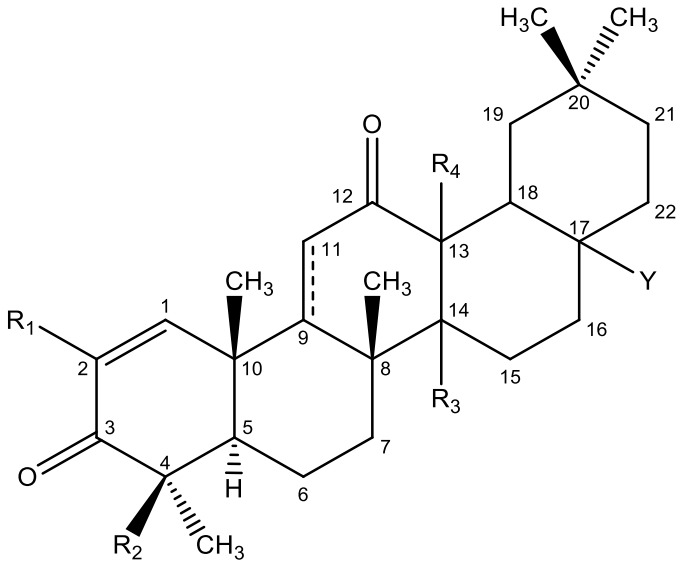
CLAIMS

1. Use of a compound of the formula:



(I),

wherein:

R_1 is −CN, halo, $-CF_3$, or $-C(O)R_a$, wherein R_a is −OH, $alkoxy_{(C1-4)}$, $-NH_2$, $alkylamino_{(C1-4)}$, or $-NH-S(O)_2-alkyl_{(C1-4)}$;

R_2 is hydrogen or methyl;

R_3 and R_4 are each independently hydrogen, hydroxy, methyl or as defined below when either of these groups is taken together with group R_c; and

Y is:

−H, −OH, −SH, −CN, −F, $-CF_3$, $-NH_2$ or −NCO;

$alkyl_{(C\leq8)}$, $cycloalkyl_{(C\leq8)}$, $alkenyl_{(C\leq8)}$, $alkynyl_{(C\leq8)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq8)}$, $heterocycloalkyl_{(C\leq12)}$, $alkoxy_{(C\leq8)}$, $cycloalkoxy_{(C\leq8)}$, $aryloxy_{(C\leq12)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $cycloalkylamino_{(C\leq8)}$, $dialkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$, $aralkylamino_{(C\leq8)}$, $alkylthio_{(C\leq8)}$, $acylthio_{(C\leq8)}$, $alkylsulfonylamino_{(C\leq8)}$, $cycloalkylsulfonylamino_{(C\leq8)}$, or substituted versions of any of these groups;

$-alkanediyl_{(C\leq8)}-R_b$, $-alkenediyl_{(C\leq8)}-R_b$, or a substituted version of any of these groups, wherein R_b is:

hydrogen, hydroxy, halo, amino or mercapto; or

heteroaryl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, aralkylamino$_{(C\leq 8)}$, heteroarylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −OC(O)NH−alkyl$_{(C\leq 8)}$, or a substituted version of any of these groups;

$-(CH_2)_mC(O)R_c$, wherein m is 0–6 and R_c is:

hydrogen, hydroxy, halo, amino, −NHOH, or mercapto; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −NH−alkoxy$_{(C\leq 8)}$, −NH–heterocycloalkyl$_{(C\leq 8)}$, −NH–amido$_{(C\leq 8)}$, or a substituted version of any of these groups;

R_c and R_3, taken together, are −O− or $-NR_d-$, wherein R_d is hydrogen or alkyl$_{(C\leq 4)}$; or

R_c and R_4, taken together, are −O− or $-NR_d-$, wherein R_d is hydrogen or alkyl$_{(C\leq 4)}$; or

$-NHC(O)R_e$, wherein R_e is:

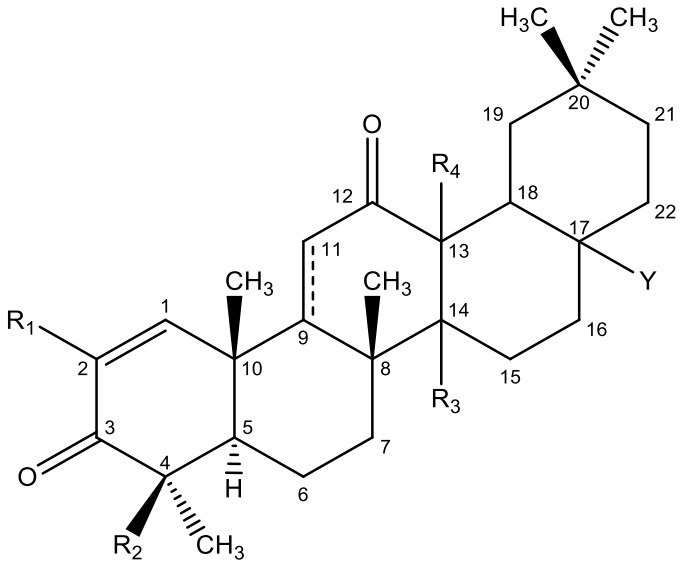
hydrogen, hydroxy, amino; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a patient infected with SARS-CoV-2, wherein the medicament comprises a pharmaceutically effective amount of the compound.

