Figure 1

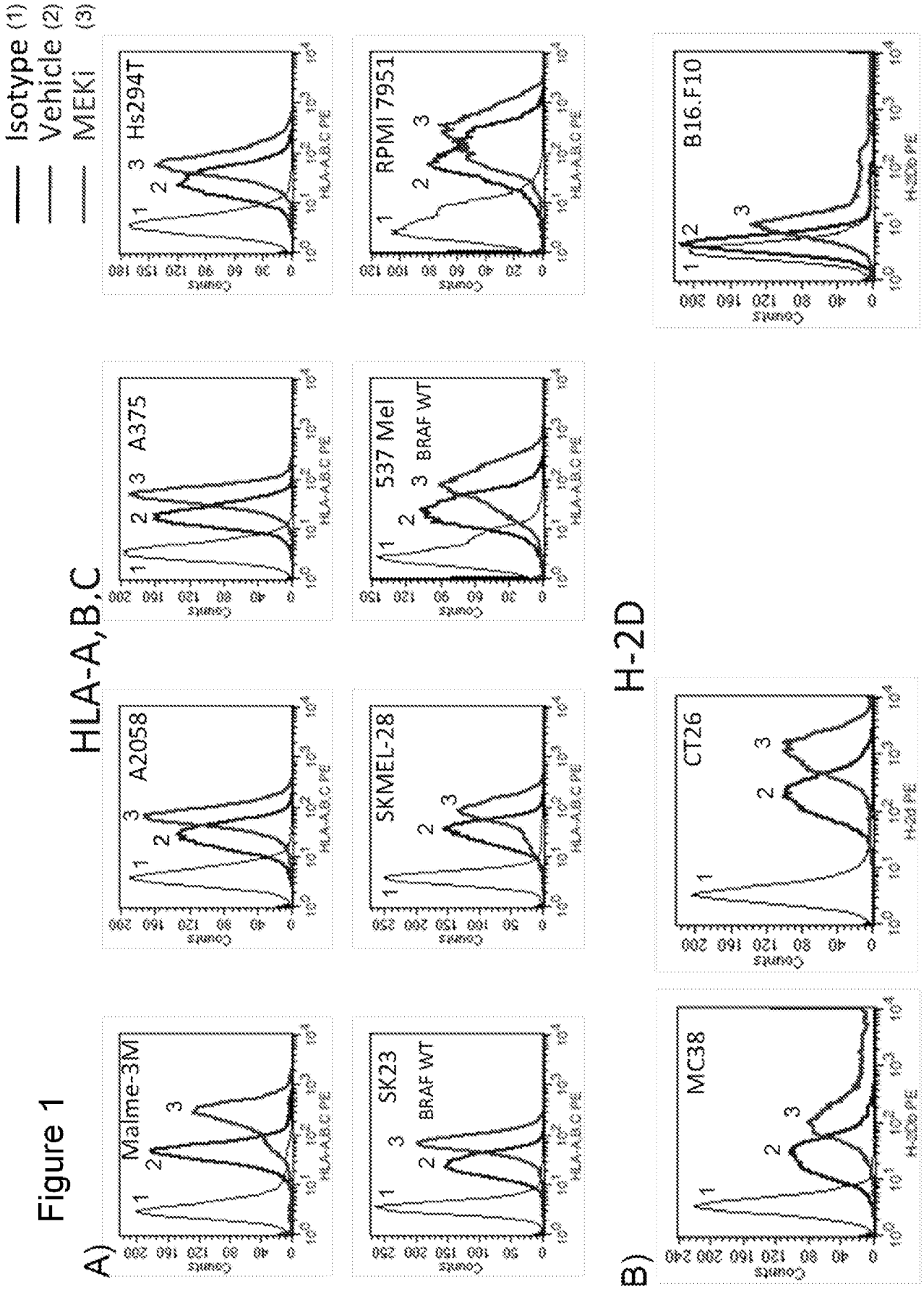

Isotype (1)
Vehicle (2)
MEKi (3)
A)
HLA-A,B,C
Malme-3M
A2058
A375
Hs294T
SK23
BRAF WT
SKMEL-28
537 Mel
BRAF WT
RPMI 7951
B)
H-2D
MC38
CT26
B16.F10
Counts
HLA-A,B,C PE
H-2Db PE

