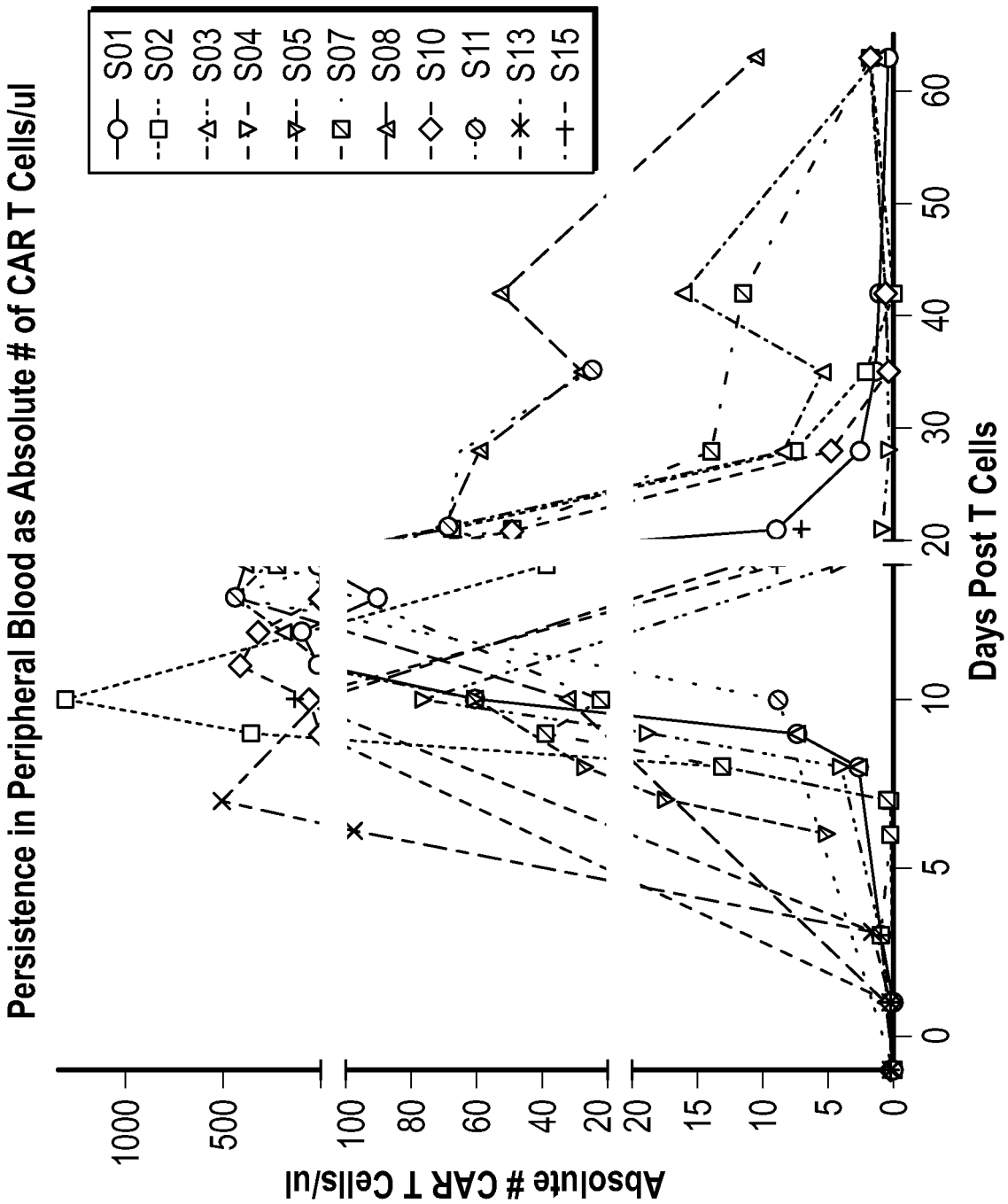

Persistence in Peripheral Blood as Absolute # of CAR T Cells/ul
S01
S02
S03
S04
S05
S07
S08
S10
S11
S13
S15
1000
500
100
80
60
40
20
20
15
10
5
0
Absolute # CAR T Cells/ul
0
5
10
20
30
40
50
60
Days Post T Cells

FIG. 1A

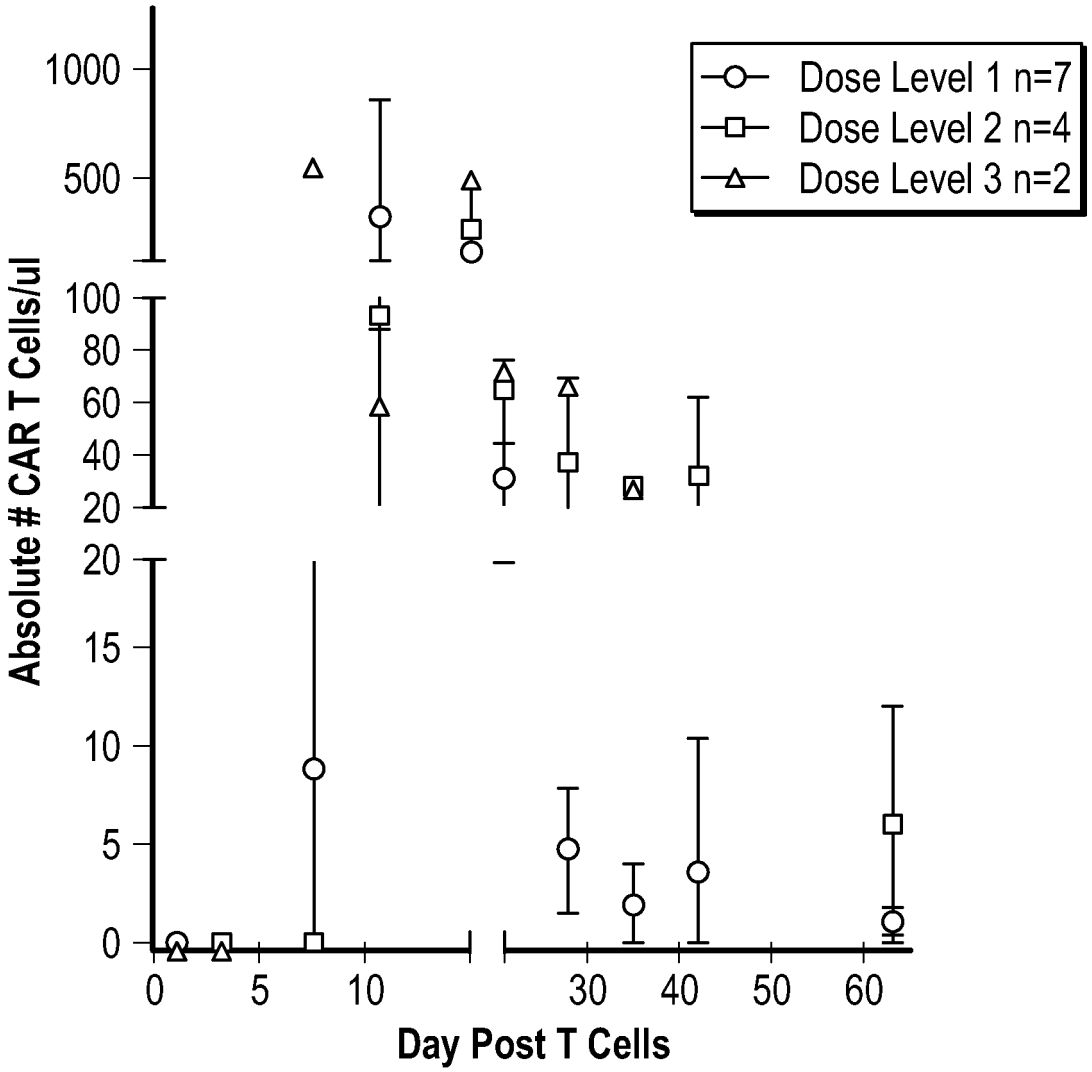

Dose Level 1 n=7
Dose Level 2 n=4
Dose Level 3 n=2
Absolute # CAR T Cells/ul
1000
500
100
80
60
40
20
20
15
10
5
0
0
5
10
30
40
50
60
Day Post T Cells

FIG. 1B

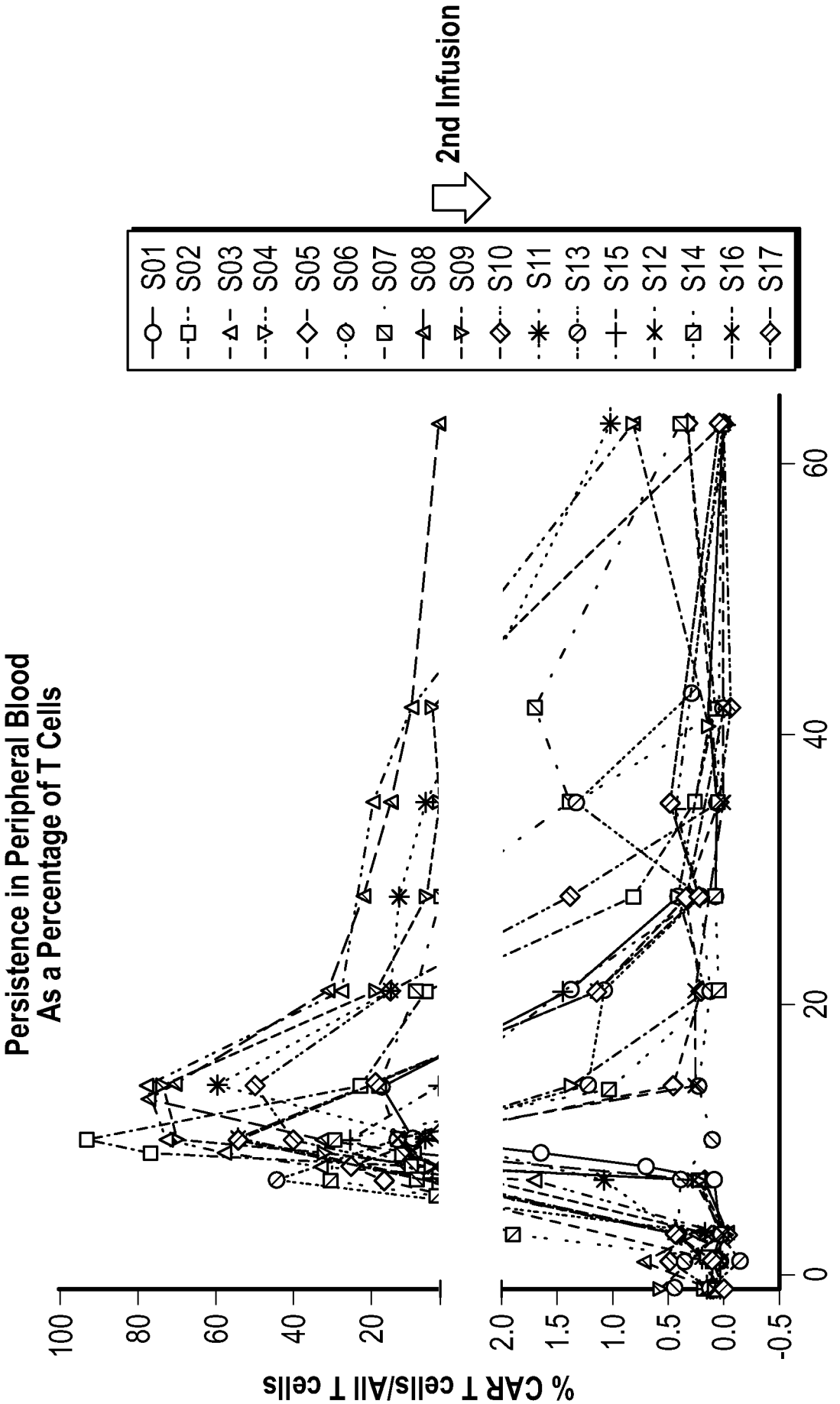

2nd Infusion
S01
S02
S03
S04
S05
S06
S07
S08
S09
S10
S11
S13
S15
S12
S14
S16
S17
Persistence in Peripheral Blood
As a Percentage of T Cells
% CAR T cells/All T cells
100
80
60
40
20
2.0
1.5
1.0
0.5
0.0
-0.5
0
20
40
60
Days Post T Cells

FIG. 2A

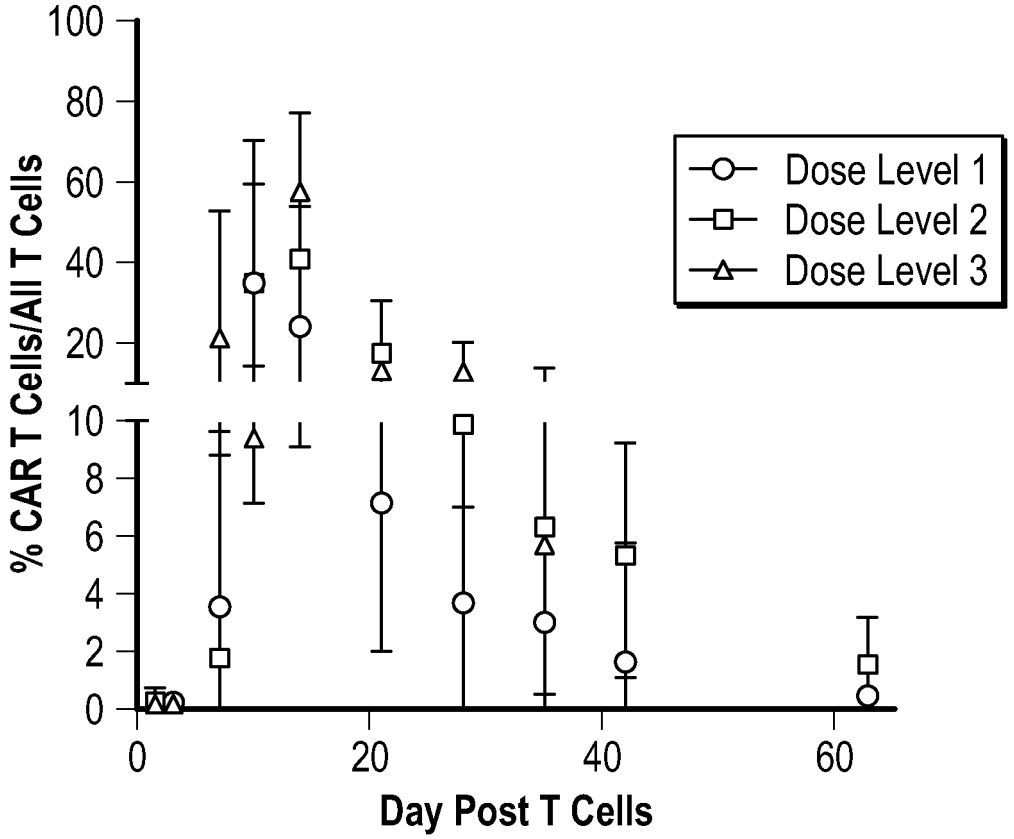

100
80
60
40
20
10
8
6
4
2
0
% CAR T Cells/All T Cells
0
20
40
60
Day Post T Cells
Dose Level 1
Dose Level 2
Dose Level 3

FIG. 2B

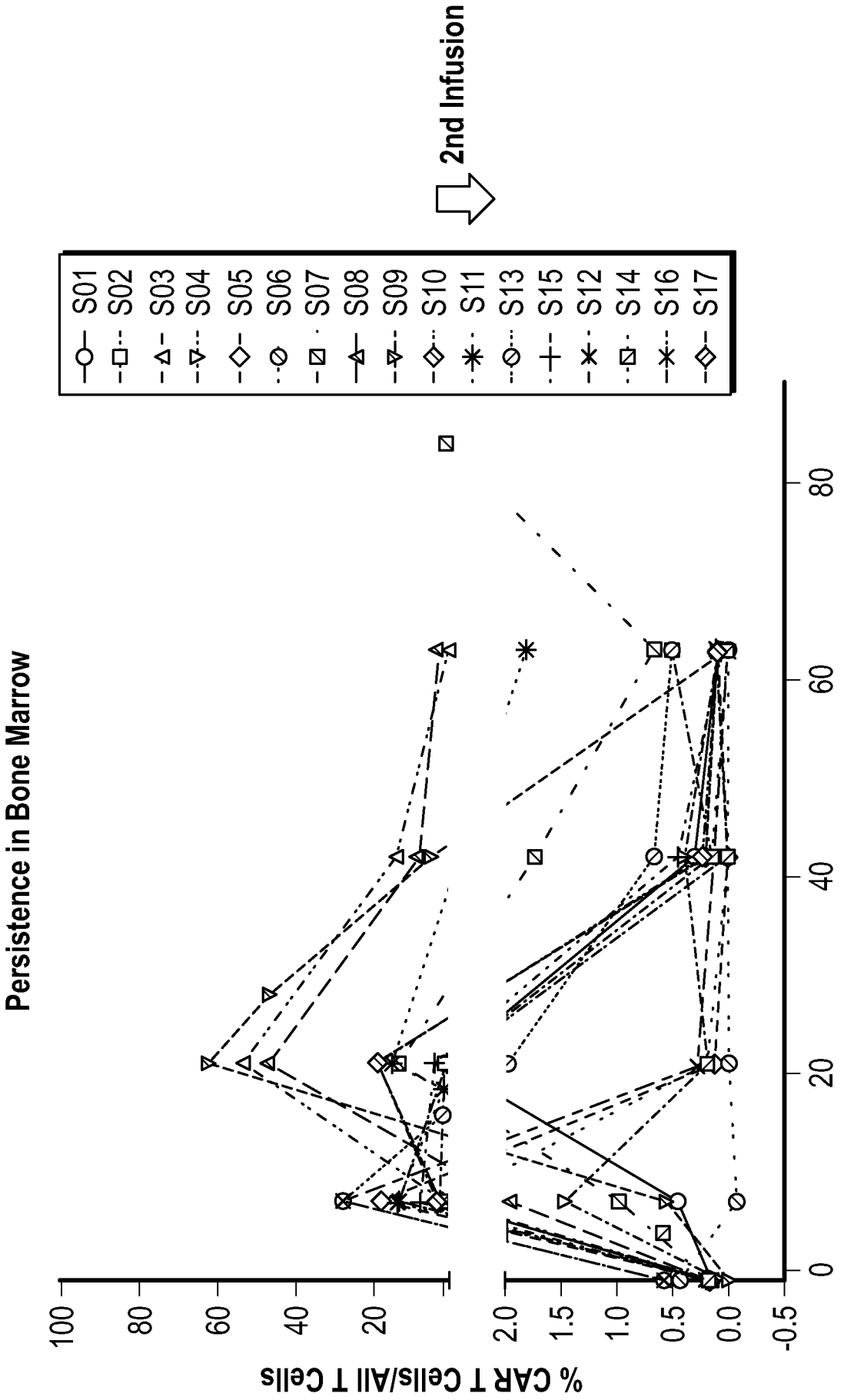

Persistence in Bone Marrow
% CAR T Cells/All T Cells
100
80
60
40
20
2.0
1.5
1.0
0.5
0.0
-0.5
0
20
40
60
80
Day Post T Cells
2nd Infusion
S01
S02
S03
S04
S05
S06
S07
S08
S09
S10
S11
S13
S15
S12
S14
S16
S17

FIG. 3A

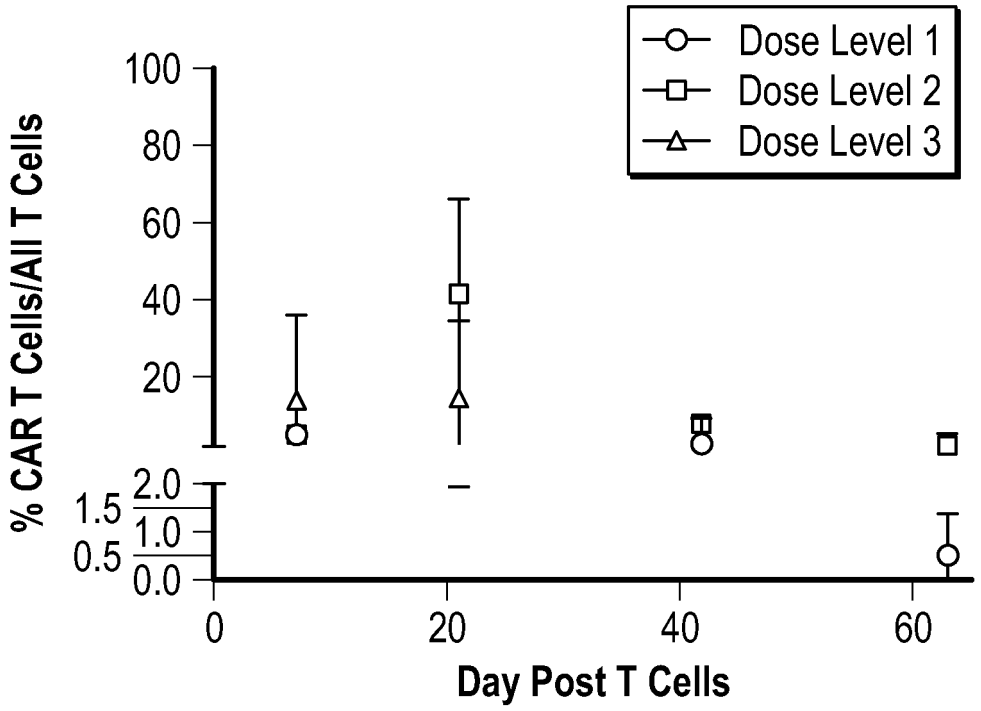

Dose Level 1
Dose Level 2
Dose Level 3
% CAR T Cells/All T Cells
100
80
60
40
20
2.0
1.5
1.0
0.5
0.0
0
20
40
60
Day Post T Cells

FIG. 3B

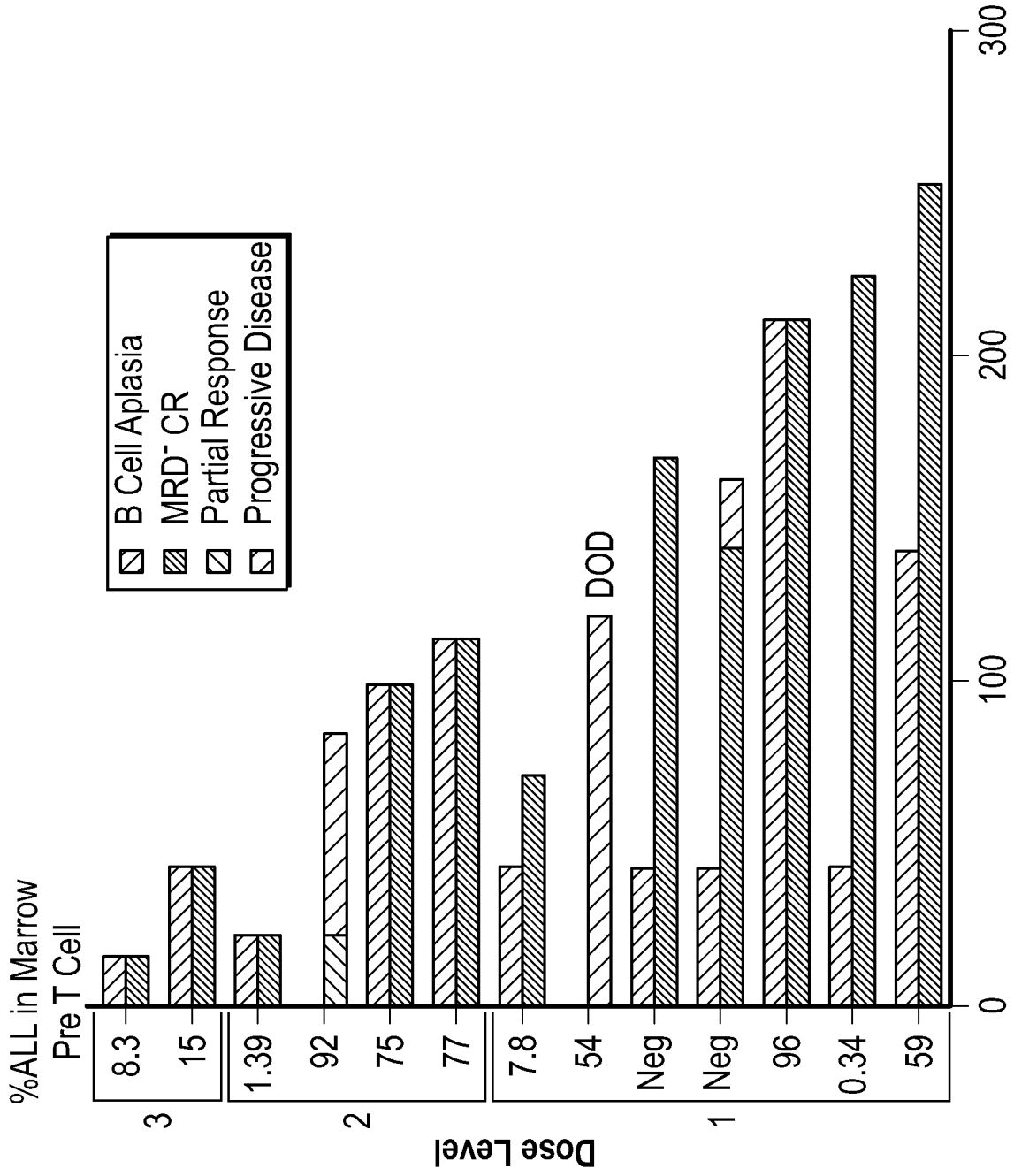

%ALL in Marrow
Pre T Cell
8.3
15
1.39
92
75
77
7.8
54
Neg
Neg
96
0.34
59
3
2
1
Dose Level
DOD
B Cell Aplasia
MRD- CR
Partial Response
Progressive Disease
0
100
200
300
Days Post T Cells

FIG. 4

SUBSTITUTE SHEET (RULE 26)

PATIENT CHARACTERISTICS

ID	Age (y)	Relapse #	# of prior HSCT	Time from most recent HSCT (mo)	Prior CD19 directed therapy	Cytogenetics	% ALL in marrow Pre T cell	Lympho-depletion	Dose Level	Response
S01	21	2	1	6	No	Ph-like	59	Cytoxan 3g/m^2	1	MRD-CR
S02	22	2	1	16	No		0.34	Cytoxan/Etoposide	1	MRD-CR
S03	21	2	1	28	No		96	Cytoxan 3gm/m^2	1	MRD-CR
S04	11	2	2	14	No		MRD neg	Cytoxan 3g/m^2	1	MRD-CR
S05	19	2	1	36	No	iAMP21, Monoso my 7	MRD neg	Cytoxan 3g/m^2	1	MRD-CR
S06	4	2	1	5	BiTE		54	Fludarabine	1	PD
S10	17	2	1	22	BiTE	Hypo-diploid	7.8	Cytoxan 3g/m^2	1	MRD-CR
S07	1	2	1	8	BiTE	t(4;11) MLL	77	Cytoxan 1.5g/m^2	2	MRD-CR
S08	23	1	1	33	No	IKZF1 delection, Ph-like	75	Cytoxan 3g/m^2	2	MRD-CR
S09	6	2	1	6	No	iAMP21	92	Cytoxan 3g/m^2	2	PR
S15	13	1	1	18	CD19 CAR pre-HSCT	Trisomy 10	1.39	Cytoxan 3g/m^2	2	MRD-CR
S11	15	2	1	59	No		15	Cytoxan 3g/m^2	3	MRD-CR
S13	8	2	1	13	No	Hypo-diploid	8.3	Cytoxan 3g/m^2	3	MRD-CR

HSCT hematopoietic stem cell transplant; BiTE blinatumomab; MPF multiparameter flow; Ph-like Philadelphia-like; iAMP21 internal amplification of chromosome 21; MRD minimal residual disease; CR complete remission; PR partial response; PD progressive disease

FIG. 5

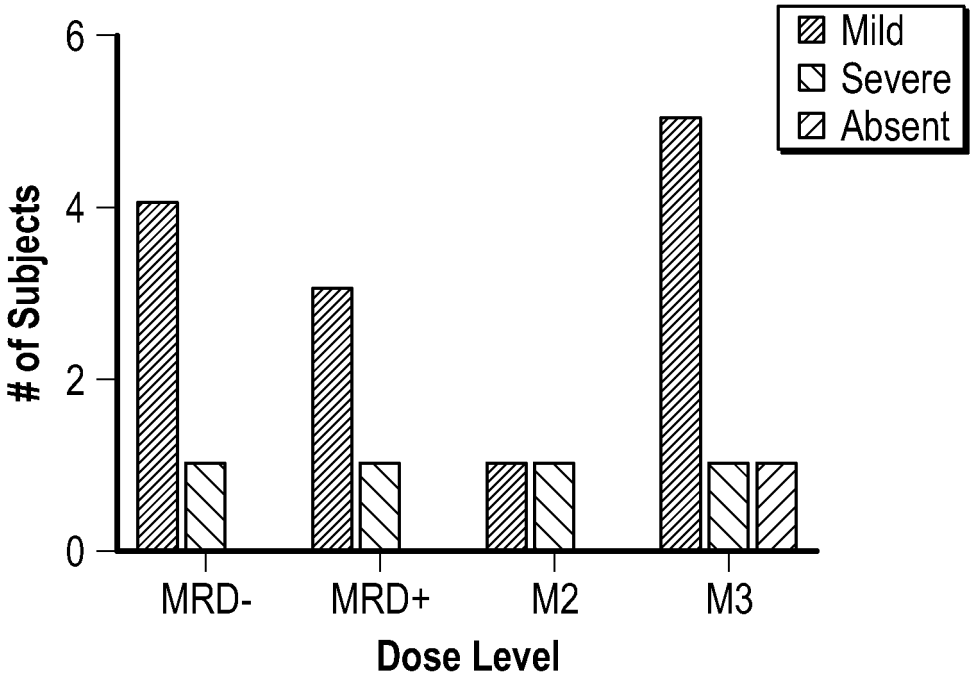

Mild
Severe
Absent
# of Subjects
0
2
4
6
MRD-
MRD+
M2
M3
Dose Level

FIG. 6A

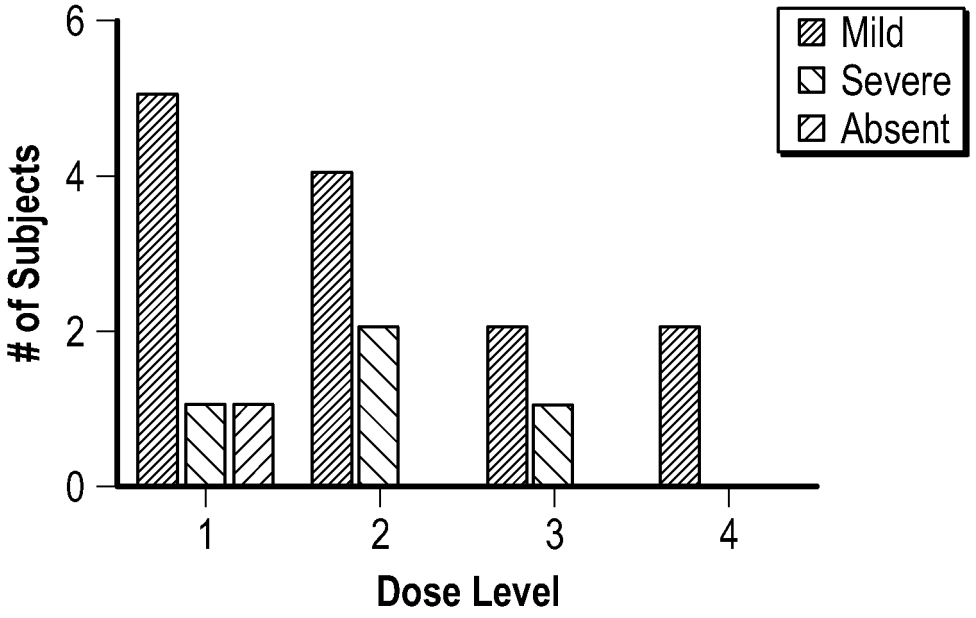

Mild
Severe
Absent
# of Subjects
0
2
4
6
1
2
3
4
Dose Level

FIG. 6B

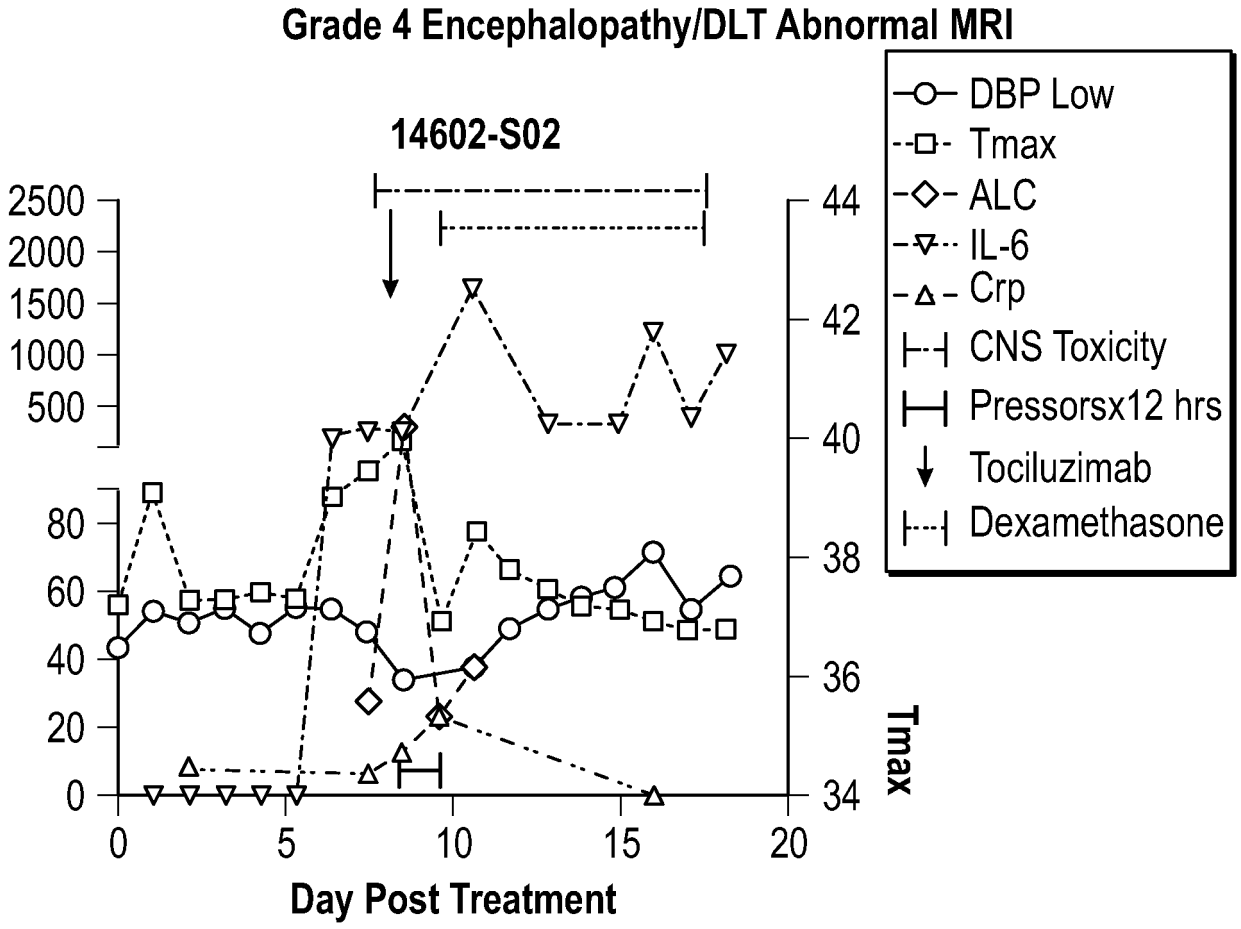

Grade 4 Encephalopathy/DLT Abnormal MRI
14602-S02
DBP Low
Tmax
ALC
IL-6
Crp
CNS Toxicity
Pressorsx12 hrs
Tociluzimab
Dexamethasone
2500
2000
1500
1000
500
80
60
40
20
0
44
42
40
38
36
34
Tmax
0
5
10
15
20
Day Post Treatment

FIG. 7A

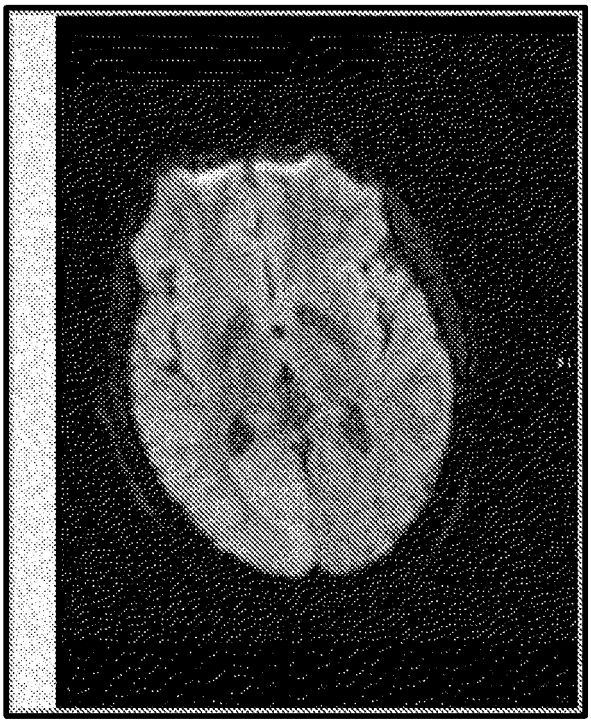


FIG. 7B

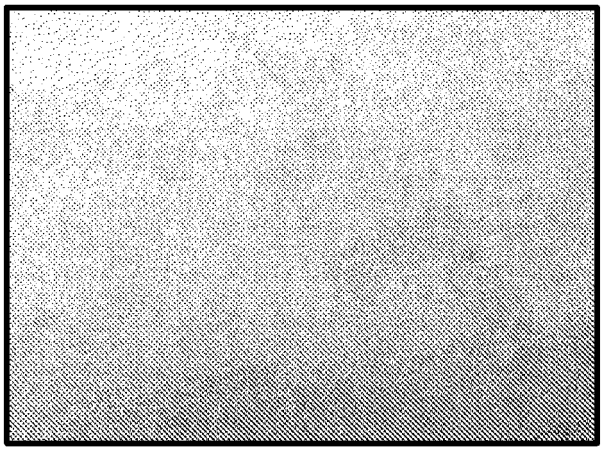


FIG. 8A

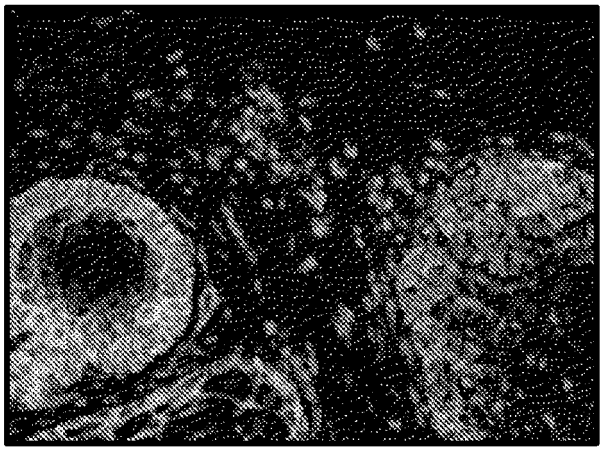


FIG. 8B

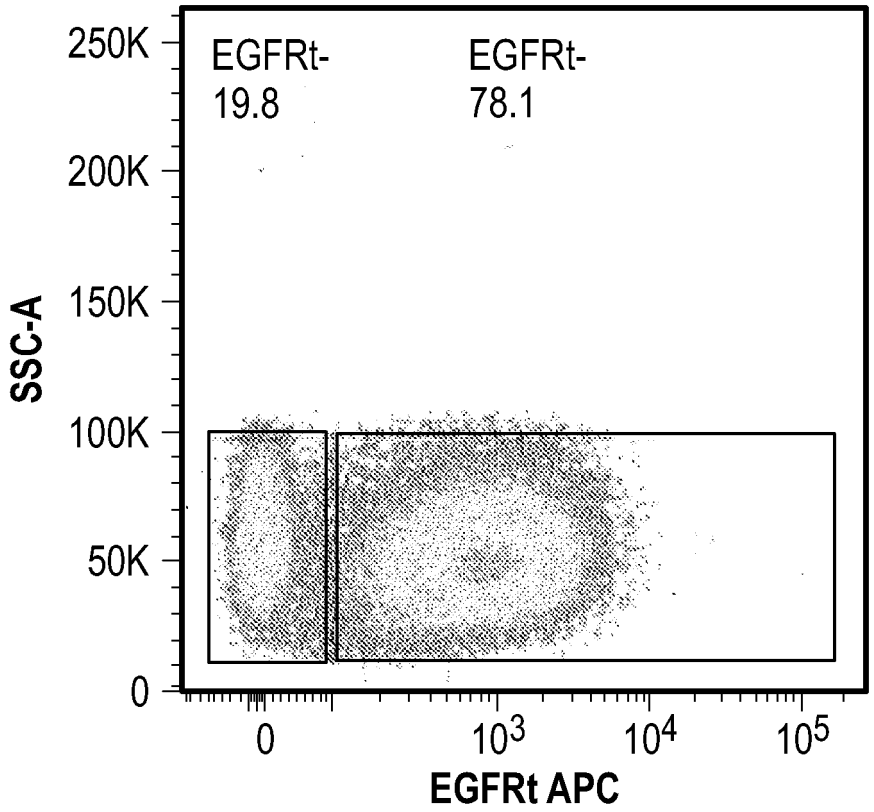


FIG. 8C

Ig or TCR Rearrangements as a Marker of MRD

ID	% of B cell reads BM pre T-cells	Day 21 BM	Day 63 BM	Later Time Point
S01	97.4	Negative (<0.0025%)	Positive (0.0016%)	Negative (<0.0002%)
S03	98.9	Positive (0.096%)	Negative (<0.0007%)	
S04	0.02	Negative (<0.0002%)	Negative (<0.0002%)	
S07	44.4	Positive (0.017%)	Positive (0.0018%)	Positive-3mo (0.0004%)
S08	88.5	Negative*(<0.0002%)	Negative (<0.0002%)	
S10	62.7	Negative (<0.0014%)	Pending	
S11	58.4/38.1	Positive (0.0071%)	Pending	

Assay performed by Adaptive Technologies. * day 42; < indicates upper bound of highest 95% confidence interval

FIG. 9

Cohort	Patient ID	Age (y)	Relapse#	Amount of disease in BM at enrollment by MPF	Current progress in study / off study
1A	14602-S01	21	2	90	In long term follow up
1A	14602-S02	22	2	0.4	In long term follow up
1A	14602-S03	21	2	90	In long term follow up
1A	14602-S04	11	2	0.04	In long term follow up
1A	14602-S05	19	2	2	In long term follow up
1A	14602-S06	4	2	54	D+42
1B	14602-S07	1	2	69	D+21
1B	14602-S08	23	1	98.6	D+7
1B	14602-S09	6	2	30	Pre T cell infusion
TBD	14602-S10	17	2	1.94	Pre T cell infusion
TBD	14602-S11	15	2	23	Pre T cell infusion
TBD	14602-S12	12	3	0.04	Pre T cell infusion

FIG. 10

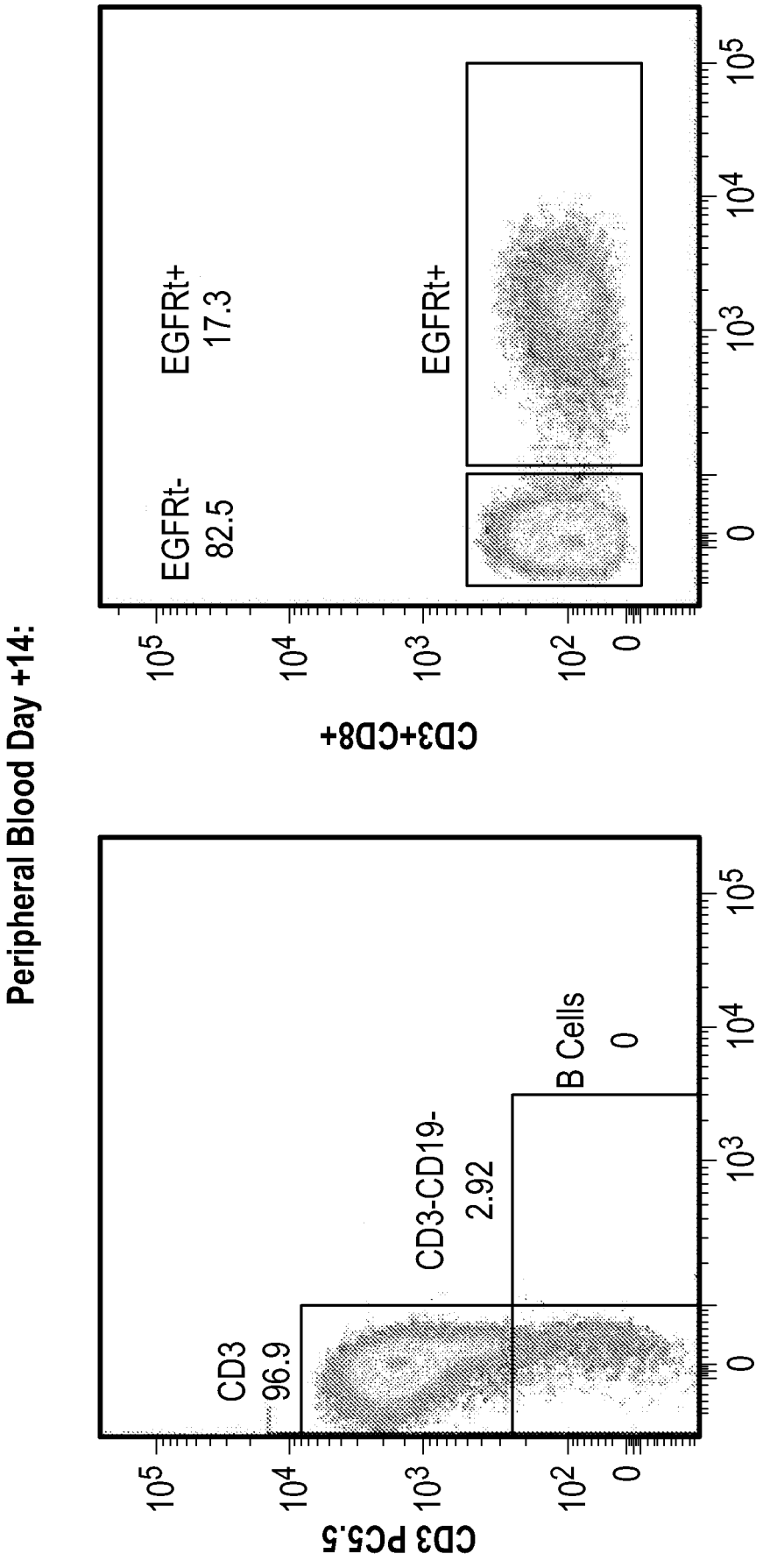


FIG. 11A

FIG. 11B

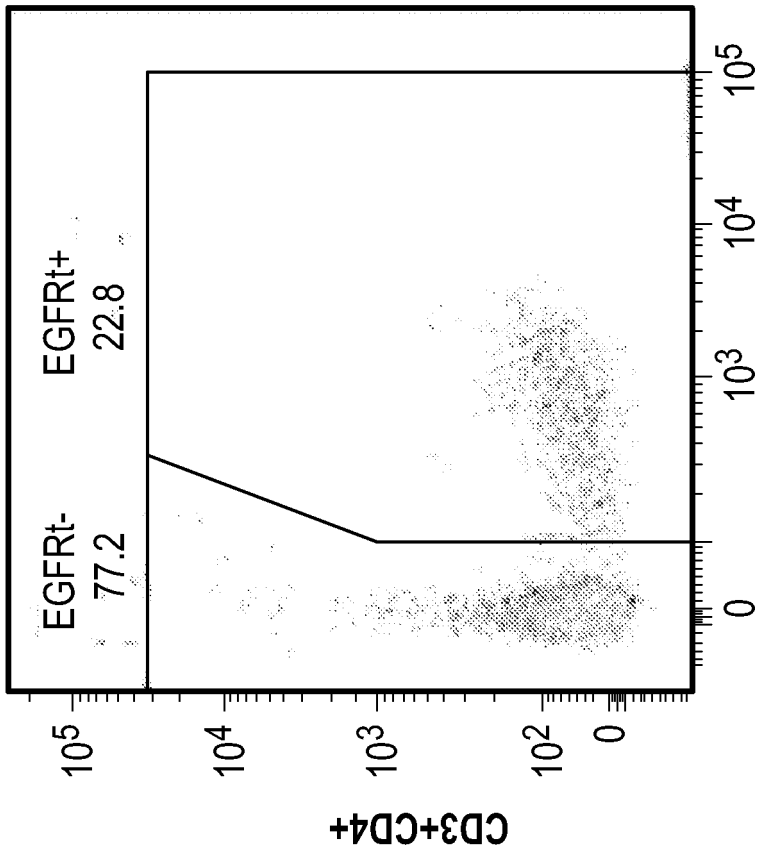


FIG. 11D

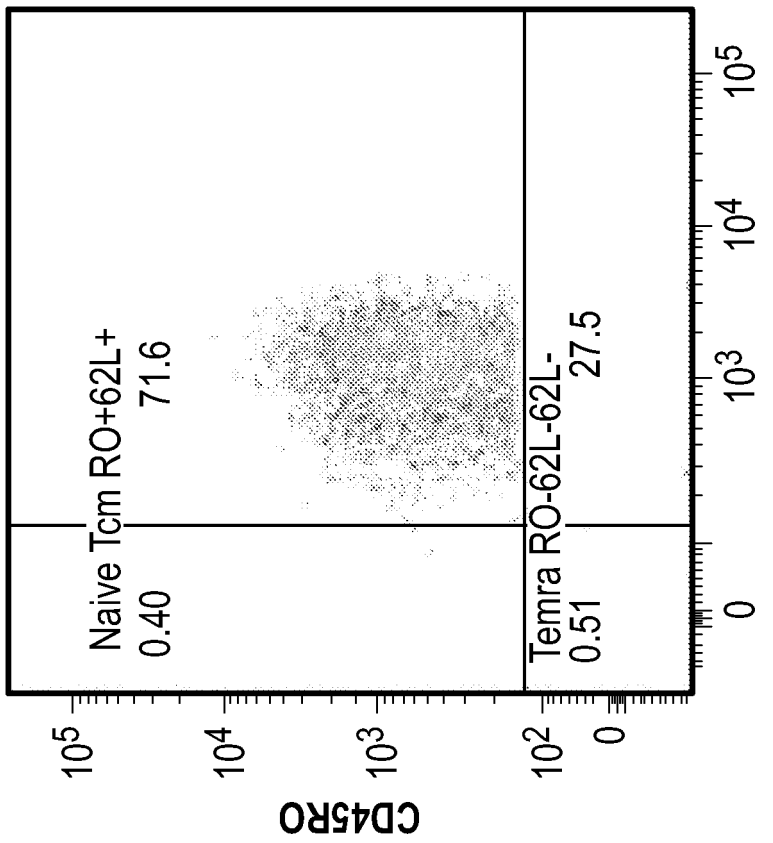


FIG. 11C

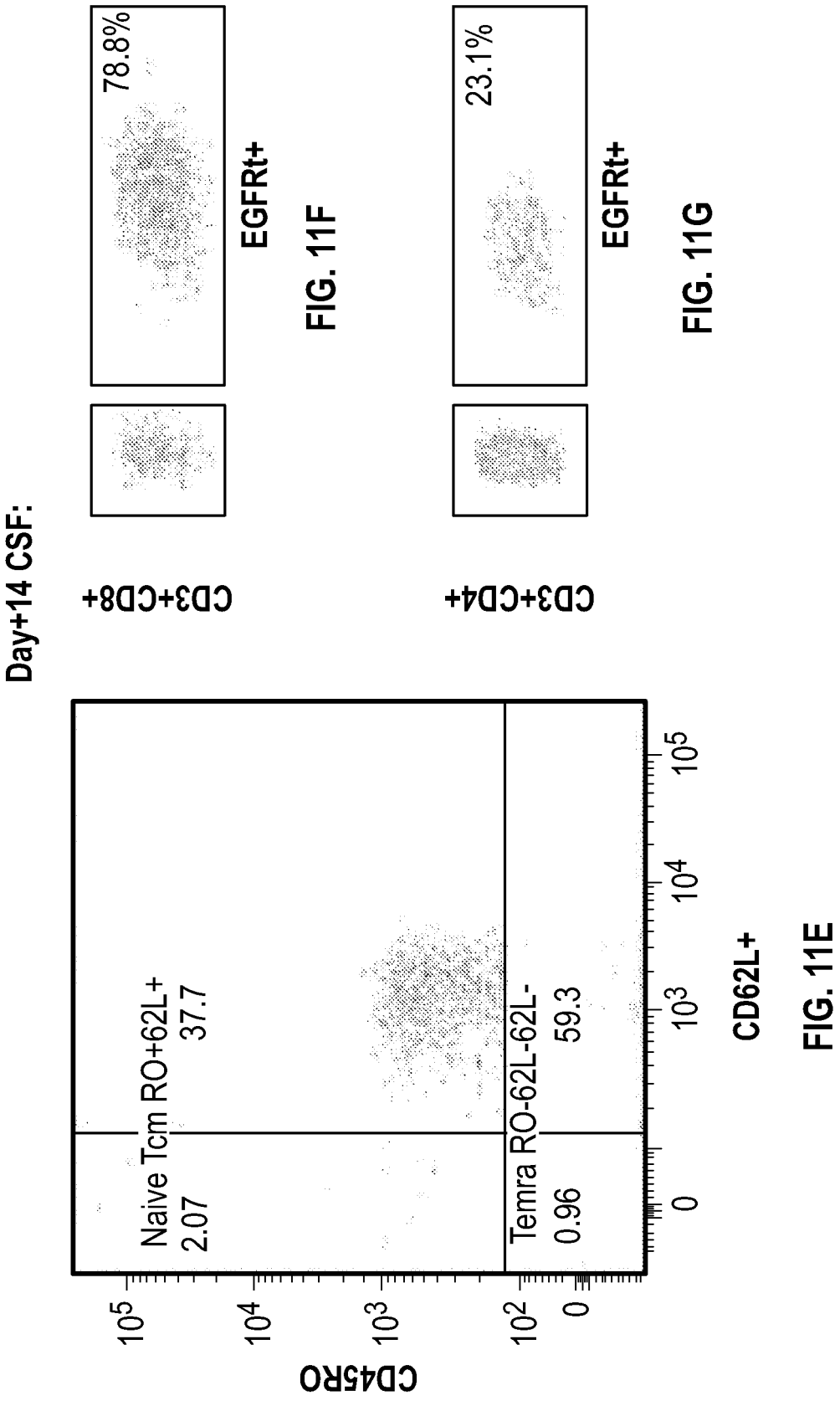


FIG. 11F

FIG. 11G

FIG. 11E

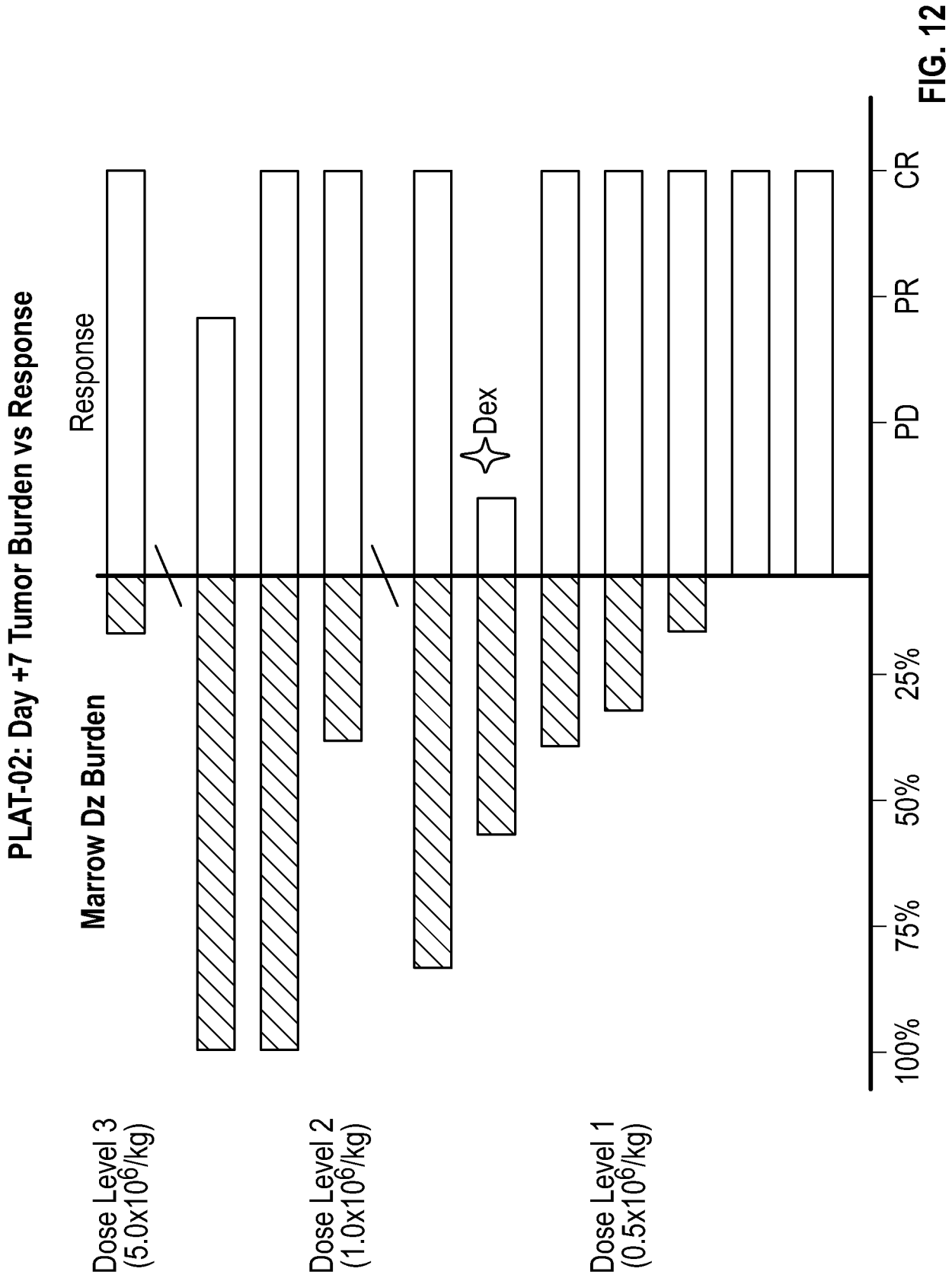

PLAT-02: Day +7 Tumor Burden vs Response
Marrow Dz Burden
Response
Dex
100%
75%
50%
25%
PD
PR
CR
Dose Level 3 (5.0x10^6/kg)
Dose Level 2 (1.0x10^6/kg)
Dose Level 1 (0.5x10^6/kg)

FIG. 12

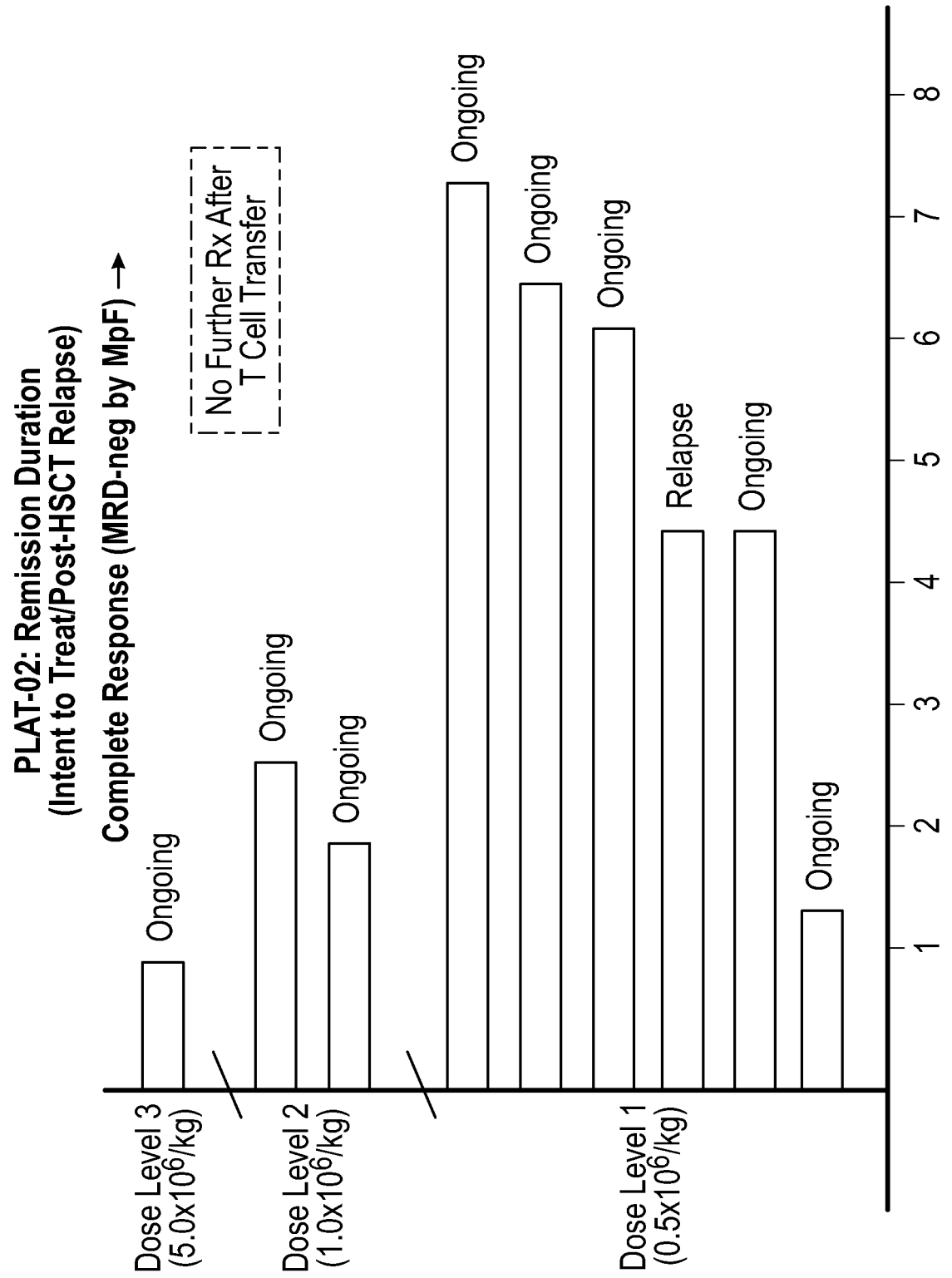

PLAT-02: Remission Duration
(Intent to Treat/Post-HSCT Relapse)
Complete Response (MRD-neg by MpF) →
No Further Rx After
T Cell Transfer
Ongoing
Ongoing
Ongoing
Ongoing
Ongoing
Ongoing
Relapse
Ongoing
Ongoing
Dose Level 3
(5.0x10^6/kg)
Dose Level 2
(1.0x10^6/kg)
Dose Level 1
(0.5x10^6/kg)
1
2
3
4
5
6
7
8
(Months)

FIG. 13

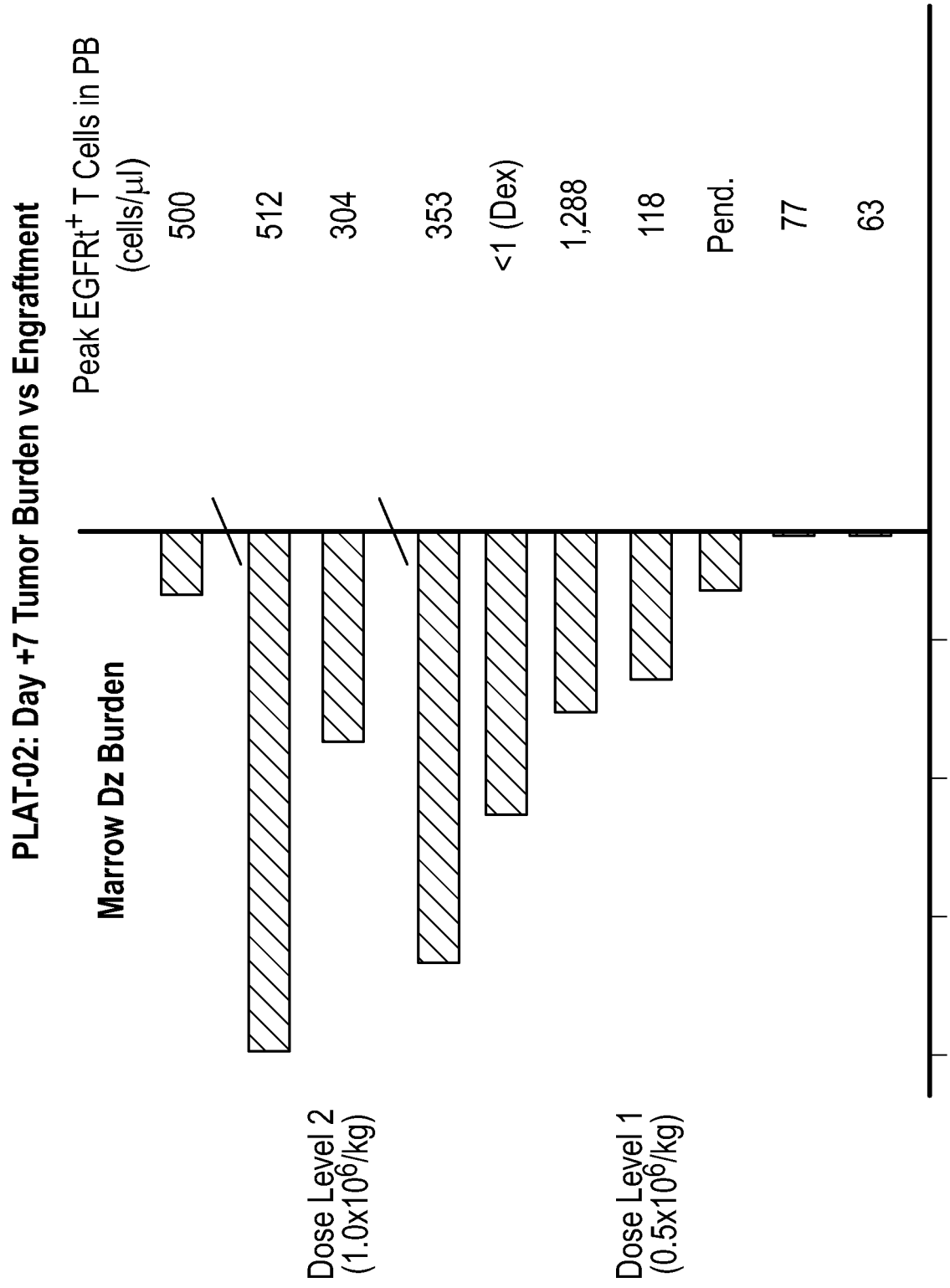

PLAT-02: Day +7 Tumor Burden vs Engraftment
Marrow Dz Burden
Peak EGFRt+ T Cells in PB (cells/µl)
500
512
304
353
<1 (Dex)
1,288
118
Pend.
77
63
Dose Level 2 (1.0x10^6/kg)
Dose Level 1 (0.5x10^6/kg)
100%
75%
50%
25%

FIG. 14

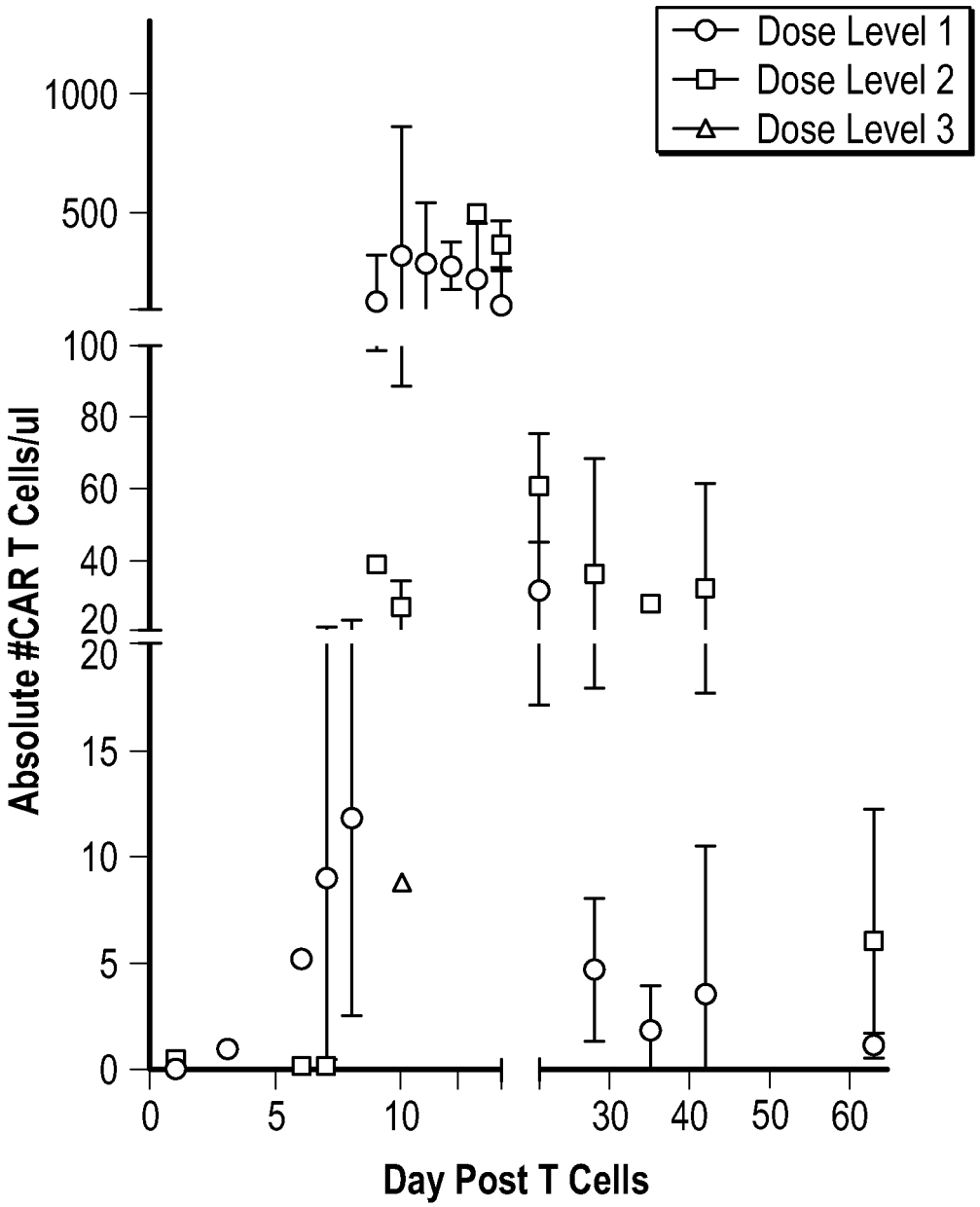

PLAT-02:Magnitude and Duration of CAR/EGFRt+ T Cell Persistence
Dose Level Absolute #CAR T-Cells/UL
Dose Level 1
Dose Level 2
Dose Level 3
Absolute #CAR T Cells/ul
1000
500
100
80
60
40
20
20
15
10
5
0
0
5
10
30
40
50
60
Day Post T Cells

FIG. 15

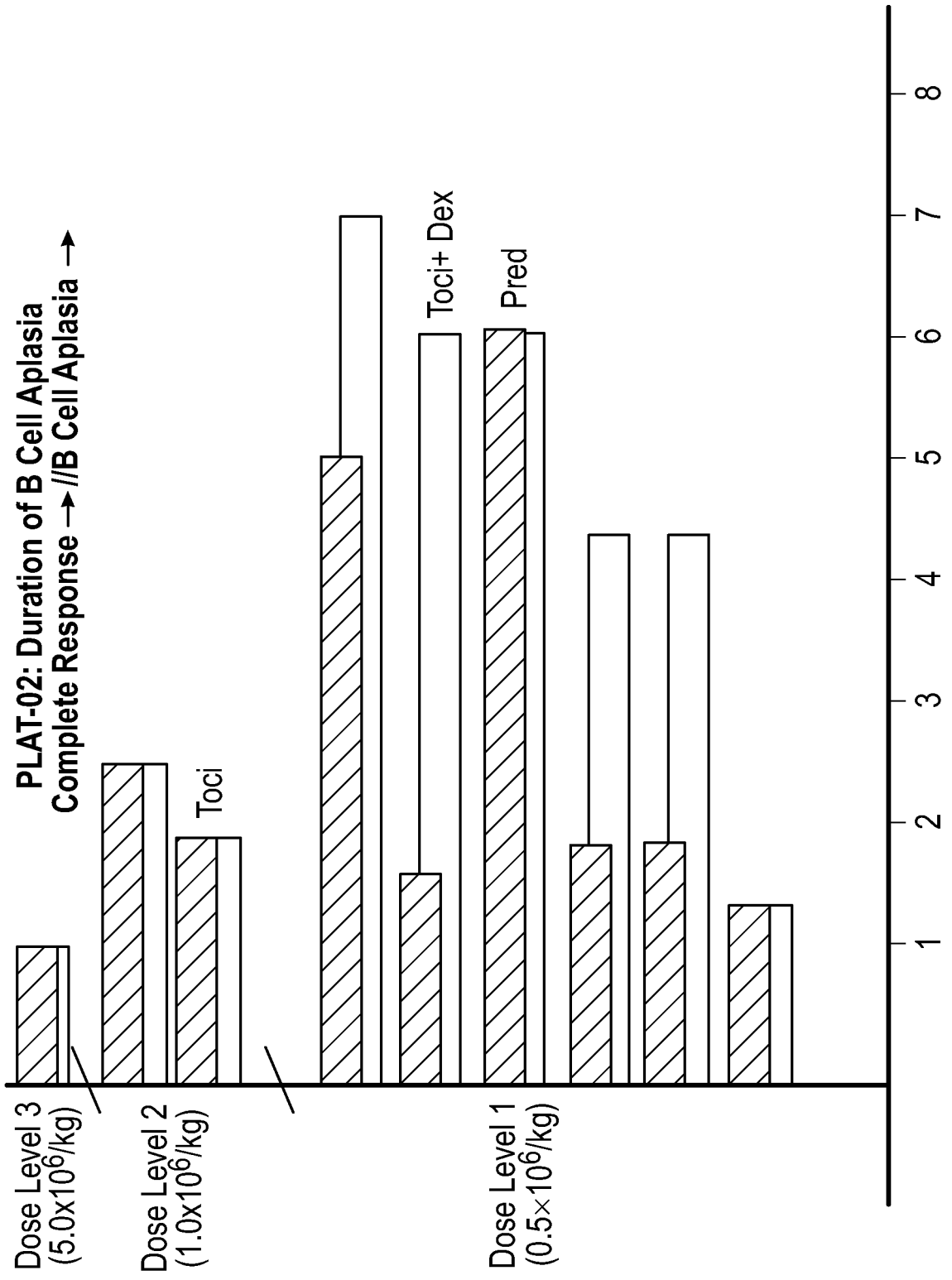

PLAT-02: Duration of B Cell Aplasia
Complete Response → //B Cell Aplasia →
Dose Level 3 (5.0x10^6/kg)
Dose Level 2 (1.0x10^6/kg)
Toci
Dose Level 1 (0.5×10^6/kg)
Toci+ Dex
Pred
1
2
3
4
5
6
7
8
(Months)

