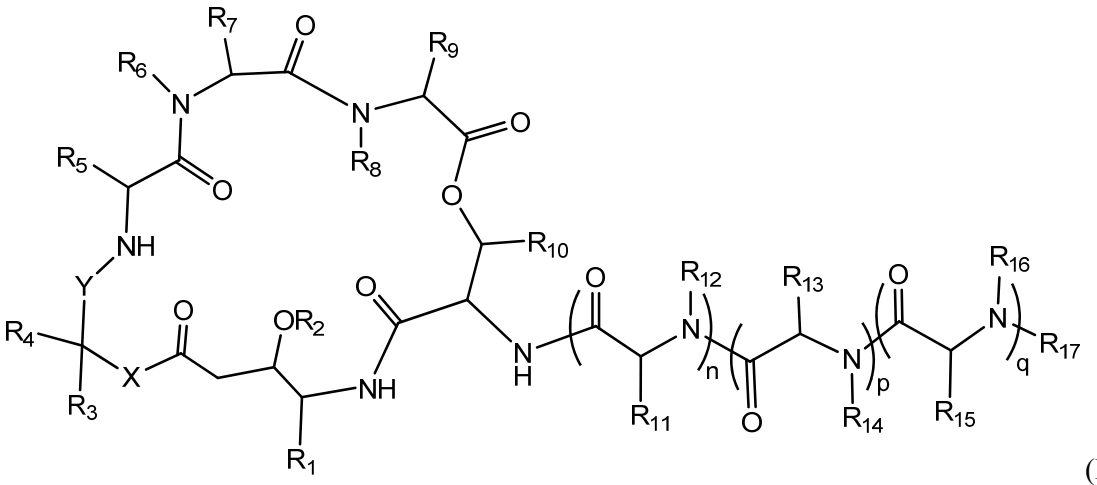
CLAIMS:

1. Use of 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;

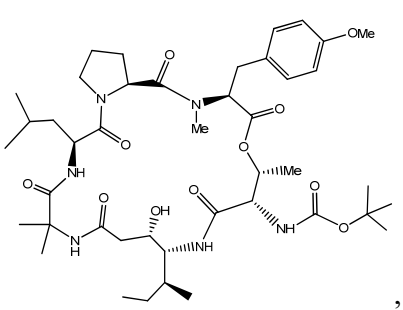
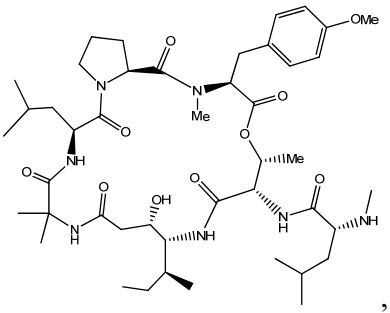
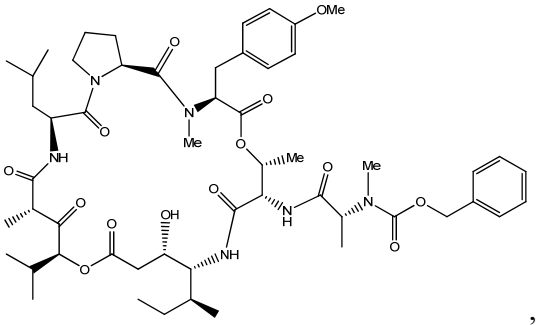
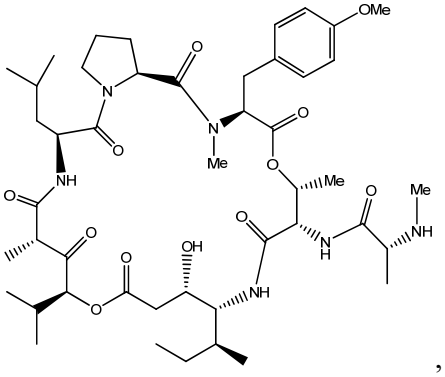
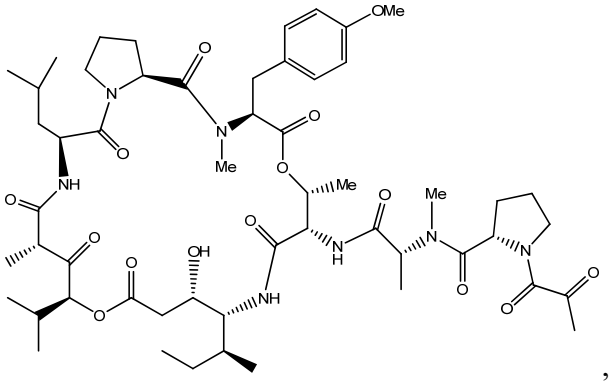
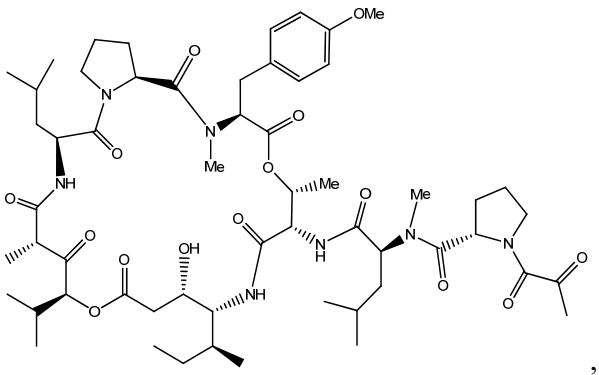
each R_7 and R_{13} is independently selected from hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_2-C_6 alkenyl, and substituted or unsubstituted C_2-C_6 alkynyl; each R_6 and R_{14} is independently selected from hydrogen and substituted or unsubstituted C_1-C_6 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;

