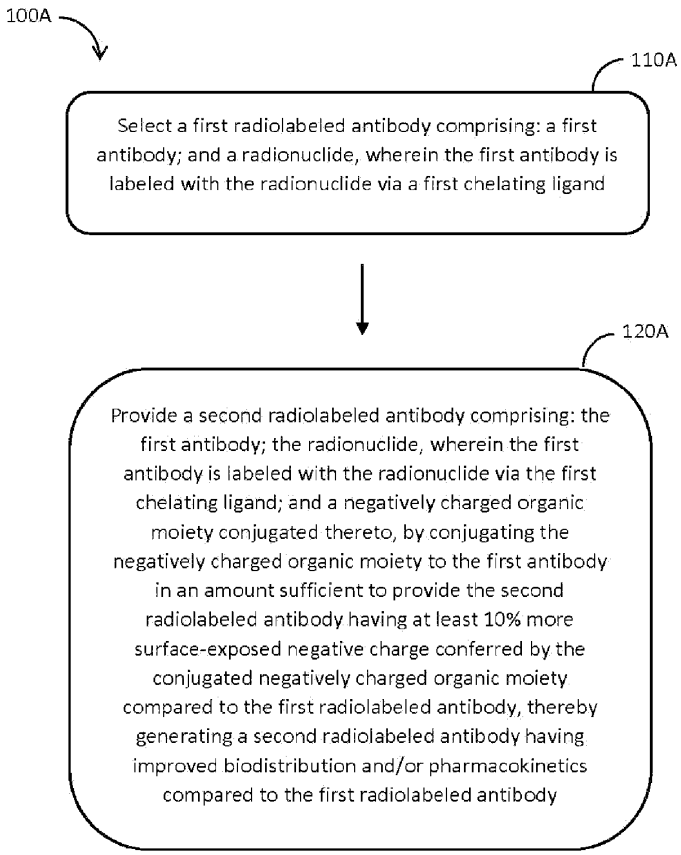
100A
110A
Select a first radiolabeled antibody comprising: a first antibody; and a radionuclide, wherein the first antibody is labeled with the radionuclide via a first chelating ligand
120A
Provide a second radiolabeled antibody comprising: the first antibody; the radionuclide, wherein the first antibody is labeled with the radionuclide via the first chelating ligand; and a negatively charged organic moiety conjugated thereto, by conjugating the negatively charged organic moiety to the first antibody in an amount sufficient to provide the second radiolabeled antibody having at least 10% more surface-exposed negative charge conferred by the conjugated negatively charged organic moiety compared to the first radiolabeled antibody, thereby generating a second radiolabeled antibody having improved biodistribution and/or pharmacokinetics compared to the first radiolabeled antibody

FIG. 1A

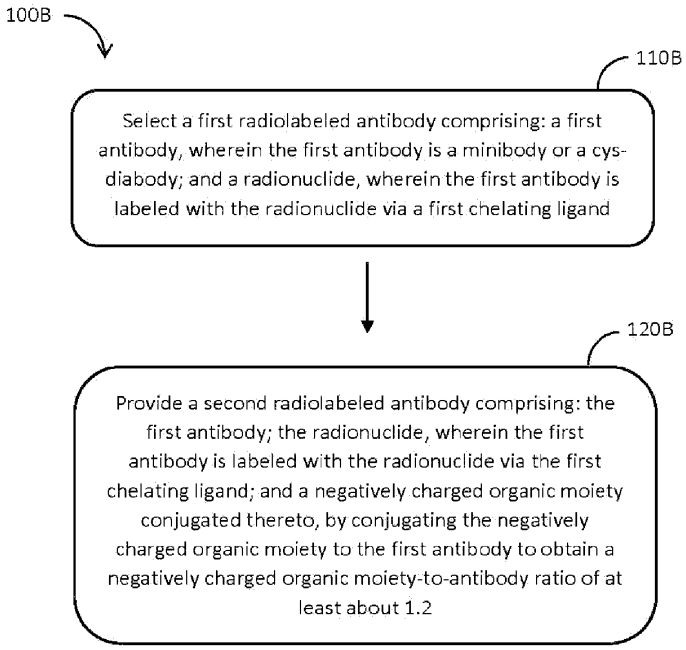
100B
110B
Select a first radiolabeled antibody comprising: a first antibody, wherein the first antibody is a minibody or a cys-diabody; and a radionuclide, wherein the first antibody is labeled with the radionuclide via a first chelating ligand
120B
Provide a second radiolabeled antibody comprising: the first antibody; the radionuclide, wherein the first antibody is labeled with the radionuclide via the first chelating ligand; and a negatively charged organic moiety conjugated thereto, by conjugating the negatively charged organic moiety to the first antibody to obtain a negatively charged organic moiety-to-antibody ratio of at least about 1.2

