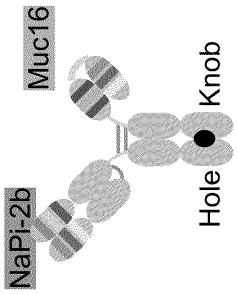


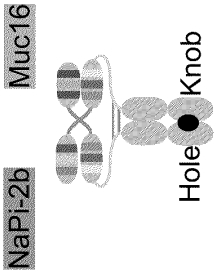
(Fab)2-Fc

FIG. 1A



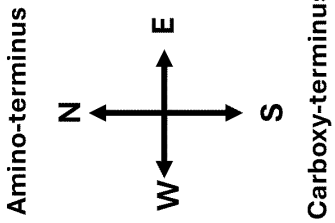
Fab/scFv-Fc

FIG. 1B



Diabody-Fc

FIG. 1C



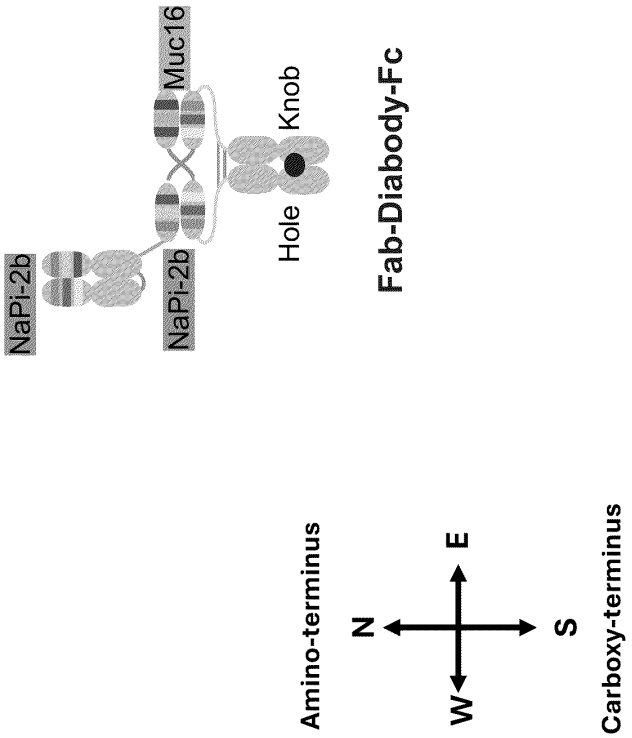
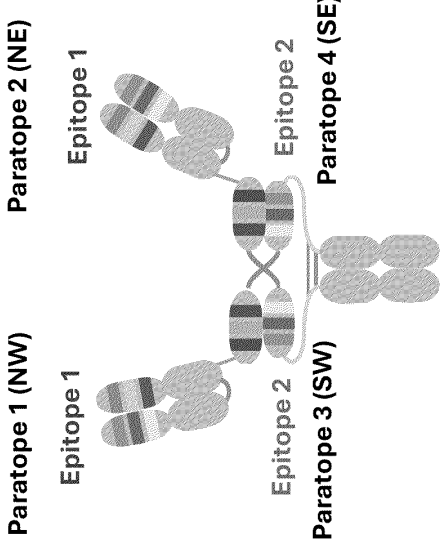

NaPi-2b
NaPi-2b
Muc16
Knob
Hole
Fab-Diabody-Fc
Amino-terminus
N
E
W
S
Carboxy-terminus

