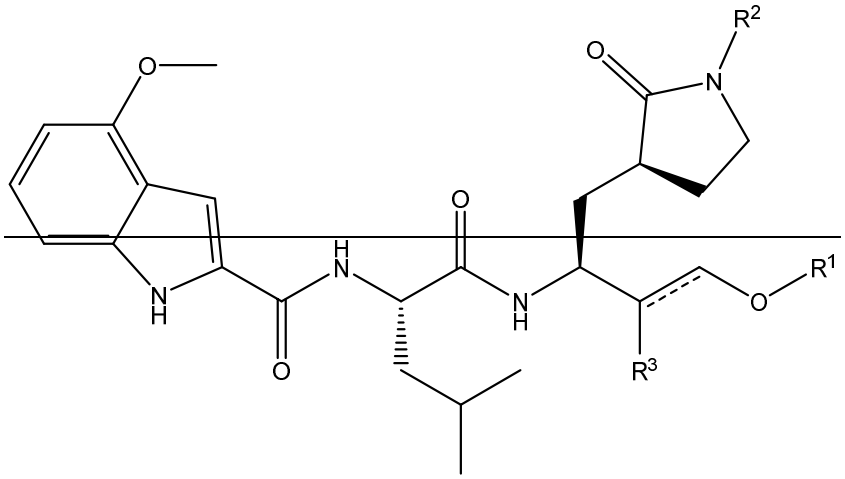
WHAT IS CLAIMED IS:

1. A compound of Formula I



I

wherein

----- is absent or a bond;

R^1 is selected from the group consisting of -CH(R^{4a})-OC(O)R^4, -C(O)OR^4, -CH(R^{4a})-OC(O)OR^4, -P(O)(OR^5)$_2$, -P(O)(C_1-C_6alkyl)(OR^5) and -C(O)N(R^6)$_2$;

R^2 is selected from the group consisting of hydrogen, -C(O)R^7, -CO_2R^7 and -C_1-C_6alkyl-OC(O)OR^7;

and when R^2 is -C(O)R^7, -CO_2R^7 or -C_1-C_6alkyl-OC(O)OR^7; then R^1 is selected from the group consisting of hydrogen, -CH(R^{4a})-OC(O)R^4, -C(O)OR^4, -CH(R^{4a})-OC(O)OR^4, -P(O)(OR^5)$_2$, -P(O)(C_1-C_6alkyl)(OR^5) and -C(O)N(R^6)$_2$;

R^3 is oxo when ----- is absent or when ----- is a bond R^3 taken together with R^1 and the oxygen to which R^1 is attached are -OC(O)O-;

R^4 and R^7 are each independently selected from the group consisting of C_1-C_6alkyl unsubstituted or substituted with one to three R^8, C_3-C_7cycloalkyl unsubstituted or substituted with one to three R^8, C_5-C_{12}bicycloalkyl unsubstituted or substituted with one to three R^8, four to seven membered heterocycloalkyl comprising one to three heteroatoms selected independently from N, O and S and which is unsubstituted or substituted with one to three R^8, C_6-C_{10}aryl unsubstituted or substituted with one to three R^8, and a five to ten membered heteroaryl comprising one to four heteroatoms

selected independently from N, O and S and which is unsubstituted or substituted with one to three R^8;

R^{4a} is hydrogen or C_1-C_6alkyl;

R^5 at each occurrence is independently hydrogen or C_1-C_6alkyl; or both R^5 groups taken together are a C_2-C_4alkylene which is optionally substituted with phenyl;

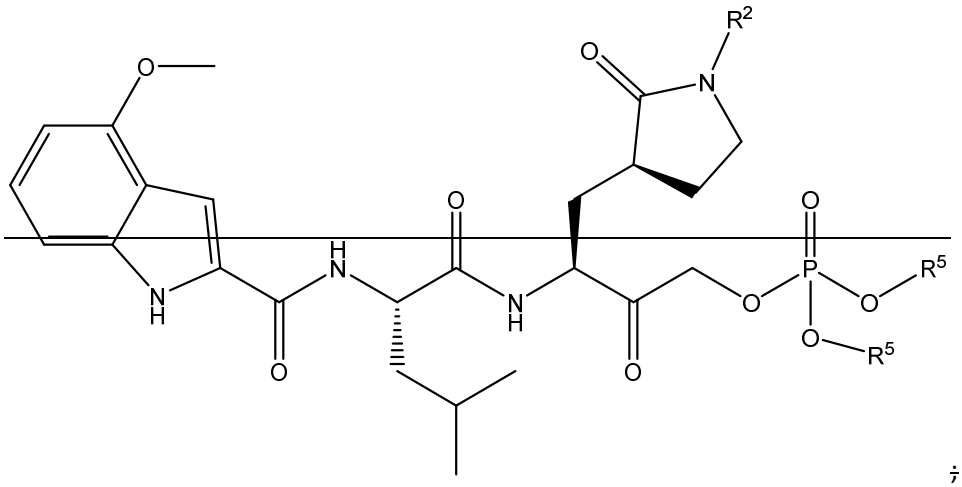
R^6 at each occurrence is independently selected from hydrogen and C_1-C_6alkyl which is unsubstituted or substituted with one to three R^8;

