CLAIMS

1. A method of identifying an asthma patient or a respiratory disorder patient who is likely to be responsive to treatment with a TH2 Pathway Inhibitor comprising determining whether the patient is Eosinophilic Inflammation Positive (EIP) using an Eosinophilic Inflammation Diagnostic Assay (EIDA), wherein the EIP status indicates that the patient is likely to be responsive to treatment with the TH2 Pathway Inhibitor, wherein the EIDA comprises the steps of:

a) determining the amount of Total Periostin in a sample obtained from said patient;

b) comparing the amount of Total Periostin determined in step a) to a reference amount; and

c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b).

2. A method of identifying an asthma patient or a respiratory disorder patient who is likely to suffer from severe exacerbations comprising determining whether the patient is Eosinophilic Inflammation Positive (EIP) using an Eosinophilic Inflammation Diagnostic Assay (EIDA), wherein the EIP status indicates that the patient is likely to suffer from an increase in severe exacerbations, wherein the EIDA comprises the steps of:

a) determining the amount of Total Periostin in a sample obtained from said patient;

b) comparing the amount of Total Periostin determined in step a) to a reference amount; and

c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b).

3. A method of identifying an asthma patient or a respiratory disorder patient who is less likely to be responsive to treatment with a TH2 Pathway Inhibitor comprising determining whether the patient is Eosinophilic Inflammation Negative (EIN) using an Eosinophilic Inflammation Diagnostic Assay (EIDA), wherein the EIN status indicates that the patient is less likely to be responsive to treatment with the TH2 Pathway Inhibitor, wherein the EIDA comprises the steps of:

a) determining the amount of Total Periostin in a sample obtained from said patient;

b) comparing the amount of Total Periostin determined in step a) to a reference amount; and

c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b).

4. A method of monitoring an asthma patient being treated with a TH2 Pathway inhibitor, comprising determining whether the patient is Eosinophilic Inflammation Positive (EIP) or Eosinophilic Inflammation Negative (EIN) using an Eosinophilic Inflammation Diagnostic Assay (EIDA), wherein the EIDA comprises the steps of:

a) determining the amount of Total Periostin in a sample obtained from said patient;

b) comparing the amount of Total Periostin determined in step a) to a reference amount; and

c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b).

5. The method of claim 4, further comprising determining a treatment regimen for the TH2 Pathway Inhibitor.

6. The method of claim 5, wherein the determination of EIP indicates continuing therapy with the TH2 Pathway Inhibitor and the determination of EIN indicates discontinuing therapy with the TH2 Pathway Inhibitor.

7. The method according to any one of claims 1-4, wherein the Total Periostin is serum periostin, which periostin is measured using an immunoassay.

8. The method according to claim 7, wherein the immunoassay is a sandwich immunoassay.

9. The method according to claim 8, wherein the sandwich immunoassay is an E4 Assay or is performed by an Elecsys® analyzer.

10. The method according to any one of claims 1-4, wherein the reference amount for EIP is selected from the group consisting of:
(a) 23ng/ml or greater when using an E4 Assay in step (a); and
(b) 50ng/ml or greater when using an Elecsys® analyzer in step (a).

11. The method according to any one of claims 1-4, wherein the reference amount for EIN is selected from the group consisting of:
(a) 21 ng/ml or lower when using an E4 Assay in step (a); and
(b) 48 ng/ml or lower when using an Elecsys® analyzer in step (a).

12. The method according to any one of claims 1-11, wherein the patient is suffering from moderate to severe asthma.

13. The method according to any one of claims 1-11, wherein the asthma or respiratory disorder is uncontrolled on a corticosteroid.

14. The method according to claim 13, wherein the corticosteroid is an inhaled corticosteroid.

15. The method according to claim 14, wherein the inhaled corticosteroid is Qvar®, Pulmicort®, Symbicort®, Aerobid®, Flovent®, Flonase®, Advair® or Azmacort®.

16. The method according to any one of claims 1-11, wherein the patient is also being treated with a second controller.

17. The method according to claim 16, wherein the second controller is a long acting bronchial dilator (LABD).

18. The method according to claim 17, wherein the LABD is (a) selected from the group consisting of: a long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline, and oral corticosteroids (OCS); or (b) selected from the group consisting of Symbicort®, Advair®, Brovana®, Foradil®, Perforomist™ and Serevent®.

