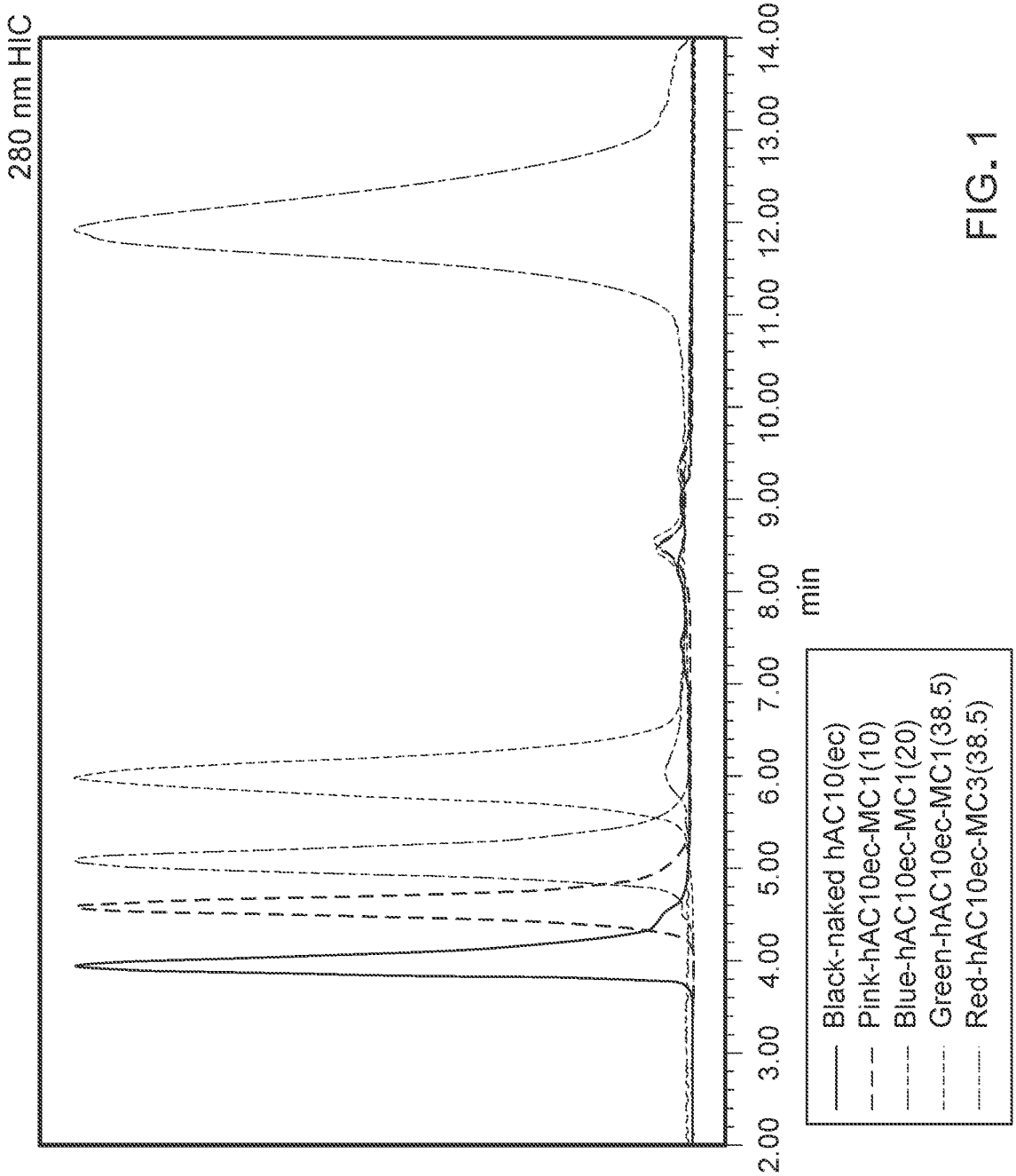

280 nm HIC
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00
10.00
11.00
12.00
13.00
14.00
min
Black-naked hAC10(ec)
Pink-hAC10ec-MC1(10)
Blue-hAC10ec-MC1(20)
Green-hAC10ec-MC1(38.5)
Red-hAC10ec-MC3(38.5)

