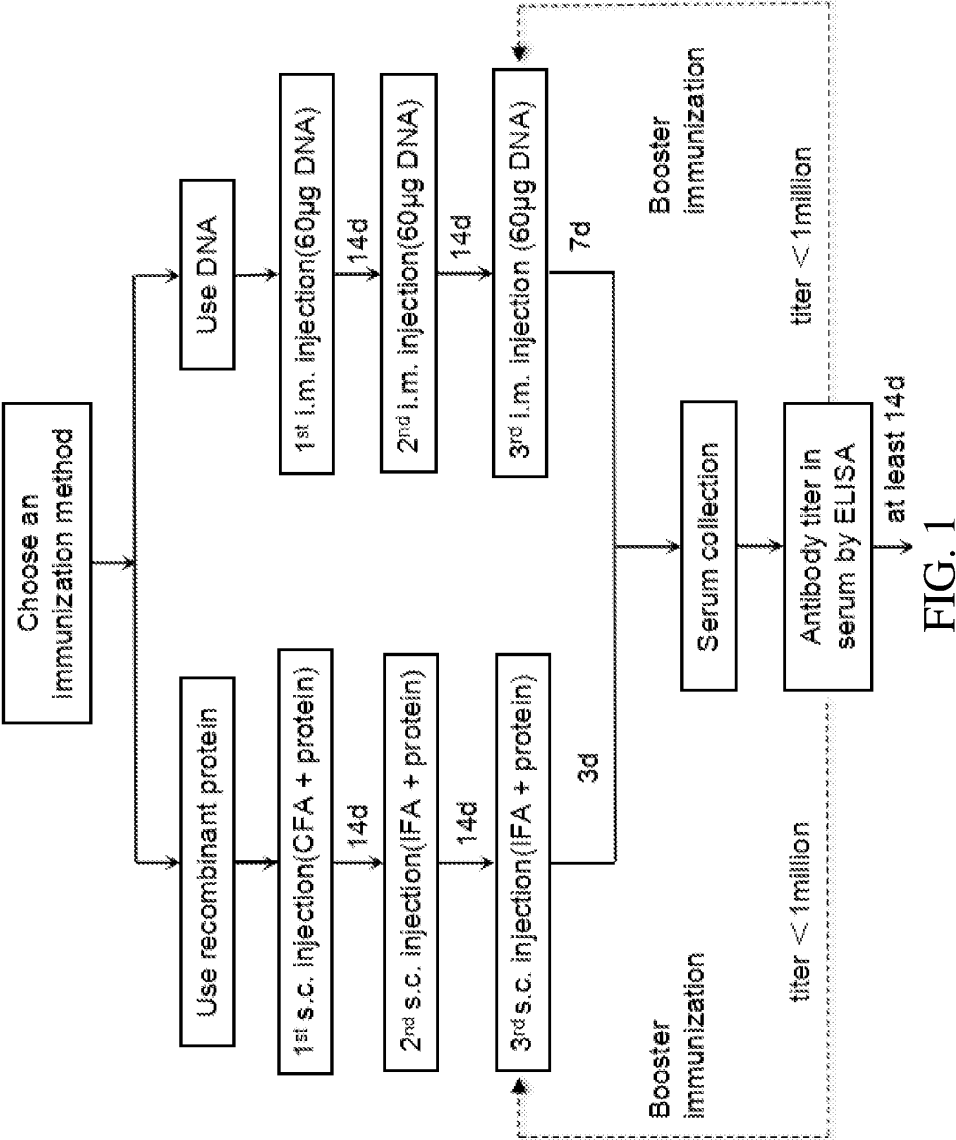




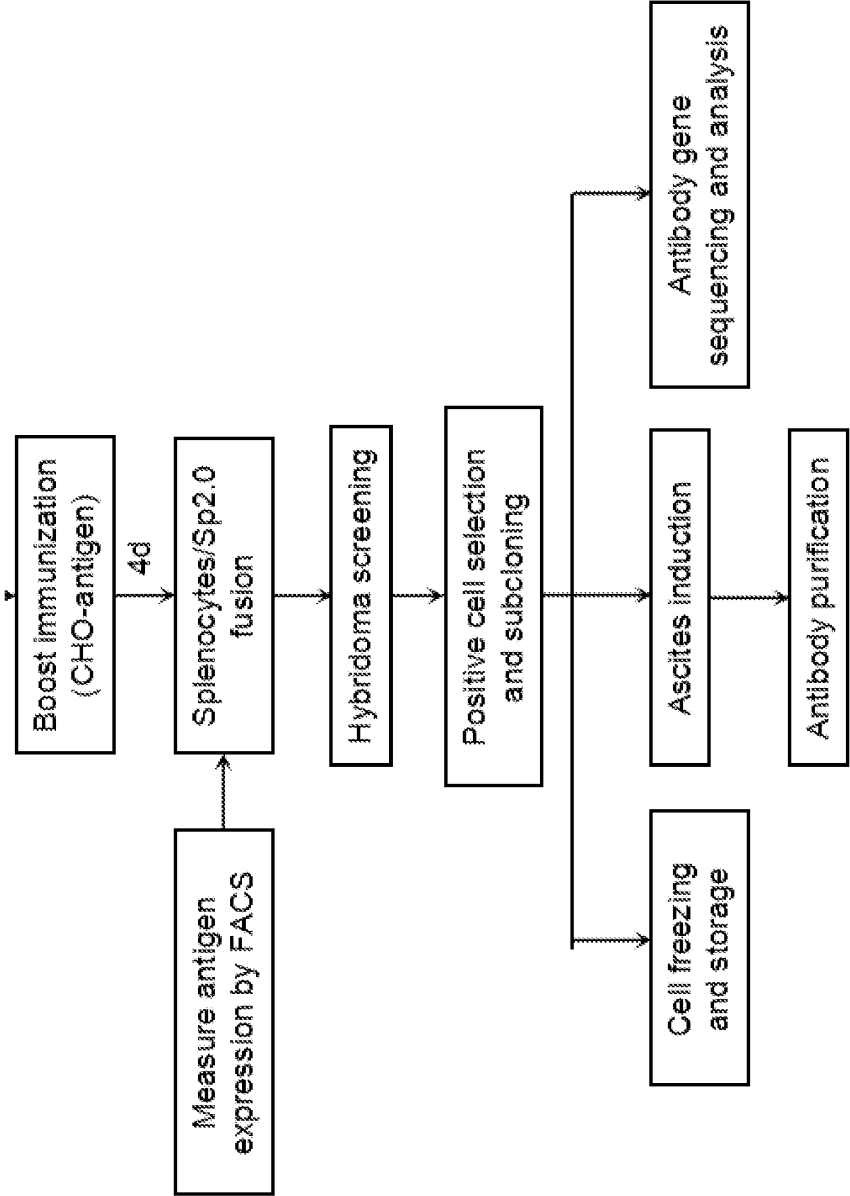


FIG. 2

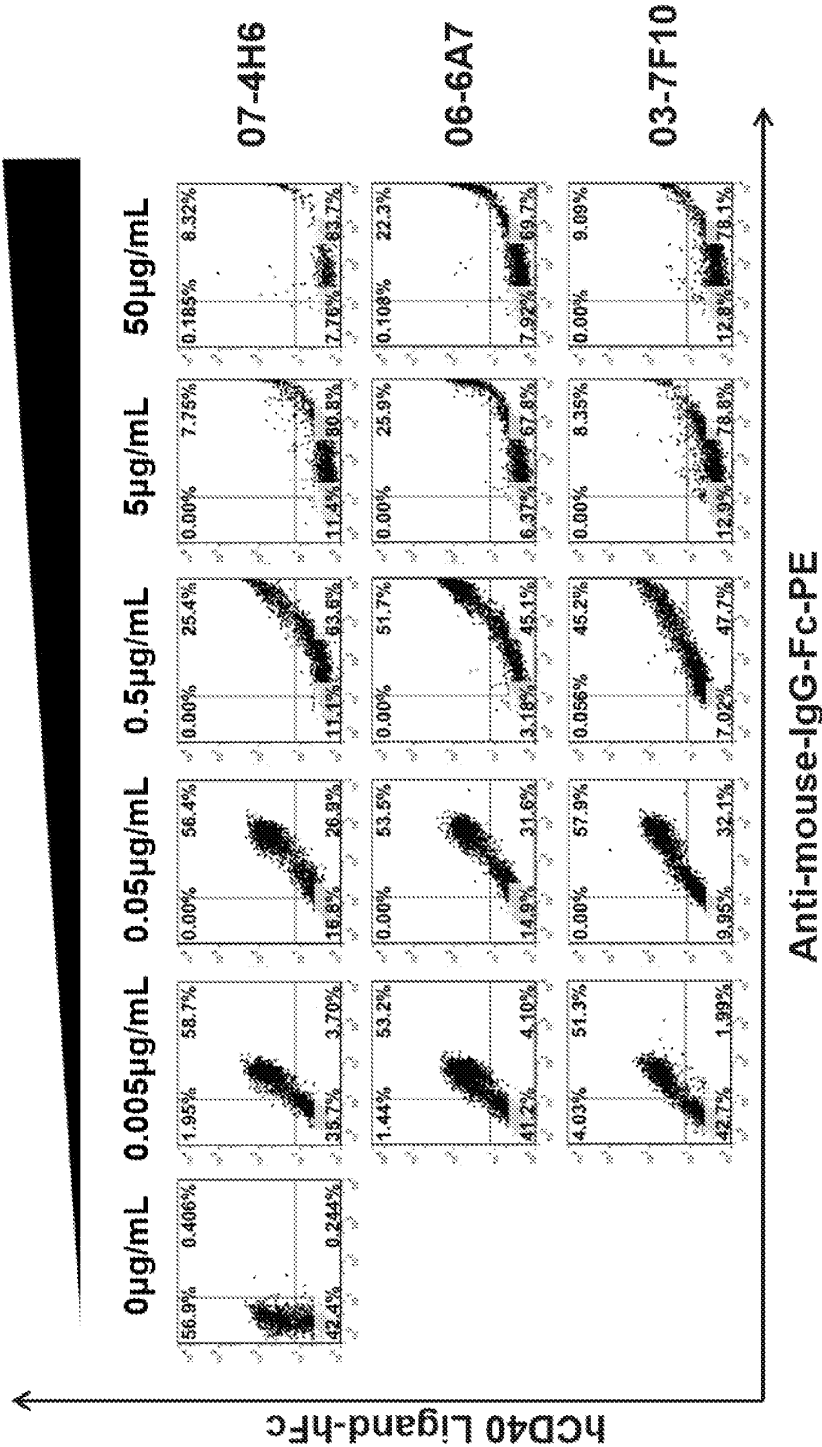


FIG. 3

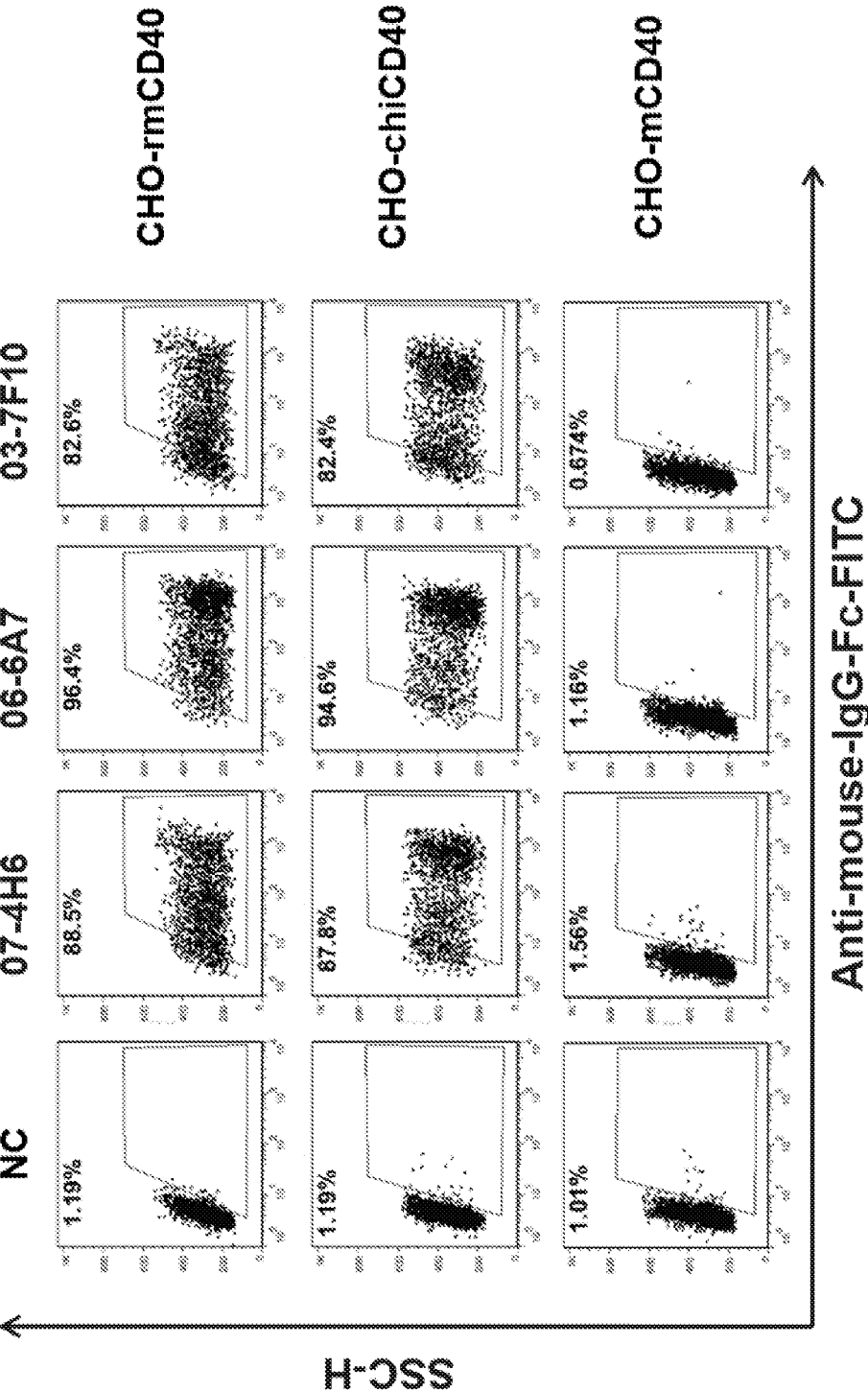


FIG. 4

