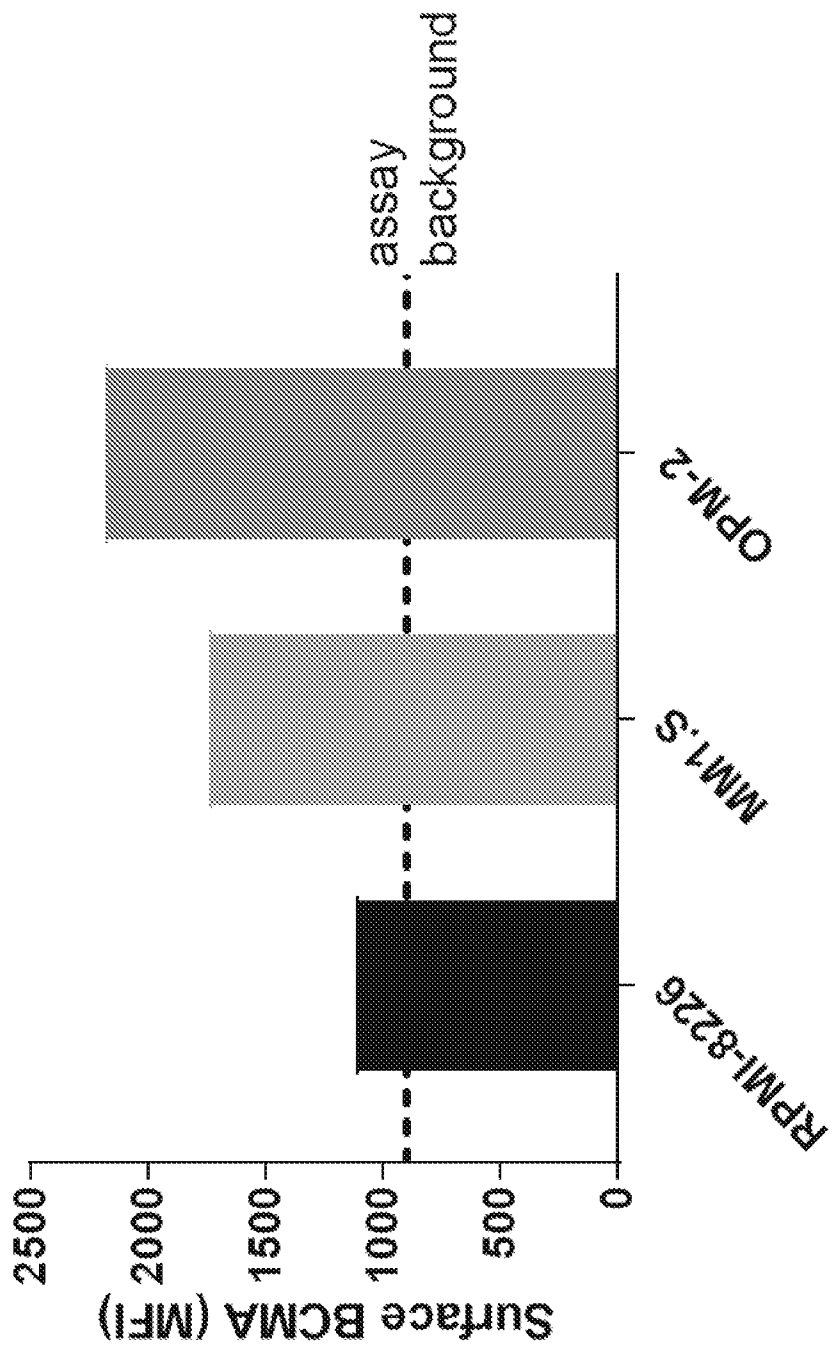

Surface BCMA (MFI)
2500
2000
1500
1000
500
0
assay
background
RPMI-8226
MM1.S
OPM-2

FIG. 1A

FIG. 1B

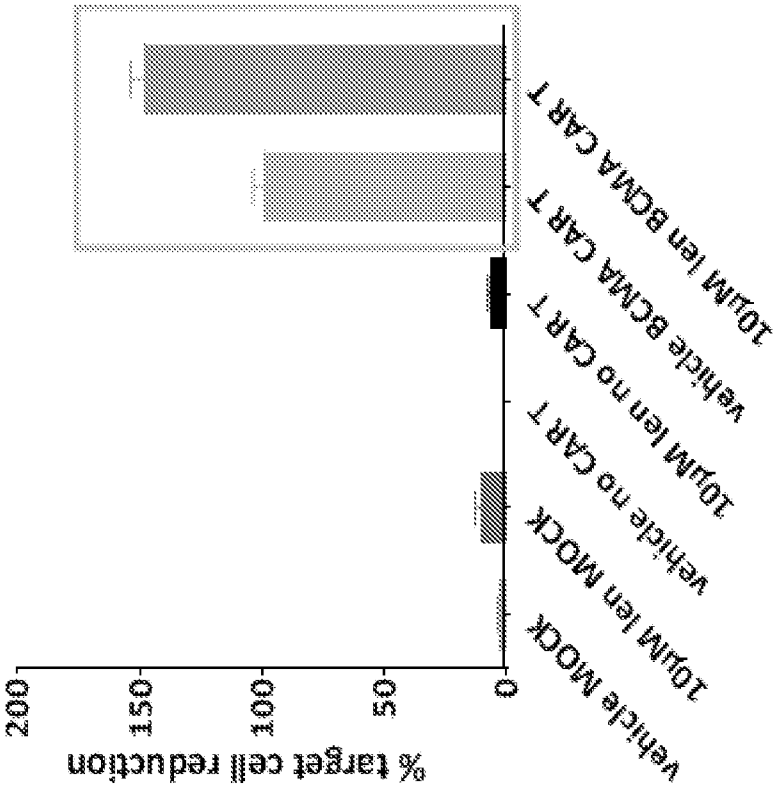
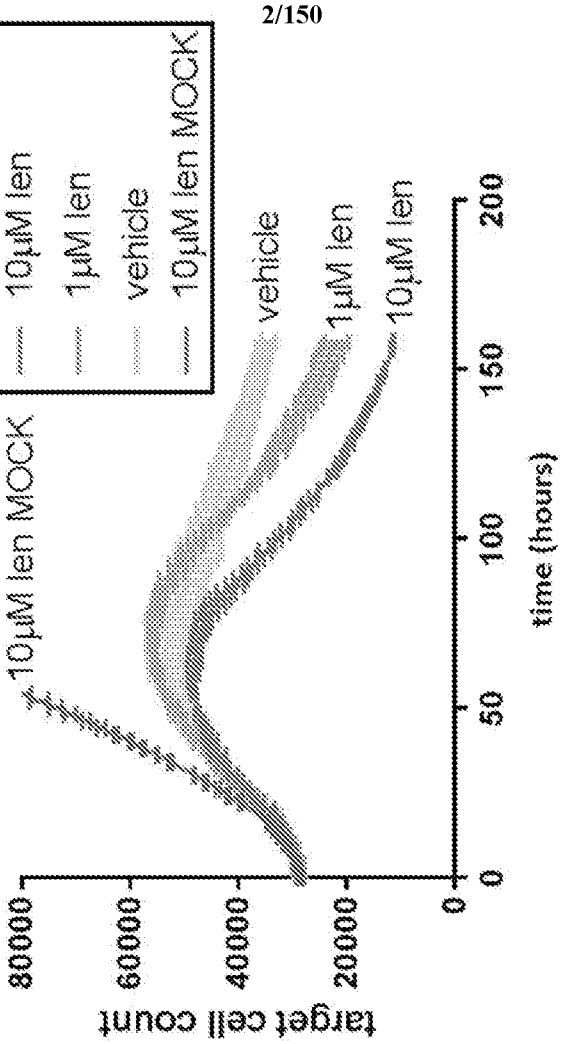

BCMA target cell: RPMI-8226
% target cell reduction
200
150
100
50
0
vehicle MOCK
10μM len MOCK
vehicle no CAR T
10μM len no CAR T
vehicle BCMA CAR T
10μM len BCMA CAR T

FIG. 1C


RPMI-8226
target cell count
80000
60000
40000
20000
0
0
50
100
150
200
time (hours)
10μM len MOCK
vehicle
1μM len
10μM len
10μM len
1μM len
vehicle
10μM len MOCK

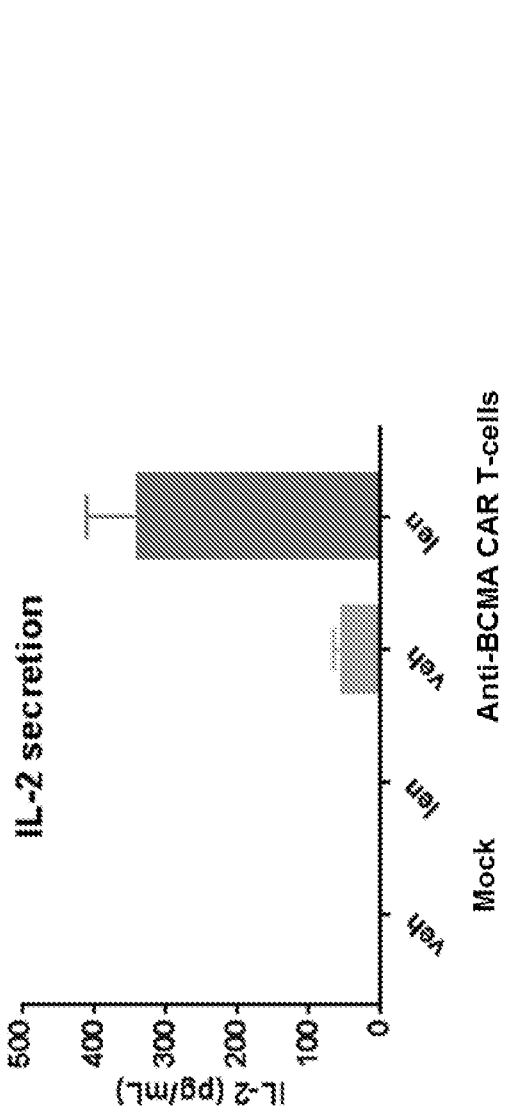


FIG. 2A

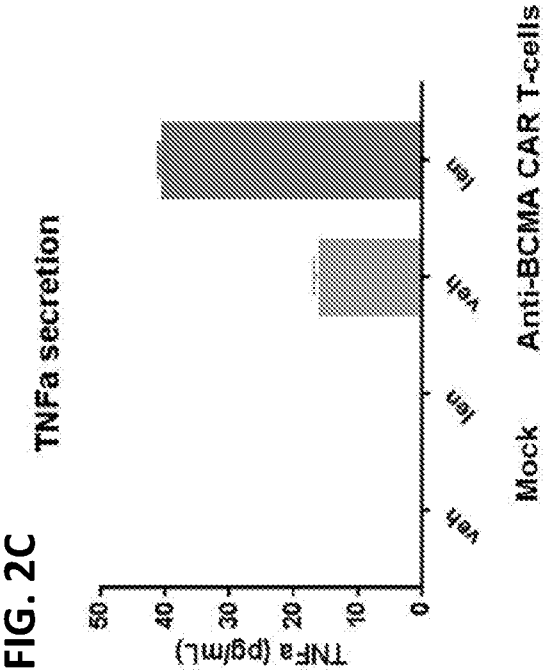


FIG. 2C

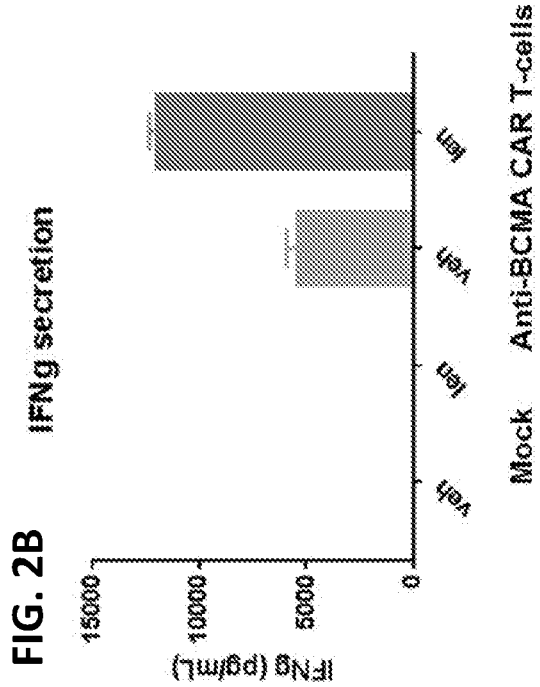


FIG. 2B

FIG. 3A

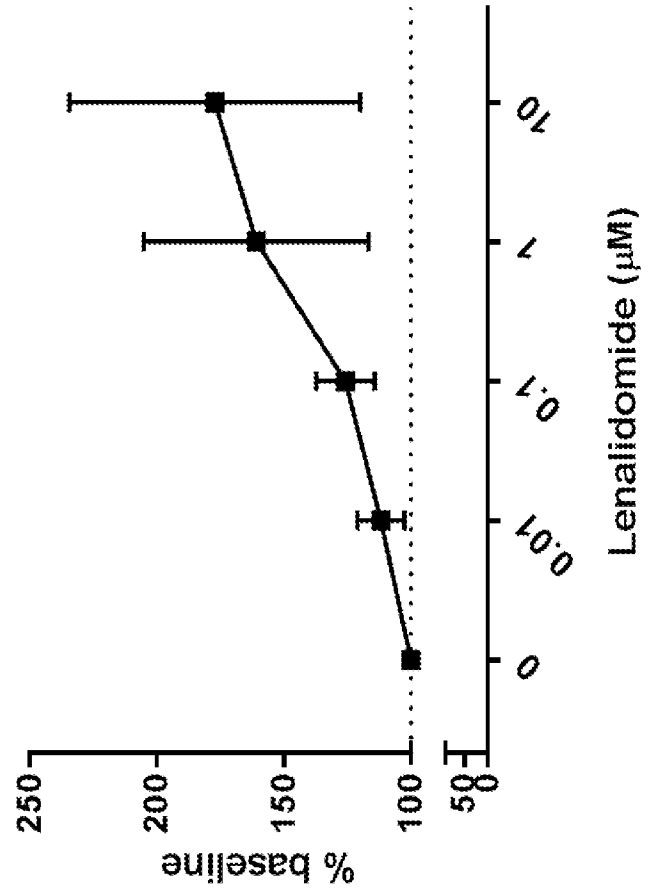

OPM2 % Killing
% baseline
250
200
150
100
50
0
0.01
0.1
1
10
Lenalidomide (μM)

FIG. 3B

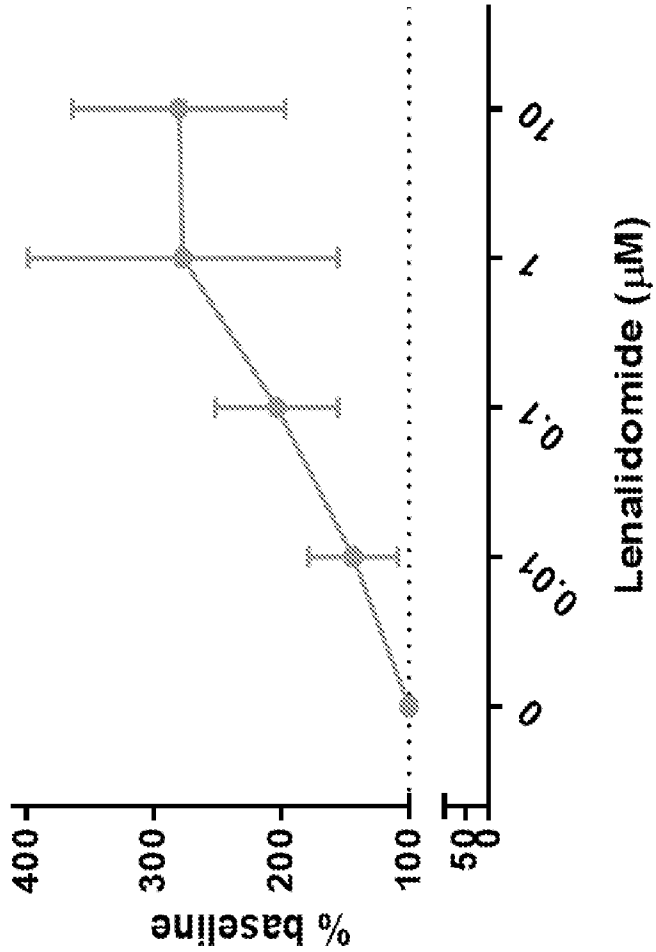

IFN-γ
% baseline
400
300
200
100
50
0
0.01
0.1
1
10
Lenalidomide (μM)

FIG. 3C

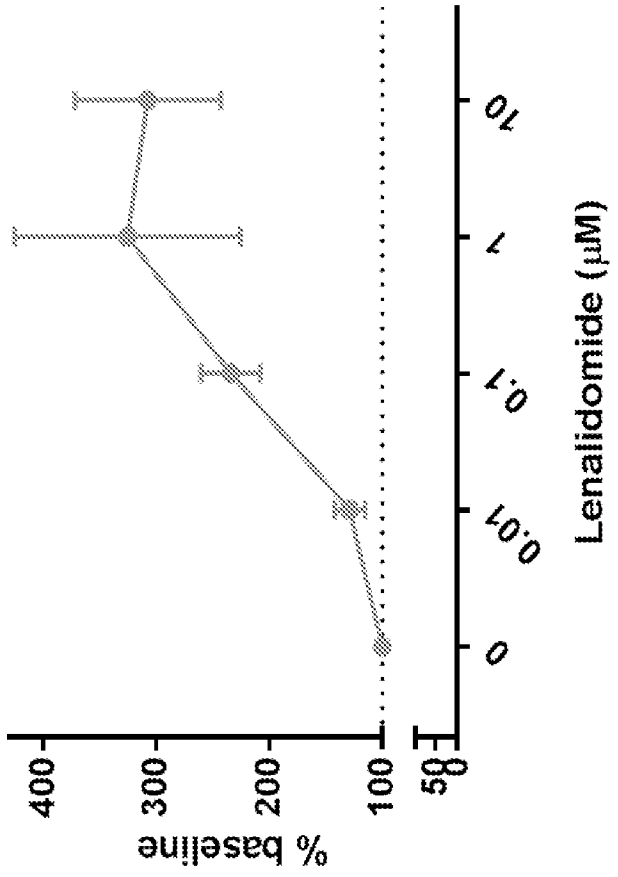

IL-2
% baseline
400
300
200
100
50
0
0
0.01
0.1
1
10
Lenalidomide (μM)

FIG. 3D

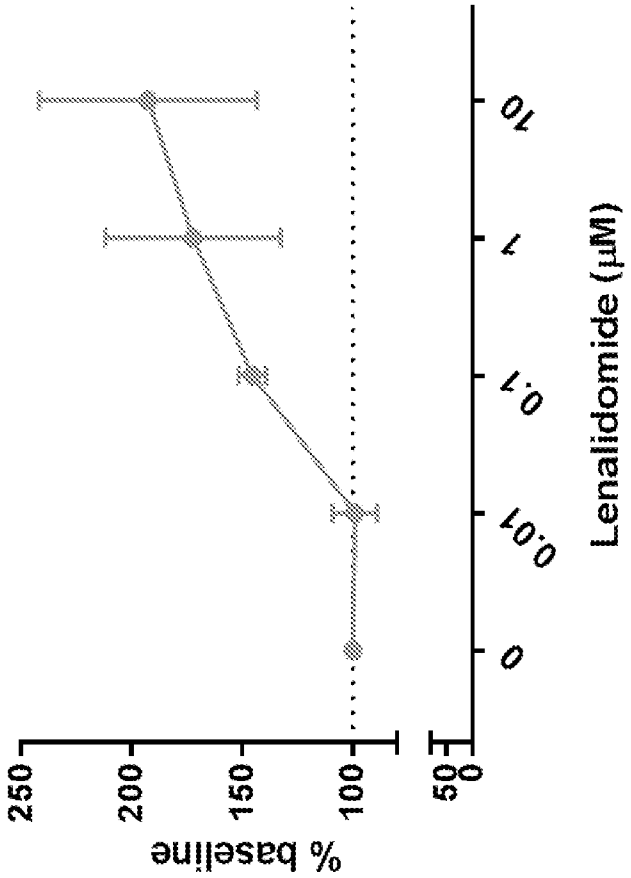
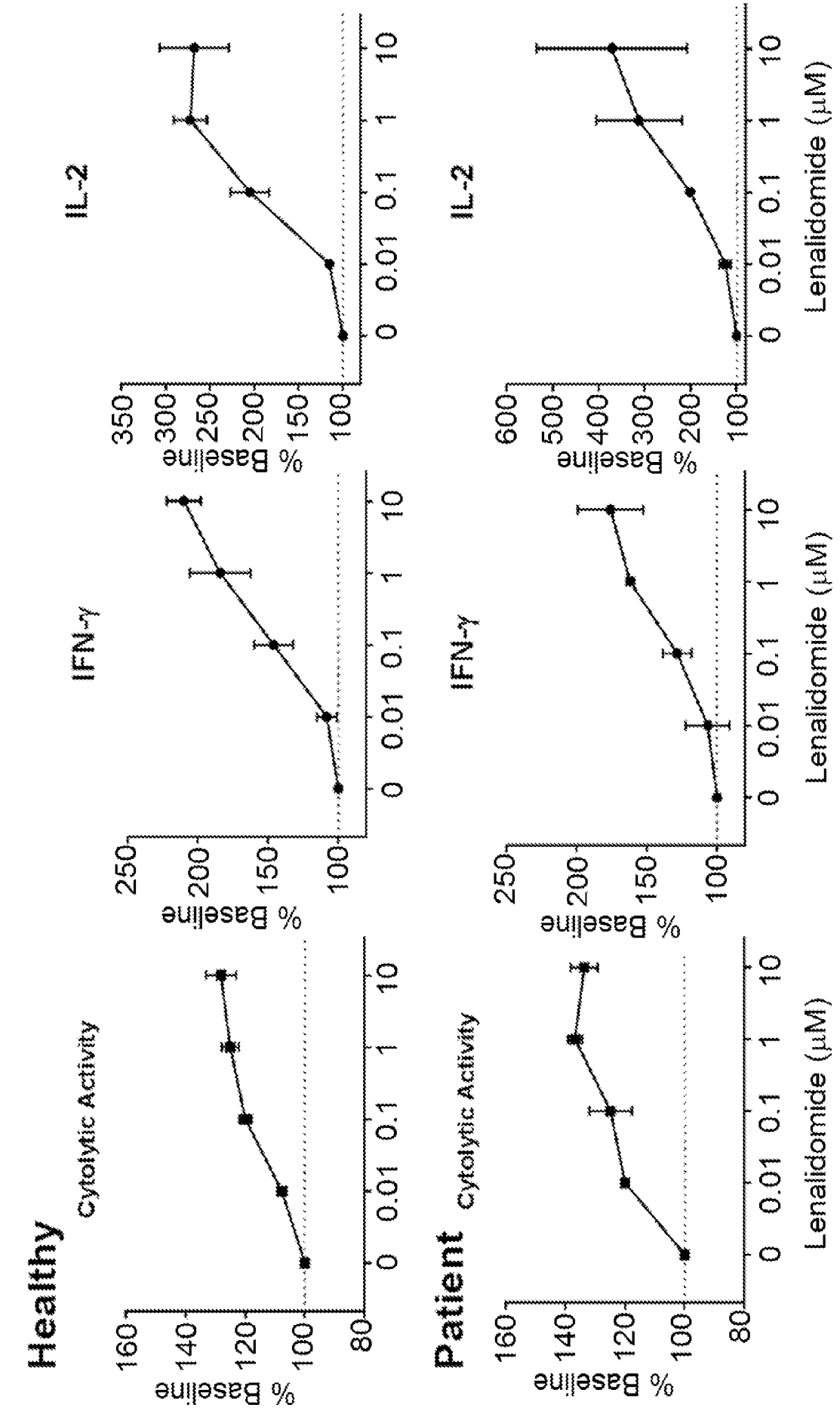

TNF-α
% baseline
250
200
150
100
50
0
0
0.01
0.1
1
10
Lenalidomide (μM)

FIG. 3E


Healthy
Cytolytic Activity
IFN-γ
IL-2
Patient
Cytolytic Activity
IFN-γ
IL-2
% Baseline
Lenalidomide (μM)
0
0.01
0.1
1
10
80
100
120
140
160
100
150
200
250
100
200
300
400
500
600
100
150
200
250
300
350

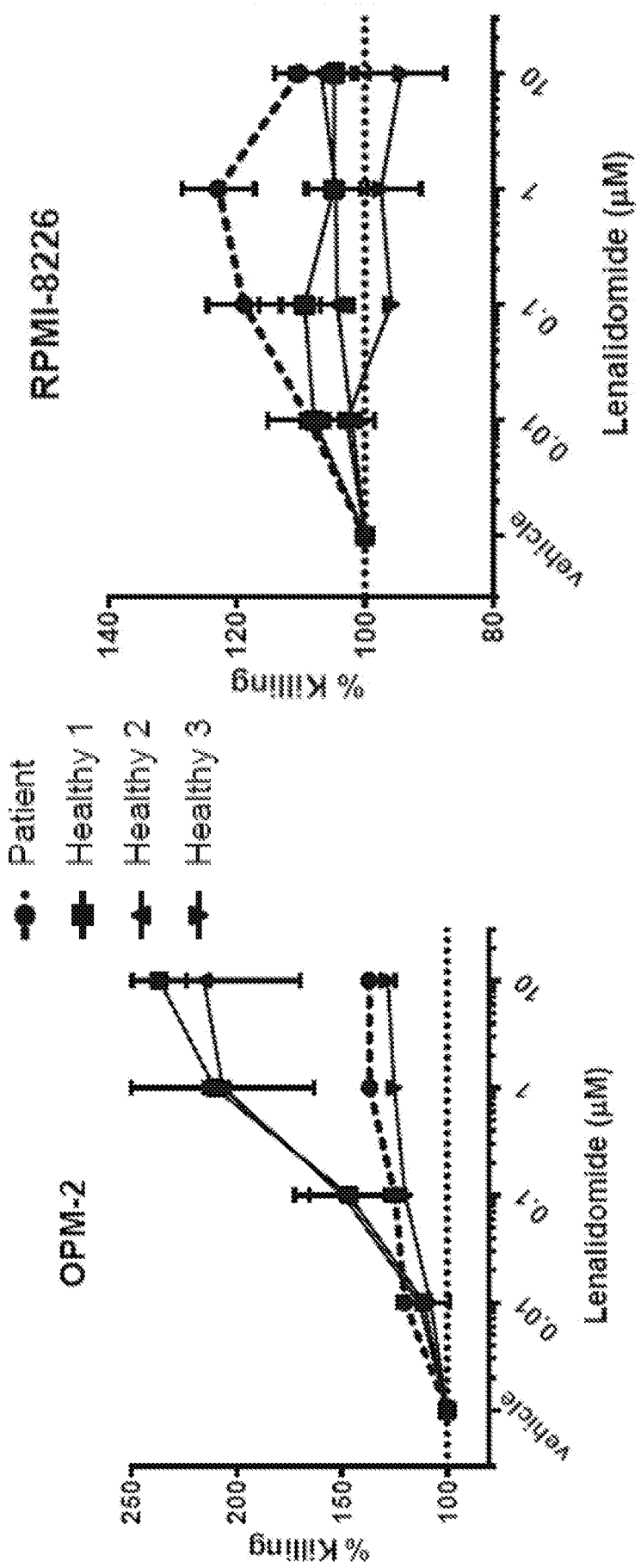

RPMI-8226
% Killing
140
120
100
80
Vehicle
0.01
0.1
1
10
Lenalidomide (μM)
Patient
Healthy 1
Healthy 2
Healthy 3
OPM-2
% Killing
250
200
150
100
Vehicle
0.01
0.1
1
10
Lenalidomide (μM)

FIG. 3F

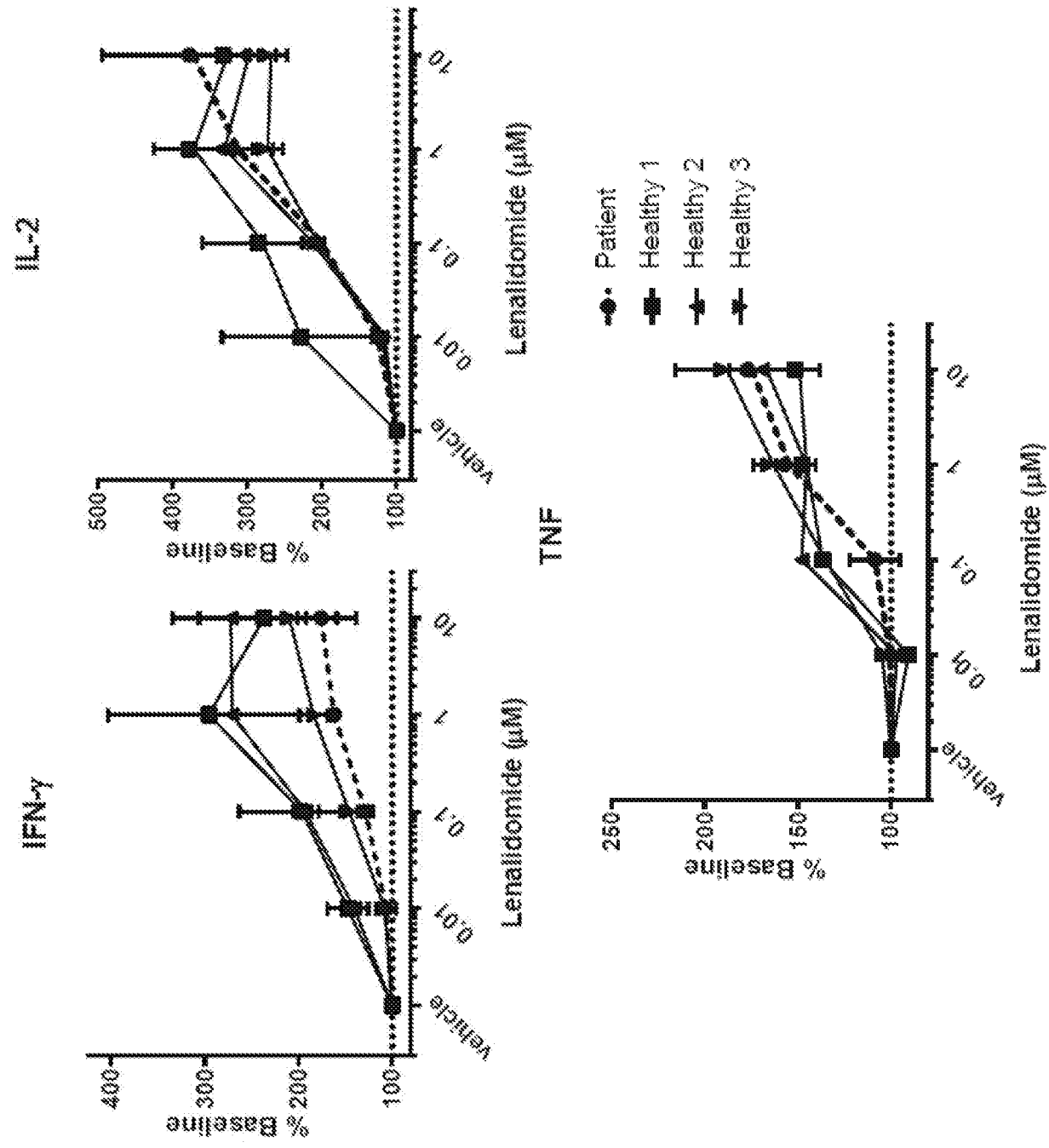

IL-2
IFN-γ
TNF
% Baseline
Lenalidomide (μM)
vehicle
0.01
0.1
1
10
Patient
Healthy 1
Healthy 2
Healthy 3

FIG. 3G

FIG. 3H

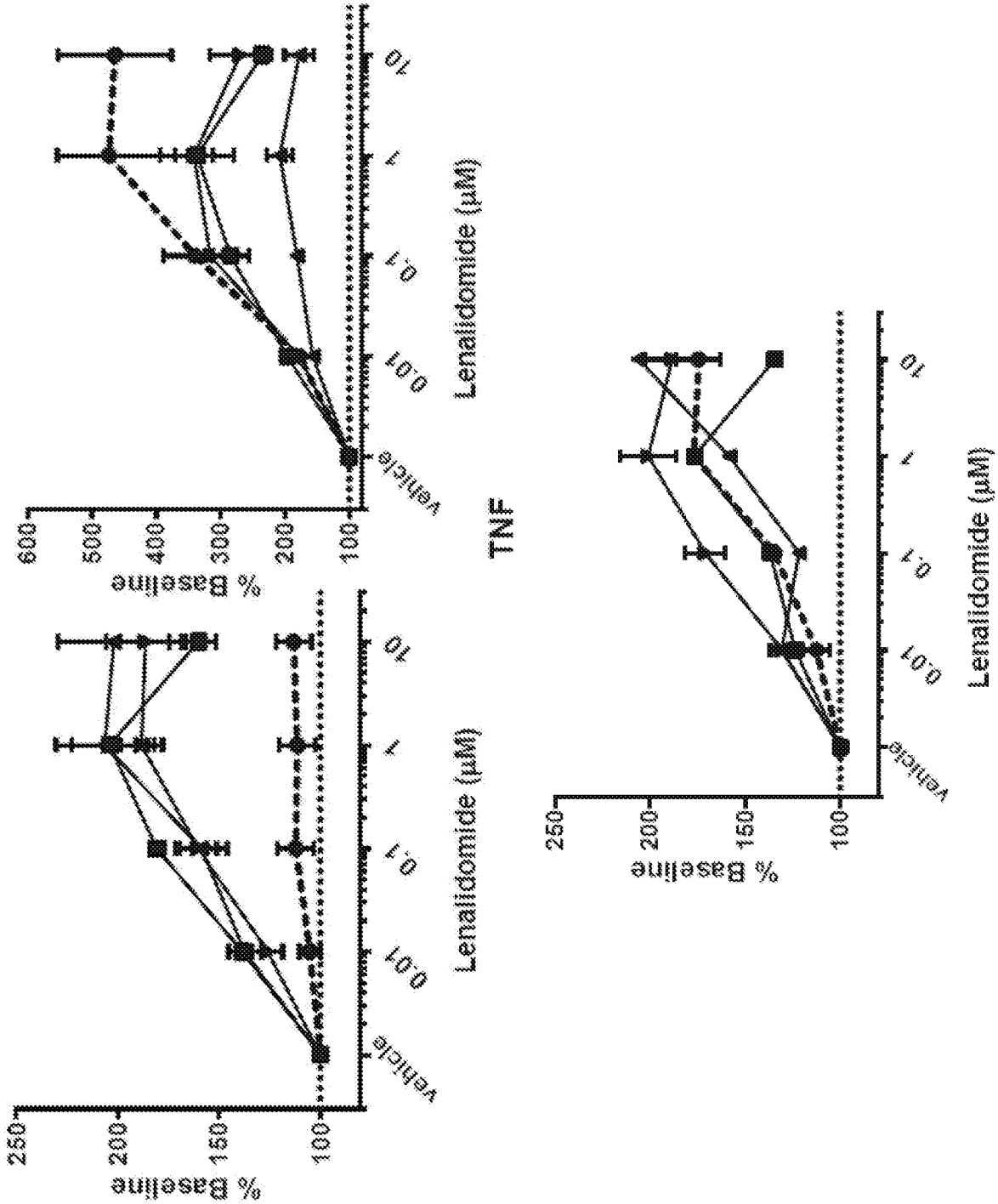
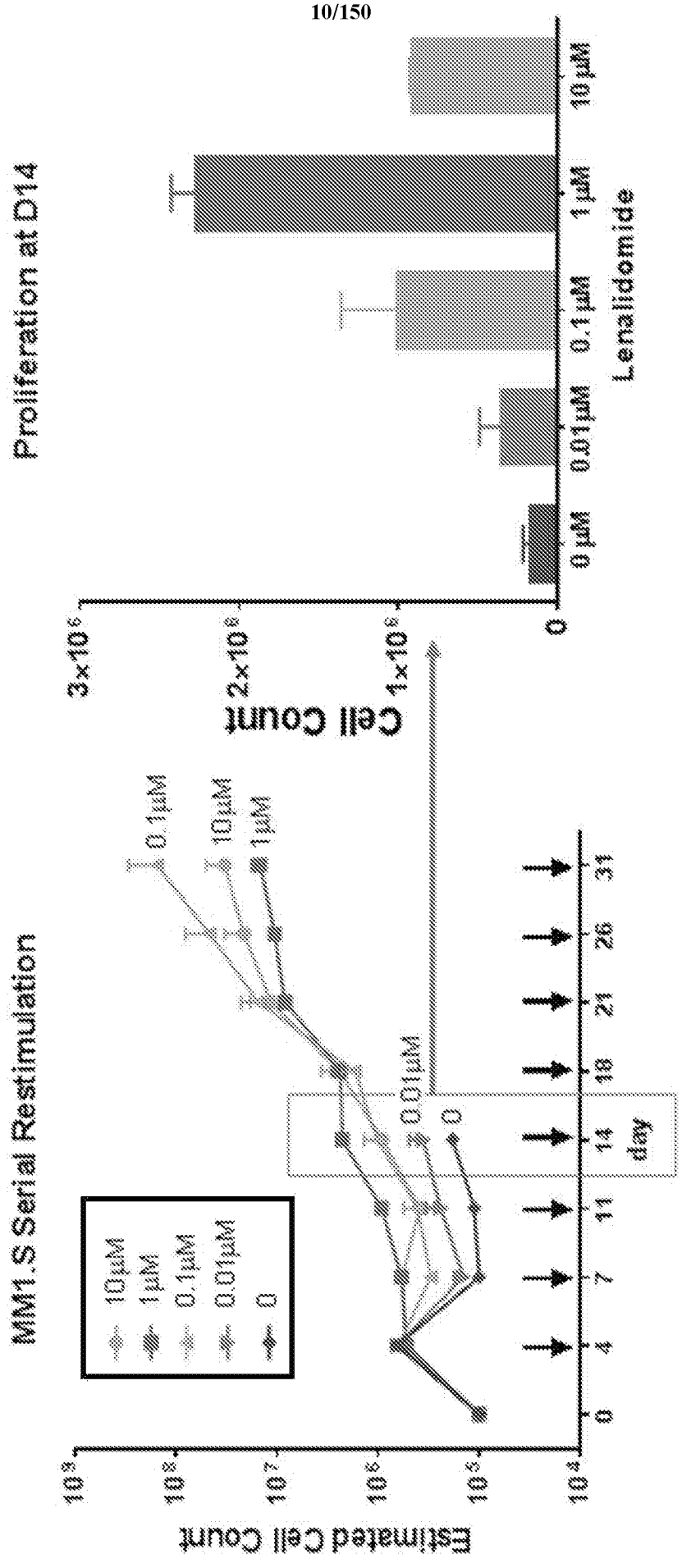

IL-2
IFN-γ
TNF
% Baseline
Lenalidomide (μM)
Vehicle
0.01
0.1
1
10
100
150
200
250
300
400
500
600

FIG. 4A


MM1.S Serial Restimulation
Estimated Cell Count
day
10μM
1μM
0.1μM
0.01μM
0
Cell Count
Proliferation at D14
Lenalidomide
0 μM
0.01μM
0.1μM
1 μM
10 μM

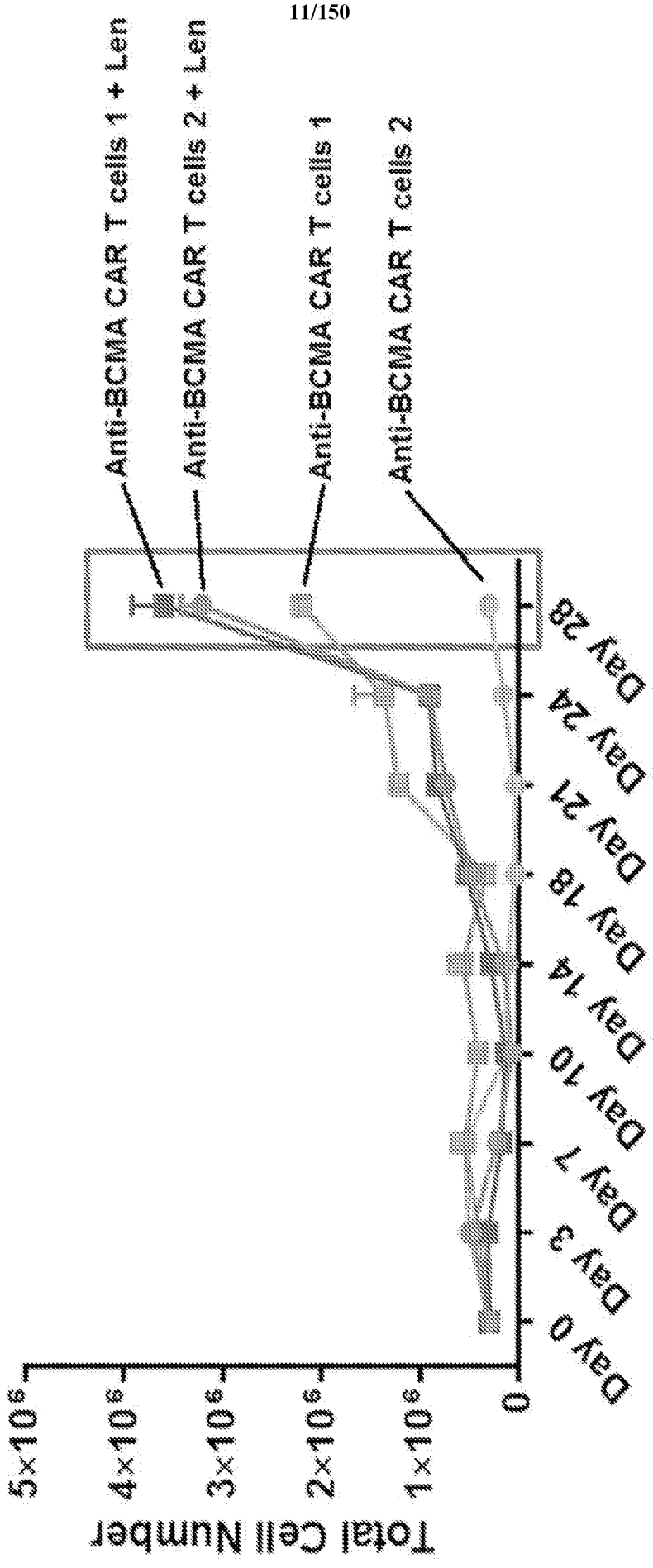

Anti-BCMA CAR T cells 1 + Len
Anti-BCMA CAR T cells 2 + Len
Anti-BCMA CAR T cells 1
Anti-BCMA CAR T cells 2
Total Cell Number
5×10⁶
4×10⁶
3×10⁶
2×10⁶
1×10⁶
0
Day 0
Day 3
Day 7
Day 10
Day 14
Day 18
Day 21
Day 24
Day 28

FIG. 4B

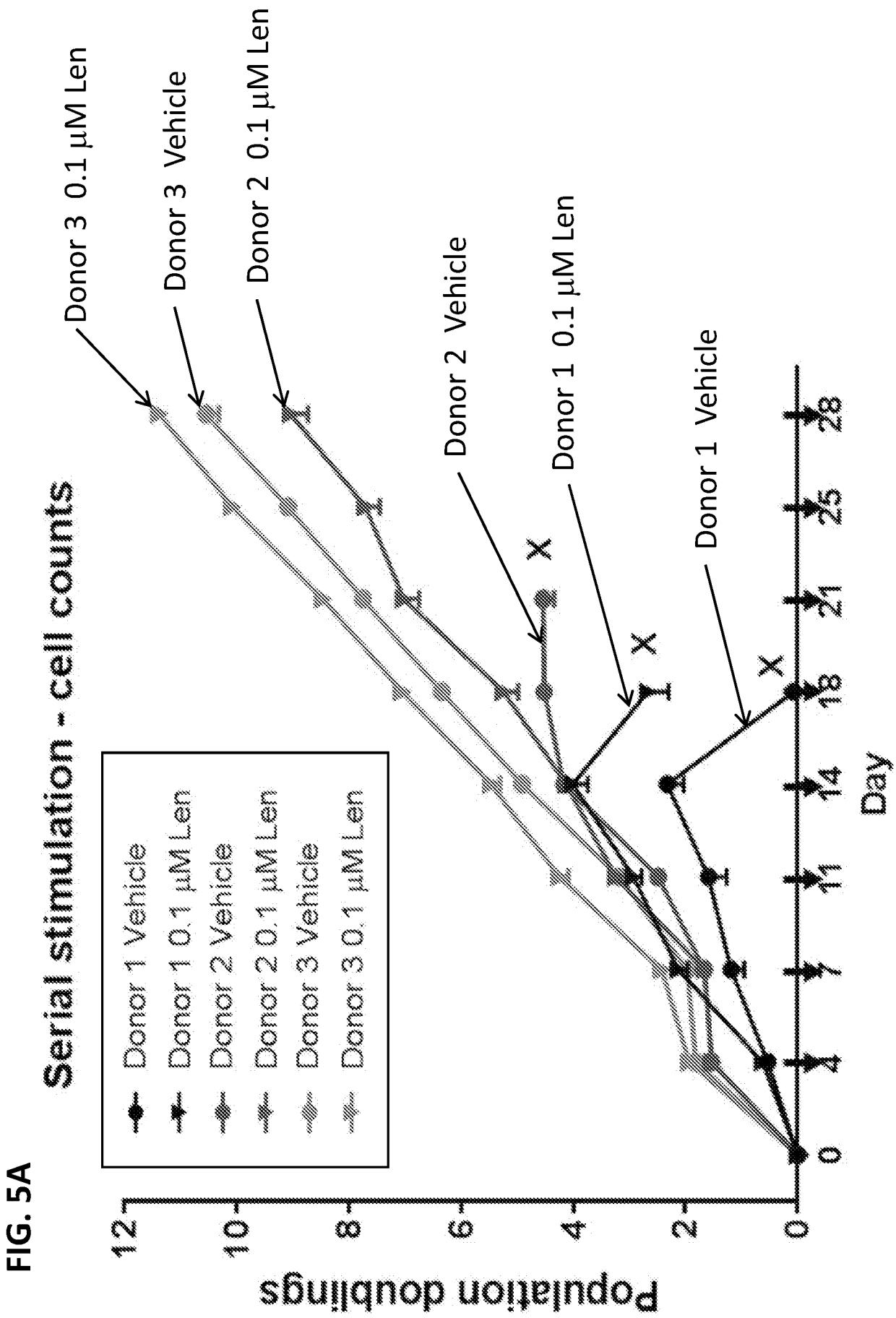

Serial stimulation - cell counts
Donor 1 Vehicle
Donor 1 0.1 µM Len
Donor 2 Vehicle
Donor 2 0.1 µM Len
Donor 3 Vehicle
Donor 3 0.1 µM Len
Donor 3 0.1 µM Len
Donor 3 Vehicle
Donor 2 0.1 µM Len
Donor 2 Vehicle
Donor 1 0.1 µM Len
Donor 1 Vehicle
Population doublings
Day
0
2
4
6
8
10
12
0
4
7
11
14
18
21
25
28

FIG. 5A

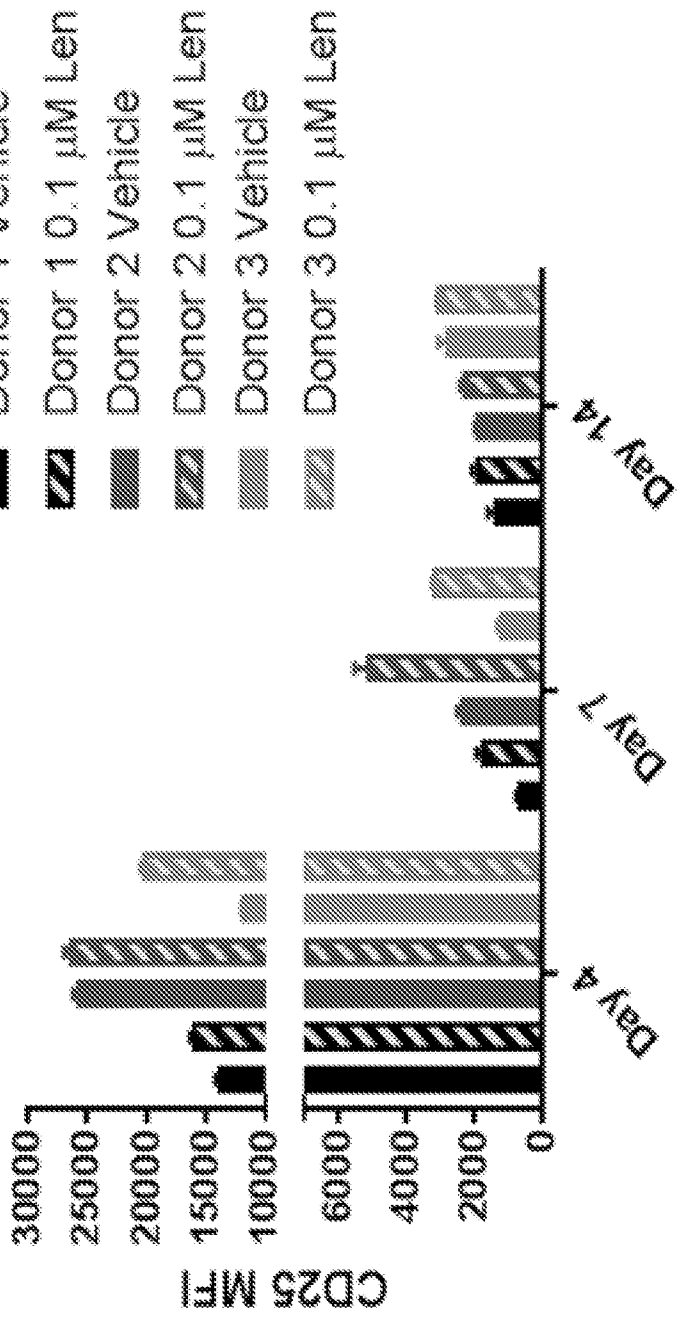
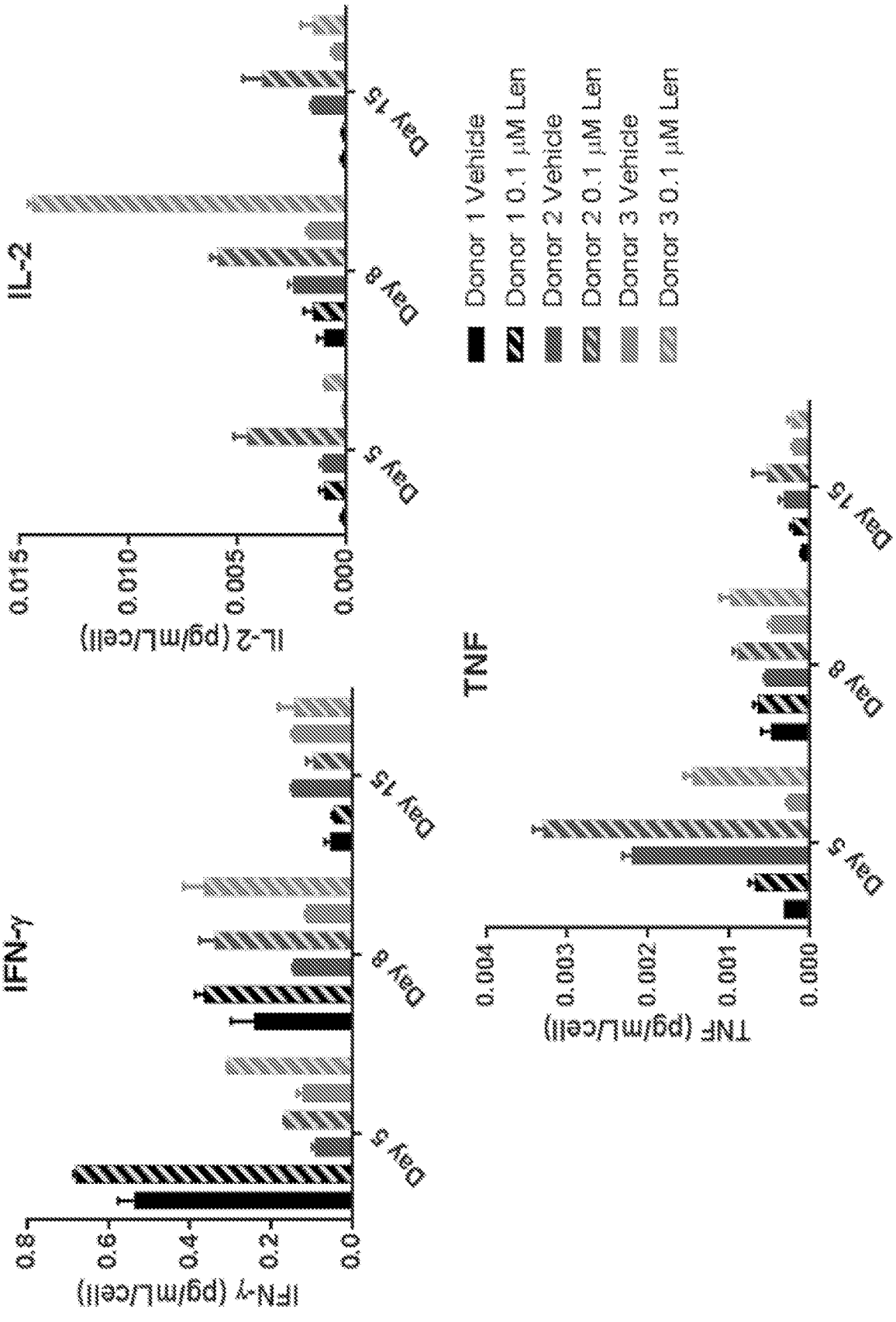

activation
Donor 1 Vehicle
Donor 1 0.1 μM Len
Donor 2 Vehicle
Donor 2 0.1 μM Len
Donor 3 Vehicle
Donor 3 0.1 μM Len
CD25 MFI
30000
25000
20000
15000
10000
6000
4000
2000
0
Day 4
Day 7
Day 14

FIG. 5B

FIG. 5C


IL-2
IL-2 (pg/mL/cell)
0.015
0.010
0.005
0.000
Day 5
Day 8
Day 15
IFN-γ
IFN-γ (pg/mL/cell)
0.8
0.6
0.4
0.2
0.0
Day 5
Day 8
Day 15
TNF
TNF (pg/mL/cell)
0.004
0.003
0.002
0.001
0.000
Day 5
Day 8
Day 15
Donor 1 Vehicle
Donor 1 0.1 μM Len
Donor 2 Vehicle
Donor 2 0.1 μM Len
Donor 3 Vehicle
Donor 3 0.1 μM Len

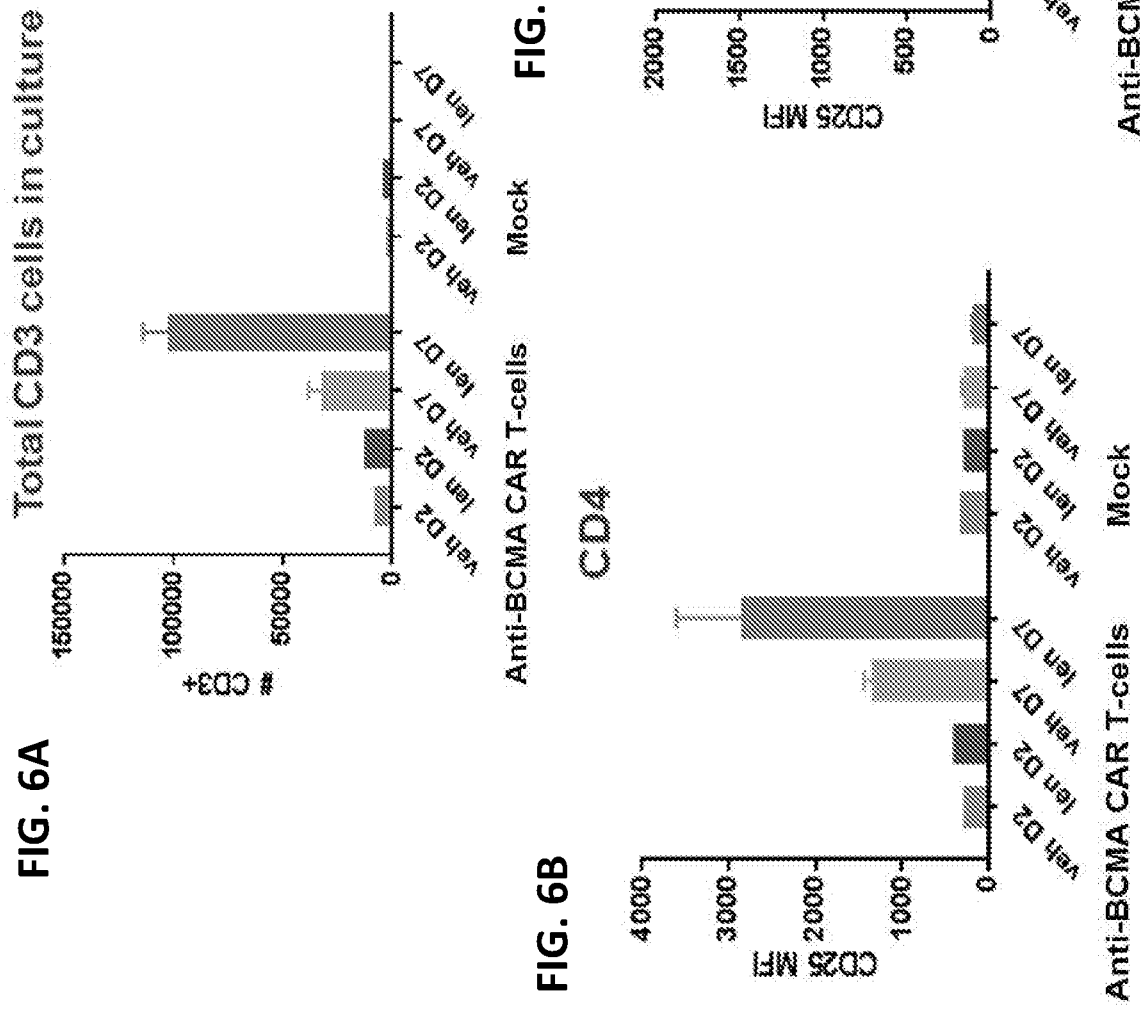


FIG. 6A

FIG. 6B

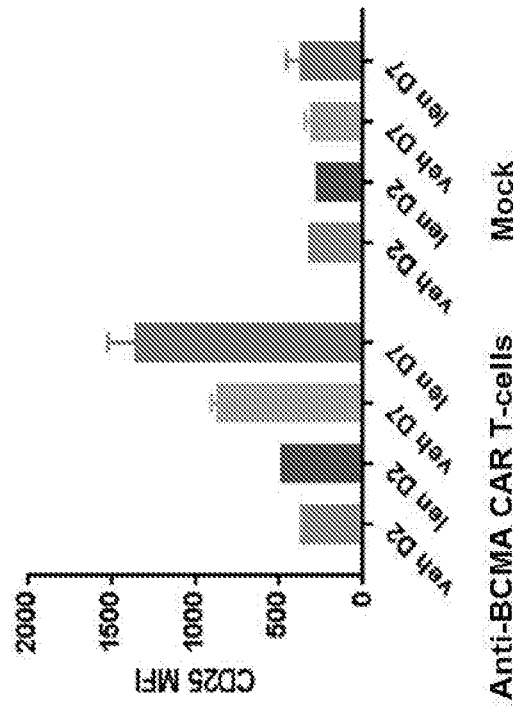


FIG. 6C

FIG. 7A

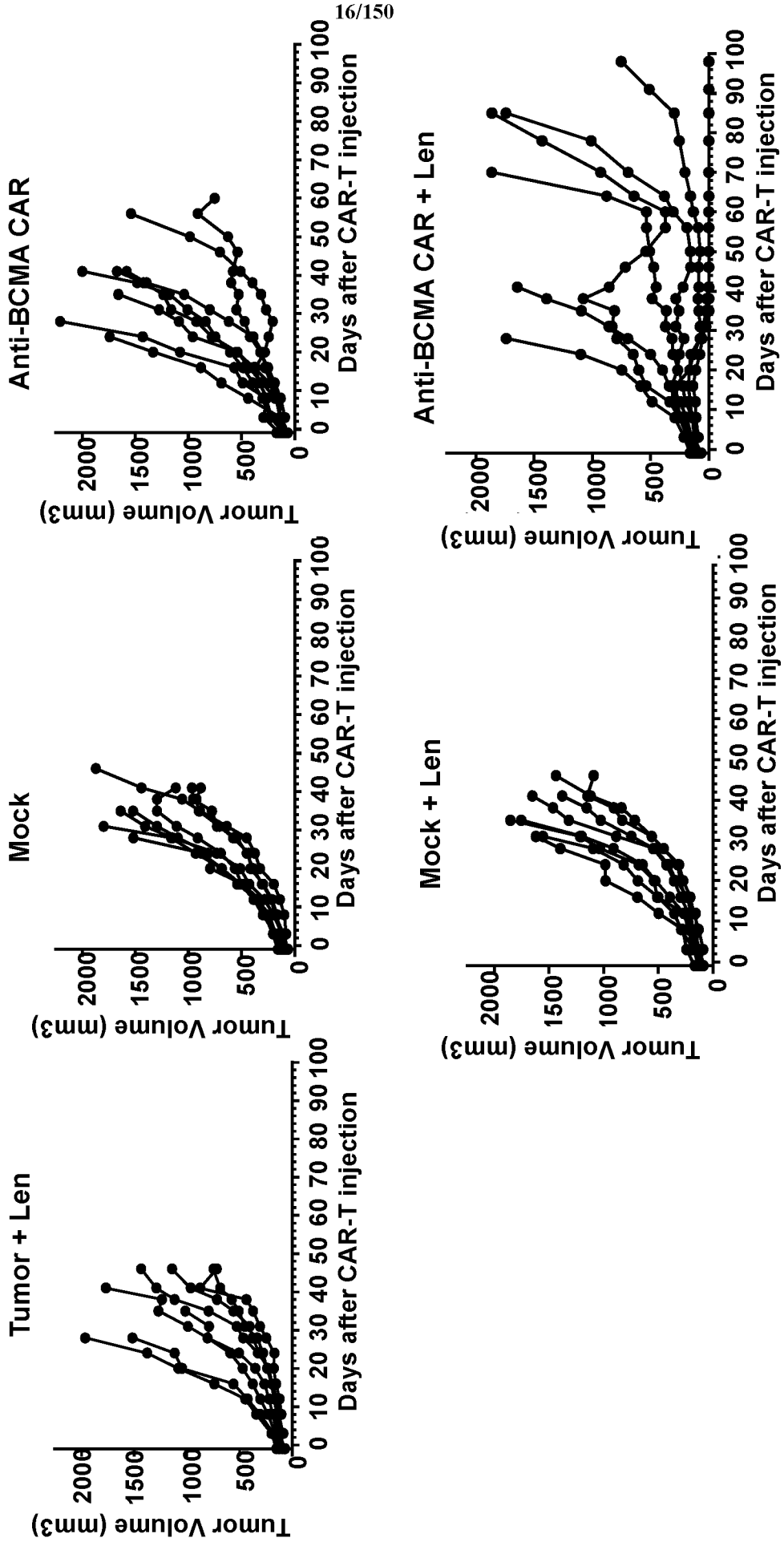
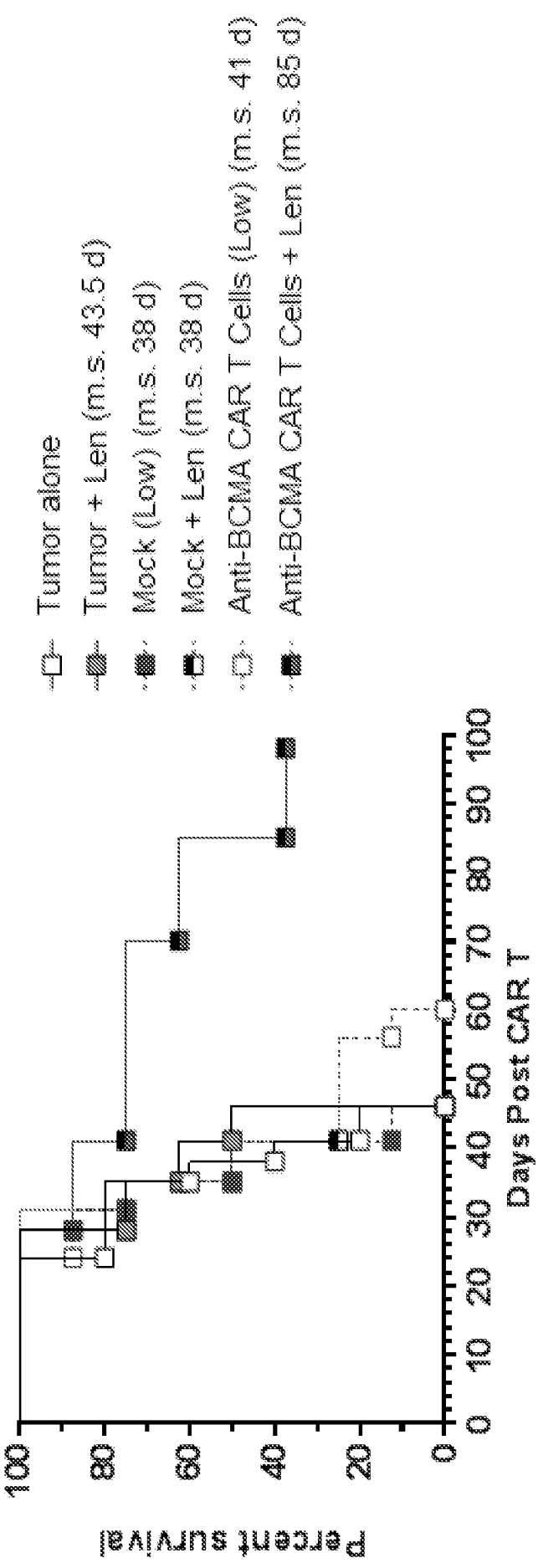

Tumor + Len
Mock
Anti-BCMA CAR
Mock + Len
Anti-BCMA CAR + Len
Tumor Volume (mm3)
0
500
1000
1500
2000
0 10 20 30 40 50 60 70 80 90 100
Days after CAR-T injection

FIG. 7B


Tumor alone
Tumor + Len (m.s. 43.5 d)
Mock (Low) (m.s. 38 d)
Mock + Len (m.s. 38 d)
Anti-BCMA CAR T Cells (Low) (m.s. 41 d)
Anti-BCMA CAR T Cells + Len (m.s. 85 d)
Percent survival
100
80
60
40
20
0
0 10 20 30 40 50 60 70 80 90 100
Days Post CAR T

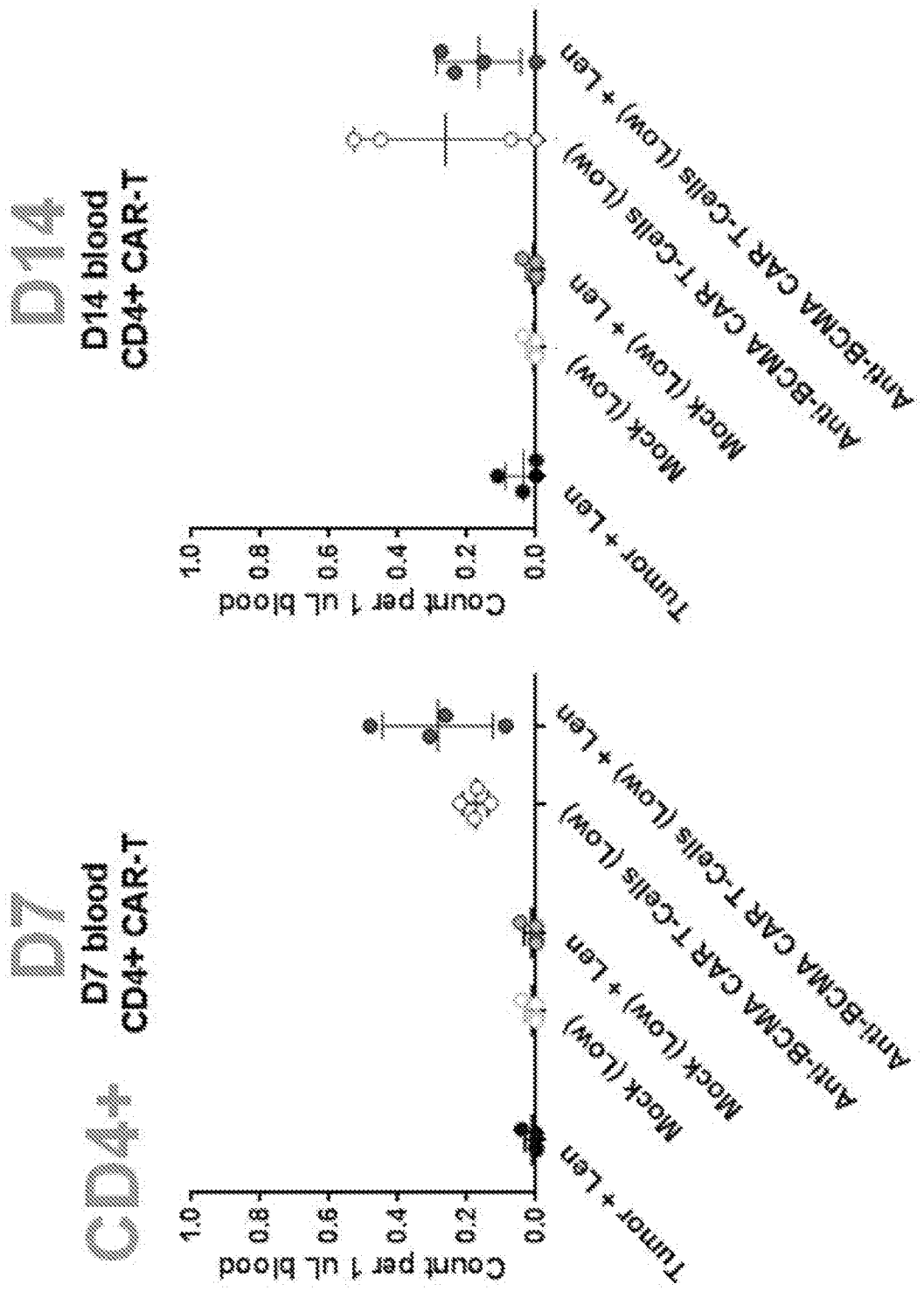

CD4+
D7
D7 blood
CD4+ CAR-T
D14
D14 blood
CD4+ CAR-T
Count per 1 uL blood
1.0
0.8
0.6
0.4
0.2
0.0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len

