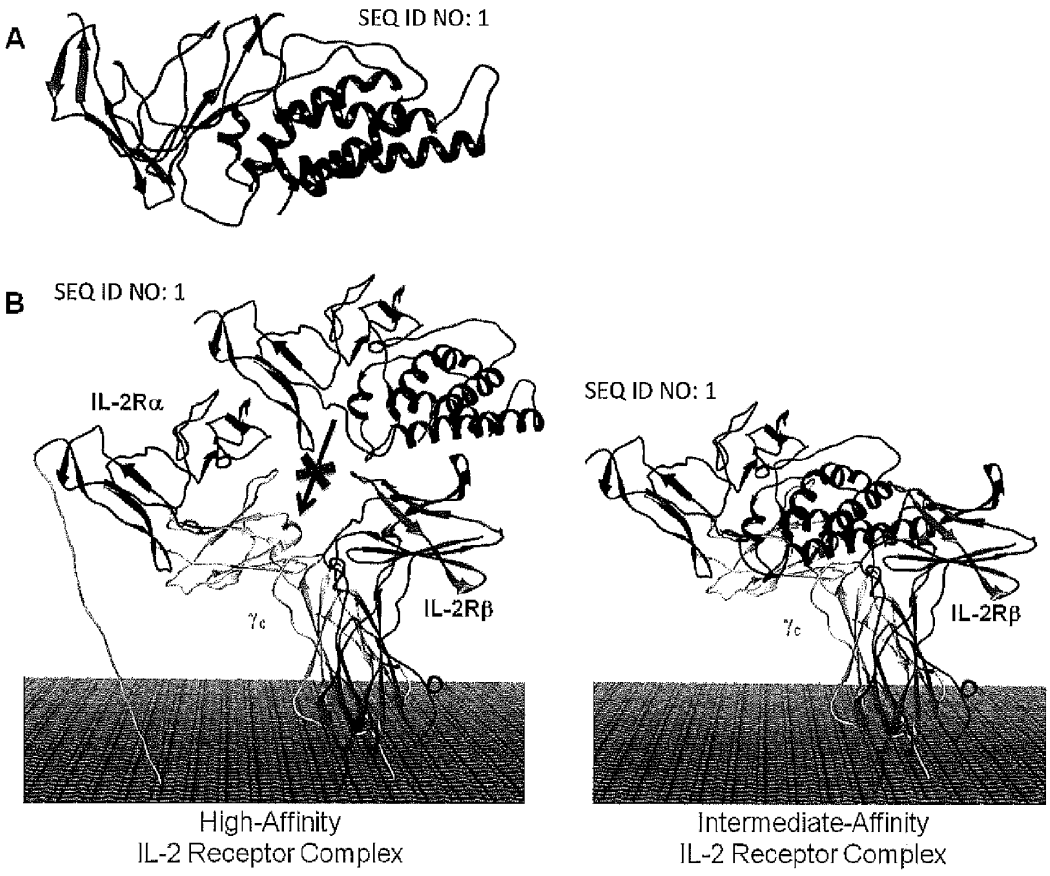

A
SEQ ID NO: 1
B
SEQ ID NO: 1
IL-2Rα
IL-2Rβ
γc
High-Affinity
IL-2 Receptor Complex
SEQ ID NO: 1
IL-2Rβ
γc
Intermediate-Affinity
IL-2 Receptor Complex

FIG. 1

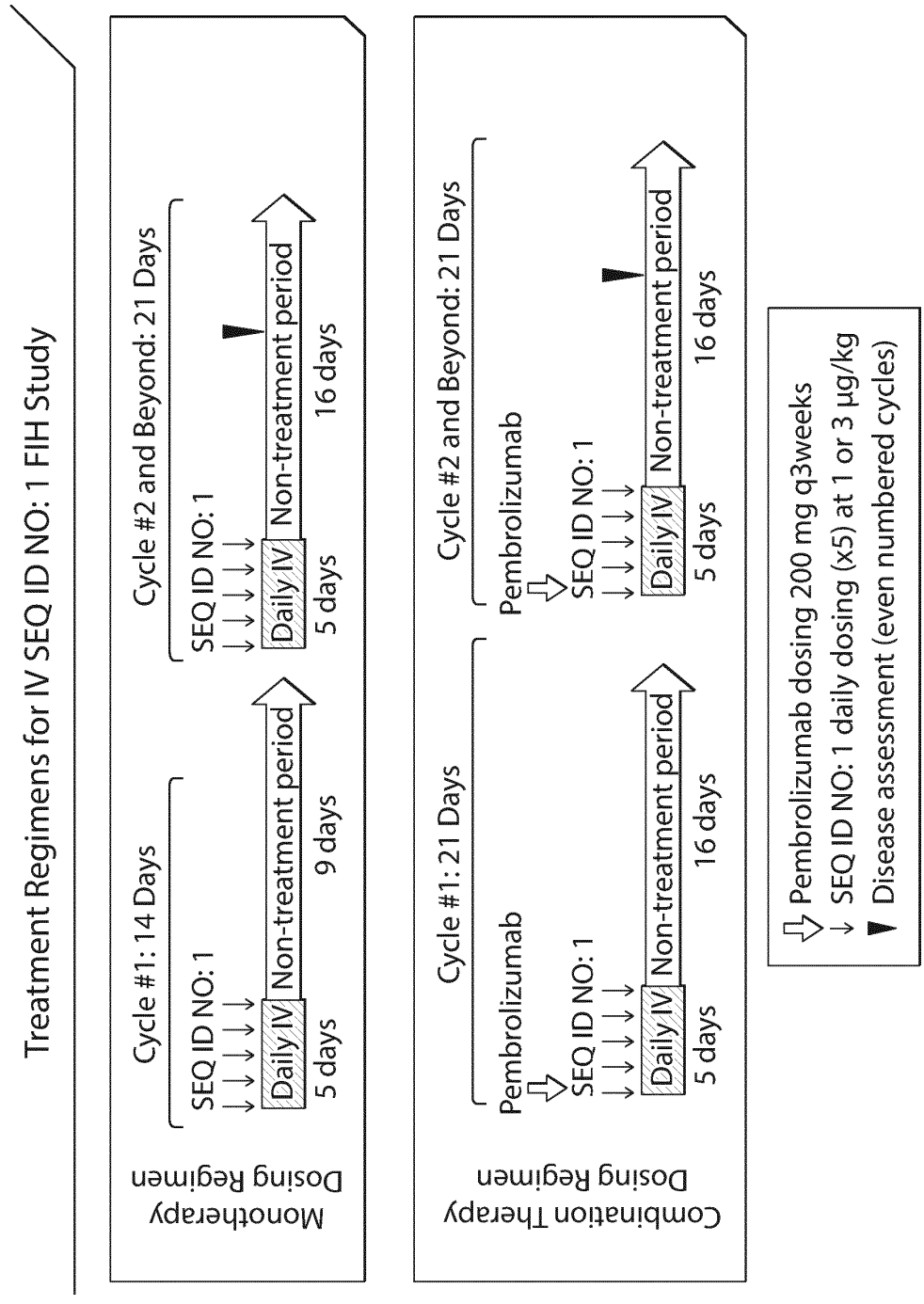
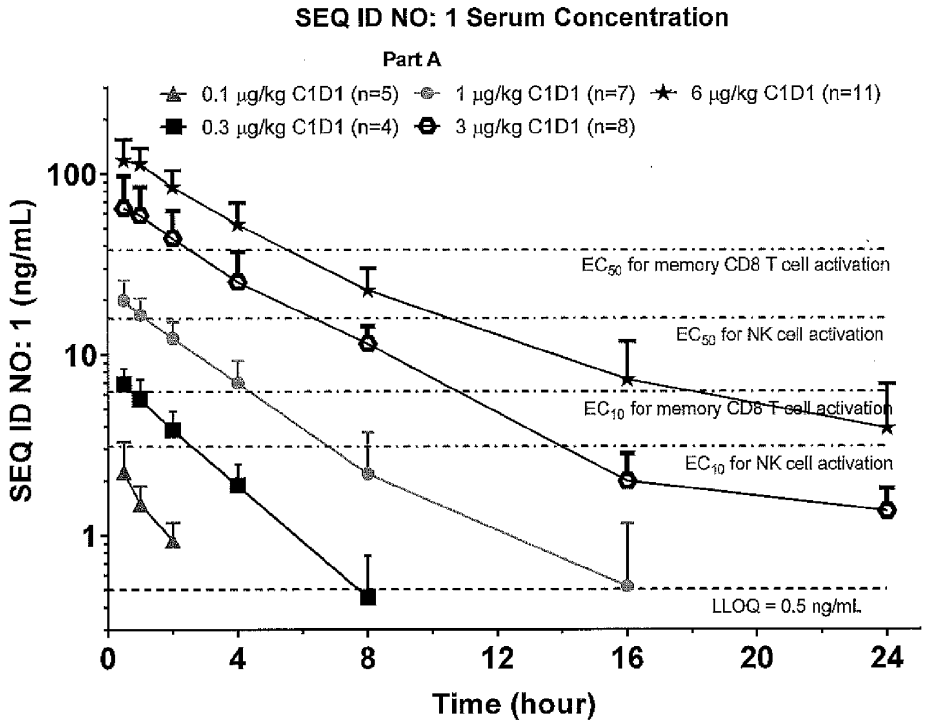

