

WHAT IS CLAIMED IS:

1. ~~A method of treating an autoimmune disease such as Sjögren's syndrome in a human patient, the method comprising administering to the patient in need thereof at least one dose of~~ Use of an isolated antibody, or antigen-binding portion thereof, that specifically binds to human CD40, wherein the antibody or antigen binding portion thereof comprises a first polypeptide portion comprising a heavy chain variable region, and a second polypeptide portion comprising a light chain variable region, wherein:

the heavy chain variable region comprises (i) a CDR1 comprising SYWMH (SEQ ID NO: 1), a CDR2 comprising QINPTTGRSQYNEKFKT (SEQ ID NO: 2), and a CDR3 comprising WGLQPFAY (SEQ ID NO: 3); and

the light chain variable region comprises a CDR1 comprising KASQDVSTAVA (SEQ ID NO: 7), a CDR2 comprising SASYRYT (SEQ ID NO: 8), and a CDR3 comprising QQHYSTPWT (SEQ ID NO: 9),

in the manufacture of a medicament for the treatment of Sjögren's syndrome in a human patient,

wherein at least one dose of the antibody, or antigen binding portion thereof is to be administered to the patient,

wherein the dose is selected from 0.3 milligrams (mg) to 1000 mg of the antibody, or antigen binding portion thereof.

~~2. The method of claim 1, wherein the autoimmune disease is Sjögren's syndrome.~~

23. The ~~use method~~ of claim 1 ~~or~~ 2, wherein the isolated antibody or antigen-binding portion thereof comprises a human IgG1 Fc domain comprising a mutation at Kabat position 238 that reduces binding to Fc-gamma-receptors (FcγRs), wherein proline 238 (P238) is mutated to one of the residues selected from the group consisting of lysine, serine, alanine, arginine, and tryptophan.

34. The use method of any one of the preceding claims, wherein the administration is sub-cutaneous and the dose is from 100 mg to 1000 mg of the antibody or antigen-binding portion thereof.

5 45. The use method of any one of the preceding claims, wherein the administration is sub-cutaneous and the dose is 100 mg, 200 mg, 300 mg, 600 mg, or 1000 mg of the antibody or antigen-binding portion thereof.

10 56. The use method of any one of the preceding claims, wherein the administration is sub-cutaneous, the dose is from 100 mg to 1000 mg of the antibody or the antigen-binding portion thereof, and the use method comprises at least four iterations of the administration administering step.

15 67. The use method of any one of the preceding claims, wherein the administration is sub-cutaneous, the dose is from 100 to 600 mg of the antibody to be administered weekly, and the use method comprises at least four iterations of the administration administering step.

20 78. The use method of ~~any one of claims 1-3~~ claim 1 or claim 2, wherein the administration is intravenous and the dose is from 0.3 mg to 1000 mg of the antibody or antigen-binding fragment thereof.

25 89. The use method of claim 78, wherein the administration is intravenous, and the dose is from 100 mg, 150 mg, 300 mg, or 600 mg of the antibody or antigen-binding fragment thereof.

910. The use method of claim 78 or 89, wherein the administration is intravenous and the dose is selected from 100 mg, 300 mg, or 600 mg of the antibody, and the use method comprises at least four iterations of the administration~~administering step~~.

5 1041. The use method of any one of claims 7-98-10, wherein the administration is intravenous and the dose is selected from 100 mg, 300 mg, or 600 mg of the antibody or the antigen-binding fragment thereof to be administered weekly, and the use method comprises at least four iterations of the administration~~administering step~~.

10 1142. The use method of any one of the preceding claims, wherein the antibody or antigen-binding fragment thereof is to be administered in combination with an immunosuppressive/immunomodulatory and/or anti-inflammatory agent,

15 wherein the antibody or antigen-binding fragment thereof and the immunosuppressive/immunomodulatory and/or anti-inflammatory agent are to be administered sequentially;

wherein the antibody or antigen-binding fragment thereof and the immunosuppressive/immunomodulatory and/or anti-inflammatory agent are to be administered simultaneously; or

20 wherein the antibody or antigen-binding fragment thereof and the immunosuppressive/immunomodulatory and/or anti-inflammatory agent are formulated in a single composition.

