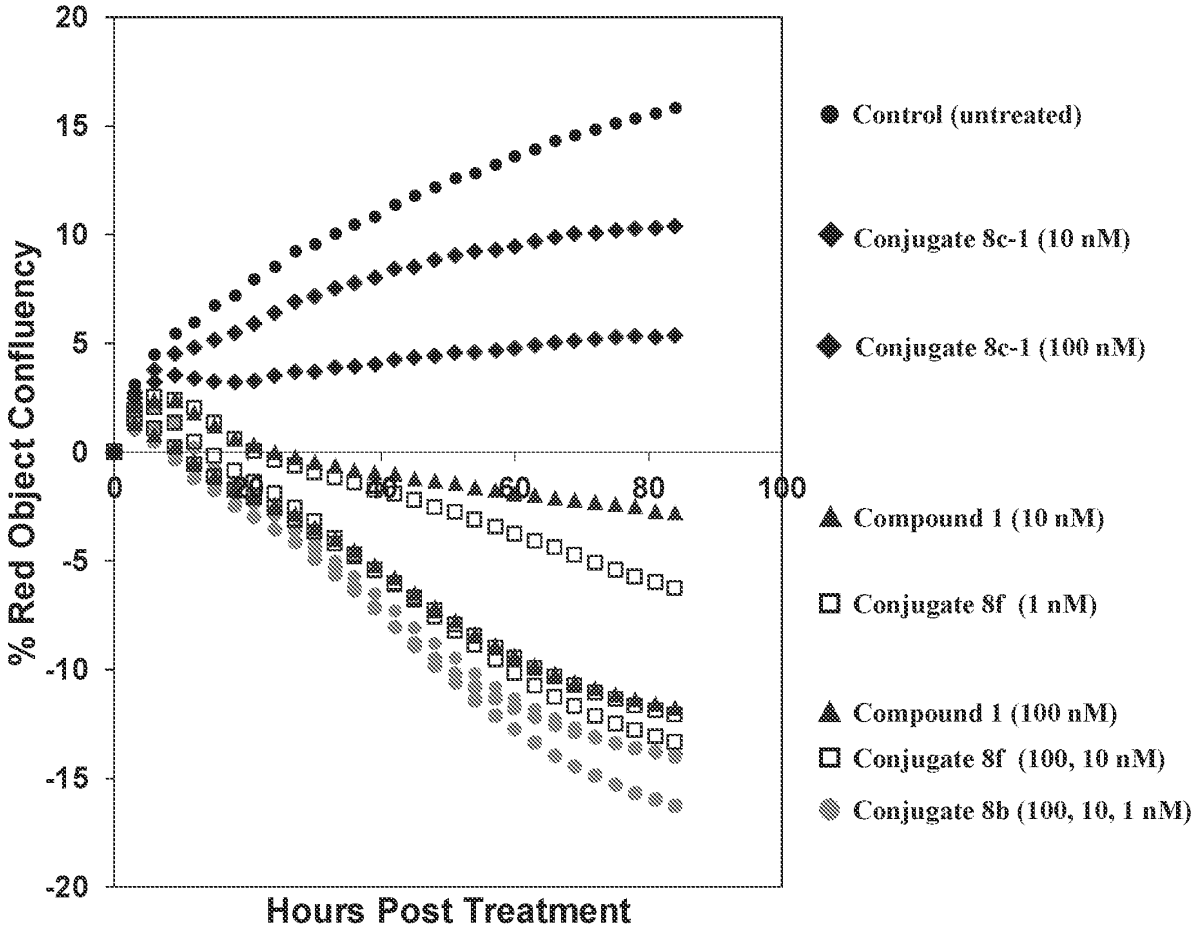

20
15
10
5
0
-5
-10
-15
-20
0
20
40
60
80
100
% Red Object Confluency
Hours Post Treatment
Control (untreated)
Conjugate 8c-1 (10 nM)
Conjugate 8c-1 (100 nM)
Compound 1 (10 nM)
Conjugate 8f (1 nM)
Compound 1 (100 nM)
Conjugate 8f (100, 10 nM)
Conjugate 8b (100, 10, 1 nM)

FIG 1A

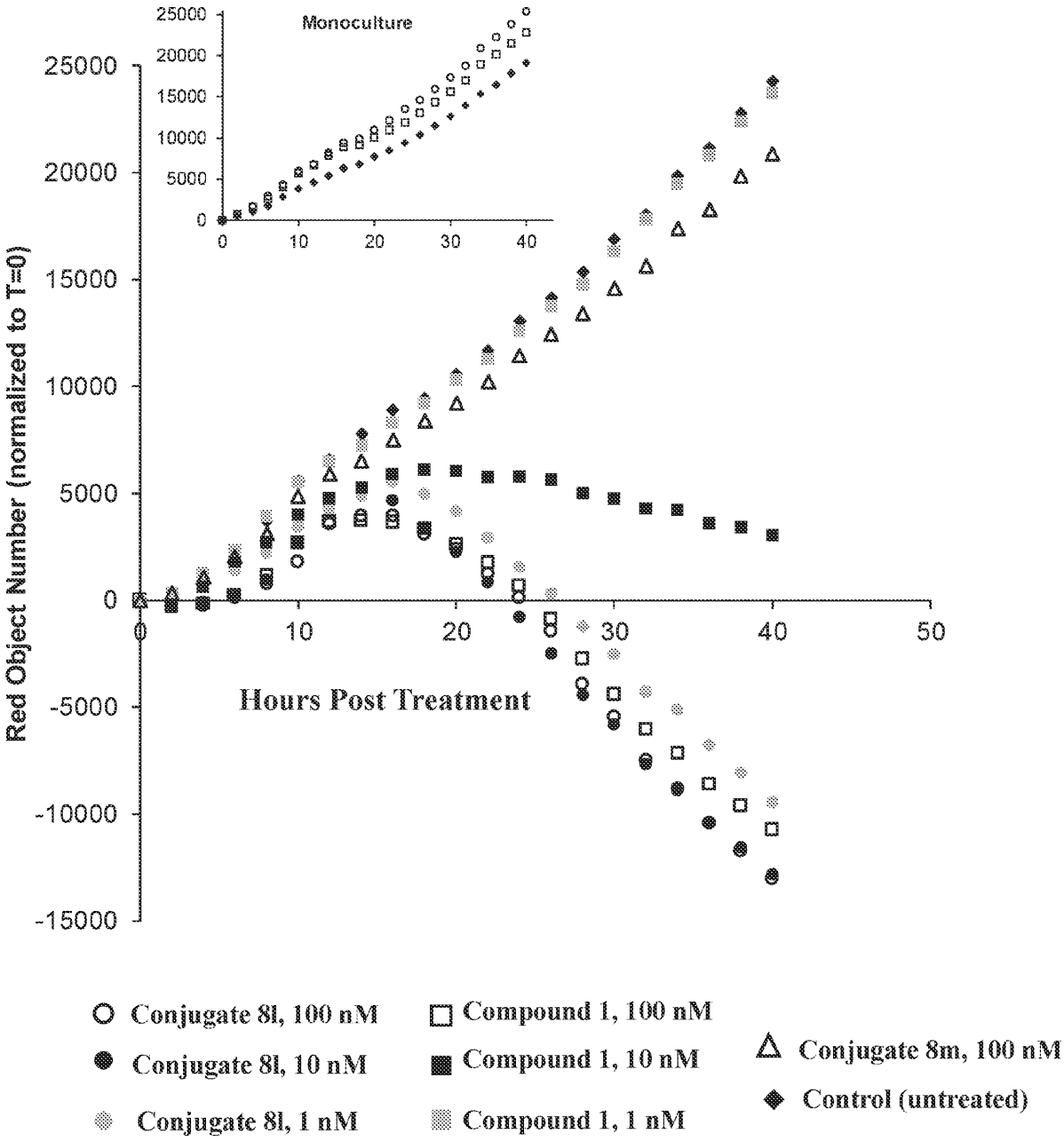

Monoculture
25000
20000
15000
10000
5000
0
0
10
20
30
40
Red Object Number (normalized to T=0)
25000
20000
15000
10000
5000
0
-5000
-10000
-15000
0
10
20
30
40
50
Hours Post Treatment
Conjugate 8l, 100 nM
Conjugate 8l, 10 nM
Conjugate 8l, 1 nM
Compound 1, 100 nM
Compound 1, 10 nM
Compound 1, 1 nM
Conjugate 8m, 100 nM
Control (untreated)

FIG 1B

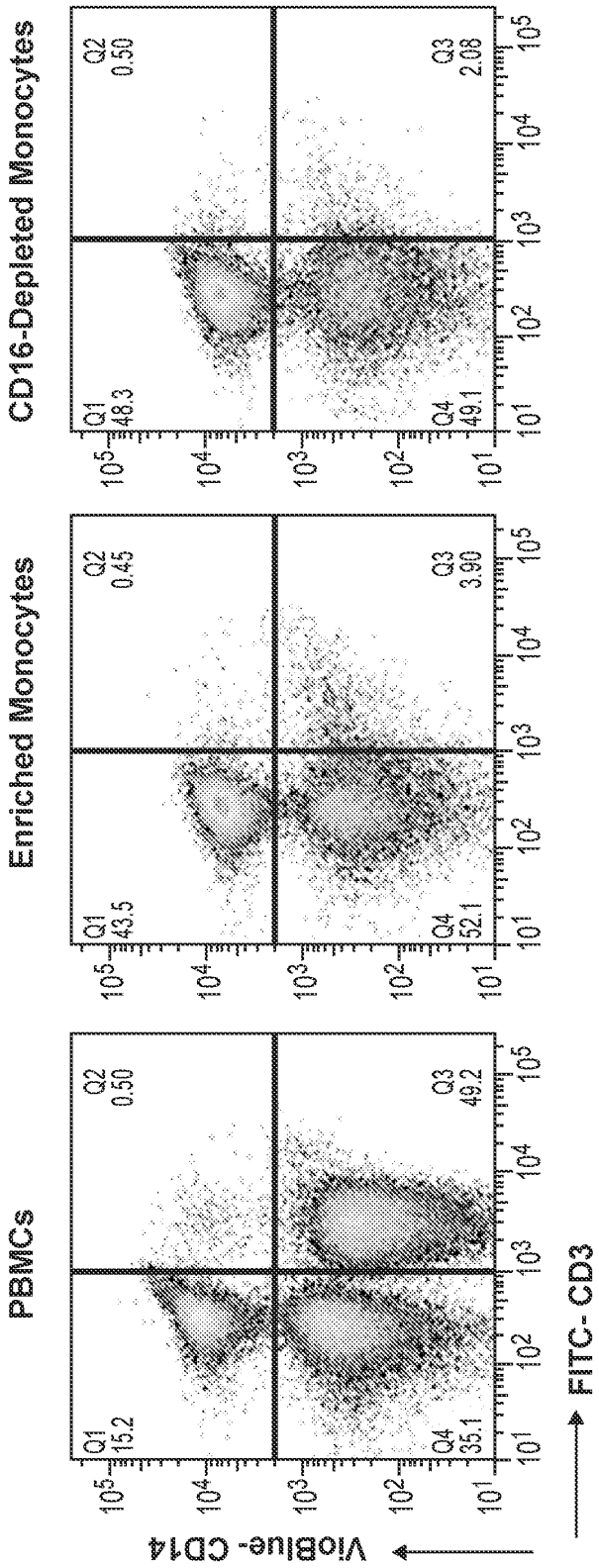

CD16-Depleted Monocytes
Enriched Monocytes
PBMCs
Q1 48.3
Q2 0.50
Q3 2.08
Q4 49.1
Q1 43.5
Q2 0.45
Q3 3.90
Q4 52.1
Q1 15.2
Q2 0.50
Q3 49.2
Q4 35.1
VioBlue- CD14
FITC- CD3

FIG 2

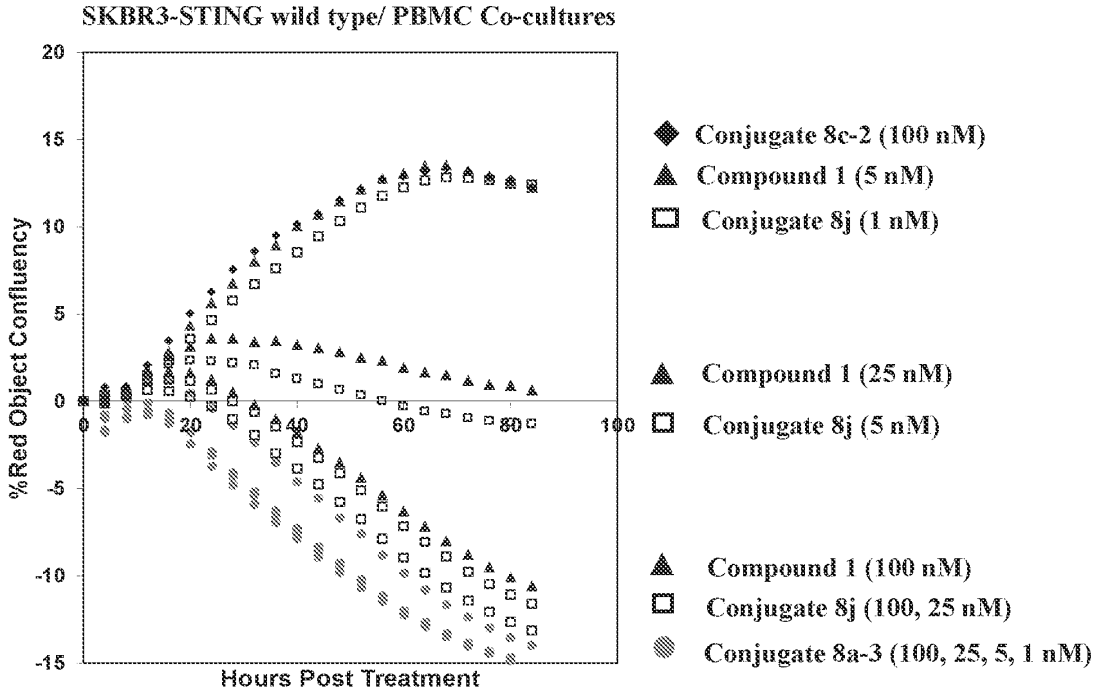

SKBR3-STING wild type/ PBMC Co-cultures
%Red Object Confluency
Hours Post Treatment
Conjugate 8c-2 (100 nM)
Compound 1 (5 nM)
Conjugate 8j (1 nM)
Compound 1 (25 nM)
Conjugate 8j (5 nM)
Compound 1 (100 nM)
Conjugate 8j (100, 25 nM)
Conjugate 8a-3 (100, 25, 5, 1 nM)

FIG 3A

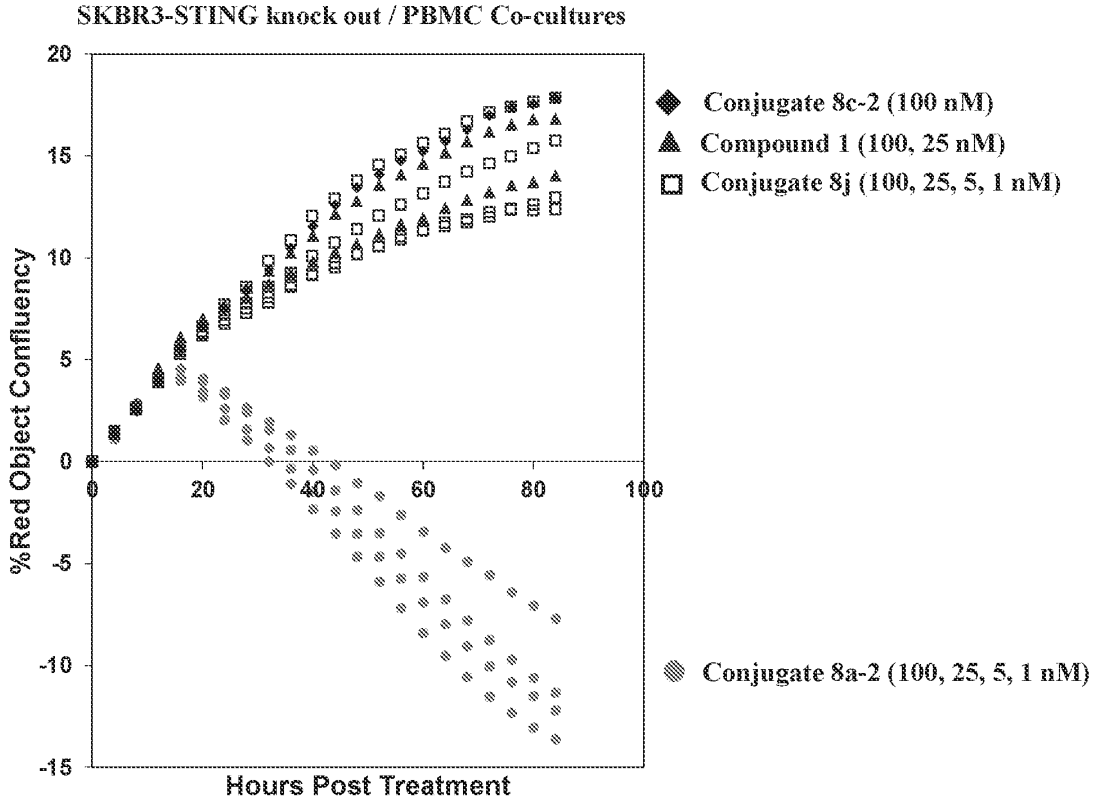

SKBR3-STING knock out / PBMC Co-cultures
%Red Object Confluency
Hours Post Treatment
Conjugate 8c-2 (100 nM)
Compound 1 (100, 25 nM)
Conjugate 8j (100, 25, 5, 1 nM)
Conjugate 8a-2 (100, 25, 5, 1 nM)

