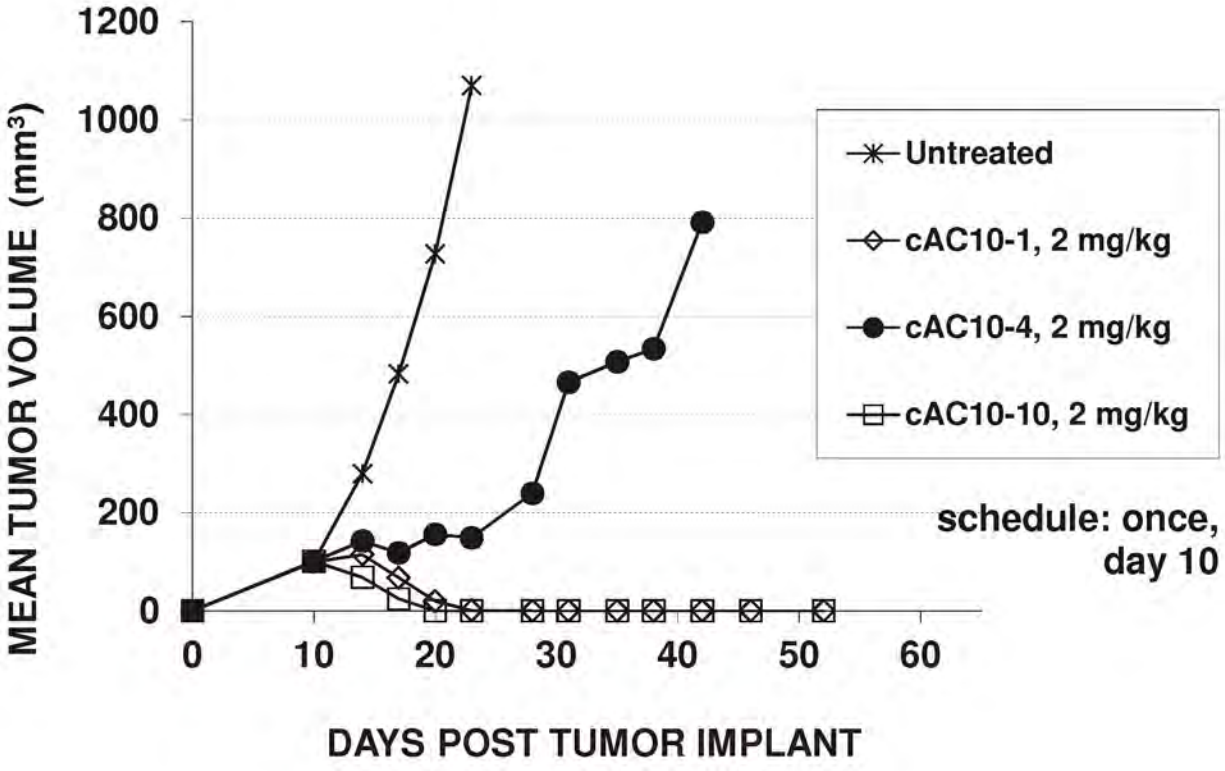

MEAN TUMOR VOLUME (mm³)
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
DAYS POST TUMOR IMPLANT
Untreated
cAC10-1, 2 mg/kg
cAC10-4, 2 mg/kg
cAC10-10, 2 mg/kg
schedule: once, day 10

Figure 1

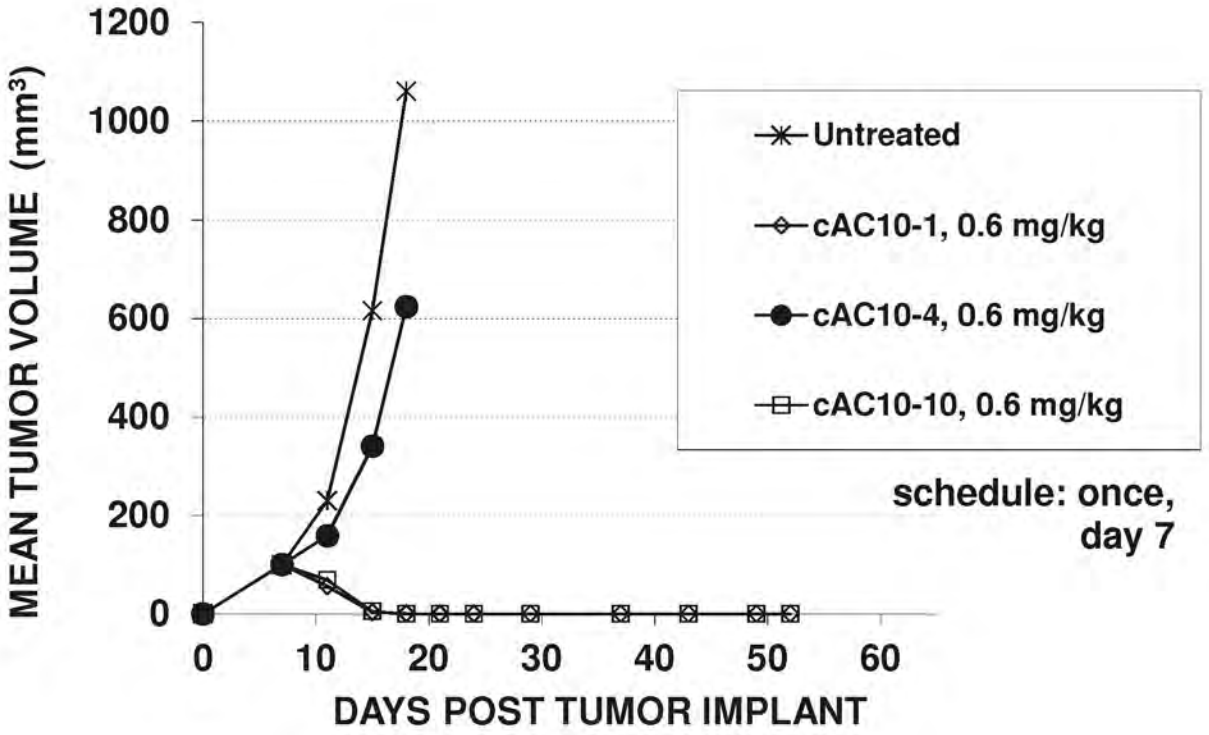

MEAN TUMOR VOLUME (mm³)
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
DAYS POST TUMOR IMPLANT
Untreated
cAC10-1, 0.6 mg/kg
cAC10-4, 0.6 mg/kg
cAC10-10, 0.6 mg/kg
schedule: once, day 7

Figure 2

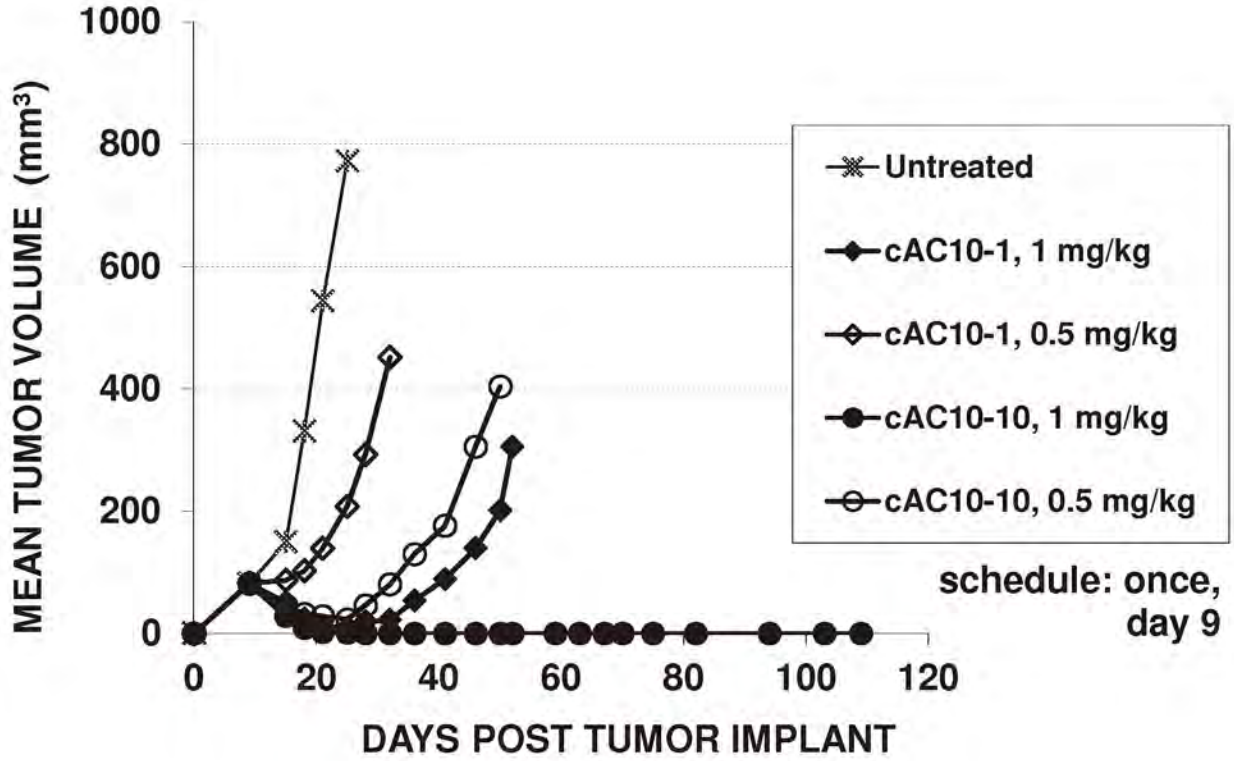

1000
800
600
400
200
0
MEAN TUMOR VOLUME (mm³)
0
20
40
60
80
100
120
DAYS POST TUMOR IMPLANT
Untreated
cAC10-1, 1 mg/kg
cAC10-1, 0.5 mg/kg
cAC10-10, 1 mg/kg
cAC10-10, 0.5 mg/kg
schedule: once, day 9

