CLAIMS

What is claimed is:

1. A method for treating allergic asthma in a subject in need thereof comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-33 (IL-33) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16.

2. The method of claim 1, wherein the 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.

3. The method of claim 1 or 2, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 18 and a light chain comprising the amino acid sequence of SEQ ID NO: 20.

4. The method of any one of claims 1-3, wherein the antibody or antigen-binding fragment thereof is administered intravenously at a dose of 10 mg/kg.

5. The method of any one of claims 1-3, wherein the antibody or antigen binding fragment thereof is administered subcutaneously at a dose of about 0.1 mg to about 600 mg, about 100 mg to about 400 mg, or about 300 mg.

6. The method of any one of claims 1-3 or 5, wherein the antibody or antigen binding fragment thereof is administered subcutaneously at an initial dose of about 600 mg or about 300 mg.

7. The method of any one of claims 1-3, 5 or 6, wherein the antibody or antigen binding fragment thereof is administered subcutaneously in one or more secondary doses of about 300 mg.

8. A method for treating allergic asthma in a subject in need thereof comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-4R (IL-4R) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 21, 22 and 23, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25 and 26.

9. The method of claim 8, wherein the 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.

10. The method of claim 8 or 9, wherein the antibody or antigen-binding fragment thereof comprises dupilumab.

11. The method of any one of claims 8-10, wherein the antibody or antigen binding fragment thereof is administered at a dose of about 0.1 mg to about 600 mg, about 100 mg to about 400 mg, or about 300 mg.

12. The method of any one of claims 8-11, wherein the antibody or antigen binding fragment thereof is administered at an initial dose of about 600 mg.

13. The method of any one of claims 8-11, wherein the antibody or antigen binding fragment thereof is administered in one or more secondary doses of about 300 mg.

14. The method of any one of claims 1-13, wherein the antibody or antigen-binding fragment thereof is administered every week (q1w), every other week (q2w), every three weeks (q3w), or every four weeks (q4w).

15. The method of any one of claims 1-14, wherein the antibody or antigen-binding fragment thereof is administered every other week (q2w).

16. The method of any one of claims 1-3 and 5-15, wherein the antibody or antigen-binding fragment thereof is administered subcutaneously.

17. The method of any one of claims 1-3 and 5-16, wherein the antibody or antigen-binding fragment thereof is administered subcutaneously using an autoinjector, a needle and syringe, or a pen delivery device.

18. A method for treating allergic asthma in a subject in need thereof comprising administering to the subject:

an initial dose of about 600 mg of an antibody or antigen-binding fragment thereof that specifically binds interleukin-4R (IL-4R) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 21, 22 and 23, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25 and 26; and

one or more subsequent doses of about 300 mg of the antibody or antigen-binding fragment thereof.

19. The method of claim 18, wherein the 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.

20. A method for treating allergic asthma in a subject in need thereof comprising administering to the subject:

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

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

21. The method of claim 20, 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.

22. The method of claim 20 or 21, wherein the first antibody or antigen-binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO; 18 and a light chain comprising the amino acid sequence of SEQ ID NO: 20.

23. The method of any one of claims 20-22, 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.

24. The method of any one of claims 20-23, wherein the second antibody or antigen-binding fragment thereof comprises dupilumab.

25. The method of any one of claims 20-24, wherein the second antibody or antigen binding fragment thereof is administered at a dose of about 0.1 mg to about 600 mg, about 100 mg to about 400 mg, or about 300 mg.

26. The method of any one of claims 20-25, wherein the second antibody or antigen binding fragment thereof is administered at an initial dose of about 600 mg.

27. The method of any one of claims 20-25, wherein the second antibody or antigen binding fragment thereof is administered in one or more subsequent doses of about 300 mg of the antibody or antigen binding fragment thereof.

28. The method of any one of claims 20-27, wherein the second antibody or antigen-binding fragment thereof is administered every week (q1w), every other week (q2w), once every three weeks (q3w), or once every four weeks (q4w).

29. The method of claim of any one of claims 20-28, wherein the second antibody or antigen-binding fragment thereof is administered every other week (q2w).

