the early and late asthmatic responses and suppressed biomarkers of Th2 inflammation following inhaled allergen challenge.[24]

[0006] The present disclosure describes a randomized, placebo-controlled, dose-ranging trial of tezepelumab in patients whose disease was inadequately controlled with medium to high doses of ICS/LABA.

SUMMARY

[0007] The anti-TSLP antibody described herein addresses an unmet need in asthma patients in which other medications may not control moderate to severe asthma. For example, the antibody therapy may improve asthma in eosinophil (EOS)-low patients and may provide a more powerful exacerbation reduction in EOS-high patients.

[0007a] In one aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0007b] In another aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every two weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to

SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b), wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0007c] In yet another aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 210 mg at an interval of every 4 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0007d] In yet another aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 210 mg at an interval of every 4 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain

variable domain of (b), wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0007e] In a further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 70 to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2, wherein the antibody is an IgG2 antibody.

[0007f] In a further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing the frequency of asthma exacerbation in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0007g] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing the frequency of asthma exacerbation in a subject, comprising that the subject is to be administered dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino

acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

[0007h] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating chronic obstructive pulmonary disease (COPD) in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0007i] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating chronic obstructive pulmonary disease (COPD) in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of

amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

[0007j] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing ACQ-6 score in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0007k] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing ACQ-6 score in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

[0007l] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject having a non-eosinophilic profile or a low eosinophil profile, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

[0007m] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject having a Th2 low profile, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

[0007n] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing ACQ-6 score in a subject having a low eosinophil profile, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

[0007o] In a still further aspect, the disclosure refers to the use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing ACQ-6 score in a subject having a Th2 low profile, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

[0008] The disclosure provides a method for treating asthma in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0009] Also contemplated is a method for treating asthma in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 70 mg to 280 mg at an interval of every two weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide

sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b), wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0010] In various examples, the antibody or antibody variant is administered every 4 weeks.

[0011] In various examples, the antibody or antibody variant is administered at a dose of 70 mg, at a dose of 210 mg or at a dose of 280 mg every 2 weeks or every 4 weeks.

[0012] The disclosure also provides a method for treating asthma in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 210 mg at an interval of every 4 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0013] The disclosure further provides a method for treating asthma in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 210 mg at an interval of every 4 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent

conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b), wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0014] In various examples, the anti-TSLP antibody variant has substantially similar pK characteristics as tezepelumab in humans.

[0015] In various examples, the antibody or antibody variant is administered for a period of at least 4 months, 6 months, 9 months, 1 year or more.

[0016] In various examples, the anti-TSLP antibody or antibody variant thereof is bivalent and selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a recombinant antibody, an antigen-binding antibody fragment, a single chain antibody, a monomeric antibody, a diabody, a triabody, a tetrabody, a Fab fragment, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, and an IgG4 antibody.

[0017] In one example, the anti-TSLP antibody variant is selected from the group consisting of a diabody, a triabody, a tetrabody, a Fab fragment, a single domain antibody, an scFv, wherein the dose is adjusted such that the binding sites are equimolar to those dosed by bivalent antibodies.

[0018] In various examples, the antibody is an IgG2 antibody.

[0019] In one example, the antibody or antibody variant is a human antibody.

[0020] In various examples, the antibody is tezepelumab. In various examples, the tezepelumab is an IgG2 antibody having the full length heavy and light chain amino acid sequences set out in SEQ ID NOs: 105 and 106, respectively.

[0021] In various examples, the antibody or antibody variant further comprises a pharmaceutically acceptable carrier or excipient.

[0022] In various examples, the asthma is severe asthma. It is further contemplated that the asthma is eosinophilic or non-eosinophilic asthma, optionally the asthma is low eosinophil asthma.

[0023] Data presented herein demonstrates an anti-TSLP antibody that substantially affects two important markers of inflammation of asthma: blood eosinophil counts and the fraction of exhaled nitric oxide. The data show that an anti-TSLP antibody reduces the level of both inflammatory markers, reduces the asthma exacerbation rate, improves lung function irrespective of asthma phenotype (eosinophilic (allergic and nonallergic) and noneosinophilic/low eosinophilic asthma), and blocks at least two important inflammatory pathways in asthma. The anti-TSLP antibody, therefore, is able to treat a patient having either asthma phenotype: eosinophilic (allergic and nonallergic) or noneosinophilic/low eosinophilic asthma. Accordingly, provided herein is a method of treating a patient having low eosinophil asthma comprising administering an anti-TSLP antibody as described herein. Also contemplated is a method for treating a subject having asthma characterized by a low Th2 profile comprising administering an anti-TSLP antibody. In various examples, the antibody is tezepelumab or another anti-TSLP antibody described in the art. Exemplary antibodies are described further in the Detailed Description.

