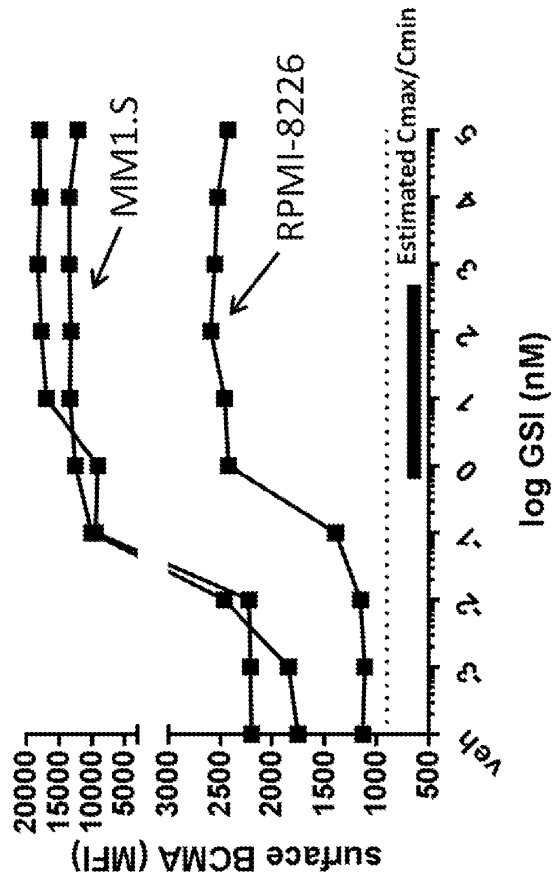

OPM2
MM1.S
RPMI-8226
Estimated Cmax/Cmin
surface BCMA (MFI)
20000
15000
10000
5000
3000
2500
2000
1500
1000
500
veh
log GSI (nM)

FIG. 1

FIG. 2A

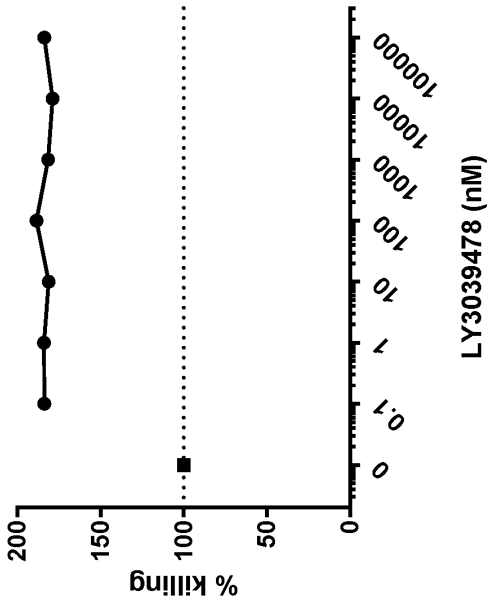

% killing
200
150
100
50
0
0
0.1
1
10
100
1000
10000
100000
LY3039478 (nM)

FIG. 2B

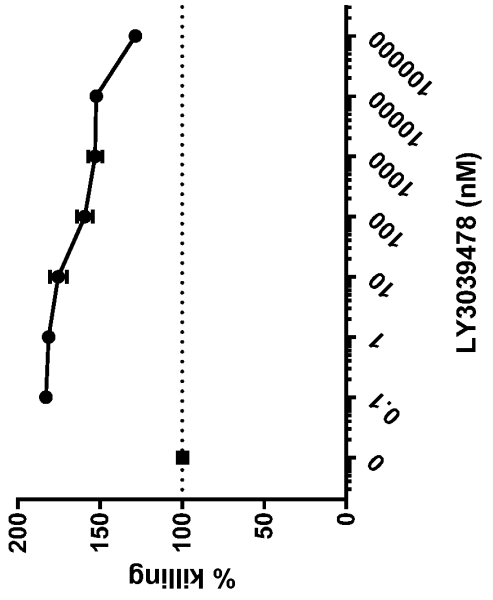

% killing
200
150
100
50
0
0
0.1
1
10
100
1000
10000
100000
LY3039478 (nM)

FIG. 2C

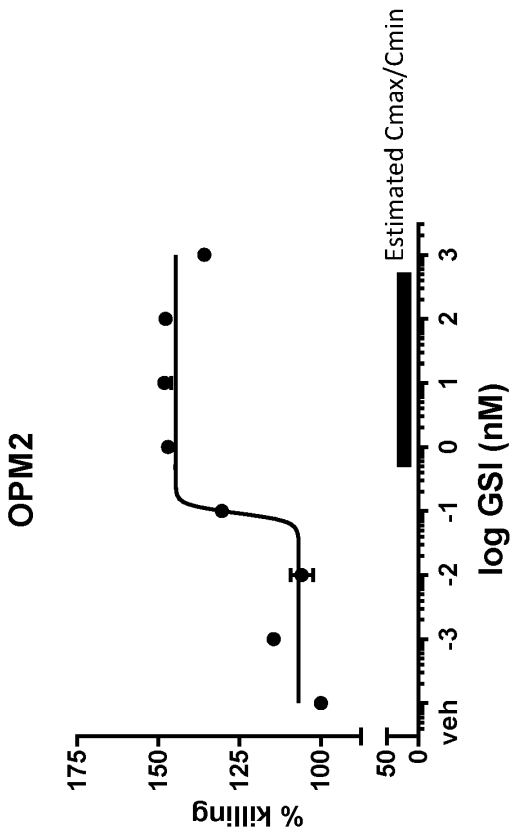

OPM2
% killing
175
150
125
100
Estimated Cmax/Cmin
50
0
veh
-3
-2
-1
0
1
2
3
log GSI (nM)

FIG. 3B

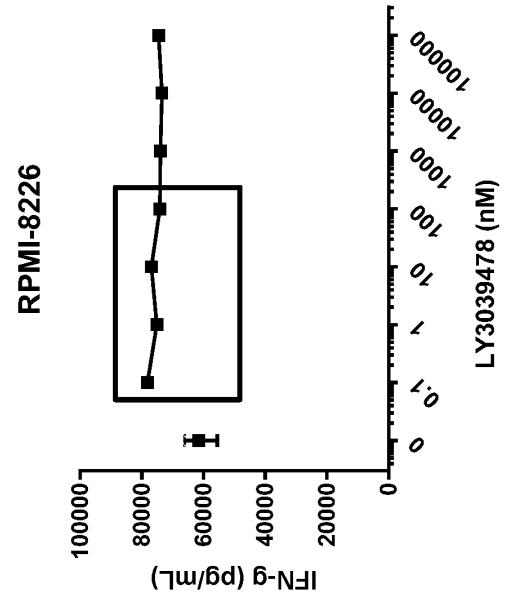

RPMI-8226
IFN-g (pg/mL)
100000
80000
60000
40000
20000
0
0
0.1
1
10
100
1000
10000
100000
LY3039478 (nM)

FIG. 3A

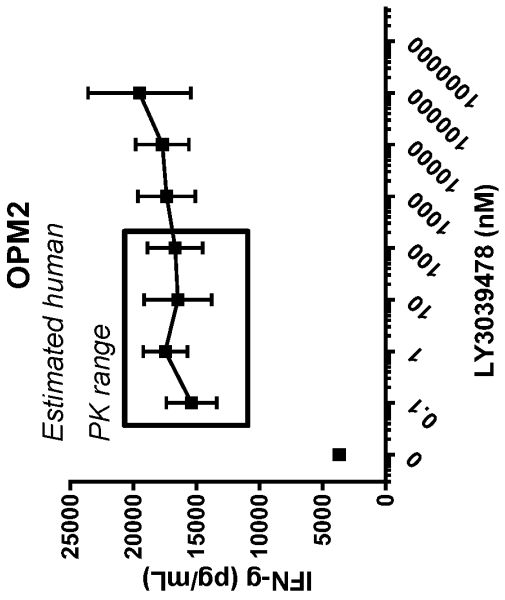

OPM2
Estimated human
PK range
IFN-g (pg/mL)
25000
20000
15000
10000
5000
0
0
0.1
1
10
100
1000
10000
100000
1000000
LY3039478 (nM)

