in chronic autoimmune inflammation and the modulation of IL-23 activity could provide promising therapies against autoimmune diseases.

There is therefore a need for antagonist molecules against IL-23 with beneficial pharmacological properties, which can be used as therapeutic agents to treat diseases, in particular immunological and autoimmune diseases in humans.

Accordingly, one aim of the present invention is to provide anti-IL-23 antagonist molecules, in particular anti-IL-23 antagonist molecules which have high binding affinity to IL-23.

A further aim of the present invention is to provide anti-IL-23 antagonist molecules, which have high specificity for IL-23.

A further aim of the present invention is to provide anti-IL-23 antagonists, which have high blocking activity for the association of IL-23 and its receptor.

A further aim of the present invention is to provide anti-IL-23 antagonists, which have potent cellular activity.

A further aim of the present invention is to provide anti-IL-23 antagonists, which have a favorable bioavailability.

A further aim of the present invention is to provide anti-IL-23 antagonists, which have favorable biophysical properties.

Further aims of the present invention include combinations of any of the aims set forth above.

Summary ~~of the Invention~~

The present ~~invention~~disclosure addresses the above needs and provides antibodies that bind to the p19 subunit of the IL-23 protein. There is provided~~In one aspect,~~ an antibody of the present ~~invention~~disclosure that binds to human IL-23 with high affinity. There is provided~~In another aspect,~~ an antibody of the present ~~invention~~disclosure that inhibits the IL-23 stimulated production of IL-17 from mouse splenocytes. There is provided~~In another aspect,~~ an antibody of the present ~~invention~~disclosure that does not bind to nor antagonize IL-12, which is a closely related family member to IL-23.

In one embodiment, the present ~~invention~~disclosure provides anti-IL-23p19 antibodies that are derived from mouse hybridomas, for example monoclonal antibodies. In one embodiment, the present ~~invention~~disclosure provides full length anti-IL-23p19 antibodies. In

another embodiment, the present ~~invention~~disclosure provides anti-IL-23p19 humanized antibodies, for example humanized monoclonal anti-IL-23p19 antibodies, for example full length humanized monoclonal anti-IL-23p19 antibodies. There is provided~~In one aspect,~~ a humanized antibody of the present ~~invention~~disclosure that binds to human IL-23 with high affinity. There is provided~~In another aspect,~~ a humanized antibody of the present ~~invention~~disclosure that also binds to cynomolgus IL-23 with high affinity. Further, there is provided~~In a further aspect,~~ a humanized antibody of the present ~~invention~~disclosure that inhibits IL-23-induced STAT3 phosphorylation in DB cells. There is provided~~In another aspect,~~ a humanized antibody of the present ~~invention~~disclosure that antagonizes the action of IL-23 by binding to the p19 subunit of IL-23, for example as measured by the inhibition of cytokines such as IL-17 and IL-22, whose production is stimulated by IL-23. There is provided~~In a further aspect,~~ a humanized antibody of the present ~~invention~~disclosure that has a favorable pharmacokinetic (PK) profile. There is provided~~In a further aspect,~~ a humanized antibody of the present ~~invention~~disclosure that has favorable biophysical properties, such as quality, stability or solubility, for example as defined by the percentage of antibody in monomer form.

Further embodiments encompass DNA molecules encoding antibodies of the present ~~invention~~disclosure, expression vectors and host cells comprising such DNA molecules, and methods of making antibodies of the present ~~invention~~disclosure. The present ~~invention~~disclosure further provides therapeutic uses for the antibodies of the present ~~invention~~disclosure, in particular against immunological and autoimmune diseases.

In one aspect, there is provided a humanized anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises:

a) a light chain variable region comprising the amino acid sequence of SEQ ID NO:19 *(CDR1-L)*; the amino acid sequence of SEQ ID NO:20 *(CDR2-L)*; and the amino acid sequence of SEQ ID NO:21 *(CDR3-L)*; and

b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 66 or 67*(CDR1-H)*; the amino acid sequence of SEQ ID NO:64 *(CDR2-H)*; and the amino acid sequence of SEQ ID NO:65 *(CDR3-H)*.

In another aspect, there is provided an antibody or antigen-binding fragment described herein for use in medicine.