[0024] In various examples, the subject is an adult. In various examples, the subject is a child or adolescent.

[0025] It is contemplated that administration of the anti-TSLP antibody or antibody variant decreases eosinophils in blood, sputum, broncheoalveolar fluid, or lungs of the subject.

[0026] It is further contemplated that administration of the anti-TSLP antibody or antibody variant shifts cell counts in the subject from a Th2 high population to a Th2 low population.

[0027] In various examples, administration of the anti-TSLP antibody or antibody variant improves one or more measures of asthma in a subject selected from the group consisting of forced expiratory volume (FEV), FEV_1 reversibility, forced vital capacity (FVC), FeNO, Asthma Control Questionnaire-6 score and AQLQ(S)+12 score.

[0028] In one example, the administration improves one or more symptoms of asthma as measured by an asthma symptom diary.

[0029] Further provided is a method for treating asthma in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 70 to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising:

i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2, wherein the antibody is an IgG2 antibody.

[0030] In various examples, the IgG2 the antibody is administered every 2 weeks or every 4 weeks.

[0031] In various examples, the IgG2 antibody is administered at a dose of 70 mg, 210 mg or 280 mg every 2 weeks or every 4 weeks.

[0032] Also provided is a method of reducing the frequency of asthma exacerbation in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0033] Further contemplated is a method of reducing the frequency of asthma exacerbation in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a

sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

[0034] It is contemplated that the dosing and antibody and antibody variant types referenced above apply to each method contemplated herein.

[0035] In various examples, the antibody or antibody variant further comprises a pharmaceutically acceptable carrier or excipient.

[0036] In various examples, the administration delays the time to an asthma exacerbation compared to a subject not receiving the anti-TSLP antibody.

[0037] In various examples, the administration reduces frequency of or levels of co-administered therapy in the subject. Optionally, the co-administered therapy is inhaled corticosteroids (ICS), long-acting β2 agonist (LABA), leukotriene receptor antagonists (LTRA), long-acting anti-muscarinics (LAMA), cromones, short- acting β2 agonist (SABA), and theophylline or oral corticosteroids.

[0038] In various examples, the administration eliminates the need for corticosteroid therapy.

[0039] In various examples, the administration is subcutaneous or intravenous.

[0040] Also provided herein is a method of treating chronic obstructive pulmonary disease (COPD) comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0041] Also provided is a method of treating chronic obstructive pulmonary disease (COPD) in a subject comprising administering a therapeutically effective amount of an anti-

TSLP antibody or antibody variant in a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

[0042] Also provided herein is a method for reducing ACQ-6 score in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain comprising: i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3; ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4; iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and b. a heavy chain variable domain comprising: i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6; ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

[0043] Further provided is a method for reducing ACQ-6 score in a subject comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant in a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises a. a light chain variable domain selected from the group consisting of: i. a sequence of amino acids at least 80% identical to SEQ ID NO:12; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and b. a heavy chain variable

domain selected from the group consisting of: i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10; ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9; iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

[0044] Provided herein is a method for reducing ACQ-6 score in a subject having a low eosinophil profile comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity. Also provided is a method for reducing ACQ-6 score in a subject having a Th2 low profile comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

[0045] Also contemplated is a method for treating asthma in a subject, including severe asthma, eosinophilic or non-eosinophilic asthma and low eosinophil asthma comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

[0046] In various examples, the subject has an eosinophil count less than 250 cells/μL at start of treatment.

[0047] Also provided is a method for treating asthma in a subject having a Th2 low profile comprising administering a therapeutically effective amount of an anti-TSLP antibody or antibody variant, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

[0048] In various examples, the subject has a Th2 profile of IgE less than or equal to 100 IU/ml or eosinophil count of less than 140 cells/μL at the time of diagnosis.