30. The method of any one of claims 20-29, wherein the second antibody or antigen-binding fragment thereof is administered subcutaneously.

31. The method of any one of claims 20-30, wherein the second antibody or antigen-binding fragment thereof is administered subcutaneously using an autoinjector, a needle and syringe, or a pen delivery device.

32. The method of any one of claims 20-31, wherein the first antibody or antigen binding fragment thereof is administered subcutaneously at a dose of about 0.1 mg to about 600 mg, about 100 mg to about 400 mg, or about 300 mg.

33. The method of any one of claims 20-32, wherein the first antibody or antigen binding fragment thereof is administered subcutaneously at an initial dose of about 600 mg or about 300 mg.

34. The method of any one of claims 20-33, wherein the first antibody or antigen binding fragment thereof is administered subcutaneously in one or more secondary doses of about 300 mg.

35. The method of any one of claims 20-30, wherein the first antibody or antigen-binding fragment thereof is administered intravenously at a dose of 10 mg/kg.

36. A method for treating allergic asthma in a subject in need thereof comprising administering to the subject:

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

wherein the first antibody or antigen-binding fragment thereof is administered at a single dose of 10 mg/kg; and

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

wherein the second antibody or antigen-binding fragment thereof is administered at an initial dose of 600 mg and one or more subsequent doses of about 300 mg.

37. The method of any one of the preceding claims, wherein the allergic asthma is mild allergic asthma.

38. The method of claim 37, wherein the allergic asthma is mild persistent allergic asthma.

39. The method of any one of the preceding claims, wherein the subject is allergic to house dust mite allergen (HDM).

40. The method of any one of the preceding claims, wherein the subject is a non-smoker.

41. The method of any one of the preceding claims, wherein the subject is clinically stable and requires short-acting inhaled β2 agonist (SABA) use on a per needed basis to control asthma symptoms.

42. The method of any one of the preceding claims, wherein loss of asthma control (LOAC) is reduced in the subject.

43. The method of any one of the preceding claims, wherein an asthma symptom selected from the group consisting of cough, wheezing, and short-acting inhaled β2 agonist use is reduced in the subject.

44. The method of any one of the preceding claims, wherein one or more asthma-associated parameter(s) are improved in the subject.

45. The method of claim 44, wherein the asthma-associated parameter is 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%, and reduction of the frequency or the dosage of short-acting inhaled β2 agonist use in the subject.

46. The method of claim 45, wherein pre-bronchodilator FEV1 is improved in the subject.

47. The method of any one of the preceding claims, wherein blood eosinophil levels are reduced in the subject.

48. The method of any one of the preceding claims, wherein one or both of asthma control questionnaire 5-question version (ACQ-5) score and asthma quality of life questionnaire with standardized activities (AQLQ) score are improved in the subject.

49. The method of any one of the preceding claims, wherein the frequency or the dosage of SABA use in the subject is reduced in the subject.

50. The method of any one of the preceding claims, wherein bronchial allergen challenge (BAC)-induced lung inflammation is reduced in the subject.

51. The method of any one of the preceding claims, wherein a type 2 cytokine level is decreased in the subject.

52. The method of claim 51, wherein the type 2 cytokine is one or both of IL-13 and IL-5.

53. The method of any one of the preceding claims, wherein a cytokine level or a chemokine level is decreased in the subject, wherein the cytokine or the chemokine is selected from the group consisting of tumor necrosis factor-alpha (TNFα), thymus and activation-regulated chemokine (TARC), pulmonary and activation-regulated chemokine (PARC), CCL1, CCL26, FCER2, SIGLEC8, CCL17, and eotaxin-3.

54. The method of any one of the preceding claims, wherein early allergen response (EAR) or late allergen response (LAR) is reduced in the subject.

55. The method of any one of the preceding claims, wherein FEV1 is improved in the subject by at least 20%, 30%, 40%, 50%, 60%, or 70%.

55. The method of any one of the preceding claims, wherein FeNO levels are reduced in the subject.

57. The method of any one of the preceding claims, wherein serum levels of sST2, IL-33, calcitonin, or matrix metalloproteinase-12 (MMP12) are reduced in the subject.

