

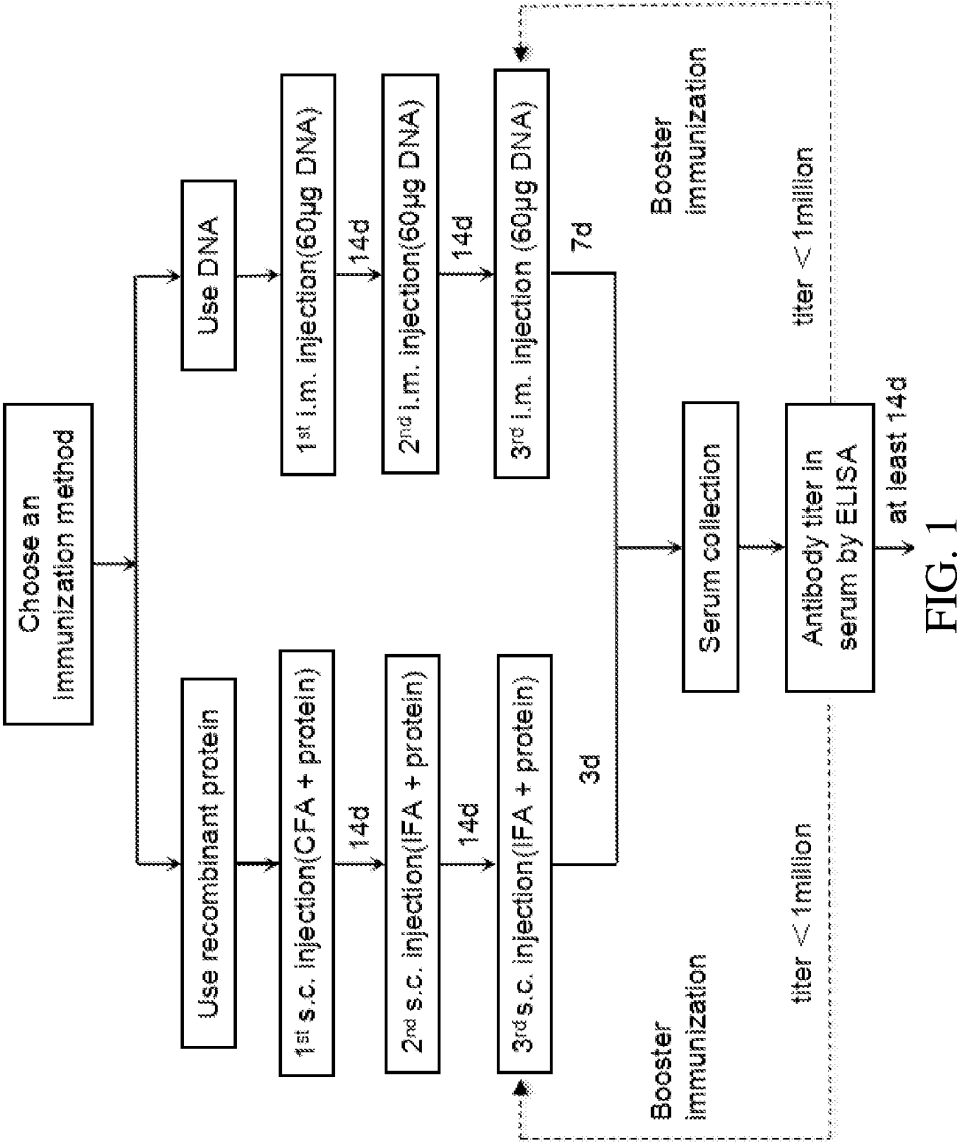


FIG. 1

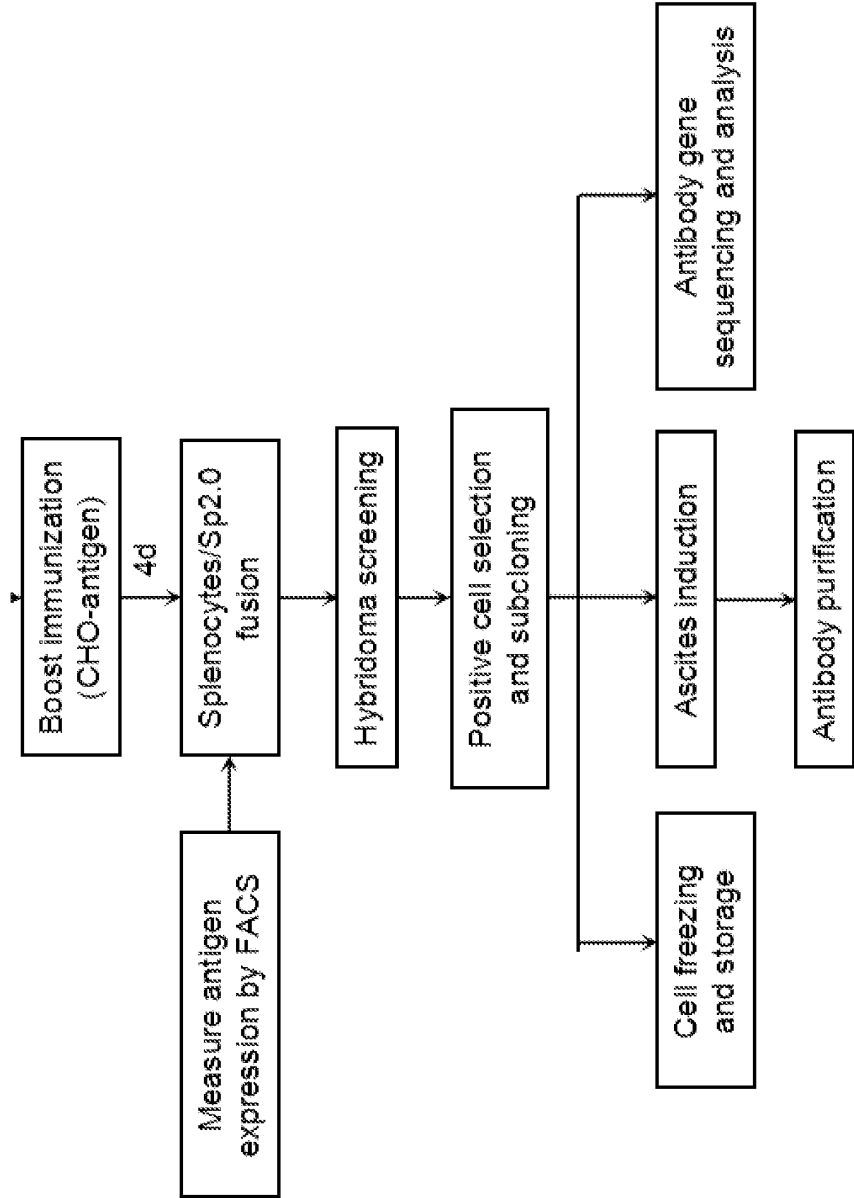


FIG. 2

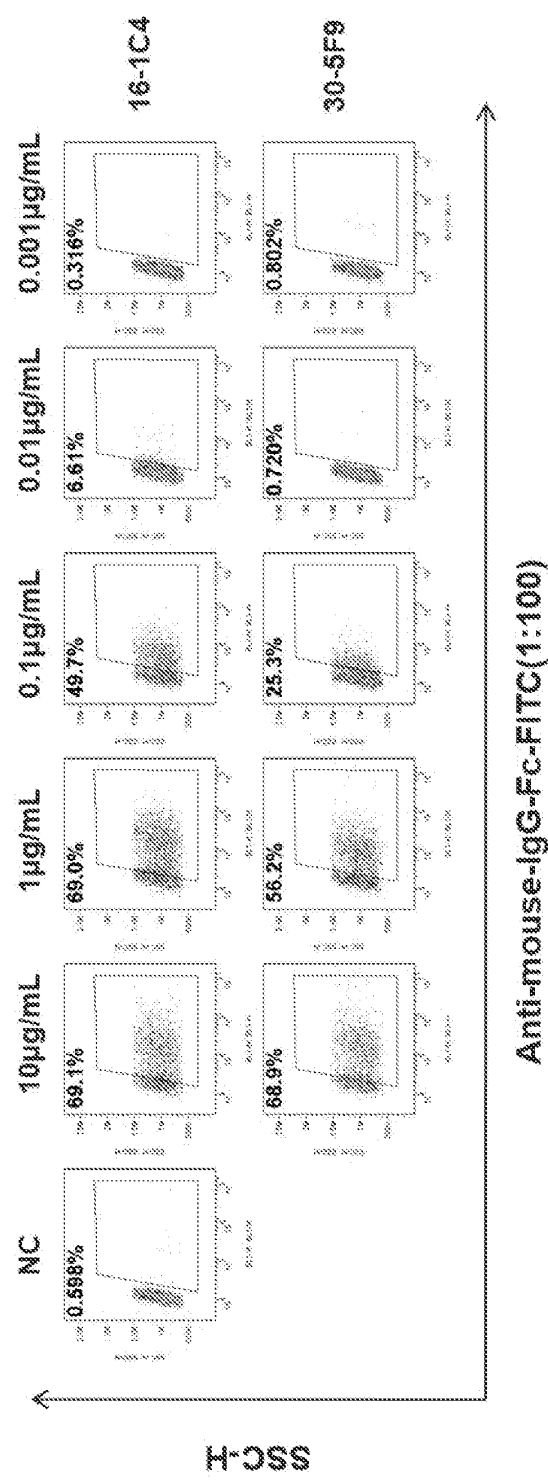


FIG. 3

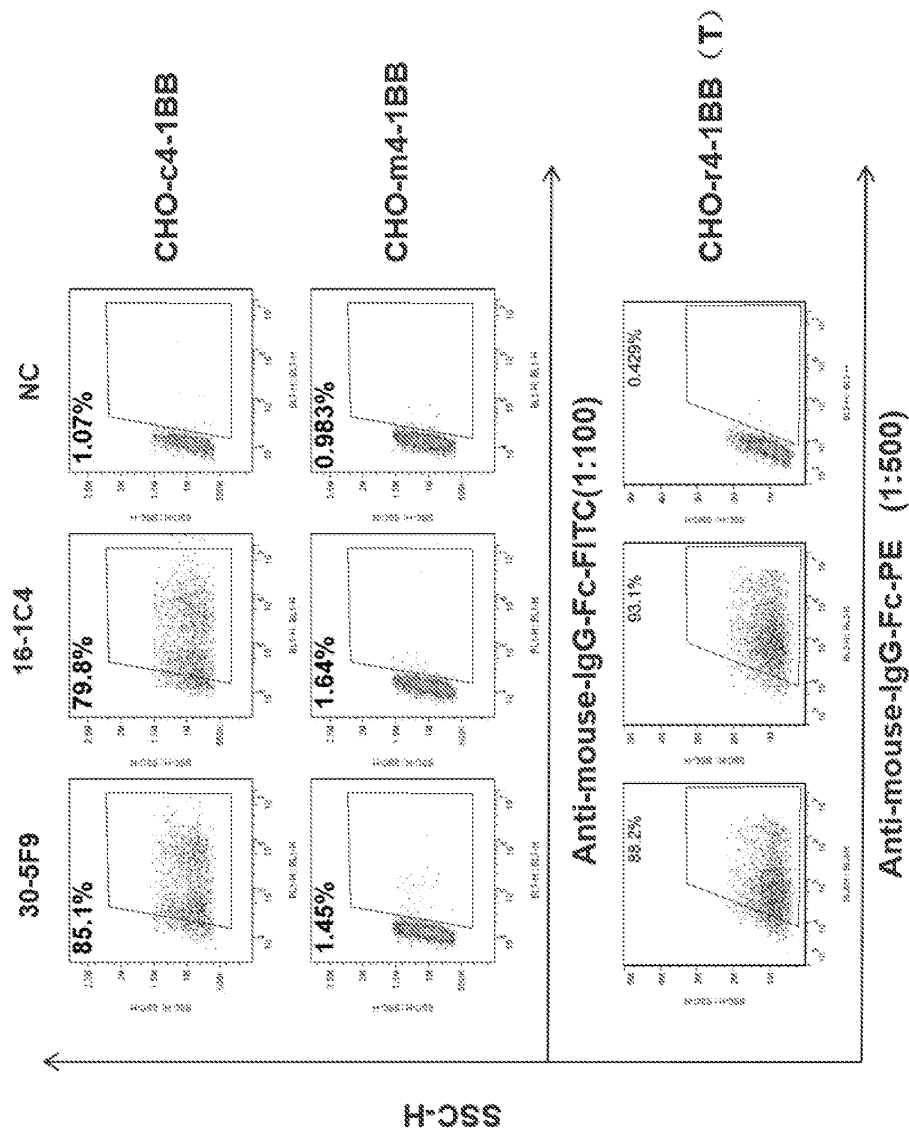


FIG. 4

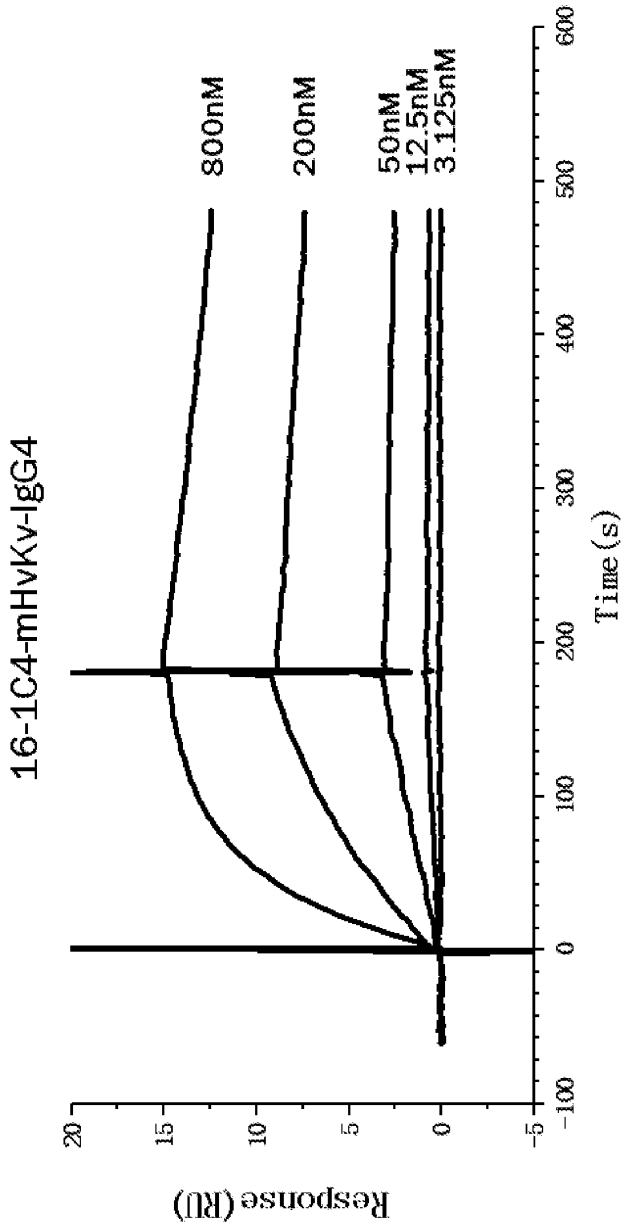


FIG. 5

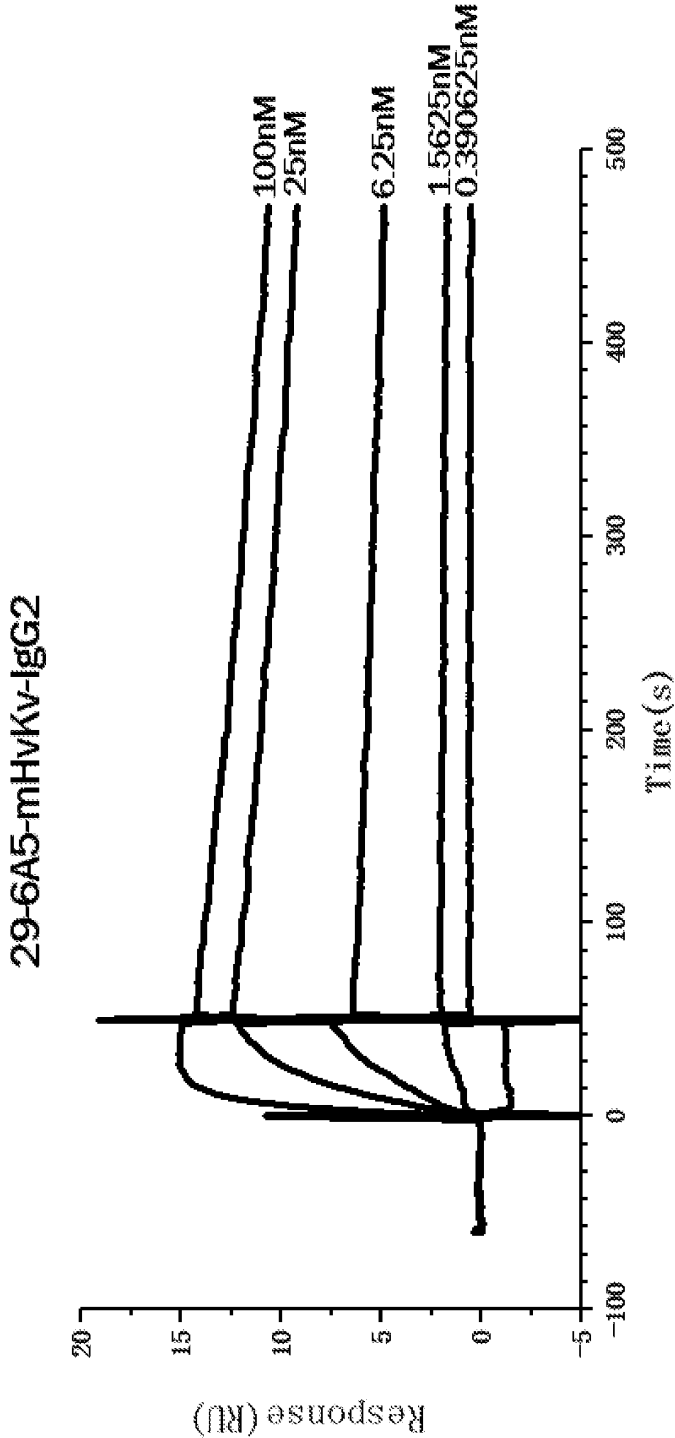


FIG. 6

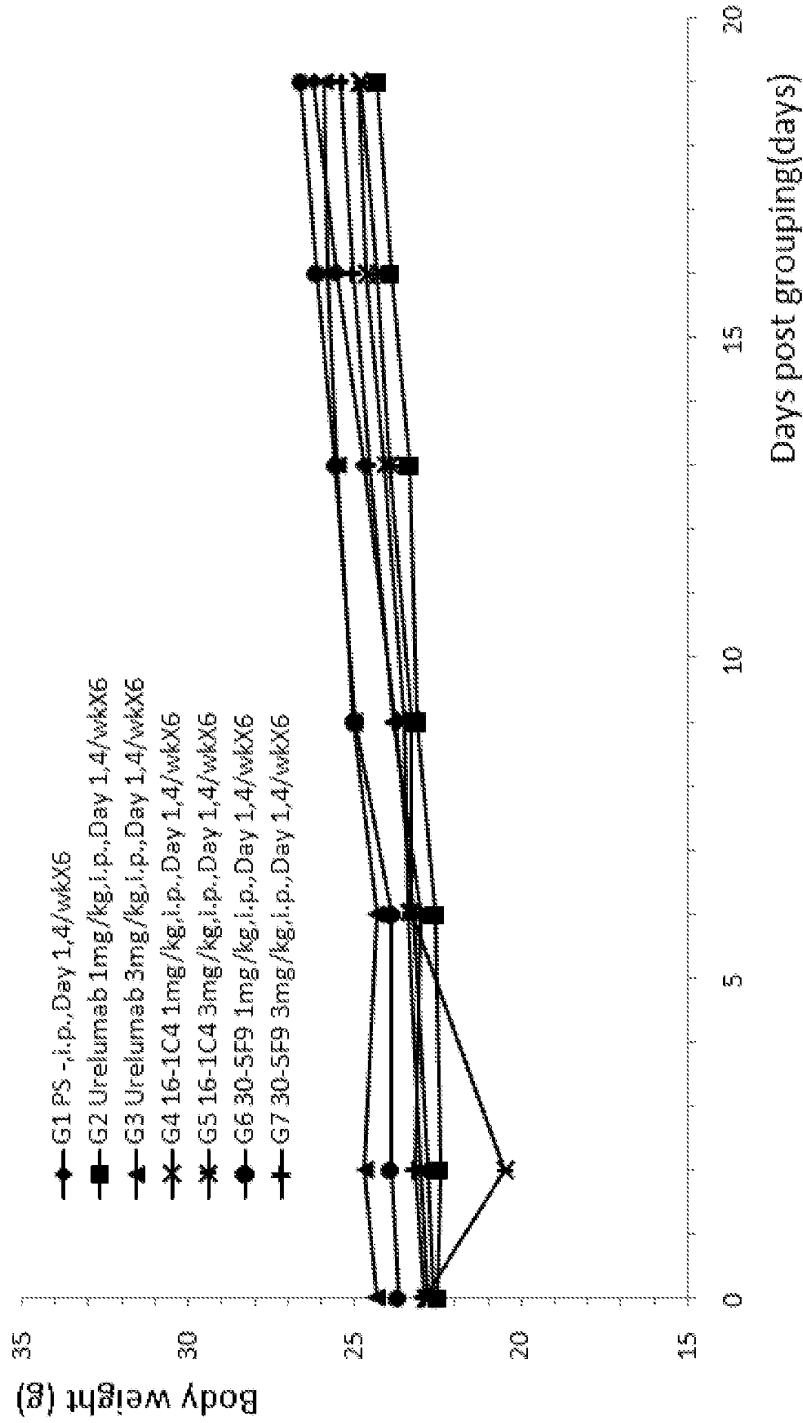


FIG. 7

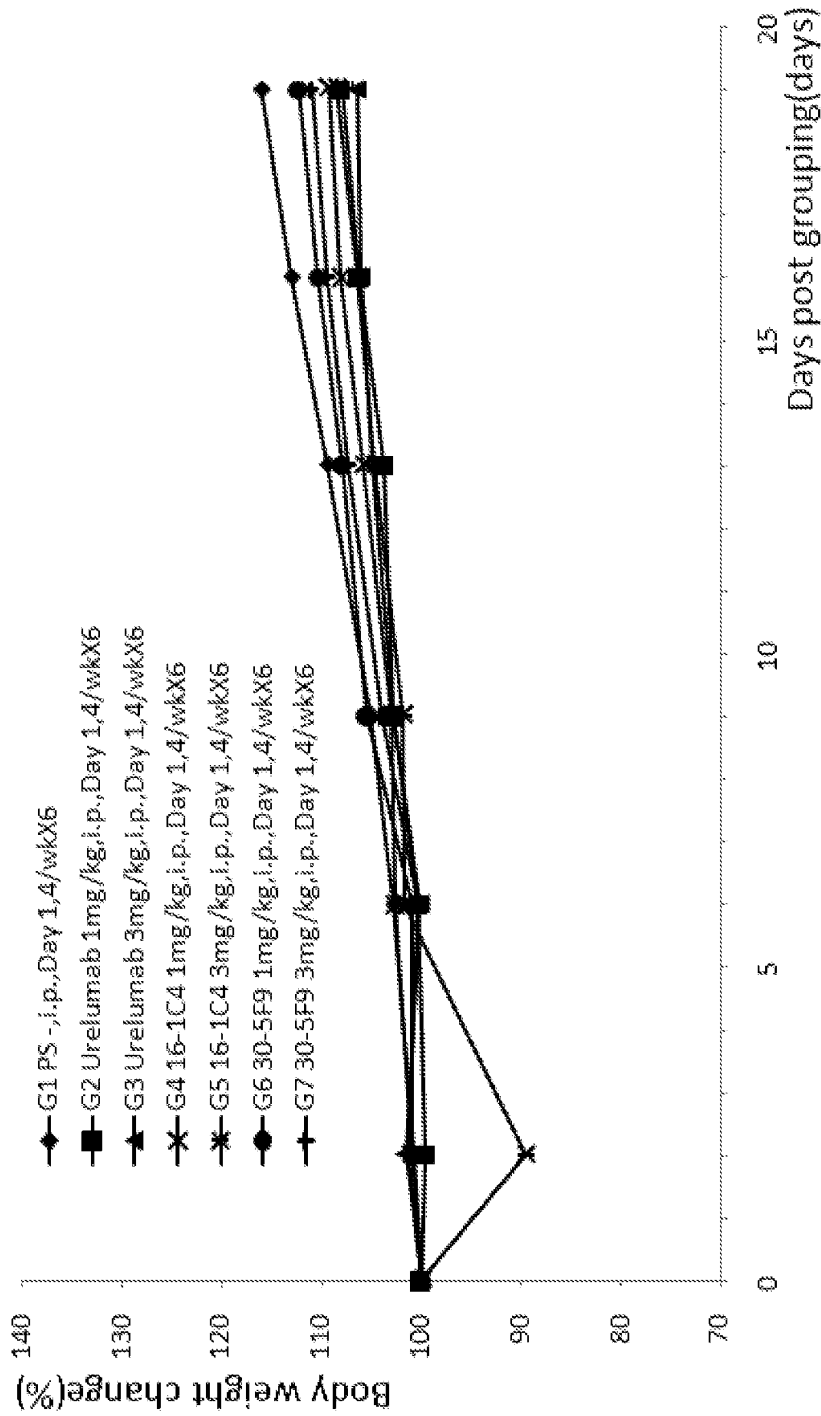


FIG. 8

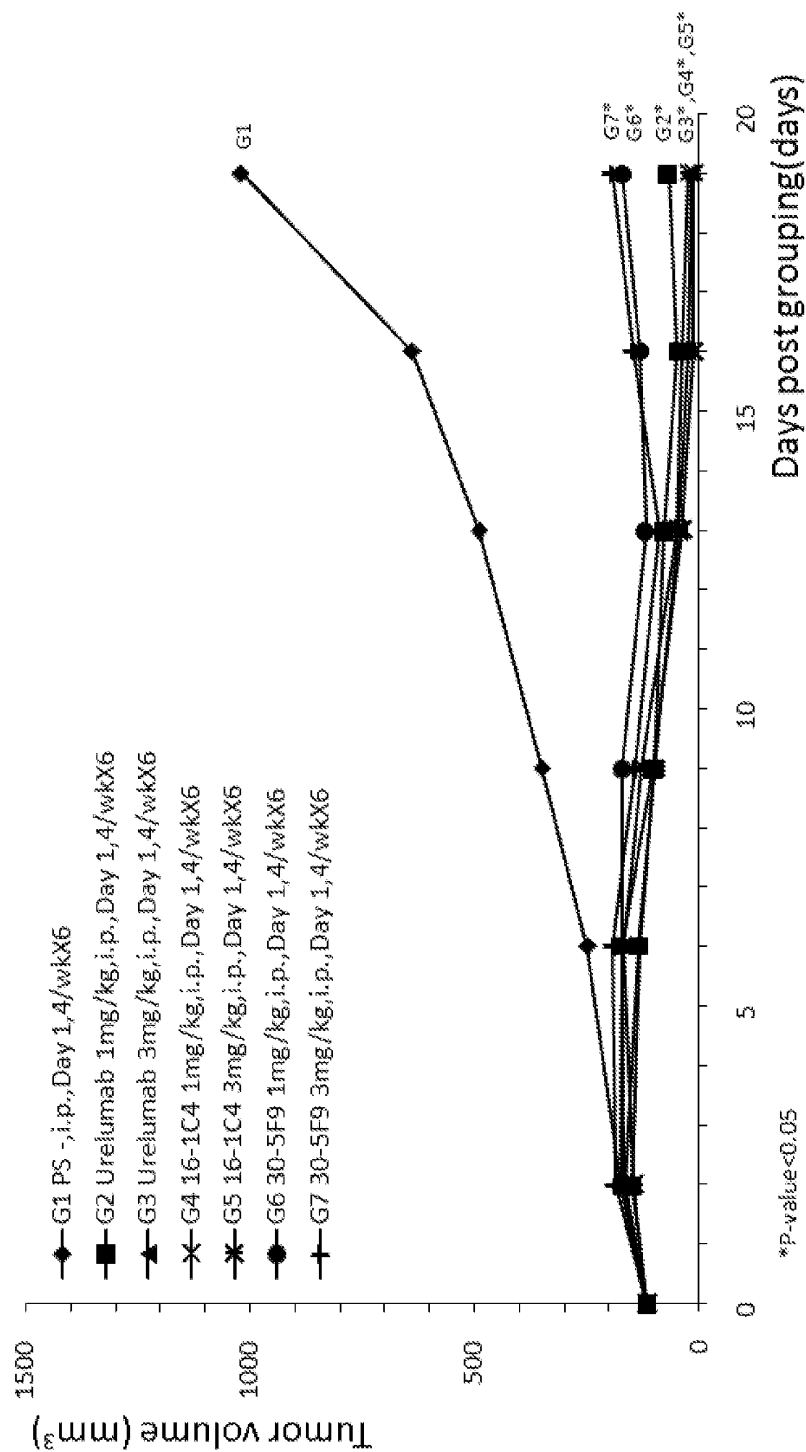


FIG. 9

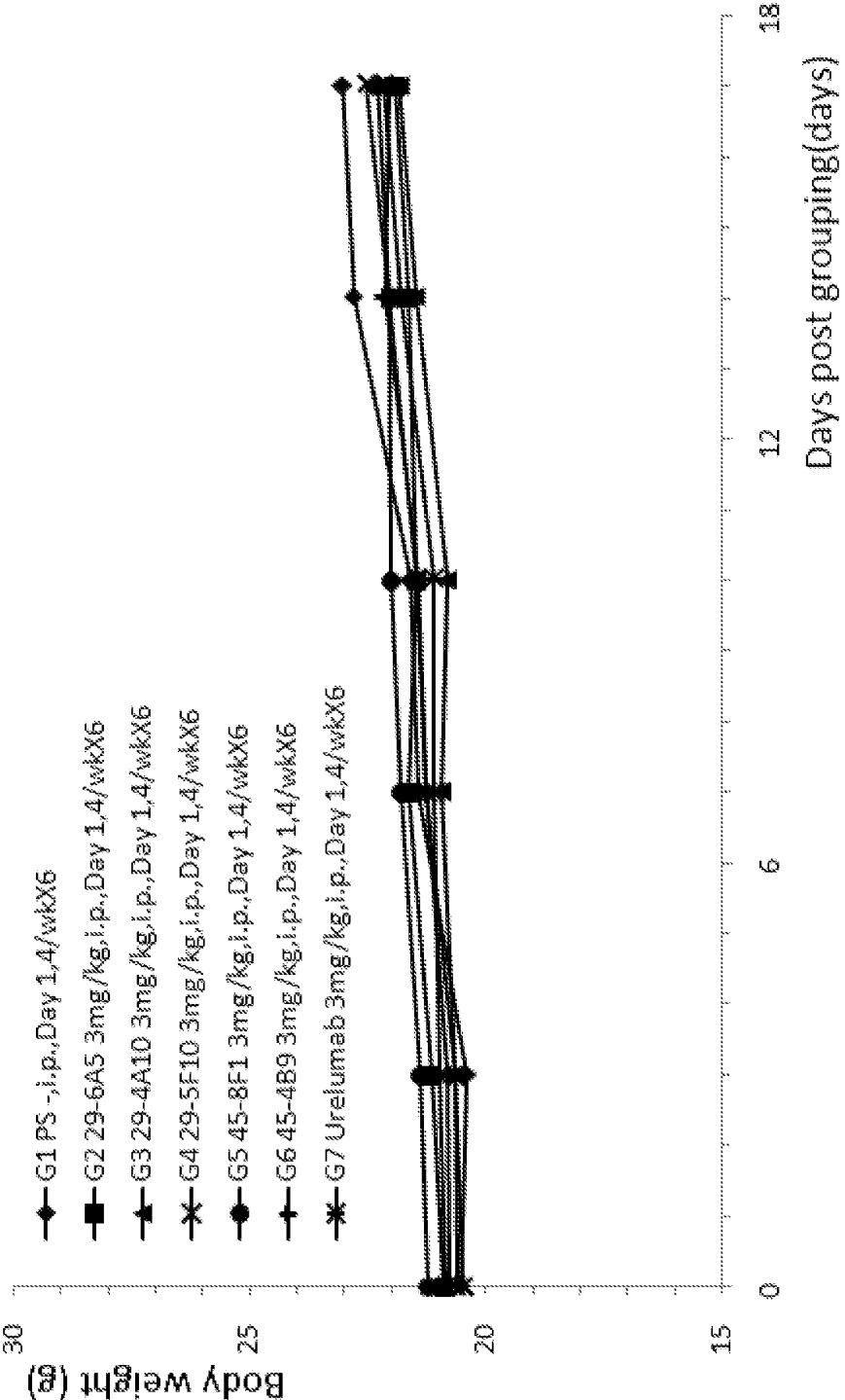


FIG. 10

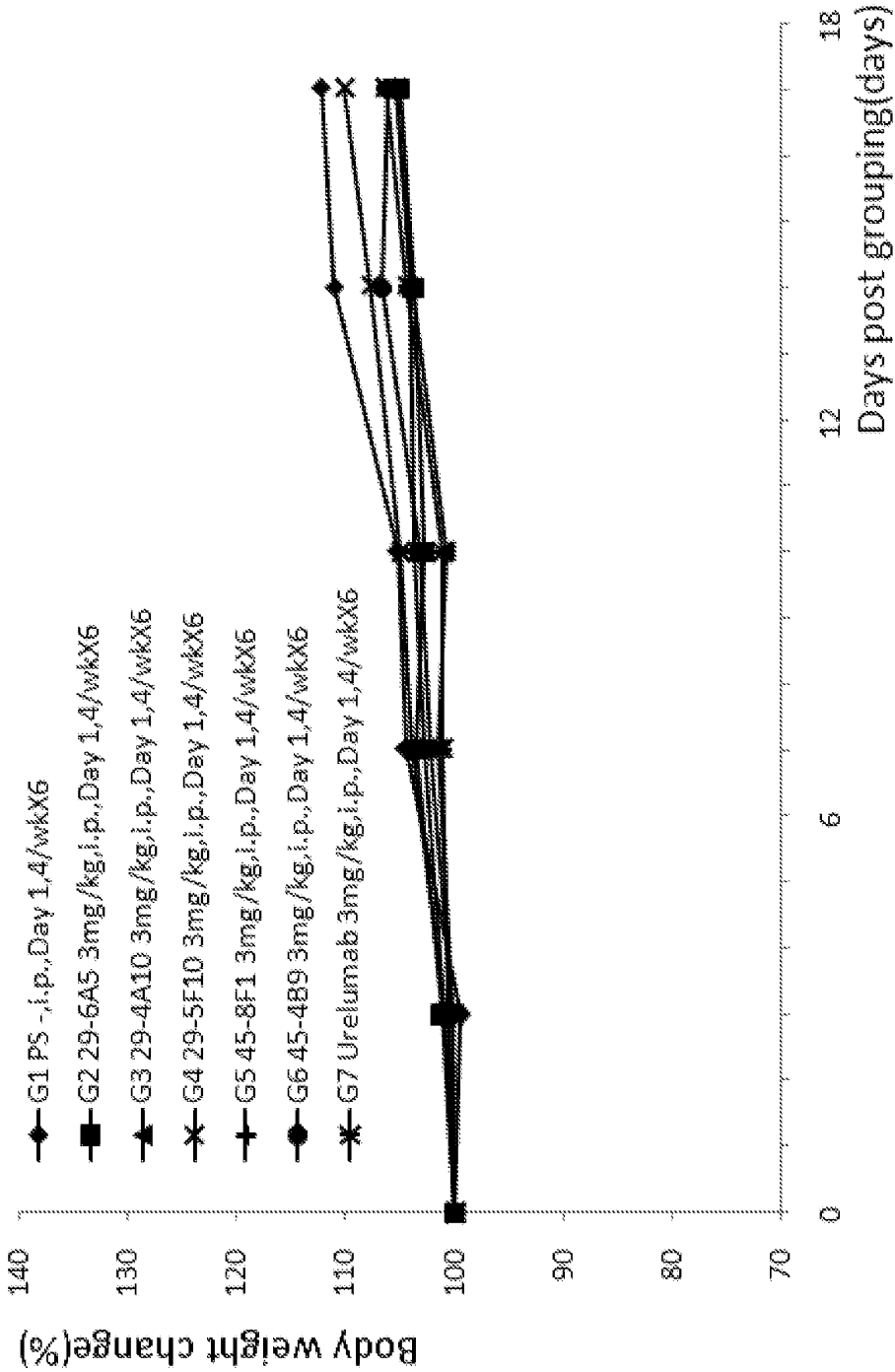


FIG. 11

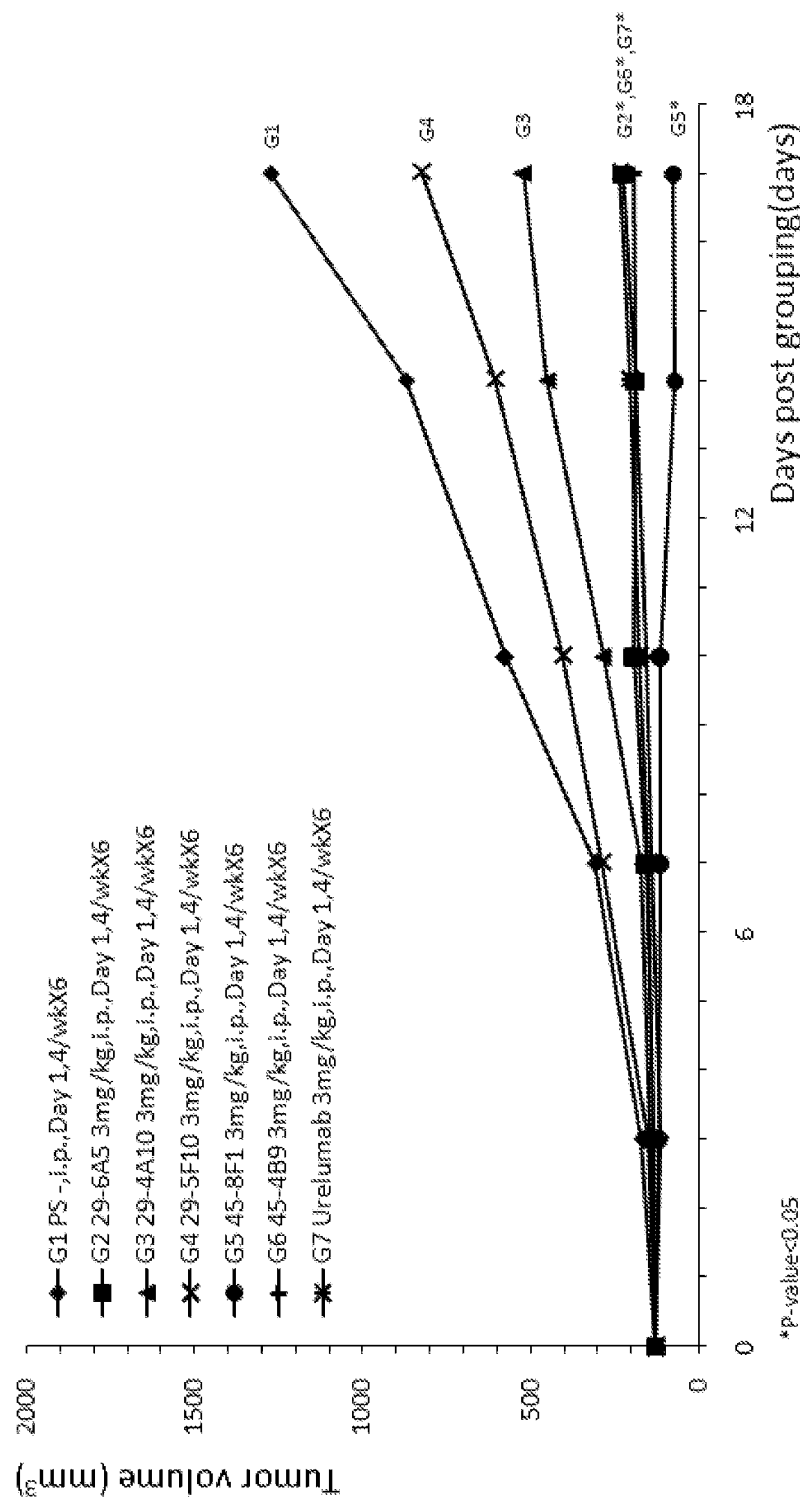


FIG. 12

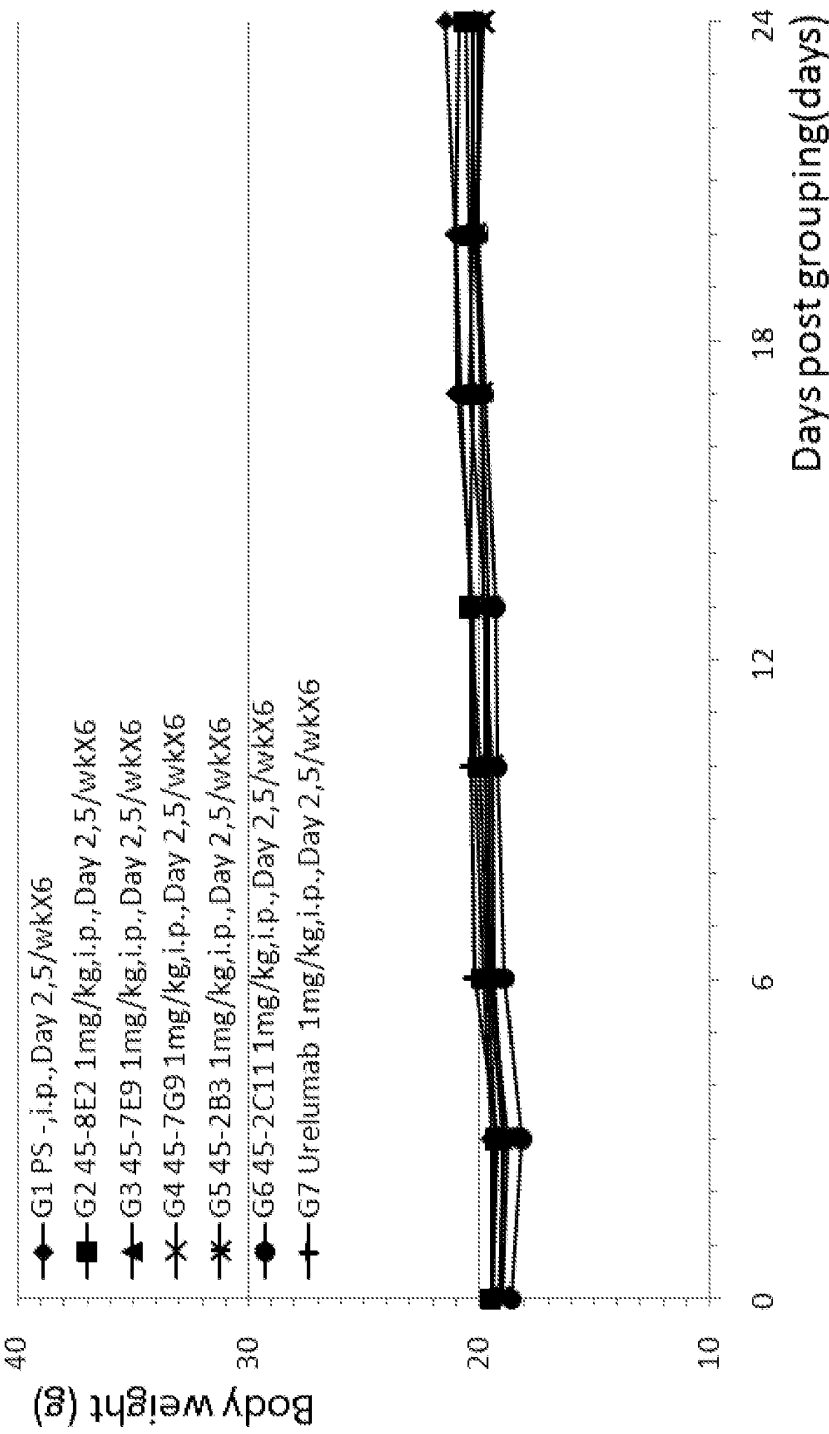


FIG. 13

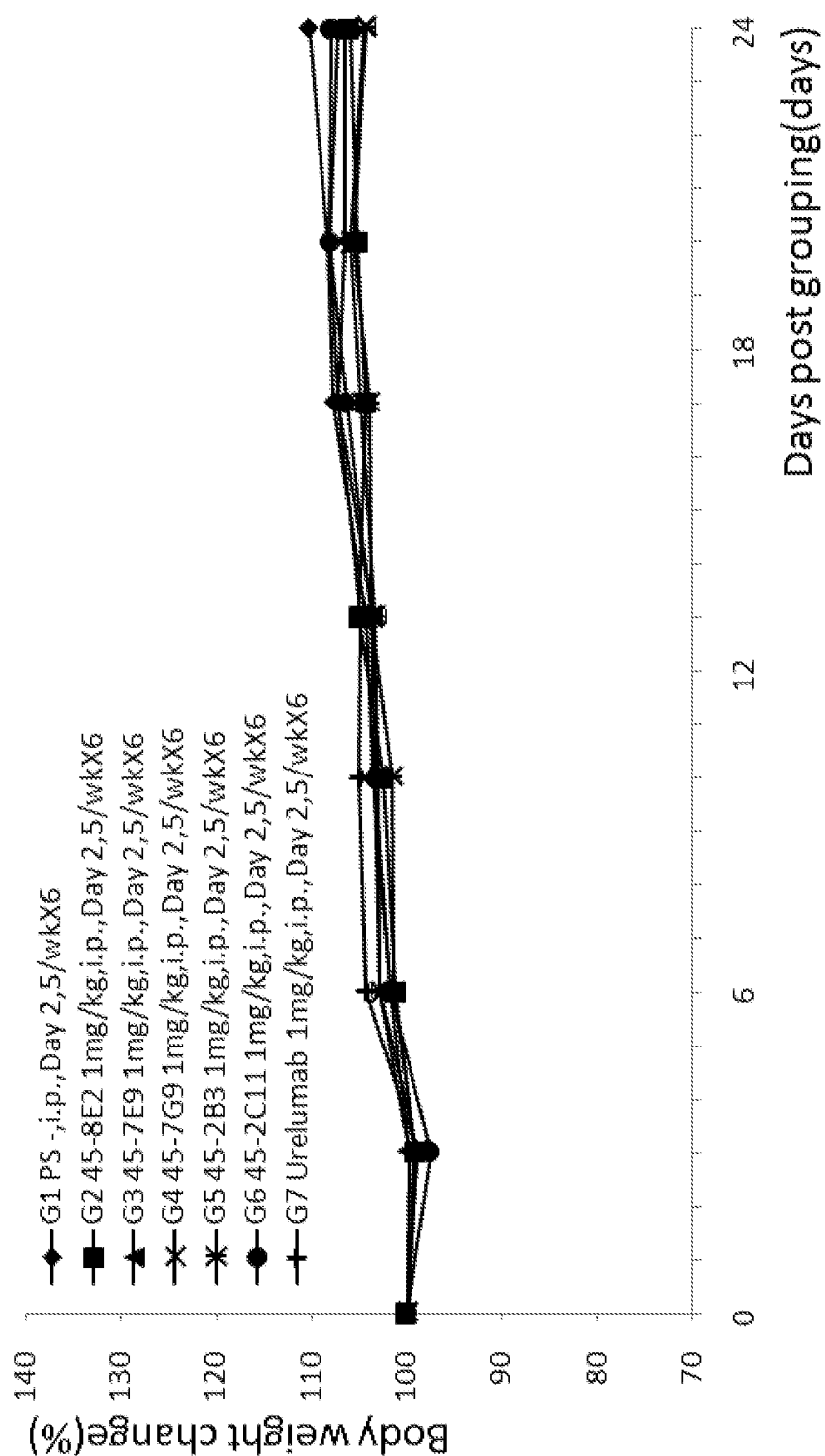


FIG. 14

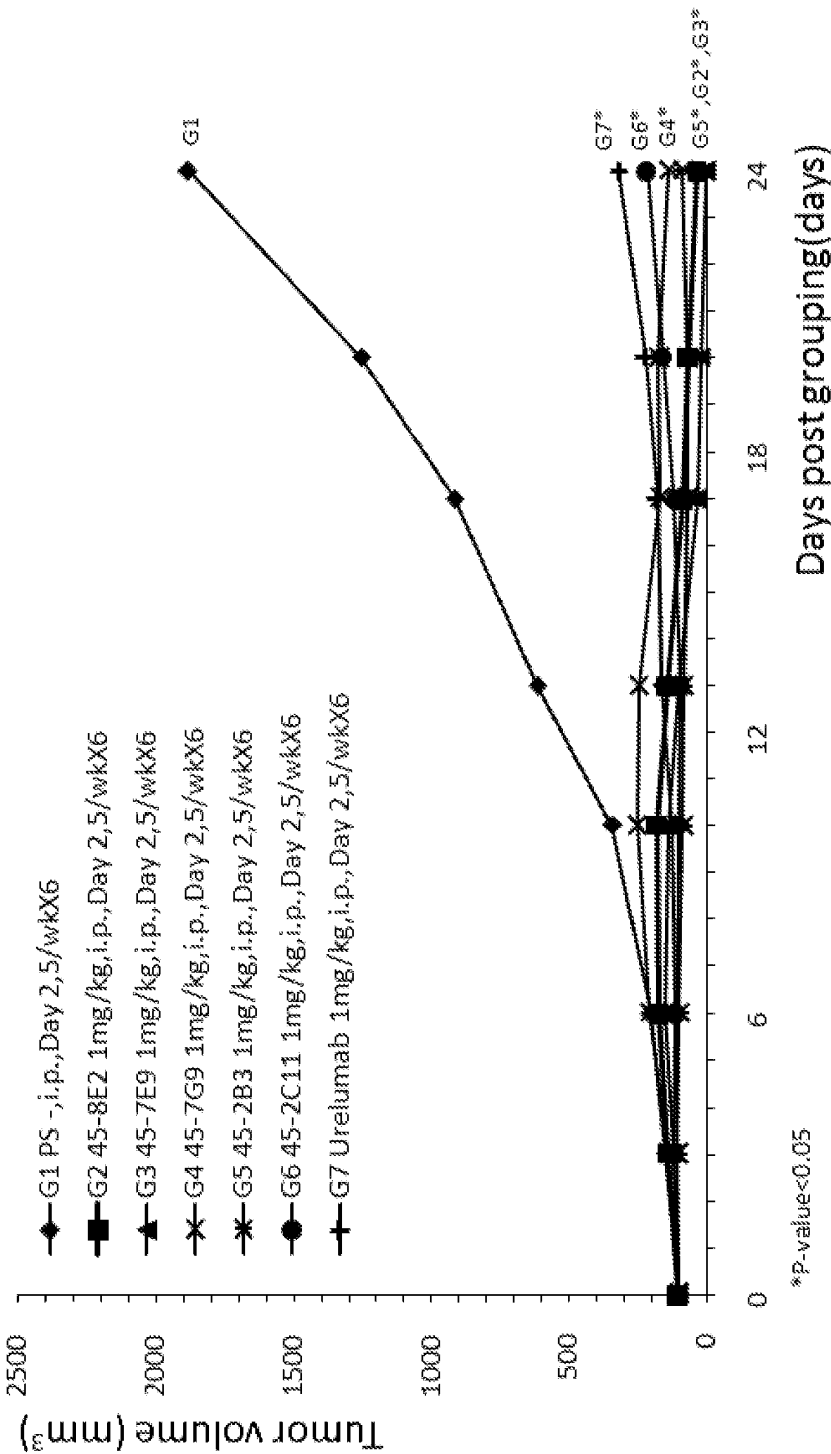


FIG. 15

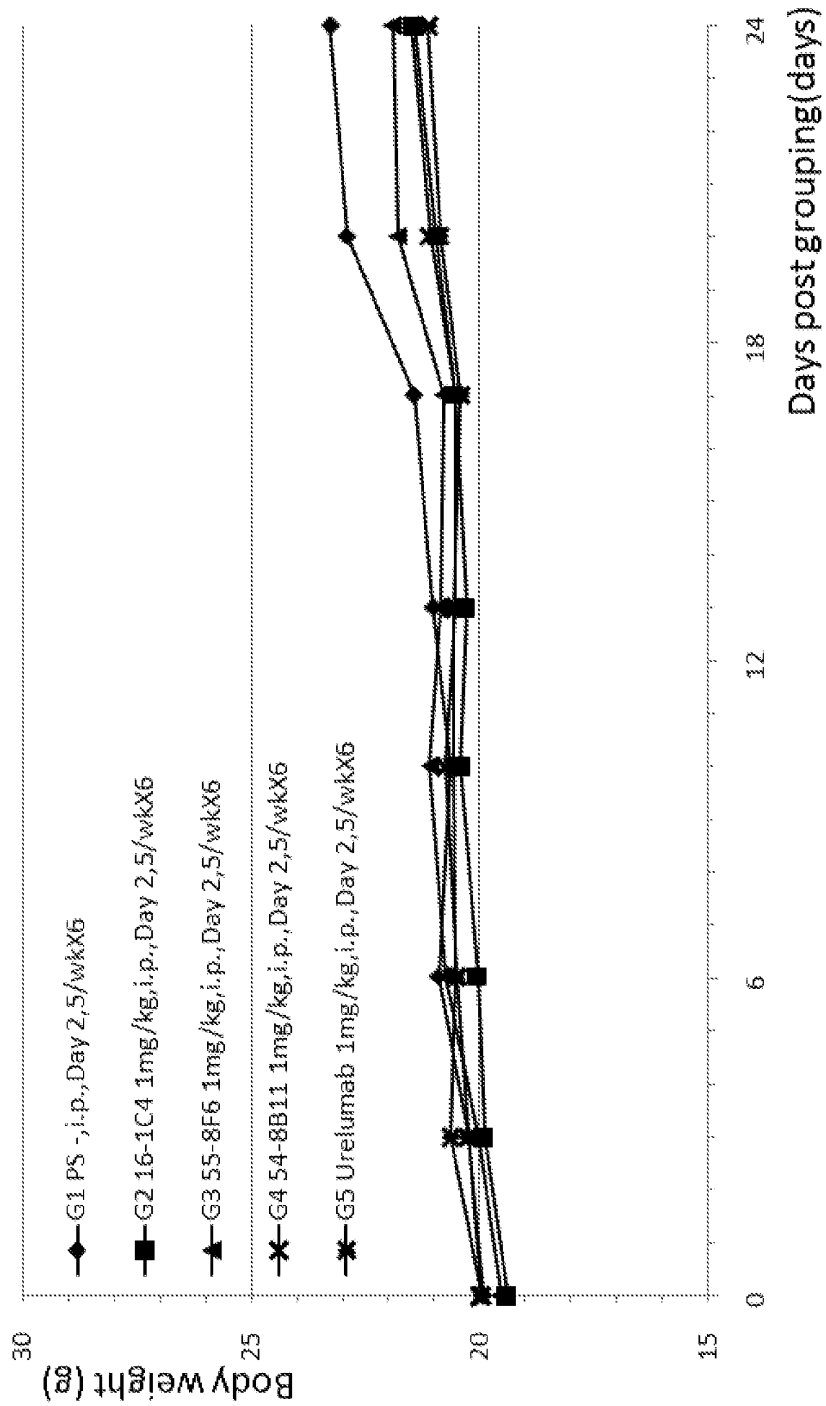


FIG. 16

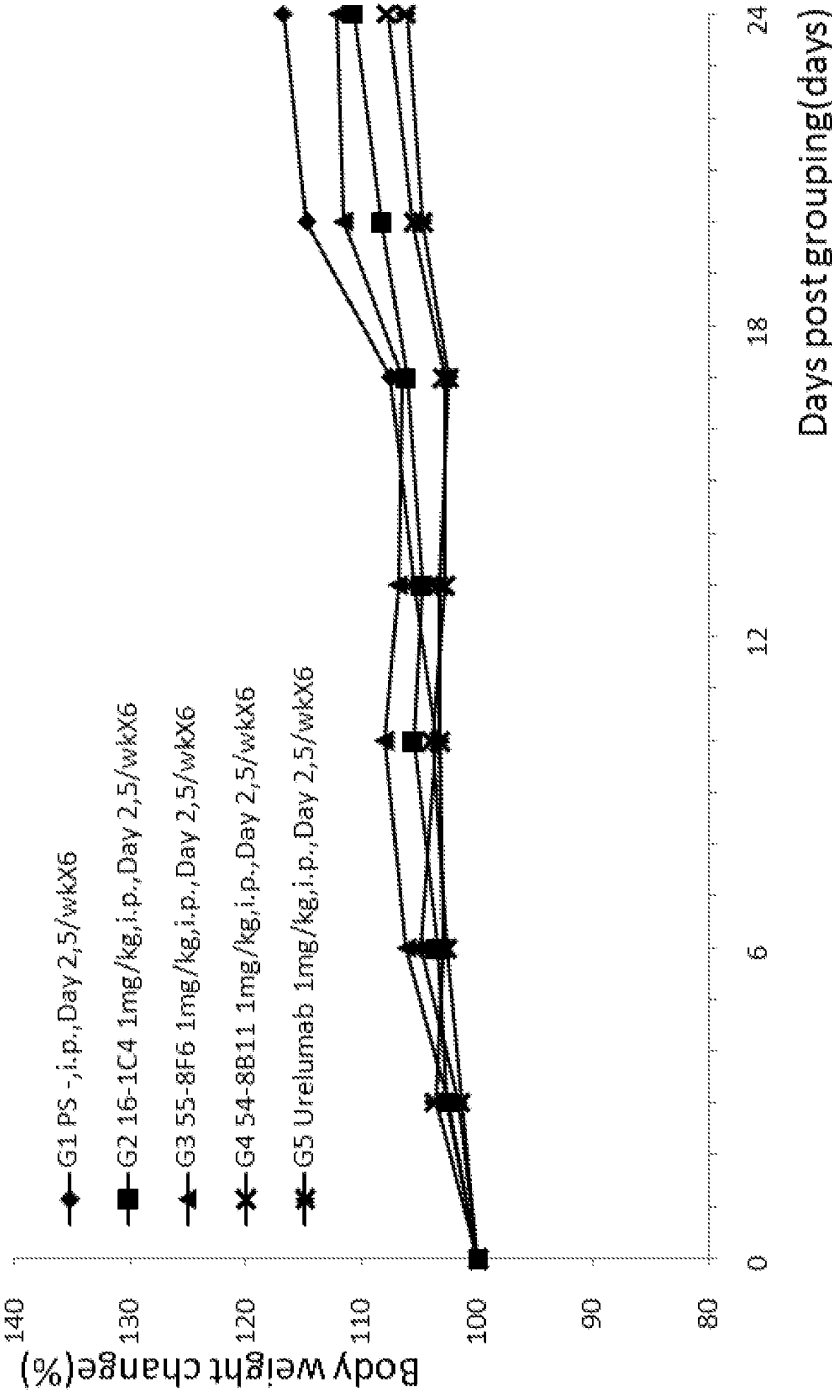


FIG. 17

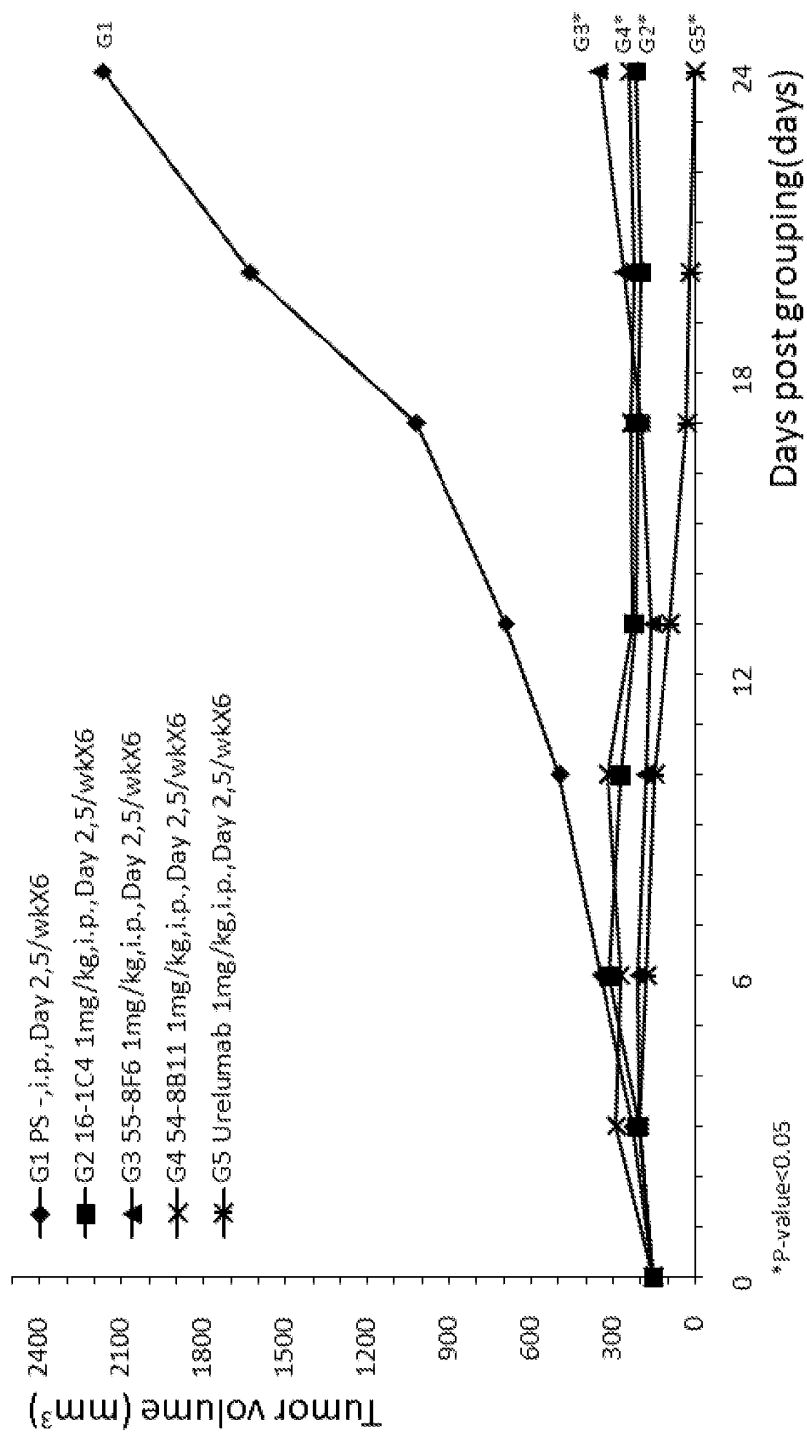


FIG. 18

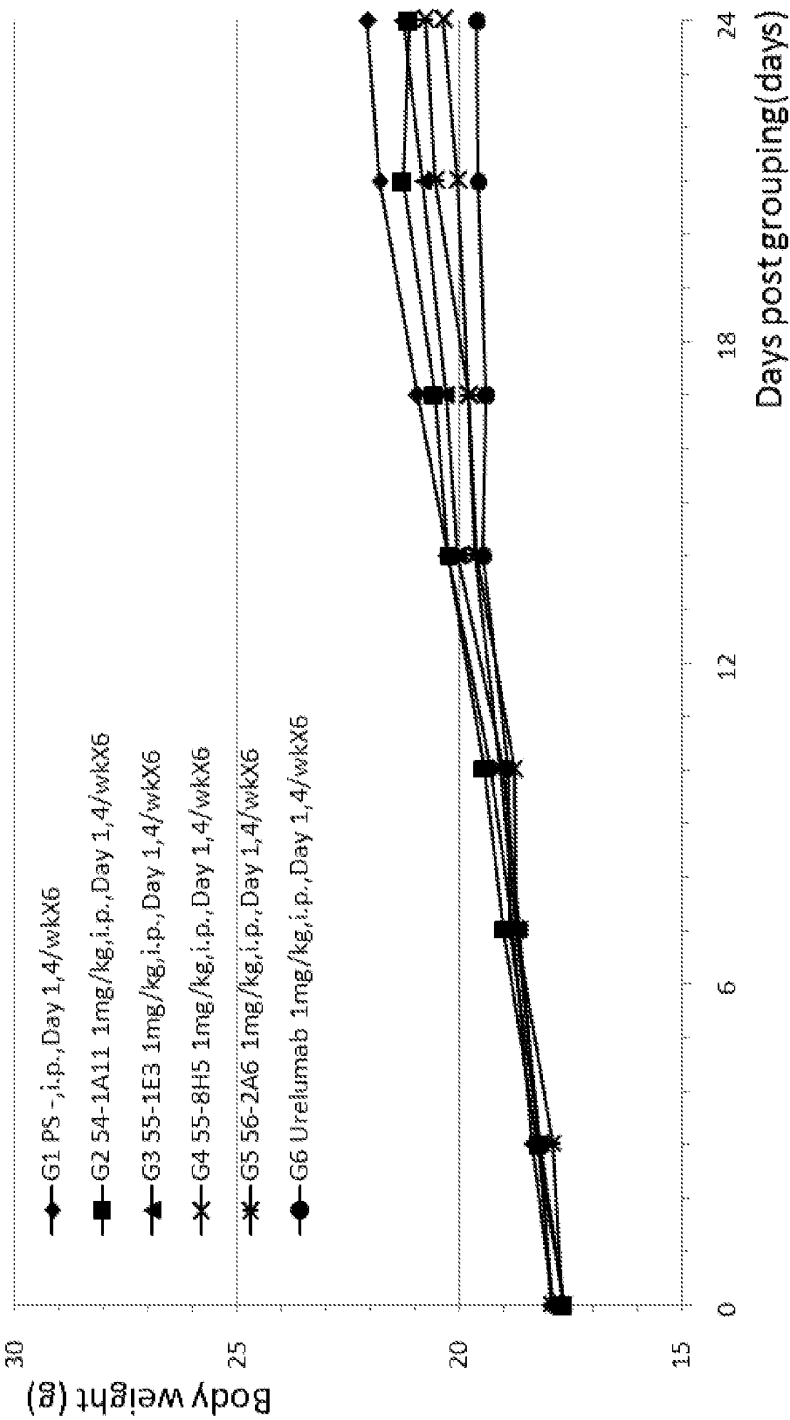


FIG. 19

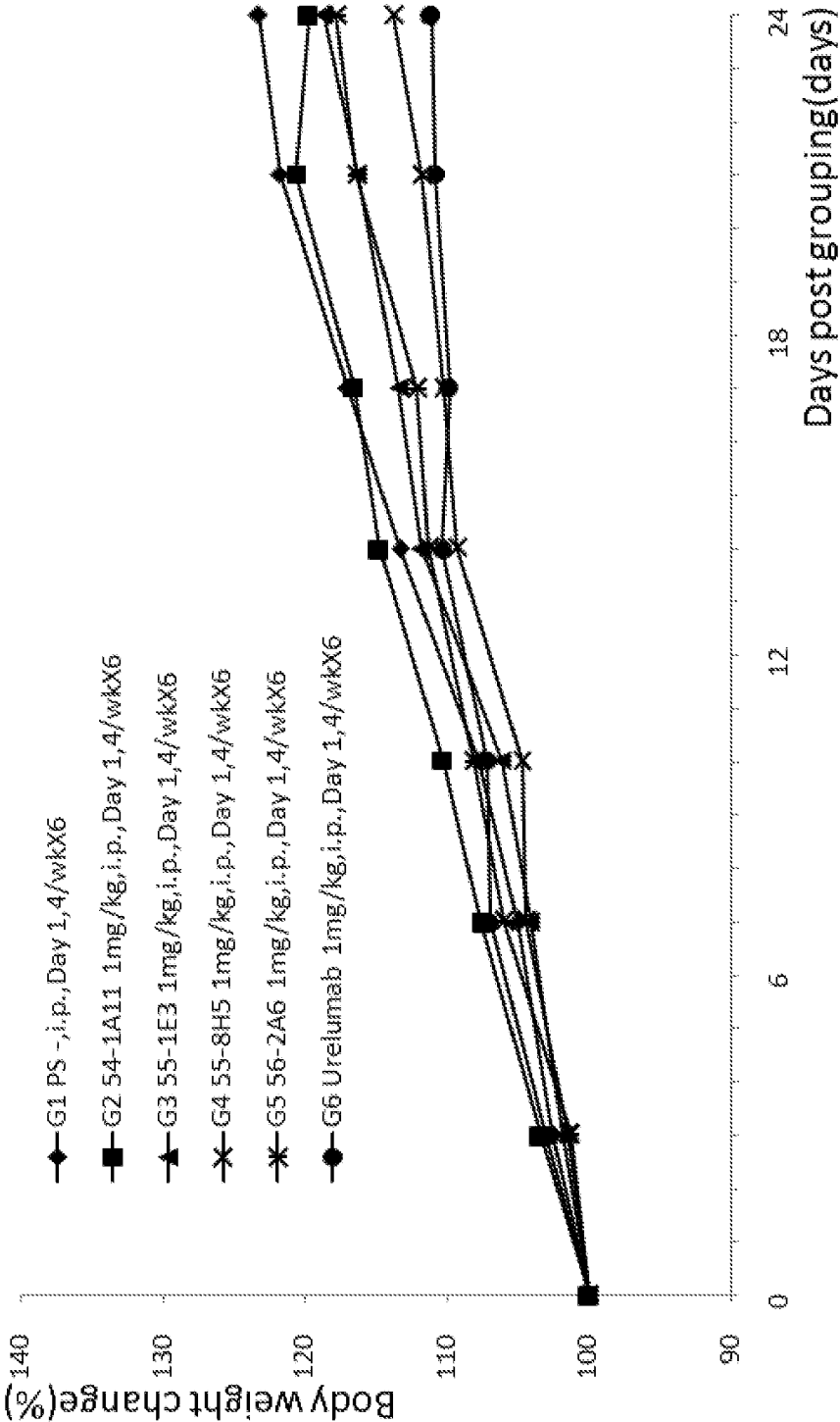


FIG. 20

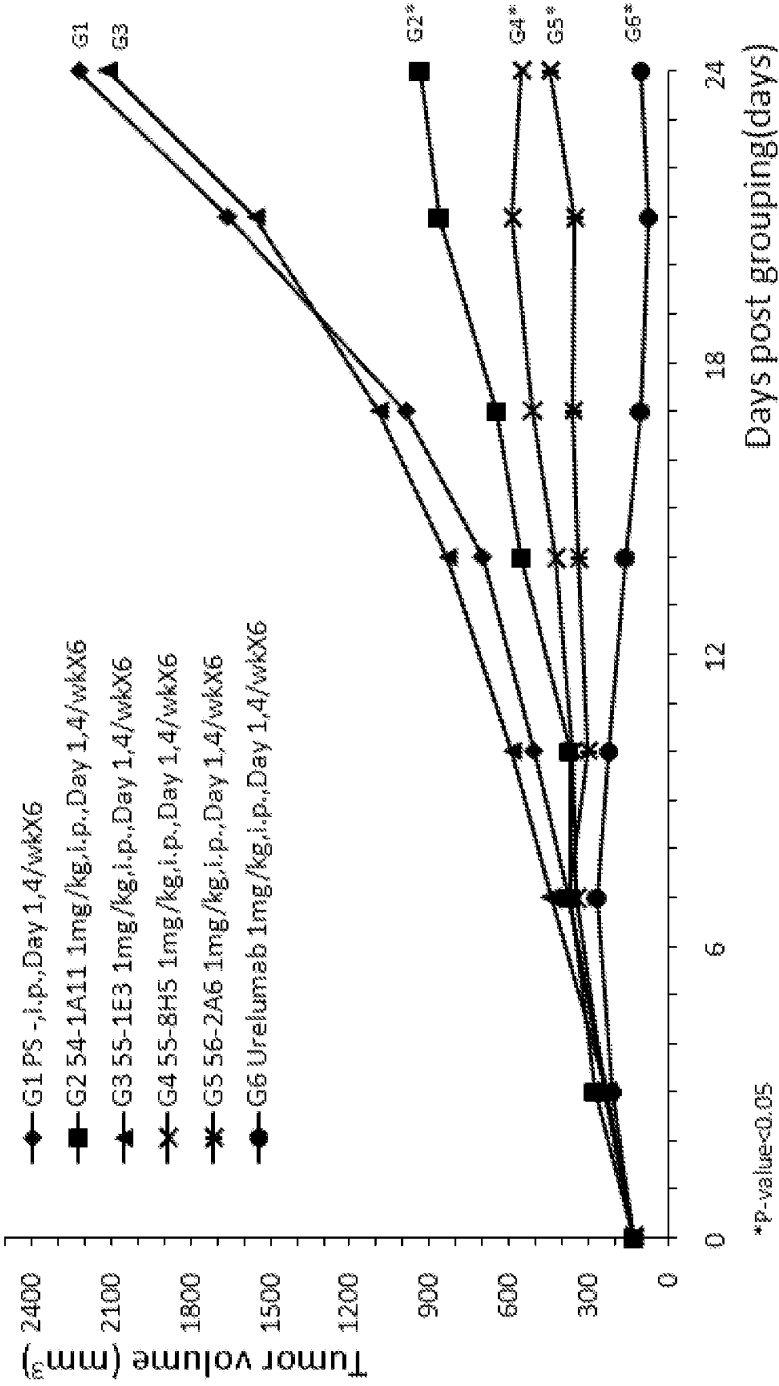


FIG. 21

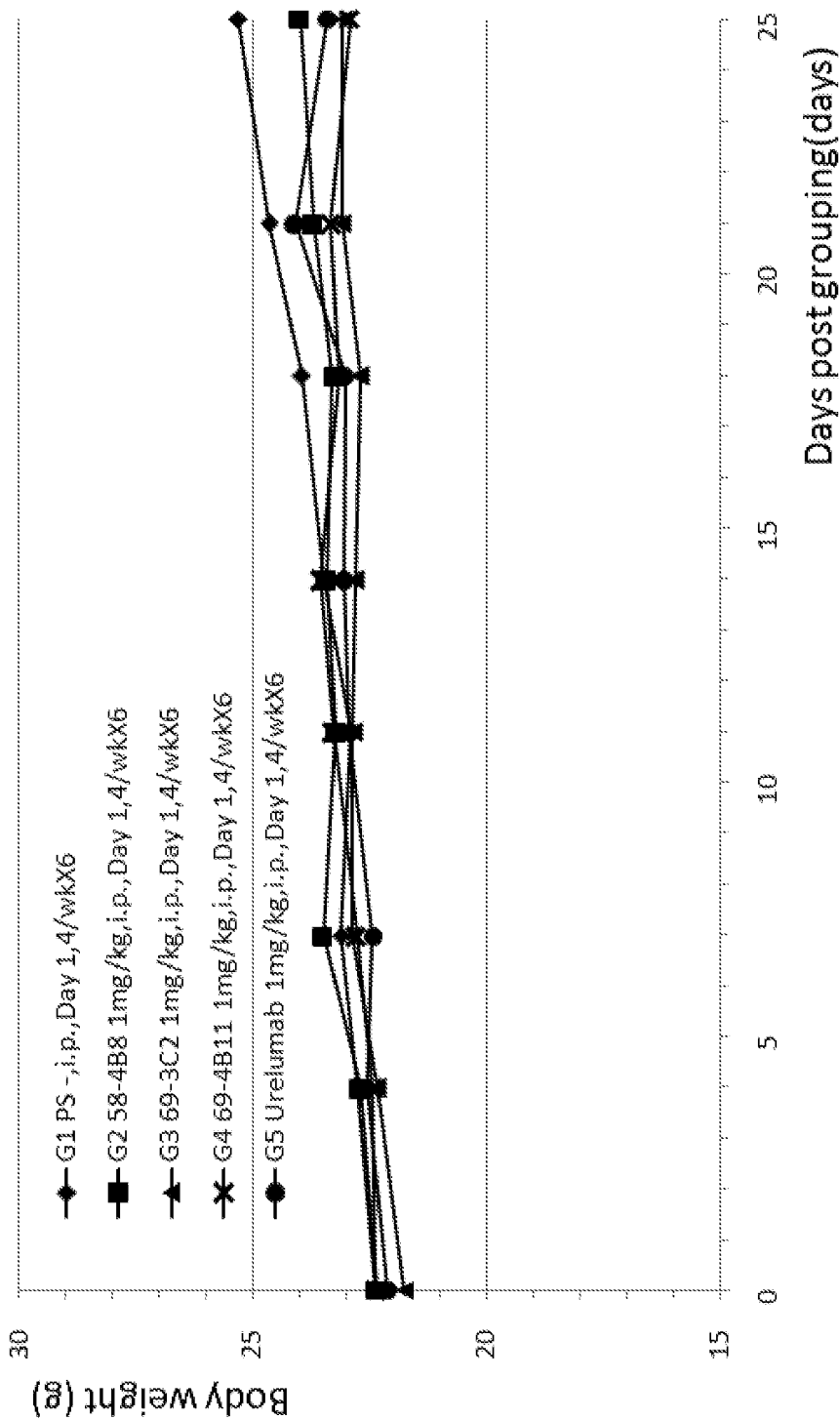


FIG. 22

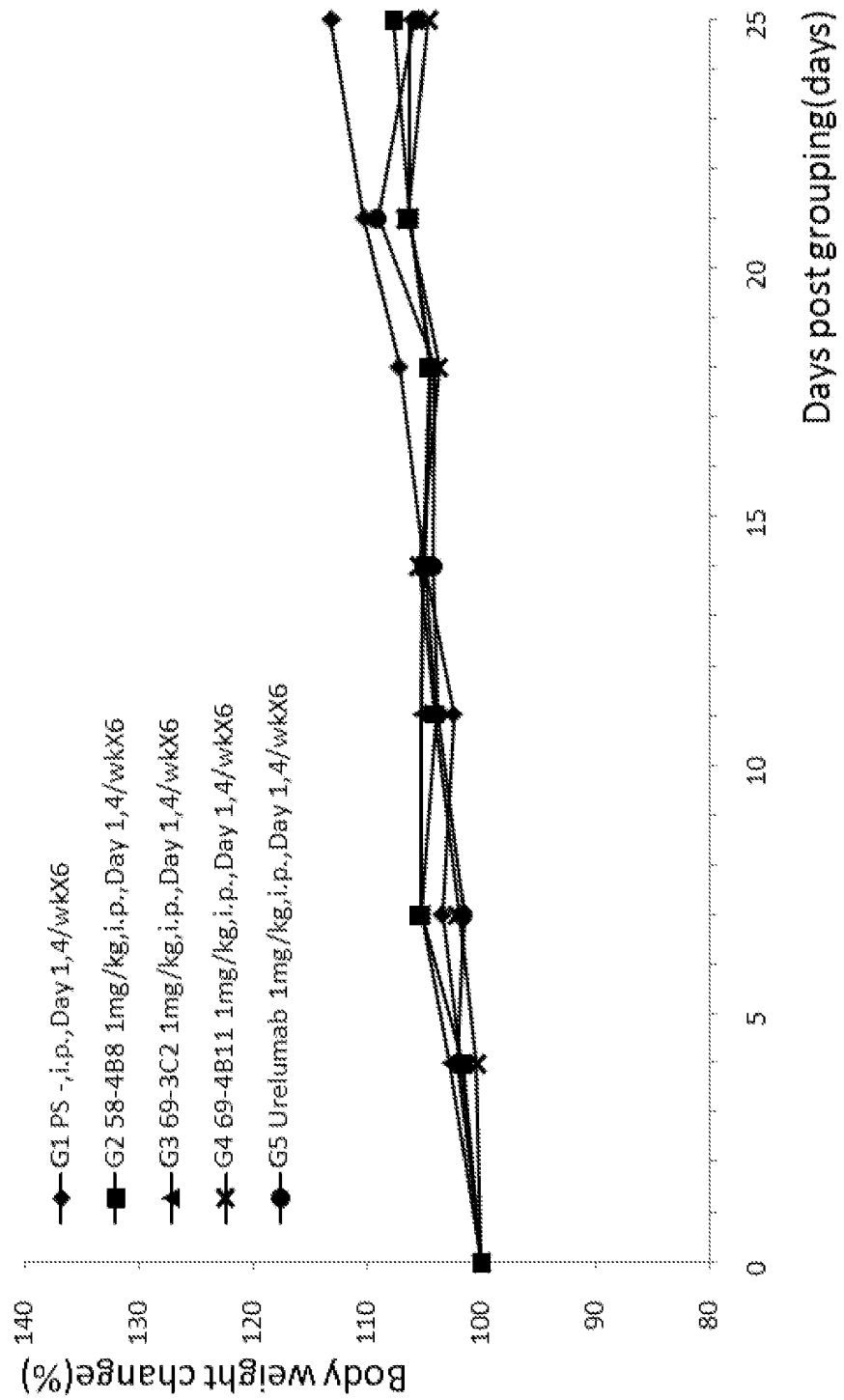


