

to one another. Five loops located at the interface of these domains are primarily responsible for engaging IL-22 residues in the ligand-receptor complex. The IL-22 residues that contribute to receptor binding are clustered at two sites in the ligand, site 1a and site 1b. Insights into the critical residues contributed by both the receptor and the ligand have revealed ways in which this interaction could be disrupted to abrogate IL-22 signalling as a therapeutic strategy.

Interleukin-20 and interleukin-24 are expressed by monocytes and keratinocytes and similar to IL-22, these cytokines have been found to play a role in skin homeostasis and pathology. It follows, that strategies to inhibit or reduce signalling downstream of IL-22R by blocking the binding of ligands that activate this receptor could have therapeutic utility, particularly in the treatment of skin conditions such as psoriasis and atopic dermatitis.

Antibodies that bind to IL-22R and block the interaction between IL-22 and IL-22R have been developed. For example, WO2011/061119 describes a humanised IL-22R antibody produced from a mouse anti-human monoclonal antibody originally described in WO2006/047249. This humanised antibody, which will be referred to herein as “280-346-TSY” was shown to inhibit IL-22 signalling via IL-22RA in a cell proliferation assay, and inhibited IL-23-induced ear inflammation in a mouse model of psoriasis.

## **SUMMARY**

The present disclosure improves upon the state of the art by providing antibodies, or antigen binding fragments thereof, which bind to the cytokine receptor IL-22R, and exhibit properties that are different to IL-22R antibodies described in the prior art. The antibodies or antigen binding fragments thereof typically exhibit combinations of properties that are distinct and in certain cases superior, to the properties of the prior art IL-22R antibodies, particularly the humanised IL-22R antibody described in WO2011/061119. The properties of these antibodies can be particularly advantageous with regard to use in human therapy, particularly for the treatment of conditions such as psoriasis, psoriatic arthritis and atopic dermatitis.

In a first example, the present disclosure provides an antibody, or an antigen binding fragment thereof, which binds to human IL-22R, wherein the antibody or antigen binding fragment thereof binds to an epitope within the IL-22R protein that does not include Tyr60.

In certain examples, the antibodies or antigen binding fragments thereof possess one or more additional properties selected from the following:

- (i) the ability to bind an epitope of human IL-22R located at least in part in the D2 domain of the IL-22R protein;
- 5 (ii) the ability to bind human IL-22R with high affinity;
- (iii) the ability to block binding of IL-22 to human IL-22R;
- (iv) the ability to inhibit IL-22 dependent activation of IL-22R;
- (v) the ability to inhibit IL-20 dependent activation of IL-22R;
- (vi) the ability to inhibit IL-22 and IL-20 dependent activation of IL-22R; and
- 10 (vii) lack of cross-reactivity with murine IL-22R.

The antibodies or antigen binding fragments may exhibit high human homology, as defined elsewhere herein. In certain examples, the antibodies or antigen binding fragments thereof comprise a heavy chain variable domain (VH) and a light chain variable domain (VL) wherein the VH and/or VL domains or one or more complementarity determining regions (CDRs) thereof are derived from an animal of the *Camelidae* family i.e. are camelid-derived. The antibodies or antigen binding fragments exhibiting high human homology or having at least one camelid-derived CDR sequence, VH and/or VL domain may be humanised or germlined variants of VH or VL domains from camelid conventional antibodies, wherein the terms "humanised" and "germlined" are as defined elsewhere herein.

In non-limiting examples the disclosure provides the following antibodies, or antigen binding fragments thereof, which are defined by reference to specific structural characteristics, i.e. specified amino acid sequences of either the CDRs (one or more of SEQ ID NOs: 2, 4, 6, 9, 11, 13, 34, 36, 41, 43 (heavy chain CDRs) or SEQ ID NOs: 16, 18, 20, 23, 25, 27, 47, 54, 57, 59 (light chain CDRs)) or entire variable domains (one or more of SEQ ID NOs: 29, 31, 63, 65 (heavy chain variable domains) or SEQ ID NOs: 30, 32, 62, 64, 66 (light chain variable domains)). All of these antibodies bind to the human cytokine receptor IL-22R.

In one aspect, the present disclosure refers to an antibody, or an antigen-binding fragment thereof, which binds to human interleukin 22 receptor (IL-22R) protein, wherein the antibody or antigen-binding fragment comprises a heavy chain variable domain (VH) and a light chain variable domain (VL), the VH comprising a combination of variable heavy chain CDR sequences: HCDR3 comprising SEQ ID NO: 6; HCDR2 comprising SEQ ID NO: 36; and HCDR1 comprising SEQ ID NO: 34, and the VL comprising combination of variable light chain CDR sequences: LCDR3 comprising SEQ ID NO: 54; LCDR2 comprising SEQ ID NO: 47; and LCDR1 comprising SEQ ID NO: 16.