Figure 3

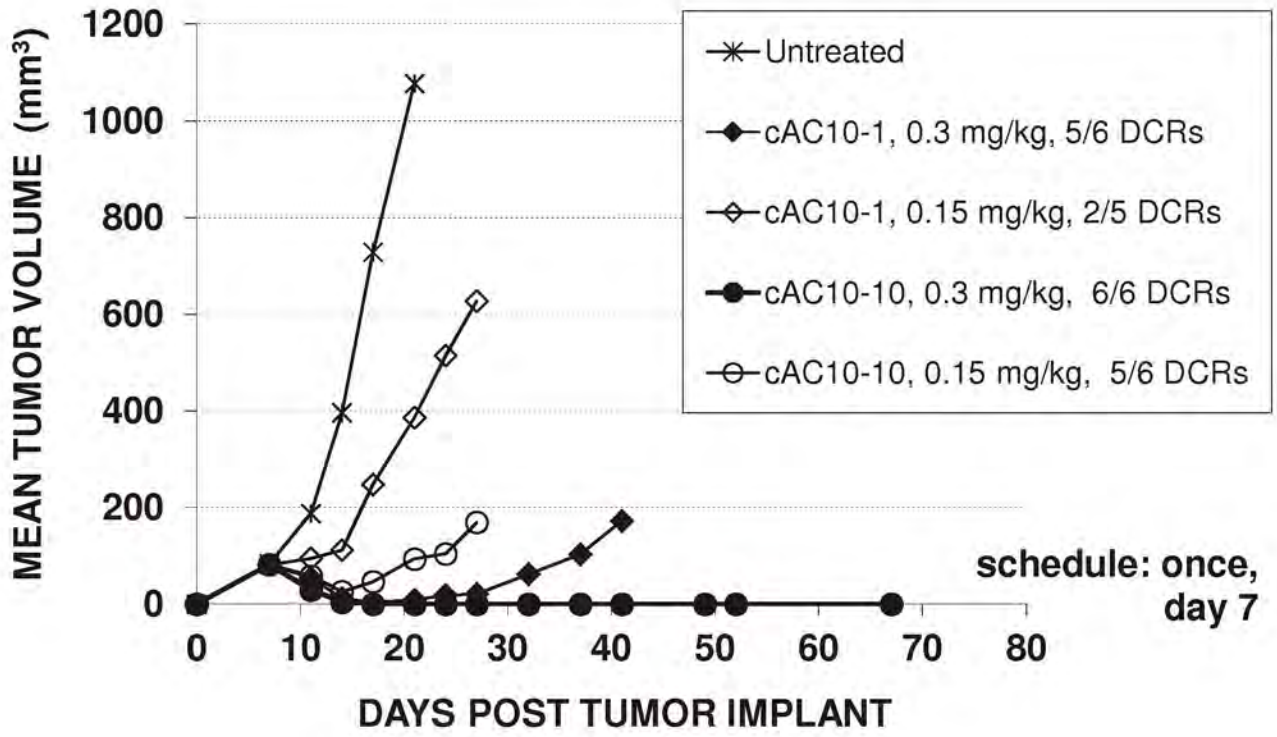

MEAN TUMOR VOLUME (mm³)
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
70
80
DAYS POST TUMOR IMPLANT
Untreated
cAC10-1, 0.3 mg/kg, 5/6 DCRs
cAC10-1, 0.15 mg/kg, 2/5 DCRs
cAC10-10, 0.3 mg/kg, 6/6 DCRs
cAC10-10, 0.15 mg/kg, 5/6 DCRs
schedule: once, day 7

Figure 4

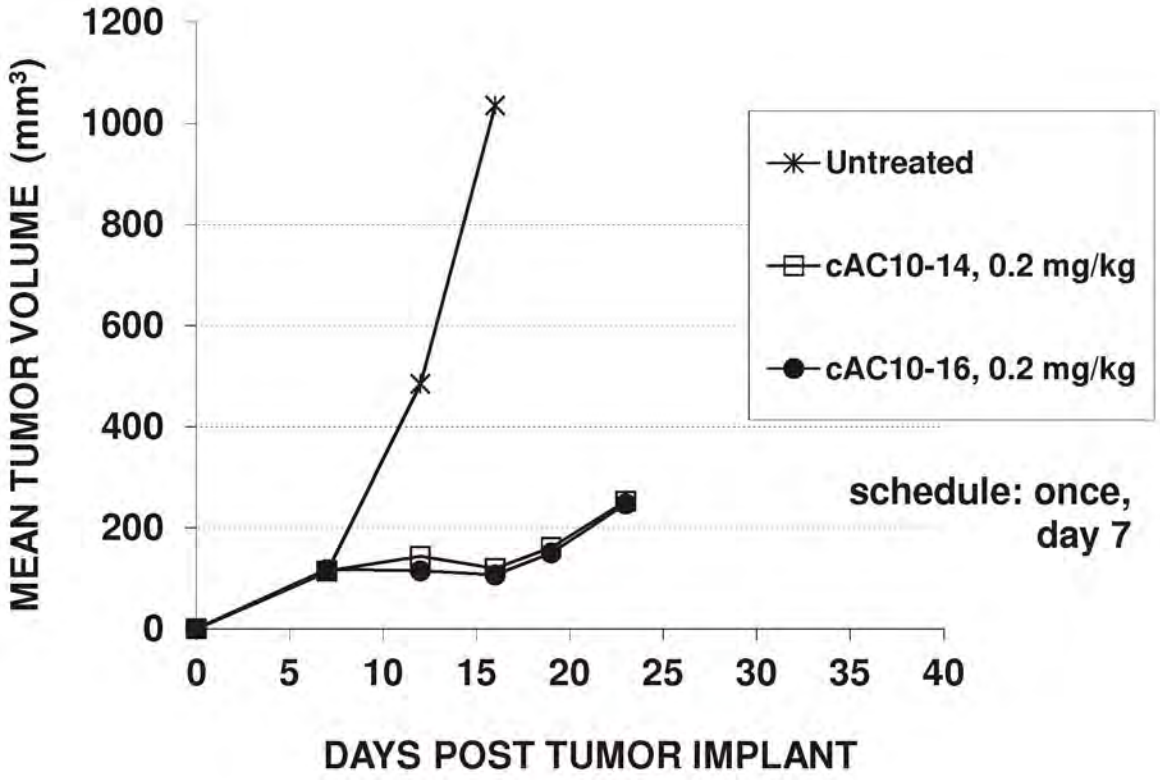

MEAN TUMOR VOLUME (mm³)
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
35
40
DAYS POST TUMOR IMPLANT
Untreated
cAC10-14, 0.2 mg/kg
cAC10-16, 0.2 mg/kg
schedule: once, day 7

Figure 5

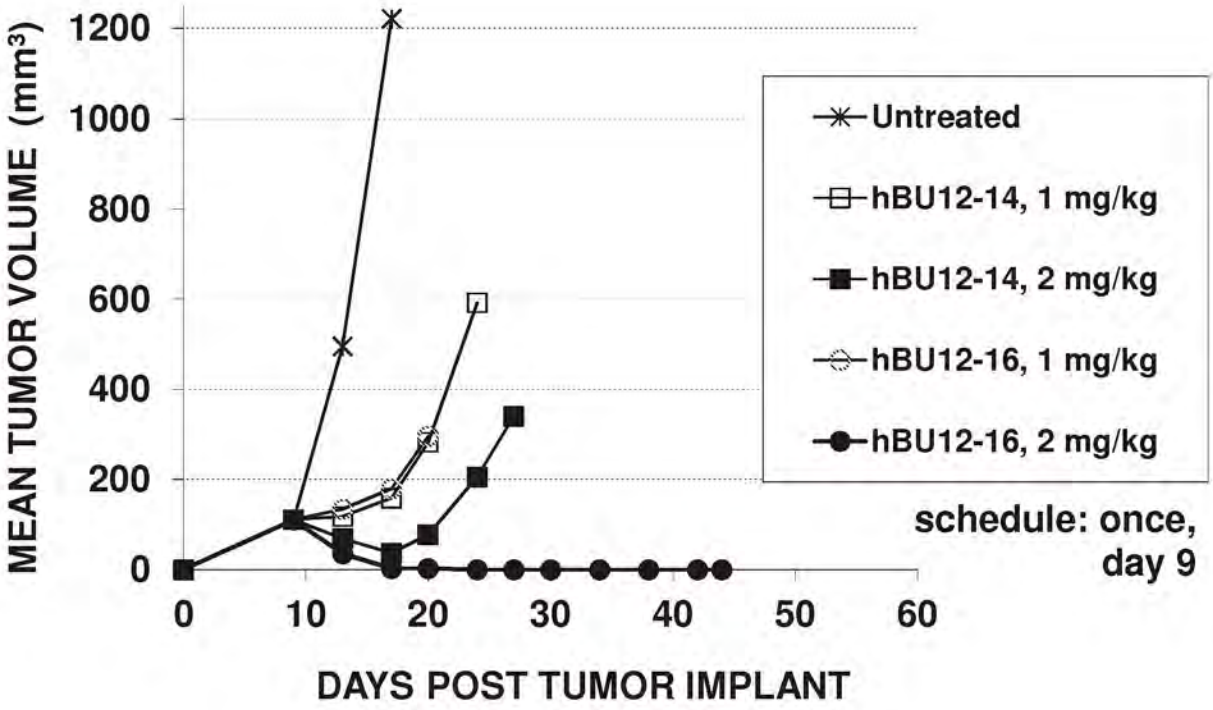

MEAN TUMOR VOLUME (mm³)
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
DAYS POST TUMOR IMPLANT
Untreated
hBU12-14, 1 mg/kg
hBU12-14, 2 mg/kg
hBU12-16, 1 mg/kg
hBU12-16, 2 mg/kg
schedule: once, day 9