Figure 2

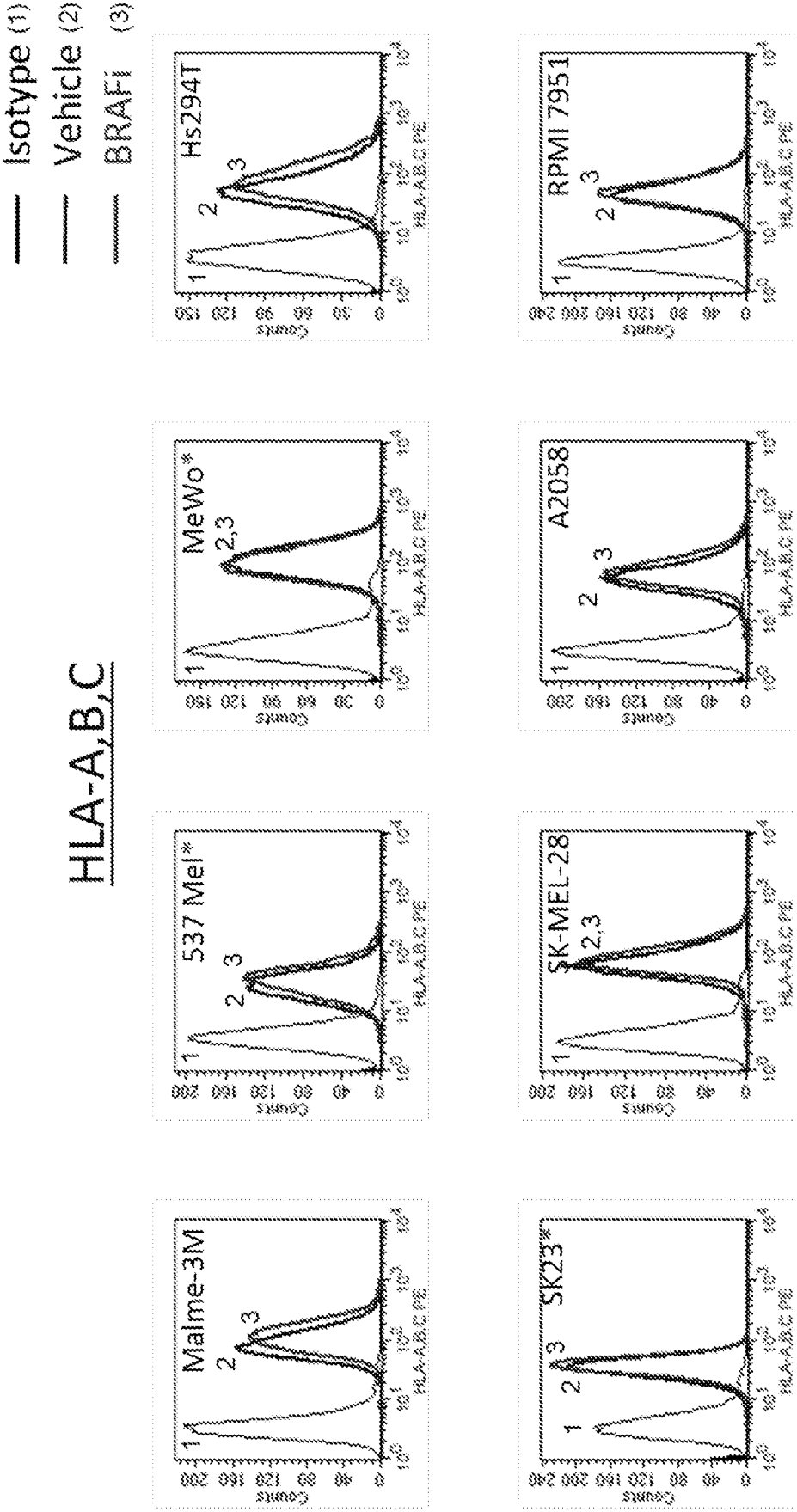
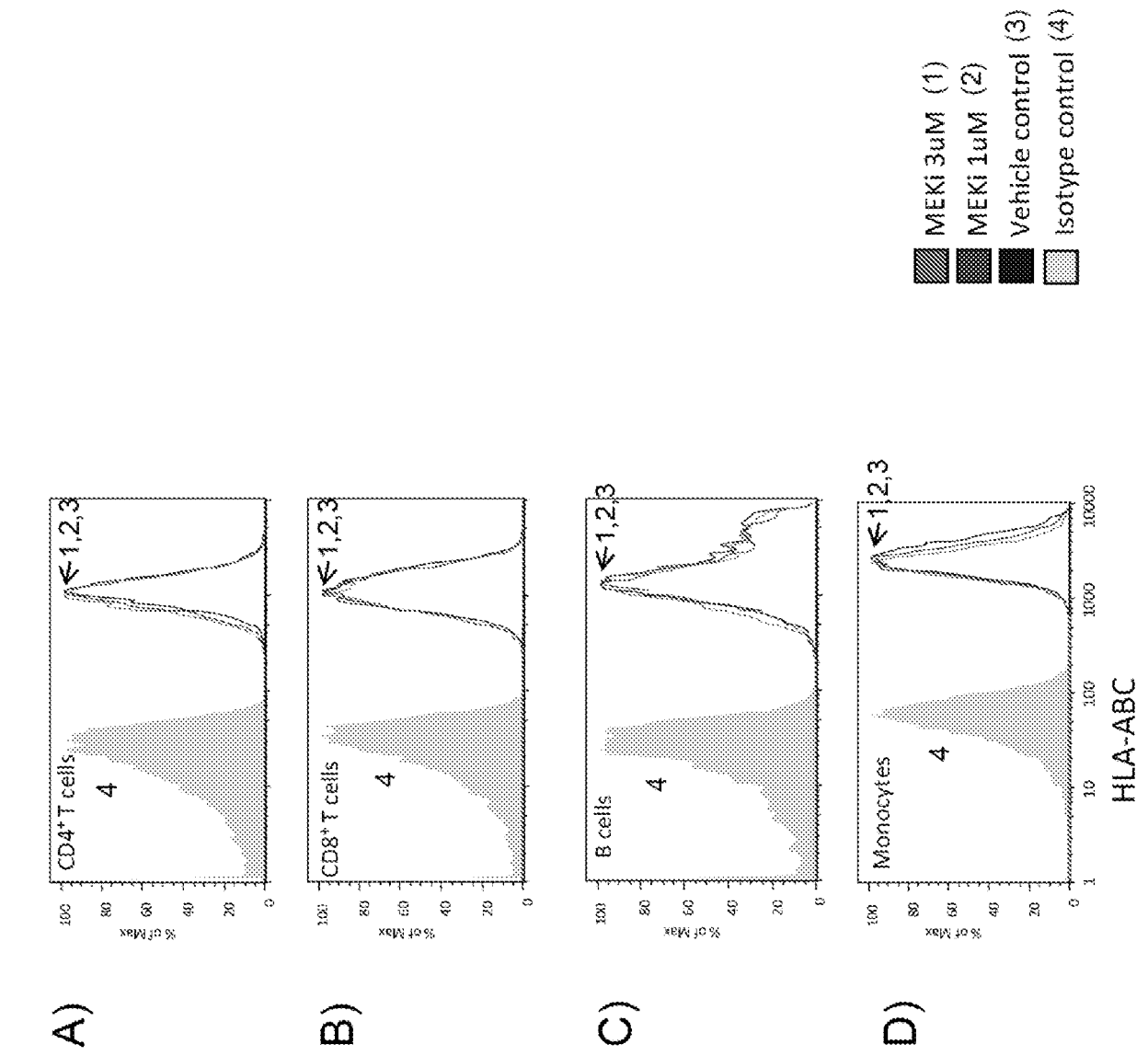

Isotype (1)
Vehicle (2)
BRAFi (3)
HLA-A,B,C
Hs294T
MeWo*
537 Mel*
A2058
RPMI 7951
SK-MEL-28
Malme-3M
SK23*
Counts
HLA-A,B,C PE

Figure 3


A)
B)
C)
D)
CD4+ T cells
CD8+ T cells
B cells
Monocytes
1,2,3
4
% of Max
HLA-ABC
MEKi 3uM (1)
MEKi 1uM (2)
Vehicle control (3)
Isotype control (4)