or both R^6 groups taken together with the nitrogen to which they are attached are a four- to seven-membered heterocycloalkyl optionally comprising an additional one to three heteroatoms independently selected from N, O and S; wherein said heterocycloalkyl is unsubstituted or substituted with one to three R^8; and

R^8 at each occurrence is independently selected from halo, hydroxy, cyano, C_1-C_3alkyl, C_1-C_3alkoxy, C_1-C_3alkoxyC_1-C_3alkyl, C_3-C_6cycloalkyl, C_3-C_6cycloalkoxy, di(C_1-C_3alkyl)amino, (C_1-C_3alkyl)amino, amino, di(C_1-C_3alkyl)amino-C_1-C_3alkyl, (C_1-C_3alkyl)amino-C_1-C_3alkyl, amino-C_1-C_3alkyl and four to seven membered heterocycloalkyl comprising one to three heteroatoms selected independently from N, O and S;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

2. The compound of claim 1 of the formula Ie



Ie

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

3. The compound of claim 2 wherein

R^2 is selected from the group consisting of hydrogen, $-C(O)CH_3$, $-CO_2CH_3$, $-CH_2OC(O)OCH_3$ and $-CH(CH_3)OC(O)OCH_3$; and

R^5 at each occurrence is independently selected from the group consisting of hydrogen, methyl, ethyl, isopropyl and t- butyl; or both R^5 groups taken together are $-CH(Phenyl)CH_2CH_2-$;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

4. The compound of claim 3 selected from the group consisting of

(1S)-1-{(3S)-3-[(2S)-4-[(dimethoxyphosphoryl)oxy]-2-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-3-oxobutyl]-2-oxopyrrolidin-1-yl}ethyl methyl carbonate;

(3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate;

(3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dimethyl phosphate;

(3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dipropan-2-yl phosphate;

(3S)-4-[(3S)-1-acetyl-2-oxopyrrolidin-3-yl]-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxobutyl dimethyl phosphate;

4-methoxy-N-[(2S)-4-methyl-1-({(2S)-4-[(2-oxido-4-phenyl-1,3,2-dioxaphosphinan-2-yl)oxy]-3-oxo-1-[(3S)-2-oxopyrrolidin-3-yl]butan-2-yl}amino)-1-oxopentan-2-yl]-1H-indole-2-carboxamide;

diethyl (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl phosphate; and

methyl (3S)-3-[(2S)-4-[(dimethoxyphosphoryl)oxy]-2-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-3-oxobutyl]-2-oxopyrrolidine-1-carboxylate;

or a pharmaceutically acceptable salt, solvate or hydrate thereof.

5. The compound of claim 4 which is (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate; or a pharmaceutically acceptable salt, solvate or hydrate thereof.

6. The compound of claim 5 which is in the form of a hydrate.

7. The compound of claim 6 which is a crystalline (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate hydrate.

8. The compound of claim 7 which is crystalline (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate Form 1 hydrate having one or more characteristics selected from the group consisting of a powder X-ray diffraction pattern, a ^{13}C solid state NMR spectrum and a Raman spectrum;

wherein the powder X-ray diffraction pattern characteristic is selected from

a) a powder X-ray diffraction pattern comprising peaks at 4.1 ± 0.2 and 7.2 ± 0.2 degrees 2-Theta;
b) a powder X-ray diffraction pattern comprising peaks at 4.1 ± 0.2, 7.2 ± 0.2 and 10.4 ± 0.2 degrees 2-Theta; and
c) a powder X-ray diffraction pattern comprising peaks at 4.1 ± 0.2, 7.2 ± 0.2, 10.4 ± 0.2 and 14.5 ± 0.2 degrees 2-Theta;

