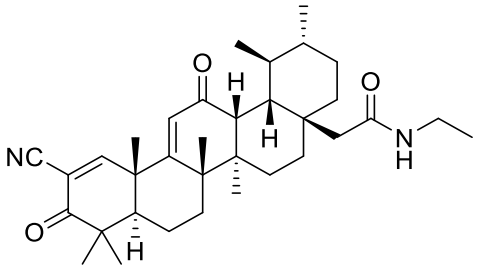

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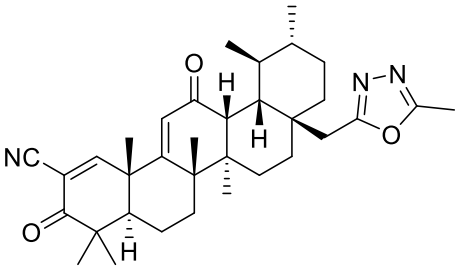

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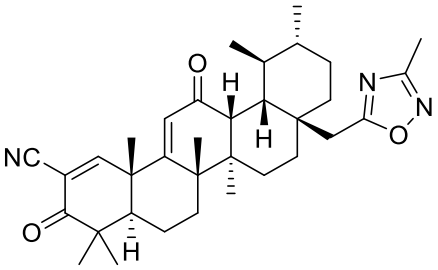

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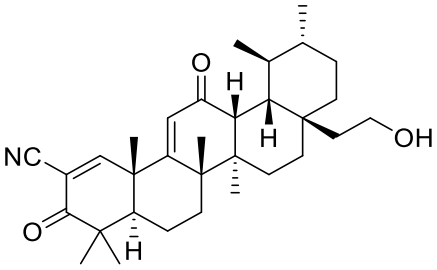
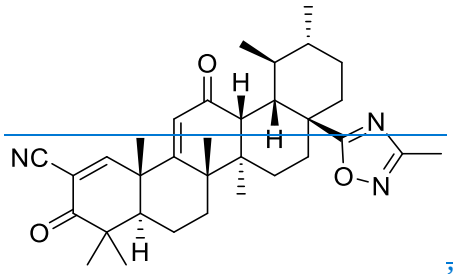


;
,

or a pharmaceutically acceptable salt thereof.