FIG. 1B

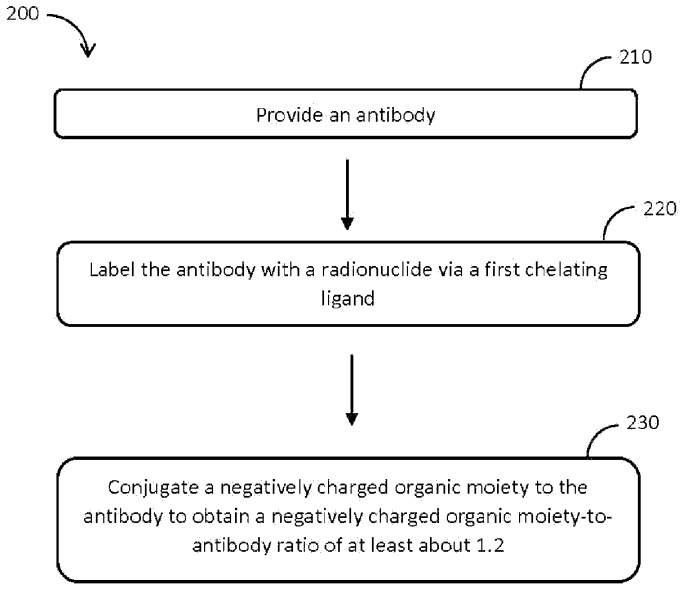
200
210
Provide an antibody
220
Label the antibody with a radionuclide via a first chelating ligand
230
Conjugate a negatively charged organic moiety to the antibody to obtain a negatively charged organic moiety-to-antibody ratio of at least about 1.2

FIG. 2

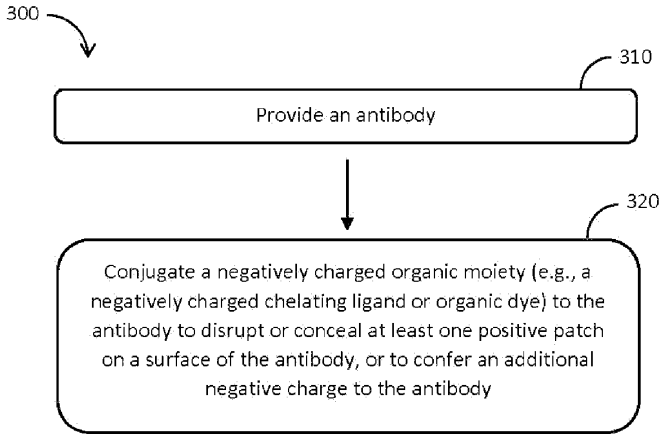
300
310
Provide an antibody
320
Conjugate a negatively charged organic moiety (e.g., a negatively charged chelating ligand or organic dye) to the antibody to disrupt or conceal at least one positive patch on a surface of the antibody, or to confer an additional negative charge to the antibody

