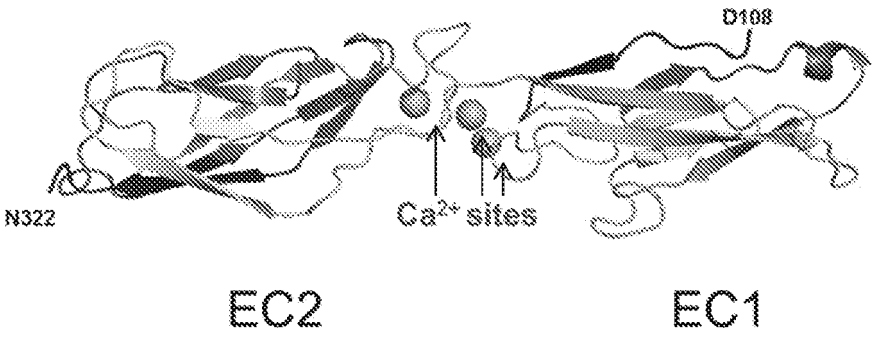

Figure 1

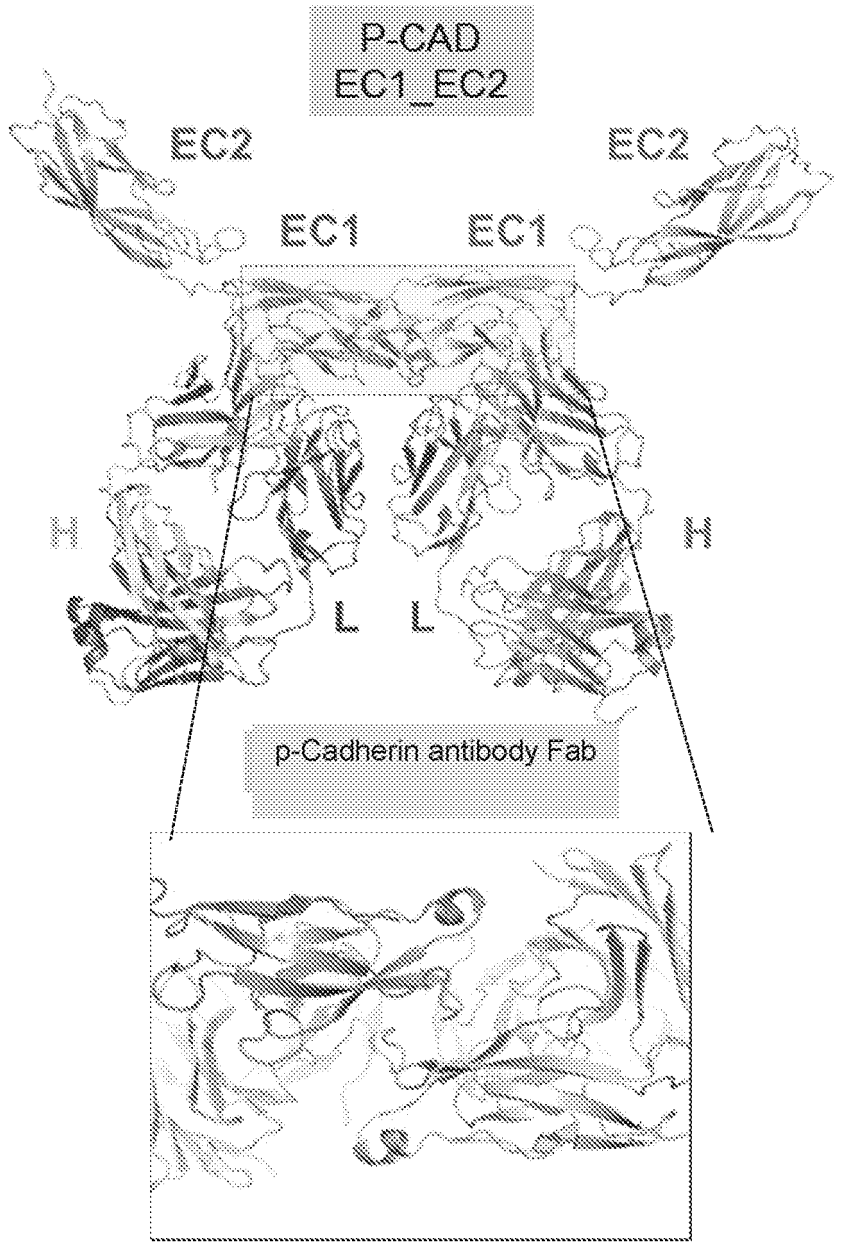

Figure 2

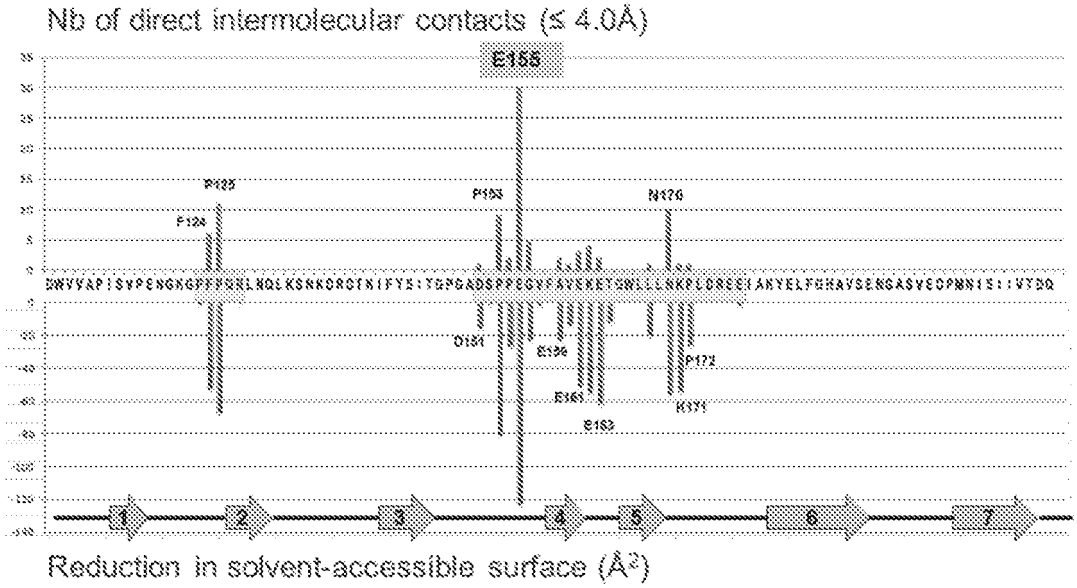
Nb of direct intermolecular contacts (≤ 4.0Å)
E155
P125
P124
P153
N176
D151
E156
E161
E163
P172
K171
1
2
3
4
5
6
7
Reduction in solvent-accessible surface (Å²)

Figure 3

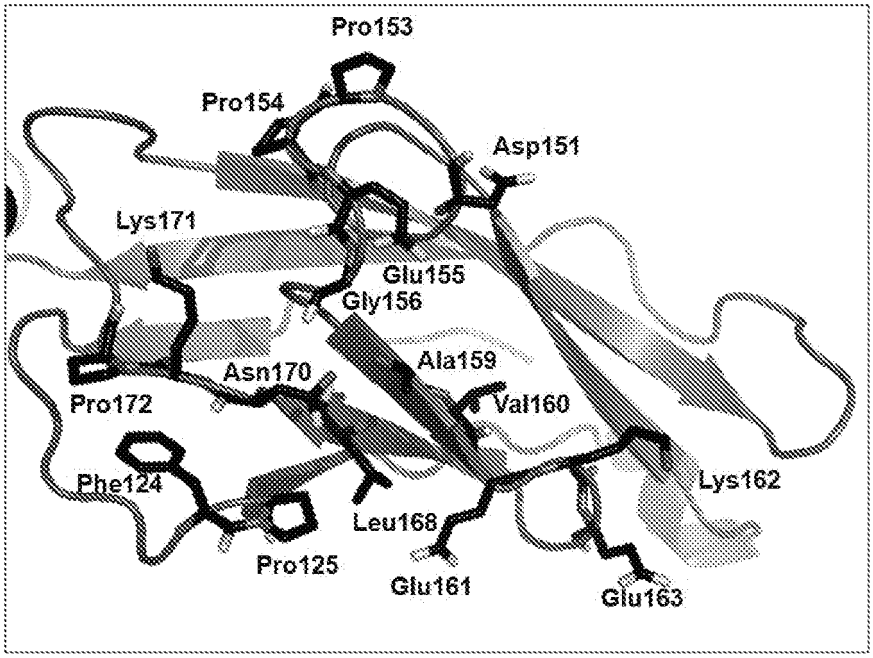
Pro153
Pro154
Asp151
Lys171
Glu155
Gly156