FIG. 3D

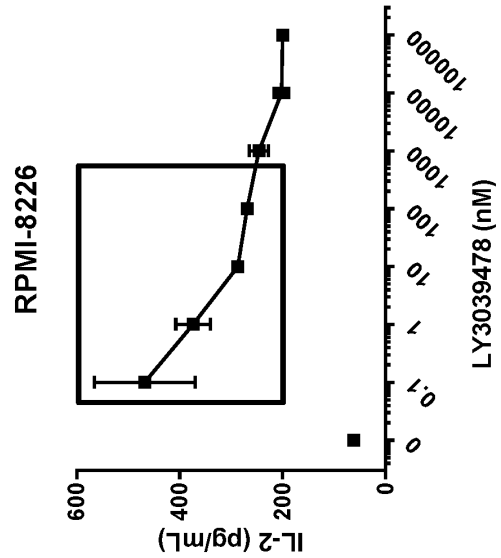
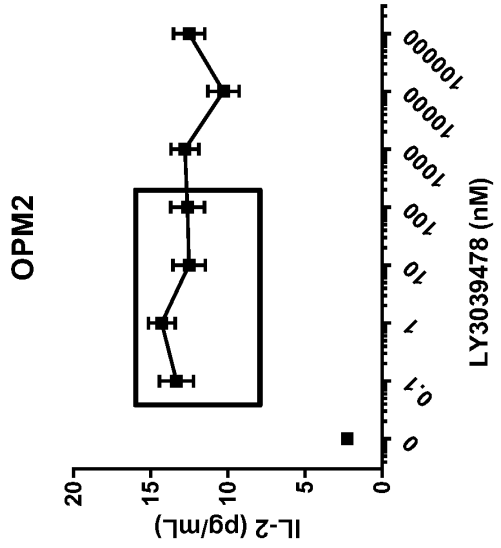

RPMI-8226
IL-2 (pg/mL)
0
200
400
600
LY3039478 (nM)
0
0.1
1
10
100
1000
10000
100000

FIG. 3C


OPM2
IL-2 (pg/mL)
0
5
10
15
20
LY3039478 (nM)
0
0.1
1
10
100
1000
10000
100000

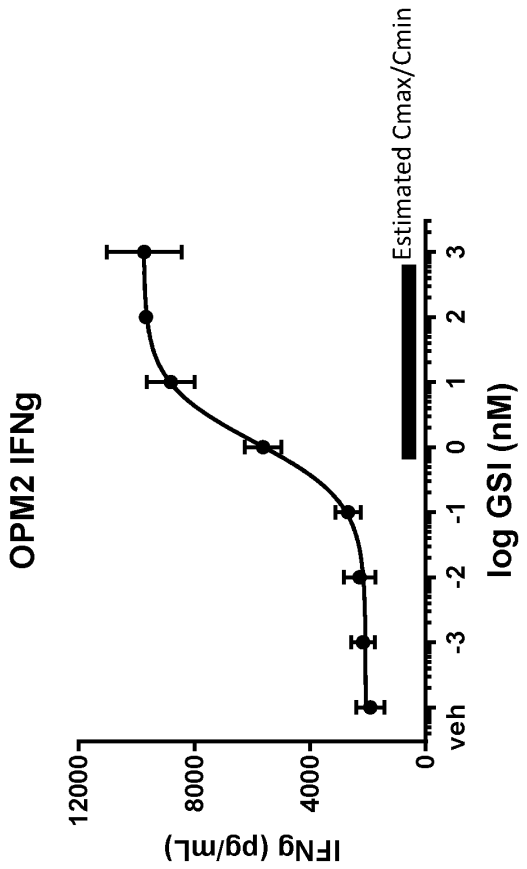

OPM2 IFNg
IFNg (pg/mL)
12000
8000
4000
0
veh
-3
-2
-1
0
1
2
3
log GSI (nM)
Estimated Cmax/Cmin

FIG. 3E

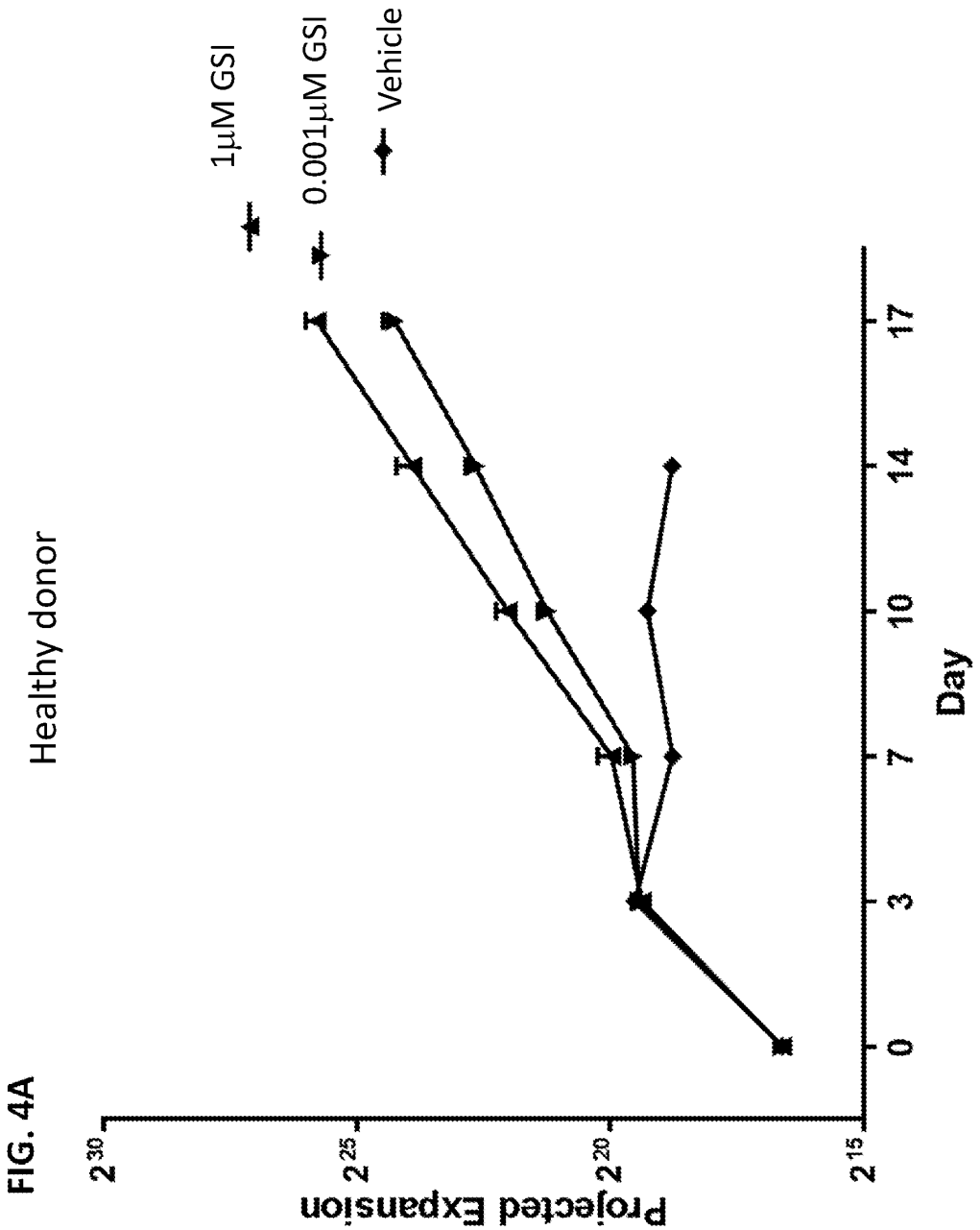

Healthy donor
1μM GSI
0.001μM GSI
Vehicle
Projected Expansion
2^{30}
2^{25}
2^{20}
2^{15}
0
3
7
10
14
17
Day