FIG 3B

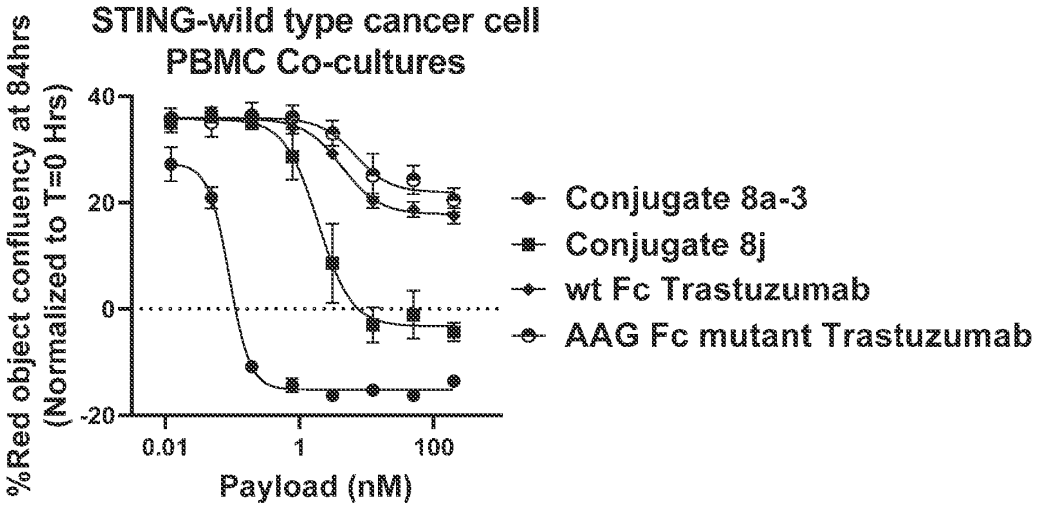

STING-wild type cancer cell
PBMC Co-cultures
%Red object confluency at 84hrs
(Normalized to T=0 Hrs)
40
20
0
-20
0.01
1
100
Payload (nM)
Conjugate 8a-3
Conjugate 8j
wt Fc Trastuzumab
AAG Fc mutant Trastuzumab

FIG 4A

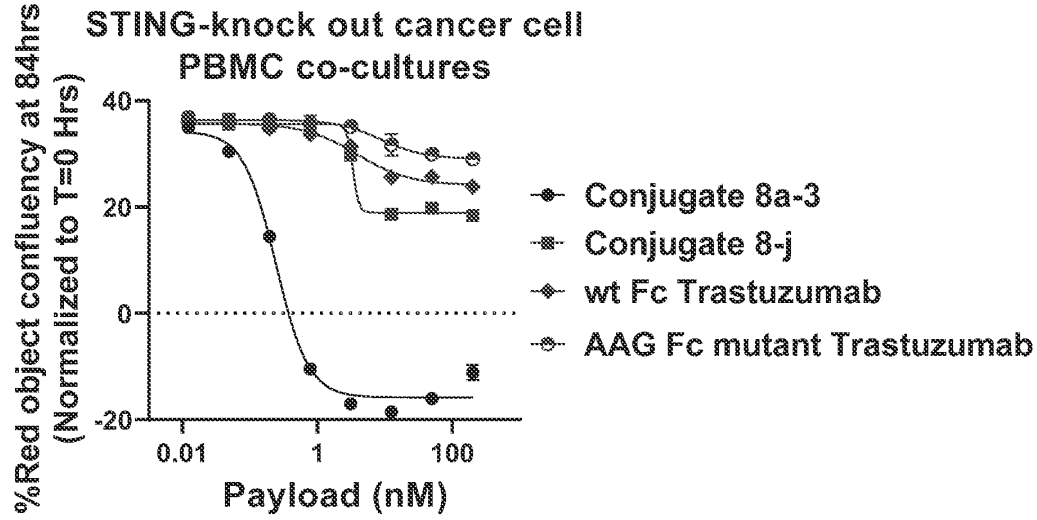

STING-knock out cancer cell
PBMC co-cultures
%Red object confluency at 84hrs
(Normalized to T=0 Hrs)
40
20
0
-20
0.01
1
100
Payload (nM)
Conjugate 8a-3
Conjugate 8-j
wt Fc Trastuzumab
AAG Fc mutant Trastuzumab

FIG 4B

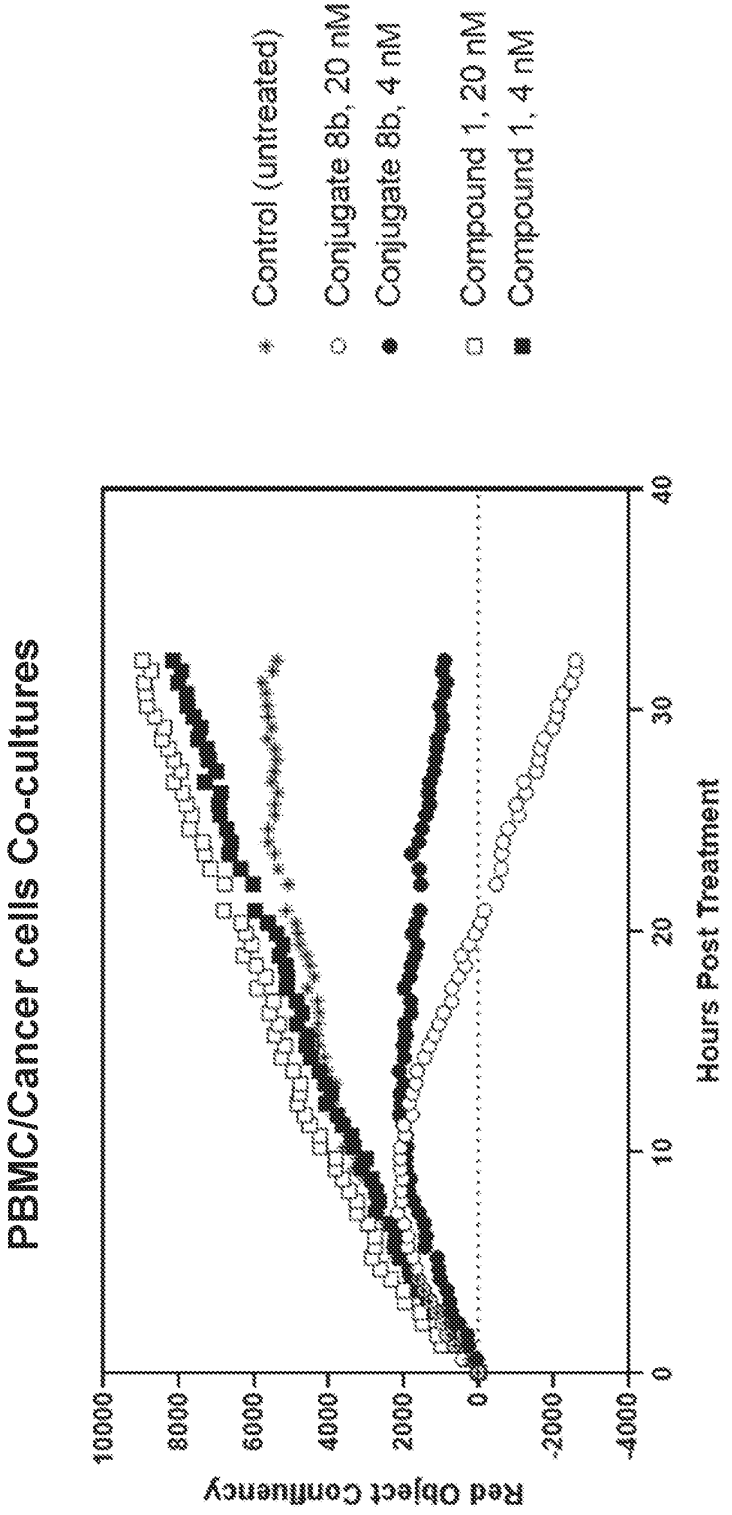

PBMC/Cancer cells Co-cultures
Control (untreated)
Conjugate 8b, 20 nM
Conjugate 8b, 4 nM
Compound 1, 20 nM
Compound 1, 4 nM
Red Object confluency
10000
8000
6000
4000
2000
0
-2000
-4000
0
10
20
30
40
Hours Post Treatment

FIG 5A

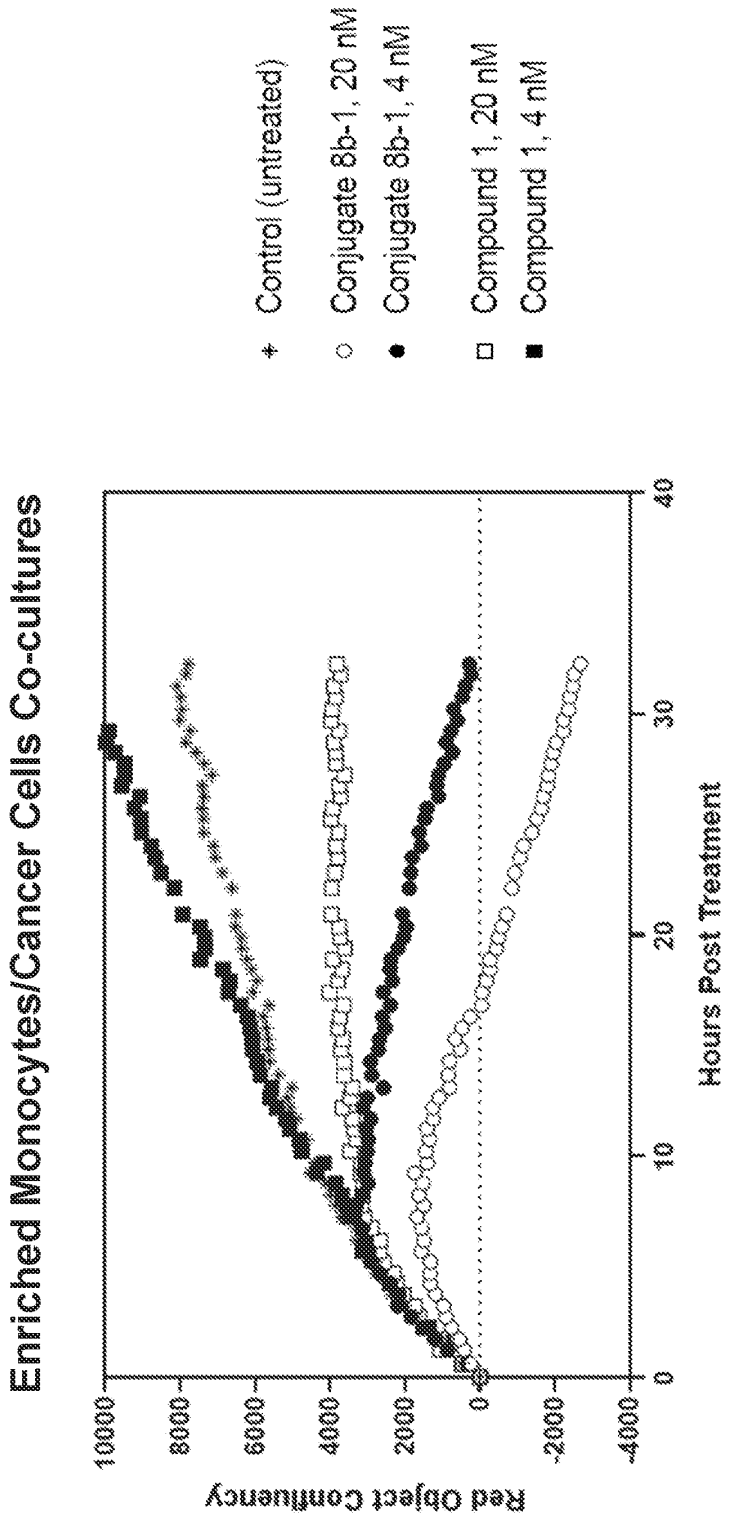

Enriched Monocytes/Cancer Cells Co-cultures
Control (untreated)
Conjugate 8b-1, 20 nM
Conjugate 8b-1, 4 nM
Compound 1, 20 nM
Compound 1, 4 nM
Red object confluency
10000
8000
6000
4000
2000
0
-2000
-4000
0
10
20
30
40
Hours Post Treatment

FIG 5B

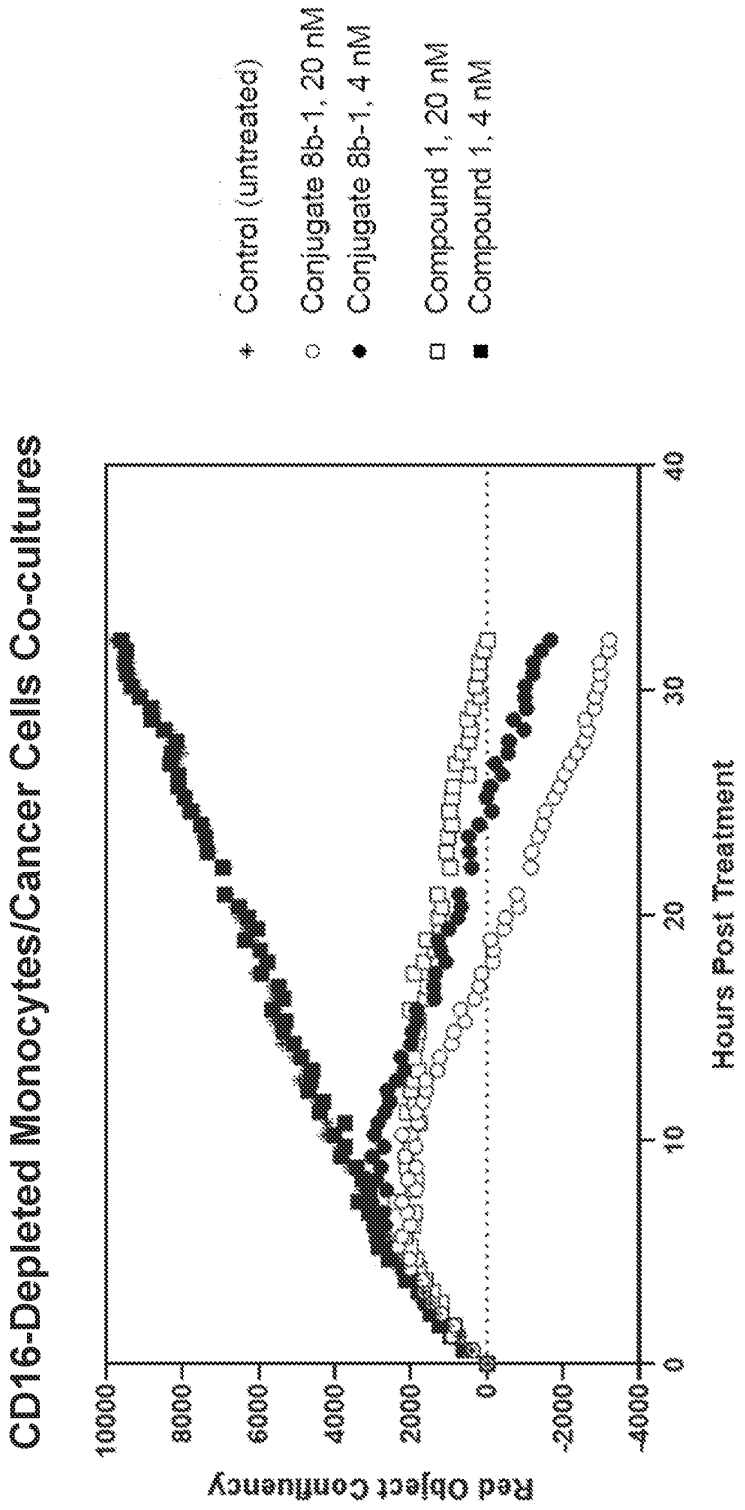

CD16-Depleted Monocytes/Cancer Cells Co-cultures
Control (untreated)
Conjugate 8b-1, 20 nM
Conjugate 8b-1, 4 nM
Compound 1, 20 nM
Compound 1, 4 nM
Red Object Confluency
10000
8000
6000
4000
2000
0
-2000
-4000
0
10
20
30
40
Hours Post Treatment

