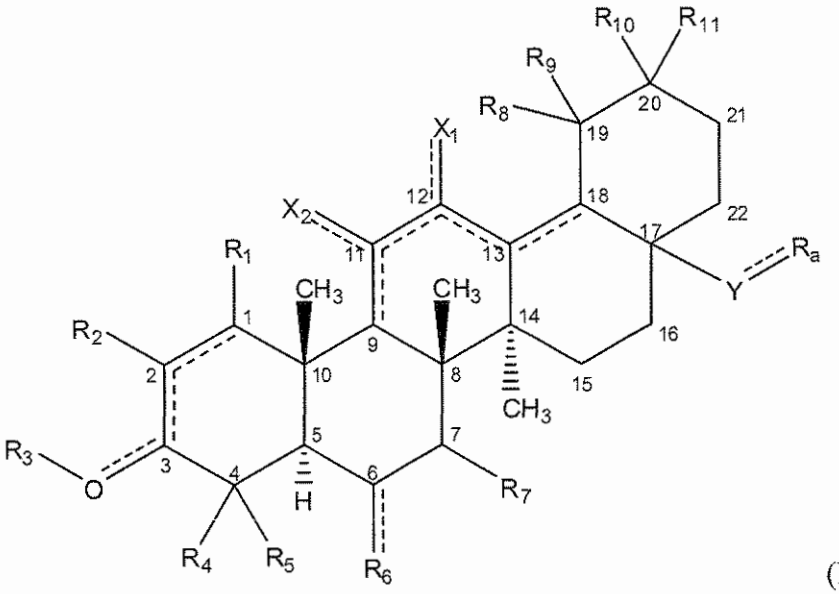
SUMMARY OF THE INVENTION

The present invention refers to subject matter as defined in the attached set of claims.

In one ~~aspect~~example, the present disclosure ~~provides~~discloses new compounds with antioxidant and anti-inflammatory properties, methods for their manufacture, and methods for their use. Compounds covered by the generic or specific formulas below or specifically named may be referred to herein as "compounds of the invention," "compounds of the present disclosure," or "oleanolic acid derivatives."

In one ~~aspect~~example, the present disclosure ~~provides~~discloses compounds of the formula:



(I)

wherein:

Y is alkanediyl$_{(C\leq 8)}$, alkenediyl$_{(C\leq 8)}$, alkynediyl$_{(C\leq 8)}$, or a substituted version of any of these groups;

R_a is:

hydrogen, hydroxy, halo, amino, nitro, cyano, azido, phosphate, 1,3-dioxoisoindolin-2-yl, mercapto or silyl; or

alkyl$_{(C\leq 12)}$, alkenyl$_{(C\leq 12)}$, alkynyl$_{(C\leq 12)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 12)}$, heteroaralkyl$_{(C\leq 12)}$, acyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 12)}$, alkenyloxy$_{(C\leq 12)}$, alkynyloxy$_{(C\leq 12)}$, aryloxy$_{(C\leq 12)}$, aralkoxy$_{(C\leq 12)}$, heteroaryloxy$_{(C\leq 12)}$, heteroaralkoxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 12)}$, alkylamino$_{(C\leq 12)}$, dialkylamino$_{(C\leq 12)}$, alkenylamino$_{(C\leq 12)}$, alkynylamino$_{(C\leq 12)}$, arylamino$_{(C\leq 12)}$, aralkylamino$_{(C\leq 12)}$, heteroarylamino$_{(C\leq 12)}$, heteroaralkylamino$_{(C\leq 12)}$, alkylsulfonylamino$_{(C\leq 12)}$, amido$_{(C\leq 12)}$, alkylthio$_{(C\leq 12)}$, alkenylthio$_{(C\leq 12)}$, alkynylthio$_{(C\leq 12)}$, arylthio$_{(C\leq 12)}$, aralkylthio$_{(C\leq 12)}$, heteroarylthio$_{(C\leq 12)}$, heteroaralkylthio$_{(C\leq 12)}$, acylthio$_{(C\leq 12)}$, thioacyl$_{(C\leq 12)}$, alkylsulfonyl$_{(C\leq 12)}$,

R_3 is:

absent or hydrogen;

$alkyl_{(C\leq 8)}$, $aryl_{(C\leq 8)}$, $aralkyl_{(C\leq 8)}$, $acyl_{(C\leq 8)}$, or a substituted version of any of these groups; or

a substituent convertible *in vivo* to hydrogen;

provided that R_3 is absent when the oxygen atom to which it is bound is part of a double bond, further provided that when R_3 is absent the oxygen atom to which it is bound is part of a double bond;

R_4 and R_5 are each independently $alkyl_{(C\leq 8)}$ or substituted $alkyl_{(C\leq 8)}$;

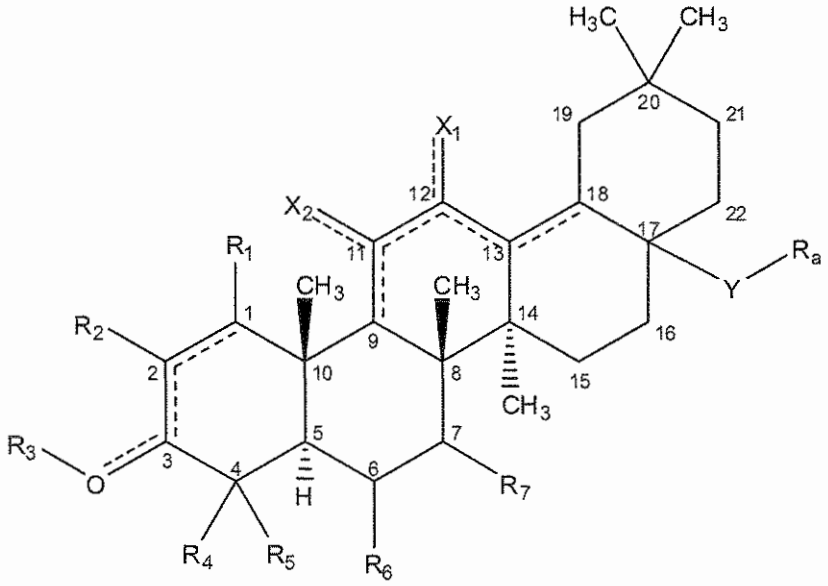
R_6 is hydrogen, hydroxy or oxo; and

R_7 is hydrogen or hydroxy;

R_8, R_9, R_{10} and R_{11} are each independently hydrogen, hydroxy, $alkyl_{(C\leq 8)}$, substituted $alkyl_{(C\leq 8)}$, $alkoxy_{(C\leq 8)}$ or substituted $alkoxy_{(C\leq 8)}$;

or pharmaceutically acceptable salts, esters, hydrates, solvates, tautomers, prodrugs, or optical isomers thereof.

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

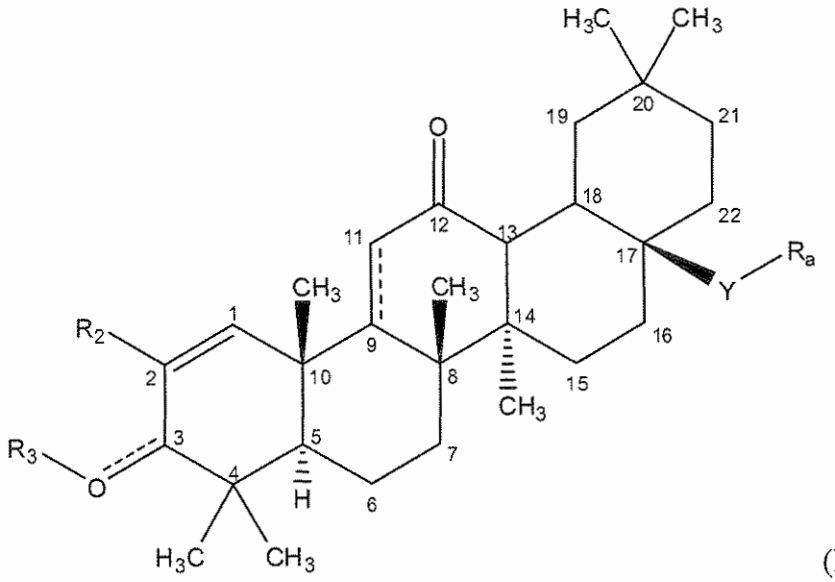


(II)

wherein:

Y is $alkanediyl_{(C\leq 8)}$, $alkenediyl_{(C\leq 8)}$, $alkynediyl_{(C\leq 8)}$, or a substituted version of any of these groups;

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



(III)

wherein:

Y is alkanediyl$_{(C\leq5)}$ or substituted alkanediyl$_{(C\leq5)}$;

R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, or cyano; or

alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, acyl$_{(C\leq12)}$, alkoxy$_{(C\leq12)}$, alkenyloxy$_{(C\leq12)}$, alkynyloxy$_{(C\leq12)}$, aryloxy$_{(C\leq12)}$, aralkoxy$_{(C\leq12)}$, heteroaryloxy$_{(C\leq12)}$, heteroaralkoxy$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, alkenylamino$_{(C\leq12)}$, alkynylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, alkylsulfonylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, arylsulfonyl$_{(C\leq12)}$, arylsulfinyl$_{(C\leq12)}$, alkylphosphate$_{(C\leq12)}$, dialkylphosphate$_{(C\leq12)}$, or a substituted version of any of these groups; or

Y and R_a form a three to five-membered ring, such that Y and R_a are further connected to one another through one or more of –O– and alkanediyl$_{(C1\text{-}3)}$, further wherein Y is –CH– and R_a is $-CH_2-$;

R_2 is:

cyano, hydroxy, halo or amino; or

fluoroalkyl$_{(C\leq8)}$, alkenyl$_{(C\leq8)}$, alkynyl$_{(C\leq8)}$, aryl$_{(C\leq8)}$, heteroaryl$_{(C\leq8)}$, acyl$_{(C\leq8)}$, alkoxy$_{(C\leq8)}$, aryloxy$_{(C\leq8)}$, acyloxy$_{(C\leq8)}$, alkylamino$_{(C\leq8)}$, arylamino$_{(C\leq8)}$, amido$_{(C\leq8)}$, or a substituted version of any of these groups; and

R_3 is:

absent or hydrogen;

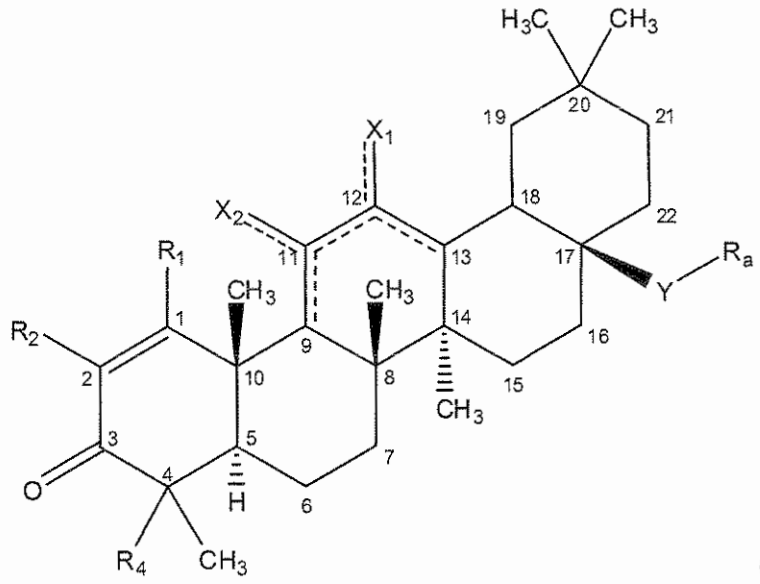
alkyl$_{(C\leq8)}$, aryl$_{(C\leq8)}$, aralkyl$_{(C\leq8)}$, acyl$_{(C\leq8)}$, or a substituted version of any of these groups; or

a substituent convertible *in vivo* to hydrogen;

provided that R_3 is absent when the oxygen atom to which it is bound is part of a double bond, further provided that when R_3 is absent the oxygen atom to which it is bound is part of a double bond;

or pharmaceutically acceptable salts, esters, hydrates, solvates, tautomers, prodrugs, or optical isomers thereof.