~~137. The compound of claim 136, wherein the compound is further defined as:~~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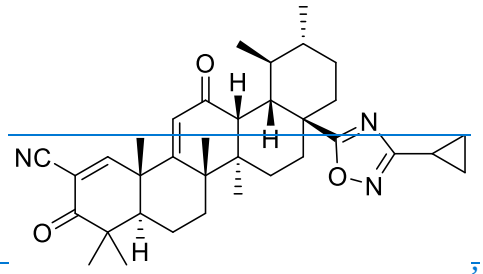
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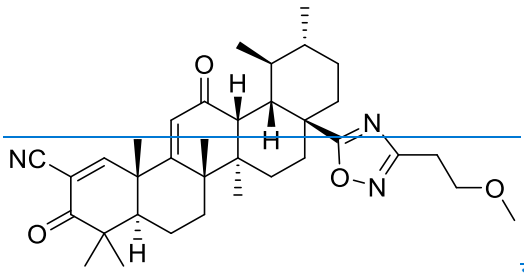
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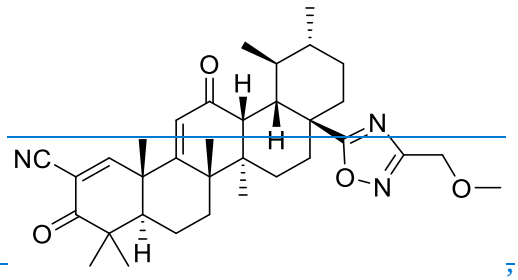
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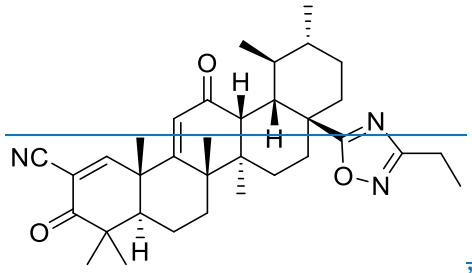
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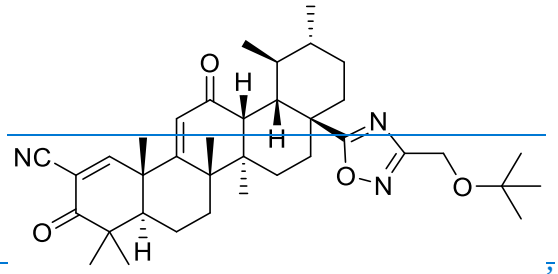
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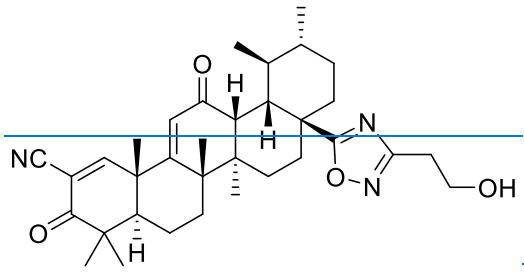
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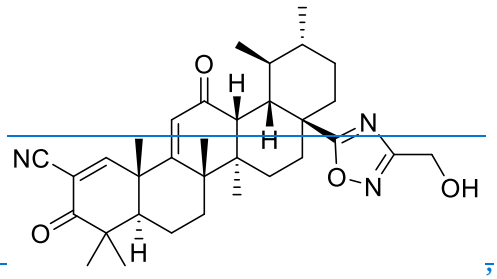
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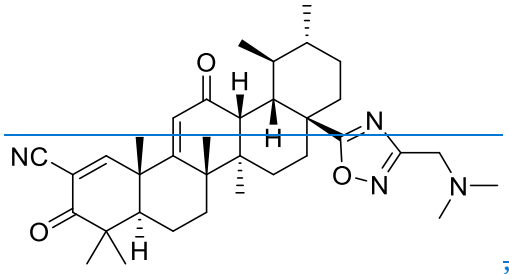
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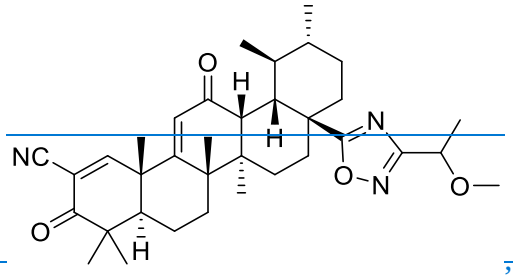
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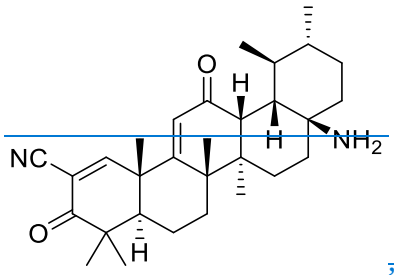
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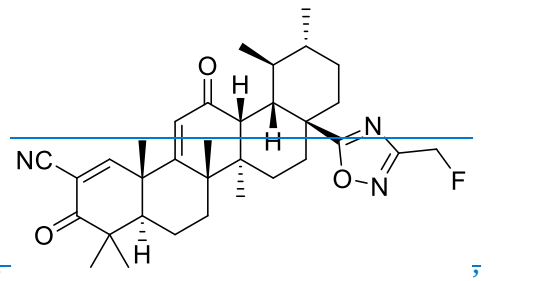
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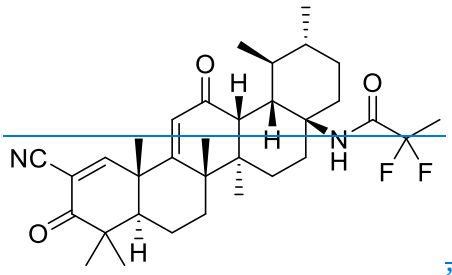

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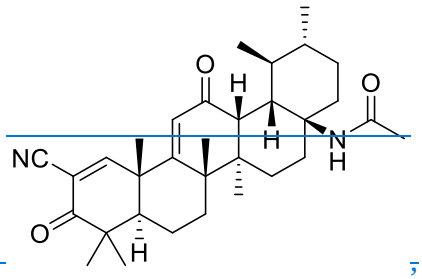