FIG 5C

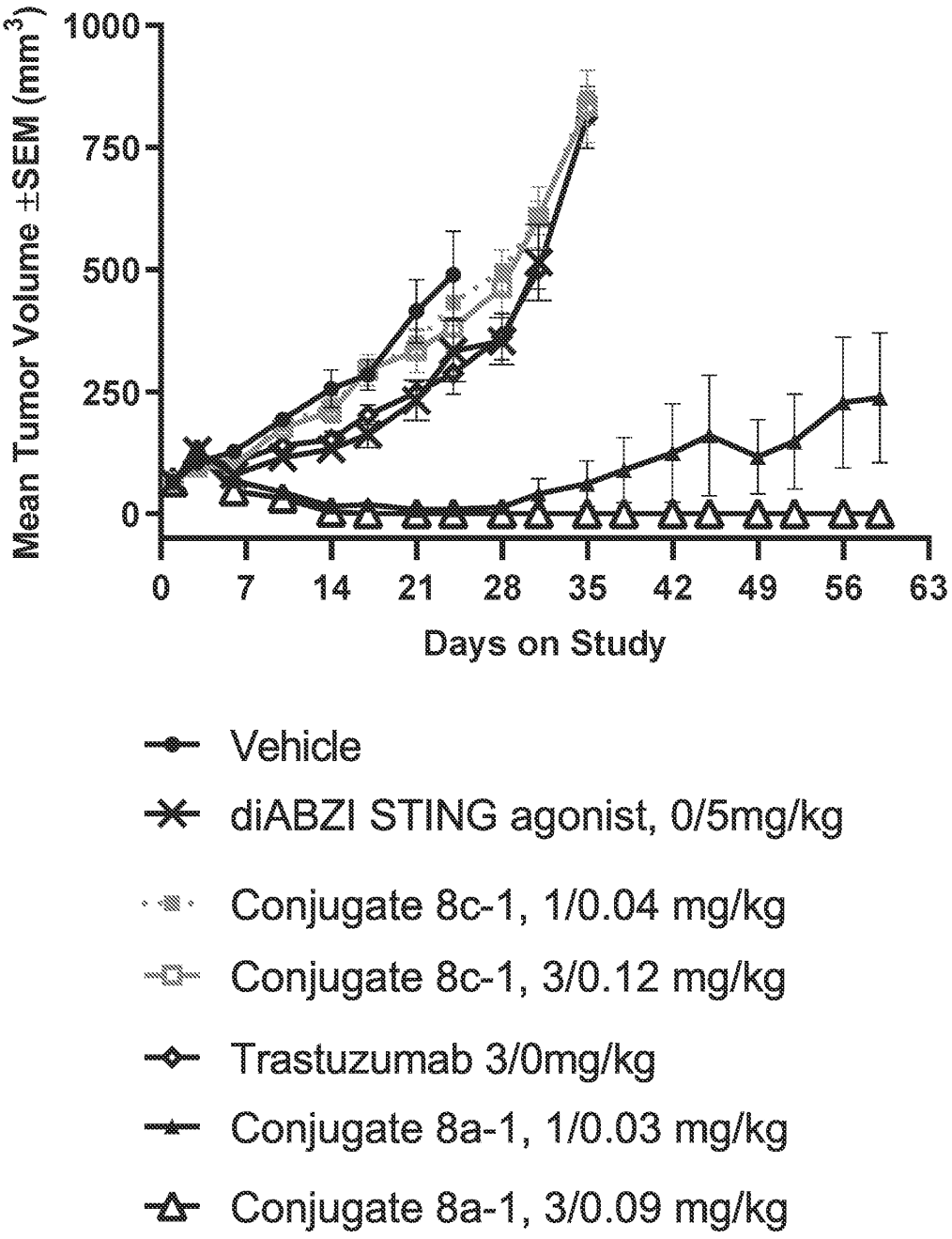

Mean Tumor Volume ±SEM (mm3)
1000
750
500
250
0
0
7
14
21
28
35
42
49
56
63
Days on Study
Vehicle
diABZI STING agonist, 0/5mg/kg
Conjugate 8c-1, 1/0.04 mg/kg
Conjugate 8c-1, 3/0.12 mg/kg
Trastuzumab 3/0mg/kg
Conjugate 8a-1, 1/0.03 mg/kg
Conjugate 8a-1, 3/0.09 mg/kg

FIG 6

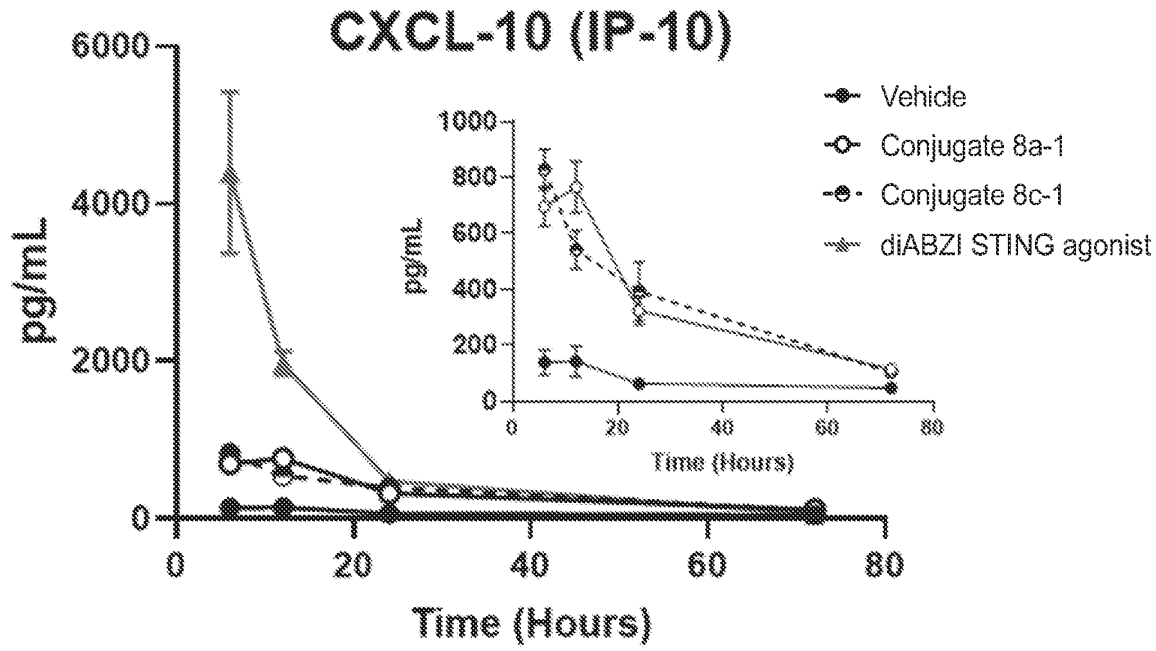

CXCL-10 (IP-10)
6000
4000
2000
0
pg/mL
0
20
40
60
80
Time (Hours)
1000
800
600
400
200
0
pg/mL
0
20
40
60
80
Time (Hours)
Vehicle
Conjugate 8a-1
Conjugate 8c-1
diABZI STING agonist

FIG 7A

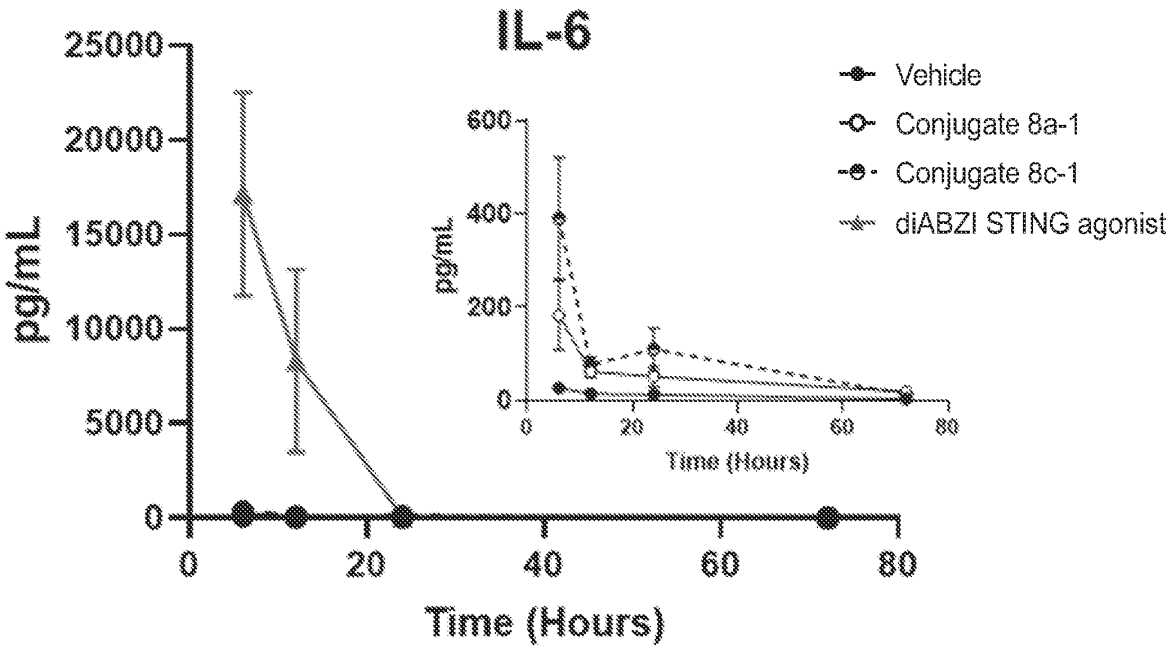

IL-6
25000
20000
15000
10000
5000
0
pg/mL
0
20
40
60
80
Time (Hours)
600
400
200
0
pg/mL
0
20
40
60
80
Time (Hours)
Vehicle
Conjugate 8a-1
Conjugate 8c-1
diABZI STING agonist

FIG 7B

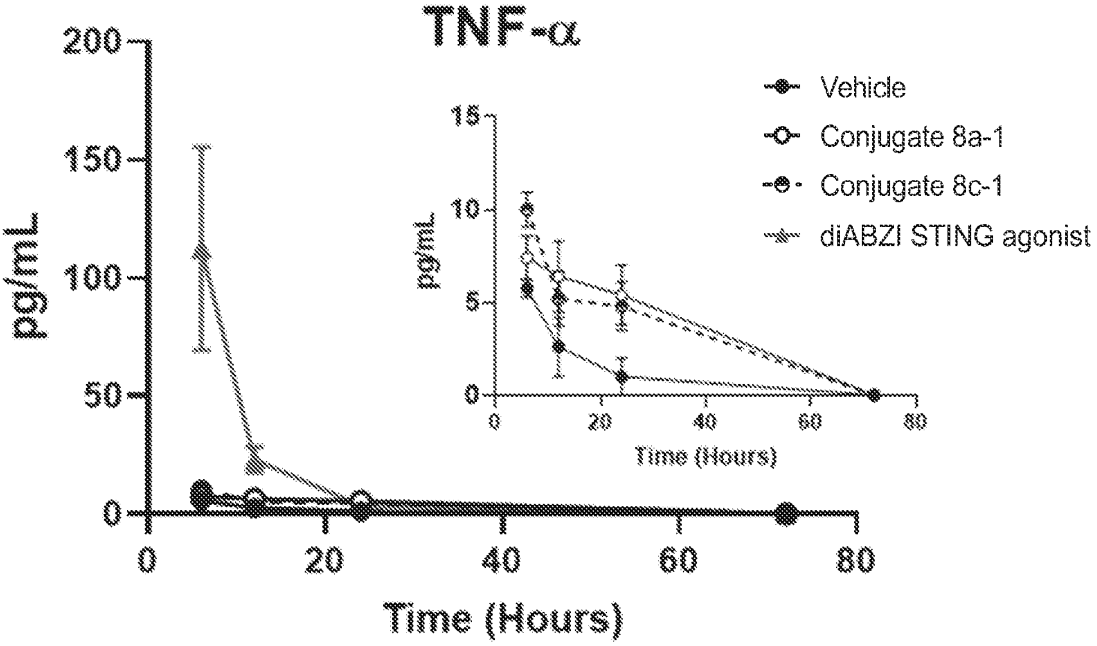

TNF-α
Vehicle
Conjugate 8a-1
Conjugate 8c-1
diABZI STING agonist
pg/mL
Time (Hours)
200
150
100
50
0
0
20
40
60
80
15
10
5
0
0
20
40
60
80
pg/mL
Time (Hours)

FIG 7C

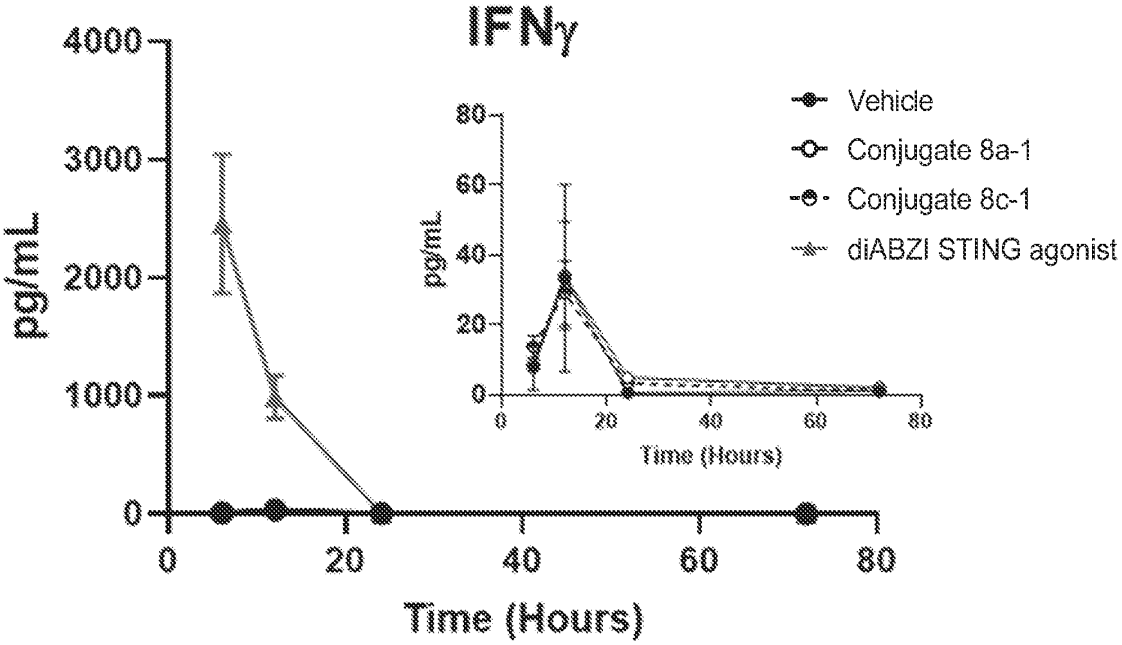

IFNγ
Vehicle
Conjugate 8a-1
Conjugate 8c-1
diABZI STING agonist
pg/mL
Time (Hours)
4000
3000
2000
1000
0
0
20
40
60
80
80
60
40
20
0
0
20
40
60
80
pg/mL
Time (Hours)