In particular examples, the antibodies defined by the following structural characteristics may exhibit high human homology, as defined herein. The antibodies may be monoclonal antibodies produced by recombinant means. The CDRs of the following IL-22R antibodies may be camelid-derived, i.e. derived from conventional antibodies raised by immunisation of camelids (specifically llama). The disclosure also provides humanised or human germlined variants, affinity variants and variants containing conservative amino acid substitutions, as defined herein.

Examples of the IL-22R antibodies of the disclosure are now further described by reference to structural characteristics.

In one example, there is provided an antibody or antigen binding fragment thereof, which binds to the cytokine receptor IL-22R, said antibody or antigen binding fragment comprising a heavy chain variable domain (VH) comprising a heavy chain CDR3 selected from:

SEQ ID NO: 6 [VGFSGTYYES], or sequence variant thereof

SEQ ID NO: 13 [PPGPFKAHYNGMKY], or sequence variant thereof,

SEQ ID NO: 43 [PPGPFKAHYNGAKY], or sequence variant thereof,

wherein the sequence variant comprises one, two or three amino acid substitutions (e.g. conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

The heavy chain variable domain of the antibody or antigen binding fragment thereof may alternatively or in addition comprise a heavy chain CDR2 selected from:

SEQ ID NO: 4 [SIYNDGSNTAYSDSVKG], or sequence variant thereof,

SEQ ID NO: 11 [GIHISGGITYYLDVKG], or sequence variant thereof,

SEQ ID NO: 36 [SIYNDASNTAYSDSVKG], or sequence variant thereof,

SEQ ID NO: 41 [GIHISGGITYYTDSVKG], or sequence variant thereof,

wherein the sequence variant comprises one, two or three amino acid substitutions (e.g. conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

The heavy chain variable domain of the antibody or antigen binding fragment thereof may alternatively or in addition comprise a heavy chain CDR1 selected from:

SEQ ID NO: 2 [SYDMS], or sequence variant thereof,

SEQ ID NO: 9 [SYFMS], or sequence variant thereof,

SEQ ID NO: 34 [SYDMN], or sequence variant thereof,

wherein the sequence variant comprises one, two or three amino acid substitutions (e.g. conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

Alternatively or in addition, the antibodies or antigen binding fragment thereof, which bind to the cytokine receptor IL-22R, may comprise a light chain variable domain (VL) comprising a light chain CDR3 selected from:

SEQ ID NO: 20 [QSGSSSANAV], or sequence variant thereof,

SEQ ID NO: 27 [ASYRLYADYV], or sequence variant thereof,  
 SEQ ID NO: 54 [QSGSSSSNAV], or sequence variant thereof,  
 wherein the sequence variant comprises one, two or three amino acid substitutions (e.g. conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

The light chain variable domain of the antibody or antigen binding fragment thereof may alternatively or in addition comprise a light chain CDR2 selected from:

SEQ ID NO: 18 [GNNNRPS], or sequence variant thereof  
 SEQ ID NO: 25 [KVNTRSS], or sequence variant thereof,  
 SEQ ID NO: 47 [GQNNRPS], or sequence variant thereof,  
 SEQ ID NO: 59 [EVNKRSS], or sequence variant thereof,  
 wherein the sequence variant comprises one, two or three amino acid substitutions (e.g. conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

The light chain variable domain of the antibody or antigen binding fragment thereof may alternatively or in addition comprise a light chain CDR1 selected from:

SEQ ID NO: 16 [QGGYYAH], or sequence variant thereof  
 SEQ ID NO: 23 [TGTSRDIGDYNYS], or sequence variant thereof,  
 SEQ ID NO: 57 [TGTSSDIGSYNYVS], or sequence variant thereof,  
 wherein the sequence variant comprises one, two or three amino acid substitutions (e.g. conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

In certain examples, there is provided an antibody or antigen binding fragment thereof, which binds to the cytokine receptor IL-22R, the antibody or antigen binding fragment thereof comprising a combination of variable heavy chain CDR3 (HCDR3), variable heavy chain CDR2 (HCDR2) and variable heavy chain CDR1 (HCDR1) wherein the combination is selected from the group consisting of:

- (i) HCDR3 comprising SEQ ID NO: 6; HCDR2 comprising SEQ ID NO: 36; HCDR1 comprising SEQ ID NO: 34;
- (ii) HCDR3 comprising SEQ ID NO: 43; HCDR2 comprising SEQ ID NO: 41; HCDR1 comprising SEQ ID NO: 9;
- (iii) HCDR3 comprising SEQ ID NO: 6; HCDR2 comprising SEQ ID NO: 4; HCDR1 comprising SEQ ID NO: 2; and

(iv) HCDR3 comprising SEQ ID NO: 13; HCDR2 comprising SEQ ID NO: 11; HCDR1 comprising SEQ ID NO: 9.

