

FIG. 1B

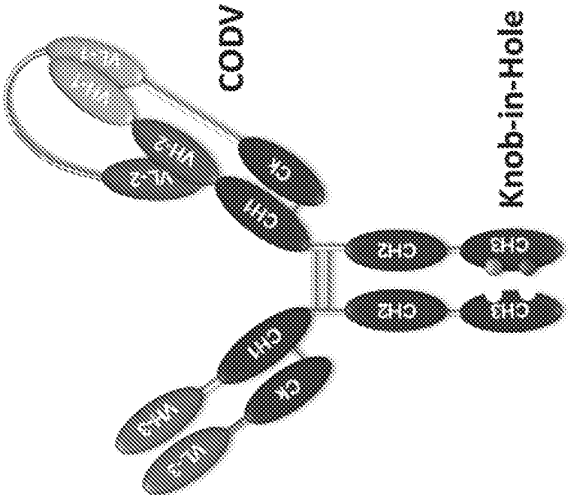


FIG. 1A

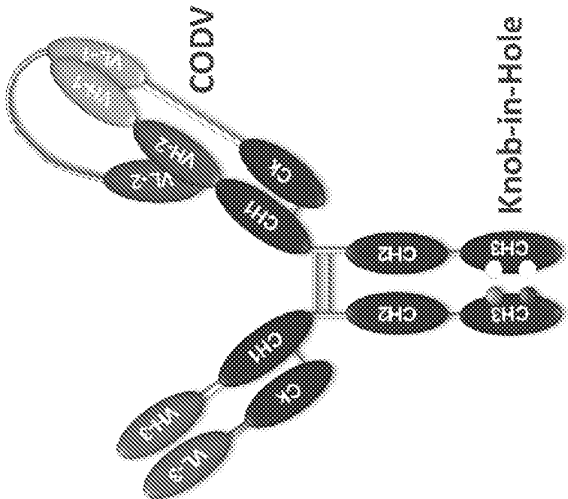


FIG. 1C

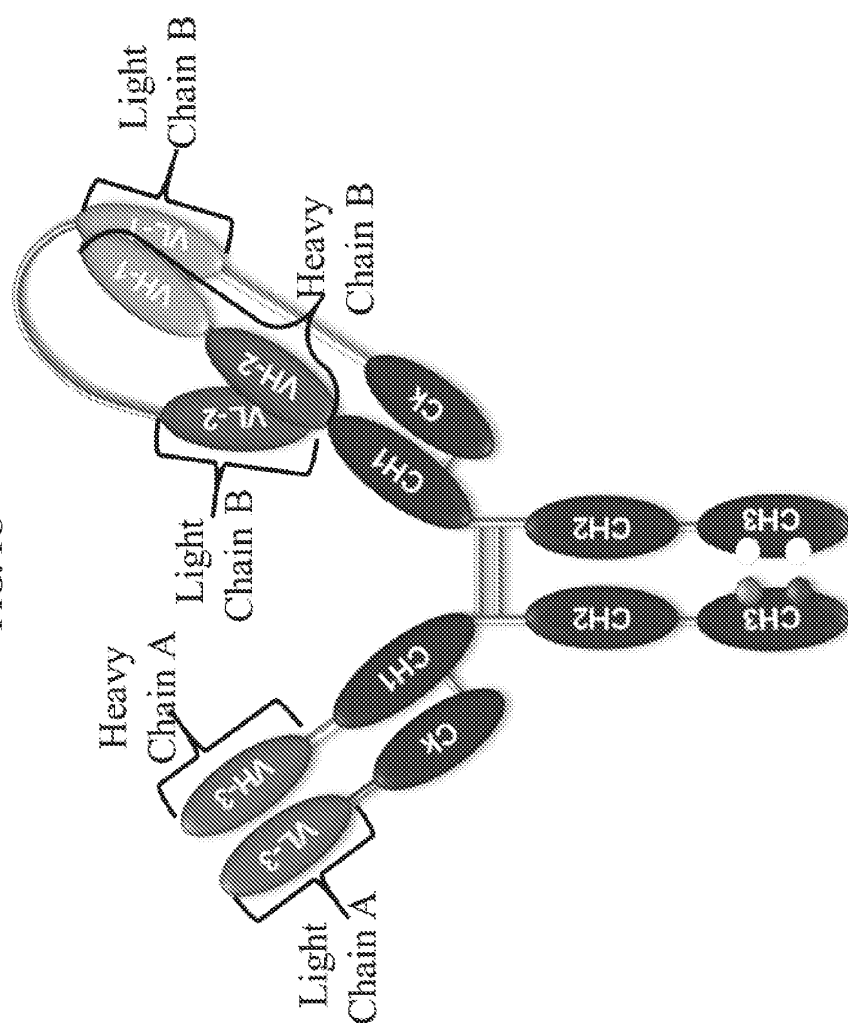
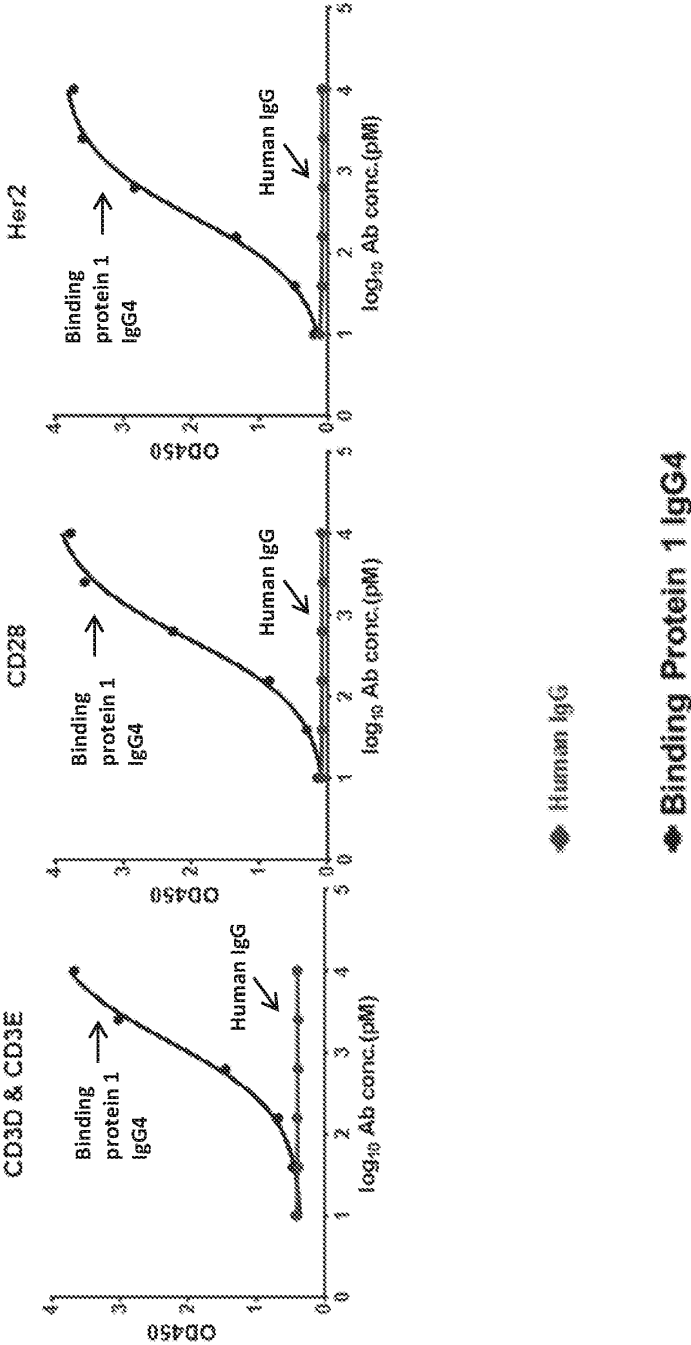
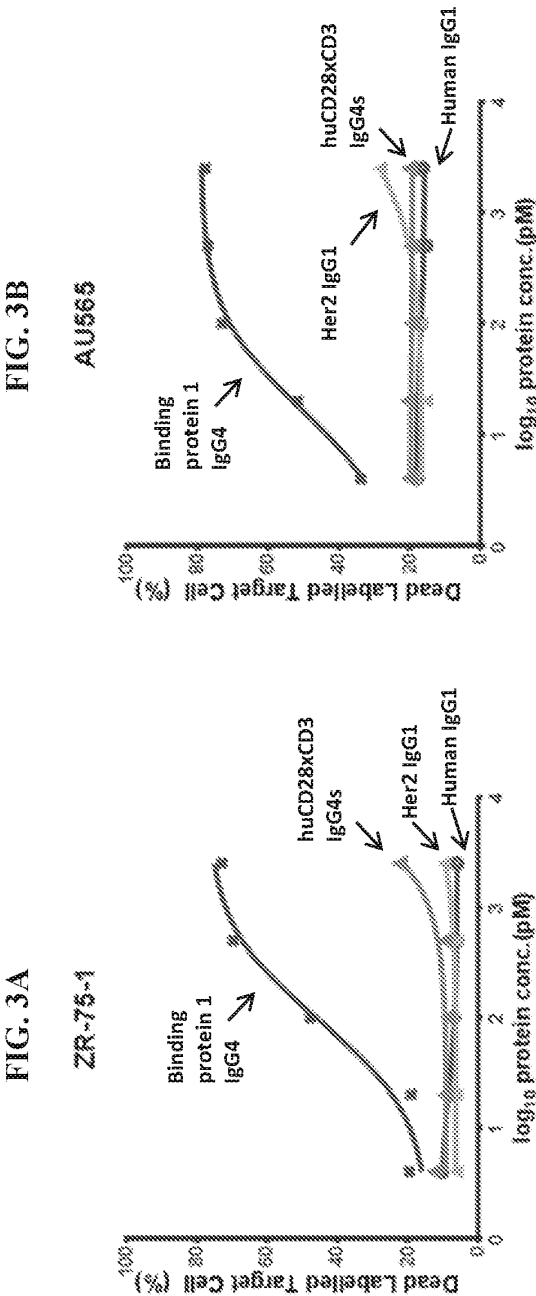


FIG. 2





- huCD28 x CD3 IgG4s
- Binding Protein 1 IgG4
- Her2 IgG1
- human IgG1

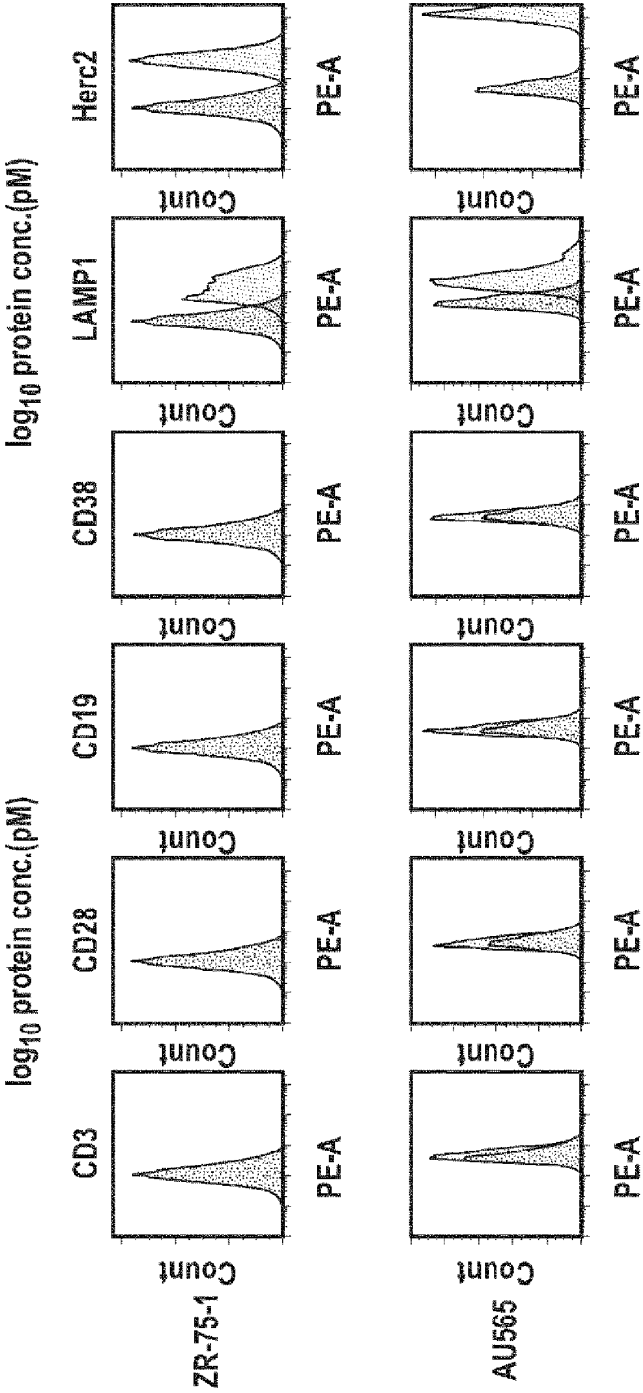
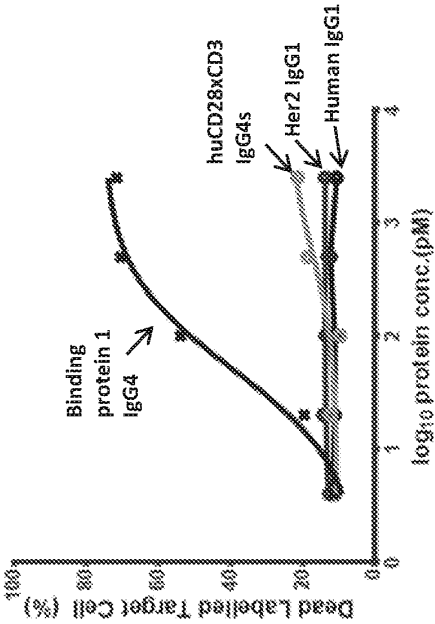
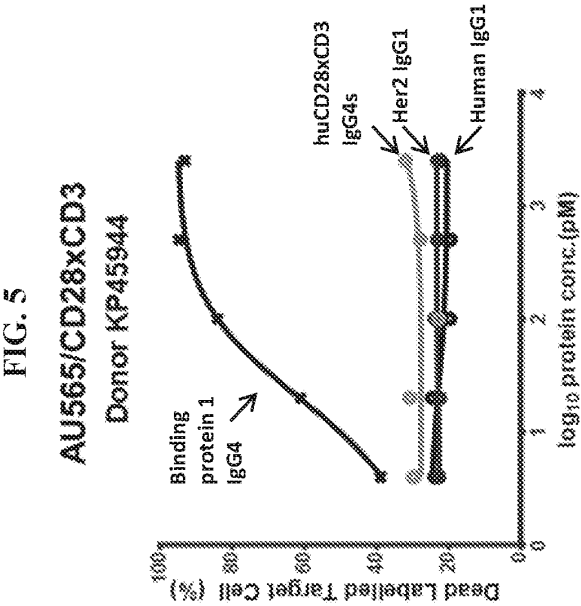