FIG 7D

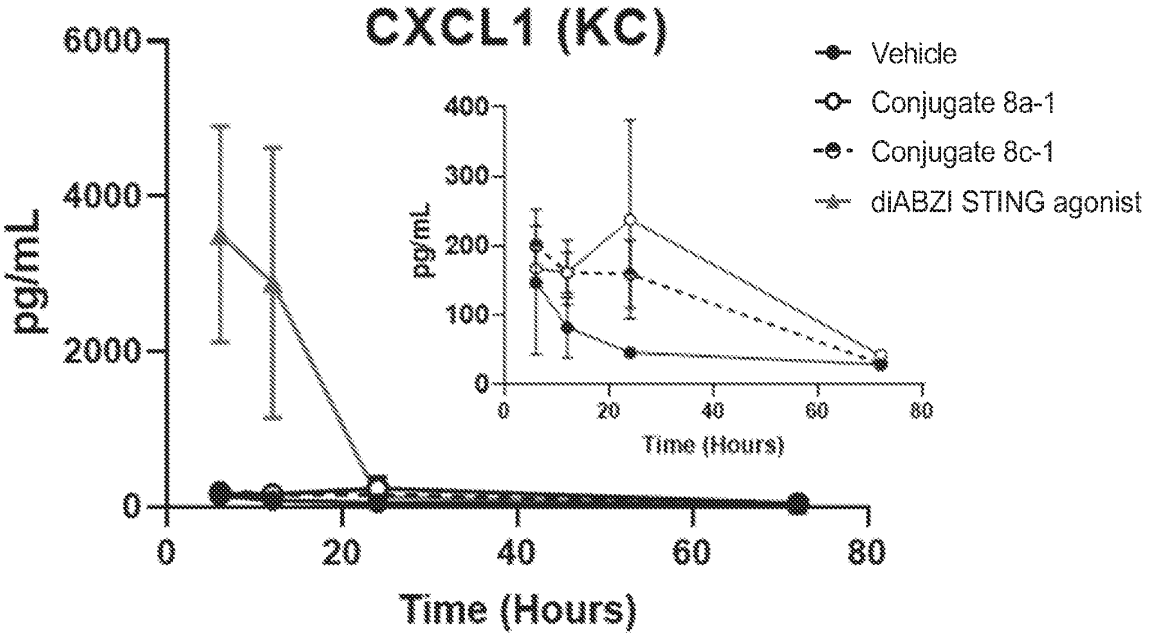

CXCL1 (KC)
Vehicle
Conjugate 8a-1
Conjugate 8c-1
diABZI STING agonist
pg/mL
Time (Hours)
6000
4000
2000
0
0
20
40
60
80
400
300
200
100

FIG 7E

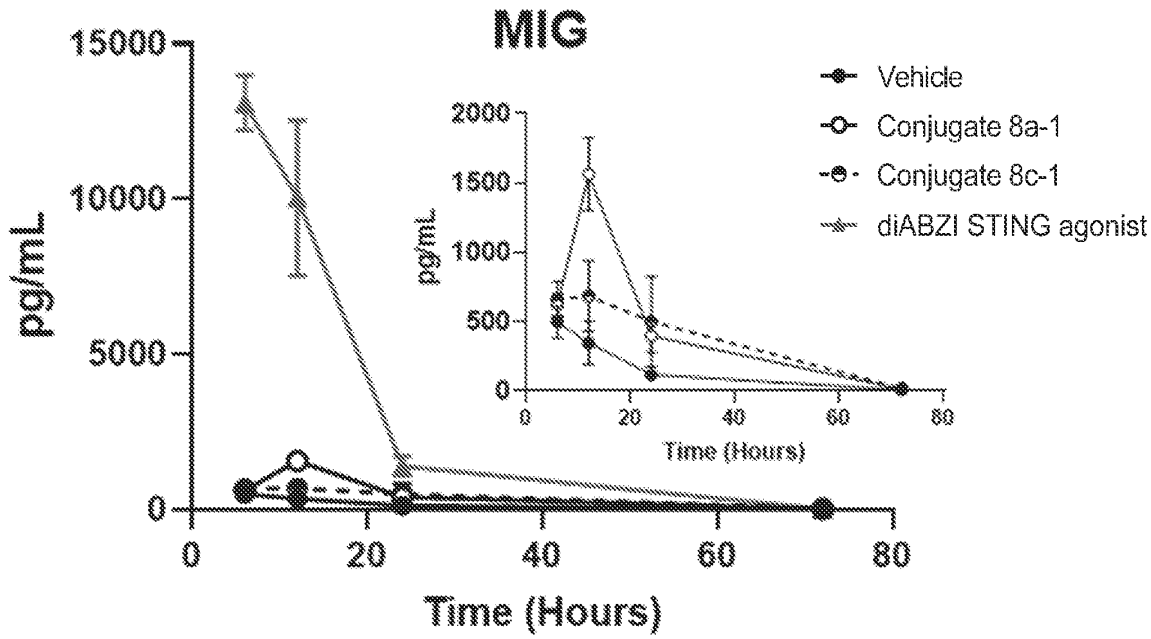

MIG
Vehicle
Conjugate 8a-1
Conjugate 8c-1
diABZI STING agonist
pg/mL
Time (Hours)
15000
10000
5000
0
0
20
40
60
80
2000
1500
1000
500

FIG 7F

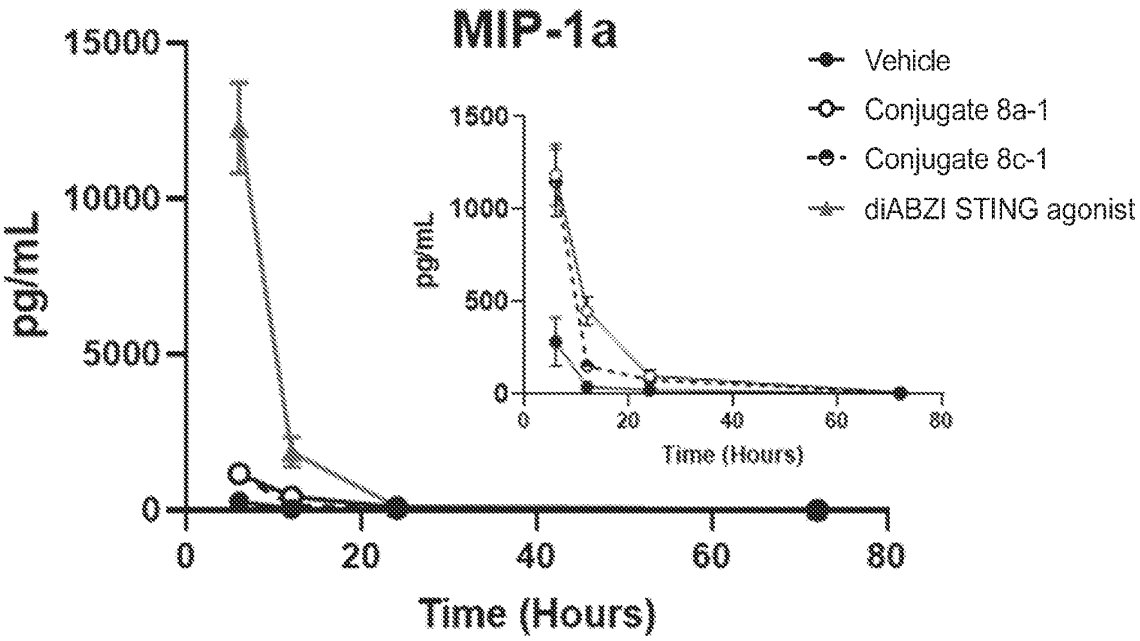

MIP-1a
15000
10000
5000
0
pg/mL
0
20
40
60
80
Time (Hours)
1500
1000
500
0
pg/mL
0
20
40
60
80
Time (Hours)
Vehicle
Conjugate 8a-1
Conjugate 8c-1
diABZI STING agonist

FIG 7G

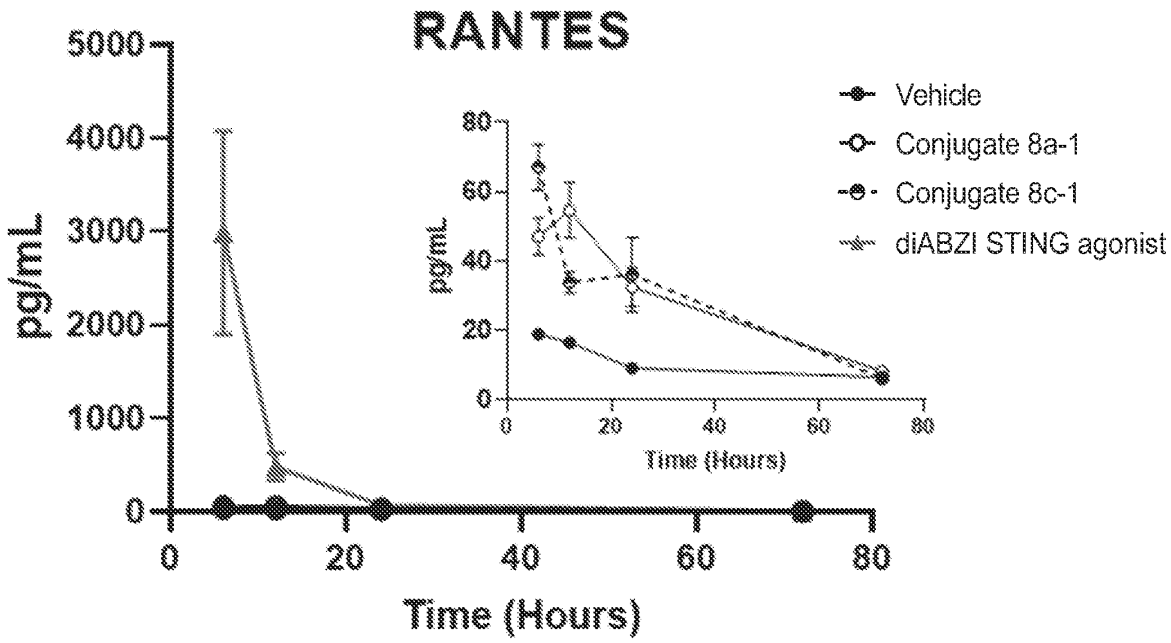

RANTES
5000
4000
3000
2000
1000
0
pg/mL
0
20
40
60
80
Time (Hours)
80
60
40
20
0
pg/mL
0
20
40
60
80
Time (Hours)
Vehicle
Conjugate 8a-1
Conjugate 8c-1
diABZI STING agonist

FIG 7H

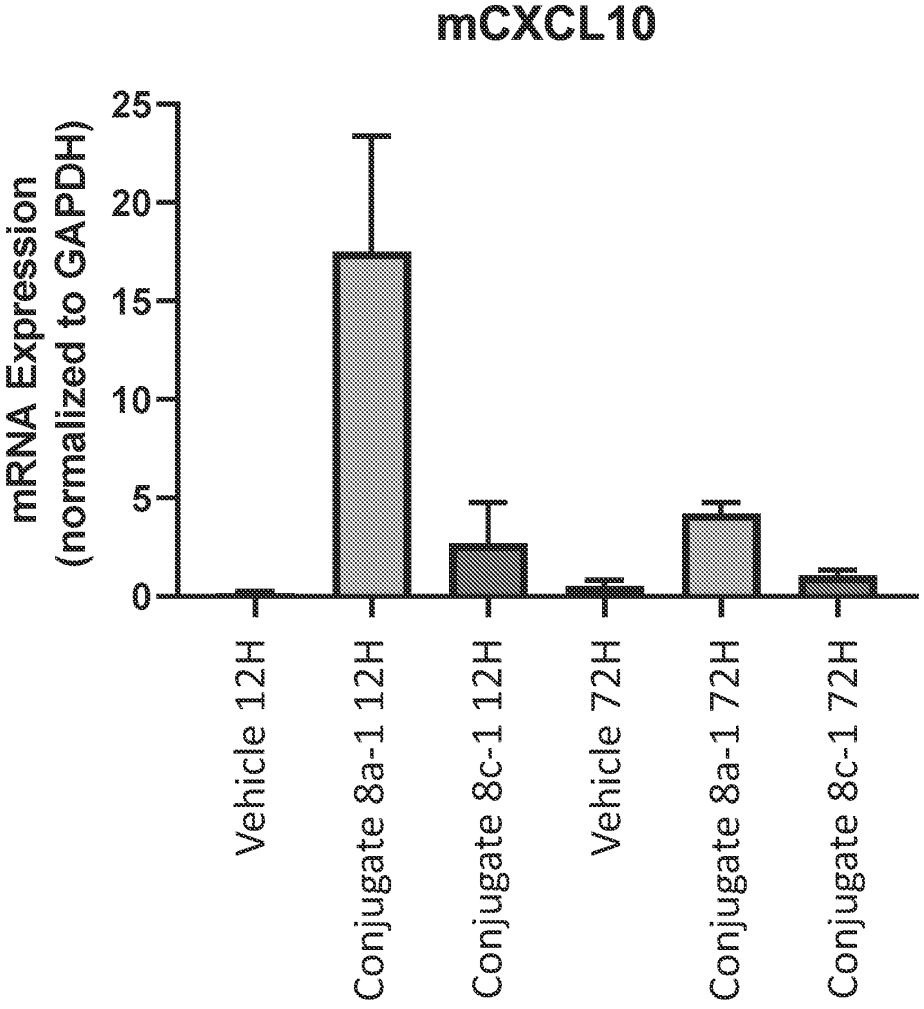

mCXCL10
mRNA Expression
(normalized to GAPDH)
25
20
15
10
5
0
Vehicle 12H
Conjugate 8a-1 12H
Conjugate 8c-1 12H
Vehicle 72H
Conjugate 8a-1 72H
Conjugate 8c-1 72H

FIG 8A

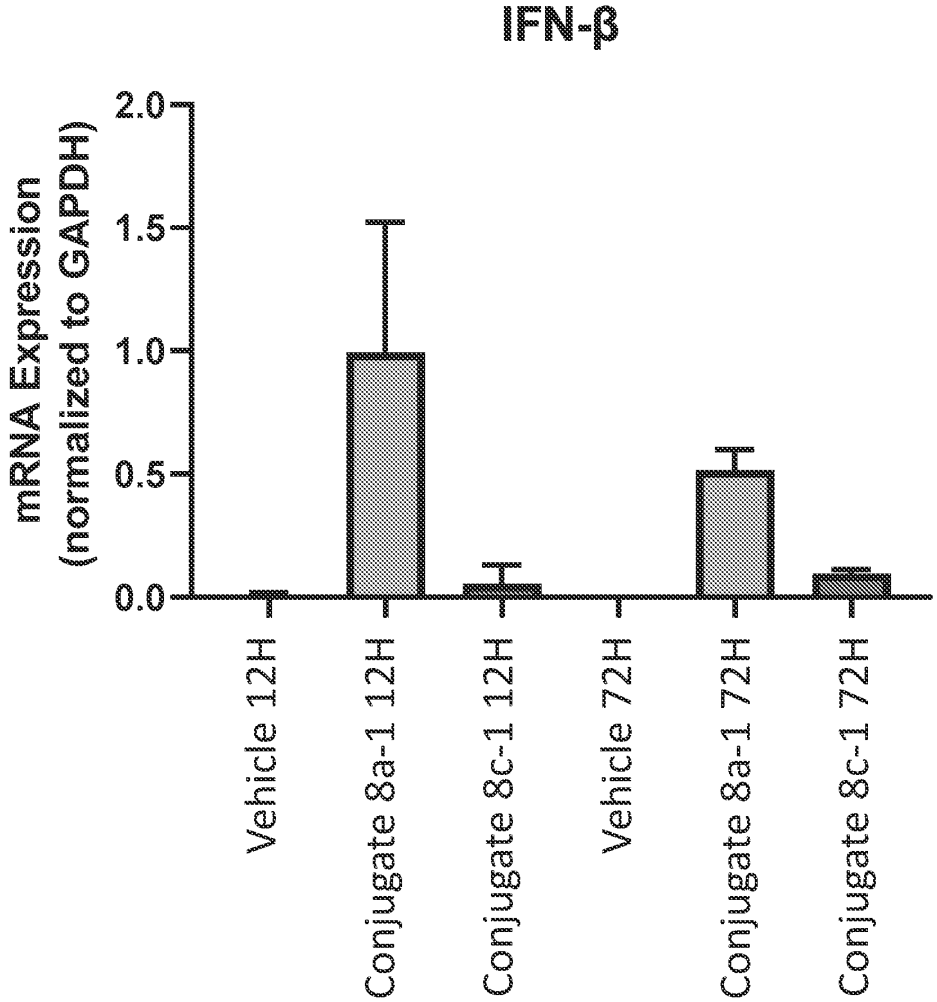

IFN-β
mRNA Expression
(normalized to GAPDH)
2.0
1.5
1.0
0.5
0.0
Vehicle 12H
Conjugate 8a-1 12H
Conjugate 8c-1 12H
Vehicle 72H
Conjugate 8a-1 72H
Conjugate 8c-1 72H

