FIG. 1A

Anti-CXCR4 Fab BMS-936564/F7/MDX-1338 VH

V segment: 3-48
D segment: 4-23
J segment: JH6b

```
    Q   V   Q   L   V   Q   S   G   G   G   L   V   Q   P   G   G   S   L
  1 CAG GTG CAG CTG GTG CAG TCT GGG GGA GGC TTG GTA CAG CCT GGG GGG TCC CTG

                                                        CDR1
                                                    ~~~~~~~~~~~~~~~~~~~
    R   L   S   C   A   A   A   G   F   T   F   S   S   Y   S   M   N   W
 55 AGA CTC TCC TGT GCA GCC GCT GGA TTC ACC TTC AGT AGC TAT AGC ATG AAC TGG

                                                            CDR2
                                                        ~~~~~~~~~~~~~~~~~~~
    V   R   Q   A   P   G   K   G   L   E   W   V   S   Y   I   S   S   R
109 GTC CGC CAG GCT CCA GGG AAG GGG CTG GAG TGG GTT TCA TAC ATT AGT AGT AGA

                    CDR2
    ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
    S   R   T   I   Y   Y   A   D   S   V   K   G   R   F   T   I   S   R
163 AGT AGA ACC ATA TAC TAC GCA GAC TCT GTG AAG GGC CGA TTC ACC ATC TCC AGA


    D   N   A   K   N   S   L   Y   L   Q   M   N   S   L   R   D   E   D
217 GAC AAT GCC AAG AAC TCA CTG TAT CTG CAA ATG AAC AGC CTG AGA GAC GAG GAC

                                            CDR3
                                    ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
    T   A   V   Y   Y   C   A   R   D   Y   G   G   Q   P   P   Y   Y   Y
271 ACG GCT GTG TAT TAC TGT GCG AGA GAT TAC GGT GGT CAA CCC CCT TAC TAC TAC

        CDR3
    ~~~~~~~~~~~~~~~~~~~~~~~~
    Y   Y   G   M   D   V   W   G   Q   G   T   T   V   T   V   S   S
325 TAC TAC GGT ATG GAC GTC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA
```

FIG. 1B

Anti-CXCR4 Fab BMS-936564/F7/MDX-1338 VK

V segment: L15
J segment: JK1

```
   A   I   R   M   T   Q   S   P   S   S   L   S   A   S   V   G   D   R
1 GCC ATC CGG ATG ACC CAG TCT CCA TCC TCA CTG TCT GCA TCT GTA GGA GAC AGA

                                CDR1
                        ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
   V   T   I   T   C   R   A   S   Q   G   I   S   S   W   L   A   W   Y
55 GTC ACC ATC ACT TGT CGG GCG AGT CAG GGT ATT AGC AGC TGG TTA GCC TGG TAT

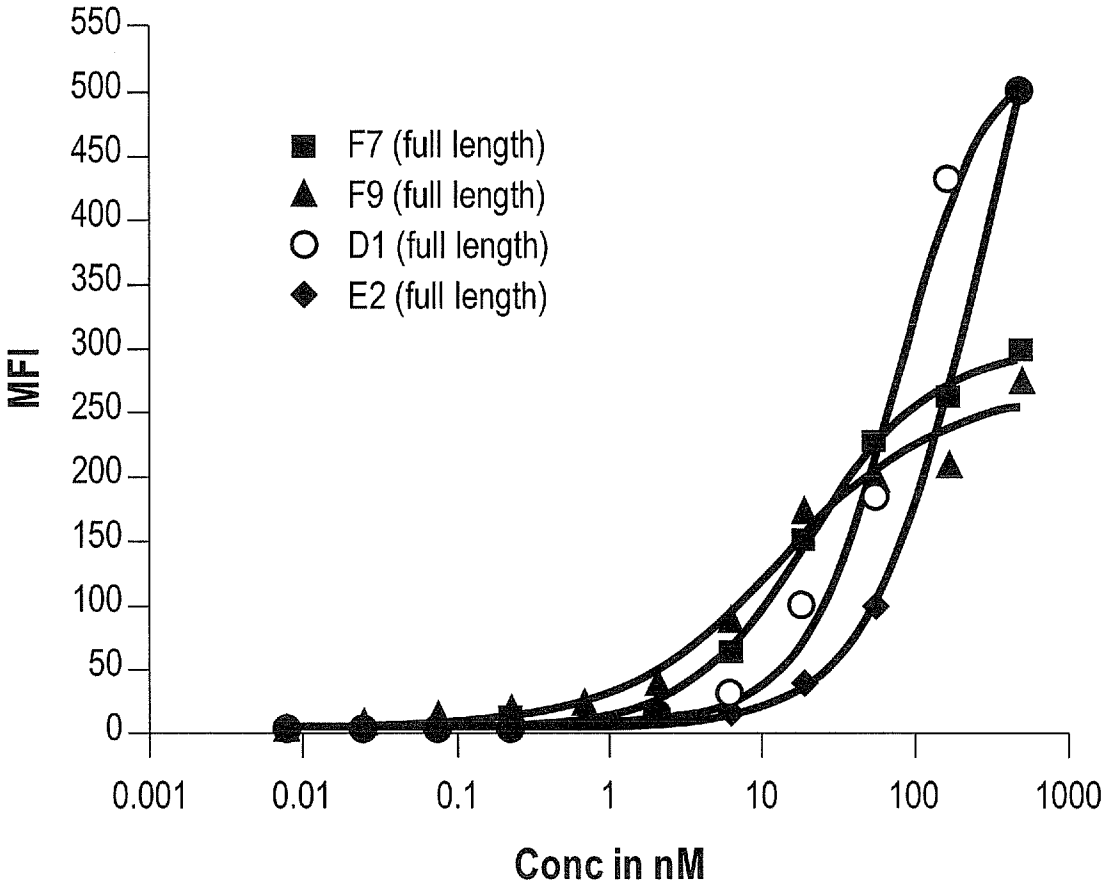
                                                        CDR2
                                                ~~~~~~~~~~~~~~~~~~~~
   Q   Q   K   P   E   K   A   P   K   S   L   I   Y   A   A   S   S   L
109 CAG CAG AAA CCA GAG AAA GCC CCT AAG TCC CTG ATC TAT GCT GCA TCC AGT TTG

    CDR2
    ~~~~~~~
   Q   S   G   V   P   S   R   F   S   G   S   G   S   G   T   D   F   T
163 CAA AGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA TCT GGG ACA GAT TTC ACT

                                                                CDR3
                                                                ~~~~~~~
   L   T   I   S   S   L   Q   P   E   D   F   V   T   Y   Y   C   Q   Q
217 CTC ACC ATC AGC AGC CTG CAG CCT GAA GAT TTT GTA ACT TAT TAC TGC CAA CAG

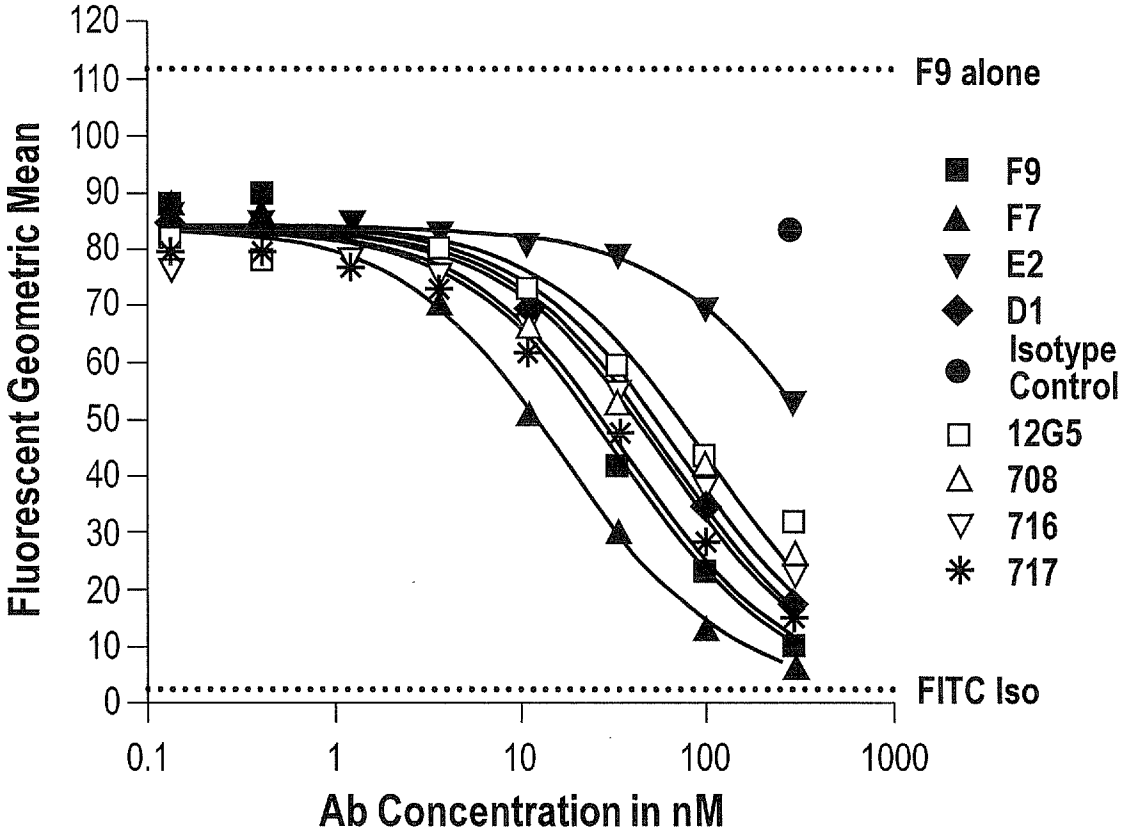
        CDR3
    ~~~~~~~~~~~~~~~~~~~~~~~~~~~
   Y   N   S   Y   P   R   T   F   G   Q   G   T   K   V   E   I   K
271 TAT AAT AGT TAC CCT CGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA
```

FIG. 2



	F7 (full length)	F9 (full length)	D1 (full length)	E2 (full length)
EC50	21.11	13.96	79.87	289.8

FIG. 3



	F9	F7	E2	D1	12G5	708	716	717
EC50	34.39	17.01	468.8	59.17	101.9	76.32	64.68	38.79

FIG. 4A

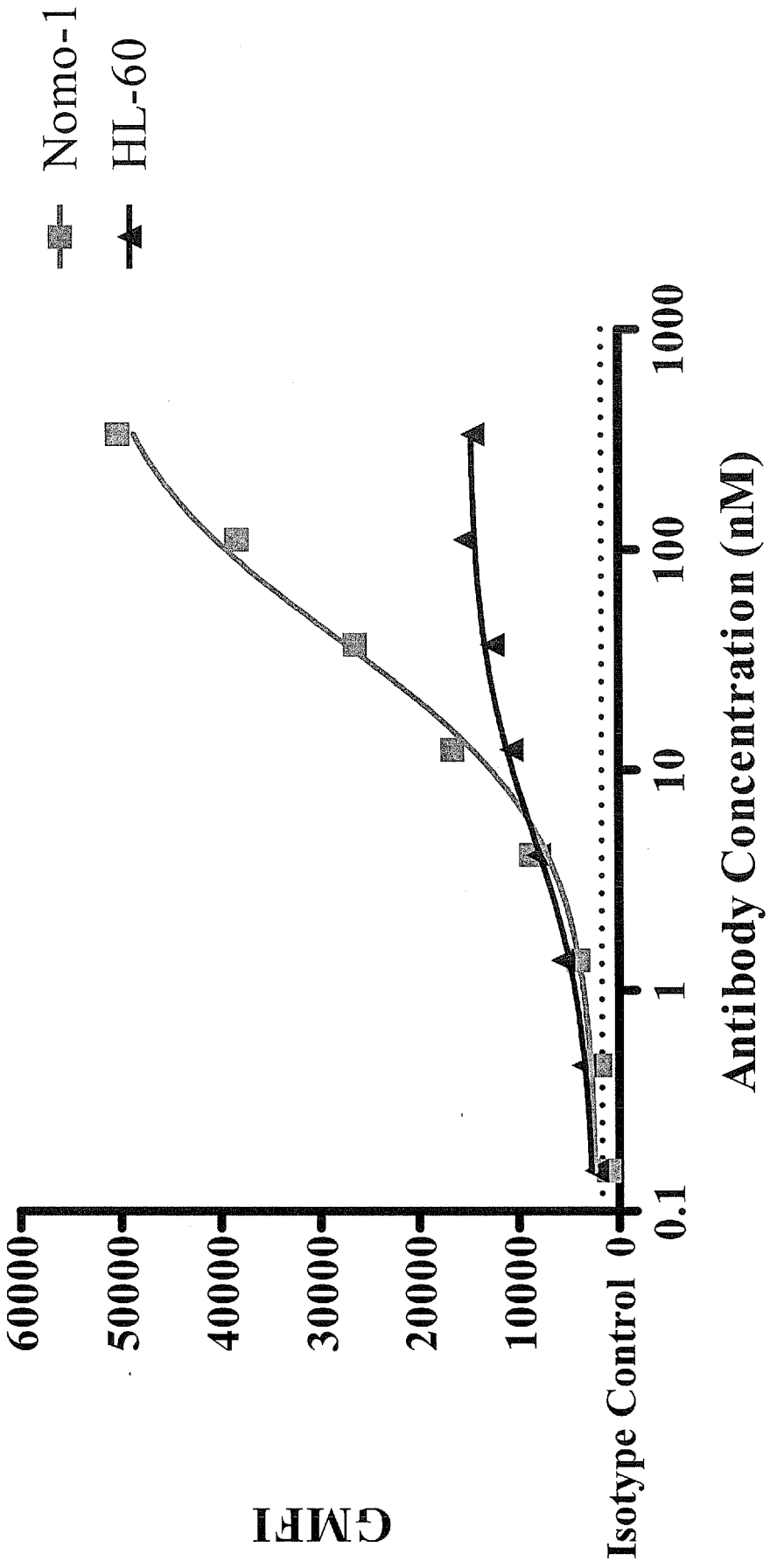

AML Cell Lines
Nomo-1
HL-60
GMFI
60000
50000
40000
30000
20000
10000
0
Isotype Control
0.1
1
10
100
1000
Antibody Concentration (nM)

FIG. 4B

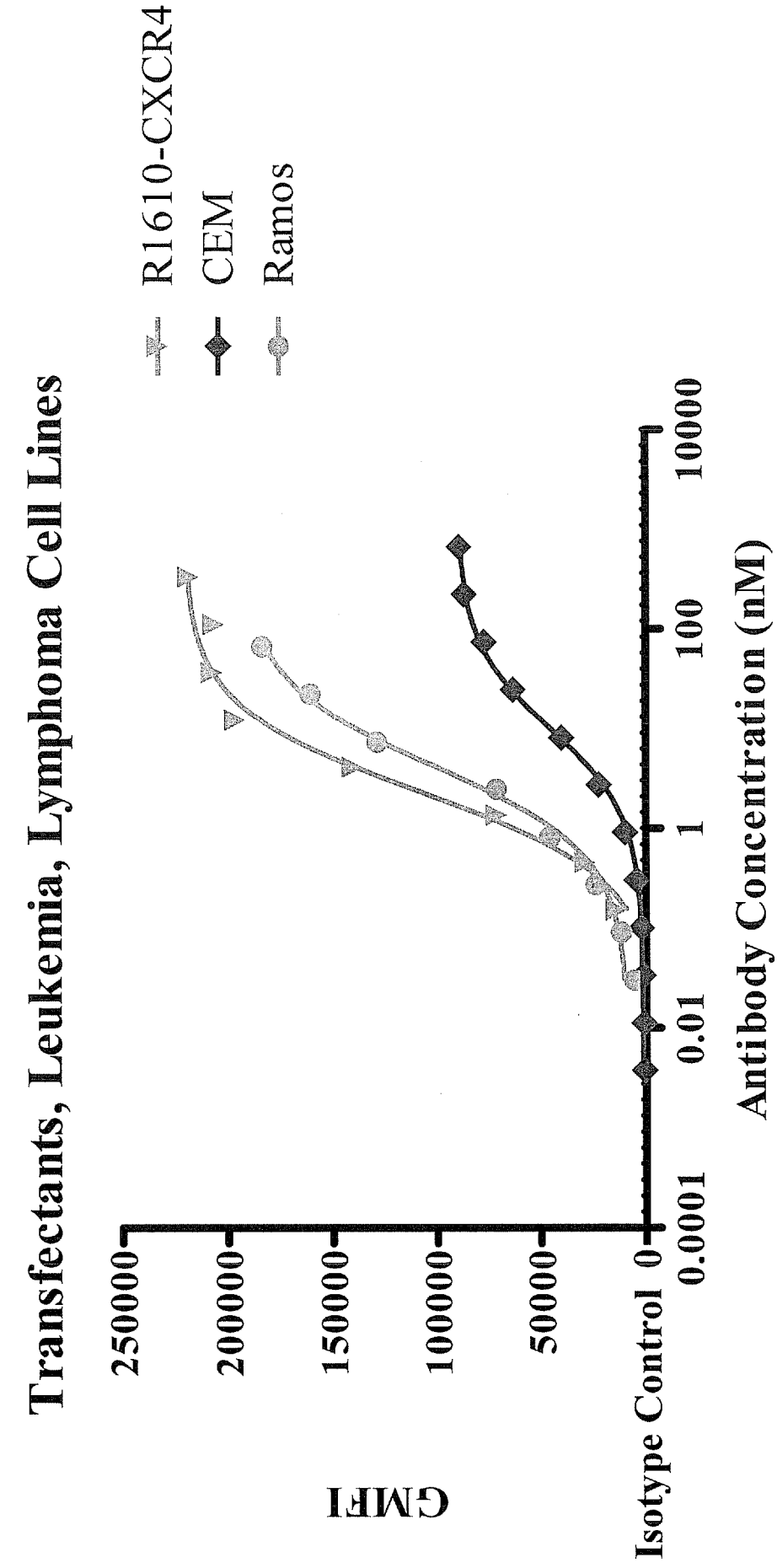

Transfectants, Leukemia, Lymphoma Cell Lines
R1610-CXCR4
CEM
Ramos
GMFI
250000
200000
150000
100000
50000
0
Isotype Control
0.0001
0.01
1
100
10000
Antibody Concentration (nM)