FIG. 8A

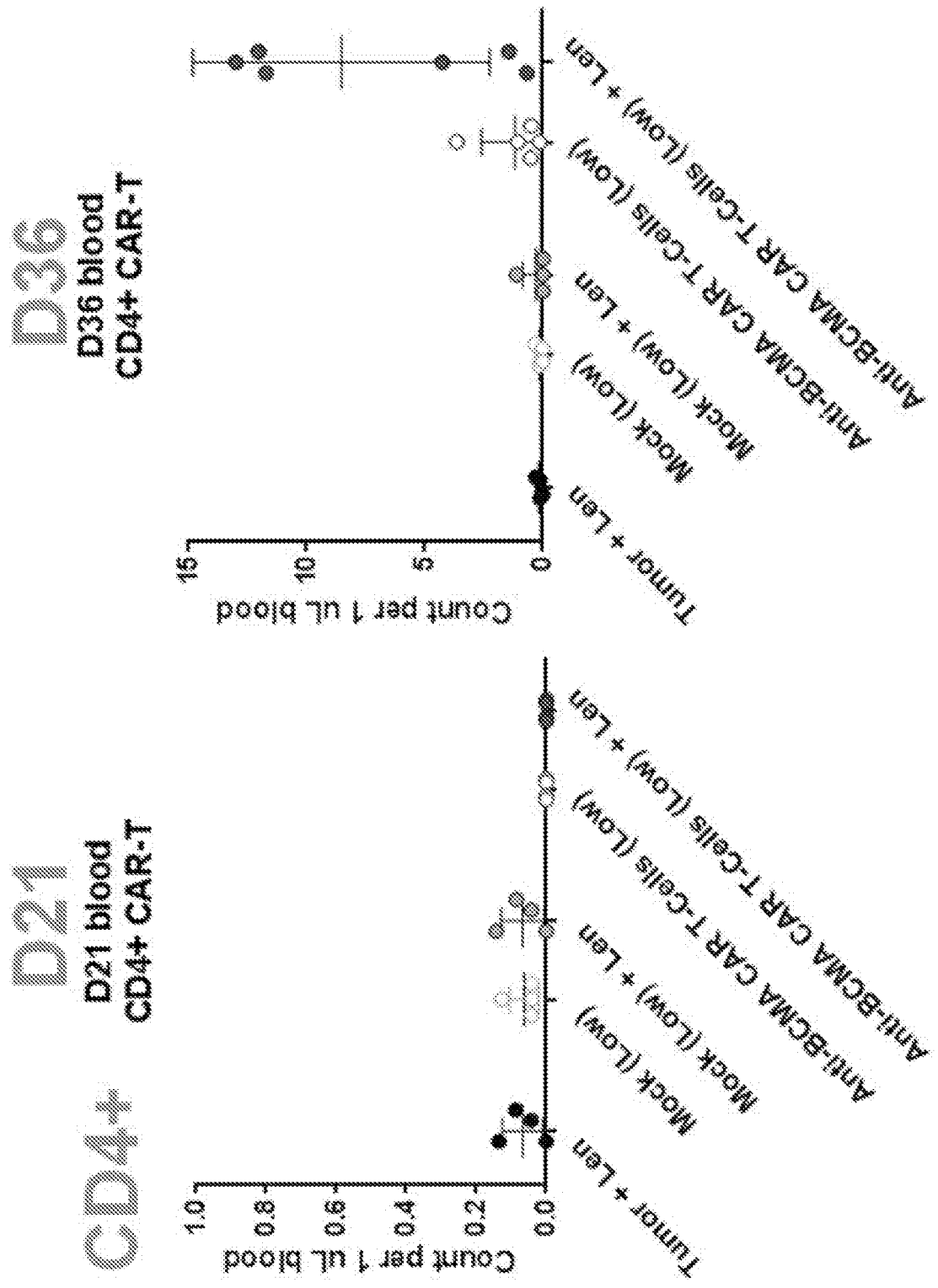

CD4+
D21
D21 blood
CD4+ CAR-T
Count per 1 uL blood
1.0
0.8
0.6
0.4
0.2
0.0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len
D36
D36 blood
CD4+ CAR-T
Count per 1 uL blood
15
10
5
0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len

FIG. 8B

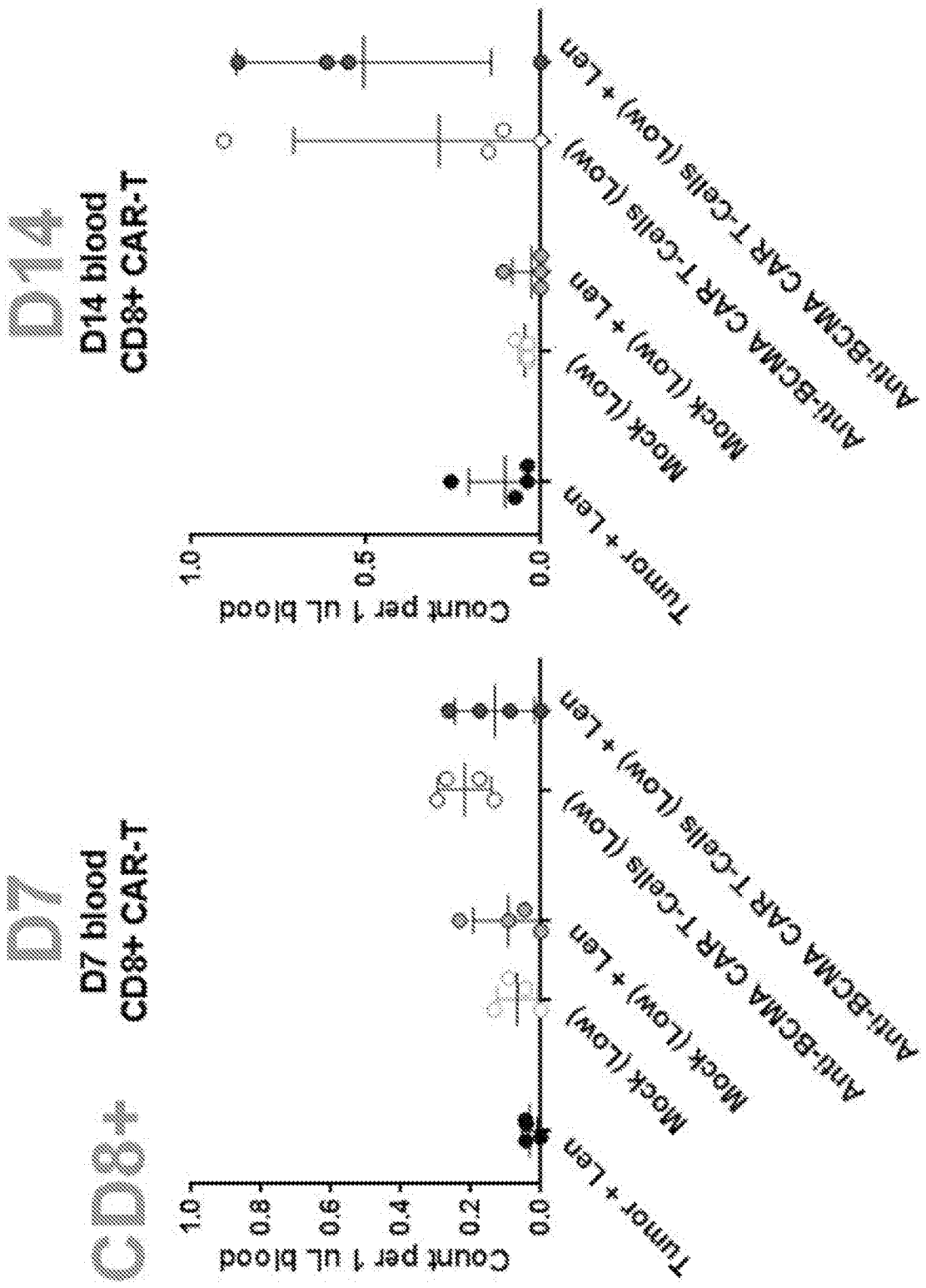

CD8+
D7
D7 blood
CD8+ CAR-T
Count per 1 uL blood
1.0
0.8
0.6
0.4
0.2
0.0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-cells (Low)
Anti-BCMA CAR T-cells (Low) + Len
D14
D14 blood
CD8+ CAR-T
Count per 1 uL blood
1.0
0.5
0.0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-cells (Low)
Anti-BCMA CAR T-cells (Low) + Len

FIG. 8C

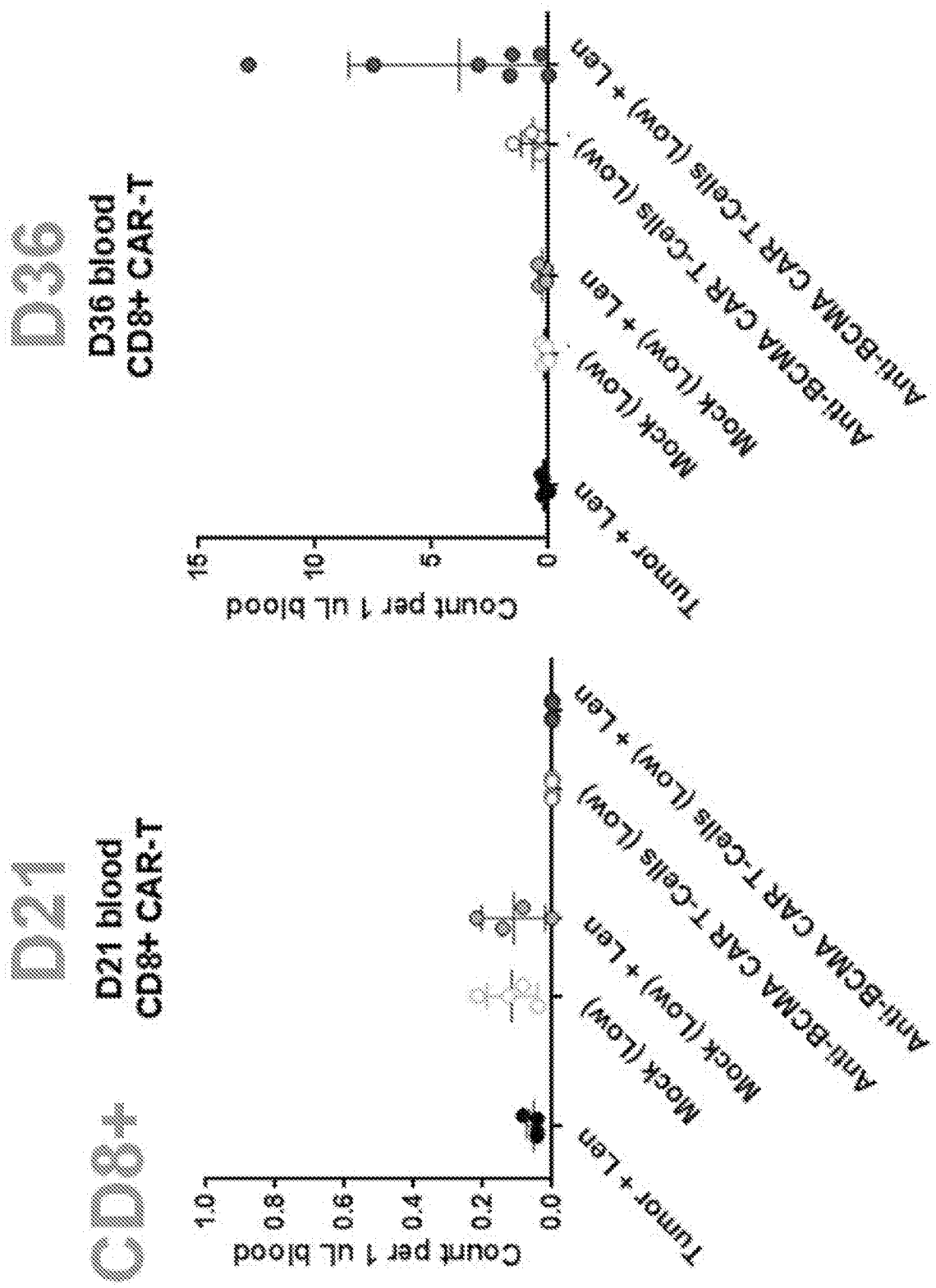

CD8+
D21
D21 blood
CD8+ CAR-T
Count per 1 uL blood
1.0
0.8
0.6
0.4
0.2
0.0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len
D36
D36 blood
CD8+ CAR-T
Count per 1 uL blood
15
10
5
0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len

FIG. 8D

FIG. 8E

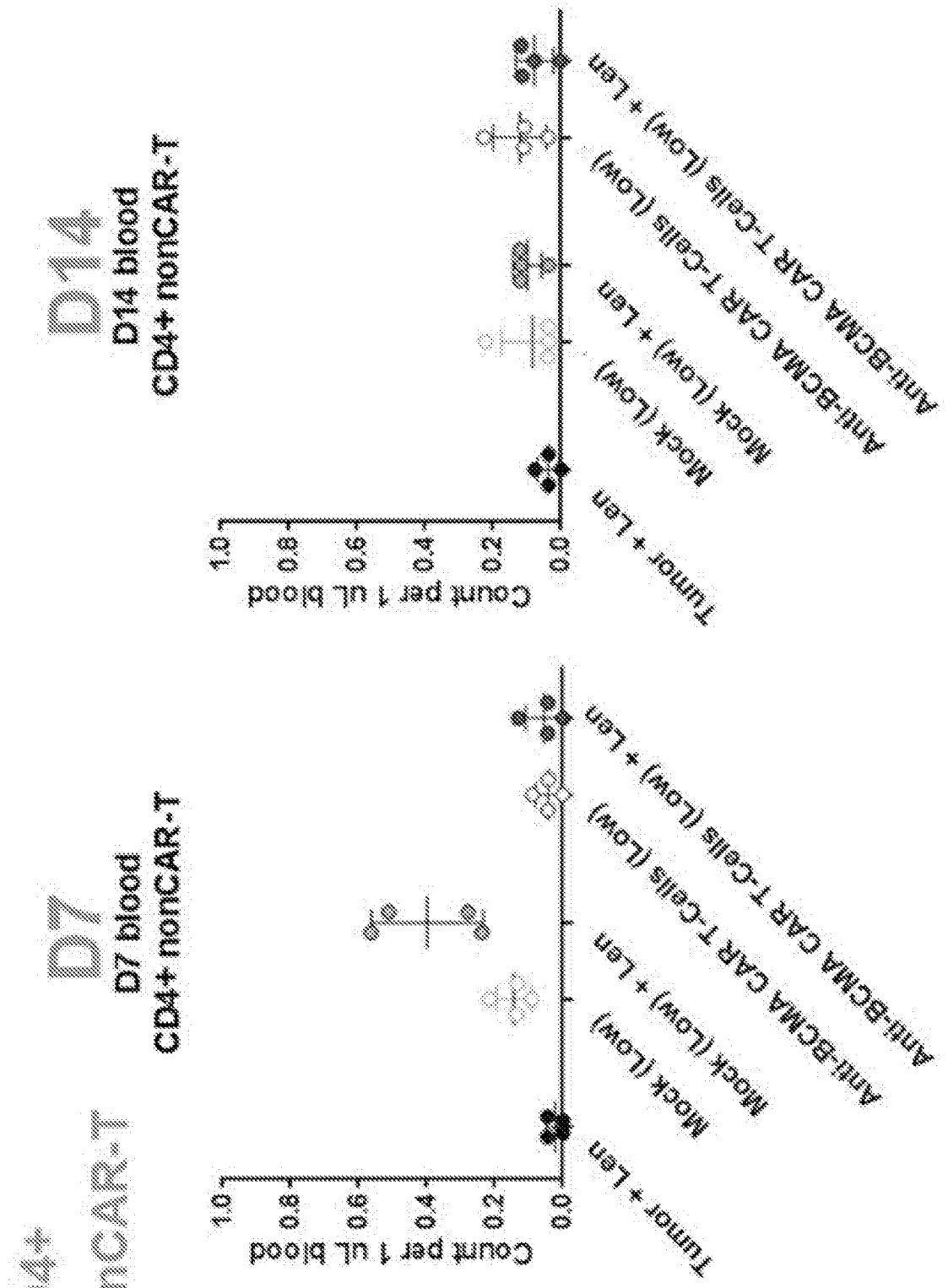

CD4+
nonCAR-T
D7
D7 blood
CD4+ nonCAR-T
D14
D14 blood
CD4+ nonCAR-T
Count per 1 uL blood
1.0
0.8
0.6
0.4
0.2
0.0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len

FIG. 8F

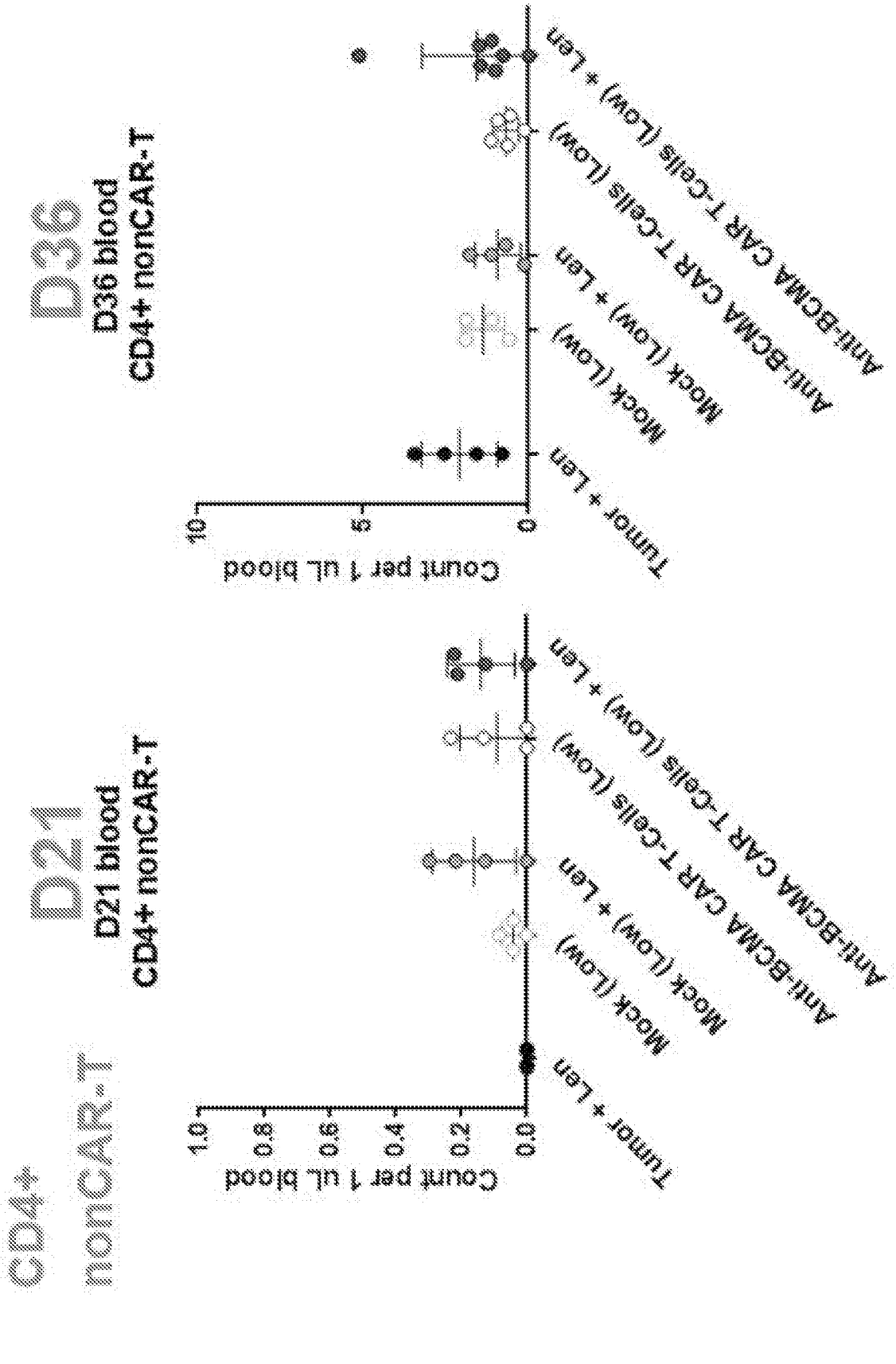
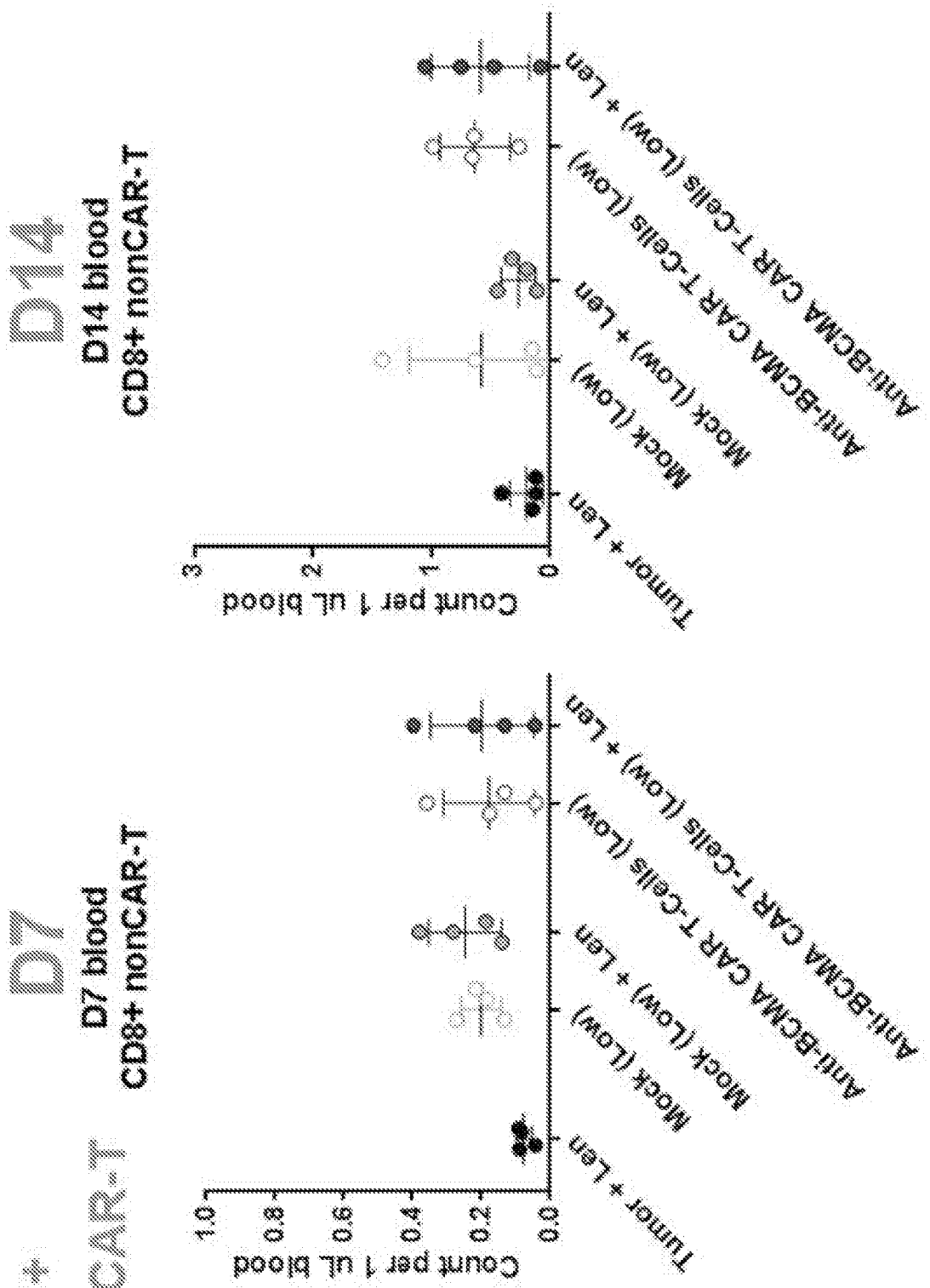

CD4+
nonCAR-T
D21
D21 blood
CD4+ nonCAR-T
Count per 1 uL blood
1.0
0.8
0.6
0.4
0.2
0.0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len
D36
D36 blood
CD4+ nonCAR-T
Count per 1 uL blood
10
5
0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len

FIG. 8G


CD8+
nonCAR-T
D7
D7 blood
CD8+ nonCAR-T
Count per 1 uL blood
1.0
0.8
0.6
0.4
0.2
0.0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len
D14
D14 blood
CD8+ nonCAR-T
Count per 1 uL blood
3
2
1
0
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len

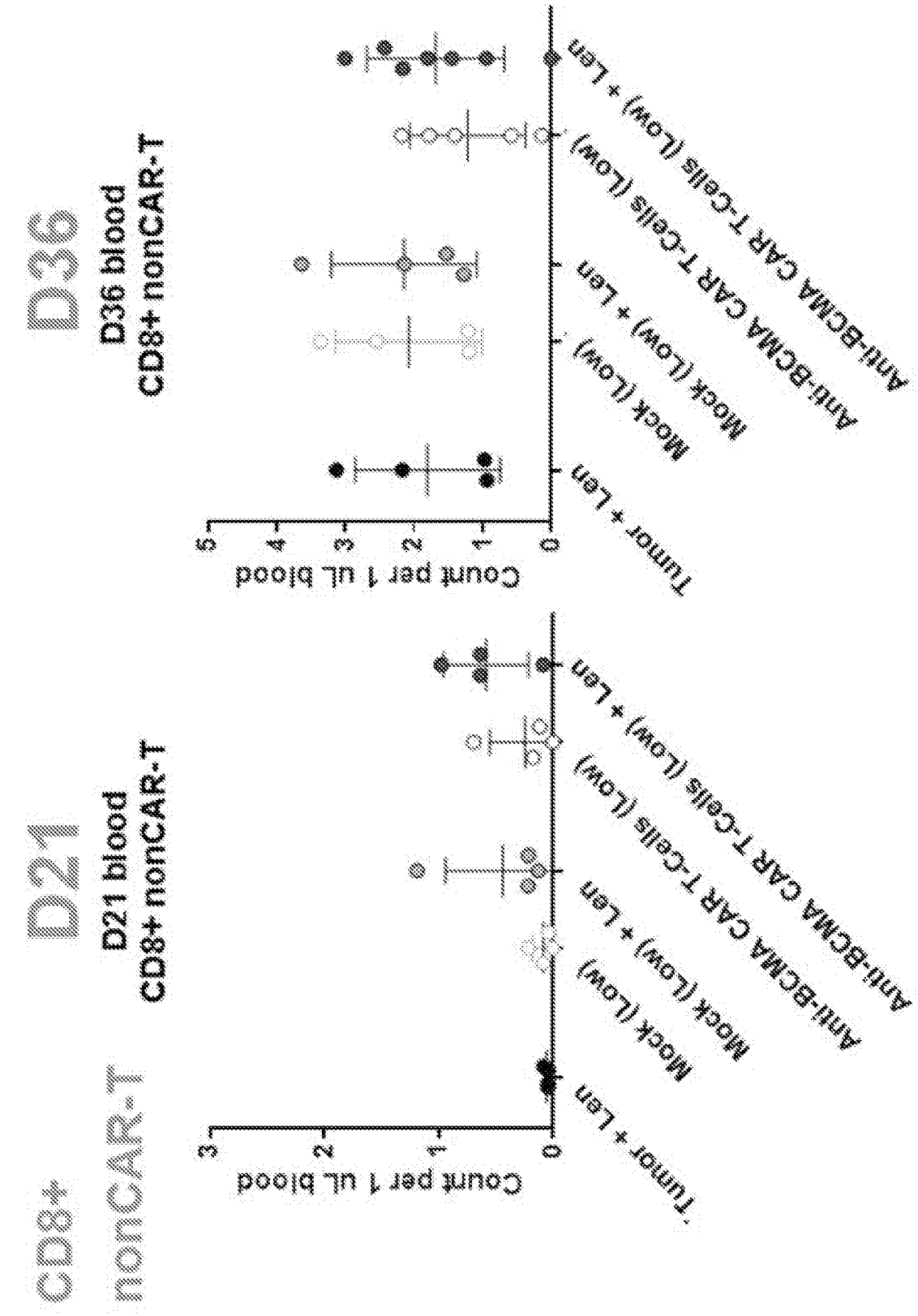

CD8+
nonCAR-T
D21
D21 blood
CD8+ nonCAR-T
Count per 1 uL blood
0
1
2
3
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len
D36
D36 blood
CD8+ nonCAR-T
Count per 1 uL blood
0
1
2
3
4
5
Tumor + Len
Mock (Low)
Mock (Low) + Len
Anti-BCMA CAR T-Cells (Low)
Anti-BCMA CAR T-Cells (Low) + Len

FIG. 8H

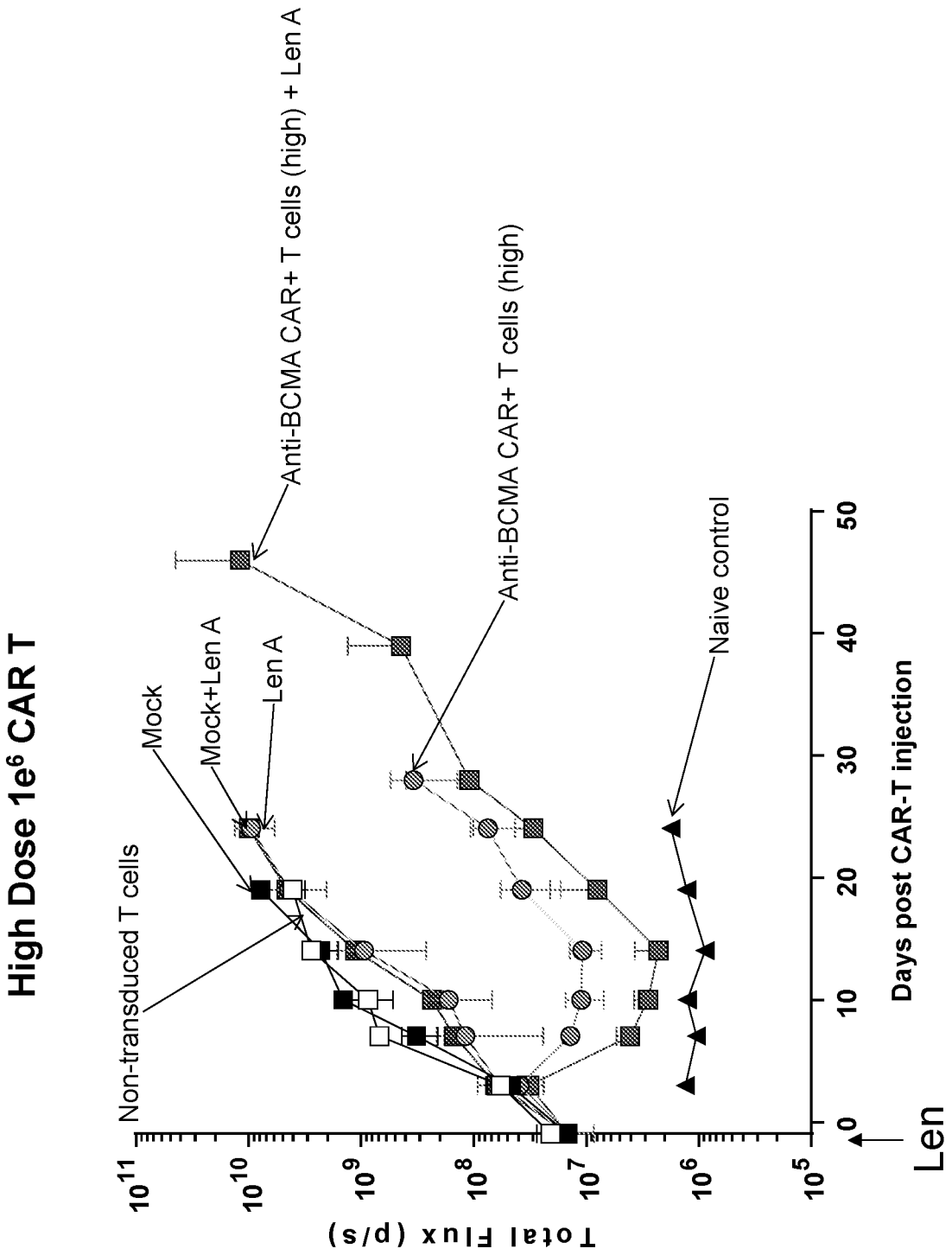

High Dose 1e6 CAR T
Anti-BCMA CAR+ T cells (high) + Len A
Anti-BCMA CAR+ T cells (high)
Naive control
Non-transduced T cells
Mock
Mock+Len A
Len A
Total Flux (p/s)
Days post CAR-T injection
Len

FIG. 9A

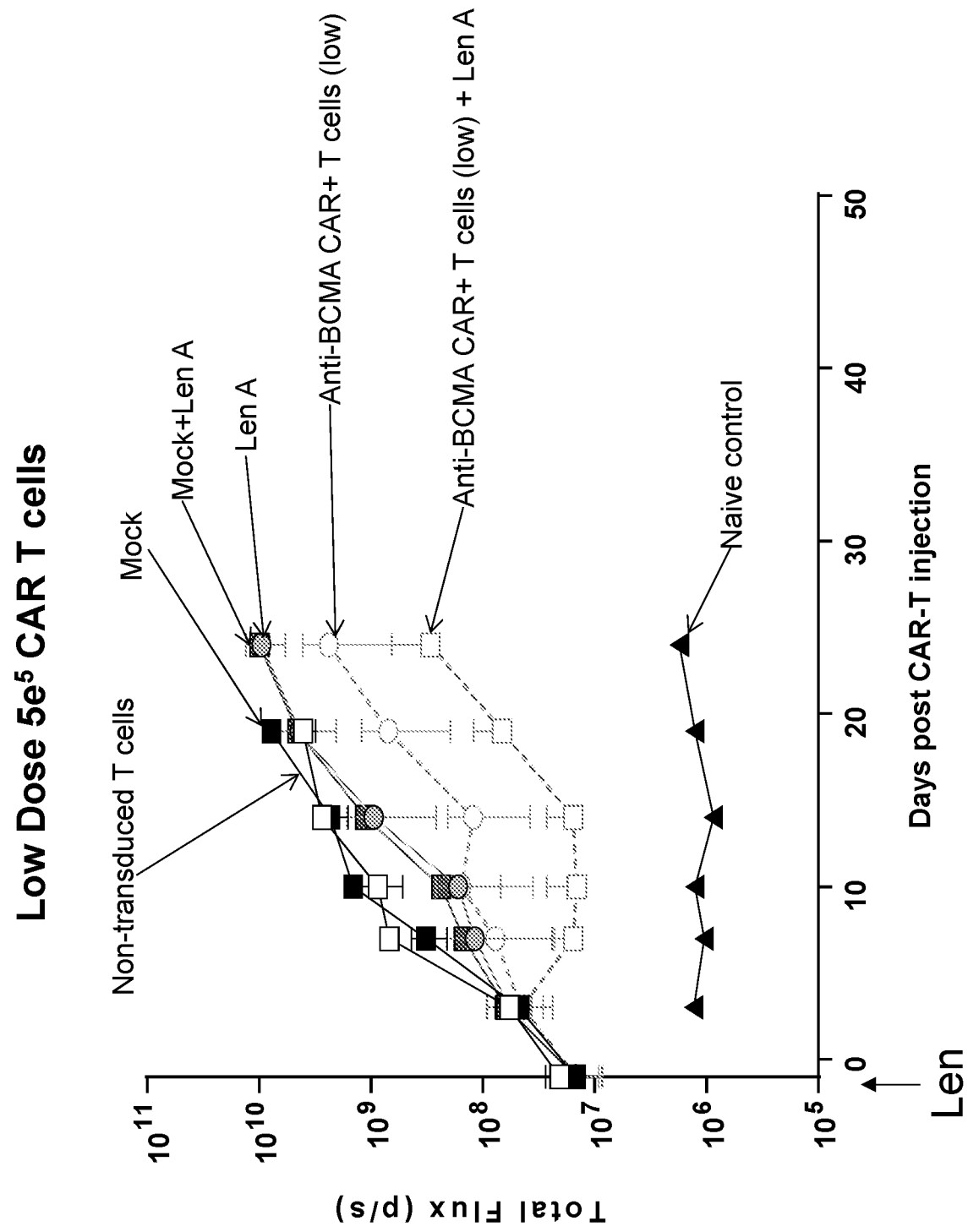
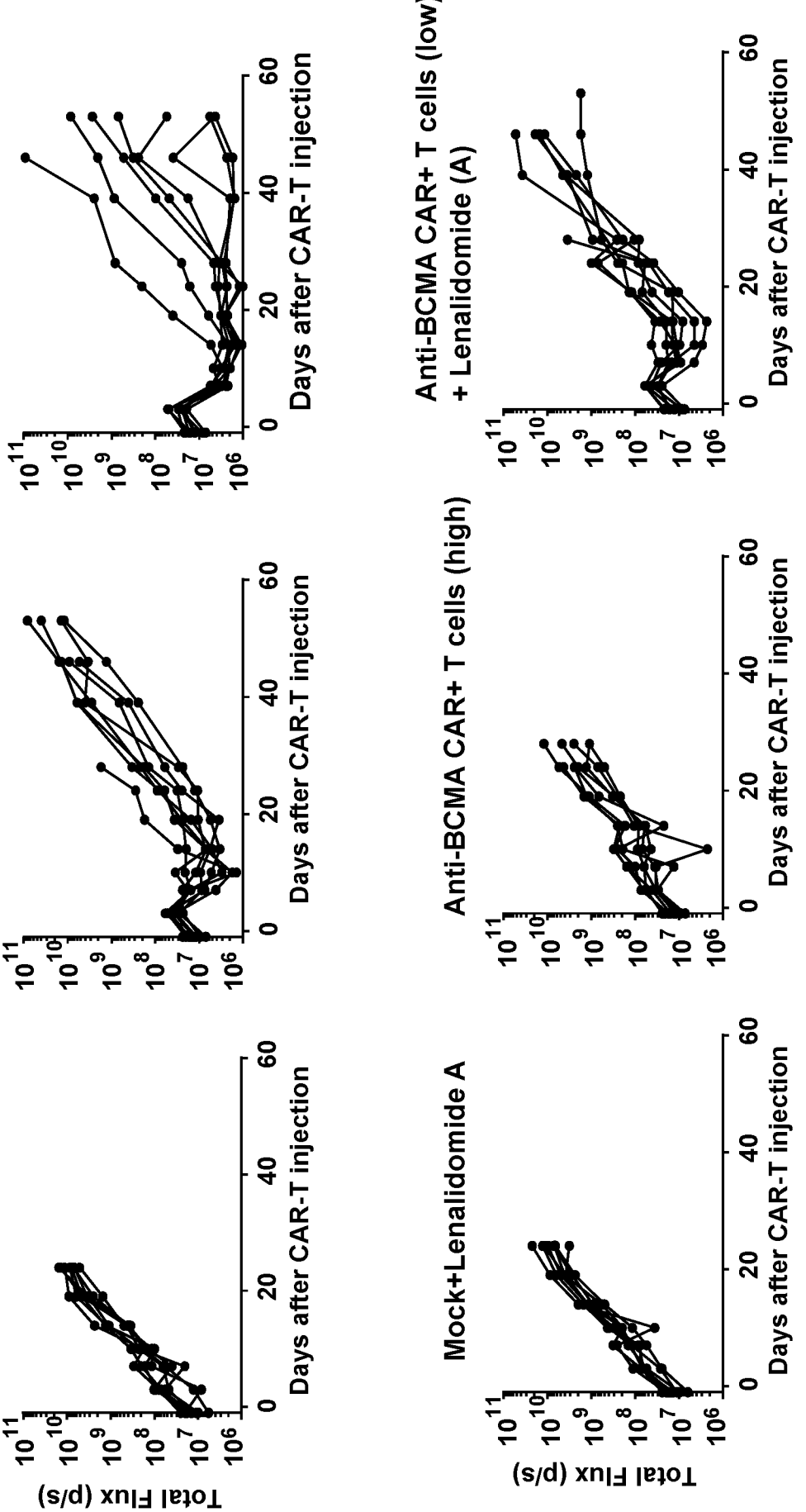

Low Dose 5e5 CAR T cells
Non-transduced T cells
Mock
Mock+Len A
Len A
Anti-BCMA CAR+ T cells (low)
Anti-BCMA CAR+ T cells (low) + Len A
Naive control
Total Flux (p/s)
Days post CAR-T injection
Len

FIG. 9B

FIG. 9C


Lenalidomide A*
Anti-BCMA CAR+ T cells (high)
Anti-BCMA CAR+ T cells (high) + Lenalidomide (A)
Mock+Lenalidomide A
Anti-BCMA CAR+ T cells (high)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (A)
Total Flux (p/s)
Days after CAR-T injection
0
20
40
60
10^{6}
10^{7}
10^{8}
10^{9}
10^{10}
10^{11}

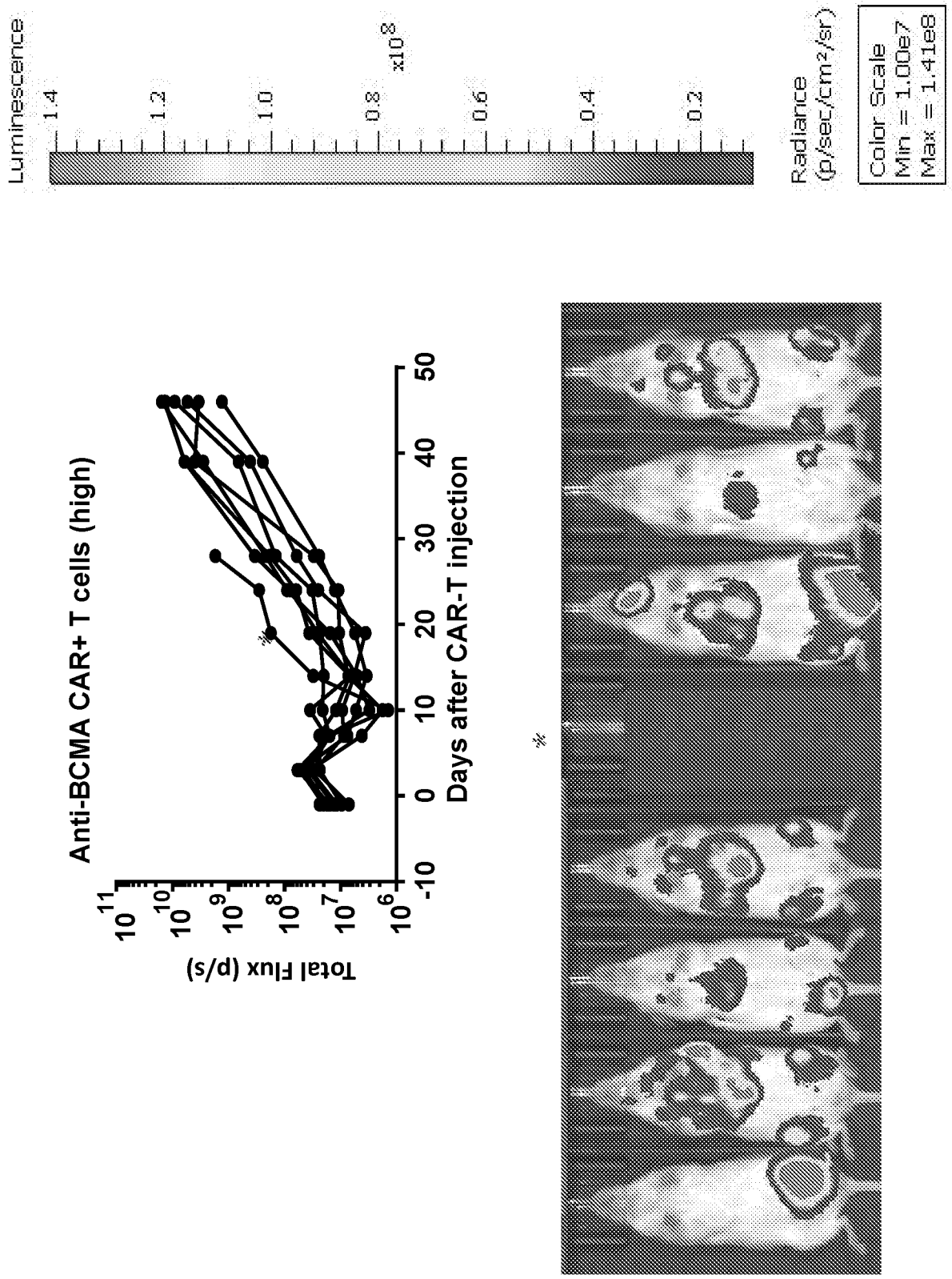

Luminescence
1.4
1.2
1.0
0.8
x10^8
0.6
0.4
0.2
Radiance (p/sec/cm²/sr)
Color Scale
Min = 1.00e7
Max = 1.41e8
Anti-BCMA CAR+ T cells (high)
Total Flux (p/s)
10^11
10^10
10^9
10^8
10^7
10^6
-10
0
10
20
30
40
50
Days after CAR-T injection

FIG. 9D

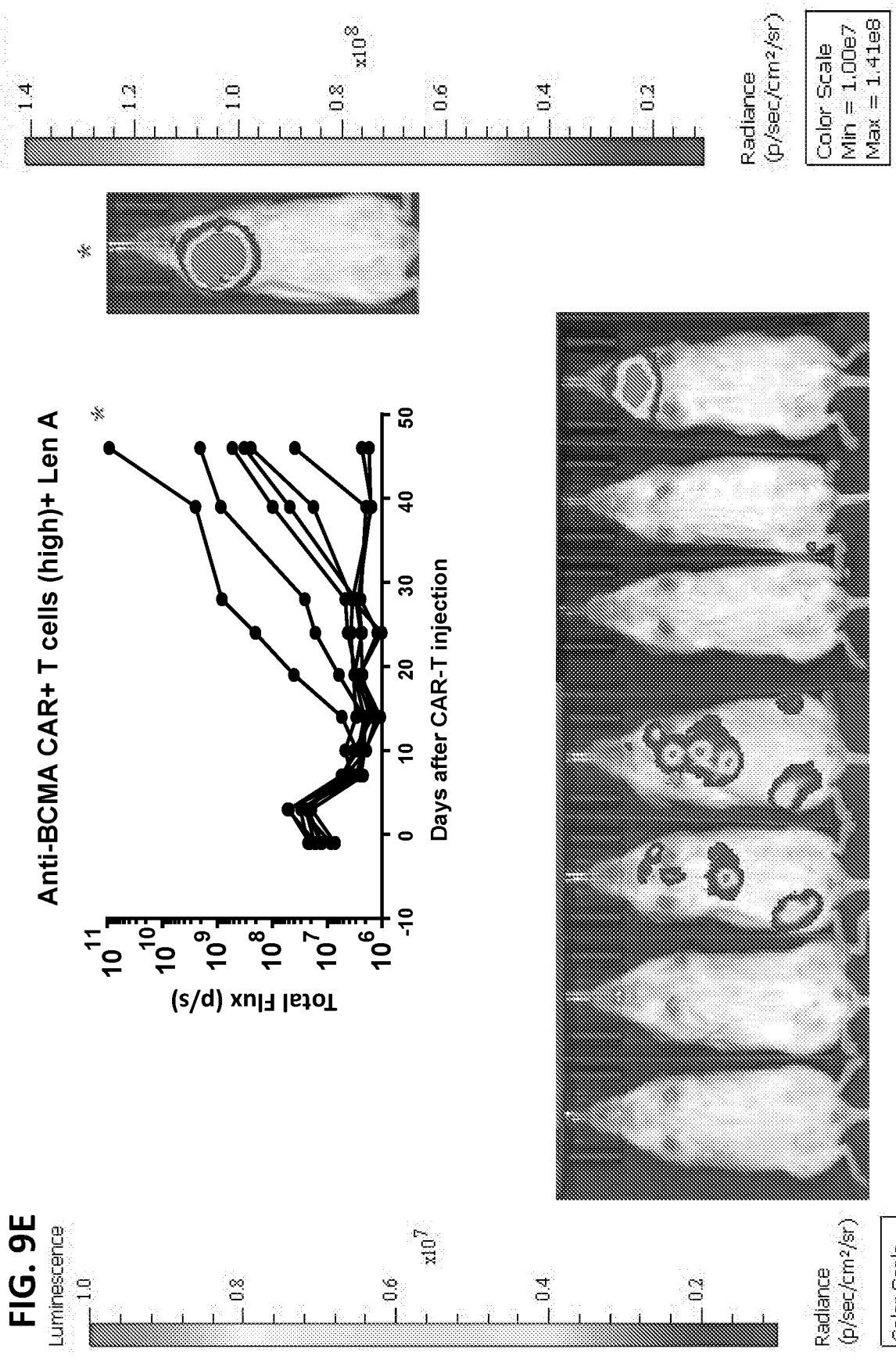

Anti-BCMA CAR+ T cells (high)+ Len A
Total Flux (p/s)
Days after CAR-T injection
Luminescence
Radiance (p/sec/cm²/sr)
Color Scale Min = 1.00e7 Max = 1.41e8
Luminescence
Radiance (p/sec/cm²/sr)
Color Scale Min = 1.00e6 Max = 1.00e7

FIG. 9E

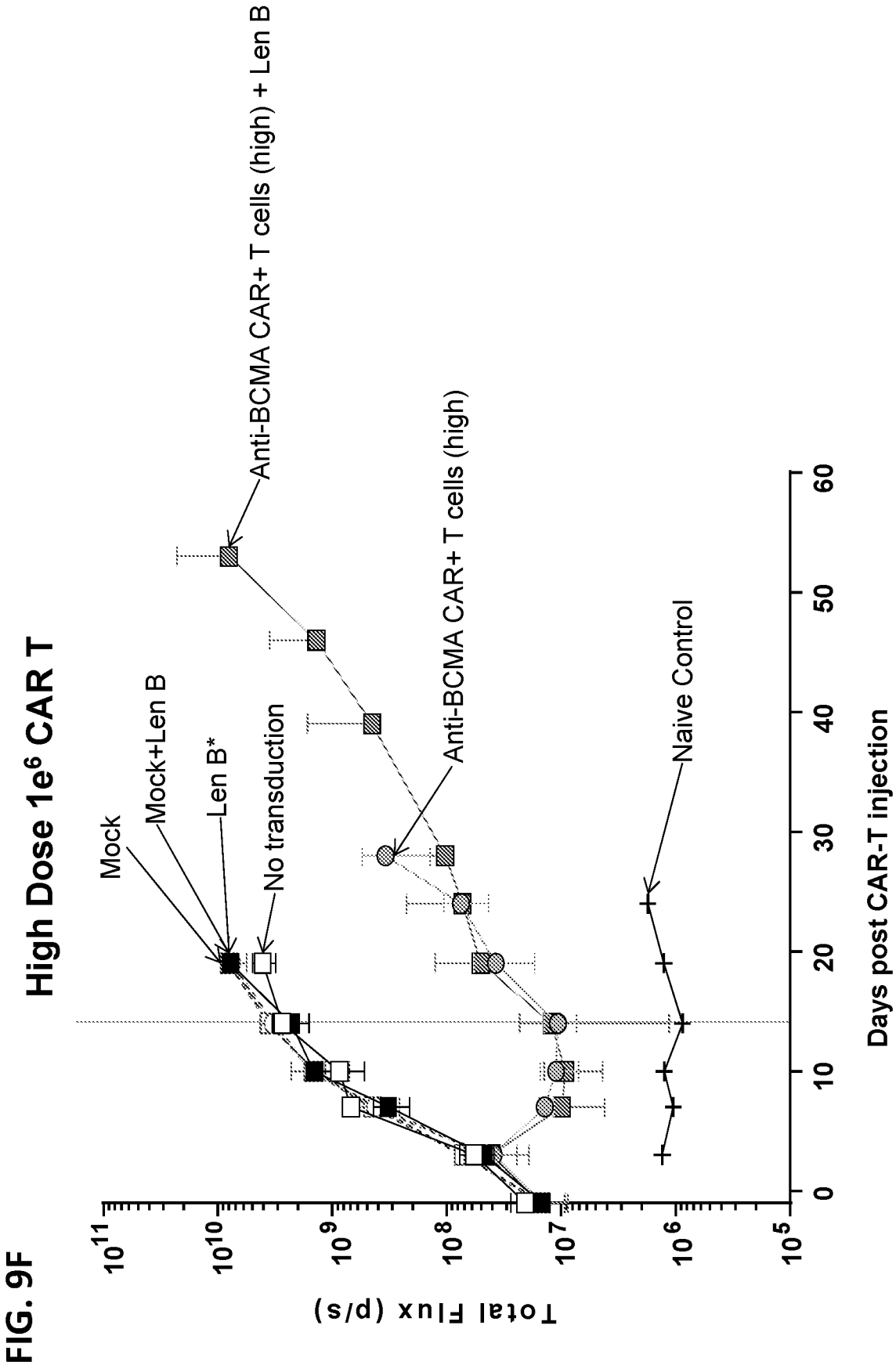

High Dose 1e6 CAR T
Anti-BCMA CAR+ T cells (high) + Len B
Mock
Mock+Len B
Len B*
No transduction
Anti-BCMA CAR+ T cells (high)
Naive Control
Total Flux (p/s)
Days post CAR-T injection
10^11
10^10
10^9
10^8
10^7
10^6
10^5
0
10
20
30
40
50
60

FIG. 9F

FIG. 9G

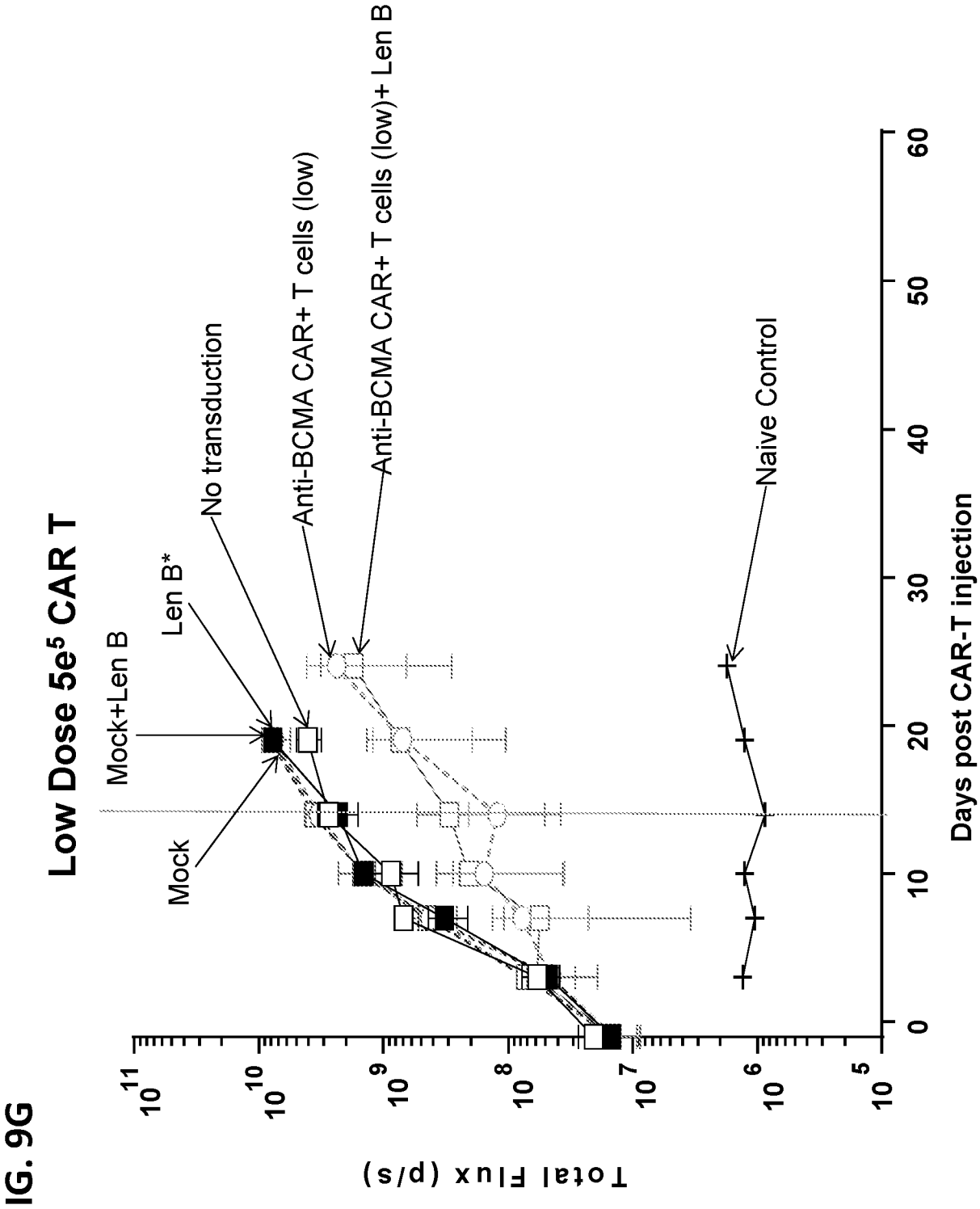
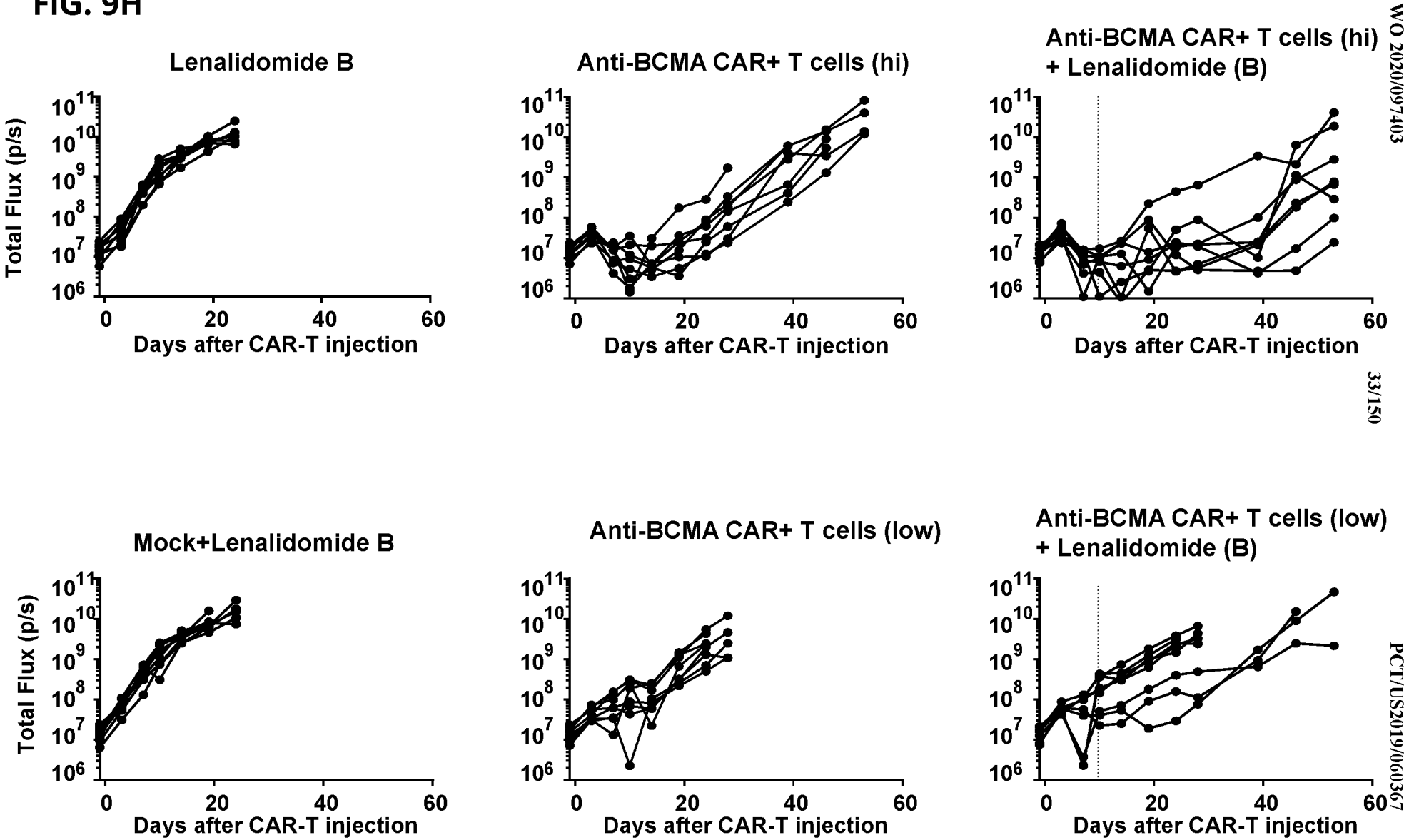

Low Dose 5e5 CAR T
Mock+Len B
Len B*
No transduction
Anti-BCMA CAR+ T cells (low)
Anti-BCMA CAR+ T cells (low)+ Len B
Mock
Naive Control
Total Flux (p/s)
Days post CAR-T injection

FIG. 9H


Lenalidomide B
Anti-BCMA CAR+ T cells (hi)
Anti-BCMA CAR+ T cells (hi) + Lenalidomide (B)
Mock+Lenalidomide B
Anti-BCMA CAR+ T cells (low)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (B)
Total Flux (p/s)
Days after CAR-T injection

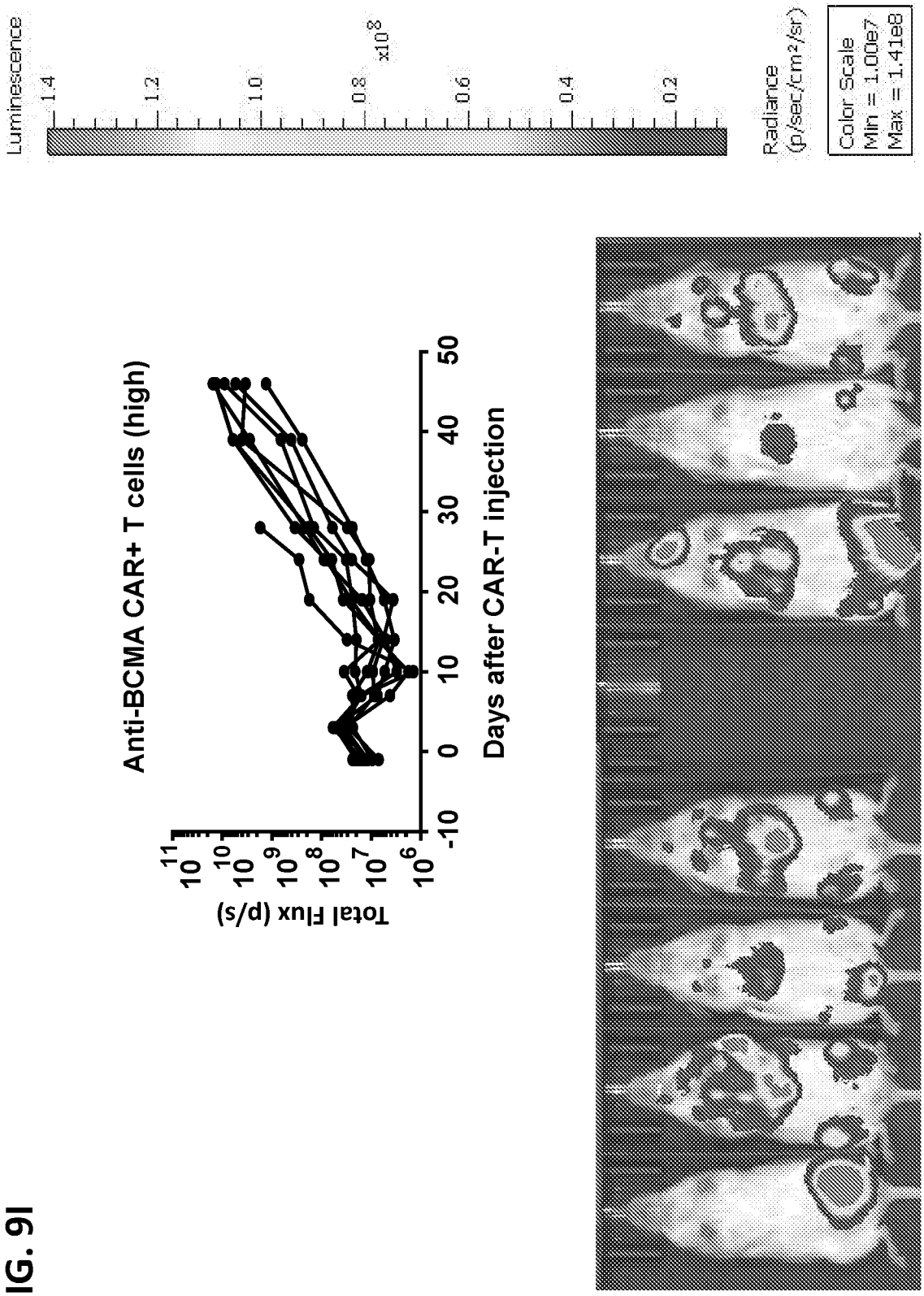

Luminescence
1.4
1.2
1.0
0.8
x10^8
0.6
0.4
0.2
Radiance
(p/sec/cm²/sr)
Color Scale
Min = 1.00e7
Max = 1.41e8
Anti-BCMA CAR+ T cells (high)
Total Flux (p/s)
10^11
10^10
10^9
10^8
10^7
10^6
-10
0
10
20
30
40
50
Days after CAR-T injection

FIG. 9I

FIG. 9J

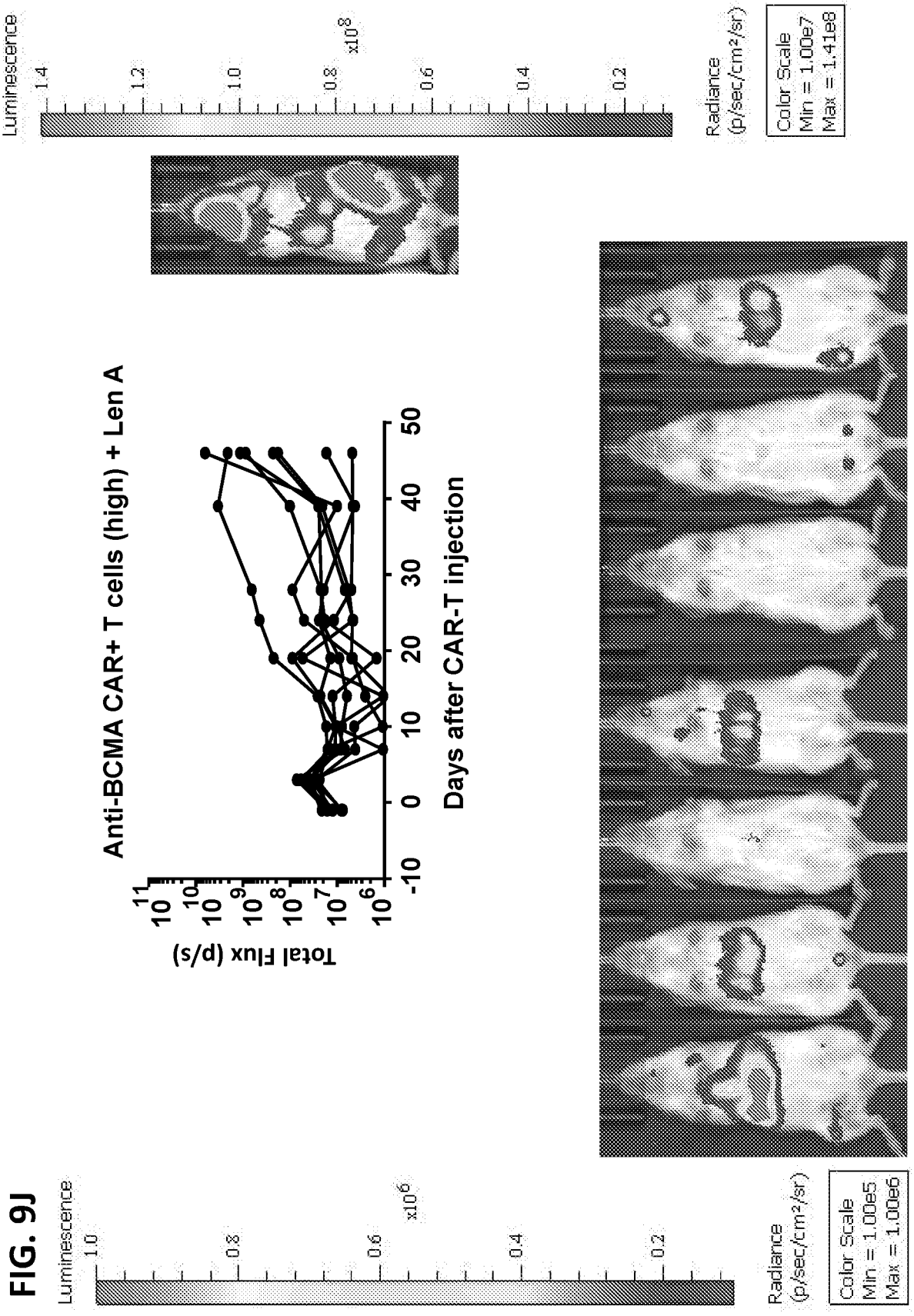

Luminescence
1.0
0.8
0.6
0.4
0.2
x10^6
Radiance (p/sec/cm²/sr)
Color Scale
Min = 1.00e5
Max = 1.00e6
Anti-BCMA CAR+ T cells (high) + Len A
Total Flux (p/s)
Days after CAR-T injection
-10
0
10
20
30
40
50
Luminescence
1.4
1.2
1.0
0.8
0.6
0.4
0.2
x10^8
Radiance (p/sec/cm²/sr)
Color Scale
Min = 1.00e7
Max = 1.41e8