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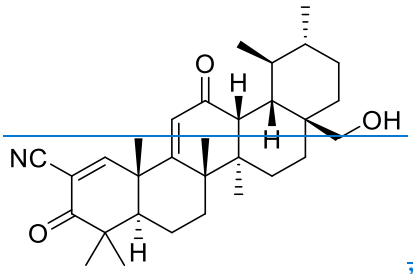

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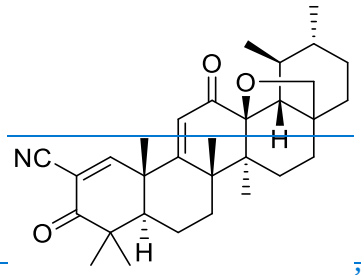

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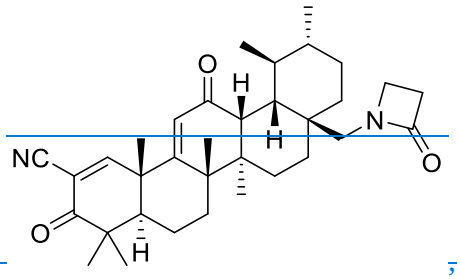

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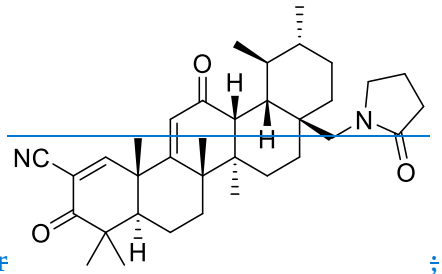
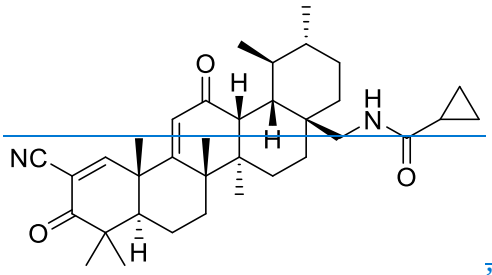


or ;

~~or a pharmaceutically acceptable salt thereof.~~

~~138. The compound of claim 136, wherein the compound is further defined as:~~



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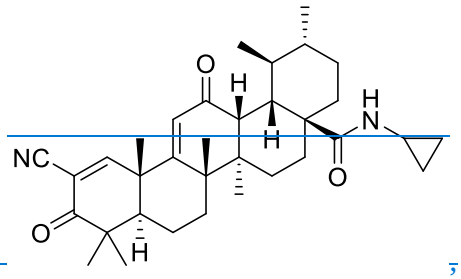

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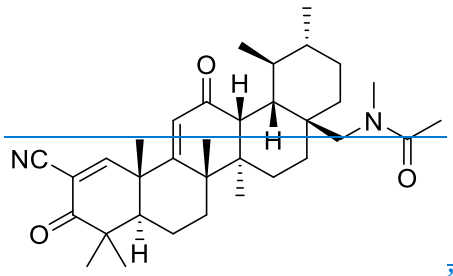

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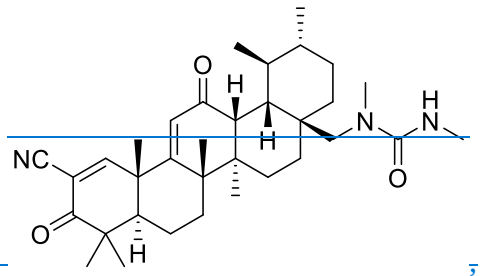

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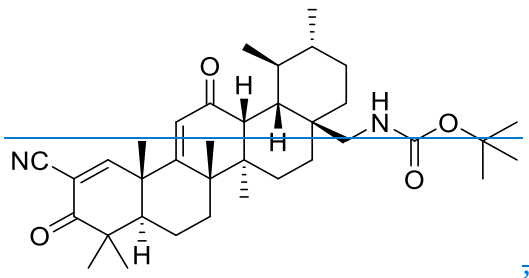