FIG. 4A

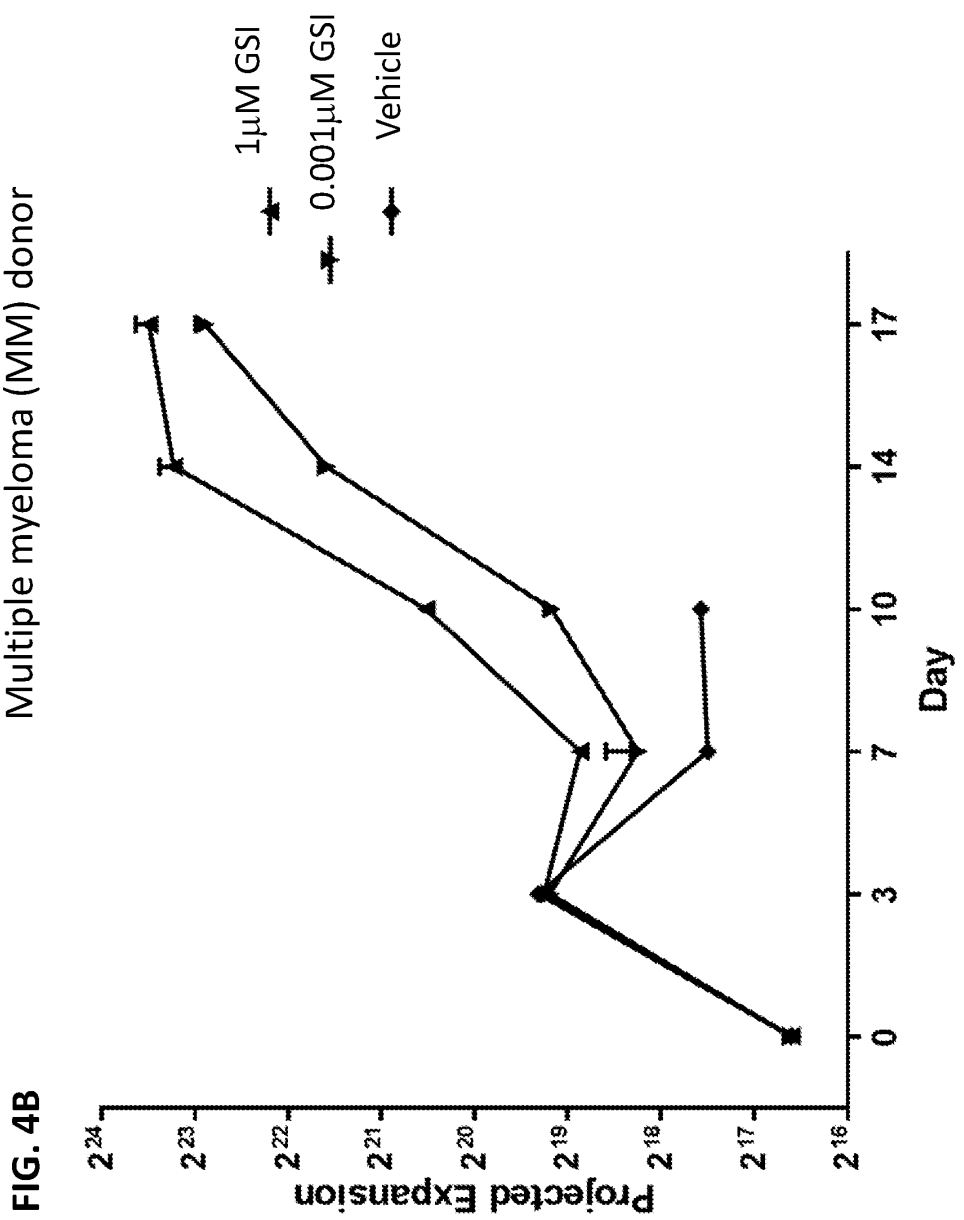
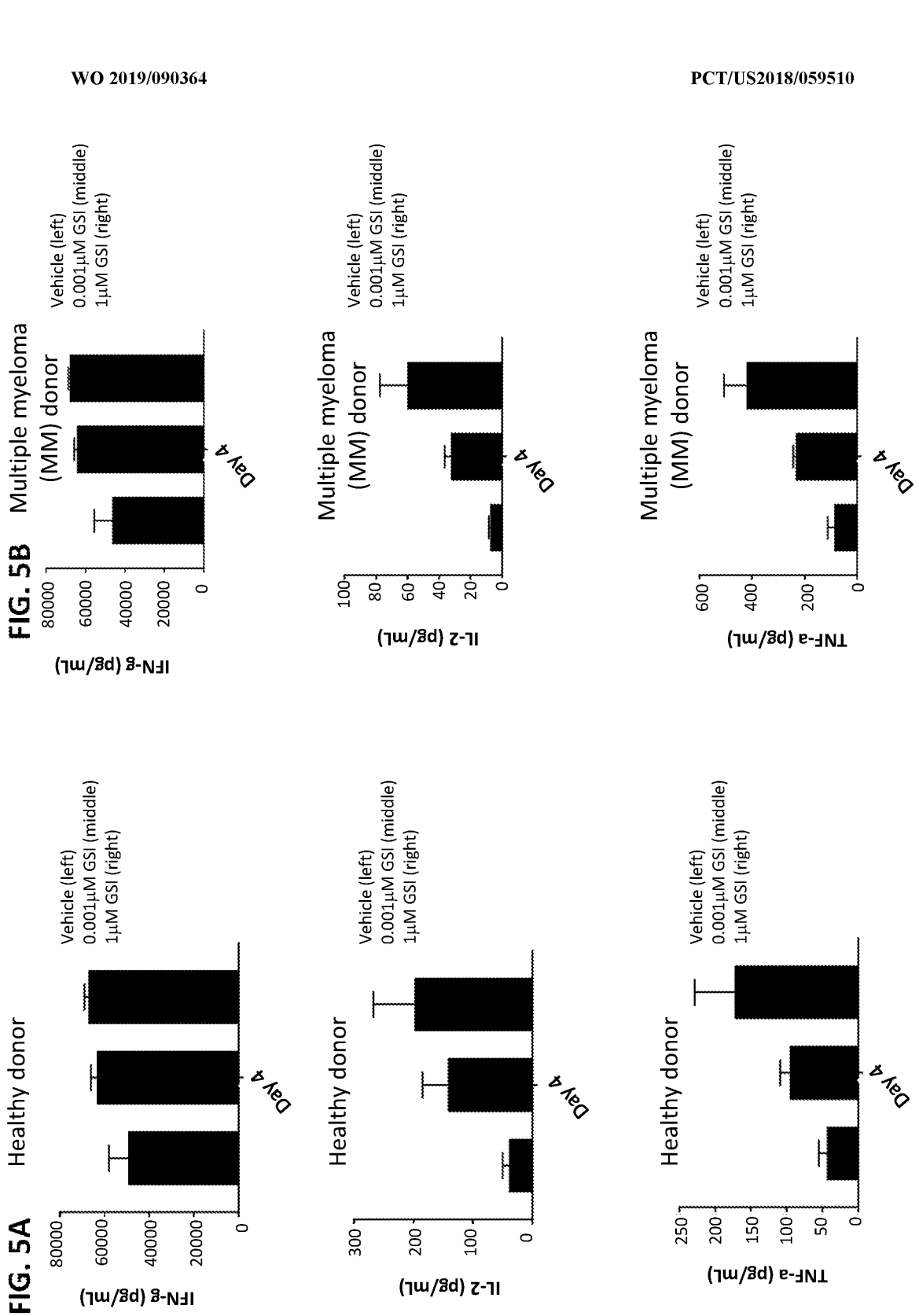

Multiple myeloma (MM) donor
1μM GSI
0.001μM GSI
Vehicle
Projected Expansion
2^{24}
2^{23}
2^{22}
2^{21}
2^{20}
2^{19}
2^{18}
2^{17}
2^{16}
0
3
7
10
14
17
Day

FIG. 4B


FIG. 5A
Healthy donor
IFN-g (pg/mL)
80000
60000
40000
20000
0
Day 4
Vehicle (left)
0.001μM GSI (middle)
1μM GSI (right)
IL-2 (pg/mL)
300
200
100
0
TNF-a (pg/mL)
250
200
150
100
50
FIG. 5B
Multiple myeloma (MM) donor
100
80
60
40
600
400

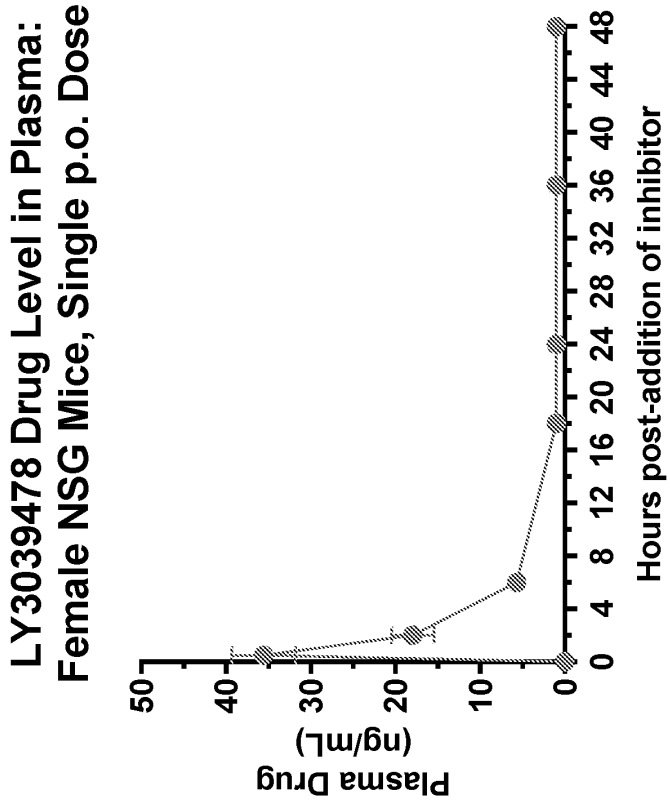

LY3039478 Drug Level in Plasma:
Female NSG Mice, Single p.o. Dose
Plasma Drug (ng/mL)
0
10
20
30
40
50
0 4 8 12 16 20 24 28 32 36 40 44 48
Hours post-addition of inhibitor