FIG. 3

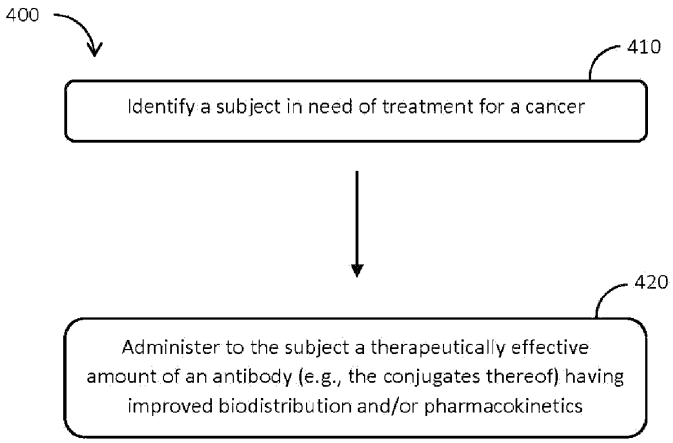
400
410
Identify a subject in need of treatment for a cancer
420
Administer to the subject a therapeutically effective amount of an antibody (e.g., the conjugates thereof) having improved biodistribution and/or pharmacokinetics

FIG. 4

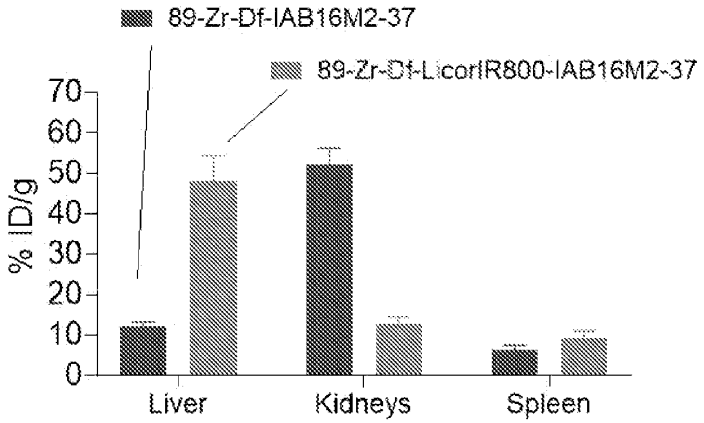
89-Zr-Df-IAB16M2-37
89-Zr-Df-LicorIR800-IAB16M2-37
% ID/g
70
60
50
40
30
20
10
0
Liver
Kidneys
Spleen

FIG. 5

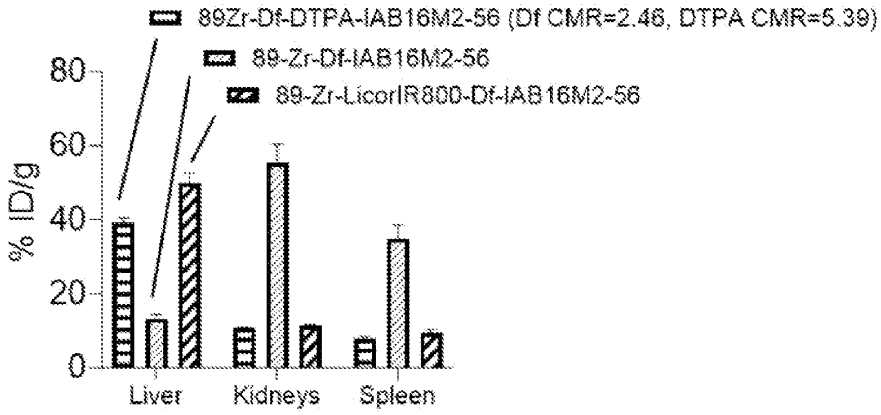
89Zr-Df-DTPA-IAB16M2-56 (Df CMR=2.46, DTPA CMR=5.39)
89-Zr-Df-IAB16M2-56
89-Zr-LicorIR800-Df-IAB16M2-56
% ID/g
80
60
40
20
0
Liver
Kidneys
Spleen

