[0012] However, unlike IL4, IL13 is not involved in the differentiation of naïve T cells into Th2 cells (Zurawski et al., Immunol. Today, 15: 19 (1994)). IL13 up-regulates FcεRI and thus helps in IgE priming of mast cells (de Vries, Allergy Clin. Immunol. 102: 165 (1998). In monocytes/macrophages, IL13 up-regulates expression of CD23 and MHC class I and class II antigens, down-regulate the expression of Fcγ and CD14, and inhibit antibody-dependent cytotoxicity (de Waal Malefyt et al., J. Immunol., 151: 6370 (1993), Chomarat et al., Int. Rev. Immunol., 17: 1 (1998)). IL13, but not IL4, promotes eosinophil survival, activation, and recruitment (Horie et al., Intern. Med., 36: 179 (1997), Luttmann et al., J. Immunol. 157: 1678 (1996), Pope et al., J. Allergy Clin. Immunol., 108: 594 (2001). IL13 also manifests important functions on nonhematopoietic cells, such as smooth muscle cells, epithelial cells, endothelial cells and fibroblast cells. IL13 enhances proliferation and cholinergic-induced contractions of smooth muscles (Wills-Karp, J. Allergy Clin. Immunol., 107: 9 (2001). In epithelial cells IL13 is a potent inducer of chemokine production (Li et al., J. Immunol., 162: 2477 (1999), alters mucociliary differentiation (Laoukili et al., J. Clin. Invest., 108: 1817 (2001), decreases ciliary beat frequency of ciliated epithelial cells (Laoukili et al., J. Clin. Invest., 108: 1817 (2001), and results in goblet cell metaplasia (Zhu et al., J. Clin. Invest., 103: 779 (1999), Grunig et al., Science, 282: 2261 (1998)). In endothelial cells IL13 is a potent inducer of vascular cell adhesion molecule 1 (VCAM-1) which is important for recruitment of eosinophils (Bochner et al., J. Immunol., 154: 799 (1995)). In human dermal fibroblasts IL13 induces type 1 collagen synthesis in human dermal fibroblasts (Roux et al., J. Invest. Dermatol., 103: 444 (1994)).

[0013] IL-13 antagonists, including anti-IL-13 antibodies have previously been described. See, e.g., Intn'l Patent Application Pub. No. WO 2005/062967. Such antibodies have also been developed as human therapeutics. The results of one clinical study with one anti-IL-13 antibody, lebrikizumab, has been described in Corren et al., New Engl. J. Med. 365:1088-1098 (2011).

[0014] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety for any purpose.

SUMMARY

[0015] The compositions and methods of the ~~invention~~ disclosure are based, at least in part, on the definition of at least three new and distinct molecular phenotypes (also referred to herein as molecular subtypes) of idiopathic pulmonary fibrois (IPF). The IPF molecular subtypes described herein were defined based on differential gene expression between the subtypes. In

addition, compositions and methods of the ~~invention~~ disclosure are based, at least in part, on the identification of serum or blood biomarkers that are prognostic for survival of IPF patients. Such biomarkers are particularly useful for identifying and selecting IPF patients for therapeutic treatment according to the methods of the ~~invention~~disclosure. The terms "molecular phenotype" and "molecular subtype" are used interchangeably herein.

[0015a] In a first aspect, there is provided 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 one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the gene is COMP or the combination of genes comprises COMP, wherein an elevated expression level of the one or the combination of genes, or an elevated expression level of the one or the combination of proteins, is indicative of a prognosis for shortened survival compared to median survival and wherein a reduced expression level of the one or the combination of genes, or a reduced expression level of the one or the combination of proteins, is indicative of a prognosis for increased survival compared to median survival.

[0016] Accordingly, in one ~~aspect~~embodiment, methods of prognosing or of aiding prognosis of idiopathic pulmonary fibrosis (IPF) are provided. In certain embodiments, a biological sample is obtained from the patient and the expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes is measured. In certain embodiments, an elevated expression level of the one or the combination of genes or elevated expression of the one or the combination of proteins encoded by the one or the combination of genes, is indicative of a prognosis for shortened survival compared to median survival. In certain embodiments, reduced expression of the one or the combination of genes or reduced expression of the one or the combination of proteins encoded by the one or the combination of genes, is indicative of a prognosis for increased survival compared to median survival. In one embodiment, the one or the combination of genes is selected from any of Table 2, Table 3, Table 4, or Table 5. In one embodiment, the one or the combination of genes is selected from MUCL1, MUC4, MUC20, PRR7, PRR15, SPRR1B, SPRR2D, KRT5, KRT6B, KRT13, KRT14, KRT15, KRT17, SERPINB3, SERPINB4, SERPINB5, SERPINB13, CLCA2, TRPV4, BBS5, MMP3, and SAA4. In one embodiment, the one or the combination of genes is selected from CXCR3, CXCR5, CXCL13, CCR6, CCR7, CD19, MS4A1 (CD20), BLK, BLNK, FCRLA, FCRL2, FCRL5, CD79A, CD79B, CD27, CD28, CD1A, CD1B, CD1C, CD1E, IGHV1-69, IGLJ3, IGJ, IGHV3-48, IGLV3-21, IGKV1-5, IGHG1, IGKC, IGLV6-57, IGK@, IGHA1, IGKV2-

