

[0013] In some embodiments, an Eosinophilic Inflammation Diagnostic Assay (EIDA) is provided.

[0014] In some embodiments, methods of identifying an asthma patient or a respiratory disorder patient who is likely to be responsive to treatment with a TH2 pathway inhibitor are provided. In some embodiments, the method comprises 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.

[0015] In some embodiments, methods of identifying an asthma patient or a respiratory disorder patient who is likely to suffer from severe exacerbations are provided. In some embodiments, the method comprises 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. In some embodiments, the methods comprise obtaining a biological sample from the patient, measuring the mRNA level of at least one, at least two, or at least three markers in the sample selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2, comparing the mRNA level detected in the sample to a reference level, and predicting that the patient is likely to suffer from severe exacerbations when the mRNA level measured in the sample is elevated compared to the reference level. In one aspect, there is provided a method of identifying an asthma patient or a respiratory disorder patient as likely to suffer from severe exacerbations, the method comprising: obtaining a biological sample from the patient, measuring the mRNA level of at least one, at least two, or at least three markers in the sample selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2, comparing the mRNA level detected in the sample to a reference level, and predicting that the patient is likely to suffer from severe exacerbations when the mRNA level measured in the sample is elevated compared to the reference level. In some embodiments, the methods comprise (a) measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6,

GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient; (b) comparing the mRNA level measured in (a) to a reference level; and (c) identifying the patient as more likely to suffer from severe exacerbations when the mRNA level measured in (a) is above the reference level. In one aspect, there is provided a method of identifying an asthma patient or a respiratory disorder patient as likely to suffer from severe exacerbations, the method comprising: (a) measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient; (b) comparing the mRNA level measured in (a) to a reference level; and (c) identifying the patient as more likely to suffer from severe exacerbations when the mRNA level measured in (a) is above the reference level. In some embodiments, the measuring the mRNA levels comprises amplification. In some embodiments, the measuring the mRNA levels comprises quantitative PCR. In some embodiments, the measuring the mRNA levels comprises amplifying the mRNA and detecting the amplified product, thereby measuring the level of the mRNA. In some embodiments, the reference level is the median level of the respective marker in a reference population. In some embodiments, the at least one, at least two, or at least three

IDO1, and CACNG6 in a sample obtained from the patient; and b) comparing the levels of the at least one, at least two, or at least three markers determined in step a) to a reference level. In some embodiments, the EIDA further comprises c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b). In some embodiments, a method further comprises selecting a therapy comprising a TH2 pathway inhibitor if the patient is a responder.

**[0023]** In any of the embodiments described herein, the EIDA may comprise the steps of a) determining the level of at least one, at least two, or three markers selected from HSD3B7, SIGLEC8, and GPR44 in a sample obtained from the patient; and b) comparing the levels of the at least one, at least two, or at least three markers determined in step a) to a reference level. In some embodiments, the EIDA further comprises c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step b). In some embodiments, a method further comprises selecting a therapy comprising a TH2 pathway inhibitor if the patient is a responder.

**[0024]** In some embodiments, methods of predicting the response of a patient suffering from asthma or a respiratory disorder to a therapy comprising a TH2 pathway inhibitor are provided. In some embodiments, the method comprises obtaining a biological sample from the patient and measuring the mRNA level of at least one, at least two, or at least three markers in the sample selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2. In some embodiments, the method comprises comparing the mRNA level detected in the sample to a reference level. In some embodiments, the method comprises predicting that the patient will respond to the therapy when the mRNA level measured in the sample is elevated compared to the reference level and predicting that the patient will not respond to the therapy when the mRNA level measured in the sample is reduced compared to the reference level. In one aspect, there is provided a method of predicting the response of a patient suffering from asthma or a respiratory disorder to a therapy comprising a TH2 pathway inhibitor, the method comprising: obtaining a biological sample from the patient, measuring the mRNA level of at least one, at least two, or at least three markers in the sample selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2,

comparing the mRNA level detected in the sample to a reference level, and predicting that the patient will respond to the therapy when the mRNA level measured in the sample is elevated compared to the reference level and predicting that the patient will not respond to the therapy when the mRNA level measured in the sample is reduced compared to the reference level. In some of the above embodiments, the mRNA level of at least one, at least two, at least three, or four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 is measured.

**[0025]** In some embodiments, methods of predicting responsiveness of an asthma patient or a respiratory disorder patient to a TH2 pathway inhibitor treatment are provided. In some embodiments, the method comprises measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44,

MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient. In some embodiments, an elevated mRNA level compared to a reference level identifies the patient as one who is likely to respond to the TH2 pathway inhibitor treatment. In one aspect, there is provided a method of predicting responsiveness of an asthma patient or a respiratory disorder patient to a TH2 pathway inhibitor treatment, the method comprising measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient, wherein elevated mRNA level compared to a reference level identifies the patient as one who is likely to respond to the TH2 pathway inhibitor treatment. In some of the above embodiments, the mRNA level of at least one, at least two, at least three, or four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 is measured.

**[0026]** In some embodiments, methods of identifying a patient suffering from asthma or a respiratory disorder as likely to respond to a therapy comprising a TH2 pathway inhibitor are provided. In some embodiments, the method comprises measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient. In some embodiments, the method further comprises comparing the measured mRNA level to a reference level. In some embodiments, ~~the~~ the method comprises identifying the patient as more likely to respond to the therapy comprising the TH2 pathway inhibitor when the measured mRNA level is above the reference level. In one aspect, there is provided a method of identifying a patient suffering from asthma or a respiratory disorder as likely to respond to a therapy comprising a TH2 pathway inhibitor, the method comprising: (a) measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient; (b) comparing the mRNA level measured in (a) to a reference level; and

(c) identifying the patient as more likely to respond to the therapy comprising the TH2 pathway inhibitor when the mRNA level measured in (a) is above the reference level. In some of the above embodiments, the mRNA level of at least one, at least two, at least three, or four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 is measured.