FIG. 3C

FIG. 4
ZR-75-1/CD28xCD3
Donor KP45926



- huCD28 x CD3 IgG4s
- Binding Protein 1 IgG4
- Her2 IgG1
- human IgG1

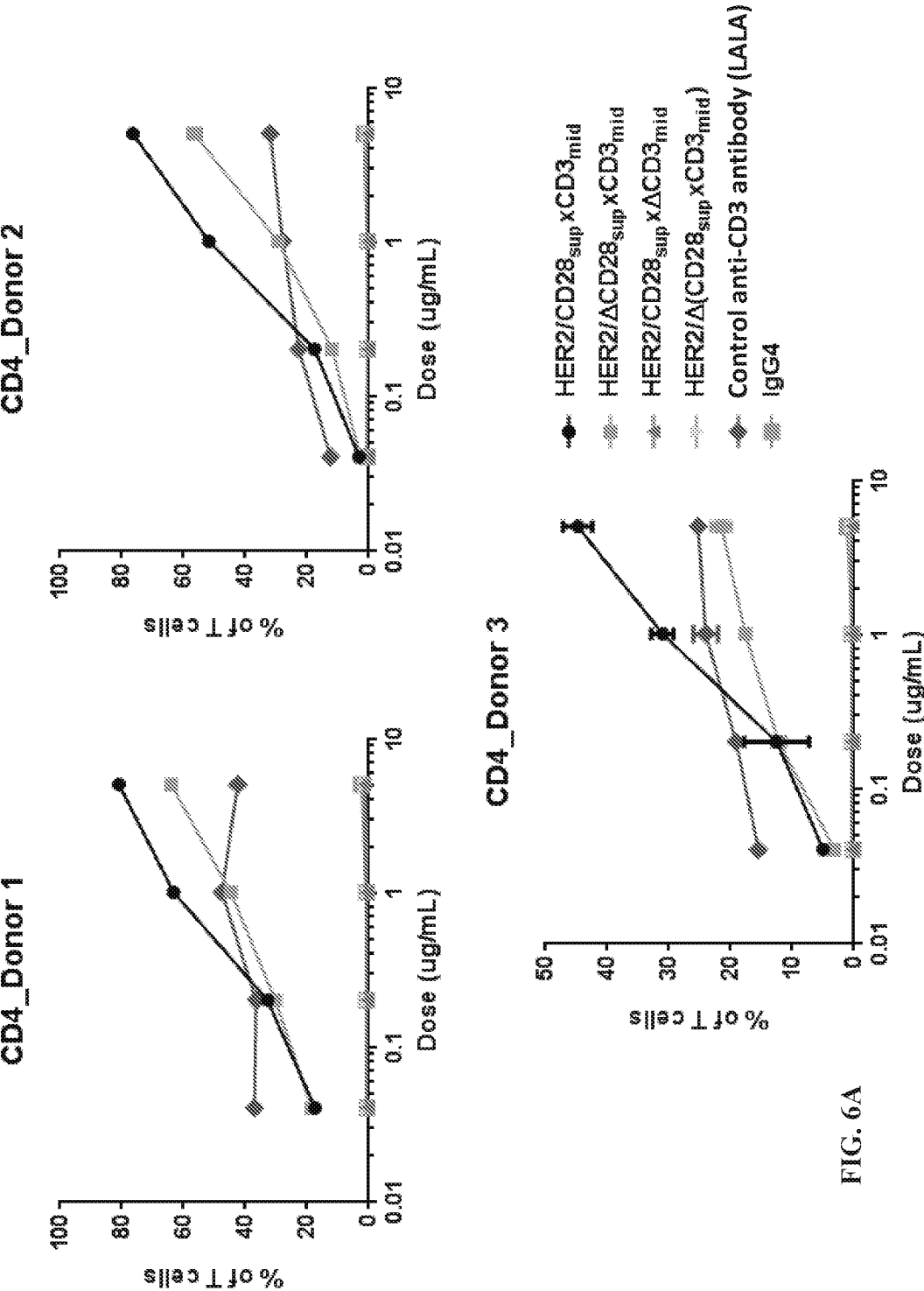


FIG. 6A

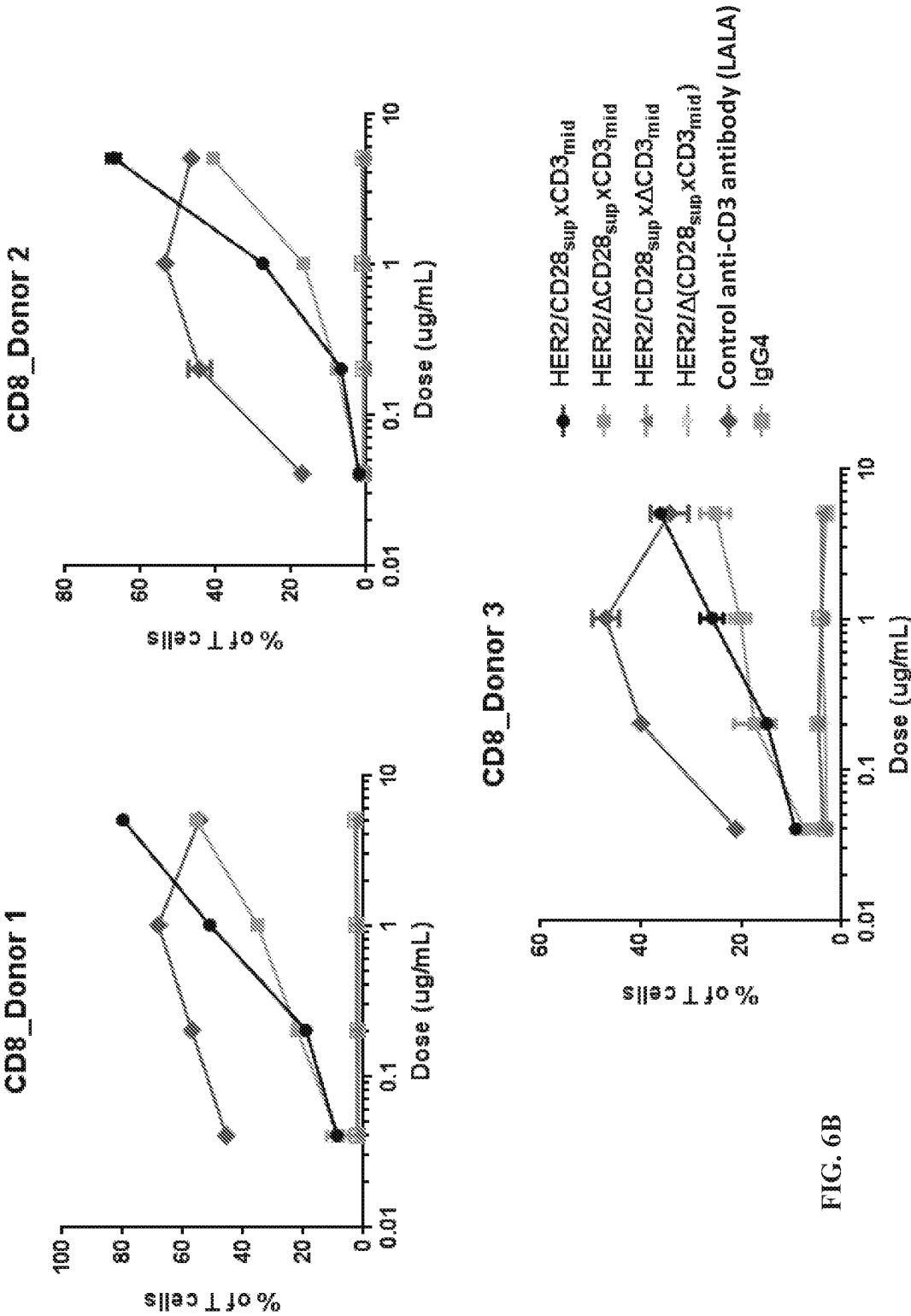


FIG. 6B

FIG. 7B

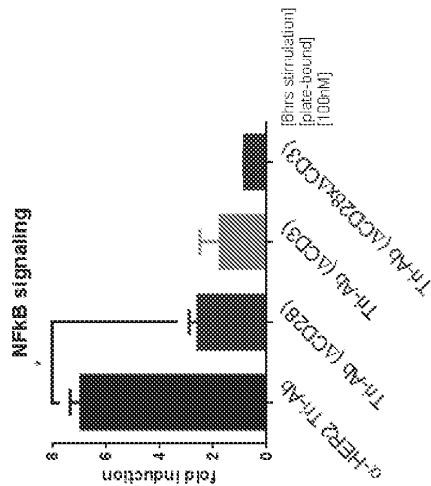


FIG. 7A

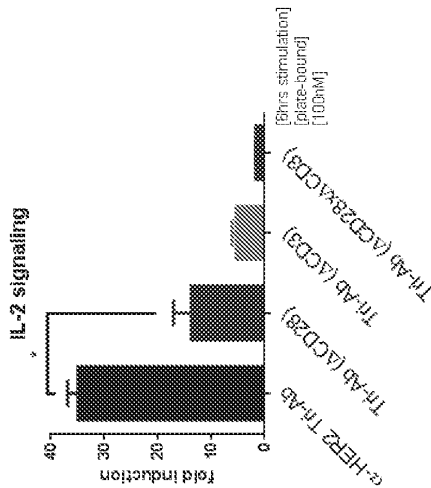


FIG. 7C

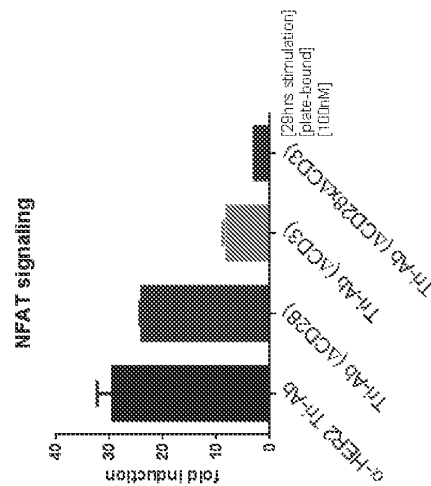
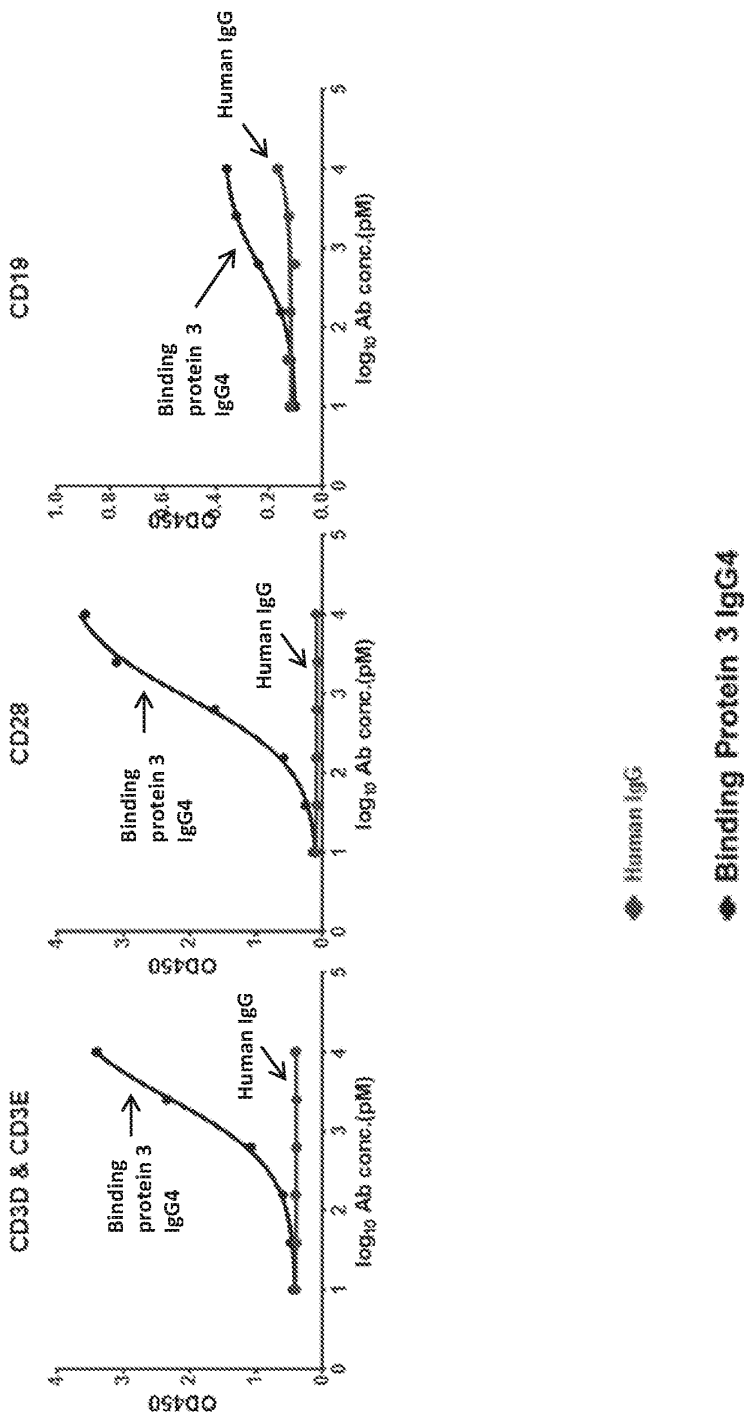