2. The use of claim 1, wherein the patient has been identified as not having a history of left-sided heart failure or wherein the patient does not show evidence of left ventricular dysfunction.

3. Use of a compound of the formula:



(I),

wherein:

R_1 is −CN, halo, $-CF_3$, or $-C(O)R_a$, wherein R_a is −OH, $alkoxy_{(C1-4)}$, $-NH_2$, $alkylamino_{(C1-4)}$, or $-NH-S(O)_2-alkyl_{(C1-4)}$;

R_2 is hydrogen or methyl;

R_3 and R_4 are each independently hydrogen, hydroxy, methyl or as defined below when either of these groups is taken together with group R_c; and

Y is:

−H, −OH, −SH, −CN, −F, $-CF_3$, $-NH_2$ or −NCO;

$alkyl_{(C\leq8)}$, $cycloalkyl_{(C\leq8)}$, $alkenyl_{(C\leq8)}$, $alkynyl_{(C\leq8)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq8)}$, $heterocycloalkyl_{(C\leq12)}$, $alkoxy_{(C\leq8)}$, $cycloalkoxy_{(C\leq8)}$, $aryloxy_{(C\leq12)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $cycloalkylamino_{(C\leq8)}$, $dialkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$, $aralkylamino_{(C\leq8)}$, $alkylthio_{(C\leq8)}$, $acylthio_{(C\leq8)}$,

alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, or substituted versions of any of these groups;

−alkanediyl$_{(C\leq 8)}$−R_b, −alkenediyl$_{(C\leq 8)}$−R_b, or a substituted version of any of these groups, wherein R_b is:

hydrogen, hydroxy, halo, amino or mercapto; or

heteroaryl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, aralkylamino$_{(C\leq 8)}$, heteroarylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −OC(O)NH−alkyl$_{(C\leq 8)}$, or a substituted version of any of these groups;

$-(CH_2)_mC(O)R_c$, wherein m is 0–6 and R_c is:

hydrogen, hydroxy, halo, amino, −NHOH, or mercapto; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −NH−alkoxy$_{(C\leq 8)}$, −NH–heterocycloalkyl$_{(C\leq 8)}$, −NH–amido$_{(C\leq 8)}$, or a substituted version of any of these groups;

R_c and R_3, taken together, are −O− or −NR_d−, wherein R_d is hydrogen or alkyl$_{(C\leq 4)}$; or

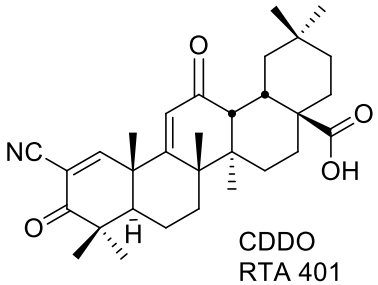
R_c and R_4, taken together, are −O− or −NR_d−, wherein R_d is hydrogen or alkyl$_{(C\leq 4)}$; or

−NHC(O)R_e, wherein R_e is:

hydrogen, hydroxy, amino; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a patient infected with SARS-CoV-2, wherein the medicament comprises a pharmaceutically effective amount of the compound, and

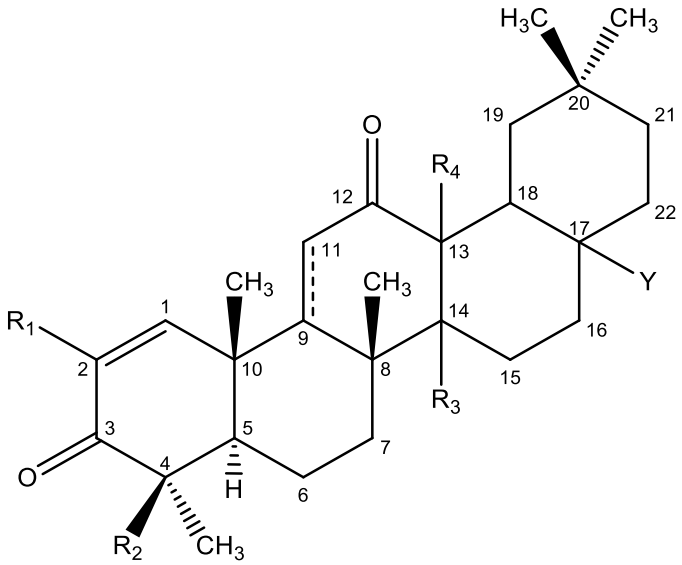


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wherein the compound is not .

