

WE CLAIM:

1. An isolated antibody or antigen-binding protein fragment thereof which is an~~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 ~~that~~ of claim 1 which is produced by a method comprising:

~~binds to a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 227 at residues 113-119, 113-122, 116-119, 116-122, 264-271, 267-271, 268-271, 268-276, 268-277 and/or 271-276;~~

~~or,~~

~~(i) specifically binds to the same epitope on IL36R as a reference(a) introducing one or more polynucleotides encoding the heavy and light chain immunoglobulin variable regions of said antibody or antigen-binding fragment thereof; or into an isolated host cell;~~

~~(ii) competes for binding to IL36R polypeptide with a reference antibody or antigen-binding fragment thereof,~~

~~wherein the reference(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 comprises:from the host cell and/or medium in which the host cell is grown.~~

~~(a) a heavy chain immunoglobulin or variable region thereof that comprises CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 138, 154,170, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220 or 224; or a variant thereof; and/or~~

~~(b) a light chain immunoglobulin or variable region thereof that comprises CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 26, 42, 58, 74, 90, 106, 122, 146, 162, 182, 186, 190, 194, 198, 202, 206, 210, 214, 218, 222 or 226; or a variant thereof.~~

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

4. A composition or kit comprising:

~~(i) a heavy chain immunoglobulin or variable region thereof that comprises CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof that comprises the~~

~~amino acid sequence set forth in SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 138, 154, 170, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220 or 224; or a variant thereof; and/or~~

~~(ii) a light chain immunoglobulin or variable region thereof that comprises CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 26, 42, 58, 74, 90, 106, 122, 146, 162, 182, 186, 190, 194, 198, 202, 206, 210, 214, 218, 222 or 226; or a variant thereof.~~

~~3. The an antibody or antigen-binding protein of any one of claimsfragment thereof of claim 1-
2.~~

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 or variable region thereof comprising an

a CDR-H1 comprising the amino acid sequence having at least 90% set forth in SEQ ID NO: 4,

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

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 138, 154, 170, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220 or 224; and/or 8, and

~~(b) a light chain immunoglobulin or variable region thereof comprising an amino acid sequence having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 10, 26, 42, 58, 74, 90, 106, 122, 146, 162, 182, 186, 190, 194, 198, 202, 206, 210, 214, 218, 222 or 226.~~

~~4. The antigen-binding protein of any one of claims 1-3 comprising:~~

~~(a) a heavy chain immunoglobulin or variable region thereof comprising the CDR-H1, CDR-H2 and CDR-H3 of a heavy chain immunoglobulin or variable region thereof comprising an amino acid sequence set forth in SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 138, 154, 170, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220 or 224, and at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 138, 154, 170, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220 or 224; and/or~~

~~(b) an light chain immunoglobulin or variable region thereof comprising the CDR-L1, CDR-L2 and CDR-L3 of a light chain immunoglobulin or variable region thereof comprising an amino acid sequence set forth in SEQ ID NO: 10, 26, 42, 58, 74, 90, 106, 122, 146, 162, 182, 186, 190, 194, 198, 202, 206, 210, 214, 218, 222 or 226, and at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO: 10, 26, 42, 58, 74, 90, 106, 122, 146, 162, 182, 186, 190, 194, 198, 202, 206, 210, 214, 218, 222 or 226.~~

~~5. The antigen-binding protein of any one of claims 1-4 comprising:~~

~~a heavy chain immunoglobulin or variable region thereof that comprises:~~

~~CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO: 4, or a variant thereof;~~

~~a CDR-H2L1 comprising the amino acid sequence set forth in SEQ ID NO: 6, or a variant thereof; and 12,~~

a CDR-H3L2 comprising the amino acid sequence set forth in SEQ ID NO: 8, or a variant thereof14, and

and/or

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, or a variant thereof;

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

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 24, or a variant thereofand

and/or

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, or a variant thereof;

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

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 40, ~~or a variant thereof~~and