Treatment Regimens for IV SEQ ID NO: 1 FIH Study
Monotherapy Dosing Regimen
Cycle #1: 14 Days
SEQ ID NO: 1
Daily IV
5 days
Non-treatment period
9 days
Cycle #2 and Beyond: 21 Days
SEQ ID NO: 1
Daily IV
5 days
Non-treatment period
16 days
Combination Therapy Dosing Regimen
Cycle #1: 21 Days
Pembrolizumab
SEQ ID NO: 1
Daily IV
5 days
Non-treatment period
16 days
Cycle #2 and Beyond: 21 Days
Pembrolizumab
SEQ ID NO: 1
Daily IV
5 days
Non-treatment period
16 days
Pembrolizumab dosing 200 mg q3weeks
SEQ ID NO: 1 daily dosing (x5) at 1 or 3 µg/kg
Disease assessment (even numbered cycles)

FIG. 2


SEQ ID NO: 1 Serum Concentration
Part A
0.1 µg/kg C1D1 (n=5)
1 µg/kg C1D1 (n=7)
6 µg/kg C1D1 (n=11)
0.3 µg/kg C1D1 (n=4)
3 µg/kg C1D1 (n=8)
SEQ ID NO: 1 (ng/mL)
100
10
1
EC50 for memory CD8 T cell activation
EC50 for NK cell activation
EC10 for memory CD8 T cell activation
EC10 for NK cell activation
LLOQ = 0.5 ng/mL
0
4
8
12
16
20
24
Time (hour)

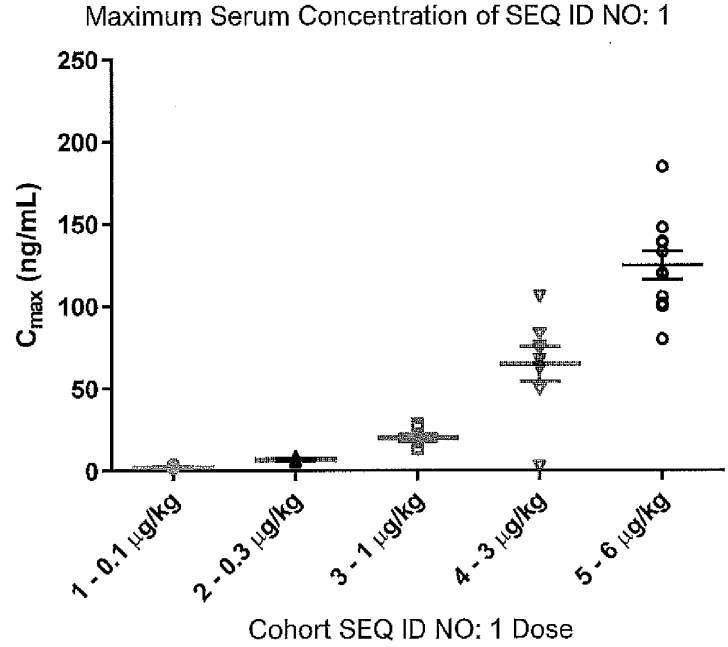

Maximum Serum Concentration of SEQ ID NO: 1
Cmax (ng/mL)
250
200
150
100
50
0
1 - 0.1 µg/kg
2 - 0.3 µg/kg
3 - 1 µg/kg
4 - 3 µg/kg
5 - 6 µg/kg
Cohort SEQ ID NO: 1 Dose

FIG. 3

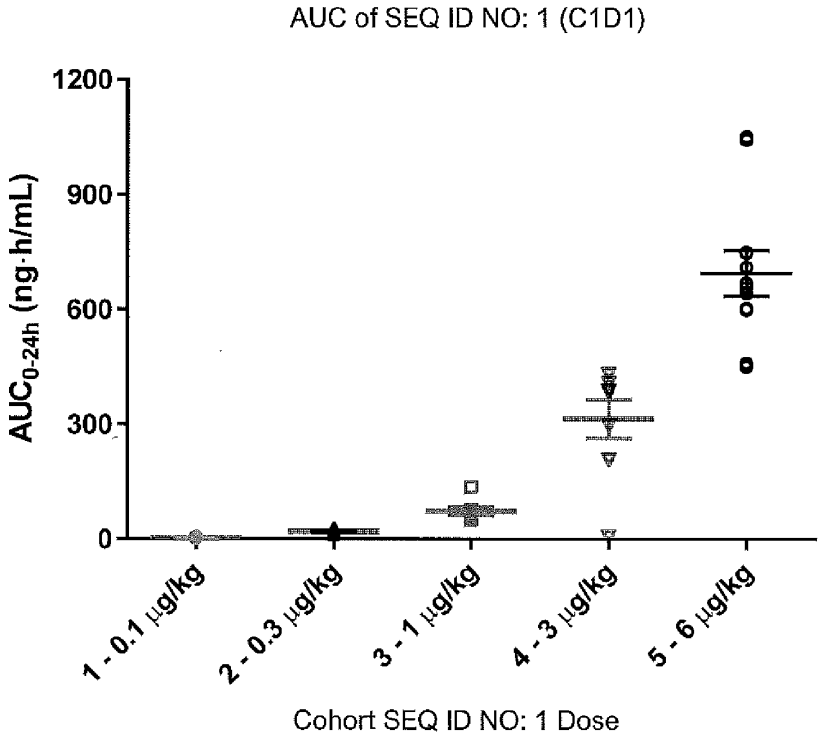

AUC of SEQ ID NO: 1 (C1D1)
1200
900
600
300
0
AUC0-24h (ng·h/mL)
1 - 0.1 µg/kg
2 - 0.3 µg/kg
3 - 1 µg/kg
4 - 3 µg/kg
5 - 6 µg/kg
Cohort SEQ ID NO: 1 Dose

FIG. 3 cont...

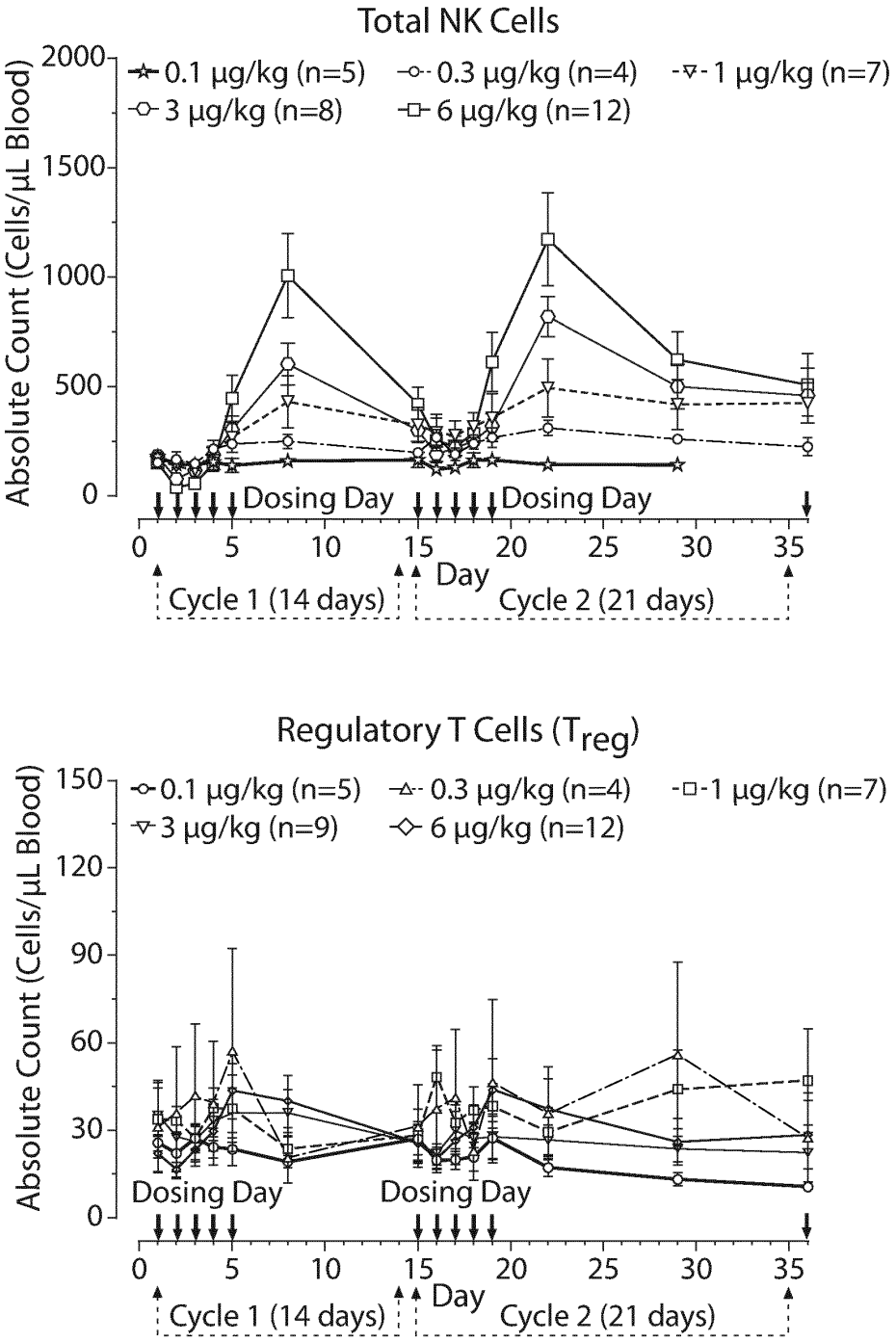
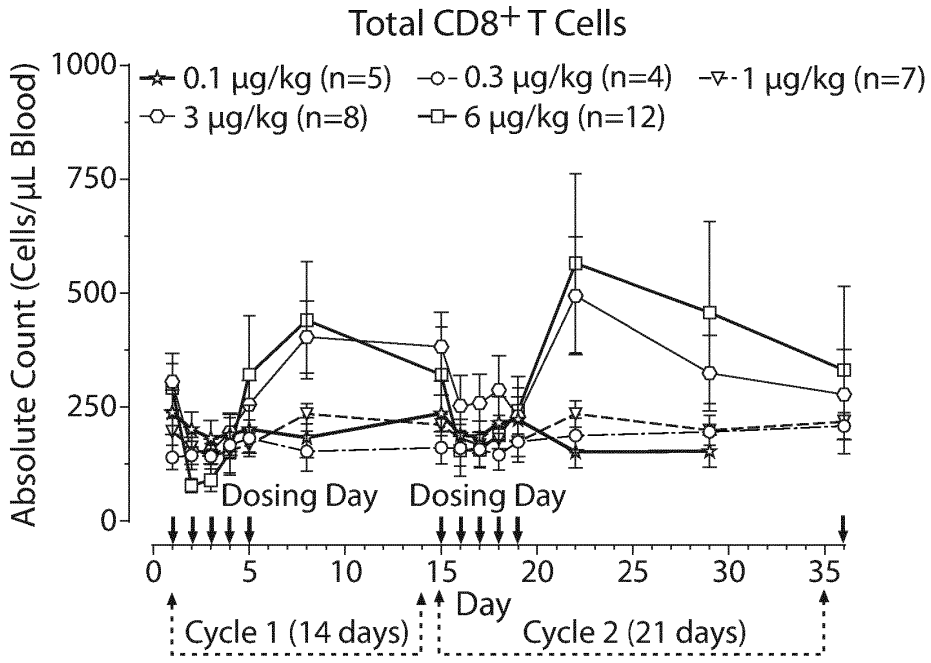