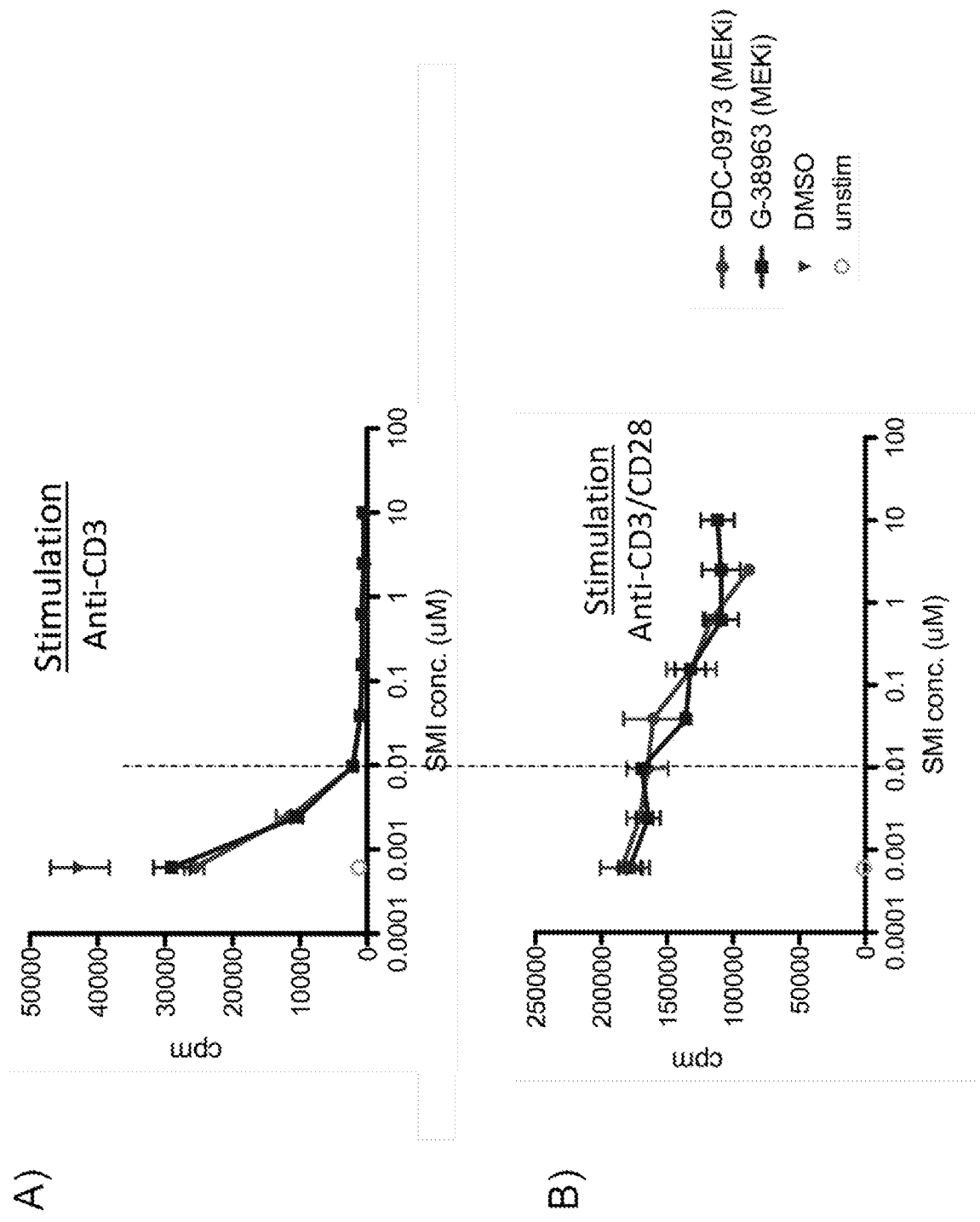

A)
Stimulation
Anti-CD3
cpm
50000
40000
30000
20000
10000
0
0.0001
0.001
0.01
0.1
1
10
100
SMI conc. (uM)
B)
Stimulation
Anti-CD3/CD28
cpm
250000
200000
150000
100000
50000
0
SMI conc. (uM)
GDC-0973 (MEKi)
G-38963 (MEKi)
DMSO
unstim

Figure 4

Figure 5

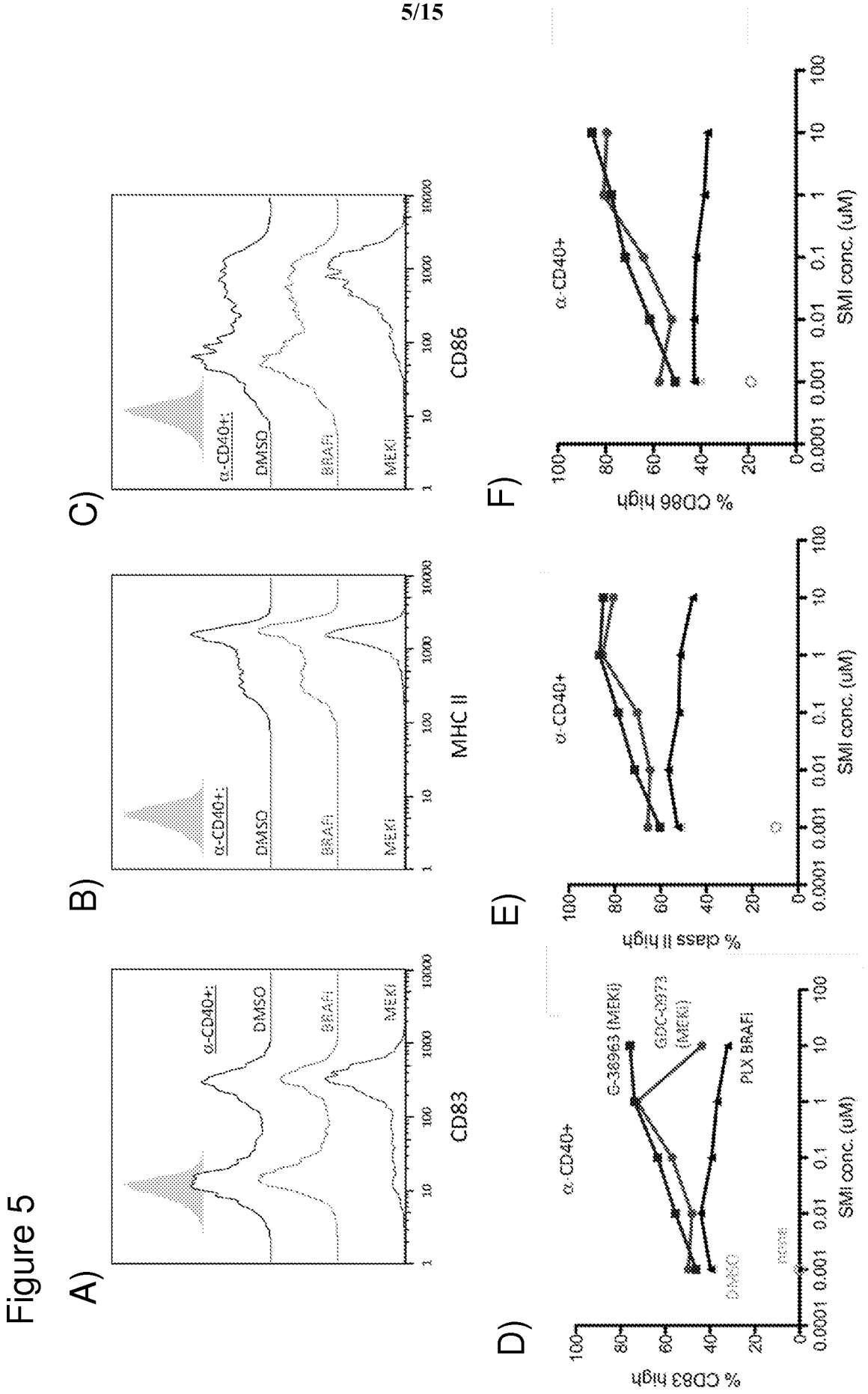

A)
B)
C)
α-CD40+
DMSO
BRAFi
MEKi
CD83
MHC II
CD86
D)
E)
F)
α-CD40+
G-38963 (MEKi)
GDC-0973 (MEKi)
PLX BRAFi
% CD83 high
% class II high
% CD86 high
SMI conc. (uM)

