ANTIBODIES TARGETING IL-13 AND TSLP AND USES THEREOF

CROSS-REFERENCE

[0001] This application claims the benefit of Chinese Invention Patent Application No. 2024103926119, filed April 2, 2024, and Chinese Invention Patent Application No. 202510130727X, filed February 5, 2025, each of which is incorporated herein by reference in its entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled 70060-701_601_SL.xml, created on March 25, 2025, which is 77,784 bytes in size. The information in the electronic format of the Sequence Listing is incorporated by reference in its entirety.

SUMMARY

[0003] Disclosed herein is an antibody or an antigen-binding fragment thereof, comprising a first antigen-binding region that binds to interleukin 13 (IL-13) and a second antigen-binding region that binds to thymic stromal lymphopoietin (TSLP), wherein the first antigen-binding region comprises a first heavy chain variable region (VH1) and a first light chain variable region (VL1) and the second antigen-binding region comprises a second heavy chain variable region (VH2) and a second light chain variable region (VL2), wherein: VH1 comprises: complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 24; CDR2 comprising the amino acid sequence of SEQ ID NO: 25 or 26; and CDR3 comprising the amino acid sequence of SEQ ID NO: 27; VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. Disclosed herein is an antibody or an antigen-binding fragment thereof, comprising a first antigen-binding region that binds to IL-13 and a second antigen-binding region that binds to TSLP, wherein the first antigen-binding region comprises a VH1 and a VL1 and the second antigen-binding region comprises a VH2 and a VL2, wherein: VH1 comprises CDR1 comprising the amino acid sequence of SEQ ID NO: 24; CDR2 comprising the amino acid sequence of SEQ ID NO: 25 or 26; and CDR3 comprising the amino acid sequence of SEQ ID NO: 27; VL1 comprises CDR1, CDR2, and CDR3

comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 54, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. In some embodiments, wherein: VH1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 24, 25, and 27, respectively; VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. In some embodiments, wherein: VH1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 24, 25, and 27, respectively; VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 54, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. In some embodiments, wherein: VH1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28 or 50; or VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, wherein: VH1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28 or 50; and VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, wherein: VH1 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28 or 50; or VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33 or 51. In some embodiments, wherein: VH1 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28 or 50; and VL2 comprises an amino acid sequence as

set forth in SEQ ID NO: 33 or 51. In some embodiments, wherein: VH1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33. In some embodiments, wherein: VH1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33. In some embodiments, wherein: VH1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 33. In some embodiments, wherein: VH1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 33. In some embodiments, wherein: VH1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 33. In some embodiments, wherein: VH1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 33. In some embodiments, wherein: VH1 comprises the amino acid sequence of SEQ ID NO: 52; VL1 comprises the amino acid sequence of SEQ ID NO: 53; VH2 comprises the amino acid sequence of SEQ ID NO: 28; or VL2 comprises the amino acid sequence of SEQ ID NO: 33. In some embodiments, wherein: VH1 comprises the amino acid sequence of SEQ ID NO: 52; VL1 comprises the amino acid sequence of SEQ ID NO: 53; VH2 comprises the amino acid sequence of SEQ ID NO: 28; and VL2 comprises the amino acid sequence of SEQ ID NO: 33.

[0004] In some embodiments, wherein VH1, VL1, VH2, or VL2 comprises a charge pair mutation comprising a substitution of: an amino acid residue of positive charge with an amino acid residue of negative charge; an amino acid residue of negative charge with an amino acid residue of positive charge; a neutral amino acid residue with an amino acid residue of positive charge; or a neutral amino acid residue with an amino acid residue of negative charge, wherein the charge pair mutation increases the association between VH1 and VL1 or the association between VH2 and VL2. In some embodiments, wherein the charge pair mutation of VH1, VL1, VH2, or VL2 comprises: a substitution of glutamine (Q) with glutamic acid (E); or a substitution of glutamine (Q) with lysine (K). In some embodiments, wherein: the charge pair mutation of VH1 or VH2 comprises a substitution of glutamine (Q) with glutamic acid (E) at amino acid residue 39 according to the Kabat numbering scheme (Q39E); the charge pair mutation of VH1 or VH2 comprises a substitution of glutamine (Q) with lysine (K) at amino acid residue 39 according to the Kabat numbering scheme (Q39K); the charge pair mutation of VL1 or VL2 comprises a substitution of glutamine (Q) with lysine (K) at amino acid residue 38 according to the Kabat numbering scheme (Q38K); or the charge pair mutation of VL1 or VL2 comprises a substitution of glutamine (Q) with glutamic acid (E) at amino acid residue 38 according to the Kabat numbering scheme (Q38E). In some embodiments, wherein: the charge pair mutation of VH1 comprises Q39E; and the charge pair mutation of VL1 comprises Q38K. In some embodiments, wherein: the charge pair mutation of VH1 comprises Q39K; and the charge pair mutation of VL1 comprises Q38E. In some embodiments, wherein: the charge pair mutation of VH2 comprises Q39E; and the charge pair mutation of VL2 comprises Q38K. In some embodiments, wherein: the charge pair mutation of VH2 comprises Q39K; and the charge pair mutation of VL2 comprises Q38E. In some embodiments, wherein: the charge pair mutation of VH1 comprises Q39K; the charge pair mutation of VL1 comprises Q38E; the charge pair mutation of VH2 comprises Q39E; and the charge pair mutation of VL2 comprises Q38K. In some embodiments, wherein: the charge pair mutation of VH1 comprises Q39E; the charge pair mutation of VL1 comprises Q38K; the charge pair mutation of VH2 comprises Q39K; and the charge pair mutation of VL2 comprises Q38E. In some embodiments, the antibody or antigen-binding fragment thereof further comprises a first heavy chain comprising VH1 and a constant region comprising CH1 domain, CH2 domain, or CH3 domain, a first light chain comprising VL1 and constant (CL) domain, a second heavy chain comprising VH2 and a constant region comprising CH1 domain, CH2 domain, or CH3 domain, or a second light chain comprising VL2 and CL domain. In some embodiments, the antibody or antigen-binding fragment thereof further comprises the first heavy chain comprising VH1 and a constant region comprising CH1 domain, CH2 domain,

and CH3 domain, the first light chain comprising VL1 and CL domain, the second heavy chain comprising VH2 and a constant region comprising CH1 domain, CH2 domain, and CH3 domain, and a second light chain comprising VL2 and CL domain. In some embodiments, wherein: the CH1 domain of the first heavy chain or the CL domain of the first light chain comprises a second charge pair mutation that increases the association between the first heavy chain and the first light chain; or the CH1 domain of the second heavy chain or the CL domain of the second light chain comprises the second charge pair mutation that increases the association between the second heavy chain and the second light chain. In some embodiments, wherein the second charge pair mutation comprises a substitution of: an amino acid residue of positive charge with an amino acid residue of negative charge; an amino acid residue of negative charge with an amino acid residue of positive charge; a neutral amino acid residue with an amino acid residue of positive charge; or a neutral amino acid residue with an amino acid residue of negative charge. In some embodiments, wherein the second charge pair mutation comprises a substitution of lysine (K) with glutamic acid (E). In some embodiments, wherein the CH1 domain of the first heavy chain or the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising:a substitution of lysine (K) with glutamic acid (E) at amino acid residue 147 according to the EU numbering (K147E); or a substitution of lysine (K) with glutamic acid (E) at amino acid residue 213 according to the EU numbering (K213E). In some embodiments, wherein the CH1 domain of the first heavy chain comprises the second charge pair mutation comprising K147E and K213E. In some embodiments, the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising K147E and K213E. In some embodiments, the CH1 domain of the first heavy chain comprises the second charge pair mutation comprising K147E and K213E and the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising K147E and K213E. In some embodiments, the antibody or antigen-binding fragment thereof further comprises a fragment antigen-binding (Fab) region, a Fab', a F(ab')2, or a single chain variable fragment (scFv). In some embodiments, the antibody or antigen-binding fragment thereof further comprises a fragment crystallizable (Fc) region. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an immunoglobulin (Ig) G, IgA, IgM, IgE, or IgD. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgG1, IgG2, IgG3, or IgG4. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgG1. In some embodiments, the Fc region comprises a knob-into-hole mutation. In some embodiments, the knob-into-hole mutation comprises: a substitution of tyrosine (Y) with cysteine (C) at amino acid residue 349 according to the EU numbering (Y349C); a substitution of serine (S) with cysteine (C) at

amino acid residue 354 according to the EU numbering (S354C); a substitution of threonine (T) with tryptophan (W) at amino acid residue 366 according to the EU numbering (T366W); a substitution of threonine (T) with serine (S) at amino acid residue 366 according to the EU numbering (T366S); a substitution of threonine (T) with tyrosine (Y) at amino acid residue 366 according to the EU numbering (T366Y); a substitution of leucine (L) with alanine (A) at amino acid residue 368 according to the EU numbering (L368A); a substitution of phenylalanine (F) with alanine (A) at amino acid residue 405 according to the EU numbering (F405A); a substitution of phenylalanine (F) with tryptophan (W) at amino acid residue 405 according to the EU numbering (F405W); a substitution of tyrosine (Y) with alanine (A) at amino acid residue 407 according to the EU numbering with (Y407A); a substitution of tyrosine (Y) with threonine (T) at amino acid residue 407 according to the EU numbering with (Y407T); or a substitution of tyrosine (Y) with valine (V) at amino acid residue 407 according to the EU numbering with (Y407V). In some embodiments, the Fc region of the first heavy chain comprises the knob-into-hole mutation comprising T366S, L368A, and Y407V; and the Fc region of the second heavy chain comprises the knob-into-hole mutation comprising T366W. In some embodiments, the Fc region of the first heavy chain comprises the knob-into-hole mutation comprising Y349C, T366S, L368A, and Y407V; and the Fc region of the second heavy chain comprises the knob-into-hole mutation comprising S354C and T366W. In some embodiments, the Fc region comprises a second amino acid mutation that increases the half-life of the antibody or antigen-binding fragment thereof. In some embodiments, the second amino acid mutation increases the binding of the antibody or antigen-binding fragment thereof to neonatal Fc receptor (FcRn). In some embodiments, the Fc region comprises a third amino acid mutation that reduces the binding affinity of the antibody or antigen-binding fragment thereof to Fc-gamma receptor (FcγR) or complement component 1q (C1q). In some embodiments, the second amino acid mutation comprises: a substitution of methionine (M) with leucine (L) at amino acid residue 428 according to the EU numbering (M428L); or a substitution of asparagine (N) with alanine (A) at amino acid residue 434 according to the EU numbering (N434A). In some embodiments, the second amino acid mutation comprises M428L and N434A. In some embodiments, the Fc region of the first heavy chain comprises the second amino acid mutation comprising M428L or N434A; and the Fc region of the second heavy chain comprises the second amino acid mutation comprising M428L or N434A. In some embodiments, the Fc region of the first heavy chain comprises the second amino acid mutation comprising M428L and N434A; and the Fc region of the second heavy chain comprises the second amino acid mutation comprising M428L and N434A. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ

ID NO: 42; the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 42; the first light chain comprises the amino acid sequence of SEQ ID NO: 44; the second heavy chain comprises the amino acid sequence of SEQ ID NO: 38; or the second light chain comprises the amino acid sequence of SEQ ID NO: 40. In some embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 42; the first light chain comprises the amino acid sequence of SEQ ID NO:

44; the second heavy chain comprises the amino acid sequence of SEQ ID NO: 38; and the second light chain comprises the amino acid sequence of SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 60; the first light chain comprises the amino acid sequence of SEQ ID NO: 61; the second heavy chain comprises the amino

acid sequence of SEQ ID NO: 66; or the second light chain comprises the amino acid sequence of SEQ ID NO: 67. In some embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 60; the first light chain comprises the amino acid sequence of SEQ ID NO: 61; the second heavy chain comprises the amino acid sequence of SEQ ID NO: 66; and the second light chain comprises the amino acid sequence of SEQ ID NO: 67.

[0005] In some embodiments, the antibody or antigen-binding fragment thereof comprises a multispecific antibody or antigen binding fragment thereof. In some embodiments, the multispecific antibody or antigen-binding fragment thereof comprises a bispecific antibody or antigen binding fragment thereof. In some embodiments, the antibody or antigen-binding fragment thereof has a technical advantage, technical effect, and/or a technical improvement compared with a second antibody or an antigen-binding fragment thereof that binds to IL-13, TSLP, or IL-13 and TSLP. In some embodiments, the second antibody that binds to IL-13, TSLP, or IL-13 and TSLP comprises Lunsekimig or an analog thereof, Lebrikizumab or an analog thereof, or Tezepelumab or an analog thereof. In some embodiments, the technical advantage, technical effect, and/or technical improvement includes or relates to therapeutic activity, stability, immunogenicity, affinity, toxicity, potency, specificity, pharmacokinetics, pharmacodynamics, or a property not exhibited by the second antibody or antigen-binding fragment thereof that binds to IL-13, TSLP, or IL-13 and TSLP. In some embodiments, the technical advantage, technical effect, and/or a technical improvement includes or relates to a binding affinity to IL-13, TSLP, or IL-13 and TSLP, an ability to inhibit IL-13-mediated biological activity, an ability to inhibit TSLP-mediated biological activity, or an ability to inhibit a biological activity mediated by IL-13 and TSLP. In some embodiments, the technical advantage, technical effect, and/or technical improvement includes or relates to a reduced immunogenicity, an increased stability, an increased binding affinity to IL-13, TSLP, or IL-13 and TSLP, an increased ability to inhibit IL-13-mediated activation of STAT6, an increased ability to inhibit IL-13-mediated cell proliferation, an increased ability to inhibit TSLP-mediated thymus and activation regulated chemokine (TARC) release, an increased ability to inhibit TSLP-mediated cell proliferation, an increased ability to inhibit TSLP-mediated activation of STAT5, an increased ability to inhibit IgE production, an increased ability to inhibit an inflammatory or allergic response, a reduced dosing frequency, an increased ability to inhibit cytokine production, a better therapeutic effect on an allergic or inflammatory disease, an increased serum half-life, an increased thermostability, an increased binding affinity to a neonatal Fc receptor (FcRn), a reduced binding affinity to a Fc-gamma receptor (FcγR), or a reduced binding affinity to complement component 1q (C1q).

[0006] Disclosed herein is a nucleic acid molecule encoding the antibody or antigen-binding fragment thereof disclosed herein. In some embodiments, the nucleic acid molecule comprises: a first nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 29; a second nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 34; a third nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 55; or a fourth nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises: the first nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises: the first nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 55 or the fourth nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises: the first nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises: the first nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises: the first nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises: the first nucleic acid sequence set forth in SEQ ID NO: 29; the second nucleic acid sequence set forth in SEQ ID NO: 34; the third nucleic acid sequence set forth in SEQ ID NO: 55; or the fourth nucleic acid sequence set forth in SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises: the first nucleic acid sequence set forth in SEQ ID NO: 29; the second nucleic acid sequence set forth in SEQ ID NO: 34; the third nucleic acid sequence set forth in SEQ ID NO: 55; and the fourth nucleic acid sequence set forth in SEQ ID NO: 56. In some embodiments, the nucleic

acid molecule comprises: a first nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 39; a second nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 41; a third nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 43; or a fourth nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises: the first nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises: the first nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises: the first nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises: the first nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises: the first nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises: the first nucleotide sequence set forth in SEQ ID NO: 39; the second nucleotide sequence set forth in SEQ ID NO: 41; the third nucleotide sequence set forth in SEQ ID NO: 43; or the fourth nucleotide sequence set forth in SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises: the first nucleotide sequence set forth in SEQ ID NO: 39; the second nucleotide sequence set forth in SEQ ID NO: 41; the third nucleotide sequence set forth in SEQ ID NO: 43; and the fourth nucleotide sequence set forth in SEQ ID NO: 45. Disclosed herein is a vector comprising the nucleic acid molecule disclosed herein. Disclosed herein is a host cell comprising the nucleic acid molecule disclosed herein or the vector disclosed herein.

[0007] Disclosed herein is a pharmaceutical composition comprising (i) the antibody or antigen-binding fragment thereof disclosed herein; and (ii) a pharmaceutically acceptable carrier or excipient. In some embodiments, the pharmaceutical composition further comprises a second therapeutic agent. In some embodiments, the second therapeutic agent is selected from the group comprising an antibody, a chemotherapeutic agent, and a small molecule drug. Disclosed herein is a conjugate comprising the antibody or antigen-binding fragment thereof disclosed herein, and a chemical moiety conjugated thereto. In some embodiments, the chemical moiety is selected from a group comprising a therapeutic agent, a detectable moiety, and an immunostimulatory molecule.

[0008] Disclosed herein is a method for treating a disease in a subject, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein. In some embodiments, the disease comprises an inflammatory disease, an autoimmune disease, or an allergic disease. In some embodiments, the disease comprises a type 2 inflammatory response-related disease. In some embodiments, the disease comprises an IL-13 mediated disease, a TSLP mediated disease, or both. In some embodiments, the disease is selected from the group comprising atopic dermatitis, allergic inflammation, asthma, urticaria, chronic obstructive pulmonary disease, eosinophilic esophagitis, rheumatoid arthritis, multiple sclerosis, idiopathic pulmonary fibrosis, eczema, eosinophilic gastroenteritis, Crohn's disease, systemic sclerosis, ulcerative colitis, and chronic rhinosinusitis with nasal polyps. In some embodiments, the disease is selected from the group comprising allergic rhinitis, allergic sinusitis, allergic conjunctivitis, hand eczema, and asthmatic eczema. In some embodiments, the method further comprises administering a second therapeutic agent to the subject. In some embodiments, the second therapeutic agent is selected from a group comprising an antibody, a chemotherapeutic agent, and a small molecule drug. Disclosed herein is a method for inhibiting or eliminating IgE in a subject, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein. In some embodiments, the subject is human.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosure will be obtained by reference to the following detailed description that sets forth exemplary embodiments, in which the principles of the present disclosure are utilized, and the accompanying drawings below:

[0010] Fig. 1A shows an exemplary structure of the anti-TSLP/IL-13 bispecific antibody TSLP/IL-13 BsAb disclosed herein.

[0011] Figs. 1B-1O show the detection results of binding affinities of 228B/C-1 humanized antibodies in transient supernatants to hIL-13.

[0012] Figs. 2A-2C show the results of activities of 228B/C-1 humanized antibodies inhibiting hIL-13-induced STAT6 activation. Therein, A: the activity of H1K1 inhibiting hIL-13-induced STAT6 activation; B: the activity of H2K1 inhibiting hIL-13-induced STAT6 activation; and C: the activity of H3K1 inhibiting hIL-13-induced STAT6 activation.

[0013] Fig. 3 shows the results of activity of 228B/C-1 humanized antibody H3K1 inhibiting hIL-13-induced TF-1 cell proliferation.

[0014] Fig. 4 shows the results of activity of 228B/C-1 humanized antibody H3K1 inhibiting hIL-13-induced release of TARC from PBMCs.

[0015] Figs. 5A-5C show that TSLP/IL-13 BsAb inhibits hTSLP induction. Therein, A: the activity of TSLP/IL-13 BsAb inhibiting hTSLP-induced STAT5 activation; B: the activity of TSLP/IL-13 BsAb inhibiting hTSLP-induced Ba/f3- TSLPR-IL7Rα cell proliferation; and C: the activity of TSLP/IL-13 BsAb inhibiting hTSLP-induced release of TARC from PBMCs.

[0016] Figs. 6A-6C show that TSLP/IL-13 BsAb inhibits hIL-13 induction. Therein, A: the activity of TSLP/IL-13 BsAb inhibiting hIL-13-induced STAT6 activation; B: the activity of TSLP/IL-13 BsAb inhibiting hIL-13-induced TF-1 cell proliferation; and C: the activity of TSLP/IL-13 BsAb inhibiting hIL-13-induced release of TARC from PBMCs.

[0017] Fig. 7 shows that TSLP/IL-13 BsAb inhibits hTSLP + hIL-13-induced release of TARC from PBMCs.

[0018] Figs. 8A-8C show the in vivo efficacy results of TSLP/IL-13 BsAb in an MC903-induced hTSLP/TSLPR humanized mouse dermatitis model. Therein, A: the influence of TSLP/IL-13 BsAb on the change of the ear thickness of hTSLP/TSLPR humanized mice; B: the influence of TSLP/IL-13 BsAb on the serum IgE level in hTSLP/TSLPR humanized mice; and C: the influence of TSLP/IL-13 BsAb and ref2 nanobody on the change of the ear thickness of hTSLP/TSLPR humanized mice.

[0019] Figs. 9A-9B shows the in vivo efficacy results of TSLP/IL-13 BsAb in an MC903-induced hIL-13 humanized mouse dermatitis model. Therein, A: the influence of TSLP/IL-13 BsAb on the change of the ear thickness of hIL-13 humanized mice; and B: the influence of TSLP/IL-13 BsAb on the serum IgE level in hIL-13 humanized mice.

[0020] Fig. 10 shows the results of the influence of TSLP/IL-13 BsAb on body weight in a B-hIL13 mouse asthma model. Data are shown as mean ± SEM, n = 6; Dunnett's test was performed after one-way ANOVA.

[0021] Fig. 11 shows the results of the influence of TSLP/IL-13 BsAb on the number of nose scratching and the number of sneezes in the B-hIL13 mouse asthma model. Data are shown as mean ± SEM, n = 6; ## $P < 0.01$, #### $P < 0.001$ compared with a control group; * $P < 0.05$, ** $P < 0.05$ compared with model groups; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

[0022] Figs. 12A-12B shows the results of the influence of TSLP/IL-13 BsAb on airway hyperresponsiveness in the B-hIL13 mouse asthma model. Data are shown as mean ± SEM, n = 6; # $P < 0.05$ compared with a control group; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

[0023] Fig. 13 shows the results of the influence of TSLP/IL-13 BsAb on the number of inflammatory cells in the airway BALF in the B-hIL13 mouse asthma model. Data are shown as mean ± SEM, n = 6; # $P < 0.05$, ## $P < 0.01$, ### $P < 0.001$ compared with a control group; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared with model groups; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

[0024] Fig. 14 shows the results of the influence of TSLP/IL-13 BsAb on the serum total IgE and OVA-sIgE levels in the B-hIL13 mouse asthma model. Data are shown as mean ± SEM, n = 6; ## $P < 0.01$ compared with a control group; * $P < 0.05$ compared with model groups; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

[0025] Fig. 15 shows a pathological diagram of eosinophil infiltration into the lung tissue in the B-hIL13 mouse asthma model by TSLP/IL-13 BsAb. Data are shown as mean ± SEM, n = 6. #### $P < 0.001$, compared with a control group; * $P < 0.05$, compared with model groups. Dunnett's test was performed after One-way ANOVA.

[0026] Fig. 16 shows the results of the influence of TSLP/IL-13 BsAb on the pathological scores of H&E staining of lung tissues in the B-hIL13 mouse asthma model. Data are shown as mean ± SEM, n = 6. ### $P < 0.001$, compared with a control group; * $P < 0.05$, compared with model groups. Dunnett's test was performed after One-way ANOVA.

[0027] Fig. 17 shows the results of the influence of TSLP/IL-13 BsAb on the metaplastic proliferation of airway goblet epithelial cells in the B-hIL13 mouse asthma model, wherein green arrows denote goblet epithelial cell positive expression and green circles denote mucus secretion.

Data are shown as mean ± SEM, n = 6; ## P < 0.01 compared with a control group; ** P < 0.01 compared with model groups; Mann-Whitney U test was performed after one-way ANOVA.

[0028] Fig. 18 shows the results of the influence of TSLP/IL-13 BsAb on the number of lung tissue mast cells and degranulation in the B-hIL13 mouse asthma model, wherein green arrows denote degranulated cells. Data are shown as mean ± SEM, n = 6; ## P < 0.01 compared with a control group; ** P < 0.01 compared with model groups; Mann-Whitney U test was performed after one-way ANOVA.

[0029] Figs. 19A-19B show the results of the influence of TSLP/IL-13 BsAb on the degranulation rate of lung tissue mast cells in the B-hIL13 mouse asthma model. Data are shown as mean ± SEM, n = 6; # P < 0.05 compared with a control group; ** P < 0.01 compared with model groups; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

[0030] Figs. 20A-20C show the results of the influence of TSLP/IL-13 BsAb on the increase of the ear thickness and mouse body weight in an MC903-induced B-hIL-13 mouse dermatitis model. One-way ANOVA analysis, #### P < 0.0001 compared with a control group; ** P < 0.01 compared with model groups.

[0031] Figs. 21A-21B show the results of the influence of TSLP/IL-13 BsAb on ear skin lesions in the MC903-induced B-hIL-13 mouse dermatitis model. One-way ANOVA analysis, #### P < 0.0001 compared with a control group; **** P < 0.0001 compared with model groups.

[0032] Fig. 22 shows the results of the influence of TSLP/IL-13 BsAb on the serum total IgE level in the MC903-induced B-hIL-13 mouse dermatitis model. One-way ANOVA analysis.

[0033] Figs. 23A-23C show the results of the influence of TSLP/IL-13 BsAb on the ear thickness of the right ear in an MC903-induced B-hTSLP/hTSLPR mouse dermatitis model. One-way ANOVA analysis, #### P < 0.0001, compared with a control group, and ** P < 0.01, compared with model groups.

[0034] Fig. 24 shows that TSLP/IL-13 BsAb inhibits hTSLP-induced STAT5 activation.

[0035] Fig. 25 shows that TSLP/IL-13 BsAb inhibits hTSLP-induced Ba/f3-TSLPR-IL7Rα cell proliferation.

[0036] Fig. 26 shows the thermal stability assay profile of TSLP/IL-13 BsAb.

[0037] Fig. 27 shows the results of the influence of TSLP/IL-13 BsAb on TSLP-induced TARC release from PBMCs.

[0038] Fig. 28 shows the results of the influence of TSLP/IL-13 BsAb on TSLP + IL-13-induced TARC release from PBMCs.

[0039] Fig. 29 shows the results of immunogenicity of TSLP/IL-13 BsAb.

[0040] Fig. 30 shows the results of the influence of TSLP/IL-13 BsAb on mouse body weight in an OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

[0041] Figs. 31A-31B show that TSLP/IL-13 BsAb reduces the number of mouse nose scratching and sneezing in the OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a control group: ###P < 0.001; compared with model groups: *P < 0.05, **P < 0.01, ***P < 0.001.

[0042] Figs. 32A-32B shows the results of the influence of TSLP/IL-13 BsAb on alleviation of airway hyperresponsiveness in the OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a control group: ##P < 0.01, ####P < 0.001; compared with model groups: *P < 0.05, **P < 0.01, ***P < 0.001.

[0043] Fig. 33 shows that TSLP/IL-13 BsAb reduces the number of inflammatory cells in BALF in the OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 11 - 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a control group: ###P < 0.001; compared with model groups: *P < 0.05, **P < 0.01, ***P < 0.001.

[0044] Fig. 34 shows that TSLP/IL-13 BsAb reduces total IgE and OVA-sIgE levels in serum in the OVA-induced B-hTSLP/hTSLPW mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a blank control group: ###P < 0.001; compared with a model control group: *P < 0.05, **P < 0.01, ***P < 0.001. Serum OVA-sIgE levels on Day 20 and Day 28 are represented as OD values, and serum assays of the mice in the control group all showed negative (< Reference), and serum assays of the mice in the model group, TSLP/IL-13 BsAb (3, 10, and 30 mg/kg) group and KLH (30 mg/kg) group all showed positive (> Reference).

[0045] Fig. 35 shows that TSLP/IL-13 BsAb inhibits h-TSLP and MUC5AC mRNA expression in the lung tissue in the OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a control group: ###P < 0.001; compared with model groups: *P < 0.05, **P < 0.01.

[0046] Fig. 36 shows the results of the influence of TSLP/IL-13 BsAb on the inflammation scores of H&E-staining of lung tissues in the OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a control group: ###P < 0.001; compared with model groups: **P < 0.01.

[0047] Fig. 37 shows a pathological diagram of TSLP/IL-13 BsAb inhibiting eosinophilic infiltration into the lung tissue in the OVA-induced B-hTSLP/hTSLPR mice asthma model.

[0048] Fig. 38 shows the results of the influence of TSLP/IL-13 BsAb on the airway goblet epithelial cell positive rate in the OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a control group: ###P < 0.001; compared with model groups: *P < 0.05, **P < 0.01.

[0049] Fig. 39 shows a pathological diagram of TSLP/IL-13 BsAb reducing airway goblet epithelial cell metaplastic proliferation in the OVA-induced B-hTSLP/hTSLPR mouse asthma model.

[0050] Fig. 40 shows the results of the influence of TSLP/IL-13 BsAb on the degranulation rate of mast cells of the lung tissue in the OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a control group: ###P < 0.001; compared with model groups: *P < 0.05, **P < 0.01.

[0051] Fig. 41 shows a pathological diagram of TSLP/IL-13 BsAb inhibiting mast cell degranulation in lung tissues in the OVA-induced B-hTSLP/hTSLPR mouse asthma model.

[0052] Fig. 42 shows the results of the influence of TSLP/IL-13 BsAb on the positive rate of peri-airway collagen deposition in lung tissues in the OVA-induced B-hTSLP/hTSLPR mouse asthma model. Data are shown as mean ± SEM, n = 12; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. Compared with a control group: ###P < 0.001; compared with model groups: *P < 0.05, **P < 0.01.

[0053] Fig. 43 shows a pathological diagram of TSLP/IL-13 BsAb reducing peri-airway collagen deposition in lung tissues in the OVA-induced B-hTSLP/hTSLPR mouse asthma model.

[0054] Fig. 44 shows the influence of TSLP/IL-13 BsAb on the body weight of mice in the MC903-induced B-hTSLP/hTSLPR mouse dermatitis model. Data are shown as mean ± SEM, n = 11; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

[0055] Fig. 45 shows the inhibitory effect of TSLP/IL-13 BsAb on the increase of the ear thickness in the MC903-induced B-hTSLP/hTSLPR mice. Data are shown as mean ± SEM, n = 11; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. One way ANOVA, compared with a control group, ####P < 0.0001, compared with model groups, *P < 0.05, ****P < 0.0001.

[0056] Fig. 46 shows the inhibitory effect of TSLP/IL-13 BsAb on skin lesions in the MC903-induced B-hTSLP/hTSLPR mice. Data are shown as mean ± SEM, n = 11; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. One way ANOVA, compared with a control group, ####P < 0.0001; compared with model groups, ****P < 0.0001.

[0057] Fig. 47 shows that TSLP/IL-13 BsAb inhibits lymph node enlargement on the drainage side of the right ear in B-hTSLP/hTSLPR mice. Data are shown as mean ± SEM, n = 11; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. One way ANOVA, compared with a control group, ####P < 0.0001; compared with model groups, ***P < 0.001, ****P < 0.0001.

[0058] Fig. 48 shows that TSLP/IL-13 BsAb reduces the serum total IgE level in the MC903-induced B-hTSLP/hTSLPR mice. Data are shown as mean ± SEM, n = 11; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. One way ANOVA, ##P < 0.01 compared with a control group; *P < 0.05 compared with model groups.

[0059] Fig. 49 shows that TSLP/IL-13 BsAb inhibits the expression of cytokines in ear tissues of the MC903-induced B-hTSLP/hTSLPR mice. Data are shown as mean ± SEM, n = 11; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. One way ANOVA, ###P < 0.001, ####P < 0.0001, compared with a control group; compared with model groups, ***P < 0.001, ****P < 0.0001.

[0060] Fig. 50 shows a pathological diagram of TSLP/IL-13 BsAb reducing the inflammation scores of ear tissues in the MC903-induced B-hTSLP/hTSLPR mice. Data are shown as mean ± SEM, n = 11; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA. One way ANOVA, ####P < 0.0001 compared with a control group; compared with model groups, *P < 0.05, **P < 0.01, ***P < 0.001.

[0061] Fig. 51 shows that TSLP/IL-13 BsAb CM512 reduces the inflammation scores of ear tissues in the MC903-induced B-hTSLP/hTSLPR mice. Data are shown as mean ± SEM, n = 11; Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way

ANOVA. One way ANOVA, ####P < 0.0001 compared with a control group; compared with model groups, *P < 0.05, **P < 0.01, ***P < 0.001.

[0062] Figs. 52A-52B show a Biacore sensorgram of TSLP/IL-13 BsAb binding to FcγRI.

[0063] Figs. 53A-53B show a Biacore sensorgram of TSLP/IL-13 BsAb binding to FcγRIIAH131.

[0064] Figs. 54A-54B show a Biacore sensorgram of TSLP/IL-13 BsAb binding to FcγRIIB.

[0065] Figs. 55A-55B show a Biacore sensorgram of TSLP/IL-13 BsAb binding to FcγRIIIAV158.

[0066] Figs. 56A-56B show a Biacore sensorgram of TSLP/IL-13 BsAb binding to FcγRIIIAF158.

[0067] Figs. 57A-57B show a Biacore sensorgram of TSLP/IL-13 BsAb binding to FcRn at pH 7.4.

[0068] Figs. 58A-58B show a Biacore sensorgram of TSLP/IL-13 BsAb binding to FcRn at pH 6.0.

[0069] Figs. 59A-59B show a Biacore sensorgram of TSLP/IL-13 BsAb binding to C1q.

[0070] Fig. 60 shows the activity of TSLP/IL-13 BsAb binding to IL-13 of different species.

[0071] Fig. 61 shows the activity of Anti-KLH hIgG1 binding to IL-13 of different species.

[0072] Fig. 62 shows the activity of TSLP/IL-13 BsAb binding to TSLP of different species.

[0073] Fig. 63 shows the activity of Anti-KLH hIgG1 binding to TSLP of different species.

[0074] Fig. 64 shows the activity of TSLP/IL-13 BsAb blocking IL-13/IL-13Rα1 complex from binding to IL-4Rα.

[0075] Fig. 65 shows the activity of TSLP/IL-13 BsAb blocking TSLP from binding to TSLPR.

[0076] Fig. 66 shows the activity of TSLP/IL-13 BsAb blocking TSLP from binding to cell surface TSLPR.

DETAILED DESCRIPTION OF THE INVENTION

[0077] The foregoing features and advantages of the present invention and additional features and advantages thereof will be more clearly understood hereinafter by referring to the accompanying drawings and the detailed description of the following embodiments.

[0078] The embodiments described herein with reference to the accompanying drawings are explanatory, exemplary, and intended for a general understanding of the invention. The embodiments should not be construed as limiting the scope of the present invention. Identical or similar elements and elements having the same or similar function are denoted throughout the specification with the same reference numerals.

[0079] Thymic Stromal Lymphopoietin (TSLP) is a cytokine of the Interleukin-7 (IL-7) family, is mainly secreted by epithelial cells, and is a key cytokine for regulating type 2 inflammatory responses, and it acts on a variety of cells, such as dendritic cells (DC), T cells, B cells, mast cells, basophils and eosinophils, and is involved in regulating cell proliferation and activation, and the like.

Epithelial cells secrete cytokines such as TSLP, Interleukin-25 (IL-25) and Interleukin-33 (IL-33) after stimulation by allergens or pathogens, and TSLP acts directly on DC cells and induces DC cells to express OX40L (also known as CD252 or TNFSF4), which in turn promotes naive T cells to differentiate into pro-inflammatory Th2 cells and secret cytokines such as Interleukin-4 (IL-4), Interleukin-5 (IL-5) and Interleukin-13 (IL-13); meanwhile, TSLP can also directly act on Type 2 innate lymphoid cells (ILC2) to secrete IL-5 and IL-13 and enhance Type 2 inflammatory responses. In addition, TSLP is also involved in the regulation of non-Type 2 inflammatory responses. TSLP can induce DC cells to secrete cytokines Interleukin-6 (IL-6) and Interleukin-23 (IL-23), both of which are crucial for the differentiation of naive T cells into Th17 cells.

[0080] IL-13 is one of the core cytokines for the type 2 inflammatory response and is mainly secreted by cells such as Th2, ILC2, mast cells, B cells, and macrophages. IL-13 activates downstream signaling by binding to a receptor complex consisting of IL-13Rα1 and IL-4Rα, and its receptors are expressed on cells such as B cells, mast cells, eosinophils, monocytes, epithelial cells, fibroblasts, and smooth muscle cells. In addition, IL-13 can also bind to IL-13Rα2, which has no obvious intracellular signaling domain and is considered to be a decoy receptor for IL-13. IL-13 can induce B cell proliferation and secretion of IgE and promote recruitment and activation of eosinophils. IL-13 can also act on endothelial cells, smooth muscle cells, fibroblasts, epithelial cells, and the like, and initiate goblet cell proliferation, increased mucus secretion, tissue remodeling, etc.

[0081] Currently, Tezepelumab, an antibody targeting TSLP, has been approved for the treatment of asthma patients; and Tralokinumab and Lebrikizumab, antibodies targeting IL-13, have been approved for the treatment of atopic dermatitis patients. However, there are still many patients who respond poorly or do not respond to these treatments. Targeting both TSLP and IL-13 is promising to provide a more effective treatment option for patients with diseases associated with inflammatory responses.

[0082] Provided herein are a bispecific antibody against IL-13 and TSLP and use thereof, particularly a monoclonal antibody against IL-13, a bispecific antibody against IL-13 and TSLP, a nucleic acid comprising a nucleotide sequence encoding the antibody, a vector comprising the nucleic acid, and a host cell comprising the nucleic acid or the vector. Also disclosed are a pharmaceutical composition and a conjugate comprising the antibody, and a method of treatment by using the antibody.

[0083] In the present invention, scientific and technical terms used herein have the meanings as generally understood by those skilled in the art, unless otherwise indicated. Moreover, the terms and laboratory procedures related to protein and nucleic acid chemistry, molecular biology, cell and

tissue culture, microbiology, immunology, as used herein, are all terms and routine procedures widely used in the respective fields. Meanwhile, for a better understanding of the present invention, definitions and explanations of relevant terms are provided below.