**[0027]** In some embodiments, methods of treating patients having asthma or a respiratory disorder are provided. In some embodiments, the method comprises measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient. In some embodiments, the method comprises comparing the measured mRNA level to a reference level. In some embodiments, the method comprises identifying the patient as more likely to respond a therapy comprising a TH2 pathway inhibitor when the measured mRNA level is above the reference level. In some embodiments, the method comprises administering the therapy when the measured mRNA level is above the reference level, thereby treating the asthma or respiratory disorder. In one aspect, there is provided use of a TH2 pathway inhibitor in the manufacture of a medicament for treating a patient having asthma or a respiratory disorder, the treatment comprising: (a) measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient; (b) comparing the mRNA level measured in (a) to a reference level; (c) identifying the patient as more likely to respond a therapy comprising a TH2 pathway inhibitor when the mRNA level measured in (a) is above the reference level; and (d) administering the therapy when the mRNA level measured in (a) is above the reference level, thereby treating the asthma or respiratory disorder. In some of the above embodiments, the mRNA level of at least one, at least two, at least three, or four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 is measured.

**[0028]** In some embodiments, a method of treating asthma or a respiratory disorder in a patient comprises administering to the patient a therapeutically effective amount of a TH2

pathway inhibitor, wherein a biological sample obtained from the patient has been determined to have elevated mRNA levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2. In one aspect, there is provided use of a TH2 pathway inhibitor in the manufacture of a medicament for treating asthma or a respiratory disorder in a patient, wherein a biological sample obtained from the patient has been determined to have elevated mRNA levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2, compared to the mRNA levels of the respective markers in a reference population. In some of the above embodiments, elevated mRNA levels of at least one, at least two, at least three, or four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 has been determined.

**[0029]** In some embodiments, a method of treating asthma or a respiratory disorder in a patient comprises administering to the patient a therapeutically effective amount of a TH2 pathway inhibitor, wherein the patient has been selected for treatment based on elevated mRNA levels in biological sample obtained from the patient of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2. In one aspect, there is provided use of a TH2 pathway inhibitor in the manufacture of a medicament for treating asthma or a respiratory disorder in a patient, wherein the patient has been selected for treatment based on elevated mRNA levels in biological sample obtained from the patient of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2, compared to the mRNA levels of the respective markers in a reference population. In some of the above embodiments, elevated mRNA levels of at least one, at least two, at least three, or four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 has been determined.

**[0030]** In any of the methods described herein, the at least one, at least two, or at least three markers may be selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2. In any of the methods described herein, the at least one, at least two, or at least three markers may be selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44. In any of the methods described herein, the at least one, at least two, or at least three markers may be selected from CCL23, IDO1, HSD3B7, and CACNG6. In any of the methods described herein, the at least one, at least two, or three markers may be selected from CCL23, IDO1, and CACNG6. In any of the methods described herein, the at least one, at least two, or three markers may be selected from HSD3B7, SIGLEC8, and GPR44. In any of the methods described herein, the at least one, at least two, or at least three markers or four markers may be selected from SIGLEC8, CCL23, CACNG6, and GPR44.

**[0031]** In any of the embodiments described herein, determining the levels of at least one marker may comprise amplification. In any of the embodiments described herein, determining the levels of at least one marker may comprise RT-PCR. In any of the embodiments described herein, determining the levels of at least one marker may comprise quantitative PCR. In any of the embodiments described herein, measuring the mRNA levels

[0039] In certain embodiments, the anti-IL-13 antibody is a bispecific antibody. In certain embodiments, the anti-IL-13 antibody is a bispecific antibody that also binds IL-4.

[0040] In any of the embodiments described herein, the TH2 pathway inhibitor may be an anti-IgE antibody. In certain embodiments, 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:1 and the variable light chain is SEQ ID NO:2 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 has the sequence of SEQ ID NO: 3 [GFTFSDYGIA]; (b) the HVR-H2 has the sequence of SEQ ID NO: 4 [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 has the sequence of SEQ ID NO: 5 [ARDNWDAMDY]; (d) the HVR-L1 has the sequence of SEQ ID NO: 6 [RSSQSLVHNNANTYLH]; (e) the HVR-L2 has the sequence of SEQ ID NO: 7 [KVSNRFS]; (f) the HVR-L3 has the sequence of SEQ ID NO: 8 [SQNTLVPWT]. In some embodiments, the anti-IgE antibody is an anti-M1' antibody.

[0041] In some embodiments, the anti-M1' antibody is administered subcutaneously at a flat dose of 150 mg once every 12 weeks, 300 mg once every 4 weeks or 450 mg once every 12 weeks. In some embodiments, the anti-M1' antibody is administered subcutaneously at a flat dose of 150 mg once every 12 weeks. In some embodiments, the anti-M1' antibody is administered subcutaneously at a flat dose of 450 mg once every 12 weeks. In some embodiments, an additional dose of the anti-M1' antibody is administered subcutaneously four weeks after administration of an initial dose.

[0042] In one embodiment, a patient treated with a TH2 pathway inhibitor according to this ~~invention~~ disclosure is also treated with one, two, three or more therapeutic agents. In one embodiment, the patient is an asthma patient. According to one embodiment, the patient is treated with the TH2 pathway inhibitor and one, two, three or more therapeutic agents, wherein at least one therapeutic agent, other than the TH2 inhibitor, is a corticosteroid, a leukotriene antagonist, a LABA, a corticosteroid/LABA combination composition, a theophylline, cromolyn sodium, nedocromil sodium, omalizumab, a LAMA, a MABA, a 5-Lipoxygenase Activating Protein (FLAP) inhibitor, or an enzyme PDE-4 inhibitor.