FIG. 10A

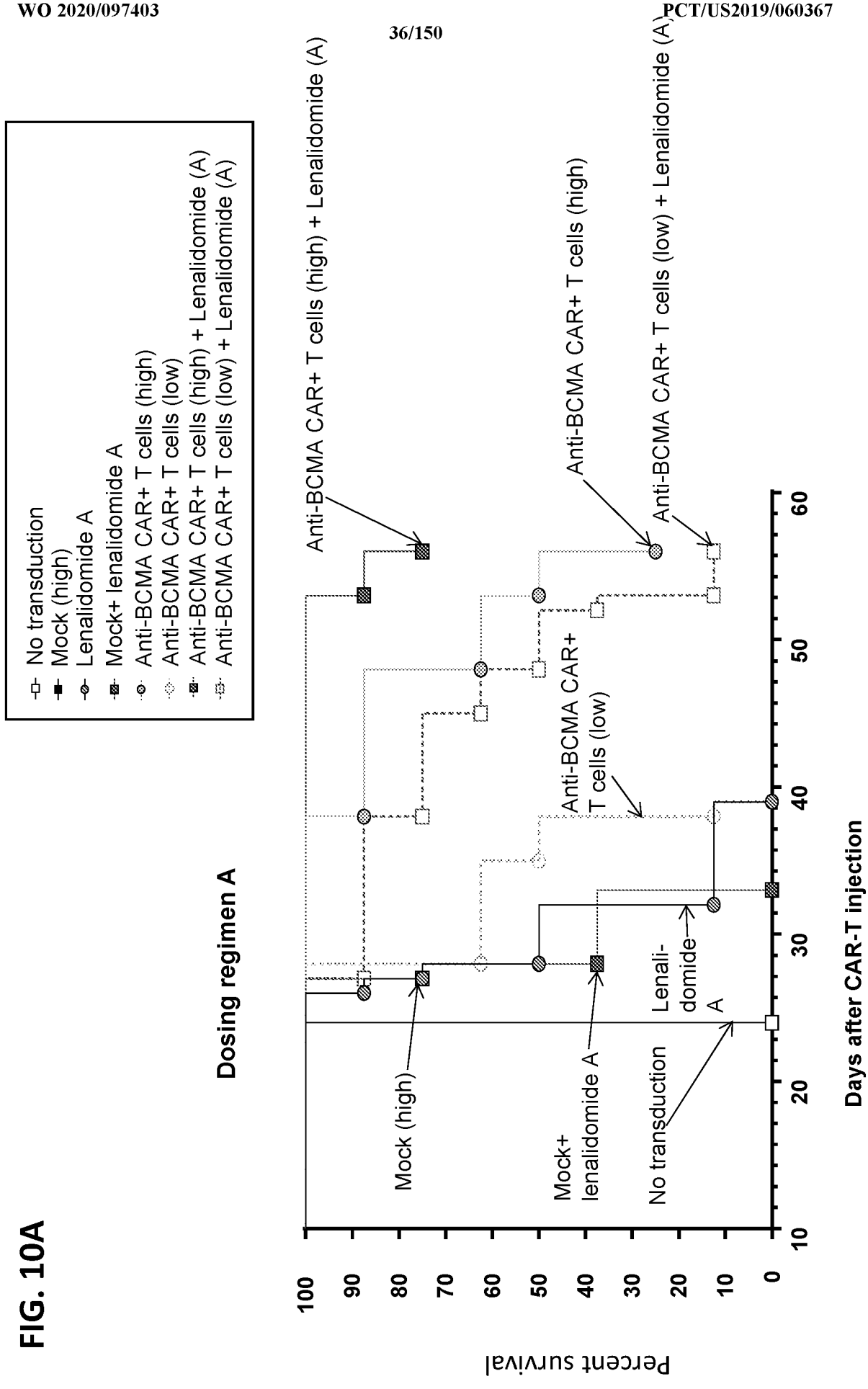

No transduction
Mock (high)
Lenalidomide A
Mock+ lenalidomide A
Anti-BCMA CAR+ T cells (high)
Anti-BCMA CAR+ T cells (low)
Anti-BCMA CAR+ T cells (high) + Lenalidomide (A)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (A)
Dosing regimen A
Anti-BCMA CAR+ T cells (high) + Lenalidomide (A)
Anti-BCMA CAR+ T cells (high)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (A)
Anti-BCMA CAR+ T cells (low)
Mock (high)
Mock+ lenalidomide A
No transduction
Lenali-domide A
Percent survival
Days after CAR-T injection
0
10
20
30
40
50
60
70
80
90
100

FIG. 10B

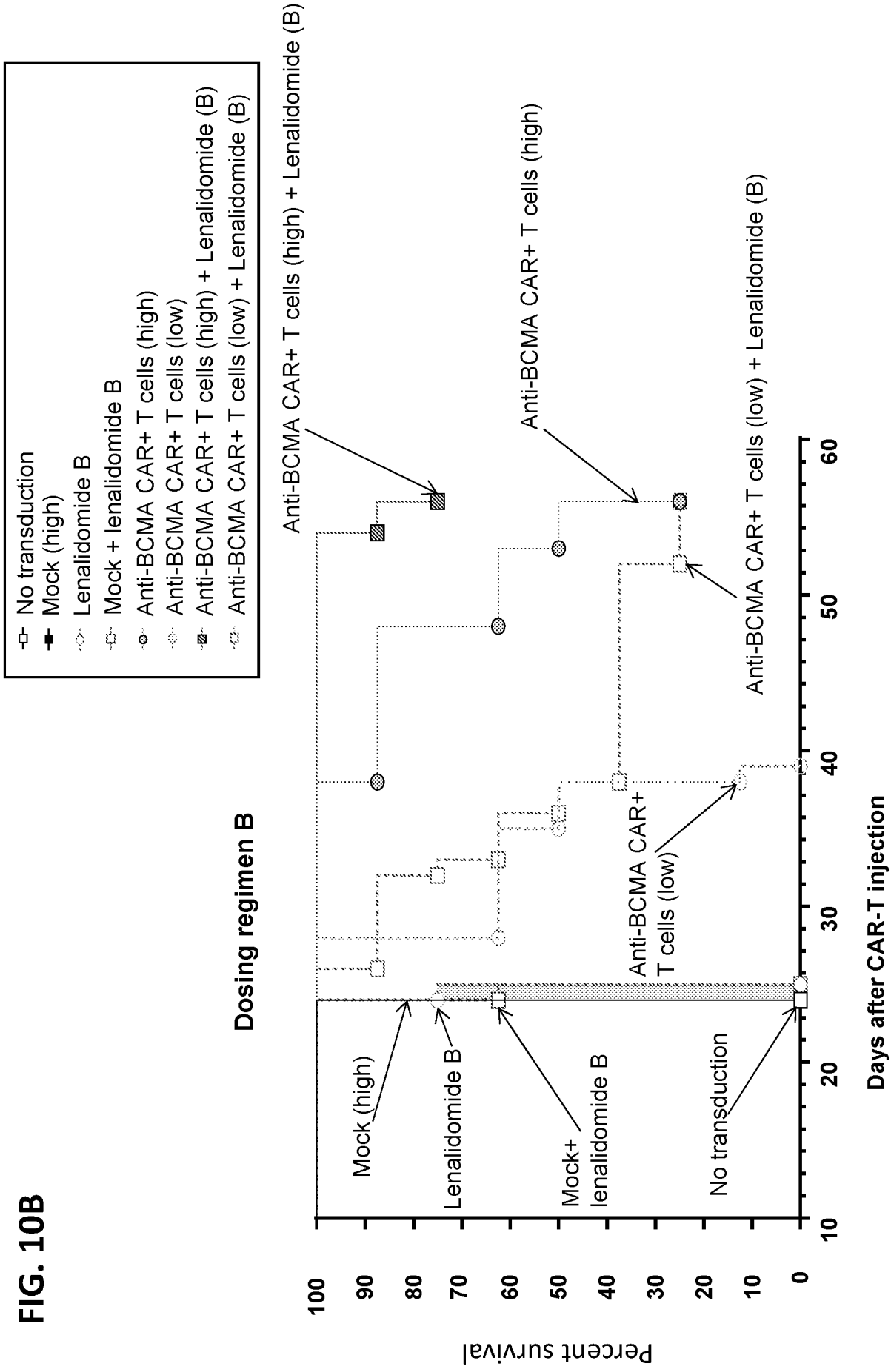

No transduction
Mock (high)
Lenalidomide B
Mock + lenalidomide B
Anti-BCMA CAR+ T cells (high)
Anti-BCMA CAR+ T cells (low)
Anti-BCMA CAR+ T cells (high) + Lenalidomide (B)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (B)
Dosing regimen B
Percent survival
Days after CAR-T injection
Mock (high)
Lenalidomide B
Mock+ lenalidomide B
No transduction
Anti-BCMA CAR+ T cells (low)
Anti-BCMA CAR+ T cells (high)
Anti-BCMA CAR+ T cells (high) + Lenalidomide (B)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (B)

FIG. 10C

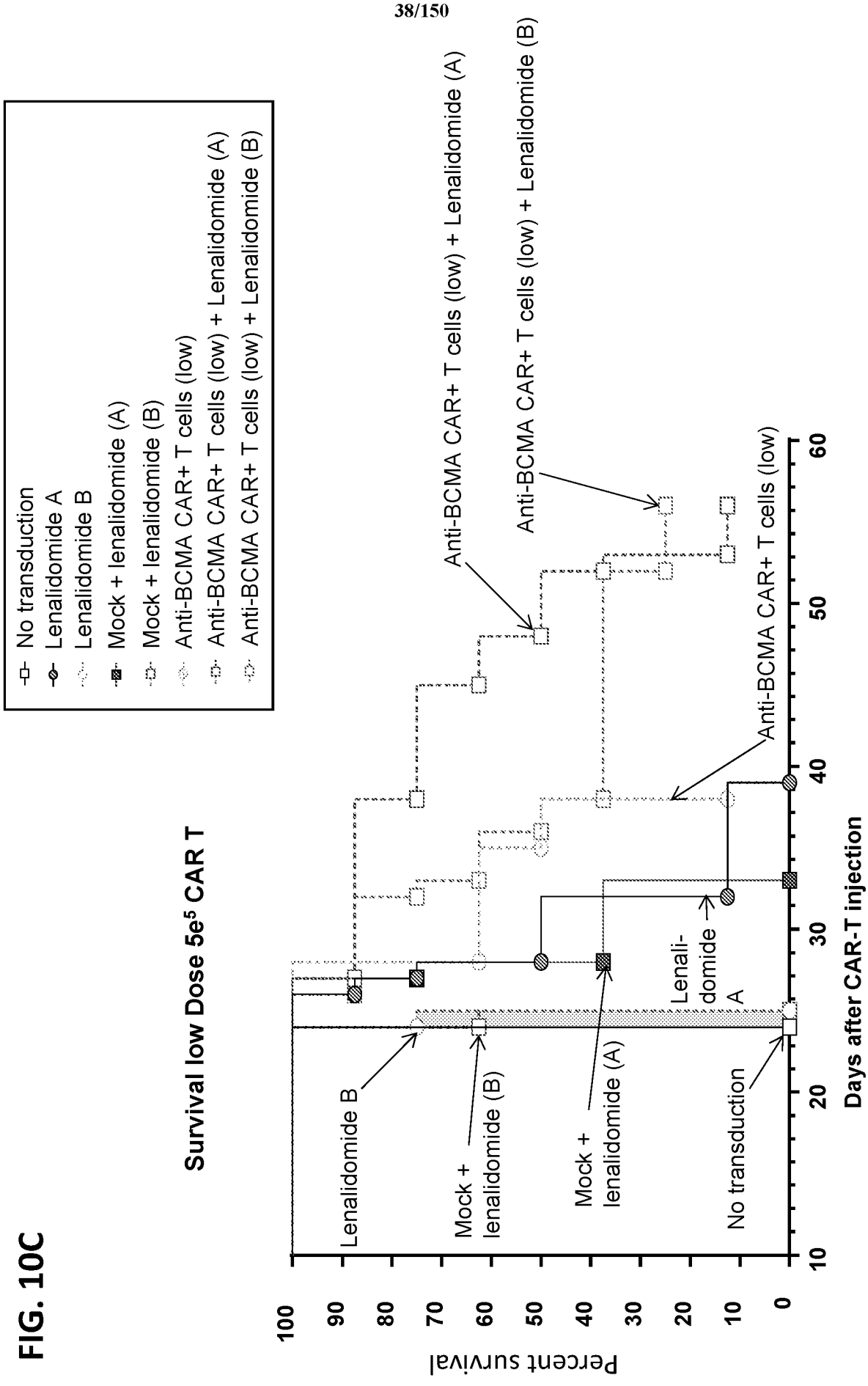

No transduction
Lenalidomide A
Lenalidomide B
Mock + lenalidomide (A)
Mock + lenalidomide (B)
Anti-BCMA CAR+ T cells (low)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (A)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (B)
Survival low Dose 5e5 CAR T
Percent survival
Days after CAR-T injection
Lenalidomide B
Mock + lenalidomide (B)
Mock + lenalidomide (A)
No transduction
Lenali-domide A
Anti-BCMA CAR+ T cells (low) + Lenalidomide (A)
Anti-BCMA CAR+ T cells (low) + Lenalidomide (B)
Anti-BCMA CAR+ T cells (low)

FIG. 10D

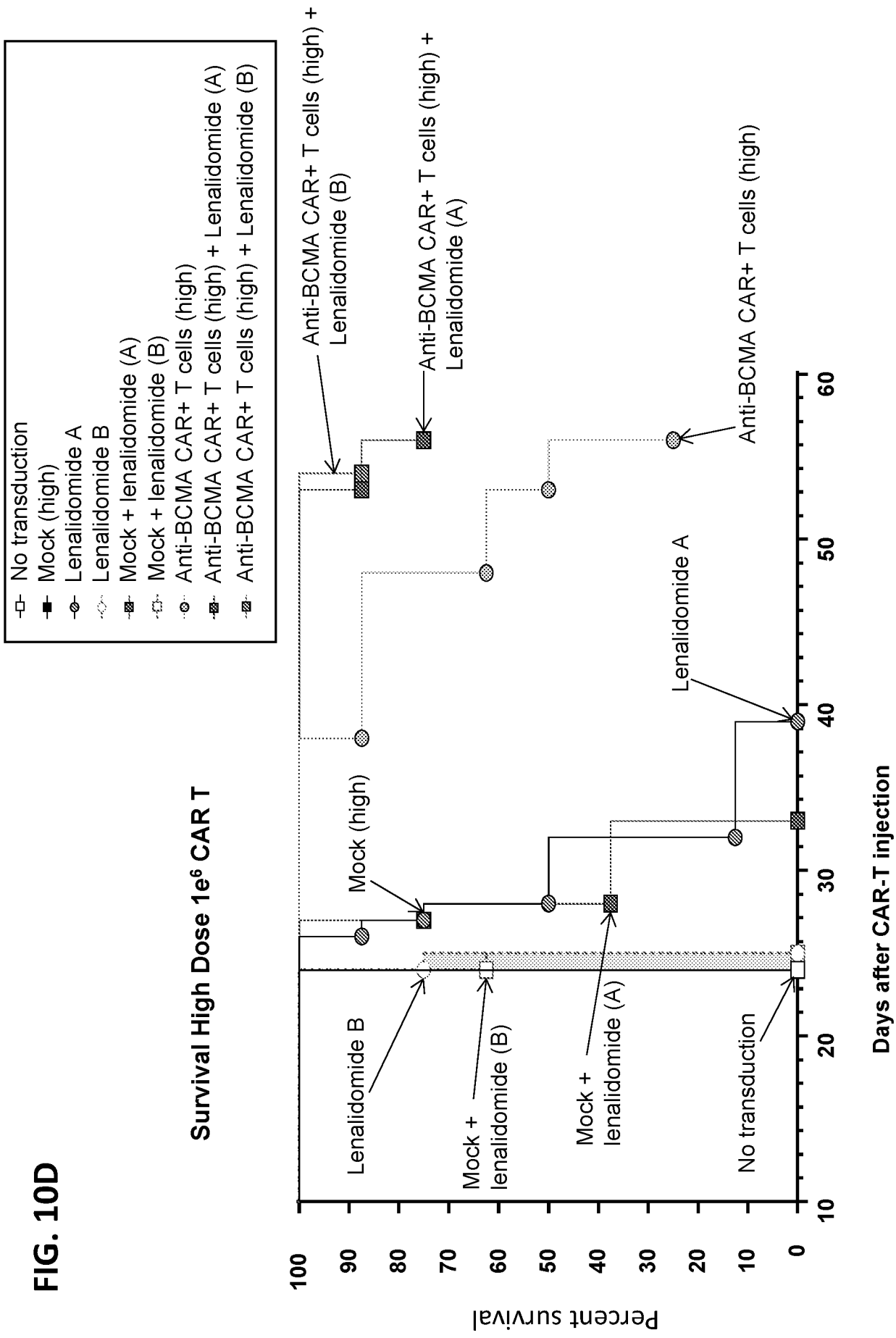
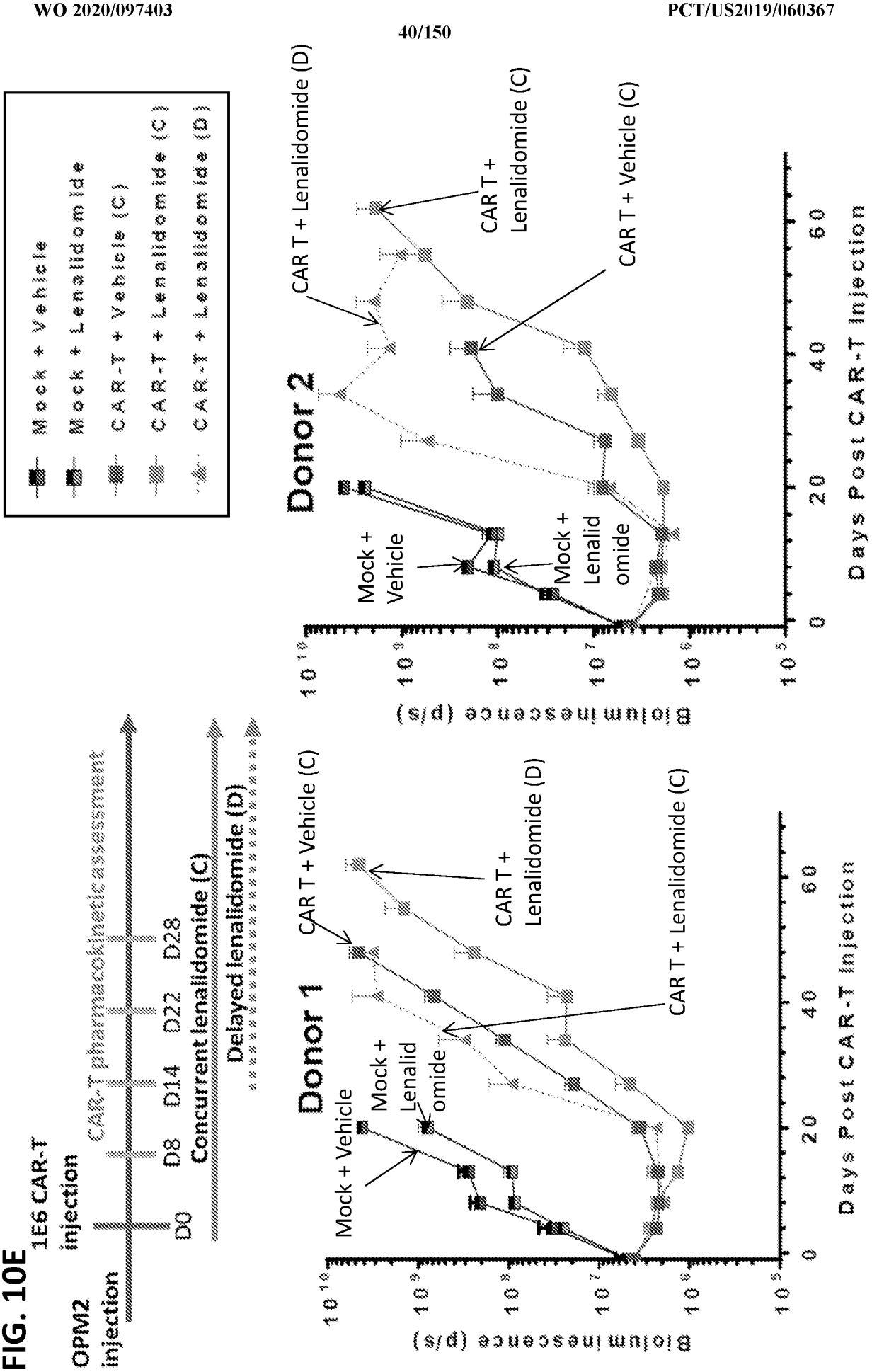

Survival High Dose 1e6 CAR T
No transduction
Mock (high)
Lenalidomide A
Lenalidomide B
Mock + lenalidomide (A)
Mock + lenalidomide (B)
Anti-BCMA CAR+ T cells (high)
Anti-BCMA CAR+ T cells (high) + Lenalidomide (A)
Anti-BCMA CAR+ T cells (high) + Lenalidomide (B)
Anti-BCMA CAR+ T cells (high) + Lenalidomide (B)
Anti-BCMA CAR+ T cells (high) + Lenalidomide (A)
Anti-BCMA CAR+ T cells (high)
Mock (high)
Lenalidomide A
Lenalidomide B
Mock + lenalidomide (B)
Mock + lenalidomide (A)
No transduction
Percent survival
Days after CAR-T injection
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60

FIG. 10E


1E6 CAR-T injection
OPM2 injection
CAR-T pharmacokinetic assessment
D0
D8
D14
D22
D28
Concurrent lenalidomide (C)
Delayed lenalidomide (D)
Mock + Vehicle
Mock + Lenalidomide
CAR-T + Vehicle (C)
CAR-T + Lenalidomide (C)
CAR-T + Lenalidomide (D)
Donor 1
Donor 2
Mock + Vehicle
Mock + Lenalidomide
CAR T + Vehicle (C)
CAR T + Lenalidomide (D)
CAR T + Lenalidomide (C)
Bioluminescence (p/s)
Days Post CAR-T Injection

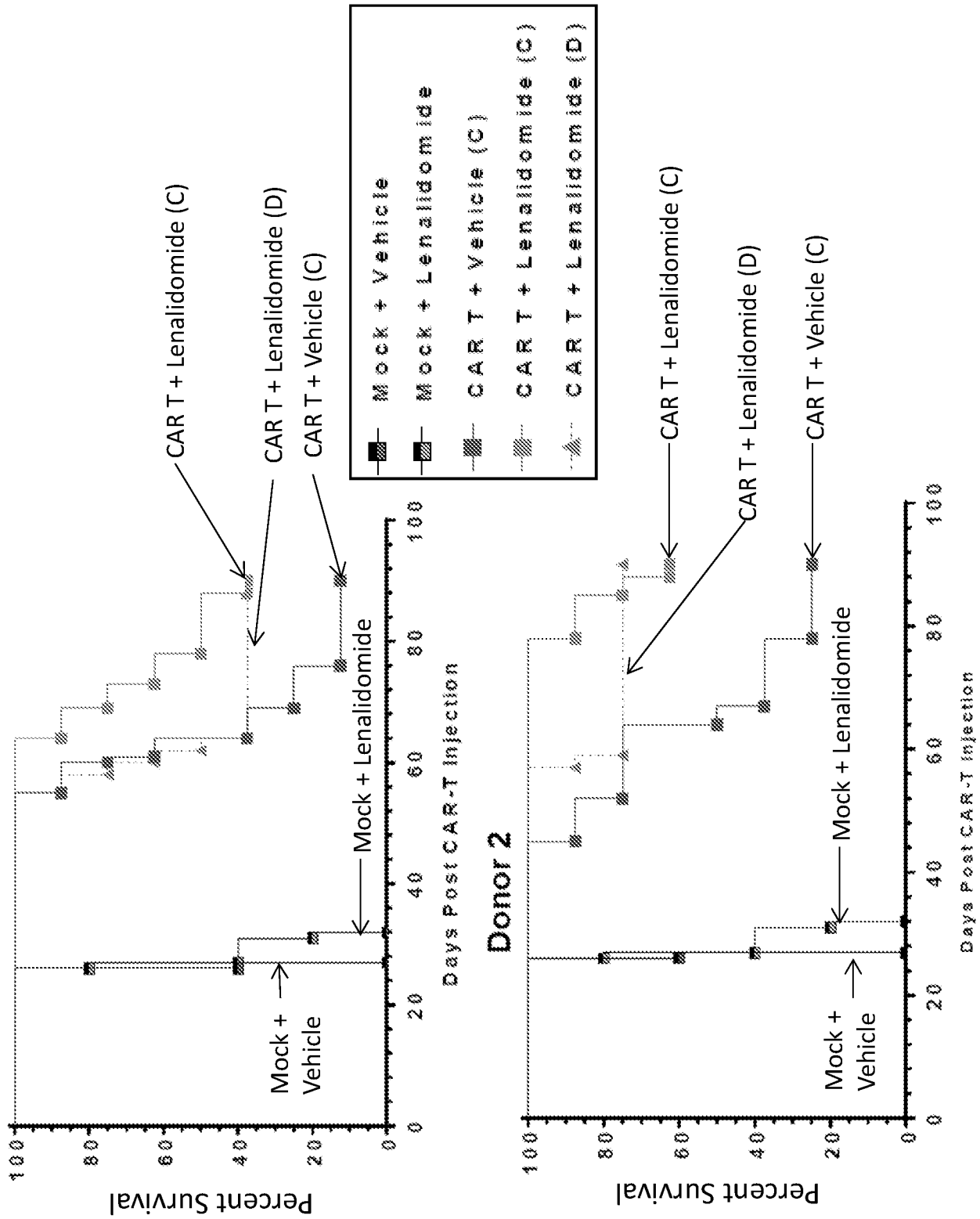

Donor 1
Donor 2
Percent Survival
Days Post CAR-T Injection
Mock + Vehicle
Mock + Lenalidomide
CAR T + Vehicle (C)
CAR T + Lenalidomide (D)
CAR T + Lenalidomide (C)
0
20
40
60
80
100

FIG. 10F

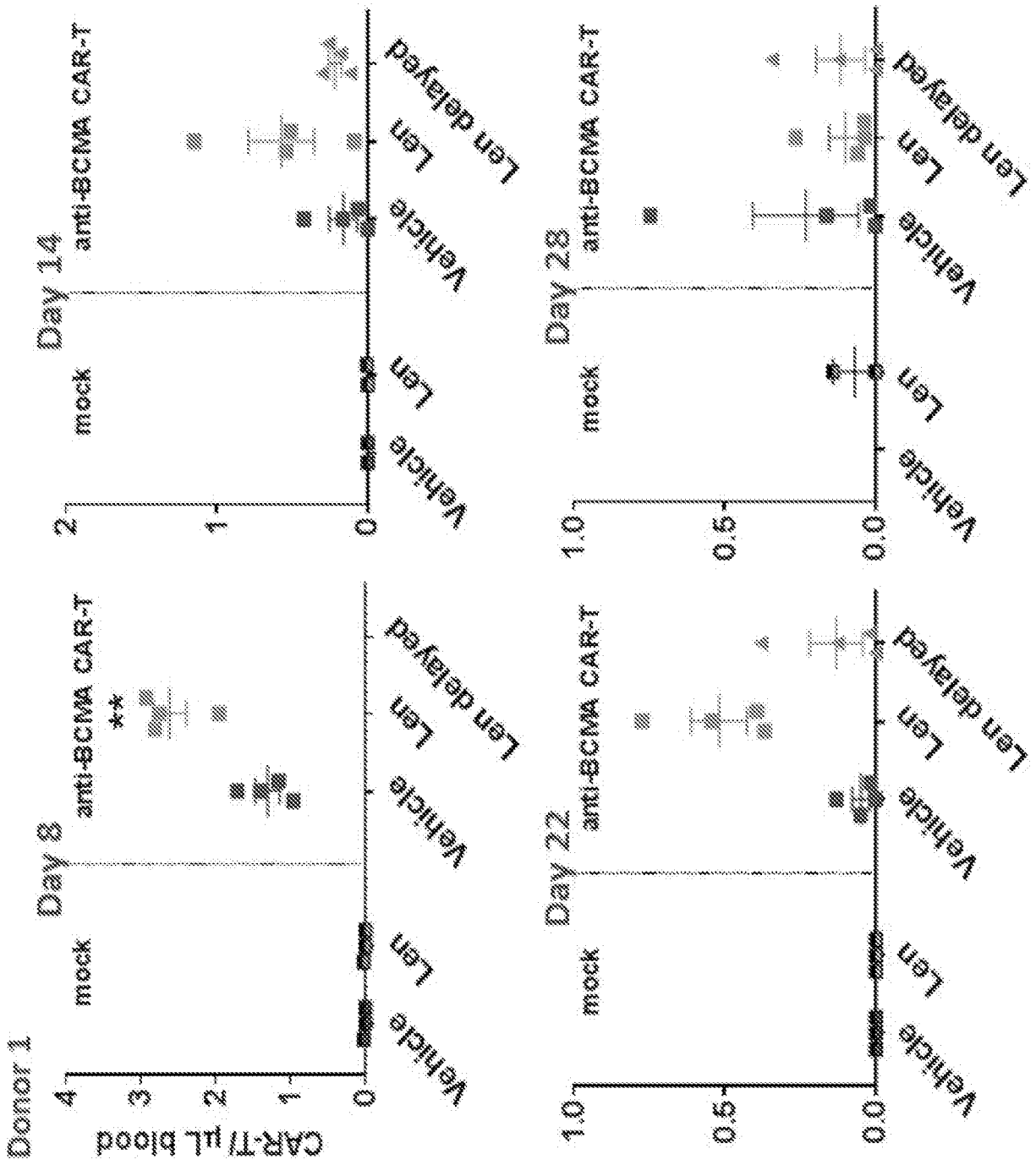

Donor 1
CAR-T/ µL blood
Day 8
Day 14
Day 22
Day 28
mock
anti-BCMA CAR-T
Vehicle
Len
Len delayed
**

FIG. 10G

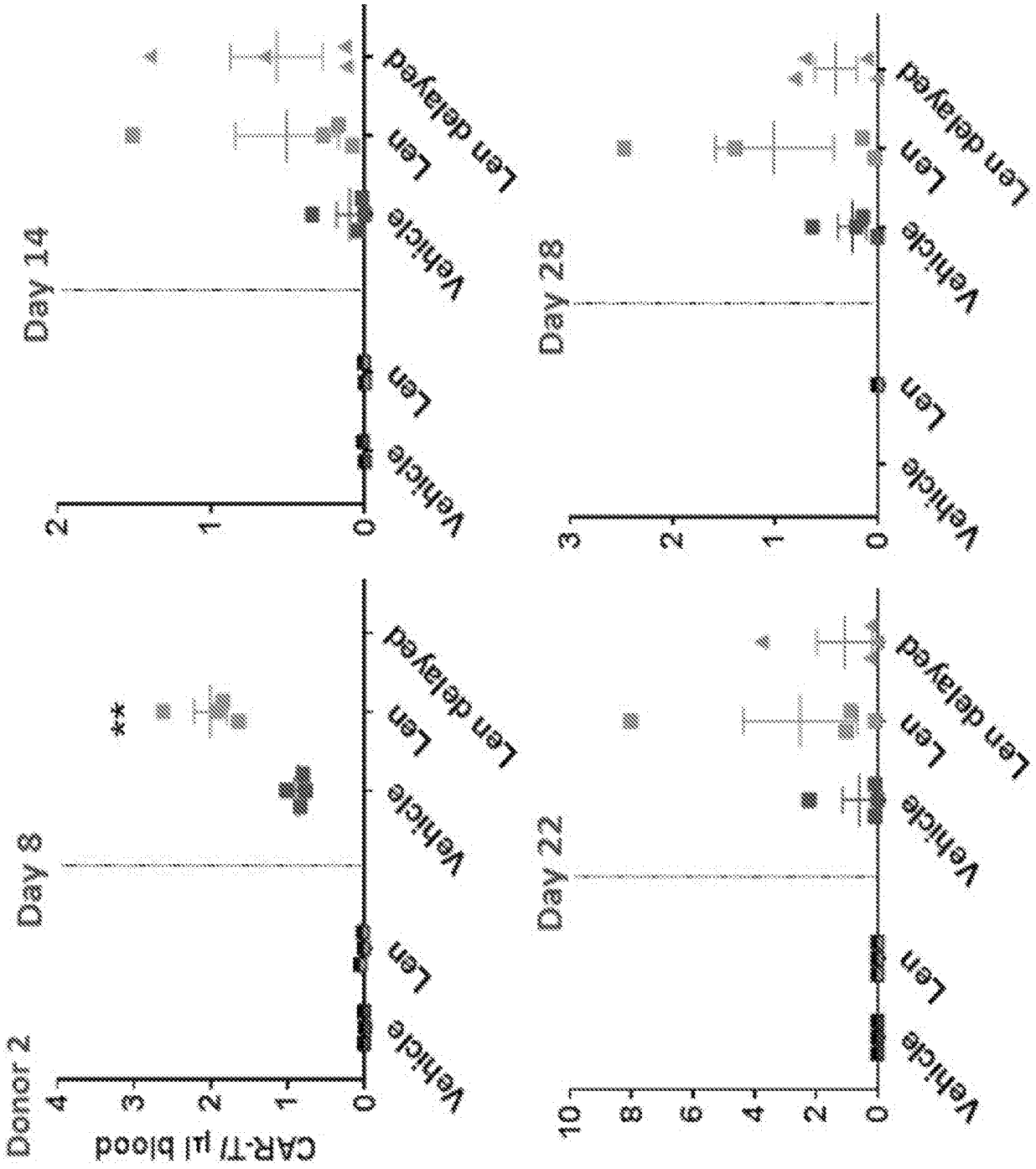

Donor 2
CAR-T/ µl blood
Day 8
Day 14
Day 22
Day 28
Vehicle
Len
Len delayed
**

FIG. 10H

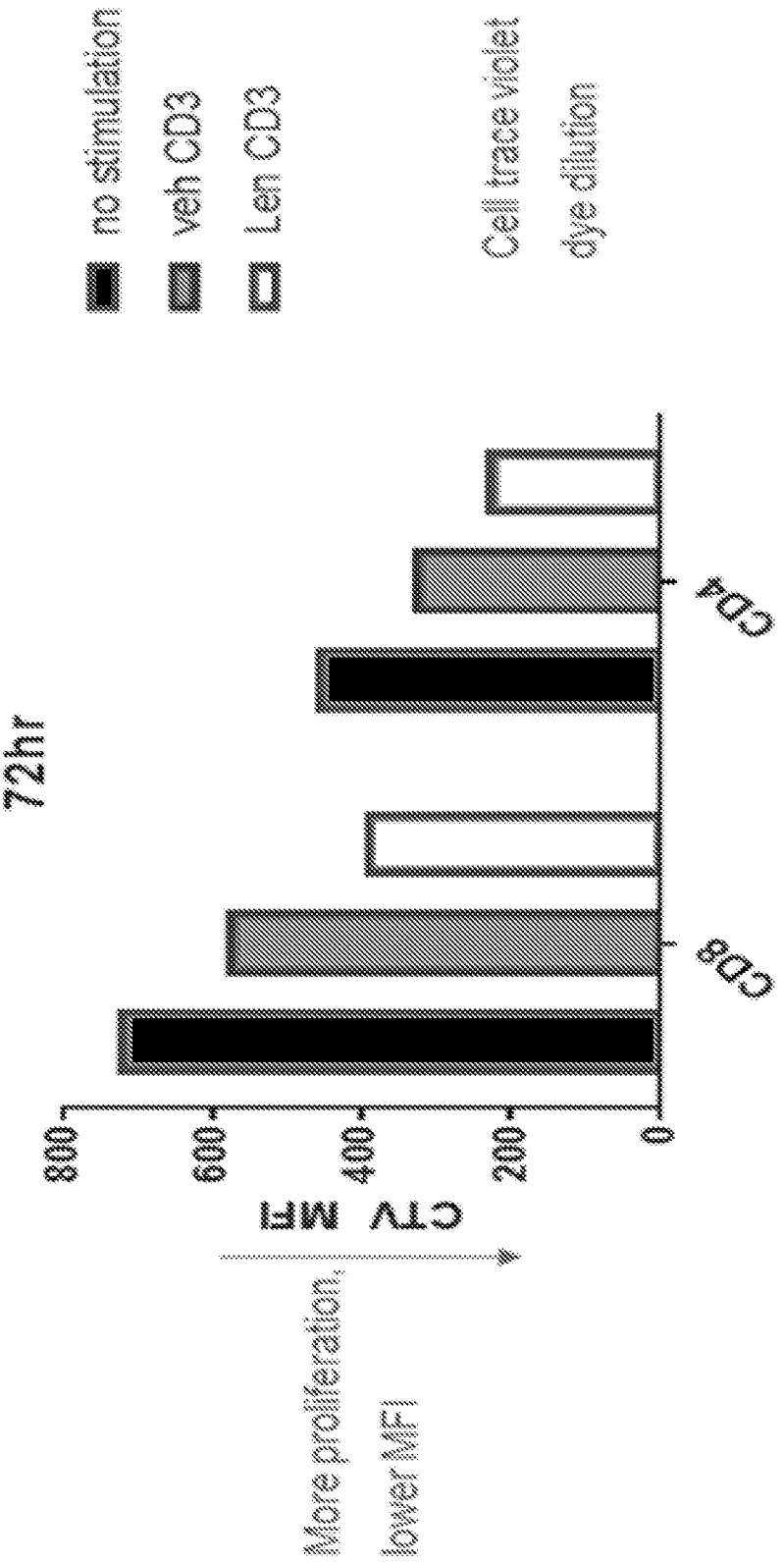

no stimulation
veh CD3
Len CD3
Cell trace violet
dye dilution
72hr
CD4
CD8
CTV MFI
800
600
400
200
0
More proliferation,
lower MFI

FIG. 11

FIG. 12A

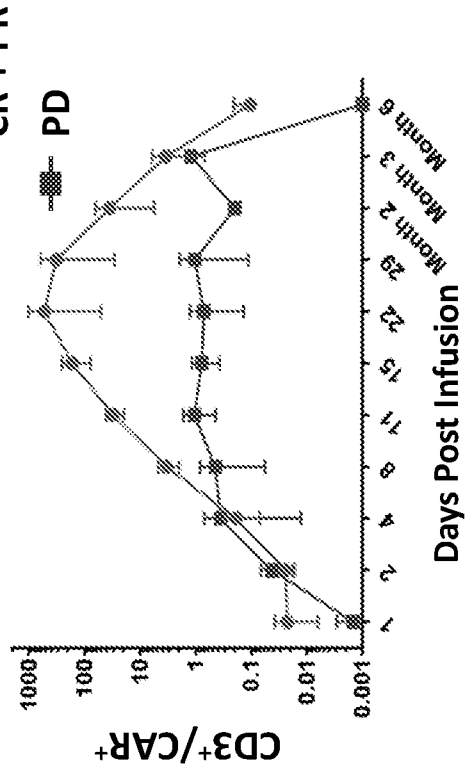


FIG. 12B

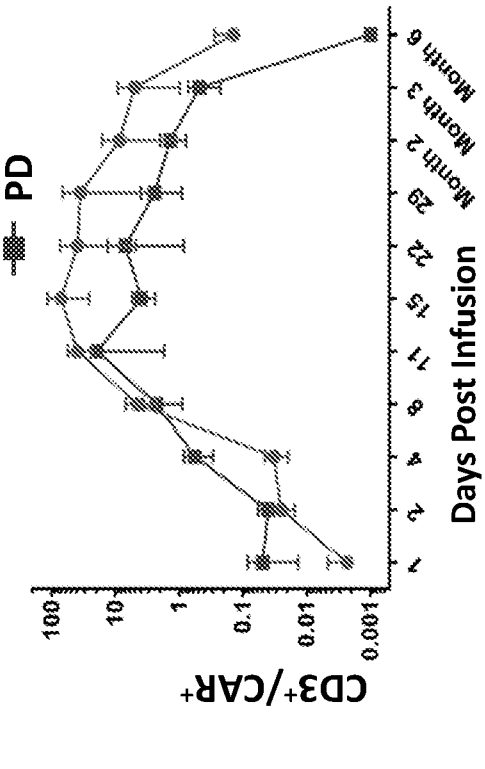


FIG. 12C

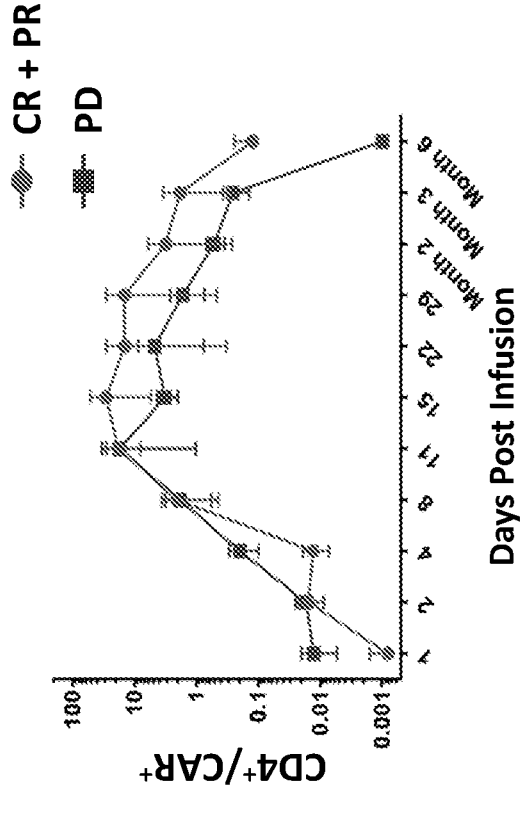


FIG. 12D

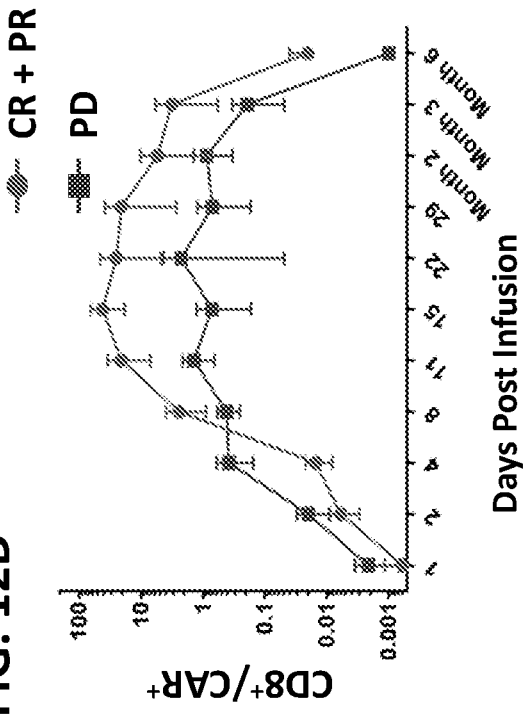


FIG. 13A

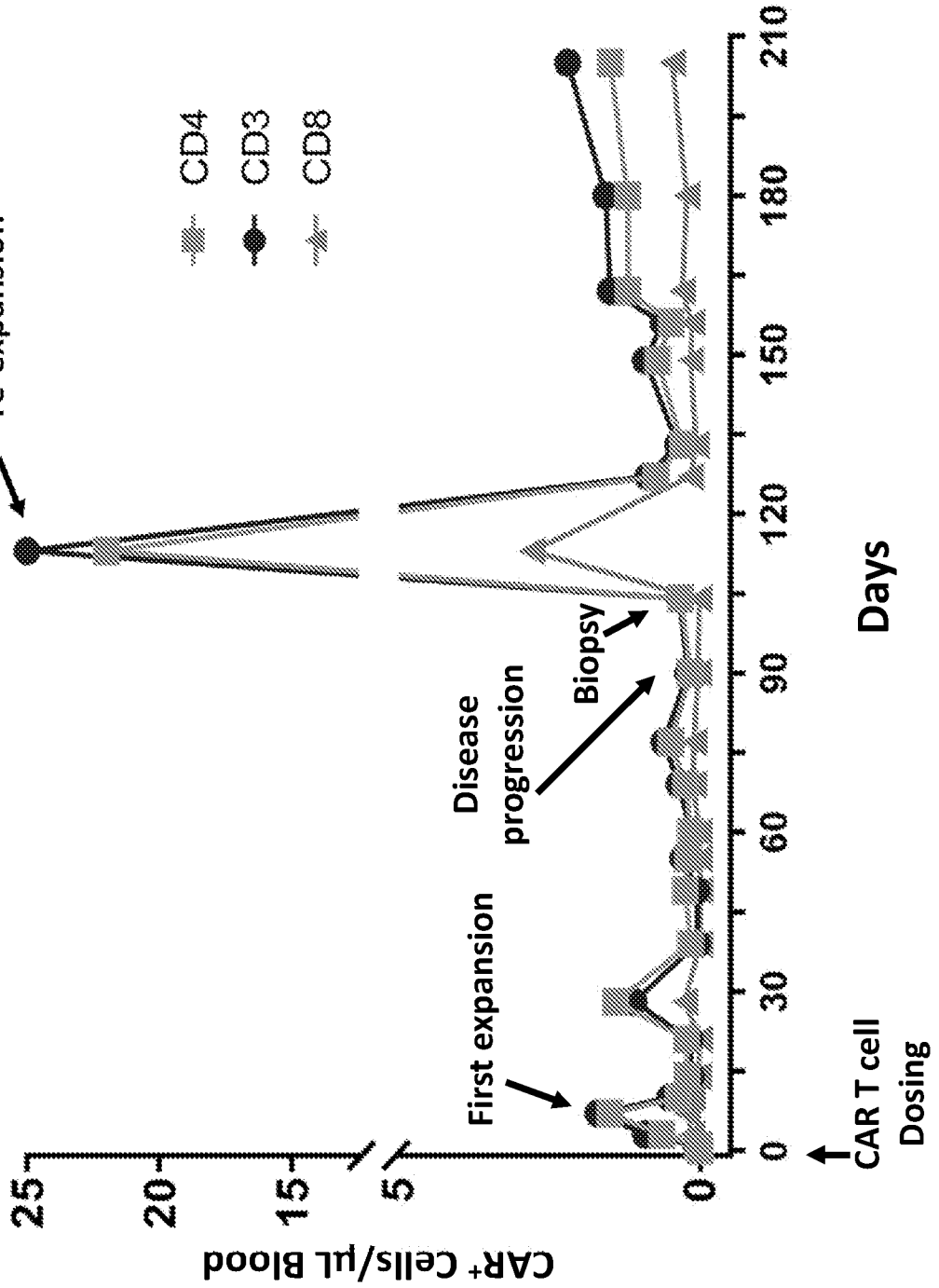

CAR+ Cells/μL Blood
25
20
15
5
0
0
30
60
90
120
150
180
210
Days
CAR T cell Dosing
First expansion
Disease progression
Biopsy
Spontaneous re-expansion
CD4
CD3
CD8

FIG. 13D



FIG. 13G

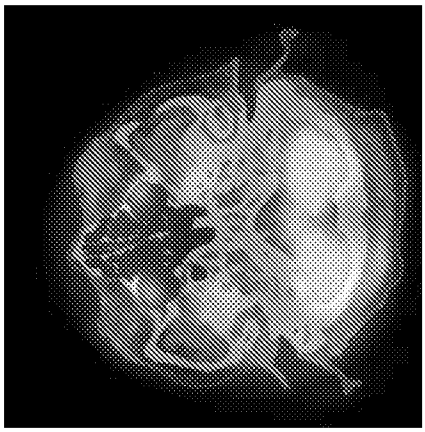


FIG. 13C

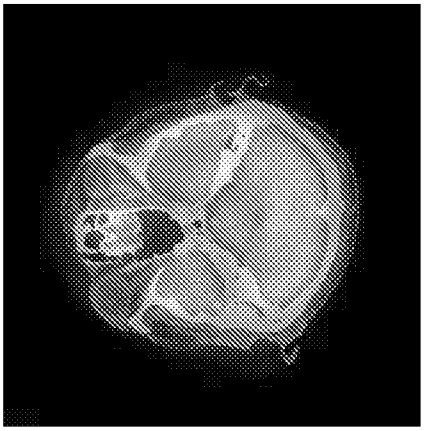


FIG. 13F

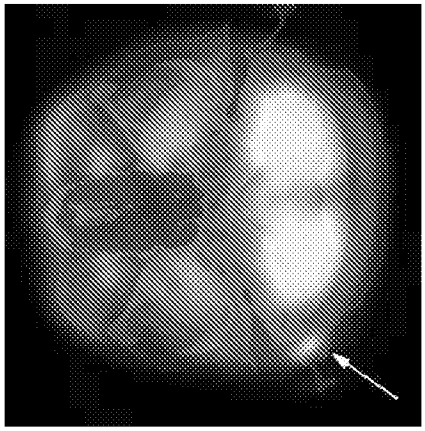


FIG. 13B

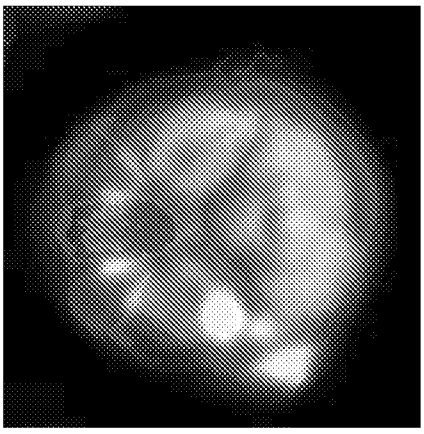


FIG. 13E

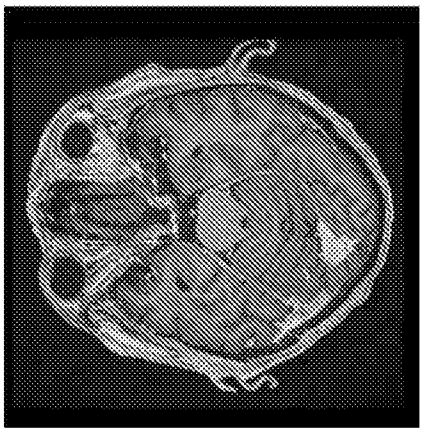


FIG. 14

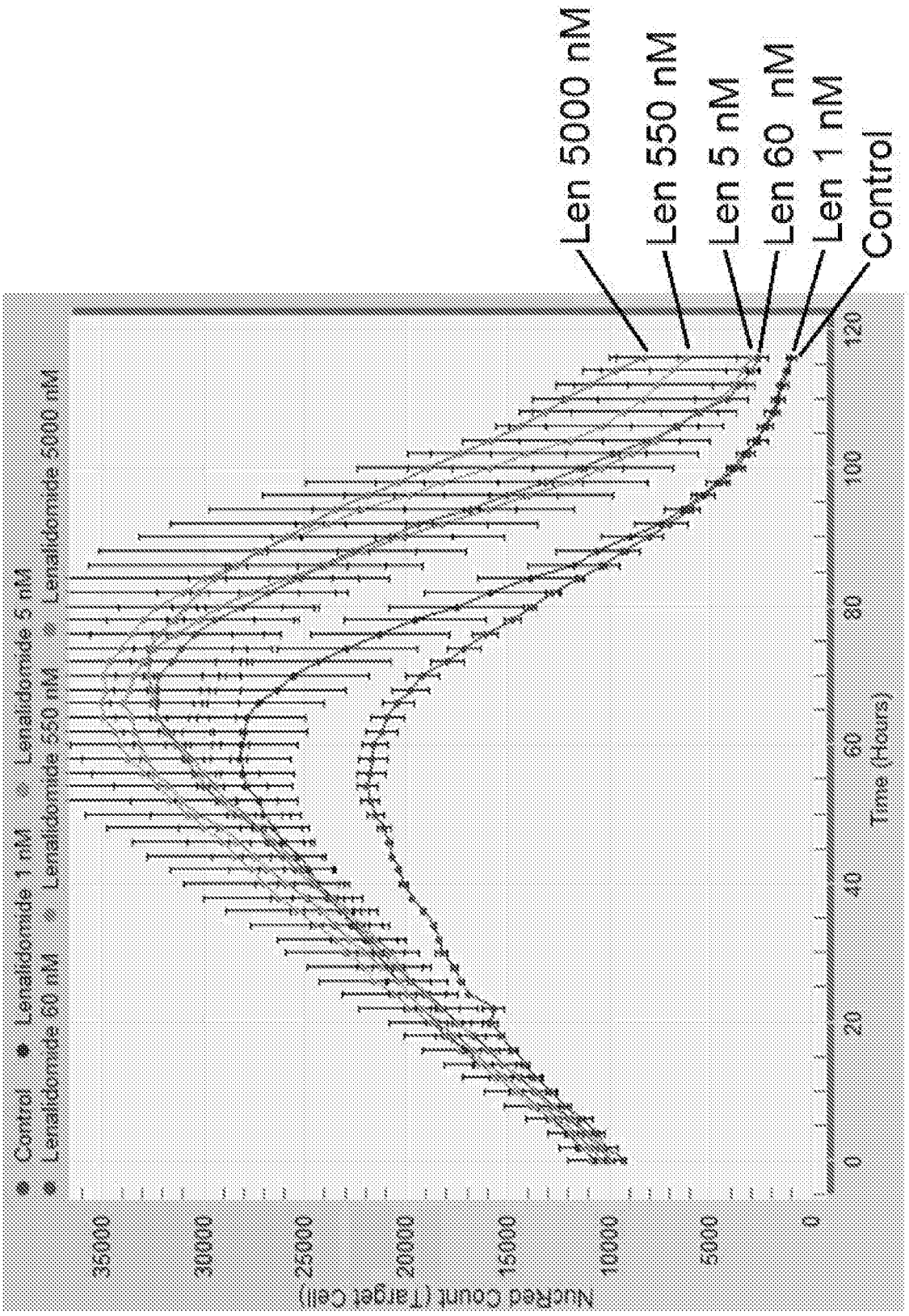

Control
Lenalidomide 1 nM
Lenalidomide 5 nM
Lenalidomide 60 nM
Lenalidomide 550 nM
Lenalidomide 5000 nM
Len 5000 nM
Len 550 nM
Len 5 nM
Len 60 nM
Len 1 nM
Control
NucRed Count (Target Cell)
35000
30000
25000
20000
15000
10000
5000
0
0
20
40
60
80
100
120
Time (Hours)

FIG. 15B

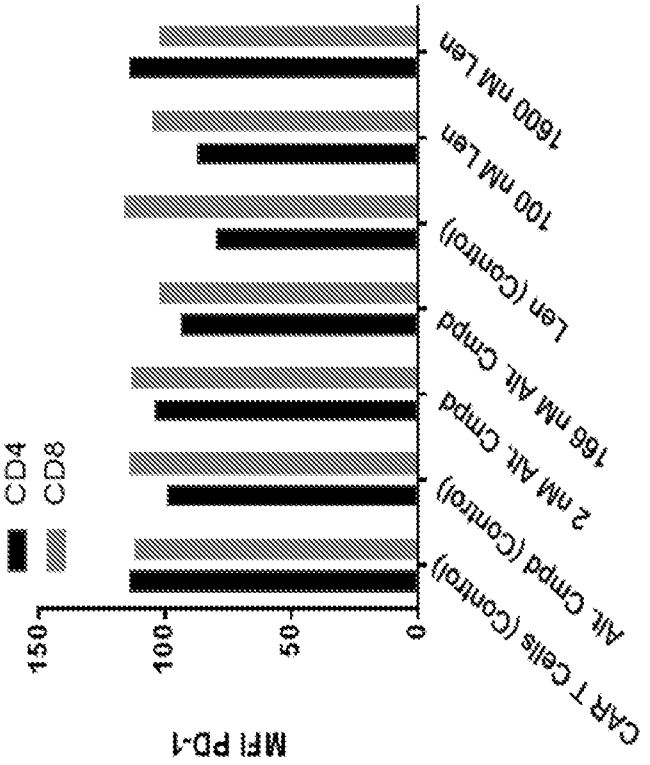


FIG. 15A

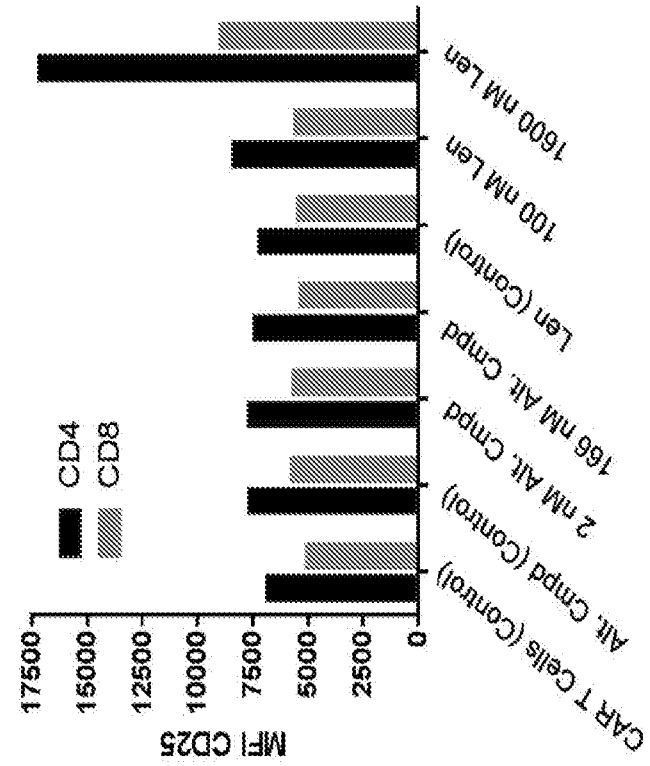


FIG. 16

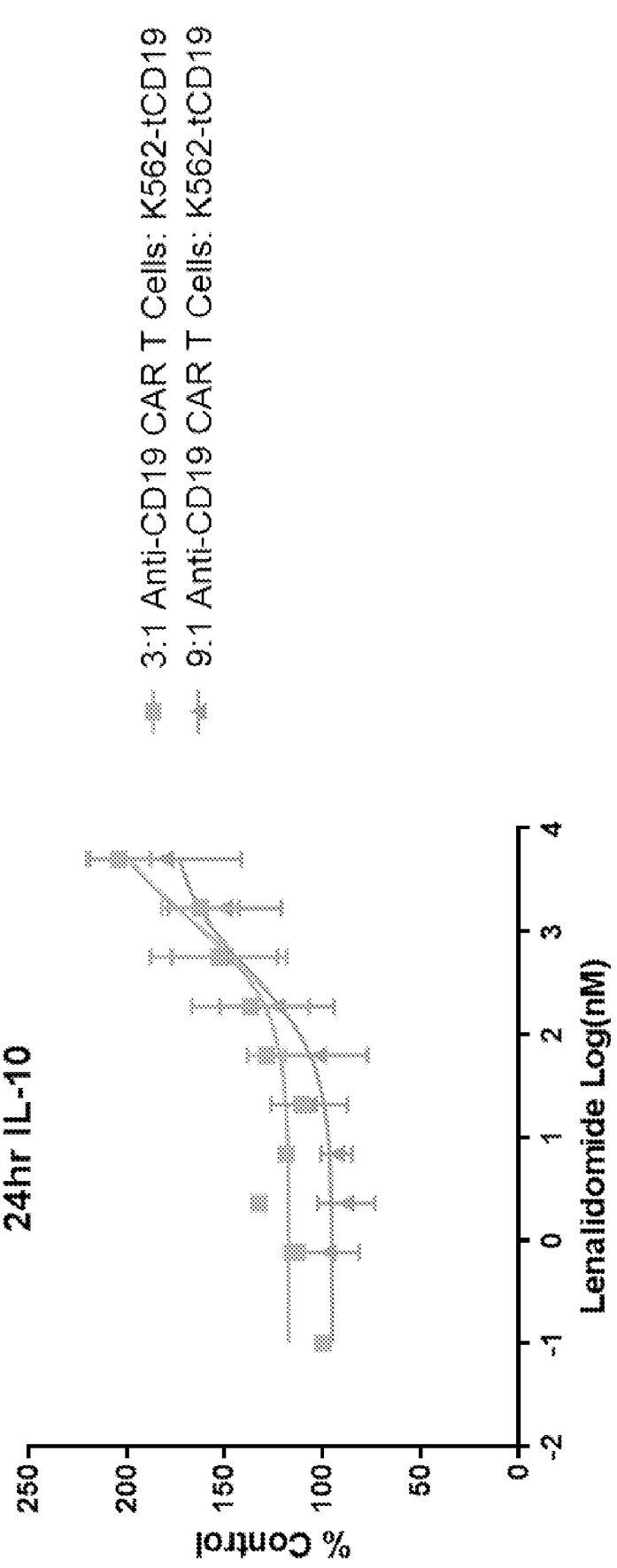

24hr IL-10
% Control
250
200
150
100
50
0
-2
-1
0
1
2
3
4
Lenalidomide Log(nM)
3:1 Anti-CD19 CAR T Cells: K562-tCD19
9:1 Anti-CD19 CAR T Cells: K562-tCD19

FIG. 17A

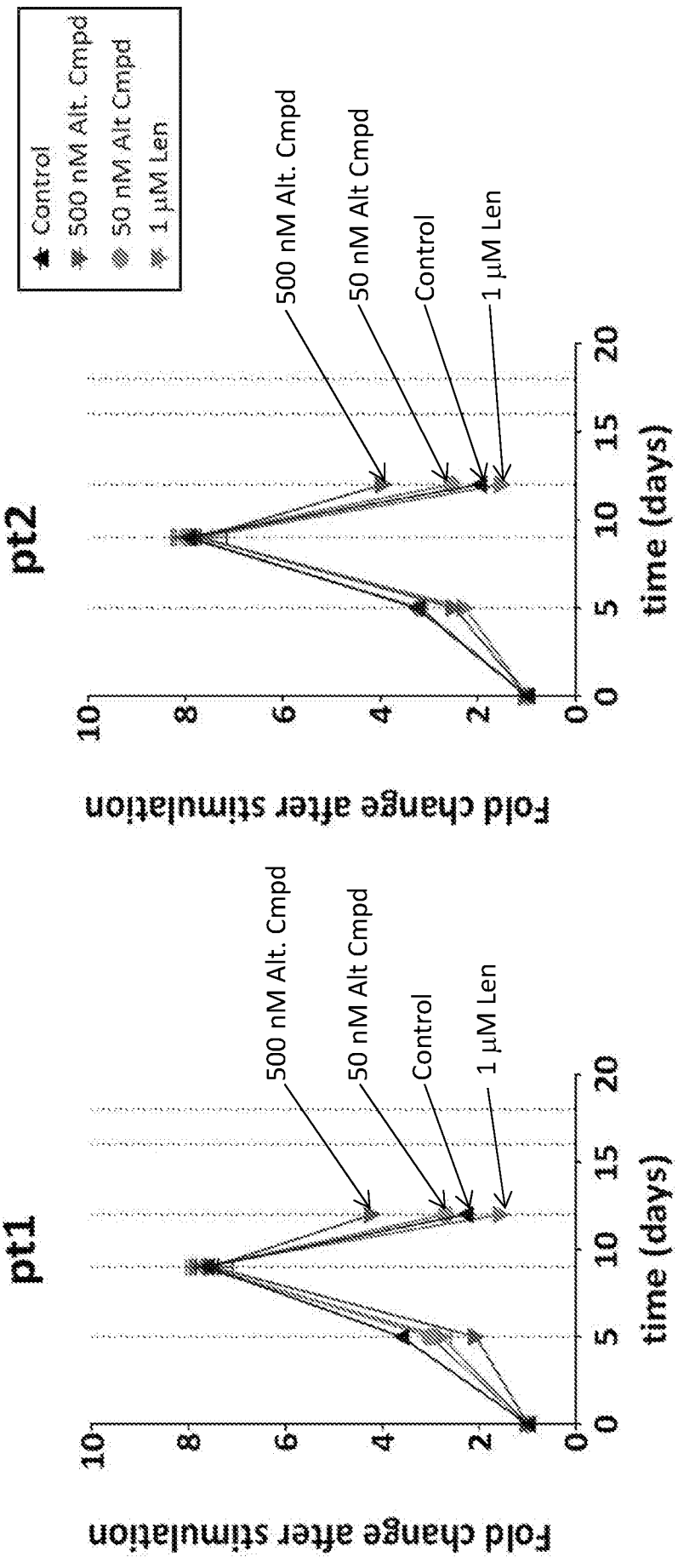

pt1
pt2
Fold change after stimulation
time (days)
0
2
4
6
8
10
0
5
10
15
20
Control
500 nM Alt. Cmpd
50 nM Alt Cmpd
1 µM Len