FIG. 6

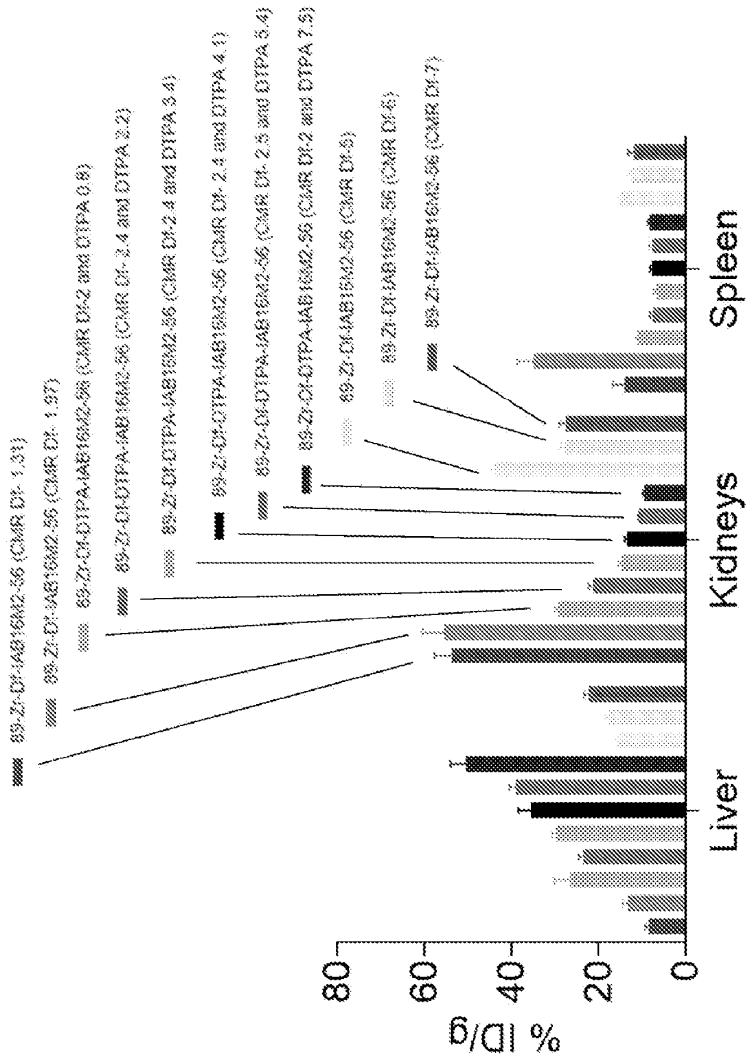
89-Zr-DF-IAB16M2-56 (CMR Df- 1.31)
89-Zr-Df-IAB16M2-56 (CMR Df- 1.97)
89-Zr-Df-DTPA-IAB16M2-56 (CMR Df-2 and DTPA 0.8)
89-Zr-Df-DTPA-IAB16M2-56 (CMR Df- 3.4 and DTPA 2.2)
89-Zr-Df-DTPA-IAB16M2-56 (CMR Df-2.4 and DTPA 3.4)
89-Zr-Df-DTPA-IAB16M2-56 (CMR Df- 2.4 and DTPA 4.1)
89-Zr-Df-DTPA-IAB16M2-56 (CMR Df- 2.5 and DTPA 5.4)
89-Zr-Df-DTPA-IAB16M2-56 (CMR Df-2 and DTPA 7.5)
89-Zr-Df-IAB16M2-56 (CMR Df-5)
89-Zr-Df-IAB16M2-56 (CMR Df-6)
89-Zr-Df-IAB16M2-56 (CMR Df-7)
% ID/g
0
20
40
60
80
Liver
Kidneys
Spleen

