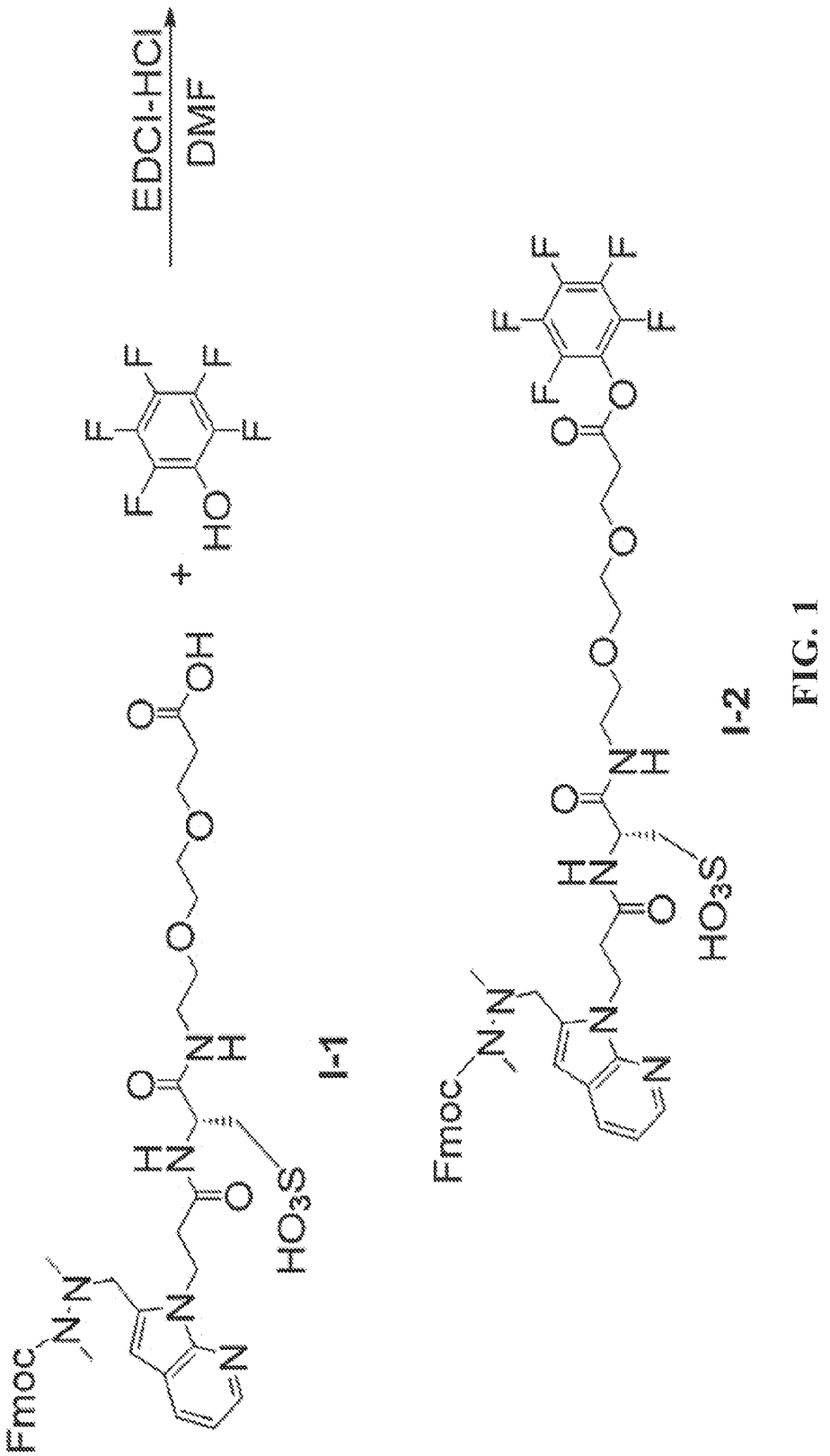


FIG. 1

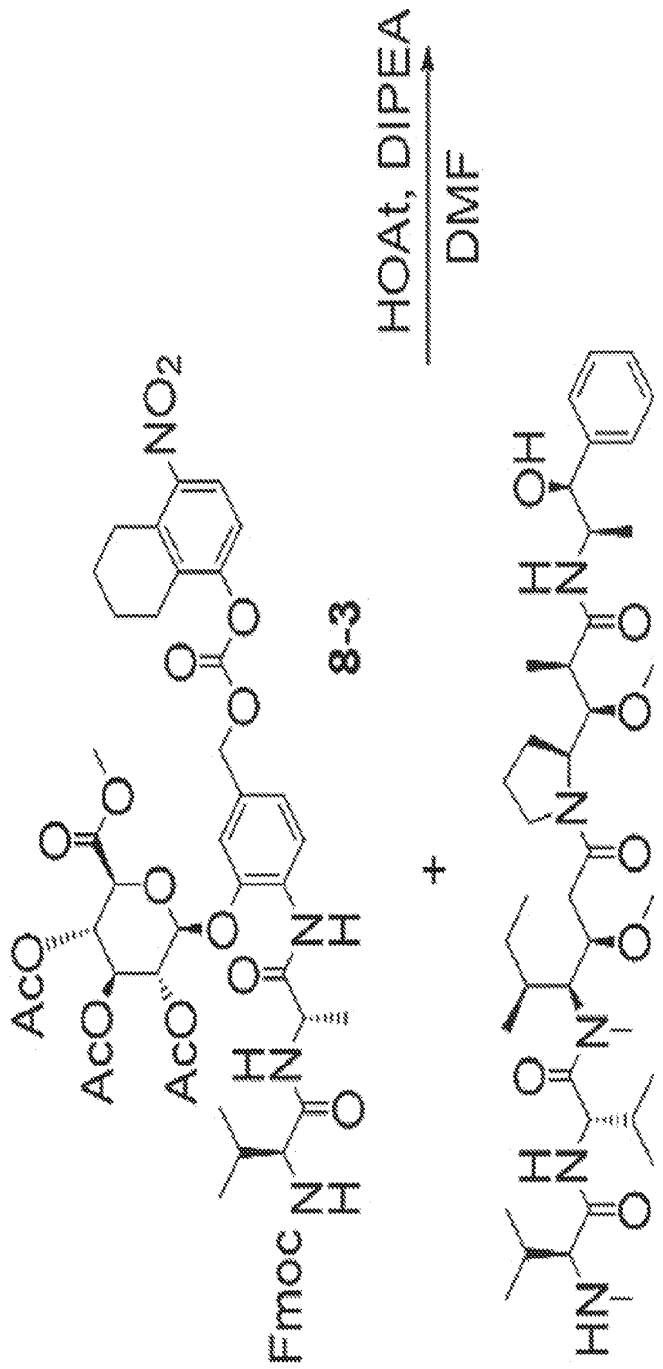


FIG. 1 (cont.)

