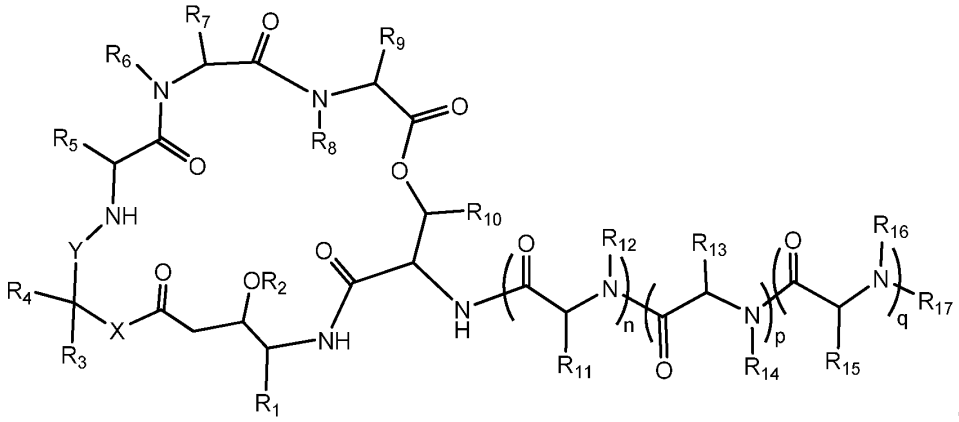
CLAIMS:

1. A compound of general formula **I**



(**I**)

wherein X is selected from O and NH;

Y is selected from CO and –COCH(CH_3)CO-;

each n and p is independently selected from 0 and 1, and q is selected from 0, 1 and 2;

each R_1, R_3, R_5, R_9, R_{11}, and R_{15} is independently selected from hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_2-C_6 alkenyl, and substituted or unsubstituted C_2-C_6 alkynyl;

R_2 is selected from hydrogen, COR_a, $COOR_a$, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_2-C_6 alkenyl, and substituted or unsubstituted C_2-C_6 alkynyl;

each R_4, R_8, R_{10}, R_{12}, and R_{16} is independently selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl;

each R_7 and R_{13} is independently selected from hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_2-C_6 alkenyl, and substituted or unsubstituted C_2-C_6 alkynyl; each R_6 and R_{14} is independently selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl; or R_6 and R_7 and/or R_{13} and R_{14} together with the corresponding N atom and C atom to which they are attached may form a substituted or unsubstituted heterocyclic group;

R_{17} is selected from hydrogen, COR_a, $COOR_a$, $CONHR_b$, $COSR_c$, $(C{=}NR_b)OR_a$, $(C{=}NR_b)NHR_b$, $(C{=}NR_b)SR_c$, $(C{=}S)OR_a$, $(C{=}S)NHR_b$, $(C{=}S)SR_c$, SO_2R_c, SO_3R_c, substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, substituted or unsubstituted C_2-C_{12} alkynyl, substituted or unsubstituted aryl, and substituted or unsubstituted heterocyclic group, with the proviso that when n, p, and q are 0 then R_{17} is not hydrogen; and

each R_a, R_b, and R_c is independently selected from hydrogen, substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, substituted or unsubstituted C_2-C_{12} alkynyl,

substituted or unsubstituted aryl, and substituted or unsubstituted heterocyclic group;

or a pharmaceutically acceptable salt or stereoisomer thereof, for use in the treatment of coronavirus (CoV) infection.

2. A compound according to claim 1, wherein R_3 and R_4 are independently selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl; preferably wherein R_3 is isopropyl and R_4 is hydrogen.

3. A compound according to claim 1 or claim 2 of general formula **II**, wherein R_3 and R_4 are methyl.

4. A compound according to any preceding claim, wherein R_{11} is selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl; preferably wherein R_{11} is methyl or isobutyl.

5. A compound according to any preceding claim, of general formula **III** wherein R_{11} is methyl and n=1.

6. A compound according to any preceding claim, wherein R_1, R_5, R_9, and R_{15} are independently selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl; preferably wherein R_1 is selected from sec-butyl and isopropyl, R_5 is isobutyl, R_9 is p-methoxybenzyl, and R_{15} is selected from methyl and benzyl.

7. A compound according to any preceding claim, wherein R_8, R_{10}, R_{12}, and R_{16} are independently selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl; preferably wherein R_8, R_{10} and R_{12} are methyl, and R_{16} is hydrogen.