FIG. 23

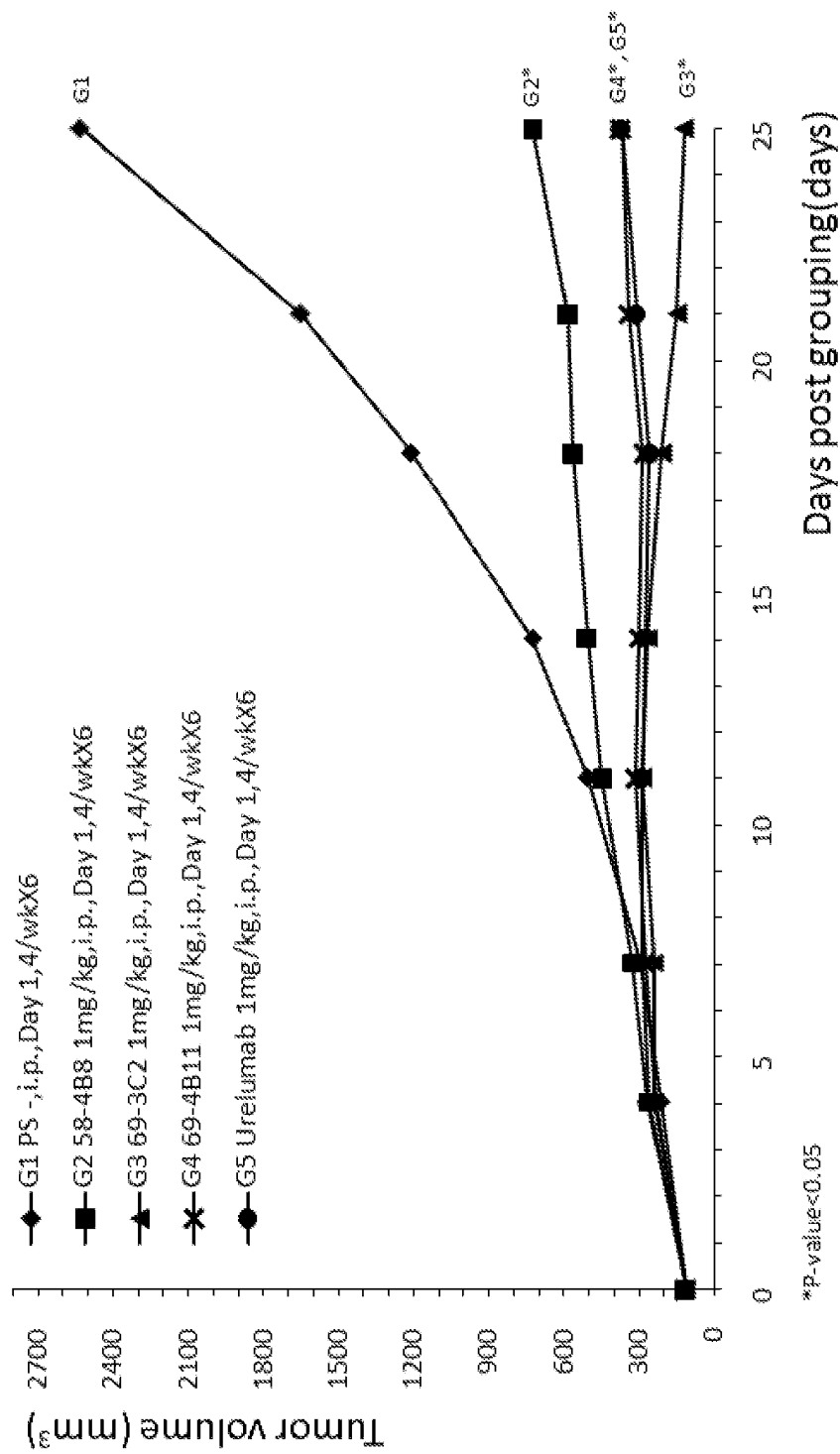


FIG. 24

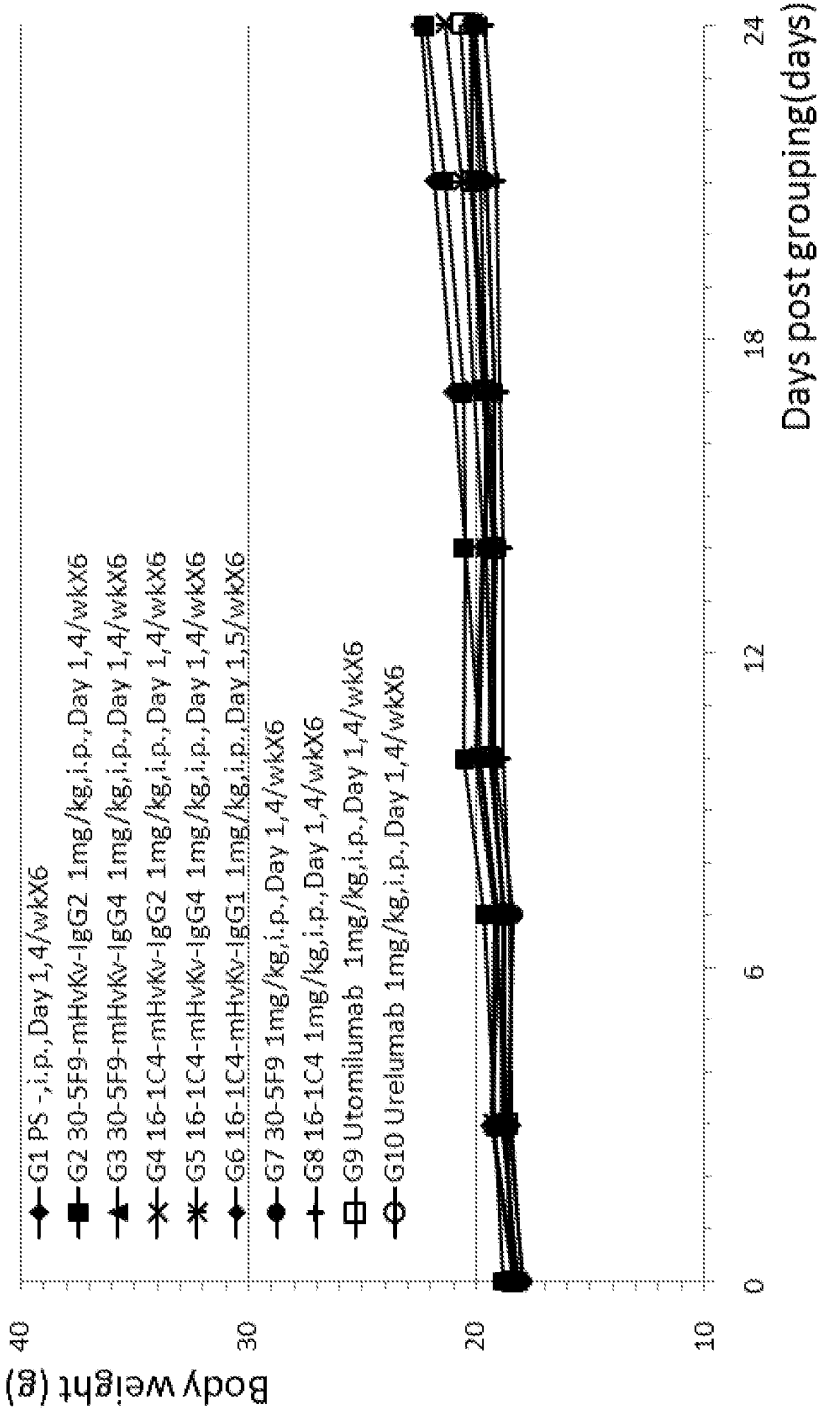


FIG. 25

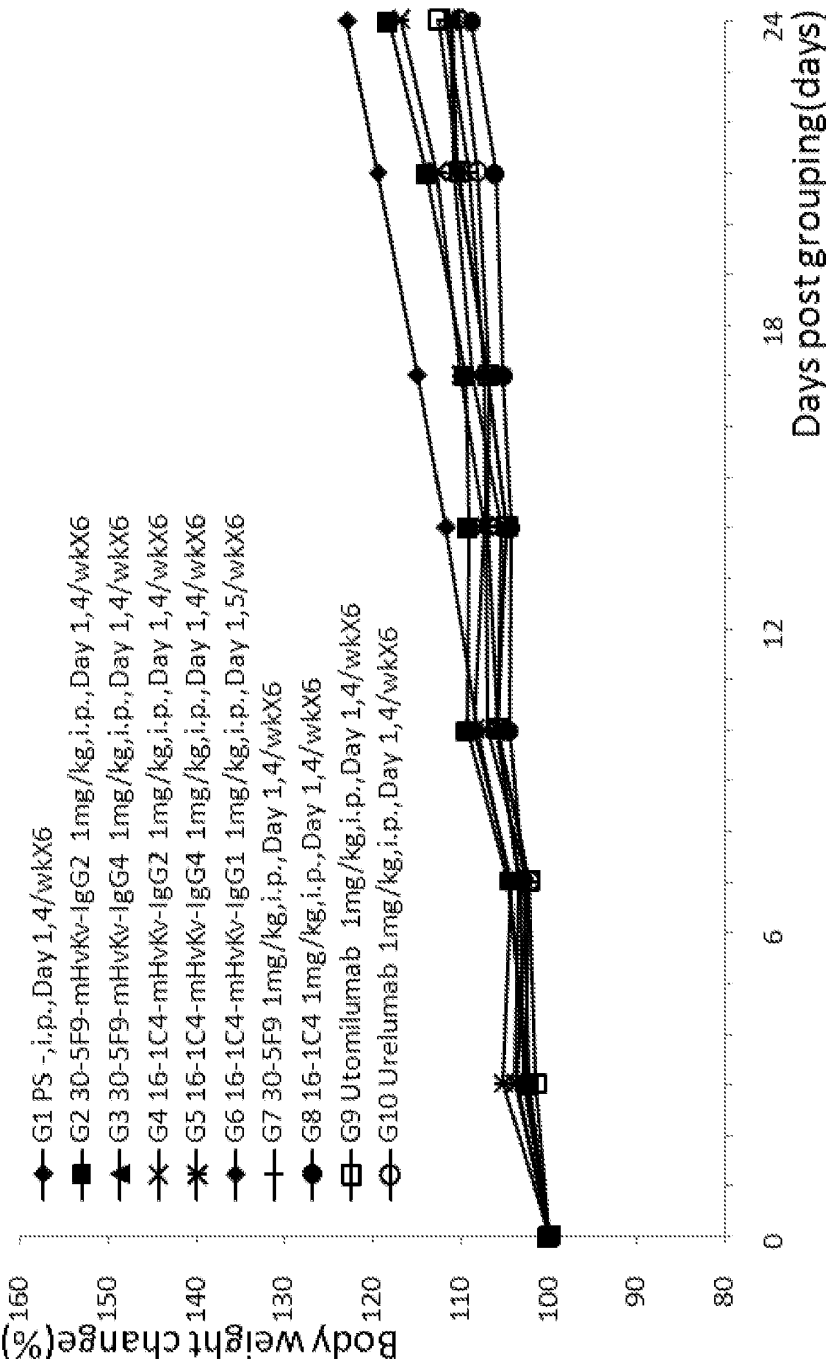


FIG. 26

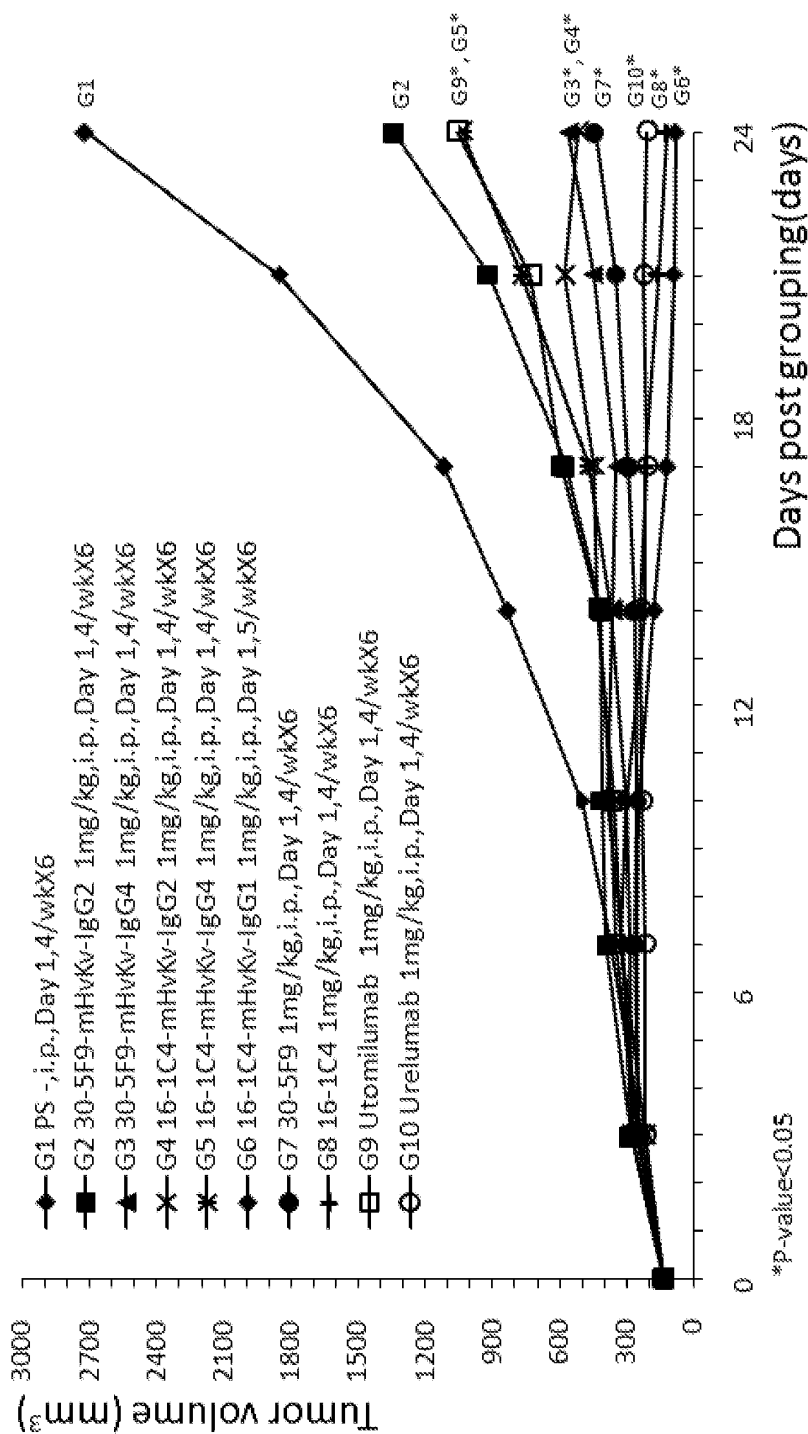


FIG. 27

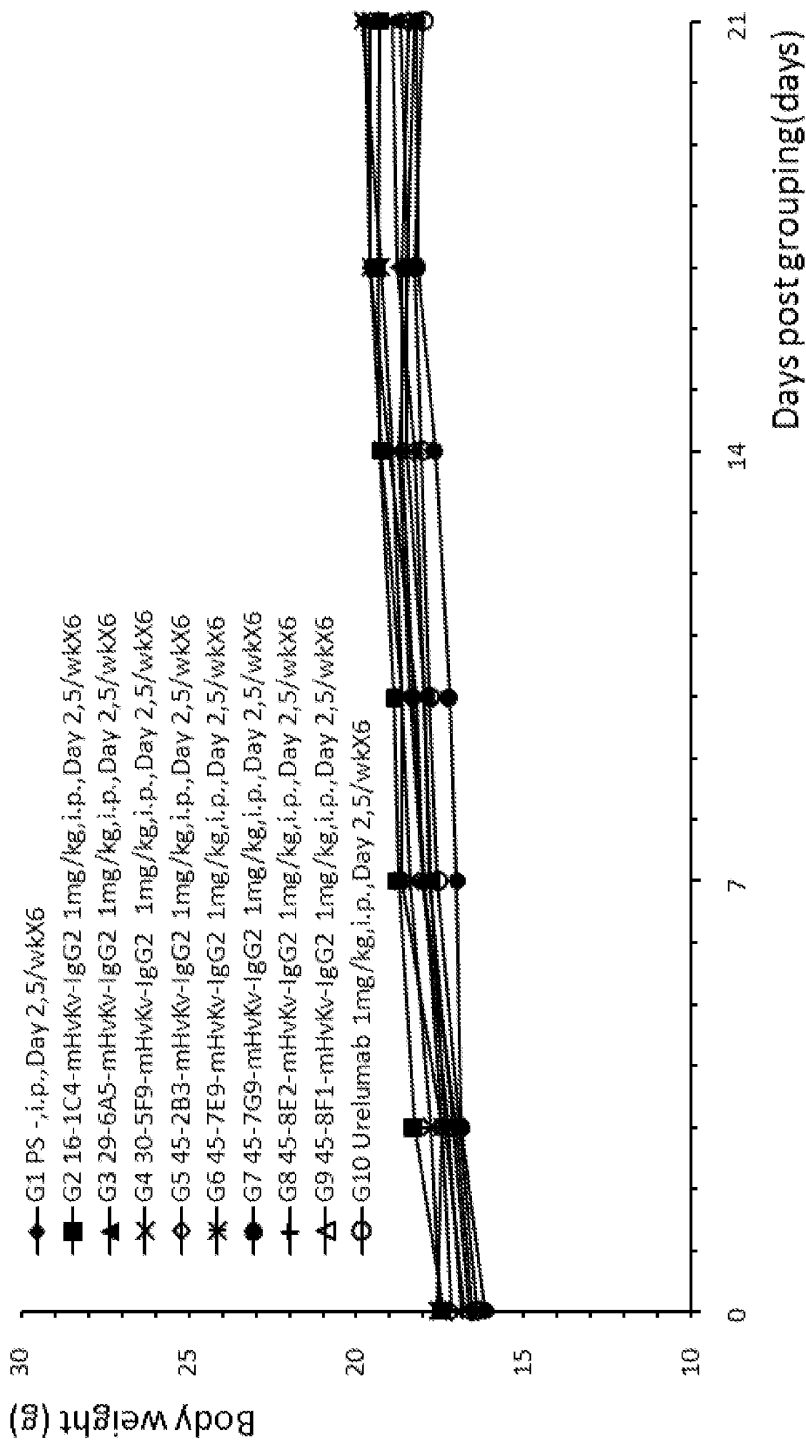


FIG. 28

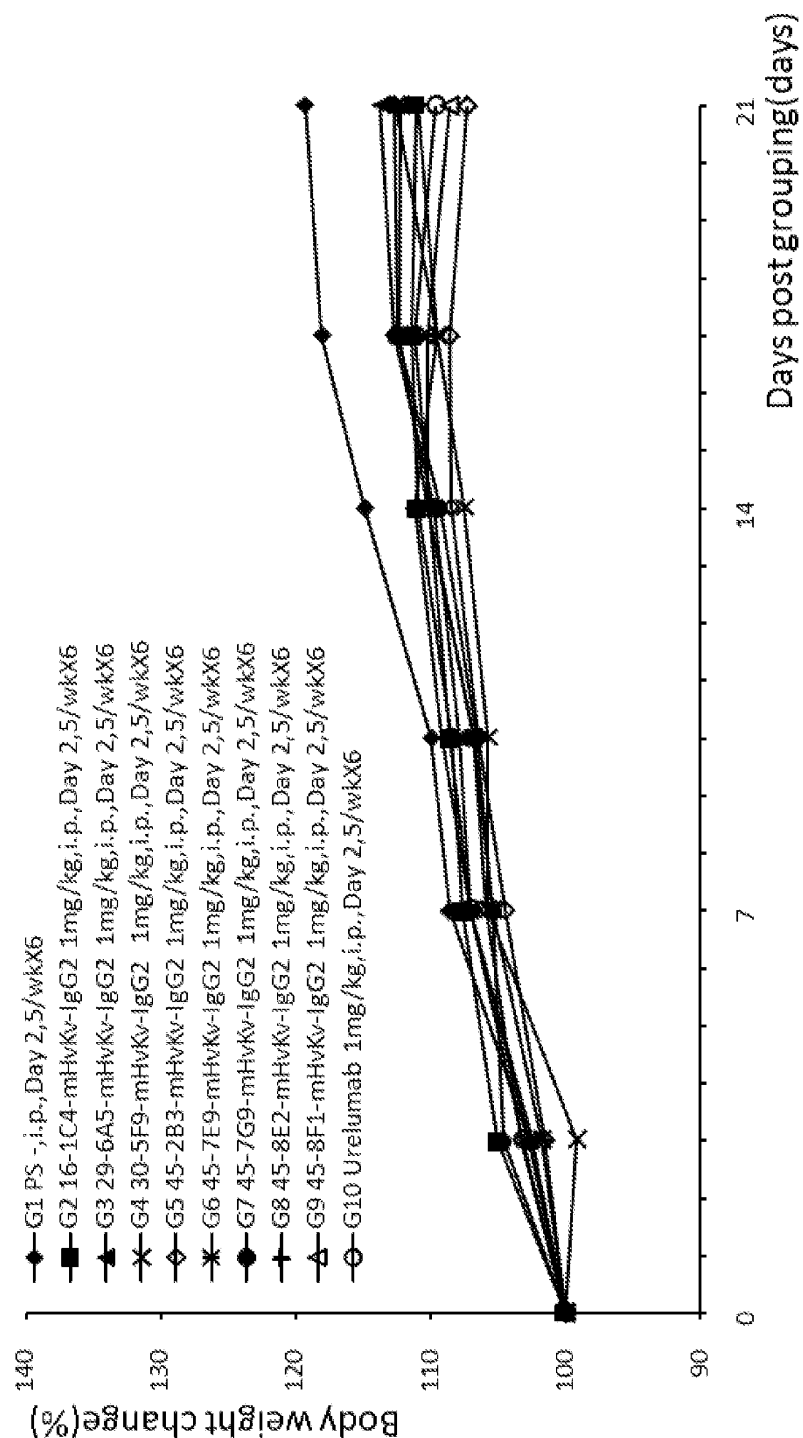


FIG. 29

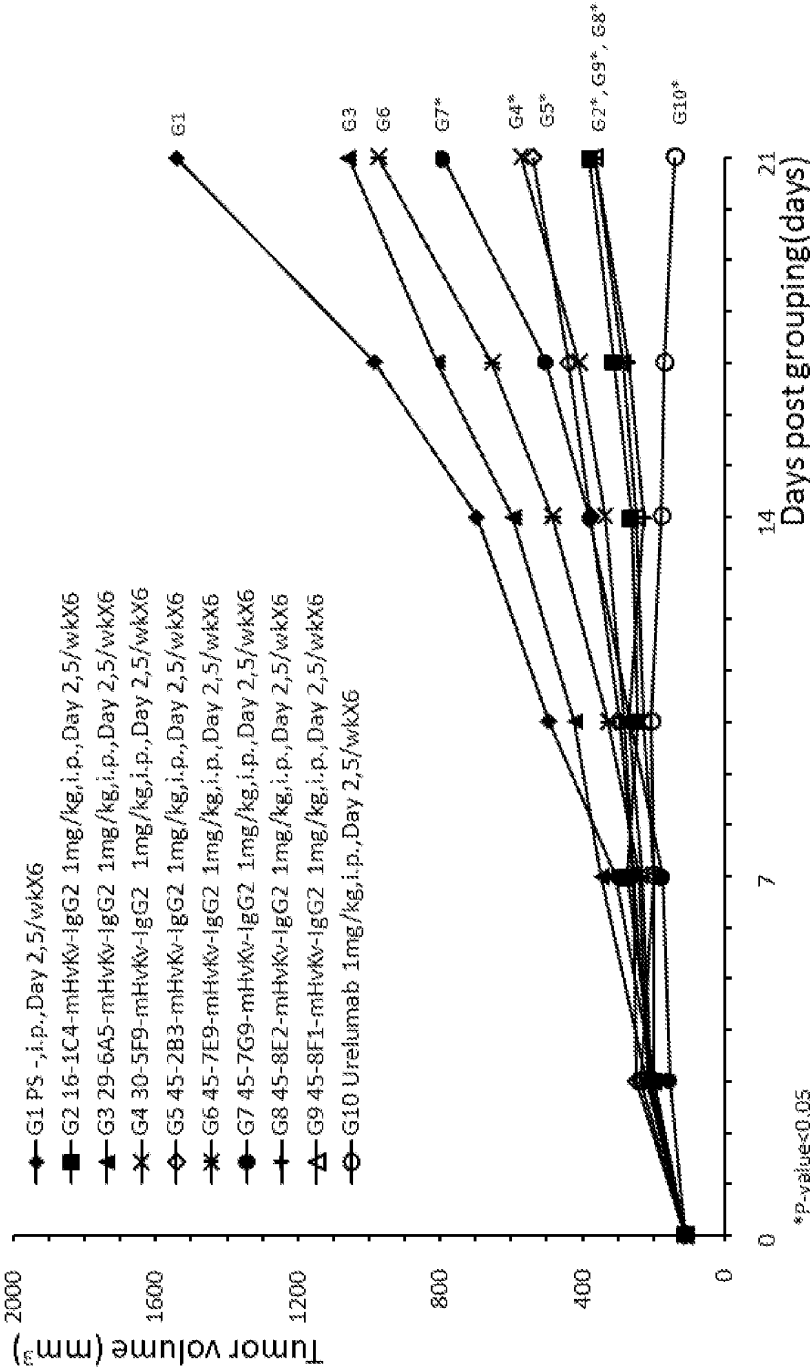


FIG. 30

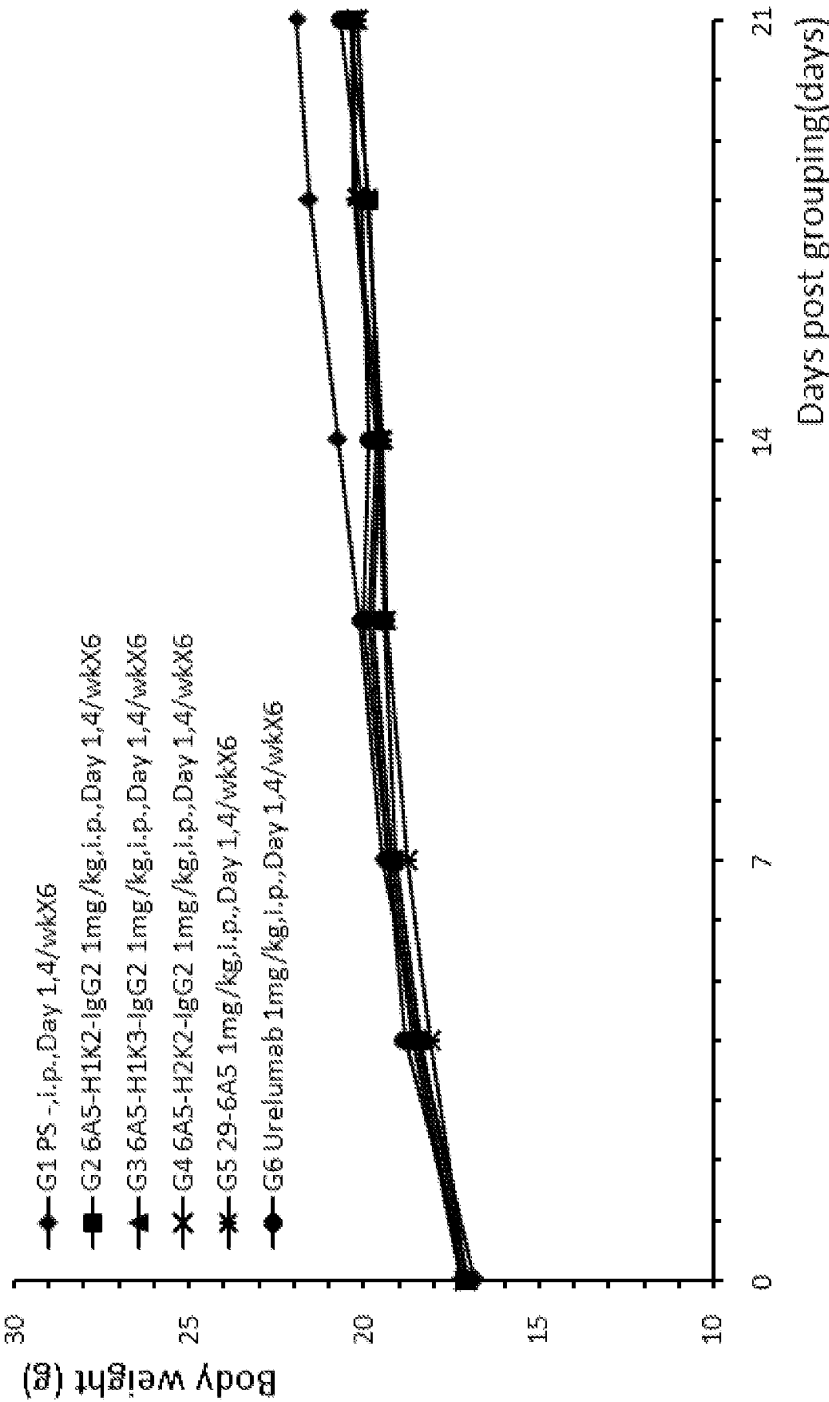


FIG. 31

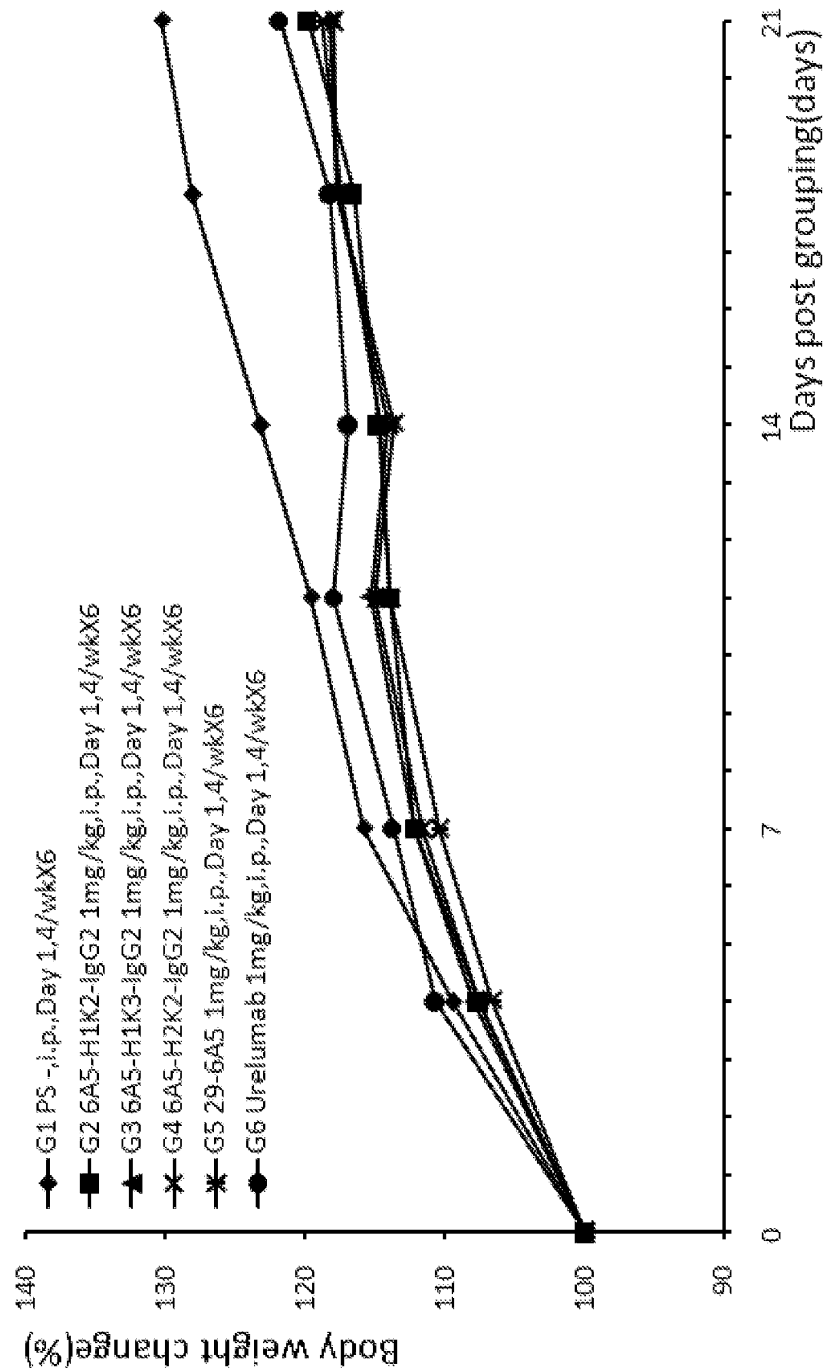


FIG. 32

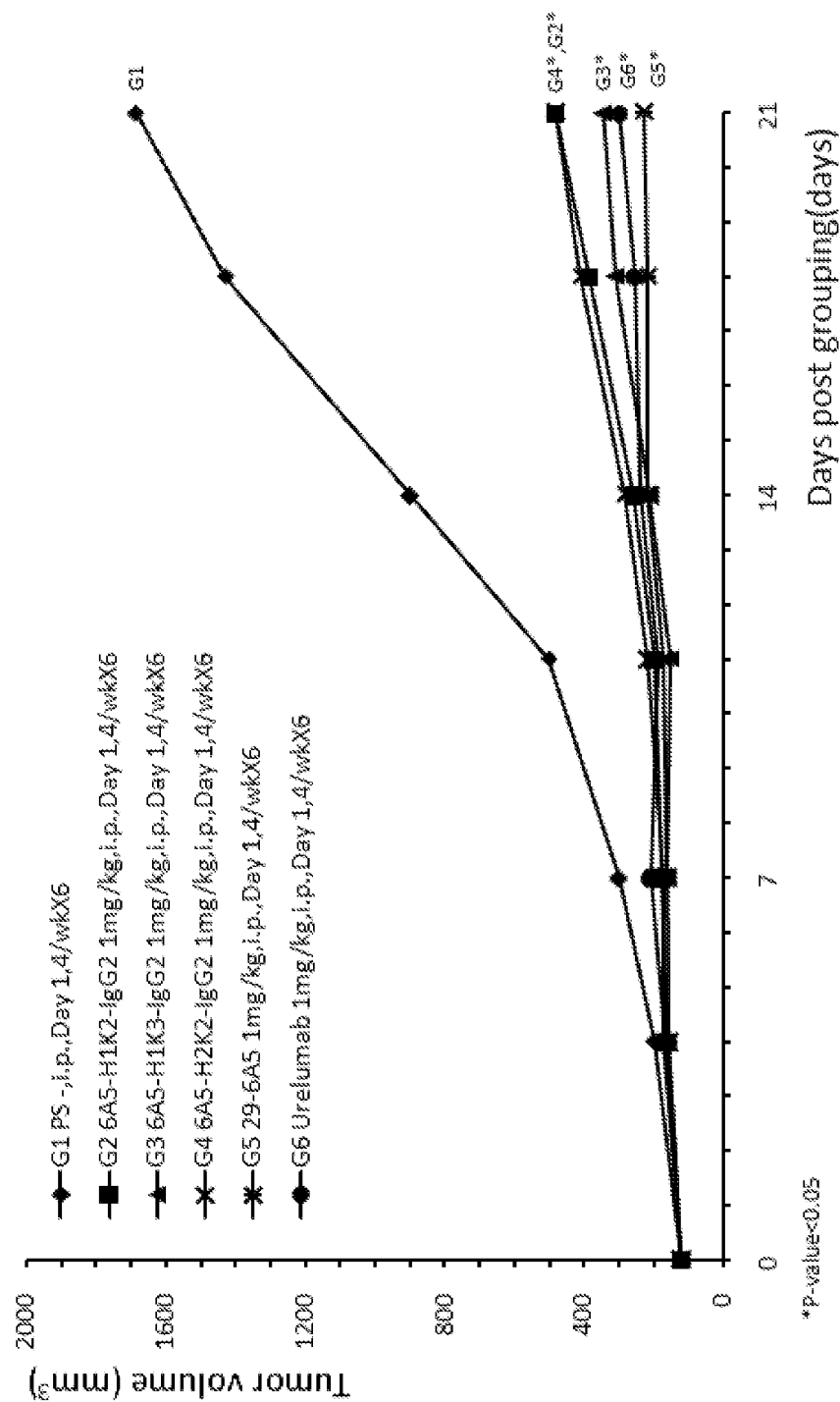


FIG. 33

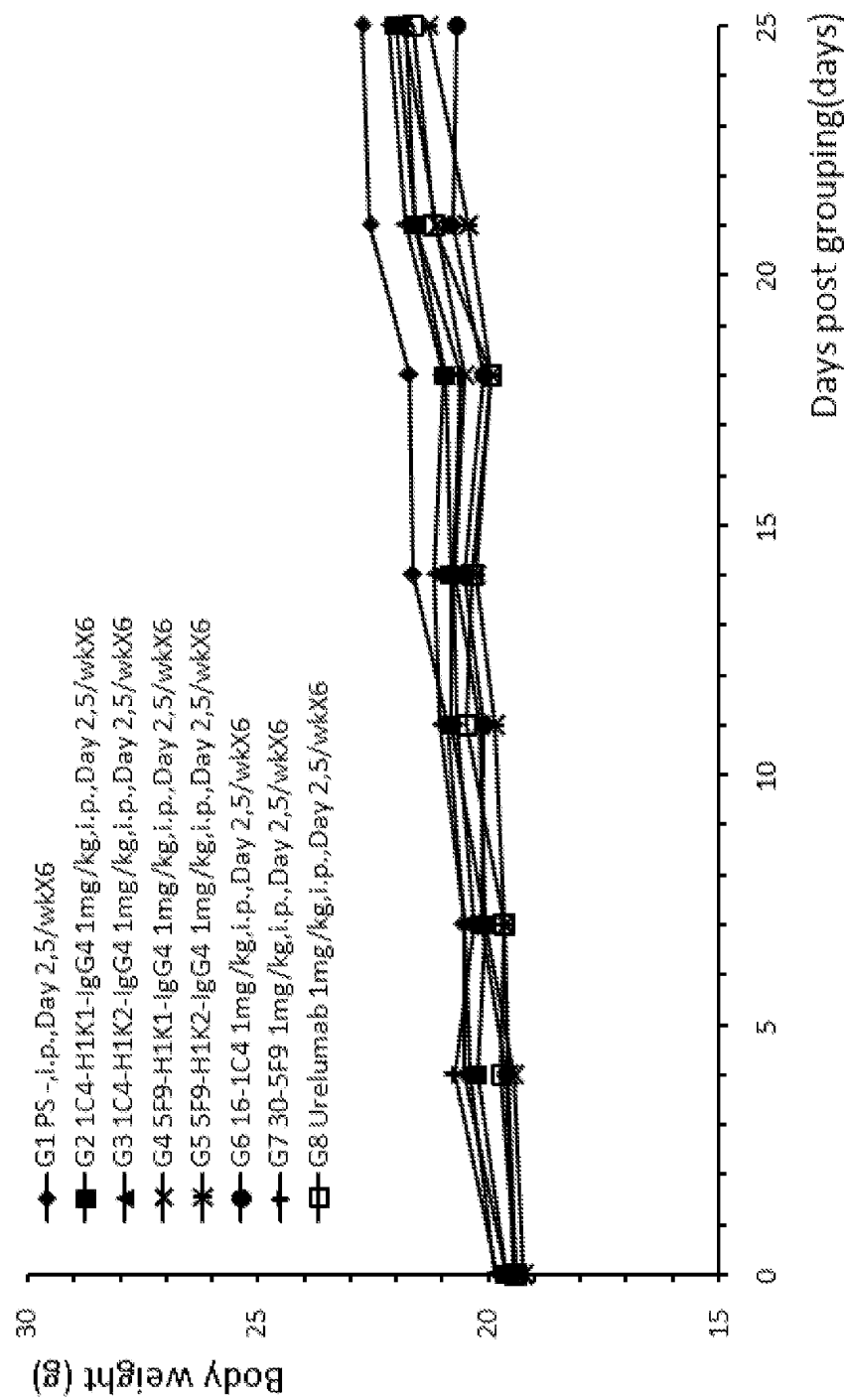


FIG. 34

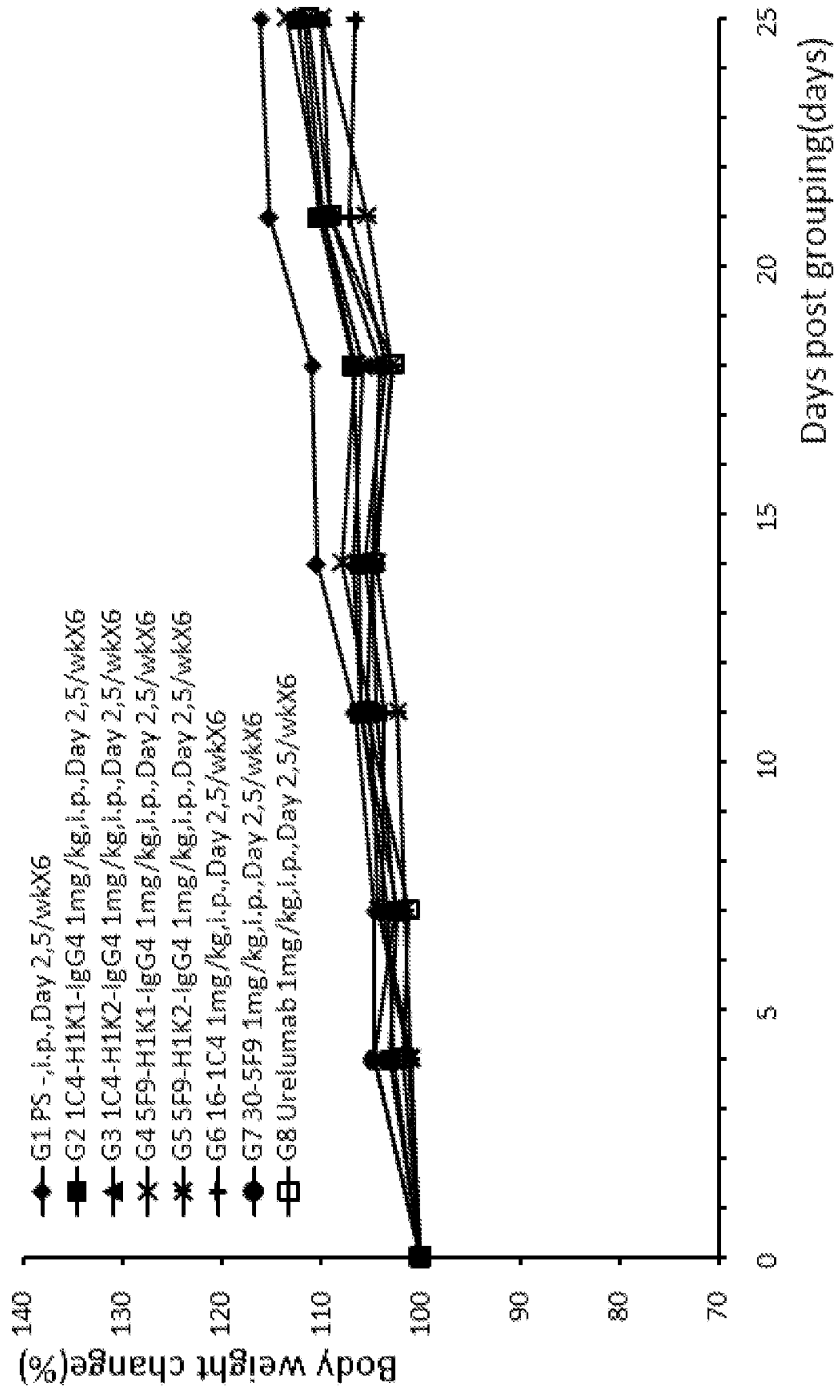


FIG. 35

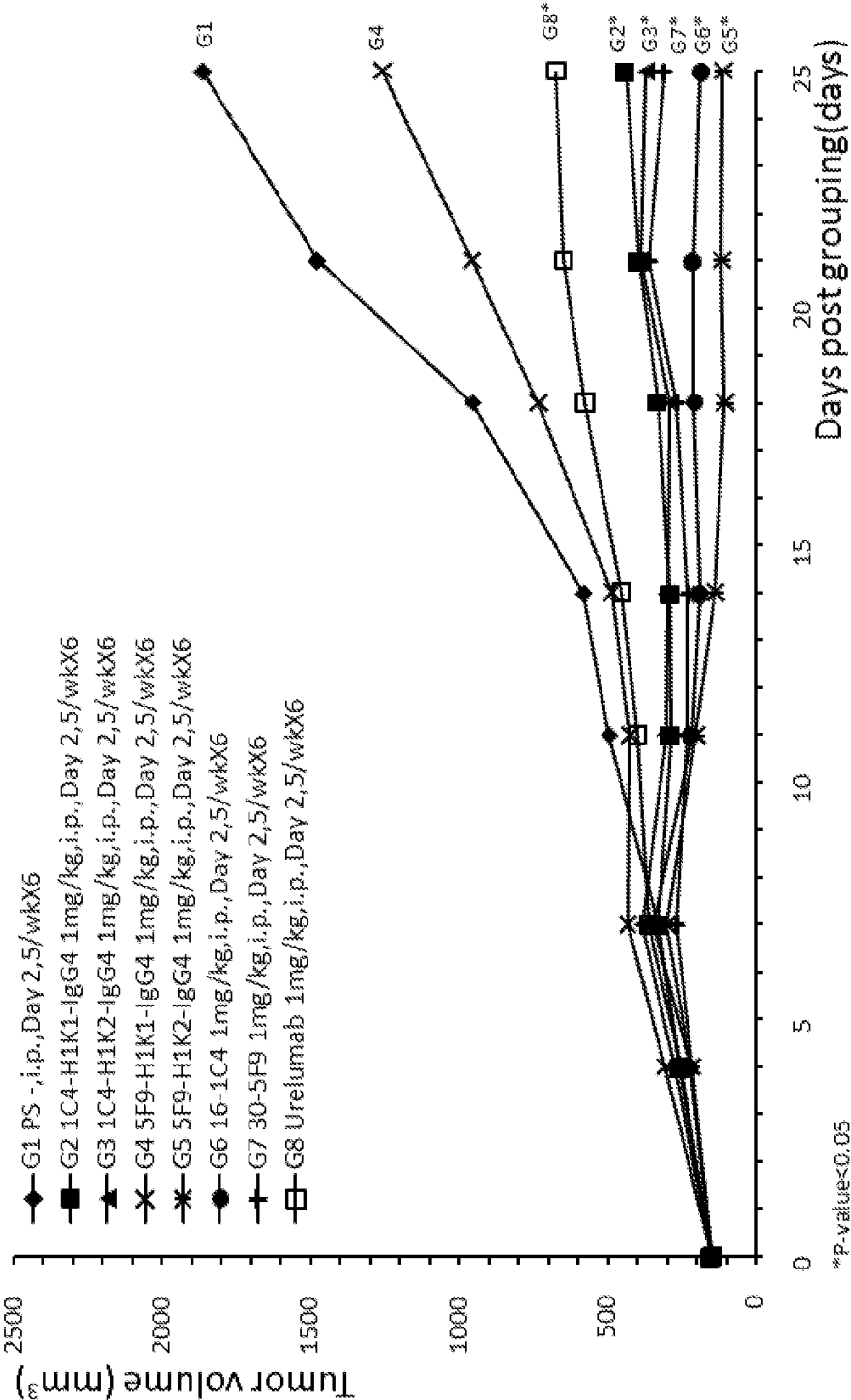


FIG. 36

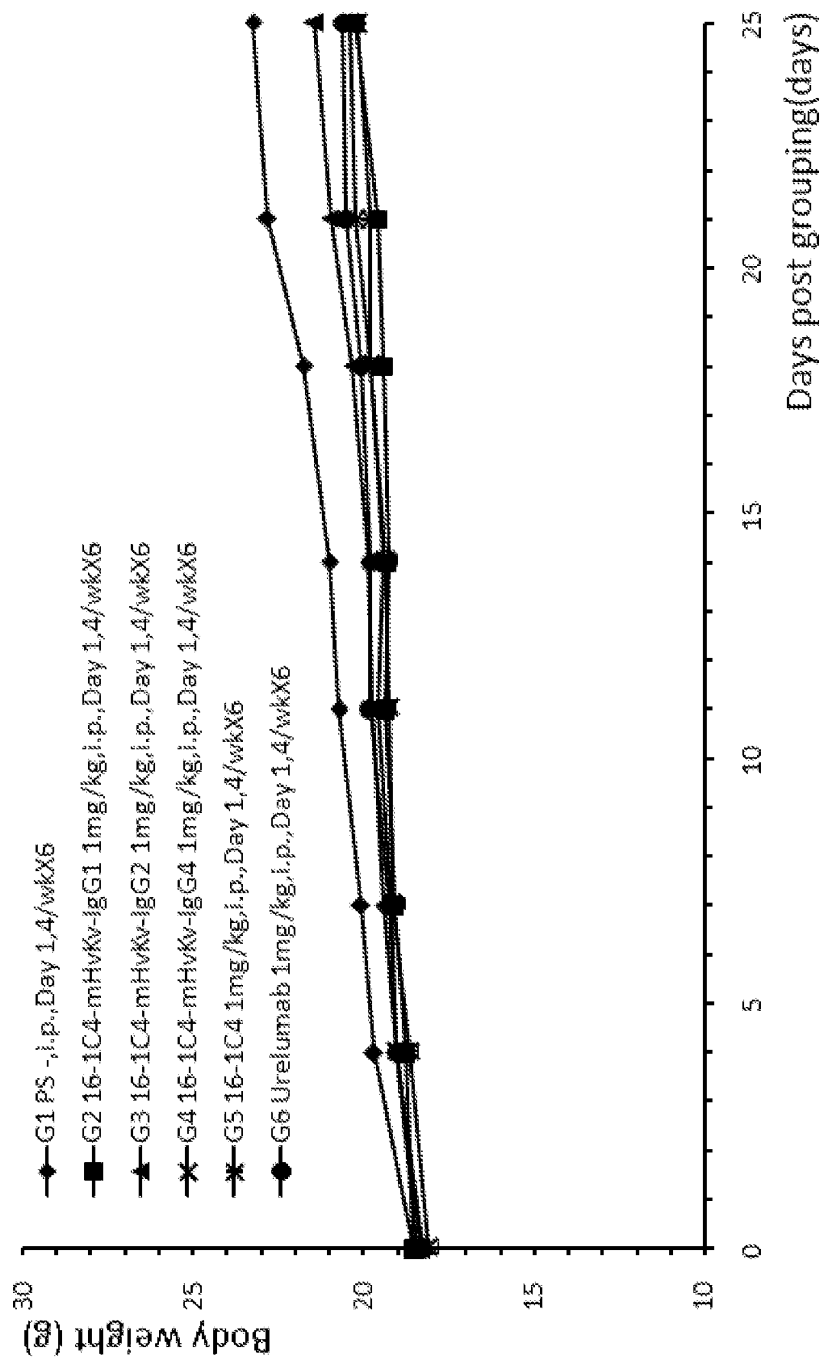


FIG. 37

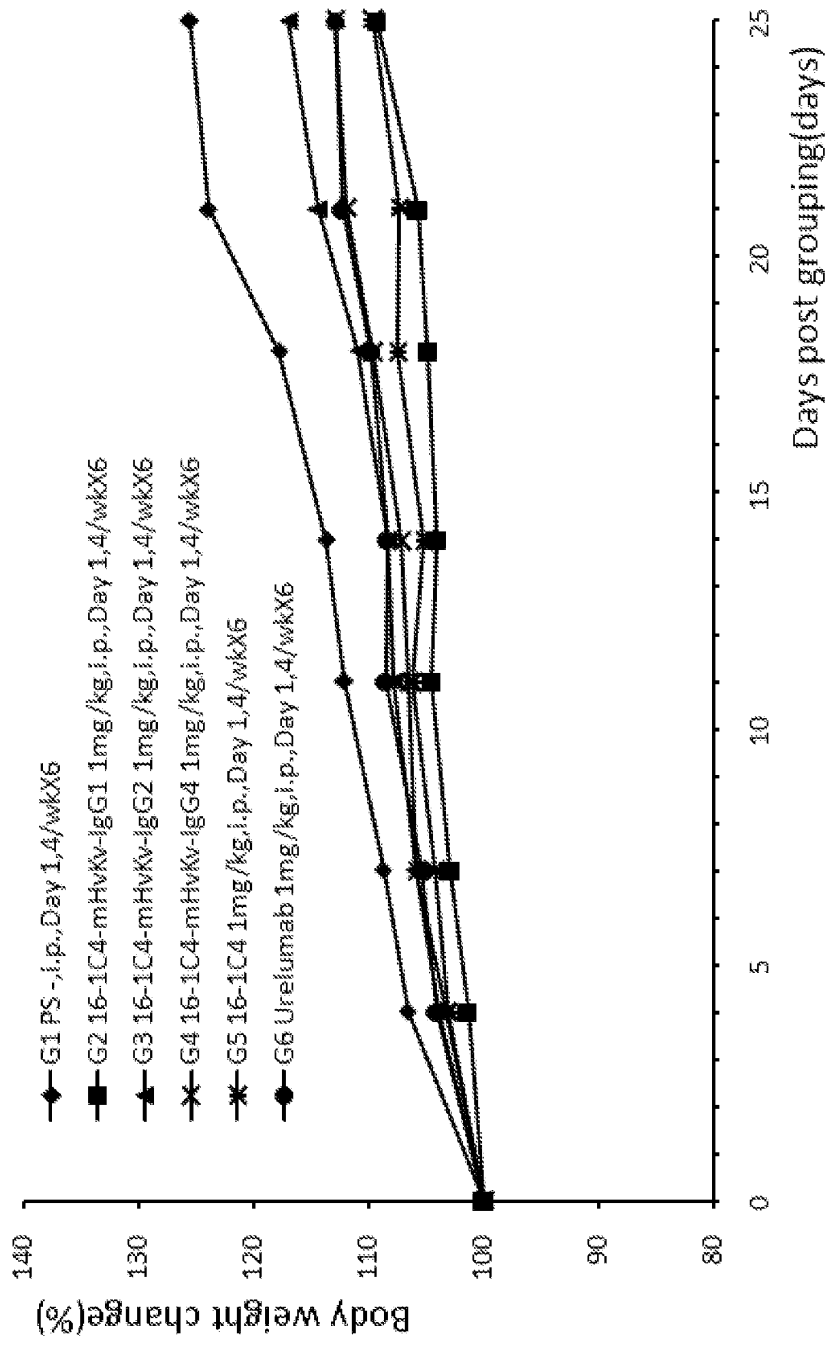


FIG. 38

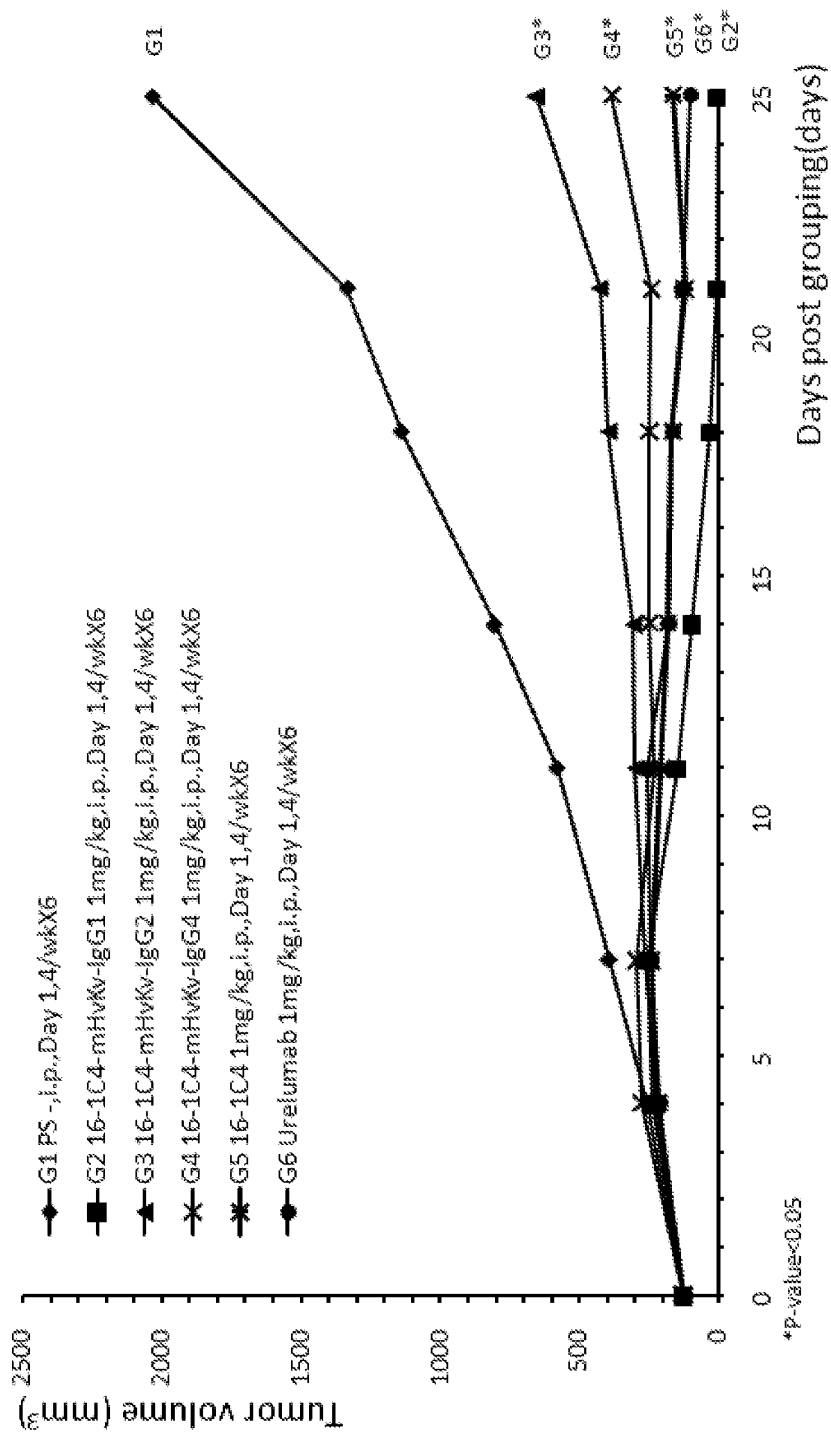


FIG. 39

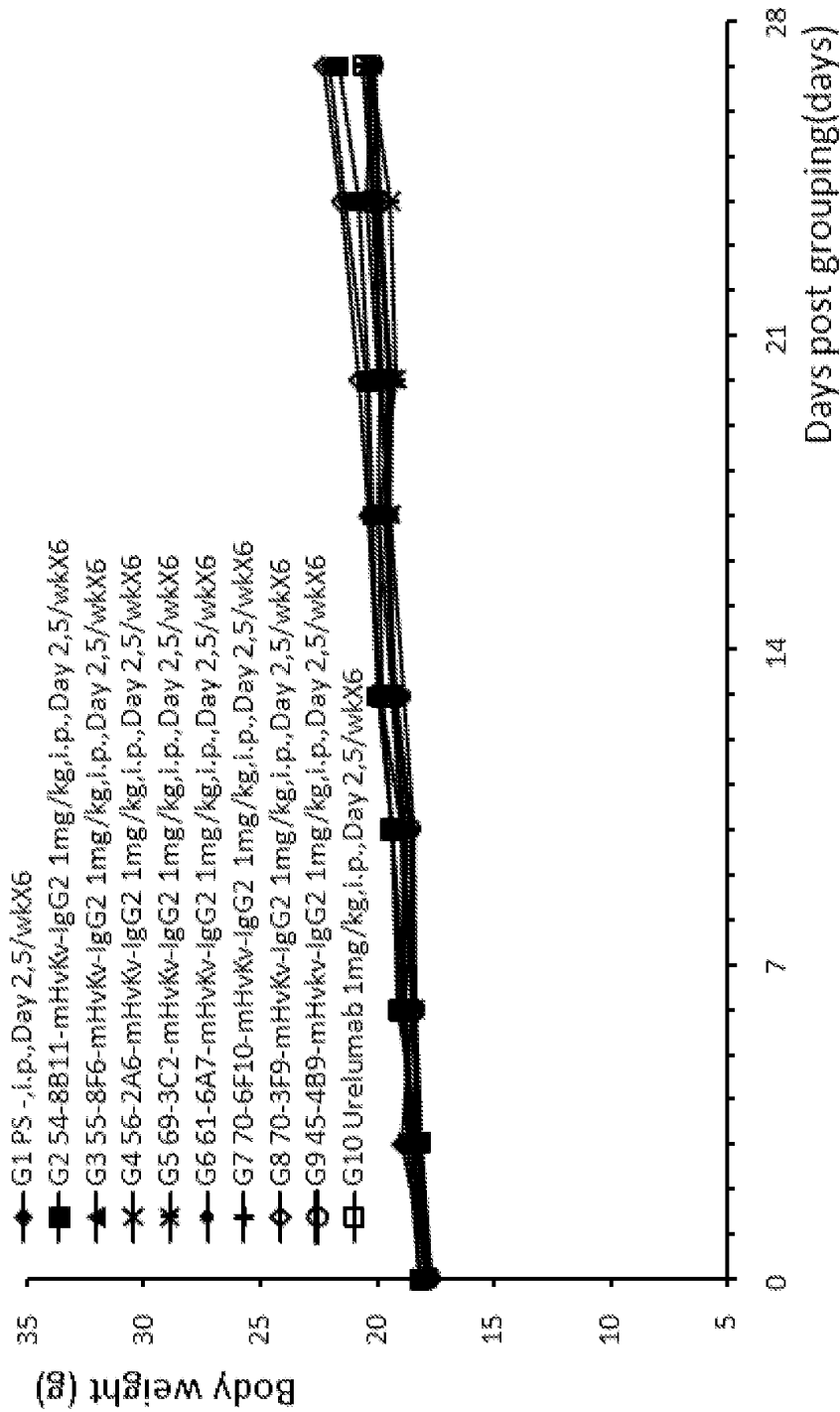


FIG. 40

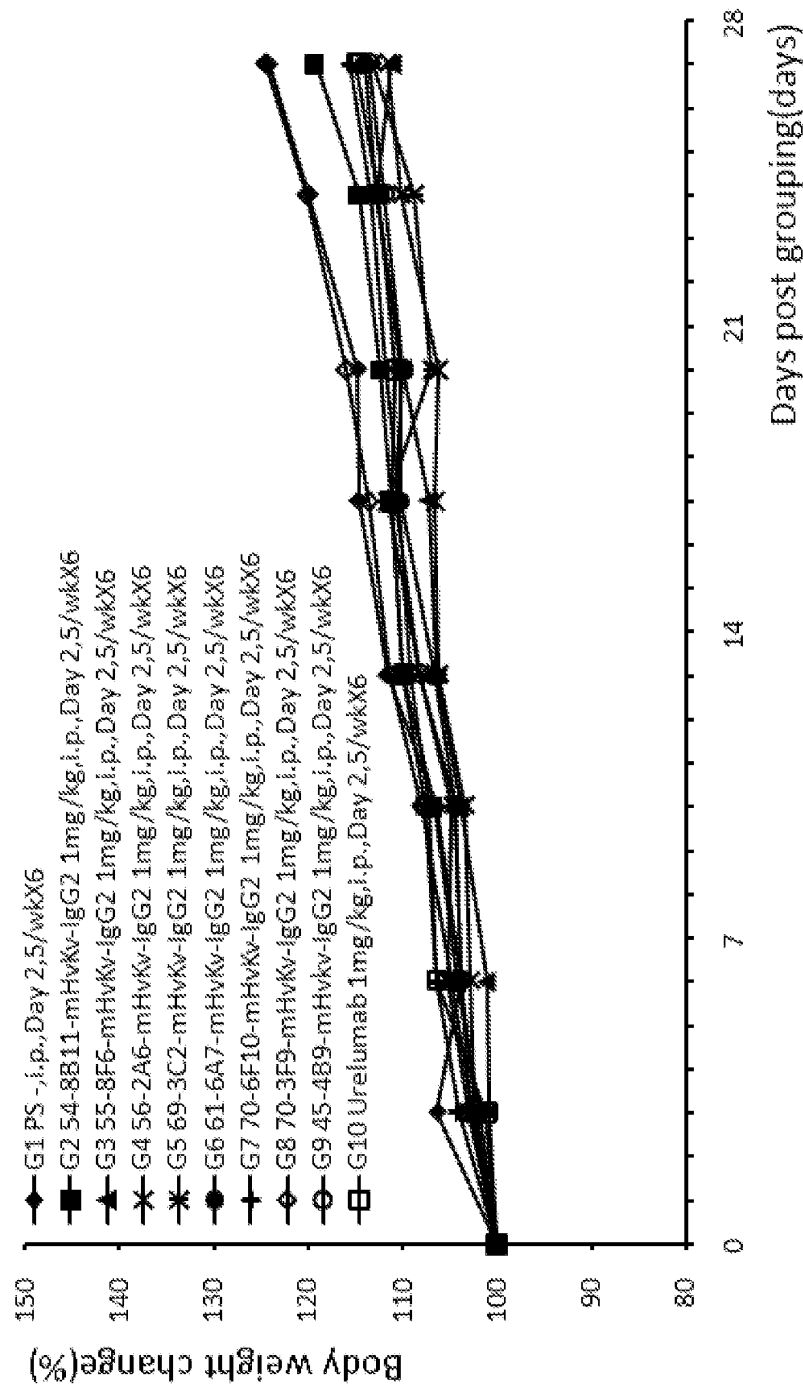


FIG. 41

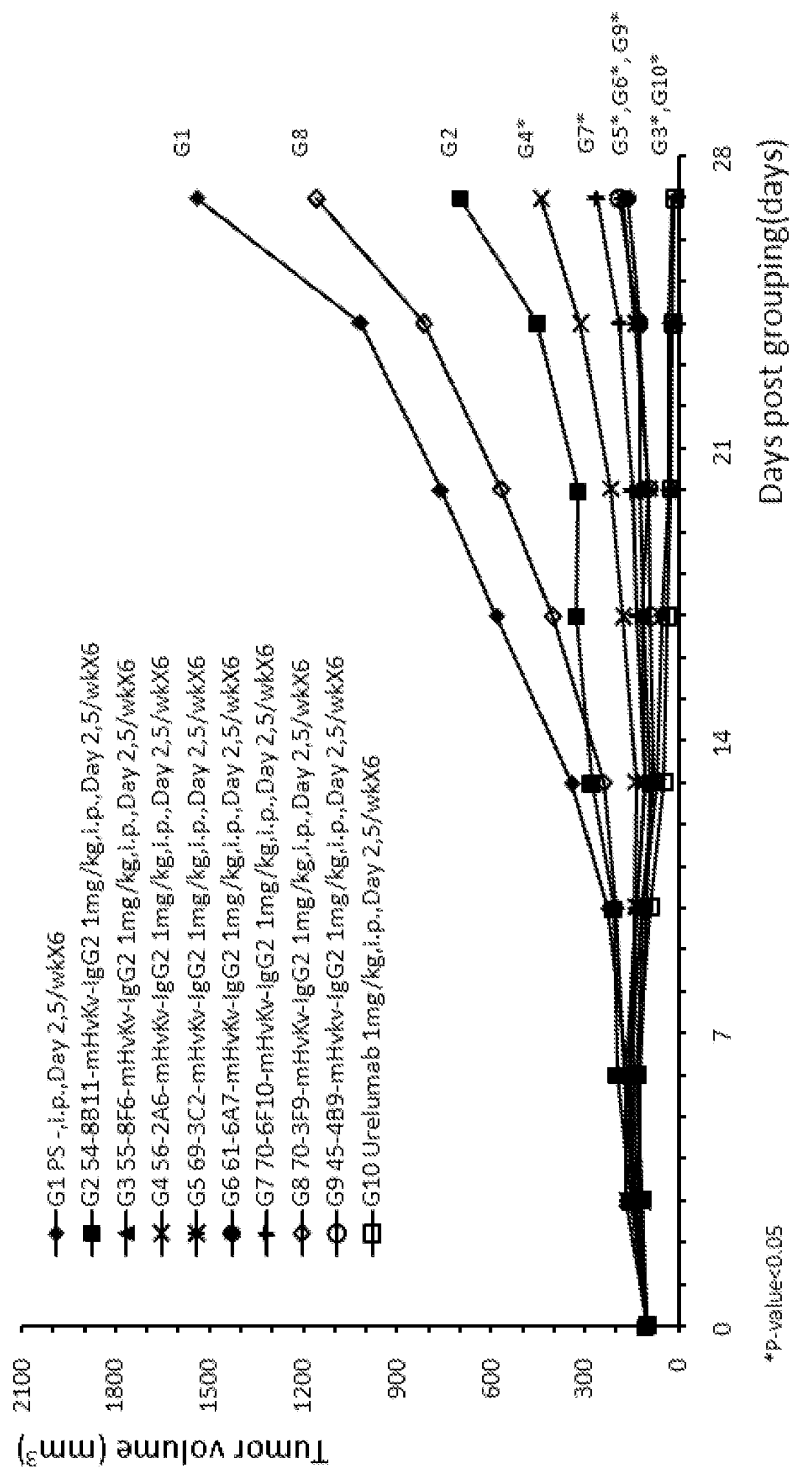


FIG. 42

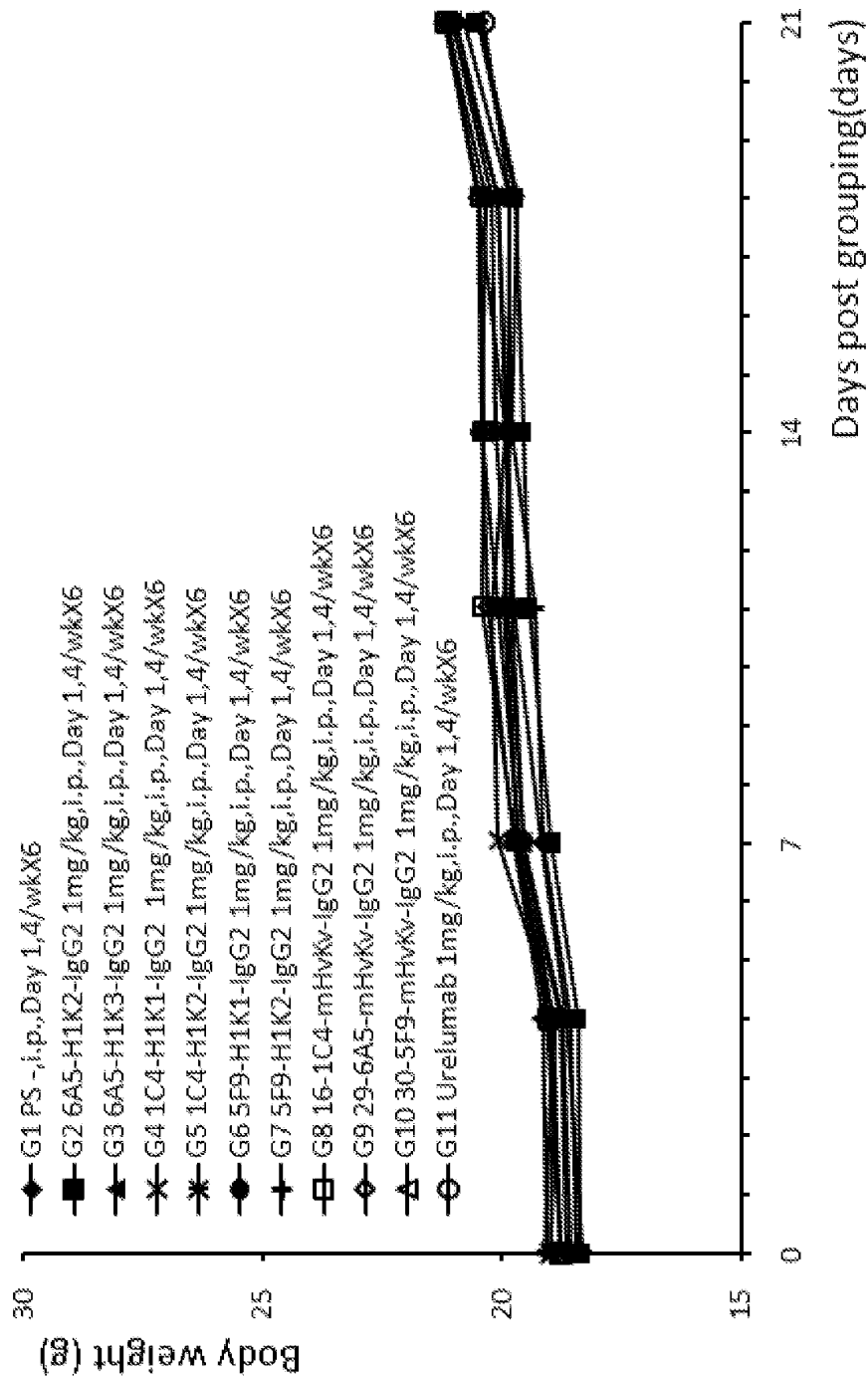


FIG. 43

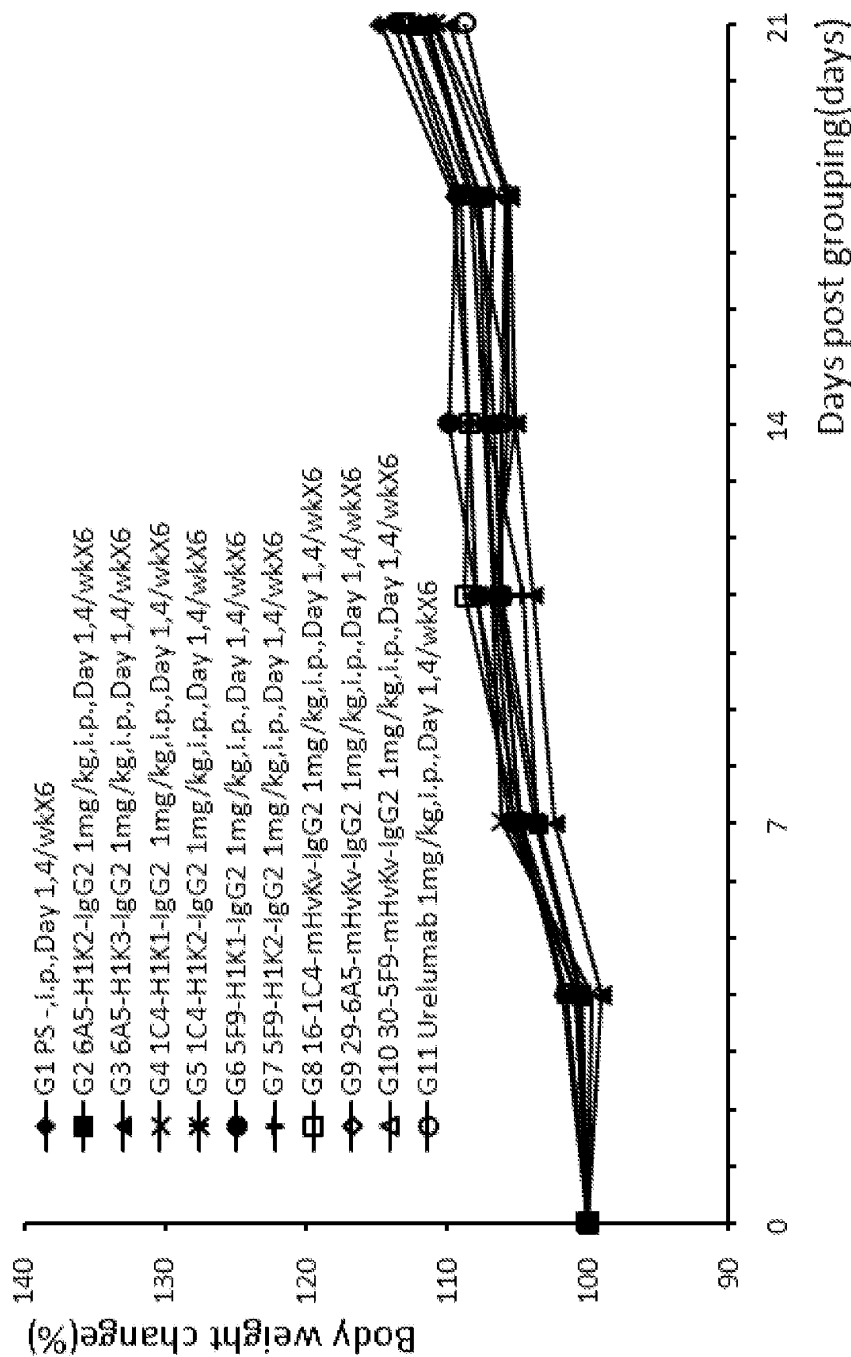


FIG. 44

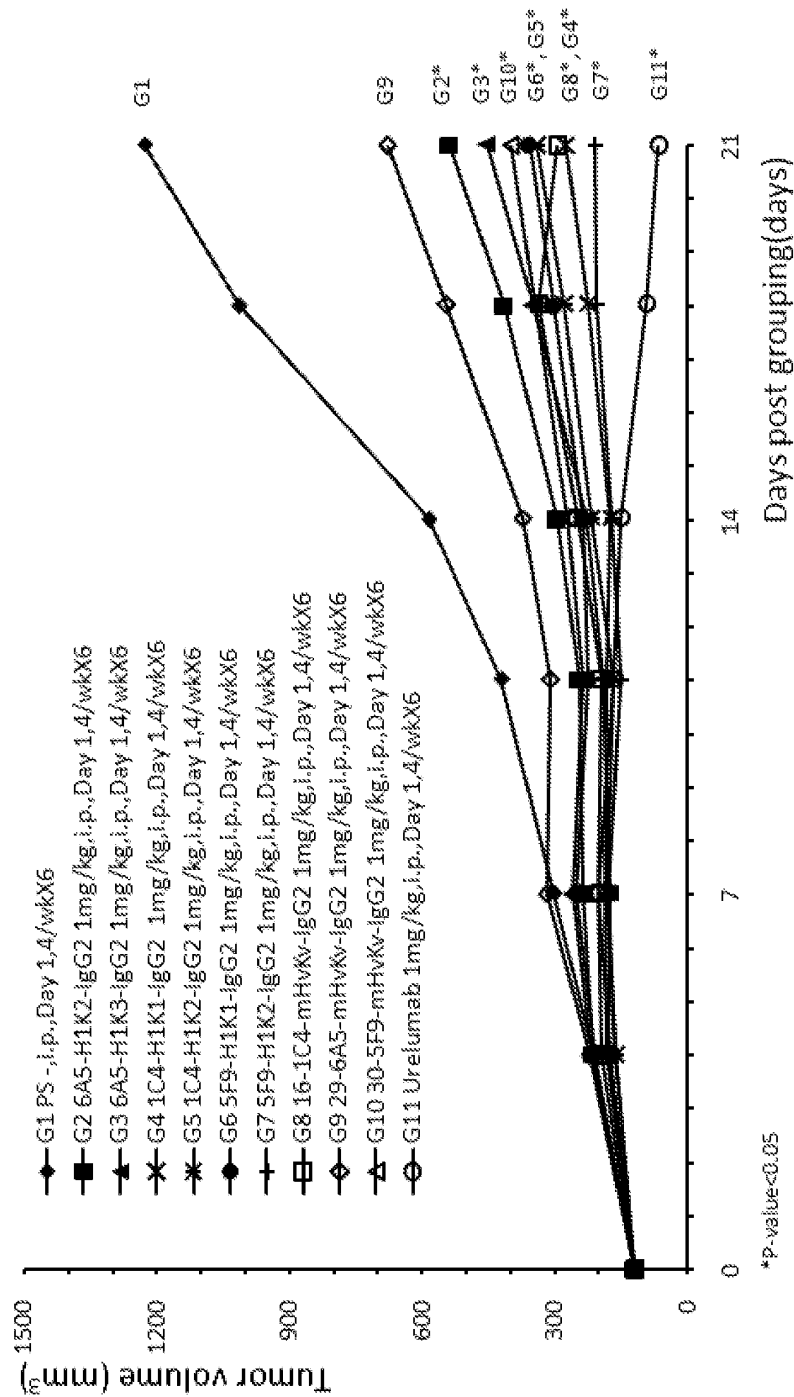


FIG. 45