FIG. 4C

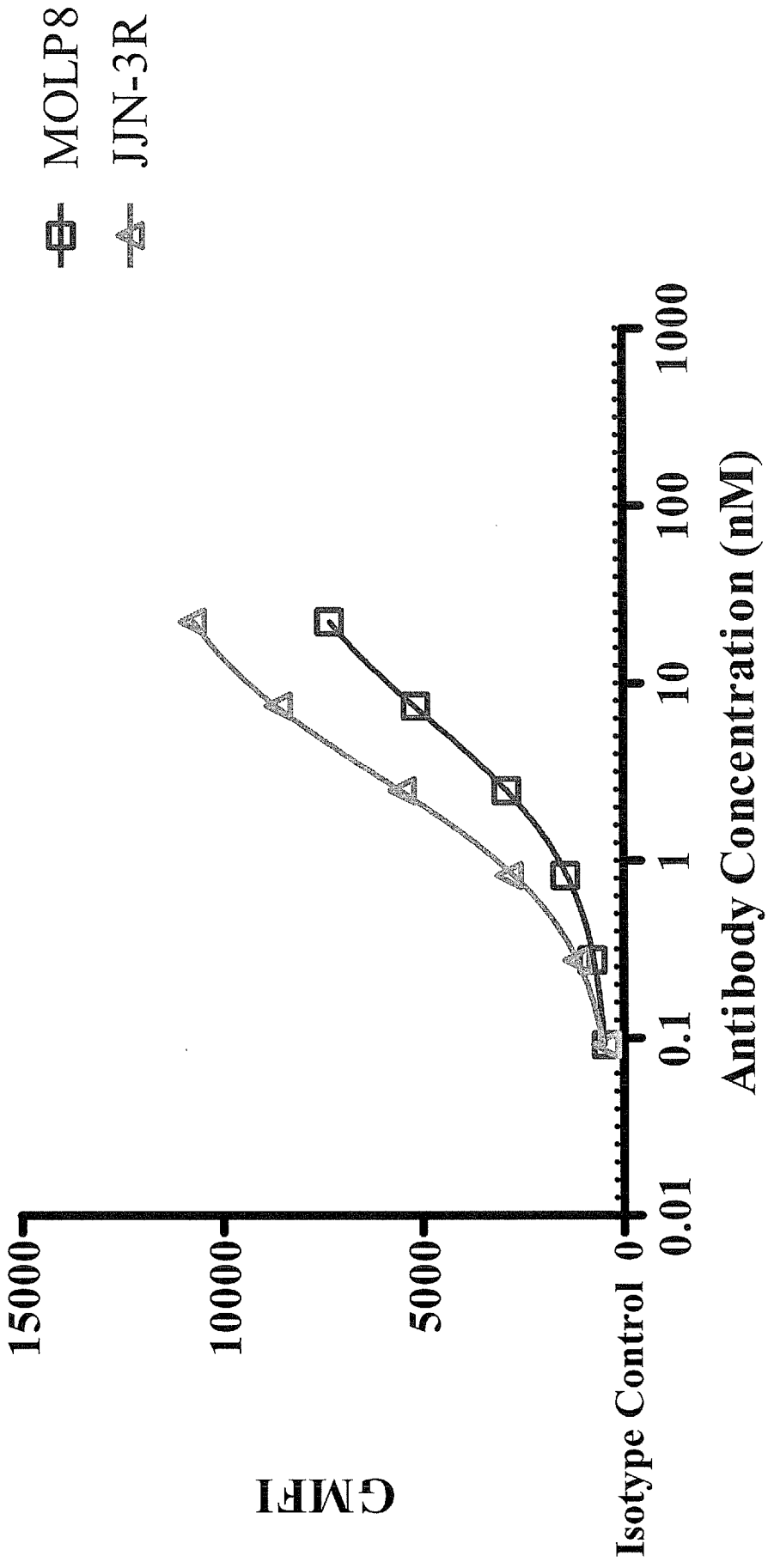

MM Cell Lines
MOLP8
JJN-3R
GMFI
15000
10000
5000
0
Isotype Control
0.01
0.1
1
10
100
1000
Antibody Concentration (nM)

FIG. 4D

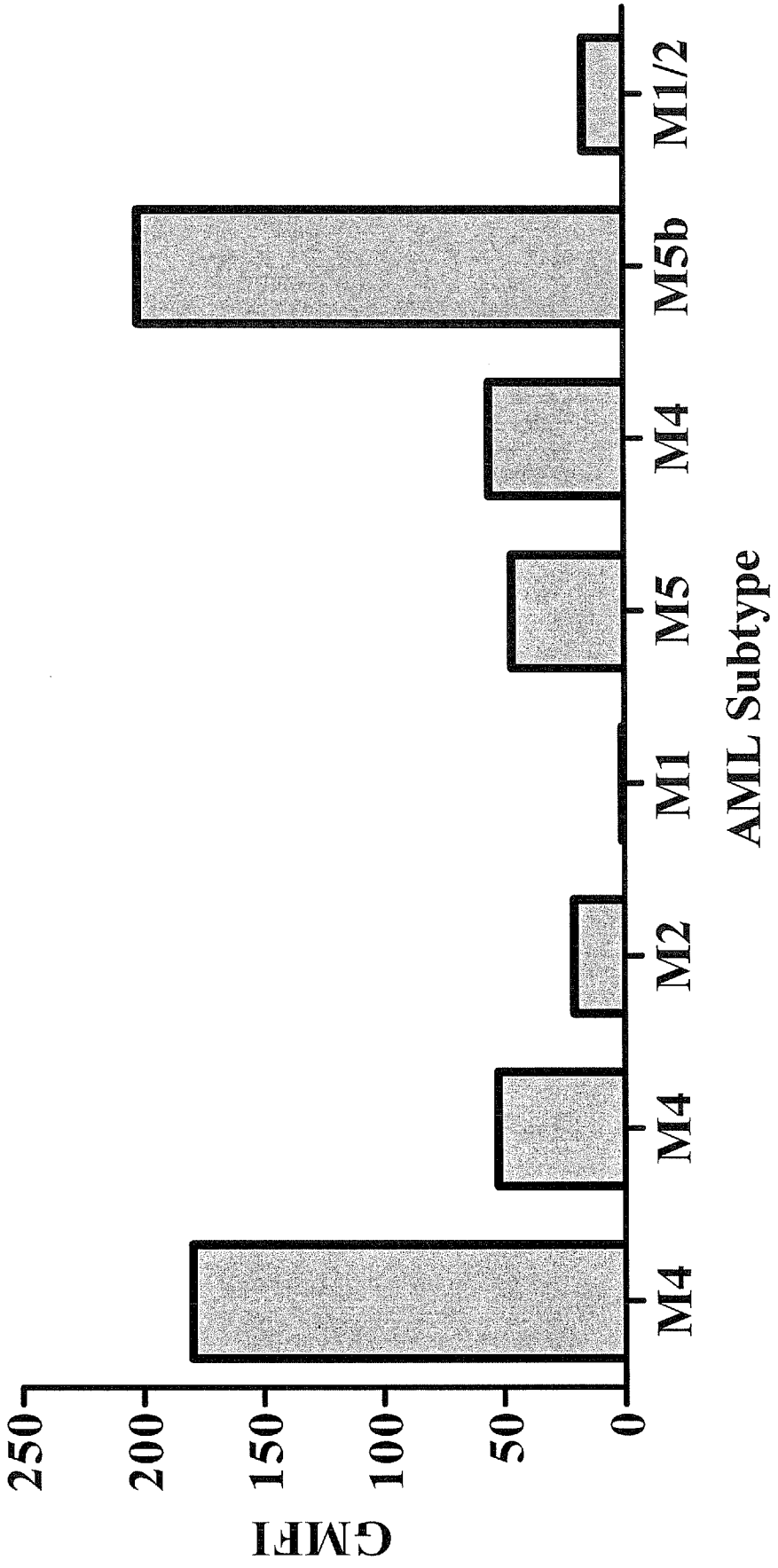
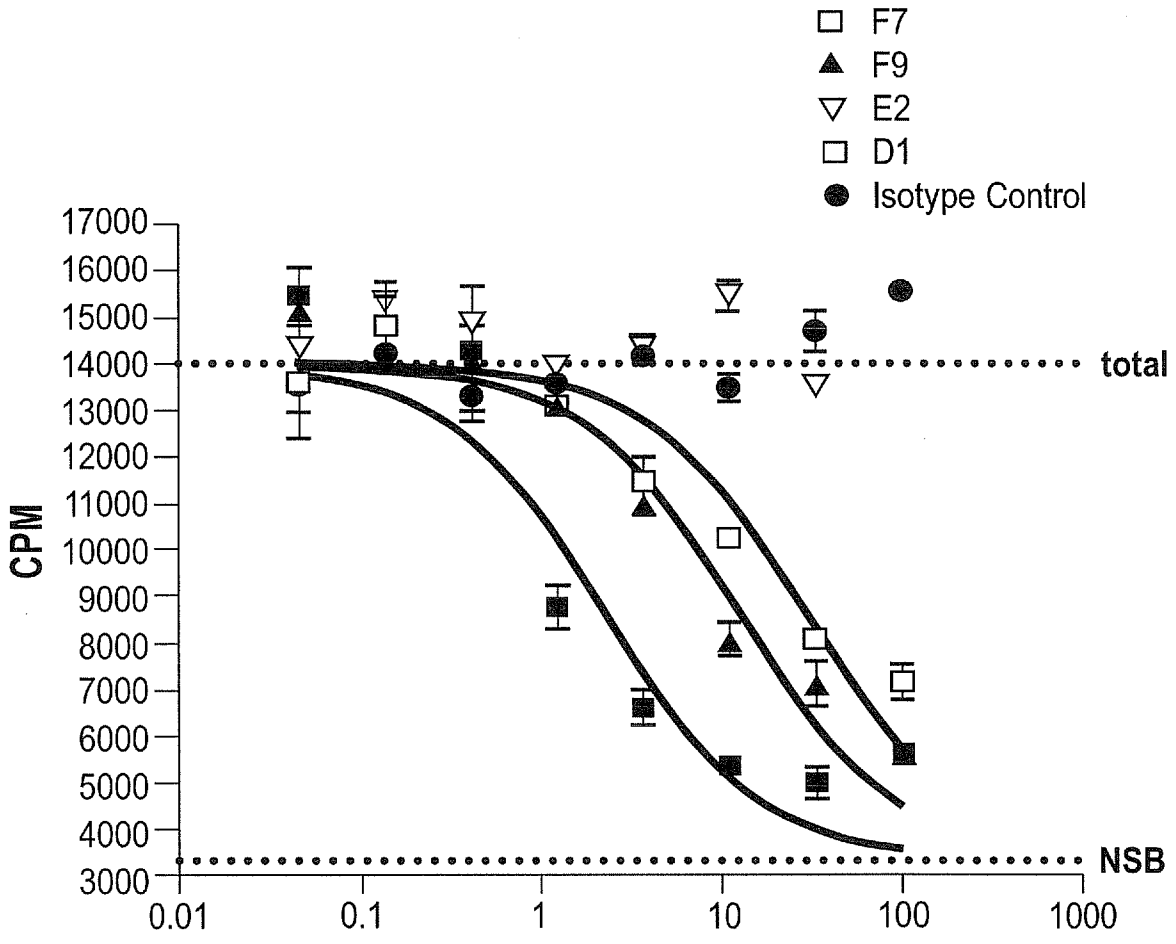

AML Patients PBMC
GMFI
250
200
150
100
50
0
M4
M4
M2
M1
M5
M4
M5b
M1/2
AML Subtype

FIG. 5



	F7	F9	D1
EC50	2.256	12.51	28.60

FIG. 6A

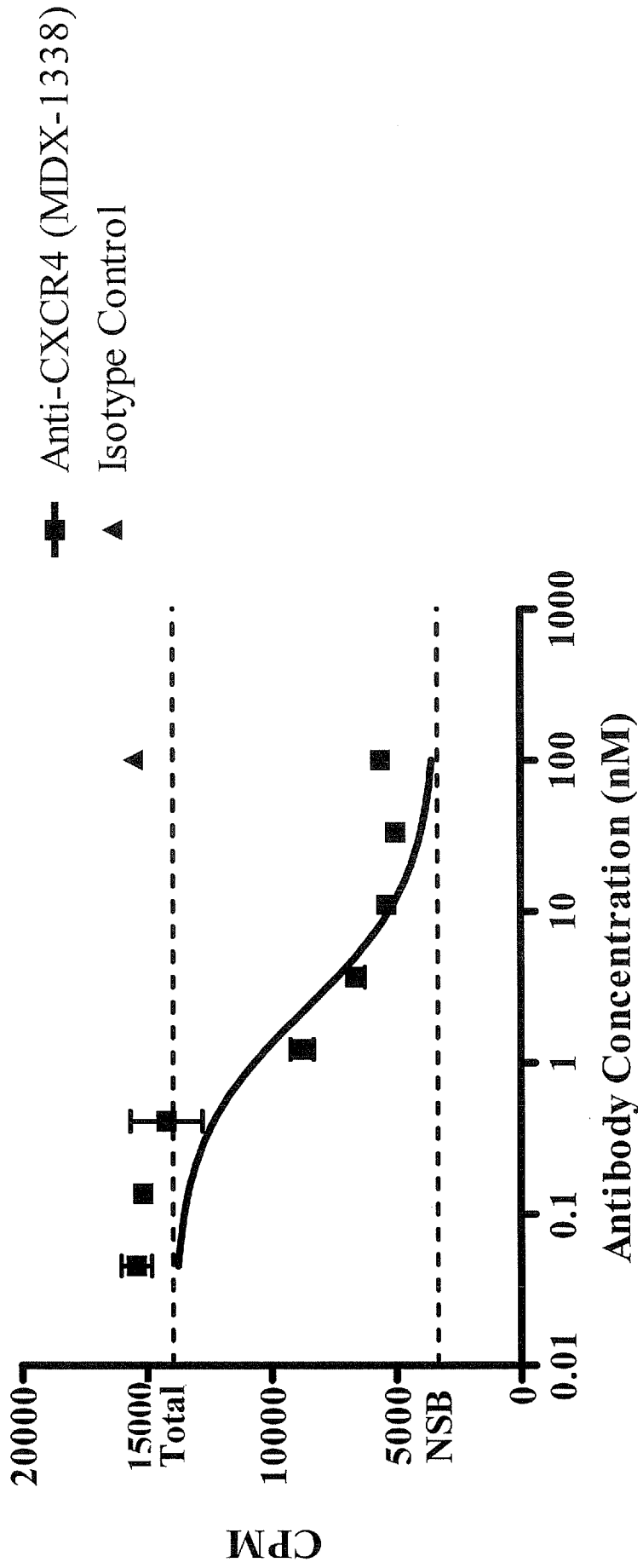

CEM Cells
Anti-CXCR4 (MDX-1338)
Isotype Control
CPM
20000
15000
Total
10000
5000
NSB
0
0.01
0.1
1
10
100
1000
Antibody Concentration (nM)

FIG. 6B

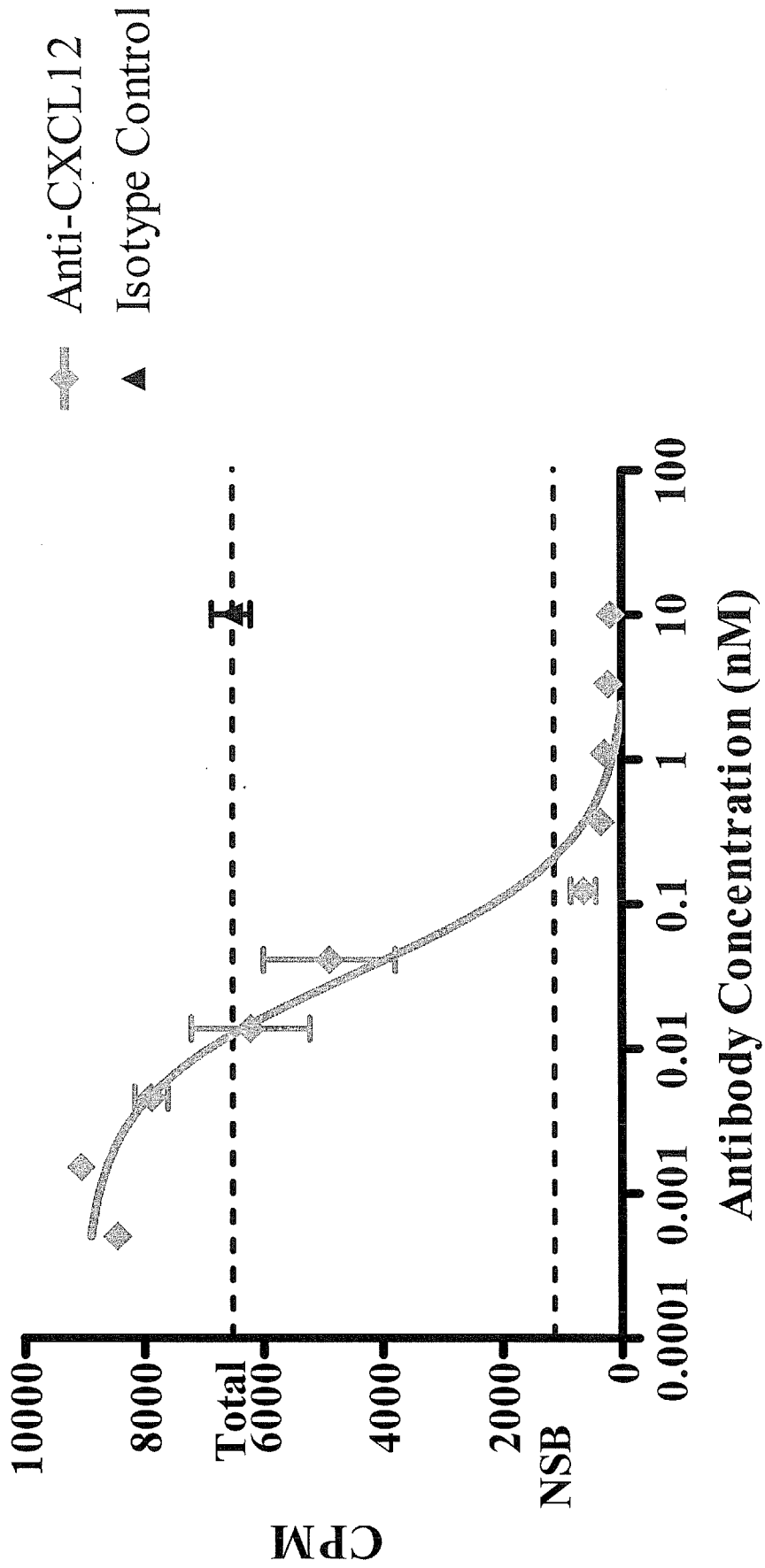

CEM Cells
Anti-CXCL12
Isotype Control
CPM
10000
8000
Total
6000
4000
2000
NSB
0
0.0001
0.001
0.01
0.1
1
10
100
Antibody Concentration (nM)