wherein the ^{13}C solid state NMR spectrum characteristic is selected from

a) ^{13}C solid state NMR spectrum comprising peaks at 21.7, 153.8 and 172.2 ppm; each peak ± 0.2 ppm;

b) a ^{13}C solid state NMR spectrum comprising peaks at 21.7, 153.8, 172.2 and 118.6 ppm; each peak ± 0.2 ppm; and

c) a ^{13}C solid state NMR spectrum comprising peaks at 21.7, 153.8, 172.2, 118.6 and 57.8 ppm; each peak ± 0.2 ppm; and

wherein the Raman spectrum characteristic is selected from

a) a Raman spectrum comprising Raman peaks at 1271, 1421 and 1217 cm^{-1}; each peak ± 2 cm^{-1};

b) a Raman spectrum comprising Raman peaks at 1271, 1421, 1217 and 1640 cm^{-1}; each peak ± 2 cm^{-1}; and

c) a Raman spectrum comprising Raman peaks at 1271, 1421, 1217, 1640 and 3074 cm^{-1}; each peak ± 2 cm^{-1}.

9. The compound of claim 5 which is in the form of a methyl ethyl ketone solvate.

10. The compound of claim 9 which is a crystalline (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, methyl ethyl ketone solvate.

11. The compound of claim 10 which is crystalline (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, methyl ethyl ketone solvate having one or more characteristics selected from the group consisting of a powder X-ray diffraction pattern, a ^{13}C NMR spectrum and a Raman spectrum;

wherein the powder X-ray diffraction pattern characteristic is selected from

a) a powder X-ray diffraction pattern comprising peaks at 7.7 ± 0.2, 8.1 ± 0.2 and 23.1 ± 0.2 degrees 2-Theta;

b) a powder X-ray diffraction pattern comprising peaks at 7.7 ± 0.2, 8.1 ± 0.2, 23.1 ± 0.2 and 17.0 ± 0.2 degrees 2-Theta; and

c) a powder X-ray diffraction pattern comprising peaks at 7.7 ± 0.2, 8.1 ± 0.2, 23.1 ± 0.2, 17.0 ± 0.2 and 25.8 ± 0.2 degrees 2-Theta;

wherein the ^{13}C solid state NMR spectrum characteristic is selected from

a) a ^{13}C solid state NMR spectrum comprising peaks at 7.2, 206.4 and 215.8 ppm; each ± 0.2 ppm;
b) a ^{13}C solid state NMR spectrum comprising peaks at 7.2, 206.4, 215.8 and 42.2 ppm; each ± 0.2 ppm; and
c) a ^{13}C solid state NMR spectrum comprising peaks at 7.2, 206.4, 215.8, 42.2 and 101.2 ppm; each ± 0.2 ppm; and

wherein the Raman spectrum characteristic is selected from

a) a Raman spectrum comprising peaks at 1511, 1644 and 3081 cm^{-1}; each ± 2 cm^{-1};

b) a Raman spectrum comprising peaks at 1511, 1644, 3081 and 1265 cm^{-1}; each ± 2 cm^{-1}; and

c) a Raman spectrum comprising peaks at 1511, 1644, 3081,1265 and 446 cm^{-1}; each ± 2 cm^{-1}.

12. The compound of claim 5 which is in the form of a dimethylsulfoxide solvate.

13. The compound of claim 12 which is crystalline (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, dimethylsulfoxide solvate.

14. The compound of claim 13 which is crystalline (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, dimethylsulfoxide solvate having one or more characteristics selected from the group consisting of a powder X-ray diffraction pattern, a ^{13}C solid state NMR spectrum and a Raman spectrum;

wherein the powder X-ray diffraction pattern characteristic is selected from

a) a powder X-ray diffraction pattern comprising peaks at 7.4 ± 0.2, 14.8 ± 0.2 and 26.2 ± 0.2 degrees 2-Theta;

b) a powder X-ray diffraction pattern comprising peaks at 7.4 ± 0.2, 14.8 ± 0.2, 26.2 ± 0.2 and 10.8 ± 0.2 degrees 2-Theta; and

c) a powder X-ray diffraction pattern comprising peaks at 7.4 ± 0.2, 14.8 ± 0.2, 26.2 ± 0.2, 10.8 ± 0.2 and 22.3 ± 0.2 degrees 2-Theta;