FIG. 8



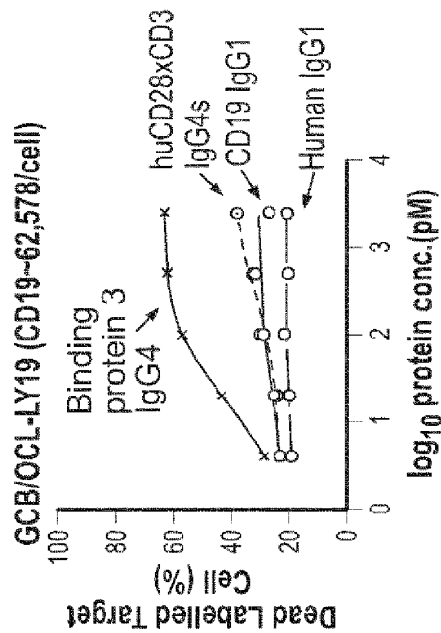


FIG. 9A

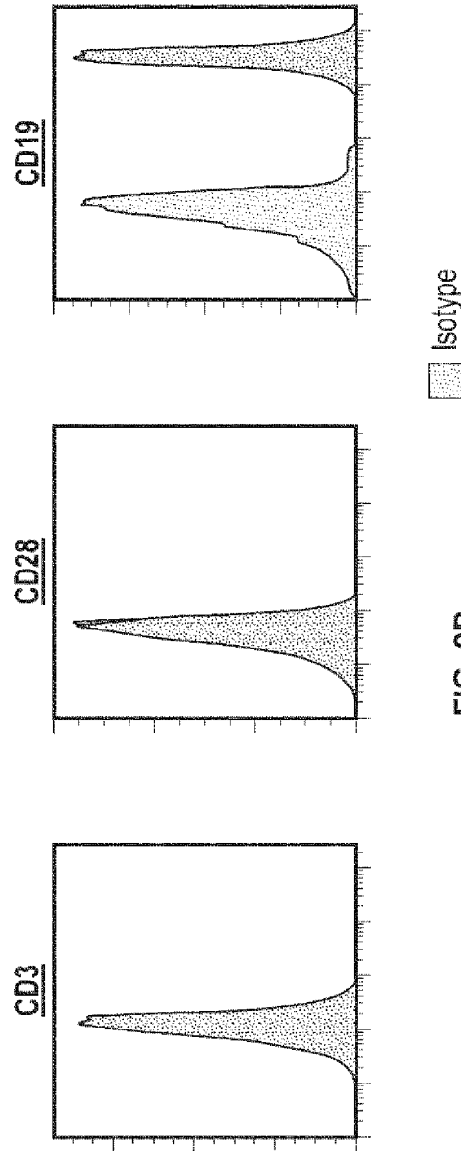


FIG. 9B

FIG. 9C

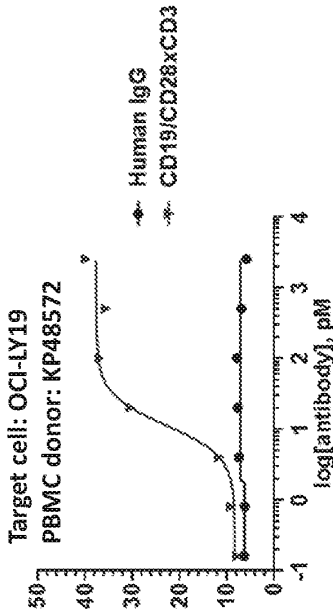


FIG. 9D

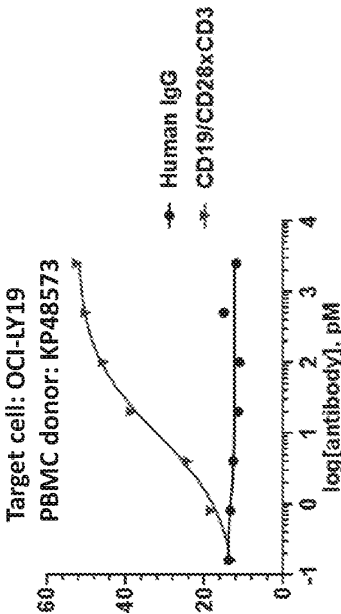


FIG. 9E

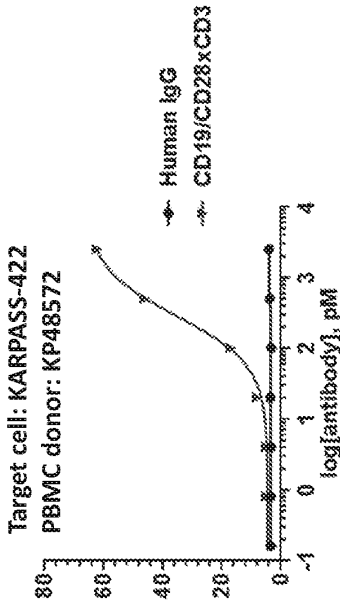


FIG. 9F

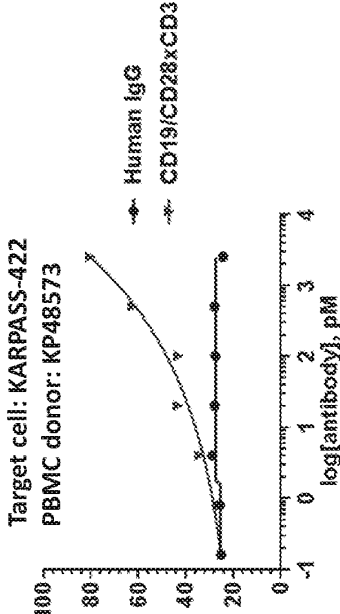


FIG. 9G

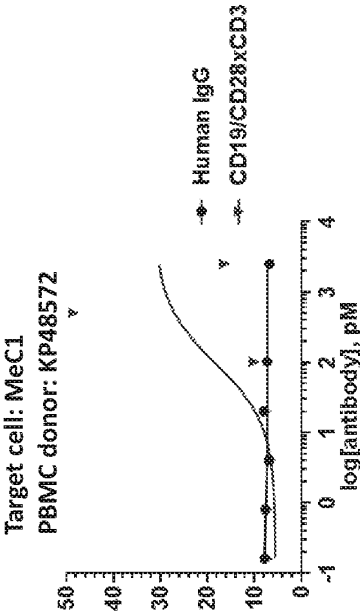


FIG. 9H

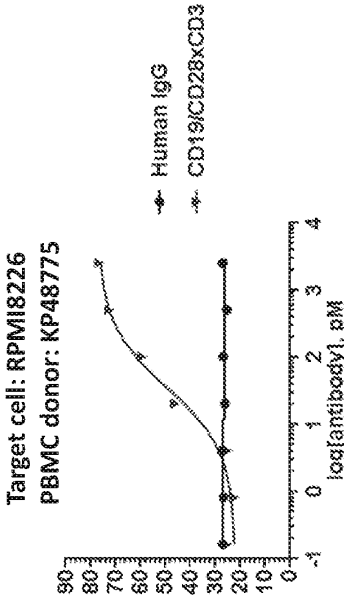


FIG. 9I

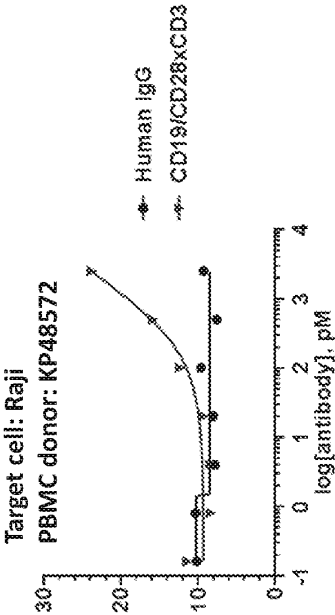


FIG. 9J

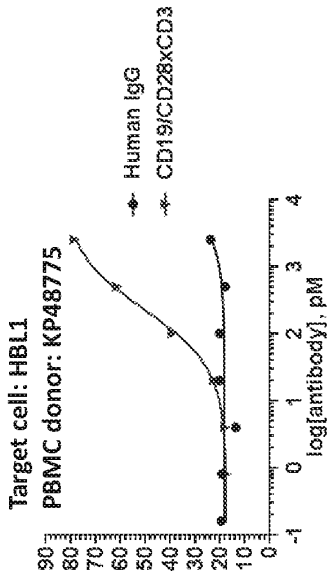


FIG. 9L

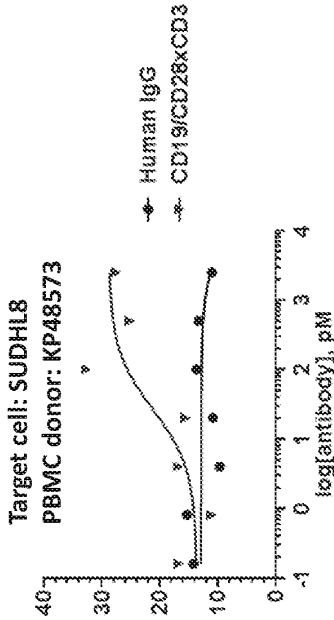


FIG. 9N

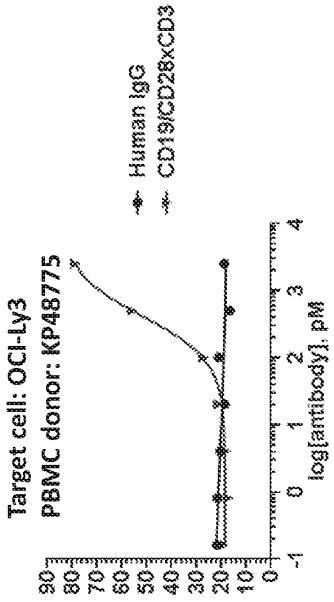


FIG. 9K

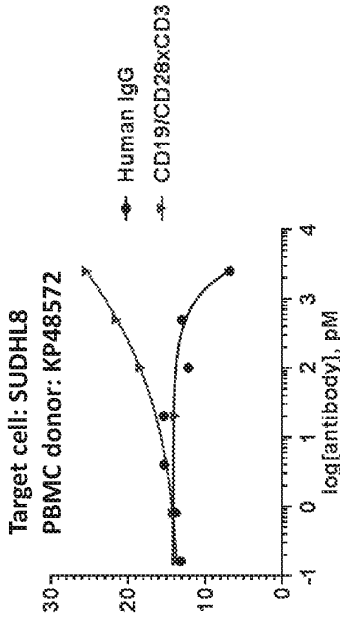


FIG. 9M

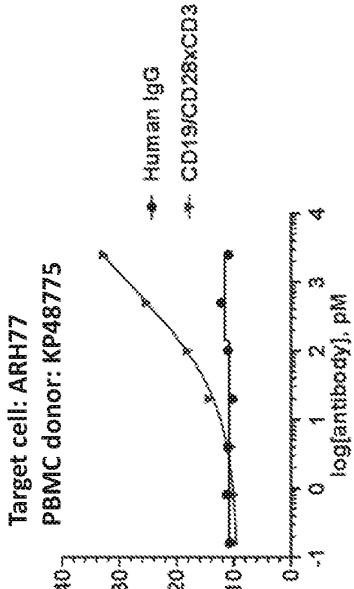


FIG. 10

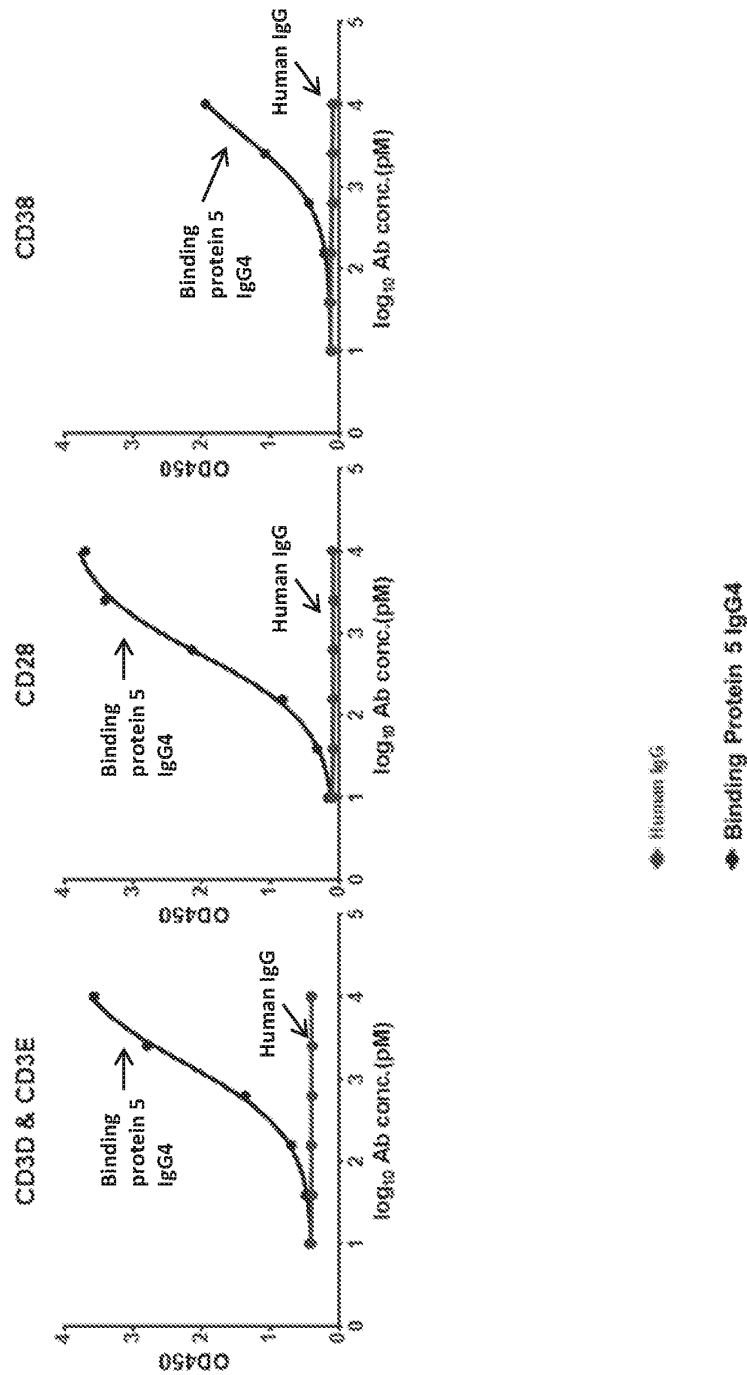


FIG. 11B

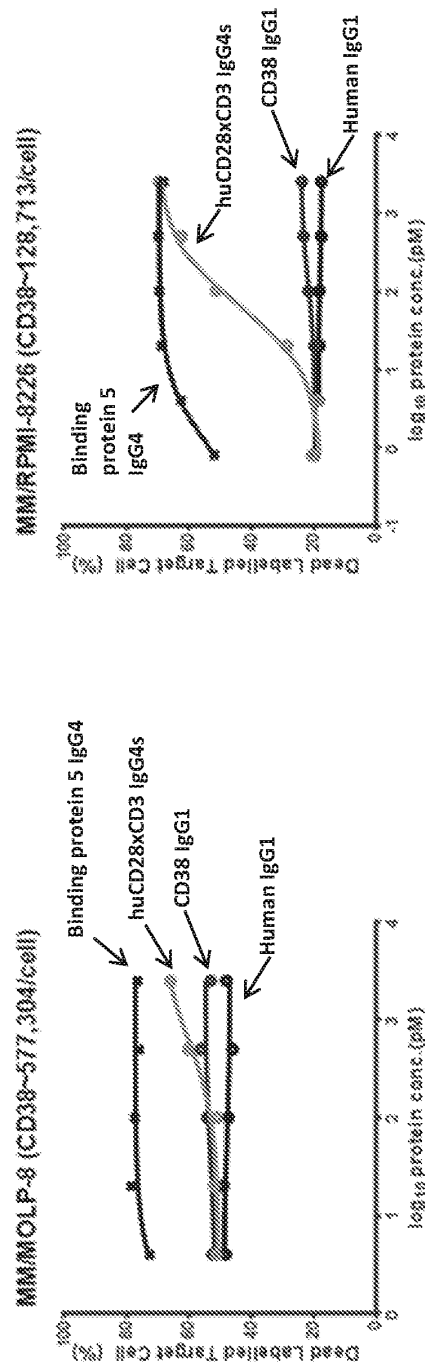


FIG. 11A

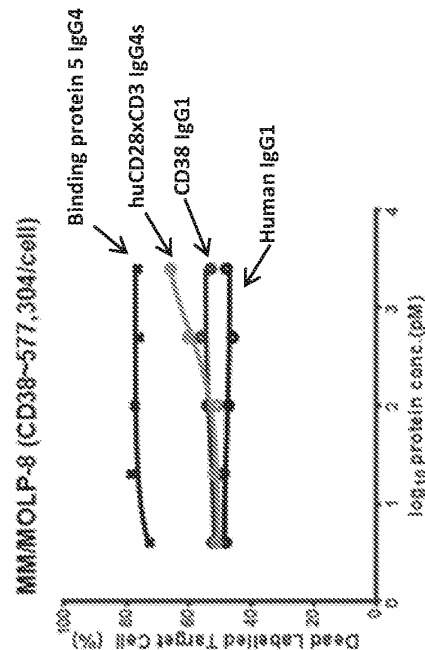
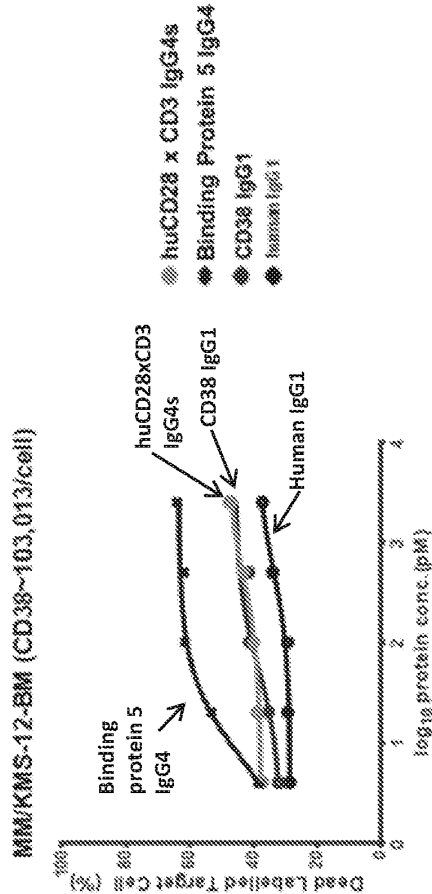


FIG. 11C



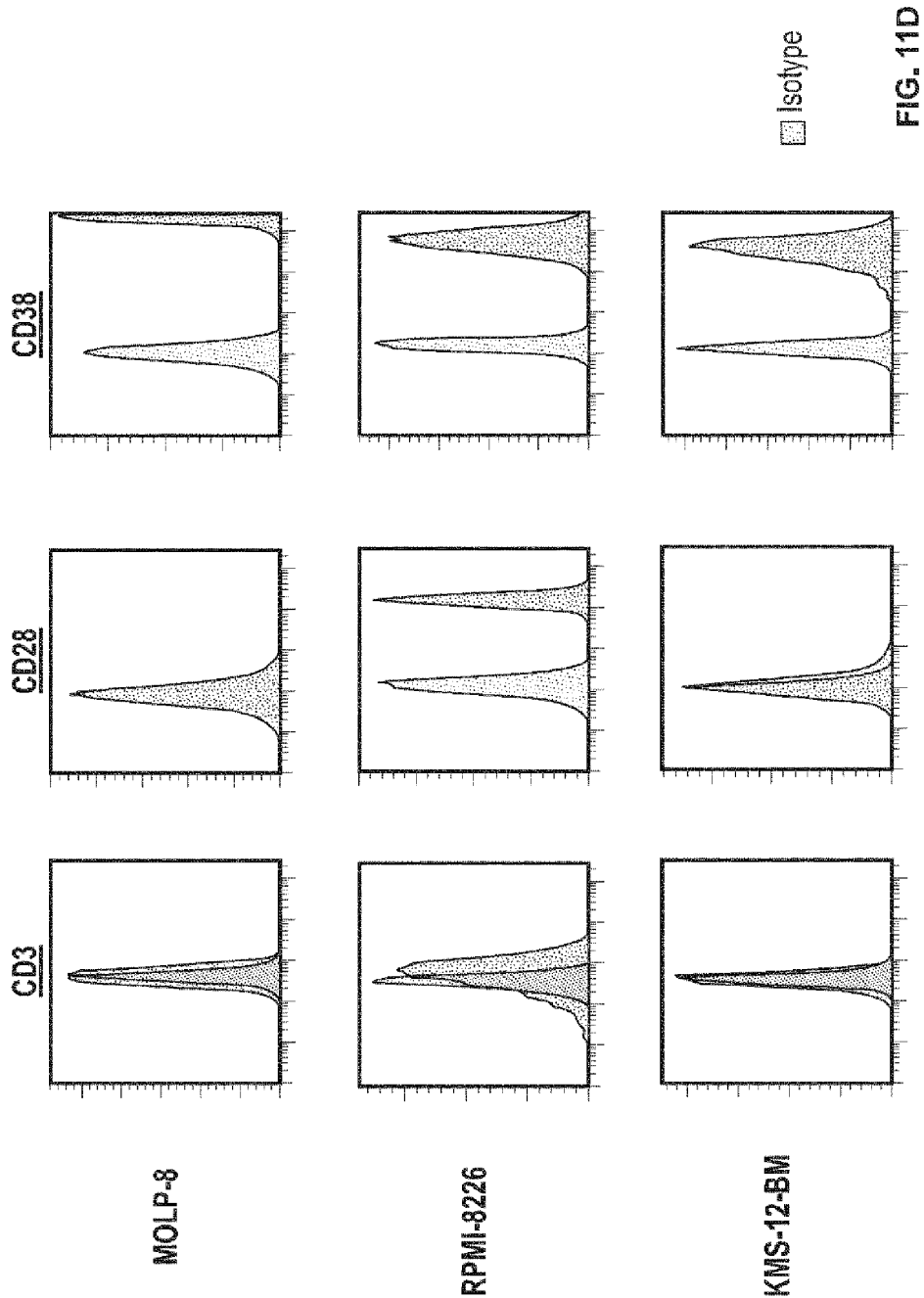


FIG. 11D

FIG. 12A

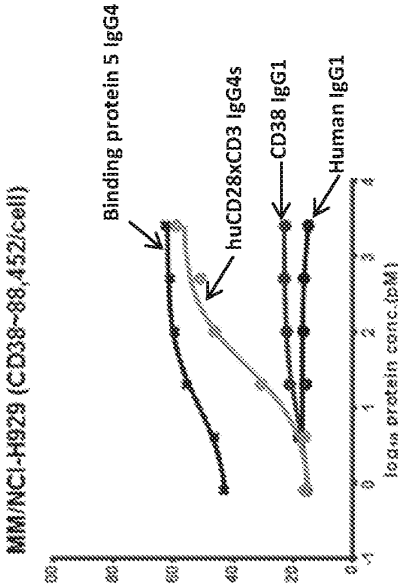


FIG. 12B

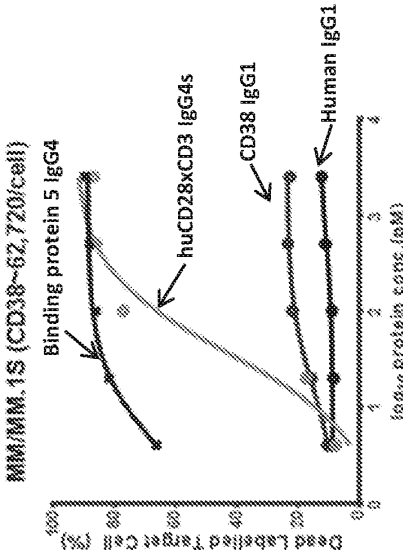
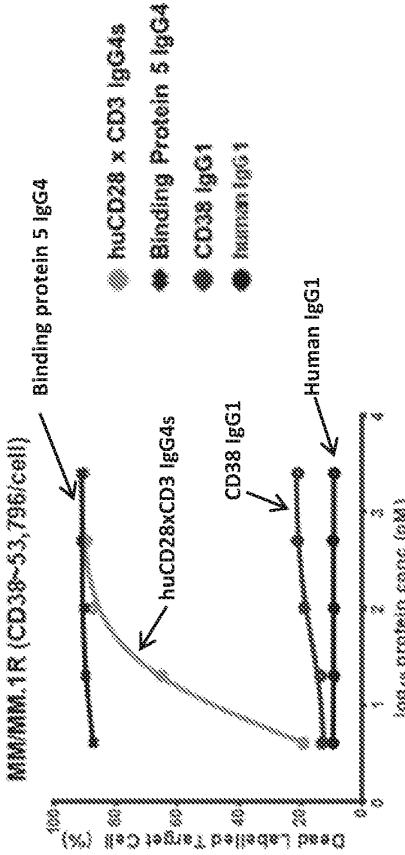