[0049] In various examples, the antibody is tezepelumab or another anti-TSLP antibody described in the art, e.g., in Table A. Exemplary antibodies are described further in the Detailed Description.

Brief Description of the Drawings

[0050] Figures 1A-1D show the effects of antibody treatment at the different doses in various measures of asthma symptoms. Figure 1A, asthma exacerbation rate; Figure 1B, changes from baseline in the postbronchodilator FEV1; Figure 1C, change from baseline in ACQ-6; Figure 1D, change from baseline in AQLQ score.

[0051] Figures 2A-2B show the effects of antibody treatment in patients receiving glucocorticoids. Figure 2A: Lines within the squares represent the median, the diamond symbol represents the mean, the boxes represent the 25^{th} to 75^{th} percentile and the whiskers represent the range (highest and lowest value). Figure 2B: Histogram of baseline inhaled glucocorticoid dose (fluticasone equivalents).

WHAT IS CLAIMED:

1. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain comprising:

i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3;

ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4;

iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and

b. a heavy chain variable domain comprising:

i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6;

ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and

iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

2. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every two weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain selected from the group consisting of:

i. a sequence of amino acids at least 80% identical to SEQ ID NO:12;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and

b. a heavy chain variable domain selected from the group consisting of:

i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b), wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

3. The use of any one of claims 1 or 2 wherein the antibody or antibody variant is to be administered every 4 weeks.

4. The use of any one of claims 1 to 3 wherein the antibody or antibody variant is to be administered at a dose of 70 mg.

5. The use of any one of claims 1 to 3 wherein the antibody or antibody variant is to be administered at a dose of 210 mg.

6. The use of any one of claims1 to 3 wherein the antibody or antibody variant is to be administered at a dose of 280 mg.

7. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 210 mg at an interval of every 4 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain comprising:

i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3;

ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4;

iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and

b. a heavy chain variable domain comprising:

i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6;

ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and

iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

8. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 210 mg at an interval of every 4 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain selected from the group consisting of:

i. a sequence of amino acids at least 80% identical to SEQ ID NO:12;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and

b. a heavy chain variable domain selected from the group consisting of:

i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b), wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

9. The use of any one of the preceding claims wherein the antibody or antibody variant is to be administered for a period of at least 4 months, 6 months, 9 months, 1 year or more.

10. The use of any one of the preceding claims, wherein said anti-TSLP antibody or antibody variant thereof is bivalent and selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a recombinant antibody, an antigen-binding antibody fragment, a single chain antibody, a monomeric antibody, a diabody, a triabody, a tetrabody, a Fab fragment, , an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, and an IgG4 antibody.

11. The use of claim 8, wherein said anti-TSLP antibody variant is selected from the group consisting of a diabody, a triabody, a tetrabody, a Fab fragment, single domain antibody, scFv, wherein the dose is adjusted such that the binding sites to be equimolar to the those dosed by bivalent antibodies.

12. The use of any one of the preceding claims, wherein the antibody is an IgG2 antibody.

13. The use of any one of the preceding claims, wherein the antibody or antibody variant is a human antibody.

14. The use of any one of the preceding claims wherein, the antibody or antibody variant further comprises a pharmaceutically acceptable carrier or excipient.

15. The use of any one of the preceding claims wherein, wherein the asthma is severe asthma.

16. The use of any one of the preceding claims, wherein the asthma is eosinophilic or non-eosinophilic asthma.

17. The use any one of the preceding claims, wherein the asthma is low eosinophil asthma.

18. The use of any one of the preceding claims, wherein the subject is an adult.

19. The use of any one of the preceding claims, wherein the subject is a child or adolescent.

20. The useof any one of the preceding claims, wherein the administration decreases eosinophils in blood, sputum, broncheoalveolar fluid, or lungs of the subject.

21. The use of any one of the preceding claims, wherein the administration shifts cell counts in the subject from a Th2 high population to a Th2 low population.

22. The use of any one of the preceding claims, wherein the administration improves one or more measures of asthma in a subject selected from the group consisting of

forced expiratory volume (FEV), FEV_1 reversibility, forced vital capacity (FCV), FeNO, Asthma Control Questionnaire-6 score and AQLQ(S)+12 score.

23. The use of any one of the preceding claims, wherein the administration improves one or more symptoms of asthma as measured by an asthma symptom diary.

24. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject, comprising that the subject is to be administered a dose of 70 to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain comprising:

i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3;

ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4;

iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and

b. a heavy chain variable domain comprising:

i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6;

ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and

iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2, wherein the antibody is an IgG2 antibody.

25. The use of claim 24 wherein the antibody is to be administered every 4 weeks.

26. The use of claim 24 or 25 wherein the antibody is to be administered at a dose of 70 mg.

27. The use of any one of claims 24 to 25 wherein the antibody is to be administered at a dose of 210 mg.

28. The use of any one of claims 24 to 25 wherein the antibody is to be administered at a dose of 280 mg.

29. The use of any one of the preceding claims wherein the antibody is tezepelumab.

30. The use of claim 29 wherein the antibody is an IgG2 antibody, and has the full length heavy and light chain sequences set out in SEQ ID NOs: 105 and 106, respectively.

31. The use of any one of the preceding claims wherein the antibody variant has substantially similar pK characteristics as tezepelumab in humans.

32. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing the frequency of asthma exacerbation in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain comprising:

i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3;

ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4;

iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and

b. a heavy chain variable domain comprising:

i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6;

ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and

iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

33. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing the frequency of asthma exacerbation in a subject, comprising that the subject is to be administered dose of 70 mg to

280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain selected from the group consisting of:

i. a sequence of amino acids at least 80% identical to SEQ ID NO:12;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and

b. a heavy chain variable domain selected from the group consisting of:

i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

34. The use of any one of claims 32 or 33 wherein the antibody or antibody variant is to be administered every 4 weeks.

35. The use of any one of claims 32 or 33 wherein the antibody or antibody variant is to be administered at a dose of 70 mg.

36. The use of any one of claims 32 or 33 wherein the antibody or antibody variant is to be administered at a dose of 210 mg.

37. The use of any one of claims 32 or 33 wherein the antibody or antibody variant is to be administered at a dose of 280 mg.

38. The use of any one of claims 32 to 37 wherein the antibody or antibody variant is to be administered for a period of at least 4 months, 6 months, 9 months, 1 year or more.

39. The use of any one of claims 32 to 38, wherein said anti-TSLP antibody or antibody variant is selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a recombinant antibody, an antigen-binding antibody fragment, a single chain antibody, a monomeric antibody, a diabody, a

triabody, a tetrabody, a Fab fragment, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, and an IgG4 antibody .

40. The use of any one of claims 32 to 39, wherein antibody or antibody variant is an IgG2 antibody.

41. The use of any one of claims 32 to 40, wherein the antibody or antibody variant is a human antibody.

42. The use of any one of claims 32 to 41 wherein, the antibody or antibody variant further comprises a pharmaceutically acceptable carrier or excipient.

43. The use of any one of claims 32 to 42 wherein the administration delays the time to an asthma exacerbation compared to a subject not receiving the anti-TSLP antibody.

44. The use of any one of claims 32 to 43 wherein the administration reduces frequency of or levels of co-administered therapy in the subject.

45. The use of claim 44 wherein the co-administered therapy is inhaled corticosteroids (ICS), long-acting β2 agonist (LABA), leukotriene receptor antagonists (LTRA), long-acting anti-muscarinics (LAMA),cromones, short- acting β2 agonist (SABA), and theophylline or oral corticosteroids.

46. The use of claim 44, wherein the administration eliminates the need for corticosteroid therapy.

47. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating chronic obstructive pulmonary disease (COPD) in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain comprising:

i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3;

ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4;

iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and

b. a heavy chain variable domain comprising:

i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6;

ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and

iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

48. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating chronic obstructive pulmonary disease (COPD) in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain selected from the group consisting of:

i. a sequence of amino acids at least 80% identical to SEQ ID NO:12;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and

b. a heavy chain variable domain selected from the group consisting of:

i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

49. The use of any one of the preceding claims wherein the administration is subcutaneous or intravenous.

50. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing ACQ-6 score in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of

every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain comprising:

i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3;

ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4;

iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and

b. a heavy chain variable domain comprising:

i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6;

ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and

iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antigen binding protein specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

51. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing ACQ-6 score in a subject, comprising that the subject is to be administered a dose of 70 mg to 280 mg at an interval of every 2 weeks, wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain selected from the group consisting of:

i. a sequence of amino acids at least 80% identical to SEQ ID NO:12;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and

b. a heavy chain variable domain selected from the group consisting of:

i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b).