wherein the ^{13}C solid state NMR spectrum characteristic is selected from

a) a ^{13}C solid state NMR spectrum comprising peaks at 173.4 ± 0.2, 210.7 ± 0.2 and 26.2 ± 0.2 ppm;

b) a ^{13}C solid state NMR spectrum comprising peaks at 173.4 ± 0.2, 210.7 ± 0.2, 26.2 ± 0.2 and 22.8 ± 0.2 ppm; and

c) a ^{13}C solid state NMR spectrum comprising peaks at 173.4 ± 0.2, 210.7 ± 0.2, 26.2 ± 0.2, 22.8 ± 0.2 and 25.5 ± 0.2 ppm; and

wherein the Raman spectrum characteristic is a Raman spectrum comprising peaks at 1717 ± 2 and 675 ± 2 cm^{-1}.

15. The compound of claim 5 which is in the form of a dimethylsulfoxide solvate hydrate.

16. The compound of claim 15 which is crystalline (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, dimethylsulfoxide solvate hydrate.

17. The compound of claim 16 which is crystalline (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, dimethylsulfoxide solvate hydrate having a powder X-ray diffraction pattern characteristic;

wherein the X-ray powder diffraction pattern characteristic is selected from

a) a powder X-ray diffraction pattern comprising peaks at 14.5 ± 0.2, 25.6 ± 0.2 and 26.6 ± 0.2 degrees 2-Theta;
b) a powder X-ray diffraction pattern comprising peaks at 14.5 ± 0.2, 25.6 ± 0.2, 26.6 ± 0.2 and 21.9 ± 0.2 degrees 2-Theta; and
c) a powder X-ray diffraction pattern comprising peaks at 14.5 ± 0.2, 25.6 ± 0.2, 26.6 ± 0.2, 21.9 ± 0.2, 17.8 ± 0.2 degrees 2-Theta.

18. The compound of claim 5 which is (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate.

19. The compound of claim 18 which is amorphous (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate.

20. The compound of claim 19 which is amorphous (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate having one or more characteristics selected from the group consisting of a ^{13}C solid state NMR spectrum and a combination of a ^{13}C solid state NMR spectrum and a ^{31}P solid state NMR spectrum;

wherein the ^{13}C solid state NMR spectrum characteristic is selected from

a) a ^{13}C solid state NMR spectrum comprising peaks at 175.0 ± 0.4, 204 ± 1.5 and 181.8 ± 0.4 ppm;

b) a ^{13}C solid state NMR spectrum comprising peaks at 175.0 ± 0.4, 204 ± 1.5, 181.8 ± 0.4 and 54.8 ± 0.2 ppm; and

c) a ^{13}C solid state NMR spectrum comprising peaks at 175.0 ± 0.4, 204 ± 1.5, 181.8 ± 0.4, 54.8 ± 0.2 and 162.9 ± 0.2 ppm; and

the combination of a ^{13}C solid state NMR spectrum and a ^{31}P solid state NMR spectrum is a ^{13}C solid state NMR spectrum comprising peaks at 175.0 ± 0.4 and 204 ± 1.5 and a ^{31}P solid state NMR spectrum with a peak at -0.8 ± 0.2 ppm.

21. The compound of claim 5 which is (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, sodium salt.

22. The compound of claim 21 which is amorphous (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, sodium salt.

23. The compound of claim 22 which is amorphous (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate sodium salt having one or more characteristics selected from the group consisting of a ^{13}C solid state NMR spectrum and a combination of a ^{13}C solid state NMR spectrum and a ^{31}P solid state NMR spectrum;

wherein the ^{13}C solid state NMR spectrum characteristic is selected from

a) a ^{13}C solid state NMR spectrum comprising peaks at 126.0 ± 0.4 ppm, 181.0 ± 0.4 ppm and 208.0 ± 1.5 ppm;

b) a ^{13}C solid state NMR spectrum comprising peaks at 126.0 ± 0.4 ppm, 181.0 ± 0.4 ppm, 208.0 ± 1.5 ppm and 174.1 ± 0.4 ppm 175.0 ± 0.4 ppm; and

c) a ^{13}C solid state NMR spectrum comprising peaks at 126.0 ± 0.4 ppm, 181.0 ± 0.4 ppm, 208.0 ± 1.5 ppm, 174.1 ± 0.4 ppm and 163.1 ± 0.2 ppm; and

the combination of a ^{13}C solid state NMR spectrum and a ^{31}P solid state NMR spectrum is a ^{13}C solid state NMR spectrum comprising peaks at 126.0 ± 0.4 ppm, 181.0 ± 0.4 ppm and a ^{31}P solid state NMR spectrum with a peak at 1.9 ± 0.2 ppm.