According to one ~~aspect~~ embodiment of the ~~invention~~ disclosure, a TH2 pathway inhibitor is administered to an asthma patient diagnosed as EIP status, wherein the diagnosis comprises the use of an EID assay (alone or in combination with other assays) to determine the EIP status. In one further

embodiment, the asthma patient is uncontrolled on a corticosteroid prior to the treatment. In another embodiment, the asthma patient is also being treated with a second controller. In one embodiment, the second controller is a corticosteroid, a LABA or a leukotriene antagonist. In a further embodiment, the asthma patient is suffering from moderate to severe asthma. Thus, in one embodiment, the patient to be treated with the TH2 pathway inhibitor is a moderate to severe asthma patient who is uncontrolled on a corticosteroid prior to treatment with the TH2 pathway inhibitor, and then is treated with the TH2 pathway inhibitor and one, two, three or more controllers. In one embodiment, at least one of the controllers is a corticosteroid. In a further embodiment, such patient is treated with a TH2 pathway inhibitor, a corticosteroid and another controller. In another embodiment, the patient is suffering from mild asthma but is not being treated with a corticosteroid. It should be understood that the therapeutic agents may have different treatment cycles as compared with the TH2 inhibitor and, consequently can be administered at different times compared to the TH2 inhibitor as a part of the patient's treatment. Therefore, according to one embodiment, a method of treatment according to this ~~invention~~-disclosure comprises the steps of administering to a patient a TH2 pathway inhibitory and optionally, administering at least one, two or three additional therapeutic agents. In one embodiment, the TH2 pathway inhibitor is present in a composition with another therapeutic agent. In another embodiment, the TH2 pathway inhibitor is not present in a composition with another therapeutic agent.

[0043] According to another embodiment, the ~~invention~~-disclosure comprises a method for treating asthma comprising administering an anti-IL-13 antibody comprising a VH comprising a sequence selected from SEQ ID NOs: 9, 19, and 21, and VL comprising a sequence selected from SEQ ID NO: 10, 20, and 22; 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; as a flat dose. In one embodiment an anti-IL13 antibody comprising a VH comprising a sequence selected from SEQ ID NOs: 9, 19, and 21 and VL comprising a sequence selected from SEQ ID NO: 10, 20, and 22 is administered as a flat dose (i.e., not weight dependent) of between 125-1000 mg, or a flat dose of 37.5 mg, or a flat dose of 125 mg, or a flat dose of 250 mg, or a flat dose of 500 mg, by subcutaneous injection or by intravenous injection, at a frequency of time selected from: every 2 weeks, every 3 weeks, and every 4 weeks. In one embodiment an anti-IL13 antibody comprising HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, and HVRL3, the respective HVRs

having 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 is administered as a flat dose (i.e., not weight dependent) of between 125-1000 mg, or a flat dose of 37.5 mg, or a flat dose of 125 mg, or a flat dose of 250 mg, or a flat dose of 500 mg, by subcutaneous injection or by intravenous injection, at a frequency of time selected from: every 2 weeks, every 3 weeks, and every 4 weeks. In one embodiment, the anti-IL13 antibody is lebrikizumab, which is administered as a flat dose (i.e., not weight dependent) of between 125-1000 mg, or a flat dose of 37.5 mg, or a flat dose of 125 mg, or a flat dose of 250 mg, or a flat dose of 500 mg, by subcutaneous injection or by intravenous injection, at a frequency of time selected from: every 2 weeks, every 3 weeks, and every 4 weeks. In some embodiments, the patient is diagnosed with EIP using an EID Assay described herein.

[0044] According to another embodiment, an antibody comprising VH comprising a sequence selected from SEQ ID NOs: 9, 19, and 21, and VL comprising a sequence selected from SEQ ID NO: 10, 20, and 22 is administered to treat asthma in a therapeutically effective amount sufficient to reduce the rate of exacerbations of the patient over time or improve FEV<sub>1</sub>. In yet another embodiment, the ~~invention-disclosure~~ comprises a method for treating asthma comprising administering an anti-IL-13 antibody comprising a VH comprising a sequence selected from SEQ ID NOs: 9, 19, and 21, and VL comprising a sequence selected from SEQ ID NO: 10, 20, and 22 or an anti-IL13 antibody comprising HVRH1, HVRH2, HVRH3, HVRL1, HVRL2, and HVRL3, the respective HVRs having 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 as a flat dose (i.e., not weight dependent) of 37.5 mg, or a flat dose of 125 mg, or a flat dose of 250 mg. In certain embodiments, the dose is administered by subcutaneous injection once every 4 weeks for a period of time. In certain embodiments, the period of time is 6 months, one year, two years, five years, ten years, 15 years, 20 years, or the lifetime of the patient. In certain embodiments, the asthma is severe asthma and the patient is inadequately controlled or uncontrolled on inhaled corticosteroids plus a second controller medication. In some embodiments, the patient is diagnosed with EIP status using an EID Assay to determine EIP status and the patient is selected for treatment with an anti-IL13 antibody as described above. In another embodiment, the method comprises treating an asthma patient with an anti-IL13 antibody as described above where the patient was previously diagnosed with EIP status using an EID Assay described herein to determine EIP status. In one embodiment, the asthma patient is age 18 or older. In one embodiment, the

asthma patient is age 12 to 17 and the anti-IL13 is administered in as a flat dose of 250 mg or a flat dose of 125 mg. In one embodiment, the asthma patient is age 6 to 11 and the anti-IL13 antibody is administered in as a flat dose of 125 mg or a flat dose of 62.5 mg.