FIG. 12C



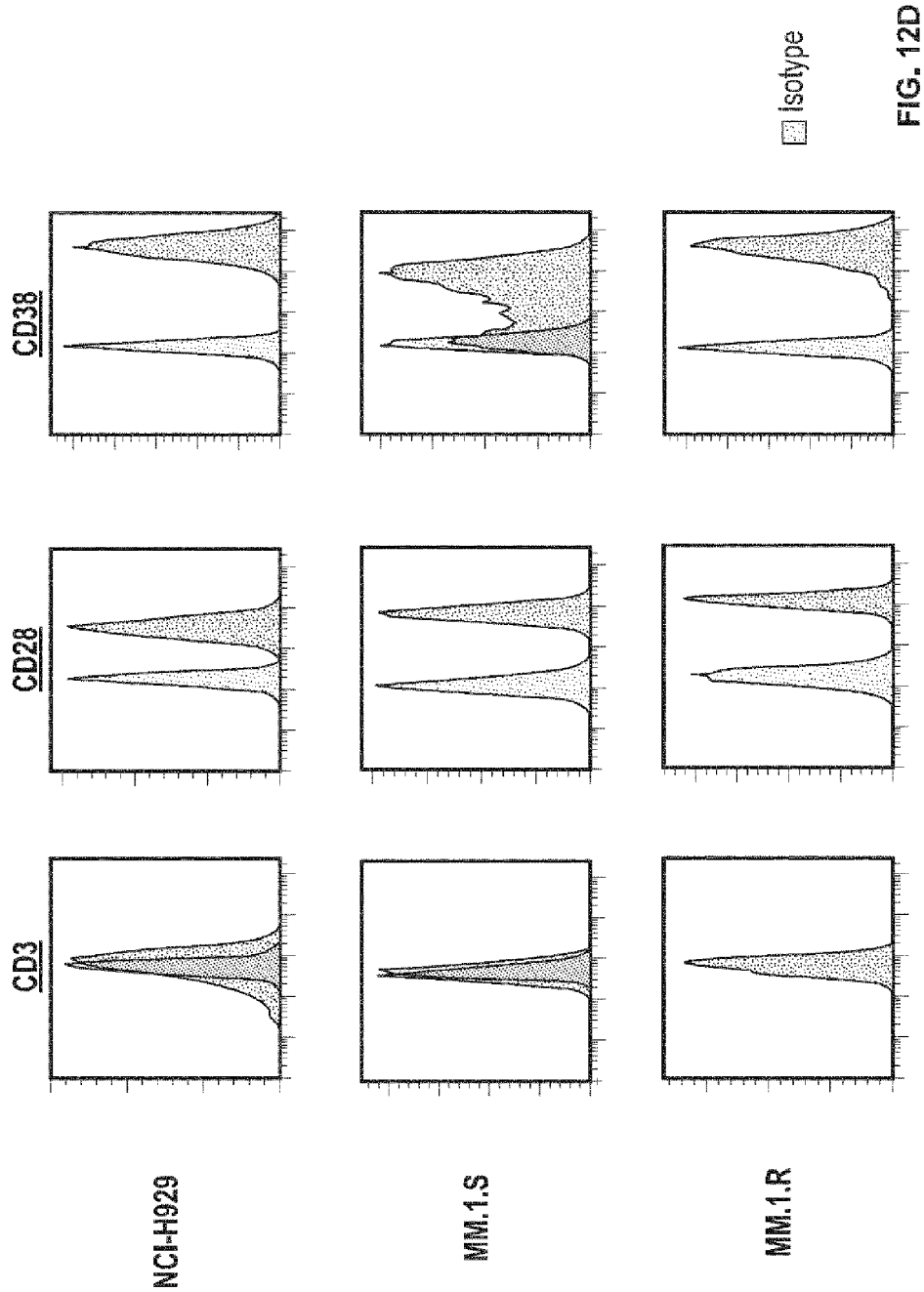


FIG. 13A

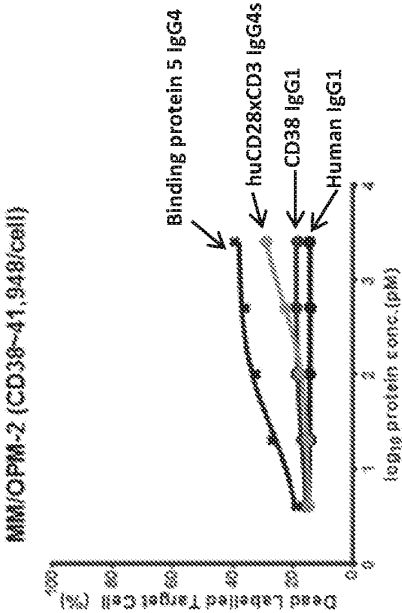


FIG. 13B

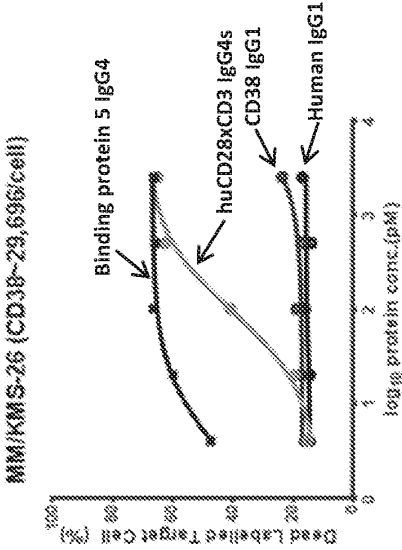
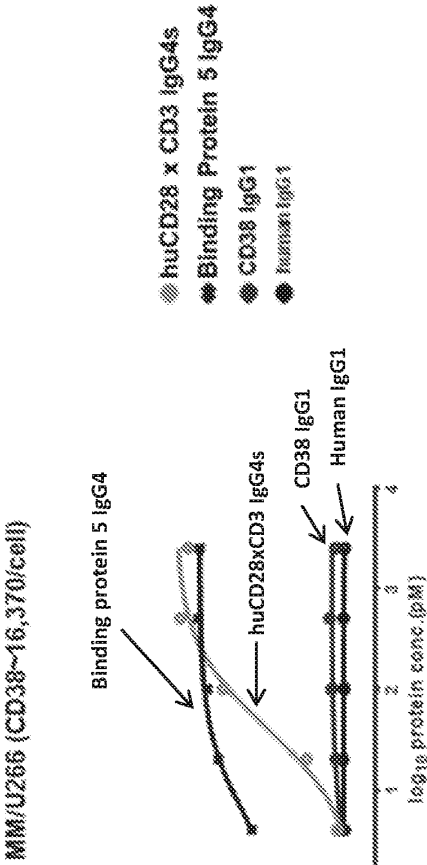


FIG. 13C



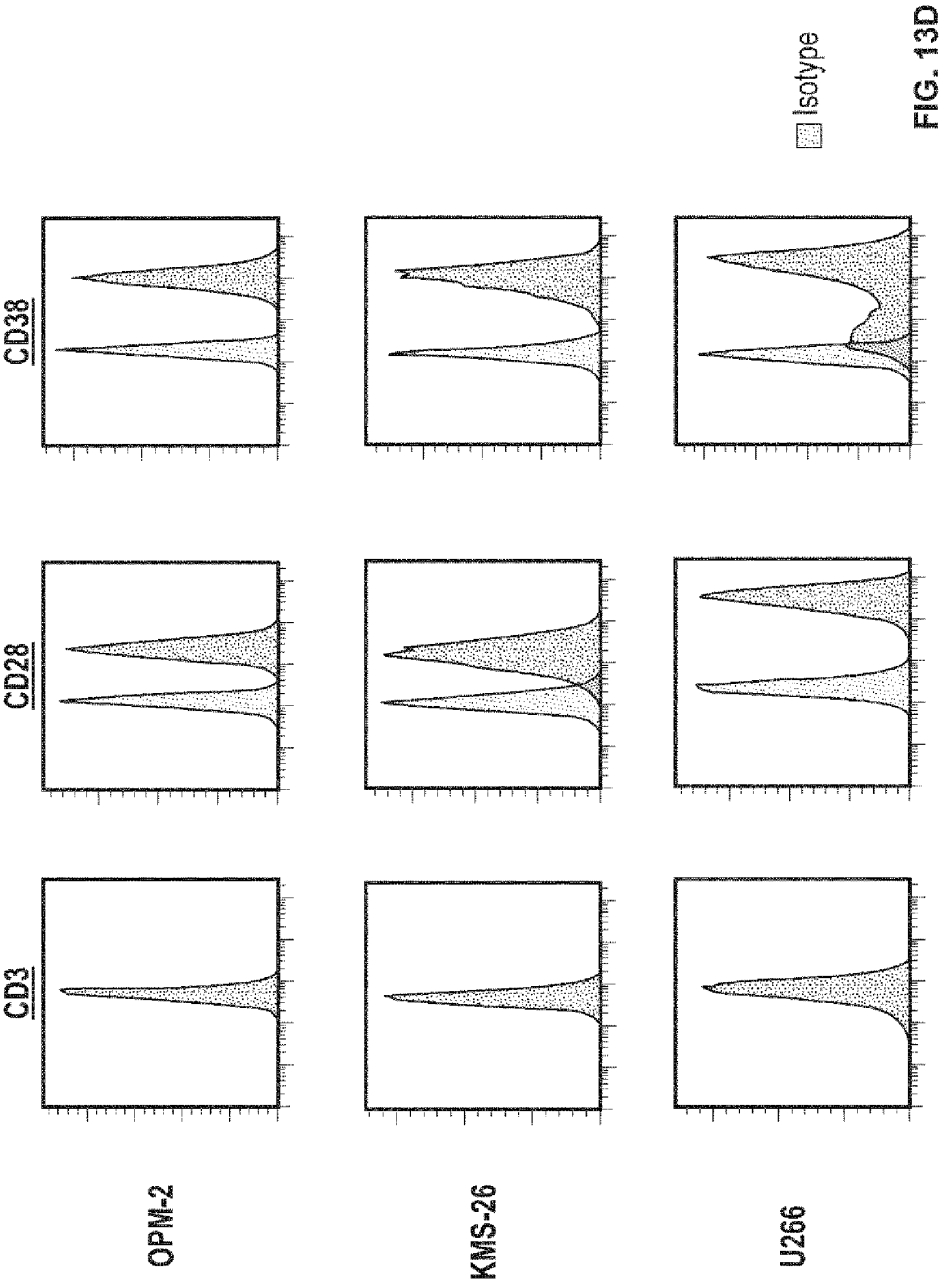
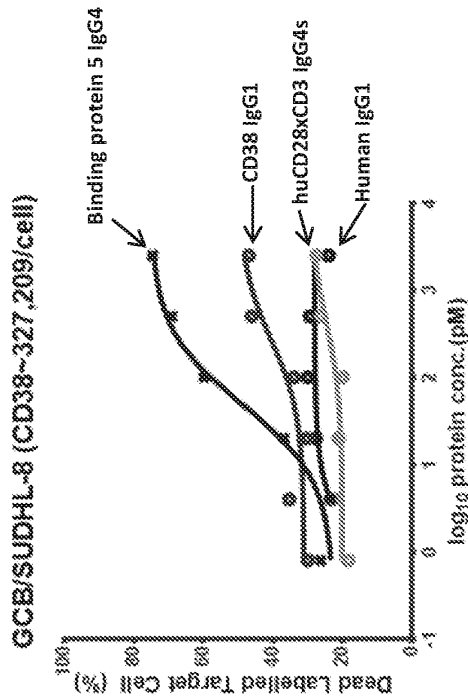
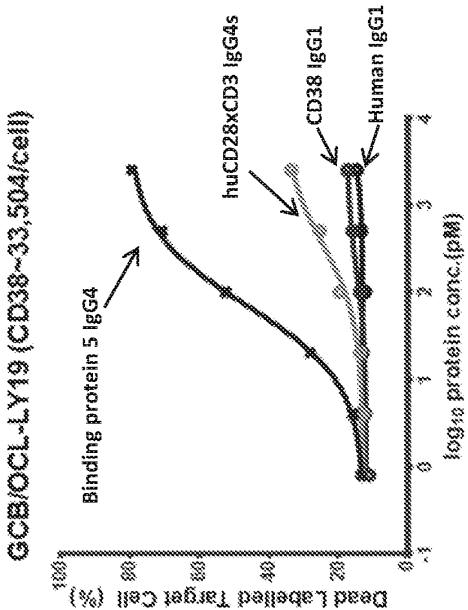


