CLAIMS

What is claimed is:

1. A method of treating or preventing viremia caused by a virus in a subject in need thereof, the method comprising administering pirfenidone to the subject.

2. A method of treating or preventing viremia-induced disease in a subject in need thereof, the method comprising administering pirfenidone to the subject.

3. A method of treating COVID-19 and/or COVID-19 disease caused by a SARS-CoV-2 variant thereof in a subject in need thereof, the method comprising administering pirfenidone to the subject.

4. A method of treating or preventing an infection with a virus in a subject in need thereof, the method comprising administering pirfenidone to the subject.

5. A method of inhibiting an inflammatory response by one or more pro-inflammatory cytokines in a subject in need thereof, the method comprising administering pirfenidone to the subject.

6. A method of inhibiting a cascade by one or more pro-inflammatory cytokines in a subject in need thereof, the method comprising administering pirfenidone to the subject.

7. A method of reducing elevated levels of one or more markers of inflammation in a subject in need thereof with viremia caused by a virus, the method comprising administering pirfenidone to the subject.

8. The method of any one of claims 1-7, wherein the pirfenidone is formulated in one or more extended-release pills, wherein each of the one or more extended-release pills comprises the pirfenidone and one or more excipients.

9. The method of any one of claims 1-8, wherein each of the one or more extended-release pills comprises approximately 100 mg to approximately 850 mg of pirfenidone.

10. The method of any one of claims 1-9, wherein each of the one or more extended-release pills comprises approximately 600 mg of pirfenidone.

11. The method of any one of claims 1-10, wherein a C_{max} from a first dose of the one or more extended-release pills is between approximately 1.0 µg/mL to 10.0 µg/mL.

12. The method of any one of claims 1-11, wherein the C_{max} from a first dose of the one or more extended-release pills is between approximately 1.0 µg/mL to 4.0 µg/mL.

13. The method of any one of claims 1-7, wherein the pirfenidone is formulated in one or more sustained-release pills, wherein each of the one or more sustained-release pills comprises the pirfenidone and one or more excipients.

14. The method of any one of claims 1-8 or 13, wherein each of the one or more sustained-release pills comprises approximately 100 mg to approximately 850 mg of pirfenidone.

15. The method of any one of claims 1-9 or 14, wherein each of the one or more sustained-release pills comprises approximately 600 mg of pirfenidone.

16. The method of any one of claims 1-10 or 15, wherein a C_{max} from a first dose of the one or more sustained-release pills is between approximately 1.0 µg/mL to 10.0 µg/mL.

17. The method of any one of claims 1-11 or 16, wherein the C_{max} from a first dose of the one or more sustained-release pills is between approximately 1.0 µg/mL to 4.0 µg/mL.

18. The method of any one of claims 1-17, wherein a T_{max} is between approximately 1.5 hours to 8.0 hours.

19. The method of any one of claims 1-18, wherein the T_{max} is between approximately 3.0 hours to approximately 5.0 hours.

20. The method of any one of claims 1-19, wherein an AUC_{0-t} is between approximately 10.0 µg*hours/mL to approximately 30.0 µg*hours/mL.

21. The method of any one of claims 1-20, wherein the half-life ($T_{1/2}$) is between approximately 1.6 hours to approximately 8.0 hours.

22. The method of any one of claims 7-21, wherein the one or more excipients comprise one or more excipients selected from the group consisting of a compression binder, diluent, disintegrant, coating agent, rate-controlling polymer, anti-caking agent, adsorbent, lubricant, and glidant.

23. The method of any one of claims 7-22, wherein at least one excipient of the one or more excipients is selected from the group consisting of hydroxypropylmethylcellulose (HPMC), microcrystalline cellulose, silicon dioxide, and sodium stearyl fumarate.

24. The method of any one of claims 7-23, wherein each of the one or more sustained-release pills comprises:

a) approximately 100 mg to approximately 850 mg of pirfenidone;
b) microcrystalline cellulose;
c) low viscosity HPMC;
d) high viscosity HPMC;
e) silicon dioxide; and
f) sodium stearyl fumarate.

25. The method of any one of claims 7-23, wherein each of the one or more extended-release pills comprises:

a) approximately 100 mg to approximately 850 mg of pirfenidone;
b) microcrystalline cellulose;
c) low viscosity HPMC;
d) high viscosity HPMC;

e) silicon dioxide; and

f) sodium stearyl fumarate.