~~and/or~~

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, ~~or a variant thereof~~;

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 54, ~~or a variant thereof~~; and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 56, ~~or a variant thereof~~

~~and/or~~

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, ~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 70, ~~or a variant thereof;~~ and

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

and/or

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, ~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 86, ~~or a variant thereof;~~ and

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

and/or

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, ~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 102, ~~or a variant thereof;~~ and

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

~~and/or~~

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, ~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 118, ~~or a variant thereof;~~ and

~~and~~

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

and/or

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, ~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 134, ~~or a variant thereof;~~ and

and

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

and/or

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, ~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 142, ~~or a variant thereof;~~ and

and

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

and/or

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, ~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 158, ~~or a variant thereof;~~ and

and

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

and/or

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, ~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 174, ~~or a variant thereof;~~ and

and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 176, ~~or a variant thereof~~and

and/or

a light chain immunoglobulin ~~or variable region thereof that comprises:~~

~~CDR-L1 comprising~~

~~the amino acid sequence set forth in SEQ ID NO: 12, or a variant thereof;~~

~~CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14, or a variant thereof;~~
~~and~~

~~CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 16, or a variant thereof~~
~~and/or~~

~~CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 28, or a variant thereof;~~

~~CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 30, or a variant thereof;~~
~~and~~

~~CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 32, or a variant thereof~~
~~and/or~~

~~CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 44, or a variant thereof;~~
~~CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 46, or a variant thereof;~~
~~and~~
~~CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 48, or a variant thereof~~
~~and/or~~

~~CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 60, or a variant thereof;~~
~~CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 62, or a variant thereof;~~
~~and~~
~~CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 64, or a variant thereof~~
~~and/or~~

~~CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 76, or a variant thereof;~~
~~CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 78, or a variant thereof;~~
~~and~~
~~CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 80, or a variant thereof~~
~~and/or~~

~~CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 92, or a variant thereof;~~
~~CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 94, or a variant thereof;~~
~~and~~
~~CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 96, or a variant thereof~~
~~and/or~~

~~CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 108, or a variant thereof;~~
~~CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 110, or a variant thereof;~~
~~and~~
~~CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 112, or a variant thereof~~
~~and/or~~

~~CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124, or a variant thereof;~~

a ~~CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, or a variant thereof;~~ and
and

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

and/or

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

CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 150, or a variant thereof;

and

CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 152, or a variant thereof

and/or

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

CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 166, or a variant thereof;

and

CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO: 168, or a variant thereof.

611. The antibody or antigen-binding fragment thereof of any one of claims of claim 10 comprising:

(1-5 comprising:)

(1)

a heavy chain immunoglobulin or variable region thereof comprising

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

or a variant thereof;

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

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 8, or a variant thereof;
and at least 90% identical to SEQ ID NO: 2, and

a light chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 12,

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 14, ~~or a variant thereof;~~ and

and

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

(2)

a heavy chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 22, ~~or a variant thereof;~~ and

and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 24, ~~or a variant thereof;~~

and at least 90% identical to SEQ ID NO: 18 and

a light chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 30, ~~or a variant thereof;~~ and

and

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

(3)

a heavy chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 38, ~~or a variant thereof;~~ and

~~and~~

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 40, ~~or a variant thereof;~~

and at least 90% identical to SEQ ID NO: 34, and

a light chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 46, ~~or a variant thereof;~~ and

~~and~~

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

(4)

a heavy chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 54, ~~or a variant thereof;~~ and

~~and~~

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

~~thereof;~~

and at least 90% identical to SEQ ID NO: 50, and

a light chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 62, ~~or a variant thereof;~~ and

~~and~~

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

(5)

a heavy chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 70, ~~or a variant thereof;~~ and

