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(54) Title: TRIPLE COMBINATION ANTIBODY THERAPIES

Figure 1A

Human IgG1 constant region

ASTKGPSVFPLAPSSKISNCTAALGCLVVDYDFPPQTVSWNSGALISCVHTFPAVLQSGSLYSISVTVVPSSSLGTQYICNVNHRKPSNTKVD
KRVKPKSDNTHFTCPAPPELLGGPSVFLPPKSTLTLMSTEDTAVTCVYVDSHEDPEVFNQYVNCVYDNCVEVFNAAKTREEDQNSTYRAVSV
FTLQHQDWLNGKEVCKVSNKALPAPKEPKAKGQPRFQVYTLPSRREDMTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDG
SFHYSLKTYDPSRWQGNVYFSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 1)

Human IgG1 D269A constant region

ASTKGPSVFPLAPSSKISNCTAALGCLVVDYDFPPQTVSWNSGALISCVHTFPAVLQSGSLYSISVTVVPSSSLGTQYICNVNHRKPSNTKVD
KRVKPKSDNTHFTCPAPPELLGGPSVFLPPKSTLTLMSTEDTAVTCVYVDSHEDPEVFNQYVNCVYDNCVEVFNAAKTREEDQNSTYRAVSV
FTLQHQDWLNGKEVCKVSNKALPAPKEPKAKGQPRFQVYTLPSRREDMTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDG
SFHYSLKTYDPSRWQGNVYFSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 2)

Human IgG1 N297A constant region

ASTKGPSVFPLAPSSKISNCTAALGCLVVDYDFPPQTVSWNSGALISCVHTFPAVLQSGSLYSISVTVVPSSSLGTQYICNVNHRKPSNTKVD
KRVKPKSDNTHFTCPAPPELLGGPSVFLPPKSTLTLMSTEDTAVTCVYVDSHEDPEVFNQYVNCVYDNCVEVFNAAKTREEDQNSTYRAVSV
FTLQHQDWLNGKEVCKVSNKALPAPKEPKAKGQPRFQVYTLPSRREDMTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDG
SFHYSLKTYDPSRWQGNVYFSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 3)

Human IgG2 constant region

ASTKGPSVFPLAPSSKISNCTAALGCLVVDYDFPPQTVSWNSGALISCVHTFPAVLQSGSLYSISVTVVPSSSLGTQYICNVNHRKPSNTKVD
KRVKPKSDNTHFTCPAPPELLGGPSVFLPPKSTLTLMSTEDTAVTCVYVDSHEDPEVFNQYVNCVYDNCVEVFNAAKTREEDQNSTYRAVSV
FTLQHQDWLNGKEVCKVSNKALPAPKEPKAKGQPRFQVYTLPSRREDMTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDG
SFHYSLKTYDPSRWQGNVYFSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 4)

Human IgG3 constant region

ASTKGPSVFPLAPSSKISNCTAALGCLVVDYDFPPQTVSWNSGALISCVHTFPAVLQSGSLYSISVTVVPSSSLGTQYICNVNHRKPSNTKVD
KRVKPKSDNTHFTCPAPPELLGGPSVFLPPKSTLTLMSTEDTAVTCVYVDSHEDPEVFNQYVNCVYDNCVEVFNAAKTREEDQNSTYRAVSV
FTLQHQDWLNGKEVCKVSNKALPAPKEPKAKGQPRFQVYTLPSRREDMTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDG
SFHYSLKTYDPSRWQGNVYFSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 5)

Figure 1B

Human IgG4 constant region (Wild Type)

ASTKGPSVFPLAPSSKISNCTAALGCLVVDYDFPPQTVSWNSGALISCVHTFPAVLQSGSLYSISVTVVPSSSLGTQYICNVNHRKPSNTKVD
KRVKPKSDNTHFTCPAPPELLGGPSVFLPPKSTLTLMSTEDTAVTCVYVDSHEDPEVFNQYVNCVYDNCVEVFNAAKTREEDQNSTYRAVSV
FTLQHQDWLNGKEVCKVSNKALPAPKEPKAKGQPRFQVYTLPSRREDMTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDG
SFHYSLKTYDPSRWQGNVYFSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 6)

Human IgG4 constant region (S211P hinge mutant)

ASTKGPSVFPLAPSSKISNCTAALGCLVVDYDFPPQTVSWNSGALISCVHTFPAVLQSGSLYSISVTVVPSSSLGTQYICNVNHRKPSNTKVD
KRVKPKSDNTHFTCPAPPELLGGPSVFLPPKSTLTLMSTEDTAVTCVYVDSHEDPEVFNQYVNCVYDNCVEVFNAAKTREEDQNSTYRAVSV
FTLQHQDWLNGKEVCKVSNKALPAPKEPKAKGQPRFQVYTLPSRREDMTKNQVSLTCLVKGFPYSDIAVEWESNGQPENNYKTPPVLDSDG
SFHYSLKTYDPSRWQGNVYFSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 7)

Human kappa light chain

RTVAASFVTHFTDEQKSGTASVYCLLNNTYPRKAVQWVNDALQSNQSVTEQSDSDYSLSTLTLSKADYEGHKVYACDYTHQGL
SSPVTGSMNIGLC (SEQ ID NO: 8)

Human lambda light chain

QDTPKAPSVTLFPFSEELQANKATLVCLISDFYPYCAVTVAWKADSSPVKAGVETTPKSKQSNKKYAAASYLSLTPEQWKSIRSYSCQVTHGSG
TVETKTVAFTECS (SEQ ID NO: 9)

(57) Abstract: The present invention is directed to triple combination therapies with anti-TIGIT antibodies, anti-PVRIG antibodies, and checkpoint inhibitors, including anti-PD-1 or anti-PD-L1 antibodies.

[Continued on next page]

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- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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