Total NK Cells
0.1 µg/kg (n=5)
0.3 µg/kg (n=4)
1 µg/kg (n=7)
3 µg/kg (n=8)
6 µg/kg (n=12)
Absolute Count (Cells/µL Blood)
2000
1500
1000
500
0
Dosing Day
Dosing Day
0
5
10
15
20
25
30
35
Day
Cycle 1 (14 days)
Cycle 2 (21 days)
Regulatory T Cells (T_{reg})
0.1 µg/kg (n=5)
0.3 µg/kg (n=4)
1 µg/kg (n=7)
3 µg/kg (n=9)
6 µg/kg (n=12)
Absolute Count (Cells/µL Blood)
150
120
90
60
30
0
Dosing Day
Dosing Day
0
5
10
15
20
25
30
35
Day
Cycle 1 (14 days)
Cycle 2 (21 days)

FIG. 4


Total CD8+ T Cells
Absolute Count (Cells/µL Blood)
1000
750
500
250
0
0.1 µg/kg (n=5)
0.3 µg/kg (n=4)
1 µg/kg (n=7)
3 µg/kg (n=8)
6 µg/kg (n=12)
Dosing Day
Dosing Day
0
5
10
15
20
25
30
35
Day
Cycle 1 (14 days)
Cycle 2 (21 days)

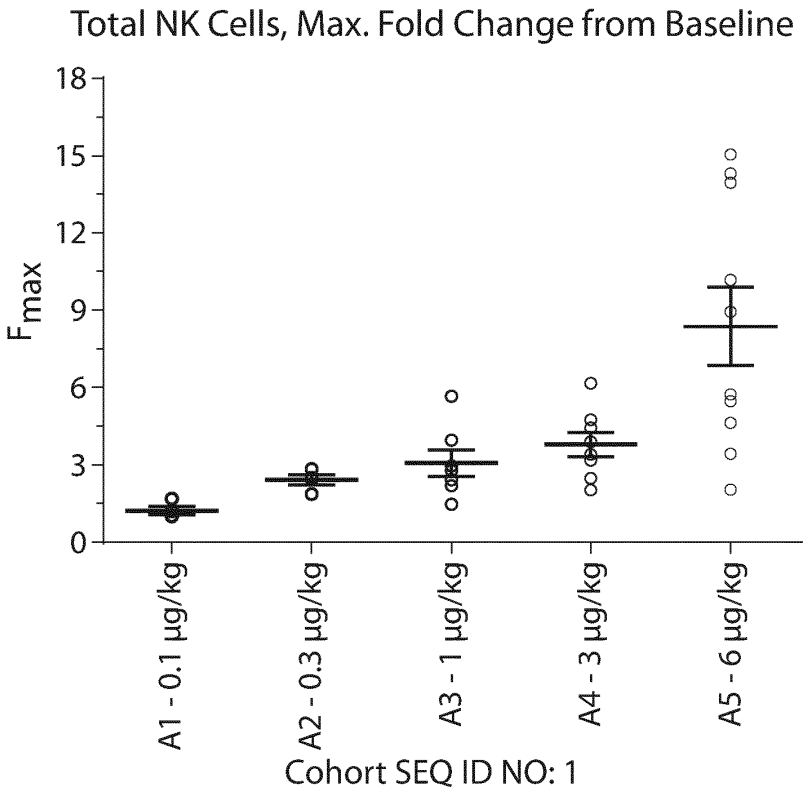
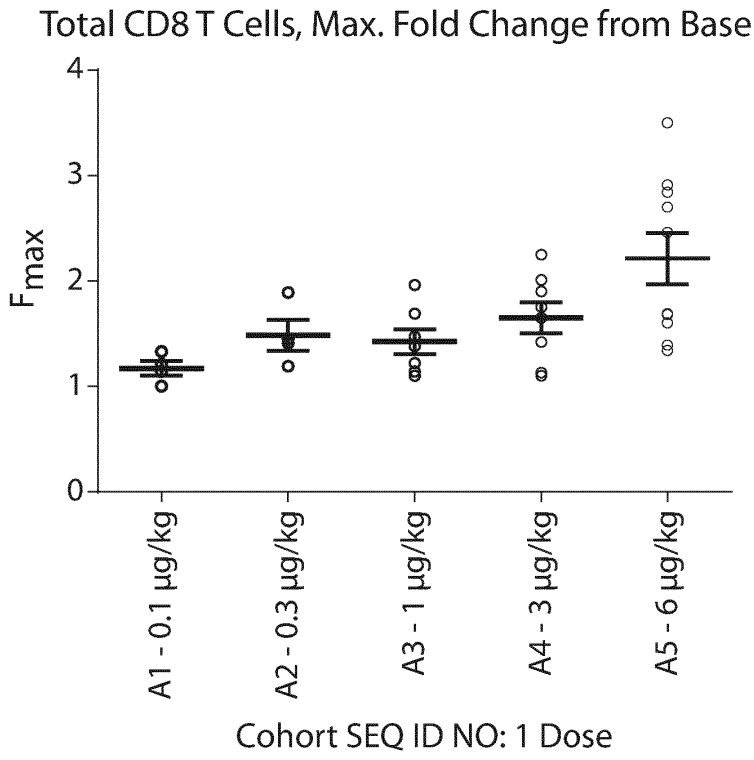

Total NK Cells, Max. Fold Change from Baseline
Fmax
18
15
12
9
6
3
0
A1 - 0.1 µg/kg
A2 - 0.3 µg/kg
A3 - 1 µg/kg
A4 - 3 µg/kg
A5 - 6 µg/kg
Cohort SEQ ID NO: 1

FIG. 4 Cont.


Total CD8 T Cells, Max. Fold Change from Baseline
Fmax
0
1
2
3
4
A1 - 0.1 µg/kg
A2 - 0.3 µg/kg
A3 - 1 µg/kg
A4 - 3 µg/kg
A5 - 6 µg/kg
Cohort SEQ ID NO: 1 Dose

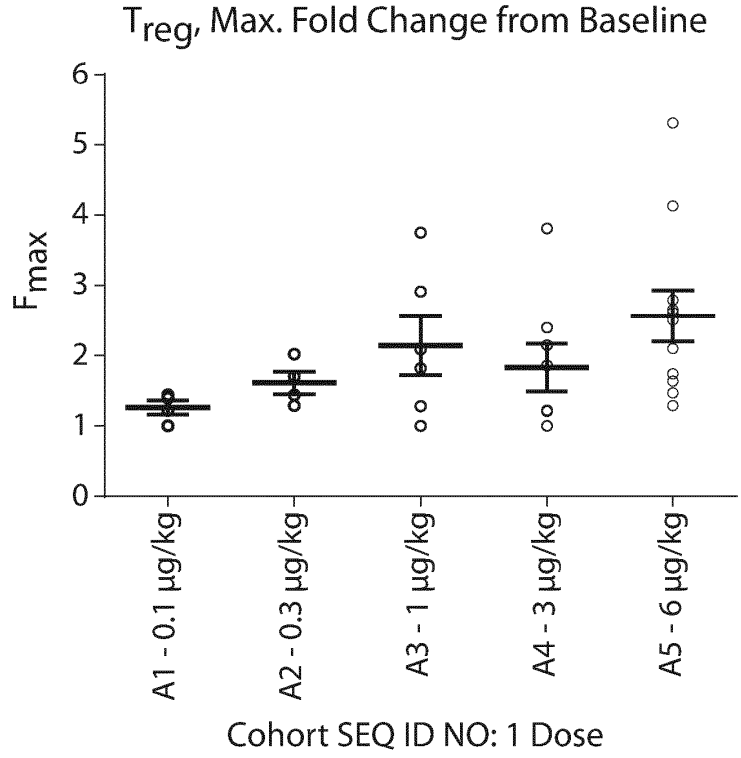

Treg, Max. Fold Change from Baseline
Fmax
0
1
2
3
4
5
6
A1 - 0.1 µg/kg
A2 - 0.3 µg/kg
A3 - 1 µg/kg
A4 - 3 µg/kg
A5 - 6 µg/kg
Cohort SEQ ID NO: 1 Dose

FIG. 4 Cont.