FIG. 6

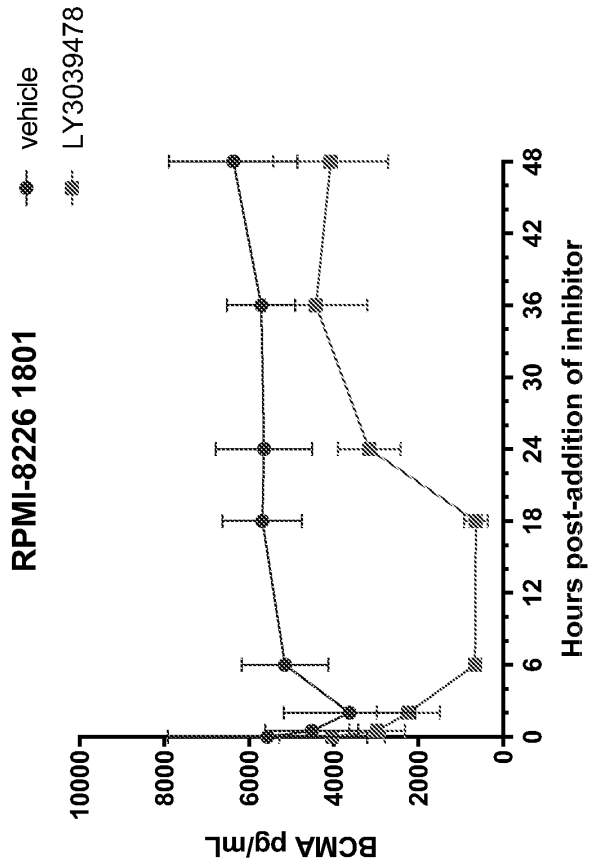

RPMI-8226 1801
vehicle
LY3039478
BCMA pg/mL
10000
8000
6000
4000
2000
0
0
6
12
18
24
30
36
42
48
Hours post-addition of inhibitor

FIG. 7

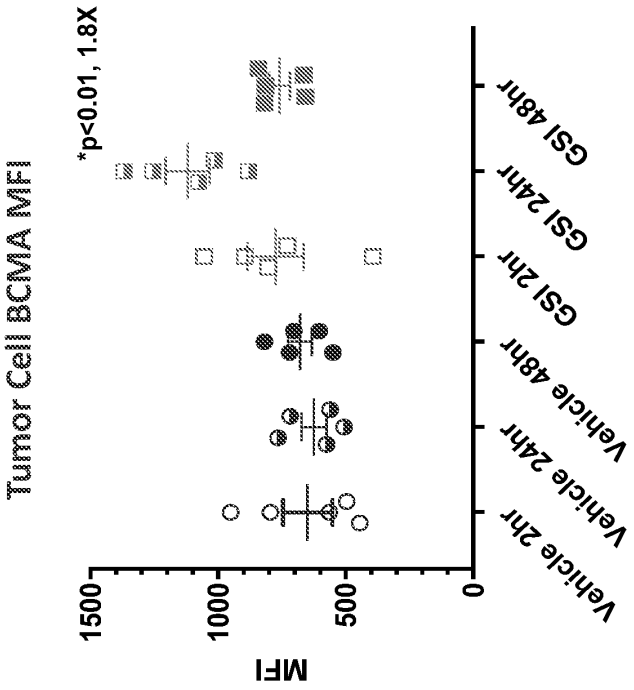

Tumor Cell BCMA MFI
*p<0.01, 1.8X
MFI
1500
1000
500
0
Vehicle 2hr
Vehicle 24hr
Vehicle 48hr
GSI 2hr
GSI 24hr
GSI 48hr

FIG. 8

FIG. 9A

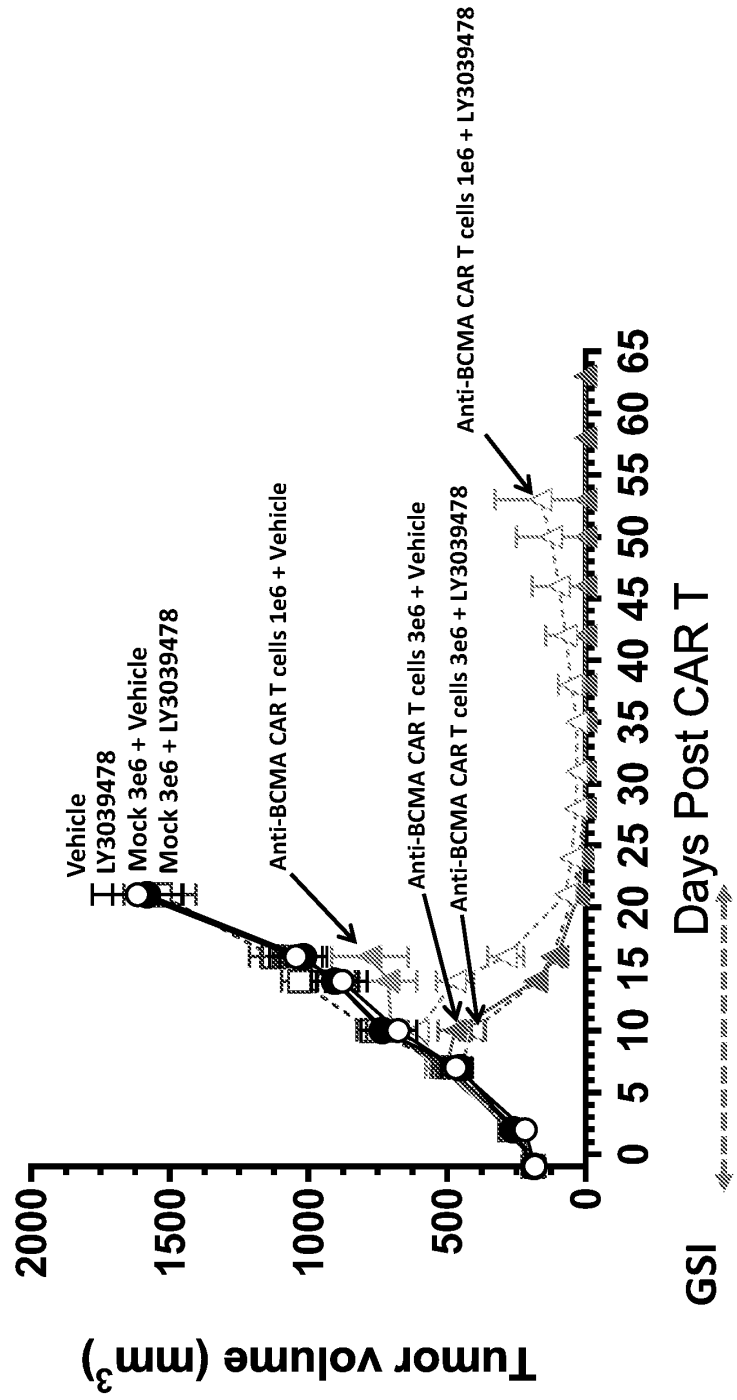

Tumor Volume
Vehicle
LY3039478
Mock 3e6 + Vehicle
Mock 3e6 + LY3039478
Anti-BCMA CAR T cells 1e6 + Vehicle
Anti-BCMA CAR T cells 3e6 + Vehicle
Anti-BCMA CAR T cells 3e6 + LY3039478
Anti-BCMA CAR T cells 1e6 + LY3039478
Tumor volume (mm3)
2000
1500
1000
500
0
0 5 10 15 20 25 30 35 40 45 50 55 60 65
Days Post CAR T
GSI

FIG. 9B

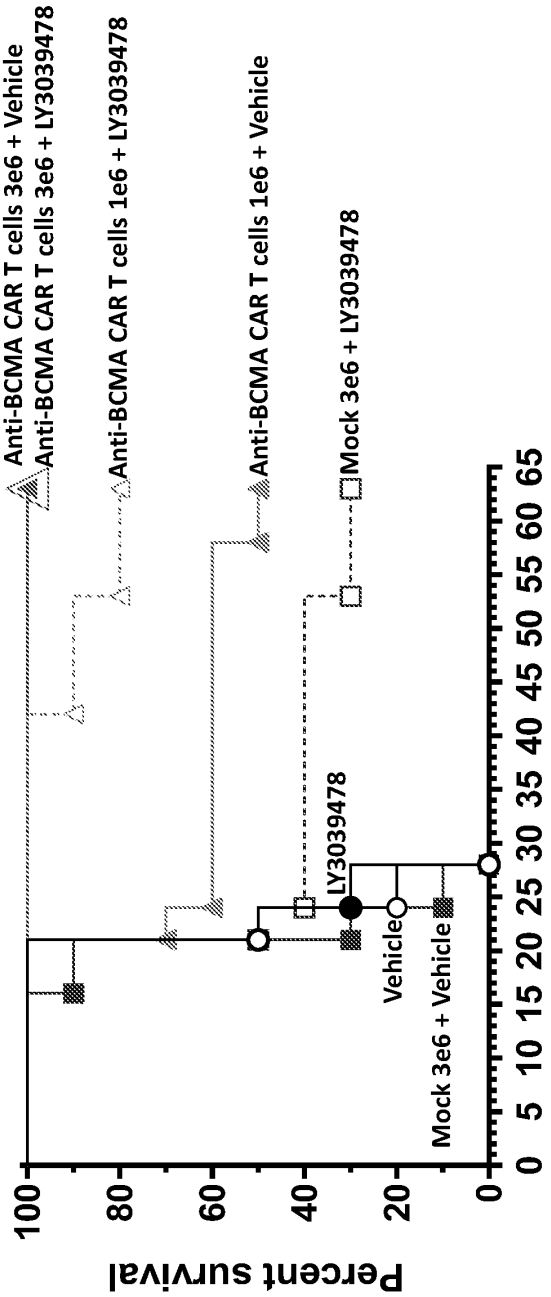

Anti-BCMA CAR T cells 3e6 + Vehicle
Anti-BCMA CAR T cells 3e6 + LY3039478
Anti-BCMA CAR T cells 1e6 + LY3039478
Anti-BCMA CAR T cells 1e6 + Vehicle
Mock 3e6 + LY3039478
LY3039478
Vehicle
Mock 3e6 + Vehicle
Percent survival
100
80
60
40
20
0
0 5 10 15 20 25 30 35 40 45 50 55 60 65
Days Post CAR T

