

What is claimed is:

1. Use of a therapeutically effective amount of an IL-4/IL-13 pathway inhibitor and a plasma cell ablating agent in the manufacture of a medicament for reducing or eliminating allergen-specific serum IgE in a subject having an allergic disease or disorder, a mast cell activation disorder or mastocytosis;

wherein the IL-4/IL-13 pathway inhibitor is an anti-IL-4R antibody or antigen-binding fragment thereof or an anti-IL-4/IL-13 bispecific antibody or antigen-binding fragment thereof; and

wherein the plasma cell ablating agent is an anti-BCMA/anti-CD3 bispecific antibody or antigen-binding fragment thereof comprising (a) a first antigen-binding domain that specifically binds to BCMA; and (b) a second antigen-binding domain that specifically binds CD3.

2. ~~The~~ Use of a therapeutically effective amount of an IL-4/IL-13 pathway inhibitor and a plasma cell ablating agent in the manufacture of a medicament for treating allergy or preventing or reducing the severity of an allergic reaction to an allergen in a subject having an allergic disease or disorder, a mast cell activation disorder, or mastocytosis;

wherein the IL-4/IL-13 pathway inhibitor is an anti-IL-4R antibody or antigen-binding fragment thereof or an anti-IL-4/IL-13 bispecific antibody or antigen-binding fragment thereof; and

wherein the plasma cell ablating agent is an anti-BCMA/anti-CD3 bispecific antibody or antigen-binding fragment thereof comprising (a) a first antigen-binding domain that specifically binds to BCMA; and (b) a second antigen-binding domain that specifically binds CD3.

3. ~~The~~ Use of a plasma cell ablating agent in the manufacture of a medicament for treating allergy or preventing or reducing the severity of an allergic reaction to an allergen in a subject having an allergic disease or disorder, a mast cell activation disorder, or mastocytosis, wherein the subject is on a background therapy regimen comprising one or more doses of an IL-4/IL-13 pathway inhibitor; wherein the IL-4/IL-13 pathway inhibitor is an anti-IL-4R antibody or an anti-IL-4/IL-13 bispecific antibody or antigen-binding fragment thereof; and

wherein the plasma cell ablating agent is an anti-BCMA/anti-CD3 bispecific antibody or antigen-binding fragment thereof comprising (a) a first antigen-binding domain that specifically binds to BCMA; and (b) a second antigen-binding domain that specifically binds CD3.

4. The use of any one of claims 1-3, wherein the allergic disease or disorder is selected from the group consisting of allergic asthma, hay fever, chronic urticaria, food allergy, pollen allergy, and allergy due to an environmental (non-food) allergen.

5. The use of any one of claims 1-4, wherein the subject is at a risk of anaphylaxis due to an allergen.

6. The use of any one of claims 1-5, wherein the subject has a seasonal allergy.

7. The use of any one of claims 1-6, wherein the subject has a severe allergy.

8. The use of any one of claims 1-7, wherein the subject has an allergy due to one or more allergens selected from the group consisting of milk, a dairy product, egg, celery, sesame, wheat, meat, soy, fish, a fruit, shellfish, a sugar, peanut, a legume, a tree nut, dust, dust mite, pollen, insect venom, mold, animal fur, animal dander, wool, latex, a metal, a household cleaner, a detergent, medication, cosmetics, perfumes, a drug such as penicillin, sulfonamides, or salicylate, therapeutic monoclonal antibodies (*e.g.*, cetuximab), ragweed, grass and birch.

9. The use of any one of claims 1-8, wherein the allergen is contained in or derived from a food item selected from the group consisting of milk, a dairy product, egg, celery, sesame, wheat, meat, fruit, soy, fish, shellfish, a sugar, peanut, a legume, and a tree nut.

10. The use of any one of claims 1-8, wherein the allergen is a non-food allergen selected from the group consisting of dust, dust mite, pollen, insect venom, mold, animal fur, animal dander, wool, latex, a metal, a household cleaner, a detergent, medication, cosmetics, perfumes, a drug such as penicillin, sulfonamides, or salicylate, therapeutic monoclonal antibodies (*e.g.*, cetuximab), ragweed, grass and birch.

11. ~~The~~ Use of an IL-4/IL-13 pathway inhibitor and a plasma cell ablating agent in the preparation of a medicament for increasing the efficacy and/or tolerability of an immunotherapy regimen in a subject having an allergy, wherein the medicament is to be administered to the subject prior to or concurrent with the immunotherapy regimen;

wherein the IL-4/IL-13 pathway inhibitor is an anti-IL-4R antibody or antigen-binding fragment thereof or an anti-IL-4/IL-13 bispecific antibody or antigen-binding fragment thereof; and

wherein the plasma cell ablating agent is an anti-BCMA/anti-CD3 bispecific antibody or antigen-binding fragment thereof comprising (a) a first antigen-binding domain that specifically binds to BCMA; and (b) a second antigen-binding domain that specifically binds CD3.