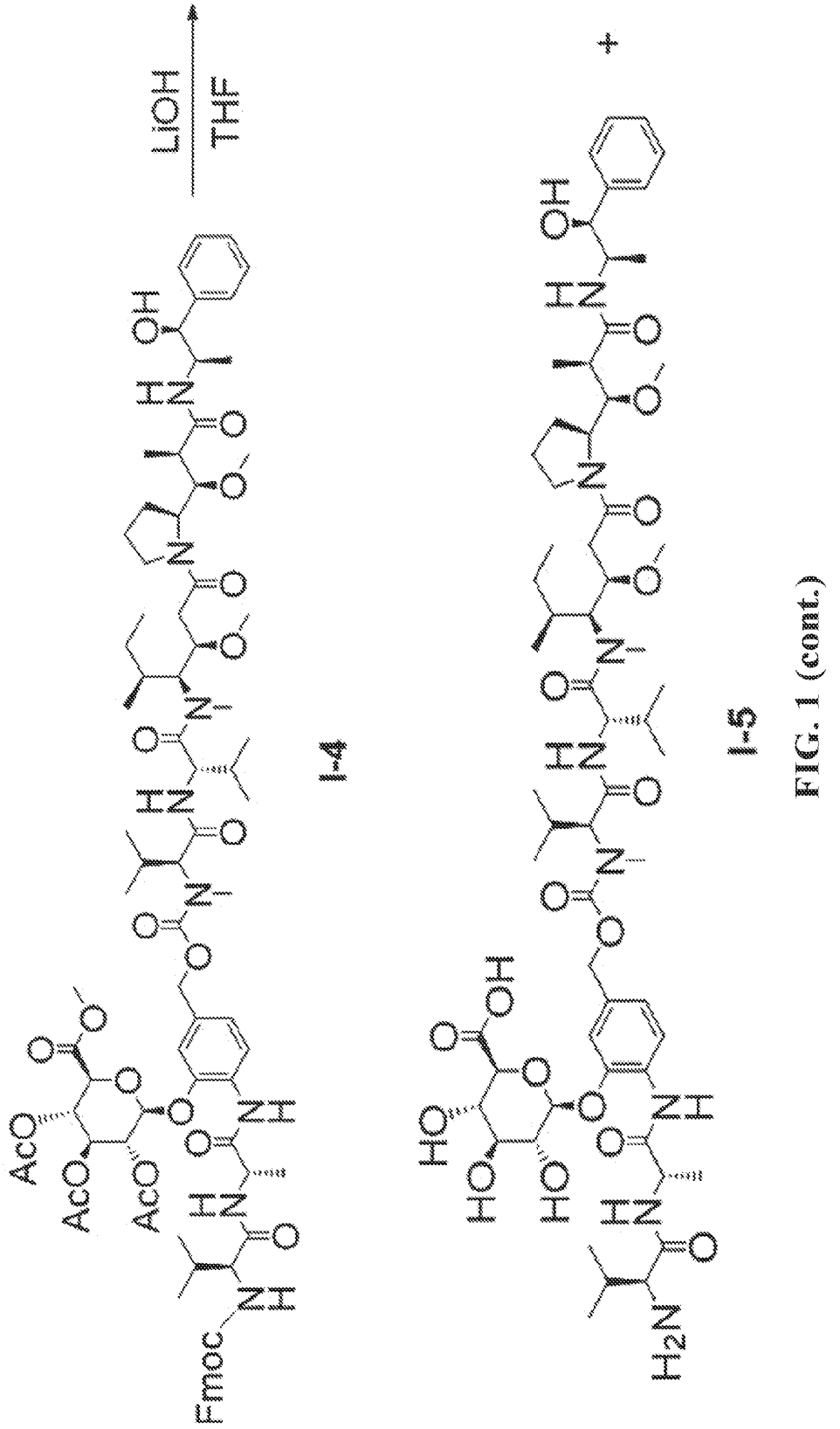


FIG. 1 (cont.)

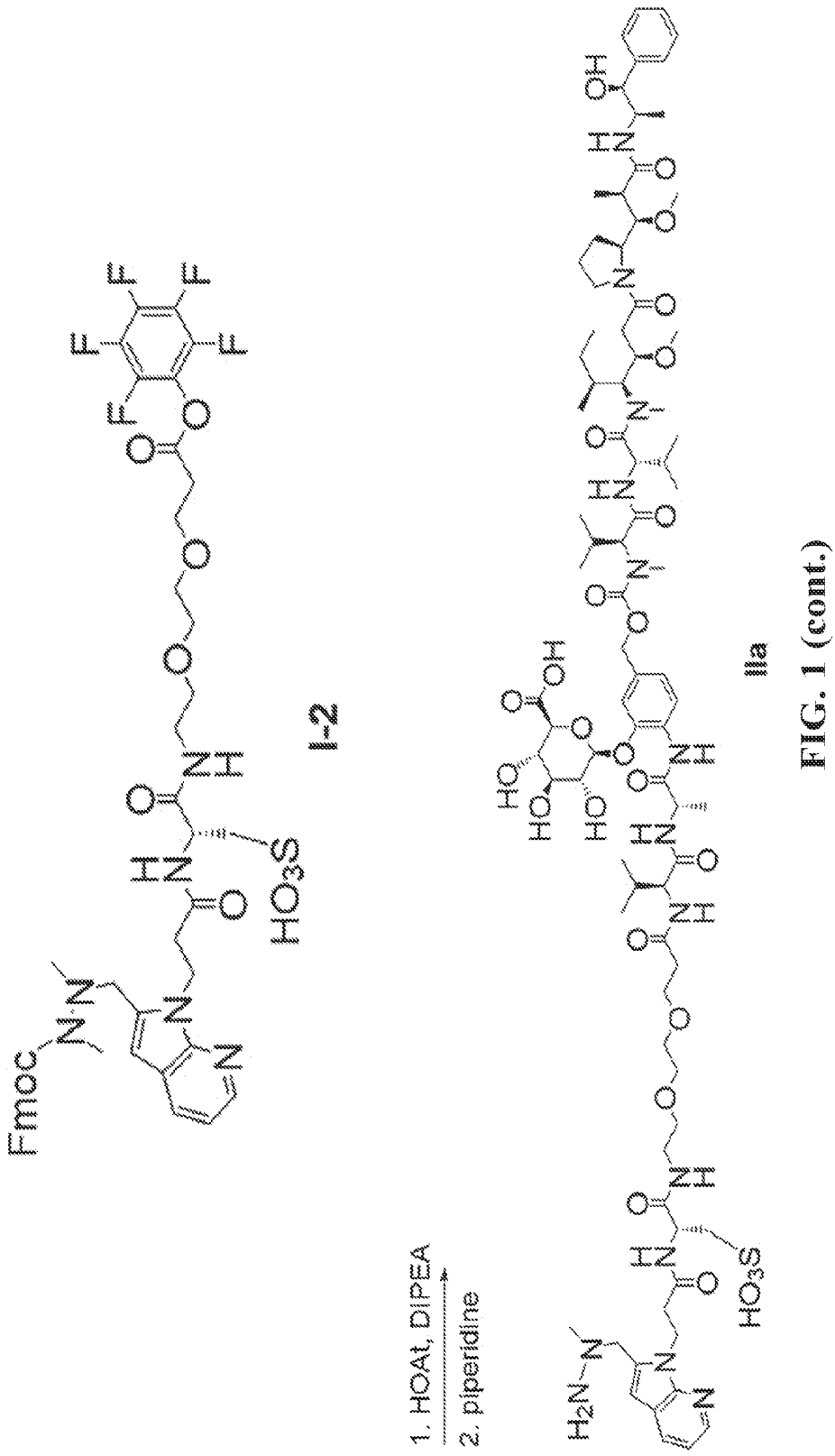


FIG. 1 (cont.)