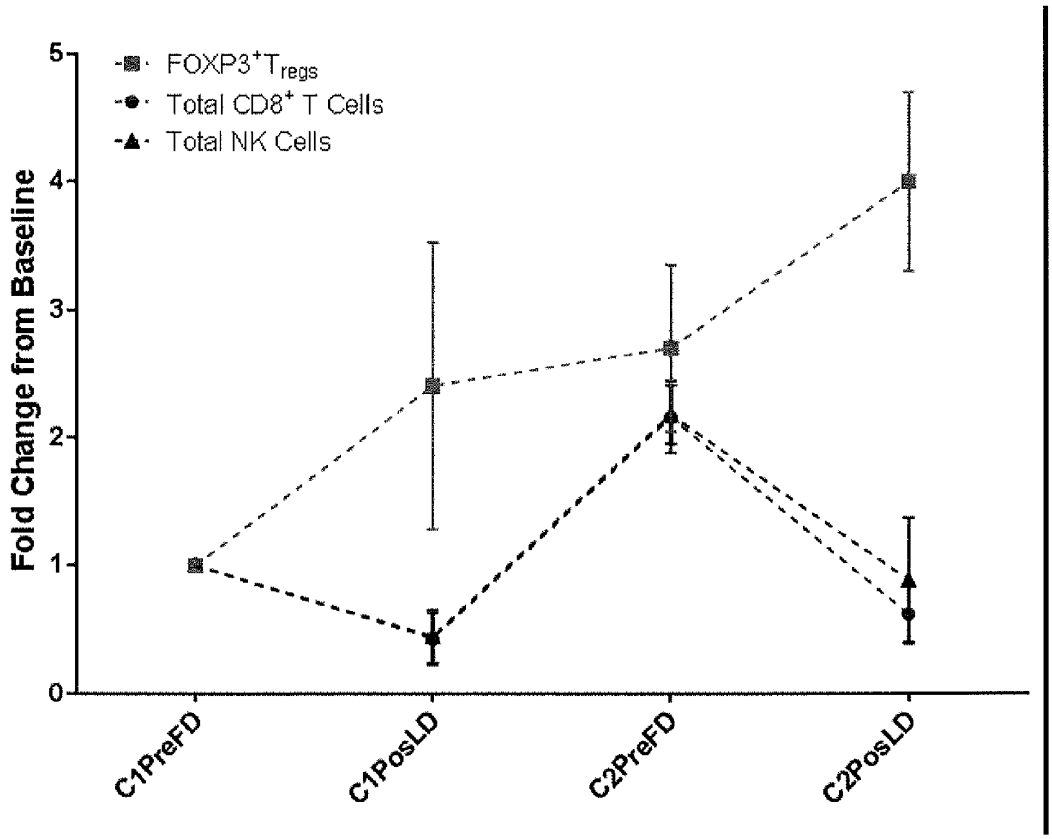

FOXP3+Tregs
Total CD8+ T Cells
Total NK Cells
Fold Change from Baseline
0
1
2
3
4
5
C1PreFD
C1PosLD
C2PreFD
C2PosLD

FIG. 5

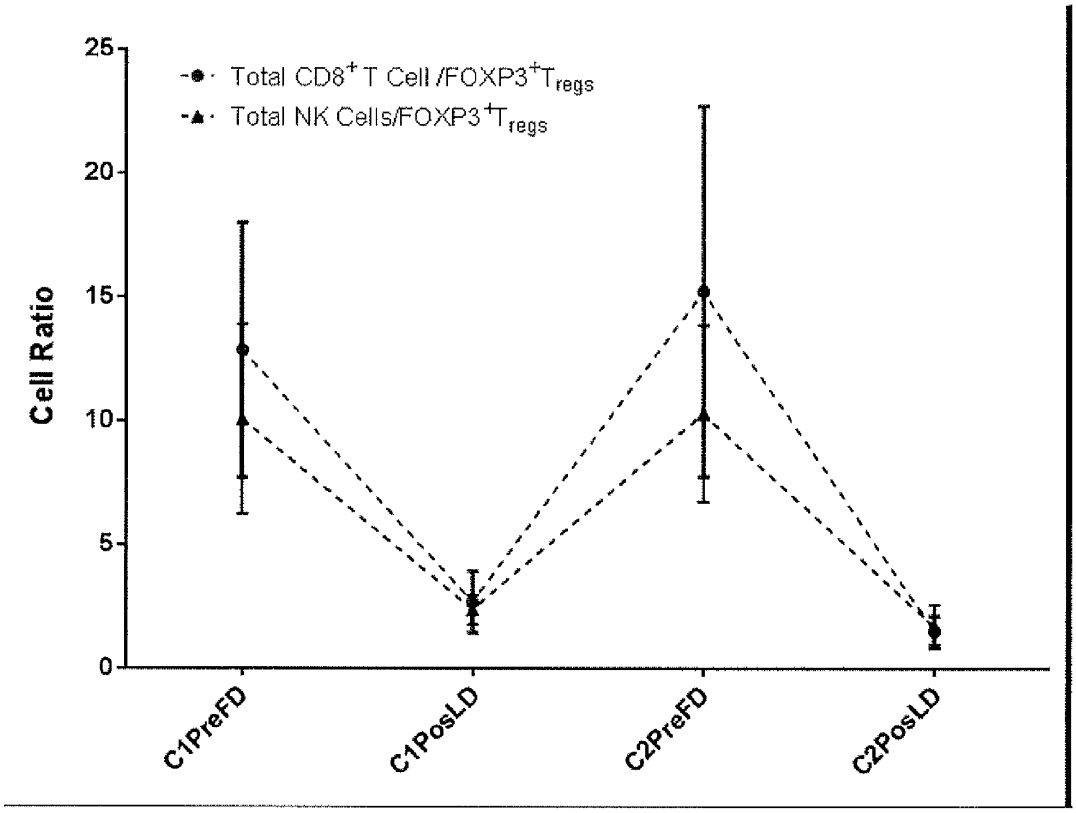

Total CD8+ T Cell /FOXP3+Tregs
Total NK Cells/FOXP3+Tregs
Cell Ratio
25
20
15
10
5
0
C1PreFD
C1PosLD
C2PreFD
C2PosLD