19. The method according to any one of claims 1-16, wherein the TH2 Pathway Inhibitor is selected from the group consisting of:
(a) a TH2 Pathway Inhibitor that inhibits the target ITK, BTK , IL-9 (e.g., MEDI-528), IL-5 (e.g., Mepolizumab, CAS No. 196078-29-2; resilizumab), IL-13 (e.g., IMA-026, IMA-638 (also referred to as, anrukinzumab, INN No. 910649-32-0; QAX-576; IL4/IL13 trap), tralokinumab (also referred to as CAT-354, CAS No. 1044515-88-9); AER-001, ABT-308 (also referred to as humanized 13C5.5 antibody), IL-4 (e.g., AER-001, IL4/IL13 trap), OX40L, TSLP, IL-25, IL-33 and IgE (e.g., XOLAIR®, QGE-031; MEDI-4212); and receptors such as: IL-9 receptor, IL-5 receptor (e.g., MEDI-563 (benralizumab, CAS No. 1044511-01-4), IL-4receptor alpha (e.g., AMG-317, AIR-645), IL-13receptoralpha1 (e.g., R-1671) and IL-13receptoralpha2, OX40, TSLP-R, IL-7Ralpha (a co-receptor for TSLP), IL17RB (receptor for IL-25), ST2 (receptor for IL-33), CCR3, CCR4, CRTH2 (e.g., AMG-853, AP768, AP-761, MLN6095, ACT129968), FcepsilonRI, FcepsilonRII/CD23 (receptors for IgE), Flap (e.g., GSK2190915), Syk kinase (R-343, PF3526299); CCR4 (AMG-761), TLR9 (QAX-935), or is a multi-cytokine inhibitor of CCR3, IL5, IL3, GM-CSF (e.g., TPI ASM8);
(b) an anti-IL13/IL4 pathway inhibitor or an anti IgE binding agent;
(c) an anti-IL-13 antibody; and (d) an anti-IgE antibody.

20. The method according to claim 19(c), wherein the anti-IL-13 antibody is selected from a group consisting of (a) an antibody comprising a VH comprising SEQ ID NO:9 and VL comprising SEQ ID NO:10, an anti-IL13 antibody comprising HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, and HVRL3, wherein the respective HVRs have the amino acid sequence of

SEQ ID NO.: 11, SEQ ID NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, SEQ ID NO.: 15, and SEQ ID NO.: 16 or lebrikizumab; and (b) a bispecific antibody that also binds IL-4.

21. The method according to claim 19(d), wherein the anti-IgE antibody is (i) the XOLAIR® antibody, (ii) anti-M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain is SEQ ID NO:24 and the variable light chain is SEQ ID NO:25 or (iii) an anti- M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain further comprises an HVR-H1, HVR-H2 and HVR-H3, and the variable light chain further comprises and HVR-L1, HVR, L2 and HVR-L3 and: (a) the HVR-H1 is residues 26-35 of SEQ ID NO:24, [GFTFSDYGIA]; (b) the HVR-H2 is residues 49-66 of SEQ ID NO:24, [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 is residues 97-106 of SEQ ID NO:24, [ARDNWDAMDY]; (d) the HVR-L1 is residues 24-39 of SEQ ID NO:25, [RSSQSLVHNNANTYLH]; (e) the HVR-L2 is residues 55-61 of SEQ ID NO:25, [KVSNRFS]; (f) the HVR-L3 is residues 94-102 of SEQ ID NO:25 [SQNTLVPWT].

22. Use of a kit for detecting Total Periostin in a biological sample that has been obtained from an asthma patient for stratifying/classifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 Pathway Inhibitor.

23. The use according to claim 22, wherein the Total Periostin is detected using an EIDA, which EIDA comprises the steps of:

a) determining the amount of Total Periostin in a sample obtained from an asthma patient

b) comparing the amount of Total Periostin determined in step a) to a reference amount.

c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b).

24. The use according to claim 22 or claim 23, wherein the Total Periostin is serum periostin, which periostin is a measured using an immunoassay.

25. The use according to claim 24, wherein the immunoassay is a sandwich immunoassay.

26. The use according to claim 25, wherein the sandwich immunoassay is performed by an Elecsys® analyzer.

27. The use according to claim 23, wherein the reference amount for a responder is selected from the group consisting of:
(a) 23ng/ml or greater when using the E4 Assay in step a; and
(b) 50ng/ml or greater when using the Elecsys® periostin assay in step a.

28. The use according to claims 22-27, wherein the patient is suffering from moderate to severe asthma.

29. The use according to claims 22-27, wherein the asthma or respiratory disorder is uncontrolled on a corticosteroid.

30. The use according to claim 29, wherein the corticosteroid is an inhaled corticosteroid

31. The use according to claim 30, wherein the inhaled corticosteroid is Qvar®, Pulmicort®, Symbicort®, Aerobid®, Flovent®, Flonase®, Advair® or Azmacort®.

32. The use according to claims 22-30, wherein the patient is also being treated with a second controller.

33. The use according to claim 32, wherein the second controller is a long acting bronchial dilator (LABD).

34. The use according to claim 33, wherein the LABD is a LABA, LTRA, LAMA, theophylline, or OCS.

35. The use according to claim 34, wherein the LABD is Symbicort®, Advair®, Brovana®, Foradil®, PerforomistTM or Serevent®.