58. The method of any one of the preceding claims, wherein serum levels of CCL26, CCL17, or SIGLEC8 are reduced in the subject.

59. The method of any one of the preceding claims, wherein serum levels of ASAP1-IT1, AX747757, BC042385, PABPC1P2, AB209315, AX748268, TCEAL5, CCL13, CLC, CACNG8, GPR82, GATA1, PRSS33, FFAR3, LGALS12, ASB2, PTGDR2, IL-13, IL-5, PTGDS, or RD3 are reduced in the subject.

60. A method for reducing a cytokine level or a chemokine level in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-33 (IL-33) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16.

61. The method of claim 60, wherein the cytokine is one or both of IL-13 and IL-5.

62. The method of claim 60 or 61, wherein the cytokine or chemokine is selected from the group consisting of TNFα, TARC, PARC, CCL1, CCL26, FCER2, SIGLEC8, CCL17 and eotaxin-3.

63. The method of any one of claims 60-62, wherein serum levels of sST2, IL-33, calcitonin or MMP12 are reduced in the subject.

64. The method of any one of claims 60-63, wherein serum levels of CCL26, CCL17 or SIGLEC8 are reduced in the subject.

65. A method for reducing expression of one or more allergic asthma signature genes in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-33 (IL-33) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16.

66. The method of claim 65, wherein the one or more allergic asthma signature genes are selected from the group consisting of BC042385, AB209315, LOC100607117, BC035084, LOC145474, AX747853, TIMP1, NT5DC2, LOC541471, AREG, PTPN7, RUNDC3, XXYLT1, FAM159A, PTGDS, TESC, ITGB2-AS1, D0574721, CLDN9, LOC100132052, AGAP7, NBEAL2, NTNG2, FLJ45445, KCNH3, POU51P3, OUG1, KIF21B, HSPA7, GAPT, BX6485Q2, PRR52, P1K3R6, LTC4S, CLEC11A, TRABD2A, DLGAP3, VDR, DKFZp686M11215, SIGLEC12, BC016361, BC052769, and RHOH.

67. The method of claim 65 or 66, wherein the one or more allergic asthma signature genes are selected from the group consisting of ASAP1-IT1, AX747757, BC042385, PABPC1P2, AB209315, AX748268, TCEAL5, CCL17, CCL13, CCL26, CLC, CACNG8, GPR82, GATA1, PRSS33, FFAR3, LGALS12, ASB2, PTGDR2, SIGLEC8, IL13, IL5, PTGDS and RD3.

68. A method for reducing expression of any combination of type 2 inflammatory cytokine and type 2 chemokine signature genes in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-33 (IL-33) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16.

69. The method of claim 68, wherein the type 2 inflammatory cytokine and chemokine signature genes are selected from the group consisting of IL-5, CCL1, IL-13, GATA2, CCL26, FCER2, CACNG8, CLC, GATA1, LGALS12, SIGLEC8, GGT5, CCL17 and MMP10.

70. The method of claim 68 or 69, wherein the one or more type 2 inflammatory cytokine and chemokine signature genes are selected from the group consisting of IL-5, CCL1, IL-13, CCL26, FCER2, SIGLEC8, GGT5 and CCL17.

71. A method for reducing expression of one or more eosinophil signature genes in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-33 (IL-33) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16.

72. The method of claim 71, wherein the one or more one or more eosinophil signature genes are selected from the group consisting of IL1RL1, ADARB1, SIGLEC8, ASB2, VSTM1, SYNE1, CLC, PTPN7 and HDC.

73. A method for reducing expression of one or more type 2 inflammatory signature genes in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-33 (IL-33) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16.

74. The method of claim 73, wherein the one or more type 2 inflammatory signature genes are selected from the group consisting of IL-4, IL-13, CCL26, CCL13, CCL17. CCL11, POSTN, IL-5 and IL-9.

75. The method of any one of claims 60-74, wherein the anti-IL-33 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.

76. The method of any one of claims 60-75, wherein the anti-IL-33 antibody or antigen-binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO; 18 and a light chain comprising the amino acid sequence of SEQ ID NO: 20.

77. A method for reducing a cytokine level or a chemokine level in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-4 receptor (IL-4R) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 21, 22 and 23, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25 and 26.