24. A pharmaceutical composition comprising a therapeutically effective amount of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, or a pharmaceutically acceptable salt, solvate or hydrate thereof according to any one of claims 5 to 23 together with a pharmaceutically acceptable carrier.

25. The pharmaceutical composition of claim 24 wherein the pharmaceutical composition further comprises a buffering agent.

26. The pharmaceutical composition of claim 25 wherein:

a) the pharmaceutically acceptable salt is selected from the group consisting of benzathine, calcium, choline, diethylamine, diolamine, magnesium, meglumine, lysine, piperazine, potassium, tris(hydroxymethyl)aminomethane and sodium;

b) the molar ratio of the salt counterion to the (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate in the pharmaceutically acceptable salt is approximately 0.5:1 to approximately 3:1; and

c) the buffering agent is selected from the group consisting of phosphoric acid, citric acid, maleic acid, tartaric acid, lactic acid and acetic acid.

27. The pharmaceutical composition of claim 26 wherein:

a) the pharmaceutically acceptable salt is sodium;

b) the molar ratio of the sodium counterion to the (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate in the pharmaceutically acceptable salt is approximately 0.5:1 to approximately 2:1;

c) the buffering agent is citric acid; and

d) the molar ratio of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate to citric acid is approximately 2:1 to approximately 10:1.

28. The pharmaceutical composition of any one of claims 24 to 27 wherein the composition is in the form of a powder or lyophile wherein the solution pH of the reconstituted formulation is in the range of 2 to 6.

29. The pharmaceutical composition of claim 28 wherein the solution pH of the reconstituted formulation is in the range of 3 to 5.

30. The pharmaceutical composition of any one of claims 24 to 29 wherein the pharmaceutical composition further comprises one or more stabilizing agents.

31. The pharmaceutical composition of claim 30 wherein the one or more stabilizing agents are selected from the group consisting of dextrans, sucrose, lactose, trehalose, mannitol, sorbitol, glucose, raffinose, glycine, histidine, polyvinyl pyrrolidones, and polyethylene glycols.

32. The pharmaceutical composition of claim 30 wherein the one or more stabilizing agents are selected from the group consisting of polyethylene glycol 300, polyethylene glycol 400 and polyethylene glycol 3350.

33. The pharmaceutical composition of claim 32 wherein the total amount of the one or more stabilizing agents is up to approximately 15% w/w of the formulation.

34. The pharmaceutical composition of any one of claims 24 to 33 wherein the pharmaceutical composition further comprises one or more solubilizing agents.

35. The pharmaceutical composition of claim 34 wherein the solubilizing agent is selected from the group consisting of polysorbate 20, polyethoxylated castor oil, polyethylene glycol (15)-hydroxystearate, hydroxypropyl-beta-cyclodextrin, sulfobutylether-beta cyclodextrin, gamma cyclodextrin, and polysorbate 80.

36. The pharmaceutical composition of claim 35 wherein the solubilizing agent is polysorbate 80 and the buffering agent is citric acid.

37. The pharmaceutical composition of claim 36 wherein the composition is a powder or lyophile which, when reconstituted with water for injection, 0.9% saline or 5% w/v provides an aqueous solution wherein the concentration of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl

dihydrogen phosphate or a pharmaceutically acceptable salt thereof is about 1 mg/mL to about 200 mg/mL.

38. The pharmaceutical composition of claim 37 wherein the solution pH of the formulation after reconstitution is in the range of about 3 to about 5.

39. The pharmaceutical composition of claim 38, which after reconstitution has a polysorbate 80 concentration is up to approximately 5% w/w.

40. The pharmaceutical composition of claim 37 wherein the pharmaceutical powder or lyophile has a water content of less than about 1%.

41. The pharmaceutical composition of any one of claims 24 to 40 which is an aqueous solution suitable for parenteral administration or is reconstituted with water for injection, 0.9% saline or 5% w/v dextrose to form an aqueous solution suitable for parenteral administration.