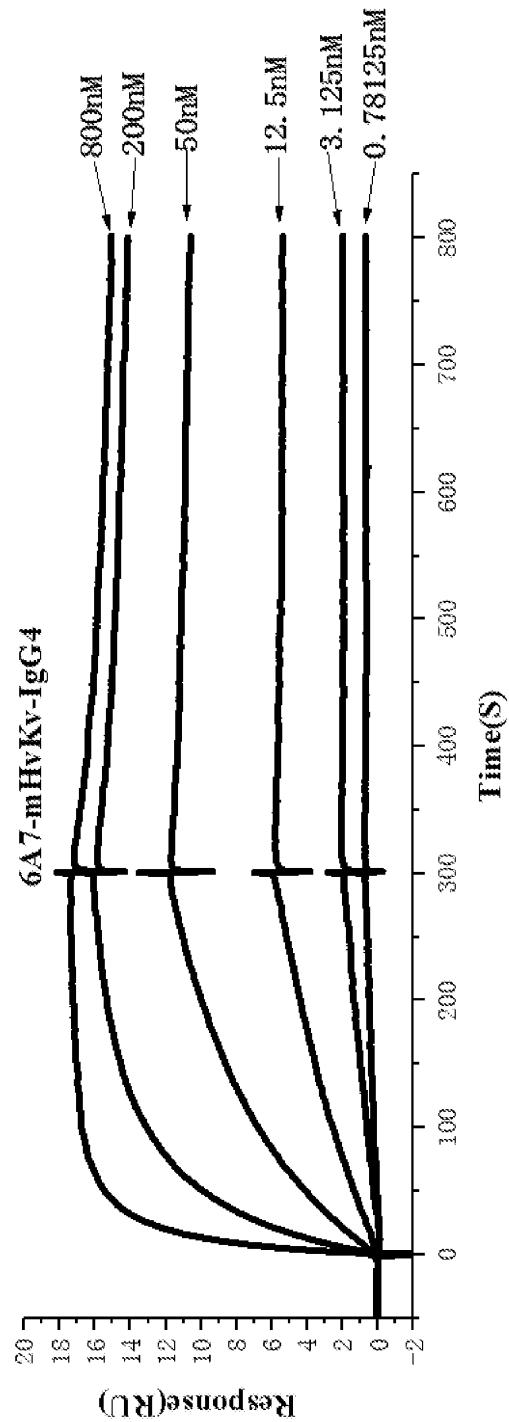


FIG. 5

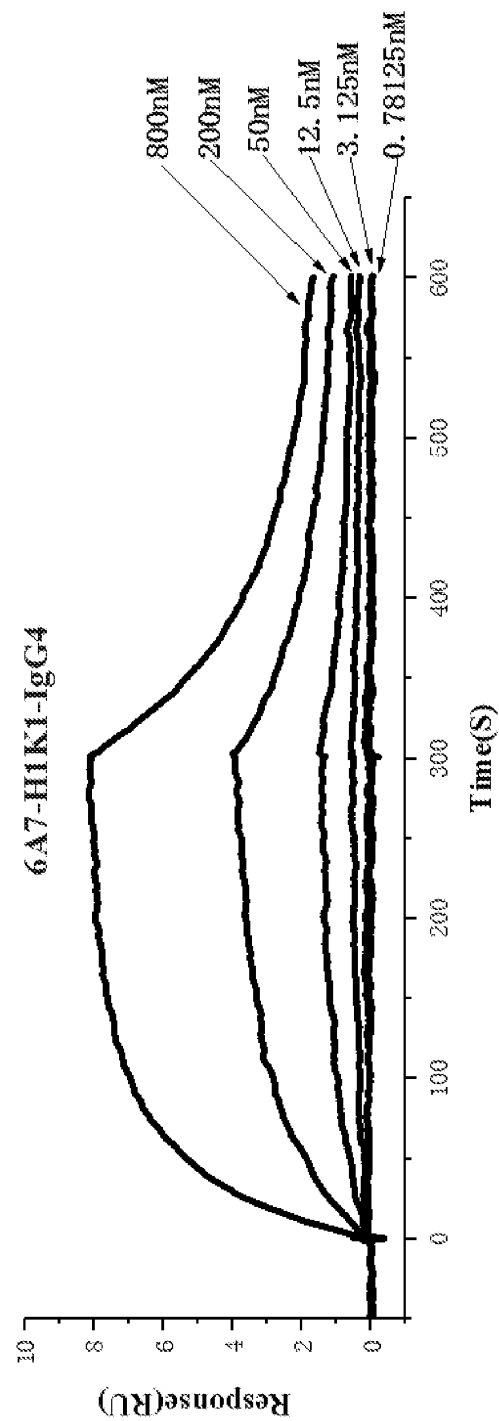


FIG. 6

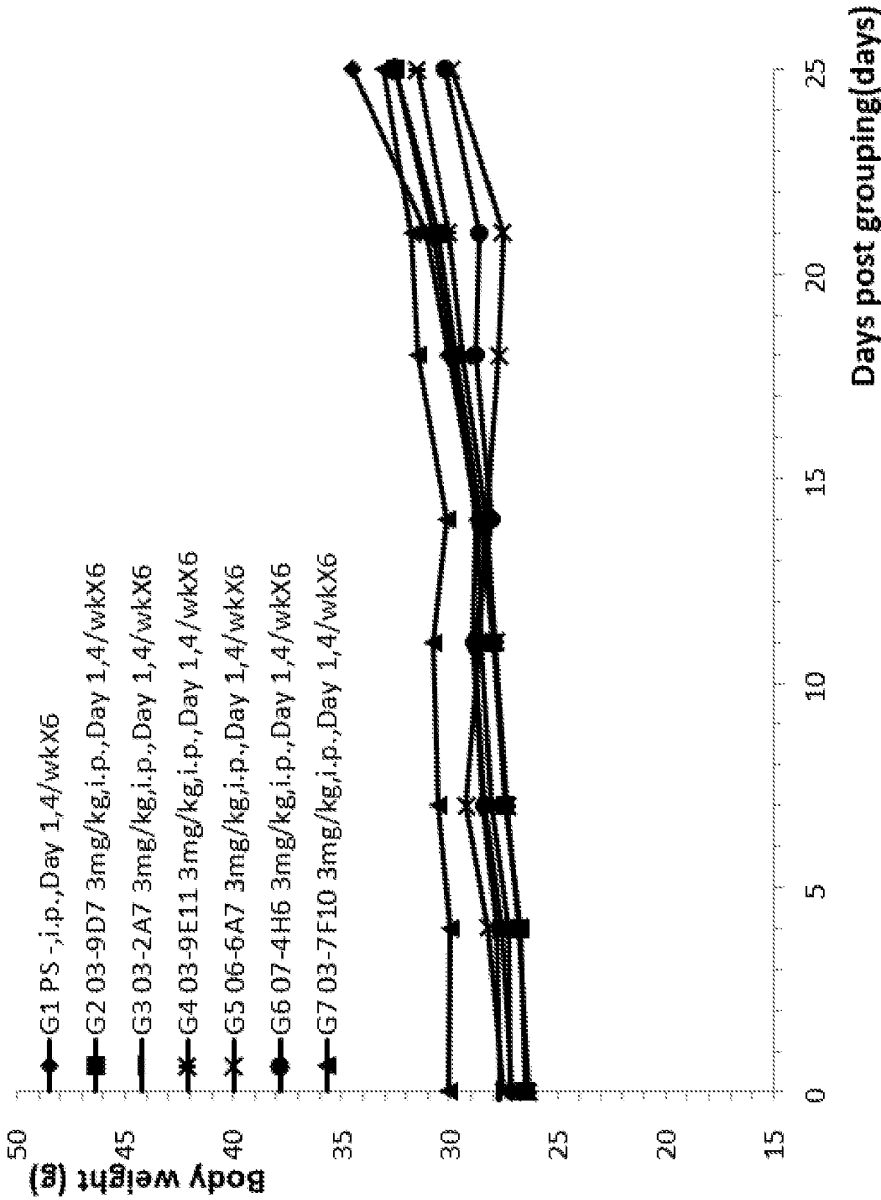


FIG. 7

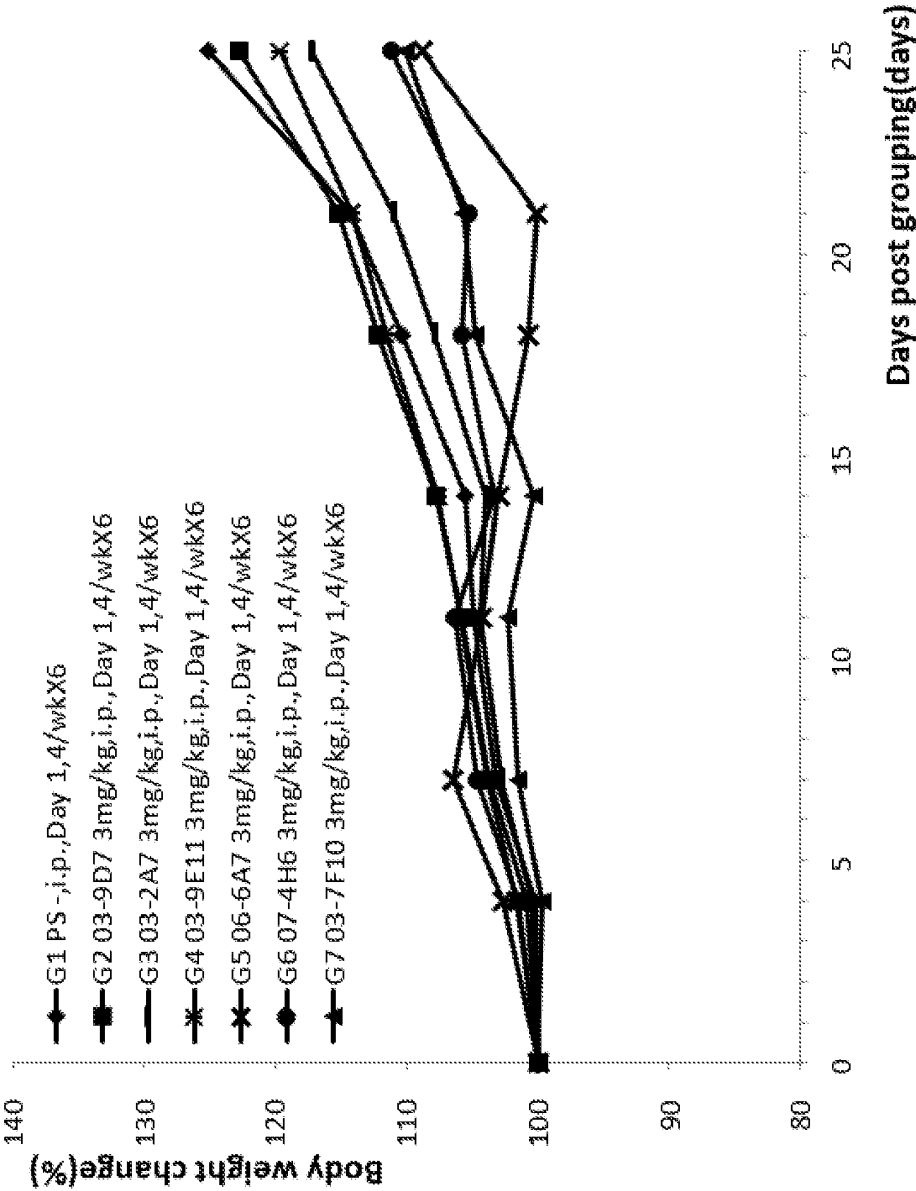


FIG. 8