36. The use according to claims 22-34, wherein the TH2 Pathway Inhibitor is selected from the group consisting of: (a) a TH2 pathway Inhibitor that inhibits the target ITK, BTK , IL-9 (e.g., MEDI-528), IL-5 (e.g., Mepolizumab, CAS No. 196078-29-2; resilizumab), IL-13 (e.g., IMA-026, IMA-638 (also referred to as, anrukinzumab, INN No. 910649-32-0; QAX-576; IL4/IL13 trap), tralokinumab (also referred to as CAT-354, CAS No. 1044515-88-9); AER-001, ABT-308 (also referred to as humanized 13C5.5 antibody), IL-4 (e.g., AER-001, IL4/IL13 trap), OX40L, TSLP, IL-25, IL-33 and IgE (e.g., XOLAIR, QGE-031; MEDI-4212); and receptors such as: IL-9 receptor, IL-5 receptor (e.g., MEDI-563 (benralizumab, CAS No. 1044511-01-4), IL-4receptor alpha (e.g., AMG-317, AIR-645), IL-13receptoralpha1 (e.g., R-1671) and IL-13receptoralpha2, OX40, TSLP-R, IL-7Ralpha (a co-receptor for TSLP), IL17RB (receptor for IL-25), ST2 (receptor for IL-33), CCR3, CCR4, CRTH2 (e.g., AMG-853, AP768, AP-761, MLN6095, ACT129968), FcepsilonRI, FcepsilonRII/CD23 (receptors for IgE), Flap (e.g., GSK2190915), Syk kinase (R-343, PF3526299); CCR4 (AMG-761), TLR9 (QAX-935) or is a multi-cytokine inhibitor of CCR3, IL5, IL3, GM-CSF (e.g., TPI ASM8);
(b) an anti-IL13/IL4 pathway inhibitor or an anti IgE binding agent;
(c) an anti-IL-13 antibody; and (d) an anti-IgE antibody.

37. The use according to claim 36(c), wherein the anti-IL-13 antibody is selected from the group consisting of: (i) an antibody comprising a VH comprising SEQ ID NO:9 and VL comprising SEQ ID NO:10, an anti-IL13 antibody comprising HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, and HVRL3, wherein the respective HVRs have the amino acid sequence of SEQ ID NO.: 11, SEQ ID NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, SEQ ID NO.: 15, and SEQ ID NO.: 16 or lebrikizumab; and
(ii) a bispecific antibody that also binds IL-4.

38. The use according to claim 36(d), wherein the anti-IgE antibody is (i) the XOLAIR® antibody, (ii) anti-M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain is SEQ ID NO:24 and the variable light chain is SEQ ID NO:25 or (iii) an anti- M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain further comprises an HVR-H1, HVR-H2 and HVR-H3, and the variable light chain further comprises and HVR-L1, HVR, L2 and HVR-L3 and: (a) the HVR-H1 is residues 26-35 of SEQ ID NO:24, [GFTFSDYGIA]; (b) the HVR-H2 is residues 49-66 of SEQ ID NO:24, [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 is residues 97-106 of SEQ ID NO:24, [ARDNWDAMDY]; (d) the HVR-L1 is residues 24-39 of SEQ ID NO:25, [RSSQSLVHNNANTYLH]; (e) the HVR-L2 is residues 55-61 of SEQ ID NO:25, [KVSNRFS]; (f) the HVR-L3 is residues 94-102 of SEQ ID NO:25. [SQNTLVPWT].

39. A kit for measuring the Total Periostin in a biological sample obtained from an asthma patient or a patient suffering from a respiratory disorder, wherein the kit comprises either (1) a first nucleic acid molecule that hybridizes to a second nucleic acid molecule, wherein the second nucleic acid molecule encodes Total Periostin or a portion thereof, or (2) the kit comprises an antibody that binds to Total Periostin.

40. The kit according to claim 39, comprising a package insert containing information describing the uses according to any one of claims 22-38.

41. A kit for diagnosing an asthma subtype in a patient comprising:

(1) determining the levels of Total Periostin in a serum sample obtained from the patient and the protein expressions levels in the serum sample for one or more proteins selected from TARC and MCP-4; and

(2) instructions for measuring the expression levels of the Total Periostin and one or more proteins selected from TARC and MCP-4 in the serum sample, wherein the elevated expression levels of any one, combination or all of said proteins is indicative of the asthma subtype.

42. The kit according to claim 41, wherein the kit further comprises a package insert for determining whether an asthma patient or respiratory disorder patient is EIP or EIN.

43. The kit according to claim 42, wherein the kit further comprises a packet insert selected from the group consisting of (a) a package insert for determining whether an asthma patient is likely to respond to a TH2 Pathway Inhibitor; and (b) a package insert containing information describing the uses according to any one of claims 22-38.

44. The kit according to claims 39-43, further comprising an empty container to hold a biological sample.

45. The kit according to claims 39-43, wherein the kit comprises two anti-periostin antibodies for use in an immunoassay for determining Total Periostin levels.

CLAIMS:

1. A method of identifying an asthma patient or a respiratory disorder patient who is likely to be responsive to treatment with a TH2 Pathway Inhibitor comprising determining whether the patient is Eosinophilic Inflammation Positive (EIP) using an Eosinophilic Inflammation Diagnostic Assay (EIDA), wherein the EIP status indicates that the patient is likely to be responsive to treatment with the TH2 Pathway Inhibitor.