[0084] ***Definitions***

[0085] As used herein, the singular forms "an," "a," and "the" include plural objects unless the context clearly indicates otherwise. Thus, for example, references to "an antibody" include plural antibodies and, in some embodiments, references to "an antibody" include multiple antibodies, and the like.

[0086] Unless otherwise indicated or defined, the term "comprising" and variants thereof such as "including" and "containing" should be understood to mean including the indicated elements or steps or element groups or step groups, without excluding any other elements or steps or element groups or step groups.

[0087] As used herein, the term "antibody" refers to an immunoglobulin molecule that has the ability to bind specifically to a particular antigen. Such molecules typically comprise two heavy (H) chains and two light (L) chains interconnected by disulfide bonds. Each heavy chain consists of a heavy chain variable region (or domain) (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region consists of three domains CH1, CH2 and CH3. Each light chain consists of a light chain variable region (or domain) (abbreviated herein as VL) and a light chain constant region. The light chain constant region consists of a domain CL. The variable regions of the antibody heavy and light chains contain binding domains that interact with antigens. The constant region of the antibody can mediate the binding of the immunoglobulin to host tissue or factors, which include various cells of the immune system (e.g., effector cells) and components of the complement system such as C1q (a first component of the classical pathway of complement activation).

[0088] The heavy chain of the immunoglobulin can be divided into three functional regions: a Fd region, a hinge region, and a Fc region (a crystallizable fragment.) The Fd region contains VH and CH1 domains and binds to the light chain to form a Fab (an antigen-binding fragment). The Fc fragment is responsible for immunoglobulin effector functions, including, for example, complement binding and binding to the homologous Fc receptor of effector cells. The hinge region found in the IgG, IgA and IgD immunoglobulin classes acts as a flexible spacer, allowing the Fab portion to move freely in space relative to the Fc region. The hinge domains are structurally diverse, varying in both sequence and length between immunoglobulin classes and subclasses.

[0089] Based on crystallographic studies, the immunoglobulin hinge region can be further subdivided structurally and functionally into three regions: an upper hinge, a core hinge, and a lower hinge. The upper hinge includes the amino acids from the carboxyl terminus of CH1 to the first residue restricting movement in the hinge, generally the first cysteine residue that forms an interchain disulfide bond between the two heavy chains. The length of the upper hinge region is associated with the fragment flexibility of the antibody. The core hinge region contains the disulfide bond between the heavy chains. The lower hinge region connects the amino terminus of the CH2 domain and includes residues in the CH2 domain. Conformational changes allowed by the structure and flexibility of the polypeptide sequence in the hinge region of immunoglobulins can affect the effector functions of the Fc portion of the antibody.

[0090] The "Light Chain Variable Region" (VL) or "Heavy Chain Variable Region" (VH) consists of "framework" regions separated by three "Complementarity-Determining Regions" or "CDRs." The framework regions are used to align CDRs that specifically bind to antigenic epitopes. CDRs comprise amino acid residues in the antibody that are primarily responsible for antigen binding. Both the VL and VH domains contain the following framework regions (FR) and CDR regions from the amino terminus to the carboxyl terminus: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4. CDR1, CDR2, and CDR3 of the VL domain are also referred to herein as LCDR1, LCDR2, and LCDR3, respectively; and CDR1, CDR2, and CDR3 of the VH domain are also referred to herein as HCDR1, HCDR2, and HCDR3, respectively.

[0091] The amino acid arrangement of each of the VL domain and the VH domain is consistent with any conventional definition of CDR. Conventional definitions include the Kabat definition (Kabat, Sequences of Proteins of Immunological Interest (National Institutes of Health, Bethesda, MD, 1987 and 1991)), the Chothia definition (Chothia and Lesk, J. Mol. Biol. 196:901-917, 1987; Chothia et al., Nature 342:878-883, 1989); and a composite of the Chothia Kabat CDR, wherein CDR-H1 is a composite of the Chothia CDR and the Kabat CDR; AbM definition used by Oxford Molecular's antibody modeling software; and the CONTACT definition of Martin et al. (world wide web bioinfo.org.uk/abs). Kabat provides a widely used numbering convention (Kabat numbering system), wherein the corresponding residues between different heavy chains or between different light chains are assigned the same numberings. The present disclosure may use CDRs defined according to any one of these numbering systems, but preferred embodiments use Kabat-defined CDRs.

[0092] Based on the amino acid sequences of the constant regions of the heavy chains of antibodies, immunoglobulin molecules can be classified into five types (isotypes): IgA, IgD, IgE, IgG, and IgM, and can be further classified into different subtypes, e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2.

Based on the amino acid sequences of the light chains, the light chains of antibodies can be categorized into lambda (λ) chains and kappa (κ) chains.

[0093] As used herein, the term "antibody" should be understood in its broadest sense and includes monoclonal antibodies (including full-length monoclonal antibodies), antibody fragments, and multispecific antibodies (e.g., bispecific antibodies) containing at least two antigen-binding regions. Antibodies may contain additional modifications, such as non-naturally occurring amino acids, mutations in the Fc region, and mutations in glycosylation sites. Antibodies also include post-translationally modified antibodies, fusion proteins containing the antigenic determinants of antibodies, and immunoglobulin molecules containing any other modifications to the antigen recognition sites, as long as these antibodies exhibit desired biological activities.

[0094] As used herein, the term "monoclonal antibody" refers to an antibody obtained from a substantially homogeneous population of antibodies. I.e., except a few naturally occurring possible mutations, each antibody constituting the population is identical. Monoclonal antibodies are highly specific and directed against a single antigen. The term "monoclonal antibody" herein is not limited to antibodies produced by hybridoma technology and also should not be construed as requiring antibodies produced by any particular methods.

[0095] The term "bispecific antibody" should be understood in the context of the present invention to mean an antibody having two different antigen-binding regions defined by different antibody sequences. This can be understood as binding to different targets, but also includes binding to different epitopes of one target. The term "bispecific antibody" as used herein should be understood in its broadest sense, including full-length bispecific antibodies and antigen-binding fragments thereof. Bispecific antibodies may contain additional modifications such as non-naturally occurring amino acids, mutations in the Fc region, and mutations in glycosylation sites. Bispecific antibodies also include post-translationally modified antibodies, fusion proteins containing antigenic determinants of antibodies, and immunoglobulin molecules containing any other modifications to the antigen recognition sites, as long as these antibodies exhibit desired biological activities.

[0096] As used herein, the term "antigen-binding fragment" of an antibody refers to one or more fragments of an antibody that retain the ability to specifically bind to the antigen. It has been shown that the antigen-binding function of an antibody can be implemented by a fragment of a full-length antibody.

[0097] Examples of antigen-binding fragments covered by the term "antigen-binding portion" of an antibody include: (i) Fab fragments, which are monovalent fragments consisting of VL, VH, CL and CH1 domains; (ii) $F(ab')_2$ fragments, which are bivalent fragments comprising two Fab fragments

linked by a disulfide bond in the hinge region; (iii) Fab' fragments, which are essentially Fab having a partial hinge region; (iv) Fd fragments, which consist of VH and CH1 domains; (v) Fd' fragments, which have VH and CH1 domains and one or more cysteine residues at the C-terminus of the CH1 domain; (vi) Fv fragments, which consist of VL and VH domains of a single arm of the antibody; (vii) dAb fragments, which consist of a VH domain; (viii) isolated complementarity-determining regions (CDR); and (ix) nanobodies, heavy chain variable regions comprising a single variable domain and two constant domains. In addition, although the two VL and VH domains of the Fv fragment are encoded by different genes, recombinant methods may be used to connect them via a synthetic linker to enable them to be made into a single protein chain in which the VL and VH regions are paired up to form a monovalent molecule (referred to as single-chain Fv (scFv)). Such single-chain antibodies are also intended to be encompassed within the term "antigen-binding fragment" of an antibody. In addition, the term also includes "straight chain antibodies" comprising a pair of tandem Fd fragments (VH-CH1-VH-CH1), which together with a complementary light chain polypeptide form an antigen-binding region, as well as modified forms of any of the foregoing fragments which retain antigen-binding activities.

[0098] These antigen-binding fragments can be obtained by using conventional techniques known to those skilled in the art, and the fragments are screened for efficacy in the same manner as intact antibodies.

[0099] As used herein, the term "binding" or "specifically binding" refers to a non-random binding reaction between two molecules such as an antibody and its target antigen. The binding specificity of an antibody can be determined based on affinity and/or avidity. Affinity represents an equilibrium constant of antigen-antibody dissociation (KD) and is a measure of the strength of binding between an antigenic determinant and an antigen-binding site of an antibody: the smaller the value of KD, the stronger the strength of binding between the antigenic determinant and the antibody. Alternatively, affinity can also be represented as an affinity constant (KA), which is 1/KD.

[00100] Avidity is a measure of the strength of binding between an antibody and a relevant antigen. Avidity relates to affinity between an antigenic determinant and an antigen-binding site of an antibody as well as the number of relevant binding sites present on the antibody. Typically, while binding to an antigen, an antibody will bind to the antigen with a dissociation constant (KD) as follows: 10^{-5} M to 10^{-12} M or less, and preferably 10^{-7} M to 10^{-12} M or less, and more preferably 10^{-8} M to 10^{-12} M, and/or with binding affinities as follows: at least 10^{7} M^{-1}, preferably at least 10^{8} M^{-1}, and more preferably at least 10^{9} M^{-1}, such as at least 10^{12} M^{-1}. It is generally accepted that any K_D value greater than 10^{-4} M indicates non-specifically binding. The specifically binding of an antibody

to an antigen or antigenic determinant can be determined in any known suitable manner, including, for example, Scatchard analysis and/or competitive binding assays such as radio-immunoassays (RIA), enzyme immunoassays (EIA) and sandwich competition assays, as well as various variants thereof known in the art.

[00101] The term "epitope" refers to a site on an antigen to which an antibody binds. The epitope may be formed from consecutive amino acids or non-consecutive amino acids juxtaposed by the tertiary folding of one or more proteins. The epitopes formed from consecutive amino acids (also referred to as linear epitopes) are typically retained during exposure to denaturing solvents, while the epitopes formed from the tertiary folding (also referred to as conformational epitopes) are typically lost during treatment with denaturing solvents. The epitopes typically comprise at least 3, more typically at least 5 or 8-10 amino acids in a unique spatial conformation. The epitope defines the minimal binding site of an antibody and is therefore a specific target for the antibody or an antigen-binding fragment thereof.

[00102] As used herein, the term "sequence identity" refers to the extent to which two sequences (amino acids) have the same residue at the same position after alignment. For example, "an amino acid sequence is X% identical with SEQ ID NO: Y" means that the amino acid sequence has an identity of X% with SEQ ID NO: Y and is described as X% of the residues in the amino acid sequence being identical with residues in the sequence disclosed in SEQ ID NO: Y. Typically, a computer program is used to perform such calculations. Exemplary programs for comparing and aligning sequence pairs include ALIGN, FASTA, gapped BLAST, BLASTP, BLASTN, or GCG.

[00103] As used herein, the term "percent (%) amino acid sequence identity" with respect to a sequence is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as EMBOSS MATCHER, EMBOSS WATER, EMBOSS STRETCHER, EMBOSS NEEDLE, EMBOSS LALIGN, BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared.

[00104] In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino

acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows: 100 times the fraction X/Y, where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program.

[00105] In addition, while determining a degree of sequence identity between two amino acid sequences, the skilled person may consider so-called "conserved" amino acid substitutions, which can generally be described as an amino acid substitution in which an amino acid residue is replaced by another amino acid residue having a similar chemical structure, which has hardly any or substantially no effect on the function, activity, or other biological properties of the polypeptide. Such conserved amino acid substitutions are well known in the art.

[00106] Such a conserved substitution is preferably a substitution of one amino acid in the following groups (a) to (e) substituted by another amino acid residue in the same group: (a) small aliphatic, nonpolar or weakly polar residues: Ala, Ser, Thr, Pro and Gly; (b) polar, negatively charged residues and (uncharged) amides thereof: Asp, Asn, Glu and Gln; (c) polar, positively charged residues: His, Arg and Lys; (d) large aliphatic, nonpolar residues: Met, Leu, Ile, Val and Cys; and (e) aromatic residues: Phe, Tyr and Trp.

[00107] Particularly preferable conserved substitutions are the following: Ala to Gly or to Ser; Arg to Lys; Asn to Gln or to His; Asp to Glu; Cys to Ser; Gln to Asn; Glu to Asp; Gly to Ala or to Pro; His to Asn or to Gln; Ile to Leu or to Val; Leu to Ile or to Val; Lys to Arg, to Gln or to Glu; Met to Leu, to Tyr or to Ile; Phe to Met, to Leu or to Tyr; Ser to Thr; Thr to Ser; Trp to Tyr; Tyr to Trp; and/or Phe to Val, to Ile or to Leu.

[00108] As used herein, the term "vector" is intended to refer to a nucleic acid molecule capable of transporting another nucleic acid to which it is attached.

[00109] As used herein, the term "host cell" refers to a cell into which an expression vector has been introduced.

[00110] The term "pharmaceutically acceptable" means that a carrier or excipient is compatible with other components of a composition and is not substantially toxic to a recipient

thereof, and/or that such a carrier or excipient is approved or useful for inclusion in a pharmaceutical composition for parenteral administration to humans.

[00111] As used herein, the terms "treat," "treatment," "treating," or the like refer to administering a medicament or performing a procedure for the purpose of obtaining effects. These effects may be prophylactic in terms of completely or partially preventing a disease or a symptom thereof, and/or may be therapeutic in terms of achieving a partial or complete cure of a disease and/or a symptom of the disease. As used herein, "treating" can include treating a disease or disorder (e.g., an inflammatory disease) in a mammal, particularly a human, and include: (a) preventing occurrence of the disease or symptoms of the disease in a subject who may be susceptible to the disease (e.g., including a disease that may be associated with or caused by the primary disease) but has not yet been diagnosed with the disease; (b) suppressing the disease, i.e., stopping its progression; and (c) mitigating the disease, i.e., causing the disease to subside. Treatment may refer to an indicator of any success in the treatment or amelioration or prevention of cancer, including any objective or subjective parameters such as a reduction in symptoms; mitigation; elimination of disease symptoms or making the disease or disorder more tolerable to the patient; slowing the rate of deterioration or decline; or making the final node of deterioration less debilitating. The treatment or amelioration of symptoms is based on one or more objective or subjective parameters; including the results of a physician's examination. Accordingly, the term "treatment" includes administration of the antibody or composition or conjugate disclosed herein to prevent or delay, mitigate, or arrest or inhibit the progression of a symptom or condition associated with a disease (e.g., an inflammatory disease). The term "therapeutic effect" refers to the reduction, elimination, or prevention of a disease, disease symptoms, or disease side effects in a subject.

[00112] As used herein, the term "effective amount" means an amount administered to a subject to treat a disease that is sufficient to achieve treatment of the disease.

[00113] As used herein, the term "subject" means any mammalian subject for whom a diagnosis, treatment or therapy is desired. The term "mammal" for therapeutic purposes refers to any animal categorized as a mammal, including humans, domestic animals, and laboratory, zoo, sport or pet animals such as dogs, horses, cats, cows, sheep, goats, pigs, mice, rats, rabbits, guinea pigs, and monkeys.

[00114] A disease associated with a type 2 inflammatory response is inflammation mediated primarily by Th2 cells, type 2 innate lymphoid cells, and relevant cytokines. When a human body is exposed to different environmental or plant and animal allergens, a type 2 inflammatory response may develop in the body, and in turn may involve multiple systems of skin, respiratory and

gastrointestinal tracts, inducing a type 2 inflammatory disease. The disease associated with the type 2 inflammatory response have the following immunopathological characteristics in the affected tissues/organs:

i) increased type 2 immune cells (Th2 and ILC2 cells, etc.) and increased expression of relevant cytokines (IL-4, IL-5, IL-13, IL-25, IL-31, IL-33, TSLP, etc.);

ii) activation and proliferation of effector cells (e.g., B cells activated into plasma cells) or activation by recruitment (e.g., mast cells, basophils and eosinophils (EOS));

iii) possibly accompanied by an increase in total IgE and/or specific IgE; and

iv) manifestations of inflammatory responses such as dilatation of microcirculation of the locally affected organs, increased permeability, increased exudation, and infiltration of relevant cells.

[00115] The following reference antibodies are used herein:

ref1: IL-13 monoclonal antibody Lebrikizumab and its heavy chain and light chain sequences are SEQ ID NOs: 57 and 58, respectively;

ref2: TSLP/IL-13 nanobody Lunsekimig and its sequence is SEQ ID NO: 59; and

ref3: TSLP monoclonal antibody and its heavy chain and light chain sequences are SEQ ID NOs: 64 and 65, respectively.

Multi-specific Antibodies and Use Thereof

[00116] Disclosed herein are antibodies that bind to IL-13 and TSLP. In some embodiments, an antibody disclosed herein comprises a multispecific antibody that binds to IL-13 and TSLP. In some embodiments, the multispecific disclosed herein comprises a bispecific antibody that binds to IL-13 and TSLP. Disclosed herein is an antibody or an antigen-binding fragment thereof, comprising a first antigen-binding region that binds to interleukin 13 (IL-13) and a second antigen-binding region that binds to thymic stromal lymphopoietin (TSLP). In some embodiments, the first antigen-binding region comprises a first heavy chain variable region (VH1) and a first light chain variable region (VL1). In some embodiments, the second antigen-binding region comprises a second heavy chain variable region (VH2) and a second light chain variable region (VL2). In some embodiments, VH1 comprises complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 24. In some embodiments, VH1 comprises CDR2 comprising the amino acid sequence of SEQ ID NO: 25 or 26. In some embodiments, VH1 comprises CDR2 comprising the amino acid sequence of SEQ ID NO: 25. In some embodiments, VH1 comprises CDR2 comprising the amino acid sequence of SEQ ID NO: 26. In some embodiments, VH1 comprises CDR3 comprising the amino acid sequence of SEQ ID NO: 27. In some embodiments, VL1 comprises

CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively. In some embodiments, VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively. In some embodiments, VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively.

[00117] Disclosed herein is an antibody or an antigen-binding fragment thereof, comprising a first antigen-binding region that binds to IL-13 and a second antigen-binding region that binds to TSLP, wherein the first antigen-binding region comprises a first heavy chain variable region (VH1) and a first light chain variable region (VL1) and the second antigen-binding region comprises a second heavy chain variable region (VH2) and a second light chain variable region (VL2), wherein: (a) VH1 comprises: complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 24; CDR2 comprising the amino acid sequence of SEQ ID NO: 25 or 26; and CDR3 comprising the amino acid sequence of SEQ ID NO: 27; (b) VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; (c) VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively; and d) VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. Disclosed herein is an antibody or an antigen-binding fragment thereof, comprising a first antigen-binding region that binds to IL-13 and a second antigen-binding region that binds to TSLP, wherein the first antigen-binding region comprises a VH1 and a VL1 and the second antigen-binding region comprises a VH2 and a VL2, wherein: VH1 comprises CDR1 comprising the amino acid sequence of SEQ ID NO: 24; CDR2 comprising the amino acid sequence of SEQ ID NO: 25 or 26; and CDR3 comprising the amino acid sequence of SEQ ID NO: 27; VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 54, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. In some embodiments, VH1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 24, 25, and 27, respectively; VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. In some embodiments, VH1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of

SEQ ID NOs: 24, 26, and 27, respectively; VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. In some embodiments, wherein: VH1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 24, 25, and 27, respectively; VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 54, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. In some embodiments, wherein: VH1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 24, 26, and 27, respectively; VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively; VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 54, 31, and 32, respectively; and VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively.

[00118] In some embodiments, VH1 comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52. In some embodiments, VH1 comprises the amino acid sequence of any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52. In some embodiments, VL1 comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53. In some embodiments, VL1 comprises the amino acid sequence of any one of SEQ ID NOs: 1, 3, 46, and 53. VH2 comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 28 or 50. In some embodiments, VH2 comprises the amino acid sequence of SEQ ID NO: 28 or 50. In some embodiments, VL2 comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VL2 comprises the amino acid sequence of SEQ ID

NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 91% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 91% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 92% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 92% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 93% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 93% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 94% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 94% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 95% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 95% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 96% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 96% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and

53; VH2 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 97% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 97% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 98% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 98% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises an amino acid sequence with at least 99% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises an amino acid sequence with at least 99% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 28 or 50; and/or VL2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises the amino acid sequence of any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises the amino acid sequence of any one SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises the amino acid sequence of SEQ ID NO: 28 or 50; or VL2 comprises the amino acid sequence of SEQ ID NO: 33 or 51. In some embodiments, VH1 comprises the amino acid sequence of any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52; VL1 comprises the amino acid sequence of any one SEQ ID NOs: 1, 3, 46, and 53; VH2 comprises the amino acid sequence of SEQ ID NO: 28 or 50; and VL2 comprises the amino acid sequence of SEQ ID NO: 33 or 51.

[00119] In some embodiments, VH1 comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 52. In some embodiments, VH1 comprises the amino acid sequence of SEQ ID NO: 52. In some embodiments, VL1 comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 53. In some embodiments, VL1 comprises the amino acid sequence of SEQ ID NO: 53. VH2

comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 28. In some embodiments, VH2 comprises the amino acid sequence of SEQ ID NO: 28. In some embodiments, VL2 comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 33. In some embodiments, VL2 comprises the amino acid sequence of SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 33. In some embodiments, VH1

comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 96% sequence

identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 28; or VL2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 52; VL1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 53; VH2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 28; and VL2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 33. In some embodiments, VH1 comprises the amino acid sequence of SEQ ID NO: 52; VL1 comprises the amino acid sequence of SEQ ID NO: 53; VH2 comprises the amino acid sequence of SEQ ID NO: 28; or VL2 comprises the amino acid sequence of SEQ ID NO: 33. In some embodiments, VH1 comprises the amino acid sequence of SEQ ID NO: 52; VL1 comprises the amino acid sequence of SEQ ID NO: 53; VH2 comprises the amino acid sequence of SEQ ID NO: 28; and VL2 comprises the amino acid sequence of SEQ ID NO: 33.

[00120] In some embodiments, VH1, VL1, VH2, or VL2 of the antibody or antigen-binding fragment thereof comprises a charge pair mutation comprising a substitution of: an amino acid

residue of positive charge with an amino acid residue of negative charge; an amino acid residue of negative charge with an amino acid residue of positive charge; a neutral amino acid residue with an amino acid residue of positive charge; or a neutral amino acid residue with an amino acid residue of negative charge, wherein the charge pair mutation increases the association between VH1 and VL1 or the association between VH2 and VL2. In some embodiments, VH1 and VL1 each comprises the charge pair mutation that increases the association between VH1 and VL1. In some embodiments, VH2 and VL2 each comprises the charge pair mutation that increases the association between VH2 and VL2. In some embodiments, the charge pair mutation of VH1, VL1, VH2, or VL2 comprises a substitution of glutamine (Q) with glutamic acid (E); or a substitution of glutamine (Q) with lysine (K). In some embodiments, the charge pair mutation of VH1, VL1, VH2, or VL2 comprises a substitution of glutamine (Q) with glutamic acid (E); and a substitution of glutamine (Q) with lysine (K). In some embodiments, the charge pair mutation of VH1 or VH2 comprises a substitution of glutamine (Q) with glutamic acid (E) at amino acid residue 39 according to the Kabat numbering scheme (Q39E). In some embodiments, the charge pair mutation of VH1 or VH2 comprises a substitution of glutamine (Q) with lysine (K) at amino acid residue 39 according to the Kabat numbering scheme (Q39K). In some embodiments, the charge pair mutation of VL1 or VL2 comprises a substitution of glutamine (Q) with lysine (K) at amino acid residue 38 according to the Kabat numbering scheme (Q38K). In some embodiments, the charge pair mutation of VL1 or VL2 comprises a substitution of glutamine (Q) with glutamic acid (E) at amino acid residue 38 according to the Kabat numbering scheme (Q38E). In some embodiments, the charge pair mutation of VH1 comprises Q39E; and the charge pair mutation of VL1 comprises Q38K. In some embodiments, the charge pair mutation of VH1 comprises Q39K; and the charge pair mutation of VL1 comprises Q38E. In some embodiments, the charge pair mutation of VH2 comprises Q39E; and the charge pair mutation of VL2 comprises Q38K. In some embodiments, the charge pair mutation of VH2 comprises Q39K; and the charge pair mutation of VL2 comprises Q38E. In some embodiments, the charge pair mutation of VH1 comprises Q39K; the charge pair mutation of VL1 comprises Q38E; the charge pair mutation of VH2 comprises Q39E; and the charge pair mutation of VL2 comprises Q38K. In some embodiments, the charge pair mutation of VH1 comprises Q39E; the charge pair mutation of VL1 comprises Q38K; the charge pair mutation of VH2 comprises Q39K; and the charge pair mutation of VL2 comprises Q38E.

[00121] In some embodiments, the antibody or antigen-binding fragment thereof further comprises a first heavy chain comprising VH1 and a constant region comprising CH1 domain, CH2 domain, or CH3 domain, a first light chain comprising VL1 and constant (CL) domain, a second

heavy chain comprising VH2 and a constant region comprising CH1 domain, CH2 domain, or CH3 domain, or a second light chain comprising VL2 and CL domain. In some embodiments, the antibody or antigen-binding fragment thereof further comprises the first heavy chain comprising VH1 and a constant region comprising CH1 domain, CH2 domain, and CH3 domain, the first light chain comprising VL1 and CL domain, the second heavy chain comprising VH2 and a constant region comprising CH1 domain, CH2 domain, and CH3 domain, and a second light chain comprising VL2 and CL domain. In some embodiments, the CH1 domain of the first heavy chain or the CL domain of the first light chain comprises a second charge pair mutation that increases the association between the first heavy chain and the first light chain. In some embodiments, the CH1 domain of the second heavy chain or the CL domain of the second light chain comprises the second charge pair mutation that increases the association between the second heavy chain and the second light chain. In some embodiments, the second charge pair mutation comprises a substitution of: an amino acid residue of positive charge with an amino acid residue of negative charge; an amino acid residue of negative charge with an amino acid residue of positive charge; a neutral amino acid residue with an amino acid residue of positive charge; or a neutral amino acid residue with an amino acid residue of negative charge. In some embodiments, the second charge pair mutation comprises a substitution of lysine (K) with glutamic acid (E). In some embodiments, the CH1 domain of the first heavy chain or the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising: a substitution of lysine (K) with glutamic acid (E) at amino acid residue 147 according to the EU numbering (K147E); or a substitution of lysine (K) with glutamic acid (E) at amino acid residue 213 according to the EU numbering (K213E). In some embodiments, the CH1 domain of the first heavy chain comprises the second charge pair mutation comprising K147E and K213E. In some embodiments, the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising K147E and K213E. In some embodiments, the CH1 domain of the first heavy chain comprises the second charge pair mutation comprising K147E and K213E and the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising K147E and K213E.

[00122] In some embodiments, the antibody or antigen-binding fragment thereof further comprises a fragment antigen-binding (Fab) region, a Fab', a $F(ab')_2$, or a single chain variable fragment (scFv). In some embodiments, the antibody or antigen-binding fragment thereof further comprises a Fab. In some embodiments, the antibody or antigen-binding fragment thereof further comprises a scFv. In some embodiments, the first heavy chain or the second heavy chain comprises a Fab or scFv. In some embodiments, the first heavy chain and the second heavy chain each comprises

a Fab. In some embodiments, the first heavy chain and the second heavy chain each comprises a scFv. In some embodiments, the first heavy chain comprises a Fab and the second heavy chain comprises a scFv. In some embodiments, the first heavy chain comprises a scFv and the second heavy chain comprises a Fab. In some embodiments, the antibody or antigen-binding fragment thereof further comprises a fragment crystallizable (Fc) region. In some embodiments, the first heavy chain and the second heavy chain each comprises a Fc region. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an immunoglobulin (Ig) G, IgA, IgM, IgE, or IgD. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgG. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgA. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgM. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgE. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgD. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgG1, IgG2, IgG3, or IgG4. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgG1. In some embodiments, the antibody or antigen-binding fragment thereof further comprises an IgG4.

[00123] In some embodiments, the Fc region comprises a knob-into-hole mutation. In some embodiments, the Fc region of the first heavy chain or the Fc region of the second heavy chain comprises the knob-into-hole mutation. In some embodiments, the Fc region of the first heavy chain and the Fc region of the second heavy chain each comprises the knob-into-hole mutation. In some embodiments, the knob-into-hole mutation comprises a substitution of tyrosine (Y) with cysteine (C) at amino acid residue 349 according to the EU numbering (Y349C); a substitution of serine (S) with cysteine (C) at amino acid residue 354 according to the EU numbering (S354C); a substitution of threonine (T) with tryptophan (W) at amino acid residue 366 according to the EU numbering (T366W); a substitution of threonine (T) with serine (S) at amino acid residue 366 according to the EU numbering (T366S); a substitution of threonine (T) with tyrosine (Y) at amino acid residue 366 according to the EU numbering (T366Y); a substitution of leucine (L) with alanine (A) at amino acid residue 368 according to the EU numbering (L368A); a substitution of phenylalanine (F) with alanine (A) at amino acid residue 405 according to the EU numbering (F405A); a substitution of phenylalanine (F) with tryptophan (W) at amino acid residue 405 according to the EU numbering (F405W); a substitution of tyrosine (Y) with alanine (A) at amino acid residue 407 according to the EU numbering with (Y407A); a substitution of tyrosine (Y) with threonine (T) at amino acid residue 407 according to the EU numbering with (Y407T); or a substitution of tyrosine (Y) with valine (V)

at amino acid residue 407 according to the EU numbering with (Y407V). In some embodiments, the Fc region of the first heavy chain comprises the knob-into-hole mutation comprising T366S, L368A, and Y407V; and the Fc region of the second heavy chain comprises the knob-into-hole mutation comprising T366W. In some embodiments, the Fc region of the first heavy chain comprises the knob-into-hole mutation comprising T366W; and the Fc region of the second heavy chain comprises the knob-into-hole mutation comprising T366S, L368A, and Y407V. In some embodiments, the Fc region of the first heavy chain comprises the knob-into-hole mutation comprising Y349C, T366S, L368A, and Y407V; and the Fc region of the second heavy chain comprises the knob-into-hole mutation comprising S354C and T366W. In some embodiments, The Fc region of the first heavy chain comprises the knob-into-hole mutation comprising S354C and T366W; and the Fc region of the second heavy chain comprises the knob-into-hole mutation comprising Y349C, T366S, L368A, and Y407V. In some embodiments, the Fc region comprises a second amino acid mutation that increases the half-life of the antibody or antigen-binding fragment thereof. In some embodiments, the second amino acid mutation increases the binding of the antibody or antigen-binding fragment thereof to neonatal Fc receptor (FcRn). In some embodiments, the Fc region comprises a third amino acid mutation that reduces the binding affinity of the antibody or antigen-binding fragment thereof to Fc-gamma receptor (FcγR) or complement component 1q (C1q). In some embodiments, the second amino acid mutation comprises: a substitution of methionine (M) with leucine (L) at amino acid residue 428 according to the EU numbering (M428L); or a substitution of asparagine (N) with alanine (A) at amino acid residue 434 according to the EU numbering (N434A). In some embodiments, the second amino acid mutation comprises M428L and N434A. In some embodiments, the Fc region of the first heavy chain comprises the second amino acid mutation comprising M428L or N434A; and the Fc region of the second heavy chain comprises the second amino acid mutation comprising M428L or N434A. In some embodiments, the Fc region of the first heavy chain comprises the second amino acid mutation comprising M428L and N434A. In some embodiments, the Fc region of the second heavy chain comprises the second amino acid mutation comprising M428L and N434A. In some embodiments, the Fc region of the first heavy chain comprises the second amino acid mutation comprising M428L and N434A; and the Fc region of the second heavy chain comprises the second amino acid mutation comprising M428L and N434A.

[00124] In some embodiments, the first heavy chain comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 42. In some embodiments, the first heavy chain comprises the amino acid

sequence of SEQ ID NO: 42. In some embodiments, the first light chain comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 44. In some embodiments, the first light chain comprises the amino acid sequence of SEQ ID NO: 44. In some embodiments, the second heavy chain comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 38. In some embodiments, the second heavy chain comprises the amino acid sequence of SEQ ID NO: 38. In some embodiments, the second light chain comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 40. In some embodiments, the second light chain comprises the amino acid sequence of SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain

comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 95%

sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 98% sequence identity to SEQ

ID NO: 38; and the second light chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 38; or the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 42; the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 44; the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 38; and the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 40. In some embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 42; the first light chain comprises the amino acid sequence of SEQ ID NO: 44; the second heavy chain comprises the amino acid sequence of SEQ ID NO: 38; or the second light chain comprises the amino acid sequence of SEQ ID NO: 40. In some embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 42; the first light chain comprises the amino acid sequence of SEQ ID NO: 44; the second heavy chain comprises the amino acid sequence of SEQ ID NO: 38; and the second light chain comprises the amino acid sequence of SEQ ID NO: 40.

[00125] In some embodiments, the first heavy chain comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 60. In some embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 60. In some embodiments, the first light chain comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 61. In some embodiments, the first light chain comprises the amino acid sequence of SEQ ID NO: 61. In some embodiments, the second heavy chain comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 66. In some embodiments, the second heavy chain comprises the amino acid sequence of SEQ ID NO: 66. In some embodiments, the second light chain comprises an amino acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 67. In some embodiments, the second light chain comprises the amino acid sequence of SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 91% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 92% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 60; the first light chain comprises an

amino acid sequence with at least 93% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 93% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 94% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least

96% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 96% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 97% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 98% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 66; or the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 67. In some embodiments, the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 60; the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 61; the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 66; and the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 67. In some

embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 60; the first light chain comprises the amino acid sequence of SEQ ID NO: 61; the second heavy chain comprises the amino acid sequence of SEQ ID NO: 66; or the second light chain comprises the amino acid sequence of SEQ ID NO: 67. In some embodiments, the first heavy chain comprises the amino acid sequence of SEQ ID NO: 60; the first light chain comprises the amino acid sequence of SEQ ID NO: 61; the second heavy chain comprises the amino acid sequence of SEQ ID NO: 66; and the second light chain comprises the amino acid sequence of SEQ ID NO: 67.

[00126] In some embodiments, the antibody or antigen-binding fragment thereof comprises a multispecific antibody or antigen binding fragment thereof. In some embodiments, the multispecific antibody or antigen-binding fragment thereof comprises a bispecific antibody or antigen binding fragment thereof. In some embodiments, the multispecific antibody or antigen-binding fragment thereof comprises a trispecific antibody or antigen binding fragment thereof. In some embodiments, the antibody or antigen-binding fragment thereof has a technical advantage, technical effect, and/or a technical improvement compared with a second antibody or an antigen-binding fragment thereof that binds to IL-13, TSLP, or IL-13 and TSLP. In some embodiments, the second antibody that binds to IL-13, TSLP, or IL-13 and TSLP comprises Lunsekimig or an analog thereof, Lebrikizumab or an analog thereof, or Tezepelumab or an analog thereof. In some embodiments, the second antibody that binds to IL-13, TSLP, or IL-13 and TSLP comprises a TSLP antibody. In some embodiments, the second antibody that binds to IL-13, TSLP, or IL-13 and TSLP comprises an IL-13 antibody. In some embodiments, the second antibody that binds to IL-13, TSLP, or IL-13 and TSLP comprises a bispecific antibody that binds to IL-13 and TSLP. In some embodiments, the second antibody that binds to IL-13, TSLP, or IL-13 and TSLP comprises a trispecific antibody that binds to IL-13 and TSLP. In some embodiments, the second antibody that binds to IL-13, TSLP, or IL-13 and TSLP comprises a multispecific antibody that binds to IL-13 and TSLP. In some embodiments, the technical advantage, technical effect, and/or technical improvement includes or relates to therapeutic activity, stability, immunogenicity, affinity, toxicity, potency, specificity, pharmacokinetics, pharmacodynamics, or a property not exhibited by the second antibody or antigen-binding fragment thereof that binds to IL-13, TSLP, or IL-13 and TSLP. In some embodiments, the technical advantage, technical effect, and/or a technical improvement includes or relates to a binding affinity to IL-13, TSLP, or IL-13 and TSLP, an ability to inhibit IL-13-mediated biological activity, an ability to inhibit TSLP-mediated biological activity, or an ability to inhibit a biological activity mediated by IL-13 and TSLP. In some embodiments, the technical advantage, technical effect, and/or technical improvement includes or relates to a reduced immunogenicity, an increased

stability, an increased binding affinity to IL-13, TSLP, or IL-13 and TSLP, an increased ability to inhibit IL-13-mediated activation of STAT6, an increased ability to inhibit IL-13-mediated cell proliferation, an increased ability to inhibit TSLP-mediated thymus and activation regulated chemokine (TARC) release, an increased ability to inhibit TSLP-mediated cell proliferation, an increased ability to inhibit TSLP-mediated activation of STAT5, an increased ability to inhibit IgE production, an increased ability to inhibit an inflammatory or allergic response, a reduced dosing frequency, an increased ability to inhibit cytokine production, a better therapeutic effect on an allergic or inflammatory disease, an increased serum half-life, an increased thermostability, an increased binding affinity to a neonatal Fc receptor (FcRn), a reduced binding affinity to a Fc-gamma receptor (FcγR), or a reduced binding affinity to complement component 1q (C1q).

