

CLAIMS

WHAT IS CLAIMED IS:

1. A method of prognosing or of aiding prognosis of idiopathic pulmonary fibrosis (IPF) in a patient comprising measuring in a biological sample obtained from the patient the expression of a combination of three or more genes, or expression of a combination of three or more proteins encoded by the combination of three or more genes, wherein the three or more genes are selected from COMP, MMP3, YKL-40, CXCL13, SAA4 (constitutive SAA) and SPP1 (OPN), wherein the combination of three or more genes comprises MMP3, wherein an elevated expression level of the combination of three or more genes, or an elevated expression level of the combination of three or more proteins, is indicative of a prognosis for shortened survival compared to median survival and wherein a reduced expression level of the combination of three or more genes, or a reduced expression level of the combination of three or more proteins, is indicative of a prognosis for increased survival compared to median survival.
2. The method of claim 1, wherein the combination of three or more genes comprises YKL-40.
3. The method of claim 1, wherein the combination of three or more genes further comprises MMP7.
4. The method of claim 1, wherein the combination of three or more genes further comprises a gene selected from CCL11, CCL13, CCL17, and CCL18.
5. The method of claim 1, wherein the combination of three or more genes comprises MMP3 and SAA4 (constitutive SAA).
6. The method of claim 4 wherein the combination of three or more genes comprises YKL-40 and CCL18.
7. The method of claim 4, comprising measuring the expression level of CXCL13.
8. The method of claim 4, comprising measuring the expression level of MMP3.
9. The method of claim 4, comprising measuring the expression level of SAA4 (constitutive SAA).
10. The method of claim 4, wherein the patient is on immunomodulatory therapy.
11. The method of any one of claims 1-10, wherein the biological sample is selected from lung tissue, serum, and plasma.
12. A method of prognosing or of aiding prognosis of IPF in a patient comprising determining a total baseline biomarker score in a biological sample obtained from the patient,
wherein the determining of the total baseline biomarker score comprises measuring the protein expression level of COMP and at least one of CXCL13 and OPN, and assigning a score of 0 if the expression level is below the median for CXCL13, OPN, and COMP,

respectively, and assigning a score of 1 if the expression level is above the median for CXCL13, OPN, and COMP, respectively, wherein the determining of the total baseline biomarker score further comprises measuring the protein expression level of YKL-40 and assigning a score of 0 if the expression level is below the median for YKL-40 and assigning a score of 1 if the expression level is above the median for YKL-40, and wherein the determining of the total baseline biomarker score further comprises adding each individual score to obtain the total baseline biomarker score,

wherein a total baseline biomarker score of two or above is indicative of a prognosis of shortened survival compared to median survival and wherein a total baseline biomarker score of zero or one is indicative of a prognosis of increased survival compared to the median survival.

13. The method of claim 12, wherein the total baseline biomarker score of the patient is two or above and the patient is selected for treatment with a candidate therapeutic agent in a clinical study, wherein the candidate therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody, N-acetylcysteine, anti-TGF- β antibody, anti- α v β 6 integrin antibody, anti-CTGF antibody, anti-CCL2 antibody, somatostatin analog, angiotensin II inhibitor, carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor.

14. The method of claim 13, wherein:

- a) the anti-LOXL2 antibody is GS-6624;
- b) the anti-TGF- β antibody is GC1008;
- c) the anti- α v β 6 integrin antibody is STX-100;
- d) the anti-CTGF antibody is FG-3019;
- e) the anti-CCL2 antibody is CNTO 888;
- f) the somatostatin analog is SOM230 or octreotide;
- g) the angiotensin II inhibitor is losartan; or
- h) the tyrosine kinase inhibitor is BIBF1120.