42. A method of treating a coronavirus infection in a patient, the method comprising administering a therapeutically effective amount of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate; or a pharmaceutically acceptable salt, solvate or hydrate thereof according to any one of claims 5 to 23 to a patient in need thereof.

43. The method of claim 42 wherein the coronavirus infection is COVID-19.

44. The method of claim 43 wherein about 0.1 g to about 5 g of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate; or a pharmaceutically acceptable salt, solvate or hydrate thereof is administered daily.

45. The method of claim 44 wherein about 0.1 to about 1 g (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate; or a pharmaceutically acceptable salt, solvate or hydrate thereof is intravenously administered daily.

46. A method of treating COVID-19 in a patient, the method comprising administering a pharmaceutical composition according to claim 41 to a patient in need of treatment thereof.

47. The method of any one of claims 42 to 46 wherein one or more additional therapeutic agents are administered to the patient.

48. The method of claim 47 wherein the one or more additional therapeutic agent is selected from the group consisting of remdesivir, galidesivir, favilavir/avifavir, mulnupiravir (MK-4482/EIDD 2801), AT-527, AT-301, BLD-2660, favipiravir, camostat, SLV213 emtrictabine/tenofivir, clevudine, dalcetrapib, boceprevir, ABX464, dexamethasone, hydrocortisone, convalescent plasma, gelsolin (Rhu-p65N), monoclonal antibodies, regdanvimab (Regkirova), ravulizumab (Ultomiris), VIR-7831/VIR-7832, BRII-196/BRII-198, COVI-AMG/COVI DROPS (STI-2020), bamlanivimab (LY-CoV555), mavrilimab, leronlimab (PRO140), AZD7442, lenzilumab, infliximab, adalimumab, JS 016, STI-1499 (COVIGUARD), lanadelumab (Takhzyro), canakinumab (Ilaris), gimsilumab, otilimab, casirivimab/imdevimab (REGN-Cov2), MK-7110 (CD24Fc/SACCOVID), heparin, apixaban, tocilizumab (Actemra), sarilumab (Kevzara), apilimod dimesylate, DNL758, PB1046, dapaglifozin, abivertinib, ATR-002, bemcentinib, acalabrutinib, baricitinib, tofacitinib, losmapimod, famotidine, niclosamide and diminazene.

49. The method of claim 48 wherein the one or more additional agent is selected from the group consisting of remdesivir, dexamethasone, malnupiravir, bamlanivimab, tofacitinib and baricitinib.

50. (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate; or a pharmaceutically acceptable salt thereof.

CLAIMS

1. A pharmaceutical composition comprising (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyldihydrogen phosphate, sodium citrate buffer, PEG400 and PEG3350.

2. The pharmaceutical composition of claim 1 wherein the composition is an aqueous solution.

3. The pharmaceutical composition of claim 2 wherein the aqueous solution comprises 100 mg/mL of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate, 40 mM sodium citrate buffer, 10 mg/mL PEG400 and 10 mg/mL PEG3350.

4. The pharmaceutical composition of claim 3 wherein the pH of the aqueous solution is 4.0.

5. The pharmaceutical composition of claim 1 wherein the molar ratio of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate to sodium citrate buffer is 4.5 to 1.

6. The pharmaceutical composition of claim 1 wherein the weight ratio of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate to PEG400 is 10 to 1.

7. The pharmaceutical composition of claim 1 wherein the weight ratio of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate to PEG3350 is 10 to 1.

8. The pharmaceutical composition of claim 1 wherein the molar ratio of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-

yl]butyl dihydrogen phosphate to sodium citrate buffer is 4.5 to 1, the weight ratio of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate to PEG400 is 10 to 1 and the weight ratio of (3S)-3-({N-[(4-methoxy-1H-indol-2-yl)carbonyl]-L-leucyl}amino)-2-oxo-4-[(3S)-2-oxopyrrolidin-3-yl]butyl dihydrogen phosphate to PEG3350 is 10 to 1.

9. The pharmaceutical composition of any one of claims 1 and 5 to 8 wherein the pharmaceutical composition is a lyophile.

10. The pharmaceutical composition of claim 8 wherein the pharmaceutical composition is an amorphous lyophile with a single Tg of 76.3°C as determined by mDSC.

11. Use of a pharmaceutical composition of any one of 1 to 8 for treatment of a coronavirus infection in a patient.

12. The use of claim 1 wherein the coronavirus infection is COVID-19.