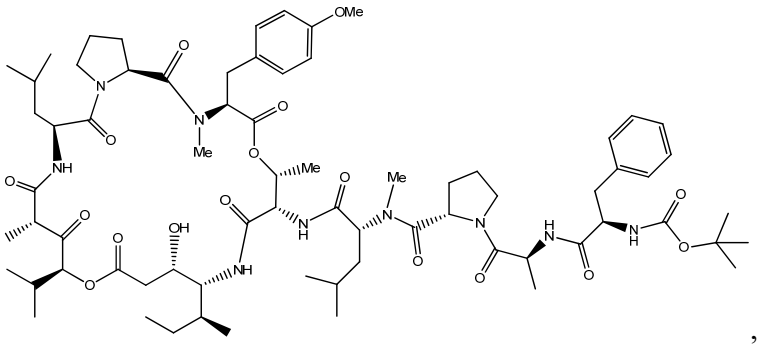
R_{17} is selected from hydrogen, COR_a, $COOR_a$, $CONHR_b$, $COSR_c$, $(C{=}NR_b)OR_a$, $(C{=}NR_b)NHR_b$, $(C{=}NR_b)SR_c$, $(C{=}S)OR_a$, $(C{=}S)NHR_b$, $(C{=}S)SR_c$, SO_2R_c, SO_3R_c, substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, substituted or 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;

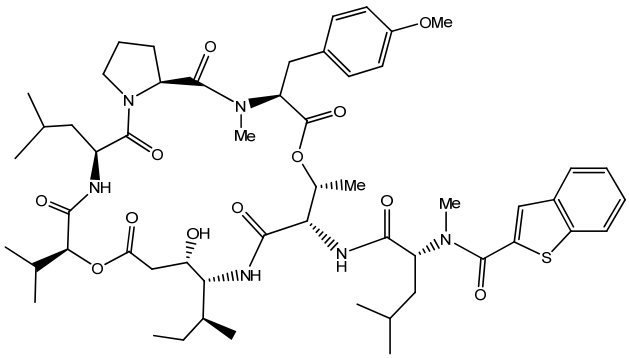
or a pharmaceutically acceptable salt or stereoisomer thereof, in the manufacture of a medicament for the treatment of coronavirus (CoV) infection.