15. The method of claim 13, wherein the anti-IL-13 agent is lebrikizumab.

16. The method of claim 13, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.

17. The method of claim 16, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.

18. The method of claim 17, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.

19. The method of claim 13, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

20. A method of prognosing or of aiding prognosis of IPF in a patient comprising determining a total baseline biomarker score in a biological sample obtained from the patient,

wherein the determining of the total baseline biomarker score comprises measuring the protein expression level of COMP or MMP3 and COMP, and assigning a score of 0 if the expression level is below the median for MMP3 and COMP, respectively, and assigning a score of 1 if the expression level is above the median for MMP3 and COMP, respectively, wherein the determining of the total baseline biomarker score further comprises measuring the protein expression level of YKL-40 and assigning a score of 0 if the expression level is below the median for YKL-40 and assigning a score of 1 if the expression level is above the median for YKL-40, and wherein the determining of the total baseline biomarker score further comprises adding each individual score to obtain the total baseline biomarker score,

wherein a total baseline biomarker score of one or above is indicative of a prognosis of shortened survival compared to median survival and wherein a total baseline biomarker score of zero is indicative of a prognosis of increased survival compared to the median survival.

21. The method of any one of claims 12-20, wherein the biological sample is selected from serum and plasma.

22. The method of claim 20, wherein the total baseline biomarker score of the patient is one or above and the patient is selected for treatment with a candidate therapeutic agent in a clinical study, wherein the candidate therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody, N-acetylcysteine, anti-TGF- β antibody, anti- α v β 6 integrin antibody, anti-CTGF antibody, anti-CCL2 antibody, somatostatin analog, angiotensin II inhibitor, carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor.

23. The method of claim 22, wherein:

a) the anti-LOXL2 antibody is GS-6624;

b) the anti-TGF- β antibody is GC1008;

c) the anti- α v β 6 integrin antibody is STX-100;

- d) the anti-CTGF antibody is FG-3019;
 - e) the anti-CCL2 antibody is CNTO 888;
 - f) the somatostatin analog is SOM230 or octreotide;
 - g) the angiotensin II inhibitor is losartan; or
 - h) the tyrosine kinase inhibitor is BIBF1120.
24. The method of claim 22, wherein the anti-IL-13 agent is lebrikizumab.
25. The method of claim 22, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.
26. The method of claim 22, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.
27. The method of claim 26, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.
28. The method of claim 27, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.
29. Use of an IPF therapeutic agent in the manufacture of a medicament for the treatment of an IPF patient previously determined to have a prognosis of shortened survival according to the method of any one of claims 1-12, 20, or 21.
30. The use of claim 29, wherein the IPF therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody, N-acetylcysteine, anti-TGF- β antibody, anti- α v β 6 integrin antibody, anti-CTGF antibody, anti-CCL2 antibody, somatostatin analog, angiotensin II inhibitor, carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor.
31. The use of claim 30, wherein:
- a) the anti-LOXL2 antibody is GS-6624;
 - b) the anti-TGF- β antibody is GC1008;
 - c) the anti- α v β 6 integrin antibody is STX-100;
 - d) the anti-CTGF antibody is FG-3019;
 - e) the anti-CCL2 antibody is CNTO 888;
 - f) the somatostatin analog is SOM230 or octreotide;

g) the angiotensin II inhibitor is losartan; or

h) the tyrosine kinase inhibitor is BIBF1120.

32. The use of claim 30, wherein the anti-IL-13 agent is lebrikizumab.

33. The use of claim 30, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.

34. The use of claim 33, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.

35. The use of claim 34, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.

36. The use of any one of claims 32-35, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg.

37. The use of claim 36, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose of 250 mg.

38. Use of an IPF therapeutic agent in the manufacture of a medicament for the treatment of an IPF patient, provided that the patient has a baseline score of two or above determined according to the method of claim 12.

39. Use of an IPF therapeutic agent in the manufacture of a medicament for the treatment of an IPF patient, provided that the patient has a baseline score of one or above determined according to the method of claim 20.

40. The use of claim 38 or claim 39, wherein the IPF therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody, N-acetylcysteine, anti-TGF- β antibody, anti- α v β 6 integrin antibody, anti-CTGF antibody, anti-CCL2 antibody, somatostatin analog, angiotensin II inhibitor, carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor.