Figure 6

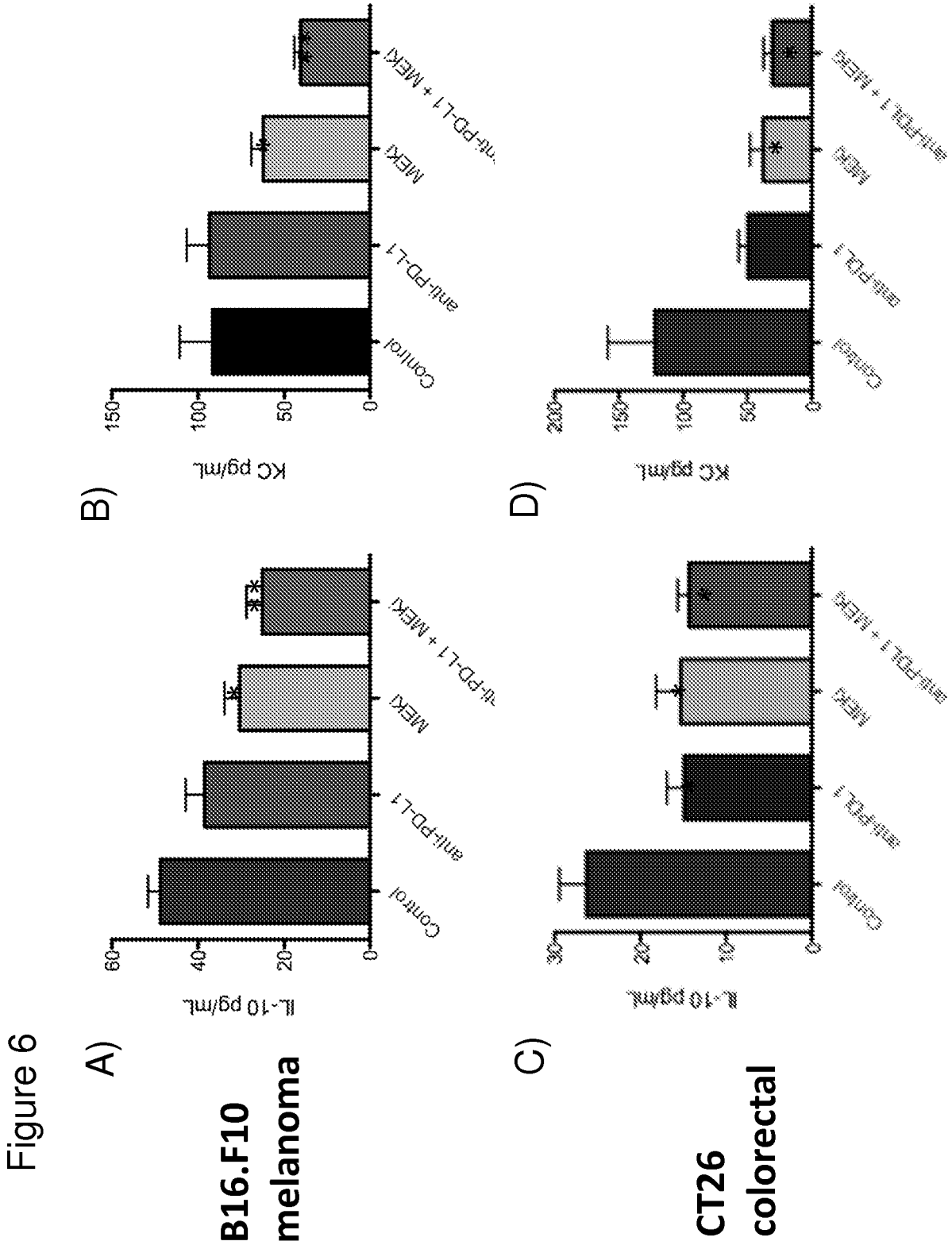

A)
B16.F10 melanoma
IL-10 pg/mL
60
40
20
0
Control
anti-PD-L1
MEKi
anti-PD-L1 + MEKi
B)
KC pg/mL
150
100
50
0
Control
anti-PD-L1
MEKi
anti-PD-L1 + MEKi
C)
CT26 colorectal
IL-10 pg/mL
30
20
10
0
Control
anti-PDL1
MEKi
anti-PDL1 + MEKi
D)
KC pg/mL
200
150
100
50
0
Control
anti-PDL1
MEKi
anti-PDL1 + MEKi

Figure 7

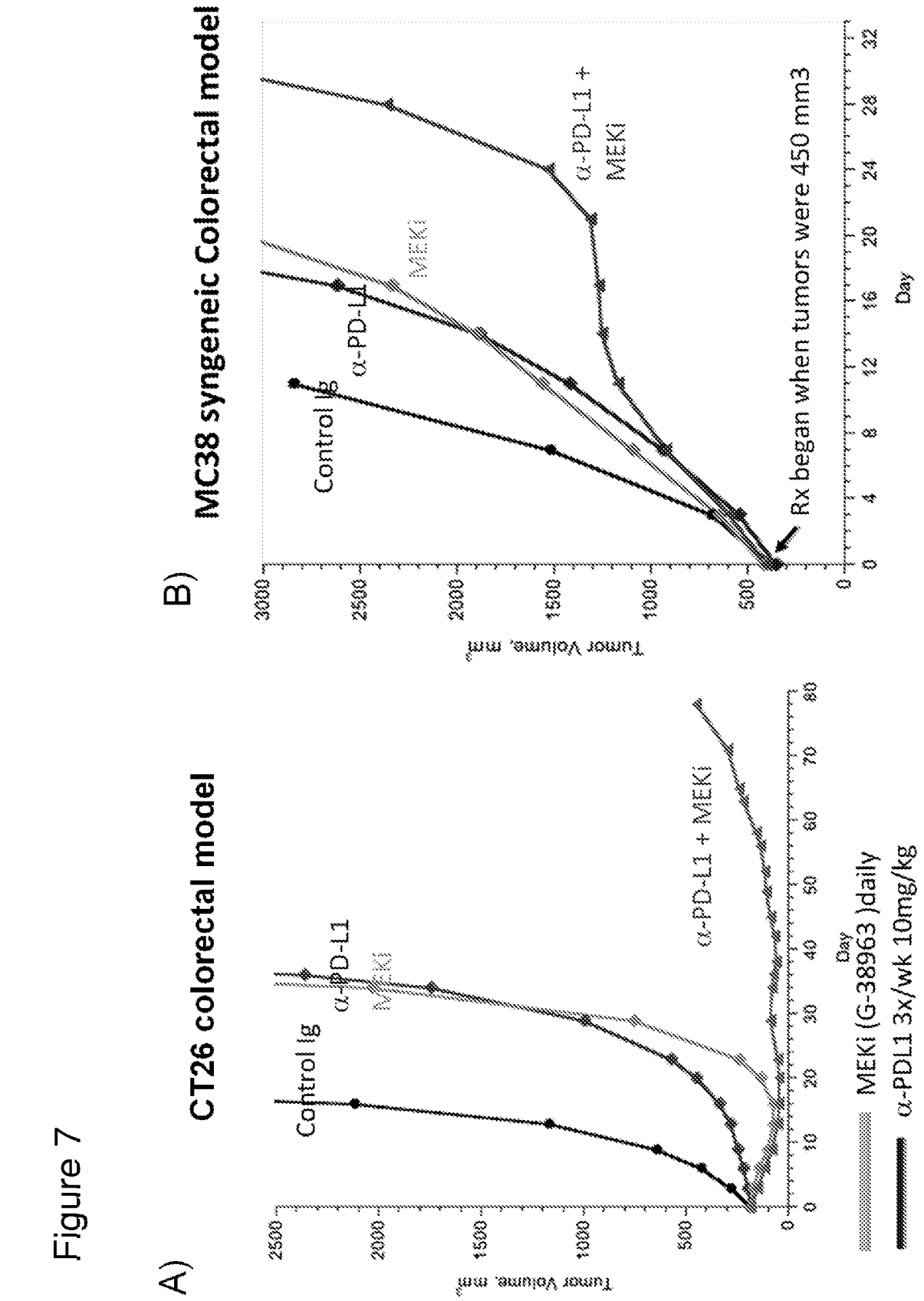

A)
CT26 colorectal model
Tumor Volume, mm3
Day
Control Ig
α-PD-L1
MEKi
α-PD-L1 + MEKi
MEKi (G-38963)daily
α-PDL1 3x/wk 10mg/kg
B)
MC38 syngeneic Colorectal model
Tumor Volume, mm3
Day
Control Ig
α-PD-L1
MEKi
α-PD-L1 + MEKi
Rx began when tumors were 450 mm3