FIG. 1

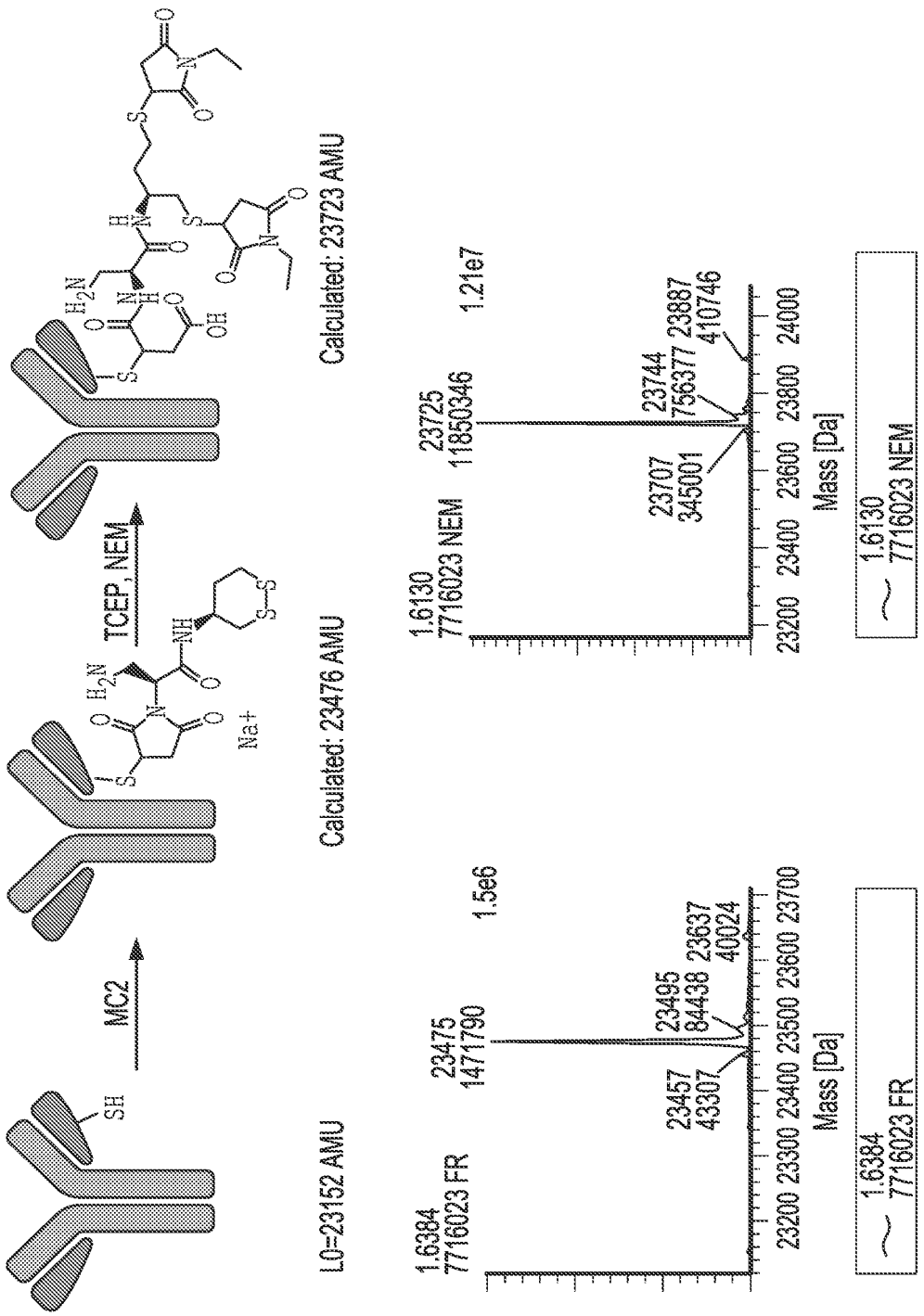

SH
MC2
TCEP, NEM
Na+
L0=23152 AMU
Calculated: 23476 AMU
Calculated: 23723 AMU
1.6384
7716023 FR
23475
1471790
1.5e6
23457
43307
23495
84438
23637
40024
23200 23300 23400 23500 23600 23700
Mass [Da]
1.6384
7716023 FR
1.6130
7716023 NEM
23725
11850346
1.21e7
23707
345001
23744
756377
23887
410746
23200 23400 23600 23800 24000
Mass [Da]
1.6130
7716023 NEM