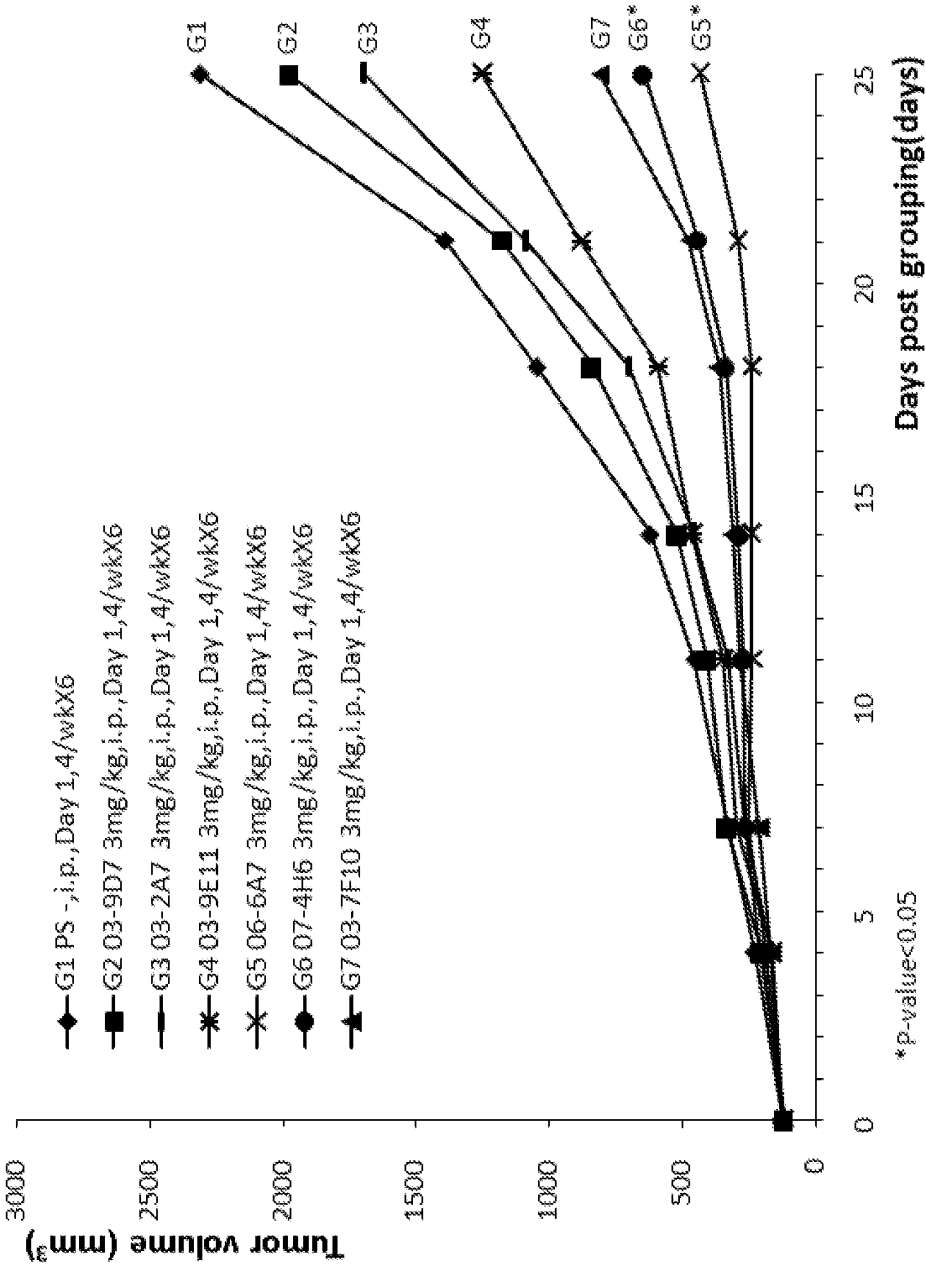


FIG. 9

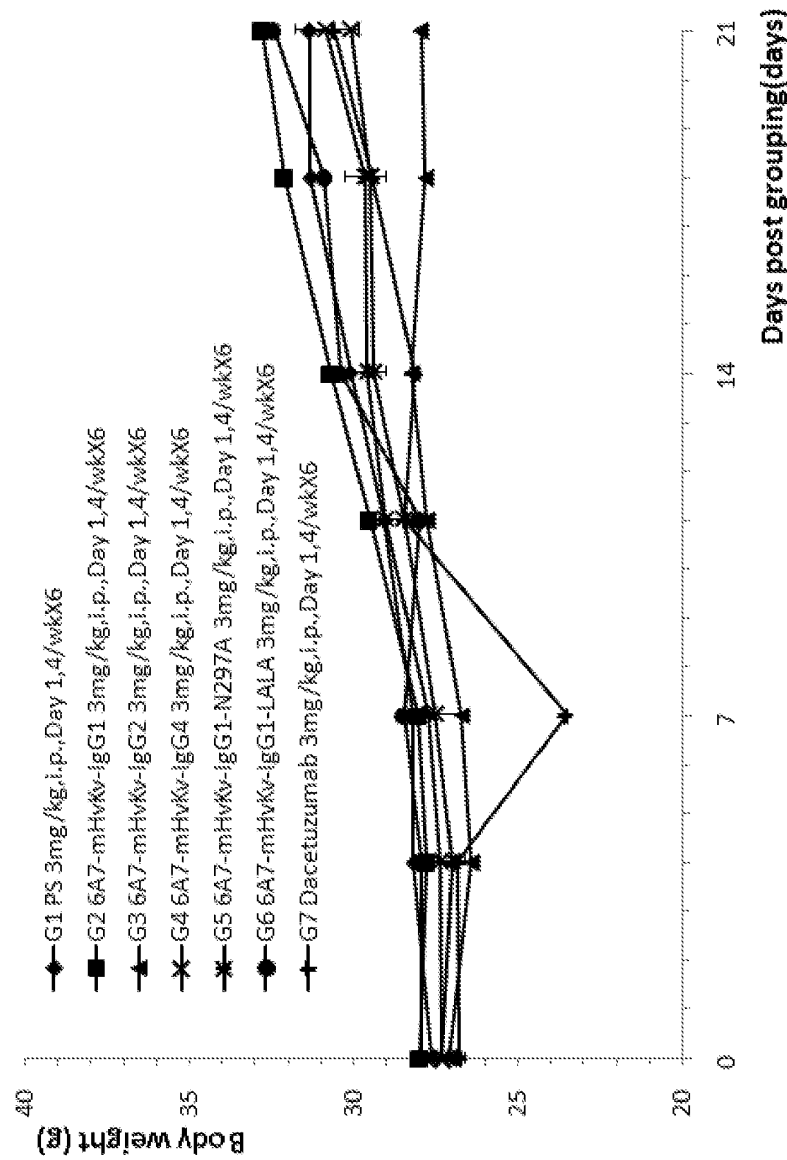


FIG. 10

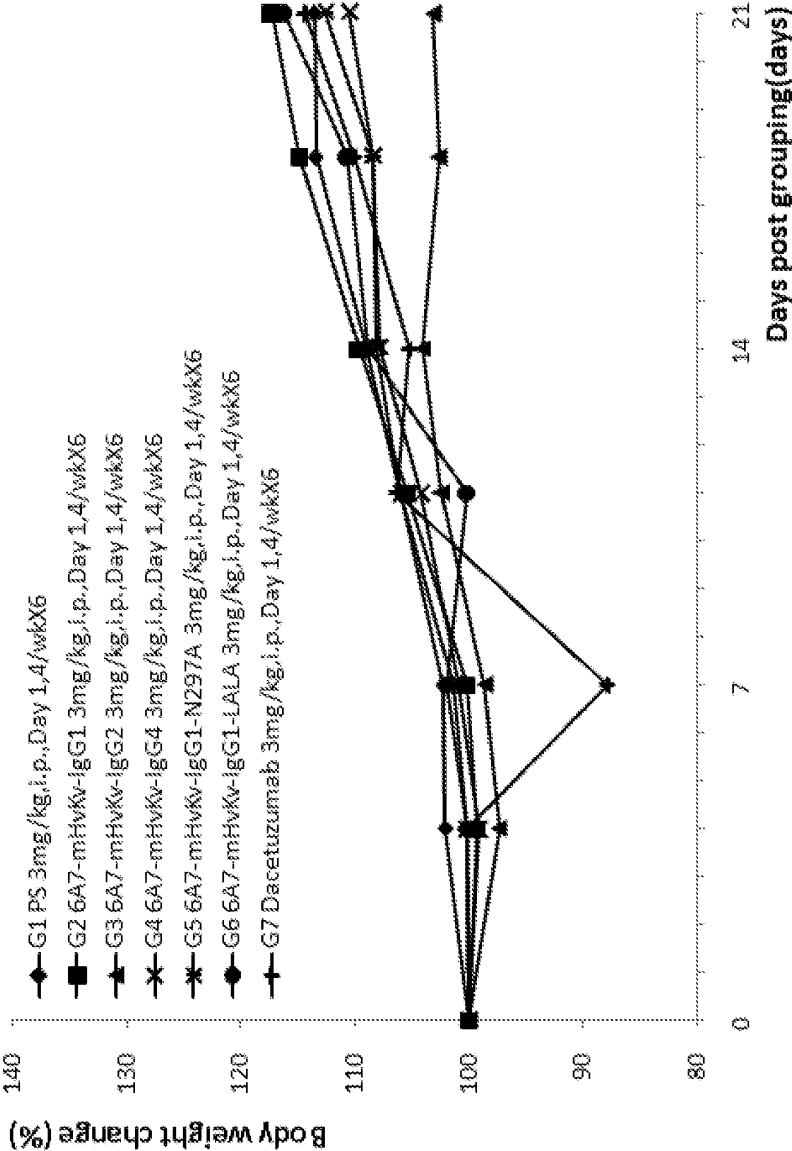


FIG. 11

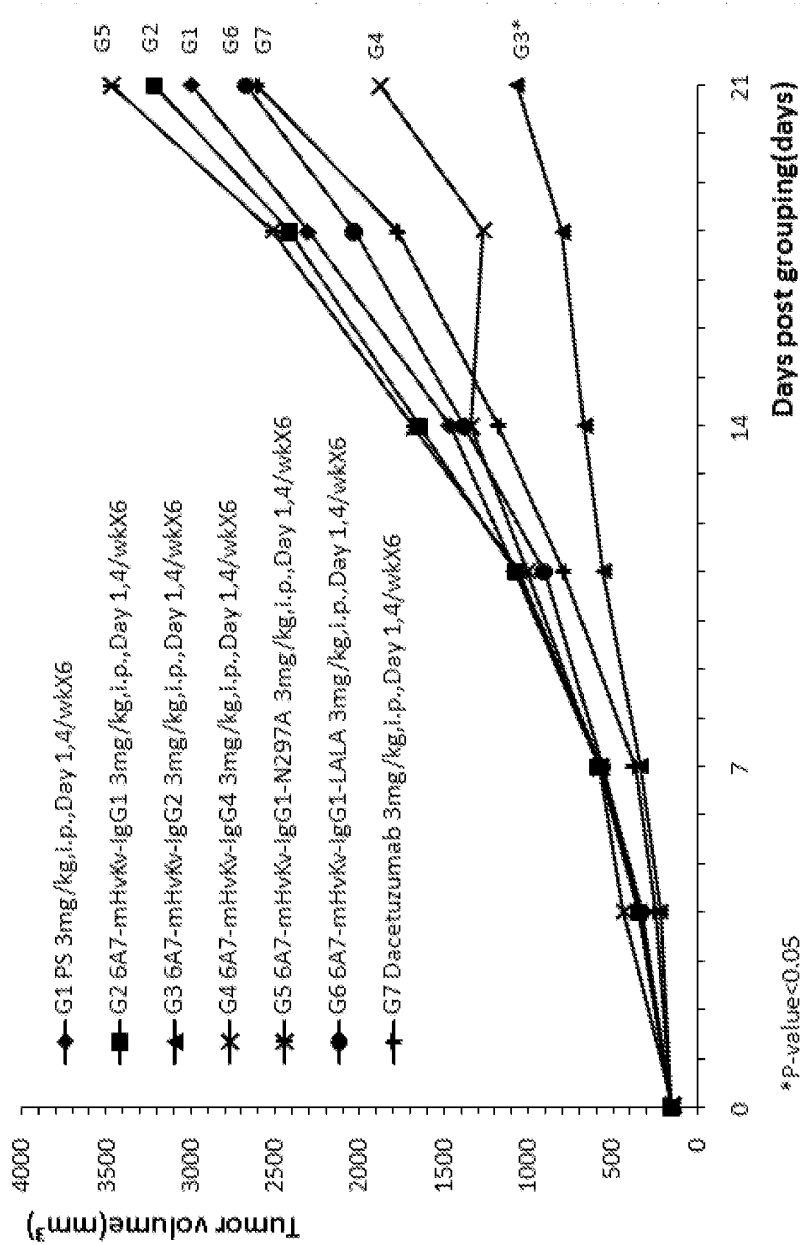


FIG. 12