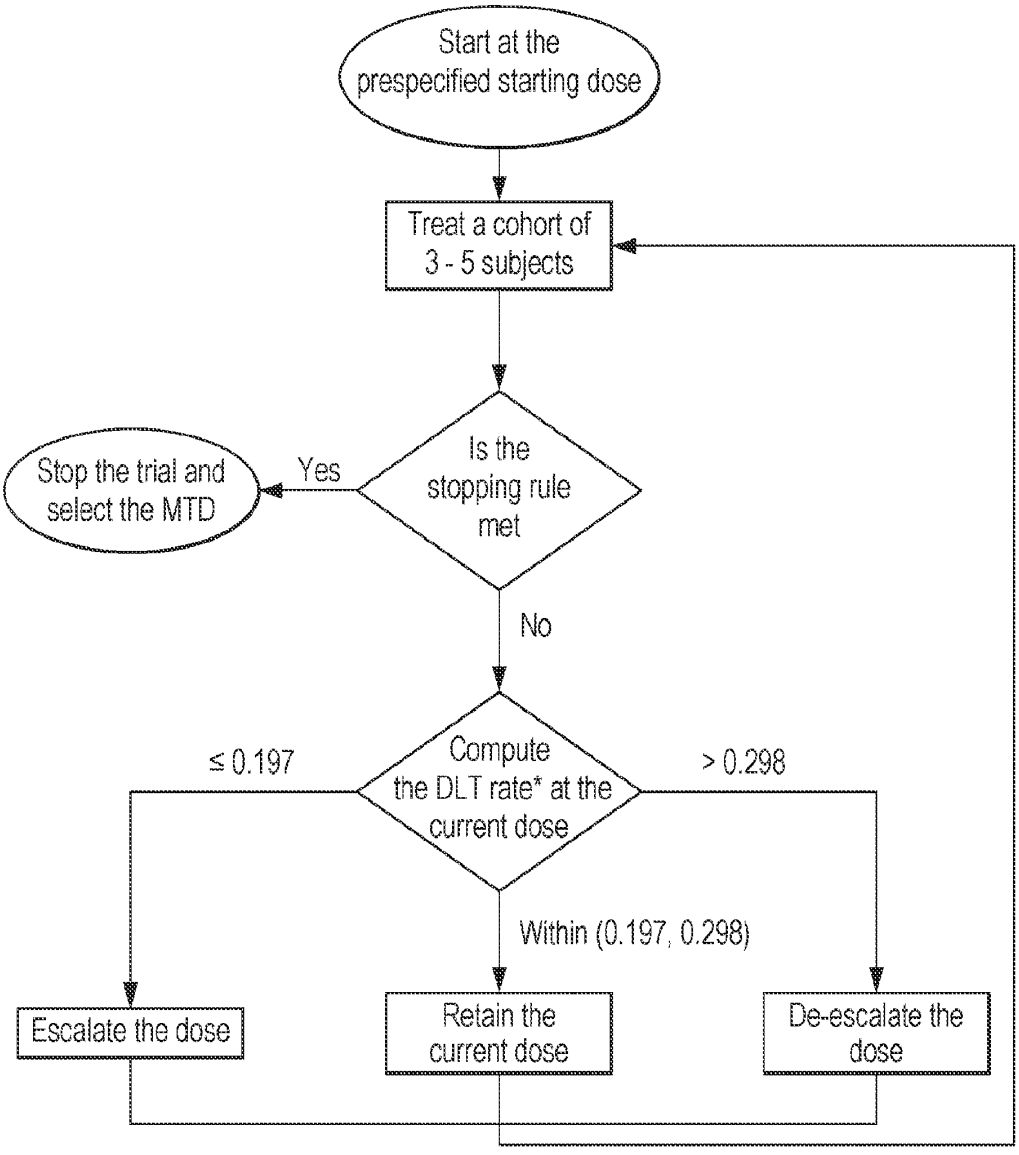
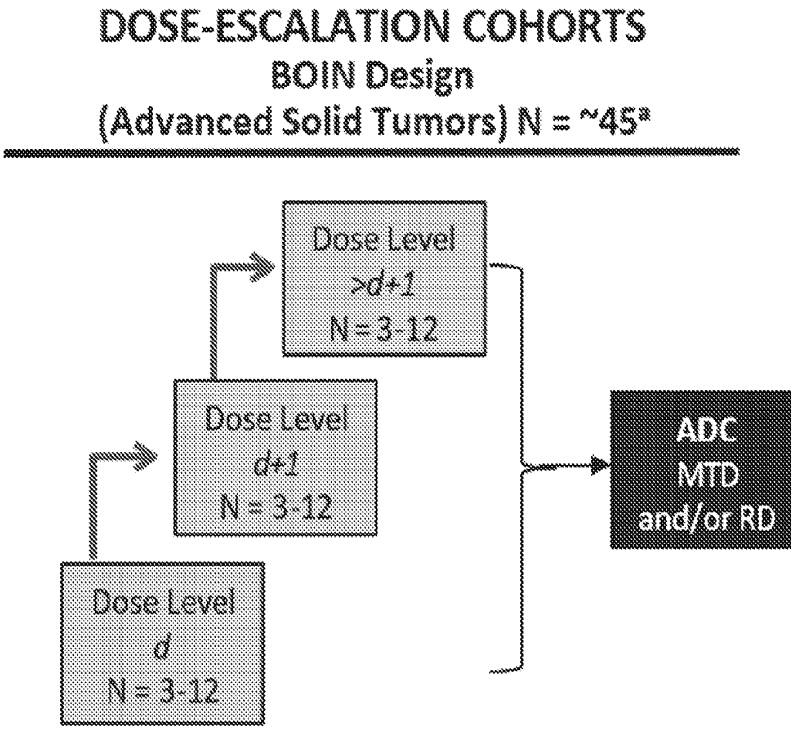

Start at the prespecified starting dose
Treat a cohort of 3 - 5 subjects
Is the stopping rule met
Yes
Stop the trial and select the MTD
No
Compute the DLT rate* at the current dose
≤ 0.197
> 0.298
Within (0.197, 0.298)
Escalate the dose
Retain the current dose
De-escalate the dose

FIG. 2


DOSE-ESCALATION COHORTS
BOIN Design
(Advanced Solid Tumors) N = ~45a
Dose Level
>d+1
N = 3-12
Dose Level
d+1
N = 3-12
Dose Level
d
N = 3-12
ADC
MTD
and/or RD

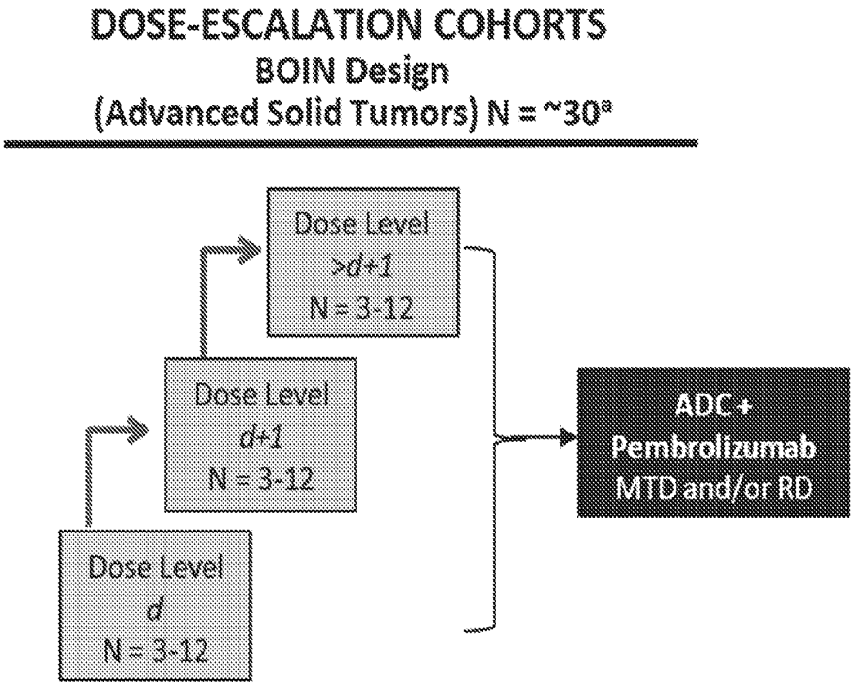

DOSE-ESCALATION COHORTS
BOIN Design
(Advanced Solid Tumors) N = ~30a
Dose Level
>d+1
N = 3-12
Dose Level
d+1
N = 3-12
Dose Level
d
N = 3-12
ADC +
Pembrolizumab
MTD and/or RD

FIG. 3

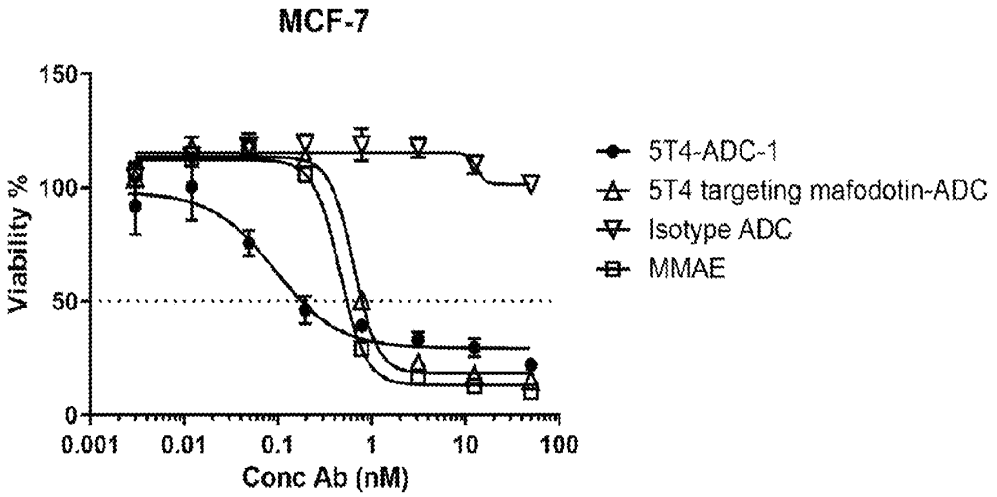

MCF-7
Viability %
150
100
50
0
0.001
0.01
0.1
1
10
100
Conc Ab (nM)
5T4-ADC-1
5T4 targeting mafodotin-ADC
Isotype ADC
MMAE