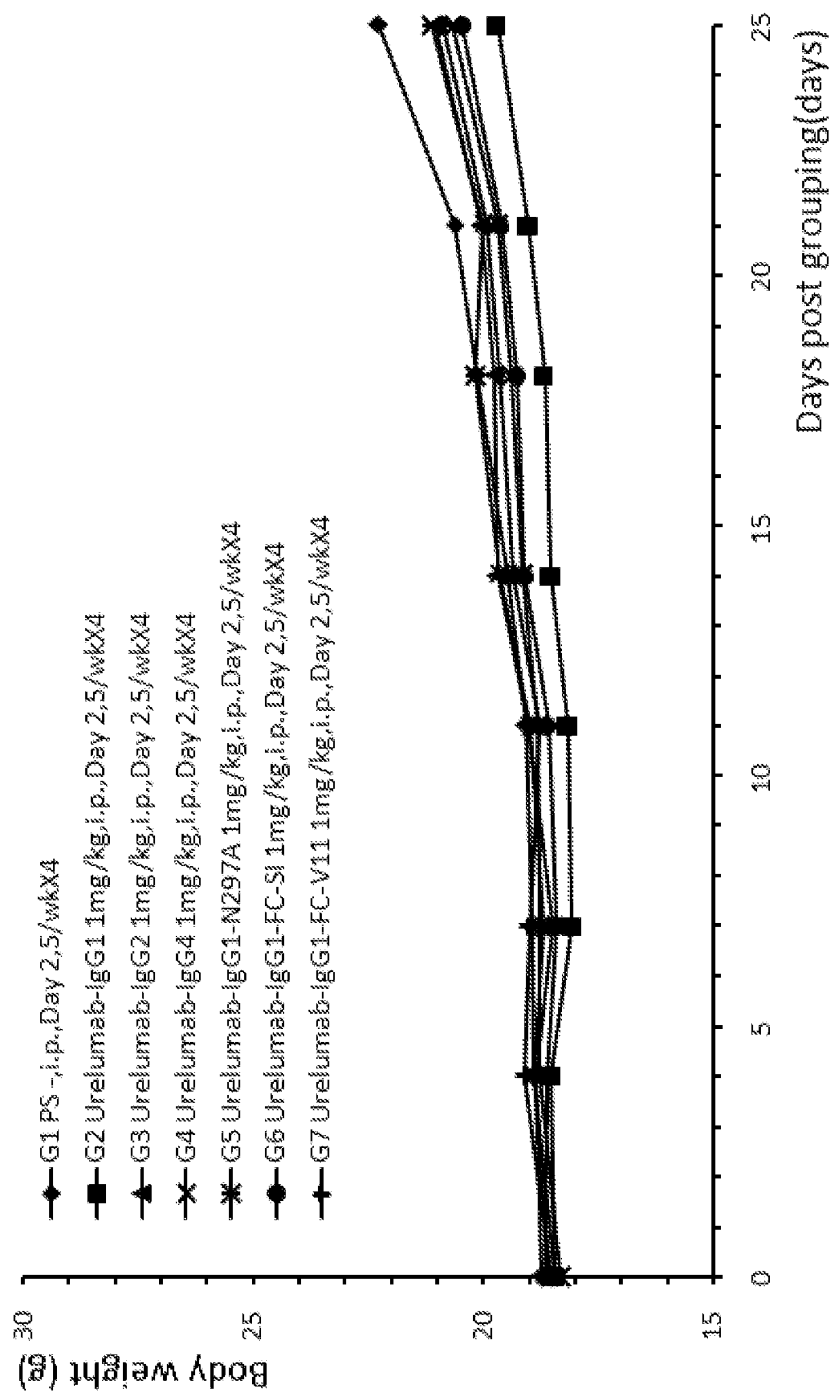


FIG. 46

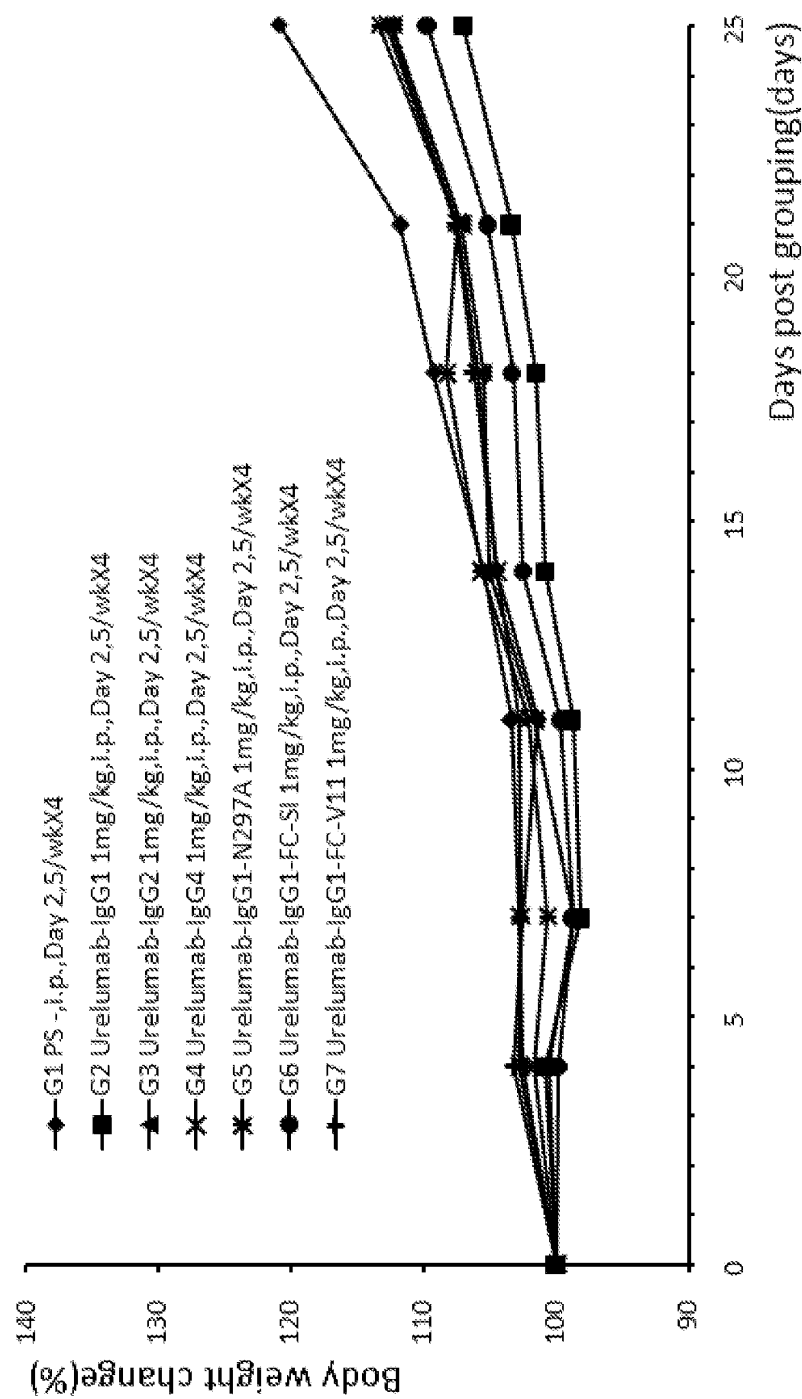


FIG. 47

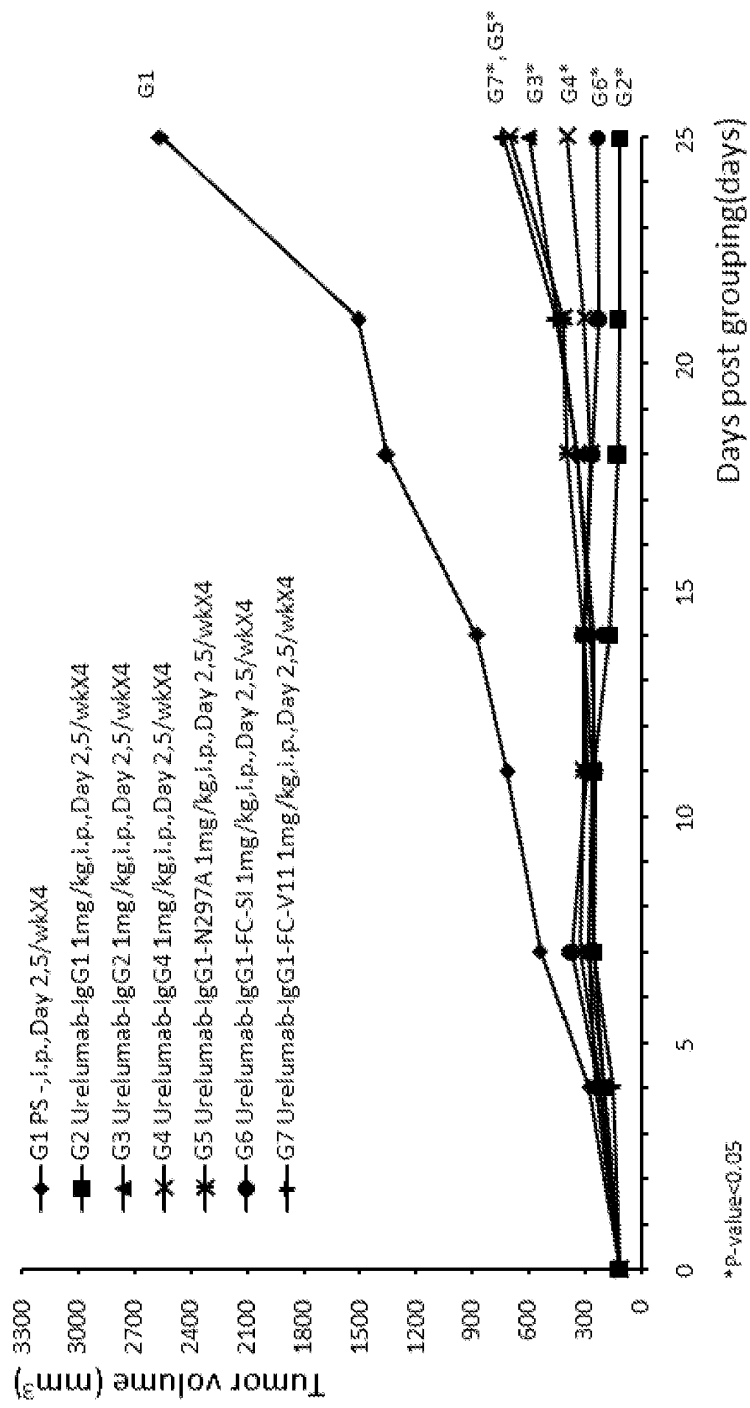


FIG. 48

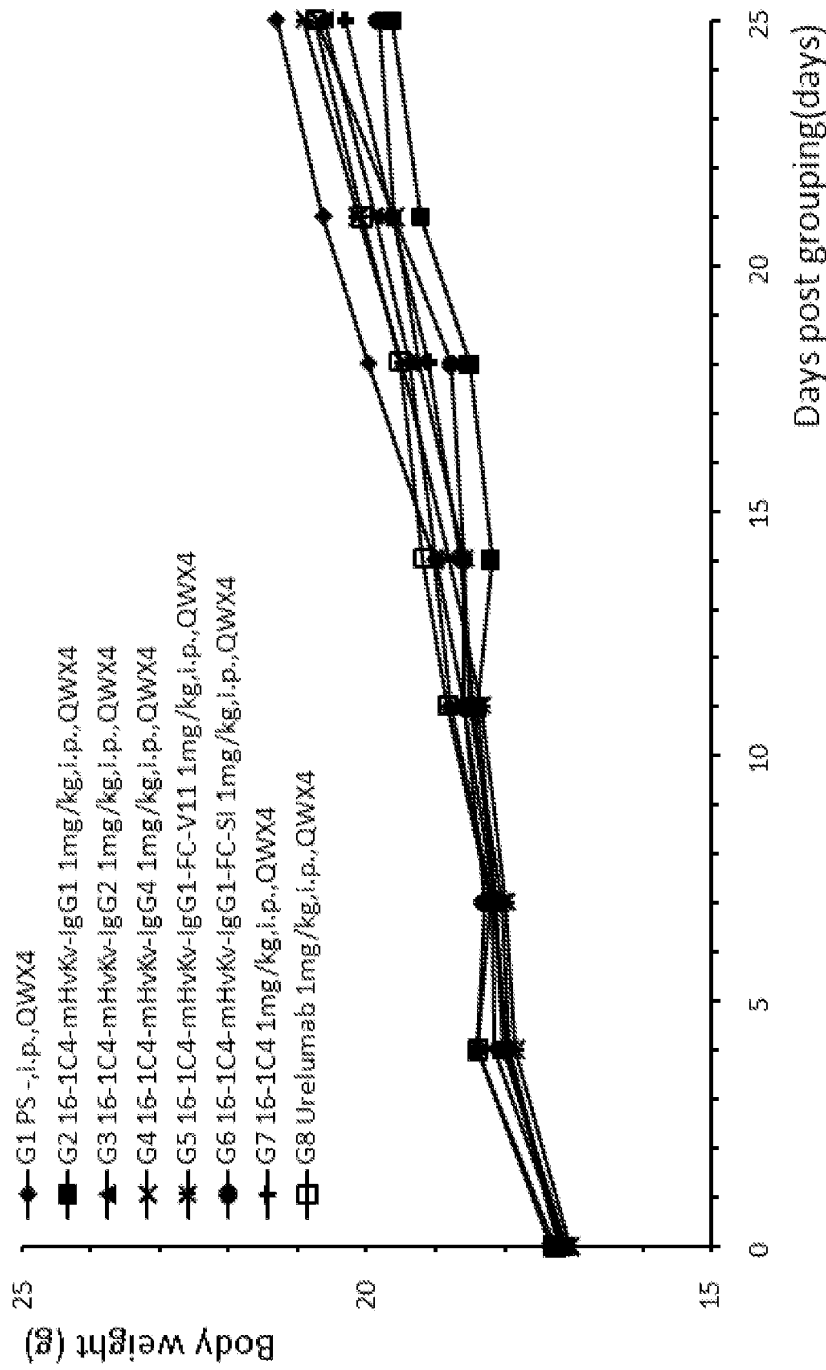


FIG. 49

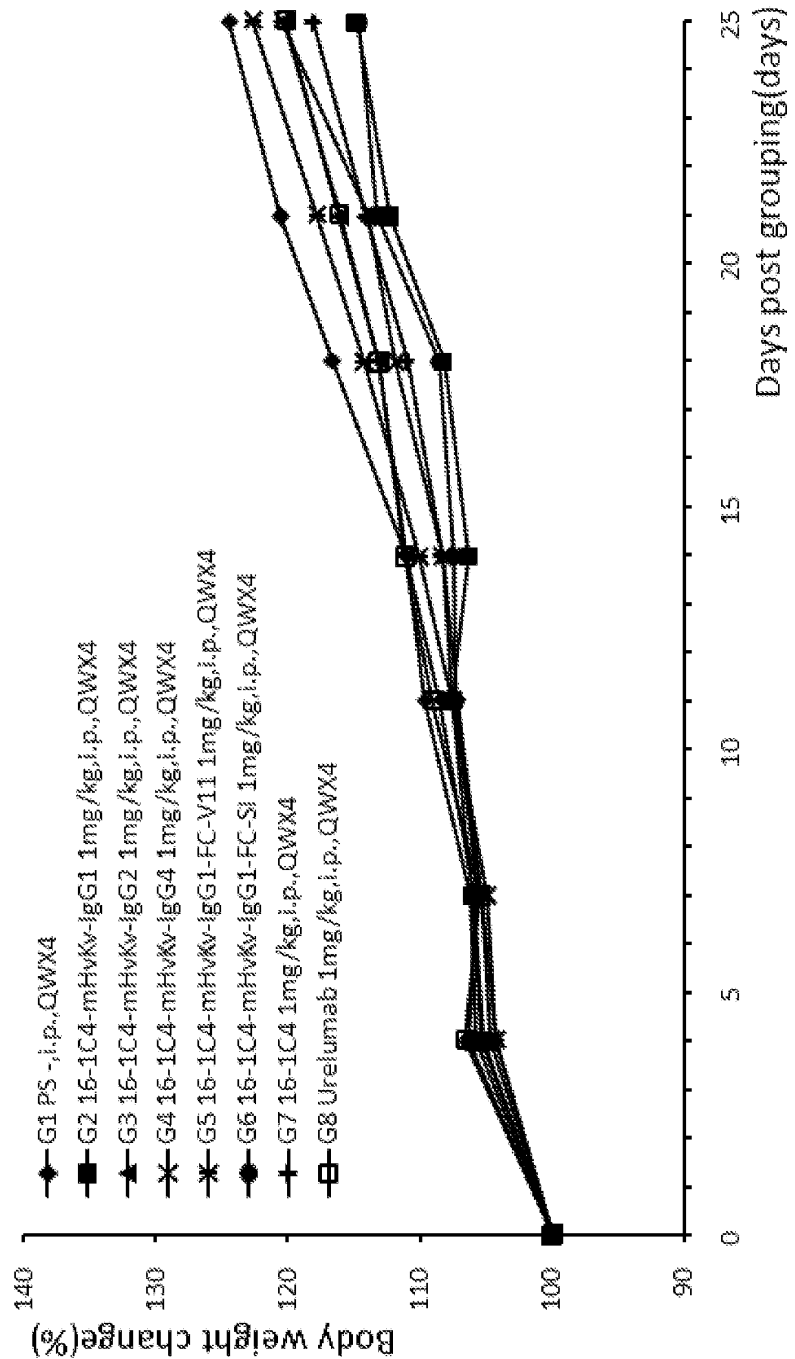


FIG. 50

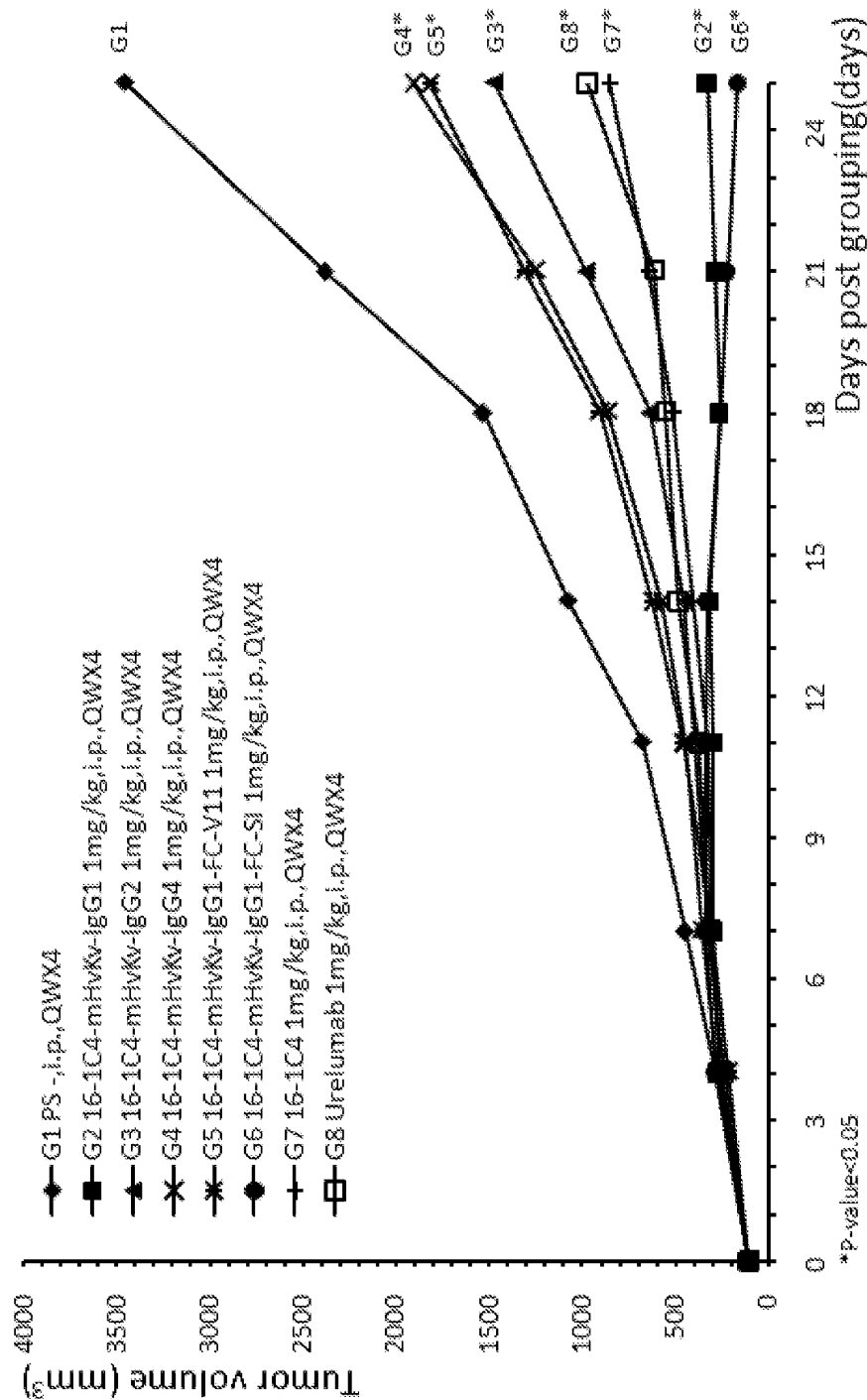


FIG. 51

FIG. 52

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:
16-1C4 or humanized 16-1C4	SSYIN	1	WIFAGTGGTYYN QKFTG	2	HSPRATLED F	3	RASSSVNHMH	4	ATSNLAS	5	QQWSSN PYT	6
29-6A5 or humanized 29-6A5	SYWIN	7	NIYPSDSYTNYN QKFKD	8	TWEEFYDSV FDY	9	KASQDINSYLS	10	RANRLVD	11	LQYDELP PT	12
30-5F9 or humanized 30-5F9	TYDIS	13	VIWTTGGGTNYS SFMS	14	VDY	15	RSSQSLVHSNG NTYLH	16	KVSNRES	17	SQNTHVP WT	18
45-2B3 or humanized 45-2B3	TSWM N	19	RIYPGDGD TDYN GRFKG	20	LDGYEVEFY FDY	21	KSSQSLLYSNG KTYLN	22	LVSKLDS	23	FQGT HFP WT	24
45-4B9 or humanized 45-4B9	TYVM Y	25	YINPYNDDIRYNE KFKG	26	QGGDY	27	RASKNINKYLA	28	SGSTLQS	29	QQYNEYP LT	30
45-7E9 or humanized 45-7E9	TYGVH	31	VIWSDGNTDYN DAFIS	32	NSITSVSFDC	33	KASQNVGTTV A	34	SASYRYS	35	QQYNSYP LT	36
45-7G9 or humanized 45-7G9	NYWI H	37	NIYPASDYTN YDE KFKN	38	GYFGSLDY	39	RASQPIGTGIH	40	SASESIS	41	QQSYSW PTT	42