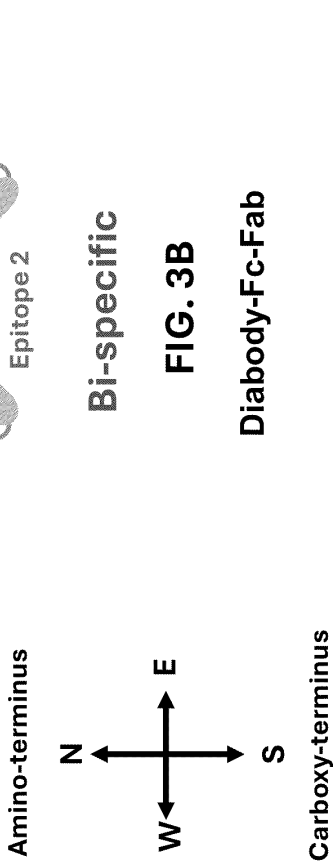
FIG. 2



Bi-specific

FIG. 3A

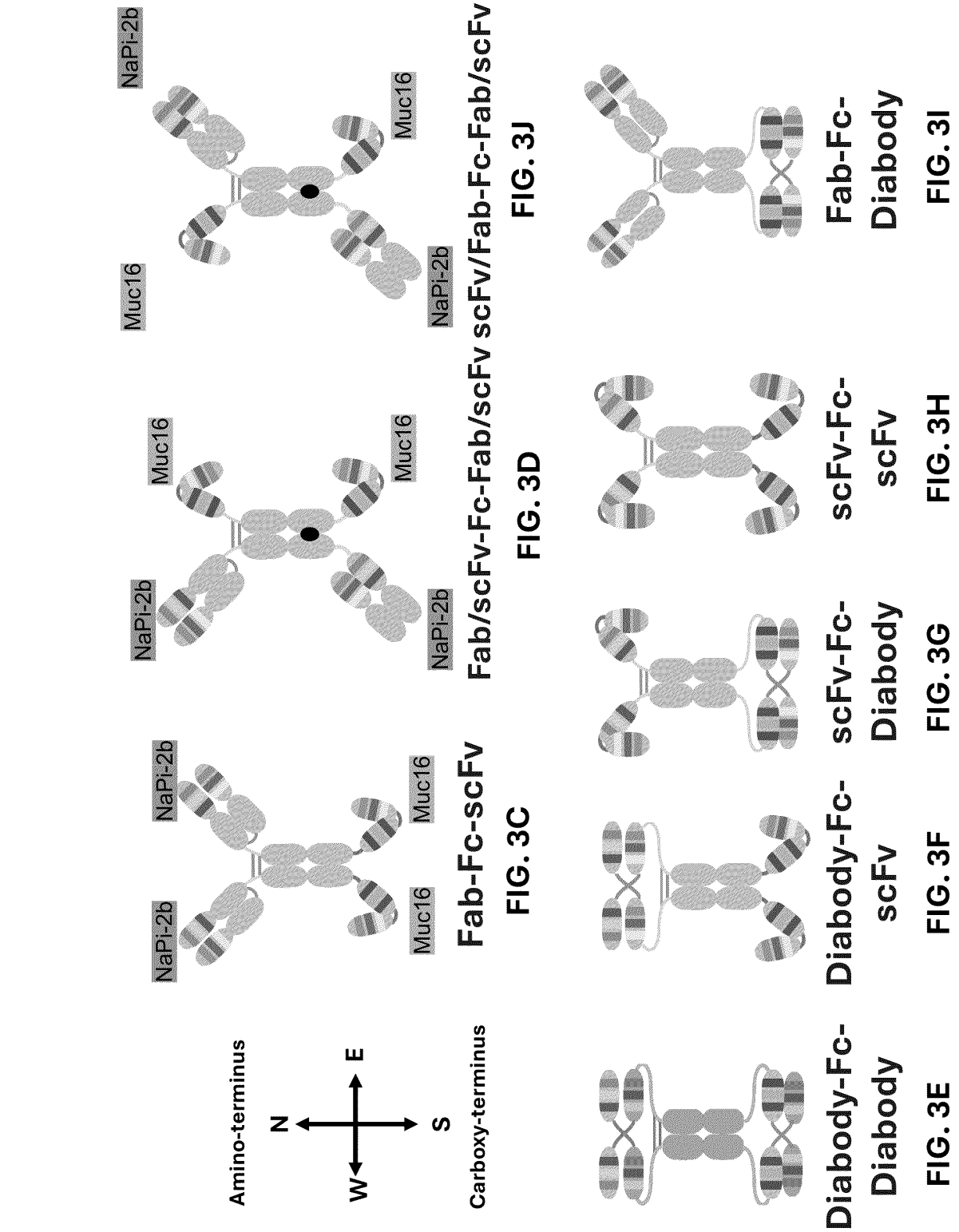
Fab-diabody-Fc

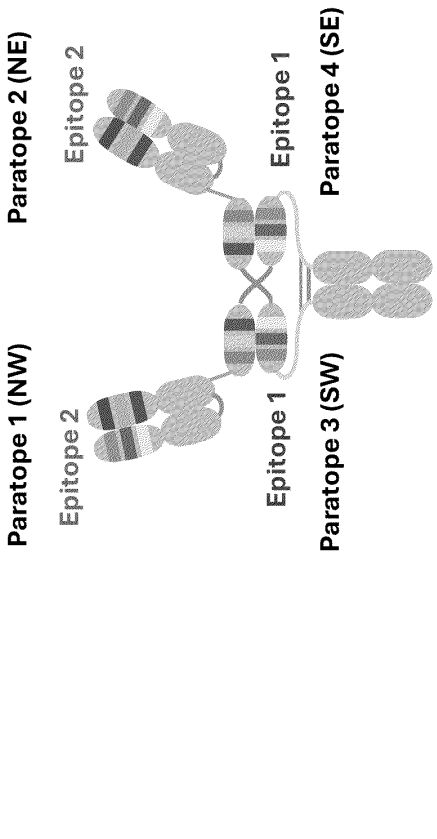


Bi-specific

FIG. 3B

Diabody-Fc-Fab


Amino-terminus
Carboxy-terminus
N
E
W
S
NaPi-2b
Muc16
Diabody-Fc-Diabody
FIG. 3E
Diabody-Fc-scFv
FIG. 3F
scFv-Fc-Diabody
FIG. 3G
scFv-Fc-scFv
FIG. 3H
Fab-Fc-scFv
FIG. 3C
Fab/scFv-Fc-Fab/scFv
FIG. 3D
scFv/Fab-Fc-Fab/scFv
FIG. 3J
Fab-Fc-Diabody
FIG. 3I