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



(IV)

wherein:

Y is alkanediyl$_{(C\leq8)}$, alkenediyl$_{(C\leq8)}$, alkynediyl$_{(C\leq8)}$, or a substituted version of any of these groups;

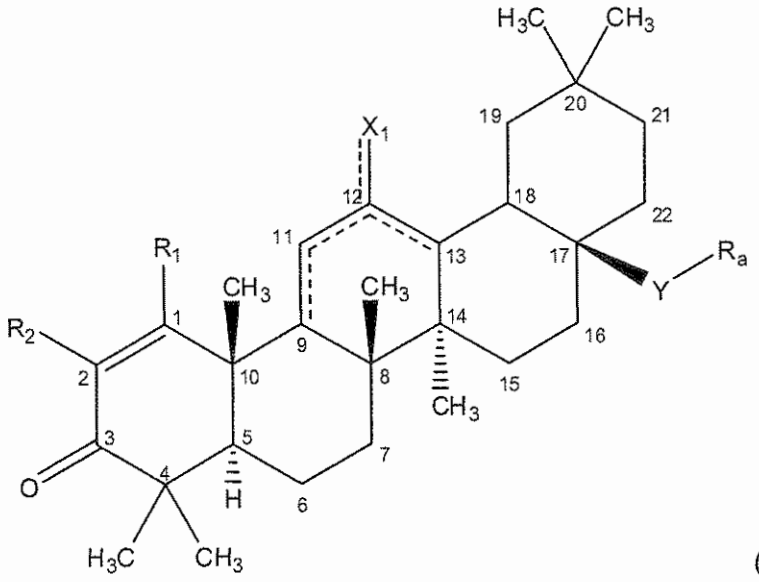
R_a is:

hydrogen, hydroxy, halo, amino, nitro, cyano, azido, phosphate, 1,3-dioxoisoindolin-2-yl, mercapto or silyl; or

alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, acyl$_{(C\leq12)}$, alkoxy$_{(C\leq12)}$, alkenyloxy$_{(C\leq12)}$,

or pharmaceutically acceptable salts, esters, hydrates, solvates, tautomers, prodrugs, or optical isomers thereof.

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



(V)

wherein:

Y is alkanediyl$_{(C\leq 8)}$, alkenediyl$_{(C\leq 8)}$, alkynediyl$_{(C\leq 8)}$, or a substituted version of any of these groups;

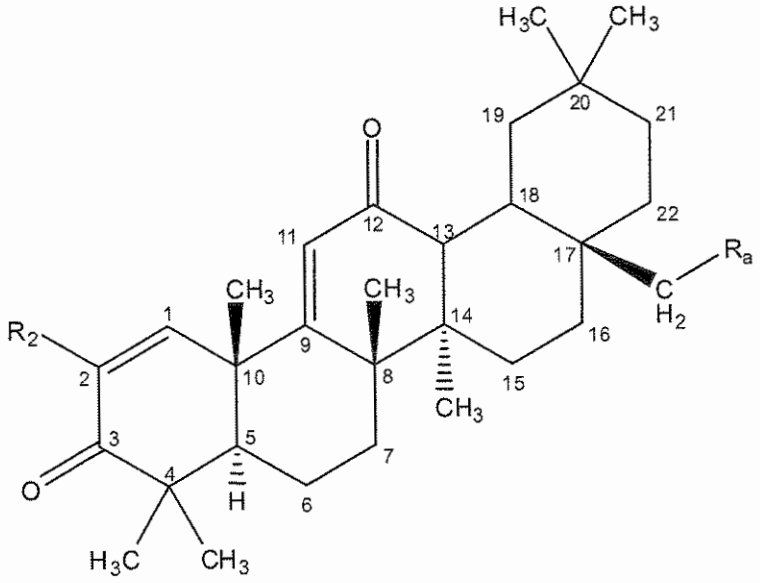
R_a is:

hydrogen, hydroxy, halo, amino, nitro, cyano, azido, phosphate, 1,3-dioxoisoindolin-2-yl, mercapto or silyl; or

alkyl$_{(C\leq 12)}$, alkenyl$_{(C\leq 12)}$, alkynyl$_{(C\leq 12)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 12)}$, heteroaralkyl$_{(C\leq 12)}$, acyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 12)}$, alkenyloxy$_{(C\leq 12)}$, alkynyloxy$_{(C\leq 12)}$, aryloxy$_{(C\leq 12)}$, aralkoxy$_{(C\leq 12)}$, heteroaryloxy$_{(C\leq 12)}$, heteroaralkoxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 12)}$, alkylamino$_{(C\leq 12)}$, dialkylamino$_{(C\leq 12)}$, alkenylamino$_{(C\leq 12)}$, alkynylamino$_{(C\leq 12)}$, arylamino$_{(C\leq 12)}$, aralkylamino$_{(C\leq 12)}$, heteroarylamino$_{(C\leq 12)}$, heteroaralkylamino$_{(C\leq 12)}$, amido$_{(C\leq 12)}$, arylsulfonyl$_{(C\leq 12)}$, arylsulfinyl$_{(C\leq 12)}$, alkylphosphate$_{(C\leq 12)}$, dialkylphosphate$_{(C\leq 12)}$, alkylphosphate$_{(C\leq 12)}$, dialkylphosphate$_{(C\leq 12)}$, or or a substituted version of any of these groups; or

Y and R_a form a three to five-membered ring, such that Y and R_a are further connected to one another through one or more of –O– and alkanediyl$_{(C1\text{-}3)}$, further wherein Y is –CH– and R_a is $–CH_2–$;

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



(VI)

wherein:

R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, or cyano; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $alkenyloxy_{(C\leq12)}$, $alkynyloxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$, $aralkoxy_{(C\leq12)}$, $heteroaryloxy_{(C\leq12)}$, $heteroaralkoxy_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $alkenylamino_{(C\leq12)}$, $alkynylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $arylsulfonyl_{(C\leq12)}$, $arylsulfinyl_{(C\leq12)}$, $alkylphosphate_{(C\leq12)}$, $dialkylphosphate_{(C\leq12)}$, or a substituted version of any of these groups; and

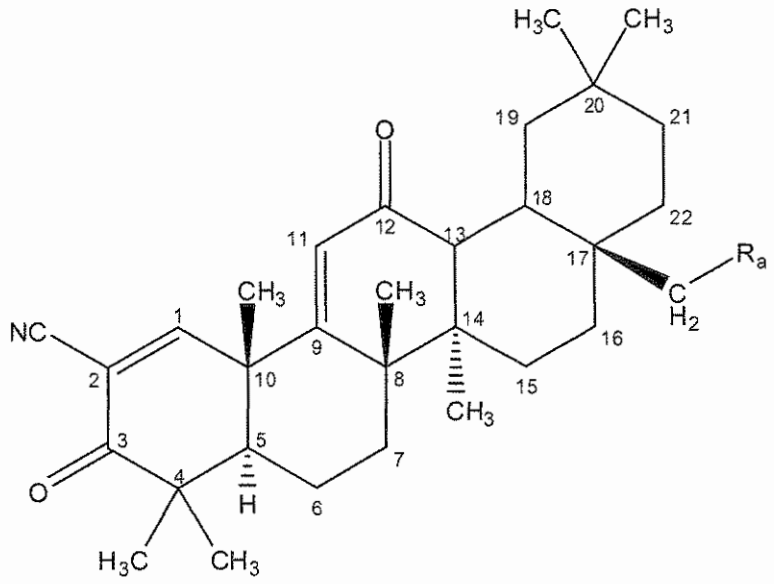
R_2 is:

cyano, hydroxy, halo or amino; or

$fluoroalkyl_{(C\leq8)}$, $alkenyl_{(C\leq8)}$, $alkynyl_{(C\leq8)}$, $aryl_{(C\leq8)}$, $heteroaryl_{(C\leq8)}$, $acyl_{(C\leq8)}$, $alkoxy_{(C\leq8)}$, $aryloxy_{(C\leq8)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$, $amido_{(C\leq8)}$, or a substituted version of any of these groups;

or pharmaceutically acceptable salts, esters, hydrates, solvates, tautomers, prodrugs, or optical isomers thereof.

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



(VII)

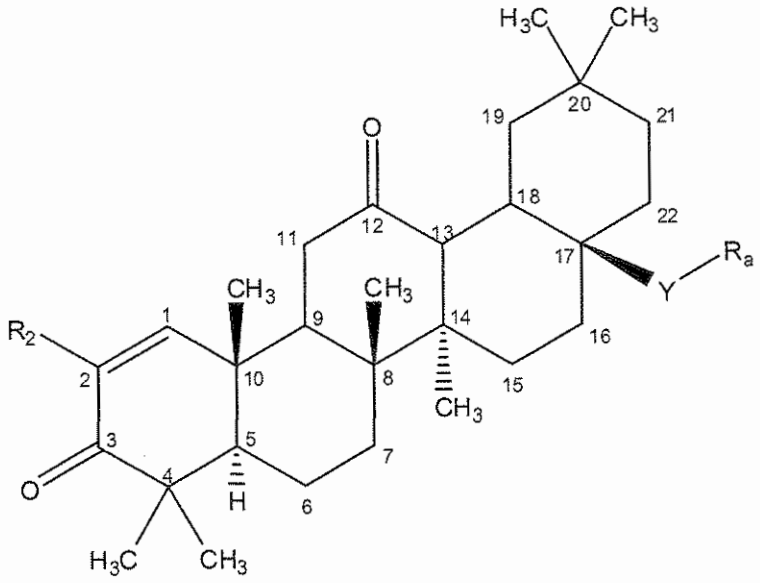
wherein R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, or cyano; or

alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, acyl$_{(C\leq12)}$, alkoxy$_{(C\leq12)}$, alkenyloxy$_{(C\leq12)}$, alkynyloxy$_{(C\leq12)}$, aryloxy$_{(C\leq12)}$, aralkoxy$_{(C\leq12)}$, heteroaryloxy$_{(C\leq12)}$, heteroaralkoxy$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, alkenylamino$_{(C\leq12)}$, alkynylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, arylsulfonyl$_{(C\leq12)}$, arylsulfinyl$_{(C\leq12)}$, alkylphosphate$_{(C\leq12)}$, dialkylphosphate$_{(C\leq12)}$, or a substituted version of any of these groups;

or pharmaceutically acceptable salts, esters, hydrates, solvates, tautomers, prodrugs, or optical isomers thereof.