26. The method of any one of claims 7-23 or 25, wherein each of the one or more extended-release pills comprises:

a) approximately 100 mg to approximately 850 mg of pirfenidone;

b) approximately 100 mg to 125 mg microcrystalline cellulose;

c) approximately 50.0 mg to 100.0 mg low viscosity HPMC;

d) approximately 30.0 mg to 50.0 mg high viscosity HPMC;

e) approximately 5.0 mg to 10.0 mg silicon dioxide; and

f) approximately 5.0 mg to 10.0 mg sodium stearyl fumarate.

27. The method of any one of claims 1-24, wherein the one or more sustained-release pills are formulated as tablets, capsules, or gel capsules.

28. The method of any one of claims 1-23 or 25-27, wherein the one or more extended-release pills are formulated as tablets, capsules, or gel capsules.

29. The method of any one of claims 1-23 or 25-28, wherein the one or more extended -release pills are formulated as tablets.

30. The method of any one of claims 1, 2, or 7-29, wherein the viremia is selected from the group consisting of primary viremia, secondary viremia, active viremia, and passive viremia.

31. The method of any one of claims 1, 2, or 7-30, wherein the viremia caused by the virus is viremia caused by an RNA virus or a DNA virus.

32. The method of any one of claims 2 or 7-31, wherein the viremia-induced disease is caused by an infection with a virus.

33. The method of any one of claims 5 or 8-32, wherein the inflammatory response is induced by an infection with a virus.

34. The method of any one of claims 4 or 8-33, wherein the infection with the virus is infection with an RNA virus or a DNA virus.

35. The method of claim 34, wherein the viremia caused by an RNA virus is viremia caused by a coronavirus.

36. The method of claim 34 or 35, wherein the infection with the RNA virus is an infection with a coronavirus.

37. The method of any one of claims 34-36, wherein the coronavirus is severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).

38. The method of any one of claims 34-36, wherein the coronavirus is a SARS-CoV-2 variant of B.1.1.7, B.1.351, B.1.525, B.1.526, P.1, B.1.427, B.1.429, and/or SARS-CoV-2 variants with the Q677P and/or L452R mutations.

39. The method of any one of claims 34-38, wherein the coronavirus causes coronavirus disease 2019 (COVID-19).

40. The method of any one of claims 34-38, wherein the coronavirus is severe acute respiratory syndrome-associated coronavirus (SARS-CoV).

41. The method of any one of claims 34-38, wherein the coronavirus is Middle East respiratory syndrome coronavirus (MERS-CoV).

42. The method of any one of claims 1-41, wherein the subject develops fibrosis.

43. The method of any one of claims 1-42, wherein the fibrosis is lung fibrosis or liver fibrosis.

44. The method of any one of claims 1-43, wherein the subject has one or more contraindications for standard immediate-release pirfenidone.

45. The method of any one of claims 1-44, wherein the subject has liver disease, liver damage, or a liver injury.

46. The method of any one of claims 1-45, wherein the subject has liver disease with a Pugh-Child score of class A, class B, or class C.

47. The method of any one of claims 45 or 46, wherein the liver disease is chronic liver disease.

48. The method of any one of claims 1-47, wherein the pirfenidone is formulated in one or more extended-release tablets, the subject has one or more liver contraindications for standard-release pirfenidone; and each of the one or more extended-release tablets comprises:

a) approximately 100 mg to approximately 850 mg of pirfenidone;
b) approximately 100 mg to 125 mg microcrystalline cellulose;
c) approximately 50.0 mg to 100.0 mg low viscosity HPMC;
d) approximately 30.0 mg to 50.0 mg high viscosity HPMC;
e) approximately 5.0 mg to 10.0 mg silicon dioxide; and
f) approximately 5.0 mg to 10.0 mg sodium stearyl fumarate.

49. The method of any one of claims 1-48, comprising blocking and/or reducing an inflammatory response.

50. The method of any one of claims 1-49, comprising inhibiting the inflammatory response by one or more pro-inflammatory cytokines.

51. The method of any one of claims 1-50, wherein the inflammatory response is a cascade by the one or more pro-inflammatory cytokines.

52. The method of any one of claims 1-51, wherein the inflammatory response results in acute respiratory distress syndrome (ARDS).

53. The method of any one of claims 1-52, wherein the subject has elevated levels of one or more markers of inflammation.

54. The method of claim 53, wherein the one or more markers of inflammation are selected from the group consisting of D-dimers, C-reactive protein (CRP), ferritin, and lactic acid dehydrogenase (LDH).