8. A compound according to any preceding claim, wherein R_6 and R_{14} are independently selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl; preferably wherein R_6 is selected from hydrogen and methyl, and R_{14} is hydrogen.

9. A compound according to any preceding claim, wherein R_7 and R_{13} are independently selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl; preferably wherein R_7 is methyl and R_{13} is selected from hydrogen, methyl, isopropyl, isobutyl, and 3-amino-3-oxopropyl.

10. A compound according to any of claims 1 to 7, wherein R_6 and R_7 and/or R_{13} and R_{14} together with the corresponding N atom and C atom to which they are attached form a substituted or unsubstituted pyrrolidine group.

11. A compound according to any preceding claim, wherein R_2 is selected from hydrogen, substituted or unsubstituted C_1-C_6 alkyl, and COR_a, and wherein R_a is a substituted or unsubstituted C_1-C_6 alkyl; preferably wherein R_2 is hydrogen.

12. A compound according to any preceding claim, wherein R_{17} is selected from hydrogen, COR_a, $COOR_a$, $CONHR_b$, $(C=S)NHR_b$, and SO_2R_c, and wherein each R_a, R_b, and R_c is independently selected from substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_2-C_6 alkenyl, substituted or unsubstituted C_2-C_6 alkynyl, substituted or unsubstituted aryl, and substituted or unsubstituted heterocyclic group; preferably wherein R_{17} is selected from hydrogen, COObenzyl, CObenzo[b]thiophen-2-yl, SO_2(p-methylphenyl), $COCOCH_3$ and $COOC(CH_3)_3$.

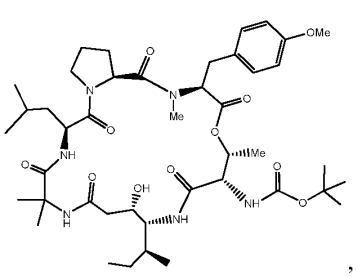
13. A compound according to any preceding claim, wherein X is NH.

14. A compound according to any of claims 1 to 12, wherein X is O.

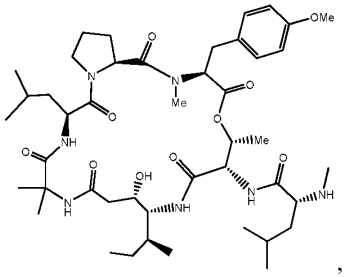
15. A compound according to any preceding claim wherein Y is CO.

16. A compound according to any of claims 1 to 14, wherein Y is –COCH(CH_3)CO-.

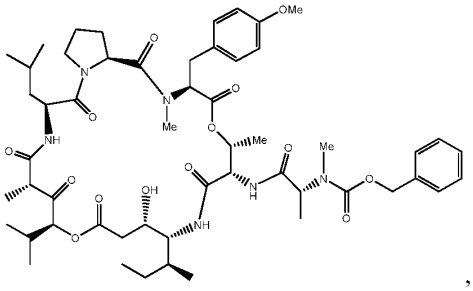
17. A compound according to claim 1 having the following structure:



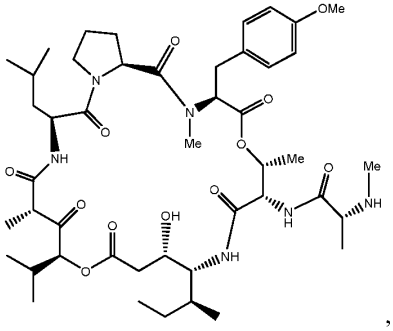
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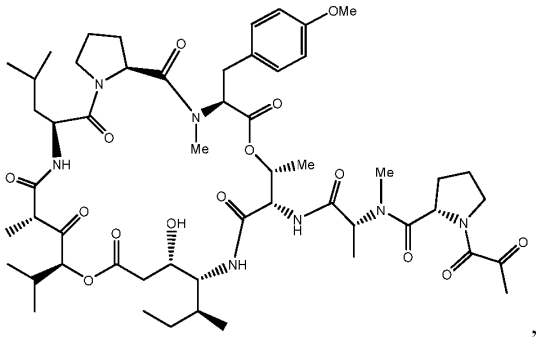
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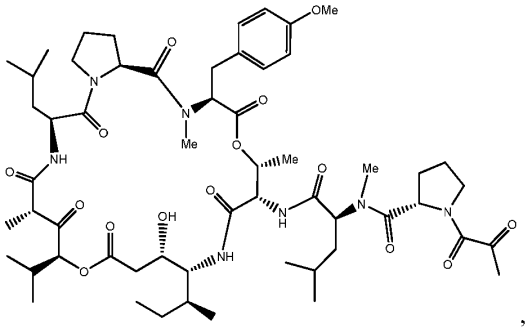
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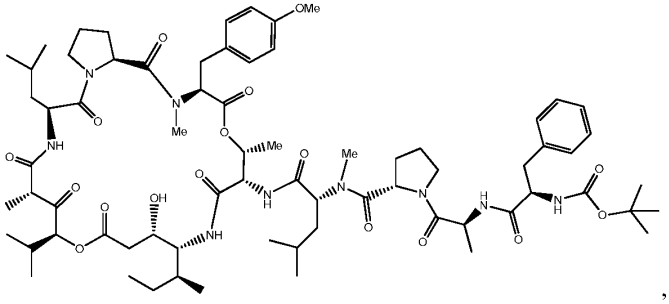
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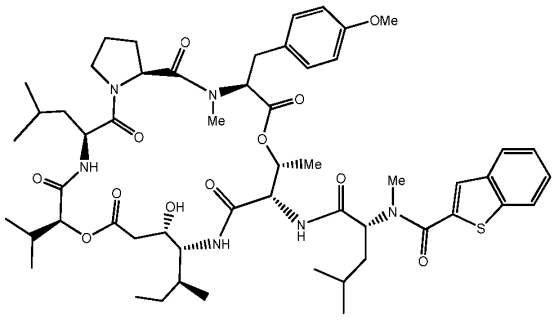
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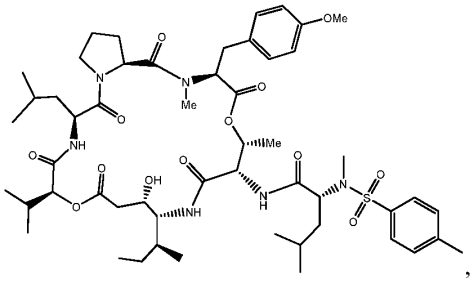
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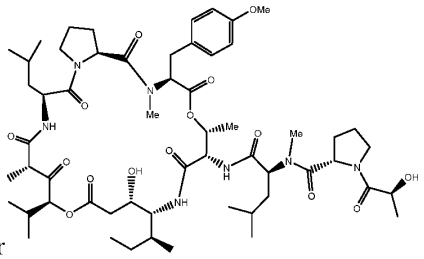
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or pharmaceutically acceptable salts or stereoisomers thereof.

18. A compound according to claim 1, wherein the compound is PLD, or pharmaceutically acceptable salts or stereoisomers thereof.

19. A compound according to claim 1, wherein the compound is didemninB, or pharmaceutically acceptable salts or stereoisomers thereof.

20. A compound according to any of the preceding claims, for use in the treatment of CoV infection, wherein the CoV is SARS-CoV-2.

21. A compound according to any one of claims 1 to 20, for use in the treatment of COVID-19 and/or for use in the treatment of pneumonia caused by COVID-19.

22. A compound according to any preceding claim, wherein the CoV infection is mild infection; and/or wherein the CoV infection is moderate infection; and/or wherein the CoV infection is severe infection.

23. A compound according to any preceding claim, wherein the CoV infection is acute CoV infection, preferably wherein the CoV infection is acute COVID-19 infection; and/or wherein the CoV infection is ongoing symptomatic CoV infection, preferably wherein the CoV infection is ongoing symptomatic COVID-19 infection; and/or wherein the CoV infection is post-CoV syndrome, CoV persistent or long CoV; preferably wherein the CoV infection is post-COVID-19 syndrome, COVID persistent or long COVID.

24. A compound according to claim 23, wherein the post-CoV syndrome, CoV persistent or long CoV include one or more symptoms arising from the cardiovascular, respiratory, gastrointestinal, neurological, musculoskeletal, metabolic, renal, dermatological, otolaryngological, haematological and autonomic systems; psychiatric problems, generalised pain, fatigue and/or persisting fever.