**[0045]** The present ~~invention-disclosure~~ provides a therapeutic agent that is a TH2 pathway inhibitor for use in treating asthma or a respiratory disorder in a patient, wherein the patient is EIP. In some embodiments, the target for inhibition in the TH2 pathway is selected from: IL-9, IL-5, IL-13, IL-4, OX40L, TSLP, IL-25, IL-33 and IgE; and receptors such as: IL-9 receptor, IL-5 receptor, IL-4receptor alpha, IL-13receptoralpha1 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, FcepsilonRI and FcepsilonRII/CD23 (receptors for IgE). In one embodiment, the patient to be treated according to the methods of the present ~~invention-disclosure~~ is suffering from mild to severe asthma, optionally moderate to severe asthma, and whose asthma is uncontrolled on a corticosteroid. In some embodiments, the patient to be treated in addition to having elevated levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2, or at least one, at least two, or at least three markers selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2, or at least one, at least two, or at least three markers selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44, or at least one, at least two, or at least three markers selected from CCL23, IDO1, HSD3B7, and CACNG6, or at least one, at least two, or all three markers selected from CCL23, IDO1, and CACNG6, or at least one, at least two, or all three of the markers selected from HSD3B7, SIGLEC8, and GPR44, or at least one, at least two, at least three, or all four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44, has a FE<sub>No</sub> level greater than 21 ppb, or greater than 35 ppb.

**[0045a]** In one aspect, there is provided use of a kit for determining the level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample obtained from an asthma patient or respiratory disorder patient for stratifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 pathway inhibitor.

**[0046]** In another ~~aspect~~embodiment, uses of a kit for measuring the levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a sample obtained from an asthma patient for stratifying/classifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 pathway inhibitor. In certain embodiments, the use comprises the steps of: (a) determining the levels of at least

one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a sample obtained from an asthma patient; (b) comparing the levels of the one or more markers determined in step (a) to a reference level; and (c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step (b).

[0047] In another ~~aspect~~embodiment, uses of a kit for measuring the levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2 in a sample obtained from an asthma patient for stratifying/classifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 pathway inhibitor. In certain embodiments, the use comprises the steps of: (a) determining the levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2 in a sample obtained from an asthma patient; (b) comparing the levels of the one or more markers determined in step (a) to a reference level; and (c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step (b).

[0048] In another ~~aspect~~embodiment, uses of a kit for measuring the levels of at least one, at least two, or at least three markers selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44 in a sample obtained from an asthma patient for stratifying/classifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 pathway inhibitor. In certain embodiments, the use comprises the steps of: (a) determining the levels of at least one, at least two, or at least three markers selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44 in a sample obtained from an asthma patient; (b) comparing the levels of the one or more markers determined in step (a) to a reference level; and (c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step (b).

[0049] In another ~~aspect~~embodiment, uses of a kit for measuring the levels of at least one, at least two, or at least three markers selected from CCL23, IDO1, HSD3B7, and CACNG6, or uses of a kit for measuring the levels of at least one, at least two, at least three, or all four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 in a sample obtained from an asthma patient for stratifying/classifying asthma patients into likely responders and non-

responders for therapeutic treatment with a TH2 pathway inhibitor. In certain embodiments, the use comprises the steps of: (a) determining the levels of at least one, at least two, or at least three markers selected from CCL23, IDO1, HSD3B7, and CACNG6, or determining the levels of at least one, at least two, at least three, or all four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 in a sample obtained from an asthma patient; (b) comparing the levels of the one or more markers determined in step (a) to a reference level; and (c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step (b).

**[0050]** In another ~~aspect~~embodiment, uses of a kit for measuring the levels of at least one, at least two, or all three markers selected from CCL23, IDO1, and CACNG6, or uses of a kit for measuring the levels of at least one, at least two, at least three, or all four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 in a sample obtained from an asthma patient for stratifying/classifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 pathway inhibitor. In certain embodiments, the use comprises the steps of: (a) determining the levels of at least one, at least two, or all three markers selected from CCL23, IDO1, and CACNG6, or determining the levels of at least one, at least two, at least three, or all four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 in a sample obtained from an asthma patient; (b) comparing the levels of the one or more markers determined in step (a) to a reference level; and (c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step (b).

**[0051]** In another ~~aspect~~embodiment, uses of a kit for measuring the levels of at least one, at least two, or all three markers selected from HSD3B7, SIGLEC8, and GPR44 in a sample obtained from an asthma patient for stratifying/classifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 pathway inhibitor. In certain embodiments, the use comprises the steps of: (a) determining the levels of at least one, at least two, or all three markers selected from HSD3B7, SIGLEC8, and GPR44 in a sample obtained from an asthma patient; (b) comparing the levels of the one or more markers determined in step (a) to a reference level; and (c) stratifying said patient into the category of responder or non-responder based on the comparison obtained in step (b).

**[0052]** In any of the embodiments described herein, determining the levels of at least one marker may comprise amplification. In any of the embodiments described herein, determining the levels of at least one marker may comprise RT-PCR. In any of the embodiments described herein, determining the levels of at least one marker may comprise

the sequence of SEQ ID NO: 4 [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 has the sequence of SEQ ID NO: 5 [ARDNWDAMDY]; (d) the HVR-L1 has the sequence of SEQ ID NO: 6 [RSSQSLVHNNANTYLH]; (e) the HVR-L2 has the sequence of SEQ ID NO: 7 [KVSNRFS]; (f) the HVR-L3 has the sequence of SEQ ID NO: 8 [SQNTLVPWT]. In some embodiments, the anti-IgE antibody is an anti-M1' antibody.