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



(VIII)

wherein:

Y is alkanediyl$_{(C\leq3)}$ or substituted alkanediyl$_{(C\leq3)}$;

R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, or cyano; or

alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, acyl$_{(C\leq12)}$, alkoxy$_{(C\leq12)}$, alkenyloxy$_{(C\leq12)}$, alkynyloxy$_{(C\leq12)}$, aryloxy$_{(C\leq12)}$, aralkoxy$_{(C\leq12)}$, heteroaryloxy$_{(C\leq12)}$, heteroaralkoxy$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, alkenylamino$_{(C\leq12)}$, alkynylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, arylsulfonyl$_{(C\leq12)}$, arylsulfinyl$_{(C\leq12)}$, alkylphosphate$_{(C\leq12)}$, dialkylphosphate$_{(C\leq12)}$, or a substituted version of any of these groups; and

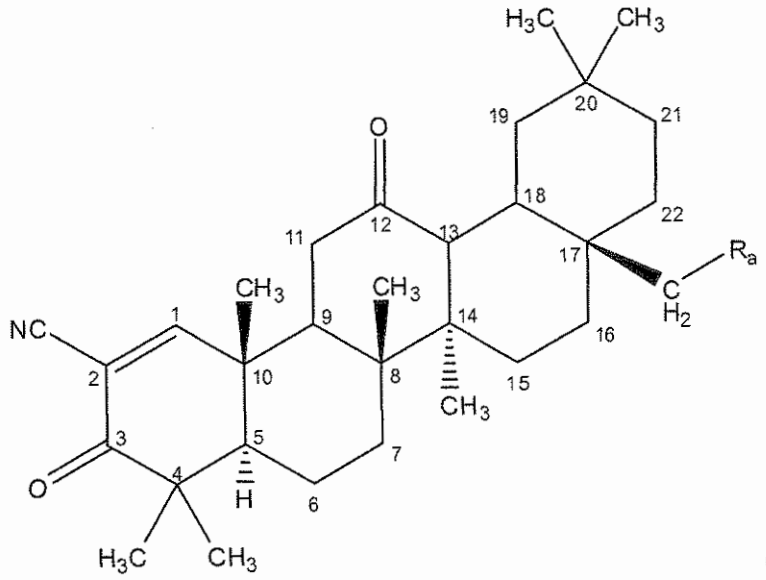
R_2 is:

cyano, hydroxy, halo or amino; or

fluoroalkyl$_{(C\leq8)}$, alkenyl$_{(C\leq8)}$, alkynyl$_{(C\leq8)}$, aryl$_{(C\leq8)}$, heteroaryl$_{(C\leq8)}$, acyl$_{(C\leq8)}$, alkoxy$_{(C\leq8)}$, aryloxy$_{(C\leq8)}$, acyloxy$_{(C\leq8)}$, alkylamino$_{(C\leq8)}$, arylamino$_{(C\leq8)}$, amido$_{(C\leq8)}$, or a substituted version of any of these groups;

or pharmaceutically acceptable salts, esters, hydrates, solvates, tautomers, prodrugs, or optical isomers thereof.

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



(IX)

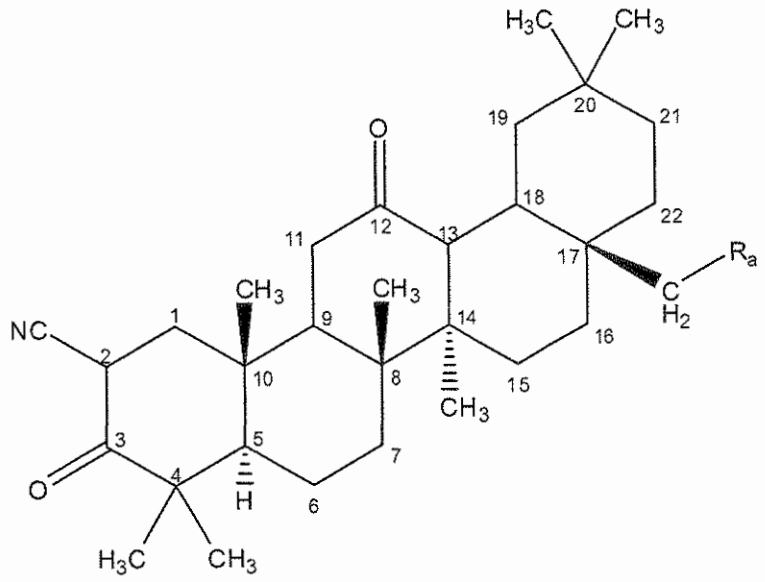
wherein R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, or cyano; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $alkenyloxy_{(C\leq12)}$, $alkynyloxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$, $aralkoxy_{(C\leq12)}$, $heteroaryloxy_{(C\leq12)}$, $heteroaralkoxy_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $alkenylamino_{(C\leq12)}$, $alkynylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $arylsulfonyl_{(C\leq12)}$, $arylsulfinyl_{(C\leq12)}$, $alkylphosphate_{(C\leq12)}$, $dialkylphosphate_{(C\leq12)}$, or a substituted version of any of these groups;

or pharmaceutically acceptable salts, esters, hydrates, solvates, tautomers, prodrugs, or optical isomers thereof.

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



(X)

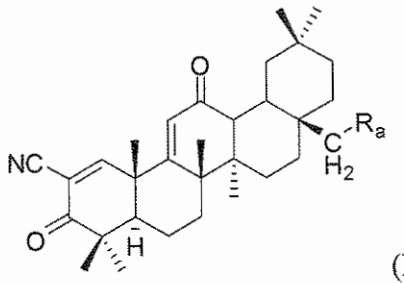
wherein R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, or cyano; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $alkenyloxy_{(C\leq12)}$, $alkynyloxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$, $aralkoxy_{(C\leq12)}$, $heteroaryloxy_{(C\leq12)}$, $heteroaralkoxy_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $alkenylamino_{(C\leq12)}$, $alkynylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $arylsulfonyl_{(C\leq12)}$, $arylsulfinyl_{(C\leq12)}$, $alkylphosphate_{(C\leq12)}$, $dialkylphosphate_{(C\leq12)}$, or a substituted version of any of these groups;

or salts, esters, hydrates, solvates, tautomers, or optical isomers thereof.

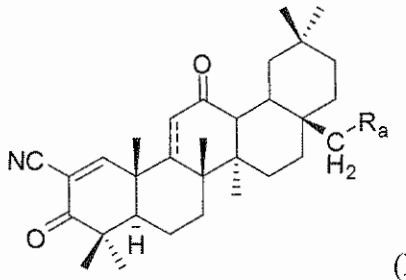
In some ~~embodiments~~examples, the compound is further defined as:



(XI)

wherein R_a is hydroxy, cyano, $acyl_{(C\leq 8)}$, substituted $acyl_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, or substituted $acyl_{(C\leq 8)}$; or pharmaceutically acceptable salts, hydrates, solvates, tautomers, or optical isomers thereof.

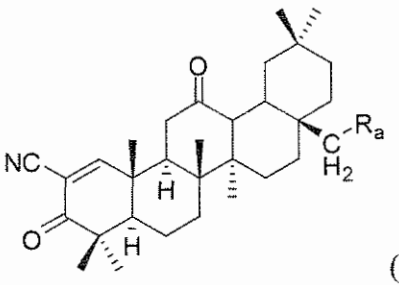
In some ~~embodiments~~examples, the compound is further defined as:



(XII)

wherein R_a is hydroxy, cyano, $acyl_{(C\leq 8)}$, substituted $acyl_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, substituted $acyl_{(C\leq 8)}$, $amido_{(C\leq 8)}$, or substituted $amido_{(C\leq 8)}$; or pharmaceutically acceptable salts, hydrates, solvates, tautomers, or optical isomers thereof.

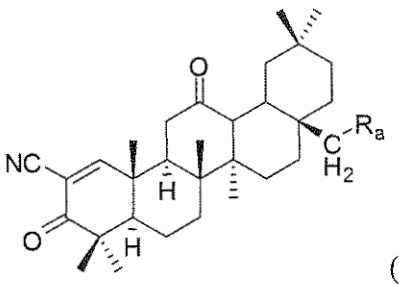
In some ~~embodiments~~examples, the compound is further defined as:



(XIII)

wherein R_a is hydroxy, cyano, $acyl_{(C\leq 8)}$, substituted $acyl_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, or substituted $acyl_{(C\leq 8)}$; or pharmaceutically acceptable salts, hydrates, solvates, tautomers, or optical isomers thereof.

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



(XIV)

wherein R_a is $alkylamino_{(C\leq 12)}$, $dialkylamino_{(C\leq 12)}$, $alkenylamino_{(C\leq 12)}$, $alkynylamino_{(C\leq 12)}$, $arylamino_{(C\leq 12)}$, $aralkylamino_{(C\leq 12)}$, $heteroarylamino_{(C\leq 12)}$, $heteroaralkylamino_{(C\leq 12)}$, $alkylsulfonylamino_{(C\leq 12)}$, or $amido_{(C\leq 12)}$, or a substituted version of any of these groups.

In a variation of each of the above ~~embodiments~~examples containing a Y group, Y can be alkanediyl$_{(C1-4)}$ or substituted alkanediyl$_{(C1-4)}$. In other variations, Y can be $-CH_2-$. In other variations, Y can be $-C(OH)HCH_2-$. In other variations, Y can be $-C\equiv C-$.

In a variation of each of the above ~~embodiments~~examples containing a X_1 group, X_1 can be OR_b and R_b is absent. In a variation of each of the above ~~embodiments~~examples containing an X_2 group, X_2 can be is hydrogen.

In a variation of each of the above ~~embodiments~~examples containing an R_a group, R_a can be $-OH$. In other variations, R_a can be $-CN$. In other variations, R_a can be $-Cl$. In other variations, R_a can be is $-Br$. In other variations, R_a can be $-H$. In other variations, R_a can be acyl$_{(C1-6)}$ or substituted acyl$_{(C1-6)}$. In other variations, R_a can be acyl$_{(C4-6)}$ or substituted acyl$_{(C4-6)}$. In other variations, R_a can be acyl$_{(C1-4)}$ or substituted acyl$_{(C1-4)}$. In other variations, R_a can be acyl$_{(C1-3)}$ or substituted acyl$_{(C1-3)}$. In other variations, R_a can be selected from the group consisting of $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, and $-C(=O)NHCH_2CF_3$. In other variations, R_a can be acyloxy$_{(C1-8)}$ or substituted acyloxy$_{(C1-3)}$. In other variations, R_a can be substituted acyloxy$_{(C1-3)}$. In other variations, R_a can be acyloxy$_{(C2-8)}$. In other variations, R_a can comprises a fluoro group. In other variations, R_a can comprises a trifluoromethyl group. In other variations, R_a can be alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, alkenylamino$_{(C\leq12)}$, alkynylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, alkylsulfonylamino$_{(C\leq12)}$, or amido$_{(C\leq12)}$, or a substituted version of any of these groups. In other variations, R_a can be arylsulfonyl$_{(C\leq8)}$ or arylsulfinyl$_{(C\leq8)}$. In other variations, R_a can be $-OP(O)(OH)_2$. In other variations, R_a can be alkylphosphate$_{(C\leq12)}$ or dialkylphosphate$_{(C\leq12)}$. In other variations, R_a can be dialkylphosphate$_{(C\leq8)}$. In other variations, R_a can be $-OP(O)(OEt)_2$. In other variations, R_a can be 1,3-dioxoisoindolin-2-yl. In a variation of each of the above ~~embodiments~~examples containing a $-Y-R_a$ group, $-Y-R_a$ can be oxirane-2-yl. In another variation of each of the above ~~embodiments~~examples containing a $-Y-R_a$ group, $-Y-R_a$ can be 1,3-dioxolan-4-yl.