2. A method of identifying an asthma patient or a respiratory disorder patient who is likely to suffer from severe exacerbations comprising determining whether the patient is Eosinophilic Inflammation Positive (EIP) using an Eosinophilic Inflammation Diagnostic Assay (EIDA), wherein the EIP status indicates that the patient is likely to suffer from an increase in severe exacerbations.

3. A method of identifying an asthma patient or a respiratory disorder patient who is less likely to be responsive to treatment with a TH2 Pathway Inhibitor comprising determining whether the patient is Eosinophilic Inflammation Negative (EIN) using an Eosinophilic Inflammation Diagnostic Assay (EIDA), wherein the EIN status indicates that the patient is less likely to be responsive to treatment with the TH2 Pathway Inhibitor.

4. A method of monitoring an asthma patient being treated with a TH2 Pathway inhibitor, comprising determining whether the patient is Eosinophilic Inflammation Positive (EIP) or Eosinophilic Inflammation Negative (EIN) using an Eosinophilic Inflammation Diagnostic Assay (EIDA).

5. The method of claim 4, further comprising determining a treatment regimen for the TH2 Pathway Inhibitor.

6. The method of claim 5, wherein the determination of EIP indicates continuing therapy with the TH2 Pathway Inhibitor and the determination of EIN indicates discontinuing therapy with the TH2 Pathway Inhibitor.

7. The method according to claims 1-4, wherein the EIDA comprises the steps of:

a) determining the amount of Total Periostin in a sample obtained from an asthma patient;

b) comparing the amount of Total Periostin determined in step a) to a reference amount; and

c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b).

8. The method according to claim 7, wherein the Total Periostin is serum periostin, which periostin is measured using an immunoassay.

9. The method according to claim 8, wherein the immunoassay is a sandwich immunoassay.

10. The method according to claim 9, wherein the sandwich immunoassay is an E4 Assay or is performed by an Elecsys® analyzer.

11. The method according to claim 7, wherein the reference amount for EIP is selected from the group consisting of: (a) 23ng/ml or greater when using an E4 Assay in step (a);and

(b) 50ng/ml or greater when using an Elecsys® analyzer in step (a).

12. The method according to claim 7, wherein the reference amount for EIN is selected from the group consisting of: (a) 21 ng/ml or lower when using an E4 Assay in step (a); and

(b) 48 ng/ml or lower when using an Elecsys® analyzer in step (a).

13. The method according to any one of claims 1-12, wherein the patient is suffering from moderate to severe asthma.

14. The method according to any one of claims 1-12, wherein the asthma or respiratory disorder is uncontrolled on a corticosteroid.

~~15. The method according to claim 14, wherein the corticosteroid is an inhaled corticosteroid.~~

16. The method according to claim 15, wherein the inhaled corticosteroid is Qvar®, Pulmicort®, Symbicort®, Aerobid®, Flovent®, Flonase®, Advair® or Azmacort®.

17. The method according to any one of claims 1-12, wherein the patient is also being treated with a second controller.

18. The method according to claim 17, wherein the second controller is a long acting bronchial dilator (LABD).

19. The method according to claim 18, wherein the LABD is (a) selected from the group consisting of: a long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline, and oral corticosteroids (OCS); or

(b) selected from the group consisting of Symbicort®, Advair®, Brovana®, Foradil®, Perforomist™ and Serevent®.

20. The method according to any one of claims 1-17, wherein the TH2 Pathway Inhibitor is selected from the group consisting of: (a) a TH2 Pathway Inhibitor that inhibits the target ITK, BTK , IL-9 (e.g., MEDI-528), IL-5 (e.g., Mepolizumab, CAS No. 196078-29-2; resilizumab), IL-13 (e.g., IMA-026, IMA-638 (also referred to as, anrukinzumab, INN No. 910649-32-0; QAX-576; IL4/IL13 trap), tralokinumab (also referred to as CAT-354, CAS No. 1044515-88-9); AER-001, ABT-308 (also referred to as humanized 13C5.5 antibody), IL-4 (e.g., AER-001, IL4/IL13 trap), OX40L, TSLP, IL-25, IL-33 and IgE (e.g., XOLAIR®, QGE-031; MEDI-4212); and receptors such as: IL-9 receptor, IL-5 receptor (e.g., MEDI-563 (benralizumab, CAS No. 1044511-01-4), IL-4receptor alpha (e.g., AMG-317, AIR-645), IL-13receptoralpha1 (e.g., R-1671) and IL-13receptoralpha2, OX40, TSLP-R, IL-7Ralpha (a co-receptor for TSLP), IL17RB (receptor for IL-25), ST2 (receptor for IL-33), CCR3, CCR4, CRTH2 (e.g., AMG-853, AP768, AP-761, MLN6095, ACT129968), FcepsilonRI, FcepsilonRII/CD23 (receptors for IgE), Flap (e.g., GSK2190915), Syk kinase (R-343, PF3526299); CCR4 (AMG-761), TLR9 (QAX-935), or is a multi-cytokine inhibitor of CCR3, IL5, IL3, GM-CSF (e.g., TPI ASM8);

(b) an anti-IL13/IL-4 pathway inhibitor or an anti-IgE binding agent;

(c) an anti-IL-13 antibody; and (d) an anti-IgE antibody.