25. A compound according to any preceding claim, for use in the treatment of a patient with signs and symptoms of CoV infection (preferably COVID-19) for up to 4 weeks; and/or for use in the treatment of a patient with signs and symptoms of CoV infection (preferably COVID-19) from 4 weeks to 12 weeks; and/or for use in the treatment of a patient with signs and symptoms of CoV infection, preferably COVID-19, for more than 12 weeks.

26. A compound according to any preceding claim, for use in the prophylaxis, reduction or

treatment of COVID persistent, long COVID or post-COVID syndrome; preferably wherein the prophylaxis, reduction or treatment minimises the likelihood that a patient suffers from COVID persistent, long COVID or post-COVID syndrome symptoms; and/or reduces the severity of such symptoms; further preferably wherein the treatment minimising the symptoms of CoV infection.

27. A compound according to any preceding claim, wherein the treatment reduces the infectivity of CoV patients; including wherein the patient is asymptomatic or not very symptomatic patients yet has a high viral load.

28. A compound for use according to any preceding claim, wherein the compound is administered in combination with a corticosteroid, preferably dexamethasone.

29. A compound for use according to claim 28, wherein the compound and corticosteroid are administered concurrently, separately or sequentially.

30. A compound for use according to any one of claims 1 to 29, wherein the compound is administered according to a regimen of a daily dose for 10 days, 9 days, 8 days, 7 days, 6 days, 5 days, 4 days, 3 days, 2 days or 1 day; preferably 2-5 days, 3-5 days, or 3, 4 or 5 days; most preferably 3 days or 5 days; most preferably 3 days.

31. A compound for use according to any one of claims 1 to 30, wherein the compound is administered at a dose of 5mg a day or less, 4.5mg a day or less, 4mg a day or less, 3.5mg a day or less, 3mg a day or less, 2.5mg a day or less or 2mg a day or less; 0.5 mg/day, 1 mg/day, 1.5 mg/day, 2 mg/day, 2.5 mg/day, 3 mg/day, 3.5 mg/day, 4 mg/day, 4.5 mg/day, or 5mg/day; preferably 1 mg/day, 1.5 mg/day, 2 mg/day or 2.5 mg/day; more preferably 1.5-2.5 mg/day; most preferably 1.5 mg/day, 2.0 mg/day or 2.5 mg/day.

32. A compound for use according to any one of claims 1 to 31, wherein the compound is administered at a total dose of 1-50 mg, 1-40 mg, 1-30 mg, 1-20 mg, 1-15 mg, 3-15 mg, 3-12 mg, 4-12 mg, 4-10 mg, or 4.5-10 mg; 4mg, 4.5mg, 5mg, 5.5mg, 6mg, 6.5mg, 7mg, 7.5mg, 8mg, 8.5mg, 9mg, 9.5mg or 10mg; preferably 4.5mg, 5mg, 6mg, 7.5mg, 8mg, 9mg or 10mg; more preferably 4.5-7.5 mg/day.

33. A compound for use according to any one of claims 1 to 32, wherein the compound is administered by infusion.

34. A compound for use according to claim 33, wherein the infusion is a 1 hour infusion, a 1.5 hour infusion, a 2 hour infusion or a 3 hour infusion, preferably a 1.5 hour infusion.

35. A compound for use according to any one of claims 1 to 34, wherein 1.5 mg of plitidepsin is administered as a 1.5-hour infusion, once a day for 3 consecutive days; or wherein 2 mg of plitidepsin is administered as a 1.5-hour infusion, once a day for 3 consecutive days; or wherein 2.5 mg of plitidepsin is administered as a 1.5-hour infusion, once a day for 3 consecutive days; or wherein 1 mg of plitidepsin is administered as a 1.5-hour infusion, once a day for 5 consecutive days; or wherein 2 mg of plitidepsin is administered as a 1.5-hour infusion, once a day for 5 consecutive days.

36. A compound for use according to any one of claims 1 to 35, wherein the compound is administered using a loading dose and a maintenance dose.

