CLAIMS

1. Use of a first antibody or antigen-binding fragment thereof and a second antibody or antigen-binding fragment thereof for the preparation of a medicament for treating asthma in a subject in need thereof, wherein the subject has a blood eosinophil count of greater than 300 cells per μL, and a blood periostin level of greater than or equal to 74.4 ng/mL, wherein the first antibody or antigen-binding fragment thereof is formulated for administration as:

an initial dose of 300 mg; and

one or more maintenance doses of 300 mg

wherein the first antibody or antigen-binding fragment thereof specifically binds to interleukin-33 (IL-33) and comprises three heavy chain complementary determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and three light chain complementary determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16, and

wherein the second antibody or antigen-binding fragment thereof is formulated for administration as:

an initial dose of 300 mg; and

one or more maintenance doses of 300 mg

wherein the second antibody or antigen-binding fragment thereof specifically binds to interleukin-4 receptor (IL-4R) and comprises three heavy chain complementary determining region (HCDR) sequences comprising SEQ ID NOs: 21, 22, and 23, and three light chain complementary determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25, and 26.

2. The use of claim 1, wherein:

(a) the medicament reduces loss of asthma control (LOAC) in the subject;

(b) the medicament improves one or more asthma-associated parameters selected from the group consisting of forced expiratory volume in 1 second (FEV1), peak expiratory flow (PEF), forced vital capacity (FVC), forced expiratory flow (FEF) 25%-75%, frequency or dosage of a long-acting β2 adrenergic agonist (LABA), frequency or dosage of an inhaled corticosteroid, and frequency or dosage of a systemic steroid;

(c) the medicament improves pre-bronchodilator FEV1;

(d) the medicament reduces the frequency or the dosage of the long-acting β2 adrenergic agonist (LABA), the frequency or the dosage of the inhaled corticosteroid, or the frequency or the dosage of the systemic steroid;

(e) the medicament improves one or both of asthma control questionnaire 5-question version (ACQ-5) score and asthma quality of life questionnaire with standardized activities (AQLQ) score;

(f) the asthma is moderate-to-severe asthma that is not well-controlled on a background therapy; and/or

(g) the medicament reduces blood eosinophil levels.

3. The use of claim 1 or 2, wherein the first antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2 and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 10.

4. The use of any one of claims 1 to 3, wherein the first antibody or antigen-binding fragment thereof or the second antibody or antigen-binding fragment thereof is formulated for:

(a) administration every other week;

(b) subcutaneous administration;

(c) administration as two injections; or

(d) administration with an autoinjector, a needle, and syringe, or a pen delivery device.

5. The use of claim any one of claims 1 to 4, wherein the second antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 27 and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 28.

6. The use of any one of claims 1 to 5, wherein the first antibody or antigen-binding fragment thereof is formulated for administration as two injections and the second antibody or antigen-binding fragment thereof is formulated for administration as one injection.

7. The use of any one of claims 1 to 6, wherein the medicament is for administration in combination with an administration of at least one additional therapeutic agent to the subject.

8. The use of claim 7, wherein the at least one additional therapeutic agent comprises one or both of an ICS and a LABA.

9. The use of claim 8, wherein the ICS is fluticasone or budesonide, and/or the LABA is salmeterol or formoterol.

10. Use of a first antibody or antigen-binding fragment thereof that specifically binds to interleukin-33 (IL-33) and a second antibody or antigen-binding fragment thereof that specifically binds to interleukin-4 receptor (IL-4R) for the preparation of a medicament for reducing an asthma patient's dependence on one or both of an inhaled corticosteroid (ICS) and a long-acting β2 adrenergic agonist (LABA) for the treatment of one or more asthma exacerbations,

wherein the asthma patient has a blood eosinophil count of greater than 300 cells per μL and a blood periostin level of greater than or equal to 74.4 ng/mL, and has moderate-to-severe asthma that is partially controlled or uncontrolled with a background asthma therapy with ICS, a LABA, or a combination thereof,

wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof are formulated for:

administration to the asthma patient at an initial dose of 300 mg and one or more maintenance doses of 300 mg for an initial treatment period while maintaining the asthma patient's background asthma therapy for the initial treatment period; and

gradually reducing or eliminating the dosage of the ICS, the LABA or the combination thereof is to be administered to the asthma patient over the course of a subsequent treatment period while continuing the administration of the first and second antibody or antigen-binding fragment thereof to the asthma patient, and

wherein the first antibody or antigen-binding fragment thereof comprises three heavy chain complementary determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and

three light chain complementary determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16, and

wherein the second antibody or antigen-binding fragment thereof comprises three heavy chain complementary determining region (HCDR) sequences comprising SEQ ID NOs: 21, 22, and 23, and three light chain complementary determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25, and 26.

11. The use of claim 10,

(a) wherein the ICS is fluticasone, budesonide, or mometasone, and the LABA is salmeterol or formoterol;

(b) wherein the ICS/LABA combination is selected from the group consisting of fluticasone/salmeterol, budesonide/formoterol, and mometasone/formoterol;

(c) wherein the medicament eliminates the dosage of one or both of the LABA and the ICS at the end of the initial treatment period; or

(d) wherein the medicament gradually reduces or eliminates the dosage of one or both of the LABA and the ICS over the course of 2 to 8 weeks.

12. The use of claims 10 or 11, wherein:

(a) the medicament reduces loss of asthma control (LOAC) in the subject;

(b) the medicament improves one or more asthma-associated parameters selected from the group consisting of forced expiratory volume in 1 second (FEV1), peak expiratory flow (PEF), forced vital capacity (FVC), forced expiratory flow (FEF) 25%-75%, frequency or dosage of a long-acting β2 adrenergic agonist (LABA), frequency or dosage of an inhaled corticosteroid, and frequency or dosage of a systemic steroid;

(c) the medicament improves pre-bronchodilator FEV1;

(d) the medicament reduces the frequency or the dosage of the long-acting β2 adrenergic agonist (LABA), the frequency or the dosage of the inhaled corticosteroid, or the frequency or the dosage of the systemic steroid;

(e) the medicament improves one or both of asthma control questionnaire 5-question version (ACQ-5) score and asthma quality of life questionnaire with standardized activities (AQLQ) score;

(f) the asthma is moderate-to-severe asthma that is not well-controlled on a background therapy; and/or

(g) the medicament reduces blood eosinophil levels.

13. The use of any one of claims 10 to 12, wherein the first antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2 and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 10.

14. The use of any one of claims 10 to 13, wherein the second antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 27 and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 28.