FIG. 14A



- huCD28 x CD3 IgG4s
- Binding Protein 5 IgG4
- CD38 IgG1
- human IgG1

FIG. 14B



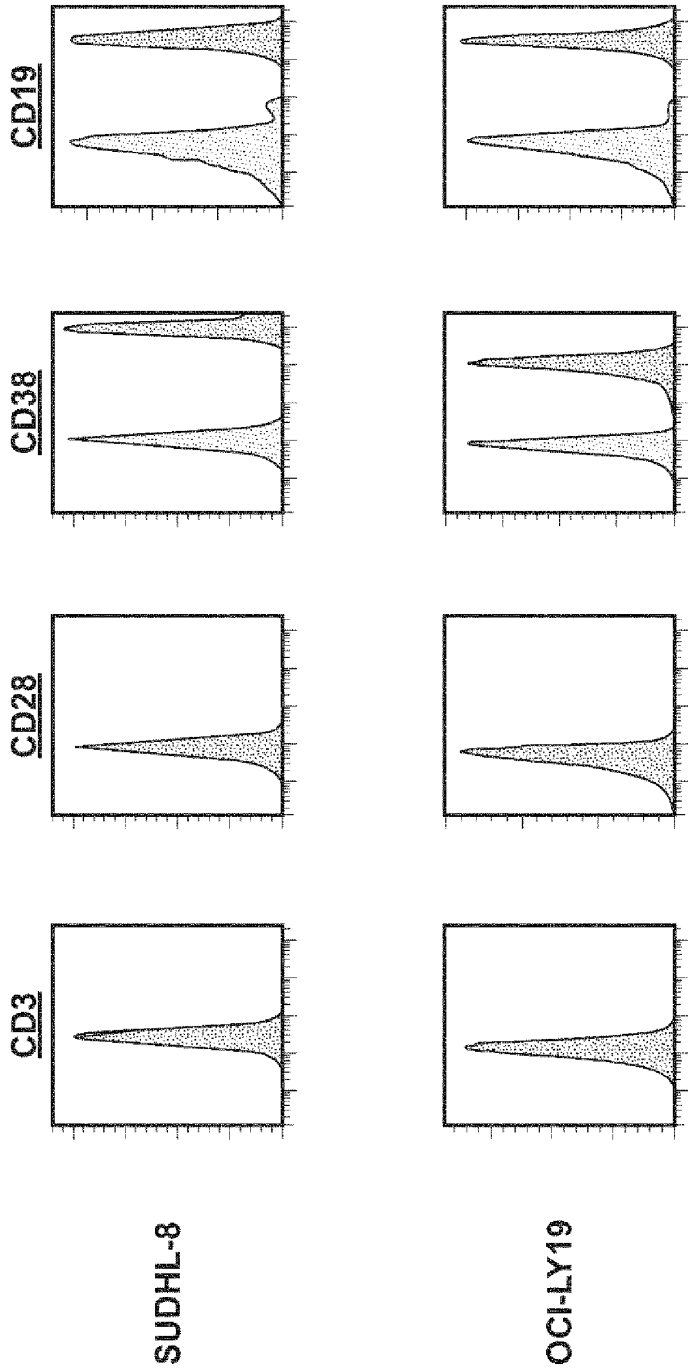


FIG. 14C

FIG. 15A

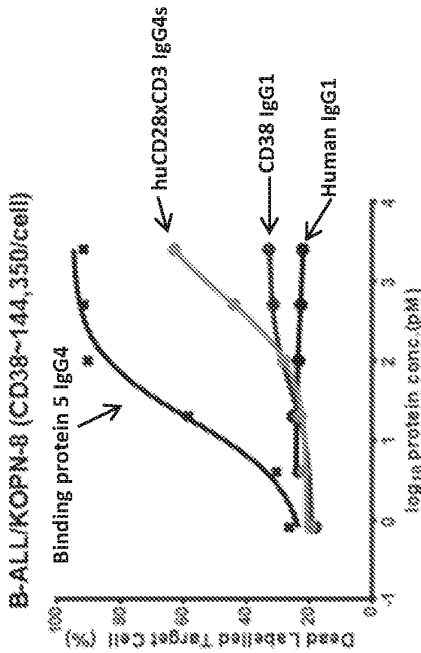


FIG. 15B

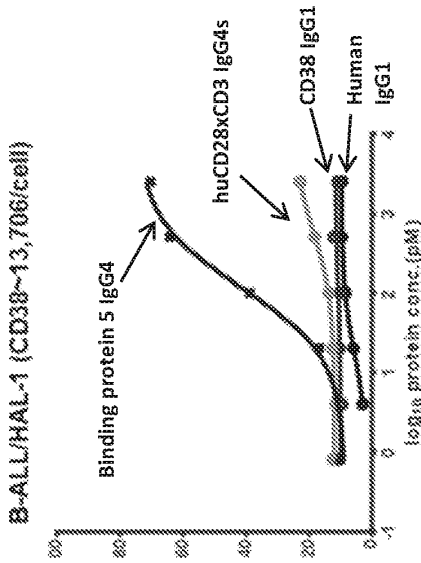
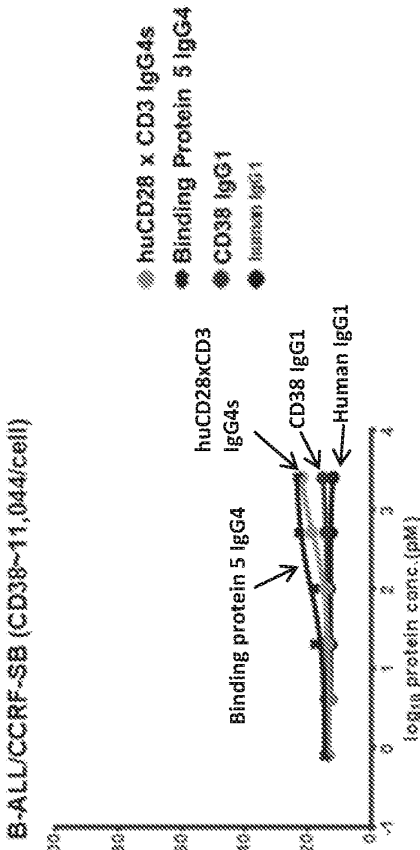


FIG. 15C



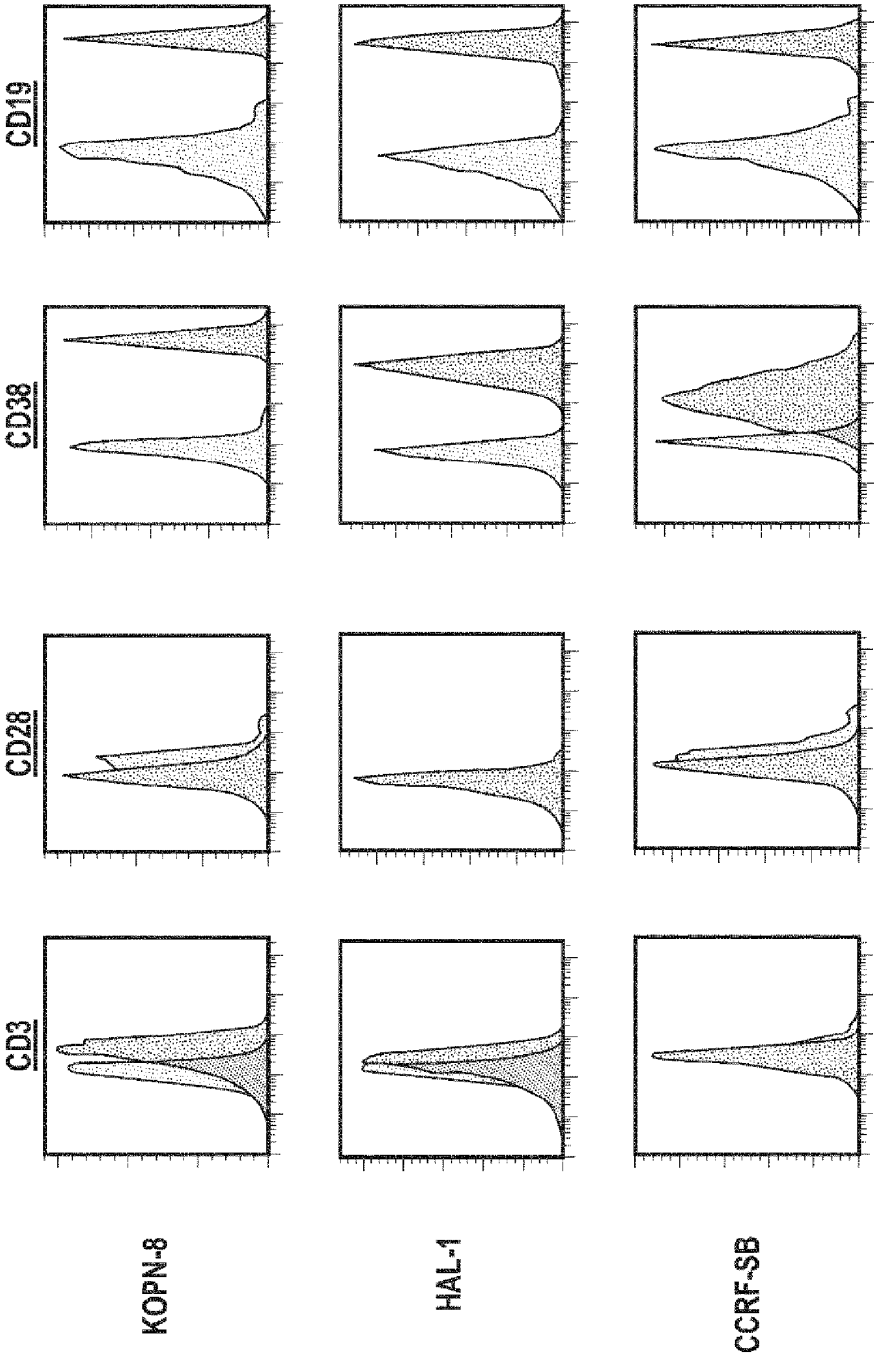


FIG. 15D

FIG. 16

MM/RPMI (CD38~128,713/cell)
Donor PK45926

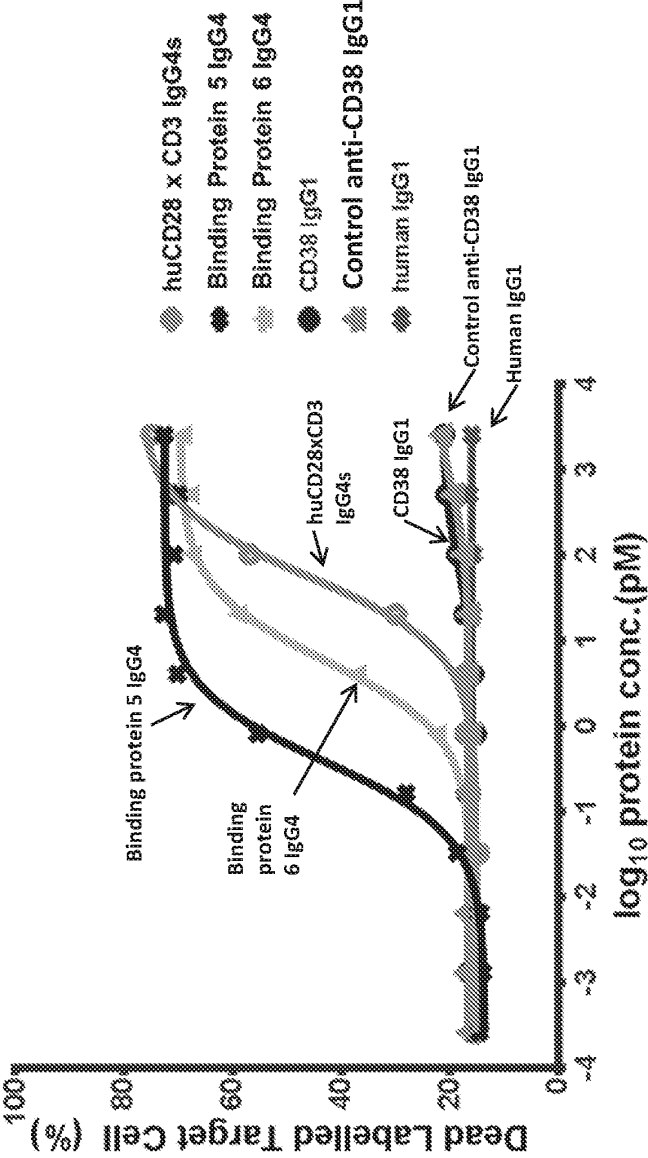


FIG. 17A

IL-2 signaling

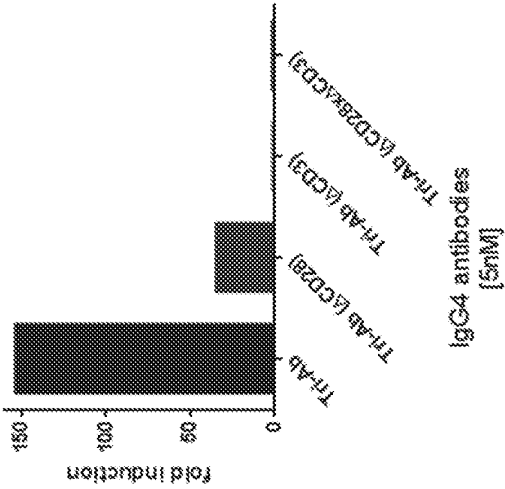
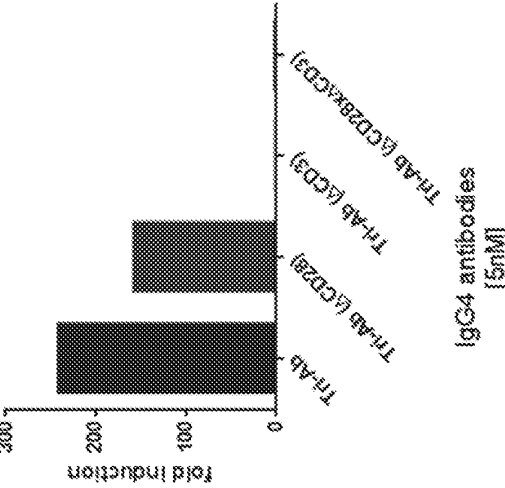


FIG. 17B

NFAT signaling



5 hr stimulation

FIG. 18A

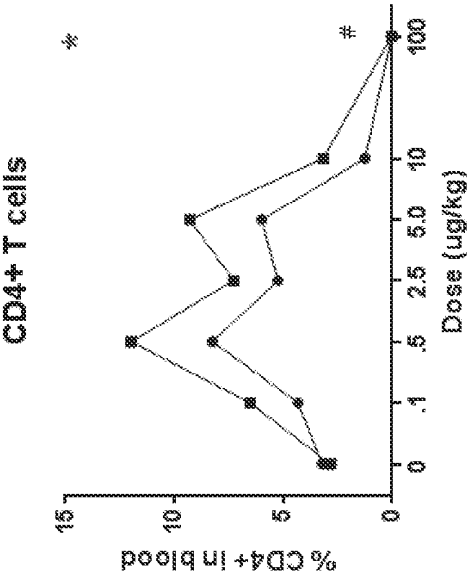


FIG. 18B

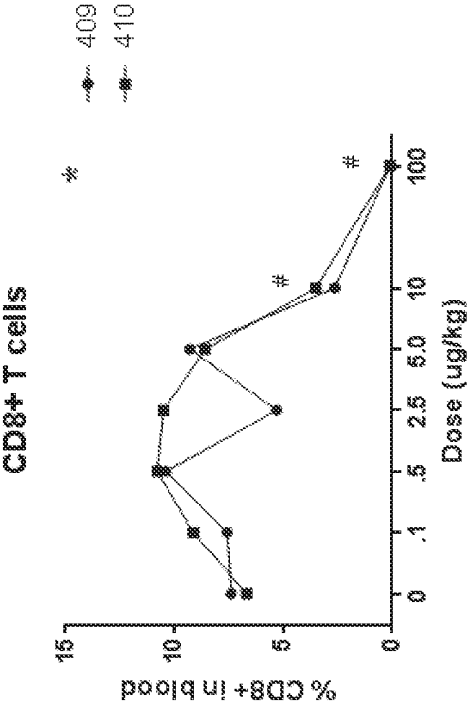


FIG. 18C

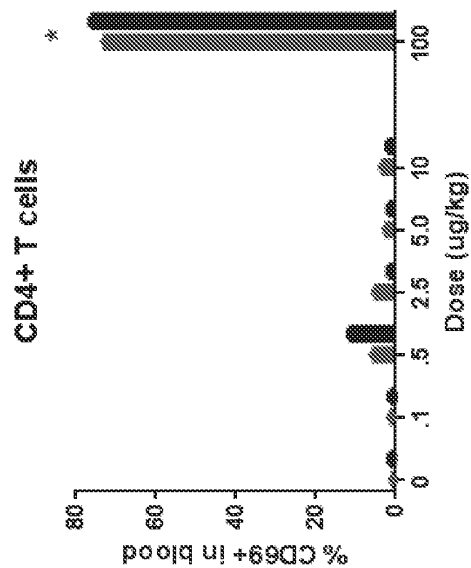
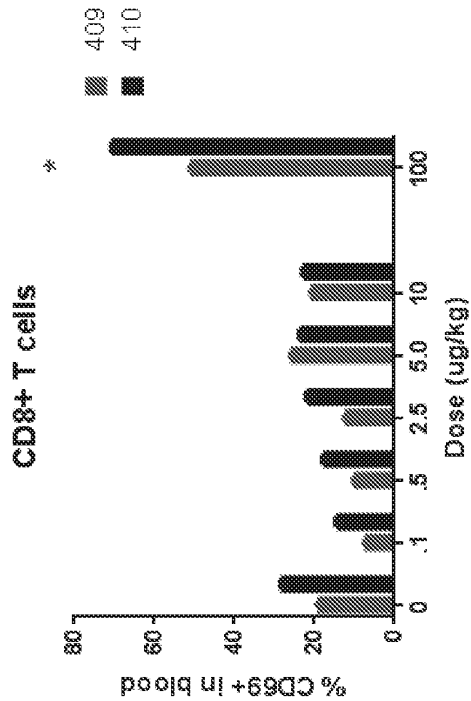