FIG. 7

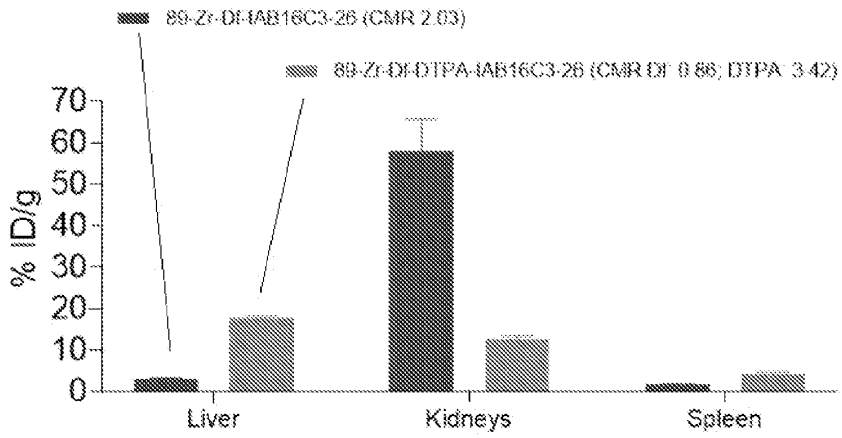
89-Zr-Df-IAB16C3-26 (CMR 2.03)
89-Zr-Df-DTPA-IAB16C3-26 (CMR Df: 0.86; DTPA: 3.42)
% ID/g
70
60
50
40
30
20
10
0
Liver
Kidneys
Spleen

FIG. 8

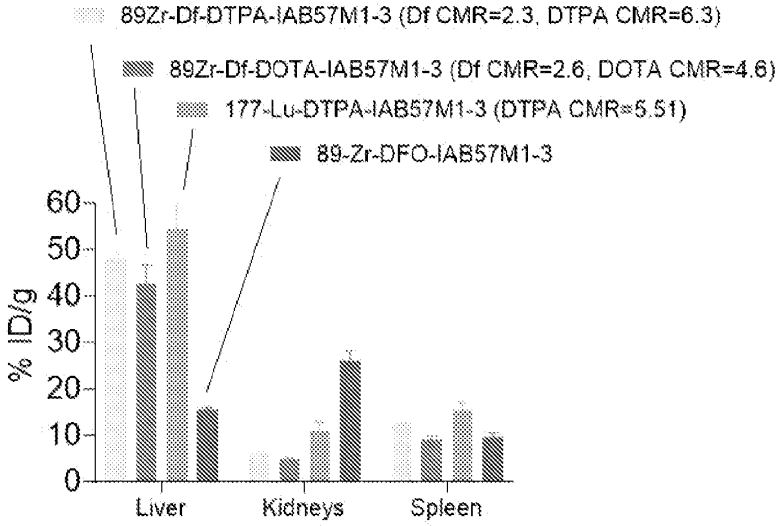
89Zr-Df-DTPA-IAB57M1-3 (Df CMR=2.3, DTPA CMR=6.3)
89Zr-Df-DOTA-IAB57M1-3 (Df CMR=2.6, DOTA CMR=4.6)
177-Lu-DTPA-IAB57M1-3 (DTPA CMR=5.51)
89-Zr-DFO-IAB57M1-3
% ID/g
60
50
40
30
20
10
0
Liver
Kidneys
Spleen

FIG. 9

M1 orientation

S	V_L	L	V_H	H	C_H3

M2 orientation

S	V_H	L	V_L	H	C_H3

S = signal peptide
V_H = Variable domain of heavy chain
L = linker
V_L = Variable domain of light chain
H = hinge
C_H3 = C_H3 domain