[00127] Disclosed herein is a nucleic acid molecule encoding the antibody or antigen-binding fragment thereof disclosed herein. In some embodiments, the nucleic acid molecule encodes the antibody or antigen-binding fragment thereof or a portion thereof. In some embodiments, the nucleic acid molecule is used to express or manufacture the antibody or antigen-binding fragment thereof or a portion thereof. In some embodiments, the nucleic acid molecule comprises a first nucleic acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 29. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence of SEQ ID NO: 29. In some embodiments, the nucleic acid molecule comprises a second nucleic acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 34. In some embodiments, the nucleic acid molecule comprises the second nucleic acid sequence of SEQ ID NO: 34. In some embodiments, the nucleic acid molecule comprises a third nucleic acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 55. In some embodiments, the nucleic acid molecule comprises the third nucleic acid sequence of SEQ ID NO: 55. In some embodiments, the nucleic acid molecule comprises a fourth nucleic acid sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the fourth nucleic acid sequence of SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises a first nucleic acid sequence with at least 90%

sequence identity to SEQ ID NO: 29; a second nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 34; a third nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 55; or a fourth nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 91% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 91% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 91% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 91% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 91% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 91% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 91% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 91% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 92% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 92% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 92% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 92% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 92% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 92% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 92% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 92% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 93% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 93% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 93% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 93% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 93% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 93% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 93% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 93% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the

first nucleic acid sequence with at least 94% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 94% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 94% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 94% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 94% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 94% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 94% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 94% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 96% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 96% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 96% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 96% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 96% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 96% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 96% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 96% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 97% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 97% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 97% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 97% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 97% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 97% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 97% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 97% sequence identity to SEQ ID NO: 56. In

some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 98% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 98% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 98% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 98% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 98% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 98% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 98% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 98% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 55; or the fourth nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 29; the second nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 34; the third nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 55; and the fourth nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence set forth in SEQ ID NO: 29; the second nucleic acid sequence set forth in SEQ ID NO: 34; the third nucleic acid sequence set forth in SEQ ID NO: 55; or the fourth nucleic acid sequence set forth in SEQ ID NO: 56. In some embodiments, the nucleic acid molecule comprises the first nucleic acid sequence set forth in SEQ ID NO: 29; the second nucleic acid sequence set forth in SEQ ID NO: 34; the third nucleic acid sequence set forth in SEQ ID NO: 55; and the fourth nucleic acid sequence set forth in SEQ ID NO: 56.

[00128] In some embodiments, the nucleic acid molecule comprises a first nucleotide sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 39. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence of SEQ ID NO: 39. In some embodiments, the nucleic acid molecule comprises a second nucleotide sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 41. In some embodiments, the nucleic acid molecule comprises the second nucleotide sequence of SEQ ID NO:

41. In some embodiments, the nucleic acid molecule comprises a third nucleotide sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 43. In some embodiments, the nucleic acid molecule comprises the third nucleotide sequence of SEQ ID NO: 43. In some embodiments, the nucleic acid molecule comprises a fourth nucleotide sequence with at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the fourth nucleotide sequence of SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises a first nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 39; a second nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 41; a third nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 43; or a fourth nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 91% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 91% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 91% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 91% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 91% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 91% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 91% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 91% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 92% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 92% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 92% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 92% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 92% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 92% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 92% sequence identity to SEQ ID NO: 43; and the fourth

nucleotide sequence with at least 92% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 93% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 93% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 93% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 93% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 93% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 93% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 93% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 93% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 94% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 94% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 94% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 94% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 94% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 94% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 94% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 94% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 96% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 96% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 96% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 96% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 96% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 96% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 96% sequence

identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 96% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 97% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 97% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 97% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 97% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 97% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 97% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 97% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 97% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 98% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 98% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 98% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 98% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 98% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 98% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 98% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 98% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 43; or the fourth nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 39; the second nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 41; the third nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 43; and the fourth nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence set forth in SEQ ID NO: 39; the second nucleotide sequence set forth in SEQ ID NO: 41; the third nucleotide sequence set forth in SEQ ID NO: 43; or the fourth nucleotide sequence set forth in SEQ ID NO: 45. In some embodiments, the nucleic acid molecule comprises the first nucleotide sequence set forth in SEQ ID NO: 39; the second nucleotide sequence set forth in SEQ ID NO: 41; the third nucleotide sequence set forth in SEQ ID NO: 43; and the fourth nucleotide sequence set forth in SEQ ID NO: 45.

[00129] Disclosed herein is a vector comprising the nucleic acid molecule disclosed herein. In some embodiments, the vector comprises any expression vector disclosed herein. Disclosed herein is a host cell comprising the nucleic acid molecule disclosed herein or the vector disclosed herein. Disclosed herein is a pharmaceutical composition comprising (i) the antibody or antigen-binding fragment thereof; and (ii) a pharmaceutically acceptable carrier or excipient. In some embodiments, the pharmaceutical composition further comprises a second therapeutic agent. In some embodiments, the second therapeutic agent is selected from the group comprising an antibody, a chemotherapeutic agent, and a small molecule drug. Disclosed herein is a conjugate comprising the antibody or antigen-binding fragment thereof disclosed herein, and a chemical moiety conjugated thereto. In some embodiments, the chemical moiety is selected from a group comprising a therapeutic agent, a detectable moiety, and an immunostimulatory molecule.

[00130] Disclosed herein is a method for treating a disease in a subject, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein. Disclosed herein is a method for treating a disease in a subject, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof disclosed herein. Disclosed herein is a method for treating a disease in a subject, comprising administering to the subject an effective amount of the pharmaceutical composition disclosed herein. Disclosed herein is a method for treating a disease in a subject, comprising administering to the subject an effective amount of the conjugate disclosed herein. In some embodiments, the disease comprises an inflammatory disease, an autoimmune disease, or an allergic disease. In some embodiments, the disease comprises a type 2 inflammatory response-related disease. In some embodiments, the disease comprises an IL-13 mediated disease, a TSLP mediated disease, or both. In some embodiments, the disease is selected from the group comprising atopic dermatitis, allergic inflammation, asthma, urticaria, chronic obstructive pulmonary disease, eosinophilic esophagitis, rheumatoid arthritis, multiple sclerosis, idiopathic pulmonary fibrosis, eczema, eosinophilic gastroenteritis, Crohn's disease, systemic sclerosis, ulcerative colitis, and chronic rhinosinusitis with nasal polyps. In some embodiments, the disease comprises asthma. In some embodiments, the disease comprises atopic dermatitis. In some embodiments, the disease is selected from the group comprising allergic rhinitis, allergic sinusitis, allergic conjunctivitis, hand eczema, and asthmatic eczema. In some embodiments, the method further comprises administering a second therapeutic agent to the subject. In some embodiments, the second therapeutic agent is selected from a group comprising an antibody, a chemotherapeutic agent, and a small molecule drug.

[00131] Disclosed herein is a method for inhibiting or eliminating IgE in a subject, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein. Disclosed herein is a method for inhibiting or eliminating IgE in a subject, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof disclosed herein. Disclosed herein is a method for inhibiting or eliminating IgE in a subject, comprising administering to the subject an effective amount the pharmaceutical composition disclosed herein. Disclosed herein is a method for inhibiting or eliminating IgE in a subject, comprising administering to the subject an effective amount of the conjugate disclosed herein. In some embodiments, the subject is human.

[00132] In an aspect, the present disclosure provides a bispecific antibody or an antigen-binding fragment thereof, comprising a first antigen-binding region binding to IL-13 and a second antigen-binding region binding to TSLP, the first antigen-binding region comprising a first light chain variable region (VL1) and a first heavy chain variable region (VH1), and the second antigen-binding region comprising a second light chain variable region (VL2) and a second heavy chain variable region (VH2), wherein the VL1 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 21-23, respectively; the VH1 comprises HCDR 1 having an amino acid sequence as set forth in SEQ ID NO: 24, HCDR 2 having an amino acid sequence as set forth in SEQ ID NO: 25 or 26, and HCDR 3 having an amino acid sequence as set forth in SEQ ID NO: 27; the VL2 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 35-37, respectively; and the VH2 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 30-32, respectively. In some embodiments, the VL1 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 21-23, respectively; the VH1 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 24, 25 and 27, respectively; the VL2 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 35-37, respectively; and the VH2 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 30-32, respectively. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3, and 46; the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19; the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO:

33 or 51; and the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28 or 50. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3, and 46; the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, and 13; the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 33; and the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 13. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino

acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 9; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO:

28. In some embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 5; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In some embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 7; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In some embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 11; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In some embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 13; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In some embodiments, the antibody comprises: a first heavy chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 42, a first light chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 44, a second heavy chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 38, and a second light chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 40. In some embodiments, the antibody comprises a first heavy chain having an amino acid sequence as set forth in SEQ ID NO: 42, a first light chain having an amino acid sequence as set forth in SEQ ID NO: 44, a second heavy chain having an amino acid sequence as set forth in SEQ ID NO: 38, and a second light chain having an amino acid sequence as set forth in SEQ ID NO: 40. In another aspect, the present disclosure provides an antibody specifically binding to IL-L3, or an antigen-binding fragment thereof, comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3, and 46, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID

NOs: 5, 7, 9, 11, 13, 15, 17, and 19. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 13. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid

sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 13. In some embodiments, the antibody is an isotype selected from IgG, IgA, IgM, IgE and IgD. In some embodiments, the antibody is a subtype selected from IgG1, IgG2, IgG3 and IgG4. In some embodiments, the antigen-binding fragment is selected from Fab, Fab', $F(ab')_2$, Fv, scFv and ds-scFv. In some embodiments, the antibody is a monoclonal antibody, a bispecific antibody, or a multispecific antibody. In some embodiments, the antibody is a bispecific antibody

that further comprises a second antigen-binding region binding to a second antigen. In yet another aspect, the present disclosure provides a nucleic acid, comprising a nucleotide sequence encoding the bispecific antibody or an antigen-binding fragment thereof disclosed herein, or the antibody or an antigen-binding fragment thereof disclosed herein. In some embodiments, the nucleic acid comprises: a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 2 or 4, a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 6, 8, 10, 12, 14, 16, 18, and 20, a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 29, and a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 34. In some embodiments, the nucleic acid comprises: a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 39, a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 41, a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 43, and a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 45. In another aspect, the present disclosure provides a vector comprising the nucleic acid disclosed herein. In another aspect, the present disclosure provides a host cell comprising the nucleic acid disclosed herein or the vector disclosed herein. In another aspect, the present disclosure provides a pharmaceutical composition comprising: (i) the bispecific antibody or an antigen-binding fragment thereof disclosed herein, or the antibody or an antigen-binding fragment thereof disclosed herein; and (ii) a pharmaceutically acceptable carrier or excipient. In some embodiments, the pharmaceutical composition further comprises a second therapeutic agent. In some embodiments, the second therapeutic agent is selected from an antibody, a chemotherapeutic agent and a small molecule drug. In another aspect, the present disclosure provides a conjugate comprising the bispecific antibody or an antigen-binding fragment thereof disclosed herein, or the antibody or an antigen-binding fragment thereof disclosed herein, and a chemical moiety conjugated therewith. In some embodiments, the chemical moiety is selected from a therapeutic agent, a detectable moiety and an immunostimulatory molecule. In yet another aspect, the present disclosure provides a method for treating a disease associated with a type 2 inflammatory response in a subject, comprising administering to the subject an effective amount of

the bispecific antibody or an antigen-binding fragment thereof disclosed herein, the antibody or an antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein. In some embodiments, the disease is a disease mediated by IL-13 and/or TSLP (e.g., an inflammatory disease and an autoimmune disease). In some embodiments, the disease is selected from allergic inflammation (e.g., allergic rhinitis, allergic sinusitis, and allergic conjunctivitis), asthma, atopic dermatitis, urticaria, chronic obstructive pulmonary disease, eosinophilic esophagitis, rheumatoid arthritis, multiple sclerosis, idiopathic pulmonary fibrosis, eczema (e.g., hand eczema, and asthmatic eczema), eosinophilic gastroenteritis, Crohn's disease, systemic sclerosis, ulcerative colitis, and chronic rhinosinusitis with nasal polyps. In some embodiments, the method further comprises administering to the subject a second therapeutic agent. In some embodiments, the second therapeutic agent is selected from an antibody, a chemotherapeutic agent and a small molecule drug. In another aspect, the present disclosure provides a method for inhibiting IgE antibody production in a subject, comprising administering to the subject an effective amount of the bispecific antibody or an antigen-binding fragment thereof disclosed herein, the antibody or an antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein.

[00133] Disclosed herein are bispecific antibodies or an antigen-binding fragments thereof, comprising a first antigen-binding region binding to IL-13 and a second antigen-binding region binding to TSLP, the first antigen-binding region comprising a first light chain variable region (VL1) and a first heavy chain variable region (VH1), the second antigen-binding region comprising a second light chain variable region (VL2) and a second heavy chain variable region (VH2), wherein the VL1 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 21-23, respectively; the VH1 comprises HCDR 1 having an amino acid sequence as set forth in SEQ ID NO: 24, HCDR 2 having an amino acid sequence as set forth in SEQ ID NO: 25 or 26, and HCDR 3 having an amino acid sequence as set forth in SEQ ID NO: 27; the VL2 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 35-37, respectively; and the VH2 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 30-32, respectively. In some embodiments, the VL1 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 21-23, respectively; the VH1 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 24, 25 and 27, respectively; the VL2 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 35-37, respectively; and the VH2 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 30-32, respectively. In some embodiments, the VL1 comprises LCDRs 1-3 having an amino acid sequence

as set forth in SEQ ID NOs: 21-23, respectively; the VH1 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 24, 26 and 27, respectively; the VL2 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 35-37, respectively; and the VH2 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 30-32, respectively. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3, and 46; the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19; the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 33 or 51; and the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28 or 50. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3, and 46; the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, and 13; the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 33; and the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1 or 3; the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19; the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 33; and the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1; the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least

85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19; the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 33; and the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3; the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19; the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 33; and the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at

least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 13. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments,

the VL1 comprises a functional variant of an amino acid sequence as set forth in SEQ ID NOs: 1, 3 or 46, which is formed by inserting, deleting and/or substituting one or more amino acids therein, provided that the functional variant retains the ability to bind to IL-13. In some embodiments, the VH1 comprises a functional variant of an amino acid sequence as set forth in SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17 or 19, which is formed by inserting, deleting and/or substituting one or more amino acids therein, provided that the functional variant retains the ability to bind to IL-13. In some embodiments, the VL2 comprises a functional variant of an amino acid sequence as set forth in SEQ ID NO: 33 or 51, which is formed by inserting, deleting and/or substituting one or more amino acids therein, provided that the functional variant retains the ability to bind to TSLP. In some embodiments, the VH2 comprises a functional variant of an amino acid sequence as set forth in SEQ ID NO: 28 or 50, which is formed by inserting, deleting and/or substituting one or more amino acids therein, provided that the functional variant retains the ability to bind to TSLP. The functional variant comprises or is composed of an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.1%, at least 99.2%, at least 99.3%, at least 99.4%, at least 99.5%, at least 99.6%, at least 99.7%, at least 99.8%, or at least 99.9% with an amino acid sequence of a parent polypeptide. In a content of the functional variant, the number of amino acids inserted, deleted and/or substituted is preferably no more than 40% of the total number of amino acids in a parent amino acid sequence, more preferably no more than 35%, more preferably 1% to 33%, more preferably 5% to 30%, more preferably 10% to 25%, and more preferably 15% to 20%. For example, the number of amino acids inserted, deleted and/or substituted may be 1 to 20, preferably 1 to 10, more preferably 1 to 7, even more preferably 1 to 5, and most preferably 1 to 2. In preferred embodiments, the number of amino acids inserted, deleted and/or substituted is 1, 2, 3, 4, 5, 6 or 7. In some embodiments, insertion, deletion and/or substitution may be performed in a framework region (FR), e.g., in FR1, FR2, FR3 and/or FR4.

[00134] In some embodiments, the substitution of one or more amino acids may be a conserved substitution of one or more amino acids. Such a conserved substitution is preferably a substitution of one amino acid in the following groups (a) to (e) substituted by another amino acid residue in the same group: (a) small aliphatic, nonpolar or weakly polar residues: Ala, Ser, Thr, Pro and Gly; (b) polar, negatively charged residues and (uncharged) amides thereof: Asp, Asn, Glu and Gln; (c) polar, positively charged residues: His, Arg and Lys; (d) large aliphatic, nonpolar residues: Met, Leu, Ile, Val and Cys; and (e) aromatic residues: Phe, Tyr and Trp. Particularly preferred conserved substitutions are the following: Ala to Gly or to Ser; Arg to Lys; Asn to Gln or to His;

Asp to Glu; Cys to Ser; Gln to Asn; Glu to Asp; Gly to Ala or to Pro; His to Asn or to Gln; Ile to Leu or to Val; Leu to Ile or to Val; Lys to Arg, to Gln or to Glu; Met to Leu, to Tyr or to Ile; Phe to Met, to Leu or to Tyr; Ser to Thr; Thr to Ser; Trp to Tyr; Tyr to Trp; and/or Phe to Val, to Ile or to Leu. In preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 9; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 5; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 7; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 11; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 13; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 5; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 7; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 9; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 11; and the VL2

comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 5; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 7; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 9; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. In other preferred embodiments, the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 11; and the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28. The bispecific antibody disclosed herein may comprise an Fc region of the antibody, which comprises CH2 and CH3 domains. The Fc region may be any isotype, including but not limited to IgG1, IgG2, IgG3 and IgG4, and may comprise one or more mutations or modifications. In one embodiment, the Fc region is an IgG1 or IgG4 isotype or derived therefrom, optionally having one or more mutations or modifications. In one embodiment, the Fc region is human IgG1 Fc. In one embodiment, the Fc region is human IgG4 Fc. In some embodiments, the Fc region comprises a modification or mutation that is capable of inhibiting Fc homodimerization, e.g., a knob-into-hole mutation in CH3 of the Fc region. The knob can be generated at the CH3 domain interface of the first IgG Fc chain by substituting a smaller amino acid side chain with a larger one (e.g., T366W); and the hole can be generated in a juxtaposition at the CH3 interface of the second IgG Fc chain by substituting a larger amino acid side chain with a smaller one (e.g., Y407V). The amino acid residues forming the knob are typically naturally occurring amino acid residues and are selected from arginine (R), phenylalanine (F), tyrosine (Y) and tryptophan (W). In some preferred embodiments, the amino acid residues are tryptophan and tyrosine. In one embodiment, the original residue forming the knob has a small side chain volume, such as alanine, asparagine, aspartic acid, glycine, serine, threonine, or valine. Exemplary amino acid substitutions in the CH3 domain to form the knob include, but are not limited to, T366W, T366Y, or F405W substitutions.The amino acid residues forming the hole are typically naturally

occurring amino acid residues and are selected from alanine (A), serine (S), threonine (T), and valine (V). In some preferred embodiments, the original residue forming the hold has a large side chain volume, such as tyrosine, arginine, phenylalanine, or tryptophan. Exemplary amino acid substitutions in the CH3 domain to form the hole include, but are not limited to, T366S, L368A, F405A, Y407A, Y407T, and Y407V substitutions. In preferred embodiments, the knob comprises T366W substitution and the hole comprises T366S, L368A, and Y407V substitutions. In some embodiments, CH3 in one heavy chain comprises T366S, L368A, and Y407V mutations, and CH3 in the other heavy chain comprises T366W mutation.

In some embodiments, CH1 and CL comprise amino acid mutations capable of promoting dimerization of heavy and light chains, such as mutations of positively charged amino acids (e.g., K and R) to negatively charged amino acids (e.g., E, Q, D, and N) in one of CH1 and CL, and mutations of negatively charged amino acids to positively charged amino acids in the other. In preferred embodiments, CH1 comprises K158E and K224E mutations, and CL comprises E143R and Q144K mutations. The bispecific antibodies of the present invention may also comprise a charge pair mutation to improve the association between the specific domains and to reduce bispecific antibody mismatches. The charge pair mutation allows a domain having the charge pair mutation to preferentially associate with another domain having a complementary charge pair mutation by affecting the charge of amino acids in the surface of the domain. In some embodiments, the charge pair mutation may be in CH3. In specific embodiments, the charge pair mutations are T366K in one heavy chain CH3 and L351D in another heavy chain CH3. In some embodiments, the charge pair mutations may be in VL and VH. In specific embodiments, the charge pair mutation is a charge pair mutation at the VH/VL interface. In preferred embodiments, the charge pair mutations at the VH/VL interface are Q39E in VH and Q38K in VL, or Q39K in VH and Q38E in VL. In preferred embodiments, the bispecific antibody of the present invention comprises Q39E in VH and Q38K in VL. In some embodiments, the Fc region has a reduced effector function, such as reduced ADCC, ADCP, CDC, and/or Clq, FcγRI, FcγRII, or FcγRIIIA binding. For example, the Fc region may be an IgGl isotype, or a non-IgGl type, such as IgG2, IgG3, or IgG4, which has been mutated such that the ability to mediate effector functions is reduced or even eliminated. For example, the Fc region may comprise an amino acid sequence having one or more of the following amino acid substitutions as compared to the wild-type sequence: E233P, L234A, L234F, L235A, L235E, G237A, N297A, N297D, P331S, and P329G. In preferred embodiments, the Fc region comprises L234A and L235A (LA mutations). In one embodiment, the Fc region comprises a mutation that removes an Asn-linked glycosylated receptor site, or a mutation that is otherwise manipulated to alter glycosylation

properties. For example, in the IgG1 Fc region, a N297Q mutation may be used to remove the Asn-linked glycosylation site. Thus, in specific embodiments, the Fc region comprises an IgG1 sequence having a N297Q mutation. In further embodiments, the Fc region is glycoengineered to reduce fucose and therefore enhance ADCC, e.g., by adding compounds to the culture medium during antibody production or by using FUT8 knockout cells. Alternatively, ADCC may be optimized. In another embodiment, the Fc region is engineered to enhance complement activation. In some embodiments, the antibody comprises: a first heavy chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 42, a first light chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 44, a second heavy chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 38, and a second light chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 40.

[00135] In some embodiments, the first heavy chain comprises a functional variant of an amino acid sequence as set forth in SEQ ID NO: 42, which is formed by inserting, deleting and/or substituting one or more amino acids therein, provided that the functional variant retains the ability to bind to IL-13. In some embodiments, the first light chain comprises a functional variant of an amino acid sequence as set forth in SEQ ID NO: 44, which is formed by inserting, deleting and/or substituting one or more amino acids therein, provided that the functional variant retains the ability to bind to IL-13. In some embodiments, the second heavy chain comprises a functional variant of an amino acid sequence as set forth in SEQ ID NO: 38, which is formed by inserting, deleting and/or substituting one or more amino acids therein, provided that the functional variant retains the ability to bind to TSLP. In some embodiments, the second heavy chain comprises a functional variant of an amino acid sequence as set forth in SEQ ID NO: 40, which is formed by inserting, deleting and/or substituting one or more amino acids therein, provided that the functional variant retains the ability to bind to TSLP. The functional variant comprises or is composed of an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.1%, at least 99.2%, at least 99.3%, at least 99.4%, at least 99.5%, at least 99.6%, at least 99.7%, at least 99.8%, or at least 99.9% with an amino acid sequence of a parent polypeptide. In some embodiments, the number of amino acids inserted, deleted and/or substituted is preferably no more than 40% of the total number of amino acids in a parent amino acid

sequence, more preferably no more than 35%, more preferably 1% to 33%, more preferably 5% to 30%, more preferably 10% to 25%, and more preferably 15% to 20%. For example, the number of amino acids inserted, deleted and/or substituted may be 1 to 50, preferably 1 to 20, more preferably 1 to 10, and even more preferably 1 to 5. In preferred embodiments, the number of amino acids inserted, deleted and/or substituted is 1, 2, 3, 4, 5, 6 or 7. In some embodiments, insertion, deletion and/or substitution may be performed in a frame region (FR), e.g., in FR1, FR2, FR3 and/or FR4; and/or in a constant region, e.g., in CL, CH1, CH2 and/or CH3. In some embodiments, the substitution of one or more amino acids may be a conserved substitution of one or more amino acids. Examples of the conserved substitution are as described above. In preferred embodiments, the antibody comprises a first heavy chain having an amino acid sequence as set forth in SEQ ID NO: 42, a first light chain having an amino acid sequence as set forth in SEQ ID NO: 44, a second heavy chain having an amino acid sequence as set forth in SEQ ID NO: 38, and a second light chain having an amino acid sequence as set forth in SEQ ID NO: 40.

[00136] ***Anti-IL-13 Antibody***

[00137] The present disclosure provides an antibody specifically binding to IL-L3, or an antigen-binding fragment thereof, comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3, 46 and 53; and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3 and 53, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 53, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid

sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 53, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 52. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 13. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH comprises an amino acid

sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence as set forth in any one selected from SEQ ID NOs: 1, 3, 46 and 53, and the VH comprises an amino acid sequence as set forth in any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence as set forth in

any one selected from SEQ ID NOs: 1, 3 and 53, and the VH comprises an amino acid sequence as set forth in any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 53, and the VH comprises an amino acid sequence as set forth in any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an amino acid sequence as set forth in any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19 and 52. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 53, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 52. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 13. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 11. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 5. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 7. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 9. In some embodiments, the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an

amino acid sequence as set forth in SEQ ID NO: 11. Based on the amino acid sequences of the constant regions of the heavy chains of antibodies, immunoglobulin molecules can be classified into five types (isotypes): IgA, IgD, IgE, IgG, and IgM, and can be further classified into different subtypes, e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2. Based on the amino acid sequences of the light chains, the light chains of antibodies can be categorized into lambda (λ) chains and kappa (κ) chains. The antibodies disclosed herein may be any type or subtype as described above. In some embodiments, the antibody is an isotype selected from IgG, IgA, IgM, IgE and IgD. In some embodiments, the antibody is a subtype selected from IgG1, IgG2, IgG3 and IgG4. In preferred embodiments, the antibody is IgG1 or IgG4 antibody. The antibody disclosed herein may be an intact antibody or an antigen-binding fragment thereof. The antigen-binding fragment may be any fragment of the antibody that retains the ability to specifically bind to IL-13. Examples of the antigen-binding fragment include, but are not limited to: Fab fragments; F(ab')2 fragments; Fab' fragments; Fd fragments; Fd' fragments; Fv fragments; scFv fragments; dAb fragments; isolated complementarity-determining regions (CDR); nanobodies; a linear antibody consisting of a pair of tandem Fd fragments (VH-CH1-VH-CH1); as well as modified forms of any of the foregoing fragments which retain antigen-binding activities. In some embodiments, the antigen-binding fragment is selected from Fab, Fab', $F(ab')_2$, Fv, scFv and ds-scFv. In preferred embodiments, the antigen-binding fragment is Fab. In another preferable embodiment, the antigen-binding fragment is Fv. In another preferable embodiment, the antigen-binding fragment is scFv. In some embodiments, the antibody is a monoclonal antibody, a bispecific antibody or a multispecific antibody. In some embodiments, the antibody is a bispecific antibody that further comprises a second antigen-binding region binding to a second antigen. In some embodiments, the second antigen is a pro-inflammatory cytokine, preferably a cytokine promoting a type 2 inflammatory response, e.g., IL-4, IL-5, IL-13, IL-25, IL-31, IL-33, and TSLP.

[00138] ***Nucleic Acid***

[00139] Disclosed herein are nucleic acids, comprising a nucleotide sequence encoding the antibody or an antigen-binding fragment thereof disclosed herein, or the antibody or an antigen-binding fragment thereof disclosed herein. The term "nucleic acid" includes single- and double-stranded nucleotide polymers. Nucleic acids may be ribonucleotides or deoxyribonucleotides or modified forms of any type of nucleotides. The modifications include base modifications such as bromouridine and inosine derivatives, ribose modifications such as 2',3'-dideoxyribose, and internucleotide linkages modifications such as phosphorothioate, phosphorodithioate,

selenophosphate, diselenophosphate, phenyl phosphonothioate, anilinephosphate and aminophosphate. In some embodiments, the present invention provides a nucleic acid molecule encoding a sequence of any one of the heavy chain variable regions disclosed herein. The present invention also provides a nucleic acid molecule that is at least 90%, at least 95%, at least 98% or at least 99% identical with a nucleic acid encoding a sequence of any one of the heavy chain variable regions disclosed herein. In some embodiments, the present invention provides a nucleic acid molecule encoding a sequence of any one of the light chain variable regions disclosed herein. The present invention also provides a nucleic acid molecule that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical with a nucleic acid encoding a sequence of any one of the light chain variable regions disclosed herein. In some embodiments, the nucleic acid disclosed herein comprises: a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 2 or 4, a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 6, 8, 10, 12, 14, 16, 18, and 20, a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 29, and a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 34. In preferred embodiments, the nucleic acid disclosed herein comprises a nucleotide sequence as set forth in SEQ ID NO: 2 or 4, a nucleotide sequence as set forth in any one selected from SEQ ID NOs: 6, 8, 10, 12, 14, 16, 18, and 20, a nucleotide sequence as set forth in SEQ ID NO: 29, and a nucleotide sequence as set forth in SEQ ID NO: 34. In some embodiments, the present invention provides a nucleic acid molecule encoding the heavy chain sequence disclosed herein. The present invention also provides a nucleic acid molecule that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical with a nucleic acid encoding the heavy chain sequence disclosed herein. In some embodiments, the present invention provides a nucleic acid molecule encoding the light chain sequence disclosed herein. The present invention also provides a nucleic acid molecule that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical with a nucleic acid encoding the light chain sequence disclosed herein. In some embodiments, the nucleic acid disclosed herein comprises: a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 39, a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 41, a nucleotide sequence having a sequence identity of at

least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 43, and a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 45. In preferred embodiments, the nucleic acid disclosed herein comprises a nucleotide sequence as set forth in SEQ ID NO: 39, a nucleotide sequence as set forth in SEQ ID NO: 41, a nucleotide sequence as set forth in SEQ ID NO: 43, and a nucleotide sequence as set forth in SEQ ID NO: 45. In some embodiments, the nucleic acid is ribonucleic acid (RNA) or deoxyribonucleic acid (DNA). In some embodiments, the present invention provides ribonucleic acid (RNA) comprising a nucleotide sequence encoding an antibody disclosed herein. In some embodiments, the present invention provides deoxyribonucleic acid (DNA) comprising a deoxynucleotide sequence encoding an antibody disclosed herein. In some embodiments, the deoxyribonucleic acid (DNA) may be introduced in vivo into a human cell. In some embodiments, the deoxyribonucleic acid (DNA) of the present invention is contained in a vector or delivery agent. In some embodiments, the deoxyribonucleic acid (DNA) of the present invention is integrated into a genome of a cell. In some embodiments, the ribonucleic acid (RNA) may be introduced in vivo into a human cell. In some embodiments, the ribonucleic acid (RNA) of the present invention is contained in a vector or delivery agent.

[00140] ***Vector***

[00141] The present disclosure provides a vector comprising a nucleic acid disclosed herein.

[00142] In some embodiments, the vector is an expression vector capable of expressing a polypeptide comprising heavy or light chain variable regions of an antibody. For example, the present invention provides an expression vector comprising any of the nucleic acid molecules described above. Any vectors may be suitable for the present disclosure. In some embodiments, the vector is a viral vector. In some embodiments, the vectors are retrovirus vectors, DNA vectors, murine leukemia virus vectors, SFG vectors, plasmids, RNA vectors, adenovirus vectors, baculovirus vectors, Epstein Barr virus vectors, papovavirus vectors, poxvirus vectors, herpes simplex virus vectors, adenovirus-associated vectors (AAV), lentivirus vectors, or any combination thereof. Suitable exemplary vectors include, for example, pGAR, pBABE-puro, pBABE-neo largeTcDNA, pBABE-hygro-hTERT, pMKO.1 GFP, MSCV-IRES-GFP, pMSCV PIG (Puro IRES GFP empty plasmid), pMSCV-loxp-dsRed-loxp-eGFP-Puro-WPRE, MSCV IRES luciferase, pMIG, MDH1-PGK-GFP_2.0, TtRMPVIR, pMSCV-IRES-mCherry FP, pRetroX GFP T2A Cre, pRXTN, pLncEXP, and pLXIN-Luc. The expression vector may be any suitable recombinant expression vector. Suitable vectors include vectors, designed for proliferation and amplification or for

expression or both, such as plasmids and viruses. For example, the vectors may be selected from pUC series (Fermentas Life Sciences, Glen Burnie, Md.), pBluescript series (Stratagene, LaJolla, Calif.), pET series (Novagen, Madison, Wis.), pGEX series (Pharmacia Biotech, Uppsala, Sweden) and pEX series (Clontech, Palo Alto, Calif.). Bacteriophage vectors such as λGT10, λGT11, λZapII (Stratagene), λEMBL4, and λNM1149 may also be used. Examples of plant expression vectors that may be used in the present disclosure include pBI01, pBI101.2, pBI101.3, pBI121, and pBIN19 (Clontech). Examples of animal expression vectors that can be used in the present disclosure include pcDNA, pEUK-Cl, pMAM, and pMAMneo (Clontech). Recombinant expression vectors may be prepared by using standard recombinant DNA techniques described in, for example, Sambrook et al., Molecular Cloning: A Laboratory Manual, 3rd ed., Cold Spring Harbor Press, Cold Spring Harbor, N.Y. 2001; and Ausubel et al., Current Protocols in Molecular Biology, Greene Publishing Associates and John Wiley & Sons, NY, 1994. Cyclic or linear expression vector constructs may be prepared to contain replication system functionality in prokaryotic or eukaryotic host cells. The replication system may be derived from, for example, COLEL, 2μ plasmid, λ, SV40, and bovine papillomavirus. For example, the vector may be an adenovirus vector comprising a nucleotide sequence encoding an antibody disclosed herein. The vector may be administered to a subject and then enter into cells of the subject, thereby integrating the nucleotide sequence encoding the antibody disclosed herein into the genome of the cell, and subsequently the cell expressing the antibody disclosed herein.

[00143] ***Host Cells***

[00144] The present disclosure provides a host cell comprising the nucleic acid disclosed herein or the vector disclosed herein.

[00145] Any cells may be used as a host cell for the nucleic acid or vector of the present disclosure. In some embodiments, the cell may be a prokaryotic cell, a fungal cell, a yeast cell, or a higher eukaryotic cell such as a mammalian cell. Suitable prokaryotic cells include, but are not limited to, eubacteria such as Gram-negative or Gram-positive organisms such as *Enterobactehaceae*, e.g., *Escherichia*, e.g., *E. coli*; *Enterobacter*; *Erwinia*; *Klebsiella*; *Proteus*; *Salmonella*, e.g., *Salmonella typhimurium*; *Serratia*, e.g., *Serratia marcescans* and *Shigella*; *Bacilli*, such as *B. subtilis* and *B. licheniformis*; *Pseudomonas*, such as *P. aeruginosa*; and *Streptomyces*. In some embodiments, the cell is a human cell. In some embodiments, the cell is an immune cell. In some embodiments, the host cell comprises, for example, a CHO cell, such as a CHOS cell and a CHO-K1 cell, or a HEK293 cell, such as HEK293A, HEK293T, and HEK293FS. The host cells of

the present invention are prepared by introducing *in vitro* or *ex vivo* the vector disclosed herein or the nucleic acid disclosed herein. The host cells of the present invention may be administered to a subject *in vivo*, and the host cells express the antibody disclosed herein *in vivo*. The present invention provides host cells in which any of the vectors described above have been introduced. The present invention also provides a method for preparing the antibody of the present invention, comprising: a) culturing the host cell disclosed herein under conditions suitable for producing the antibody; and b) obtaining the antibody from the culture.

[00146] ***Pharmaceutical Compositions***

[00147] The present disclosure provides a pharmaceutical composition, comprising the bispecific antibody or an antigen-binding fragment thereof disclosed herein, or the antibody or an antigen-binding fragment thereof disclosed herein, and a pharmaceutically acceptable carrier or excipient. The antibody or an antigen-binding fragment thereof or agent (also referred to herein as "active compound") of the present invention, as well as their derivatives, fragments, analogues and homologues, may be incorporated into a pharmaceutical composition suitable for administration. Such a composition typically comprises an antibody or an antigen-binding fragment thereof or agent and a pharmaceutically acceptable carrier. As used herein, the term "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersing media, coatings, anti-bacterial agents and anti-fungal agents, isotonic agents and absorption-delaying agents, and the like, which are compatible with administration of the drug. Preferred examples of such carriers or excipients include, but are not limited to, water, saline, Ringer's solution, dextrose solution and 5% human serum albumin. Liposomes and non-aqueous vehicles such as non-volatile oils may also be used. The use of such media and agents for pharmaceutical active substances is well known in the art. Unless any conventional medium or agent is incompatible with the active compounds, it is contemplated for use in the composition. Supplementary active compounds may also be incorporated into the composition. In some embodiments, the pharmaceutical composition further comprises a second therapeutic agent. In some embodiments, the second therapeutic agent is selected from an antibody, a chemotherapeutic agent, and a small molecule drug. The pharmaceutical composition of the present invention may be formulated to be compatible with its intended routes of administration. Examples of routes of administration include parenteral administration, such as intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (i.e., topical), transmucosal, and rectal administration. Solutions or suspensions for parenteral, intradermal or subcutaneous application may include the following components: a sterile diluent, such as water for injection, saline solution, non-

volatile oil, polyethylene glycol, glycerol, propylene glycol, or other synthetic solvents; antimicrobials, such as benzyl alcohol or methylparaben; antioxidants, such as ascorbic acid or sodium bisulfite; chelating agents, such as ethylenediaminetetraacetic acid (EDTA); buffers, such as acetate, citrate, or phosphate; and agents for regulating tonicity, such as sodium chloride or dextrose. Values of pH may be adjusted with an acid or base, such as hydrochloric acid or sodium hydroxide. Parenteral preparations may be encapsulated in ampoules, disposable syringes, or multi-dose vials made of glass or plastic. The pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (if water soluble) or dispersions and sterile powders for the temporary preparation of sterile injectable solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be a fluid present at an easily injectable level. It must be stable under conditions of preparation and storage and must be protected against the contaminating effects of microorganisms such as bacteria and fungi. The carrier may be a solvent or a dispersing medium containing, for example, water, ethanol, polyols (e.g. glycerol, propylene glycol and liquid polyethylene glycol), and suitable mixtures thereof. Suitable fluidity may be maintained, for example, by the use of an envelope such as lecithin, by maintaining a desired particle size in the case of a dispersion, and by using surfactants. Microbial action may be prevented by various antimicrobial agents and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, and thimerosal. In many cases, preferably, the composition includes isotonic agents, such as saccharides, polyols such as mannitol, sorbitol, sodium chloride. The absorption of the injectable composition may be prolonged by including absorption-delaying agents, such as aluminum monostearate and gelatin in the composition. Sterile injectable solutions may be prepared as follows: incorporating a desired amount of the active compound and an ingredient or a combination of ingredients (as desired) enumerated above in a suitable solvent, followed by filtration sterilization. Typically, the dispersion is prepared by introducing the active compound into a sterile vehicle containing basic dispersing media and desired other ingredients from those enumerated above. In the case of sterile powders for preparing sterile injectable solutions, the preparation method is vacuum drying and freeze drying to produce a powder of the active ingredient plus any other desired ingredients from the previously sterile filtered solution thereof. Oral compositions typically include inert diluents or edible carriers. They may be encapsulated in gelatin capsules or pressed into tablets. For the purpose of oral therapeutic administration, the active compound may be mixed with an excipient and used in the form of tablets, lozenges or capsules. Oral compositions may also be prepared by using a fluid carrier used as a mouthwash, wherein the

compound in the fluid carrier is administered orally and rinsed and spit out or swallowed. Pharmaceutically compatible binding agents and/or adjuvant materials may be included as part of the composition. Tablets, pills, capsules, lozenges or the like may contain any of the following ingredients or compounds of similar properties: binding agents, such as microcrystalline cellulose, tragacanth gum or gelatin; excipients, such as starch or lactose, disintegrants, such as alginate, Primogel, or corn starch; lubricants, such as magnesium stearate or Sterotes; glidants, such as colloidal silicon dioxide; sweetening agents, such as sucrose or saccharin; or flavoring agents, such as peppermint oil, methyl salicylate, or orange flavoring. For inhalation administration, the compound is delivered as an aerosol spray from a pressure vessel or a dispenser or nebulizer containing a suitable propellant (e.g. gas such as carbon dioxide). Systemic administration may also be performed in a transmucosal or transdermal manner. For transmucosal or transdermal administration, a penetrant suitable for the barrier to be penetrated is used in the formulation. Such penetrants are generally known in the art and include, for example, detergents, bile salts and fusidic acid derivatives for transmucosal administration. Transmucosal administration may be accomplished by using nasal sprays or suppositories. For transdermal administration, the active compounds are formulated as ointments, salves, gels or creams well known in the art. The active compound may also be prepared into a suppository form (e.g., using conventional suppository matrices such as cocoa butter and other glycerides) or a retention enema for rectal delivery.