Alternatively or in addition, the antibodies or antigen binding fragment thereof, which bind to the cytokine receptor IL-22R may comprise a combination of variable light chain CDR3 (LCDR3), variable light chain CDR2 (LCDR2) and variable light chain CDR1 (LCDR1) selected from the group consisting of:

(i) LCDR3 comprising SEQ ID NO: 54; LCDR2 comprising SEQ ID NO: 47; LCDR1 comprising SEQ ID NO: 16;

(ii) LCDR3 comprising SEQ ID NO: 27; LCDR2 comprising SEQ ID NO: 59; LCDR1 comprising SEQ ID NO: 57;

(iii) LCDR3 comprising SEQ ID NO: 20; LCDR2 comprising SEQ ID NO: 47; LCDR1 comprising SEQ ID NO: 16;

(iv) LCDR3 comprising SEQ ID NO: 20; LCDR2 comprising SEQ ID NO: 18; LCDR1 comprising SEQ ID NO: 16; and

(v) LCDR3 comprising SEQ ID NO: 27; LCDR2 comprising SEQ ID NO: 25; LCDR1 comprising SEQ ID NO: 23.

In certain examples, provided herein are antibodies or antigen binding fragments thereof, which bind to the cytokine receptor IL-22R, wherein the antibodies or antigen binding fragments comprise a combination of variable heavy chain CDR3 (HCDR3), variable heavy chain CDR2 (HCDR2) and variable heavy chain CDR1 (HCDR1), variable light chain CDR3 (LCDR3), variable light chain CDR2 (LCDR2) and variable light chain CDR1 (LCDR1) according to the examples described below.

In one example, provided herein is an antibody or antigen binding fragment thereof, which binds to the cytokine receptor IL-22R and comprises the combination of VH and VL CDR sequences: HCDR3 comprising SEQ ID NO: 6; HCDR2 comprising SEQ ID NO: 36; HCDR1 comprising SEQ ID NO: 34; LCDR3 comprising SEQ ID NO: 54; LCDR2 comprising SEQ ID NO: 47; and LCDR1 comprising SEQ ID NO: 16.

In one example, provided herein is an antibody or antigen binding fragment thereof, which binds to the cytokine receptor IL-22R and comprises the combination of VH and VL CDR sequences: HCDR3 comprising SEQ ID NO: 43; HCDR2 comprising SEQ ID NO: 41; HCDR1 comprising SEQ ID NO: 9; LCDR3 comprising SEQ ID NO: 27; LCDR2 comprising SEQ ID NO: 59; and LCDR1 comprising SEQ ID NO: 57.

In one example, provided herein is an antibody or antigen binding fragment thereof, which binds to the cytokine receptor IL-22R and comprises the combination of VH and VL CDR sequences: HCDR3 comprising SEQ ID NO: 6; HCDR2 comprising SEQ ID NO: 4; HCDR1 comprising SEQ ID NO: 2; LCDR3 comprising SEQ ID NO: 20; LCDR2 comprising SEQ ID NO: 47; and LCDR1 comprising SEQ ID NO: 16.

In one example, provided herein is an antibody or antigen binding fragment thereof, which binds to the cytokine receptor IL-22R and comprises the combination of VH and VL CDR sequences: HCDR3 comprising SEQ ID NO: 6; HCDR2 comprising SEQ ID NO: 4; HCDR1 comprising SEQ ID NO: 2; LCDR3 comprising SEQ ID NO: 20; LCDR2 comprising SEQ ID NO: 18; and LCDR1 comprising SEQ ID NO: 16.

In one example, provided herein is an antibody or antigen binding fragment thereof, which binds to the cytokine receptor IL-22R and comprises the combination of VH and VL CDR sequences: HCDR3 comprising SEQ ID NO: 13; HCDR2 comprising SEQ ID NO: 11; HCDR1 comprising SEQ ID NO: 9; LCDR3 comprising SEQ ID NO: 27; LCDR2 comprising SEQ ID NO: 25; and LCDR1 comprising SEQ ID NO: 23.