In a variation of each of the above ~~embodiments~~examples containing an R_1 group, R_1 can be $-H$, $-OH$ or $-F$. In some of these variations, R_1 can be $-H$. In a variation of each of the above ~~embodiments~~examples containing an R_2 group, R_2 can be $-CN$. In other variations, R_2 can be $-CF_3$. In other variations, R_2 can be a substituted acyl$_{(C1-3)}$. In other variations, R_2 can be $-C(=O)NHS(=O)_2CH_3$. In a variation of each of the above ~~embodiments~~examples containing an R_3 group, R3 can be absent. In a variation of each of the above ~~embodiments~~examples containing an R_4 group, R_4 can be methyl. In other variations, R_4 can be hydroxymethyl.

In a variation of each of the above ~~embodiments~~examples containing an R_4 and/or an R_5 group, R_4 and/or R_5 can each independently be methyl. In a variation of each of the above ~~embodiments~~examples containing an R_6 and/or an R_7 group, R_6 and/or R_7 can each independently be hydrogen. In a variation of each of the above ~~embodiments~~examples containing an R_8 and/or an R_9 group, R_8 and/or R_9 can each independently be hydrogen. In a variation of each of the above ~~embodiments~~examples containing an R_{10} and/or an R_{11} group, R_{10} and/or R11 can each independently be methyl.

In some variations of one or more of the above ~~embodiments~~examples, Y, R_a, and carbon numbers 13, 17 and 18 form a ring, wherein Y is alkanediyl$_{(C=1)}$ or substituted alkanediyl$_{(C=1)}$ and R_a is –O–. In some variations of one or more of the above ~~embodiments~~examples, the bond between carbons 9 and 11 is a single bond. In some variations of one or more of the above ~~embodiments~~examples, the bond between carbons 9 and 11 is a double bond.

Examples of specific compounds ~~provided~~disclosed by the present disclosure include:

methyl-2-((4a*R*,6a*R*,6b*S*,8a*R*,12a*S*,14a*R*,14b*S*)-11-cyano-2,2,6a,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-octadecahydropicen-4a-yl)acetate,

2-((4a*R*,6a*R*,6b*S*,8a*R*,12a*S*,14a*R*,14b*S*)-11-cyano-2,2,6a,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-octadecahydropicen-4a-yl)acetic acid,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14b*R*)-8a-(hydroxymethyl)-4,4,6a,6b,11,11,14b-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,

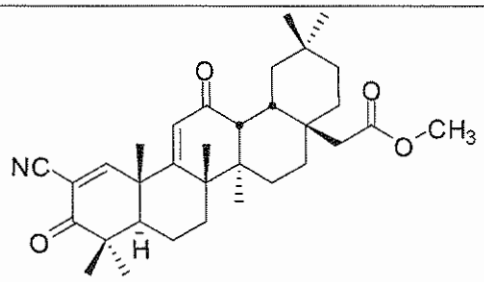
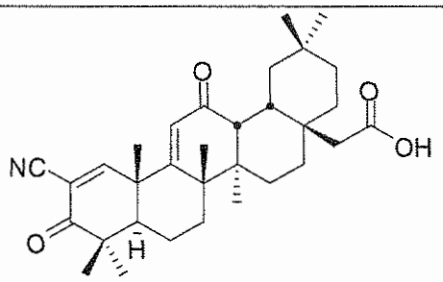
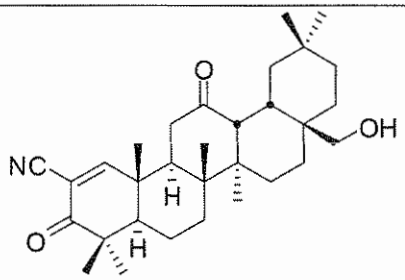
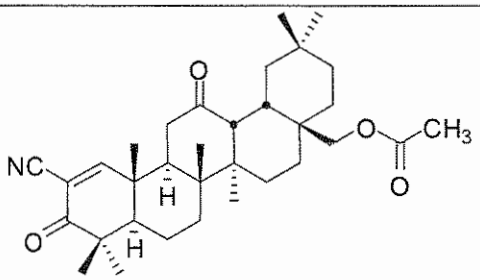
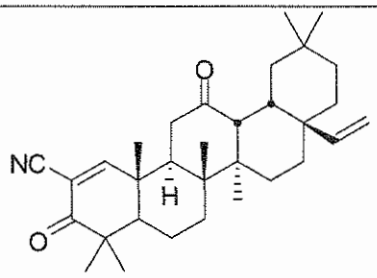
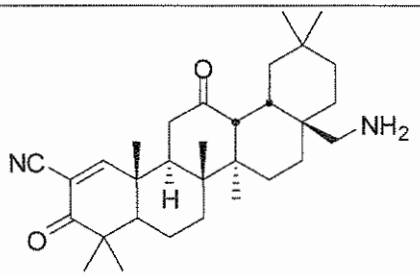
((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl acetate,

(6a*R*,6b*R*,8a*R*,12a*S*,12b*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-vinyl-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

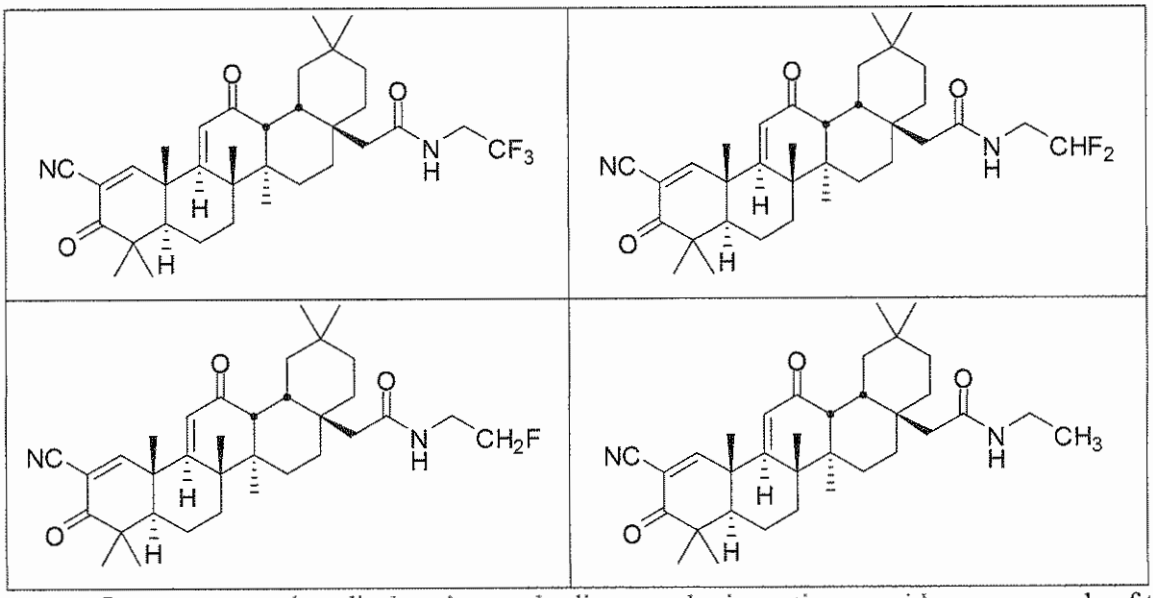
(6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14b*R*)-8a-(aminomethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-(2,2,2-trifluoroethyl)acetamide.

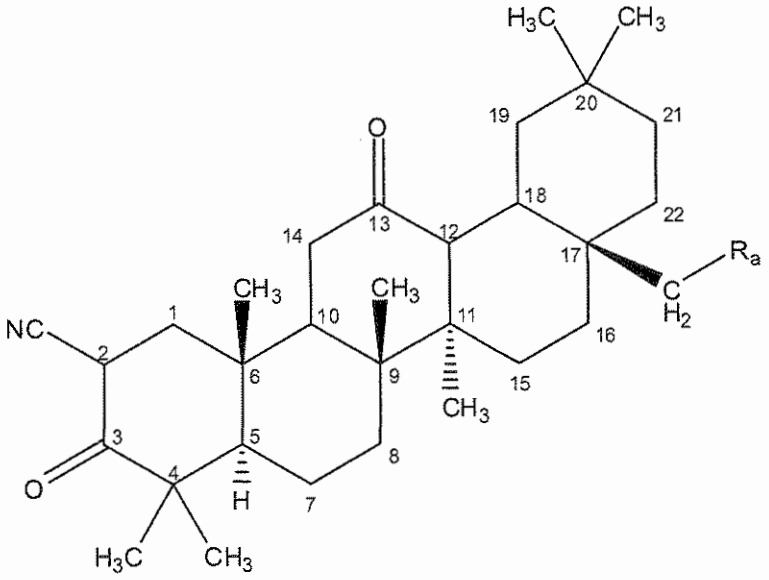
Non-limiting examples of compounds disclosed hereinprovided by this invention include the compounds according to the formulas shown below, as well as or pharmaceutically acceptable salts thereof. In certain embodimentsexamples, these compounds are substantially free from other optical isomers thereof.

 63194 (402-50)	 63199 (402-54)
 63202 (402-63)	 63204 (402-65)
 63213	 63214

In some ~~embodiments~~examples, one or more of the following compounds is contemplated:

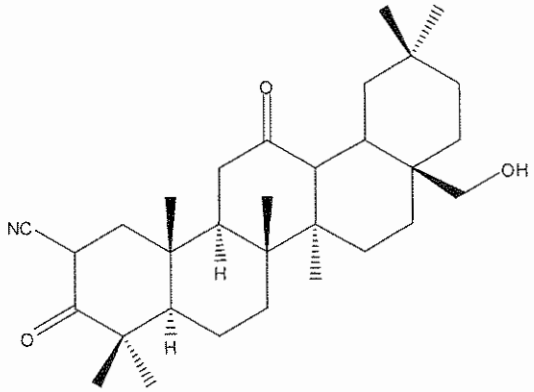


In some examples, disclosed are~~embodiments, the invention provides~~ compounds of the formula:



(XV),

wherein R_a is: hydrogen, hydroxy, halo, amino or cyano; or $alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $alkenyloxy_{(C\leq12)}$, $alkynyloxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$, $aralkoxy_{(C\leq12)}$, $heteroaryloxy_{(C\leq12)}$, $heteroaralkoxy_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $alkenylamino_{(C\leq12)}$, $alkynylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, or a substituted version of any of these groups; or salts, esters, hydrates, solvates, tautomers, or optical isomers thereof. For example, disclosed herein is~~the invention provides~~:



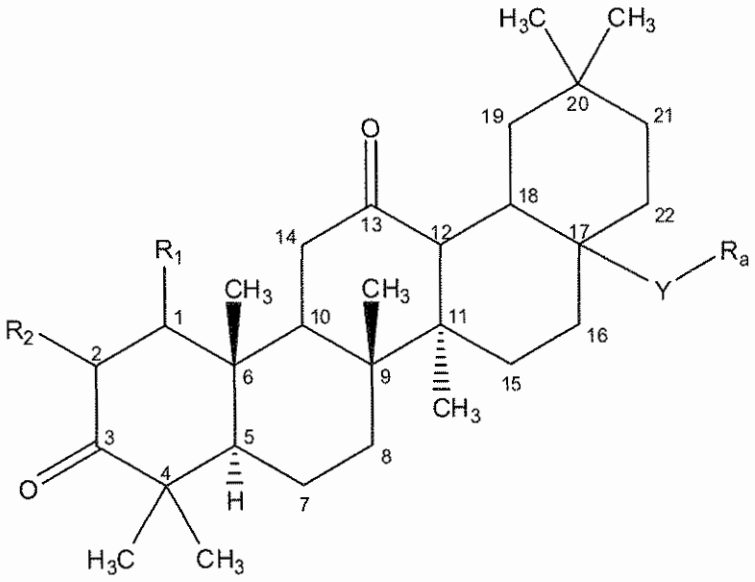
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or salts, hydrates, solvates, tautomers, or optical isomers thereof.