FIG. 16

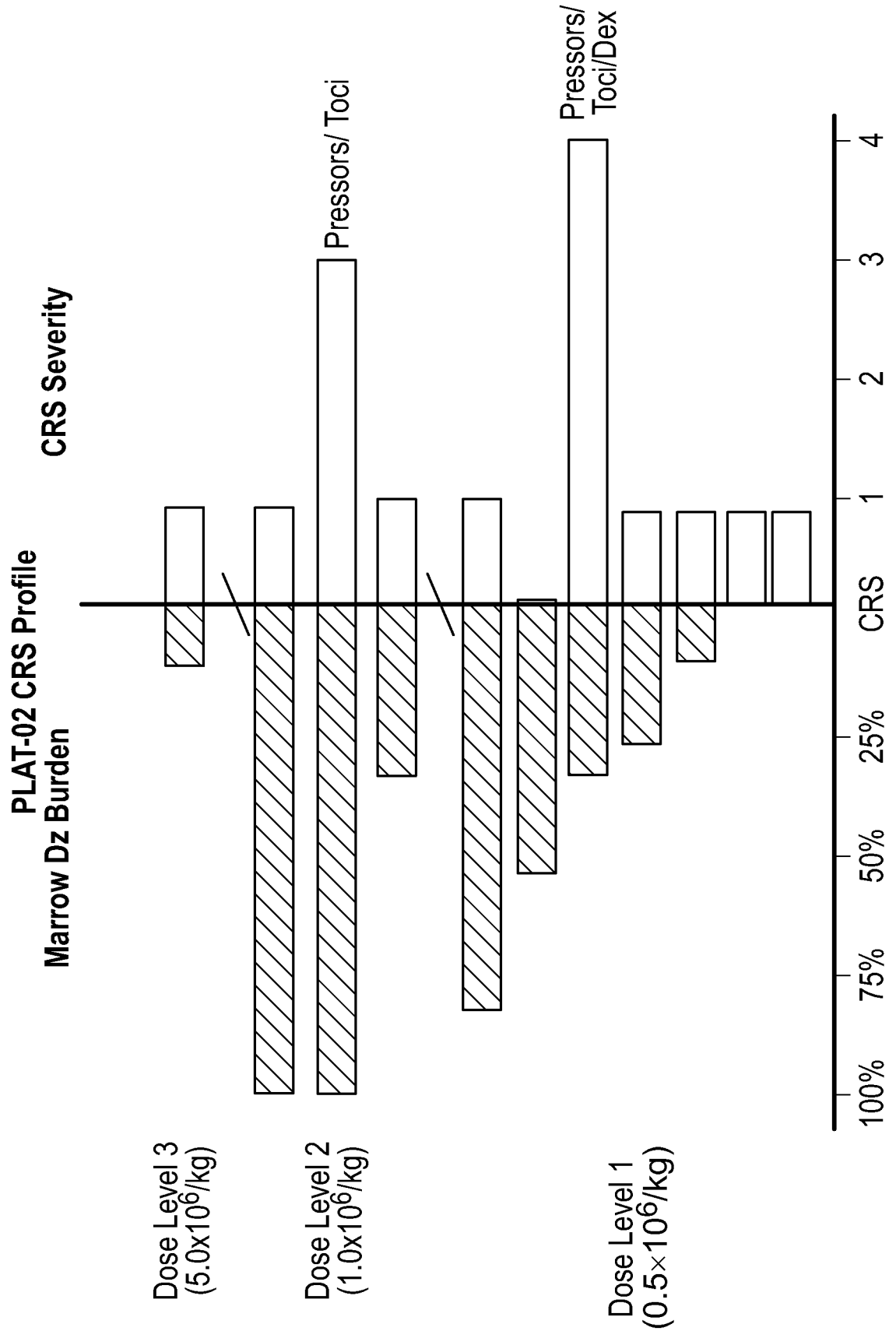

PLAT-02 CRS Profile
Marrow Dz Burden
CRS Severity
Pressors/ Toci
Pressors/
Toci/Dex
Dose Level 3
(5.0x10^6/kg)
Dose Level 2
(1.0x10^6/kg)
Dose Level 1
(0.5×10^6/kg)
100%
75%
50%
25%
CRS
1
2
3
4

FIG. 17

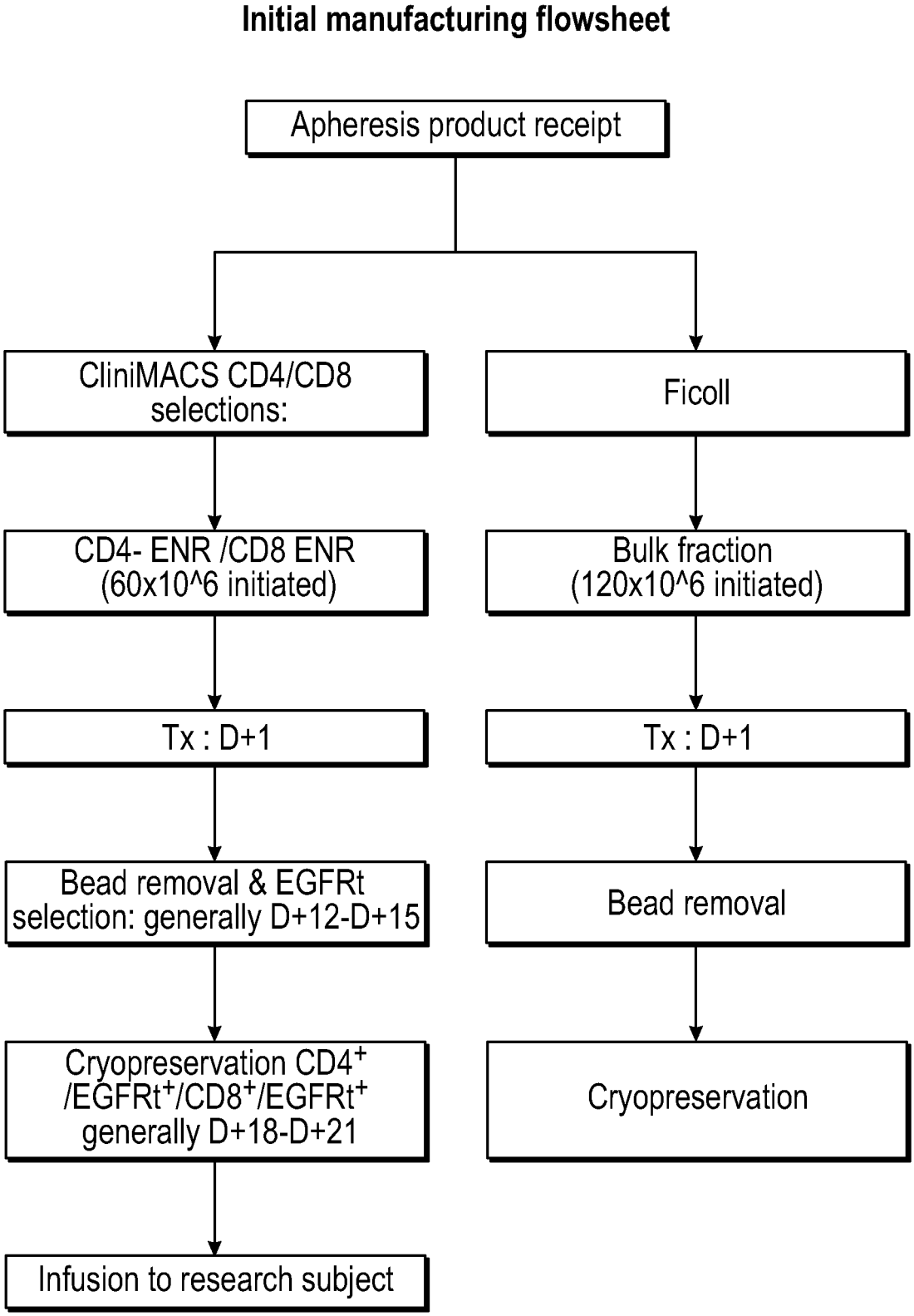

Initial manufacturing flowsheet
Apheresis product receipt
CliniMACS CD4/CD8 selections:
Ficoll
CD4- ENR /CD8 ENR (60x10^6 initiated)
Bulk fraction (120x10^6 initiated)
Tx : D+1
Tx : D+1
Bead removal & EGFRt selection: generally D+12-D+15
Bead removal
Cryopreservation CD4+ /EGFRt+/CD8+/EGFRt+ generally D+18-D+21
Cryopreservation
Infusion to research subject

FIG. 18A

Current manufacturing flowsheet

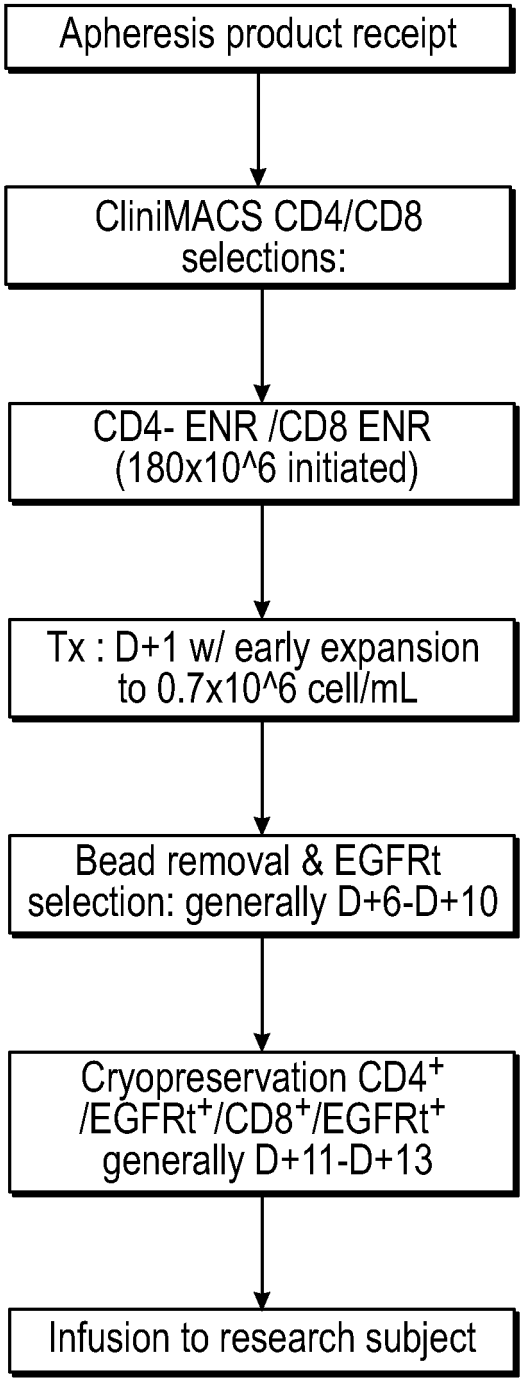


FIG. 18B

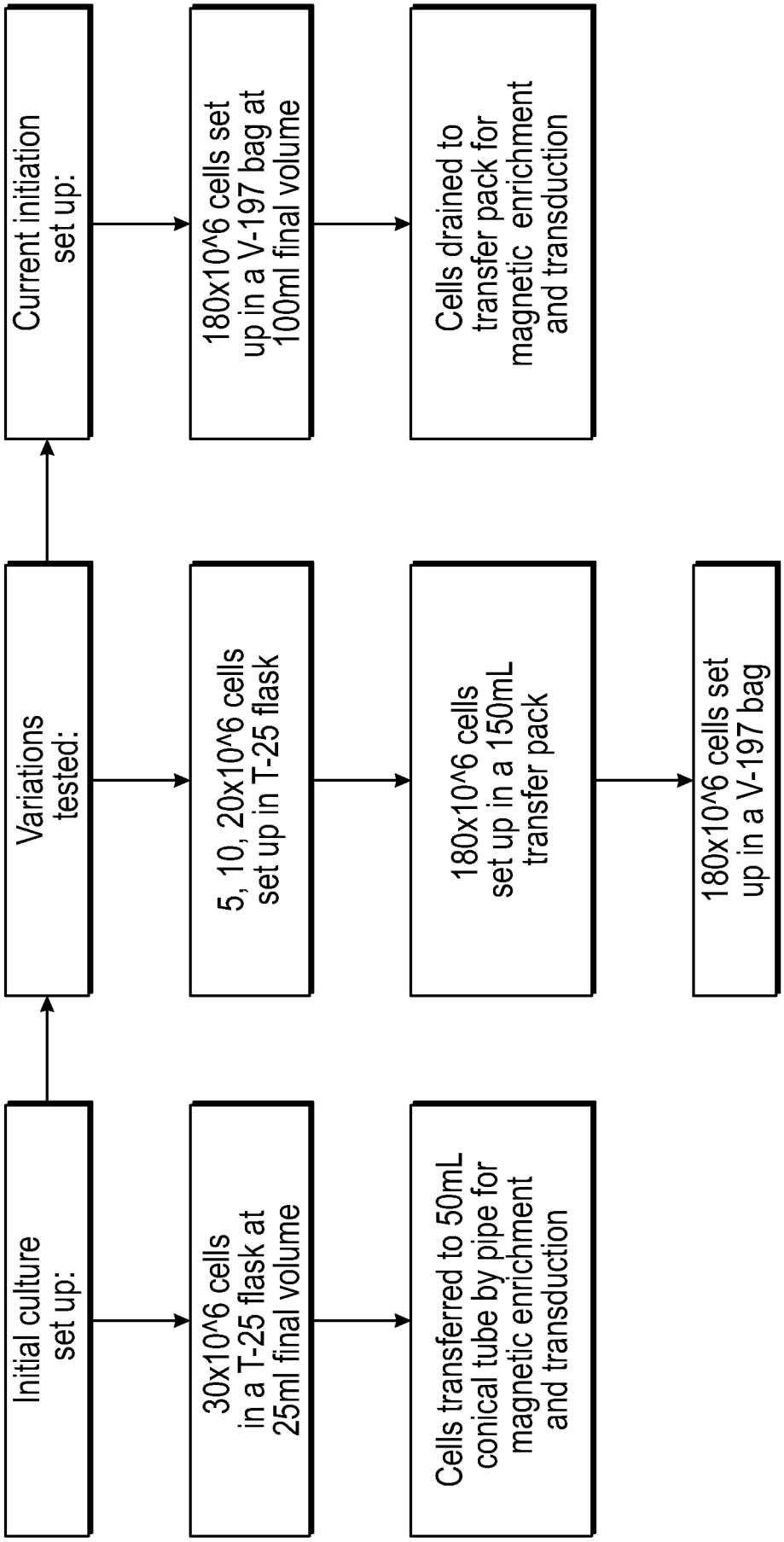

Initial culture set up:
30x10^6 cells in a T-25 flask at 25ml final volume
Cells transferred to 50mL conical tube by pipe for magnetic enrichment and transduction
Variations tested:
5, 10, 20x10^6 cells set up in T-25 flask
180x10^6 cells set up in a 150mL transfer pack
180x10^6 cells set up in a V-197 bag
Current initiation set up:
180x10^6 cells set up in a V-197 bag at 100ml final volume
Cells drained to transfer pack for magnetic enrichment and transduction

FIG. 19

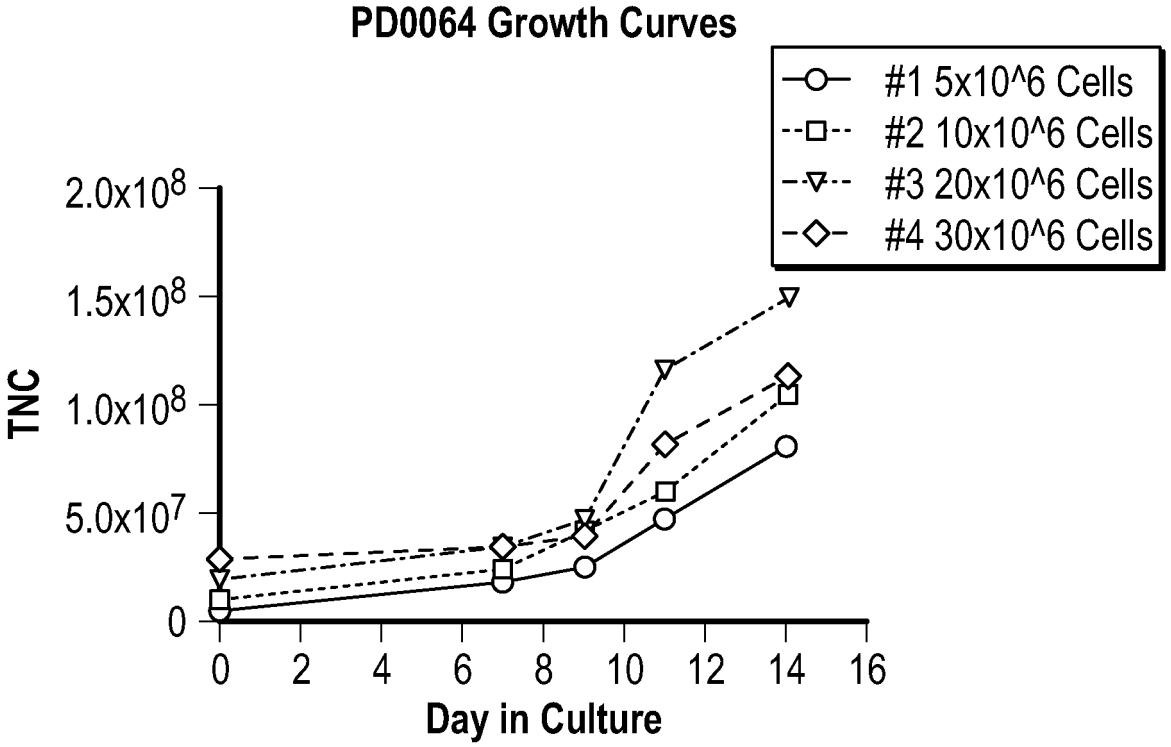


FIG. 20A

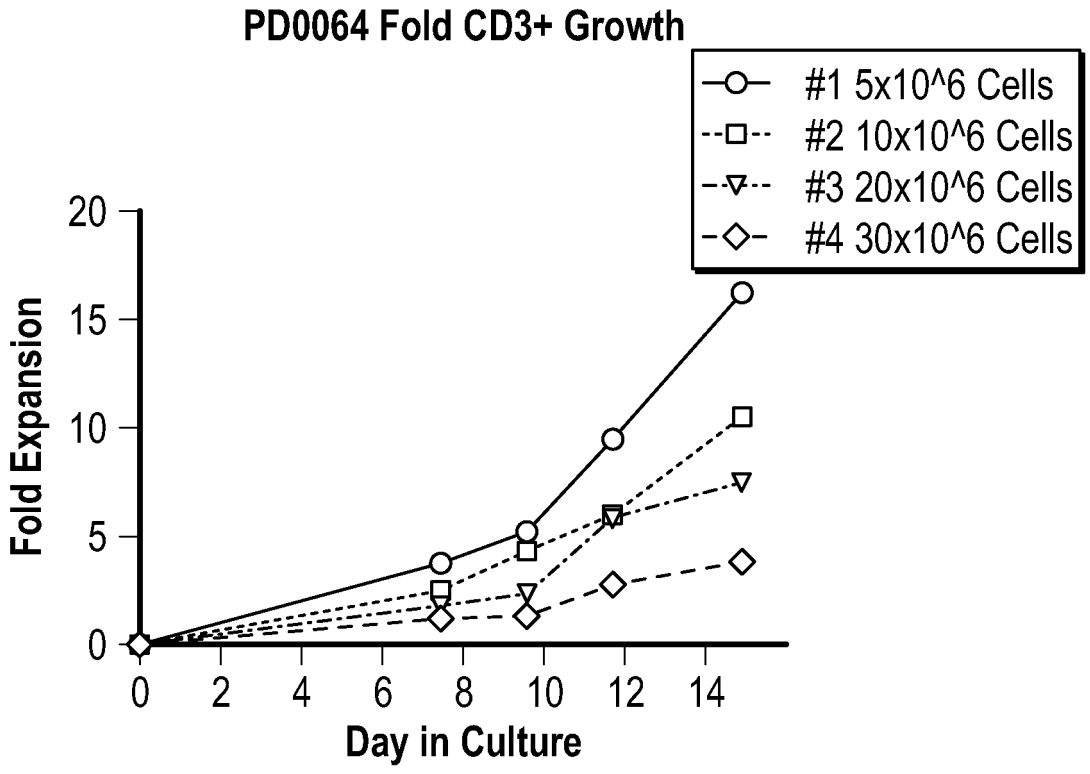


FIG. 20B

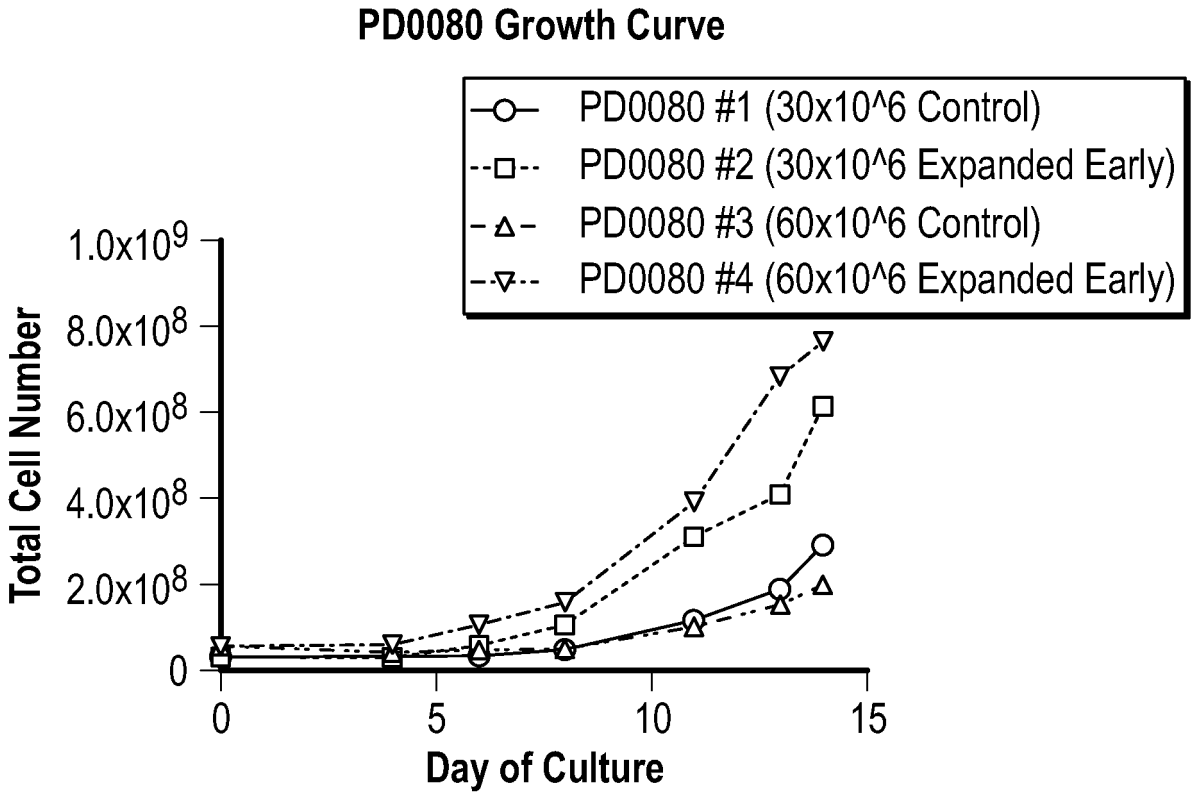


FIG. 20C

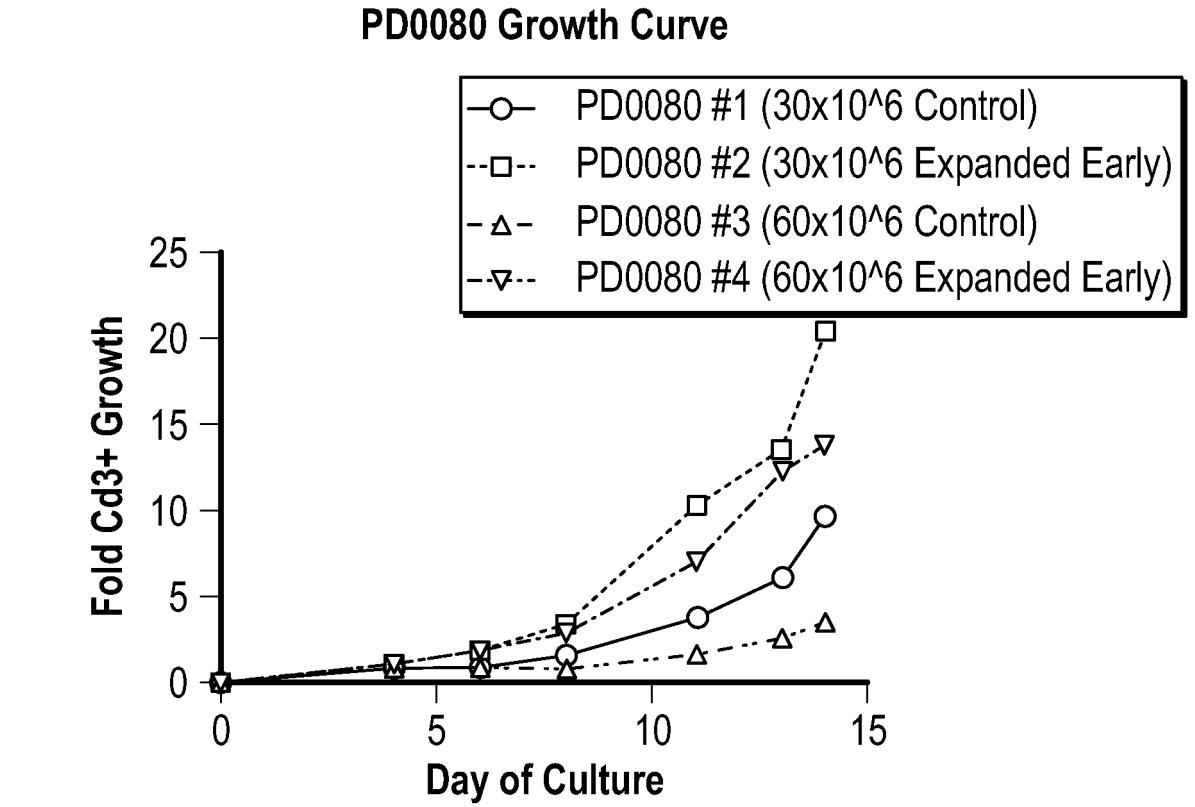


FIG. 20D

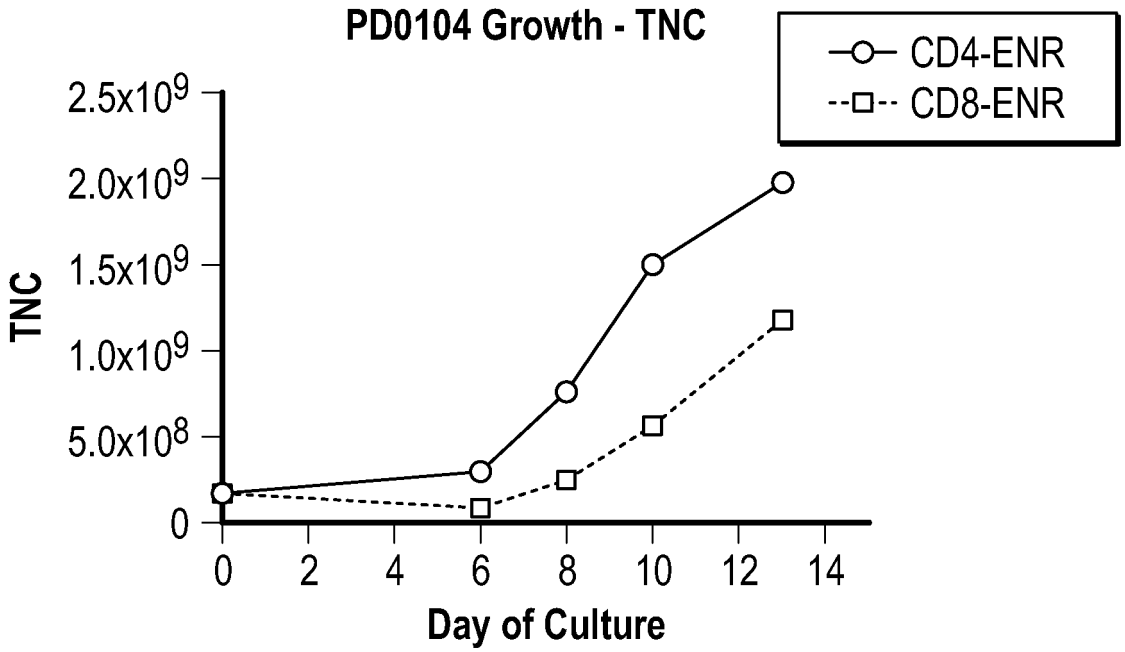


FIG. 21A

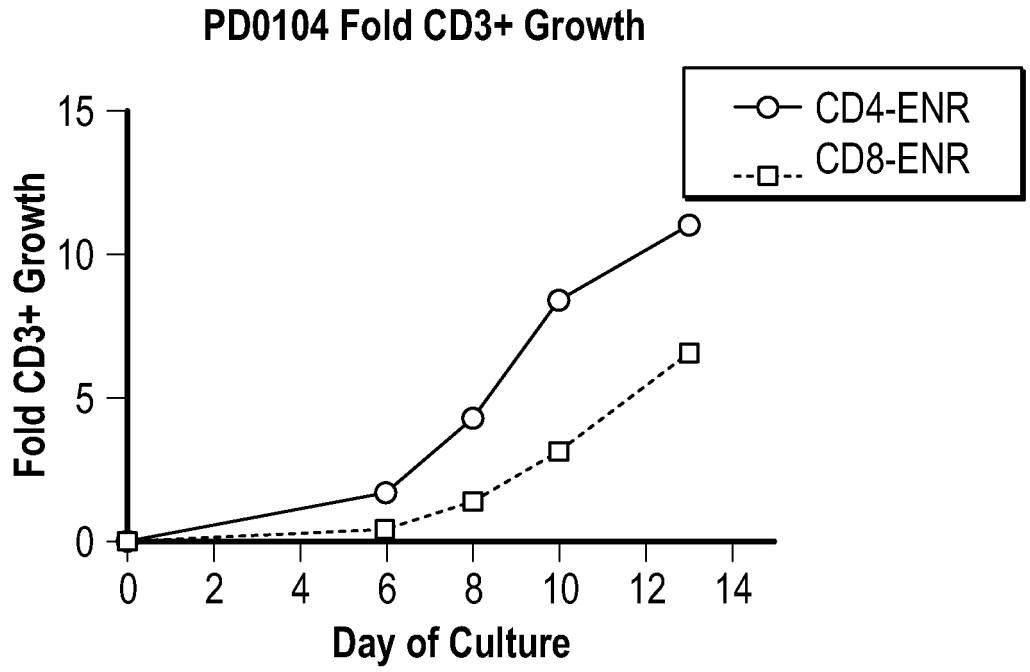


FIG. 21B

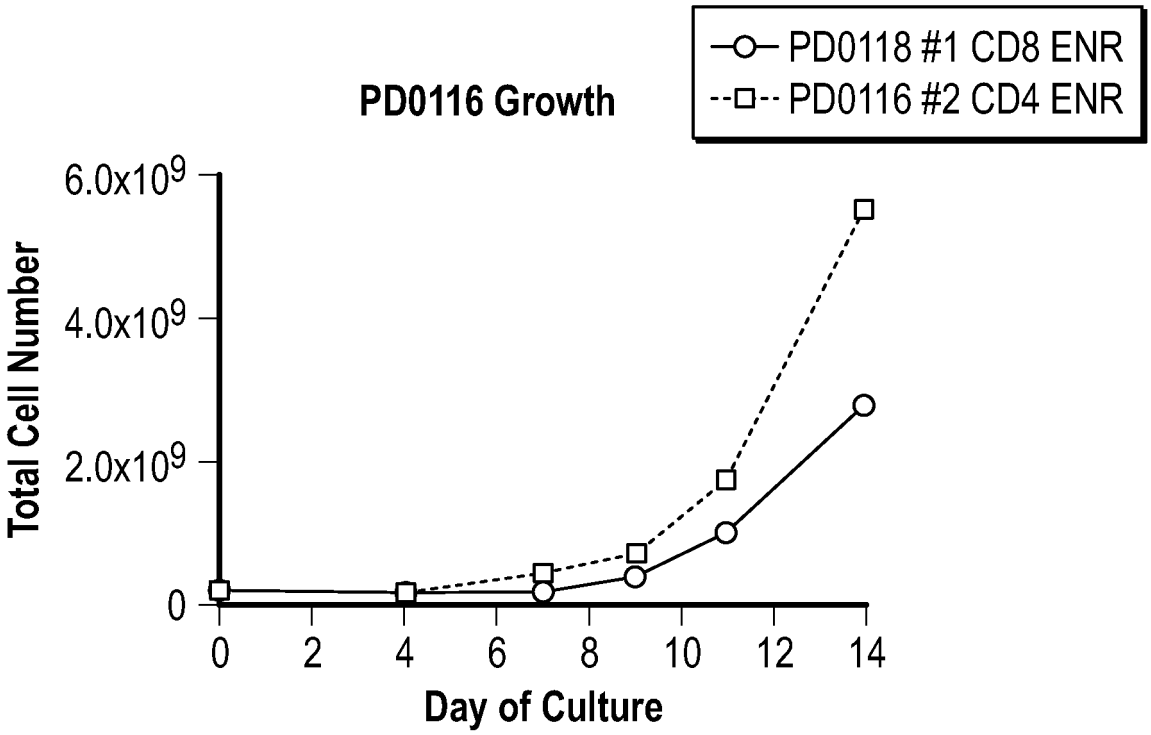


FIG. 21C

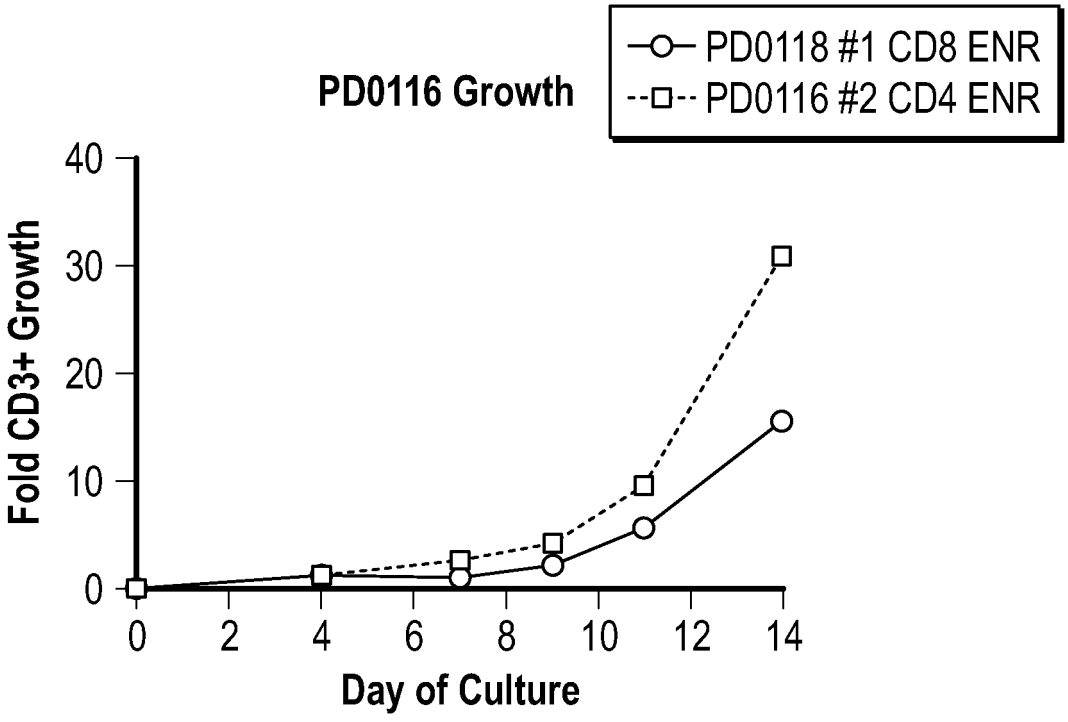


FIG. 21D

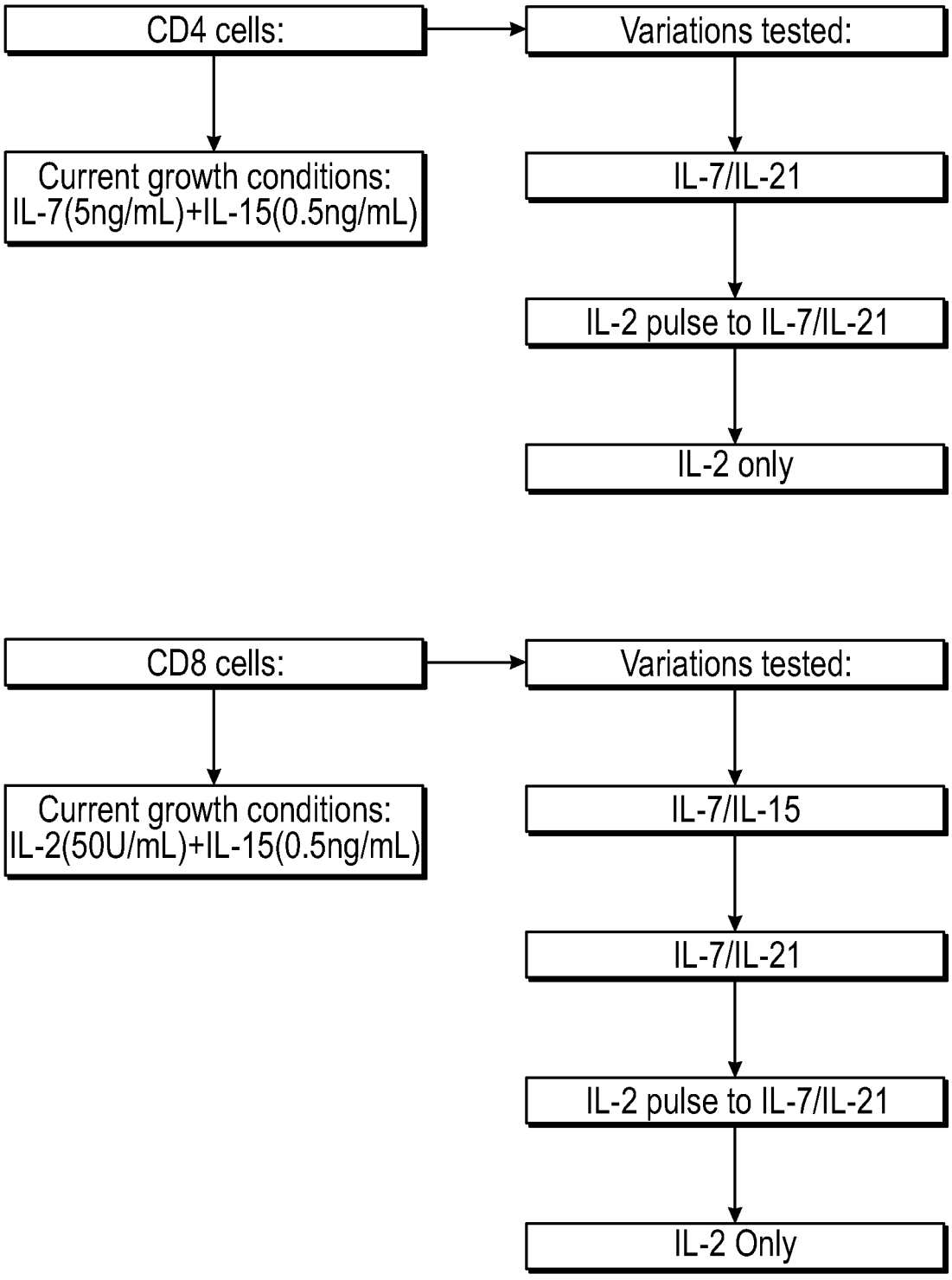

CD4 cells:
Variations tested:
Current growth conditions:
IL-7(5ng/mL)+IL-15(0.5ng/mL)
IL-7/IL-21
IL-2 pulse to IL-7/IL-21
IL-2 only
CD8 cells:
Variations tested:
Current growth conditions:
IL-2(50U/mL)+IL-15(0.5ng/mL)
IL-7/IL-15
IL-7/IL-21
IL-2 pulse to IL-7/IL-21
IL-2 Only

FIG. 22

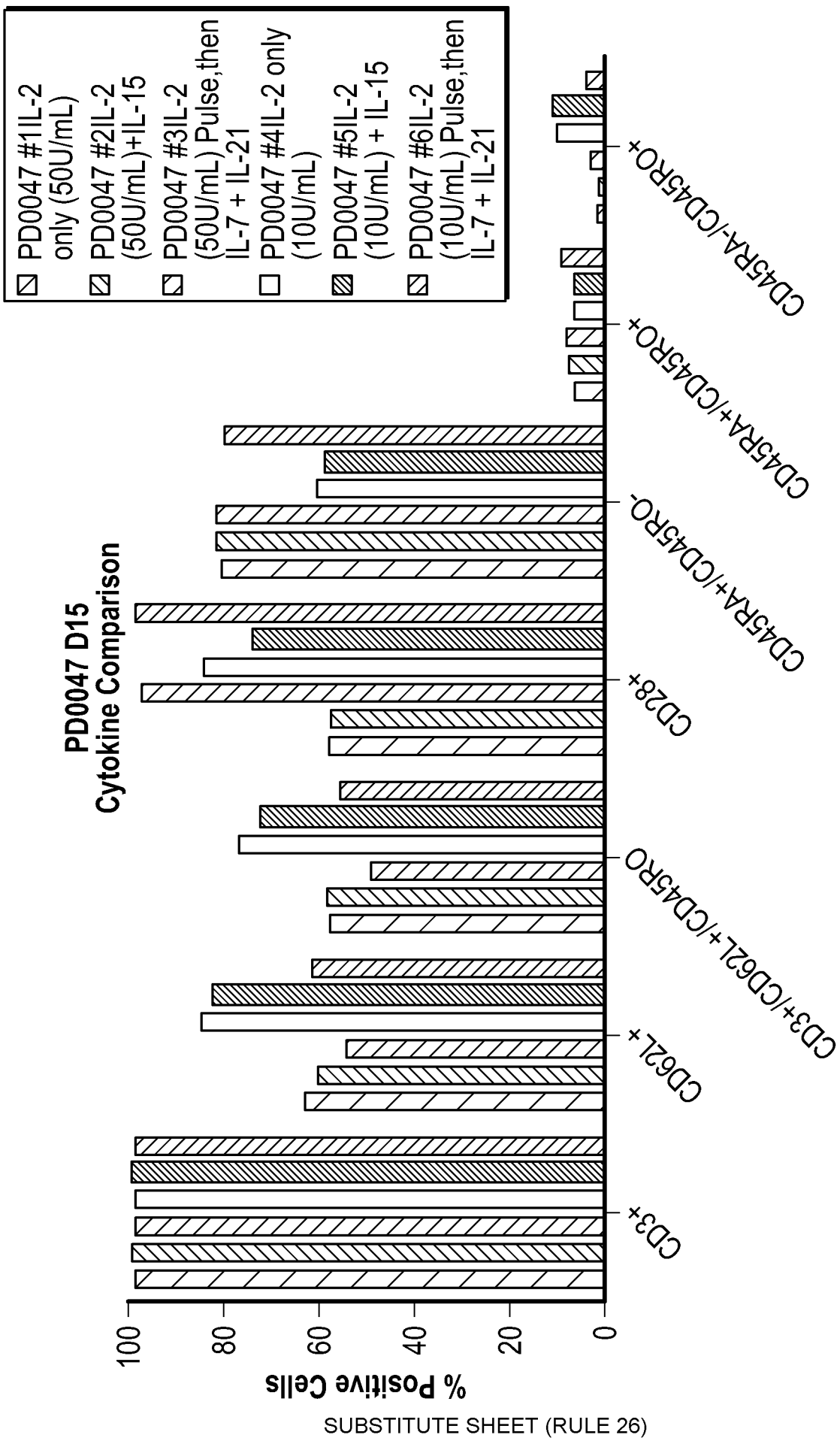

PD0047 D15
Cytokine Comparison
% Positive Cells
100
80
60
40
20
0
CD3+
CD62L+
CD3+/CD62L+/CD45RO-
CD28+
CD45RA+/CD45RO-
CD45RA+/CD45RO+
CD45RA-/CD45RO+
PD0047 #1IL-2 only (50U/mL)
PD0047 #2IL-2 (50U/mL)+IL-15
PD0047 #3IL-2 (50U/mL) Pulse,then IL-7 + IL-21
PD0047 #4IL-2 only (10U/mL)
PD0047 #5IL-2 (10U/mL) + IL-15
PD0047 #6IL-2 (10U/mL) Pulse,then IL-7 + IL-21

FIG. 23A

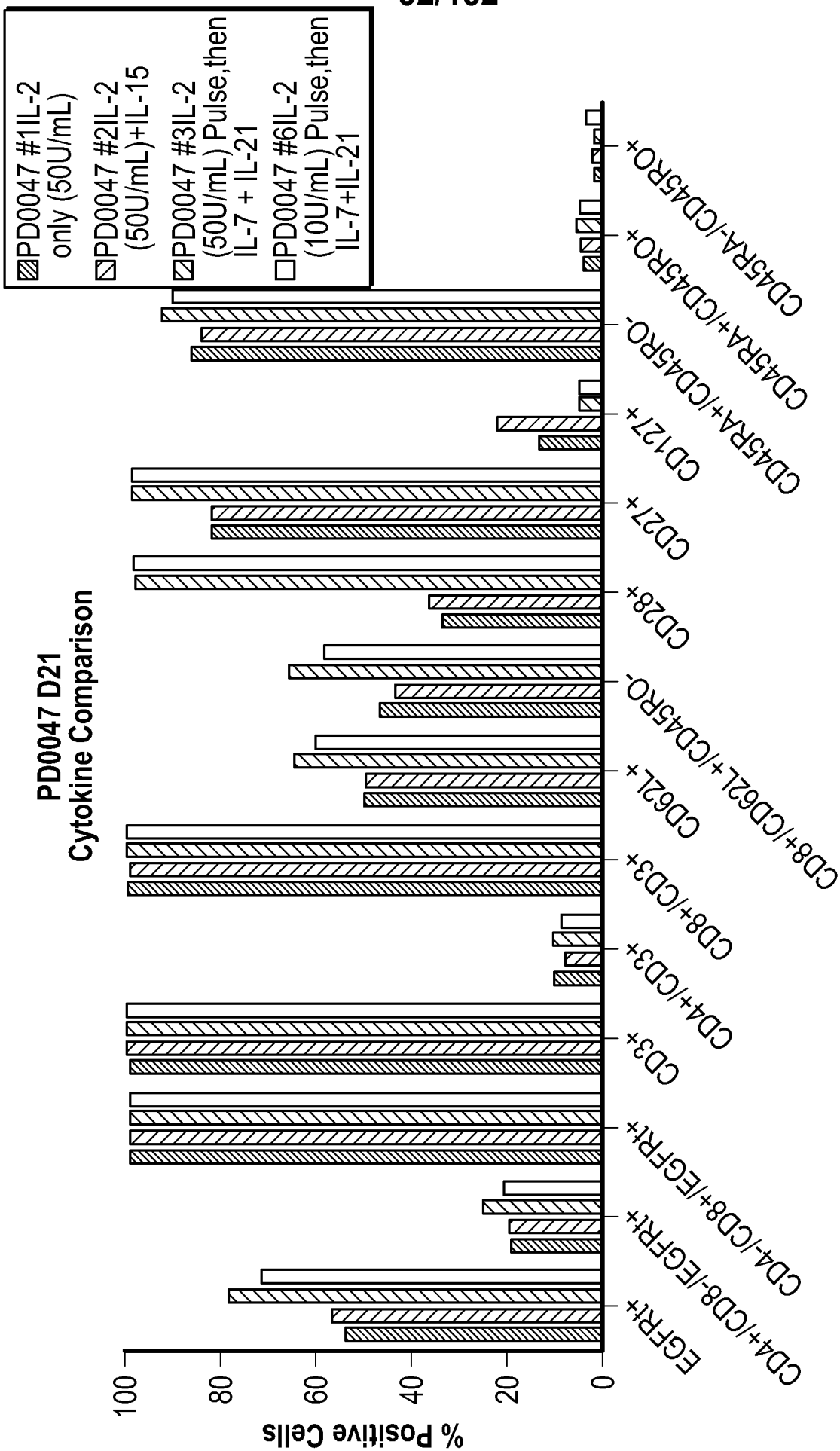

PD0047 D21
Cytokine Comparison
PD0047 #1IL-2 only (50U/mL)
PD0047 #2IL-2 (50U/mL)+IL-15
PD0047 #3IL-2 (50U/mL) Pulse,then IL-7 + IL-21
PD0047 #6IL-2 (10U/mL) Pulse,then IL-7+IL-21
% Positive Cells
100
80
60
40
20
0
EGFRt+
CD4+/CD8-/EGFRt+
CD4-/CD8+/EGFRt+
CD3+
CD4+/CD3+
CD8+/CD3+
CD8+/CD62L+/CD45RO-
CD62L+
CD28+
CD27+
CD127+
CD45RA+/CD45RO-
CD45RA+/CD45RO+
CD45RA-/CD45RO+
PD0047
Starting Material: PD0038 CD8 Enriched Tx: D1
Vector: ZRX-014
Note: #4 and #5 terminated on D18

FIG. 23B

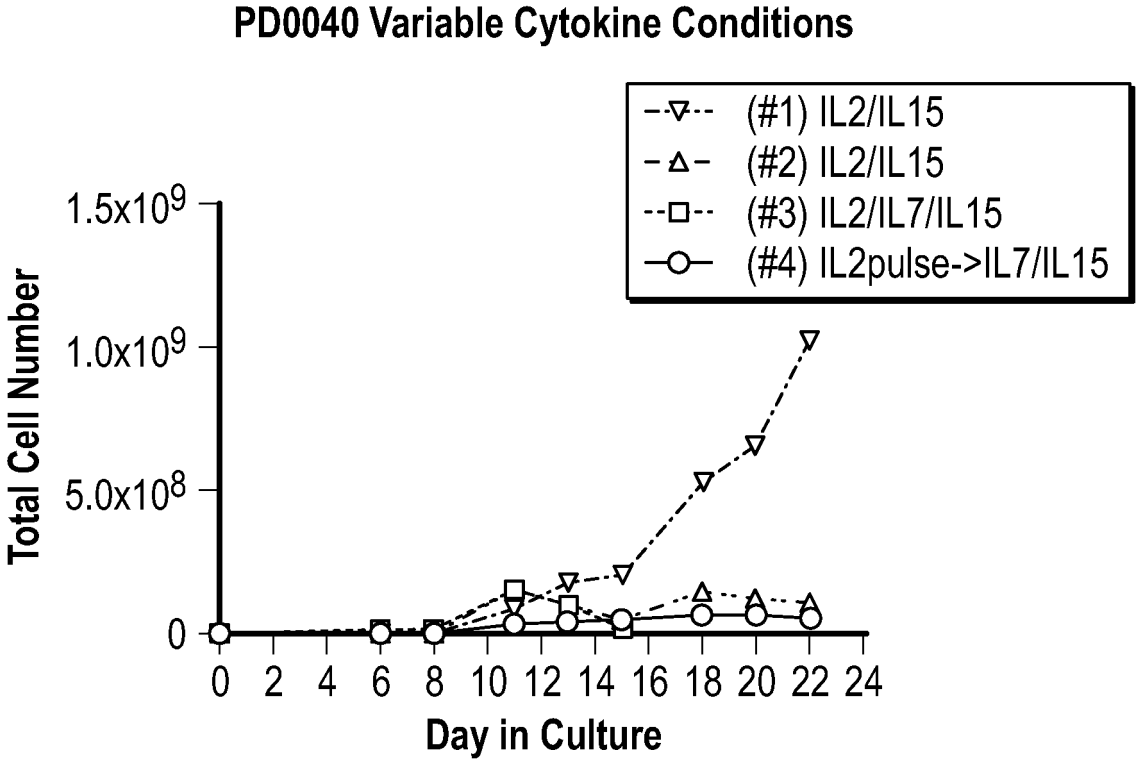


FIG. 23C

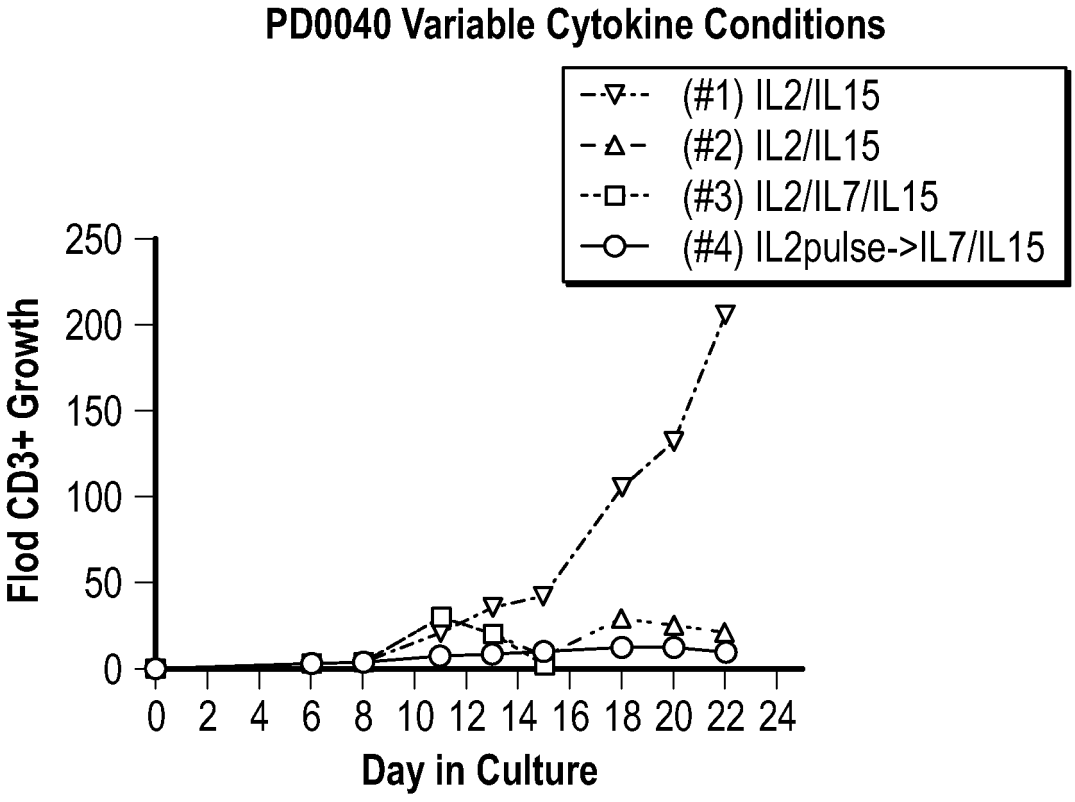


FIG. 23D

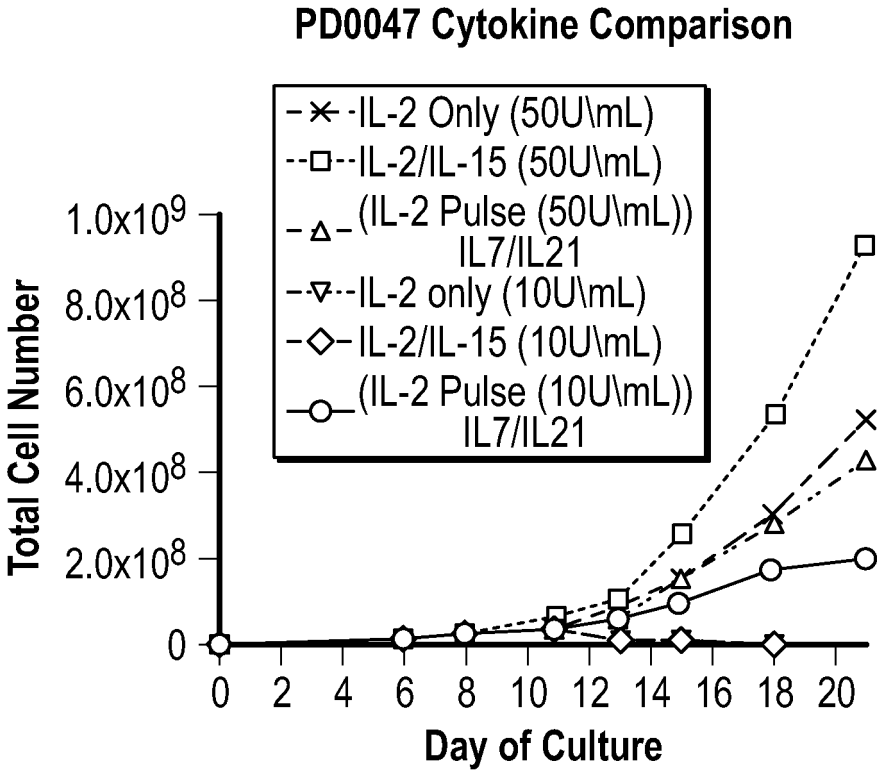


FIG. 23E

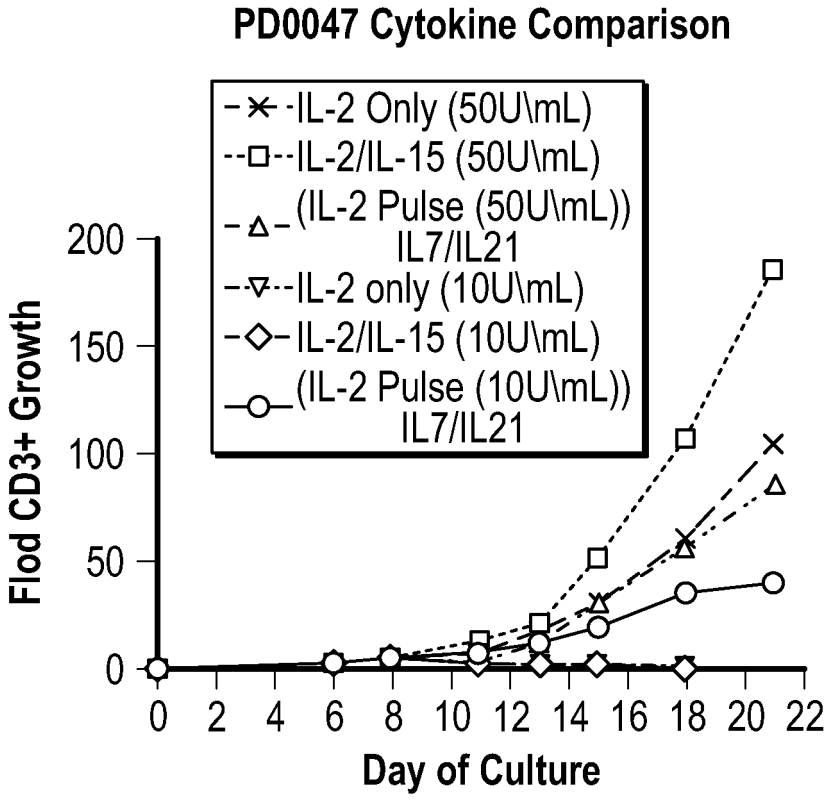


FIG. 23F

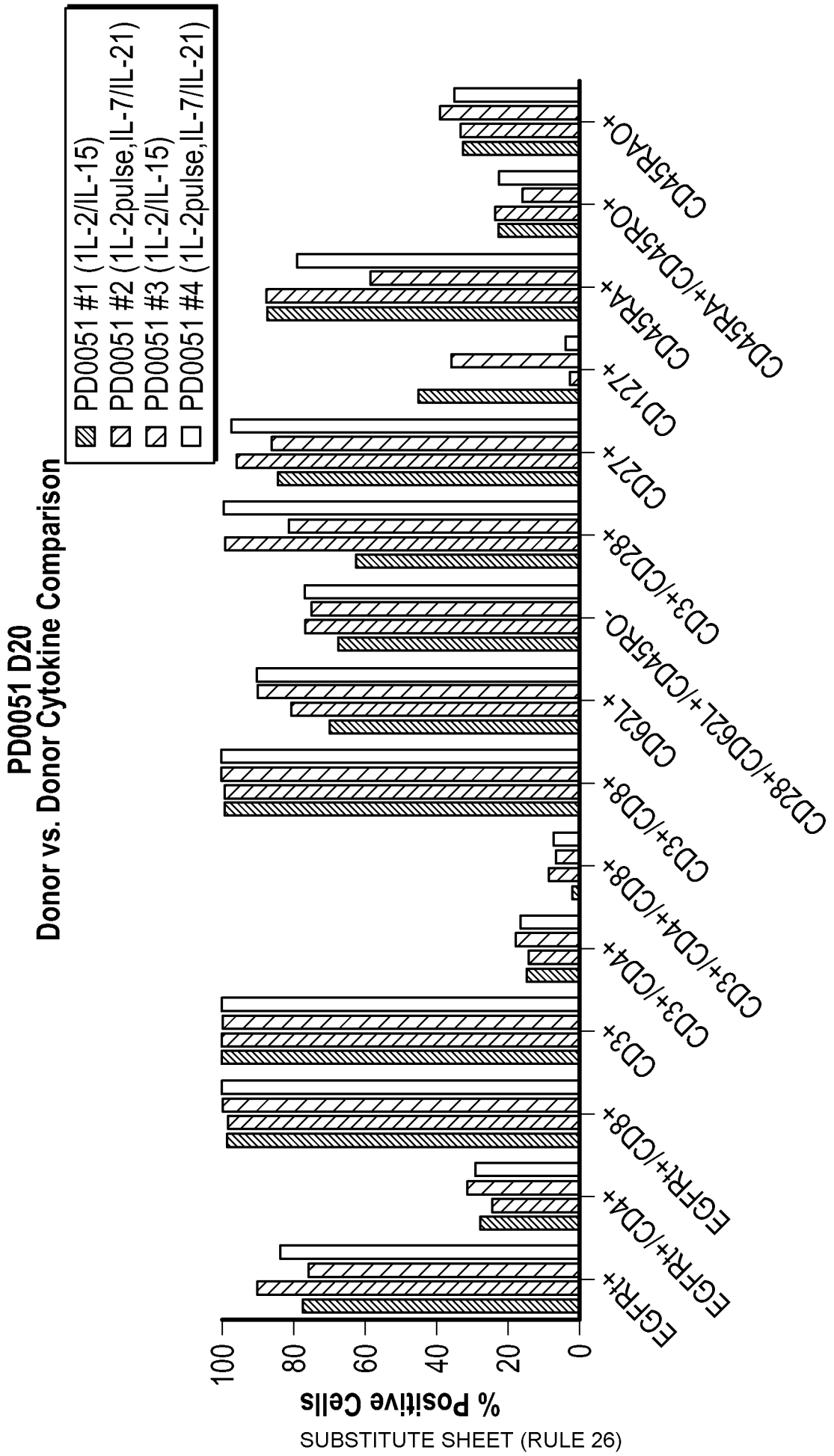

PD0051 D20
Donor vs. Donor Cytokine Comparison
PD0051 #1 (1L-2/IL-15)
PD0051 #2 (1L-2pulse,IL-7/IL-21)
PD0051 #3 (1L-2/IL-15)
PD0051 #4 (1L-2pulse,IL-7/IL-21)
% Positive Cells
100
80
60
40
20
0
EGFRt+
EGFRt+/CD4+
EGFRt+/CD8+
CD3+
CD3+/CD4+
CD3+/CD4+/CD8+
CD3+/CD8+
CD62L+
CD28+/CD62L+/CD45RO-
CD3+/CD28+
CD27+
CD127+
CD45RA+
CD45RA+/CD45RO+
CD45RAO+

FIG. 24A

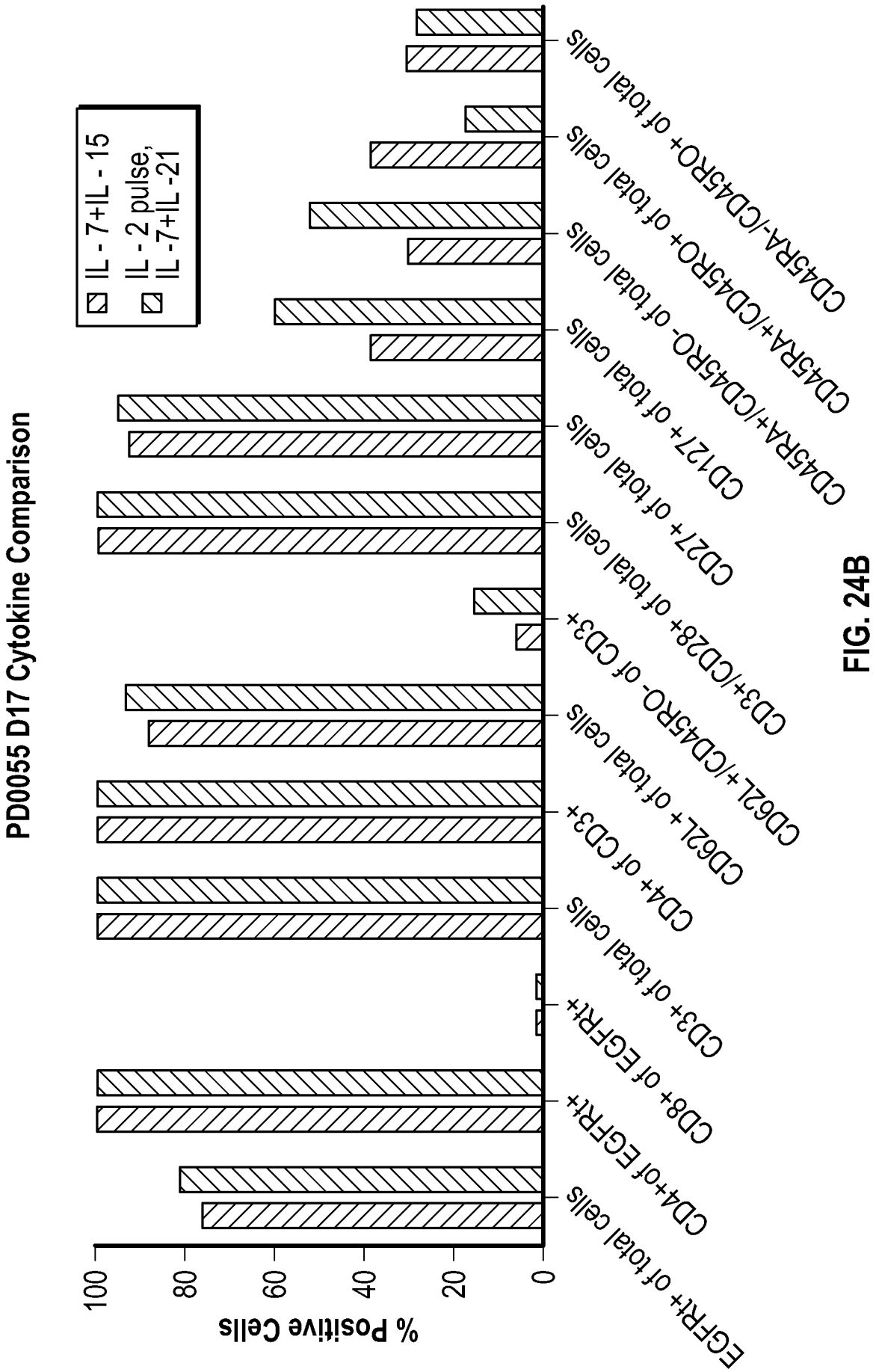

PD0055 D17 Cytokine Comparison
IL - 7+IL - 15
IL - 2 pulse, IL -7+IL -21
% Positive Cells
0
20
40
60
80
100
EGFRt+ of total cells
CD4+of EGFRt+
CD8+ of EGFRt+
CD3+ of total cells
CD4+ of CD3+
CD62L+ of total cells
CD62L+/CD45RO- of CD3+
CD3+/CD28+ of total cells
CD27+ of total cells
CD127+ of total cells
CD45RA+/CD45RO- of total cells
CD45RA+/CD45RO+ of total cells
CD45RA-/CD45RO+ of total cells

FIG. 24B

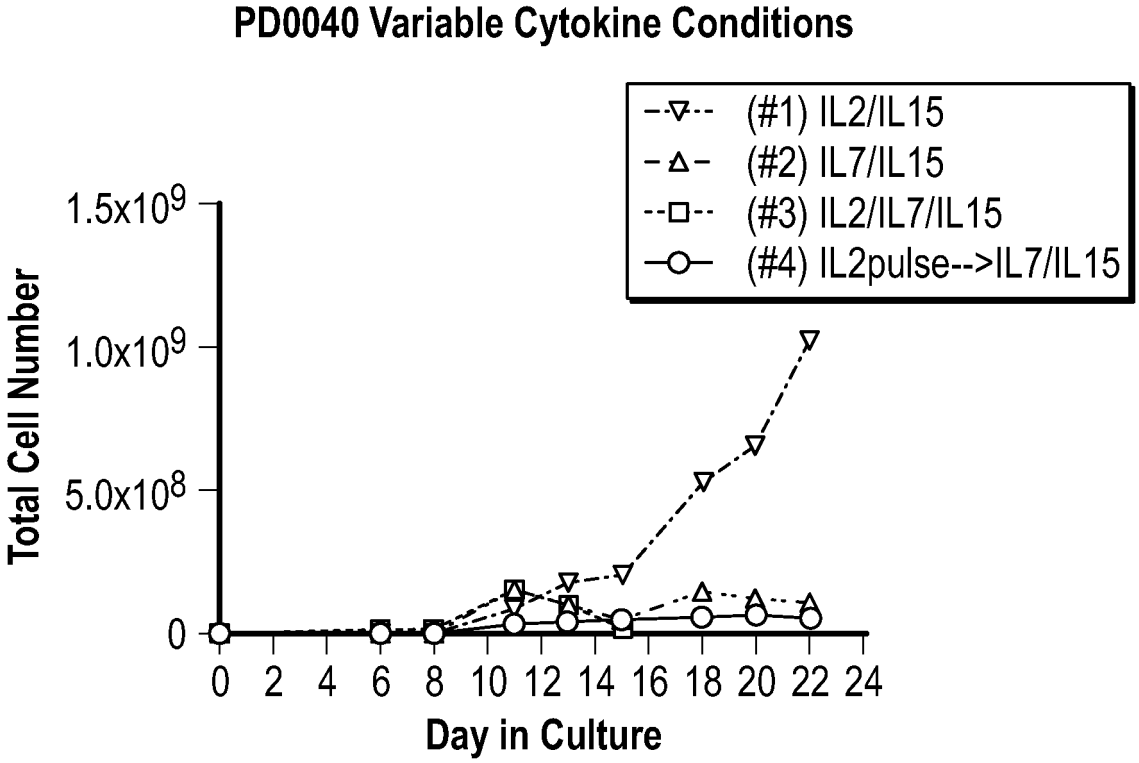


FIG. 24C

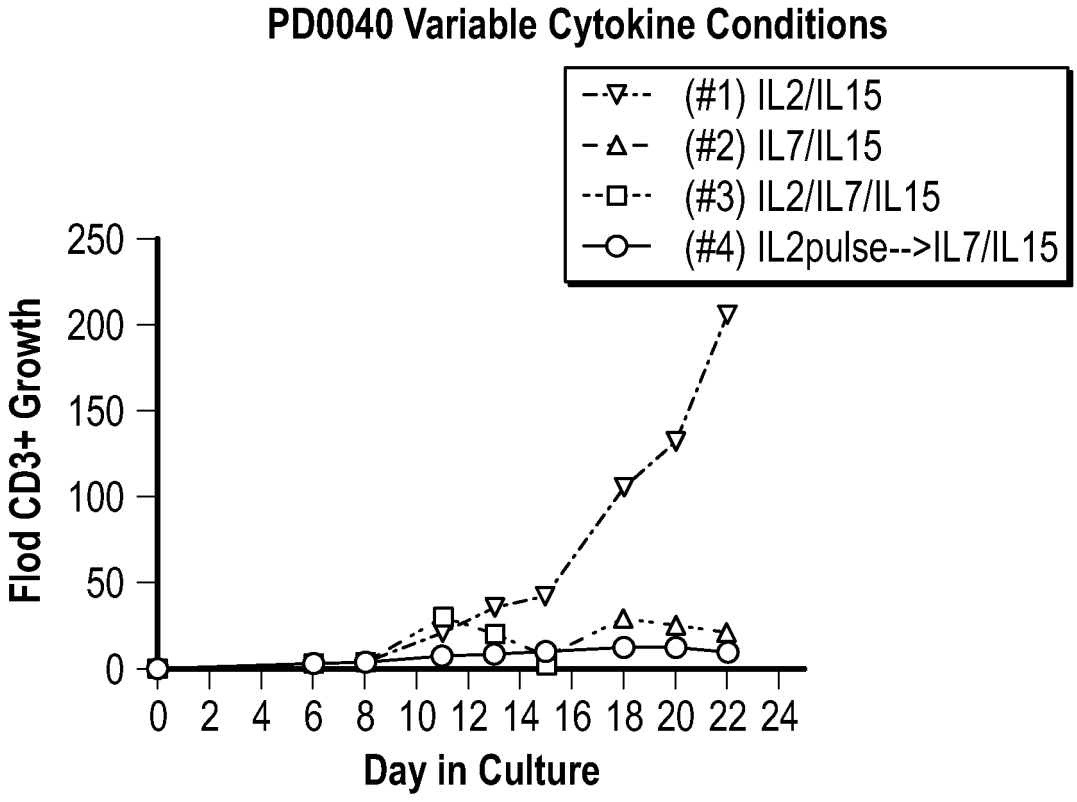


FIG. 24D

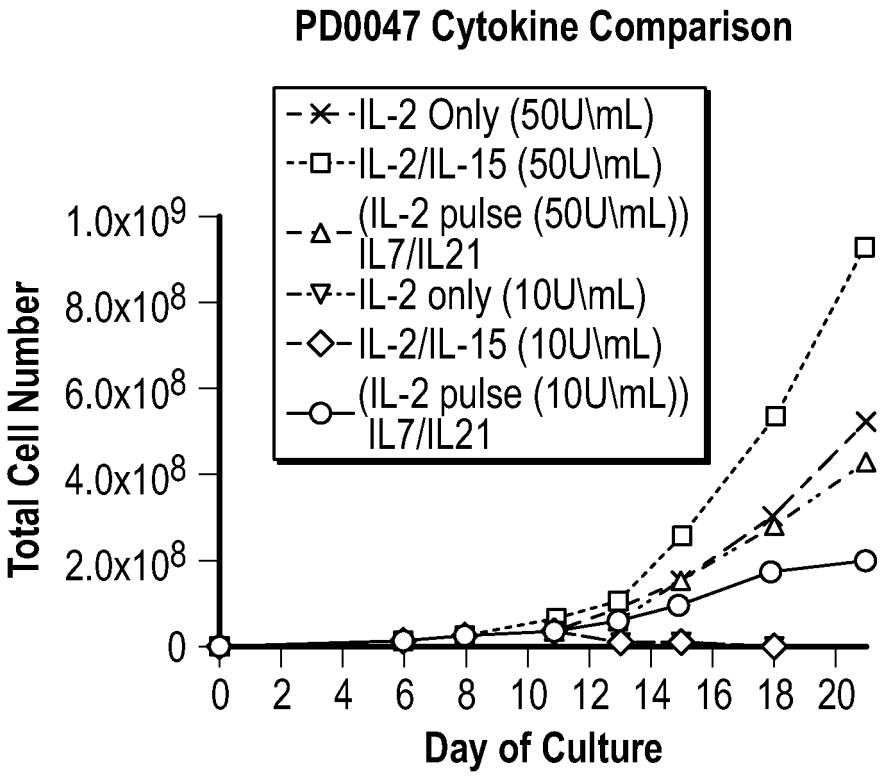


FIG. 24E

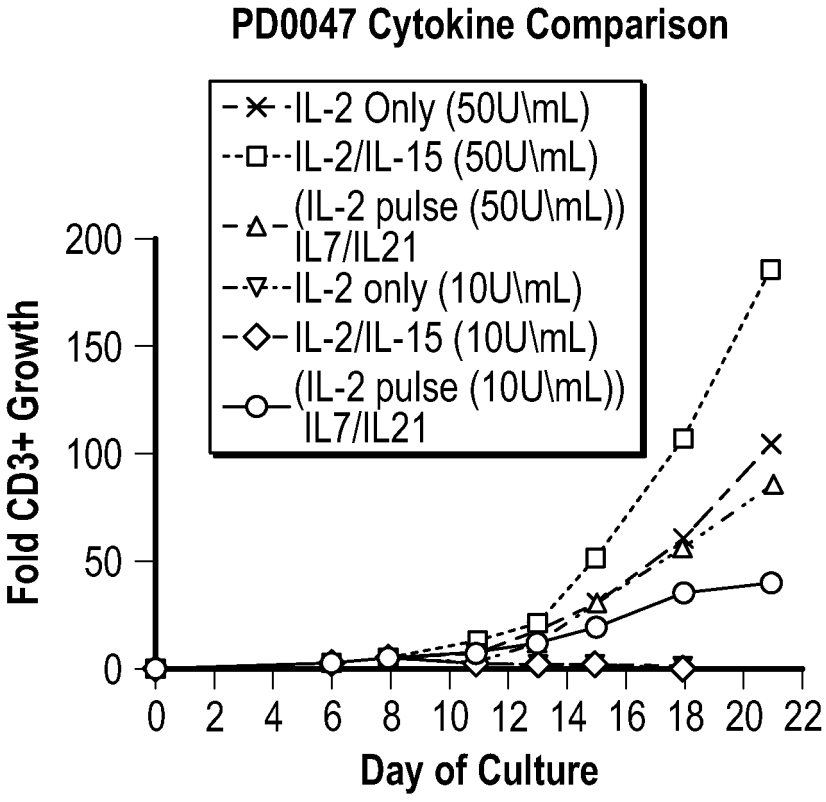


FIG. 24F

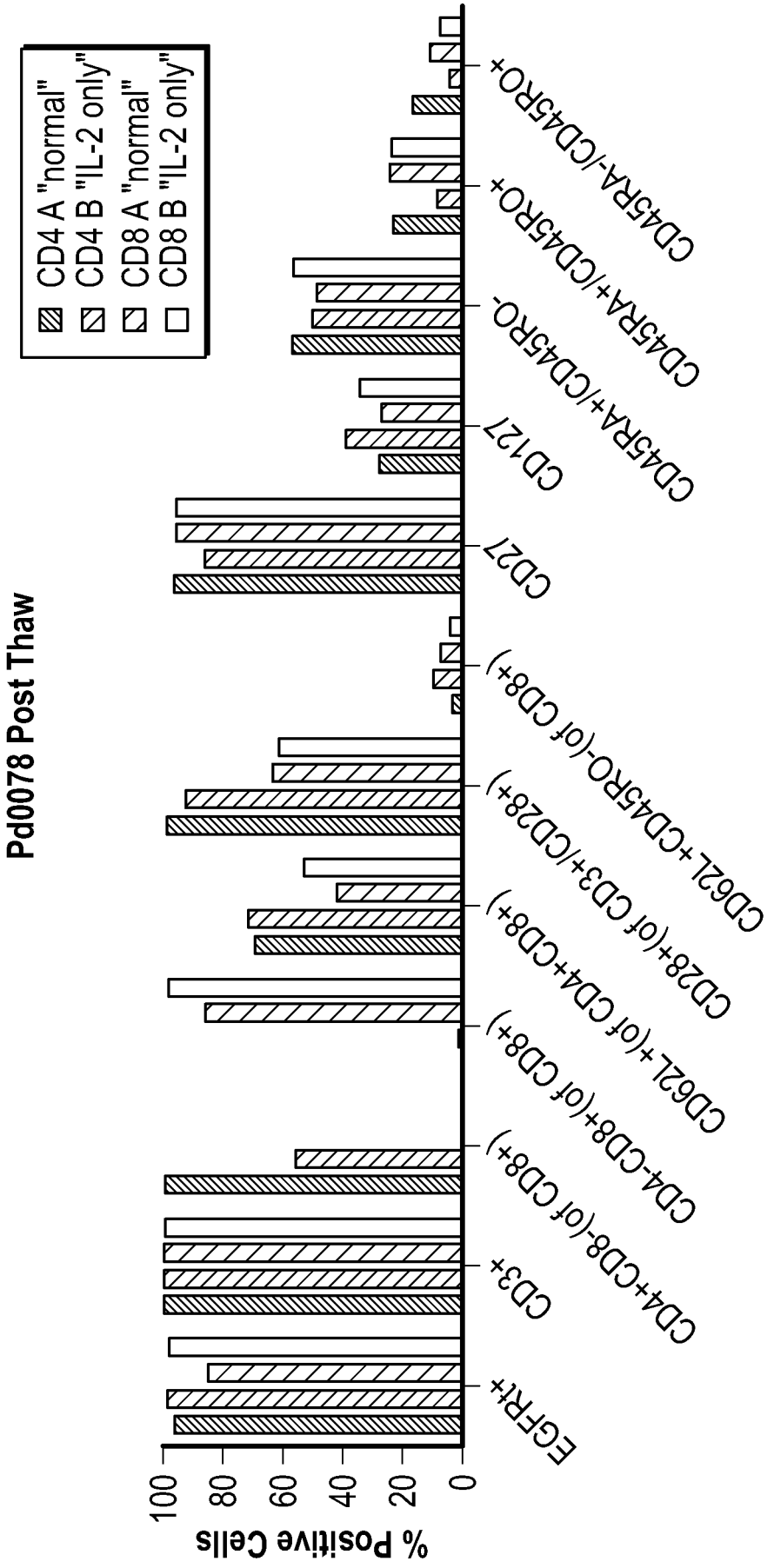

Pd0078 Post Thaw
% Positive Cells
100
80
60
40
20
0
CD4 A "normal"
CD4 B "IL-2 only"
CD8 A "normal"
CD8 B "IL-2 only"
EGFRt+
CD3+
CD4+CD8-(of CD8+)
CD4-CD8+(of CD8+)
CD62L+(of CD4+CD8+)
CD28+(of CD3+/CD28+)
CD62L+CD45RO-(of CD8+)
CD27
CD127
CD45RA+/CD45RO-
CD45RA+/CD45RO+
CD45RA-/CD45RO+