12. The use of claim 11, wherein the immunotherapy is oral immunotherapy.
13. The use of claim 11, wherein the immunotherapy is subcutaneous immunotherapy.
14. The use of any one of claims 11-13, wherein the subject has a food allergy.
15. The use of claim 14, wherein the subject has an allergy to milk, a dairy product, egg, celery, sesame, wheat, meat, fruit, soy, fish, shellfish, a sugar, peanut, a legume, or a tree nut.
16. The use of any one of claims 11-13, wherein the subject has an allergy to a non-food allergen selected from the group consisting of dust, dust mite, pollen, insect venom, mold, animal fur, animal dander, wool, latex, a metal, a household cleaner, a detergent, cosmetics, perfume, a drug, a therapeutic monoclonal antibody, ragweed, grass and birch.
17. The use of any one of claims 11-16, wherein the medicament is to be administered prior to the onset of the immunotherapy regimen.
18. The use of any one of claims 11-17, wherein the medicament is to be administered concurrently with the immunotherapy regimen.
19. The use of any one of claims 1-18, wherein the IL-4/IL-13 pathway inhibitor is ~~selected from the group consisting of an anti-IL-4 antibody, an anti-IL-13 antibody, an anti-IL-4/IL-13 bispecific antibody, an IL-4 receptor (IL-4R) inhibitor, an IL-4 trap, an IL-13 trap, and an anti-IL-4R~~ an anti-IL-4/IL-13 bispecific antibody.
20. The use of ~~any one of claims 1-19~~ claim 19, wherein the ~~anti-IL-4/IL-13 pathway inhibitor~~ anti-IL-4/IL-13 pathway inhibitor ~~is an anti-IL-4 antibody~~ is an anti-IL-4/IL-13 bispecific antibody ~~romilkimab~~.
21. The use of any one of claims 1-~~19~~ 18, wherein the IL-4/IL-13 pathway inhibitor is an anti-IL-~~13~~ 4R antibody.
22. The use of ~~any one of claims 1-19~~ claim 19, wherein the IL-4/IL-13 pathway inhibitor is an ~~anti-IL-4/IL-13 bispecific antibody~~.
23. ~~The use of any one of claims 1-19, wherein the IL-4/IL-13 pathway inhibitor is an IL-4R inhibitor.~~
24. ~~The use of any one of claims 1-19, wherein the IL-4/IL-13 pathway inhibitor is an anti-IL-4R antibody.~~
25. ~~The use of claim 24~~ claim 21, wherein the anti-IL-4R antibody comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three

light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 has the amino acid sequence of SEQ ID NO: 3, HCDR2 has the amino acid sequence of SEQ ID NO: 4, HCDR3 has the amino acid sequence of SEQ ID NO: 5, LCDR1 has the amino acid sequence of SEQ ID NO: 6, LCDR2 has the amino acid sequence of SEQ ID NO: 7, and LCDR3 has the amino acid sequence of SEQ ID NO: 8.

2623. The use of claim 2522, wherein the anti-IL-4R antibody comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 2.

2724. The use of any one of claims 24, 21-23, wherein the anti-IL-4R antibody comprises a heavy chain and a light chain, wherein the heavy chain has an amino acid sequence of SEQ ID NO: 9.

2825. The use of any one of claims 24-26, 21-23, wherein the anti-IL-4R antibody comprises a heavy chain and a light chain, wherein the light chain has an amino acid sequence of SEQ ID NO: 10.

2926. The use of any one of claims 24, 21-23, wherein the anti-IL-4R antibody comprises a heavy chain and a light chain, wherein the heavy chain has an amino acid sequence of SEQ ID NO: 9 and the light chain has an amino acid sequence of SEQ ID NO: 10.

3027. The use of any one of claims 1-29, 18 or 21-26, wherein the IL-4/IL-13 pathway inhibitor is dupilumab ~~or a bioequivalent thereof~~.

~~31. The use of any one of claims 1-19, wherein the IL-4/IL-13 pathway inhibitor is selected from the group consisting of dupilumab, pascolizumab, AMG317, MEDI2045, MEDI9314, tralokinumab, lebrikzumab, anrukinzumab, dectrekumab, GSK679586, MEDI7836, romilkimab, an IL-4 trap, an IL-13 trap, AER-003, and pitrakinra.~~

~~32. The use of any one of claims 1-31, wherein the plasma cell ablating agent is selected from the group consisting of a B-cell maturation antigen (BCMA) targeting agent, a proteasome inhibitor, a histone deacetylase inhibitor, a BAFF inhibitor, and an APRIL inhibitor.~~