,

wherein R_a is: hydrogen, hydroxy, halo, amino or cyano; or $alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $alkenyloxy_{(C\leq12)}$, $alkynyloxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$, $aralkoxy_{(C\leq12)}$, $heteroaryloxy_{(C\leq12)}$, $heteroaralkoxy_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $alkenylamino_{(C\leq12)}$, $alkynylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, or a substituted version of any of these groups; or salts, esters, hydrates, solvates, tautomers, or optical isomers thereof.

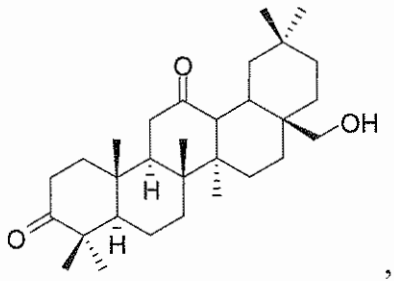
In some examples, disclosed herein are~~embodiments, the invention provides~~ compounds of the formula:



(XVI),

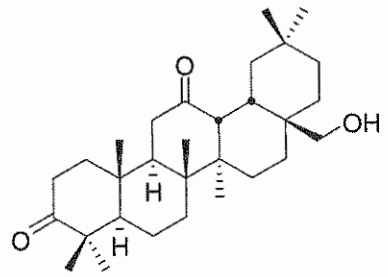
wherein: Y is $alkanediyl_{(C\leq8)}$, $alkenediyl_{(C\leq8)}$, $alkynediyl_{(C\leq8)}$, or a substituted version of any of these groups; R_a is: hydrogen, hydroxy, halo, amino, nitro, cyano, azido, mercapto or silyl; or $alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $alkenyloxy_{(C\leq12)}$, $alkynyloxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$,

aralkoxy$_{(C\leq12)}$, heteroaryloxy$_{(C\leq12)}$, heteroaralkoxy$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, alkenylamino$_{(C\leq12)}$, alkynylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, alkylsulfonylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, alkylthio$_{(C\leq12)}$, alkenylthio$_{(C\leq12)}$, alkynylthio$_{(C\leq12)}$, arylthio$_{(C\leq12)}$, aralkylthio$_{(C\leq12)}$, heteroarylthio$_{(C\leq12)}$, heteroaralkylthio$_{(C\leq12)}$, acylthio$_{(C\leq12)}$, thioacyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, alkenylsulfonyl$_{(C\leq12)}$, alkynylsulfonyl$_{(C\leq12)}$, arylsulfonyl$_{(C\leq12)}$, aralkylsulfonyl$_{(C\leq12)}$, alkylammonium$_{(C\leq12)}$, alkylsulfonium$_{(C\leq12)}$, alkylsilyl$_{(C\leq12)}$, or a substituted version of any of these groups; R_1 is: hydrogen, cyano, hydroxy, halo or amino; or alkyl$_{(C\leq8)}$, alkenyl$_{(C\leq8)}$, alkynyl$_{(C\leq8)}$, aryl$_{(C\leq8)}$, aralkyl$_{(C\leq8)}$, heteroaryl$_{(C\leq8)}$, heteroaralkyl$_{(C\leq8)}$, acyl$_{(C\leq8)}$, alkoxy$_{(C\leq8)}$, aryloxy$_{(C\leq8)}$, acyloxy$_{(C\leq8)}$, alkylamino$_{(C\leq8)}$, arylamino$_{(C\leq8)}$, amido$_{(C\leq8)}$, or a substituted version of any of these groups; R_2 is: cyano, hydroxy, halo or amino; or alkenyl$_{(C\leq8)}$, alkynyl$_{(C\leq8)}$, aryl$_{(C\leq8)}$, heteroaryl$_{(C\leq8)}$, acyl$_{(C\leq8)}$, alkoxy$_{(C\leq8)}$, aryloxy$_{(C\leq8)}$, acyloxy$_{(C\leq8)}$, alkylamino$_{(C\leq8)}$, arylamino$_{(C\leq8)}$, amido$_{(C\leq8)}$, or a substituted version of any of these groups; or salts, esters, hydrates, solvates, tautomers, or optical isomers thereof. For example, disclosed is~~the invention provides~~:



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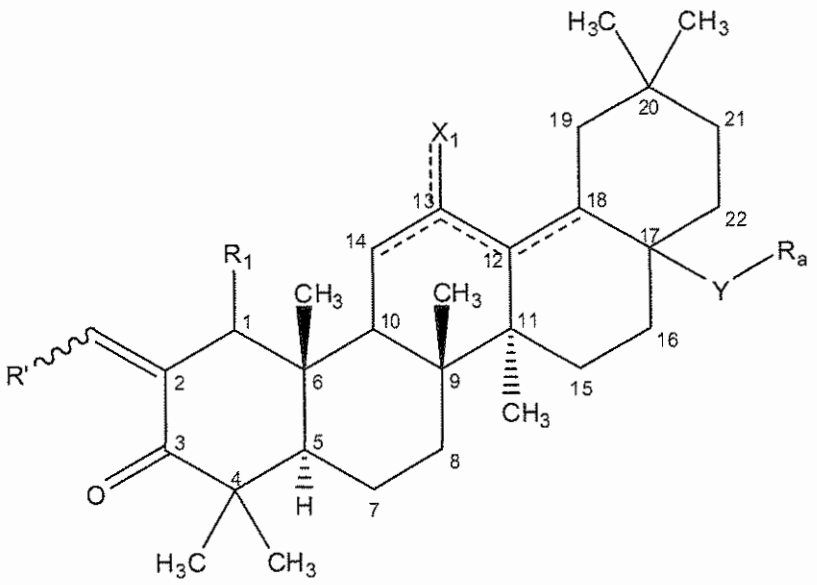
or salts, hydrates, solvates, tautomers, or optical isomers thereof, such as:



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In some ~~embodiments~~examples, this optical isomer is substantially free from other optical isomers thereof.

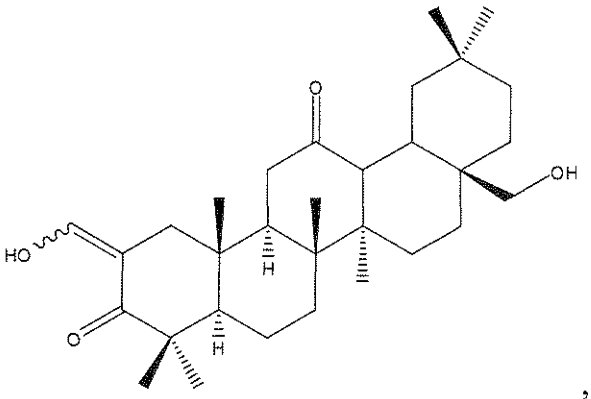
In some examples, disclosed are~~embodiments, the invention provides~~ compounds of the formula:



(XVII),

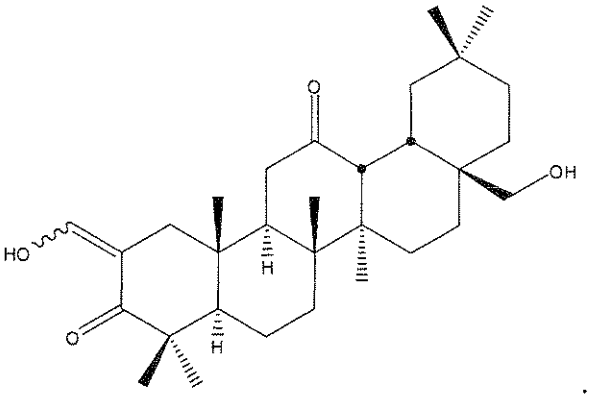
wherein: Y is alkanediyl$_{(C\leq8)}$, alkenediyl$_{(C\leq8)}$, alkynediyl$_{(C\leq8)}$, or a substituted version of any of these groups; R_a is: hydrogen, hydroxy, halo, amino, nitro, cyano, azido, mercapto or silyl; or alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, acyl$_{(C\leq12)}$, alkoxy$_{(C\leq12)}$, alkenyloxy$_{(C\leq12)}$, alkynyloxy$_{(C\leq12)}$, aryloxy$_{(C\leq12)}$, aralkoxy$_{(C\leq12)}$, heteroaryloxy$_{(C\leq12)}$, heteroaralkoxy$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, alkenylamino$_{(C\leq12)}$, alkynylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, alkylsulfonylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, alkylthio$_{(C\leq12)}$, alkenylthio$_{(C\leq12)}$, alkynylthio$_{(C\leq12)}$, arylthio$_{(C\leq12)}$, aralkylthio$_{(C\leq12)}$, heteroarylthio$_{(C\leq12)}$, heteroaralkylthio$_{(C\leq12)}$, acylthio$_{(C\leq12)}$, thioacyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, alkenylsulfonyl$_{(C\leq12)}$, alkynylsulfonyl$_{(C\leq12)}$, arylsulfonyl$_{(C\leq12)}$, aralkylsulfonyl$_{(C\leq12)}$, alkylammonium$_{(C\leq12)}$, alkylsulfonium$_{(C\leq12)}$, alkylsilyl$_{(C\leq12)}$, or a substituted version of any of these groups; X_1 is: OR_b, NR_bR_c, or SR_b, wherein R_b and R_c are each independently: hydrogen; alkyl$_{(C\leq8)}$, aryl$_{(C\leq8)}$, aralkyl$_{(C\leq8)}$, acyl$_{(C\leq8)}$, or a substituted version of any of these groups; or provided that R_b is absent when the atom to which it is bound is part of a double bond, further provided that when R_b is absent the atom to which it is bound is part of a double bond; and R_1 is: hydrogen, cyano, hydroxy, halo or amino; or alkyl$_{(C\leq8)}$, alkenyl$_{(C\leq8)}$, alkynyl$_{(C\leq8)}$, aryl$_{(C\leq8)}$, aralkyl$_{(C\leq8)}$, heteroaryl$_{(C\leq8)}$, heteroaralkyl$_{(C\leq8)}$, acyl$_{(C\leq8)}$, alkoxy$_{(C\leq8)}$, aryloxy$_{(C\leq8)}$, acyloxy$_{(C\leq8)}$, alkylamino$_{(C\leq8)}$, arylamino$_{(C\leq8)}$, amido$_{(C\leq8)}$, or a substituted version of any of these groups; R′ is hydroxy, alkoxy$_{(C\leq12)}$, substituted alkoxy$_{(C\leq12)}$, aryloxy$_{(C\leq12)}$, substituted aryloxy$_{(C\leq12)}$, aralkoxy$_{(C\leq12)}$, substituted aralkoxy$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, or substituted acyloxy$_{(C\leq12)}$; or salts, esters, hydrates, solvates, tautomers, or optical isomers thereof. In

some of these ~~embodiments~~examples, R′ is acetyloxy. In other of these ~~embodiments~~examples, R′ is hydroxy. For example, disclosed herein is~~the invention provides~~:



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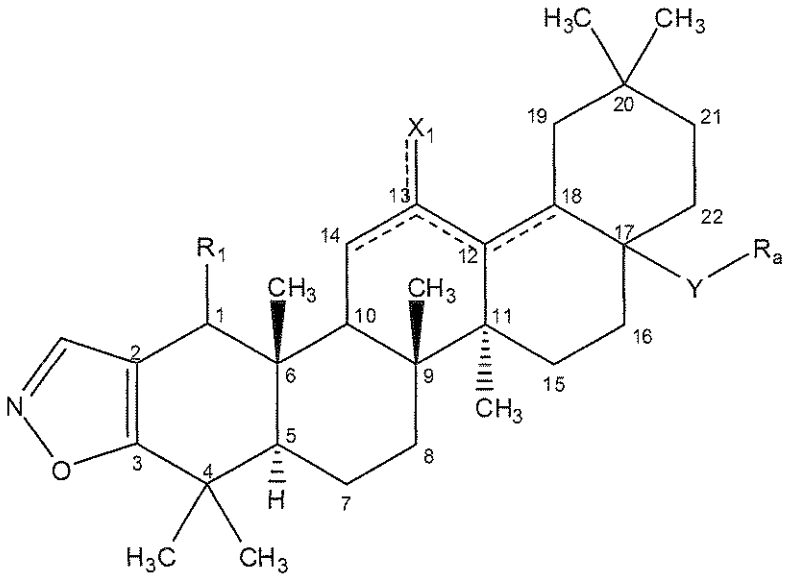
or salts, hydrates, solvates, tautomers, or optical isomers thereof, such as:



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In certain ~~embodiments~~examples, this optical isomer is substantially free from other optical isomers thereof.

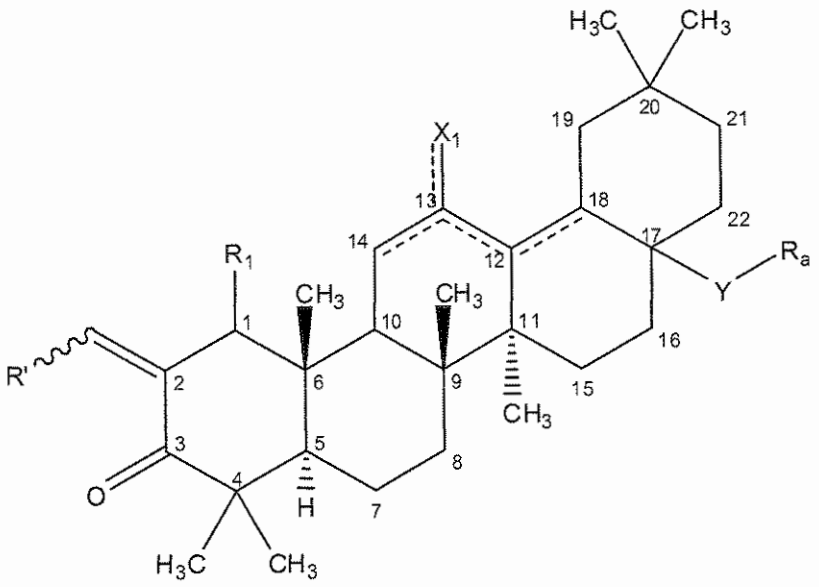
In some examples, disclosed are~~embodiments, the invention provides~~ compounds of the formula:



(XVIII),

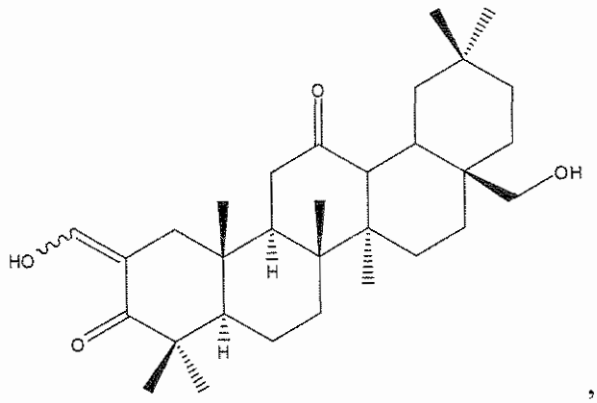
wherein: Y is alkanediyl$_{(C\leq 8)}$, alkenediyl$_{(C\leq 8)}$, alkynediyl$_{(C\leq 8)}$, or a substituted version of any of these groups; R_a is: hydrogen, hydroxy, halo, amino, nitro, cyano, azido, mercapto or silyl; or alkyl$_{(C\leq 12)}$, alkenyl$_{(C\leq 12)}$, alkynyl$_{(C\leq 12)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 12)}$, heteroaralkyl$_{(C\leq 12)}$, acyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 12)}$, alkenyloxy$_{(C\leq 12)}$, alkynyloxy$_{(C\leq 12)}$, aryloxy$_{(C\leq 12)}$, aralkoxy$_{(C\leq 12)}$, heteroaryloxy$_{(C\leq 12)}$, heteroaralkoxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 12)}$, alkylamino$_{(C\leq 12)}$, dialkylamino$_{(C\leq 12)}$, alkenylamino$_{(C\leq 12)}$, alkynylamino$_{(C\leq 12)}$, arylamino$_{(C\leq 12)}$, aralkylamino$_{(C\leq 12)}$, heteroarylamino$_{(C\leq 12)}$, heteroaralkylamino$_{(C\leq 12)}$, alkylsulfonylamino$_{(C\leq 12)}$, amido$_{(C\leq 12)}$, alkylthio$_{(C\leq 12)}$, alkenylthio$_{(C\leq 12)}$, alkynylthio$_{(C\leq 12)}$, arylthio$_{(C\leq 12)}$, aralkylthio$_{(C\leq 12)}$, heteroarylthio$_{(C\leq 12)}$, heteroaralkylthio$_{(C\leq 12)}$, acylthio$_{(C\leq 12)}$, thioacyl$_{(C\leq 12)}$, alkylsulfonyl$_{(C\leq 12)}$, alkenylsulfonyl$_{(C\leq 12)}$, alkynylsulfonyl$_{(C\leq 12)}$, arylsulfonyl$_{(C\leq 12)}$, aralkylsulfonyl$_{(C\leq 12)}$, alkylammonium$_{(C\leq 12)}$, alkylsulfonium$_{(C\leq 12)}$, alkylsilyl$_{(C\leq 12)}$, or a substituted version of any of these groups; X_1 is: OR_b, NR_bR_c, or SR_b, wherein R_b and R_c are each independently: hydrogen; alkyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, acyl$_{(C\leq 8)}$, or a substituted version of any of these groups; or provided that R_b is absent when the atom to which it is bound is part of a double bond, further provided that when R_b is absent the atom to which it is bound is part of a double bond; and R_1 is: hydrogen, cyano, hydroxy, halo or amino; or alkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heteroaralkyl$_{(C\leq 8)}$, acyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, or a substituted version of any of these groups; or salts, esters, hydrates, solvates, tautomers, or optical isomers thereof. For example, disclosed herein is~~the invention provides~~:

In some examples, disclosed are~~embodiments, the invention provides~~ compounds of the formula:



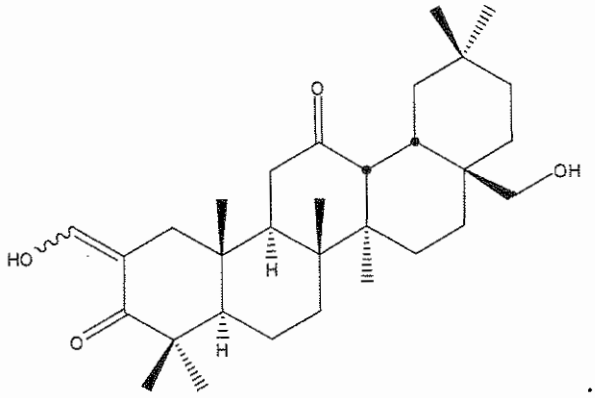
(XIX),

wherein: Y is alkanediyl$_{(C\leq 8)}$, alkenediyl$_{(C\leq 8)}$, alkynediyl$_{(C\leq 8)}$, or a substituted version of any of these groups; R_a is: hydrogen, hydroxy, halo, amino, nitro, cyano, azido, mercapto or silyl; or alkyl$_{(C\leq 12)}$, alkenyl$_{(C\leq 12)}$, alkynyl$_{(C\leq 12)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 12)}$, heteroaralkyl$_{(C\leq 12)}$, acyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 12)}$, alkenyloxy$_{(C\leq 12)}$, alkynyloxy$_{(C\leq 12)}$, aryloxy$_{(C\leq 12)}$, aralkoxy$_{(C\leq 12)}$, heteroaryloxy$_{(C\leq 12)}$, heteroaralkoxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 12)}$, alkylamino$_{(C\leq 12)}$, dialkylamino$_{(C\leq 12)}$, alkenylamino$_{(C\leq 12)}$, alkynylamino$_{(C\leq 12)}$, arylamino$_{(C\leq 12)}$, aralkylamino$_{(C\leq 12)}$, heteroarylamino$_{(C\leq 12)}$, heteroaralkylamino$_{(C\leq 12)}$, alkylsulfonylamino$_{(C\leq 12)}$, amido$_{(C\leq 12)}$, alkylthio$_{(C\leq 12)}$, alkenylthio$_{(C\leq 12)}$, alkynylthio$_{(C\leq 12)}$, arylthio$_{(C\leq 12)}$, aralkylthio$_{(C\leq 12)}$, heteroarylthio$_{(C\leq 12)}$, heteroaralkylthio$_{(C\leq 12)}$, acylthio$_{(C\leq 12)}$, thioacyl$_{(C\leq 12)}$, alkylsulfonyl$_{(C\leq 12)}$, alkenylsulfonyl$_{(C\leq 12)}$, alkynylsulfonyl$_{(C\leq 12)}$, arylsulfonyl$_{(C\leq 12)}$, aralkylsulfonyl$_{(C\leq 12)}$, alkylammonium$_{(C\leq 12)}$, alkylsulfonium$_{(C\leq 12)}$, alkylsilyl$_{(C\leq 12)}$, or a substituted version of any of these groups; X_1 is: OR_b, NR_bR_c, or SR_b, wherein R_b and R_c are each independently: hydrogen; alkyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, acyl$_{(C\leq 8)}$, or a substituted version of any of these groups; or provided that R_b is absent when the atom to which it is bound is part of a double bond, further provided that when R_b is absent the atom to which it is bound is part of a double bond; and R_1 is: hydrogen, cyano, hydroxy, halo or amino; or alkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heteroaralkyl$_{(C\leq 8)}$, acyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, or a substituted version of any of these groups; R′ is hydroxy, alkoxy$_{(C\leq 12)}$, substituted alkoxy$_{(C\leq 12)}$, aryloxy$_{(C\leq 12)}$, substituted aryloxy$_{(C\leq 12)}$, aralkoxy$_{(C\leq 12)}$, substituted aralkoxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 12)}$, or substituted acyloxy$_{(C\leq 12)}$; or salts, esters, hydrates, solvates, tautomers, or optical isomers thereof. In some of these ~~embodiments~~examples, R′ is acetyloxy. In other of these ~~embodiments~~examples, R′ is hydroxy. For example, disclosed herein is~~the invention provides~~:



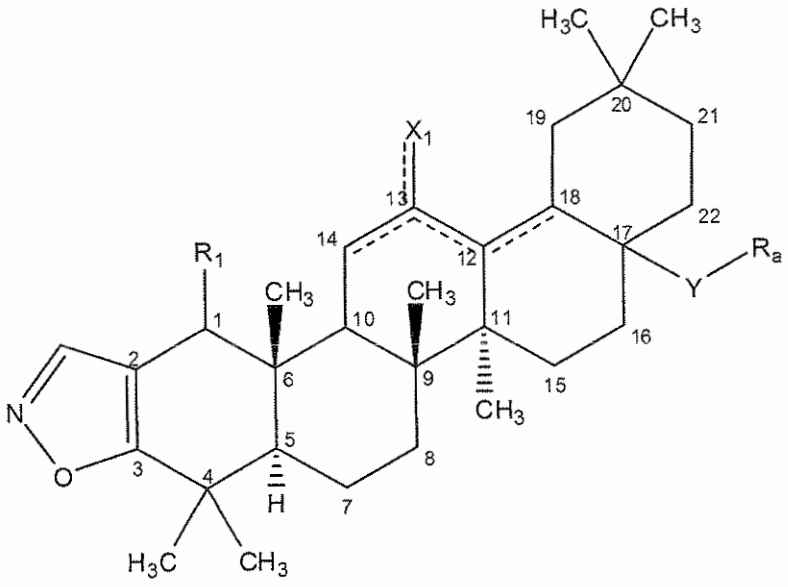
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or salts, hydrates, solvates, tautomers, or optical isomers thereof, such as:



In certain ~~embodiments~~examples, this optical isomer is substantially free from other optical isomers thereof.