52. The use of any one of the preceding claims wherein the administration is subcutaneous or intravenous.

53. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject having a non-eosinophilic profile or a low eosinophil profile, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

54. The use of claim 53 wherein the anti-TSLP antibody or anti-TSLP antibody variant is selected from an antibody described in Table A:

TABLE A

WO2017/042701	An anti-TSLP antibody comprising a heavy chain (HC) CDR1 comprising the sequence of SEQ ID NO: 13, a HC CDR2 comprising the sequence of SEQ ID NO: 14, and a HC CDR3 comprising the sequence of SEQ ID NO: 15; An anti-TSLP antibody comprising a light chain (LC) CDR1 comprising the sequence of SEQ ID NO: 16, a LC CDR2 comprising the sequence of SEQ ID NO: 17, a LC CDR3 comprising the sequence of SEQ ID NO: 18; An anti-TSLP antibody comprising a heavy chain (HC) CDR1 comprising the sequence of SEQ ID NO: 19, a HC CDR2 comprising the sequence of SEQ ID NO: 20, a HC CDR3 comprising the sequence of SEQ ID NO:15; An anti-TSLP antibody comprising a light chain (LC) CDR1 comprising the sequence of SEQ ID NO: 21, a LC CDR2 comprising the sequence of SEQ ID NO: 22, a LC CDR3 comprising the sequence of SEQ ID NO: 23; An anti-TSLP antibody comprising a HC variable region comprising the sequence of SEQ ID NO: 26 and/or a LC variable region comprising the sequence of SEQ ID NO: 27; An anti-TSLP antibody comprising a HC variable region comprising the sequence of SEQ ID NO: 28 and/or a LC variable region comprising the sequence of SEQ ID NO: 29; An anti-TSLP antibody that comprises a paratope comprising at least one

	of the following residues: Thr28, Asp31, Tyr32, Trp33, Asp56, Glu101, Ile102, Tyr103, Tyr104, Tyr105 of a heavy chain sequence of SEQ ID NO: 26 or Gly28, Ser29, Lys30, Tyr31, Tyr48, Asp50, Asn51, Glu52, Asn65, and Trp92 of a light chain sequence of SEQ ID NO:27; An anti-TSLP antibody that specifically binds an epitope in human TSLP, wherein the epitope comprises at least one of the following residues: Lys38, Ala41, Leu44, Ser45, Thr46, Ser48, Lys49, Ile52, Thr53, Ser56, Gly57, Thr58, Lys59, Lys101, Gln145, and Arg149 of SEQ ID NO: 30;
WO2016/142426	An anti-TSLP antibody comprising the amino acid sequence of SEQ ID NO: 31; An anti-TSLP antibody comprising a CDR1 comprising the sequence of SEQ ID NO: 32; a CDR2 comprising the sequence of SEQ ID NO: 33, and a CDR3 comprising the sequence of SEQ ID NO: 34; An anti-TSLP antibody comprising a CDR1 comprising the sequence of SEQ ID NO: 32; a CDR2 comprising the sequence of SEQ ID NO: 35, and a CDR3 comprising the sequence of SEQ ID NO: 34; An anti-TSLP antibody comprising a variant of the CDR1 of SEQ ID NO: 31 wherein the residue corresponding to residue 28 in SEQ ID NO:31 is Pro, the residue corresponding to residue 30 in SEQ ID NO:31 is Arg, the residue corresponding to residue 31 in SEQ ID NO:31 is Asn, the residue corresponding to residue 32 in SEQ ID NO: 31 is Trp and the residue corresponding to residue 34 in SEQ ID NO: 31 is Asp; An anti-TSLP antibody comprising a variant of the CDR2 of SEQ ID NO: 31 wherein the residue corresponding to residue 50 in SEQ ID NO:31 is Gly, the residue corresponding to residue 53 in SEQ ID NO:31 is His and the residue corresponding to residue 55 in SEQ ID NO:31 is Gln; An anti-TSLP antibody comprising a variant of the CDR3 of SEQ ID NO: 31 wherein the residue corresponding to residue 91 in SEQ ID NO:31 is He, Leu, Val or Phe, the residue corresponding to residue 92 in SEQ ID NO:31 is Gly or Ala, the residue corresponding to residue 93 in SEQ ID NO:31 is Glu, Phe, Asp or Ser and the residue corresponding to residue 94 in SEQ ID NO:31 is Asp.
WO2010/017468	An anti-TSLP antibody (9B7) comprising a HC CDR3 comprising the sequence of SEQ ID NO:38, wherein the other CDRs of the HC and LC comprise the sequences of SEQ ID NOs: 36, 37, and 39-41; An anti-TSLP antibody (6C5) comprising a HC CDR3 comprising the