4. The use of claim 3, wherein the patient has been identified as not having a history of left-sided heart failure or wherein the patient does not show evidence of left ventricular dysfunction.

5. Use of a compound of the formula:



(I),

wherein:

R_1 is −CN, halo, $-CF_3$, or $-C(O)R_a$, wherein R_a is −OH, $alkoxy_{(C1-4)}$, $-NH_2$, $alkylamino_{(C1-4)}$, or $-NH-S(O)_2-alkyl_{(C1-4)}$;

R_2 is hydrogen or methyl;

R_3 and R_4 are each independently hydrogen, hydroxy, methyl or as defined below when either of these groups is taken together with group R_c; and

Y is:

−H, −OH, −SH, −CN, −F, $-CF_3$, $-NH_2$ or −NCO;

$alkyl_{(C\leq8)}$, $cycloalkyl_{(C\leq8)}$, $alkenyl_{(C\leq8)}$, $alkynyl_{(C\leq8)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq8)}$, $heterocycloalkyl_{(C\leq12)}$, $alkoxy_{(C\leq8)}$, $cycloalkoxy_{(C\leq8)}$, $aryloxy_{(C\leq12)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $cycloalkylamino_{(C\leq8)}$, $dialkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$, $aralkylamino_{(C\leq8)}$, $alkylthio_{(C\leq8)}$, $acylthio_{(C\leq8)}$, $alkylsulfonylamino_{(C\leq8)}$, $cycloalkylsulfonylamino_{(C\leq8)}$, or substituted versions of any of these groups;

$-alkanediyl_{(C\leq8)}-R_b$, $-alkenediyl_{(C\leq8)}-R_b$, or a substituted version of any of these groups, wherein R_b is:

hydrogen, hydroxy, halo, amino or mercapto; or

$heteroaryl_{(C\leq8)}$, $alkoxy_{(C\leq8)}$, $cycloalkoxy_{(C\leq8)}$, $alkenyloxy_{(C\leq8)}$, $aryloxy_{(C\leq8)}$, $aralkoxy_{(C\leq8)}$, $heteroaryloxy_{(C\leq8)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $cycloalkylamino_{(C\leq8)}$, $dialkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$, $aralkylamino_{(C\leq8)}$, $heteroarylamino_{(C\leq8)}$, $alkylsulfonylamino_{(C\leq8)}$, $cycloalkylsulfonylamino_{(C\leq8)}$, $amido_{(C\leq8)}$, $-OC(O)NH-alkyl_{(C\leq8)}$, or a substituted version of any of these groups;

$-(CH_2)_mC(O)R_c$, wherein m is 0–6 and R_c is:

hydrogen, hydroxy, halo, amino, −NHOH, or mercapto; or

$alkyl_{(C\leq8)}$, $cycloalkyl_{(C\leq8)}$, $alkenyl_{(C\leq8)}$, $alkynyl_{(C\leq8)}$, $aryl_{(C\leq8)}$, $aralkyl_{(C\leq8)}$, $heteroaryl_{(C\leq8)}$, $heterocycloalkyl_{(C\leq8)}$, $alkoxy_{(C\leq8)}$, $cycloalkoxy_{(C\leq8)}$, $alkenyloxy_{(C\leq8)}$, $aryloxy_{(C\leq8)}$, $aralkoxy_{(C\leq8)}$, $heteroaryloxy_{(C\leq8)}$,

acyloxy$_{(C\leq8)}$, alkylamino$_{(C\leq8)}$, cycloalkylamino$_{(C\leq8)}$, dialkylamino$_{(C\leq8)}$, arylamino$_{(C\leq8)}$, alkylsulfonylamino$_{(C\leq8)}$, cycloalkylsulfonylamino$_{(C\leq8)}$, amido$_{(C\leq8)}$, −NH−alkoxy$_{(C\leq8)}$, −NH–heterocycloalkyl$_{(C\leq8)}$, −NH–amido$_{(C\leq8)}$, or a substituted version of any of these groups;

R_c and R_3, taken together, are −O− or −NR_d−, wherein R_d is hydrogen or alkyl$_{(C\leq4)}$; or

R_c and R_4, taken together, are −O− or −NR_d−, wherein R_d is hydrogen or alkyl$_{(C\leq4)}$; or

−NHC(O)R_e, wherein R_e is:

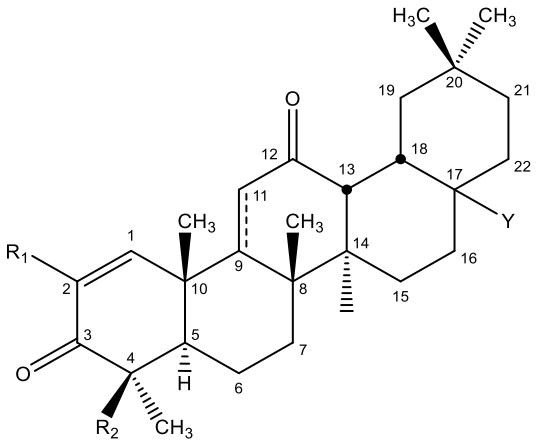
hydrogen, hydroxy, amino; or

alkyl$_{(C\leq8)}$, cycloalkyl$_{(C\leq8)}$, alkenyl$_{(C\leq8)}$, alkynyl$_{(C\leq8)}$, aryl$_{(C\leq8)}$, aralkyl$_{(C\leq8)}$, heteroaryl$_{(C\leq8)}$, heterocycloalkyl$_{(C\leq8)}$, alkoxy$_{(C\leq8)}$, cycloalkoxy$_{(C\leq8)}$, aryloxy$_{(C\leq8)}$, aralkoxy$_{(C\leq8)}$, heteroaryloxy$_{(C\leq8)}$, acyloxy$_{(C\leq8)}$, alkylamino$_{(C\leq8)}$, cycloalkylamino$_{(C\leq8)}$, dialkylamino$_{(C\leq8)}$, arylamino$_{(C\leq8)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a patient infected with SARS-CoV-2, wherein the medicament comprises a pharmaceutically effective amount of the compound, and

wherein the patient has been identified as not having a history of left-sided heart failure or wherein the patient does not show evidence of left ventricular dysfunction.

6. The use of any one of claims 1-5, wherein the compound is further defined as:



(II),

wherein:

R_1 is −CN, halo, $-CF_3$, or $-C(O)R_a$, wherein R_a is −OH, $alkoxy_{(C1-4)}$, $-NH_2$, $alkylamino_{(C1-4)}$, or $-NH-S(O)_2-alkyl_{(C1-4)}$;

R_2 is hydrogen or methyl;

Y is:

−H, −OH, −SH, −CN, −F, $-CF_3$, $-NH_2$ or −NCO;

$alkyl_{(C\leq8)}$, $cycloalkyl_{(C\leq8)}$, $alkenyl_{(C\leq8)}$, $alkynyl_{(C\leq8)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq8)}$, $heterocycloalkyl_{(C\leq12)}$, $alkoxy_{(C\leq8)}$, $cycloalkoxy_{(C\leq8)}$, $aryloxy_{(C\leq12)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $cycloalkylamino_{(C\leq8)}$, $dialkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$, $aralkylamino_{(C\leq8)}$, $alkylthio_{(C\leq8)}$, $acylthio_{(C\leq8)}$, $alkylsulfonylamino_{(C\leq8)}$, $cycloalkylsulfonylamino_{(C\leq8)}$, or substituted versions of any of these groups;

$-alkanediyl_{(C\leq8)}-R_b$, $-alkenediyl_{(C\leq8)}-R_b$, or a substituted version of any of these groups, wherein R_b is:

hydrogen, hydroxy, halo, amino or mercapto; or

$heteroaryl_{(C\leq8)}$, $alkoxy_{(C\leq8)}$, $cycloalkoxy_{(C\leq8)}$, $alkenyloxy_{(C\leq8)}$, $aryloxy_{(C\leq8)}$, $aralkoxy_{(C\leq8)}$, $heteroaryloxy_{(C\leq8)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $cycloalkylamino_{(C\leq8)}$, $dialkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$, $aralkylamino_{(C\leq8)}$, $heteroarylamino_{(C\leq8)}$, $alkylsulfonylamino_{(C\leq8)}$, $cycloalkylsulfonylamino_{(C\leq8)}$, $amido_{(C\leq8)}$, $-OC(O)NH-alkyl_{(C\leq8)}$, or a substituted version of any of these groups;

