CLAIMS

What is claimed is:

1. An anti-IgE antibody, or antigen binding agent, comprising a heavy chain variable region comprising a complementarity determining region, CDR-H1, with an amino acid sequence which is Seq. ID No. 14, CDR-H2, with an amino acid sequence which is Seq. ID No. 16, CDR-H3, with an amino acid sequence which is Seq. ID No. 18, and a light chain variable region comprising a complementarity determining region, CDR-L1, with an amino acid sequence which is Seq. ID No. 29, CDR-L2, with an amino acid sequence which is Seq. ID No. 50 or 51, CDR-L3, with an amino acid sequence which is Seq. ID No. 33; wherein the light chain variable region further comprises a framework region, FR-L3, with an amino acid sequence selected from Seq. ID No. 32 which has one, two, three, four, five, six, seven or more amino acid substitutions to strengthen the interaction of the anti-IgE antibody, or antigen binding agent, with the Cε2 domain of human IgE; and wherein:

a. the FR-L3 region is mutated at position S60 (Kabat) to M , R, K, N, Q or T;
b. the FR-L3 region is mutated at position S67 (Kabat) to M;
c. the FR-L3 region is mutated at position S77 (Kabat) to R; and/or
d. the FR-L3 region is mutated at position Q79 (Kabat) to R.

2. An anti-IgE antibody, or antigen binding agent, comprising a heavy chain variable region and a light chain variable region, wherein:

a. the heavy chain variable region comprises a CDR-H1 with an amino acid sequence which is Seq ID No. 14, a CDR-H2 with an amino acid sequence which is Seq ID No. 16 and a CDR-H3 with an amino acid sequence which is Seq ID No. 18 and the light chain variable region comprises CDR-L1 with an amino acid sequence which is Seq ID No. 29, a CDR-L2 with an amino acid sequence which is Seq ID No. 50, a CDR-L3 with an amino acid sequence which is Seq ID No. 33 and a framework region FW-L3 with an amino acid sequence which is Seq ID No. 131 or 138; or
b. the heavy chain variable region comprises an amino acid sequence which is Seq ID No. 1 and the light chain variable region comprises an amino acid sequence selected from Seq ID No. 132 or 139.

3. The anti-IgE antibody, or antigen binding agent of claim 2 further comprising a light chain constant region, wherein the light chain variable region and the light chain constant region VL-CL have an amino acid sequence selected from Seq ID No. 136 or 145 optionally comprising a signal sequence which has an amino acid sequence which is Seq ID No. 160.

4. The anti-IgE antibody, or antigen binding agent, of claims 2 or 3, further comprising a heavy chain constant region, CH1.

5. The anti-IgE antibody, or antigen binding agent, of claim 4, wherein the heavy chain variable region and heavy chain constant region, VH-CH1, has an amino acid sequence which is Seq. ID No. 5.

6. The anti-IgE antibody, or antigen binding agent, of claims 1-5 which is selected from the group consisting of: a Fab fragment, modified Fab' fragment, Fab' fragment, $F(ab')_2$ fragment, Fv, scFv, scab, a diabody, bispecific antibody, triabody, FabFv, Fab-Fv-Fv, tribody, or a $(Fab\text{-}Fv)^2$-Fc.

7. The anti-IgE antibody of claim 6 which is a Fab fragment linked directly or via a linker to a scFv that binds to a serum carrier protein, such as human serum albumin.

8. The anti-IgE antibody of claim 7 wherein the scFv comprises a heavy chain variable region and a light chain variable region, preferably linked via a linker having Seq. ID No. 151, wherein the heavy chain variable region comprises a CDR-H1 with an amino acid sequence which is Seq ID No. 152, a CDR-H2 with an amino acid sequence which is Seq ID No. 153 and a CDR-H3 with an amino acid sequence which is Seq ID No. 154 and the light chain variable region comprises CDR-L1 with an amino acid sequence which is Seq ID No. 155, a CDR-L2 with an amino acid sequence which is Seq ID No. 156, a CDR-L3 with an amino acid sequence which is Seq ID No. 157.