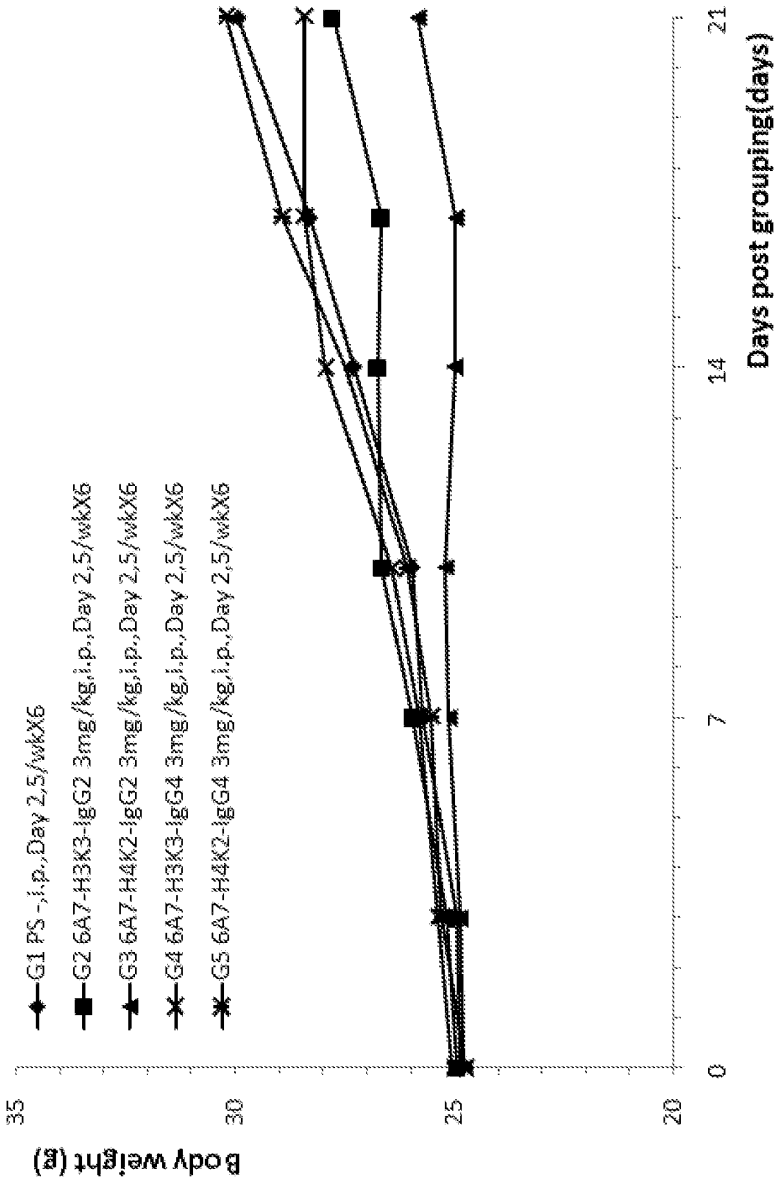


FIG. 13

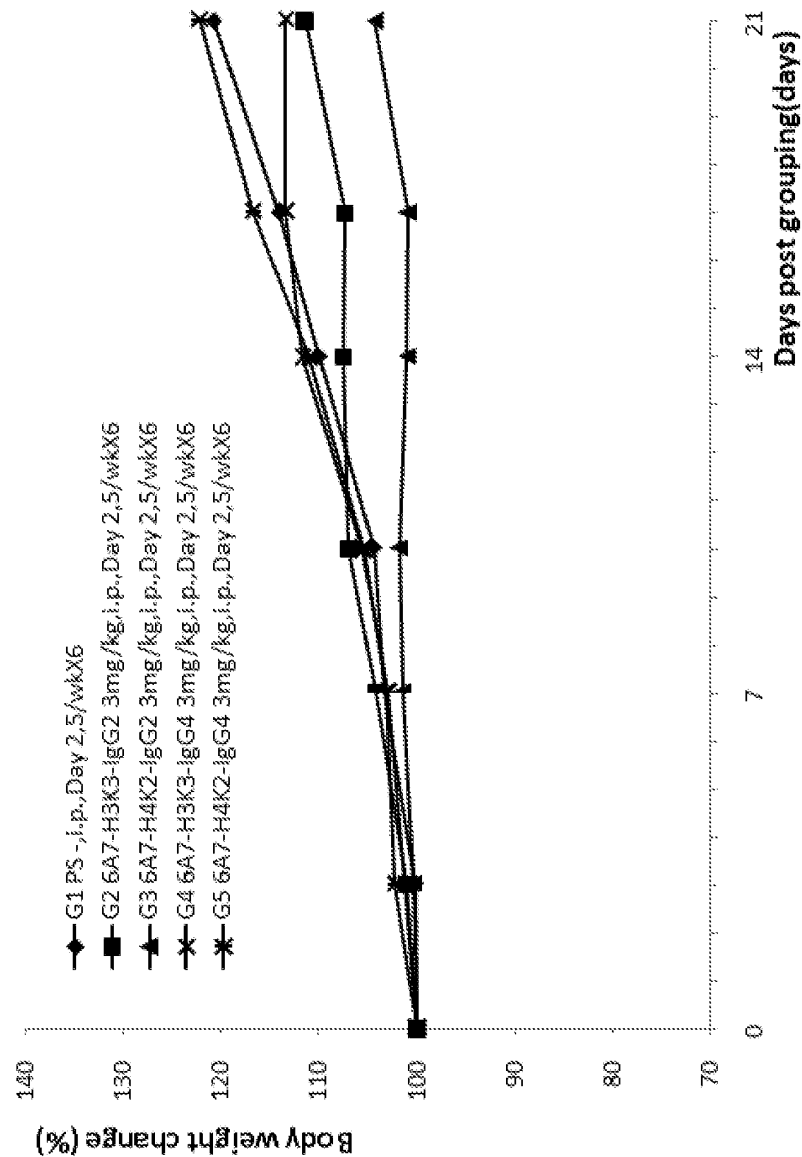


FIG. 14

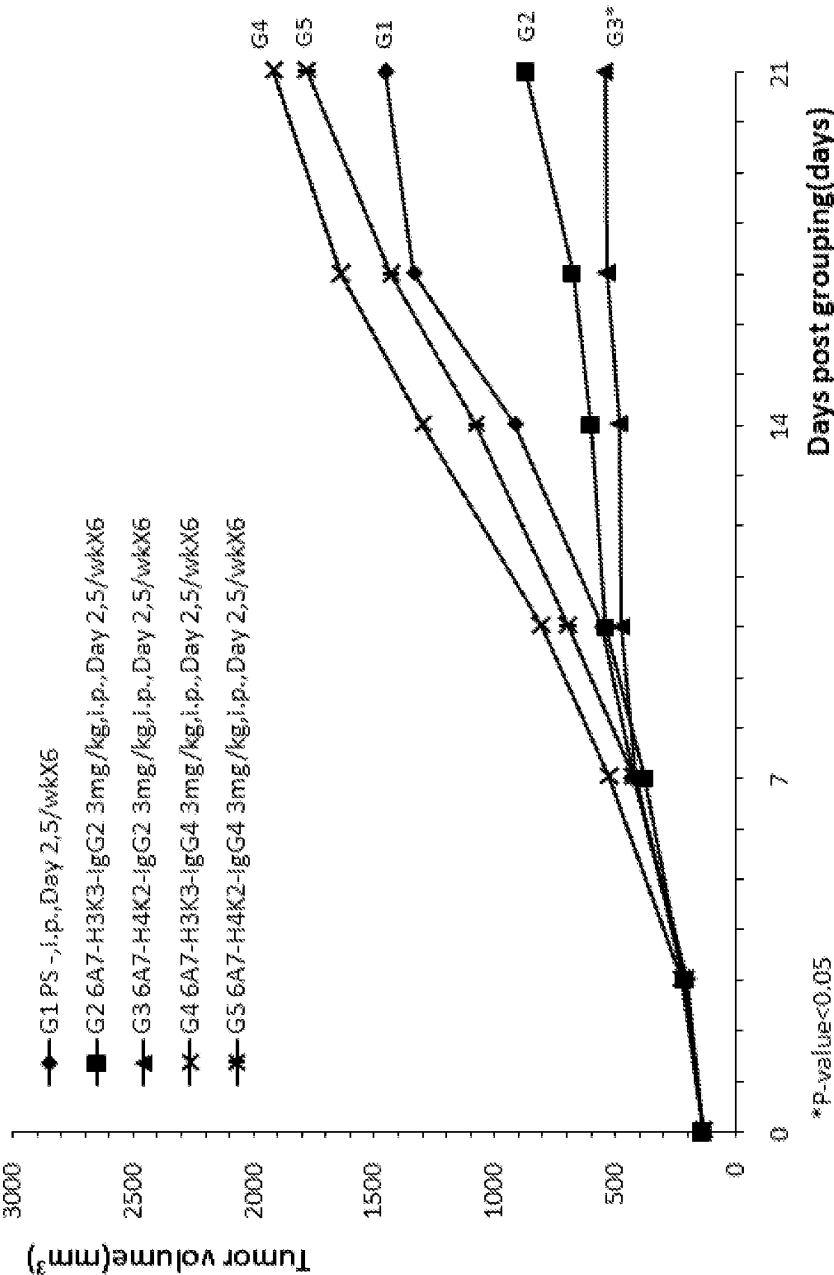


FIG. 15

Kabat CDR

Ab	VH CDR1	SEQ ID:	VH CDR2	SEQ ID:	VH CDR3	SEQ ID:	VL CDR1	SEQ ID:	VL CDR2	SEQ ID:	VL CDR3	SEQ ID:
03-7F10 or humanized 03-7F10	DYYM Y	1	YISYGGDSTFYPD TVRG	2	PAPSAHSY LDY	3	RASQDISNYLN	4	YVTSRLHS	5	QQGKTLP FT	6
06-6A7 or humanized 06-6A7	SYIY	7	GINPRINGGTNFN EKFS	8	HGNGVY	9	RSSQSLLHSNG NTYLH	10	QVSNRFS	11	SQTTHVP WT	12
07-4H6 or humanized 07-4H6	SGYW N	13	FISYSGSTYYTPSL KS	14	FRYDDGVD Y	15	RASHEISGYLS	16	AASTLAS	17	LQYSSVP WT	18