24, IGKV1D-8, IGHM. In one embodiment, the one or the combination of genes is selected from COL1A1, COL1A2, COL5A2, COL12A1, COL14A1, COL15A1, COL16A1, COL18A1, CTHRC1, HGF, IGFBP7, SCGF (CLEC11A); LOXL1, LOXL2; GLI1, GLI2, SMO; SFRP2, DIO2, CDH11, POSTN, and TGFB3. In certain embodiments, the gene expression level is measured by assaying for mRNA levels. In certain embodiments, the assay comprises a PCR method and/or the use of a microarray chip. In one embodiment, the PCR method is qPCR. In one embodiment, the PCR method is multiplex-PCR. In certain embodiments, kits include at least one enzyme selected from a nuclease, a ligase, and a polymerase. In certain embodiments, the protein expression level is measured by an immunoassay. In certain embodiments, immunoassay kits are provided comprising one or

more antibodies that bind to one or more proteins encoded by one of the genes identified above.

[0017] In yet a further embodiment of the methods above, the one or the combination of genes is selected from CHI3L1 (YKL-40), CCL11, CCL13, CCL17, CCL18, COMP, CXCL13, MMP3, MMP7, SAA4 (constitutive SAA), POSTN, AND SPP1 (OPN). In another embodiment, the one or the combination of genes is selected from YKL-40, CCL11, CCL13, CCL17, CCL18, MMP7, CXCL13, COMP, SAA and OPN. In still another embodiment, the one or the combination of genes is selected from SAA, MMP3, CXCL13, OPN, COMP, and YKL-40. In another embodiment, the one or the combination of genes is selected from POSTN, MMP3, and CXCL13. In a still further embodiment, the expression level of YKL-40 or the expression level of CCL18 and/or the expression level of CXCL13 is measured. In yet another embodiment, the expression level of MMP3 and/or the expression level of SAA is measured. In certain embodiments, the gene expression level is measured by assaying for mRNA levels. In certain embodiments, the assay comprises a PCR method and/or the use of a microarray chip. In one embodiment, the PCR method is qPCR. In one embodiment, the PCR method is multiplex-PCR. In certain embodiments, kits include at least one enzyme selected from a nuclease, a ligase, and a polymerase. In certain embodiments, the protein expression level is measured by an immunoassay. In certain embodiments, immunoassay kits are provided comprising one or more antibodies that bind to one or more proteins encoded by one of the genes identified above.

[0018] In certain embodiments of the methods described above, the patient is on immunomodulatory therapy. In another embodiment, the biological sample is selected from lung tissue, serum, and plasma.

[0019] In one ~~aspect~~embodiment, gene expression according to the methods described above is measured by microarray. In another ~~aspect~~embodiment gene expression is measured by real-time quantitative polymerase chain reaction (qPCR). In another ~~aspect~~embodiment, gene expression is measured by multiplex-PCR. According to another embodiment, gene expression is measured by observing protein expression levels of one or more of the genes described above. According to another embodiment, expression of a gene of interest is considered elevated when compared to a healthy control or a reference subject if the relative mRNA level of the gene of interest is greater than 2 fold of the level of a control or reference gene mRNA. According to another embodiment, the relative mRNA level of the gene of interest is greater than 3 fold, fold, 10 fold, 15 fold, 20 fold, 25 fold, or 30 fold compared to a healthy control or reference gene expression level. In one ~~aspect~~embodiment, the gene expression level is measured by a

method selected from a PCR method, a microarray method, or an immunoassay method. In one embodiment, the microarray method comprises the use of a microarray chip having one or more nucleic acid molecules that can hybridize under stringent conditions to a nucleic acid molecule encoding a gene mentioned above or having one or more polypeptides (such as peptides or antibodies) that can bind to one or more of the proteins encoded by the genes mentioned above. In one embodiment, the PCR method is qPCR. In one embodiment, the PCR method is multiplex-PCR. According to one embodiment, the immunoassay method comprises binding an antibody to protein expressed from a gene mentioned above in a patient sample and determining if the protein level from the patient sample is elevated. In certain embodiments, the immunoassay method is an enzyme-linked immunosorbent assay (ELISA).

[0019a] In a second aspect, there is provided 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.

[0020] In another ~~aspect~~embodiment, methods of prognosing or of aiding prognosis of IPF in a patient are provided where a biological sample is obtained from the patient and a total baseline biomarker score is determined. In certain embodiments, the determining of the total baseline biomarker score comprises measuring the protein expression level of at least one of CXCL13, OPN, and COMP 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. In certain embodiments, a total baseline biomarker score of two or above is indicative of a prognosis of shortened survival compared to median survival. In certain embodiments, a total baseline biomarker score of zero or one is indicative of a prognosis of increased survival compared to the median survival. In certain embodiments, the protein expression level is measured by an immunoassay. In certain embodiments, immunoassay kits are provided comprising one or more antibodies that bind to one or more proteins encoded by CXCL13, OPN, COMP and/or YKL-40.

