

IL-2 receptor exists in three states

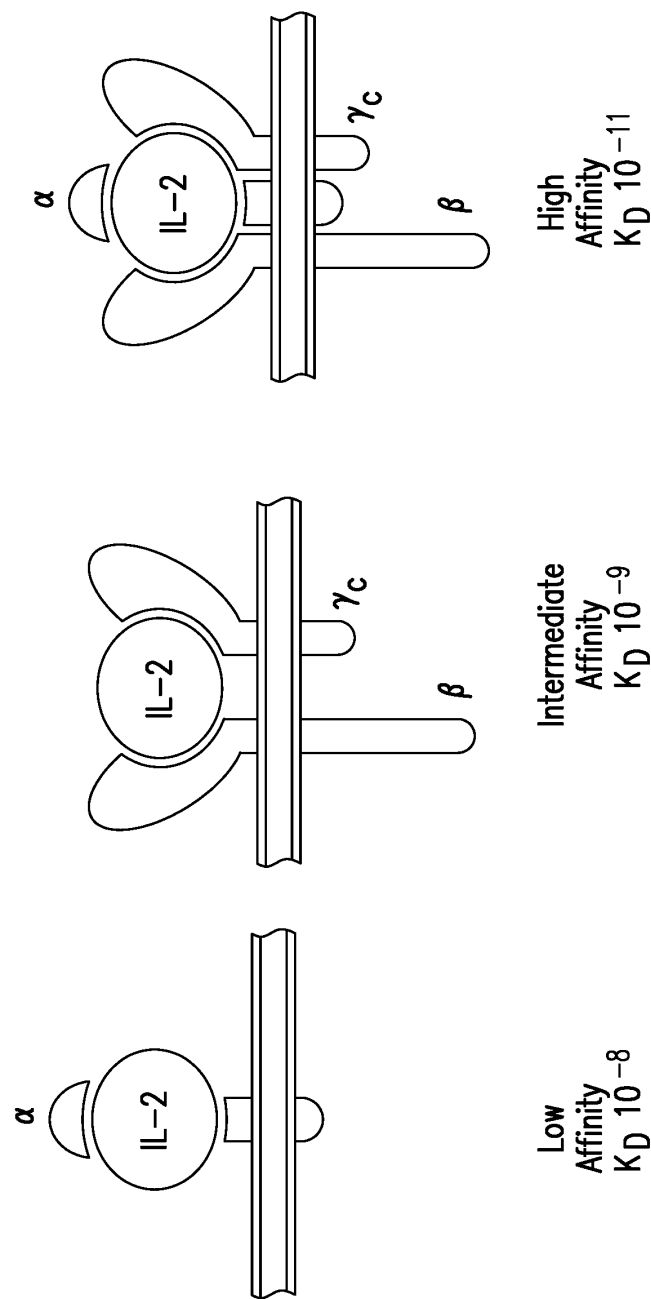


FIG.1

- 1 × AId-6HIS
- 2 ▢ AId-6HIS_K34D
- 3 = AId-6HIS_T36D
- 4 □ AId-6HIS_R37G
- 5 △ AId-6HIS_T40D
- 6 ▽ AId-6HIS_F41L
- 7 ○ AId-6HIS_K42G
- 8 ● AId-6HIS_Y44V

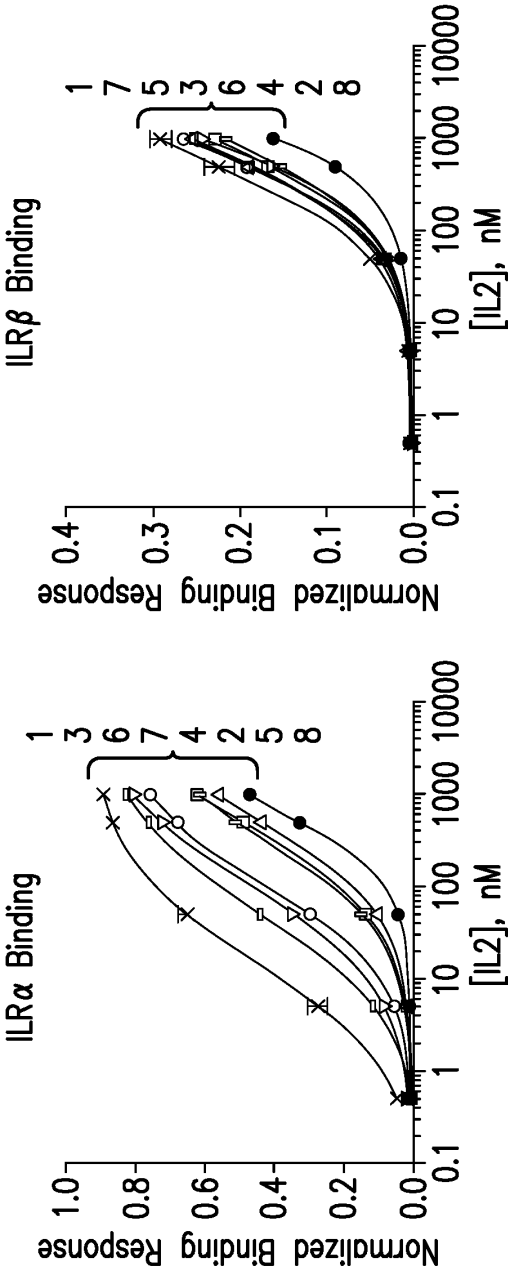


FIG.2A

- 1 × Ald-6HIS
- 2 □ Ald-6HIS_E60T
- 3 = Ald-6HIS_E61S
- 4 □ Ald-6HIS_K63G
- 5 △ Ald-6HIS_P64A
- 6 ▽ Ald-6HIS_E67G
- 7 ○ Ald-6HIS_L71I

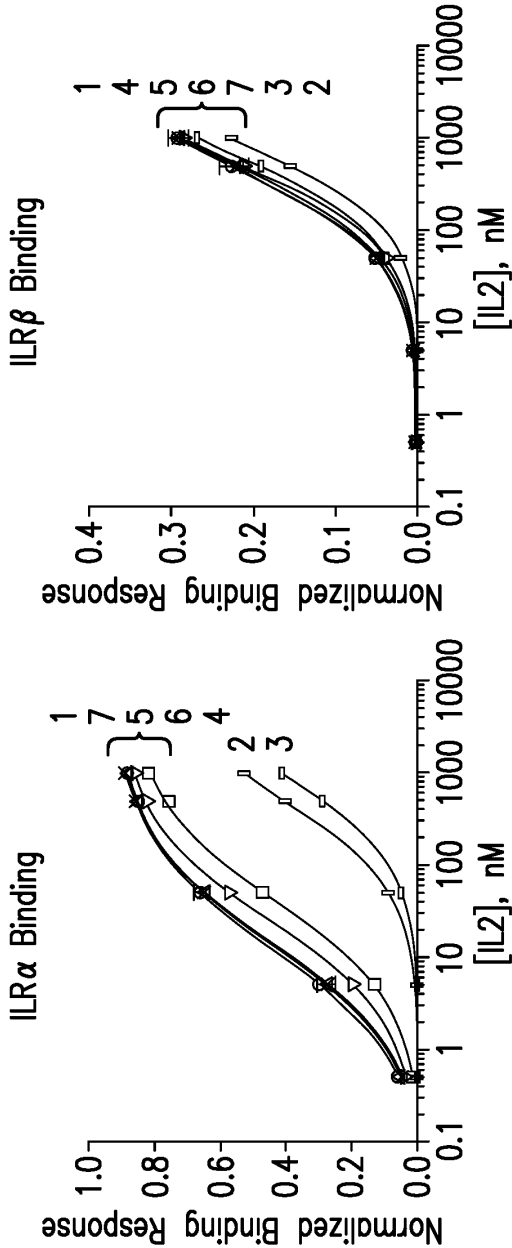


FIG.2B

- 1 × Ald-6HIS
- 2 ▯ Ald-6HIS_E60T/E61S
- 3 ▮ Ald-6HIS_E60T/P64A
- 4 □ Ald-6HIS_E61S/P64A
- 5 △ Ald-6HIS_E61S/Y106A
- 6 ▽ Ald-6HIS_E60T/E61S/P64A
- 7 ○ Ald-6HIS_E61S/P64A/Y106A
- 8 ● Ald-6HIS_E61S