FIG. 10A

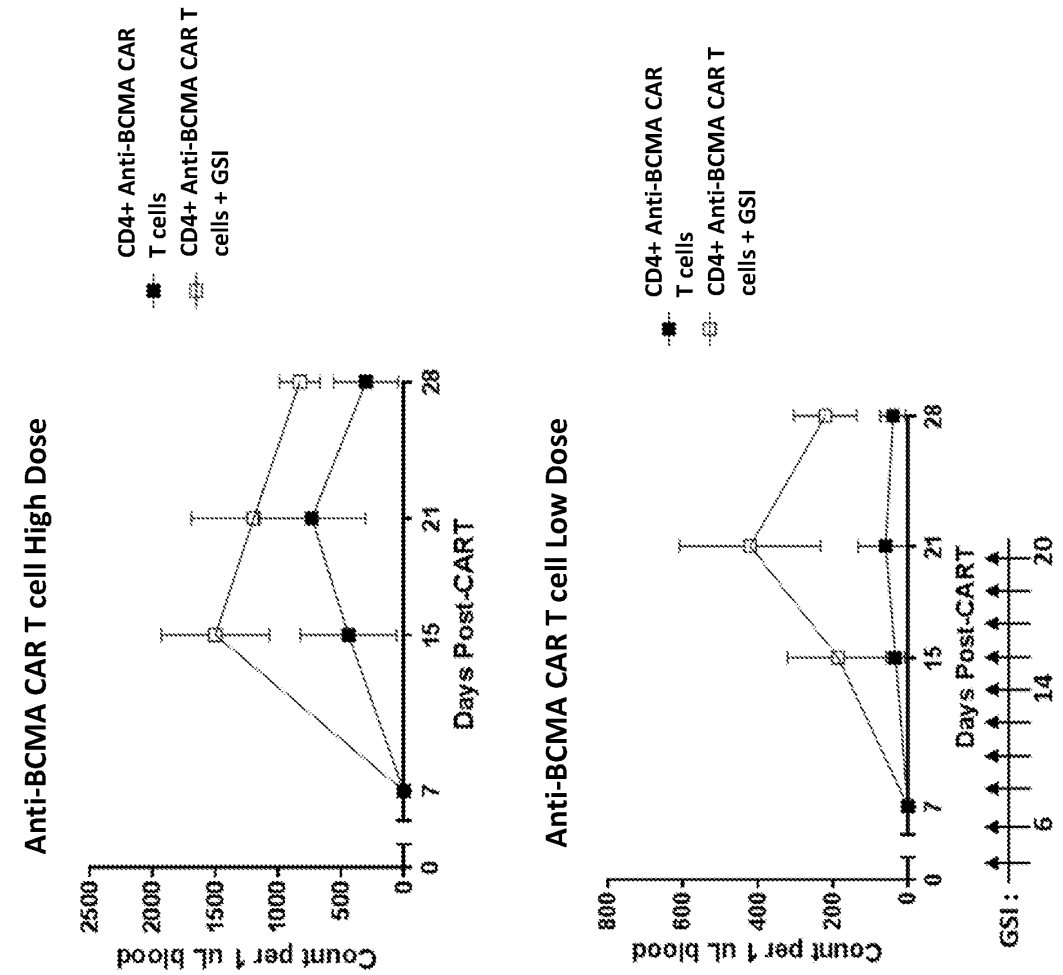

Anti-BCMA CAR T cell High Dose
CD4+ Anti-BCMA CAR T cells
CD4+ Anti-BCMA CAR T cells + GSI
Count per 1 uL blood
2500
2000
1500
1000
500
0
0
7
15
21
28
Days Post-CART
Anti-BCMA CAR T cell Low Dose
CD4+ Anti-BCMA CAR T cells
CD4+ Anti-BCMA CAR T cells + GSI
Count per 1 uL blood
800
600
400
200
0
0
7
15
21
28
Days Post-CART
GSI :
6
14
20

FIG. 10B

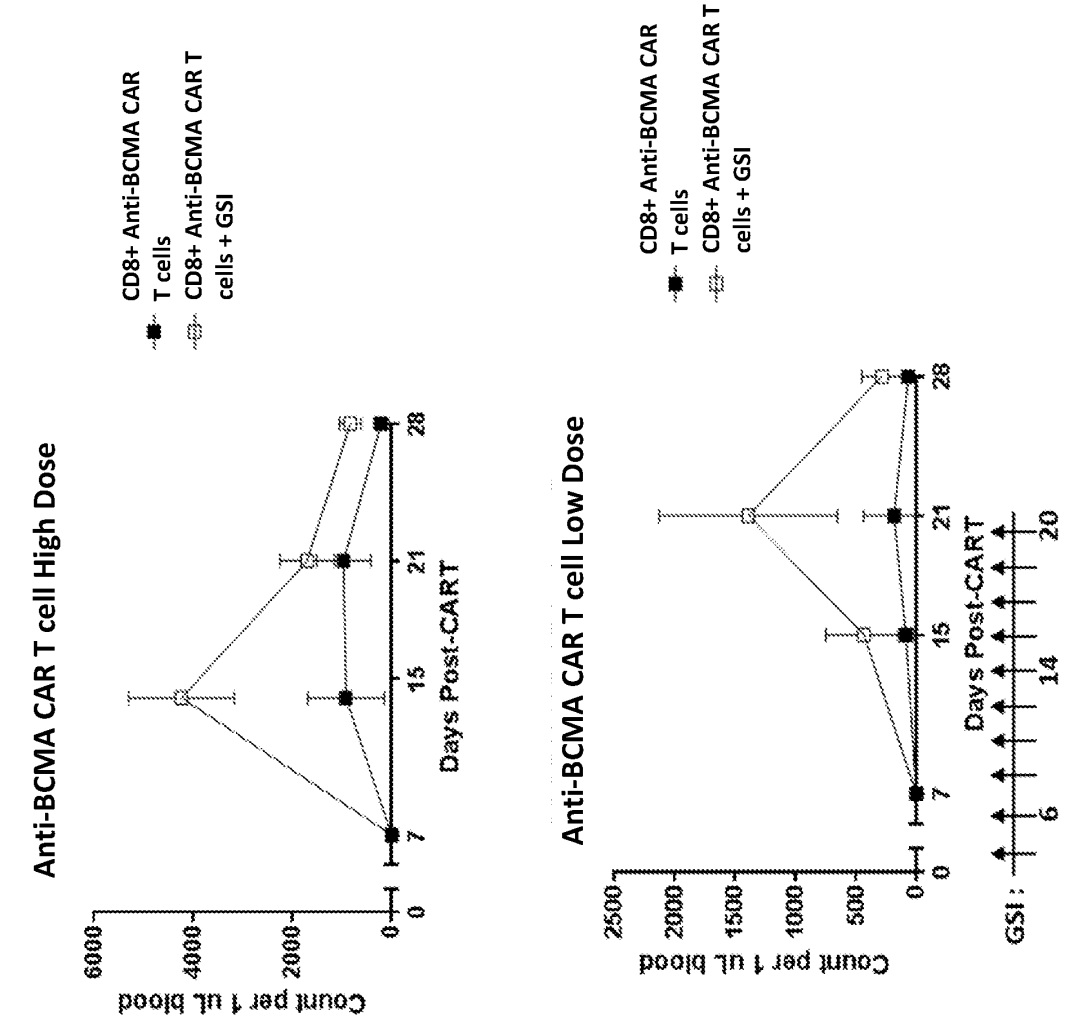

Anti-BCMA CAR T cell High Dose
CD8+ Anti-BCMA CAR T cells
CD8+ Anti-BCMA CAR T cells + GSI
Count per 1 uL blood
6000
4000
2000
0
0
7
15
21
28
Days Post-CART
Anti-BCMA CAR T cell Low Dose
CD8+ Anti-BCMA CAR T cells
CD8+ Anti-BCMA CAR T cells + GSI
Count per 1 uL blood
2500
2000
1500
1000
500
0
0
7
15
21
28
Days Post-CART
GSI :
6
14
20