2. The use according to claim 1, the compound having the following structure:

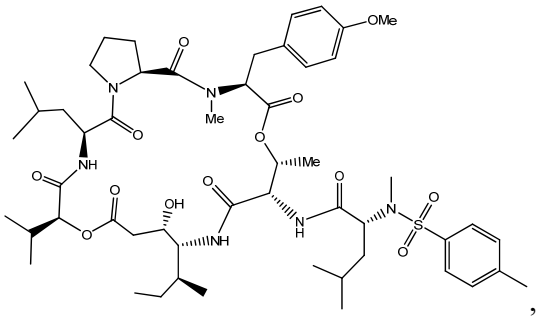

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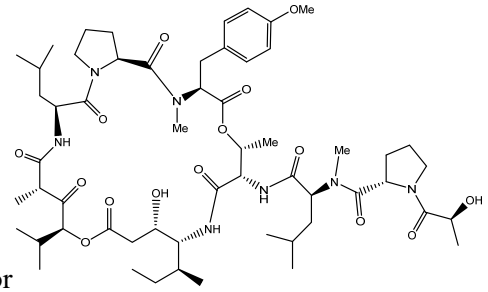
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, or



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or pharmaceutically acceptable salts or stereoisomers thereof.

3. The use according to claim 1, wherein the compound is PLD, or pharmaceutically acceptable salts or stereoisomers thereof.

4. The use according to claim 1, wherein the compound is didemninB, or pharmaceutically acceptable salts or stereoisomers thereof.

5. The use according to any of the preceding claims, for the treatment of CoV infection, wherein the CoV is SARS-CoV-2; preferably

the treatment of COVID-19 and/or for use in the treatment of pneumonia caused by COVID-19.

6. 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.

7. 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.

8. A compound according to claim 7, 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.

9. 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.

10. 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.

11. 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.

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

13. A compound for use according to claim 12, wherein the compound and corticosteroid are administered concurrently, separately or sequentially.

14. The use according to any one of claims 1 to 13, 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.

15. A compound for use according to any one of claims 1 to 14, 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.

16. A compound for use according to any one of claims 1 to 15, 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.

17. The use according to any one of claims 1 to 16, wherein the compound is administered by infusion; preferably

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.

18. A compound for use according to any one of claims 1 to 17, 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.

19. The use according to any one of claims 1 to 18, wherein the compound is administered using a loading dose and a maintenance dose; including

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.

20. The use according to any one of claims 1 to 19, 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.

21. A compound for use according to claim 20, 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.

22. A compound for use according to claim 21, wherein the corticosteroid is administered intravenously on days when the compound is administered but is administered by oral administration or IV on subsequent days.

23. A compound for use according to any one of claims 20 to 22, 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; preferably

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.

24. A compound for use according to any one of claims 1 to 23, 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).

25. A compound for use according to any one of claims 20 to 24, wherein the corticosteroid is administered 20 to 30 minutes prior to starting treatment with the compound according to any one of claims 1 to 4.

26. A compound for use according to any one of claims 1 to 25, wherein on Days 4 and 5, patients receive ondansetron (or equivalent) 4 mg twice a day PO.

27. The use according to any one of claims 1 to 26, wherein the compound is administered as a single dose (on day 1).

28. A compound for use according to claim 27, 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.

29. A compound for use according to any one of claims 27 to 28, wherein the compound is administered as a 1.5-hour infusion.

30. A compound for use according to any one of claims 27 to 29, wherein a corticosteroid is administered according to the regimen according to any one of claims 20 to 25.

31. A compound for use according to any one of claims 1 to 30, 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).

32. The use according to any preceding claim, in the manufacture of a medicament for the 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 31, 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.

33. The use according to any preceding claim, in the manufacture of a medicament for 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 31, 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.

34. The use according to any preceding claim, in the manufacture of a medicament for 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 31, or a pharmaceutically acceptable salt or stereoisomer thereof; preferably wherein the CoV is SARS-CoV-2.

35. 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 34 or a pharmaceutically acceptable salt or stereoisomer thereof.

36. Use of a compound as defined in any of claims 1 to 34 or a pharmaceutically acceptable salt or stereoisomer thereof and a corticosteroid in the manufacture of a medicament for the treatment of CoV infection.

37. A pharmaceutical package comprising a compound as defined in any of claims 1 to 34 and a corticosteroid, optionally further comprising instructions according to any one of claims 1 to 34.

38. A kit comprising the compound as defined in any of claims 1 to 34, optionally and a corticosteroid, together with instructions for treating CoV infections, said instructions according to any one of claims 1 to 34.