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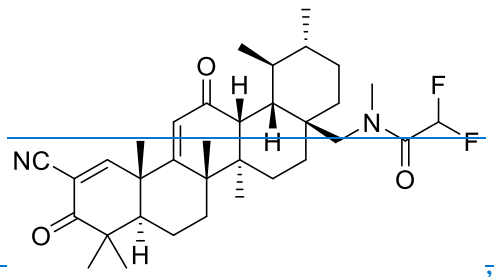

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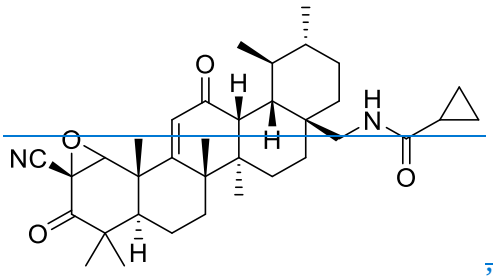

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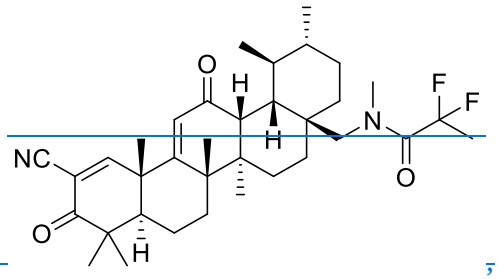

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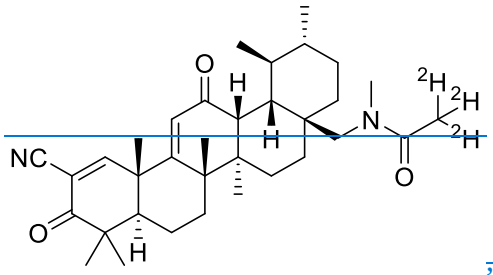
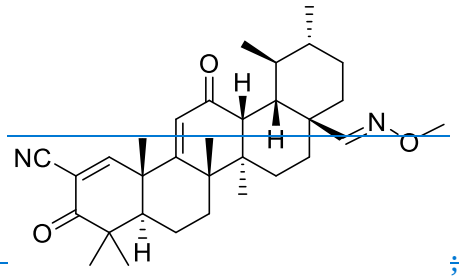


~~, or~~



~~;~~

~~or a pharmaceutically acceptable salt thereof.~~

~~139. The compound according to any one of claims 1-135, wherein the compound is further defined as:~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-(3-methyl-1,2,4-oxadiazol-5-yl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(2-methoxyethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(methoxymethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-ethyl-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(tert-butoxymethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(2-hydroxyethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(hydroxymethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-((dimethylamino)methyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(1-methoxyethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-amino-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(fluoromethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~N-((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-2,2-difluoropropanamide;~~

~~N-((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)acetamide;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(hydroxymethyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aR,6bS,11R,12S,12aR,12bS,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-4,4a,5,6,6a,6b,7,8,10,11,12,12a,13,14b-tetradecahydro-3H,9H-12b,8a-(epoxymethano)picene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((2-oxoazetidin-1-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile; or~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((2-oxopyrrolidin-1-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)cyclopropanecarboxamide;~~

~~(1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-N-cyclopropyl-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicene-4a(2H)-carboxamide;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-hydroxy-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-fluoro-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-N-methylacetamide;~~

1-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-1,3-dimethylurea;

tert-butyl (((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)carbamate;

N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)acetamide;

1-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-3-methylurea;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-((1H-imidazol-1-yl)methyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-((1H-tetrazol-1-yl)methyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-((1H-1,2,3-triazol-1-yl)methyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((2-oxooxazolidin-3-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-((1H-pyrazol-1-yl)methyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-((1H-1,2,4-triazol-1-yl)methyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-

~~3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-((3-methyl-2-oxoimidazolidin-1-yl)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(((2-hydroxyethyl)amino)methyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-(oxazolidin-3-ylmethyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-((4-methyl-1H-1,2,3-triazol-1-yl)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(azetidin-1-ylmethyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)acetamide-2,2,2-d3;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)propionamide;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((5-oxopyrazolidin-1-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-2,2-difluoropropanamide;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-2,2-difluoroacetamide;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((2-oxoimidazolidin-1-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-2,2-difluoro-N-methylacetamide;~~