FIG. 11

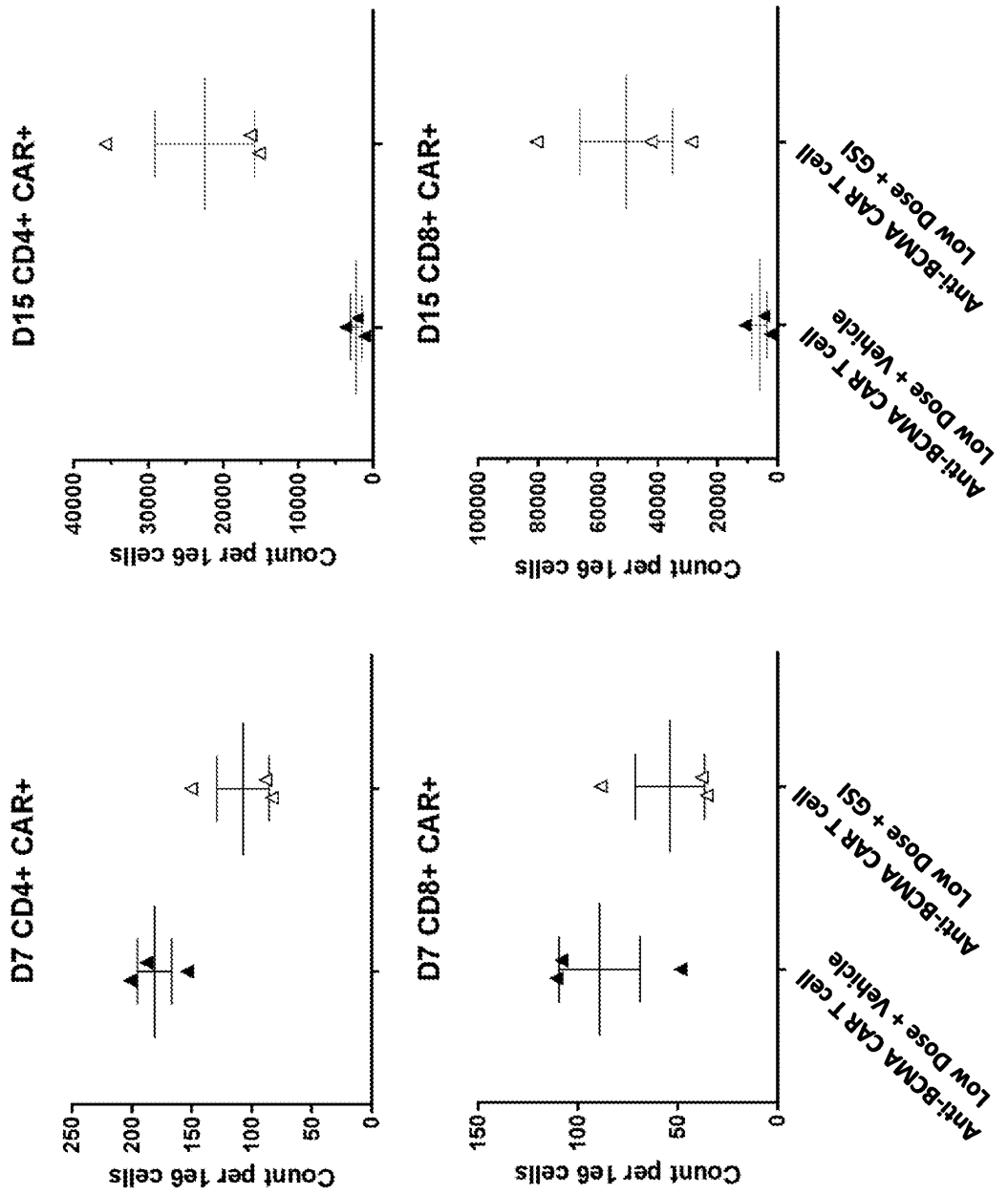

D7 CD4+ CAR+
Count per 1e6 cells
250
200
150
100
50
0
D7 CD8+ CAR+
Count per 1e6 cells
150
100
50
0
D15 CD4+ CAR+
Count per 1e6 cells
40000
30000
20000
10000
0
D15 CD8+ CAR+
Count per 1e6 cells
100000
80000
60000
40000
20000
0
Anti-BCMA CAR T cell
Low Dose + Vehicle
Anti-BCMA CAR T cell
Low Dose + GSI