~~33. The use of claim 32, wherein the BCMA targeting agent is selected from the group consisting of an anti-BCMA/anti-CD3 bispecific antibody, a chimeric antigen receptor against BCMA ("BCMA CAR"), and an anti-BCMA antibody conjugated to a cytotoxic agent ("BCMA ADC").~~

~~34. The use of any one of claims 1-33, wherein the plasma cell ablating agent is an anti-BCMA/anti-CD3 bispecific antibody or antigen-binding fragment thereof comprising (a) a first antigen-binding domain that specifically binds to BCMA; and (b) a second antigen-binding domain that specifically binds CD3.~~

~~35. The use of claim 34~~28. The use of any one of claims 1-27, wherein the first antigen-binding domain comprises three heavy chain CDRs (HCDR1, HCDR2 and HCDR3) contained with a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 12, and three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 20.

3629. The use of claim 3528, wherein HCDR1 has the amino acid sequence of SEQ ID NO: 14, HCDR2 has the amino acid sequence of SEQ ID NO: 16, HCDR3 has the amino acid sequence of SEQ ID NO: 18, LCDR1 has the amino acid sequence of SEQ ID NO: 22, LCDR2 has the amino acid sequence of SEQ ID NO: 24, and LCDR3 has the amino acid sequence of SEQ ID NO: 26.

3730. The use of ~~any one of claims 34-36~~claim 28 or 29, wherein the second antigen-binding domain comprises three heavy chain CDRs (HCDR1, HCDR2 and HCDR3) contained with a heavy chain variable region (HCVR) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs: 28 and 36, and three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 20.

3831. The use of claim 3730, wherein HCDR1 has the amino acid sequence of SEQ ID NO: 30 or 38, HCDR2 has the amino acid sequence of SEQ ID NO: 32 or 40, HCDR3 has the amino acid sequence of SEQ ID NO: 34 or 42, LCDR1 has the amino acid sequence of SEQ ID NO: 22, LCDR2 has the amino acid sequence of SEQ ID NO: 24, and LCDR3 has the amino acid sequence of SEQ ID NO: 26.

3932. The use of ~~claim 34~~any one of claims 1-27, wherein the anti-BCMA/anti-CD3 bispecific antibody or antigen-binding fragment thereof comprises:

(a) a first antigen-binding domain that comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 14, 16, and 18, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 22, 24, and 26; and

(b) a second antigen binding domain that comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 30, 32, and 34, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 22, 24, and 26.

~~4033.~~ The use of ~~claim 34~~any one of claims 1-27, wherein the anti-BCMA/anti-CD3 bispecific antibody or antigen-binding fragment thereof comprises:

(a) a first antigen-binding domain that comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 14, 16, and 18, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 22, 24, and 26; and

(b) a second antigen binding domain that comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 38, 40, and 42, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 22, 24, and 26.

~~4134.~~ The use of any one of claims 1-~~4018~~, wherein ~~IgE production is blocked, and allergen-specific IgE is eliminated from the serum in the subject as compared to a subject treated with either the:~~

the IL-4/IL-13 pathway inhibitor is an anti-IL-4R antibody or antigen-binding fragment thereof that comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 has the amino acid sequence of SEQ ID NO: 3, HCDR2 has the amino acid sequence of SEQ ID NO: 4, HCDR3 has the plasma-cell-ablating agent amino acid sequence of SEQ ID NO: 5, LCDR1 has the amino acid sequence of SEQ ID NO: 6, LCDR2 has the amino acid sequence of SEQ ID NO: 7, and LCDR3 has the amino acid sequence of SEQ ID NO: 8; and

the anti-BCMA/anti-CD3 bispecific antibody or antigen-binding fragment thereof comprises (i) a first antigen-binding domain that comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 14, 16, and 18, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 22, 24, and 26; and (ii) a ~~monotherapy~~second antigen binding domain that comprises HCDR1, HCDR2, and HCDR3 domains, respectively, comprising the amino acid

sequences of SEQ ID NOs: 38, 40, and 42, and LCDR1, LCDR2, and LCDR3 domains, respectively, comprising the amino acid sequences of SEQ ID NOs: 22, 24, and 26.

~~4235~~. The use of any one of claims 1-~~4134~~, wherein at least one additional therapeutic agent or therapy is to be administered to the subject.

~~4336~~. The use of claim ~~4235~~, wherein the additional therapeutic agent is selected from the group consisting of an IgE antagonist, an anti-histamine, an anti-inflammatory agent, a corticosteroid, a leukotriene antagonist, a mast cell inhibitor, a bronchial dilator, a decongestant, epinephrine, an IL-1 antagonist, an IL-5 antagonist, an IL-31 antagonist, an IL-33 antagonist, an IL-25 antagonist, interferon γ , a TNF antagonist, and a TSLP antagonist.