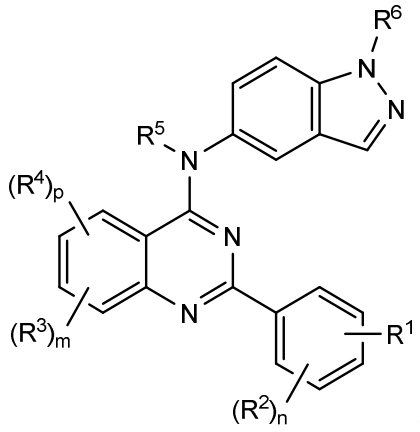
What is claimed:

1. Use of a ROCK2 inhibitor in the manufacture of a medicament for treating a viral infection in a subject in need thereof.
2. Use of a ROCK2 inhibitor in the manufacture of a medicament for preventing a viral infection in a subject at risk for the viral infection.
3. Use of a ROCK2 inhibitor in the manufacture of a medicament for treating Kawasaki disease, PMIS, or PIMS-TS associated with a viral infection in a subject in need thereof.
4. Use of a ROCK2 inhibitor in the manufacture of a medicament for the treatment or prevention of sequelae resulting from a viral infection in a subject in need thereof.
5. The use of any one of claims 1-4, wherein the ROCK2 inhibitor is a ROCK2 selective inhibitor.
6. The use of any one of claims 1-5, wherein the ROCK2 inhibitor is a ribonucleic acid (RNA).
7. The use of claim 6, wherein the ROCK2 inhibitor is an antisense RNA, a small interfering RNA or a microRNA.
8. The use of any one of claims 1-5, wherein the ROCK2 inhibitor is a compound having the structure of Formula I:



(I)

or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof, wherein:

R^1 is selected from the group consisting of —O—$(CH_2)_rCO_2R^{12}$, —O—$(CH_2)_y$, —C(═O)$NR^{13}R^{14}$, —O—$(CH_2)_y$, -heteroaryl, —O—$(CH_2)_y$, -cycloalkyl, —O—C(═O)—$(CH_2)_y$, —$NR^{13}R^{14}$, —O—$(CH_2)_z$—$NR^{13}R^{14}$, —NH—C(═O)—$(CH_2)_y$, —$NR^{13}R^{14}$, —NH—C(═O)—X—R^{15}, and —NH—$(CH_2)_y$, —$NR^{13}R^{14}$;

R^{12} is selected from the group consisting of C_1-C_6 alkyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{16}R^{17}$, —(C_1-C_6 alkyl)-C(═O)$NR^{16}R^{17}$, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted at one or more carbon atoms by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

R^{13} and R^{14} are independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{16}R^{17}$, —(C_1-C_6 alkyl)-C(═O)$NR^{16}R^{17}$, aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{13} and R^{14} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

X is absent or selected from a -O, NH, and C_1-C_6 alkyl;

R^{15} is selected from the group consisting of heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{15} is selected from —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{16}R^{17}$, —CO_2R^{18}, —O—$(CH_2)_x$—CO_2R^{18}, and —C(═O)$NR^{16}R^{17}$;

R^{16} and R^{17} are independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents

independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{16} and R^{17} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

R^{18} is selected from the group consisting of H, aryl, aralkyl, heteroaryl, C_1-C_6 alkyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{16}R^{17}$, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoroalkyl;

x is selected from 0 to 6;

y is selected from 0 to 6;

z is selected from 2 to 6;

each R^2 is independently selected from the group consisting of lower alkyl, CN, halo, hydroxy, lower alkoxy, amino, and perfluoro lower alkyl;

each R^3 is independently selected from the group consisting of lower alkyl, CN, halo, hydroxy, lower alkoxy, amino, and perfluoro lower alkyl;

R^4 is selected from H, —$(CH_2)_a$—$NR^{43}R^{44}$, —Y—R^{42}, —O—$(CH_2)_a$—CO_2R^{42}, —O—$(CH_2)_a$—C(=O)$NR^{43}R^{44}$, —O—$(CH_2)_a$-heteroaryl, —O—$(CH_2)_a$-cycloalkyl, —O—C(=O)—$(CH_2)_a$—$NR^{43}R^{44}$, —O—$(CH_2)_c$—$N^{43}R^{44}$, —NH—C(=O)—Y—R^{45}, —NH—C(=O)—$(CH_2)_a$—$NR^{43}R^{44}$;

R^{42} is selected from the group consisting of C_1-C_6 alkyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{46}R^{47}$, —(C_1-C_6 alkyl)-C(=O)$N^{46}R^{47}$, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), each of which may be optionally substituted at one or more carbon atoms by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