In another aspect, there is provided a pharmaceutical composition comprising an antibody or antigen-binding fragment described herein and a pharmaceutically acceptable carrier.

In another aspect, there is provided an isolated polynucleotide comprising a sequence encoding a light chain variable region of an antibody or antibody fragment having the amino acid sequence of SEQ ID NO:158, 160, 162 or 164, and encoding a heavy chain variable region of an antibody or antibody fragment having the amino acid sequence of SEQ ID NO: 166 or 168.

In another aspect, there is provided an expression vector comprising the polynucleotide described herein.

In another aspect, there is provided a host cell comprising:

a) an isolated polynucleotide comprising a sequence encoding a light chain variable region of an antibody or antibody fragment having the amino acid sequence of SEQ ID NO:158, 160, 162 or 164; and

b) an isolated polynucleotide comprising a sequence encoding a heavy chain variable region of an antibody or antibody fragment having the amino acid sequence of SEQ ID NO: 166 or 168.

In another aspect, there is provided a host cell comprising:

a) an isolated polynucleotide comprising a sequence encoding a light chain of an antibody having the amino acid sequence of SEQ ID NO:174 or 180; and

b) an isolated polynucleotide comprising a sequence encoding a heavy chain of an antibody having the amino acid sequence of SEQ ID NO:176 or 178.

In another aspect, there is provided a method for producing an antibody or antigen-binding fragment comprising:

a) obtaining a host cell described herein; and

b) cultivating the host cell.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof comprising a light chain CDR1 (L-CDR1) sequence of SEQ ID NO:1, 4, 6, 7, 8, 11, 15, 18, 19, 22, 27 or 30; a light chain CDR2 (L-CDR2) sequence of SEQ ID NO:2, 5, 9, 12, 16, 20, 23, 25, 28 or 31; a light chain CDR3 (L-CDR3) sequence of SEQ ID NO:3, 10, 13, 14, 17, 21, 24, 26, 29, or 32; a heavy chain CDR1 (H-CDR1) sequence of SEQ ID NO:33, 36, 38, 40, 43, 45, 48, 51, 54, 57, 60, 63, 66, 67, 68, 69, 77 or 80; a heavy chain CDR2 (H-CDR2) sequence of SEQ ID NO:34, 39, 41, 46, 49, 52, 55, 58, 61, 64, 70, 72, 73, 75, 78 or 81; and a heavy chain CDR3 (H-CDR3) sequence of SEQ ID NO:35, 37, 42, 44, 47, 50, 53, 56, 59, 62, 65, 71, 74, 76, 79 or 82. In one embodiment, the anti-IL-23p19 antibody or antigen-binding fragment thereof comprises a light chain variable region comprising a

L-CDR1 listed above, a L-CDR2 listed above and a L-CDR3 listed above, and a heavy chain variable region comprising a H-CDR1 listed above, a H-CDR2 listed above and a H-CDR3 listed above.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:1, 2, 3, 33, 34, and 35, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:4, 5, 3, 36, 34 and 37, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:1, 2, 3, 38, 39 and 35, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:6, 2, 3, 40, 41 and 42, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:7, 2, 3, 43, 41 and 44, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:8, 9, 10, 45, 46 and 47, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:8, 9, 10, 48, 49 and 50, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:11, 12, 13, 51, 52 and 53, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:7, 2, 14, 54, 55 and 56, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:15, 16, 17, 57, 58 and 59, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:18, 16, 17, 60, 61 and 62, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:19, 20, 21, 63, 66, 67 or 68, 64 and 65, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:22, 23, 24, 69, 70 and 71, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:22, 25, 26, 55, 72 and 71, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:8, 9, 10, 45, 73 and 74, respectively; or a L-

CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:27, 28, 29, 45, 75 and 76, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:8, 9, 10, 77, 78 and 79, respectively; or a L-CDR1, a L-CDR2, a L-CDR3, a H-CDR1, a H-CDR2 and a H-CDR3 sequence of SEQ ID NO:30, 31, 32, 80, 81 and 82, respectively. In one embodiment, the anti-IL-23p19 antibody or antigen-binding fragment thereof comprises a light chain variable region comprising a L-CDR1, L-CDR2 and L-CDR3 combination listed above, and a heavy chain variable region comprising a H-CDR1, H-CDR2 and H-CDR3 combination listed above.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:84 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:121; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:86 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:123; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:88 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:125; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:90 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:127; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:91 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:128; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:93 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:130; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:95 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:132; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:97 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:134; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:99 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:136; or a light

chain variable region comprising the amino acid sequence of SEQ ID NO:101 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:138; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:103 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:140; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:105 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:142; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:107 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:144; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:109 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:146; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:111 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:148; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:113 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:150; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:115 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:152; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:117 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:154; or a light chain variable region comprising the amino acid sequence of SEQ ID NO:119 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:156.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:158, 160, 162 and 164 and a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:166, 168, 170 and 172.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment

thereof has a K_D for IL-23 of less than 40pM, or a K_D for IL-23 of less than 20pM, or K_D for IL-23 of less than 10pM or K_D for IL-23 of less than 1pM.

In a further embodiment, the present ~~invention~~disclosure provides an anti-IL-23p19 antibody or antigen-binding fragment thereof that binds to human IL-23p19 at an epitope consisting of amino acid residues 108 to 126 and amino acid residues 137 to 151 of SEQ ID NO: 181.

In a further embodiment, the present ~~invention~~disclosure provides an anti-IL-23p19 antibody or antigen-binding fragment thereof that competitively binds to human IL-23p19 with an antibody of the present ~~invention~~disclosure. In one embodiment~~enbodiment~~, the present ~~invention~~disclosure provides an anti-IL-23p19 antibody or antigen-binding fragment thereof that competitively binds to human IL-23p19 with a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO:174 and a heavy chain comprising the amino acid sequence of SEQ ID NO:176. In one embodiment~~enbodiment~~, the present ~~invention~~disclosure provides an anti-IL-23p19 antibody or antigen-binding fragment thereof that competitively binds to human IL-23p19 with a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO:174 and a heavy chain comprising the amino acid sequence of SEQ ID NO:178. In one embodiment~~enbodiment~~, the present ~~invention~~disclosure provides an anti-IL-23p19 antibody or antigen-binding fragment thereof that competitively binds to human IL-23p19 with a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO:180 and a heavy chain comprising the amino acid sequence of SEQ ID NO:176. In one embodiment~~enbodiment~~, the present ~~invention~~disclosure provides an anti-IL-23p19 antibody or antigen-binding fragment thereof that competitively binds to human IL-23p19 with a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 180 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 178.

In one embodiment, the anti-IL-23p19 antibody is a humanized antibody. In one embodiment, the anti-IL-23p19 antibody is a monoclonal antibody. In one embodiment,

the anti-IL-23p19 antibody is a full length antibody. In one embodiment, the anti-IL-23p19 antibody is a humanized monoclonal antibody, for example a full length humanized monoclonal antibody. In one embodiment the antigen-binding fragment is a Fab, $F(ab')_2$, or single chain Fv fragment. In one embodiment, the antigen-binding fragment comprises a light chain variable region and a heavy chain variable region.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises the amino acid sequence of SEQ ID NO:19 *(CDR1-L)*; the amino acid sequence of SEQ ID NO:20 *(CDR2-L)*; the amino acid sequence of SEQ ID NO:21 *(CDR3-L)*: the amino acid sequence of SEQ ID NO:63, 66, 67 or 68 *(CDR1-H)*; the amino acid sequence of SEQ ID NO:64 *(CDR2-H)*; and the amino acid sequence of SEQ ID NO:65 *(CDR3-H)*.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises the amino acid sequence of SEQ ID NO:19 *(CDR1-L)*; the amino acid sequence of SEQ ID NO:20 *(CDR2-L)*; the amino acid sequence of SEQ ID NO:21 *(CDR3-L)*: the amino acid sequence of SEQ ID NO:66 *(CDR1-H)*; the amino acid sequence of SEQ ID NO:64 *(CDR2-H)*; and the amino acid sequence of SEQ ID NO:65 *(CDR3-H)*.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:19 *(CDR1-L)*; the amino acid sequence of SEQ ID NO:20 *(CDR2-L)*; and the amino acid sequence of SEQ ID NO:21 *(CDR3-L)*; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 63, 66, 67 or 68 *(CDR1-H)*; the amino acid sequence of SEQ ID NO:64 *(CDR2-H)*; and the amino acid sequence of SEQ ID NO:65 *(CDR3-H)*.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 or antigen-binding fragment thereof antibody, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:19 *(CDR1-L)*; the amino acid sequence of SEQ ID NO:20 *(CDR2-L)*; and the amino acid sequence of SEQ ID NO:21 *(CDR3-L)*; and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:66 *(CDR1-H)*; the amino acid sequence of SEQ ID NO:64 *(CDR2-H)*; and the amino acid sequence of SEQ ID NO:65 *(CDR3-H)*.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of any one of SEQ ID NO:158, 160, 162 or 164; and a heavy chain variable region comprising the amino acid sequence any one of SEQ ID NO:166, 168, 170 or 172.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:160 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:166.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:160 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:168.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of