~~and~~

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 72, ~~or a variant thereof;~~

and at least 90% identical to SEQ ID NO: 66;

and

a light chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 78, ~~or a variant thereof;~~ and

and

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

(6)

a heavy chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 86, ~~or a variant thereof;~~ and

and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 88, ~~or a variant thereof;~~

and at least 90% identical to SEQ ID NO: 82, and

a light chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 94, ~~or a variant thereof;~~ and

and

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

(7)

a heavy chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 102, ~~or a variant thereof;~~ and

~~and~~

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 104, ~~or a variant thereof;~~

~~and~~ at least 90% identical to SEQ ID NO: 98, and

a light chain immunoglobulin ~~or variable region thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 110, ~~or a variant thereof;~~ and

~~and~~

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

(8)

a heavy chain immunoglobulin ~~or variable region thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 118, ~~or a variant thereof;~~ and

~~and~~

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 120, ~~or a variant thereof;~~

~~and~~

~~a light chain immunoglobulin or variable region thereof comprising~~

~~a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124, or a variant thereof;~~

~~a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, or a variant thereof; 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, or a variant thereof; and at least 90% identical to SEQ ID NO: 122;~~

(9)

~~a heavy chain immunoglobulin or variable region thereof comprising~~

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

~~or a variant thereof;~~

~~a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 134, or a variant thereof; and~~

~~and~~

~~a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 136, or a variant thereof;~~

~~and~~

~~a light chain immunoglobulin or variable region thereof comprising~~

~~a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124, or a variant thereof;~~

~~a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, or a variant thereof; 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, ~~or a variant thereof~~ and at least 90% identical to SEQ ID NO: 122;

(10)

a heavy chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 142, ~~or a variant thereof;~~ and

~~and~~

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 144, ~~or a variant thereof;~~

and at least 90% identical to SEQ ID NO: 138, and

a light chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 150, ~~or a variant thereof;~~ and

~~and~~

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

(11)

a heavy chain immunoglobulin ~~or~~-variable region ~~thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 158, ~~or a variant thereof;~~ and

and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 160, ~~or a variant thereof;~~

and at least 90% identical to SEQ ID NO: 154, and

a light chain immunoglobulin ~~or variable region thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 166, ~~or a variant thereof;~~ and

and

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

or

(12)

a heavy chain immunoglobulin ~~or variable region thereof~~ comprising

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

~~or a variant thereof;~~

a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO: 174, ~~or a variant thereof;~~ and

and

a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO: 176, ~~or a variant thereof;~~

and

~~a light chain immunoglobulin or variable region thereof comprising~~

~~a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO: 124, or a variant thereof;~~

~~a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO: 126, or a variant thereof;~~ 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, ~~or a variant thereof~~ and at least 90% identical to SEQ ID NO: 122.

7. The claim 10

12. An isolated antibody or antigen-binding protein of any one of claims 1-6 ~~fragment thereof~~ which specifically binds to Interleukin-36 Receptor (IL36R) comprising:

~~(a) a heavy chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 138, 154, 170, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220 or 224, or a variant thereof;~~

~~and/or~~

~~(b) a light chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 26, 42, 58, 74, 90, 106, 122, 146, 162, 182, 186, 190, 194, 198, 202, 206, 210, 214, 218, 222 or 226, or a variant thereof.~~

8. The antigen-binding protein of any one of claims 1-7 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; ~~and/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.

913. The antibody or antigen-binding protein fragment thereof of ~~any one of claims 1-8~~ claim 12 wherein the heavy chain immunoglobulin variable region is linked to an IgG, ~~IgG1 or IgG4~~ heavy chain constant region and the light chain immunoglobulin variable region is linked to a kappa ~~or lambda~~ light chain constant region.

~~10-14.~~ The antibody or antigen-binding protein fragment thereof of ~~any one of claims 1-9~~ 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; ~~and/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.

~~11. An~~ 15. The antibody or antigen-binding protein fragment thereof of any one of claims 1-10 claim 12 which is an antibody ~~or antigen-binding fragment thereof~~.

~~12~~ 16. The antibody or antigen-binding protein fragment thereof of any one of claims 1-11 claim 12 which is multispecific.