**[0060]** In any of the embodiments described herein, the patient may be 0-17 years old, 2-17 years old, 2-6 years old, 6-11 years old, 8-17 years old, 12-17 years old, 2 years old or older, 6 years old or older, or 12 years old or older. In some embodiments, the patient is 18 years or older. In any of the embodiments described herein, the patient may be a human.

**[0060a]** In one aspect, there is provided a kit for stratifying an asthma patient or a respiratory disorder patient wherein the kit comprises:

a) reagents for measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a sample obtained from the patient; and

b) instructions for (i) measuring the mRNA levels of the at least one, at least two, or at least three markers, (ii) comparing the levels of the at least one, at least two, or at least three markers to a reference level, and (iii) stratifying said patient into the category of responder or non-responder based on the comparison.

**[0061]** In yet another ~~aspect~~ embodiment, kits for measuring the levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample obtained from an asthma patient or a patient suffering from a respiratory disorder are provided. In some embodiments, the kit comprises instructions for (i) measuring the mRNA levels of the at least one, at least two, or at least three markers, (ii) comparing the levels of the at least one, at least two, or at least three markers to a reference level, and (iii) stratifying said patient into the category of responder or non-responder based on the comparison. In some embodiments, the kit comprises at least one, at least two, or at least three first nucleic acid molecules that hybridize to at least one, at least two, or at least three second nucleic acid molecules, wherein the at least one, at least two, or at least three second nucleic acid

molecules encode at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 or a portion thereof. In certain embodiments, the kit comprises a package insert containing information describing the uses provided above.

[0062] In yet another ~~aspect~~embodiment, kits for measuring the levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2 in a biological sample obtained from an asthma patient or a patient suffering from a respiratory disorder are provided. In some embodiments, the kit comprises instructions for (i) measuring the mRNA levels of the at least one, at least two, or at least three markers, (ii) comparing the levels of the at least one, at least two, or at least three markers to a reference level, and (iii) stratifying said patient into the category of

responder or non-responder based on the comparison. In some embodiments, the kit comprises at least one, at least two, or at least three first nucleic acid molecules that hybridize to at least one, at least two, or at least three second nucleic acid molecules, wherein the at least one, at least two, or at least three second nucleic acid molecules encode at least one, at least two, or at least three markers selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2 or a portion thereof. In certain embodiments, the kit comprises a package insert containing information describing the uses provided above.

[0063] In yet another ~~aspect~~embodiment, kits for measuring the levels of at least one, at least two, or at least three markers selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44 in a biological sample obtained from an asthma patient or a patient suffering from a respiratory disorder are provided. In some embodiments, the kit comprises instructions for (i) measuring the mRNA levels of the at least one, at least two, or at least three markers, (ii) comparing the levels of the at least one, at least two, or at least three markers to a reference level, and (iii) stratifying said patient into the category of responder or non-responder based on the comparison. In some embodiments, the kit comprises at least one, at least two, or at least three first nucleic acid molecules that hybridize to at least one, at least two, or at least three second nucleic acid molecules, wherein the at least one, at least two, or at least three second nucleic acid molecules encode at least one, at least two, or at least three markers selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44 or a portion thereof. In certain embodiments, the kit comprises a package insert containing information describing the uses provided above.

[0064] In yet another ~~aspect~~embodiment, kits for measuring the levels of at least one, at least two, or at least three markers selected from CCL23, IDO1, HSD3B7, and CACNG6, or kits for measuring the levels of at least one, at least two, at least three, or all four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 in a biological sample obtained from an asthma patient or a patient suffering from a respiratory disorder are provided. In some embodiments, the kit comprises instructions for (i) measuring the mRNA levels of the at least one, at least two, or at least three markers, (ii) comparing the levels of the at least one, at least two, or at least three markers to a reference level, and (iii) stratifying said patient into the category of responder or non-responder based on the comparison. In some embodiments, the kit comprises at least one, at least two, or at least three first nucleic acid molecules that hybridize to at least one, at least two, or at least three second nucleic acid molecules, wherein

the at least one, at least two, or at least three second nucleic acid molecules encode at least one, at least two, or at least three markers selected from CCL23, IDO1, HSD3B7, and CACNG6 or a portion thereof, or at least one, at least two, or at least three selected from SIGLEC8, CCL23, CACNG6, and GPR44 or a portion thereof. In certain embodiments, the kit comprises a package insert containing information describing the uses provided above.

[0065] In yet another ~~aspect~~embodiment, kits for measuring the levels of at least one, at least two, or all three markers selected from CCL23, IDO1, and CACNG6 in a biological sample obtained from an asthma patient or a patient suffering from a respiratory disorder are provided. In some embodiments, the kit comprises instructions for (i) measuring the mRNA levels of the at least one, at least two, or at least three markers, (ii) comparing the levels of the at least one, at least two, or at least three markers to a reference level, and (iii) stratifying said patient into the category of responder or non-responder based on the comparison. In some embodiments, the kit comprises at least one, at least two, or at least three first nucleic acid molecules that hybridize to at least one, at least two, or at least three second nucleic acid molecules, wherein the at least one, at least two, or at least three second nucleic acid molecules encode at least one, at least two, or all three markers selected from CCL23, IDO1, and CACNG6 or a portion thereof. In certain embodiments, the kit comprises a package insert containing information describing the uses provided above.