FIG. 18D



* severe vomitus
p<0.05 vs. Dose 0

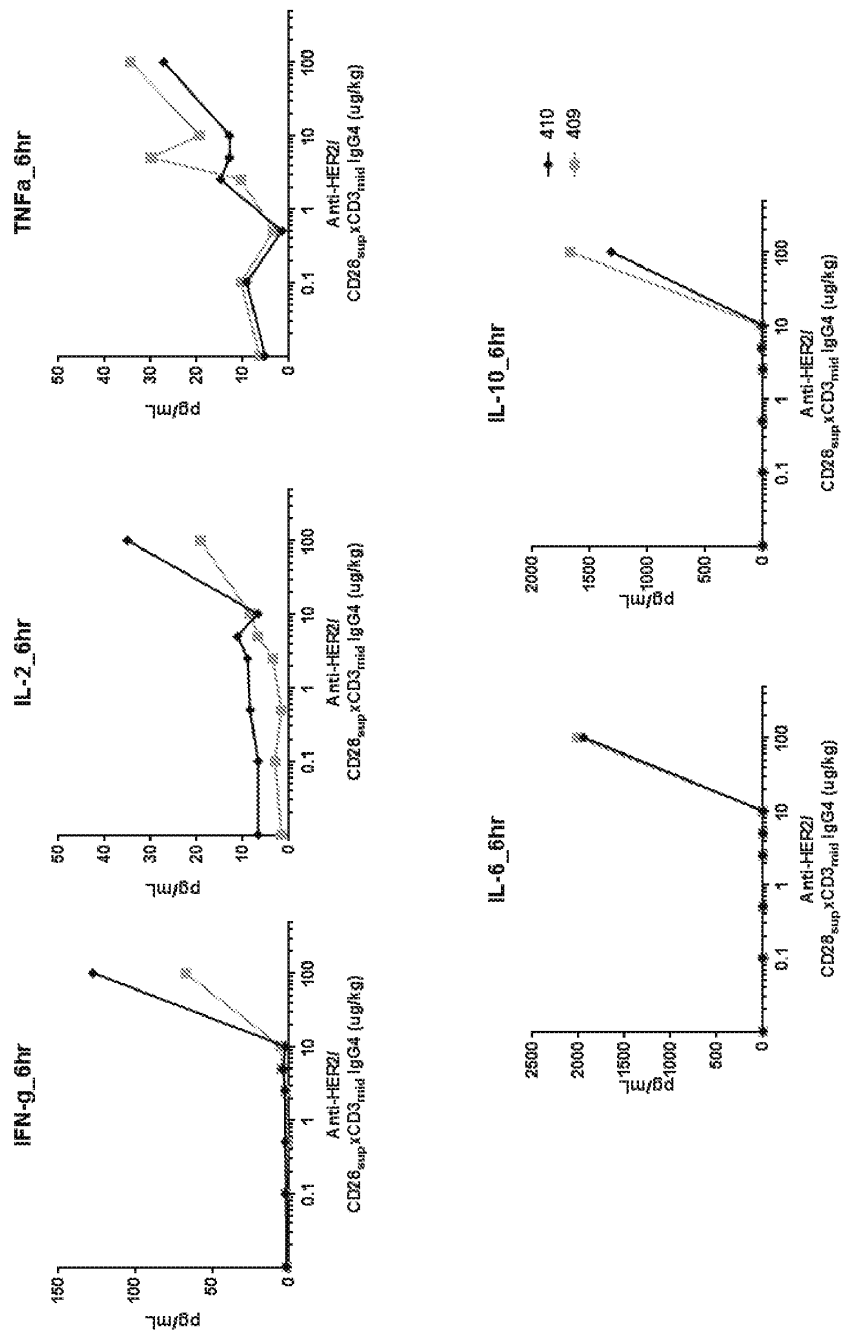


FIG. 18E

FIG. 19A

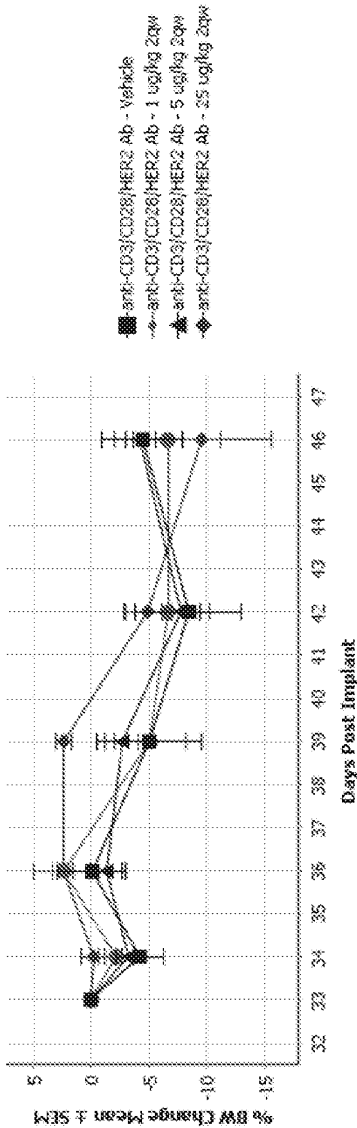
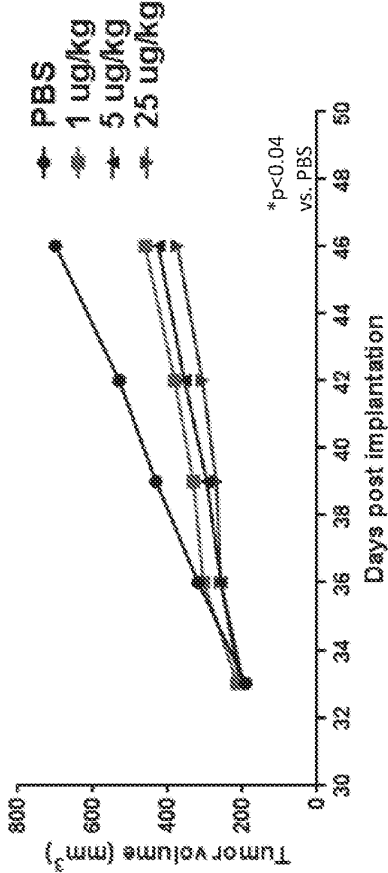


FIG. 19B



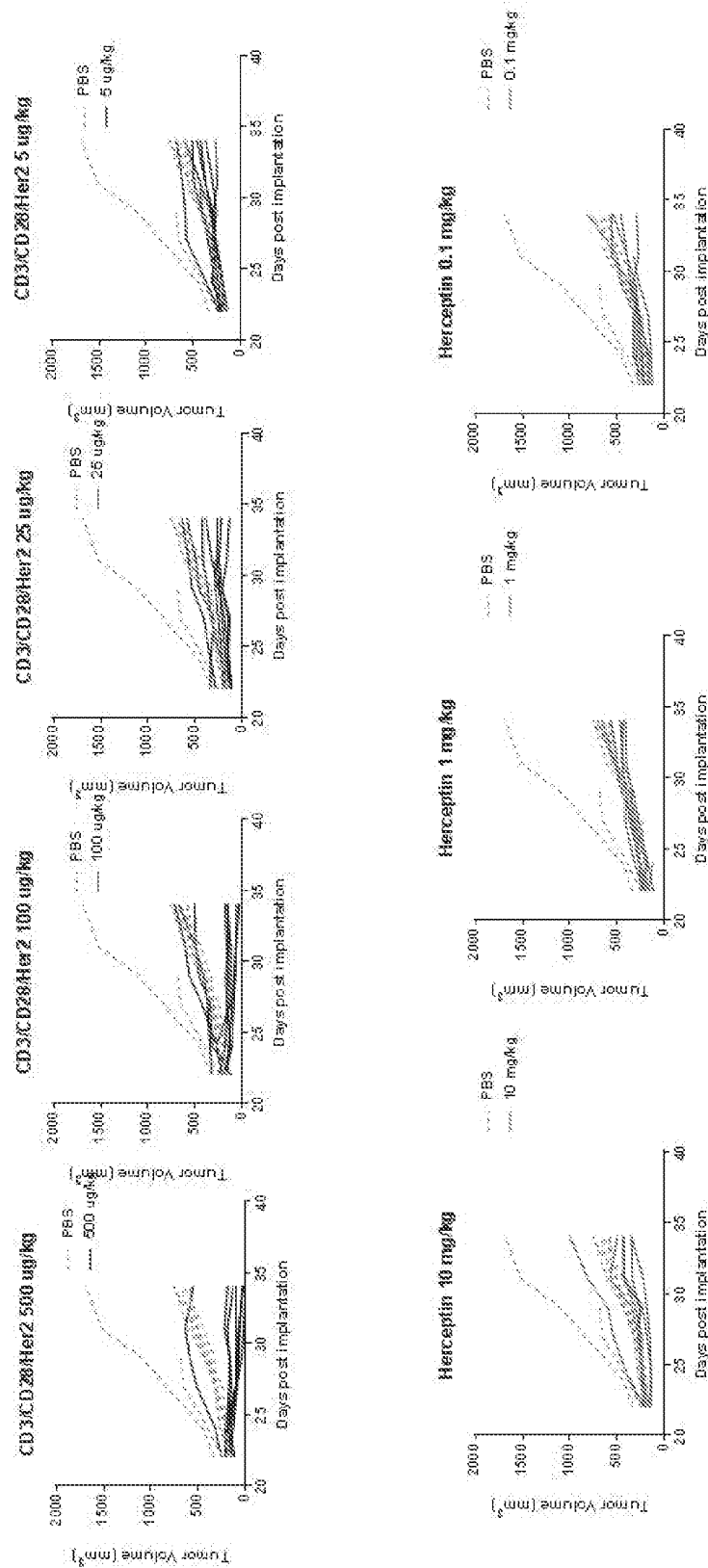


FIG. 20B

FIG. 20C

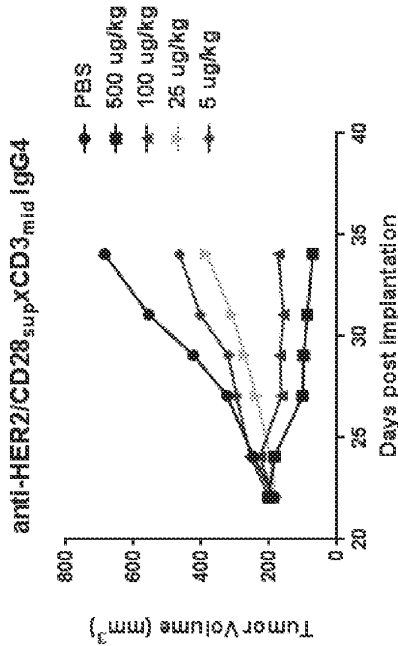


FIG. 20D

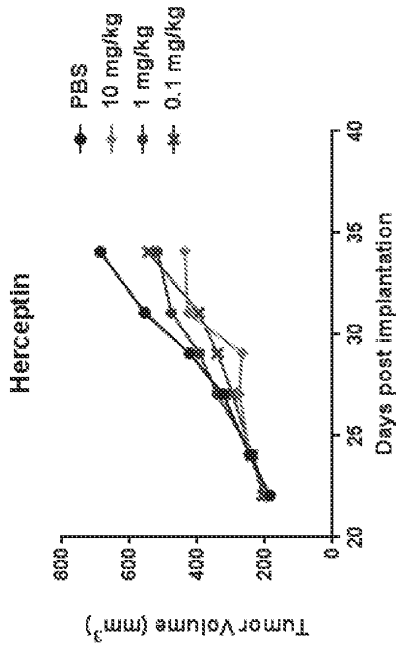


FIG. 20E

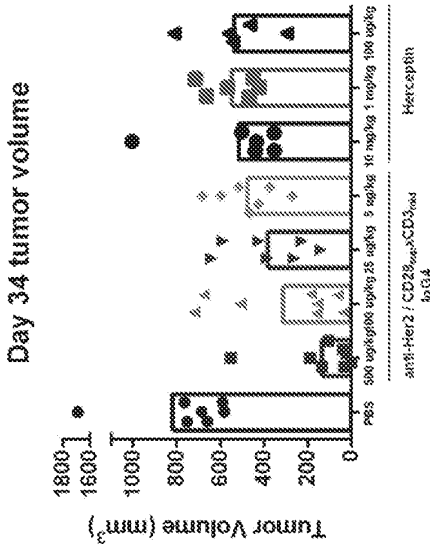
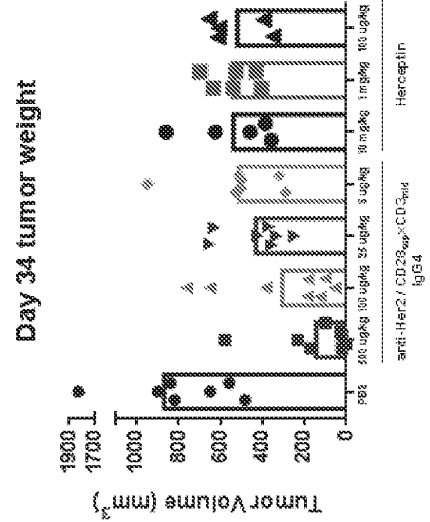