R^{43} and R^{44} are independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{46}R^{47}$, —(C_1-C_6 alkyl)-C(═O)$NR^{46}R^{47}$, aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{43} and R^{44} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

Y is absent or selected from O, NH, and C_1-C_6 alkyl;

R^{45} is selected from the group consisting of H, aryl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{46}R^{47}$, —CO_2R^{48}, —O—$(CH_2)_6$—CO_2R^{48}, and —C(═O)$NR^{46}R^{47}$;

R^{46} and R^{47} independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{46} and R^{47} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

R^{48} is selected from the group consisting of H, aryl, aralkyl, heteroaryl, C_1-C_6 alkyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{46}R^{47}$, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoroalkyl;

a is selected from 0 to 6;

b is selected from 0 to 6;

c is selected from 2 to 6;

R^5 is selected from the group consisting of H, C_1-C_6 alkyl, —$(CH_2)_d$—C(═O)—$NR^{53}R^{54}$, —C(═O)—$(CH_2)_d$—$NR^{53}R^{54}$, and —C(═O)—X—R^{55};

R^{53} and R^{54} are independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{56}R^{57}$, —(C_1-C_6 alkyl)-C(═O)$NR^{56}R^{57}$, aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{53} and R^{54} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

R^{55} is selected from the group consisting of H, aryl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{56}R^{57}$, —CO_2R^{58}, —O—$(CH_2)_e$—CO_2R^{58}, and —C(═O)$NR^{56}R^{57}$;

R^{56} and R^{57} independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{56} and R^{57} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

R^{58} is selected from the group consisting of H, aryl, aralkyl, heteroaryl, C_1-C_6 alkyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{56}R^{57}$, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoroalkyl;

d is selected from 0 to 6;

e is selected from 0 to 6;

R^6 is selected from the group consisting of H, C_1-C_6 alkyl, —$(CH_2)_r$—C(═O)—$NR^{63}R^{64}$, —C(═O)—$(CH_2)_r$—$NR^{63}R^{64}$, and —C(═O)—X—R^{65};

R^{63} and R^{64} are independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{66}R^{67}$, —(C_1-C_6 alkyl)-C(═O)$NR^{66}R^{67}$, aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{63} and R^{64} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

R^{65} is selected from the group consisting of H, aryl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{66}R^{67}$, —CO_2R, —O—(CH_2), —CO_2R^{68}, and —C(═O)$NR^{66}R^{67}$;

R^{66} and R^{67} independently selected from the group consisting of H, C_1-C_5 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{66} and R^{67} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

R^{68} is selected from the group consisting of H, aryl, aralkyl, heteroaryl, C_1-C_6 alkyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{66}R^{67}$, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoroalkyl;

r is selected from 0 to 6;

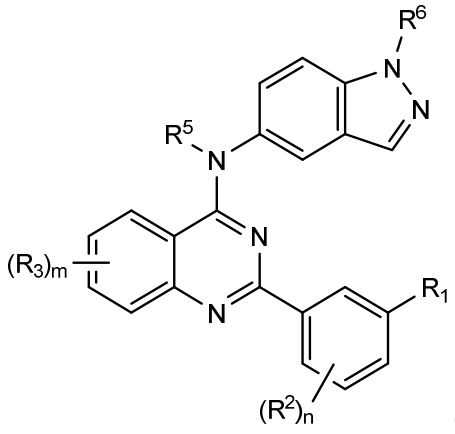
s is selected from 0 to 6;

n is selected from 0 to 4;

m is selected from 0 to 3; and

p is selected from 0 and 1.

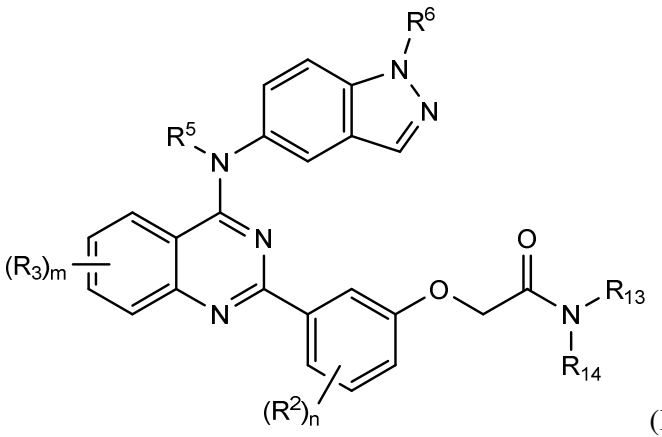
9. The use of claim 8, wherein the ROCK2 inhibitor is a compound having the structure of Formula II:



(II)

or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof, wherein: R^1, R^2, R^3, R^5, R^6, m and n are as defined in claim 8.