Ala159
Asn170
Pro172
Val160
Lys162
Phe124
Leu168
Pro125
Glu161
Glu163

Figure 4

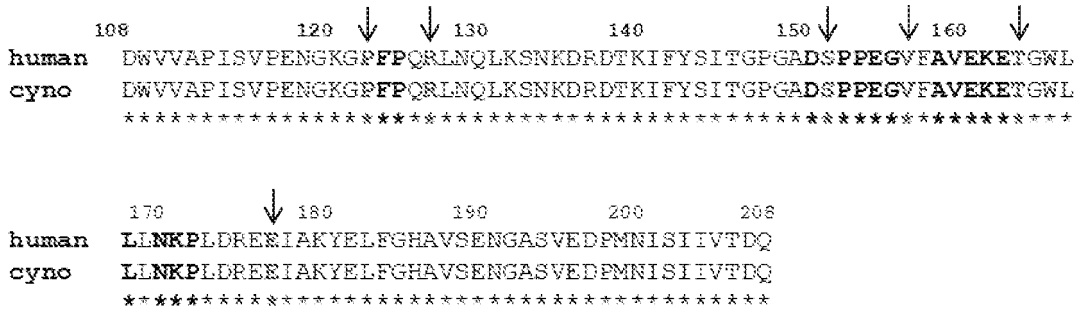
108 120 130 140 150 160
human DWVVAPISVPENGKGPFPQRLNQLKSNKDRDTKIFYSITGPGADSPPEGVFAVEKETGWL
cyno DWVVAPISVPENGKGPFPQRLNQLKSNKDRDTKIFYSITGPGADSPPEGVFAVEKETGWL
170 180 190 200 208
human LLNKPLDREEIAKYELFGHAVSENGASVEDPMNISIIVTDQ
cyno LLNKPLDREEIAKYELFGHAVSENGASVEDPMNISIIVTDQ

