

WE CLAIM:

1. An isolated antibody or antigen-binding fragment thereof which specifically binds to Interleukin-36 Receptor (IL36R) comprising:

(a) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 2, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 10;

(b) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 18, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 26;

(c) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 34, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 42;

(d) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 50, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 58;

(e) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 66, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 74;

(f) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 82, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 90;

(g) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 98, and a light chain immunoglobulin variable region

comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 106;

(h) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 114, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 122;

(i) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 130, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 122;

(j) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 138, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 146;

(k) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 154, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 162; or

(l) a heavy chain immunoglobulin variable region comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 170, and a light chain immunoglobulin variable region comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 122.

2. The antibody or antigen-binding fragment thereof of claim 1 which is produced by a method comprising:

(a) introducing one or more polynucleotides encoding the heavy and light chain immunoglobulin variable regions of said antibody or antigen-binding fragment thereof into an isolated host cell;

(b) culturing the host cell in a medium under conditions favorable to expression of the polynucleotide; and

(c) optionally, isolating the antibody or antigen-binding fragment thereof from the host cell and/or medium in which the host cell is grown.

3. The isolated antibody or antigen-binding fragment thereof of claim 2 wherein the host cell is a Chinese hamster ovary cell.

4. A composition or kit comprising an antibody or antigen-binding fragment thereof of claim 1.

5. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of claim 1 and a pharmaceutically acceptable carrier.

6. The pharmaceutical composition of claim 5 in association with a further therapeutic agent.

7. The pharmaceutical composition of claim 5 in association with a further therapeutic agent, wherein the further therapeutic agent is a member selected from the group consisting of an anti-tumor necrosis factor (TNF) alpha antibody or antigen-binding fragment thereof, one or more human TNF receptors or fragments thereof linked to an immunoglobulin, an Interleukin-17 inhibitor, an Interleukin-23 p19 inhibitor, an Interleukin-12 p40 inhibitor, guselkumab, ustekinumab, brodalumab, ixekizumab, secukinumab, infliximab, adalimumab, etanercept, dupilumab, sarilumab, tocilizumab, golimumab, abatacept, tofacitinib, abatacept, a non-steroidal anti-inflammatory drug (NSAID), ibuprofen, naproxen, acetaminophen, aspirin, celecoxib, cyclophosphamide, methotrexate, a corticosteroid, cortisone and prednisone.

8. A complex comprising an antibody or antigen-binding fragment thereof of claim 1 bound to a IL36R polypeptide.

9. A vessel or injection device comprising the antibody or antigen-binding fragment thereof of claim 1 or a pharmaceutical composition comprising said antibody or fragment and a pharmaceutically acceptable carrier.

10. An isolated antibody or antigen-binding fragment thereof which specifically binds to Interleukin-36 Receptor (IL36R) comprising:

(1)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 4,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 6, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 8, and
a light chain immunoglobulin variable region comprising
a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 12,
a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14, and
a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 16;

(2)

a heavy chain immunoglobulin variable region comprising
a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 20,
a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 22, and
a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 24, and
a light chain immunoglobulin variable region comprising
a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 28,
a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 30, and
a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 32;

(3)

a heavy chain immunoglobulin variable region comprising
a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 36,
a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 38, and
a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 40, and
a light chain immunoglobulin variable region comprising
a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 44,
a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 46, and
a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 48;

(4)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 52,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 54, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 56, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 60,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 62, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 64;

(5)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 68,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 70, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 72, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 76,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 78, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 80;

(6)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 84,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 86, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 88, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 92,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 94, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 96;

(7)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 100,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 102, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 104, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 108,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 110, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 112;

(8)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 116,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 118, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 120, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 128;

(9)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 132,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 134, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 136, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 128;

(10)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 140,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 142, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 144, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 148,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 150, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 152;

(11)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 156,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 158, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 160, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 164,
a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 166, and
a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 168;

or

(12)

a heavy chain immunoglobulin variable region comprising
a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 172,
a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 174, and
a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 176, and
a light chain immunoglobulin variable region comprising
a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124,
a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, and
a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 128.