FIG. 4A

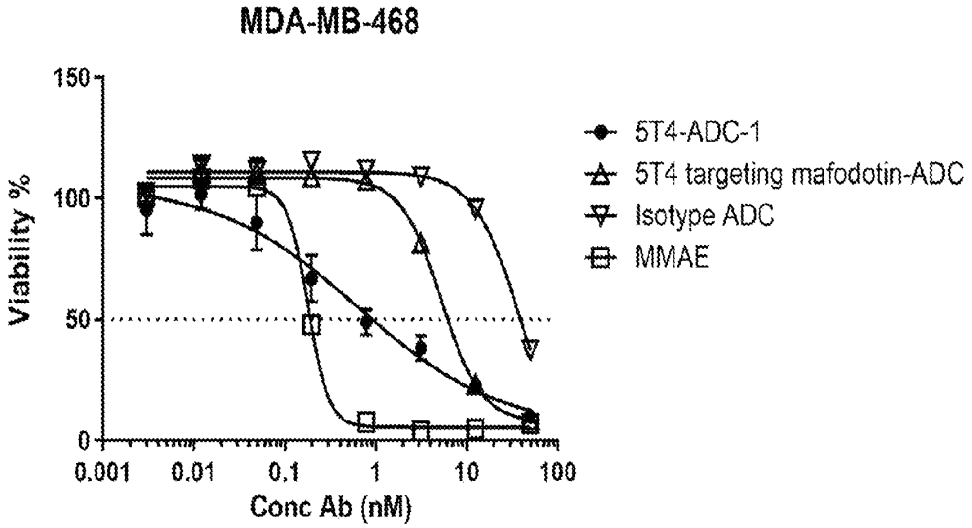

MDA-MB-468
Viability %
150
100
50
0
0.001
0.01
0.1
1
10
100
Conc Ab (nM)
5T4-ADC-1
5T4 targeting mafodotin-ADC
Isotype ADC
MMAE

FIG. 4B

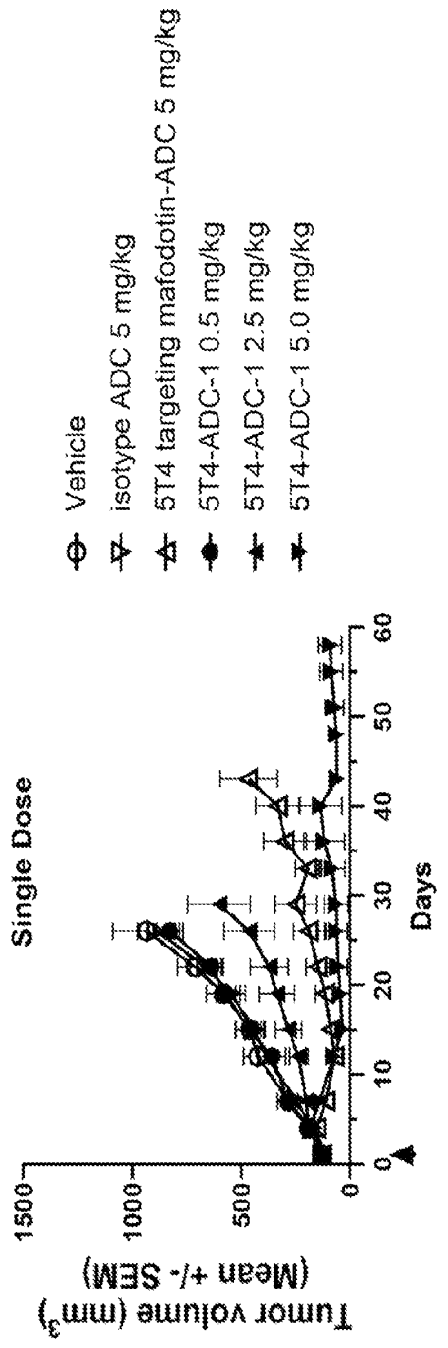

Single Dose
Vehicle
isotype ADC 5 mg/kg
5T4 targeting mafodotin-ADC 5 mg/kg
5T4-ADC-1 0.5 mg/kg
5T4-ADC-1 2.5 mg/kg
5T4-ADC-1 5.0 mg/kg
Tumor volume (mm3)
(Mean +/- SEM)
Days
0
500
1000
1500
0
10
20
30
40
50
60

FIG. 5A

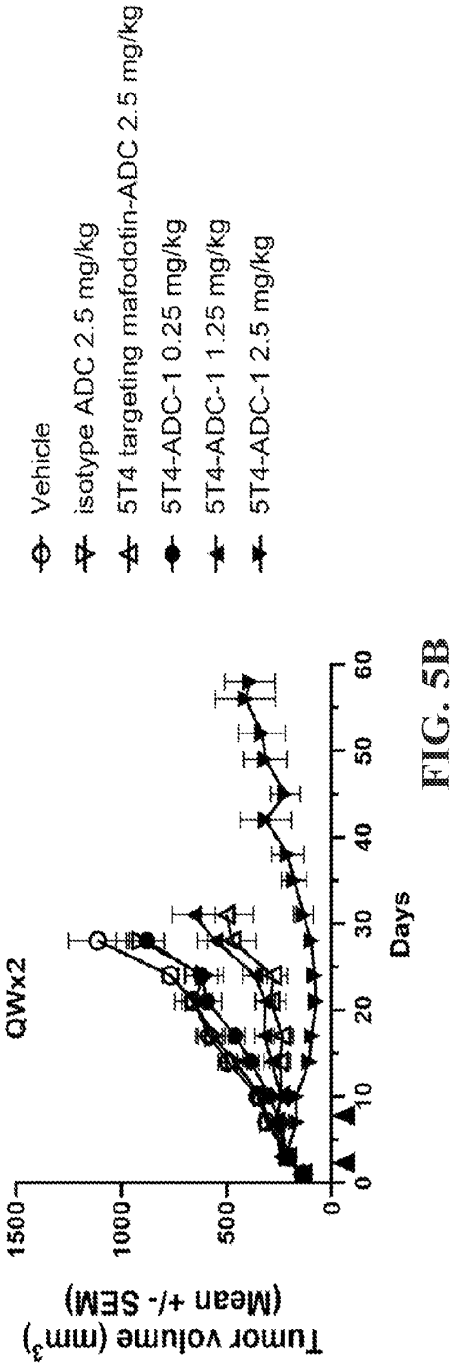

QWx2
Vehicle
isotype ADC 2.5 mg/kg
5T4 targeting mafodotin-ADC 2.5 mg/kg
5T4-ADC-1 0.25 mg/kg
5T4-ADC-1 1.25 mg/kg
5T4-ADC-1 2.5 mg/kg
Tumor volume (mm3)
(Mean +/- SEM)
Days
0
500
1000
1500
0
10
20
30
40
50
60