FIG. 25A

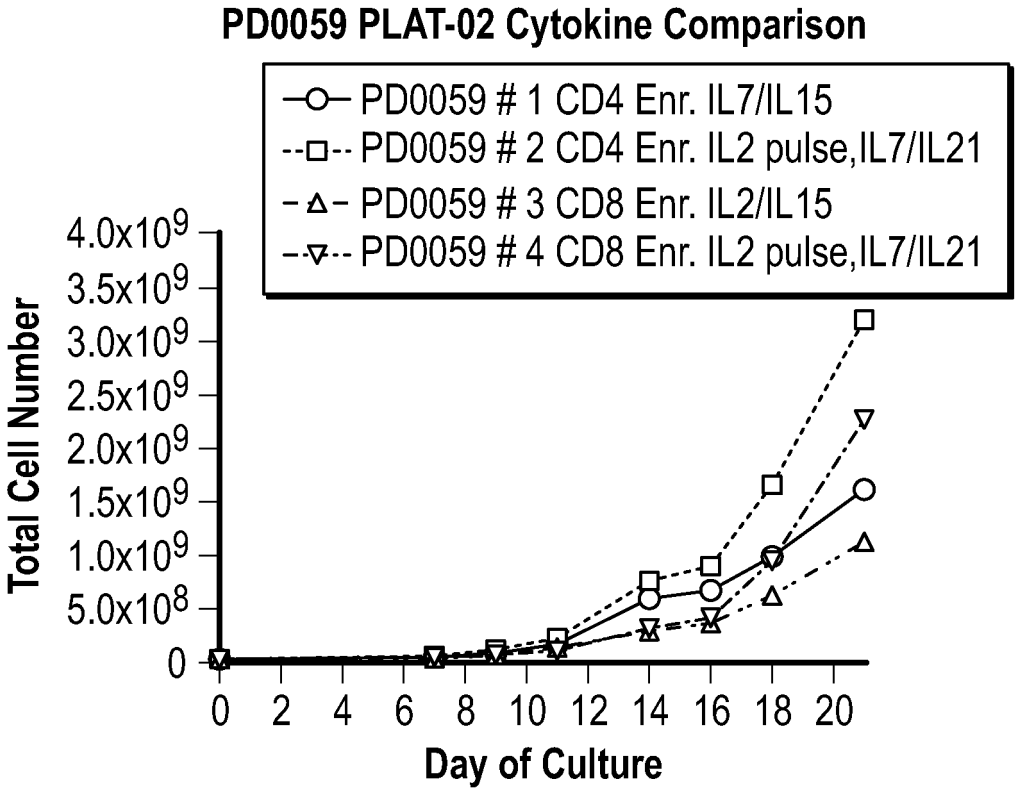


FIG. 25B1

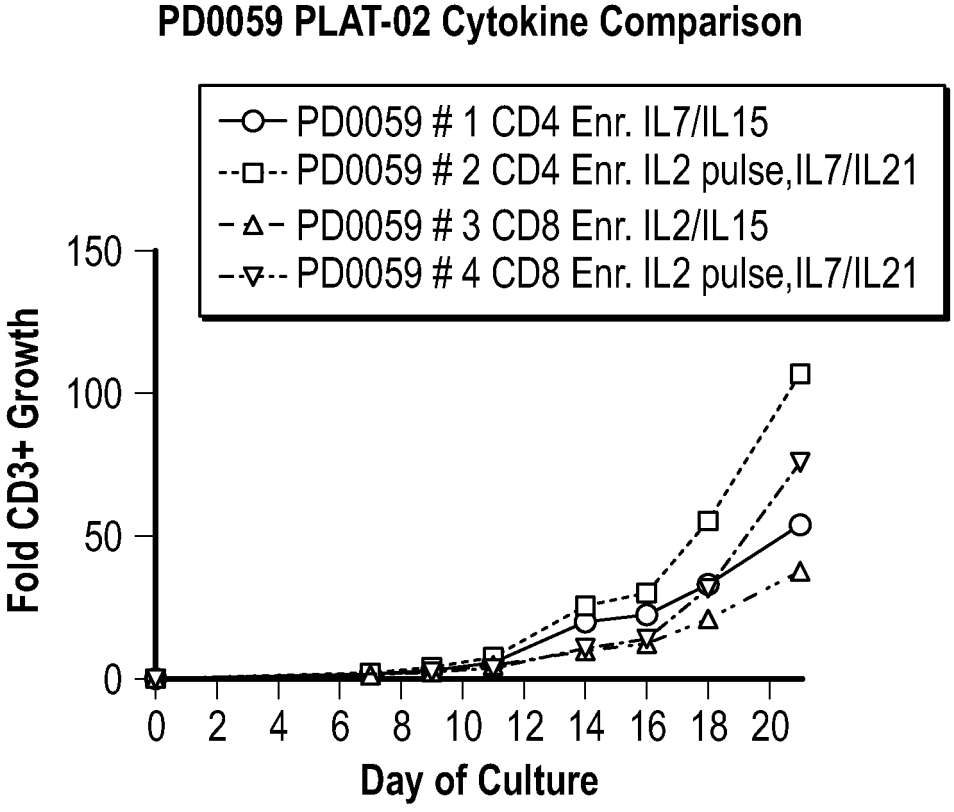


FIG. 25B2

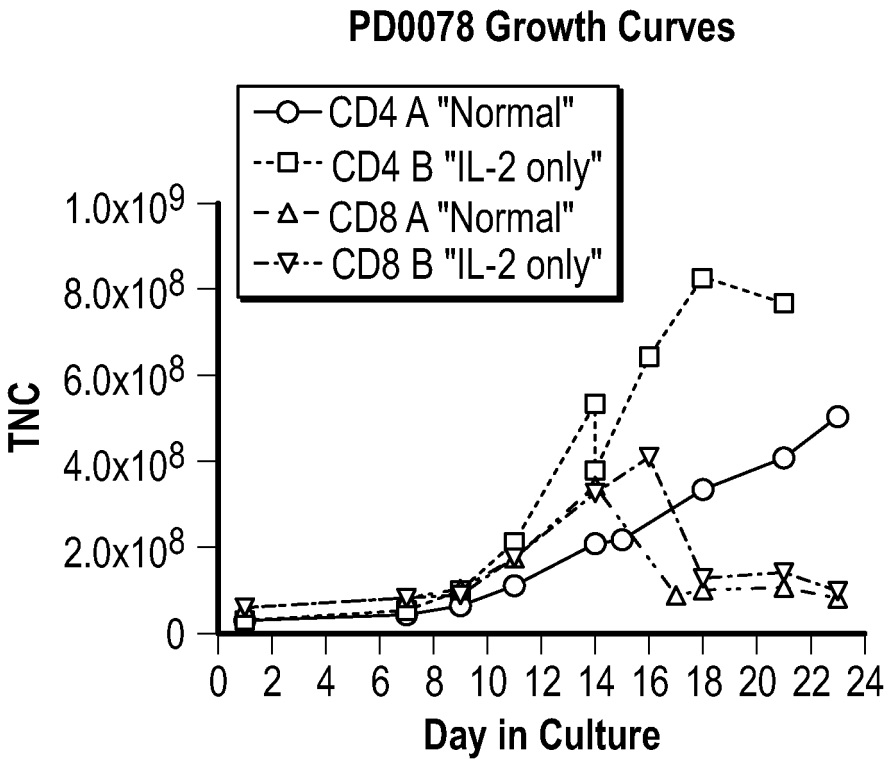


FIG. 25B3

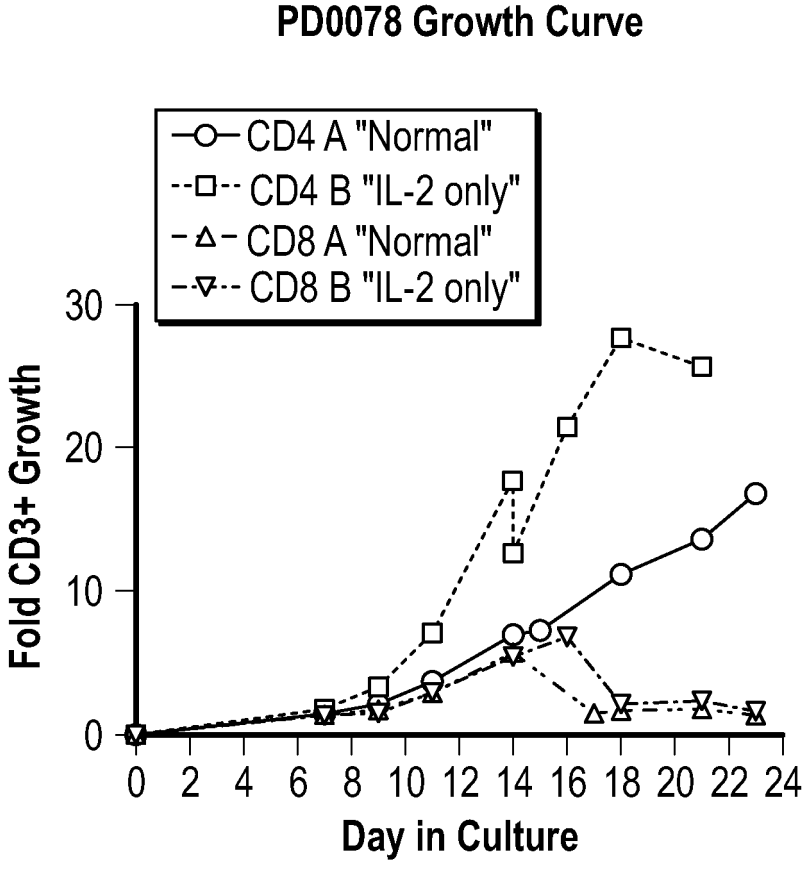


FIG. 25B4

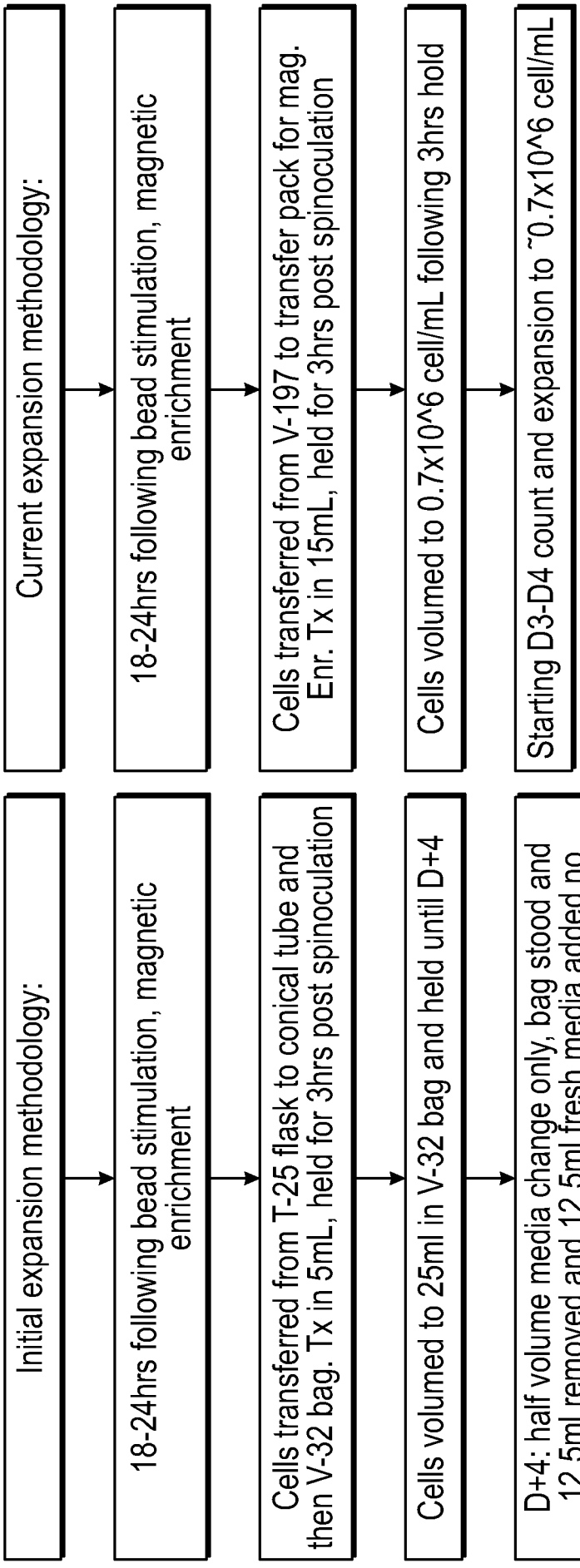

Current expansion methodology:
18-24hrs following bead stimulation, magnetic enrichment
Cells transferred from V-197 to transfer pack for mag. Enr. Tx in 15mL, held for 3hrs post spinoculation
Cells volumed to 0.7x10^6 cell/mL following 3hrs hold
Starting D3-D4 count and expansion to ~0.7x10^6 cell/mL
Initial expansion methodology:
18-24hrs following bead stimulation, magnetic enrichment
Cells transferred from T-25 flask to conical tube and then V-32 bag. Tx in 5mL, held for 3hrs post spinoculation
Cells volumed to 25ml in V-32 bag and held until D+4
D+4: half volume media change only, bag stood and 12.5ml removed and 12.5ml fresh media added no count performed. Final volume again 25mL
Starting D6-D7 count and expansion to ~0.7x10^6 cell/mL

FIG. 26

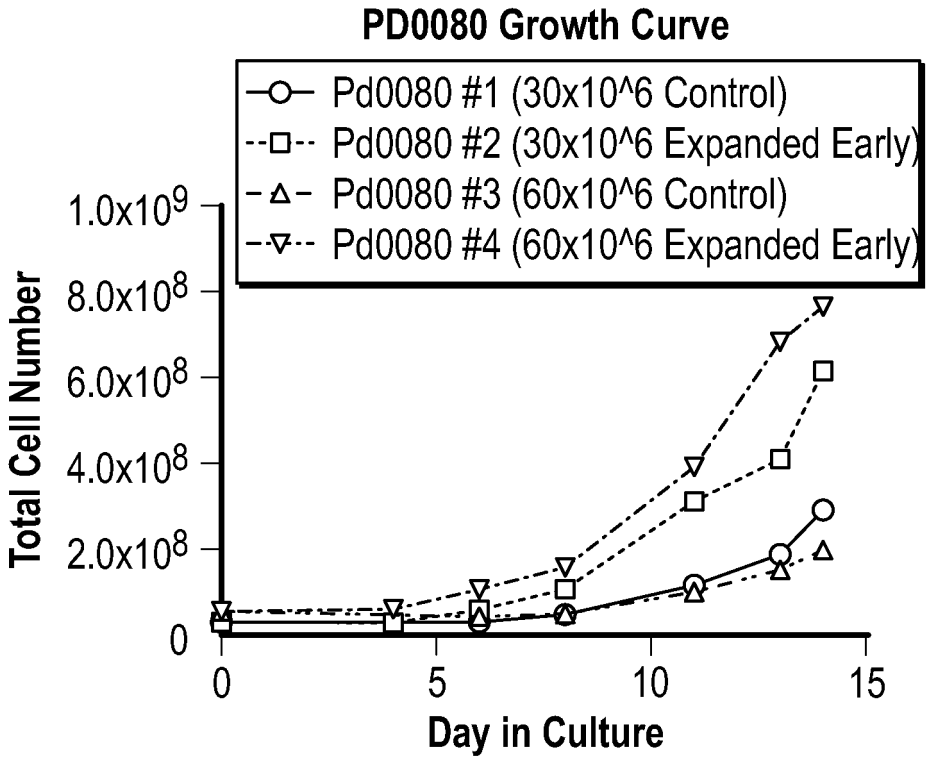


FIG. 27A

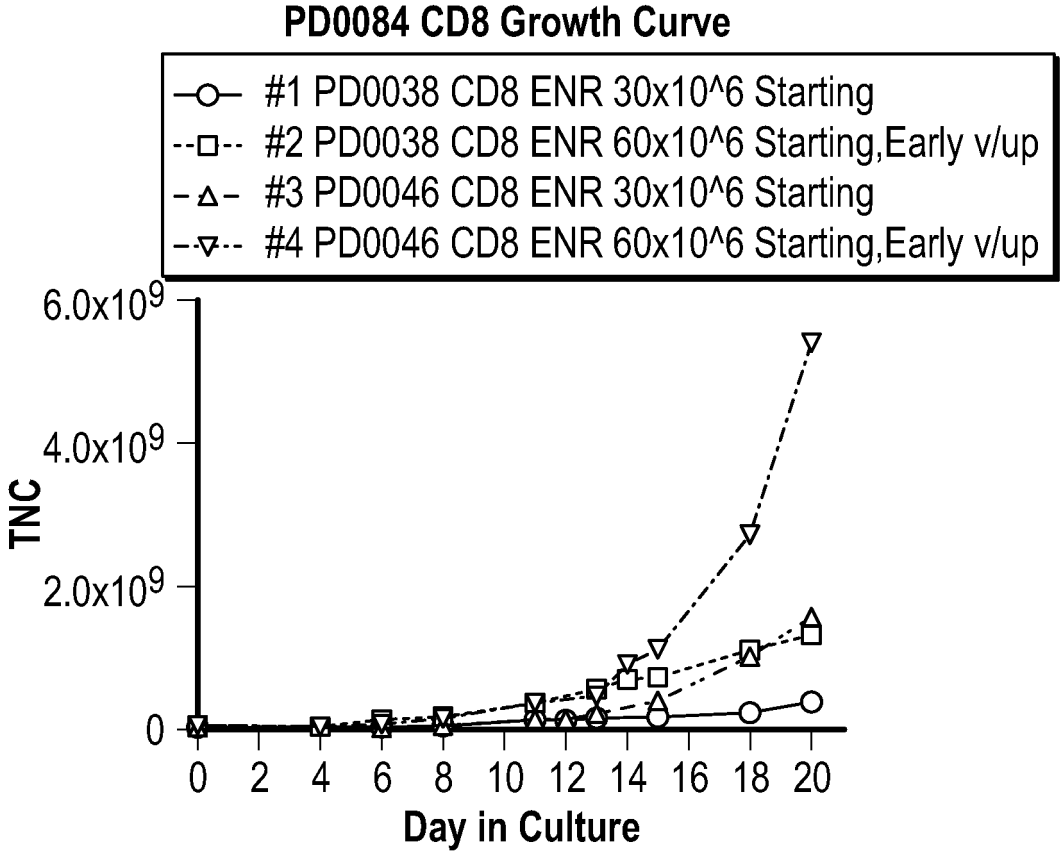


FIG. 27B

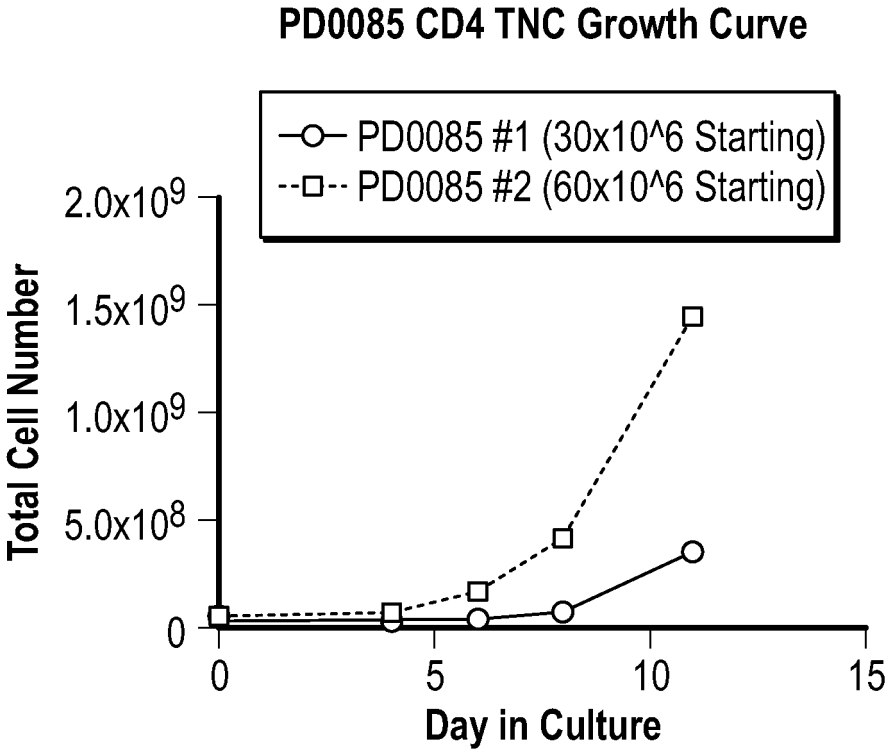


FIG. 27C

Starting Material:	PD0038 CD4/CD8 selected
Transduction:	D+1, ZRX-014
Stim Reagent:	CTS 3/28
Scale:	Full (pooled 50:50 product)

FIG. 28A

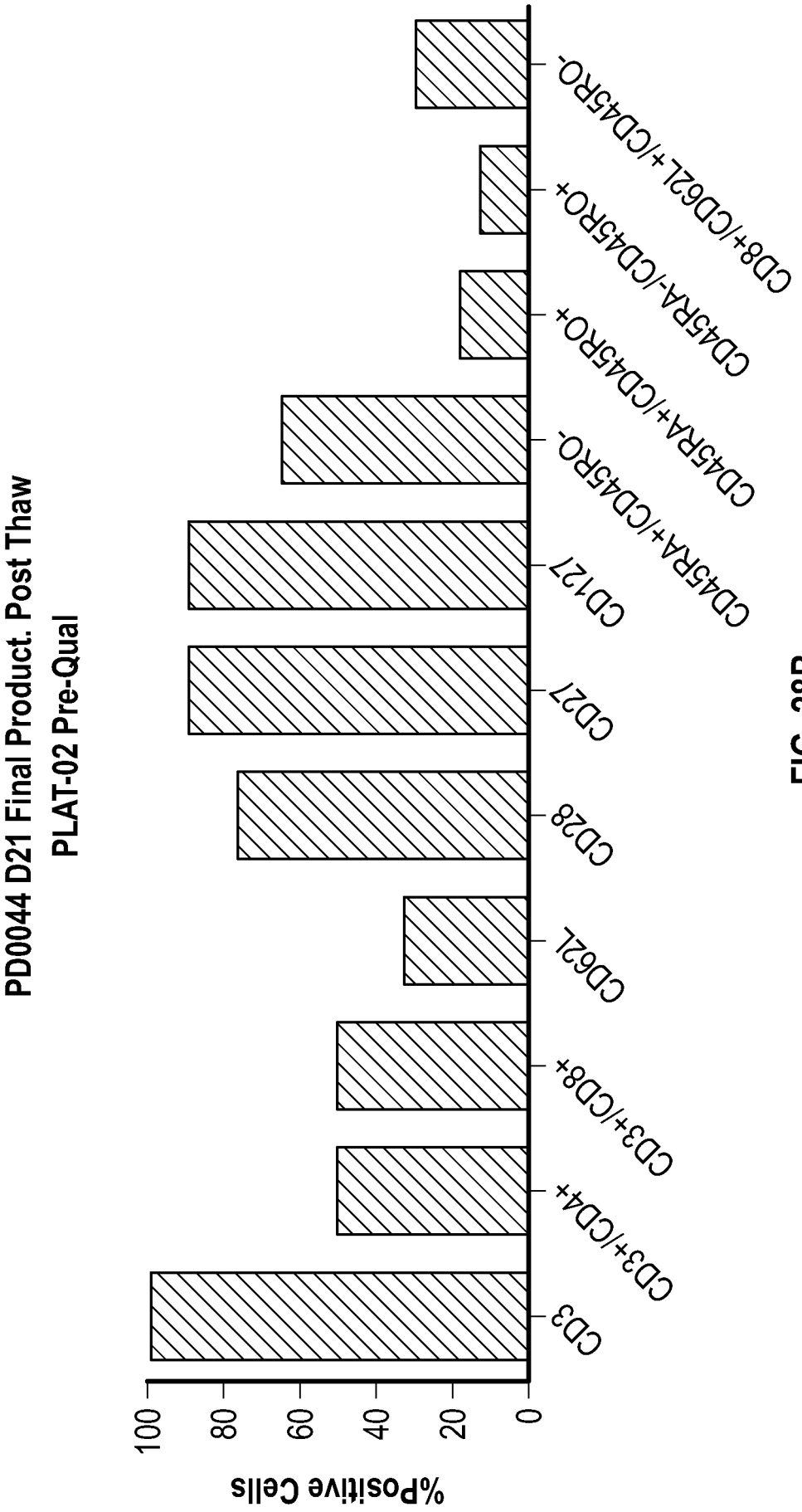

PD0044 D21 Final Product. Post Thaw
PLAT-02 Pre-Qual
%Positive Cells
0
20
40
60
80
100
CD3
CD3+/CD4+
CD3+/CD8+
CD62L
CD28
CD27
CD127
CD45RA+/CD45RO-
CD45RA+/CD45RO+
CD45RA-/CD45RO+
CD8+/CD62L+/CD45RO-

FIG. 28B

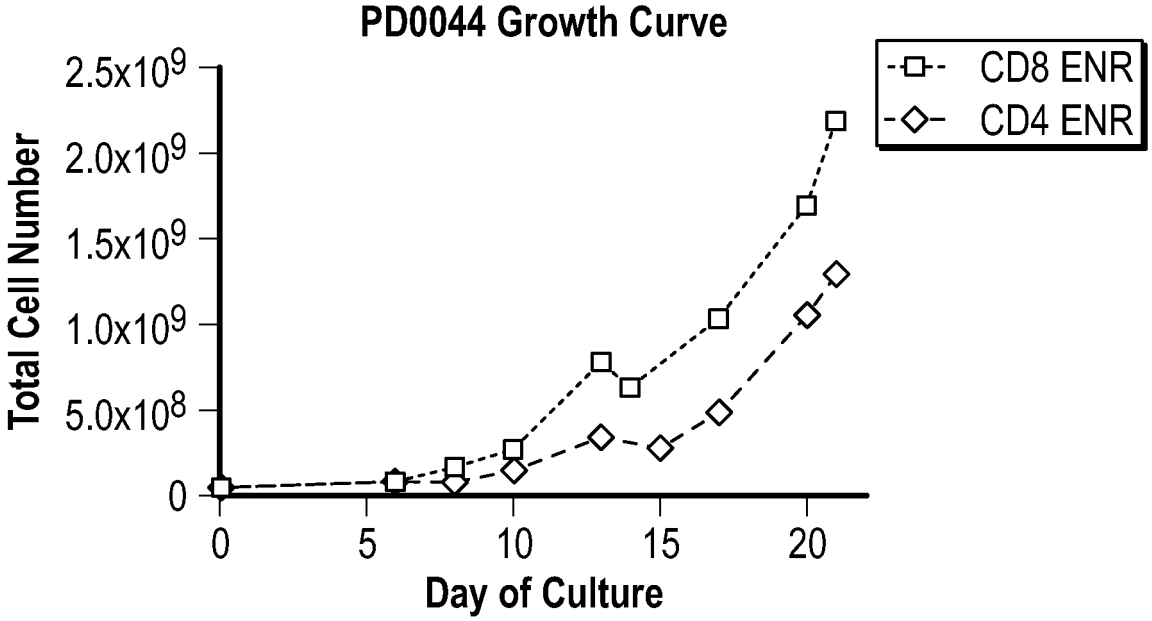


FIG. 28C

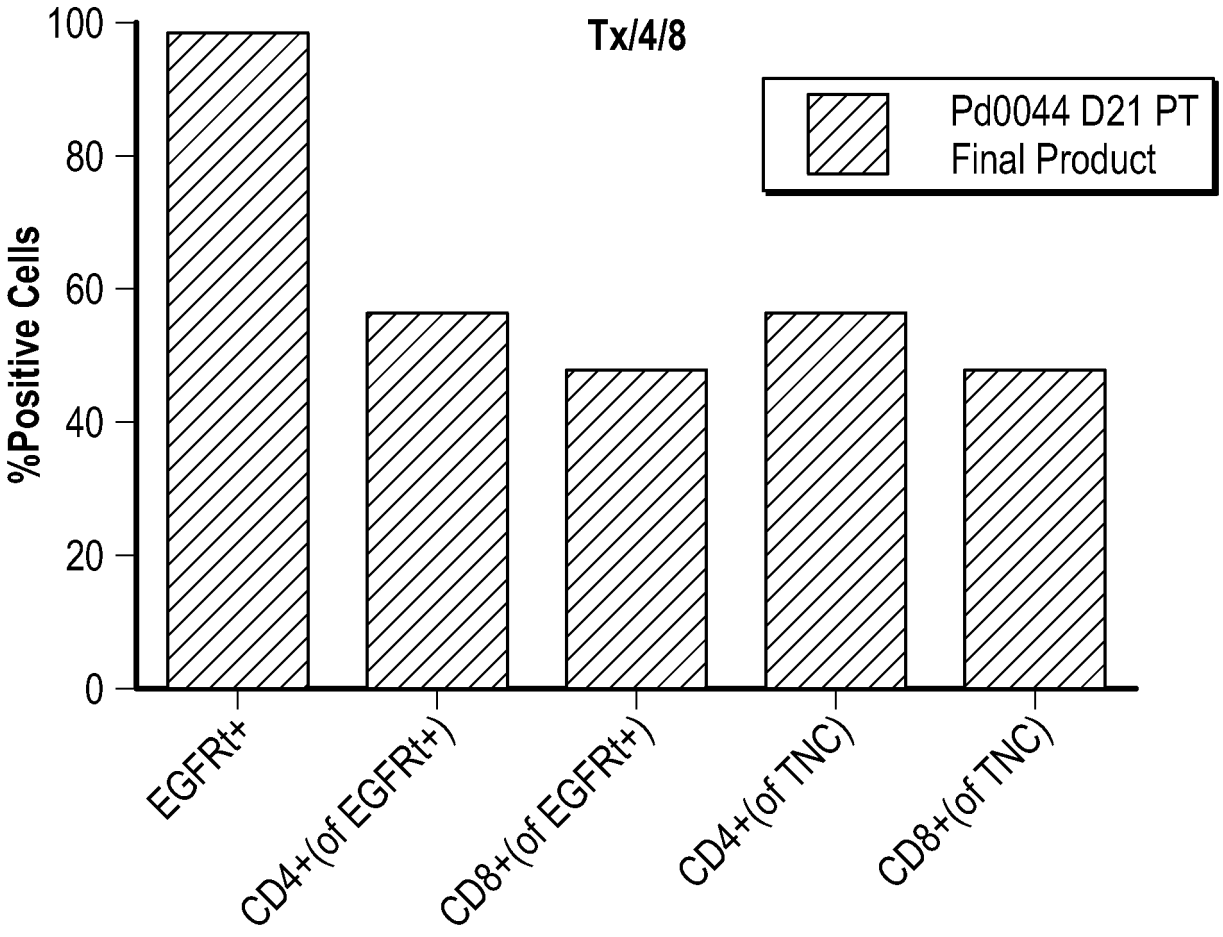


FIG. 28D

Starting Material:	Fresh,APH-NDPBMC-004
Transduction:	D+1, ZRX-014
Stim Reagent:	CTS 3/28
Scale:	Full scale

FIG. 29A

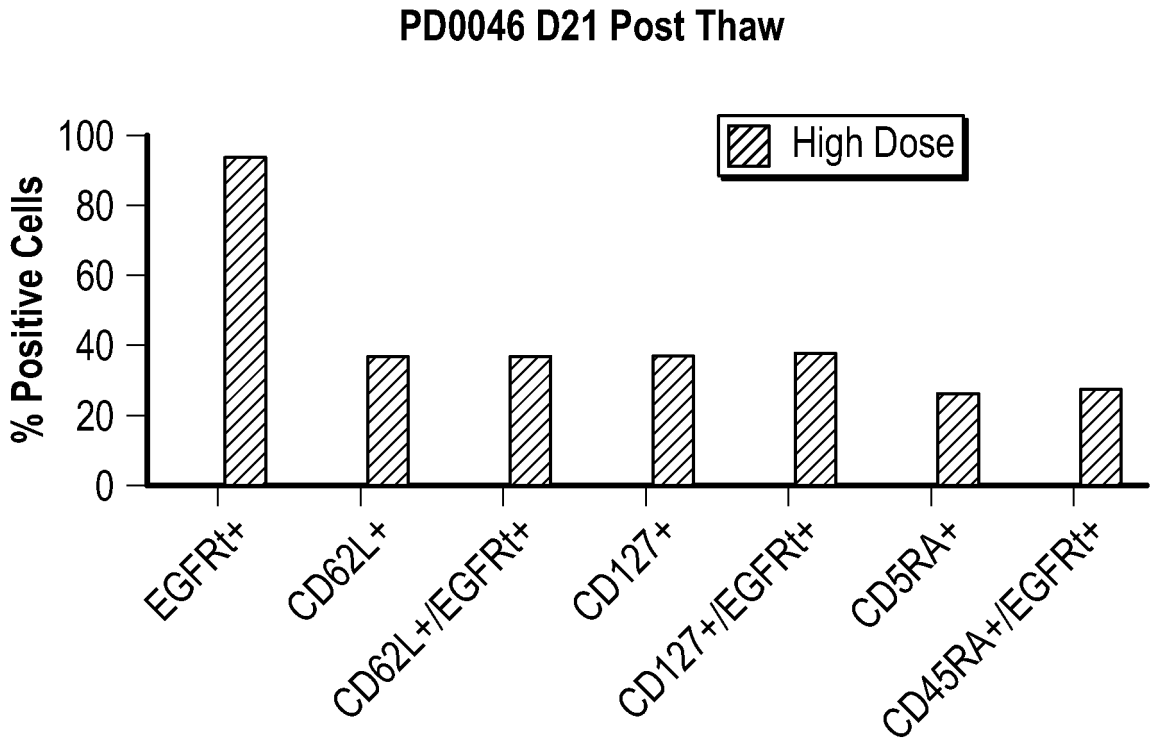


FIG. 29B

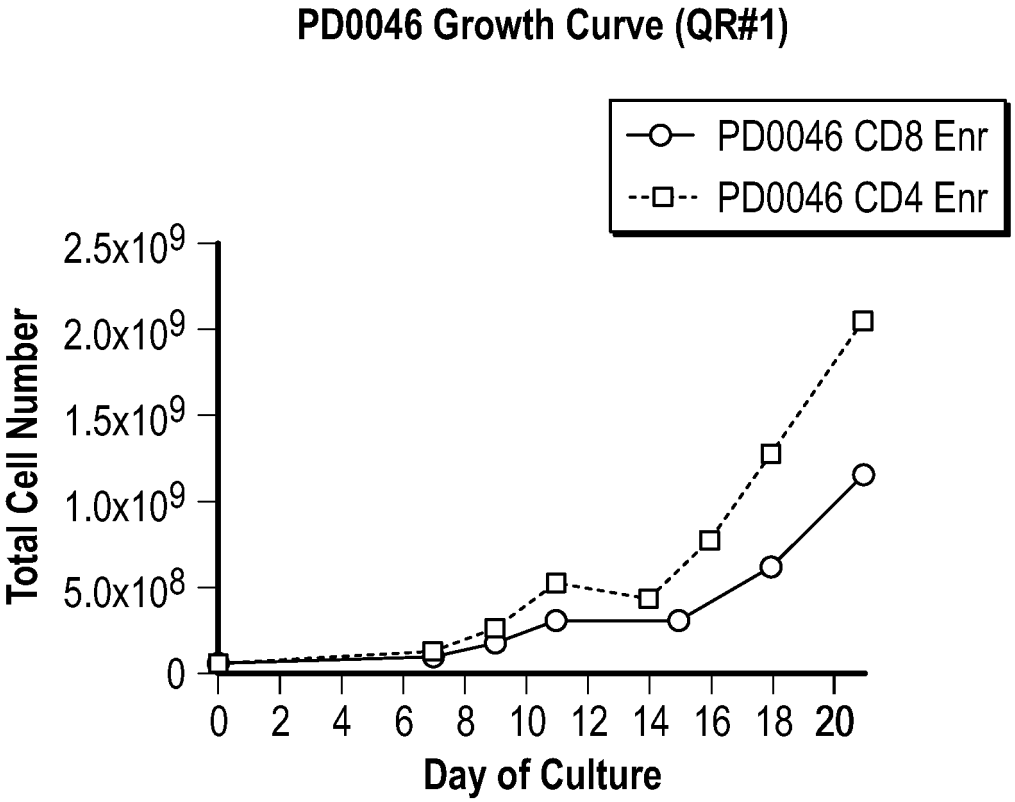

PD0046 Growth Curve (QR#1)
PD0046 CD8 Enr
PD0046 CD4 Enr
Total Cell Number
2.5x10^9
2.0x10^9
1.5x10^9
1.0x10^9
5.0x10^8
0
0 2 4 6 8 10 12 14 16 18 20
Day of Culture

FIG. 29C

Starting Material:	Fresh, APH - NDPBMC-007
Transduction:	D+1, ZRX-014
Stim Reagent:	CTS 3/28
Scale:	Fullscale

FIG. 30A

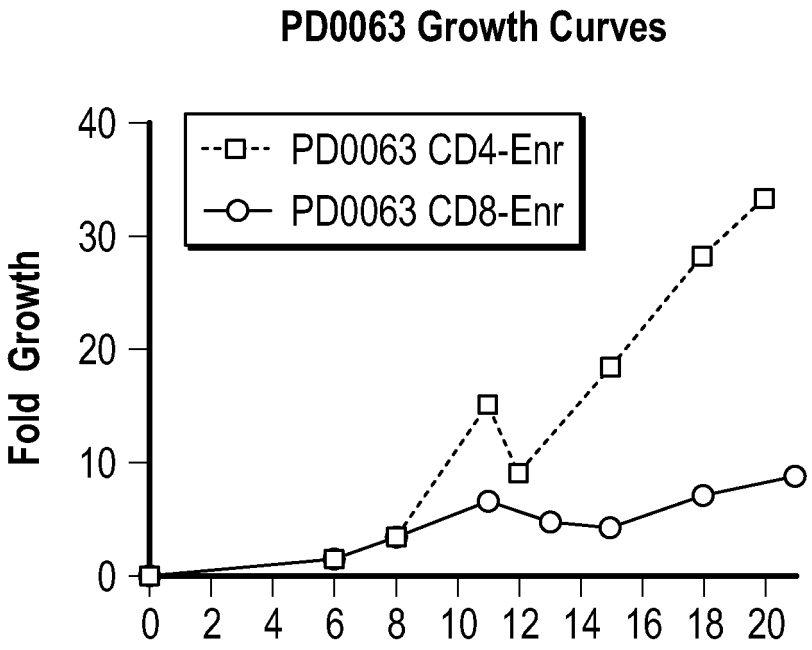


FIG. 30B

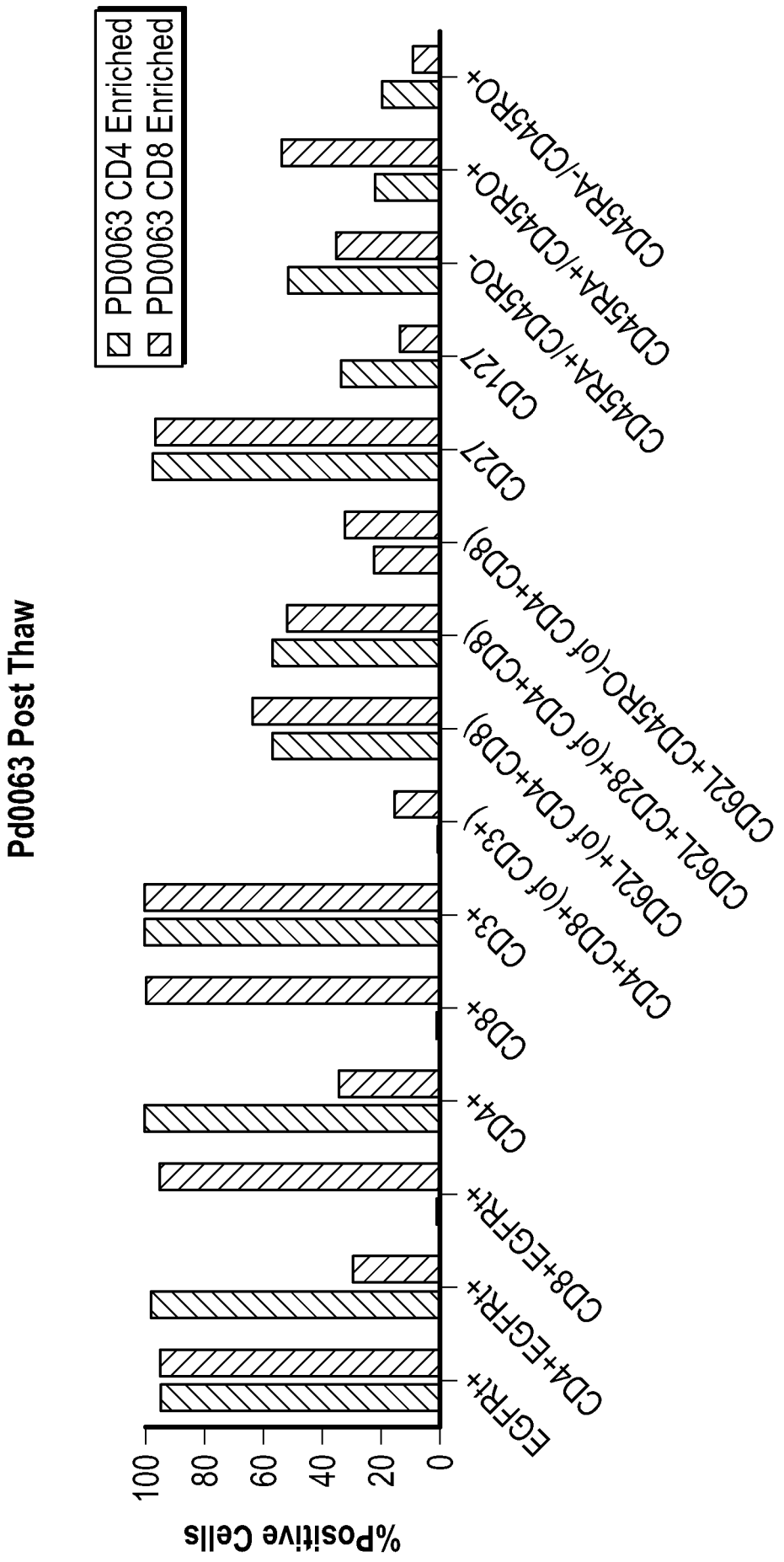

Pd0063 Post Thaw
PD0063 CD4 Enriched
PD0063 CD8 Enriched
%Positive Cells
100
80
60
40
20
0
EGFRt+
CD4+EGFRt+
CD8+EGFRt+
CD4+
CD8+
CD3+
CD4+CD8+(of CD3+)
CD62L+(of CD4+CD8)
CD62L+CD28+(of CD4+CD8)
CD62L+CD45RO-(of CD4+CD8)
CD27
CD127
CD45RA+/CD45RO-
CD45RA+/CD45RO+
CD45RA-/CD45RO+

FIG. 30C

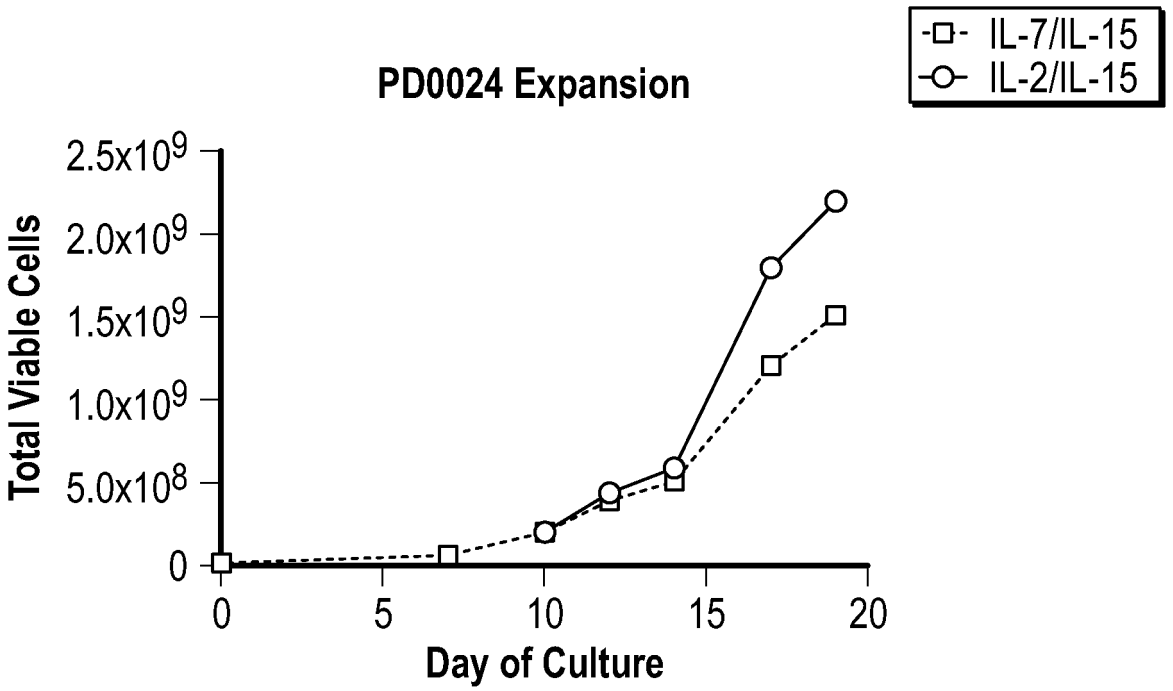


FIG. 31A1

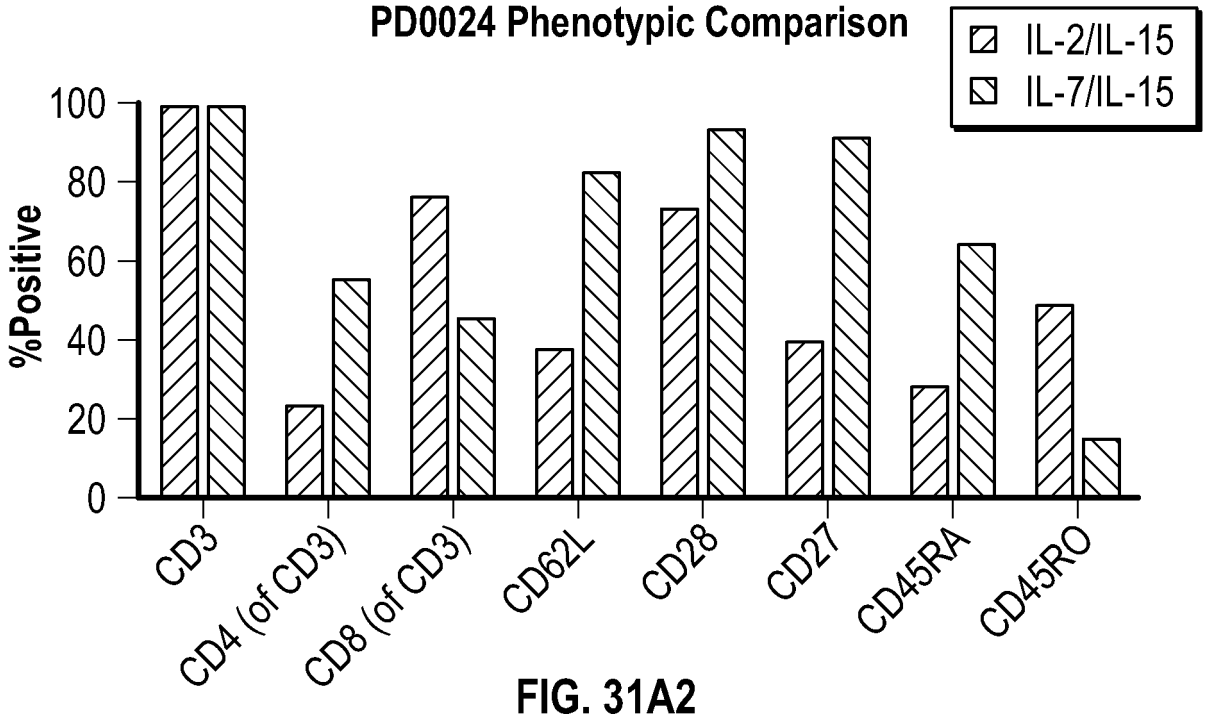


FIG. 31A2

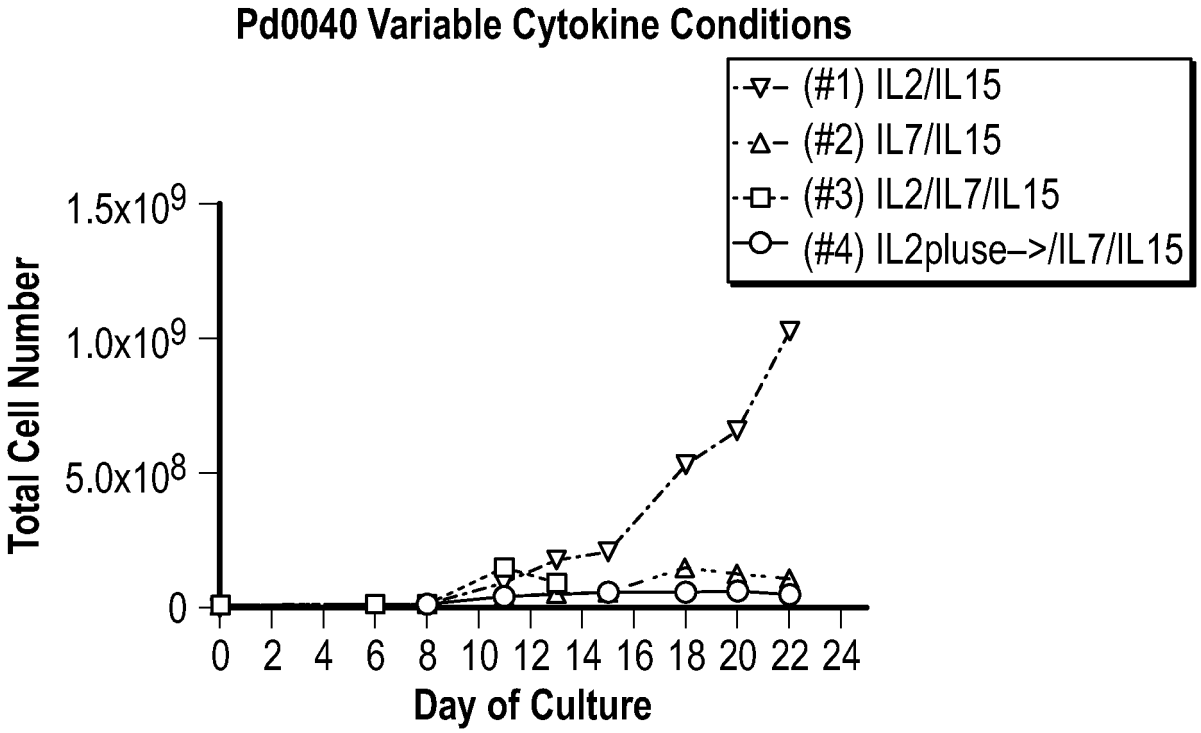


FIG. 31B1

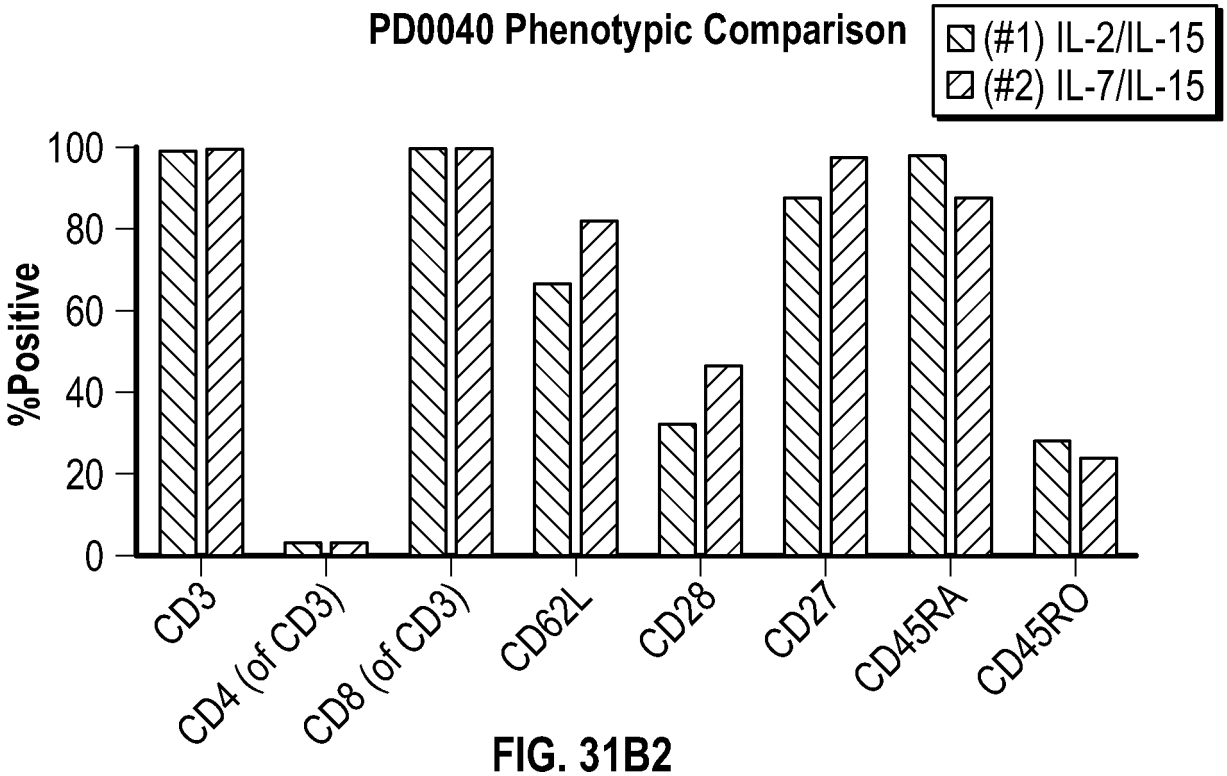


FIG. 31B2

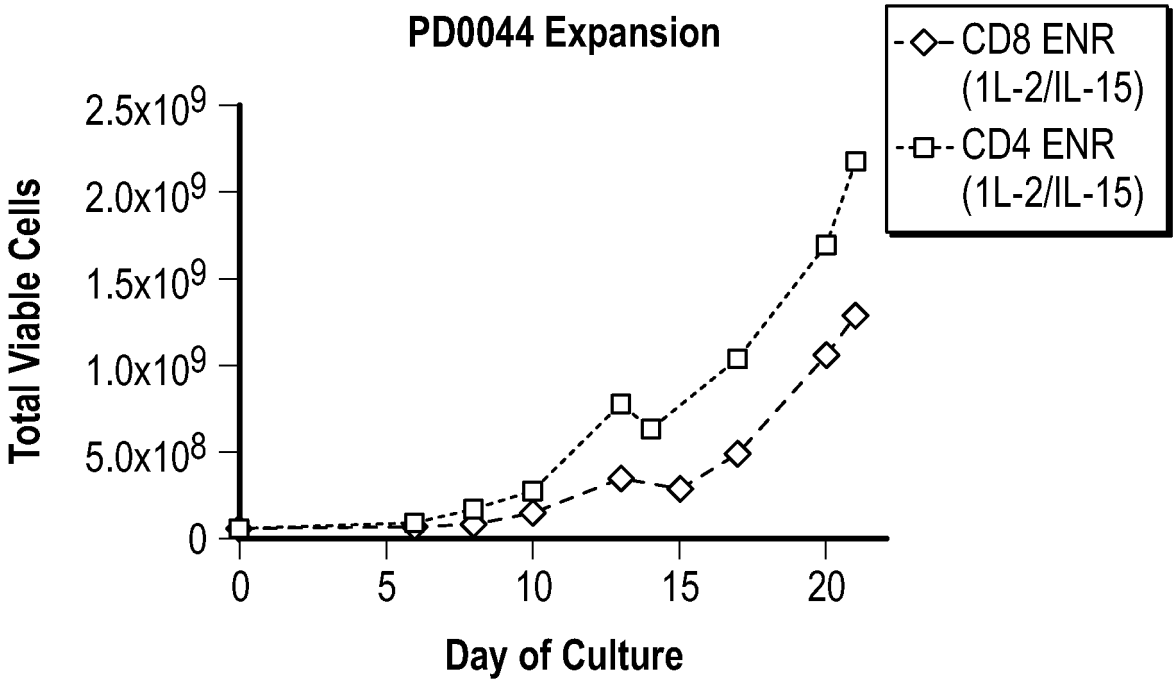
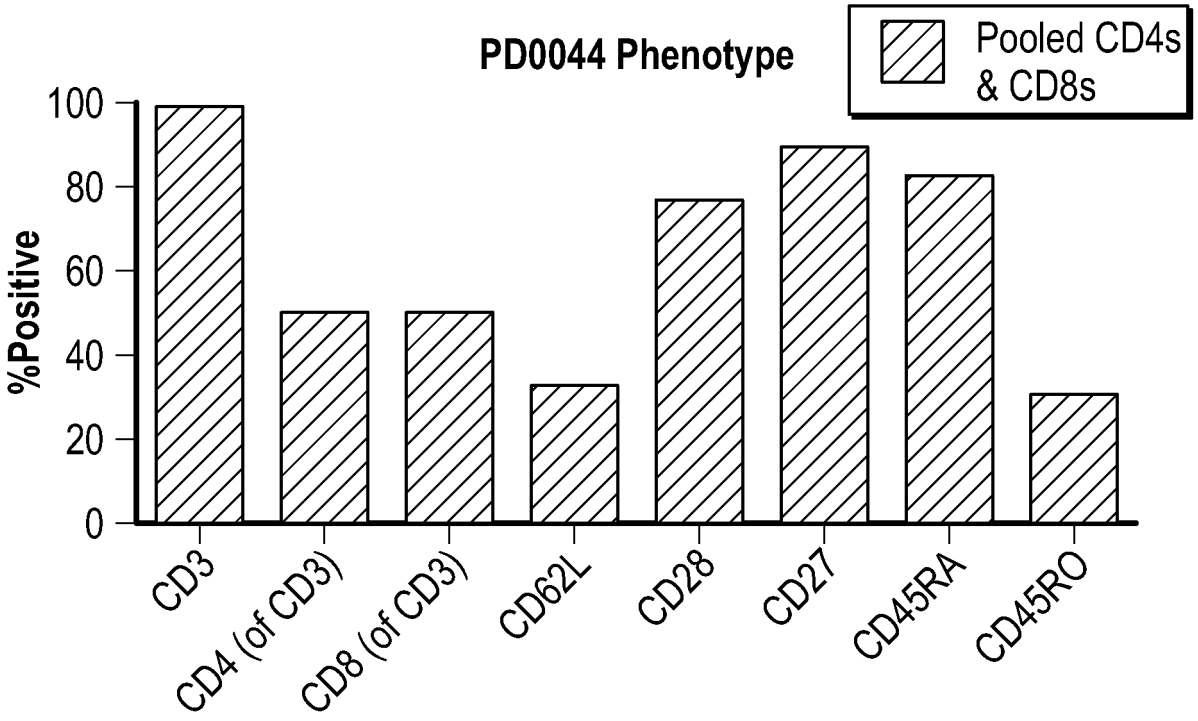


FIG. 32A1



Growing CD8-enriched cultures in IL-2/IL-15 and CD4-enriched cultures in IL-7/IL-15 yields robust expansion of both cultures and strong expression of memory phenotype (representative data shown above)

FIG. 32A2

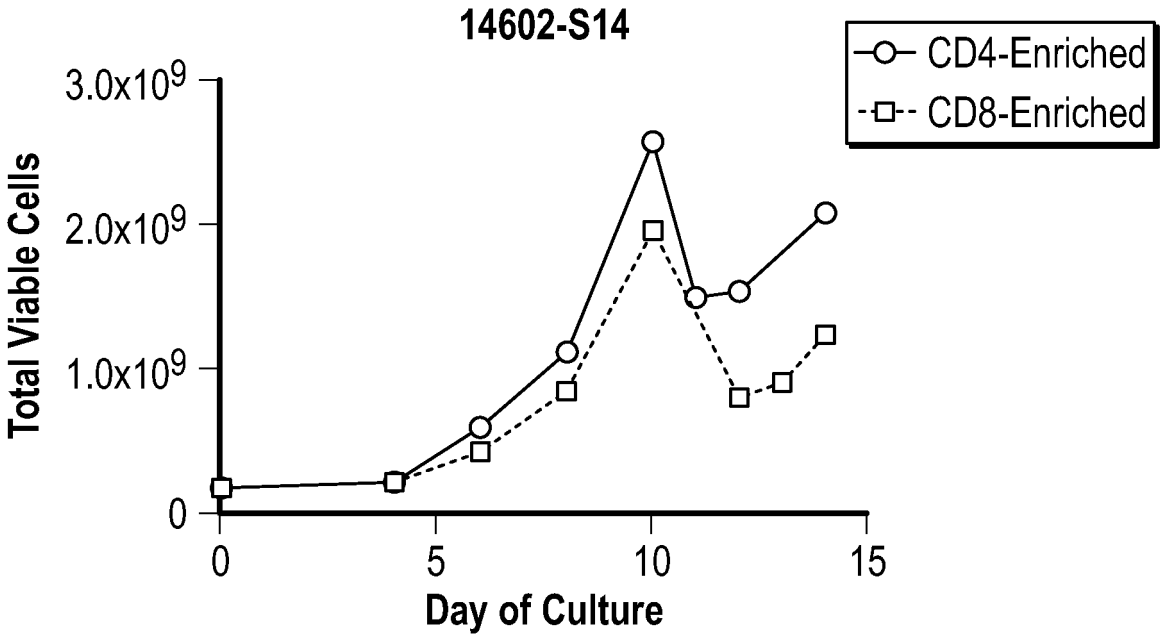
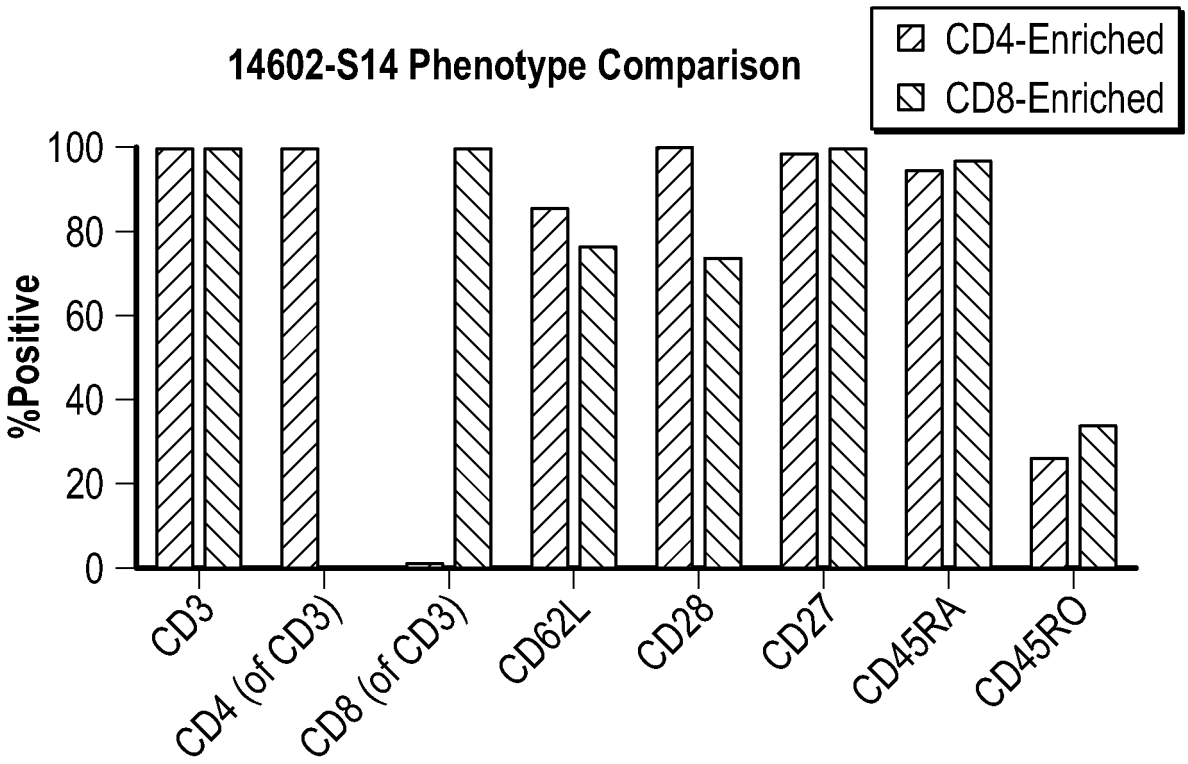
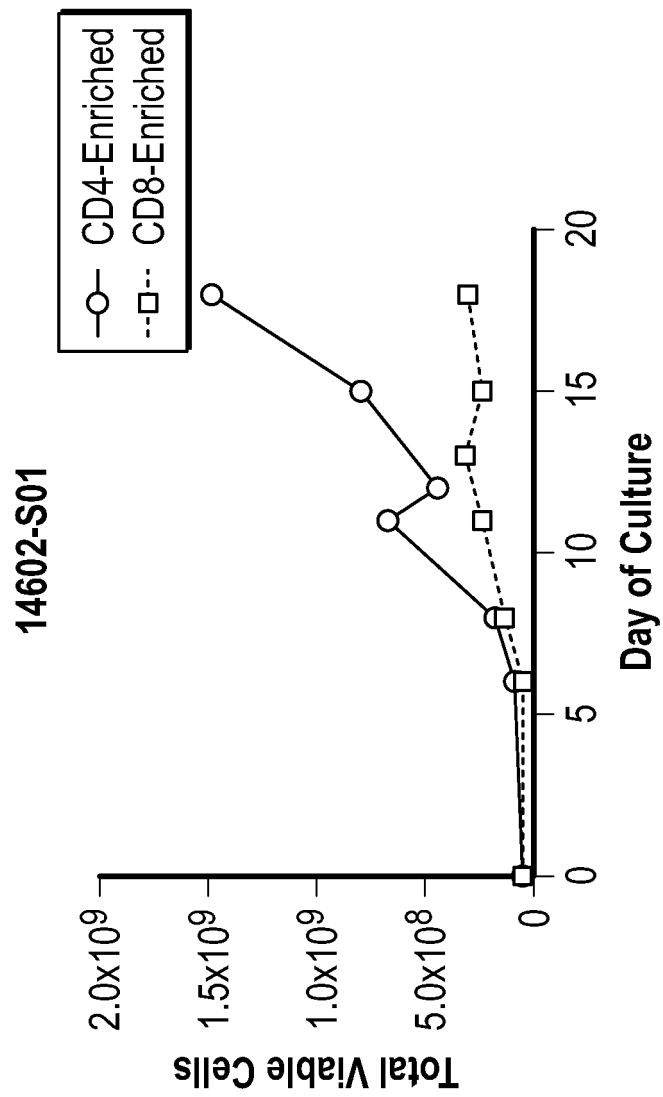


FIG. 32B1



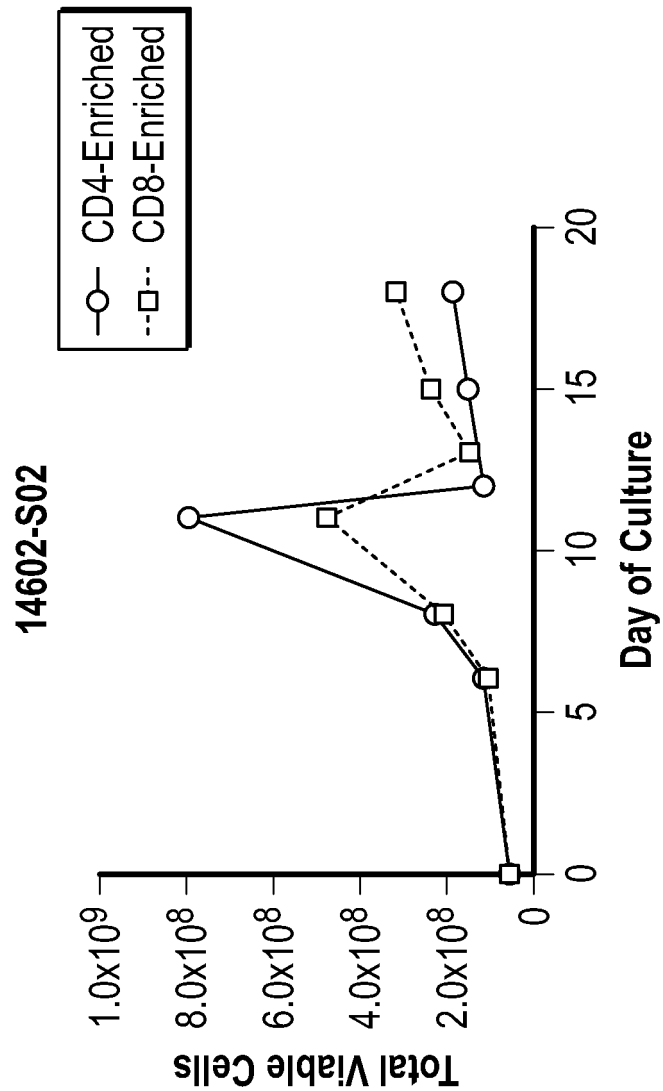
Growing CD8-enriched cultures in IL-2/IL-15 and CD4-enriched cultures in IL-7/IL-15 yields robust expansion of both cultures and strong expression of memory phenotype (representative data shown above)

FIG. 32B2



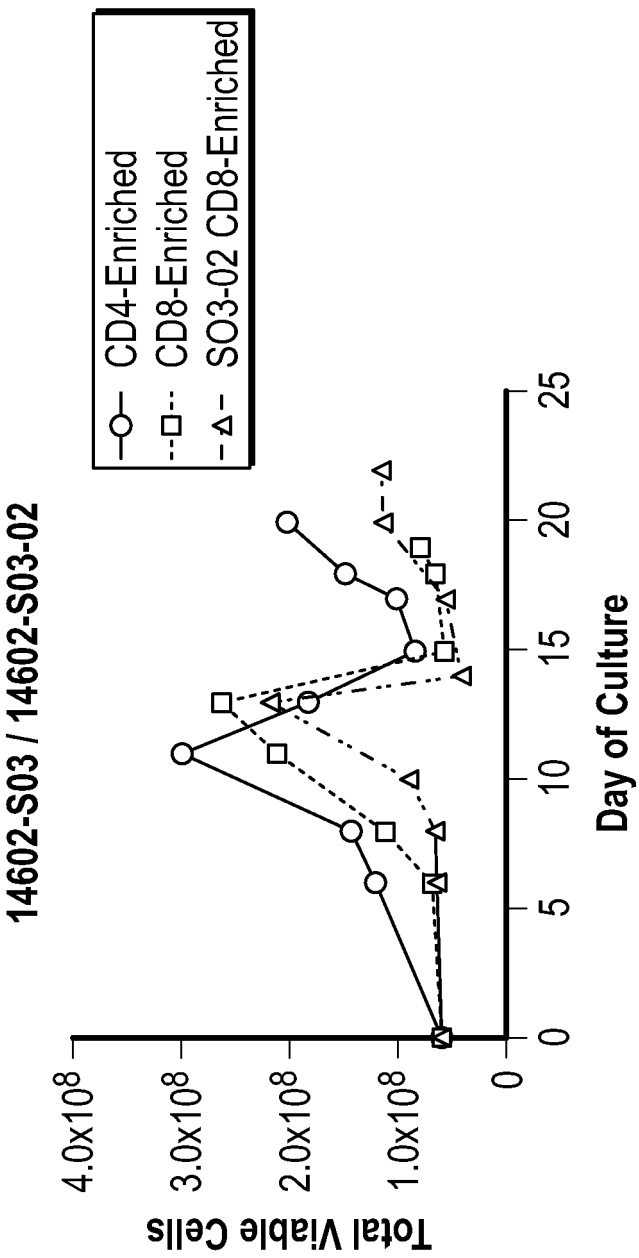
Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S01 CD4	98.7	98.3		96.6
14602-S01 CD8	98.1		96.9	92.5

FIG. 33A



Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S02 CD4	94.9	94.5		95.5
14602-S02 CD8	98.5		98.2	97.8