FIG. 6

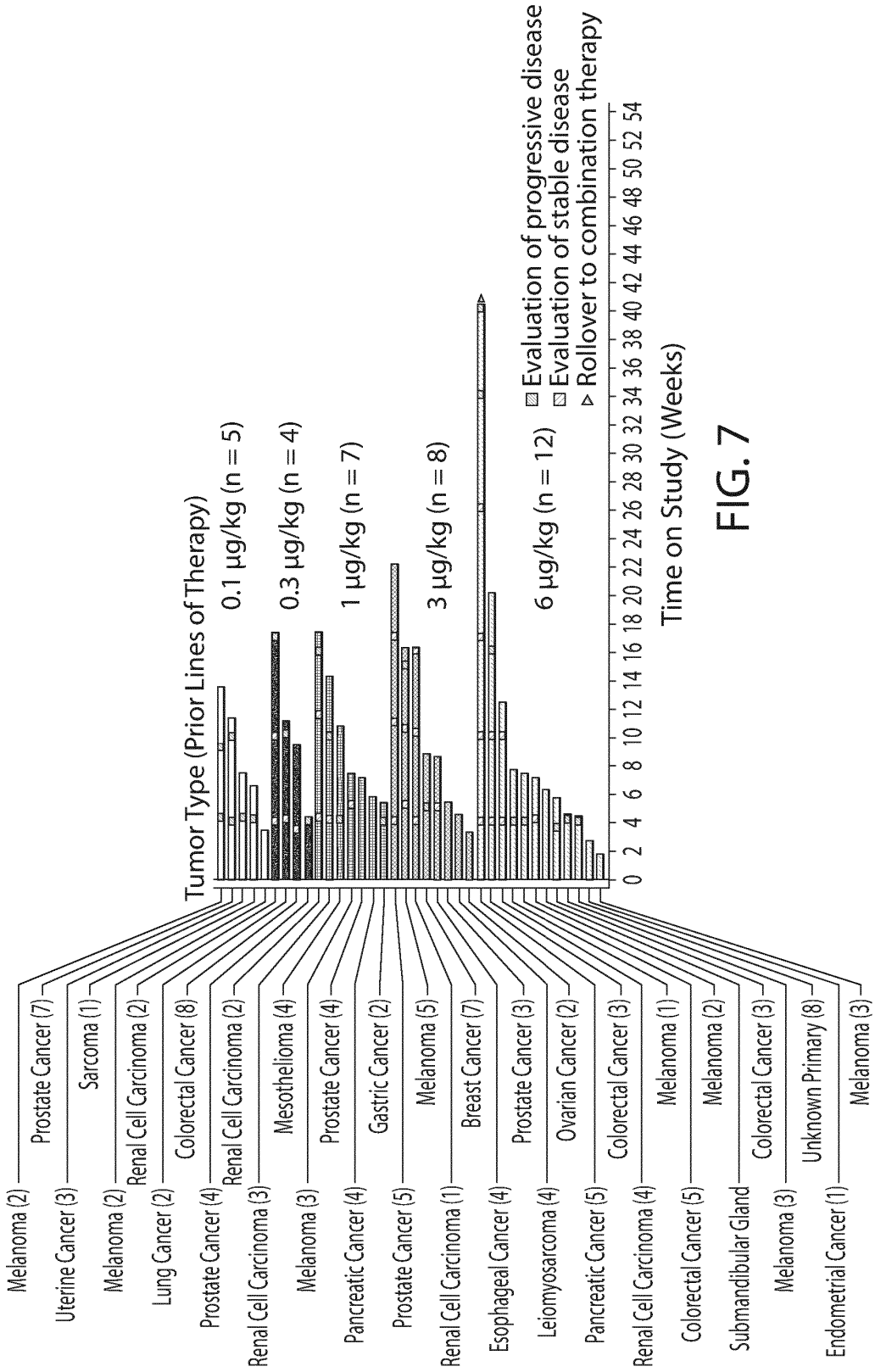

Tumor Type (Prior Lines of Therapy)
0.1 µg/kg (n = 5)
0.3 µg/kg (n = 4)
1 µg/kg (n = 7)
3 µg/kg (n = 8)
6 µg/kg (n = 12)
Evaluation of progressive disease
Evaluation of stable disease
Rollover to combination therapy
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52 54
Time on Study (Weeks)
Melanoma (2)
Prostate Cancer (7)
Uterine Cancer (3)
Sarcoma (1)
Melanoma (2)
Renal Cell Carcinoma (2)
Lung Cancer (2)
Colorectal Cancer (8)
Prostate Cancer (4)
Renal Cell Carcinoma (2)
Renal Cell Carcinoma (3)
Mesothelioma (4)
Melanoma (3)
Prostate Cancer (4)
Pancreatic Cancer (4)
Gastric Cancer (2)
Prostate Cancer (5)
Melanoma (5)
Renal Cell Carcinoma (1)
Breast Cancer (7)
Esophageal Cancer (4)
Prostate Cancer (3)
Leiomyosarcoma (4)
Ovarian Cancer (2)
Pancreatic Cancer (5)
Colorectal Cancer (3)
Renal Cell Carcinoma (4)
Melanoma (1)
Colorectal Cancer (5)
Melanoma (2)
Submandibular Gland
Colorectal Cancer (3)
Melanoma (3)
Unknown Primary (8)
Endometrial Cancer (1)
Melanoma (3)

FIG. 7

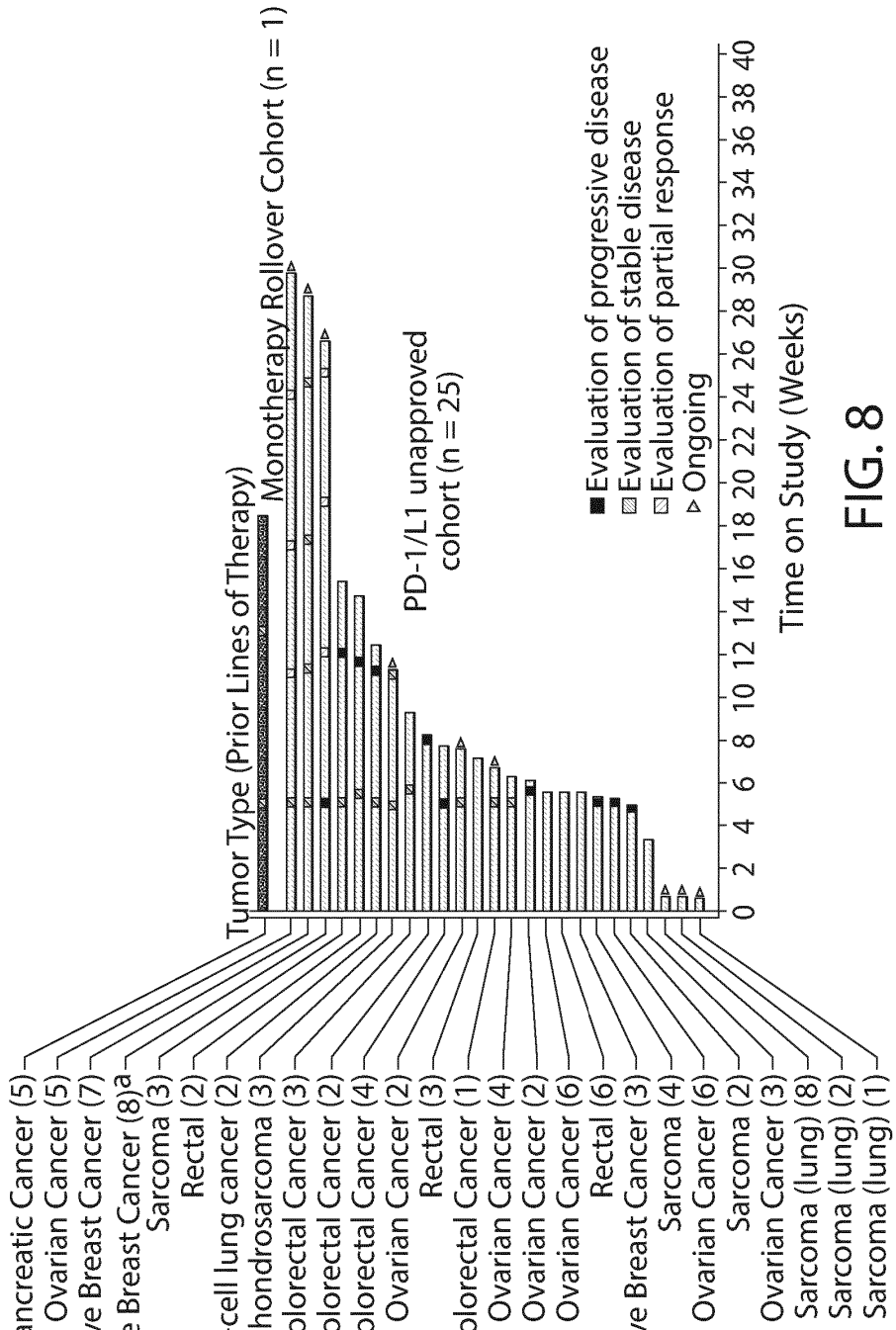

Tumor Type (Prior Lines of Therapy)
Monotherapy Rollover Cohort (n = 1)
PD-1/L1 unapproved cohort (n = 25)
Pancreatic Cancer (5)
Ovarian Cancer (5)
Triple Negative Breast Cancer (7)
Triple Negative Breast Cancer (8)a
Sarcoma (3)
Rectal (2)
Non-small-cell lung cancer (2)
Chondrosarcoma (3)
Colorectal Cancer (3)
Colorectal Cancer (2)
Colorectal Cancer (4)
Ovarian Cancer (2)
Rectal (3)
Colorectal Cancer (1)
Ovarian Cancer (4)
Ovarian Cancer (2)
Ovarian Cancer (6)
Rectal (6)
Triple Negative Breast Cancer (3)
Sarcoma (4)
Ovarian Cancer (6)
Sarcoma (2)
Ovarian Cancer (3)
Sarcoma (lung) (8)
Sarcoma (lung) (2)
Sarcoma (lung) (1)
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40
Time on Study (Weeks)
Evaluation of progressive disease
Evaluation of stable disease
Evaluation of partial response
Ongoing

FIG. 8

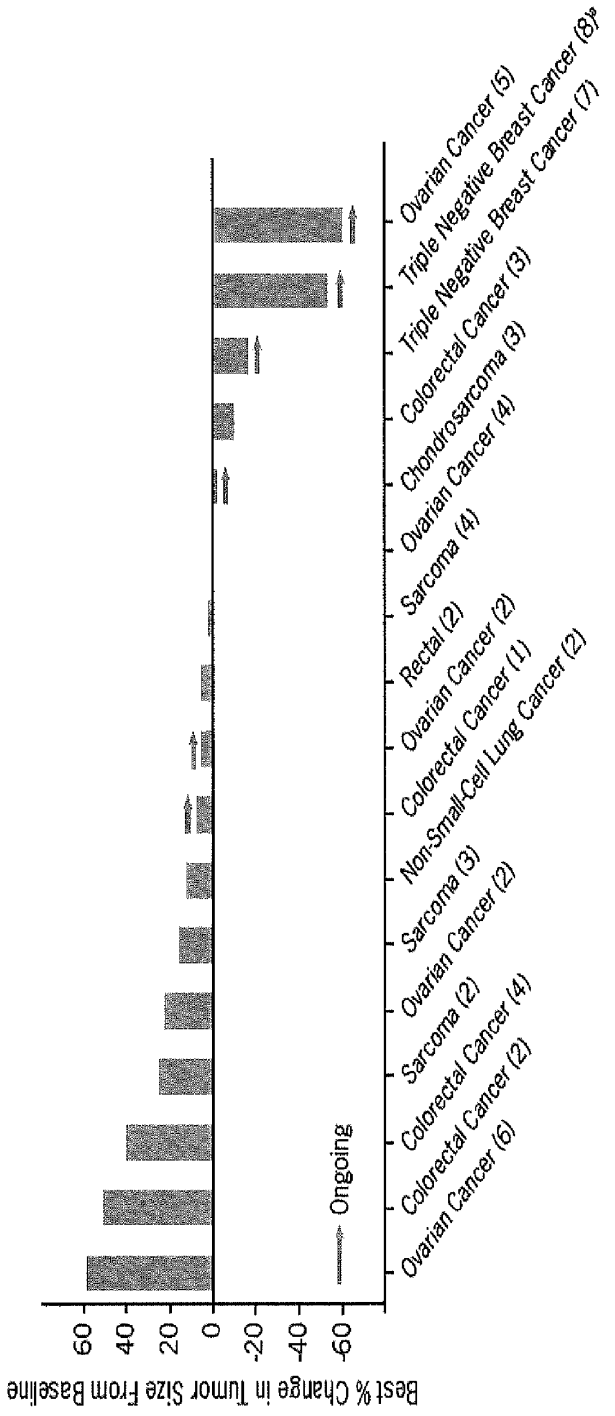

Best % Change in Tumor Size From Baseline
60
40
20
0
-20
-40
-60
Ongoing
Ovarian Cancer (6)
Colorectal Cancer (2)
Colorectal Cancer (4)
Sarcoma (2)
Ovarian Cancer (2)
Sarcoma (3)
Non-Small-Cell Lung Cancer (2)
Colorectal Cancer (1)
Ovarian Cancer (2)
Rectal (2)
Sarcoma (4)
Ovarian Cancer (4)
Chondrosarcoma (3)
Colorectal Cancer (3)
Triple Negative Breast Cancer (7)
Triple Negative Breast Cancer (8)*
Ovarian Cancer (5)
Tumor Type (Prior Lines of Therapy)