	sequence of SEQ ID NO:44, wherein the other CDRs of the HC and LC comprise the sequences of SEQ ID NOs: 42, 43, and 45-47; An anti-TSLP antibody (6A3) comprising a HC CDR3 comprising the sequence of SEQ ID NO:50, wherein the other CDRs of the HC and LC comprise the sequences of SEQ ID NOs: 48, 49, and 51-53; An anti-TSLP antibody (1A11) comprising a HC CDR3 comprising the sequence of SEQ ID NO:56, wherein the other CDRs of the HC and LC comprise the sequences of SEQ ID NOs: 54, 55, and 57-59; An anti-TSLP antibody comprising (i) heavy chain variable region of SEQ ID NO:60 and/or the light chain variable region of SEQ ID NO:61; An anti-TSLP antibody comprising (i) heavy chain variable region of SEQ ID NO: 62 and/or the light chain variable region of SEQ ID NO:63; An anti-TSLP antibody comprising (i) heavy chain variable region of SEQ ID NO: 64 and/or the light chain variable region of SEQ ID NO:65; An anti-TSLP antibody comprising (i) heavy chain variable region of SEQ ID NO:66 and/or the light chain variable region of SEQ ID NO: 67; An anti-TSLP antibody comprising (i) heavy chain variable region of SEQ ID NO: 68 and/or the light chain variable region of SEQ ID NO: 69; An anti-TSLP antibody comprising a HC CDR selected from the group consisting of SEQ ID NO:38, SEQ ID NO:44, SEQ ID NO:50 and SEQ ID NO:56, and analogs thereof; An anti-TSLP antibody comprising a heavy chain comprising the following CDRs or analogs thereof CDRH1 : RYNVH (SEQ ID NO:36), CDRH2: MIWDGGSTDYNSALKS (SEQ ID NO:37), CDRH3: NRYESG (SEQ ID NO:38), and a light chain comprising the following CDRs or analogs thereof CDRL1 : KSSQSLLNSGNRKNYLT (SEQ ID NO:39), CDRL2: WASTRES (SEQ ID NO:40), and CDRL3: QNDYTYPFTFGS (SEQ ID NO:41); or An anti-TSLP antibody comprising a heavy chain comprising the following CDRs or analogs thereof CRDH1 : AYWMS (SEQ ID NO:42),CDRH2: EINPDSSTINCTPSLKD (SEQ ID NO:43), CDRH3: RLRPFWYFDVW (SEQ ID NO:44), and a light chain comprising the following CDRs or analogs thereof CDRL1 : RSSQSIVQSNGNTYLE (SEQ ID NO:45), CDRL2: KVSNRFS (SEQ ID NO:46), and CDRL3: FQGSHVPRT (SEQ ID NO:47);