Figure 8

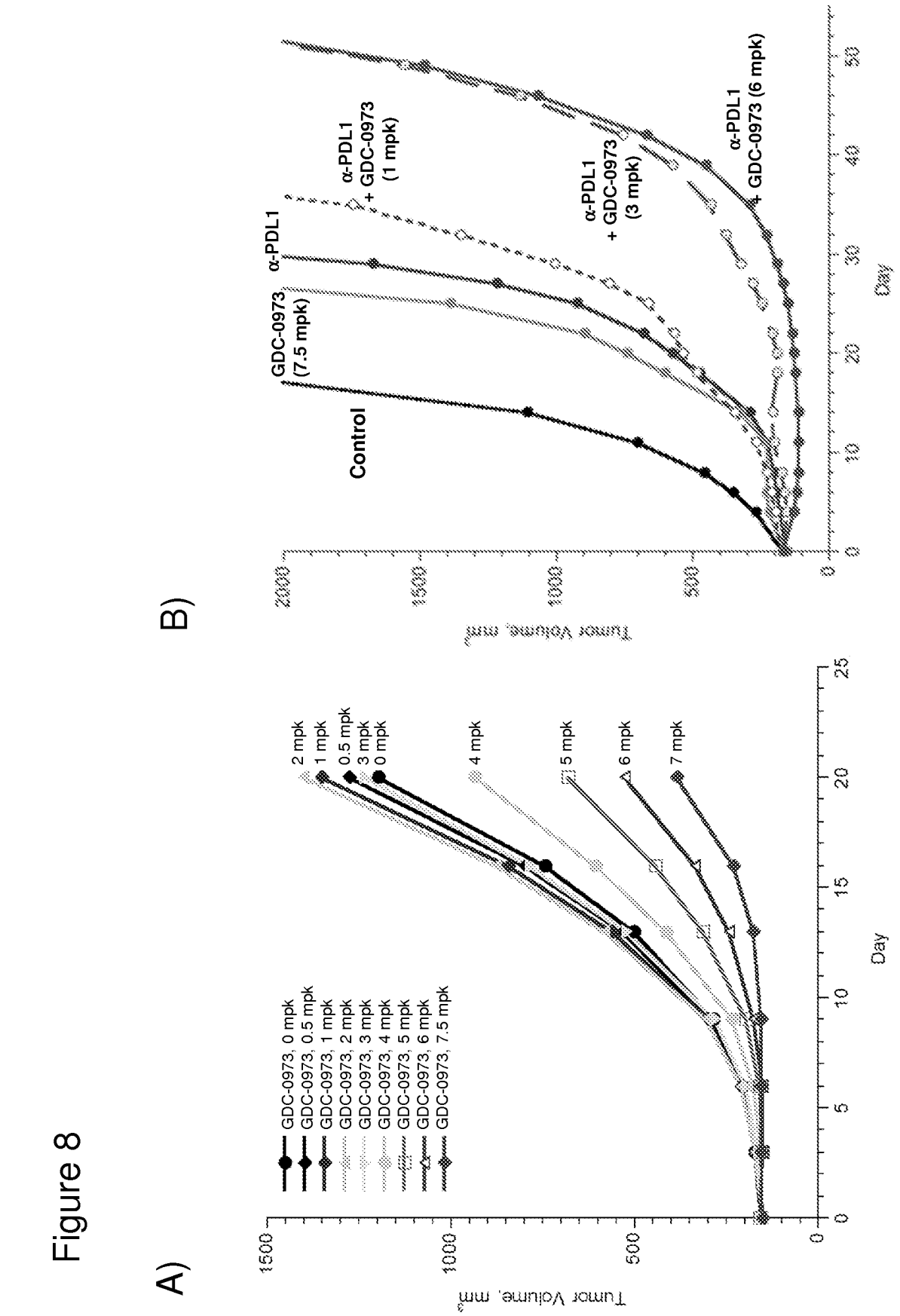
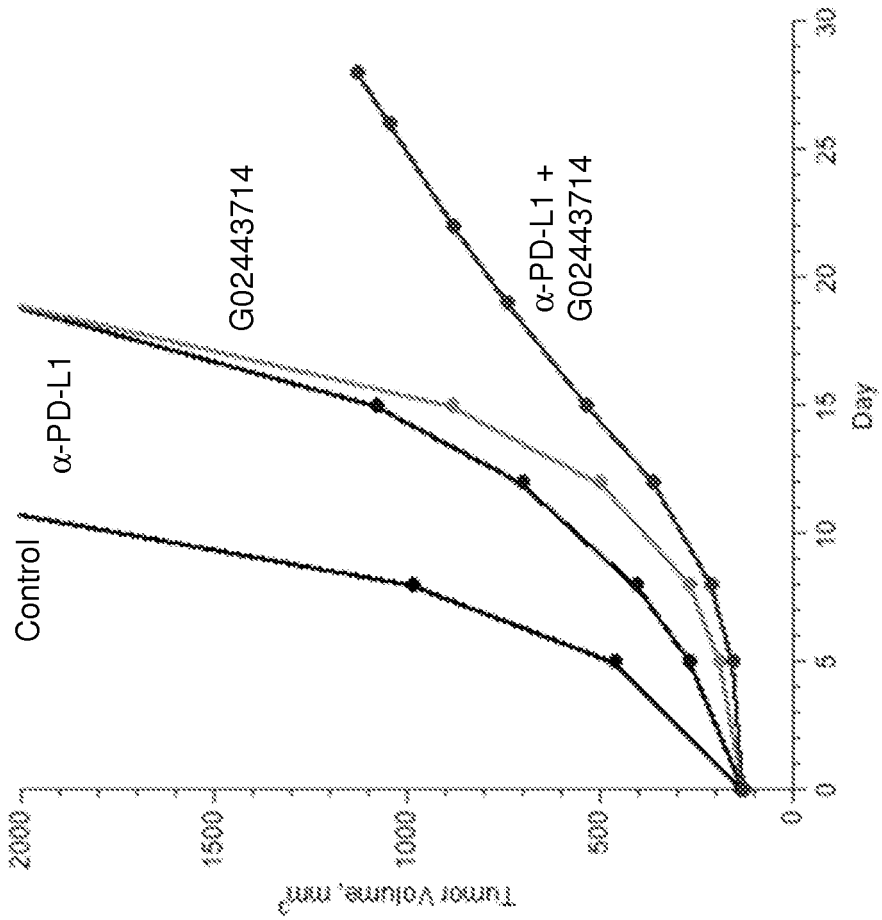

A)
GDC-0973, 0 mpk
GDC-0973, 0.5 mpk
GDC-0973, 1 mpk
GDC-0973, 2 mpk
GDC-0973, 3 mpk
GDC-0973, 4 mpk
GDC-0973, 5 mpk
GDC-0973, 6 mpk
GDC-0973, 7.5 mpk
2 mpk
1 mpk
0.5 mpk
3 mpk
0 mpk
4 mpk
5 mpk
6 mpk
7 mpk
Tumor Volume, mm3
Day
B)
α-PDL1
GDC-0973 (7.5 mpk)
Control
α-PDL1 + GDC-0973 (1 mpk)
α-PDL1 + GDC-0973 (3 mpk)
α-PDL1 + GDC-0973 (6 mpk)
Tumor Volume, mm3
Day