FIG 8B

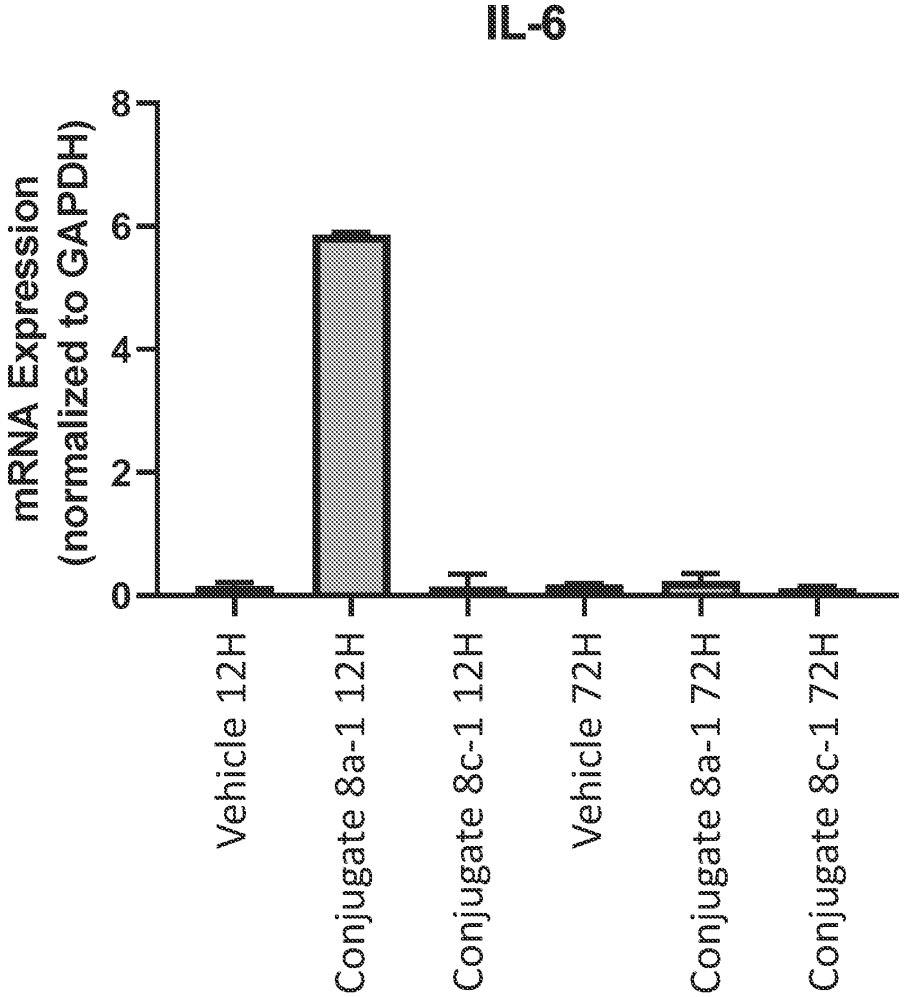

IL-6
mRNA Expression
(normalized to GAPDH)
0
2
4
6
8
Vehicle 12H
Conjugate 8a-1 12H
Conjugate 8c-1 12H
Vehicle 72H
Conjugate 8a-1 72H
Conjugate 8c-1 72H

FIG 8C

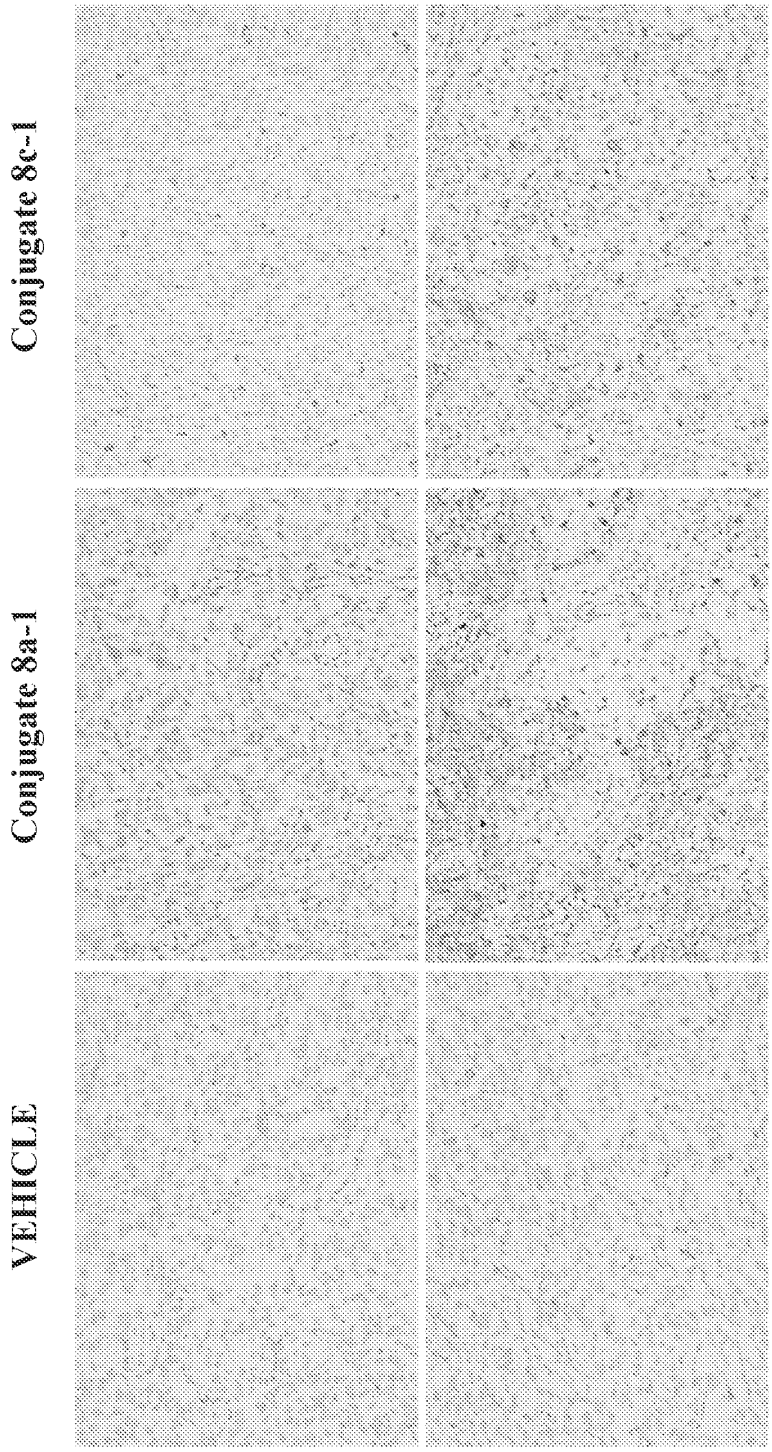


FIG 9

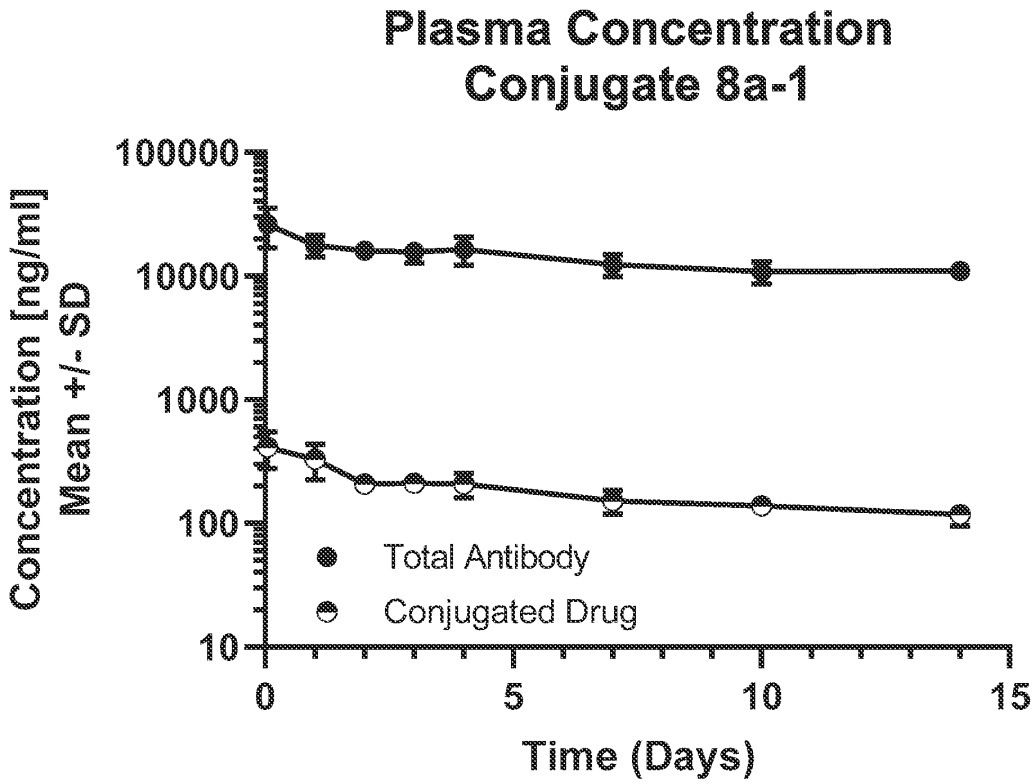

Plasma Concentration
Conjugate 8a-1
Concentration [ng/ml]
Mean +/- SD
100000
10000
1000
100
10
0
5
10
15
Time (Days)
Total Antibody
Conjugated Drug

FIG 10

Effect of IFNλ1 (IL29) or IFNλ2(IL28A) neutralizing antibodies in cancer cell and PBMC co-cultures

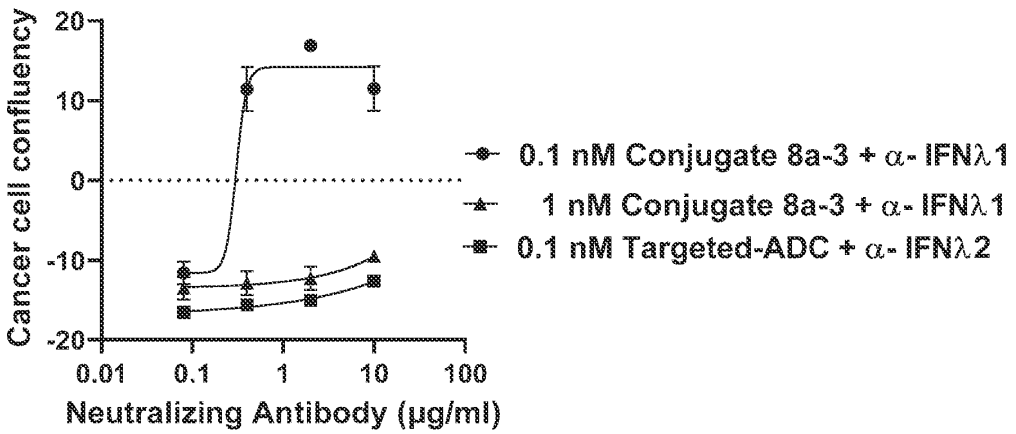


FIG 11

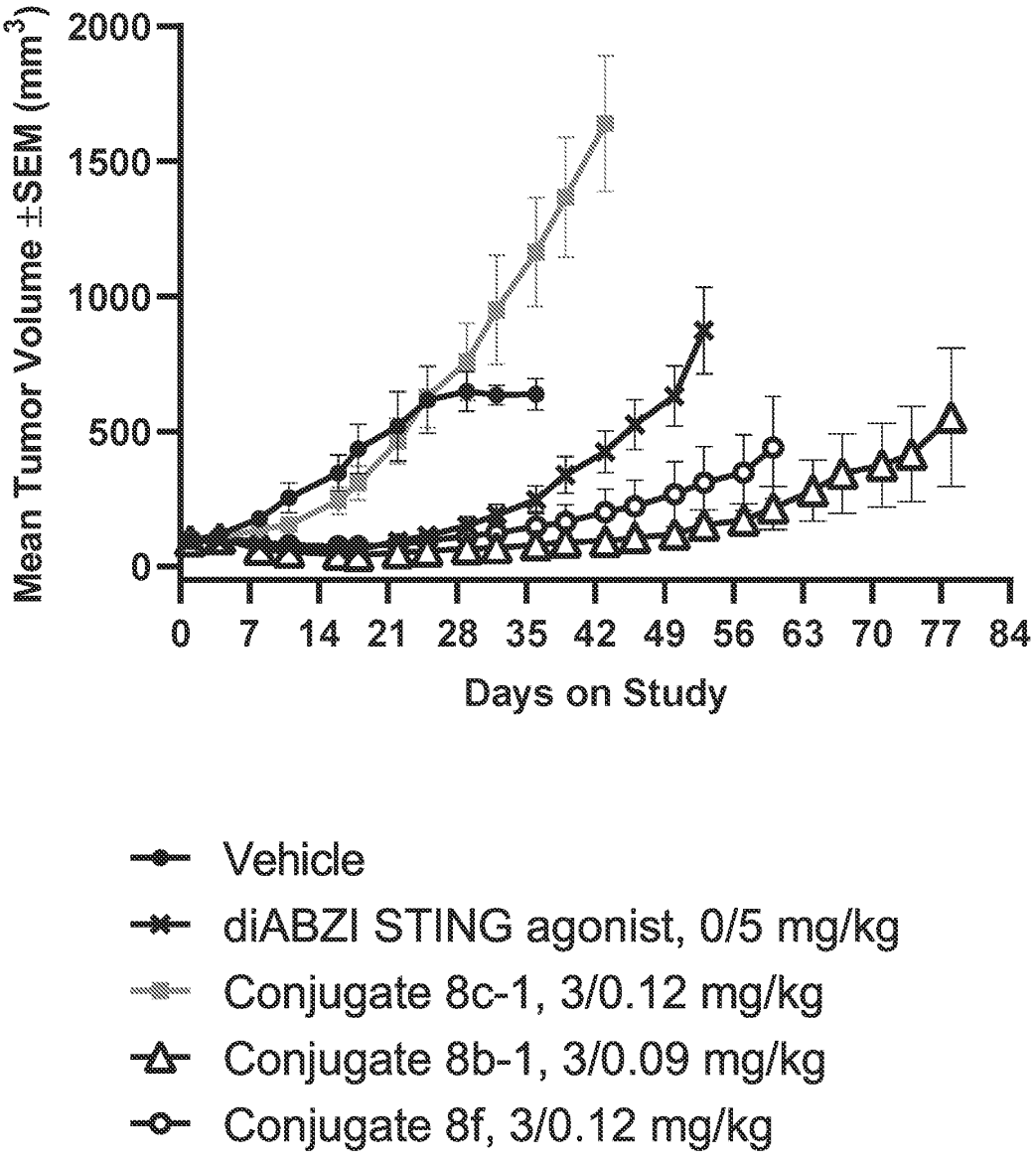

Mean Tumor Volume ±SEM (mm3)
2000
1500
1000
500
0
0 7 14 21 28 35 42 49 56 63 70 77 84
Days on Study
Vehicle
diABZI STING agonist, 0/5 mg/kg
Conjugate 8c-1, 3/0.12 mg/kg
Conjugate 8b-1, 3/0.09 mg/kg
Conjugate 8f, 3/0.12 mg/kg

FIG 12

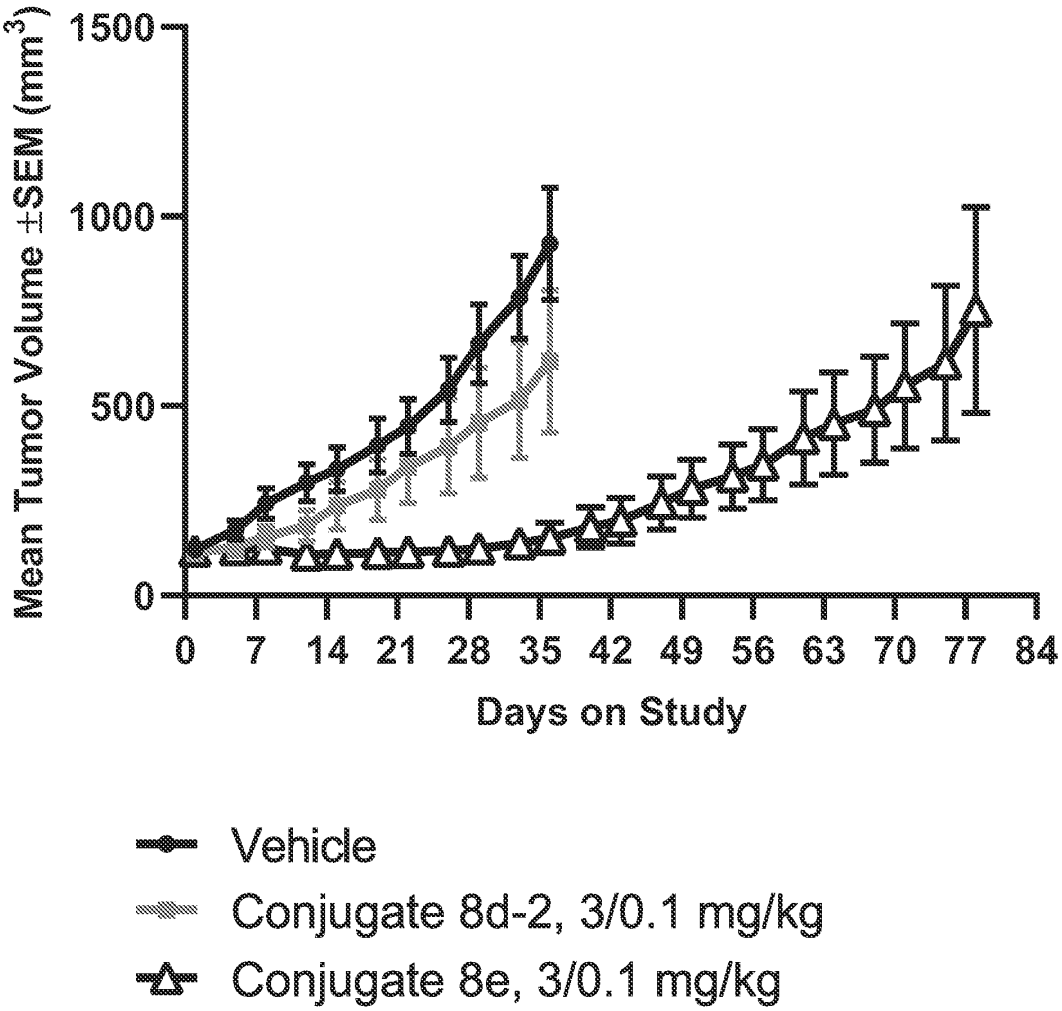

Mean Tumor Volume ±SEM (mm3)
1500
1000
500
0
0 7 14 21 28 35 42 49 56 63 70 77 84
Days on Study
Vehicle
Conjugate 8d-2, 3/0.1 mg/kg
Conjugate 8e, 3/0.1 mg/kg