45-8E11 or humanized 45-8E11	SNW MH	43	VIYPGNSDTSYN QKFKG	44	GITTAPEY	45	KASENVGIYVS	46	GASNRYT	47	GHTYNYP FT	48

45-8E2 or humanized 45-8E2	RYWM S	49	EIHPSDSSAINYTPS LKD	50	SYGRVFDY	51	RASQSIDYHLH	52	YASQIS	53	QDGHSP PT	54
45-8F1 or humanized 45-8F1	SYWM H	55	VIYVNSDTSYN QKFKG	56	GITTAPDY	57	KASENVGHIHVS	58	GASSGYN	59	GQTYSP FT	60
54-8B11 or humanized 54-8B11	NYGM N	61	WINTYTGEPTYA DDFKG	62	REYYPWVFDY Y	63	SASSSVSYMHH	64	DTSKLAS	65	FQSGYP LT	66
55-8F6 or humanized 55-8F6	SYWIN	67	NIYPSDSYTNYN QKFKD	68	FHYGSSPED N	69	RASQDISHYLN	70	YTSRLHS	71	QQGHTL PRT	72
56-2A6 or humanized 56-2A6	NYGM N	73	WINTYTGEPTYA DDFKG	74	RDYLGAMD Y	75	RASSSVSSSYL H	76	STSNLAS	77	QQYSAYL YT	78
59-5E4 or humanized 59-5E4	TYWIN	79	NIYPSDSYTNYN QKFKD	80	EAGDGTTHY AIDY	81	KASENVGTYS	82	GASNRYP	83	GQGYSYL RT	84
61-6A7 or humanized 61-6A7	DYWM H	85	WIDPENGNTIYD PKFQD	86	GLPWYFDY	87	SASSSVSDMN	88	LTSNLSS	89	QQWSGN PLT	90
69-3C2 or humanized 69-3C2	SFGM H	91	YISSGSSAIYYADT VKG	92	DWVDY	93	RASENIYSNLV	94	TATKLTN	95	QHFWDT PYT	96
70-3F9 or humanized 70-3F9	SYWIN	97	NIYPSDSYTNYNQ KFKD	98	FGSSGYPDY YTIMEY	99	RASGNIDNYLA	100	NAKTLAE	101	QQYWTIP YT	102