Figure 6

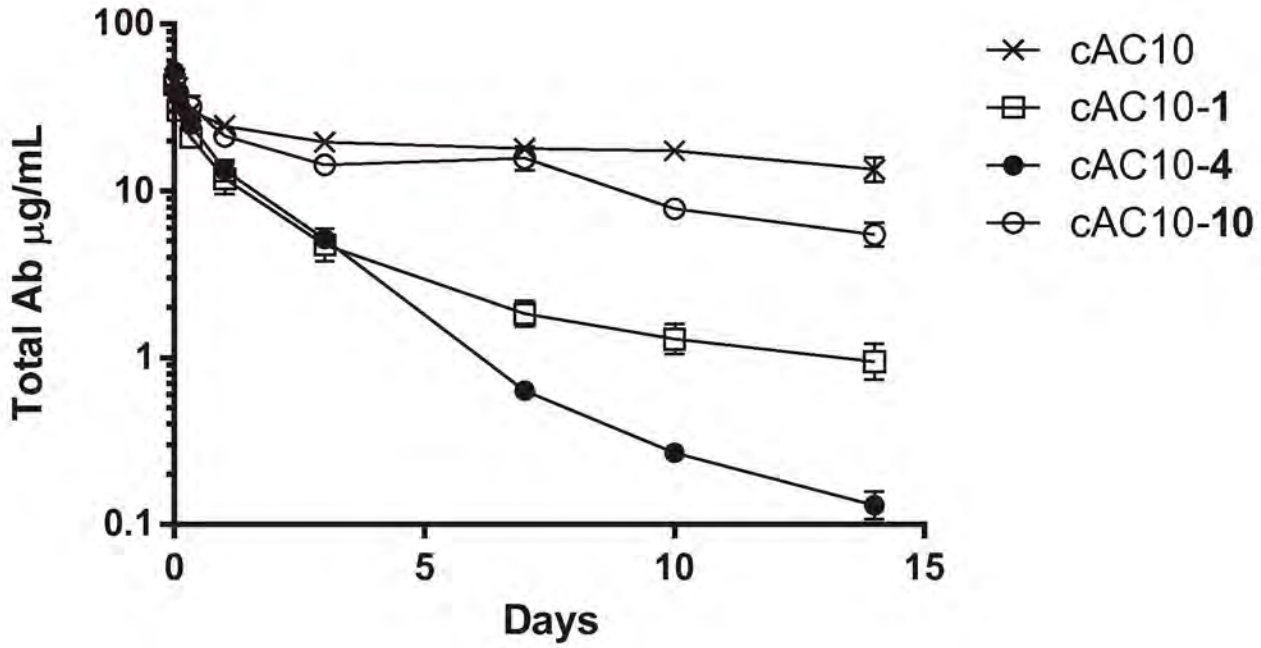

100
10
1
0.1
Total Ab µg/mL
0
5
10
15
Days
cAC10
cAC10-1
cAC10-4
cAC10-10

Figure 7

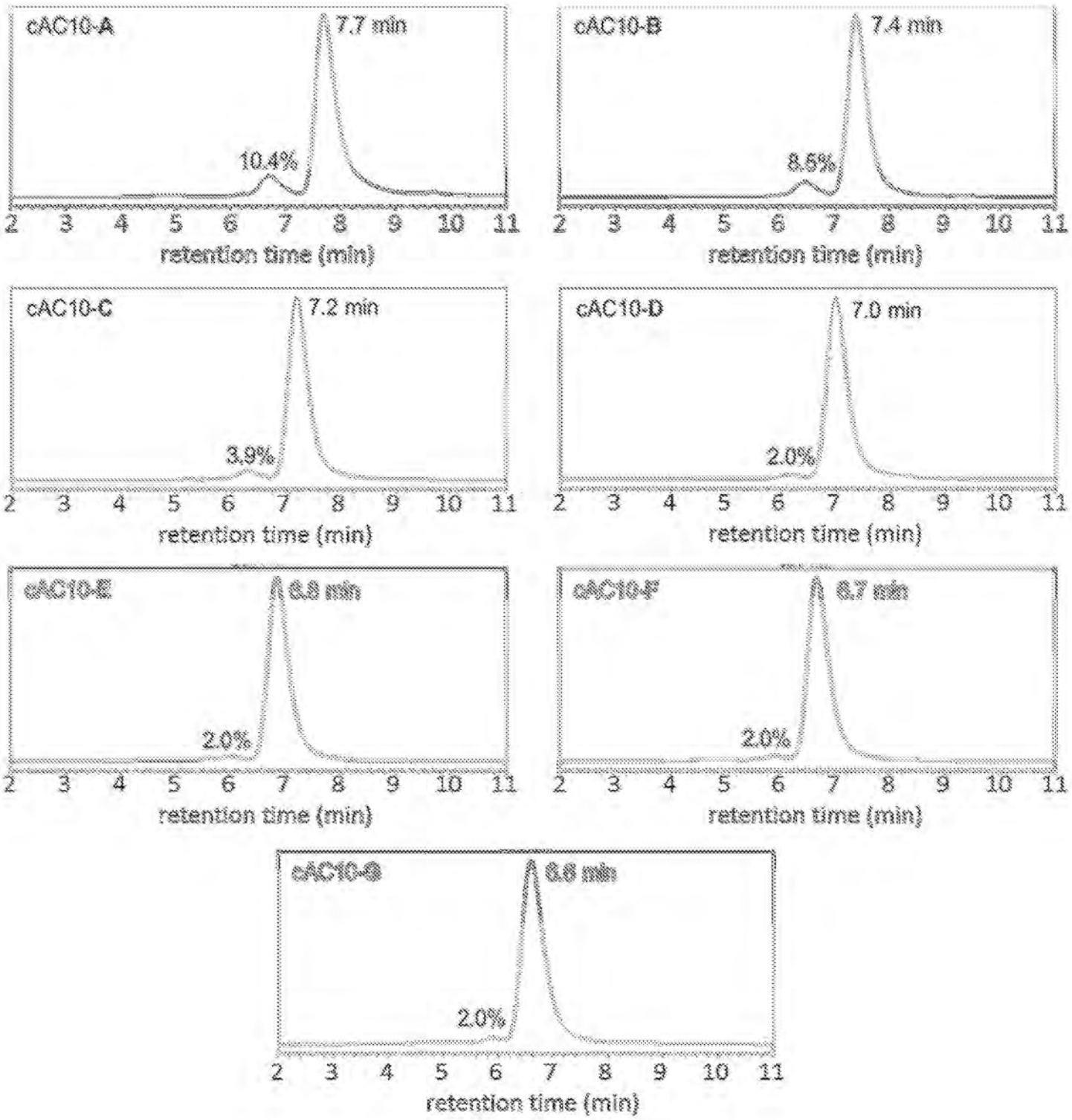

cAC10-A
7.7 min
10.4%
2 3 4 5 6 7 8 9 10 11
retention time (min)
cAC10-B
7.4 min
8.5%
2 3 4 5 6 7 8 9 10 11
retention time (min)
cAC10-C
7.2 min
3.9%
2 3 4 5 6 7 8 9 10 11
retention time (min)
cAC10-D
7.0 min
2.0%
2 3 4 5 6 7 8 9 10 11
retention time (min)
cAC10-E
6.8 min
2.0%
2 3 4 5 6 7 8 9 10 11
retention time (min)
cAC10-F
6.7 min
2.0%
2 3 4 5 6 7 8 9 10 11
retention time (min)
cAC10-G
6.6 min
2.0%
2 3 4 5 6 7 8 9 10 11
retention time (min)

Figure 8

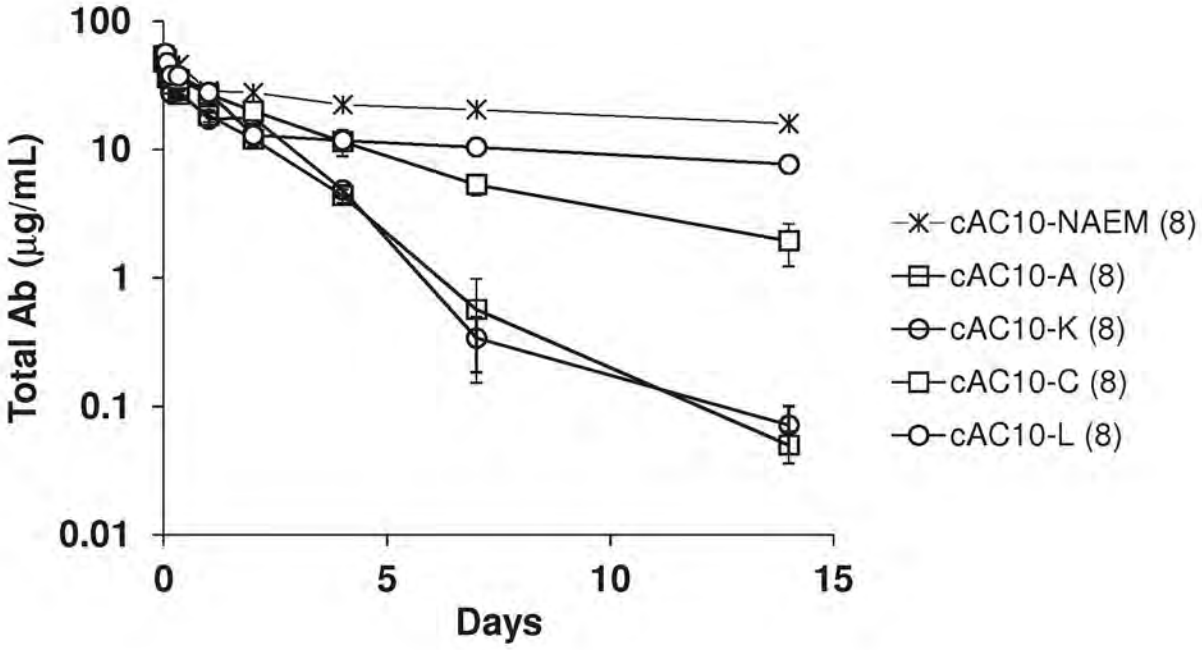

100
10
1
0.1
0.01
Total Ab (μg/mL)
0
5
10
15
Days
cAC10-NAEM (8)
cAC10-A (8)
cAC10-K (8)
cAC10-C (8)
cAC10-L (8)