FIG. 20F



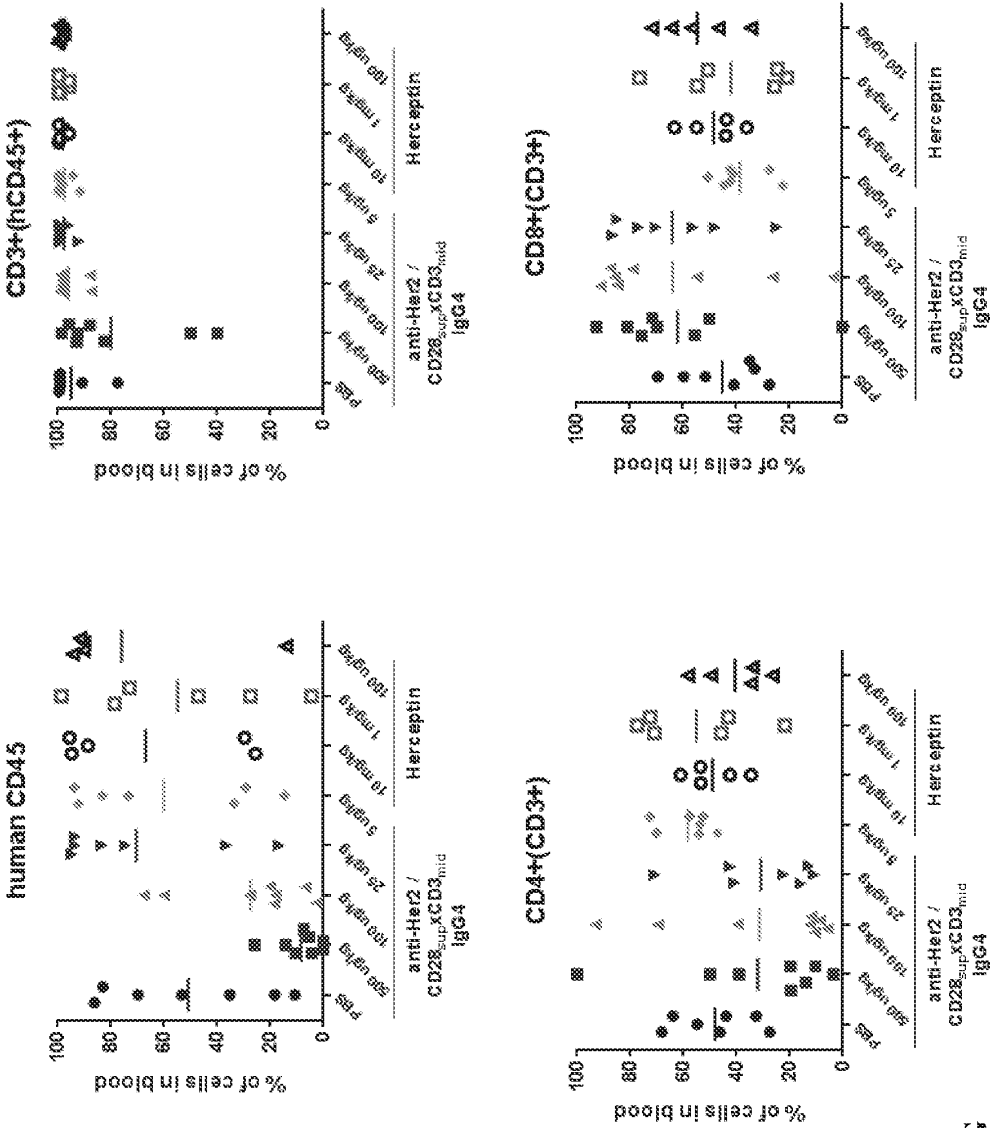


FIG. 20G

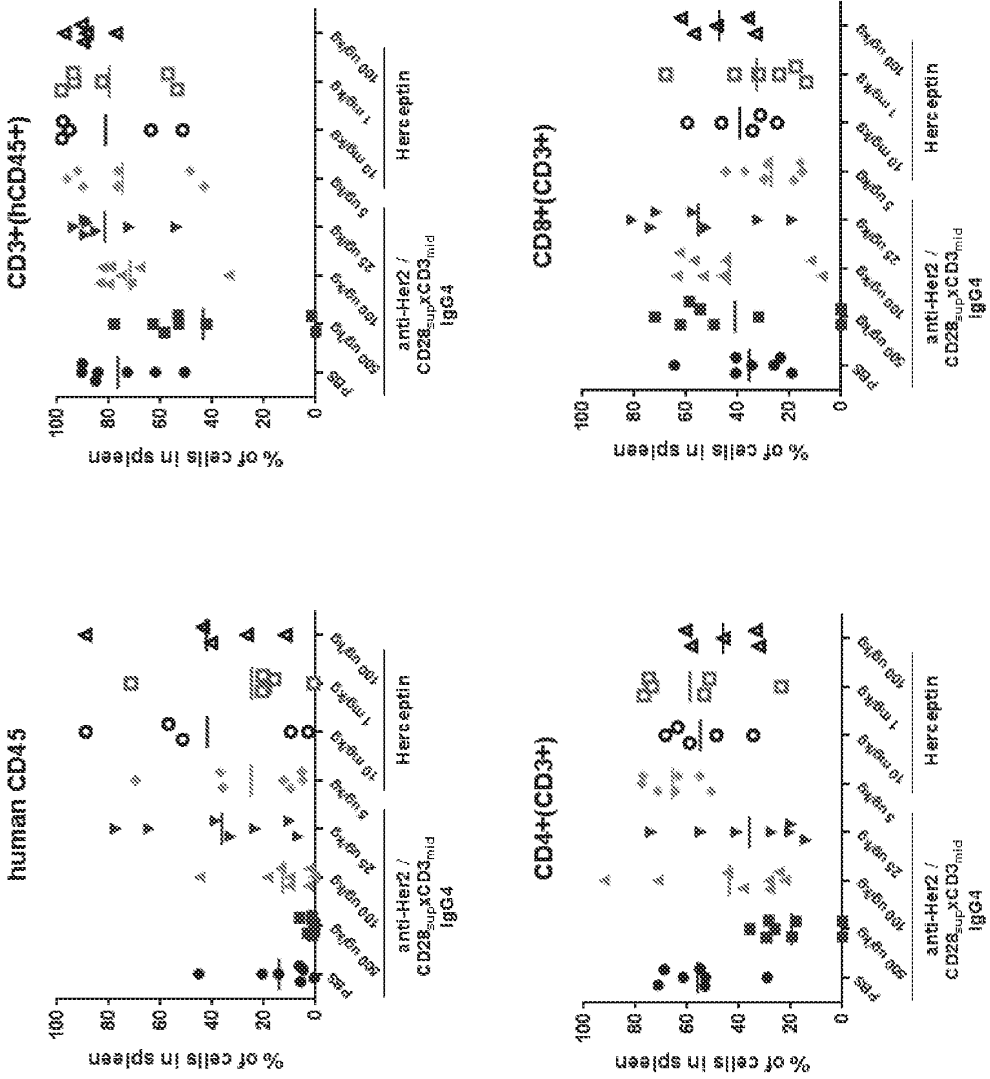


FIG. 20H

FIG. 21A

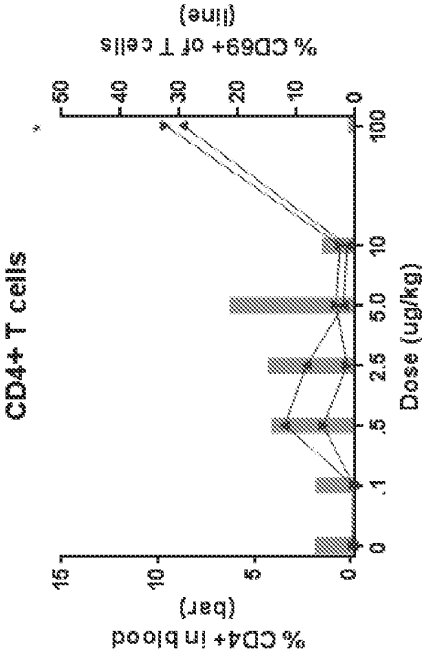
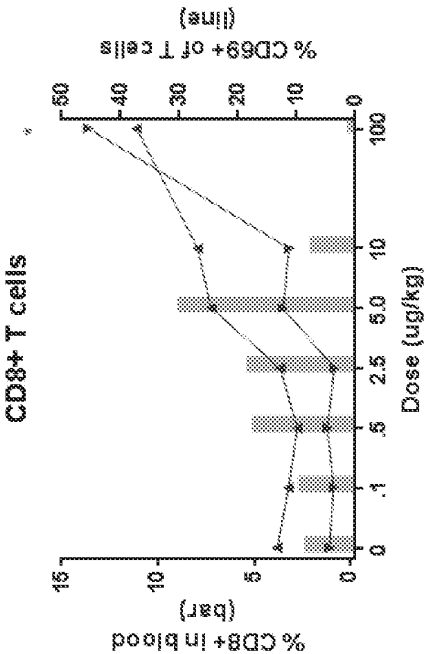


FIG. 21B



*Serious adverse event (vomiting). Animals recovered 24 hrs later.

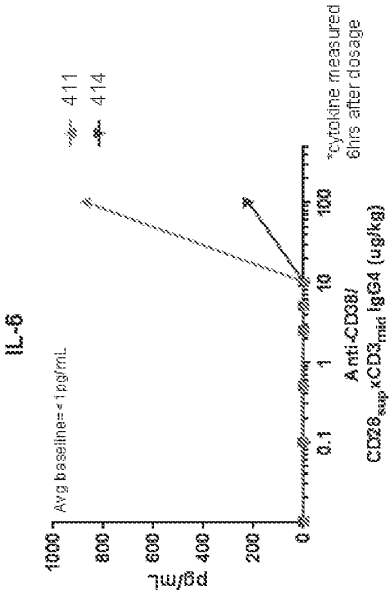


FIG. 21C

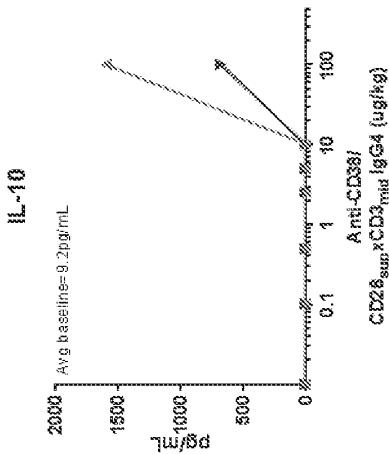


FIG. 21D

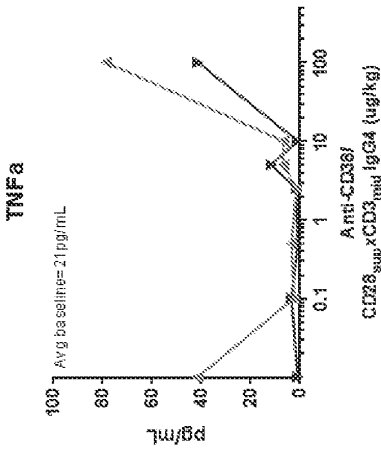


FIG. 21E

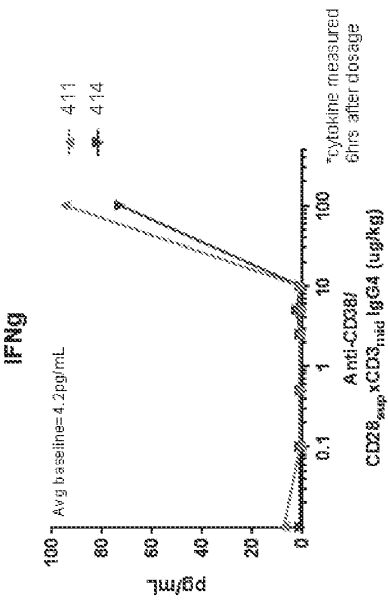


FIG. 21F

FIG. 22A

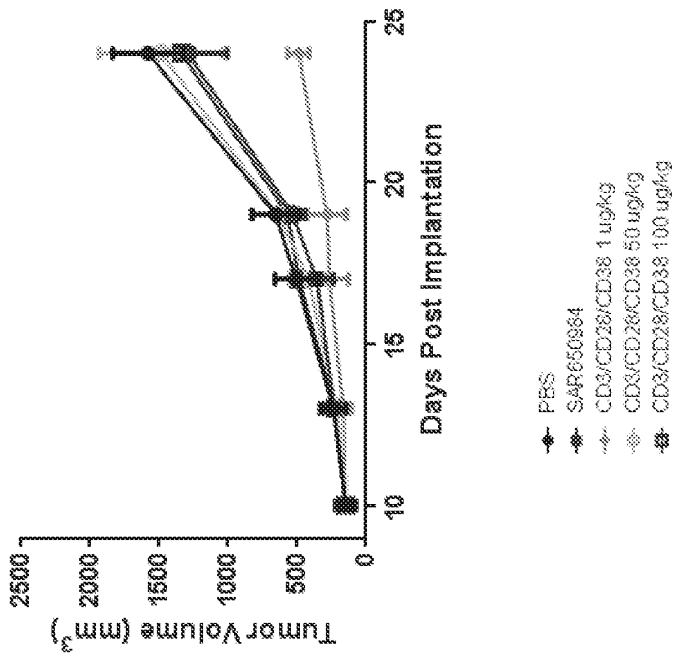
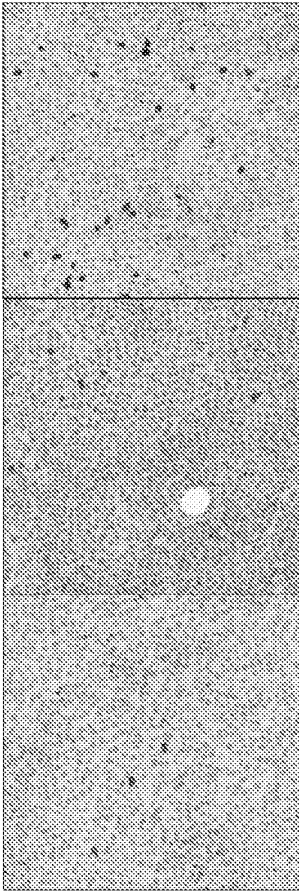
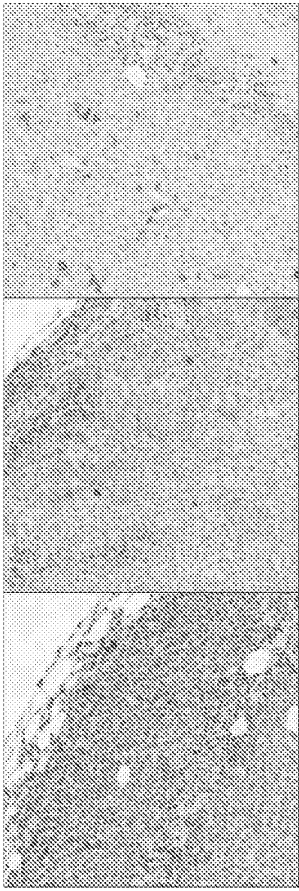


FIG. 22B



Anti-hCD8

FIG. 22C



Anti-hCD4

FIG. 23A

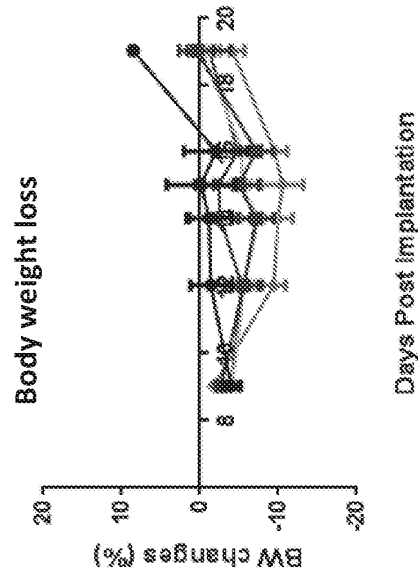
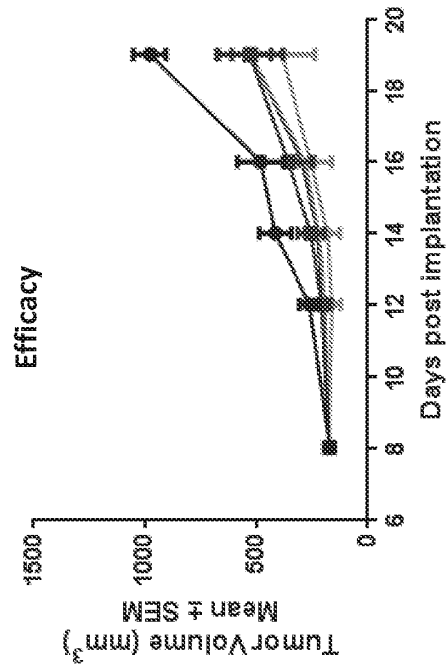


FIG. 23B



- PBS
- CD3/CD28/CD38 0.04 ug/kg
- ◆ CD3/CD28/CD38 0.2 ug/kg
- ▲ CD3/CD28/CD38 1 ug/kg
- ▼ CD3/CD28/CD38 5 ug/kg

FIG. 23C

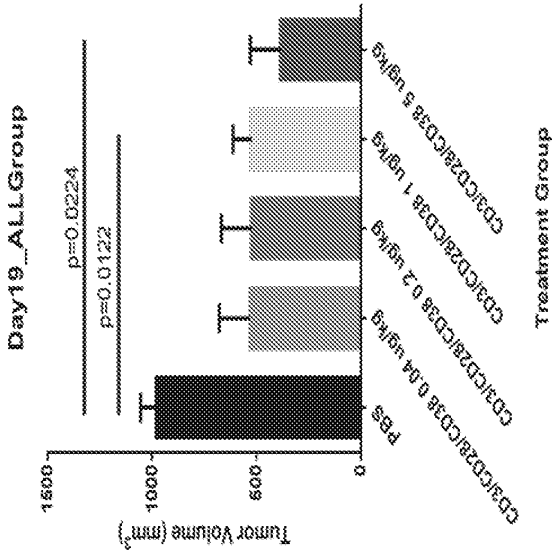


FIG. 23D

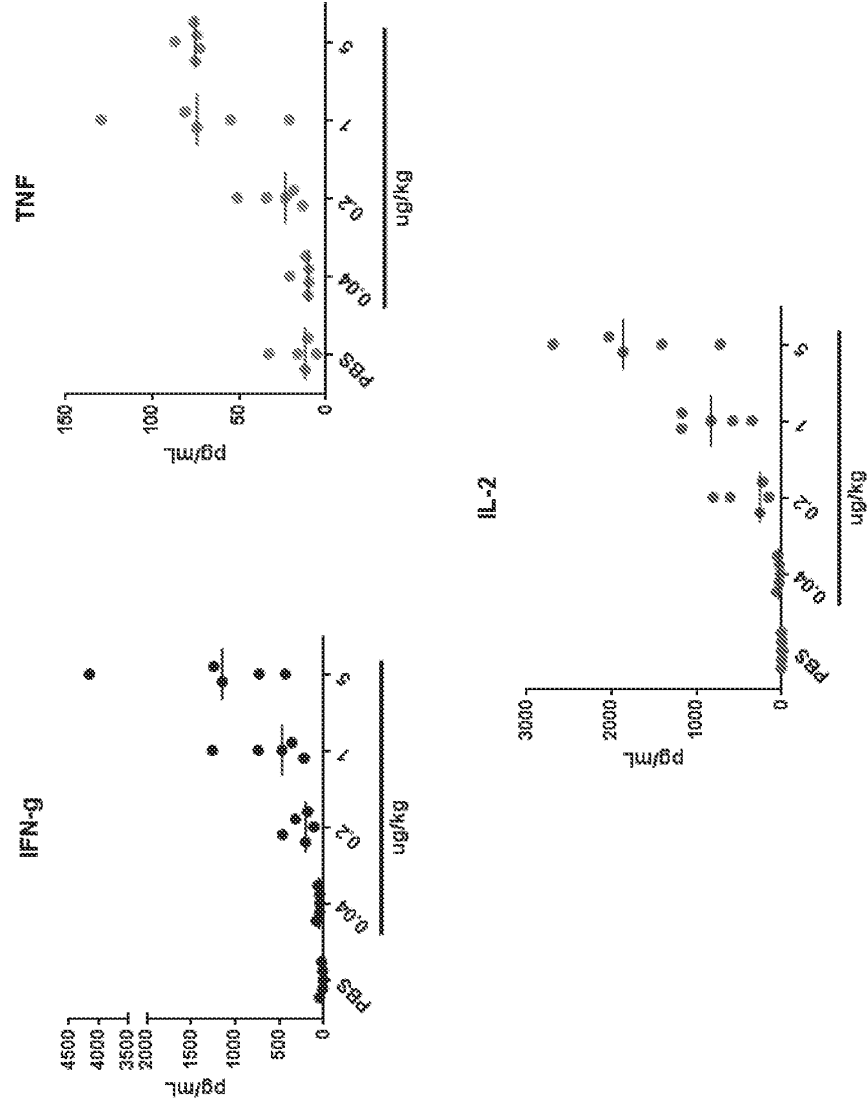


FIG. 25

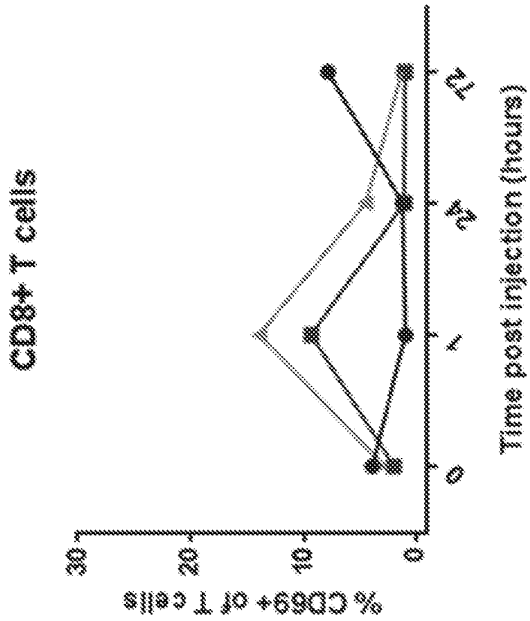
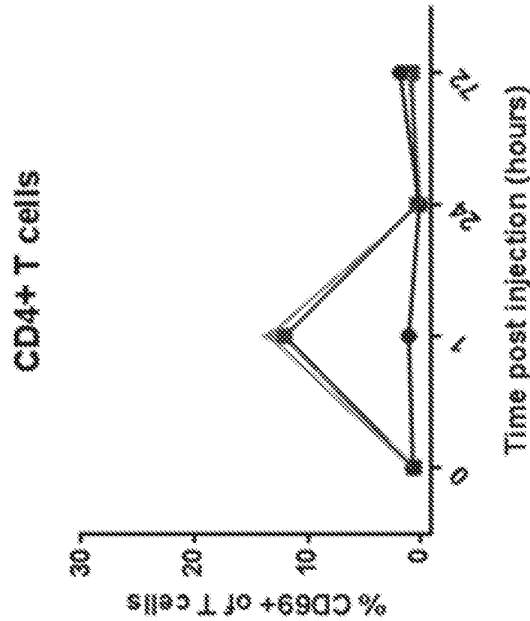