Figure 9



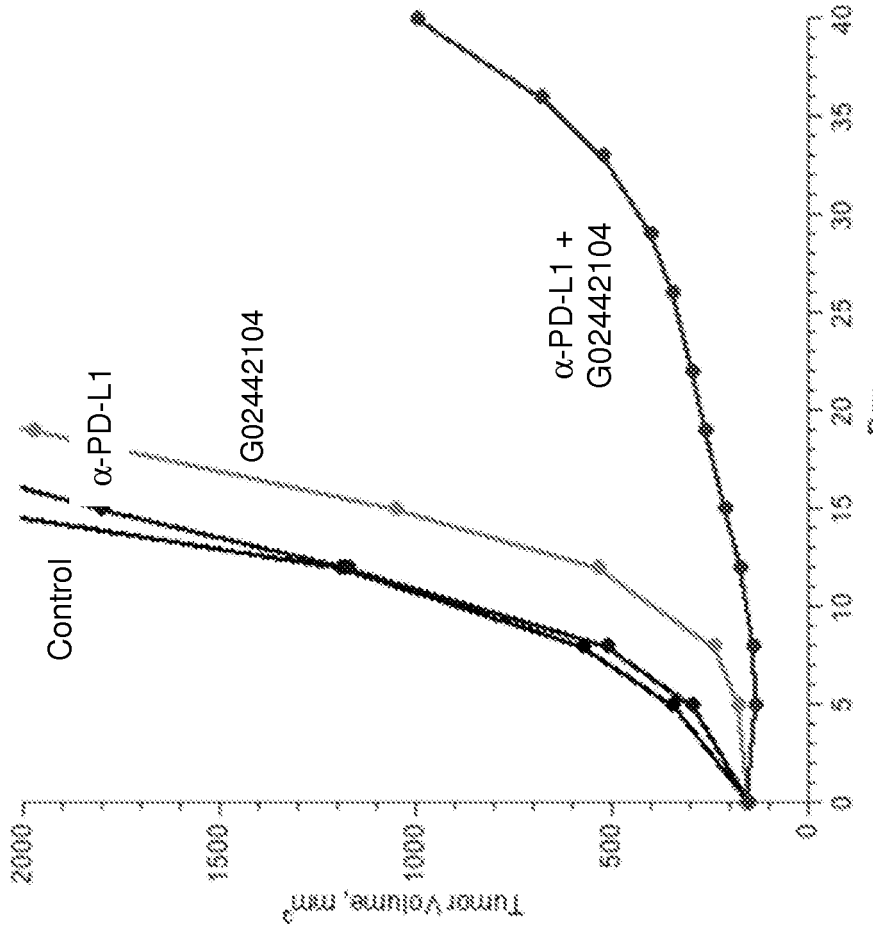
Control: TTP5X = 6.5 days, 0% TGI, 0% PR

anti-PD-L1: TTP5X = 12 days, 60% TGI, 0% PR

G02443714: TTP5X = 14 days, 75% TGI, 0% PR

anti-PD-L1 + G02443714: TTP5x = **18 days, 85% TGI, 20% PR**

Figure 10



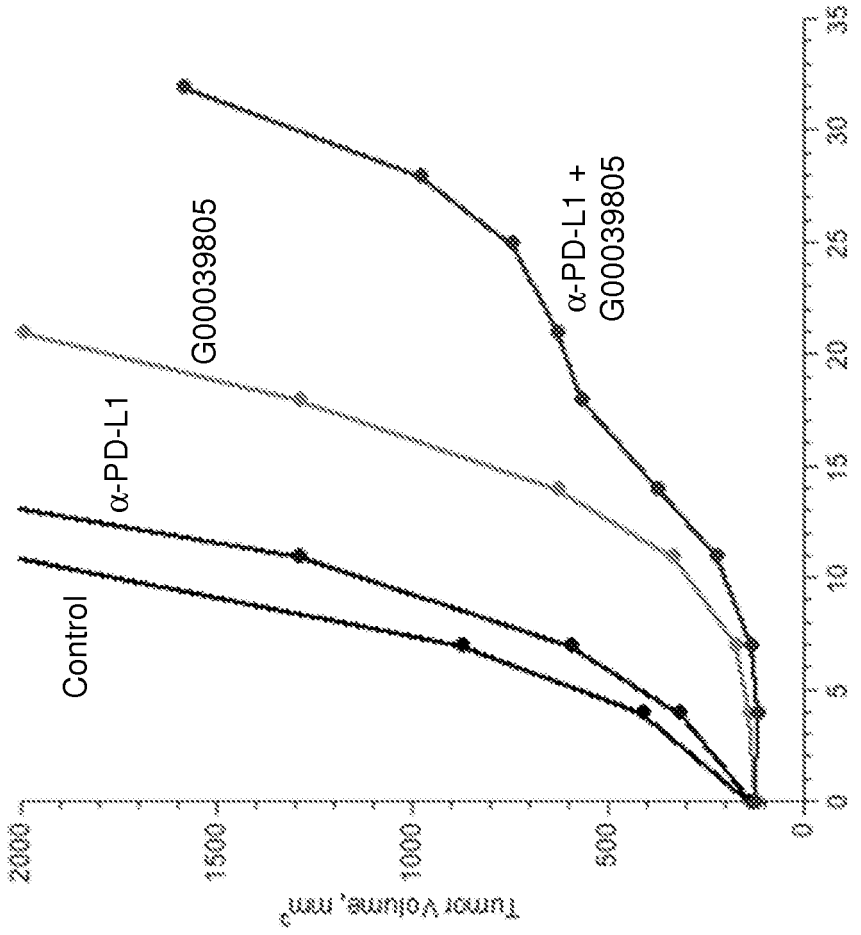
Control: TTP5X = 10 days, 0% TGI, 0% PR, 0% CR