In certain examples, provided herein are antibodies or antigen binding fragments thereof, which bind to the cytokine receptor IL-22R, wherein the antibodies or antigen binding fragments comprise a heavy chain variable domain (VH) selected from the following:

- (i) a VH comprising or consisting of the amino acid sequence of SEQ ID NO: 29 or 31
- (ii) an affinity variant or human germlined variant of a VH comprising or consisting of the amino acid sequence of SEQ ID NO: 29 or 31; or
- (iii) a VH comprising or consisting of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98%, at least 99% identity to the amino acid sequence of SEQ ID NO: 29 or 31.

Alternatively or in addition, the antibodies or antigen binding fragments may comprise a light chain variable domain (VL) selected from the following:

- (i) a VL comprising or consisting of the amino acid sequence of SEQ ID NO: 30, 32 or 62
- (ii) an affinity variant or human germlined variant of a VL comprising or consisting of the amino acid sequence of SEQ ID NO: 30, 32 or 62; or

(iii) a VL comprising or consisting of an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98%, at least 99% identity to the amino acid sequence of SEQ ID NO: 30, 32 or 62.

- 5 For examples wherein the domains of the antibodies or antigen binding fragments are defined by a particular percentage sequence identity to a reference sequence, the VH and/or VL domains may retain identical CDR sequences to those present in the reference sequence such that the variation is present only within the framework regions.
- 10 In certain examples, the antibodies of the disclosure may include the CH1 domain, hinge region, CH2 domain and CH3 domain of a human antibody, in particular human IgG1, IgG2, IgG3 or IgG4.

Particularly preferred antibodies of the present disclosure are described below.

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230C9 and antibodies related thereto

In certain examples, there is provided an isolated antibody, or antigen binding fragment thereof, which specifically binds IL-22R, said antibody or antigen binding fragment comprising a heavy chain variable domain wherein:

- 20 the variable heavy chain CDR3 sequence is SEQ ID NO:6 [VGFSGTYYES] or sequence variant thereof;

the variable heavy chain CDR2 sequence is SEQ ID NO:36 [SIYNDASNTAYSDSVKG] or sequence variant thereof; and

- the variable heavy chain CDR1 sequence is SEQ ID NO:34 [SYDMN] or sequence variant thereof, and
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wherein the sequence variant comprises one, two or three amino acid substitutions (e.g., conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

- 30 The antibody or antigen binding fragment may further comprise a light chain variable domain wherein:

the variable light chain CDR3 sequence is SEQ ID NO:54 [QSGSSSSNAV] or sequence variant thereof;

- the variable light chain CDR2 sequence is SEQ ID NO:47 [GQNNRPS] or sequence variant thereof; and
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the variable light chain CDR1 sequence is SEQ ID NO:16 [QGGYYAH] or sequence variant thereof, and

wherein the sequence variant comprises one, two or three amino acid substitutions (e.g., conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

In certain examples, there is provided an isolated antibody, or antigen binding fragment thereof, which specifically binds IL-22R, said antibody or antigen binding fragment comprising a heavy chain variable domain wherein:

- 10 the variable heavy chain CDR3 sequence comprises or consists of SEQ ID NO:6 [VGFSGTYYSES];
- the variable heavy chain CDR2 sequence comprises or consists of SEQ ID NO:36 [SIYNDASNTAYSDSVKG];
- the variable heavy chain CDR1 sequence comprises or consists of SEQ ID NO:34 [SYDMN];
- 15 the variable light chain CDR3 sequence comprises or consists of SEQ ID NO:54 [QSGSSSSNAV];
- the variable light chain CDR2 sequence comprises or consists of SEQ ID NO:47 [GQNNRPS]; and
- the variable light chain CDR1 sequence comprises or consists of SEQ ID NO:16
- 20 [QGGYYAH].

The antibodies or antigen binding fragments thereof may comprise a heavy chain variable domain (VH) comprising the amino acid sequence of SEQ ID NO: 63 and optionally a light chain variable domain (VL) comprising the amino acid sequence of SEQ ID NO: 64. In

- 25 certain examples, provided herein are monoclonal antibodies or antigen binding fragments thereof, comprising a heavy chain variable domain and a light chain variable domain, the heavy chain variable domain comprising a VH sequence with at least 85% sequence identity, or at least 90% sequence identity, or at least 95% sequence identity, or at least 97%, 98% or 99% sequence identity, to the amino acid sequence shown as SEQ ID NO:63
- 30 and/or the light chain variable domain comprising a VL with at least 85% sequence identity, or at least 90% sequence identity, or at least 95% sequence identity, or at least 97%, 98% or 99% sequence identity, to the amino acid sequence shown as SEQ ID NO:64.