11. The antibody or antigen-binding fragment of claim 10 comprising:

(1)

a heavy chain immunoglobulin variable region comprising
a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 4,
a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 6, and
a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 8, and at least
90% identical to SEQ ID NO: 2, and
a light chain immunoglobulin variable region comprising
a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 12,
a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 16, and at least 90% identical to SEQ ID NO: 10;

(2)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 20,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 22, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 24, and at least 90% identical to SEQ ID NO: 18 and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 28,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 30, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 32, and at least 90% identical to SEQ ID NO: 26;

(3)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 36,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 38, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 40, and at least 90% identical to SEQ ID NO: 34, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 44,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 46, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 48, and at least 90% identical to SEQ ID NO: 42;

(4)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 52,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 54, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 56, and at least 90% identical to SEQ ID NO: 50, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 60,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 62, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 64, and at least 90% identical to SEQ ID NO: 58;

(5)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 68,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 70, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 72, and at least 90% identical to SEQ ID NO: 66;

and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 76,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 78, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 80, and at least 90% identical to SEQ ID NO: 74;

(6)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 84,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 86, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 88, and at least 90% identical to SEQ ID NO: 82, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 92,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 94, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 96, and at least 90% identical to SEQ ID NO: 90;

(7)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 100,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 102, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 104, and at least 90% identical to SEQ ID NO: 98, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 108,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 110, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 112, and at least 90% identical to SEQ ID NO: 106;

(8)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 116,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 118, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 120, and at least 90% identical to SEQ ID NO: 114, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 128, and at least 90% identical to SEQ ID NO: 122;

(9)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 132,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 134, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 136, and at least 90% identical to SEQ ID NO: 130, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 128, and at least 90% identical to SEQ ID NO: 122;

(10)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 140,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 142, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 144, and at least 90% identical to SEQ ID NO: 138, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 148,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 150, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 152, and at least 90% identical to SEQ ID NO: 146;

(11)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 156,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 158, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 160, and at least 90% identical to SEQ ID NO: 154, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 164,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 166, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 168, and at least 90% identical to SEQ ID NO: 162;

or

(12)

a heavy chain immunoglobulin variable region comprising

a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 172,

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 174, and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 176, and at least 90% identical to SEQ ID NO: 170, and

a light chain immunoglobulin variable region comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124,

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, and

a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 128, and at least 90% identical to SEQ ID NO: 122.

claim 10

12. An isolated antibody or antigen-binding fragment thereof which specifically binds to Interleukin-36 Receptor (IL36R) comprising:

- (a) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 2, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 10;
- (b) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 18, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 26;
- (c) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 34, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 42;
- (d) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 50, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 58;
- (e) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 66, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 74;
- (f) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 82, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 90;
- (g) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 98, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 106;
- (h) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 114, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 122;
- (i) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 130, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 122;
- (j) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 138, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 146;

(k) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 154, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 162; or

(l) a heavy chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 170, and a light chain immunoglobulin variable region that comprises the amino acid sequence set forth in SEQ ID NO: 122.

13. The antibody or antigen-binding fragment thereof of claim 12 wherein the heavy chain immunoglobulin variable region is linked to an IgG heavy chain constant region and the light chain immunoglobulin variable region is linked to a kappa light chain constant region.

14. The antibody or antigen-binding fragment thereof of claim 12 comprising:

(a) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 180, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 182;

(b) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 184, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 186;

(c) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 188, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 190;

(d) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 192, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 194;

(e) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 196, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 198;

(f) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 200, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 202;

(g) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 204, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 206;

(h) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 208, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 210;

(i) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 212, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 214;

(j) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 216, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 218;

(k) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 220, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 222; or

(l) a heavy chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 224, and a light chain immunoglobulin that comprises the amino acid sequence set forth in SEQ ID NO: 226.

15. The antibody or antigen-binding fragment thereof of claim 12 which is an antibody.

16. The antibody or antigen-binding fragment thereof of claim 12 which is multispecific.

17. A polypeptide comprising:

the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NOs: 2, 10, 18, 26, 34, 42, 50, 58, 66, 74, 82, 90, 98, 106, 114, 122, 130, 138, 146, 154, 162 and 170.