SEQ ID NO:158 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:166.

In one embodiment, the present ~~invention~~disclosure further provides an anti-IL-23p19 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:158 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:168.

In one embodiment, the anti-IL-23p19 antibody is a humanized antibody. In one embodiment, the anti-IL-23p19 antibody is a monoclonal antibody. In one embodiment, the anti-IL-23p19 antibody is a full length antibody. In one embodiment, the anti-IL-23p19 antibody is a humanized monoclonal anti-IL-23p19 antibody, for example a full length humanized monoclonal antibody. In one embodiment, the antigen-binding fragment is a Fab, $F(ab')_2$, or single chain Fv fragment. In one embodiment, the antigen-binding fragment comprises a light chain variable region and a heavy chain variable region.

In one embodiment, the present ~~invention~~disclosure further provides an antibody comprising the amino acid sequence SEQ ID NO:166 or 168 linked to a human IgG1, IgG2, IgG3, IgG4, IgM, IgA or IgE heavy chain constant region. An antibody comprising the amino acid sequence of SEQ ID NO: 166 or 168 linked to a human IgG1 heavy chain constant region. An antibody comprising the amino acid sequence of SEQ ID NO:158 or 160 linked to a human kappa or lambda light chain constant region. An antibody comprising the amino acid sequence of SEQ ID NO: 158 or 160 linked to a human kappa light chain constant region.

In one embodiment, the present ~~invention~~disclosure further provides an antibody comprising the amino acid sequence of SEQ ID NO:166 or 168 linked to a human IgG1 heavy chain constant region; and the amino acid sequence of SEQ ID NO:158 or 160 linked to a human kappa light chain constant region.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain variable region comprising the amino acid sequence selected from the group consisting of any one of SEQ ID NO:158, 160, 162 and 164 and a heavy chain variable region comprising the amino acid sequence selected from the group consisting of any one of SEQ ID NO:166, 168, 170 and 172.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain variable region comprising the amino acid sequence of SEQ ID NO:160 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:166.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain variable region comprising the amino acid sequence of SEQ ID NO:160 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:168.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain variable region comprising the amino acid sequence of SEQ ID NO:158 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:166.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain variable region comprising the amino acid sequence of SEQ ID NO:158 and a heavy chain variable region comprising the amino acid sequence SEQ ID NO:168.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO:174 or 180 and a heavy chain comprising the amino acid sequence of SEQ ID NO:176 or 178.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO:174 and a heavy chain comprising the amino acid sequence of SEQ ID NO:176.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO:174 and a heavy chain comprising the amino acid sequence of SEQ ID NO:178.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO:180 and a heavy chain comprising the amino acid sequence of SEQ ID NO:176.

In one embodiment, the present ~~invention~~disclosure further provides a humanized monoclonal anti-IL-23p19 antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 180 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 178.

In a further embodiment, the present ~~invention~~disclosure relates to an anti-IL-23p19 antibody or antigen-binding fragment thereof comprising a humanized light chain variable domain comprising the CDRs of SEQ ID NO:160 and framework regions having an amino acid sequence at least 90% identical to the amino acid sequence of the framework regions of the variable domain light chain amino acid sequence of SEQ ID NO:160 and a humanized heavy chain variable domain comprising the CDRs of SEQ ID NO:166 and framework regions having an amino acid sequence at least 90% identical to the amino acid sequence of the framework regions of the variable domain heavy chain amino acid sequence of SEQ ID NO:166. In one embodiment, the anti-IL-23p19 antibody is a

humanized monoclonal antibody, for example a full length humanized monoclonal antibody.