55. The method of any one of claims 1-54, wherein the one or more markers of inflammation comprise C-reactive protein (CRP), ferritin, and lactic acid dehydrogenase (LDH).

56. The method of any one of claims 1-55, wherein the subject has elevated levels of one or more pro-inflammatory cytokines.

57. The method of claim 56, wherein the one or more pro-inflammatory cytokines are selected from the group consisting of TNF-α, IFN-γ, IL-1β, IL-6, and/or IL-12.

58. The method of any one of claims 1-57, wherein the subject has high viral burden and elevated levels of one or more markers of inflammation.

59. The method of any one of claims 1-58, wherein the subject that has high viral burden has low levels of cycle threshold (Ct).

60. The method of any one of claims 1-59, wherein the subject has pneumonia.

61. The method of any one of claims 1-60, wherein the subject has lung inflammation and/or lung fibrosis.

62. The method of any one of claims 1-61, wherein the subject has acute respiratory distress syndrome (ARDS).

63. The method of any one of claims 1-62, wherein the subject has COVID-19.

64. The method of any one of claims 1-63, wherein the pirfenidone is formulated in one or more extended-release pills, wherein each of the one or more extended-release pills

comprises the pirfenidone and one or more excipients; the coronavirus is severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and/or a SARS-CoV-2 variant thereof; and the subject has coronavirus disease 2019 (COVID-19) and/or a disease caused by a SARS-CoV-2 variant thereof.

65. The method of any one of claims 1-63, wherein the pirfenidone is formulated in one or more sustained-release pills, wherein each of the one or more sustained-release pills comprises the pirfenidone and one or more excipients; the coronavirus is severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2); and the subject has coronavirus disease 2019 (COVID-19).

66. The method of any one of claims 1-65, wherein the subject has one or more contraindications for immediate-release pirfenidone.

67. The method of any one of claims 1-65, wherein the subject has one or more contraindications for standard-release pirfenidone.

68. The method of any one of claims 1-67, wherein a daily dosage comprises approximately 400 mg to approximately 4800 mg of pirfenidone per day.

69. The method of any one of claims 1-68, wherein a daily dosage comprises approximately 800 mg to approximately 3000 mg of pirfenidone per day.

70. The method of any one of claims 1-69, wherein a daily dosage comprises approximately 1000 mg to approximately 2400 mg of pirfenidone per day.

71. The method of any one of claims 1-70, wherein the one or more sustained-release tablets are administered orally 1 to 8 times per day.

72. The method of any one of claims 1-71, wherein the one or more sustained-release pills are administered orally two times per day.

73. The method of any one of claims 1-72, wherein the one or more sustained-release pills are administered for approximately ten days or more.

74. The method of any one of claims 1-70, wherein the one or more extended-release tablets are administered orally 1 to 8 times per day.

75. The method of any one of claims 1-70 or 74, wherein the one or more extended-release pills are administered orally two times per day.

76. The method of any one of claims 1-70 or 75, wherein the one or more extended-release pills are administered for approximately ten days or more.

77. The method of any one of claims 1-70 or 74-76, wherein the one or more extended-release pills are administered for approximately fourteen days or more.

78. The method of any one of claims 1-70 or 74-76, wherein the one or more extended-release pills are administered for approximately twenty-eight days or more.

79. The method of any one of claims 1-73, wherein the one or more sustained-release pills are administered for approximately thirty days or more.

80. The method of any one of claims 1-73 or 79, wherein the one or more sustained-release pills are administered for approximately ten to approximately thirty days.

81. The method of any one of claims 1-70 or 74-78, wherein the one or more extended-release pills are administered for approximately thirty days or more.

82. The method of any one of claims 1-70 or 74-78, wherein the one or more extended-release pills are administered for approximately ten to approximately thirty days.

83. The method of any one of claims 1-70, 74-78, 81, or 82, comprising a formulation of pirfenidone that provides release of pirfenidone over 12 hours.

84. A pharmaceutical composition comprising pirfenidone and one or more excipients, for use in treating or preventing viremia caused by a virus, viremia-induced disease, COVID-19, a disease caused by a SARS-CoV-2 variant thereof, an infection with a virus, and/or ARDS caused by infection with an infectious agent in a subject in need thereof.

85. The pharmaceutical composition of claim 84, comprising pirfenidone and one or more excipients, for use in treating or preventing viremia caused by a virus, viremia-induced disease, an infection with a virus, and/or ARDS caused by infection with an infectious agent in a subject in need thereof.