70-6F10 or humanized 70-6F10	NSW MN	103	RIYPGDGDYDYN GKFKG	104	LDGNYYW YFDV	105	KSSQSLDSDG KTYLN	106	LVSCLDS	107	WQGTHT PQT	108

FIG. 53
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:
16-1C4 or humanized 16-1C4	GFTFS SSYIN	109	FAGTGG	110	HSPRATLFD F	111	RASSSVNHMH	112	ATSNLAS	113	QQWSSN PYT	114
29-6A5 or humanized 29-6A5	GYTFS SYWIN	115	YPSDSY	116	TWEFYDVS FDY	117	KASQDINSYLS	118	RANRLVD	119	LQYDELP PT	120
30-5F9 or humanized 30-5F9	GFSLT TYDIS	121	WTGGG	122	VDY	123	RSSQSLVHSNG NTYLH	124	KVSNRFS	125	SQNTHP WT	126
45-2B3 or humanized 45-2B3	GYAFS TSWM N	127	YPGDGD	128	LDGYEVFY FDY	129	KSSQSLVHSNG KTYLN	130	LVSKLDS	131	FQGTFFP WT	132
45-4B9 or humanized 45-4B9	GYTFT TYVM Y	133	NPYNDD	134	QGGDY	135	RASKNINKYLA	136	SGSTLQS	137	QQYNEYP LT	138
45-7E9 or humanized 45-7E9	GFSLT TYGVH	139	WSDGN	140	NSITSVSFDC	141	KASQNVGTTV A	142	SASYRYS	143	QQYNSYP LT	144
45-7G9 or humanized 45-7G9	GYTFS NWI H	145	YPASDY	146	GYFGSLDY	147	RASQPIGTGIH	148	SASESIS	149	QQSYSW PTT	150
45-8E11 or humanized 45-8E11	GSFT SNW MH	151	YPGNSD	152	GITTAPEY	153	KASENVGIYVS	154	GASNRYT	155	GHTYNYP FT	156
45-8E2 or humanized 45-8E2	GFDFS RYWM S	157	HPDSSA	158	SYGRVFDY	159	RASQSIDYHLH	160	YASQSIS	161	QDGHSP PT	162