Figure 5

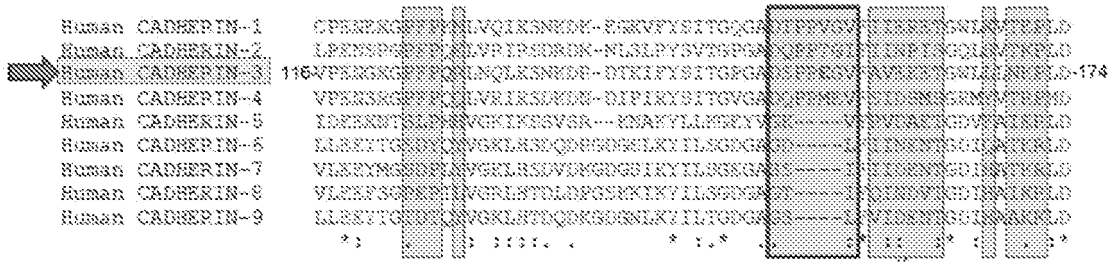
Human CADHERIN-1
Human CADHERIN-2
Human CADHERIN-3
Human CADHERIN-4
Human CADHERIN-5
Human CADHERIN-6
Human CADHERIN-7
Human CADHERIN-8
Human CADHERIN-9

Figure 6

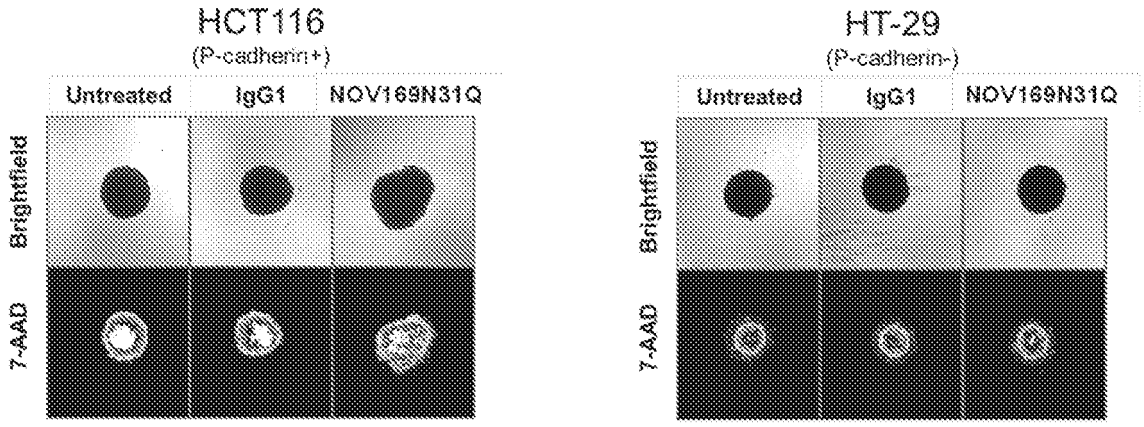
HCT116
(P-cadherin+)
Untreated
IgG1
NOV169N31Q
Brightfield
7-AAD
HT-29
(P-cadherin-)
Untreated
IgG1
NOV169N31Q
Brightfield
7-AAD

Figure 7

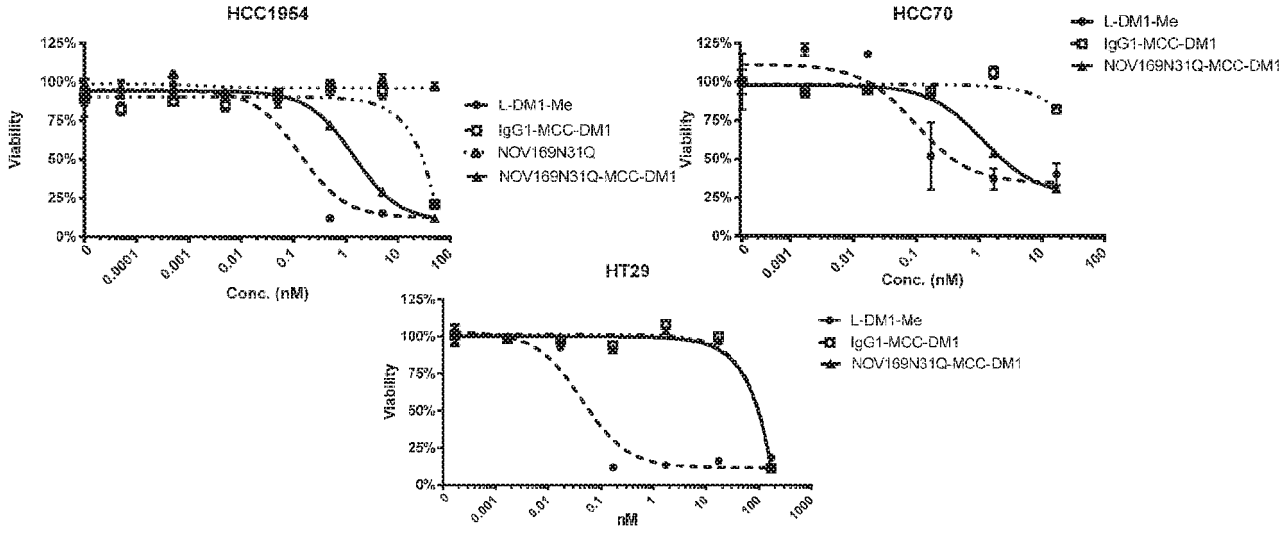
HCC1954
Viability
125%
100%
75%
50%
25%
0%
0
0.0001
0.001
0.01
0.1
1
10
100
Conc. (nM)
L-DM1-Me
IgG1-MCC-DM1
NOV169N31Q
NOV169N31Q-MCC-DM1
HCC70
Viability
125%
100%
75%
50%
25%
0%
0
0.001
0.01
0.1
1
10
100
Conc. (nM)
L-DM1-Me
IgG1-MCC-DM1
NOV169N31Q-MCC-DM1
HT29
Viability
125%
100%
75%
50%
25%
0%
0
0.001
0.01
0.1
1
10
100
1000
nM
L-DM1-Me
IgG1-MCC-DM1
NOV169N31Q-MCC-DM1