In a further embodiment, the present ~~invention~~disclosure relates to an anti-IL-23p19 antibody or antigen-binding fragment thereof comprising a humanized light chain variable domain comprising the CDRs of SEQ ID NO:160 and framework regions having an amino acid sequence at least 90% identical to the amino acid sequence of the framework regions of the variable domain light chain amino acid sequence of SEQ ID NO:160 and a humanized heavy chain variable domain comprising the CDRs of SEQ ID NO:168 and framework regions having an amino acid sequence at least 90% identical to the amino acid sequence of the framework regions of the variable domain heavy chain amino acid sequence of SEQ ID NO:168. In one embodiment, the anti-IL-23p19 antibody is a humanized monoclonal antibody, for example a full length humanized monoclonal antibody.

In a further embodiment, the present ~~invention~~disclosure relates to an anti-IL-23p19 antibody or antigen-binding fragment thereof comprising a humanized light chain variable domain comprising the CDRs of SEQ ID NO:158 and framework regions having an amino acid sequence at least 90% identical to the amino acid sequence of the framework regions of the variable domain light chain amino acid sequence of SEQ ID NO:158 and a humanized heavy chain variable domain comprising the CDRs of SEQ ID NO:166 and framework regions having an amino acid sequence at least 90% identical to the amino acid sequence of the framework regions of the variable domain heavy chain amino acid sequence of SEQ ID NO:166. In one embodiment, the anti-IL-23p19 antibody is a humanized monoclonal antibody, for example a full length humanized monoclonal antibody.

In a further embodiment, the present ~~invention~~disclosure relates to an anti-IL-23p19 antibody or antigen-binding fragment thereof comprising a humanized light chain variable ~~domain~~ comprising the CDRs of SEQ ID NO:158 and framework regions having an amino acid sequence at least 90% identical to the amino acid sequence of the framework regions

of the variable domain light chain amino acid sequence of SEQ ID NO:158 and a humanized heavy chain variable domain comprising the CDRs of SEQ ID NO:168 and framework regions having an amino acid sequence at least 90% identical to the amino acid sequence of the framework regions of the variable domain heavy chain amino acid sequence of SEQ ID NO:168. In one embodiment, the anti-IL-23p19 antibody is a humanized monoclonal antibody, for example a full length humanized monoclonal antibody.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized by a K_D for human IL-23 equal or less than 1 pM. T~~In one aspect, t~~here is no shift in binding on-rate in 50% human serum. There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it blocks IL-23 binding to human IL-23R/Fc in vitro.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it does not bind to human IL-12.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it inhibits human IL-23 induced IL-17 production in mouse splenocytes with IC_{50}'s equal or less than 20 pM.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it inhibits human IL-23 induced STAT3 phosphorylation in human DB cells with IC_{50}'s equal or less than 40 pM.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it has no predicted activity in ADCC/CDC.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it has a K_D equal or less than 1 pM for cynomolgus monkey IL-23.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it has no cross reactivity to mouse or rat IL-23.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it inhibits human IL-23 induced IL-17 and IL-22 production in a mouse ear at 80% or greater inhibition of both cytokines at 1 mg/kg.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized by a melting temperature of 83°C as determined by differential scanning calorimetry.

There is provided~~In one aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized by solubility equal or greater than 100 mg/ml, as measured by UV spectroscopy and monitored by turbidity.

There is provided~~In a further aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it is present in at least 90% monomer form, or in at least 92% monomer form, or in at least 95% monomer form in a buffer.

There is provided~~In a further aspect,~~ a humanized anti-IL-23p19 antibody of the present ~~invention~~disclosure that may be further characterized in that it remains in at least 90% monomer form, or in at least 92% monomer form, or in at least 95% monomer form in a buffer for one month or for four months.

There is provided~~In one aspect,~~ the humanized anti-IL-23p19 antibody that is a humanized monoclonal antibody, for example a full length humanized monoclonal antibody.