- For examples wherein the domains of the antibodies or antigen binding fragments are defined by a particular percentage sequence identity to a reference sequence, the VH and/or
- 35 VL domains may retain identical CDR sequences to those present in the reference sequence such that the variation is present only within the framework regions. In certain examples, the antibodies or antigen binding fragments comprising heavy chain variable domains and/or

light chain variable domains defined as having a particular percentage identity to SEQ ID NOs: 63 and 64, respectively will have the following CDR sequences:

a variable heavy chain CDR3 sequence comprising or consisting of SEQ ID NO:6 [VGFSGTYYSES];

5 a variable heavy chain CDR2 sequence comprising or consisting of SEQ ID NO:36 [SIYNDASNTAYSDSVKG];

a variable heavy chain CDR1 sequence comprising or consisting of SEQ ID NO:34 [SYDMN];

10 a variable light chain CDR3 sequence comprising or consisting of SEQ ID NO:54 [QSGSSSSNAV];

a variable light chain CDR2 sequence comprising or consisting of SEQ ID NO:47 [GQNNRPS]; and

a variable light chain CDR1 sequence comprising or consisting of SEQ ID NO:16 [QGGYYAH].

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In another aspect, the present disclosure refers to an antibody which binds to human interleukin 22 receptor (IL-22R) protein, wherein the antibody comprises a heavy chain comprising a heavy chain variable domain (VH) and a light chain comprising a light chain variable domain (VL), the VH comprising the amino acid sequence of SEQ ID NO: 63 and the VL comprising the amino acid sequence of SEQ ID NO: 64.

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The antibodies which specifically bind IL-22R may comprise at least one full-length immunoglobulin heavy chain and/or at least one full-length lambda or kappa light chain. In certain examples, the antibodies comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 67 and a light chain comprising the amino acid sequence of SEQ ID NO: 68. In certain examples, provided herein are monoclonal antibodies comprising a heavy chain with at least 85% sequence identity, or at least 90% sequence identity, or at least 95% sequence identity, or at least 97%, 98% or 99% sequence identity, to the amino acid sequence shown as SEQ ID NO:67 and/or a light chain with at least 85% sequence identity, or at least 90% sequence identity, or at least 95% sequence identity, or at least 97%, 98% or 99% sequence identity, to the amino acid sequence shown as SEQ ID NO:68. For examples wherein the chains of the antibodies are defined by a particular percentage sequence identity to a reference sequence, the heavy chain and/or light chain may retain identical CDR sequences to those present in the reference sequence such that the variation is present only outside the CDR regions.

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In another aspect, the present disclosure refers to an antibody or antigen-binding fragment thereof, which binds to human interleukin 22 receptor (IL-22R) protein, wherein the antibody or antigen-binding fragment comprises a heavy chain and a light chain, wherein the heavy chain comprises the amino acid sequence of SEQ ID NO: 67 and wherein the light chain comprises the amino acid sequence of SEQ ID NO: 68.

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#### 223G5 and antibodies related thereto

45 In certain examples, there is provided an isolated antibody, or antigen binding fragment thereof, which specifically binds IL-22R, said antibody or antigen binding fragment comprising a heavy chain variable domain wherein:

the variable heavy chain CDR3 sequence is SEQ ID NO:43 [PPGPFKAHYNGAKY] or sequence variant thereof;

the variable heavy chain CDR2 sequence is SEQ ID NO:41 [GIHISGGITYYTDVKG] or sequence variant thereof; and

the variable heavy chain CDR1 sequence is SEQ ID NO:9 [SYFMS] or sequence variant thereof, and

- 5 wherein the sequence variant comprises one, two or three amino acid substitutions (e.g., conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

The antibody or antigen binding fragment may further comprise a light chain variable domain

- 10 wherein:

the variable light chain CDR3 sequence is SEQ ID NO:27 [ASYRLYADYV] or sequence variant thereof;

the variable light chain CDR2 sequence is SEQ ID NO:59 [EVNKRSS] or sequence variant thereof; and

- 15 the variable light chain CDR1 sequence is SEQ ID NO:57 [TGTSSDIGSYNYVS] or sequence variant thereof, and

wherein the sequence variant comprises one, two or three amino acid substitutions (e.g., conservative substitutions, humanising substitutions or affinity variants) in the recited sequence.