~~2-((((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)amino)ethyl acetate;~~

~~(3aR,5aS,5bR,7aS,10R,11S,11aS,11bR,13bS)-7a-(azetidin-1-ylmethyl)-3,3,5a,5b,10,11,13b-heptamethyl-2,12-dioxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13b,13c-octadecahydropiceno[1,2-b]oxirene-1a(2H)-carbonitrile;~~

~~methyl (((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)carbamate;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-2,2-difluoro-N-methylpropanamide;~~

~~N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-N-methylacetamide-d3;~~

~~(4aR,6aR,6bS,8aS,11R,12S,12aR,14bS)-8a-((1H-1,2,4-triazol-1-yl)methyl)-12b-hydroxy-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~methyl 2-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)-3-oxopyrazolidine-1-carboxylate;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-((E)-(methoxyimino)methyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-N-methoxy-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicene-4a(2H)-carboxamide;~~

~~(1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-N-(2,2-difluoroethyl)-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicene-4a(2H)-carboxamide;~~

~~(4aR,6aR,6bR,8aS,11R,12S,12aS,12bR,13R,14bR)-4,4,6a,6b,11,12,14b-heptamethyl-3,16-dioxo-4,4a,5,6,6a,6b,7,8,9,10,11,12,12a,12b,13,14,14a,14b-octadecahydro-3H-13,8a-(epoxymethano)picene-2-carbonitrile;~~

~~1-((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-3-ethylurea;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-(1H-1,2,3-triazol-1-yl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-(2-oxopyrrolidin-1-yl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-(1H-tetrazol-1-yl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(1H-imidazol-1-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-(2-oxooxazolidin-3-yl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)cyclobutanecarboxamide;

N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)azetidine-1-carboxamide;

N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)methanesulfonamide;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(4-bromo-1H-pyrazol-1-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-(1H-pyrazol-1-yl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)ethanesulfonamide;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-((2,5-dioxopyrrolidin-1-yl)methyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

N-((1aR,3aR,5aS,5bR,7aS,10R,11S,11aS,11bR,13bS)-1a-cyano-3,3,5a,5b,10,11,13b-heptamethyl-2,12-dioxo-1a,3,3a,4,5,5a,5b,6,7,8,9,10,11,11a,11b,12,13b,13c-octadecahydropiceno[1,2-b]oxiren-7a(2H)-yl)-2,2-difluoropropanamide;

methyl ((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)carbamate;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(aminomethyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)methyl)cyclopropanesulfonamide;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-(2-oxoazetidin-1-yl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

N-(((1aR,3aR,5aS,5bR,7aS,10R,11S,11aS,11bR,13bS)-1a-cyano-3,3,5a,5b,10,11,13b-heptamethyl-2,12-dioxo-1a,3,3a,4,5,5a,5b,6,7,8,9,10,11,11a,11b,12,13b,13c-octadecahydropiceno[1,2-b]oxiren-7a(2H)-yl)methyl)cyclopropanecarboxamide;

N-(((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-octadecahydropicene-4a-carbonyl)oxy)acetimidamide;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-(5-methyl-1,3,4-oxadiazol-2-yl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)propanoic acid;

3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-N-methylpropanamide;

3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-N-ethylpropanamide;

(4aR,6aS,6bR,8aR,11R,12S,12aS,12bR,14bS)-8a-(3-(azetidine-1-yl)-3-oxopropyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-

~~3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(1aR,3aR,5aS,5bR,7aS,10R,11S,11aS,11bR,13bS)-3,3,5a,5b,10,11,13b-heptamethyl-7a-(3-methyl-1,2,4-oxadiazol-5-yl)-2,12-dioxo-3,3a,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13b,13c-octadecahydropiceno[1,2-b]oxirene-1a(2H)-carbonitrile;~~

~~3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-N-cyclopropylpropanamide;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(azetidine-1-carbonyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-(pyrrolidine-1-carbonyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-N-hydroxy-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicene-4a(2H)-carboxamide;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-(5-methyl-1,2,4-oxadiazol-3-yl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~tert-butyl (((1S,2R,4aS,6aR,6bR,8aR,12aR,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-octadecahydropicen-4a(2H)-yl)methyl)carbamate;~~