FIG. 6C

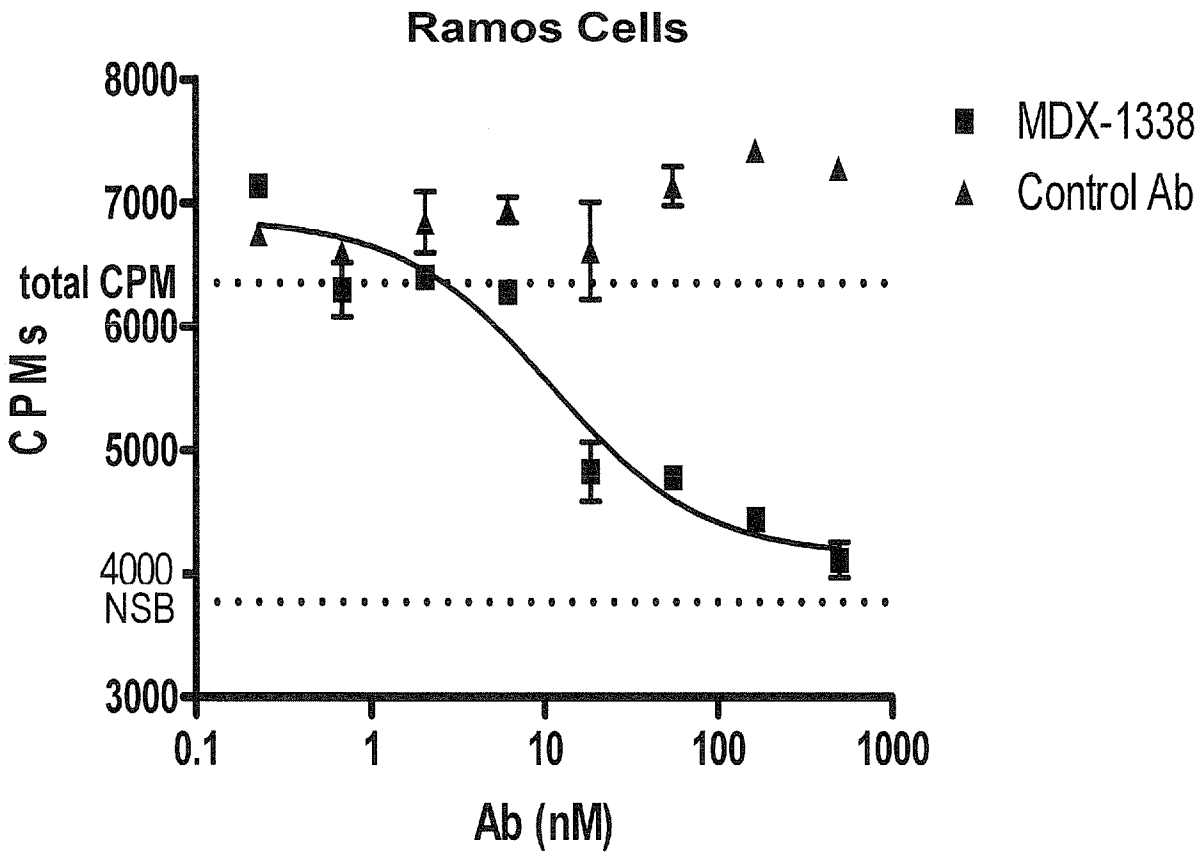
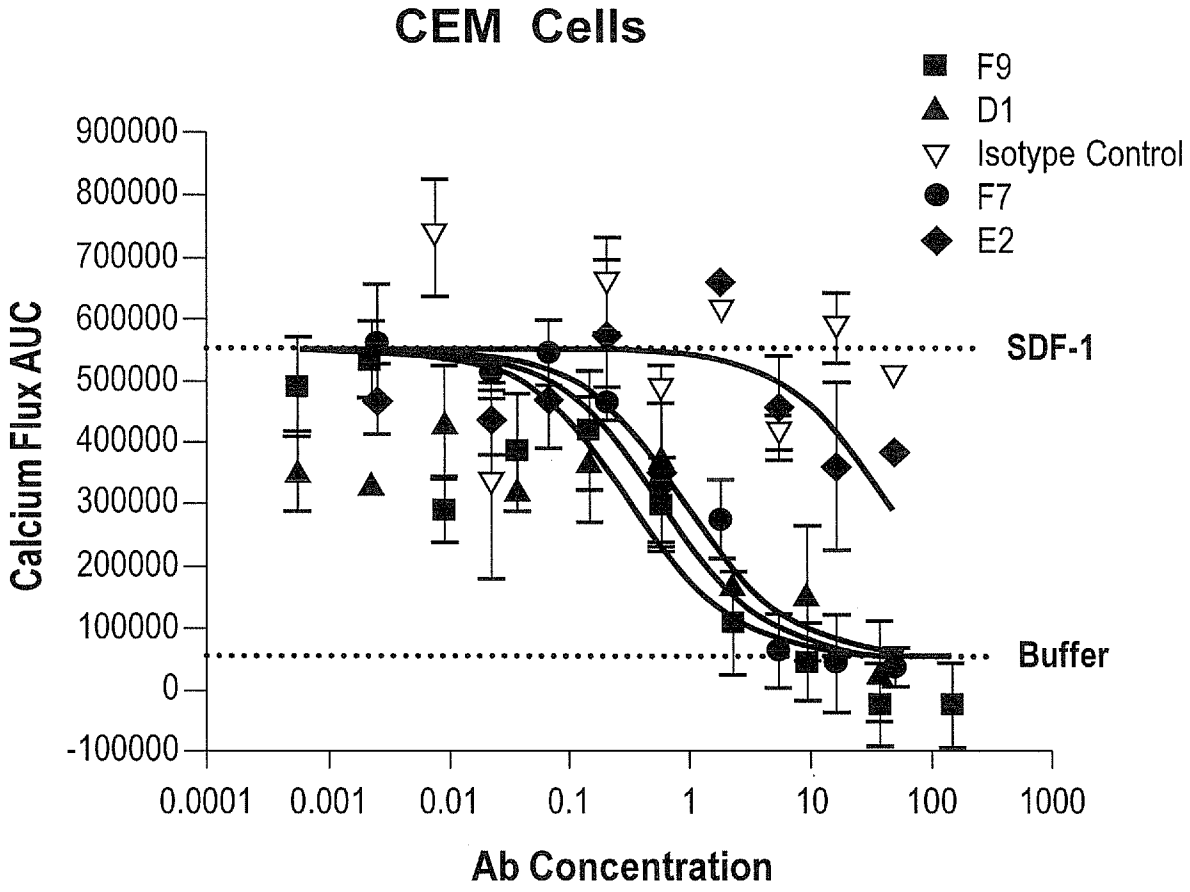

Ramos Cells
8000
7000
total CPM
6000
5000
4000
NSB
3000
CPMs
0.1
1
10
100
1000
Ab (nM)
MDX-1338
Control Ab

FIG. 7



	F9	D1	F7	E2
EC50	0.3219	0.5684	0.9046	43.92

FIG. 8A

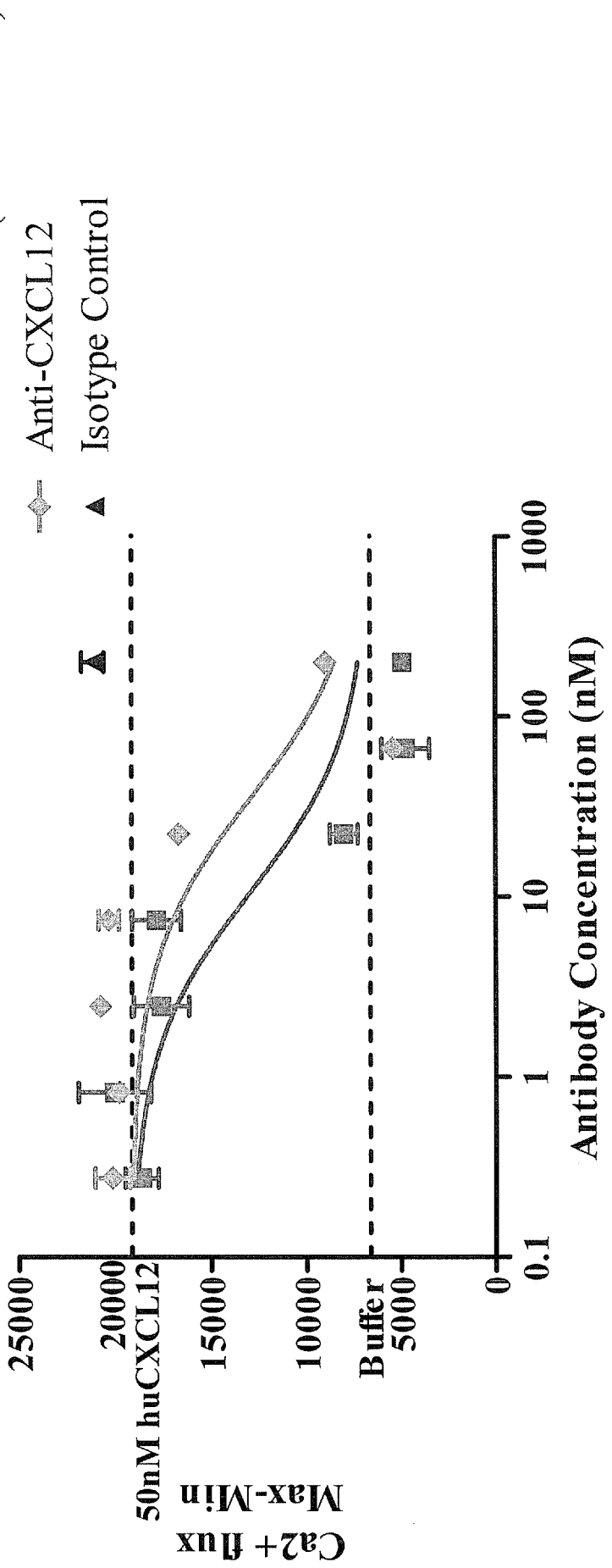

Anti-CXCR4 (MDX-1338)
Anti-CXCL12
Isotype Control
Ca2+ flux
Max-Min
50nM huCXCL12
Buffer
25000
20000
15000
10000
5000
0
0.1
1
10
100
1000
Antibody Concentration (nM)

FIG. 8B

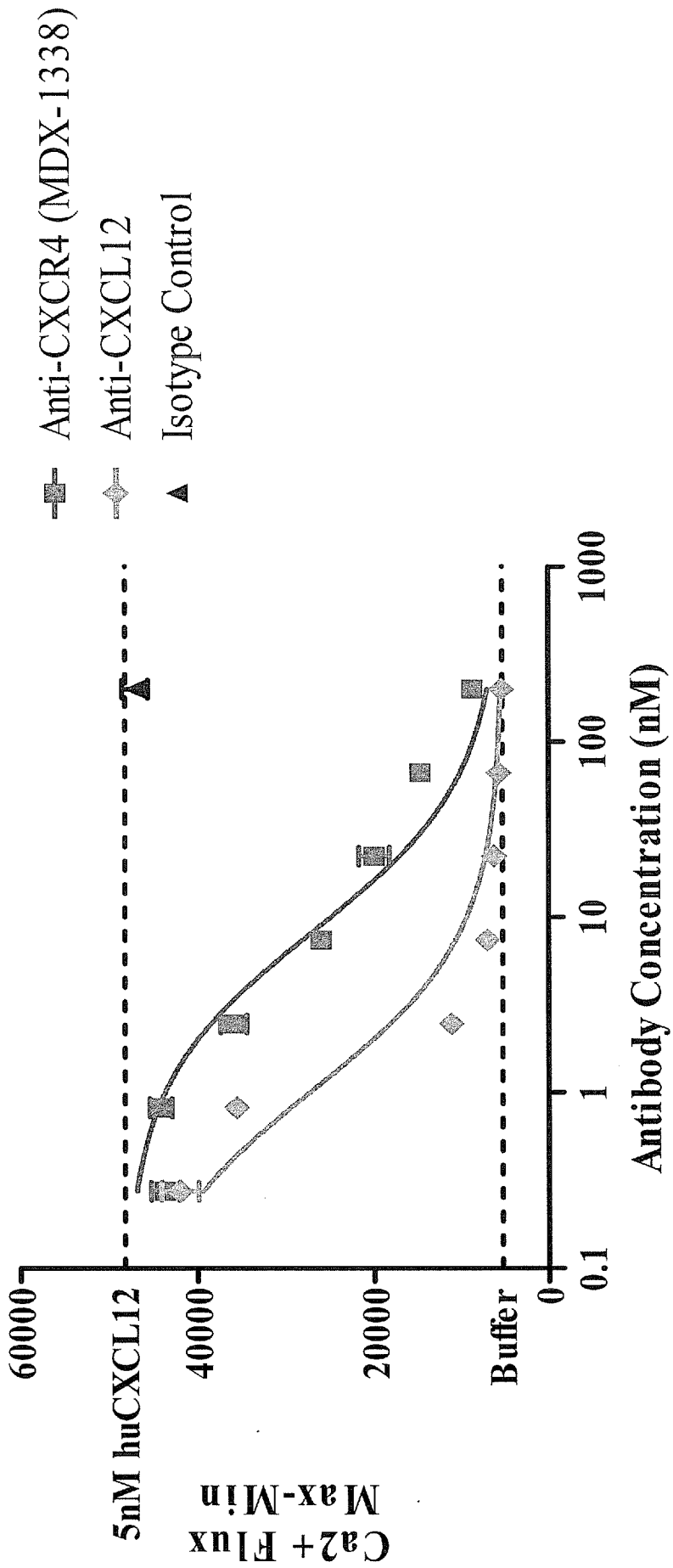
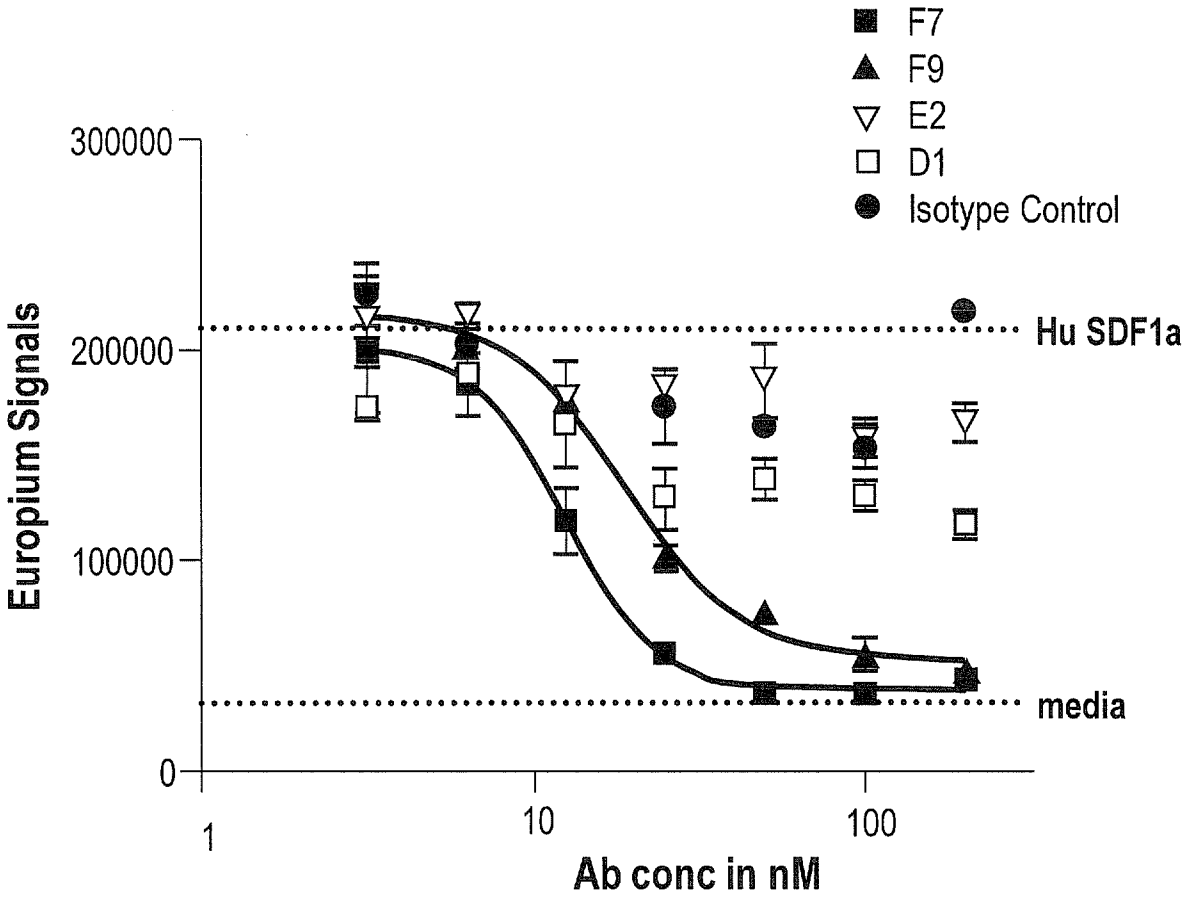

Anti-CXCR4 (MDX-1338)
Anti-CXCL12
Isotype Control
Ca2+ Flux
Max-Min
5nM huCXCL12
Buffer
60000
40000
20000
0
0.1
1
10
100
1000
Antibody Concentration (nM)

FIG. 9



	F7	F9
EC50	12.44	18.99

FIG. 10A

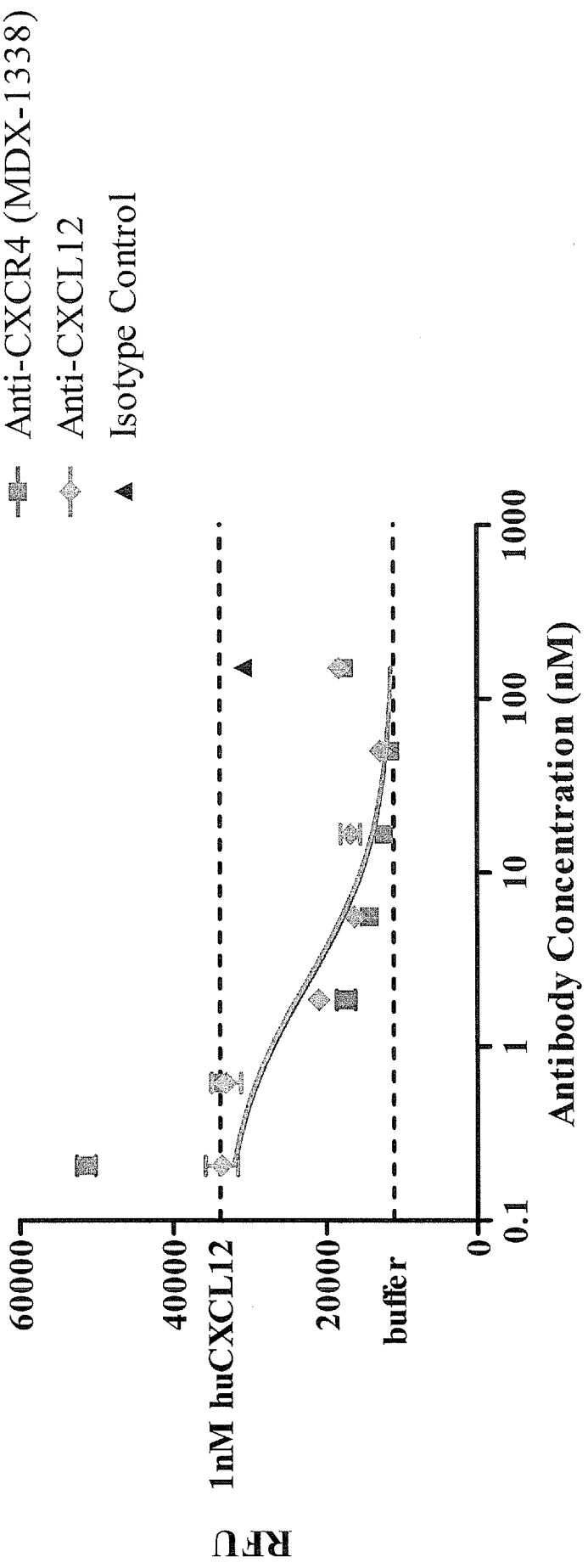

Anti-CXCR4 (MDX-1338)
Anti-CXCL12
Isotype Control
RFU
60000
40000
20000
0
1nM huCXCL12
buffer
0.1
1
10
100
1000
Antibody Concentration (nM)