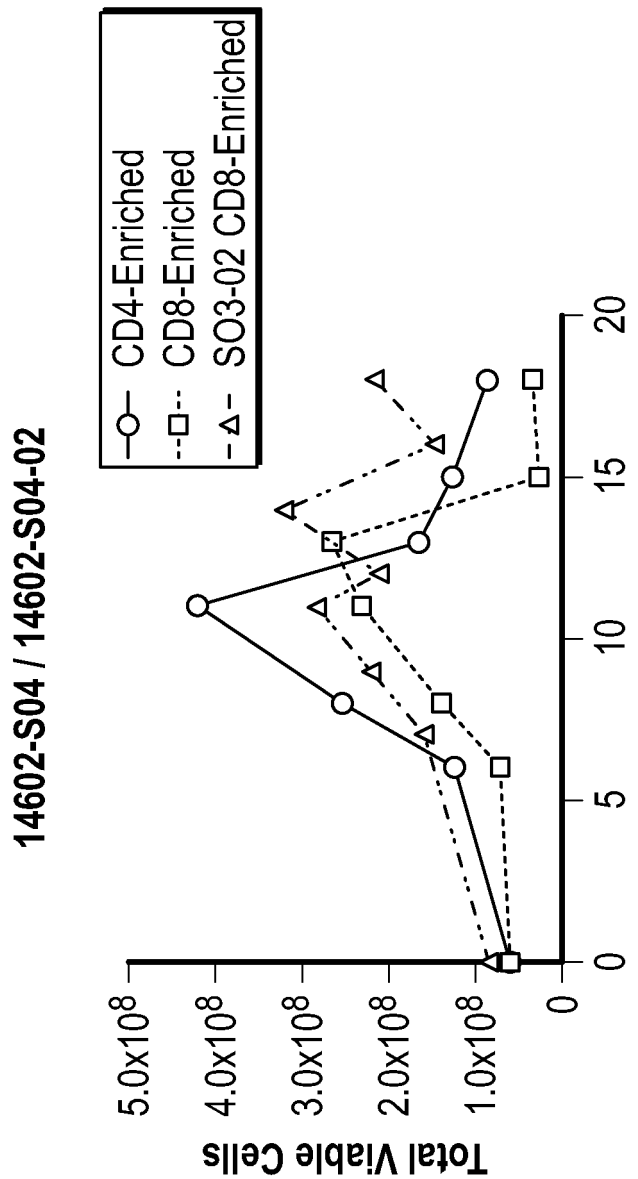
FIG. 33B



Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)	CD3	CD4+CD8- (of CD3)
14602-S03 CD4	98.3	98.2		97.2	98.5	97.7
14602-S03 CD8	93.6		93.1	96.2		
14602-S03-02 CD8	96.6		95.9			

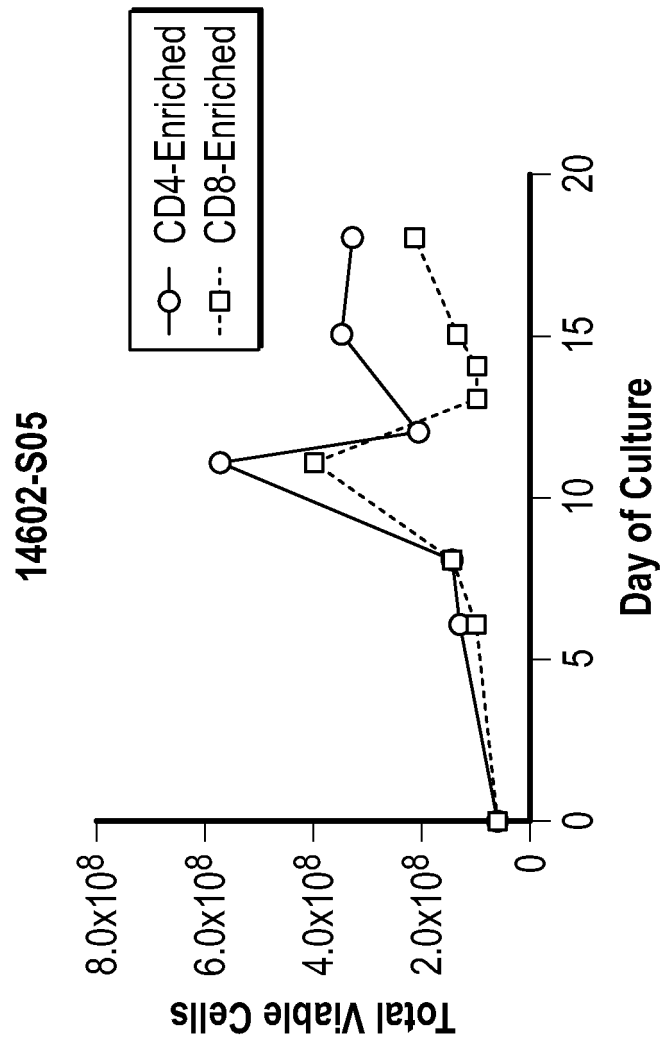
CD4-CD8+ (of CD3)	CD62L	Total CD28 from CD28(CD3)	CD27	CD127	CD45RA+/ CD45RO-	CD45RA+
0.2	60.9	97.4	98	23.7	66.2	84.9

FIG. 33C



Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S04 CD4	95.6	95.5		94.2
14602-S04-02 CD8	99.4		99.2	94.5

FIG. 34A



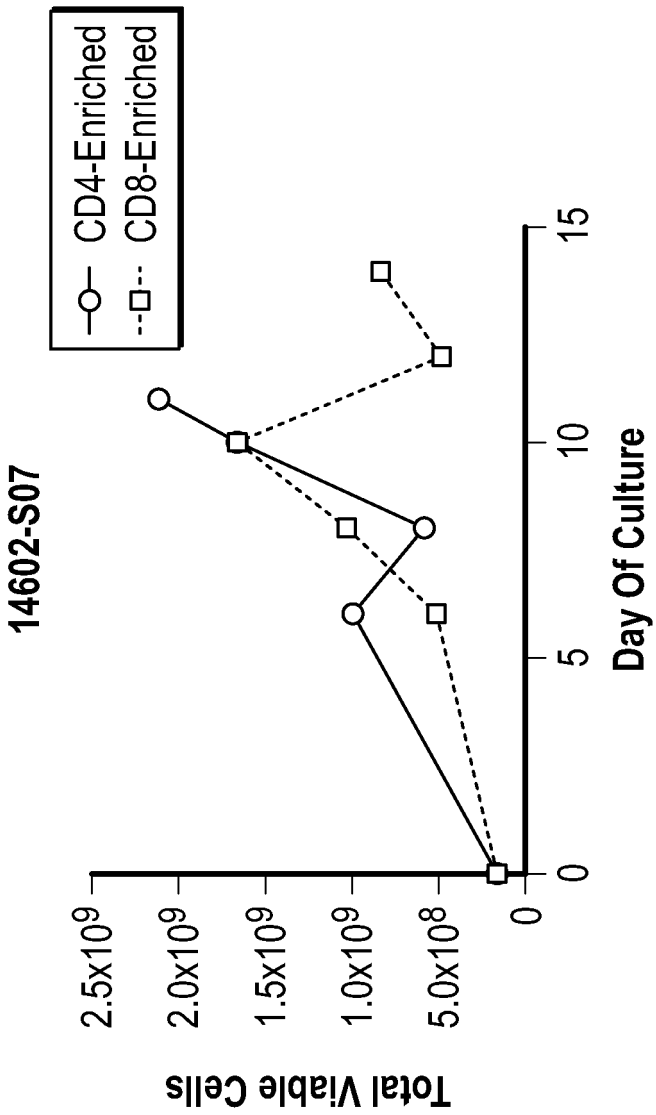
Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S05 CD4	95.2	95.1		97.7
14602-S05 CD8	97.5		97.3	96.6

FIG. 34B

Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)	CD3	CD4+CD8- (of CD3)
14602-S06 CD8	99.8		99.7	97		
14602-S06-02 CD4	98.1	98.1		98.5		
14602-S06-04 CD8	99.4		94.4	95.5	98.3	0.1

CD4-CD8+ (of CD3)	CD62L	Total CD28 from CD28(CD3)	CD27	CD127	CD45RA+/ CD45RO-	CD45RA+
98.3	49.2	57.7	99.9	70.3	48.3	99.3

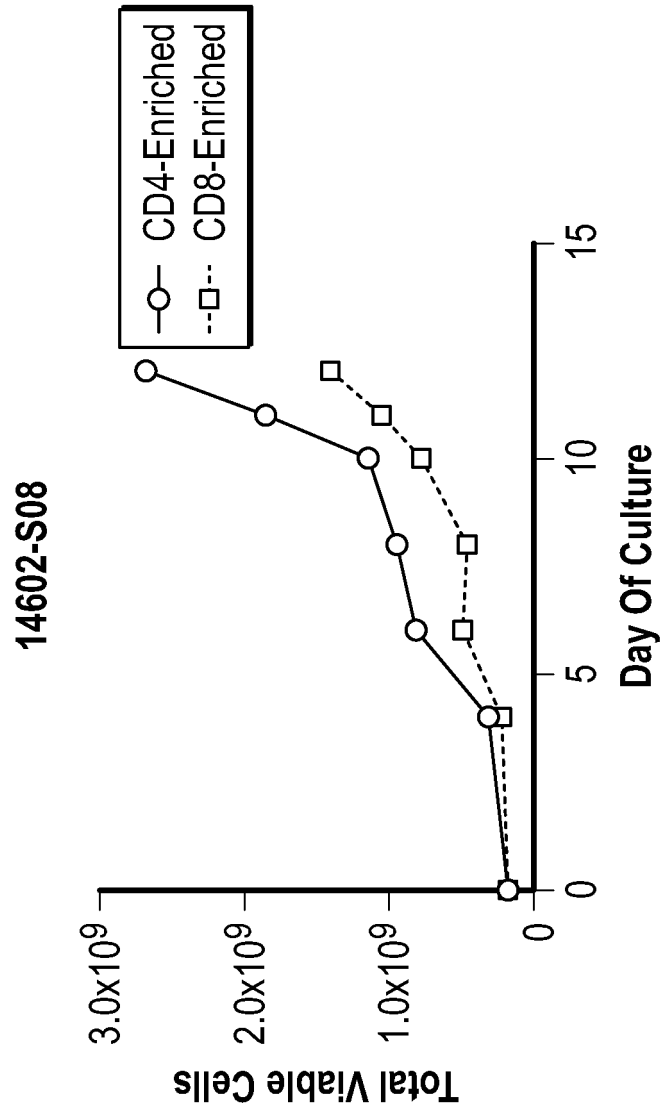
FIG. 34C



Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)	CD3	CD4+CD8- (of CD3)
14602-S07 CD4	98.6	98.5		94.1	84.3	98.7
14602-S07 CD8	99.3		99	95.2	99.6	0.7

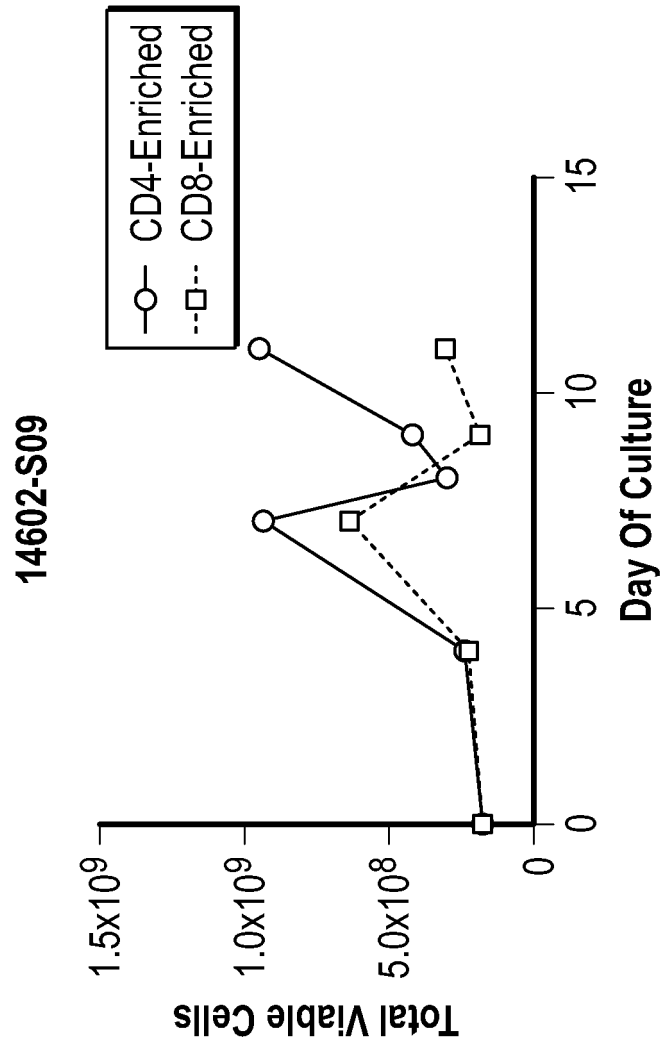
CD4-CD8+ (of CD3)	CD62L	total CD28 (from CD28/CD3)	CD27	CD127	CD45RA+/ CD45RO-	CD45RA+
0	57	98.8	99.4	37	51.4	65.5
97.3	66.1	51.2	99.8	55.6	52.8	94

FIG. 35A



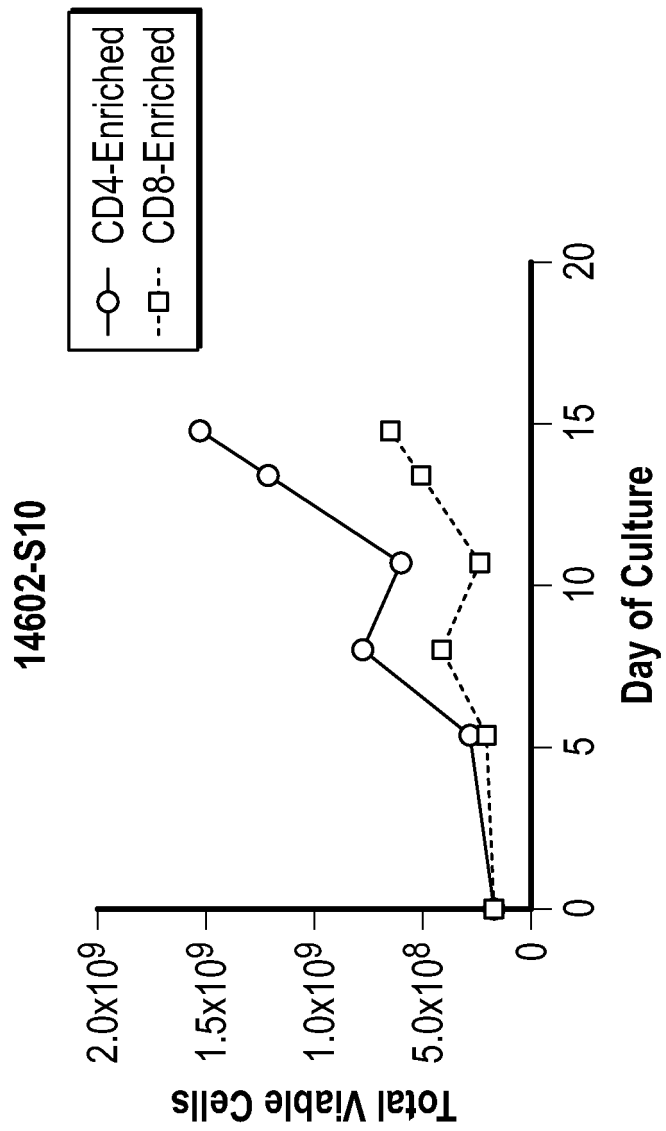
Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S08 CD4	97.4	97.3		96.1
14602-S08 CD8	97.8		97.6	95.6

FIG. 35B



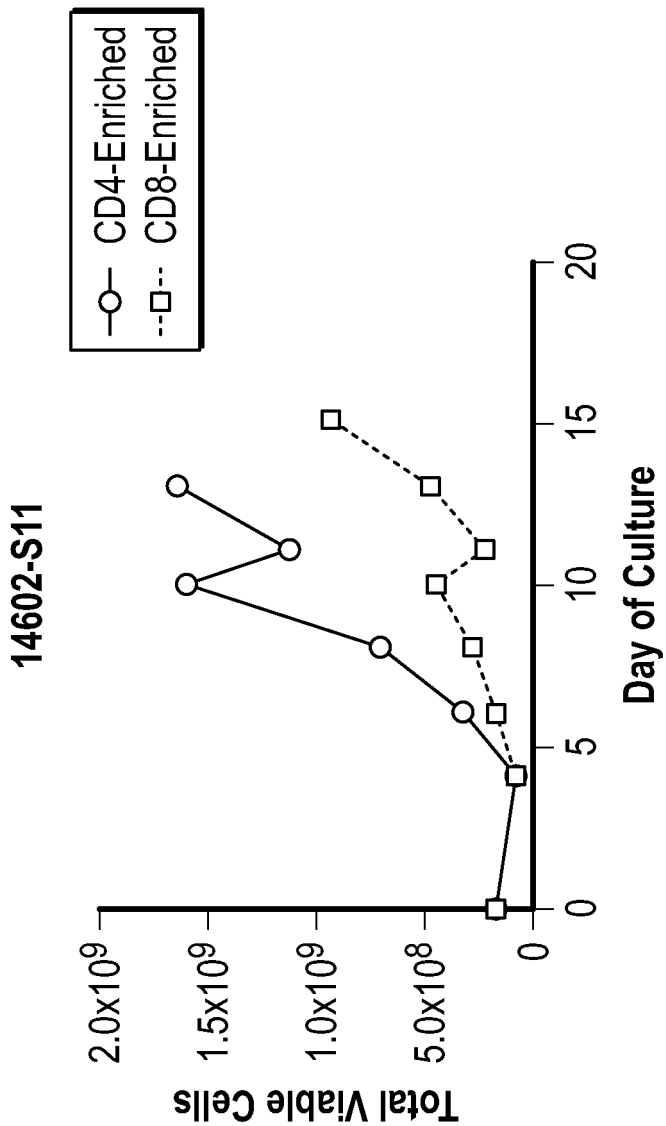
Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S09 CD4	99.4	99.4		95.2
14602-S09 CD8	99.3		99	92.5

FIG. 35C



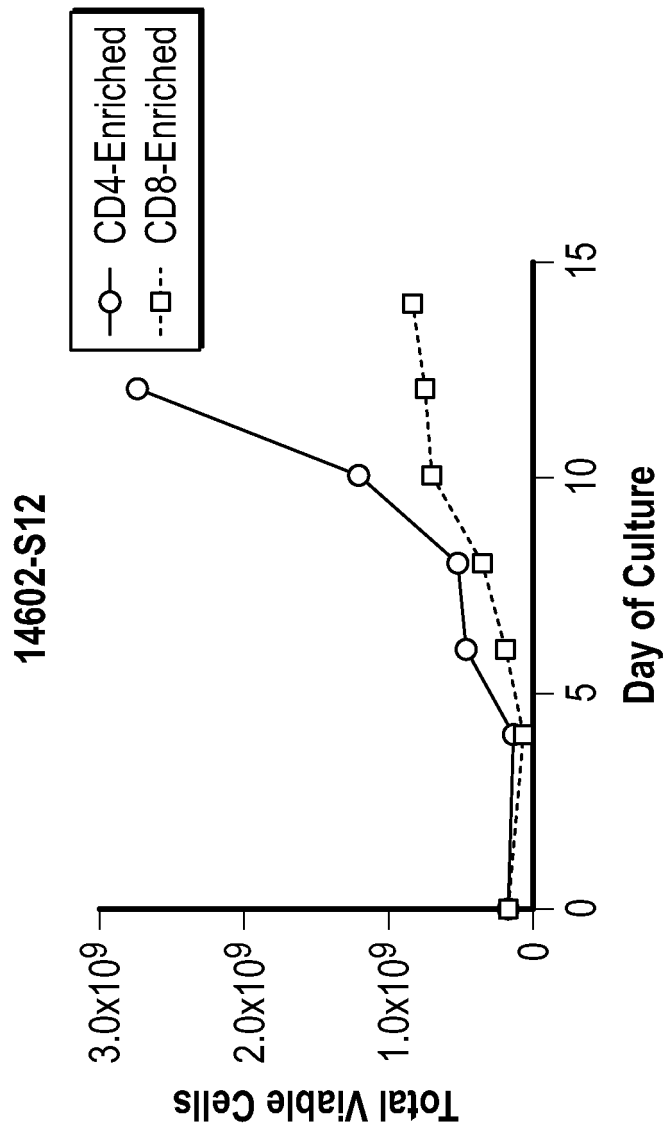
Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S10 CD4	98.6	98.4		97.7
14602-S10 CD8	97.6		93.4	96.1

FIG. 36A



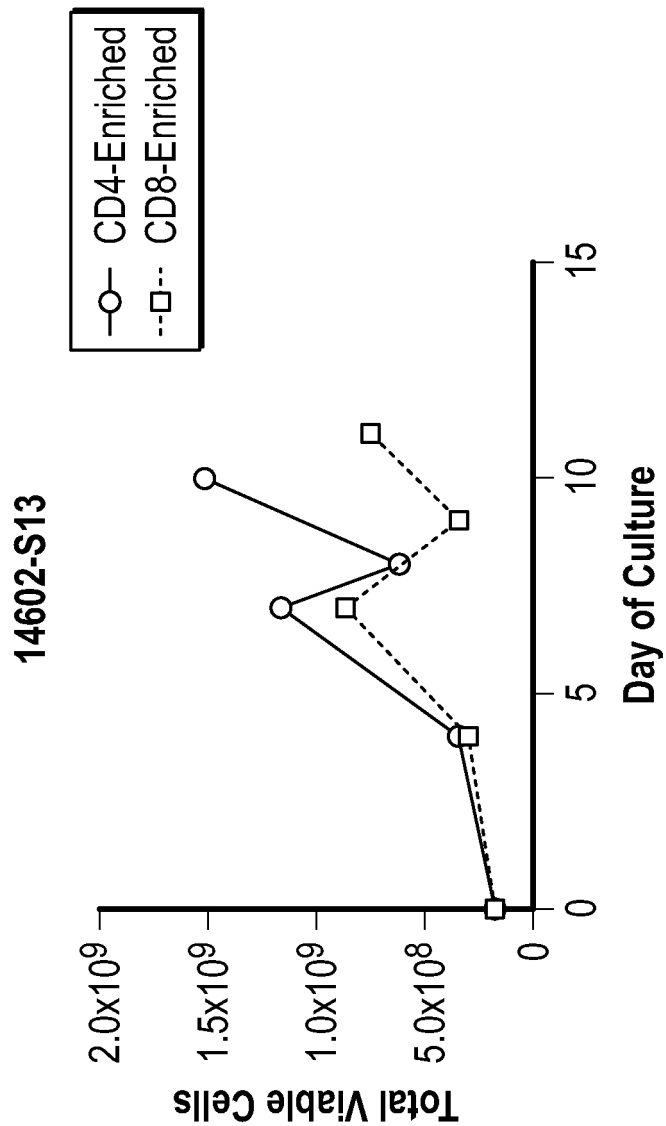
Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S11 CD4	99.2	99.1		98.1
14602-S11 CD8	97.1		97.1	93.7

FIG. 36B



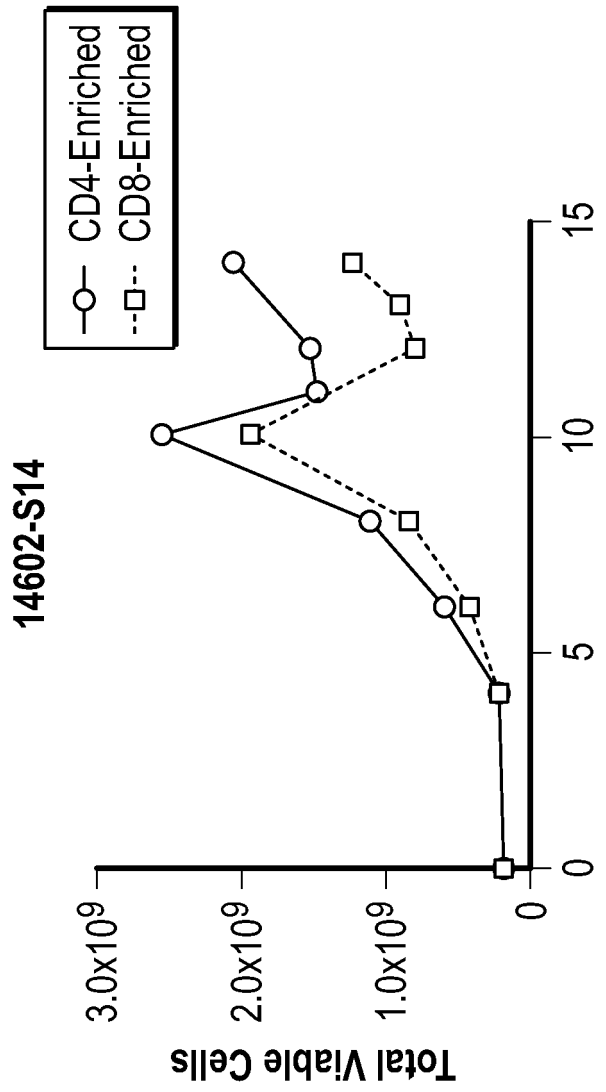
Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S12 CD4	98.7	98.7		97.3
14602-S12 CD8	99.8		99.8	94

FIG. 36C



Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S13 CD4	99.8	99.8		95.9
14602-S14 CD8	99.8		99.8	97

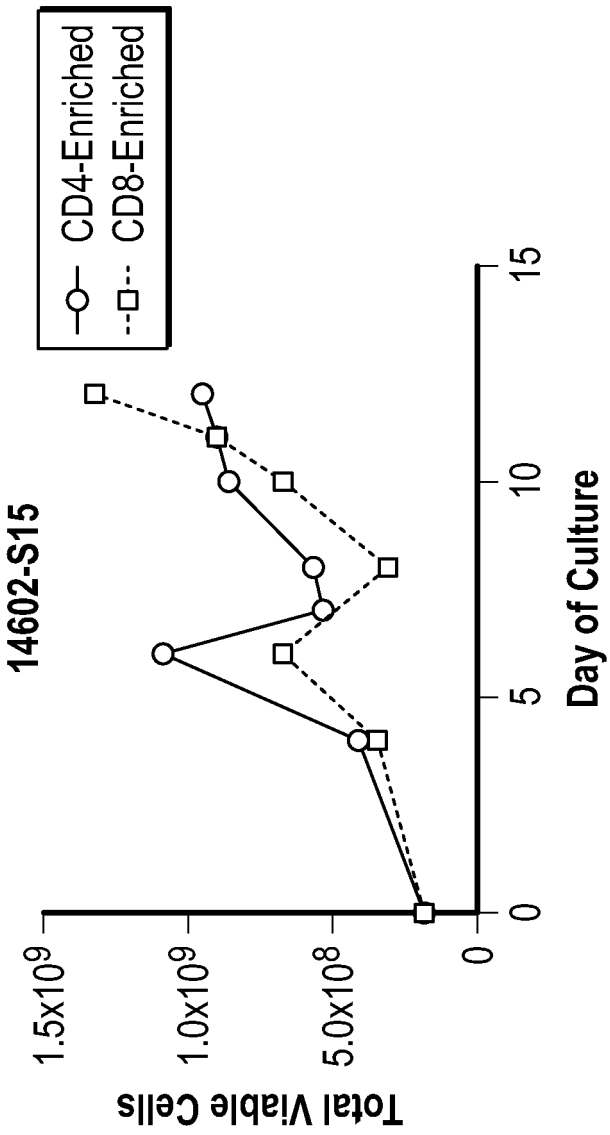
FIG. 36D



Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)	CD3	CD4+CD8- (of CD3)
14602-S14 CD4	99.4	99.4		98.4	99.8	99.5
14602-S14 CD8	99.4		99.2	95.1	99.8	0

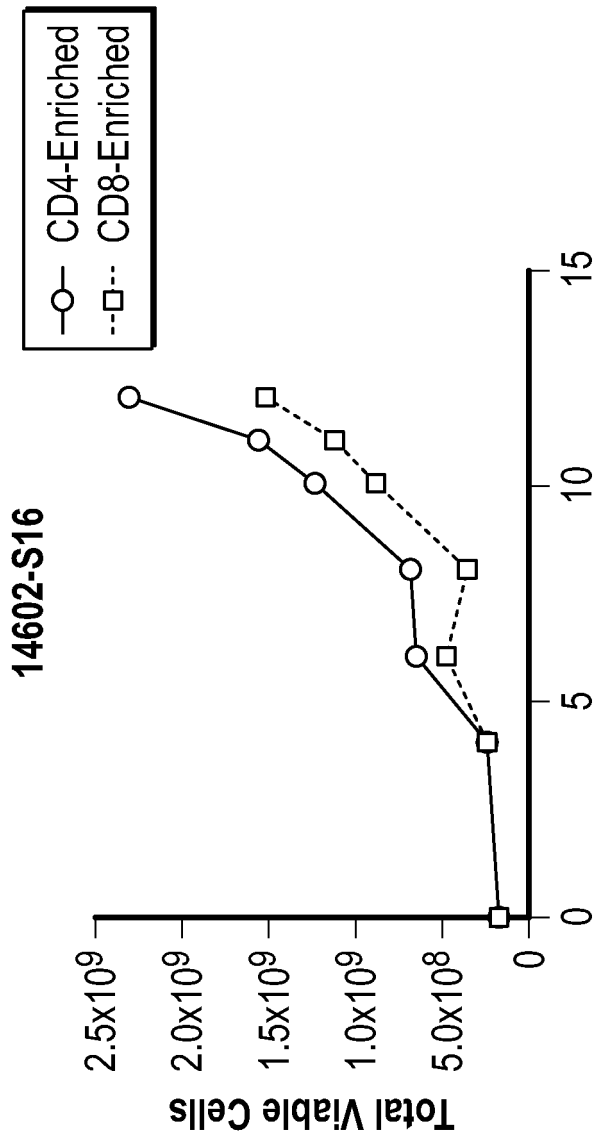
CD4-CD8+ (of CD3)	CD62L	total CD28 (from CD28/CD3)	CD27	CD127	CD45RA+/ CD45RO-	CD45RA+
0	85.3	99.4	98.3	82.5	71.3	94.1
99.5	76.1	73.6	99.4	67	63.6	96.8

FIG. 37A



Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S15 CD4	98.1	98		97.7
14602-S15 CD8	98.4		97.9	96.2

FIG. 37B



Product ID	Total EGFRt+ (pre-cryo)	CD4+/EGFRt+ (pre-cryo)	CD8+/EGFRt+ (pre-cryo)	Total EGFRt+ (release testing)
14602-S16 CD4	96.9	96.9		96.3
14602-S16 CD8	96.2		95.8	94.9

FIG. 37C

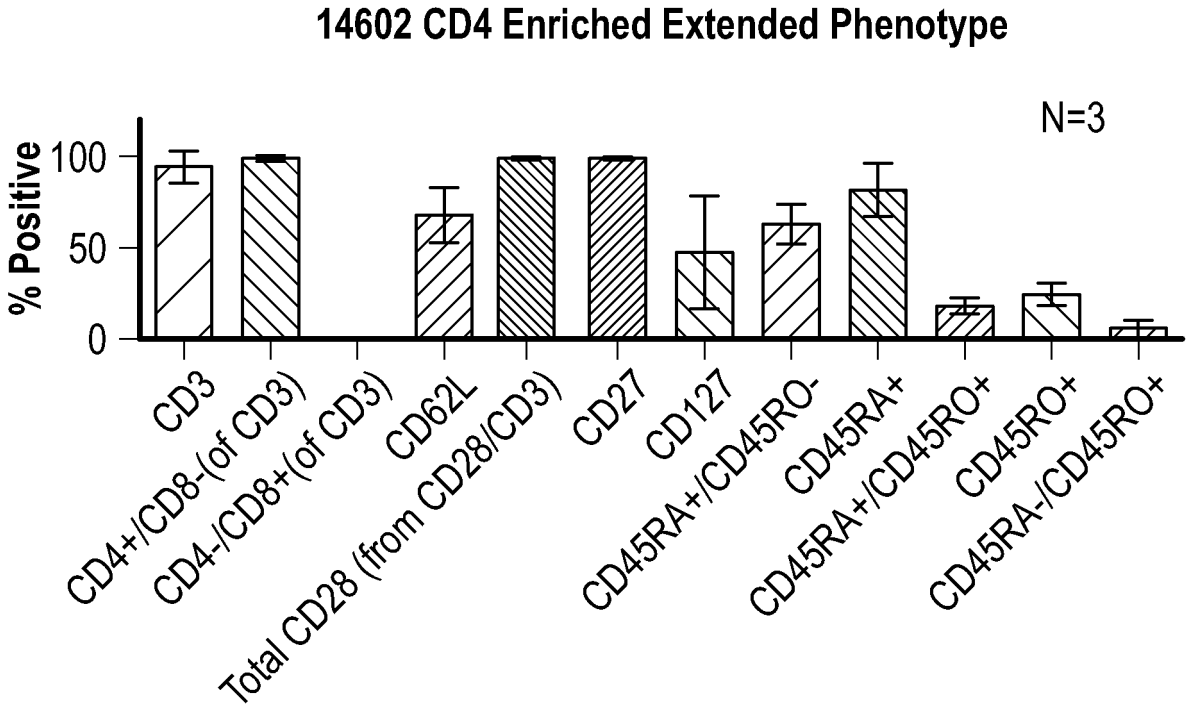


FIG. 38A

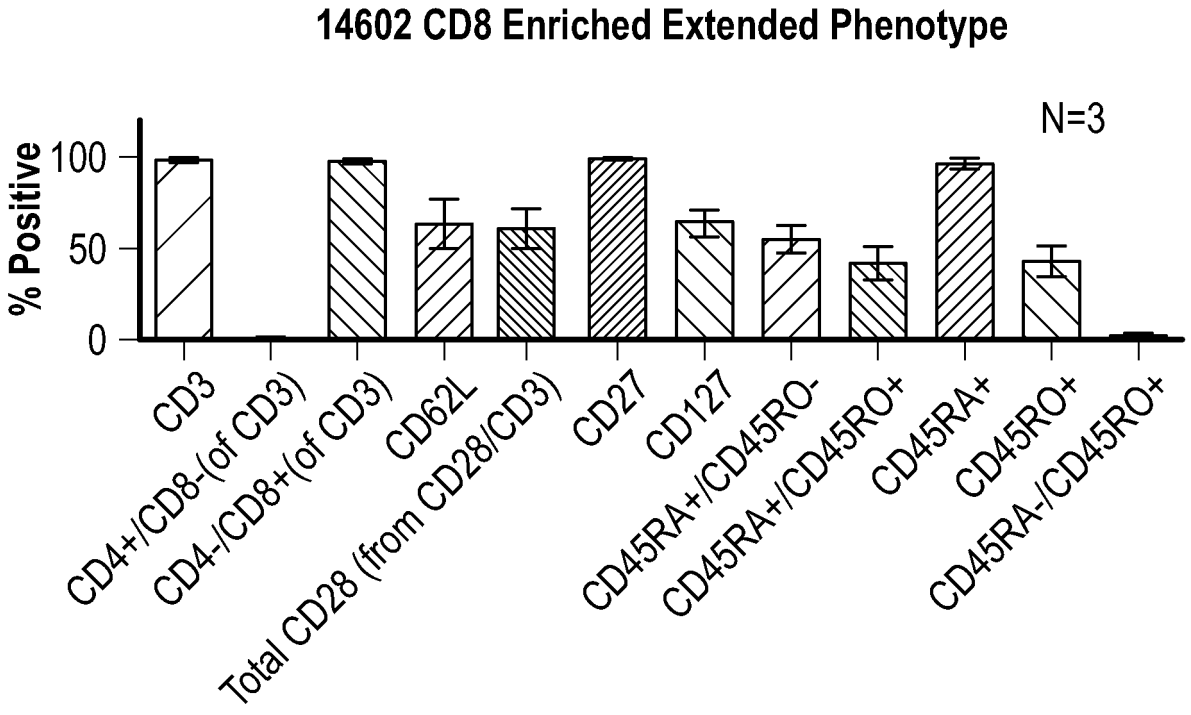


FIG. 38B

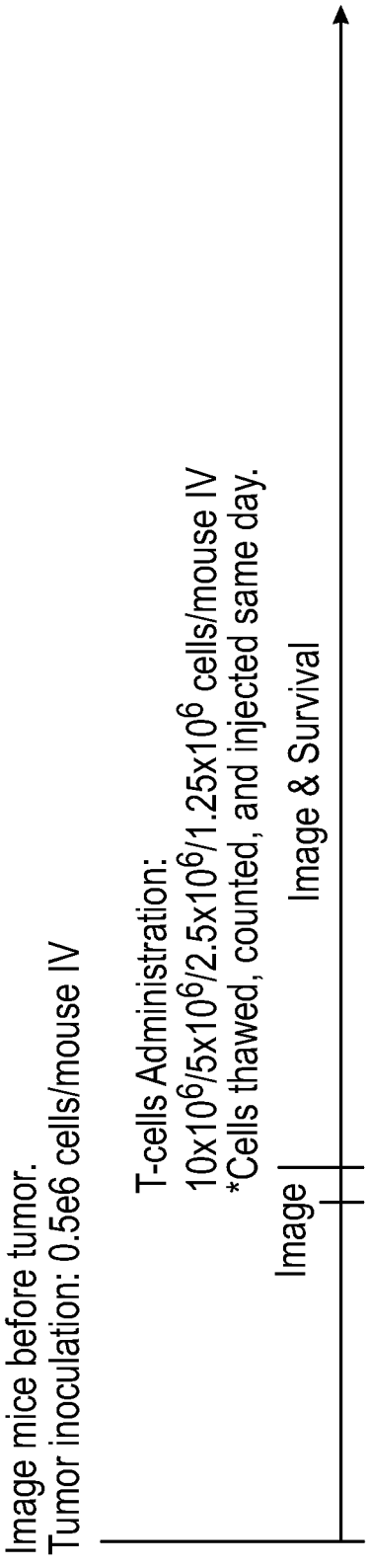

Image mice before tumor.
Tumor inoculation: 0.5e6 cells/mouse IV
T-cells Administration:
10x10^6/5x10^6/2.5x10^6/1.25x10^6 cells/mouse IV
*Cells thawed, counted, and injected same day.
Image
6 7
Image & Survival
Day 0

FIG. 39A

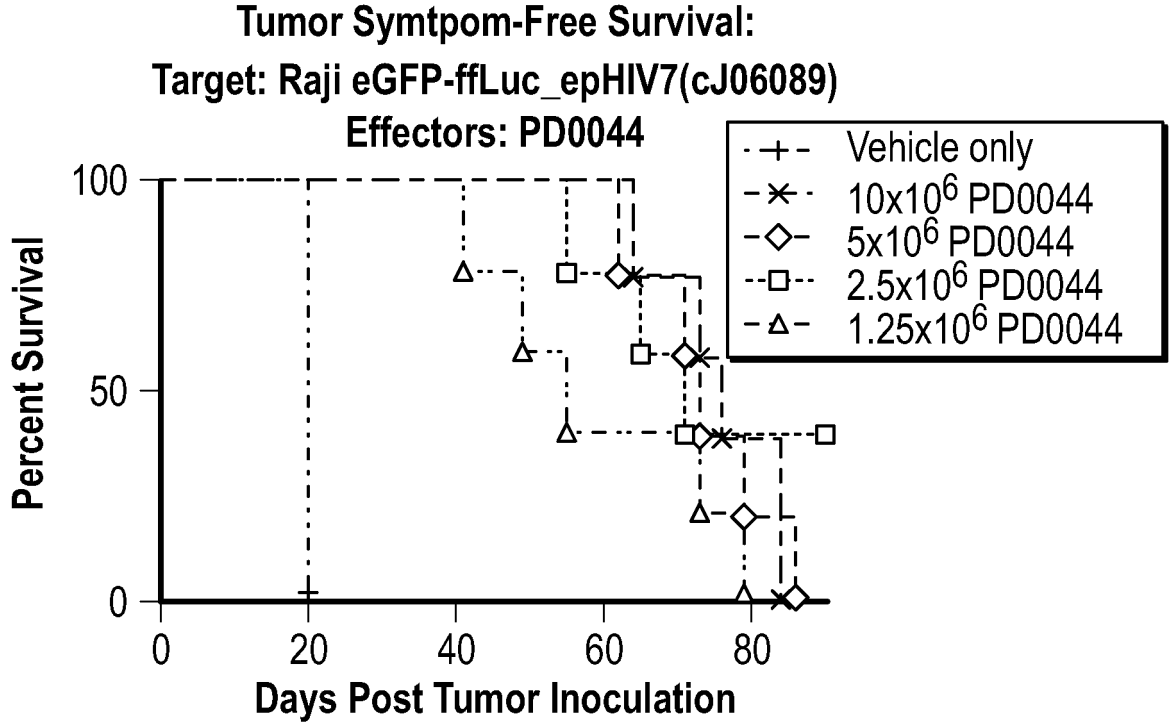


FIG. 39B1

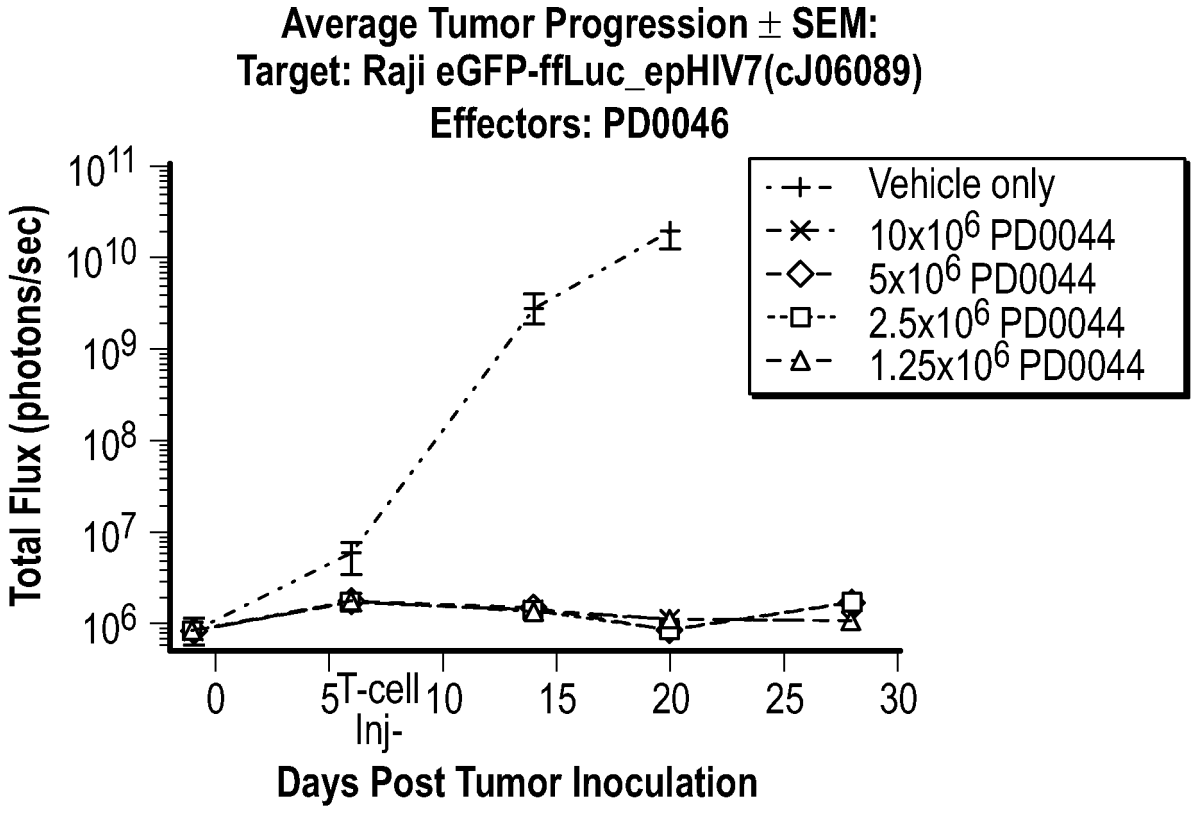


FIG. 39B2

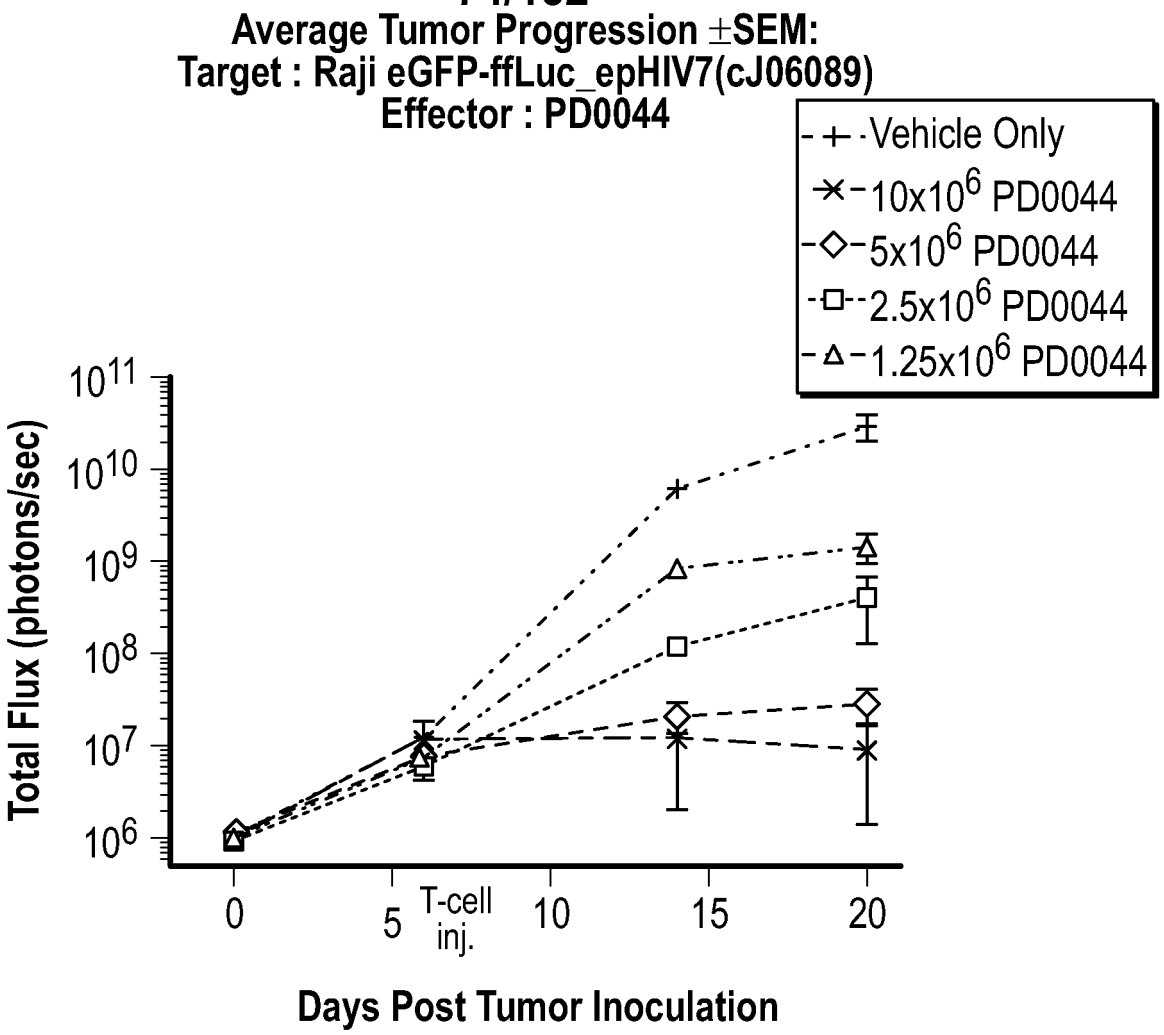


FIG. 40A

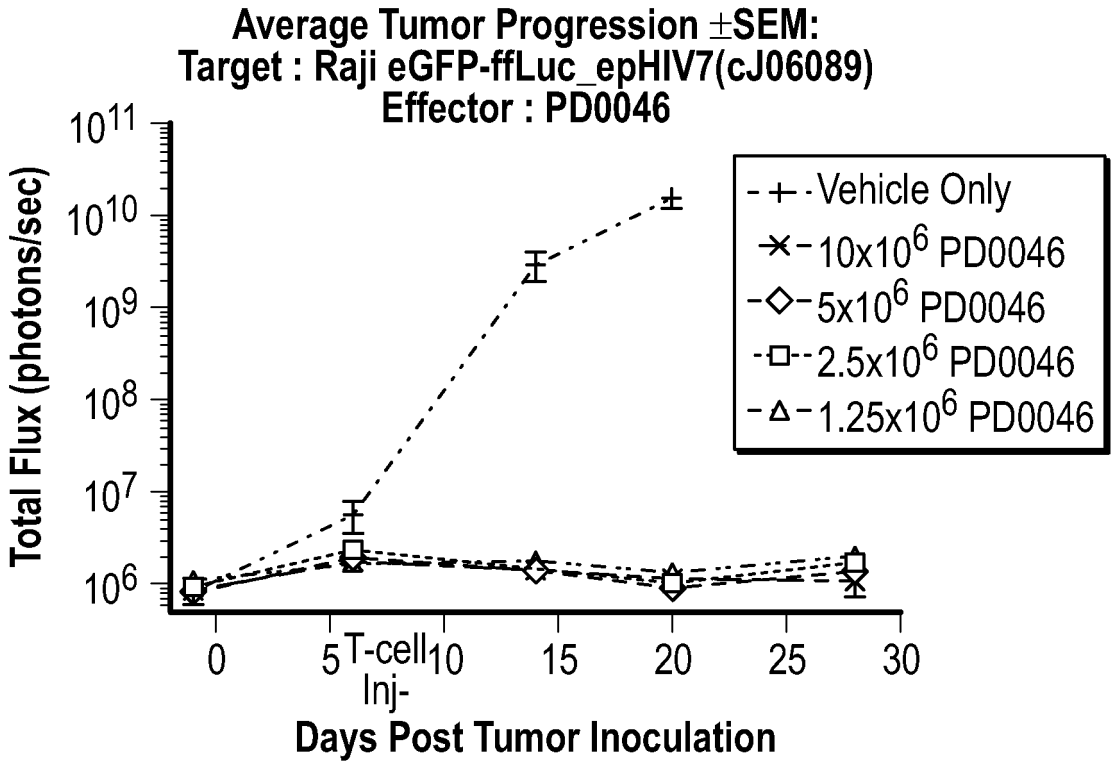


FIG. 40B

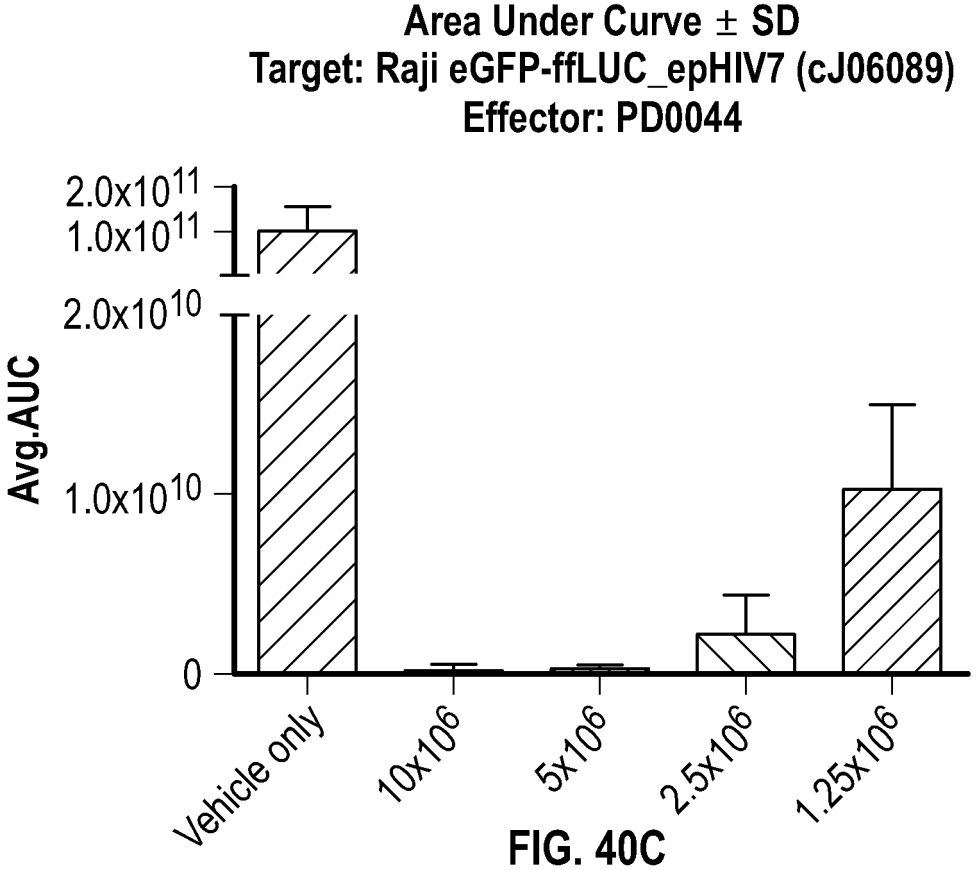


FIG. 40C

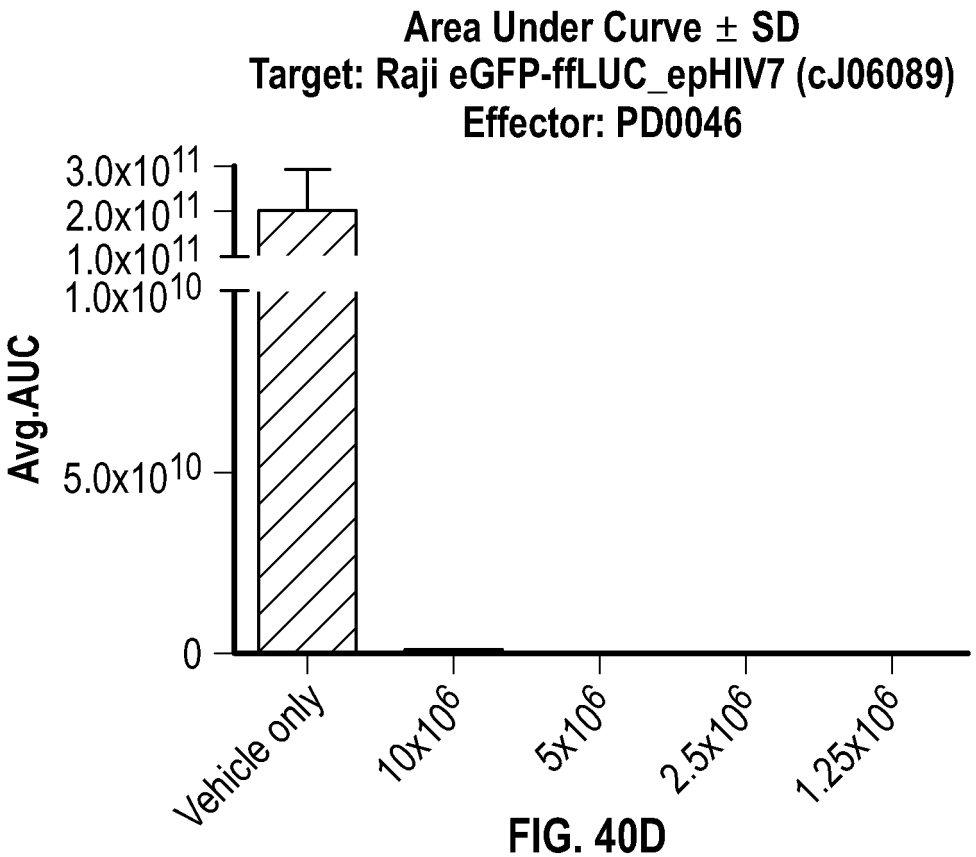


FIG. 40D

SUBSTITUTE SHEET (RULE 26)

JME13-25: Cytokine Growth Conditions

AIM(S):

1. Determine if there is an in vivo difference in killing ability between cells that have been grown in various cytokine conditions in vitro.

EXPERIMENTAL SET-UP:

(n=5 per group)

Group A: PBS only

Group B: "Normal" 1:1 EGFRt+ CD4:CD8 transduced With Zrx-014

PD0055 #1 (Donor PD0038 CD4 with 5ng/ml IL7 & 0.5ng/ml IL15, S1D14 @ 75.9% EGFRt+)

PD0051 #1 (Donor PD0038 CD8 with 50U/ml IL2 & 0.5ng/ml IL15, S1D21 @ 76.8% EGFRt+)

Group C: "Pulsed" 1:1 EGFRt+CD4:CD8 transduced with Zrx-014

PD0055 #2 (Donor PD0038 CD4 with 50U/ml IL2 pulse 5 days, then 5ng/ml IL7 & 5ng/ml IL21, S1D11 @ 81.2% EGFRt+)

PD0051 #2 (Donor PD0038 CD8 with 50U/ml IL2 pulse 5 days, then 5ng/ml IL7 & 5ng/ml IL21, S1D21 @ 89.5% EGFRt+)

*Note: Cells thawed, counted, and injected same day

Image mice before tumor

Tumor inoculation: 0.5e6 cells/mouse IV

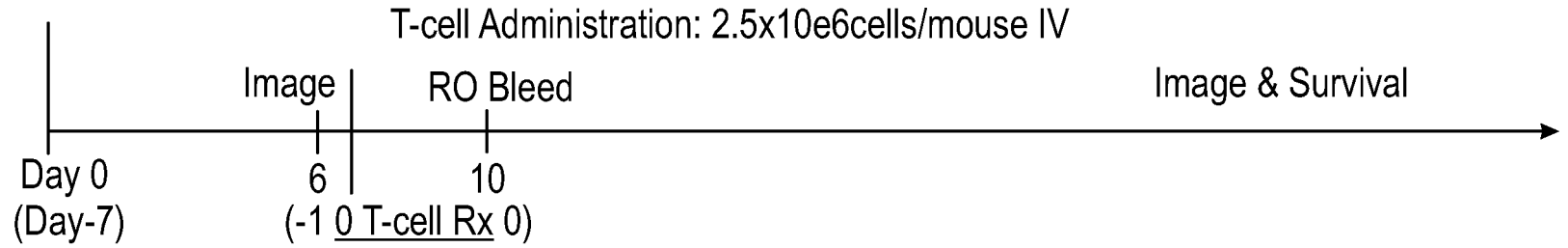


FIG. 41

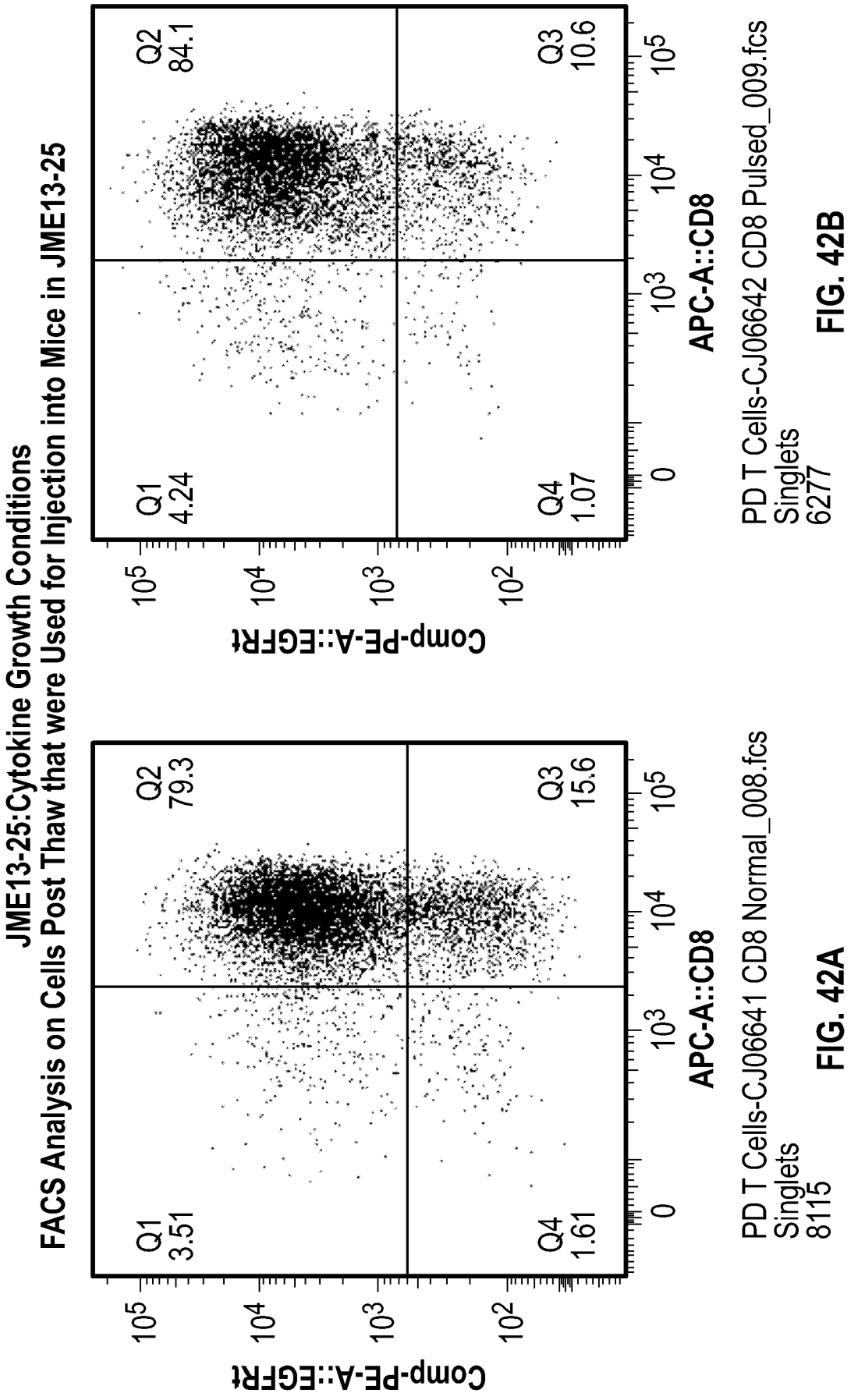


FIG. 42A

FIG. 42B

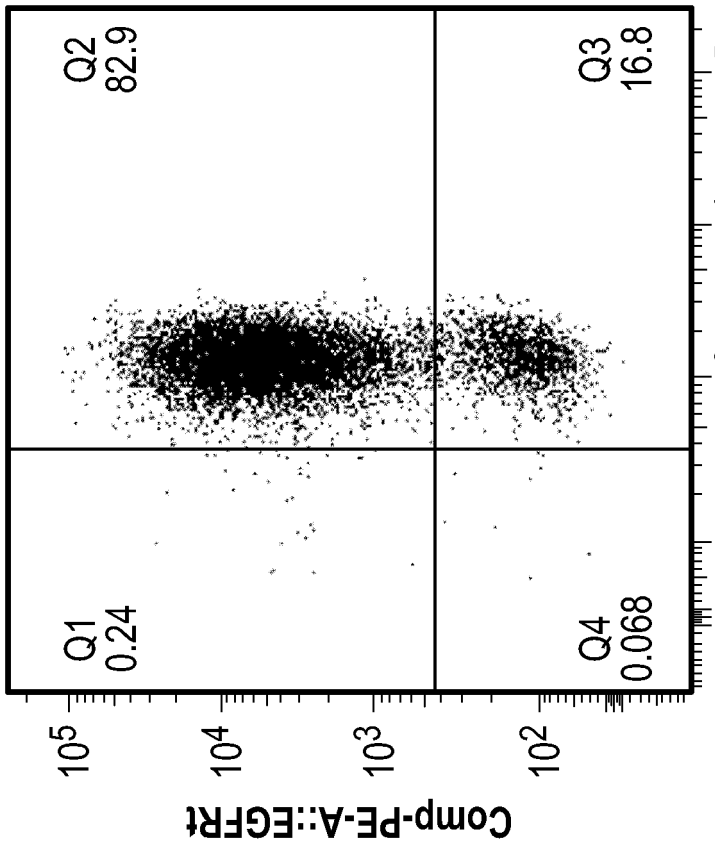


FIG. 42D

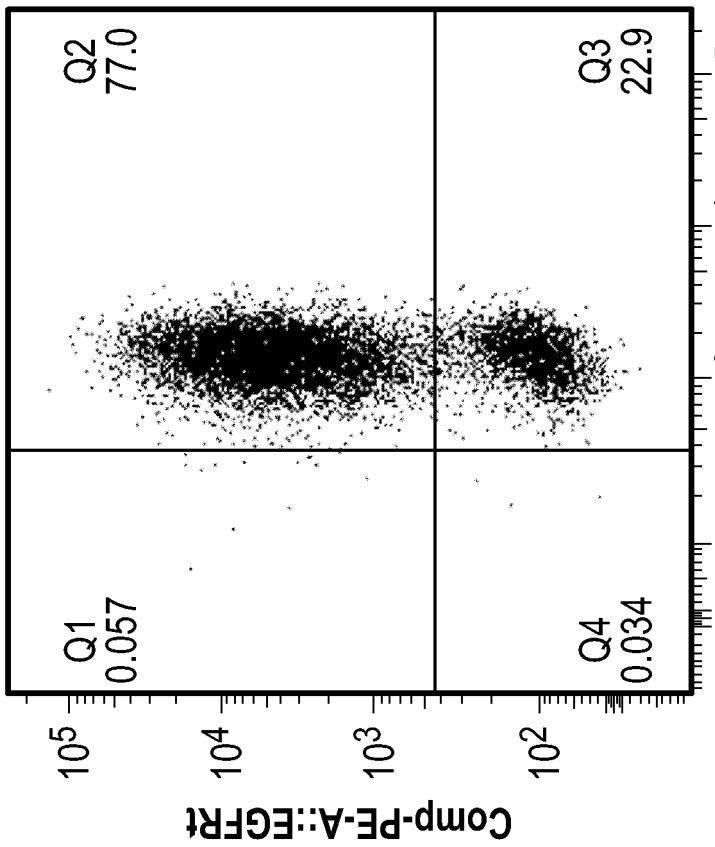


FIG. 42C

Cell Thawed out with Similar %EGFRt+

cJ#	Cell Line	Day of Freezeing EGFRt+	Day of Thaw EGFRt+
cJ06641	PD0051 #1 (CD8 in IL2/IL15)	76.8%	78.3%
cJ06642	PD0051 #2 (CD8 in IL2 pulse, IL7/IL21)	89.5%	84.1%
cJ06643	PD0055 #1 (CD4 in IL7/IL15)	75.9%	77.0%
cJ06645	PD0055 #2 (CD4 in IL2 pulse, IL7/IL21)	81.2%	82.9%

Samples collected on mixed samples left over from preparation for injection into mice.
Data acquired but not analyzed.

FIG. 42E

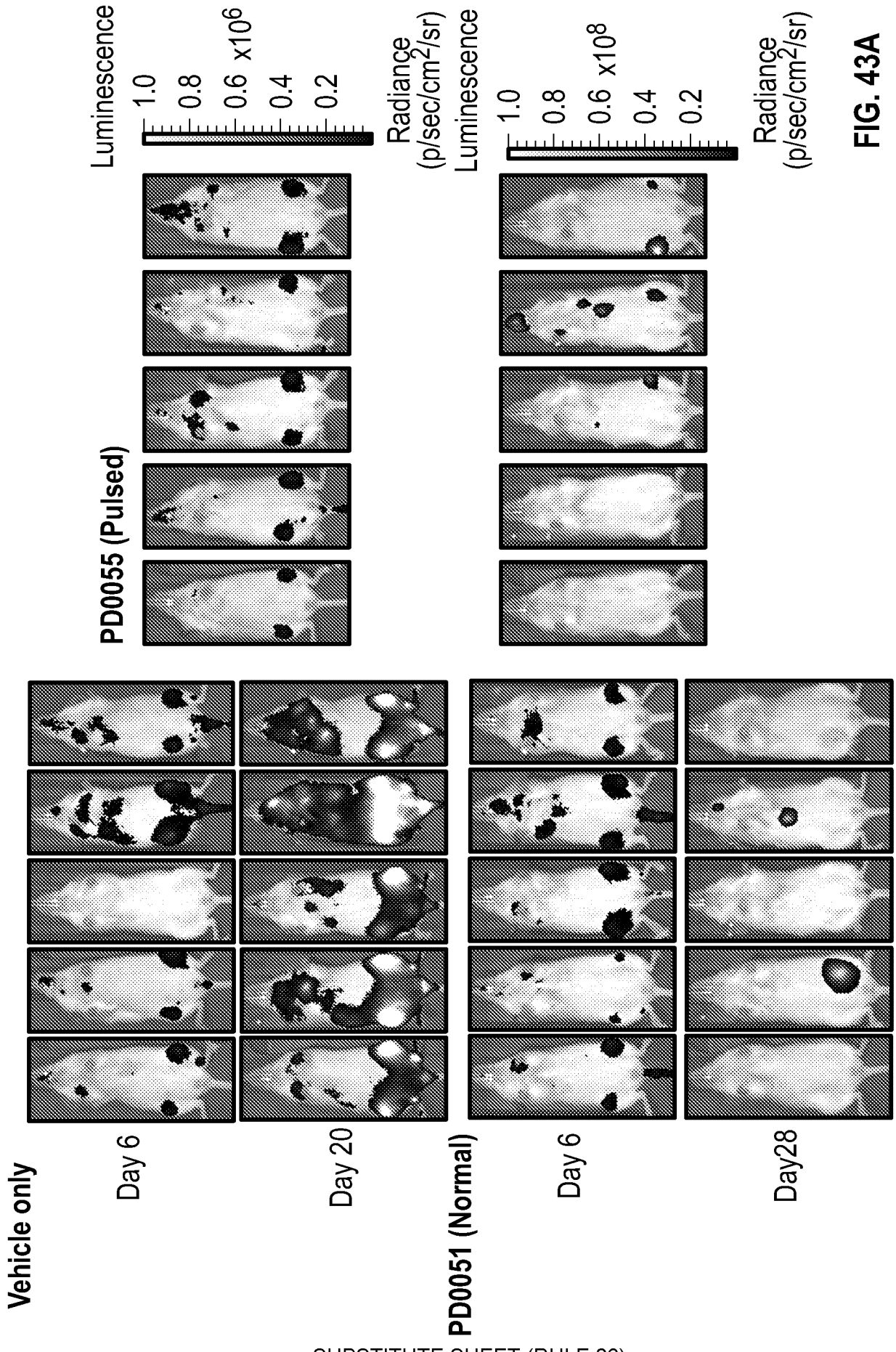

Luminescence
1.0
0.8
0.6 x10^6
0.4
0.2
Radiance (p/sec/cm2/sr)
PD0055 (Pulsed)
Luminescence
1.0
0.8
0.6 x10^8
0.4
0.2
Radiance (p/sec/cm2/sr)
Vehicle only
Day 6
Day 20
PD0051 (Normal)
Day 6
Day28

FIG. 43A

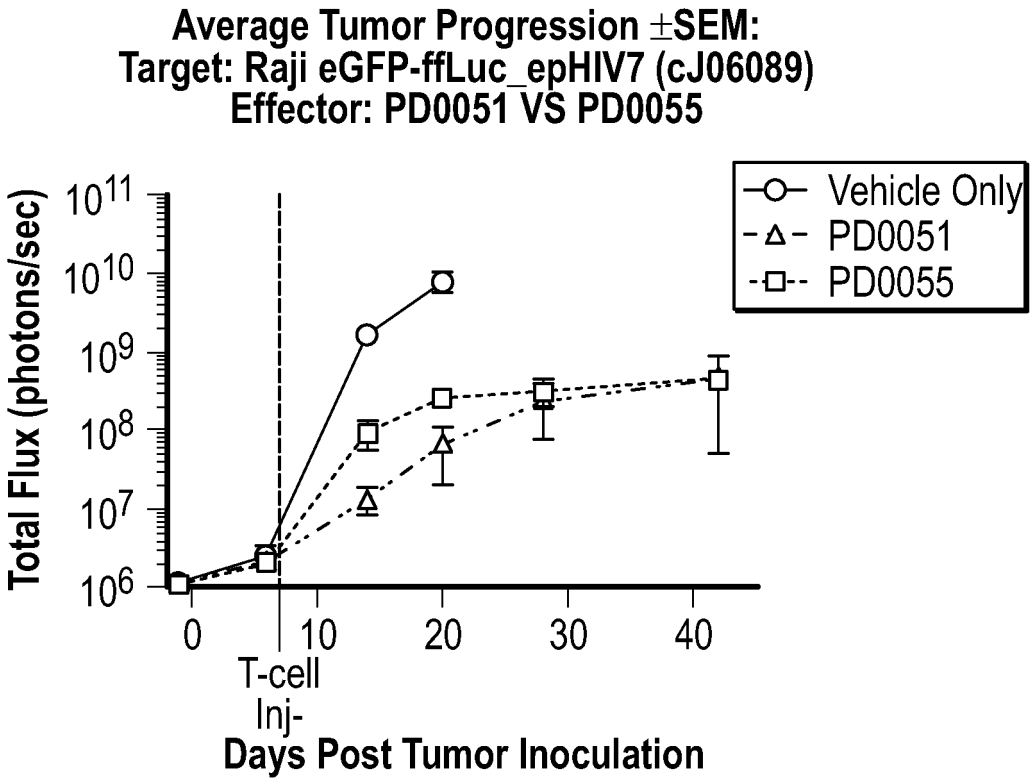


FIG. 43B

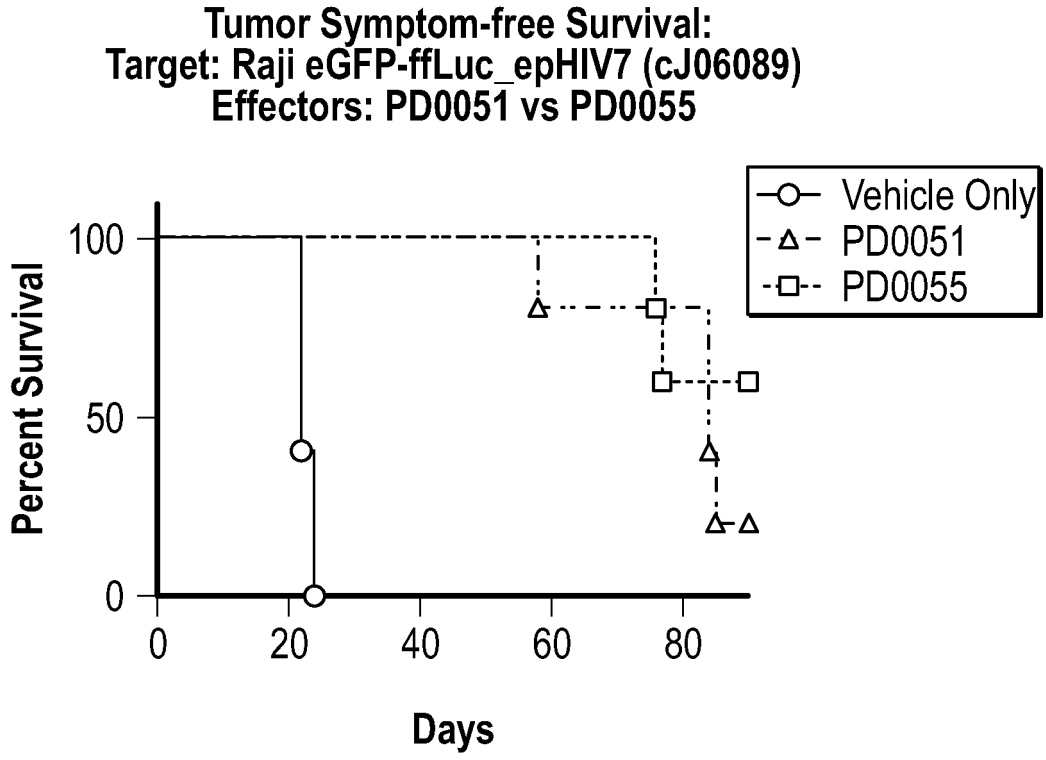


FIG. 43C

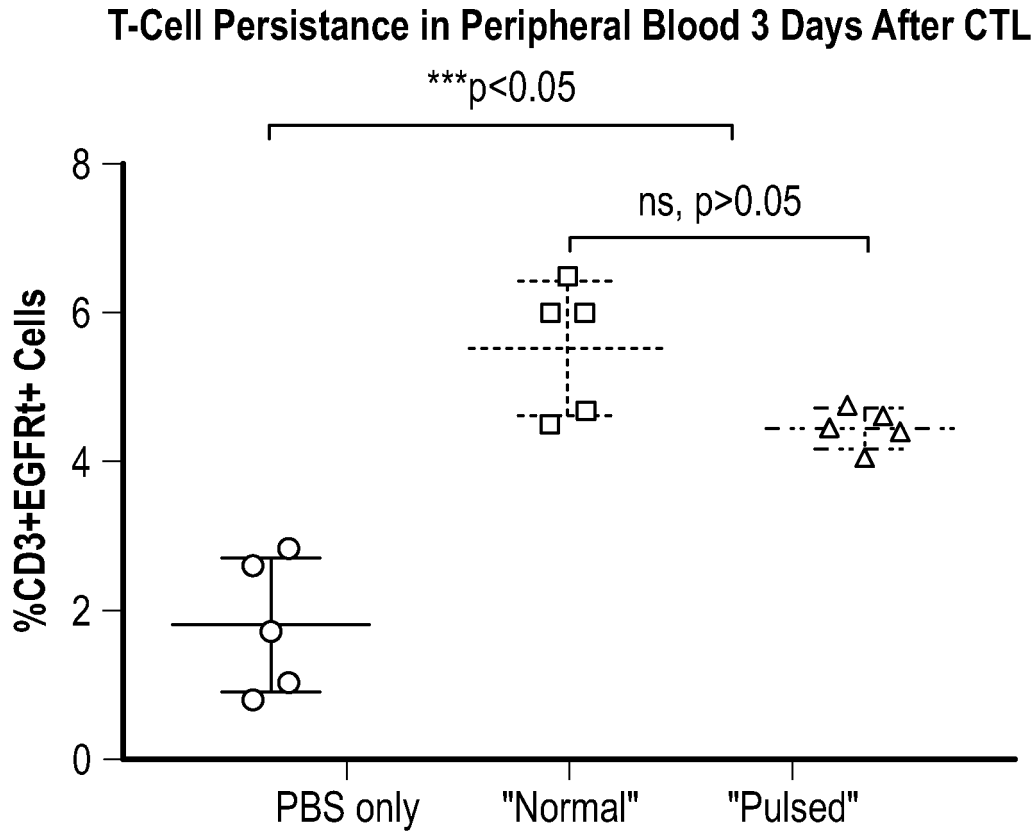


FIG. 44A

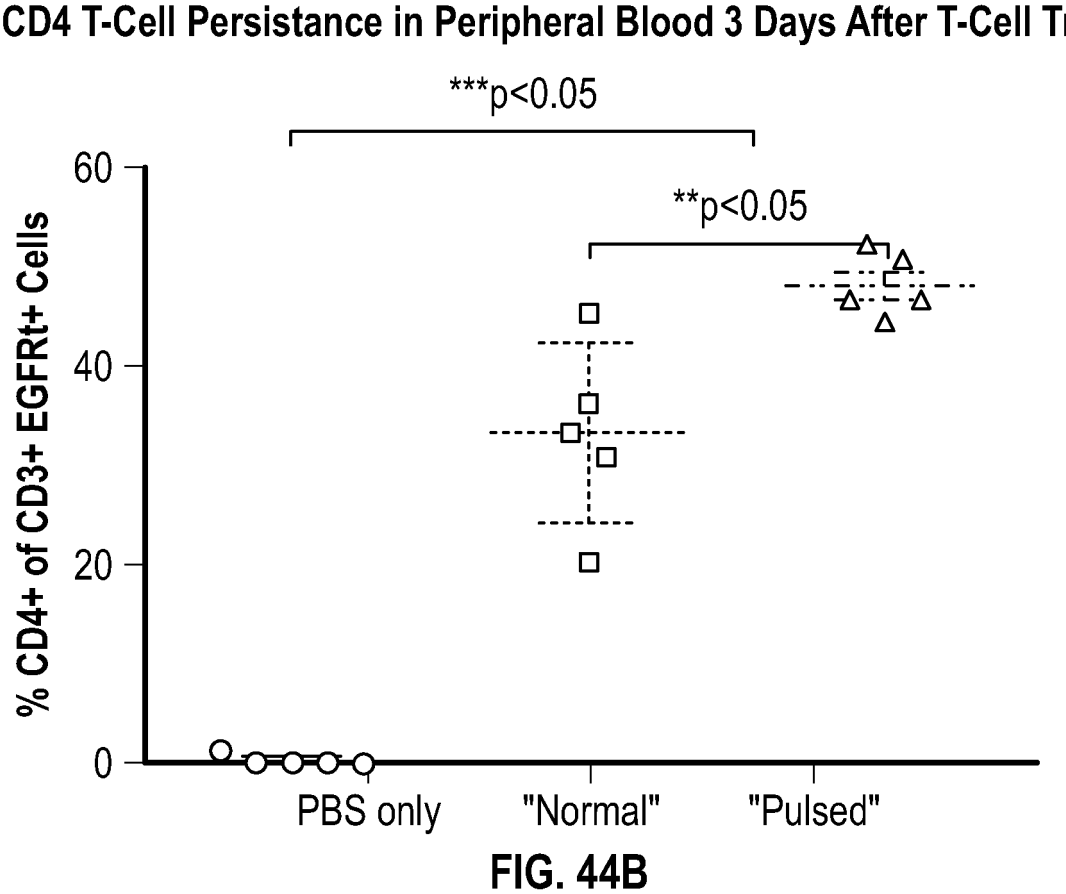
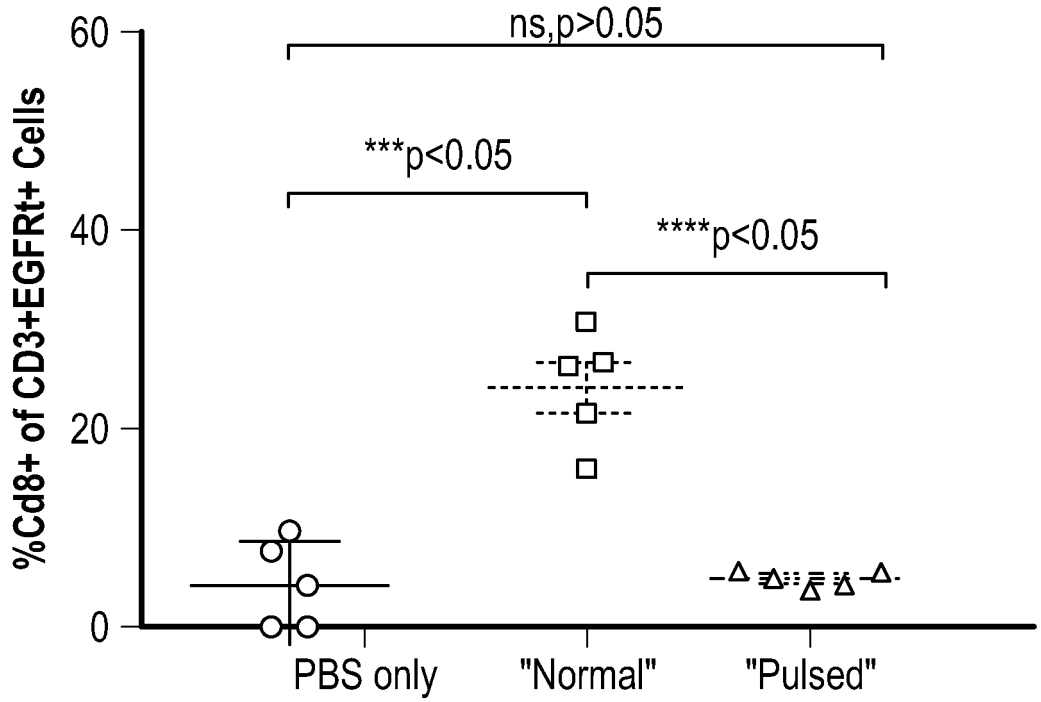


FIG. 44B

CD8 T-Cell Persistance in Peripheral Blood 3 Days After T-Cell Transfer



Caveats to Note:

- This staining is prior to inclusion of the Live/Dead stain and switching from CD3 to CD45 in optimized mouse panel.
- Lymphocyte gate is not confirmed.
- EGFRt staining in Cd3- population.
- CD4-CD8- population is present in CD3+EGFRt+ population.