~~3-((1S,2R,4aR,6aR,6bR,8aR,12aR,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-octadecahydropicen-4a(2H)-yl)-N-ethylpropanamide;~~

~~3-((1S,2R,4aR,6aR,6bR,8aR,12aR,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-~~

~~1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-octadecahydropicen-4a(2H)-yl)-N-methylpropanamide;~~

~~(4aR,6aR,6bR,8aR,11R,12S,12aS,12bR,14bR)-8a-(3-(azetidine-1-yl)-3-oxopropyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-((methylamino)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~methyl (1S,2R,4aS,6aR,6bR,8aR,12aR,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-octadecahydropicene-4a(2H)-carboxylate;~~

~~methyl 2-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)acetate;~~

~~2-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)acetic acid;~~

~~2-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-N-cyclopropylacetamide;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-formyl-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~methyl 3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)propanoate;~~

~~2-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)acetamide;~~

(4aR,6aS,6bR,8aR,11R,12S,12aS,12bR,14bS)-8a-(2-(azetidine-1-yl)-2-oxoethyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

2-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-N-methylacetamide;

methyl 3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)propanoate;

3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)propanoic acid;

3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-N-methylpropanamide;

3-((1S,2R,4aR,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-N-ethylpropanamide; or

(4aR,6aS,6bR,8aR,11R,12S,12aS,12bR,14bS)-8a-(3-(azetidin-1-yl)-3-oxopropyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

or a pharmaceutically acceptable salt thereof.

140. The compound of claim 103, wherein the compound is further defined as:

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-8a-(3-methyl-1,2,4-oxadiazol-5-yl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(2-methoxyethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(methoxymethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-ethyl-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(tert-butoxymethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(2-hydroxyethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(hydroxymethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-((dimethylamino)methyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(1-methoxyethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-amino-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-~~

~~3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(3-(fluoromethyl)-1,2,4-oxadiazol-5-yl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~N-((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)-2,2-difluoropropanamide;~~

~~N-((1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-1,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicen-4a(2H)-yl)acetamide;~~

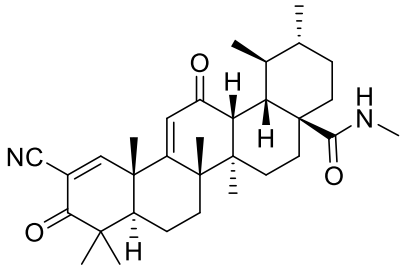
~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-8a-(hydroxymethyl)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((2-oxoazetidin-1-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile; or~~

~~(4aR,6aS,6bR,8aS,11R,12S,12aS,12bR,14bS)-4,4,6a,6b,11,12,14b-heptamethyl-3,13-dioxo-8a-((2-oxopyrrolidin-1-yl)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carbonitrile;~~

~~or a pharmaceutically acceptable salt thereof.~~

~~141~~72. A compound of the formula:



;

or a pharmaceutically acceptable salt thereof.

~~142. The compound of claim 141, wherein the compound is further defined as:~~

~~(1S,2R,4aS,6aR,6bS,8aR,12aS,14aR,14bS)-11-cyano-N,1,2,6a,6b,9,9,12a-octamethyl-10,14-dioxo-1,3,4,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-hexadecahydropicene-4a(2H)-carboxamide~~

~~or a pharmaceutically acceptable salt thereof.~~

~~143~~73. A pharmaceutical composition comprising:

(A) a compound according to any one of claims 1-~~142~~72; and

(B) an excipient.

~~144. The pharmaceutical composition of claim 143, wherein the pharmaceutical composition is formulated for administration orally, intraadiposally, intraarterially, intraarticularly, intracranially, intradermally, intralesionally, intramuscularly, intranasally, intraocularly, intrapericardially, intraperitoneally, intrapleurally, intraprostatically, intrarectally, intrathecally, intratracheally, intratumorally, intraumbilically, intravaginally, intravenously, intravesicularlly, intravitreally, liposomally, locally, mucosally, parenterally, rectally, subconjunctival, subcutaneously, sublingually, topically, transbuccally, transdermally, vaginally, in crèmes, in lipid compositions, via a catheter, via a lavage, via continuous infusion, via infusion, via inhalation, via injection, via local delivery, or via localized perfusion.~~