FIG. 9

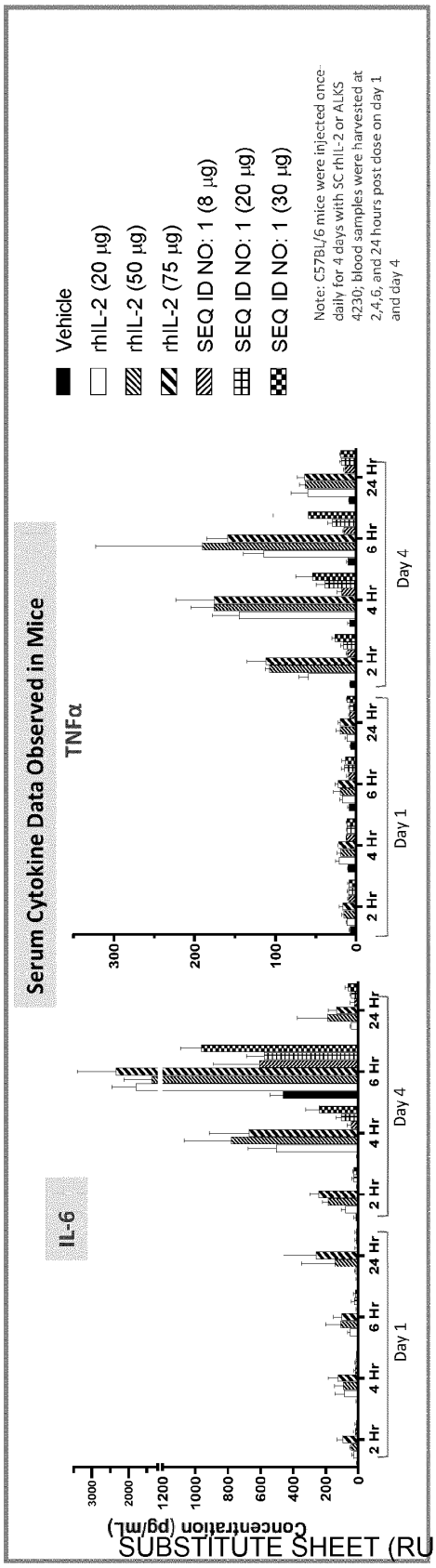

Serum Cytokine Data Observed in Mice
IL-6
TNFα
Concentration (pg/mL)
Vehicle
rhIL-2 (20 µg)
rhIL-2 (50 µg)
rhIL-2 (75 µg)
SEQ ID NO: 1 (8 µg)
SEQ ID NO: 1 (20 µg)
SEQ ID NO: 1 (30 µg)
Note: C57BL/6 mice were injected once-daily for 4 days with SC rhIL-2 or ALKS 4230; blood samples were harvested at 2,4,6, and 24 hours post dose on day 1 and day 4
Day 1
Day 4
2 Hr
4 Hr
6 Hr
24 Hr

FIG. 10

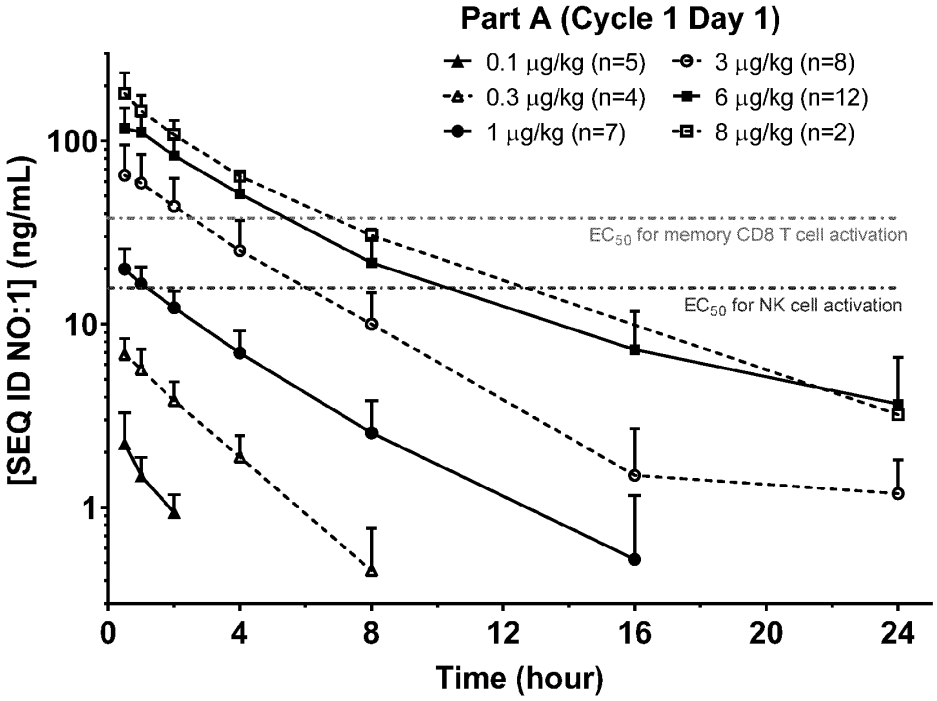

Part A (Cycle 1 Day 1)
0.1 μg/kg (n=5)
0.3 μg/kg (n=4)
1 μg/kg (n=7)
3 μg/kg (n=8)
6 μg/kg (n=12)
8 μg/kg (n=2)
EC50 for memory CD8 T cell activation
EC50 for NK cell activation
[SEQ ID NO:1] (ng/mL)
100
10
1
0
4
8
12
16
20
24
Time (hour)

FIG. 11

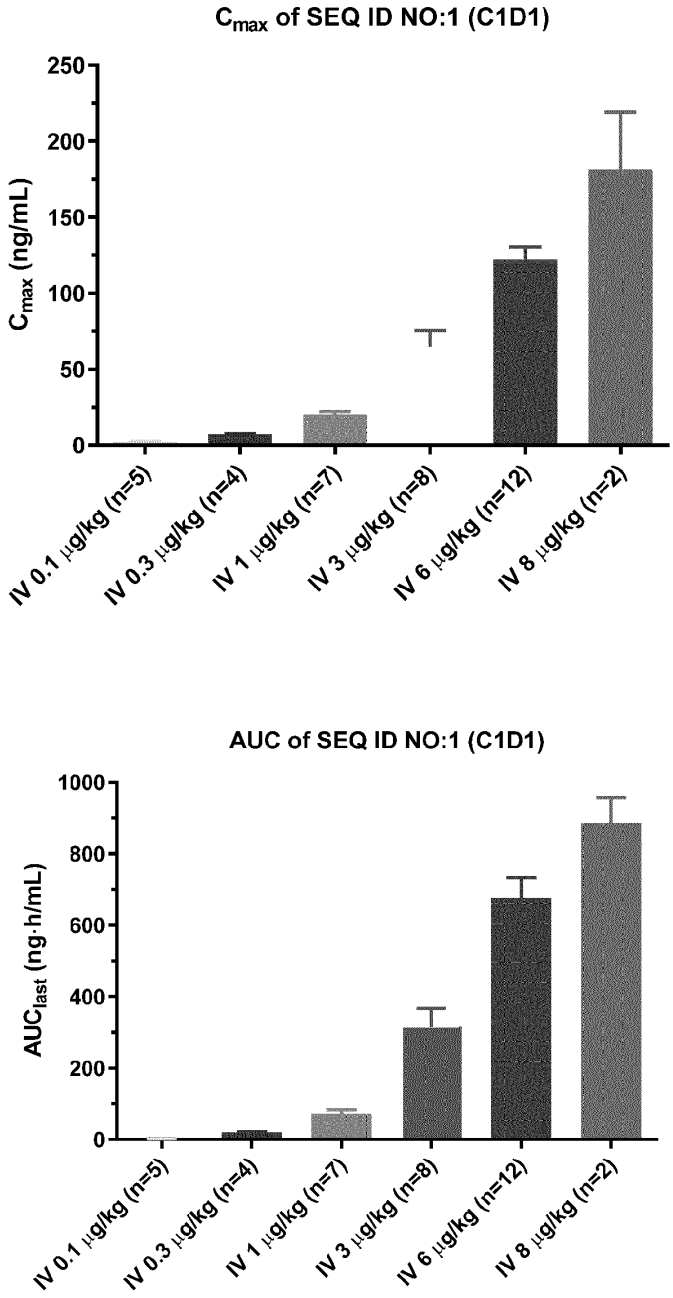

Cmax of SEQ ID NO:1 (C1D1)
Cmax (ng/mL)
250
200
150
100
50
0
IV 0.1 µg/kg (n=5)
IV 0.3 µg/kg (n=4)
IV 1 µg/kg (n=7)
IV 3 µg/kg (n=8)
IV 6 µg/kg (n=12)
IV 8 µg/kg (n=2)
AUC of SEQ ID NO:1 (C1D1)
AUClast (ng·h/mL)
1000
800
600
400
200
0
IV 0.1 µg/kg (n=5)
IV 0.3 µg/kg (n=4)
IV 1 µg/kg (n=7)
IV 3 µg/kg (n=8)
IV 6 µg/kg (n=12)
IV 8 µg/kg (n=2)