FIG. 44C

SUBSTITUTE SHEET (RULE 26)

AIM(S):

1. Determine if there is an in vivo difference in killing ability between cells that have been grown in various cytokine conditions in vitro with repeat antigen encounters.

EXPERIMENTAL SET-UP:

(n=3 per group)

Group A: PBS only

Group B: "Normal"1:1 EGFRt+CD4:CD8 transduced With Zrx-014

PD0055 #1 (Donor PD0038 CD4 with 5ng/ml IL7 & 0.5ng/ml IL15, S1D14 @ 75.9% EGFRt+)

PD0051 #1 (Donor PD0038 CD8 with 50U/ml IL2 & 0.5ng/ml IL15, S1D21 @ 76.8% EGFRt+)

Group C: "Pulsed" 1:1 EGFRt+CD4: CD8 transduced with Zrx-014

PD0055 #2 (Donor PD0038 CD4 with 50U/ml IL2 pulse 5 days, then 5ng/ml IL7& 5ng/ml IL21, S1D11 @ 81.2% EGFRt+)

PD0051 #2 (Donor PD0038 CD8 with 50U/ml IL2 pulse 5 days, then 5ng/ml IL7& 5ng/ml IL21, S1D21 @ 89.5% EGFRt+)

*Note:Cells thawed, counted, and injected same day

Image mice before tumor

Tumor inoculation: 0.5e6 cells/mouse IV

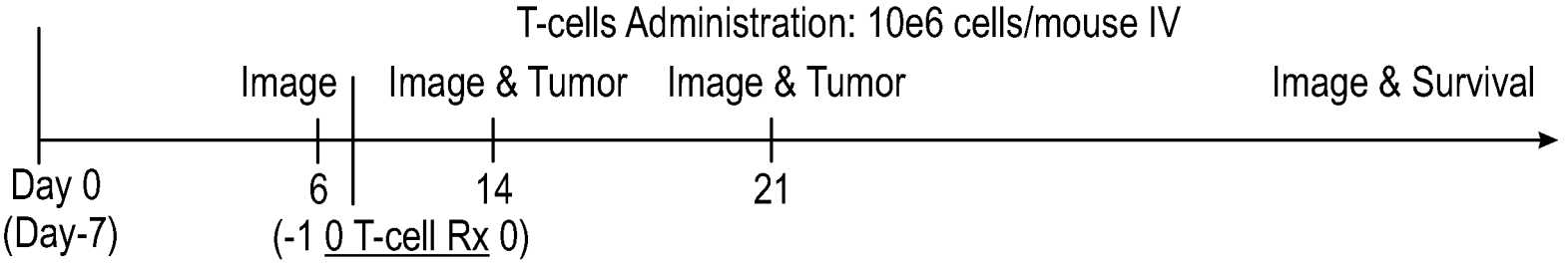


FIG. 45

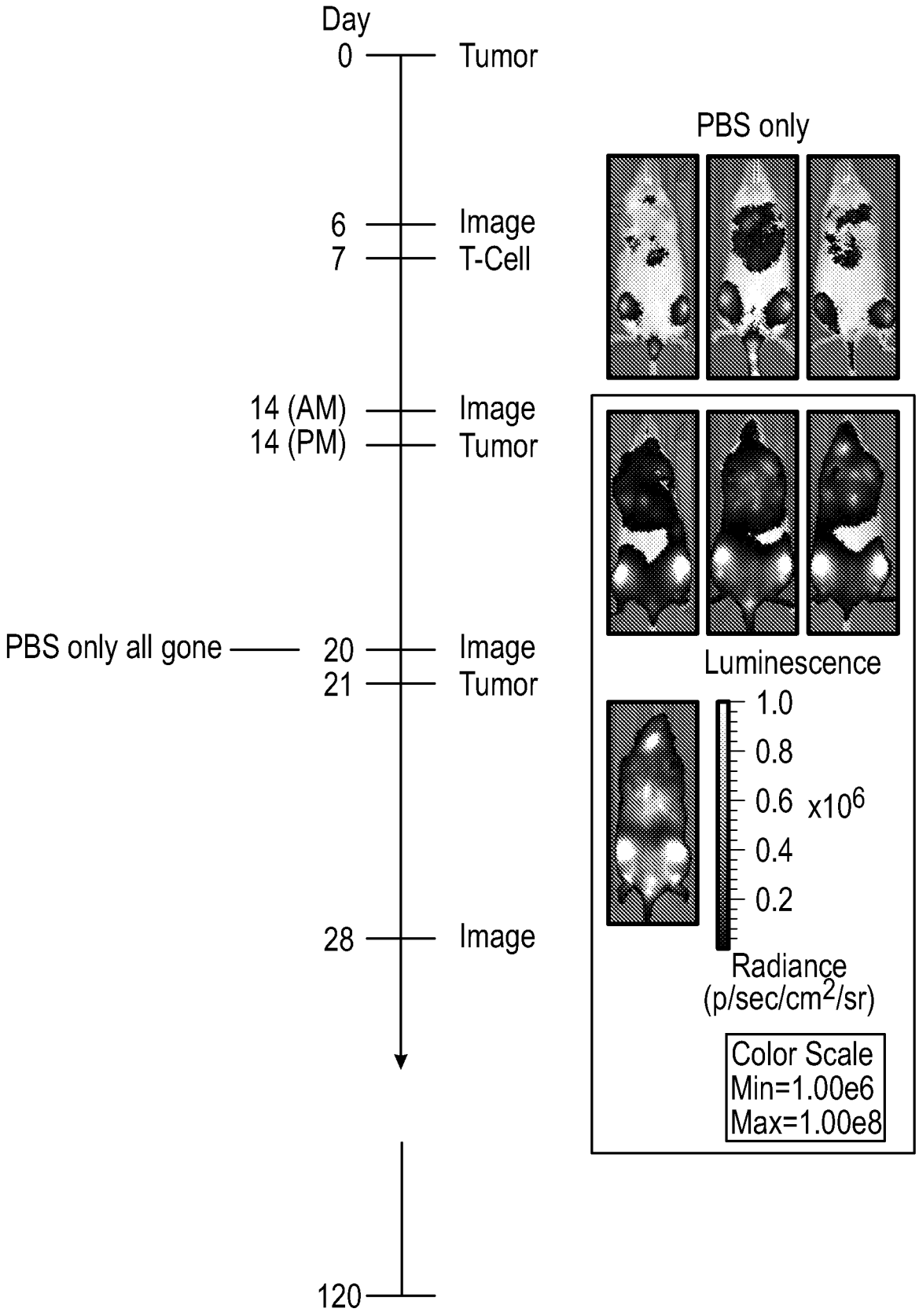

Day
0
Tumor
6
Image
7
T-Cell
14 (AM)
Image
14 (PM)
Tumor
PBS only all gone
20
Image
21
Tumor
28
Image
120
PBS only
Luminescence
1.0
0.8
0.6
x10^6
0.4
0.2
Radiance
(p/sec/cm^2/sr)
Color Scale
Min=1.00e6
Max=1.00e8

FIG. 46A

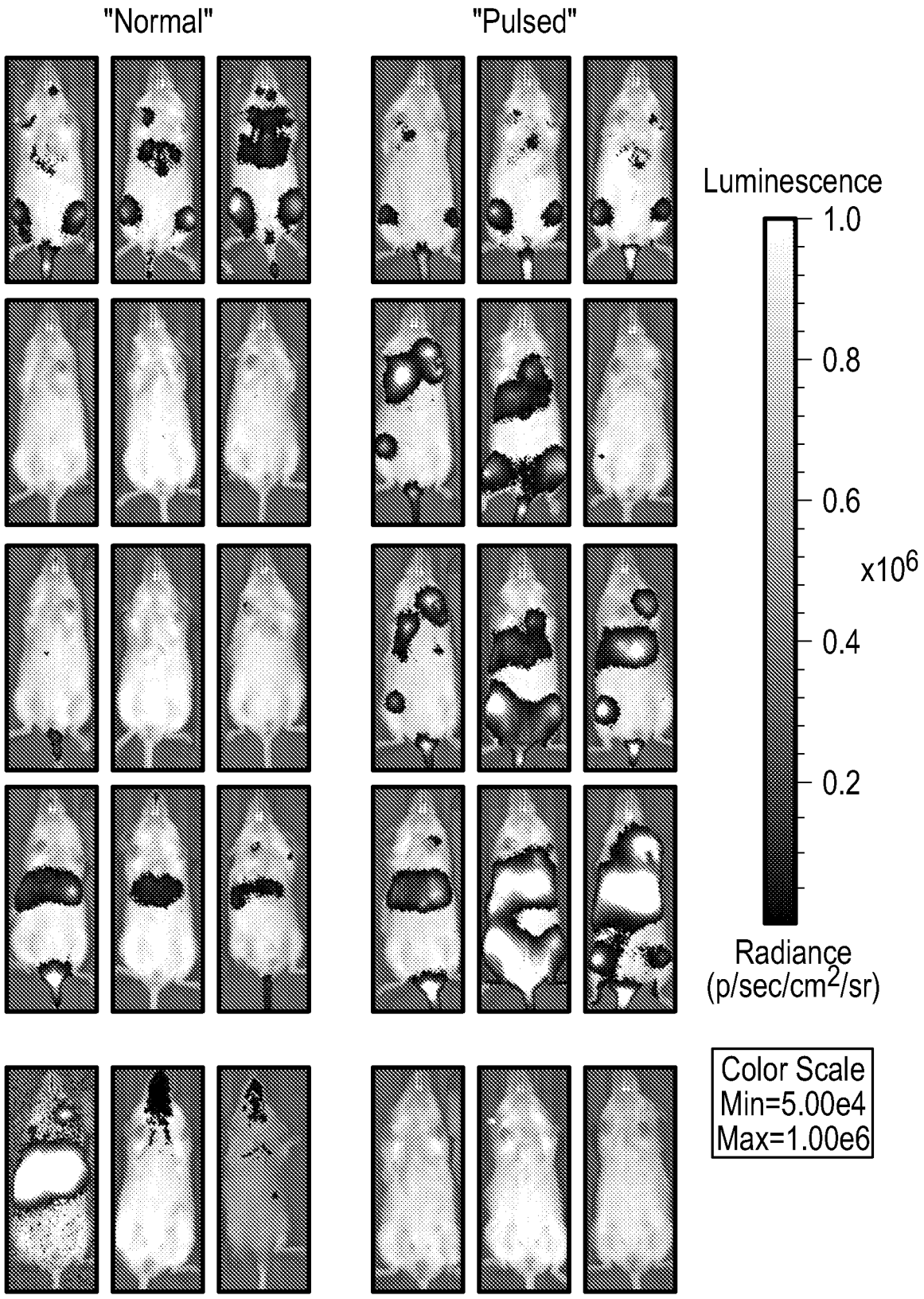

"Normal"
"Pulsed"
Luminescence
1.0
0.8
0.6
x10^6
0.4
0.2
Radiance
(p/sec/cm^2/sr)
Color Scale
Min=5.00e4
Max=1.00e6

FIG. 46B

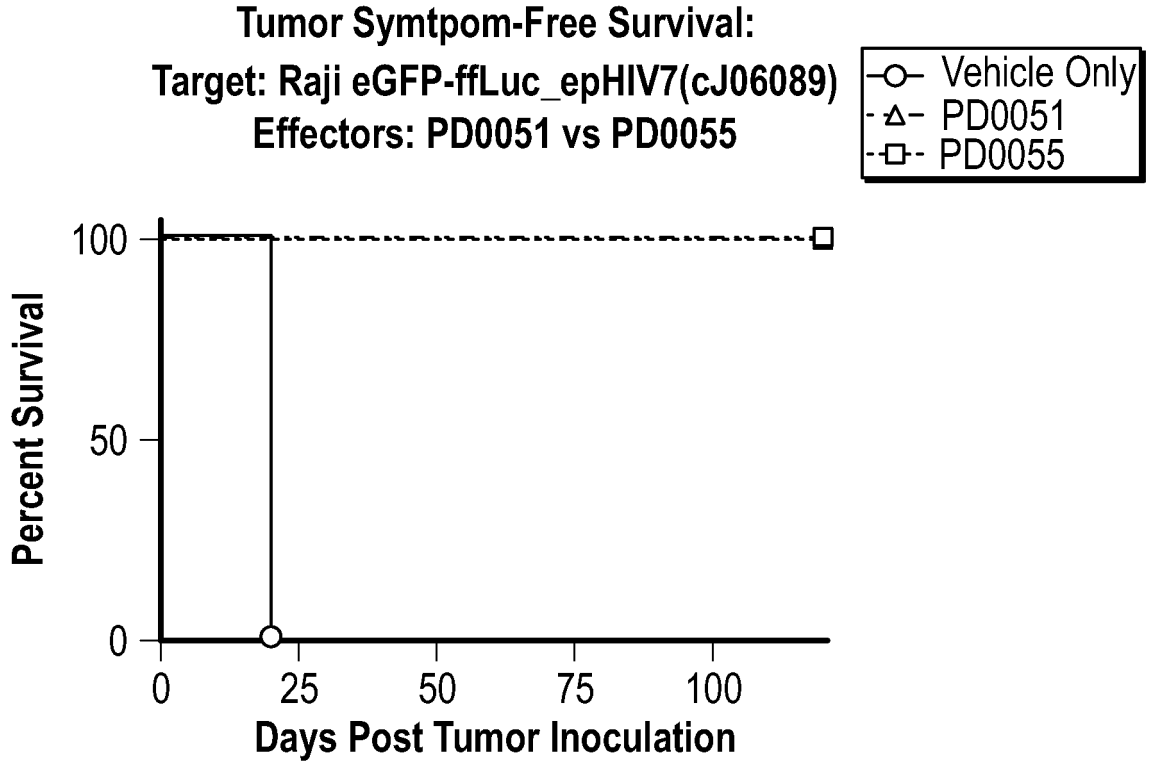


FIG. 47A

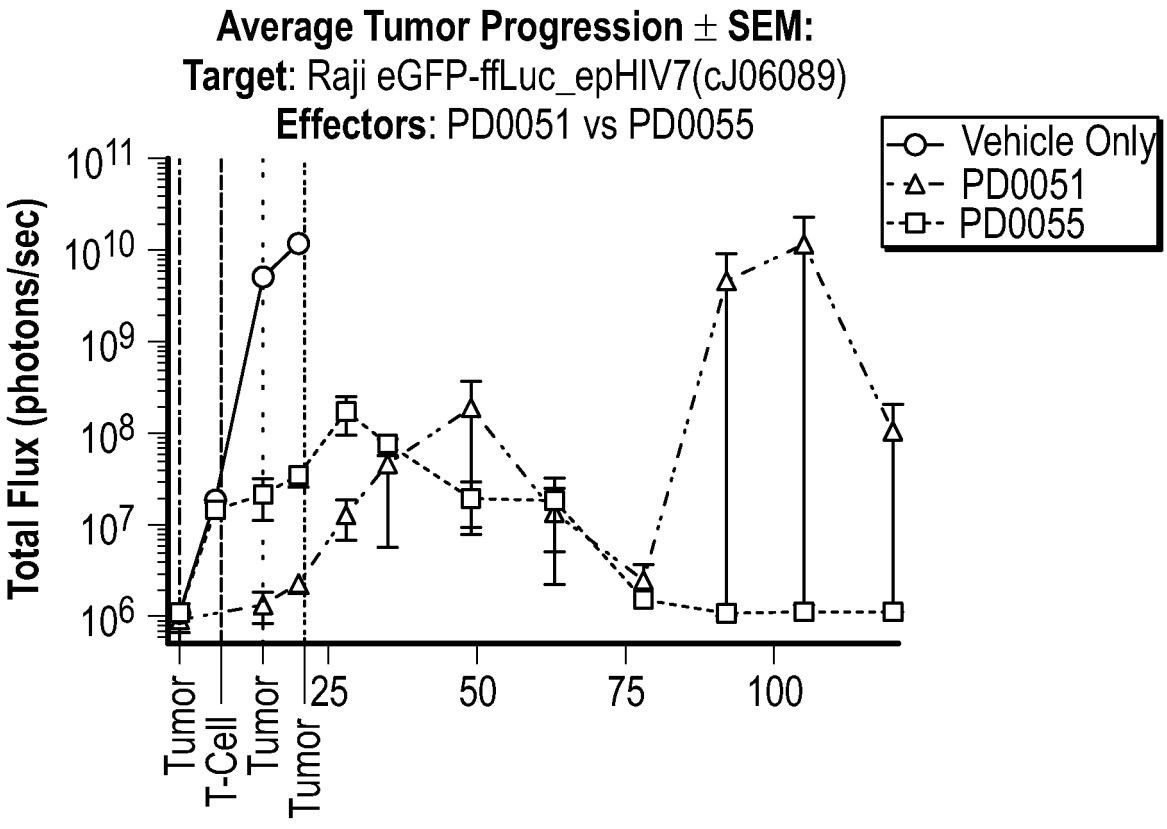


FIG. 47B

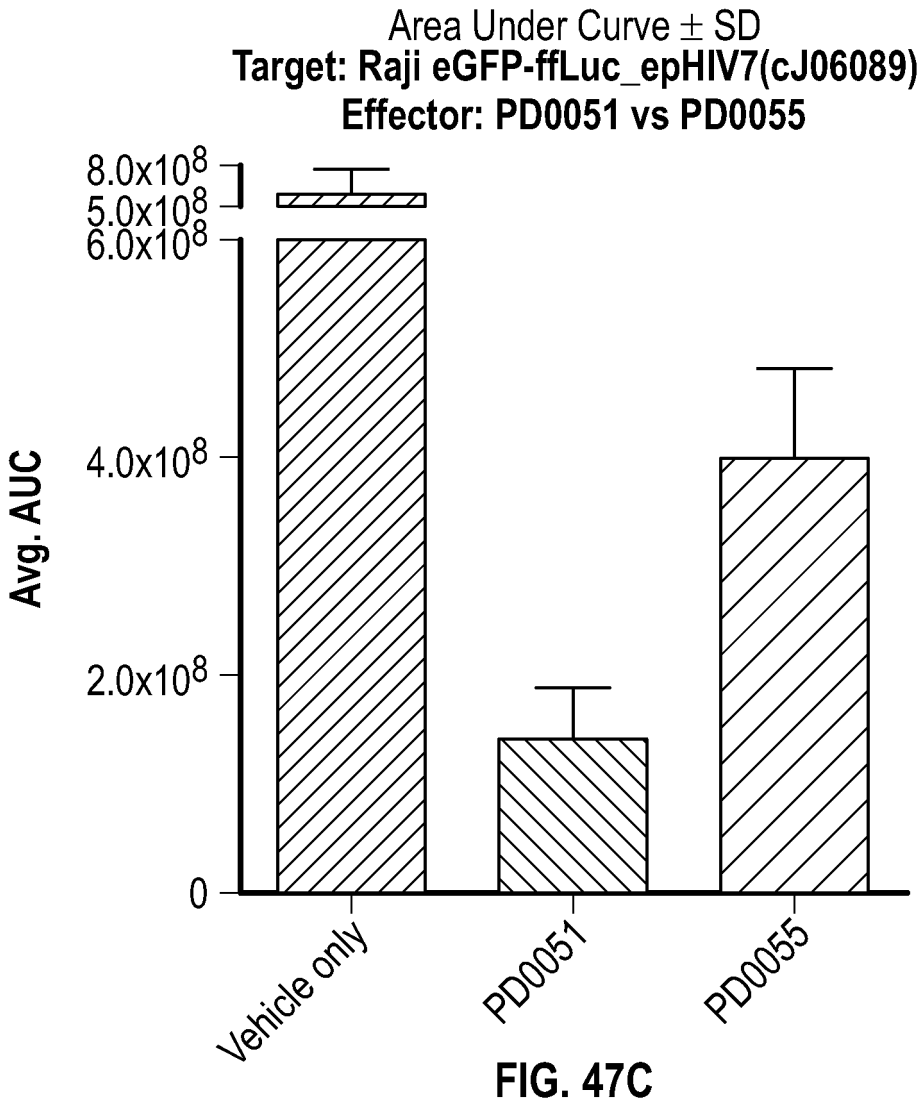

Area Under Curve ± SD
Target: Raji eGFP-ffLuc_epHIV7(cJ06089)
Effector: PD0051 vs PD0055
Avg. AUC
8.0x10^8
5.0x10^8
6.0x10^8
4.0x10^8
2.0x10^8
0
Vehicle only
PD0051
PD0055

FIG. 47C

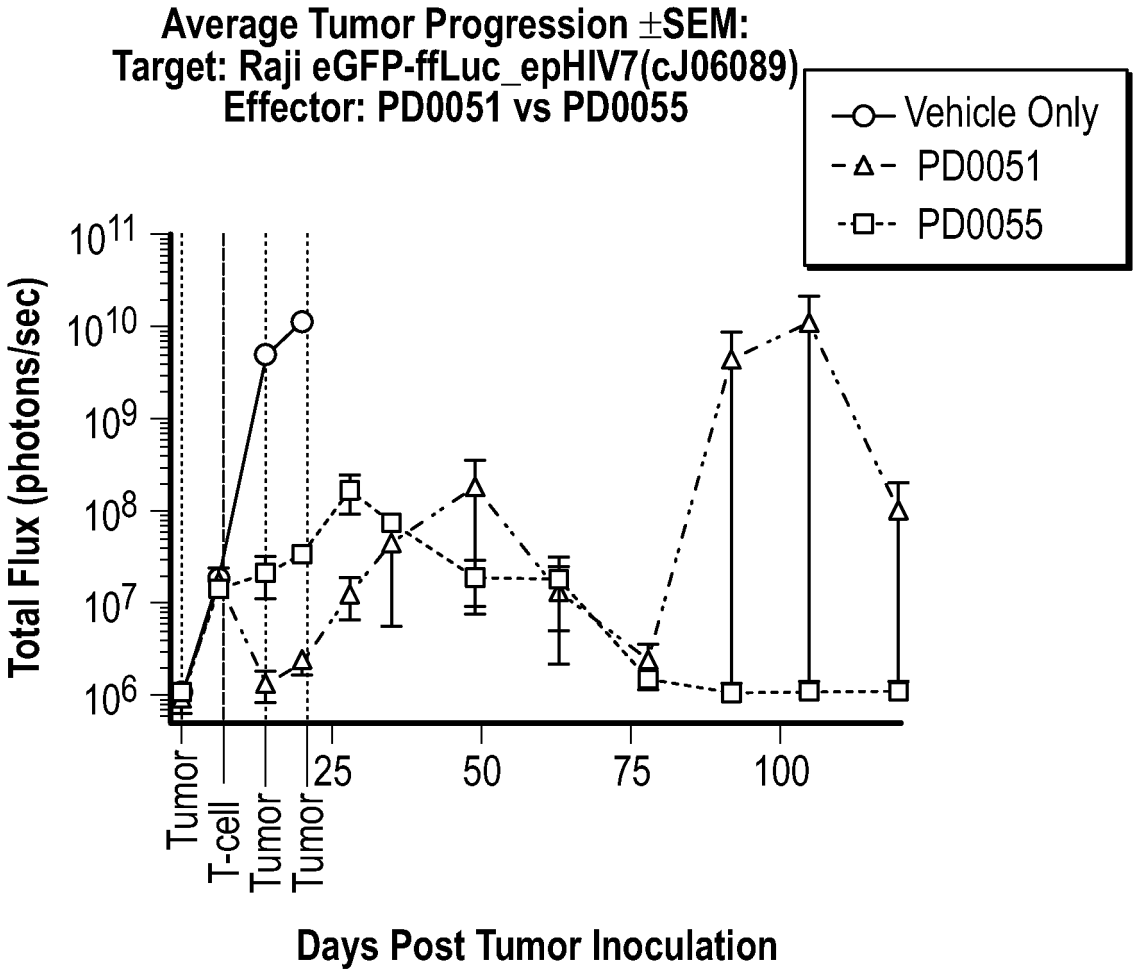


FIG. 48A

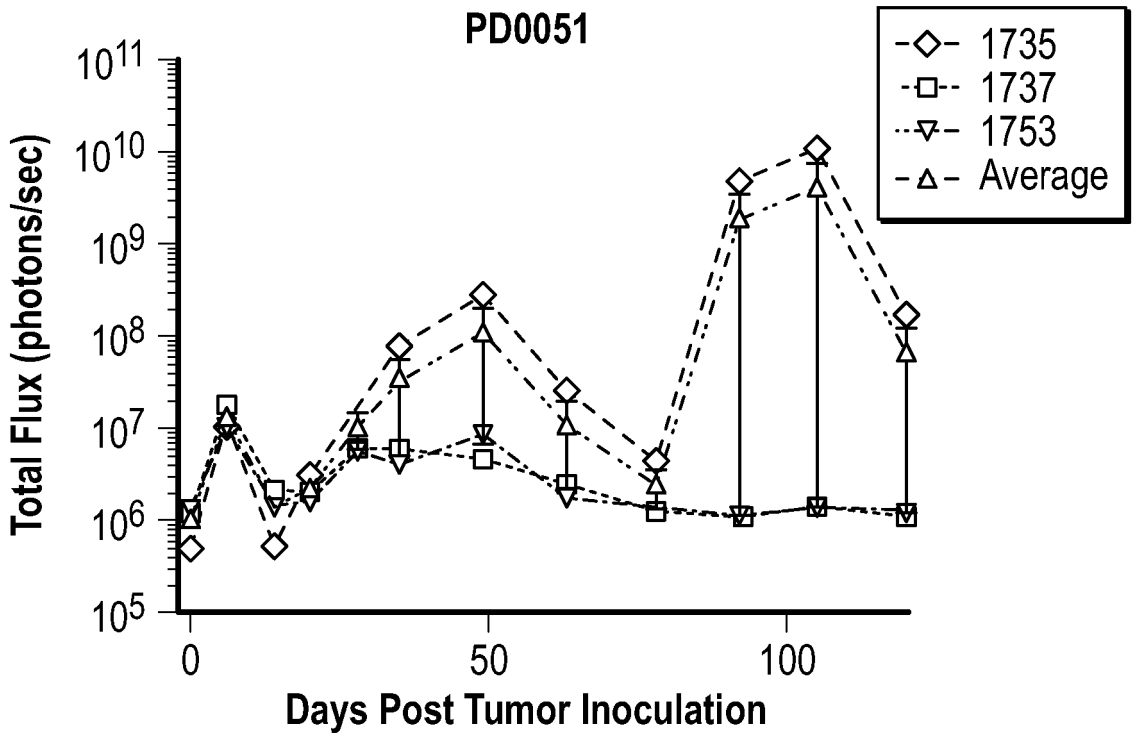


FIG. 48B

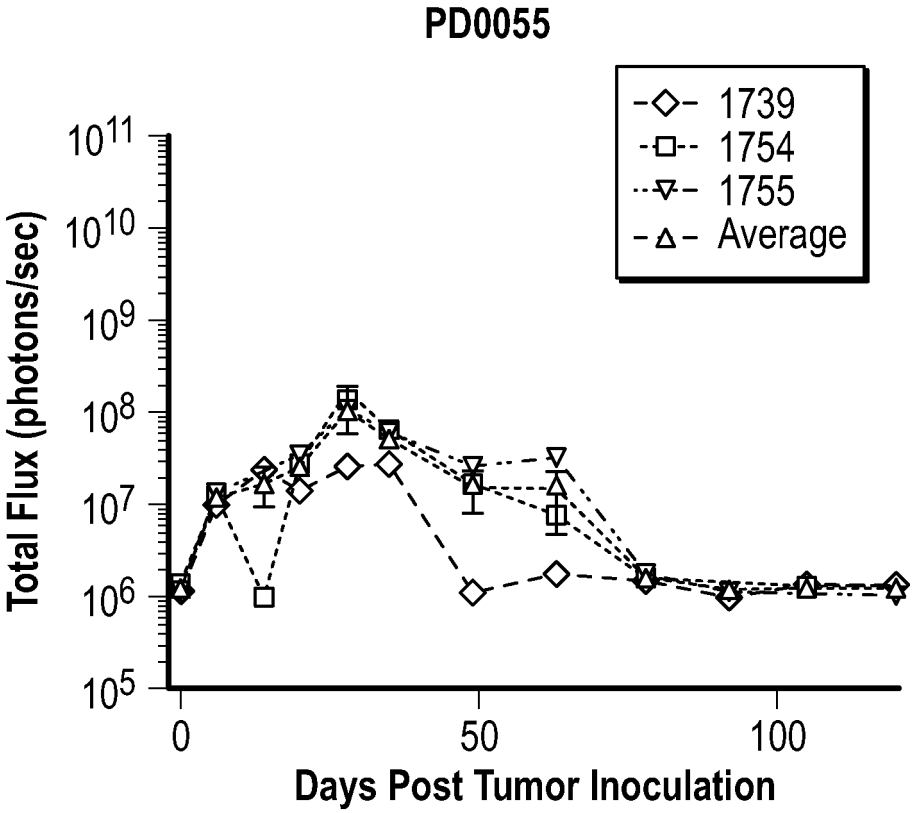


FIG. 48C

Experiment Timeline

Day 0: **Tumor Inoculation**

Day 6: Image mice

Day 7:**T-cell administration**

Day 14(AM): Image mice

Day 14(PM): **Tumor Inoculation**

Day 20: Image mice

Day 21: **Tumor Inoculation**

Day 28, 35, 49, 63, 78, 92, 105, 120: Image mice

FIG. 48D

AIM(S):

1. Determine if there is an in vivo difference in killing ability between cells that have been grown under the same conditions as PLAT-01 and PLAT-02 as well as "in between" protocols.

CONDITIONS:

Product	CD4 select (%)	CD8 select (%)	EGFRt select (CD4%/CD8%)	PD#'s
PLAT-1.0	No (28.9%)	No (72.0%)	No (79.5%)	PD0066 #6
PLAT-1.33	**Yes** (87.4%)	**Yes** (99.8%)	No (95.0%/48.0%)	PD0069 #1 & PD0070#2
PLAT-1.67	No (24.3%)	No (77.8%)	**Yes** (66.7%)	PD0069 #3
PLAT-2.0	**Yes** (99.8%)	**Yes** (99.1%)	**Yes** (94.2/94.9%)	PD0063 CD4 & PD0063 CD8

Note: All products initiated from the same donor.

EXPERIMENTAL SET-UP:

- n=5 per group
- 17 groups total
  - Dose of 1.25e6/2.5e6/5e6/10e6 per product condition
  - Additional vehicle control group
- Cells thawed, counted, and injected on same day.
- Cells injected based on EGFRt+ [and 1:1 CD4:CD8 (for selected) cells]

Tumor inoculation: 0.5e6 cells/mouse IV

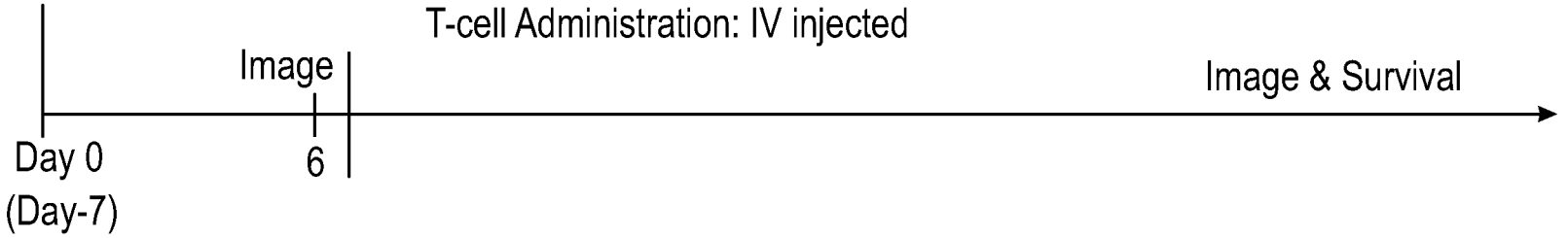


FIG. 49

SUBSTITUTE SHEET (RULE 26)

Product	CD4 select (%)	CD8 select (%)	EGFRt select (CD4%/CD8%)	PD#'s
PLAT-1.0	No (28.9%)	No (72.0%)	No (79.5%)	PD0066 #6
PLAT-1.33	**Yes** (87.4%)	**Yes** (99.8%)	No (95.0%/48.0%)	PD0069 #1 & PD0070#2
PLAT-1.67	No (24.3%)	No (77.8%)	**Yes** (66.7%)	PD0069 #3
PLAT-2.0	**Yes** (99.8%)	**Yes** (99.1%)	**Yes** (94.2/94.9%)	PD0063 CD4 & PD0063 CD8

1. Data from PLAT-1.33 is questionable as although the cells were selected for CD4 and CD8, the final %EGFRt+CD8 cells appears unusually low at 48%.

2. Data from PLAT-1.67 is questionable as final %EGFRt+ is only 66.7% even though bulk cells underwent mid-process enriched for EGFRt.

3. Animals receiving PLAT-2.0 cells developed xGvHD in both the 10 million and 5 million dose groups with the first group coming mid-study as a result of the xGvHD and the later group being confirmed for xGvHD both by physical observation and persistence of T-cells by FACS analysis of bone marrow.