FIG. 2

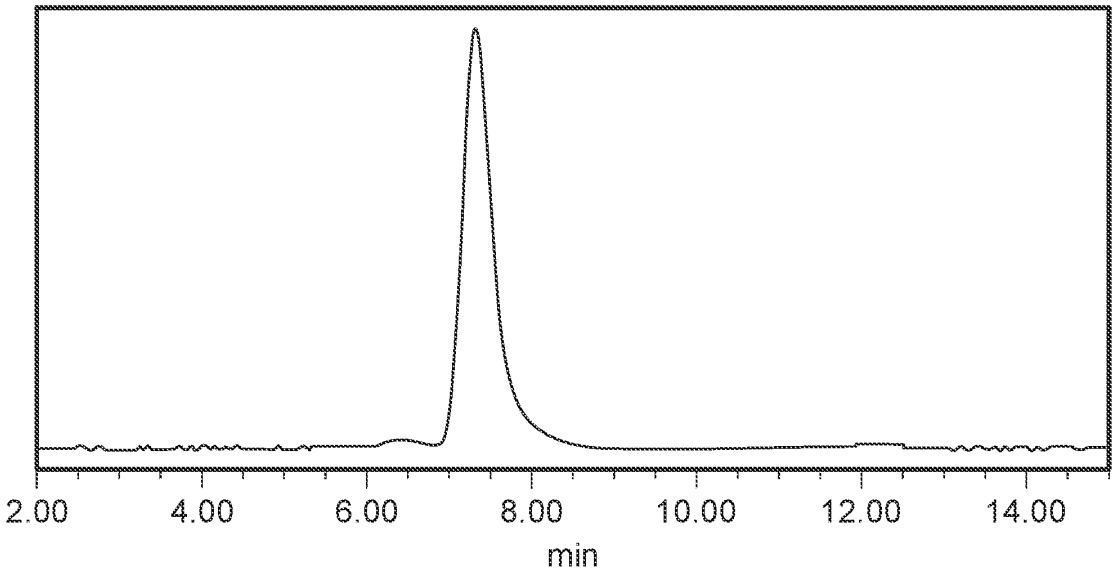

2.00
4.00
6.00
8.00
10.00
12.00
14.00
min

FIG. 3A

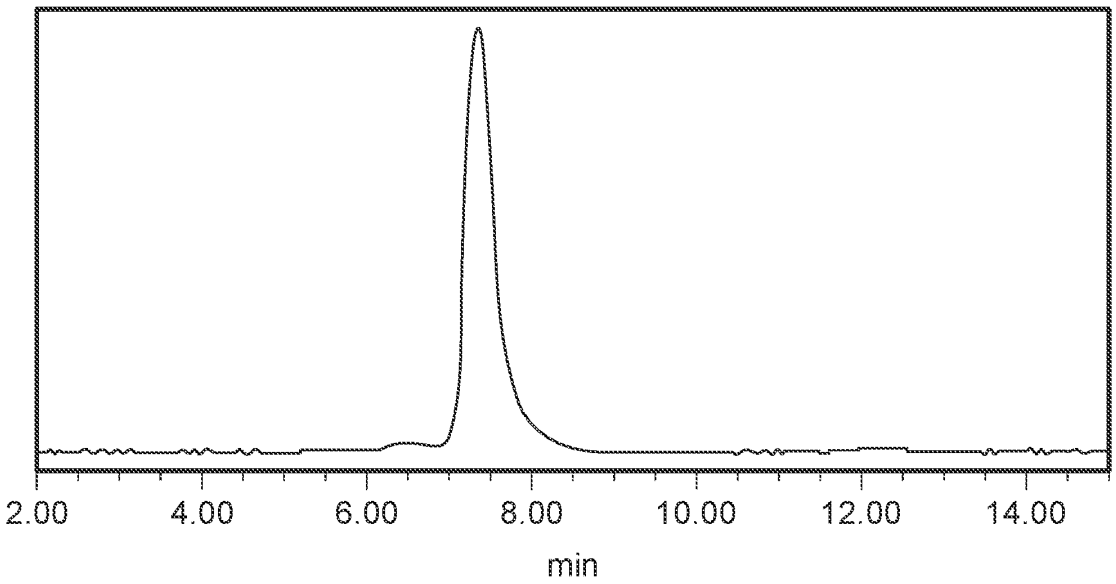

2.00
4.00
6.00
8.00
10.00
12.00
14.00
min

FIG. 3B