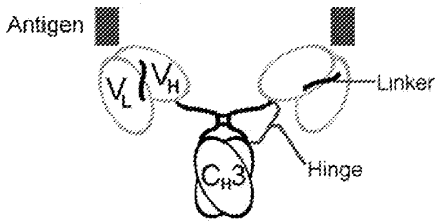

FIG. 10

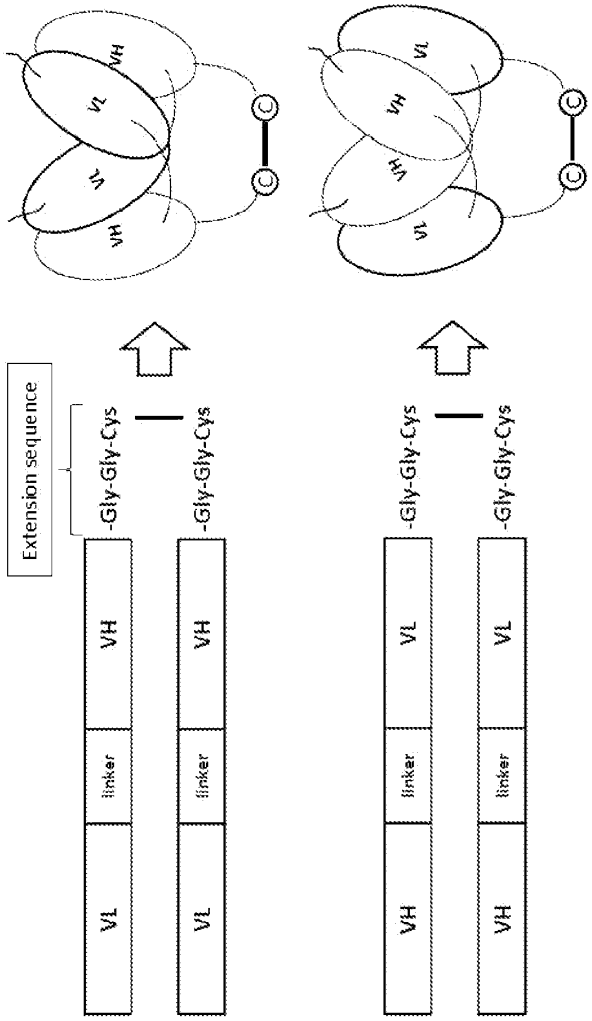
Extension sequence
-Gly-Gly-Cys
-Gly-Gly-Cys
VL
linker
VH
VL
linker
VH
-Gly-Gly-Cys
-Gly-Gly-Cys
VH
linker
VL
VH
linker
VL
VH
VL
VH
VL
VL
VH
VH
VL
C
C
C
C

FIG. 11

IAB16M2-37 (SEQ ID NO: 5)

QVQLVQSGAEVKKPGASVKVSCK**A**S**G**YTFTEYTIHWVRQAPGQRLEWIGGINPNNGIPNYNQKF
KGRVTITVDISASTAYMELSSLRSEDTAVYYCARRRIAYGYDEGHAMDYWGQGTLVTVSSGSTS
GGGSGGGSGGGGSSDIVMTQSPDSLAVSLGERATINCKSSQSLLYSRNQKNYLAWYQQKPGQPP
KLLIFWASTRESGVPDRFSGSG**S**GTDFTLTIS**R**L**EP**ED**F**AVYYCQQY**Y**SYPLTFGQGTKVEIKE
PKSSDKTHTCPPCPPCGGGSSGGGSGGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIA
VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPG

FIG. 12A

IAB16M2-56 (SEQ ID NO: 6)

QVQLVQSGAE VKKPGSSVKV SCKASGFSLT NYDINWVRQA PGQGLEWMGL IWTGGGTNYN
QKFQGRVTIT KDESISTAYM ELSSLRSEDT AVYYCVRGGP LVWYALDYWG QGTLVTVSSG
STSGGGSGGG SGGGGSSDIQ MTQSPSSLSA SVGDRVTITC KASQDVSTAV AWYQQKPGKA
PKLLIYSASY RYTGVPSRFS GSGSGTDFTL TISSLQPEDF ATYYCQQHYS NPRTFGQGTK
VEIKEPKSSD KTHTCPPCPP CGGGSSGGGS GGQPREPQVY TLPPSREEMT KNQVSLTCLV
KGFYPSDIAV EWESNGQPEN NYKTTPPVLD SDGSFFLYSK LTVDKSRWQQ GNVFSCSVME
EALHNHYTQK SLSLSPG

FIG. 12B

IAB16C3-26 (SEQ ID NO: 7)

EIVLTQSPGTLSLSPGERATLSCRASQSVSRSYLAWYQQKPGQAPRLLIIGASTRATGIP

DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQGQVIPPTFGQGTKVEIKGGGSGGGGEVQL