FIG. 50

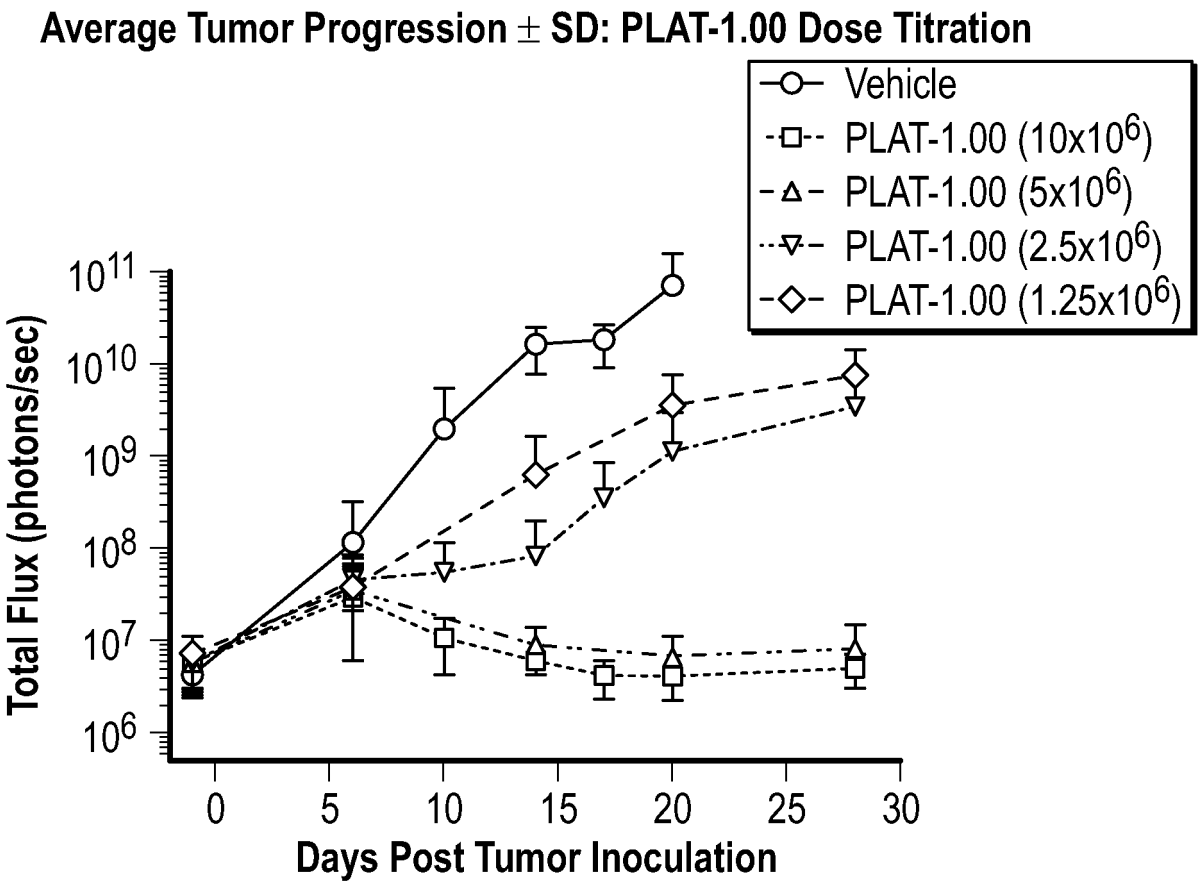


FIG. 51A

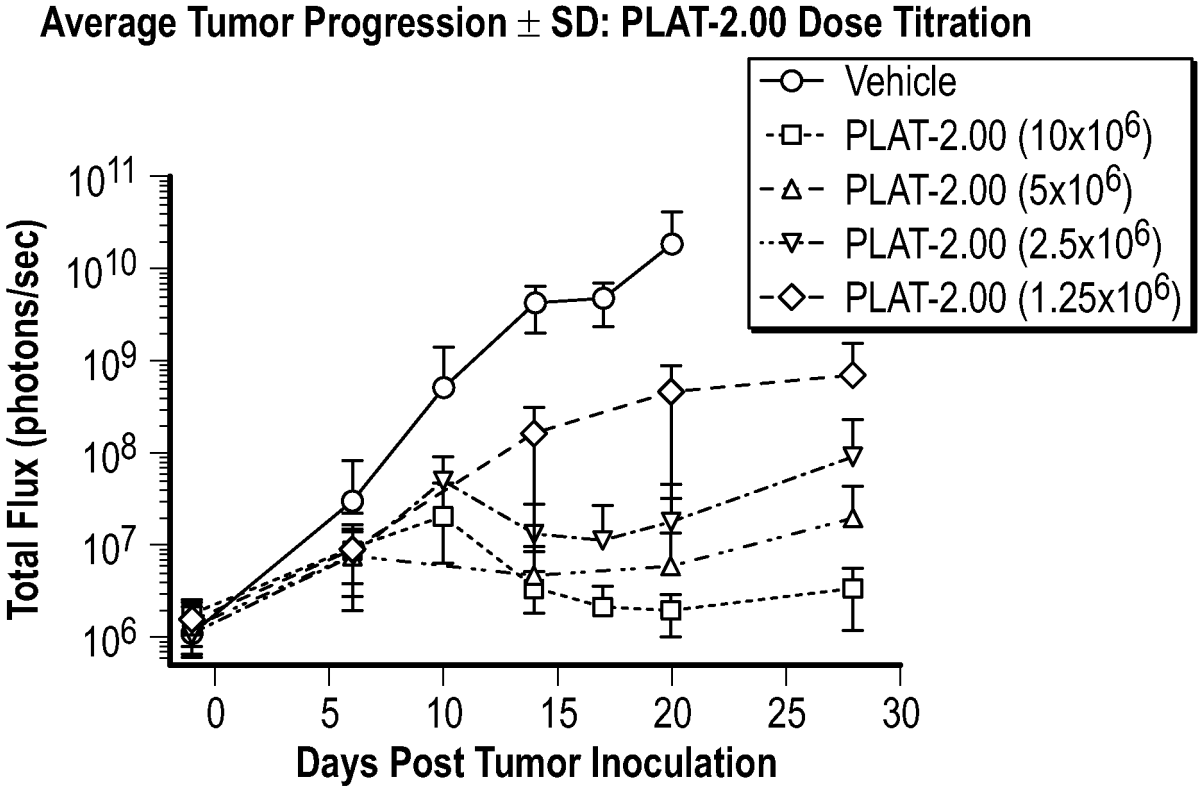


FIG. 51B

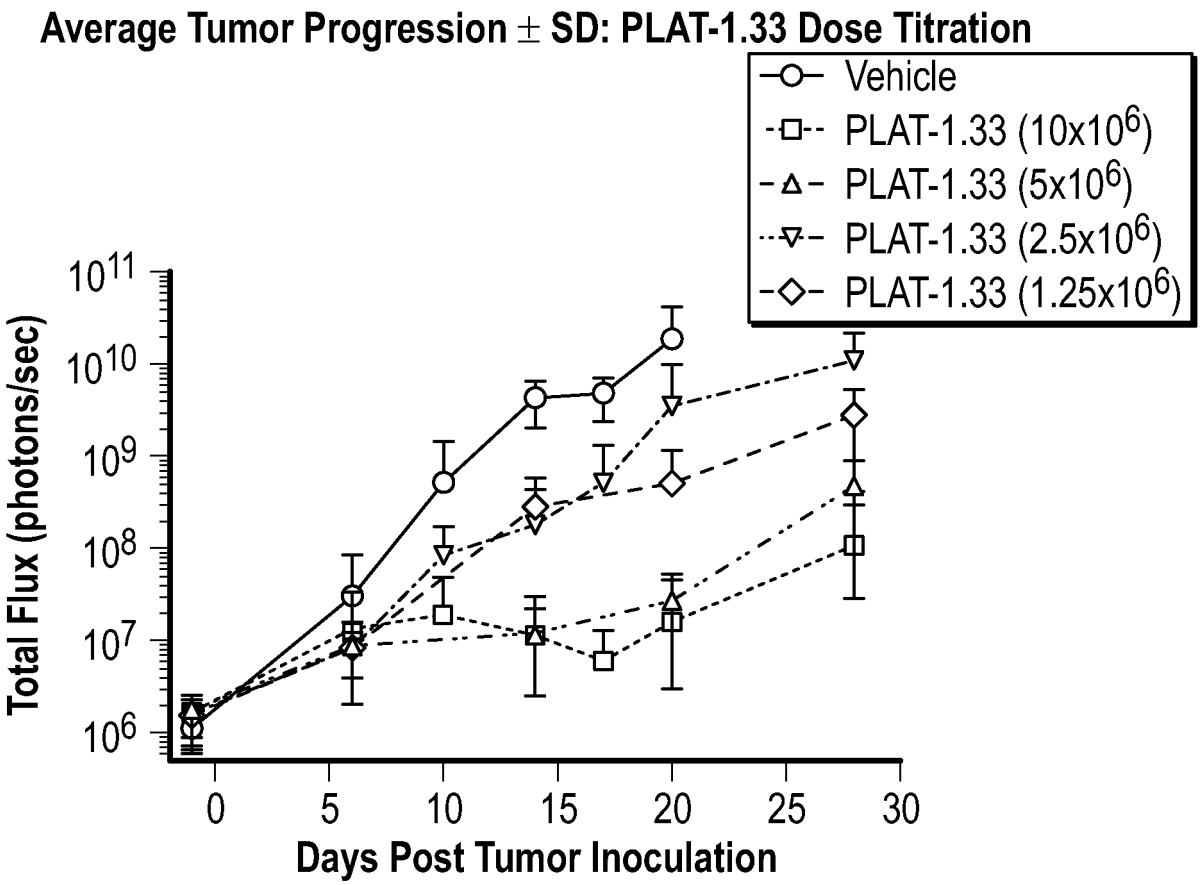


FIG. 51C

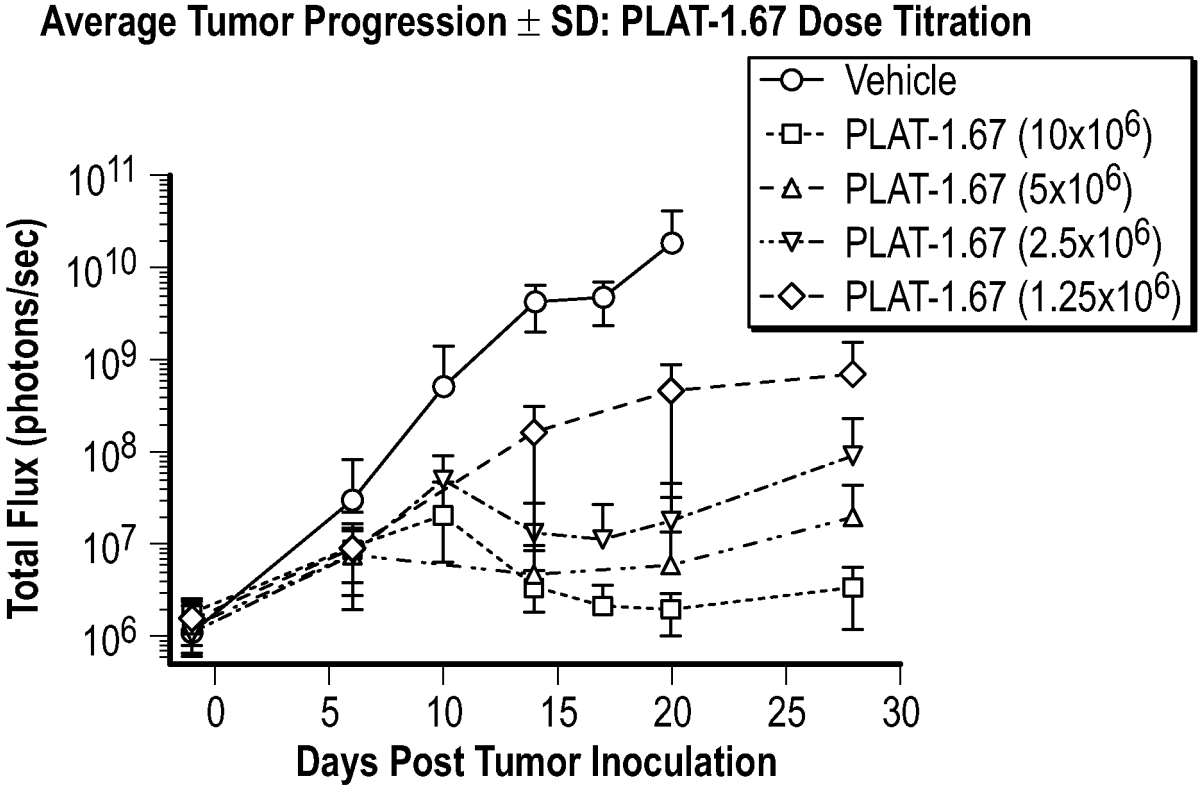


FIG. 51D

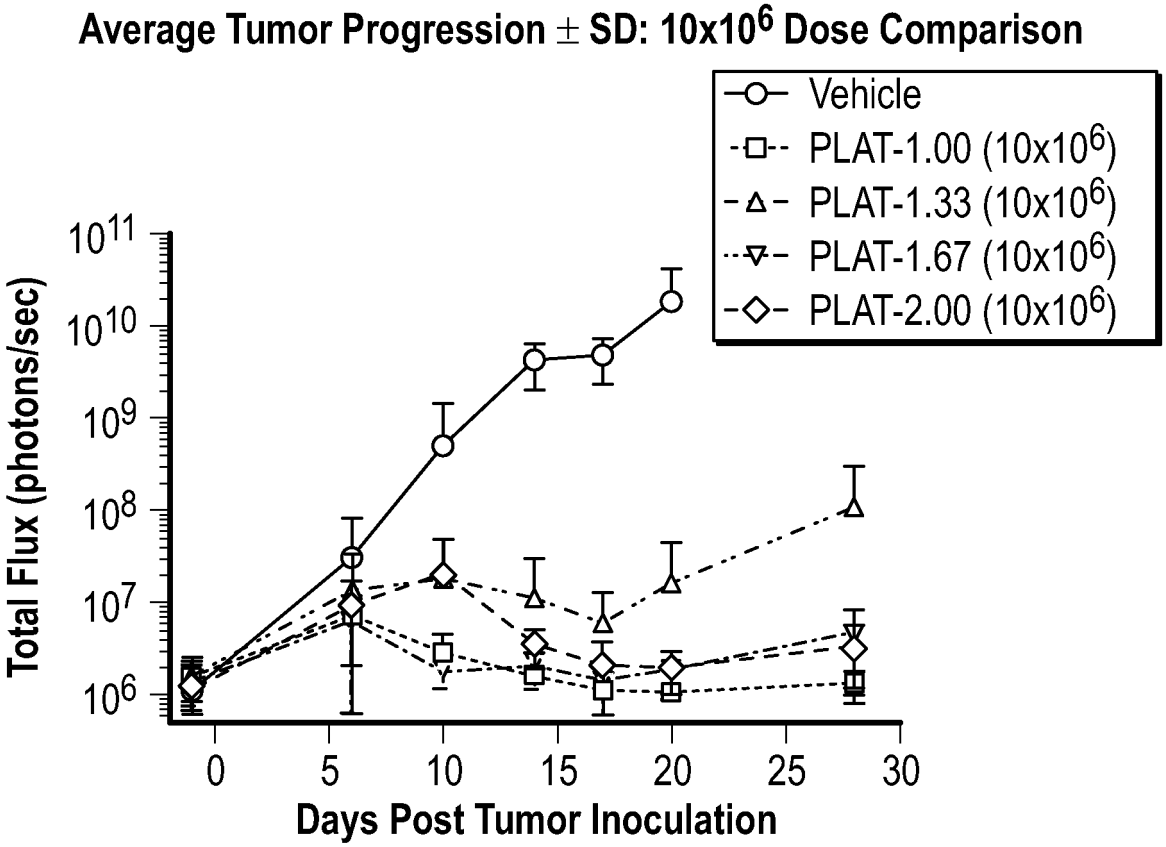


FIG. 52A

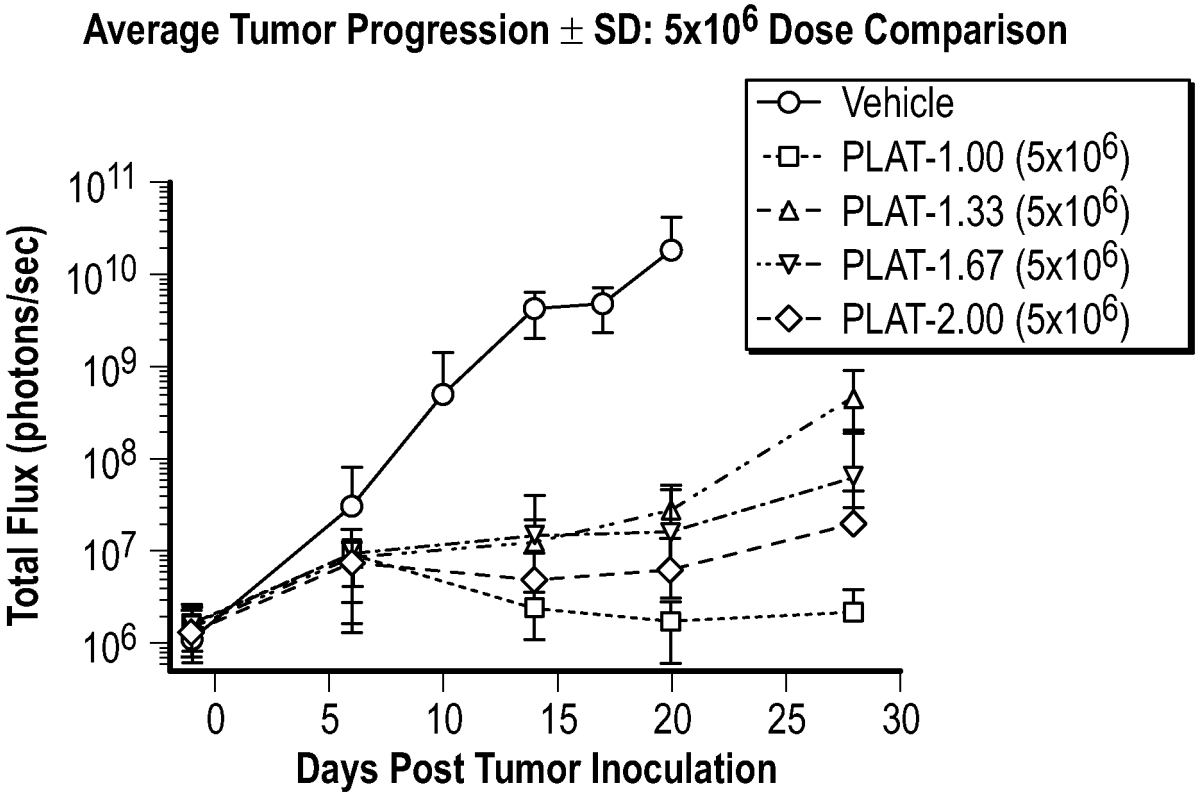


FIG. 52B

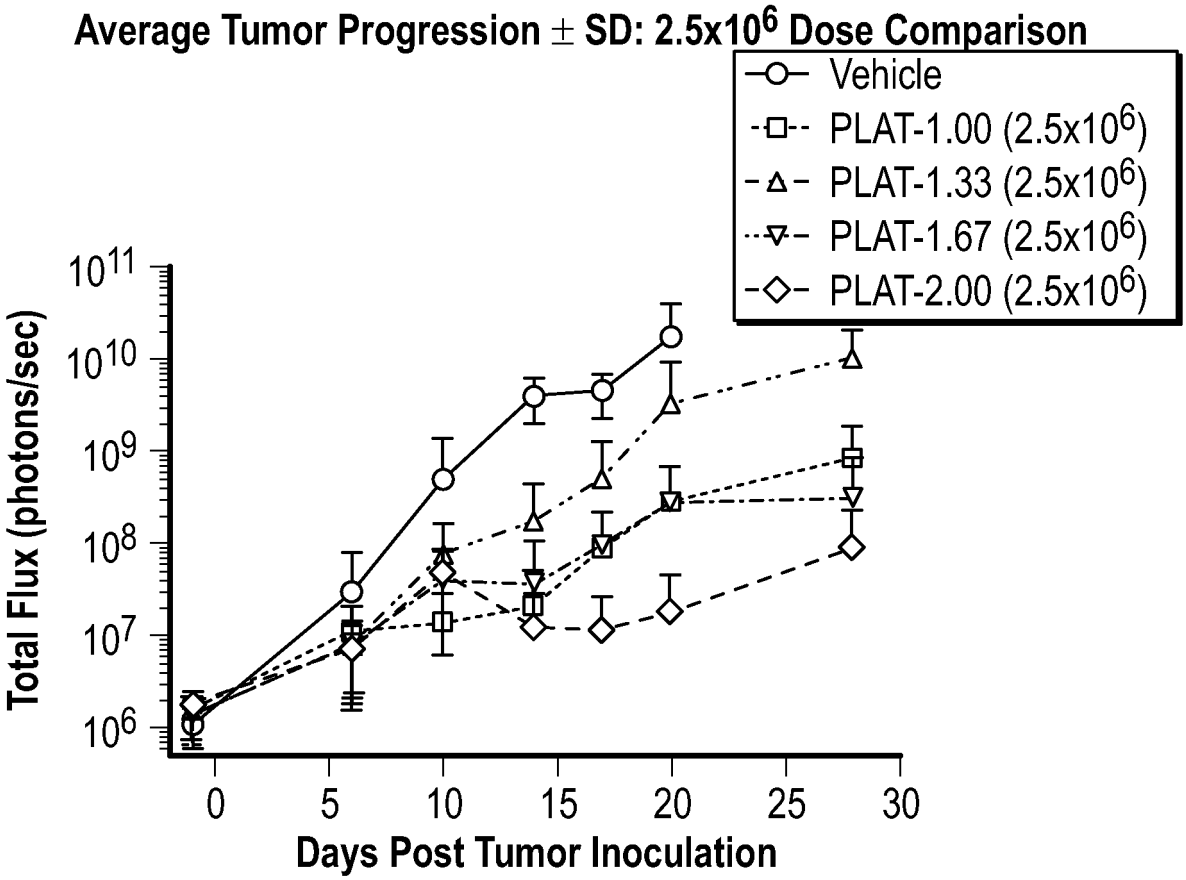


FIG. 52C

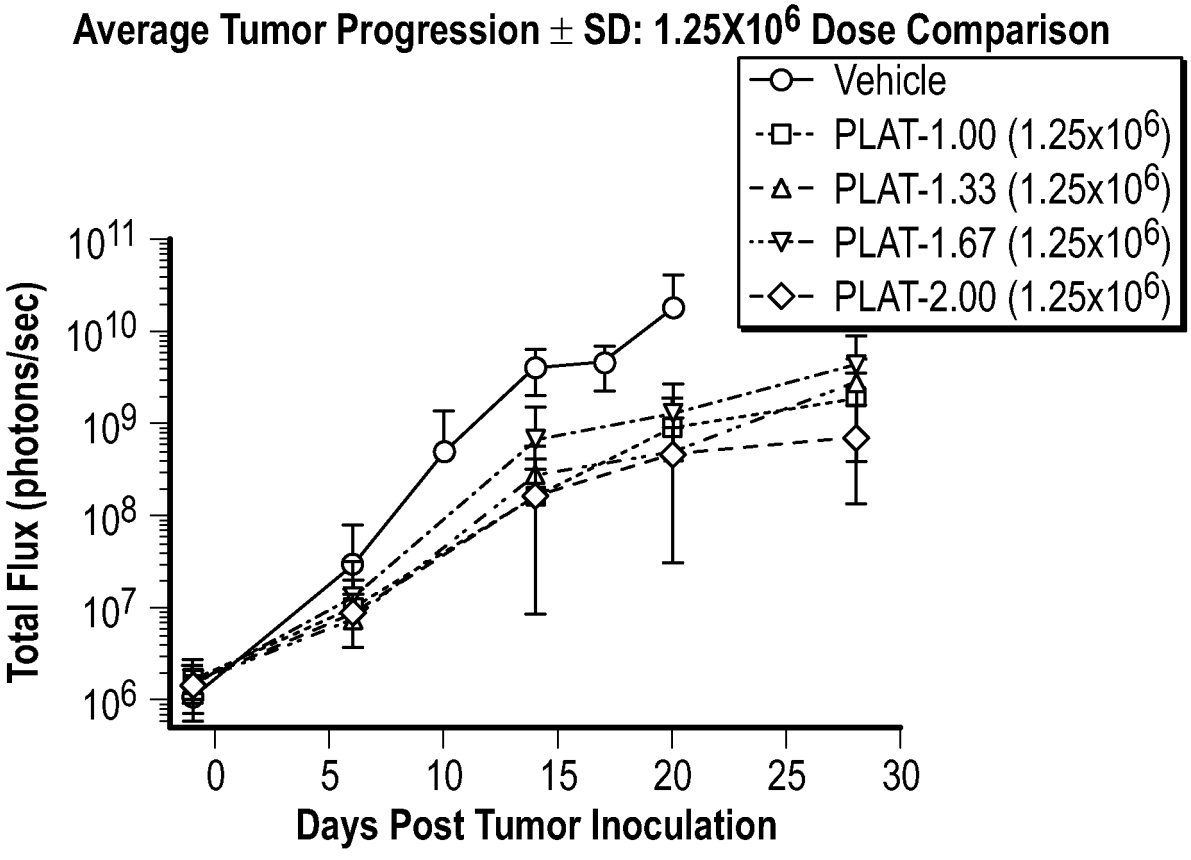


FIG. 52D

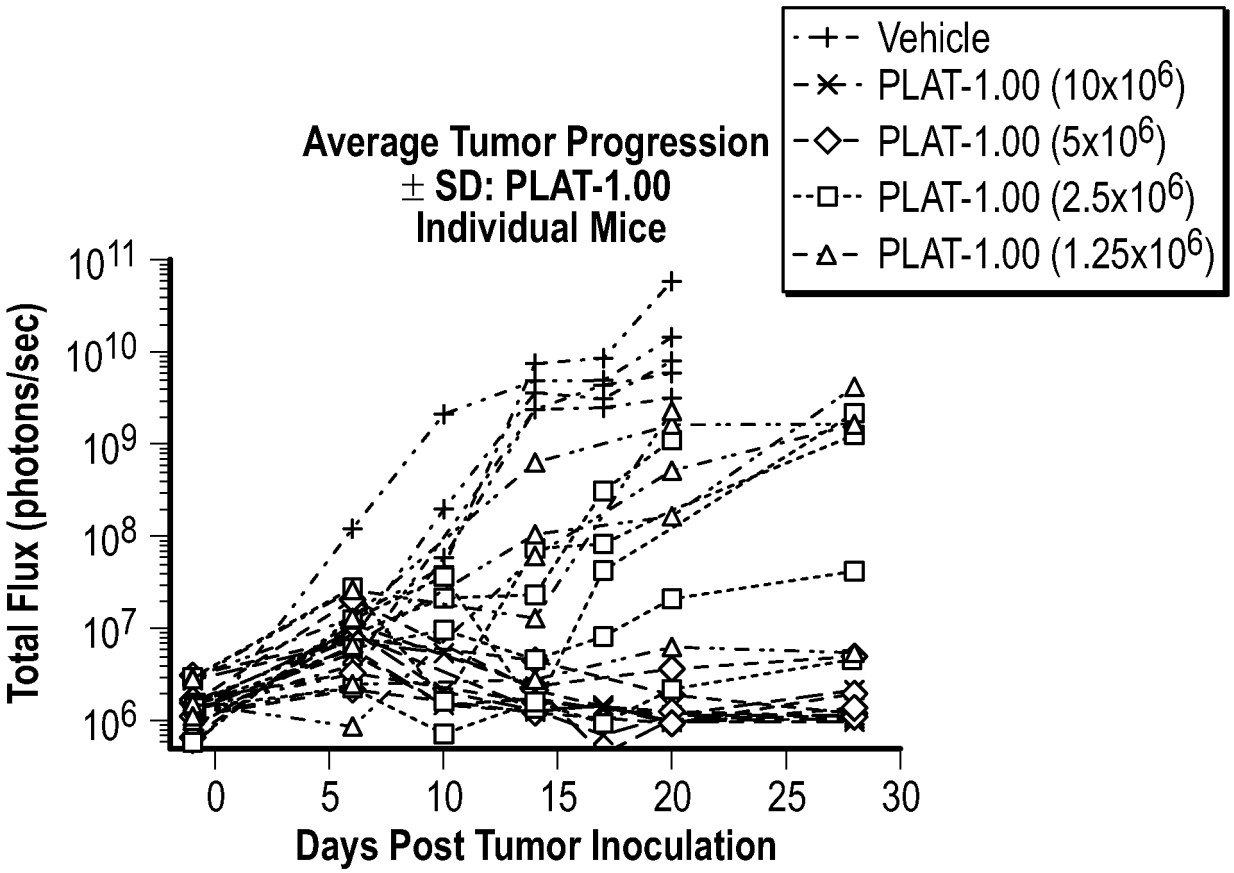


FIG. 53A1

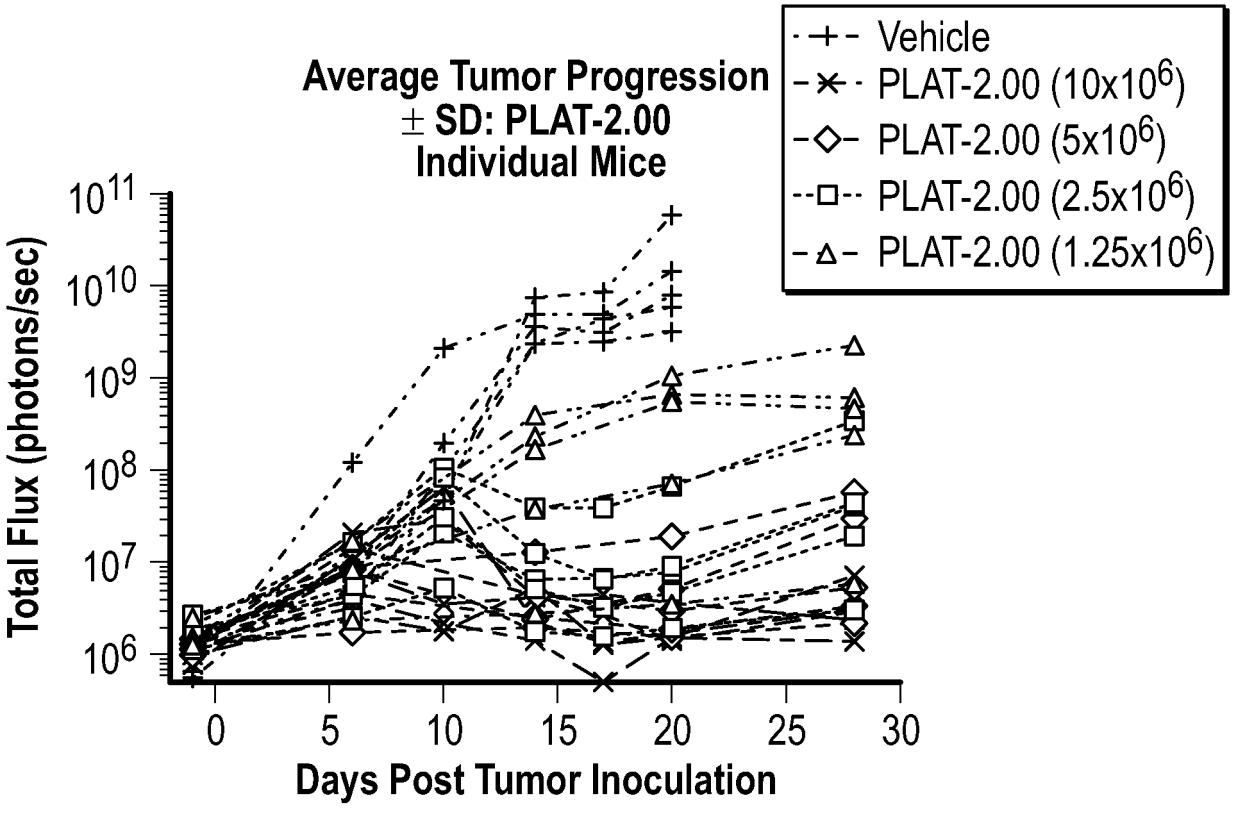


FIG. 53A2

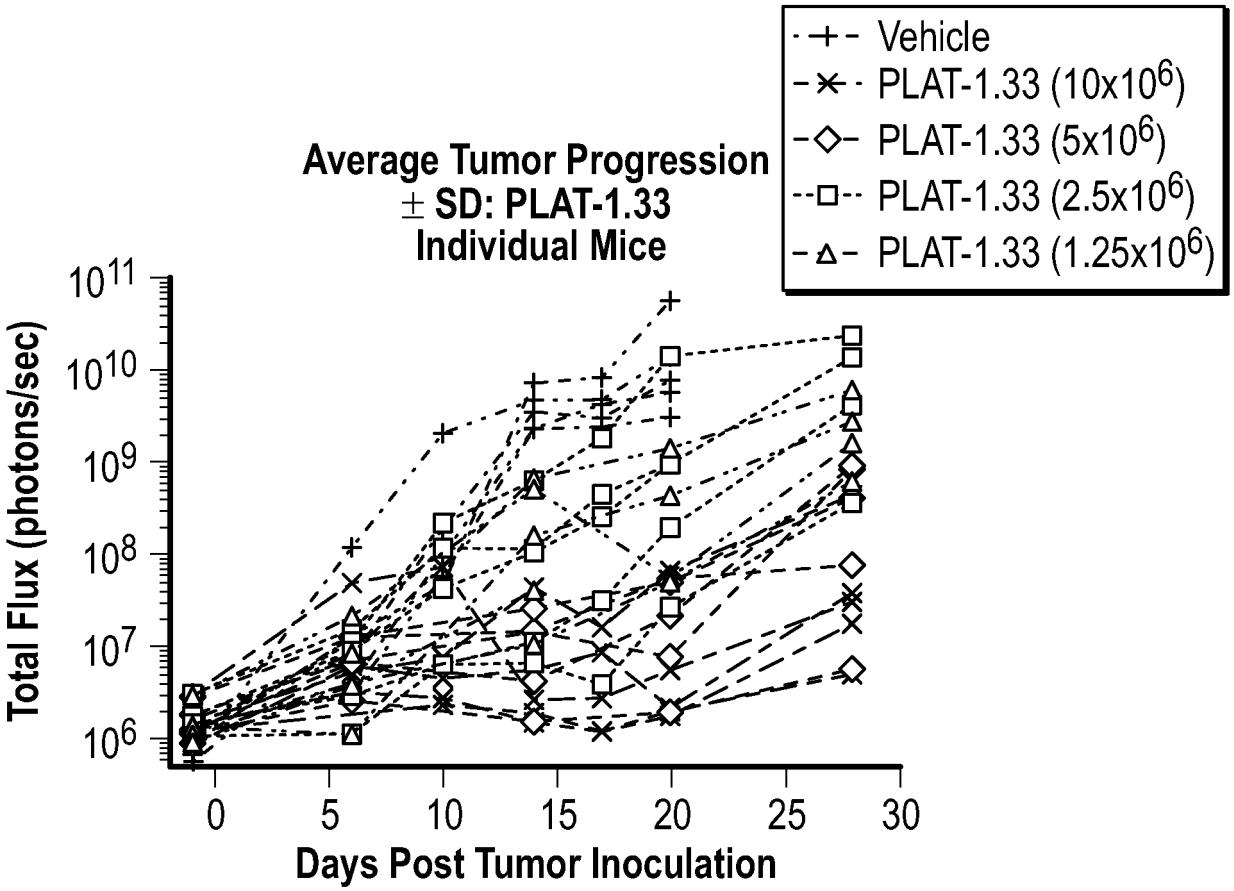


FIG. 53A3

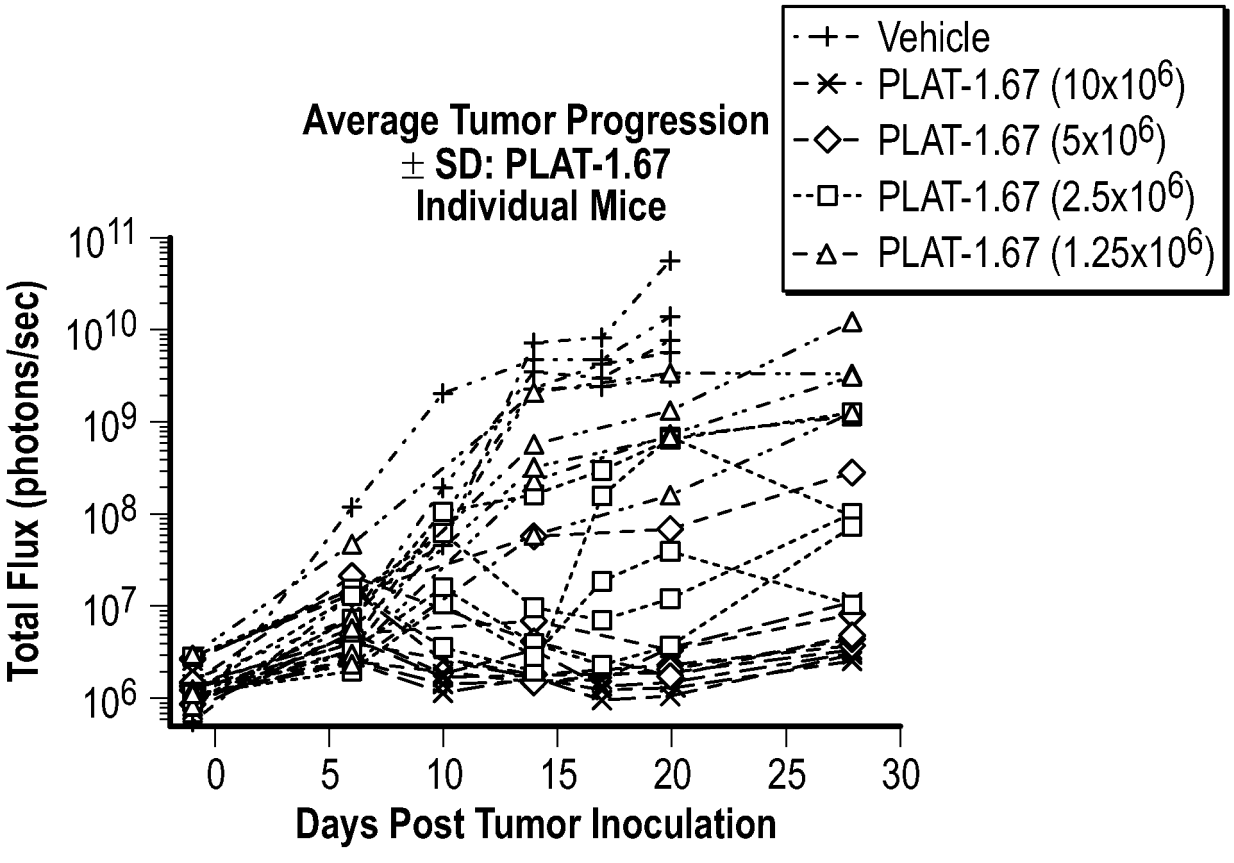


FIG. 53A4

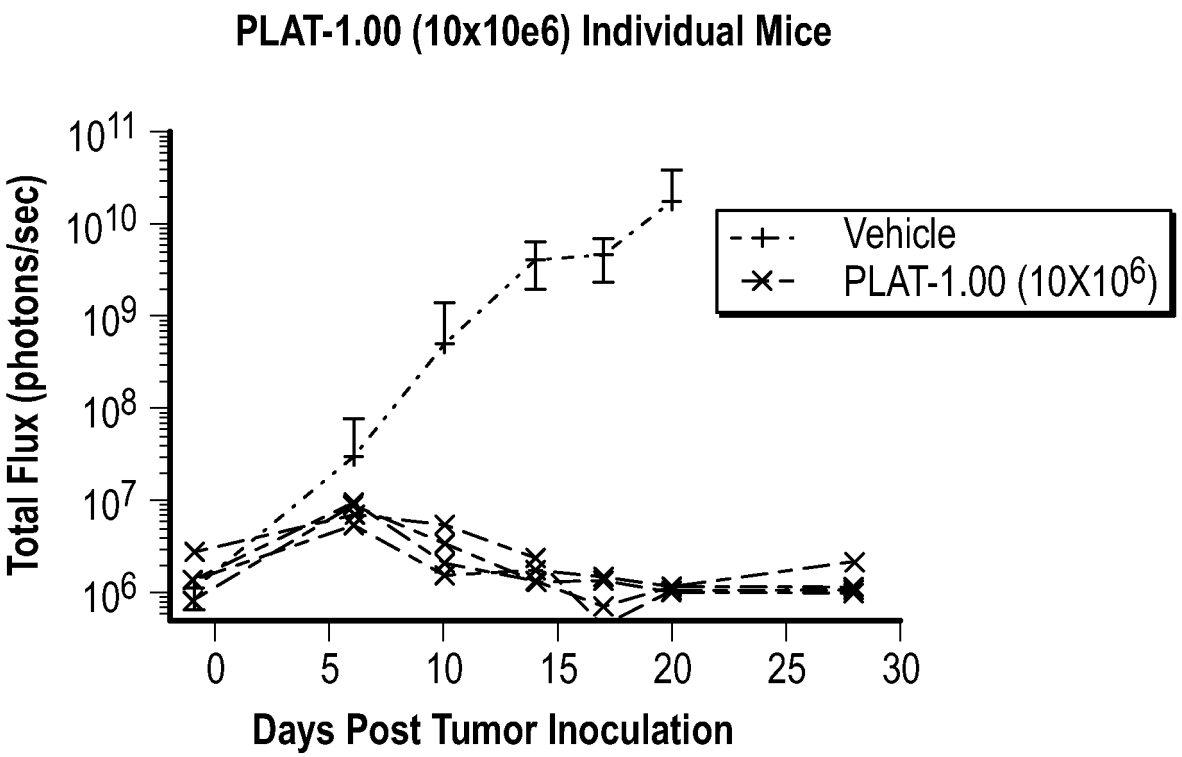


FIG. 53B1

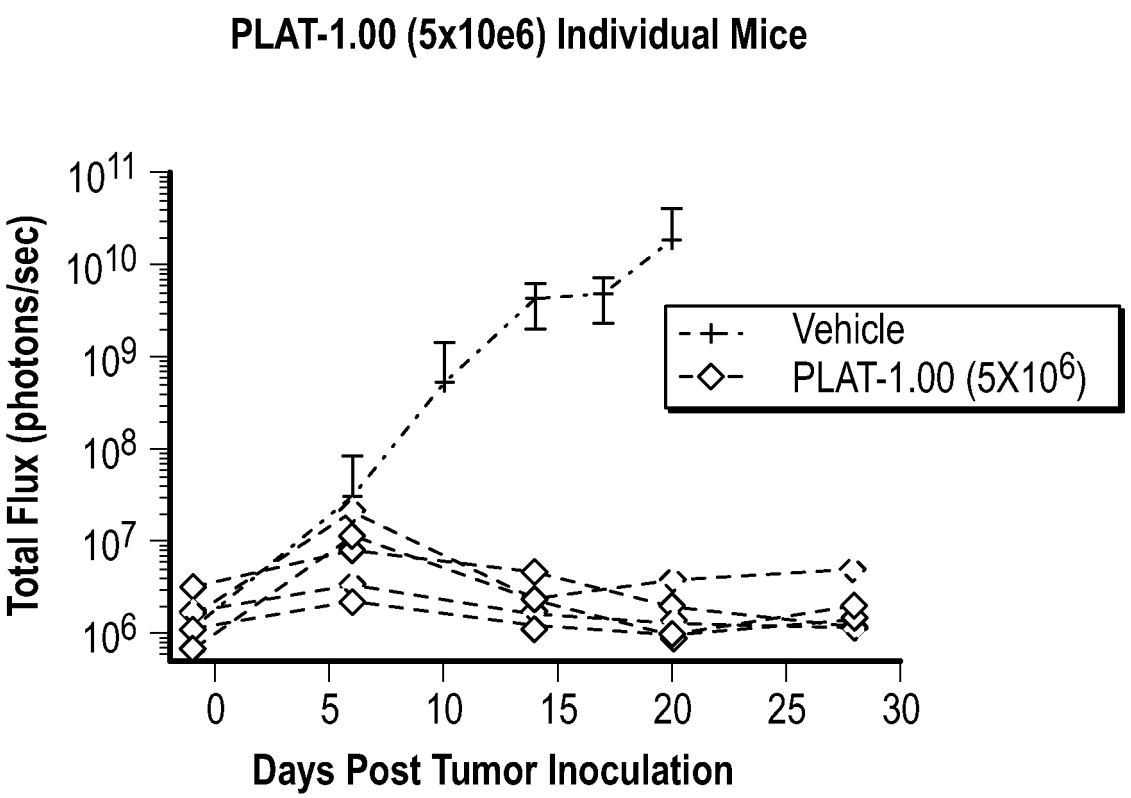


FIG. 53B2

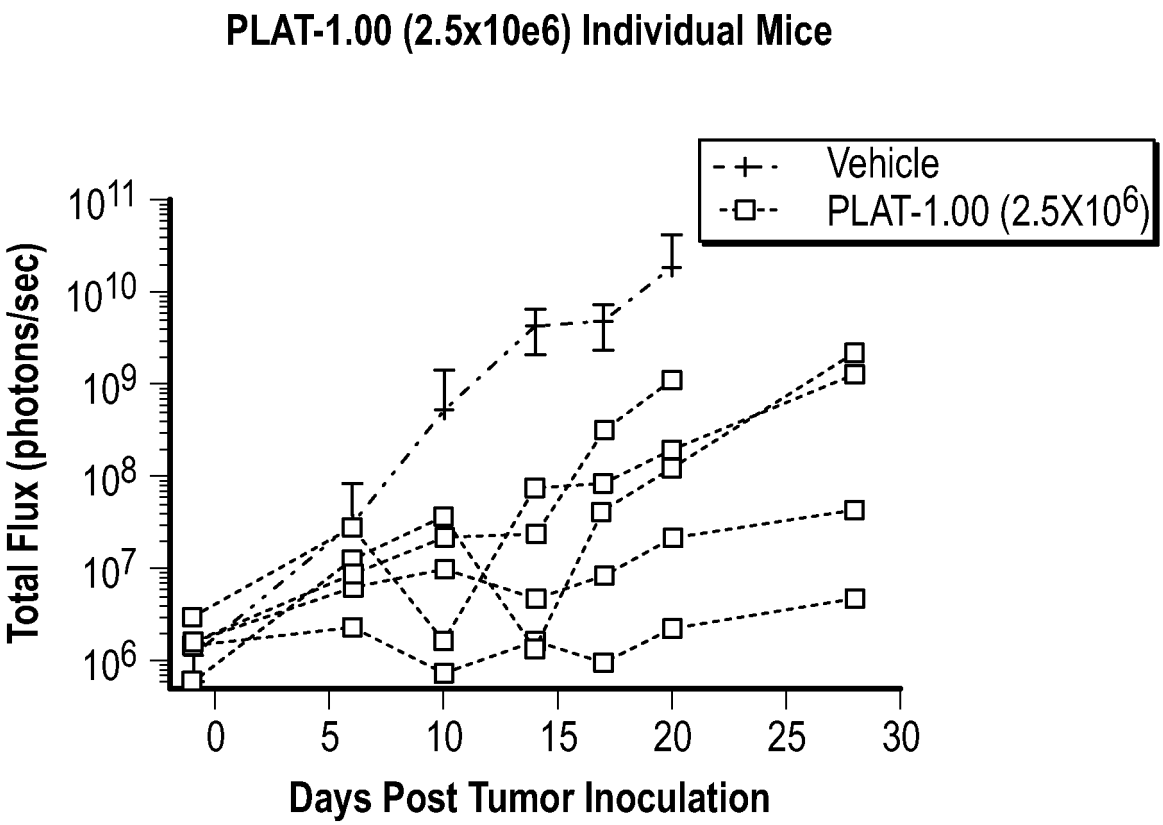


FIG. 53B3

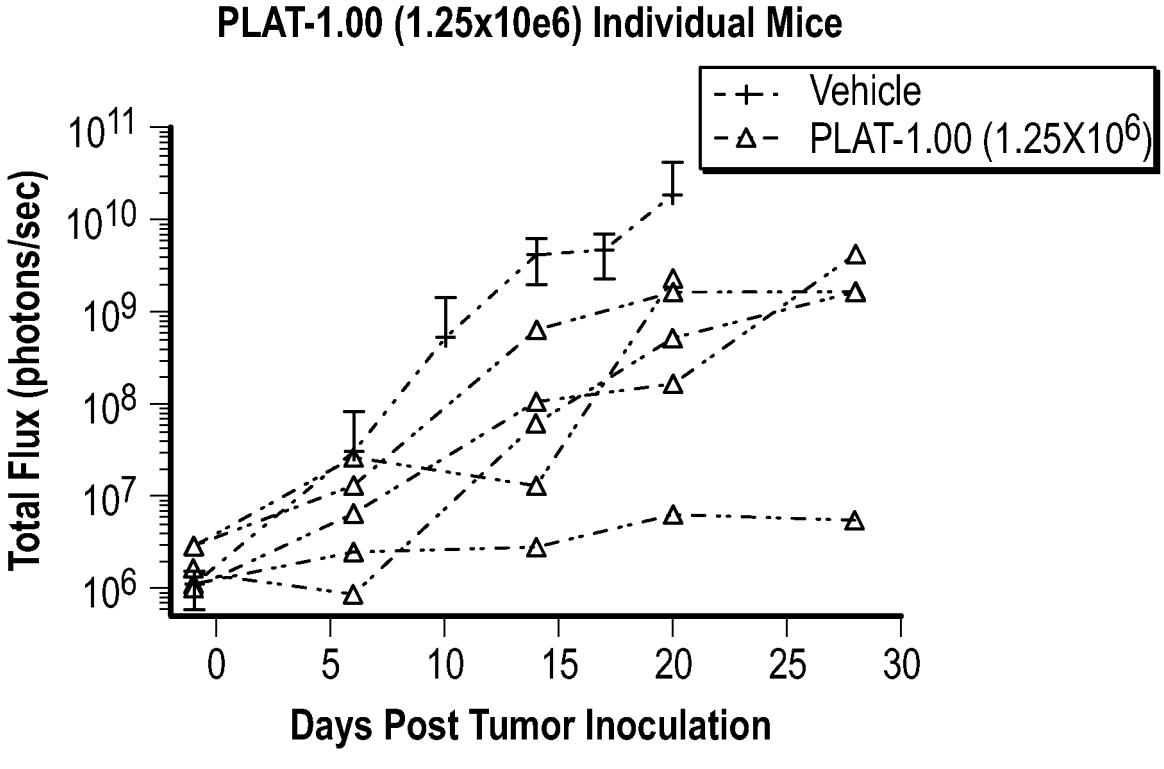


FIG. 53B4

PLAT-1.33 (10x10e6) Individual Mice

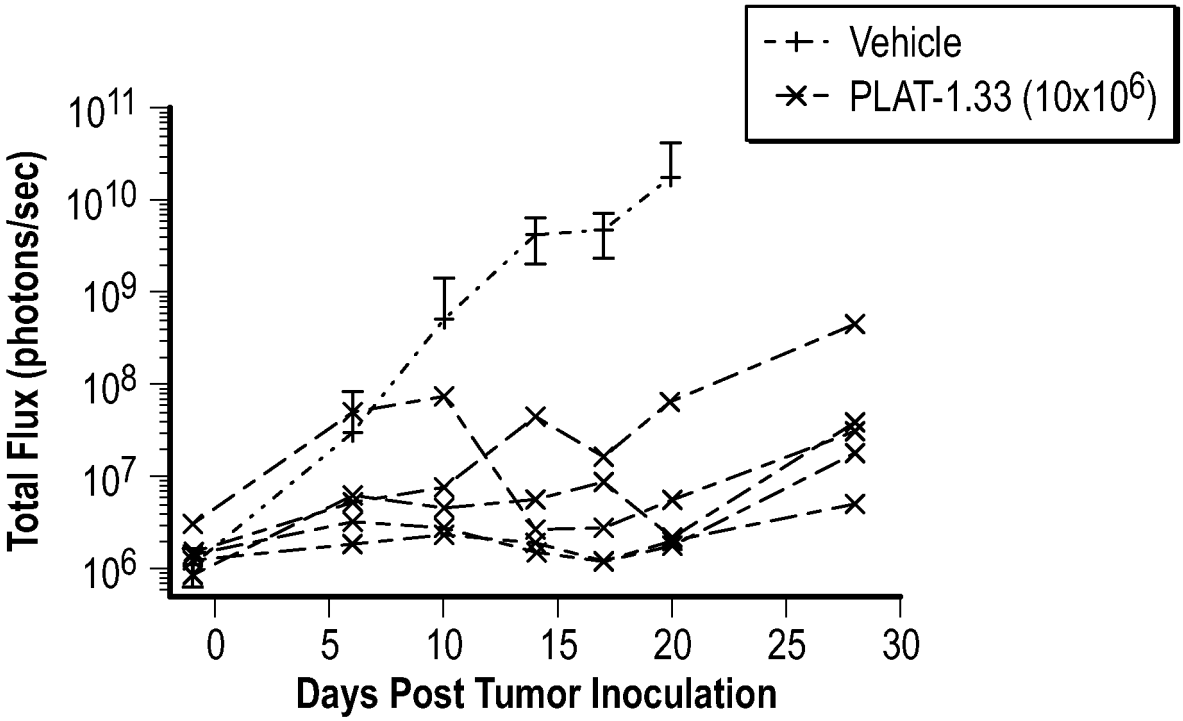


FIG. 53C1

PLAT-1.33 (5x10e6) Individual Mice

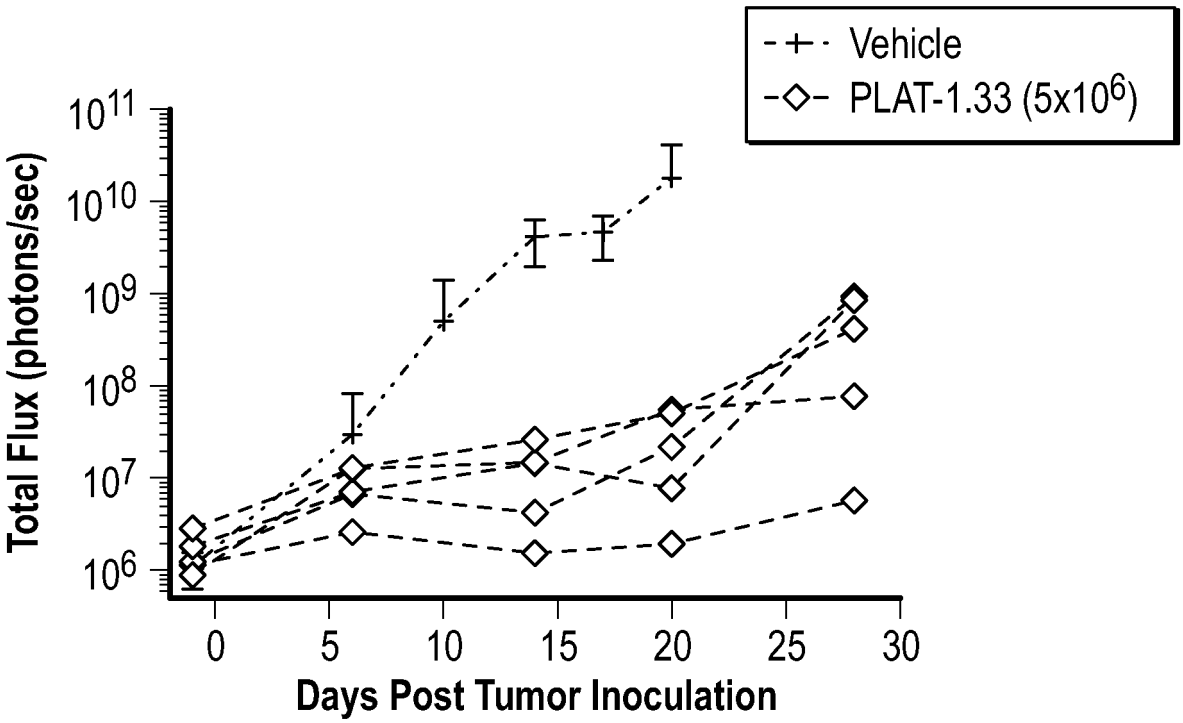


FIG. 53C2

PLAT-1.33 (2.5x10e6) Individual Mice

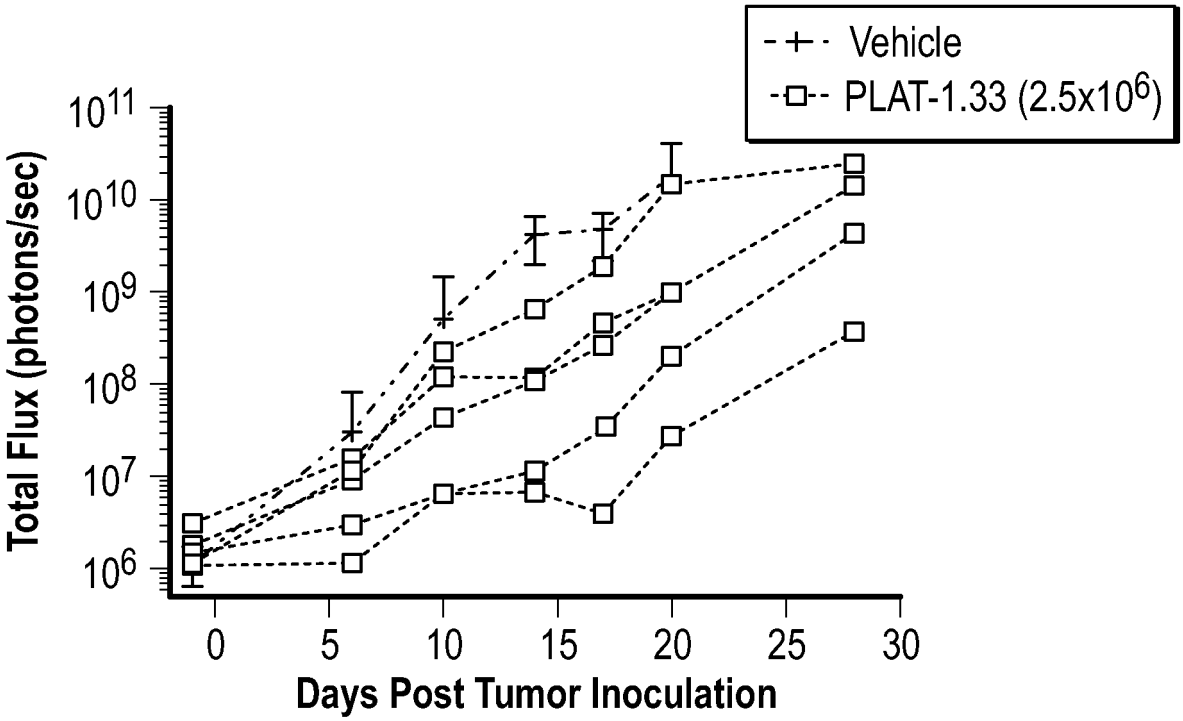


FIG. 53C3

PLAT-1.33 (1.25x10e6) Individual Mice

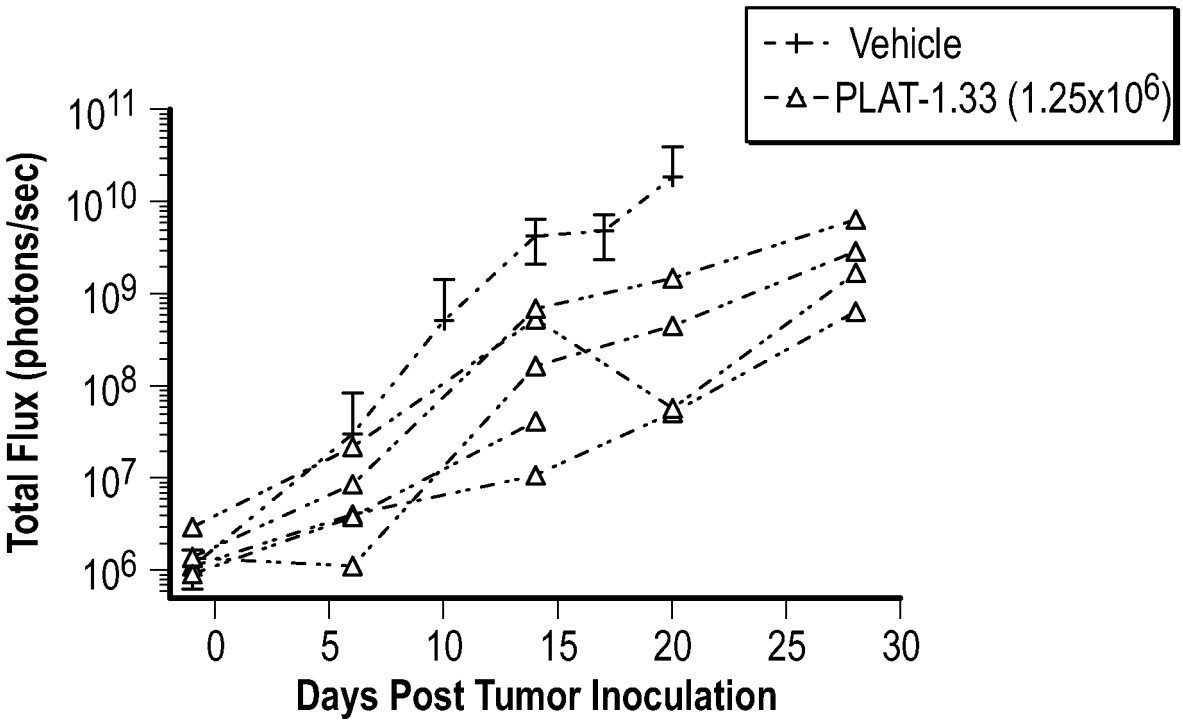


FIG. 53C4

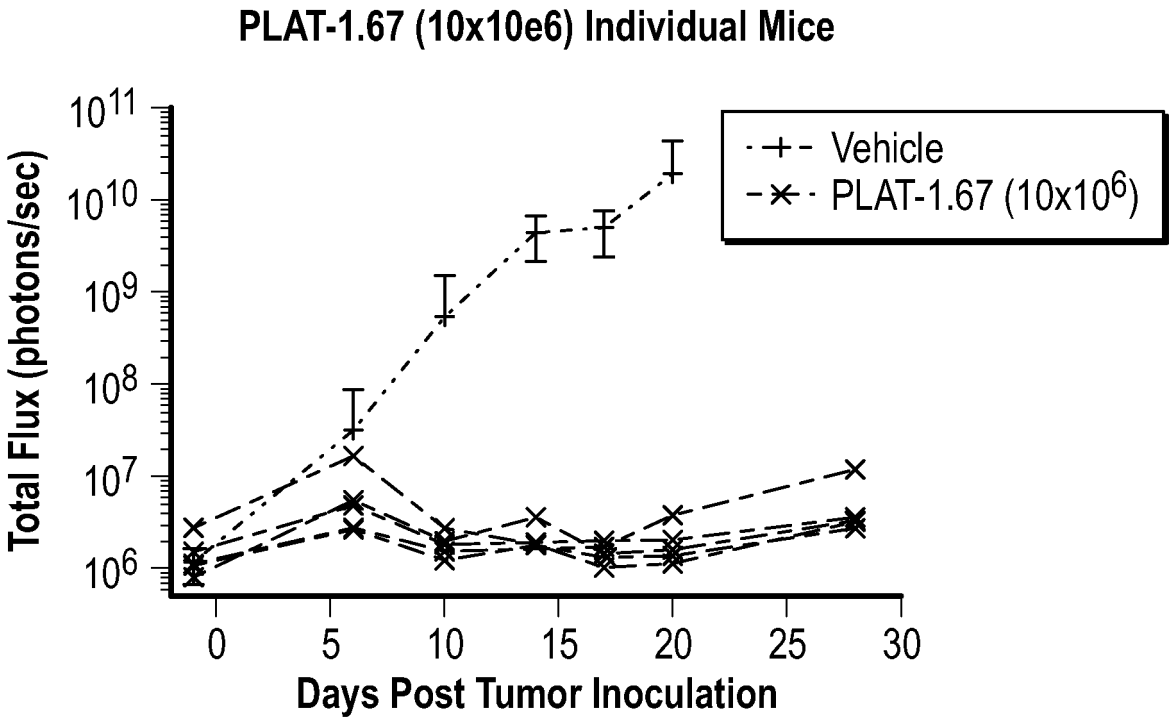


FIG. 53D1

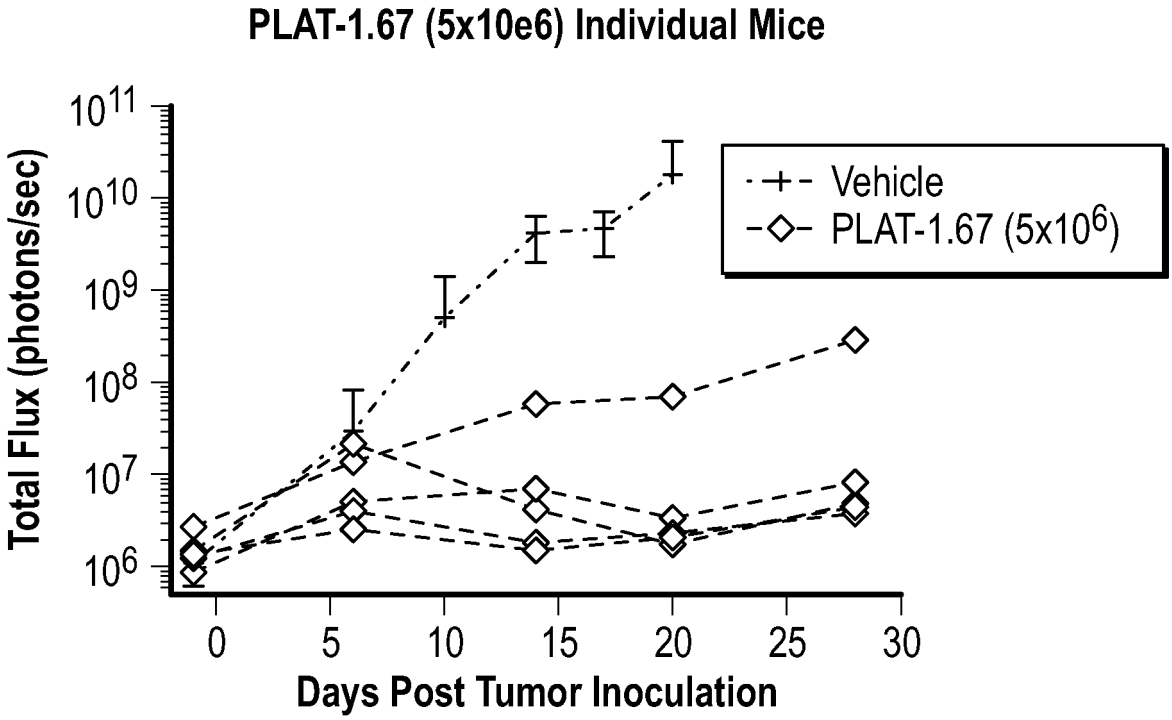


FIG. 53D2

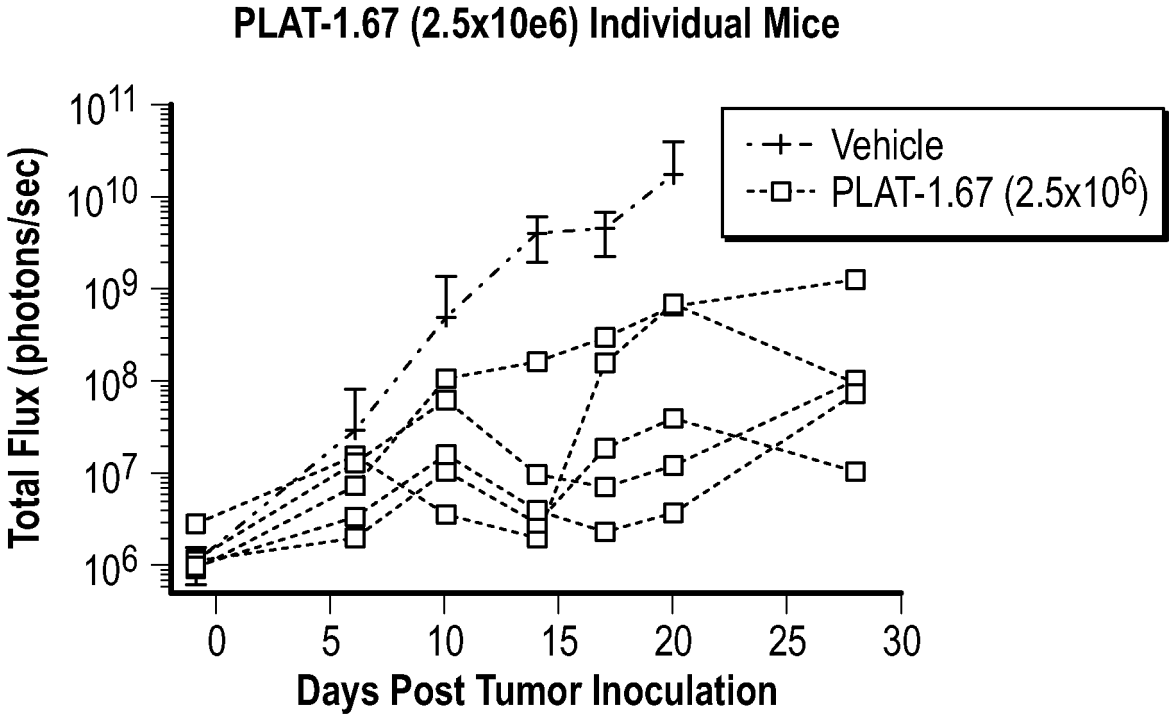


FIG. 53D3

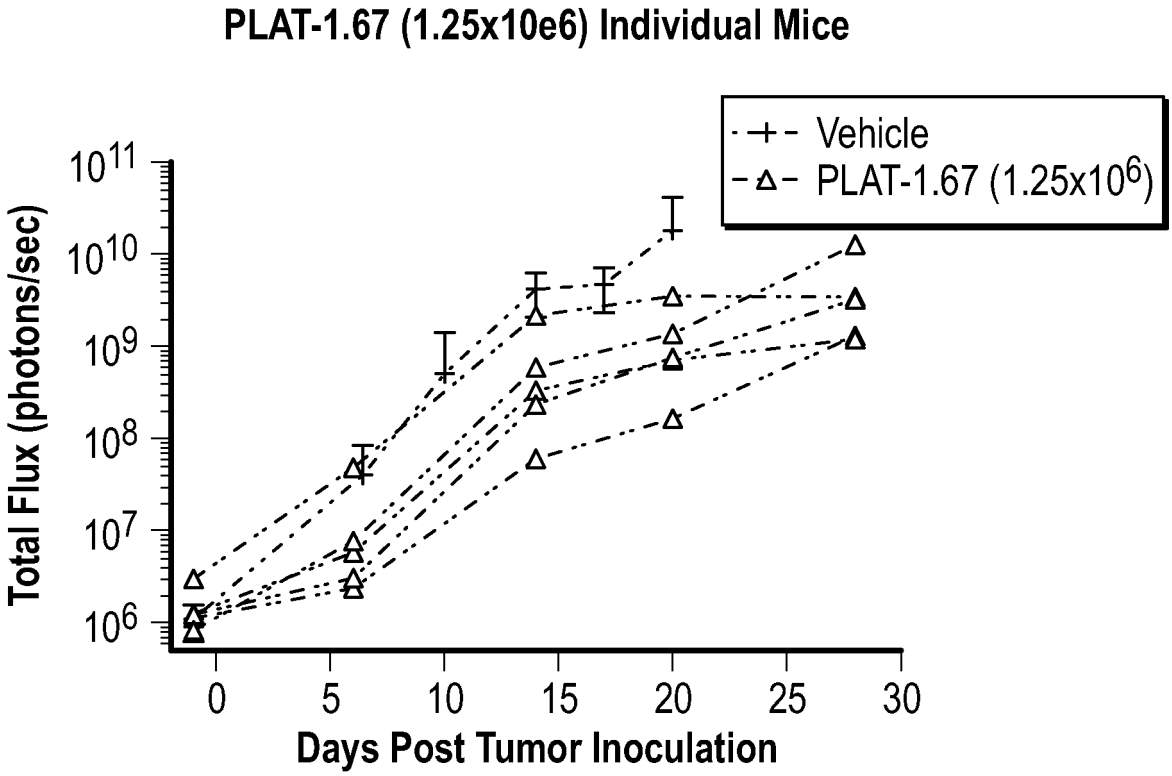


FIG. 53D4

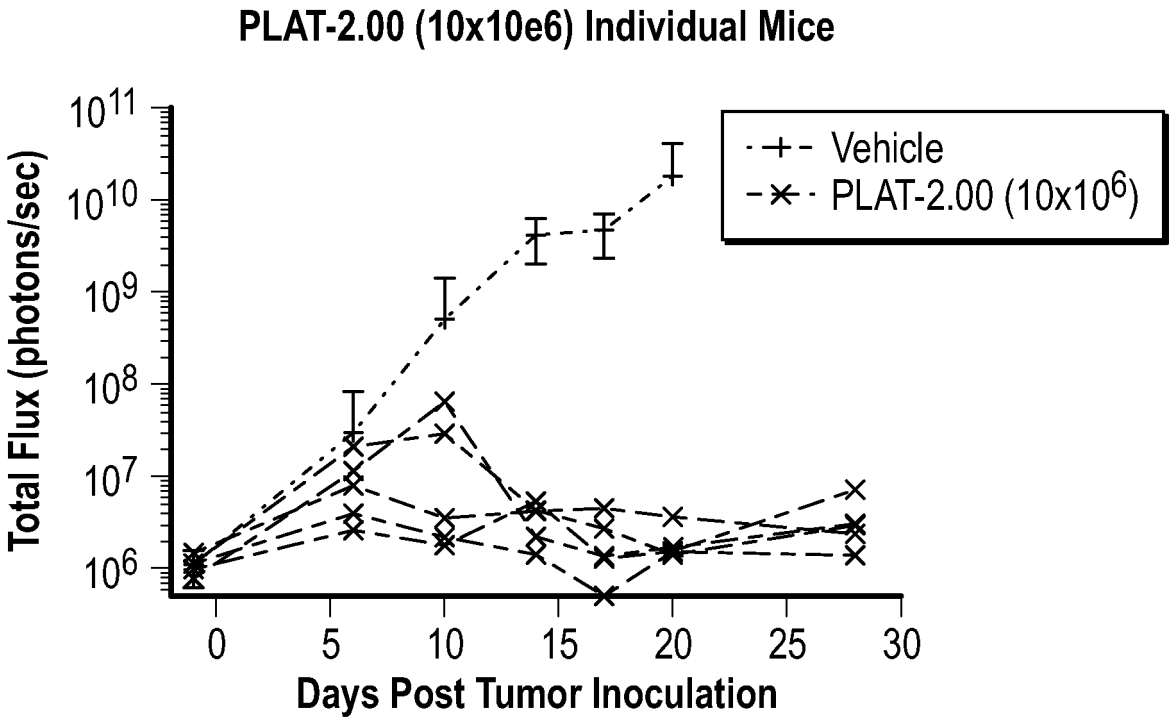


FIG. 53E1

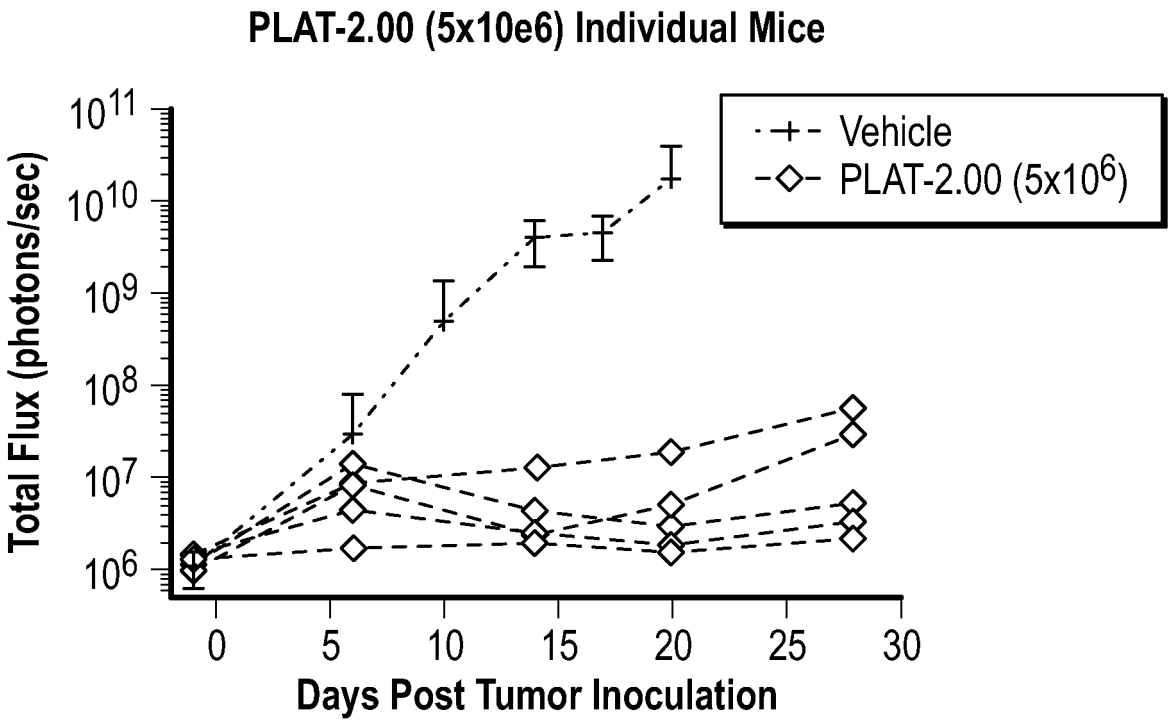


FIG. 53E2

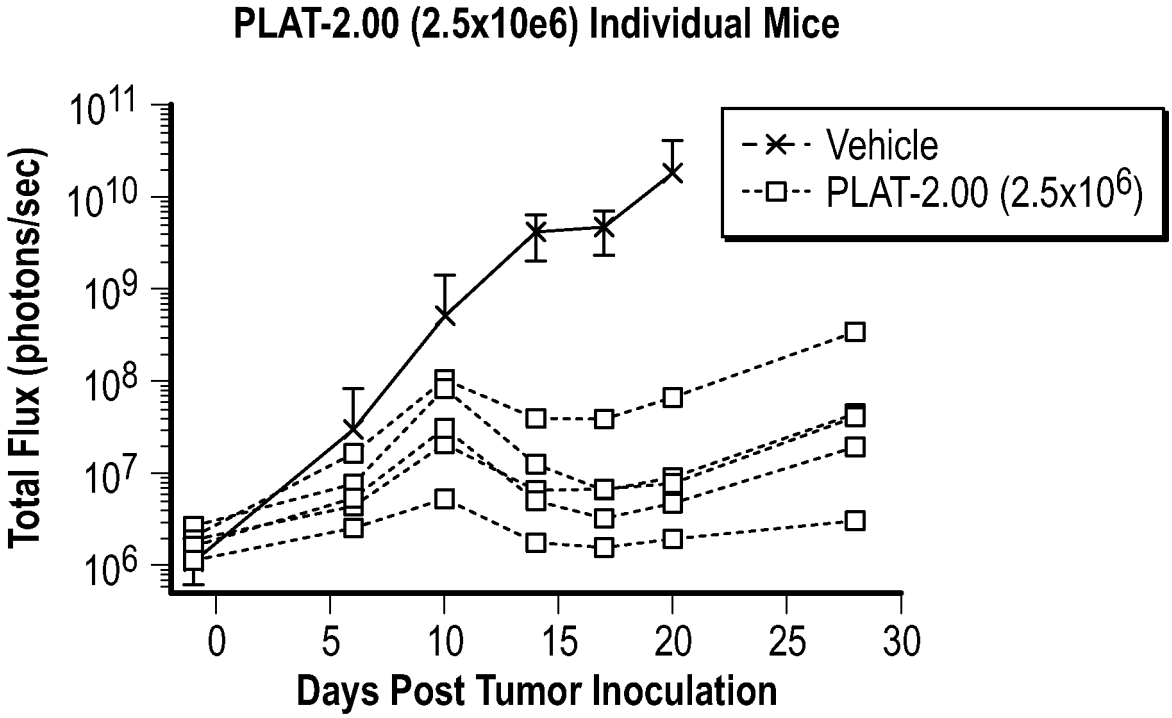


FIG. 53E3

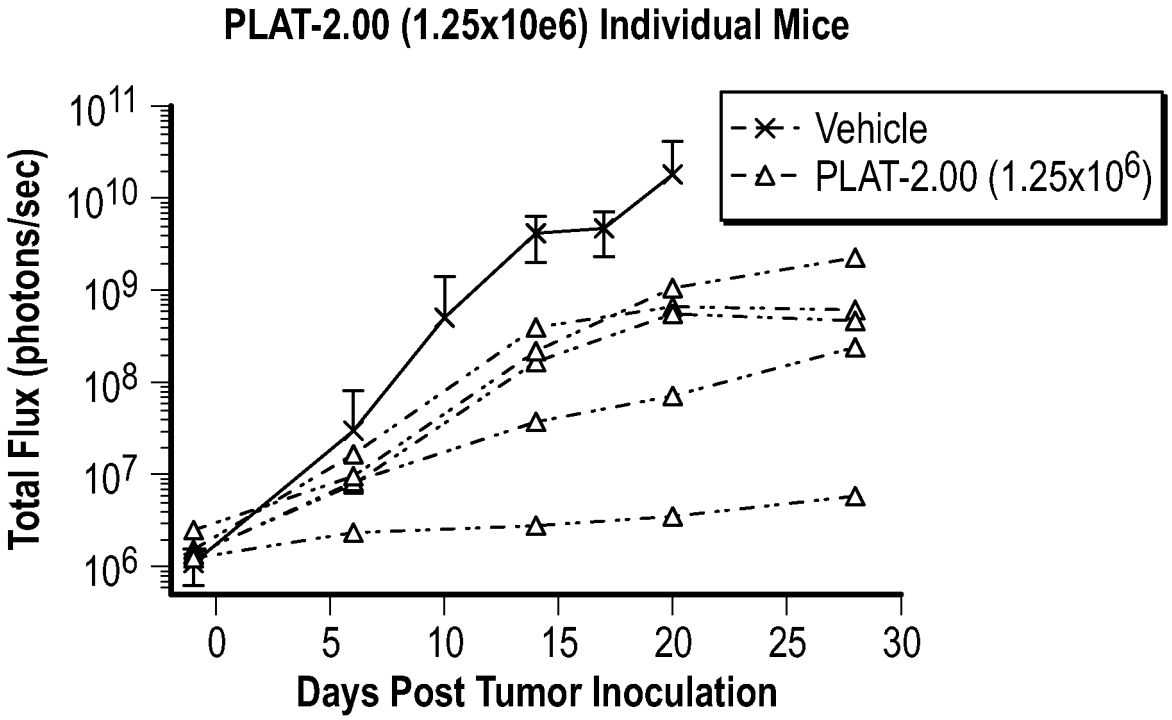


FIG. 53E4

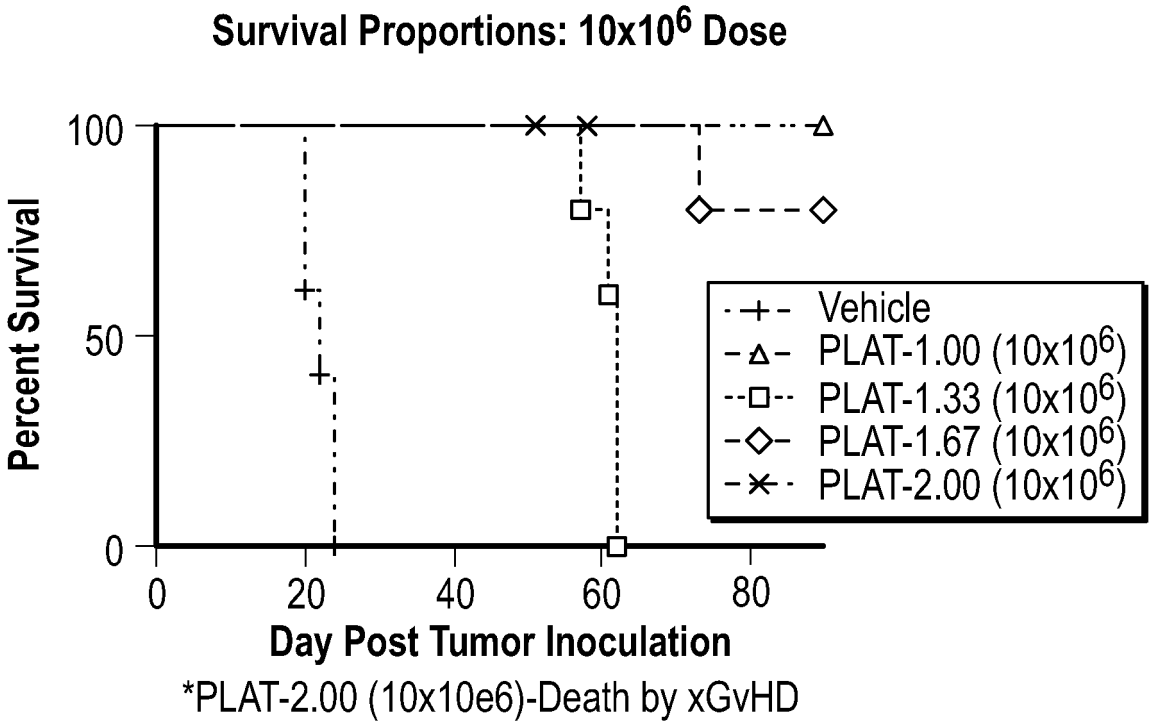


FIG. 54A

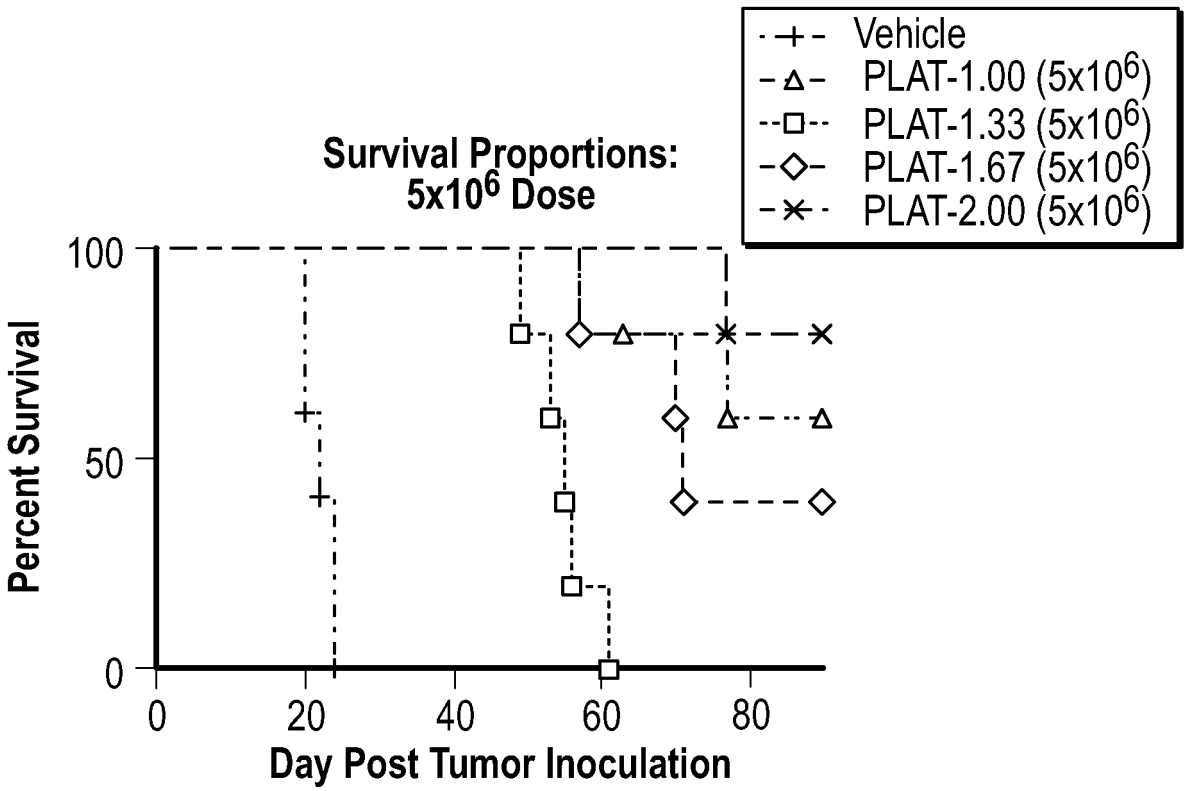


FIG. 54B

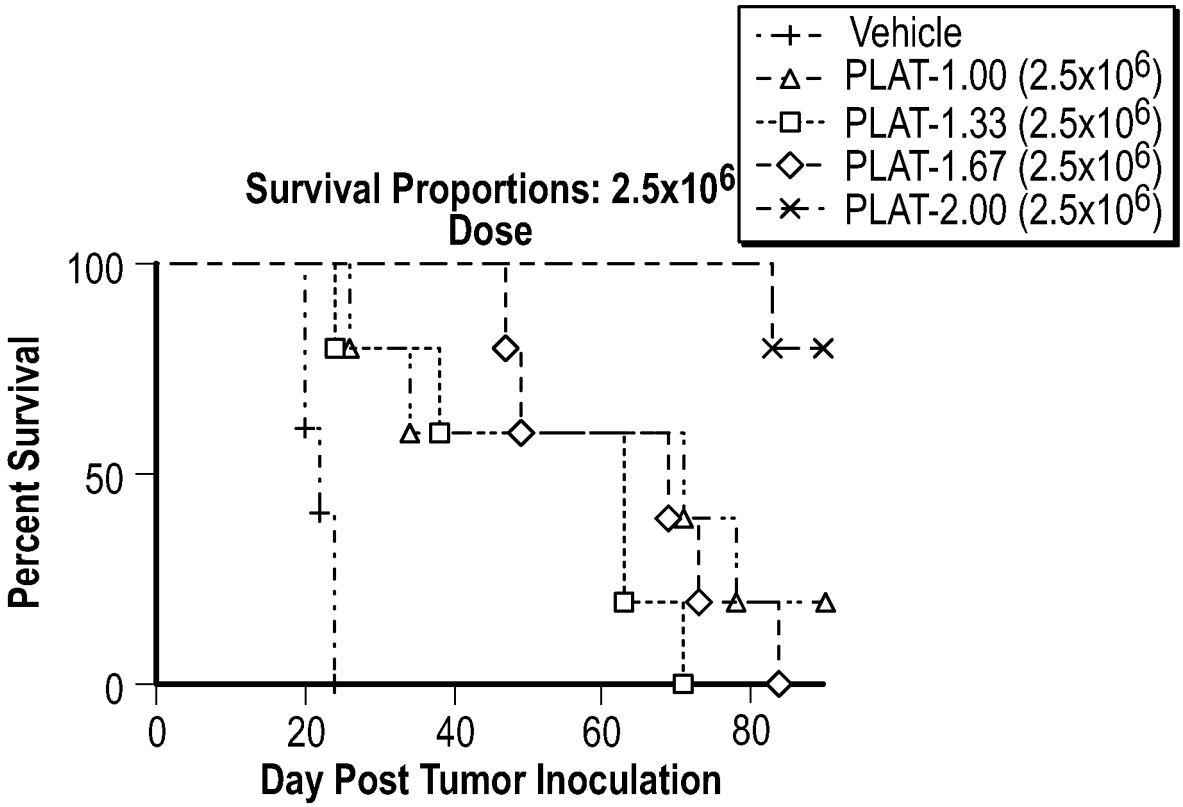


FIG. 54C

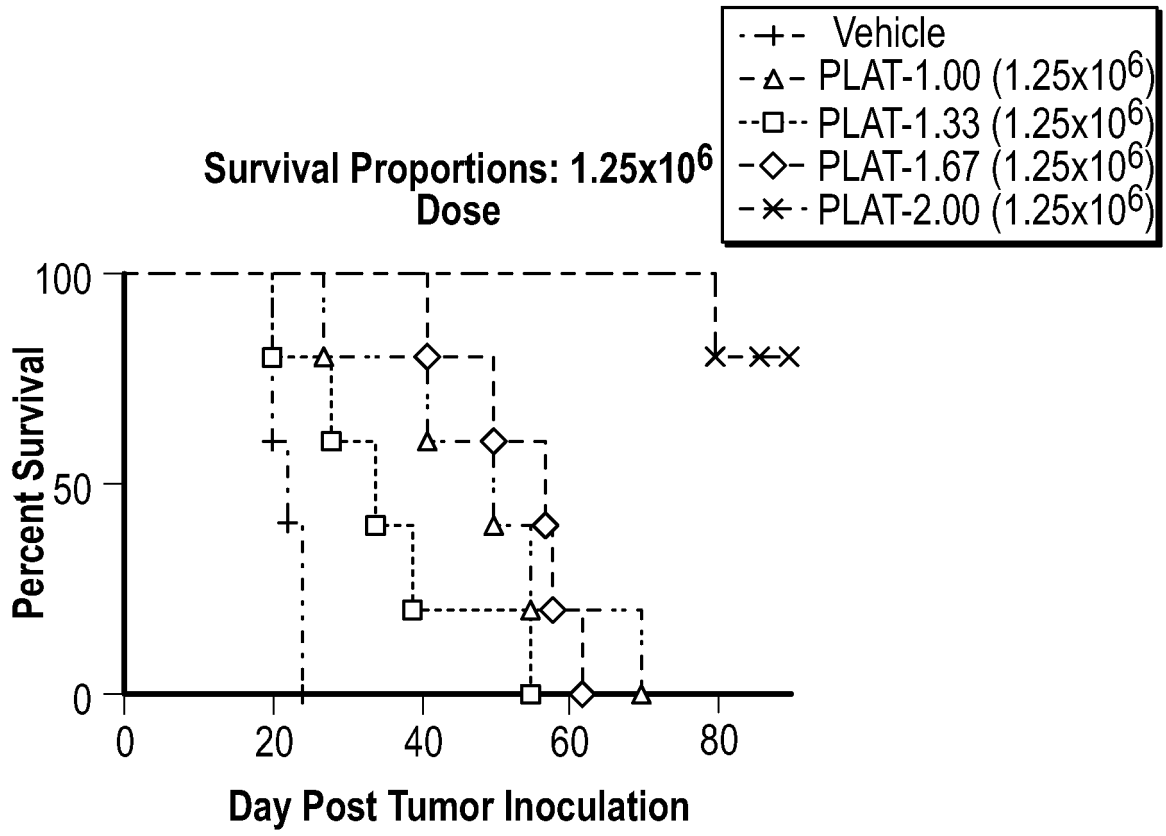


FIG. 54D

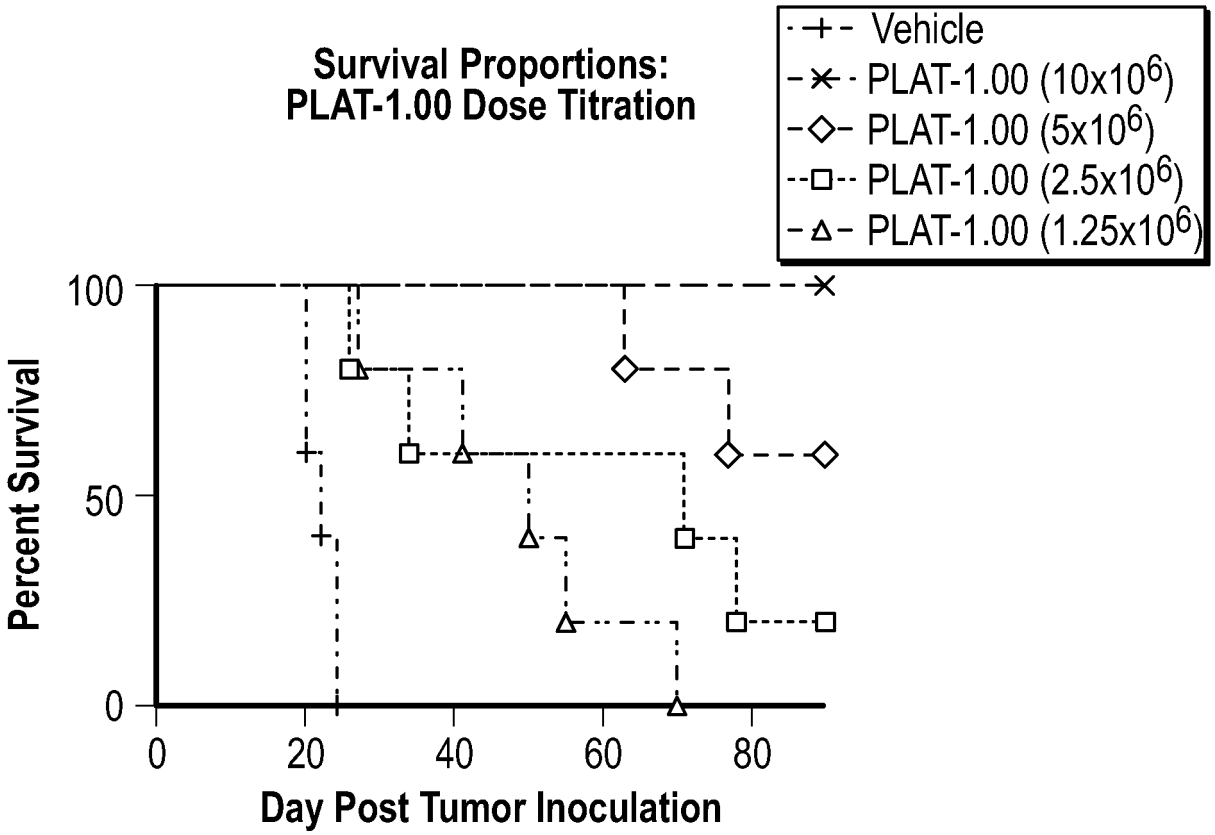
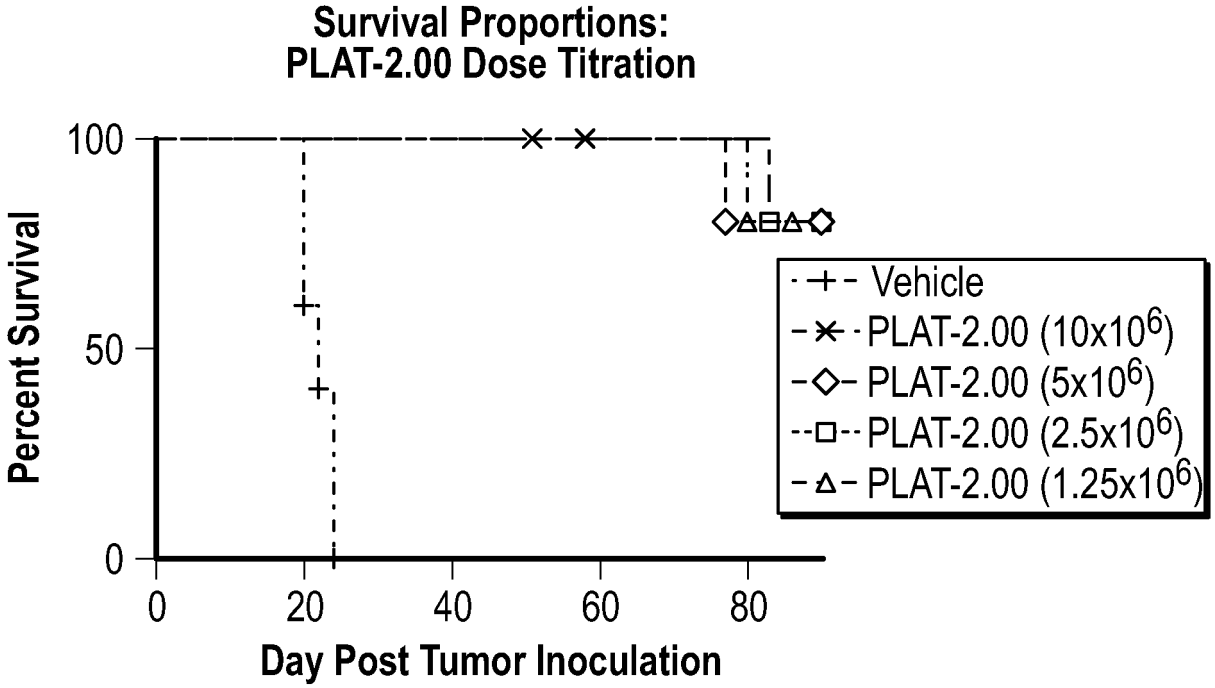


FIG. 55A



*PLAT-2.00(10x10e6)-Death by xGVHD

FIG. 55B

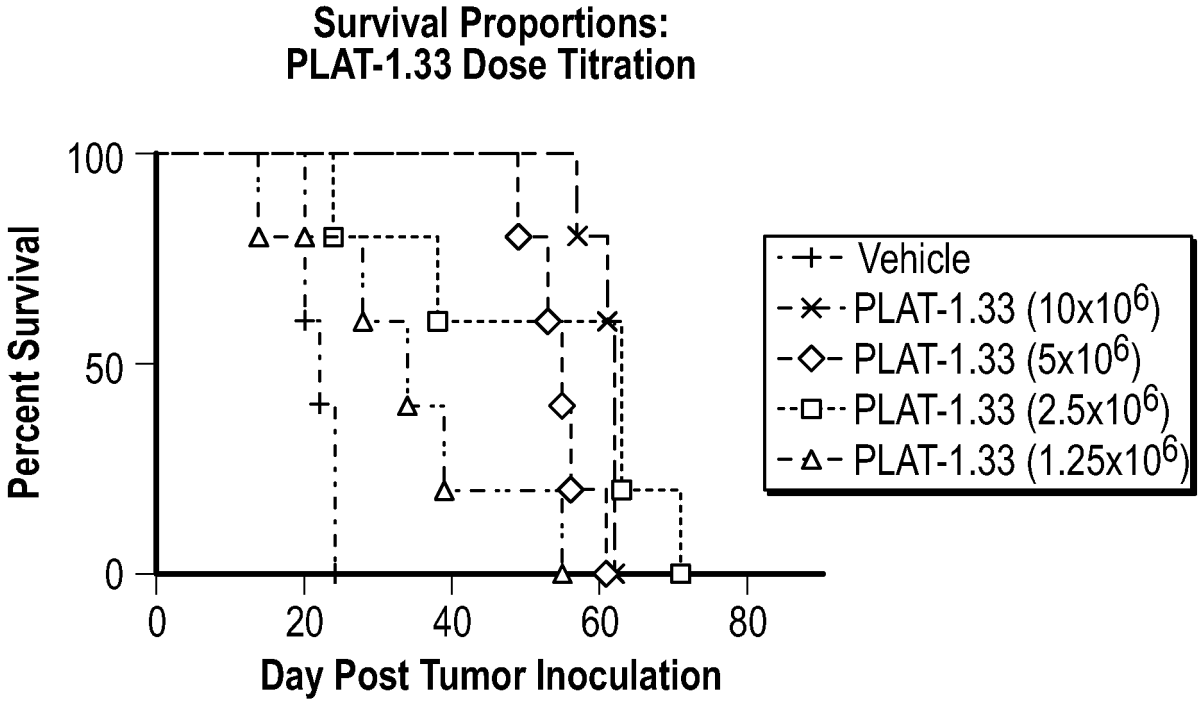


FIG. 55C

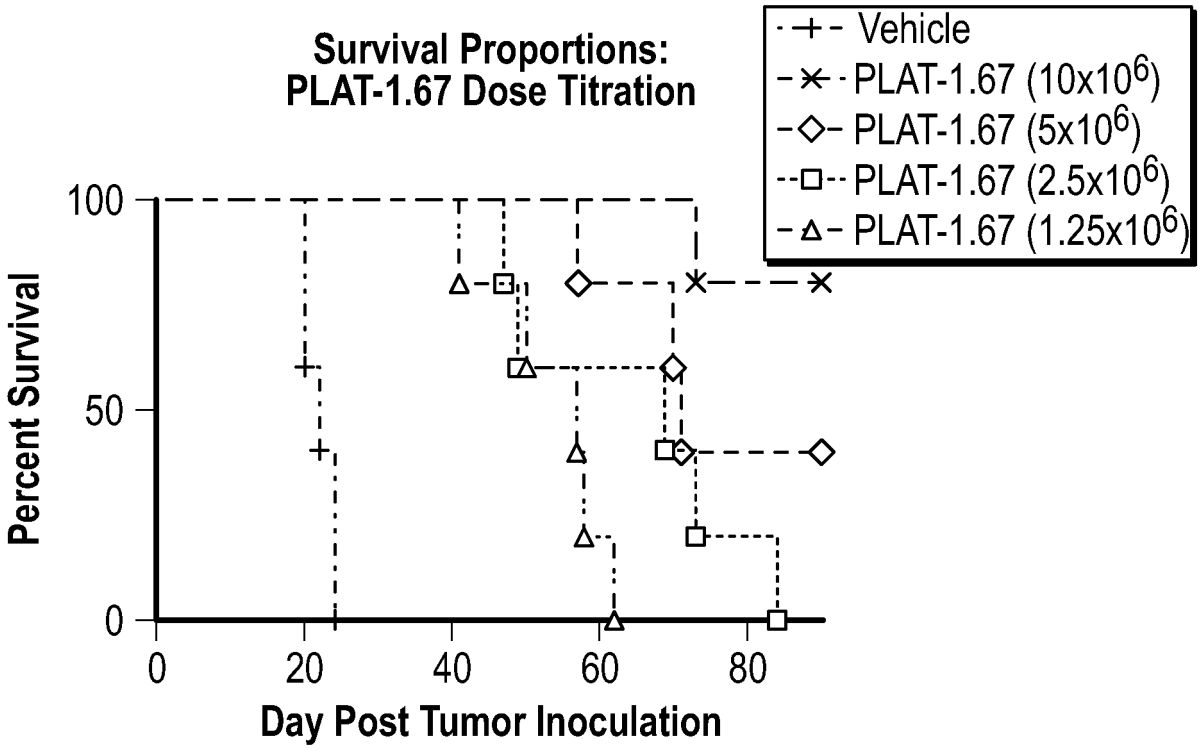


FIG. 55D

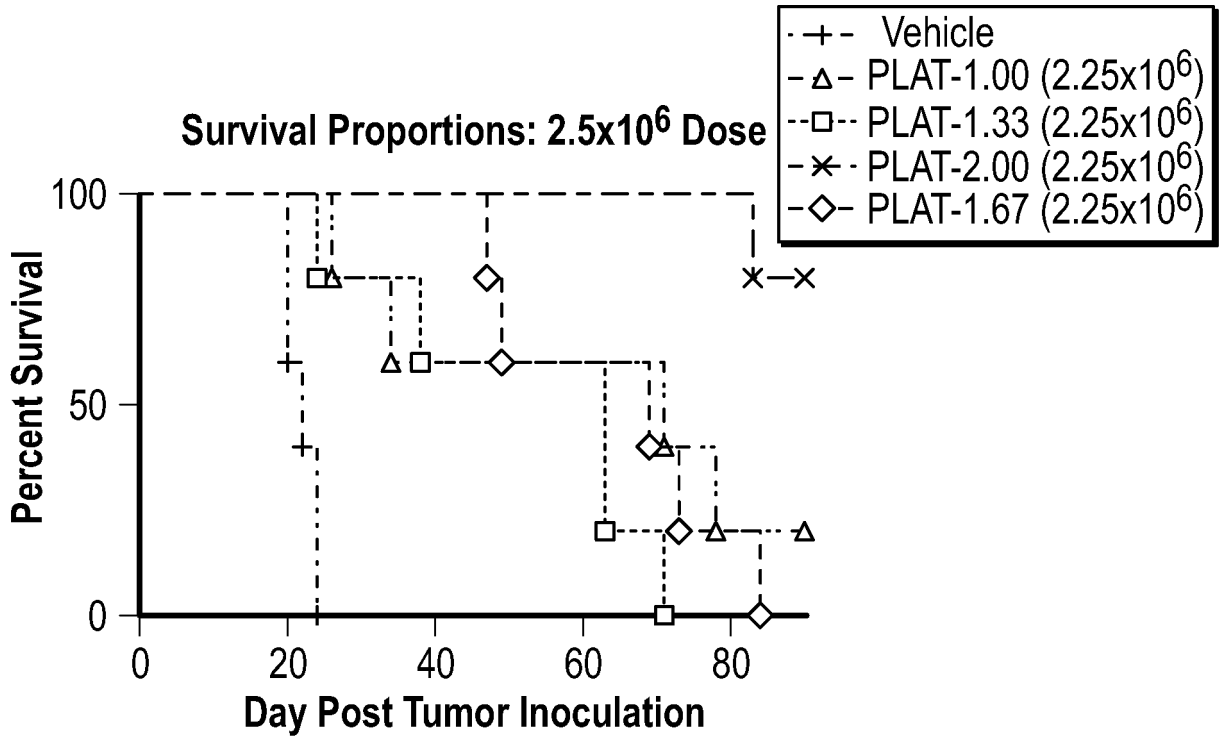


FIG. 56A

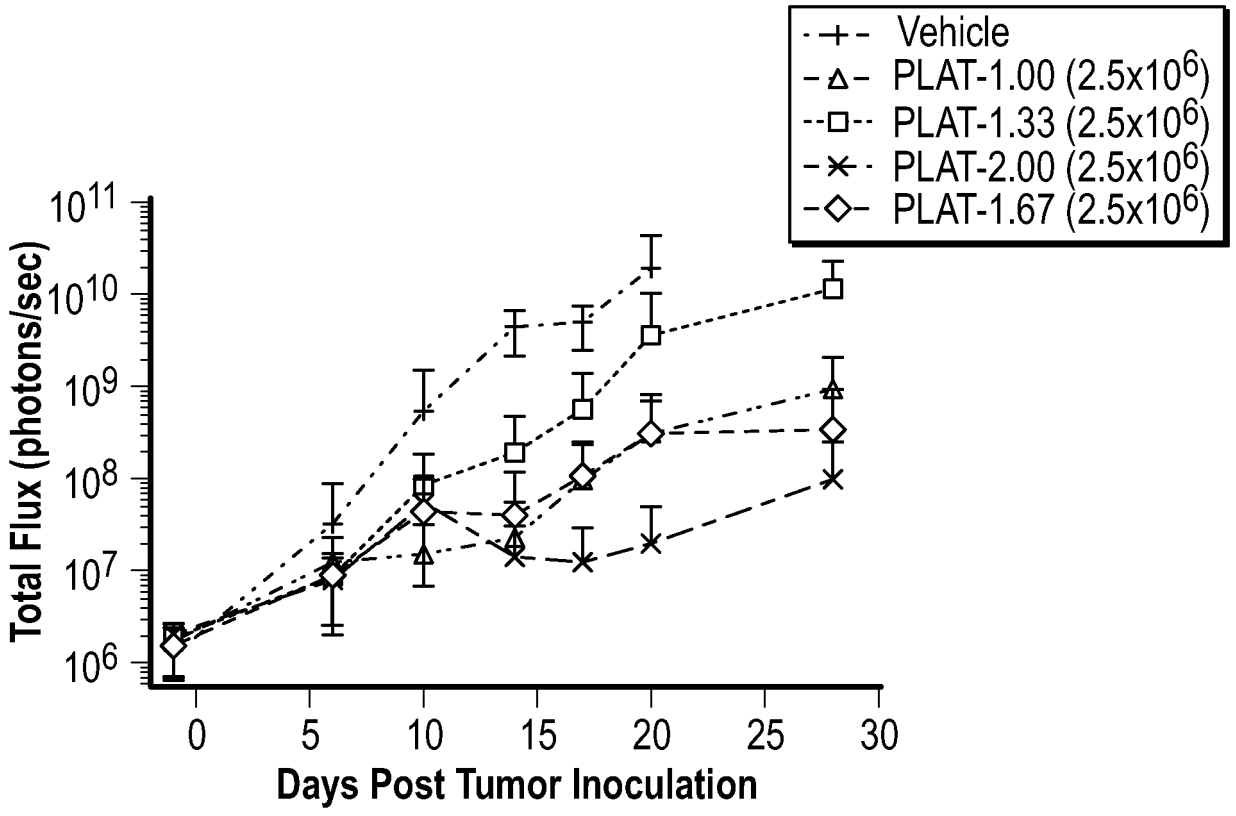


FIG. 56B

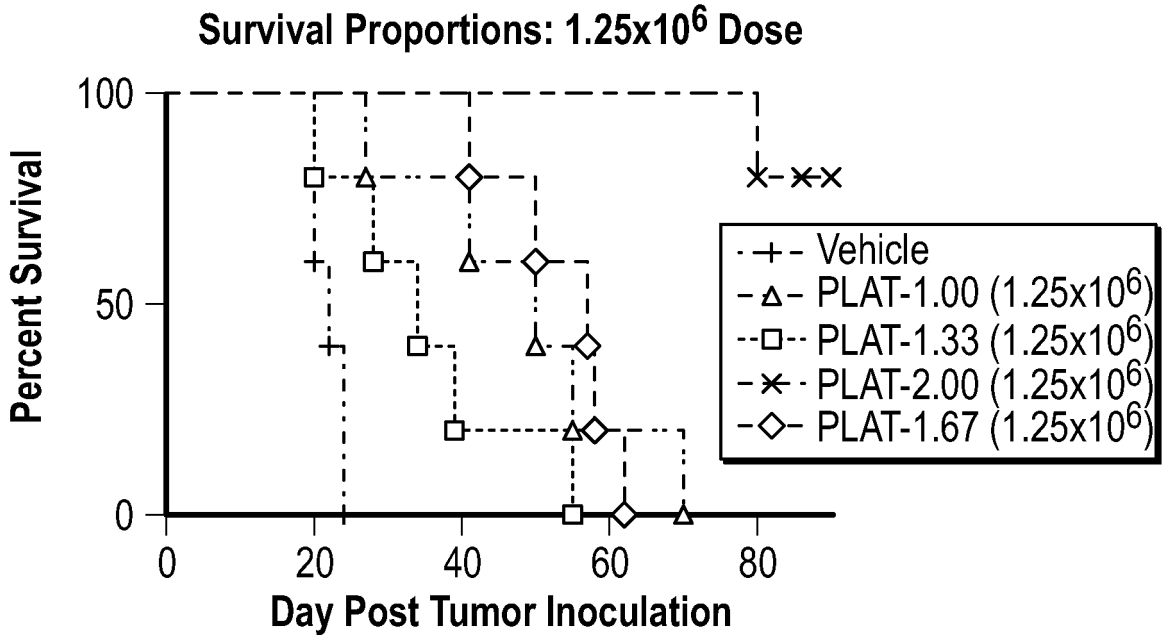


FIG. 56C

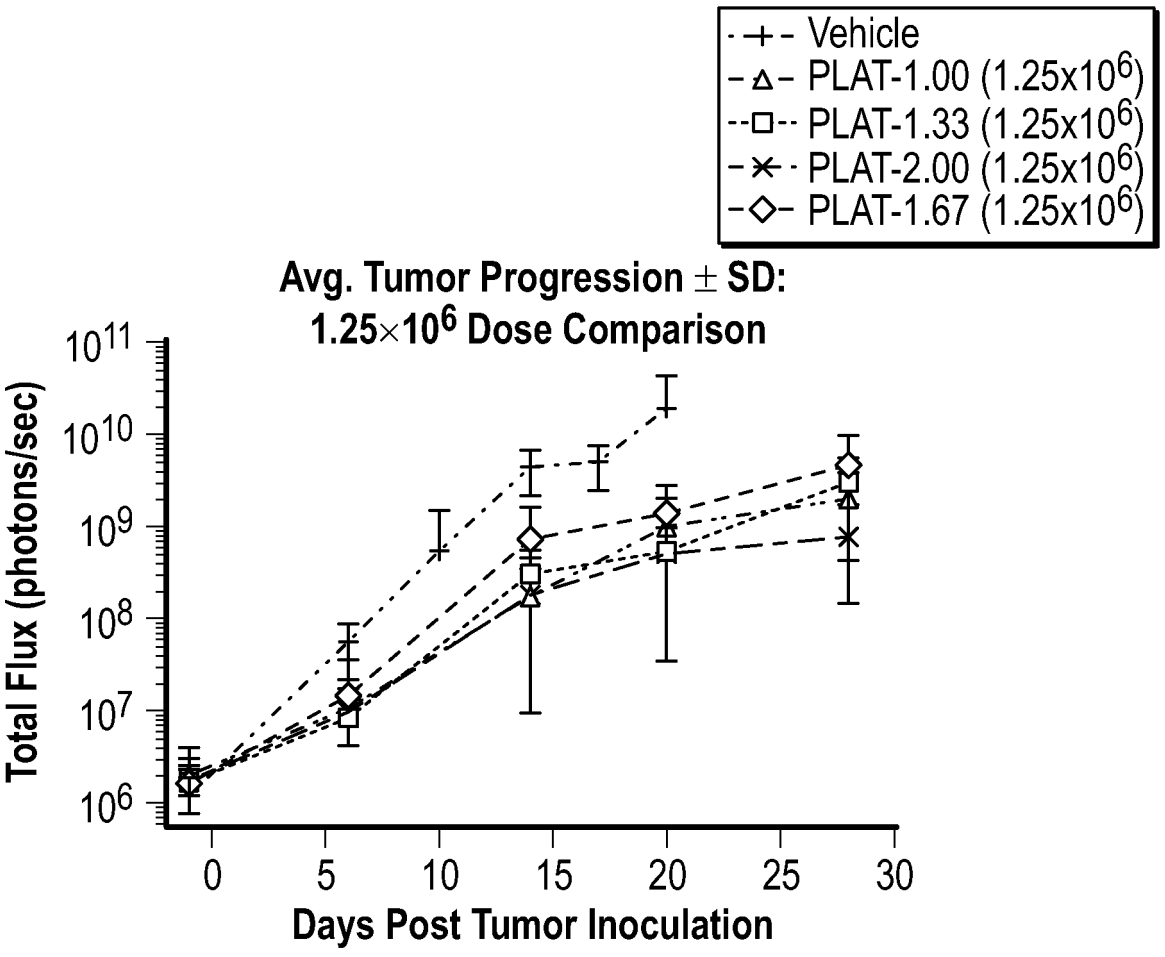


FIG. 56D

JME14-03: xenoGraft-versus-Host Disease

Symptoms/Signs xGvHD in Mice:

- Flaky skin
- Eye issues (weepy looking)
- Weight loss
- Dehydration
- Hindlimb edema

FIG. 57A

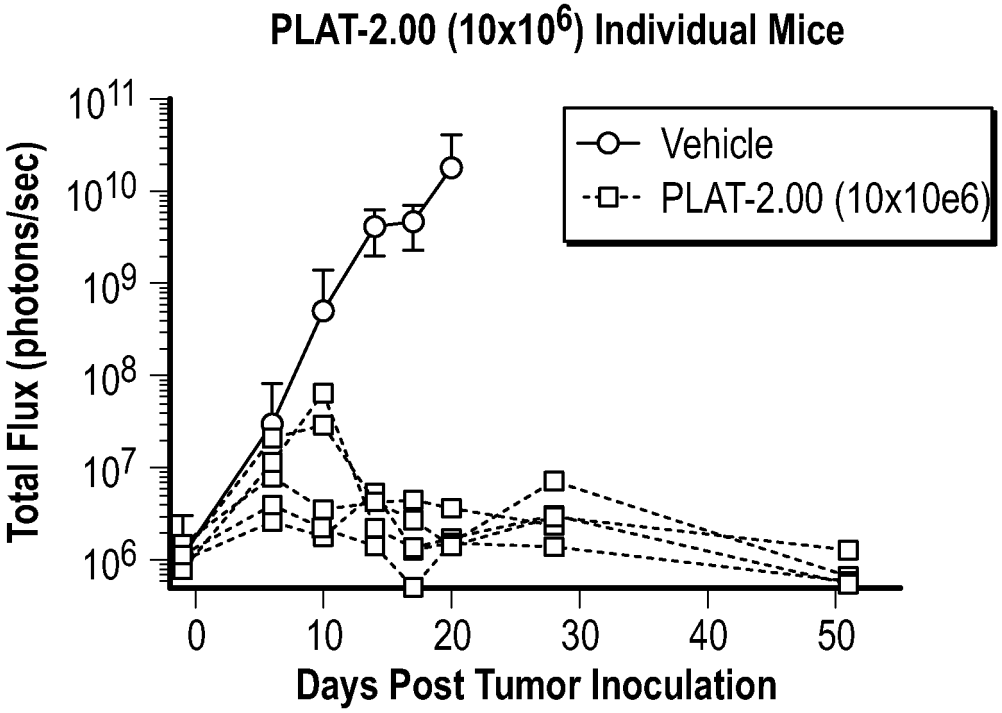
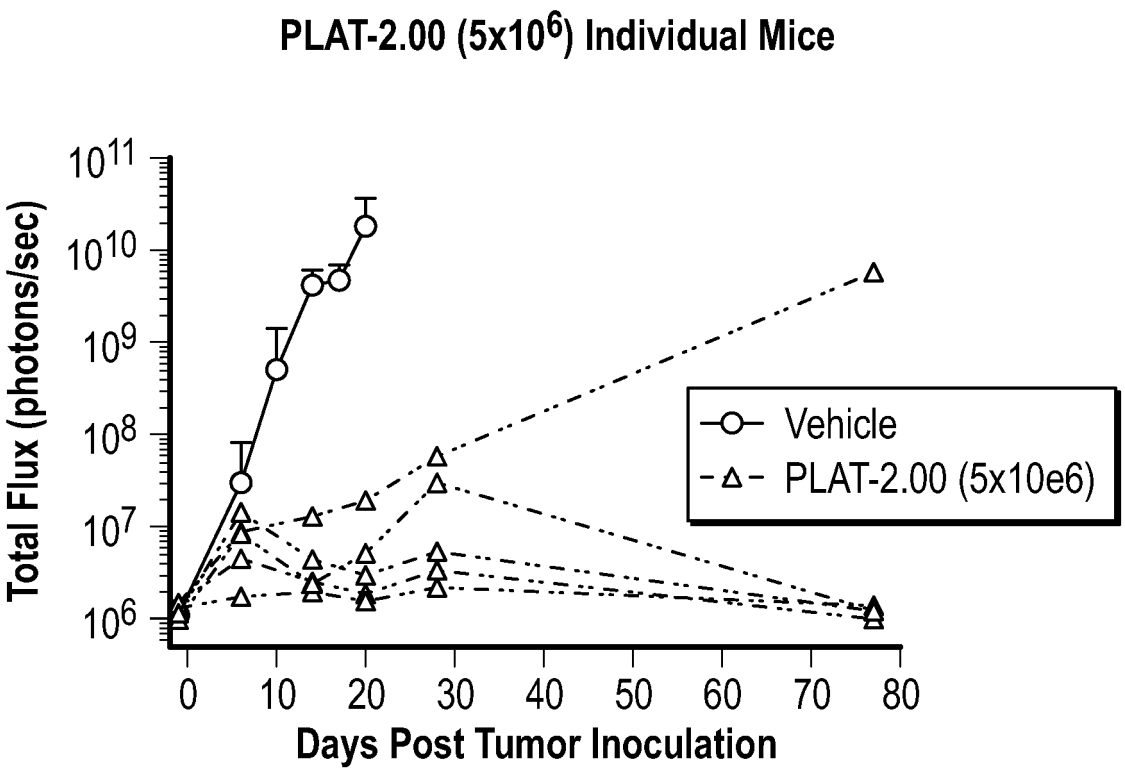


FIG. 57B



NOTE: Animals treated at 10 million and 5 million doses with PLAT-02 cells developed xGvHD. As a result animals receiving the 10 million dose were taken down day 58 post tumor or 51 days post T-cell administration. Those receiving 5 million dose were euthanized at end of study at 90 days post tumor or 83 days post T-cell administration.