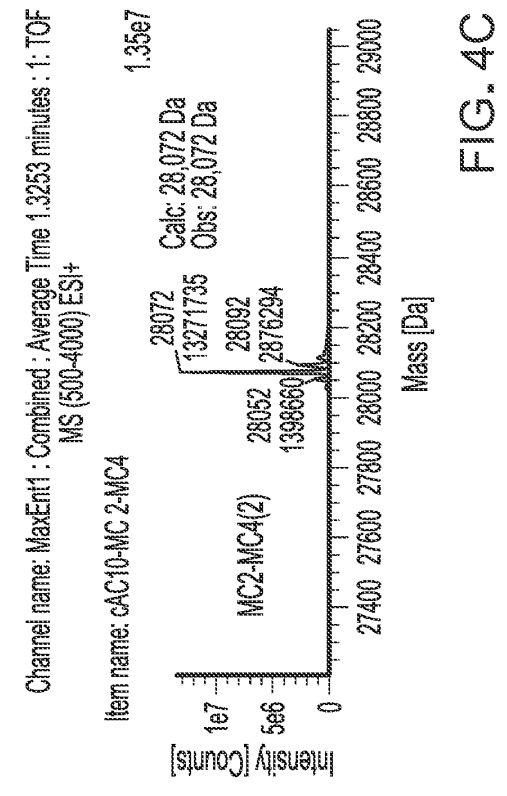


FIG. 4A

FIG. 4C

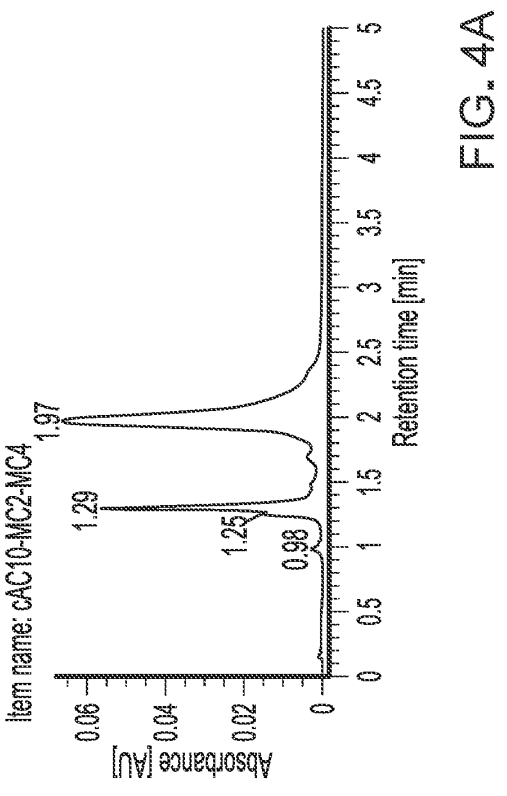


FIG. 4B

FIG. 4D

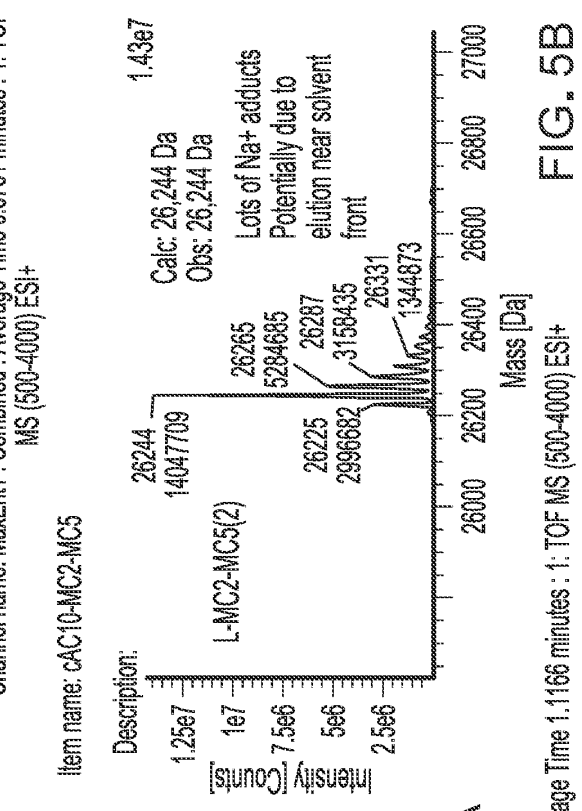


FIG. 5A

FIG. 5B

FIG. 5C

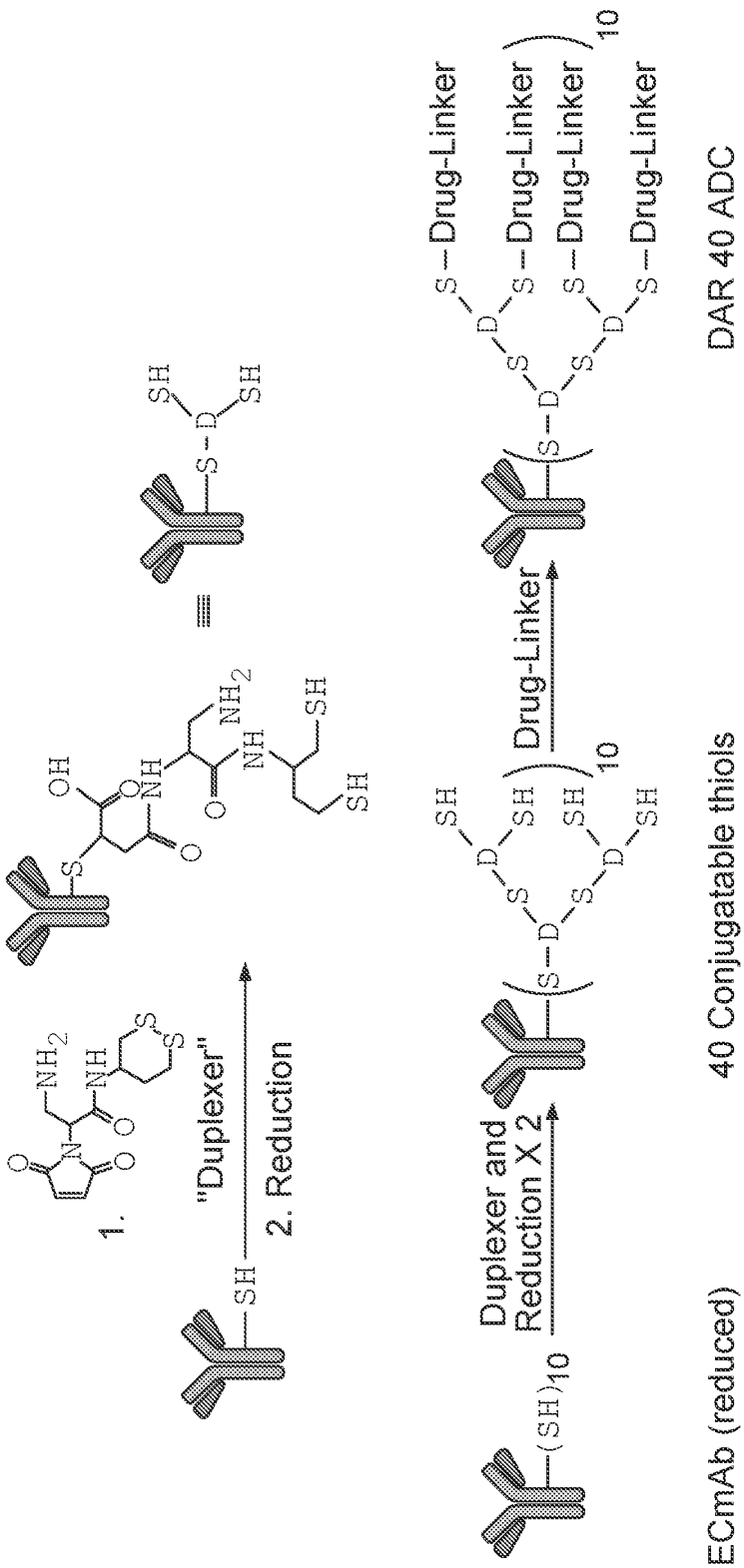