[0021] In yet still another ~~aspect~~embodiment, if the total baseline biomarker score of the patient is two or above as determined as described above, the patient is selected for treatment with a candidate therapeutic agent in a clinical study. In certain embodiments, 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-αvβ6 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). In one embodiment, the anti-IL-13 agent is lebrikizumab. In one embodiment, the anti-IL-13/anti-IL-4 agent is a bispecific antibody. In one embodiment, 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. In one embodiment, 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. In one embodiment, 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. In certain embodiments, methods of treating an IPF patient are provided where an effective amount of an IPF therapeutic agent as provided above is administered provided that the patient has a baseline score of two or above determined according to the methods described above.

[0021a] In a third aspect, there is provided 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.

[0022] In another ~~aspect~~embodiment, methods of prognosing or of aiding prognosis of IPF in a patient are provided where a biological sample is obtained from the patient and a total baseline biomarker score is determined, where the determining of the total baseline biomarker score comprises measuring the protein expression level of at least one of 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. In certain embodiments, a total baseline biomarker score of one or above is indicative of a prognosis of shortened survival compared to median survival. In certain embodiments, a total baseline biomarker score of zero is indicative of a prognosis of increased survival compared to the median survival. In certain embodiments, the protein expression level is measured by an immunoassay. In certain embodiments, immunoassay kits

are provided comprising one or more antibodies that bind to one or more proteins encoded by MMP3, COMP and/or YKL-40.

[0023] In yet still another ~~aspect~~embodiment, if the total baseline biomarker score of the patient is one or above as determined as described above with respect to expression of MMP3, COMP, and/or YKL-40, the patient is selected for treatment with a candidate therapeutic agent in a clinical study. In certain embodiments, 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-αvβ6 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). In one embodiment, the anti-IL-13 agent is lebrikizumab. In one embodiment, the anti-IL-13/anti-IL-4 agent is a bispecific antibody. In one embodiment, 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. In one embodiment, 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. In one embodiment, 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. In certain embodiments, methods of treating an IPF patient are provided where an effective amount of an IPF therapeutic agent as provided above is administered provided that the patient has a baseline score of one or above determined according to the methods described above.

[0024] In another ~~aspect~~embodiment, methods of diagnosing a molecular subtype of IPF in a subject are provided. In certain embodiments, the methods comprise measuring in a biological sample obtained from the subject expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes. In certain embodiments, the one or the combination of genes is selected from MUCL1, MUC4, MUC20, PRR7, PRR15, SPRR1B, SPRR2D, KRT5, KRT6B, KRT13, KRT14, KRT15, KRT17, SERPINB3, SERPINB4, SERPINB5, SERPINB13, CLCA2, TRPV4, BBS5, MMP3,

and SAA4, and elevated expression of the one or the combination of genes, or elevated expression of the one or the combination of proteins, is indicative of the IPF molecular subtype. In certain embodiments, the one or the combination of genes is selected from CXCR3, CXCR5, CXCL13, CCR6, CCR7, CD19, MS4A1 (CD20), TNFRSF17 (BCMA), BLK, BLNK, FCRLA, FCRL2, FCRL5, CD79A, CD79B, CD27, CD28, CD1A, CD1B, CD1C, CD1E, IGHV1-69, IGLJ3, IGJ, IGHV3-48, IGLV3-21, IGKV1-5, IGHG1, IGKC, IGLV6-57, IGK@ (immunoglobulin kappa locus), IGHA1, IGKV2-24, IGKV1D-8, IGHM, and elevated expression of the one or the combination of genes, or elevated expression of the one or the combination of proteins, is indicative of the IPF molecular subtype. In certain embodiments, the one or the combination of genes is selected from COL1A1, COL1A2, COL5A2, COL12A1, COL14A1, COL15A1, COL16A1, COL18A1, CTHRC1, HGF, IGFBP7, SCGF (CLEC11A); LOXL1, LOXL2; GLI1, GLI2, SMO; SFRP2, DIO2, CDH11, POSTN, and TGFB3, and elevated expression of the one or the combination of genes, or elevated expression of the one or the combination of proteins, is indicative of the IPF molecular subtype. In certain embodiments, the gene expression level is measured by assaying for mRNA levels. In certain embodiments, the assay comprises a PCR method and/or the use of a microarray chip. In one embodiment, the PCR method is qPCR. In one embodiment, the PCR method is multiplex-PCR. In certain embodiments, kits include at least one enzyme selected from a nuclease, a ligase, and a polymerase. In certain embodiments, the protein expression level is measured by an immunoassay. In certain embodiments, immunoassay kits are provided comprising one or more antibodies that bind to one or more proteins encoded by one of the genes identified above.

[0025] In another ~~aspect~~embodiment, the biological sample for use according to any of the above methods is lung tissue, whole blood, or serum. In certain embodiments, the biological sample is lung tissue or whole blood and the expression of the one or the combination of genes is measured using a PCR method or a microarray chip. In certain embodiments, the biological sample is serum and the expression of the one or the combination of proteins is measured using an immunoassay.