21. The method according to claim 20(c), wherein the anti-IL-13 antibody is selected from a group consisting of (a) an antibody comprising a VH comprising SEQ ID NO:9 and VL comprising SEQ ID NO:10, an anti-IL13 antibody comprising HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, and HVRL3, wherein the respective HVRs have the amino acid sequence of SEQ ID NO.: 11, SEQ ID NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, SEQ ID NO.: 15, and SEQ ID NO.: 16 or lebrikizumab; and

(b) a bispecific antibody that also binds IL-4.

22. The method according to claim 20(d), wherein the anti-IgE antibody is (i) the XOLAIR® antibody, (ii) anti-M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain is SEQ ID NO:24 and the variable light chain is SEQ ID NO:25 or (iii) an anti- M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain further comprises an HVR-H1, HVR-H2 and HVR-H3, and the variable light chain further comprises and HVR-L1, HVR, L2 and HVR-L3 and: (a) the HVR-H1 is residues 26-35 of SEQ ID NO:24, [GFTFSDYGIA]; (b) the HVR-H2 is residues 49-66 of SEQ ID NO:24, [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 is residues 97-106 of SEQ ID NO:24, [ARDNWDAMDY]; (d) the HVR-L1 is residues 24-39 of SEQ ID NO:25, [RSSQSLVHNNANTYLH]; (e) the HVR-L2 is residues 55-61 of SEQ ID NO:25, [KVSNRFS]; (f) the HVR-L3 is residues 94-102 of SEQ ID NO:25 [SQNTLVPWT].

23. Use of a kit for detecting Total Periostin in a biological sample that has been obtained from an asthma patient for stratifying/classifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 Pathway Inhibitor.

24. The use according to claim 23, wherein the Total Periostin is detected using an EIDA, which EIDA comprises the steps of:

a) determining the amount of Total Periostin in a sample obtained from an asthma patient

b) comparing the amount of Total Periostin determined in step a) to a reference amount.

c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b).

25. The use according to claim 23 or claim 24, wherein the Total Periostin is serum periostin, which periostin is a measured using an immunoassay.

26. The use according to claim 25, wherein the immunoassay is a sandwich immunoassay.

27. The use according to claim 26, wherein the sandwich immunoassay is performed by an Elecsys® analyzer.

28. The use according to claim 24, wherein the reference amount for a responder is selected from the group consisting of: (a) 23ng/ml or greater when using the E4 Assay in step a; and

(b) 50ng/ml or greater when using the Elecsys® periostin assay in step a.

29. The use according to claims 23-28, wherein the patient is suffering from moderate to severe asthma.

30. The use according to claims 23-28, wherein the asthma or respiratory disorder is uncontrolled on a corticosteroid.

31. The use according to claim 30, wherein the corticosteroid is an inhaled corticosteroid

32. The use according to claim 31, wherein the inhaled corticosteroid is Qvar®, Pulmicort®, Symbicort®, Aerobid®, Flovent®, Flonase®, Advair® or Azmacort®.

33. The use according to claims 23-31, wherein the patient is also being treated with a second controller.

34. The use according to claim 33, wherein the second controller is a long acting bronchial dilator (LABD).

35. The use according to claim 34, wherein the LABD is a LABA, LTRA, LAMA, theophylline, or OCS.

36. The use according to claim 35, wherein the LABD is Symbicort®, Advair®, Brovana®, Foradil®, PerforomistTM or Serevent®.

37. The use according to claims 23-35, wherein the TH2 Pathway Inhibitor is selected from the group consisting of: (a) a TH2 pathway Inhibitor that inhibits the target ITK, BTK , IL-9 (e.g., MEDI-528), IL-5 (e.g., Mepolizumab, CAS No. 196078-29-2; resilizumab), IL-13 (e.g., IMA-026, IMA-638 (also referred to as, anrukinzumab, INN No. 910649-32-0; QAX-576; IL4/IL13 trap), tralokinumab (also referred to as CAT-354, CAS No. 1044515-88-9); AER-001, ABT-308 (also referred to as humanized 13C5.5 antibody), IL-4 (e.g., AER-001, IL4/IL13 trap), OX40L, TSLP, IL-25, IL-33 and IgE (e.g., XOLAIR, QGE-031; MEDI-4212); and receptors such as: IL-9 receptor, IL-5 receptor (e.g., MEDI-563 (benralizumab, CAS No. 1044511-01-4), IL-4receptor alpha (e.g., AMG-317, AIR-645), IL-13receptoralpha1 (e.g., R-1671) and IL-13receptoralpha2, OX40, TSLP-R, IL-7Ralpha (a co-receptor for TSLP), IL17RB (receptor for IL-25), ST2 (receptor for IL-33), CCR3, CCR4, CRTH2 (e.g., AMG-853, AP768, AP-761, MLN6095, ACT129968), FcepsilonRI, FcepsilonRII/CD23 (receptors for IgE), Flap (e.g., GSK2190915), Syk kinase (R-343, PF3526299); CCR4 (AMG-761), TLR9 (QAX-935) or is a multi-cytokine inhibitor of CCR3, IL5, IL3, GM-CSF (e.g., TPI ASM8);

(b) an anti-IL13/IL4 pathway inhibitor or an anti IgE binding agent;

(c) an anti-IL-13 antibody; and (d) an anti-IgE antibody.