25 13.— The method of claim 12, wherein the antibody or antigen-binding fragment thereof and the immunosuppressive/immunomodulatory and/or anti-inflammatory agent are administered sequentially.

~~14. The method of claim 12, wherein the antibody or antigen-binding fragment thereof and the immunosuppressive/immunomodulatory and/or anti-inflammatory agent are administered simultaneously.~~

5 ~~15. The method of claim 12, wherein the antibody or antigen-binding fragment thereof and the immunosuppressive/immunomodulatory and/or anti-inflammatory agent are formulated in a single composition.~~

10 ~~16. The use method of any one of claims 1-15, wherein the antibody, or antigen binding portion thereof, comprises a first polypeptide portion comprising a heavy chain variable region, and a second polypeptide portion comprising a light chain variable region, wherein:~~

15 the heavy chain variable region comprises the amino acid sequence of
 QVQLVQSGAEVKKPGSSVKVCKASGYAFTSYWMHWVRQAPGQGLEWMGQINPT
TGRSQYNEKFKTRVTITADKSTSTAYMELSSLRSED~~TAVYYCAR~~WGLQPFAYWGQ
 GTLVTVSS (SEQ ID NO: 4),

20 and the light chain variable region comprises the amino acid sequence of
 DIQMTQSPSFLSASVGDRVITTCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYT
 GVPSRFGSGSGTDFTLTISSLQPEDFATYYCQQHYSTPWTFGGGTKVEIK (SEQ ID
 NO: 10).

25 ~~17. The use method of any one of claims 1-16, wherein the antibody, or antigen binding portion thereof, comprises an Fc domain which comprises an amino acid sequence selected from:~~

EPKSCDKTHTCPPCPAPELLGGKSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
 EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
 VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE
 WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH
 YTQKSLSLSPG (SEQ ID NO: 13 ; IgG1-P238K (-C-term Lys)),

30 EPKSCDKTHTCPPCPAPELLGGKSVFLFPPKPKDTLMISRTPEVTCVVVDVSH

EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE
WESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH
YTQKSLSLSPGK (SEQ ID NO: 14; IgG1-P238K),

5 *ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL*
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL
GGKSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFF
10 *LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG* (SEQ ID NO: 15; CH1-
IgG1-P238K (-C-term Lys)),

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL
GGKSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
15 *REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ*
VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFF
LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 16;
CH1-IgG1-P238K),

EPKSCDKTHTCPPCPAPELLGGKSVFLFPPKPKDTLMISRTPEVTCVVDVSHED
20 *DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV*
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPG (SEQ ID NO: 17; IgG1f-P238K (-C-term Lys)),

EPKSCDKTHTCPPCPAPELLGGKSVFLFPPKPKDTLMISRTPEVTCVVDVSHED
25 *DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV*
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 18; IgG1f-P238K),

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
30 *QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL*
GGKSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSF

FLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 19;
CH1-IgG1f-P238K (-C-term Lys)),

or

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL

5 *QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL*
GGKSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSF
FLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID No: 20;
10 CH1-IgG1f-P238K).

1418. The ~~use method~~ of any one of claims 1-1317, wherein the antibody, or antigen
binding portion thereof wherein the first polypeptide portion comprises or consists of an
amino acid sequence of

15 *QVQLVQSGAEVKKPGSSVKVSCKASGYAFT***SYWMH***WVRQAPGQGLEWMG*
QINPTTGRSQYNEKFKTR*VTITADKSTSTAYMELSSLRSEDTAVYYCAR***WGLOPF**
AYWGQGT*LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT*
SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
*CPPCPAPELLGGK***SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV**
20 *EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK*
AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP
PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID
NO: 5; HC_Y12XX-hz28-CH1-IgG1-P238K - no terminal lysine); and

the second polypeptide portion comprises or consists of the amino acid sequence of
25 *DIQMTQSPSFLSASVGDRVTITC***KASQDVSTAVA***WYQQKPGKAPKLLIY***SASYRYT**
*GVPSRFGSGSGTDFTLTISLQPEDFATYYC***QQHYSTPWT***FGGGTKVEIKRTVAAPS*
VFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL
SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 11; LC_Y12XX-
hz28-CL).