FIG. 5B

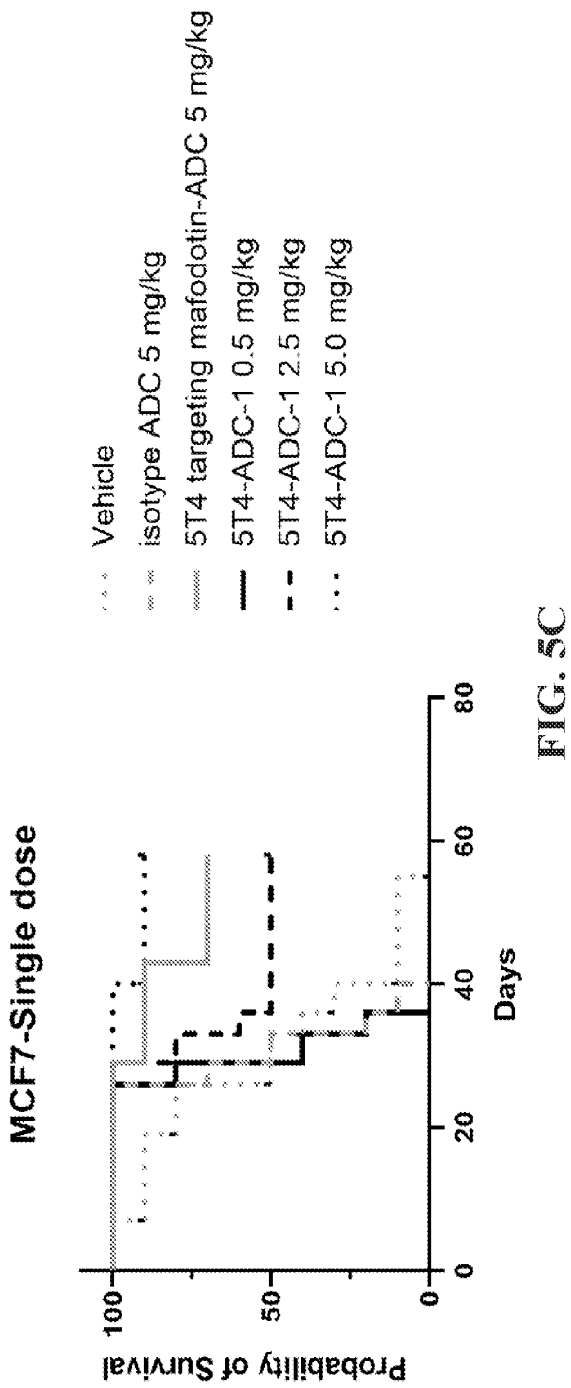

MCF7-Single dose
Probability of Survival
100
50
0
0
20
40
60
80
Days
Vehicle
isotype ADC 5 mg/kg
5T4 targeting mafodotin-ADC 5 mg/kg
5T4-ADC-1 0.5 mg/kg
5T4-ADC-1 2.5 mg/kg
5T4-ADC-1 5.0 mg/kg

FIG. 5C

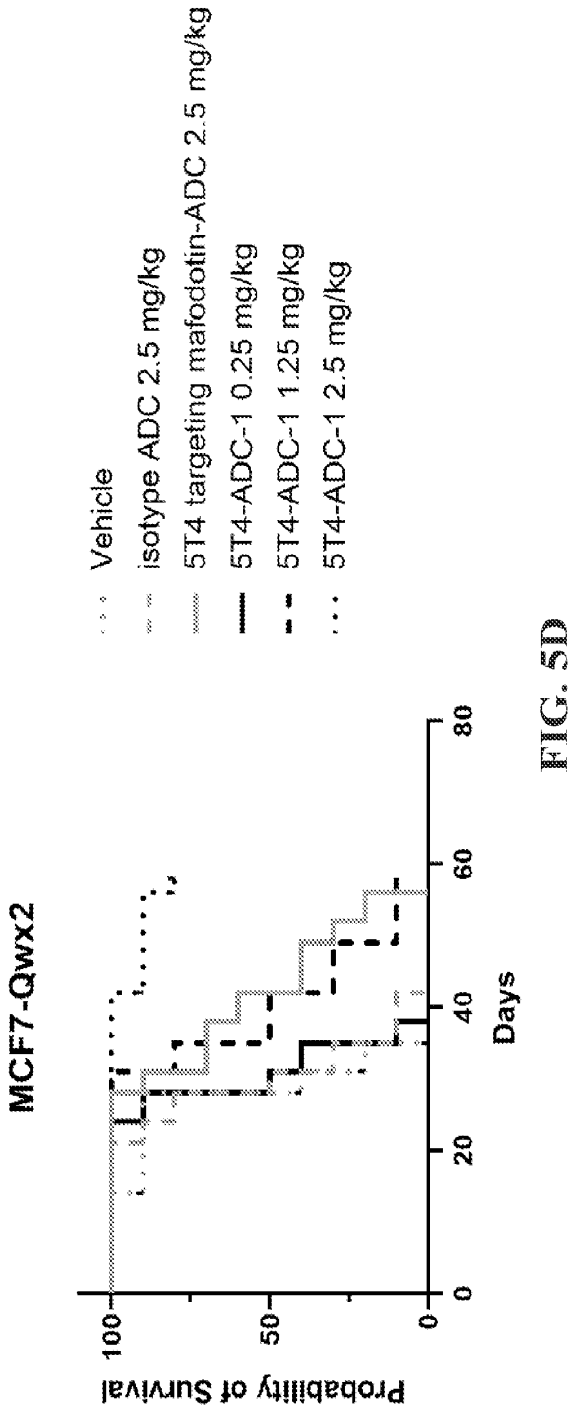

MCF7-Qwx2
Probability of Survival
100
50
0
0
20
40
60
80
Days
Vehicle
isotype ADC 2.5 mg/kg
5T4 targeting mafodotin-ADC 2.5 mg/kg
5T4-ADC-1 0.25 mg/kg
5T4-ADC-1 1.25 mg/kg
5T4-ADC-1 2.5 mg/kg

FIG. 5D

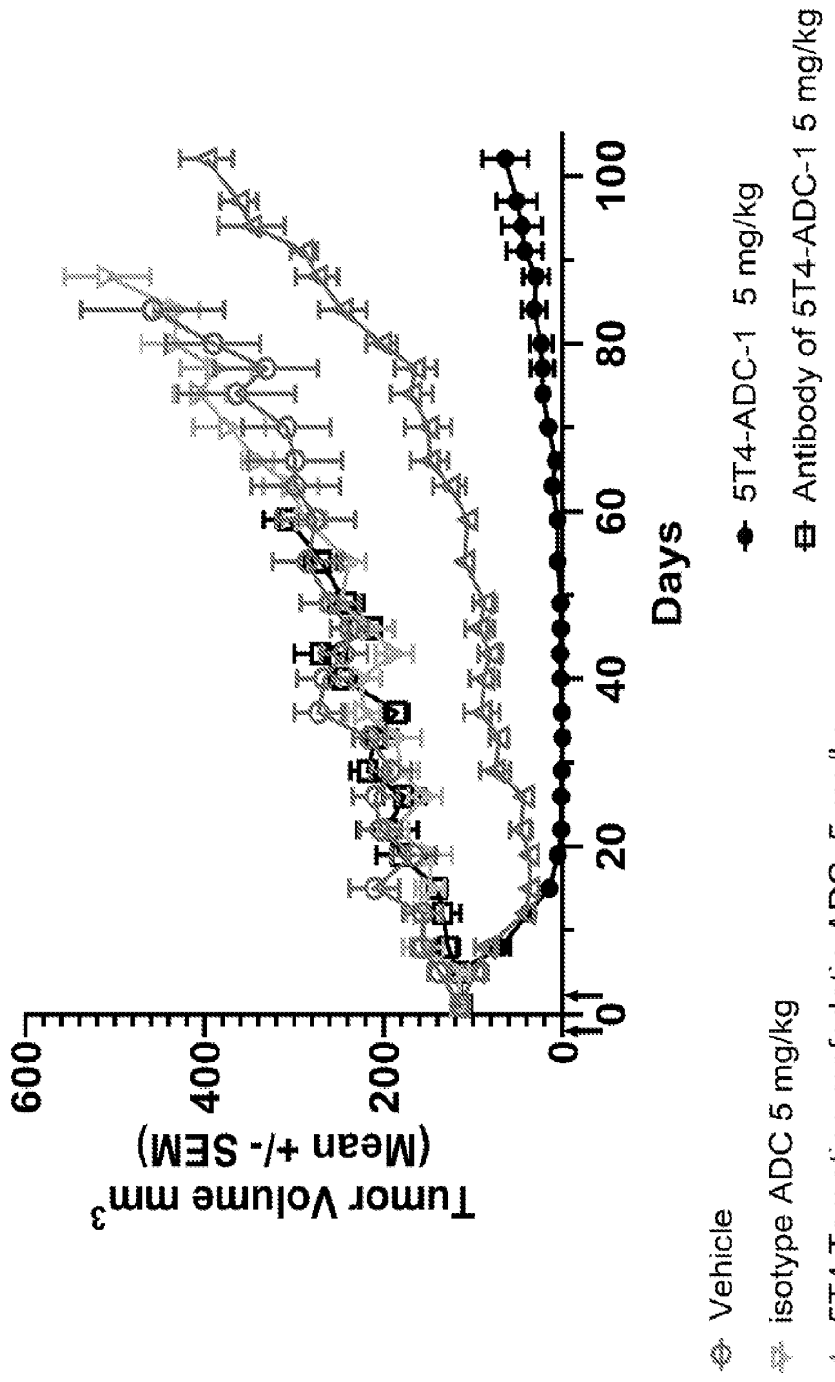

Tumor Volume mm3 (Mean +/- SEM)
600
400
200
0
0
20
40
60
80
100
Days
Vehicle
isotype ADC 5 mg/kg
5T4 Targeting mafodotin-ADC 5 mg/kg
5T4-ADC-1 5 mg/kg
Antibody of 5T4-ADC-1 5 mg/kg