$-(CH_2)_mC(O)R_c$, wherein m is 0–6 and R_c is:

hydrogen, hydroxy, halo, amino, −NHOH, or mercapto; or

$alkyl_{(C\leq8)}$, $cycloalkyl_{(C\leq8)}$, $alkenyl_{(C\leq8)}$, $alkynyl_{(C\leq8)}$, $aryl_{(C\leq8)}$, $aralkyl_{(C\leq8)}$, $heteroaryl_{(C\leq8)}$, $heterocycloalkyl_{(C\leq8)}$, $alkoxy_{(C\leq8)}$, $cycloalkoxy_{(C\leq8)}$, $alkenyloxy_{(C\leq8)}$, $aryloxy_{(C\leq8)}$, $aralkoxy_{(C\leq8)}$, $heteroaryloxy_{(C\leq8)}$, $acyloxy_{(C\leq8)}$, $alkylamino_{(C\leq8)}$, $cycloalkylamino_{(C\leq8)}$, $dialkylamino_{(C\leq8)}$, $arylamino_{(C\leq8)}$,

alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −NH−alkoxy$_{(C\leq 8)}$, −NH–heterocycloalkyl$_{(C\leq 8)}$, −NH–amido$_{(C\leq 8)}$, or a substituted version of any of these groups;

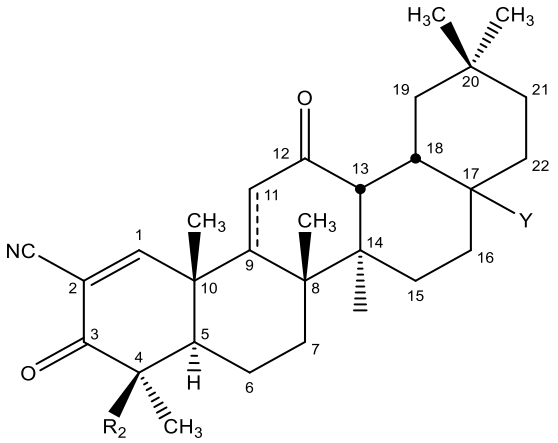
−NHC(O)R_e, wherein R_e is:

hydrogen, hydroxy, amino; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof.

7. The use of claim 6, wherein the compound is further defined as:



(III),

wherein:

R_2 is hydrogen or methyl;

Y is:

−H, −OH, −SH, −CN, −F, −CF_3, −NH_2 or −NCO;

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, aralkylamino$_{(C\leq 8)}$, alkylthio$_{(C\leq 8)}$, acylthio$_{(C\leq 8)}$,

alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, or substituted versions of any of these groups;

−alkanediyl$_{(C\leq 8)}$−R_b, −alkenediyl$_{(C\leq 8)}$−R_b, or a substituted version of any of these groups, wherein R_b is:

hydrogen, hydroxy, halo, amino or mercapto; or

heteroaryl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, aralkylamino$_{(C\leq 8)}$, heteroarylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −OC(O)NH−alkyl$_{(C\leq 8)}$, or a substituted version of any of these groups;

$-(CH_2)_mC(O)R_c$, wherein m is 0–6 and R_c is:

hydrogen, hydroxy, halo, amino, −NHOH, or mercapto; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −NH−alkoxy$_{(C\leq 8)}$, −NH–heterocycloalkyl$_{(C\leq 8)}$, −NH–amido$_{(C\leq 8)}$, or a substituted version of any of these groups;

$-NHC(O)R_e$, wherein R_e is:

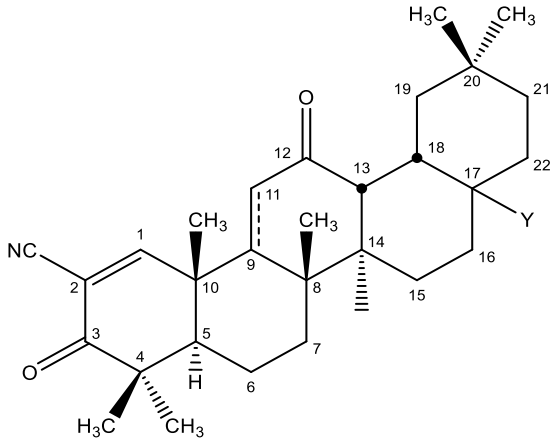
hydrogen, hydroxy, amino; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$,

cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof.

8. The use of claim 7, wherein the compound is further defined as:



(IV),

wherein:

Y is:

−H, −OH, −SH, −CN, −F, −CF_3, −NH_2 or −NCO;

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, aralkylamino$_{(C\leq 8)}$, alkylthio$_{(C\leq 8)}$, acylthio$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, or substituted versions of any of these groups;

−alkanediyl$_{(C\leq 8)}$−R_b, −alkenediyl$_{(C\leq 8)}$−R_b, or a substituted version of any of these groups, wherein R_b is:

hydrogen, hydroxy, halo, amino or mercapto; or

heteroaryl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, aralkylamino$_{(C\leq 8)}$, heteroarylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$,

−OC(O)NH−alkyl$_{(C\leq 8)}$, or a substituted version of any of these groups;