	An anti-TSLP antibody comprising a heavy chain comprising the following CDRs or analogs thereof CRDH1 : TDYAWN (SEQ ID NO:48), CDRH2: YIFYSGSTTYTPSLKS (SEQ ID NO:49), CDRH3: GGYDVNYF (SEQ ID NO:50), and a light chain comprising the following CDRs or analogs thereof CDRL1 : LASQTIGAWLA (SEQ ID NO:51), CDRL2: AATRLAD (SEQ ID NO:52), and CDRL3: QQFFSTPWT (SEQ ID NO:53); An anti-TSLP antibody comprising a heavy chain comprising the following CDRs or analogs thereof CDRH1 : GYTMN (SEQ ID NO:54), CDRH2: LINPYNGVTSYNQKFK (SEQ ID NO:55), CDRH3: GDGNYWYF (SEQ ID NO:56), and a light chain comprising the following CDRs or analogs thereof CDRL1 : SASSSVTYMHW (SEQ ID NO:57), CDRL2: EISKLAS (SEQ ID NO:58), and CDRL3: QEWNYPYTF (SEQ ID NO:59); An anti-TSLP antibody comprising a HC CDR1 comprising the sequence of SEQ ID NO: 70; a CDR2 comprising the sequence of SEQ ID NO: 71, and a CDR3 comprising the sequence of SEQ ID NO: 72; An anti-TSLP antibody comprising a LC CDR1 comprising the sequence of SEQ ID NO: 73; a CDR2 comprising the sequence of SEQ ID NO: 74, and a CDR3 comprising the sequence of SEQ ID NO: 75;
US2012/0020988	An anti-TSLP antibody comprising a heavy chain variable domain comprising a CDR1 region of SEQ ID NO: 76, a CDR2 region of SEQ ID NO:77, and CDR3 region of SEQ ID NO:78, and a light chain variable domain comprising a CDR1 region of SEQ ID NO: 79, a CDR2 region of SEQ ID NO:80, and a CDR3 region of SEQ ID NO:81. An anti-TSLP antibody comprising a heavy chain variable domain comprising SEQ ID NO:82 and a light chain variable domain comprising SEQ ID NO:83; An anti-TSLP antibody comprising a heavy chain variable domain comprising a CDR1 region of SEQ ID NO: 76 or 84, a CDR2 region of SEQ ID NO: 77 or 85, and CDR3 region of SEQ ID NO: 78, and a light chain variable domain comprising a CDR1 region of SEQ ID NO: 79 or 86, a CDR2 region of SEQ ID NO: 80, 87, or 88, and a CDR3 region of SEQ ID NO: 81. An anti-TSLP antibody comprising a heavy chain variable domain comprising a CDR1 region of SEQ ID NO: 76, a CDR2 region of SEQ ID NO:85, and CDR3 region of SEQ ID NO: 78, and a light chain variable domain comprising a CDR1 region of SEQ ID NO: 86, a CDR2 region of

	SEQ ID NO:87 and a CDR3 region of SEQ ID NO:81; An anti-TSLP antibody comprising a heavy chain variable domain comprising a CDR1 region of SEQ ID NO: 76, a CDR2 region of SEQ ID NO:85, and CDR3 region of SEQ ID NO: 78, and a light chain variable domain comprising a CDR1 region of SEQ ID NO: 86, a CDR2 region of SEQ ID NO:88 and a CDR3 region of SEQ ID NO:81; An anti-TSLP antibody comprising a heavy chain variable domain comprising a CDR1 region of SEQ ID NO: 84, a CDR2 region of SEQ ID NO:85, and CDR3 region of SEQ ID NO: 78, and a light chain variable domain comprising a CDR1 region of SEQ ID NO: 86, a CDR2 region of SEQ ID NO:88 and a CDR3 region of SEQ ID NO:81; or An anti-TSLP antibody comprising a heavy chain variable domain comprising a CDR1 region of SEQ ID NO: 76, a CDR2 region of SEQ ID NO:85, and CDR3 region of SEQ ID NO: 78, and a light chain variable domain comprising a CDR1 region of SEQ ID NO: 86, a CDR2 region of SEQ ID NO: 80 and a CDR3 region of SEQ ID NO:81. An anti-TSLP antibody comprising a heavy chain variable domain comprises SEQ ID NO:89 and a light chain variable domain comprises SEQ ID NO:90; An anti-TSLP antibody comprising a heavy chain variable domain comprises SEQ ID NO:89 and a light chain variable domain comprises SEQ ID NO:91; An anti-TSLP antibody comprising a heavy chain variable domain comprises SEQ ID NO:92 and a light chain variable domain comprises SEQ ID NO:93; An anti-TSLP antibody comprising a heavy chain variable domain comprises SEQ ID NO:89 and a light chain variable domain comprises SEQ ID NO:94,
US8637019	An anti-TSLP antibody comprising heavy chain variable region comprising: a CDR-H1 sequence comprising SEQ ID NO:95, a CDR-H2 sequence comprising SEQ ID NO:96, and a CDR-H3 sequence comprising SEQ ID NO:97; and/or an antibody light chain variable region or a TSLP-binding fragment thereof, said light chain variable region comprising: a CDR-L1 sequence comprising SEQ ID NO: 98, a CDR-L2 sequence comprising SEQ ID NO: 99, and a CDR-L3 sequence comprising SEQ ID NO: 100. An anti-TSLP antibody comprising a heavy chain variable region

	comprises the amino acid sequence of SEQ ID NO:101 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 102. An anti-TSLP antibody comprising SEQ ID NO:103 and SEQ ID NO:104.