FIG. 5E

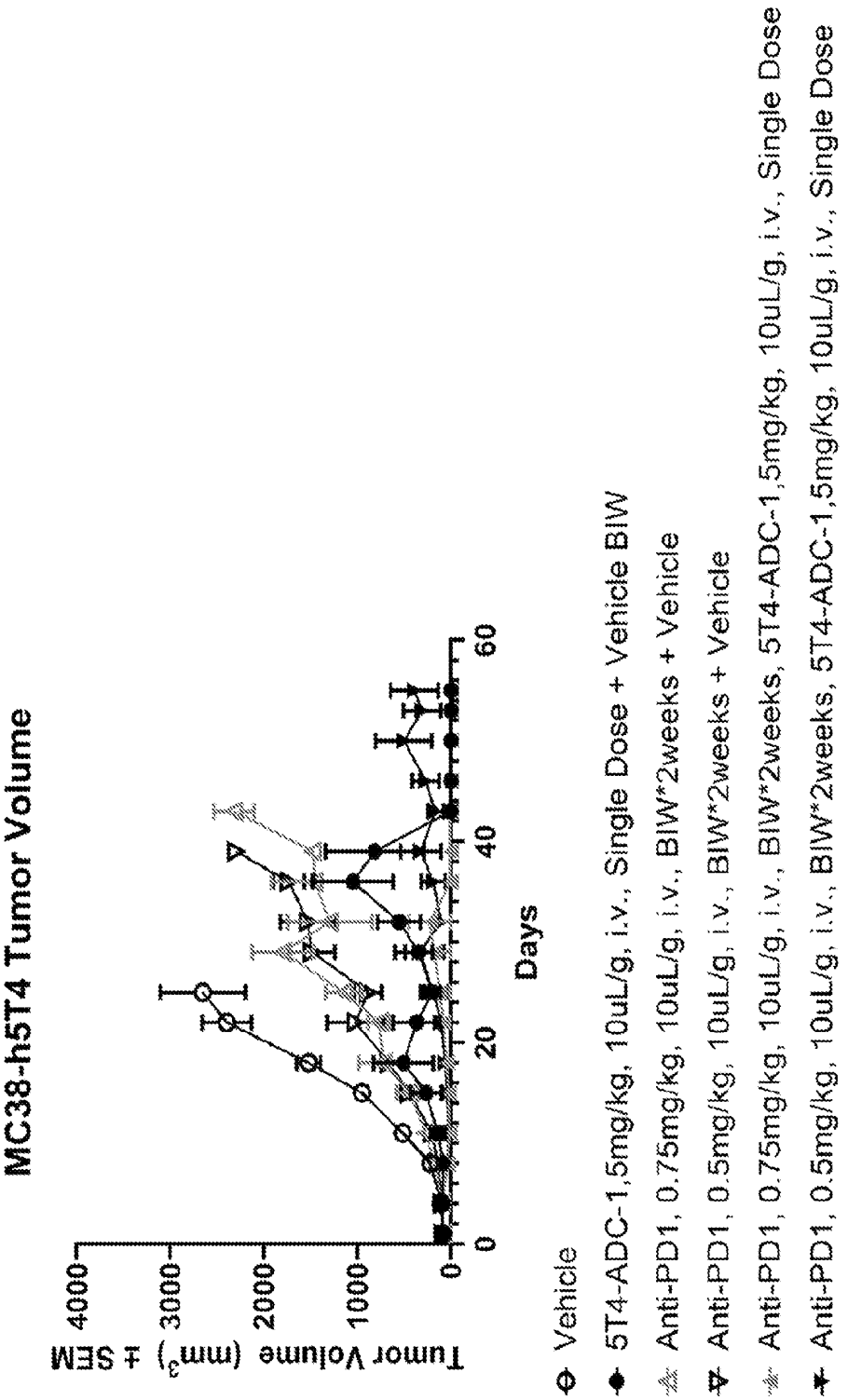

MC38-h5T4 Tumor Volume
Tumor Volume (mm3) ± SEM
4000
3000
2000
1000
0
0
20
40
60
Days
Vehicle
5T4-ADC-1,5mg/kg, 10uL/g, i.v., Single Dose + Vehicle BIW
Anti-PD1, 0.75mg/kg, 10uL/g, i.v., BIW*2weeks + Vehicle
Anti-PD1, 0.5mg/kg, 10uL/g, i.v., BIW*2weeks + Vehicle
Anti-PD1, 0.75mg/kg, 10uL/g, i.v., BIW*2weeks, 5T4-ADC-1,5mg/kg, 10uL/g, i.v., Single Dose
Anti-PD1, 0.5mg/kg, 10uL/g, i.v., BIW*2weeks, 5T4-ADC-1,5mg/kg, 10uL/g, i.v., Single Dose