38. The use according to claim 37(c), wherein the anti-IL-13 antibody is selected from the group consisting of: (i) an antibody comprising a VH comprising SEQ ID NO:9 and VL comprising SEQ ID NO:10, an anti-IL13 antibody comprising HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, and HVRL3, wherein the respective HVRs have the amino acid sequence of SEQ ID NO.: 11, SEQ ID NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, SEQ ID NO.: 15, and SEQ ID NO.: 16 or lebrikizumab; and

(b) a bispecific antibody that also binds IL-4.

39. The use according to claim 37(d), wherein the anti-IgE antibody is (i) the XOLAIR® antibody, (ii) anti-M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain is SEQ ID NO:24 and the variable light chain is SEQ ID NO:25 or (iii) an anti- M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain further comprises an HVR-H1, HVR-H2 and HVR-H3, and the variable light chain further comprises and HVR-L1, HVR, L2 and HVR-L3 and: (a) the HVR-H1 is residues 26-35 of SEQ ID NO:24, [GFTFSDYGIA]; (b) the HVR-H2 is residues 49-66 of SEQ ID NO:24, [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 is residues 97-106 of SEQ ID NO:24, [ARDNWDAMDY]; (d) the HVR-L1 is residues 24-39 of SEQ ID NO:25, [RSSQSLVHNNANTYLH]; (e) the HVR-L2 is residues 55-61 of SEQ ID NO:25, [KVSNRFS]; (f) the HVR-L3 is residues 94-102 of SEQ ID NO:25. [SQNTLVPWT].

40. A kit for measuring the Total Periostin in a biological sample obtained from an asthma patient or a patient suffering from a respiratory disorder, wherein the kit comprises either (1) a first nucleic acid molecule that hybridizes to a second nucleic acid molecule, wherein the

second nucleic acid molecule encodes Total Periostin or a portion thereof, or (2) the kit comprises an antibody that binds to Total Periostin.

41. The kit according to claim 40, comprising a package insert containing information describing the uses according to any one of claims 23-39.

42. A kit for diagnosing an asthma subtype in a patient comprising:

(1) determining the levels of Total Periostin in a serum sample obtained from the patient and optionally the protein expressions levels in the serum sample for one or more proteins selected from TARC and MCP-4; and

(2) instructions for measuring the expression levels of the Total Periostin and optionally one or more proteins selected from TARC and MCP-4 in the serum sample, wherein the elevated expression levels of any one, combination or all of said proteins is indicative of the asthma subtype.

43. The kit according to claim 42, wherein the kit further comprises a package insert for determining whether an asthma patient or respiratory disorder patient is EIP or EIN.

44. The kit according to claim 43, wherein the kit further comprises a packet insert selected from the group consisting of (a) a package insert for determining whether an asthma patient is likely to respond to a TH2 Pathway Inhibitor; and

(b) a package insert containing information describing the uses according to any one of claims 23-39.

45. The kit according to claims 40-44, further comprising an empty container to hold a biological sample.

46. The kit according to claims 40-44, wherein the kit comprises two anti-periostin antibodies for use in an immunoassay for determining Total Periostin levels.

47. Use of an anti-IL-13 antibody comprising HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, and HVRL3, wherein the respective HVRs have the amino acid sequence of SEQ ID NO.: 11, SEQ ID

NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, SEQ ID NO.: 15, and SEQ ID NO.: 16 in the manufacture of a medicament for treating an asthma or a respiratory disorder in a patient; wherein the antibody is to be administered in a 125-500mg flat dose every 2-8 weeks.

48. The use according to claim 47, wherein the patient is suffering from moderate to severe asthma.

49. The use according to claim 47 or 48, wherein the asthma or respiratory disorder is uncontrolled on a corticosteroid.

50. The use according to claim 49, wherein the asthma or respiratory disorder is selected from the group consisting of: (a) an asthma or respiratory disorder that is uncontrolled on an inhaled corticosteroid; and
(b) an asthma or respiratory disorder that is uncontrolled on a total daily dose of at least 500 mcg fluticasone propionate (FP).

51. The use according to claim 50(a), wherein the corticosteroid is an inhaled corticosteroid is Qvar®, Pulmicort®, Symbicort®, Aerobid®, Flovent®, Flonase®, Advair®, Azmacort®.