~~13. The antigen-binding protein of any one of claims 1-12 which comprises one or more of the following properties:~~

- ~~• Binds to human IL36R (IL-1RL2) with a K_D of about 2.18 nM to about 13.9 nM at 25°C or with a K_D of about 4.25 nM to about 29.5 nM at 37°C;~~
- ~~• Binds to *Macaca fascicularis* IL36R (IL-1RL2) with a K_D of about 7.87 nM to about 34.4 nM at 25°C or with a K_D of about 14.4 nM to about 58.2 nM at 37°C;~~

- ~~Binds to human IL36R (IL-1RL2) fused to a mouse IgG2a with a K_D of about 173 pM to about 5.79 nM at 25°C or with a K_D of about 205 pM to about 28.7 nM at 37°C;~~
- ~~Binds to human IL36R (IL-1RL2) fused to IL1RAcP extracellular domain expressed with mouse IgG2a Fc tag with a K_D of about 212 pM to about 14 nM at 25°C or with a K_D of about 264 pM to about 40.9 nM at 37°C;~~
- ~~Competes with H4H14699P2; H4H14700P2; H4H14706P2; H4H14708P2; H4H14709P; H4H14728P; H4H14731P; H4H14732P2; H4H14734P2; H4H14757P; H4H14758P or H4H14760P2 for binding to IL36R (IL-1RL2); optionally with the proviso that said antigen-binding protein is not APE6155 or an antigen-binding fragment thereof;~~
- ~~Blocks activation of one or more NF- κ B elements, which is/are fused to a reporter gene, in a host cell, by IL-36R (IL-1RL2) in the presence of IL-1RAcP and IL36R ligand;~~
- ~~Prevents or ameliorates skin inflammation or reduces skin thickness or total pathology score or reduces pro-inflammatory cytokine levels in a subject suffering from skin inflammation;~~
- ~~Prevents or ameliorates colitis or colon inflammation or reduces fecal levels of LCN2-17. A polypeptide in a subject with such colitis or inflammation~~

~~Protects residues (a) 113-119, 113-122, 116-119 and/or 116-122; and/or (b) 264-271, 267-271, 268-271, 268-276, 268-277 and/or 271-276, of human IL36R (IL-1RL2) comprising the amino acid sequence set forth in SEQ ID NO: 227, when bound, from digestion with pepsin and/or Protease XIII and/or deuteration in the presence of deuterium; ;~~

- ~~Binds to IL36R (IL-1RL2) comprising the amino acid sequence set forth in SEQ ID NO: 227 at residues 113-119, 113-122, 116-119, 116-122, 264-271, 267-271, 268-271, 268-276, 268-277 and/or 271-276;~~
- ~~Binds Domain II of IL36R (IL-1RL2);~~
- ~~Binds a polypeptide comprising the amino acid sequence YKQILHLGKD (SEQ ID NO: 229) (amino acids 113-122 of SEQ ID NO: 227);~~
- ~~Inhibits IL36 α , IL36 β and/or IL36 γ in *in vitro* epidermal keratinocytes, intestinal myofibroblasts and/or CD14+ monocytes, with an IC_{50} of about 1-6 nM; and/or~~

- ~~Competitively inhibits IL36 α , IL36 β and/or IL36 γ -mediated activation of NF κ B by IL36R.~~

~~14. A complex comprising an antigen-binding protein of any one of claims 1-13 bound to a IL36R polypeptide.~~

~~15. A method for making an antigen-binding protein of any one of claims 1-14 or an immunoglobulin chain thereof comprising:~~

~~(a) introducing one or more polynucleotides encoding an immunoglobulin chain of said antigen-binding protein into a host cell;~~

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

~~(c) optionally, isolating the antigen-binding protein or immunoglobulin chain from the host cell and/or medium in which the host cell is grown.~~

~~16. The method of claim 15 wherein the host cell is a Chinese hamster ovary cell.~~

~~17. An antigen-binding protein or immunoglobulin chain which is a product of the method of any one of claims 15-16.~~