FIG. 17B

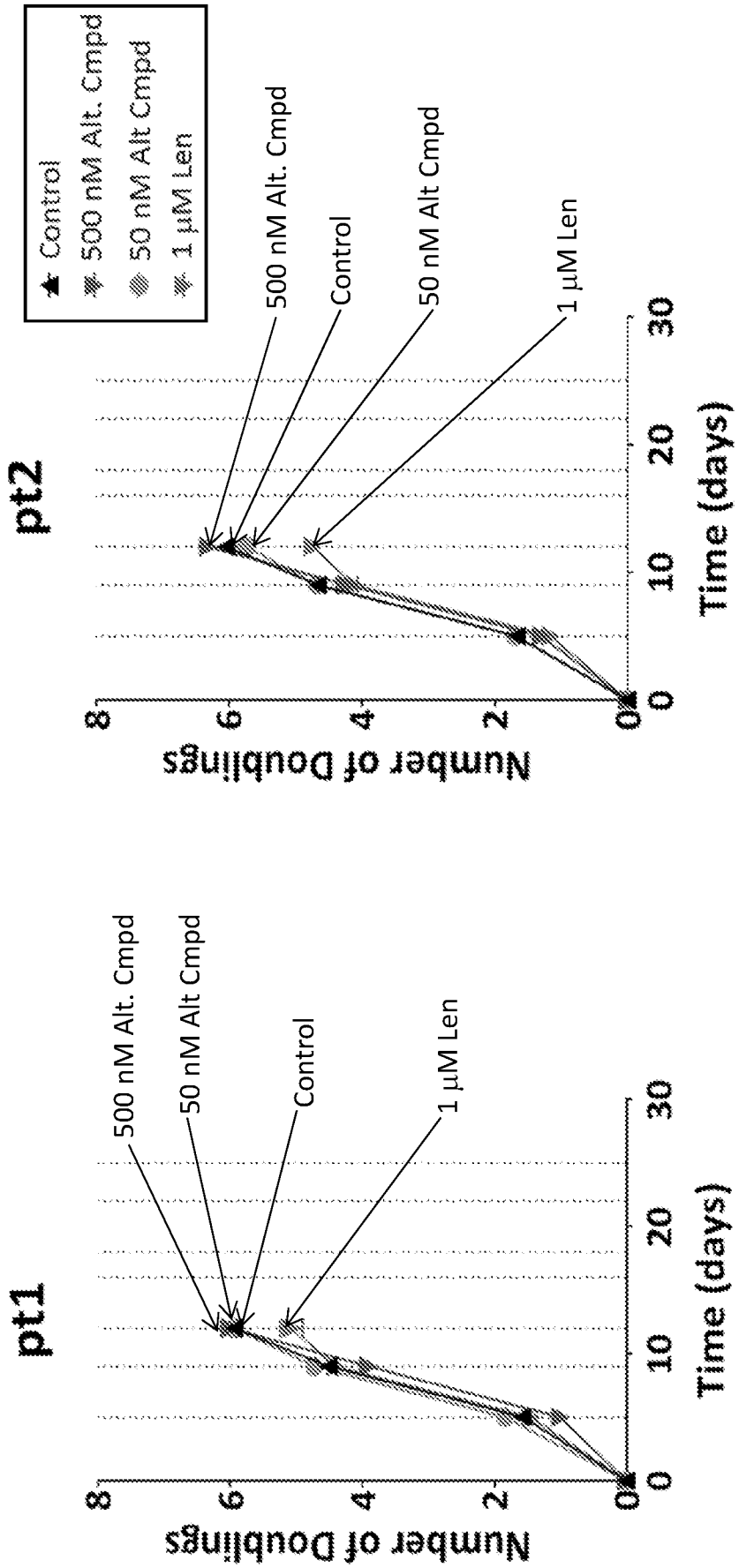
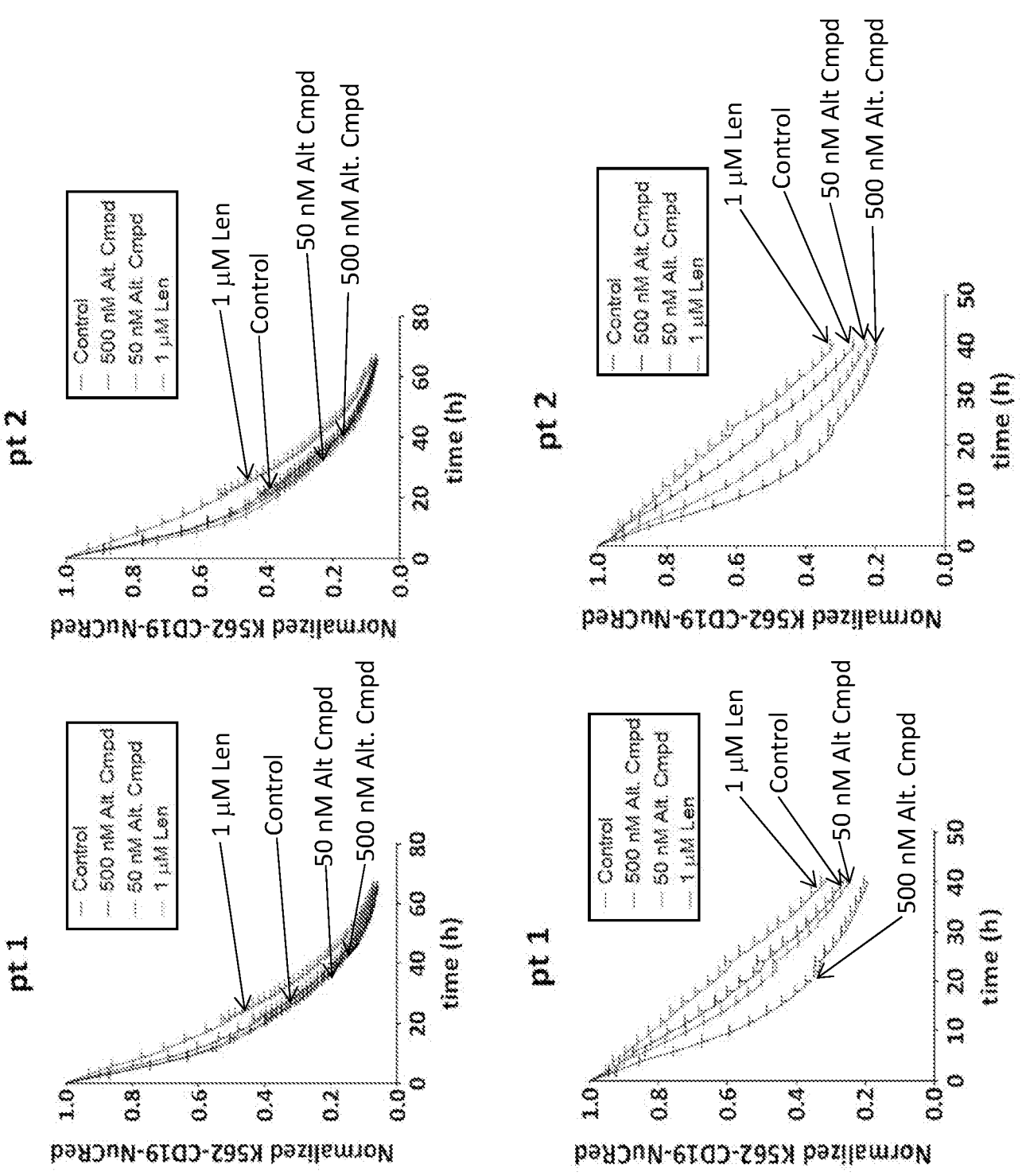
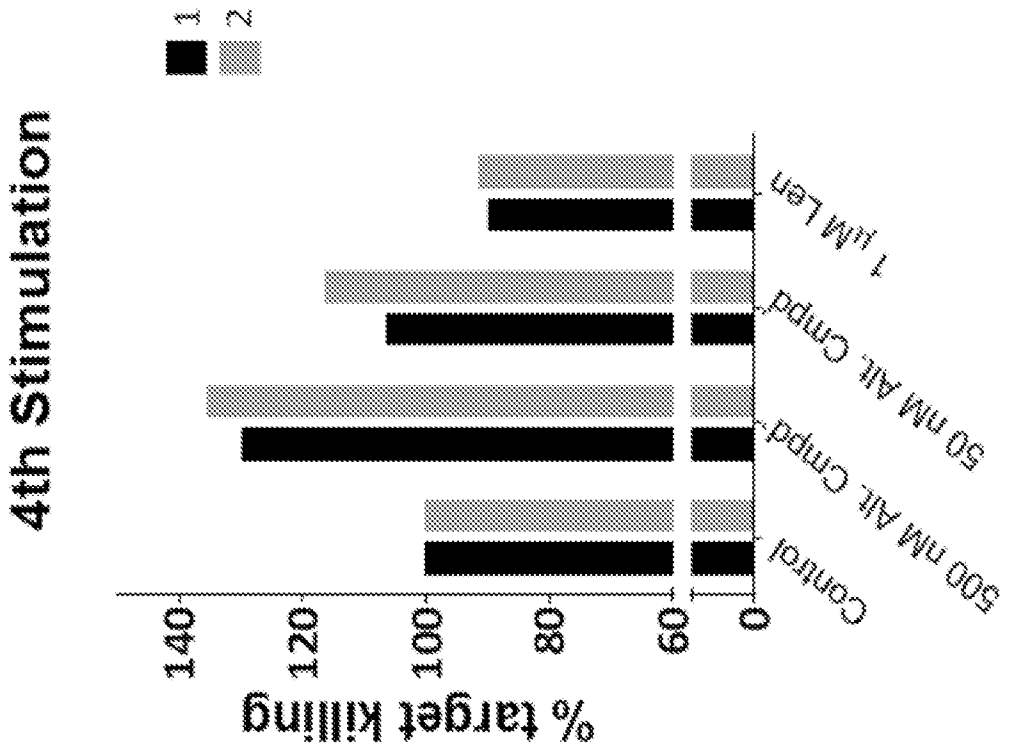

pt2
Control
500 nM Alt. Cmpd
50 nM Alt Cmpd
1 µM Len
Number of Doublings
Time (days)
0
2
4
6
8
0
10
20
30
pt1
500 nM Alt. Cmpd
50 nM Alt Cmpd
Control
1 µM Len
Number of Doublings
Time (days)

FIG. 18A


2nd Stimulation
4th Stimulation
pt 1
pt 2
Control
500 nM Alt. Cmpd
50 nM Alt. Cmpd
1 µM Len
1 µM Len
Control
50 nM Alt Cmpd
500 nM Alt. Cmpd
Normalized K562-CD19-NucRed
time (h)
0.0
0.2
0.4
0.6
0.8
1.0
0
10
20
30
40
50
60
80


4th Stimulation
1
2
% target killing
140
120
100
80
60
0
Control
500 nM Alt. Cmpd
50 nM Alt. Cmpd
1 μM Len

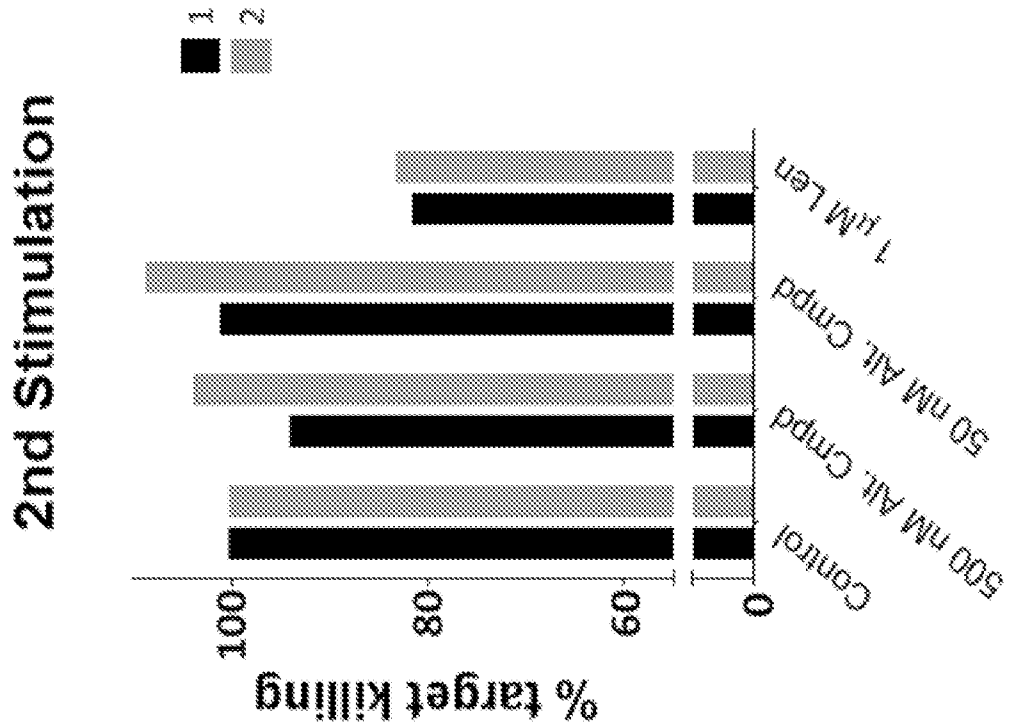

2nd Stimulation
1
2
% target killing
100
80
60
0
Control
500 nM Alt. Cmpd
50 nM Alt. Cmpd
1 μM Len

FIG. 18B

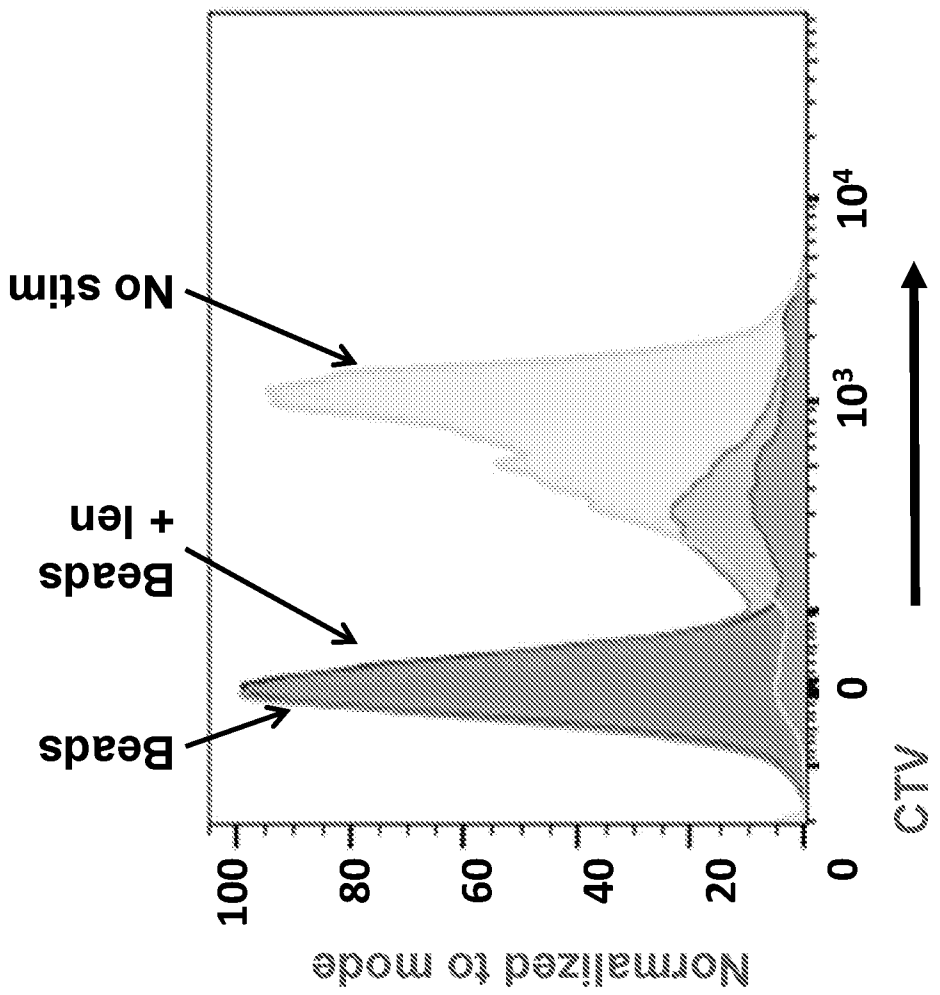

Normalized to mode
100
80
60
40
20
0
0
10^3
10^4
CTV
Beads
Beads + len
No stim

FIG. 19A

FIG. 19B

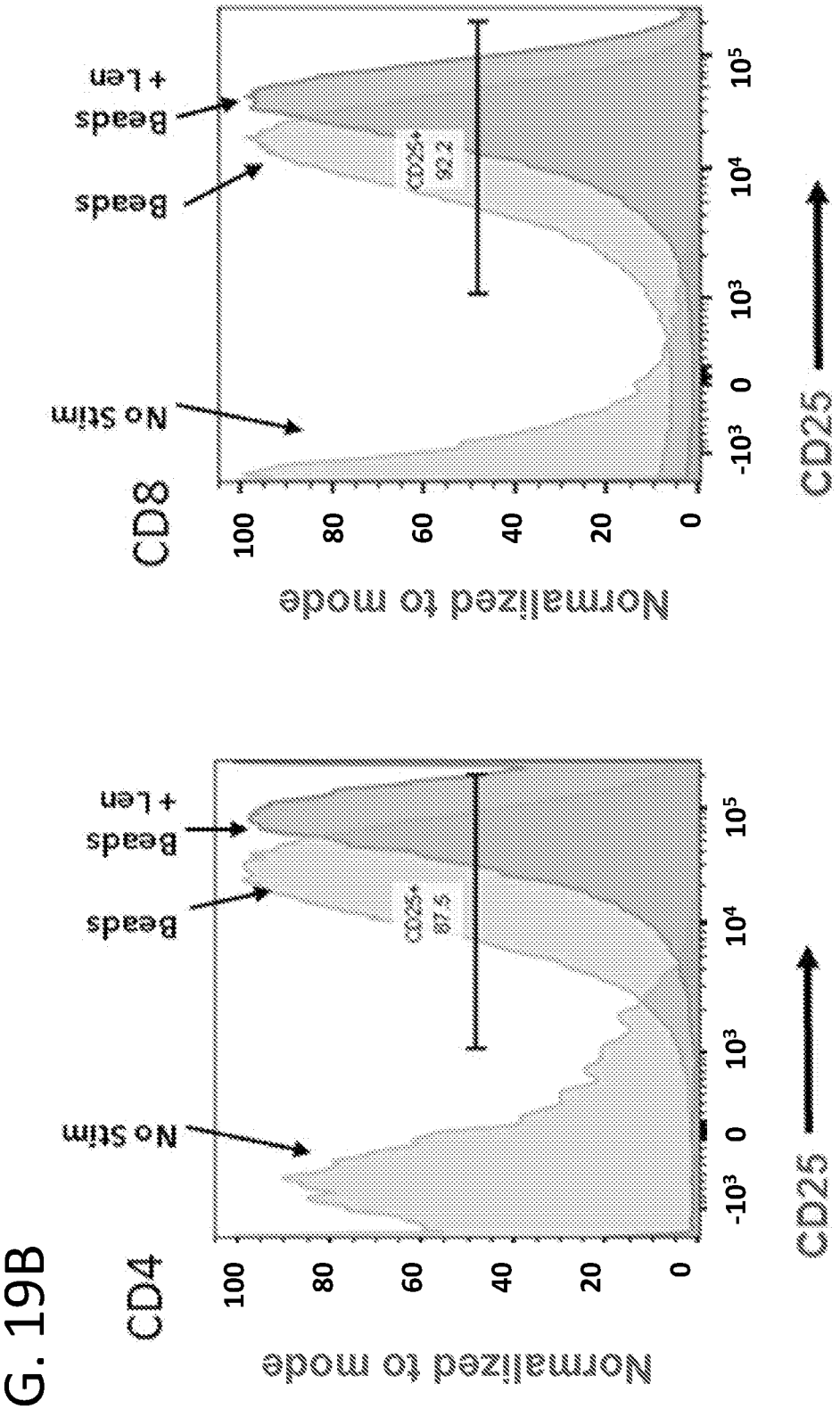

CD8
CD4
Normalized to mode
100
80
60
40
20
0
No Stim
Beads
Beads + Len
CD25+ 92.2
CD25+ 87.5
-10³
0
10³
10⁴
10⁵
CD25

FIG. 19C

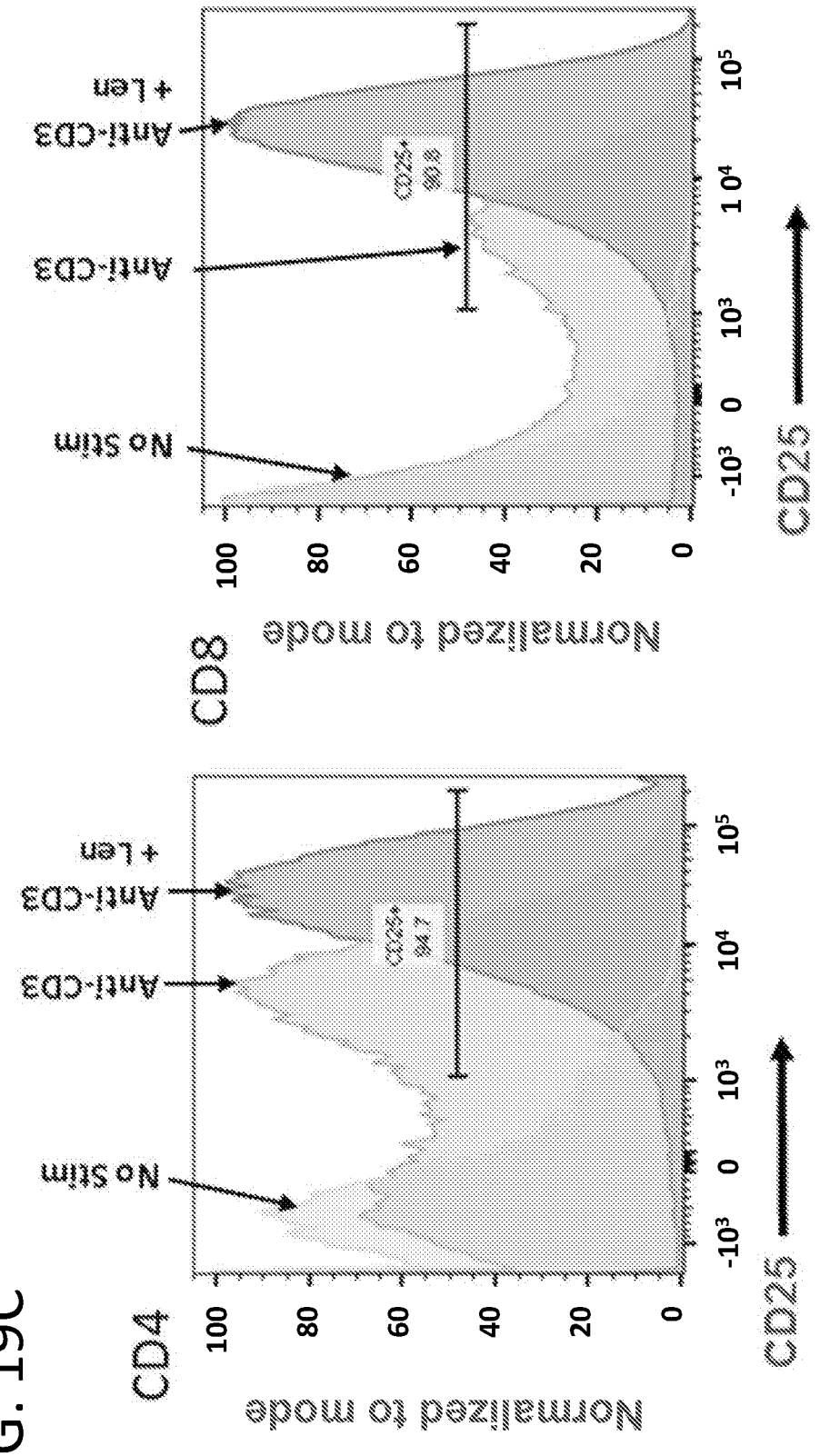

CD4
Normalized to mode
100
80
60
40
20
0
-10³
0
10³
10⁴
10⁵
CD25
No Stim
Anti-CD3
Anti-CD3 + Len
CD25+ 94.7
CD8
Normalized to mode
100
80
60
40
20
0
-10³
0
10³
10⁴
10⁵
CD25
No Stim
Anti-CD3
Anti-CD3 + Len
CD25+ 90.8

FIG. 20A

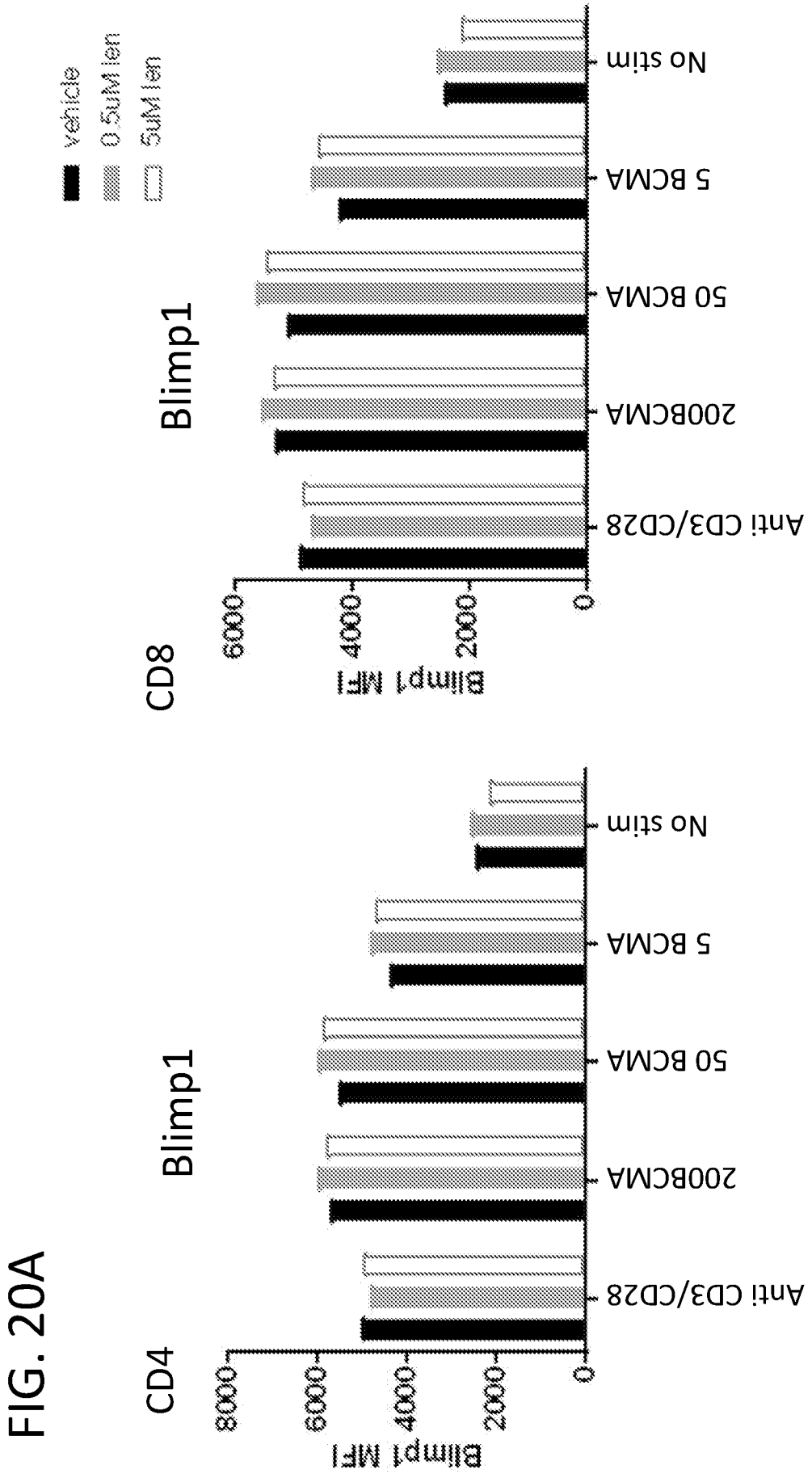

CD4
Blimp1
Blimp1 MFI
8000
6000
4000
2000
0
Anti CD3/CD28
200BCMA
50 BCMA
5 BCMA
No stim
CD8
Blimp1
Blimp1 MFI
6000
4000
2000
0
Anti CD3/CD28
200BCMA
50 BCMA
5 BCMA
No stim
vehicle
0.5uM Ien
5uM Ien

FIG. 20B

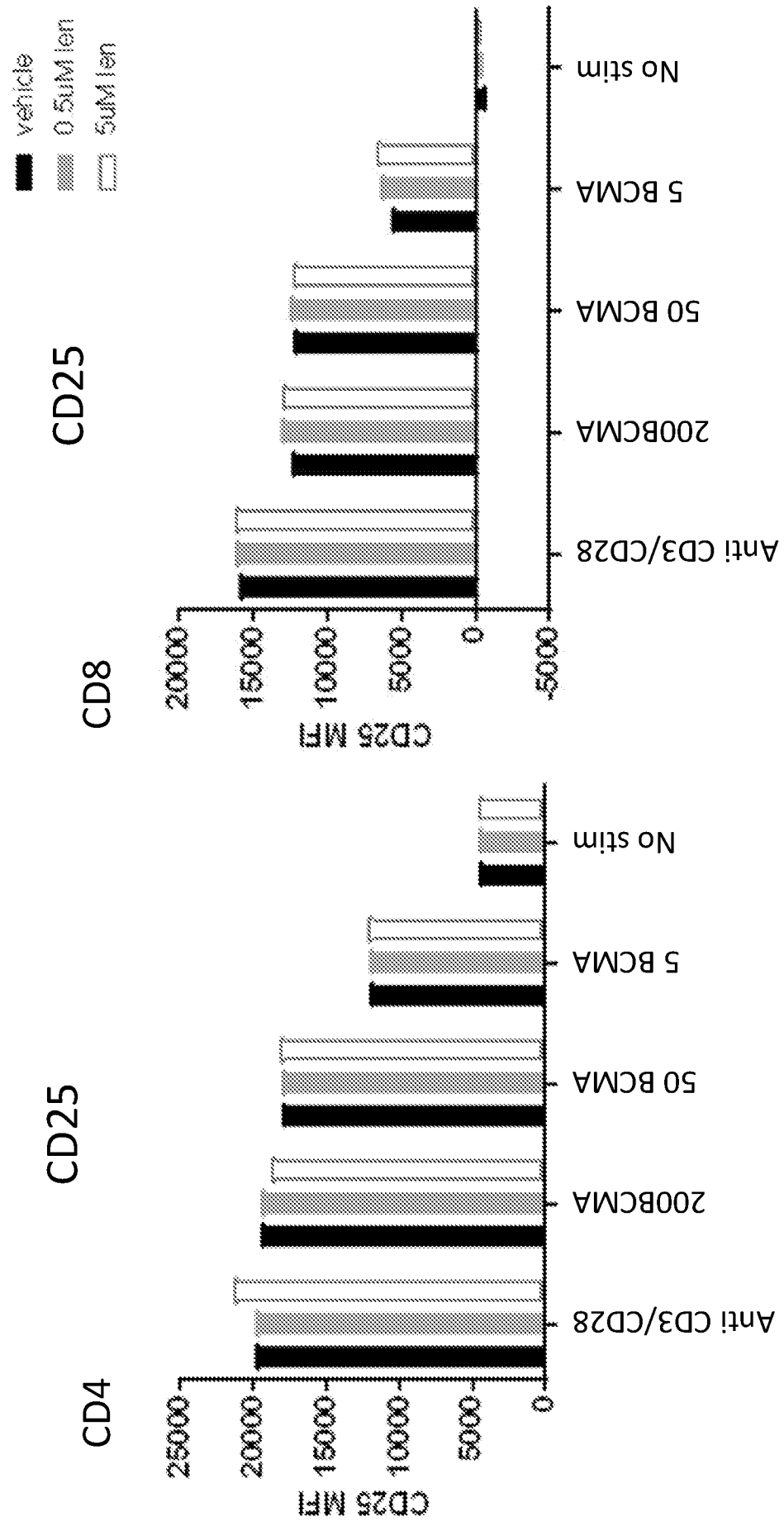

CD4
CD25
CD25 MFI
25000
20000
15000
10000
5000
0
Anti CD3/CD28
200BCMA
50 BCMA
5 BCMA
No stim
CD8
CD25
CD25 MFI
20000
15000
10000
5000
0
-5000
Anti CD3/CD28
200BCMA
50 BCMA
5 BCMA
No stim
vehicle
0.5uM Ien
5uM Ien

FIG. 20C

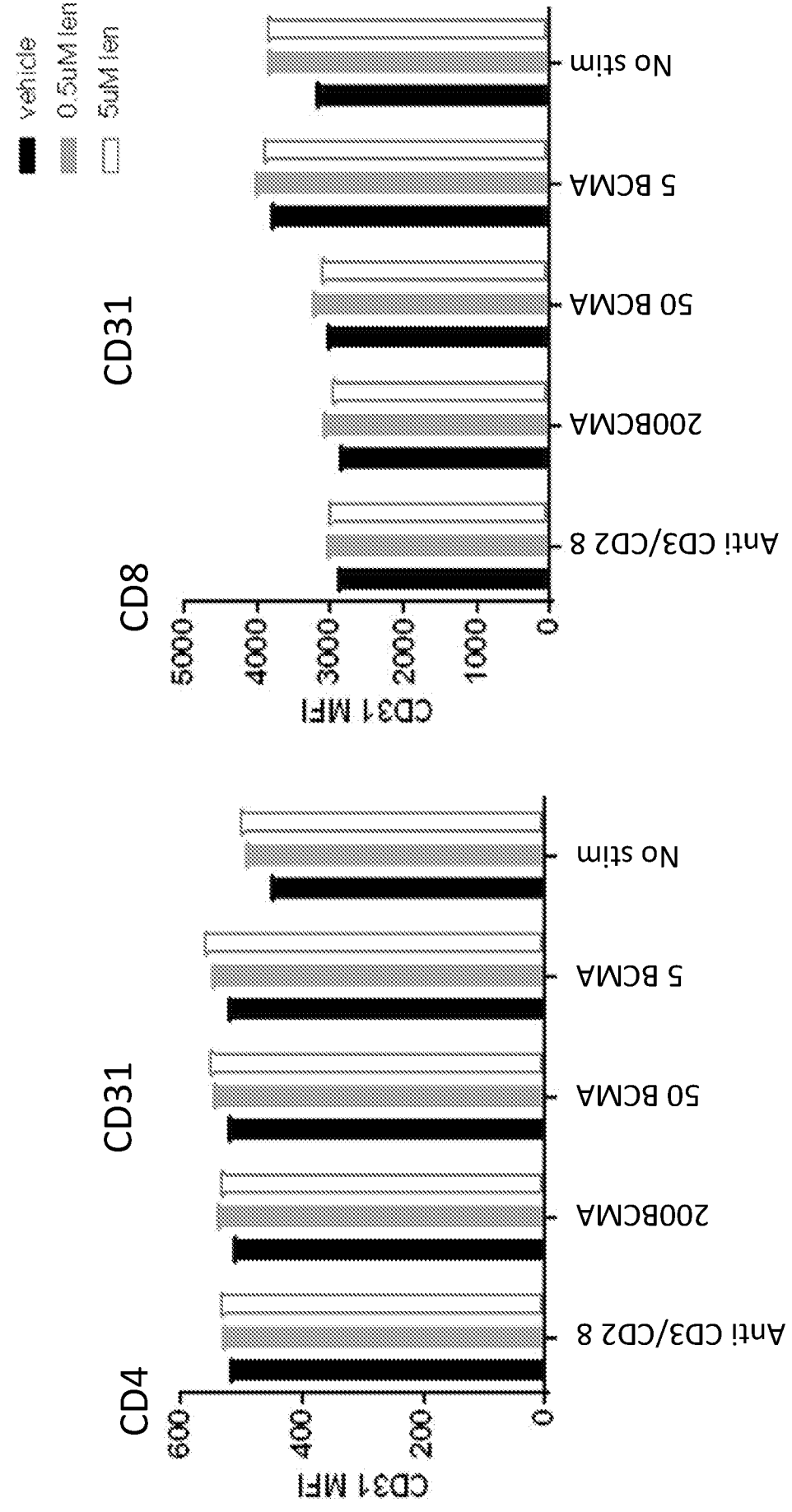
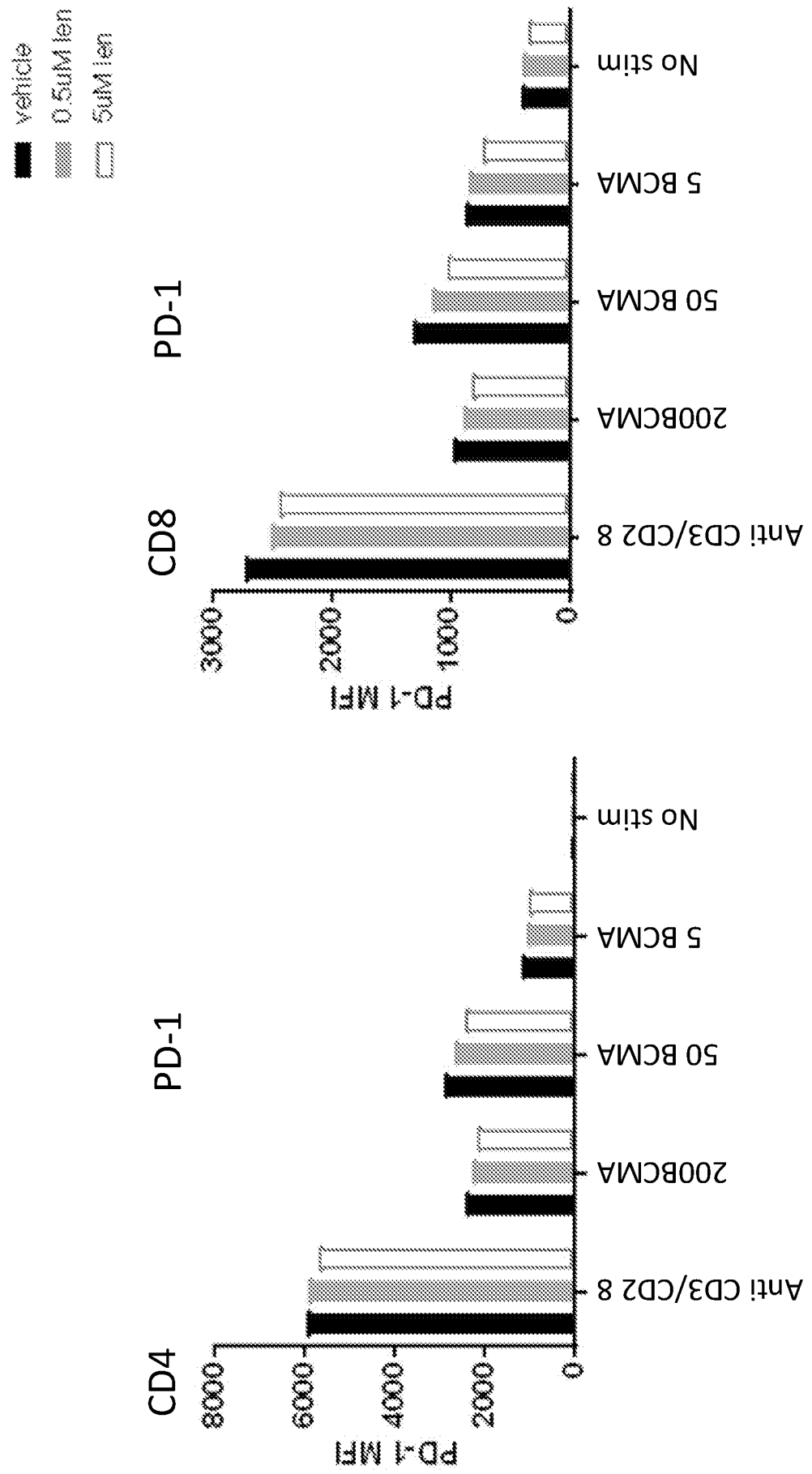

CD4
CD31
CD31 MFI
600
400
200
0
Anti CD3/CD2 8
200BCMA
50 BCMA
5 BCMA
No stim
CD8
CD31
CD31 MFI
5000
4000
3000
2000
1000
0
Anti CD3/CD2 8
200BCMA
50 BCMA
5 BCMA
No stim
vehicle
0.5uM Ien
5uM Ien

FIG. 20D


CD4
PD-1
PD-1 MFI
8000
6000
4000
2000
0
Anti CD3/CD2 8
200BCMA
50 BCMA
5 BCMA
No stim
CD8
PD-1
PD-1 MFI
3000
2000
1000
0
Anti CD3/CD2 8
200BCMA
50 BCMA
5 BCMA
No stim
vehicle
0.5uM len
5uM len

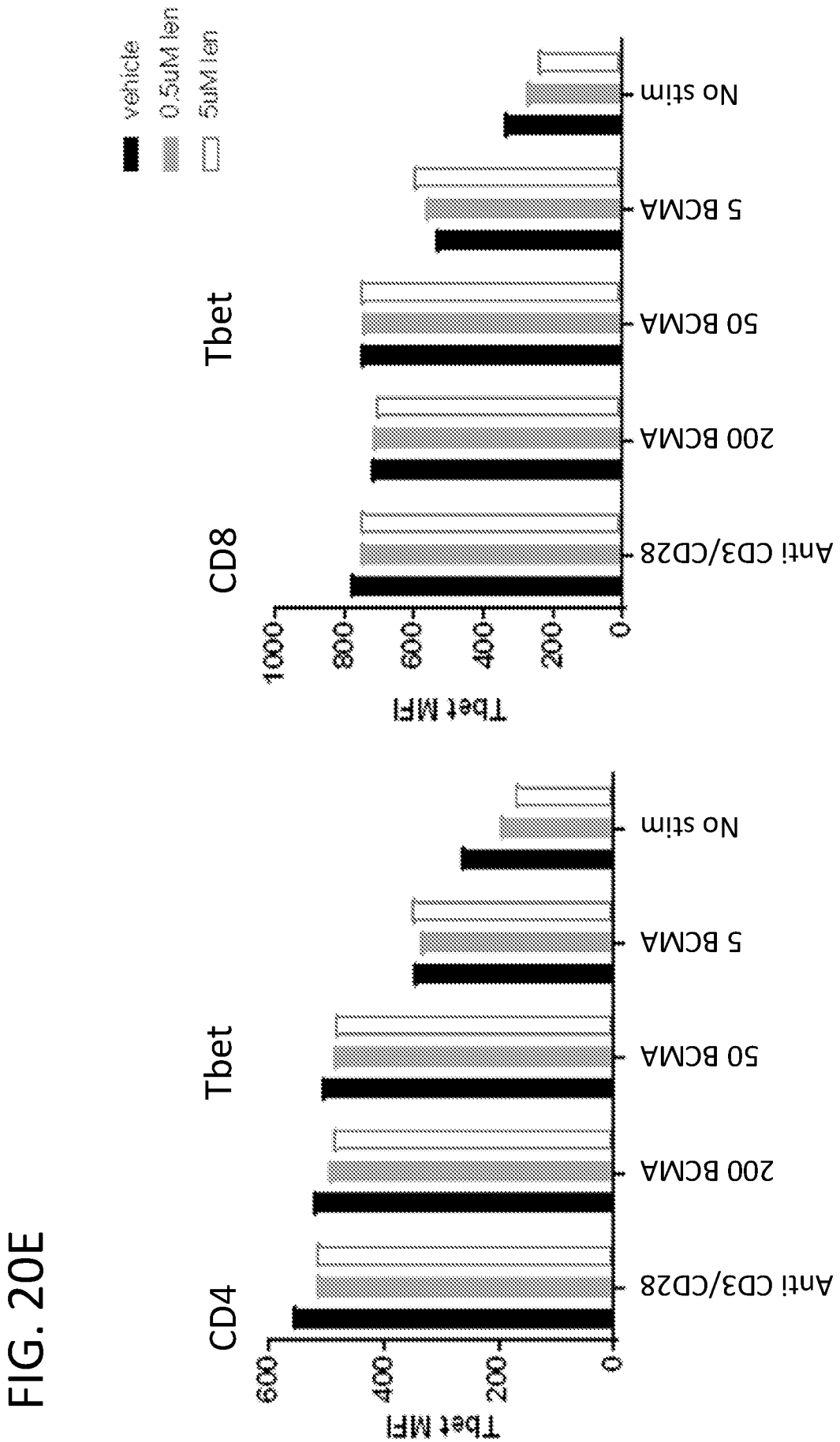

vehicle
0.5uM Ien
5uM Ien
CD8
Tbet
Tbet MFI
1000
800
600
400
200
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
CD4
Tbet
Tbet MFI
600
400
200
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim

FIG. 20E

FIG. 20F

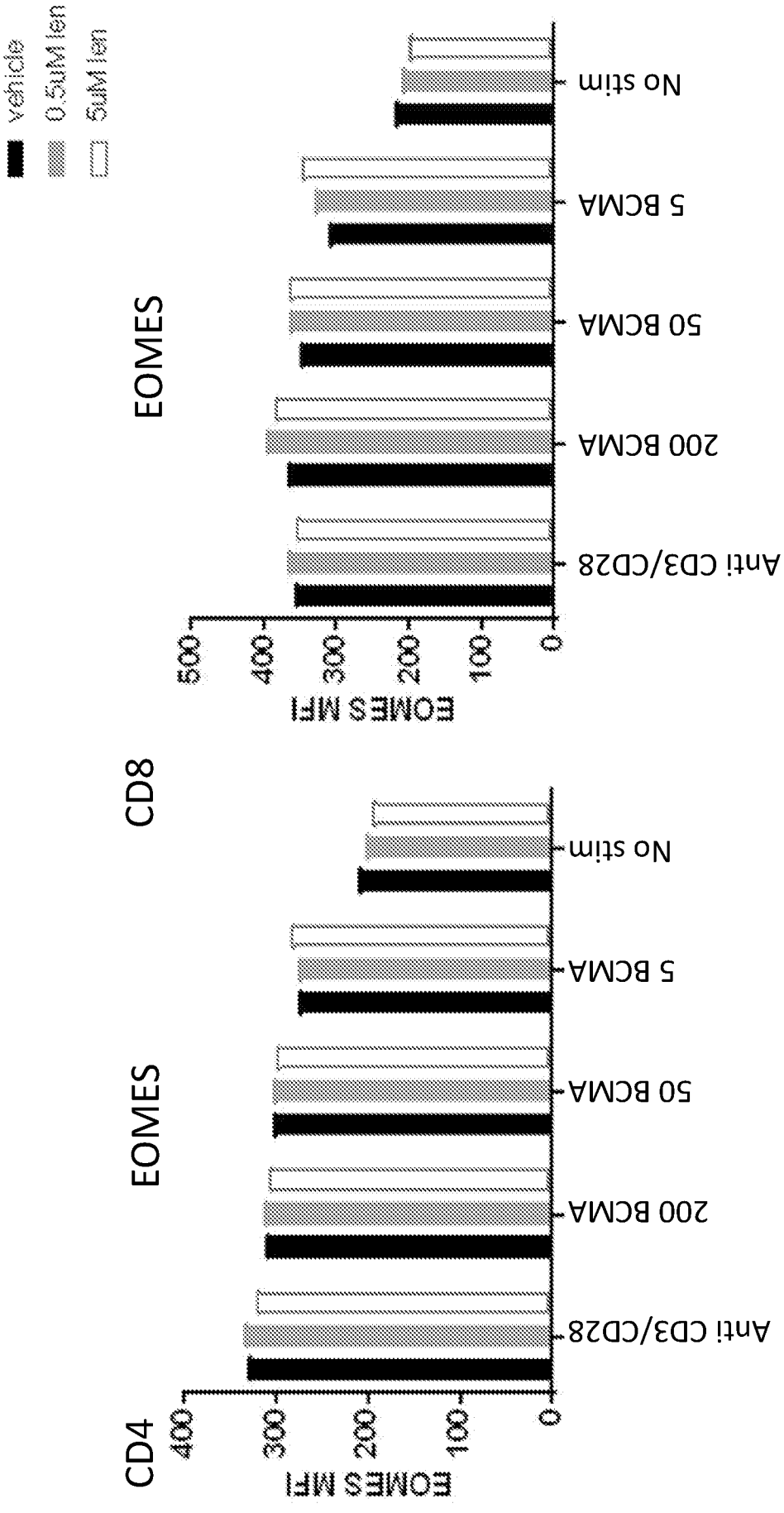

CD4
EOMES
EOMES MFI
400
300
200
100
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
CD8
EOMES
EOMES MFI
500
400
300
200
100
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
vehicle
0.5uM Ien
5uM Ien

FIG. 20G

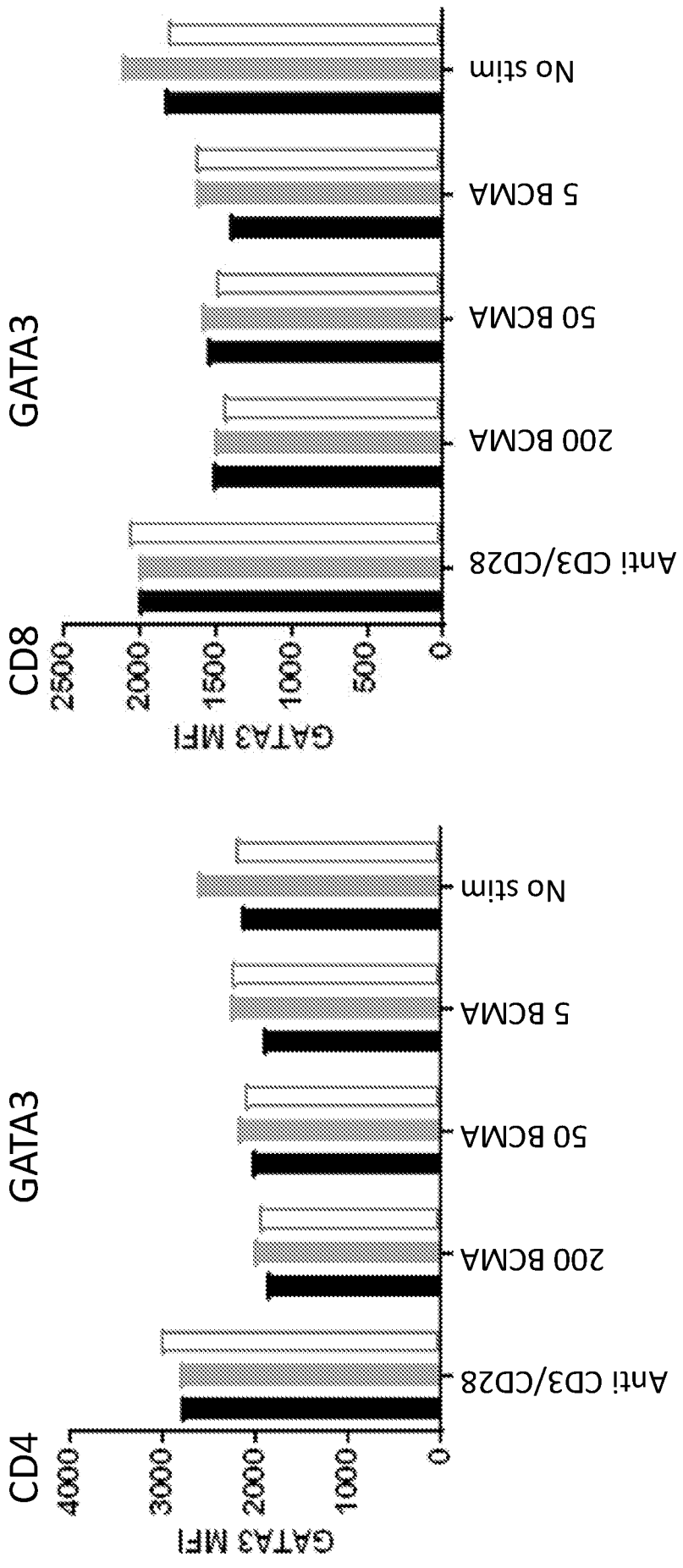

CD4
GATA3
GATA3 MFI
4000
3000
2000
1000
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
CD8
GATA3
GATA3 MFI
2500
2000
1500
1000
500
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
vehicle
0.5uM Ien
5uM Ien

FIG. 20H

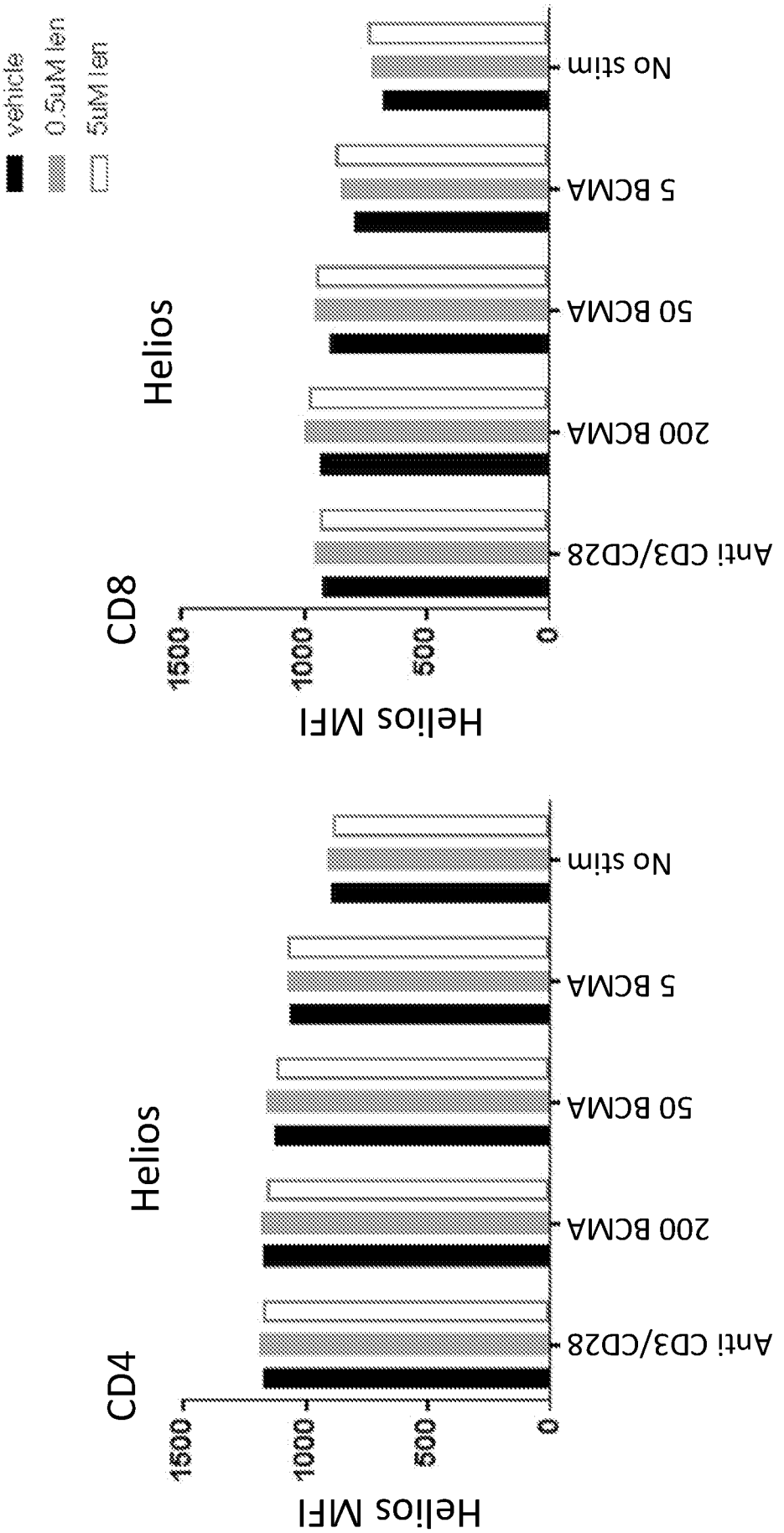

CD4
Helios
Helios MFI
1500
1000
500
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
CD8
Helios
Helios MFI
1500
1000
500
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
vehicle
0.5uM len
5uM len

FIG. 20I

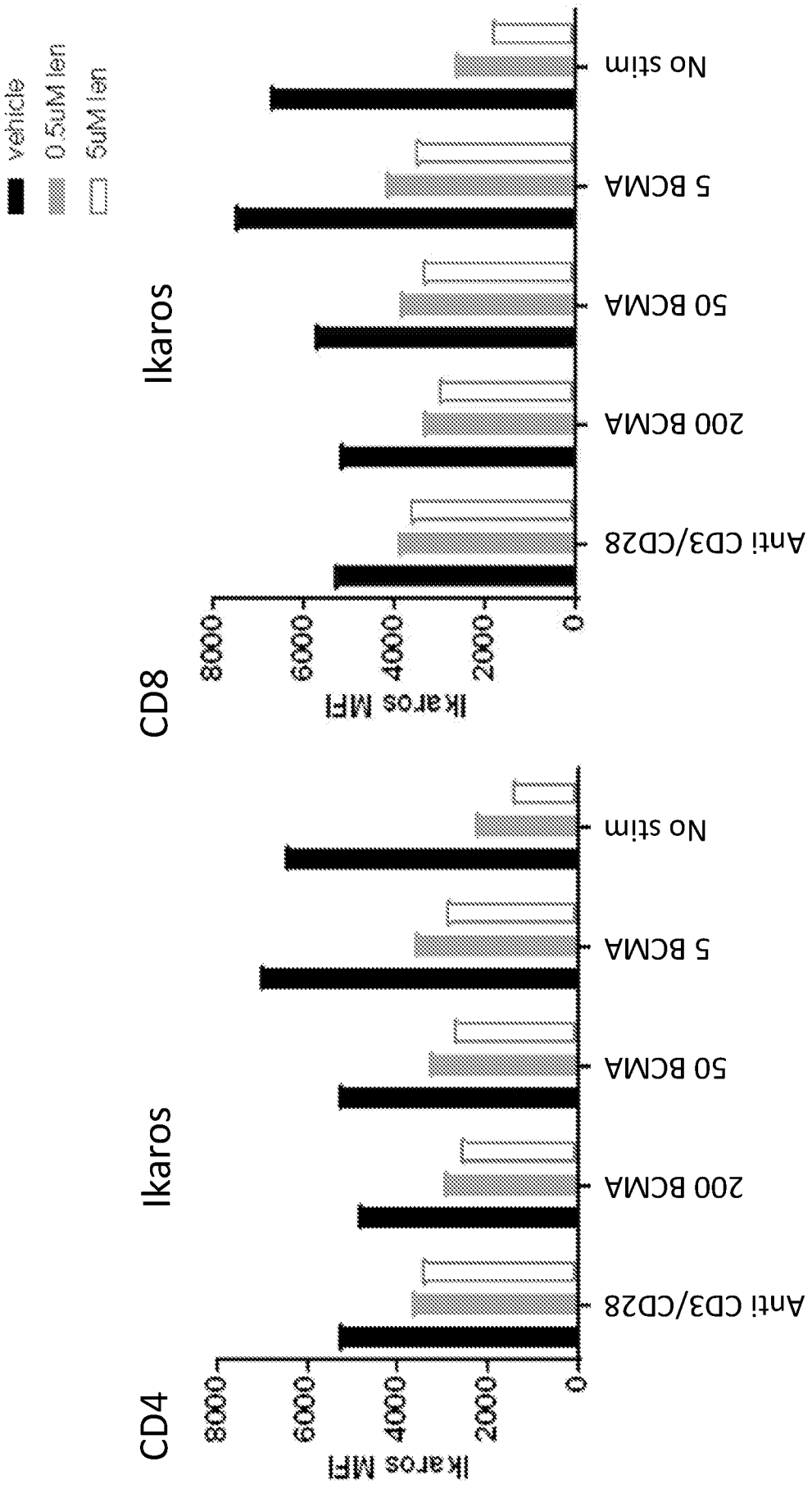

CD4
Ikaros
Ikaros MFI
8000
6000
4000
2000
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
CD8
Ikaros
Ikaros MFI
8000
6000
4000
2000
0
Anti CD3/CD28
200 BCMA
50 BCMA
5 BCMA
No stim
vehicle
0.5uM len
5uM len

FIG. 21A

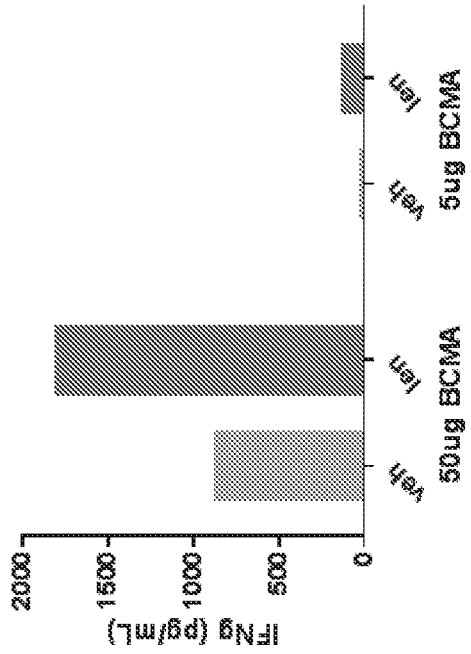


FIG. 21B

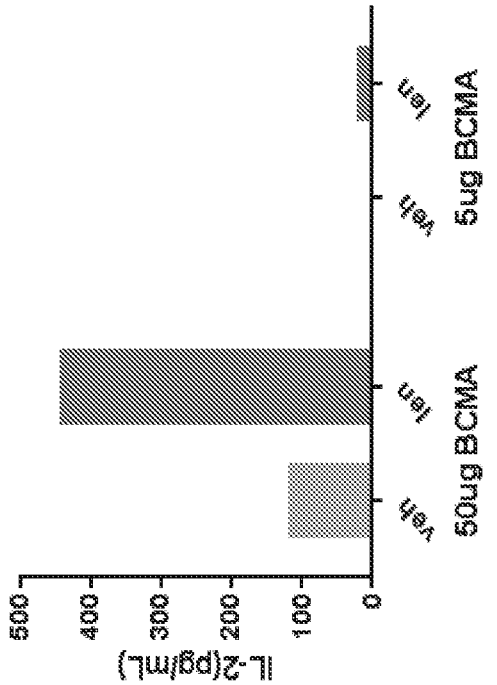


FIG. 21C

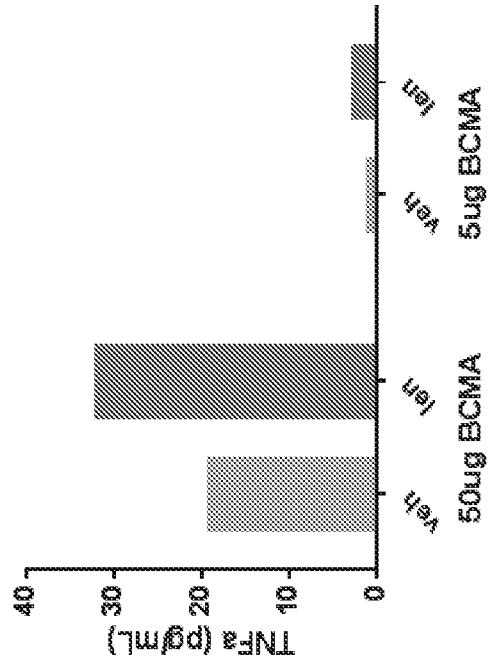
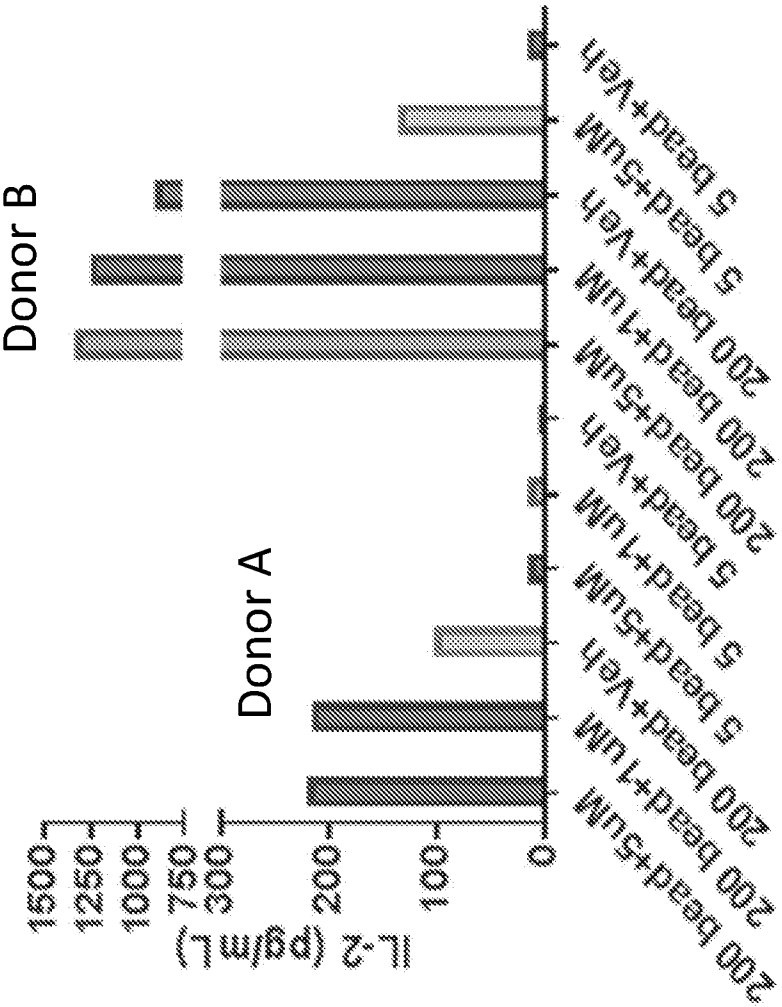


FIG. 21D


Donor B
Donor A
IL-2 (pg/mL)
1500
1250
1000
750
300
200
100
0
200 bead+5uM
200 bead+1uM
200 bead+Veh
5 bead+5uM
5 bead+1uM
5 bead+Veh
200 bead+5uM
200 bead+1uM
200 bead+Veh
5 bead+5uM
5 bead+Veh

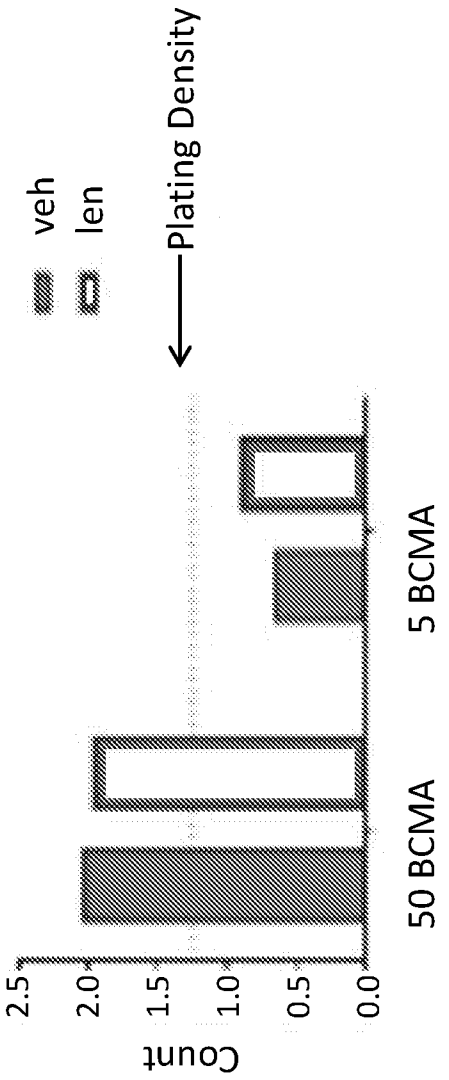


FIG. 21E

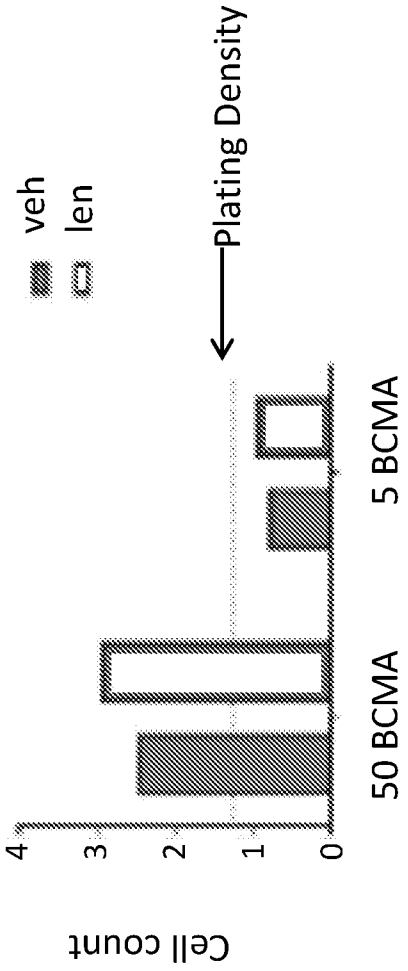
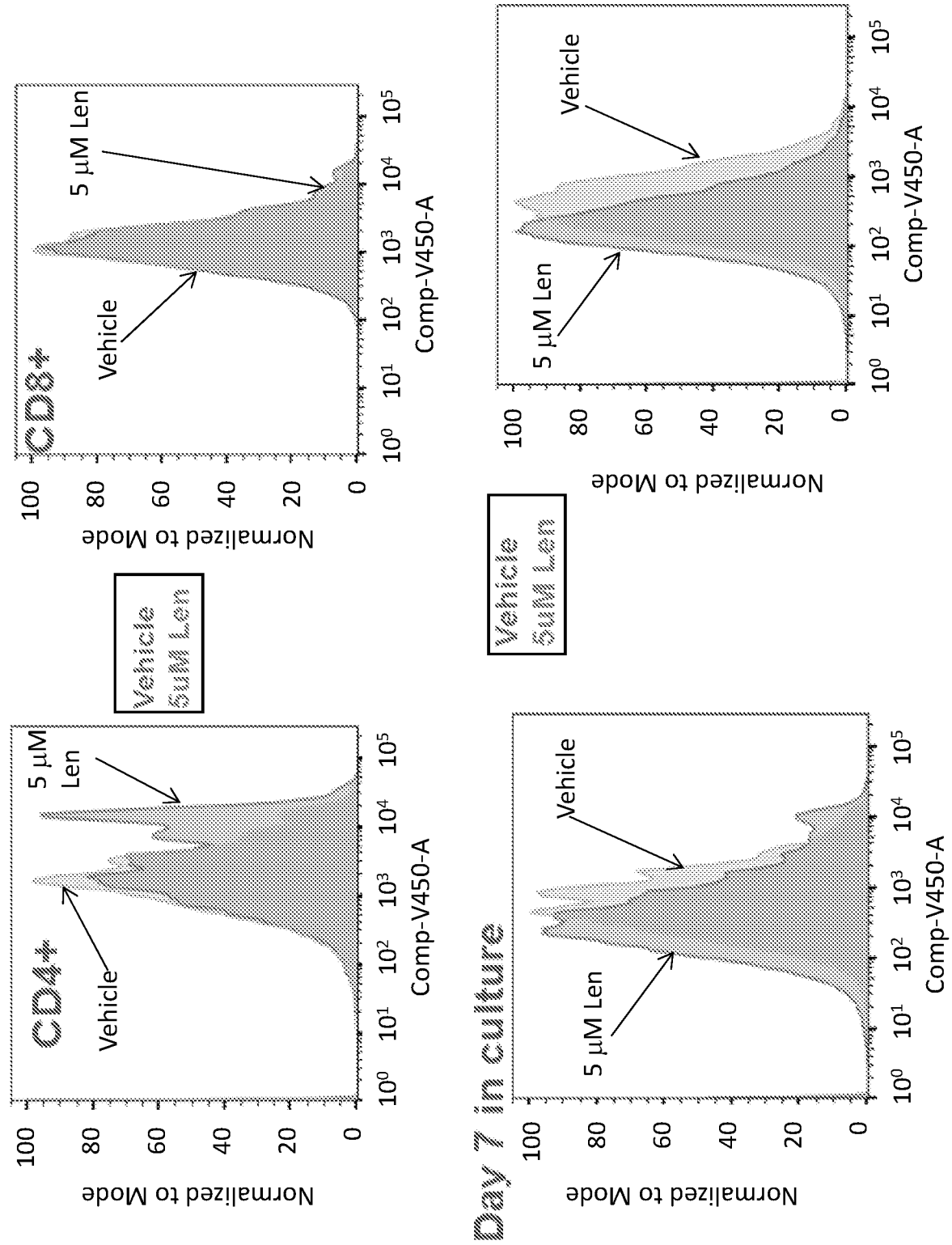