37. A compound for use according to claim 36, wherein the dosage regimen is:

a loading dose of 2.5 mg for day 1, and followed by a maintenance dose of 2 mg/day for subsequent days;

a loading dose of 2.5 mg for day 1, and followed by a maintenance dose of 1.5 mg/day for subsequent days;

a loading dose of 2.5 mg for day 1, and followed by a maintenance dose of 1 mg/day for subsequent days;

a loading dose of 2.5 mg for day 1, and followed by a maintenance dose of 0.5 mg/day for subsequent days;

a loading dose of 2 mg for day 1, and followed by a maintenance dose of 1.5 mg/day for subsequent days;

a loading dose of 2 mg for day 1, and followed by a maintenance dose of 1 mg/day for subsequent days;

a loading dose of 2 mg for day 1, and followed by a maintenance dose of 0.5 mg/day for subsequent days;

a loading dose of 1.5 mg for day 1, and followed by a maintenance dose of 1 mg/day for subsequent days;

a loading dose of 1.5 mg for day 1, and followed by a maintenance dose of 0.5 mg/day for subsequent days; or

a loading dose of 1 mg for day 1, and followed by a maintenance dose of 0.5 mg/day for subsequent days.

38. A compound for use according to any one of claims 1 to 37, wherein the compound is administered in combination with a corticosteroid, and wherein the corticosteroid is administered on the same days as administration of the compound according to any one of claims 1 to 19.

39. A compound for use according to claim 38, wherein the corticosteroid may also be administered on one or more subsequent days; preferably wherein the corticosteroid is administered with the compound on days 1-3 and the corticosteroid is further administered on one or more of days 4-10.

40. A compound for use according to claim 39, wherein the corticosteroid is administered intravenously on days when the compound is administered but is administered by oral administration or IV on subsequent days.

41. A compound for use according to any one of claims 38 to 40, wherein the corticosteroid is dexamethasone; preferably wherein dexamethasone is administered at a dose of 6.6 mg/day IV on days when the compound according to the present invention is administered.

42. A compound for use according to claim 41, wherein dexamethasone is administered at a dose of 6 mg/day oral administration or IV on subsequent days, preferably one or more of days 4, 5, 6, 7, 8, 9 and 10.

43. A compound for use according to any one of claims 1 to 42, wherein PLD is administered 1.5 mg/day intravenous (IV) combined with dexamethasone 6.6 mg/day IV on Days 1 to 3, followed by dexamethasone 6 mg/day oral administration (PO)/IV from Day 4 and up to Day 10 (as per physician judgement according to patient clinical condition and evolution); or

wherein PLD is administered 2.0 mg/day intravenous (IV) combined with dexamethasone 6.6 mg/day IV on Days 1 to 3, followed by dexamethasone 6 mg/day oral administration (PO)/IV from Day 4 and up to Day 10 (as per physician judgement according to patient clinical condition and evolution); or

wherein PLD is administered 2.5 mg/day intravenous (IV) combined with dexamethasone 6.6 mg/day IV on Days 1 to 3, followed by dexamethasone 6 mg/day oral administration (PO)/IV from Day 4 and up to Day 10 (as per physician judgement according to patient clinical condition and evolution).

44. A compound for use according to any one of claims 38 to 43, wherein the corticosteroid is administered 20 to 30 minutes prior to starting treatment with the compound according to any one of claims 1 to 19.

45. A compound for use according to any one of claims 1 to 44, wherein the patient additionally receives the following medications, preferably 20 to 30 minutes prior to starting treatment with the compound according to any one of claims 1 to 19:

Ondansetron 8 mg IV (or equivalent);

Diphenhydramine hydrochloride 25 mg IV (or equivalent); and

Ranitidine 50 mg IV (or equivalent).

46. A compound for use according to any one of claims 1 to 45, wherein on Days 4 and 5, patients receive ondansetron (or equivalent) 4 mg twice a day PO.

47. A compound for use according to any one of claims 1 to 34, wherein the compound is administered as a single dose (on day 1).

48. A compound for use according to claim 47, wherein the single dose is 1-10 mg, 4-10 mg, 4.5-10 mg, 4mg, 4.5mg, 5mg, 5.5mg, 6mg, 6.5mg, 7mg, 7.5mg, 8mg, 8.5mg, 9mg, 9.5mg or 10mg, preferably 4.5mg, 5mg, 6mg, 7.5mg, 8mg, 9mg or 10mg, more preferably 5-9 mg, 6.5-8.5 mg, 7-8 mg or most preferably 7.5 mg.

49. A compound for use according to any one of claims 47 to 48, wherein the compound is administered as a 1.5-hour infusion.

50. A compound for use according to any one of claims 47 to 49, wherein a corticosteroid is administered according to the regimen according to any one of claims 38 to 44.