anti-PD-L1: TTP5X = 10 days, -33% TGI, 10% PR, 0% CR

G02442104: TTP5X = 14 days, 1% TGI, 0% PR, 0% CR

anti-PD-L1 + G02442104: TTP5x = **37.5 days, 93% TGI, 40% PR, 10% CR**

Figure 11



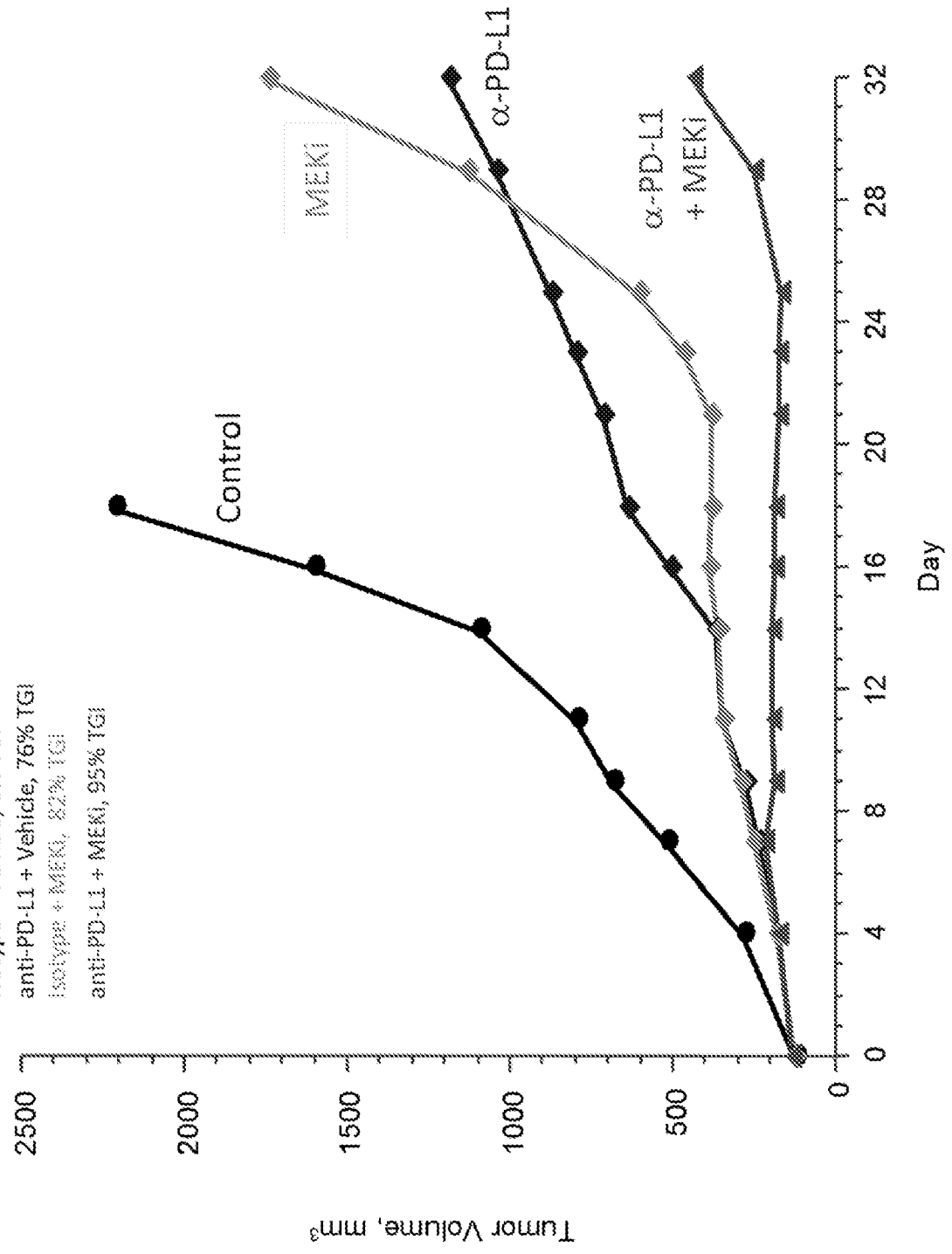
Control: TTP5X = 6 days, 0% TGI, 0% PR

anti-PD-L1: TTP5X = 7.5 days, 6% TGI, 0% PR

G00039805: TTP5X = 14.5 days, 47% TGI, 10% PR

anti-PD-L1 + G00039805: TTP5x = **22 days, 80% TGI, 30% PR**

Figure 12


Cloudman S91 melanoma model
Isotype + Vehicle, 0% TGI
anti-PD-L1 + Vehicle, 76% TGI
Isotype + MEKi, 82% TGI
anti-PD-L1 + MEKi, 95% TGI
Control
MEKi
α-PD-L1
α-PD-L1 + MEKi
Tumor Volume, mm3
2500
2000
1500
1000
500
0
0
4
8
12
16
20
24
28
32
Day

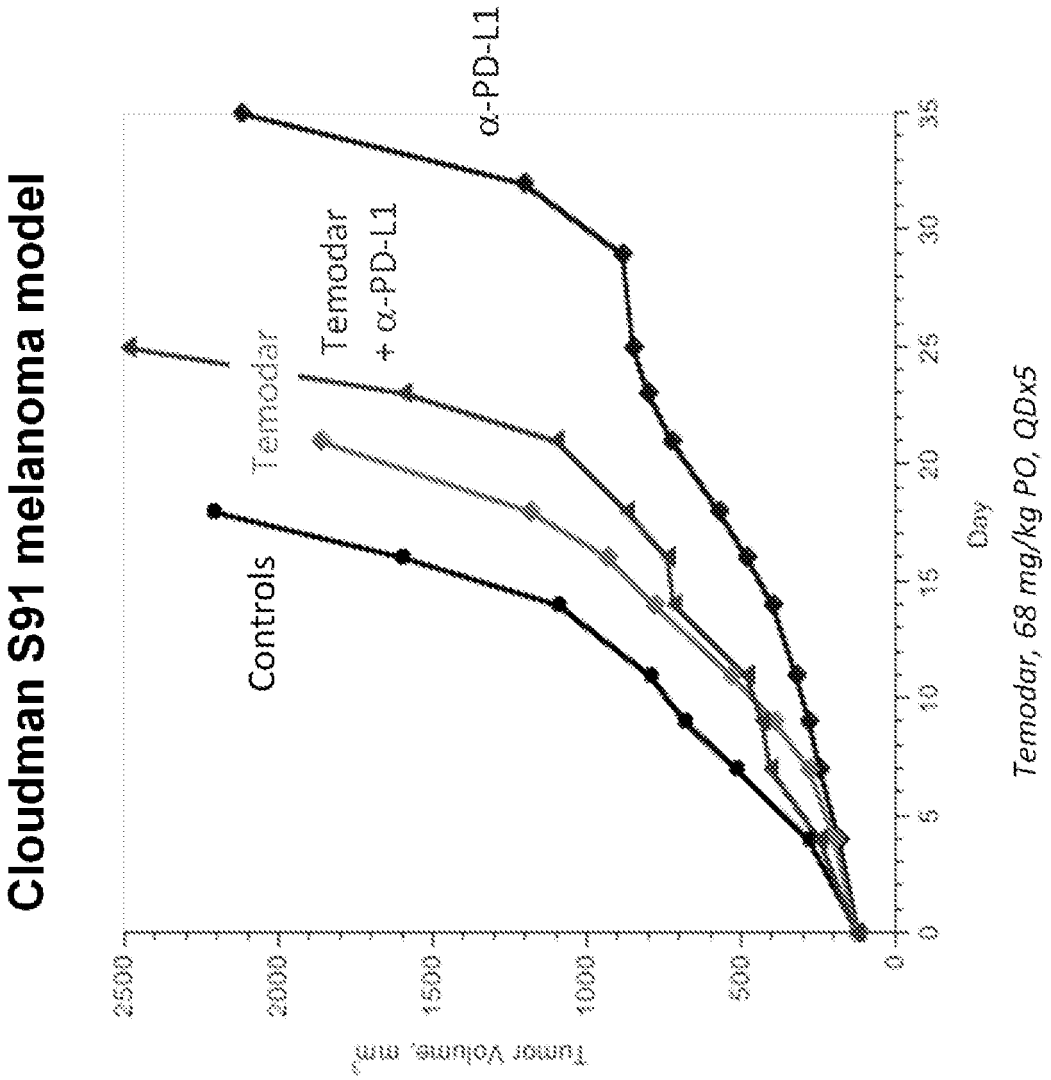

Cloudman S91 melanoma model
Tumor Volume, mm³
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
35
Day
Controls
Temodar
Temodar
+ α-PD-L1
α-PD-L1
Temodar, 68 mg/kg PO, QDx5