1.
"Duplexer"
2. Reduction
Duplexer and
Reduction X 2
Drug-Linker
ECmAb (reduced)
40 Conjugatable thiols
DAR 40 ADC

FIG. 6

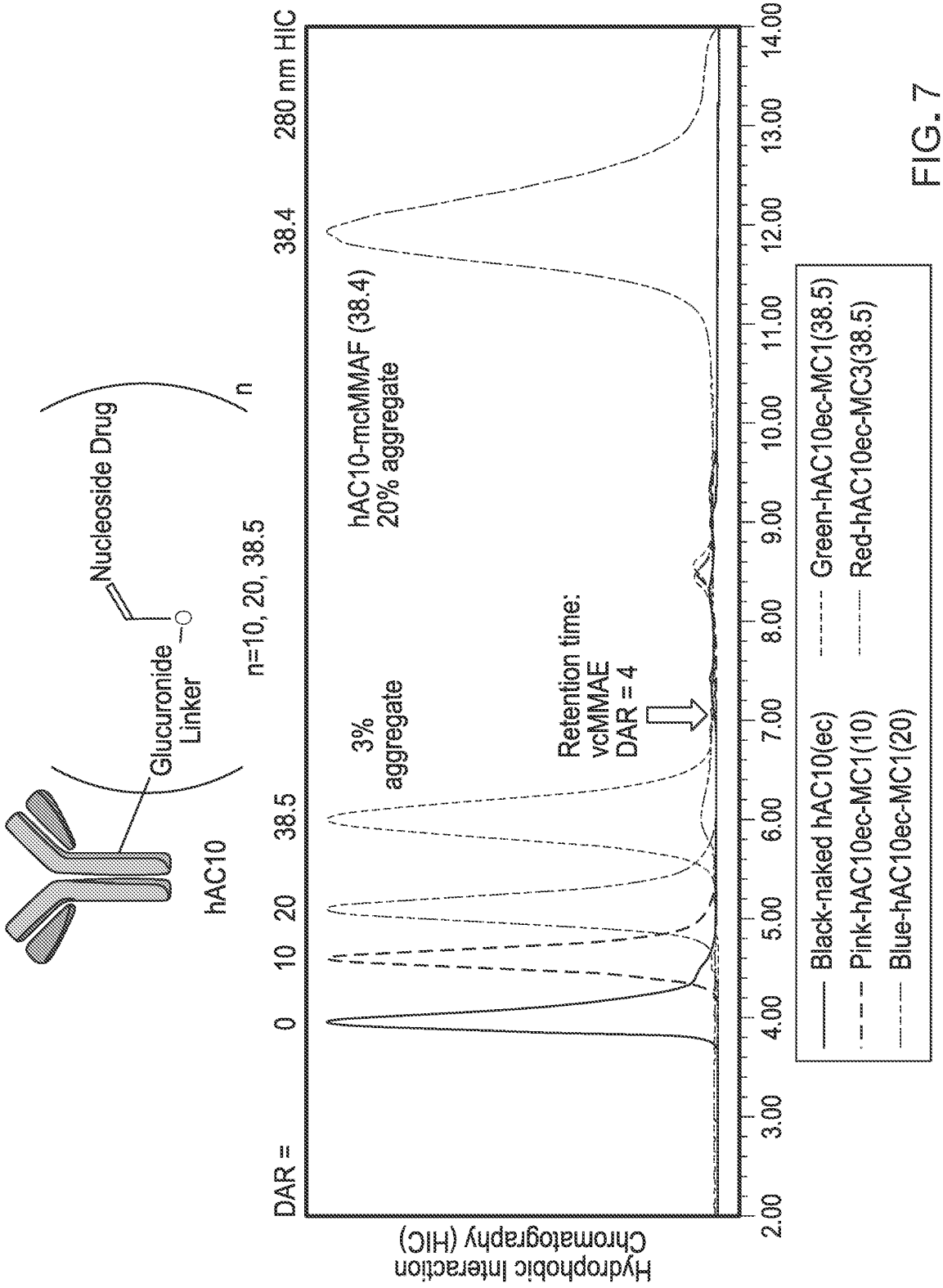
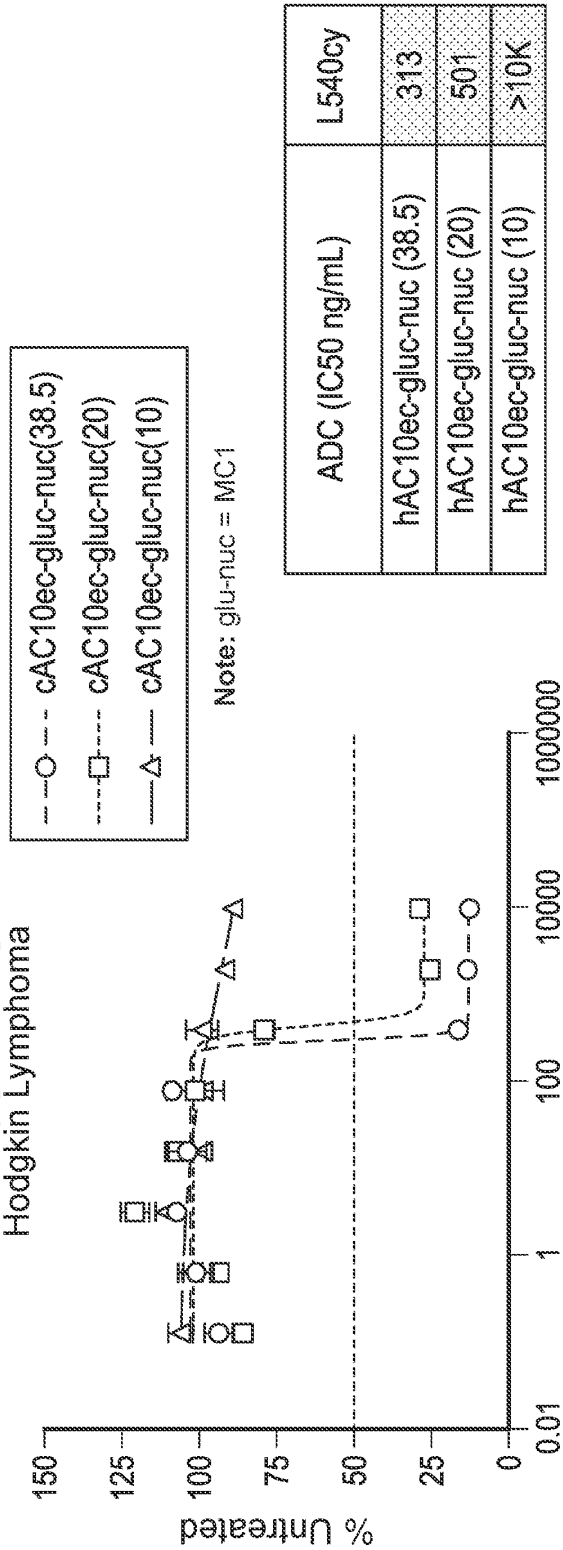