45-8F1 or humanized 45-8F1	GYSFT SYWM H	163	YPGNSD	164	GITTAPDY	165	KASENVGIHVS	166	GASSGVN	167	GQTSYSP FT	168
54-8B11 or humanized 54-8B11	KFTFT NYGM N	169	NTYTGE	170	REYYPWV FV Y	171	SASSSVSYM H	172	DTSKLAS	173	FQGS GYP LT	174
55-8F6 or humanized 55-8F6	GYIFTS YWIN	175	YPSDSY	176	FHYGSSPFD N	177	RASQDISHYLN	178	YTSRLHS	179	QQGHTL PRT	180
56-2A6 or humanized 56-2A6	GYTFT NYGM N	181	NTYTGE	182	RDYLGAMD Y	183	RASSSVSSSYL H	184	STSNLAS	185	QQYSAYL YT	186
59-5E4 or humanized 59-5E4	GYTFT TYWIN	187	YPSDSY	188	EAGDGTHY AIDY	189	KASENVGTYS	190	GASNRYP	191	GQGSYSL RT	192
61-6A7 or humanized 61-6A7	GFNIK DYWM H	193	DPENGN	194	GLPWYFDY	195	SASSSVSDMN	196	LTSNLSS	197	QQWSGN PLT	198
69-3C2 or humanized 69-3C2	GFSS SFGM H	199	SSGSSA	200	DWVDY	201	RASENIYSNLV	202	TATKLTN	203	QHFWDT PYT	204
70-3F9 or humanized 70-3F9	GYTFT SYWIN	205	FPDSY	206	FGSSGYPDY YTIMEY	207	RASGNIDNYLA	208	NAKTLAE	209	QQYWTIP YT	210
70-6F10 or humanized 70-6F10	GYAFN NSW MN	211	YPGDGD	212	LDGNYYYW YFDV	213	KSSQSLDSDG KTYLN	214	LVSKLDS	215	WQGTHF PQT	216

Protein	Amino acid sequence	SEQ ID NO.
Human 4-1BB (h4-1BB) NP_001552.2	MGNHCYNIVA TLLVLNFER TRSLQDPCSN CPAGTFCDNN RNQICSPCPP NSFSSAGGQR TCDICRQCKG VFRTRKECSS TSNAECDCTP GFHCLGAGCS MCEQDCKQGG ELTKGCKDC CFGTFNDQKR GICRPWTNCS LDGKSVLVNG TKERDVVCGP SPADLSPGAS SVTPPAPARE PGHSPQIJSF FLALTSTALL FLFFLT LRF SVVKRGRKKL LYIFKQPFMR VQTTQEEDG CSCRPEEEEE GGCEL	217
Mouse 4-1BB (m4-1BB) NP_035742.1	MGNHCYNVWV IVLLVGEK VGAVQNSCDN CQPTGTCRKY NPVCKSCPPS TFSIGGQPN CNICRVGAGY FRFKFCST HNAECIEG FHCLGPQCTR CEKDCRPGQE LTKGCKTCS LGTFDQNGT GVCRPWTNCS LDGRSVLKTG TTEKDVVCGP PVVFSFSTT ISVTPEGGPG GHSLQVLTFL LALTSALLA LIFITLLFSV LKWIRKFPK IFKQPFKTT GAAQEEEDACS CRCPQEEEGG GGGYEL	218
Monkey 4-1BB (rm4-1BB) NP_001253057.1	MGNHCYNIVA TLLVLNFER TRSLQDLCSN CPAGTFCDNN RSQICSPCPP NSFSSAGGQR TCDICRQCKG VFKTRKECSS TSNAECDIS GYHCLGAECS MCEQDCKQGG ELTKGCKDC CFGTFNDQKR GICRPWTNCS LDGKSVLVNG TKERDVVCGP SPADLSPGAS SATPPAPARE PGHSPQIJSF LALTSTVVLV LFFLVLRFS VVKRSRKKLL YIFKQPFMR VQTTQEEDGC SCRPEEEEE GGCEL	219
Chimeric 4-1BB (chi4-1BB) (Humanized 4-1BB)	MGNHCYNIVATLLVLNFERTRSLQDPCSNCPAGTFCDNNRNQICSPCPPNSFSSAGGQRTCDICRQCKGVF RTRKECSSTNAECDCTPGFHCLGAGCSMCEQDCKQGGELTKGCKDCCFGTNDQKRIGICRPWTNCSLD GKSVLVNGTKERDVVCGPSPADLSPGASSVTPPAPAREPGHSLQVLTFLALTSALLALIFITLLFSVLKWKIRK KFPHFQKPFKTTGAAQEEEDACSCRCPEEEEEGGGGYEL	220

FIG. 54

FIG. 55

Humanized antibody variable domains	Description	AMINO ACID SEQUENCE	SEQ ID NO:
1C4 Humanized heavy chain variable domain (H1)	HuVHv1: humanization percentage 83.7%; top hit to human and <i>Macaca fascicularis</i>	QVQMVSQGAEVKKPGASVKLSCKASGFTFSSSYINWLRQAPGQRL WMGWIFAGTGGTYNNQKFTGRVTITRDTASTAYMELSSLRSDTA IYCARHSPRATLDFEWGQGTTTLTVSS	221
1C4 Humanized heavy chain variable domain (H2)	HuVHv2: humanization percentage 80.6%; top hit to human and <i>Macaca fascicularis</i>	QVQMVSQGAEVKKPGASVKLSCKASGFTFSSSYINWLRQAPGQSL WIGWIFAGTGGTYNNQKFTGRVQITRDTASTAYMELSSLRSDTA YYCARHSPRATLDFEWGQGTTTLTVSS	222
1C4 Humanized heavy chain variable domain (H3)	HuVHv3: humanization percentage 79.6%; top hit to human and <i>Macaca fascicularis</i>	QVQMVSQGAEVKKPGASVKLSCKASGFTFSSSYINWLRQAPGQSL WIGWIFAGTGGTYNNQKFTGRAQITRDTASTAYMELSSLRSDTA YYCARHSPRATLDFEWGQGTTTLTVSS	223
1C4 Humanized heavy chain variable domain (H4)	HuVHv4: humanization percentage 74.5%; top hit to human and <i>Macaca fascicularis</i>	QVQMVSQGAEVKKPGASVKLSCKTSGFTFSSSYINWLRQAPGQSL WIAWIFAGTGGTYNNQKFTGRAQLTVDTASTAYMELSSLRSDTA YYCARHSPRATLDFEWGQGTTTLTVSS	224
1C4 Humanized light chain variable domain (K1)	HuVLv1: humanization percentage 84.2%; top hit to human and <i>Macaca fascicularis</i>	EIVLTQSPATLSLSPGERATLSCRASSSVNHHMWYQQKPGQAPRALI YATSNLASGIPARFSGSGSGTSFTLTISLLEPEDFAVYCCQWSSNPY TFGGGTKLEIK	225
1C4 Humanized light chain variable domain (K2)	HuVLv2: humanization percentage 83.2%; top hit to human and <i>Macaca fascicularis</i>	EIVLTQSPATLSLSPGERATLSCRASSSVNHHMWYQQKPGQAPRALI YATSNLASGIPARFSGSGSGTSFTLTISLLEPEDFAVYCCQWSSNPYT FGGGTKLEIK	226
1C4 Humanized light chain variable domain (K3)	HuVLv3: humanization percentage 78.9%; Non top hit to human and <i>Macaca fascicularis</i>	EIVLTQSPATLSLSPGERATMSCRASSSVNHHMWYQQKPGFSPRA WIYATSNLASGIPARFSGSGSGTSFTLTISLLEPEDFATYCCQWSSN PYTFGGGTKLEIK	227
1C4 Humanized light chain variable domain (K4)	HuVLv3: humanization percentage 73.7%; Non top hit to human and <i>Macaca fascicularis</i>	EIVLTQSPATLSASGERVTMSCRASSSVNHHMWYQQKPGFSPRA WIYATSNLASGIPARFSGSGSGTSVLTISLLEPEDFATYCCQWSSN PYTFGGGTKLEIK	228

FIG. 56

Humanized antibody variable domains	Description	AMINO ACID SEQUENCE	SEQ ID NO:
6A5 Humanized heavy chain variable domain (H1)	HuVHv1: humanization percentage 82.7%; top hit to human and <i>Macaca fascicularis</i>	QVQLVQSGAEVKPGSSVKLSCKASGYTSSYWINVWRQAPGQGL EWMGNIYPSDSYTNYNQKFKDRVTLTVDKSTSTAYMELSSLRSEDT AVYCTRTWEFYDSDVFEDYWGQGTLVTVSS	229
6A5 Humanized heavy chain variable domain (H2)	HuVHv2: humanization percentage 80.6%; Non top hit to human and <i>Macaca fascicularis</i>	QVQLVQSGAEVKPGSSVKLSCKASGYTSSYWINVWRQAPGQGL EWIGNIYPSDSYTNYNQKFKDRATLTVDKSTSTAYMELSSLRSEDTA VYCTRTWEFYDSDVFEDYWGQGTLVTVSS	230
6A5 Humanized heavy chain variable domain (H3)	HuVHv3: humanization percentage 78.6%; Non top hit to human and <i>Macaca fascicularis</i>	QVQLVQSGAEVKPGSSVKLSCKASGYTSSYWINVWRQAPGQGL EWIGNIYPSDSYTNYNQKFKDKATLTVDKSTSTAYMELSSLRSEDTA VYCTRTWEFYDSDVFEDYWGQGTLVTVSS	231
6A5 Humanized light chain variable domain (K1)	HuVLv1: humanization percentage 84.2%; Non top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSSLSASLGERVTITCKASQDINSYLSWYQQKPKGKPKLIY RANRLVDGVPSRFGSGSGGQDFTLTISLQpEDIATYYCLQYDELPPTF GGGTKVEIK	232
6A5 Humanized light chain variable domain (K2)	HuVLv2: humanization percentage 83.2%; Non top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSSLSASLGERVTITCKASQDINSYLSWYQQKPKGKPKKTLI YRANRLVDGVPSRFGSGSGGQDFTLTISLQPEDIAITYYCLQYDELPP TFGGGTKVEIK	233
6A5 Humanized light chain variable domain (K3)	HuVLv3: humanization percentage 82.1%; Non top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSSLSASLGERVTITCKASQDINSYLSWYQQKPKGKPKKTLI YRANRLVDGVPSRFGSGSGGQDFTLTISLQPEDIAITYYCLQYDELPP TFGGGTKVEIK	234
6A5 Humanized light chain variable domain (K4)	HuVLv3: humanization percentage 81.1%; Non top hit to human and <i>Macaca fascicularis</i>	DIQMTQSPSSLSASLGERVTITCKASQDINSYLSWYQQKPKGKPKKTLI YRANRLVDGVPSRFGSGSGGQDFTLTISLQPEDIAITYYCLQYDELPP TFGGGTKLEIK	235

FIG. 57

Humanized antibody variable domains	Description	AMINO ACID SEQUENCE	SEQ ID NO:
5F9 Humanized heavy chain variable domain (H1)	HuVHv1: humanization percentage 82.5%; top hit to human and <i>Macaca fascicularis</i>	QVQLQESGPGLVKPSSETLSLTCTVSGFSLTTYD ¹ ISWVRQPPGKGLEW IGVWWTGGGTNNSSFM ² SRVTISKDTSKNQVSLKLSSTAAADTAIYY CERVDYWGQGT ³ TVTVSS	236
5F9 Humanized heavy chain variable domain (H2)	HuVHv2: humanization percentage 79.4%; Non top hit to human and <i>Macaca fascicularis</i>	QVQLKESGPGLVKPSSETLSLTCTVSGFSLTTYD ¹ ISWVRQPPGKGLEW LGVWWTGGGTNNSSFM ² SRVTISKDTSKNQVSLKLSSTAAADTAIYY CERVDYWGQGT ³ TVTVSS	237
5F9 Humanized heavy chain variable domain (H3)	HuVHv3: humanization percentage 77.3%; Non top hit to human and <i>Macaca fascicularis</i>	QVQLKESGPGLVKPSSETLSITCTVSGFSLTTYD ¹ ISWVRQPPGKGLEWL GVWWTGGGTNNSSFM ² SRVTISKDTSKNQVSLKLSSTAAADTAIYYC ERVDYWGQGT ³ TLTVSS	238
5F9 Humanized light chain variable domain (K1)	HuVLv1: humanization percentage 91%; top hit to human and <i>Macaca fascicularis</i>	DVVM ¹ TQSP ² LSLPVTLGQPASISCRSSQSLVHSGNGNTYL ³ HW ⁴ FQQRPG QSPRL ⁵ LIYKVSNRFS ⁶ GVDPDRFSGSGGTAF ⁷ TKISRVEAEDVG ⁸ VVYCS ⁹ QNTHVPW ¹⁰ TFGGG ¹¹ TKVEIK	239
5F9 Humanized light chain variable domain (K2)	HuVLv2: humanization percentage 90%; top hit to human and <i>Macaca fascicularis</i>	DVVM ¹ TQSP ² LSLPVTLGQPASISCRSSQSLVHSGNGNTYL ³ HW ⁴ FQQRPG QSPKLL ⁵ IYKVSNRFS ⁶ GVDPDRFSGSGGTAF ⁷ TKISRVEAEDVG ⁸ VVYCS ⁹ QNTHVPW ¹⁰ TFGGG ¹¹ TKVEIK	240
5F9 Humanized light chain variable domain (K3)	HuVLv3: humanization percentage 89%; Non top hit to human and <i>Macaca fascicularis</i>	DVVM ¹ TQSP ² LSLPVTLGQPASISCRSSQSLVHSGNGNTYL ³ HW ⁴ YQQRPG QSPKLL ⁵ IYKVSNRFS ⁶ GVDPDRFSGSGGTAF ⁷ TKISRVEAEDVG ⁸ VVYCS ⁹ QNTHVPW ¹⁰ TFGGG ¹¹ TKLEIK	241
5F9 Humanized light chain variable domain (K4)	HuVLv3: humanization percentage 87%; Non top hit to human and <i>Macaca fascicularis</i>	DVVM ¹ TQSP ² LSLPVTLGDPASISCRSSQSLVHSGNGNTYL ³ HW ⁴ YLQRRPG QSPKLL ⁵ IYKVSNRFS ⁶ GVDPDRFSGSGGTAF ⁷ TKISRVEAEDVG ⁸ VVYCS ⁹ QNTHVPW ¹⁰ TFGGG ¹¹ TKLEIK	242

FIG. 58

16-1C4 ("1C4") Heavy chain variable region (SEQ ID NO: 243)
QGMQSGAELVKPGASVKLSCKTSGFTFSSYINWLKQKPGQSLFWIAWIFAGTGGTYYNQKFTGKAQLTVDTSSTAYMQFSSLTTEDSAIYYCAR
HSPRATLFDWGQGTTLTVSS

16-1C4 ("1C4") Light chain variable region (SEQ ID NO: 244)
QIVLSQSPAILASAPGEKVTMTCRASSVNHHWYQQRTGFSPKAWIYATSNLASGVPARFSGSGGTSYSLTISRVEAEDAATYYCQWSSNPYTFG
GGTKLEIK

29-6A5 ("6A5") Heavy chain variable region (SEQ ID NO: 245)
QVQLQQPGAELVRPGASVKLSCKASGYTFSSYINWVKQRPQGQLEWIGNIYPSDSYTNYNQKFKDKATLTVDKSSSTAYMQLSSPTSDDSAVYYCTR
TWEFYDVSVDYWGQGTTLTVSS

29-6A5 ("6A5") Light chain variable region (SEQ ID NO: 246)
DIKMTQSPSSMYASISGERVTITCKASQDINSYLSWFFQKPKGKSPKTLIYRANRLVDGVPSPRFGSGSGGQDYSLTISLSEYEDMGIYYCLQYDELPPTF
GGTKLEIK

30-5F9 ("5F9") Heavy chain variable region (SEQ ID NO: 247)
QVQLKESGPGLVAPSQSLITCTVSGFSLTTYDISWVRQPPGKGLEWLGVIWTGGGTNNYNSFMRLSISKDNSKNQVFLKMNSLQVDDTAIYYCERV
DYWGQGTTLTVSS

30-5F9 ("5F9") Light chain variable region (SEQ ID NO: 248)
DVVMTQTPLSLPVSLGDQASISCRSSQSLVHSGNGNTYLHWYLQKPCGQSPKLLIYKVSNRFSGVDPDRFSGSGGTAFTEFKISRVEAEDLGVIYFCSQNT
VPWTFGGGTLEIK

45-2B3 ("2B3") Heavy chain variable region (SEQ ID NO: 249)
QVQLQQSGPELVKPGASVKISCKTSGYAFSTSWMNWVKQRPQGQLEWIGRIYPGDGTDYNGRPFKATLTADKSSSTAYLQLSLTSVDSAVYFCAR
LDGYEYEVFDYWGQGTTLTVSS

45-2B3 ("2B3") Light chain variable region (SEQ ID NO: 250)
 DVVMTQTPTLTLSVTIGQPASISCKSSQSLLYSNGKTYINWLLQRPQGSPKRLIYLVSKLDSGVDPDRFTGSGGTDFTLTKISRVEAEDLGIYYCFQGT
 FPWTFGGGKLEIK

45-4B9 ("4B9") Heavy chain variable region (SEQ ID NO: 251)
 EVQLQQSGPELVKPGASVKMSCKASGYTFITYVMYWKQRPQGQLEWIGYINPYNDDIRYNEKFKGKATLTSDRSSSTAYMELSSLTSEDSAVYLCAR
 QGGDYWGQGTILTIVSS

45-4B9 ("4B9") Light chain variable region (SEQ ID NO: 252)
 DVQITQSPSYLAASPGETITVNCRAKRNINKYLAWIYQEKPGKTNKLLIYSGSTLQSGIPSRFSGSGGTDFTLTISLLEPEDFAVYHCQQYNEYPLTF
 GAGTKLEMK

45-7E9 ("7E9") Heavy chain variable region (SEQ ID NO: 253)
 QVQLKQSGPGLVQPSQSLISITCTVSGFSLTTYGVHWRQPPGKGLEWLGVIWSDGNTDYNDAFISRLSITKDNSTSQVFFKMNGLQADDTAIYYCARN
 SITSVSFDWCWGQGTTLTVSS

45-7E9 ("7E9") Light chain variable region (SEQ ID NO: 254)
 DIVMTQSQKFMSTSVGDRVSVTCKASQNVGTTVAWIYQRPQSPKALICSAARYSGVDPDRFTGSGGTDFTLTISNVQSEDLAEYFCQQYNSYPLTF
 GSGTKLEIK

45-7G9 ("7G9") Heavy chain variable region (SEQ ID NO: 255)
 QVQLQQPGSALVRPGASVKLSCKASGYTFSNYWIHWVKQRHGQGLEWIGNIYPASDYNIDEKFKNKGTLTVDTSSTAYMHLSSLTSEDSAVYYCSR
 GYFGSLDYWGQGTSTVTVSA

45-7G9 ("7G9") Light chain variable region (SEQ ID NO: 256)
 DILLTQSPAILSVPGERVSVFSCRASQPIGTGIHWYQQRTNGSPRLLIKSAESIIGIPSRFSGSGGTDFTLTINNVESSDDVDYCYCQQSYSWPPTF
 GGGTKLKIN

45-8E11 ("8E11") Heavy chain variable region (SEQ ID NO: 257)
 EVQLQQSGTVLARPASVKMSCKASGYSTSNWMHWVKORPGGLEWIGVIYPGNSDTSYNQKFKGKAKLTAVTSASTAYMELSSLTNEDSAVYYCTR
 GITTAPEYWGQGTTLTVSS

45-8E11 ("8E11") Light chain variable region (SEQ ID NO: 258)
 NIVMTQSPKSMMSVGERVTLSCKASENVGIYVSWYQQKPEQSPKLLIYGASNRYTGVPDRFTGSGSATDFTLTISVQPEDLADYHCGHTYNYPTTF
 GSGTKLEIK

45-8E2 ("8E2") Heavy chain variable region (SEQ ID NO: 259)
 EVKLLSEGGGLVQPGGSLKLSCAASGFDFSRYYMMSWVRQAPGKGLEWIGEIHDPDSSAINYTPSLKDKFII SRDNAKNTLYLQMSKVRSEDTALYYCAR
 SYIGRVFDYWGQGTTLTVSS

45-8E2 ("8E2") Light chain variable region (SEQ ID NO: 260)
 DIVMTQSPATLSVTPGDRVSLSCRASQISDYLHWYQQKSHESPRLLIKYASQSIGIPPRFSGSGSGDFTLSINSVEPEDVGMYYCQDGHSPPTTF
 GAGTKLELK

45-8F1 ("8F1") Heavy chain variable region (SEQ ID NO: 261)
 EVQLQQSGTVLARPASVKMSCKASGYSTSYWMHWVKORPGGLEWIGVIYPGNSDTSYNQKFKGKAKLTAVTSASTAYMDLSSLTNEDSAVYYCTR
 GITTAPDYWGQGTTLTVSS

45-8F1 ("8F1") Light chain variable region (SEQ ID NO: 262)
 NIVMTQSPKSMMSVGERVTLSCKASENVGIHVSWYQQKPEQSPKLLIYGASSGNGVDPDRFTGSGSATDFTLTISVQPEDLADYHCGQTYSPPTTF
 GSGTKLEIK

54-8B11 ("8B11") Heavy chain variable region (SEQ ID NO: 263)
 QIQLVQSGPELKKPGETVKISCKASKFTFTNYGMNWKQAPGKALRWMGWINTYTGEPTYADDFKGRFDFSLETSAITAYLIQINNLIKNNEDTATYFCAR
 REYYPWFVYWGQGTTLTVSA

54-8B11 ("8B11") Light chain variable region (SEQ ID NO: 264)

ENVLTQSPAIMASPGKVTMTCSASSVSVMHWYQQKSTSPKLWIYDTSKLASGVPGRFSGSGSGNSYSLTSSMEAEADVATYYCFQGGGYPLTFG
GGTKLEIK

55-8F6 ("8F6") Heavy chain variable region (SEQ ID NO: 265)
QVQLQQPGAELVRPGASVKLSCKASGYIFTSYWINWVKQRPQGQLEWIGNIYPSDSYTNYNQKFKDKATLTVDKSSSTAYMQLSSPTSEDSAVYYCTR
FHYGSSPFDNWGGQTTLTVSS

55-8F6 ("8F6") Light chain variable region (SEQ ID NO: 266)
DIQMTQSTSSLSASLGDRVVISCRASQDISHYLNWYQQKPDGTVKLLIYYTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDFATYFCQQGHTLPRTF
GGGTKLEIK

56-2A6 ("2A6") Heavy chain variable region (SEQ ID NO: 267)
QIQLVQSGPELKKPGETVKISCKASGYFTNYGMNWVKQAPGKGFKWMGWINTYTGEPTYADDFKGRFAFSLAISASTAYLQINNLIKNETATATYFCAR
RDYLGAMDYWGQTSVTVSS

56-2A6 ("2A6") Light chain variable region (SEQ ID NO: 268)
ENVLTQSPAIMASPGKVTMTCRASSVSSTSSYLHWYQQKSGASPKLWIYSTSNLASGVPARFSGSGSGTSYSLTSSVEAEDAATYYCQQYSAYLYT
FGGGTKLEIK

59-5E4 ("5E4") Heavy chain variable region (SEQ ID NO: 269)
QVQLQQPGAELVRPGASVKLSCKASGYFTTYWINWVRQRPQGQLEWIGNIYPSDSYTNYNQKFKDKASLTVDKSSNTAYMQLSSPTSEDSAVYYCAR
EAGDGTHTYYAIDYWGQTSVTVSS

59-5E4 ("5E4") Light chain variable region (SEQ ID NO: 270)
NIVMTQSPKMSMSVGERVTLSCKASENVGTIVSWYQQKPEQSPKLLIYGASNRYPGVDPDRFTGSGSATDFTLTSSLQAEADLADYHCGQGYSLRFTF
GGGTNLEIK

61-6A7 ("6A7") Heavy chain variable region (SEQ ID NO: 271)

EVQLQQSGAELVRPGALVKLSCKASGFNIKDYMHVWVRRRPEQGLEWIGWIDPENGNTIYDPKFQDKASITADTSSNTAYLQLSSLTSEDTA VYICAE
GLPWYFDYWGQGTTLTVSS

61-6A7 ("6A7") Light chain variable region (SEQ ID NO: 272)
QIILTQSPALMSASPEKVTMTCSASSVSDMNWYQQKPRSSPTPWIIYLTSNLSSGVPDRFSGSGSGTSYSLTISSEAEADAATYYCQQWSGNPLTFG
AGTRLEIK

69-3C2 ("3C2") Heavy chain variable region (SEQ ID NO: 273)
DVQLVESGGGLVQPGGSRKLSCAAAGFSFSGMHMMRQAPKEKLEWVAYISSGSSAIYYADTVKGRFTISRDNPKNTLFLQMTSLRSEDTAMYICAR
DWVDYWGQGTTLTVSS

69-3C2 ("3C2") Light chain variable region (SEQ ID NO: 274)
DIQMTQSPASLSVSVGETVTITCRASENIYSNLVWYQQKQKSPQLLVYTATKLTNGVPSRFSGSGSGTQYSLKINSLOSEDFGTYYCQHFWDTPYTF
GGGTKLEMK

70-3F9 ("3F9") Heavy chain variable region (SEQ ID NO: 275)
QVQLQQPGAELVRPGASVKLSCKASGYTFTSYWINWVKQRPQGQLEWIGNIFPSSDSTYNYNQKFKDRAKLTVDKSSSTAYMQLSSPTSEDSAVYICTR
FGSSGYPDYITMEYWGQTSVTVSS

70-3F9 ("3F9") Light chain variable region (SEQ ID NO: 276)
DIQMTQSPASLSASVGETVTITCRASGNIDNLYLAWYQQKQKSPQLLVYNAKTLAEGVPSRFSGSGSGTEYSLKINSLOPEDFGSYHCQQYWTIPYTF
GGGTKLEIK

70-6F10 ("6F10") Heavy chain variable region (SEQ ID NO: 277)
QVQLQQSGPELVKPGASVKISCKASGYAFNNSWMNWVKQRPQGQLEWIGRIYPGDGTDYNGKFKGKATLTADKSSSTAYMQLSSLTSDSAVYFCAR
LDGNYYYWYFDVWGAGTTVTVSS

70-6F10 ("6F10") Light chain variable region (SEQ ID NO: 278)
DVVMTQTPTLTLSVTIGQPASISCKSSQSLDSDGKTYLNWLLQRPQGQSPKRLIYLVSKLDSGVDPDRFTGSGSGTDFTLKISRVEAEDLGVIYCWQGTGTH
FPQTFGGGTKEIK

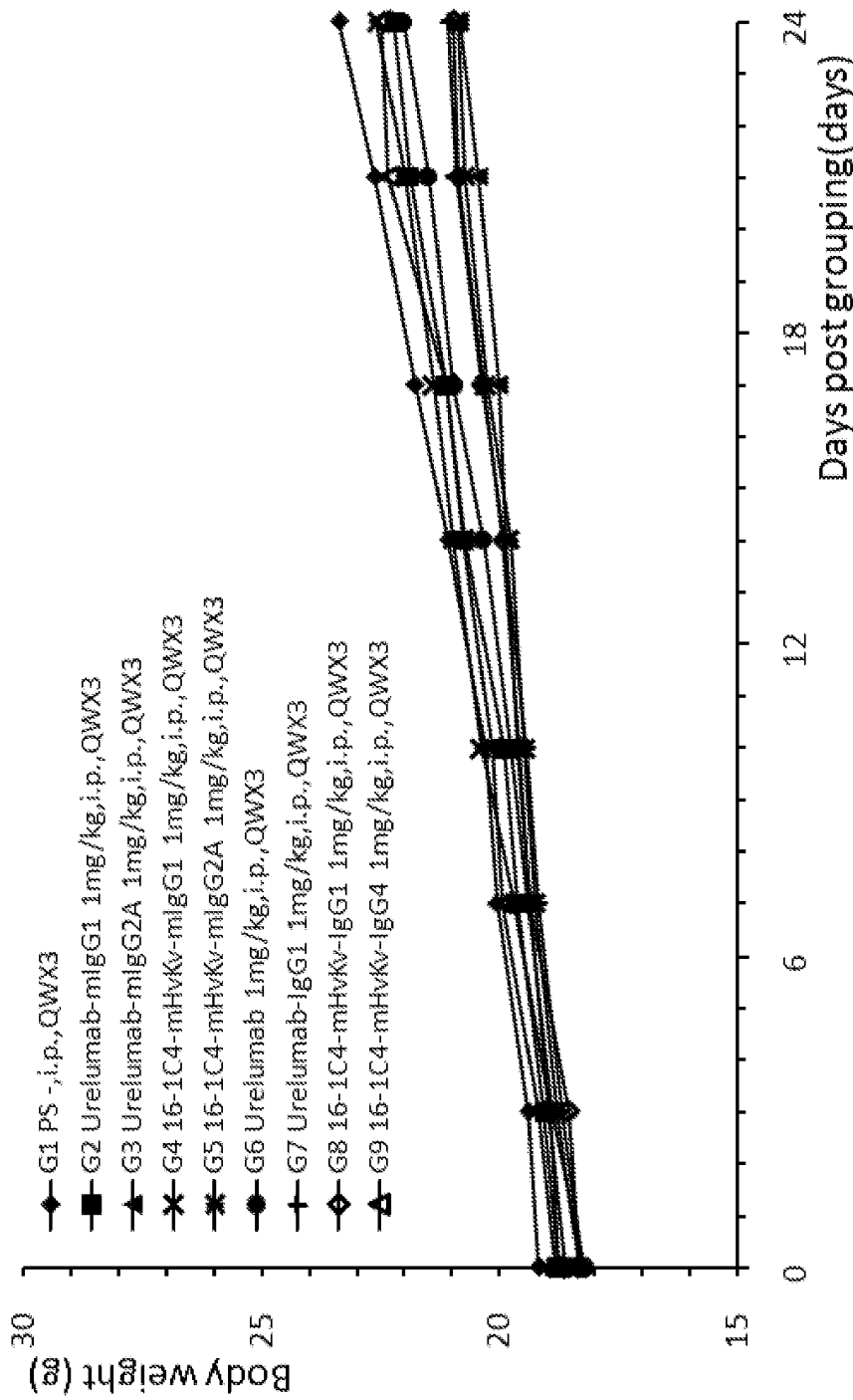


FIG. 59

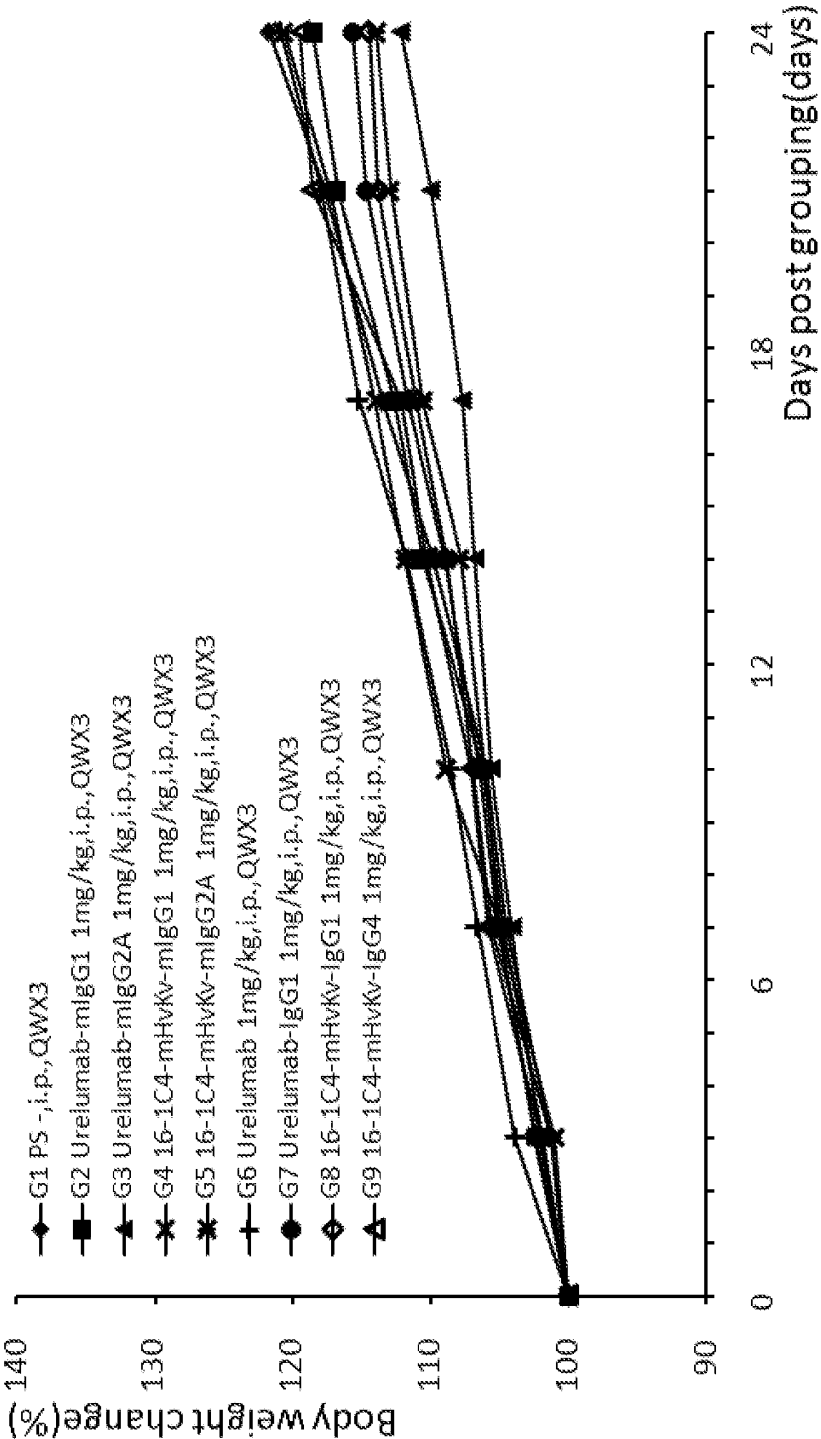
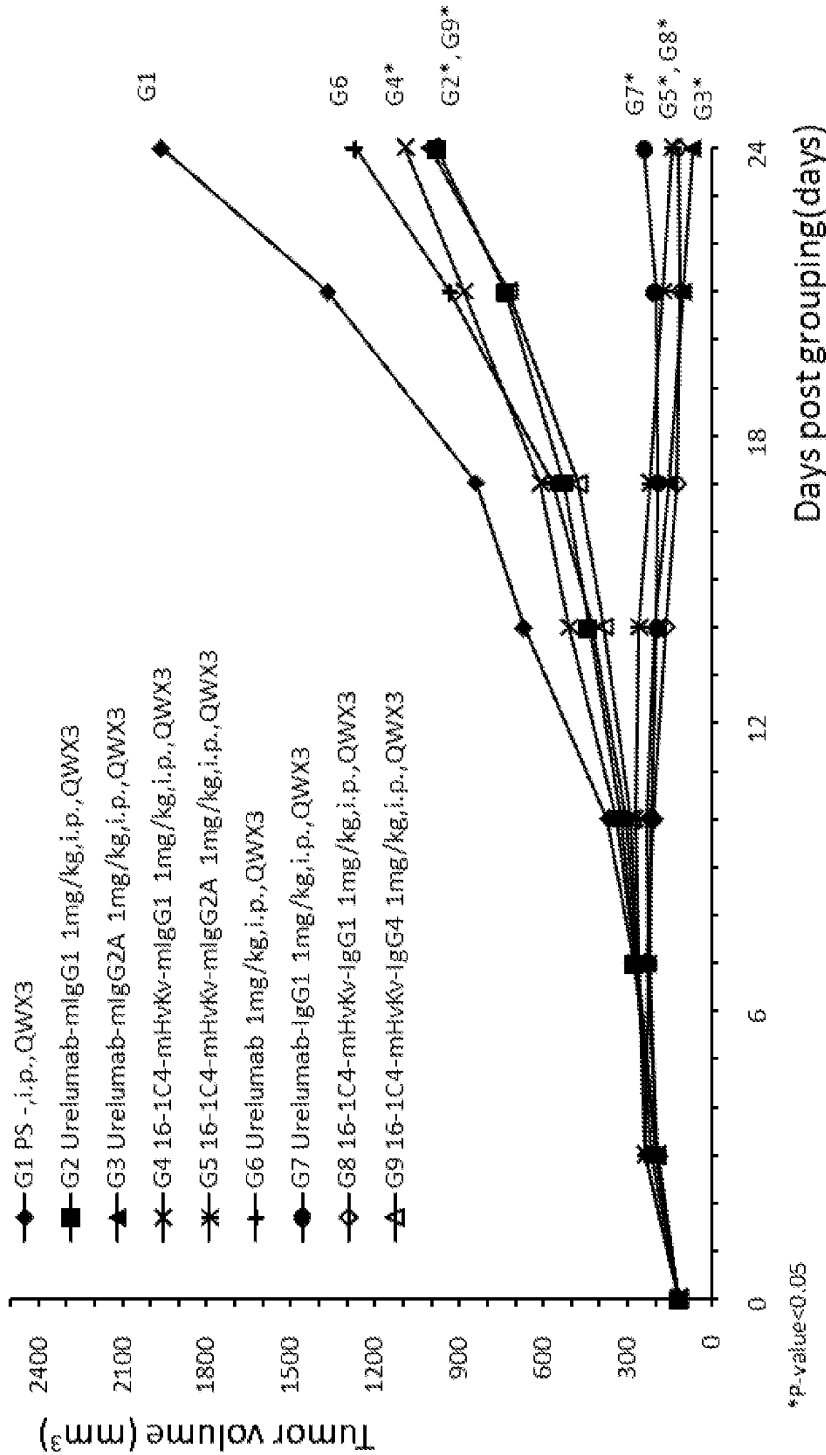