Figure 9

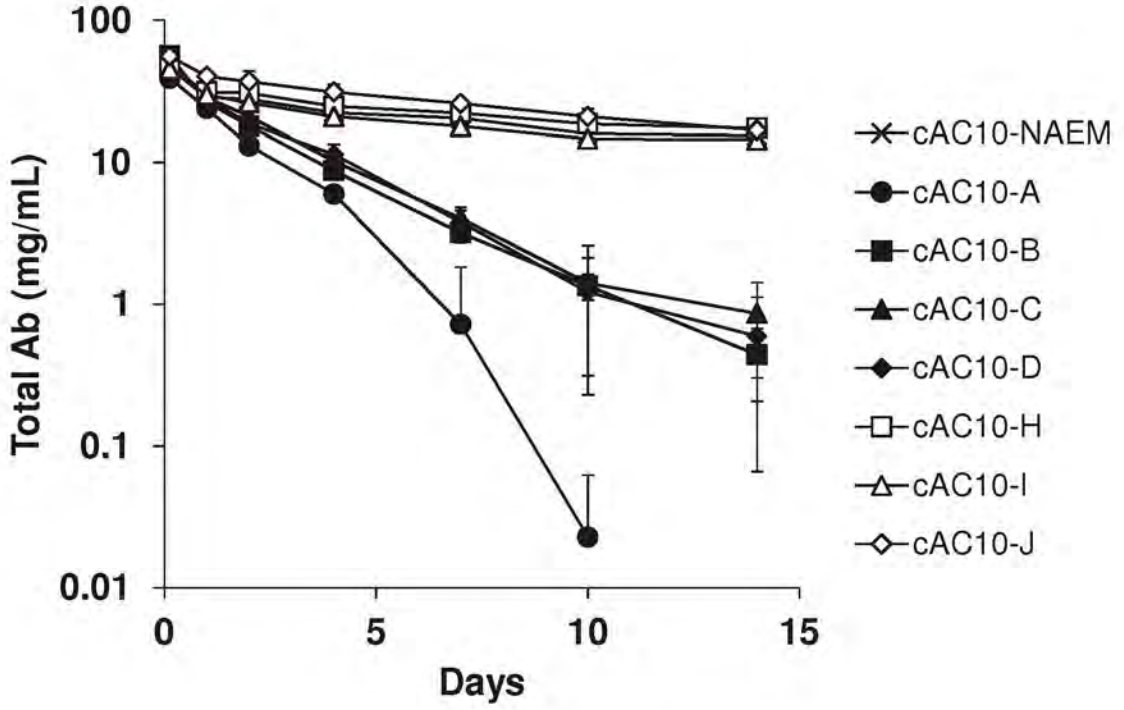

100
10
1
0.1
0.01
Total Ab (mg/mL)
0
5
10
15
Days
cAC10-NAEM
cAC10-A
cAC10-B
cAC10-C
cAC10-D
cAC10-H
cAC10-I
cAC10-J

Figure 10

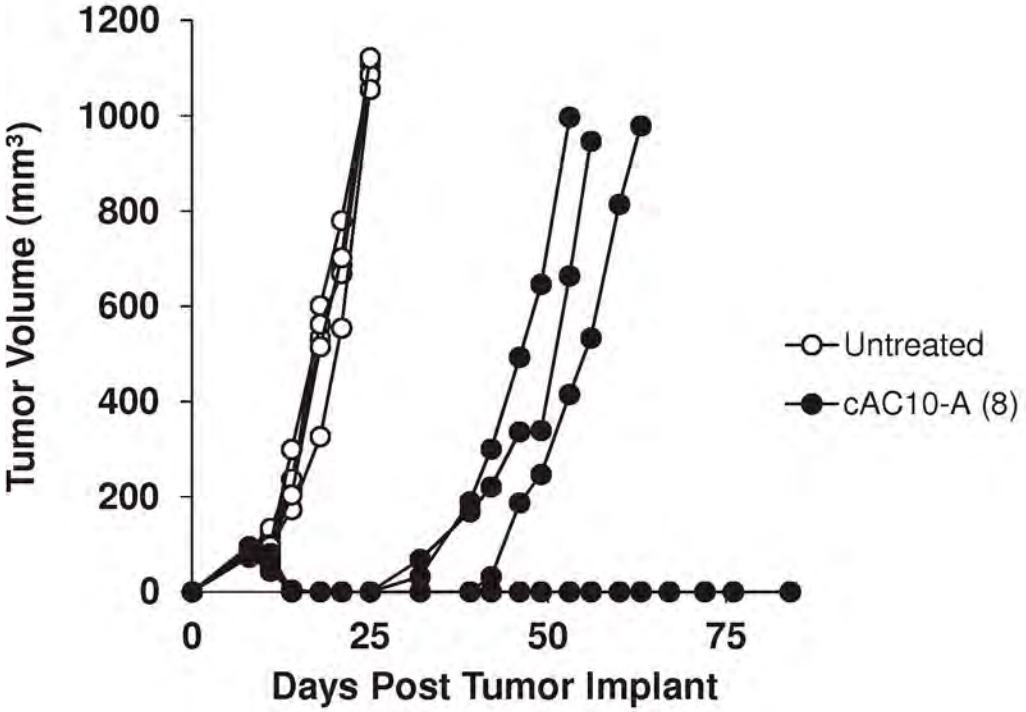

1200
1000
800
600
400
200
0
Tumor Volume (mm³)
0
25
50
75
Days Post Tumor Implant
Untreated
cAC10-A (8)

Figure 11

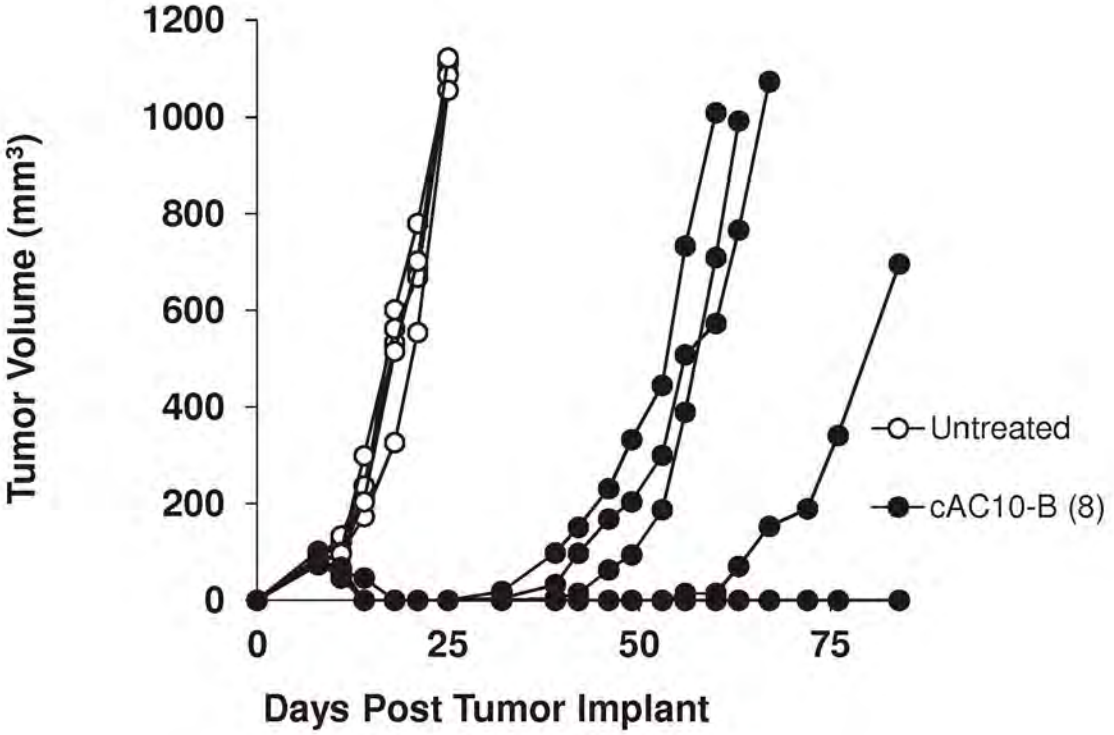

1200
1000
800
600
400
200
0
Tumor Volume (mm³)
0
25
50
75
Days Post Tumor Implant
Untreated
cAC10-B (8)