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In certain examples, there is provided an isolated antibody, or antigen binding fragment thereof, which specifically binds IL-22R, said antibody or antigen binding fragment comprising a heavy chain variable domain wherein:

the variable heavy chain CDR3 sequence comprises or consists of SEQ ID NO:43

- 25 [PPGPFKAHYNGAKY];

the variable heavy chain CDR2 sequence comprises or consists of SEQ ID NO:41

[GIHISGGITYYTDVKG];

the variable heavy chain CDR1 sequence comprises or consists of SEQ ID NO:9 [SYFMS];

the variable light chain CDR3 sequence comprises or consists of SEQ ID NO:27

- 30 [ASYRLYADYV];

the variable light chain CDR2 sequence comprises or consists of SEQ ID NO:59

[EVNKRSS]; and

the variable light chain CDR1 sequence comprises or consists of SEQ ID NO:57

[TGTSSDIGSYNYVS].

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The antibodies or antigen binding fragments thereof may comprise a heavy chain variable domain (VH) comprising the amino acid sequence of SEQ ID NO: 65 and optionally a light

chain variable domain (VL) comprising the amino acid sequence of SEQ ID NO: 66. In certain examples, provided herein are monoclonal antibodies or antigen binding fragments thereof, comprising a heavy chain variable domain and a light chain variable domain, the heavy chain variable domain comprising a VH sequence with at least 85% sequence identity, or at least 90% sequence identity, or at least 95% sequence identity, or at least 97%, 98% or 99% sequence identity, to the amino acid sequence shown as SEQ ID NO:65 and/or the light chain variable domain comprising a VL with at least 85% sequence identity, or at least 90% sequence identity, or at least 95% sequence identity, or at least 97%, 98% or 99% sequence identity, to the amino acid sequence shown as SEQ ID NO:66.

For examples wherein the domains of the antibodies or antigen binding fragments are defined by a particular percentage sequence identity to a reference sequence, the VH and/or VL domains may retain identical CDR sequences to those present in the reference sequence such that the variation is present only within the framework regions. In certain examples, the antibodies or antigen binding fragments comprising heavy chain variable domains and/or light chain variable domains defined as having a particular percentage identity to SEQ ID NOs: 65 and 66, respectively will have the following CDR sequences:

a variable heavy chain CDR3 sequence comprising or consisting of SEQ ID NO:43 [PPGPFKAHYNGAKY];

a variable heavy chain CDR2 sequence comprising or consisting of SEQ ID NO:41 [GIHISGGITYYTDSVKG];

a variable heavy chain CDR1 sequence comprising or consisting of SEQ ID NO:9 [SYFMS];

a variable light chain CDR3 sequence comprising or consisting of SEQ ID NO:27 [ASYRLYADYV];

a variable light chain CDR2 sequence comprising or consisting of SEQ ID NO:59 [EVNKRSS]; and

a variable light chain CDR1 sequence comprising or consisting of SEQ ID NO:57 [TGTSSDIGSYNYVS].

The antibodies which specifically bind IL-22R may comprise at least one full-length immunoglobulin heavy chain and/or at least one full-length lambda or kappa light chain. In certain examples, the antibodies comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 69 and a light chain comprising the amino acid sequence of SEQ ID NO: 70. In certain examples, provided herein are monoclonal antibodies comprising a heavy chain with at least 85% sequence identity, or at least 90% sequence identity, or at least 95% sequence identity, or at least 97%, 98% or 99% sequence identity, to the amino acid sequence shown as SEQ ID NO:69 and/or a light chain with at least 85% sequence

identity, or at least 90% sequence identity, or at least 95% sequence identity, or at least 97%, 98% or 99% sequence identity, to the amino acid sequence shown as SEQ ID NO:70. For examples wherein the chains of the antibodies are defined by a particular percentage sequence identity to a reference sequence, the heavy chain and/or light chain may retain identical CDR sequences to those present in the reference sequence such that the variation is present only outside the CDR regions.

Where particular antibodies, or antigen-binding regions, are identified as comprising a combination of a VH domain or heavy chain, defined by reference to a specific amino acid sequence, and a VL domain or a light chain, also defined by reference to a specific amino acid sequence, then for each specific VH/VL or heavy chain/light chain combination listed (unless otherwise stated) this definition may be taken to include antibodies, or antigen binding regions, formed by combination of a VH domain/heavy chain having at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% sequence identity to the stated VH/heavy chain amino acid sequence and a VL domain/light chain having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, or at least 99% sequence identity to the stated VL/light chain amino acid sequence. In each case the domains/chains defined by % sequence identity to the stated domain/chain amino acid sequences may retain identical CDR sequences to those present in the stated VH/VL domain or heavy/light chain amino acid sequences, whilst exhibiting amino acid sequence variation within the framework regions or other regions outside the CDR regions.