[00148] In one embodiment, the active compound is prepared with a carrier (e.g., controlled-release formulations, including implants and microencapsulated delivery systems) that will protect the compound from rapid elimination from the body. Biodegradable and biocompatible polymers may be used, such as vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyortho esters, and polylactic acid. Methods for preparing such formulations will be apparent to those skilled in the art. The present invention provides a therapeutic composition comprising the antibody or an antigen-binding fragment thereof of the present invention. The therapeutic composition according to the present invention will be administered with suitable carriers, excipients and other agents incorporated into the formulation to provide improved transfer, delivery, tolerability, etc. Many suitable formulations are found in prescriptions known to all medicinal chemists: Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, PA. These formulations include, for example, powders, pastes, ointments, jellies, waxes, oils, lipids, vesicle-containing lipids (cationic or anionic) (e.g., LIPOFECTIN™), DNA conjugates, anhydrous absorbent pastes, oil-in-water and water-in-oil emulsions, poly(ethylene glycol) emulsions (poly(ethylene glycol) of various molecular weights), semi-solid gels, and semi-solid mixtures containing poly(ethylene glycol). See also Powell

et al. "Compendium of excipients for parenteral formulations" PDA (1998) J Pharm Sci Technol 52:238-311.

[00149] ***Conjugates***

[00150] The present disclosure provides a conjugate comprising the antibody or an antigen-binding fragment thereof disclosed herein or the bispecific antibody or an antigen-binding fragment thereof disclosed herein, and a chemical moiety conjugated thereto. In the context of the present disclosure, a "conjugate" is an antibody or antibody fragment (e.g., an antigen-binding fragment) covalently linked to a chemical moiety. The chemical moiety may be, for example, a drug, a toxin, a therapeutic agent, a detectable label, a protein, a nucleic acid, a lipid, a nanoparticle, a carbohydrate, or a recombinant virus. An antibody conjugate is commonly referred to as "immunoconjugate." When the conjugate comprises an antibody attached to a drug (e.g., a cytotoxic agent), the conjugate is typically referred to as an "antibody-drug conjugate" or "ADC." The terms "conjugation" or "ligation" may refer to making two polypeptides into one consecutive polypeptide molecule. In one embodiment, the antibody is attached to the chemical moiety. In another embodiment, the antibody attached to the chemical moiety is further attached to a lipid, or other molecules to a protein or peptide to increase its half-life in vivo. The ligation may be performed chemically or recombinantly. In one embodiment, the ligation is chemical, wherein a reaction between the antibody moiety and the chemical moiety creates a covalent bond formed between the two molecules to form one molecule. A peptide linker (short peptide sequence) may optionally be included between the antibody and the chemical moiety. Any number of ways known to those skilled in the art may be used to attach the chemical moiety to the antibody of the present invention. Both covalent and non-covalent attachment ways may be used. The procedure for attaching the chemical moiety to the antibody varies depending on the chemical structure of the chemical moiety. Polypeptides typically contain a variety of functional groups; such as carboxylic acid (COOH), free amine (-NH2), or sulfhydryl (-SH) moieties, which may be used to react with suitable functional groups on the antibody to result in binding of the chemical moiety. Alternatively, the antibody is derivatized to expose or attach additional reactive functional groups. Derivatization may involve attachment of any of a number of known linker molecules. The linker may be any molecule used to attach the antibody to the chemical moiety. The linker is capable of forming a covalent bond with both the antibody and the chemical moiety. Suitable linkers are well known to those of skill in the art, and include, but are not limited to, straight or branched chain carbon linkers, heterocyclic carbon linkers, or peptide linkers. In the case where the antibody and the chemical moiety are polypeptides, the linker may be attached to the

constituent amino acids via their side groups (e.g., via disulfide bonds to cysteines) or to amino and carboxyl groups of the alpha carbon of the terminal amino acids. In certain cases, the chemical moiety is expected to be released from the antibody when the immunoconjugate reaches its target site. Thus, in these instances, the immunoconjugate will comprise a cleavable linkage near the target site. Enzymatic activities or conditions experienced by the immunoconjugate within a target cell or near the target site may promote cleavage of the linkage to release the chemical moiety from the antibody. In view of the large number of methods reported for attaching a variety of radio-diagnostic compounds, radio-therapeutic compounds, labels (e.g., enzymes or fluorescent molecules), drugs, toxins, and other agents to an antibody, a person of skill in the art will be able to determine a suitable method for attaching a given agent to an antibody or other polypeptides. The antibody disclosed herein may be derivatized or attached to another molecule (e.g., another peptide or protein). Typically, the antibody or a portion thereof is derivatized such that binding to a target antigen is not adversely affected by the derivatization or labeling. For example, the antibody may be functionally linked (by chemically coupling, gene fusion, non-covalent association, or otherwise) to one or more other molecular entities, such as another antibody (e.g., a bispecific antibody or a bivalent antibody), a detecting agent, a pharmaceutical agent, and/or a protein or peptide that may mediate the association of the antibody or the antibody moiety to another molecule (e.g., the core region of streptavidin or a polyhistidine tag). One type of derived antibodies is produced by crosslinking two or more antibodies (of the same type or different types). Suitable crosslinking agents include heterobifunctional crosslinking agents having two distinctly reactive portions (e.g., meso-maleimido benzoyl-N-hydroxysuccinimide ester) separated by a suitable spacer, or homobifunctional crosslinking agents (e.g., octanedioic acid disuccinimide ester). Such linkers are commercially available. In some embodiments of the conjugate disclosed by the present invention, the chemical moiety is selected from a therapeutic agent, a detectable moiety, and an immunostimulatory molecule. In some embodiments, the therapeutic agent includes, but is not limited to, an immunomodulator, a radioactive compound, an enzyme (e.g., perforin), a chemotherapeutic agent (e.g., cisplatin), or a toxin. In some embodiments, the therapeutic agent may be, for example, mertansine, geldanamycin, a tubulin inhibitor such as a tubulin-binding agent (e.g., auristatins), or a minor groove-binding agent such as calicheamicin. In some embodiments, the detectable moiety may be selected from biotin, streptavidin, enzymes or catalytically active fragments thereof, radionuclides, nanoparticles, paramagnetic metal ions, or fluorescent, phosphorescent, or chemiluminescent molecules. Detectable moieties for diagnostic purposes include, for example, fluorescent labels, radiolabels, enzymes, nucleic acid probes, and contrast agents. Antibodies may be

conjugated to detectable labels; for example, detectable labels capable of being detected by ELISA, spectrophotometry, flow cytometry, microscopy, or diagnostic imaging techniques (e.g., computed tomography (CT), computed axial tomography (CAT) scanning, magnetic resonance imaging (MRI), nuclear magnetic resonance imaging (NMRI), magnetic resonance tomography (MTR), ultrasonic, fiberoptic examination, and laparoscopy). Specific, non-limiting examples of detectable labels include fluorophores, chemiluminescent agents, enzymatic ligations, radioisotopes, and heavy metals or compounds (e.g., superparamagnetic iron oxide nanocrystals for detection by MRI). For example, useful detectable labels include fluorescent compounds, including fluorescein, fluorescein isothiocyanate, rhodamine, 5-dimethylamino-1-naphthalenesulfonyl chloride, phycoerythrin, lanthanide phosphorosome, and the like. Bioluminescent labels such as luciferase, green fluorescent protein (GFP) and yellow fluorescent protein (YFP) may also be used. The antibody or antigen-binding fragment may also be conjugated to enzymes useful for detection, such as horseradish peroxidase, beta-galactosidase, luciferase, alkaline phosphatase, and glucose oxidase. The antibody or antigen-binding fragment, upon conjugation to a detectable enzyme, can be detected by adding an enzyme to produce additional reagents capable of recognizing reaction products. For example, when horseradish peroxidase reagents are present, the addition of hydrogen peroxide and diaminobenzidine will result in a colored reaction product, which can be visually detected. The antibody or antigen-binding fragment may also be conjugated to biotin and detected by indirect measurement of avidin or streptavidin binding. It should be noted that the avidin itself may be conjugated to an enzyme or fluorescent label. The antibody may be fused to a self-labelled protein tag (e.g., HaloTag). For example, the protein tag may be cloned to a terminus of a constant region. HaloTag is a self-labelled protein tag derived from a bacterial enzyme (haloalkane dehalogenase), and is intended to bind covalently to a synthetic ligand. In some cases, the synthetic ligand comprises a chloroalkane linker attached to a fluorophore such as a near-infrared fluorophore (Los et al. (2008) ACS Chem Biol. 3(6):373-82). The antibody may be labelled with a magnetic agent such as gadolinium. The antibody may also be labelled with lanthanides (e.g., europium and dysprosium) and manganese. Paramagnetic particles such as superparamagnetic iron oxide may also be used as a label. The antibody may also be labelled with a predetermined polypeptide epitope recognized by a second reporter gene (e.g., leucine zipper pair sequences, a binding site of a second antibody, metal-binding domains, and epitope tags). In some embodiments, the tag is attached by a spacer arm of various lengths to reduce potential steric hindrance. The antibody may also be labelled with radiolabelled amino acids. Radiolabelling may be used for diagnostic and therapeutic purposes. For example, radiolabelling may be used to detect expression of a target antigen by X-ray, emission

spectroscopy, or other diagnostic techniques. Examples of polypeptide labelling include, but are not limited to, the following radioisotopes or radionucleotides: ^{3}H, ^{14}C, ^{15}N, ^{35}S, ^{90}Y, ^{99}Tc, ^{111}In, ^{125}I, and ^{131}I. In some embodiments, the immunostimulatory molecule is an immune effector molecule stimulating an immune response. For example, the immunostimulatory molecule may be a cytokine such as IL-2 and IFN-γ, a chemokine such as IL-8, platelet factor 4, a melanoma growth stimulating protein, a complement activator; a viral/bacterial protein domain, or a viral/bacterial peptide.

[00151] ***Treatment Methods***

[00152] The present disclosure provides a method for treating a disease associated with a type 2 inflammatory response in a subject, comprising administering to the subject an effective amount of a bispecific antibody or an antigen-binding fragment thereof disclosed herein, an antibody or an antigen-binding fragment thereof disclosed herein, a pharmaceutical composition disclosed herein, or a conjugate disclosed herein. In some embodiments, the disease is a disease mediated by IL-13 and/or TSLP (e.g., an inflammatory disease and an autoimmune disease). In some embodiments, the disease is an IL-13-mediated inflammatory disease. In some embodiments, the disease is an IL-13-mediated autoimmune disease. In some embodiments, the disease is a TSLP-mediated inflammatory disease. In some embodiments, the disease is a TSLP-mediated autoimmune disease. In some embodiments, the disease is selected from an allergic inflammatory disease (e.g., allergic rhinitis, allergic sinusitis, and allergic conjunctivitis), asthma, atopic dermatitis, urticaria, chronic obstructive pulmonary disease, eosinophilic esophagitis, rheumatoid arthritis, multiple sclerosis, idiopathic pulmonary fibrosis, eczema (e.g., hand eczema, and asthmatic eczema), eosinophilic gastroenteritis, Crohn's disease, systemic sclerosis, ulcerative colitis, and chronic rhinosinusitis with nasal polyps. In preferred embodiments, the disease is atopic dermatitis. In some embodiments, the dosage administered to the subject may vary with the embodiments, the drugs used, the methods of administration, and the site and subject to be treated. However, the dosage should be sufficient to provide a therapeutic response. A clinician is able to determine the effective amount to be administered to a human or other subjects to treat a medical condition. The precise amount required to be therapeutically effective may depend on many factors, such as the activity of the antibody and the route of administration. Dosages of the antibodies, compositions, or conjugates described herein may be administered to a mammal in a single dose or in a series of subdoses over a suitable period of time, e.g., once daily, semi-weekly, weekly, bi-weekly, semi-monthly, bi-monthly, semi-annually, or annually, as needed. A dosage unit comprising an effective amount of the antibody, composition or conjugate may be administered as a single daily dose, or a total daily dose may be administered in

two, three, four or more subdoses administered daily, as needed. The appropriate mode of administration may be selected by a physician. The route of administration may be parenteral administration, e.g., by injection, intranasal, transpulmonary or percutaneous administration. Systemic or topical administration may be performed by intravenous, intramuscular, intraperitoneal, or subcutaneous injection. In some embodiments, the antibody, composition, or conjugate is selected for parenteral delivery, for inhalation, or for delivery through the digestive tract, e.g., orally. The dosage and method of administration may vary and may be selected appropriately depending on the weight, age, conditions and the like of a subject. In some embodiments, the method further comprises administering a second therapeutic agent to the subject. In some embodiments, the antibody, composition, or conjugate disclosed herein is administered prior to, substantially concurrently with, or after administration of the second therapeutic agent. In some embodiments, the second therapeutic agent is selected from an antibody, a chemotherapeutic agent, and a small molecule drug. The present disclosure also provides a method for inhibiting IgE antibody production in a subject, comprising administering to the subject an effective amount of the bispecific antibody or an antigen-binding fragment thereof disclosed herein, the antibody or an antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein. One of pathological characteristics of a diseases associated with a type 2 inflammatory response is an increase in IgE, and therefore inhibition of IgE antibody production in a subject can be used to prevent or treat a disease associated with a type 2 inflammatory response, such as allergic inflammation (e.g., allergic rhinitis, allergic sinusitis, and allergic conjunctivitis), asthma, atopic dermatitis, urticaria, chronic obstructive pulmonary disease, eosinophilic esophagitis, rheumatoid arthritis, multiple sclerosis, idiopathic pulmonary fibrosis, eczema (e.g., hand eczema, and asthmatic eczema), eosinophilic gastroenteritis, Crohn's disease, systemic sclerosis, ulcerative colitis, and chronic rhinosinusitis with nasal polyps.

[00153] ***Medical Use***

[00154] The present disclosure provides use of the bispecific antibody or an antigen-binding fragment thereof disclosed herein, the antibody or an antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein, in preparation of a medicament useful for treating a disease associated with a type 2 inflammatory response in a subject. The present disclosure also provides the bispecific antibody or an antigen-binding fragment thereof disclosed herein, the antibody or an antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein,

for use in treating a disease associated with a type 2 inflammatory response in a subject. In some embodiments of the use disclosed herein, the disease is selected from allergic inflammation (e.g., allergic rhinitis, allergic sinusitis, and allergic conjunctivitis), asthma, atopic dermatitis, urticaria, chronic obstructive pulmonary disease, eosinophilic esophagitis, rheumatoid arthritis, multiple sclerosis, idiopathic pulmonary fibrosis, eczema (e.g., hand eczema, and asthmatic eczema), eosinophilic gastroenteritis, Crohn's disease, systemic sclerosis, ulcerative colitis, and chronic rhinosinusitis with nasal polyps. In some embodiments, the disease is selected from allergic rhinitis, allergic sinusitis, allergic conjunctivitis, hand eczema, and asthmatic eczema. In some embodiments, the bispecific antibody or an antigen-binding fragment thereof disclosed herein, the antibody or an antigen-binding fragment thereof disclosed herein, the pharmaceutical composition disclosed herein, or the conjugate disclosed herein is used in combination with a second therapeutic agent. In some embodiments, the second therapeutic agent is selected from an antibody, a chemotherapeutic agent, and a small molecule drug.

[00155] ***Kits***

[00156] The present disclosure provides a pharmaceutical package or a kit comprising one or more containers containing one or more components of the pharmaceutical composition described herein, such as the antibody or an antigen-binding fragment disclosed herein.

[00157] In specific embodiments, the kit comprises a first container containing the antibody disclosed herein. In specific embodiments, the kit comprises a first container which is a vial containing the antibody as a lyophilized sterile powder under vacuum, and the kit further comprises a second container containing a pharmaceutically acceptable fluid. In specific embodiments, provided herein is an injection device containing the antibody. In specific embodiments, the injection device comprises the antibody in a sterile solution. In specific embodiments, the injection device is a syringe. In one embodiment, the kit includes an instructional material disclosing ways to use the antibody of the present disclosure. The instructional material may be written, in electronic form (e.g., a computer diskette or CD), or visual (e.g., a video file). The kit may also include additional components to facilitate the application for which the kit is designed. Thus, for example, the kit may additionally contain a tool for detecting a label (e.g., enzyme substrates for enzymatic labelling, filter sets for detecting fluorescent labels, and suitable secondary labels such as secondary antibodies). The kit may also include buffers and other reagents routinely used to implement the particular methods. Such kits and suitable contents are well known to those of skill in the art.

[00158] Embodiments

[00159] Embodiment 1 A bispecific antibody or an antigen-binding fragment thereof comprising a first antigen-binding region binding to IL-13 and a second antigen-binding region binding to TSLP, the first antigen-binding region comprising a first light chain variable region (VL1) and a first heavy chain variable region (VH1), and the second antigen-binding region comprising a second light chain variable region (VL2) and a second heavy chain variable region (VH2), wherein

the VL1 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 21-23, respectively;

the VH1 comprises HCDR 1 having an amino acid sequence as set forth in SEQ ID NO: 24, HCDR 2 having an amino acid sequence as set forth in SEQ ID NO: 25 or 26, and HCDR 3 having an amino acid sequence as set forth in SEQ ID NO: 27;

the VL2 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 35-37, respectively; and

the VH2 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 30-32, respectively.

[00160] Embodiment 2. The bispecific antibody according to embodiment 1, or an antigen-binding fragment thereof, wherein

the VL1 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 21-23, respectively;

the VH1 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 24, 25 and 27, respectively;

the VL2 comprises LCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 35-37, respectively; and

the VH2 comprises HCDRs 1-3 having an amino acid sequence as set forth in SEQ ID NOs: 30-32, respectively.

[00161] Embodiment 3. The bispecific antibody according to embodiment 1, or an antigen-binding fragment thereof, wherein

the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3, and 46;

the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19;

the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 33 or 51; and

the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28 or 50.

[00162] Embodiment 4. The bispecific antibody according to embodiment 3, or an antigen-binding fragment thereof, wherein

the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 1, 3, and 46;

the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 5, 7, 9, 11, and 13;

the VL2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 33; and

the VH2 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 28.

[00163] Embodiment 5. The bispecific antibody according to embodiment 4, or an antigen-binding fragment thereof, wherein

(i) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9; or

(ii) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5; or

(iii) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at

least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7; or

(iv) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11; or

(v) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 1, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 13; or

(vi) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5; or

(vii) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7; or

(viii) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9; or

(ix) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 46, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11; or

(x) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 5; or

(xi) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 7; or

(xii) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 9; or

(xiii) the VL1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 3, and the VH1 comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 11.

[00164] Embodiment 6. The bispecific antibody according to embodiment 5, or an antigen-binding fragment thereof, wherein

(i) the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 9; or

(ii) the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 5; or

(iii) the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 7; or

(iv) the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 11; or

(v) the VL1 comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH1 comprises an amino acid sequence as set forth in SEQ ID NO: 13; and

the VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33, and the VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28.

[00165] Embodiment 7. The bispecific antibody according to embodiment 6, or an antigen-binding fragment thereof, wherein the antibody comprises:

a first heavy chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 42,

a first light chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 44,

a second heavy chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 38, and

a second light chain which comprises an amino acid sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 40.

[00166] Embodiment 8. The bispecific antibody according to embodiment 7, or an antigen-binding fragment thereof, wherein the antibody comprises a first heavy chain having an amino acid sequence as set forth in SEQ ID NO: 42, a first light chain having an amino acid sequence as set forth in SEQ ID NO: 44, a second heavy chain having an amino acid sequence as set forth in SEQ ID NO: 38, and a second light chain having an amino acid sequence as set forth in SEQ ID NO: 40.

[00167] Embodiment 9. An antibody specifically binding to IL-13, or an antigen-binding fragment thereof, comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein

the VL comprises an amino acid sequence as set forth in any one selected from SEQ ID NOs: 1, 3, and 46, and

the VH comprises an amino acid sequence as set forth in any one selected from SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, and 19.

[00168] Embodiment 10. The antibody according to embodiment 9, or an antigen-binding fragment thereof, wherein

(i) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 9; or

(ii) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 5; or

(iii) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 7; or

(iv) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 11; or

(v) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 13; or

(vi) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 5; or

(vii) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 7; or

(viii) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 9; or

(ix) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 46, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 11; or

(x) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 5; or

(xi) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 7; or

(xii) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 9; or

(xiii) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 3, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 11.

[00169] Embodiment 11. The antibody according to embodiment 10, or an antigen-binding fragment thereof, wherein

(i) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 9; or

(ii) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 5; or

(iii) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 7; or

(iv) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 11; or

(v) the VL comprises an amino acid sequence as set forth in SEQ ID NO: 1, and the VH comprises an amino acid sequence as set forth in SEQ ID NO: 13.

[00170] Embodiment 12. The antibody according to any one of embodiments 9-11, or an antigen-binding fragment thereof, wherein the antibody is an isotype selected from IgG, IgA, IgM, IgE and IgD.

[00171] Embodiment 13. The antibody according to any one of embodiments 9-12, or an antigen-binding fragment thereof, wherein the antibody is a subtype selected from IgG1, IgG2, IgG3 and IgG4.

[00172] Embodiment 14. The antibody according to any one of embodiments 9-13, or an antigen-binding fragment thereof, wherein the antigen-binding fragment is selected from Fab, Fab', $F(ab')_2$, Fv, scFv and ds-scFv.

[00173] Embodiment 15. The antibody according to any one of embodiments 9-14, or an antigen-binding fragment thereof, wherein the antibody is a monoclonal antibody, a bispecific antibody, or a multispecific antibody.

[00174] Embodiment 16. The antibody according to embodiment 15, or an antigen-binding fragment thereof, wherein the antibody is a bispecific antibody that further comprises a second antigen-binding region binding to a second antigen.

[00175] Embodiment 17. A nucleic acid, comprising a nucleotide sequence encoding the bispecific antibody or the antigen-binding fragment thereof according to any one of embodiments 1-8, or the antibody or the antigen-binding fragment thereof according to any one of embodiments 9-16.

[00176] Embodiment 18. The nucleic acid according to embodiment 17, which comprises:

a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 2 or 4,

a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with any one selected from SEQ ID NOs: 6, 8, 10, 12, 14, 16, 18, and 20,

a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 29, and

a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 34.

[00177] Embodiment 19. The nucleic acid according to embodiment 17, which comprises:
a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 39,
a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 41,
a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 43, and
a nucleotide sequence having a sequence identity of at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% with SEQ ID NO: 45.

[00178] Embodiment 20. A vector comprising the nucleic acid according to any one of embodiments 17-19.

[00179] Embodiment 21. A host cell, comprising the nucleic acid according to any one of embodiments 17-19, or the vector according to embodiment 20.

[00180] Embodiment 22. A pharmaceutical composition, comprising: (i) the bispecific antibody or the antigen-binding fragment thereof according to any one of embodiments 1-8, or the antibody or the antigen-binding fragment thereof according to any one of embodiments 9-16; and (ii) a pharmaceutically acceptable carrier or excipient.

[00181] Embodiment 23. The pharmaceutical composition according to embodiment 22, further comprising a second therapeutic agent.

[00182] Embodiment 24. The pharmaceutical composition according to embodiment 23, wherein the second therapeutic agent is selected from an antibody, a chemotherapeutic agent and a small molecule drug.

[00183] Embodiment 25. A conjugate, comprising the bispecific antibody or the antigen-binding fragment thereof according to any one of embodiments 1-8, or the antibody or the antigen-binding fragment thereof according to any one of embodiments 9-16, and a chemical moiety conjugated therewith.

[00184] Embodiment 26. The conjugate according to embodiment 25, wherein the chemical moiety is selected from a therapeutic agent, a detectable moiety and an immunostimulatory molecule.

[00185] Embodiment 27. A method for treating a disease associated with a type 2 inflammatory response in a subject, comprising administering to the subject an effective amount of the bispecific antibody or the antigen-binding fragment thereof according to any one of embodiments 1-8, the antibody or the antigen-binding fragment thereof according to any one of

embodiments 9-16, the pharmaceutical composition according to any one of embodiments 22-24, or the conjugate according to embodiment 25 or 26.

[00186] Embodiment 28. The method according to embodiment 27, wherein the disease is a disease mediated by IL-13 and/or TSLP (e.g., an inflammatory disease and an autoimmune disease).

[00187] Embodiment 29. The method according to embodiment 28, wherein the disease is selected from atopic dermatitis, allergic inflammation (e.g., allergic rhinitis, allergic sinusitis, and allergic conjunctivitis), asthma, urticaria, chronic obstructive pulmonary disease, eosinophilic esophagitis, rheumatoid arthritis, multiple sclerosis, idiopathic pulmonary fibrosis, eczema (e.g., hand eczema, and asthmatic eczema), eosinophilic gastroenteritis, Crohn's disease, systemic sclerosis, ulcerative colitis, and chronic rhinosinusitis with nasal polyps.

[00188] Embodiment 30. The method according to any one of embodiments 27-29, further comprising administering to the subject a second therapeutic agent.

[00189] Embodiment 31. The method according to embodiment 30, wherein the second therapeutic agent is selected from an antibody, a chemotherapeutic agent and a small molecule drug.

[00190] Embodiment 32. A method for inhibiting IgE antibody production in a subject, comprising administering to the subject an effective amount of the bispecific antibody or the antigen-binding fragment thereof according to any one of embodiments 1-8, the antibody or the antigen-binding fragment thereof according to any one of embodiments 9-16, the pharmaceutical composition according to any one of embodiments 22-24, or the conjugate according to embodiment 25 or 26.

[00191] **Examples**

[00192] The following examples are given for the purpose of illustrating various embodiments of the present invention, but are not meant to limit the invention in any way. The examples and the methods described herein currently represent preferred embodiments, are exemplary, and are not intended to limit the scope of the present invention. Variations and other uses will occur to those skilled in the art and be encompassed within the spirit of the present invention as limited by the scope of the claims.

[00193] **Example 1. humanization of murine anti-IL-13 antibody 228B/C-1**

[00194] The murine anti-IL-13 antibody 228B/C-1 is a murine parent molecule of Lebrikizumab. The light chain variable region (VL, also known as K0) of Lebrikizumab comprises LCDR1, LCDR2, and LCDR3 comprising the amino acid sequences of SEQ ID NO: 21, 22, and 23, respectively. The heavy chain variable region (VH, also known as H0) of Lebrikizumab comprises

HCDR1, HCDR2, and HCDR3 comprising the amino acid sequences of SEQ ID NO: 24, 25, and 27, respectively.

[00195] VL of Lebrikizumab comprises the amino acid sequence set forth in SEQ ID NO: 46. The nucleotide sequence set forth in SEQ ID NO: 47 encodes the VL of Lebrikizumab. VH of Lebrikizumab comprises the amino acid sequence set forth in SEQ ID NO: 48. The nucleotide sequence set forth in SEQ ID NO: 49 encodes the VH of Lebrikizumab.

[00196] The 228B/C-1 molecule is humanized by a strategy of transplanting antibody complementarity determining regions (CDRs) to improve its developability. Based on computer homology modeling, human germline genes IMGT_ hIGKV1_39 and IMGT_hIGKV3-11 with high homology to 228B/C-1 light chain framework regions were selected to perform CDR transplantation for the light chain, and human IGKJ2*01 with the highest homology was selected for FM4; human germline genes IMGT_ IGHV4-59 and IMGT_ IGHV3-33 with high homology to 228B/C-1 light chain framework regions were selected to perform CDR transplantation for the heavy chain, and human IGHJ4*01 with the highest homology was selected for FM4. Meanwhile, a computer was used to perform homology modeling and analyze the amino acid sequences of the CDR regions and adjacent framework regions, avoiding the centralized distribution of charge or hydrophobic regions on the molecular surface; and to find out the crucial amino acid residues in the antibody gene sequence for binding to the target antigen and maintaining the spatial framework by calculating the electrostatic force, van der Waals' force, hydrophilicity-hydrophobicity and entropy value. On this basis, revertant mutation sites were designed. A total of 8 humanized heavy chain variable regions H1-H8 and 2 humanized light chain variable regions K1-K2 were designed (Table 1).

Table 1. 228B/C-1 humanized antibody sequence

228B/C-1 humanized antibody	germline genes	J region genes	V region	
			amino acid sequence	nucleotide sequence
K1	MGT_hIGKV1_39	IGKJ2*01	1	2
K2	IMGT_hIGKV3-11	IGKJ2*01	3	4
H1	IMGT_ IGHV4-59	IGHJ4*01	5	6
H2	IMGT_ IGHV3-33	IGHJ4*01	7	8
H3	IMGT_ IGHV4-59	IGHJ4*01	9	10
H4	IMGT_ IGHV3-33	IGHJ4*01	11	12
H5	IMGT_ IGHV4-59	IGHJ4*01	13	14
H6	IMGT_ IGHV3-33	IGHJ4*01	15	16
H7	IMGT_ IGHV4-59	IGHJ4*01	17	18
H8	IMGT_ IGHV3-33	IGHJ4*01	19	20

[00197] K1-K2 are humanized light chain variable regions. H1-H8 are humanized heavy chain variable regions.

[00198] K1 comprises the amino acid sequence set forth in SEQ ID NO: 1. The nucleic acid encoding K1 comprises the nucleotide sequence set forth in SEQ ID NO: 2. K2 comprises the amino acid sequence set forth in SEQ ID NO: 3. The nucleic acid encoding K1 comprises the nucleotide sequence set forth in SEQ ID NO: 4.

[00199] H1 comprises the amino acid sequence set forth in SEQ ID NO: 5. The nucleic acid encoding H1 comprises the nucleotide sequence set forth in SEQ ID NO: 6. H2 comprises the amino acid sequence set forth in SEQ ID NO: 7. The nucleic acid encoding H2 comprises the nucleotide sequence set forth in SEQ ID NO: 8. H3 comprises the amino acid sequence set forth in SEQ ID NO: 9. The nucleic acid encoding H3 comprises the nucleotide sequence set forth in SEQ ID NO: 10. H4 comprises the amino acid sequence set forth in SEQ ID NO: 11. The nucleic acid encoding H4 comprises the nucleotide sequence set forth in SEQ ID NO: 12. H5 comprises the amino acid sequence set forth in SEQ ID NO: 13. The nucleic acid encoding H5 comprises the nucleotide sequence set forth in SEQ ID NO: 14. H6 comprises the amino acid sequence set forth in SEQ ID NO: 15. The nucleic acid encoding H6 comprises the nucleotide sequence set forth in SEQ ID NO: 16. H7 comprises the amino acid sequence set forth in SEQ ID NO: 17. The nucleic acid encoding H7 comprises the nucleotide sequence set forth in SEQ ID NO: 18. H8 comprises the amino acid sequence set forth in SEQ ID NO: 19. The nucleic acid encoding H8 comprises the nucleotide sequence set forth in SEQ ID NO: 20.

[00200] In the above humanized variable region sequences, the six CDRs of K1, K2, H1, H3, H4, and H5 were identical to the CDR sequences of the parent antibody Lebrikizumab; HCDR2 of H2, H6, H7, and H8 (SEQ ID NO: 26) was different from HCDR2 of the parent antibody Lebrikizumab, and the other five CDRs were identical to those of Lebrikizumab.

[00201] **Example 2. expression of 228B/C-1 humanized antibody**

[00202] 1) validation of 228B/C-1 humanized light chain and heavy chain pairing

[00203] The Lebrikizumab light chain variable region (K0) and two humanized light chain variable regions (K1, K2) were paired with the Lebrikizumab heavy chain variable region (H0) and eight humanized heavy chain variable regions (H1-H8), respectively. HEK293 cells were transiently transfected, and the supernatants were taken to capture the antibodies with a ProA probe by using the biofilm interference technique (BLI/gator prime), and then the probe was transferred to diluted human IL-13 antigen (hIL-13). Based on the signal change detected on the probe, the real-time binding signal of the antigen to the antibody was obtained, and finally the mapping was 1:1 kinetically fitted to obtain the binding affinity of the antibody to the antigen in the transiently-

transfected supernatant (Figs. 1B-1O). The light and heavy chain pairs H1K0, H2K0, H3K0, H4K0, H1K1, H2K1, H3K1, H4K1, H5K1, H1K2, H2K2, H3K2 and H4K2 with higher affinities were selected for further transient transfection, expression and purification.

[00204] 2) expression and purification of 228B/C-1 humanized antibody

[00205] The light and heavy chains were transfected into ExpiCHO cells at a ratio of 1:1 by using transfection reagents. The cells were cultured for 7 days at 37°C, 8% CO_2 and 80% humidity. After culturing, the fermentation broth was centrifuged at 4°C, 4500 rpm for 30 min and the supernatant was filtered through a 0.22 μm needle filter. Purification was performed by a gravity column using Protein A. The yields of transient transfection of the humanized antibodies are shown in Table 2. The results showed that the optimized yields of transient transfection of 228B/C-1 humanized antibodies were all better than that of the parent antibody Lebrikizumab.

Table 2. yields of transient transfection of 228B/C-1 humanized antibodies

Antibody	Yield (mg/L)	Antibody	Yield (mg/L)
Lebrikizumab	32.1	H3K1	156.4
H1K0	145.9	H4K1	215.9
H2K0	123.5	H5K1	190.8
H3K0	140.4	H1K2	137.2
H4K0	110.7	H2K2	80.7
H1K1	168.3	H3K2	103.1
H2K1	217.5	H4K2	104.8

[00206] **Example 3. activity of 228B/C-1 humanized antibody**

[00207] 1) Binding affinity to human IL-13 (hIL-13)

[00208] Surface plasmon resonance technology (SPR/Biacore T200) was used, a CM5 chip was selected, and a goat anti-hFc antibody was coupled to the chip channels Fc1-4 to capture the humanized antibody onto the chip surface through the specific high-affinity binding of the goat anti-hFc to the humanized antibody. Then the gradiently diluted hIL-13 antigen was allowed to flow through the chip surface as an analyte to determine the affinity and kinetic information of the humanized antibody to hIL-13. The data were fitted with Langmuir 1:1 kinetics or steady state mode by Biacore T200 Evaluation software 3.1 to obtain the affinities of the humanized antibodies interacting with the antigen. The affinities of H1K1 and H4K1 for hIL-13 were comparable to that of ref1 (Lebrikizumab), while the affinity of H3K1 for hIL-13 was slightly better than that of ref1 (Table 3).

Table 3. Affinity of 228B/C-1 humanized antibody

Humanized antibody	Affinity (KD, M)	Humanized antibody	Affinity (KD, M)
ref1	1.22E-14	H3K1	7.11E-15
H1K1	2.70E-14	H4K1	1.14E-14
H2K1	1.47E-13		

[00209] 2) Inhibiting hIL-13-induced STAT6 activation

[00210] HEK293-STAT6 cells were cultured with their corresponding complete culture media at 37°C, 5% CO_2, and the cell concentration was controlled to be 2×10^5 - 1×10^6 cells per 1 mL. The cells were collected by centrifugation at 4°C, 300 g for 5 min and the supernatant was discarded, and the cells were resuspended with appropriate amount of 10% FBS/DMEM solution and counted, and the cells were formulated into a cell suspension containing 6×10^5 cells per 1 mL. 50 μL of the cell suspension was sequentially added to each well in a 96-well fluorescence detection white plate and placed in an incubator at 37°C, 5% CO_2 and incubated for 16-24 h. The gradiently diluted humanized antibody was mixed with an equal volume of hIL-13 at 2 ng/ml and pre-incubated at 37°C for 30 min. 50 μl of the mixture was added to each well and incubate for 6 h at 37°C, 5% CO_2. The fluorescence detection reagent was removed from the refrigerator 2 h in advance, melt and equilibrated to room temperature (avoiding light). The cell plate was taken out half an hour in advance and equilibrated to room temperature. A multichannel pipette was used to directly add 100 μL of the aspirated fluorescent substrate solution into the cells (avoiding light), the reaction was performed at room temperature for 5-10 min, and then immediately put into a microplate reader for detection. The results showed that the activities of H1K1, H2K1 and H3K1 inhibiting hIL-13-induced STAT6 activation were comparable to that of the parent antibody Lebrikizumab (ref1) (Figs. 2A-2C).