Figure 12

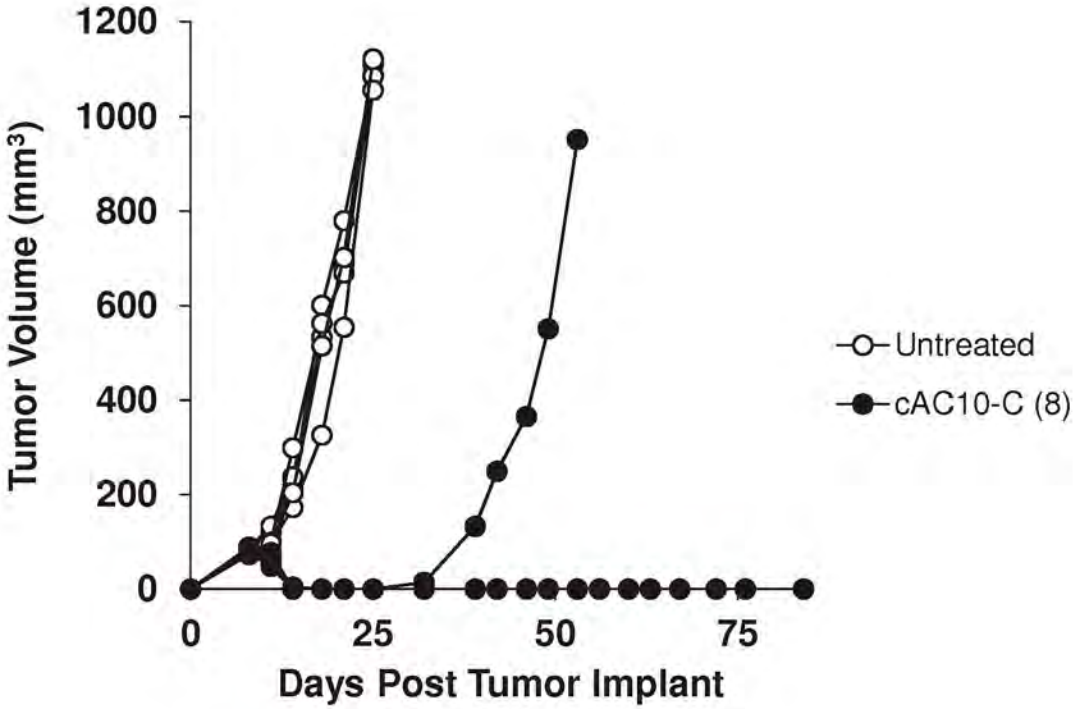

1200
1000
800
600
400
200
0
Tumor Volume (mm³)
0
25
50
75
Days Post Tumor Implant
Untreated
cAC10-C (8)

Figure 13

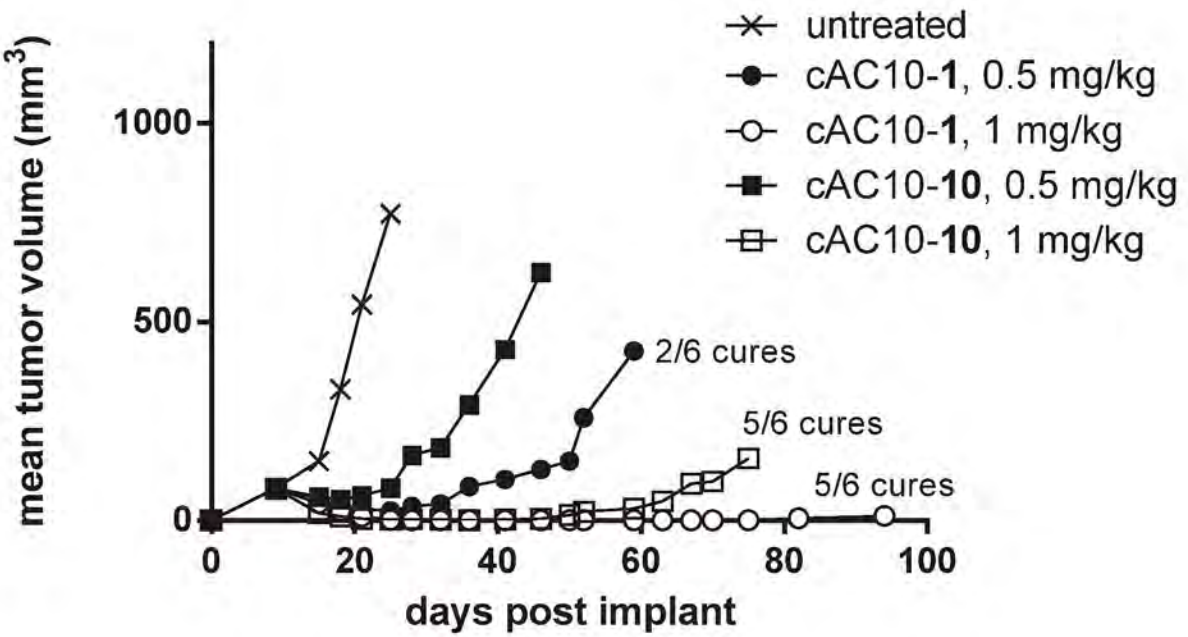

untreated
cAC10-1, 0.5 mg/kg
cAC10-1, 1 mg/kg
cAC10-10, 0.5 mg/kg
cAC10-10, 1 mg/kg
mean tumor volume (mm3)
1000
500
0
0
20
40
60
80
100
days post implant
2/6 cures
5/6 cures
5/6 cures

Figure 15

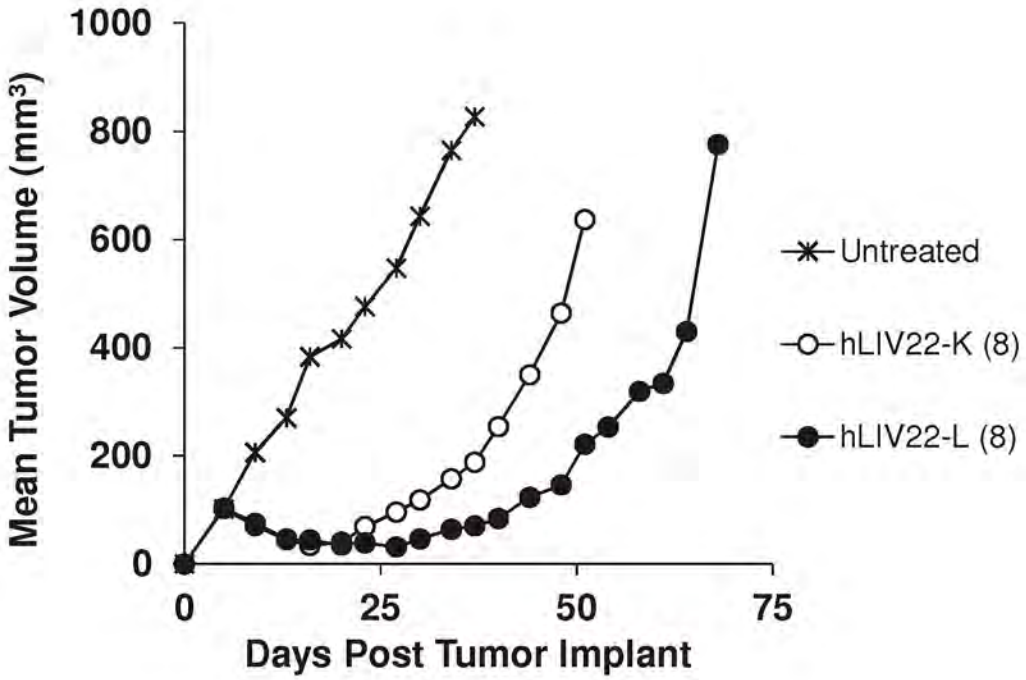

1000
800
600
400
200
0
Mean Tumor Volume (mm³)
0
25
50
75
Days Post Tumor Implant
Untreated
hLIV22-K (8)
hLIV22-L (8)

Figure 14

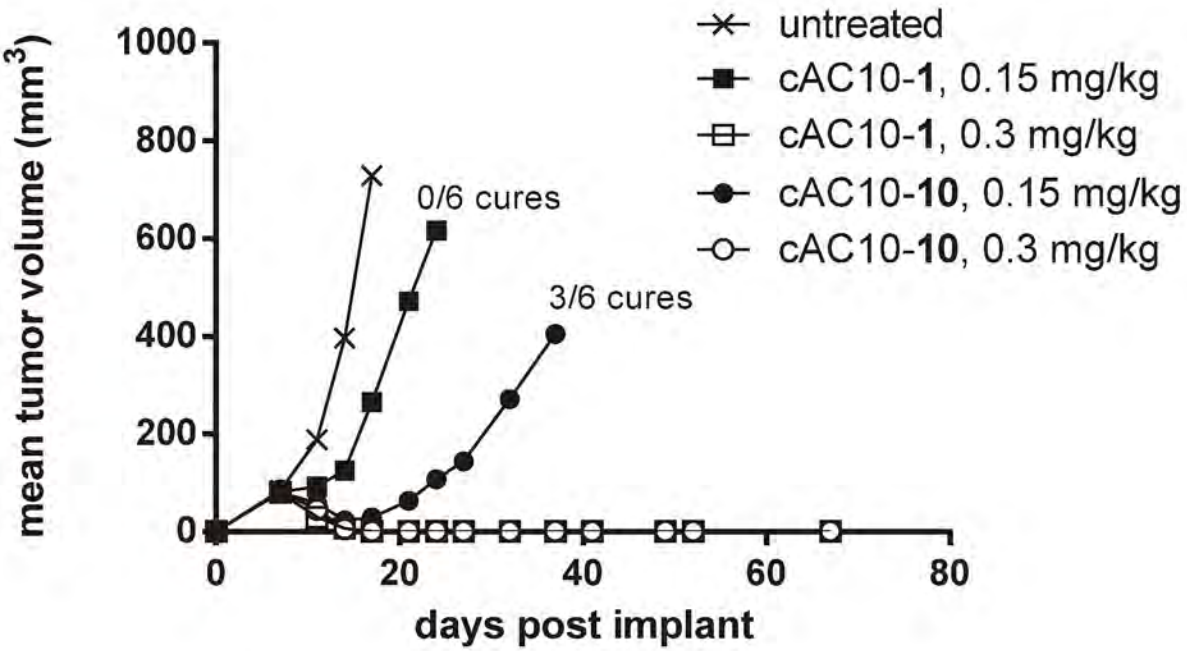

mean tumor volume (mm3)
1000
800
600
400
200
0
0
20
40
60
80
days post implant
0/6 cures
3/6 cures
untreated
cAC10-1, 0.15 mg/kg
cAC10-1, 0.3 mg/kg
cAC10-10, 0.15 mg/kg
cAC10-10, 0.3 mg/kg

