CLAIMS

What is claimed is:

1. An isolated monoclonal antibody or antigen-binding fragment thereof that binds to natural Bet v 1 or birch pollen extract (BPE), wherein the antibody or fragment thereof comprises:

(a) a heavy chain complementarity determining region (HCDR)1 comprising the amino acid sequence of SEQ ID NO: 148; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 150; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 152; a light chain complementarity determining region (LCDR)1 comprising the amino acid sequence of SEQ ID NO: 156; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 158; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 160; or

(b) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 292; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 294; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 296; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 300; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 302; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 304; or

(c) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 100; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 102; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 104; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 110; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 112; or

(d) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 116; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 118; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 120; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 124; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 126; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 128; or

(e) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 4; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 6; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 8; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 12; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 14; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

(f) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 22; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 24; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 28; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 30; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 32; or

(g) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 36; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 40; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 44; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 46; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 48; or

(h) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 52; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 54; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 56; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 60; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 62; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 64; or

(i) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 68; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 70; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 72; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 76; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 78; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 80; or

(j) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 84; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 86; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 88; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 92; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 94; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 96; or

(k) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 132; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 134; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 136; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 140; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 142; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 144; or

(l) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 164; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 166; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 168; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 172; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 174; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 176; or

(m) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 180; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 182; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 184; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 188; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 190; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 192; or

(n) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 196; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 198; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 200; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 204; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 206; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 208; or

(o) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 212; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 214; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 216; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 220; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 222; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 224; or

(p) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 228; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 230; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 232; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 236; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 238; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 240; or

(q) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 244; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 246; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 248; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 252; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 254; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 256; or

(r) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 260; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 262; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 264; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 268; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 270; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 272; or

(s) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 276; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 278; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 268; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 270; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 272; or

(t) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 284; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 286; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 288; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 268; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 270; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 272.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof is a fully human monoclonal antibody.

3. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region/light chain variable region (HCVR/LCVR) amino acid sequence pair selected from the group consisting of SEQ ID NOs: 146/154, 290/298, 98/106, 114/122, 2/10, 18/26, 34/42, 50/58, 66/74, 82/90, 130/138, 162/170, 178/186, 194/202, 210/218, 226/234, 242/250, 258/266, 274/266, and 282/266.

4. The antibody or antigen-binding fragment thereof of claim 3, comprising an HCVR comprising the amino acid sequence of SEQ ID NO: 146 and an LCVR comprising the amino acid sequence of SEQ ID NO: 154.

5. The antibody or antigen-binding fragment thereof of claim 1, wherein the BPE is from *Betula pendula, Betula nigra*, or *Betula populifolia.*

6. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof cross-reacts with one or more allergens selected from the group

consisting of Aln g1, Cor a1, Car b1, Que a1, Api g2, Api g1, Dau c1, Mal d1, Ost c1, Fag s1, and Cas s1.

7. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof binds to Bet v 1 with a K_D equal to or less than 10^{-8} M as measured by surface plasmon resonance.

8. A pharmaceutical composition comprising a therapeutically effective amount of an antibody or antigen-binding fragment thereof of claim 1 and a pharmaceutically acceptable excipient.

9. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1, comprising:

   an HCDR1 comprising the amino acid sequence of SEQ ID NO: 148; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 150; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 152; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 156; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 158; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 160.

10. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1, comprising:

    an HCDR1 comprising the amino acid sequence of SEQ ID NO: 292; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 294; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 296; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 300; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 302; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 304.

11. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1, comprising:

    an HCDR1 comprising the amino acid sequence of SEQ ID NO: 100; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 102; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 104; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 110; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 112.

12. A pharmaceutical composition comprising a therapeutically effective amount of an antibody or antigen-binding fragment thereof of claim 9 and a pharmaceutically acceptable excipient.

13. A pharmaceutical composition comprising a therapeutically effective amount of an antibody or antigen-binding fragment thereof of claim 10 and a pharmaceutically acceptable excipient.

14. A pharmaceutical composition comprising a therapeutically effective amount of an antibody or antigen-binding fragment thereof of claim 11 and a pharmaceutically acceptable excipient.

15. The antibody or antigen-binding fragment thereof of claim 3, comprising an HCVR comprising the amino acid sequence of SEQ ID NO: 290 and an LCVR comprising the amino acid sequence of SEQ ID NO: 298.

16. The antibody or antigen-binding fragment thereof of claim 3, comprising an HCVR comprising the amino acid sequence of SEQ ID NO: 98 and an LCVR comprising the amino acid sequence of SEQ ID NO: 106.

17. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof binds to a Bet v 1 amino acid sequence fragment selected from the group consisting of SEQ ID NOs: 307, 308, 309, 310, and 311.

18. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof inhibits natural Bet v 1, *Betula pendula* BPE, *Betula nigra* BPE, or *Betula populifolia* BPE binding to allergen specific IgE.