FIG. 10B

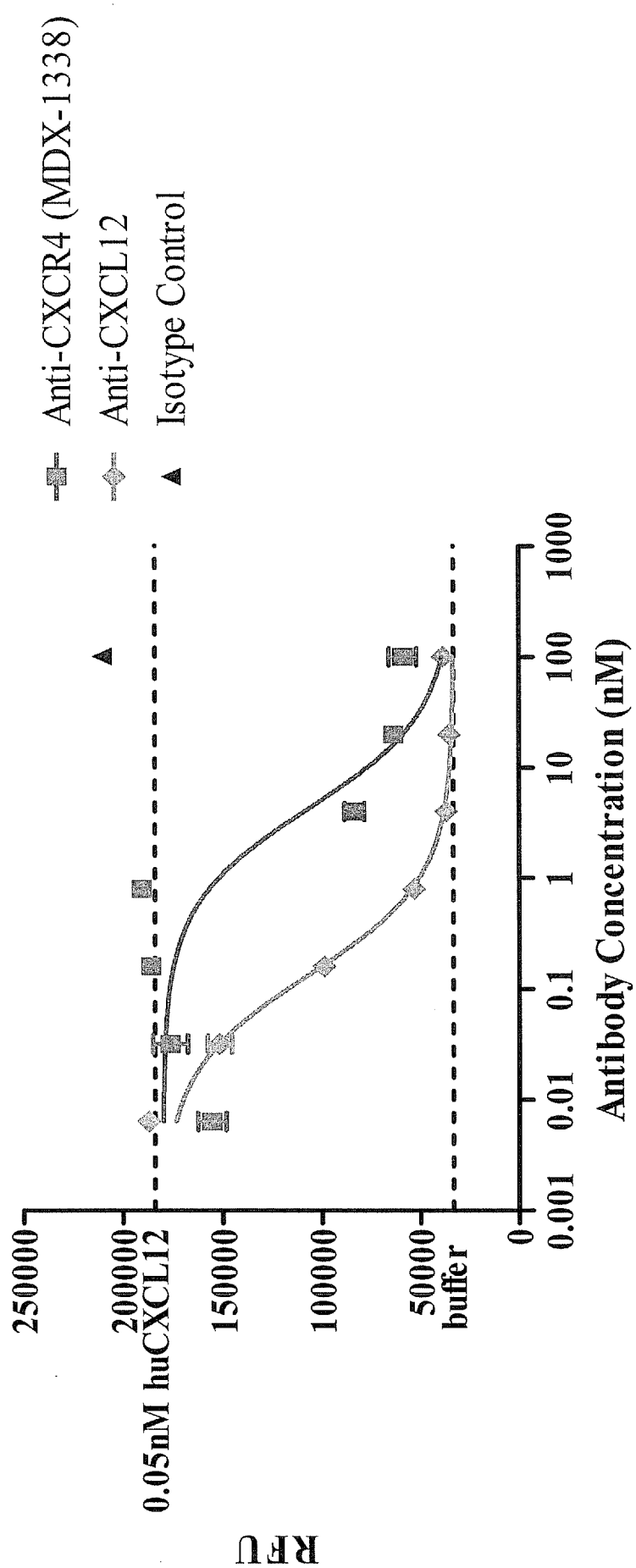

Anti-CXCR4 (MDX-1338)
Anti-CXCL12
Isotype Control
RFU
250000
200000
150000
100000
50000
0
0.05nM huCXCL12
buffer
0.001
0.01
0.1
1
10
100
1000
Antibody Concentration (nM)

FIG. 11A

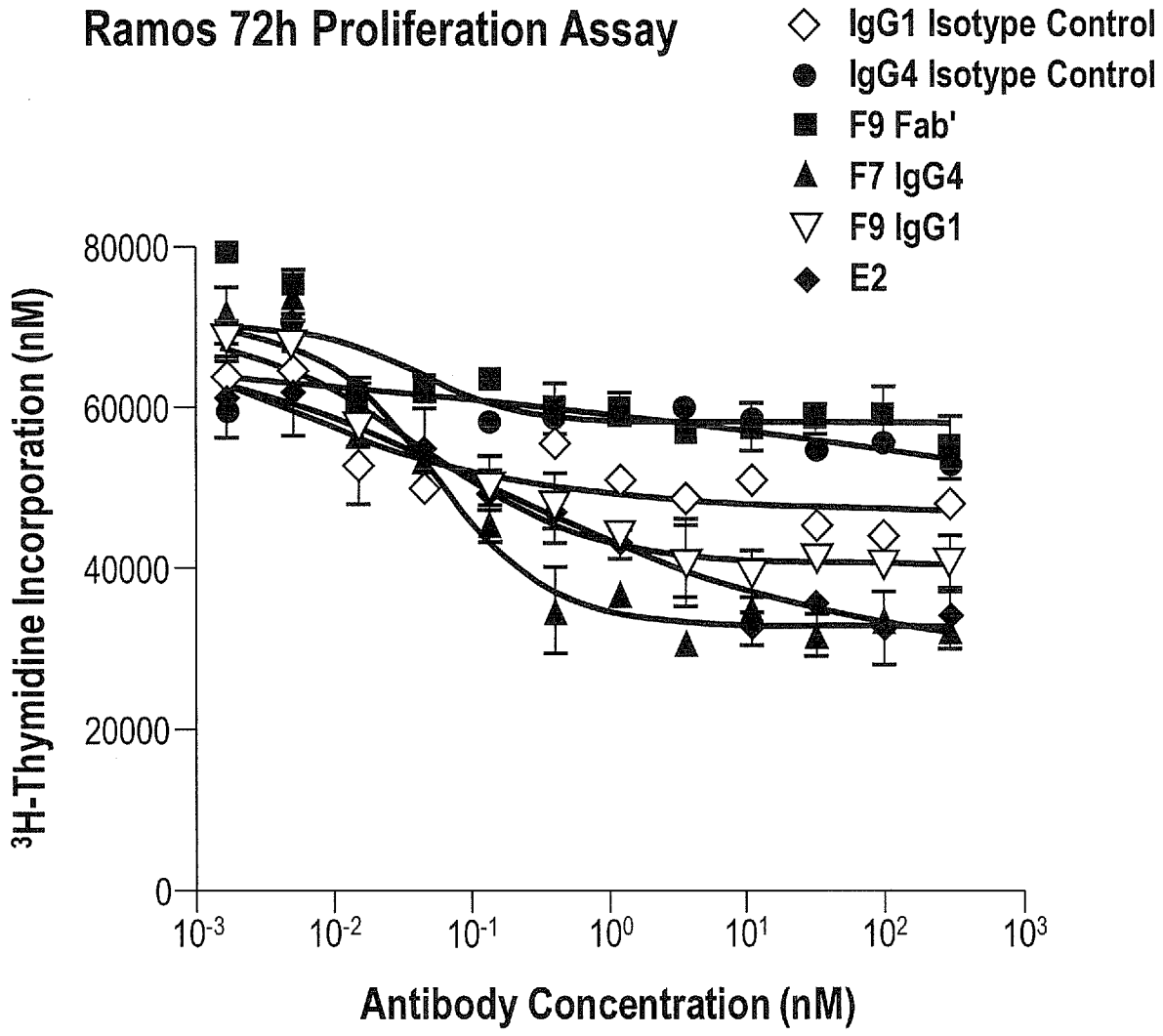

Ramos 72h Proliferation Assay
IgG1 Isotype Control
IgG4 Isotype Control
F9 Fab'
F7 IgG4
F9 IgG1
E2
3H-Thymidine Incorporation (nM)
80000
60000
40000
20000
0
10-3
10-2
10-1
100
101
102
103
Antibody Concentration (nM)

FIG. 11B

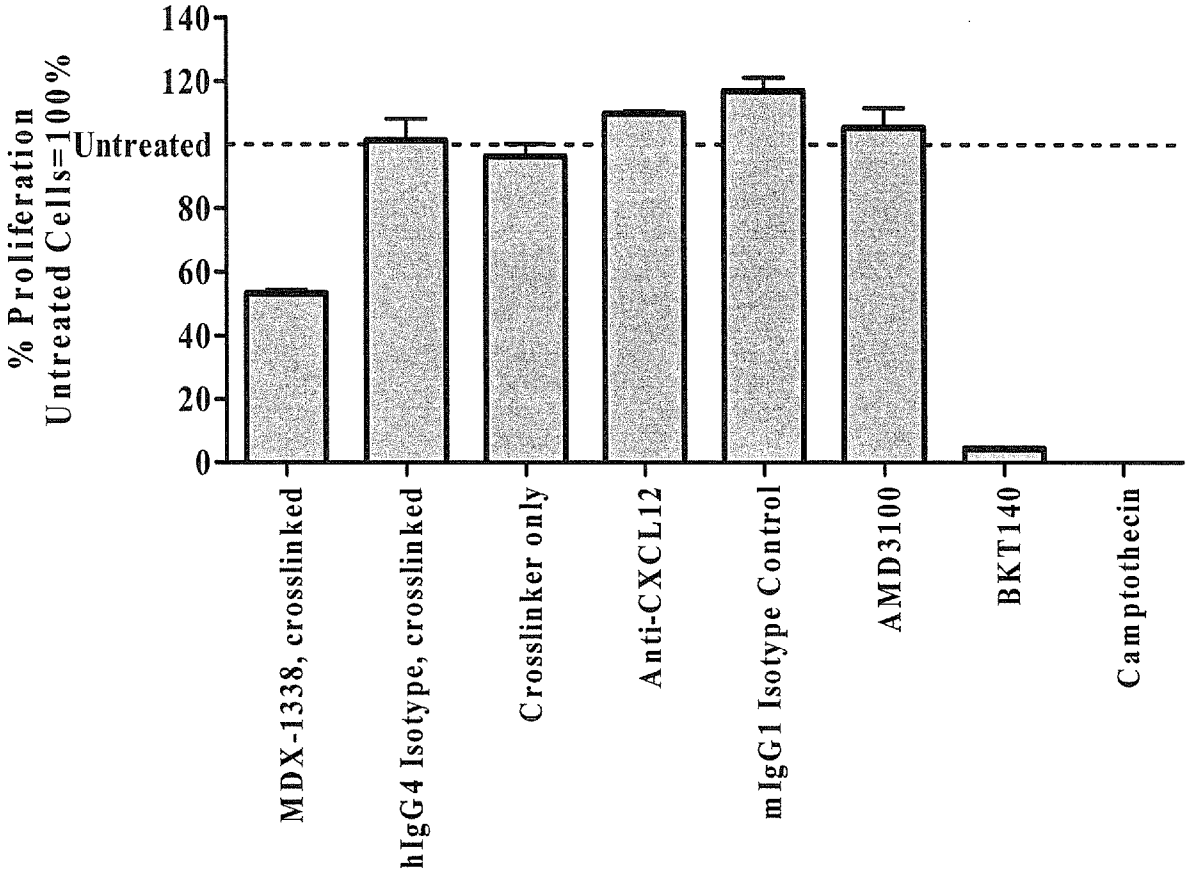

Proliferation of Ramos Cells
Abs: 41.25nM
Peptides: 100uM
CPT: 10uM
% Proliferation
Untreated Cells=100%
140
120
Untreated
80
60
40
20
0
MDX-1338, crosslinked
hIgG4 Isotype, crosslinked
Crosslinker only
Anti-CXCL12
mIgG1 Isotype Control
AMD3100
BKT140
Camptothecin

FIG. 12A

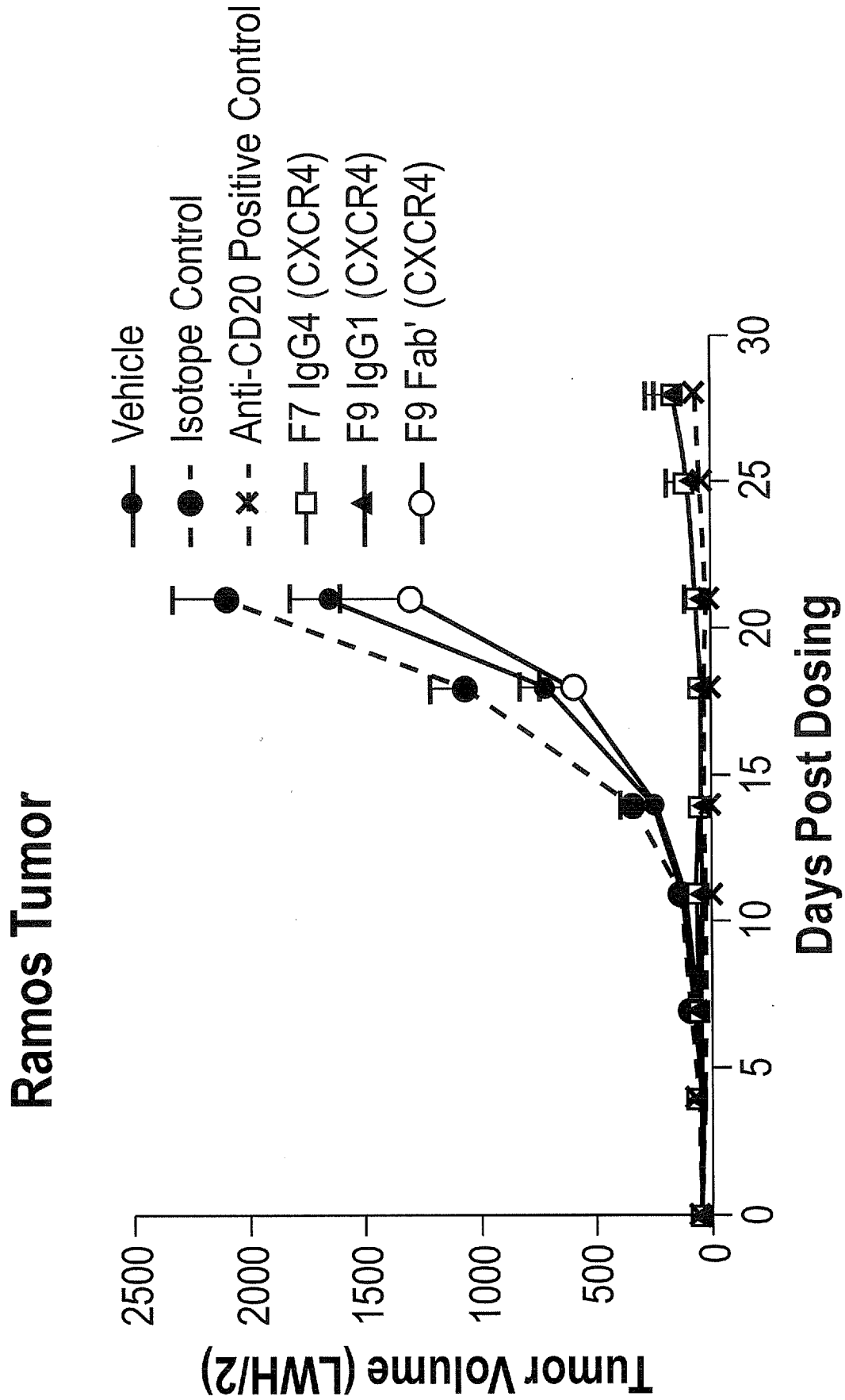

Ramos Tumor
Vehicle
Isotope Control
Anti-CD20 Positive Control
F7 IgG4 (CXCR4)
F9 IgG1 (CXCR4)
F9 Fab' (CXCR4)
Tumor Volume (LWH/2)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
Days Post Dosing