FIG. 12A

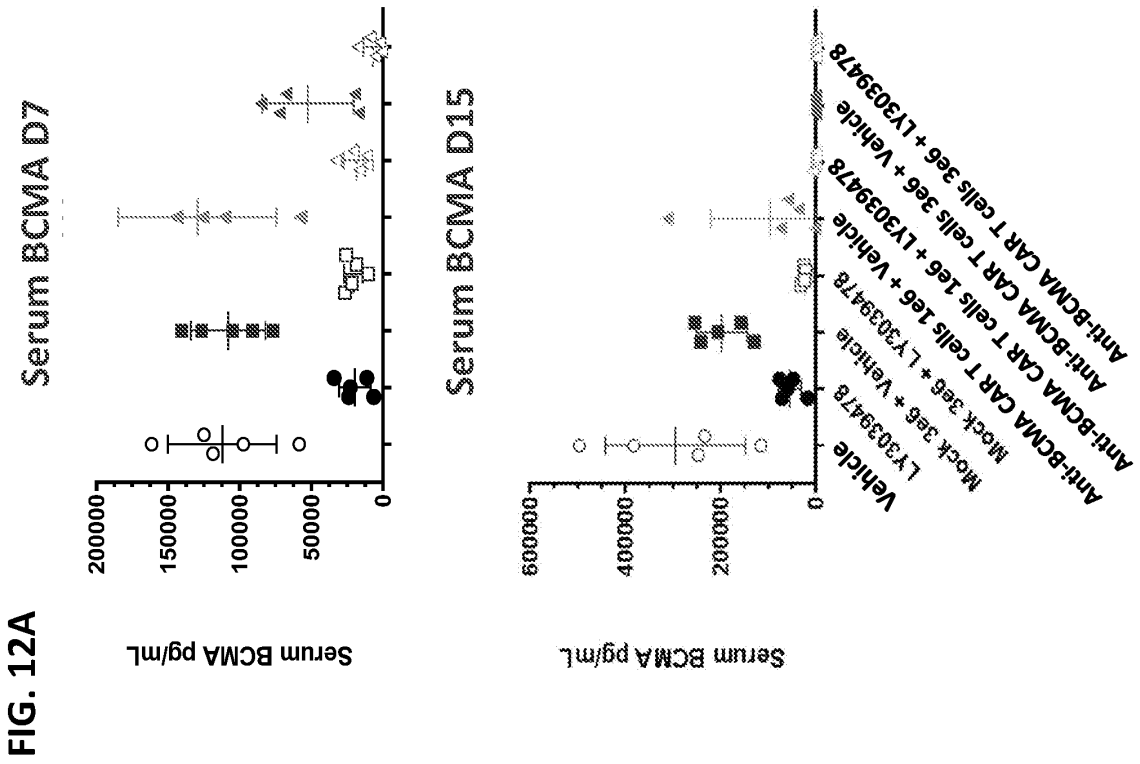


FIG. 12B

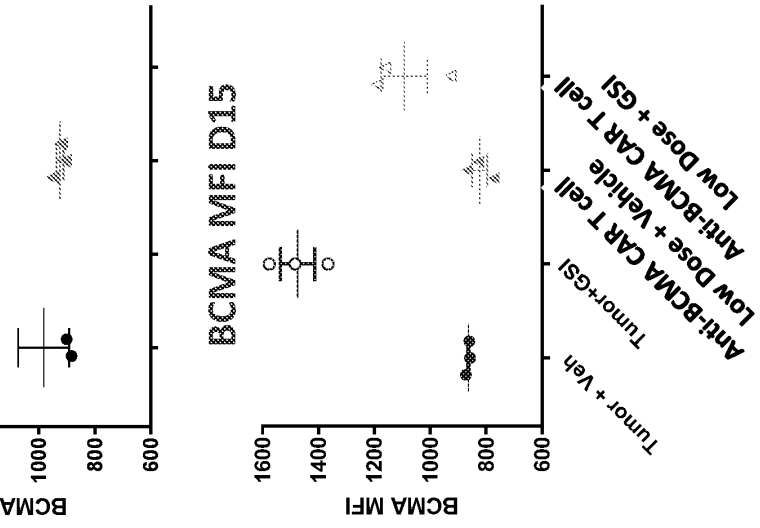
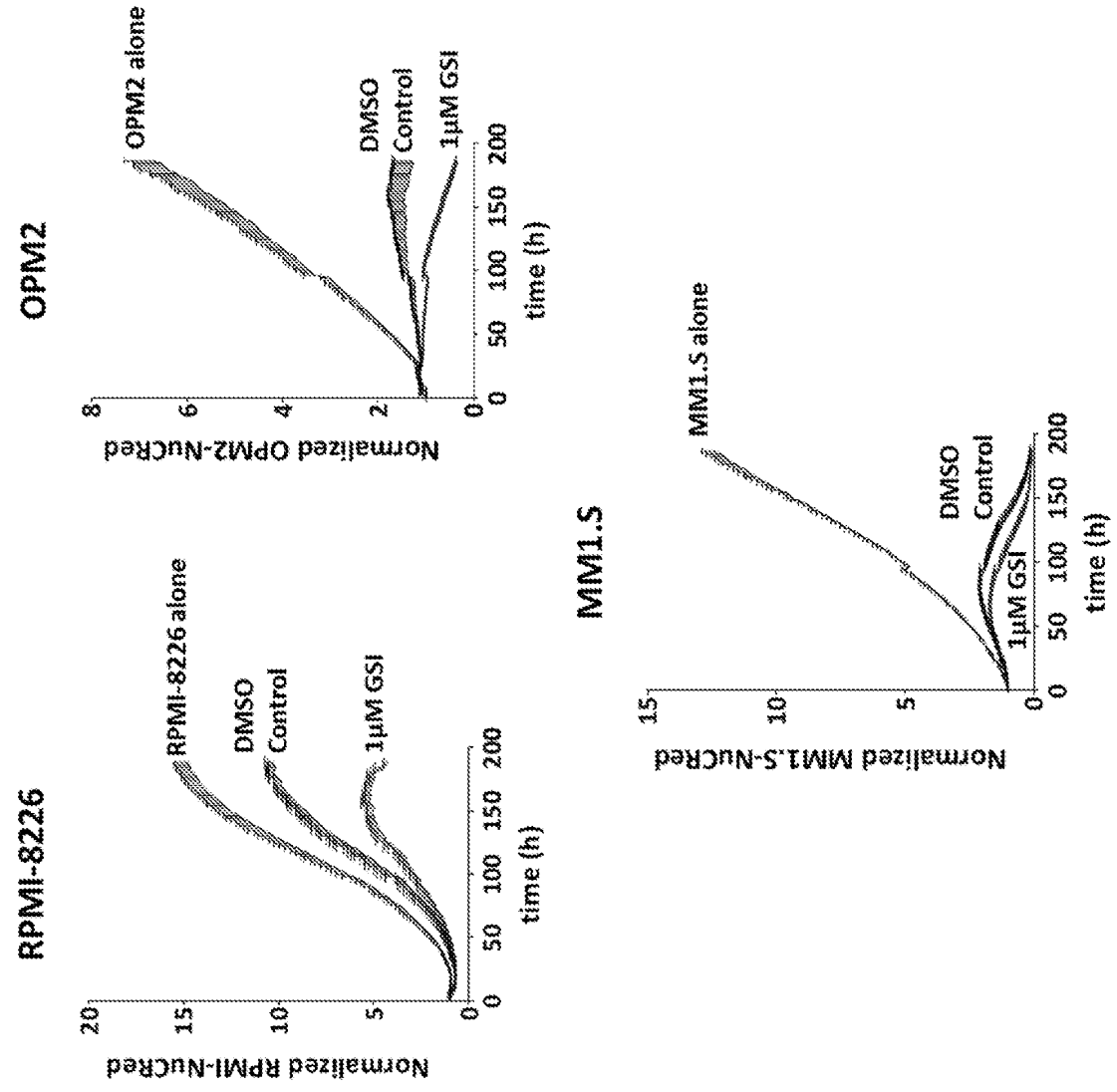


FIG. 13A


RPMI-8226
Normalized RPMI-NucRed
RPMI-8226 alone
DMSO
Control
1μM GSI
time (h)
OPM2
Normalized OPM2-NucRed
OPM2 alone
DMSO
Control
1μM GSI
time (h)
MM1.S
Normalized MM1.S-NucRed
MM1.S alone
DMSO
Control
1μM GSI
time (h)

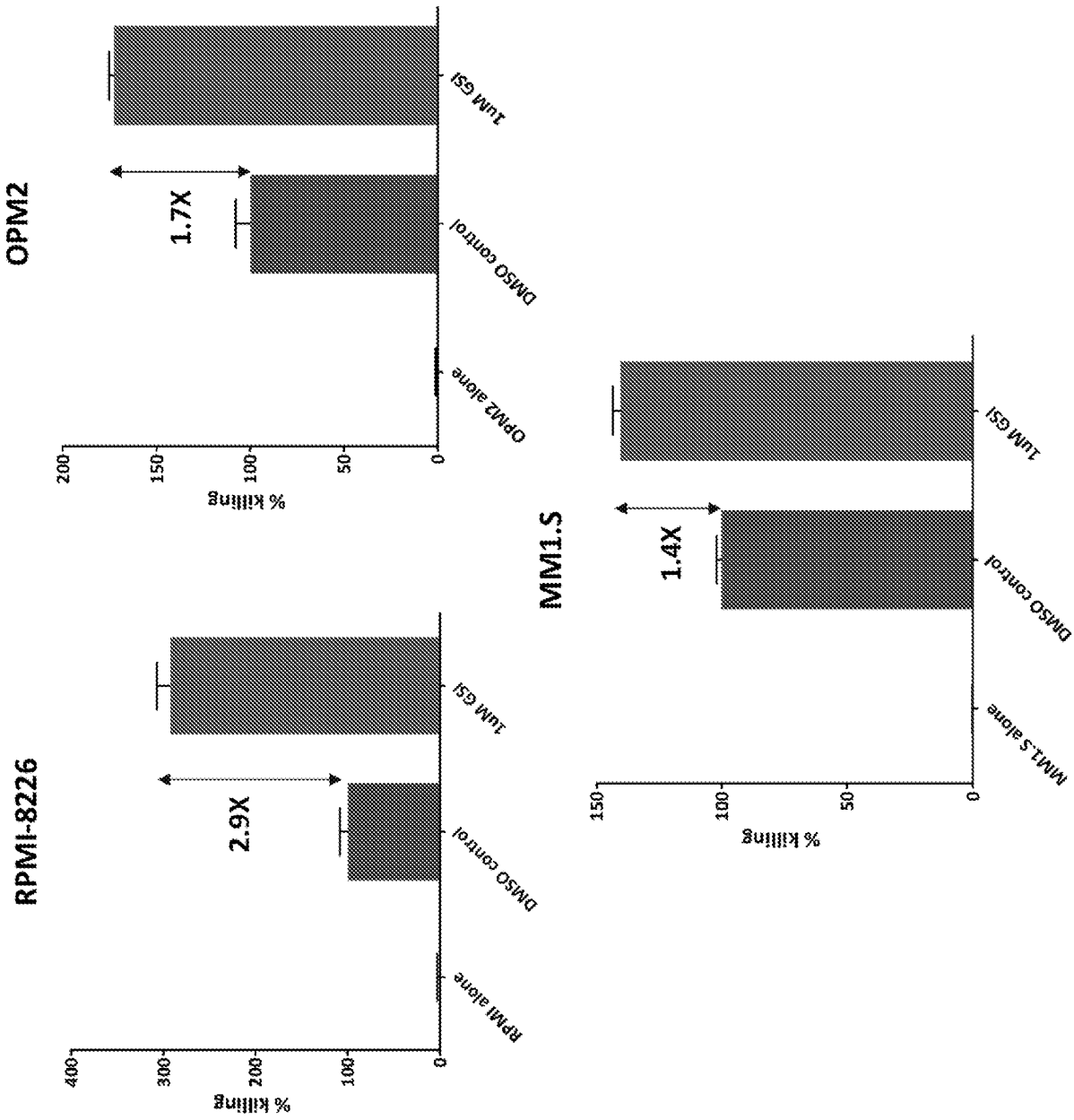

RPMI-8226
% killing
0
100
200
300
400
RPMI alone
DMSO control
2.9X
1uM GSI
OPM2
% killing
0
50
100
150
200
OPM2 alone
DMSO control
1.7X
1uM GSI
MM1.S
% killing
0
50
100
150
MM1.S alone
DMSO control
1.4X
1uM GSI