[0066] In yet another ~~aspect~~embodiment, kits for measuring the levels of at least one, at least two, or all three markers selected from HSD3B7, SIGLEC8, and GPR44 in a biological sample obtained from an asthma patient or a patient suffering from a respiratory disorder are provided. In some embodiments, the kit comprises instructions for (i) measuring the mRNA levels of the at least one, at least two, or at least three markers, (ii) comparing the levels of the at least one, at least two, or at least three markers to a reference level, and (iii) stratifying said patient into the category of responder or non-responder based on the comparison. In some embodiments, the kit comprises at least one, at least two, or at least three first nucleic acid molecules that hybridize to at least one, at least two, or at least three second nucleic acid molecules, wherein the at least one, at least two, or at least three second nucleic acid molecules encode at least one, at least two, or all three markers selected from HSD3B7, SIGLEC8, and GPR44 or a portion thereof. In certain embodiments, the kit comprises a package insert containing information describing the uses provided above.

[0067] In still yet another ~~aspect~~embodiment, kits for diagnosing an asthma subtype in a patient are provided, the kits comprising: (1) determining the levels of at least one, at least two, or at

least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a serum sample obtained from the patient; and (2) instructions for measuring the levels of the at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in the serum sample, wherein the elevated expression levels of any one, combination or all of said markers is indicative of the asthma subtype.

[0068] In still yet another aspectembodiment, kits for diagnosing an asthma subtype in a patient are provided, the kits comprising: (1) determining the levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2 in a serum sample obtained from the patient; and (2) instructions for measuring the levels of the at least one, at least two, or at least three markers selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2 in the serum sample, wherein the elevated expression levels of any one, combination or all of said markers is indicative of the asthma subtype.

[0069] In still yet another aspectembodiment, kits for diagnosing an asthma subtype in a patient are provided, the kits comprising: (1) determining the levels of at least one, at least two, or at least three markers selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44 in a serum sample obtained from the patient; and (2) instructions for measuring the levels of the at least one, at least two, or at least three markers selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44 in the serum sample, wherein the elevated expression levels of any one, combination or all of said markers is indicative of the asthma subtype.

[0070] In still yet another aspectembodiment, kits for diagnosing an asthma subtype in a patient are provided, the kits comprising: (1) determining the levels of at least one, at least two, or at least three markers selected from CCL23, IDO1, HSD3B7, and CACNG6 in a serum sample obtained from the patient; and (2) instructions for measuring the levels of the at least one, at least two, or at least three markers selected from CCL23, IDO1, HSD3B7, and CACNG6 in the serum sample, wherein the elevated expression levels of any one, combination or all of said markers is indicative of the asthma subtype.

[0071] In still yet another ~~aspect~~embodiment, kits for diagnosing an asthma subtype in a patient are provided, the kits comprising: (1) determining the levels of at least one, at least two, or all three markers selected from CCL23, IDO1, and CACNG6 in a serum sample obtained from the patient; and (2) instructions for measuring the levels of the at least one, at least two, or all three markers selected from CCL23, IDO1, and CACNG6 in the serum sample, wherein the elevated expression levels of any one, combination or all of said markers is indicative of the asthma subtype.

[0072] In still yet another ~~aspect~~embodiment, kits for diagnosing an asthma subtype in a patient are provided, the kits comprising: (1) determining the levels of at least one, at least two, or all three markers selected from HSD3B7, SIGLEC8, and GPR44 in a serum sample obtained from the patient; and (2) instructions for measuring the levels of the at least one, at least two, or all three markers selected from HSD3B7, SIGLEC8, and GPR44 in the serum sample, wherein the elevated expression levels of any one, combination or all of said markers is indicative of the asthma subtype.

[0073] In still yet another ~~aspect~~embodiment, kits for diagnosing an asthma subtype in a patient are provided, the kits comprising: (1) determining the levels of at least one, at least two, at least three, or all four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 in a serum sample obtained from the patient; and (2) instructions for measuring the levels of the at least one, at least two, at least three, or all four markers selected from SIGLEC8, CCL23, CACNG6, and GPR44 in the serum sample, wherein the elevated expression levels of any one, combination or all of said markers is indicative of the asthma subtype.

[0074] In some embodiments, the kit further comprises a package insert for determining whether an asthma patient or respiratory disorder patient is EIP or EIN. In some embodiments, the kit further comprises a package insert for determining whether an asthma patient is likely to respond to a TH2 pathway inhibitor. In some embodiments, the kit further comprises a package insert containing information describing any of the uses provided above. In some embodiments, the kit further comprises an empty container to hold a biological sample. In some embodiments, the kit comprises reagents for determining the levels of the one or more markers. In some embodiments, the reagents for determining the levels of the one or more markers include, but are not limited to, one or more first nucleic acid molecules that hybridize to one or more second nucleic acid molecules that encode one or more markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8,

CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2.

[0075] In still another ~~aspect~~embodiment, methods of treating of a patient suffering from asthma or a respiratory disease comprising administering a TH2 pathway inhibitor to the patient diagnosed as EIP are provided. In certain embodiments, the methods comprise the step of diagnosing the patient as EIP using an EID Assay. In certain embodiments, the methods further comprise the step of retreating the patient with the TH2 pathway inhibitor if the patient is determined to be EIP. In certain embodiments, serum, whole blood, PBMCs, or plasma from the patient is used to determine whether the patient is EIP.

### BRIEF DESCRIPTION OF THE DRAWINGS

[0076] **Figure 1.** Serum periostin is elevated in asthma patients under the age of 18 years but is not related to age in adult asthma patients. (A) Serum periostin level vs. age in 783 asthma patients from omalizumab studies 008, 009, 010, and EXTRA, 159 of whom were under the age of 18 years. (B) Range and distribution of serum periostin levels by study. Thick horizontal black line denotes median, box and whiskers denote interquartile and total ranges, respectively.