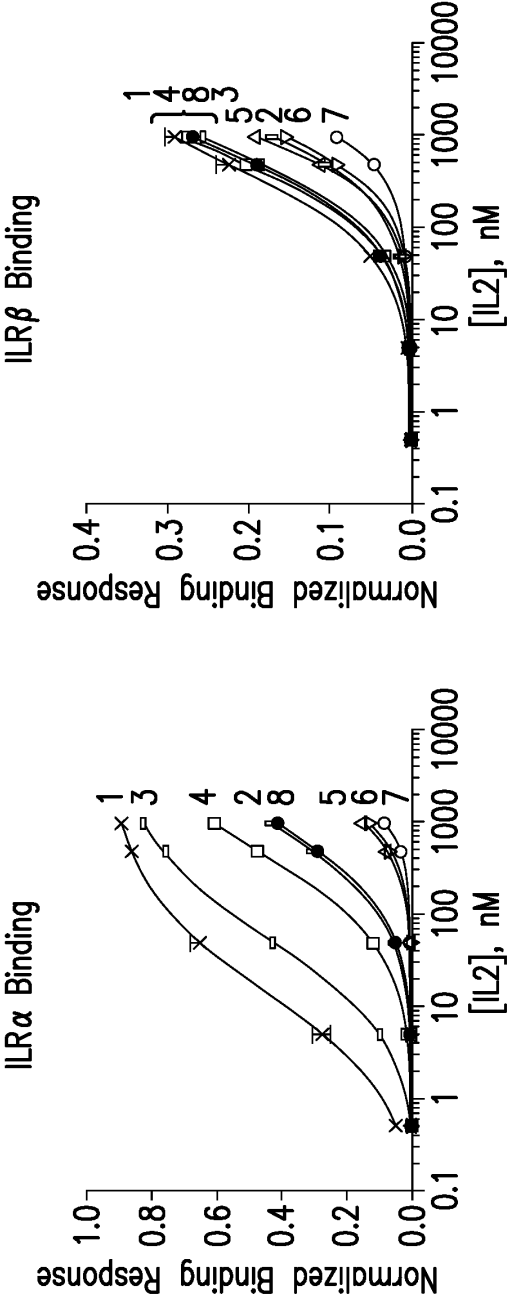


FIG.2C

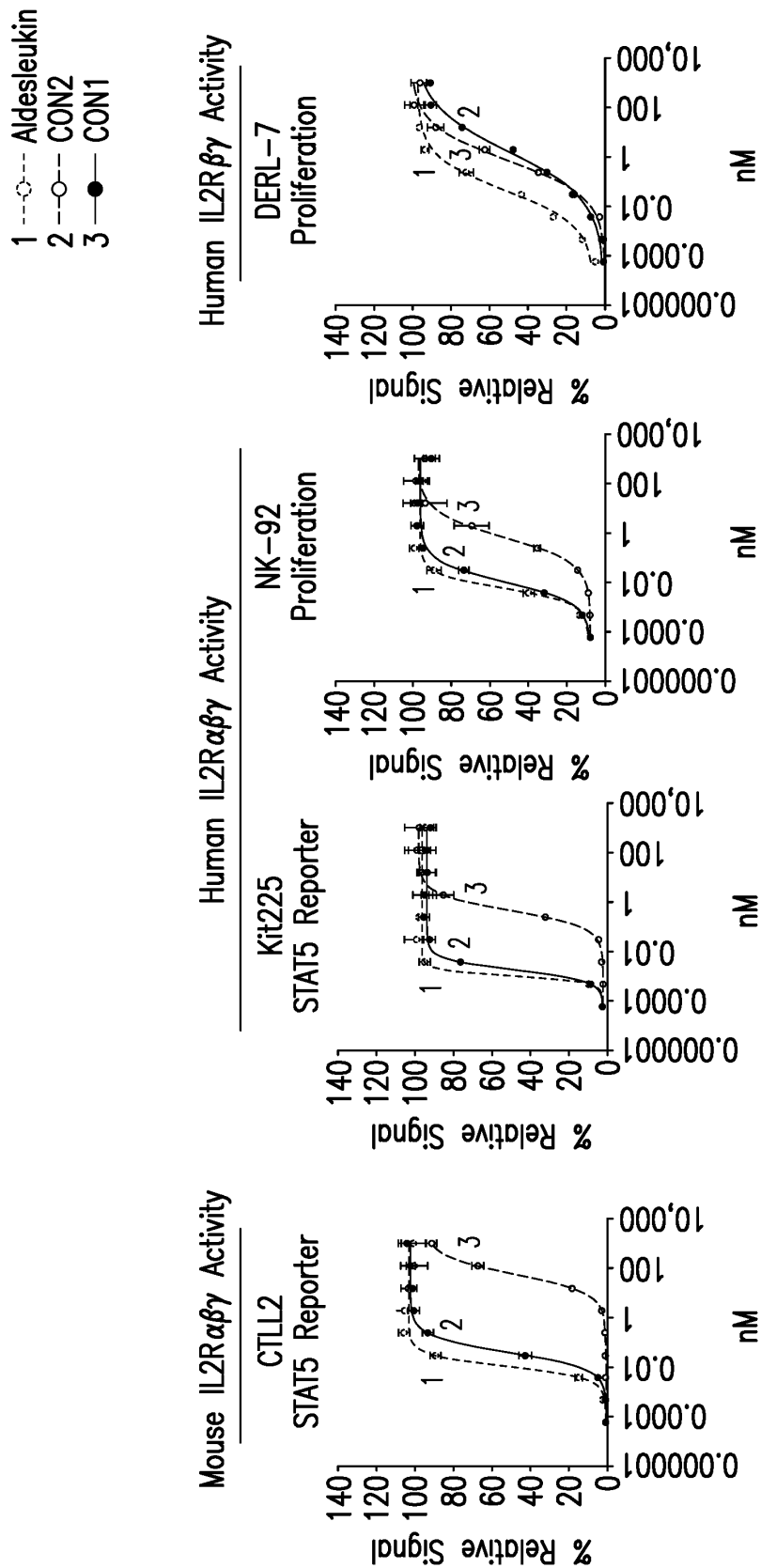


FIG.3

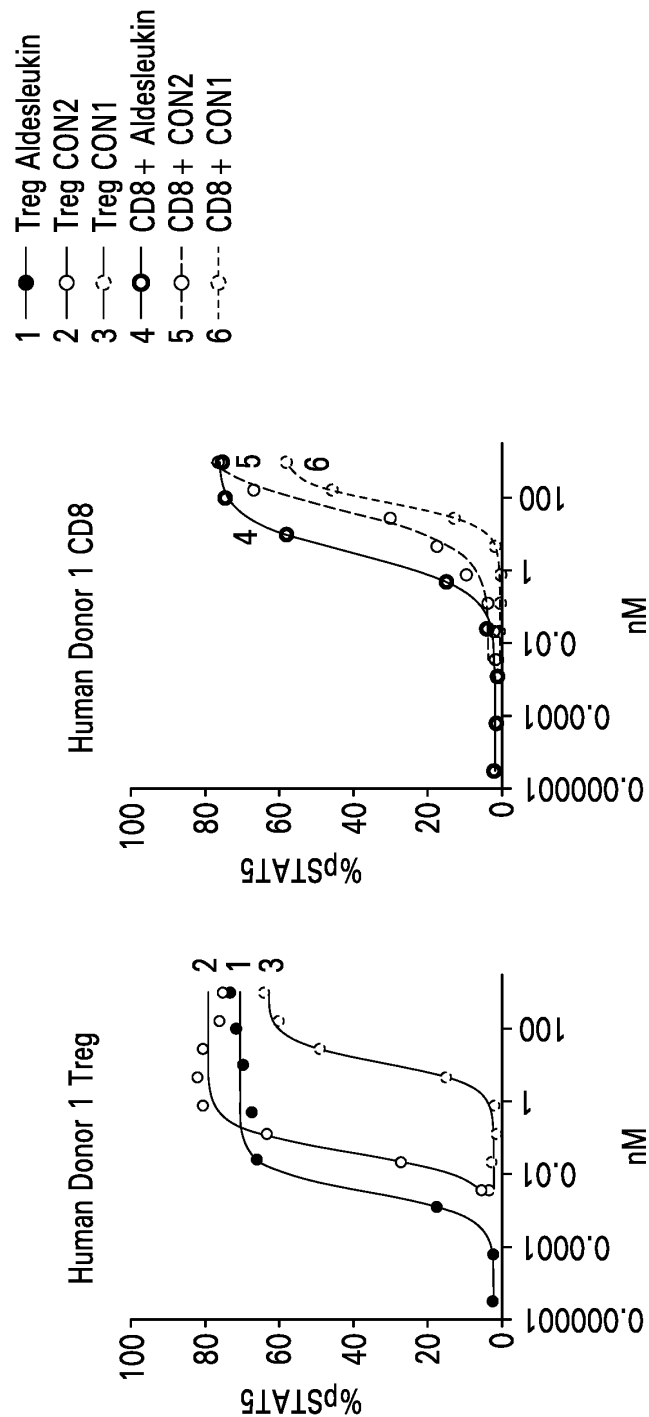


FIG.4A

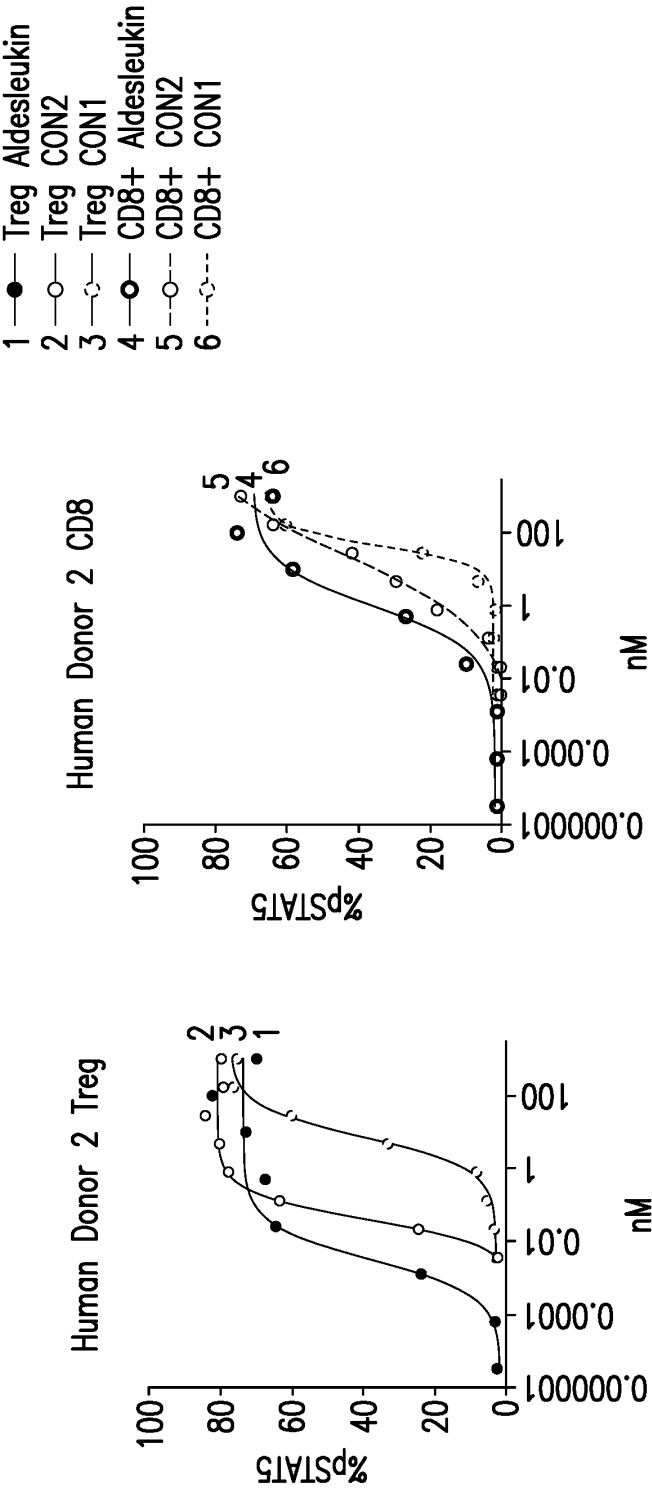


FIG.4B

Bioactivity of CON1 Relative to Other IL-2 Entities
Kit225Stat5Luc Assay

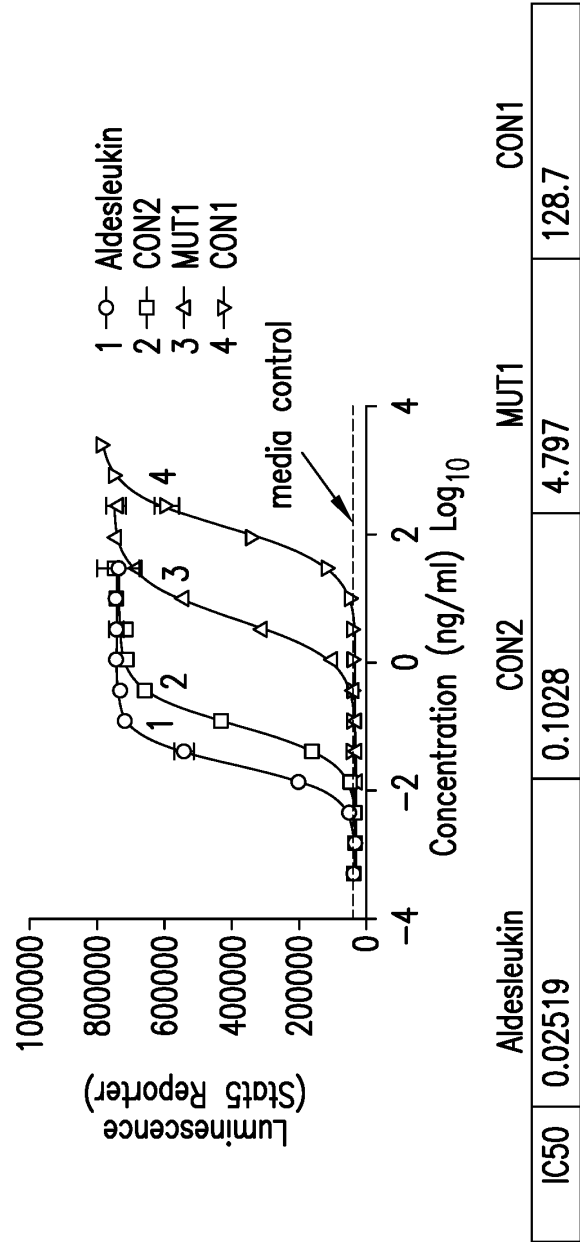


FIG. 5A

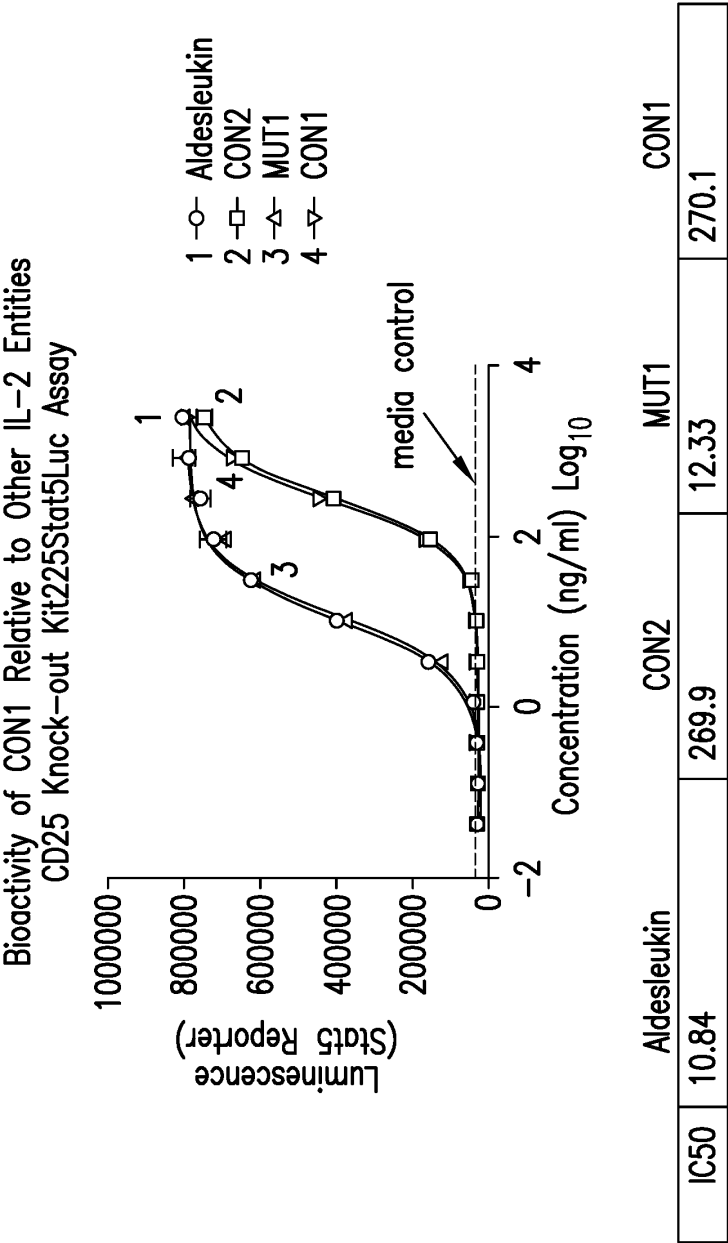


FIG.5B

