

What is Claimed:

1. A method of reducing the likelihood that an injured patient or subject at risk of an inflammatory syndrome will produce one or more of sepsis, septic shock, an acute inflammatory syndrome (whether iatrogenic or not) or acute respiratory distress syndrome, comprising administering to said patient or subject an effective amount of at least one PLA2 inhibitor and/or at least one metalloprotease inhibitor alone or in combination with at least one antibiotic.
2. The method according to claim 1 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid- as the racemic mixture or enantiomer thereof) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl}oxyacetic acid), a pharmaceutically acceptable salt thereof or a mixture thereof.
3. The method according to claim 1 or 2 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.
4. The method according to any of claims 1-3 wherein said PLA2 inhibitor and/or said metalloprotease inhibitor is combined with at least one antibiotic.
5. The method according to claim 4 wherein said antibiotic is selected from the group consisting of a penam, a carboxylpenicillin, a cephalosporin, a monobactam, a carbapenem, a fluoroquinolone, a macrolide or a mixture thereof.
6. A method of treating an injured or burned patient or subject to improve wound healing and/or to inhibit, ameliorate or reduce the likelihood of one or more of sepsis, septic

shock, acute inflammatory syndrome, including inflammatory response syndrome (SIRS) and/or acute respiratory distress syndrome (ARDS) in said patient or subject, comprising administering to said patient or subject an effective amount of at least one PLA2 inhibitor and/or a metalloprotease inhibitor in combination with an effective amount of at least one antibiotic.

7. The method according to claim 6 comprising administering to said patient or subject at least two antibiotics.

8. The method according to claim 6 or 7 wherein said antibiotic(s) is co-administered with at least one PLA2 inhibitor.

9. The method according to any of claims 6-8 wherein said antibiotic(s) is co-administered with at least one metalloprotease inhibitor.

10. The method according to any of claims 6-9 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid- as a racemic mixture or enantiomer thereof) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl}oxyacetic acid), darapladib, a pharmaceutically acceptable salt thereof or a mixture thereof.

11. The method according to any of claims 6-10 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.

12. A method of treating a patient or subject with sepsis, including early sepsis, comprising administering to said patient or subject in need, an effective amount of at least

one antibiotic and an effective amount of at least one PLA2 inhibitor and/or a metalloprotease inhibitor.

13. The method according to claim 12 comprising administering to said patient or subject at least two antibiotics.

14. The method according to claim 12 or 13 wherein said antibiotic(s) is co-administered with at least one PLA2 inhibitor.

15. The method according to any of claims 12-14 wherein said antibiotic(s) is co-administered with at least one metalloprotease inhibitor.

16. The method according to any of claims 12-15 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid- as a racemic mixture or enantiomer thereof) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl}oxyacetic acid), darapladib, a pharmaceutically acceptable salt thereof or a mixture thereof.

17. The method according to any of claims 12-16 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.

18. A method for preserving a blood sample(s) taken from a patient or subject who has injuries or burns which place the patient or subject at risk for one or more of sepsis, septic shock, acute inflammatory syndrome, including inflammatory response syndrome (SIRS) and/or acute respiratory distress syndrome (ARDS), the method comprising combining in said blood sample an effective amount of at least one PLA2 inhibitor and/or at least one

metalloprotease each alone, together or in combination with an effective amount of at least one antibiotic.

19. The method according to claim 18 wherein said blood sample is combined with at least one PLA2 inhibitor.

20. The method according to claim 18 or 19 wherein said antibiotic(s) is combined with at least one metalloprotease inhibitor.

21. The method according to any of claims 18-20 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid- as a racemic mixture or enantiomer thereof) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl)oxyacetic acid), a pharmaceutically acceptable salt thereof or a mixture thereof.

22. The method according to any of claims 18-21 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.

23. A composition comprising a blood sample(s) taken from a patient or subject who has injuries or burns which place the patient or subject at risk for one or more of sepsis, septic shock, acute inflammatory syndrome, including inflammatory response syndrome (SIRS) and/or acute respiratory distress syndrome (ARDS), in combination with an effective amount of at least one PLA2 inhibitor and/or at least one metalloprotease each alone, together or in combination with an effective amount of at least one antibiotic.

24. The composition according to claim 23 wherein said blood sample is combined with at least one PLA2 inhibitor.

25. The composition according to claim 23 or 24 wherein said composition comprises at least one antibiotic and at least one metalloprotease inhibitor.

26. The composition according to any of claims 23-25 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid- as a racemic mixture or enantiomer thereof) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl}oxyacetic acid), darapladib a pharmaceutically acceptable salt thereof or a mixture thereof.

27. The composition according to any of claims 23-26 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.

28. A pharmaceutical composition for use in treating a patient at risk for or afflicted with one or more of sepsis, septic shock, acute inflammatory syndrome, including inflammatory response syndrome (SIRS) and/or acute respiratory distress syndrome (ARDS), comprising an effective amount of at least one antibiotic in combination with at least one PLA2 inhibitor and/or at least one metalloprotease inhibitor.