[0026] In yet still another ~~aspect~~embodiment, methods of treating IPF in a patient are provided.

[0026a] In a fourth aspect, there is provided these 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 as defined in the second aspect.

[0026b] In a fifth aspect, there is provided the 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 as defined in the third aspect.

[0026c] In certain embodiments, the methods comprise administering an effective amount of an IPF therapeutic agent to the patient to treat the IPF, provided that elevated expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, has been detected in a biological sample obtained from the patient. In one embodiment, the one or the combination of genes is selected from MUCL1,

kinase inhibitor (BIBF1120). In certain embodiments, the IPF therapeutic agent is an anti-IL-13 antibody. In one embodiment, 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. In one embodiment, 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. In one embodiment, the anti-IL-13 antibody (lebrikizumab) 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. In certain embodiments, lebrikizumab is administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg. In one embodiment, lebrikizumab is administered subcutaneously once every four weeks at a flat does of 250 mg.

[0026a] In a sixth aspect, there is provided the 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 as defined herein

[0027] In ~~a further aspect~~one embodiment, methods of treating an IPF patient previously determined to have a prognosis of shortened survival according to the methods above are provided. In certain such embodiments, an effective amount of the IPF therapeutic agent is administered. In one embodiment, 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-αvβ6 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). In one embodiment, 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. In one embodiment, 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. In one embodiment, the anti-IL-13 antibody (lebrikizumab) 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. In one embodiment, the anti-IL-13 antibody is administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg. In one embodiment, the anti-IL-13 antibody is administered subcutaneously once every four weeks at a flat dose of 250 mg.

[0028] In yet a still further ~~aspect~~embodiment, the methods of treating an IPF patient with an anti-IL-13 antibody or with lebrikizumab described above 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. In one embodiment, disease progression is further indicated by decrease from baseline of $\geq$ 15% in DL_{CO} at week 52. In one embodiment, treatment with an anti-IL-13 antibody or lebrikizumab as described above results in a decrease in DL_{CO} from baseline 52 weeks after treatment is less than 15%. In one embodiment, such 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. In one embodiment, the reduction in decline from baseline in distance walked is greater than 50 meters, or greater than 30 meters, or greater than 10 meters. In certain embodiments, the treatment extends the time to a first event of acute IPF exacerbation or a first event of IPF deterioration compared to no treatment.

[0029] In one ~~aspect~~embodiment, methods of extending the time to disease progression in an IPF patient by administering an anti-IL-13 antibody or lebrikizumab are provided. In certain embodiments, the time to disease progression in treated patients is compared to no treatment. In certain embodiments, 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. In one embodiment, disease progression is further indicated by decrease from baseline of $\geq$ 15% in DL_{CO} at week 52. In one embodiment, treatment with an anti-IL-13 antibody or lebrikizumab as described above results in a decrease in DL_{CO} from baseline 52 weeks after treatment is less than 15%. In one embodiment, such 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. In one embodiment, the reduction in decline from baseline in distance walked is greater than 50 meters, or greater than 30 meters, or greater than 10 meters. In certain embodiments, the treatment extends the time to a first event of acute IPF exacerbation or a first event of IPF deterioration compared to no treatment.

[0029a] In one aspect, there is provided 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 one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the one gene is COMP or the combination of genes comprises COMP, wherein a change in expression level from the first time point to the one or more additional time points is indicative of disease progression.

[0030] In still yet another ~~aspect~~embodiment, methods of monitoring disease progression in an IPF patient are provided. In certain embodiments, the methods comprise obtaining a biological sample from the patient at a first time point and one or more additional time points, measuring in the biological samples the expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the one or the combination of genes is selected from any of Table 2, Table 3, Table 4, or Table 5, wherein a change in expression level from the first time point to the one or more additional time points is indicative of disease progression. In one embodiment, the one or the combination of genes, or the one or the combination of proteins, is selected from MUCL1, MUC4, MUC20, PRR7, PRR15, SPRR1B, SPRR2D, KRT5, KRT6B, KRT13, KRT14, KRT15, KRT17, SERPINB3, SERPINB4, SERPINB5, SERPINB13, CLCA2, TRPV4, BBS5, MMP3, and SAA4. In one embodiment, the one or the combination of genes is selected from CXCR3, CXCR5, CXCL13, CCR6, CCR7, CD19, MS4A1 (CD20), BLK, BLNK, FCRLA, FCRL2, FCRL5, CD79A, CD79B, CD27, CD28, CD1A, CD1B, CD1C, CD1E, IGHV1-69, IGLJ3, IGJ, IGHV3-48, IGLV3-21, IGKV1-5, IGHG1, IGKC, IGLV6-57, IGK@, IGHA1, IGKV2-24, IGKV1D-8, IGHM. In one embodiment, the one or the combination of genes, or the one or the combination of proteins, is selected from COL1A1, COL1A2, COL5A2, COL12A1, COL14A1, COL15A1, COL16A1, COL18A1, CTHRC1, HGF, IGFBP7, SCGF (CLEC11A); LOXL1, LOXL2; GLI1, GLI2, SMO; SFRP2, DIO2, CDH11, POSTN, and TGFB3. In one embodiment, the one or the combination of genes, or the one or the combination of proteins is selected from CHI3L1 (YKL-40), CCL11, CCL13, CCL17, CCL18, COMP, CXCL13, MMP3, MMP7, SAA4 (constitutive SAA), POSTN, AND SPP1 (OPN). In certain embodiments, a biological sample is selected from lung tissue, serum, and plasma. In certain embodiments, the gene expression level is measured by assaying for mRNA levels. In certain embodiments, the assay comprises a PCR method and/or the use of a microarray chip. In one embodiment, the PCR method is qPCR. In one embodiment, the PCR method is multiplex-PCR. In certain embodiments, kits include at