FIG 13

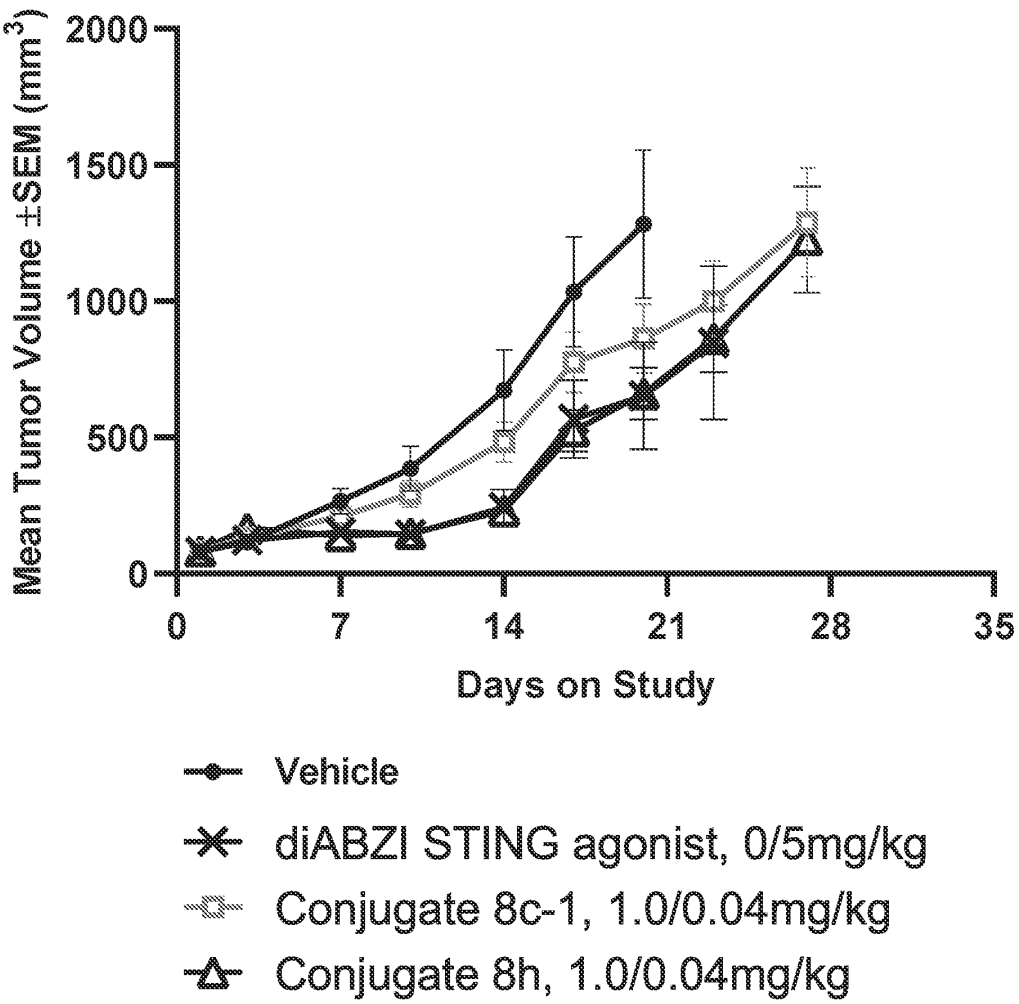

Mean Tumor Volume ±SEM (mm3)
2000
1500
1000
500
0
0
7
14
21
28
35
Days on Study
Vehicle
diABZI STING agonist, 0/5mg/kg
Conjugate 8c-1, 1.0/0.04mg/kg
Conjugate 8h, 1.0/0.04mg/kg

FIG 14

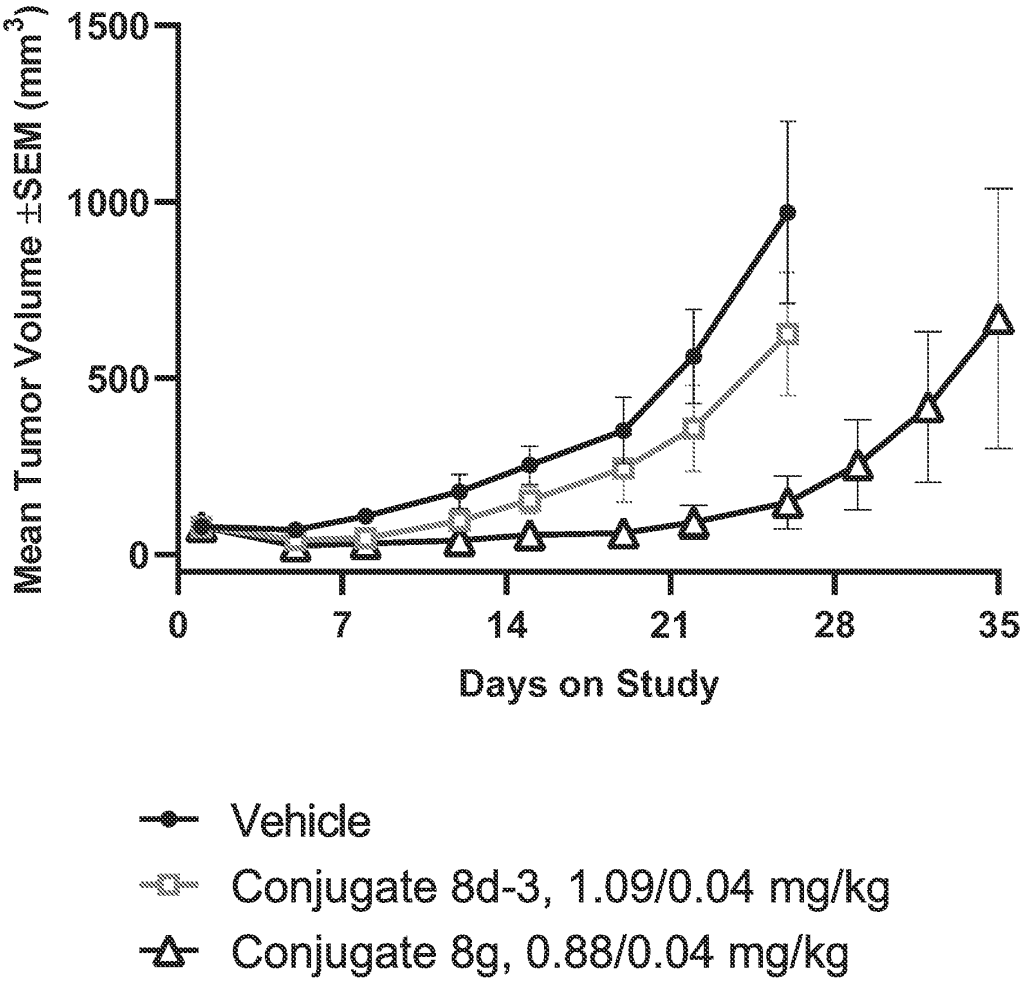

Mean Tumor Volume ±SEM (mm3)
1500
1000
500
0
0
7
14
21
28
35
Days on Study
Vehicle
Conjugate 8d-3, 1.09/0.04 mg/kg
Conjugate 8g, 0.88/0.04 mg/kg

FIG 15A

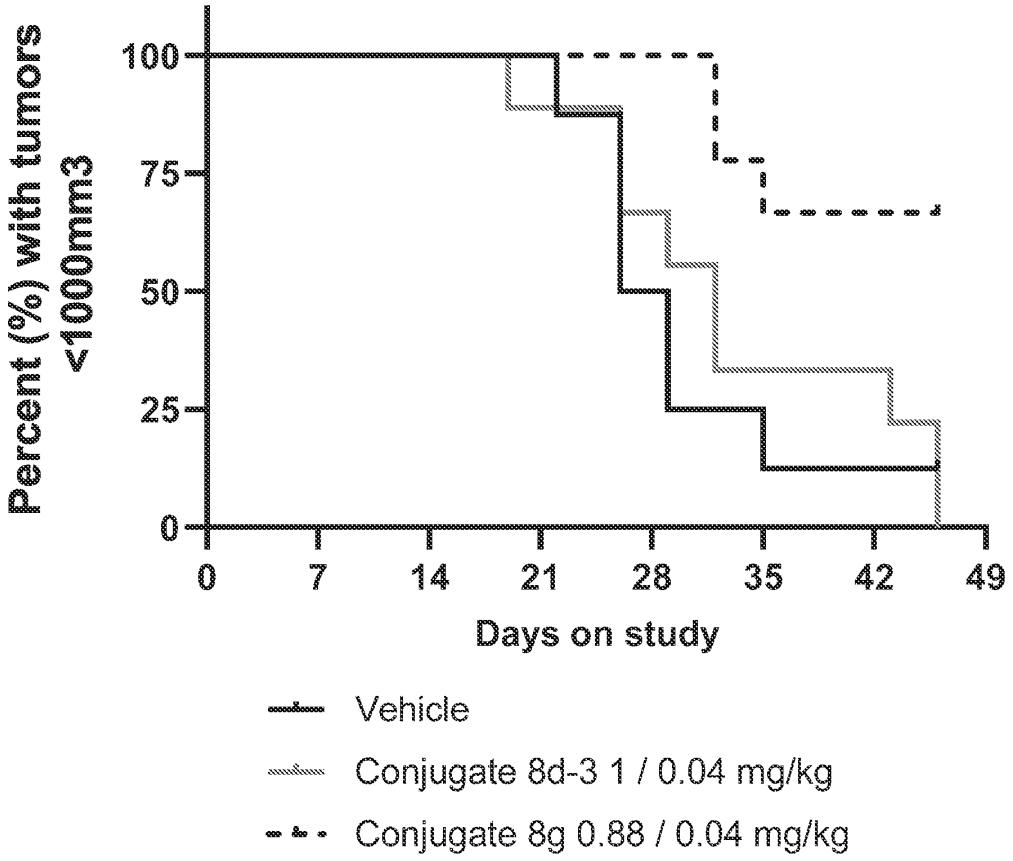

Percent (%) with tumors <1000mm3
100
75
50
25
0
0
7
14
21
28
35
42
49
Days on study
Vehicle
Conjugate 8d-3 1 / 0.04 mg/kg
Conjugate 8g 0.88 / 0.04 mg/kg

FIG 15B

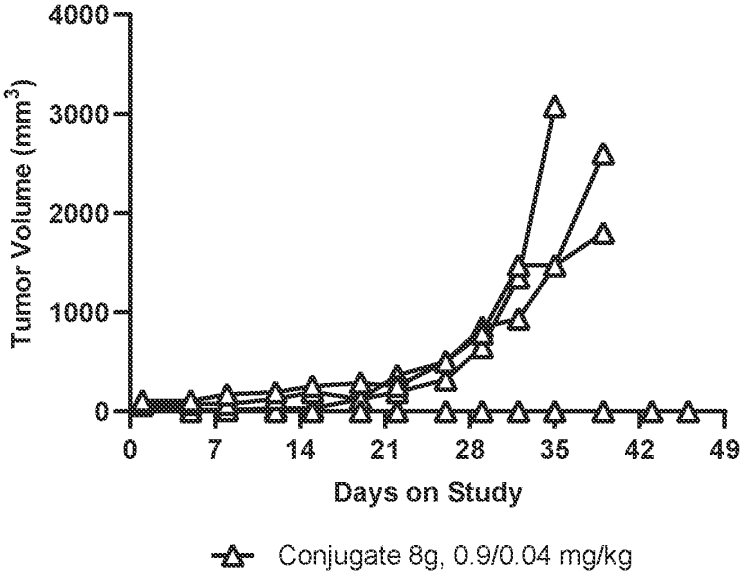

4000
3000
2000
1000
0
Tumor Volume (mm3)
0
7
14
21
28
35
42
49
Days on Study
Conjugate 8g, 0.9/0.04 mg/kg