[00211] 3) Inhibiting hIL-13-induced TF-1 cell proliferation

[00212] TF-1 cells were cultured with a cell culture containing 2 ng/ml GM-CSF at 37°C, 5% CO_2, and the cell concentration was controlled to be 1×10^5 - 1×10^6 cells per 1ml. The cells were collected by centrifugation at 300 g per minute at 4°C for 10 min, and the cell culture was formulated into a cell suspension containing 1×10^5 cells per 1 ml, and 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate, and cultured for 20 h at 37°C, 5% CO_2. Different concentrations of the humanized antibodies were mixed with 40 ng/ml of hIL-13 in equal volume, and 100 μl of the mixture was added to each well, and cultured at 37°C, 5% CO_2 for 96 h. The cell viability was determined by a Cell Titer-Glo Luminescent Cell Viability Assay kit. The results

showed that the activity of H3K1 inhibiting hIL-13-induced TF-1 cell proliferation was better than that of the parent antibody Lebrikizumab (ref1) (Fig. 3).

[00213] 4) Inhibiting hIL-13-induced TARC release from PBMCs

[00214] PBMCs were formulated into a cell suspension containing 2.5×10^6 cells per 1 ml with the cell culture, and 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate. The gradiently diluted humanized antibody was mixed with 20 ng/ml of hIL-13 in equal volume and incubated at 37°C for 30 min. 100 μl of the mixture per well was added to the cells and incubated at 37°C, 5% CO_2 for 72 h. The cell culture supernatant was taken and the amount of the released TARC in the cell culture supernatant was detected by a Human TARC/ CCL17 ELISA kit. The results showed that the activity of H3K1 inhibiting hIL-13-induced TARC release from PBMCs was comparable to that of the parent antibody Lebrikizumab (ref1) (Fig. 4).

[00215] Example 4. Construction and expression of the vector encoding anti-TSLP/IL-13 bispecific antibody

[00216] The anti-TSLP/IL-13 bispecific antibody TSLP/IL-13 BsAb (Fig. 1A) was constructed by using 228B/C-1 H3K1. The anti-TSLP VH and VL of TSLP/IL-13 BsAb were constructed based on SEQ ID Nos: 50 and 51, respective. The mismatch in the bispecific antibody was reduced by introducing charge-pairing mutations in VH and VL and Knob-into-hole mutations in Fc. In addition, mutations were introduced in the antibody Fc to extend the half-life of the bispecific antibody.

[00217] The TSLP/IL-13 BsAb bispecific antibody comprises a first antigen-binding region that binds to interleukin 13 (IL-13) and a second antigen-binding region that binds to thymic stromal lymphopoietin (TSLP). The anti-TSLP binding domain comprises a heavy chain variable region (VH) and a light chain variable region (VL). The anti-TSLP VH comprises complementary determining region (CDR)1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively. The anti-TSLP VL comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively. The anti-TSLP VH comprises the amino acid sequence set forth in SEQ ID NO: 28 which was encoded by the nucleotide sequence set forth in SEQ ID NO: 29. The anti-TSLP VL comprises the amino acid sequence set forth in SEQ ID NO: 33 which was encoded by the nucleotide sequence set forth in SEQ ID NO: 34. The anti-TSLP VH and VL of TSLP/IL-13 BsAb were obtained by introducing Q39E in the anti-TSLP VH and introducing Q38K charge pair mutation in the anti-TSLP VL described above. The anti-TSLP heavy chain of TSLP/IL-13 BsAb comprising the amino acid

sequence set forth in SEQ ID NO: 38 which was encoded by the nucleotide sequence set forth in SEQ ID NO: 39, and the anti-TSLP light chain of TSLP/IL-13 BsAb comprising the amino acid sequence set forth in SEQ ID NO: 40 which was encoded by the nucleotide sequence set forth in SEQ ID NO: 41.

[00218] The TSLP/IL-13 BsAb's IL-13 binding domain comprises a heavy chain variable region (VH) and a light chain variable region (VL). The anti- IL-13 VH comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 24, 25, and 27, respectively. The anti- IL-13 VL comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively. The anti- IL-13 VH of TSLP/IL-13 BsAb comprises the amino acid sequence set forth in SEQ ID NO: 52 which was encoded by the nucleotide sequence set forth in SEQ ID NO: 55. The anti- IL-13 VL of TSLP/IL-13 BsAb comprises the amino acid sequence set forth in SEQ ID NO: 53 which was encoded by the nucleotide sequence set forth in SEQ ID NO: 56. The anti- IL-13 VH and VL of TSLP/IL-13 BsAb were obtained by introducing Q39K in the anti- IL-13 VH and introducing Q38E charge pair mutation in the anti- IL-13 VL described above. The anti- IL-13 heavy chain of TSLP/IL-13 BsAb comprising the amino acid sequence set forth in SEQ ID NO: 42 which was encoded by the nucleotide sequence set forth in SEQ ID NO: 43, and the anti-IL-13 light chain of TSLP/IL-13 BsAb comprising the amino acid sequence set forth in SEQ ID NO: 44 which was encoded by the nucleotide sequence set forth in SEQ ID NO: 45.

[00219] A TSLP/IL-13 BsAb plasmid (heavy chain 1: light chain 1: heavy chain 2: light chain 2 = 1:2:1:2) was transfected into ExpiCHO cells with transfection reagents and cultured at 37°C, 8% CO_2, 80% humidity for 7 days. After culturing, the fermentation broth was centrifuged at 4°C, 4500 rpm, for 30 min, and the supernatant was filtered through a 0.22 μm needle filter. It was first purified by a gravity column using Protein A by loading-equilibration-rinse-elution. The protein eluted from Protein A was then subjected to gradient elution to remove antibody aggregates and fragments by using CEX with a Capto S ImpAct column as a vehicle, so as to improve protein monomer purity. The quality of TSLP/IL-13 BsAb was detected by SEC and mass spectrometry, and the results were shown in Table 4.

Table 4. yield and quality of TSLP/IL-13 BsAb expression

Antibody	Yield (mg/L)	SEC			MS
		Monomers	Aggregates	Fragments	Mismatches
TSLP/IL-13 BsAb	245.2	99.7%	0.2%	0.1%	0%

[00220] Example 5. Binding affinity of TSLP/IL-13 BsAb to TSLP and IL-13

[00221] Surface plasmon resonance technology (SPR/Biacore T200) utilizing a ProA chip was employed to capture the TSLP/IL-13 BsAb onto the chip surface. Then the gradually diluted human TSLP (hTSLP), cynomolgus monkey TSLP (cyTSLP), hIL-13, and cynomolgus monkey IL-13 (cyIL-13) antigens as analytes were allowed to flow through the chip surface to determine the affinity and kinetic information of the TSLP/IL-13 BsAb with each of the antigens. The data were fitted with Langmuir 1:1 kinetics or steady state mode by Biacore T200 Evaluation software 3.1 to obtain the affinities of the antibody interacting with the antigens. TSLP monoclonal antibody (ref3) and IL-13 monoclonal antibody Lebrikizumab (ref1) were used as controls. The results showed that TSLP/IL-13 BsAb bound to human TSLP and cynomolgus monkey TSLP with high affinities comparable to those of the TSLP monoclonal antibody (ref3); TSLP/IL-13 BsAb bound to human IL-13 and cynomolgus monkey IL-13 with high affinities comparable to those of IL-13 monoclonal antibody Lebrikizumab (ref1) (Table 5).

Table 5. Affinities of TSLP/IL-13 BsAb to antigens

Antigen	Antibody	Ka (1/Ms)	Kd (1/s)	KD (M)
hTSLP	ref3	1.11E+06	9.36E-06	8.42E-12
	TSLP/IL-13 BsAb	9.77E+05	2.01E-06	2.06E-12
cyTSLP	ref3	8.96E+05	3.17E-06	3.54E-12
	TSLP/IL-13 BsAb	6.58E+05	7.99E-08	1.22E-13
hIL-13	ref1	2.551E+6	6.22E-06	2.44E-12
	TSLP/IL-13 BsAb	2.713E+6	1.09E-05	4.00E-12
cyIL-13	ref1	3.048E+6	5.93E-06	1.95E-12
	TSLP/IL-13 BsAb	3.110E+6	2.30E-05	7.38E-12

[00222] Example 6. Activity of TSLP/IL-13 BsAb inhibiting hTSLP induction

[00223] 1) Inhibiting hTSLP-indued STAT5 activation

[00224] Ba/f3-hTSLPR-IL7Rα-STAT5 luc cells were cultured with a cell culture medium at 37°C, 5% CO_2. The cells were collected by centrifugating at 4°C, 300g for 5 min, discarding the supernatant, and washed once with 10 ml PBS. The cells were resuspended with an appropriate amount of 10% FBS/RPMI1640 solution (to maintain the cell density at 1.5×10^6 cells/mL) without antibiotics and murine IL-3 (mIL-3) cytokine, and cultured overnight in starvation at 37°C, 5% CO_2. On the following day, the cells were collected by centrifugating at 300 g for 5 min, followed by discarding the supernatant. After resuspending the cells with an appropriate amount of assay buffer

(1% FBS/RPMI1640), 100 μL of the cell suspension was taken for counting. The cell density was adjusted to 1×10^6 cells/mL, and 50 μL of the cell suspension was taken from each well and added into a 96-well sterile fluorescence assay white plate with 5×10^4 cells per well. It was placed in an incubator at 37°C, 5% CO_2 for incubation. TSLP/IL-13 BsAb antibody (18 μg/ml, 1:3 isocratic dilution) was mixed with 12 ng/ml of hTSLP in equal volume and pre-incubated at 37°C for 30 min. 50 μl of the mixture per well was added to the cells and incubated at 37°C, 5% CO_2 for 6 h. The fluorescence detection reagent was removed from the refrigerator 2 h in advance, melt and equilibrated to room temperature (avoiding light). The cell plate was taken out half an hour in advance and equilibrated to room temperature. A multichannel pipette was used to directly add 100 μL of the aspirated fluorescent substrate solution into the cells (avoiding light), the reaction was performed for 5-10 min at room temperature and then immediately put into a microplate reader for detection. TSLP monoclonal antibody (ref3) and Tezepelumab analogue (SEQ ID Nos: 68 and 69) were used as controls. The results showed that the activity of TSLP/IL-13 BsAb inhibiting hTSLP-induced STAT5 activation was slightly weaker than that of TSLP monoclonal antibody (Fig. 5A), which may be due to TSLP/IL-13 BsAb lacking one binding region for TSLP compared to the TSLP monoclonal antibody. The activity of TSLP/IL-13 BsAb inhibiting hTSLP-induced STAT5 activation was superior to that of Tezepelumab analogue (Fig. 24).

[00225] 2) Inhibiting hTSLP-induced Ba/f3-TSLPR-IL7Rα cell proliferation

[00226] Ba/f3-TSLPR-IL7Rα cells were cultured with a cell culture medium at 37°C, 5% CO_2. The cells were collected by centrifugation at 4°C, 300 g for 10 min, discarding the supernatant, and washed once with 10 ml PBS, and formulated into a cell suspension containing 1×10^5 cells per 1 ml with RPMI-1640+10%FBS culture. 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate, and cultured overnight in starvation at 37°C, 5% CO_2. TSLP/IL-13 BsAb (120 μg/ml, 3X gradient dilution) was mixed with 20 ng/ml of hTSLP in equal volume and pre-incubated at 37°C for 30 min. 100 μl of the mixture per well was added to the cells and incubated at 37°C, 5% CO_2 for 72 h. The number of cells was detected by using a CellTiter-Glo® Luminescent Cell Viability Assay kit. TSLP monoclonal antibody (ref3) and Tezepelumab analogue (SEQ ID Nos: 68 and 69) were used as controls. The results showed that the activity of TSLP/IL-13 BsAb inhibiting hTSLP-induced Ba/f3-TSLPR-IL7Rα cell proliferation was comparable to that of TSLP monoclonal antibody, and the inhibitory activity was superior to that of Tezepelumab analogue (Fig. 5B and Fig. 25).

[00227] 3) Inhibiting hTSLP-induced TARC release from PBMCs

[00228] PBMCs were formulated into a cell suspension containing 2.5×10^6 cells per 1 ml with the cell culture, and 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate. The gradiently diluted TSLP/IL-13 BsAb was mixed with 20 ng/ml of hTSLP in equal volume and incubated at 37°C for 30 min. 100 μl of the mixture per well was added to the cells and incubated at 37°C, 5% CO_2 for 72 h. The cell culture supernatant was taken and the amount of released TARC in the cell culture supernatant was detected by a Human TARC/ CCL17 ELISA kit. TSLP monoclonal antibody (ref3) was used as a control. The results showed that the activity of TSLP/IL-13 BsAb inhibiting hTSLP-induced TARC release from PBMCs was comparable to that of TSLP monoclonal antibody (Fig. 5C).

[00229] **Example 7. Activity of TSLP/IL-13 BsAb inhibiting hIL-13 induction**

[00230] 1) Inhibiting hIL-13-induced STAT6 activation

[00231] HEK293-STAT6 cells were cultured with their corresponding complete culture media at 37°C, 5% CO_2, and the cell concentration was controlled to be 2×10^5 - 1×10^6 cells per 1 mL. The cells were collected by centrifugation at 4°C, 300 g for 5 min and the supernatant was discarded, and the cells were resuspended with appropriate amount of 10% FBS/DMEM solution and counted, and the cells were formulated into a cell suspension containing 6×10^5 cells per 1 mL. 50 μL of the cell suspension was sequentially added to each well in a 96-well fluorescence detection white plate and placed in an incubator at 37°C, 5% CO_2 and incubated for 16-24 h. The gradually diluted TSLP/IL-13 BsAb was mixed with an equal volume of hIL-13 at 2 ng/ml and pre-incubated at 37°C for 30 min. 50 μl of the mixture was added to each well and incubate for 6 h at 37°C, 5% CO_2. The fluorescence detection reagent was removed from the refrigerator 2 h in advance, melt and equilibrated to room temperature (avoiding light). The cell plate was taken out half an hour in advance and equilibrated to room temperature. A multichannel pipette was used to directly add 100 μL of the aspirated fluorescent substrate solution into the cells (avoiding light), the reaction was performed at room temperature for 5-10 min, and then immediately put into a microplate reader for detection. IL-13 monoclonal antibody Lebrikizumab (ref1) and known TSLP/IL-13 bispecific nanobody Lunsekimig (ref2) were used as controls. The results showed that the activity of TSLP/IL-13 BsAb inhibiting hIL-13-induced STAT6 activation was slightly weaker than that of IL-13 monoclonal antibody (which may be due to TSLP/IL-13 BsAb lacking one binding region for IL-13 compared to the IL-13 monoclonal antibody), and superior to that of ref2 nanobody (Fig. 6A).

[00232] 2) Inhibiting hIL-13-induced TF-1 cell proliferation

[00233] TF-1 cells were cultured with a cell culture medium containing 2 ng/ml GM-CSF at 37°C, 5% CO_2, and the cell concentration was controlled to be 1×10^5 - 1×10^6 cells per 1ml. The cells were collected by centrifugation at 300 g per minute at 4°C for 10 min, and the cell culture was formulated into a cell suspension containing 1×10^5 cells per 1 ml, and 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate, and cultured for 20 h at 37°C, 5% CO_2. Different concentrations of TSLP/IL-13 BsAb were mixed with 40 ng/ml of hIL-13 in equal volume, and 100 μl of the mixture was added to each well, and cultured at 37°C, 5% CO_2 for 96 h. The cell viability was determined by a Cell Titer-Glo Luminescent Cell Viability Assay kit. IL-13 monoclonal antibody Lebrikizumab (ref1) and TSLP/IL-13 bispecific nanobody Lunsekimig (ref2) were used as controls. The results showed that the activity of TSLP/IL-13 BsAb inhibiting IL-13-induced TF-1 cell proliferation was slightly weaker than that of ref1 monoclonal antibody (which may be due to TSLP/IL-13 BsAb lacking one binding region for IL-13 compared to the IL-13 monoclonal antibody), and superior to that of ref2 nanobody (Fig. 6B).

[00234] 3) Inhibiting hIL-13-induced TARC release from PBMCs

[00235] PBMCs were formulated into a cell suspension containing 2.5×10^6 cells per 1 ml with the cell culture, and 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate. The gradiently diluted TSLP/IL-13 BsAb was mixed with 20 ng/ml of hIL-13 in equal volume and incubated at 37°C for 30 min. 100 μl of the mixture per well was added to the cells and incubated at 37°C, 5% CO_2 for 72 h. The cell culture supernatant was taken and the amount of released TARC in the cell culture supernatant was detected by a Human TARC/ CCL17 ELISA kit. IL-13 monoclonal antibody Lebrikizumab (ref1) and TSLP/IL-13 bispecific nanobody Lunsekimig (ref2) were used as controls. The results showed that the activity of TSLP/IL-13 BsAb inhibiting hIL-13-induced TARC release from PBMCs was slightly weaker than that of IL-13 monoclonal antibody (which may be due to TSLP/IL-13 BsAb lacking one binding region for IL-13 compared to the IL-13 monoclonal antibody), and superior to that of ref2 nanobody (Fig. 6C).

[00236] **Example 8. TSLP/IL-13 BsAb inhibiting hTSLP + hIL-13-induced TARC release from PBMCs**

[00237] The inhibition of the synergistic activity of TSLP and IL-13 by TSLP/IL-13 BsAb was evaluated by the release of TARC from PBMCs induced by hTSLP + hIL-13. PBMCs were formulated into a cell suspension containing 2.5×10^6 cells per 1 ml with the cell culture, and 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate. 40 ng/ml hIL-13 was mixed with 40 ng/ml hTSLP in equal volume, and then the gradually diluted TSLP/IL-13 BsAb was mixed

with 20 ng/ml of a mixture of hIL-13 and hTSLP in equal volume, and incubated at 37°C for 30 min. 100 μl of the mixture per well was added to the cells and incubated at 37°C, 5% CO_2 for 72 h. The cell culture supernatant was taken and the amount of released TARC in the cell culture supernatant was detected by a Human TARC/ CCL17 ELISA kit. IL-13 monoclonal antibody Lebrikizumab (ref1), TSLP/IL-13 bispecific nanobody Lunsekimig (ref2) and TSLP monoclonal antibody (ref3) were used as controls. The results showed that TSLP/IL-13 BsAb and ref2 nanobody could completely inhibit TARC release from PBMCs induced by hTSLP + hIL-13, and the inhibitory activity of TSLP/IL-13 BsAb was slightly better than that of ref2 nanobody, while ref1 monoclonal antibody and ref3 monoclonal antibody could not completely inhibit TARC release from PBMCs induced by hTSLP + hIL-13 (Fig. 7). This indicates that TSLP/IL-13 BsAb can exert better efficacy than that of the monoclonal antibody by blocking the signal pathways of both TSLP and IL-13.

[00238] Example 9. In vivo efficacy of TSLP/IL-13 BsAb in a MC903-induced mouse dermatitis model

[00239] 1) MC903-induced hTSLP/TSLPR humanized mouse dermatitis model

[00240] 8-10-week-old hTSLP/TSLPR humanized mice were randomly divided into 5 groups (a control group, a model group, 3 mg/kg TSLP/IL-13 BsAb dosing group, 30 mg/kg TSLP/IL-13 BsAb dosing group, and 30 mg/kg irrelevant anti-KLH antibody (SEQ ID Ns: 62 and 63, prepared according to US8734796B) dosing group), with 11 mice in each group. The anti-KLH antibody includes a heavy chain (SEQ ID NO: 62) and a light chain (SEQ ID NO: 63). Mice in the model groups and the dosing groups were applied with 20 μl MC903 (50 μM) in the right ear on days D1, D2, D3, D4, D5, D8, D9, D10, D11, and D12, and 20 μl anhydrous ethanol was applied in the control group. Each dosing group was administered the corresponding dosage of TSLP/IL-13 BsAb or Anti-KLH by subcutaneous injection on the day before modeling (D0), D3, D6, D8, D10, and D12, respectively. Changes in the thickness of the right ear of the mice were detected during the modeling and dosing. The serum of mice was taken on day D14, and the IgE level in the serum of mice were detected with a mouse IgE ELISA kit.

[00241] The results showed that 3 mg/kg and 30 mg/kg TSLP/IL-13 BsAb could significantly inhibit the increase in mouse ear thickness and significantly reduce mouse serum IgE level in the hTSLP/TSLPR humanized mouse dermatitis model (Figs. 8A and 8B).

[00242] The effect of TSLP/IL-13 BsAb were further compared with that of TSLP/IL-13 bispecific nanobody Lunsekimig (ref2) in the same mouse dermatitis model. 8-10-week-old hTSLP/TSLPR humanized mice were randomly divided into 4 groups (a control group, a model

group, 4 mg/kg TSLP/IL-13 BsAb dosing group and 4 mg/kg ref2 antibody dosing group). Mice in the model and dosing groups were applied with 20 μl MC903 (50 μM) in the right ear on days D1, D2, D3, D4, D5, D8, D9, D10, D11, D12, D14, and D15, and 20 μl anhydrous ethanol was applied in the control group. Each dosing group was administered the corresponding dosage of TSLP/IL-13 BsAb or ref2 antibody by subcutaneous injection on the day before modeling (D0), D3, D6, D8, D10, D12, and D14, respectively, and changes in the thickness of the right ear of the mice were detected during the modeling and dosing.

[00243] The results showed that 4 mg/kg TSLP/IL-13 BsAb inhibited the increase in mouse ear thickness better than ref2 antibody (Fig. 8C).

[00244] 2) MC903-induced hIL-13 humanized mouse dermatitis model

[00245] 8-10-week-old hIL-13 humanized mice were randomly divided into 5 groups (a control group, a model group, 2 mg/kg TSLP/IL-13 BsAb dosing group, 10 mg/kg TSLP/IL-13 BsAb dosing group, and 10 mg/kg irrelevant Anti-KLH antibody dosing group), with 12 mice in each group. Mice in the model and dosing groups were applied with 20 μl MC903 (50 μM) in the right ear on days D1, D2, D3, D4, D5, D8, D9, D10, D11, and D12, and 20 μl anhydrous ethanol was applied in the control group. Each dosing group was administered the corresponding dosage of TSLP/IL-13 BsAb or Anti-KLH (SEQ ID Ns: 62 and 63) by subcutaneous injection on the day before modeling (D0), D3, D6, D8, D10, and D12, respectively. Changes in the thickness of the right ear of the mice were detected during the modeling and dosing. The serum of mice was taken on day D14, and IgE level in the serum of mice were detected with a mouse IgE ELISA kit.

[00246] The results showed that in the hIL-13 humanized mouse dermatitis model, 10 mg/kg TSLP/IL-13 BsAb dosing group could significantly inhibit the increase in mouse ear thickness, and in 2 mg/kg and 10 mg/kg TSLP/IL-13 BsAb dosing groups, reduced mouse serum IgE levels could be observed (Figs. 9A and 9B).

[00247] Example 10. Pharmacokinetics (PK) of TSLP/IL-13 BsAb in human FcRn (hFcRn) humanized mouse

[00248] 6-8-week-old female hFcRn humanized mice were administered 10 mg/kg TSLP/IL-13 BsAb, IL-13 monoclonal antibody Lebrikizumab (ref1), TSLP monoclonal antibody (ref3), and TSLP/IL-13 BsAb without Fc half-life mutation (TSLP/IL-13 BsAb-WT) in a single subcutaneous injection, respectively, 4 mice per group. TSLP/IL-13 BsAb-WT includes an anti-IL-13 heavy chain (SEQ ID No: 60), an anti-IL-13 light chain (SEQ ID No: 61), an anti-TSLP heavy chain (SEQ ID No: 66), and an anti-TSLP light chain (SEQ ID No: 67). Mouse blood was collected for PK assay at

0h, 4h, D2, D3, D4, D6, D8, D15, D22, D29, D36, D43, and D54 from dosing, respectively. On D54, the half-lives of TSLP/IL-13 BsAb, TSLP/IL-13 BsAb-WT, ref1 monoclonal antibody, and ref3 monoclonal antibody were 16.8, 11.2, 11.0 and 13.3 days, respectively. It indicates that the half-life of TSLP/IL-13 BsAb is superior to other molecules and is promising to reduce the frequency of dosing for clinical patients.

[00249] Example 11. Efficacy of TSLP/IL-13 BsAb on B-hIL13 mouse asthma

[00250] Eighteen B-hIL13 mice were randomly divided into 3 groups according to body weight, with 6 mice in each group, i.e., a blank control group, a model group, and 30 mg/kg TSLP/IL-13 BsAb dosing group, respectively. On the first day of modeling, OVA $Al(OH)_3$ mixture was injected at multiple sites to induce sensitization (counted as Day 0). On Day 14, the OVA $Al(OH)_3$ mixture was injected intraperitoneally to enhance sensitization, and on Days 21-27, OVA solution was nebulized and inhaled for challenge. The first dosing was on the day before modeling (Day -1); from Day -1 to Day 19, dosing once every 4 days, totally 5 times; from Day 21 to Day 27, dosing once every 1 day, totally 4 times; and dosing by subcutaneous injection 2 h before OVA challenge. The model group was synchronously injected subcutaneously 0.9% sodium chloride injection.

[00251] **Influence on mouse body weight**

[00252] General symptom observation was performed daily during the test period, and the mice were weighed before each dosing, and the weight results were shown in Fig. 10. The results showed that there was no significant difference ($P > 0.05$) in the mouse body weights among the control group, the model group and 30 mg/kg TSLP/IL-13 BsAb dosing group.

[00253] **Influence on number of nose scratching and number of sneezes**

[00254] On Day 21 and Day 27, the number of nose scratching and the number of sneezes were counted within 30 min after OVA challenge, and the results were shown in Fig. 11 and Table 6 - Table 7. The results showed that, compared with the control group, for the mice in the model group, on Day 21 and Day 27, the number of nose scratching within 30 min of OVA challenge was significantly increased ($P < 0.01$ - 0.001), and the number of sneezes had no significant change ($P > 0.05$); compared with the model group, for the mice in 30 mg/kg TSLP/IL-13 BsAb dosing group, on Day 21 and Day 27, the number of nose scratching was significantly decreased ($P < 0.05$ - 0.01).

Table 6. numbers of nose scratching and sneezes within 30 min after OVA challenge on Day 21

Group	n	Nose scratching		Sneezes	
		Number of times	Inhibition rate (%)	Number of times	Inhibition rate (%)
Control	6	6.17±0.65	-	3.00±0.63	-
Model	6	25.00±2.66##	-	2.33±0.61	-
30 mg/kg TSLP/IL-13 BsAb dosing group	6	13.67±1.17**	45.3	0.67±0.33	71.4

[00255] The data were shown as mean ± SEM, n = 6. ## $P < 0.01$ compared with a control group; ** $P < 0.05$ compared with a model group. Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

Table 7. numbers of nose scratching and sneezes within 30 min after OVA challenge on Day 27

Group	n	Nose scratching		Sneezes	
		Number of times	Inhibition rate (%)	Number of times	Inhibition rate (%)
Control	6	12.33±1.43	-	3.50±1.43	-
Model	6	24.33±2.06###	-	2.50±0.56	-
30 mg/kg TSLP/IL-13 BsAb dosing group	6	16.33±2.01*	32.9	1.50±0.43	40.0

[00256] The data were shown as mean ± SEM, n = 6. ### $P < 0.001$ compared with a control group; * $P < 0.05$ compared with a model group. Dunnett's test was performed after one-way ANOVA, and Mann-Whitney U test was performed after one-way ANOVA.

[00257] **Influence on airway hyperresponsiveness (AHR)**

[00258] On Day 28, mice were allowed to inhale by nebulization 0, 1, 2, 4, 8, 12, 24, or 48 mg/mL acetylmethacholine (Mch) and the Mch-induced mouse airway hyperresponsiveness was detected with an EMKA Animal Lung Function Monitoring System, and the results were shown in Figs. 12A-12B. The results showed that compared with the control group, upon inhaling by nebulization various concentrations of Mch, the mice in the model group showed a trend of elevated airway resistance (Penh) ($P > 0.05$); the percentage increase in Penh increased significantly ($P < 0.05$) while inhaling by nebulization 12 and 24 mg/mL of Mch; and compared with the model group, mice in 30 mg/kg TSLP/IL-13 BsAb dosing group showed a decreasing trend in the percentage increase in Penh while inhaling by nebulization 1, 2, 4, 8, 12, 24, and 48 mg/mL Mch, and the inhibition rates were 68.2%, 57.7%, 55.4%, 47.4%, 14.1%, 29.7%, and 19.8%, respectively.

[00259] **Influence on number of inflammatory cells in BALF**

[00260] On Day 28, mice were subjected to bronchoalveolar lavage, and the total number of leukocytes, eosinophils, macrophages, and lymphocytes in the bronchoalveolar lavage fluid (BALF) was counted microscopically, and the results were shown in Fig. 13. The results showed that the numbers of leukocytes, eosinophils, macrophages and lymphocytes in BALF of mice in the model group were significantly increased compared with those in the control group ($P < 0.05$-0.001); and the numbers of leukocytes, eosinophils and macrophages in BALF of mice in the 30 mg/kg TSLP/IL-13 BsAb dosing group were significantly decreased compared with those in the model group ($P < 0.05$-0.001), and the inhibition rates were 44.2%, 80.3% and 52.7%, respectively.

[00261] **Influence on serum total IgE and OVA-sIgE levels**

[00262] On Day 20 and Day 28, blood was collected from the retro-orbital venous plexus of mice, and serum total IgE and OVA-sIgE levels were detected by ELISA, and the results were shown in Fig. 14. The results showed that compared with the control group, the serum total IgE and OVA-sIgE levels in mice in the model group on Day 20 and 28 were significantly elevated ($P < 0.01$); compared with the model group, the serum total IgE level in the 30 mg/kg TSLP/IL-13 BsAb dosing group on Day 28 was significantly decreased ($P < 0.05$), and the OVA -sIgE level had a tendency to decrease ($P > 0.05$).

[00263] **Influence on eosinophils infiltration in lung tissues**

[00264] On Day 28, lung tissues were fixed completely with 10% neutral buffered formalin solution and then sectioned with paraffin embedding. H&E staining was performed to observe eosinophilic infiltration of the lung tissues and pathological scoring was performed, the results of the pathological diagram of eosinophilic infiltration were shown in Fig. 15, and the results of the pathological scoring were shown in Fig. 16. The results of H&E staining showed that eosinophilic infiltration of lung tissues of the mice in the model group could be seen in the airway and the perivascular area ($P < 0.001$). 30 mg/kg TSLP/IL-13 BsAb dosing group could significantly inhibit eosinophil infiltration ($P < 0.05$).

[00265] **Influence on airway goblet epithelial cell metaplastic proliferation**

[00266] On Day 28, PAS staining was performed on mouse lung tissues to observe the metaplastic proliferation of goblet epithelial cells in the peri-airway of the lung tissues and to count the positive rate, and the results were shown in Fig. 17. The results of PAS staining showed that there was significant metaplastic proliferation of goblet epithelial cells in the peri-airway of the mice in the model group ($P < 0.01$), and the 30 mg/kg TSLP/IL-13 BsAb dosing group was able to

significantly reduce the airway epithelial cell mucus secretion and goblet epithelial cell metaplastic proliferation ($P < 0.01$).

[00267] **Influence on number and degranulation of lung tissue mast cells**

[00268] On Day 28, the lung tissues of mice were stained with toluidine blue, and the mast cell degranulation of the lung tissues was observed and the degranulation rate was counted, and the results were shown in Figs. 18 and 19A-19B. The results of toluidine blue staining showed that the total number of mast cells in the lung tissues of mice in the model group was significantly increased ($P < 0.05$), and there was a trend of increased mast cell degranulation ($P > 0.05$); compared with the model group, the 30 mg/kg TSLP/IL-13 BsAb dosing group was able to significantly reduce the total number of mast cells ($P < 0.01$), and had a role in reducing mast cell degranulation ($P > 0.05$).

[00269] **Conclusions**

[00270] In this Example, an OVA-induced B-hIL13 mouse asthma model was established, and the 30 mg/kg TSLP/IL-13 BsAb dosing group dosed by subcutaneous injection could significantly reduce the number of inflammatory cells in BALF, reduce the serum total IgE level, reduce the eosinophils infiltration in lung tissues, inhibit the increase in mucus secretion of airway epithelial cells and alleviate the goblet epithelial cell metaplastic proliferation; there was a tendency to improve airway hyperresponsiveness and reduce mast cell degranulation.

[00271] **Example 12. Evaluating efficacy of TSLP/IL-13 BsAb on MC903-induced B-hIL-13 mouse dermatitis model**

[00272] B-hIL-13 mice were randomly divided into 6 groups, with 12 mice in each group, i.e., a blank control group (control group), a model group (model group), TSLP/IL-13 BsAb dosing group (0.4, 2.0, and 10.0 mg/kg), and a negative control Anti-KLH hIgG1 (SEQ ID Ns: 62 and 63) (10.0 mg/kg) group, respectively. The anti-KLH antibody includes a heavy chain (SEQ ID NO: 62) and a light chain (SEQ ID NO: 63). On the first day of modeling, 20 μL of MC903 was applied in the right ear of the mice, 10 μL each in the belly and dorsal sides of the ear (counted as Day 1), for 5 consecutive days, and then paused for 2 days. From Day 8 to Day 12, the mice were applied in the right ear for 5 consecutive days, and then paused for 1 day, and the model ended on Day 14. The blank control group was applied with anhydrous ethanol synchronously. The first dosing was on the day before modeling (Day 0); and from Day 0 to Day 7, dosing once every 2 days on Day 0, Day 3, and Day 6, totally 3 times; from Day 8 to Day 14, dosing once every 1 day on Day 8, Day 10, and Day 12, totally 3 times, by subcutaneous injection. The blank control group and the model group were injected with vehicle TSLP/IL-13 BsAb blank solution synchronously.

[00273] **Influence on mouse body weight**

[00274] The mice were weighed before each dosing during the test period, and the results in Fig. 20A showed no significant difference in the body weights of the mice in each group ($P > 0.05$).

[00275] **Influence on the increase of mouse ear thickness**

[00276] From Day 0 to Day 14, the thickness of the right ear of mice in each group was measured with a spiral micrometer, and the results were shown in Figs. 20B-20C. The results showed that the ear thickness of mice in the model group was significantly increased compared with that of the blank control group ($P < 0.0001$); the TSLP/IL-13 BsAb (10.0 mg/kg) group could significantly inhibit the increase in the ear thickness of the right ear of the mice compared with that of the model group ($P < 0.01$), and the TSLP/IL-13 BsAb 0.4 mg/kg group, 2.0 mg/kg group and 10.0 mg/kg group dose-dependently inhibited the increase of the ear thickness of the right ear of mice, and the inhibition rates were 13.85%, 18.76% and 27.11%, respectively.

[00277] **Influence on ear skin lesions of mice**

[00278] From Day 0 to Day 14, clinical disease scores of skin lesion conditions of the right ear of mice in each group were performed before each dosing, and the results were shown in Figs. 21A-21B. The results showed that compared with the blank control group, the belly side of the right ear of the mice in the model group was obviously dry, deeper color, dark red, desquamated and edematous, and blood vessels on the dorsal side of the ear were significantly dilated, with a significant increase in the clinical disease scores ($P < 0.0001$); compared with the model group, the skin lesions on the belly side of the right ear of the mice in the TSLP/IL-13 BsAb (10.0 mg/kg) group were significantly alleviated, and the blood vessels on the dorsal side of the ear showed no significant tendency of dilatation, and the clinical disease scores were significantly reduced ($P < 0.0001$). The inhibition rates of the TSLP/IL-13 BsAb 0.4 mg/kg group, 2.0 mg/kg group and 10.0 mg/kg group on skin lesion conditions of the right ear of the mice were 2.61%, 11.4% and 26.32%, respectively.

[00279] **Influence on serum total IgE level of mice**

[00280] At the end of the model (Day 14), total IgE level in the serum of the mice in each group were measured by ELISA, and the results were shown in Fig. 22. The results showed that compared with the blank control group, the total IgE level in the serum of the mice in the model group had an elevated trend; compared with the model group, the total IgE level in the serum of the mice in the TSLP/IL-13 BsAb (2.0 and 10.0 mg/kg) groups showed a decreased trend. The inhibition rates of TSLP/IL-13 BsAb (2.0 and 10.0 mg/kg) groups on the total IgE level of the serum of the mice were 24.06% and 25.95%, respectively.

[00281] Example 13. Evaluation pretest of efficacy of TSLP/IL-13 BsAb on MC903-induced B-hTSLP/hTSLPR mouse dermatitis model

[00282] B-hTSLP/hTSLPR mice were randomly divided into 8 groups, i.e., a blank control group (control group), a model group (model group), TSLP/IL-13 BsAb (4.0 and 20.0 mg/kg) dosing groups, Lunsekimig analogue (SEQ ID No: 59, 4.0 and 20.0 mg/kg) dosing groups, and anti-TSLP (Ref3, 4.0 and 20.0 mg/kg) dosing groups, respectively, with 3 mice in the blank control group, and 4 mice in each of the model and dosing groups. On the first day of modeling, 20 ml of 50 Mm MC903 was applies to the mouse right ear, and 10 mL was applied to the belly and dorsal sides of the ear (counted as Day 1) for 5 consecutive days, pausing for 2 days. From Day 8 to Day 12, the mouse right ear was applied for 5 consecutive days, pausing for 1 day. From Day 14 to Day 15, the mouse right ear was applied consecutively for 2 days; the modeling ended on Day 16. The blank control group was synchronously applied with anhydrous ethanol. The first dosing was on the day before the modeling (Day 0); from Day 0 to Day 7, dosing once every 2 days on Day 0, Day 3, and Day 6, totally 3 times; from Day 8 to Day 16, dosing once every 1 day on Day 8, Day 10, Day 12, and Day 14, totally 4 times, by subcutaneous injection. The blank control group and the model group were synchronously injected with the vehicle TSLP/IL-13 BsAb blank solution. From Day 0 to Day 16, the thickness of the mouse right ear in each group was measured with a spiral micrometer, and the results were shown in Figs. 23A-23C.