least one enzyme selected from a nuclease, a ligase, and a polymerase. In certain embodiments, the protein expression level is measured by an immunoassay. In certain embodiments, immunoassay kits are provided comprising one or more antibodies that bind to one or more proteins encoded by one of the genes identified above.

[0031] In another ~~aspect~~embodiment, the methods of monitoring disease progression as described above further comprise treating the patient with a candidate therapeutic agent in a clinical study. In certain embodiments, the therapeutic agent is selected from an anti-IL-13 agent, an

CLAIMS

WHAT IS CLAIMED IS:

1. A method of prognosing or of aiding prognosis of idiopathic pulmonary fibrosis (IPF) in a patient comprising obtaining a biological sample from the patient, measuring in the biological sample the expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the one or the combination of genes is selected from any of Table 2, Table 3, Table 4, or Table 5, wherein an elevated expression level of the one or the combination of genes, or an elevated expression level of the one or the combination of proteins, is indicative of a prognosis for shortened survival compared to median survival and wherein a reduced expression level of the one or the combination of genes, or a reduced expression level of the one or the combination of proteins, is indicative of a prognosis for increased survival compared to median survival.

2. The method of claim 1, wherein the one or the combination of genes, or the one or the combination of proteins, is selected from MUCL1, MUC4, MUC20, PRR7, PRR15, SPRR1B, SPRR2D, KRT5, KRT6B, KRT13, KRT14, KRT15, KRT17, SERPINB3, SERPINB4, SERPINB5, SERPINB13, CLCA2, TRPV4, BBS5, MMP3, and SAA4.

3. The method of claim 1, wherein the one or the combination of genes is selected from CXCR3, CXCR5, CXCL13, CCR6, CCR7, CD19, MS4A1 (CD20), BLK, BLNK, FCRLA, FCRL2, FCRL5, CD79A, CD79B, CD27, CD28, CD1A, CD1B, CD1C, CD1E, IGHV1-69, IGLJ3, IGJ, IGHV3-48, IGLV3-21, IGKV1-5, IGHG1, IGKC, IGLV6-57, IGK@, IGHA1, IGKV2-24, IGKV1D-8, IGHM.

4. The method of claim 1, wherein the one or the combination of genes, or the one or the combination of proteins, is selected from COL1A1, COL1A2, COL5A2, COL12A1, COL14A1, COL15A1, COL16A1, COL18A1, CTHRC1, HGF, IGFBP7, SCGF (CLEC11A); LOXL1, LOXL2; GLI1, GLI2, SMO; SFRP2, DIO2, CDH11, POSTN, and TGFB3.

5. The method of claim 1, wherein the one or the combination of genes, or the one or the combination of proteins is selected from CHI3L1 (YKL-40), CCL11, CCL13, CCL17, CCL18, COMP, CXCL13, MMP3, MMP7, SAA4 (constitutive SAA), POSTN, AND SPP1 (OPN).

6. The method of claim 5, wherein the one or the combination of genes, or the one or the combination of proteins, is selected from MMP3 and SAA4 (constitutive SAA).

7. The method of claim 5 wherein the one or the combination of genes, or the one or the combination of proteins, is selected from YKL-40 and CCL18.

8. The method of claim 5, comprising measuring the expression level of CXCL13.

9. The method of claim 5, comprising measuring the expression level of MMP3.

10. The method of claim 5, comprising measuring the expression level of SAA4 (constitutive SAA).

11. The method of claim 5, wherein the patient is on immunomodulatory therapy.

12. The method of any one of claims 1-11, wherein the biological sample is selected from lung tissue, serum, and plasma.

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

wherein the determining of the total baseline biomarker score comprises measuring the protein expression level of at least one of CXCL13, OPN, and COMP 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.

14. The method of claim 13, 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-αvβ6 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).

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

16. The method of claim 14, 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 14, 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 obtaining a biological sample from the patient and determining a total baseline biomarker score,

wherein the determining of the total baseline biomarker score comprises measuring the protein expression level of at least one of 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 13-20, 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 (GS-6624), N-acetylcysteine, anti-TGF-β antibody (GC1008), anti-αvβ6 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).