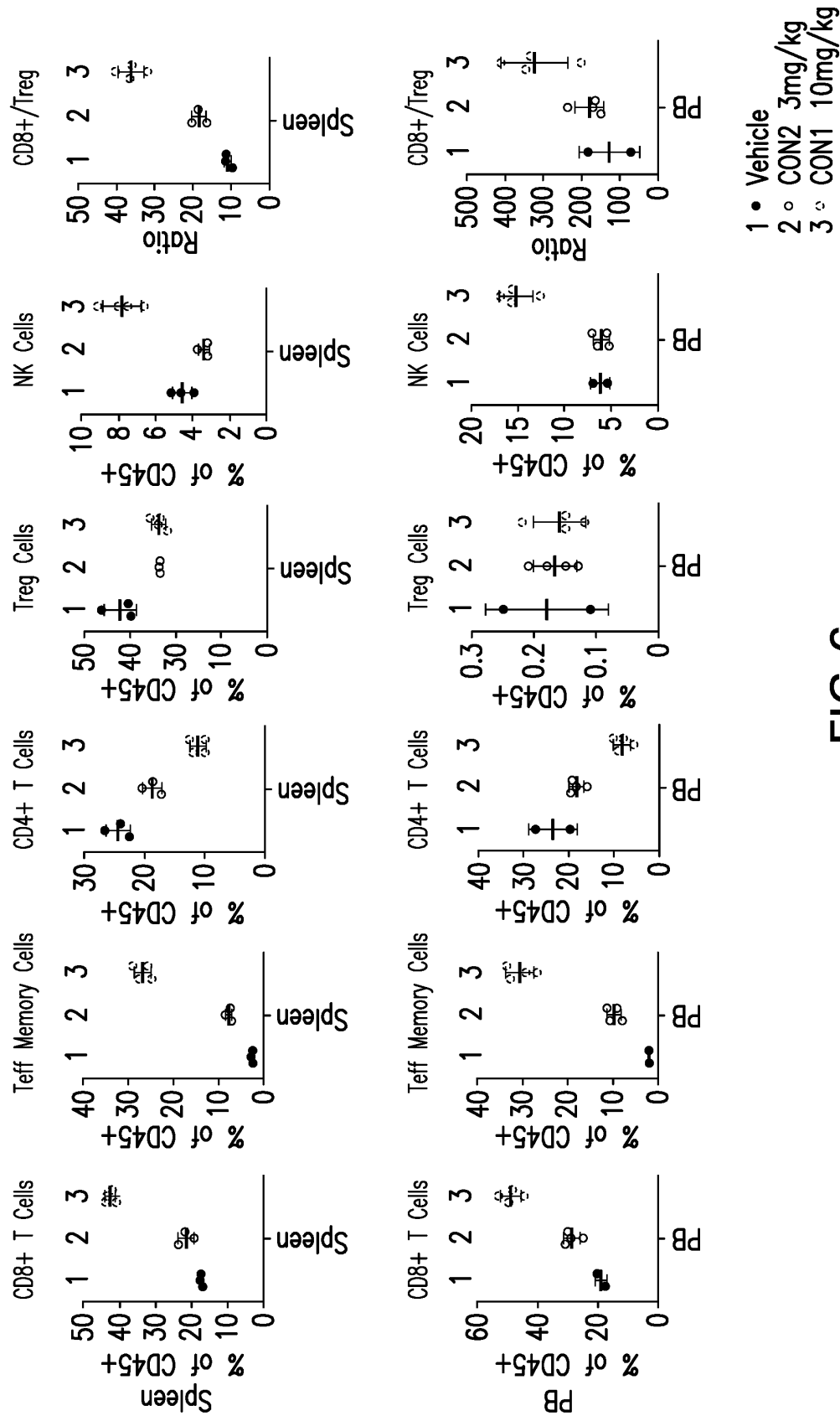


FIG.6

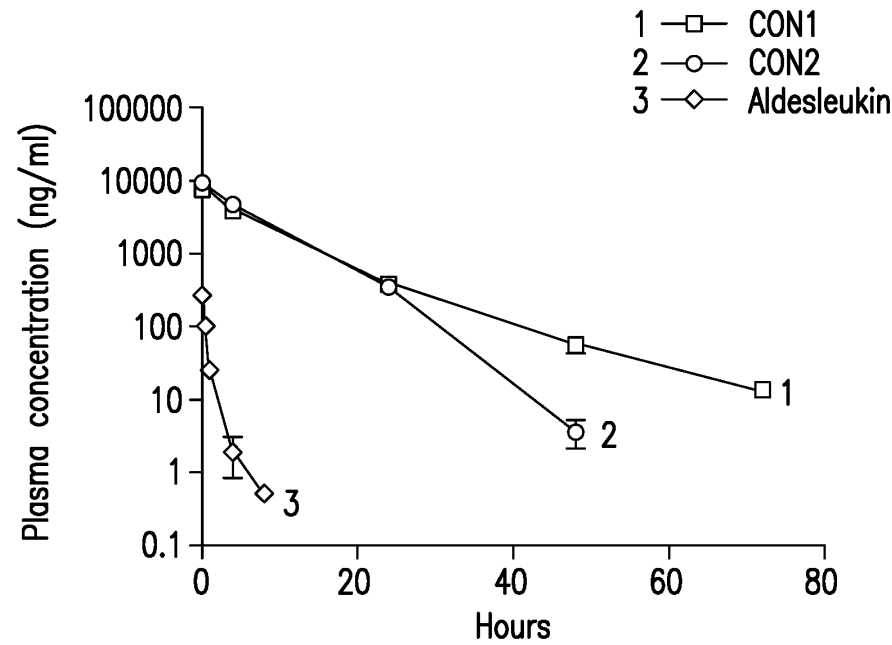


FIG.7

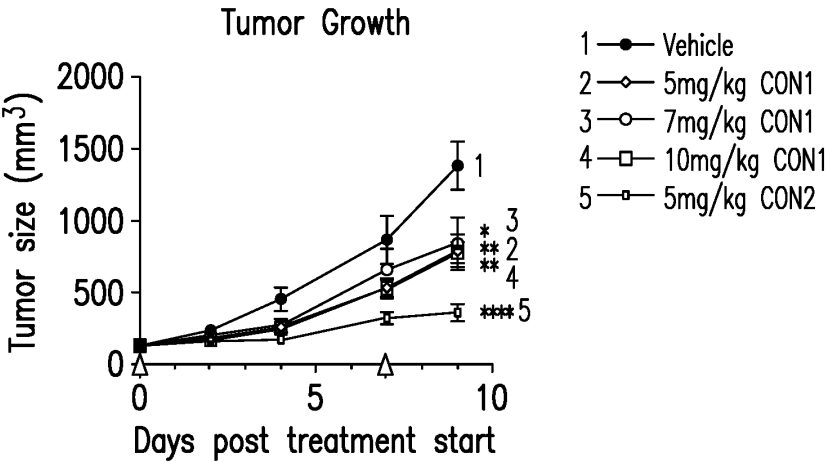


FIG.8A

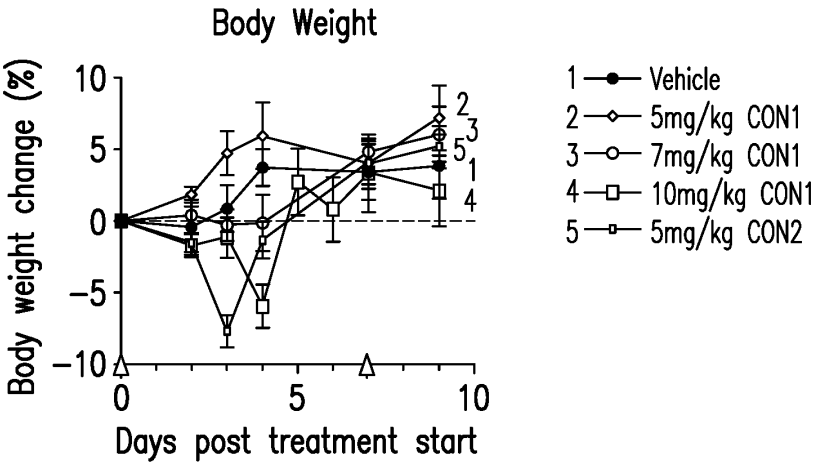


FIG.8B

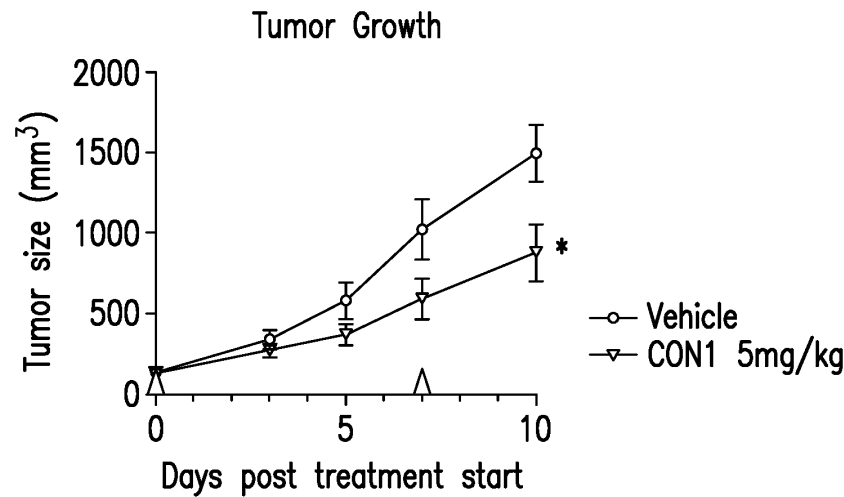


FIG.9A

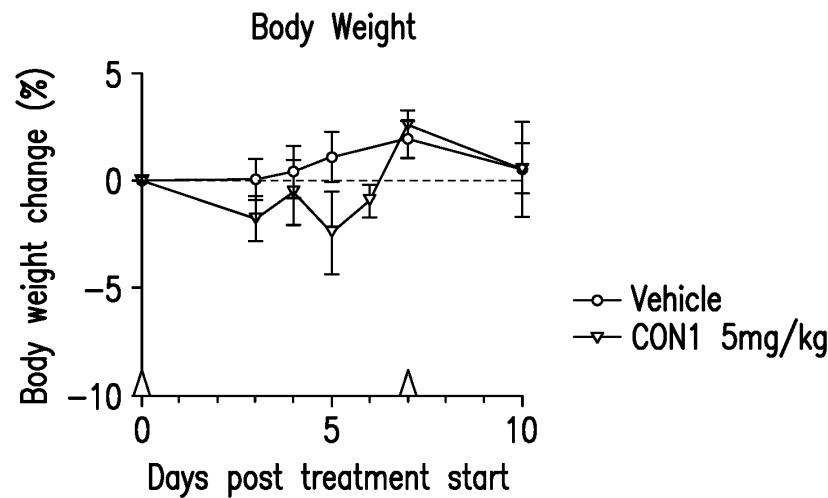


FIG.9B

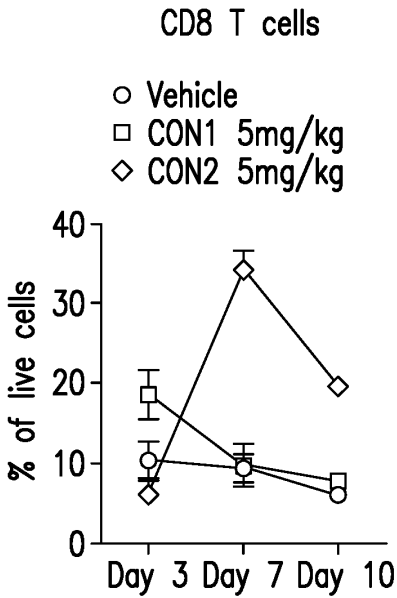


FIG.10A

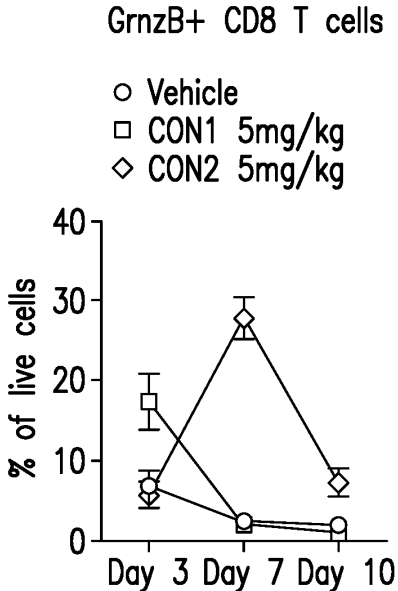


FIG.10B