41. The use of claim 40, wherein:

a) the anti-LOXL2 antibody is GS-6624;

- b) the anti-TGF- β antibody is GC1008;
 - c) the anti- α v β 6 integrin antibody is STX-100;
 - d) the anti-CTGF antibody is FG-3019;
 - e) the anti-CCL2 antibody is CNTO 888;
 - f) the somatostatin analog is SOM230 or octreotide;
 - g) the angiotensin II inhibitor is losartan; or
 - h) the tyrosine kinase inhibitor is BIBF1120.
42. The use of claim 40, wherein the anti-IL-13 agent is lebrikizumab.
43. The use of claim 40, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.
44. The use of claim 43, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.
45. The use of claim 44, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.
46. The use of any one of claims 42-45, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg.
47. The use of claim 46, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose of 250 mg.
48. The use of claim 40, wherein the IPF therapeutic agent is a combination anti-IL-13/anti-IL-4 agent.
49. The use of claim 48, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.
50. The use of any one of claims 29-49, wherein the treatment extends the time to disease progression compared to no treatment, wherein disease progression is indicated by the first occurrence of one or more of the following: (i) death; (ii) non-elective hospitalization; (iii) 10% or greater decrease from baseline in FVC.
51. The use of claim 50, wherein disease progression is further indicated by decrease from baseline of $\geq 15\%$ in DL_{CO} at week 52.

52. The use of any one of claims 29-49, wherein a decrease in DL_{CO} from baseline 52 weeks after treatment is less than 15%.
53. The use of any one of claims 29-49, wherein the treatment results in less reduction in decline from baseline in distance walked by the patient in a 6-minute walk test 52 weeks after treatment compared to no treatment.
54. The use of claim 53, wherein the reduction in decline from baseline in distance walked is greater than 50 meters, or greater than 30 meters, or greater than 10 meters.
55. The use of any one of claims 29-49, wherein the treatment extends the time to a first event of acute IPF exacerbation or a first event of IPF deterioration compared to no treatment.
56. A method of monitoring disease progression in an IPF patient comprising, measuring in biological samples obtained from the patient at a first time point and one or more additional time points the expression of a combination of three or more genes, or expression of a combination of three or more proteins encoded by the combination of three or more genes, wherein the combination of three or more genes is selected from COMP, MMP3, YKL-40, CXCL13, SAA4 (constitutive SAA) and SPP1 (OPN), wherein the combination of three or more genes comprises MMP3, wherein a change in expression level from the first time point to the one or more additional time points is indicative of disease progression.
57. The method of claim 56, wherein the combination of three or more genes comprises YKL-40.
58. The method of claim 56, wherein the combination of three or more genes further comprises MMP7.
59. The method of claim 56, wherein the combination of three or more genes further comprises a gene selected from CCL11, CCL13, CCL17, and CCL18.
60. The method of any one of claims 56-59, wherein the biological samples are selected from lung tissue, serum, and plasma.
61. The method of claim 60, wherein the biological sample is lung tissue or plasma and the expression of the one or the combination of genes is measured using a PCR method or a microarray chip.
62. The method of claim 60, wherein the biological sample is serum and the expression of the one or the combination of proteins is measured using an immunoassay.
63. The method of any one of claims 56-62, wherein the patient is to be further treated with a candidate therapeutic agent in a clinical study.
64. The method of claim 63, wherein the candidate therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-

LOXL2 antibody, N-acetylcysteine, anti-TGF- β antibody, anti- α v β 6 integrin antibody, anti-CTGF antibody, anti-CCL2 antibody, somatostatin analog, angiotensin II inhibitor, carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor.