Unless otherwise stated in the present application, % sequence identity between two amino acid sequences may be determined by comparing these two sequences aligned in an optimum manner and in which the amino acid sequence to be compared can comprise additions or deletions with respect to the reference sequence for an optimum alignment between these two sequences. The percentage of identity is calculated by determining the number of identical positions for which the amino acid residue is identical between the two sequences, by dividing this number of identical positions by the total number of positions in the comparison window and by multiplying the result obtained by 100 in order to obtain the percentage of identity between these two sequences. For example, it is possible to use the BLAST program, "BLAST 2 sequences" (Tatusova et al, "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", FEMS Microbiol Lett. 174:247-250) available on the site <http://www.ncbi.nlm.nih.gov/gorf/bl2.html>, the parameters used being those given by default (in particular for the parameters "open gap penalty": 5, and "extension gap penalty": 2; the matrix chosen being, for example, the matrix "BLOSUM 62" proposed by the

program), the percentage of identity between the two sequences to be compared being calculated directly by the program.

The IL-22R antibodies or antigen binding fragments thereof provided herein may each exhibit one, or any combination, of the following properties/features:

- the antibody or antigen binding fragment may bind to an epitope within the human IL-22R protein that does not include Tyr60;
- the antibody or antigen binding fragment may bind to an epitope located at least in part in the D2 domain of the human IL-22R protein, wherein the D2 domain is amino acid residues 125 to 228 of SEQ ID NO: 71;
- the antibody or antigen binding fragment may bind to human IL-22R with high affinity;
- the antibody or antigen binding fragment may block binding of IL-22 to IL-22R;
- the antibody or antigen binding fragment may inhibit IL-22-dependent activation of IL-22R;
- the antibody or antigen binding fragment may inhibit IL-20-dependent activation of IL-22R;
- the antibody or antigen binding fragment may inhibit IL-22-dependent activation of IL-22R and IL-20-dependent activation of IL-22R;
- the antibody or antigen binding fragment may not cross-react with murine IL-22R.

The IL-22R antibodies or antigen binding fragments thereof provided herein preferably exhibit two or more of the following properties/features:

- the antibody or antigen binding fragment binds to an epitope within human IL-22R protein that does not include Tyr60;
- the antibody or antigen binding fragment binds to human IL-22R with high affinity;
- the antibody or antigen binding fragment inhibits IL-22-dependent activation of IL-22R and IL-20-dependent activation of IL-22R.

The IL-22R antibodies, or antigen binding fragments thereof, provided herein may be chimeric antibodies. In certain examples, the antibodies or antigen binding fragments thereof contain the hinge region, CH2 domain and/or CH3 domain of a human IgG. In certain examples, the antibodies or antigen binding fragments thereof exhibit high homology to a human IgG, preferably a human IgG1, wherein "high human homology" is as defined elsewhere herein. In certain examples, the antibodies or antigen binding fragments thereof comprise a heavy chain variable domain (VH) and a light chain variable domain (VL) wherein the VH and/or VL domains or one or more complementarity

determining regions (CDRs) thereof are derived from an animal of the *Camelidae* family i.e. are camelid-derived, preferably wherein the camelid is a llama.

In further examples, the disclosure also provides polynucleotide molecules which encode the above-listed antibodies and antigen binding fragments, in addition to expression vectors comprising the polynucleotides, host cells containing the vectors and methods of recombinant expression/production of the antibodies described herein.

In a still further example, the disclosure provides a pharmaceutical composition comprising any one of the IL-22R antibodies or antigen binding fragments thereof described herein, and a pharmaceutically acceptable carrier or excipient.

In another aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody or antigen-binding fragment as disclosed herein and at least one pharmaceutically acceptable carrier or excipient.

A still further example of the disclosure concerns methods of medical treatment using the above-listed IL-22R antibodies or antigen binding fragments thereof, particularly in the prophylaxis and/or treatment of conditions such as psoriasis, psoriatic arthritis and atopic dermatitis.

These and other examples of the disclosure will be better appreciated and understood when considered in conjunction with the following description and the accompanying drawings. It should be understood, however, that the following description, while indicating various examples of the disclosure and numerous specific details thereof, is given by way of illustration and not of limitation. Many substitutions, modifications, additions and/or rearrangements may be made within the scope of the disclosure without departing from the spirit thereof, and the disclosure includes all such substitutions, modifications, additions and/or rearrangements.