Further embodiments encompass a DNA molecule encoding a variable light chain region above, a DNA molecule encoding a variable heavy chain region above, a DNA molecule encoding a light chain region above, or a DNA molecule encoding a heavy chain region above.

Further embodiments encompass an expression vector containing a DNA molecule above. In one embodiment, an expression vector comprises a DNA molecule encoding the constant heavy chain and/or the constant light chain, respectively, linked to the DNA molecule encoding the variable heavy chain and/or the variable light chain, respectively. Further embodiments encompass a host cell carrying one or more expression vectors above. In one embodiment, a host is a mammalian cell.

Further embodiments encompass a method for producing an antibody or antigen-binding fragment thereof above comprising transfecting a mammalian host cell with

one or more of the vectors above, cultivating the host cell and recovering and purifying the antibody or antigen-binding fragment thereof.

Further embodiments encompass a method for producing an antibody or antigen-binding fragment thereof above comprising obtaining a mammalian host cell comprising one or more of the vectors above, and cultivating the host cell. In one embodiment, the method further comprises recovering and purifying the antibody or antigen-binding fragment thereof.

In one embodiment, the present ~~invention~~disclosure further provides an antibody or antigen-binding fragment thereof above for use in medicine. In one embodiment, the use is the treatment of an inflammatory disease, of an autoimmune disease, of a respiratory disease, of a metabolic disorder or of cancer. In one embodiment, the use is for the treatment of psoriasis, inflammatory bowel disease (Crohn's disease, ulcerative colitis), psoriatic arthritis, multiple sclerosis, rheumatoid arthritis, or ankylosing spondylitis. In one embodiment, the use is for the treatment of psoriasis. In one embodiment, the use is for the treatment of inflammatory bowel disease.

In one embodiment, the present ~~invention~~disclosure further provides a pharmaceutical composition comprising an antibody molecule or antigen-binding fragment above and a pharmaceutically acceptable carrier.

In one embodiment, the present ~~invention~~disclosure further provides a method for treating an inflammatory disease, an autoimmune disease, a respiratory disease, a metabolic disorder or cancer comprising administering to a subject in need thereof, for example a patient, an effective amount of an anti-IL-23p19 antibody or antigen-binding fragment thereof above, or a pharmaceutical composition comprising the antibody or antigen-binding fragment thereof. In one embodiment, the antibody or antigen-binding fragment is administered by a parenteral route of administration, or is administered intravenously or subcutaneously. In one embodiment, the antibody or antigen-binding fragment is administered subcutaneously. In one embodiment, the disease is

psoriasis, inflammatory bowel disease (Crohn's disease, ulcerative colitis), psoriatic arthritis, multiple sclerosis, rheumatoid arthritis, or ankylosing spondylitis. In one embodiment, the disease is psoriasis. In one embodiment, the disease is inflammatory bowel disease.

In one embodiment, the present ~~invention~~disclosure further provides a method for inhibiting the binding of IL-23 to the IL-23 receptor on a mammalian cell, comprising administering to the cell an antibody molecule or antigen-binding fragment above, whereby signaling mediated by the IL-23 receptor is inhibited.

In one embodiment, the present ~~invention~~disclosure further provides a method for treating a subject having an IL-23-associated disorder, comprising administering to the subject an antibody or antigen-binding fragment above, which antibody or antigen-binding fragment binds to human IL-23.

In one embodiment, the present ~~invention~~disclosure further provides a method for detecting and/or quantifying IL-23 levels in a biological sample by contacting the sample with an antibody or antigen binding fragment above and detecting binding of the antibody or fragment thereof with IL-23p19. This information can be used to diagnose an IL-23-associated disorder. Thus, methods are provided for diagnosing an IL-23-associated disorder or for determining if a subject has an increased risk of developing an IL-23-associated disorder, wherein the method comprises contacting a biological sample from a subject with an antibody or antigen binding fragment above and detecting binding of the antibody or antigen binding fragment to IL-23p19 to determine the expression or concentration of IL-23.

In one embodiment, the present ~~invention~~disclosure further provides a method for inhibiting the binding of IL-23 to the IL-23 receptor on a cell, comprising administering to the cell or cellular environment an antibody or antigen-binding fragment above, whereby signaling mediated by the IL-23 receptor is inhibited.