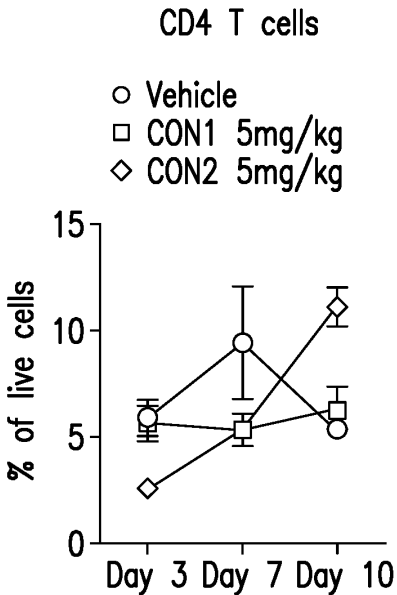


FIG.10C

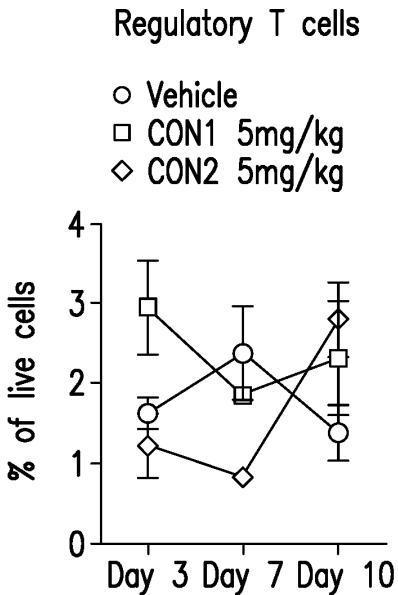


FIG.10D

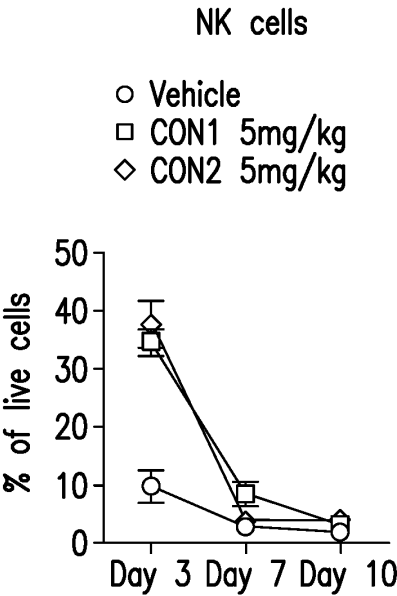


FIG.10E

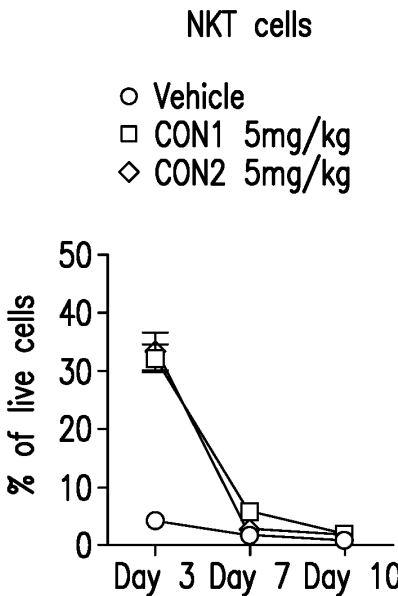


FIG.10F

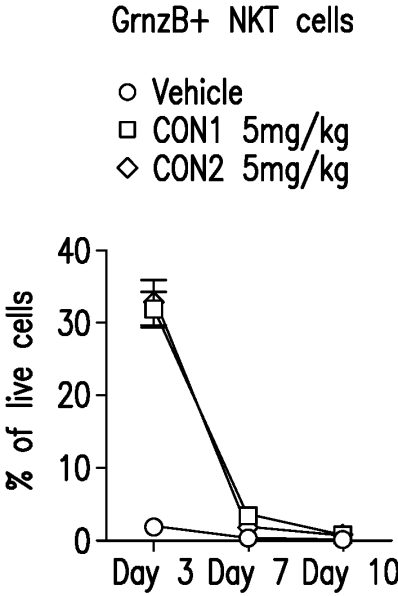


FIG.10G

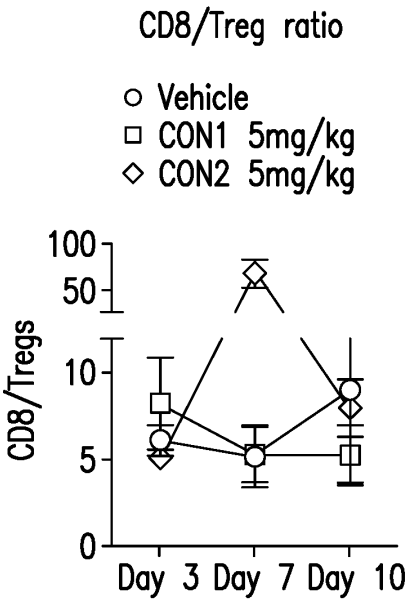


FIG.10H

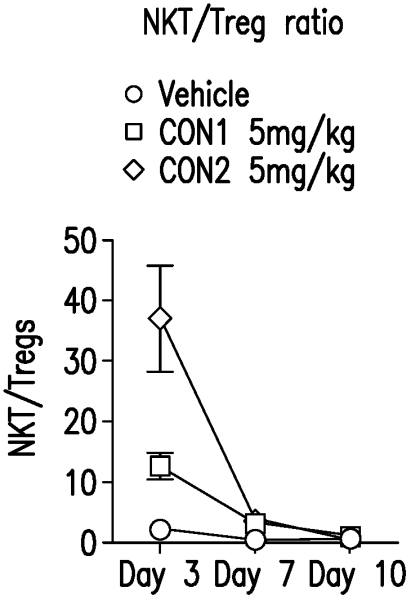


FIG.10I

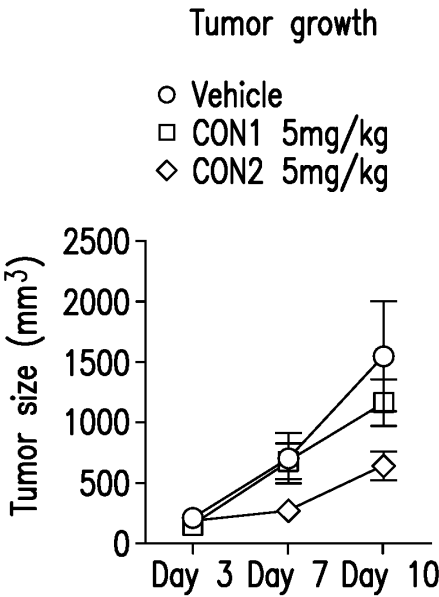


