

WHAT IS CLAIMED IS:

1. 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
5 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
10 (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
15 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 use of claim 1, wherein the isolated antibody or antigen-binding portion
20 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.

25 3. The use of any one of the preceding claims, wherein the administration is subcutaneous and the dose is from 100 mg to 1000 mg of the antibody or antigen-binding portion thereof.

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

5 5. The use of any one of the preceding claims, wherein the administration is subcutaneous, the dose is from 100 mg to 1000 mg of the antibody or the antigen-binding portion thereof, and the use comprises at least four iterations of the administration.

10 6. The use of any one of the preceding claims, wherein the administration is subcutaneous, the dose is from 100 to 600 mg of the antibody to be administered weekly, and the use comprises at least four iterations of the administration.

15 7. The use of 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.

8. The use of claim 7, 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.

20 9. The use of claim 7 or 8, wherein the administration is intravenous and the dose is selected from 100 mg, 300 mg, or 600 mg of the antibody, and the use comprises at least four iterations of the administration.

25 10. The use of any one of claims 7-9, 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 comprises at least four iterations of the administration.

11. The use 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,

wherein the antibody or antigen-binding fragment thereof and the

5 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

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

12. The use of any one of claims 1-11, 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 the amino acid sequence of

QVQLVQSGAEVKKPGSSVKVSCKASGYAFTSYWMHWVRQAPGQGLEWMGQINPT
TGRSQYNEKFKTRVTTITADKSTSTAYMELSSLRSEDTAVYYCARWGLQPFAYWGQ

20 GTLVTVSS (SEQ ID NO: 4),

and the light chain variable region comprises the amino acid sequence of

DIQMTQSPSFLSASVGDRVTTTCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYT
 GVPSRFGSGSGTDFTLTISLQPEDFATYYCQQHYSTPWTFGGGTKVEIK (SEQ ID
 NO: 10).

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13. The use of any one of claims 1-12, wherein the antibody, or antigen binding portion thereof, comprises an Fc domain which comprises an amino acid sequence selected from:

EPKSCDKTHTCPPCPAPELLGGGKSVFLFPPKPKDTLMISRTPEVTCVVVDVSH

30 EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK

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

EPKSCDKTHTCPPCPAPELLGGKSVFLFPPKPKDTLMISRTPEVTCVVDVSH
5 EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE
WESNGQPENNYKTTTPVLDSGSSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH
YTQKSLSLSPGK (SEQ ID NO: 14; IgG1-P238K),

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
10 QSSGLYSLSSVTVPPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKTHTCPPCPAPELL
GGKSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGSSFF
LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 15; CH1-
15 IgG1-P238K (-C-term Lys)),

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVTVPPSSSLGTQTYICNVNHKPSNTKVDKRVKPKSCDKTHTCPPCPAPELL
GGKSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
20 VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGSSFF
LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 16;
CH1-IgG1-P238K),

EPKSCDKTHTCPPCPAPELLGGKSVFLFPPKPKDTLMISRTPEVTCVVDVSH
DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
25 SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTTPVLDSGSSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPG (SEQ ID NO: 17; IgG1f-P238K (-C-term Lys)),

EPKSCDKTHTCPPCPAPELLGGKSVFLFPPKPKDTLMISRTPEVTCVVDVSH
DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
30 SNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEMTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTTPVLDSGSSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGK (SEQ ID NO: 18; IgG1f-P238K),

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL

QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL
GGKSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSF
5 FLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 19;
CH1-IgG1f-P238K (-C-term Lys)),

or

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

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14. The use of any one of claims 1-13, wherein the antibody, or antigen binding
portion thereof wherein the first polypeptide portion comprises or consists of an amino acid
sequence of

QVQLVQSGAEVKKPGSSVKVCKASGYAFTSYWMHWVRQAPGQGLEWMG
20 QINPTTGRSQYNEKFKTRVTITADKSTSTAYMELSSLRSEDTAVYYCARWGLQPF
AYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT
SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
CPPCPAPELLGGKSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
25 AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP
PVLDSDGSSFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (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
DIQMTQSPSFLSASVGDRVTTTCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYT
30 GVPSRFGSGSGTDFTLTISLQPEDFATYYCQQHYSTPWTFGGGTKVEIKRTVAAPS
VFIFPPSDEQLKSGTASVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL

SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 11; LC_Y12XX-hz28-CL).

15. The use of any one of claims 1-14, wherein the antibody, or antigen binding portion thereof, is antibody BMS-986325, wherein the first polypeptide portion has the amino acid sequence of

QVQLVQSGAEVKKPGSSVKVSCKASGYAFT**SYWMH**WVRQAPGQGLEWMG
QINPTTGRSQYNEKFKTRVTITADKSTSTAYMELSSLRSEDVAVYYCAR**WGLQPF**
AYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT
 10 SGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
 CPPCPAPELLGG**K**SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
 EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
 AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTP
 PVLDSGDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPG (SEQ ID

15 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**
 GVPSRFGSGSGTDFTLTISSLQPEDFATYYC**QQHYSTPWT**FGGGTKVEIKRTVAAPS
 VFIFPPSDEQLKSGTASVCLLNNFYPRFAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL
 20 *SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC* (SEQ ID NO: 11; LC_Y12XX-hz28-CL).

16. A kit comprising:

(a) a dose of antibody BMS-986325,

wherein the first polypeptide portion has the amino acid sequence of

QVQLVQSGAEVKKPGSSVKVSCKASGYAFT**SYWMH**WVRQAPGQGLEWMG
QINPTTGRSQYNEKFKTRVTITADKSTSTAYMELSSLRSEDVAVYYCAR**WGLQPF**
AYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALT
 SGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHT
 30 CPPCPAPELLGG**K**SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV

EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTP
PVLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPG (SEQ ID
NO: 5; HC_Y12XX-hz28-CH1-IgG1-P238K- no terminal lysine); and

5 the second polypeptide portion has the amino acid sequence of

DIQMTQSPSFLSASVGDRVITTCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYT
GVPSRFGSGSGTDFTLTISLQPEDFATYYCQQHYSTPWTFGGGTKVEIKRTVAAPS
VFIFPPSDEQLKSGTASVCLLNNFYPRQAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL
SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 11; LC_Y12XX-

10 hz28-CL), or

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

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
15 6.0,

and

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

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