Figure 16

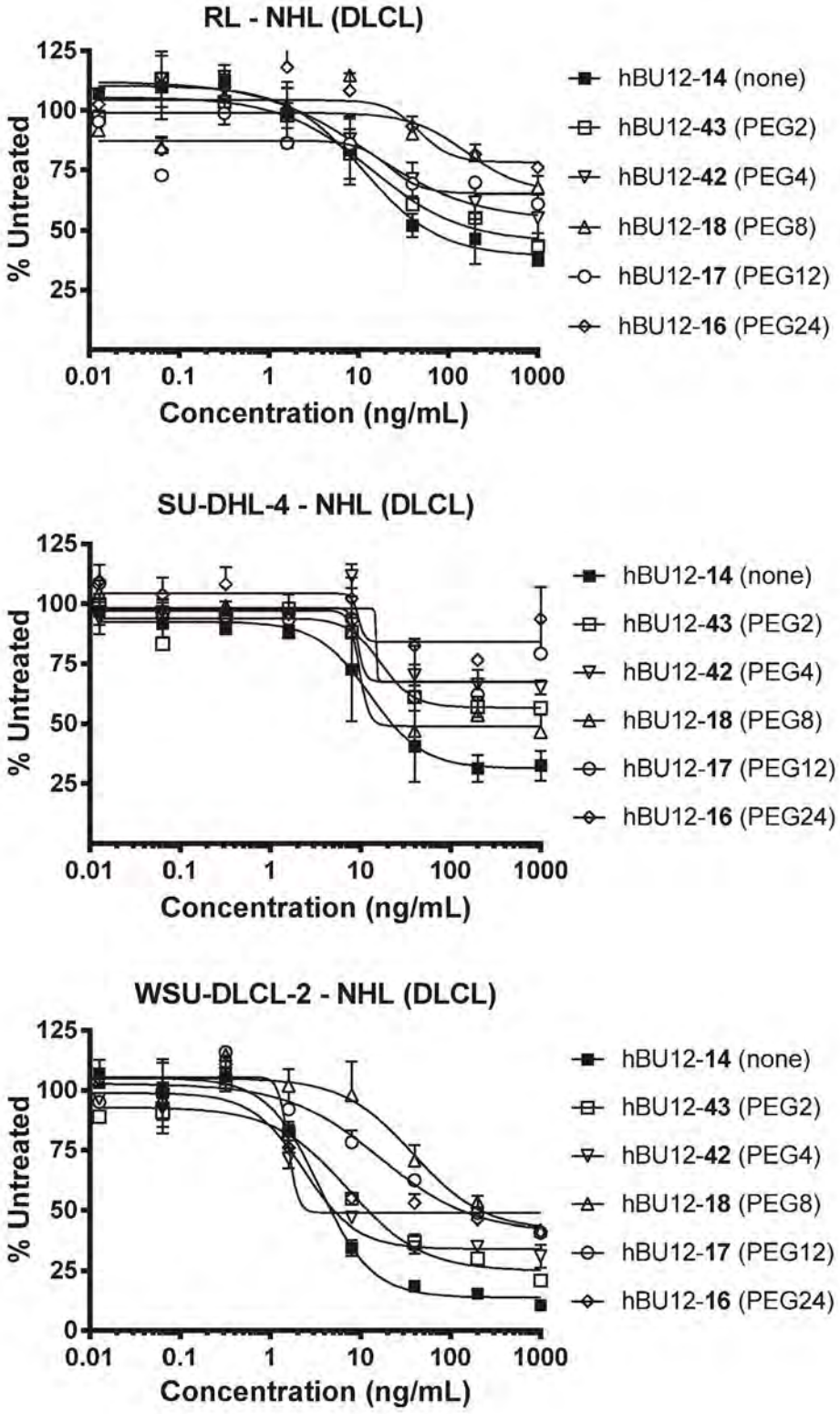

RL - NHL (DLCL)
% Untreated
125
100
75
50
25
0.01
0.1
1
10
100
1000
Concentration (ng/mL)
hBU12-14 (none)
hBU12-43 (PEG2)
hBU12-42 (PEG4)
hBU12-18 (PEG8)
hBU12-17 (PEG12)
hBU12-16 (PEG24)
SU-DHL-4 - NHL (DLCL)
% Untreated
125
100
75
50
25
0.01
0.1
1
10
100
1000
Concentration (ng/mL)
hBU12-14 (none)
hBU12-43 (PEG2)
hBU12-42 (PEG4)
hBU12-18 (PEG8)
hBU12-17 (PEG12)
hBU12-16 (PEG24)
WSU-DLCL-2 - NHL (DLCL)
% Untreated
125
100
75
50
25
0
0.01
0.1
1
10
100
1000
Concentration (ng/mL)
hBU12-14 (none)
hBU12-43 (PEG2)
hBU12-42 (PEG4)
hBU12-18 (PEG8)
hBU12-17 (PEG12)
hBU12-16 (PEG24)

Figure 17

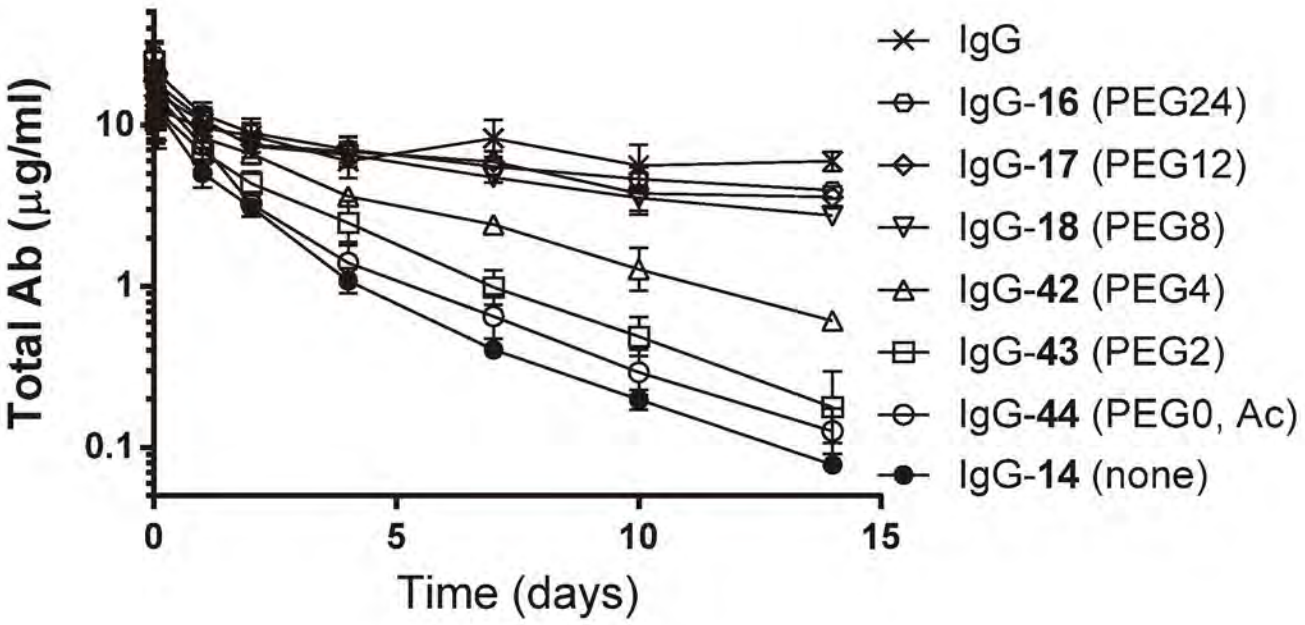

Total Ab (μg/ml)
10
1
0.1
0
5
10
15
Time (days)
IgG
IgG-16 (PEG24)
IgG-17 (PEG12)
IgG-18 (PEG8)
IgG-42 (PEG4)
IgG-43 (PEG2)
IgG-44 (PEG0, Ac)
IgG-14 (none)