Figure 8

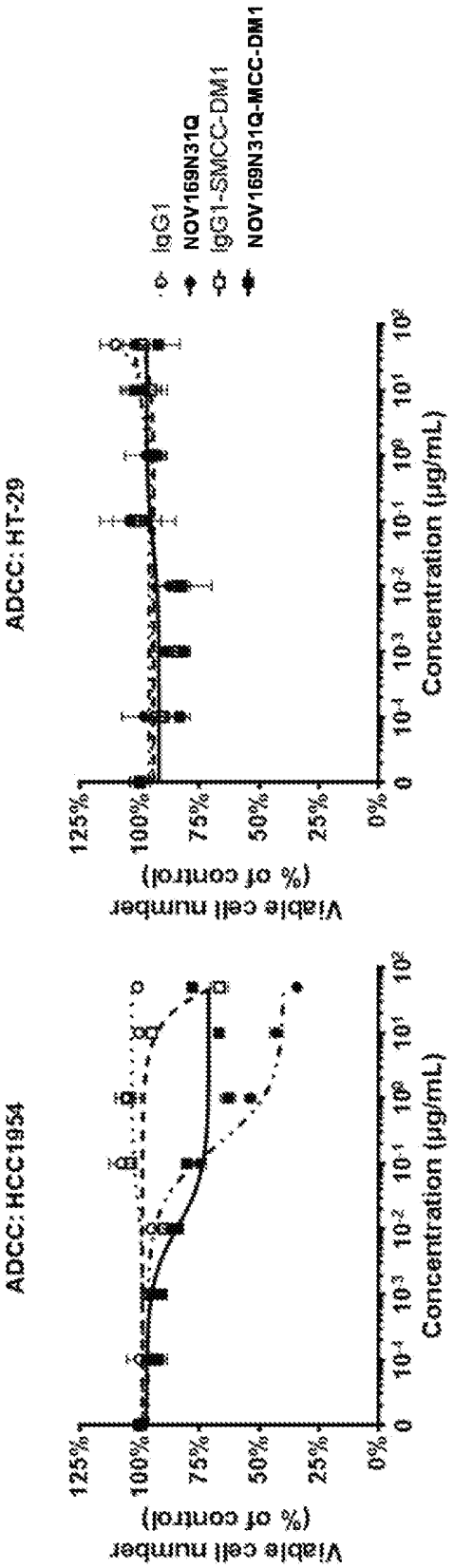
ADCC: HCC1954
ADCC: HT-29
Viable cell number (% of control)
125%
100%
75%
50%
25%
0%
0
10^{-4}
10^{-3}
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
Concentration (µg/mL)
IgG1
NOV169N31Q
IgG1-SMCC-DM1
NOV169N31Q-MCC-DM1

Figure 9

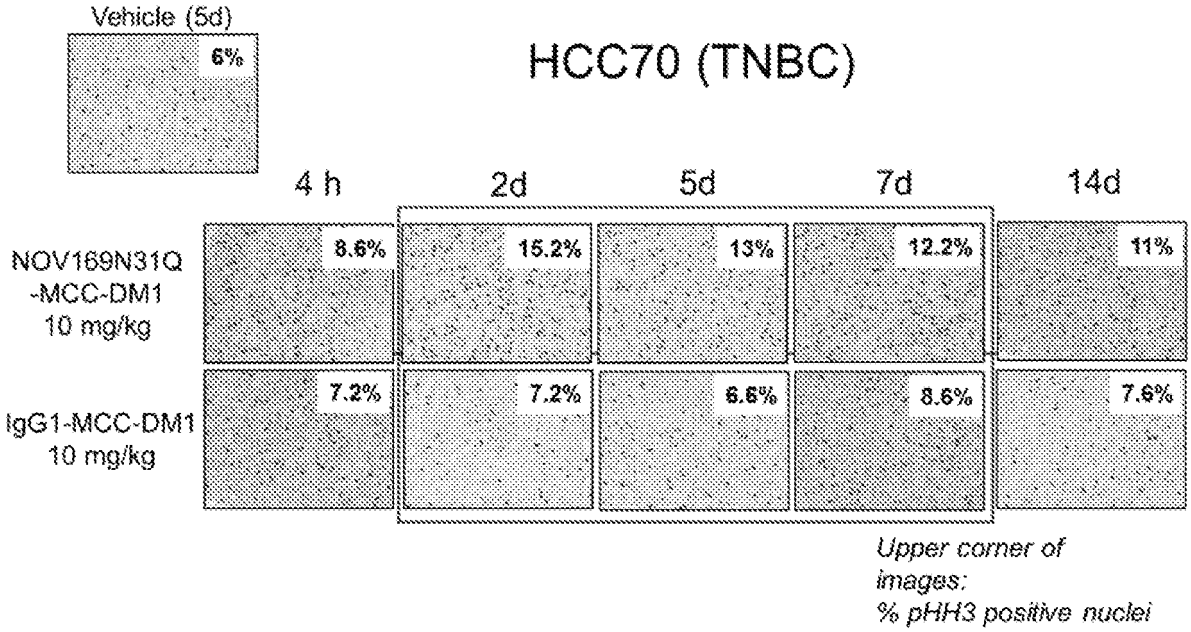
Vehicle (5d)
6%
HCC70 (TNBC)
4 h
2d
5d
7d
14d
NOV169N31Q
-MCC-DM1
10 mg/kg
8.6%
15.2%
13%
12.2%
11%
IgG1-MCC-DM1
10 mg/kg
7.2%
7.2%
6.6%
8.6%
7.6%
Upper corner of
images:
% pHH3 positive nuclei