FIG. 16

Chothia CDR

Ab	VH CDR1	SEQ ID:	VH CDR2	SEQ ID:	VH CDR3	SEQ ID:	VL CDR1	SEQ ID:	VL CDR2	SEQ ID:	VL CDR3	SEQ ID:
03-7F10 or humanized 03-7F10	GFTFSD YYMY	19	SYGGDS	20	PAPSAHSYY LDY	3	RASQDISNYLN	4	YTSRLHS	21	QQGKTLP FT	6
06-6A7 or humanized 06-6A7	GYTFISY YIY	22	NPRNGG	23	HGNGVY	9	RSSQSLLHSNG NTYLH	10	QVSNRFS	11	SQTTTHVP WT	12
07-4H6 or humanized 07-4H6	GDSVSS GYWN	24	SYSGS	25	FRYDDGVD Y	15	RASHEISGYLS	16	AASTLAS	17	LQYSSYP WT	18

FIG. 17

Protein	Amino acid sequence	SEQ ID NO:
Human CD40 (hCD40) NP_001241.1	MVRLPLQCVLWGCLLTAVHPEPPPTACREKQYLINSQCCSLCQPGQKLVSDCTETETECCLPCGESEFL DTWNRETHCHQHXYCDPNLGLRVQKGTSETDTICTCEEHWHCTSEACESCVLHRSCTSPGFGVKQIAT GVSDTICEPCPVGFFSNVSSAFKCHPWTSCETKDLVVQQAGTNKTDVCGPQDRRLRLLVPIPVVNGI LFAILLVLVFIKKVAKKPTNKAPHPKQEPQEIINFDDLPGSNTAAPVQETLHGCQPVTDGDKESRIS VQERQ	26
Mouse CD40 (mCD40) NP_035741.2	MVSLPRLCALWGCLLTAVHLGQCVCSDKQYLHDGQCCLCQPGSRLTSHCTALEKTQCHPCDSGEFS AQWNREIRCHQHRHCEPNQGLRVKKEGTAEADTVCTCKEGHCTSKDCEACAQHTPCIPGFGVMEMAT ETTDTVCHPCPVGFFSNQSSLFKCYPWTSCEDKNLEVLQKGTSTQNVICGLKSRMRALLVPIPVVNGI LITIFGVFLYIKKVVKKPKDNEILPPAARRQDPQEMEDYPGHNTAAPVQETLHGCQPVTDGDKESRI SVQERQVTDLSIALRPLV	27
Monkey CD40 (rmCD40) NP_001252791.1	MVRLPLQCVL WGCLLTAVYP EPPTACREKQ YLINSQCCSL CQPGQKLVSD CTETETECCL PCSESEFLDT WNRETRCHQH KYCDPNLGLR VQKGTSETD TICTCEEGLH CMSESCSCV PHRSCIPGFG VKQIATGVSD TICEPCPVGF FSNVSSAFK CRPWTSCETK DLVVQQAGTN KTDVVCGPQD RQRALVWPI CLGILFVILL LVLVFIKKVA KKPNDKAPHP KQEPQEIINF DDLPGSNPAA PVQETLHGCQ PVTQEDGKES RISVQERQ	28
Chimeric CD40 (chiCD40) (Humanized CD40)	MVSLPRLCALWGCLLTAVHPEPPPTACREKQYLINSQCCSLCQPGQKLVSDCTETETECCLPCGESEFL DTWNRETHCHQHXYCDPNLGLRVQKGTSETDTICTCEEHWHCTSEACESCVLHRSCTSPGFGVKQIAT GVSDTICEPCPVGFFSNVSSAFKCHPWTSCETKDLVVQQAGTNKTDVCGPQDRRLRLLVPIPVVNGI LITIFGVFLYIKKVVKKPKDNEILPPAARRQDPQEMEDYPGHNTAAPVQETLHGCQPVTDGDKESRI SVQERQVTDLSIALRPLV	29

FIG. 18

FIG. 19

Humanized antibody variable domains	Description	AMINO ACID SEQUENCE	SEQ ID NO:
Humanized heavy chain variable domain (H1) based on 7F10	HuVHv1: humanization percentage 84.7%; Not top hit to human and <i>Macaca fascicularis</i>	EVQLVESGGGLVQPGGSLRLSCATSGFTFSDYMYWVRQAPGK RLEWVAIISYGGDSTFYPDIVRGRFTISRDNAKNSLYLQMNSL RAEDTAVYYCARPAPSAHSYYLDYWGQGTLTIVSS	30
Humanized heavy chain variable domain (H2) based on 7F10	HuVHv2: humanization percentage 82.7%; Not top hit to human and <i>Macaca fascicularis</i>	EVQLVESGGGLVQPGGSLRLSCATSGFTFSDYMYWVRQAPGK RLEWVAIISYGGDSTFYPDIVRGRFTISRDNAKNSLYLQMNSL KAEDTAVYYCARPAPSAHSYYLDYWGQGTLTIVSS	31
Humanized heavy chain variable domain (H3) based on 7F10	HuVHv3: humanization percentage 78.6%; Not top hit to human and <i>Macaca fascicularis</i>	EVQLVESGGGLVQPGGSLRLSCATSGFTFSDYMYWVRQAPGK RLEWVAIISYGGDSTFYPDIVRGRFTISRDNAKNSLYLQMNSL KAEDTAVYYCARPAPSAHSYYLDYWGQGTLTIVSS	32
Humanized light chain variable domain (K1) based on 7F10	HuVLv1: humanization percentage 85.3%; top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSSLSASVGRVITICRASQDISNYLNWYQQKPGGA VKLLIYYTSRLHSGLPFRFSGSGGTDFFTISSLQPEDIAITY YCQQGKTLPTTFASGKLEIK	33
Humanized light chain variable domain (K2) based on 7F10	HuVLv2: humanization percentage 84.2%; Not top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSSLSASVGRVITICRASQDISNYLNWYQQKPGGA VKLLIYYTSRLHSGLPFRFSGSGGTDFFTISSLQPEDIAITY YCQQGKTLPTTFASGKLEIK	34
Humanized light chain variable domain (K3) based on 7F10	HuVLv3: humanization percentage 82.1%; Not top hit to human and <i>Macaca fascicularis</i>	DIQMTQSTSSLSASVGRVITICRASQDISNYLNWYQQKPGGA VKLLIYYTSRLHSGLPFRFSGSGGTDFFTISSLQPEDIAITY YCQQGKTLPTTFASGKLEIK	35
Humanized light chain variable domain (K4) based on 7F10	HuVLv4: humanization percentage 80%; Not top hit to human and <i>Macaca fascicularis</i>	DIQMTQSTSSLSASVGRVITICRASQDISNYLNWYQQKPDGT VKLLIYYTSRLHSGLPFRFSGSGGTDFFTISSLQPEDIAITY YCQQGKTLPTTFASGKLEIK	36