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

24. The method of claim 22, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

25. 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.

26. The method of claim 25, 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.

27. The method of claim 26, 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.

28. A method of diagnosing a molecular subtype of IPF in a subject, the method comprising measuring in a biological sample obtained from the subject expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the one or the combination of genes is selected from MUCL1, MUC4, MUC20, PRR7, PRR15, SPRR1B, SPRR2D, KRT5, KRT6B, KRT13, KRT14, KRT15, KRT17, SERPINB3, SERPINB4, SERPINB5, SERPINB13, CLCA2, TRPV4, BBS5, MMP3, and SAA4 wherein elevated expression of the one or the combination of genes, or elevated expression of the one or the combination of proteins, is indicative of the IPF molecular subtype.

29. A method of diagnosing a molecular subtype of IPF in a subject, the method comprising measuring in a biological sample obtained from the subject expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the one or the combination of genes is selected from CXCR3, CXCR5, CXCL13, CCR6, CCR7, CD19, MS4A1 (CD20), TNFRSF17 (BCMA),

BLK, BLNK, FCRLA, FCRL2, FCRL5, CD79A, CD79B, CD27, CD28, CD1A, CD1B, CD1C, CD1E, IGHV1-69, IGLJ3, IGJ, IGHV3-48, IGLV3-21, IGKV1-5, IGHG1, IGKC, IGLV6-57, IGK@ (immunoglobulin kappa locus), IGHA1, IGKV2-24, IGKV1D-8, IGHM, wherein elevated expression of the one or the combination of genes, or elevated expression of the one or the combination of proteins, is indicative of the IPF molecular subtype.

30. A method of diagnosing a molecular subtype of IPF in a subject, the method comprising measuring in a biological sample obtained from the subject expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the one or the combination of genes is selected from COL1A1, COL1A2, COL5A2, COL12A1, COL14A1, COL15A1, COL16A1, COL18A1, CTHRC1, HGF, IGFBP7, SCGF (CLEC11A); LOXL1, LOXL2; GLI1, GLI2, SMO; SFRP2, DIO2, CDH11, POSTN, and TGFB3, wherein elevated expression of the one or the combination of genes, or elevated expression of the one or the combination of proteins, is indicative of the IPF molecular subtype.

31. The method of any one of claims 28-30, wherein the biological sample is lung tissue, whole blood, or serum.

32. The method of any one of claims 12, 21, or 31, wherein the biological sample is lung tissue, plasma or whole blood and the expression of the one or the combination of genes is measured using a PCR method or a microarray chip.

33. The method of claim 31, wherein the biological sample is serum and the expression of the one or the combination of proteins is measured using an immunoassay.

34. A method of treating IPF in a patient comprising administering an effective amount of an IPF therapeutic agent to the patient to treat the IPF, provided that elevated expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, has been detected in a biological sample obtained from the patient, wherein the one or the combination of genes is selected from MUCL1, MUC4, MUC20, PRR7, PRR15, SPRR1B, SPRR2D, KRT5, KRT6B, KRT13, KRT14, KRT15, KRT17, SERPINB3, SERPINB4, SERPINB5, SERPINB13, CLCA2, TRPV4, BBS5, MMP3 and SAA4.

35. A method of treating IPF in a patient comprising administering an effective amount of an IPF therapeutic agent to the patient to treat the IPF, provided that elevated expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, has been detected in a biological sample obtained from the patient, wherein the one or the combination of genes is selected from CXCR3, CXCR5,

CXCL13, CCR6, CCR7, CD19, MS4A1 (CD20), TNFRSF17 (BCMA), BLK, BLNK, FCRLA, FCRL2, FCRL5, CD79A, CD79B, CD27, CD28, CD1A, CD1B, CD1C, CD1E, IGHV1-69, IGLJ3, IGJ, IGHV3-48, IGLV3-21, IGKV1-5, IGHG1, IGKC, IGLV6-57, IGK@ (immunoglobulin kappa locus), IGHA1, IGKV2-24, IGKV1D-8, IGHM.

36. A method of treating IPF in a patient comprising administering an effective amount of an IPF therapeutic agent to the patient to treat the IPF, provided that elevated expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, has been detected in a biological sample obtained from the patient, wherein the one or the combination of genes is selected from COL1A1, COL1A2, COL5A2, COL12A1, COL14A1, COL15A1, COL16A1, COL18A1, CTHRC1, HGF, IGFBP7, SCGF (CLEC11A); LOXL1, LOXL2; GLI1, GLI2, SMO; SFRP2, DIO2, CDH11, POSTN, and TGFB3.

37. The method of any one of claims 34-36, wherein the IPF therapeutic agent is selected from an anti-IL-13 agent, an anti-IL-4 agent, a combination anti-IL-13/IL-4 agent, pirfenidone, anti-LOXL2 antibody (GS-6624), N-acetylcysteine, anti-TGF-β antibody (GC1008), anti-αvβ6 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 method of claim 37, wherein the IPF therapeutic agent is an anti-IL-13 agent, wherein the IL-13 agent is an anti-IL-13 antibody, and wherein the anti-IL-13 antibody is lebrikizumab.