[00283] The results showed that the mouse ear thickness in the model group was significantly increased compared with that of the blank control group ($P < 0.0001$); the TSLP/IL-13 BsAb (4.0 and 20.0 mg/kg) groups could significantly inhibit the increase in mouse right ear thickness compared with that of the model group ($P < 0.01$), with the inhibition rates of 25.43% and 27.03%, respectively; the Lunsekimig analogue (4.0 and 20.0 mg/kg) groups could significantly inhibit the increase in mouse right ear thickness ($P < 0.01$), with the inhibition rates of 22.34% and 26.92%, respectively; the anti-TSLP (Ref3) (4.0 mg/kg) group could inhibit the increase in mouse right ear thickness, with the inhibition rate of 19.36%, but no statistical difference was observed ($P > 0.05$), and the anti-TSLP (Ref3, 20.0 mg/kg) group could significantly inhibit the increase in mouse ear thickness ($P < 0.01$) with the inhibition rate of 21.08%.

[00284] Example 14. TSLP/IL-13 BsAb thermal stability

[00285] In a 1.5 mL centrifuge tube, TSLP/IL-13 BsAb was diluted to 1 mg/mL with 1 × PBS buffer and centrifugated for 5 min at 12,000 rpm with a centrifuge. With a capillary tube reaching to the bottom of the centrifuge tube, the sample was siphoned until the capillary being full, and the

capillary was placed in a capillary tray, capped with a capillary cap, and the capillary drawer was closed. After scanning with a nanoDSF method, the particle size analysis was performed, followed by Thermal Unfolding Analysis. TSLP monoclonal antibody (Anti-TSLP, Ref3), Lebrikizumab analogue (SEQ ID Nos: 57 and 58), Tezepelumab analogue (SEQ ID Nos: 68 and 69) and Lunsekimig analogue (SEQ ID No: 59) were used as controls. The assay results were shown in Table 8 and the assay profile was shown in Fig. 26. The results showed that the Tmonset values of TSLP/IL-13 BsAb, Anti-TSLP (Ref3), Lebrikizumab analogue, Tezepelumab analogue and Lunsekimig analogue were 62.42°C, 66.00°C, 62.15°C, 59.13°C and 58.03°C, respectively, and the Tm values were 67.23°C, 70.14°C, 68.33°C, 64.42°C and 62.60°C, respectively.

[00286] Table 8. results of nanoDSF thermal stability assay

	Hydrated particle size (nm)	PDI	Tmonset (℃)	Tm (℃)
TSLP/IL-13 BsAb	5.11	0.00	62.42	67.23
TSLP monoclonal antibody	5.09	0.00	66.00	70.14
Lebrikizumab analogue	5.16	0.02	62.15	68.33
Tezepelumab analogue	5.39	0.02	59.13	64.42
Lunsekimig	3.94	0.00	58.03	62.60

[00287] Example 15. TSLP/IL-13 BsAb inhibiting TSLP-induced TARC release from PBMCs

[00288] The inhibition of TSLP by TSLP/IL-13 BsAb was evaluated by the release of TARC from PBMCs induced by TSLP. TSLP could induce PBMCs to release TARC, and TSLP/IL-13 BsAb inhibited the release of TARC upon binding to TSLP. Changes in the amount of TARC in the culture supernatant were detected by Enzyme-Linked Immunosorbent Assay (ELISA), and the half maximal inhibitory concentration (IC_{50}) of TSLP/IL-13 BSAB was calculated according to the changes, thereby evaluating the biological activity of TSLP/IL-13 BsAb for inhibiting TSLP-induced TARC release from PBMCs. The anabiotic PBMCs were formulated into a cell suspension containing 2.5×10^6 cells per 1 ml with the cell culture, and 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate. After TSLP/IL-13 BsAb, Anti-TSLP (Ref3) and Tezepelumab analogue (SEQ ID Nos: 68 and 69) were diluted to 4 μg/mL with the cell culture, in 3-fold gradient

dilutions, totally 8 dilutions, with 2 wells for each dilution; in addition, TSLP was diluted to 20 ng/mL with the cell culture. The gradiently diluted TSLP/IL-13 BSAB, Anti-TSLP (Ref3) and Tezepelumab analogue were mixed with an equal volume of TSLP, respectively, 100 μL of the mixture was added to the cells in each well, and incubated at 37°C, 5% CO_2 for 72 h. The cell culture supernatant was taken, and the TARC amount in the cell culture supernatant was detected by a human TARC ELISA kit. A linear regression equation was obtained from the TARC standard concentrations and corresponding absorbances thereof. The TARC amount in the culture supernatant was calculated from the linear regression equation and multiplied by the dilution factor to get the final amount. The results were shown in Fig. 27.

[00289] The results showed that TSLP/IL-13 BsAb, Anti-TSLP (Ref3) and Tezepelumab analogue could inhibit TSLP-induced TARC release from PBMCs, with IC_{50} of 0.32 nM, 0.26 nM and 1.12 nM, respectively. This indicates that TSLP/IL-13 BSAB can effectively inhibit TSLP-induced TARC release from PBMCs, and the inhibitory activity is better than those of Tezepelumab analogue.

[00290] Example 16. TSLP/IL-13 BsAb inhibiting TSLP + IL-13-induced TARC release from PBMCs

[00291] The inhibition of the synergistic activity of TSLP and IL-13 by TSLP/IL-13 BSAB was evaluated by the release of TARC from PBMCs induced by TSLP + IL-13. Both TSLP and IL-13 could induce the release of TARC from PBMCs. TSLP/IL-13 BsAb could inhibit the TARC release upon high affinity binding to TSLP and IL-13. Changes in the amount of TARC in the culture supernatant were detected by Enzyme-Linked Immunosorbent Assay (ELISA), and the maximum inhibition rate of TSLP/IL-13 BsAb was calculated according to the changes, thereby evaluating the biological activity of TSLP/IL-13 BsAb for inhibiting the TARC release from PBMCs cells induced by TSLP + IL-13. The anabiotic PBMCs were formulated into a cell suspension containing 2×10^6 cells per 1 ml with the cell culture, and 100 μl per well was inoculated into a flat-bottomed 96-well cell culture plate. TSLP/IL-13 BsAb, Anti-TSLP (Ref3), Lebrikizumab analogue(SEQ ID Nos: 57 and 58), Lunsekimig analogue (SEQ ID No: 59)and Tezepelumab analogue (SEQ ID Nos: 68 and 69) were diluted to 26.7 nM with the cell culture, in 3-fold gradient dilutions, totally 8 dilutions, with 2 wells for each dilution; IL-13 and TSLP were also diluted to 40 ng/mL with the cell culture. 40 ng/mL TSLP and IL-13 were mixed in equal volume. The gradually diluted antibodies were mixed with an equal volume of the mixture of TSLP and IL-13, respectively. 100 μL of the mixture was added to the cells in each well, and incubated at 37°C, 5% CO_2 for 72 h.

The cell culture supernatant was taken, and the TARC amount in the cell culture supernatant was detected by a human TARC ELISA kit. The linear regression equation was obtained from the TARC standard concentrations and corresponding absorbances thereof. The TARC amount in the culture supernatant was calculated from the linear regression equation and multiplied by the dilution factor to get the amount and calculate the inhibition rate. The results were shown in Fig. 28.

[00292] The results showed that TSLP/IL-13 BSAB, Anti-TSLP (Ref3), Lebrikizumab analogue, Lunsekimig analogue, and Tezepelumab analogue could all inhibit the release of TARC from PBMCs induced by TSLP + IL-13, with maximal inhibition rates of 93.1%, 58.4%, 77.3%, 94.0% and 49.4%, respectively. This indicates that TSLP/IL-13 BsAb can effectively inhibit the TARC release from PBMCs induced by TSLP + IL-13, and the inhibitory effect is superior to those of Anti-TSLP (Ref3), Lebrikizumab analogue and Tezepelumab analogue.

[00293] **Example 17. Immunogenicity assessment of TSLP/IL-13 BsAb**

[00294] The risk of immunogenicity of TSLP/IL-13 BsAb was preliminarily evaluated by detecting the activation of $CD4^+$ T cells by TSLP/IL-13 BsAb. The clinical immunogenicity of an agent showed a correlation with the proportion of CD134 (OX40) and CD137 (4-1BB) positive $CD4^+$ T cells. TSLP/IL-13 BsAb was co-cultured with peripheral blood monocytes (PBMCs) isolated from the peripheral blood of healthy volunteers for 48 h, and the proportion of CD134- and CD137-positive cells in $CD4^+$ T cells was measured by a flow assay to evaluate the risk of TSLP/IL-13 BsAb immunogenicity. The density of isolated and collected cells was adjusted to 2.5×10^6/mL with X-vivo15 culture medium, and 100 μL was added to a 96-well U-plate. The various antibodies and positive control were diluted to 200 μg/mL with X-vivo15 culture medium. 100 μL of diluted sample was added to the cells and incubated at 37°C, 5% CO_2 for 48 h, with KLH as the positive control, and the wells without any sample as the negative control. After 48 h, the cells were washed and stained for 48 h by adding the antibodies (50 μL/well, adding FITC anti-human CD4, APC anti-human CD137, and PE anti-human CD4), and then stained with 50 μL of PI solution for 5 min., and washed with flow buffer and then resuspended in 100 μL of PBS, and analyzed by a flow cytometer. The results were shown in Fig. 29.

[00295] The results showed that the Stimulation Index of TSLP/IL-13 BsAb, Anti-TSLP (Ref3), Lebrikizumab analogue (SEQ ID Nos: 57 and 58), Tezepelumab analogue (SEQ ID Nos: 68 and 69), and Lunsekimig analogue (SEQ ID No: 59) were 0.91, 0.97, 0.90, 1.11, and 1.12, respectively. The risk of immunogenicity was comparable in all groups and much smaller than the stimulation index of KLH in the positive control group (3.51). This indicates that TSLP/IL-13 BsAb,

Anti-TSLP (Ref3), Lebrikizumab analogue, Tezepelumab analogue and Lunsekimig analogue have comparable risks of immunogenicity and are all low immunogenic.

[00296] Example 18. Efficacy of TSLP/IL-13 BsAb on OVA-induced B-hTSLP/hTSLPR mouse asthma

[00297] B-hTSLP/hTSLPR mice were randomly divided into 6 groups according to body weight, with 12 mice in each group, i.e., a blank control group, a model group, a KLH negative control group (30 mg/kg), TSLP/IL-13 BsAb low-dosage group (3 mg/kg), TSLP/IL-13 BsAb medium-dosage group (10 mg/kg) and TSLP/IL-13 BsAb high-dosage group (30 mg/kg), respectively. On the first day of modeling, 2 mg/mL OVA $Al(OH)_3$ mixture was injected at multiple sites for sensitization, totally 0.5 mL/mouse (counted as Day 0). On Day 14, 0.2 mL OVA $Al(OH)_3$ mixture was injected intraperitoneally to enhance sensitization. On Days 21-27, OVA solution (0.9% sodium chloride injectable solution formulated in 10 mg/mL) was nebulized and inhaled for challenge. The first dosing was on the day before modeling (Day -1);from Day -1 to Day 19, dosing once every 4 days, totally 5 times; from Day 21 to Day 27, dosing once every 1 day, totally 4 times; and dosing was performed by subcutaneous injection 2 h before OVA challenge. The blank control group and model group were synchronously injected subcutaneously vehicle TSLP/IL-13 BsAb blank solution.

[00298] **Influence on mouse body weight**

[00299] General symptom observation was performed daily during modeling and dosing, and the mice in each group were weighed before each dosing, and the results were shown in Fig. 30. The results showed that there was no significant difference in the mouse body weight in the model group during modeling and dosing, compared with the blank control group ($P > 0.05$). There was no significant difference ($P > 0.05$) in the mouse body weight in the TSLP/IL-13 BsAb (3, 10, and 30 mg/kg) groups and KLH (30 mg/kg) group during modeling and dosing, compared with the model group. No significant abnormality was observed in the general symptoms of mice in all test groups.

[00300] **Influence on number of nose scratching and number of sneezes**

[00301] On Day 27, the number of mouse nose scratching and number of sneezes were counted within 30 min after OVA challenge, and the results were shown in Figs. 31A-31B. The results showed that the number of mouse nose scratching and number of sneezes in the model group were significantly increased compared with the blank control group ($P < 0.001$). Compared with the model group, the number of mouse nose scratching and number of sneezes in the TSLP/IL-13 BsAb (10 and 30 mg/kg) groups ($P < 0.05$ - 0.001) were significantly decreased, and there was no

significant difference between the TSLP/IL-13 BsAb (3 mg/kg) group and the KLH (30 mg/kg) group ($P > 0.05$); the number of mouse nose scratching and number of sneezes in the TSLP/IL-13 BsAb (3, 10, and 30 mg/kg) groups showed a dose-dependent reduction, the inhibition rates for nose scratching were 7.08%, 26.15% and 49.54%, respectively, and the inhibition rates for sneezes were 9.89%, 26.37% and 36.26%, respectively.

[00302] **Influence on Mch-induced airway hyperresponsiveness (AHR)**

[00303] On Day 28, mice were allowed to inhale by nebulization 0, 1, 2, 4, 8, 12, 24, or 48 mg/mL acetylmethacholine (Mch) and the Mch-induced mouse airway hyperresponsiveness (AHR) was detected with an EMKA Animal Lung Function Monitoring System, and at the end of the airway hyperresponsiveness assay, the assay data were exported by using the IOX Recording and Analysis Software. 3 - 5 maximum values were consecutively selected from the baseline values and the detection values after Mch nebulization respectively, to calculate the measured values and increase rates of airway resistance (Penh) and PC100, and the results were shown in Figs. 32A-32B. The results showed that in the model group, the Penh values and the increase rates of Penh at Mch 12, 24, and 48 mg/mL were significantly increased compared with the blank control group ($P < 0.01$ - 0.001). Compared with the model group, the TSLP/IL-13 BsAb (10 and 30 mg/kg) groups significantly reduced the increase in Penh values ($P < 0.05$ - 0.001), the TSLP/IL-13 BsAb (3 mg/kg) group significantly reduced the Penh values at Mch 24 mg/mL ($P < 0.05$), and the increase in the Penh values in the KLH (30 mg/kg) group was not significantly different ($P > 0.05$) at various concentrations of Mch. The inhibition rates of the Penh values in the TSLP/IL-13 BsAb (3, 10 and 30 mg/kg) groups at Mch 48 mg/mL were 23.72%, 46.33% and 57.04%, respectively. The PC100 of the blank control group, model group, TSLP/IL-13 BsAb (3, 10 and 30 mg/kg) groups and KLH (30 mg/kg) group were 10.43, 5.82, 6.75, 9.41, 13.99 and 5.21 mg/mL, respectively, which indicated that after OVA-induced mouse asthma modeling, the PC100 of the mice in the model group was decreased, and airway sensitivity was increased; and in the TSLP/IL-13 BsAb (3, 10 and 30 mg/kg) groups, the PC100 increased in a dose-dependent manner, and the airway sensitivity was decreased.

[00304] **Influence on number of inflammatory cells in bronchoalveolar lavage (BALF)**

[00305] On Day 28, after blood collection, the mice were sacrificed by cervical dislocation., the left lung and parietal lobes were ligated, and irrigated with 0.5 mL of bronchoalveolar lavage fluid (BALF) twice, and lavage fluids from the three repetition were combined and mixed thoroughly, and leukocytes, eosinophils, macrophages and lymphocytes were counted under the microscope, and the results were shown in Fig. 33. The results showed that the numbers of leukocytes, eosinophils, macrophages and lymphocytes in BALF in the model group were all

significantly increased, compared with the blank control group ($P < 0.001$). Compared with the model group, the TSLP/IL-13 BsAb (10 and 30 mg/kg) groups could significantly inhibit the increase of the total number of leukocytes and the number of eosinophils ($P < 0.01$-0.001), the TSLP/IL-13 BsAb (3 mg/kg) group could significantly inhibit the increase of the number of eosinophils ($P < 0.05$), the TSLP/IL-13 BsAb (30 mg/kg) group could significantly inhibit the increase of the number of macrophages ($P < 0.001$), the TSLP/IL-13 BsAb (3, 10, and 30 mg/kg) groups had no effect on the number of lymphocytes ($P > 0.05$), and the KLH (30 mg/kg) group had no effect on the total number of leukocytes, the number of eosinophils, macrophages, and lymphocytes ($P > 0.05$). For the TSLP/IL-13 BsAb (3, 10, and 30 mg/kg) groups, the inhibition rates of the total number of leukocytes were 17.16%, 28.82% and 41.03%, respectively, and the inhibition rates of the number of eosinophils were 32.39%, 58.74% and 69.87%, respectively.

[00306] **Influence on serum total IgE and OVA-sIgE levels**

[00307] On Day 20 and Day 28, blood was collected from the retro-orbital venous plexus of mice, and serum total IgE and OVA-sIgE levels were detected by ELISA, and the results were shown in Fig. 34. The results showed that compared with the blank control group, on Day 20 and Day 28, serum total IgE and OVA-sIgE levels were significantly elevated ($P < 0.001$). Compared with the model group, on Day 20, the TSLP/IL-13 BsAb (10 and 30 mg/kg) groups could significantly decrease serum total IgE level ($P < 0.05$ - 0.01); on Day 28, the TSLP/IL-13 BsAb (10 and 30 mg/kg) groups could significantly decrease serum total IgE and OVA-sIgE levels ($P < 0.01$ - 0.001); on Day 20 and Day 28, for the TSLP/IL-13 BsAb (3, 10, and 30 mg/kg) groups, serum total IgE level were dose-dependently reduced, on Day 20 the inhibition rates were 25.04%, 31.90% and 46.88%, respectively, and on Day 28 the inhibition rates were 7.81%, 49.91%, and 56.12%, respectively.

[00308] **Influence on h-TSLP and MUC5AC mRNA expression in lung tissues**

[00309] The lung tissue of parietal lobe was added with 1 mL of TRIzon Reagent, and homogenized, RNA was extracted and reverse-transcribed to cDNA, and IL-4, IL-5, IL-13, h-TSLP and MUC5AC mRNA expression levels in the lung tissue were detected by using q-PCR, and the results were shown in Fig. 35. The results showed that the expression levels of h-TSLP and MUC5AC mRNA in the lung tissue of the mice in the model group were significantly elevated, compared with those in the blank control group ($P < 0.001$), and the expression levels of IL-4, IL-5 and IL-13 mRNA showed an elevated trend without significant differences ($P > 0.05$). Compared with the model group, the TSLP/IL-13 BsAb (10 and 30 mg/kg) groups could significantly inhibit the increase of h-TSLP and MUC5AC mRNA expression levels in lung tissues ($P < 0.05$ - 0.01), the

inhibition rates for h-TSLP were 35.85% and 24.73%, respectively, and the inhibition rates for MUC5AC were 48.81% and 57.21%, respectively.

[00310] **Influence on eosinophils infiltration in lung tissues**

[00311] On Day 28, after alveolar lavage, the hilar portion of the left lung was taken and fixed with 10% neutral buffered formalin solution, and sectioned with paraffin embedding after complete fixation. H&E staining was performed to observe eosinophilic infiltration of the lung tissues, and pathological scoring was performed, the results of the pathological scoring were shown in Fig. 36, and the pathological diagram of eosinophilic infiltration was shown in Fig. 37. The results showed that massive eosinophilic infiltration was observed in the airways and perivascular of the lung tissues of the mice in the model group, compared with the blank control group ($P < 0.001$). Compared with the model group, the TSLP/IL-13 BsAb (10 and 30 mg/kg) groups significantly inhibited eosinophil infiltration in the airways and perivascular of mouse lung tissues in a dose-dependent manner ($P < 0.01$).

[00312] **Influence on airway goblet epithelial cell metaplastic proliferation**

[00313] On Day 28, PAS staining was performed on the mouse lung tissues to observe the metaplastic proliferation of goblet epithelial cells of peri-airway of the lung tissues, and the positive rate was counted, and the results of the positive rate were shown in Fig. 38, and the results of the pathological diagram of airway goblet epithelial cell metaplastic proliferation was shown in Fig. 39. The results of PAS staining showed that compared with the blank control group, the mouse lung tissue airway lumen interior of the model group showed a large amount of goblet epithelial cell metaplastic proliferation and mucus secretion ($P < 0.001$), and the positive rate of goblet epithelial cells was 46.37%. Compared with the model group, the TSLP/IL-13 BsAb (10 and 30 mg/kg) groups significantly inhibited the goblet epithelial cell metaplastic proliferation and mucus secretion in the mouse airway in a dose-dependent manner ($P < 0.05$-0.01), and the inhibition rates were 21.36% and 46.06%, respectively.

[00314] **Influence on lung tissue mast cells degranulation**

[00315] On Day 28, the lung tissues of mice were stained with toluidine blue, and the mast cell degranulation of the lung tissues was observed and the degranulation rate was counted. The results of the degranulation rate were shown in Fig. 40, and the results of the pathological diagram of mast cell degranulation were shown in Fig. 41. The results showed that compared with the blank control group, more mast cell degranulation was observed in the lung tissues of the mice in the model group ($P < 0.001$), and the degranulation rate was 66.10%. Compared with the model group, the TSLP/IL-13 BsAb (3, 10 and 30 mg/kg) groups significantly inhibited mast cell degranulation in

mouse lung tissues in a dose-dependent manner ($P < 0.05 - 0.01$), with inhibition rates of 30.69%, 43.27%, and 65.33%, respectively; no significant difference was observed in the KLH (30 mg/kg) group ($P > 0.05$).

[00316] **Influence on lung tissue peri-airway collagen deposition**

[00317] On Day 28, Masson's staining was performed on mouse lung tissues, and airway remodeling and peri-airway collagen deposition were observed under the microscope, and the area of the positive expression region was calculated; the results of collagen deposition positivity rate were shown in Fig. 42, and the results of the pathological diagram of peri-airway collagen deposition were shown in Fig. 43. The results showed that more collagen deposition was observed in the peri-airway of the lung tissue of the mice in the model group, compared with the blank control group ($P < 0.001$). Compared with the model group, the TSLP/IL-13 BsAb (3, 10 and 30 mg/kg) groups significantly improved peri-airway collagen deposition of mouse lung tissue in a dose-dependent manner ($P < 0.05 - 0.01$), with inhibition rates of 30.63%, 50.62%, and 57.32%, respectively; there was no significant difference in the KLH (30 mg/kg) group ($P > 0.05$).

[00318] **Conclusions**

[00319] In this Example, an OVA-induced B-hTSLP/hTSLPR mouse asthma model was successfully established, and TSLP/IL-13 BsAb administered by subcutaneous injection could significantly inhibit Mch-induced airway hyperresponsiveness; alleviate the symptoms of allergic rhinitis; reduce the increase of total number of leukocytes, number of eosinophils, and number of macrophages in BALF; decrease serum total IgE and OVA- sIgE levels; inhibit the expression of h-TSLP and MUC5AC mRNA in lung tissues; reduce eosinophil infiltration in lung tissues; inhibit the increase of mucus secretion of epithelial cells in the airways; alleviate goblet epithelial cell metaplastic proliferation; reduce the degranulation of mast cells in lung tissues; and reduce the peri-airway collagen deposition. These results demonstrate that TSLP/IL-13 BsAb has a significant anti-asthmatic effect.

[00320] **Example 19. Evaluating efficacy of TSLP/IL-13 BsAb on MC903-induced B-hTSLP/hTSLPR mouse dermatitis model**

[00321] B-hTSLP/hTSLPR mice were randomly divided into 6 groups, with 11 mice in each group, i.e., a blank control group (control group), a model group (model group), TSLP/IL-13 BsAb (0.3, 3.0, and 30.0 mg/kg) groups and a negative control Anti-KLH hIgG1 (SEQ ID Ns: 62 and 63. 30.0 mg/kg) group, respectively. On the first day of modeling (counted as Day 0), 20 μL of MC903 (50 μM) was applied to the mouse right ear, and 10 μL each to the belly and dorsal sides of the ear

for 5 consecutive days, and then paused for 2 days; from Day 7 to Day 11, the mouse right ear was applied consecutively for 5 days, and then paused for 2 days, and then the model ended on Day 13; and in the blank control group, anhydrous ethanol was applied synchronously. The first dosing was on the day before modeling (Day -1); Day -1 - Day 6, dosing once every 2 days on Day -1, Day 2, and Day 5, totally 3 times; Day 7 - Day 13, dosing once every 1 day on Day 7, Day 9, and Day 11, totally 3 times, by subcutaneous injection. The blank control group and the model group were synchronously injected with vehicle TSLP/IL-13 BsAb blank solution.

[00322] **Body weight and general symptom observation**

[00323] General symptom observation was performed daily during modeling and dosing, and the mice in each group were weighed before each dosing, and the results were shown in Fig. 44. The results showed that there was no significant difference in the mouse body weight in the model group during modeling and dosing, compared with the blank control group ($P > 0.05$). There was no significant difference ($P > 0.05$) in the mouse body weights in the TSLP/IL-13 BsAb (0.3, 3.0, and 30.0 mg/kg) groups and Anti-KLH hIgG1 (SEQ ID Ns: 62 and 63, 30.0 mg/kg) group during modeling and dosing compared with the model group.

[00324] **Inhibitory effect on the increase of mouse ear thickness**

[00325] From Day -1 to Day 13, before each dosing and on Day 12 and Day 13, the thickness of the right ear of the mice in each group was measured with a spiral micrometer, and the results were shown in Fig. 45. The results showed that, compared with the blank control group, the mouse right ear thickness in the model group was significantly increased ($P < 0.0001$). Compared with the model group, the TSLP/IL-13 BsAb (3.0 and 30.0 mg/kg) groups could significantly inhibit the increase of the mouse right ear thickness ($P < 0.05$-0.0001); the TSLP/IL-13 BsAb (0.3, 3.0, and 30.0 mg/kg) groups dose-dependently inhibited the increase of the mouse right ear thickness, and the inhibition rates were 5.45%, 17.29% and 40.48%, respectively.

[00326] **Inhibitory effect on mouse skin lesions**

[00327] From Day -1 to Day 13, before each dosing and on Day 12 and Day 13, clinical disease scores of skin lesion conditions of the right ear of mice in each group were performed, and the results were shown in Fig. 46. The results showed that compared with the blank control group, the belly side of the right ear of the mice in the model group was obviously dry, deeper color, dark red, desquamated and edematous, and the blood vessels on the dorsal side of the ear were significantly dilated, with a significant increase in the clinical disease scores ($P < 0.0001$). Compared with the model group, the skin lesions on the belly side of the right ear of the mice in the TSLP/IL-13 BsAb (30.0 mg/kg) group were significantly alleviated, and the blood vessels on the dorsal side

of the ear showed no significant tendency of dilatation, and the clinical disease scores were significantly reduced ($P < 0.0001$), and the TSLP/IL-13 BsAb (0.3, 3.0, and 30.0 mg/kg) groups reduced the skin lesions on the mouse right ear, with inhibition rates of 11.58%, 10.53%, and 40.26%, respectively.

[00328] **Inhibiting lymph node enlargement on drainage side of mouse right ear**

[00329] On Day 13, lymph nodes on the drainage side of the mouse right ear were taken and weighed, and the results were shown in Fig. 47. The results showed that the weight of lymph nodes on the drainage side of the right ear of the mice in the model group was significantly increased compared with the blank control ($P < 0.0001$). Compared with the model group, the lymph nodes on the drainage side of the mouse right ear in the TSLP/IL-13 BsAb (3.0, and 30.0 mg/kg) groups were not significantly enlarged and had no significantly increased weights ($P < 0.001$-0.0001), and the lymph nodes on the drainage side of the mouse right ear in the TSLP/IL-13 BsAb (0.3 mg/kg) group and the Anti-KLH hIgG1 (SEQ ID Ns: 62 and 63, 30.0 mg/kg) group showed no significant difference in weight ($P > 0.05$). TSLP/IL-13 BsAb (0.3, 3.0, and 30.0 mg/kg) could dose-dependently inhibit MC903-induced lymph node enlargement on the drainage side of the mouse right ear of the mice, with the inhibition rates of 19.03%, 40.48%, and 50.65%, respectively.

[00330] **Decreasing mouse serum total IgE level**

[00331] On Day 13, total IgE level in the mouse serum in each group were detected by ELISA, and the results were shown in Fig. 48. The results showed that the total IgE level in mouse serum in the model group were significantly elevated, compared with the blank control group ($P < 0.01$). Compared with the model group, the total IgE level in mouse serum in the TSLP/IL-13 BsAb (3.0, and 30.0 mg/kg) groups were significantly decreased ($P < 0.05$), and the total IgE level in mouse serum in the TSLP/IL-13 BsAb (3.0, and 30.0 mg/kg) groups were significantly decreased, with the inhibition rates of 47.79% and 46.61%, respectively.

[00332] **Inhibiting expression of cytokines in mouse ear tissue**

[00333] IL-4, IL-5 and IL-6 mRNA expression in mouse ear tissues were detected by a qPCR method, and the results were shown in Fig. 49. The results showed that IL-4 and IL-6 mRNA levels in the mouse ear tissues in the model group were significantly elevated, compared with those in the blank control group ($P < 0.001$), while IL-5 mRNA levels were not significantly elevated ($P > 0.05$). Compared with the model group, the IL-4 mRNA levels in the mouse ear tissues in the TSLP/IL-13 BsAb (3.0, and 30.0 mg/kg) groups were significantly reduced ($P < 0.001$), and the inhibition rates for IL-4 were 78.38% and 85.95%, respectively; the IL-6 mRNA levels in the mouse ear tissues in

the TSLP/IL-13 BsAb (0.3, 3.0, and 30.0 mg/kg) groups were significantly decreased ($P < 0.001$), and the inhibition rates for IL-6 were 48.02%, 73.17% and 84.49%, respectively.

[00334] **Decreasing inflammation scores of mouse ear tissue**

[00335] On Day 13, the mouse right ear tissues were stained with H&E and scored for inflammation, and the results were shown in Figs. 50 and 51. The pathological results of the mouse right ear tissues showed that the inflammation scores of the mouse ear tissues in the model group were significantly elevated, compared with those of the blank control group ($P < 0.0001$). Compared with the model group, the inflammation scores of the mouse ear tissues in the TSLP/IL-13 BsAb (3.0, and 30.0 mg/kg) groups were significantly reduced ($P < 0.01$-0.001). The TSLP/IL-13 BsAb (0.3, 3.0, and 30.0 mg/kg) groups dose-dependently reduced the inflammation scores of the mouse ear tissues, with the inhibition rates of 16.7%, 25.0% and 33.3%, respectively.

[00336] **Conclusions**

[00337] In this example, the MC903-induced B-hTSLP/hTSLPR mouse dermatitis model was successfully established, and TSLP/IL-13 BsAb administered by subcutaneous injection could significantly inhibit the increase of mouse ear thickness; improve skin lesions of mouse ear and decrease the clinical disease score; inhibit lymph node enlargement on the drainage side of the right ear; reduce total IgE level in serum; inhibit IL-4 and IL-6 mRNA expression in ear tissues; inhibit the inflammatory response of ear tissues. These results demonstrate that TSLP/IL-13 BsAb has a significant anti-dermatitis effect.

[00338] **Example 20. Studies on affinity of TSLP/IL-13 BsAb for FcγR, FcRn and C1q**

[00339] **Binding affinities for FcγRI, FcγRII and FcγRIII**

[00340] SPR/Biacore T200 was used to couple His-Tag antibody to the CM5 chip surface, and FcγRI, FcγRIIAH131, FcγRIIB, FcγRIIIAV158, and FcγRIIIAF158 were captured by the mutual binding of His-tag to His-Tag antibody, and the capture time was set to 40 s, and the flow rate was 10 μL/min, the chip was rinsed with buffer to a smooth baseline, and the gradually diluted TSLP/IL-13 BsAb was allowed to flow through the chip at a flow rate of 30 μL/min. While detecting the affinity of TSLP/IL-13 BsAb for FcγRI, the binding time of TSLP/IL-13 BsAb was set to 120 s, and the dissociation time was set to 200 s. While detecting the affinities of TSLP/ IL-13 BsAb for FcγRII and FcγRIII, the binding time of TSLP/IL-13 BsAb was set to 90 s, and the dissociation time was set to 120 s. Finally, the measured data were fitted to obtain the equilibrium dissociation constants (KDs) by regenerating with 10 mM Glycine-HCl at pH 2.0 for 30 s, the flow rate being set to 30 μL/min. The results were shown in Figs. 52A-56B. Figs. 52A-52B show that the binding of

TSLP/IL-13 BsAb and positive control antibody Anti-KLH hIgG1 (SEQ ID Ns: 62 and 63) to FcγRI was in conformity with the Langmuir 1:1 kinetic theory model, and was monovalent. The affinity KD of TSLP/IL-13 BsAb for FcγRI was 1.53 nM, and the affinity KD of positive control antibody Anti-KLH hIgG1 for FcγRI was 0.66 nM. Figs. 53A-53B and 54A-54B show that the binding of TSLP/IL-13 BsAb and positive control antibody Anti-KLH hIgG1 to FcγRII was in conformity with the Steady state model, and was monovalent. The affinity of TSLP/IL-13 BsAb for FcγRIIAH131 was 2.36 μM, and the affinity of positive control antibody Anti-KLH hIgG1 for FcγRIIAH131 was 1.11 μM (Figs. 53A-53B). TSLP/IL-13 BsAb and the positive control antibody Anti-KLH hIgG1 both bound weakly to FcγRIIB (Figs. 54A-54B). Figs. 55A-55B and 56A-56B show that the binding of TSLP/IL-13 BsAb and positive control antibody Anti-KLH hIgG1 to FcγRIII was in conformity with the Steady state model, and was monovalent. The affinity of TSLP/IL-13 BsAb for FcγRIIIAV158 was 843.7 nM, and the affinity of the positive control antibody Anti-KLH hIgG1 for FcγRIIIAV158 was 258.3 nM (Figs. 55A-55B). The affinity of TSLP/IL-13 BsAb for FcγRIIIAF158 was 1.28 μM, and the affinity of the positive control antibody Anti-KLH hIgG1 for FcγRIIIAF158 was 995.2 nM (Figs. 56A-56B).

[00341] **Binding affinity for FcRn**

[00342] SPR/Biacore T200 was used to capture FcRn onto the CM5 chip surface coupled with Tis-Tag antibody, the capture time was set to 40 s, the flow rate was 10 μL/min, the chip was rinsed with buffer to a smoothy baseline. The gradiently diluted TSLP/IL-13 BsAb and the positive control antibody Anti-KLH hIgG1 were allowed to flow through the chip at a flow rate of 30 μL/ min. The binding time was set to 80 s, the dissociation time was 110 s. The measured data were fitted to obtain the equilibrium dissociation constants by regenerating with 10 mM Glycine-HCl at pH 2.0 for 30 s, the flow rate being 30 μL/min. The results were shown in Figs. 57A-58B. Figs. 57A-57B and 58A-58B show that the binding of TSLP/IL-13 BsAb and positive control antibody Anti-KLH hIgG1 to FcRn was pH-dependent. At pH 7.4, TSLP/IL-13 BsAb and positive control antibody Anti-KLH hIgG1 weakly bound to FcRn (Figs. 57A-57B). At pH 6.0, the binding of TSLP/IL-13 BsAb and positive control antibody Anti-KLH hIgG1 to FcRn was in conformity with the Steady state model, and was monovalent. The affinity of TSLP/IL-13 BsAb for FcRn was 451.8 nM, and the affinity of positive control antibody Anti-KLH hIgG1 for FcRn was 599.3 nM (Figs. 58A-58B).

[00343] **Binding affinity for C1q**

[00344] SPR/Biacore T200 was used to capture TSLP/IL-13 BsAb and positive control antibody Anti-KLH hIgG1 into the Fc2 and Fc4 channels of the Protein L chip, the capture time was set to 40 s and the flow rate was 10 μL/min. The chip was rinsed with buffer until a smoothy

baseline, and the gradiently diluted C1q was allowed to flow sequentially through the chip at 30 μL/min. The binding time was set to 80 s, the dissociation time was 110 s, and the measured data was fitted to obtain the equilibrium dissociation constants by regenerating with 10 mM Glycine-HCl at pH 2.0 for 30 s, with the flow rate being 30 μL/min. Biacore T200 Evaluation Software 3.1 was used for analysis, and the binding of the antibody to FcγRI was fitted in Kinetics 1:1 binding mode, and other weak interactions (fast binding and fast dissociation) were fitted in Steady State mode to obtain affinity data. The results were shown in Figs. 59A-59B. Figs. 59A-59B shows that the binding of TSLP/IL-13 BsAb to C1q conformed to the Steady state model. The affinity of TSLP/IL-13 BsAb for C1q was 79.18 nM, and the affinity of the positive control antibody Anti-KLH hIgG1 for C1q was 53.62 nM.

[00345] **Conclusions**

[00346] TSLP/IL-13 BsAb can bind to FcγRI, FcγRIIAH131, FcγRIIIAV158 and FcγRIIIAF158 and C1q, and weakly bind to FcγRIIB; and bind to FcRn in a pH-dependent manner, weakly bind to FcRn at pH 7.4, and the affinity for FcRn is increased at pH 6.0 and stronger than that of the positive control antibody Anti-KLH IgG1.

[00347] **Example 21. Studies on binding of TSLP/IL-13 BsAb to IL-13 of different species**

[00348] A 96-well ELISA plate was coated with the human, cynomolgus monkey, mouse and rat IL-13 recombinant proteins, respectively, by using ELISA, after blocking, and was co-incubated with different concentrations of TSLP/IL-13 BsAb stock solution, and was labelled with anti-human Fc secondary antibody containing HRP, and was developed with TMB substrate. The absorbances at a wavelength of 450 nm were measured to calculate EC50s. The binding activities of TSLP/IL-13 BsAb to the human, cynomolgus monkey, mouse and rat IL-13 were evaluated.