FIG. 12B

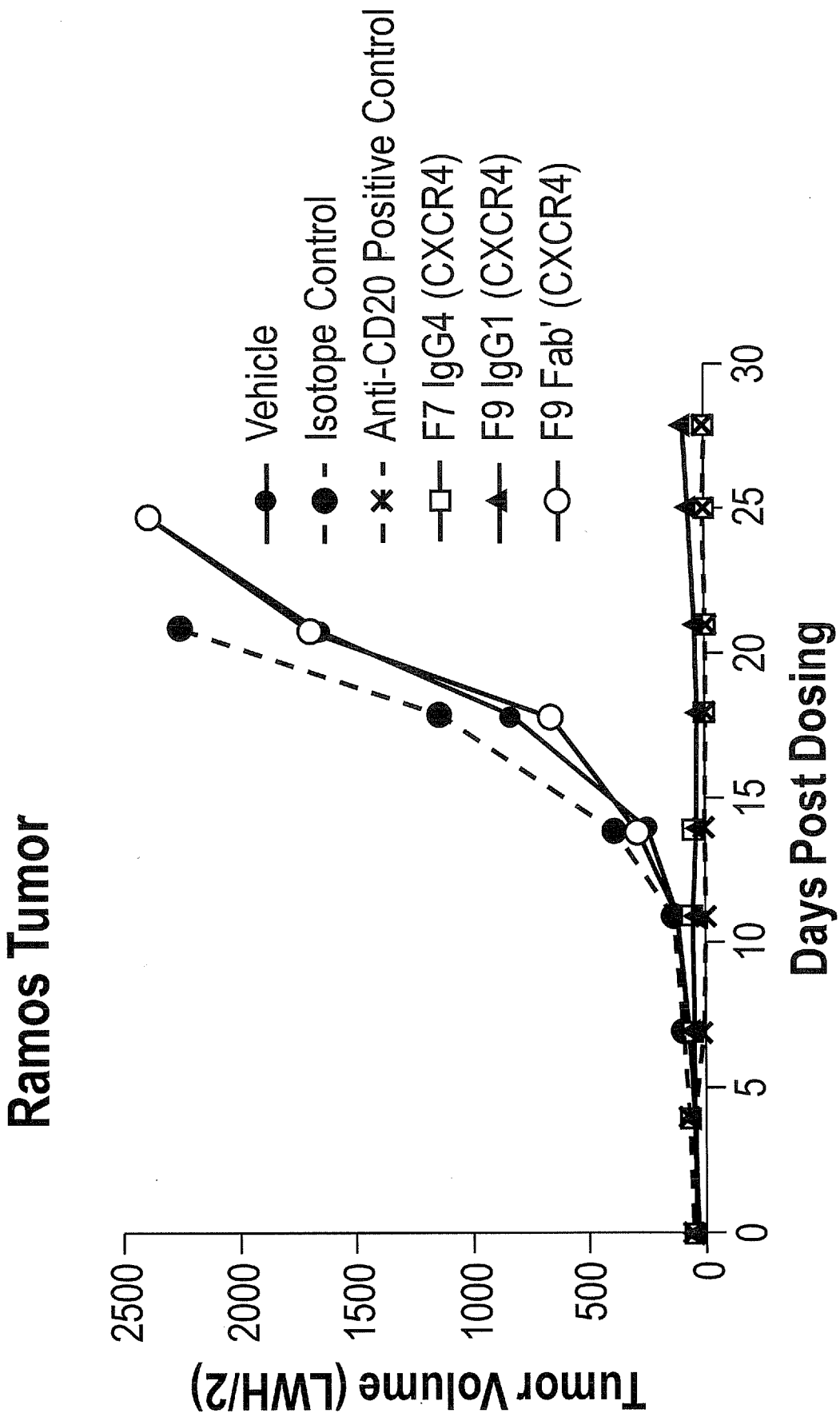

Ramos Tumor
Vehicle
Isotope Control
Anti-CD20 Positive Control
F7 IgG4 (CXCR4)
F9 IgG1 (CXCR4)
F9 Fab' (CXCR4)
Tumor Volume (LWH/2)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
Days Post Dosing

FIG. 12C

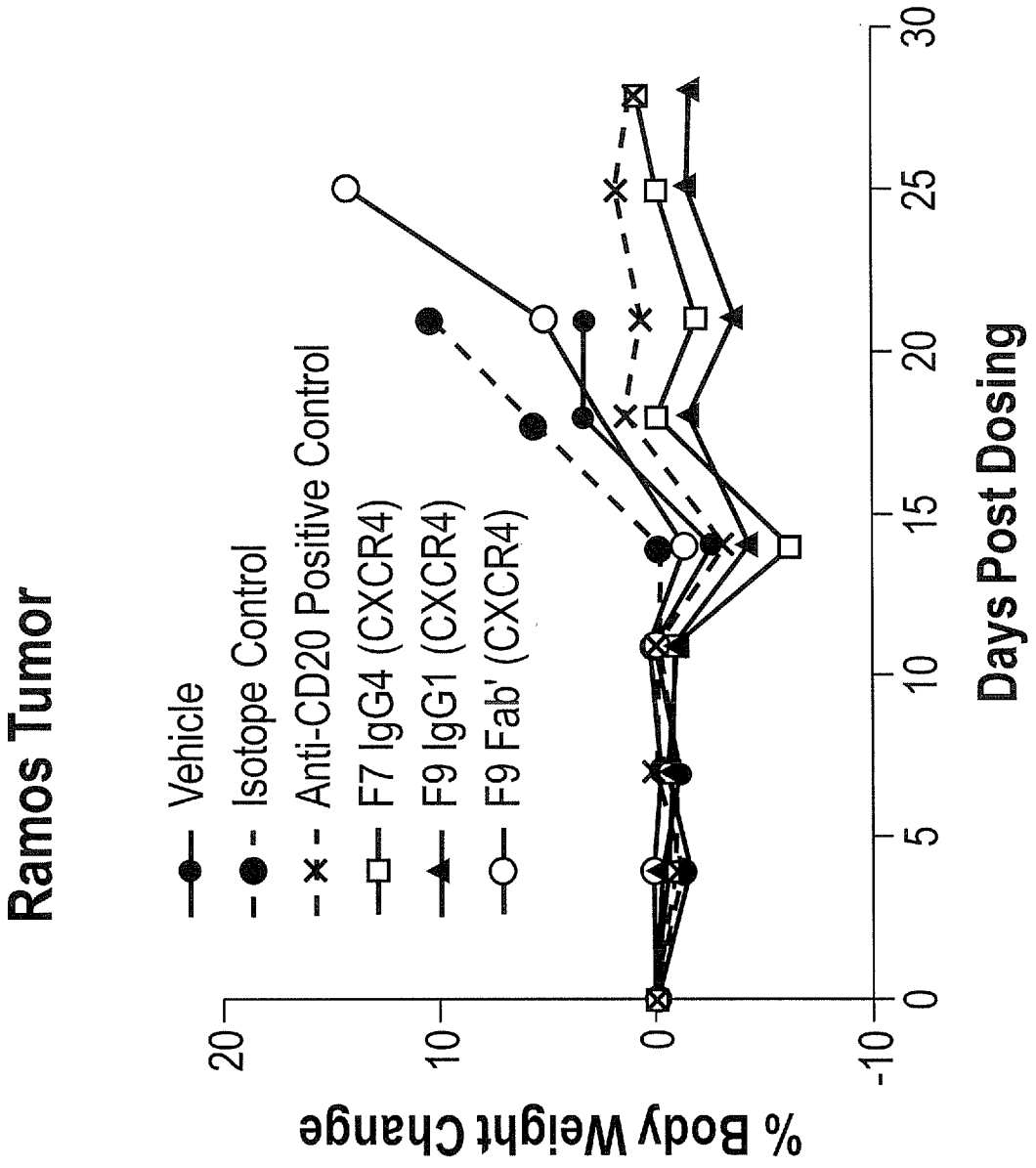

Ramos Tumor
Vehicle
Isotope Control
Anti-CD20 Positive Control
F7 IgG4 (CXCR4)
F9 IgG1 (CXCR4)
F9 Fab' (CXCR4)
% Body Weight Change
20
10
0
-10
0
5
10
15
20
25
30
Days Post Dosing

FIG. 13A

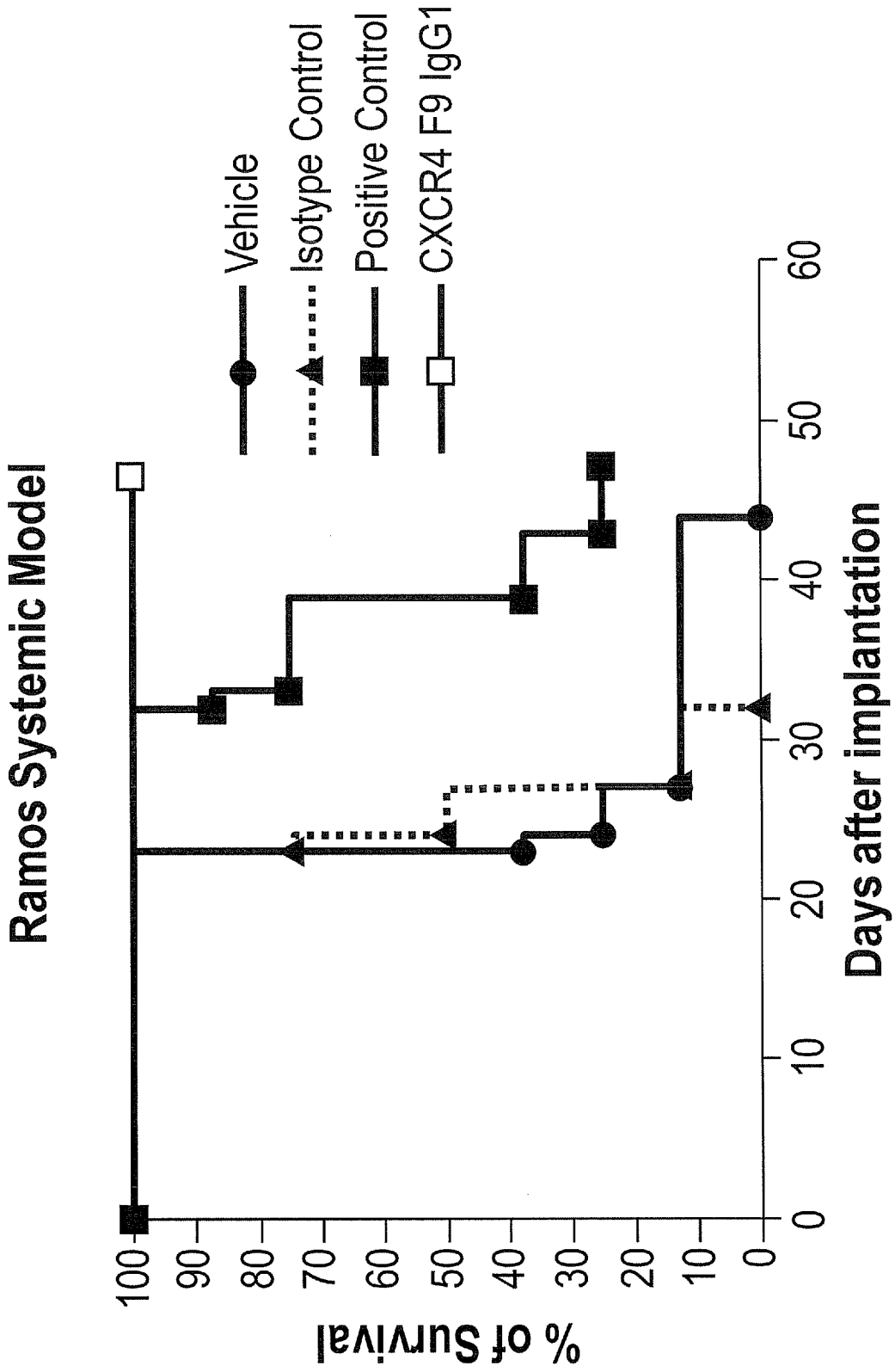

Ramos Systemic Model
Vehicle
Isotype Control
Positive Control
CXCR4 F9 IgG1
% of Survival
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
60
Days after implantation

FIG. 13B

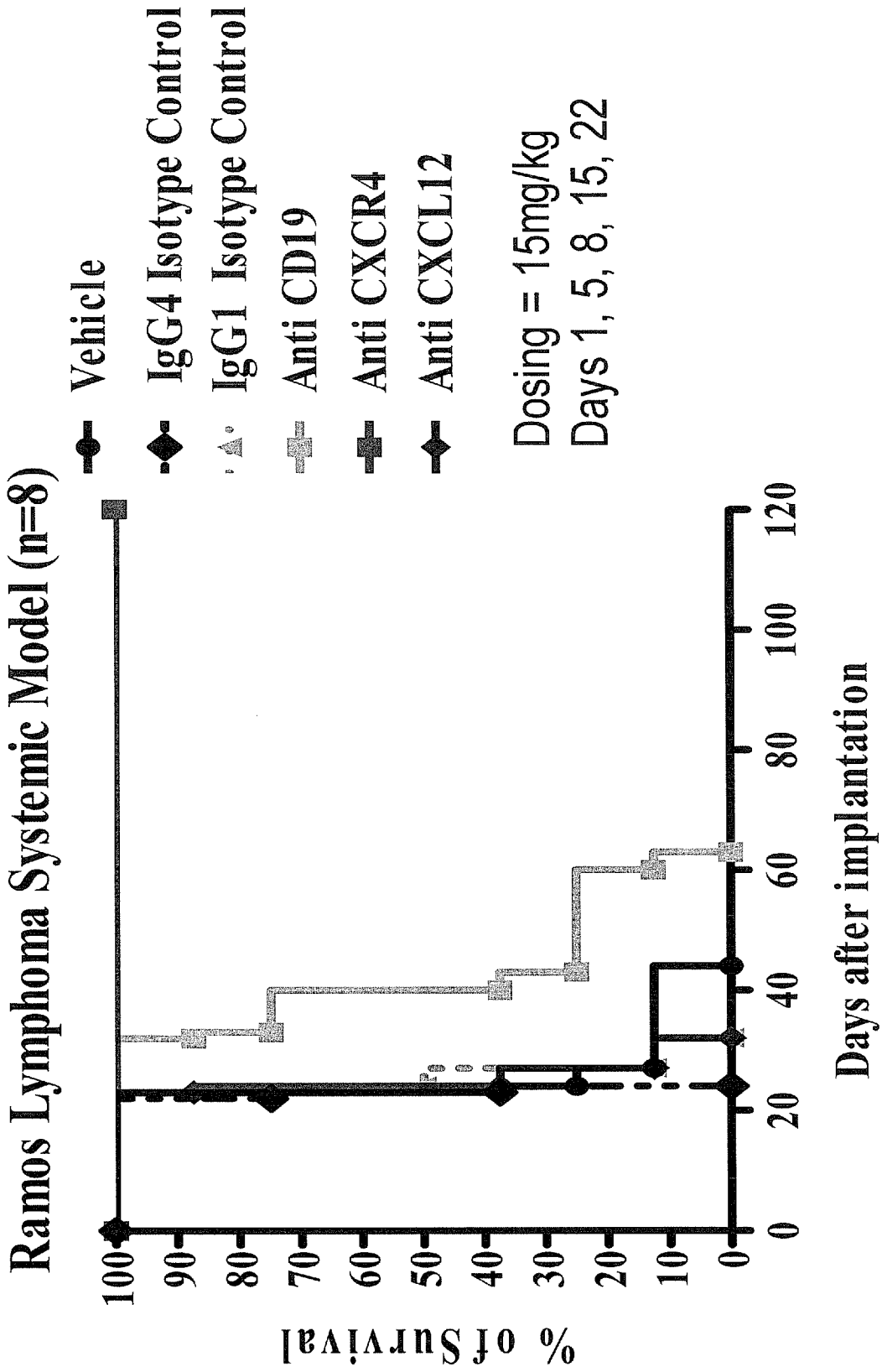

Ramos Lymphoma Systemic Model (n=8)
Vehicle
IgG4 Isotype Control
IgG1 Isotype Control
Anti CD19
Anti CXCR4
Anti CXCL12
Dosing = 15mg/kg
Days 1, 5, 8, 15, 22
% of Survival
100
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
120
Days after implantation

FIG. 14A

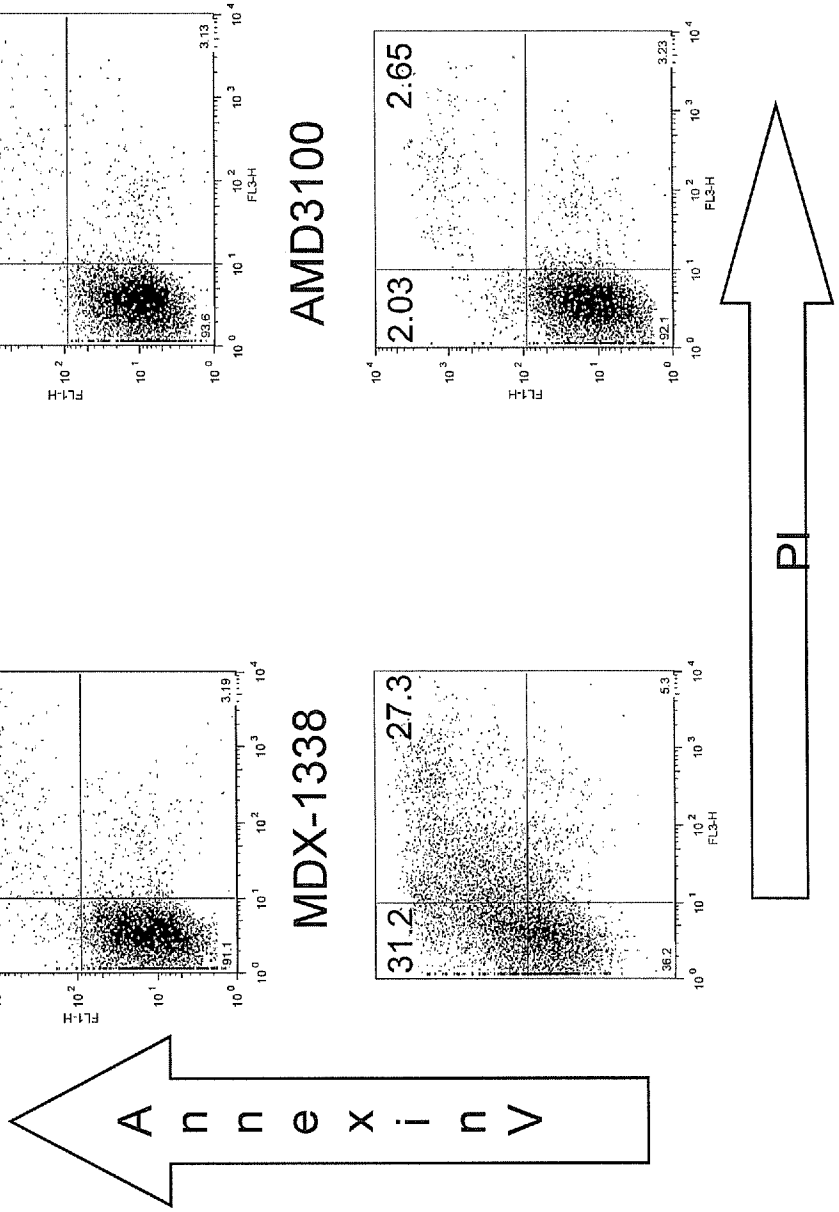

No Treatment
Isotype Control
AMD3100
MDX-1338
Annexin V
PI
1.67
4.05
0.51
2.8
31.2
27.3
2.03
2.65
FL1-H
FL3-H