FIG 16A

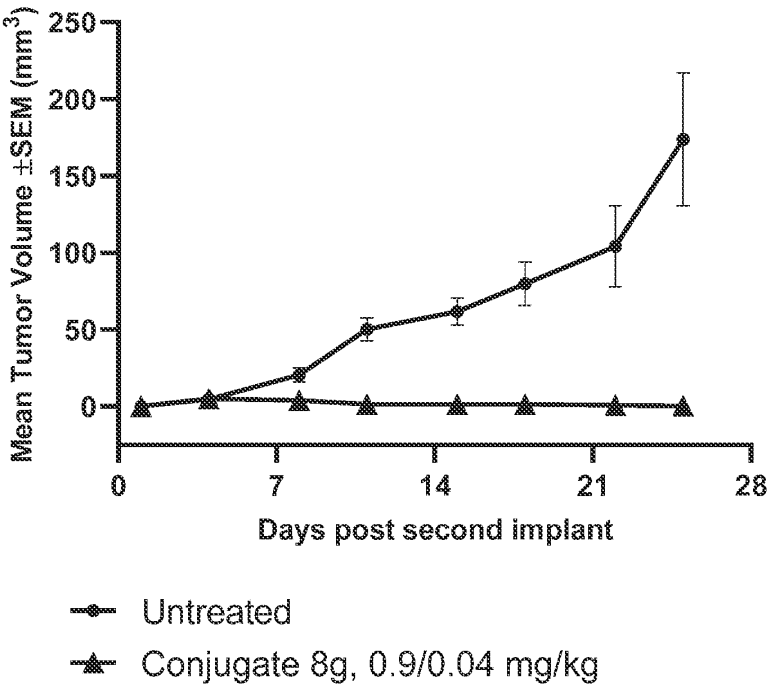


FIG 16B

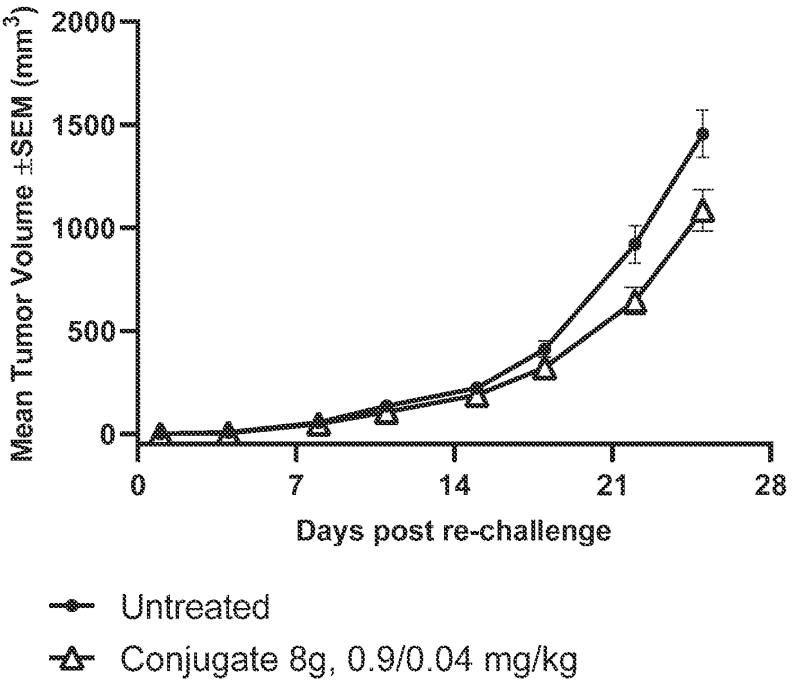


FIG 16C

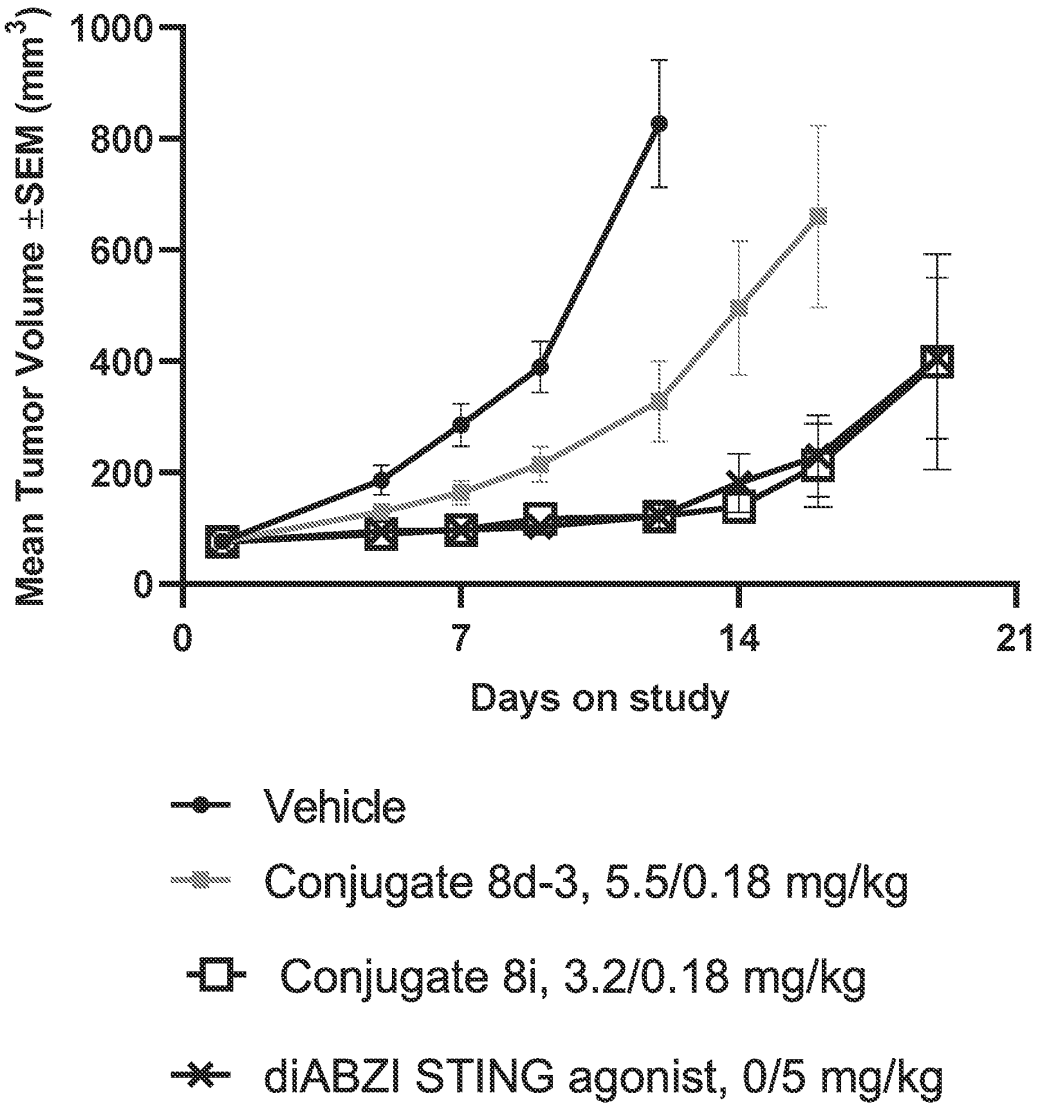

Mean Tumor Volume ±SEM (mm3)
1000
800
600
400
200
0
0
7
14
21
Days on study
Vehicle
Conjugate 8d-3, 5.5/0.18 mg/kg
Conjugate 8i, 3.2/0.18 mg/kg
diABZI STING agonist, 0/5 mg/kg

FIG 17

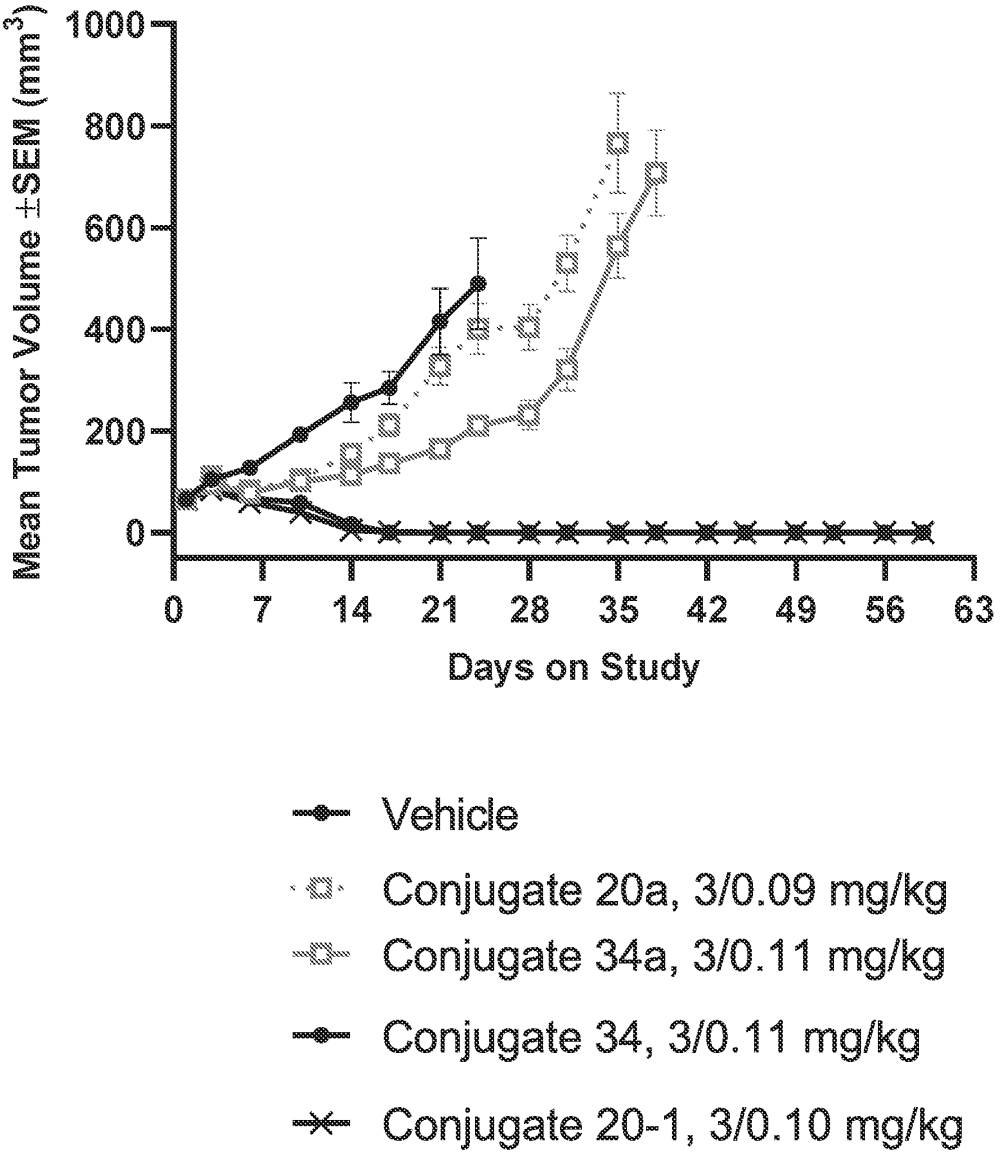

Mean Tumor Volume ±SEM (mm3)
1000
800
600
400
200
0
0
7
14
21
28
35
42
49
56
63
Days on Study
Vehicle
Conjugate 20a, 3/0.09 mg/kg
Conjugate 34a, 3/0.11 mg/kg
Conjugate 34, 3/0.11 mg/kg
Conjugate 20-1, 3/0.10 mg/kg

FIG 18

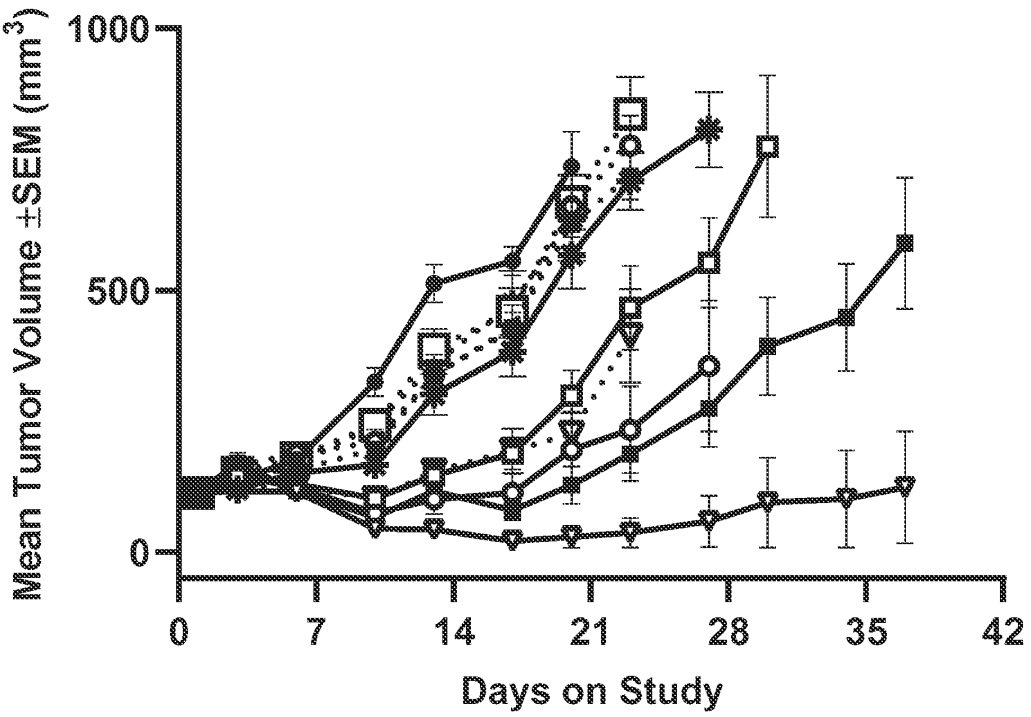
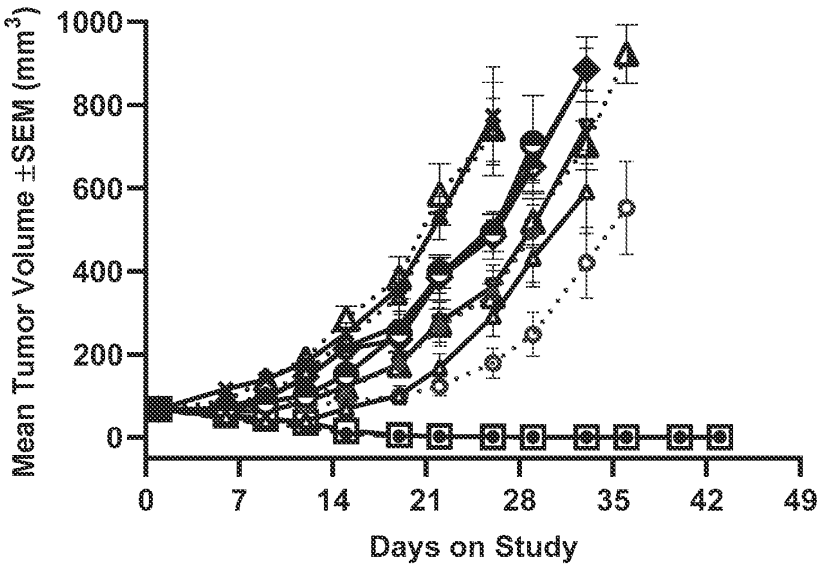

Mean Tumor Volume ±SEM (mm3)
1000
500
0
0
7
14
21
28
35
42
Days on Study
Vehicle
Conjugate 28, 0.3/0.01mg/kg
Conjugate 29, 0.2/0.01mg/kg
Conjugate 8-2, 0.3/0.01 mg/kg
Conjugate 25, 0.3/0.01 mg/kg
Conjugate 45, 0.3/0.01 mg/kg
Conjugate 45,1 /0.04 mg/kg
Conjugate 25,1/0.04 mg/kg
Conjugate 8-2, 1/0.04 mg/kg
Conjugate 29, 0.8/0.02 mg/kg
Conjugate 28, 1.0/0.03 mg/kg

FIG 19



Vehicle
diABZI STING agonist, 1.5 mg/kg, q3dx3
Compound 30, 1.5 mg/kg, q3dx3
diABZI STING agonist, 0.128 mg/kg
Compound 30, 0.128 mg/kg
Conjugate 32b-2, 3.42/0.128 mg/kg
XMT-1519, 3.00 mg/kg
Conjugate 32-5, 0.100/0.004 mg/kg
Conjugate 32-5, 0.300/0.013 mg/kg
Conjugate 32-5, 1.00/0.042 mg/kg
Conjugate 32-5, 3.00/0.128 mg/kg
Conjugate 32e, 1.00/0.039 mg/kg
Conjugate 32e, 3.00/0.117 mg/kg