[00349] The human, cynomolgus monkey, mouse and rat IL-13 were respectively formulated with a coating solution to a concentration of 1 μg/mL, 100 μL per well was added to ELISA plate, and kept at 4°C for overnight coating. The coated ELISA plate was washed and blocked, and then different concentrations of TSLP/IL-13 BsAb were added, and then incubated at room temperature for 1 h. The plate was washed, and then the prepared Anti-hFc-HRP secondary antibody solution (1:4000 dilution) was added, and the incubation at room temperature was continued for 1 h. 100 μL of prepared TMB developing solution per well was added, and then 50 μL of termination solution was added per well after 5 min of development at 37°C and avoiding light. The absorbances at a wavelength of 450 nm were read by a microplate reader. Anti-KLH hIgG1 was used as a negative

control. The results were processed by GraphPad Prism 6 software, and the EC50 was calculated by four-parameter regression calculation for curve-fitting, with the antibody concentration as the horizontal coordinate and the absorbance at 450 nm as the vertical coordinate. The results were shown in Figs. 60 and 61. Fig. 60 shows that TSLP/IL-13 BsAb binds to human and cynomolgus monkey IL-13 with EC50s of 0.45 nM and 0.56 nM, respectively, and does not bind to rat and mouse IL-13. Fig. 61 shows that the negative control Anti-KLH hIgG1 binds to none of human, cynomolgus monkey, rat and mouse IL-13.

[00350] Example 22. Studies on binding of TSLP/IL-13 BsAb to TSLP of different species

[00351] A 96-well ELISA plate was coated with the human, cynomolgus monkey, mouse and rat TSLP recombinant proteins, respectively, by using ELISA, after blocking, and was co-incubated with different concentrations of TSLP/IL-13 BsAb stock solution, and was labelled with anti-human Fc secondary antibody containing horseradish peroxidase (HRP), and was developed with TMB substrate. The absorbances at a wavelength of 450 nm were measured to calculate half-effective concentrations (EC50). The binding activities of TSLP/IL-13 BsAb to the human, cynomolgus monkey, mouse and rat TSLP were evaluated.

[00352] The human, cynomolgus monkey, mouse and rat TSLP were respectively formulated with a coating solution to a concentration of 1 μg/mL, 100 μL per well was added to ELISA plate, and kept at 4°C for overnight coating. The coated ELISA plate was washed and blocked, and then different concentrations of TSLP/IL-13 BsAb were added, and then incubated at room temperature for 1 h. The plate was washed, and then the prepared Anti-hFc-HRP secondary antibody solution (1:4000 dilution) was added, and the incubation at room temperature was continued for 1 h. 100 μL of prepared TMB developing solution per well was added, and then 50 μL of termination solution was added per well after 5 min of development at 37°C and avoiding light. The absorbances at a wavelength of 450 nm were read by a microplate reader. Anti-KLH hIgG1 was used as a negative control. The results were processed by GraphPad Prism 6 software, and the EC50 was calculated by four-parameter regression calculation for curve-fitting, with the antibody concentration as the horizontal coordinate and the absorbance at 450 nm as the vertical coordinate. The results were shown in Figs. 62 and 63. Fig. 62 shows that TSLP/IL-13 BsAb binds to human and cynomolgus monkey TSLP with EC50s of 0.05 nM and 0.11 nM, respectively, and does not bind to rat and mouse TSLP. Fig. 63 shows that the negative control Anti-KLH hIgG1 binds to none of human, cynomolgus monkey, rat and mouse TSLP.

[00353] Example 23. Studies on TSLP/IL-13 BsAb blocking IL-13/IL-13Rα1 complex from binding to IL- 4Rα

[00354] IL-4Rα was immobilized on the CM5 chip by amino coupling using surface plasmon resonance technique (SPR/Biacore T200), and then the IL-13/IL-13Rα1 complex was incubated with the gradiently diluted TSLP/IL-13 BsAb and then was allowed to flow over the chip surface as an analyte to evaluate the activity of TSLP/IL-13 BsAb blocking the IL-13/IL-13Rα1 complex from binding to IL-4Rα by the binding signal of the analyte.

[00355] Channel 4 of the CM5 chip was selected, the coupling volume was set to 3000 RU, at a flow rate of 10 μL/min, and the coupling reagent (Amine Coupling Kit) and 30 μg/mL IL-4Rα were added to complete the coupling. Channel 4-3 was selected, the gradiently diluted TSLP/IL-13 BsAb and IL-13/IL-13Rα1 mixture were added sequentially, and the binding time was set to 100 s, for a dissociation time of 60 s, at a flow rate of 30 μL/min, for a regeneration time of 30 s, at a flow rate of 30 μL/min. In the data analysis software Biacore T200 Evaluation Software, find the corresponding data file, Report Point select baseline to get the curve profile; exporting to the final binding signal, GraphPad Prism software was used to process, with the sample to be tested as the horizontal coordinate, resonance unit (RU) as the vertical coordinate to make a graph. Anti-KLH hIgG1 was used as a negative control. The results were shown in Fig. 64. Fig. 64 shows that TSLP/IL-13 BsAb effectively blocked the IL-13/IL-13Rα1 complex from binding to IL-4Rα, and the negative control Anti-KLH hIgG1 had no blocking effect.

[00356] Example 24. Studies on activity of TSLP/IL-13 BsAb blocking TSLP from binding to a TSLP receptor (TSLPR)

[00357] A 96-well ELISA plate was coated with TSLPR-hFc recombinant protein by using Enzyme-Linked Immunosorbent Assay (ELISA), after blocking, and a volume ratio of 1:1 mixture of TSLP/IL-13 BsAb and TSLP-mFc recombinant protein was added, and then the absorbance was measured at a wavelength of 450 nm after development with the horseradish peroxidase (HRP)-labelled anti-mFc secondary antibody. The half-effective inhibitory concentration (IC50) of TSLP/IL-13 BsAb was determined, and thereby the activity of TSLP/IL-13 BsAb blocking TSLP from binding to TSLPR was evaluated.

[00358] TSLPR-hFc was diluted to 1 μg/mL with a coating solution, and 100 μL per well was added to the ELISA plate, and kept at 4°C for overnight coating. The coated ELISA plate was washed and blocked, and then 100 μL per well the diluted TSLP/IL-13 BsAb stock solution, the negative control Anti-KLH hIgG1, and a mixed solution of 200 ng/mL TSLP-mFc respectively were

added, 2 wells for each dilution, and then incubated at room temperature for 1 h. The plate was washed each well, and then the prepared Anti-mFc-HRP secondary antibody solution (1:4000 dilution) was added, and the incubation at room temperature was continued for 1 h. 100 μL of prepared TMB developing solution per well was added, and then 50 μL of termination solution was added per well after 5 min of development at 37°C and avoiding light. The absorbances at a wavelength of 450 nm were read by a microplate reader. The results were processed by GraphPad Prism 6 software, and the IC50 was calculated by four-parameter regression calculation for curve-fitting, with the antibody concentration as the horizontal coordinate and the absorbance at 450 nm as the vertical coordinate. The results were shown in Fig. 65. Fig. 65 shows that TSLP/IL-13 BsAb effectively blocked TSLP from binding to TSLPR with an IC50 of 7.26 nM; the negative control Anti-KLH hIgG1 had no blocking activity.

[00359] Example 25. Studies on activity of TSLP/IL-13 BsAb blocking TSLP from binding to cell surface TSLP receptor (TSLPR)

[00360] By using flow cytometry, different concentrations of TSLP/IL-13 BsAb stock solution and TSLP-mFc fusion protein were pre-incubated, and then the mixed solution was incubated with TSLPR- expressing cells of interest, and the binding of TSLP to cell surface TSLPR was detected, and then the half-effective inhibitory concentration (IC50) was calculated, and the activity of TSLP/IL-13 BsAb blocking TSLP from binding to cell surface TSLPR was evaluated.

[00361] BA/F3-TSLPR-IL7Rα cells were cultured with a cell culture medium at 37°C, 5% CO2. The cells were centrifugated for 10 min, collected, and the cell density was adjusted to 1×10^7 cells per 1 mL with a blocking solution, and blocked in an ice bath for 30 min. Antibody dilutions and TSLP solution were prepared simultaneously, and 60 μL of the diluted antibody solution was mixed with 60 μL of TSLP solution, and incubated for 30 min at 37°C. The density of cells was adjusted to 5×10^5 cells per 1 mL by adding a flow buffer, and 100 μL was inoculated into a U-type 96-well cell culture plate, centrifugated to discard the supernatant, 100 μL of antibody-TSLP mixture was added to each well and incubated with the cells for 60 min at 4°C. After incubation, the cells were washed with 200 μL of the flow buffer, and 50 μL of the diluted solution of APC secondary antibody in each well was used to label the to-be-tested on the cell surface, and the cells were incubated for 20 min on ice, and then washed. 50 μL of the PI solution in each well was added, was incubated for 5 min on ice, washed, and the cells were resuspended with 50 μL of PBS. The average fluorescence intensity of the cells was read by a flow cytometer, and the results were recorded. The fluorescence value of PI-negative cell population APC was analyzed by GraphPad Prism 6 software,

and the IC50 was calculated by four-parameter regression calculation method with the antibody concentration as the horizontal coordinate and the average fluorescence intensity of APC as the vertical coordinate. Anti-KLH hIgG1 was used as the negative control. The results are shown in Fig. 66. Fig. 66 shows that TSLP/IL-13 BsAb effectively blocked TSLP from binding to cell surface TSLPR with an IC50 of 1.46 nM, and the negative control Anti-KLH hIgG1 had no significant blocking activity.

[00362] Example 26. Exemplary Amino Acid and Nucleic Acid Sequences

[00363] Tables 9, 10 and 11 illustrate the amino acid and nucleic acid sequences related to antibodies disclosed herein.

[00364] Table 9. Exemplary Amino Acid Sequences of First Antigen-Binding Region that Binds to IL-13 and Other Antibodies

Description of Sequences	Amino Acid Sequences (Amino terminus to Carboxyl terminus)	SEQ ID NO:
Anti-IL13 VL-CDR1 (TSLP/IL-13 BsAb)	RASKSVDSYGNSFMH	21
Anti-IL13 VL-CDR2 (TSLP/IL-13 BsAb)	LASNLES	22
Anti-IL13 VL-CDR3 (TSLP/IL-13 BsAb)	QQNNEDPRT	23
Anti-IL13 VH-CDR1 (TSLP/IL-13 BsAb)	AYSVN	24
Anti-IL13 VH-CDR2 (TSLP/IL-13 BsAb)	MIWGDGKIVYNSALKS	25
Anti-IL13 VH-CDR3 (TSLP/IL-13 BsAb)	DGYYPYAMDN	27
Anti-IL13 VH-CDR2 (H2, H6, H7, H8)	MIWGDGKIVYNSAVKS	26
Anti-IL-13 VL (K0) (Lebrikizumab/ref1)	DIVMTQSPDSLSVSLGERATINC**RASKSVDSYGNS FMH**WYQQKPGQPPKLLIY**LASNLES**GVPDRFSGS GSGTDFTLTISSLQAEDVAVYYC**QQNNEDPRT**FG GGTKVEIK	46
Anti-IL-13 VL (K1)	DIQMTQSPSSLSASVGDRVTITC**RASKSVDSYGNS FMH**WYQQKPGKAPKLLIY**LASNLES**GVPSRFSGS GSGTDFTLTISSLQPEDFATYYC**QQNNEDPRT**FG QGTKLEIK	1
Anti-IL-13 VL (K2)	EIVLTQSPATLSLSPGERATLSC**RASKSVDSYGNS FMH**WYQQKPGQAPRLLIY**LASNLES**GIPARFSGS GSGTDFTLTISSLEPEDFAVYYC**QQNNEDPRT**FG QGTKLEIK	3
Anti-IL-13 VL (TSLP/IL-13 BsAb)	DIQMTQSPSSLSASVGDRVTITC**RASKSVDSYGNS FMH**WYQEKPGKAPKLLIY**LASNLES**GVPSRFSGS	53

Description of Sequences	Amino Acid Sequences (Amino terminus to Carboxyl terminus)	SEQ ID NO:
	GSGTDFTLTISSLQPEDFATYYC**QQNNEDPRT**FG QGTKLEIK	
Anti-IL-13 VH (H0) (Lebrikizumab/ref1)	QVTLRESGPALVKPTQTLTLTCTVSGFSLS**AYSVN** WIRQPPGKALEWLA**MIWGDGKIVYNSALKS**RLT ISKDTSKNQVVLTMTNMDPVDTATYYCAG**DGYY PYAMDN**WGQGSLVTVSS	48
Anti-IL-13 VH (H1)	QVQLQESGPGLVKPSETLSLTCTVSGFSLS**AYSVN** WIRQPPGKGLEWIG**MIWGDGKIVYNSALKS**RVTI SKDTSKNQVVLKLSSVTAADTAVYYCAG**DGYYP YAMDN**WGQGTLVTVSS	5
Anti-IL-13 VH (H2)	QVQLVESGGGVVQPGRSLRLSCAVSGFSLS**AYSV N**WVRQAPGKGLEWVA**MIWGDGKIVYNSAVKS** RLTISKDNSKNTVYLQMNSLRAEDTAVYYCAG**D GYYPYAMDN**WGQGTLVTVSS	7
Anti-IL-13 VH (H3)	QVQLQESGPGLVKPSETLSLTCTVSGFSLS**AYSVN** WIRQPPGKGLEWIG**MIWGDGKIVYNSALKS**RVTI SKDTSKNQVSLKLSSVTAADTAVYYCAG**DGYYP YAMDN**WGQGTLVTVSS	9
Anti-IL-13 VH (H4)	QVQLQESGPGLVKPSETLSLTCTVSGFSLS**AYSVN** WIRQPPGKGLEWIG**MIWGDGKIVYNSALKS**RVTI SKDTSKNQFSLKLSSVTAADTAVYYCAG**DGYYP YAMDN**WGQGTLVTVSS	11
Anti-IL-13 VH (H5)	QVQLQESGPGLVKPSETLSLTCTVSGFSLS**AYSVN** WIRQPPGKGLEWIG**MIWGDGKIVYNSALKS**RVTI SVDTSKNQFSLKLSSVTAADTAVYYCAG**DGYYP YAMDN**WGQGTLVTVSS	13
Anti-IL-13 VH (H6)	QVQLVESGGGVVQPGRSLRLSCAVSGFSLS**AYSV N**WVRQAPGKGLEWVA**MIWGDGKIVYNSAVKS** RLTISKDNSKNTLYLQMNSLRAEDTAVYYCAG**D GYYPYAMDN**WGQGTLVTVSS	15
Anti-IL-13 VH (H7)	QVQLVESGGGVVQPGRSLRLSCAVSGFSLS**AYSV N**WVRQAPGKGLEWVA**MIWGDGKIVYNSAVKS** RLTISRDNSKNTLYLQMNSLRAEDTAVYYCAG**D GYYPYAMDN**WGQGTLVTVSS	17
Anti-IL-13 VH (H8)	QVQLVESGGGVVQPGRSLRLSCAVSGFSLS**AYSV N**WVRQAPGKGLEWVA**MIWGDGKIVYNSAVKS** RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAG**DG YYPYAMDN**WGQGTLVTVSS	19
Anti-IL-13 VH (TSLP/IL-13 BsAb)	QVQLQESGPGLVKPSETLSLTCTVSGFSLS**AYSVN** WIRKPPGKGLEWIG**MIWGDGKIVYNSALKS**RVTI SKDTSKNQVSLKLSSVTAADTAVYYCAG**DGYYP YAMDN**WGQGTLVTVSS	52
Anti-IL-13 Heavy Chain (TSLP/IL-13 BsAb)	QVQLQESGPGLVKPSETLSLTCTVSGFSLS**AYSVN** WIRKPPGKGLEWIG**MIWGDGKIVYNSALKS**RVTI SKDTSKNQVSLKLSSVTAADTAVYYCAG**DGYYP YAMDN**WGQGTLVTVSSASTKGPSVFPLAPSSKST	42

Description of Sequences	Amino Acid Sequences (Amino terminus to Carboxyl terminus)	SEQ ID NO:
	SGGTAALGCLVEDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDERVEPKSCDKTHTCPPCPAPELLGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVCTLPPSREEMTKNQVSLSCAVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKL TVDKSRWQQGNVFSCSVLHEALHAHYTQKSLSLS PGK	
Anti-IL-13 Light Chain (TSLP/IL-13 BsAb)	DIQMTQSPSSLSASVGDRVTITC**RASKSVDSYGNS FMH**WYQEKPGKAPKLLIY**LASNLES**GVPSRFSGS GSGTDFTLTISSLQPEDFATYYC**QQNNEDPRT**FG QGTKLEIKRTVAAPSVFIFPPSDKQLKSGKASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGL SSPVTKSFNRGEC	44
Anti-IL-13 Heavy Chain (Lebrikizumab/ref1/ Lebrikizumab analog)	QVTLRESGPALVKPTQTLTLTCTVSGFSLS**AYSVN** WIRQPPGKALEWLA**MIWGDGKIVYNSALKS**RLT ISKDTSKNQVVLTMTNMDPVDTATYYCAG**DGYY PYAMDN**WGQGSLVTVSSASTKGPSVFPLAPCSRS TSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVD HKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIA VEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSL GK	57
Anti-IL-13 Light Chain (Lebrikizumab/ref1/ Lebrikizumab analog)	DIVMTQSPDSLSVSLGERATINC**RASKSVDSYGNS FMH**WYQQKPGQPPKLLIY**LASNLES**GVPDRFSGS GSGTDFTLTISSLQAEDVAVYYC**QQNNEDPRT**FG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGL SSPVTKSFNRGEC	58
Anti-IL-13/Anti-TSLP (Lunsekimig/ref2/ Lunsekimig analog)	DVQLVESGGGVVQPGGSLRLSCAASGRTFSSYRM GWFRQAPGKEREFVAALSGDGYSTYTANSVKGR FTISRDNSKNTVYLQMNSLRPEDTALYYCAAKLQ YVSGWSYDYPYWGQGTLVTVSSGGGGSGGGGS GGGGSGGGGSGGGGSGGGGSGGGGSEVQLVESG GGVVQPGGSLRLSCAASGFTFNNYAMKWVRQAP GKGLEWVSSITTGGGSTDYADSVKGRFTISRDNS KNTLYLQMNSLRPEDTALYYCANVPFGYYSEHFS	59

Description of Sequences	Amino Acid Sequences (Amino terminus to Carboxyl terminus)	SEQ ID NO:
	GLSFDYRGQGTLVTVSSGGGGSGGGSEVQLVESG GGVVQPGGSLRLSCAASGSGFGVNILYWYRQAA GIERELIASITSGGITNYVDSVKGRFTISRDNSENT MYLQMNSLRAEDTGLYYCASRNIFDGTTEWGQG TLVTVSSGGGGSGGGSEVQLVESGGGVVQPGGSL RLSCAASGFTFRSFGMSWVRQAPGKGPEWVSSIS GSGSDTLYADSVKGRFTISRDNSKNTLYLQMNSL RPEDTALYYCTIGGSLSRSSQGTLVTVSSGGGGSG GGSEVQLVESGGGVVQPGGSLRLSCAASGFTFAD YDYDIGWFRQAPGKEREGVSCISNRDGSTYYADS VKGRFTISRDNSKNTVYLQMNSLRPEDTALYYCA VEIHCDDYGVENFDFDPWGQGTLVTVSSA	
Anti-IL-13 Heavy Chain (TSLP/IL-13 BsAb-WT)	QVQLQESGPGLVKPSETLSLTCTVSGFSLSAYSVN WIRKPPGKGLEWIGMIWGDGKIVYNSALKSRVTI SKDTSKNQVSLKLSSVTAADTAVYYCAGDGYYP YAMDNWGQGTLVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVEDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDERVEPKSCDKTHTCPPCPAPELLGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVCTLPPSREEMTKNQVSLSCAVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKL TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK	60
Anti-13 Light Chain (TSLP/IL-13 BsAb-WT)	DIQMTQSPSSLSASVGDRVTITCRASKSVDSYGNS FMHWYQEKPGKAPKLLIYLASNLESGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCQQNNEDPRTFGQ GTKLEIKRTVAAPSVFIFPPSDKQLKSGKASVVCL LNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLS SPVTKSFNRGEC	61
Anti-KLH Heavy Chain (Anti-KLH)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYH MHWVRQAPGQGLEWMGWINPNSGGTNYAQKFQ GRVTMTRDTSISTAYMELSRLRSDDTAVYYCARD RGSYYWFDPWGQGTLVTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYIC NVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	62

Description of Sequences	Amino Acid Sequences (Amino terminus to Carboxyl terminus)	SEQ ID NO:
	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	
Anti-KLH Light Chain (Anti-KLH)	DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	63

[00365] **Table 10. Exemplary Amino Acid Sequences of Second Antigen-Binding Region that Binds to TSLP**

Description of Sequences	Amino Acid Sequences (Amino terminus to Carboxyl terminus)	SEQ ID NO:
Anti-TSLP VL-CDR1 (TSLP/IL-13 BsAb)	RTSENIYSYLA	35
Anti-TSLP VL-CDR2 (TSLP/IL-13 BsAb)	FAKTLTD	36
Anti-TSLP VL-CDR3 (TSLP/IL-13 BsAb)	QHHYGTPWT	37
Anti-TSLP VH-CDR1 (TSLP/IL-13 BsAb)	DYWMH	30
Anti-TSLP VH-CDR2 (TSLP/IL-13 BsAb)	IIDPSDSDTSLNQKFQG	31
Anti-TSLP VH-CDR3 (TSLP/IL-13 BsAb)	SLDGYYDY	32
Anti-TSLP VH-CDR1 (1A)	TDYWMH	54
Anti-TSLP VL (K-0)	DIQMTQSPSSLSASVGDRVTITC**RTSENIYSYLA**WYQQKPGKAPKLLIY**FAKTLTD**GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC**QHHYGTPWT**FGQGTKVEIK	51
Anti-TSLP VH (H-0)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFT**DYWMH**WVRQAPGQGLEWMG**IIDPSDSDTSLNQKFQG**RVTITADTSTSTAYMELSSLRSEDTAVYYCAR**SLDGYYDY**WGQGTLVTVSS	50
Anti-TSLP VH (TSLP/IL-13 BsAb)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFT**DYWMH**WVREAPGQGLEWMG**IIDPSDSDTSLNQKFQG**	28

Description of Sequences	Amino Acid Sequences (Amino terminus to Carboxyl terminus)	SEQ ID NO:
	RVTITADTSTSTAYMELSSLRSEDTAVYYCAR**SLD GYYDY**WGQGTLVTVSS	
Anti-TSLP VL (TSLP/IL-13 BsAb)	DIQMTQSPSSLSASVGDRVTITC**RTSENIYSYLA**W YQKKPGKAPKLLIY**FAKTLTD**GVPSRFSGSGSGTD FTLTISSLQPEDFATYYC**QHHYGTPWT**FGQGTKV EIK	33
Anti-TSLP Heavy Chain (TSLP/IL-13 BsAb)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFT**DYW MH**WVREAPGQGLEWMG**IIDPSDSDTSLNQKFQG** RVTITADTSTSTAYMELSSLRSEDTAVYYCAR**SLD GYYDY**WGQGTLVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKP SNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP REPQVYTLPPCREEMTKNQVSLWCLVKGFYPSDIA VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVLHEALHAHYTQKSLSLSPGK	38
Anti-TSLP Light Chain (TSLP/IL-13 BsAb)	DIQMTQSPSSLSASVGDRVTITC**RTSENIYSYLA**W YQKKPGKAPKLLIY**FAKTLTD**GVPSRFSGSGSGTD FTLTISSLQPEDFATYYC**QHHYGTPWT**FGQGTKV EIKGQPKAAPSVTLFPPSSEELQANEATLVCLISDF YPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYA ASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAP TECS	40
Anti-TSLP Heavy Chain (Ref3)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTDYW MHWVRQAPGQGLEWMGIIDPSDSDTSLNQKFQGR VTITADTSTSTAYMELSSLRSEDTAVYYCARSLDG YYDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	64
Anti-TSLP Light Chain (Ref3)	DIQMTQSPSSLSASVGDRVTITCRTSENIYSYLAWY QQKPGKAPKLLIYFAKTLTDGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQHHYGTPWTFGQGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLS STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC	65

Description of Sequences	Amino Acid Sequences (Amino terminus to Carboxyl terminus)	SEQ ID NO:
Anti-TSLP Heavy Chain (TSLP/IL-13 BsAb-WT）	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTDYW MHWVREAPGQGLEWMGIIDPSDSDTSLNQKFQGR VTITADTSTSTAYMELSSLRSEDTAVYYCARSLDG YYDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	66
Anti-TSLP Light Chain (TSLP/IL-13 BsAb-WT）	DIQMTQSPSSLSASVGDRVTITCRTSENIYSYLAWY QKKPGKAPKLLIYFAKTLTDGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQHHYGTPWTFGQGTKVEI KGQPKAAPSVTLFPPSSEELQANEATLVCLISDFYP GAVTVAWKADSSPVKAGVETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTE CS	67
Anti-TSLP Heavy Chain (Tezepelumab analog)	QMQLVESGGGVVQPGRSLRLSCAASGFTFRTYGM HWVRQAPGKGLEWVAVIWYDGSNKHYADSVKG RFTITRDNSKNTLNLQMNSLRAEDTAVYYCARAP QWELVHEAFDIWGQGTMVTVSSASTKGPSVFPLA PCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTC NVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTV VHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQ PREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLT VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP GK	68
Anti-TSLP Light Chain (Tezepelumab analog)	SYVLTQPPSVSVAPGQTARITCGGNNLGSKSVHW YQQKPGQAPVLVVYDDSDRPSWIPERFSGSNSGNT ATLTISRGEAGDEADYYCQVWDSSSDHVVFGGGT KLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLIS DFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNK YAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTV APTECS	69

[00366] **Table 11. Exemplary Nucleic Acid Sequences Encoding Antibody Constructs**

Description of Sequences	Nucleotide Sequences	SEQ ID NO:
Anti-IL13 VL (K0) (Lebrikizumab)	GACATCGTGATGACACAGAGCCCTGACAGCCTG TCCGTGTCTCTGGGAGAGAGAGCCACCATCAAC TGCAGAGCCAGCAAGAGCGTGGACAGCTACGG CAACAGCTTCATGCACTGGTATCAGCAGAAGCC CGGCCAGCCTCCTAAGCTGCTGATCTACCTGGC CAGCAACCTGGAAAGCGGCGTGCCAGATAGAT TCAGCGGCTCTGGCTCTGGCACCGACTTCACCC TGACAATCAGTTCCCTGCAGGCCGAGGATGTGG CCGTGTACTACTGCCAGCAGAACAACGAGGAC CCCAGAACATTCGGCGGAGGCACCAAGGTGGA AATCAA	47
Anti-IL13 VL (K1)	GACATCCAGATGACACAGAGCCCTAGCAGCCT GTCTGCCAGCGTGGGAGACAGAGTGACCATCA CCTGTAGAGCCAGCAAGAGCGTGGACAGCTAC GGCAACAGCTTCATGCACTGGTATCAGCAGAAG CCCGGCAAGGCCCCTAAGCTGCTGATCTACCTG GCCAGCAACCTGGAAAGCGGCGTGCCATCTAG ATTCAGCGGCTCTGGCTCTGGCACCGACTTCAC CCTGACAATCTCTAGCCTGCAGCCTGAGGACTT CGCCACCTACTACTGCCAGCAGAACAACGAGG ACCCCAGAACATTCGGCCAGGGCACCAAGCTG GAAATCAAG	2
Anti-IL13 VL (K2)	GAGATCGTGCTGACACAGAGCCCTGCCACACTG TCACTGTCTCCAGGCGAGAGAGCCACACTGAGC TGTAGAGCCAGCAAGAGCGTGGACAGCTACGG CAACAGCTTCATGCACTGGTATCAGCAGAAGCC CGGCCAGGCTCCTAGACTGCTGATCTACCTGGC CAGCAACCTGGAATCTGGCATCCCCGCTAGATT CAGCGGCTCTGGCTCTGGCACAGACTTCACCCT GACAATCAGCAGCCTGGAACCTGAGGACTTCGC CGTGTACTACTGCCAGCAGAACAACGAGGACC CCAGAACATTCGGCCAGGGCACCAAGCTGGAA ATCAAG	4
Anti-IL13 VH (H0) (Lebrikizumab)	CAAGTGACCCTGAGAGAGTCTGGACCCGCTCTG GTCAAGCCCACACAGACCCTGACACTGACCTGT ACCGTGTCCGGCTTCAGCCTGTCTGCCTACAGC GTGAACTGGATCAGACAGCCTCCTGGCAAGGCC CTGGAATGGCTGGCTATGATCTGGGGCGACGGC AAGATCGTGTACAACAGCGCCCTGAAGTCCAG ACTGACCATCAGCAAGGACACCAGCAAGAACC AGGTGGTGCTGACCATGACCAACATGGACCCTG TGGACACCGCCACCTACTACTGTGCTGGCGACG GCTACTACCCCTACGCCATGGATAATTGGGGCC AGGGCTCTCTGGTCACCGTGTCATCT	49
Anti-IL13 VH (H1)	CAGGTTCAGCTGCAAGAGTCTGGACCTGGCCTG GTCAAGCCTAGCGAGACACTGAGCCTGACCTGT	6

Description of Sequences	Nucleotide Sequences	SEQ ID NO:
	ACCGTGTCTGGCTTCAGCCTGAGCGCCTACAGC GTGAACTGGATCAGACAGCCTCCTGGCAAAGG CCTGGAATGGATCGGAATGATCTGGGGCGACG GCAAGATCGTGTACAACAGCGCCCTGAAGTCCA GAGTGACCATCAGCAAGGACACCAGCAAGAAC CAGGTGGTGCTGAAGCTGAGCAGCGTGACAGC CGCTGATACCGCCGTGTACTATTGTGCTGGCGA CGGCTACTACCCCTACGCCATGGATAATTGGGG CCAGGGCACACTGGTCACCGTGTCATCT	
Anti-IL13 VH (H2)	CAGGTGCAGCTGGTTGAATCTGGTGGCGGAGTG GTGCAGCCTGGCAGATCTCTGAGACTGAGCTGT GCCGTGTCTGGCTTCAGCCTGTCTGCCTACTCTG TGAACTGGGTCCGACAGGCTCCTGGCAAAGGA CTGGAATGGGTCGCCATGATCTGGGGCGACGGC AAGATCGTGTACAACAGCGCCGTGAAGTCCAG ACTGACCATCAGCAAGGACAACAGCAAGAACA CCGTGTACCTGCAGATGAACAGCCTGAGAGCCG AGGACACCGCCGTGTACTATTGTGCTGGCGACG GCTACTACCCCTACGCCATGGATAATTGGGGCC AGGGCACACTGGTCACCGTGTCATCT	8
Anti-IL13 VH (H3)	CAGGTTCAGCTGCAAGAGTCTGGACCTGGCCTG GTCAAGCCTAGCGAGACACTGAGCCTGACCTGT ACCGTGTCTGGCTTCAGCCTGAGCGCCTACAGC GTGAACTGGATCAGACAGCCTCCTGGCAAAGG CCTGGAATGGATCGGAATGATCTGGGGCGACG GCAAGATCGTGTACAACAGCGCCCTGAAGTCCA GAGTGACCATCAGCAAGGACACCAGCAAGAAC CAGGTGAGCCTGAAGCTGAGCAGCGTGACAGC CGCTGATACCGCCGTGTACTATTGTGCTGGCGA CGGCTACTACCCCTACGCCATGGATAATTGGGG CCAGGGCACACTGGTCACCGTGTCATCT	10
Anti-IL13 VH (H4)	CAGGTTCAGCTGCAAGAGTCTGGACCTGGCCTG GTCAAGCCTAGCGAGACACTGAGCCTGACCTGT ACCGTGTCTGGCTTCAGCCTGAGCGCCTACAGC GTGAACTGGATCAGACAGCCTCCTGGCAAAGG CCTGGAATGGATCGGAATGATCTGGGGCGACG GCAAGATCGTGTACAACAGCGCCCTGAAGTCCA GAGTGACCATCAGCAAGGACACCAGCAAGAAC CAGTTCAGCCTGAAGCTGAGCAGCGTGACAGCC GCTGATACCGCCGTGTACTATTGTGCTGGCGAC GGCTACTACCCCTACGCCATGGATAATTGGGGC CAGGGCACACTGGTCACCGTGTCATCT	12
Anti-IL13 VH (H5)	CAGGTTCAGCTGCAAGAGTCTGGACCTGGCCTG GTCAAGCCTAGCGAGACACTGAGCCTGACCTGT ACCGTGTCTGGCTTCAGCCTGAGCGCCTACAGC GTGAACTGGATCAGACAGCCTCCTGGCAAAGG	14

Description of Sequences	Nucleotide Sequences	SEQ ID NO:
	CCTGGAATGGATCGGAATGATCTGGGGCGACG GCAAGATCGTGTACAACAGCGCCCTGAAGTCCA GAGTGACCATCAGCGTGGACACCAGCAAGAAC CAGTTCAGCCTGAAGCTGAGCAGCGTGACAGCC GCTGATACCGCCGTGTACTATTGTGCTGGCGAC GGCTACTACCCCTACGCCATGGATAATTGGGGC CAGGGCACACTGGTCACCGTGTCATCT	
Anti-IL13 VH (H6)	CAGGTGCAGCTGGTTGAATCTGGTGGCGGAGTG GTGCAGCCTGGCAGATCTCTGAGACTGAGCTGT GCCGTGTCTGGCTTCAGCCTGTCTGCCTACTCTG TGAACTGGGTCCGACAGGCTCCTGGCAAAGGA CTGGAATGGGTCGCCATGATCTGGGGCGACGGC AAGATCGTGTACAACAGCGCCGTGAAGTCCAG ACTGACCATCAGCAAGGACAACAGCAAGAACA CCCTGTACCTGCAGATGAACAGCCTGAGAGCCG AGGACACCGCCGTGTACTATTGTGCTGGCGACG GCTACTACCCCTACGCCATGGATAATTGGGGCC AGGGCACACTGGTCACCGTGTCATCT	16
Anti-IL13 VH (H7)	CAGGTGCAGCTGGTTGAATCTGGTGGCGGAGTG GTGCAGCCTGGCAGATCTCTGAGACTGAGCTGT GCCGTGTCTGGCTTCAGCCTGTCTGCCTACTCTG TGAACTGGGTCCGACAGGCTCCTGGCAAAGGA CTGGAATGGGTCGCCATGATCTGGGGCGACGGC AAGATCGTGTACAACAGCGCCGTGAAGTCCAG ACTGACCATCAGCAGAGACAACAGCAAGAACA CCCTGTACCTGCAGATGAACAGCCTGAGAGCCG AGGACACCGCCGTGTACTATTGTGCTGGCGACG GCTACTACCCCTACGCCATGGATAATTGGGGCC AGGGCACACTGGTCACCGTGTCATCT	18
Anti-IL13 VH (H8)	CAGGTGCAGCTGGTTGAATCTGGTGGCGGAGTG GTGCAGCCTGGCAGATCTCTGAGACTGAGCTGT GCCGTGTCTGGCTTCAGCCTGTCTGCCTACTCTG TGAACTGGGTCCGACAGGCTCCTGGCAAAGGA CTGGAATGGGTCGCCATGATCTGGGGCGACGGC AAGATCGTGTACAACAGCGCCGTGAAGTCCAG ATTCACCATCAGCAGAGACAACAGCAAGAACA CCCTGTACCTGCAGATGAACAGCCTGAGAGCCG AGGACACCGCCGTGTACTATTGTGCTGGCGACG GCTACTACCCCTACGCCATGGATAATTGGGGCC AGGGCACACTGGTCACCGTGTCATCT	20
Anti-IL-13 VL (TSLP/IL-13 BsAb)	GACATCCAGATGACACAGAGCCCTAGCAGCCT GTCTGCCAGCGTGGGAGACAGAGTGACCATCA CCTGTAGAGCCAGCAAGAGCGTGGACAGCTAC GGCAACAGCTTCATGCACTGGTATCAGGAGAA GCCCGGCAAGGCCCCTAAGCTGCTGATCTACCT GGCCAGCAACCTGGAAAGCGGCGTGCCATCTA	56