FIG. 12

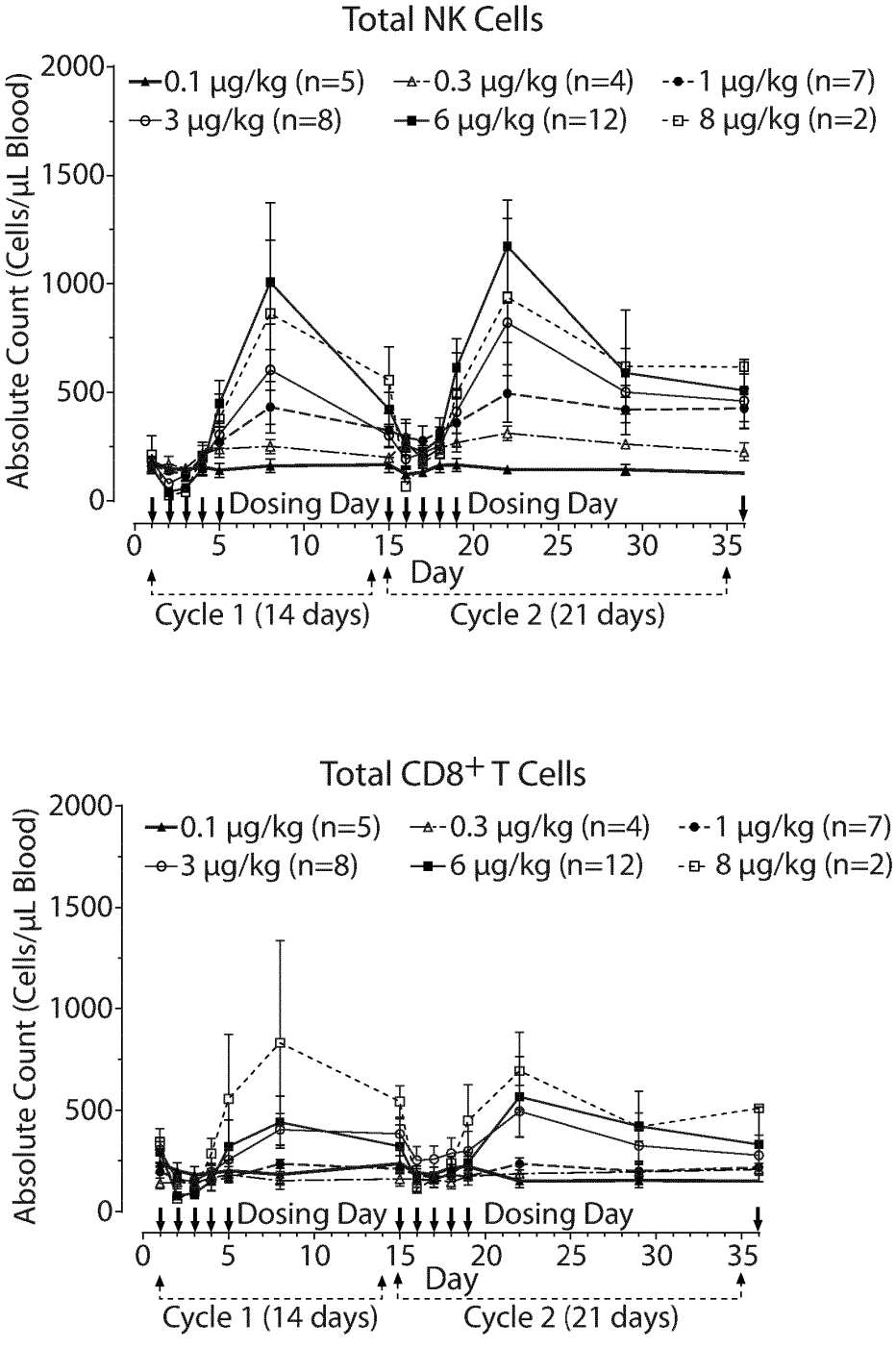

Total NK Cells
0.1 µg/kg (n=5)
0.3 µg/kg (n=4)
1 µg/kg (n=7)
3 µg/kg (n=8)
6 µg/kg (n=12)
8 µg/kg (n=2)
Absolute Count (Cells/µL Blood)
2000
1500
1000
500
0
Dosing Day
Dosing Day
0
5
10
15
20
25
30
35
Day
Cycle 1 (14 days)
Cycle 2 (21 days)
Total CD8+ T Cells
0.1 µg/kg (n=5)
0.3 µg/kg (n=4)
1 µg/kg (n=7)
3 µg/kg (n=8)
6 µg/kg (n=12)
8 µg/kg (n=2)
Absolute Count (Cells/µL Blood)
2000
1500
1000
500
0
Dosing Day
Dosing Day
0
5
10
15
20
25
30
35
Day
Cycle 1 (14 days)
Cycle 2 (21 days)

FIG. 13

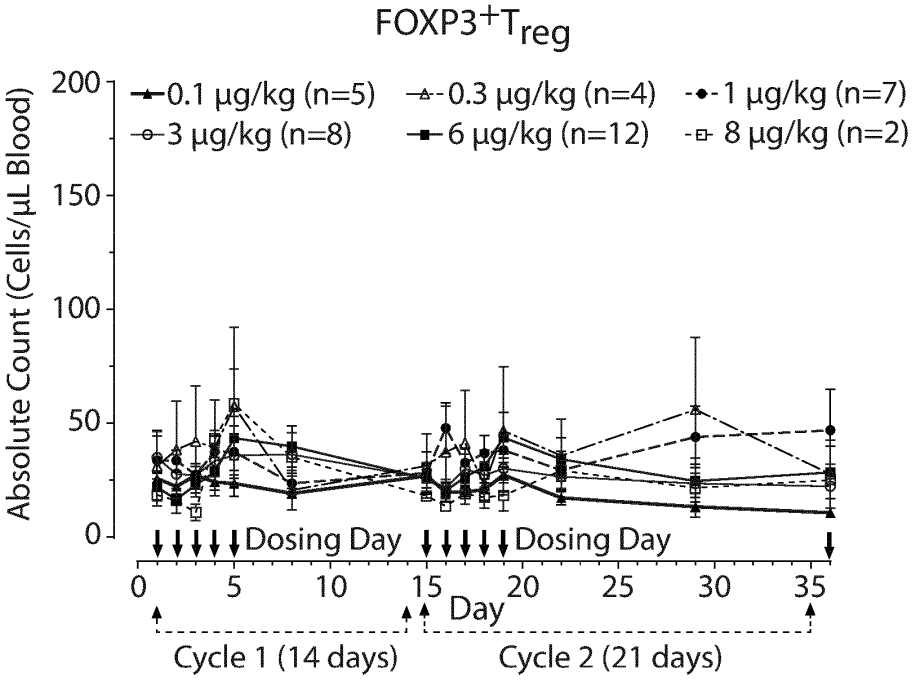

FOXP3+Treg
0.1 µg/kg (n=5)
0.3 µg/kg (n=4)
1 µg/kg (n=7)
3 µg/kg (n=8)
6 µg/kg (n=12)
8 µg/kg (n=2)
Absolute Count (Cells/µL Blood)
200
150
100
50
0
Dosing Day
Dosing Day
0
5
10
15
20
25
30
35
Day
Cycle 1 (14 days)
Cycle 2 (21 days)

FIG. 13 Cont.