~~145. The pharmaceutical composition of claim 144, wherein the pharmaceutical composition is formulated for oral administration.~~

~~146. The pharmaceutical composition of claim 144, wherein the pharmaceutical composition is formulated for administration via injection.~~

~~147. The pharmaceutical composition of claim 146, wherein the pharmaceutical composition is formulated for intraarterial administration, intramuscular administration, intraperitoneal administration, or intravenous administration.~~

~~148. The pharmaceutical composition of claim 144, wherein the pharmaceutical composition is formulated for administration topically.~~

~~149. The pharmaceutical composition of claim 148, wherein the pharmaceutical composition is formulated for topical administration to the skin or to the eye.~~

~~150. The pharmaceutical composition according to any one of claims 143-149, wherein the pharmaceutical composition is formulated as a unit dose.~~

~~15174~~. ~~A method of treating or preventing a disease or disorder in a patient in need thereof comprising administering to the patient a pharmaceutically effective amount of a~~The compound or pharmaceutical composition according to any one of claims 1-~~150~~73 for use in treatment or prevention of a disease or disorder in a patient.

~~152. The method of claim 151, wherein the patient is a mammal.~~

~~153. The method of claim 152, wherein the patient is a human.~~

75. Use of a compound or pharmaceutical composition according to any one of claims 1-73 in the manufacture of a medicament for the treatment or prevention of a disease or disorder in a patient.

~~154~~76. The ~~method~~use of claim ~~151~~75, wherein the disease or disorder is a condition associated with inflammation and/or oxidative stress.

~~155. The method of claim 151, wherein the disease or disorder is cancer.~~

~~156. The method of claim 151, wherein the disease or disorder is a cardiovascular disease.~~

~~157. The method of claim 156, wherein the cardiovascular disease is atherosclerosis.~~

~~158. The method of claim 151, wherein the disease or disorder is an autoimmune disease.~~

~~159. The method of claim 158, wherein the autoimmune disease is Crohn's disease, rheumatoid arthritis, lupus, or psoriasis.~~

~~160. The method of claim 151, wherein the disease or disorder is a neurodegenerative disease.~~

~~161. The method of claim 160, wherein the neurodegenerative disease is Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, or Huntington's disease.~~

~~162. The method of claim 151, wherein the disease or disorder is chronic kidney disease, diabetes, mucositis, inflammatory bowel disease, dermatitis, sepsis, ischemia reperfusion injury (including complications from sickle cell anemia), influenza, osteoarthritis, osteoporosis, pancreatitis, asthma, chronic obstructive pulmonary disease, cystic fibrosis, idiopathic pulmonary fibrosis, multiple sclerosis, muscular dystrophy, cachexia, or graft-versus-host disease.~~

~~163. The method of claim 151, wherein the disease or disorder is an eye disease.~~

~~164. The method of claim 163, wherein the eye disease is uveitis, glaucoma, macular degeneration, or retinopathy.~~

~~165. The method of claim 151, wherein the disease or disorder is neuropsychiatric.~~

~~166. The method of claim 165, wherein the neuropsychiatric disease or disorder is schizophrenia, depression, bipolar disorder, epilepsy, post-traumatic stress disorder, attention deficit disorder, autism, or anorexia nervosa.~~

~~167. The method of claim 151, wherein the disease or disorder is associated with mitochondrial dysfunction.~~

~~168. The method of claim 167, wherein the disease or disorder associated with mitochondrial dysfunction is Friedreich's ataxia.~~

~~169. The method of claim 151, wherein the disease or disorder is chronic pain.~~

~~170. The method of claim 151, wherein the disease or disorder is neuropathic pain.~~

~~171~~77. Use of ~~T~~the compound or pharmaceutical composition according to any one of claims 1-73 in the manufacture of a medicament for the ~~use in A method of inhibiting~~inhibition of nitric oxide production ~~comprising administering to a patient in need thereof an amount of a compound or composition of claims 1-170 sufficient to cause inhibition of IFN-γ induced nitric oxide production~~ in one or more cells of ~~the~~ a patient.