FIG. 13B

FIG. 13C

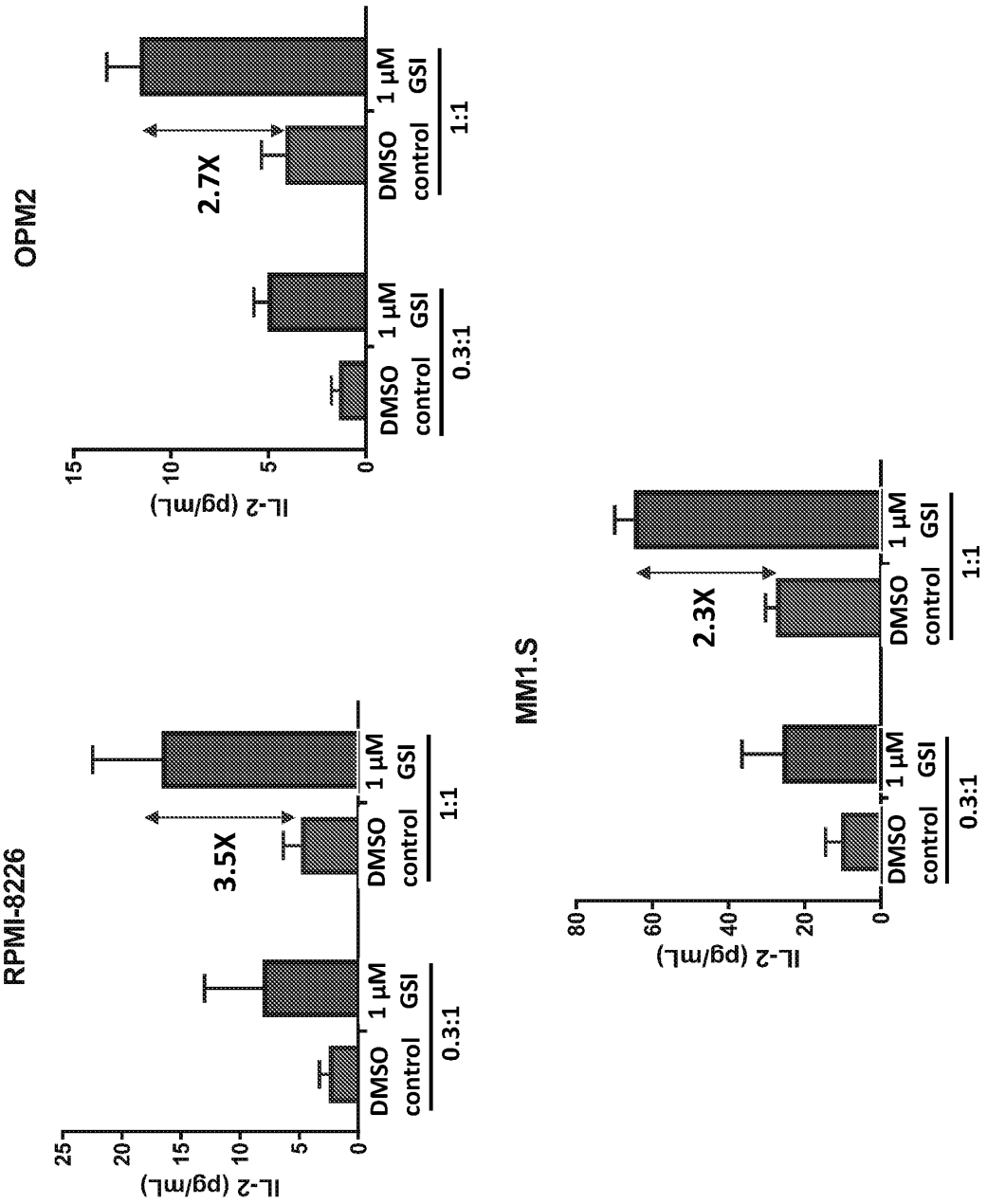

OPM2
IL-2 (pg/mL)
0
5
10
15
2.7X
DMSO
control
1 μM
GSI
0.3:1
1:1
RPMI-8226
IL-2 (pg/mL)
0
5
10
15
20
25
3.5X
DMSO
control
1 μM
GSI
0.3:1
1:1
MM1.S
IL-2 (pg/mL)
0
20
40
60
80
2.3X
DMSO
control
1 μM
GSI
0.3:1
1:1

FIG. 14

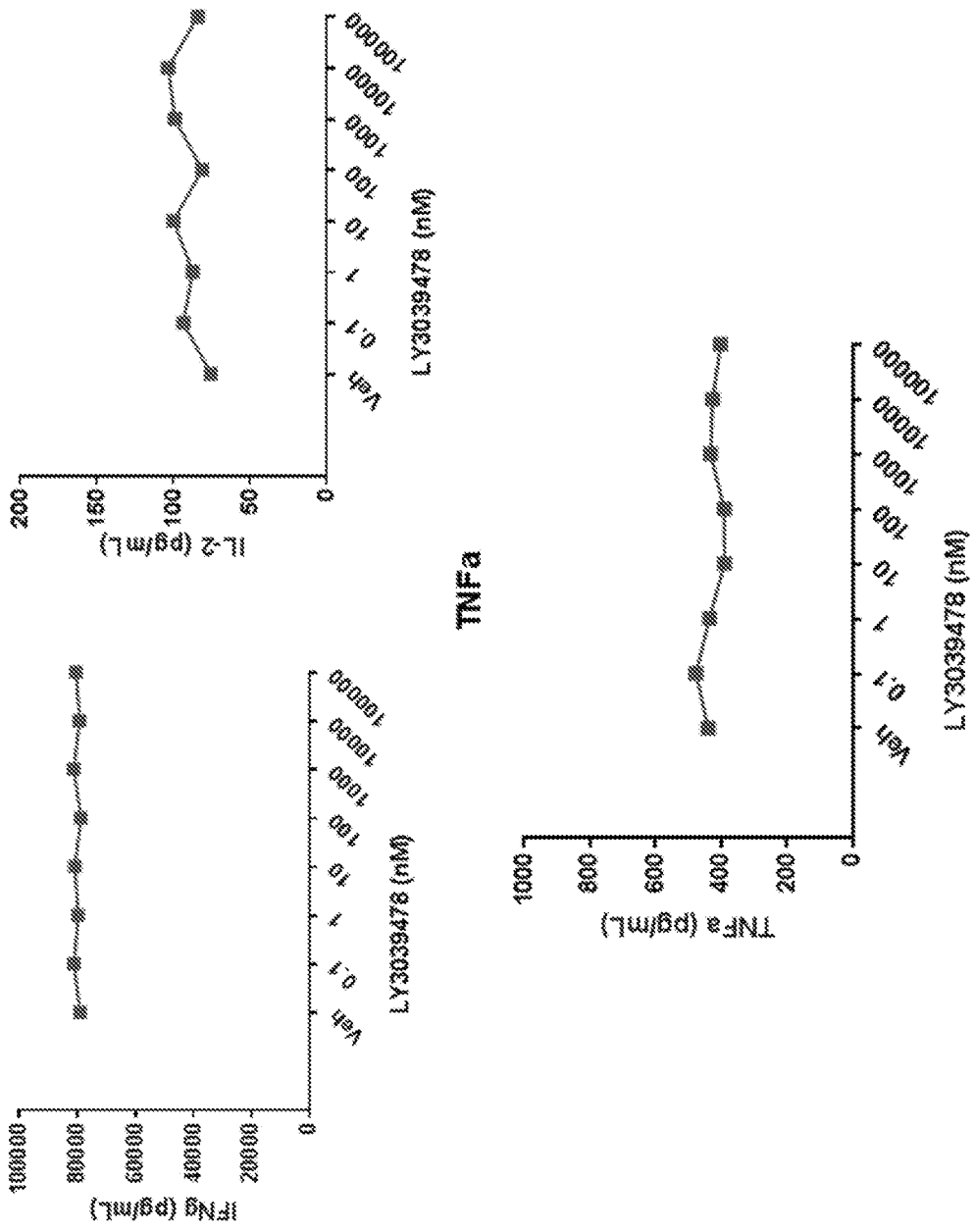

IL-2
IL-2 (pg/mL)
200
150
100
50
0
Veh
0.1
1
10
100
1000
10000
100000
LY3039478 (nM)
IFNg
IFNg (pg/mL)
100000
80000
60000
40000
20000
0
Veh
0.1
1
10
100
1000
10000
100000
LY3039478 (nM)
TNFa
TNFa (pg/mL)
1000
800
600
400
200
0
Veh
0.1
1
10
100
1000
10000
100000
LY3039478 (nM)

FIG. 15B

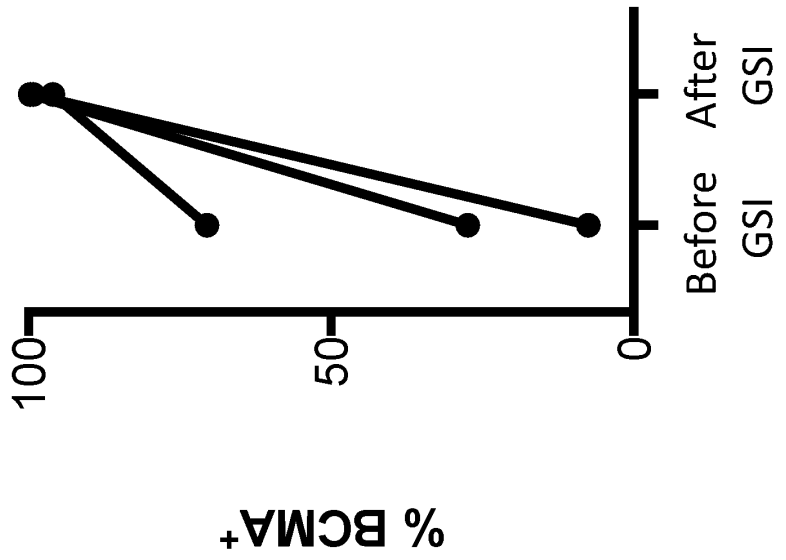


FIG. 15A