9. The anti-IgE antibody of claims 7 or 8, wherein the Fab fragment comprises a heavy chain variable region and a light chain variable region, wherein:

a. the heavy chain variable region comprises a CDR-H1 with an amino acid sequence which is Seq ID No. 14, a CDR-H2 with an amino acid sequence which is Seq ID No. 16 and a CDR-H3 with an amino acid sequence which is Seq ID No. 18 and the light chain variable region comprises CDR-L1 with an amino acid sequence which is Seq ID No. 29, a CDR-L2 with an amino acid sequence which is Seq ID No. 50, a CDR-L3 with an amino acid sequence which is Seq ID No. 33 and a

framework region FW-L3 with an amino acid sequence which is Seq ID No. 131 or 138; or

b. the heavy chain variable region comprises an amino acid sequence which is Seq ID No. 1 and the light chain variable region comprises an amino acid sequence selected from Seq ID No. 132 or 139.

10. An isolated DNA sequence encoding the heavy and/or light chain(s) of an anti-IgE antibody, or antigen binding agent, of claims 1-9.

11. A cloning or expression vector comprising one or more DNA sequences selected from Seq. ID No. 36, Seq. ID No. 38, Seq. ID No. 40, or Seq. ID No. 42, or Seq. ID No. 133, or Seq ID No. 135, or Seq ID No. 137, or Seq ID No. 140, or Seq. ID No. 142, or Seq ID No. 144; wherein optionally the cloning or expression vector further comprising one or more DNA sequences selected from Seq. ID No. 2, Seq. ID No. 4, Seq. ID No. 6, Seq. ID No. 8, Seq. ID No. 10, or Seq. ID No. 12 or Seq. ID No. 148.

12. A pharmaceutical composition comprising the anti-IgE antibody, or antigen binding agent, of claims 1-9, in combination with one or more of a pharmaceutically acceptable excipient, diluent or carrier.

13. The anti-IgE antibody, or antigen binding agent, of claims 1-9, or a composition of claim 12 for use as a medicament.

14. The anti-IgE antibody, or antigen binding agent of claims 1-9, or composition of claim 12, for use in the treatment or prevention of one or more of: allergy ; allergic asthma; severe asthma; moderate asthma; chronic spontaneous urticaria; chronic idiopathic urticaria; perennial allergic rhinitis; seasonal allergic rhinitis; acute asthma exacerbations; acute bronchospasm; status asthmaticus; hyper IgE syndrome; allergic bronchopulmonary aspergillosis; prevention of anaphylactic reactions; food allergy; atopic dermatitis; allergic rhinitis; bee venom sensitivity; idiopathic anaphylaxis; peanut allergy; latex allergy; inflammatory skin diseases; urticaria (solar, cold-induced, local heat-induced, and/or delayed pressure-induced); cutaneous mastocytosis; systemic mastocytosis; eosinophil-associated gastrointestinal disorder; bullous pemphigoid; interstitial cystitis; nasal polyps; idiopathic angioedema; or non-allergic asthma.

15. Use of the anti-IgE antibody, or antigen binding agent of claims 1-9, or composition of claim 12, in the manufacture of a medicament for the treatment or prevention of one or

more of: allergy ; allergic asthma; severe asthma; moderate asthma; chronic spontaneous urticaria; chronic idiopathic urticaria; perennial allergic rhinitis; seasonal allergic rhinitis; acute asthma exacerbations; acute bronchospasm; status asthmaticus; hyper IgE syndrome; allergic bronchopulmonary aspergillosis; prevention of anaphylactic reactions; food allergy; atopic dermatitis; allergic rhinitis; bee venom sensitivity; idiopathic anaphylaxis; peanut allergy; latex allergy; inflammatory skin diseases; urticaria (solar, cold-induced, local heat-induced, and/or delayed pressure-induced); cutaneous mastocytosis; systemic mastocytosis; eosinophil-associated gastrointestinal disorder; bullous pemphigoid; interstitial cystitis; nasal polyps; idiopathic angioedema; or non-allergic asthma.