~~1519.~~ The ~~use method~~ of any one of claims 1-~~1418~~, wherein the antibody, or antigen binding portion thereof, is antibody BMS-986325, wherein the first polypeptide portion has the amino acid sequence of

QVQLVQSGAEVKKPGSSVKV SCKASGYAFT**SYWMH**WVRQAPGQGLEWMG
 5 **QINPTTGRSQYNEKFKT**RVTTITADKSTSTAYMELSSLRSEDTAVYYCAR**WGLQPF**
AYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT
 SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
 CPPCPAPELLGG**K**SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
 EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
 10 AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTP
 PVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPG (SEQ ID
 NO: 5; HC_Y12XX-hz28-CH1-IgG1-P238K - no terminal lysine); and

the second polypeptide portion has the amino acid sequence of
 DIQMTQSPSFLSASVGDRVTTTC**KASQDVSTAVA**WYQQKPGKAPKLLIY**SASYRYT**
 15 GVPSRFGSGSGTDFTLTISSLQPEDFATYYC**QQHYSTPWT**FGGGTKVEIKRTVAAPS
 VFIFPPSDEQLKSGTASVCLNNFYPRKAVQWVKVDNALQSGNSQESVTEQDSKDSYSTSL
 SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 11; LC_Y12XX-
 hz28-CL).

20 ~~1620.~~ A kit ~~for treating an autoimmune disease such as Sjögren's Syndrome in a~~
~~human patient, the kit comprising:~~

_____ (a) a dose of antibody BMS-986325,

wherein the first polypeptide portion has the amino acid sequence of

QVQLVQSGAEVKKPGSSVKV SCKASGYAFT**SYWMH**WVRQAPGQGLEWMG
 25 **QINPTTGRSQYNEKFKT**RVTTITADKSTSTAYMELSSLRSEDTAVYYCAR**WGLQPF**
AYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT
 SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
 CPPCPAPELLGG**K**SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
 EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
 30 AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTP
 PVLDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPG (SEQ ID

NO: 5; HC_Y12XX-hz28-CH1-IgG1-P238K- no terminal lysine); and

the second polypeptide portion has the amino acid sequence of

DIQMTQSPSFLSASVGDRVITTCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYT
GVPSRFGSGSGTDFTLTISSLQPEDFATYYCQQHYSTPWTFGGGTKVEIKRTVAAPS

5 VFIFPPSDEQLKSGTASVCLLNFPYQKQWVNDNALQSGNSQESVTEQDSKDYSL
SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 11; LC_Y12XX-
hz28-CL), or

wherein the dose of antibody BMS-986325 ranges from 0.3 milligrams (mg) to 1000
mg, or

10 wherein the dose of antibody BMS-986325 is a formulation comprising 20 mM
histidine, 250 mM sucrose, 50 micromolar pentetic acid, and 0.05% (w/v) polysorbate 80, pH
6.0,

and

15 (b) instructional material for using the antibody in the use method of any one
of claims 1-15~~19~~.

~~21. The kit of claim 20, wherein the dose of antibody BMS-986325 ranges from~~
~~0.3 milligram (mg) to 1000 mg.~~

20 ~~22. The kit of claim 20 or 21, wherein the dose of antibody BMS-986325 is a~~
~~formulation comprising 20 mM histidine, 250 mM sucrose, 50 micromolar pentetic acid and~~
~~0.05% (w/v) polysorbate 80, pH 6.0.~~