86. The pharmaceutical composition of claim 84 or 85, wherein the pirfenidone is formulated in one or more sustained-release pills, wherein each of the one or more sustained-release pills comprises the pirfenidone and the one or more excipients.

87. The pharmaceutical composition of claim 84 or 85, wherein the pirfenidone is formulated in one or more extended-release pills, wherein each of the one or more extended-release pills comprises the pirfenidone and the one or more excipients.

88. The pharmaceutical composition of claim 84-87, wherein the viremia-induced disease is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).

89. The pharmaceutical composition of claim 84-88, wherein the infection with the virus is infection with SARS-CoV-2.

90. The pharmaceutical composition of any one of claims 84-89, wherein the subject has COVID-19.

91. Use of pirfenidone for treating or preventing viremia caused by a virus, viremia-induced disease, COVID-19, a disease caused by a SARS-CoV-2 variant thereof, an infection with a virus, and/or ARDS caused by infection with an infectious agent in a subject in need thereof.

92. A kit comprising a pharmaceutical composition comprising pirfenidone and one or more excipients, for use in treating or preventing viremia caused by a virus, viremia-induced disease, COVID-19, a disease caused by a SARS-CoV-2 variant thereof, an infection with a virus, and/or ARDS caused by infection with an infectious agent; and

instructions for administering to a subject or contacting a biological sample with the pharmaceutical composition.

CLAIMS

What is claimed is:

1. Use of pirfenidone in the manufacture of a medicament for the treatment of COVID-19 and/or COVID-19 disease caused by a SARS-CoV-2 variant thereof in a subject in need thereof, wherein pirfenidone is to be administered to the subject.

2. Use of pirfenidone in the manufacture of a medicament for the treatment or prevention of viremia caused by a virus in a subject in need thereof, wherein pirfenidone is to be administered to the subject.

3. Use of pirfenidone in the manufacture of a medicament for the treatment or prevention of viremia-induced disease in a subject in need thereof, wherein pirfenidone is to be administered to the subject.

4. Use of pirfenidone in the manufacture of a medicament for the treatment or prevention of an infection with a virus in a subject in need thereof, wherein pirfenidone is to be administered to the subject.

5. Use of pirfenidone in the manufacture of a medicament for the inhibition of (a) an inflammatory response or (b) a cascade by one or more pro-inflammatory cytokines in a subject in need thereof, wherein pirfenidone is to be administered to the subject.

6. Use of pirfenidone in the manufacture of a medicament for the reduction of elevated levels of one or more markers of inflammation in a subject in need thereof with viremia caused by a virus, wherein pirfenidone is to be administered to the subject.

7. The use of any one of claims 1-6, wherein pirfenidone is formulated in:

(a) extended-release pills, wherein each of the extended-release pills comprises pirfenidone and one or more excipients; or

(b) sustained-release pills, wherein each of the sustained-release pills comprises pirfenidone and one or more excipients.

8. The use of claim 7, wherein each of the extended-release pills or sustained-release pills comprises:

(a) approximately 100 mg to approximately 850 mg of pirfenidone; or

(b) approximately 600 mg of pirfenidone.

9. The use of claim 7 or 8, wherein a C_{max} from a first dose of the extended-release pills or sustained-release pills is between approximately:

(a) 1.0 μg/mL to 10.0 μg/mL; or

(b) 1.0 μg/mL to 4.0 μg/mL.

10. The use of any one of claims 7-9, wherein a T_{max} from a first dose of the extended-release pills or sustained-release pills is between approximately:

(a) 1.5 hours to approximately 8.0 hours; or

(b) 3.0 hours to approximately 5.0 hours.

11. The use of any one of claims 7-10, wherein the one or more excipients are selected from the group consisting of compression binders, diluents, disintegrants, coating agents, rate-controlling polymers, anti-caking agents, adsorbents, lubricants, and glidants.

12. The use of any one of claims 7-11, wherein each of the sustained-release pills or extended-release pills comprises:

a) approximately 100 mg to approximately 850 mg of pirfenidone;
b) microcrystalline cellulose;
c) low viscosity HPMC;
d) high viscosity HPMC;
e) silicon dioxide; and
f) sodium stearyl fumarate;

optionally, wherein each of the sustained-release pills or extended-release pills comprises:

i) approximately 100 mg to approximately 850 mg of pirfenidone;
ii) approximately 100 mg to 125 mg microcrystalline cellulose;
iii) approximately 50.0 mg to 100.0 mg low viscosity HPMC;
iv) approximately 30.0 mg to 50.0 mg high viscosity HPMC;
v) approximately 5.0 mg to 10.0 mg silicon dioxide; and
vi) approximately 5.0 mg to 10.0 mg sodium stearyl fumarate.