LESGGGLVQPGGSLRLSCAASGFTFSSHAMSWVRQAPGKGLEWVSAIWASGEQYYADSVK

GRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKGWLGNFDYWGQGTLVTVSSGGCPPCPP

C

FIG. 12C

IAB57M1-3

METDTLLLWVLLLWVPGSTG

EIVMTQSPATLSVSPGERATLSCKASQSVSNDVVWYQQ**KPGQAPR**LLIYDASNRYTGIPARFSGSGSGTE
FTLTISSLQSEDFAVYYCQQDYTSPWTFGQGTKLEIKGSTSGGGSGGGSGGGGSSQVQLVQSGAEVKKPG
ASVKVSCKASGYTFTNYGMNWVRQAPGQGLEWMGWINTYTGEPTYADDFKGRVTMTTDTSTSTAYMELRS
LRSDDTAVYYCARIGDSSPSDYWGQGTLVTVSSEP**KSSDK**THTCPPCPPCGGGSSGGGSGGQPREPQVYT
LPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 3)

FIG. 12D

IgG1:

SEQ ID No.: 9

IGHG1*01
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID No.: 10

IGHG1*03
GQPREPQVYTLPPSR**E**H**M**TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID No.: 11

IGHG1*04
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
QQGN**I**FSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID No.: 12

IGHG1*07
GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMHE**G**LHNHYTQKSLSLSPGK

IgG2:

SEQ ID No.: 13

IGHG2*01
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID No.: 14

IGHG2*06
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI**S**VEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID No.: 15

IGHG2*15
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY**N**TTPPMLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMHEALHNHYTQKSLSLSPGK

FIG. 13

IgG3:

SEQ ID No.: 16

IGHG3*01
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSGQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHNRFTQKSLSLSPGK

SEQ ID No.: 17

IGHG3*03
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSGQPENNYNTTPP**V**LDSDGSFFLYS**R**LTVDKSRW
Q**E**GN**V**FSCSVMHEALHNRFTQKSLSLSPGK

SEQ ID No.: 18

IGHG3*06
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSGQPENNY**K**TTPPMLDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHNRFTQKSLSLSPGK

SEQ ID No.: 19

IGHG3*08
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES**N**GQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHNRFTQKSLSLSPGK

SEQ ID No.: 20

IGHG3*13
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSGQPENNY**K**TTPPMLDSDGSFFLYSKLTVDKSRW
Q**E**GNIFSCSVMHEALHNRFTQKSLSLSPGK

SEQ ID No.: 21

IGHG3*14
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES**N**GQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHNR**Y**TQKSLSLSPGK

SEQ ID No.: 22

IGHG3*15
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES**N**GQPENNY**K**TTPPMLDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHNR**Y**TQKSLSLSPGK

FIG. 13 continued

SEQ ID No.: 23

IGHG3*17
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIA**M**EWESSGQPENNY**K**TTPP**V**LDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHNH**Y**TQKSLSLSPGK

SEQ ID No.: 24

IGHG3*20
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES**N**GQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHNR**Y**TQKSLSLSPGK

SEQ ID No.: 25

IGHG3*22
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES**N**GQPENNYNTTPPMLDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHN**HY**TQKSLSLSPGK

SEQ ID No.: 26

IGHG3*23
GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESSGQPENNY**K**TTPP**V**LDSDGSFFLYSKLTVDKSRW
QQGNIFSCSVMHEALHN**HY**TQKSLSLSPGK

IgG4:

SEQ ID No.: 27

IGHG4*01
GQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRW
QEGNVFSCSVMHEALHNHYTQKSLSLSLGK

SEQ ID No.: 28

IGHG4*03
GQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS**K**LTVDKSRW
QEGNVFSCSVMHEALHNHYTQKSLSLSLGK

SEQ ID No.: 29

IGHG4*05
GQPREPQVYTLPPS**R**EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRW
QEGNVFSCSVMHEALHNHYTQKSLSLSLGK

FIG. 13 continued