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(54) Title: METHOD OF TREATING AN AUTOIMMUNE DISEASE WITH ANTAGONISTIC CD40 MONOCLONAL ANTI-BODIES

FIGURE 1

BMS-986325 Heavy Chain Amino Acid Sequence:

QVQLVQSGAEVKKPGSSVKVSCKASGYAFTSYNMHWVRQAPGQGLEWMGQINPTTGRSQYN
EKFKTRVTITADKSTSTAYMELSSLRSEDTAVYYCARWGLQPFAYWGQGLTVTVSSASTKG
PSVFPPLAPSSKSTSGGTAAALGCLVKDYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSL
SVVTVPSSSLGTQTYICNVNHHKPSNTKVDKRAVEPKSCDKTHTCPPCPAPELLGGKSVFLFP
PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSV
MHEALHNHYTQKSLSLSPG
(SEQ ID NO: 5)

BMS-986325 Light Chain Amino Acid Sequence:

DIQMTQSPSFLSASVGDRTVITCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYTVGPSR
FSGSGSGTDFTLTISLQPEDFATYYCQQHYSTPWTFGGGTKVEIKRTVAAPSVFIFPPSD
EQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSLTLSL
ADYBKHKVYACEVTHQGLSSPVTKSPNRGEC
(SEQ ID NO: 11)

(57) Abstract: A method of treating an autoimmune disease such as Sjögren's Syndrome is provided. The method comprises administration of an antibody or an antigen binding portion thereof that specifically binds an epitope of CD40 associated with antagonism. The antibody or the antigen binding portion thereof does not exhibit CD40 agonist activity in either *in vitro* or *in vivo* preclinical testing. The antibody inhibits CD40L-induced signaling on DCs, resulting at least in part to reduced production of pro-inflammatory cytokines, and reduction of cell surface activation markers, CD86 and CD54. The antibodies can comprise an Fc region containing a mutation that reduces or eliminates binding to Fc receptors, reducing or eliminating Fc gamma receptor (FcγR)-mediated cross-linking or clustering.

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WO 2022/046942 A1

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