

CORRECTED VERSION

(19) World Intellectual Property
Organization
International Bureau(43) International Publication Date
06 December 2018 (06.12.2018)

WIPO | PCT

(10) International Publication Number

WO 2018/220446 A9



(51) International Patent Classification:
A61K 39/395 (2006.01) C07K 16/28 (2006.01)

(21) International Application Number:
PCT/IB2018/000696

(22) International Filing Date:
01 June 2018 (01.06.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

62/513,960	01 June 2017 (01.06.2017)	US
62/515,452	05 June 2017 (05.06.2017)	US
62/538,563	28 July 2017 (28.07.2017)	US
62/547,051	17 August 2017 (17.08.2017)	US
62/582,756	07 November 2017 (07.11.2017)	US
62/618,005	16 January 2018 (16.01.2018)	US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP,

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(54) Title: TRIPLE COMBINATION ANTIBODY THERAPIES

Figure 1A

Human IgG1 constant region
ASTKGVSVFTLAPMSKSGCTAALGCLVKDYFPEPVVSWNSGAILSGVHTFPAVLQSSGLYSIVSSVTVPSRSGTQTYTCNVNHRKPSNKTVD
KRVSKVCKPTCPAPFELCGSVFLFPKPKDTLMISRTPEVTCVVDVSHDPEVKFNWYVDGVEVHNAKTRPEEQVSTYRVSVV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTSKARGQPREPQVYTLPSRREMTKNQVSLCLVKGYFSDIAVEWESNGQPENNYKTPPVLDSDGE
FLYSYLTVDKSRWQQGNVPSVSMHLEAHNHTYQKSLSPCK (SEQ ID NO: 1)

Human IgG1 206A constant region
ASTKGVSVFTLAPMSKSGCTAALGCLVKDYFPEPVVSWNSGAILSGVHTFPAVLQSSGLYSIVSSVTVPSRSGTQTYTCNVNHRKPSNKTVD
KRVSKVCKPTCPAPFELCGSVFLFPKPKDTLMISRTPEVTCVVDVSHDPEVKFNWYVDGVEVHNAKTRPEEQVSTYRVSVV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTSKARGQPREPQVYTLPSRREMTKNQVSLCLVKGYFSDIAVEWESNGQPENNYKTPPVLDSDGE
FLYSYLTVDKSRWQQGNVPSVSMHLEAHNHTYQKSLSPCK (SEQ ID NO: 2)

Human IgG1 207A constant region
ASTKGVSVFTLAPMSKSGCTAALGCLVKDYFPEPVVSWNSGAILSGVHTFPAVLQSSGLYSIVSSVTVPSRSGTQTYTCNVNHRKPSNKTVD
KRVSKVCKPTCPAPFELCGSVFLFPKPKDTLMISRTPEVTCVVDVSHDPEVKFNWYVDGVEVHNAKTRPEEQVSTYRVSVV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTSKARGQPREPQVYTLPSRREMTKNQVSLCLVKGYFSDIAVEWESNGQPENNYKTPPVLDSDGE
FLYSYLTVDKSRWQQGNVPSVSMHLEAHNHTYQKSLSPCK (SEQ ID NO: 3)

Human IgG2 constant region
ASTKGVSVFTLAPMSKSGCTAALGCLVKDYFPEPVVSWNSGAILSGVHTFPAVLQSSGLYSIVSSVTVPSRSGTQTYTCNVNHRKPSNKTVD
KRVSKVCKPTCPAPFELCGSVFLFPKPKDTLMISRTPEVTCVVDVSHDPEVKFNWYVDGVEVHNAKTRPEEQVSTYRVSVV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTSKARGQPREPQVYTLPSRREMTKNQVSLCLVKGYFSDIAVEWESNGQPENNYKTPPVLDSDGE
FLYSYLTVDKSRWQQGNVPSVSMHLEAHNHTYQKSLSPCK (SEQ ID NO: 4)

Human IgG3 constant region
ASTKGVSVFTLAPMSKSGCTAALGCLVKDYFPEPVVSWNSGAILSGVHTFPAVLQSSGLYSIVSSVTVPSRSGTQTYTCNVNHRKPSNKTVD
KRVSKVCKPTCPAPFELCGSVFLFPKPKDTLMISRTPEVTCVVDVSHDPEVKFNWYVDGVEVHNAKTRPEEQVSTYRVSVV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTSKARGQPREPQVYTLPSRREMTKNQVSLCLVKGYFSDIAVEWESNGQPENNYKTPPVLDSDGE
FLYSYLTVDKSRWQQGNVPSVSMHLEAHNHTYQKSLSPCK (SEQ ID NO: 5)

Figure 1B

Human IgG1 constant region (Wild Type)
ASTKGVSVFTLAPMSKSGCTAALGCLVKDYFPEPVVSWNSGAILSGVHTFPAVLQSSGLYSIVSSVTVPSRSGTQTYTCNVNHRKPSNKTVD
KRVSKVCKPTCPAPFELCGSVFLFPKPKDTLMISRTPEVTCVVDVSHDPEVKFNWYVDGVEVHNAKTRPEEQVSTYRVSVV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTSKARGQPREPQVYTLPSRREMTKNQVSLCLVKGYFSDIAVEWESNGQPENNYKTPPVLDSDGE
FLYSYLTVDKSRWQQGNVPSVSMHLEAHNHTYQKSLSPCK (SEQ ID NO: 6)

Human IgG4 constant region (S24P hinge mutant)
ASTKGVSVFTLAPMSKSGCTAALGCLVKDYFPEPVVSWNSGAILSGVHTFPAVLQSSGLYSIVSSVTVPSRSGTQTYTCNVNHRKPSNKTVD
KRVSKVCKPTCPAPFELCGSVFLFPKPKDTLMISRTPEVTCVVDVSHDPEVKFNWYVDGVEVHNAKTRPEEQVSTYRVSVV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTSKARGQPREPQVYTLPSRREMTKNQVSLCLVKGYFSDIAVEWESNGQPENNYKTPPVLDSDGE
FLYSYLTVDKSRWQQGNVPSVSMHLEAHNHTYQKSLSPCK (SEQ ID NO: 7)

Human kappa light chain
RTVAAPSFTPTSDQKSCSTASVCLLNFTYPRFAKQWKEVINALQGNGQRVSTQPKDSTSLSTLSKADYERKRVYACLVTHQGL
SPVITKSNRGEI (SEQ ID NO: 8)

Human lambda light chain
GQPKAAISYELTTSSELAQANKATVLCVLSYVEGAVVAVAKLSRSPYKACVLEETPSKQSNKCAASSTLSLTPQWKSHEISQVTHKUS
TVKTVAPTECS (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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KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

- (84) Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

- *with international search report (Art. 21(3))*

(48) Date of publication of this corrected version:

26 December 2019 (26.12.2019)

(15) Information about Correction:

see Notice of 26 December 2019 (26.12.2019)

Previous Correction:

see Notice of 22 August 2019 (22.08.2019)