FIG. 60



*p-value<0.05

FIG. 61

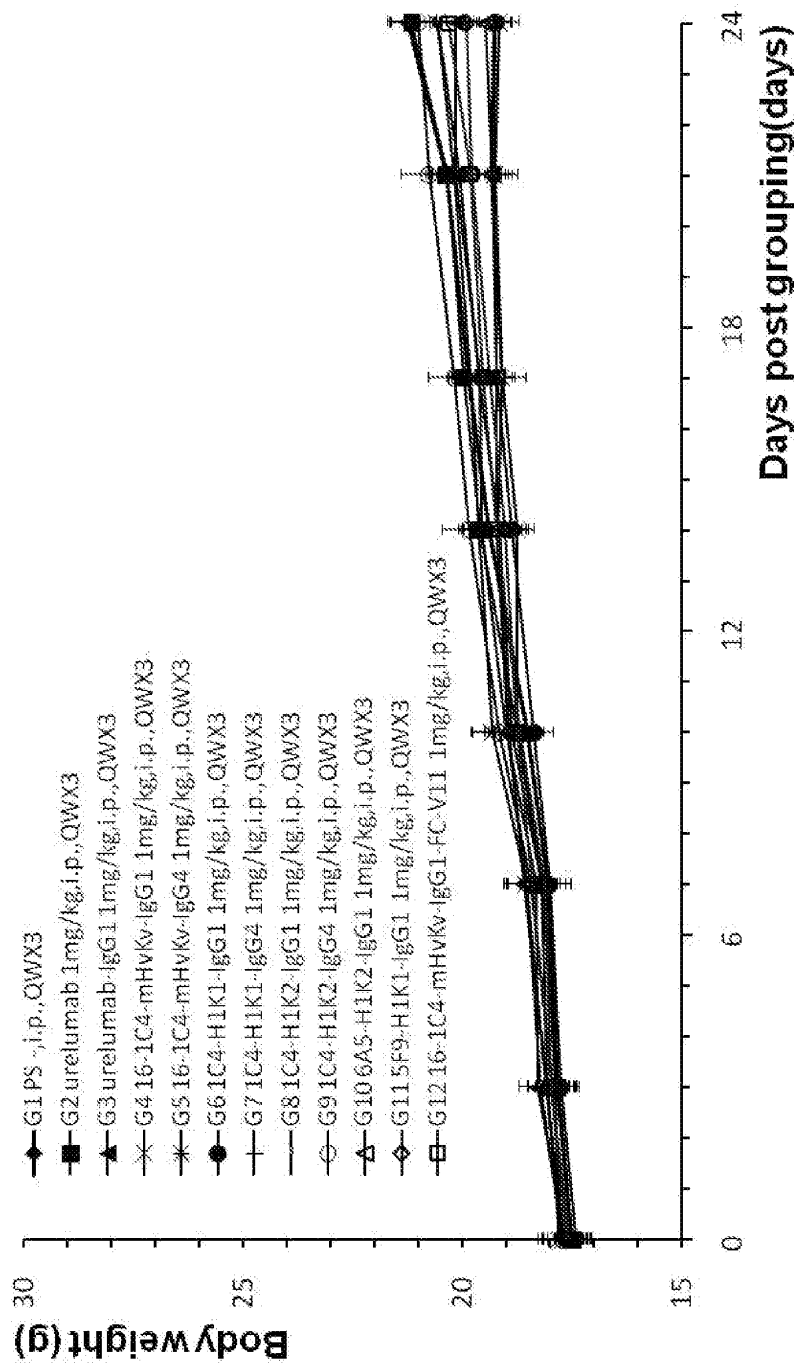


FIG. 62

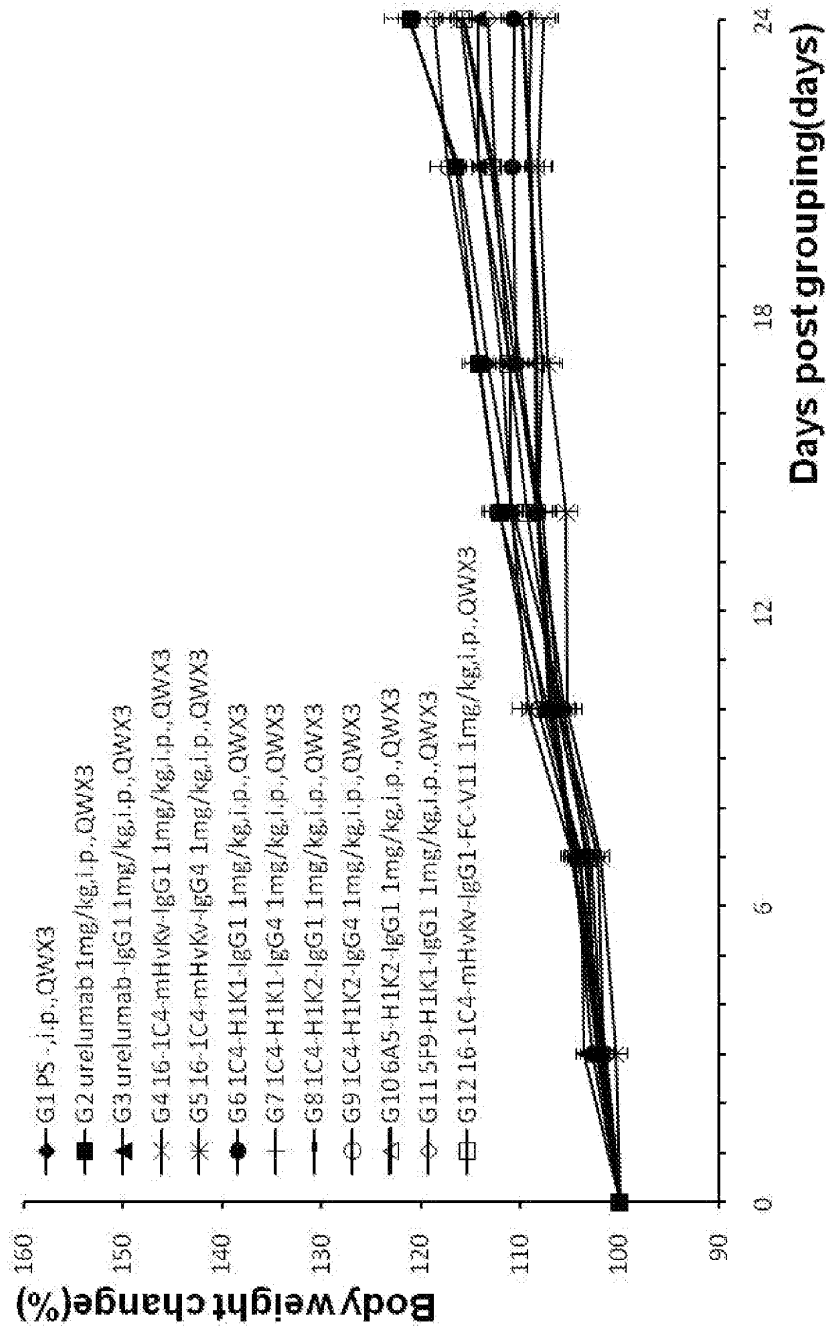


FIG. 63

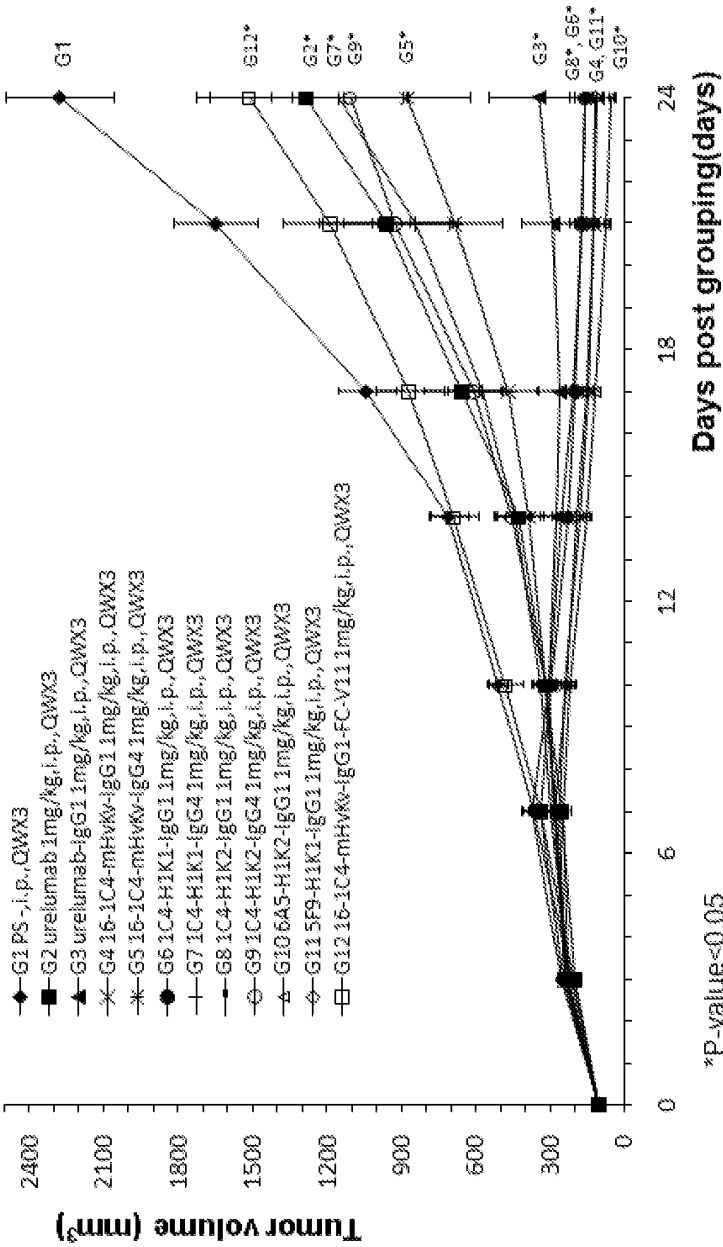


FIG. 64

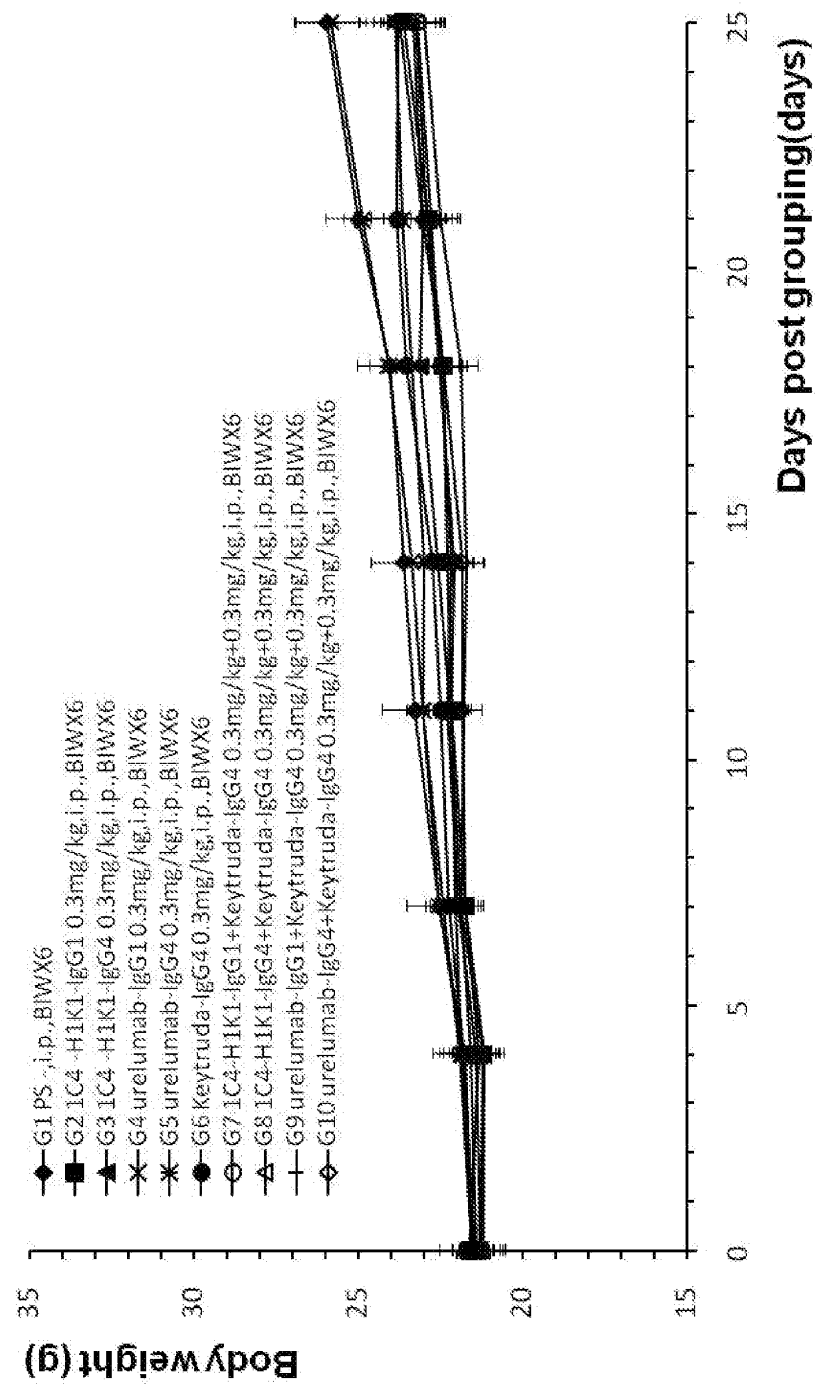


FIG. 65

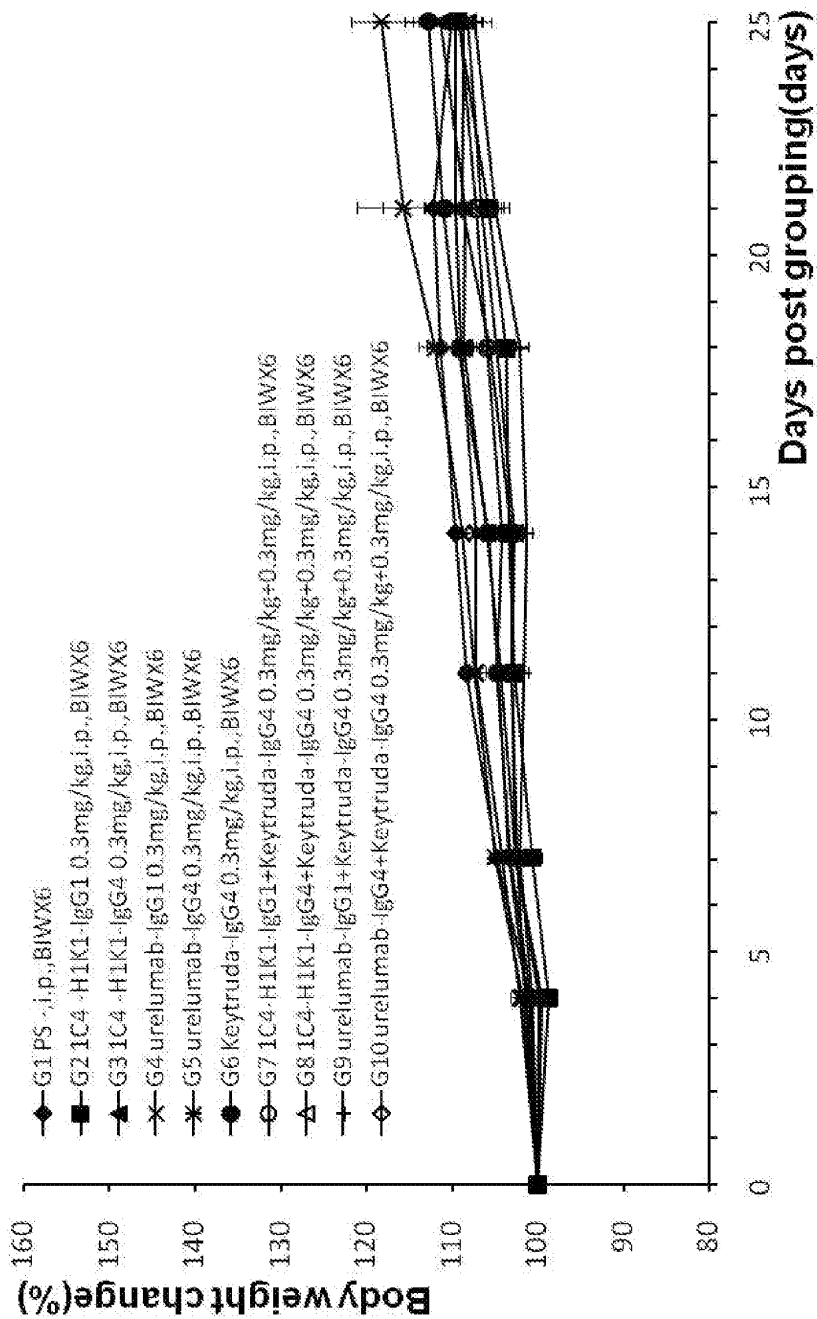


FIG. 66

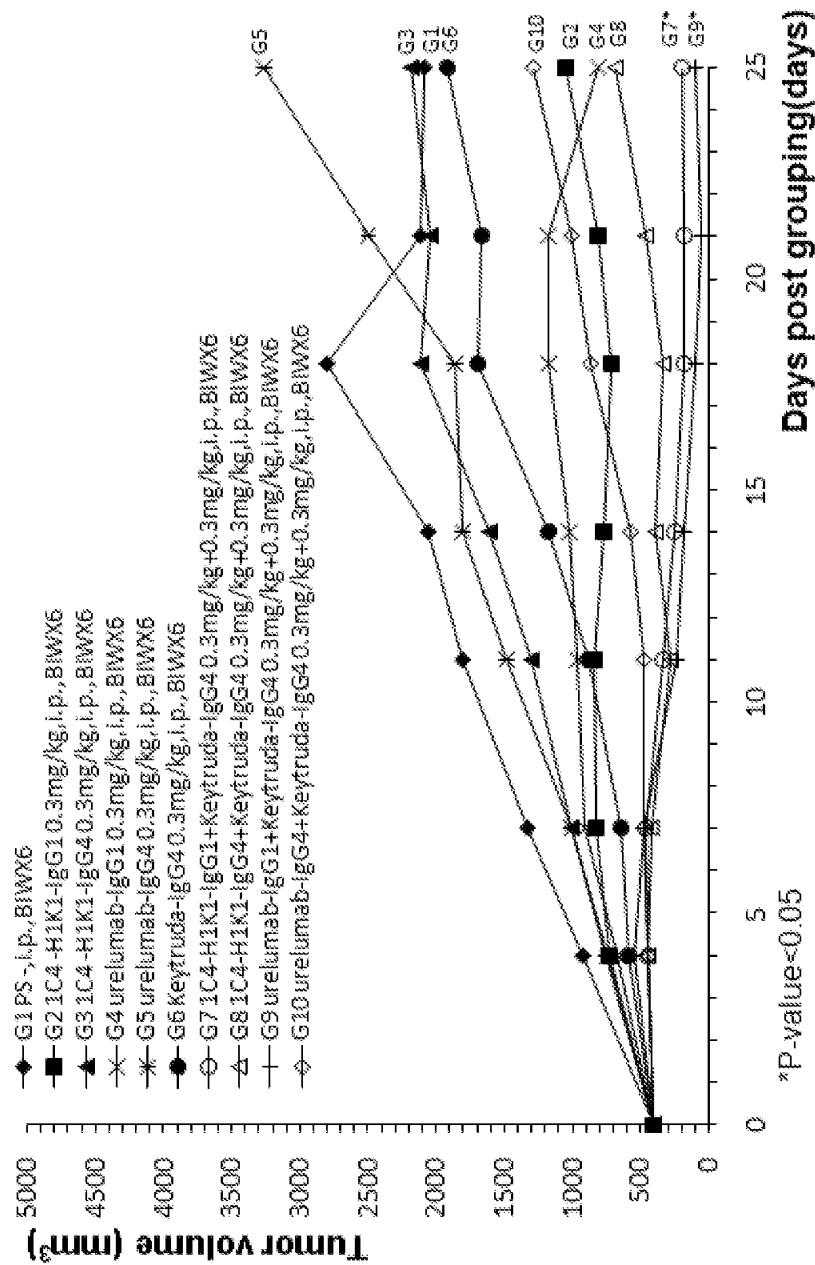


FIG. 67

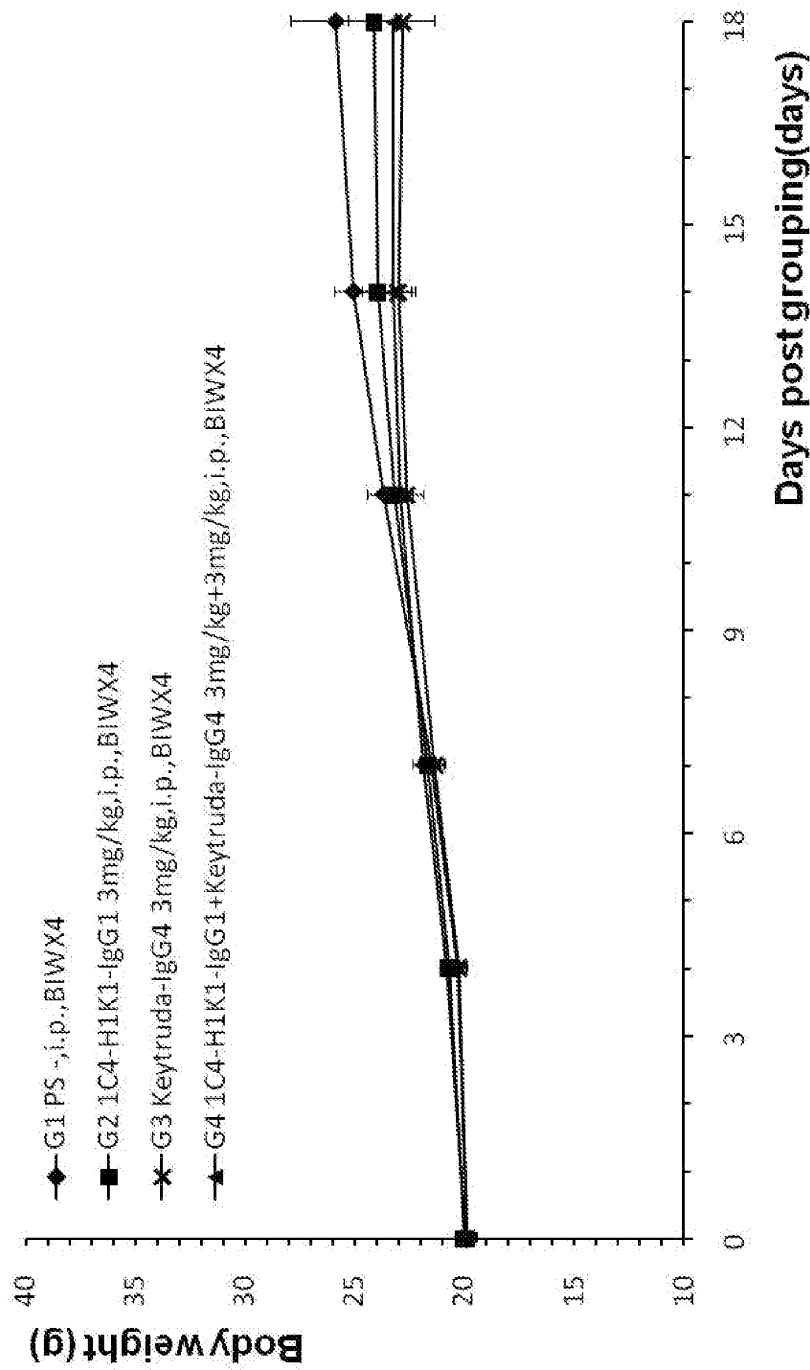


FIG. 68

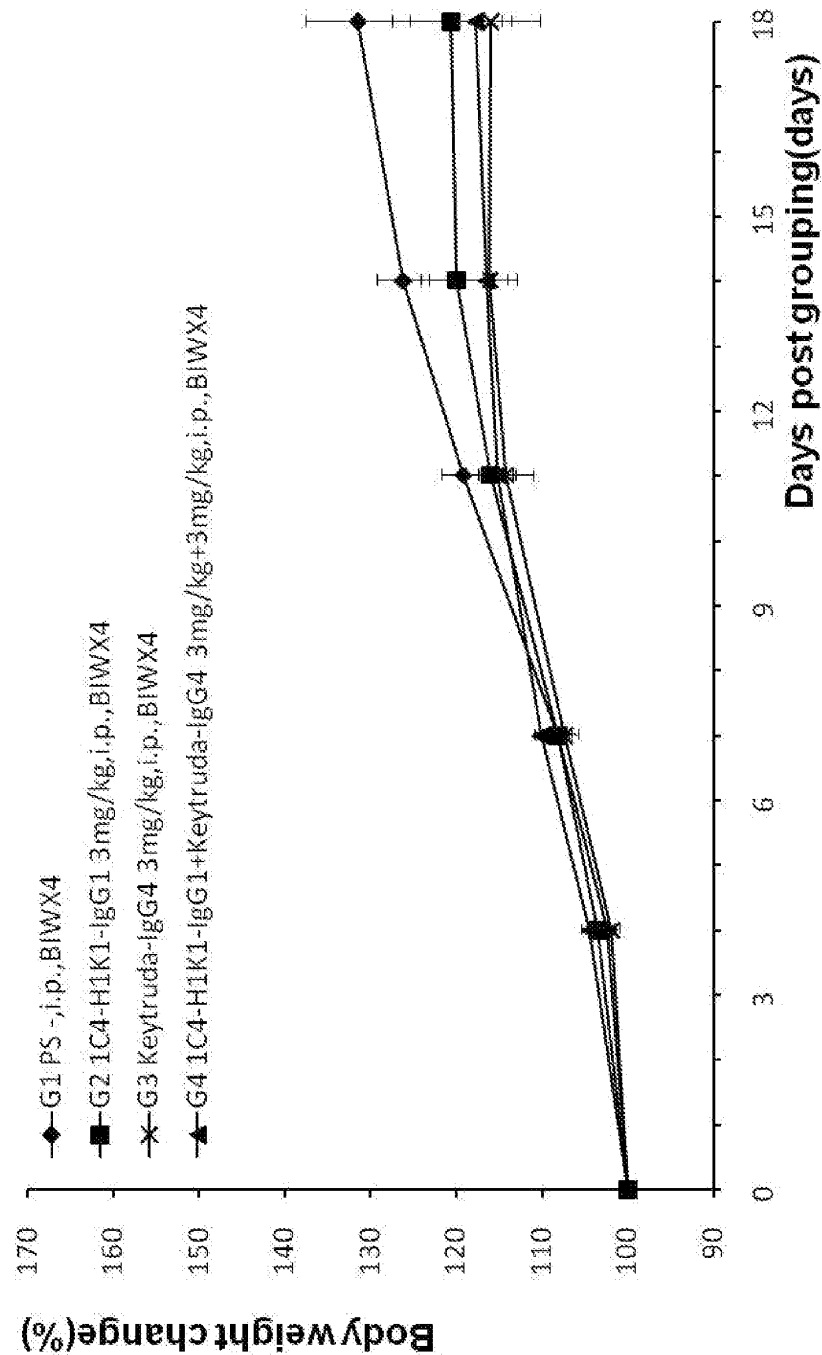


FIG. 69

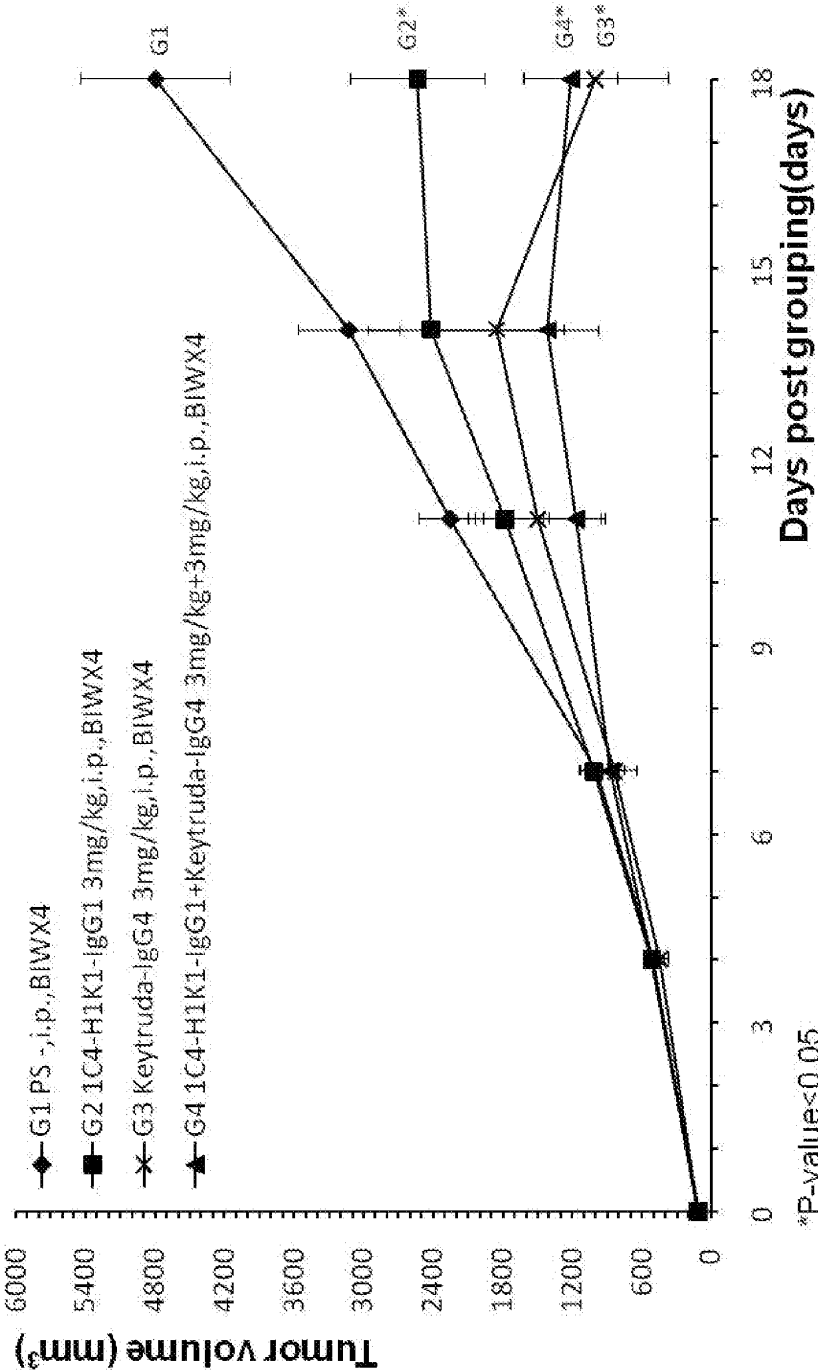


FIG. 70

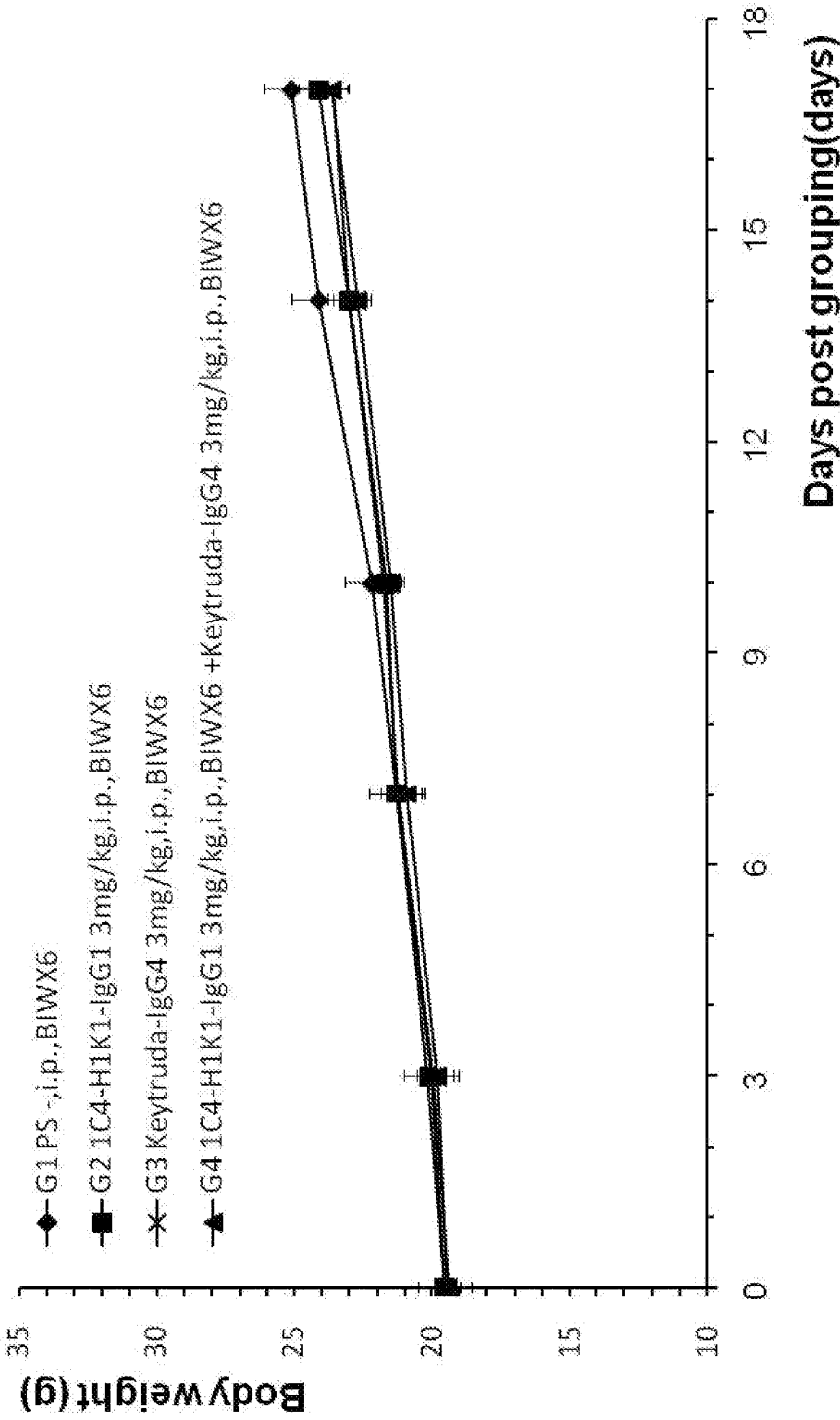


FIG. 71

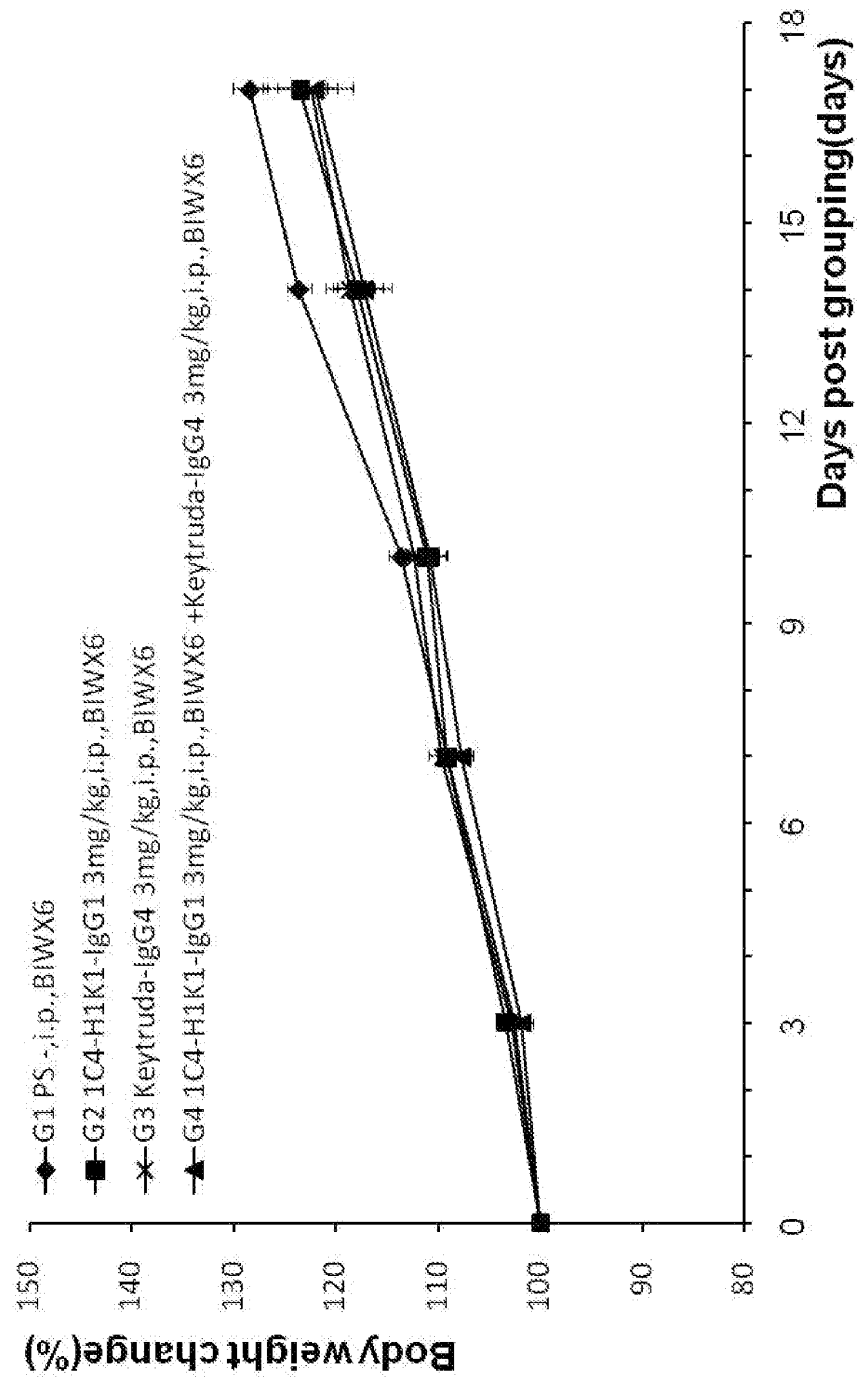


FIG. 72

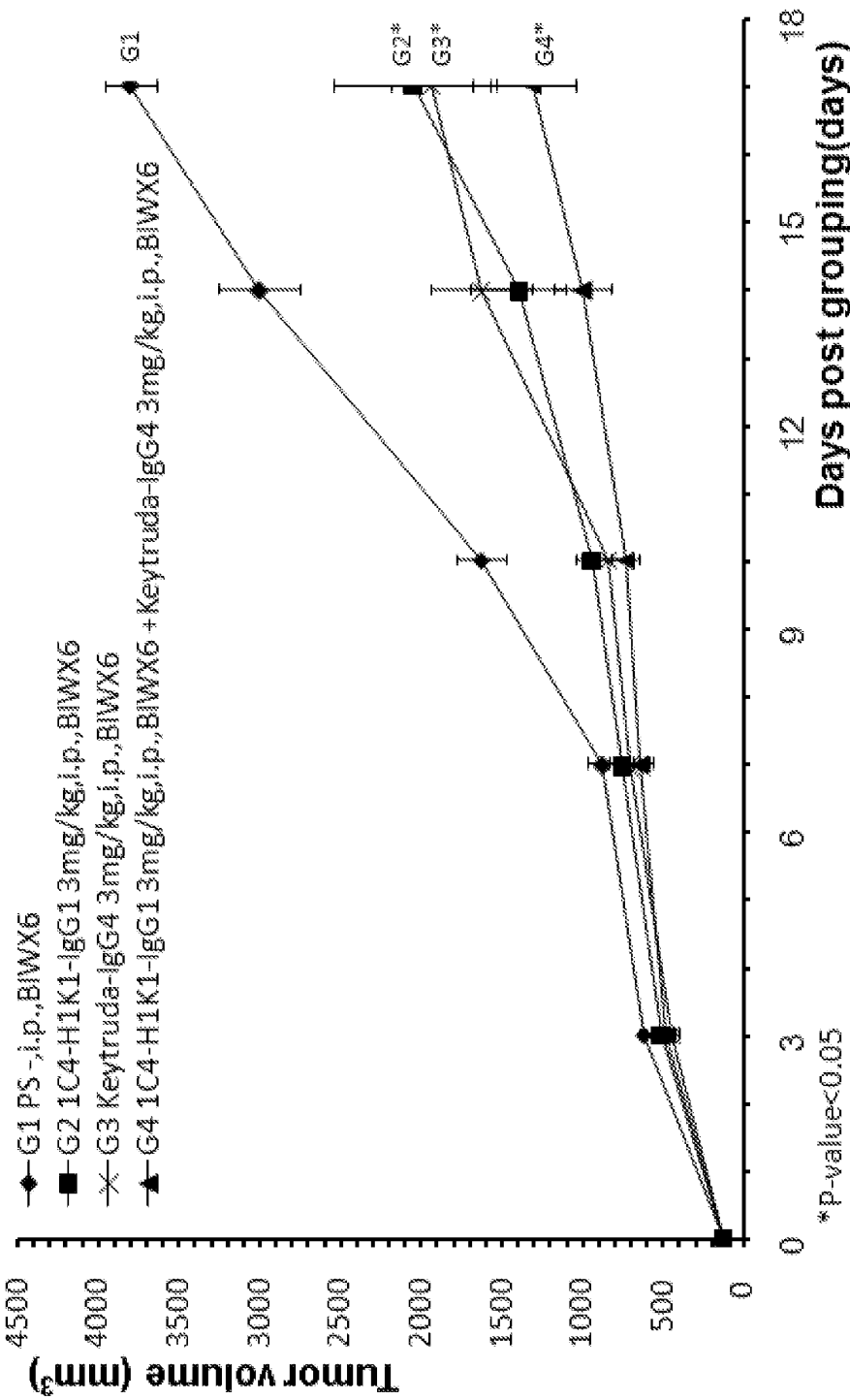


FIG. 73

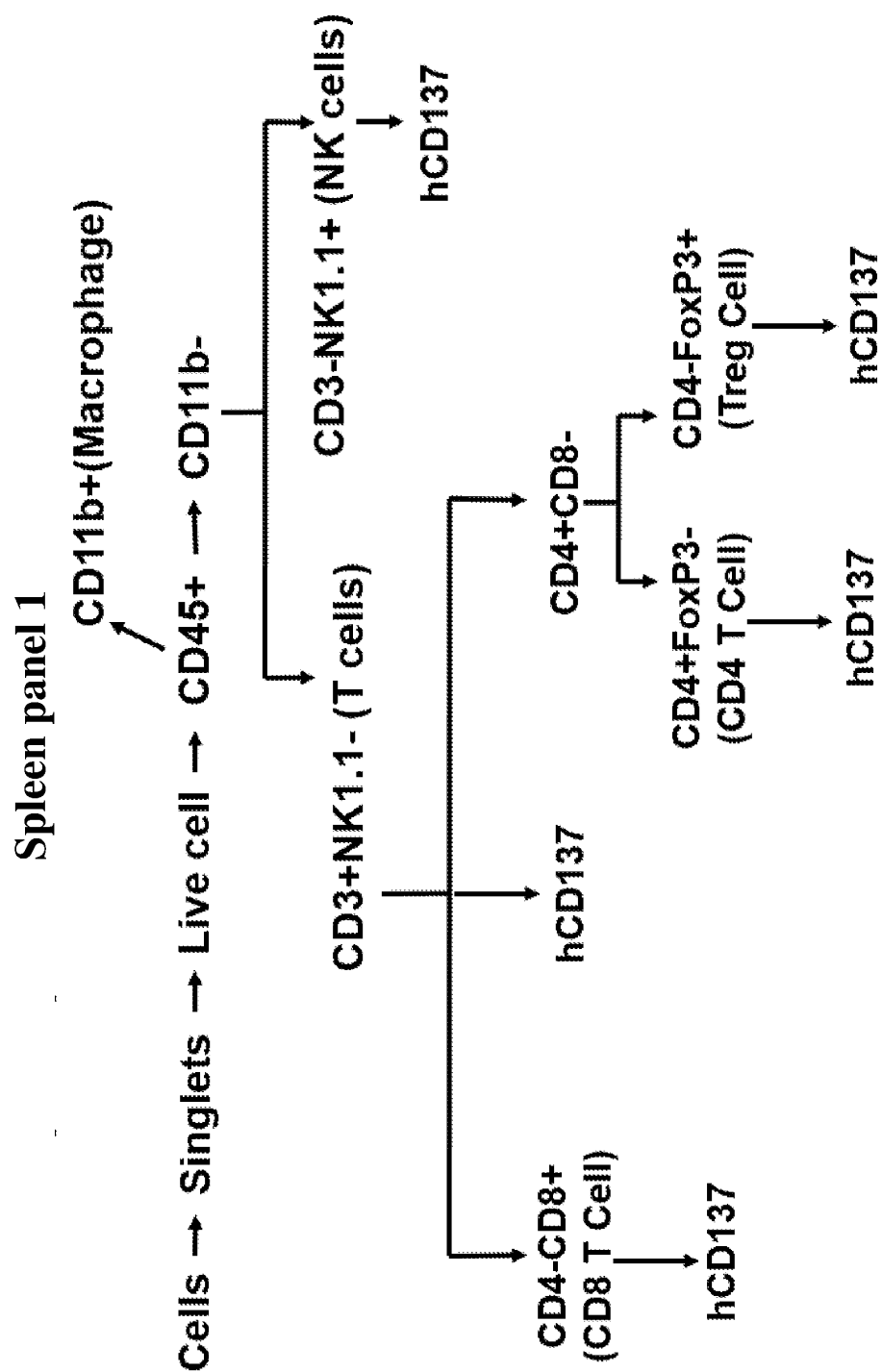


FIG. 74

Spleen panel 2

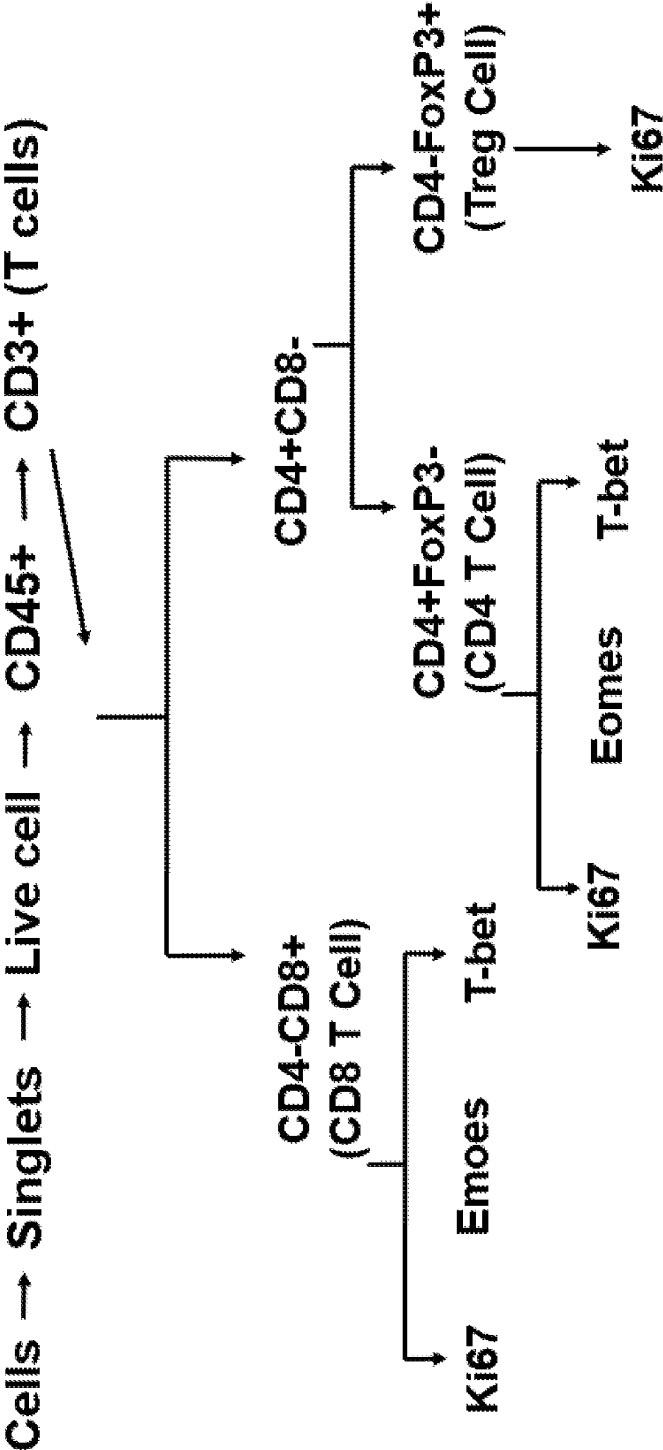


FIG. 75

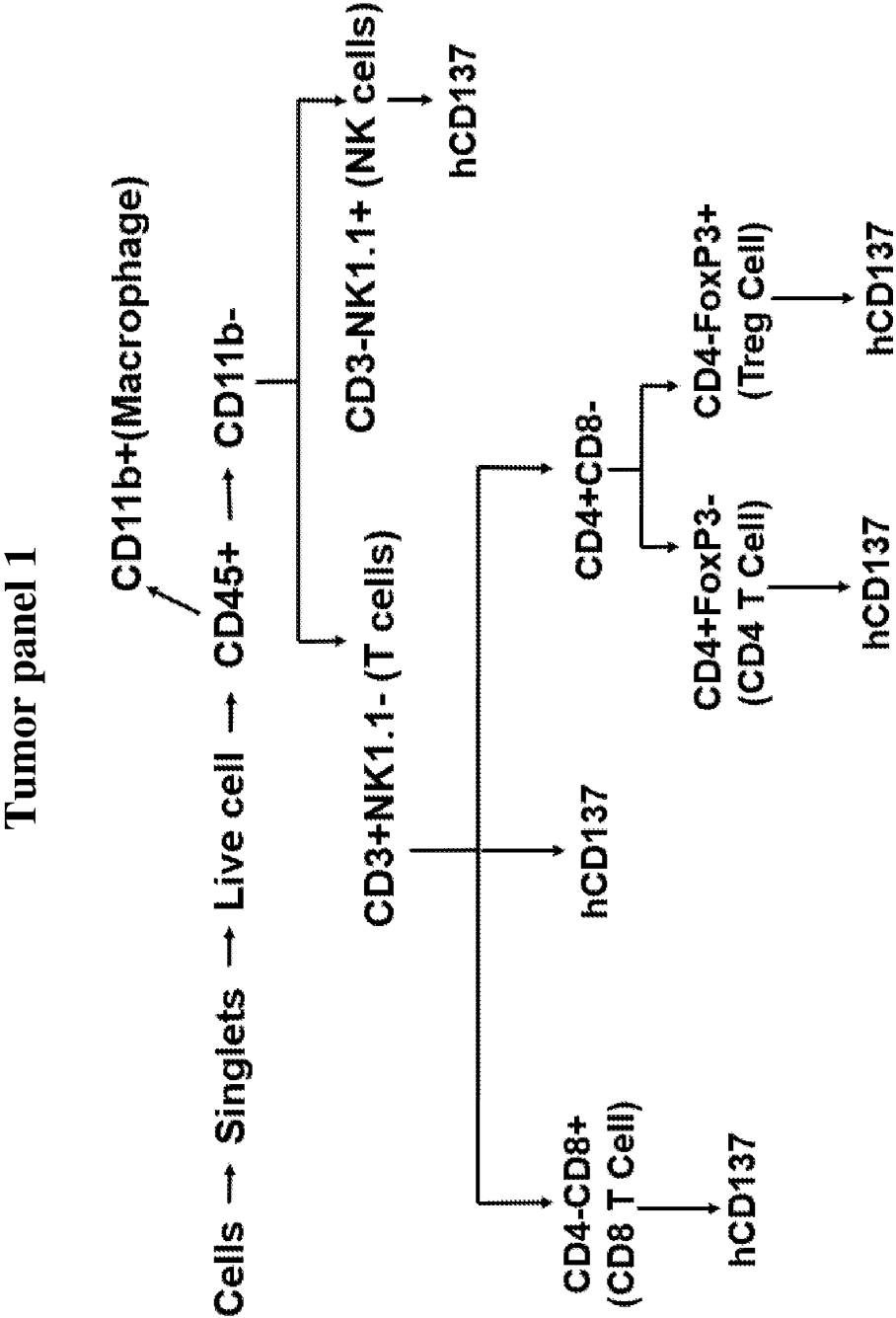


FIG. 76