FIG. 6A

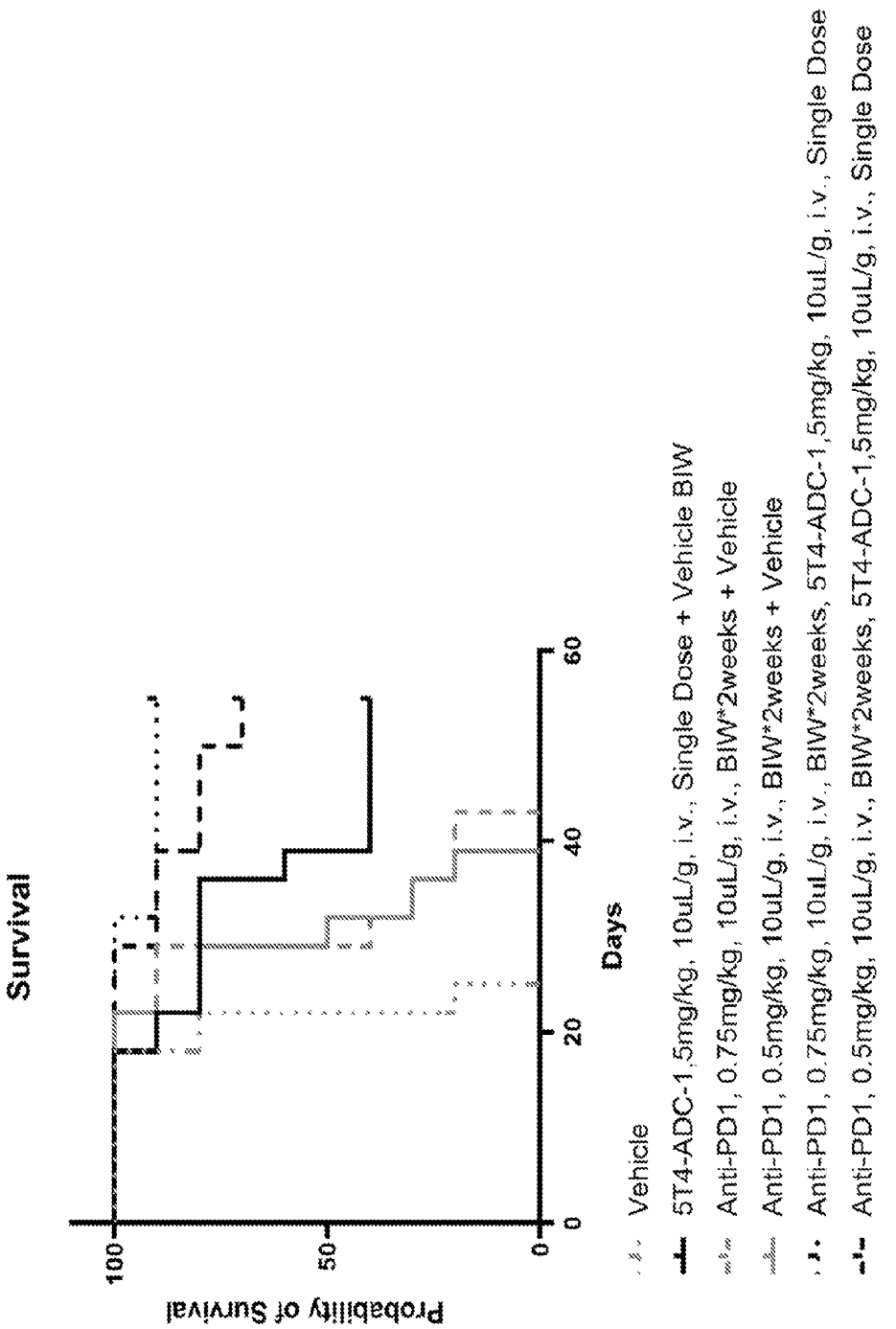

Survival
Probability of Survival
100
50
0
0
20
40
60
Days
Vehicle
5T4-ADC-1.5mg/kg, 10uL/g, i.v., Single Dose + Vehicle BIW
Anti-PD1, 0.75mg/kg, 10uL/g, i.v., BIW*2weeks + Vehicle
Anti-PD1, 0.5mg/kg, 10uL/g, i.v., BIW*2weeks + Vehicle
Anti-PD1, 0.75mg/kg, 10uL/g, i.v., BIW*2weeks, 5T4-ADC-1,5mg/kg, 10uL/g, i.v., Single Dose
Anti-PD1, 0.5mg/kg, 10uL/g, i.v., BIW*2weeks, 5T4-ADC-1,5mg/kg, 10uL/g, i.v., Single Dose

FIG. 6B

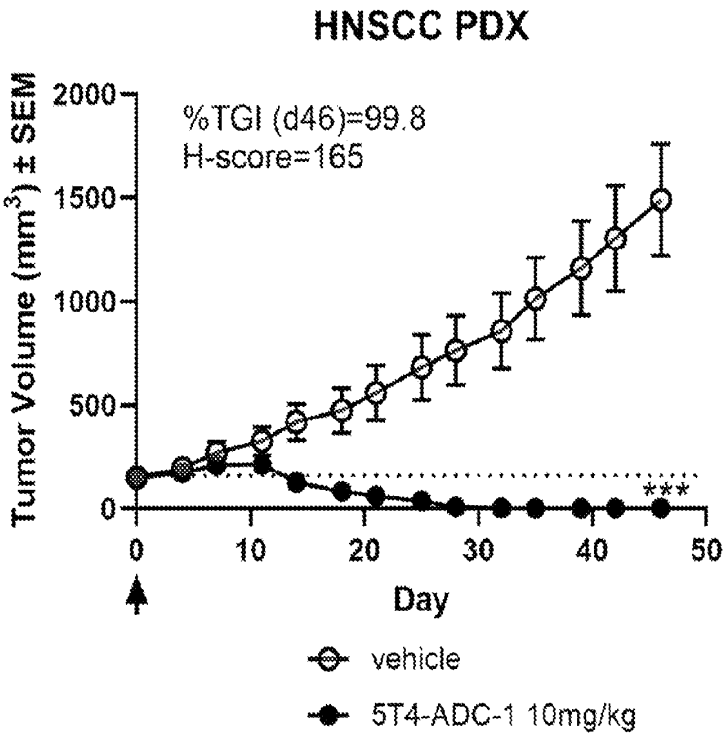

HNSCC PDX
%TGI (d46)=99.8
H-score=165
Tumor Volume (mm3) ± SEM
2000
1500
1000
500
0
***
0
10
20
30
40
50
Day
vehicle
5T4-ADC-1 10mg/kg

FIG. 7A

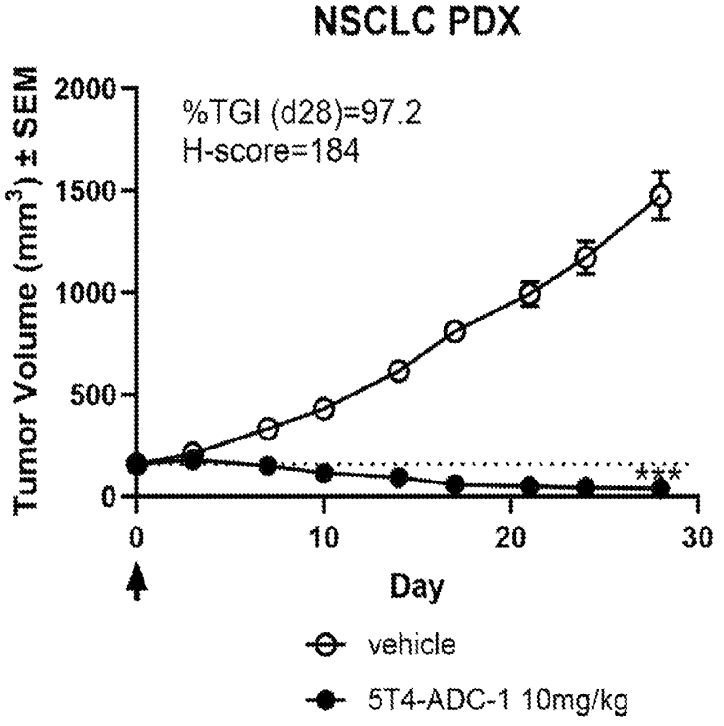

NSCLC PDX
%TGI (d28)=97.2
H-score=184
Tumor Volume (mm3) ± SEM
2000
1500
1000
500
0
***
0
10
20
30
Day
vehicle
5T4-ADC-1 10mg/kg

FIG. 7B

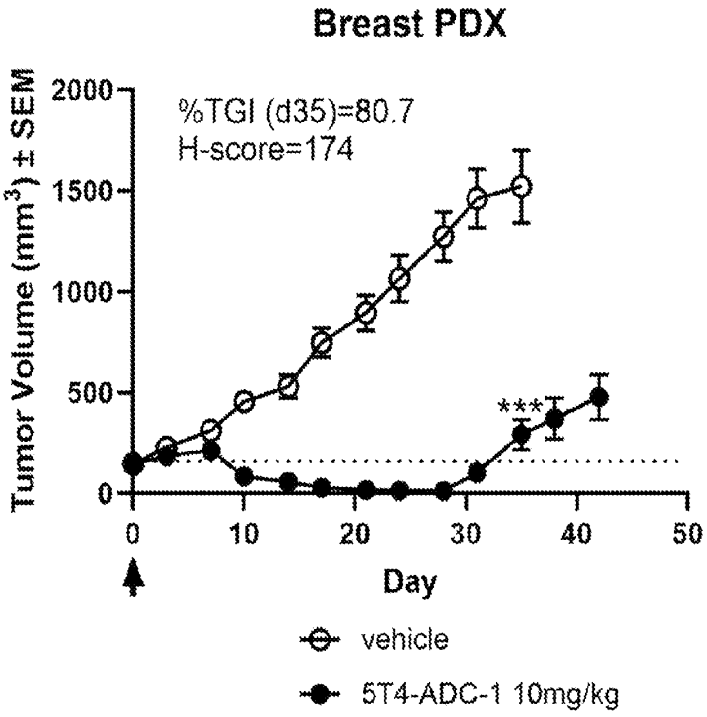

Breast PDX
%TGI (d35)=80.7
H-score=174
Tumor Volume (mm3) ± SEM
2000
1500
1000
500
0
***
0
10
20
30
40
50
Day
vehicle
5T4-ADC-1 10mg/kg