FIG. 14B

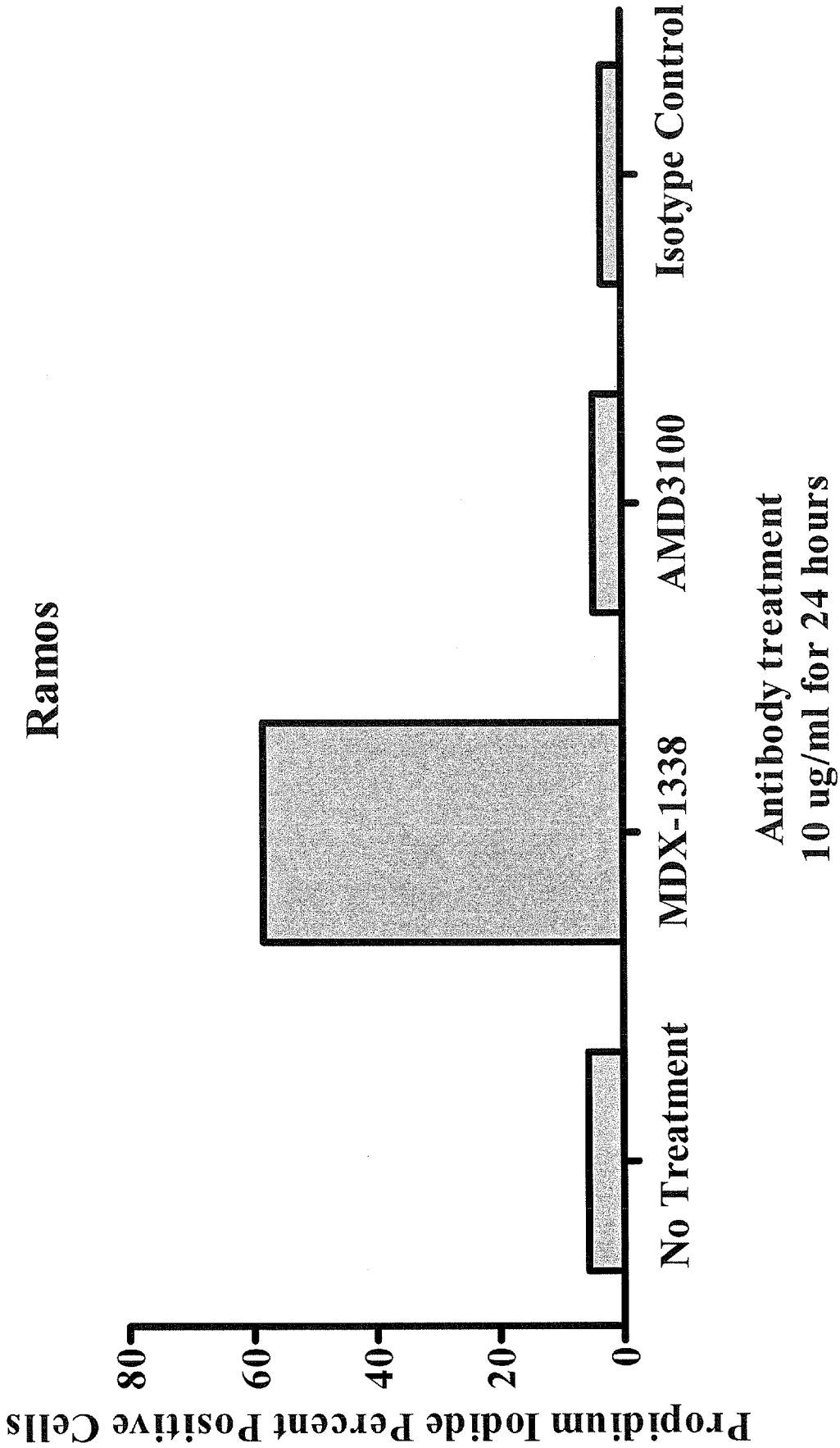

Ramos
Propidium Iodide Percent Positive Cells
0
20
40
60
80
No Treatment
MDX-1338
AMD3100
Isotype Control
Antibody treatment
10 ug/ml for 24 hours

FIG. 15A

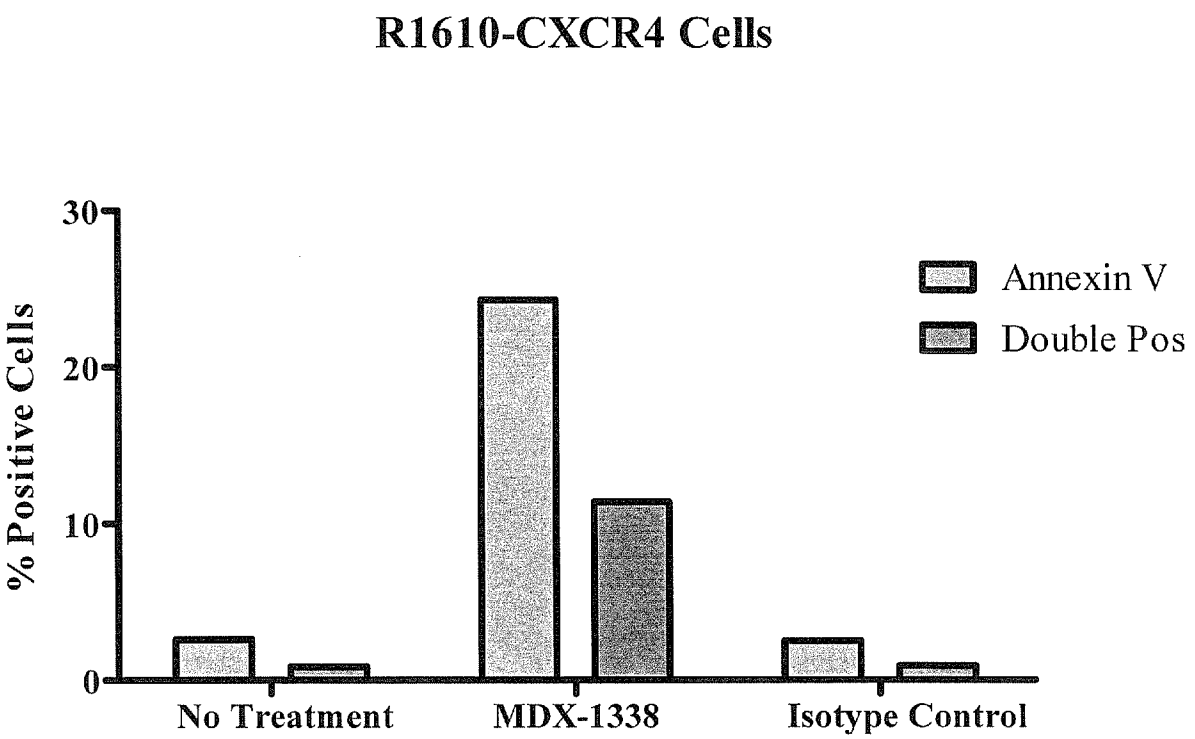


FIG. 15B

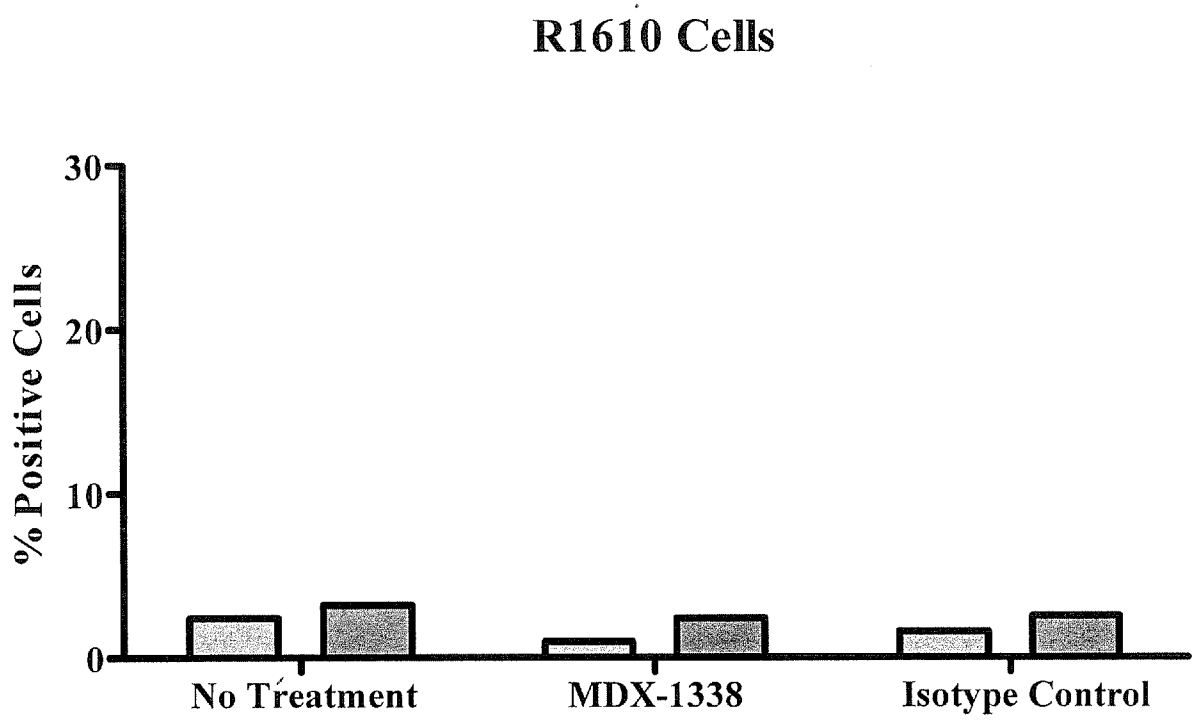


FIG. 16

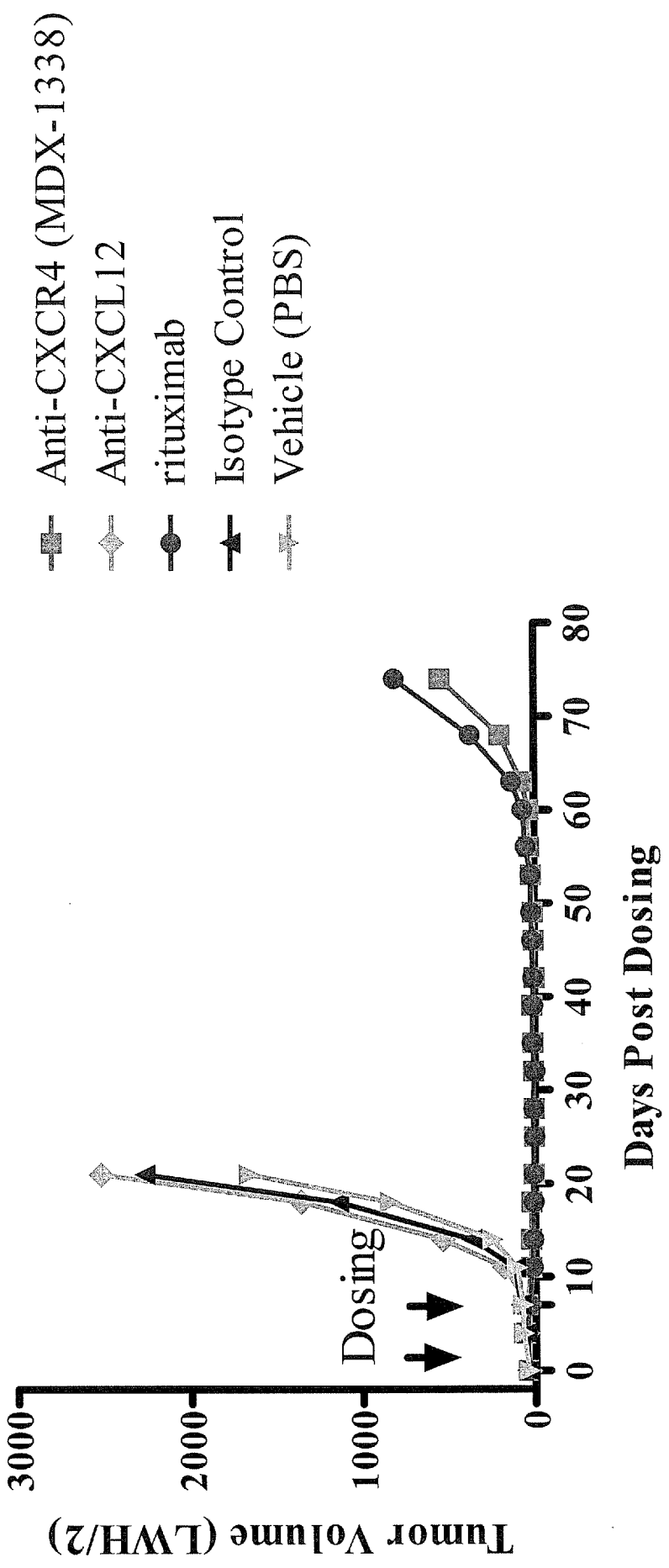

Ramos B Cell Lymphoma Xenograft
Anti-CXCR4 (MDX-1338)
Anti-CXCL12
rituximab
Isotype Control
Vehicle (PBS)
Dosing
Tumor Volume (LWH/2)
Days Post Dosing
0
1000
2000
3000
0
10
20
30
40
50
60
70
80

FIG. 17A

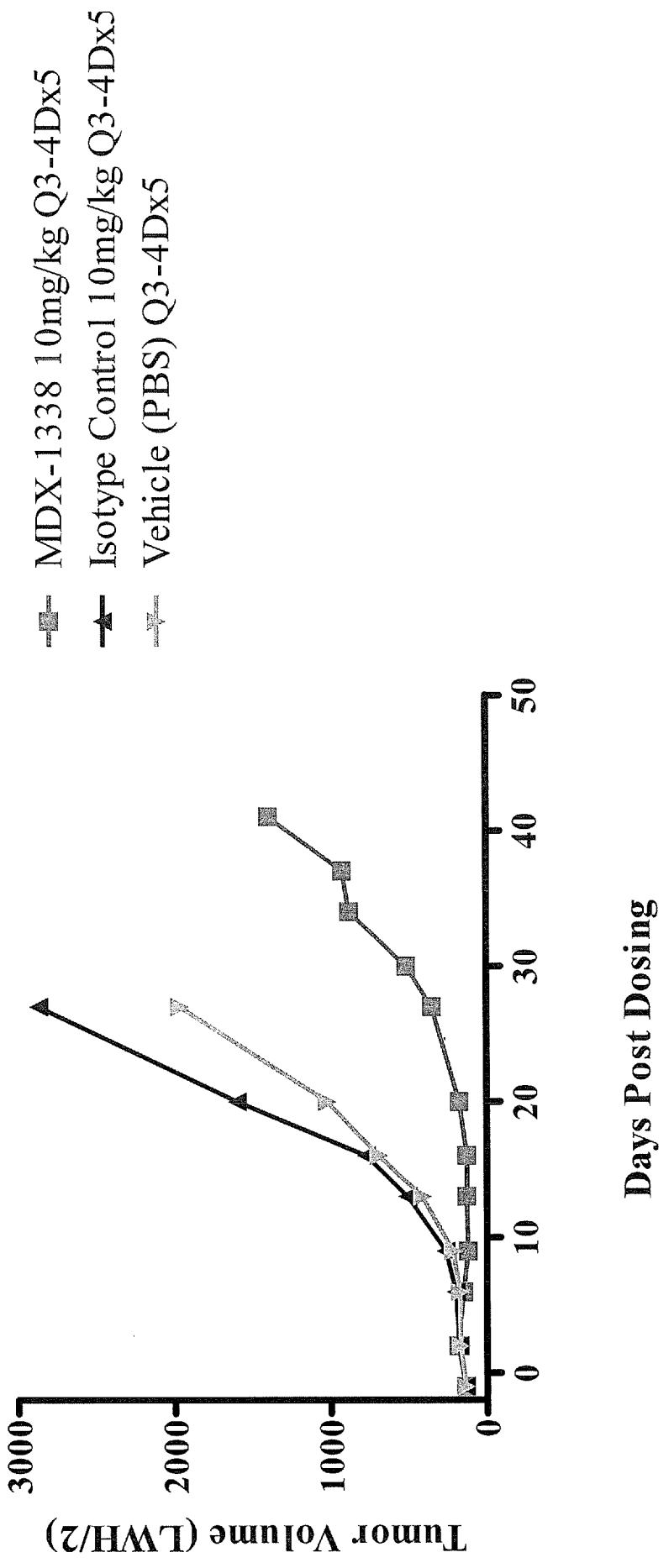

HL60
Median Tumor Growth
MDX-1338 10mg/kg Q3-4Dx5
Isotype Control 10mg/kg Q3-4Dx5
Vehicle (PBS) Q3-4Dx5
Tumor Volume (LWH/2)
3000
2000
1000
0
0
10
20
30
40
50
Days Post Dosing

FIG. 17B

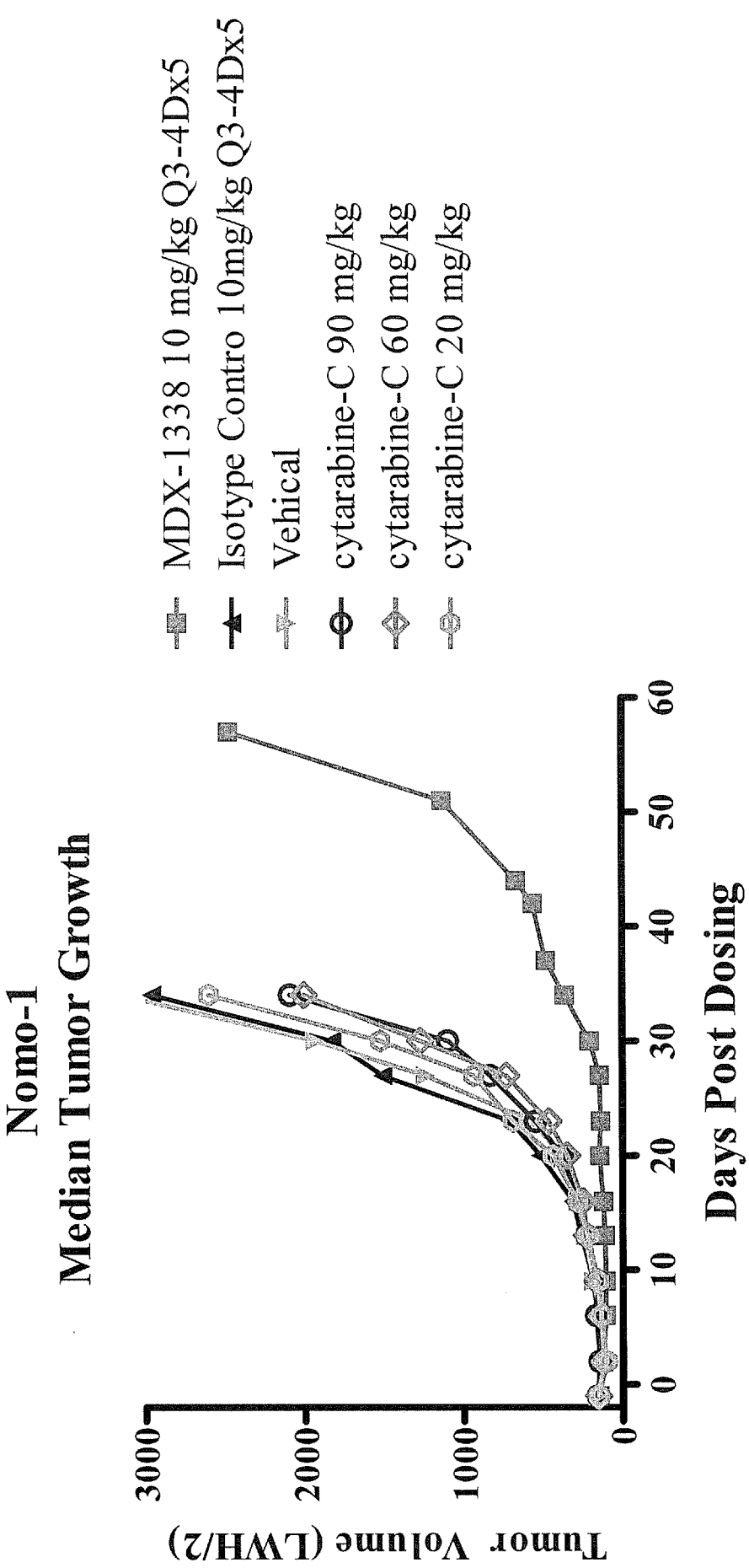

Nomo-1
Median Tumor Growth
MDX-1338 10 mg/kg Q3-4Dx5
Isotype Contro 10mg/kg Q3-4Dx5
Vehical
cytarabine-C 90 mg/kg
cytarabine-C 60 mg/kg
cytarabine-C 20 mg/kg
Tumor Volume (LWH/2)
3000
2000
1000
0
0
10
20
30
40
50
60
Days Post Dosing