52. The use according to claim any one of claims 47-51, wherein the patient is being treated with a second controller.

53. The use according to any one of claims 47-52, wherein the patient is continuing to be treated with a corticosteroid, optionally an inhaled corticosteroid, during the treatment with the anti-IL13 antibody.

54. The use according to claim 53, wherein the patient is continuing to be treated with a second controller during the treatment with the anti-IL-13 antibody.

55. The use according to claim 52 or claim 54, wherein the second controller is a long acting bronchial dilator.

~~56. The use according to claim 55, wherein the long acting bronchial dilator is a LABA, LTRA,~~ LAMA, theophylline, or OCS.

57. The use according to claim 56, wherein the patient is selected from the group consisting of:
(a) a patient which has been determined to be EIP;

(b) a patient which has been determined to be EIP using the kit according to any one of claims 40-46;

(c) a patient which has been determined to be EIP using the method of any one of claims 7-11.

58. The use according to any one of claims 47-57, wherein the patient is to be administered a flat dose of 125 mg or 250 mg every four weeks.

59. The use according to claim 58, wherein the patient is selected from the group consisting of
(a) a patient who is 18 years or older;

(b) a patient who is 12-17 years old or 12 years old and older; and

(c) a patient who is 6-11 years old or 6 years old and older.

60. The use according to any of claims 47-59, wherein the anti-IL-13 antibody is to be administered subcutaneously.

61. The use according to claim 60, wherein the anti-IL-13 antibody is to be administered using a prefilled syringe or autoinjector device.

62. The use according to claim 47, wherein the asthma patient to be treated is 18 years old or older and has serum periostin at $\geq$ 50 ng/mL and is uncontrolled on an inhaled corticosteroid and a second controller medication.

~~63. The use according to claim 60, wherein the serum periostin is selected from the group~~ consisting of: (a) a serum periostin which is measured using the method of any one of claims 7-10 and 11(b);
(b) a serum periostin which is measured using the kit of any one of claims 40-46.

64. The use according to any of claims 47-63, wherein the anti-IL-13 antibody is selected from the group consisting of (a) an antibody comprising a VH comprising SEQ ID NO:9 and a VL comprising SEQ ID NO:10; and (b)lebrikizumab.

65. The use according to claim 59(b), wherein the asthma patient is 12 years old and above and uncontrolled on an inhaled corticosteroid and a second controller medication.

66.Use of lebrikizumab in the manufacture of a medicament for treating asthma or a respiratory disease in a patient, wherein the treatment results in a relative improvement in FEV1 of greater than 5% compared to before treatment with lebrikizumab.

67. The use according to claim 66, wherein the relative improvement in FEV1 is greater than 8% compared to before treatment with lebrikizumab.

68. Use of lebrikizumab in the manufacture of a medicament for treating asthma or a respiratory disease in a patient, wherein the treatment results in a reduction in severe exacerbations.

69.Use of a TH2 Pathway Inhibitor in the manufacture of a medicament for otreating of a patient suffering from asthma or a respiratory disease in a patient diagnosed as EIP.

70. The use according to claim 69, wherein the patient has been diagnosed as EIP using a Total Periostin Assay.

71. The use according to claim 69 or claim 70, wherein the patient is retreated with the TH2 Pathway Inhibitor if the patient is determined to be EIP.

72. The use according to any one of claims 69-71, wherein serum from the patient is used to determine whether the patient is EIP.

73. The use according to any one of claims 69-71, wherein the EIP status is diagnosed using an EIDA in which the assay comprises the steps of:

a) determining the amount of Total Periostin in a sample obtained from the patient;

b) comparing the amount of Total Periostin determined in step a) to a reference amount; and

c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step (b).

74. The use according to claim 73, wherein the Total Periostin is serum periostin, which periostin is measured using an immunoassay.

75. The use according to claim 74, wherein the immunoassay is a sandwich immunoassay.

76. The use according to claim 75, wherein the sandwich immunoassay is performed by an Elecsys® analyzer.

77. The use according to any one of claims 73-76, wherein the reference amount is selected from the group consisting of: (i) 23ng/ml or greater when using the E4 Assay in step (a); and

(b) 50ng/ml or greater when using the Elecsys® periostin assay in step a.

78. The use according to claims 69-77, wherein the patient is suffering from moderate to severe asthma.

79. The use according to claims 69-78, wherein the asthma or respiratory disorder is uncontrolled on a corticosteroid.

80. The use according to claim 79, wherein the corticosteroid is an inhaled corticosteroid.

81. The use according to claim 80, wherein the inhaled corticosteroid is Qvar®, Pulmicort®, Symbicort®, Aerobid®, Flovent®, Flonase®, Advair® or Azmacort®.

82. The use according to claims 69-80, wherein the patient is also being treated with a second controller.

83. The use according to claim 82, wherein the second controller is a long acting bronchial dilator (LABD).

84. The use according to claim 83, wherein the LABD is selected from the group consisting of:
(a) a LABA, LTRA, LAMA, theophylline, or OCS; and
(b) Symbicort®, Advair®, Brovana®, Foradil®, PerforomistTM or Serevent®.