FIG.10J

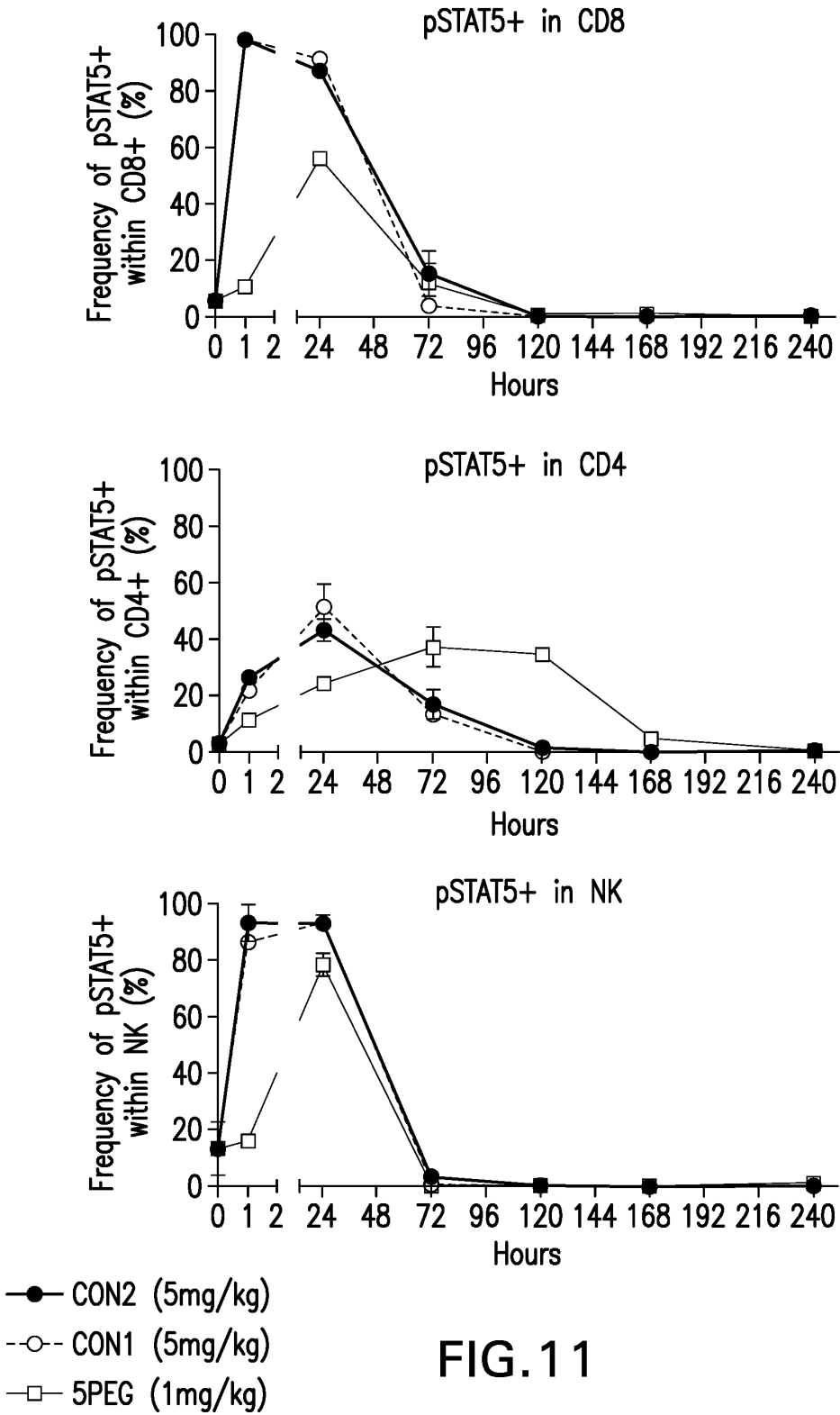


FIG.11

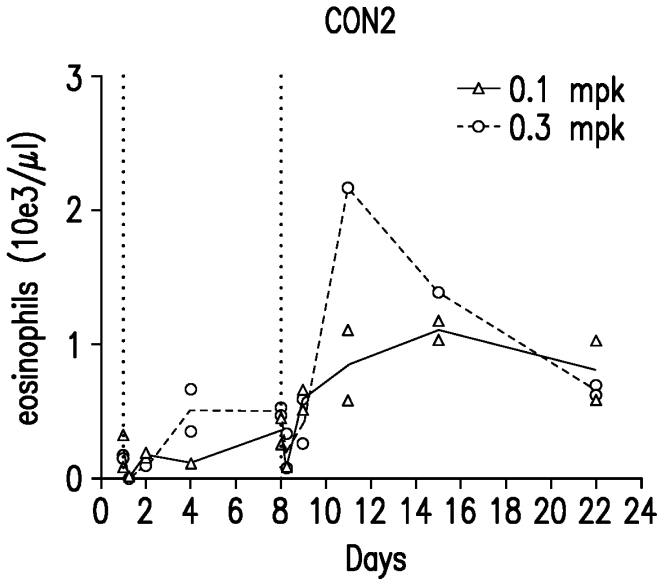


FIG.12A

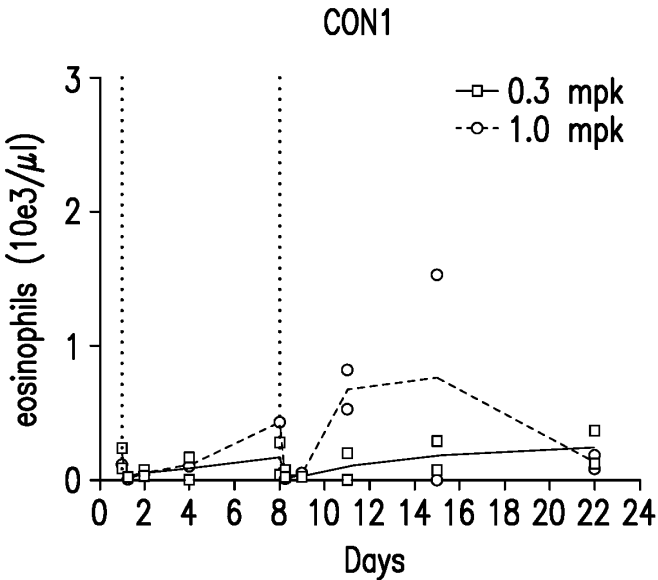


FIG.12B

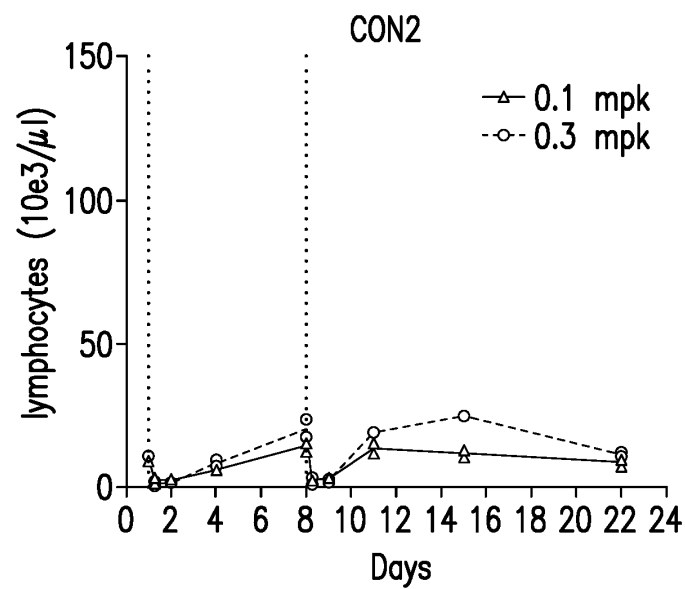


FIG.12C

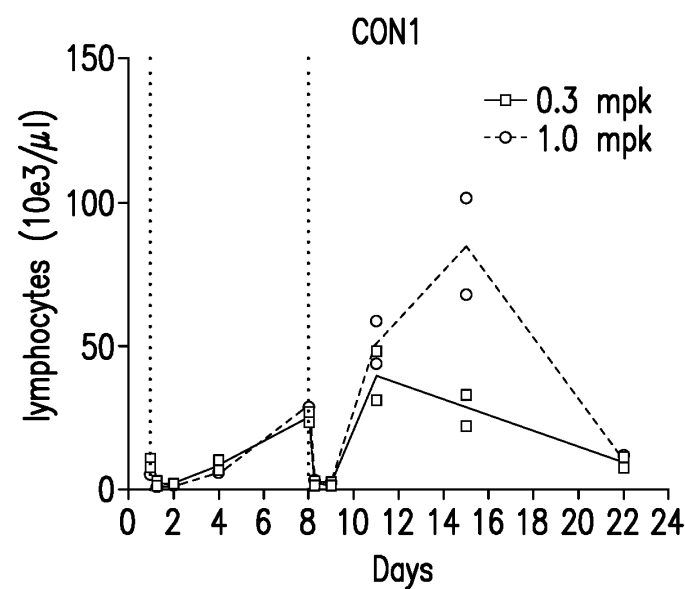


FIG.12D

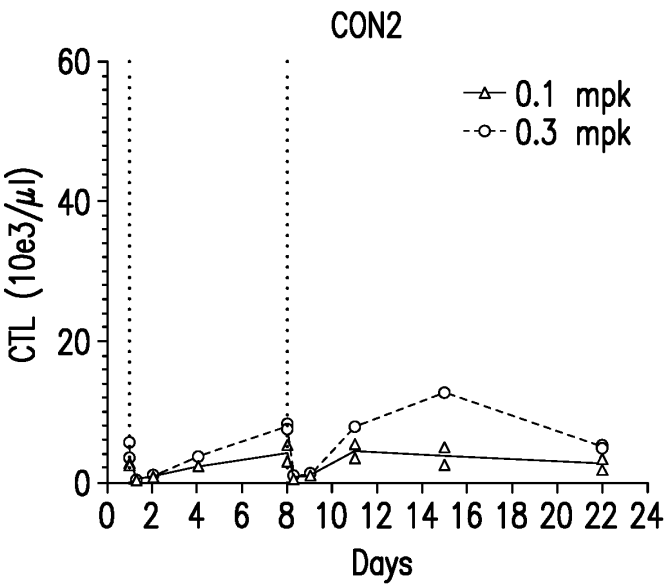


FIG.12E

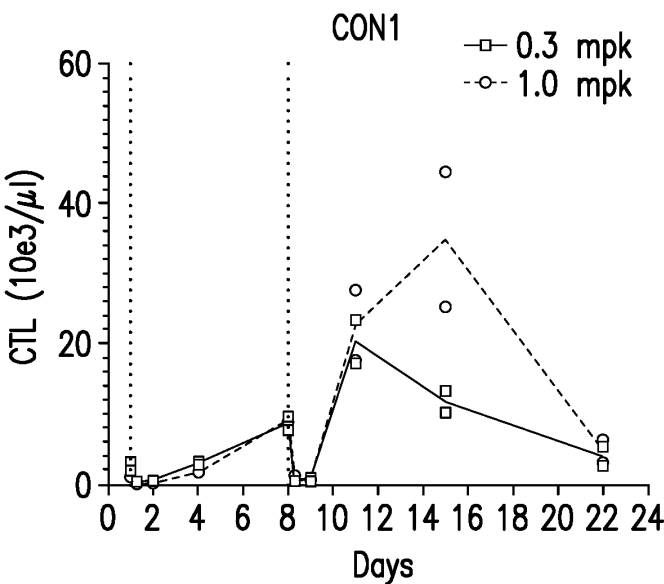


FIG.12F