Figure 10

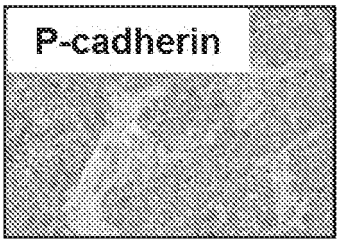

Figure 11A

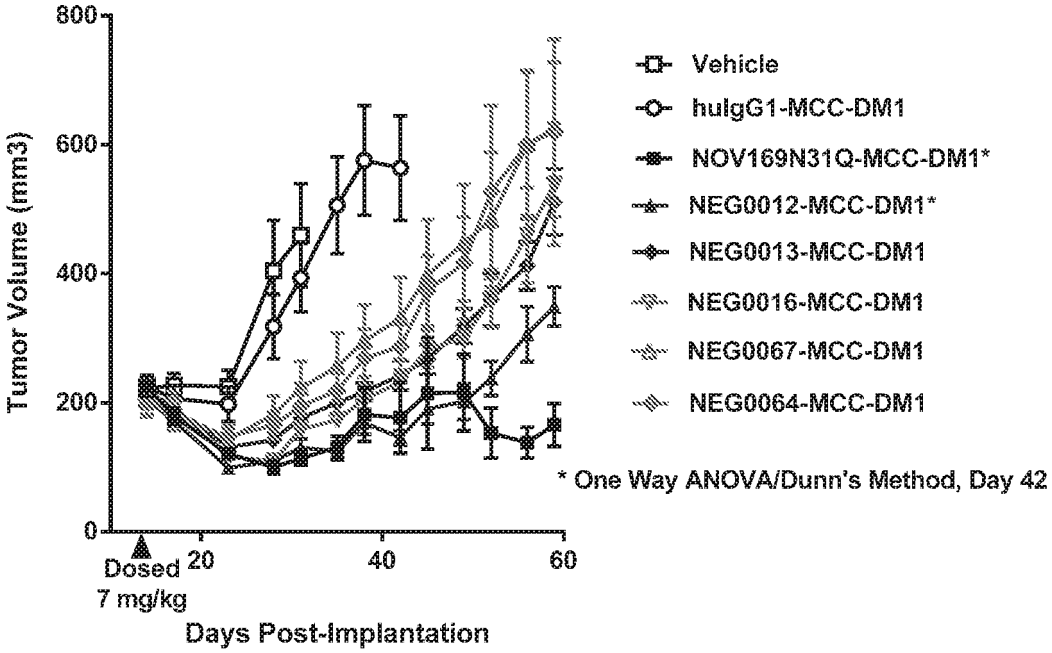

Figure 11B

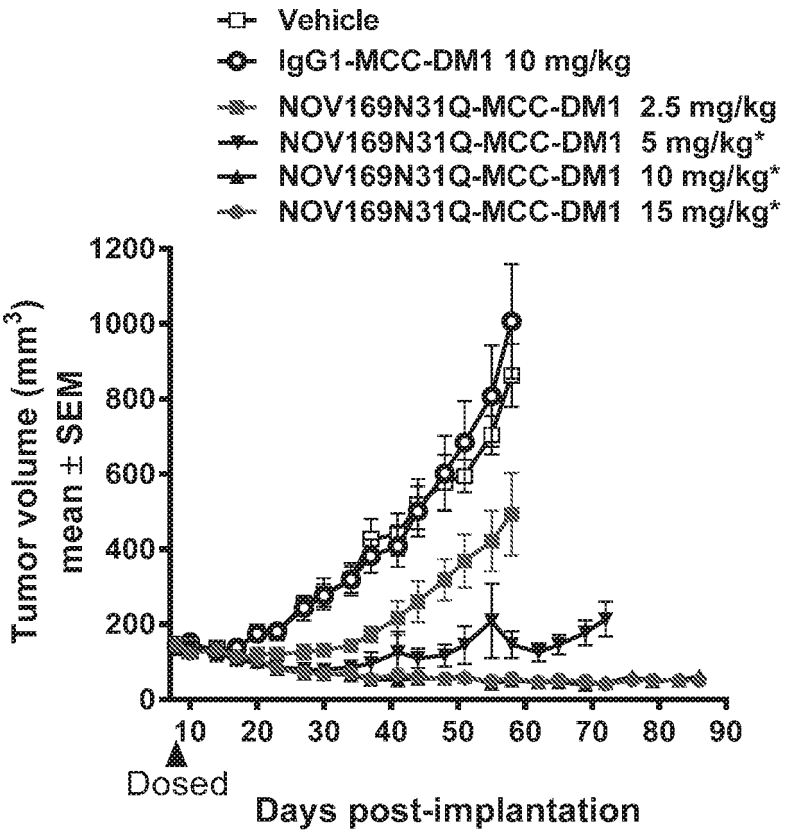
Vehicle
IgG1-MCC-DM1 10 mg/kg
NOV169N31Q-MCC-DM1 2.5 mg/kg
NOV169N31Q-MCC-DM1 5 mg/kg*
NOV169N31Q-MCC-DM1 10 mg/kg*
NOV169N31Q-MCC-DM1 15 mg/kg*
Tumor volume (mm3) mean ± SEM
1200
1000
800
600
400
200
0
10
20
30
40
50
60
70
80
90
Dosed
Days post-implantation