FIG. 21F

FIG. 21G


Day 4 in culture Cell trace violet dye dilution assay
CD4+
Vehicle
5 µM Len
CD8+
Vehicle
5 µM Len
Vehicle
5uM Len
Day 7 in culture
Vehicle
5 µM Len
Vehicle
5 µM Len
Normalized to Mode
Comp-V450-A
0
20
40
60
80
100
10^0
10^1
10^2
10^3
10^4
10^5

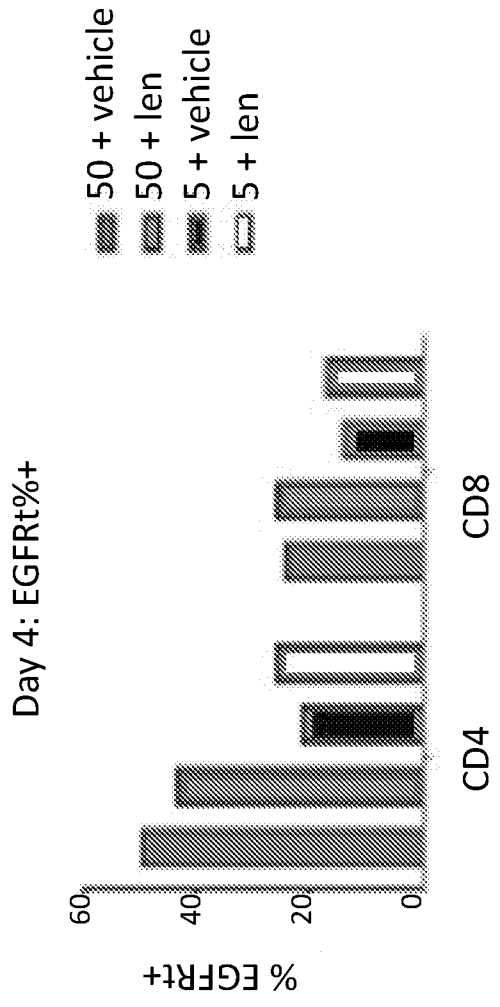


FIG. 21H

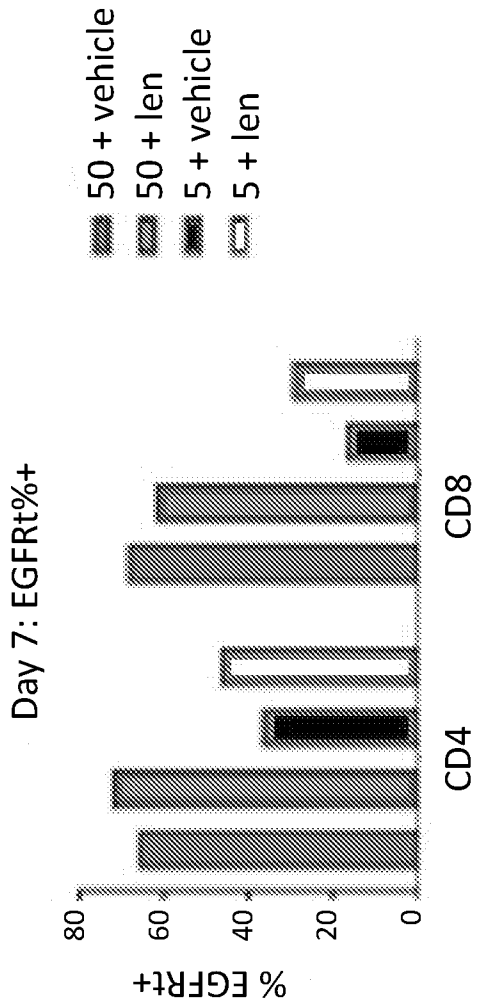


FIG. 21I

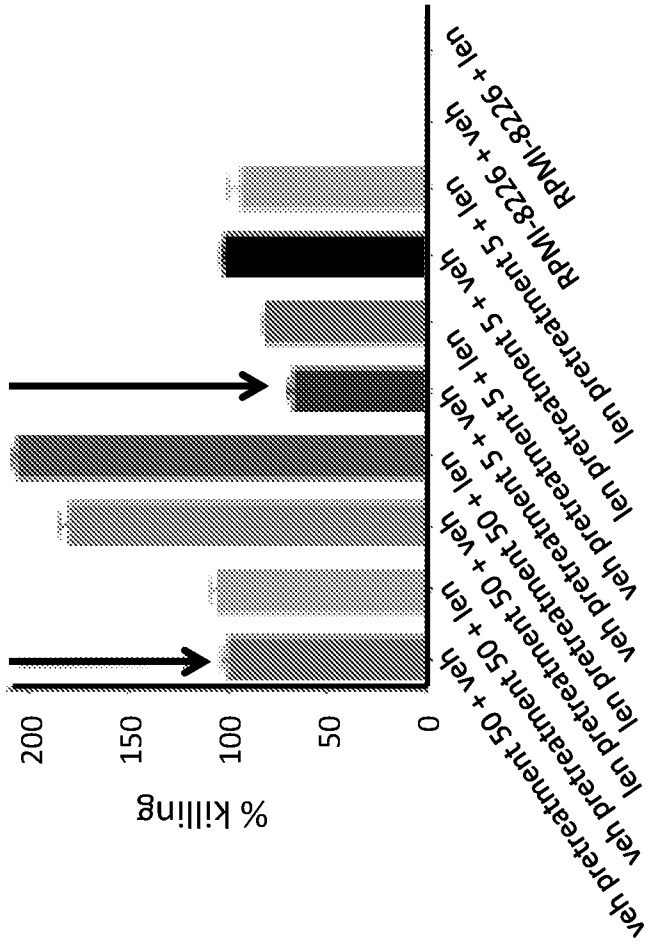

% killing
0
50
100
150
200
veh pretreatment 50 + veh
veh pretreatment 50 + len
len pretreatment 50 + veh
len pretreatment 50 + len
veh pretreatment 5 + veh
veh pretreatment 5 + len
len pretreatment 5 + veh
len pretreatment 5 + len
RPMI-8226 + veh
RPMI-8226 + len

FIG. 21J

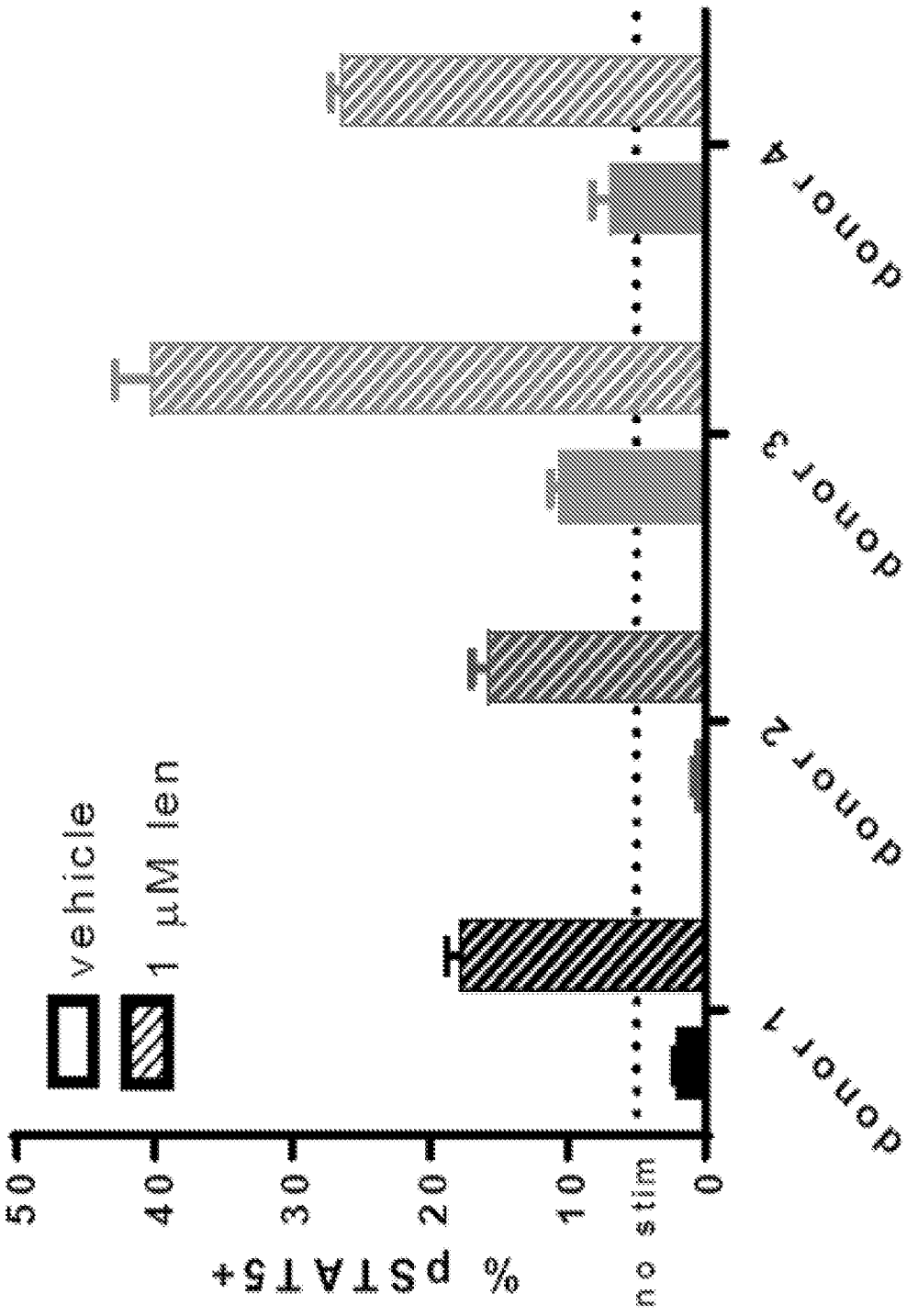
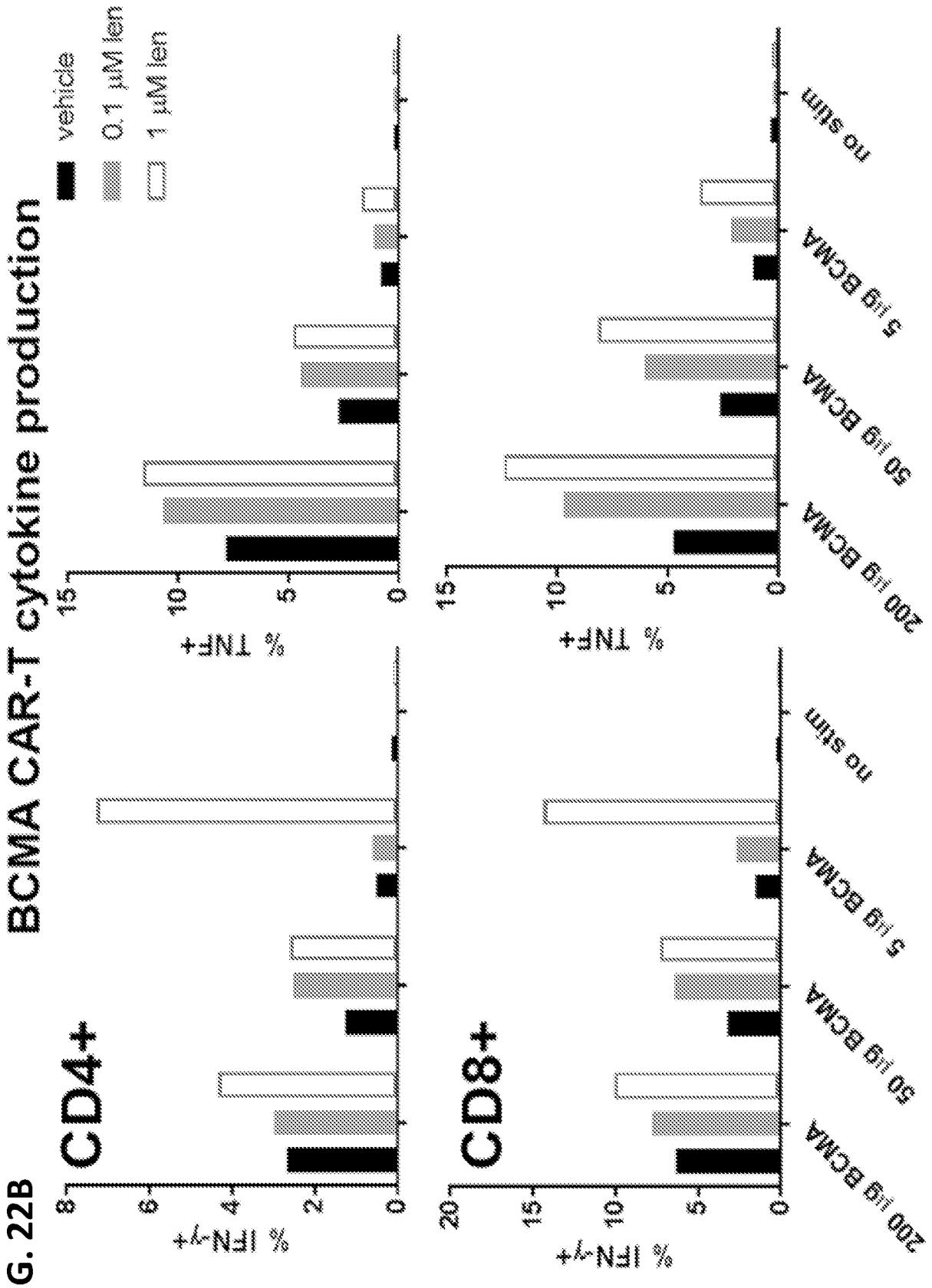

2 hour CAR stimulation
vehicle
1 µM len
% pSTAT5+
50
40
30
20
10
0
no stim
donor 1
donor 2
donor 3
donor 4

FIG. 22A

FIG. 22B


BCMA CAR-T cytokine production
vehicle
0.1 µM len
1 µM len
CD4+
CD8+
% IFN-γ+
% TNF+
no stim
5 µg BCMA
50 µg BCMA
200 µg BCMA

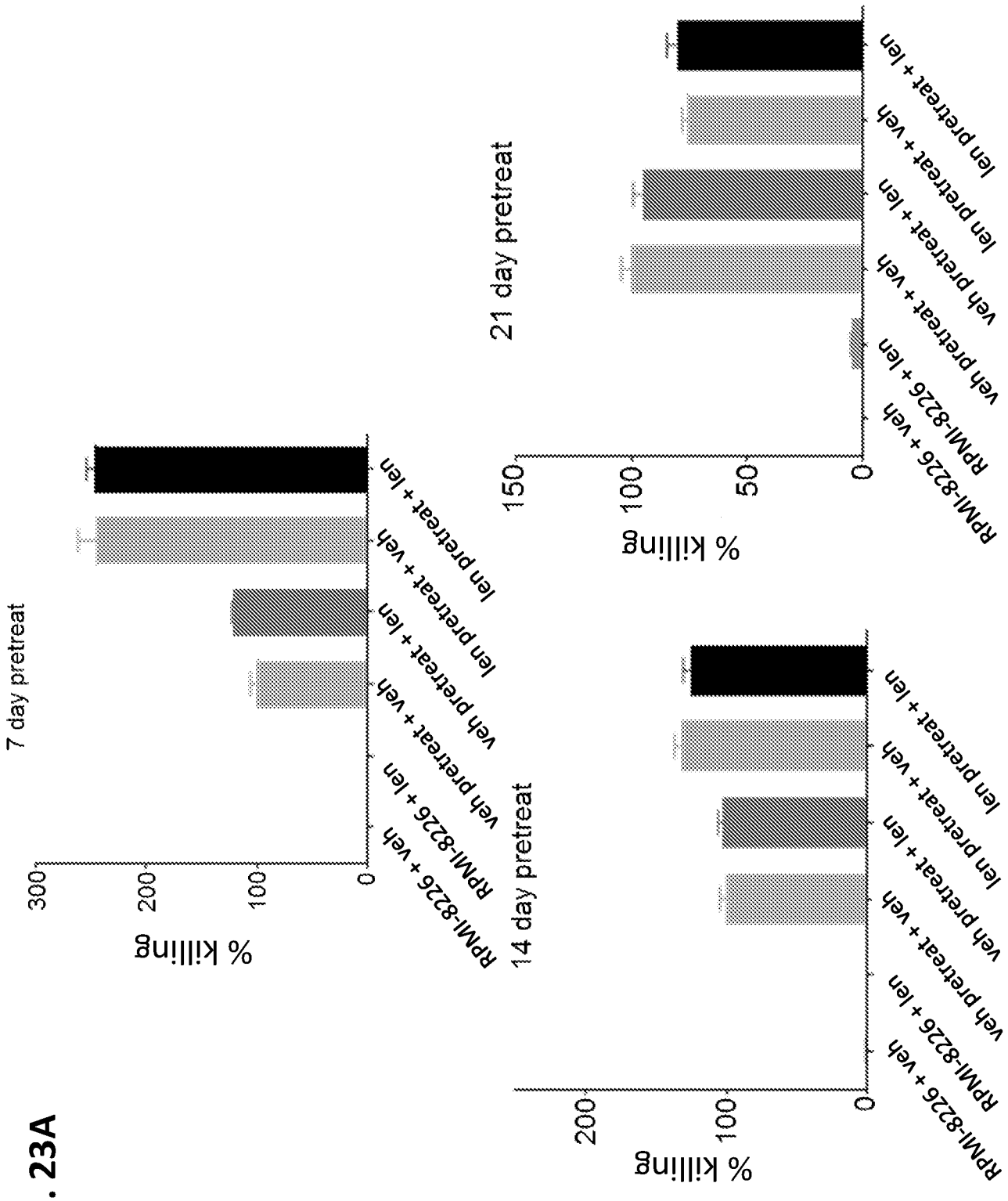

7 day pretreat
% killing
300
200
100
0
RPMI-8226 + veh
RPMI-8226 + len
veh pretreat + veh
veh pretreat + len
len pretreat + veh
len pretreat + len
14 day pretreat
% killing
200
100
0
RPMI-8226 + veh
RPMI-8226 + len
veh pretreat + veh
veh pretreat + len
len pretreat + veh
len pretreat + len
21 day pretreat
% killing
150
100
50
0
RPMI-8226 + veh
RPMI-8226 + len
veh pretreat + veh
veh pretreat + len
len pretreat + veh
len pretreat + len

FIG. 23A

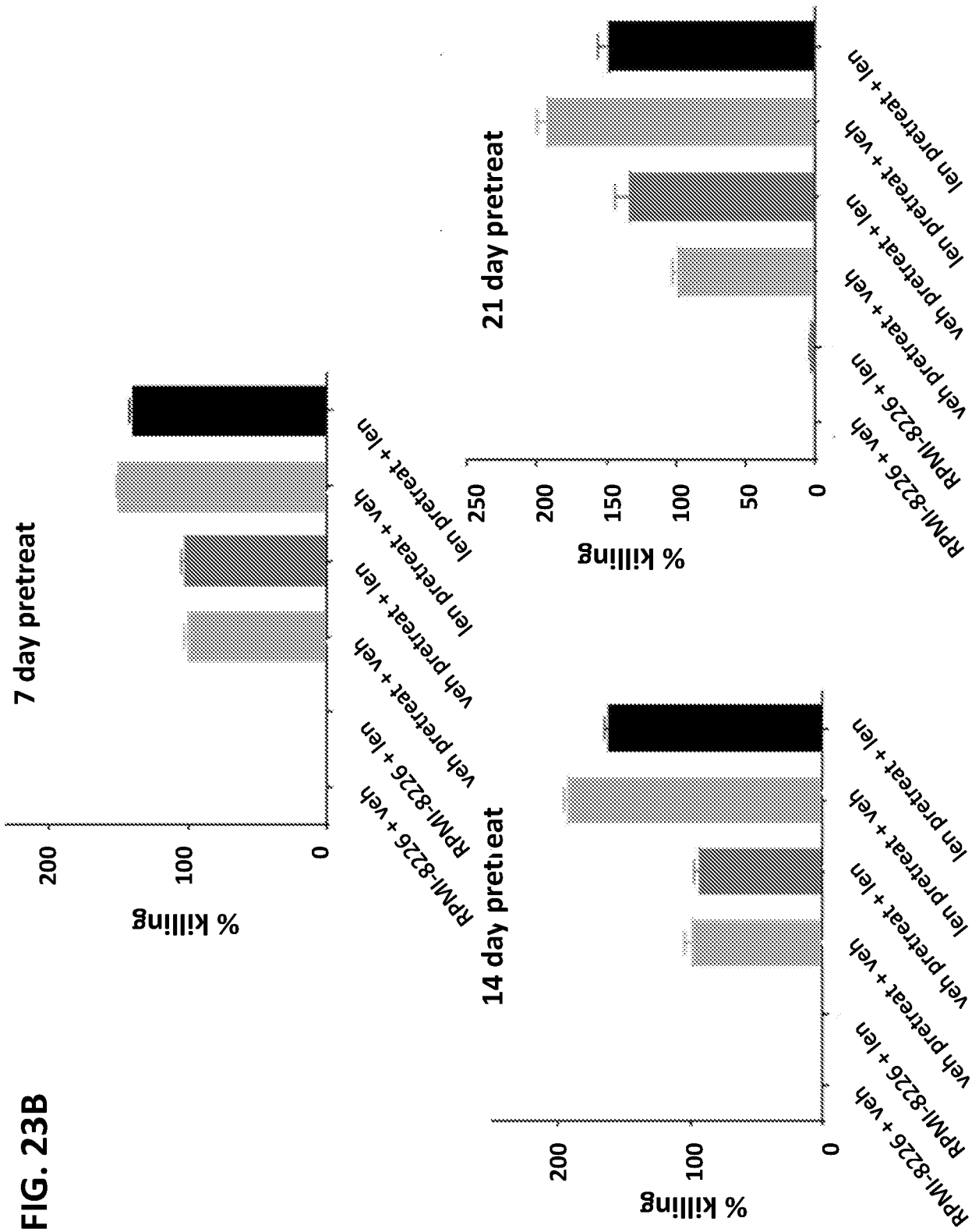

7 day pretreat
% killing
0
100
200
RPMI-8226 + veh
RPMI-8226 + len
veh pretreat + veh
veh pretreat + len
len pretreat + veh
len pretreat + len
14 day pretreat
% killing
0
100
200
RPMI-8226 + veh
RPMI-8226 + len
veh pretreat + veh
veh pretreat + len
len pretreat + veh
len pretreat + len
21 day pretreat
% killing
0
50
100
150
200
250
RPMI-8226 + veh
RPMI-8226 + len
veh pretreat + veh
veh pretreat + len
len pretreat + veh
len pretreat + len

FIG. 23B

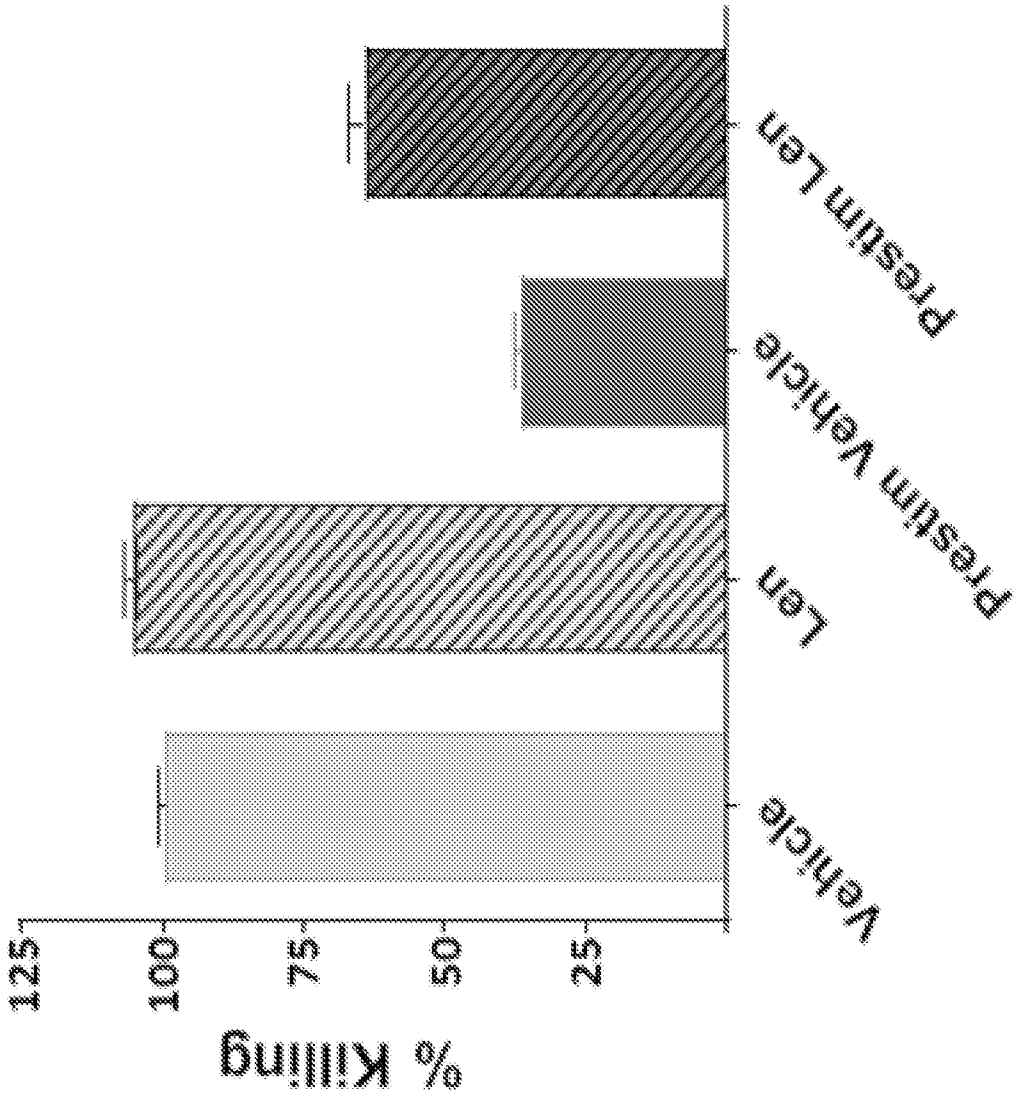

% Killing
125
100
75
50
25
Vehicle
Len
Presilin Vehicle
Presilin Len

FIG. 24A

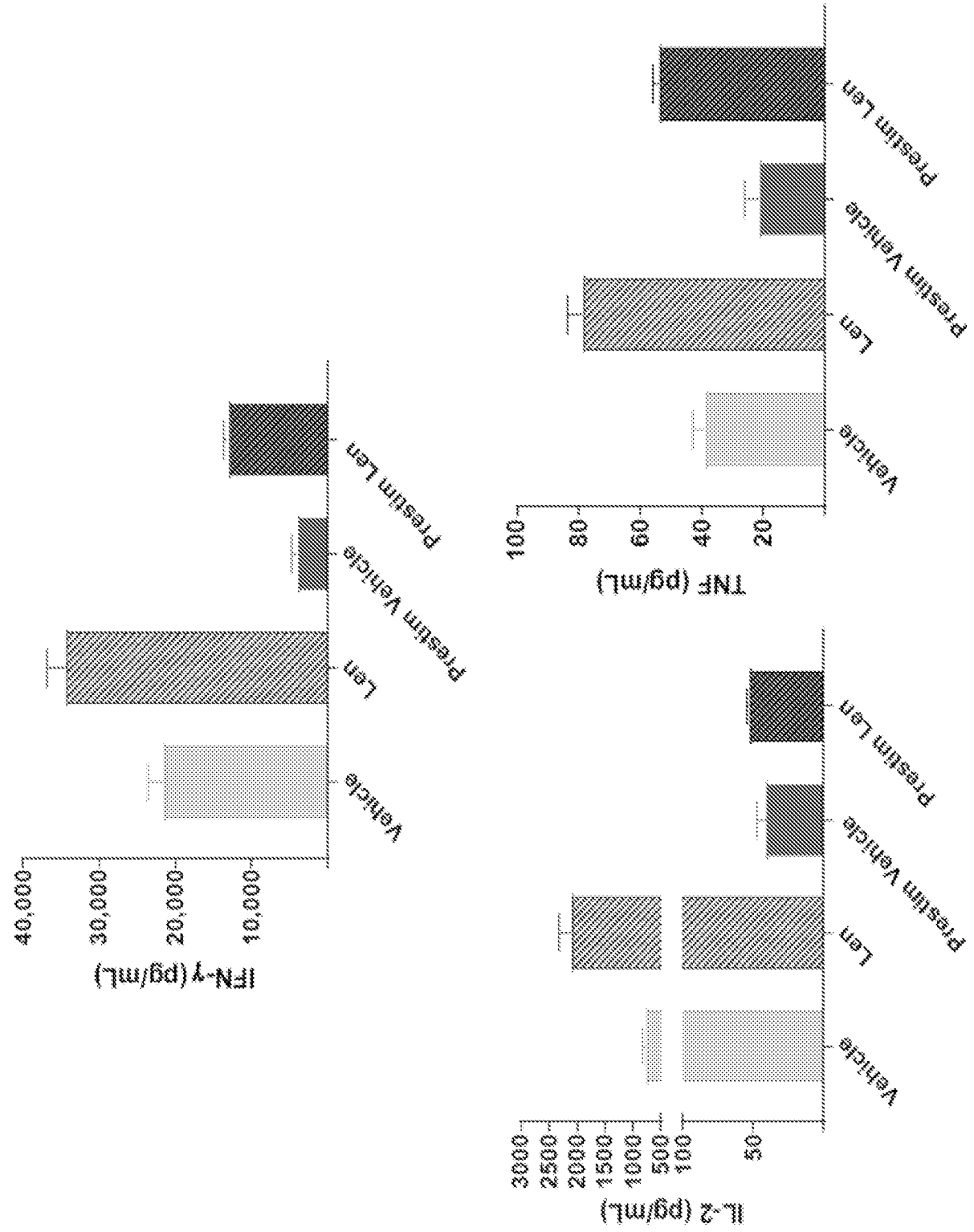

IFN-γ (pg/mL)
40,000
30,000
20,000
10,000
Vehicle
Len
Presatin Vehicle
Presatin Len
TNF (pg/mL)
100
80
60
40
20
Vehicle
Len
Presatin Vehicle
Presatin Len
IL-2 (pg/mL)
3000
2500
2000
1500
1000
500
100
50
Vehicle
Len
Presatin Vehicle
Presatin Len

FIG. 24B

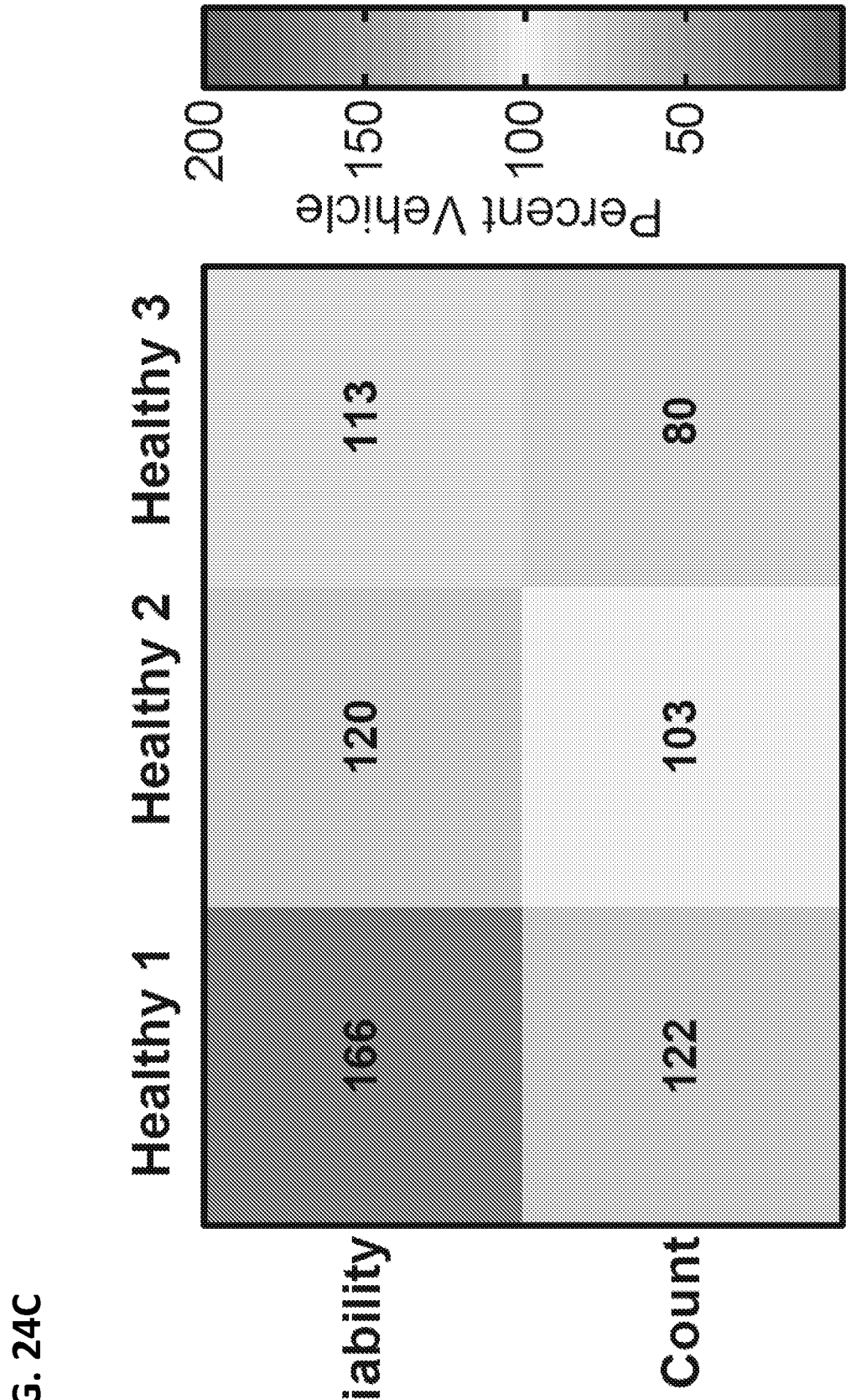

Healthy 1
Healthy 2
Healthy 3
166
120
113
122
103
80
Viability
Count
200
150
100
50
Percent Vehicle

FIG. 24C

FIG. 24D

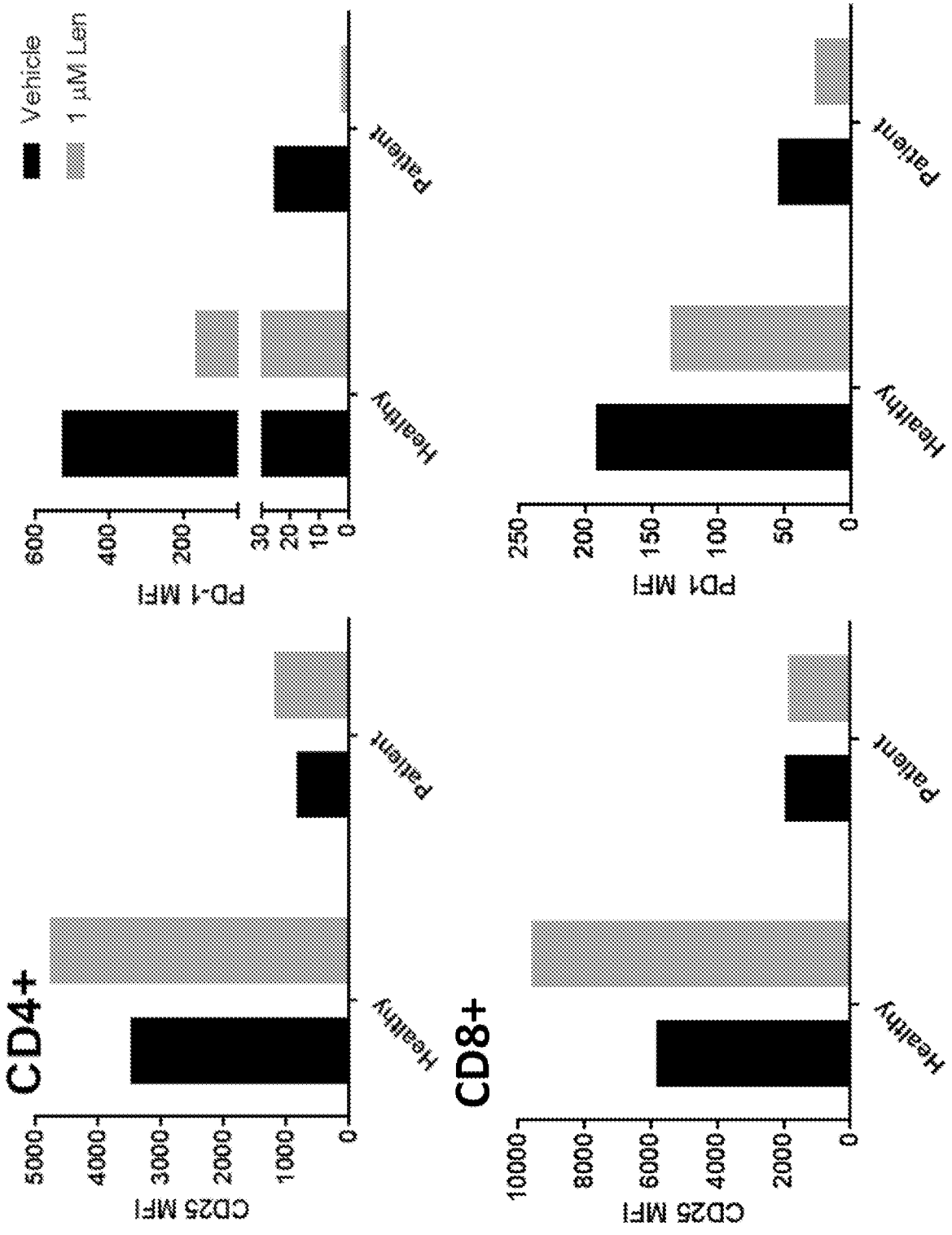
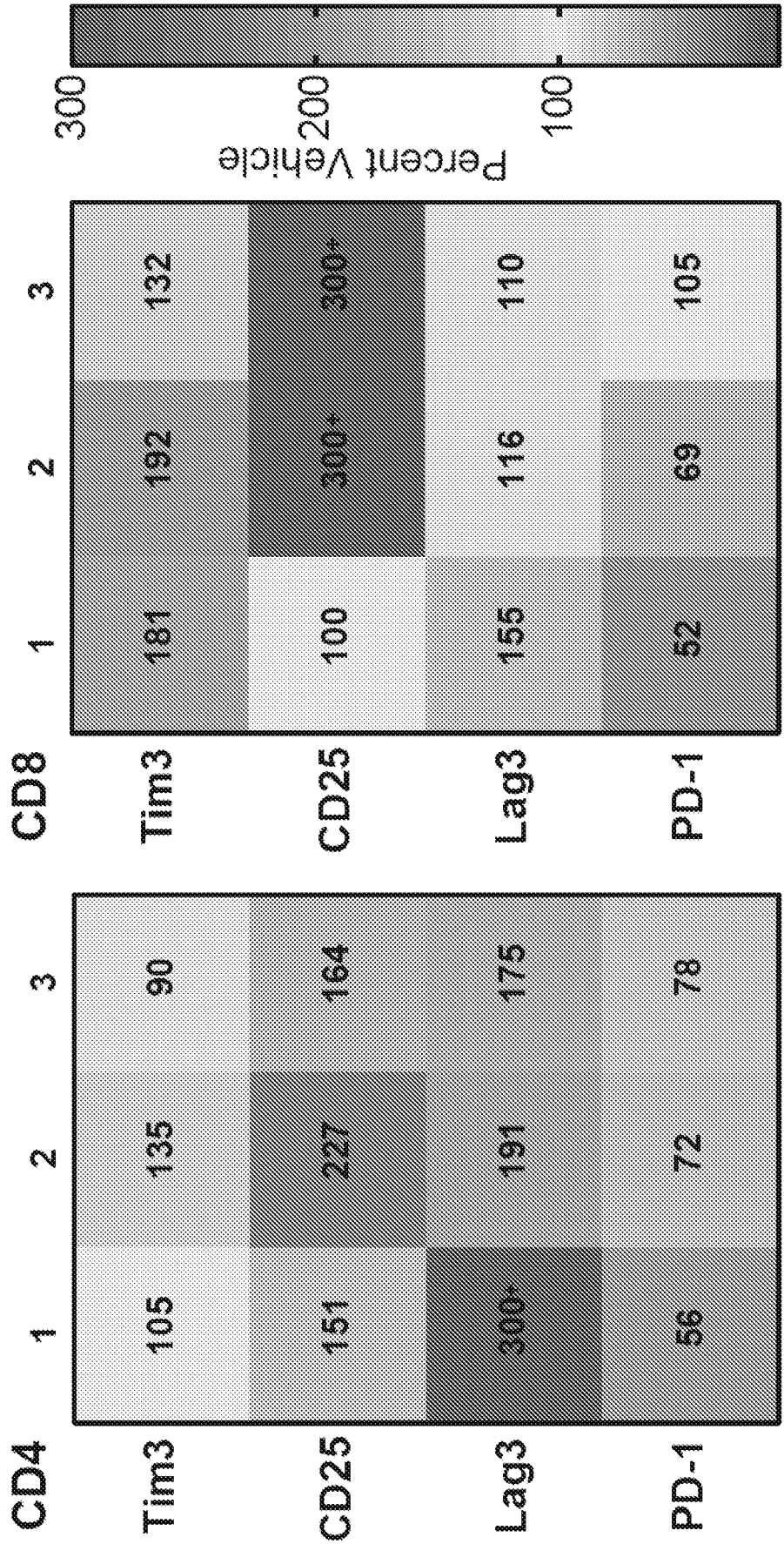

CD4+
CD8+
Vehicle
1 μM Len
CD25 MFI
PD-1 MFI
PD1 MFI
Healthy
Patient
0
1000
2000
3000
4000
5000
6000
8000
10000
10
20
30
200
400
600
50
100
150
250

FIG. 24E


CD4
1
2
3
Tim3
105
135
90
CD25
151
227
164
Lag3
300+
191
175
PD-1
56
72
78
CD8
1
2
3
Tim3
181
192
132
CD25
100
300+
300+
Lag3
155
116
110
PD-1
52
69
105
Percent Vehicle
300
200
100

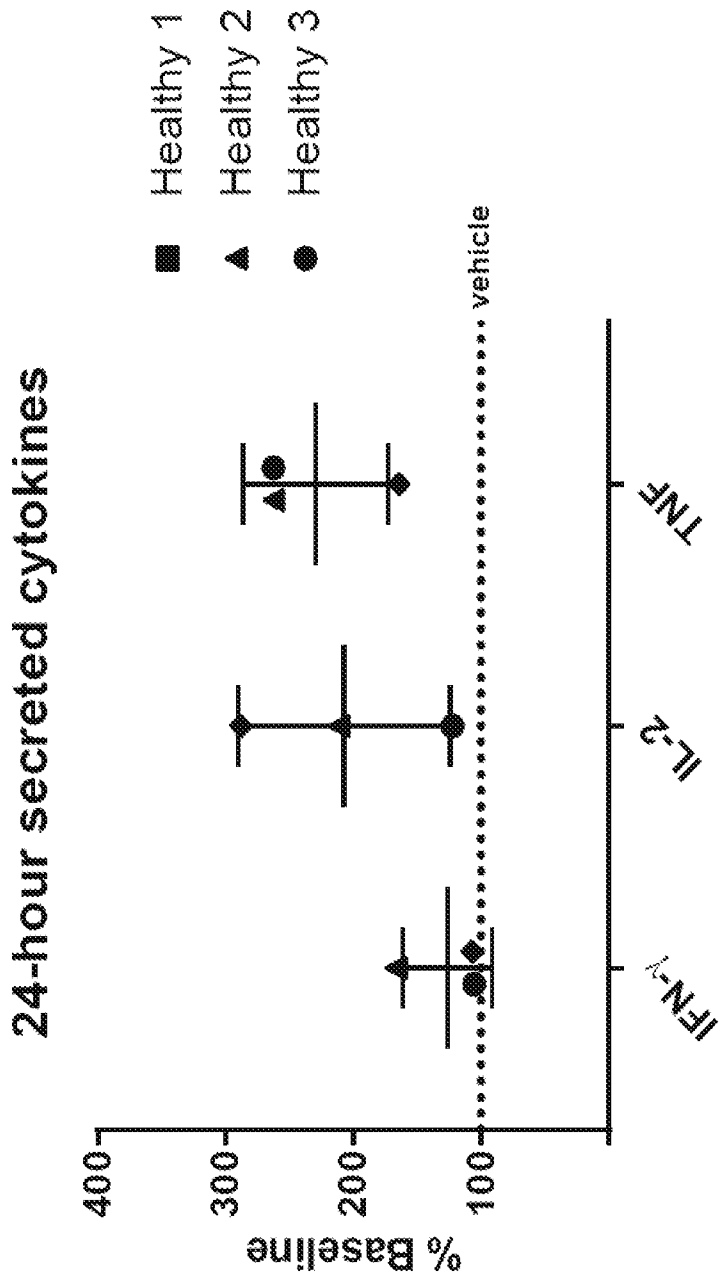

24-hour secreted cytokines
Healthy 1
Healthy 2
Healthy 3
vehicle
% Baseline
400
300
200
100
IFN-γ
IL-2
TNF

FIG. 25A

FIG. 25B

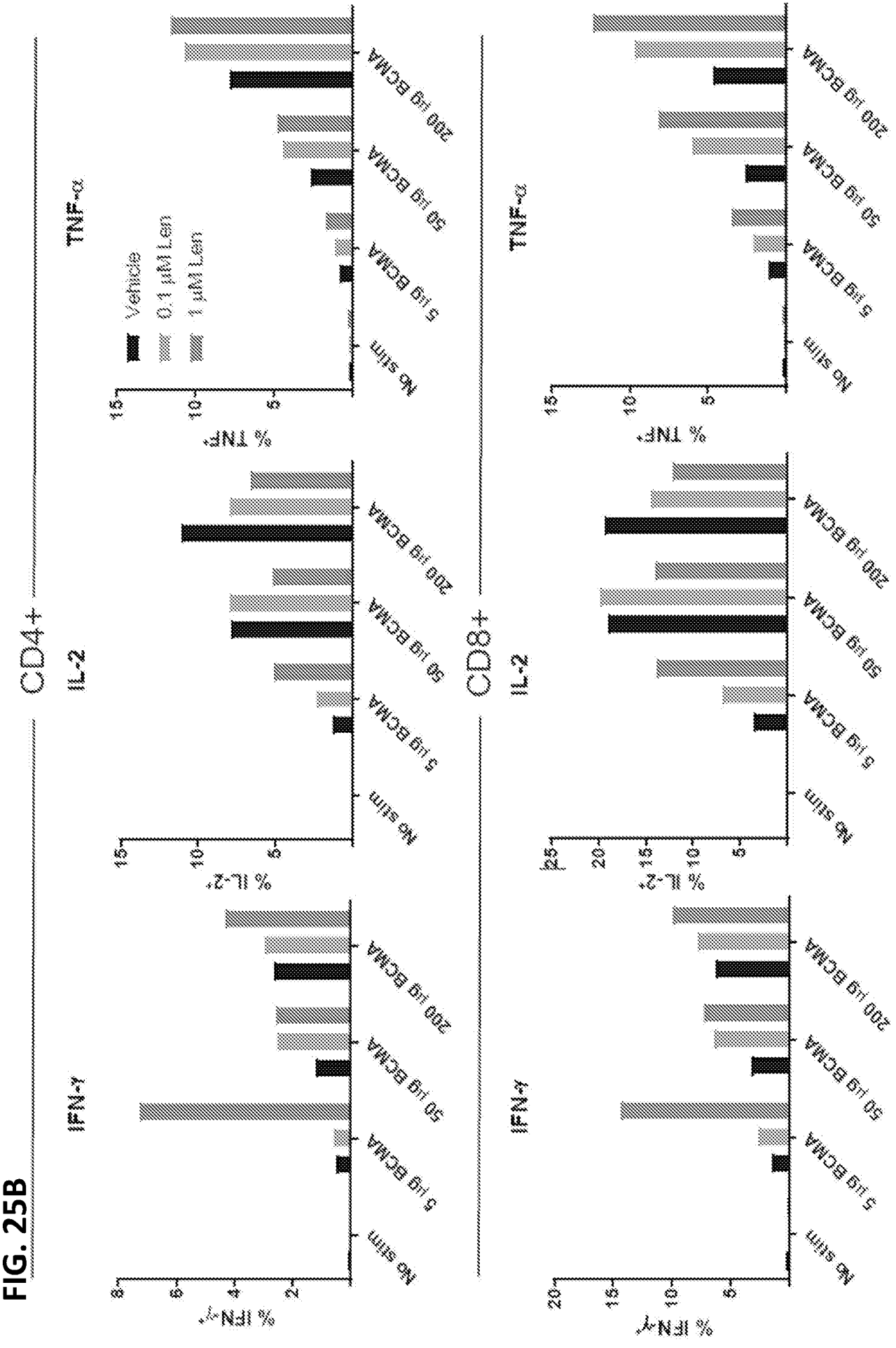

CD4+
CD8+
TNF-α
IL-2
IFN-γ
% TNF+
% IL-2+
% IFN-γ+
Vehicle
0.1 μM Len
1 μM Len
No stim
5 μg BCMA
50 μg BCMA
200 μg BCMA

FIG. 25C

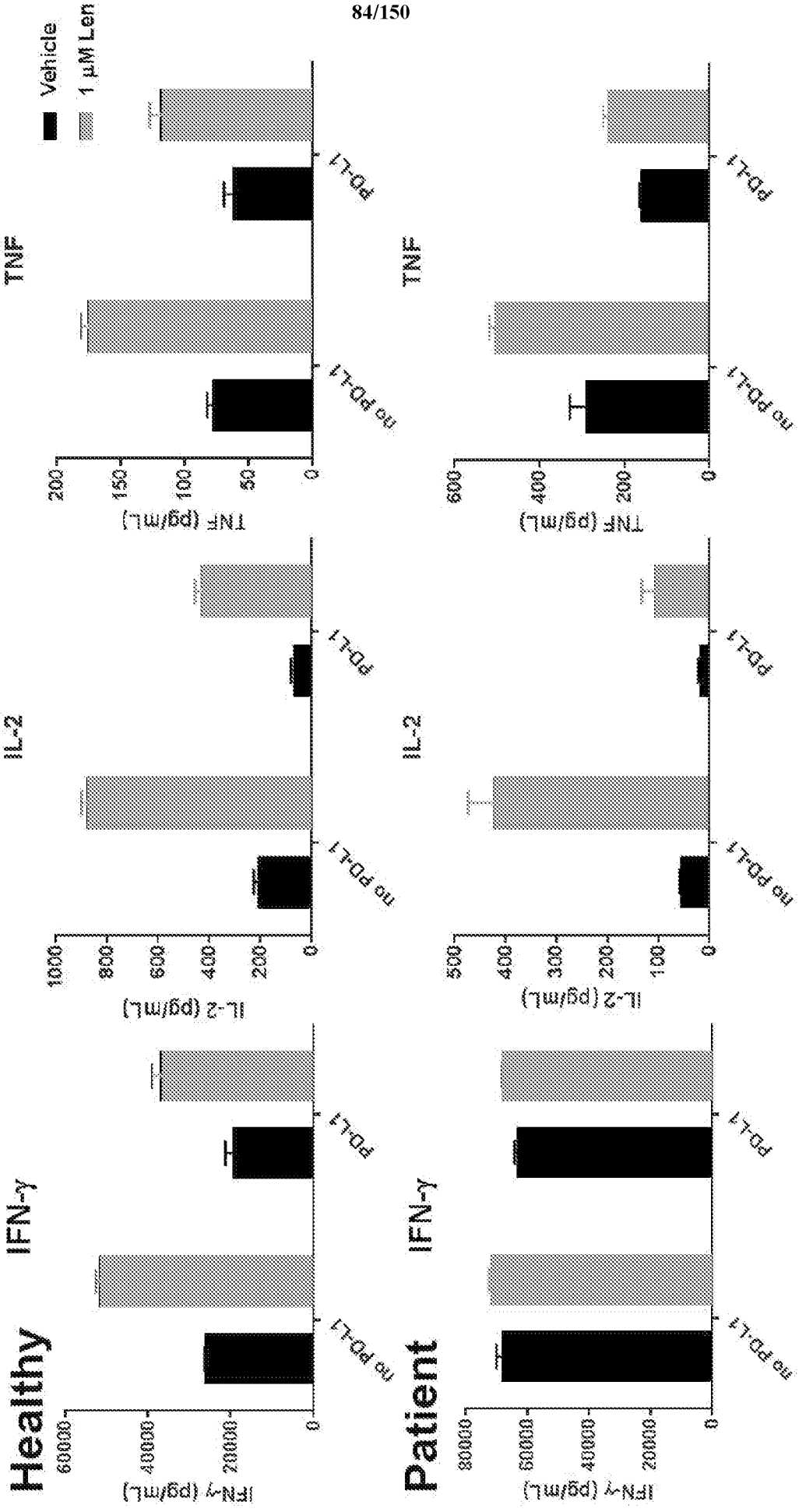
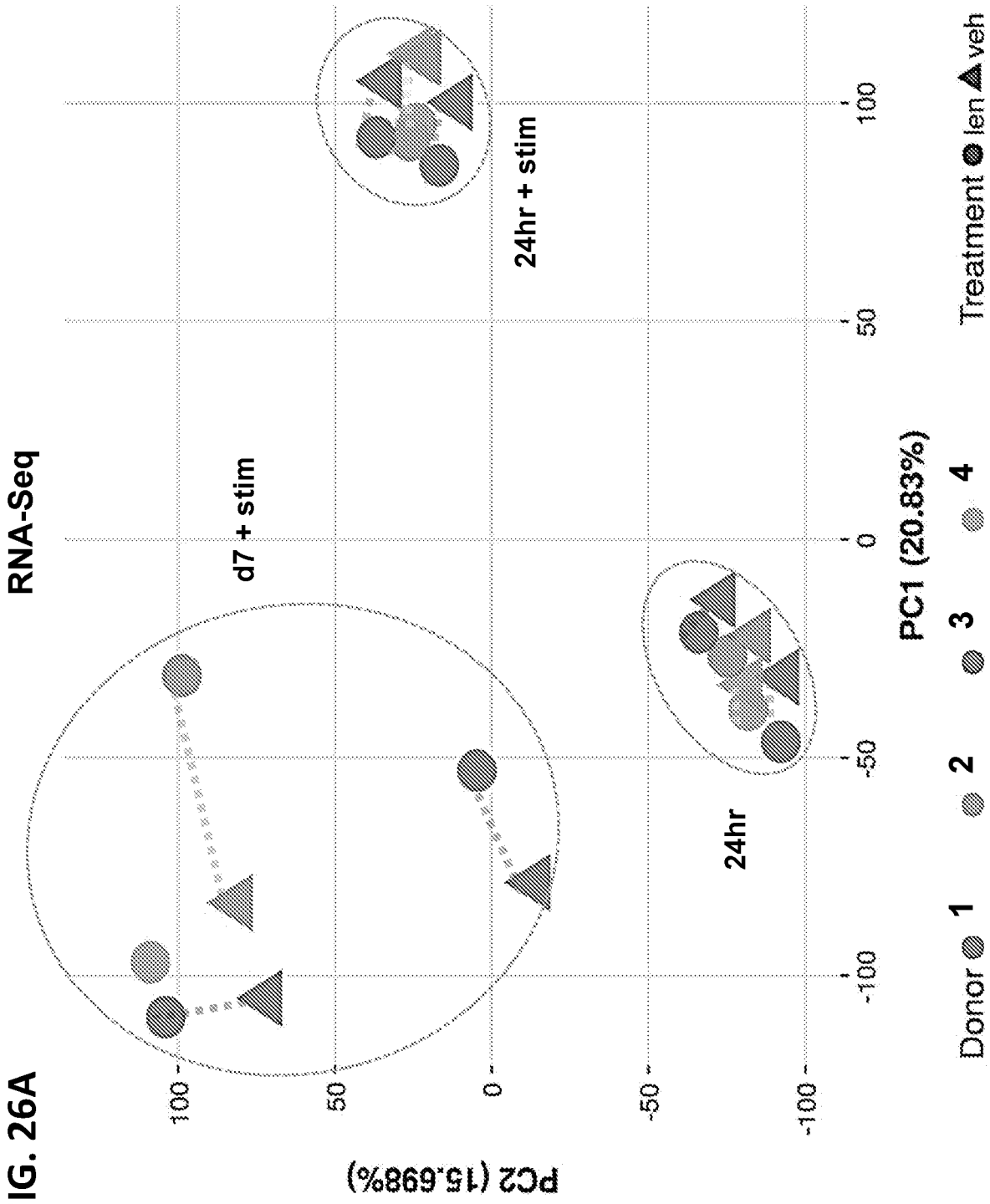

Healthy
Patient
IFN-γ
IL-2
TNF
Vehicle
1 μM Len
IFN-γ (pg/mL)
IL-2 (pg/mL)
TNF (pg/mL)
no PD-L1
PD-L1

FIG. 26A


RNA-Seq
d7 + stim
24hr + stim
24hr
PC2 (15.698%)
PC1 (20.83%)
100
50
0
-50
-100
Donor 1 2 3 4
Treatment len veh

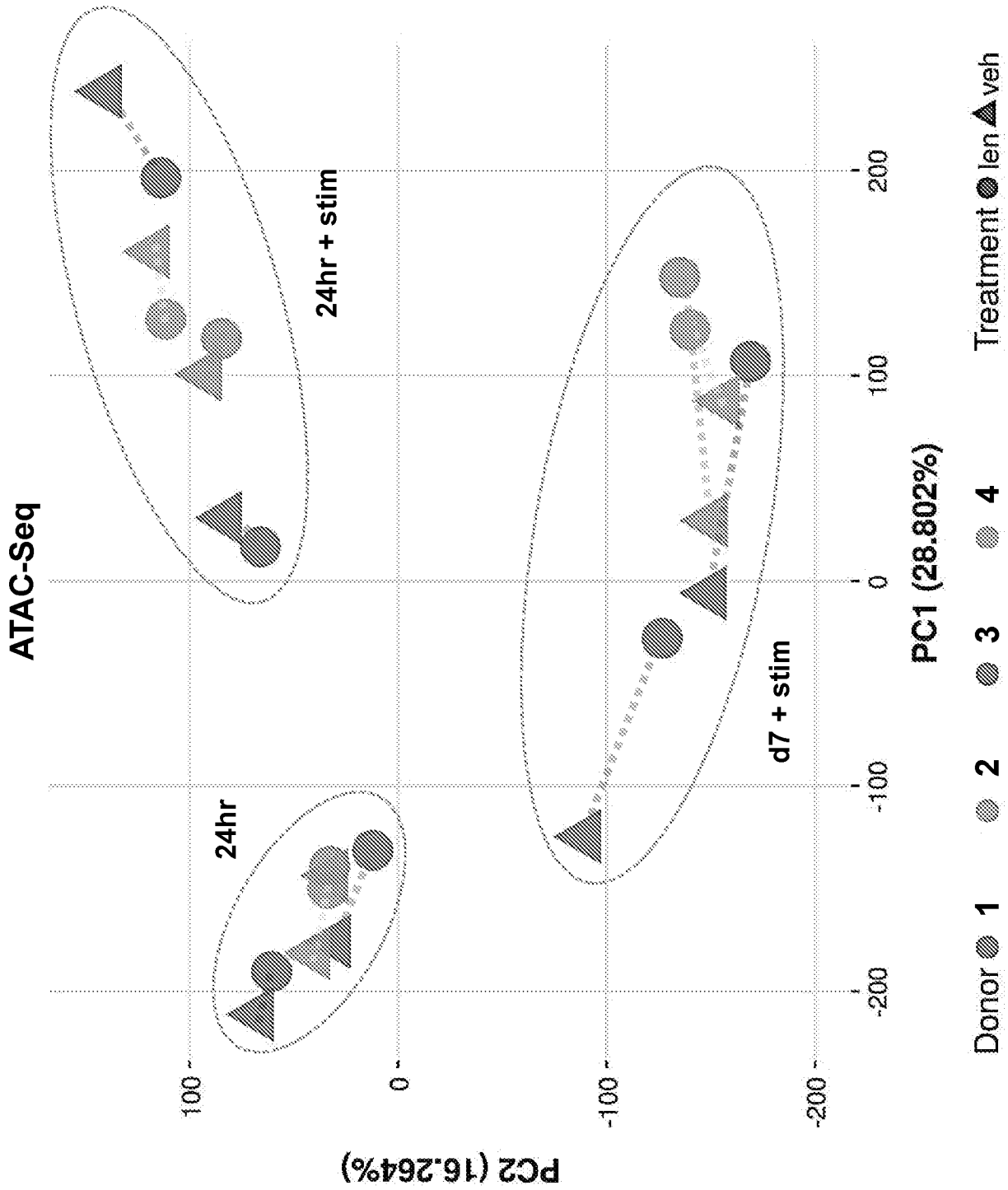
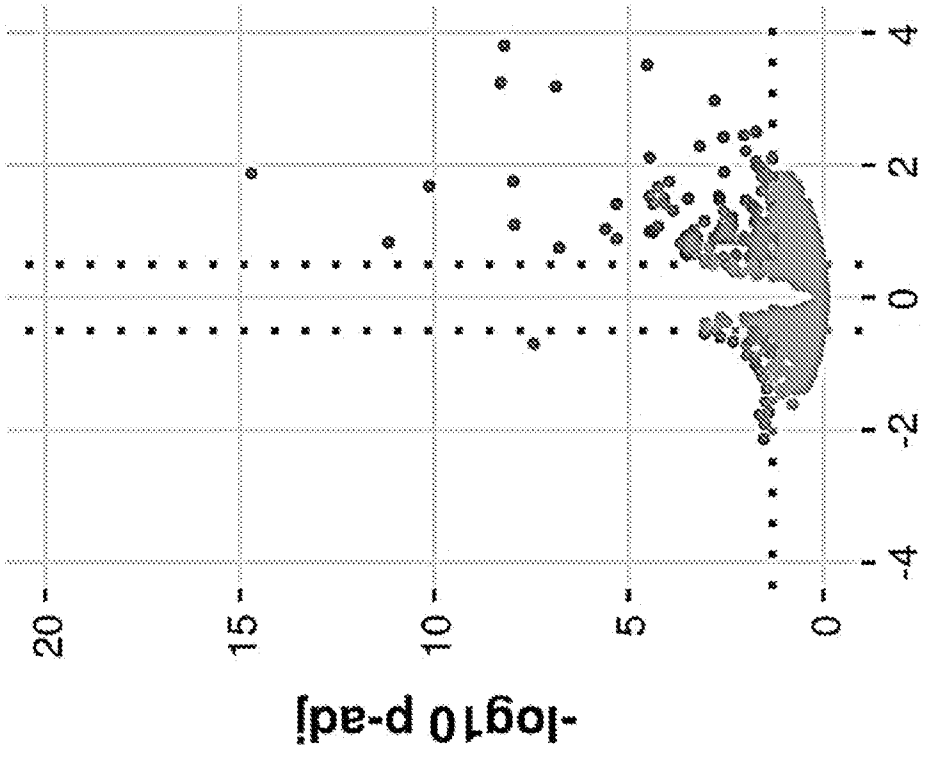

ATAC-Seq
24hr
24hr + stim
d7 + stim
PC1 (28.802%)
PC2 (16.264%)
100
0
-100
-200
200
Donor 1 2 3 4
Treatment len veh

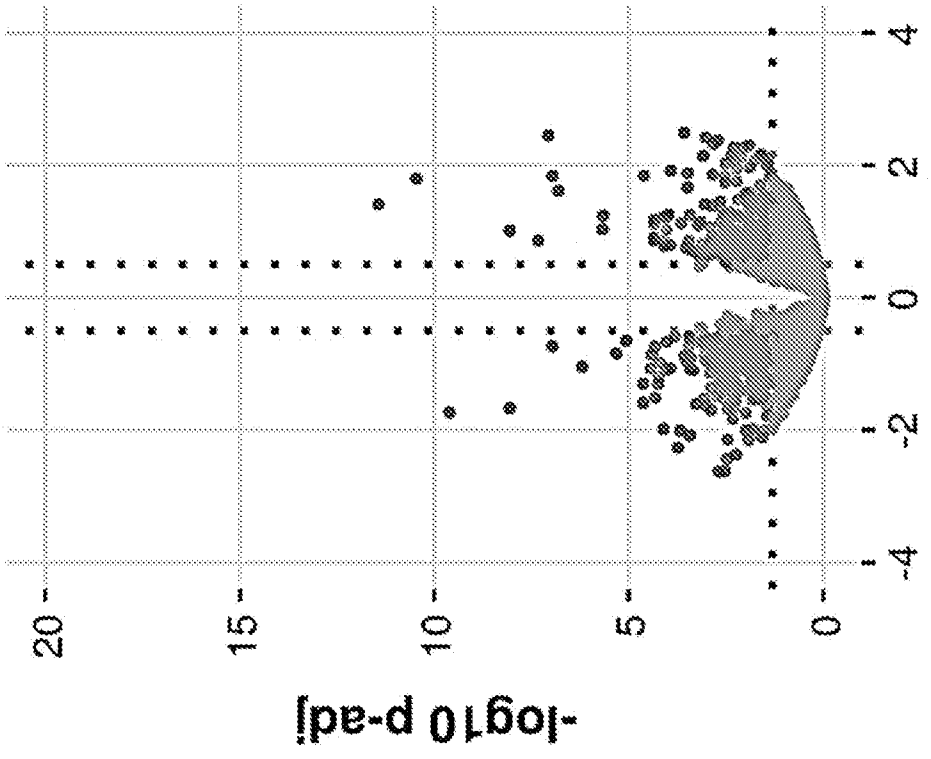
FIG. 26B

FIG. 27A 24hr: Len/Vehicle



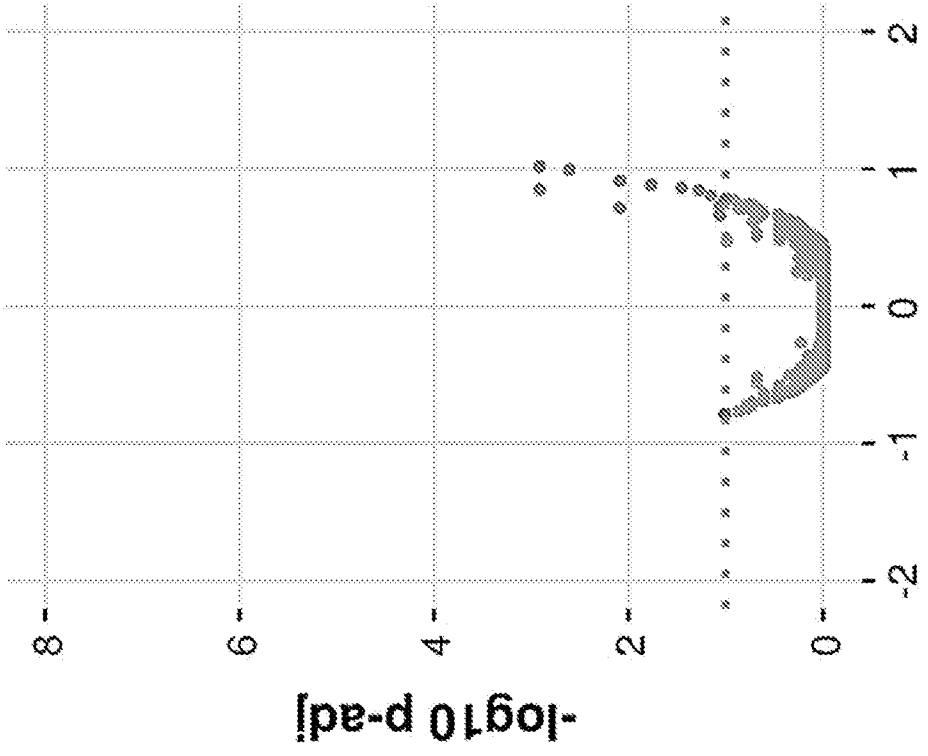
log2 fold change		
down	up	total
37	177	214

FIG. 27B d7: Len/Vehicle



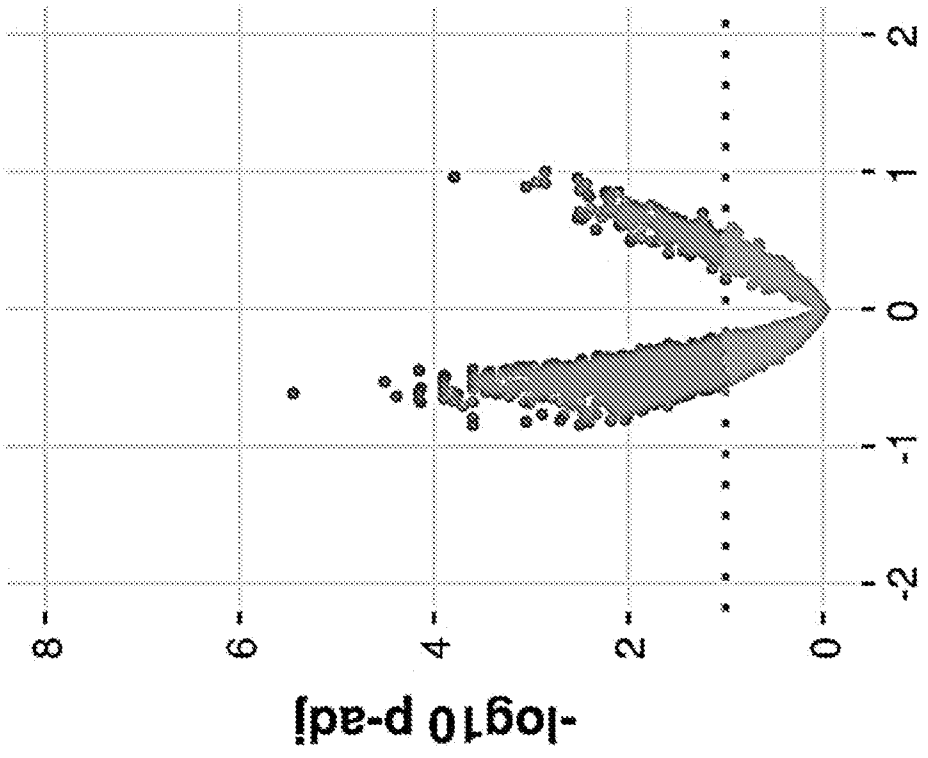
log2 fold change		
down	up	total
255	328	583