Nucleoside Drug
Glucuronide Linker
hAC10
n
n=10, 20, 38.5
DAR =
0
10
20
38.5
38.4
280 nm HIC
hAC10-mcMMAF (38.4)
20% aggregate
3% aggregate
Retention time:
vcMMAE
DAR = 4
Hydrophobic Interaction Chromatography (HIC)
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00
10.00
11.00
12.00
13.00
14.00
Black-naked hAC10(ec)
Green-hAC10ec-MC1(38.5)
Pink-hAC10ec-MC1(10)
Red-hAC10ec-MC3(38.5)
Blue-hAC10ec-MC1(20)

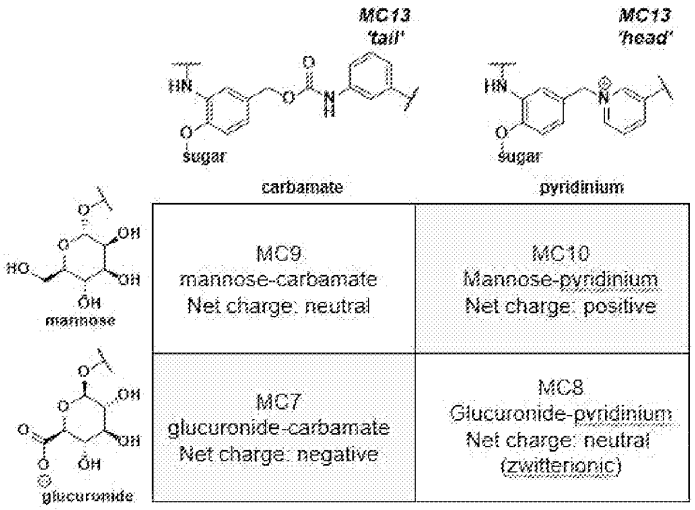
FIG. 7



ADC (IC50 ng/mL)	L540cy
hAC10ec-gluc-nuc (38.5)	313
hAC10ec-gluc-nuc (20)	501
hAC10ec-gluc-nuc (10)	>10K

In vitro cytotoxic activity of variably loaded dendrimeric nucleoside payload cAC10 (anti-CD30) ADCs against Hodgkin lymphoma line L540cy.