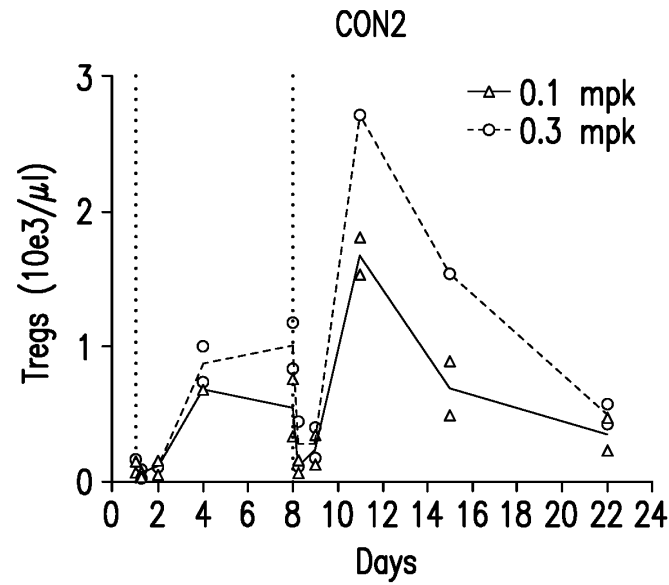


FIG.12G

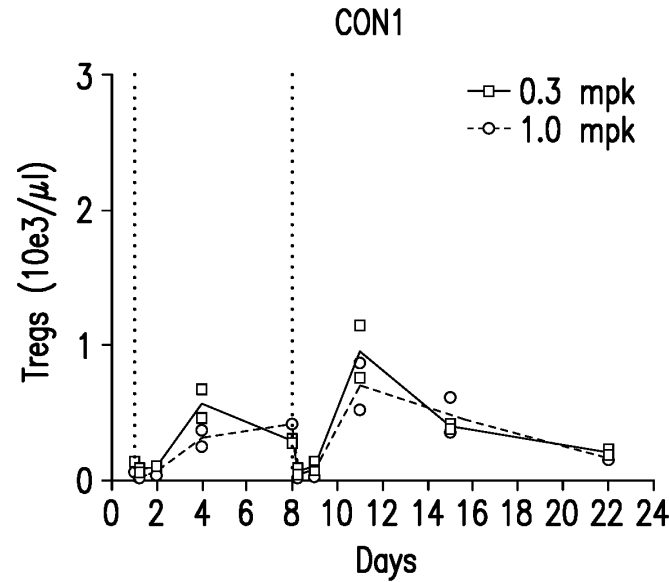


FIG.12H

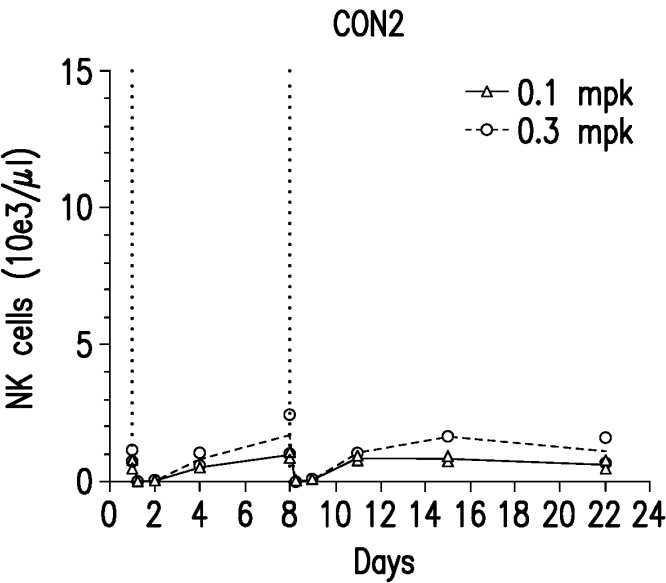


FIG.12I

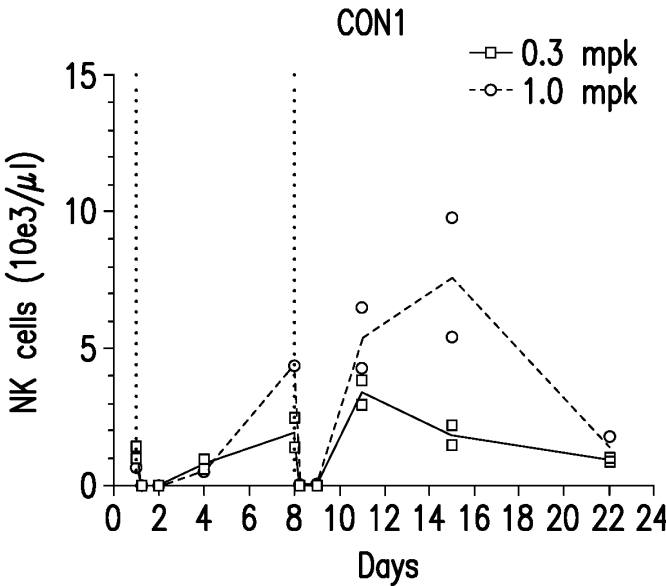


FIG.12J

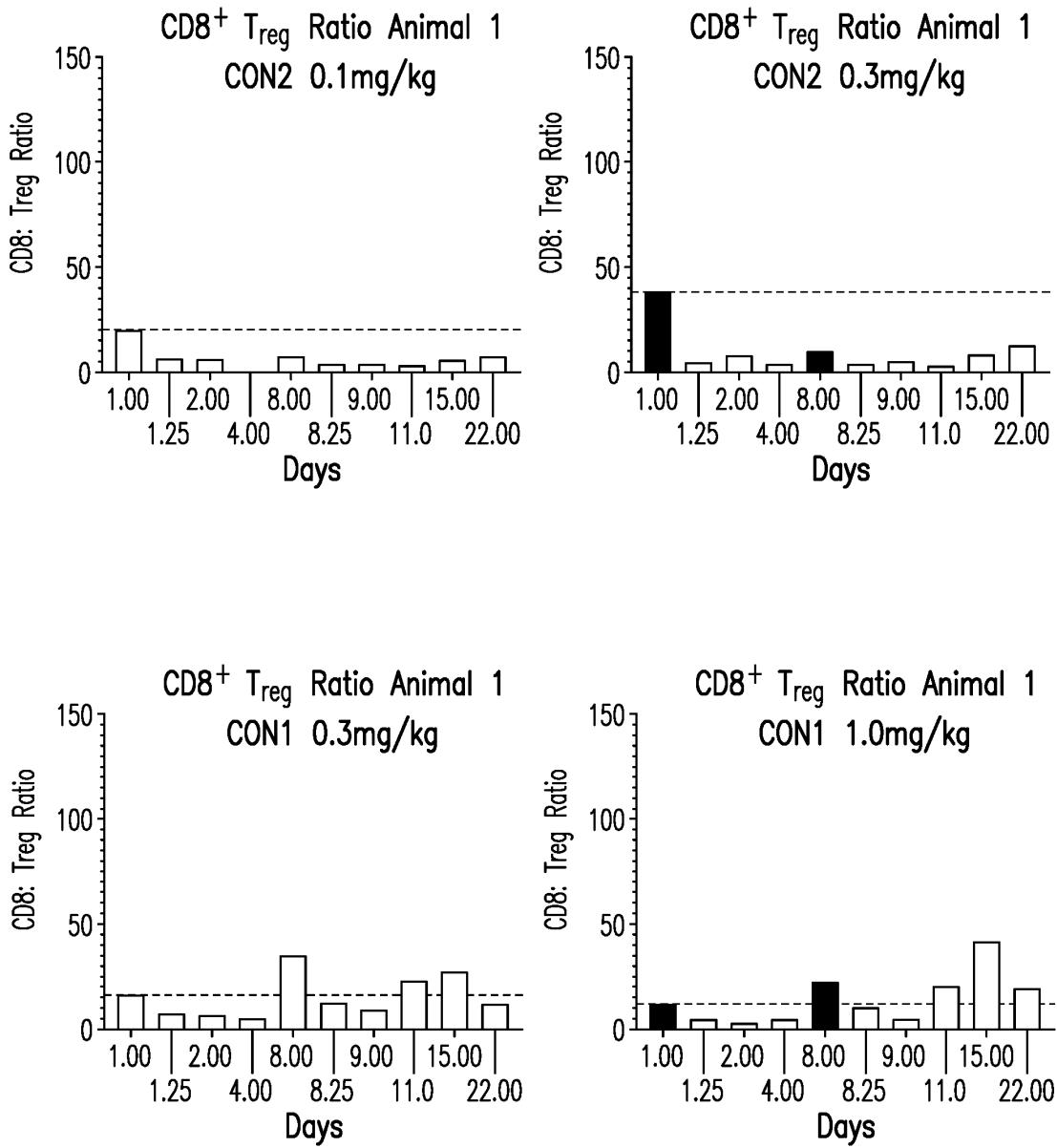


FIG.13A

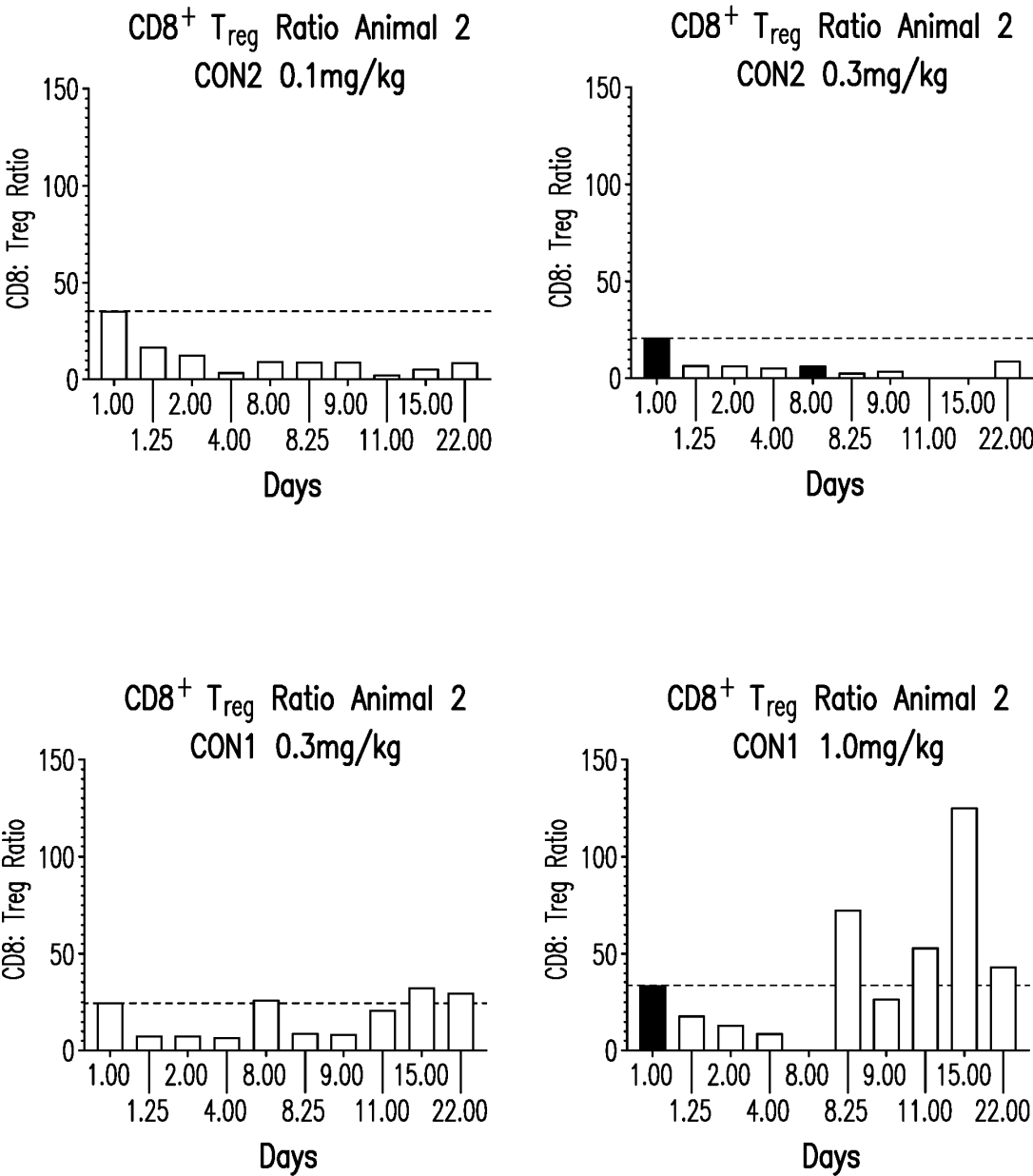


FIG.13B

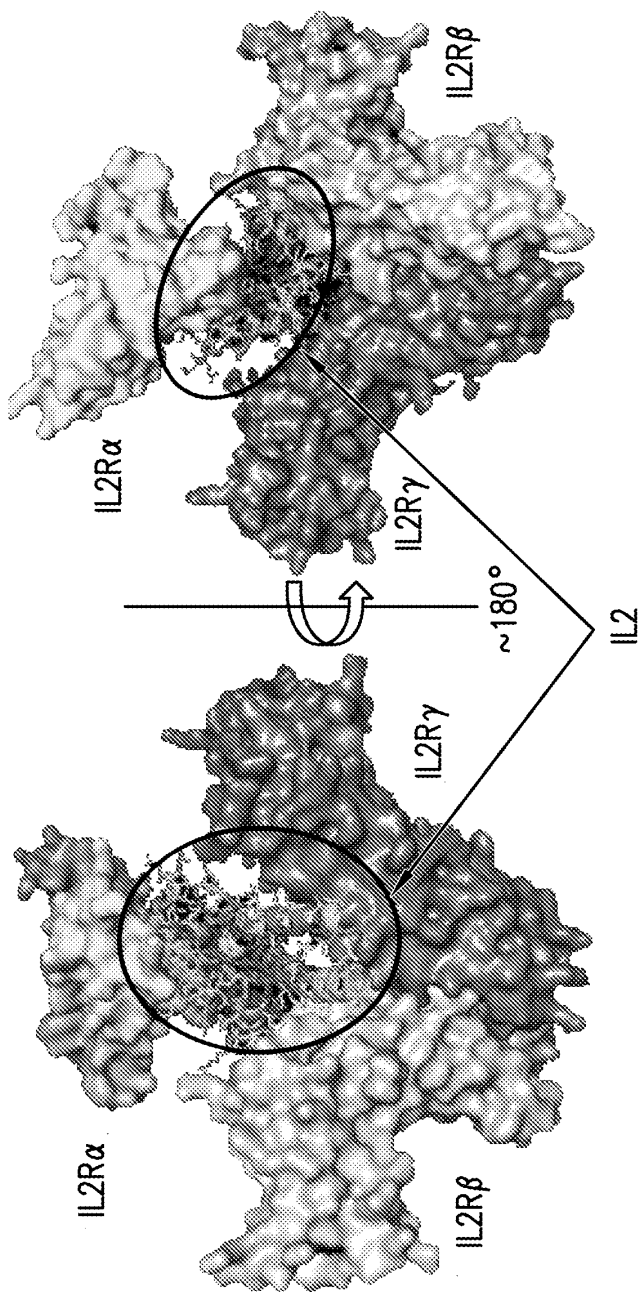
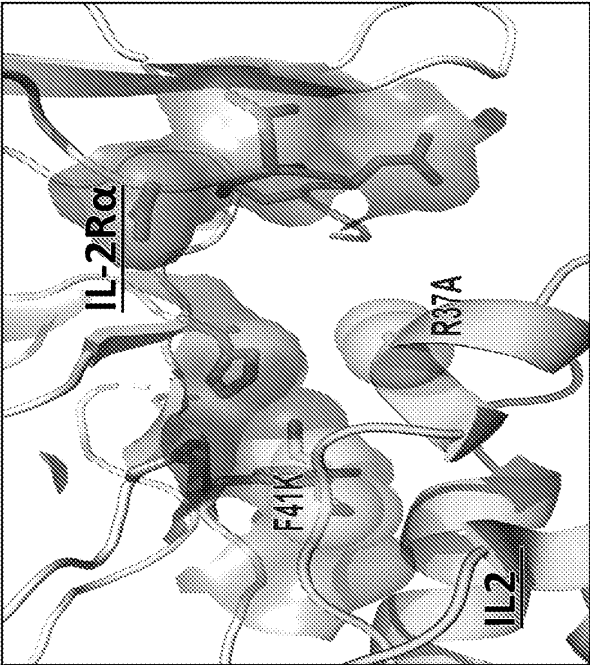