Description of Sequences	Nucleotide Sequences	SEQ ID NO:
	GATTCAGCGGCTCTGGCTCTGGCACCGACTTCA CCCTGACAATCTCTAGCCTGCAGCCTGAGGACT TCGCCACCTACTACTGCCAGCAGAACAACGAGG ACCCCAGAACATTCGGCCAGGGCACCAAGCTG GAAATCAAG	
Anti-IL-13 VH (TSLP/IL-13 BsAb)	CAGGTTCAGCTGCAAGAGTCTGGACCTGGCCTG GTCAAGCCTAGCGAGACACTGAGCCTGACCTGT ACCGTGTCTGGCTTCAGCCTGAGCGCCTACAGC GTGAACTGGATCAGAAAGCCTCCTGGCAAAGG CCTGGAATGGATCGGAATGATCTGGGGCGACG GCAAGATCGTGTACAACAGCGCCCTGAAGTCCA GAGTGACCATCAGCAAGGACACCAGCAAGAAC CAGGTGAGCCTGAAGCTGAGCAGCGTGACAGC CGCTGATACCGCCGTGTACTATTGTGCTGGCGA CGGCTACTACCCCTACGCCATGGATAATTGGGG CCAGGGCACACTGGTCACCGTGTCATCT	55
Anti-TSLP VL (TSLP/IL-13 BsAb)	GACATCCAGATGACACAGAGCCCTAGCAGCCT GTCTGCCAGCGTGGGAGACAGAGTGACCATCA CCTGTAGAACCAGCGAGAACATCTACAGCTACC TGGCCTGGTATCAGAAGAAGCCTGGCAAGGCTC CCAAGCTGCTGATCTACTTCGCCAAGACACTGA CCGACGGCGTGCCCTCTAGATTCAGCGGATCTG GCTCTGGCACCGACTTCACCCTGACAATCTCTA GCCTGCAGCCTGAGGACTTCGCCACCTACTACT GCCAGCACCACTACGGCACACCTTGGACATTCG GCCAGGGCACCAAGGTGGAAATCAAG	34
Anti-TSLP VH (TSLP/IL-13 BsAb)	CAGGTTCAGCTGGTTCAGTCTGGCGCCGAAGTG AAGAAACCTGGCAGCAGCGTGAAGGTGTCCTG CAAGGCTAGCGGCTACACATTCACCGACTACTG GATGCACTGGGTCCGAGAGGCTCCAGGACAGG GACTTGAGTGGATGGGCATCATCGACCCCAGCG ACAGCGACACAAGCCTGAACCAGAAATTCCAG GGCAGAGTGACCATCACCGCCGACACCTCTACA AGCACCGCCTACATGGAACTGAGCAGCCTGAG AAGCGAGGACACCGCCGTGTACTACTGTGCCAG ATCTCTGGACGGCTACTACGATTACTGGGGCCA GGGAACCCTGGTCACCGTTTCTTCT	29
Anti-IL-13 Heavy Chain (TSLP/IL-13 BsAb)	CAGGTTCAGCTGCAAGAGTCTGGACCTGGCCTG GTCAAGCCTAGCGAGACACTGAGCCTGACCTGT ACCGTGTCTGGCTTCAGCCTGAGCGCCTACAGC GTGAACTGGATCAGAAAGCCTCCTGGCAAAGG CCTGGAATGGATCGGAATGATCTGGGGCGACG GCAAGATCGTGTACAACAGCGCCCTGAAGTCCA GAGTGACCATCAGCAAGGACACCAGCAAGAAC CAGGTGAGCCTGAAGCTGAGCAGCGTGACAGC CGCTGATACCGCCGTGTACTATTGTGCTGGCGA	43

Description of Sequences	Nucleotide Sequences	SEQ ID NO:
	CGGCTACTACCCCTACGCCATGGATAATTGGGG CCAGGGCACACTGGTCACCGTGTCATCTGCTAG CACCAAGGGCCCATCCGTCTTCCCCCTGGCACC CTCCTCCAAGAGCACCTCTGGGGGCACAGCGGC CCTGGGCTGCCTGGTCGAAGATTACTTCCCCGA ACCGGTGACGGTGTCGTGGAACTCAGGCGCCCT GACCAGCGGCGTGCACACCTTCCCGGCTGTCCT ACAGTCCTCAGGACTCTACTCCCTCAGCAGCGT GGTGACCGTGCCCTCCAGCAGCTTGGGCACCCA GACCTACATCTGCAACGTGAATCACAAGCCCAG CAACACCAAGGTGGACGAGAGAGTTGAGCCCA AATCTTGTGACAAAACTCACACATGCCCACCGT GCCCAGCACCTGAACTCCTGGGGGGACCGTCAG TCTTCCTCTTCCCCCCAAAACCCAAGGACACCC TCATGATCTCCCGGACCCCTGAGGTCACATGCG TGGTGGTGGACGTGAGCCACGAAGACCCTGAG GTCAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCATAATGCCAAGACAAAGCCGCGGGAGGA GCAGTACAACAGCACGTACCGTGTGGTCAGCGT CCTCACCGTCCTGCACCAGGACTGGCTGAATGG CAAGGAGTACAAGTGCAAGGTCTCCAACAAAG CCCTCCCAGCCCCCATCGAGAAAACCATCTCCA AAGCCAAAGGGCAGCCCCGAGAACCACAGGTG TGCACCCTGCCCCCATCCCGGGAGGAGATGACC AAGAACCAGGTCAGCCTGTCGTGCGCAGTCAA AGGCTTCTATCCCAGCGACATCGCCGTGGAGTG GGAGAGCAATGGGCAGCCGGAGAACAACTACA AGACCACGCCTCCCGTGCTGGACTCCGACGGCT CCTTCTTCCTCGTGAGCAAGCTCACCGTGGACA AGAGCAGGTGGCAGCAGGGGAACGTCTTCTCA TGCTCCGTGCTGCATGAGGCTCTGCACGCCCAC TACACGCAGAAGTCCCTCTCCCTGTCTCCGGGT AAA	
Anti-IL-13 Light Chain (TSLP/IL-13 BsAb)	GACATCCAGATGACACAGAGCCCTAGCAGCCT GTCTGCCAGCGTGGGAGACAGAGTGACCATCA CCTGTAGAGCCAGCAAGAGCGTGGACAGCTAC GGCAACAGCTTCATGCACTGGTATCAGGAGAA GCCCGGCAAGGCCCCTAAGCTGCTGATCTACCT GGCCAGCAACCTGGAAAGCGGCGTGCCATCTA GATTCAGCGGCTCTGGCTCTGGCACCGACTTCA CCCTGACAATCTCTAGCCTGCAGCCTGAGGACT TCGCCACCTACTACTGCCAGCAGAACAACGAGG ACCCCAGAACATTCGGCCAGGGCACCAAGCTG GAAATCAAGCGAACTGTGGCTGCACCATCTGTC TTCATCTTCCCGCCATCTGATAAACAGTTGAAA TCTGGAAAAGCCTCTGTTGTGTGCCTGCTGAAT	45

Description of Sequences	Nucleotide Sequences	SEQ ID NO:
	AACTTCTATCCCAGAGAGGCCAAAGTACAGTGG AAGGTGGATAACGCCCTCCAATCGGGTAACTCC CAGGAGAGTGTCACAGAGCAGGACAGCAAGGA CAGCACCTACAGCCTCAGCAGCACCCTGACGCT GAGCAAAGCAGACTACGAGAAACACAAAGTCT ACGCCTGCGAAGTCACCCATCAGGGCCTGAGCT CGCCCGTCACAAAGAGCTTCAACAGGGGAGAG TGT	
Anti-TSLP Heavy Chain (TSLP/IL-13 BsAb)	CAGGTTCAGCTGGTTCAGTCTGGCGCCGAAGTG AAGAAACCTGGCAGCAGCGTGAAGGTGTCCTG CAAGGCTAGCGGCTACACATTCACCGACTACTG GATGCACTGGGTCCGAGAGGCTCCAGGACAGG GACTTGAGTGGATGGGCATCATCGACCCCAGCG ACAGCGACACAAGCCTGAACCAGAAATTCCAG GGCAGAGTGACCATCACCGCCGACACCTCTACA AGCACCGCCTACATGGAACTGAGCAGCCTGAG AAGCGAGGACACCGCCGTGTACTACTGTGCCAG ATCTCTGGACGGCTACTACGATTACTGGGGCCA GGGAACCCTGGTCACCGTTTCTTCTGCTAGCAC CAAGGGCCCATCCGTCTTCCCCCTGGCACCCTC CTCCAAGAGCACCTCTGGGGGCACAGCGGCCCT GGGCTGCCTGGTCAAGGACTACTTCCCCGAACC GGTGACGGTGTCGTGGAACTCAGGCGCCCTGAC CAGCGGCGTGCACACCTTCCCGGCTGTCCTACA GTCCTCAGGACTCTACTCCCTCAGCAGCGTGGT GACCGTGCCCTCCAGCAGCTTGGGCACCCAGAC CTACATCTGCAACGTGAATCACAAGCCCAGCAA CACCAAGGTGGACAAGAGAGTTGAGCCCAAAT CTTGTGACAAAACTCACACATGCCCACCGTGCC CAGCACCTGAACTCCTGGGGGGACCGTCAGTCT TCCTCTTCCCCCCAAAACCCAAGGACACCCTCA TGATCTCCCGGACCCCTGAGGTCACATGCGTGG TGGTGGACGTGAGCCACGAAGACCCTGAGGTC AAGTTCAACTGGTACGTGGACGGCGTGGAGGT GCATAATGCCAAGACAAAGCCGCGGGAGGAGC AGTACAACAGCACGTACCGTGTGGTCAGCGTCC TCACCGTCCTGCACCAGGACTGGCTGAATGGCA AGGAGTACAAGTGCAAGGTCTCCAACAAAGCC CTCCCAGCCCCCATCGAGAAAACCATCTCCAAA GCCAAAGGGCAGCCCCGAGAACCACAGGTGTA CACCCTGCCCCCATGCCGGGAGGAGATGACCA AGAACCAGGTCAGCCTGTGGTGCCTGGTCAAAG GCTTCTATCCCAGCGACATCGCCGTGGAGTGGG AGAGCAATGGGCAGCCGGAGAACAACTACAAG ACCACGCCTCCCGTGCTGGACTCCGACGGCTCC TTCTTCCTCTATAGCAAGCTCACCGTGGACAAG	39

Description of Sequences	Nucleotide Sequences	SEQ ID NO:
	AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGC TCCGTGCTGCATGAGGCTCTGCACGCCCACTAC ACGCAGAAGTCCCTCTCCCTGTCTCCGGGTAAA	
Anti-TSLP Light Chain (TSLP/IL-13 BsAb)	GACATCCAGATGACACAGAGCCCTAGCAGCCT GTCTGCCAGCGTGGGAGACAGAGTGACCATCA CCTGTAGAACCAGCGAGAACATCTACAGCTACC TGGCCTGGTATCAGAAGAAGCCTGGCAAGGCTC CCAAGCTGCTGATCTACTTCGCCAAGACACTGA CCGACGGCGTGCCCTCTAGATTCAGCGGATCTG GCTCTGGCACCGACTTCACCCTGACAATCTCTA GCCTGCAGCCTGAGGACTTCGCCACCTACTACT GCCAGCACCACTACGGCACACCTTGGACATTCG GCCAGGGCACCAAGGTGGAAATCAAGGGACAG CCCAAGGCGGCGCCCTCGGTCACTCTGTTCCCG CCCTCCTCTGAGGAGCTTCAAGCCAACGAGGCC ACACTGGTGTGTCTCATAAGTGACTTCTATCCG GGAGCCGTGACAGTGGCCTGGAAGGCAGATAG CAGCCCCGTCAAGGCGGGAGTGGAGACCACCA CACCCTCCAAACAAAGCAACAACAAGTACGCG GCCAGCAGCTACCTGAGCCTGACGCCTGAGCAG TGGAAGTCCCACAGAAGCTACAGCTGCCAGGTC ACGCATGAAGGGAGCACCGTGGAGAAGACAGT GGCCCCTACAGAATGTTCA	41

TSLP= Thymic Stromal Lymphopoietin
IL-13= interleukin 13
CDR= Complementarity Determining Region
VH=Heavy Chain Variable Region
VL= Light Chain Variable Region
HC=Heavy Chain
LC=Light Chain

[00367] Although preferred embodiments of the present invention have been shown and described herein, it will be apparent to those skilled in the art that these embodiments are provided as examples only. Many variants, variations and substitutions will occur to those skilled in the art without departing from the present invention. It should be understood that various alternatives to the embodiments described herein may be employed. The following claims are intended to define the scope of the present invention and cover methods and structures and their equivalents within the scope of these claims.

CLAIMS

WHAT IS CLAIMED IS:

1. An antibody or an antigen-binding fragment thereof, comprising a first antigen-binding region that binds to interleukin 13 (IL-13) and a second antigen-binding region that binds to thymic stromal lymphopoietin (TSLP), wherein the first antigen-binding region comprises a first heavy chain variable region (VH1) and a first light chain variable region (VL1) and the second antigen-binding region comprises a second heavy chain variable region (VH2) and a second light chain variable region (VL2), wherein:

(a) VH1 comprises:

(i) complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 24;

(ii) CDR2 comprising the amino acid sequence of SEQ ID NO: 25 or 26; and

(iii) CDR3 comprising the amino acid sequence of SEQ ID NO: 27;

(b) VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively;

(c) VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively; and

(d) VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein:

(a) VH1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 24, 25, and 27, respectively;

(b) VL1 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 21, 22, and 23, respectively;

(c) VH2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 30, 31, and 32, respectively; and

(d) VL2 comprises CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NOs: 35, 36, and 37, respectively.

3. The antibody or antigen-binding fragment thereof of claim 1 or 2, wherein:

(a) VH1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52;

(b) VL1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53;

(c) VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28 or 50; or

(d) VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33 or 51.

4. The antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein:

(a) VH1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52;

(b) VL1 comprises an amino acid sequence with at least 90% sequence identity to any one of SEQ ID NOs: 1, 3, 46, and 53;

(c) VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28 or 50; and

(d) VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33 or 51.

5. The antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein:

(a) VH1 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52;

(b) VL1 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 46, and 53;

(c) VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28 or 50; or

(d) VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33 or 51.

6. The antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein:

(a) VH1 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 5, 7, 9, 11, 13, 15, 17, 19, 48, and 52;

(b) VL1 comprises an amino acid sequence as set forth in any one of SEQ ID NOs: 1, 3, 46, and 53;

(c) VH2 comprises an amino acid sequence as set forth in SEQ ID NO: 28 or 50; and

(d) VL2 comprises an amino acid sequence as set forth in SEQ ID NO: 33 or 51.

7. The antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein:

(a) VH1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 52;

(b) VL1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 53;

(c) VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28; or

(d) VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33.

8. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 7, wherein:

(a) VH1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 52;

(b) VL1 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 53;

(c) VH2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 28; and

(d) VL2 comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 33.

9. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 7-8, wherein:

(a) VH1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 52;

(b) VL1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 53;

(c) VH2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 28; or

(d) VL2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 33.

10. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 7-9, wherein:

(a) VH1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 52;

(b) VL1 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 53;

(c) VH2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 28; and

(d) VL2 comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 33.

11. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 7-10, wherein:

(a) VH1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 52;

(b) VL1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 53;

(c) VH2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 28; or

(d) VL2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 33.

12. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 7-11, wherein:

(a) VH1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 52;

(b) VL1 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 53;

(c) VH2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 28; and

(d) VL2 comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 33.

13. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 7-12, wherein:

(a) VH1 comprises the amino acid sequence of SEQ ID NO: 52;

(b) VL1 comprises the amino acid sequence of SEQ ID NO: 53;

(c) VH2 comprises the amino acid sequence of SEQ ID NO: 28; or

(d) VL2 comprises the amino acid sequence of SEQ ID NO: 33.

14. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 7-13, wherein:

(a) VH1 comprises the amino acid sequence of SEQ ID NO: 52;

(b) VL1 comprises the amino acid sequence of SEQ ID NO: 53;

(c) VH2 comprises the amino acid sequence of SEQ ID NO: 28; and

(d) VL2 comprises the amino acid sequence of SEQ ID NO: 33.

15. The antibody or antigen-binding fragment thereof of any one of claims 1-14, wherein VH1, VL1, VH2, or VL2 comprises a charge pair mutation comprising a substitution of:

(a) an amino acid residue of positive charge with an amino acid residue of negative charge;

(b) an amino acid residue of negative charge with an amino acid residue of positive charge;

(c) a neutral amino acid residue with an amino acid residue of positive charge; or

(d) a neutral amino acid residue with an amino acid residue of negative charge,

wherein the charge pair mutation increases the association between VH1 and VL1 or the association between VH2 and VL2.

16. The antibody or antigen-binding fragment thereof of claim 15, wherein the charge pair mutation of VH1, VL1, VH2, or VL2 comprises:

(a) a substitution of glutamine (Q) with glutamic acid (E); or

(b) a substitution of glutamine (Q) with lysine (K).

17. The antibody or antigen-binding fragment thereof of claim 15 or 16, wherein:

(a) the charge pair mutation of VH1 or VH2 comprises a substitution of glutamine (Q) with glutamic acid (E) at amino acid residue 39 according to the Kabat numbering scheme (Q39E);

(b) the charge pair mutation of VH1 or VH2 comprises a substitution of glutamine (Q) with lysine (K) at amino acid residue 39 according to the Kabat numbering scheme (Q39K);

(c) the charge pair mutation of VL1 or VL2 comprises a substitution of glutamine (Q) with lysine (K) at amino acid residue 38 according to the Kabat numbering scheme (Q38K); or

(d) the charge pair mutation of VL1 or VL2 comprises a substitution of glutamine (Q) with glutamic acid (E) at amino acid residue 38 according to the Kabat numbering scheme (Q38E).

18. The antibody or antigen-binding fragment thereof of claim 17, wherein:

(a) the charge pair mutation of VH1 comprises Q39E; and

(b) the charge pair mutation of VL1 comprises Q38K.

19. The antibody or antigen-binding fragment thereof of claim 17, wherein:

(a) the charge pair mutation of VH1 comprises Q39K; and

(b) the charge pair mutation of VL1 comprises Q38E.

20. The antibody or antigen-binding fragment thereof of claim 17 or 19, wherein:

(a) the charge pair mutation of VH2 comprises Q39E; and

(b) the charge pair mutation of VL2 comprises Q38K.

21. The antibody or antigen-binding fragment thereof of claim 17 or 18, wherein:

(a) the charge pair mutation of VH2 comprises Q39K; and

(b) the charge pair mutation of VL2 comprises Q38E.

22. The antibody or antigen-binding fragment thereof of any one of claims 17, 19, and 20, wherein:

(a) the charge pair mutation of VH1 comprises Q39K;

(b) the charge pair mutation of VL1 comprises Q38E;

(c) the charge pair mutation of VH2 comprises Q39E; and

(d) the charge pair mutation of VL2 comprises Q38K.

23. The antibody or antigen-binding fragment thereof of any one of claims 17, 18, and 21, wherein:

(a) the charge pair mutation of VH1 comprises Q39E;

(b) the charge pair mutation of VL1 comprises Q38K;

(c) the charge pair mutation of VH2 comprises Q39K; and

(d) the charge pair mutation of VL2 comprises Q38E.

24. The antibody or antigen-binding fragment thereof of any one of claims 1-23, further comprising a first heavy chain comprising VH1 and a constant region comprising CH1 domain, CH2 domain, or CH3 domain, a first light chain comprising VL1 and constant (CL) domain, a second heavy chain comprising VH2 and a constant region comprising CH1 domain, CH2 domain, or CH3 domain, or a second light chain comprising VL2 and CL domain.

25. The antibody or antigen-binding fragment thereof of claims 24, further comprising the first heavy chain comprising VH1 and a constant region comprising CH1 domain, CH2 domain, and CH3 domain, the first light chain comprising VL1 and CL domain, the second heavy chain comprising VH2 and a constant region comprising CH1 domain, CH2 domain, and CH3 domain, and a second light chain comprising VL2 and CL domain.

26. The antibody or antigen-binding fragment thereof of claim 24 or 25, wherein:

(a) the CH1 domain of the first heavy chain or the CL domain of the first light chain comprises a second charge pair mutation that increases the association between the first heavy chain and the first light chain; or

(b) the CH1 domain of the second heavy chain or the CL domain of the second light chain comprises the second charge pair mutation that increases the association between the second heavy chain and the second light chain.

27. The antibody or antigen-binding fragment thereof of claim 26, wherein the second charge pair mutation comprises a substitution of:

(a) an amino acid residue of positive charge with an amino acid residue of negative charge;

(b) an amino acid residue of negative charge with an amino acid residue of positive charge;

(c) a neutral amino acid residue with an amino acid residue of positive charge; or

(d) a neutral amino acid residue with an amino acid residue of negative charge.

28. The antibody or antigen-binding fragment thereof of claim 26 or 27, wherein the second charge pair mutation comprises a substitution of lysine (K) with glutamic acid (E).

29. The antibody or antigen-binding fragment thereof of claim 28, wherein the CH1 domain of the first heavy chain or the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising:

(a) a substitution of lysine (K) with glutamic acid (E) at amino acid residue 147 according to the EU numbering (K147E); or

(b) a substitution of lysine (K) with glutamic acid (E) at amino acid residue 213 according to the EU numbering (K213E).

30. The antibody or antigen-binding fragment thereof of claim 29, wherein the CH1 domain of the first heavy chain comprises the second charge pair mutation comprising K147E and K213E.

31. The antibody or antigen-binding fragment thereof of claim 29, wherein the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising K147E and K213E.

32. The antibody or antigen-binding fragment thereof of any one of claims 29-31, wherein the CH1 domain of the first heavy chain comprises the second charge pair mutation comprising K147E and K213E and the CH1 domain of the second heavy chain comprises the second charge pair mutation comprising K147E and K213E.

33. The antibody or antigen-binding fragment thereof of any one of claims 1-32, further comprising a fragment antigen-binding (Fab) region, a Fab', a $F(ab')_2$, or a single chain variable fragment (scFv).

34. The antibody or antigen-binding fragment thereof of any one of claims 1-33, further comprising a fragment crystallizable (Fc) region.

35. The antibody or antigen-binding fragment thereof of claims 1-34, further comprising an immunoglobulin (Ig) G, IgA, IgM, IgE, or IgD.

36. The antibody or antigen-binding fragment thereof of claim 35, further comprising an IgG1, IgG2, IgG3, or IgG4.

37. The antibody or antigen-binding fragment thereof of claim 36, further comprising an IgG1.

38. The antibody or antigen-binding fragment thereof of any one of claims 34-37, wherein the Fc region comprises a knob-into-hole mutation.

39. The antibody or antigen-binding fragment thereof of claim 38, wherein the knob-into-hole mutation comprises:

(a) a substitution of tyrosine (Y) with cysteine (C) at amino acid residue 349 according to the EU numbering (Y349C);

(b) a substitution of serine (S) with cysteine (C) at amino acid residue 354 according to the EU numbering (S354C);

(c) a substitution of threonine (T) with tryptophan (W) at amino acid residue 366 according to the EU numbering (T366W);

(d) a substitution of threonine (T) with serine (S) at amino acid residue 366 according to the EU numbering (T366S);

(e) a substitution of threonine (T) with tyrosine (Y) at amino acid residue 366 according to the EU numbering (T366Y);

(f) a substitution of leucine (L) with alanine (A) at amino acid residue 368 according to the EU numbering (L368A);

(g) a substitution of phenylalanine (F) with alanine (A) at amino acid residue 405 according to the EU numbering (F405A);

(h) a substitution of phenylalanine (F) with tryptophan (W) at amino acid residue 405 according to the EU numbering (F405W);

(i) a substitution of tyrosine (Y) with alanine (A) at amino acid residue 407 according to the EU numbering with (Y407A);

(j) a substitution of tyrosine (Y) with threonine (T) at amino acid residue 407 according to the EU numbering with (Y407T); or

(k) a substitution of tyrosine (Y) with valine (V) at amino acid residue 407 according to the EU numbering with (Y407V).

40. The antibody or antigen-binding fragment thereof of claim 39, wherein:

(a) the Fc region of the first heavy chain comprises the knob-into-hole mutation comprising T366S, L368A, and Y407V; and

(b) the Fc region of the second heavy chain comprises the knob-into-hole mutation comprising T366W.

41. The antibody or antigen-binding fragment thereof of claim 39 or 40, wherein:

(a) the Fc region of the first heavy chain comprises the knob-into-hole mutation comprising Y349C, T366S, L368A, and Y407V; and

(b) the Fc region of the second heavy chain comprises the knob-into-hole mutation comprising S354C and T366W.

42. The antibody or antigen-binding fragment thereof of any one of claims 34-41, wherein the Fc region comprises a second amino acid mutation that increases the half-life of the antibody or antigen-binding fragment thereof.

43. The antibody or antigen-binding fragment thereof of claim 42, wherein the second amino acid mutation increases the binding of the antibody or antigen-binding fragment thereof to neonatal Fc receptor (FcRn).

44. The antibody or antigen-binding fragment thereof of any one of claims 34-43, wherein the Fc region comprises a third amino acid mutation that reduces the binding affinity of the antibody or antigen-binding fragment thereof to Fc-gamma receptor (FcγR) or complement component 1q (C1q).

45. The antibody or antigen-binding fragment thereof of any one of claims 42- 44, wherein the second amino acid mutation comprises:

(a) a substitution of methionine (M) with leucine (L) at amino acid residue 428 according to the EU numbering (M428L); or

(b) a substitution of asparagine (N) with alanine (A) at amino acid residue 434 according to the EU numbering (N434A).

46. The antibody or antigen-binding fragment thereof of claim 45, wherein the second amino acid mutation comprises M428L and N434A.

47. The antibody or antigen-binding fragment thereof of claim 45 or 46, wherein:

(a) the Fc region of the first heavy chain comprises the second amino acid mutation comprising M428L or N434A; and

(b) the Fc region of the second heavy chain comprises the second amino acid mutation comprising M428L or N434A.

48. The antibody or antigen-binding fragment thereof of any one of claims 45-47, wherein:

(a) the Fc region of the first heavy chain comprises the second amino acid mutation comprising M428L and N434A; and

(b) the Fc region of the second heavy chain comprises the second amino acid mutation comprising M428L and N434A.

49. The antibody or antigen-binding fragment thereof of any one of claims 24-48, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 42;

(b) the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 44;

(c) the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 38; or

(d) the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 40.

50. The antibody or antigen-binding fragment thereof of any one of claims 24-48, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 42;

(b) the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 44;

(c) the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 38; and

(d) the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 40.

51. The antibody or antigen-binding fragment thereof of any one of claims 24-48, wherein :

(a) the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 42;

(b) the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 44;

(c) the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 38; or

(d) the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 40.

52. The antibody or antigen-binding fragment thereof of any one of claims 24-48, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 42;

(b) the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 44;

(c) the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 38; and

(d) the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 40.

53. The antibody or antigen-binding fragment thereof of any one of claims 24-48, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 42;

(b) the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 44;

(c) the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 38; or

(d) the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 40.

54. The antibody or antigen-binding fragment thereof of any one of claims 24-48, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 42;

(b) the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 44;

(c) the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 38; and

(d) the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 40.

55. The antibody or antigen-binding fragment thereof of any one of claims 24-48, wherein:

(a) the first heavy chain comprises the amino acid sequence of SEQ ID NO: 42;

(b) the first light chain comprises the amino acid sequence of SEQ ID NO: 44;

(c) the second heavy chain comprises the amino acid sequence of SEQ ID NO: 38; or

(d) the second light chain comprises the amino acid sequence of SEQ ID NO: 40.

56. The antibody or antigen-binding fragment thereof of any one of claims 24-48, wherein:

(a) the first heavy chain comprises the amino acid sequence of SEQ ID NO: 42;

(b) the first light chain comprises the amino acid sequence of SEQ ID NO: 44;

(c) the second heavy chain comprises the amino acid sequence of SEQ ID NO: 38; and

(d) the second light chain comprises the amino acid sequence of SEQ ID NO: 40.

57. The antibody or antigen-binding fragment thereof of any one of claims 24-44, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 60;

(b) the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 61;

(c) the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 66; or

(d) the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 67.

58. The antibody or antigen-binding fragment thereof of any one of claims 24-44, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 60;

(b) the first light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 61;

(c) the second heavy chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 66; and

(d) the second light chain comprises an amino acid sequence with at least 90% sequence identity to SEQ ID NO: 67.

59. The antibody or antigen-binding fragment thereof of any one of claims 24-44, wherein :

(a) the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 60;

(b) the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 61;

(c) the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 66; or

(d) the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 67.

60. The antibody or antigen-binding fragment thereof of any one of claims 24-44, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 60;

(b) the first light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 61;

(c) the second heavy chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 66; and

(d) the second light chain comprises an amino acid sequence with at least 95% sequence identity to SEQ ID NO: 67.

61. The antibody or antigen-binding fragment thereof of any one of claims 24-44, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 60;

(b) the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 61;

(c) the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 66; or

(d) the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 67.

62. The antibody or antigen-binding fragment thereof of any one of claims 24-44, wherein:

(a) the first heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 60;

(b) the first light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 61;

(c) the second heavy chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 66; and

(d) the second light chain comprises an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 67.

63. The antibody or antigen-binding fragment thereof of any one of claims 24-44, wherein:

(a) the first heavy chain comprises the amino acid sequence of SEQ ID NO: 60;

(b) the first light chain comprises the amino acid sequence of SEQ ID NO: 61;

(c) the second heavy chain comprises the amino acid sequence of SEQ ID NO: 66; or

(d) the second light chain comprises the amino acid sequence of SEQ ID NO: 67.

64. The antibody or antigen-binding fragment thereof of any one of claims 24-44, wherein:

(a) the first heavy chain comprises the amino acid sequence of SEQ ID NO: 60;

(b) the first light chain comprises the amino acid sequence of SEQ ID NO: 61;

(c) the second heavy chain comprises the amino acid sequence of SEQ ID NO: 66; and

(d) the second light chain comprises the amino acid sequence of SEQ ID NO: 67.

65. The antibody or antigen-binding fragment thereof of any one of claims 1-64, wherein the antibody or antigen-binding fragment thereof comprises a multispecific antibody or antigen binding fragment thereof.

66. The antibody or antigen-binding fragment thereof of claim 65, wherein the multispecific antibody or antigen-binding fragment thereof comprises a bispecific antibody or antigen binding fragment thereof.

67. The antibody or antigen-binding fragment thereof of any one of claims 1-66, wherein the antibody or antigen-binding fragment thereof has a technical advantage, technical effect, and/or a technical improvement compared with a second antibody or an antigen-binding fragment thereof that binds to IL-13, TSLP, or IL-13 and TSLP.

68. The antibody or antigen-binding fragment thereof of claim 67, wherein the second antibody that binds to IL-13, TSLP, or IL-13 and TSLP comprises Lunsekimig or an analog thereof, Lebrikizumab or an analog thereof, or Tezepelumab or an analog thereof.

69. The antibody or antigen-binding fragment thereof of claim 67 or 68, wherein the technical advantage, technical effect, and/or technical improvement includes or relates to therapeutic activity, stability, immunogenicity, affinity, toxicity, potency, specificity, pharmacokinetics, pharmacodynamics, or a property not exhibited by the second antibody or antigen-binding fragment thereof that binds to IL-13, TSLP, or IL-13 and TSLP.

70. The antibody or antigen-binding fragment thereof of any one of claims 67-69, wherein the technical advantage, technical effect, and/or a technical improvement includes or relates to a binding affinity to IL-13, TSLP, or IL-13 and TSLP, an ability to inhibit IL-13-mediated biological activity, an ability to inhibit TSLP-mediated biological activity, or an ability to inhibit a biological activity mediated by IL-13 and TSLP.

71. The antibody or antigen-binding fragment thereof of any one of claims 67-70, wherein the technical advantage, technical effect, and/or technical improvement includes or relates to a reduced immunogenicity, an increased stability, an increased binding affinity to IL-13, TSLP, or IL-13 and TSLP, an increased ability to inhibit IL-13-mediated activation of STAT6, an increased ability to inhibit IL-13-mediated cell proliferation, an increased ability to inhibit TSLP-mediated thymus and activation regulated chemokine (TARC) release, an increased ability to inhibit TSLP-mediated cell

proliferation, an increased ability to inhibit TSLP-mediated activation of STAT5, an increased ability to inhibit IgE production, an increased ability to inhibit an inflammatory or allergic response, a reduced dosing frequency, an increased ability to inhibit cytokine production, a better therapeutic effect on an allergic or inflammatory disease, an increased serum half-life, an increased thermostability, an increased binding affinity to a neonatal Fc receptor (FcRn), a reduced binding affinity to a Fc-gamma receptor (FcγR), or a reduced binding affinity to complement component 1q (C1q).

72. A nucleic acid molecule encoding the antibody or antigen-binding fragment thereof of any one of claims 1-71.

73. The nucleic acid molecule of claim 72, comprising:

(a) a first nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 29;

(b) a second nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 34;

(c) a third nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 55; or

(d) a fourth nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 56.

74. The nucleic acid molecule of claim 73, comprising:

(a) the first nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 29;

(b) the second nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 34;

(c) the third nucleic acid sequence with at least 90% sequence identity SEQ ID NO: 55; and

(d) the fourth nucleic acid sequence with at least 90% sequence identity to SEQ ID NO: 56.

75. The nucleic acid molecule of claim 73, comprising:

(a) the first nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 29;

(b) the second nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 34;

(c) the third nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 55; or

(d) the fourth nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 56.

76. The nucleic acid molecule of claim 73, comprising:

(a) the first nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 29;

(b) the second nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 34;

(c) the third nucleic acid sequence with at least 95% sequence identity SEQ ID NO: 55; and

(d) the fourth nucleic acid sequence with at least 95% sequence identity to SEQ ID NO: 56.

77. The nucleic acid molecule of claim 73, comprising:

(a) the first nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 29;

(b) the second nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 34;

(c) the third nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 55; or

(d) the fourth nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 56.

78. The nucleic acid molecule of claim 73, comprising:

(a) the first nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 29;

(b) the second nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 34;

(c) the third nucleic acid sequence with at least 99% sequence identity SEQ ID NO: 55; and

(d) the fourth nucleic acid sequence with at least 99% sequence identity to SEQ ID NO: 56.

79. The nucleic acid molecule of claim 73, comprising:

(a) the first nucleic acid sequence set forth in SEQ ID NO: 29;

(b) the second nucleic acid sequence set forth in SEQ ID NO: 34;

(c) the third nucleic acid sequence set forth in SEQ ID NO: 55; or

(d) the fourth nucleic acid sequence set forth in SEQ ID NO: 56.

80. The nucleic acid molecule of claim 73, comprising:

(a) the first nucleic acid sequence set forth in SEQ ID NO: 29;

(b) the second nucleic acid sequence set forth in SEQ ID NO: 34;

(c) the third nucleic acid sequence set forth in SEQ ID NO: 55; and

(d) the fourth nucleic acid sequence set forth in SEQ ID NO: 56.

81. The nucleic acid molecule of any one of claims 72-80, comprising:

(a) a first nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 39;

(b) a second nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 41;

(c) a third nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 43; or

(d) a fourth nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 45.

82. The nucleic acid molecule of claim 81, comprising:

(a) the first nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 39;

(b) the second nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 41;

(c) the third nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 43; and

(d) the fourth nucleotide sequence with at least 90% sequence identity to SEQ ID NO: 45.

83. The nucleic acid molecule of claim 81, comprising:

(a) the first nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 39;

(b) the second nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 41;

(c) the third nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 43; or

(d) the fourth nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 45.

84. The nucleic acid molecule of claim 81, comprising:

(a) the first nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 39;

(b) the second nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 41;

(c) the third nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 43; and

(d) the fourth nucleotide sequence with at least 95% sequence identity to SEQ ID NO: 45.

85. The nucleic acid molecule of claim 81, comprising:

(a) the first nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 39;

(b) the second nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 41;

(c) the third nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 43; or

(d) the fourth nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 45.

86. The nucleic acid molecule of claim 81, comprising:

(a) the first nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 39;

(b) the second nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 41;

(c) the third nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 43; and

(d) the fourth nucleotide sequence with at least 99% sequence identity to SEQ ID NO: 45.

87. The nucleic acid molecule of claim 81, comprising:

(a) the first nucleotide sequence set forth in SEQ ID NO: 39;

(b) the second nucleotide sequence set forth in SEQ ID NO: 41;

(c) the third nucleotide sequence set forth in SEQ ID NO: 43; or

(d) the fourth nucleotide sequence set forth in SEQ ID NO: 45.

88. The nucleic acid molecule of claim 81, comprising:

(a) the first nucleotide sequence set forth in SEQ ID NO: 39;

(b) the second nucleotide sequence set forth in SEQ ID NO: 41;

(c) the third nucleotide sequence set forth in SEQ ID NO: 43; and

(d) the fourth nucleotide sequence set forth in SEQ ID NO: 45.

89. A vector comprising the nucleic acid molecule of any one of claims 72-88.

90. A host cell comprising the nucleic acid molecule of any one of claims 72-88 or the vector of claim 89.

91. A pharmaceutical composition comprising (i) the antibody or antigen-binding fragment thereof of any one of claims 1-71; and (ii) a pharmaceutically acceptable carrier or excipient.

92. The pharmaceutical composition of claim 91, further comprising a second therapeutic agent.

93. The pharmaceutical composition of claim 92, wherein the second therapeutic agent is selected from the group comprising an antibody, a chemotherapeutic agent, and a small molecule drug.

94. A conjugate comprising the antibody or antigen-binding fragment thereof of any one of claims 1-71, and a chemical moiety conjugated thereto.

95. The conjugate of claim 94, wherein the chemical moiety is selected from a group comprising a therapeutic agent, a detectable moiety, and an immunostimulatory molecule.

96. A method for treating a disease in a subject, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof of any one of claims 1-71, the pharmaceutical composition of any one of claims 91-93, or the conjugate of claim 94 or 95.

97. The method of claim 96, wherein the disease comprises an inflammatory disease, an autoimmune disease, or an allergic disease.

98. The method of claim 96 or 97, wherein the disease comprises a type 2 inflammatory response-related disease.

99. The method of any one of claims 96-98, wherein the disease comprises an IL-13 mediated disease, a TSLP mediated disease, or both.

100. The method of any one of claims 96-99, wherein the disease is selected from the group comprising atopic dermatitis, allergic inflammation, asthma, urticaria, chronic obstructive pulmonary disease, eosinophilic esophagitis, rheumatoid arthritis, multiple sclerosis, idiopathic pulmonary fibrosis, eczema, eosinophilic gastroenteritis, Crohn's disease, systemic sclerosis, ulcerative colitis, and chronic rhinosinusitis with nasal polyps.

101. The method of any one of claims 96-100, wherein the disease is selected from the group comprising allergic rhinitis, allergic sinusitis, allergic conjunctivitis, hand eczema, and asthmatic eczema.

102. The method of any one of claims 96-101, further comprising administering a second therapeutic agent to the subject.

103. The method of claim 102, wherein the second therapeutic agent is selected from a group comprising an antibody, a chemotherapeutic agent, and a small molecule drug.

104. A method for inhibiting or eliminating IgE in a subject, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof of any one of claims 1-71, the pharmaceutical composition of any one of claims 91-93, or the conjugate of claim 94 or 95.

105. The method of any one of claims 96-104, wherein the subject is human.