85. The use according to claim 68-80, wherein the TH2 Pathway Inhibitor is selected from the group consisting of: (a) a TH2 Pathway Inhibitor which inhibits the target ITK, BTK , IL-9 (e.g., MEDI-528), IL-5 (e.g., Mepolizumab, CAS No. 196078-29-2; resilizumab), IL-13 (e.g., IMA-026, IMA-638 (also referred to as, anrukinzumab, INN No. 910649-32-0; QAX-576; IL4/IL13 trap), tralokinumab (also referred to as CAT-354, CAS No. 1044515-88-9); AER-001, ABT-308 (also referred to as humanized 13C5.5 antibody), IL-4 (e.g., AER-001, IL4/IL13 trap), OX40L, TSLP, IL-25, IL-33 and IgE (e.g., XOLAIR, QGE-031; MEDI-4212); and receptors such as: IL-9 receptor, IL-5 receptor (e.g., MEDI-563 (benralizumab, CAS No. 1044511-01-4), IL-4receptor alpha (e.g., AMG-317, AIR-645), IL-13receptoralpha1 (e.g., R-1671) and IL-13receptoralpha2, OX40, TSLP-R, IL-7Ralpha (a co-receptor for TSLP), IL17RB (receptor for IL-25), ST2 (receptor for IL-33), CCR3, CCR4, CRTH2 (e.g., AMG-853, AP768, AP-761, MLN6095, ACT129968), FcepsilonRI, FcepsilonRII/CD23 (receptors for IgE), Flap (e.g., GSK2190915), Syk kinase (R-343,

~~PF3526299); CCR4 (AMG-761), TLR9 (QAX-935) or is a multi-cytokine inhibitor of CCR3,~~ IL5, IL3, GM-CSF (e.g., TPI ASM8);

(b) an anti-IL13/IL4 pathway inhibitor or an anti IgE binding agent; and (c) an anti-IgE antibody.

86. The use according to claim 85(b), wherein the anti-IL-13/IL4 pathway inhibitor is an anti-anti-IL-13 antibody.

87. The use according to claim 86, wherein the anti-IL-13 antibody is selected from the group consisting of: (a) an antibody comprising a VH comprising SEQ ID NO:9 and VL comprising SEQ ID NO:10, an anti-IL13 antibody comprising HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, and HVRL3, wherein the respective HVRs have the amino acid sequence of SEQ ID NO.: 11, SEQ ID NO.: 12, SEQ ID NO.: 13, SEQ ID NO.: 14, SEQ ID NO.: 15, and SEQ ID NO.: 16 or lebrikizumab; and

(b) a bispecific antibody that also binds IL-4.

88. The use according to claim 85(c), wherein the anti-IgE antibody is (i) the XOLAIR® antibody, (ii) anti-M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain is SEQ ID NO:24 and the variable light chain is SEQ ID NO:25 or (iii) an anti- M1' antibody comprising a variable heavy chain and a variable light chain, wherein the variable heavy chain further comprises an HVR-H1, HVR-H2 and HVR-H3, and the variable light chain further comprises and HVR-L1, HVR, L2 and HVR-L3 and: (a) the HVR-H1 is residues 26-35 of SEQ ID NO:24, [GFTFSDYGIA]; (b) the HVR-H2 is residues 49-66 of SEQ ID NO:24, [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 is residues 97-106 of SEQ ID NO:24, [ARDNWDAMDY]; (d) the HVR-L1 is residues 24-39 of SEQ ID NO:25, [RSSQSLVHNNANTYLH]; (e) the HVR-L2 is residues 55-61 of SEQ ID NO:25, [KVSNRFS]; (f) the HVR-L3 is residues 94-102 of SEQ ID NO:25 [SQNTLVPWT].

89. A method for evaluating adverse events in a patient associated with treatment of asthma with lebrikizumab comprising the steps of monitoring the number and/or severity of events that are exacerbations, community-acquired pneumonia, anaphylaxis, musculoskeletal pains, musculoskeletal disorders, connective tissue pains or connective tissue disorders.

90. The method according to claim 89, wherein the musculoskeletal or connective tissue disorder is arthralgia, back pain, pain in extremity, myalgia, neck pain, arthritis, bone development abnormalities, bursitis, costochondritis, exostosis, flank pain, musculoskeletal chest pain, musculoskeletal pain, pain in jaw or tendinitis.

91. An anti-periostin antibody comprising the HVR sequences of SEQ ID NO:1 and the HVR sequences of SEQ ID NO:2.

92. The antibody according to claim 91, wherein the antibody comprises the sequences of SEQ ID NO:1 and SEQ ID NO:2.

93. An anti-periostin antibody comprising the HVR sequences of SEQ ID NO:3 and the HVR sequences of SEQ ID NO:4.

94. The antibody according to claim 93, wherein the antibody comprises the sequences of SEQ ID NO:3 and SEQ ID NO:4.

95. A Total Periostin Assay comprising the use of the antibodies claims 91 and 93.