Figure 12

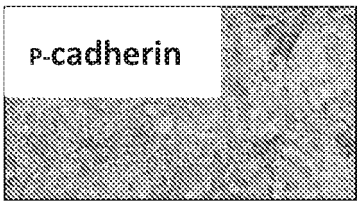

Figure 13A

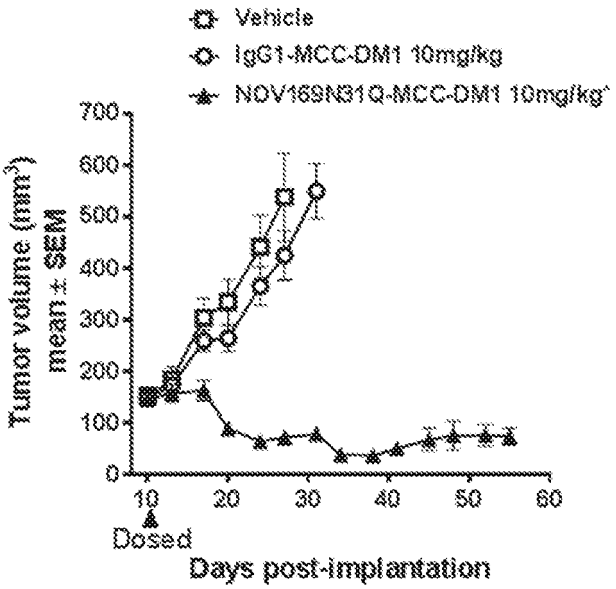

Figure 13B

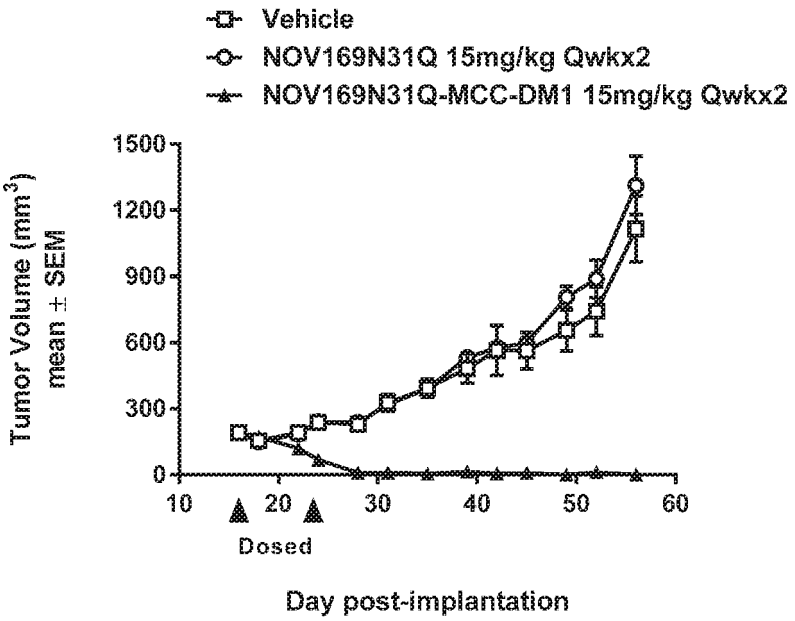

Figure 13C

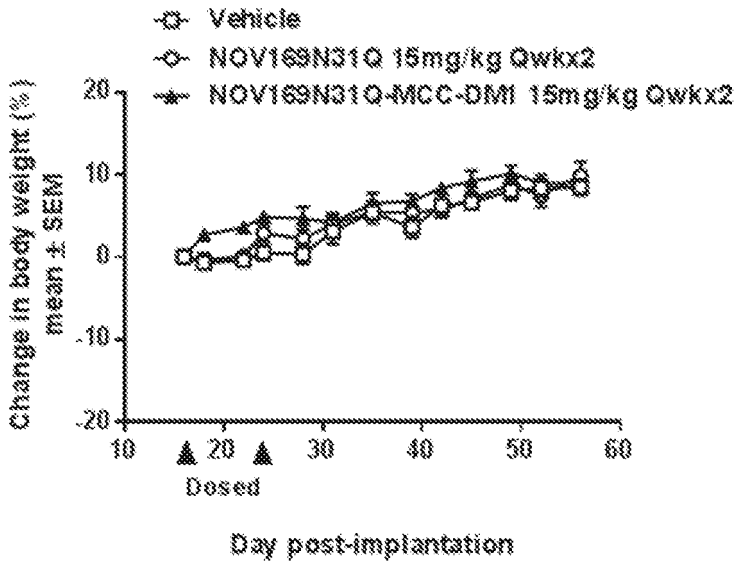

Figure 13D

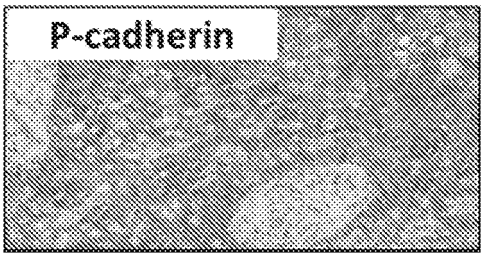

Figure 14A

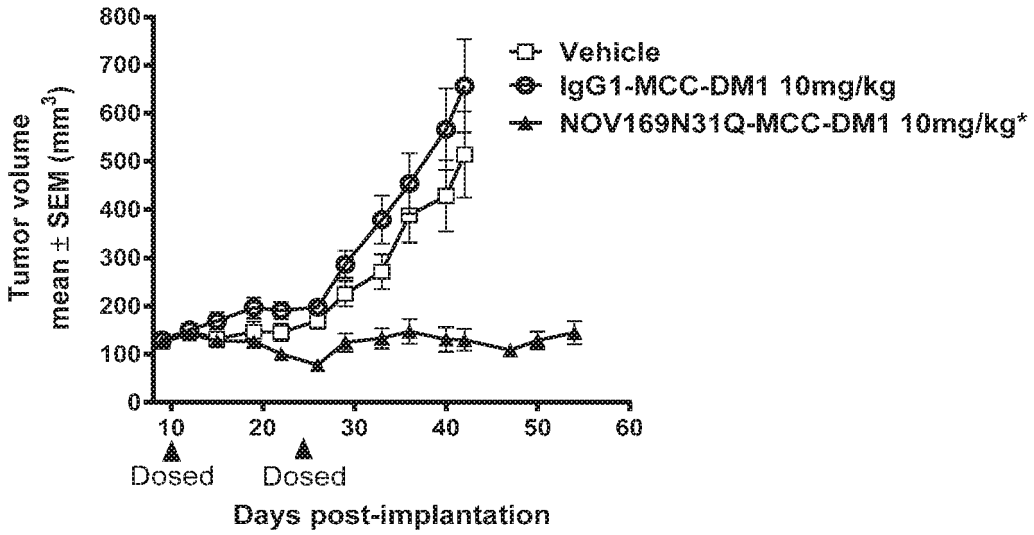