Figure 18

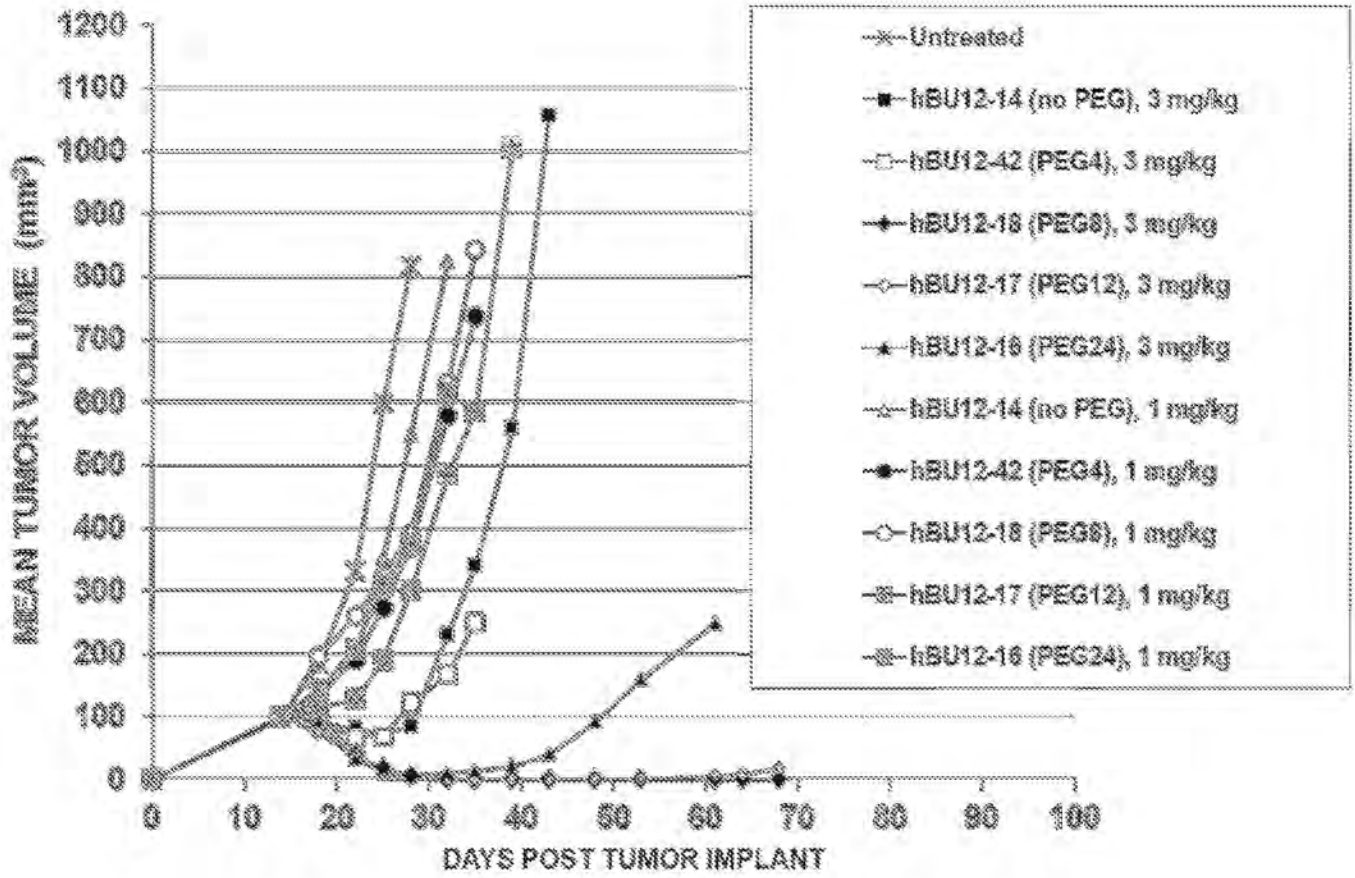

MEAN TUMOR VOLUME (mm²)
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
0
10
20
30
40
50
60
70
80
90
100
DAYS POST TUMOR IMPLANT
Untreated
hBU12-14 (no PEG), 3 mg/kg
hBU12-42 (PEG4), 3 mg/kg
hBU12-18 (PEG8), 3 mg/kg
hBU12-17 (PEG12), 3 mg/kg
hBU12-16 (PEG24), 3 mg/kg
hBU12-14 (no PEG), 1 mg/kg
hBU12-42 (PEG4), 1 mg/kg
hBU12-18 (PEG8), 1 mg/kg
hBU12-17 (PEG12), 1 mg/kg
hBU12-16 (PEG24), 1 mg/kg

Figure 19

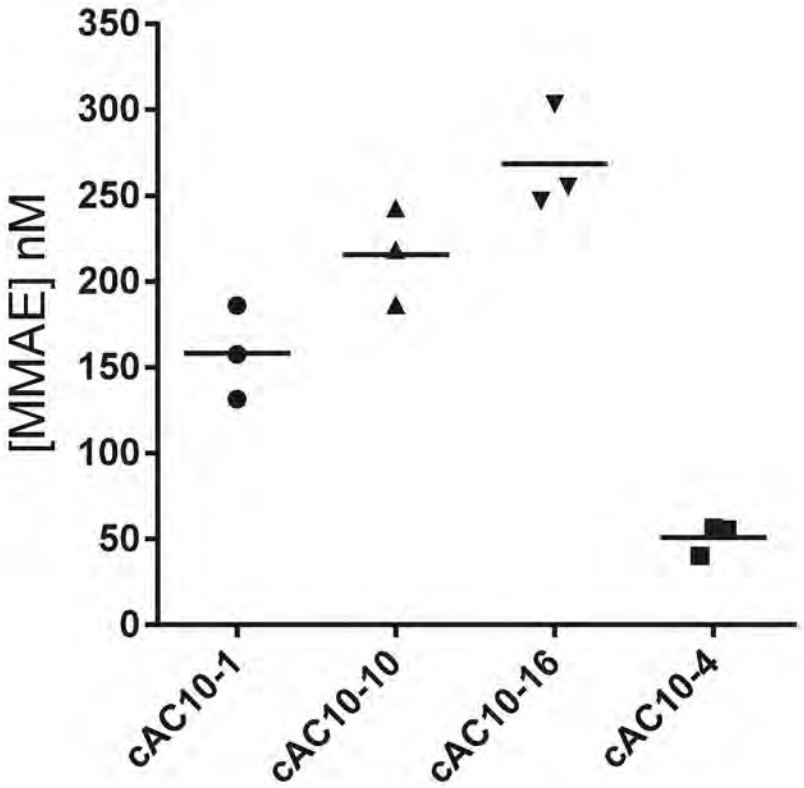

350
300
250
200
150
100
50
0
[MMAE] nM
cAC10-1
cAC10-10
cAC10-16
cAC10-4

Figure 20

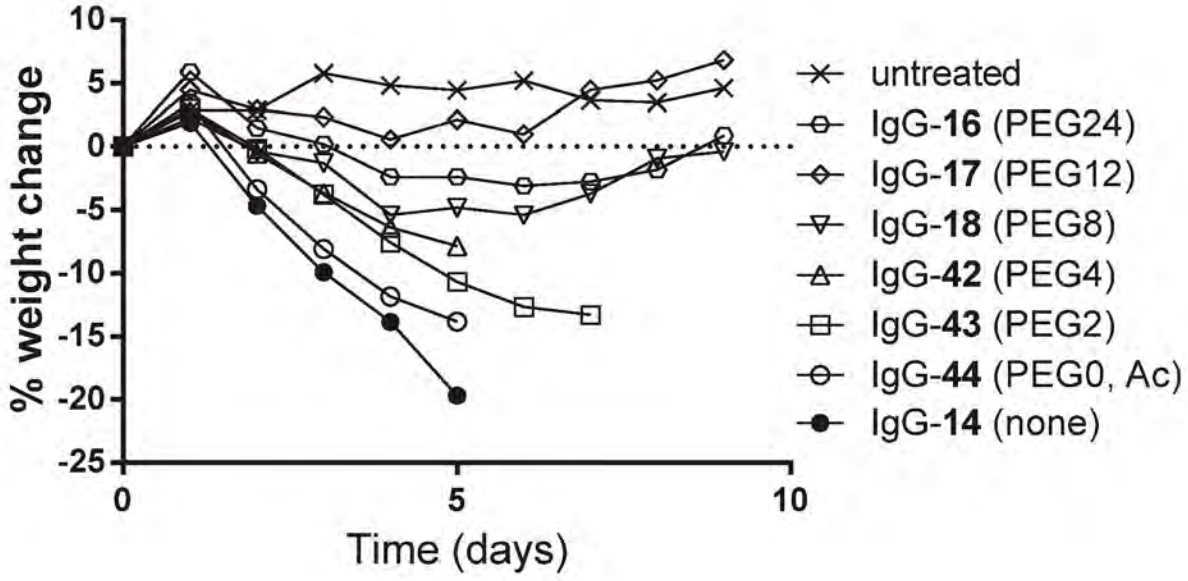

% weight change
10
5
0
-5
-10
-15
-20
-25
0
5
10
Time (days)
untreated
IgG-16 (PEG24)
IgG-17 (PEG12)
IgG-18 (PEG8)
IgG-42 (PEG4)
IgG-43 (PEG2)
IgG-44 (PEG0, Ac)
IgG-14 (none)