FIG. 18A

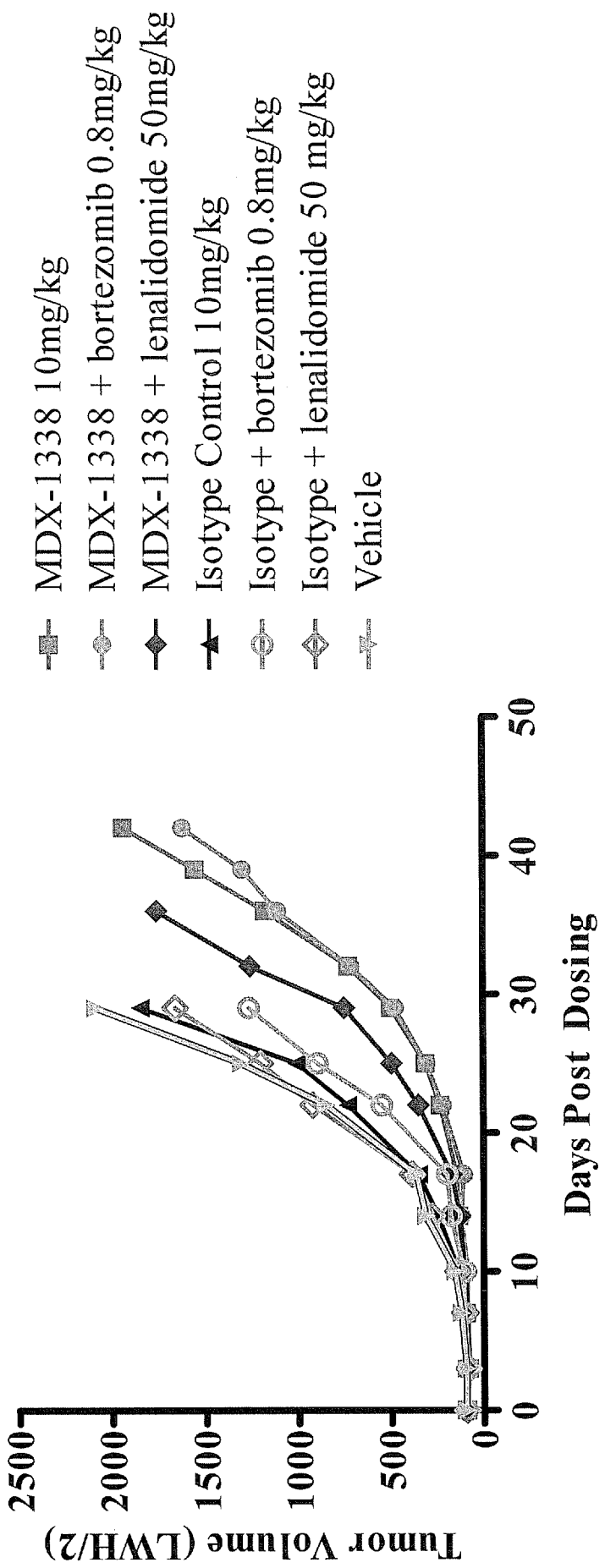

MOLP8
Median Tumor Volumes
MDX-1338 10mg/kg
MDX-1338 + bortezomib 0.8mg/kg
MDX-1338 + lenalidomide 50mg/kg
Isotype Control 10mg/kg
Isotype + bortezomib 0.8mg/kg
Isotype + lenalidomide 50 mg/kg
Vehicle
Tumor Volume (LWH/2)
2500
2000
1500
1000
500
0
0
10
20
30
40
50
Days Post Dosing

FIG. 18B

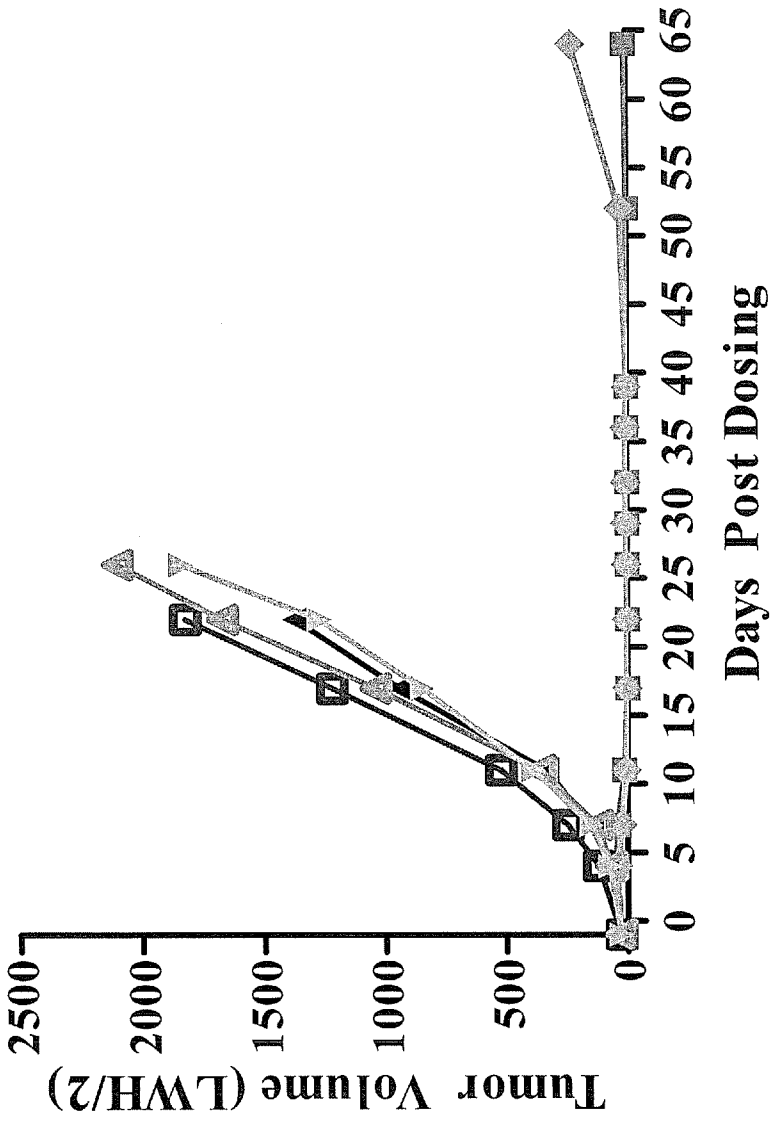

JJN3-R
Median Tumor Growth
MDX-1338 30 mg/kg IP
MDX-1338 10 mg/kg IP
Isotype Control 30 mg/kg IP
bortezomib 0.8 mg/kg IV
lenalidomide 50 mg/kg IP
Vehicle 0.3 ml IP
Tumor Volume (LWH/2)
2500
2000
1500
1000
500
0
0 5 10 15 20 25 30 35 40 45 50 55 60 65
Days Post Dosing

FIG. 18C

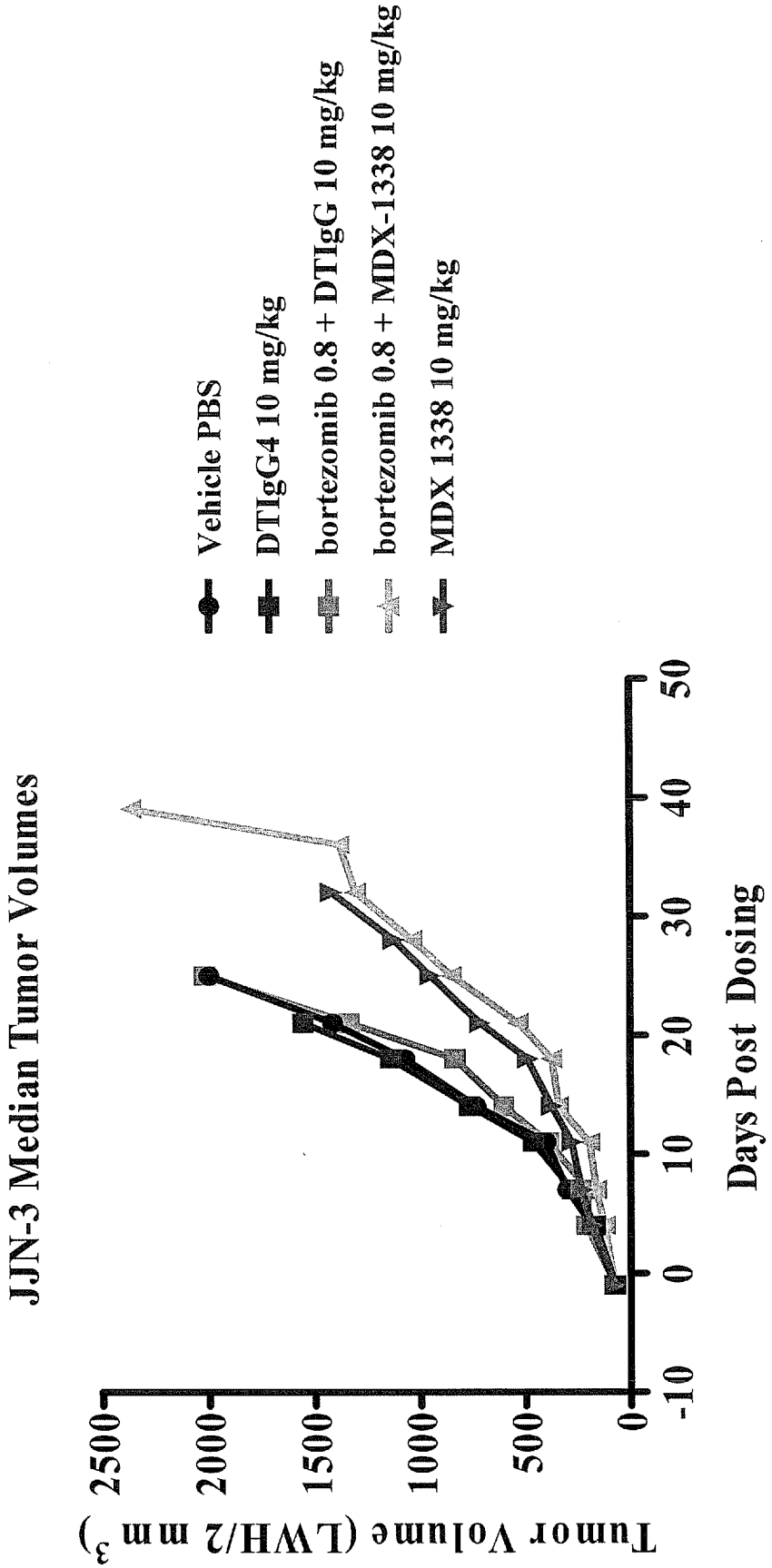

JJN-3 Median Tumor Volumes
Vehicle PBS
DTIgG4 10 mg/kg
bortezomib 0.8 + DTIgG 10 mg/kg
bortezomib 0.8 + MDX-1338 10 mg/kg
MDX 1338 10 mg/kg
Tumor Volume (LWH/2 mm 3)
2500
2000
1500
1000
500
0
-10
0
10
20
30
40
50
Days Post Dosing

FIG. 18D

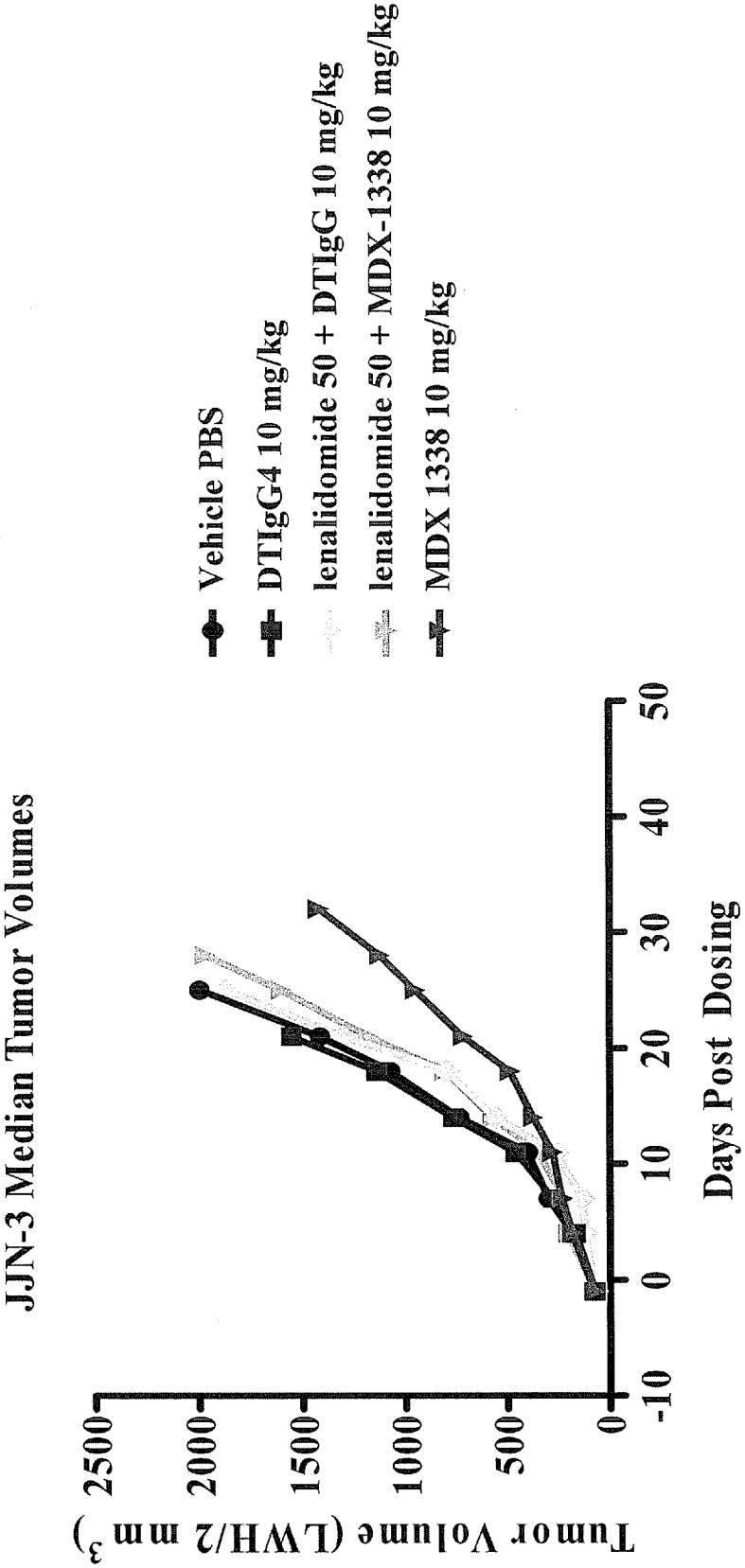

JJN-3 Median Tumor Volumes
Vehicle PBS
DTIgG4 10 mg/kg
lenalidomide 50 + DTIgG 10 mg/kg
lenalidomide 50 + MDX-1338 10 mg/kg
MDX 1338 10 mg/kg
Tumor Volume (LWH/2 mm 3)
2500
2000
1500
1000
500
0
-10
0
10
20
30
40
50
Days Post Dosing

FIG. 18E

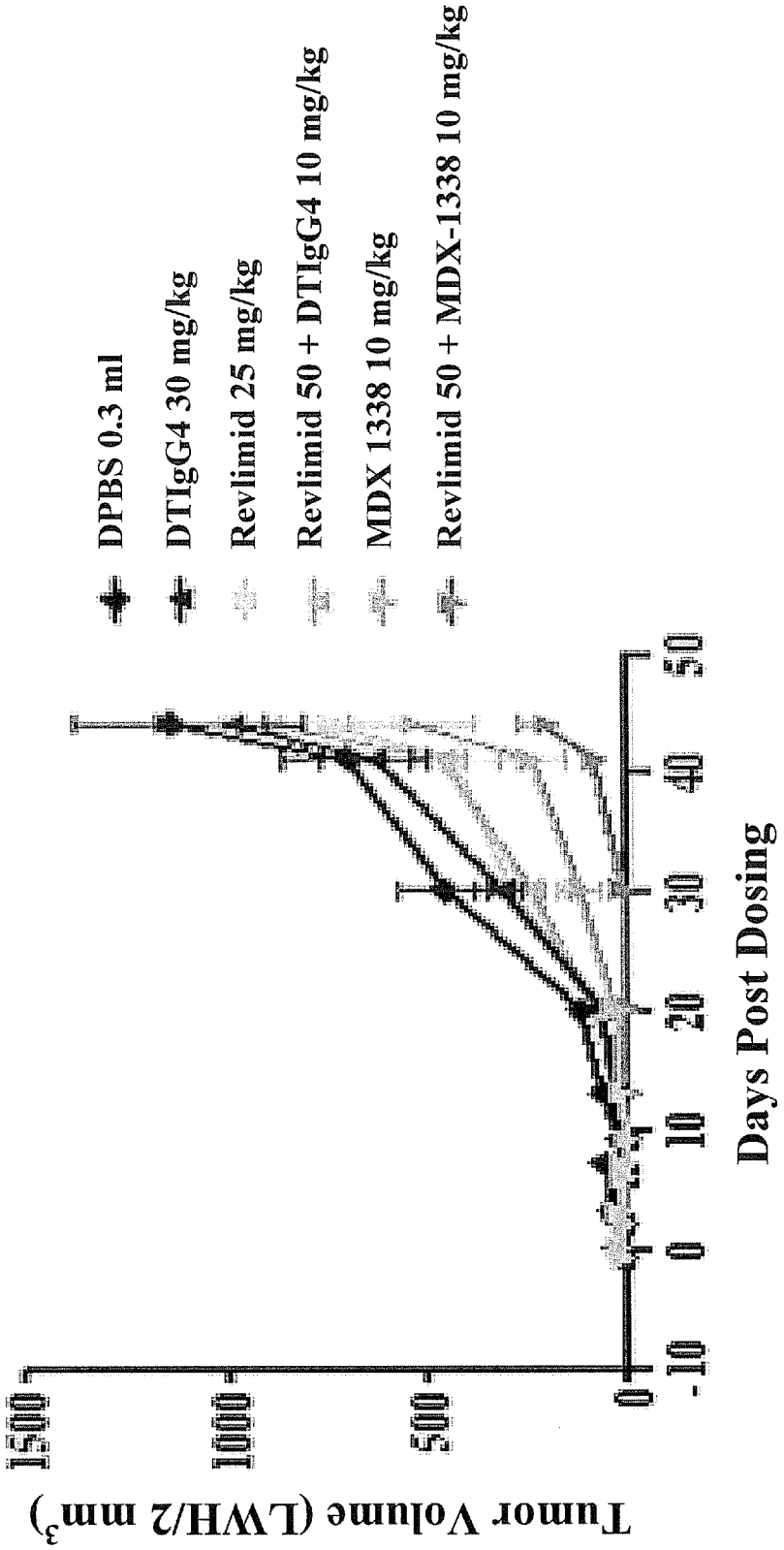

MDX-1338-050 RPMI-8226 Mean Tumor Volumes
DPBS 0.3 ml
DTIgG4 30 mg/kg
Revlimid 25 mg/kg
Revlimid 50 + DTIgG4 10 mg/kg
MDX 1338 10 mg/kg
Revlimid 50 + MDX-1338 10 mg/kg
Tumor Volume (LWH/2 mm³)
1500
1000
500
0
-10
0
10
20
30
40
50
Days Post Dosing