FIG. 27C 24hr: Len/Vehicle



down	up	total
2	13	15

FIG. 27D d7: Len/Vehicle



down	up	total
2510	294	2804

FIG. 28A

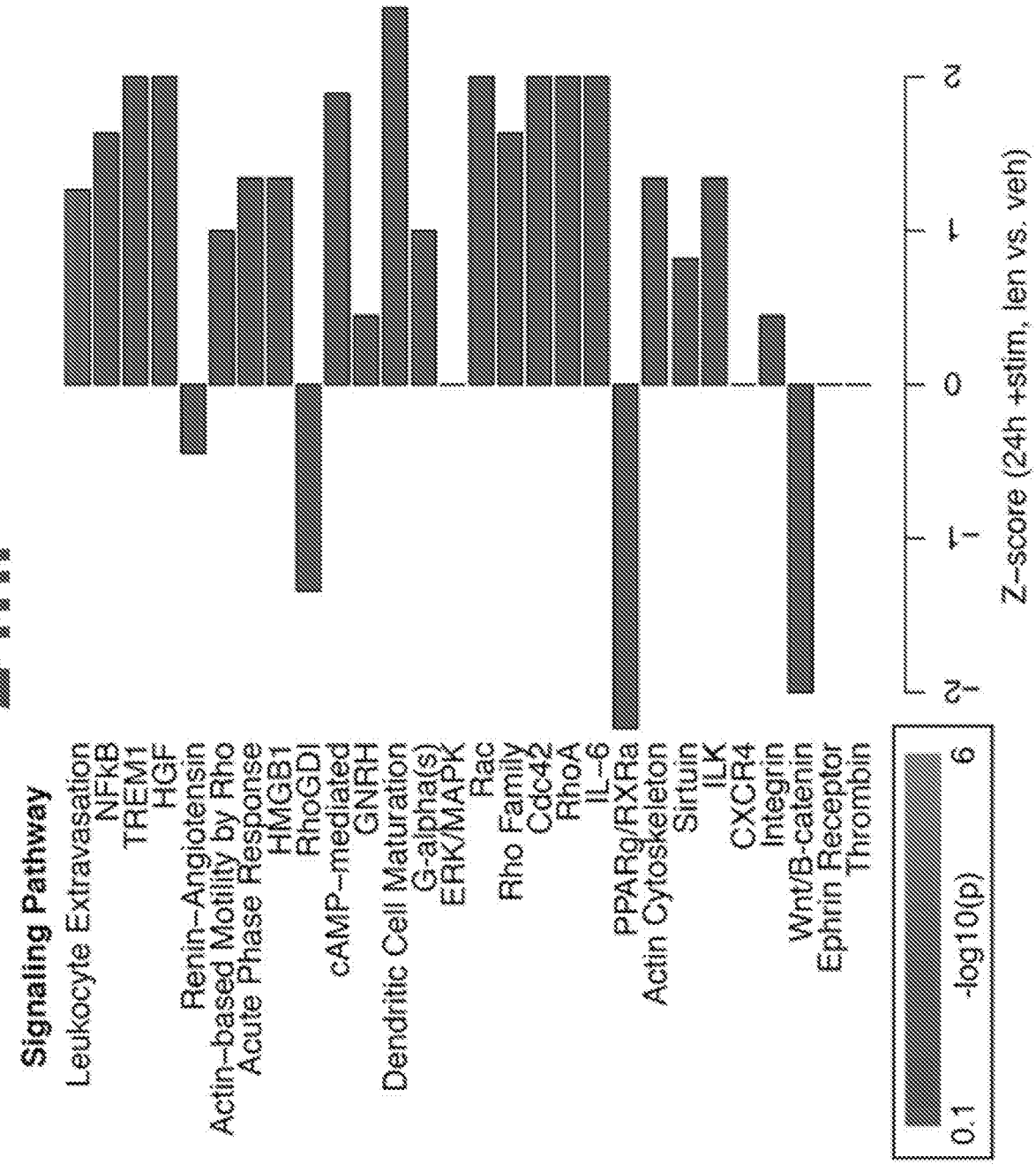
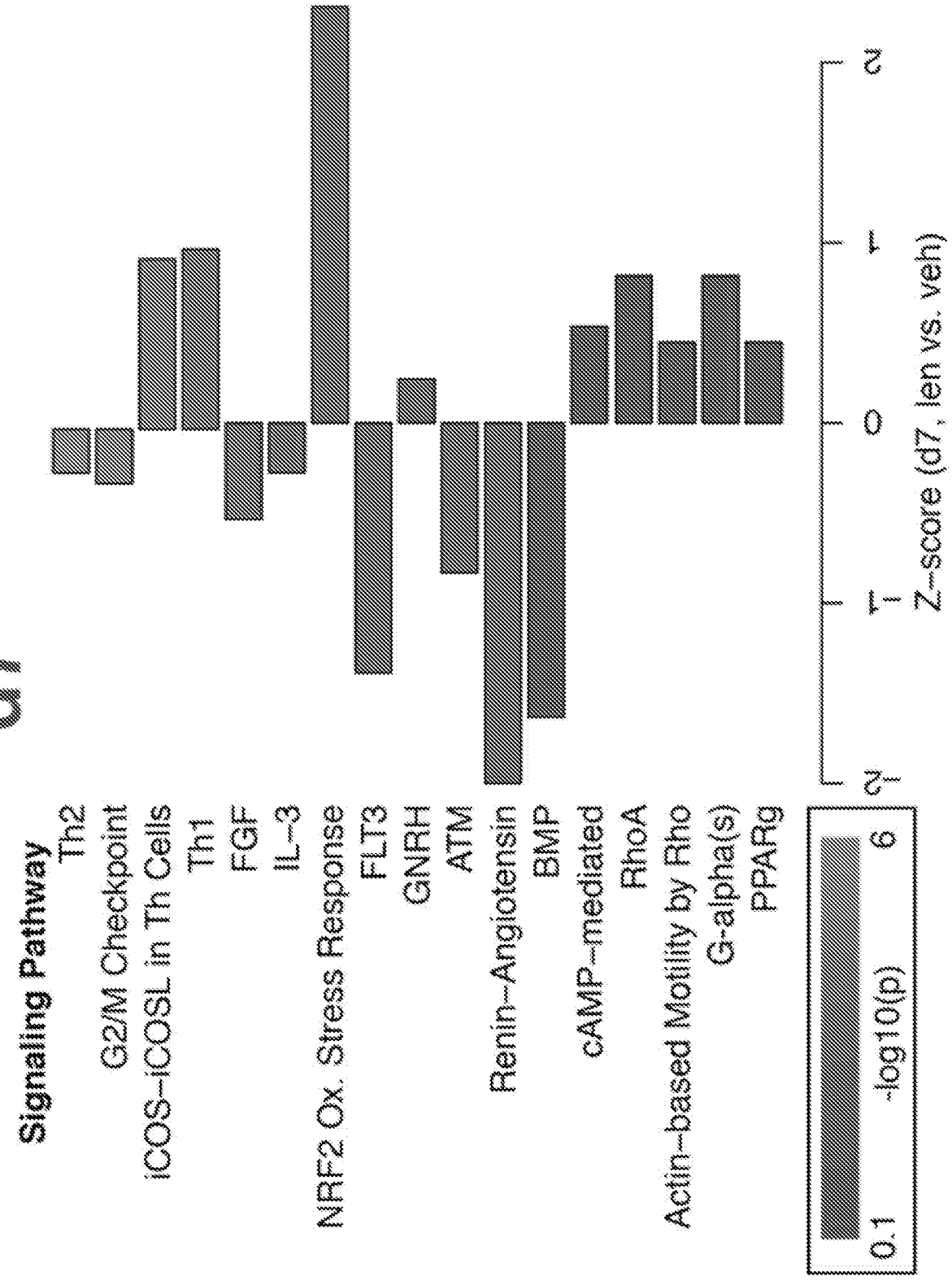

24hr
Signaling Pathway
Leukocyte Extravasation
NFkB
TREM1
HGF
Renin–Angiotensin
Actin–based Motility by Rho
Acute Phase Response
HMGB1
RhoGDI
cAMP–mediated
GNRH
Dendritic Cell Maturation
G-alpha(s)
ERK/MAPK
Rac
Rho Family
Cdc42
RhoA
IL–6
PPARg/RXRa
Actin Cytoskeleton
Sirtuin
ILK
CXCR4
Integrin
Wnt/B-catenin
Ephrin Receptor
Thrombin
0.1
-log10(p)
6
-2
-1
0
1
2
Z–score (24h +stim, len vs. veh)

FIG. 28B


d7
Signaling Pathway
Th2
G2/M Checkpoint
iCOS–iCOSL in Th Cells
Th1
FGF
IL–3
NRF2 Ox. Stress Response
FLT3
GNRH
ATM
Renin–Angiotensin
BMP
cAMP–mediated
RhoA
Actin–based Motility by Rho
G-alpha(s)
PPARg
-log10(p)
0.1
6
-2
-1
0
1
2
Z–score (d7, len vs. veh)

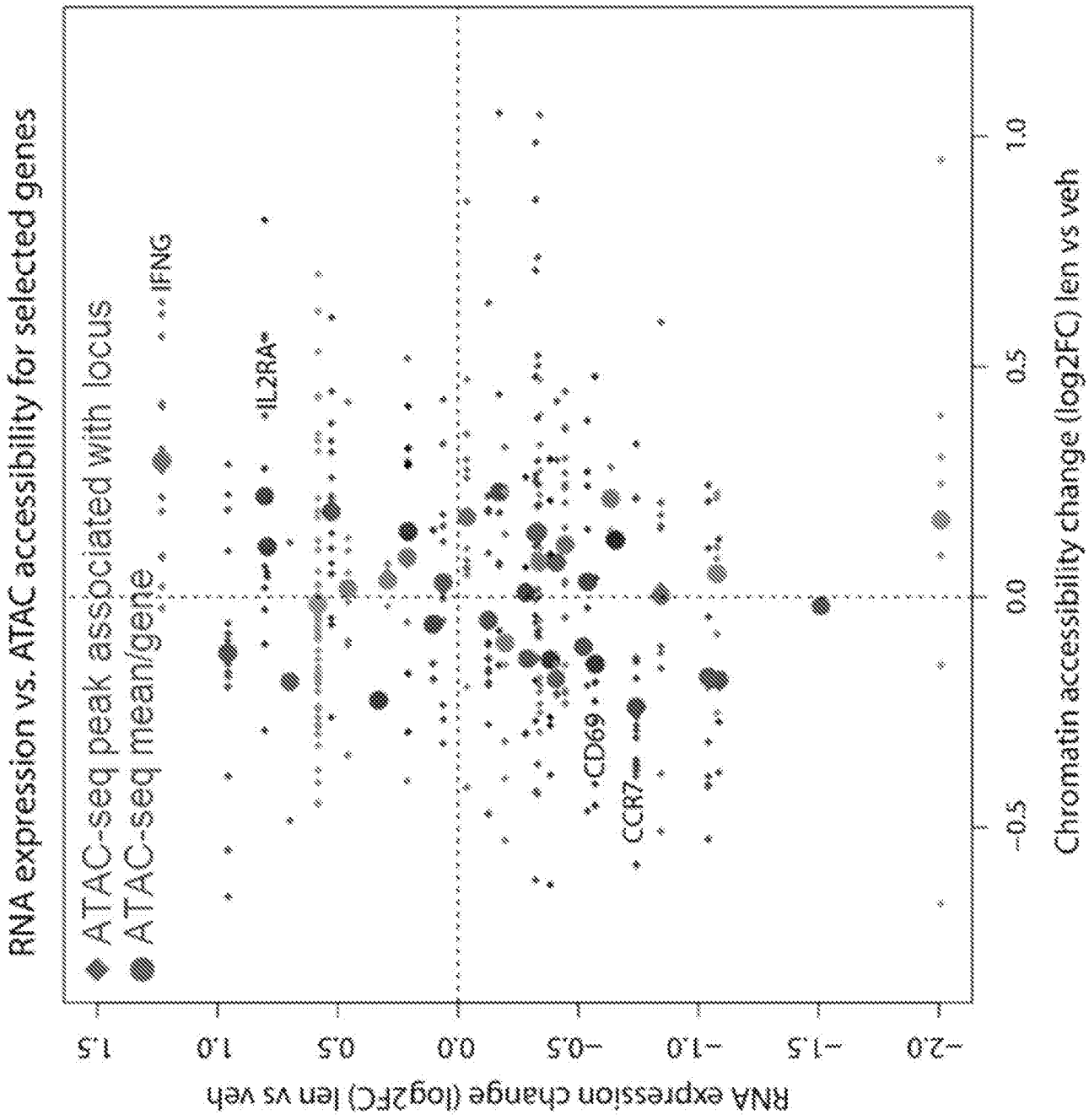
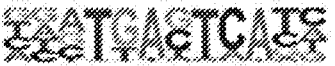
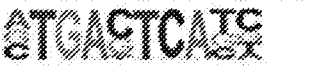
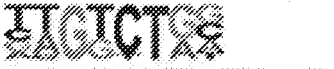
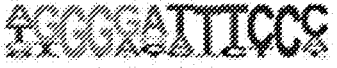

RNA expression vs. ATAC accessibility for selected genes
ATAC-seq peak associated with locus
ATAC-seq mean/gene
IFNG
IL2RA
CD69
CCR7
RNA expression change (log2FC) len vs veh
1.5
1.0
0.5
0.0
−0.5
−1.0
−1.5
−2.0
−0.5
0.0
0.5
1.0
Chromatin accessibility change (log2FC) len vs veh

FIG. 29

FIG. 30

Motif Name	Motif	Log P-value	% of Target Sequences with Motif
Atf3(bZIP)/GBM-ATF3		-7.66E+01	61.90%
BATF(bZIP)/Th17-BATF		-7.54E+01	61.56%
Fra1(bZIP)/BT549-Fra1		-7.39E+01	58.50%
AP-1(bZIP)/ThioMac-PU.1		-7.33E+01	62.24%
JunB(bZIP)/DendriticCells-Junb		-7.17E+01	58.16%
Fosl2(bZIP)/3T3L1-Fosl2		-6.18E+01	46.94%
Jun-AP1(bZIP)/K562-cJun		-5.14E+01	39.12%
Smad3(MAD)/NPC-Smad3		-4.50E+01	56.46%
NFkB-p65(RHD)/GM12787-p65		-4.41E+01	29.59%
RUNX1(Runt)/Jurkat-RUNX1		-4.04E+01	50.00%
RUNX(Runt)/HPC7-Runx1		-3.77E+01	41.16%
Bach2(bZIP)/OCILy7-Bach2		-3.62E+01	26.53%

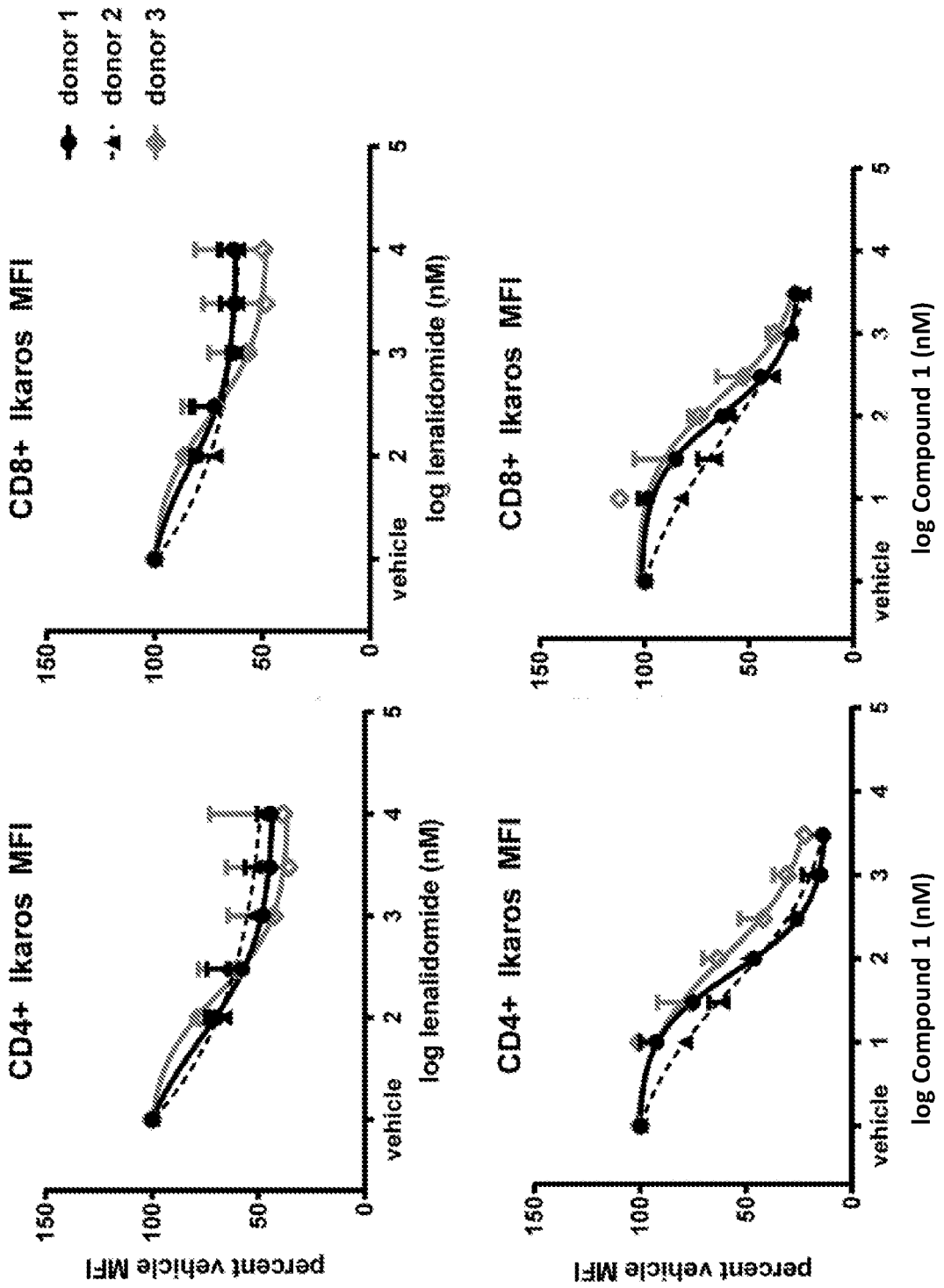
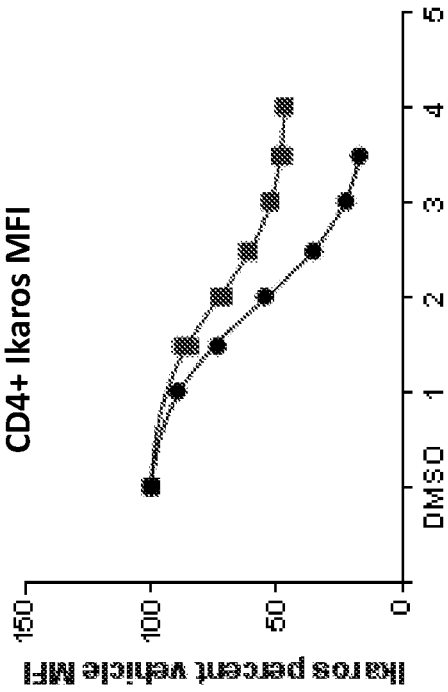
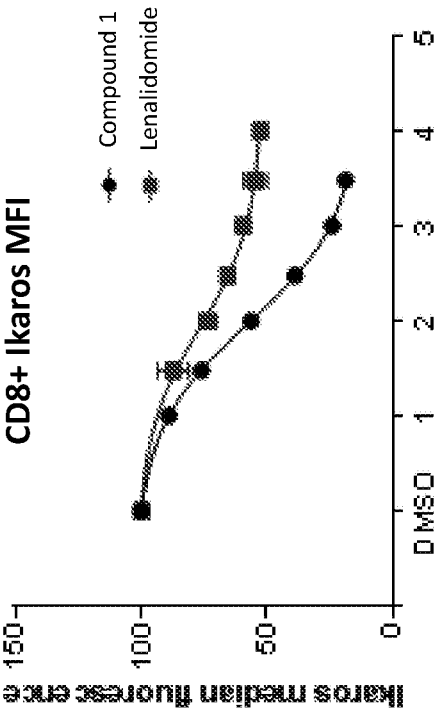

donor 1
donor 2
donor 3
CD8+ Ikaros MFI
CD4+ Ikaros MFI
percent vehicle MFI
150
100
50
0
vehicle
1
2
3
4
5
log lenalidomide (nM)
log Compound 1 (nM)

FIG. 31A

FIG. 31B



	Compound 1	Lenalidomide
EC50	82	93.55



	Compound 1	Lenalidomide
EC50	93.39	84.59

FIG. 31C

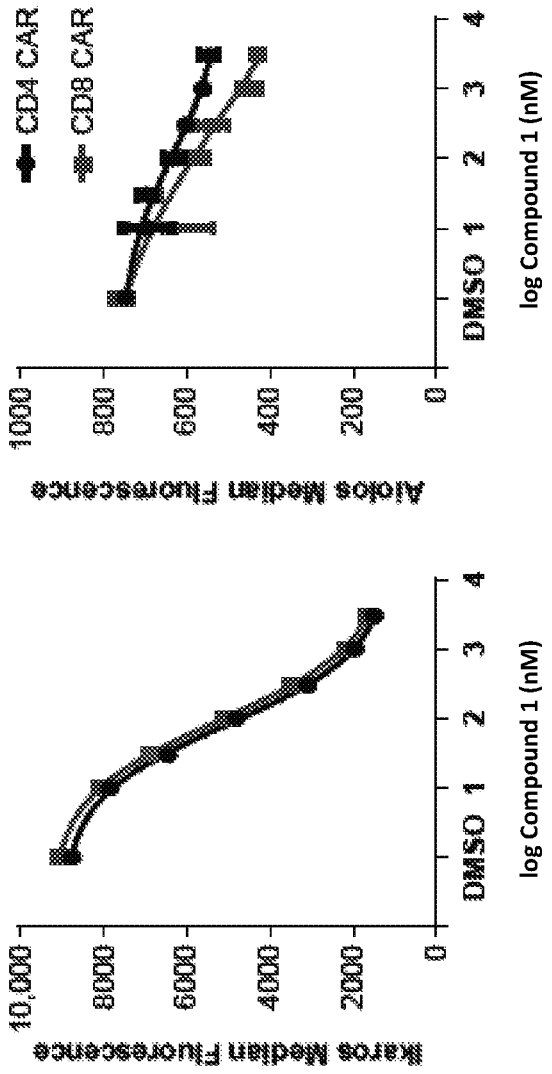

CD4 CAR
CD8 CAR
Aloxos Median Fluorescence
1000
800
600
400
200
0
DMSO
1
2
3
4
log Compound 1 (nM)
Karos Median Fluorescence
10,000
8000
6000
4000
2000
0
DMSO
1
2
3
4
log Compound 1 (nM)

FIG. 32A

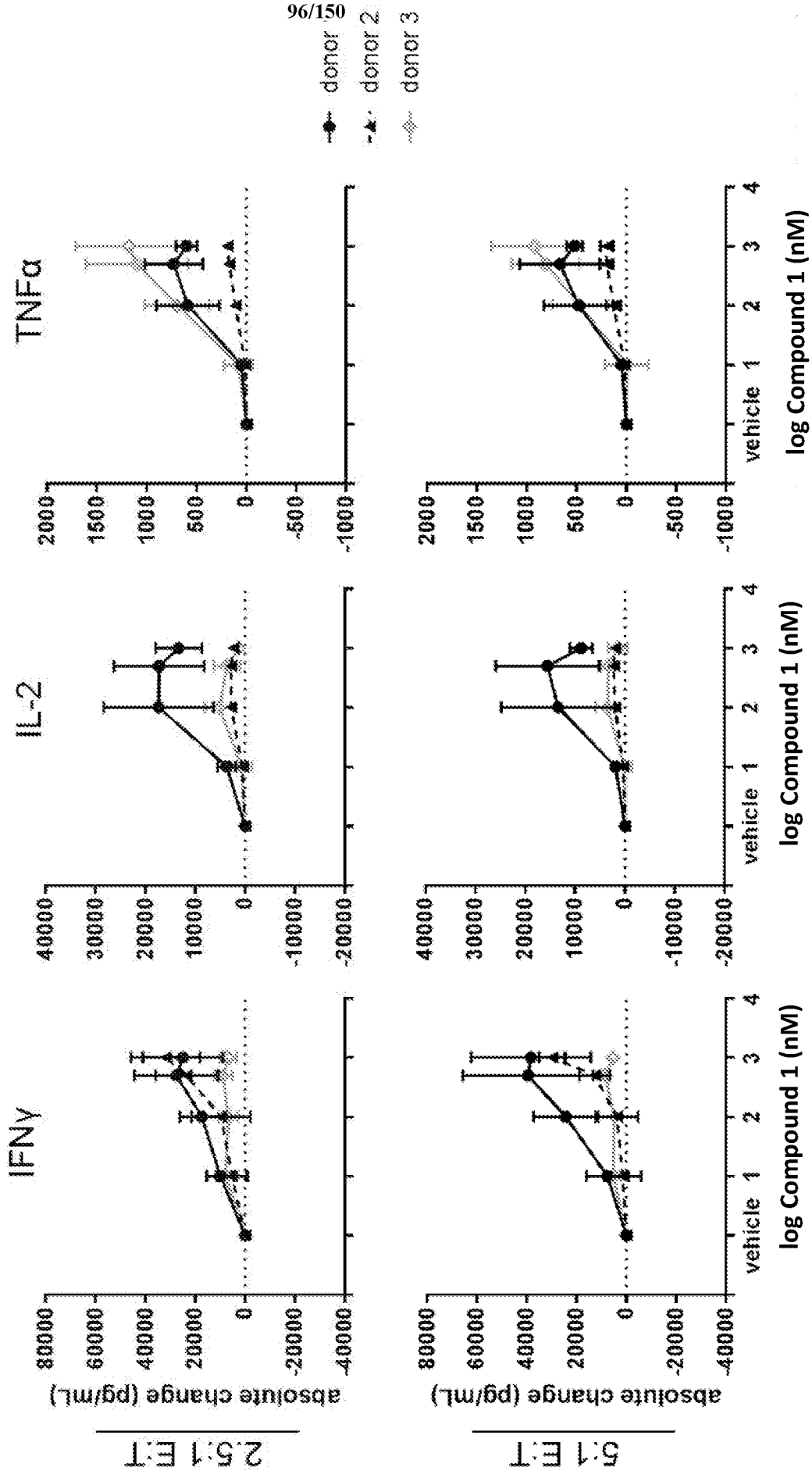
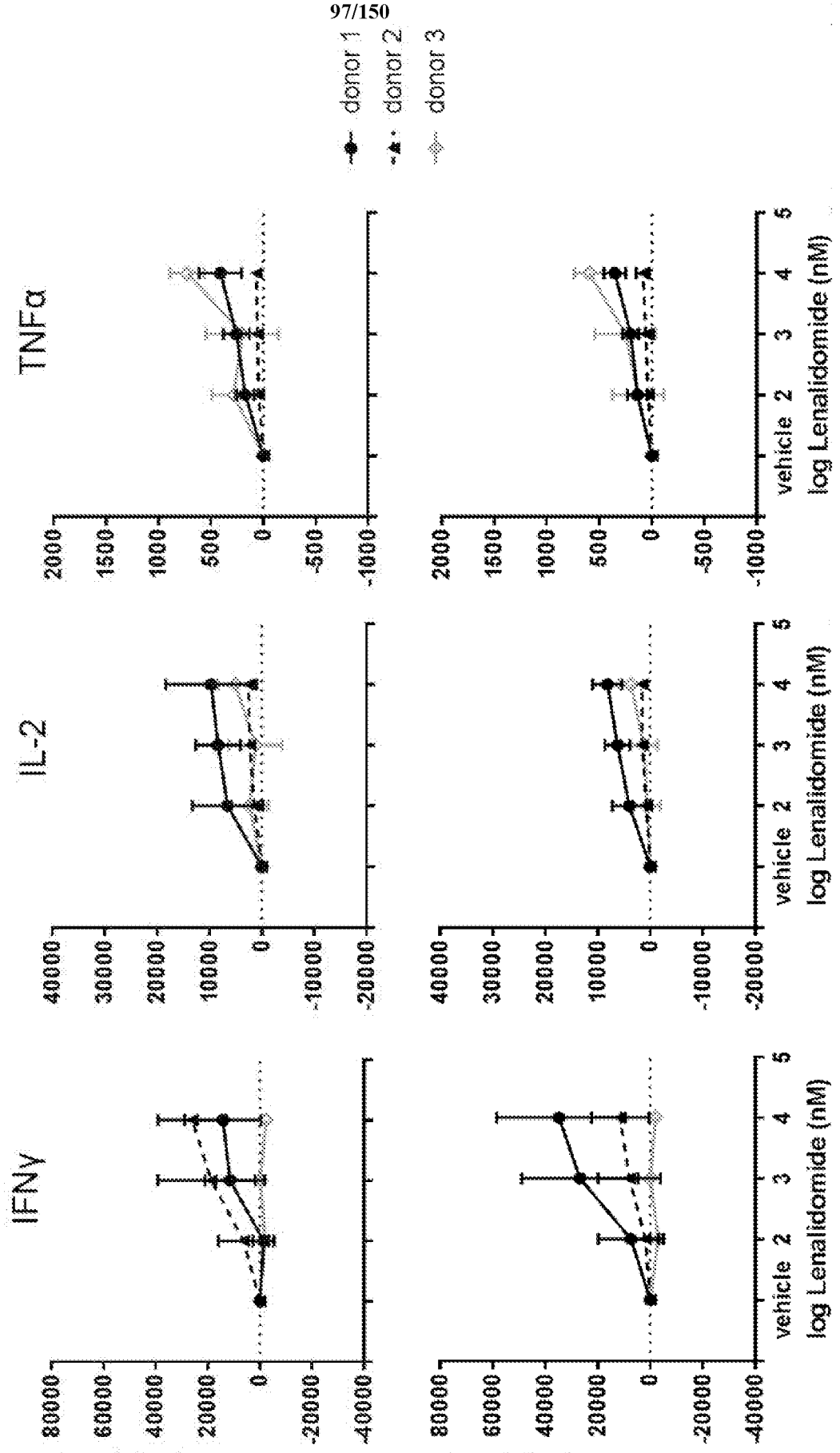

IFNγ
IL-2
TNFα
donor
donor 2
donor 3
2.5:1 E:T
5:1 E:T
absolute change (pg/mL)
log Compound 1 (nM)
vehicle
80000
60000
40000
20000
0
-20000
-40000
30000
10000
-10000
2000
1500
1000
500
-500
-1000
1
2
3
4

FIG. 32B


IFNγ
IL-2
TNFα
donor 1
donor 2
donor 3
2.5:1 E:T
5:1 E:T
absolute change (pg/mL)
log Lenalidomide (nM)
vehicle
80000
60000
40000
20000
0
-20000
-40000
30000
10000
-10000
2000
1500
1000
500
-500
-1000
2
3
4
5

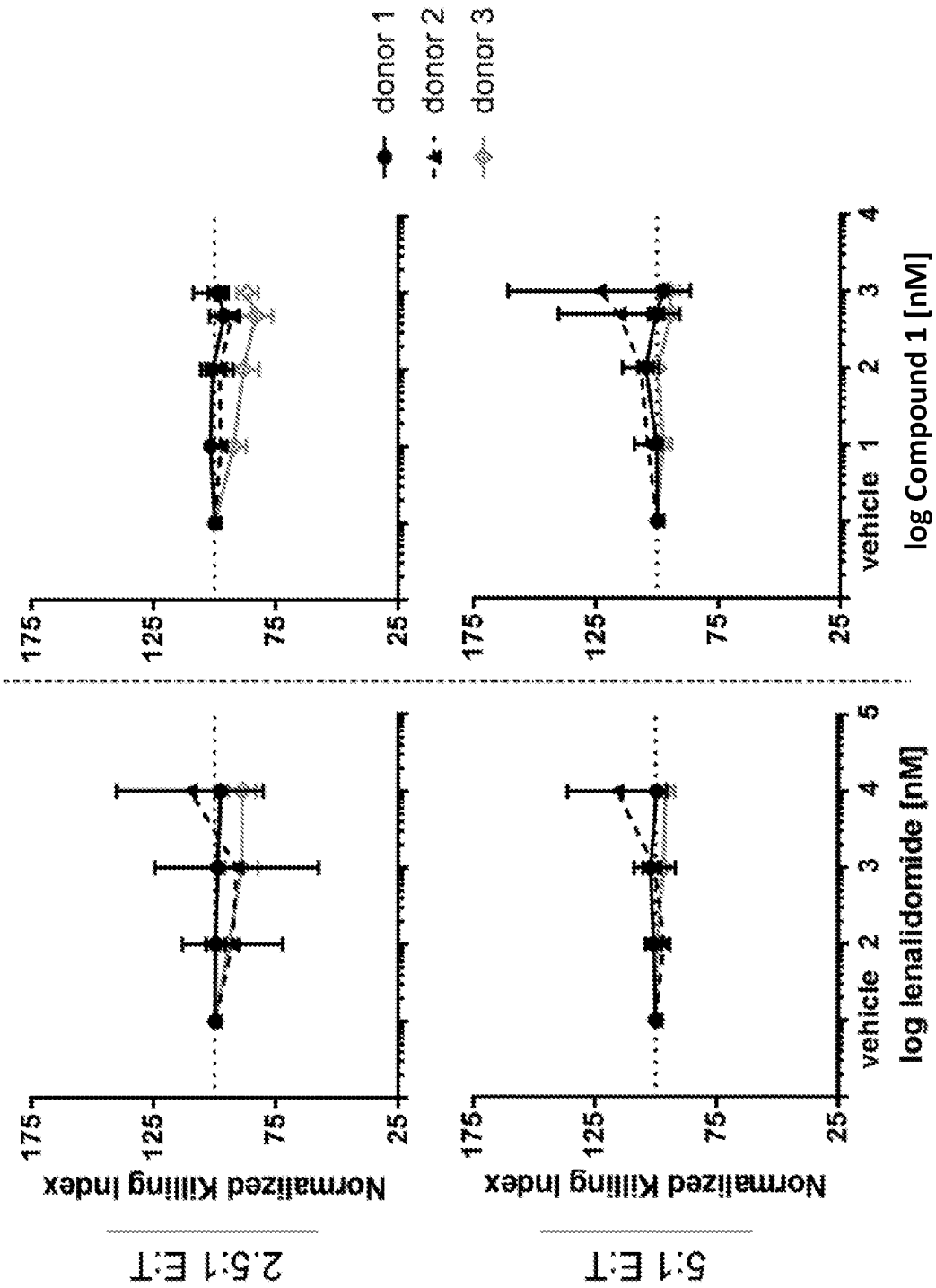

donor 1
donor 2
donor 3
2.5:1 E:T
5:1 E:T
Normalized Killing Index
175
125
75
25
vehicle
1
2
3
4
5
log lenalidomide [nM]
log Compound 1 [nM]

FIG. 33A

FIG. 33B

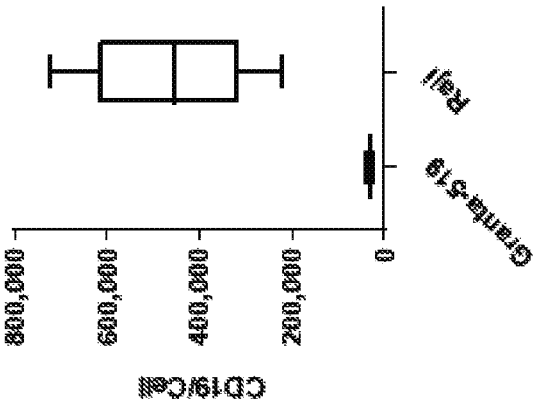


FIG. 33C

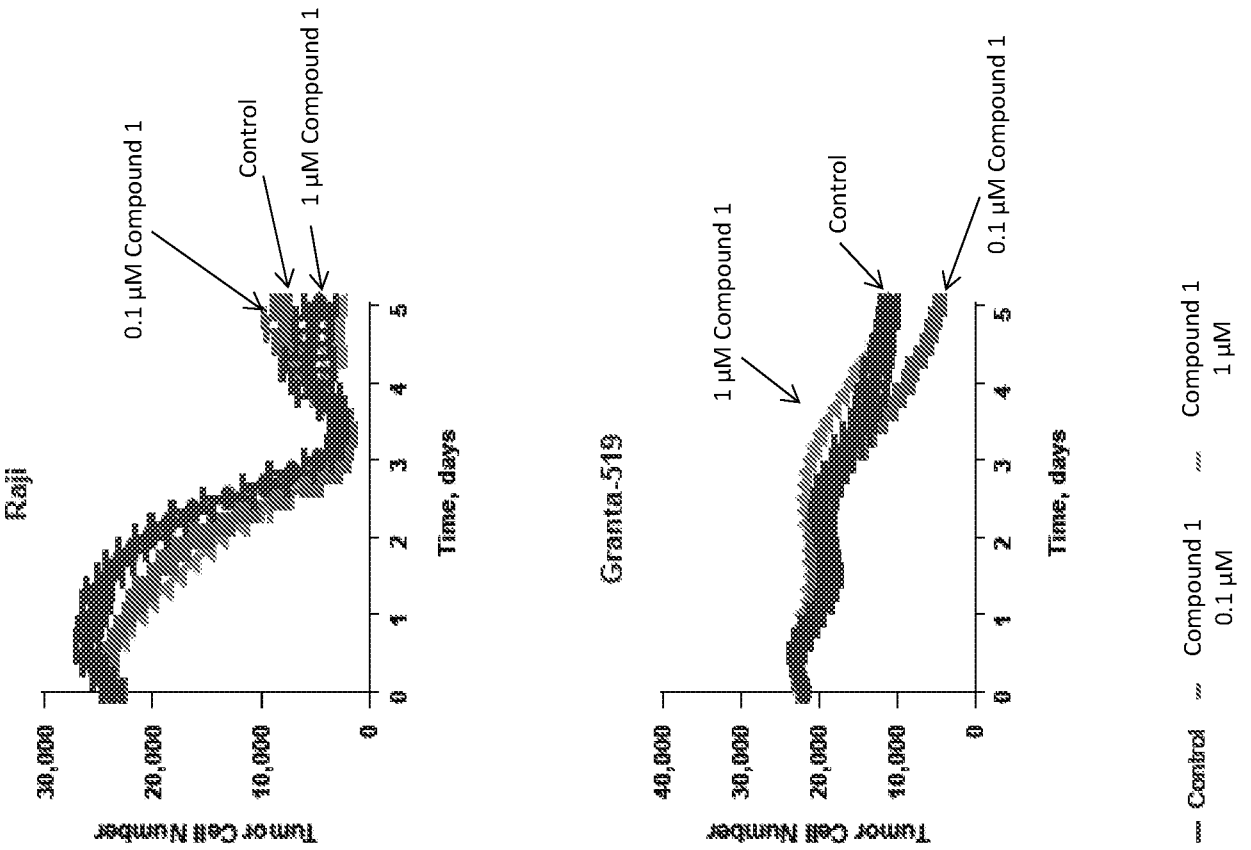

Raji
0.1 µM Compound 1
Control
1 µM Compound 1
Tumor Cell Number
Time, days
Granta-519
1 µM Compound 1
Control
0.1 µM Compound 1
Tumor Cell Number
Time, days
Control
Compound 1 0.1 µM
Compound 1 1 µM

FIG. 33D

FIG. 34A

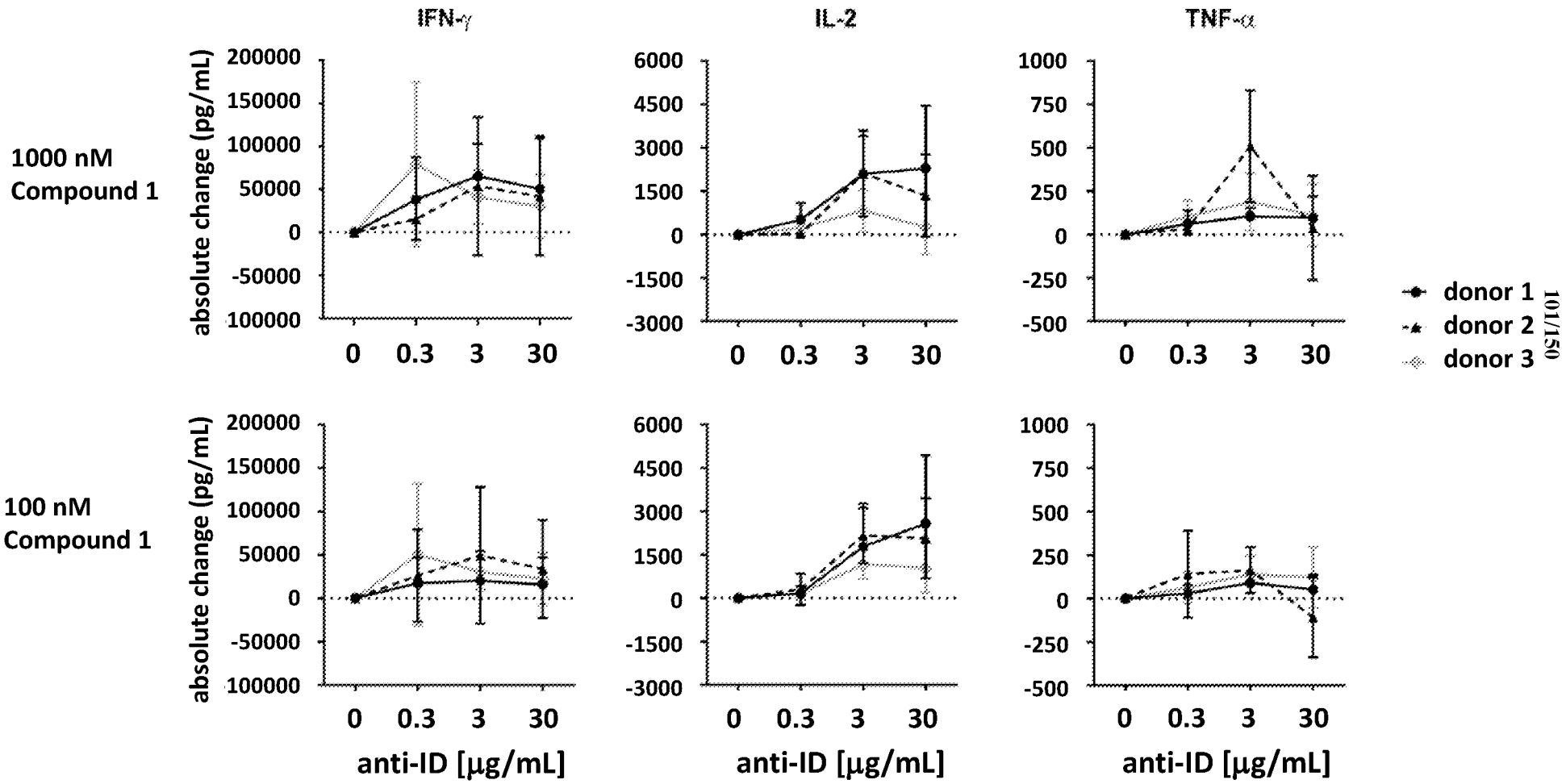

IFN-γ
IL-2
TNF-α
1000 nM Compound 1
100 nM Compound 1
absolute change (pg/mL)
200000
150000
100000
50000
0
-50000
100000
6000
4500
3000
1500
0
-1500
-3000
1000
750
500
250
0
-250
-500
0
0.3
3
30
anti-ID [µg/mL]
donor 1
donor 2
donor 3

FIG. 34B

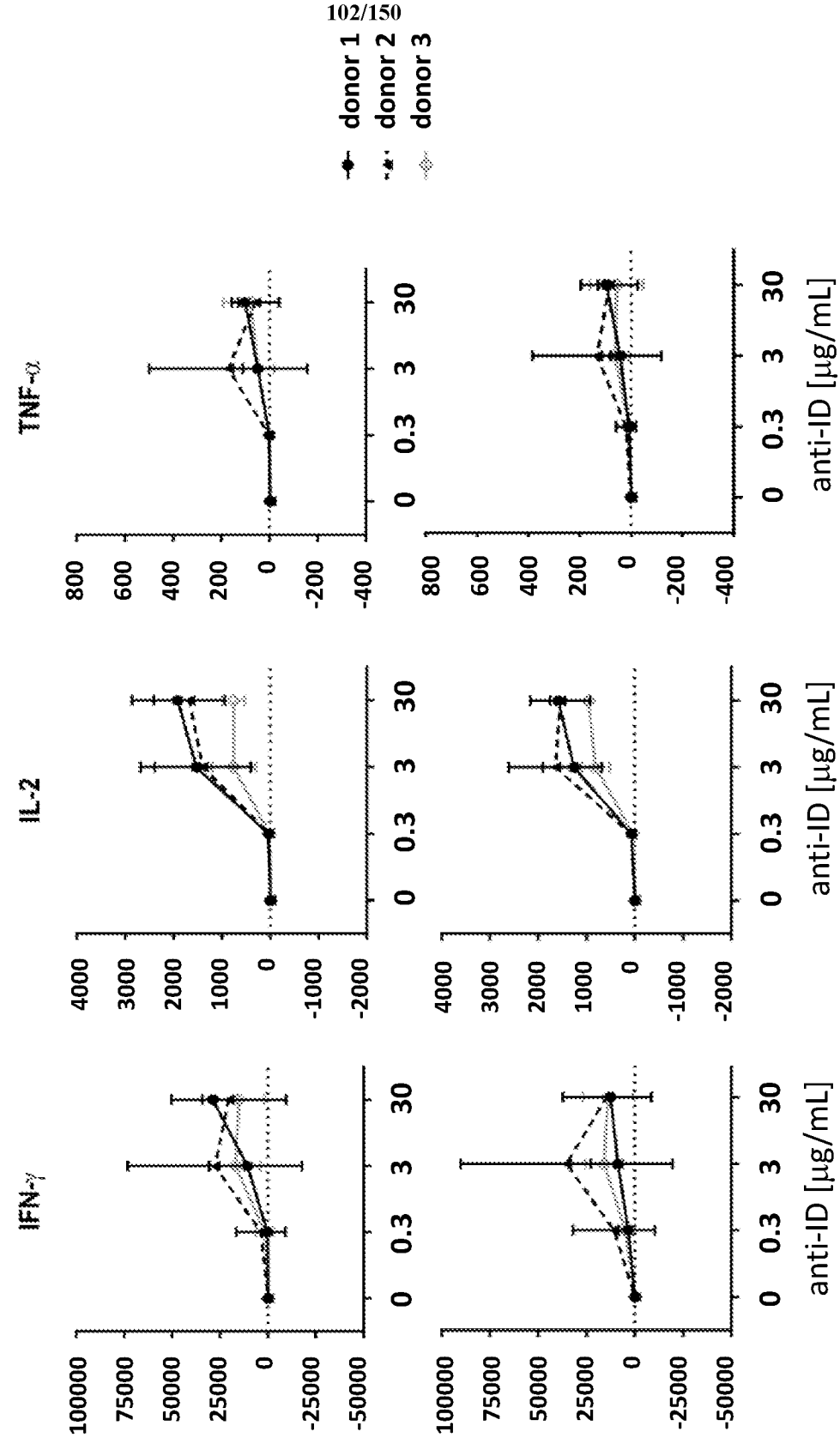
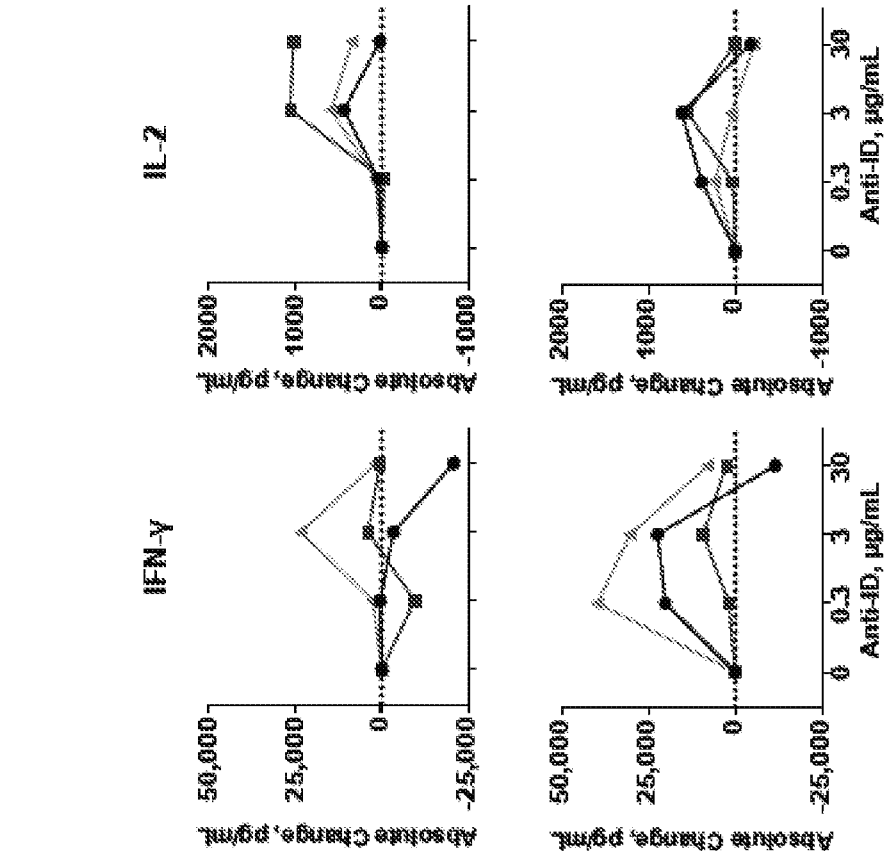

donor 1
donor 2
donor 3
IFN-γ
IL-2
TNF-α
5000 nM Len
500 nM Len
absolute change (pg/mL)
anti-ID [μg/mL]
100000
75000
50000
25000
0
-25000
-50000
4000
3000
2000
1000
-1000
-2000
800
600
400
200
-200
-400
0
0.3
3
30

FIG. 34C


IFN-γ
IL-2
100 nM Compound 1
1000 nM Compound 1
Absolute Change, pg/mL
50,000
25,000
0
-25,000
2000
1000
0
-1000
0
0.3
3
30
Anti-ID, µg/mL

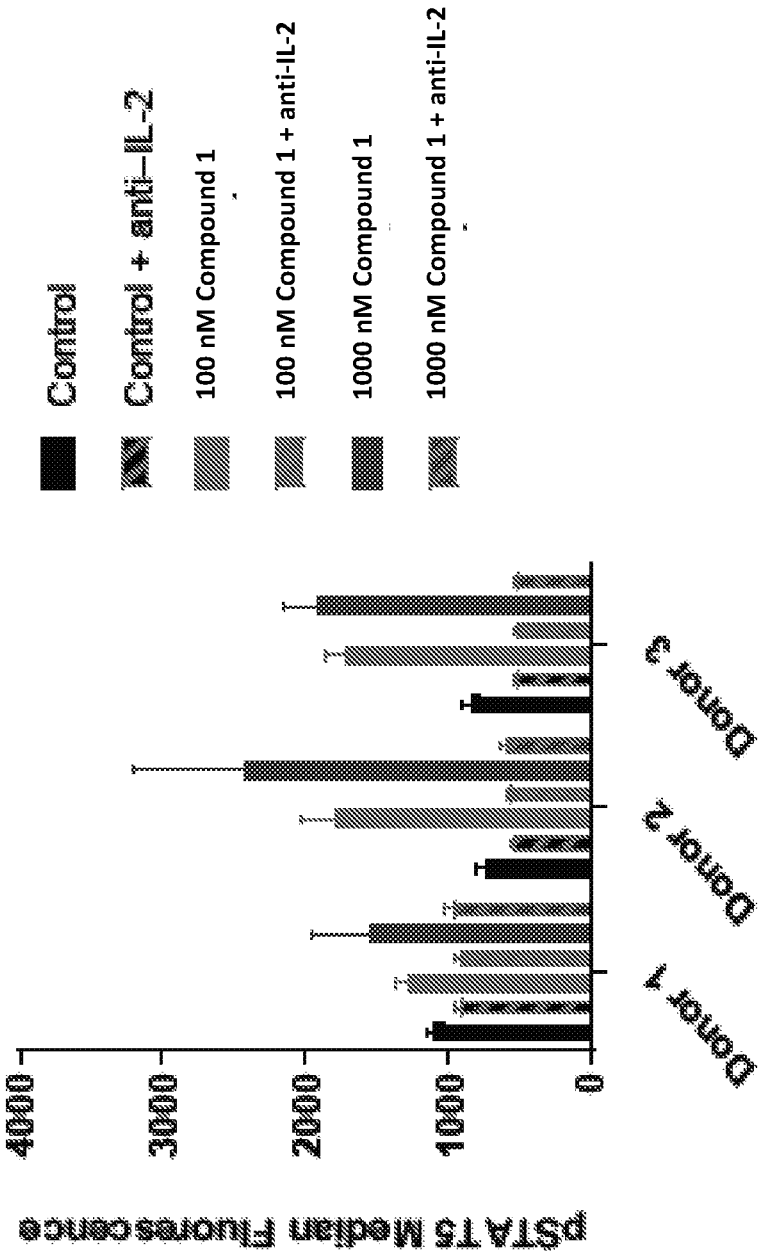

Control
Control + anti-IL-2
100 nM Compound 1
100 nM Compound 1 + anti-IL-2
1000 nM Compound 1
1000 nM Compound 1 + anti-IL-2
pSTAT5 Median Fluorescence
4000
3000
2000
1000
0
Donor 1
Donor 2
Donor 3

FIG. 34D

FIG. 35A

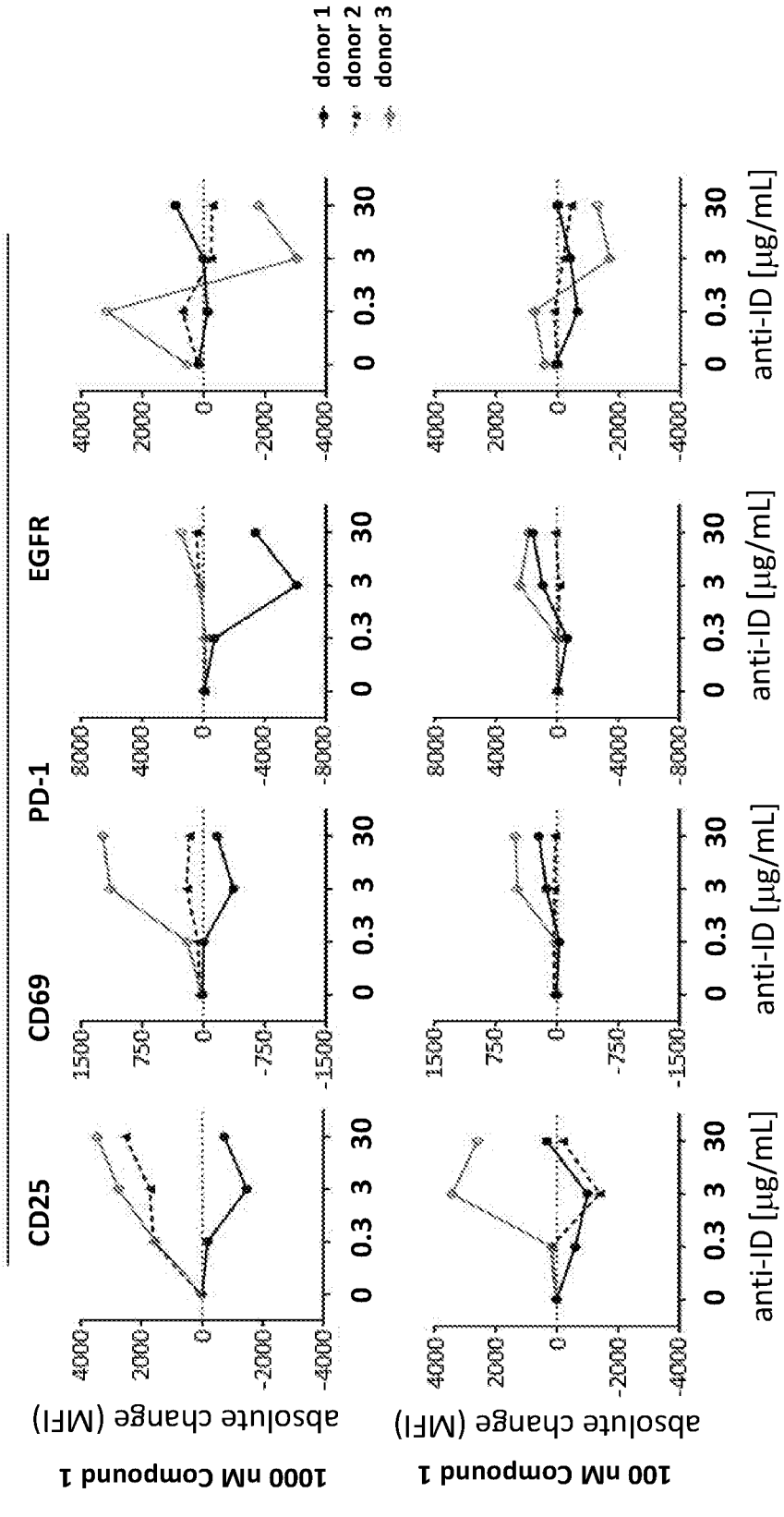

CD4+CAR+
CD25
CD69
PD-1
EGFR
1000 nM Compound 1
100 nM Compound 1
absolute change (MFI)
anti-ID [µg/mL]
0 0.3 3 30
donor 1
donor 2
donor 3

FIG. 35B

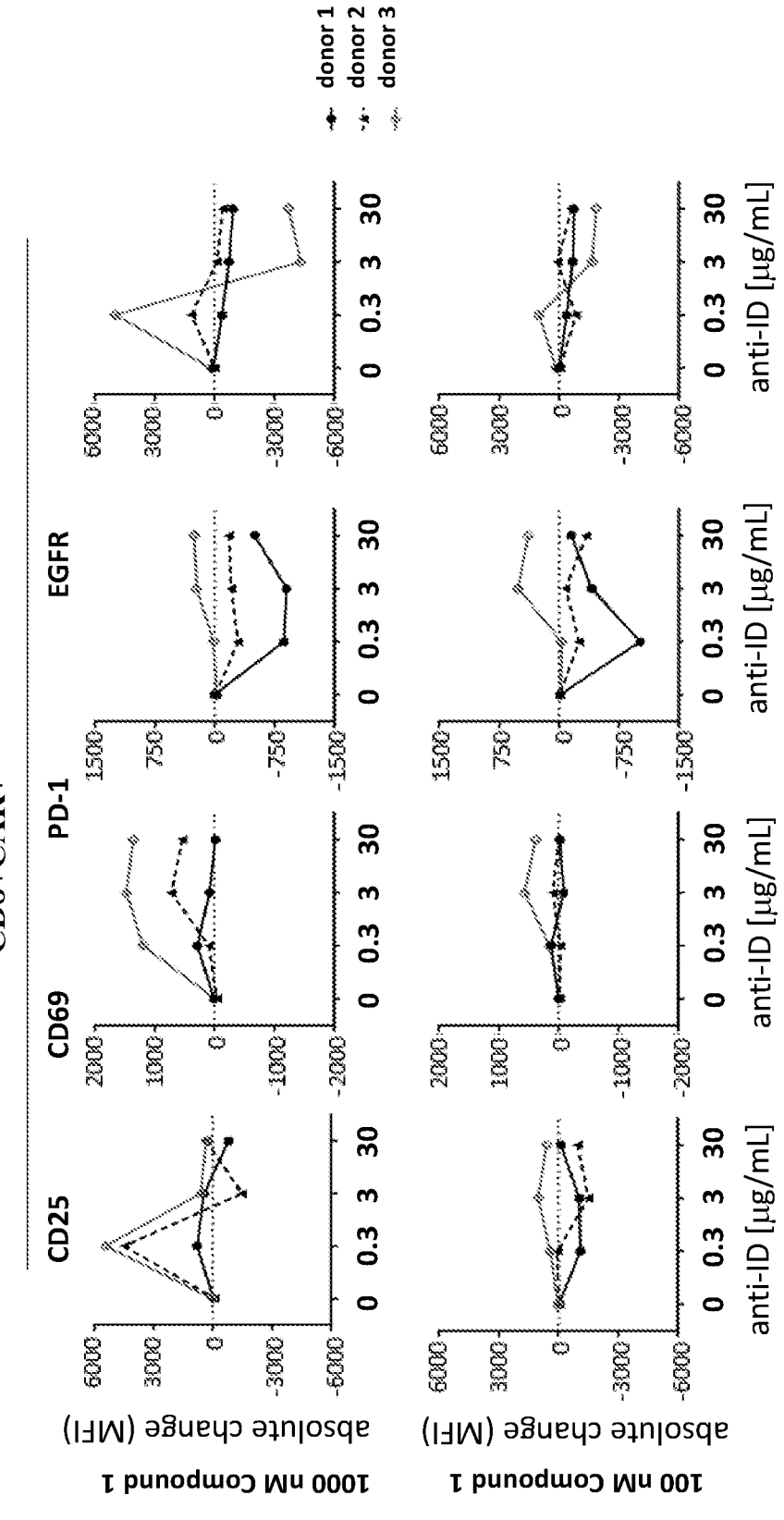

CD8+CAR+
CD25
CD69
PD-1
EGFR
donor 1
donor 2
donor 3
1000 nM Compound 1
100 nM Compound 1
absolute change (MFI)
anti-ID [µg/mL]
0 0.3 3 30
6000
3000
0
-3000
-6000
2000
1000
-1000
-2000
1500
750
-750
-1500

FIG. 36A

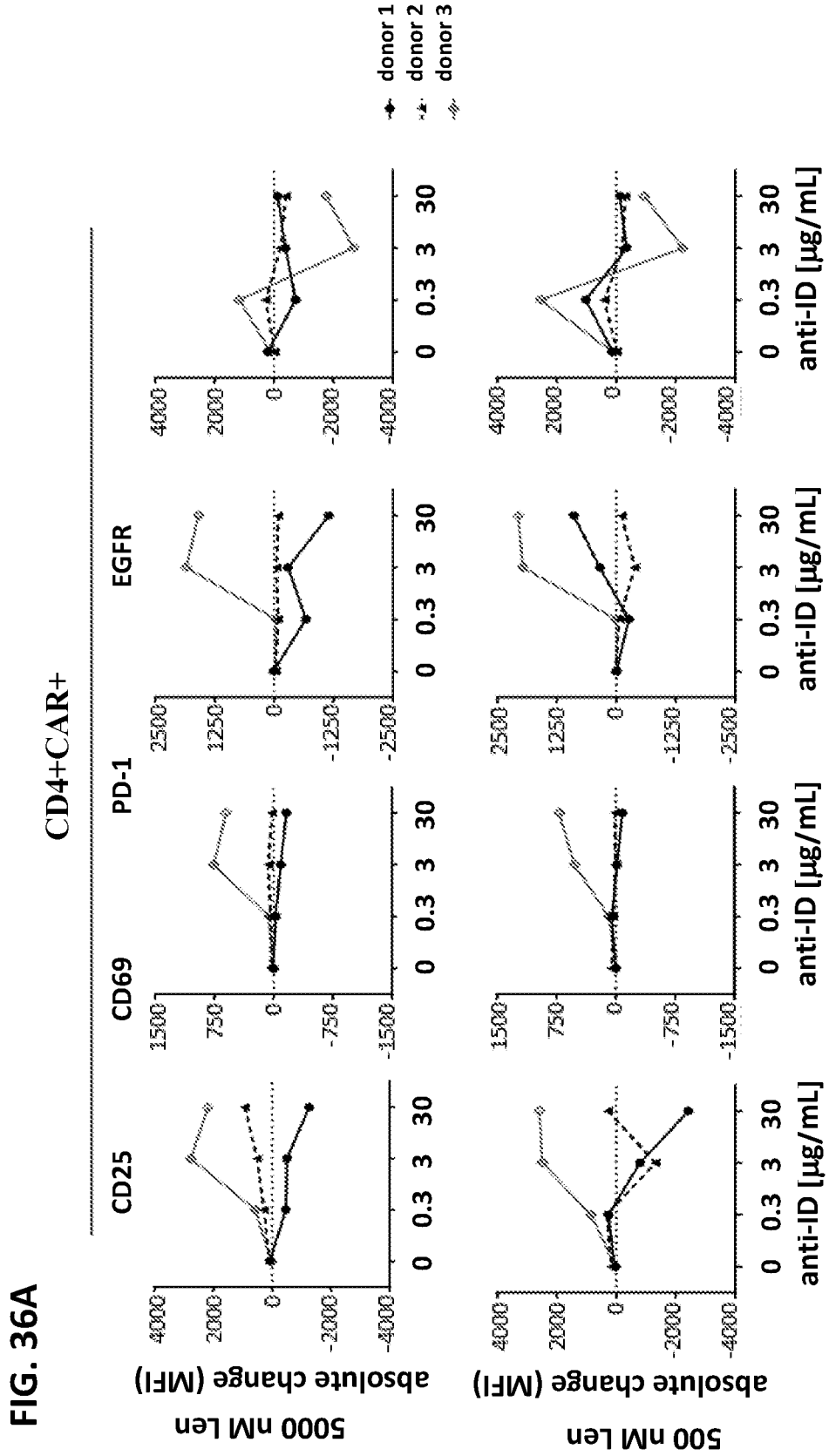

CD4+CAR+
CD25
CD69
PD-1
EGFR
donor 1
donor 2
donor 3
5000 nM Len
500 nM Len
absolute change (MFI)
anti-ID [µg/mL]
0 0.3 3 30
4000
2000
0
-2000
-4000
1500
750
-750
-1500
2500
1250
-1250
-2500

FIG. 36B

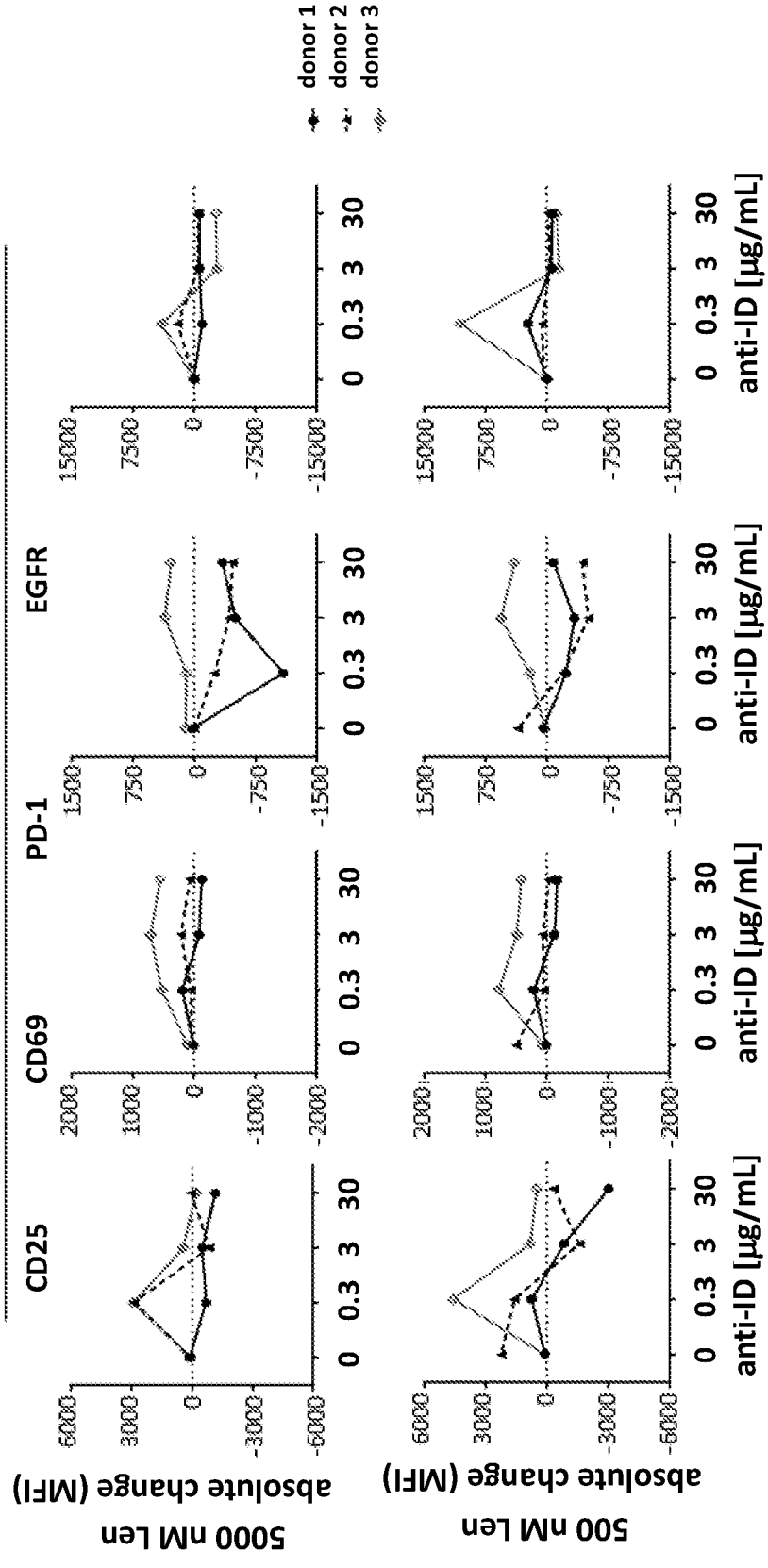

CD8+CAR+
CD25
CD69
PD-1
EGFR
donor 1
donor 2
donor 3
5000 nM Len
500 nM Len
absolute change (MFI)
anti-ID [µg/mL]
0 0.3 3 30
6000
3000
0
-3000
-6000
2000
1000
-1000
-2000
1500
750
-750
-1500
15000
7500
-7500
-15000