FIG.14A

Panel B – Mutant IL-2 R37A/F41K substitutions
at the IL-2R α interface



Panel A – Native IL-2 R37/F41
at the IL-2R α interface

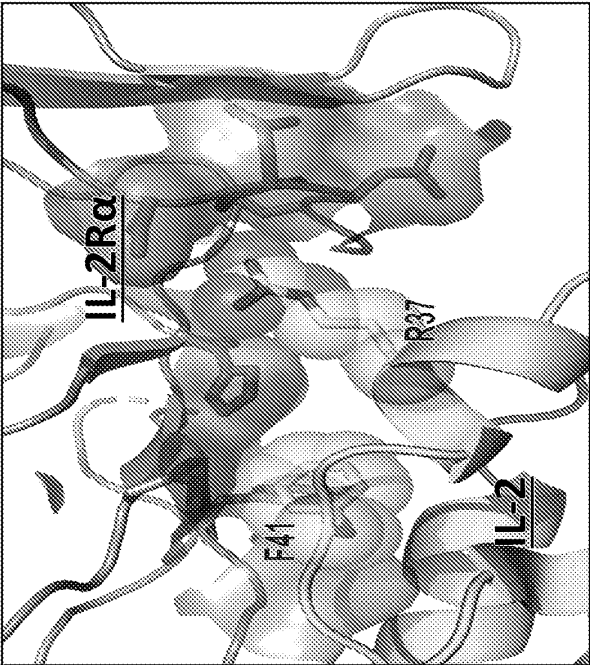


FIG.14B

Aldesleukin [numbering scheme A]

	1	2	3	4	5	6	7
123456789	0	123456789	0	123456789	0	123456789	0
123456789	0	123456789	0	123456789	0	123456789	0
PTSSSTKKTQL	QLEHLLLDL	QMIILNG	INNYKNPKL	TRML	TFKFYMPKK	ATELKHLC	LEELKPLEEVLNLA
8	9	0	1	1	1	1	1
3456789	0	123456789	0	123456789	0	123456789	0
3456789	0	123456789	0	123456789	0	123456789	0
QSKNFHLRPRDL	ISNINVIVLEL	KGSETTFMCE	YADETAT	IVEFLNRW	ITFSQSI	IISTLT	

(SEQ ID NO: 2)

FIG. 15B

Aldesleukin [numbering scheme B]

1	2	3	4	5	6	7
234567890	1234567890	1234567890	1234567890	1234567890	1234567890	1234567890
PTSSSTKKTQLQLEHLLDLQMI	LNGINNYKNPKL	TRMLTFKFYMPKKAT	ELKHLQC	LEEEELKPLEE	VNL	LA

8	9	0	1	1	1	1
4567890	1234567890	1234567890	1234567890	1234567890	1234567890	1234567890
QSKNFHLRPRDL	ISNINVIVLELKGSETTFMCE	YADETAT	IVEFLNRWI	TFSQSI	I	STLT

(SEQ ID NO: 2)

FIG.15C

X is pAMF conjugated to PEG1
Amino acid substitutions are in bold and underlined

FIG. 15D

Tumor volume
Efficacy of Aldesleukin
+/- mDX400 in CT26

□ Iso + Vehicle
○ mDX400 (10) + Vehicle
--- Iso + Aldesleukin (1)
● mDX400 (10) + Aldesleukin (1)

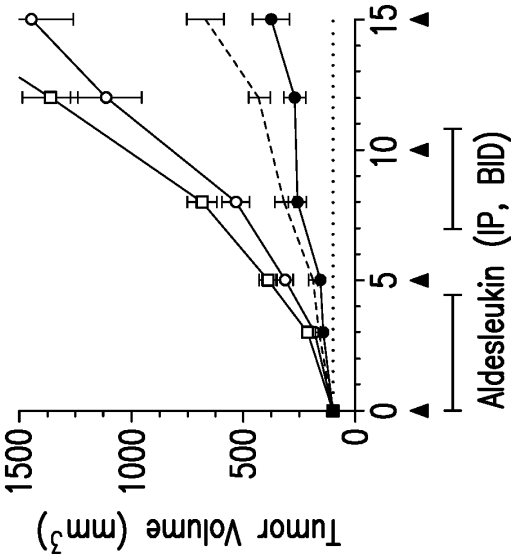
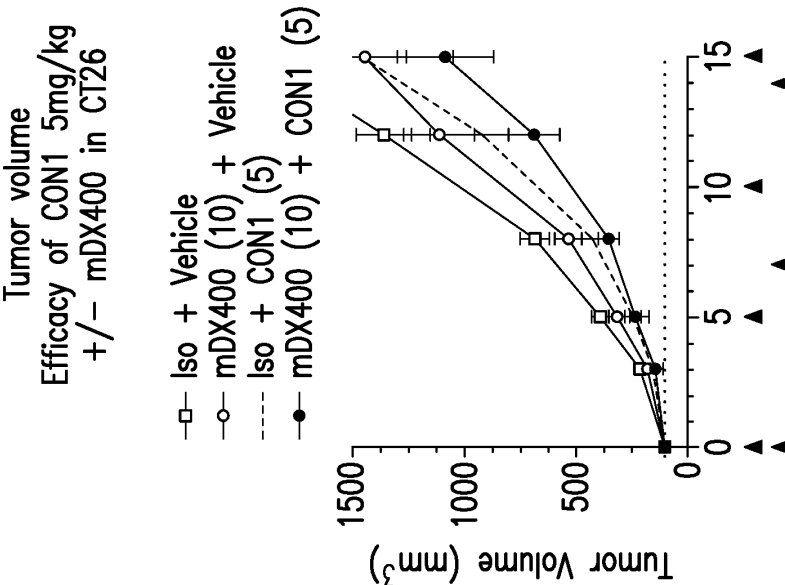


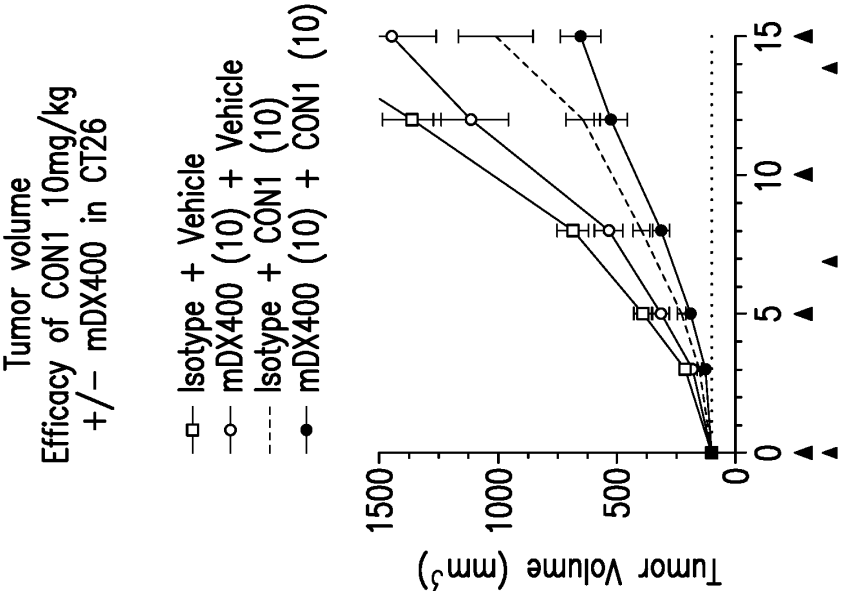
FIG.16A

Treatment	Dose (mg/kg)	Day 15 TGI%	CR/PR
Isotype (Iso) + Vehicle			
Mdx400 + Vehicle		25	
Iso + Aldesleukin	1	68	1CR
mDX400 + Aldesleukin	1	85	1CR



Treatment	Dose (mg/kg)	Day 15 TGI%	CR/PR
Isotype (Iso) + Vehicle			
Mdx400 + Vehicle		25	
Iso + CON1	5	24	
mDX400 + CON1	5	45	

FIG.16B



Treatment	Dose (mg/kg)	Day 15 TGI%	CR/PR
Isotype (Iso) + Vehicle			
Mdx400 + Vehicle		25	
Iso + CON1	10	49	
mDX400 + CON1	10	69	1PR