FIG. 18F

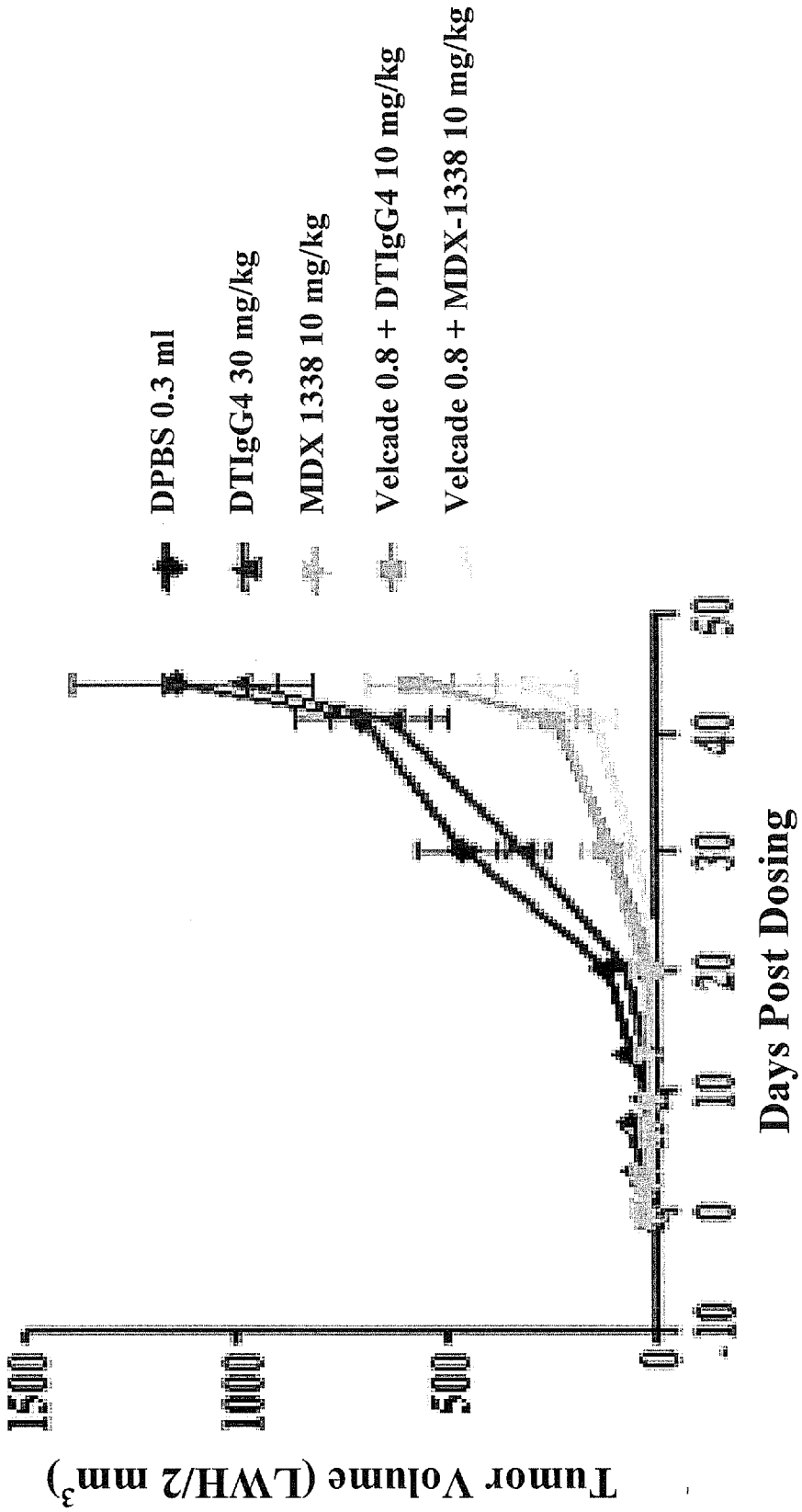

MDX-1338-050 RPMI-8226 Mean Tumor Volumes
DPBS 0.3 ml
DTIgG4 30 mg/kg
MDX 1338 10 mg/kg
Velcade 0.8 + DTIgG4 10 mg/kg
Velcade 0.8 + MDX-1338 10 mg/kg
Tumor Volume (LWH/2 mm3)
1500
1000
500
0
-10
0
10
20
30
40
50
Days Post Dosing

FIG. 18G

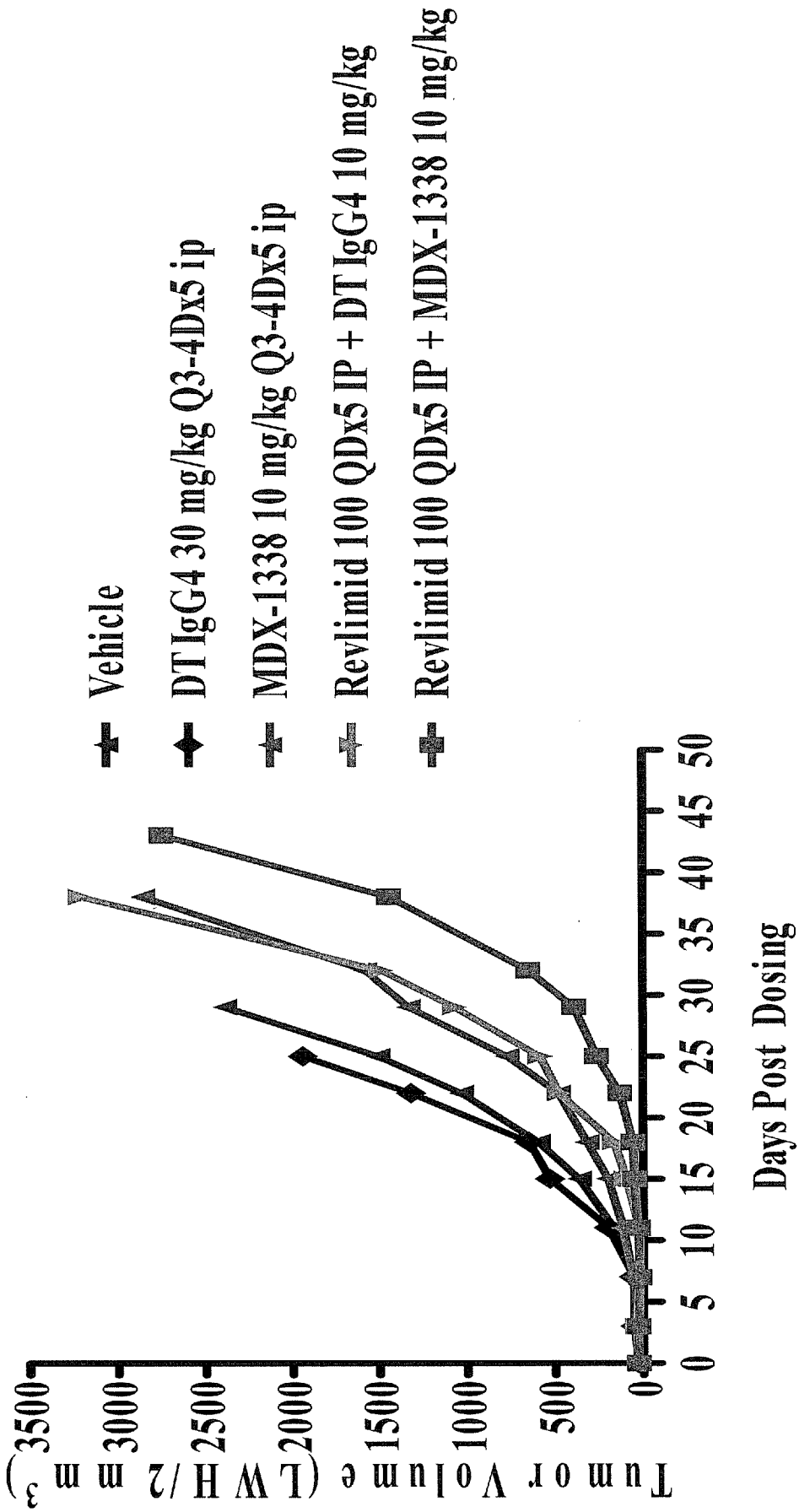

MDX-1338-049 MM1S Median Tumor Volumes
Vehicle
DT IgG4 30 mg/kg Q3-4Dx5 ip
MDX-1338 10 mg/kg Q3-4Dx5 ip
Revlimid 100 QDx5 IP + DT IgG4 10 mg/kg
Revlimid 100 QDx5 IP + MDX-1338 10 mg/kg
Tumor Volume (L W H /2 mm 3)
0
500
1000
1500
2000
2500
3000
3500
0 5 10 15 20 25 30 35 40 45 50
Days Post Dosing

FIG. 18H

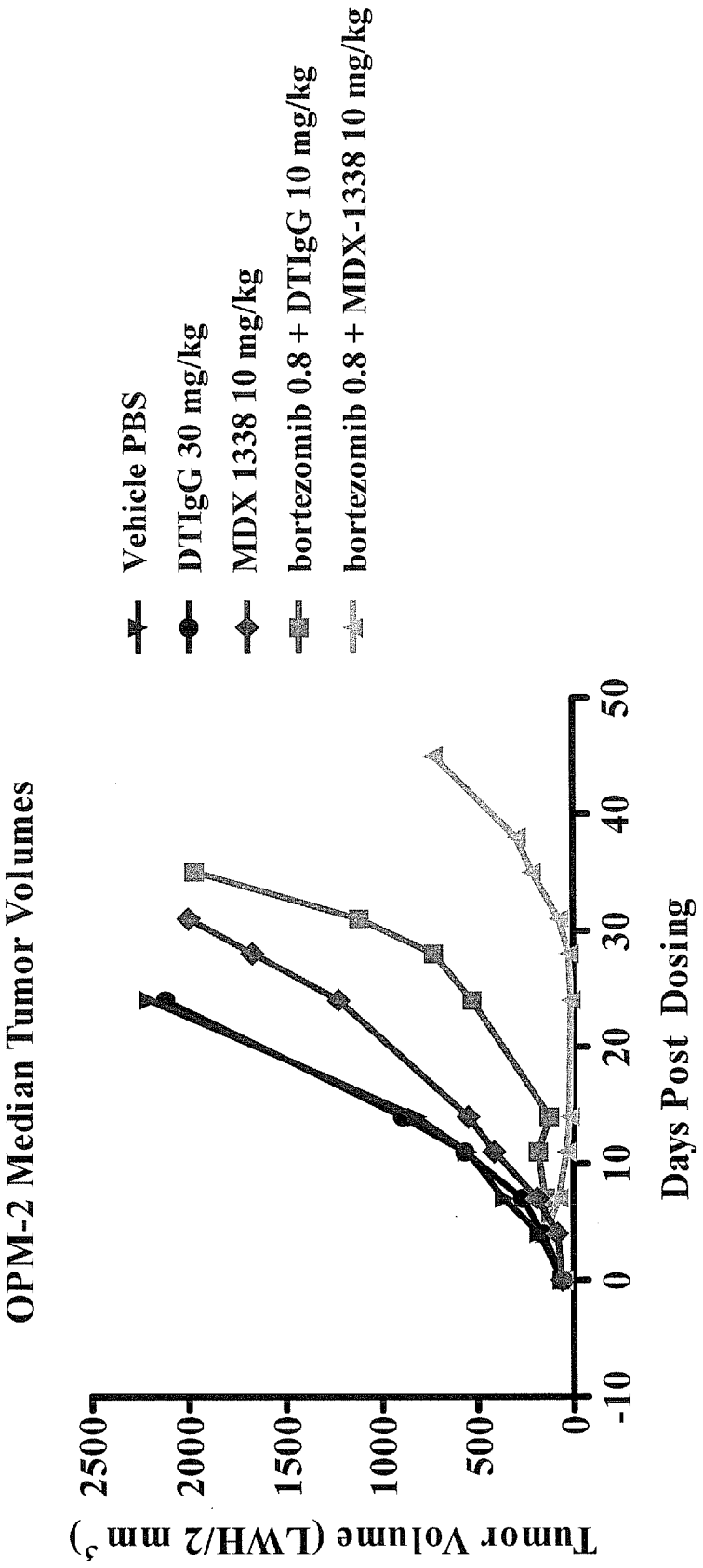
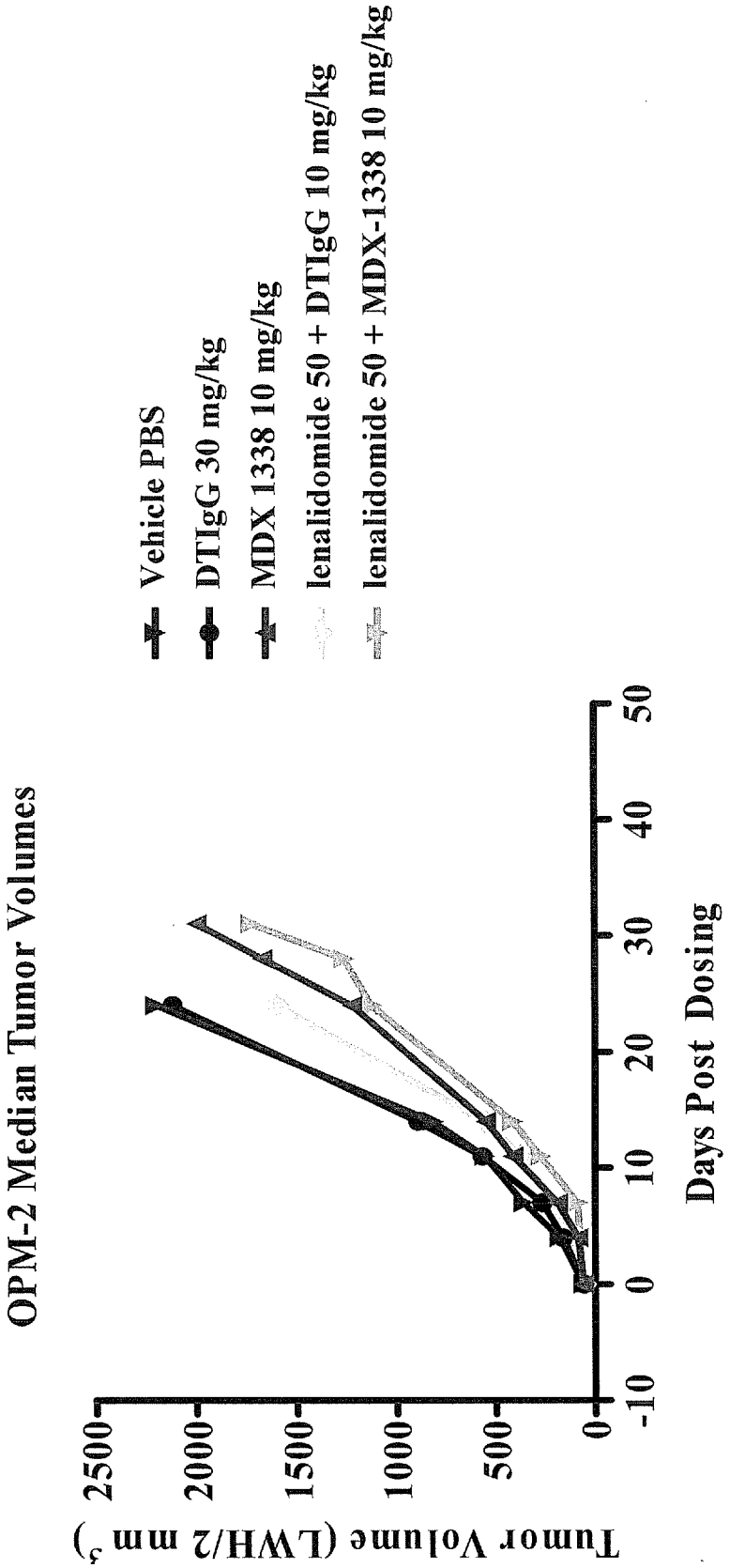

OPM-2 Median Tumor Volumes
Vehicle PBS
DTIgG 30 mg/kg
MDX 1338 10 mg/kg
bortezomib 0.8 + DTIgG 10 mg/kg
bortezomib 0.8 + MDX-1338 10 mg/kg
Tumor Volume (LWH/2 mm³)
2500
2000
1500
1000
500
0
-10
0
10
20
30
40
50
Days Post Dosing

FIG. 18I


OPM-2 Median Tumor Volumes
Vehicle PBS
DTIgG 30 mg/kg
MDX 1338 10 mg/kg
lenalidomide 50 + DTIgG 10 mg/kg
lenalidomide 50 + MDX-1338 10 mg/kg
Tumor Volume (LWH/2 mm ³)
2500
2000
1500
1000
500
0
-10
0
10
20
30
40
50
Days Post Dosing