Figure 14B

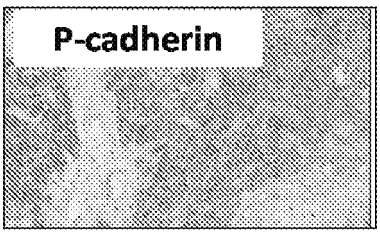

Figure 15A

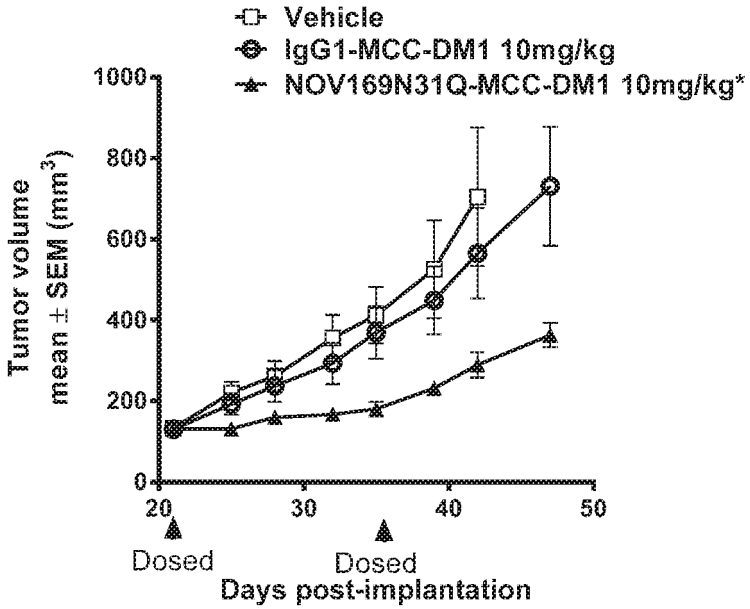

Figure 15B

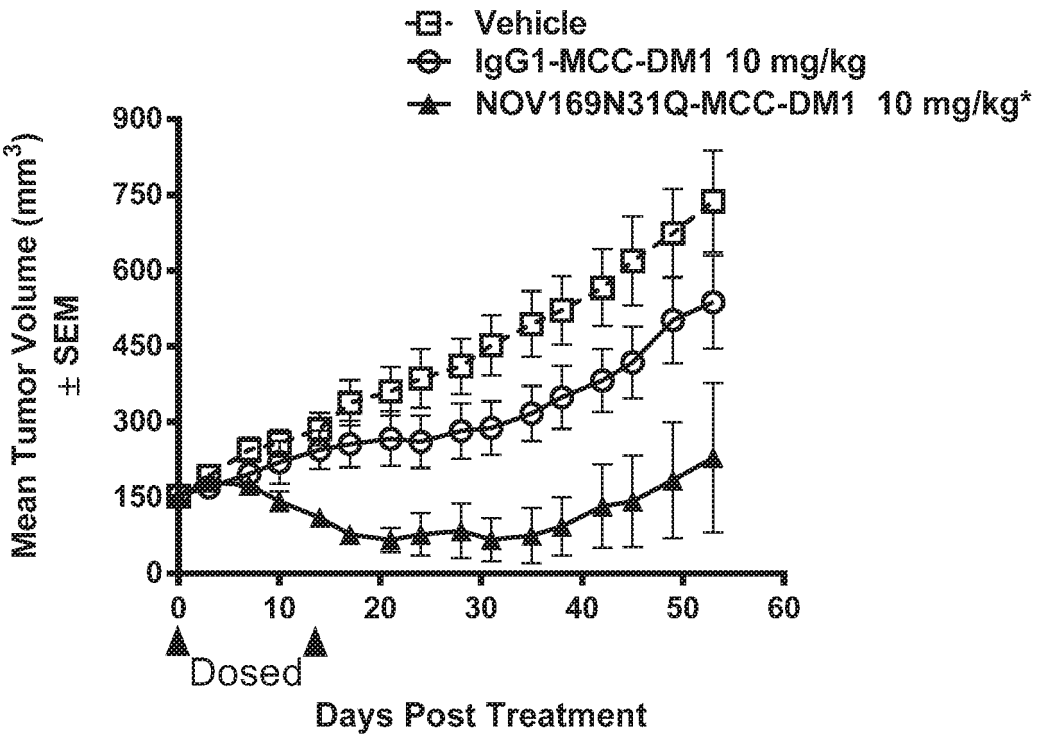
Vehicle
IgG1-MCC-DM1 10 mg/kg
NOV169N31Q-MCC-DM1 10 mg/kg*
Mean Tumor Volume (mm3) ± SEM
900
750
600
450
300
150
0
0
10
20
30
40
50
60
Dosed
Days Post Treatment