Figure 13

Figure 14

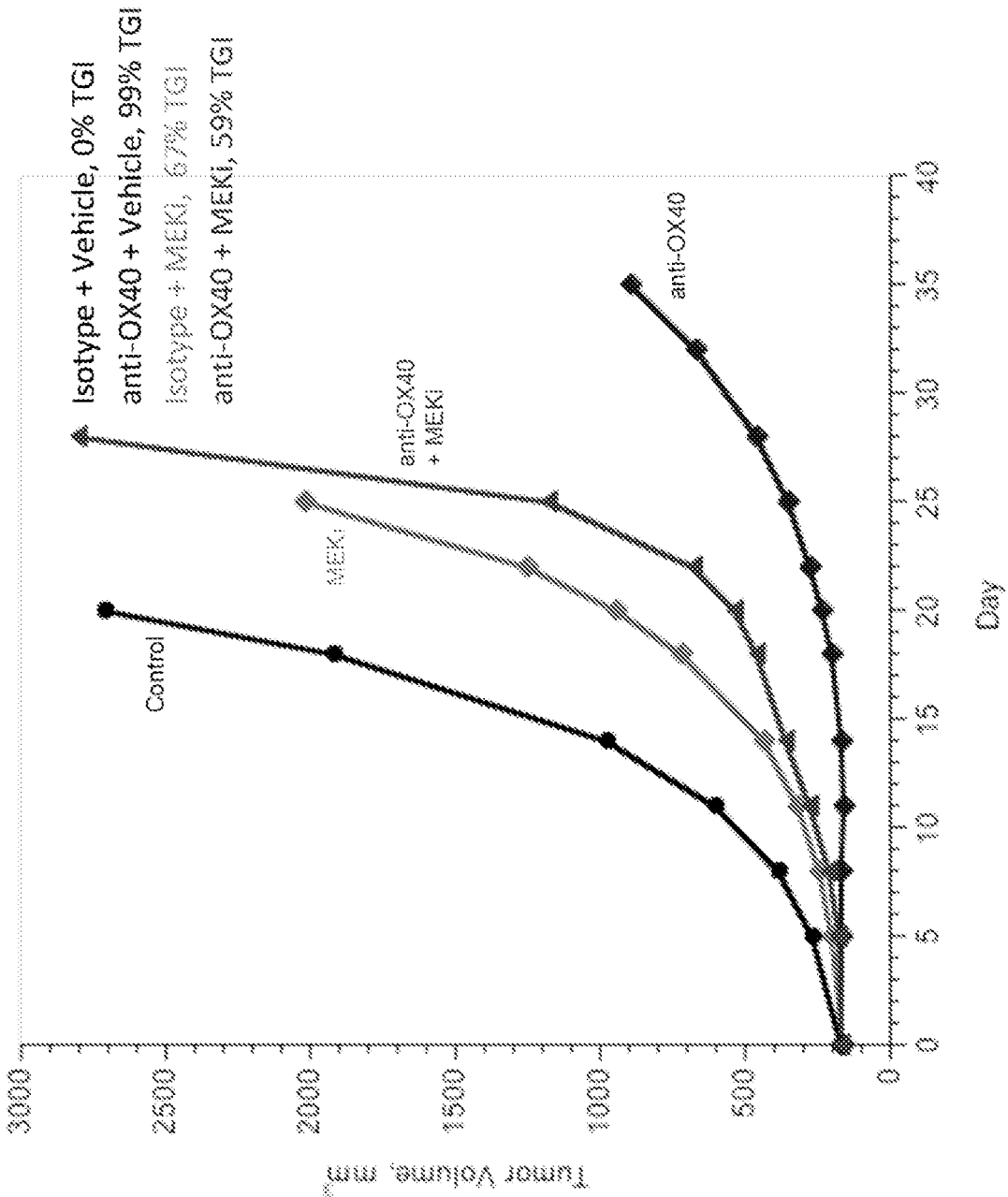
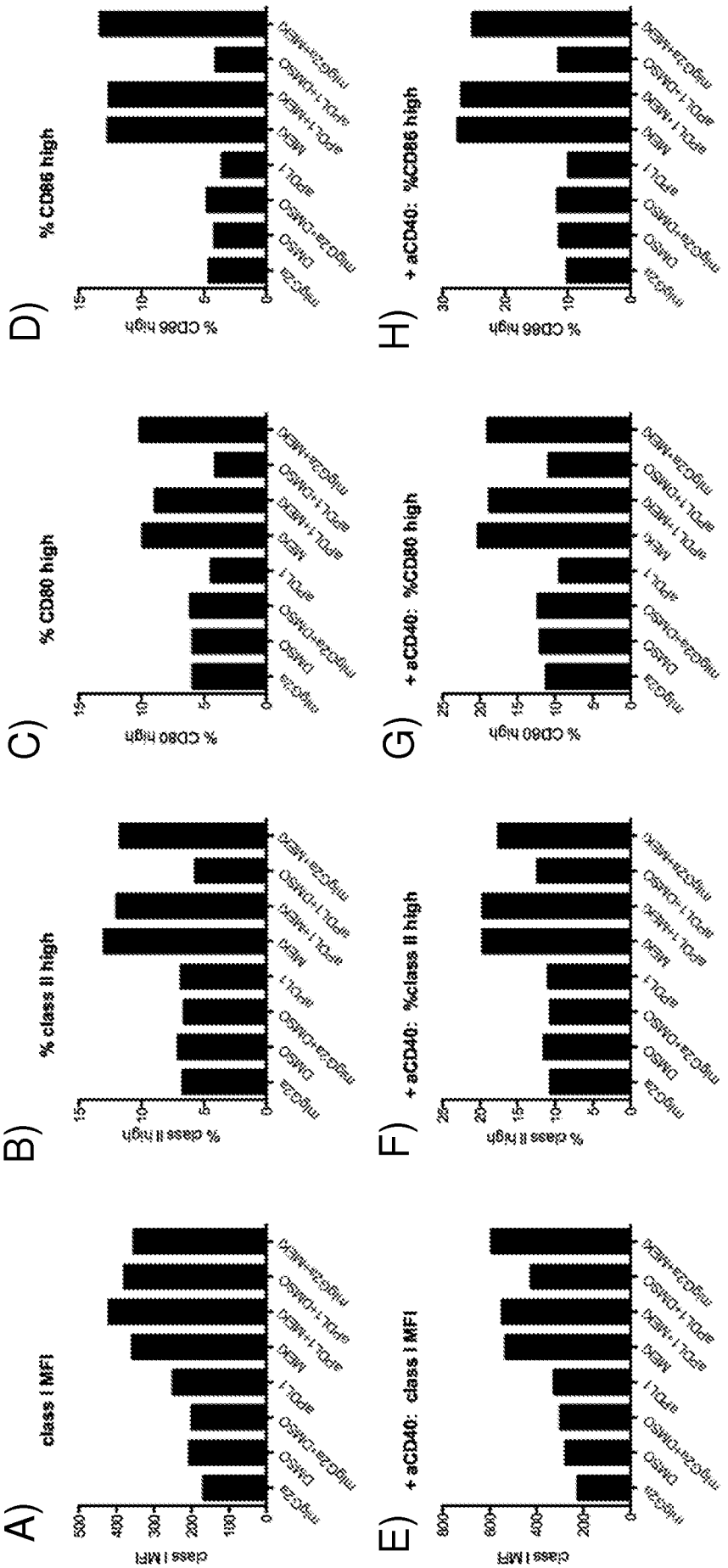

MC38 syngeneic colorectal model
Isotype + Vehicle, 0% TGI
anti-OX40 + Vehicle, 99% TGI
Isotype + MEKi, 67% TGI
anti-OX40 + MEKi, 59% TGI
Control
MEKi
anti-OX40 + MEKi
anti-OX40
Tumor Volume, mm3
Day
0
500
1000
1500
2000
2500
3000
0
5
10
15
20
25
30
35
40

Figure 15


A)
class I MFI
B)
% class II high
C)
% CD80 high
D)
% CD86 high
E)
+ aCD40: class I MFI
F)
+ aCD40: %class II high
G)
+ aCD40: %CD80 high
H)
+ aCD40: %CD86 high
mIgG2a
DMSO
mIgG2a+DMSO
aPDL1
aPDL1+MEK
MEKi
aPDL1+DMSO
aPDL1+MEKi
mIgG2a+MEK
mIgG2a+MEKi