51. A compound for use according to any one of claims 47 to 50, wherein the following prophylactic medications are administered 20-30 minutes prior to administration with a compound of the present invention:

Ondansetron 8 mg IV (or equivalent), particularly in slow infusion of 15 minutes;

Diphenhydramine hydrochloride 25 mg IV (or equivalent);

Ranitidine 50 mg IV (or equivalent).

52. A compound for use according to any one of claims 47 to 51, wherein ondansetron 4 mg orally is given every 12 hours for 3 days after administration of a compound of the present invention.

53. A compound for use according to any preceding claim, wherein dexamethasone is dexamethasone phosphate and is administered at a dose of 8 mg if administered on days when a compound of the invention is administered (equating to a dose of 6.6 mg base) and is administered at a dose of 7.2 mg if administered thereafter (equating to a dose of 6 mg base).

54. A pharmaceutical composition comprising a compound as defined in any of claims 1 to 53, or a pharmaceutically acceptable salt or stereoisomer thereof, and a pharmaceutically acceptable carrier, for use in the treatment of coronavirus (CoV) infection; preferably wherein the CoV is SARS-CoV-2.

55. Use of a compound as defined in any of claims 1 to 53, or a pharmaceutically acceptable salt or stereoisomer thereof, in the manufacture of a medicament for the treatment of CoV infection; preferably wherein the CoV is SARS-CoV-2.

56. A method of treating a CoV infection, wherein the method comprises administering to an individual in need thereof, a therapeutically effective amount of a compound as defined in any of claims 1 to 53, or a pharmaceutically acceptable salt or stereoisomer thereof; preferably wherein the CoV is SARS-CoV-2.

57. A method of prophylaxis, reduction or treatment of CoV persistent, long CoV or post-CoV syndrome, wherein the method comprises administering to an individual in need thereof, a therapeutically effective amount of a compound as defined in any of claims 1 to 53, or a pharmaceutically acceptable salt or stereoisomer thereof; preferably wherein the CoV is SARS-CoV-2; optionally wherein the treatment minimises the likelihood that a patient suffers from COVID persistent, long COVID or post-COVID syndrome symptoms; and/or reduces the severity of such symptoms.

58. A method of reducing the infectivity of CoV patients, wherein the method comprises administering to an individual in need thereof, a therapeutically effective amount of a compound as defined in any of claims 1 to 53, or a pharmaceutically acceptable salt or stereoisomer thereof; preferably wherein the CoV is SARS-CoV-2; optionally wherein the patient is asymptomatic or not very symptomatic yet has a high viral load.

59. A method of minimising the symptoms of CoV infection, wherein the method comprises administering to an individual in need thereof, a therapeutically effective amount of a compound

as defined in any of claims 1 to 53, or a pharmaceutically acceptable salt or stereoisomer thereof; preferably wherein the CoV is SARS-CoV-2.

60. A corticosteroid for use in the treatment of CoV infection, wherein the corticosteroid is administered in combination with a compound according to any one of claims 1 to 53.

61. A compound according to any one of claims 1 to 19 and a corticosteroid for use in the treatment of CoV infection; wherein the use is according to any one of claims 1 to 53.

62. A method of treatment of CoV infection, the method comprising administering a combination therapy of compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof and a corticosteroid to a patient in need thereof, thereby treating the CoV infection; wherein said method is as defined in any one of claims 1 to 53.

63. Use of a compound as defined in any of claims 1 to 53 or a pharmaceutically acceptable salt or stereoisomer thereof, in the manufacture of a medicament for the treatment of CoV infection; wherein said treatment includes administration of a corticosteroid.

64. Use of a corticosteroid in the manufacture of a medicament for the treatment of CoV infection; wherein said treatment includes administration of a compound as defined in any of claims 1 to 53 or a pharmaceutically acceptable salt or stereoisomer thereof.

65. Use of a compound as defined in any of claims 1 to 53 or a pharmaceutically acceptable salt or stereoisomer thereof and a corticosteroid in the manufacture of a medicament for the treatment of CoV infection.

66. A pharmaceutical package comprising a compound as defined in any of claims 1 to 53 and a corticosteroid, optionally further comprising instructions according to any one of claims 1 to 53.

67. A kit comprising the compound as defined in any of claims 1 to 53 together with instructions for treating CoV infections.

68. A kit comprising a compound as defined in any of claims 1 to 53 and a corticosteroid together with instructions for treating CoV infections.