39. The method 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 method 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 method 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 method of any one of claims 38-41, wherein the anti-IL-13 antibody is administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg.

43. The method of claim 42, wherein the anti-IL-13 antibody is administered subcutaneously once every four weeks at a flat dose of 250 mg.

44. The method of claim 37, wherein the IPF therapeutic agent is a combination anti-IL-13/anti-IL-4 agent.

45. The method of claim 44, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

46. A method of treating an IPF patient previously determined to have a prognosis of shortened survival according to the method of any one of claims 1-13, 20, or 21 comprising administering an effective amount of an IPF therapeutic agent.

47. The method of claim 46, 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-αvβ6 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).

48. The method of claim 47, wherein the anti-IL-13 agent is lebrikizumab.

49. The method of claim 47 , 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.

50. The method of claim 49, 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.

51. The method of claim 50, 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.

52. The method of any one of claims 48-51, wherein the anti-IL-13 antibody is administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg.

53. The method of claim 52, wherein the anti-IL-13 antibody is administered subcutaneously once every four weeks at a flat dose of 250 mg.

54. A method of treating an IPF patient comprising administering an effective amount of an IPF therapeutic agent, provided that the patient has a baseline score of two or above determined according to the method of claim 13.

55. A method of treating an IPF patient comprising administering an effective amount of an IPF therapeutic agent, provided that the patient has a baseline score of one or above determined according to the method of claim 20.

56. The method of claim 54 or claim 55, 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-αvβ6 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).

57. The method of claim 56, wherein the anti-IL-13 agent is lebrikizumab.

58. The method of claim 56 , 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.

59. The method of claim 58, 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.

60. The method of claim 59, 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.

61. The method of any one of claims 57-60, wherein the anti-IL-13 antibody is administered subcutaneously once every four weeks at a flat dose selected from 125 mg, 250 mg, and 500 mg.

62. The method of claim 61, wherein the anti-IL-13 antibody is administered subcutaneously once every four weeks at a flat dose of 250 mg.

63. The method of claim 56, wherein the IPF therapeutic agent is a combination anti-IL-13/anti-IL-4 agent.

64. The method of claim 63, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

65. The method of any one of claims 34-64, 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.

66. The method of claim 65, wherein disease progression is further indicated by decrease from baseline of $\geq$ 15% in DL_{CO} at week 52.

67. The method of any one of claims 34-64, wherein a decrease in DL_{CO} from baseline 52 weeks after treatment is less than 15%.

68. The method of any one of claims 34-64, 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.

69. The method of claim 68, 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.

70. The method of any one of claims 34-64, 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.

71. A method of monitoring disease progression in an IPF patient comprising obtaining a biological sample from the patient at a first time point and one or more additional time points, measuring in the biological samples the expression of one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the one or the combination of genes is selected from any of Table 2, Table 3, Table 4, or Table 5, wherein a change in expression level from the first time point to the one or more additional time points is indicative of disease progression.

72. The method of claim 71, wherein the one or the combination of genes, or the one or the combination of proteins, is selected from MUCL1, MUC4, MUC20, PRR7, PRR15, SPRR1B, SPRR2D, KRT5, KRT6B, KRT13, KRT14, KRT15, KRT17, SERPINB3, SERPINB4, SERPINB5, SERPINB13, CLCA2, TRPV4, BBS5, MMP3, and SAA4.

73. The method of claim 71, wherein the one or the combination of genes is selected from CXCR3, CXCR5, CXCL13, CCR6, CCR7, CD19, MS4A1 (CD20), BLK, BLNK, FCRLA, FCRL2, FCRL5, CD79A, CD79B, CD27, CD28, CD1A, CD1B, CD1C, CD1E, IGHV1-69, IGLJ3, IGJ, IGHV3-48, IGLV3-21, IGKV1-5, IGHG1, IGKC, IGLV6-57, IGK@, IGHA1, IGKV2-24, IGKV1D-8, IGHM.

74. The method of claim 71, wherein the one or the combination of genes, or the one or the combination of proteins, is selected from COL1A1, COL1A2, COL5A2, COL12A1, COL14A1, COL15A1, COL16A1, COL18A1, CTHRC1, HGF, IGFBP7, SCGF (CLEC11A); LOXL1, LOXL2; GLI1, GLI2, SMO; SFRP2, DIO2, CDH11, POSTN, and TGFB3.

75. The method of claim 71, wherein the one or the combination of genes, or the one or the combination of proteins is selected from CHI3L1 (YKL-40), CCL11, CCL13, CCL17, CCL18, COMP, CXCL13, MMP3, MMP7, SAA4 (constitutive SAA), POSTN, AND SPP1 (OPN).

76. The method of any one of claims 71-75, wherein the biological samples are selected from lung tissue, serum, and plasma.

77. The method of claim 76, 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.

78. The method of claim 76, wherein the biological sample is serum and the expression of the one or the combination of proteins is measured using an immunoassay.

79. The method of any one of claims 71-78, further comprising treating the patient with a candidate therapeutic agent in a clinical study.