FIG. 57C

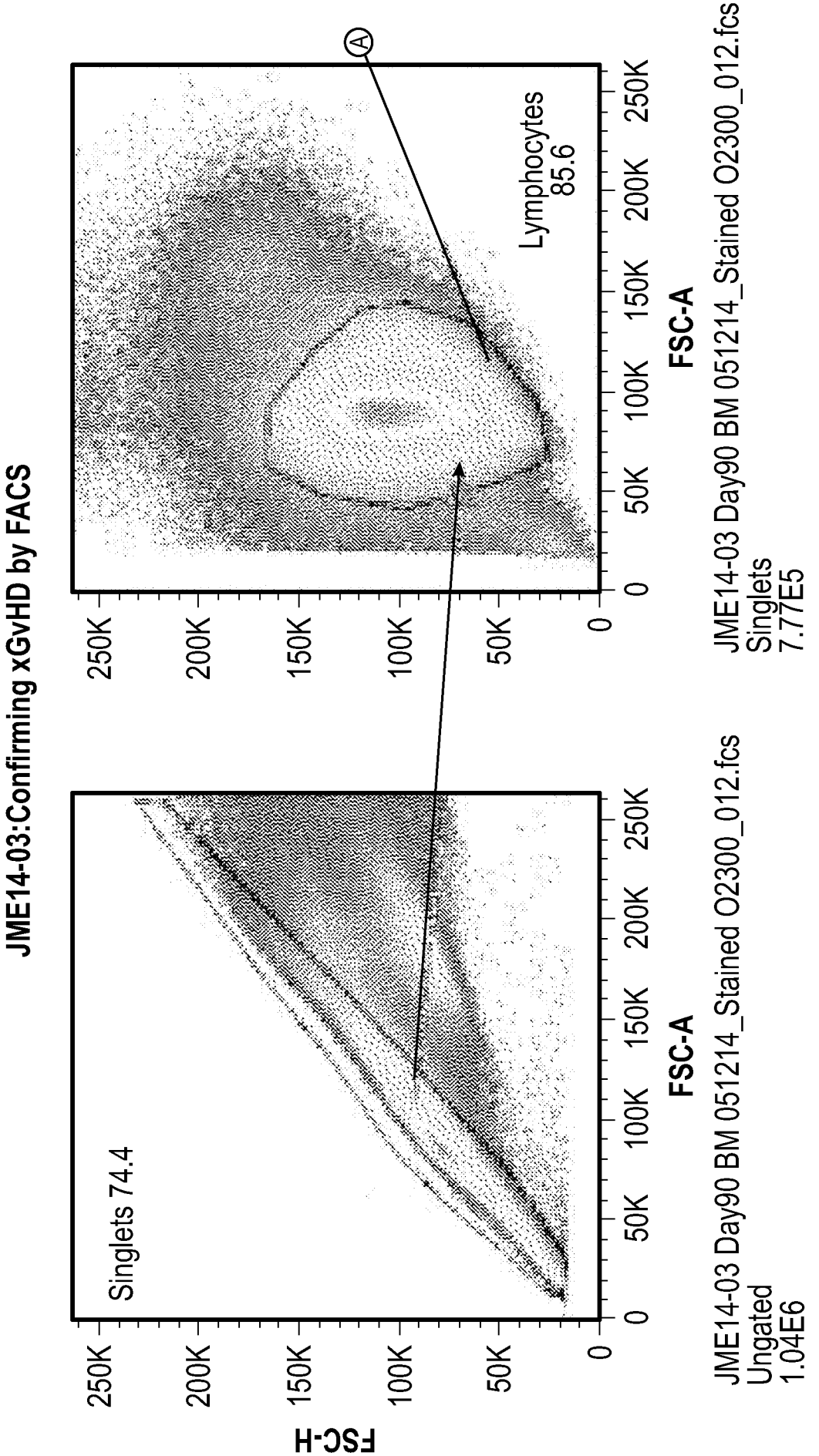


FIG. 58A1

FIG. 58A2

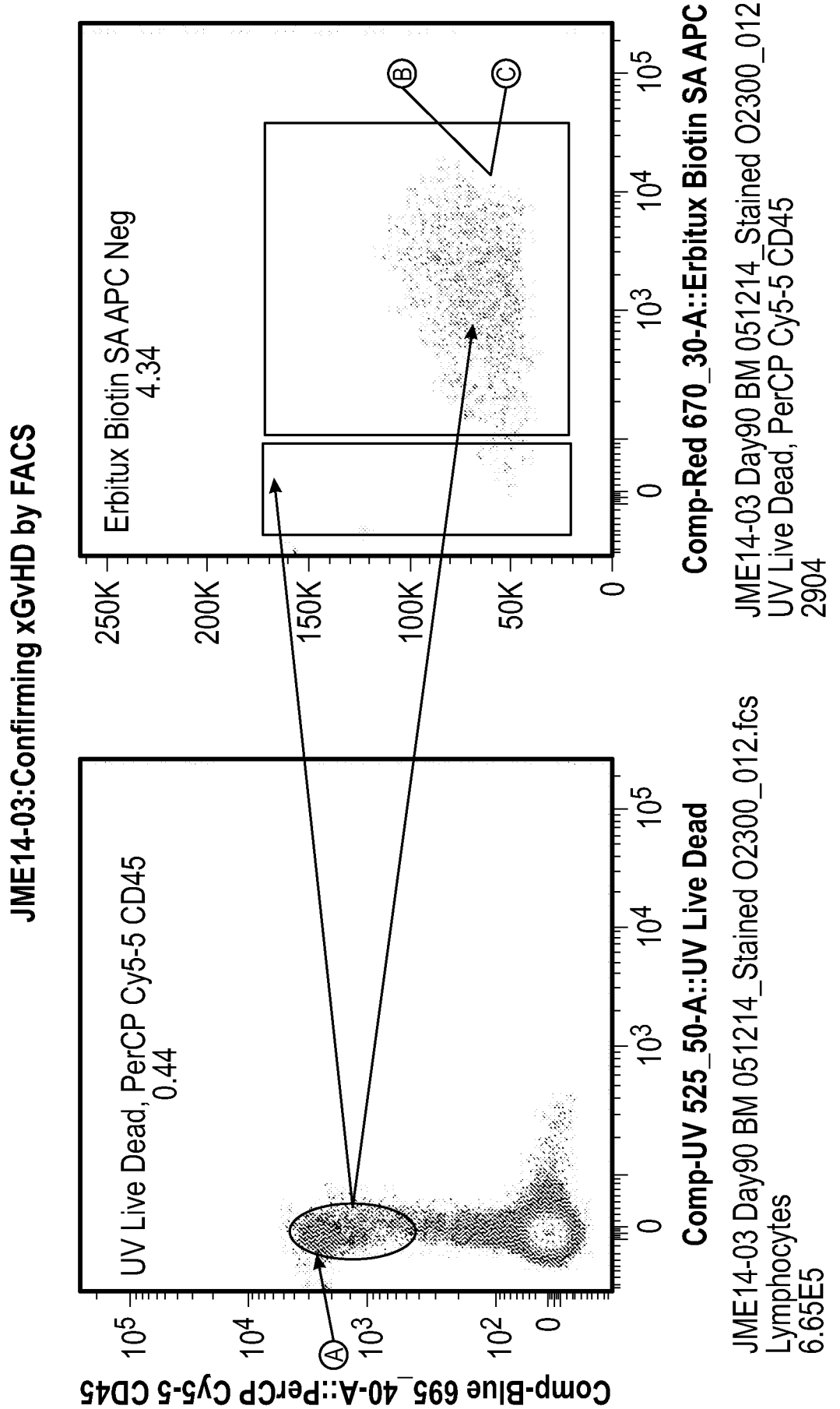


FIG. 58A3

FIG. 58A4

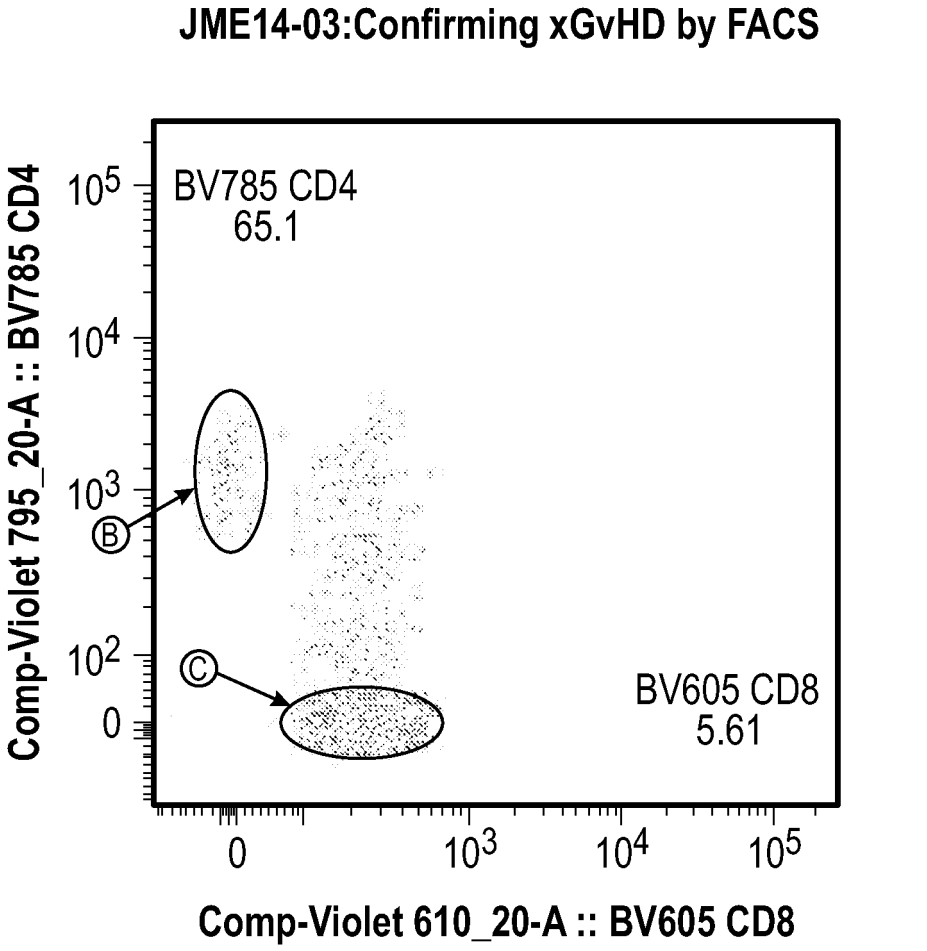

JME14-03:Confirming xGvHD by FACS
BV785 CD4
65.1
BV605 CD8
5.61
Comp-Violet 795_20-A :: BV785 CD4
Comp-Violet 610_20-A :: BV605 CD8
JME14-03 Day90 BM 051214_Stained O2300_012.fcs
Erbitux Biotin SA APC Pos
2761

FIG. 58A5

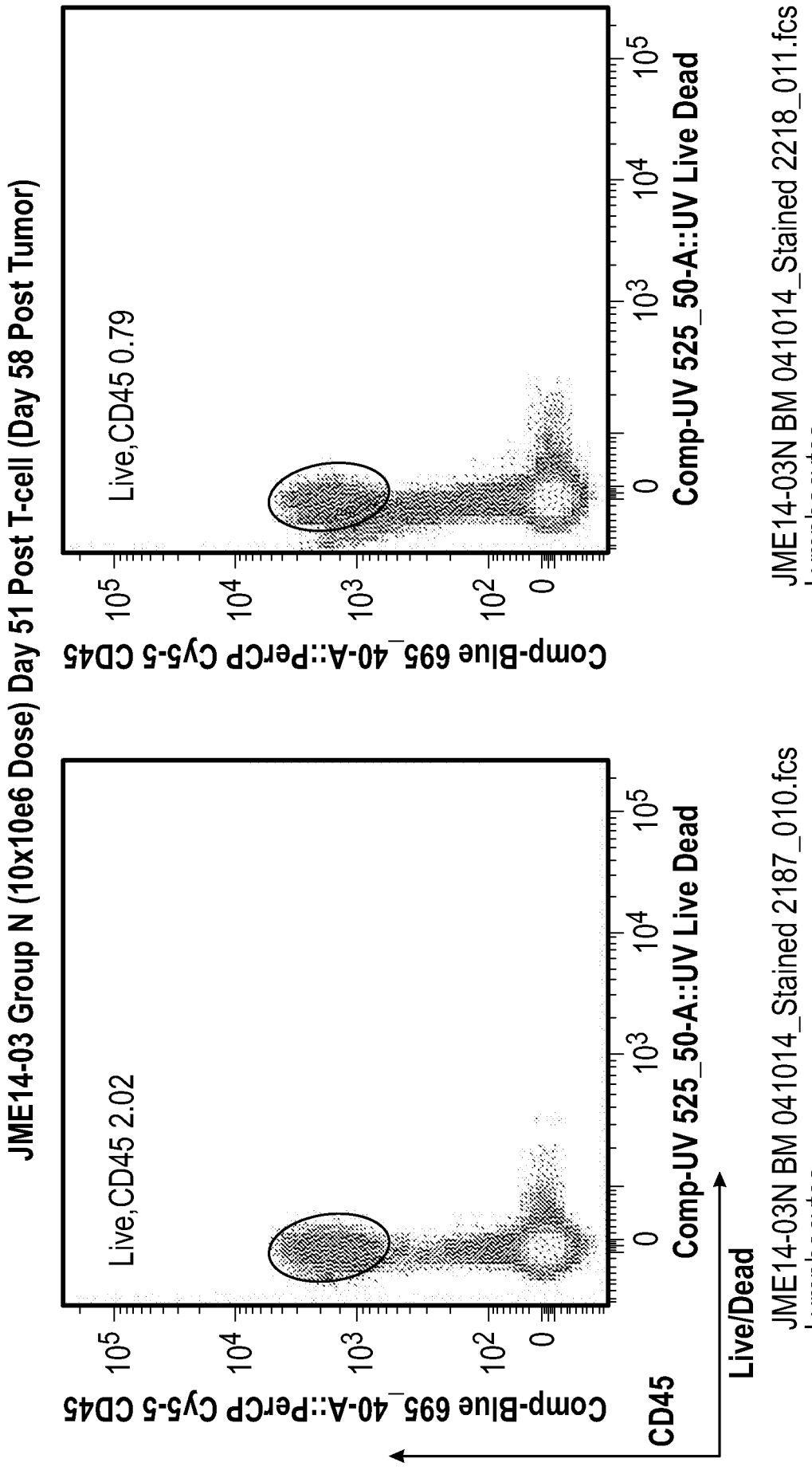


FIG. 58B1

FIG. 58B2

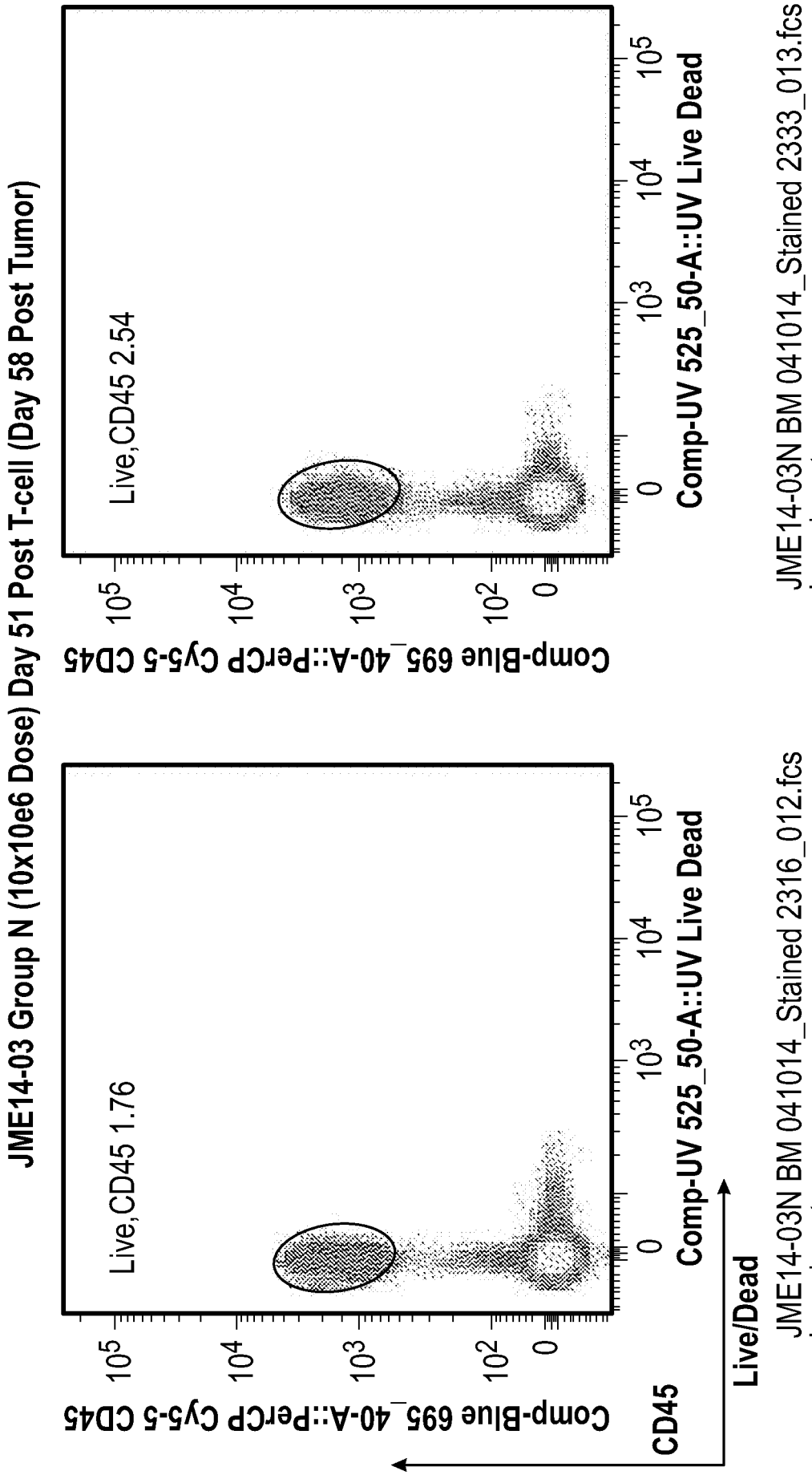


FIG. 58B3

FIG. 58B4

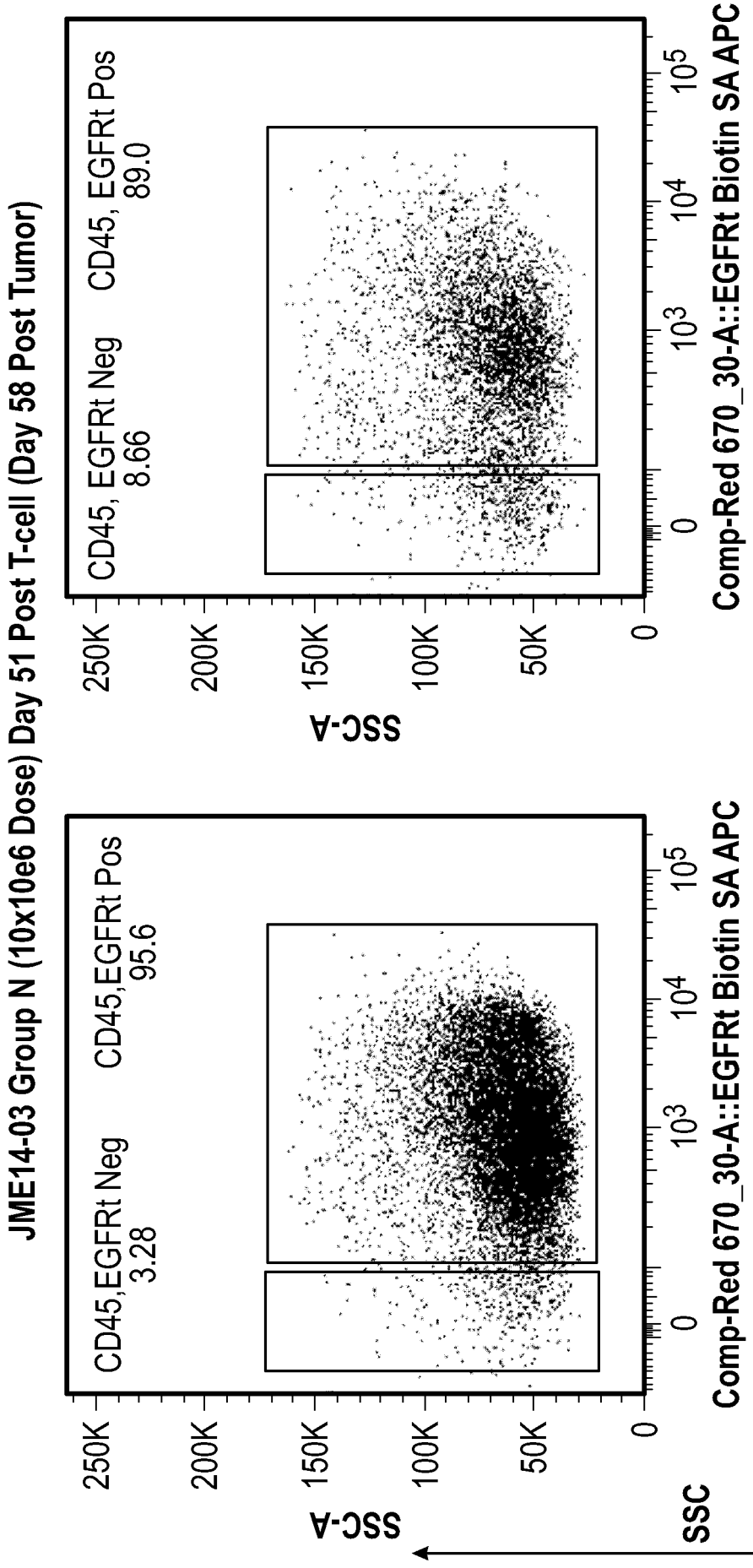


FIG. 58B5

FIG. 58B6

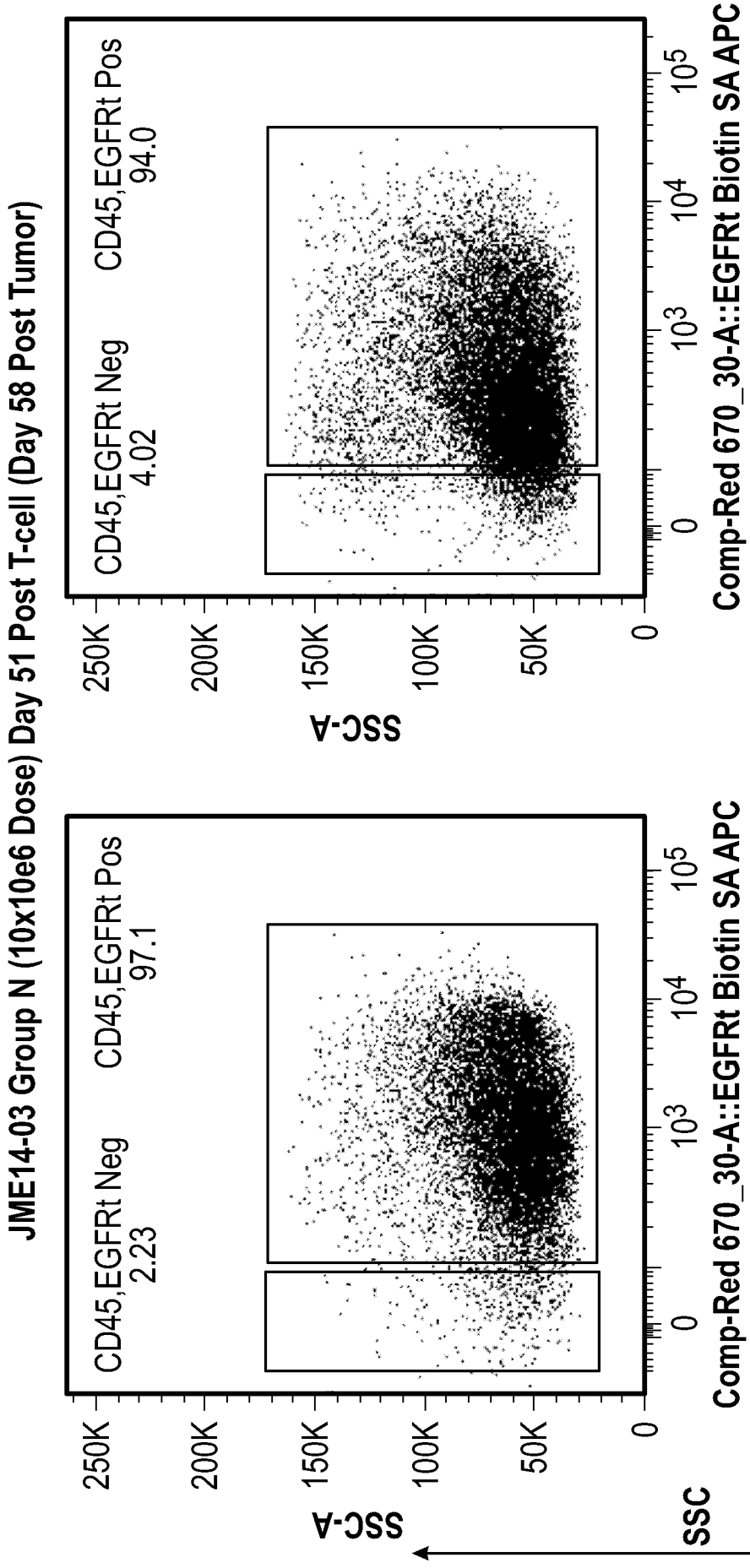


FIG. 58B7

FIG. 58B8

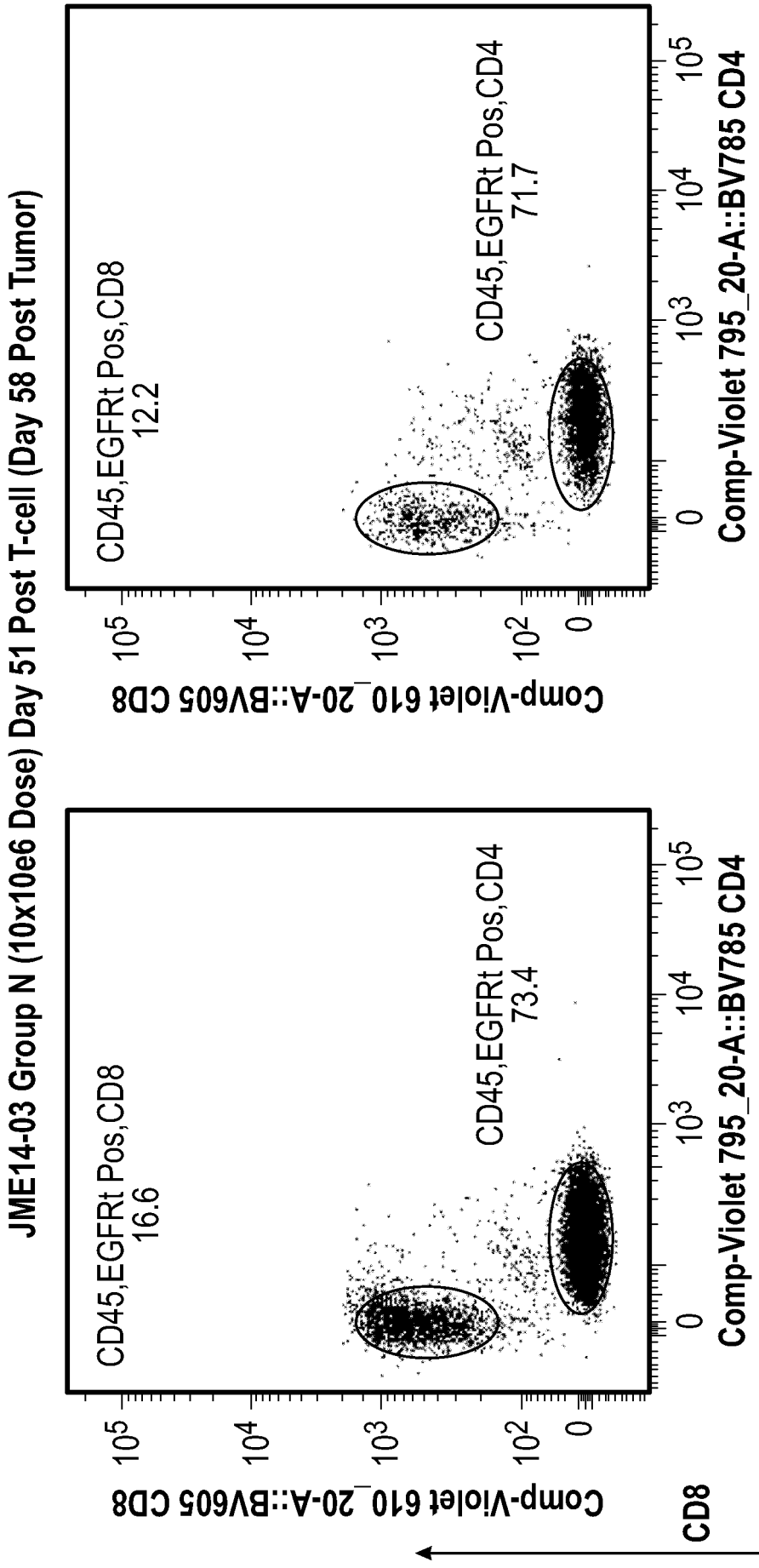


FIG. 58B9

FIG. 58B10

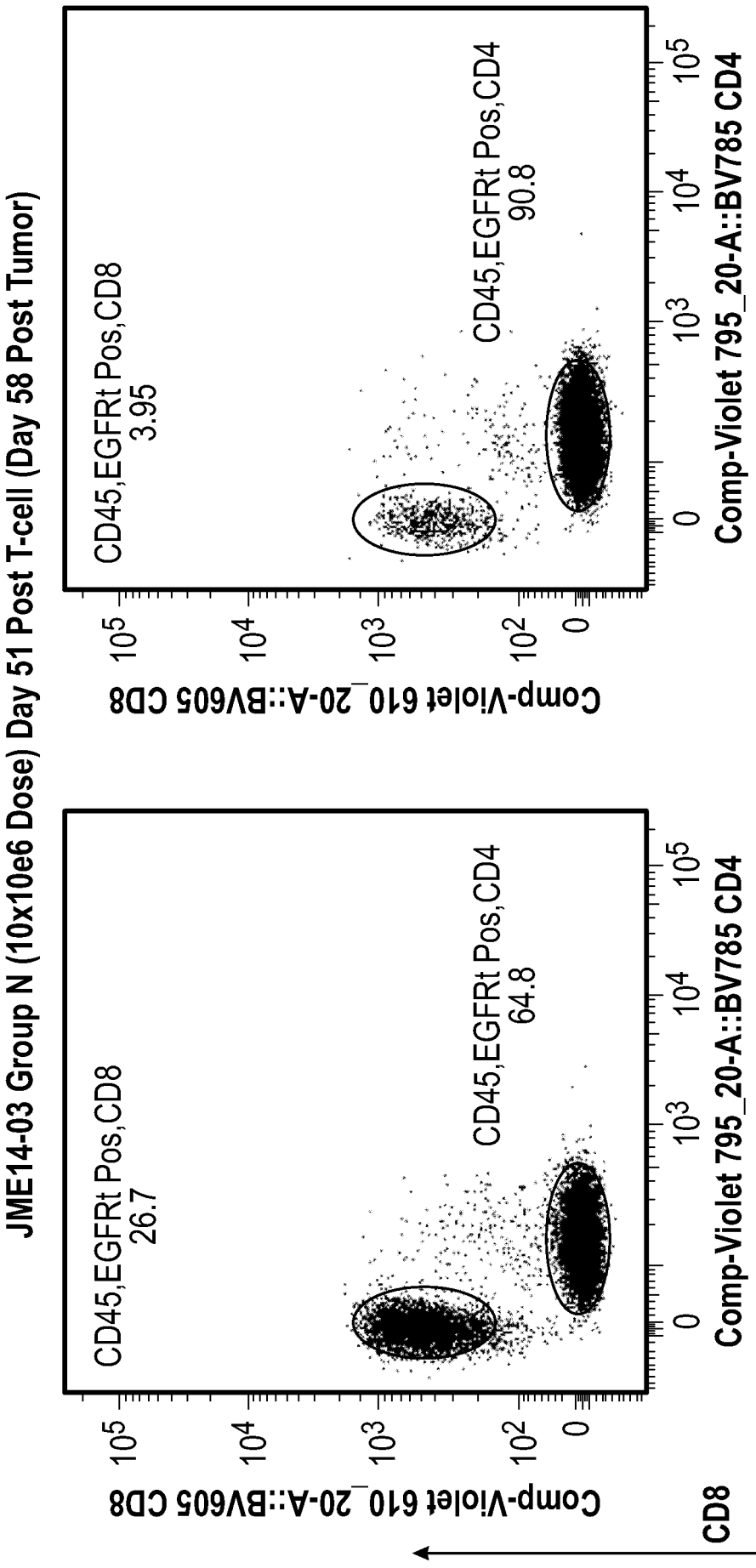


FIG. 58B11

FIG. 58B12

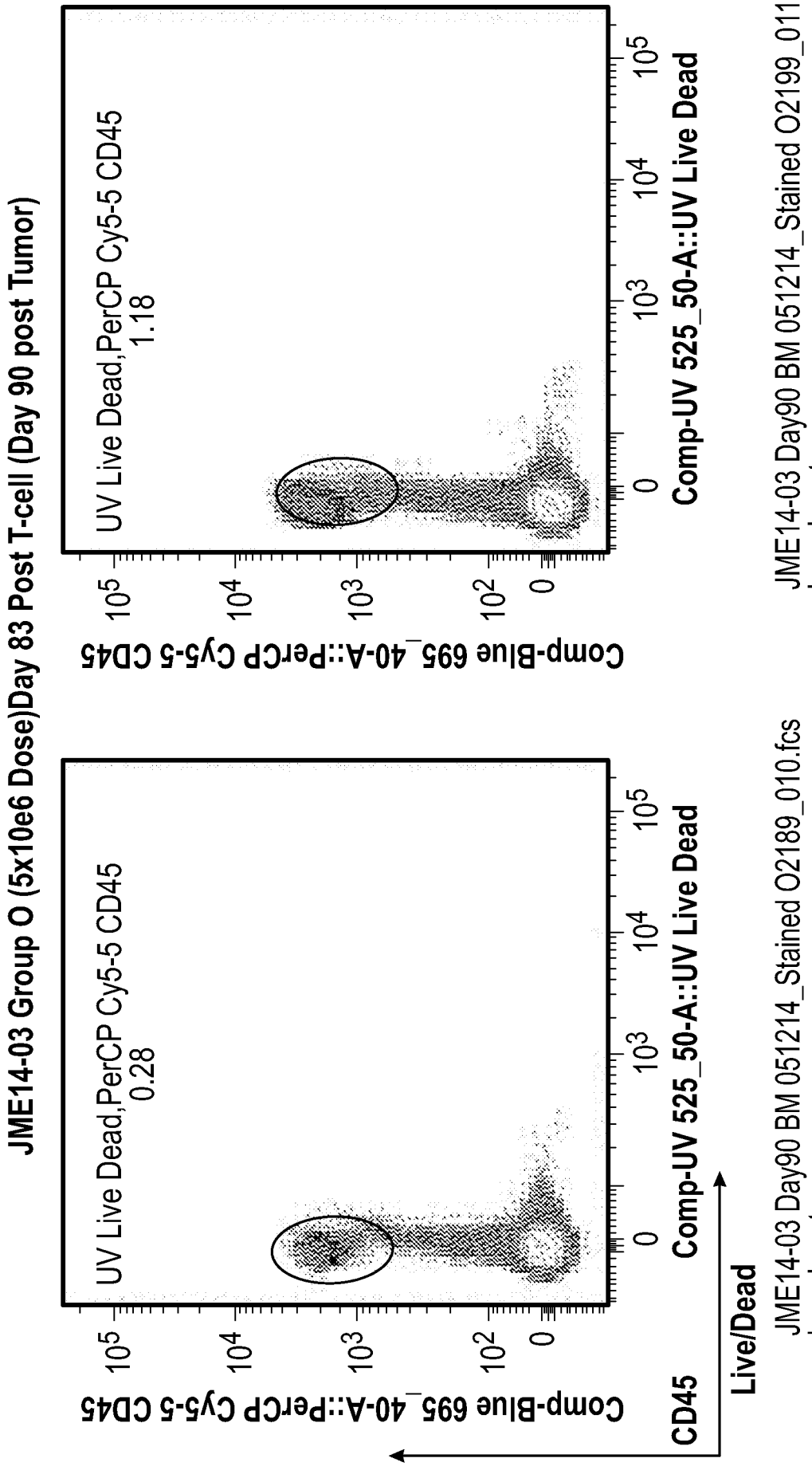
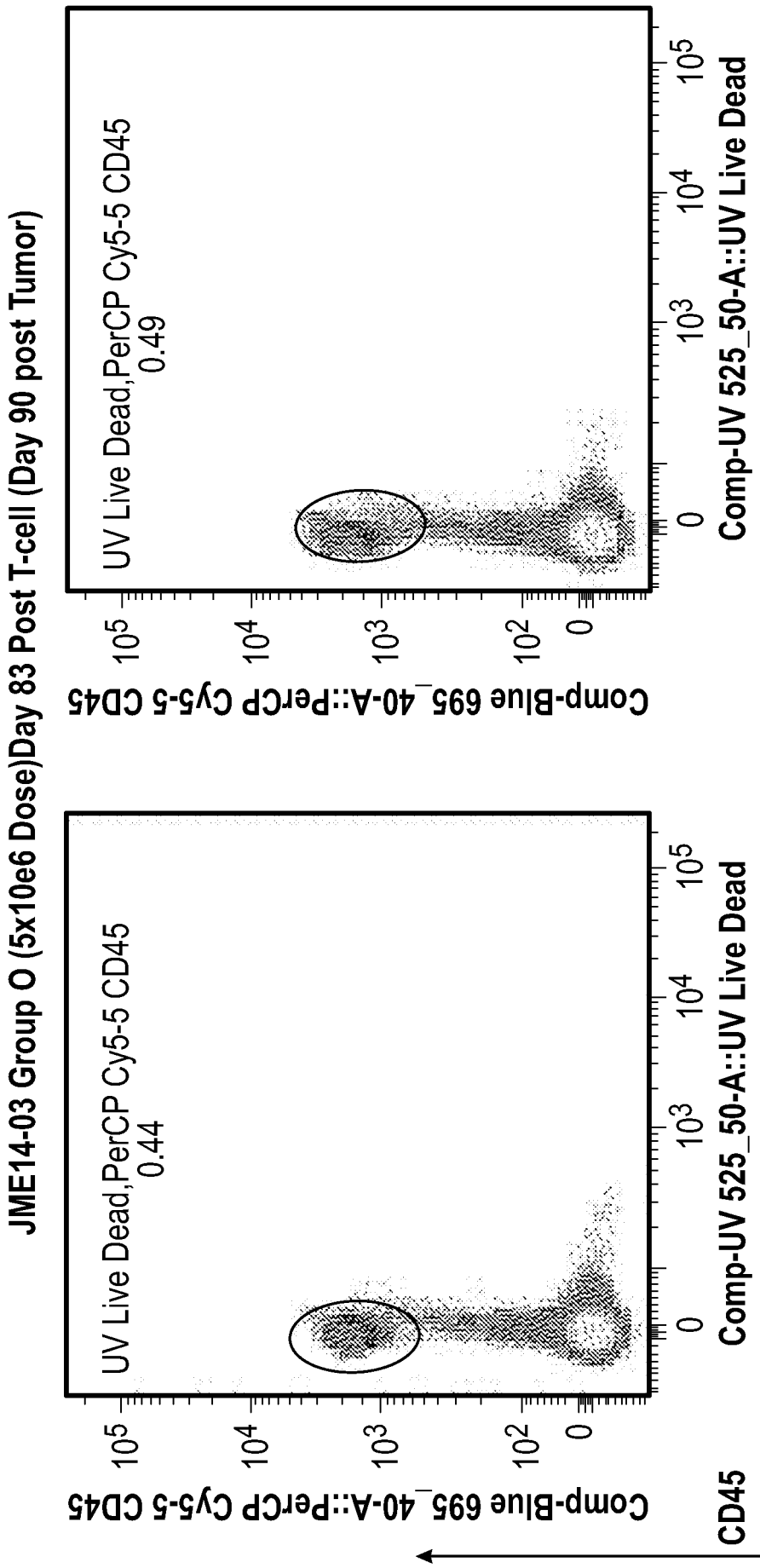


FIG. 58C1

FIG. 58C2



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FIG. 58C3

FIG. 58C4

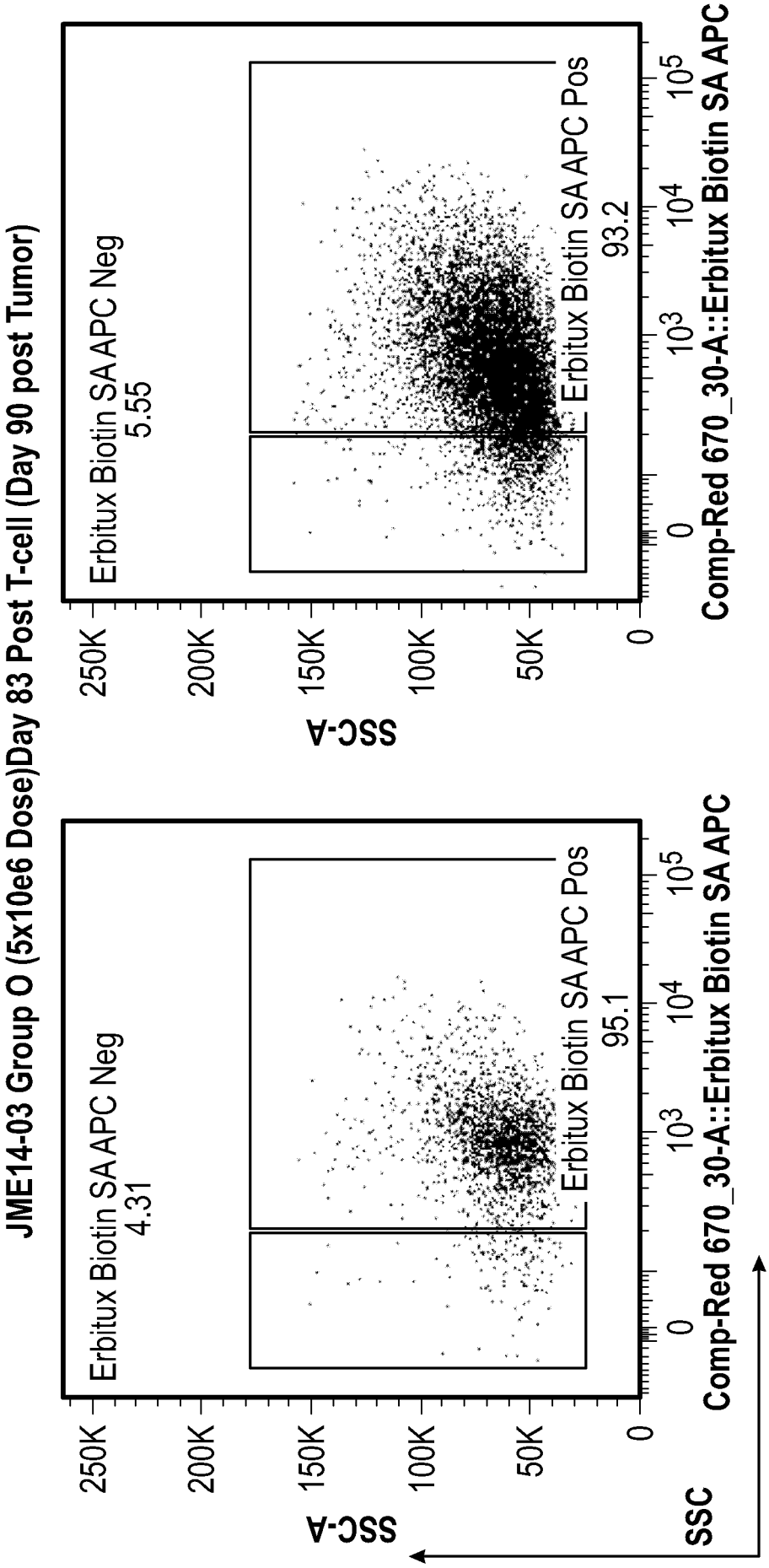


FIG. 58C5

FIG. 58C6

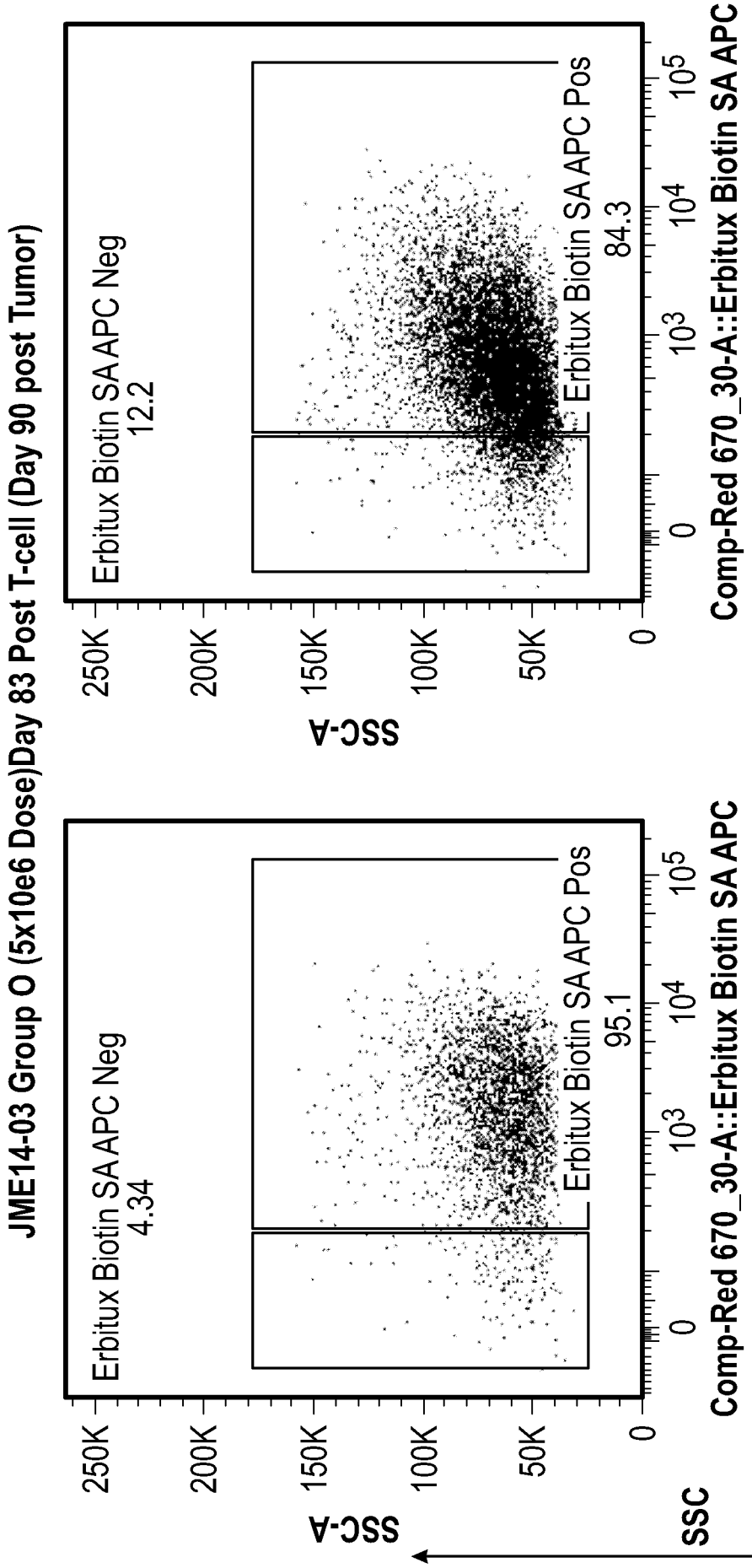


FIG. 58C7

FIG. 58C8

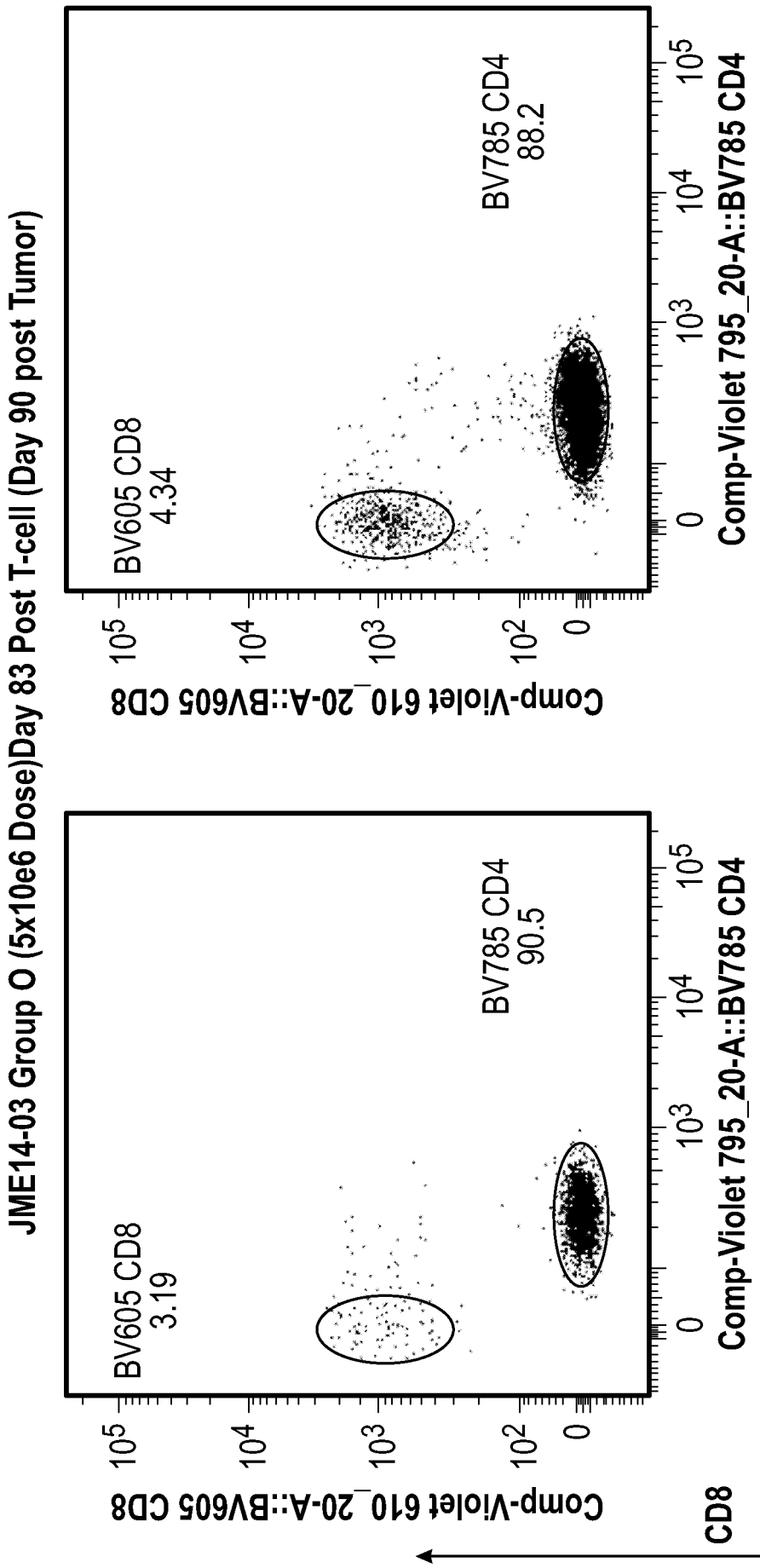
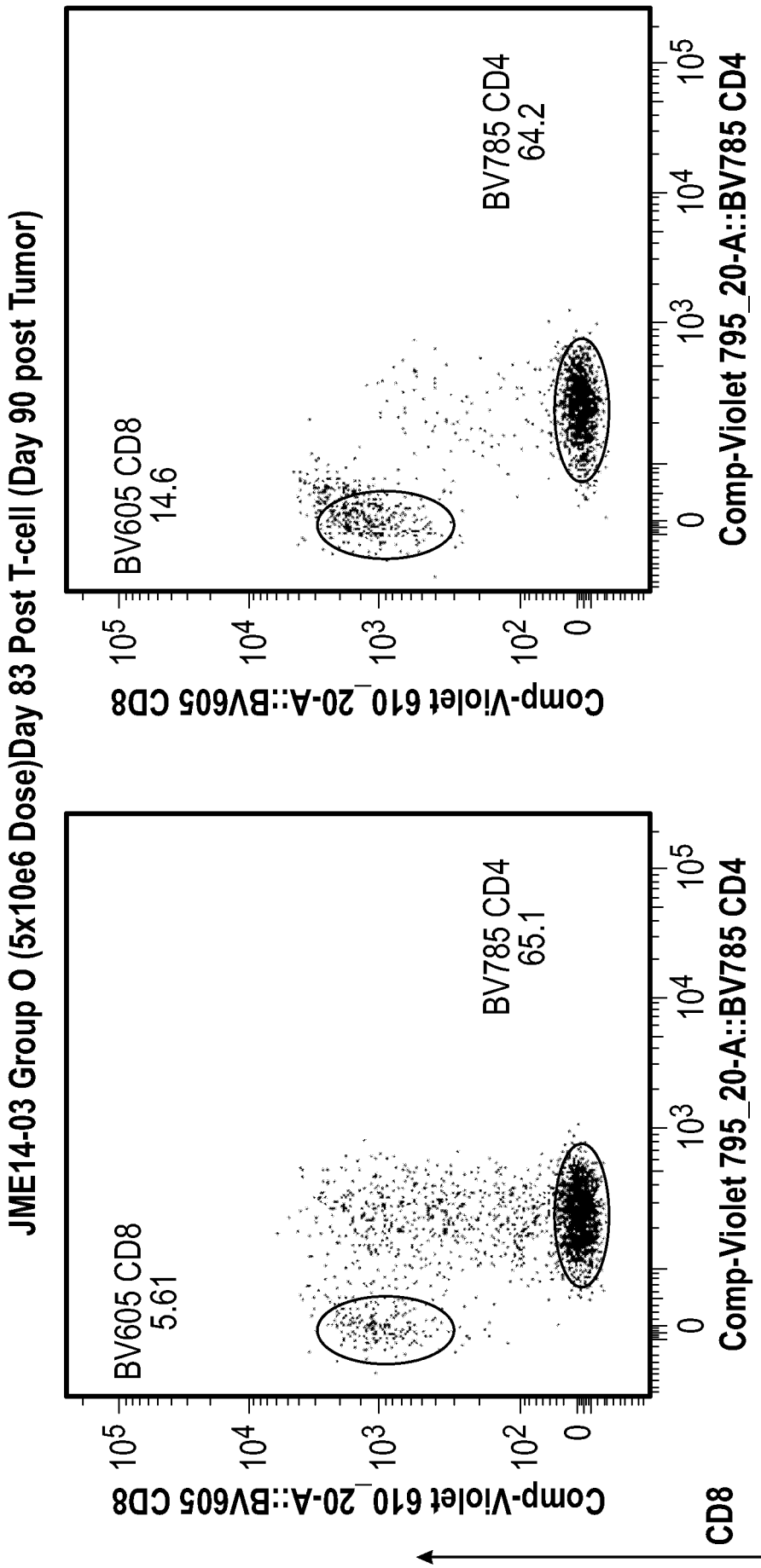


FIG. 58C9

FIG. 58C10



iLabber ELN #EXP-14-CW6241

FIG. 58C11

FIG. 58C12

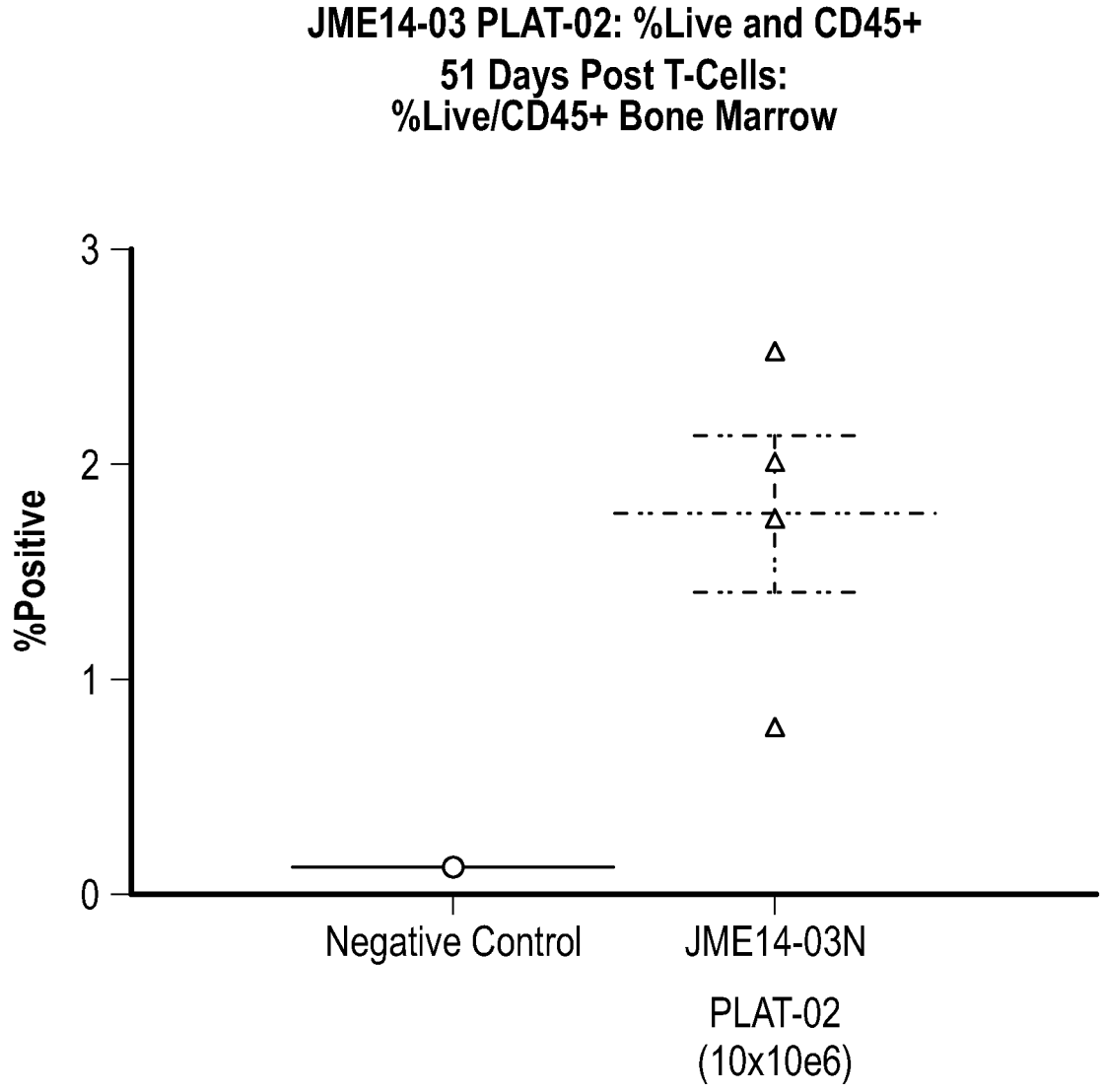

JME14-03 PLAT-02: %Live and CD45+
51 Days Post T-Cells:
%Live/CD45+ Bone Marrow
%Positive
3
2
1
0
Negative Control
JME14-03N
PLAT-02
(10x10e6)