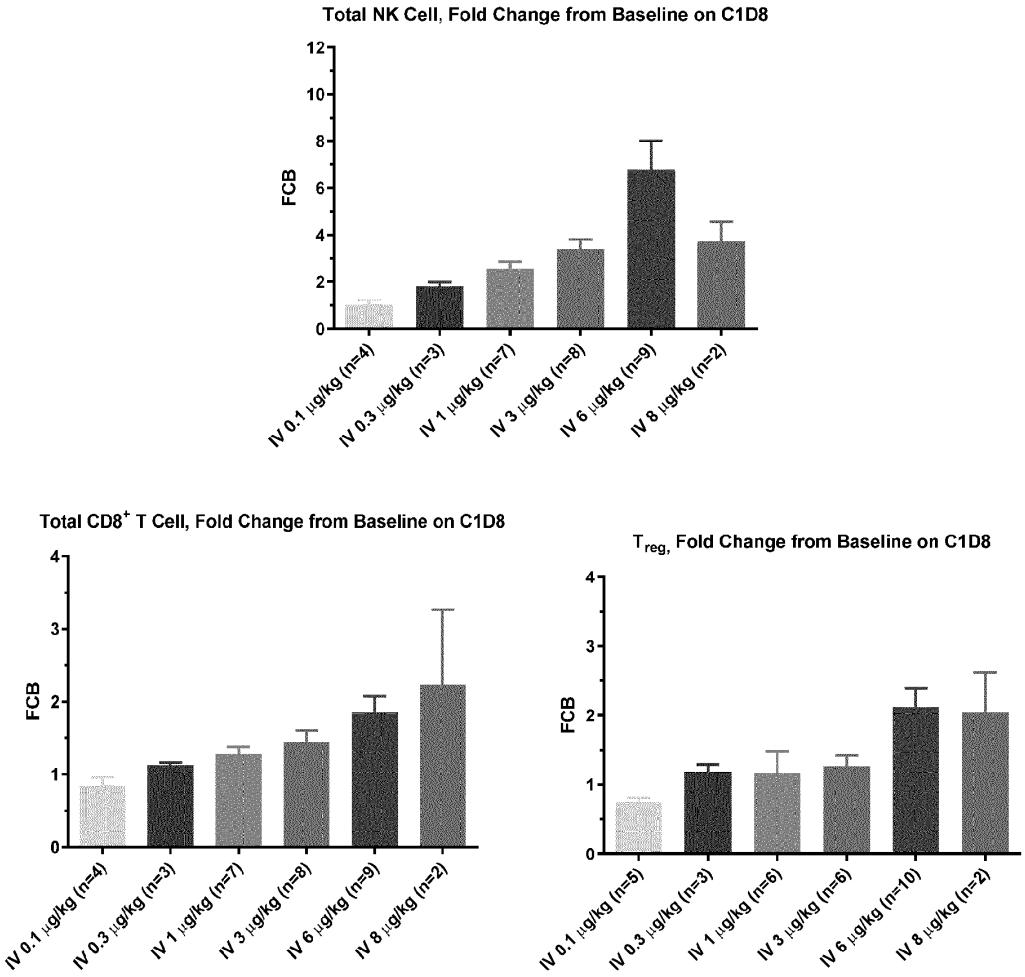

Total NK Cell, Fold Change from Baseline on C1D8
FCB
12
10
8
6
4
2
0
IV 0.1 µg/kg (n=4)
IV 0.3 µg/kg (n=3)
IV 1 µg/kg (n=7)
IV 3 µg/kg (n=8)
IV 6 µg/kg (n=9)
IV 8 µg/kg (n=2)
Total CD8+ T Cell, Fold Change from Baseline on C1D8
FCB
4
3
2
1
0
IV 0.1 µg/kg (n=4)
IV 0.3 µg/kg (n=3)
IV 1 µg/kg (n=7)
IV 3 µg/kg (n=8)
IV 6 µg/kg (n=9)
IV 8 µg/kg (n=2)
Treg, Fold Change from Baseline on C1D8
FCB
4
3
2
1
0
IV 0.1 µg/kg (n=5)
IV 0.3 µg/kg (n=3)
IV 1 µg/kg (n=6)
IV 3 µg/kg (n=6)
IV 6 µg/kg (n=10)
IV 8 µg/kg (n=2)

FIG. 14

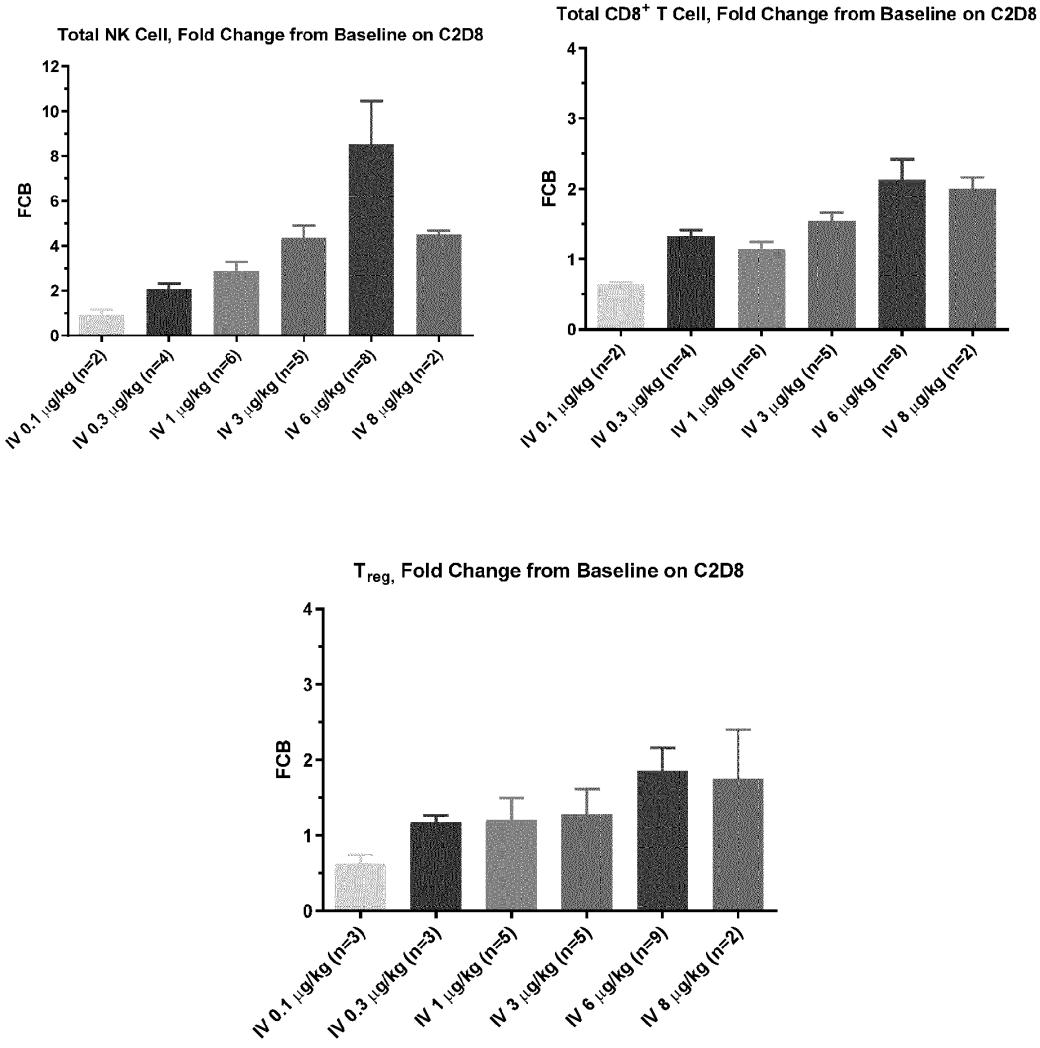

Total NK Cell, Fold Change from Baseline on C2D8
FCB
0
2
4
6
8
10
12
IV 0.1 µg/kg (n=2)
IV 0.3 µg/kg (n=4)
IV 1 µg/kg (n=6)
IV 3 µg/kg (n=5)
IV 6 µg/kg (n=8)
IV 8 µg/kg (n=2)
Total CD8+ T Cell, Fold Change from Baseline on C2D8
FCB
0
1
2
3
4
IV 0.1 µg/kg (n=2)
IV 0.3 µg/kg (n=4)
IV 1 µg/kg (n=6)
IV 3 µg/kg (n=5)
IV 6 µg/kg (n=8)
IV 8 µg/kg (n=2)
Treg, Fold Change from Baseline on C2D8
FCB
0
1
2
3
4
IV 0.1 µg/kg (n=3)
IV 0.3 µg/kg (n=3)
IV 1 µg/kg (n=5)
IV 3 µg/kg (n=5)
IV 6 µg/kg (n=9)
IV 8 µg/kg (n=2)

FIG. 14 (cont)

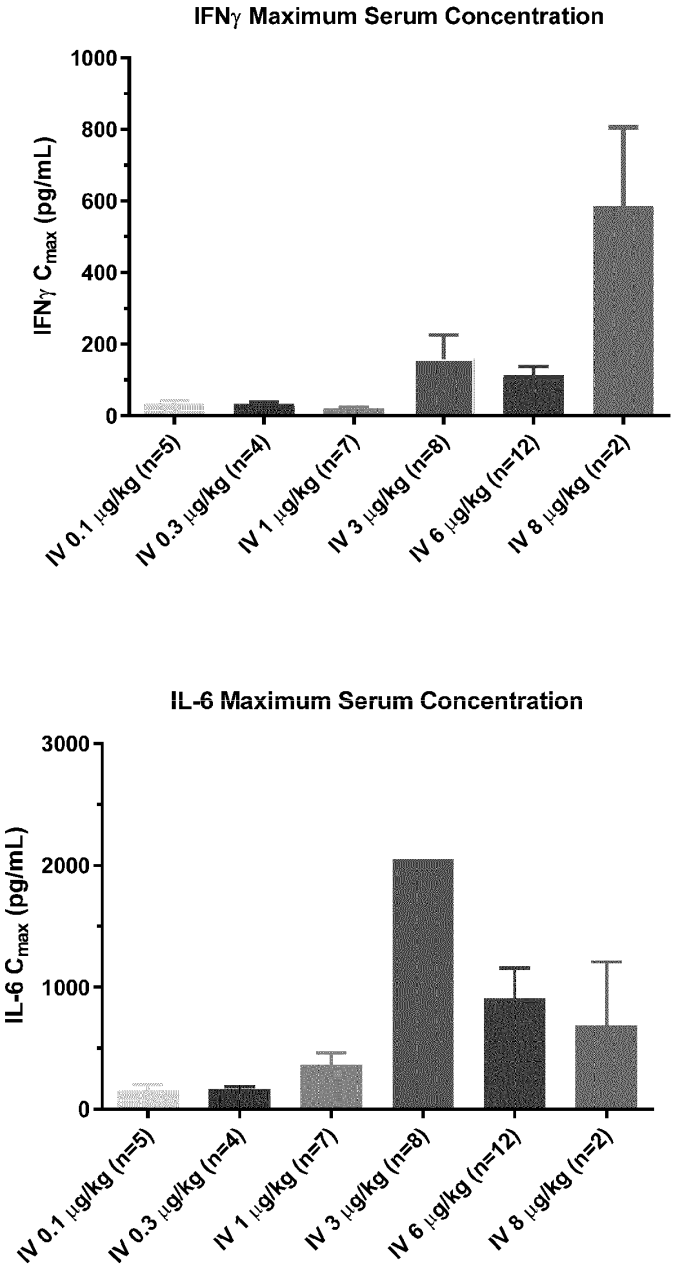

IFNγ Maximum Serum Concentration
IFNγ Cmax (pg/mL)
1000
800
600
400
200
0
IV 0.1 µg/kg (n=5)
IV 0.3 µg/kg (n=4)
IV 1 µg/kg (n=7)
IV 3 µg/kg (n=8)
IV 6 µg/kg (n=12)
IV 8 µg/kg (n=2)
IL-6 Maximum Serum Concentration
IL-6 Cmax (pg/mL)
3000
2000
1000
0
IV 0.1 µg/kg (n=5)
IV 0.3 µg/kg (n=4)
IV 1 µg/kg (n=7)
IV 3 µg/kg (n=8)
IV 6 µg/kg (n=12)
IV 8 µg/kg (n=2)

FIG. 15