55. The use of any one of claims 32 to 54 wherein the anti-TSLP antibody is tezepelumab.

56. The use of claim 55 wherein the antibody is an IgG2 antibody, and has the full length heavy and light chain sequences set out in SEQ ID NOs: 105 and 106, respectively.

57. The use of any one of claims 32 to 56 wherein the antibody variant has substantially similar pK characteristics as tezepelumab in humans.

58. The use of any one of claims 53, 54, or 55 wherein the subject has an eosinophil count less than 250 cells/µL at start of treatment.

59. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for treating asthma in a subject having a Th2 low profile, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

60. The use of claim 59 wherein the subject has a Th2 profile of IgE less than or equal to 100 IU/ml or eosinophil count of less than 140 cells/µL at the time of diagnosis.

61. The uses of claim 59 or 60 wherein the antibody or antibody variant is selected from an antibody described in Table A.

62. The use of claim 59 or 60 where in the antibody is tezepelumab.

63. The use of claim 62 wherein the antibody is an IgG2 antibody, and has the full length heavy and light chain sequences set out in SEQ ID NOs: 105 and 106, respectively.

64. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing ACQ-6 score in a subject having a low eosinophil profile, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

65. The use of claim 64 wherein the anti-TSLP antibody or anti-TSLP antibody variant is selected from an antibody described in Table A.

66. The use of claim 64 wherein the anti-TSLP antibody is tezepelumab.

67. The use of claim 66 wherein the antibody is an IgG2 antibody, and has the full length heavy and light chain sequences set out in SEQ ID NOs: 105 and 106, respectively.

68. The use of claims 64, 65, or 66 wherein the subject has an eosinophil count less than 250 cells/µL at start of treatment.

68. Use of a therapeutically effective amount of an anti-TSLP antibody or antibody variant in the manufacture of a medicament for reducing ACQ-6 score in a subject having a Th2 low profile, wherein the antibody or antibody variant binding to TSLP inhibits TSLP activity.

69. The use of claim 68 wherein the subject has a Th2 profile of IgE less than or equal to 100 IU/ml or eosinophil count of less than 140 cells/µL at the time of diagnosis.

70. The uses of claims 68 or 69 wherein the antibody or antibody variant is selected from an antibody described in Table A.

71. The use of claims 68 or 69 where in the antibody is tezepelumab.

72. The use of claim 71 wherein the antibody is an IgG2 antibody, and has the full length heavy and light chain sequences set out in SEQ ID NOs: 105 and 106, respectively.

73. The use of any one of claims 53-72 wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain comprising:

i. a light chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:3;

ii. a light chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:4;

iii. a light chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:5; and

b. a heavy chain variable domain comprising:

i. a heavy chain CDR1 sequence comprising the amino acid sequence set forth in SEQ ID NO:6;

ii. a heavy chain CDR2 sequence comprising the amino acid sequence set forth in SEQ ID NO:7, and

iii. a heavy chain CDR3 sequence comprising the amino acid sequence set forth in SEQ ID NO:8, wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

74. The use of any one of claims 53-72 wherein both binding sites of the antibody have identical binding to TSLP, and the antibody comprises

a. a light chain variable domain selected from the group consisting of:

i. a sequence of amino acids at least 80% identical to SEQ ID NO:12;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:11;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:11; and

b. a heavy chain variable domain selected from the group consisting of:

i. a sequence of amino acids that is at least 80% identical to SEQ ID NO:10;

ii. a sequence of amino acids encoded by a polynucleotide sequence that is at least 80% identical to SEQ ID NO:9;

iii. a sequence of amino acids encoded by a polynucleotide that hybridizes under moderately stringent conditions to the complement of a polynucleotide consisting of SEQ ID NO:9; or c. a light chain variable domain of (a) and a heavy chain variable domain of (b), wherein the antibody specifically binds to a TSLP polypeptide as set forth in amino acids 29-159 of SEQ ID NO:2.

75. The use of any one of claims 53-74 wherein the antibody or antibody variant is to be administered every 4 weeks.

76. The use any one of claims 53-75 wherein the administration is subcutaneous or intravenous.