FIG. 59A

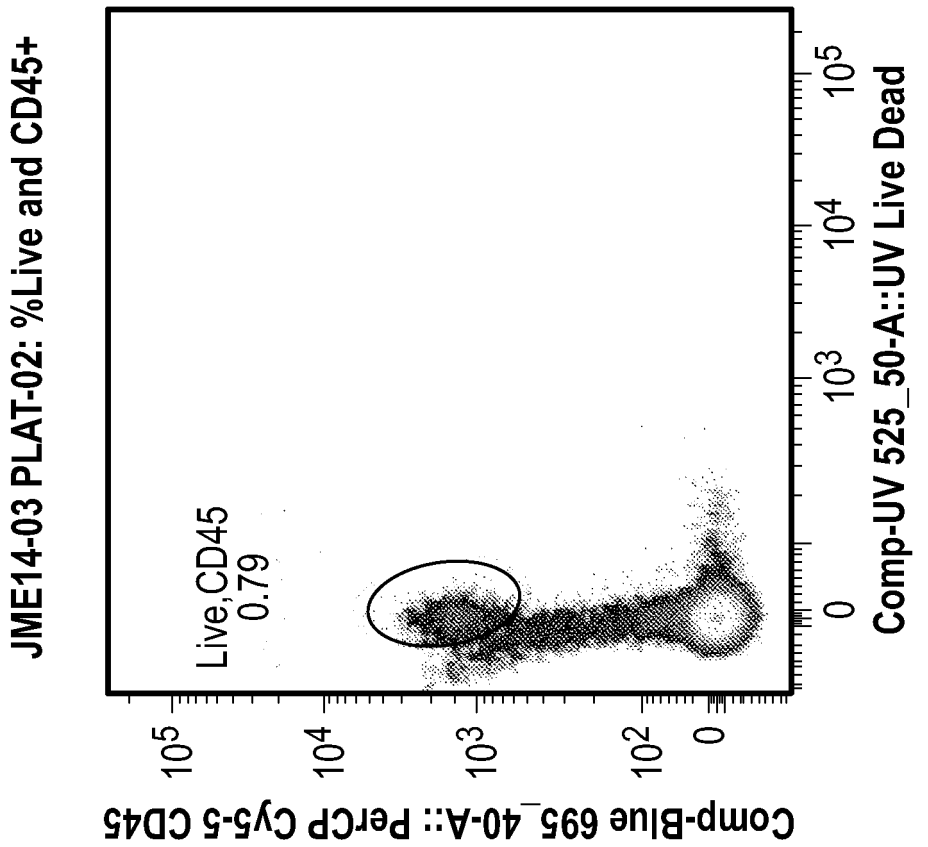


FIG. 59B2

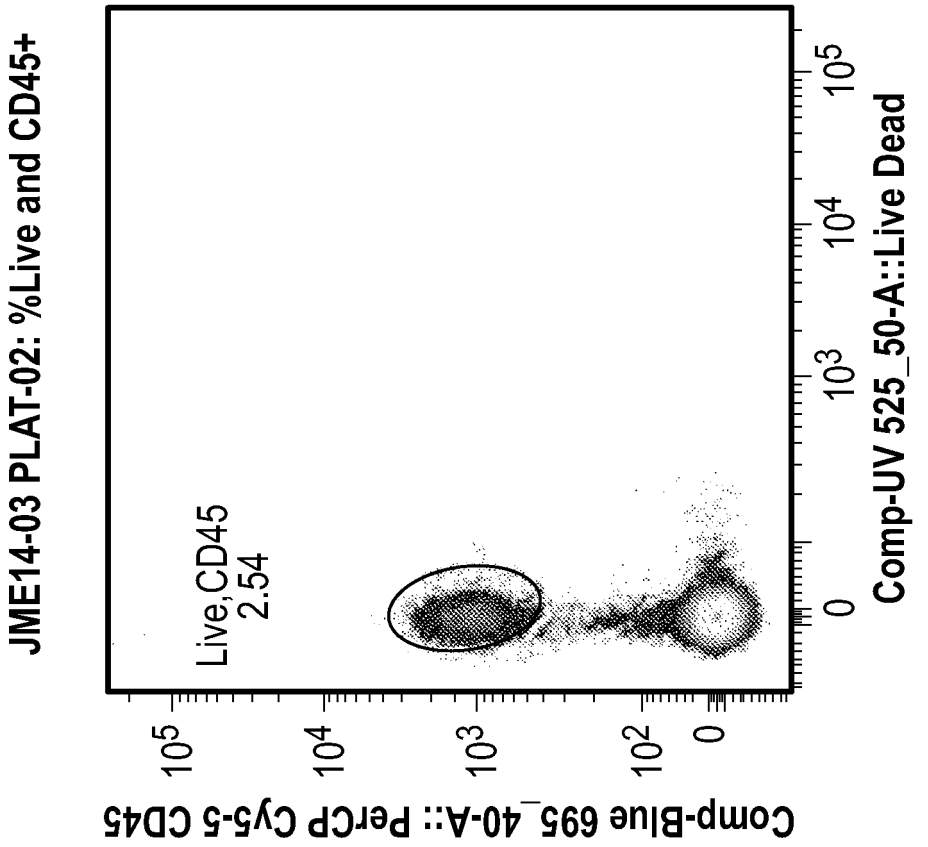


FIG. 59B1

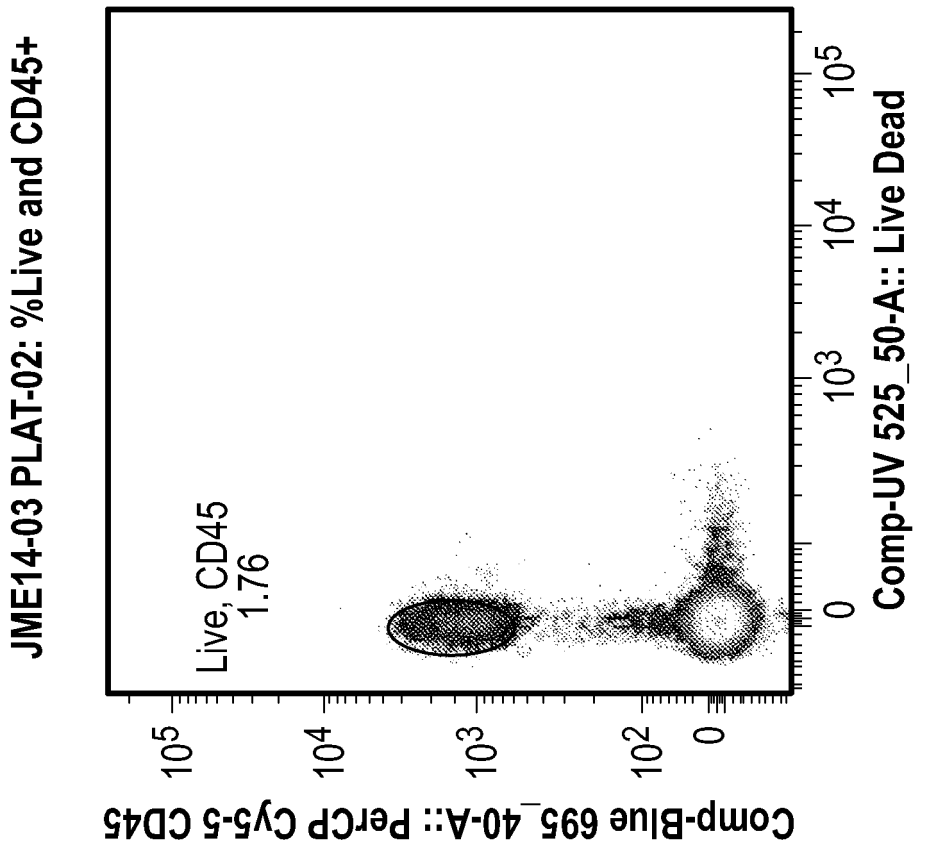


FIG. 59B4

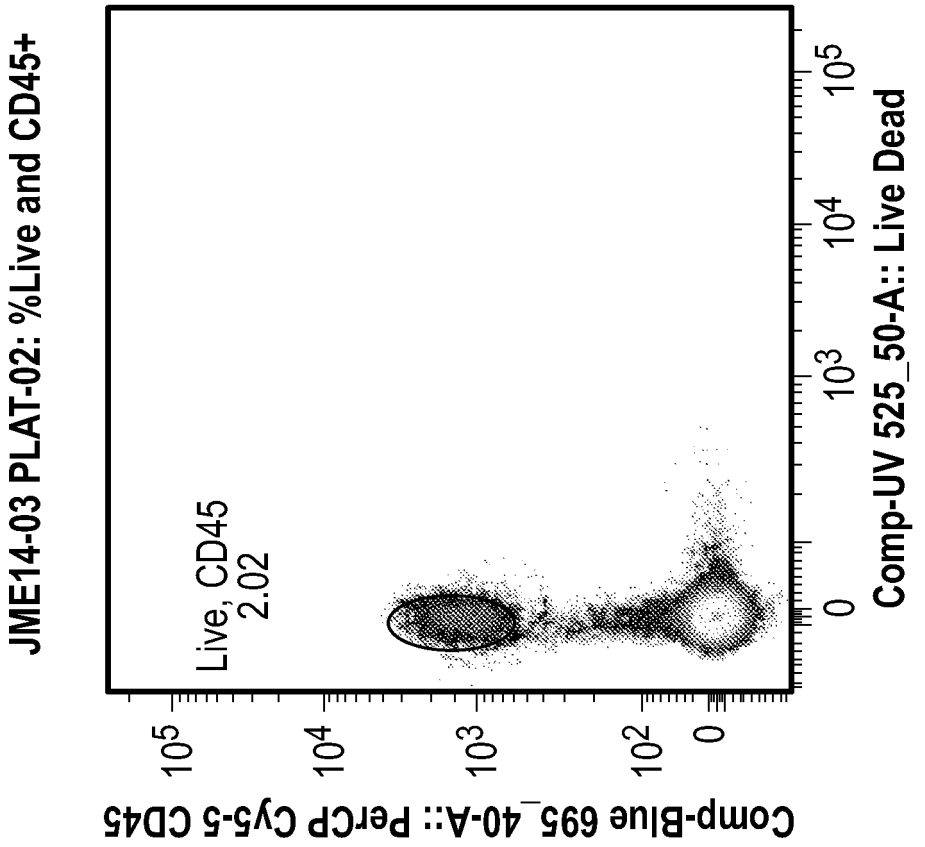


FIG. 59B3

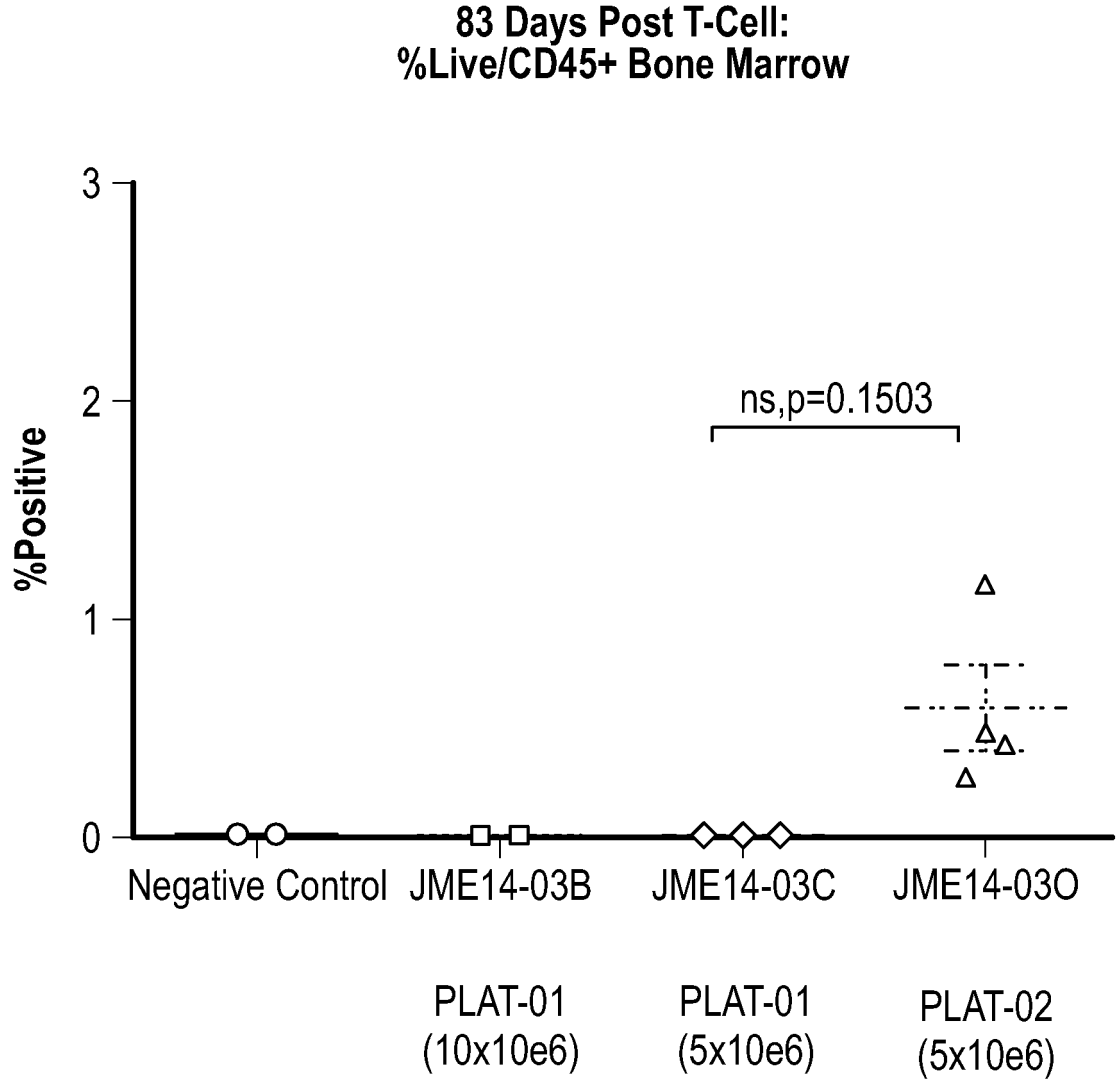

83 Days Post T-Cell:
%Live/CD45+ Bone Marrow
%Positive
3
2
1
0
ns,p=0.1503
Negative Control
JME14-03B
JME14-03C
JME14-03O
PLAT-01
(10x10e6)
PLAT-01
(5x10e6)
PLAT-02
(5x10e6)

FIG. 59C

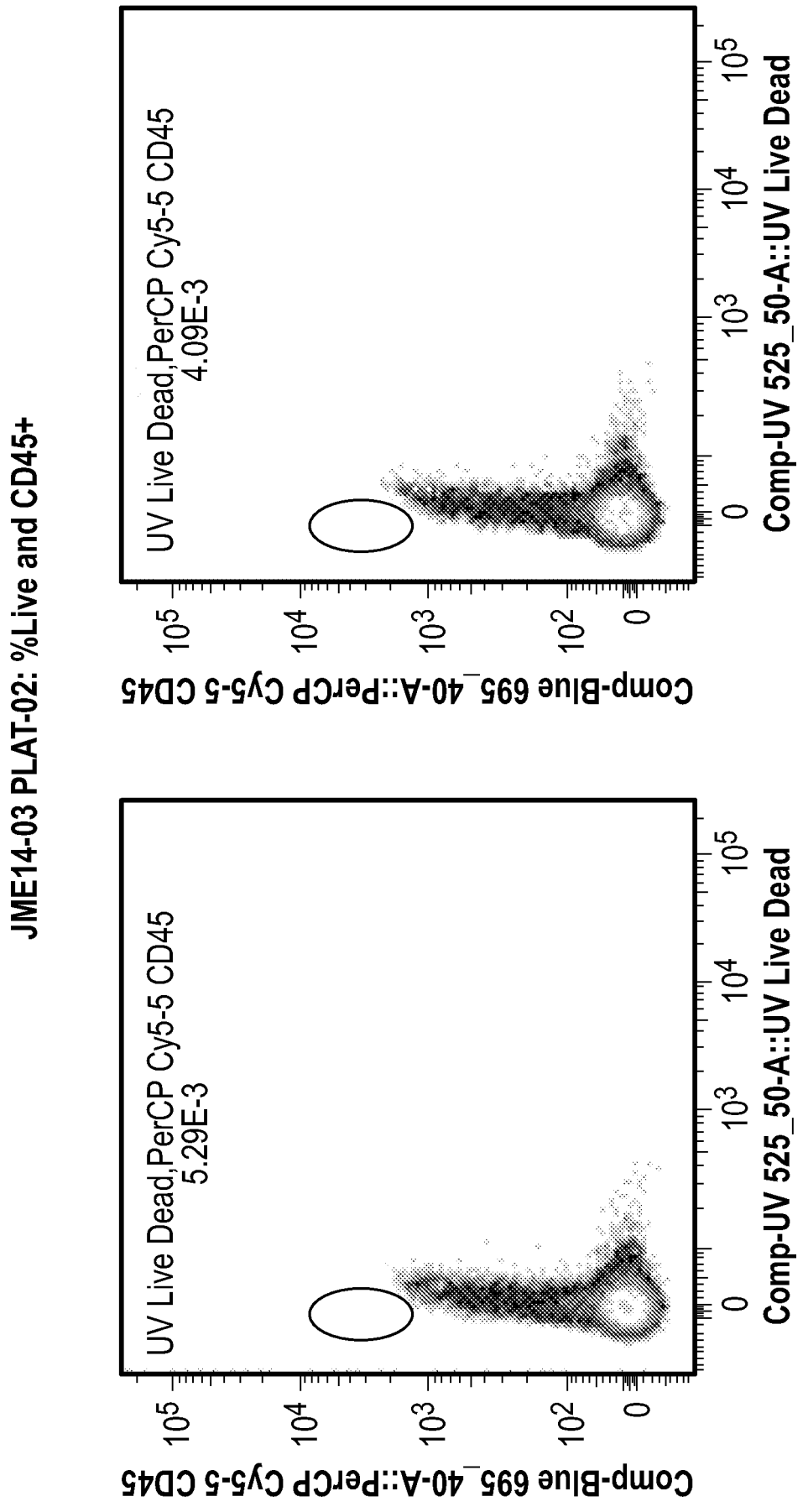


FIG. 59D1

FIG. 59D2

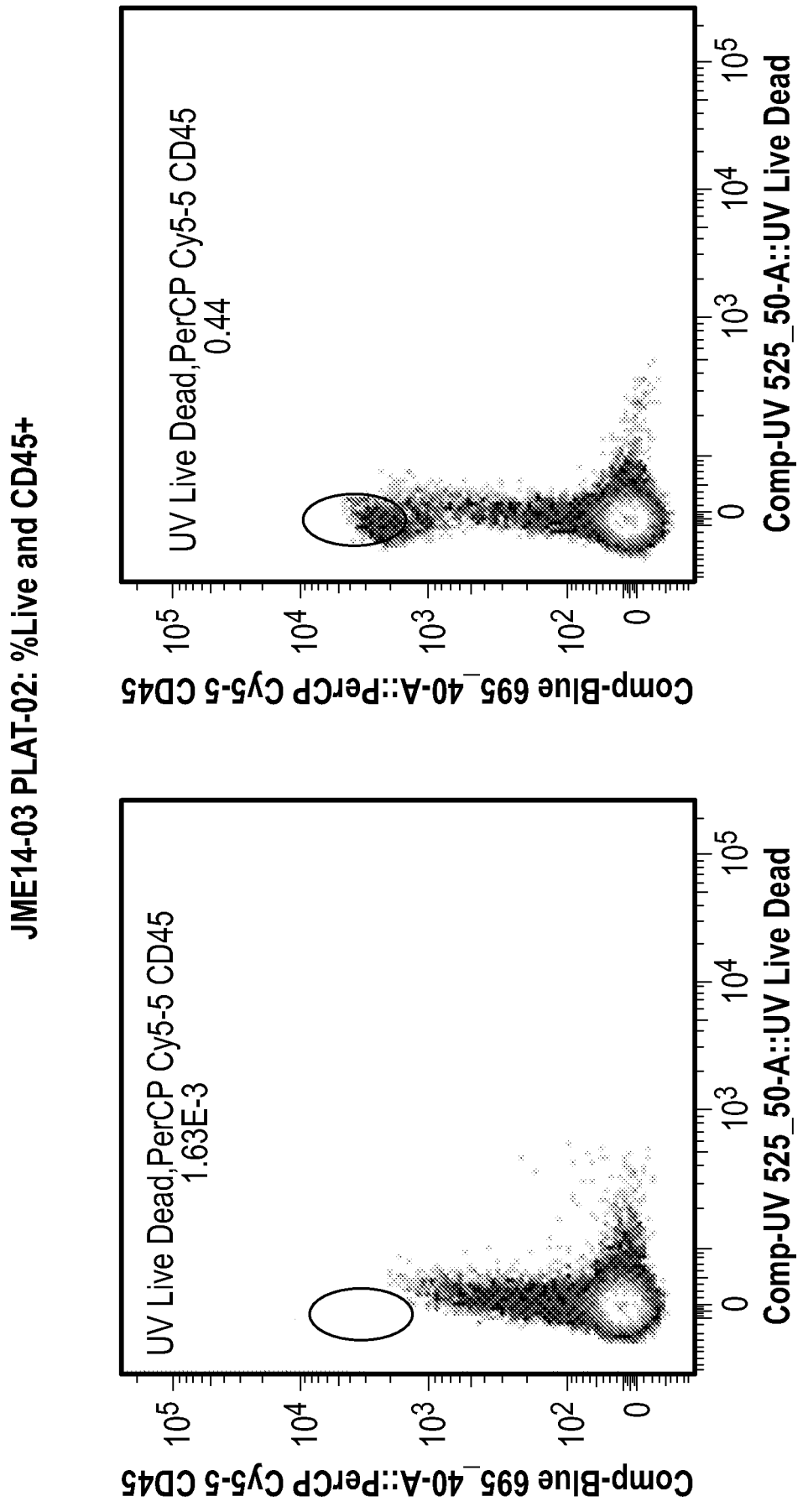


FIG. 59D3

FIG. 59D4

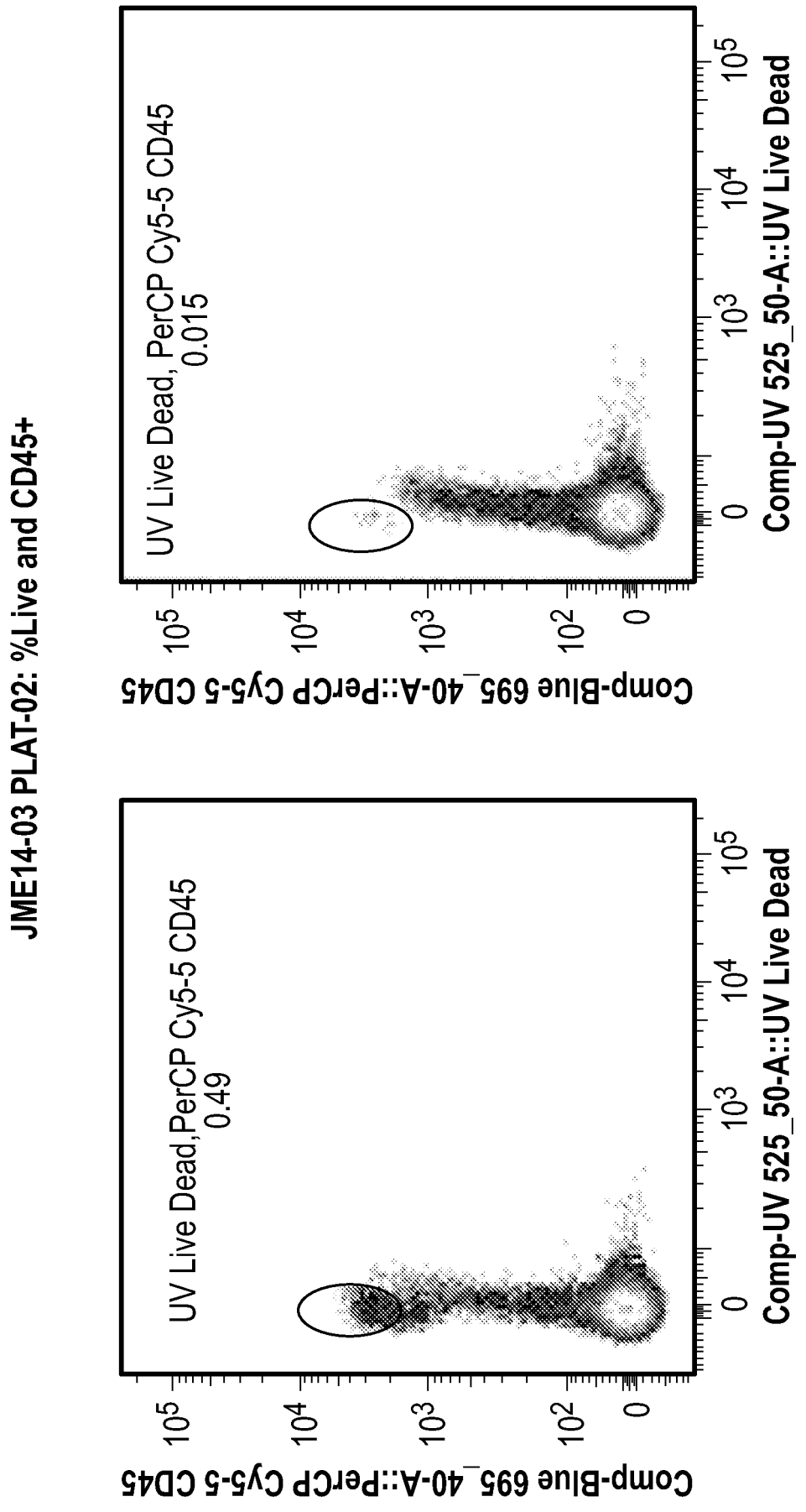


FIG. 59D5

FIG. 59D6

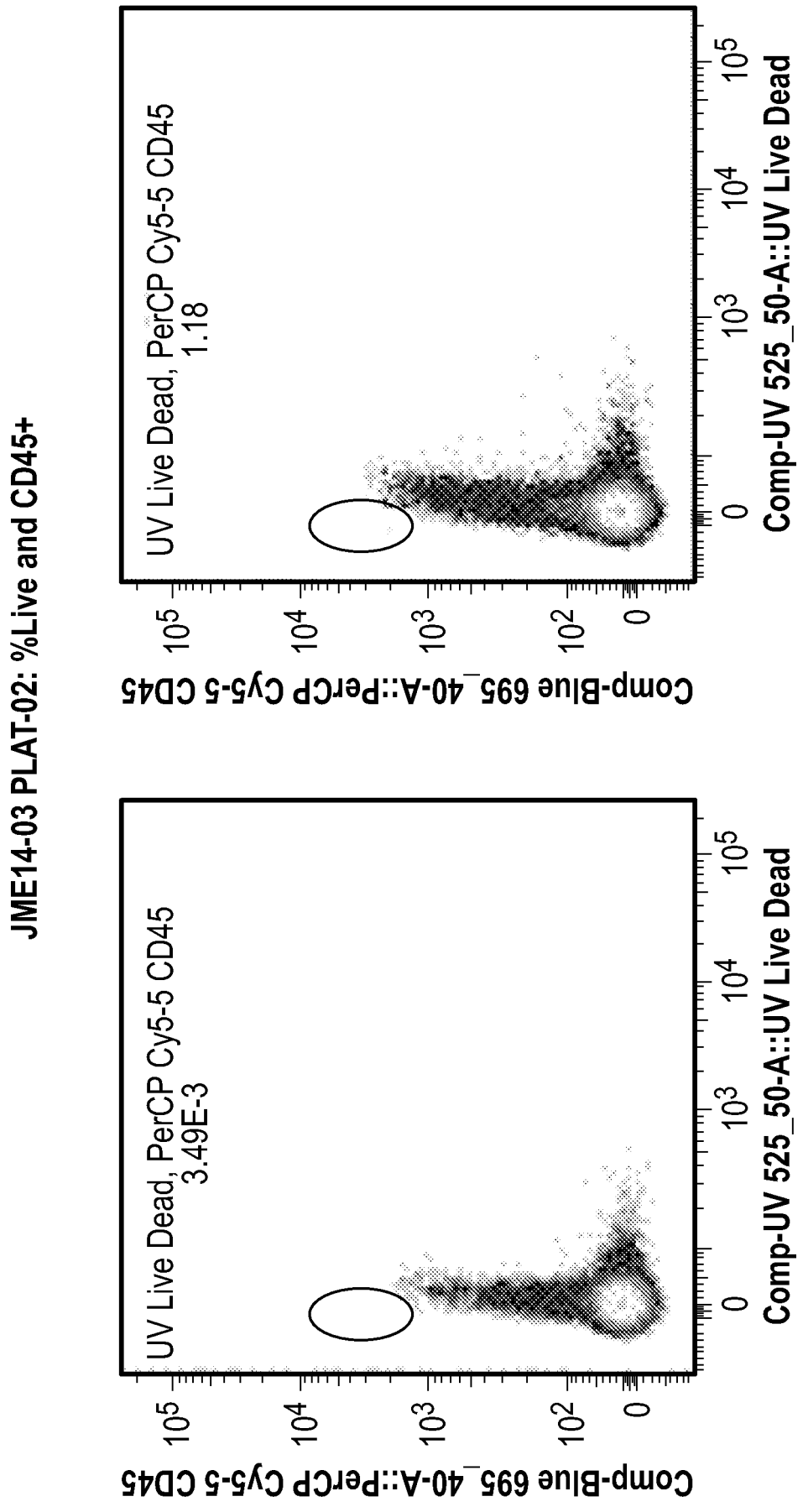


FIG. 59D7

FIG. 59D8

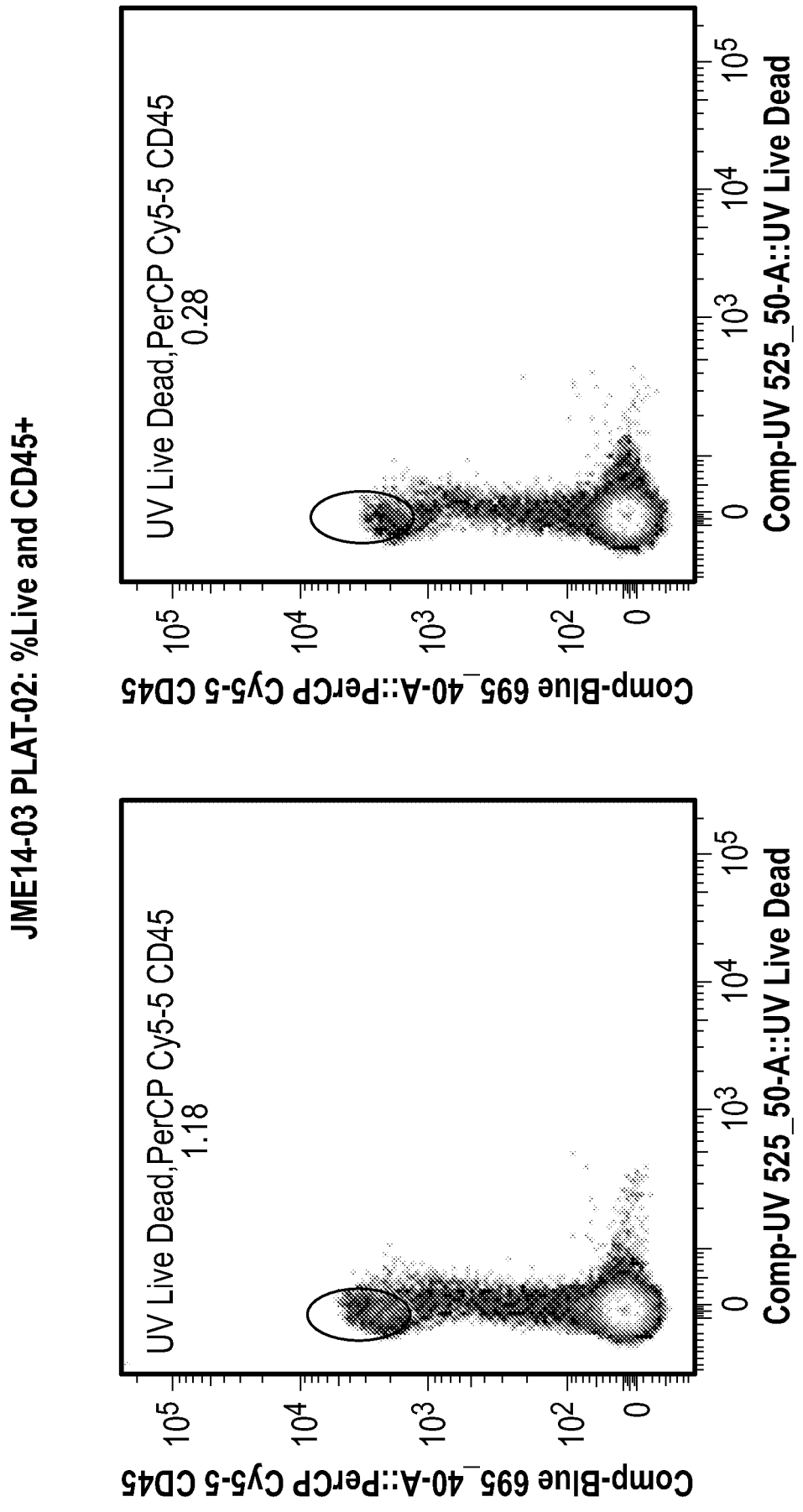


FIG. 59D9

FIG. 59D10

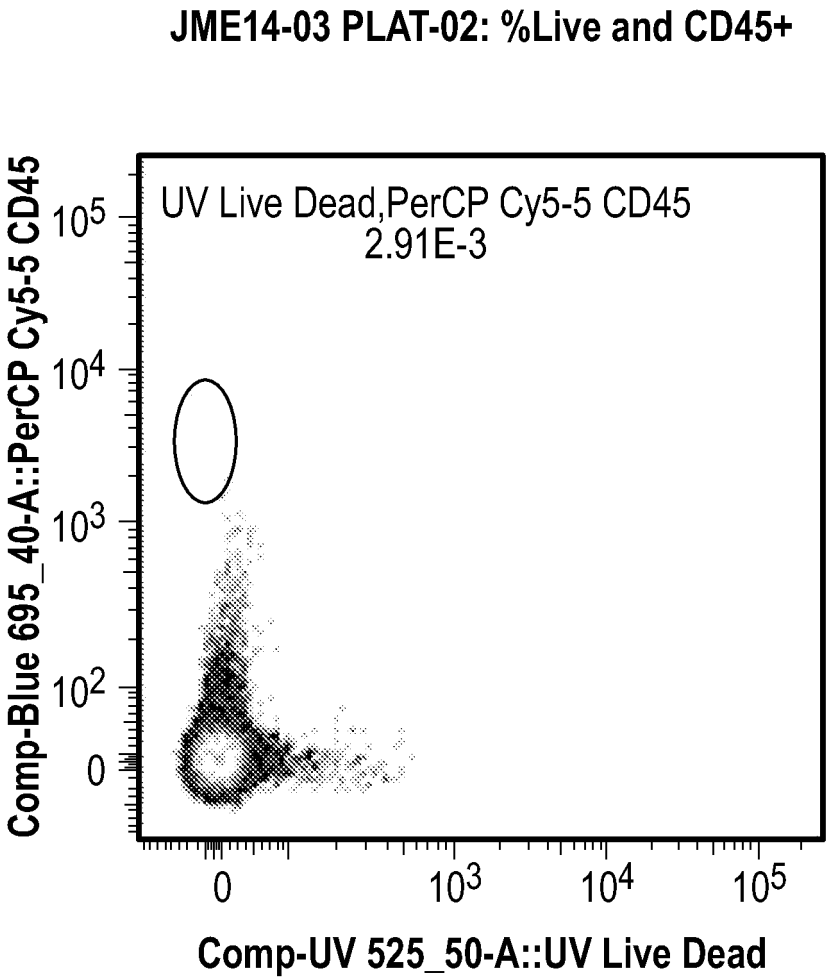

JME14-03 PLAT-02: %Live and CD45+
UV Live Dead,PerCP Cy5-5 CD45
2.91E-3
Comp-Blue 695_40-A::PerCP Cy5-5 CD45
10^5
10^4
10^3
10^2
0
0
10^3
10^4
10^5
Comp-UV 525_50-A::UV Live Dead

FIG. 59D11

JME14-03 PLAT-02, 5 Million T-Cell Dose Group:%EGFRt+ of Live, CD45+
51 Days Post T-Cells:
%EGFRt of CD45+ Bone Marrow

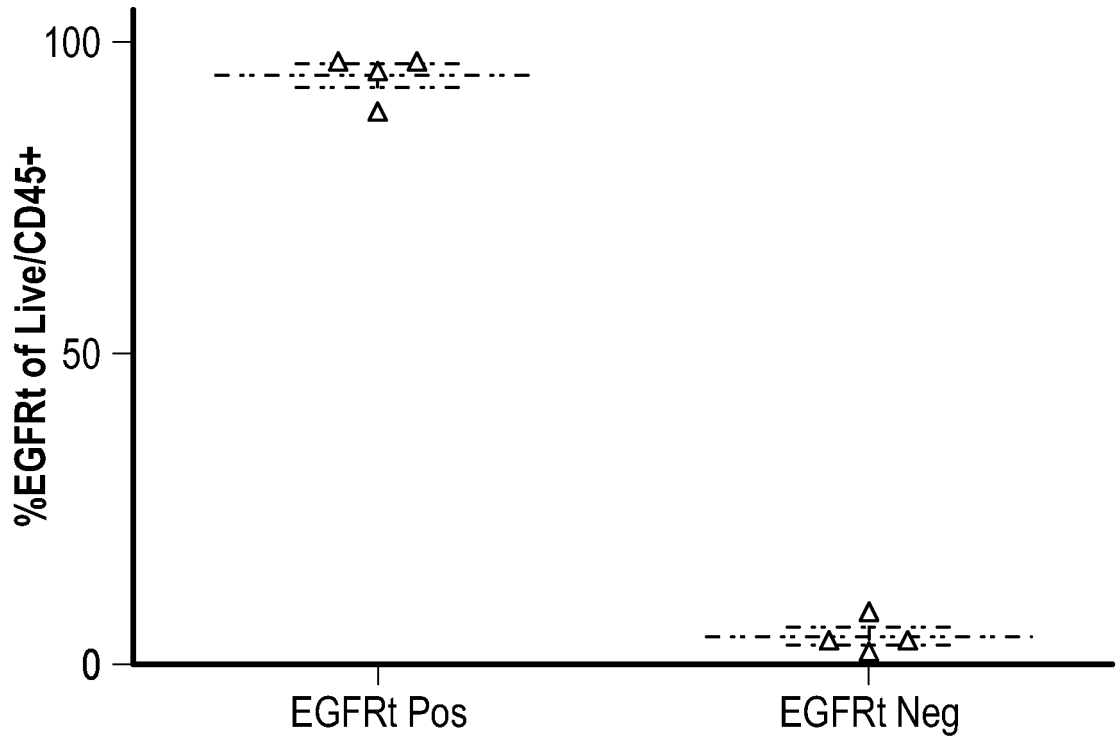


FIG. 59E

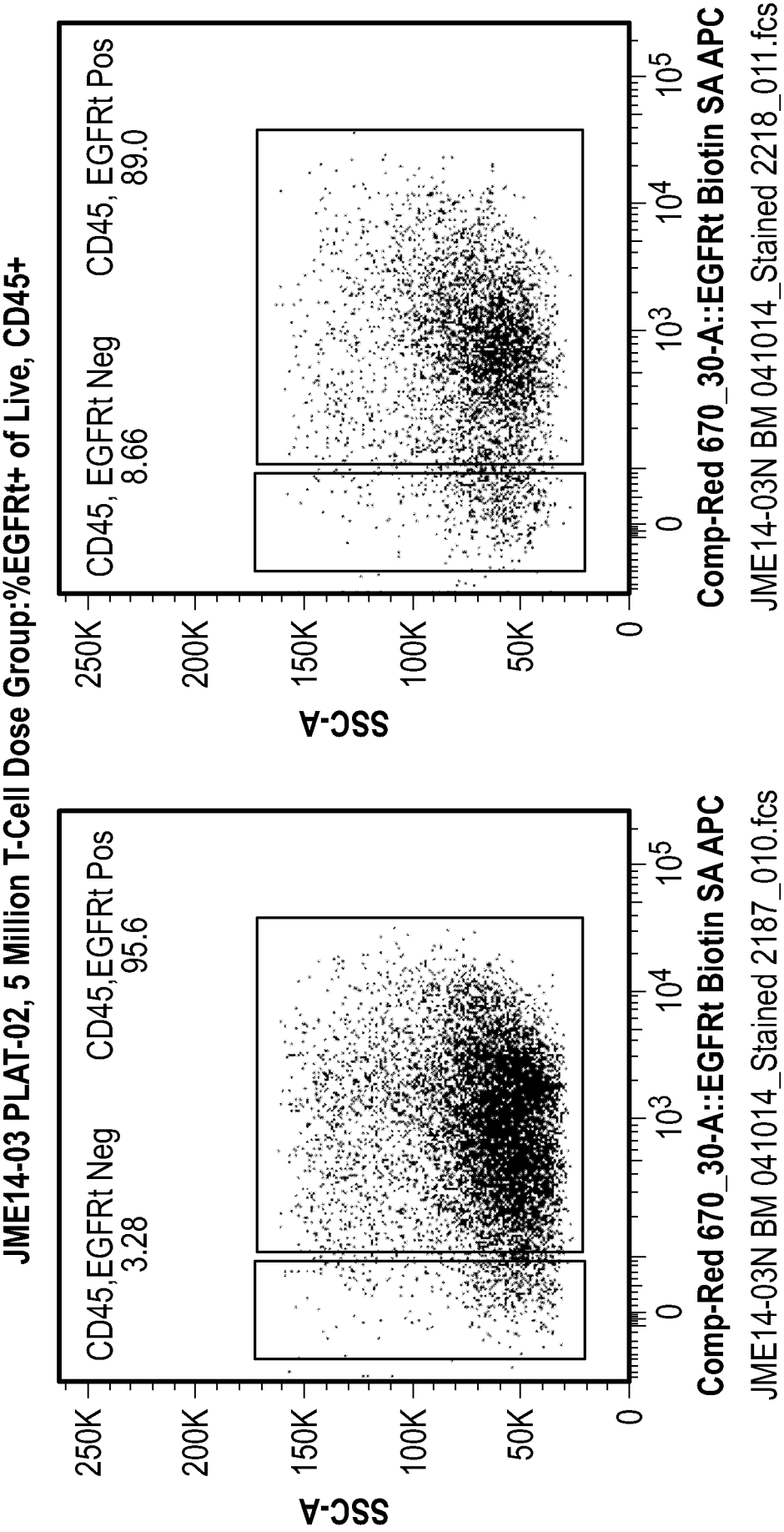


FIG. 59F1

FIG. 59F2

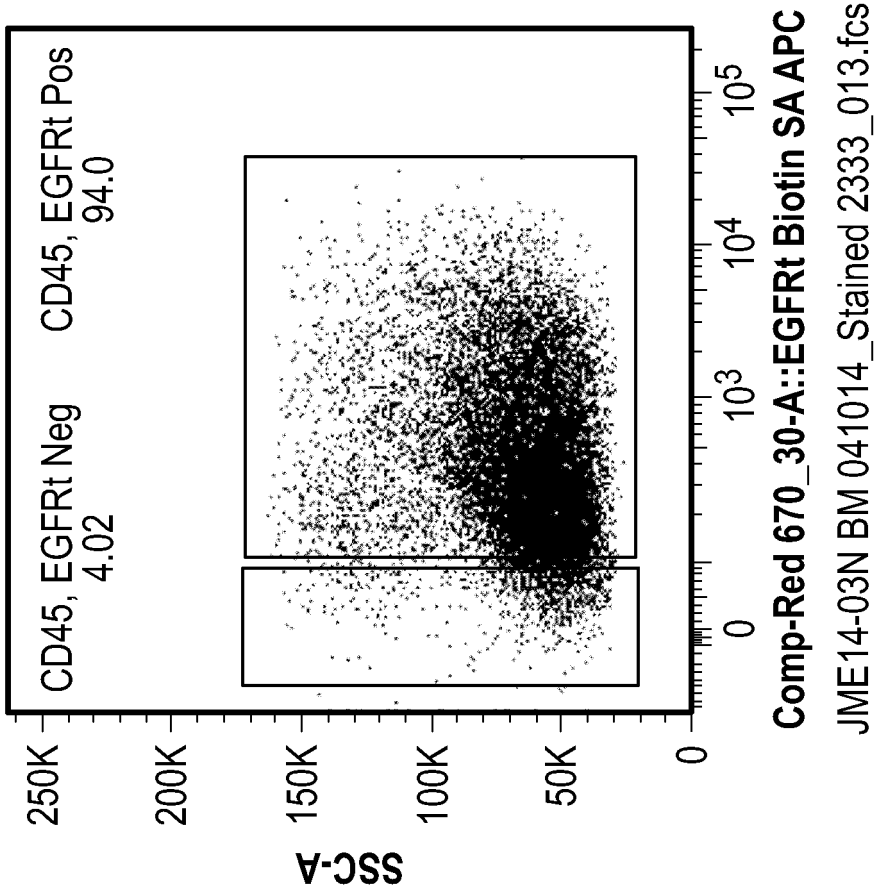


FIG. 59F4

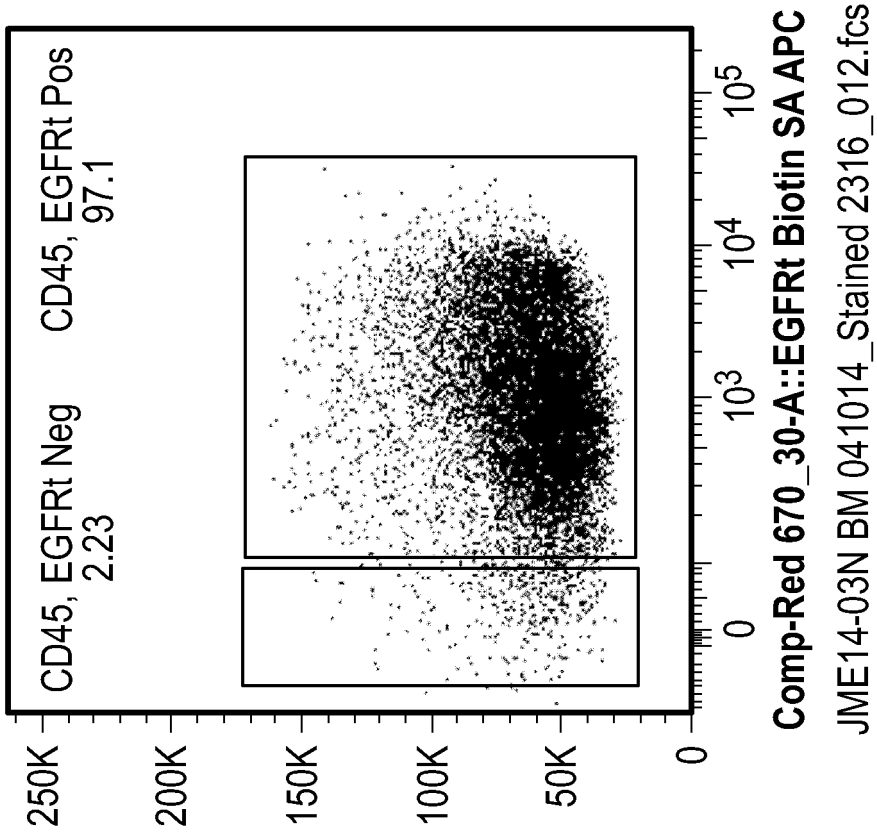


FIG. 59F3

JME14-03 PLAT-02, 5 Million T-Cell Dose Group:%EGFRt+ of Live, CD45+
83 Days Post T-Cells:
%EGFRt of CD45+ Bone Marrow

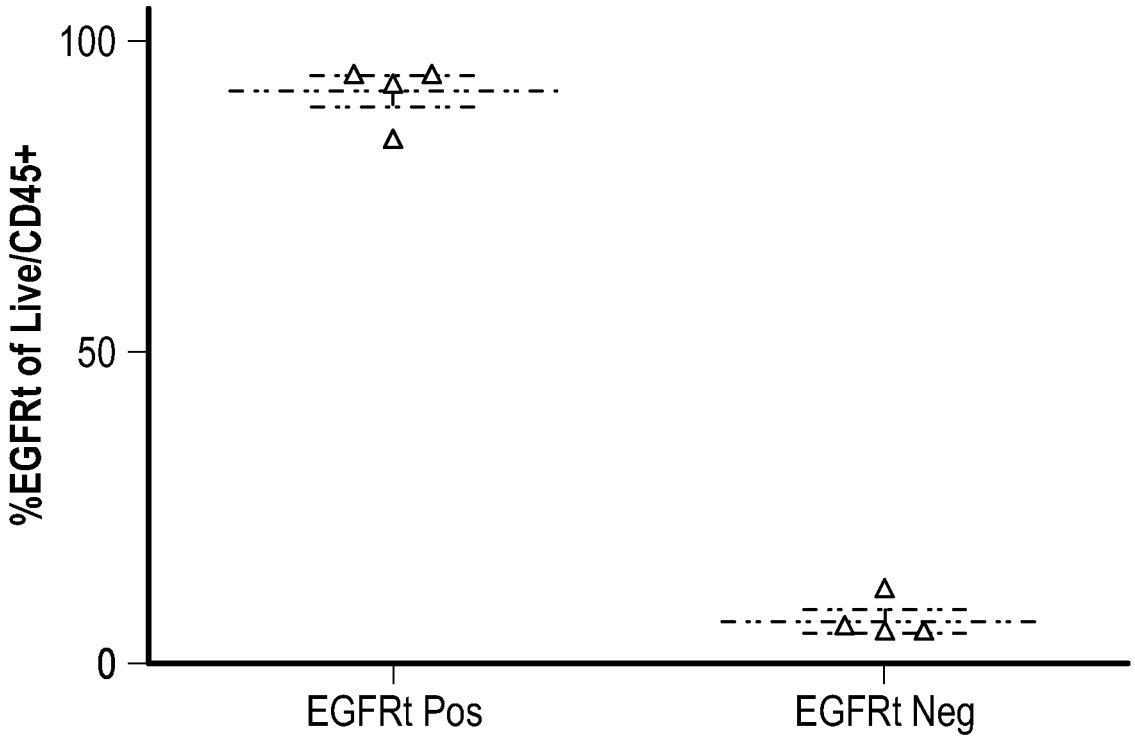


FIG. 59G

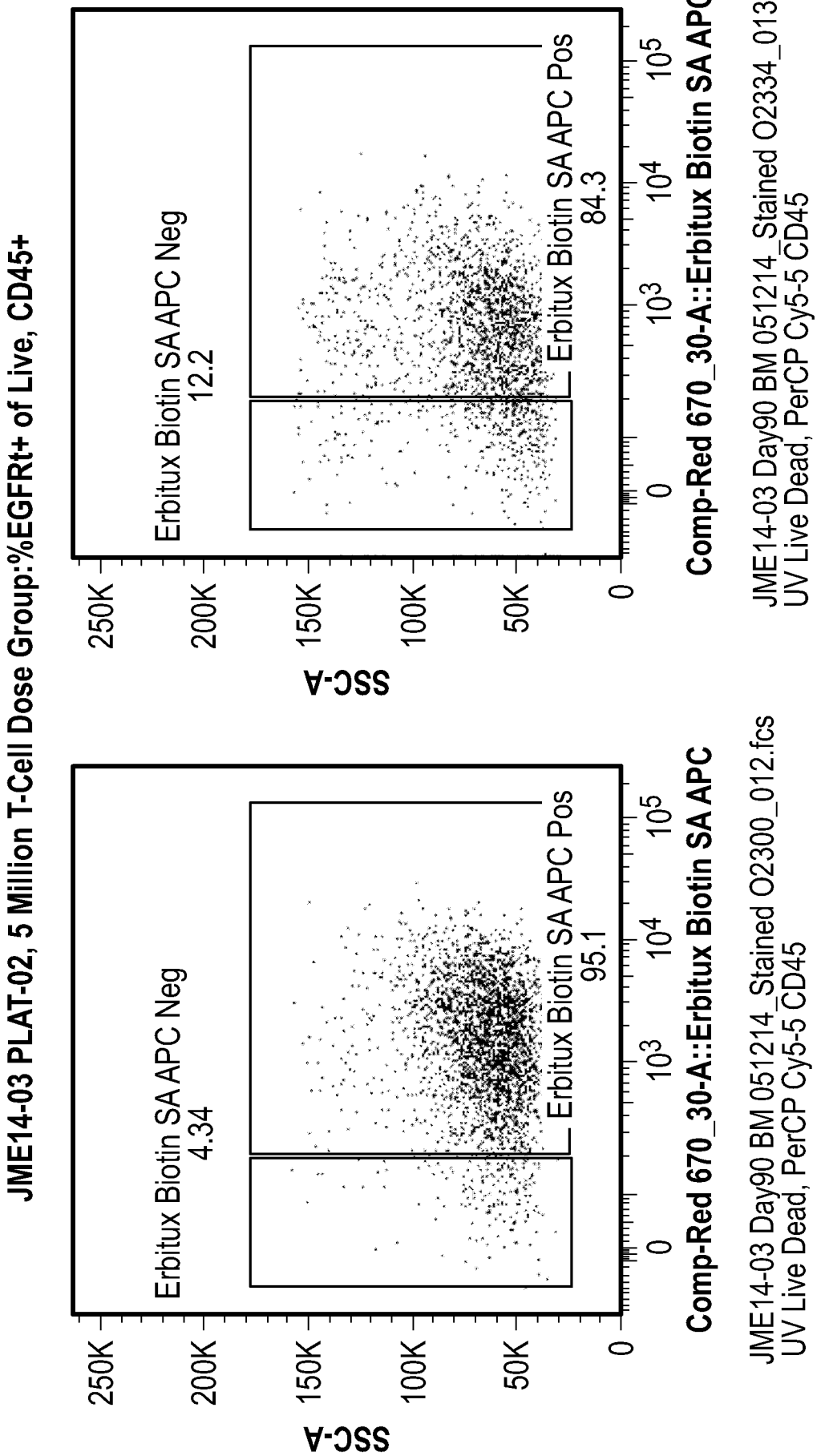


FIG. 59H1

FIG. 59H2

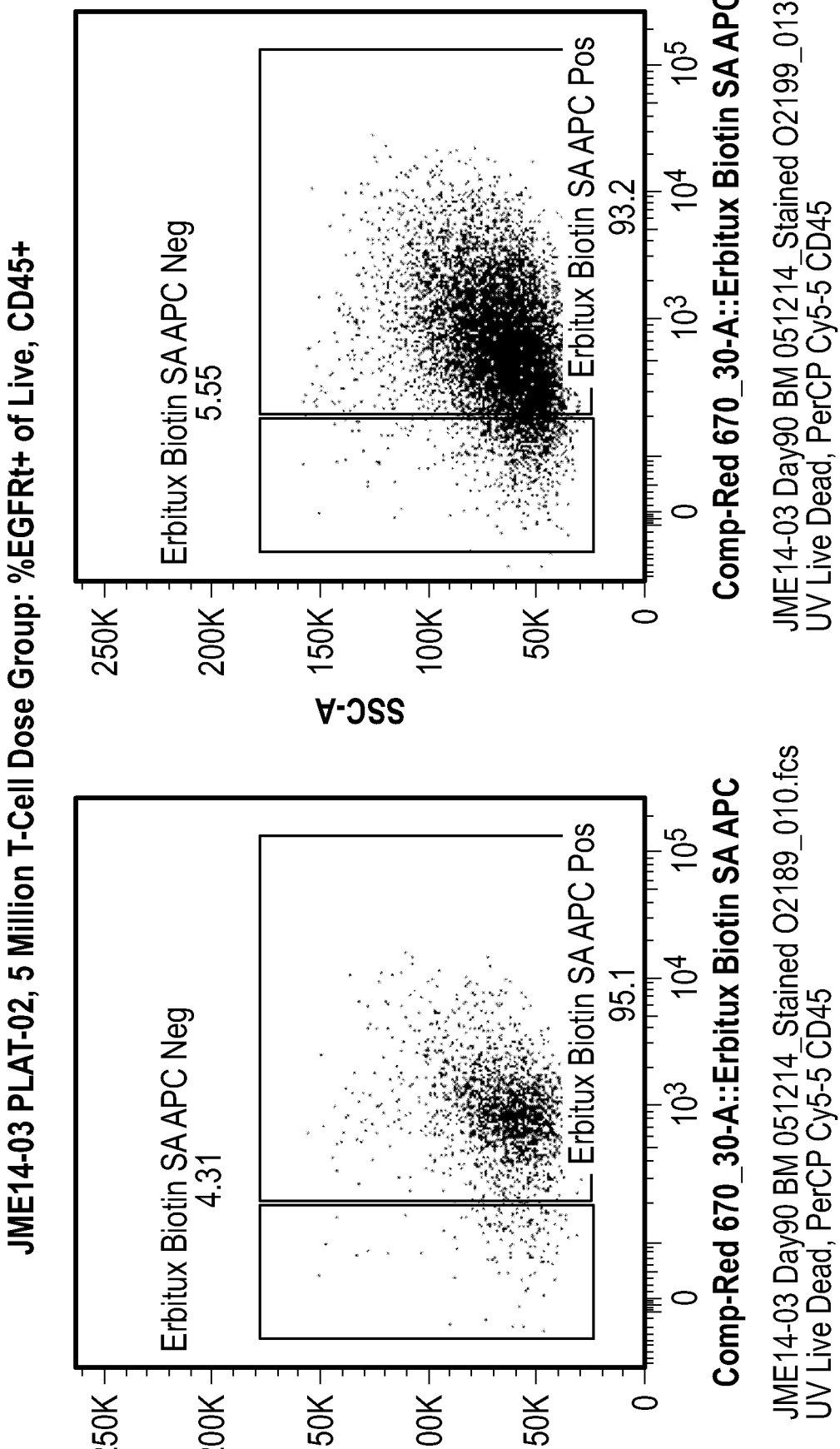


FIG. 59H3

FIG. 59H4

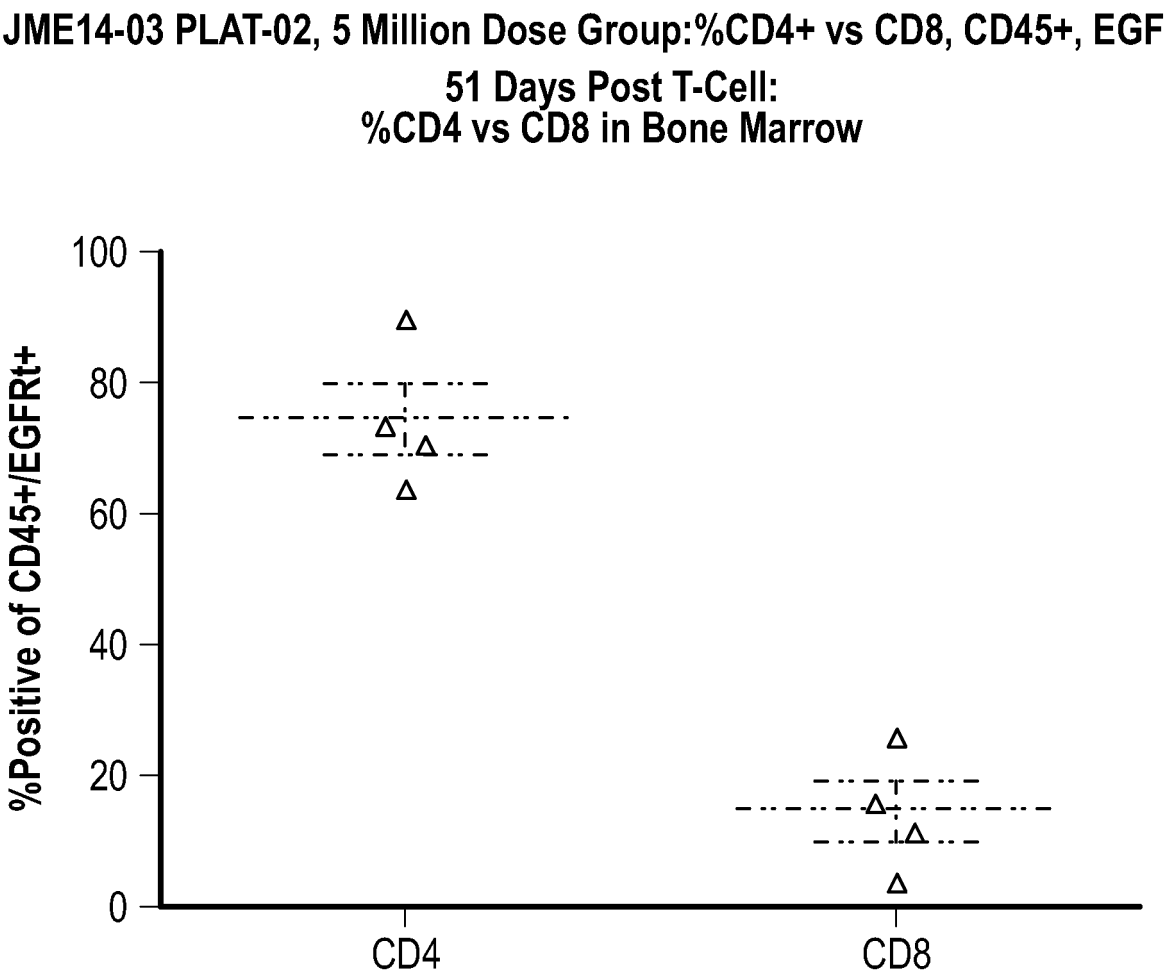

JME14-03 PLAT-02, 5 Million Dose Group:%CD4+ vs CD8, CD45+, EGFRt+
51 Days Post T-Cell:
%CD4 vs CD8 in Bone Marrow
%Positive of CD45+/EGFRt+
100
80
60
40
20
0
CD4
CD8

FIG. 60A

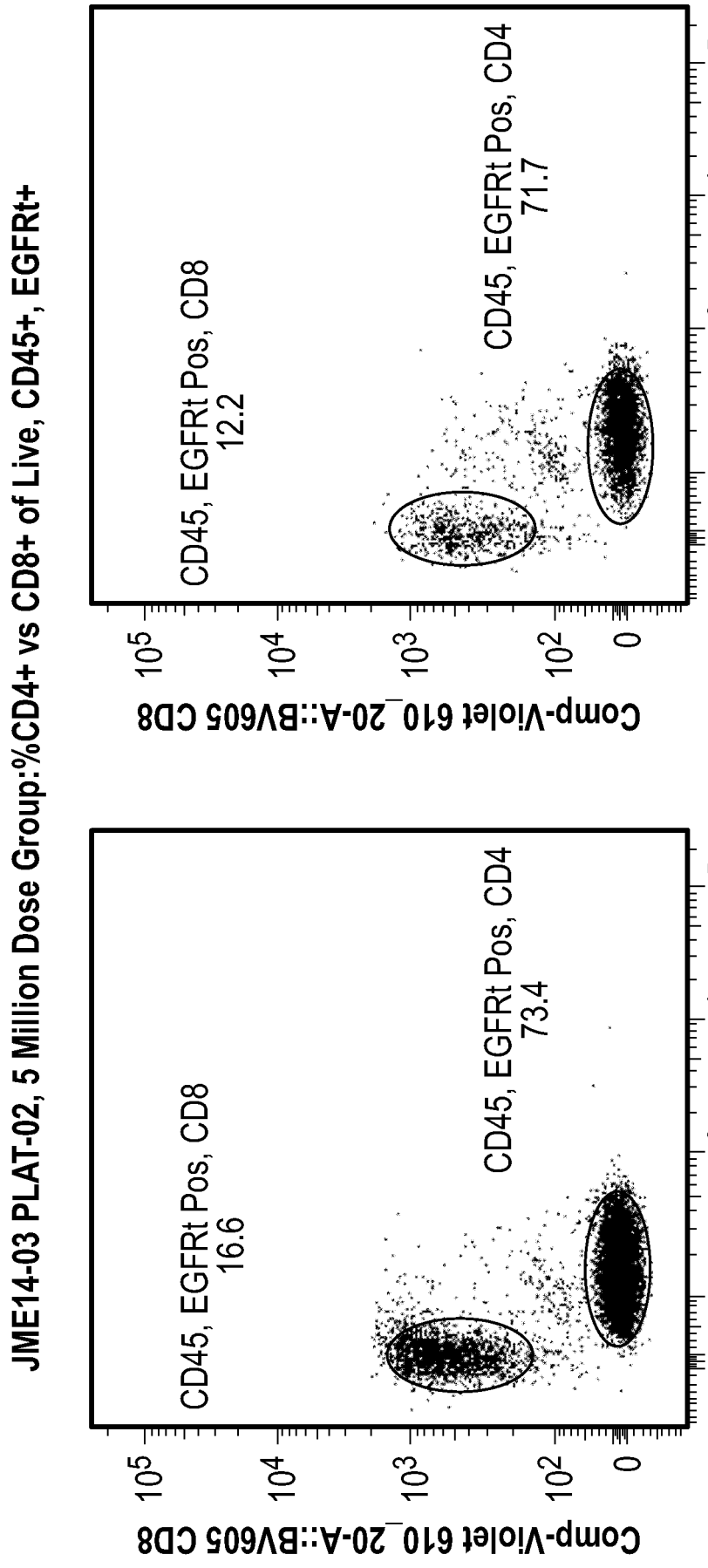


FIG. 60B1

FIG. 60B2

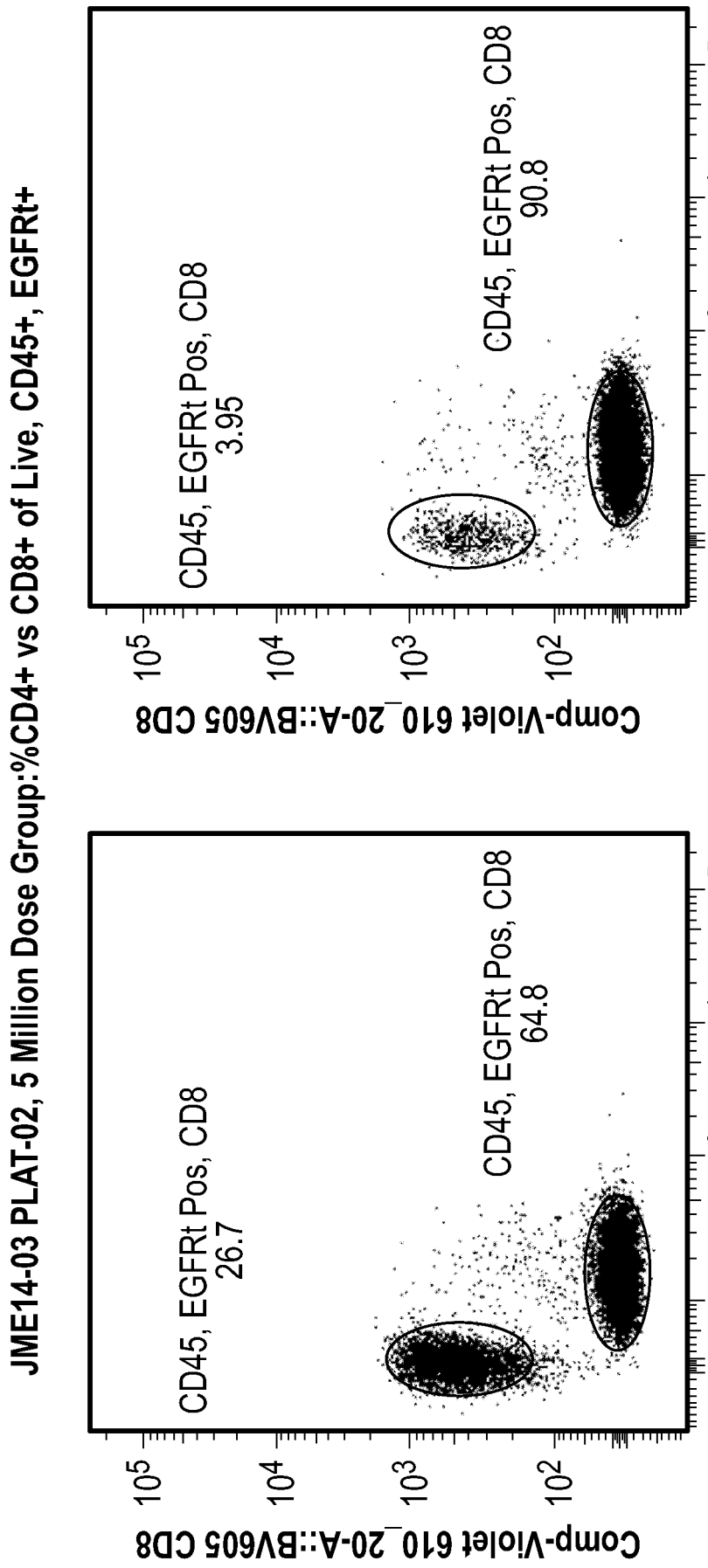


FIG. 60B3

FIG. 60B4

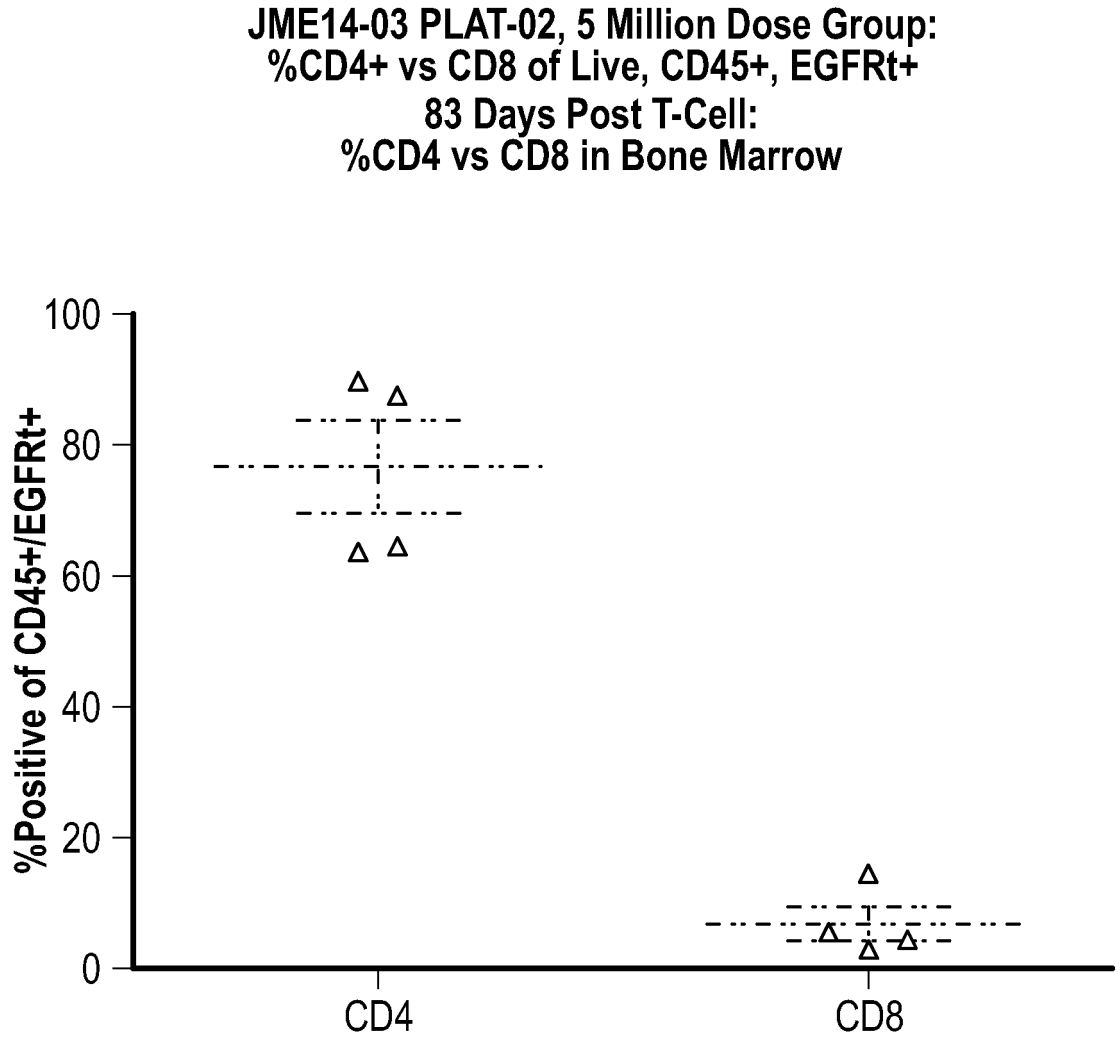

JME14-03 PLAT-02, 5 Million Dose Group:
%CD4+ vs CD8 of Live, CD45+, EGFRt+
83 Days Post T-Cell:
%CD4 vs CD8 in Bone Marrow
%Positive of CD45+/EGFRt+
100
80
60
40
20
0
CD4
CD8

FIG. 60C

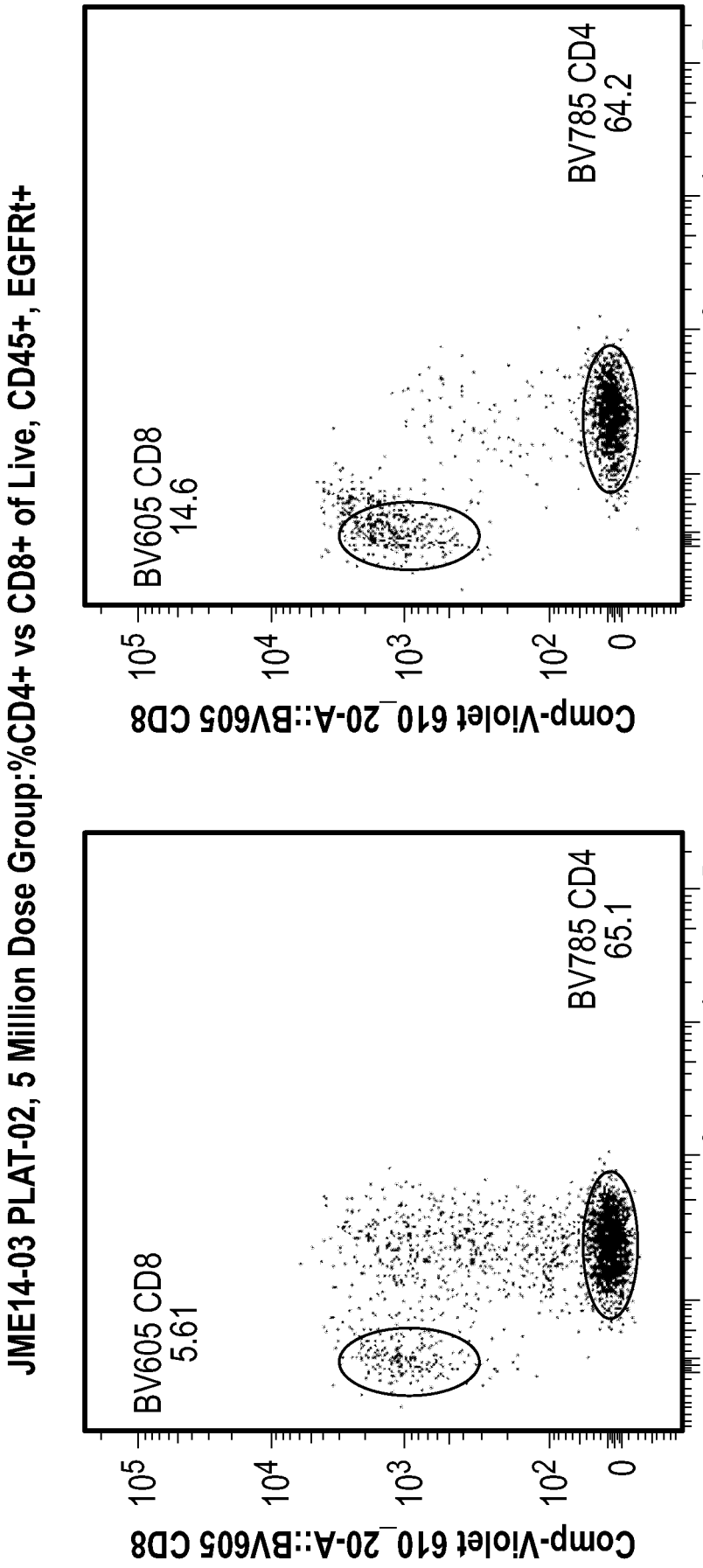


FIG. 60D1

FIG. 60D2

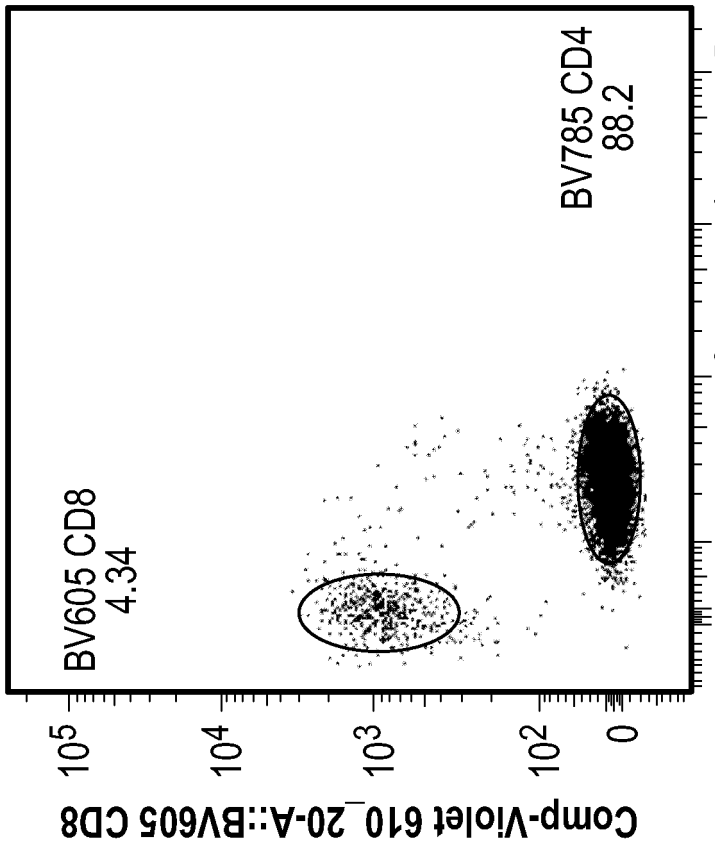


FIG. 60D4

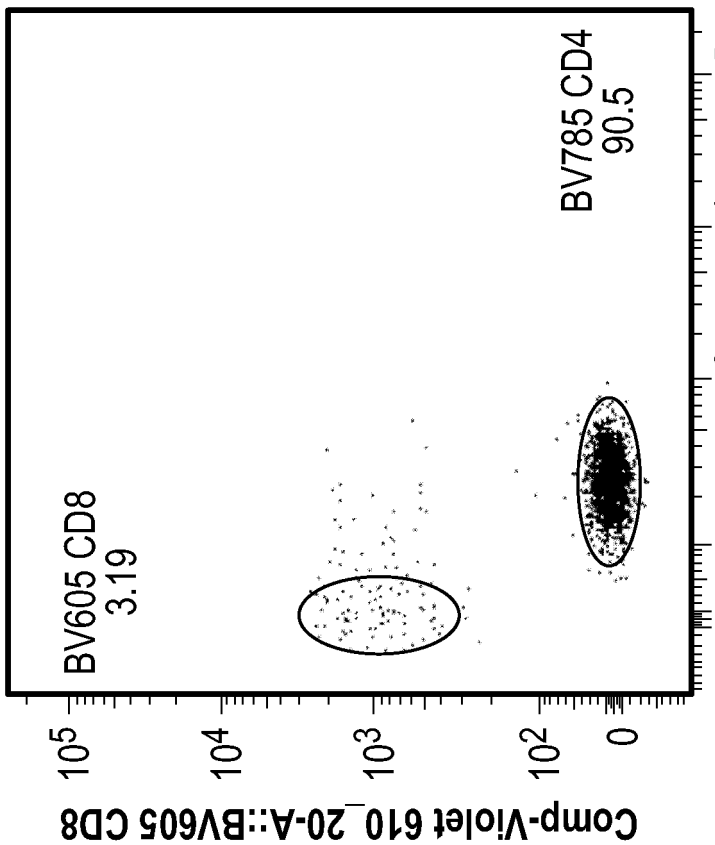


FIG. 60D3

JME14-03 Group N, Day 51 post T-cell

Sample	Lymphocytes	Live, CD45+	EGFRt+	CD4+	CD8+
PLAT-02 (10x10e6)	4.91e5 (87.2%)	9937 (2.02%)	9498 (95.6%)	6976 (73.4%)	1576 (16.6%)
PLAT-02 (10x10e6)	5.83e5 (84.2%)	4631 (0.79%)	4121 (89.0%)	3443 (71.7%)	504 (12.2%)
PLAT-02 (10x10e6)	7.07e5 (91.2%)	12376 (1.76%)	12116 (97.1%)	7851 (64.8%)	3234 (26.7%)
PLAT-02 (10x10e6)	5.96e5 (88.4%)	15132 (2.54%)	14217 (94.0%)	12907 (90.8%)	561 (3.95%)
Neg. Control	120212 (87.6%)	156 (0.13%)	145 (92.9%)	51 (35.2%)	45 (31.0%)

JME14-03 Day 90 post T-cell

Sample	Lymphocytes	Live, CD45+	EGFRt+	CD4+	CD8+
PLAT-02 (5x10e6)	7.91e5 (87.2%)	2206 (0.28%)	2099 (95.1%)	1899 (90.5%)	67 (3.19%)
PLAT-02 (5x10e6)	7.81e5 (86.9%)	9221 (1.18%)	8594 (93.2%)	7583 (88.2%)	373 (4.34%)
PLAT-02 (5x10e6)	76.65e5 (85.6%)	2904 (0.44%)	2761 (95.1%)	1798 (65.1%)	155 (5.61%)
PLAT-02 (5x10e6)	4.31e5 (81.5%)	2115 (0.49%)	1783 (84.3%)	1145 (64.2%)	260 (14.6%)
Neg. Control	7.51e5 (83.1%)	109 (0.015%)	79 (72.5%)	48 (60.8%)	8 (10.1%)
Neg. Control	5.29e5 (78.6%)	28 (5.29e-3%)	10 (28%)	0 (0%)	0 (0%)
PLAT-01 (10x10e6)	6.15e6 (80.3%)	27 (4.09e-3%)	19 (70.4%)	6 (31.6%)	1 (5.26%)
PLAT-01 (10x10e6)	6.44e6 (81.1%)	26 (4.04e-3%)	15 (57.7%)	8 (53.3%)	2 (13.3%)
PLAT-01 (5x10e6)	6.77e5 (80.9%)	11 (1.63e-3)	5 (45.5%)	1 (20.0%)	0 (0%)
PLAT-01 (5x10e6)	7.73e5 (80.3%)	27 (3.49e-3)	11 (40.7%)	3 (27.3%)	0 (0%)
PLAT-01 (5x10e6)	7.56e5 (84.5%)	22 (2.91e-3)	16 (72.7%)	5 (31.2%)	8 (50%)

FIG. 61