## **BRIEF DESCRIPTION OF DRAWINGS**

**Figure 1** shows the different receptor complexes that mediate signalling via the cytokines IL-22, IL-20 and IL-24. IL-22R is capable of forming a heterodimeric complex with two different receptor partners, IL-10R $\beta$  (or IL-10R2) and IL-20R $\beta$  (or IL-20R2), and activation of these different complexes by ligand binding triggers signalling via intracellular downstream pathways.

**Figure 2** shows the full-length amino acid sequence of human IL-22R (SEQ ID NO: 71).

**CLAIMS**

1. An antibody, or an antigen-binding fragment thereof, which binds to human interleukin 22 receptor (IL-22R) protein, wherein the antibody or antigen-binding fragment comprises a heavy chain variable domain (VH) and a light chain variable domain (VL), the VH comprising a combination of variable heavy chain CDR sequences: HCDR3 comprising SEQ ID NO: 6; HCDR2 comprising SEQ ID NO: 36; and HCDR1 comprising SEQ ID NO: 34, and the VL comprising combination of variable light chain CDR sequences: LCDR3 comprising SEQ ID NO: 54; LCDR2 comprising SEQ ID NO: 47; and LCDR1 comprising SEQ ID NO: 16.
2. The antibody or antigen-binding fragment of claim 1, wherein the VH domain and/or the VL domain is a humanised or germlined variant of a camelid-derived VH or VL domain.
3. The antibody or antigen-binding fragment of claim 1 which contains the hinge region, CH2 domain and/or CH3 domain of a human IgG.
4. A pharmaceutical composition comprising the antibody or antigen-binding fragment according to claim 1 and at least one pharmaceutically acceptable carrier or excipient.
5. The antibody or antigen-binding fragment of claim 1, wherein the VH comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 63.
6. The antibody or antigen-binding fragment of claim 1, wherein the VH comprises the amino acid sequence of SEQ ID NO: 63.
7. The antibody or antigen-binding fragment of claim 1, wherein the VL comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 64.
8. The antibody or antigen-binding fragment of claim 1, wherein the VL comprises the amino acid sequence of SEQ ID NO: 64.
9. An antibody or antigen-binding fragment thereof, which binds to human interleukin 22 receptor (IL-22R) protein, wherein the antibody or antigen-binding fragment comprises a heavy chain and a light chain, wherein the heavy chain comprises the amino acid sequence of SEQ ID NO: 67 and wherein the light chain comprises the amino acid sequence of SEQ ID NO: 68.

10. A pharmaceutical composition comprising the antibody or antigen-binding fragment according to claim 9 and at least one pharmaceutically acceptable carrier or excipient.
11. An antibody which binds to human interleukin 22 receptor (IL-22R) protein, wherein the antibody comprises a heavy chain comprising a heavy chain variable domain (VH) and a light chain comprising a light chain variable domain (VL), the VH comprising the amino acid sequence of SEQ ID NO: 63 and the VL comprising the amino acid sequence of SEQ ID NO: 64.
12. The antibody of claim 11, further comprising the hinge region, CH2 domain and/or CH3 domain of a human IgG1 antibody.
13. The antibody of claim 11, wherein the heavy chain comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 67.
14. The antibody of claim 11, wherein the heavy chain comprises an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 67.
15. The antibody of claim 11, wherein the heavy chain comprises an amino acid sequence at least 98% identical to the amino acid sequence of SEQ ID NO: 67.
16. The antibody of claim 11, wherein the heavy chain comprises an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 67.
17. The antibody of claim 11, wherein the heavy chain comprises the amino acid sequence of SEQ ID NO: 67.
18. The antibody of claim 11, wherein the light chain comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 68.
19. The antibody of claim 11, wherein the light chain comprises an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 68.
20. The antibody of claim 11, wherein the light chain comprises an amino acid sequence at least 98% identical to the amino acid sequence of SEQ ID NO: 68.

21. The antibody of claim 11, wherein the light chain comprises the amino acid sequence of SEQ ID NO: 68.
22. The antibody of claim 11, wherein the heavy chain comprises an amino acid sequence at  
5 least 95% identical to the amino acid sequence of SEQ ID NO: 67 and wherein the light  
chain comprises an amino acid sequence at least 95% identical to the amino acid sequence  
of SEQ ID NO: 68.
23. A pharmaceutical composition comprising the antibody or antigen-binding fragment  
10 according to claim 11 and at least one pharmaceutically acceptable carrier or excipient.