[0077] **Figure 2.** Relationship between blood eosinophils and age is continuous across pediatric and adult asthma patients. (A) Blood eosinophil counts vs. age in 2028 asthma patients from omalizumab studies 008, 009, 010, and EXTRA, 413 of whom were under the age of 18 years. (B) Range and distribution of blood eosinophil counts by study. Thick horizontal black line denotes median, box and whiskers denote interquartile and total ranges, respectively.

[0078] **Figure 3.** Serum periostin levels and blood eosinophil counts are positively correlated in adult but not pediatric asthma patients. (A) adults in the EXTRA study; (B) adults in the MILLY study; (C) patients age 12-17 in EXTRA; (D) patients age 6-12 in study 010. rS, Spearman's rank-order correlation coefficient.

[0079] **Figure 4.** Different cellular distribution of eosinophil-related genes in peripheral blood. Selected genes correlated with blood eosinophil counts in EXTRA are variably expressed in isolated peripheral blood leukocyte populations in GSE3982 (Liu et al. (2006) J Allergy Clin Immunol 118: 496-503). (A) SIGLEC8 expression is mainly restricted to eosinophils. (B) CLC expression is restricted to eosinophils and basophils. (C) CSF1 expression is distributed across multiple peripheral blood leukocyte types including

8. The method according to claim 4, wherein the TH2 pathway inhibitor is an anti-IgE antibody.

9. The method according to claim 8, 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:1 and the variable light chain is SEQ ID NO:2 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 has the sequence of SEQ ID NO: 3 [GFTFSDYGIA]; (b) the HVR-H2 has the sequence of SEQ ID NO: 4 [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 has the sequence of SEQ ID NO: 5 [ARDNWDAMDY]; (d) the HVR-L1 has the sequence of SEQ ID NO: 6 [RSSQSLVHNNANTYLH]; (e) the HVR-L2 has the sequence of SEQ ID NO: 7 [KVSNRFS]; (f) the HVR-L3 has the sequence of SEQ ID NO: 8 [SQNTLVPWT].

10. Use of a TH2 pathway inhibitor in the manufacture of a medicament for A  
~~method of treating a patient having asthma or a respiratory disorder, the method treatment~~  
comprising:

- (a) measuring the mRNA level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample from the patient;
- (b) comparing the mRNA level measured in (a) to a reference level;
- (c) identifying the patient as more likely to respond a therapy comprising a TH2 pathway inhibitor when the mRNA level measured in (a) is above the reference level; and
- (d) administering the therapy when the mRNA level measured in (a) is above the reference level, thereby treating the asthma or respiratory disorder.

11. The method or use according to any one of the preceding claims, wherein measuring the mRNA levels comprises amplification.

12. The method or use according to claim 11, wherein measuring the mRNA levels comprises quantitative PCR.
13. The method or use according to any one of the preceding claims, wherein measuring the mRNA levels comprises amplifying the mRNA and detecting the amplified product, thereby measuring the level of the mRNA.
14. The method or use according to any one of the preceding claims, wherein the reference level is the median level of the respective marker in a reference population.
15. ~~A method of~~ Use of a TH2 pathway inhibitor in the manufacture of a medicament for treating asthma or a respiratory disorder in a patient, comprising administering to the patient a therapeutically effective amount of a TH2 pathway inhibitor, wherein a biological sample obtained from the patient has been determined to have elevated mRNA levels of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2, compared to the mRNA levels of the respective markers in a reference population.
16. ~~A method of~~ Use of a TH2 pathway inhibitor in the manufacture of a medicament for treating asthma or a respiratory disorder in a patient, comprising administering to the patient a therapeutically effective amount of a TH2 pathway inhibitor, wherein the patient has been selected for treatment based on elevated mRNA levels in biological sample obtained from the patient of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2, compared to the mRNA levels of the respective markers in a reference population.
17. The ~~use method~~ according to claim 15 or claim 16, wherein the mRNA levels were determined by a method comprising amplification.
18. The ~~use method~~ according to claim 17, wherein the mRNA levels were determined by a method comprising quantitative PCR.

19. The ~~use~~method according to any one of claims 15 to 18, wherein the mRNA levels were determined by a method comprising amplifying the mRNA and detecting the amplified product.

20. The ~~use~~method of any one of claims 15 to 19, wherein the reference level is the median level of the respective marker in a reference population.

21. The ~~use~~method according to any one of claim 15 to 20, wherein the TH2 pathway inhibitor is an inhibitor of ITK, BTK, IL-9 (e.g., MEDI-528), IL-5 (e.g., Mepolizumab, CAS No. 196078-29-2; reslizumab), IL-13 (e.g., IMA-026, IMA-638 (also referred to as, anrunkinumab, 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; quilizumab); 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, dupilumab), 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).

22. The ~~use~~method according to any one of claims 15 to 21, wherein the TH2 pathway inhibitor is an anti-IL13/IL4 pathway inhibitor or an anti IgE binding agent.

23. The ~~use~~method according to any one of claims 15 to 21, wherein the TH2 pathway inhibitor is an anti-IL-13 antibody.

24. The ~~use~~method according to claim 23, wherein the anti-IL-13 antibody is an antibody comprising a VH comprising a sequence selected from SEQ ID NOs: 9, 19, and 21, and VL comprising a sequence selected from SEQ ID NO: 10, 20, and 22; 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.

25. The ~~use method~~ according to claim 24, wherein the patient is to be administered a flat dose of 37.5 mg, or 125 mg or 250 mg every four weeks.

26. The ~~use method~~ according to any one of claims 23 to 25, wherein the anti-IL-13 antibody is to be administered subcutaneously.

27. The ~~use method~~ according to any one of claims 23 to 26, wherein the anti-IL-13 antibody is to be administered using a prefilled syringe or autoinjector device.