FIG. 8



Charge-variant linkers for MC13

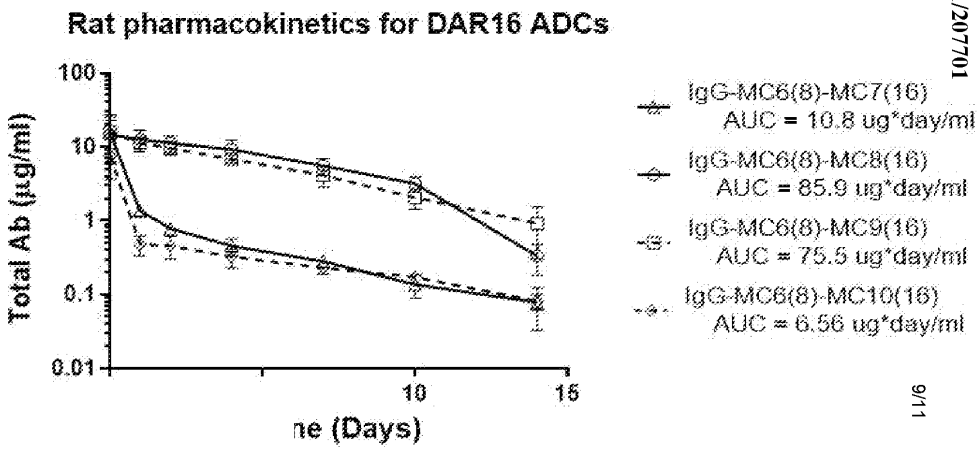


FIG. 9

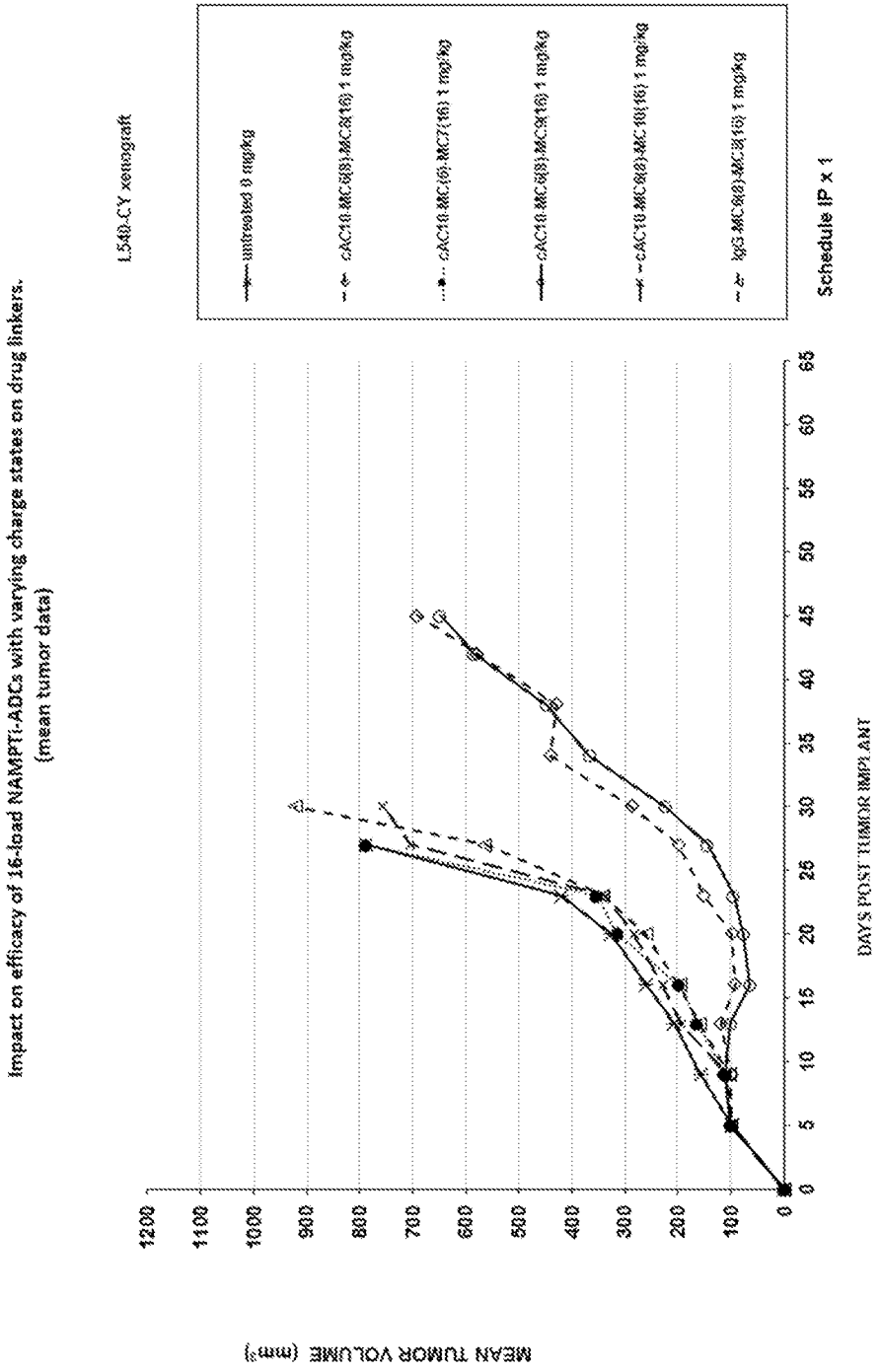

Impact on efficacy of 16-load NAMPTi-ADCs with varying charge states on drug linkers.
(mean tumor data)
L540-CY xenograft
untreated 0 mg/kg
cAC10.MC(6)-MC3(16) 1 mg/kg
cAC10.MC(6)-MC7(16) 1 mg/kg
cAC10.MC(8)-MC3(16) 1 mg/kg
cAC10.MC(8)-MC10(16) 1 mg/kg
Schedule IP x 1
MEAN TUMOR VOLUME (mm³)
DAYS POST TUMOR IMPLANT