−$(CH_2)_m$C(O)R_c, wherein m is 0–6 and R_c is:

hydrogen, hydroxy, halo, amino, −NHOH, or mercapto; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −NH−alkoxy$_{(C\leq 8)}$, −NH–heterocycloalkyl$_{(C\leq 8)}$, −NH–amido$_{(C\leq 8)}$, or a substituted version of any of these groups;

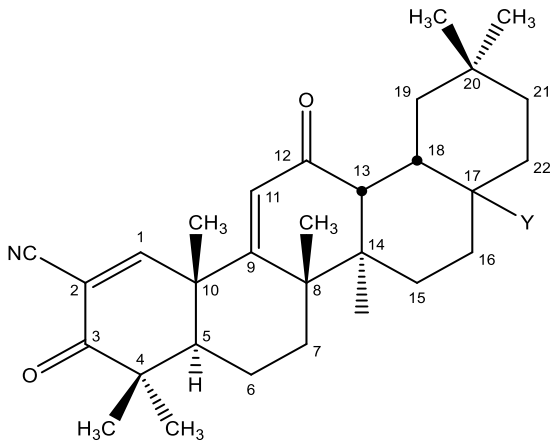
−NHC(O)R_e, wherein R_e is:

hydrogen, hydroxy, amino; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof.

9. The use of claim 8, wherein the compound is further defined as:



(V),

wherein:

Y is:

−H, −OH, −SH, −CN, −F, $-CF_3$, $-NH_2$ or −NCO;

$alkyl_{(C\leq 8)}$, $cycloalkyl_{(C\leq 8)}$, $alkenyl_{(C\leq 8)}$, $alkynyl_{(C\leq 8)}$, $aryl_{(C\leq 12)}$, $aralkyl_{(C\leq 12)}$, $heteroaryl_{(C\leq 8)}$, $heterocycloalkyl_{(C\leq 12)}$, $alkoxy_{(C\leq 8)}$, $cycloalkoxy_{(C\leq 8)}$, $aryloxy_{(C\leq 12)}$, $acyloxy_{(C\leq 8)}$, $alkylamino_{(C\leq 8)}$, $cycloalkylamino_{(C\leq 8)}$, $dialkylamino_{(C\leq 8)}$, $arylamino_{(C\leq 8)}$, $aralkylamino_{(C\leq 8)}$, $alkylthio_{(C\leq 8)}$, $acylthio_{(C\leq 8)}$, $alkylsulfonylamino_{(C\leq 8)}$, $cycloalkylsulfonylamino_{(C\leq 8)}$, or substituted versions of any of these groups;

$-alkanediyl_{(C\leq 8)}-R_b$, $-alkenediyl_{(C\leq 8)}-R_b$, or a substituted version of any of these groups, wherein R_b is:

hydrogen, hydroxy, halo, amino or mercapto; or

$heteroaryl_{(C\leq 8)}$, $alkoxy_{(C\leq 8)}$, $cycloalkoxy_{(C\leq 8)}$, $alkenyloxy_{(C\leq 8)}$, $aryloxy_{(C\leq 8)}$, $aralkoxy_{(C\leq 8)}$, $heteroaryloxy_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, $alkylamino_{(C\leq 8)}$, $cycloalkylamino_{(C\leq 8)}$, $dialkylamino_{(C\leq 8)}$, $arylamino_{(C\leq 8)}$, $aralkylamino_{(C\leq 8)}$, $heteroarylamino_{(C\leq 8)}$, $alkylsulfonylamino_{(C\leq 8)}$, $cycloalkylsulfonylamino_{(C\leq 8)}$, $amido_{(C\leq 8)}$, $-OC(O)NH-alkyl_{(C\leq 8)}$, or a substituted version of any of these groups;

$-(CH_2)_mC(O)R_c$, wherein m is 0–6 and R_c is:

hydrogen, hydroxy, halo, amino, −NHOH, or mercapto; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, alkenyloxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, cycloalkylsulfonylamino$_{(C\leq 8)}$, amido$_{(C\leq 8)}$, −NH−alkoxy$_{(C\leq 8)}$, −NH–heterocycloalkyl$_{(C\leq 8)}$, −NH–amido$_{(C\leq 8)}$, or a substituted version of any of these groups;

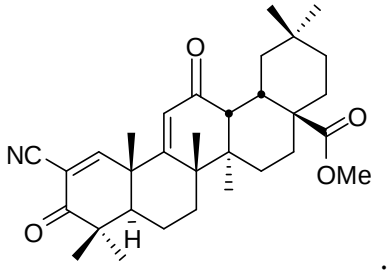
−NHC(O)R_e, wherein R_e is:

hydrogen, hydroxy, amino; or

alkyl$_{(C\leq 8)}$, cycloalkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 8)}$, aralkyl$_{(C\leq 8)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 8)}$, alkoxy$_{(C\leq 8)}$, cycloalkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 8)}$, aralkoxy$_{(C\leq 8)}$, heteroaryloxy$_{(C\leq 8)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, cycloalkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, or a substituted version of any of these groups;