65. The method of claim 64, wherein:

- a) the anti-LOXL2 antibody is GS-6624;
- b) the anti-TGF- β antibody is GC1008;
- c) the anti- α v β 6 integrin antibody is STX-100;
- d) the anti-CTGF antibody is FG-3019;
- e) the anti-CCL2 antibody is CNTO 888;
- f) the somatostatin analog is SOM230 or octreotide;
- g) the angiotensin II inhibitor is losartan; or
- h) the tyrosine kinase inhibitor is BIBF1120.

66. The method of claim 64, wherein the anti-IL-13 agent is lebrikizumab.

67. The method of claim 64, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.

68. The method of claim 67, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.

69. The method of claim 68, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of prognosing or of aiding prognosis of idiopathic pulmonary fibrosis (IPF) in a patient comprising measuring in a biological sample obtained from the patient the expression of a combination of three or more genes, or expression of a combination of three or more proteins encoded by the combination of three or more genes, wherein the three or more genes are selected from COMP, MMP3, YKL-40, CXCL13, SAA4 (constitutive SAA) and SPP1 (OPN), wherein the combination of three or more genes comprises MMP3, wherein an elevated expression level of the combination of three or more genes, or an elevated expression level of the combination of three or more proteins, is indicative of a prognosis for shortened survival compared to median survival and wherein a reduced expression level of the combination of three or more genes, or a reduced expression level of the combination of three or more proteins, is indicative of a prognosis for increased survival compared to median survival.
2. The method of claim 1, wherein the combination of three or more genes comprises YKL-40.
3. The method of claim 1, wherein the combination of three or more genes further comprises MMP7.
4. The method of claim 1, wherein the combination of three or more genes further comprises a gene selected from CCL11, CCL13, CCL17, and CCL18.
5. The method of claim 1, wherein the combination of three or more genes comprises MMP3 and SAA4 (constitutive SAA).
6. The method of claim 4 wherein the combination of three or more genes comprises YKL-40 and CCL18.
7. The method of claim 4, comprising measuring the expression level of CXCL13.
8. The method of claim 4, comprising measuring the expression level of MMP3.
9. The method of claim 4, comprising measuring the expression level of SAA4 (constitutive SAA).
10. The method of claim 4, wherein the patient is on immunomodulatory therapy.
11. The method of any one of claims 1-10, wherein the biological sample is selected from lung tissue, serum, and plasma.
12. A method of prognosing or of aiding prognosis of IPF in a patient comprising determining a total baseline biomarker score in a biological sample obtained from the patient, wherein the determining of the total baseline biomarker score comprises measuring the protein expression level of COMP and at least one of CXCL13 and OPN, and assigning a score of 0 if the expression level is below the median for CXCL13, OPN, and COMP,

respectively, and assigning a score of 1 if the expression level is above the median for CXCL13, OPN, and COMP, respectively, wherein the determining of the total baseline biomarker score further comprises measuring the protein expression level of YKL-40 and assigning a score of 0 if the expression level is below the median for YKL-40 and assigning a score of 1 if the expression level is above the median for YKL-40, and wherein the determining of the total baseline biomarker score further comprises adding each individual score to obtain the total baseline biomarker score,

wherein a total baseline biomarker score of two or above is indicative of a prognosis of shortened survival compared to median survival and wherein a total baseline biomarker score of zero or one is indicative of a prognosis of increased survival compared to the median survival.

13. The method of claim 12, wherein the total baseline biomarker score of the patient is two or above and the patient is selected for treatment with a candidate therapeutic agent in a clinical study, wherein the candidate therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody (GS-6624), N-acetylcysteine, anti-TGF- β antibody (GC1008), anti- $\alpha v \beta 6$ integrin antibody (STX-100), anti-CTGF antibody (FG-3019), anti-CCL2 antibody (CNTO 888), somatostatin analog (SOM230, octreotide), antitensin II inhibitor (losartan), carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor (BIBF1120).