FIG. 7C

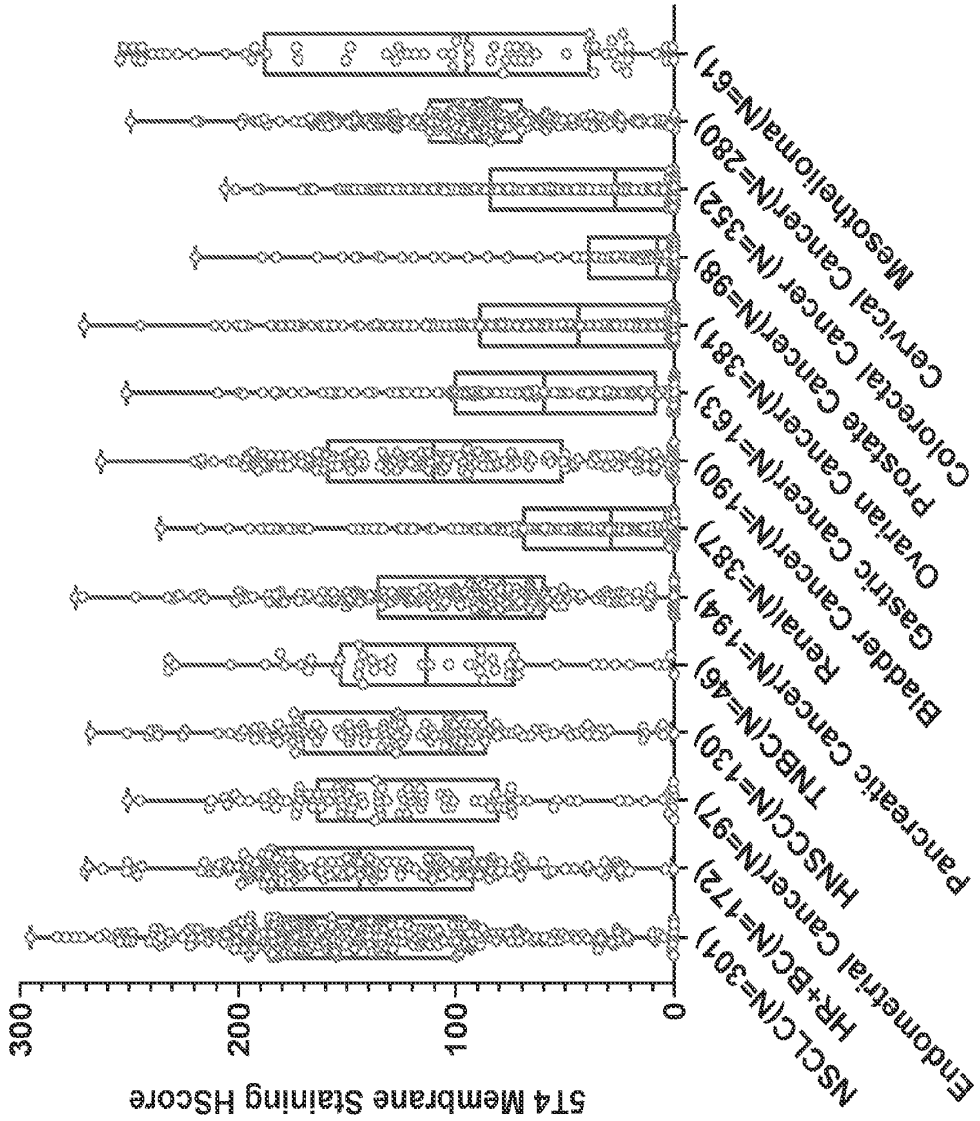

5T4 Membrane Staining HScore
300
200
100
0
NSCLC(N=301)
HR+BC(N=172)
Endometrial Cancer(N=97)
HNSCC(N=130)
TNBC(N=46)
Pancreatic Cancer(N=194)
Renal(N=387)
Bladder Cancer(N=190)
Gastric Cancer(N=163)
Ovarian Cancer(N=381)
Prostate Cancer(N=98)
Colorectal Cancer (N=352)
Cervical Cancer(N=280)
Mesothelioma(N=61)

FIG. 8A

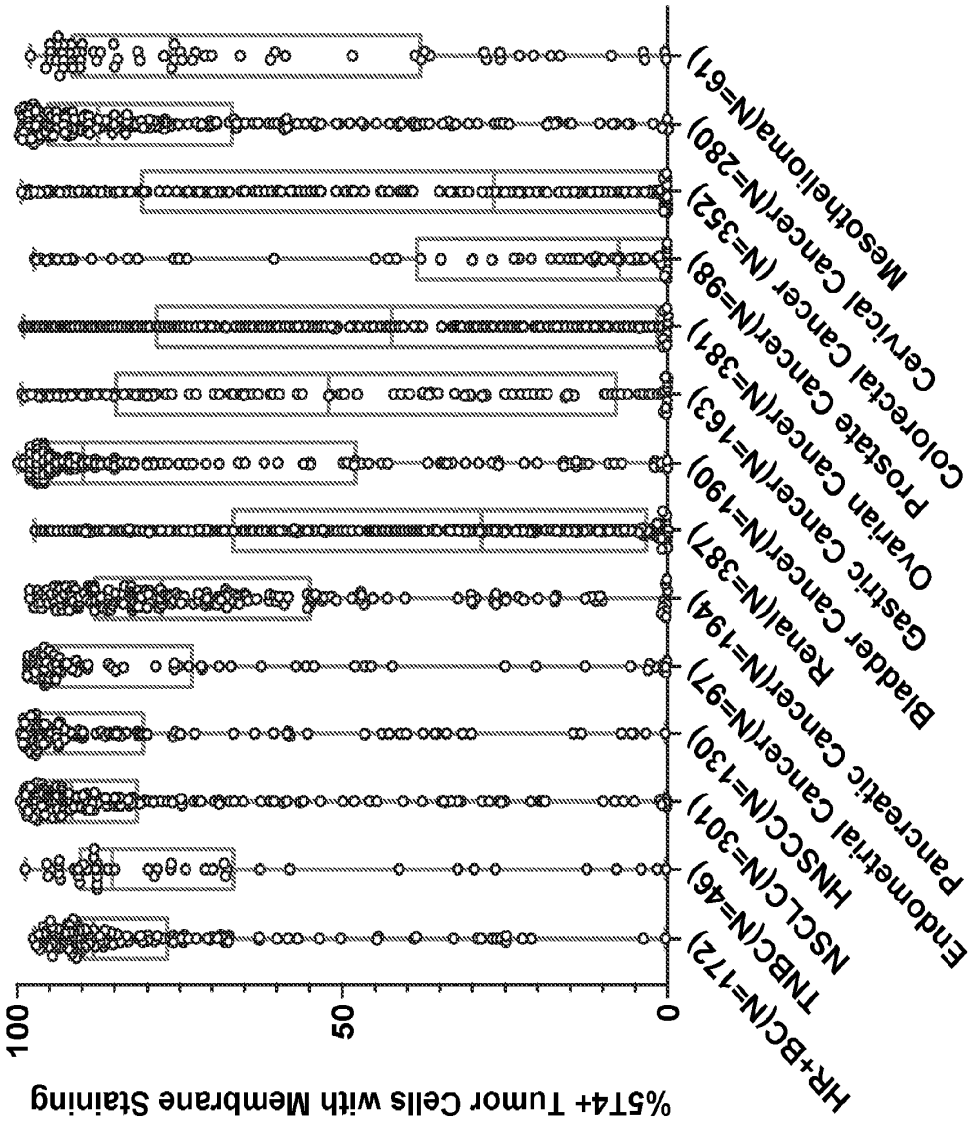

%5T4+ Tumor Cells with Membrane Staining
100
50
0
HR+BC(N=172)
TNBC(N=46)
NSCLC(N=301)
HNSCC(N=130)
Endometrial Cancer(N=97)
Pancreatic Cancer(N=194)
Bladder Cancer(N=387)
Renal(N=190)
Gastric Cancer(N=163)
Ovarian Cancer(N=381)
Prostate Cancer(N=98)
Colorectal Cancer (N=352)
Cervical Cancer(N=280)
Mesothelioma(N=61)

FIG. 8B