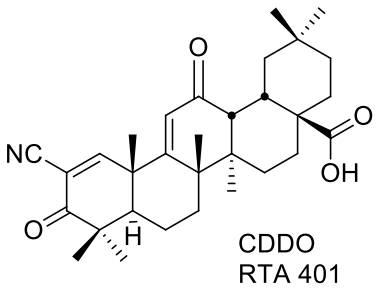
or a pharmaceutically acceptable salt thereof.

10. The use of claim 9, wherein the compound is further defined as:



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11. The use of any one of claims 1-9, wherein the compound is not



CDDO
RTA 401

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12. The use according to any one of claims 1-11, wherein the patient has radiographic infiltrates by imaging prior to treatment.

13. The use of claim 12, wherein the imaging is a chest X-ray or CT scan.

14. The use according to any one of claims 1-13, wherein the patient's blood oxygen saturation, at rest, is at most 94% prior to treatment.

15. The use according to any one of claims 1-14, wherein the patient requires supplemental oxygen prior to treatment.

16. The use according to any one of claims 1-15, wherein the patient requires non-invasive ventilation prior to treatment.

17. The use according to any one of claims 1-16, wherein the patient requires mechanical ventilation for up to 2 days prior to treatment.

18. The use according to any one of claims 1-11, wherein the medicament is for treating or preventing COVID-19 in a patient in need thereof.

19. The use according to any one of claim 1-11, wherein the coronavirus is a betacoronavirus.

20. The use according to any one of claims 1-11, wherein the coronavirus is a severe acute respiratory syndrome-related (SARS) coronavirus.

21. The use according to any one of claims 1-18, wherein the coronavirus is SARS-CoV-2.

22. The use according to any one of claims 1-21, wherein the medicament is for inhibiting replication of SARS-CoV-2 in the patient.

23. The use according to any one of claims 1-22, wherein the medicament is for suppressing or preventing systemic inflammation in the patient.

24. The use of claim 23, wherein the medicament is for suppressing or preventing a cytokine storm in the patient.

25. The use according to any one of claims 1-23, wherein the medicament is for suppressing or preventing lung inflammation in the patient.

26. The use according to any one of claims 1-25, wherein the medicament is for treating or preventing inflammation-induced liver damage in the patient.

27. The use according to any one of claims 1-26, wherein the medicament is for treating or preventing acute lung injury in the patient.

28. The use according to any one of claims 1-27, wherein the medicament is for treating or preventing kidney damage in the patient.

29. The use according to any one of claims 1-28, wherein the medicament is for treating or preventing acute kidney injury in the patient.

30. The use according to any one of claims 1-29, wherein the medicament is for improving kidney function in the patient.

31. The use according to any one of claims 1-30, wherein the medicament is for increasing the patient's estimated glomerular filtration rate (eGFR).

32. The use according to any one of claims 1-31, wherein the medicament is for treating or preventing acute respiratory distress syndrome in the patient.

33. The use according to any one of claims 1-32, wherein the medicament is for treating or preventing seizures in the patient.

34. The use according to any one of claims 1-33, wherein the medicament is for treating or preventing brain inflammation in the patient.

35. The use according to any one of claims 1-34, wherein the medicament is for reducing the hospitalization time of the patient.

36. The use according to any one of claims 1-35, wherein the medicament is for reducing the time spent in the intensive care unit.

37. The use according of any one of claims 1-34, wherein the medicament is for delaying the need for hospitalization of the patient.

38. The use according of any one of claims 1-37, wherein the medicament is for increasing the probability of survival of the patient.

39. The use according of any one of claims 1-38, wherein the medicament is for preventing the need for non-invasive mechanical ventilation.

40. The use according of any one of claims 1-39, wherein the medicament is for preventing the need for invasive mechanical ventilation.

41. The use according of any one of claims 1-40, wherein the medicament is for preventing respiratory failure.

42. The use according to any one of claims 1-41, wherein the medicament is for lowering the patient's WHO score.

43. The use according of any one of claims 1-42, wherein the medicament is for preventing the need for renal replacement therapy.

44. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as a crystalline form having an X-ray diffraction pattern (CuKα) comprising significant diffraction peaks at about 8.8, 12.9, 13.4, 14.2 and 17.4 °2θ.