14. The method of claim 13, wherein the anti-IL-13 agent is lebrikizumab.

15. The method of claim 13, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.

16. The method of claim 15, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.

17. The method of claim 16, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.

18. The method of claim 13, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

19. A method of prognosing or of aiding prognosis of IPF in a patient comprising determining a total baseline biomarker score in a biological sample obtained from the patient,

wherein the determining of the total baseline biomarker score comprises measuring the protein expression level of COMP or MMP3 and COMP, and assigning a score of 0 if the expression level is below the median for MMP3 and COMP, respectively, and assigning a score of 1 if the expression level is above the median for MMP3 and COMP, respectively, wherein the determining of the total baseline biomarker score further comprises measuring the protein expression level of YKL-40 and assigning a score of 0 if the expression level is below the median for YKL-40 and assigning a score of 1 if the expression level is above the median for YKL-40, and wherein the determining of the total baseline biomarker score further comprises adding each individual score to obtain the total baseline biomarker score,

wherein a total baseline biomarker score of one or above is indicative of a prognosis of shortened survival compared to median survival and wherein a total baseline biomarker score of zero is indicative of a prognosis of increased survival compared to the median survival.

20. The method of any one of claims 12-19, wherein the biological sample is selected from serum and plasma.

21. The method of claim 19, wherein the total baseline biomarker score of the patient is one or above and the patient is selected for treatment with a candidate therapeutic agent in a clinical study, wherein the candidate therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody (GS-6624), N-acetylcysteine, anti-TGF- β antibody (GC1008), anti- α v β 6 integrin antibody (STX-100), anti-CTGF antibody (FG-3019), anti-CCL2 antibody (CNTO 888), somatostatin analog (SOM230, octreotide), antiotensin II inhibitor (losartan), carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor (BIBF1120).

22. The method of claim 21, wherein the anti-IL-13 agent is lebrikizumab.

23. The method of claim 21, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

24. The method of claim 21, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.

25. The method of claim 24, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.
26. The method of claim 25, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.
27. Use of an IPF therapeutic agent in the manufacture of a medicament for the treatment of an IPF patient previously determined to have a prognosis of shortened survival according to the method of any one of claims 1-12, 19, or 20.
28. The use of claim 27, wherein the IPF therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody (GS-6624), N-acetylcysteine, anti-TGF- β antibody (GC1008), anti- α v β 6 integrin antibody (STX-100), anti-CTGF antibody (FG-3019), anti-CCL2 antibody (CNTO 888), somatostatin analog (SOM230, octreotide), antiotensin II inhibitor (losartan), carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor (BIBF1120).
29. The use of claim 28, wherein the anti-IL-13 agent is lebrikizumab.
30. The use of claim 28, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.
31. The use of claim 30, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.
32. The use of claim 31, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.
33. The use of any one of claims 29-32, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg.
34. The use of claim 33, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose of 250 mg.

35. Use of an IPF therapeutic agent in the manufacture of a medicament for the treatment of an IPF patient, provided that the patient has a baseline score of two or above determined according to the method of claim 12.
36. Use of an IPF therapeutic agent in the manufacture of a medicament for the treatment of an IPF patient, provided that the patient has a baseline score of one or above determined according to the method of claim 19.
37. The use of claim 35 or claim 36, wherein the IPF therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody (GS-6624), N-acetylcysteine, anti-TGF- β antibody (GC1008), anti- α v β 6 integrin antibody (STX-100), anti-CTGF antibody (FG-3019), anti-CCL2 antibody (CNTO 888), somatostatin analog (SOM230, octreotide), antiotensin II inhibitor (losartan), carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor (BIBF1120).
38. The use of claim 37, wherein the anti-IL-13 agent is lebrikizumab.
39. The use of claim 37, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.
40. The use of claim 39, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.
41. The use of claim 40, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.
42. The use of any one of claims 38-41, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg.
43. The use of claim 42, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose of 250 mg.
44. The use of claim 37, wherein the IPF therapeutic agent is a combination anti-IL-13/anti-IL-4 agent.
45. The use of claim 44, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