Figure 21

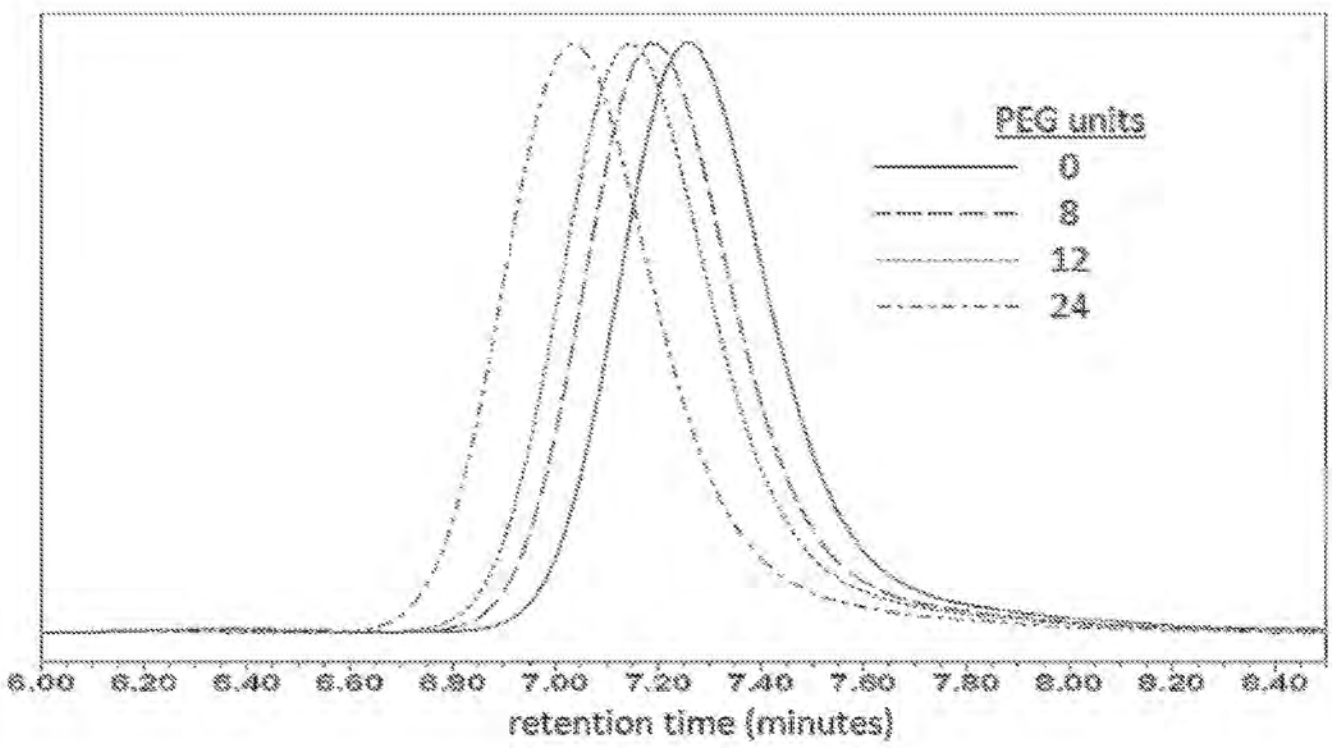

PEG units
0
8
12
24
6.00
6.20
6.40
6.60
6.80
7.00
7.20
7.40
7.60
7.80
8.00
8.20
8.40
retention time (minutes)

Figure 22

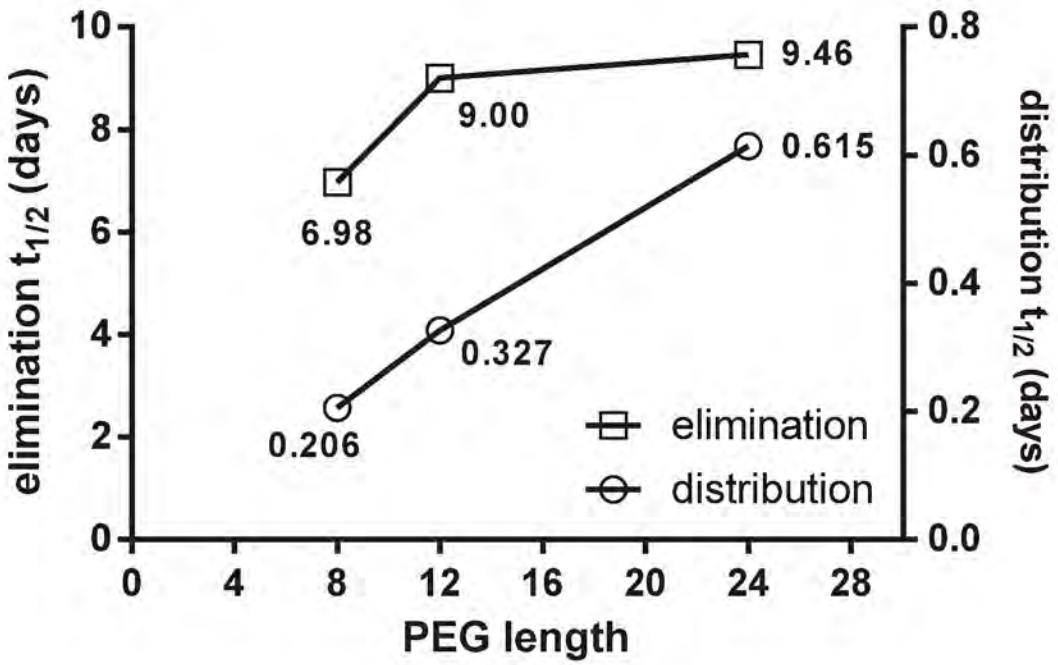

elimination $t_{1/2}$ (days)
distribution $t_{1/2}$ (days)
PEG length
9.46
9.00
6.98
0.615
0.327
0.206
elimination
distribution
0
2
4
6
8
10
0.0
0.2
0.4
0.6
0.8
0
4
8
12
16
20
24
28

Figure 23

SEQUENCE LISTING

<110> Seattle Genetics, Inc.

<120> PEGYLATED DRUG-LINKERS FOR IMPROVED LIGAND-DRUG CONJUGATE PHARMACOKINETICS

<130> 2700-00114PC

<150> 61/891,320
<151> 2013-10-15

<150> 61/941,904
<151> 2014-02-19

<150> 61/947,742
<151> 2014-03-04

<150> 61/975,318
<151> 2014-04-04

<160> 10

<170> PatentIn version 3.5

<210> 1
<211> 117
<212> PRT
<213> Mus musculus

<400> 1

```
Gln Ile Gln Leu Gln Gln Ser Gly Pro Glu Val Val Lys Pro Gly Ala
1               5                  10                  15


Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Tyr Ile Thr Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Trp Ile Tyr Pro Gly Ser Gly Asn Thr Lys Tyr Asn Glu Lys Phe
    50                  55                  60


Lys Gly Lys Ala Thr Leu Thr Val Asp Thr Ser Ser Ser Thr Ala Phe
65                  70                  75                  80


Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95
```

```
Ala Asn Tyr Gly Asn Tyr Trp Phe Ala Tyr Trp Gly Gln Gly Thr Gln
            100                 105                 110

Val Thr Val Ser Ala
        115
```

<210> 2
<211> 111
<212> PRT
<213> mus musculus

<400> 2

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Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Phe Asp
            20                  25                  30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

Lys Val Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65                  70                  75                  80

Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
                85                  90                  95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 3
<211> 118
<212> PRT
<213> Artificial

<220>
<223> Humanized murine sequence

<400> 3

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Lys Trp Met
        35                  40                  45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Ala Phe
    50                  55                  60

Lys Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Tyr Gly Asp Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Ser
        115
```

<210> 4
<211> 112
<212> PRT
<213> Artificial

<220>
<223> Humanized murine sequence

<400> 4

```
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1               5                   10                  15

Glu Arg Ala Thr Ile Asn Cys Arg Ala Ser Lys Ser Val Ser Thr Ser
            20                  25                  30

Gly Tyr Ser Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45
```

```
Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln His Ser Arg
                85                  90                  95

Glu Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105                 110
```

<210> 5
<211> 120
<212> PRT
<213> Artificial

<220>
<223> Humanized murine sequence

<400> 5

```
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Thr Ser
            20                  25                  30

Gly Met Gly Val Gly Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
        35                  40                  45

Trp Ile Gly His Ile Trp Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ala
    50                  55                  60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65                  70                  75                  80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
                85                  90                  95

Cys Ala Arg Met Glu Leu Trp Ser Tyr Tyr Phe Asp Tyr Trp Gly Gln
            100                 105                 110
```

```
Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  6
<211>  107
<212>  PRT
<213>  Artificial

<220>
<223>  Humanized murine sequence

<400>  6

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1               5                   10                  15


Glu Arg Ala Thr Leu Ser Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
            20                  25                  30


His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
        35                  40                  45


Asp Thr Ser Lys Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
    50                  55                  60


Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65                  70                  75                  80


Asp Val Ala Val Tyr Tyr Cys Phe Gln Gly Ser Val Tyr Pro Phe Thr
                85                  90                  95


Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
            100                 105


<210>  7
<211>  330
<212>  PRT
<213>  homo sapiens

<400>  7

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15
```

```
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225                 230                 235                 240
```

```
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330
```

<210> 8
<211> 106
<212> PRT
<213> homo sapiens

<400> 8

```
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1               5                   10                  15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
            20                  25                  30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
        35                  40                  45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
    50                  55                  60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65                  70                  75                  80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
```

```
                85                  90                  95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
            100                 105
```

<210> 9
<211> 117
<212> PRT
<213> heavy chain variable region

<400> 9

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

Tyr Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Tyr Pro Gly Ser Gly Asn Thr Lys Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Asn Tyr Gly Asn Tyr Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115
```

<210> 10
<211> 111
<212> PRT
<213> light chain variable region

<400> 10

```
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
```

```
1               5                   10                  15

Glu Arg Ala Thr Ile Asn Cys Lys Ala Ser Gln Ser Val Asp Phe Asp
            20                  25                  30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
        35                  40                  45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65                  70                  75                  80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Ser Asn
                85                  90                  95

Glu Asp Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105                 110
```