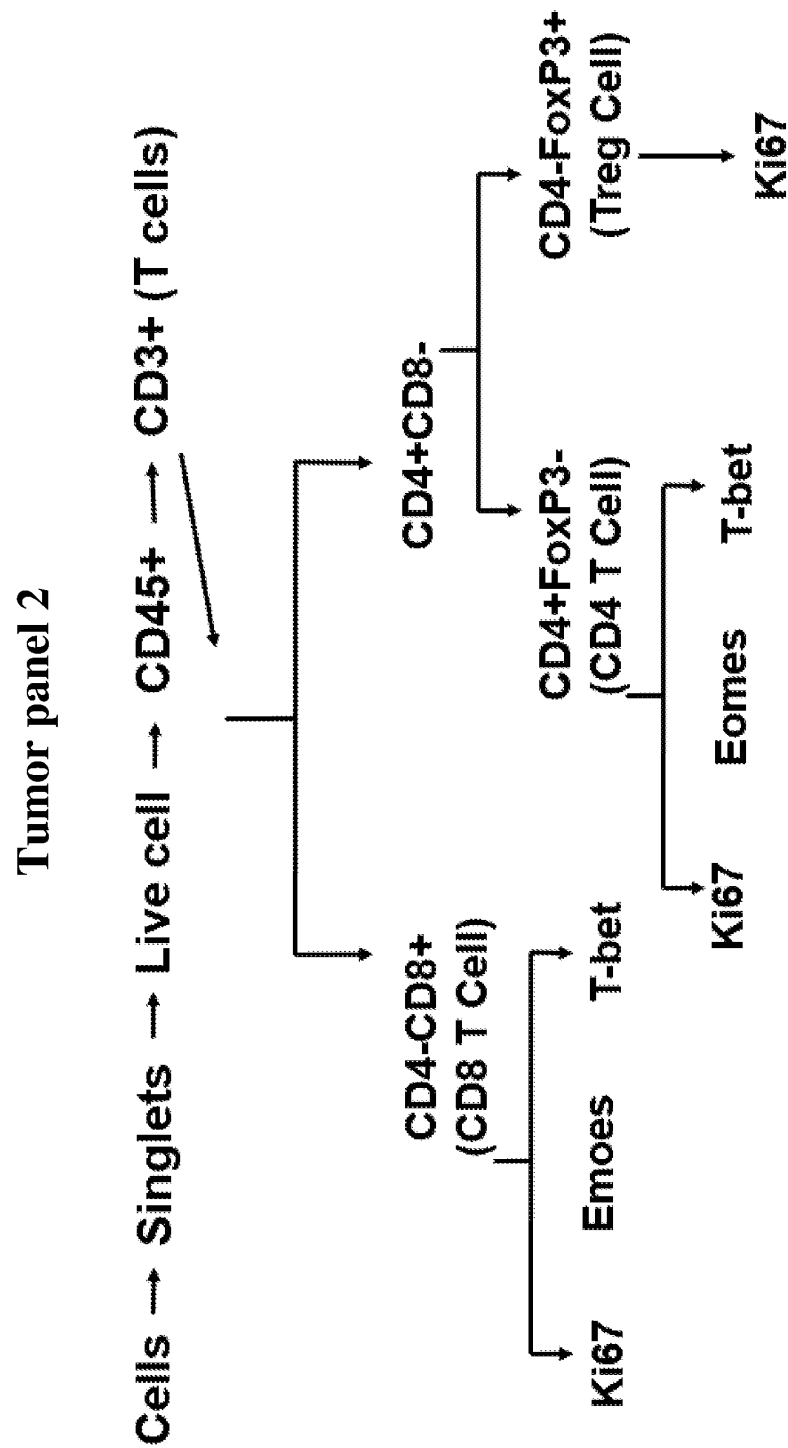


FIG. 77

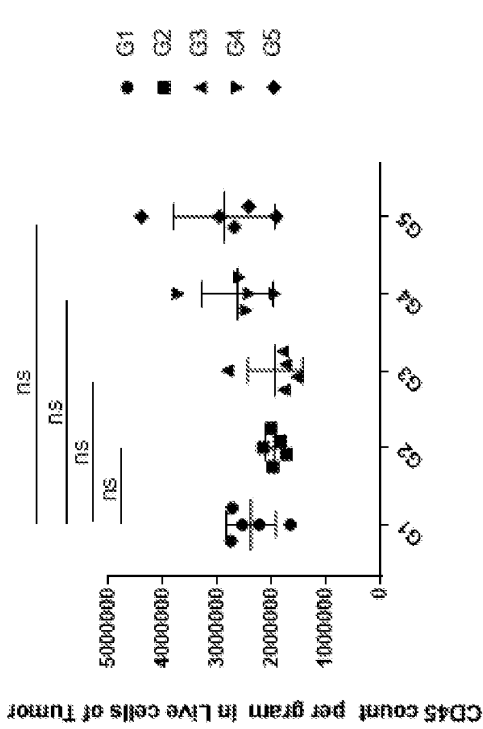


FIG. 78B

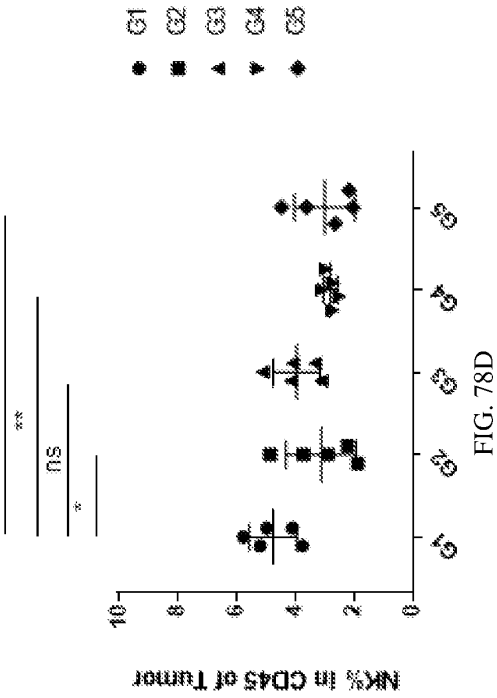


FIG. 78D

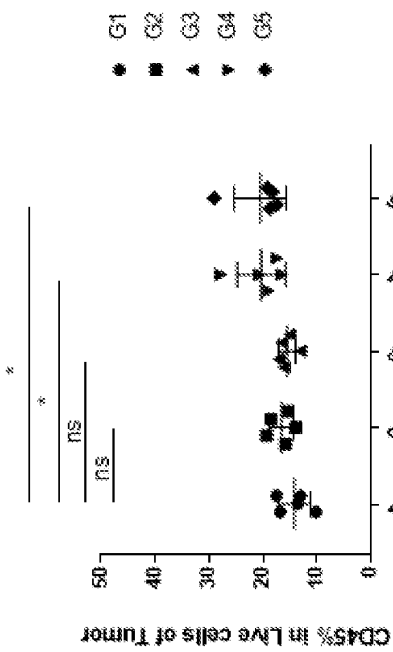


FIG. 78A

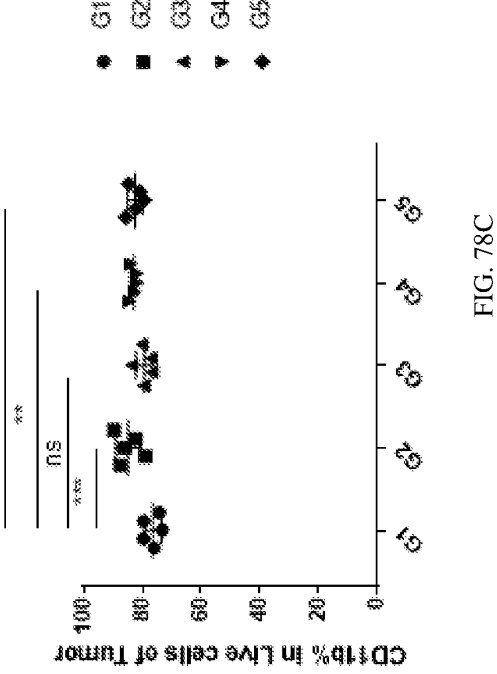
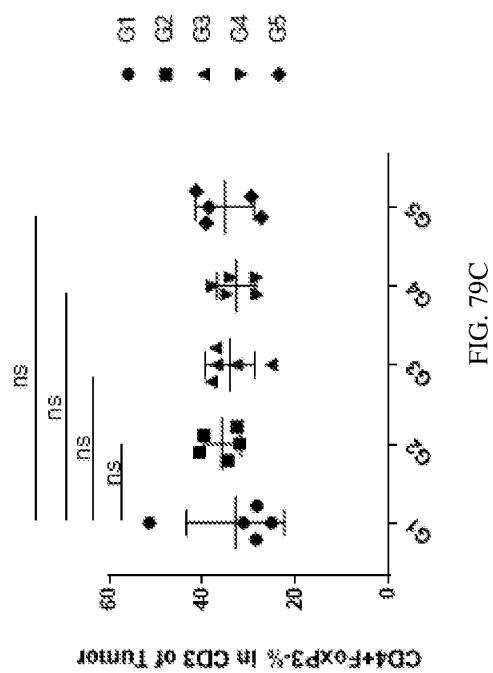
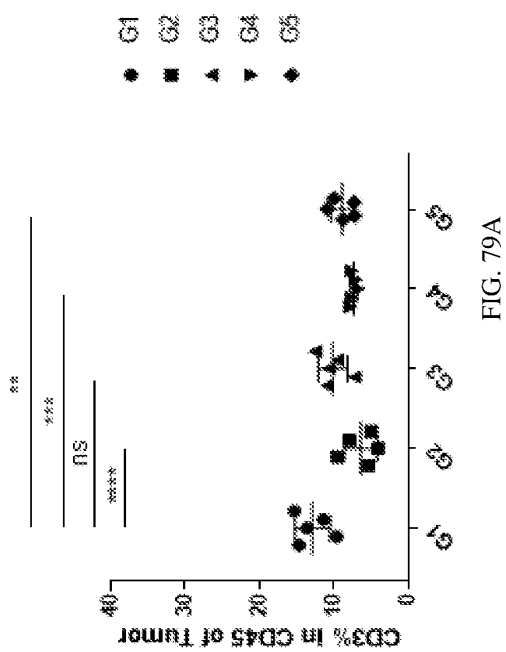
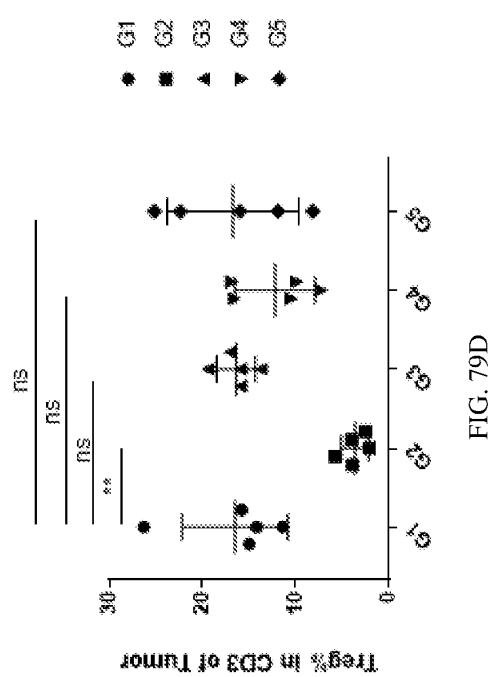
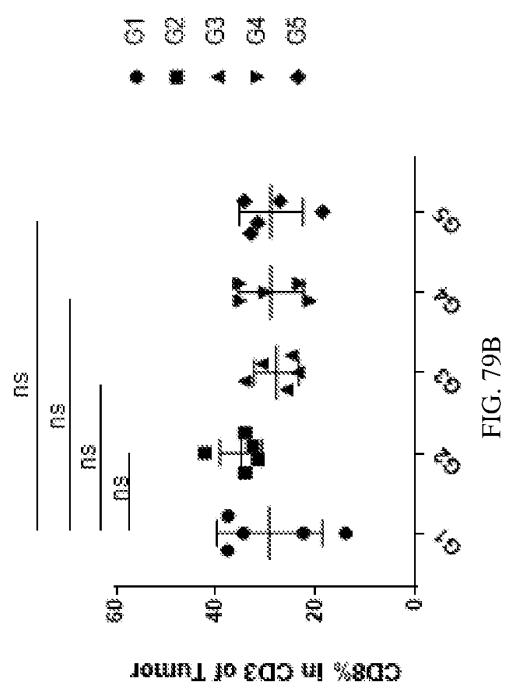


FIG. 78C



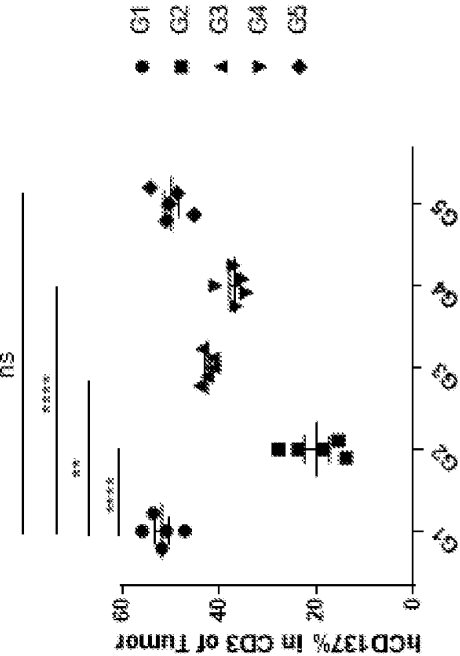


FIG. 80B

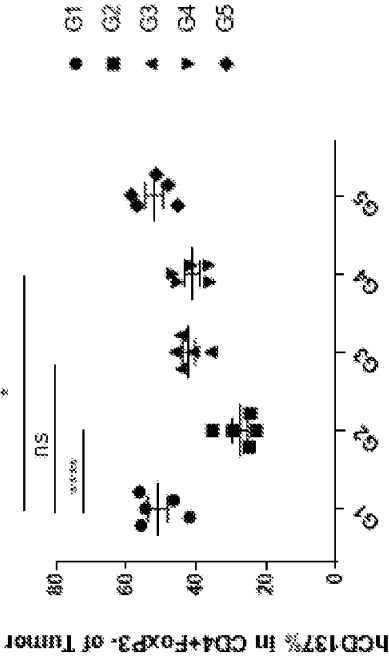


FIG. 80D

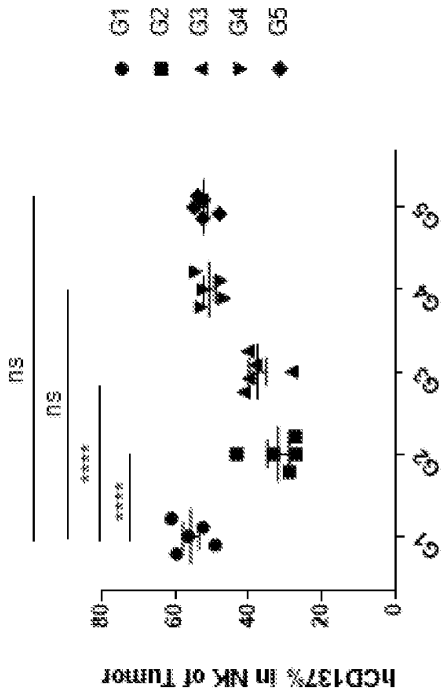


FIG. 80A

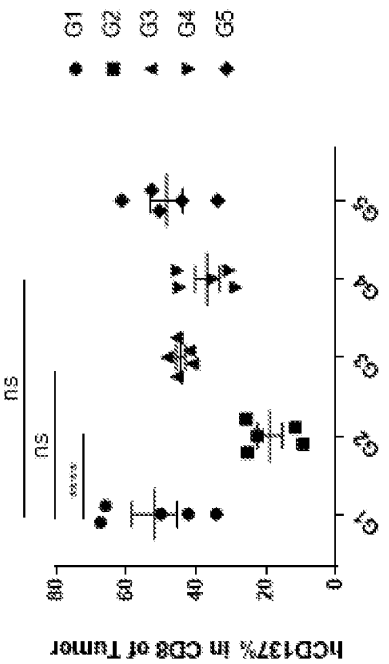


FIG. 80C

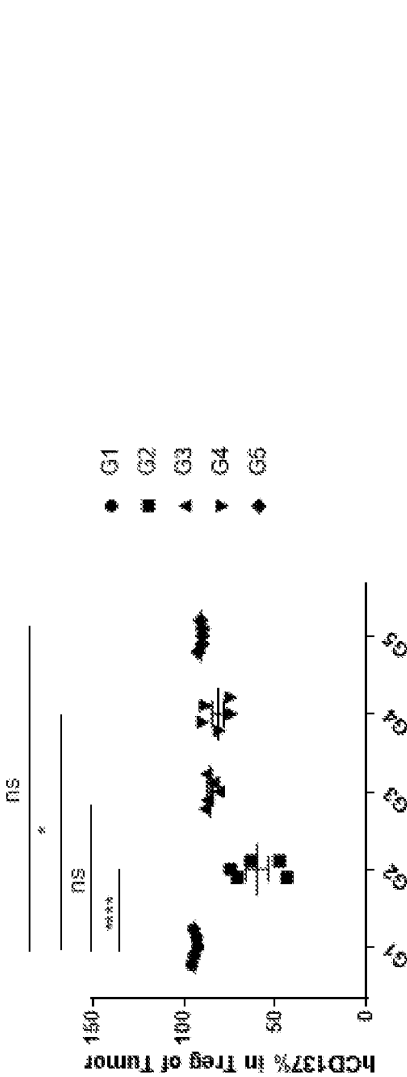
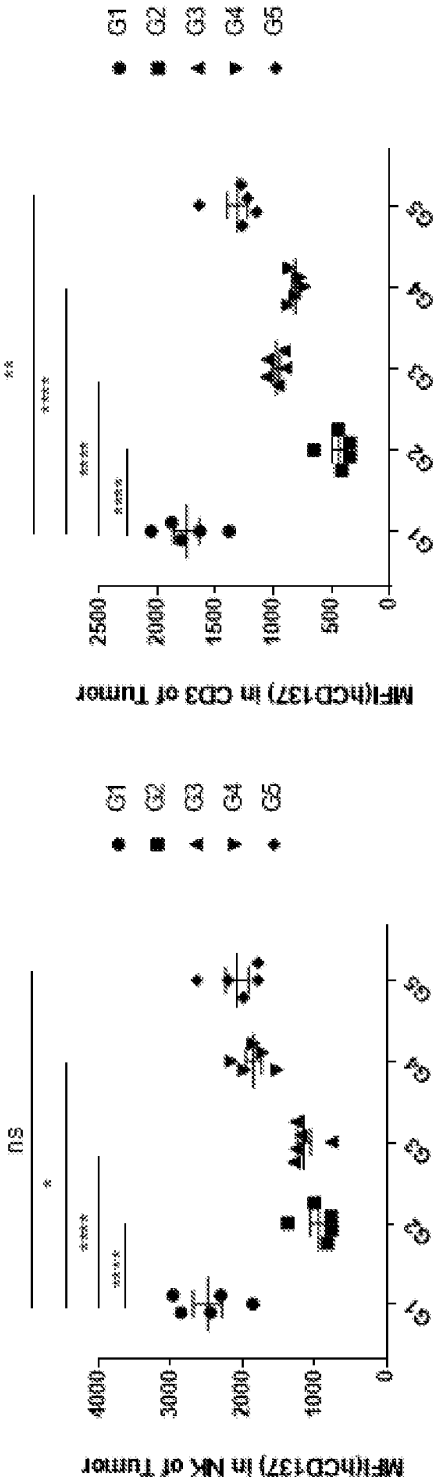


FIG. 80E



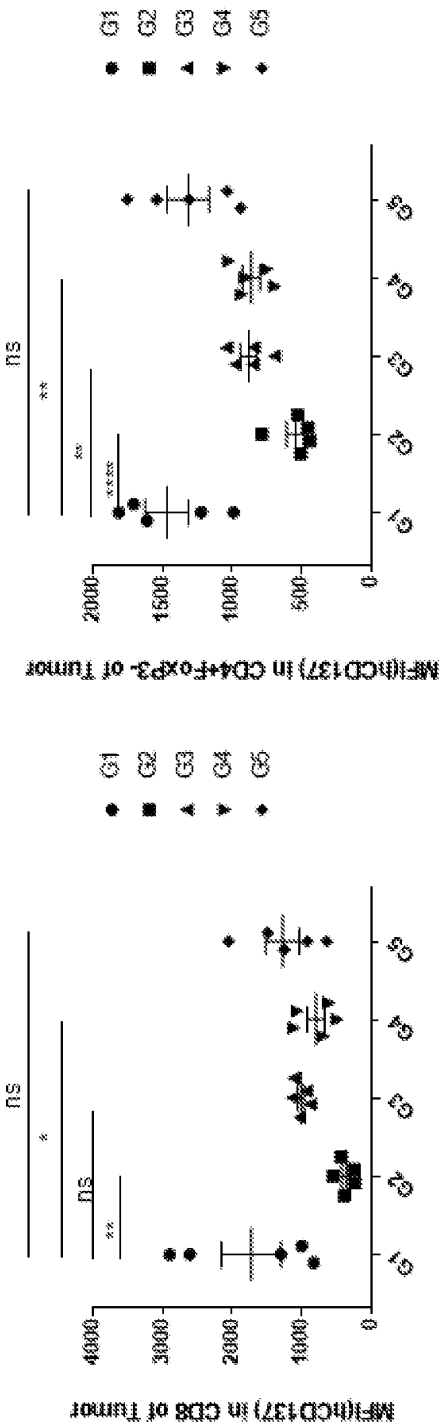


FIG. 81D

FIG. 81C

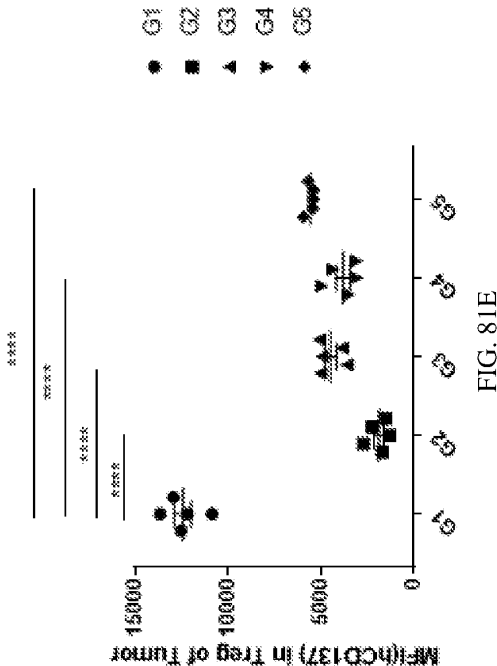


FIG. 81E