46. The use of any one of claims 27-45, wherein the treatment extends the time to disease progression compared to no treatment, wherein disease progression is indicated by the first occurrence of one or more of the following: (i) death; (ii) non-elective hospitalization; (iii) 10% or greater decrease from baseline in FVC.
47. The use of claim 46, wherein disease progression is further indicated by decrease from baseline of $\geq 15\%$ in DL_{CO} at week 52.
48. The use of any one of claims 27-45, wherein a decrease in DL_{CO} from baseline 52 weeks after treatment is less than 15%.
49. The use of any one of claims 27-45, wherein the treatment results in less reduction in decline from baseline in distance walked by the patient in a 6-minute walk test 52 weeks after treatment compared to no treatment.
50. The use of claim 49, wherein the reduction in decline from baseline in distance walked is greater than 50 meters, or greater than 30 meters, or greater than 10 meters.
51. The use of any one of claims 27-45, wherein the treatment extends the time to a first event of acute IPF exacerbation or a first event of IPF deterioration compared to no treatment.
52. A method of monitoring disease progression in an IPF patient comprising, measuring in biological samples obtained from the patient at a first time point and one or more additional time points the expression of a combination of three or more genes, or expression of a combination of three or more proteins encoded by the combination of three or more genes, wherein the combination of three or more genes is selected from COMP, MMP3, YKL-40, CXCL13, SAA4 (constitutive SAA) and SPP1 (OPN), wherein the combination of three or more genes comprises MMP3, wherein a change in expression level from the first time point to the one or more additional time points is indicative of disease progression.
53. The method of claim 52, wherein the combination of three or more genes comprises YKL-40.
54. The method of claim 52, wherein the combination of three or more genes further comprises MMP7.
55. The method of claim 52, wherein the combination of three or more genes further comprises a gene selected from CCL11, CCL13, CCL17, and CCL18.
56. The method of any one of claims 52-55, wherein the biological samples are selected from lung tissue, serum, and plasma.
57. The method of claim 56, wherein the biological sample is lung tissue or plasma and the expression of the one or the combination of genes is measured using a PCR method or a microarray chip.

58. The method of claim 56, wherein the biological sample is serum and the expression of the one or the combination of proteins is measured using an immunoassay.

59. The method of any one of claims 52-58, wherein the patient is to be further treated with a candidate therapeutic agent in a clinical study.

60. The method of claim 59, wherein the candidate therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/anti-IL-4 agent, pirfenidone, anti-LOXL2 antibody (GS-6624), N-acetylcysteine, anti-TGF- β antibody (GC1008), anti- α v β 6 integrin antibody (STX-100), anti-CTGF antibody (FG-3019), anti-CCL2 antibody (CNTO 888), somatostatin analog (SOM230, octreotide), antiotensin II inhibitor (losartan), carbon monoxide, thalidomide, tetrathiomolybdate, doxycycline, minocycline, and tyrosine kinase inhibitor (BIBF1120).

61. The method of claim 60, wherein the anti-IL-13 agent is lebrikizumab.

62. The method of claim 60, wherein the anti-IL-13 agent is an anti-IL-13 antibody comprising three heavy chain CDRs, CDR-H1 having the amino acid sequence of SEQ ID NO.: 1, CDR-H2 having the amino acid sequence of SEQ ID NO.: 2, and CDR-H3 having the amino acid sequence of SEQ ID NO.: 3, and three light chain CDRs, CDR-L1 having the amino acid sequence of SEQ ID NO.: 4, CDR-L2 having the amino acid sequence of SEQ ID NO.: 5, and CDR-L3 having the amino acid sequence of SEQ ID NO.: 6.

63. The method of claim 62, wherein the anti-IL-13 antibody comprises a heavy chain variable region having the amino acid sequence of SEQ ID NO.: 7 and a light chain variable region having the amino acid sequence of SEQ ID NO.: 9.

64. The method of claim 63, wherein the anti-IL-13 antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO.: 10 and a light chain having the amino acid sequence of SEQ ID NO.: 14.