Humanized antibody variable domains	Description	AMINO ACID SEQUENCE	SEQ ID NO:
Humanized heavy chain variable domain (H1) based on 6A7	HuVHv1: humanization percentage 84.7%; top hit to human and <i>Macaca fascicularis</i>	QVLVQSGAEVKKPGASVKVSCKASGYTFISYYIYVVRQAPGQ GLEWMGGINPRNGGTNFEKFKSRVTLTVDTSTSTAYMELSRL RSEDTAVYYCARHNGVYWGQGTITVTVSS	37
Humanized heavy chain variable domain (H2) based on 6A7	HuVHv2: humanization percentage 82.7%; top hit to human and <i>Macaca fascicularis</i>	QVLVQSGAEVKKPGASVKVSCKASGYTFISYYIYVVRQAPGQ GLEWIGGINPRNGGTNFEKFKSRATLTVDTSTSTAYMELSRL RSEDTAVYYCARHNGVYWGQGTITVTVSS	38
Humanized heavy chain variable domain (H3) based on 6A7	HuVHv3: humanization percentage 81.6%; top hit to human and <i>Macaca fascicularis</i>	QVLVQSGAEVKKPGASVKVSCKASGYTFISYYIYVVRQAPGQ GLEWIGGINPRNGGTNFEKFKSRATLTVDTSTSTAYMELSRL RSEDTAVYYCTRHNHNGVYWGQGTITVTVSS	39
Humanized heavy chain variable domain (H4) based on 6A7	HuVHv4: humanization percentage 79.6%; top hit to human and <i>Macaca fascicularis</i>	QVLVQSGAEVKKPGASVKLSCKASGYTFISYYIYVVKQAPGQ GLEWIGGINPRNGGTNFEKFKSRATLTVDTSTSTAYMELSRL RSEDTAVYYCTRHNHNGVYWGQGTITVTVSS	40
Humanized light chain variable domain (K1) based on 6A7	HuLV1: humanization percentage 91%; top hit to human and <i>Macaca fascicularis</i>	DVVMTQSPSLPVLGQPASISCRSSQSLHNSNGNTYLHWfqq rPGQSPNHLIYQVSNRFGVDPDRFSGSGGTDFTLKISRVEAE DvGVYyCSQTTHVPWTFGGgTKvEIK	41
Humanized light chain variable domain (K2) based on 6A7	HuLV2: humanization percentage 88%; Not top hit to human and <i>Macaca fascicularis</i>	DVVMTQSPSLPVLGQPASISCRSSQSLHNSNGNTYLHWYQQ rPGQSPNHLIYQVSNRFGVDPDRFSGSGGTDFTLKISRVEAE DVGvYfCSQTTHVPWTFGGgTKvEIK	42
Humanized light chain variable domain (K3) based on 6A7	HuLV3: humanization percentage 87%; Not top hit to human and <i>Macaca fascicularis</i>	DVVMTQSPSLPVLGDPASISCRSSQSLHNSNGNTYLHWYQQ rPGQSPNHLIYQVSNRFGVDPDRFSGSGGTDFTLKISRVEAE DVGvYfCSQTTHVPWTFGGgTKLEIK	43

FIG. 20

Humanized antibody variable domains	Description	AMINO ACID SEQUENCE	SEQ ID NO:
Humanized heavy chain variable domain (H1) based on 4H6	HuVHv1: humanization percentage 88.9%; top hit to human and <i>Macaca fascicularis</i>	QVQLQESGPGLVKPSQTLSTCTVSGDSVSSGYWNWIRKHPG KKLEWIGFISYSGSTYYTPSLKSRVTISRDTSKNQFSLKLS VTAADTAVYYCARFRYYDDGVDYWGQGTLLTVSS	44
Humanized heavy chain variable domain (H2) based on 4H6	HuVHv2: humanization percentage 87.9%; top hit to human and <i>Macaca fascicularis</i>	EVQLQESGPGLVKPSQTLSTCTVSGDSVSSGYWNWIRKHPG KKLEWIGFISYSGSTYYTPSLKSRVTISRDTSKNQFSLKLS VTAADTAVYYCARFRYYDDGVDYWGQGTLLTVSS	45
Humanized heavy chain variable domain (H3) based on 4H6	HuVHv3: humanization percentage 83.8%; top hit to human and <i>Macaca fascicularis</i>	EVQLQESGPGLVKPSQTLSTCTVSGDSVSSGYWNWIRKHPG KKLEYMGFISYSGSTYYTPSLKSRITISRDTSKNQFSLKLS VTAADTAVYFCARFRYYDDGVDYWGQGTLLTVSS	46
Humanized heavy chain variable domain (H4) based on 4H6	HuVHv4: humanization percentage 82.8%; top hit to human and <i>Macaca fascicularis</i>	EVQLQESGPGLVKPSQTLSTCTVSGDSVSSGYWNWIRKFPFG KKLEYMGFISYSGSTYYTPSLKSRITISRDTSKNQFSLKLS VTAADTAVYFCARFRYYDDGVDYWGQGTLLTVSS	47
Humanized light chain variable domain (K1) based on 4H6	HuVLv1: humanization percentage 87.4%; top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSAMSASVGDRVTITCRASHEISGYLSWfQQKPgG VIKRLINAASTLASGVPSRFSGRSGTefLTIsSLQPEDFA tYYCLQYSSYPWTFGGGTKLEIK	48
Humanized light chain variable domain (K2) based on 4H6	HuVLv2: humanization percentage 84.2%; top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSAMSASVGDRVTITCRASHEISGYLSWfQQKPgG TIKRLINAASTLASGVPSRFSGRSGTefLTIsSLQPEDFA DYYCLQYSSYPWTFGGGTKLEIK	49
Humanized light chain variable domain (K3) based on 4H6	HuVLv3: humanization percentage 83.2%; top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSAMSASVGDRVTITCRASHEISGYLSWfQQKPgG TIKRLINAASTLASGVPSRFSGRSGTefLTIsSLQPEDFA DYYCLQYSSYPWTFGGGTKLEIK	50
Humanized light chain variable domain (K4) based on 4H6	HuVLv4: humanization percentage 82.1%; Not top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSAMSASVGDRVTITCRASHEISGYLSWfQQKPgG TIKRLINAASTLASGVPSRFSGRSGTefLTIsSLQPEDFA DYYCLQYSSYPWTFGGGTKLEIK	51

FIG. 21

03-7F10 ("7F10") Heavy chain variable region (SEQ ID NO: 52)
EVLIVSGGLVQPGSLKLSCATSGFTFSDYMYWVRQTPEKRLEWVAIISYGGDSTFYPDTVRGRFTISRDNAKNALYLQMSRLKSEDTAVYYCAR
PAPSAHSYYLDYWGQGTTLTVSS

03-7F10 ("7F10") Light chain variable region (SEQ ID NO: 53)
DIQMTQTSSLSASLGDVITISCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLHSLGPSRFSGSGSGTDYSLTISNLEQEDIATYYCQQGKTLPTTF
ASGTKLEIK

06-6A7 ("6A7") Heavy chain variable region (SEQ ID NO: 54)
QVQLQQPGAELVKPGASVKLSCKASGYTFISYIYVWVKQRPQGQGLEWIGGINPRNGGTNFKFKSKATLTVDKSSSTAYMQLSLTSSEDSAVYYCTR
HGNGVYWGQGTTLTVSS

06-6A7 ("6A7") Light chain variable region (SEQ ID NO: 55)
DVVMTQTPLSLPVSLGDAQSISCRSSQSLLSHNGNTYLHWYLQKPGQSPNHLIYQVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYFCSQTH
VPWTFGGGTKLEIK

07-4H6 ("4H6") Heavy chain variable region (SEQ ID NO: 56)
EVKLQESGPSLVKPSQTLSTCSVTGDSVSSGYWNWIRKPPGNKLEYMGFIYSYSGSTYYTPSLKSRISITRDTSKNQFYQLNSVTTEDTATYFCARF
RRYDDGVDYWGQGTTLTVSS

07-4H6 ("4H6") Light chain variable region (SEQ ID NO: 57)
DIQMTQSPSSLSASLGERSLTCSRASHEISGYLSWIQQKPDGTIKRLINAASTLASGVPKRFSGRSGSEYSLTINSLESEDFADYYCLQYSSYPWTF
GGGTKLEIK

FIG. 22