29. The composition according to claim 28 comprising at least one PLA2 inhibitor.

30. The composition according to claim 28 or 29 comprising at least one metalloprotease inhibitor.

31. The composition according to any of claims 28-30 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid- as a racemic mixture or enantiomer thereof) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl}oxyacetic acid), darapladib, a pharmaceutically acceptable salt thereof or a mixture thereof.

32. The composition according to any of claims 28-31 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.

33. A method of inhibiting or reducing the likelihood of a COVID-19/cytokine release syndrome in a patient at risk of same comprising administering to said patient at risk at least one PLA2 inhibitor and/or at least one metalloprotease inhibitor.

34. The method according to claim 33 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid- as a racemic mixture) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl}oxyacetic acid), a pharmaceutically acceptable salt thereof or a mixture thereof.

35. The method according to claim 33 or 34 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.

36. The method according to any of claims 1-3 wherein said PLA2 inhibitor and/or said metalloprotease inhibitor are combined.

37. A method of treating neo-natal acute respiratory distress syndrome (neo-natal ARDS), including meconium aspiration syndrome in a patient in need comprising administering to said patient at least one PLA2 inhibitor.

38. The method according to claim 37 wherein said PLA2 inhibitor is LY315920, LY333013, AZD2716, as an enantiomerically enriched species or as a racemic mixture or mixtures thereof.

39. The method according to either of claims 37 or 38 wherein said neo-natal ARDS is meconium aspiration syndrome (MAS).

40. A method of treating a patient or subject in need at risk for or afflicted with anthrax or severe acute respiratory syndrome coronavirus infection (SARS or SARS-CoV2), comprising administering to said patient or subject an effective amount of at least one PLA2 inhibitor and/or a metalloprotease inhibitor and optionally at least one antibiotic to provide an unexpected inhibition, amelioration and/or avoidance of sepsis, septic shock, acute inflammatory syndrome, including inflammatory response syndrome (SIRS) and/or acute respiratory distress syndrome (ARDS) in the patient or subject.

41. The method according to claim 40 comprising administering to said patient or subject at least two antibiotics in combination with said PLA2 inhibitor(s) and/or said metalloprotease inhibitor(s).

42. The method according to 40 or 41 wherein at least one PLA2 inhibitor is administered to said patient.

43. The method according to any of claims 40-42 wherein at least one metalloprotease inhibitor is administered to said patient or subject.

44. The method according to any of claims 40-43 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid- as a racemic mixture or enantiomer thereof) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl}oxyacetic acid), darapladib, a pharmaceutically acceptable salt thereof or a mixture thereof.

45. The method according to any of claims 40-44 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.

46. The method according to any of claims 1-17 and 33-45 wherein said PLA2 inhibitor and said metalloprotease inhibitor are co-administered.

47. The method according to any of claims 18-22 wherein said PLA2 inhibitor and said metalloprotease inhibitor(s) are used together.

48. The composition according to any of claims 23-32 comprising at least one PLA2 inhibitor and at least one metalloprotease inhibitor.

49. The method according to any of claims 1-22 and 33-45 wherein said metalloprotease inhibitor is prinomastat.

50. The composition according to any of claims 23-32 wherein said PLA2 inhibitor is varespladib, methylvarespladib, AZD2716 (as a racemic mixture or as the "R" enantiomer), a pharmaceutically acceptable salt thereof or a mixture thereof.

51. The method according to any of claims 1-22 and 33-45 wherein said PLA2 inhibitor is varespladib, methylvarespladib, AZD2716 (as a racemic mixture or as the "R" enantiomer), a pharmaceutically acceptable salt thereof or a mixture thereof.

52. The composition according to any of claims 23-32 wherein said PLA2 inhibitor is varespladib, methylvarespladib, AZD2716 (as a racemic mixture or as the "R" enantiomer), a pharmaceutically acceptable salt thereof or a mixture thereof.

53. A pharmaceutical composition comprising a therapeutically effective amount of at least one PLA2 inhibitor, at least one metalloprotease inhibitor or a mixture thereof in combination with an antibiotic.

54. The composition according to claim 53 wherein said antibiotic is a penam, a carboxypenicillin, a cephalosporin, a monobactam, a carbapenem, a fluoroquinolone, a macrolide or a mixture thereof.

55. The composition according to claim 53 wherein said antibiotic is ciprofloxacin, levofloxacin, moxifloxacin, penicillin G, doxycycline, chloramphenicol, ofloxacin or mixtures thereof.

56. The composition according to any of claims 53-55 wherein said PLA2 inhibitor is varespladib (LY315920), methyl varespladib (LY333013), AZD2716-R,S (3-(5'-Benzyl-2'-

carbamoylbiphenyl-3-yl)propanoic acid- as a racemic mixture or enantiomer thereof) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl}oxyacetic acid), darapladib, a pharmaceutically acceptable salt thereof or a mixture thereof.

57. The method according to any of claims 53-56 wherein said metalloprotease inhibitor is prinomastat, BB-94 (marimastat), BB-2516 (batimastat), vorinostat, cefixime and doxycycline, a pharmaceutically acceptable salt thereof or a mixture thereof.