80. The method of claim 79, 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-αvβ6 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).

81. The method of claim 80, wherein the anti-IL-13 agent is lebrikizumab.

82. The method of claim 80 , 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.

83. The method of claim 82, 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.

84. The method of claim 83, 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 one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the gene is COMP or the combination of genes comprises COMP, wherein an elevated expression level of the one or the combination of genes, or an elevated expression level of the one or the combination of proteins, is indicative of a prognosis for shortened survival compared to median survival and wherein a reduced expression level of the one or the combination of genes, or a reduced expression level of the one or the combination of proteins, is indicative of a prognosis for increased survival compared to median survival.

2. The method of claim 1, wherein the combination of genes comprises MMP3.

3. The method of claim 1, wherein the combination of genes comprises YKL-40.

4. The method of claim 1, wherein the combination of genes comprises MMP7.

5. The method of claim 1, wherein the combination of genes is selected from any of Table 2, Table 3, Table 4 or Table 5.

6. The method of claim 1, wherein the combination of genes comprises a gene selected from CHI3L1 (YKL-40), CCL11, CCL13, CCL17, CCL18, CXCL13, MMP3, MMP7, SAA4 (constitutive SAA), POSTN, and SPP1 (OPN).

7. The method of claim 6, wherein the combination of genes comprises a gene selected from MMP3 and SAA4 (constitutive SAA).

8. The method of claim 6 wherein the combination of genes comprises a gene selected from YKL-40 and CCL18.

9. The method of claim 6, comprising measuring the expression level of CXCL13.

10. The method of claim 6, comprising measuring the expression level of MMP3.

11. The method of claim 6, comprising measuring the expression level of SAA4 (constitutive SAA).

12. The method of claim 6, wherein the patient is on immunomodulatory therapy.

13. The method of any one of claims 1-12, wherein the biological sample is selected from lung tissue, serum, and plasma.

14. 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.

15. The method of claim 14, 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-αvβ6 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).

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

17. The method of claim 15, 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.

18. The method of claim 17, 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.

19. The method of claim 18, 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.

20. The method of claim 15, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

21. 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.

22. The method of any one of claims 14-21, wherein the biological sample is selected from serum and plasma.

23. The method of claim 21, 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-αvβ6 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).

24. The method of claim 23, wherein the anti-IL-13 agent is lebrikizumab.

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

26. The method of claim 23, 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 1-14, 21, or 22.

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 (GS-6624), N-acetylcysteine, anti-TGF-β antibody (GC1008), anti-αvβ6 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).

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

32. 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.

33. The use of claim 32, 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.

34. The use of claim 33, 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.

35. The use of any one of claims 31-34, 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.

36. The use of claim 35, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose of 250 mg.

37. 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 14.

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 one or above determined according to the method of claim 21.

39. The use of claim 37 or claim 38, 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-αvβ6 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).

40. The use of claim 39, wherein the anti-IL-13 agent is lebrikizumab.

41. The use of claim 39 , 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.

42. The use of claim 41, 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.

43. The use of claim 42, 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.

44. The use of any one of claims 40-42, 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.

45. The use of claim 44, wherein the anti-IL-13 antibody is to be administered subcutaneously once every four weeks at a flat dose of 250 mg.

46. The use of claim 39, wherein the IPF therapeutic agent is a combination anti-IL-13/anti-IL-4 agent.

47. The use of claim 46, wherein the anti-IL-13/anti-IL-4 agent is a bispecific antibody.

48. The use of any one of claims 29-47, 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.

49. The use of claim 48, wherein disease progression is further indicated by decrease from baseline of $\geq$ 15% in DL_{CO} at week 52.

50. The use of any one of claims 29-47, wherein a decrease in DL_{CO} from baseline 52 weeks after treatment is less than 15%.

51. The use of any one of claims 29-47, 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.

52. The use of claim 51, 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.

53. The use of any one of claims 29-47, 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.

54. 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 one or a combination of genes, or expression of one or a combination of proteins encoded by the one or the combination of genes, wherein the one gene is COMP or the combination of genes comprises COMP, wherein a change in expression level from the first time point to the one or more additional time points is indicative of disease progression.

55. The method of claim 54, wherein the combination of genes comprises MMP3.

56. The method of claim 54, wherein the combination of genes comprises YKL-40.

57. The method of claim 54, wherein the combination of genes comprises MMP7.

58. The method of claim 54, wherein the combination of genes comprises a gene selected from CHI3L1 (YKL-40), CCL11, CCL13, CCL17, CCL18, CXCL13, MMP3, MMP7, SAA4 (constitutive SAA), POSTN, and SPP1 (OPN).

59. The method of claim 54, wherein the combination of genes is selected from any of Table 2, Table 3, Table 4 or Table 5.

60. The method of any one of claims 54-59, 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 54-62, 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 (GS-6624), N-acetylcysteine, anti-TGF-β antibody (GC1008), anti-αvβ6 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).

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

66. 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.

67. The method of claim 66, 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.

68. The method of claim 67, 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.