~~18. A polypeptide comprising:~~

~~(a) CDR-H1, CDR-H2, and CDR-H3 of a heavy chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 2, 18, 34, 50, 66, 82, 98, 114, 130, 138, 154, 170, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220 or 224, or a variant thereof; and/or~~

~~(b) CDR-L1, CDR-L2, and CDR-L3 of a light chain immunoglobulin or variable region thereof that comprises the amino acid sequence set forth in SEQ ID NO: 10, 26, 42, 58, 74, 90, 106, 122, 146, 162, 182, 186, 190, 194, 198, 202, 206, 210, 214, 218, 222 or 226, or a variant thereof;~~

~~or,~~

~~(c) the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO: 1-226, or a variant thereof NOs: 2, 10, 18, 26, 34, 42, 50, 58, 66, 74, 82, 90, 98, 106, 114, 122, 130, 138, 146, 154, 162 and 170.~~

~~19. A polynucleotide encoding the polypeptide of claim 18.~~

~~20. A vector comprising the polynucleotide of claim 19.~~

~~21. A host cell comprising the antigen-binding protein or immunoglobulin chain or polypeptide or polynucleotide or vector of any one of claims 1-13, 17, 18, 19 or 20.~~

~~22. A composition or kit comprising one or more of the antigen-binding proteins of any one of claims 1-13 and 17, optionally in association with a further therapeutic agent.~~

~~23. A pharmaceutical composition comprising the antigen-binding protein of any one of claims 1-13 and 17 and a pharmaceutically acceptable carrier and, optionally, a further therapeutic agent.~~

~~24. The composition or kit of any one of claims 22-23 in association with a further therapeutic agent which is an anti-inflammatory agent.~~

~~25. The composition or kit of any one of claims 22-24 wherein the further therapeutic agent is a member selected from the group consisting of an anti-TNF α antibody or antigen-binding fragment thereof, one or more human TNF receptors or fragments thereof linked to an immunoglobulin, an IL17 inhibitor, an IL23p19 inhibitor, an IL12p40 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.~~

~~26. A vessel or injection device comprising the antigen-binding protein or composition of any one of claims 1-13, 17 or 22-25.~~

~~27. A method for treating or preventing an IL-36R-mediated disease in a subject in need thereof, comprising administering a therapeutically effective amount of antigen-binding protein of any one of claims 1-13 or 17 optionally in association with a further therapeutic agent.~~

~~28. A method for treating or preventing: an inflammatory disorder, an autoimmune disorder, deficiency of interleukin IL-36 receptor antagonist (DITRA) syndrome, impetigo herpetiformis, acrodermatitis, a skin neutrophilic pustular disease, a pustular disease, psoriasis, generalized pustular psoriasis, psoriasis vulgaris, palmoplantar pustular psoriasis, palmoplantar pustulosis, colitis, airway inflammation, joint inflammation, kidney inflammation, alopecia areata, skin inflammation, acanthosis, hyperkeratosis, kindler syndrome, systemic lupus erythematosus (SLE), nephrotic syndrome, ANCA (anti-neutrophil cytoplasmic antibody)-associated vasculopathies, tubulointerstitial lesions or glomerulonephritis; comprising administering a therapeutically effective amount of antigen-binding protein of any one of claims 1-13 or 17 optionally in association with a further therapeutic agent.~~

~~29. The method of any one of claims 27-28, for treating or preventing psoriasis or inflammatory bowel disease.~~

~~30. A method for administering an antigen-binding protein of any one of claims 1-13 or 17 into the body of a subject comprising injecting the antigen-binding protein into the body of the subject, optionally in association with a further therapeutic agent.~~

~~31. The method of claim 30 wherein the antigen-binding protein is injected into the body of the subject subcutaneously, intravenously or intramuscularly.~~

~~32. The method of any one of claims 27-31 wherein the subject has a homozygous or heterozygous *IL36RN* mutation genotype.~~