FIG.16C

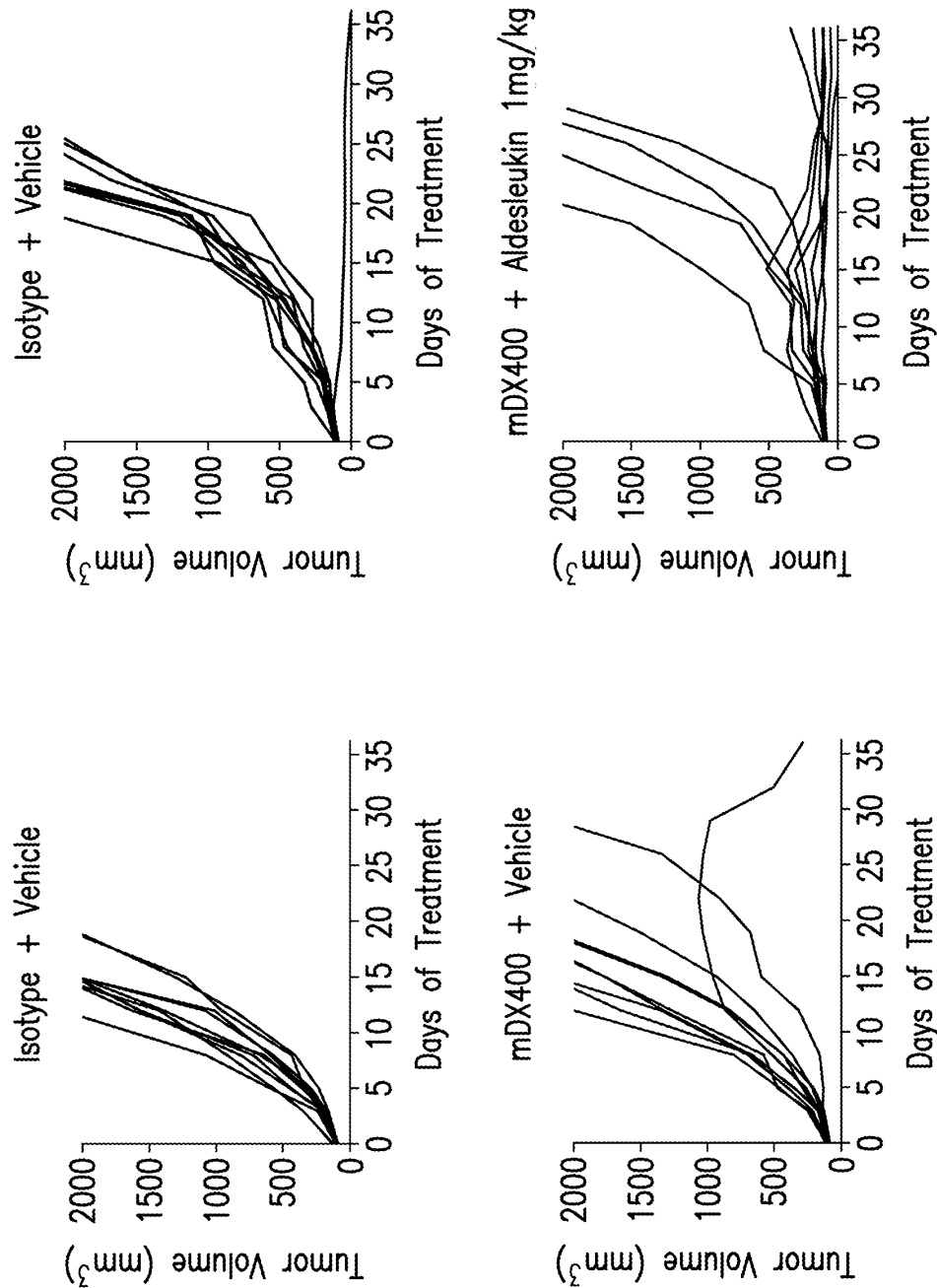


FIG.17A

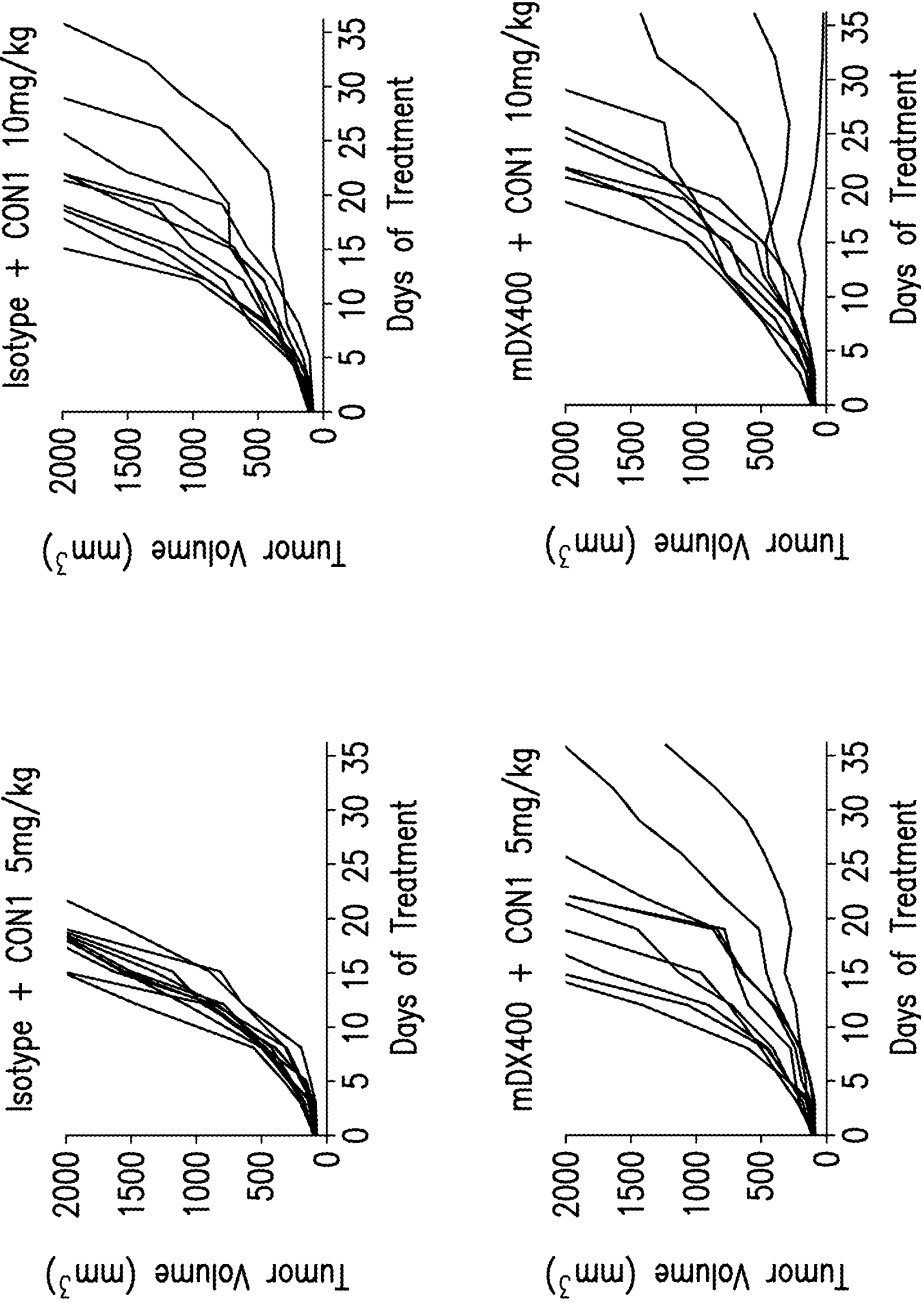


FIG.17B

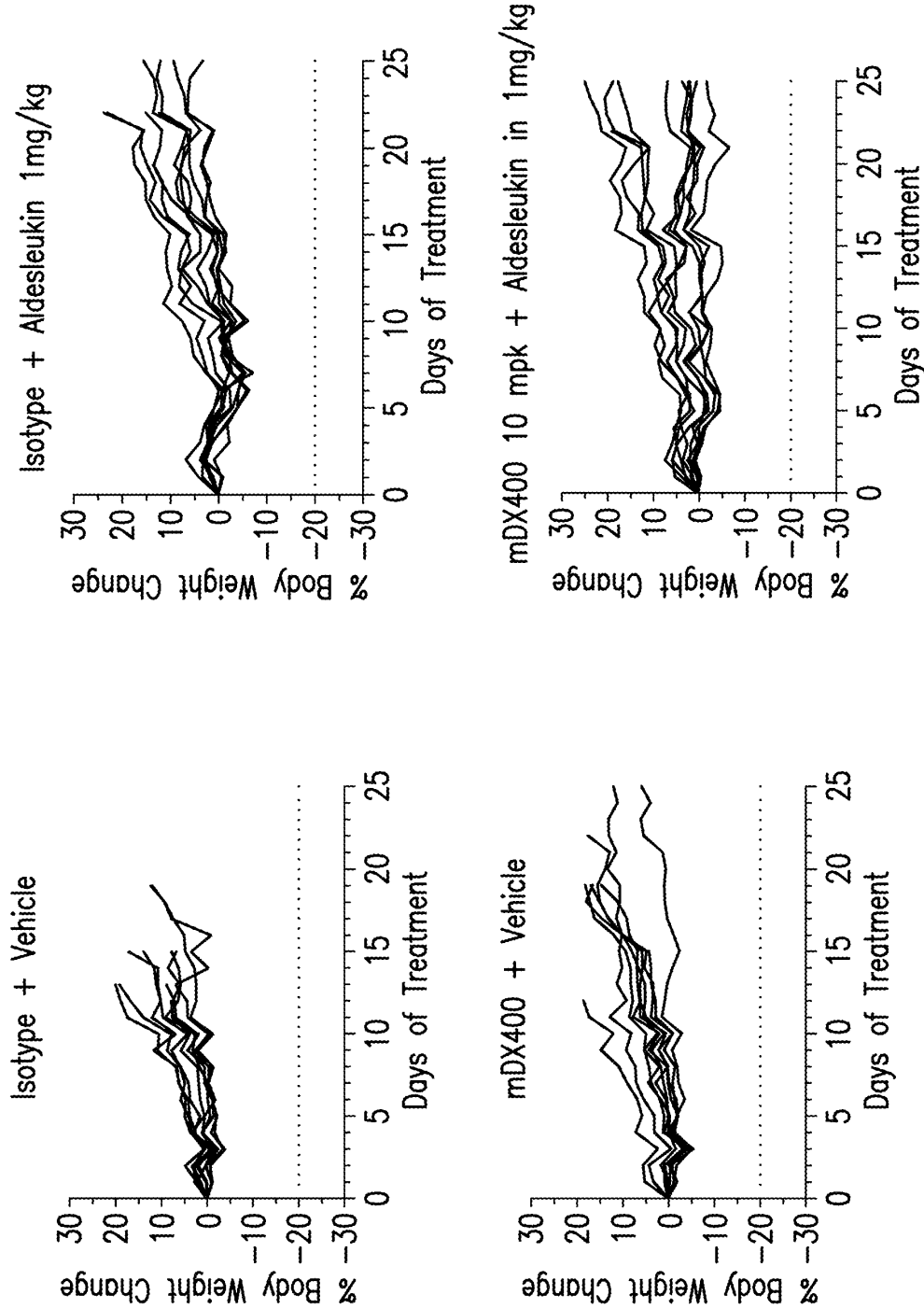


FIG.18A

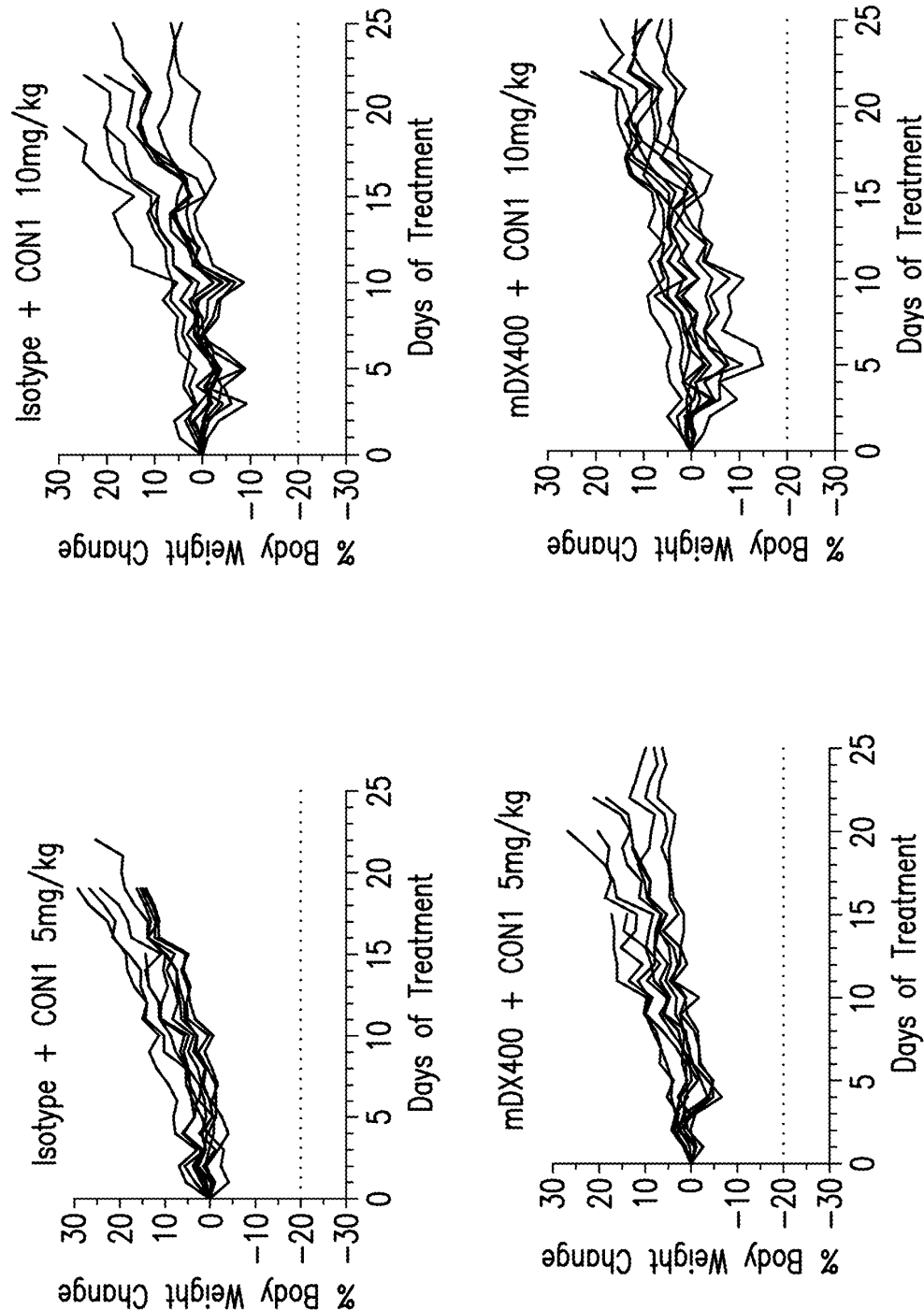


FIG.18B