28. The ~~use method~~ of claim 23, wherein the anti-IL-13 antibody is a bispecific anti-IL-13 antibody.

29. The ~~use method~~ according to claim 28, wherein the bispecific anti-IL13 antibody binds IL-13 and IL-4.

30. The ~~use method~~ according to claim 22, wherein the TH2 pathway inhibitor is an anti-IgE antibody.

31. The ~~use method~~ according to claim 30, 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:1 and the variable light chain is SEQ ID NO:2 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 has the sequence of SEQ ID NO: 3 [GFTFSDYGIA]; (b) the HVR-H2 has the sequence of SEQ ID NO: 4 [AFISDLAYTIYYADTVTG]; (c) the HVR-H3 has the sequence of SEQ ID NO: 5 [ARDNWDAMDY]; (d) the HVR-L1 has the sequence of SEQ ID NO: 6 [RSSQSLVHNNANTYLH]; (e) the HVR-L2 has the sequence of SEQ ID NO: 7 [KVSNRFS]; (f) the HVR-L3 has the sequence of SEQ ID NO: 8 [SQNTLVPWT].

32. The ~~use~~method according to claim 31, wherein the anti-IgE antibody is an anti-M1' antibody.

33. The ~~use~~method according to claim 31, wherein the anti-M1' antibody is to be administered subcutaneously at a flat dose of 150 mg once every 12 weeks, 300 mg once every 4 weeks or 450 mg once every 12 weeks.

34. The ~~use~~method according to claim 33, wherein the anti-M1' antibody is to be administered subcutaneously at a flat dose of 150 mg once every 12 weeks.

35. The ~~use~~method according to claim 33, wherein the anti-M1' antibody is to be administered subcutaneously at a flat dose of 450 mg once every 12 weeks.

36. The ~~use~~method according to claim 34 or claim 35, ~~further comprising subcutaneous administration of wherein an additional dose is to be further administered subcutaneously~~ four weeks after administration of an initial dose.

37. The method or use according to any one of the preceding claims, wherein the at least one, at least two, or at least three markers are selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2.

38. The method or use according to any one of claims 1 to 36, wherein the at least one, at least two, or at least three markers are selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44.

39. The method or use according to any one of claims 1 to 36, wherein the at least one, at least two, or at least three markers are selected from CCL23, IDO1, HSD3B7, and CACNG6.

40. The method or use according to any one of claims 1 to 36, wherein the at least one, at least two, or three markers are selected from CCL23, IDO1, and CACNG6.

41. The method or use according to any one of claims 1 to 36, wherein the at least one, at least two, or three markers are selected from HSD3B7, SIGLEC8, and GPR44.

42. The method or use according to any one of claims 1 to 36, wherein the at least one, at least two, at least three, or four markers are selected from SIGLEC8, CCL23, CACNG6, and GPR44.

43. The method or use according to any one of the preceding claims, wherein if the mRNA level is elevated, the patient is Eosinophilic Inflammation Positive (EIP).

44. The method or use according to any one of the preceding claims, wherein the patient is suffering from moderate to severe asthma.

45. The method or use according to any one of the preceding claims, wherein the asthma or respiratory disorder is uncontrolled on a corticosteroid.

46. The method or use according to claim 45, wherein the corticosteroid is an inhaled corticosteroid.

47. The method or use according to claim 46, wherein the inhaled corticosteroid is Qvar®, Pulmicort®, Symbicort®, Aerobid®, Flovent®, Flonase®, Advair® or Azmacort®.

48. The method or use according to any one of the preceding claims, wherein the patient is being treated with a second controller.

49. The method or use according to claim 48, wherein the second controller is a long acting bronchial dilator (LABD).

50. The method or use according to claim 49, wherein the LABD is a long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline, or oral corticosteroids (OCS).

51. The method or use according to claim 49, wherein the LABD is Symbicort®, Advair®, Brovana®, Foradil®, Perforomist™ or Serevent®.

52. The method or use according to any one of the preceding claims, wherein the patient is 0-17 years old, 2-17 years old, 2-6 years old, 6-11 years old, 8-17 years old, 12-17 years old, 2 years old or older, 6 years old or older, or 12 years old or older.

53. The method or use according to claim 52, wherein the patient is 18 years or older.

54. The method or use according to any one of the preceding claims, wherein the patient is a human.

55. The method or use according to any one of the preceding claims, wherein the biological sample is selected from blood, serum, plasma, and peripheral blood mononuclear cells (PBMCs)

56. The method or use according to claim 55, wherein the biological sample is PBMCs.

57. Use of a kit for determining the level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, LGALS12, IDO1, THBS4, OLIG2, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, SORD, ASB2, CACNG6, GPR44, MGAT3, SLC47A1, SMPD3, CCR3, CLC, CYP4F12, and ABTB2 in a biological sample obtained from an asthma patient or respiratory disorder patient for stratifying asthma patients into likely responders and non-responders for therapeutic treatment with a TH2 pathway inhibitor.

58. The use according to claim 57, wherein the kit is for determining the level of at least one, at least two, or at least three markers selected from CSF1, MEIS2, CCL23, HSD3B7, SORD, CACNG6, MGAT3, SLC47A1, and ABTB2.

59. The use according to claim 57, wherein the kit is for determining the level of at least one, at least two, or at least three markers selected from MEIS2, LGALS12, IDO1, ALOX15, SIGLEC8, CCL23, PYROXD2, HSD3B7, CACNG6, and GPR44.

60. The use according to claim 57, wherein the kit is for determining the level of at least one, at least two, or at least three markers selected from CCL23, IDO1, HSD3B7, and CACNG6.