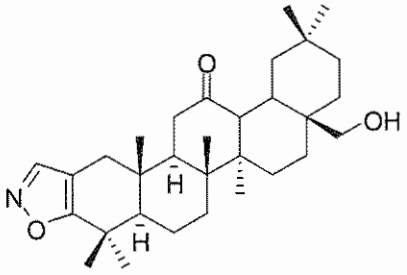
In some examples, disclosed are~~embodiments, the invention provides~~ compounds of the formula:



(XX),

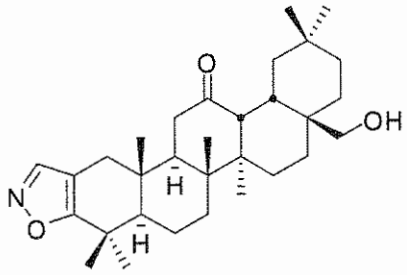
wherein: Y is alkanediyl$_{(C\leq 8)}$, alkenediyl$_{(C\leq 8)}$, alkynediyl$_{(C\leq 8)}$, or a substituted version of any of these groups; R_a is: hydrogen, hydroxy, halo, amino, nitro, cyano, azido, mercapto or silyl; or alkyl$_{(C\leq 12)}$, alkenyl$_{(C\leq 12)}$, alkynyl$_{(C\leq 12)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 12)}$, heteroaralkyl$_{(C\leq 12)}$, acyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 12)}$, alkenyloxy$_{(C\leq 12)}$, alkynyloxy$_{(C\leq 12)}$, aryloxy$_{(C\leq 12)}$, aralkoxy$_{(C\leq 12)}$, heteroaryloxy$_{(C\leq 12)}$, heteroaralkoxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 12)}$, alkylamino$_{(C\leq 12)}$, dialkylamino$_{(C\leq 12)}$, alkenylamino$_{(C\leq 12)}$, alkynylamino$_{(C\leq 12)}$, arylamino$_{(C\leq 12)}$, aralkylamino$_{(C\leq 12)}$, heteroarylamino$_{(C\leq 12)}$, heteroaralkylamino$_{(C\leq 12)}$, alkylsulfonylamino$_{(C\leq 12)}$, amido$_{(C\leq 12)}$, alkylthio$_{(C\leq 12)}$, alkenylthio$_{(C\leq 12)}$, alkynylthio$_{(C\leq 12)}$, arylthio$_{(C\leq 12)}$, aralkylthio$_{(C\leq 12)}$, heteroarylthio$_{(C\leq 12)}$, heteroaralkylthio$_{(C\leq 12)}$, acylthio$_{(C\leq 12)}$, thioacyl$_{(C\leq 12)}$, alkylsulfonyl$_{(C\leq 12)}$, alkenylsulfonyl$_{(C\leq 12)}$, alkynylsulfonyl$_{(C\leq 12)}$, arylsulfonyl$_{(C\leq 12)}$, aralkylsulfonyl$_{(C\leq 12)}$, alkylammonium$_{(C\leq 12)}$, alkylsulfonium$_{(C\leq 12)}$, alkylsilyl$_{(C\leq 12)}$, or a substituted version of any of

these groups; X_1 is: OR_b, NR_bR_c, or SR_b, wherein R_b and R_c are each independently: hydrogen; $alkyl_{(C\leq8)}$, $aryl_{(C\leq8)}$, $aralkyl_{(C\leq8)}$, $acyl_{(C\leq8)}$, or a substituted version of any of these groups; or provided that R_b is absent when the atom to which it is bound is part of a double bond, further provided that when R_b is absent the atom to which it is bound is part of a double bond; and R_1 is: hydrogen, cyano, hydroxy, halo or amino; or $alkyl_{(C\leq8)}$, $alkenyl_{(C\leq8)}$, $alkynyl_{(C\leq8)}$, $aryl_{(C\leq8)}$, $aralkyl_{(C\leq8)}$, $heteroaryl_{(C\leq8)}$, $heteroaralkyl_{(C\leq8)}$, $acyl_{(C\leq8)}$, $alkoxy_{(C\leq8)}$, $aryloxy_{(C\leq8)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$, $amido_{(C\leq8)}$, or a substituted version of any of these groups; or salts, esters, hydrates, solvates, tautomers, or optical isomers thereof. For example, disclosed are~~the invention provides~~:



,

or salts, hydrates, solvates, tautomers, or optical isomers thereof, such as:



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In certain ~~embodiments~~examples, this optical isomer is substantially free from other optical isomers thereof.

In a variation of each of the above ~~embodiments~~examples containing a Y group, Y can be $alkanediyl_{(C1-4)}$ or substituted $alkanediyl_{(C1-4)}$. In some of these variations, Y can be $-CH_2-$. In a variation of each of the above ~~embodiments~~examples containing an X_1 group, X_1 can be OR_b and R_b can be absent.

In a variation of each of the above ~~embodiments~~examples containing an R_a group, R_a can be $-OH$. In other variations, R_a can be $acyl_{(C1-6)}$ or substituted $acyl_{(C1-6)}$. In some of these variations, R_a can be $acyl_{(C4-6)}$ or substituted $acyl_{(C4-6)}$. In some of these variations, R_a can be $acyl_{(C1-4)}$ or substituted $acyl_{(C1-4)}$. In some of these variations, R_a can be $acyl_{(C1-3)}$ or substituted $acyl_{(C1-3)}$. In some of these variations, R_a can be selected from the group

consisting of $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, and $-C(=O)NHCH_2CF_3$. In still other variations, R_a can be $acyloxy_{(C1-3)}$ or substituted $acyloxy_{(C1-3)}$.

In a variation of each of the above ~~embodiments~~examples containing an R_1 group, R_1 can be $-H$, $-OH$ or $-F$. In some of these variations, R_1 can be $-H$. In a variation of each of the above ~~embodiments~~examples containing an R_2 group, R_2 can be $-CN$. In other variations, R_2 can be a substituted $acyl_{(C1-3)}$. For example, R_2 can be $-C(=O)NHS(=O)_2CH_3$.

In some ~~embodiments~~examples, ~~the invention provides~~disclosed are compounds useful for preventing and/or treating diseases or disorders whose pathology involves oxidative stress, inflammation, and/or dysregulation of inflammatory signaling pathways. In some variations, the diseases or disorders can be characterized by overexpression of inducible nitric oxide synthase (iNOS) and/or inducible cyclooxygenase (COX-2) in affected tissues. In some variations, the diseases or disorders can be characterized by overproduction of reactive oxygen species (ROS) or reactive nitrogen species (RNS) such as superoxide, hydrogen peroxide, nitric oxide or peroxynitrite in affected tissues. In some variations, the disease or disorder is characterized by excessive production of inflammatory cytokines or other inflammation-related proteins such as TNFα, IL-6, IL-1, IL-8, ICAM-1, VCAM-1, and VEGF. Such diseases or disorders may, in some ~~embodiments~~examples, involve undesirable proliferation of certain cells, as in the case of cancer (*e.g.*, solid tumors, leukemias, myelomas, lymphomas, and other cancers), fibrosis associated with organ failure, or excessive scarring. Non limiting examples of the disease or disorder include: lupus, rheumatoid arthritis, juvenile-onset diabetes, multiple sclerosis, psoriasis, and Crohn's disease. Further non-limiting examples include cardiovascular diseases, such as atherosclerosis, heart failure, myocardial infarction, acute coronary syndrome, restenosis following vascular surgery, hypertension, and vasculitis; neurodegenerative or neuromuscular diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease, ALS, and muscular dystrophy; neurological disorders such as epilepsy and dystonia; neuropsychiatric conditions such as major depression, bipolar disorder, post-traumatic stress disorder, schizophrenia, anorexia nervosa, ADHD, and autism-spectrum disorders; retinal diseases such as macular degeneration, diabetic retinopathy, glaucoma, and retinitis; chronic and acute pain syndromes, including inflammatory and neuropathic pain; hearing loss and tinnitus; diabetes and complications of diabetes, including metabolic syndrome, diabetic nephropathy, diabetic neuropathy, and diabetic ulcers; respiratory diseases such as asthma, chronic obstructive pulmonary disease, acute respiratory distress syndrome,

and cystic fibrosis; inflammatory bowel diseases; osteoporosis, osteoarthritis, and other degenerative conditions of bone and cartilage; acute or chronic organ failure, including renal failure, liver failure (including cirrhosis and hepatitis), and pancreatitis; ischemia-reperfusion injury associated with thrombotic or hemorrhagic stroke, subarachnoid hemorrhage, cerebral vasospasm, myocardial infarction, shock, or trauma; complications of organ or tissue transplantation including acute or chronic transplant failure or rejection and graft-versus-host disease; skin diseases including atopic dermatitis and acne; sepsis and septic shock; excessive inflammation associated with infection, including respiratory inflammation associated with influenza and upper respiratory infections; mucositis associated with cancer therapy, including radiation therapy or chemotherapy; and severe burns.

In some ~~embodiments~~examples, compounds of the present disclosure are in the form of pharmaceutically acceptable salts. In other ~~embodiments~~examples, compounds of the present disclosure are not be in the form of a pharmaceutically acceptable salts.

In some ~~embodiments~~examples, compounds of the present disclosure can be esters of the above formulas. The ester may, for example, result from a condensation reaction between a hydroxy group of the formula and the carboxylic acid group of biotin.

In some ~~embodiments~~examples, the compounds of the present disclosure can be present as a mixture of stereoisomers. In other ~~embodiments~~examples, the compounds of the present disclosure are present as single stereoisomers.

In some ~~embodiments~~examples, compounds of the present disclosure may be inhibitors of IFN-γ-induced nitrous oxide (NO) production in macrophages, for example, having an IC_{50} value of less than 0.2 μM.