FIG. 24



- CD38_{SB}19 x CD28_{sup} x CD3_{mid} IgG4
- CD28_{sup} x CD3_{mid} IgG4
- CD28_{sup} IgG4

FIG. 26B

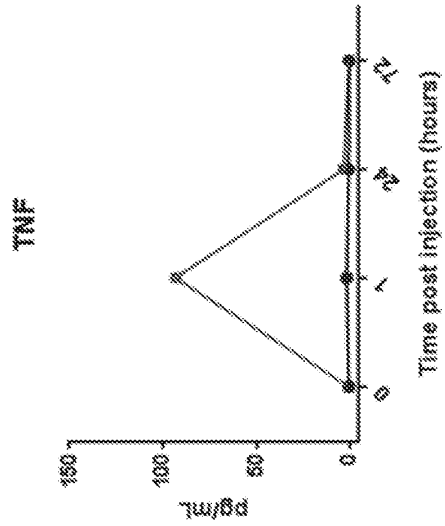


FIG. 26A

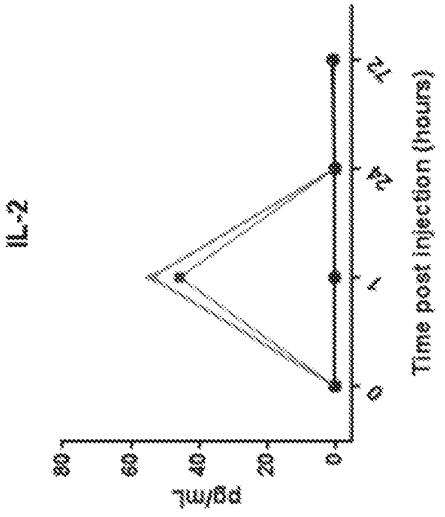
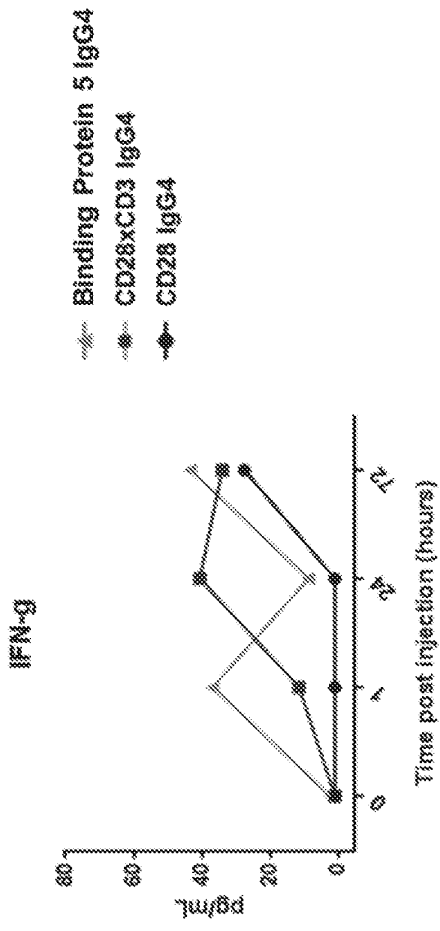


FIG. 26C



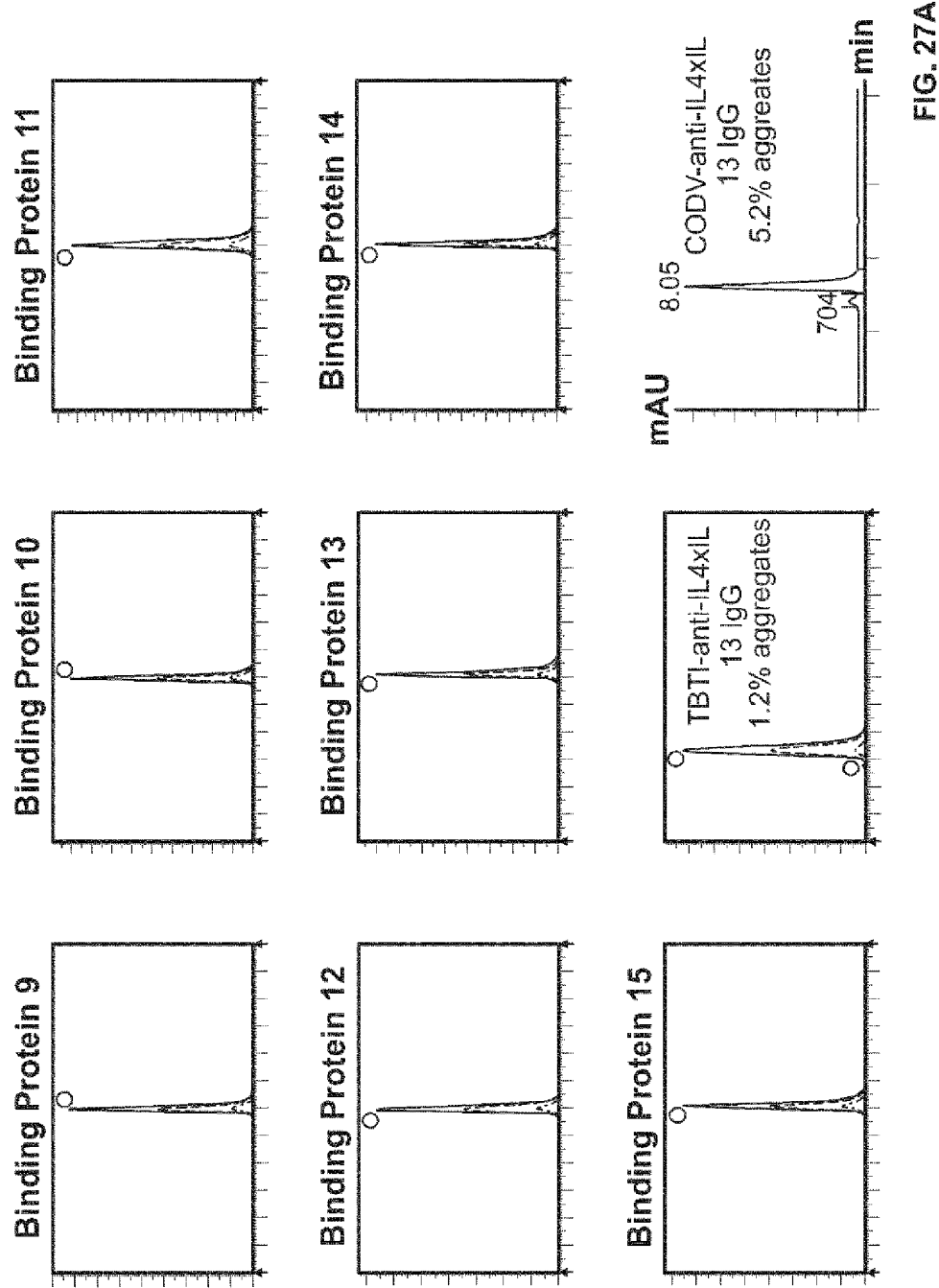


FIG. 27A

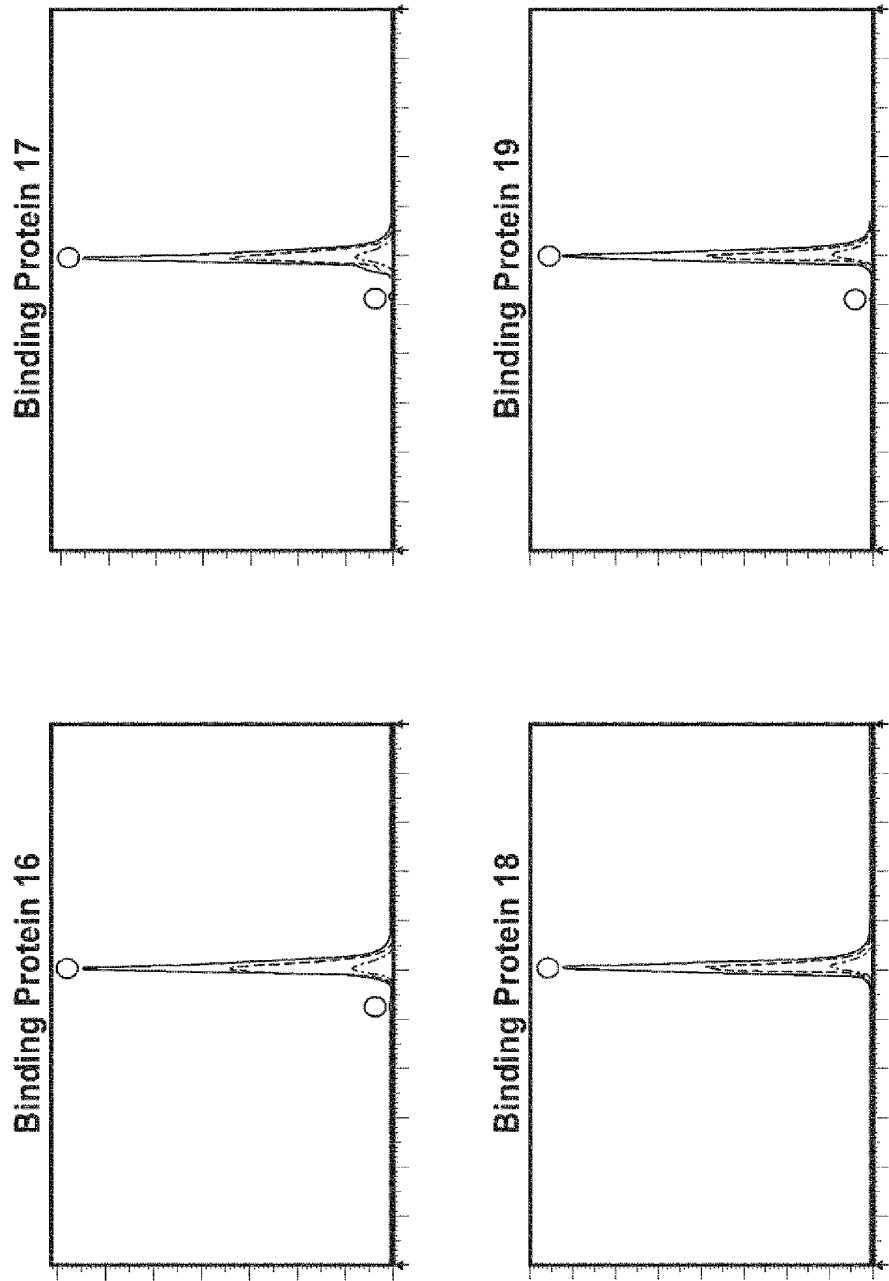


FIG. 27B

FIG. 28A

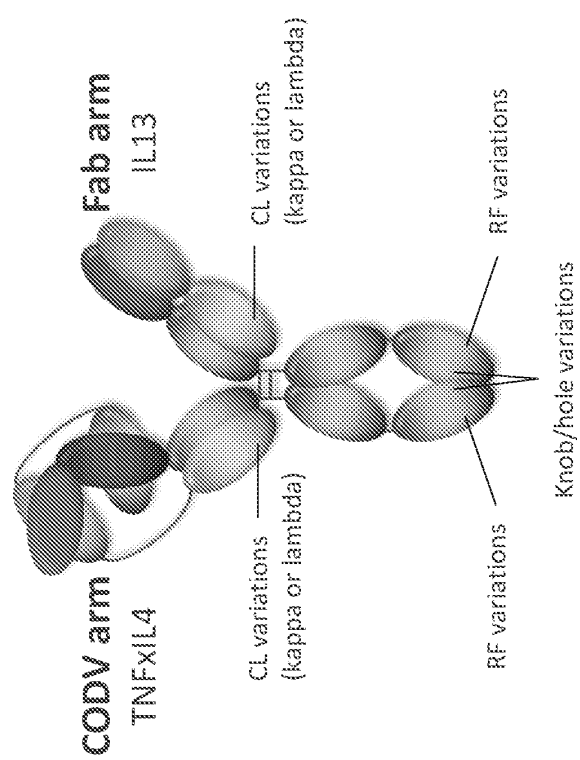
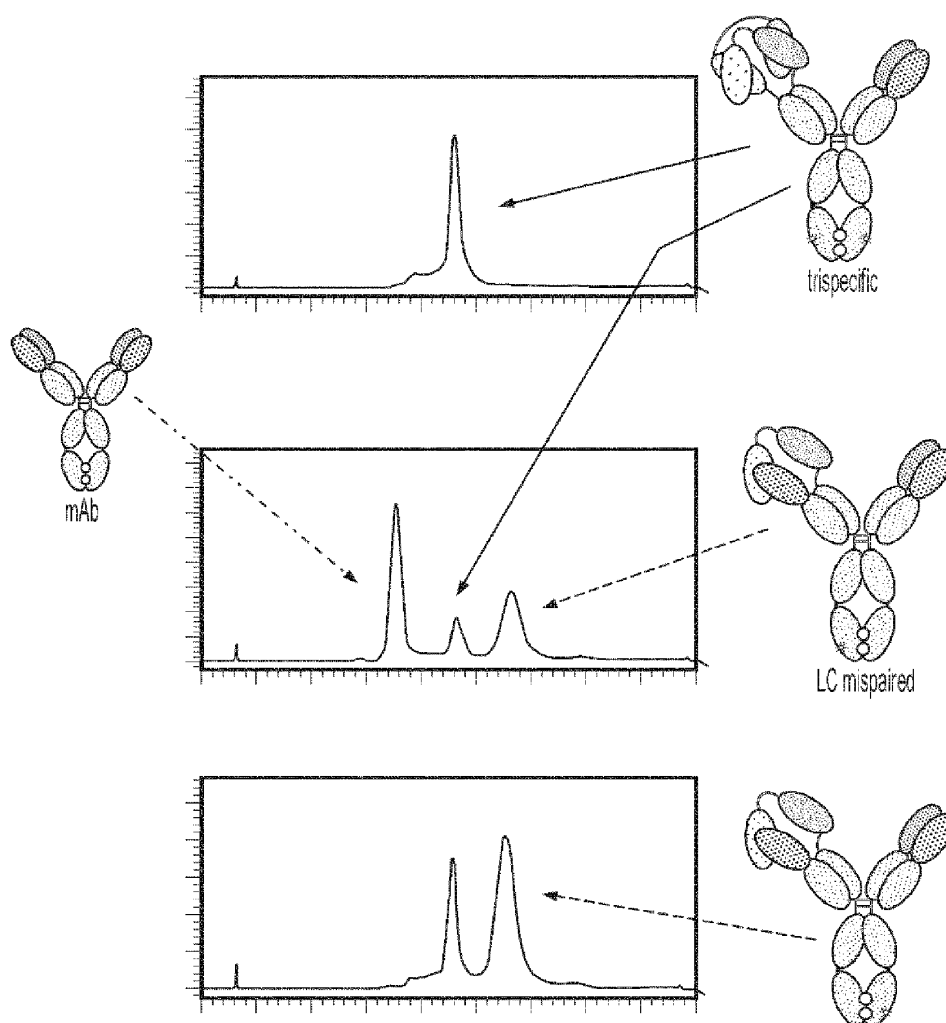


FIG. 28B

CODV- arm	Fab- arm	CODV- arm	Fab- arm	RF mutation
Kappa	Kappa	Hole	Knob	no RF
Kappa	Kappa	Hole	Knob	Hole
Kappa	Kappa	Hole	Knob	Knob
Kappa	lambda	Knob	Hole	no RF
Kappa	lambda	Knob	Hole	Hole
Kappa	lambda	Knob	Hole	Knob
lambda	Kappa	Knob	Hole	no RF
lambda	Kappa	Knob	Hole	Hole
lambda	Kappa	Knob	Hole	Knob
Kappa	Kappa	Knob	Hole	no RF
Kappa	Kappa	Knob	Hole	Hole
Kappa	Kappa	Knob	Hole	Knob
Kappa	lambda	Hole	Knob	no RF
Kappa	lambda	Hole	Knob	Hole
Kappa	lambda	Hole	Knob	Knob
lambda	Kappa	Hole	Knob	no RF
lambda	Kappa	Hole	Knob	Hole
lambda	Kappa	Hole	Knob	Knob

**FIG. 29**

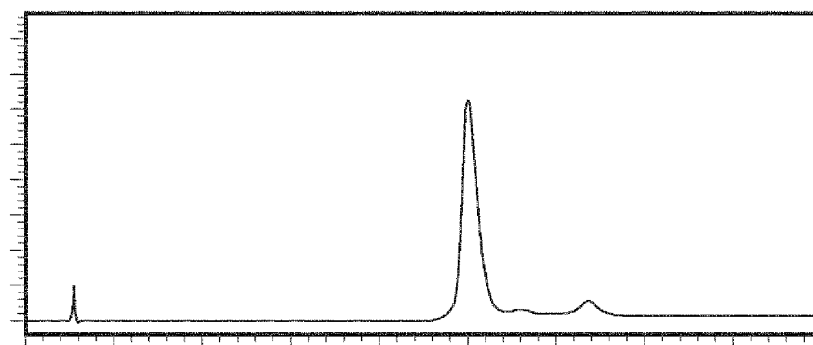


FIG. 30A