78. The method of claim 77, wherein the cytokine is one or both of IL-13 and IL-5.

79. The method of claim 77 or 78, wherein the cytokine or chemokine is selected from the group consisting of TNFα, TARC, PARC, CCL1, CCL26, FCER2, SIGLEC8, CCL17 and eotaxin-3.

80. The method of any one of claims 77-79, wherein serum levels of sST2, IL-33, calcitonin or MMP12 are reduced in the subject.

81. The method of any one of claims 77-80, wherein serum levels of CCL26, CCL17 or SIGLEC8 are reduced in the subject.

82. A method for reducing expression of one or more allergic asthma signature genes in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-4 receptor (IL-4R) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID

NOs: 21, 22 and 23, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25 and 26.

83. The method of claim 82, wherein the one or more allergic asthma signature genes are selected from the group consisting of BC042385, AB209315, LOC100607117, BC035084, LOC145474, AX747853, TIMP1, NT5DC2, LOC541471, AREG, PTPN7, RUNDC3, XXYLT1, FAM159A, PTGDS, TESC, ITGB2-AS1, D0574721, CLDN9, LOC100132052, AGAP7, NBEAL2, NTNG2, FLJ45445, KCNH3, POU51P3, OUG1, KIF21B, HSPA7, GAPT, BX6485Q2, PRR52, P1K3R6, LTC4S, CLEC11A, TRABD2A, DLGAP3, VDR, DKFZp686M11215, SIGLEC12, BC016361, BC052769, and RHOH.

84. The method of claim 82 or 83, wherein the one or more allergic asthma signature genes are selected from the group consisting of ASAP1-IT1, AX747757, BC042385, PABPC1P2, AB209315, AX748268, TCEAL5, CCL17, CCL13, CCL26, CLC, CACNG8, GPR82, GATA1, PRSS33, FFAR3, LGALS12, ASB2, PTGDR2, SIGLEC8, IL13, IL5, PTGDS and RD3.

85. A method for reducing expression of any combination of type 2 inflammatory cytokine and type 2 chemokine signature genes in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-4 receptor (IL-4R) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 21, 22 and 23, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25 and 26.

86. The method of claim 85, wherein the type 2 inflammatory cytokine and chemokine signature genes are selected from the group consisting of IL-5, CCL1, IL-13, GATA2, CCL26, FCER2, CACNG8, CLC, GATA1, LGALS12, SIGLEC8, GGT5, CCL17 and MMP10.

87. The method of claim 85 or 86, wherein the one or more type 2 inflammatory cytokine and chemokine signature genes are selected from the group consisting of IL-5, CCL1, IL-13, CCL26, FCER2, SIGLEC8, GGT5 and CCL17.

88. A method for reducing expression of one or more eosinophil signature genes in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-4 receptor (IL-4R) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 21, 22 and 23, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25 and 26.

89. The method of claim 88, wherein the one or more one or more eosinophil signature genes are selected from the group consisting of IL1RL1, ADARB1, SIGLEC8, ASB2, VSTM1, SYNE1, CLC, PTPN7 and HDC.

90. A method for reducing expression of one or more type 2 inflammatory signature genes in a subject having allergic asthma, comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds interleukin-4 receptor (IL-4R) and comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 21, 22 and 23, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 24, 25 and 26.

91. The method of claim 90, wherein the one or more type 2 inflammatory signature genes are selected from the group consisting of IL-4, IL-13, CCL26, CCL13, CCL17. CCL11, POSTN, IL-5 and IL-9.

92. The method of any one of claims 77-91, wherein the 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.

93. The method of any one of claims 77-92, wherein the antibody or antigen-binding fragment thereof comprises dupilumab.

94. The method of any one of claims 60-76, further comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds IL-4R, wherein the

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

95. The method of any one of claims 77-93, further comprising administering to the subject an antibody or antigen-binding fragment thereof that specifically binds IL-33, wherein the antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining region (HCDR) sequences comprising SEQ ID NOs: 4, 6 and 8, and three light chain complementarity determining region (LCDR) sequences comprising SEQ ID NOs: 12, 14 and 16.