45. The use of claim 44, wherein the X-ray diffraction pattern (CuKα) is substantially as shown in FIG. 1A or FIG. 1B.

46. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as an amorphous form having an X-ray diffraction pattern (CuKα) with a peak at approximately 13.5 °2θ, substantially as shown in FIG. 1C, and a transition glass temperature (T_g).

47. The use of claim 46, wherein the T_g value is in the range of about 120 °C to about 135 °C.

48. The use of claim 47, wherein the T_g value is in the range of about 125 °C to about 130 °C.

49. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as a crystalline form having an X-ray diffraction pattern (CuKα) comprising significant diffraction peaks at about 6.2, 12.4, 15.4, 18.6 and 24.9 °2θ.

50. The use of claim 49, wherein the crystalline form is further characterized by one, two, three, four or five additional diffraction peaks selected from the group consisting of 8.6, 13.3, 13.7, 17.1 and 21.7 °2θ.

51. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as a crystalline form having an X-ray diffraction pattern (CuKα) comprising significant diffraction peaks at about 3.6, 7.1, 10.8, 12.4 and 16.5 °2θ.

52. The use of claim 51, wherein the crystalline form is further characterized by one, two, three, four or five additional diffraction peaks selected from the group consisting of 12.9, 13.9, 14.8, 18.6 and 20.6°2θ.

53. The use of either claim 51 or 52, wherein the crystalline form is further characterized by a Raman spectrum having peaks at 2949, 1671, 1618 and 1464 ± 4 cm^{-1}.

54. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as a toluene solvate crystalline form having an X-ray diffraction pattern (CuKα) comprising diffraction peaks at about 9.65, 7.58, 7.18, 6.29, 6.06, 5.47, 5.21, 4.77 and 3.07 °2θ.

55. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as a semi-dioxane solvate crystalline form having an X-ray diffraction pattern (CuKα) comprising diffraction peaks at about 10.01, 7.09, 6.84, 6.23, 5.29, 5.20, 5.10, 4.84, and 4.61 °2θ.

56. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as a semi-tetrahydrofuran solvate crystalline form having an X-ray diffraction pattern (CuKα) comprising diffraction peaks at about 10.00, 7.14, 6.80, 6.65, 6.10, 5.62, 5.29, 4.88, and 4.50 °2θ.

57. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as a methanol solvate crystalline form having an X-ray diffraction pattern (CuKα) comprising diffraction peaks at about 8.86, 8.45, 8.17, 7.90, 7.26, 4.67, 6.63, 6.46, and 3.64 °2θ.

58. The use according to any one of claims 10-43, wherein at least a portion of the compound is present as an anhydrous crystalline form having an X-ray diffraction pattern (CuKα) comprising diffraction peaks at about 12.05, 8.90, 8.49, 8.13, 7.92, 7.29, 6.64, 4.67 and 3.65 °2θ.

59. The use according to any one of claims 10-43, wherein at least a portion of the compound is present a dihydrate crystalline form having an X-ray diffraction pattern (CuKα) comprising diffraction peaks at about 8.81, 8.48, 7.91, 7.32, 5.09, 4.24, 3.58, 3.36 and 3.17 °2θ.

60. The use according to any one of claims 1-59, wherein the therapeutically effective amount is a daily dose from about 0.1 mg to about 300 mg of the compound.

61. The use of claim 60, wherein the daily dose is from about 0.5 mg to about 200 mg of the compound.

62. The use of claim 61, wherein the daily dose is from about 1 mg to about 150 mg of the compound.

63. The use of claim 62, wherein the daily dose is from about 1 mg to about 75 mg of the compound.

64. The use of claim 63, wherein the daily dose is from about 1 mg to about 20 mg of the compound.

65. The use of claim 60, wherein the daily dose is from about 2.5 mg to about 30 mg of the compound.

66. The use of claim 65, wherein the daily dose is about 2.5 mg of the compound.

67. The use of claim 65, wherein the daily dose is about 5 mg of the compound.

68. The use of claim 65, wherein the daily dose is about 10 mg of the compound.

69. The use of claim 65, wherein the daily dose is about 15 mg of the compound.

70. The use of claim 65, wherein the daily dose is about 20 mg of the compound.

71. The use of claim 65, wherein the daily dose is about 30 mg of the compound.

72. The use according to any one of claims 1-59, wherein the medicament is formulated for administration orally, intraarterially or intravenously.

73. The use according to any one of claims 1-59, wherein the medicament is formulated as a hard or soft capsule or a tablet.

74. The use according to any one of claims 1-59, wherein the medicament is formulated as a solid dispersion comprising (i) the compound and (ii) an excipient.

75. The use of claim 74, wherein the excipient is a methacrylic acid – ethyl acrylate copolymer.

76. The use of claim 75, wherein the copolymer comprises methacrylic acid and ethyl acrylate at a 1:1 ratio.