FIG. 37A

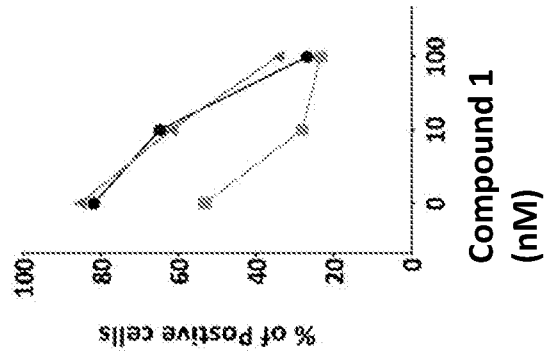
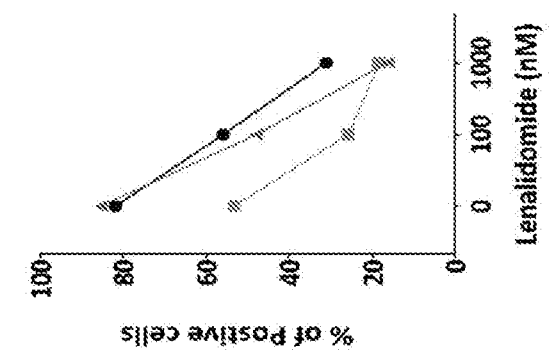
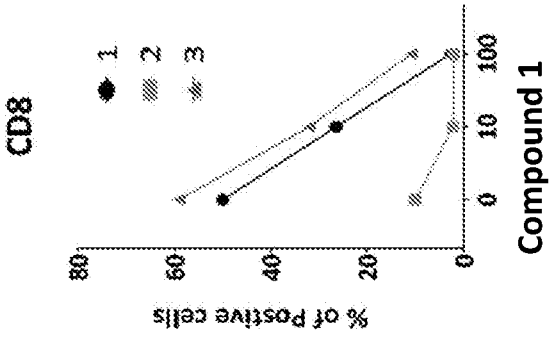


FIG. 37B





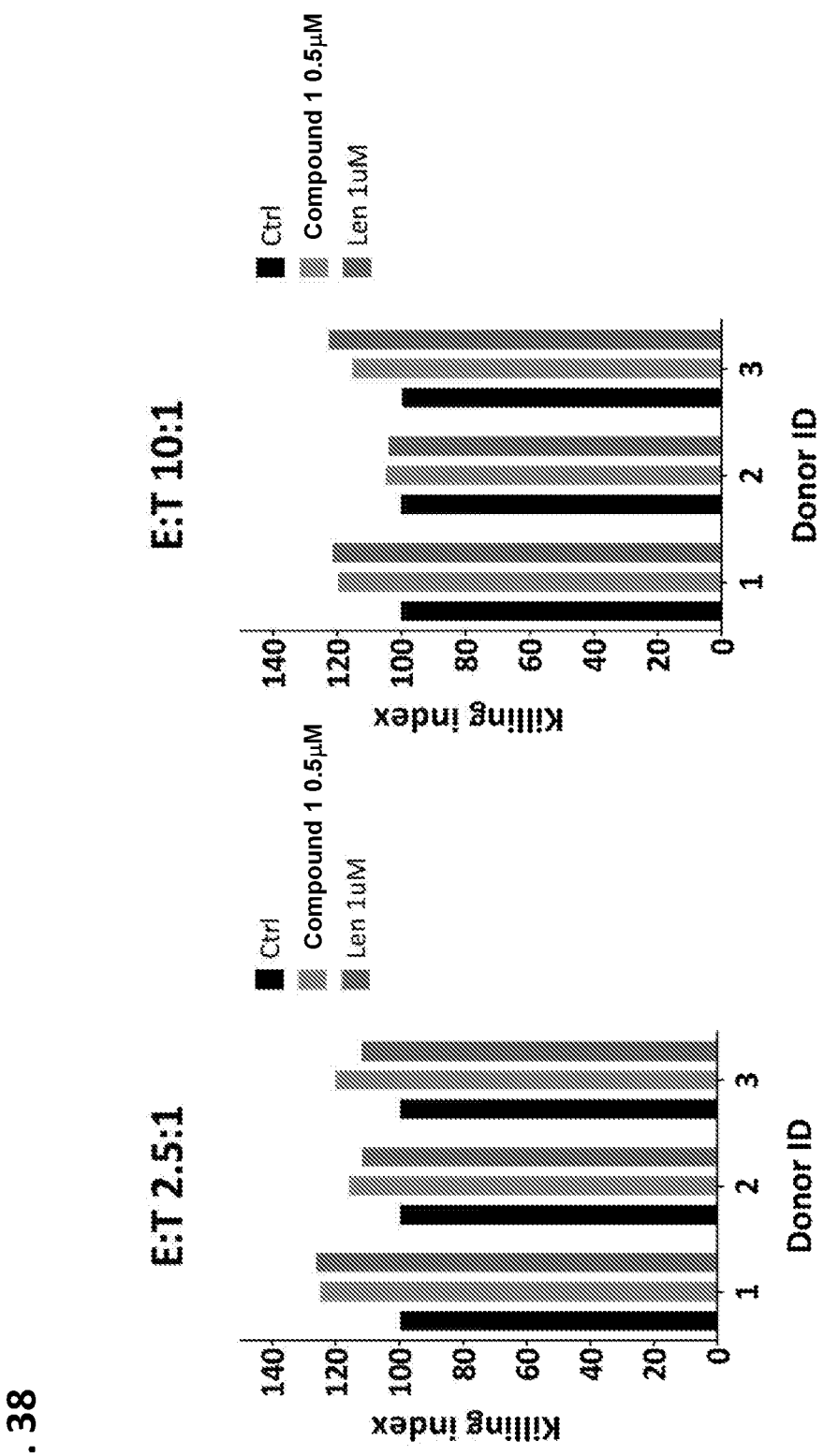
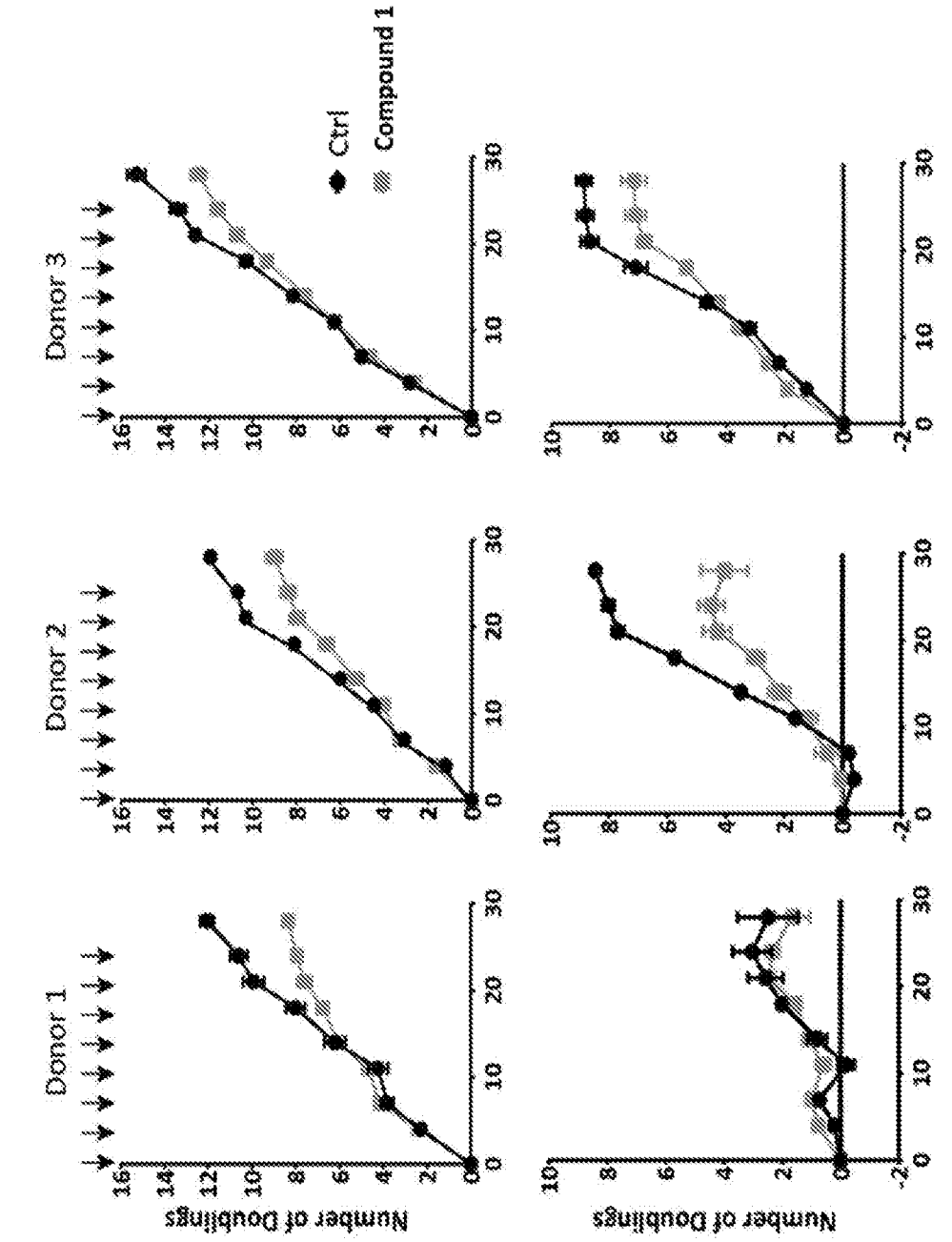

E:T 10:1
Ctrl
Compound 1 0.5μM
Len 1uM
Killing index
0
20
40
60
80
100
120
140
1
2
3
Donor ID
E:T 2.5:1
Ctrl
Compound 1 0.5μM
Len 1uM
Killing index
0
20
40
60
80
100
120
140
1
2
3
Donor ID

FIG. 38

FIG. 39A


Donor 1
Donor 2
Donor 3
Ctrl
Compound 1
E:T
2.5:1
10:1
Number of Doublings

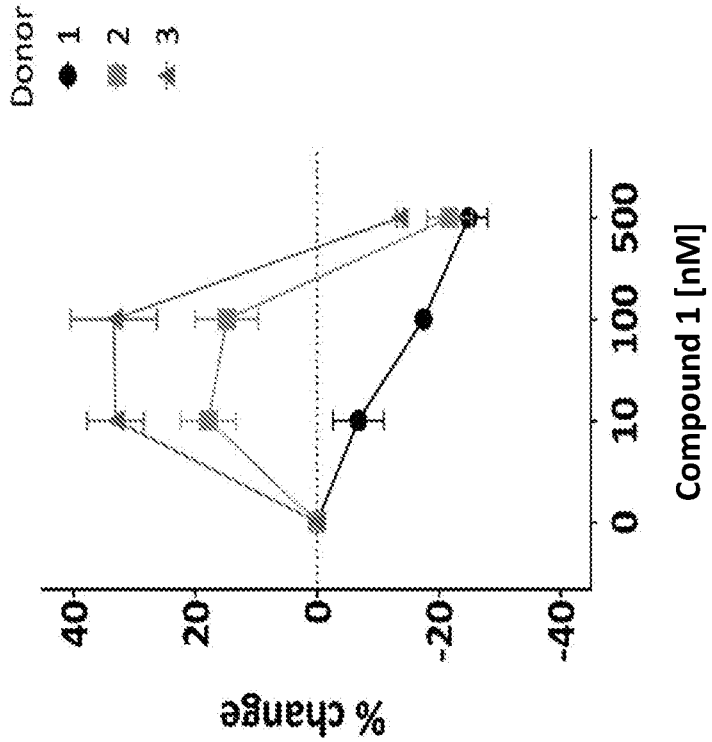


FIG. 39B

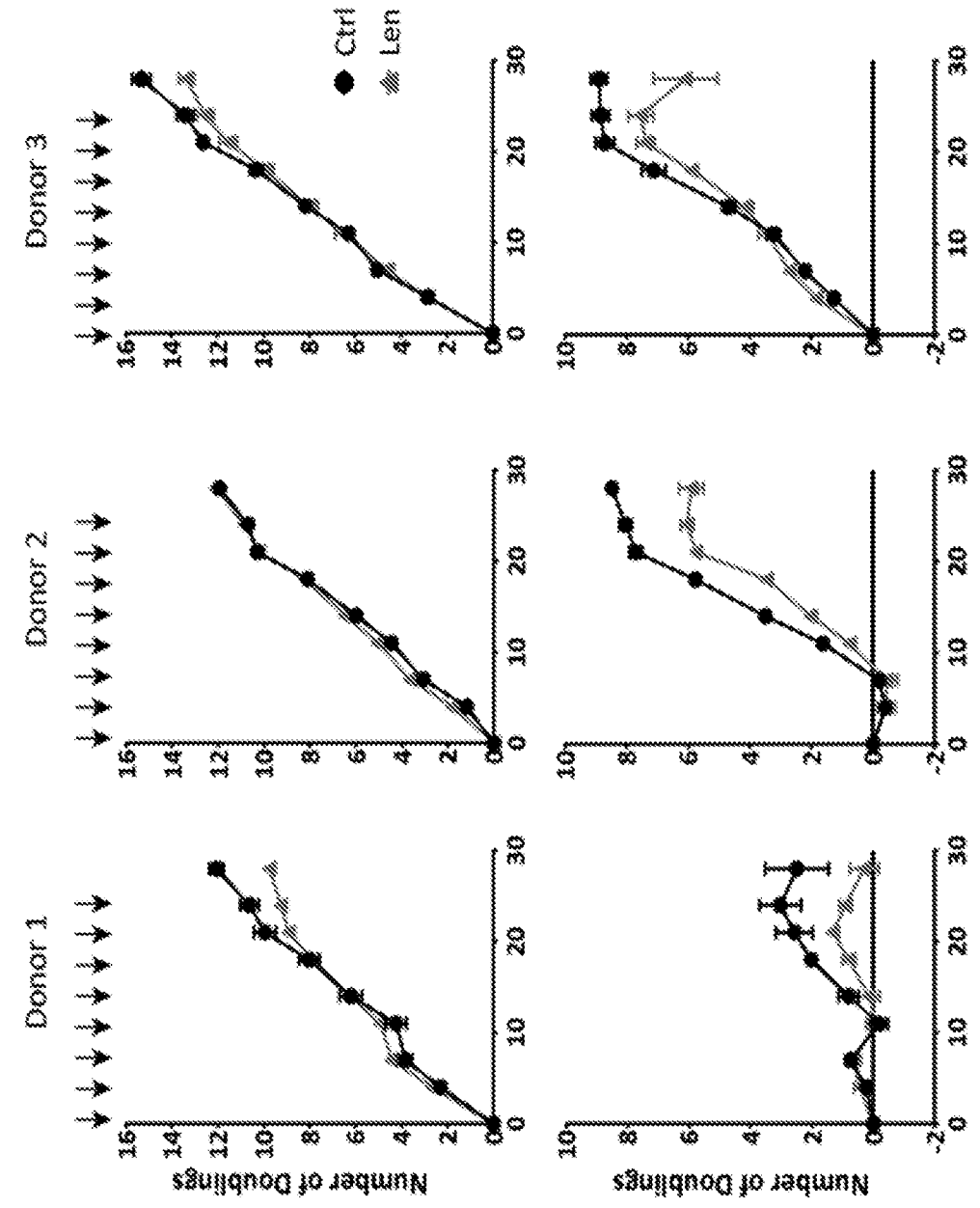

Donor 1
Donor 2
Donor 3
Ctrl
Len
Number of Doublings
E:T
2.5:1
10:1

FIG. 40A

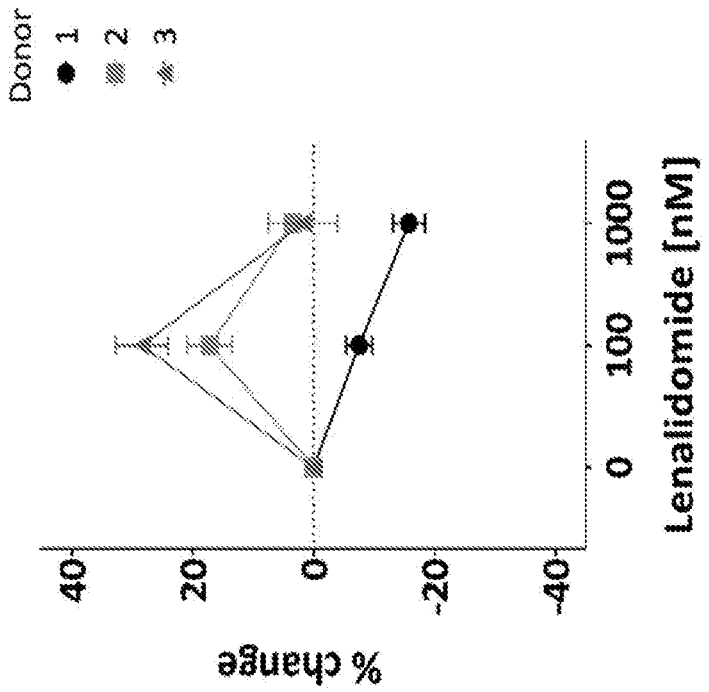


FIG. 40B

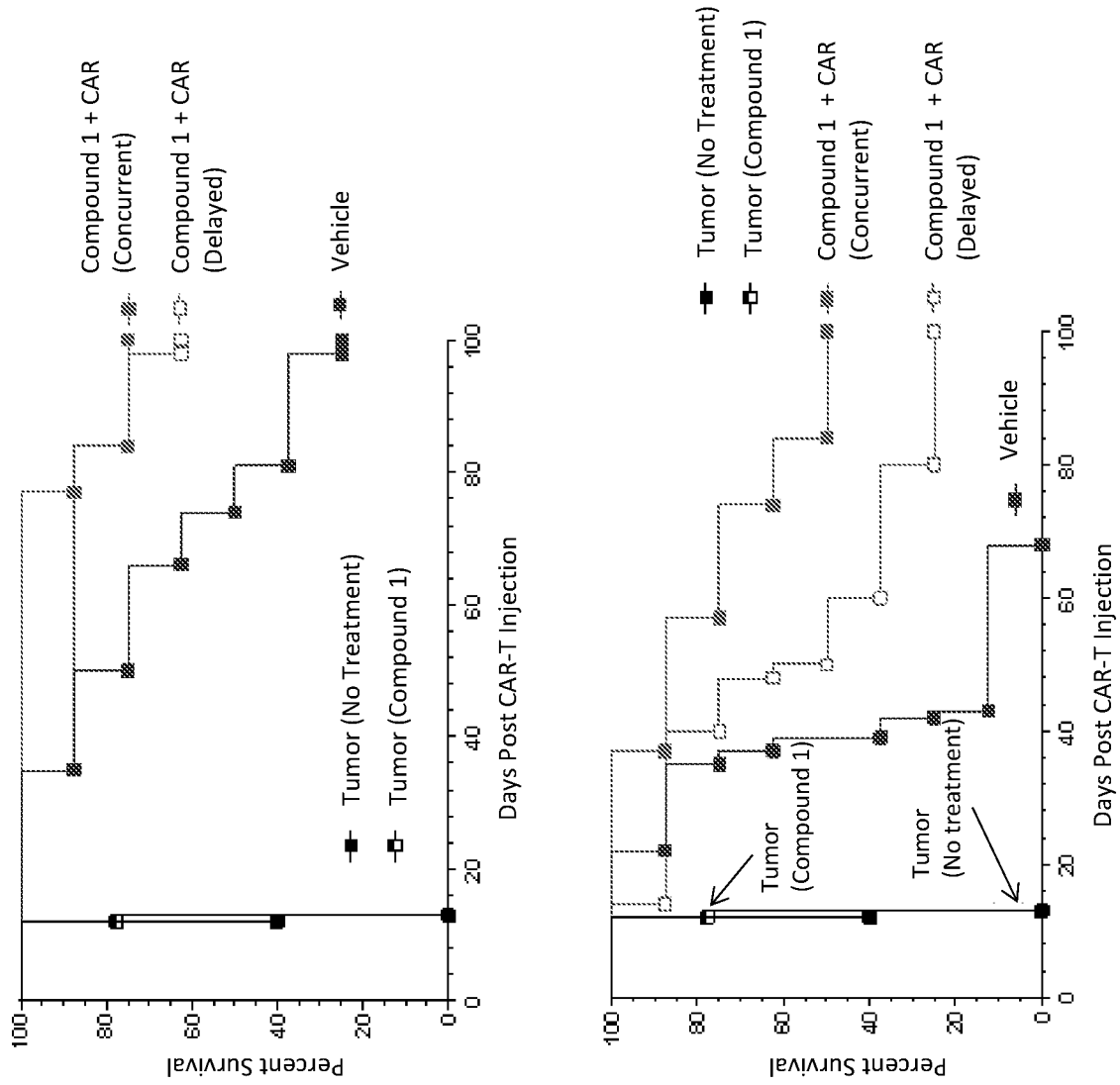

Compound 1 + CAR (Concurrent)
Compound 1 + CAR (Delayed)
Vehicle
Tumor (No Treatment)
Tumor (Compound 1)
Percent Survival
Days Post CAR-T Injection
0
20
40
60
80
100

FIG. 41

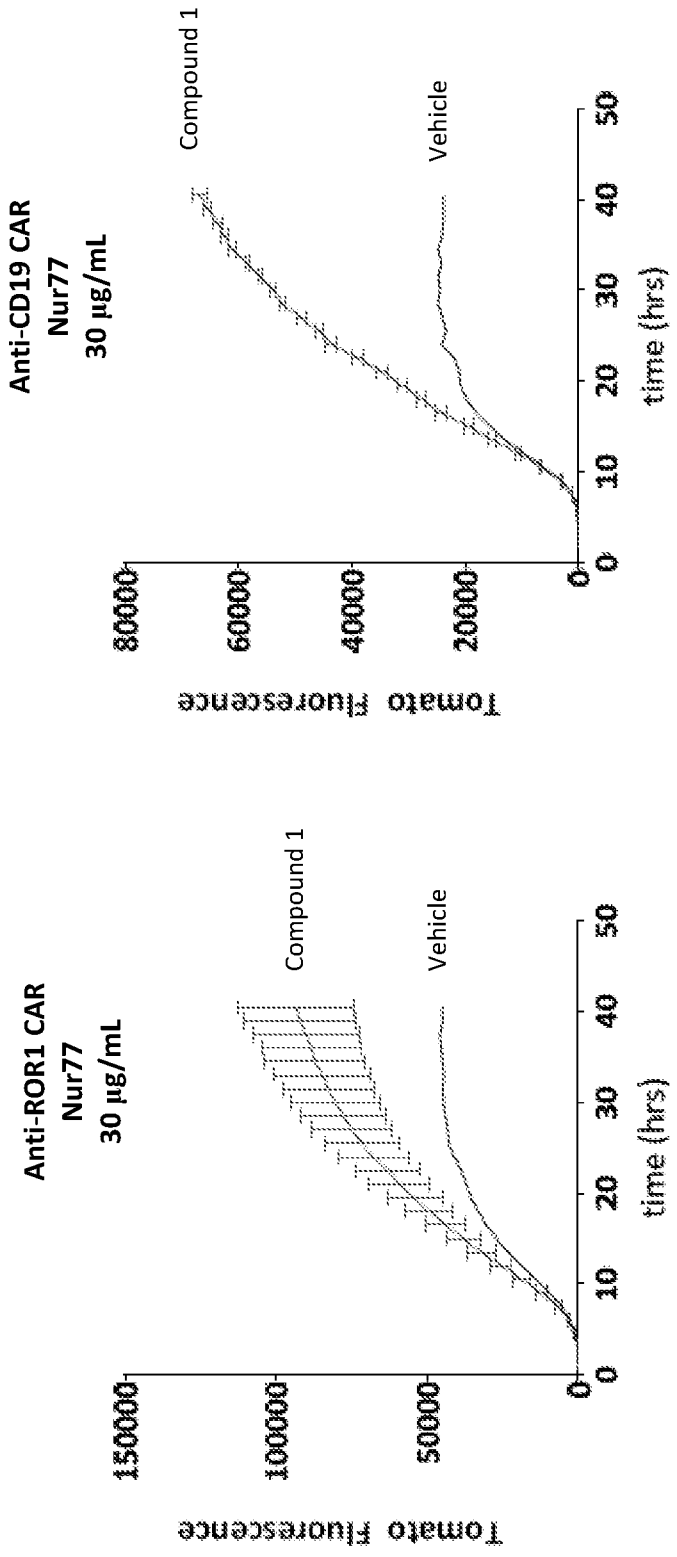

Anti-ROR1 CAR
Nur77
30 µg/mL
Compound 1
Vehicle
Tomato Fluorescence
150000
100000
50000
0
0
10
20
30
40
50
time (hrs)
Anti-CD19 CAR
Nur77
30 µg/mL
Compound 1
Vehicle
Tomato Fluorescence
80000
60000
40000
20000
0
0
10
20
30
40
50
time (hrs)

FIG. 42

FIG. 43A

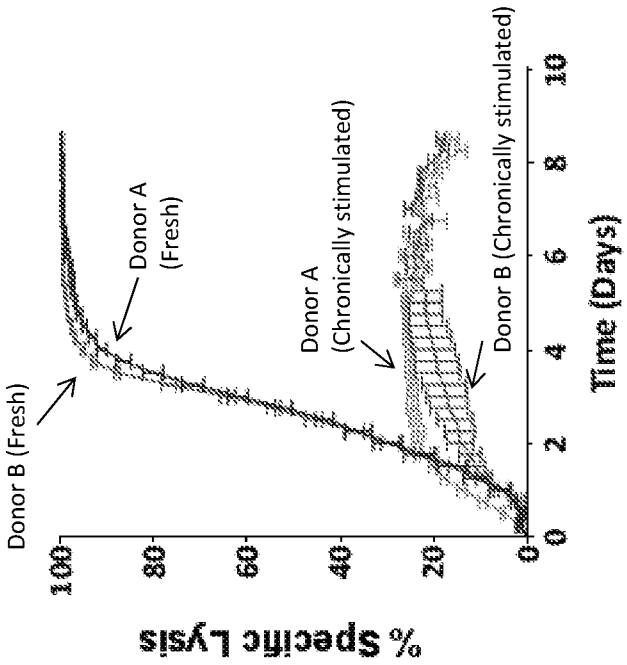
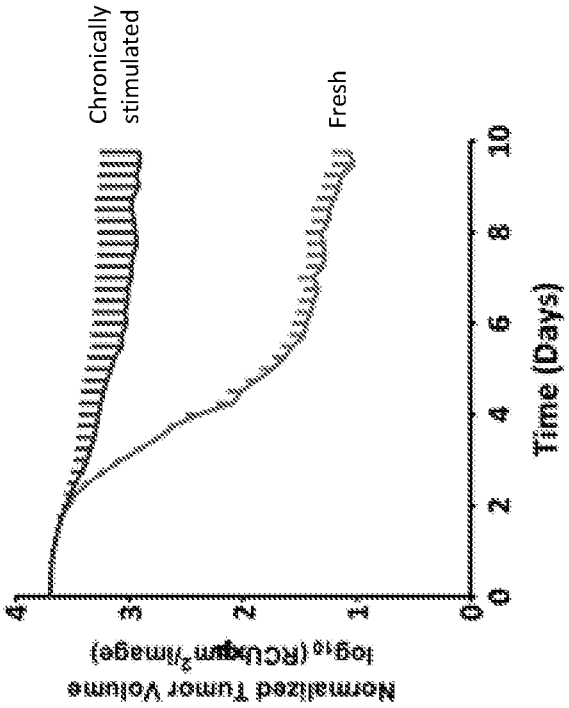


FIG. 43B



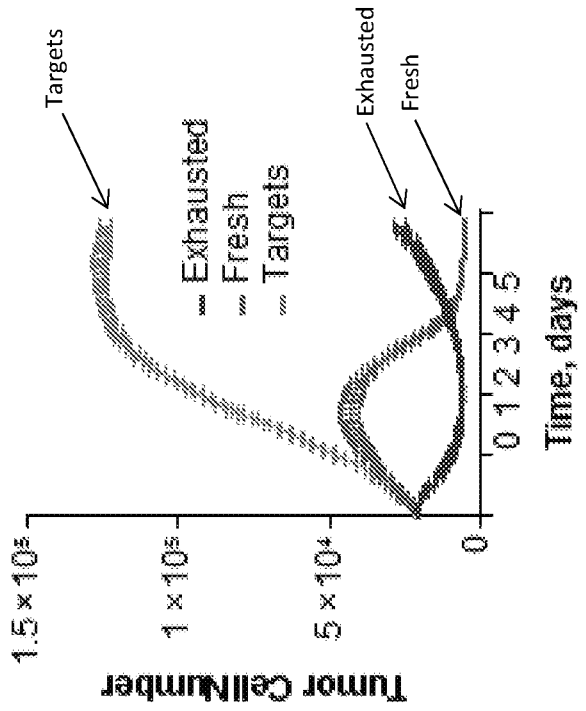
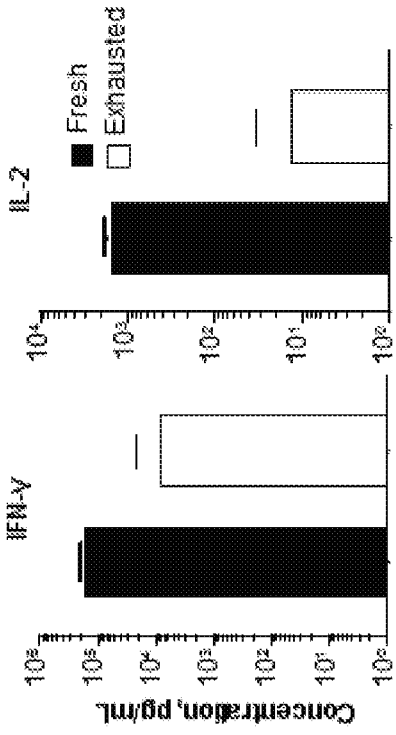


FIG. 43C



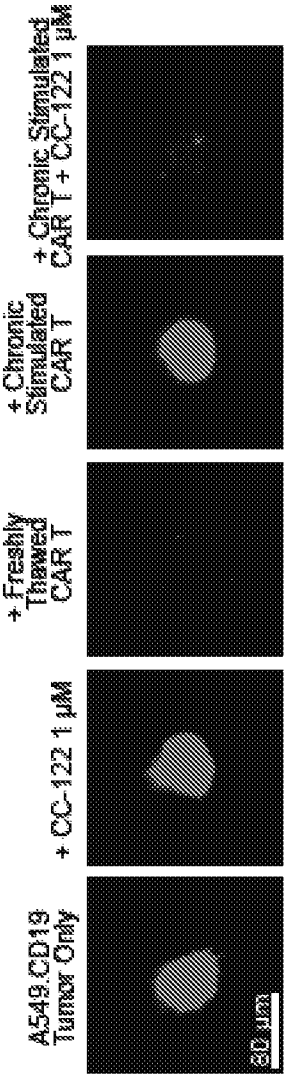


FIG. 43D

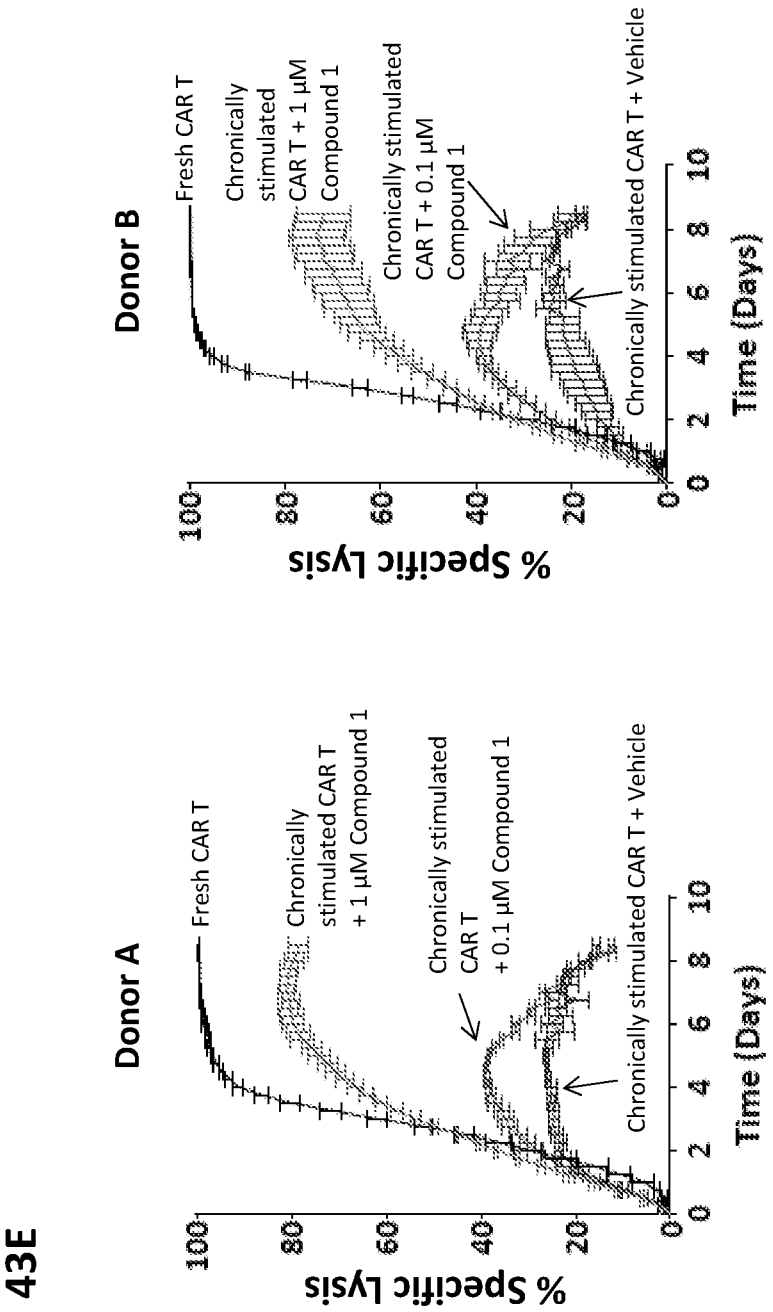

Donor A
Donor B
% Specific Lysis
Time (Days)
0
20
40
60
80
100
0
2
4
6
8
10
Fresh CAR T
Chronically stimulated CAR T + 1 µM Compound 1
Chronically stimulated CAR T + 0.1 µM Compound 1
Chronically stimulated CAR T + Vehicle

FIG. 43E

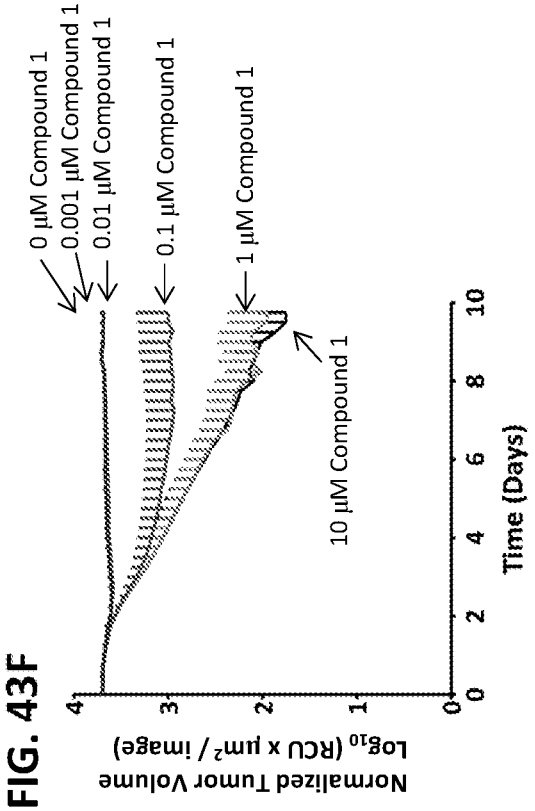


FIG. 43F

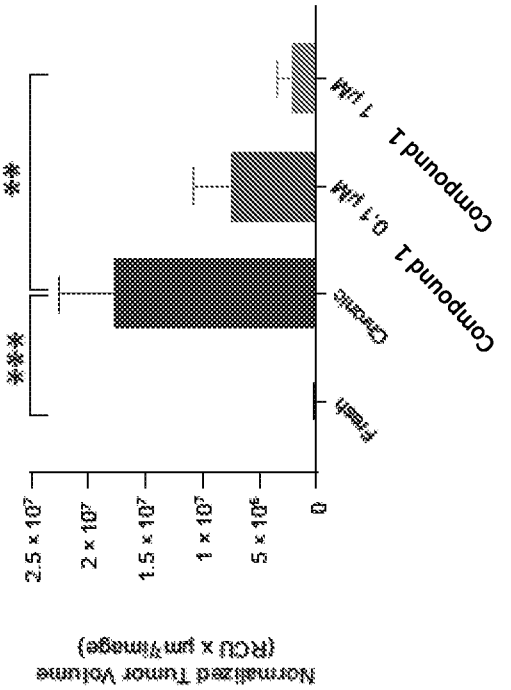


FIG. 43H

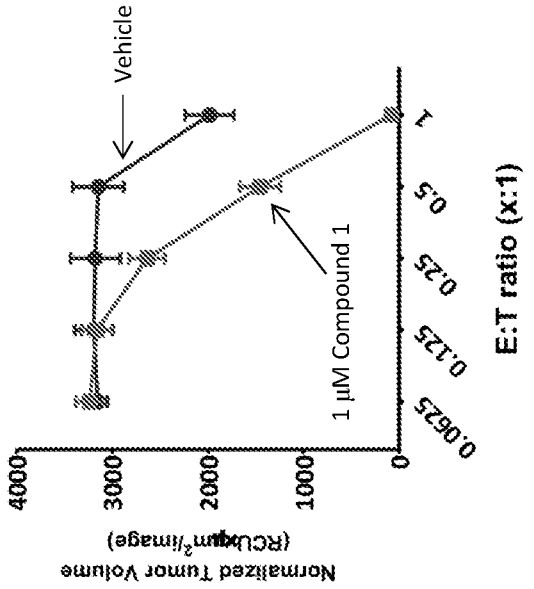
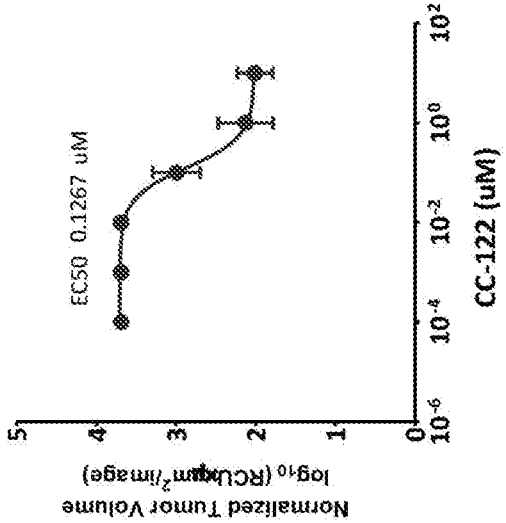


FIG. 43G



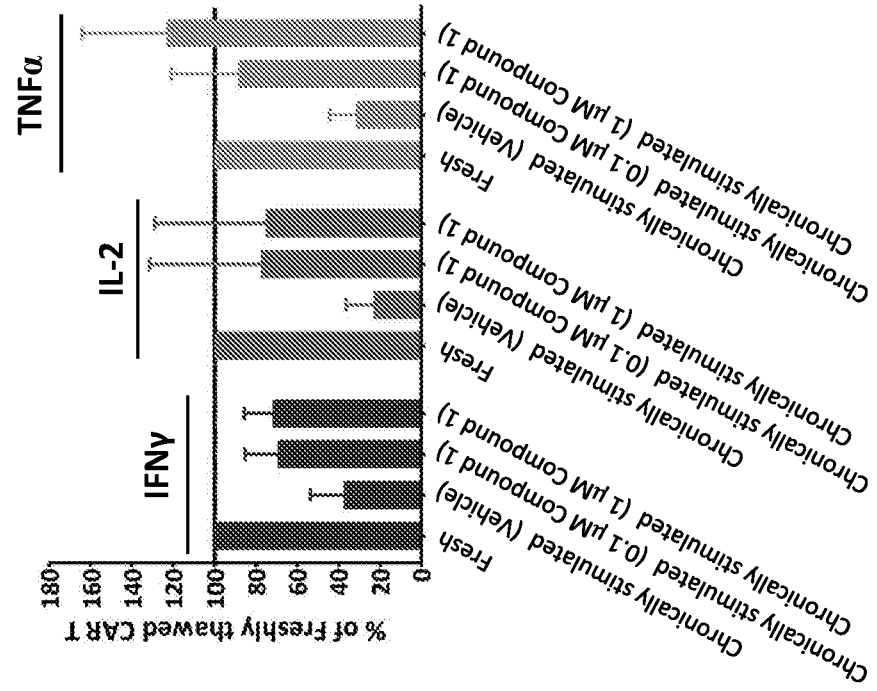


FIG. 43J

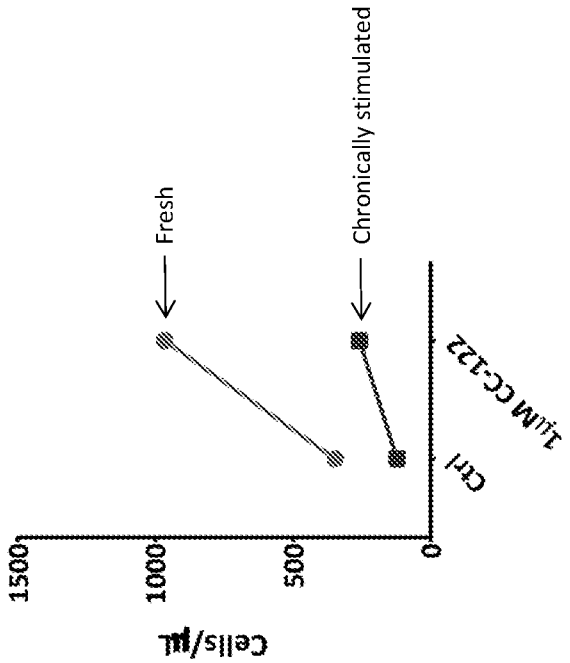


FIG. 43I

FIG. 43L

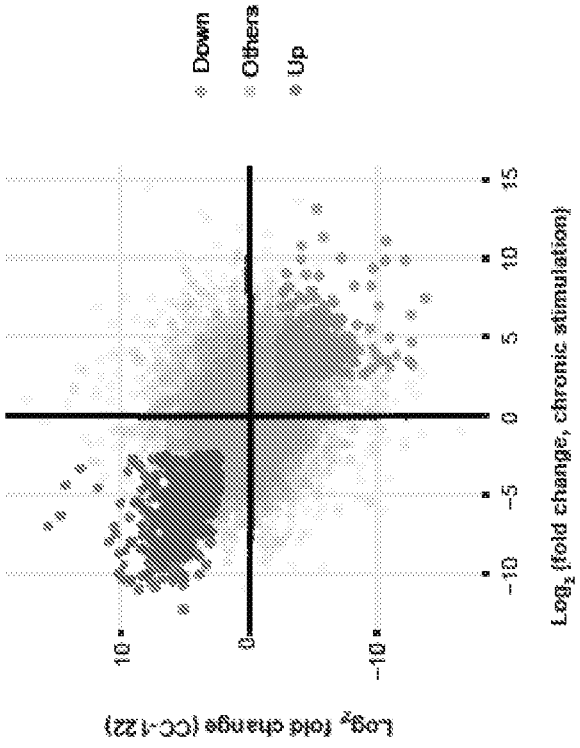
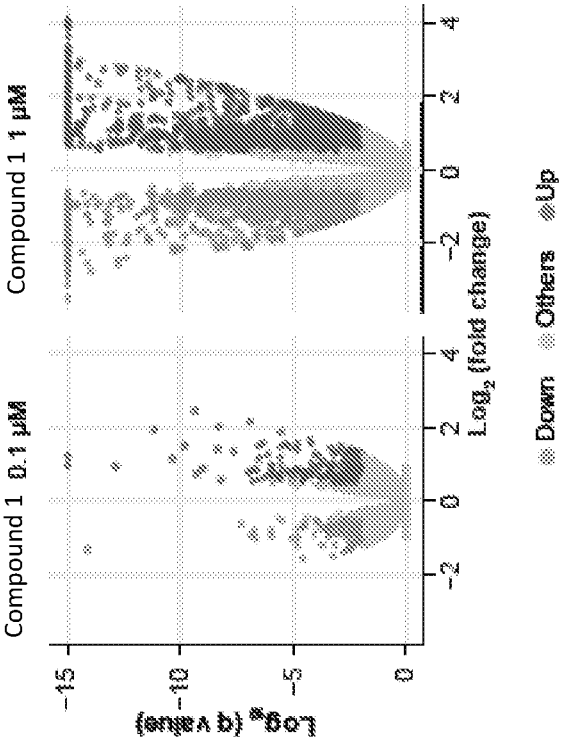


FIG. 43K



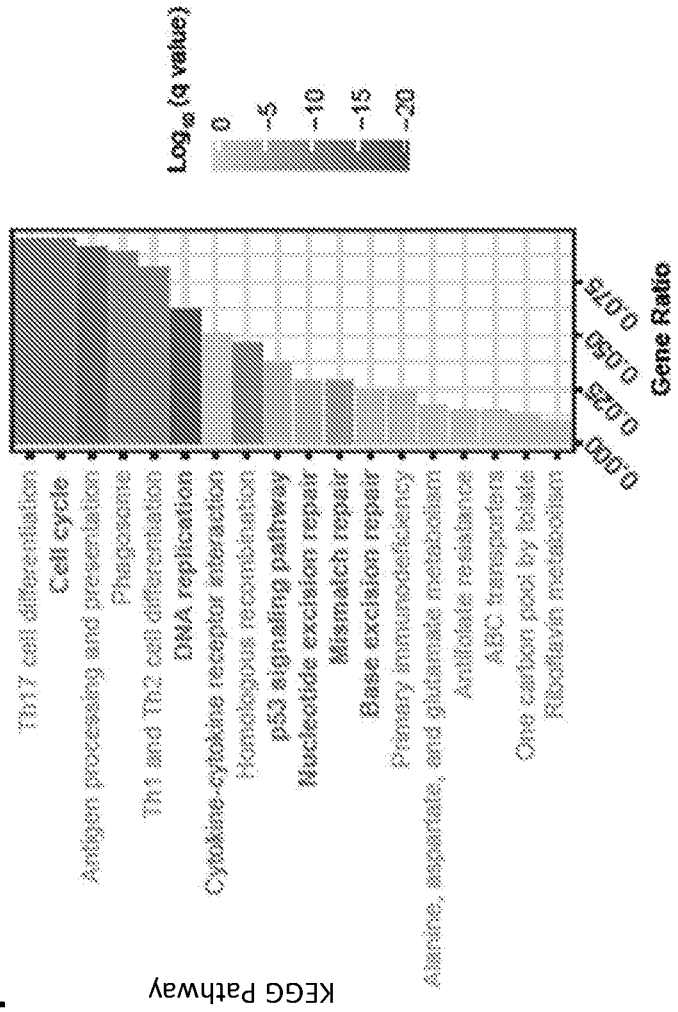

Log10(q value)
0
-5
-10
-15
-20
Gene Ratio
0.075
0.050
0.025
0.000
KEGG Pathway
Th17 cell differentiation
Cell cycle
Antigen processing and presentation
Phagosome
Th1 and Th2 cell differentiation
DNA replication
Cytokine-cytokine receptor interaction
Homologous recombination
p53 signaling pathway
Nucleotide excision repair
Mismatch repair
Base excision repair
Primary immunodeficiency
Alanine, aspartate, and glutamate metabolism
Antifolate resistance
ABC transporters
One carbon pool by folate
Nonfarm metabolism

FIG. 43M

FIG. 44A

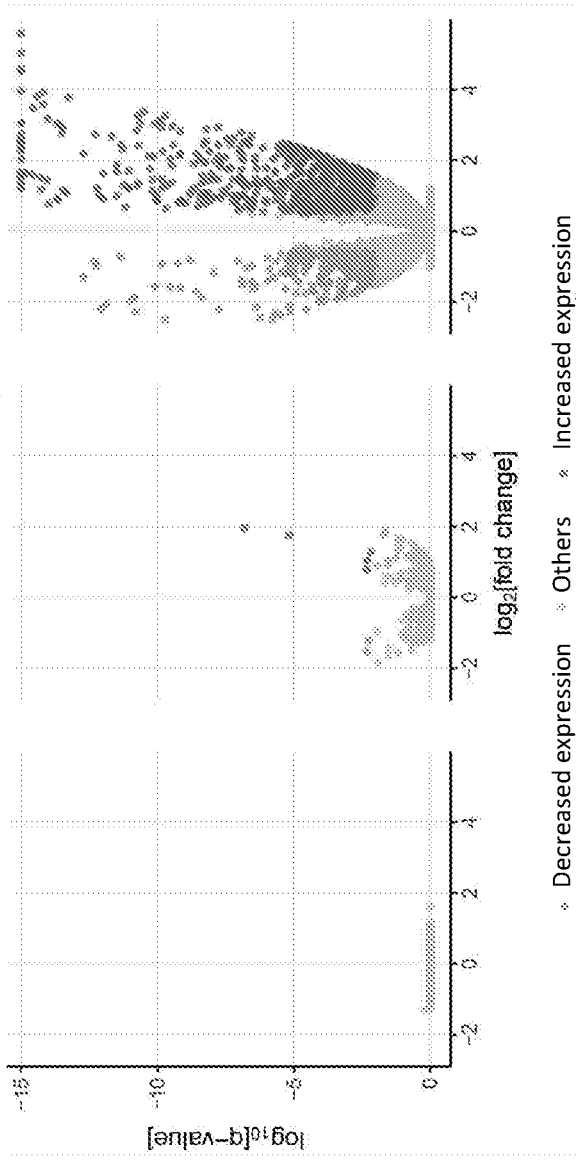

IL2
Compound 1 (0.1 μM)
Compound 1 (1 μM)
log10[q-value]
log2[fold change]
Decreased expression
Others
Increased expression

FIG. 44B

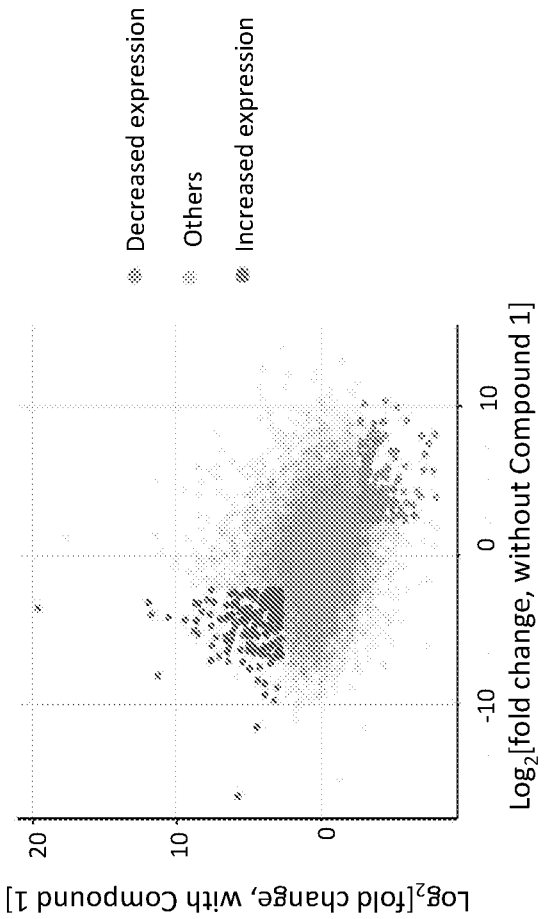


FIG. 44C

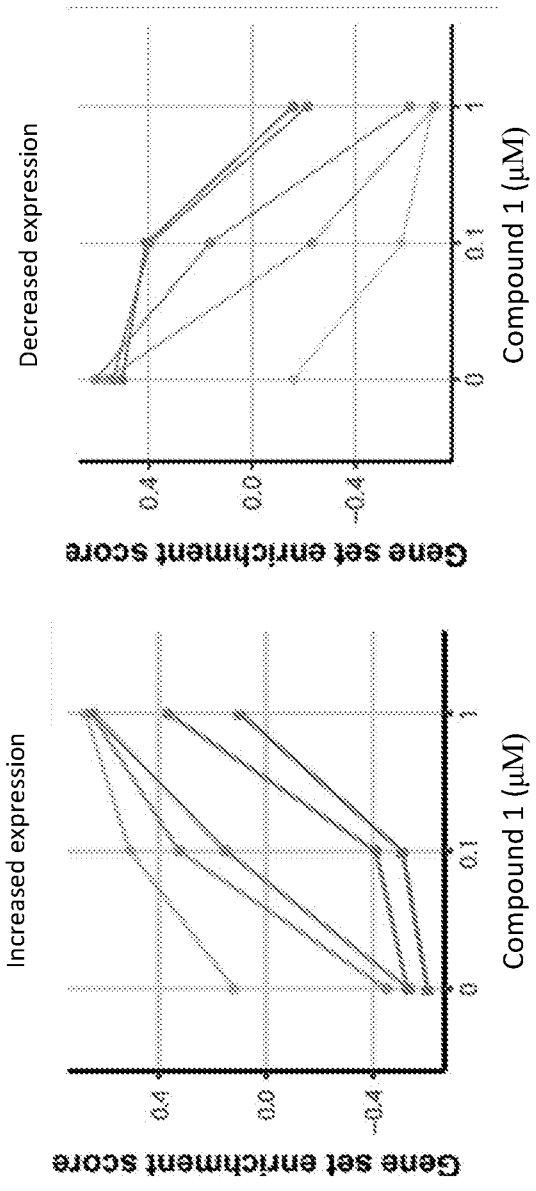
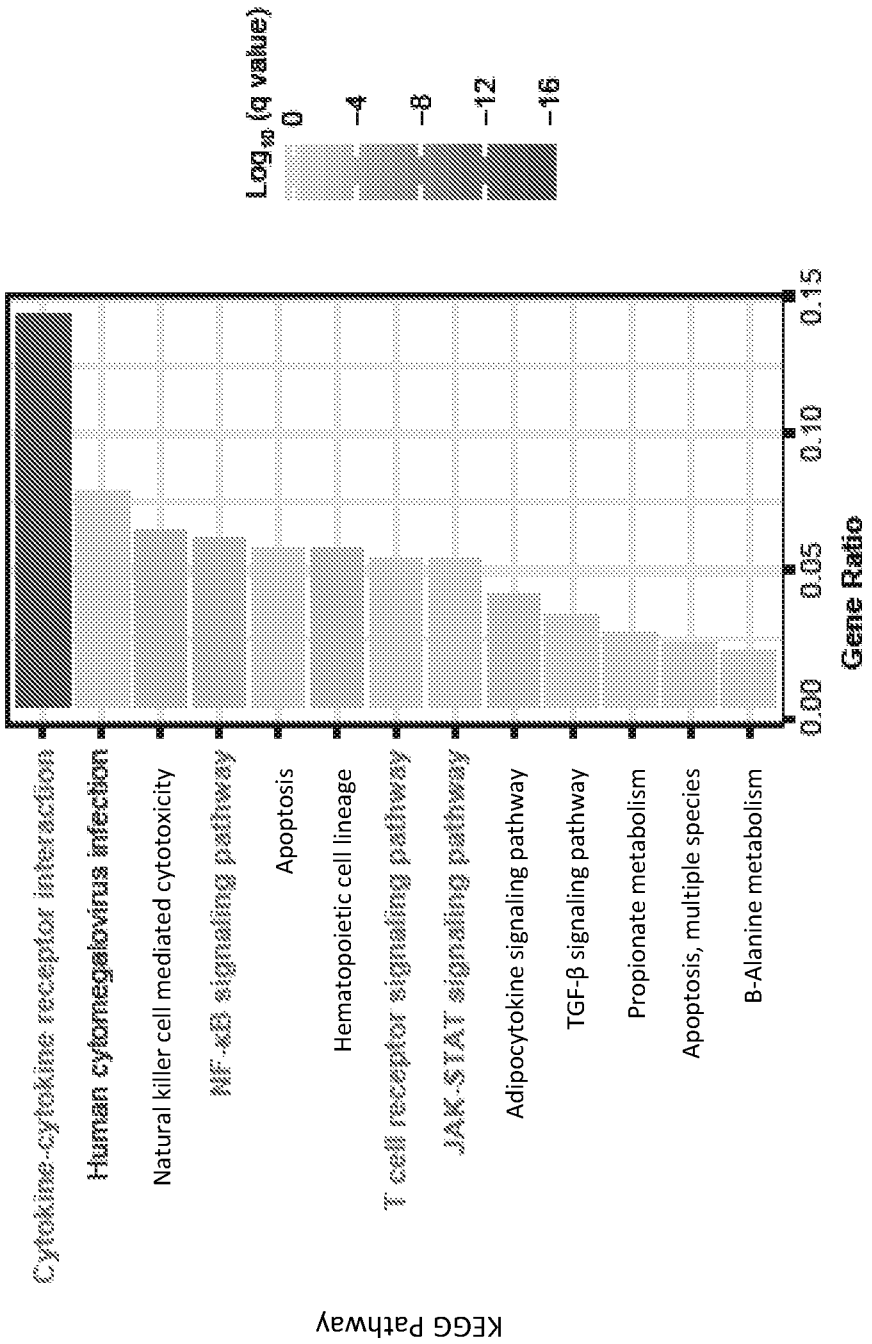


FIG. 44D


Log10 (q value)
0
-4
-8
-12
-16
Cytokine-cytokine receptor interaction
Human cytomegalovirus infection
Natural killer cell mediated cytotoxicity
MF-κB signaling pathway
Apoptosis
Hematopoietic cell lineage
T cell receptor signaling pathway
JAK-STAT signaling pathway
Adipocytokine signaling pathway
TGF-β signaling pathway
Propionate metabolism
Apoptosis, multiple species
B-Alanine metabolism
KEGG Pathway
0.00
0.05
0.10
0.15
Gene Ratio

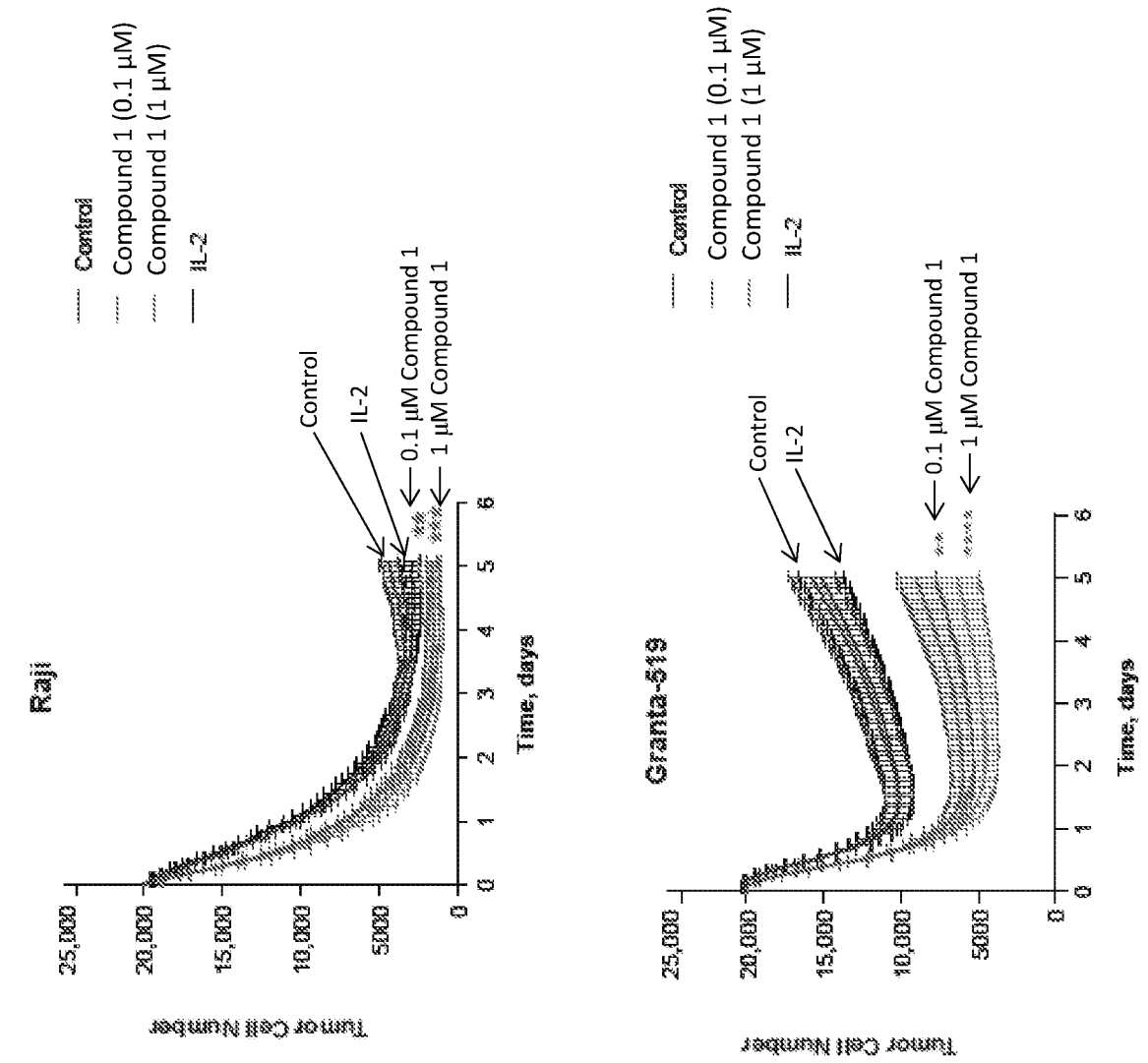

Raji
Granta-519
Control
Compound 1 (0.1 µM)
Compound 1 (1 µM)
IL-2
Control
IL-2
0.1 µM Compound 1
1 µM Compound 1
Tumor Cell Number
Time, days
0
5000
10,000
15,000
20,000
25,000
1
2
3
4
5
6

FIG. 44E

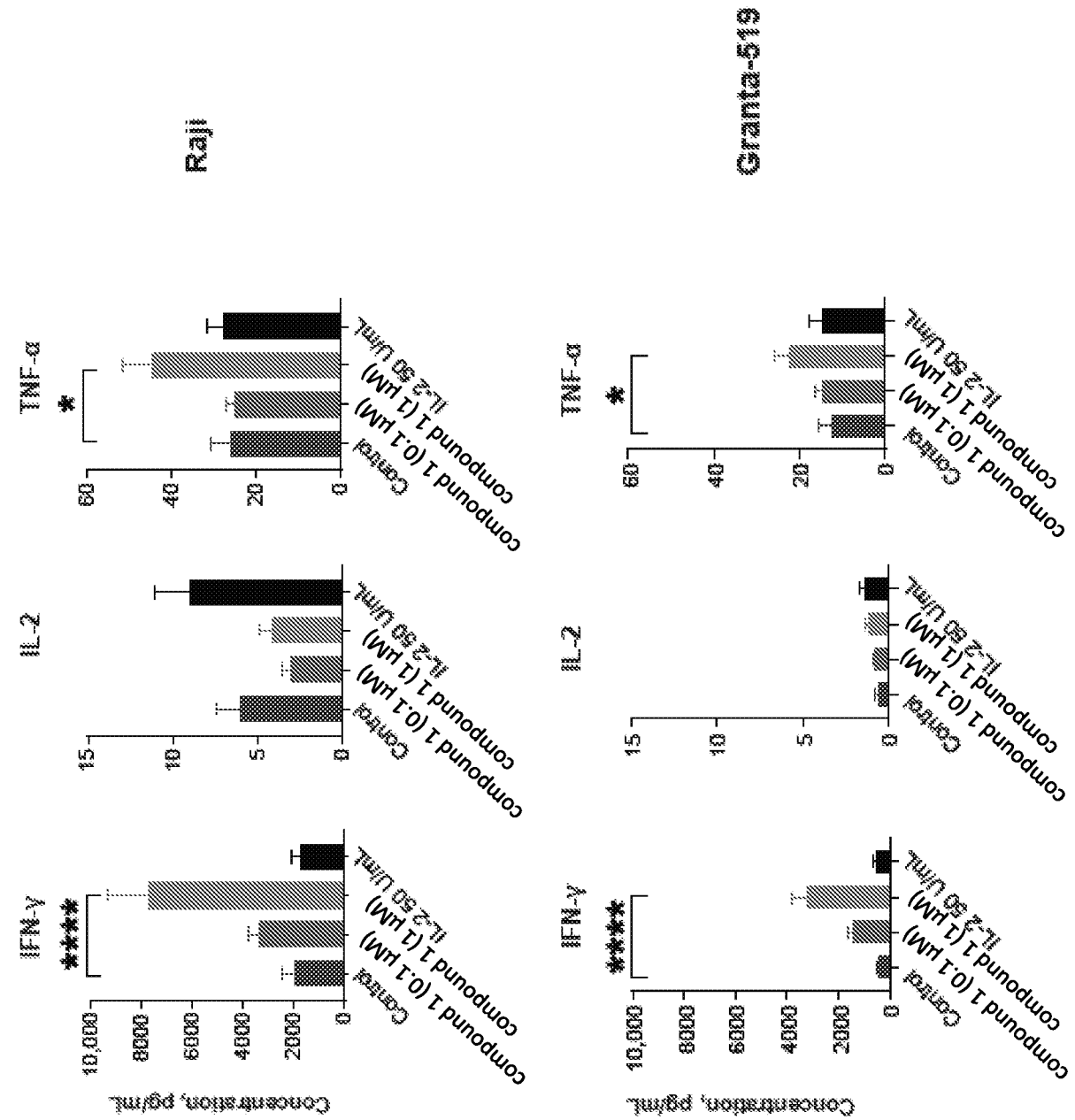
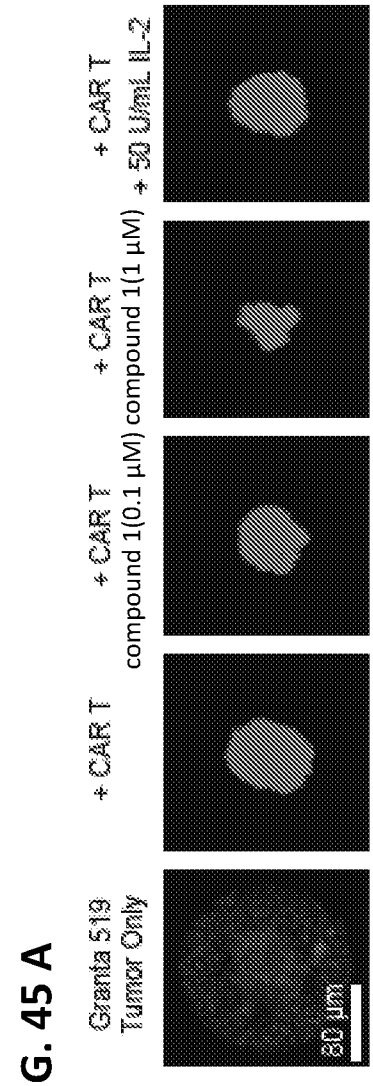
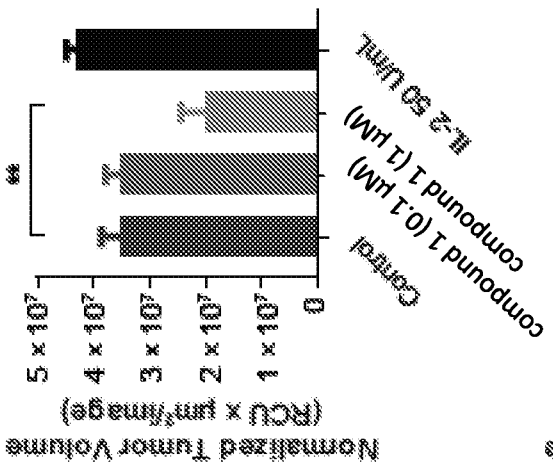

Raji
Granta-519
IFN-γ
IL-2
TNF-α
Concentration, pg/mL
****
*
Control
Compound 1 (0.1 μM)
Compound 1 (1 μM)
IL-2 50 U/mL