FIG 20

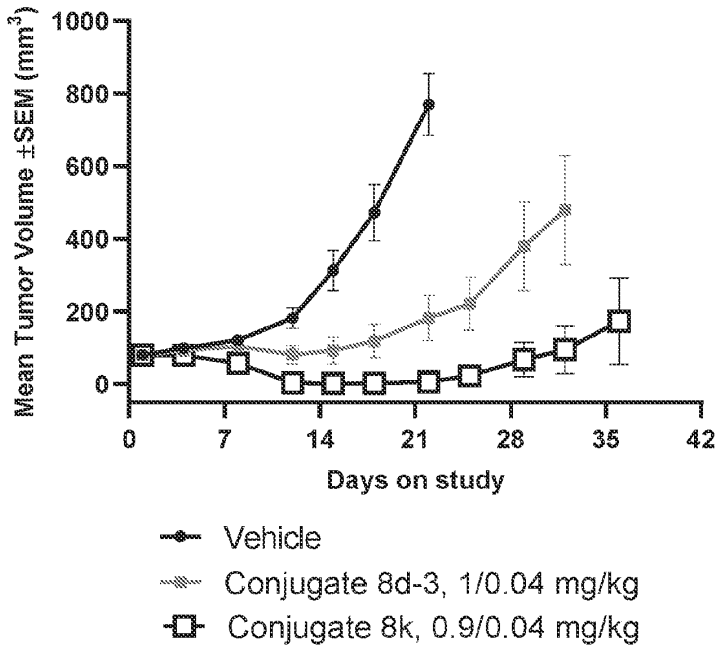


FIG. 21A

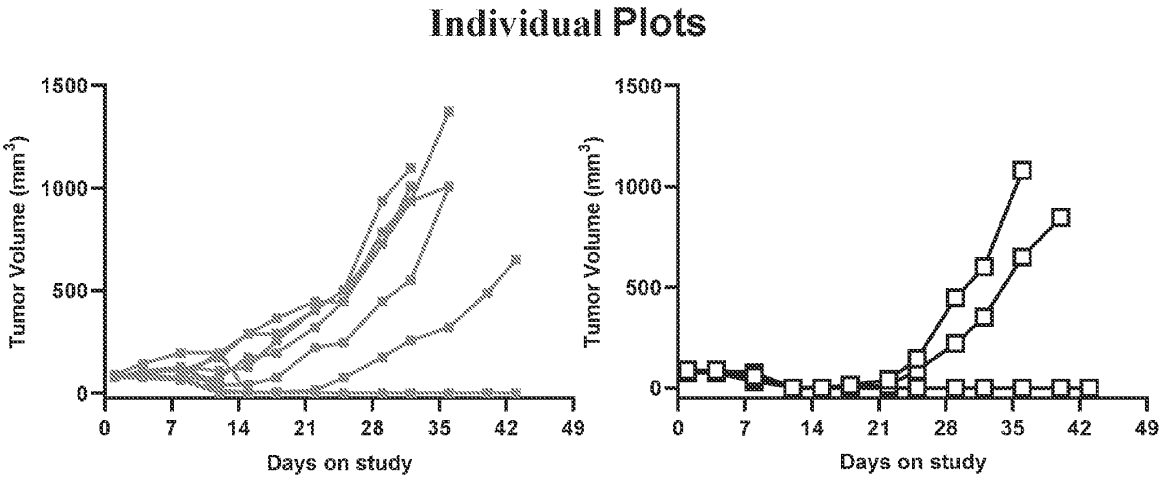


FIG. 21B

FIG. 21C

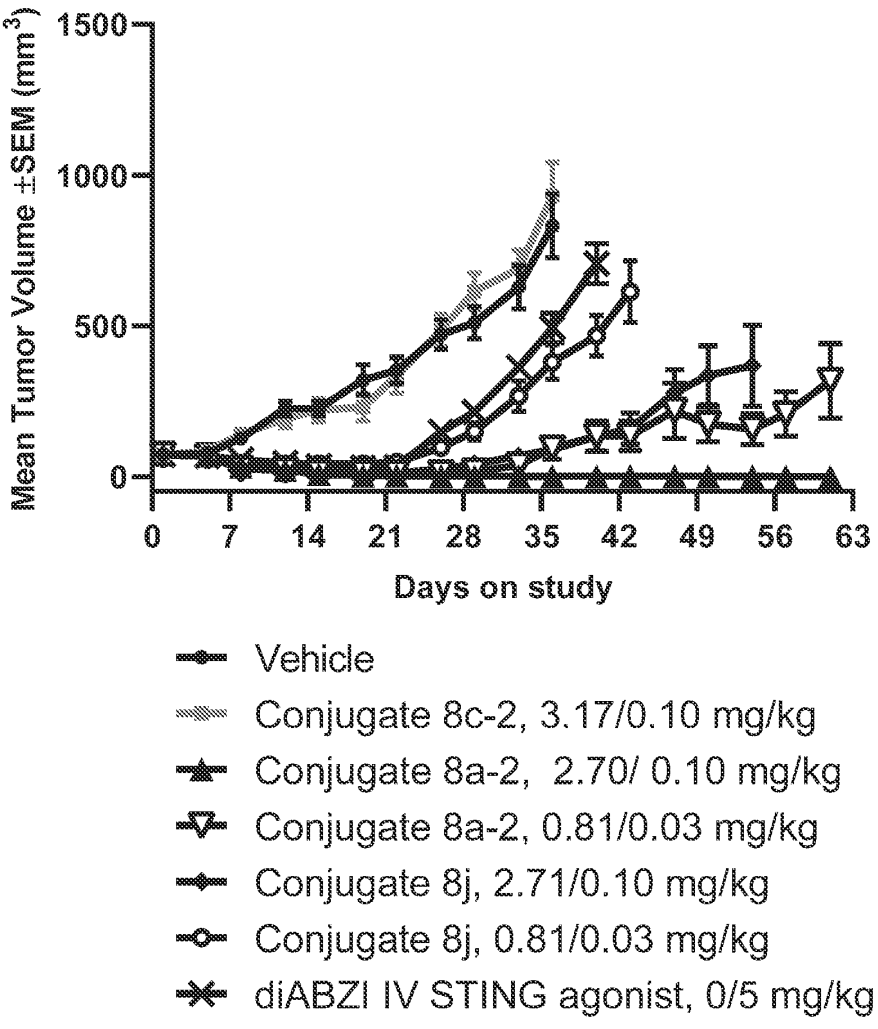

Mean Tumor Volume ±SEM (mm3)
1500
1000
500
0
0
7
14
21
28
35
42
49
56
63
Days on study
Vehicle
Conjugate 8c-2, 3.17/0.10 mg/kg
Conjugate 8a-2, 2.70/ 0.10 mg/kg
Conjugate 8a-2, 0.81/0.03 mg/kg
Conjugate 8j, 2.71/0.10 mg/kg
Conjugate 8j, 0.81/0.03 mg/kg
diABZI IV STING agonist, 0/5 mg/kg

FIG 22

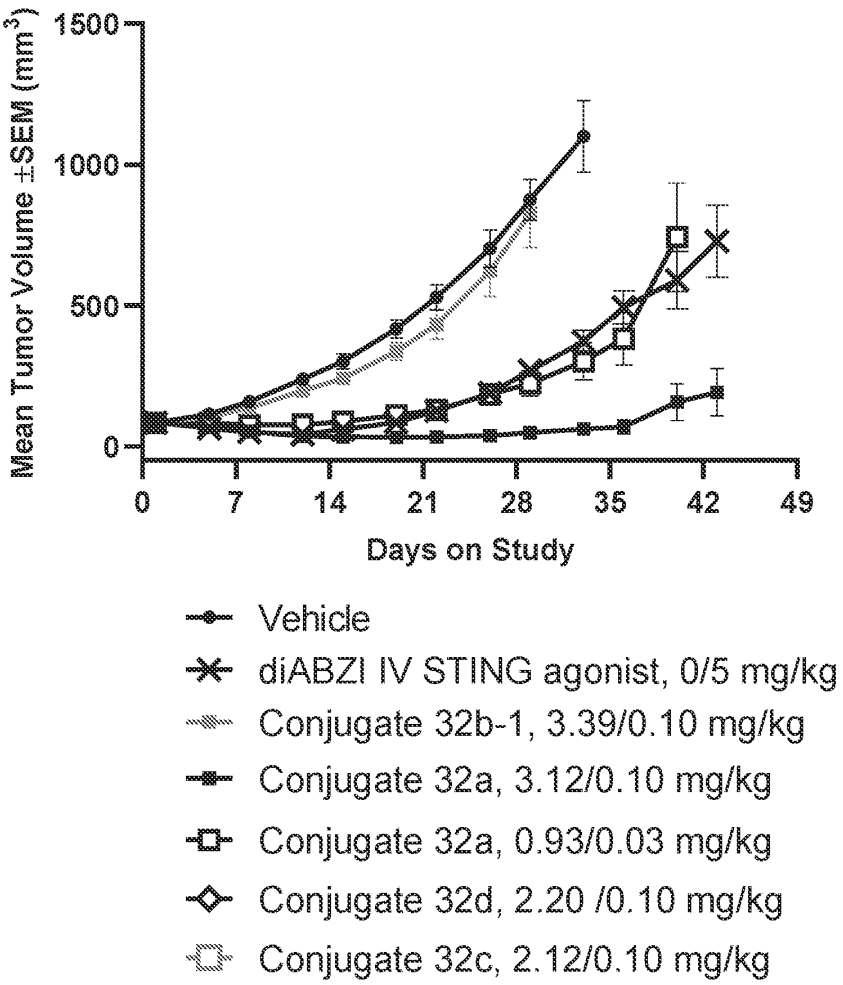
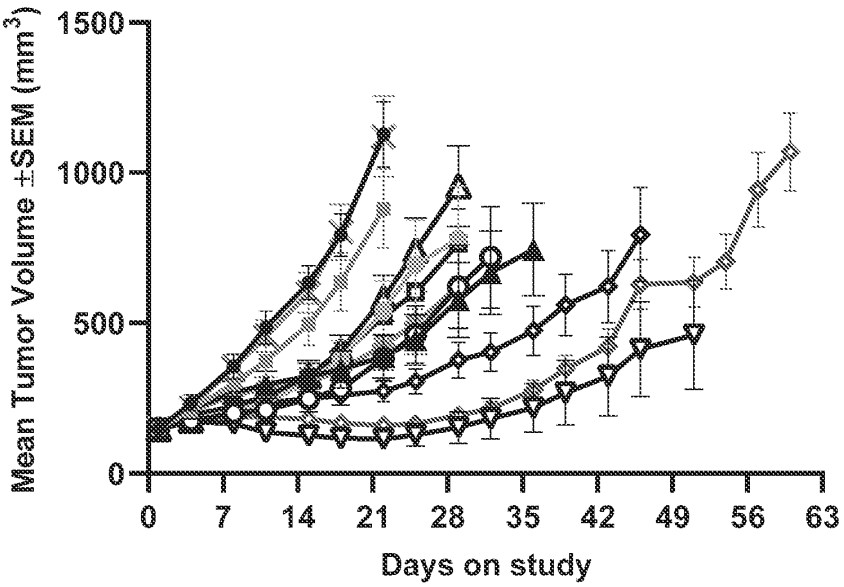

Mean Tumor Volume ±SEM (mm3)
1500
1000
500
0
0
7
14
21
28
35
42
49
Days on Study
Vehicle
diABZI IV STING agonist, 0/5 mg/kg
Conjugate 32b-1, 3.39/0.10 mg/kg
Conjugate 32a, 3.12/0.10 mg/kg
Conjugate 32a, 0.93/0.03 mg/kg
Conjugate 32d, 2.20 /0.10 mg/kg
Conjugate 32c, 2.12/0.10 mg/kg

FIG 23



- Vehicle
- Rituximab AF-HPA ADC, 0.75/0.023 mg/kg + Conjugate 8c-2, 4.0/0.126 mg/kg
- XMT-1535 AF-HPA ADC, 0.75/0.024 mg/kg
- Conjugate 8b-2, 4.0/0.142 mg/kg
- Conjugate 8b-2, 2.0/0.071 mg/kg
- XMT-1535 AF-HPA ADC, 0.75/0.024 mg/kg + Conjugate 8c-2, 4.0/0.126 mg/kg
- Rituximab AF-HPA ADC, 0.75/0.023 mg/kg + Conjugate 8b-2, 4.0/0.142 mg/kg
- Rituximab AF-HPA ADC, 0.75/0.023 mg/kg + Conjugate 8b-2, 2.0 /0.071 mg/kg
- XMT-1535 AF-HPA ADC, 0.75/0.024 mg/kg + Conjugate 8b-2, 4.0/0.142 mg/kg
- XMT-1535 AF-HPA ADC, 0.75/0.024 mg/kg + Conjugate 8b-2, 2.0/0.071 mg/kg
- XMT-1535 AF-HPA ADC, 0.75/0.024 mg/kg +XMT-1535, 4.0/0 mg/kg
- XMT-1535, 4.75/0 mg/kg

FIG 24

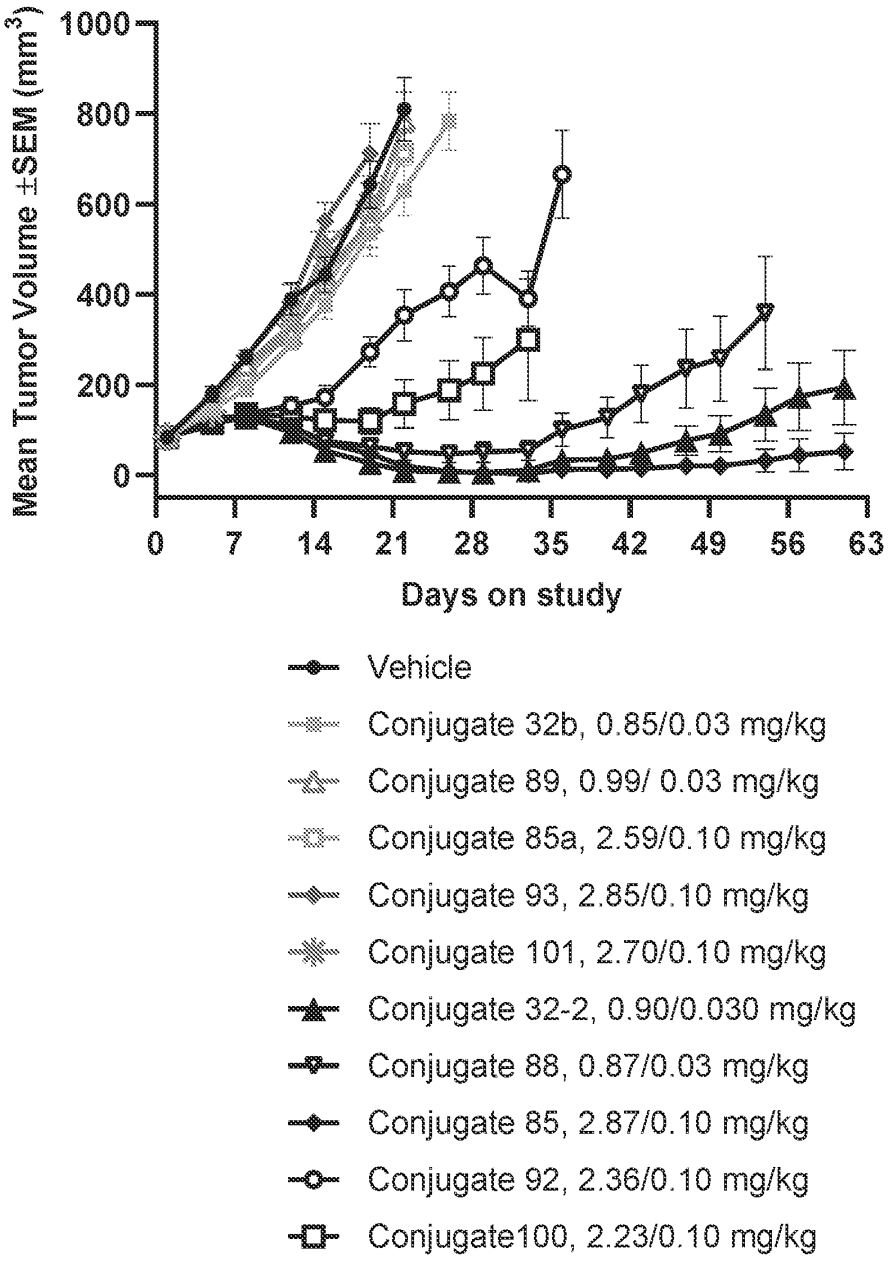

Mean Tumor Volume ±SEM (mm3)
1000
800
600
400
200
0
0
7
14
21
28
35
42
49
56
63
Days on study
Vehicle
Conjugate 32b, 0.85/0.03 mg/kg
Conjugate 89, 0.99/ 0.03 mg/kg
Conjugate 85a, 2.59/0.10 mg/kg
Conjugate 93, 2.85/0.10 mg/kg
Conjugate 101, 2.70/0.10 mg/kg
Conjugate 32-2, 0.90/0.030 mg/kg
Conjugate 88, 0.87/0.03 mg/kg
Conjugate 85, 2.87/0.10 mg/kg
Conjugate 92, 2.36/0.10 mg/kg
Conjugate100, 2.23/0.10 mg/kg

FIG 25

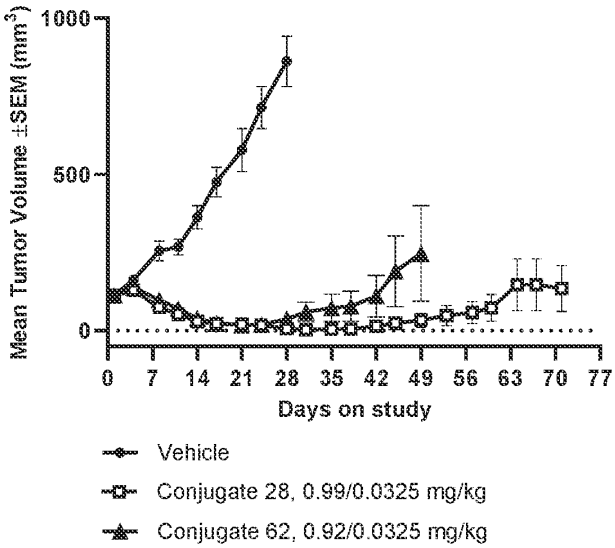

Mean Tumor Volume ±SEM (mm3)
1000
500
0
0 7 14 21 28 35 42 49 56 63 70 77
Days on study
Vehicle
Conjugate 28, 0.99/0.0325 mg/kg
Conjugate 62, 0.92/0.0325 mg/kg

FIG 26

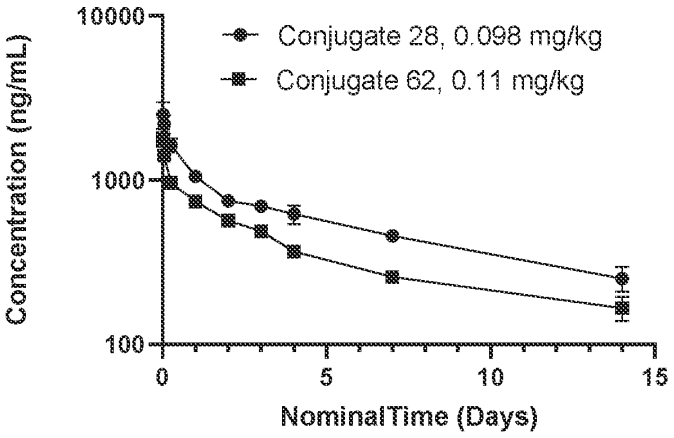

Concentration (ng/mL)
10000
1000
100
0 5 10 15
NominalTime (Days)
Conjugate 28, 0.098 mg/kg
Conjugate 62, 0.11 mg/kg

FIG 27