FIG. 10

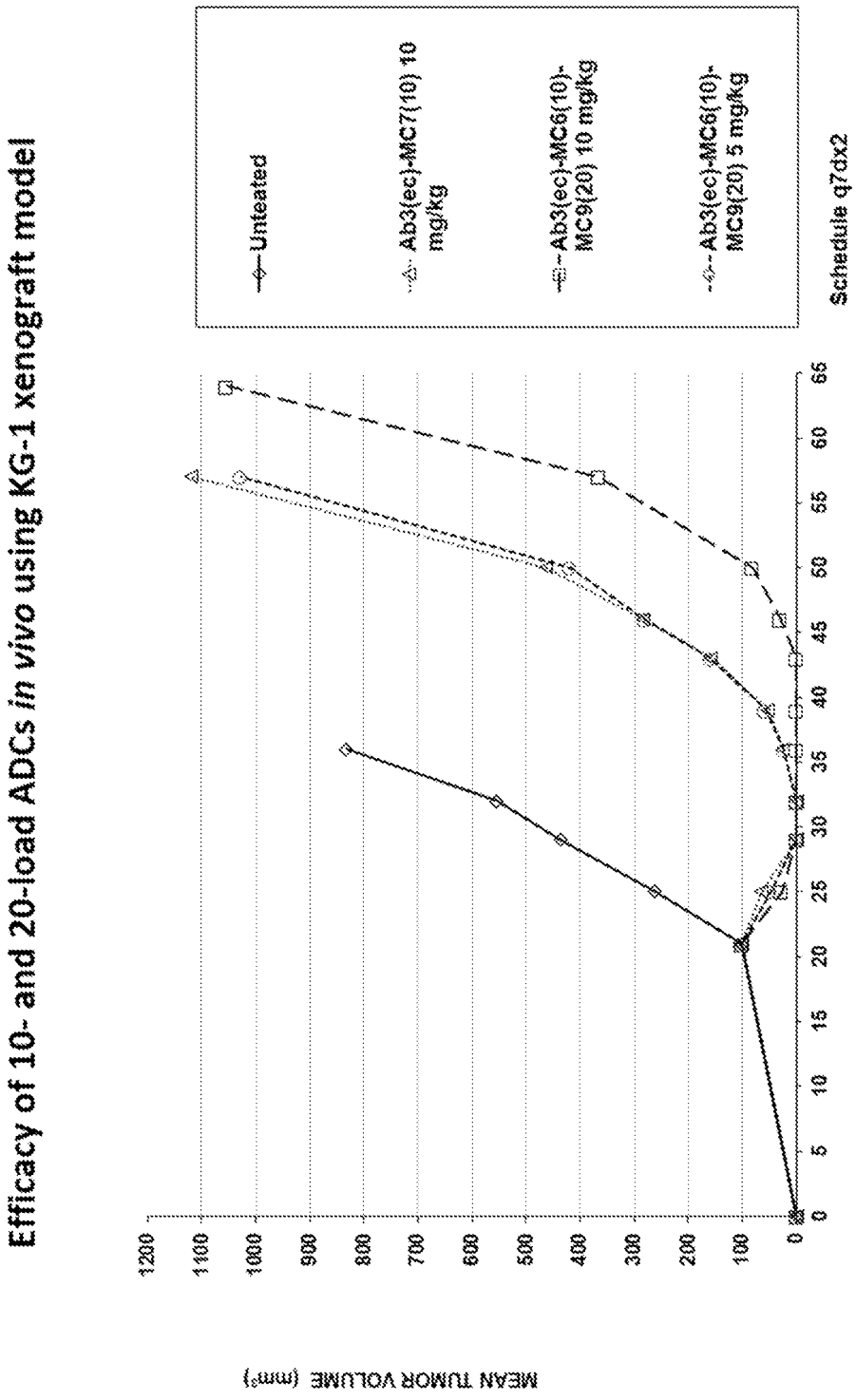

Efficacy of 10- and 20-load ADCs in vivo using KG-1 xenograft model
Untreated
Ab3(ec)-MC7(10) 10 mg/kg
Ab3(ec)-MC6(10)-MC9(20) 10 mg/kg
Ab3(ec)-MC6(10)-MC9(20) 5 mg/kg
Schedule q7dx2
MEAN TUMOR VOLUME (mm³)
DAYS POST TUMOR IMPLANT
0
100
200
300
400
500
600
700
800
900
1000
1100
1200
0
5
10
15
20
25
30
35
40
45
50
55
60
65

FIG. 11