13. The use of any one of claims 7-12, wherein the sustained-release pills or extended-release pills are formulated as tablets, capsules, or gel capsules.

14. The use of any one of claims 2, 3, and 6-13, wherein the viremia is:

(a) selected from the group consisting of primary viremia, secondary viremia, active viremia, and passive viremia; and/or

(b) caused by an RNA virus or a DNA virus; wherein the RNA virus is a coronavirus.

15. The use of claim 14, wherein the coronavirus is:

(a) severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2);

(b) SARS-CoV-2 variant of B.1.1.7, B.1.351, B.1.525, B.1.526, P.1, B.1.427, B.1.429, and/or SARS-CoV-2 variants with the Q677P and/or L452R mutations;

(c) severe acute respiratory syndrome-associated coronavirus (SARS-CoV); or

(d) Middle East respiratory syndrome coronavirus (MERS-CoV).

16. The use of any one of claims 1-15, wherein the subject develops fibrosis;

optionally, wherein the fibrosis is lung fibrosis or liver fibrosis.

17. The use of any one of claims 1-16, comprising:

(a) blocking and/or reducing an inflammatory response;

(b) inhibiting the inflammatory response by one or more pro-inflammatory cytokines; optionally, wherein the inflammatory response:

(i) is a cascade by the one or more pro-inflammatory cytokines; or

(ii) results in acute respiratory distress syndrome (ARDS).

18. The use of any one of claims 1-17, wherein the subject has elevated levels of one or more:

(a) markers of inflammation; optionally, wherein the one or more markers of inflammation are selected from the group consisting of D-dimers, C-reactive protein (CRP), ferritin, and lactic acid dehydrogenase (LDH); and/or

(b) pro-inflammatory cytokines; optionally, wherein the one or more pro-inflammatory cytokines are selected from the group consisting of TNF-α, IFN-γ, IL-1β, IL-6, and IL-12.

19. The use of any one of claims 1-18, wherein the subject has:

(a) high viral burden and elevated levels of one or more markers of inflammation;

(b) high viral burden has low levels of cycle threshold (Ct);

(c) pneumonia;

(d) lung inflammation and/or lung fibrosis;

(e) acute respiratory distress syndrome (ARDS);

(f) COVID-19; and/or

(g) liver disease, liver damage, or a liver injury;

optionally, wherein the liver disease is chronic liver disease.

20. The use of any one of claims 1-19, wherein pirfenidone is formulated in extended-release pills or sustained-release pills, wherein each of the extended-release pills or sustained-release pills comprises pirfenidone and one or more excipients; the coronavirus is severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and/or a SARS-CoV-2 variant thereof; and the subject has coronavirus disease 2019 (COVID-19) and/or a disease caused by a SARS-CoV-2 variant thereof.

21. The use of any one of claims 1-20, wherein the subject has one or more contraindications for:

(a) immediate-release pirfenidone; or

(b) standard-release pirfenidone.

22. The use of any one of claims 1-21, wherein a daily dose of pirfenidone comprises:

(a) approximately 400 mg to approximately 4800 mg of pirfenidone per day;

(b) approximately 800 mg to approximately 3000 mg of pirfenidone per day; or

(c) approximately 1000 mg to approximately 2400 mg of pirfenidone per day.

23. The use of any one of claims 7-22, wherein the sustained-release tablets or extended-release tablets are to be administered orally:

(a) 1 to 8 times per day; or

(b) two times per day.

24. The use of any one of claims 7-23, wherein the extended-release pills are to be administered for approximately:

(a) ten days or more or

(b) fourteen days or more; or

(c) twenty-eight days or more.

25 The use of any one of claims 7-23, wherein the extended-release pills or sustained-release pills are to be administered for approximately:

(a) thirty days or more; or

(b) ten to approximately thirty days.

26. The use of any one of claims 1-25, comprising a formulation of pirfenidone that provides release of pirfenidone over 12 hours.

27. A kit comprising a pharmaceutical composition comprising pirfenidone and one or more excipients, for use in treating or preventing viremia caused by a virus, viremia-induced disease, COVID-19, a disease caused by a SARS-CoV-2 variant thereof, an infection with a virus, and/or ARDS caused by infection with an infectious agent; and

instructions for administering to a subject with the pharmaceutical composition.