10. The use of claim 9, wherein the ROCK2 inhibitor is a compound having the structure of Formula III:



(III)

or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof, wherein:

R^{13} and R^{14} are independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), —(C_1-C_6 alkyl)-$NR^{16}R^{17}$, —(C_1-C_6 alkyl)-C(═O)$NR^{16}R^{17}$, aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{13} and R^{14} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

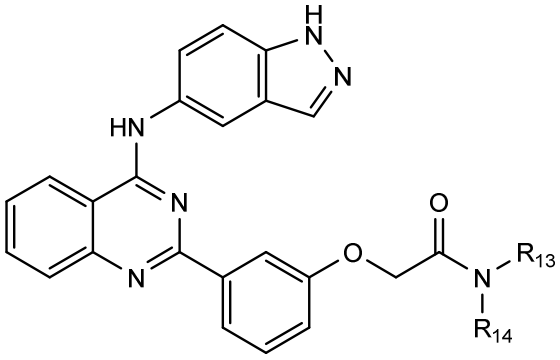
R^{16} and R^{17} are independently selected from the group consisting of H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, —(C_1-C_6 alkyl)-O—(C_1-C_6 alkyl), aryl, aralkyl, heteroaryl, C_3-C_7 cycloalkyl, 3-10 membered heterocyclic ring containing up to 3 heteroatoms, each of which may be optionally substituted by from 1 to 3 substituents

independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

or R^{16} and R^{17} may be taken together to form 3-10 membered heterocyclic ring having up to 3 heteroatoms which is optionally substituted by from 1 to 3 substituents independently selected from halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, oxo, hydroxy, amino, cyano and C_1-C_3 perfluoro alkyl;

wherein each of R^2, R^3, R^5, R^6, m and n are as defined in claim 8.

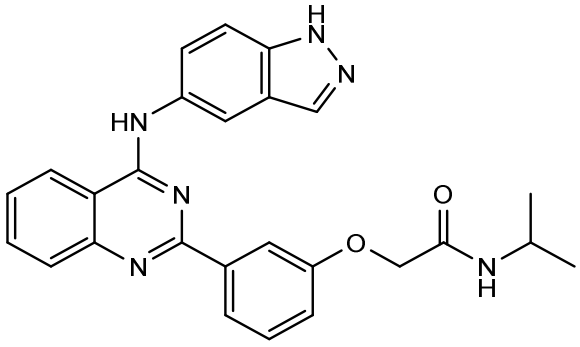
11. The use of claim 10, wherein the ROCK2 inhibitor is a compound having the structure of Formula IV:



(IV)

or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof, wherein: R^{13} and R^{14} are as defined in claim 10.

12. The use of claim 11, wherein the ROCK2 inhibitor is the compound (2-(3-(4-((1H-indazol-5-yl)amino)quinazolin-2-yl)phenoxy)-N-isopropylacetamide), having the chemical structure of Compound 1:



(Compound 1),

or a pharmaceutically acceptable salt, ester, stereoisomer, polymorph, solvate, N-oxide, or isotopically labeled compound thereof.

13. The use according to any one of claims 1 to 12, wherein the viral infection is caused by a coronavirus.

14. The use according to any one of claims 1 to 13, wherein the viral infection is caused by SARS-CoV-1, SARS-CoV-2 or MERS-CoV.

15. The use according to any one of claims 1 to 14, wherein the viral infection is caused by SARS-CoV-2.

16. The use according to claim 15, wherein the viral infection is caused by a Delta or Omicron variant of SARS-CoV-2.

17. The use according to any one of claims 4 to 16, wherein the sequelae resulting from the viral infection include one or more of the group consisting of fatigue, dyspnea, cough, arthralgia, myalgia, headache, chest pain, fever, palpitations, myocardial inflammation, ventricular dysfunction, stroke, pulmonary function abnormalities, pulmonary fibrosis, renal dysfunction rash, alopecia, olfactory and/or gustatory dysfunction, sleep dysregulation, cognitive impairment altered, memory impairment, depression, anxiety, changes in mood, and combinations thereof.

18. The use according to any one of claims 4 to 17, wherein the sequelae is pulmonary fibrosis.

19. The use according to any one of claims 1 to 18, wherein the medicament is to be administered with at least one other therapeutic agent.

20. The use according to claim 19, wherein the at least one other therapeutic agent is selected from the group consisting of an antiviral agent, a corticosteroid, an anti-inflammatory signal transduction modulator, a β2-adrenoreceptor agonist bronchodilator, an anticholinergic, a mucolytic agent, hypertonic saline, and combinations thereof.

21. The use according to claim 19, wherein the at least one other therapeutic agent comprises remdesivir.

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