Figure 16

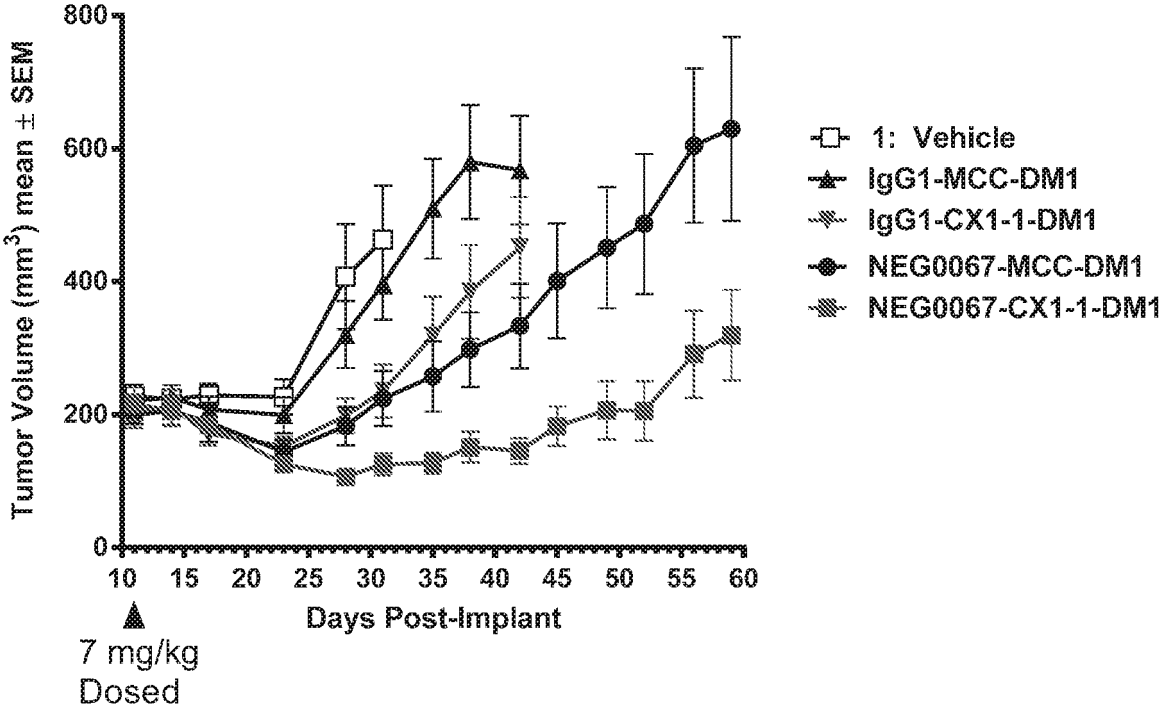
800
600
400
200
0
Tumor Volume (mm3) mean ± SEM
10 15 20 25 30 35 40 45 50 55 60
Days Post-Implant
7 mg/kg
Dosed
1: Vehicle
IgG1-MCC-DM1
IgG1-CX1-1-DM1
NEG0067-MCC-DM1
NEG0067-CX1-1-DM1

Figure 17

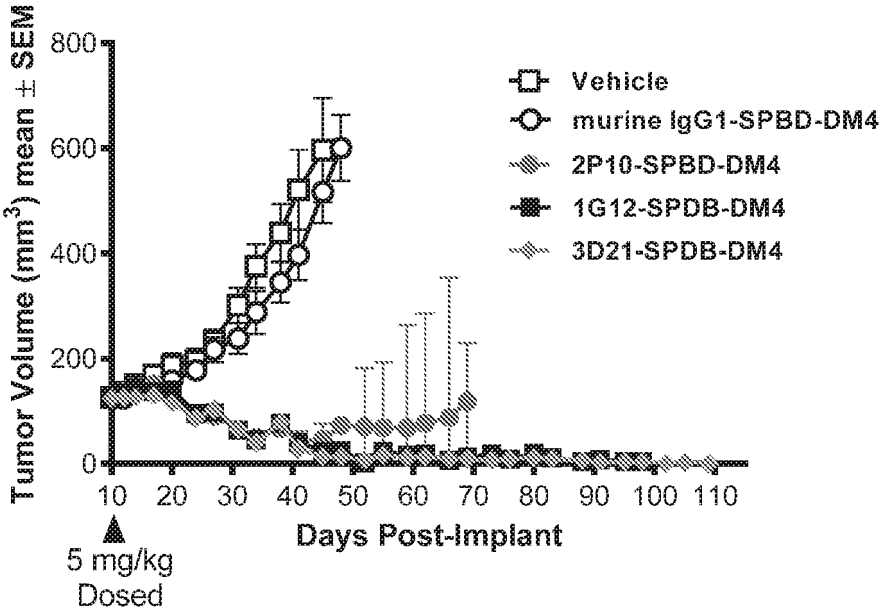
Tumor Volume (mm3) mean ± SEM
800
600
400
200
0
10 20 30 40 50 60 70 80 90 100 110
Days Post-Implant
5 mg/kg
Dosed
Vehicle
murine IgG1-SPBD-DM4
2P10-SPBD-DM4
1G12-SPDB-DM4
3D21-SPDB-DM4

Figure 18