Other general ~~aspects~~examples of the present disclosure contemplate a pharmaceutical composition comprising as an active ingredient a compound of the present disclosure and a pharmaceutically acceptable carrier. The composition may, for example, be adapted for administration by a route selected from the group consisting of orally, intraadiposally, intraarterially, intraarticularly, intracranially, intradermally, intralesionally, intramuscularly, intranasally, intraocularally, intrapericardially, intraperitoneally, intrapleurally, intraprostaticaly, intrarectally, intrathecally, intratracheally, intratumorally, intraumbilically, intravaginally, intravenously, intravesicularlly, intravitreally, liposomally, locally, mucosally, orally, 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,

via localized perfusion, bathing target cells directly, or any combination thereof. In particular ~~embodiments~~examples, the composition may be formulated for oral delivery. In particular ~~embodiments~~examples, the composition is formulated as a hard or soft capsule, a tablet, a syrup, a suspension, a wafer, or an elixir. In certain ~~embodiments~~examples, the soft capsule is a gelatin capsule. Certain compositions may comprise a protective coating, such as those compositions formulated for oral delivery. Certain compositions further comprise an agent that delays absorption, such as those compositions formulated for oral delivery. Certain compositions may further comprise an agent that enhances solubility or dispersibility, such as those compositions formulated for oral delivery. Certain compositions may comprise a compound of the present disclosure, wherein the compound is dispersed in a liposome, an oil and water emulsion or a water and oil emulsion.

Yet another general ~~aspect~~example of the present disclosure contemplates a therapeutic method comprising administering a pharmaceutically effective amount of a compound of the present disclosure to a subject. The subject may, for example, be a human. These or any other methods of the present disclosure may further comprise identifying a subject in need of treatment.

Another method of the present disclosure contemplates a method of treating cancer in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure. The cancer may be any type of cancer, such as a carcinoma, sarcoma, lymphoma, leukemia, melanoma, mesothelioma, multiple myeloma, or seminoma. Other types of cancers include cancer of the bladder, blood, bone, brain, breast, central nervous system, colon, endometrium, esophagus, genitourinary tract, head, larynx, liver, lung, neck, ovary, pancreas, prostate, spleen, small intestine, large intestine, stomach, or testicle. In these or any other methods, the subject may be a primate. This or any other method may further comprise identifying a subject in need of treatment. The subject may have a family or patient history of cancer. In certain ~~embodiments~~examples, the subject has symptoms of cancer. The compounds ~~of the invention~~ disclosed herein may be administered *via* any method described herein, such as locally. In certain ~~embodiments~~examples, the compound is administered by direct intratumoral injection or by injection into tumor vasculature. In certain ~~embodiments~~examples, the compounds may be administered systemically. The compounds may be administered intravenously, intra-arterially, intramuscularly, intraperitoneally, subcutaneously or orally, in certain ~~embodiments~~examples.

In certain ~~embodiments~~examples regarding methods of treating cancer in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the

present disclosure, the pharmaceutically effective amount is 0.1 – 1000 mg/kg. In certain ~~embodiments~~examples, the pharmaceutically effective amount is administered in a single dose per day. In certain ~~embodiments~~examples, the pharmaceutically effective amount is administered in two or more doses per day. The compound may be administered by contacting a tumor cell during *ex vivo* purging, for example. The method of treatment may comprise any one or more of the following: a) inducing cytotoxicity in a tumor cell; b) killing a tumor cell; c) inducing apoptosis in a tumor cell; d) inducing differentiation in a tumor cell; or e) inhibiting growth in a tumor cell. The tumor cell may be any type of tumor cell, such as a leukemia cell. Other types of cells include, for example, a bladder cancer cell, a breast cancer cell, a lung cancer cell, a colon cancer cell, a prostate cancer cell, a liver cancer cell, a pancreatic cancer cell, a stomach cancer cell, a testicular cancer cell, a brain cancer cell, an ovarian cancer cell, a lymphatic cancer cell, a skin cancer cell, a brain cancer cell, a bone cancer cell, or a soft tissue cancer cell.

Combination treatment therapy is also contemplated by the present disclosure. For example, regarding methods of treating cancer in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure, the method may further comprise a treatment selected from the group consisting of administering a pharmaceutically effective amount of a second drug, radiotherapy, gene therapy, and surgery. Such methods may further comprise (1) contacting a tumor cell with the compound prior to contacting the tumor cell with the second drug, (2) contacting a tumor cell with the second drug prior to contacting the tumor cell with the compound, or (3) contacting a tumor cell with the compound and the second drug at the same time. The second drug may, in certain ~~embodiments~~examples, be an antibiotic, anti-inflammatory, anti-neoplastic, anti-proliferative, anti-viral, immunomodulatory, or immunosuppressive. The second drug may be an alkylating agent, androgen receptor modulator, cytoskeletal disruptor, estrogen receptor modulator, histone-deacetylase inhibitor, HMG-CoA reductase inhibitor, prenyl-protein transferase inhibitor, retinoid receptor modulator, topoisomerase inhibitor, or tyrosine kinase inhibitor. In certain ~~embodiments~~examples, the second drug is 5-azacitidine, 5-fluorouracil, 9-cis-retinoic acid, actinomycin D, alitretinoin, all-trans-retinoic acid, annamycin, axitinib, belinostat, bevacizumab, bexarotene, bosutinib, busulfan, capecitabine, carboplatin, carmustine, CD437, cediranib, cetuximab, chlorambucil, cisplatin, cyclophosphamide, cytarabine, dacarbazine, dasatinib, daunorubicin, decitabine, docetaxel, dolastatin-10, doxifluridine, doxorubicin, doxorubicin, epirubicin, erlotinib, etoposide, etoposide, gefitinib, gemcitabine, gemtuzumab ozogamicin, hexamethylmelamine, idarubicin, ifosfamide,

Another general method of the present disclosure entails a method of treating or preventing a cardiovascular disease in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure. The cardiovascular disease may be, for example, atherosclerosis, cardiomyopathy, congenital heart disease, congestive heart failure, myocarditis, rheumatic heart disease, valve disease, coronary artery disease, endocarditis, or myocardial infarction. Combination therapy is also contemplated for such methods. For example, such methods may further comprise administering a pharmaceutically effective amount of a second drug. The second drug may be, for example, a cholesterol lowering drug, an anti-hyperlipidemic, a calcium channel blocker, an anti-hypertensive, or an HMG-CoA reductase inhibitor. Non-limiting examples of second drugs include amlodipine, aspirin, ezetimibe, felodipine, lacidipine, lercanidipine, nicardipine, nifedipine, nimodipine, nisoldipine or nitrendipine. Other non-limiting examples of second drugs include atenolol, bucindolol, carvedilol, clonidine, doxazosin, indoramin, labetalol, methyldopa, metoprolol, nadolol, oxprenolol, phenoxybenzamine, phentolamine, pindolol, prazosin, propranolol, terazosin, timolol or tolazoline. The second drug may be, for example, a statin, such as atorvastatin, cerivastatin, fluvastatin, lovastatin, mevastatin, pitavastatin, pravastatin, rosuvastatin or simvastatin.

Methods of treating or preventing a neurodegenerative disease in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure are also contemplated. The neurodegenerative disease may, for example, be selected from the group consisting of Parkinson's disease, Alzheimer's disease, multiple sclerosis (MS), Huntington's disease and amyotrophic lateral sclerosis. In particular ~~embodiments~~examples, the neurodegenerative disease is Alzheimer's disease. In particular ~~embodiments~~examples, the neurodegenerative disease is MS, such as primary progressive, relapsing-remitting secondary progressive or progressive relapsing MS. The subject may be, for example, a primate. The subject may be a human.

In particular ~~embodiments~~examples of methods of treating or preventing a neurodegenerative disease in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure, the treatment suppresses the demyelination of neurons in the subject's brain or spinal cord. In certain ~~embodiments~~examples, the treatment suppresses inflammatory demyelination. In certain ~~embodiments~~examples, the treatment suppresses the transection of neuron axons in the subject's brain or spinal cord. In certain ~~embodiments~~examples, the treatment suppresses the transection of neurites in the subject's brain or spinal cord. In certain ~~embodiments~~examples, the treatment suppresses neuronal apoptosis in the subject's brain or

spinal cord. In certain ~~embodiments~~examples, the treatment stimulates the remyelination of neuron axons in the subject's brain or spinal cord. In certain ~~embodiments~~examples, the treatment restores lost function after an MS attack. In certain ~~embodiments~~examples, the treatment prevents a new MS attack. In certain ~~embodiments~~examples, the treatment prevents a disability resulting from an MS attack.

One general ~~aspect~~example of the present disclosure contemplates a method of treating or preventing a disorder characterized by overexpression of iNOS genes in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure.

Another general ~~aspect~~example of the present disclosure contemplates a method of inhibiting IFN-γ-induced nitric oxide production in cells of a subject, comprising administering to said subject a pharmaceutically effective amount of a compound of the present disclosure.

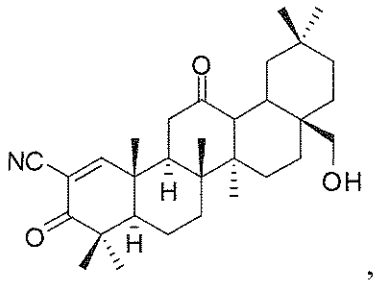
Yet another general method of the present disclosure contemplates a method of treating or preventing a disorder characterized by overexpression of COX-2 genes in a subject, comprising administering to the subject a pharmaceutically effective amount of compound of the present disclosure.

Methods of treating renal/kidney disease (RKD) in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure are also contemplated. See U.S. Patent Application 12/352,473, which is incorporated by reference herein in its entirety. The RKD may result from, for example, a toxic insult. The toxic insult may result from, for example, an imaging agent or a drug. The drug may be a chemotherapeutic, for example. The RKD may result from ischemia/reperfusion injury, in certain ~~embodiments~~examples. In certain ~~embodiments~~examples, the RKD results from diabetes or hypertension. The RKD may result from an autoimmune disease. The RKD may be further defined as chronic RKD, or acute RKD.

In certain methods of treating renal/kidney disease (RKD) in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure, the subject has undergone or is undergoing dialysis. In certain ~~embodiments~~examples, the subject has undergone or is a candidate to undergo kidney transplant. The subject may be a primate. The primate may be a human. The subject in this or any other method may be, for example, a cow, horse, dog, cat, pig, mouse, rat or guinea pig.

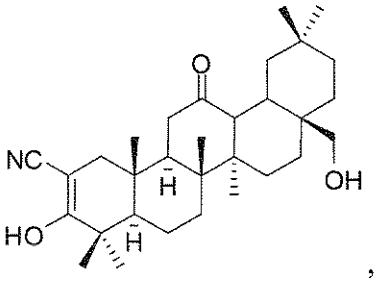
Also contemplated by the present disclosure is a method for improving glomerular filtration rate or creatinine clearance in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure.

Methods of synthesizing compounds of the present disclosure are also contemplated. In particular ~~embodiments~~examples, such methods can comprise a method of making a target compound defined of the formula:



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comprising reacting a compound of the formula:



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with an oxidizing agent under a set of conditions to form the target compound.

Kits are also contemplated by the present disclosure, such as a kit comprising: a compound of the present disclosure; and instructions which comprise one or more forms of information selected from the group consisting of indicating a disease state for which the compound is to be administered, storage information for the compound, dosing information and instructions regarding how to administer the compound. The kit may comprise a compound of the present disclosure in a multiple dose form.

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 embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention 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.