FIG. 44F

FIG. 45 A





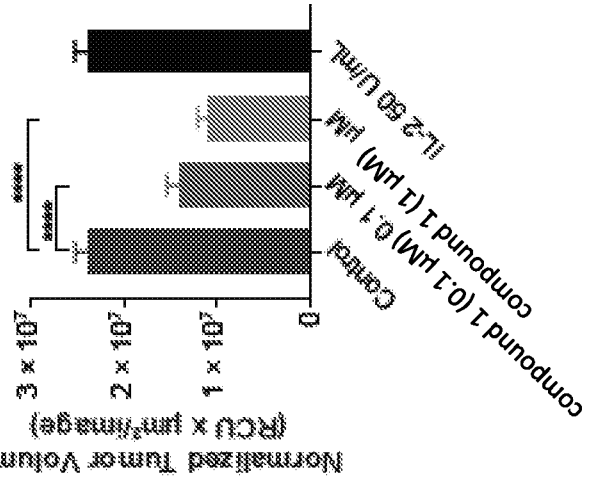


FIG. 45 B

FIG. 45 C

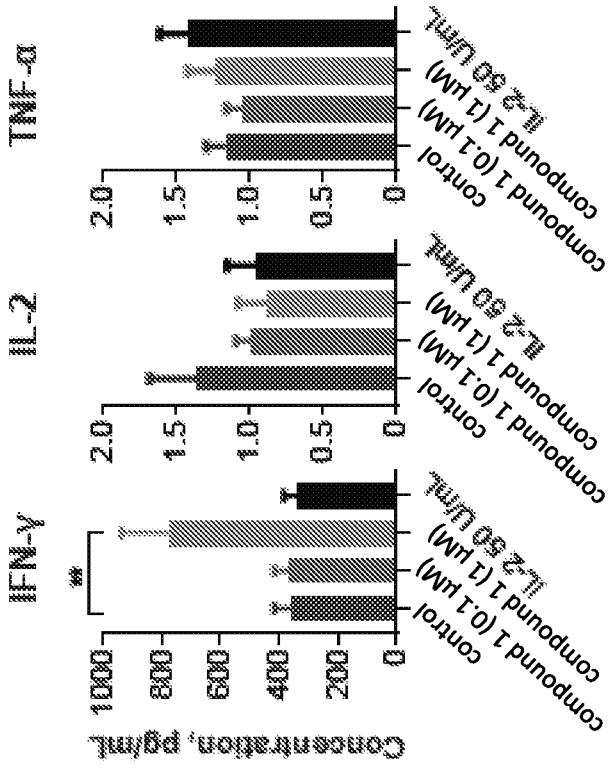


FIG. 45 D

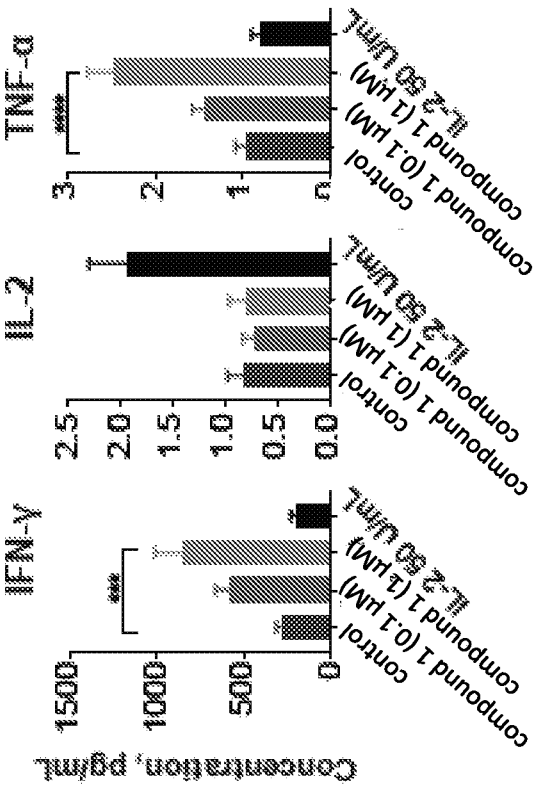
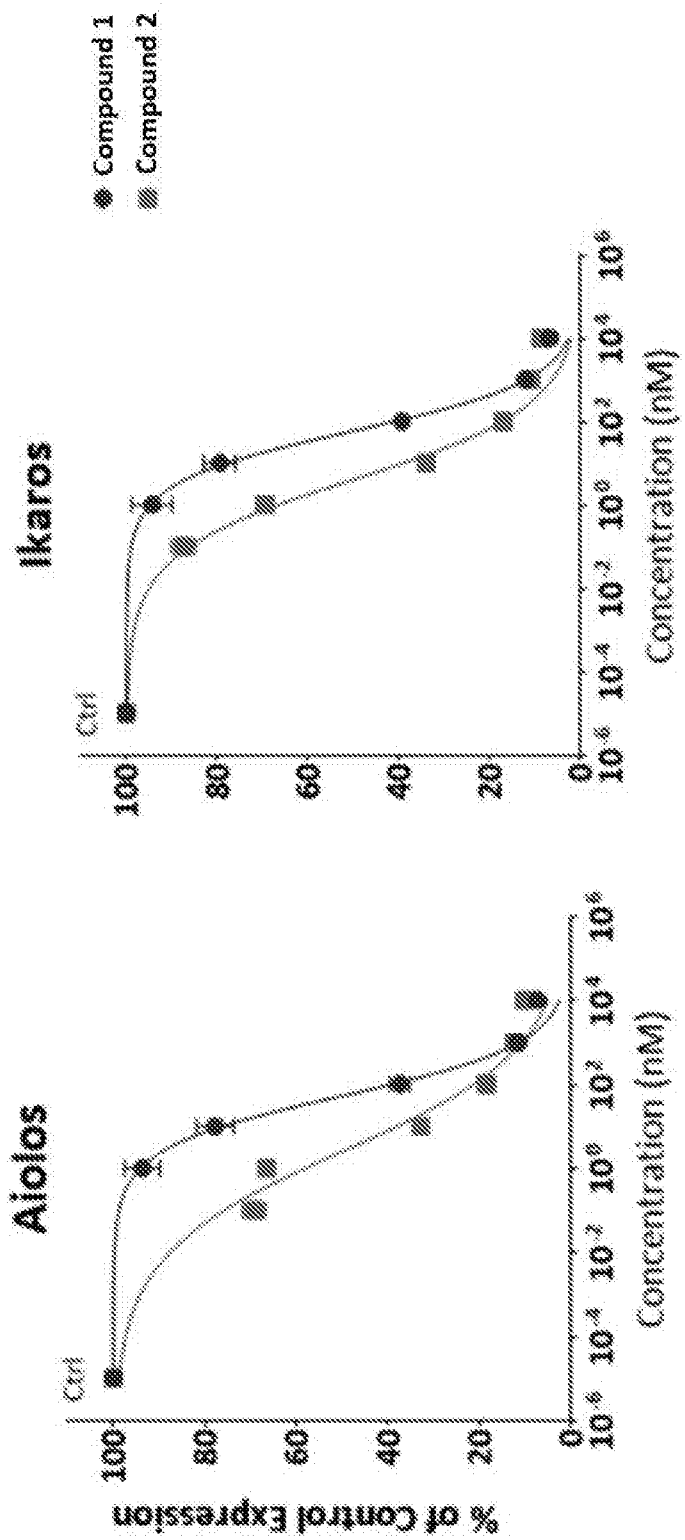


FIG. 46


Compound 1
Compound 2
Ikaros
Aiolos
Ctrl
% of Control Expression
Concentration (nM)
100
80
60
40
20
0
10^{-6}
10^{-4}
10^{-2}
10^{0}
10^{2}
10^{4}
10^{6}

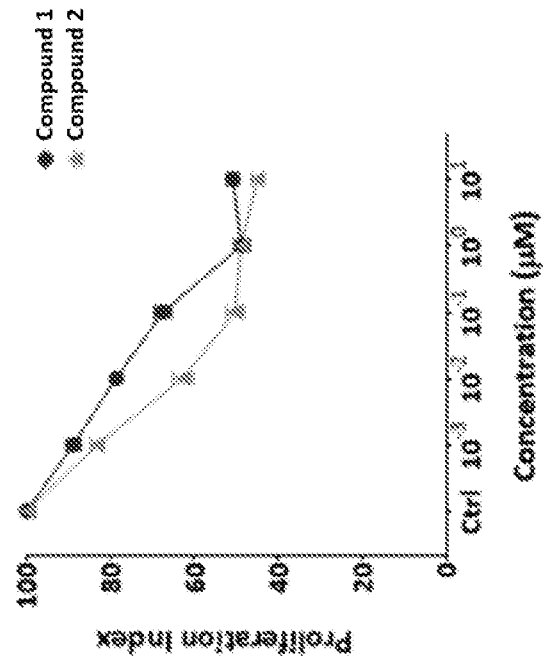


FIG. 47A

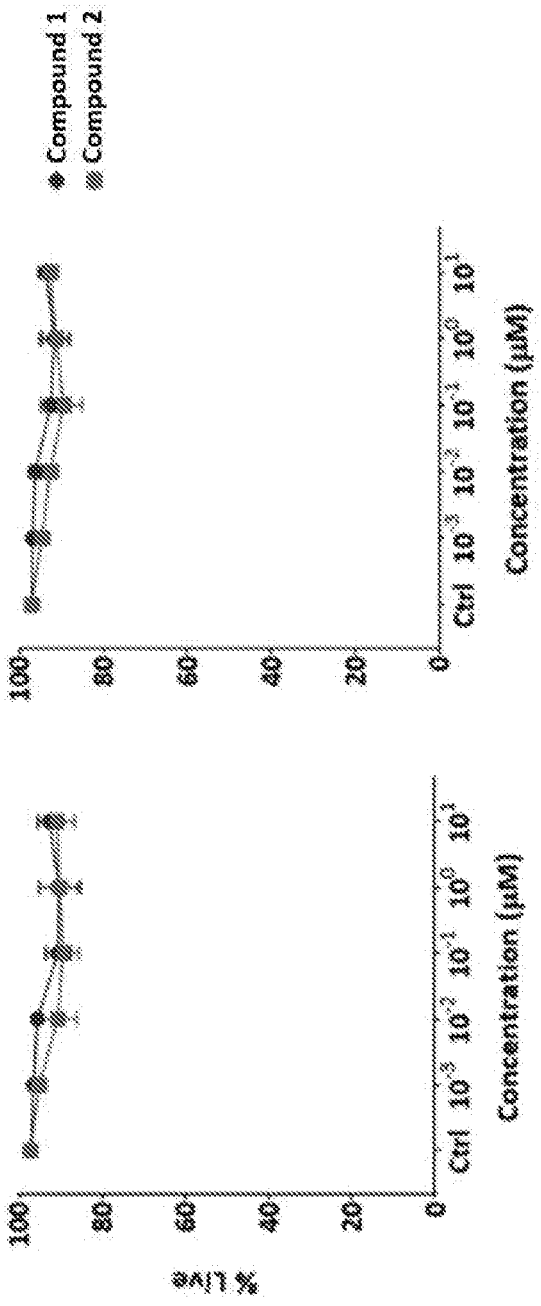


FIG. 47B

FIG. 47C

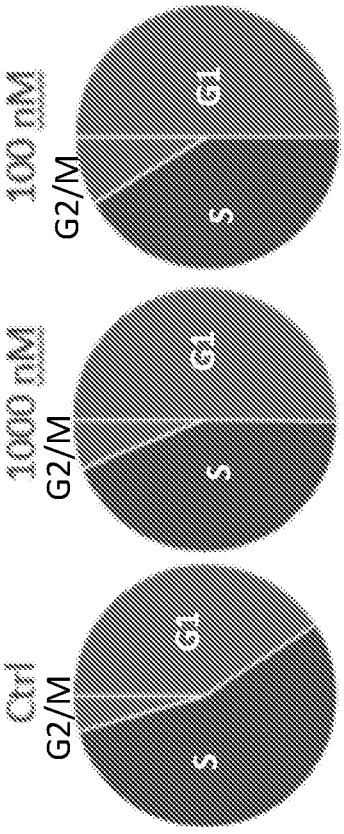


FIG. 47D

FIG. 47E

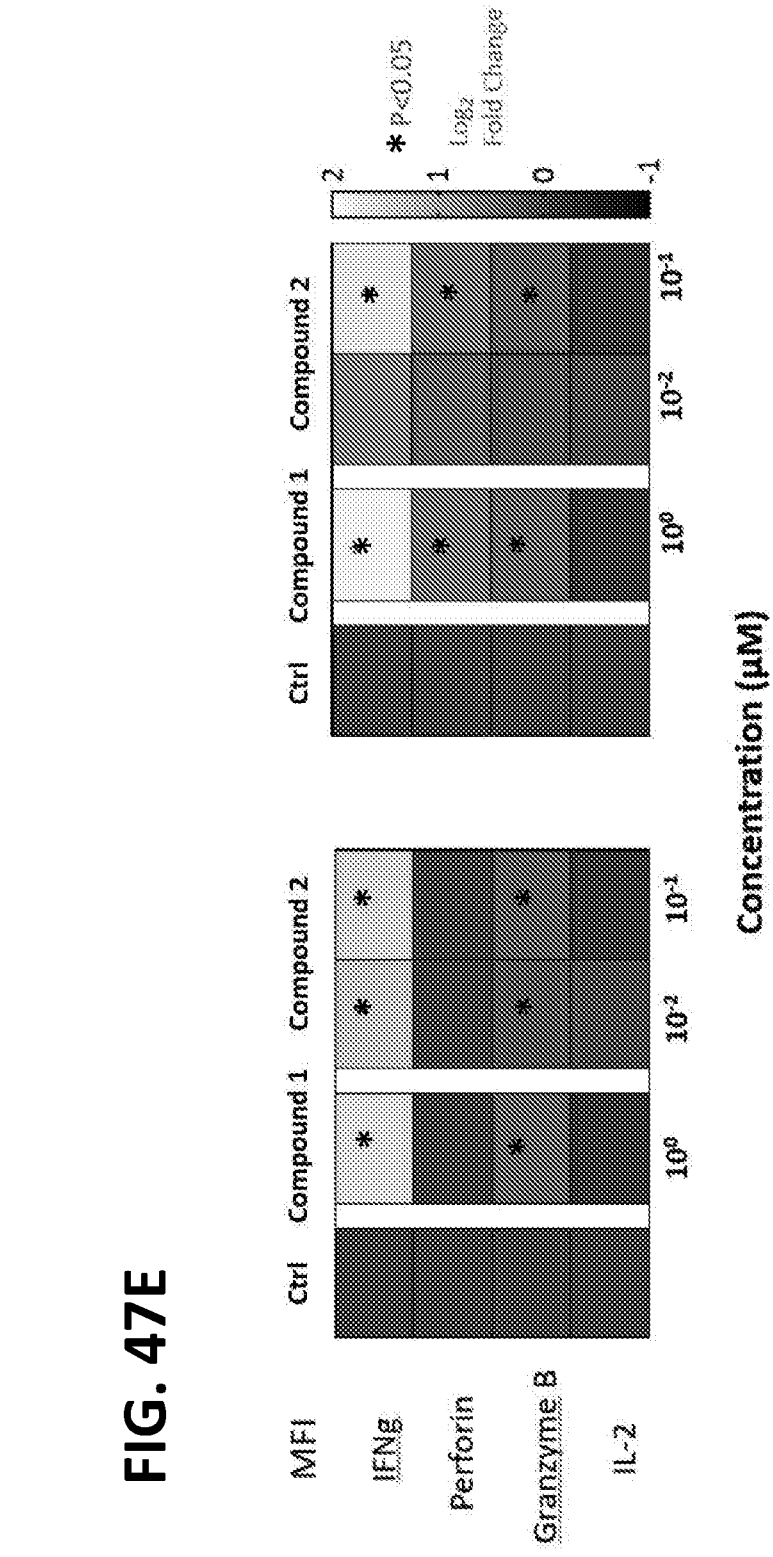

MFI
IFNg
Perforin
Granzyme B
IL-2
Ctrl
Compound 1
Compound 2
10^{0}
10^{-2}
10^{-4}
Concentration (μM)
* p<0.05
Log2 Fold Change
2
1
0
-1

FIG. 48A

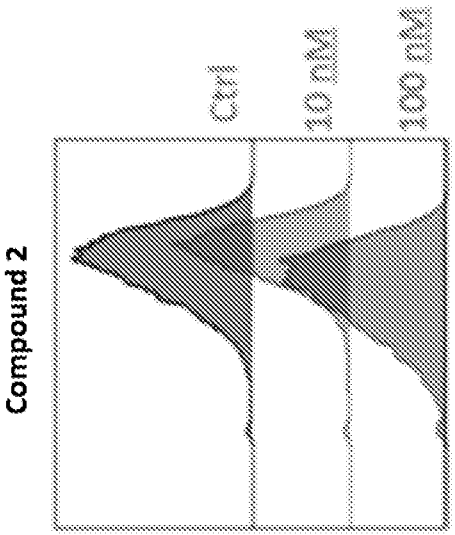
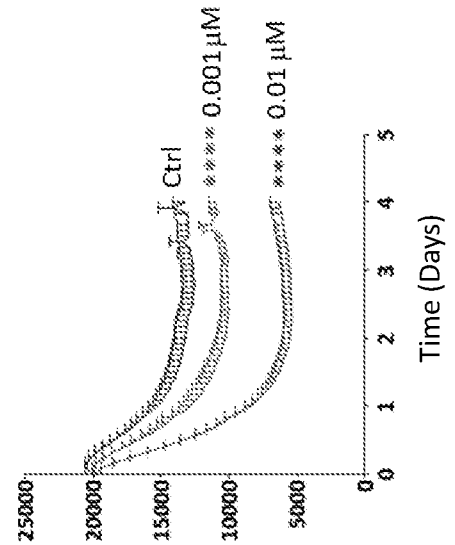
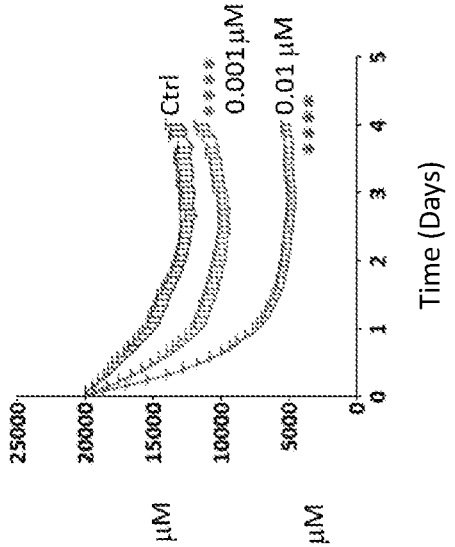


FIG. 48B





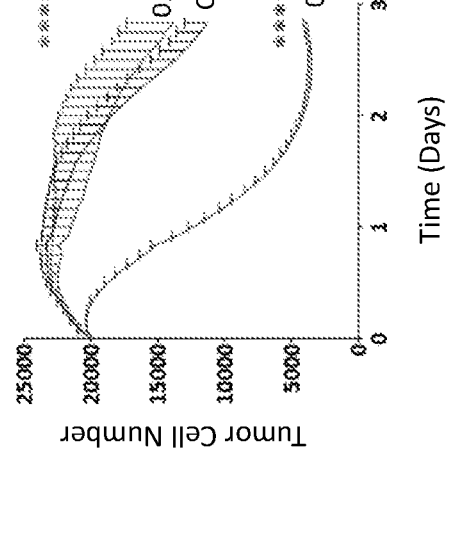


FIG. 48C

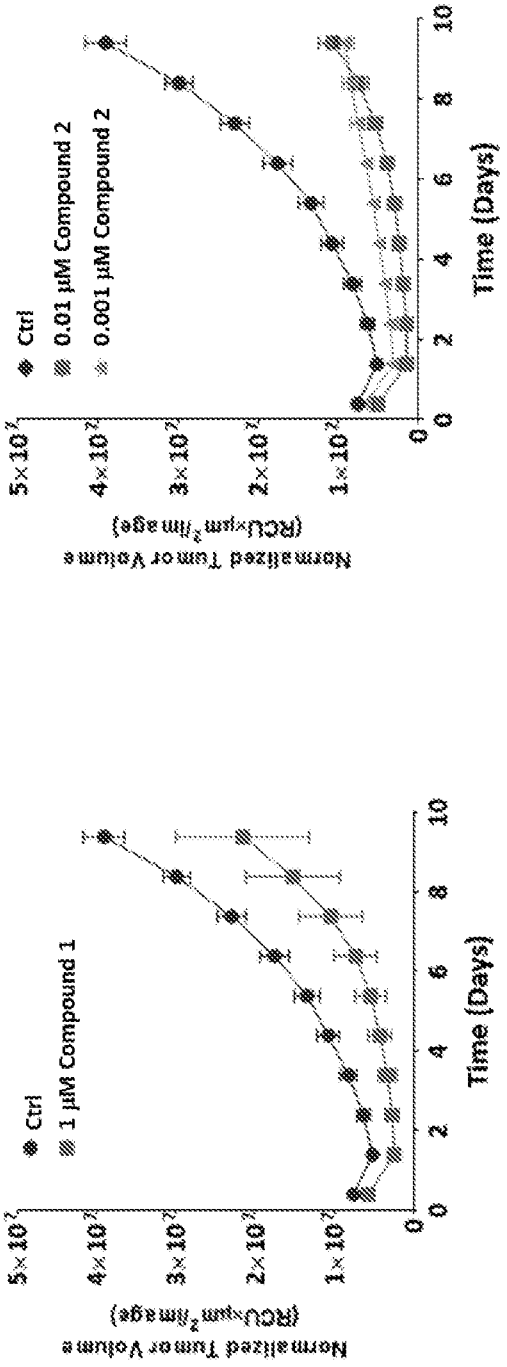


FIG. 48D

FIG. 48E

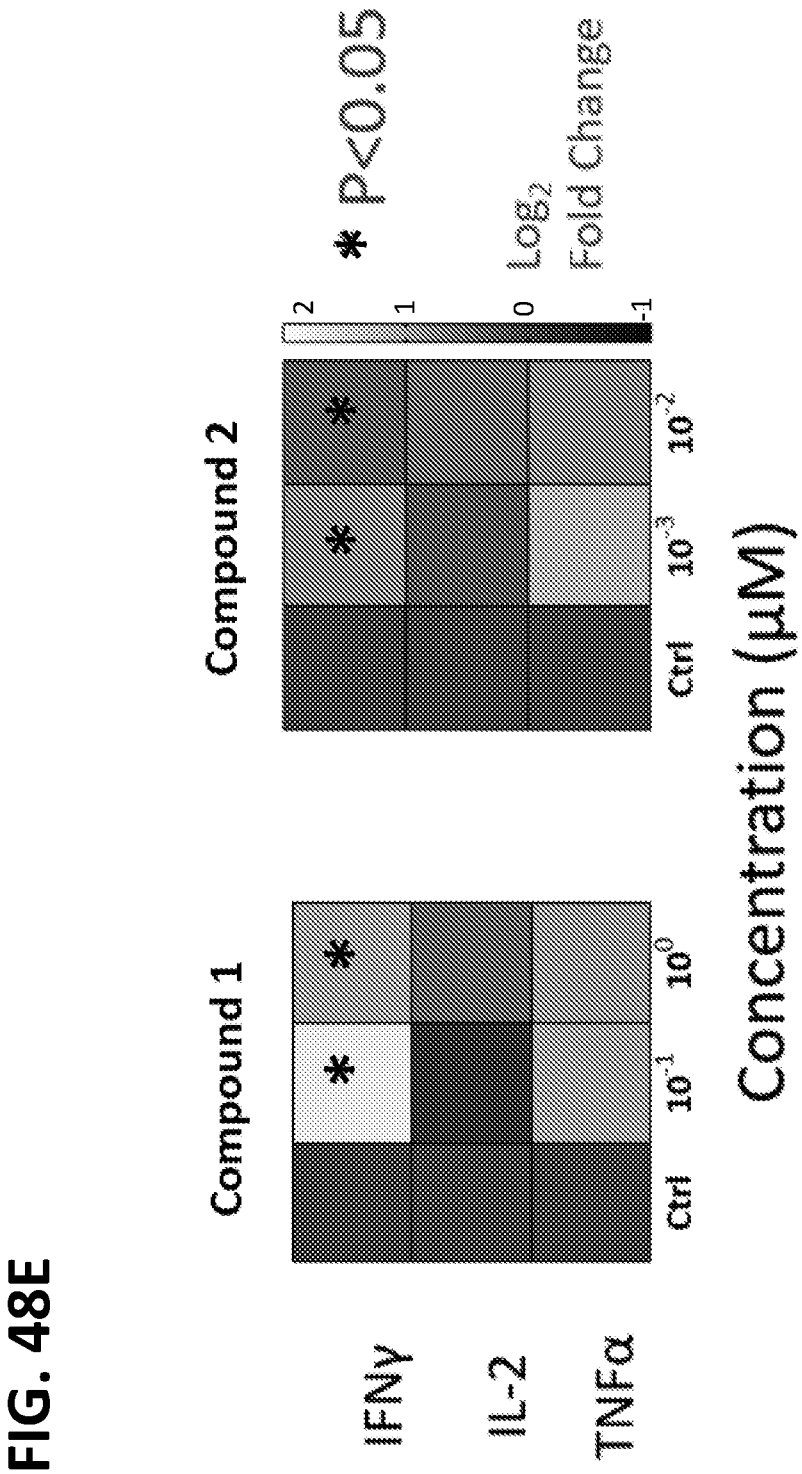

Compound 1
Compound 2
IFNγ
IL-2
TNFα
Ctrl
10^{-1}
10^{0}
10^{-3}
10^{-2}
Concentration (μM)
* P<0.05
Log_2 Fold Change
2
1
0
-1

FIG. 49A

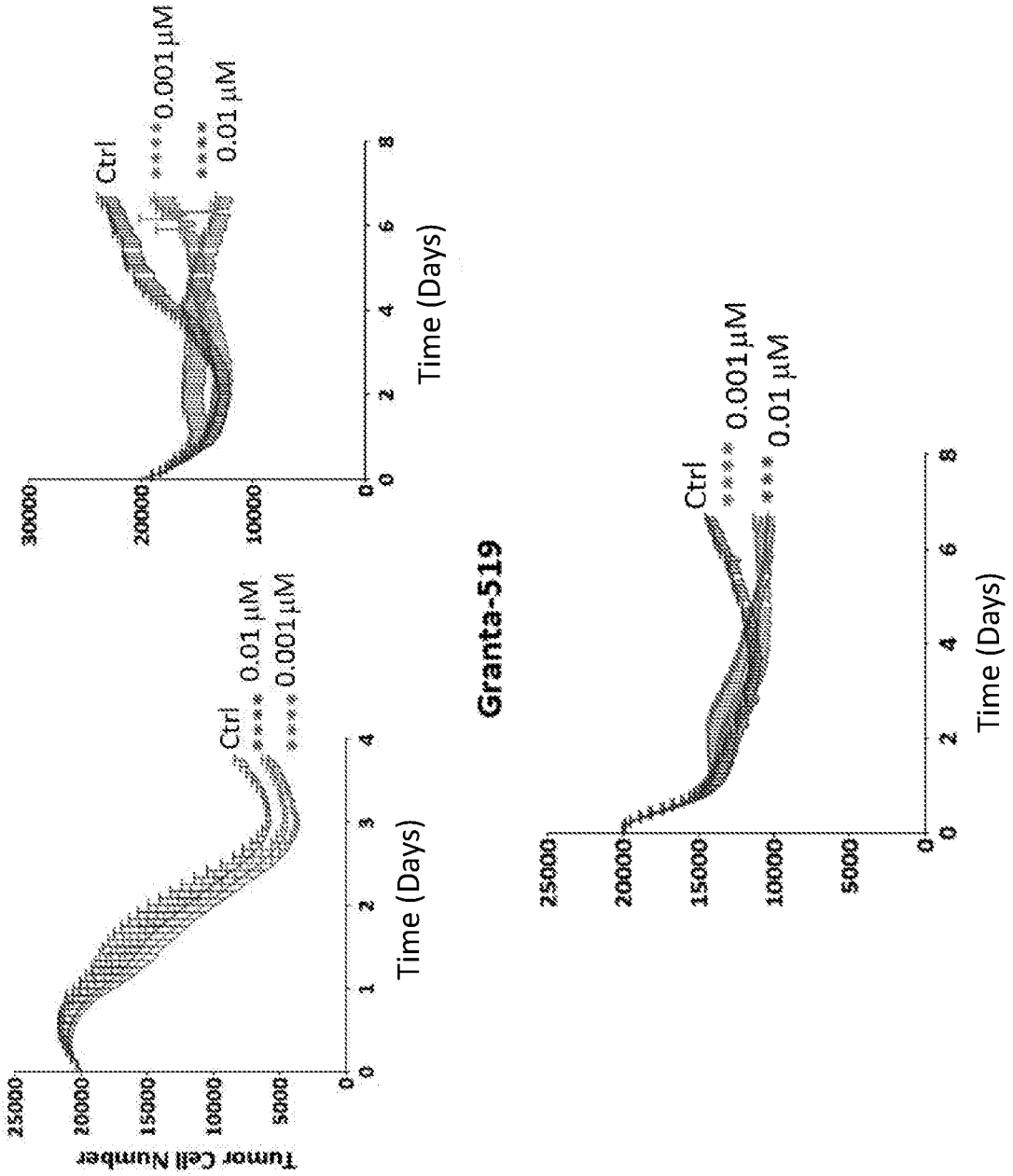

K562.CD19
Tumor Cell Number
Time (Days)
Ctrl
**** 0.01 µM
**** 0.001 µM
Raji
Time (Days)
Ctrl
**** 0.001 µM
**** 0.01 µM
Granta-519
Time (Days)
Ctrl
**** 0.001 µM
*** 0.01 µM

FIG. 49B

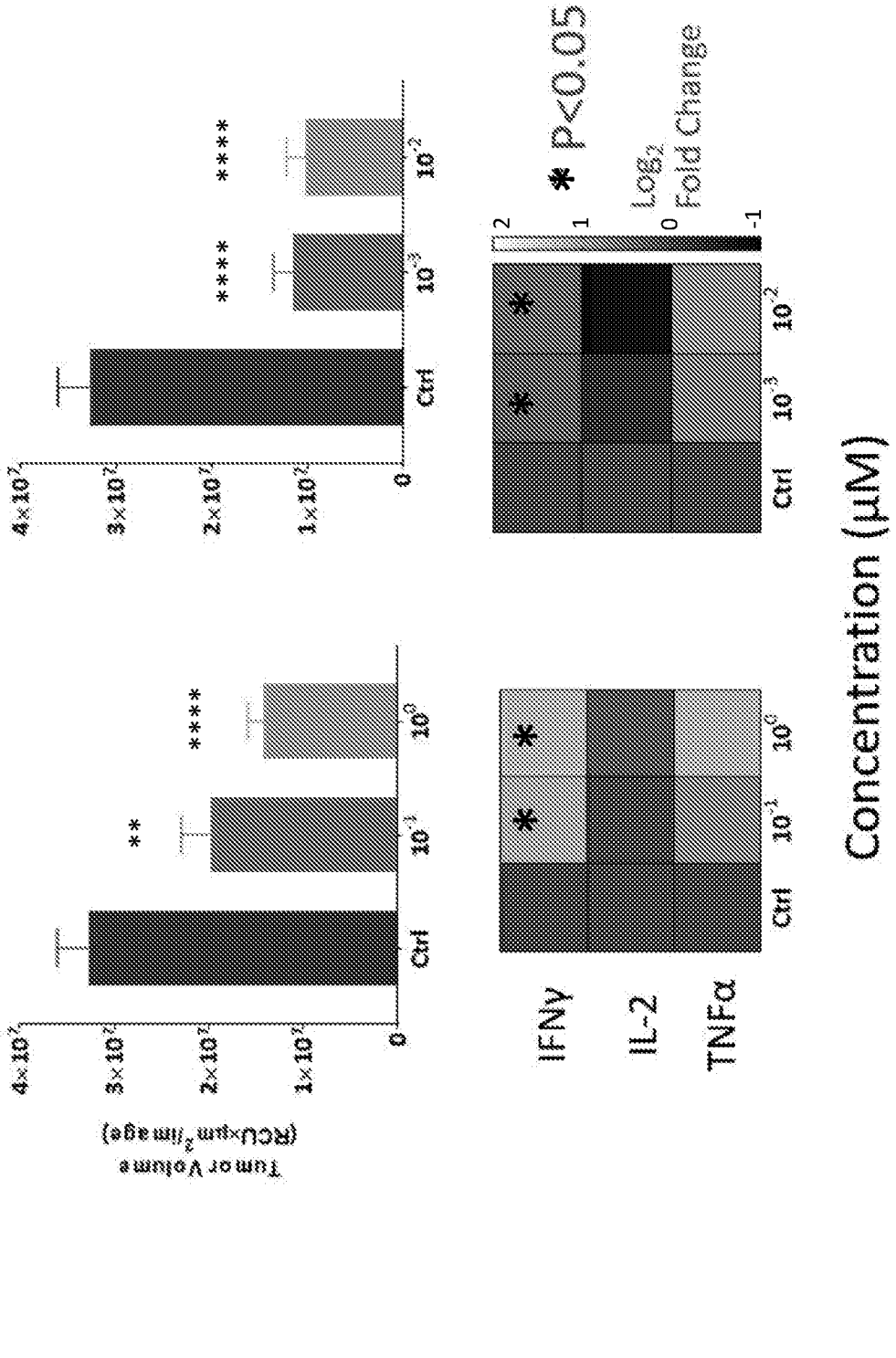
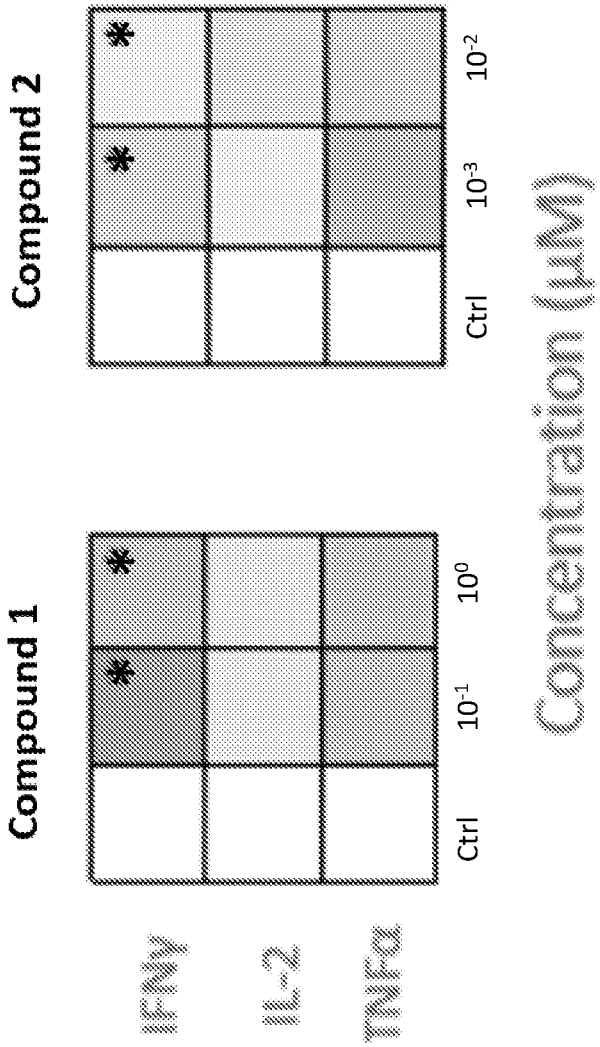

Compound 1
Compound 2
Tumor Volume
(RCU×μm²/Image)
4×10⁷
3×10⁷
2×10⁷
1×10⁷
0
Ctrl
10⁻¹
10⁰
10⁻³
10⁻²
**
****
IFNγ
IL-2
TNFα
* P<0.05
Log₂
Fold Change
2
1
0
-1
Concentration (μM)

FIG. 49C


Compound 1
Compound 2
IFNγ
IL-2
TNFα
Ctrl
10-1
100
Ctrl
10-3
10-2
Concentration (μM)

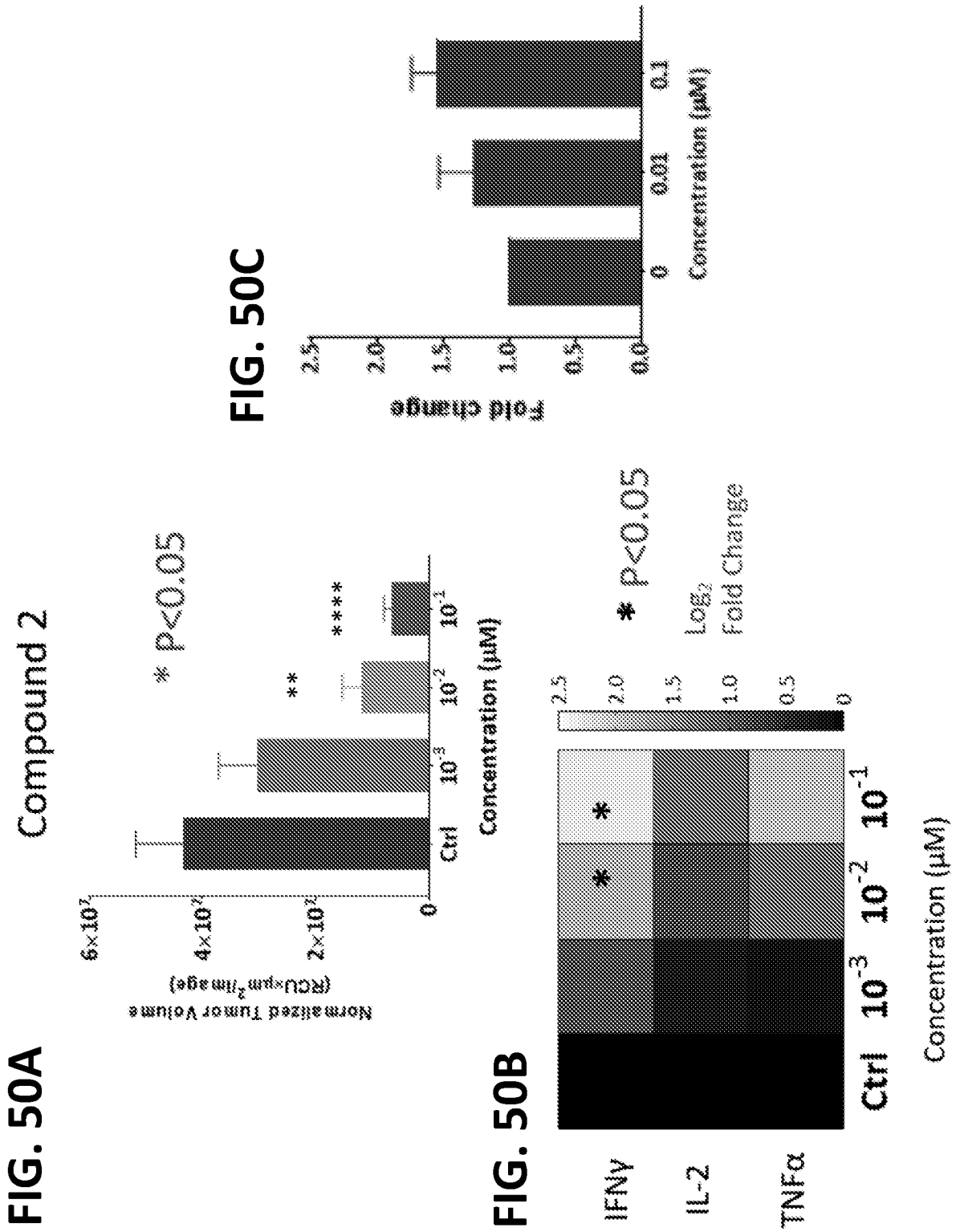

FIG. 50A
Compound 2
* P<0.05
Normalized Tumor Volume
(RCU×μm²/Image)
6×10⁷
4×10⁷
2×10⁷
0
**
****
Ctrl
10⁻³
10⁻²
10⁻¹
Concentration (μM)
FIG. 50B
* P<0.05
Log2 Fold Change
2.5
2.0
1.5
1.0
0.5
0
IFNγ
IL-2
TNFα
Ctrl
10⁻³
10⁻²
10⁻¹
Concentration (μM)
FIG. 50C
Fold change
2.5
2.0
1.5
1.0
0.5
0.0
0
0.01
0.1
Concentration (μM)

FIG. 51A

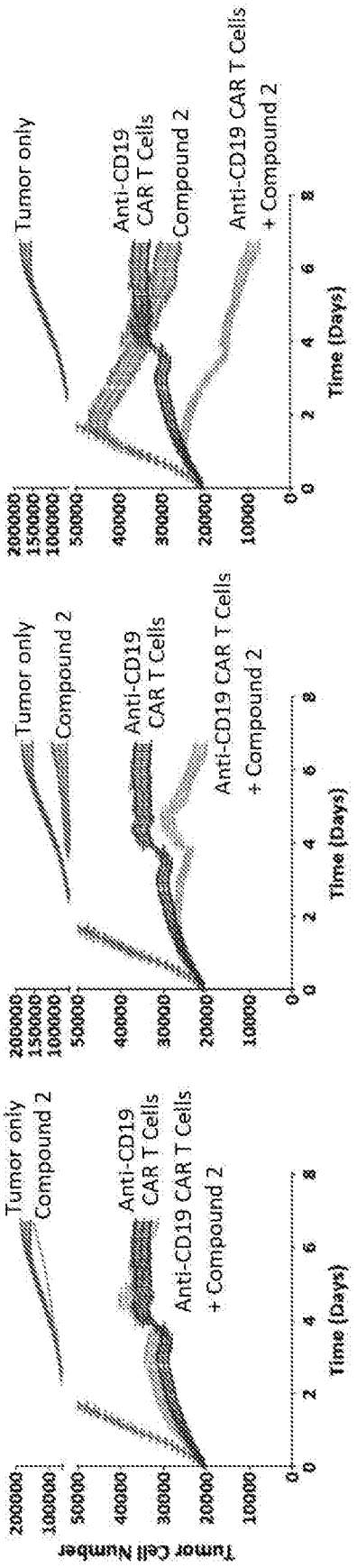


FIG. 51B

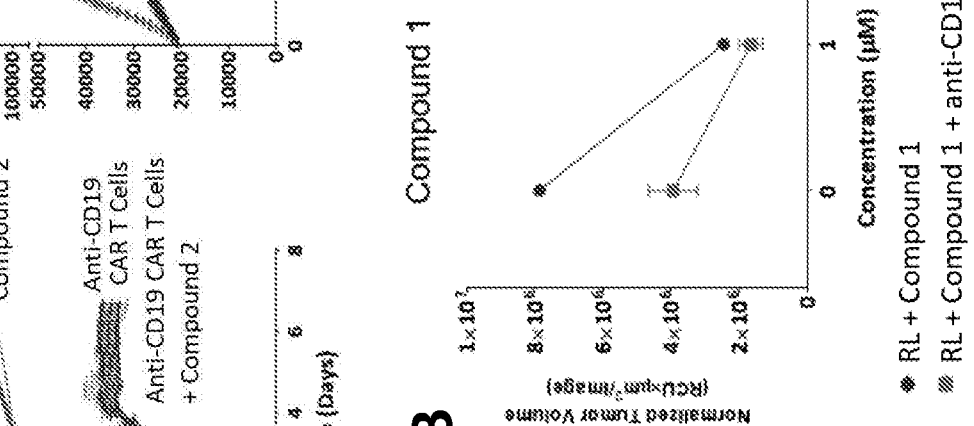


FIG. 51C

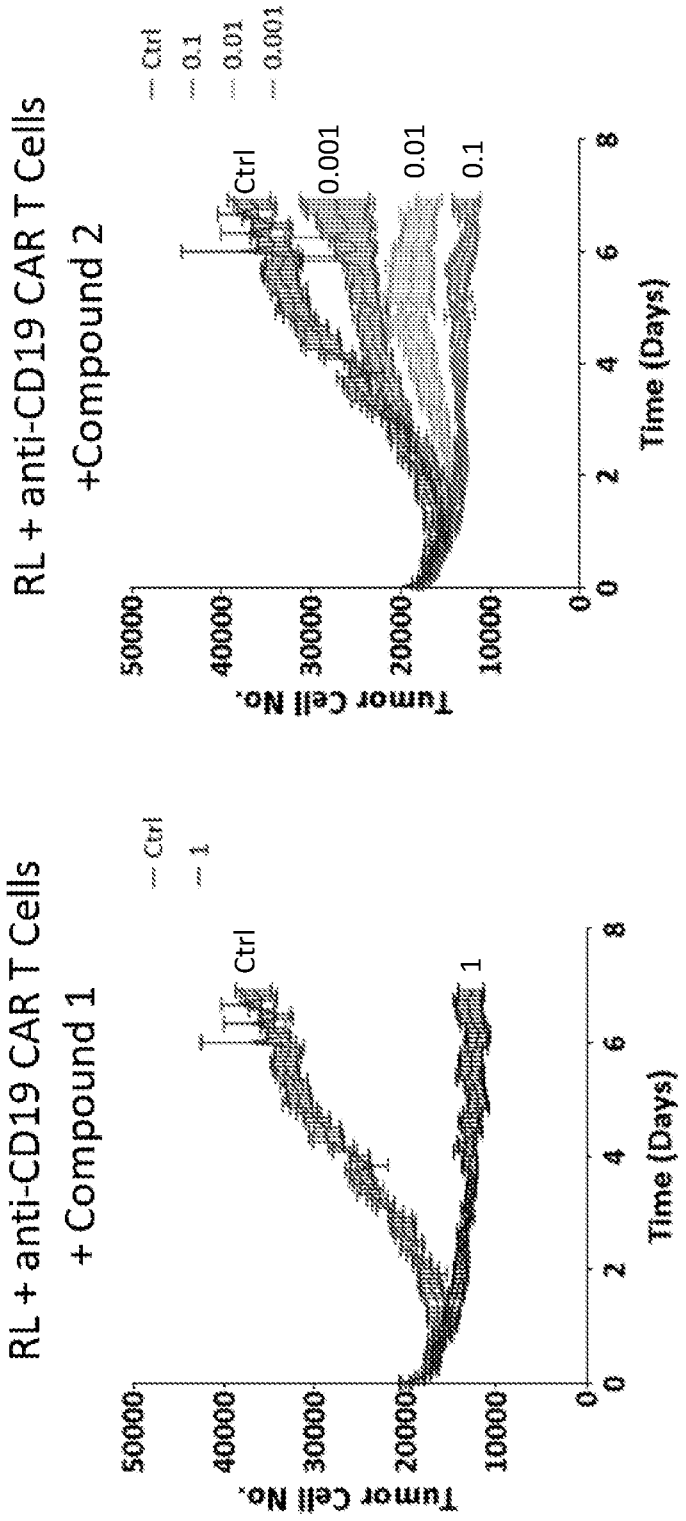

RL + anti-CD19 CAR T Cells
+ Compound 1
Ctrl
1
Tumor Cell No.
Time (Days)
RL + anti-CD19 CAR T Cells
+Compound 2
Ctrl
0.1
0.01
0.001
Tumor Cell No.
Time (Days)

FIG. 52

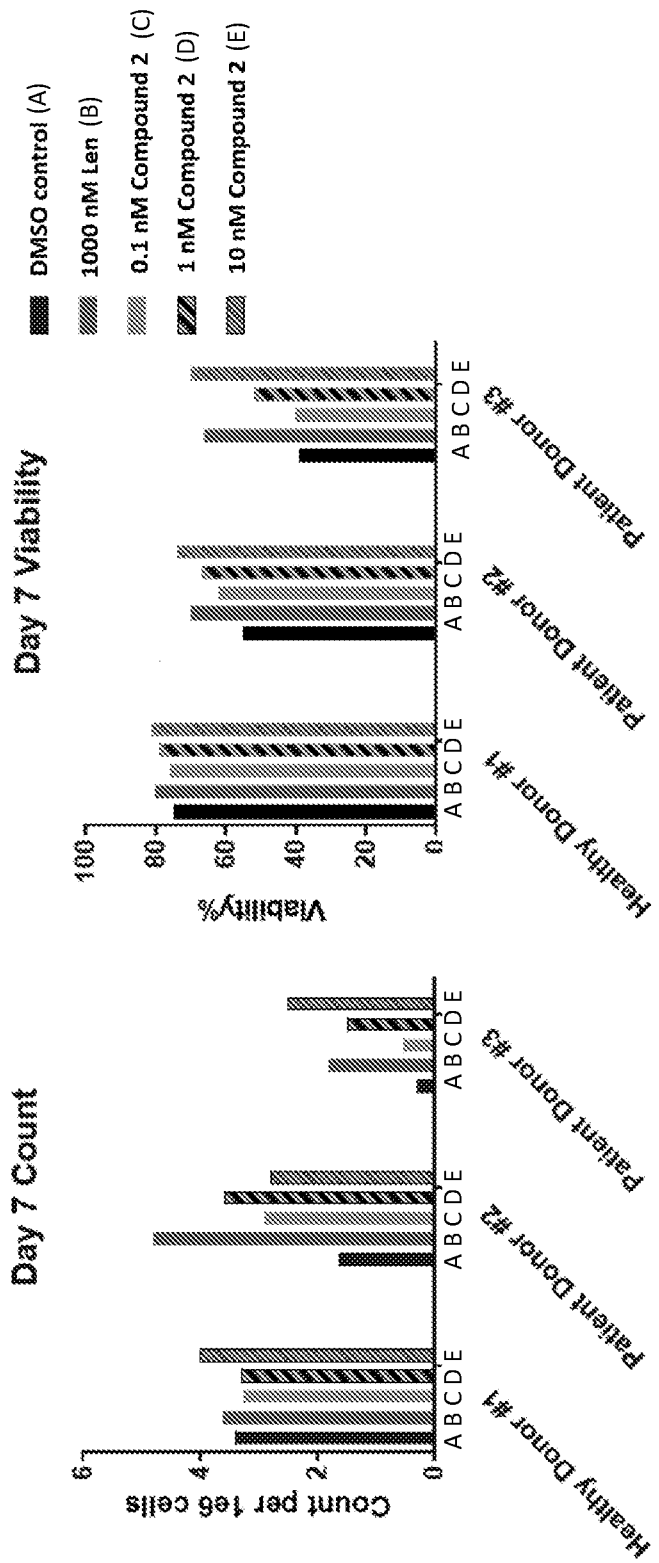

DMSO control (A)
1000 nM Len (B)
0.1 nM Compound 2 (C)
1 nM Compound 2 (D)
10 nM Compound 2 (E)
Day 7 Viability
Viability%
0
20
40
60
80
100
A B C D E
Healthy Donor #1
Patient Donor #2
Patient Donor #3
Day 7 Count
Count per 1e6 cells
0
2
4
6
A B C D E
Healthy Donor #1
Patient Donor #2
Patient Donor #3

FIG. 53A

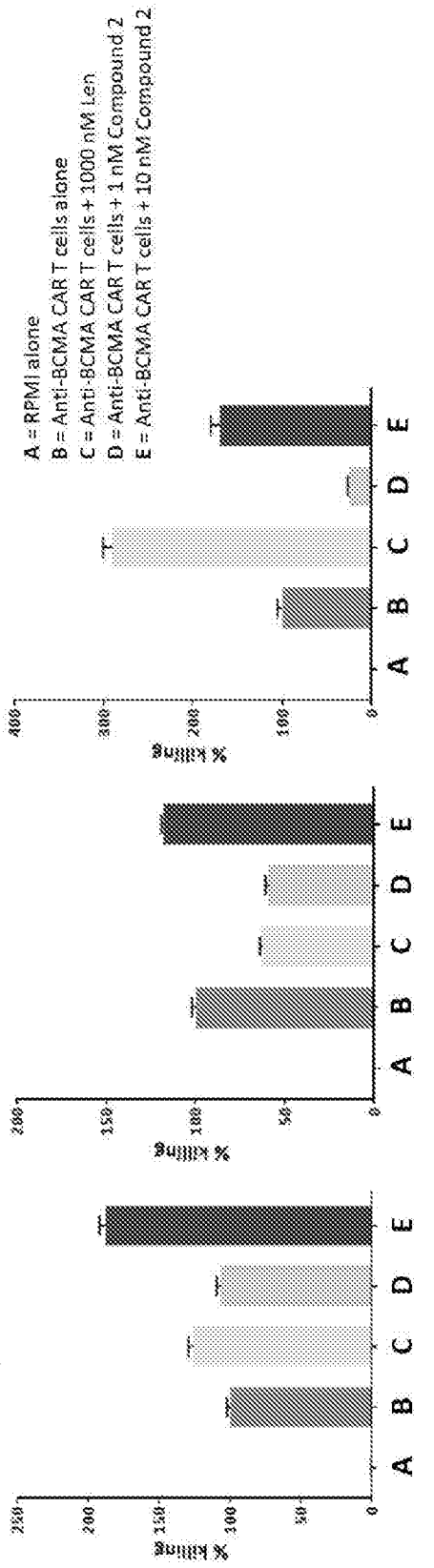


FIG. 53B

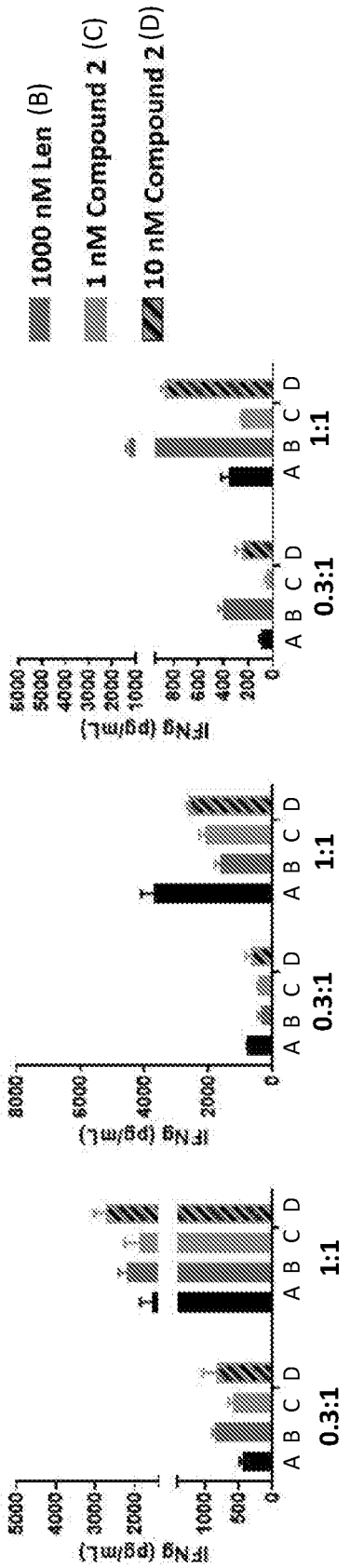


FIG. 53C

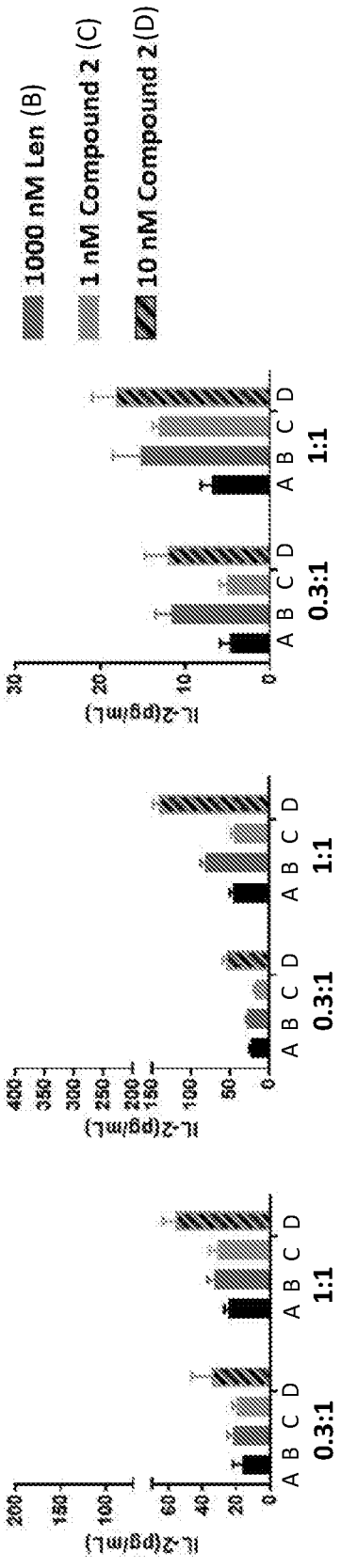


FIG. 53D

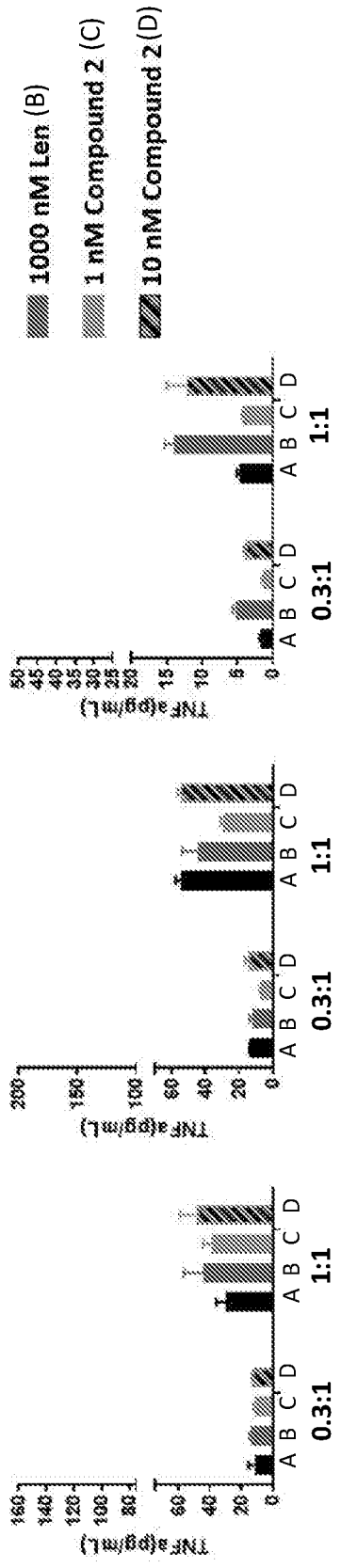


FIG. 54A

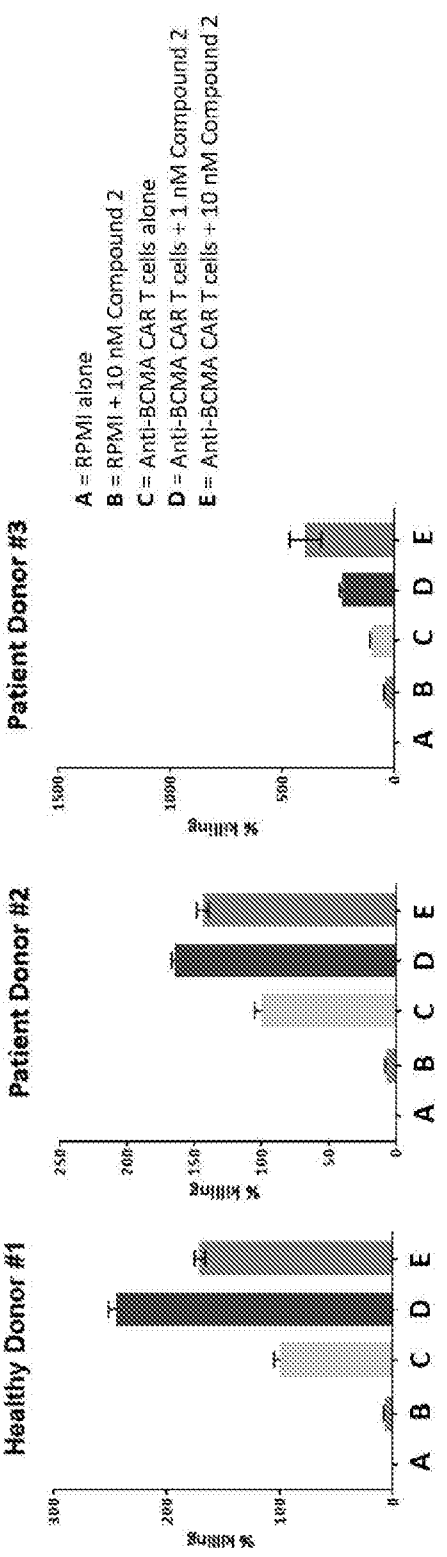


FIG. 54B

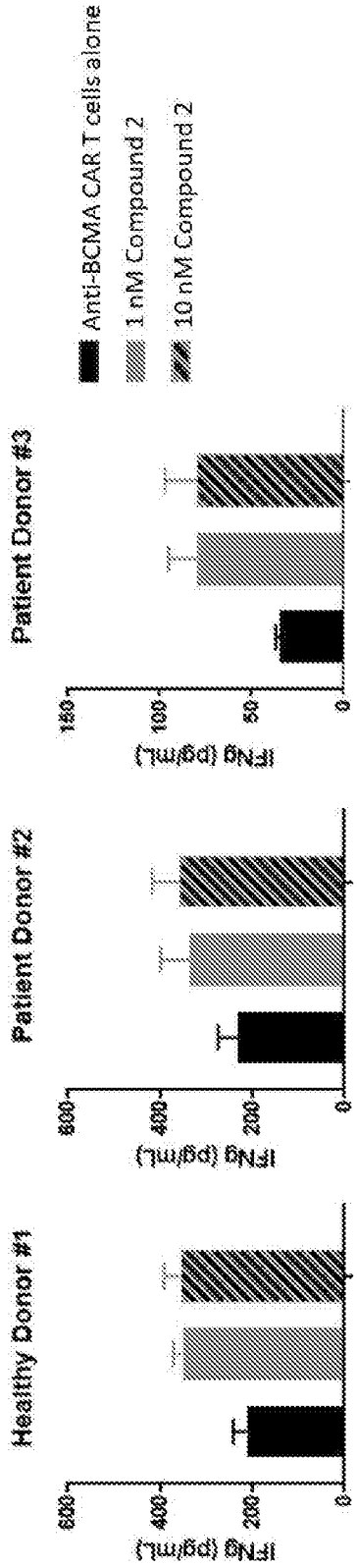


FIG. 54C

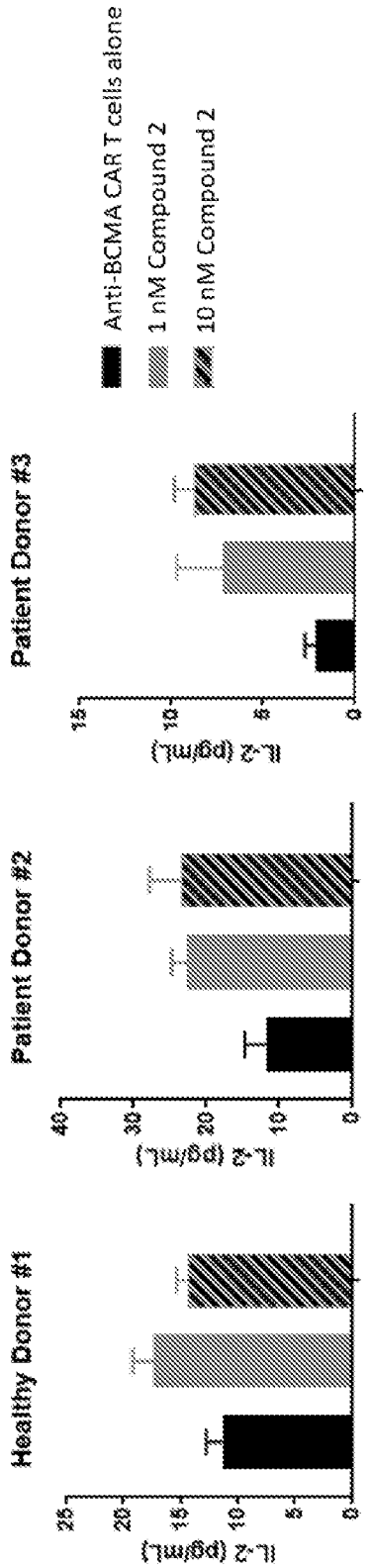


FIG. 54D

FIG. 55A

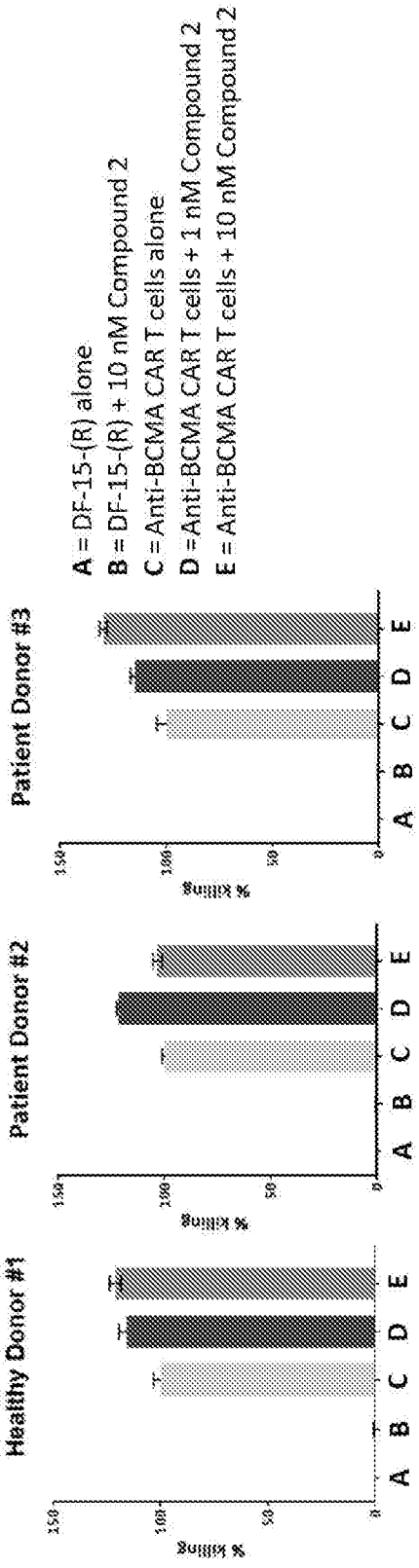


FIG. 55B

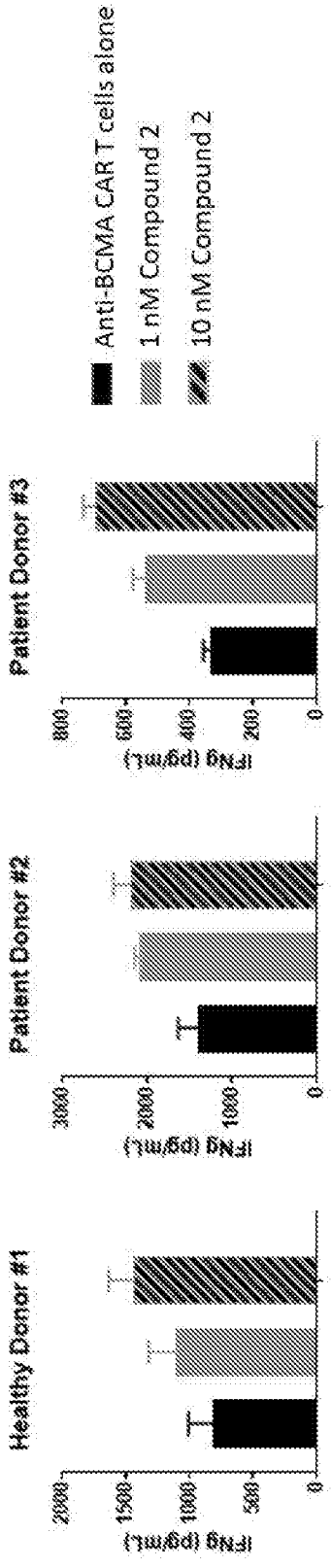


FIG. 55C

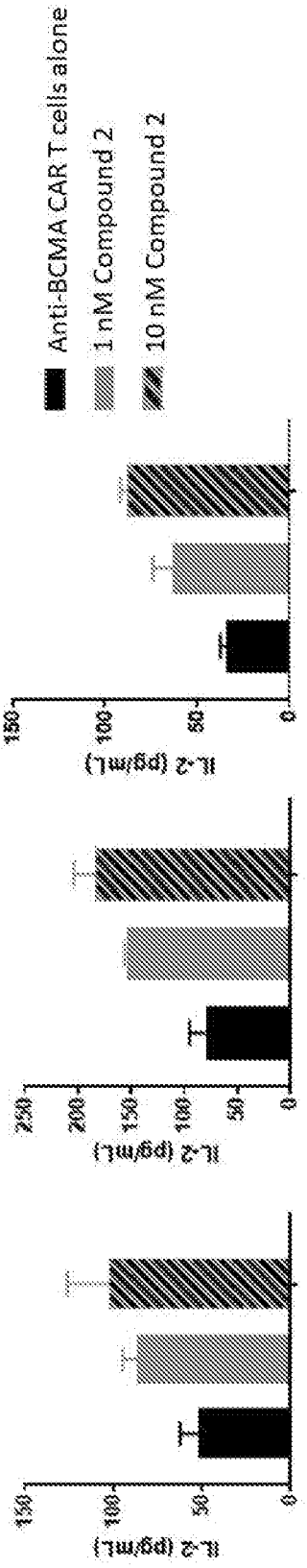


FIG. 55D