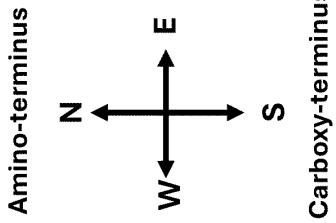


Bi-specific

FIG. 4A

Bi-specific

FIG. 4B



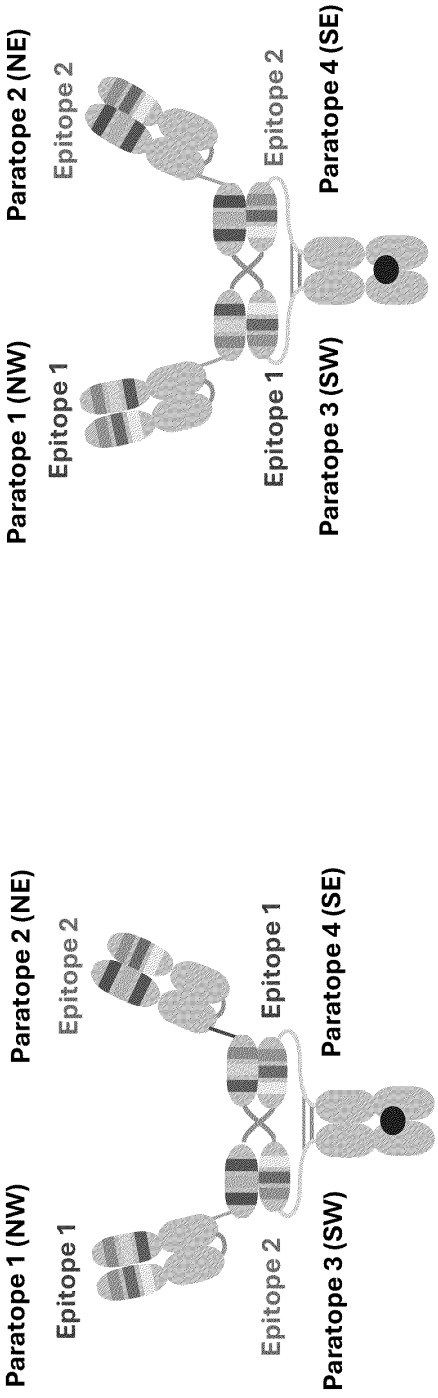
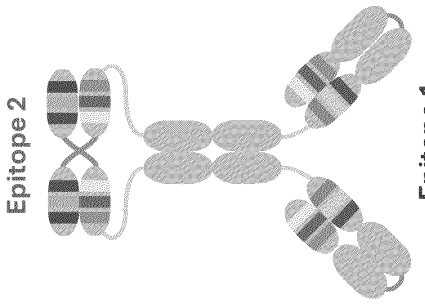

Paratope 1 (NW)
Epitope 1
Epitope 2
Paratope 2 (NE)
Paratope 3 (SW)
Epitope 2
Epitope 1
Paratope 4 (SE)
Bi-specific

FIG. 4C

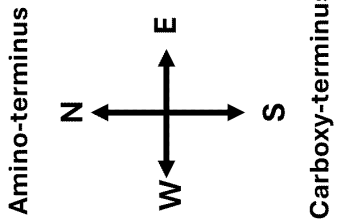
Paratope 1 (NW)
Epitope 1
Epitope 2
Paratope 2 (NE)
Paratope 3 (SW)
Epitope 2
Epitope 1
Paratope 4 (SE)
Bi-specific
Amino-terminus
N
E
W
S
Carboxy-terminus

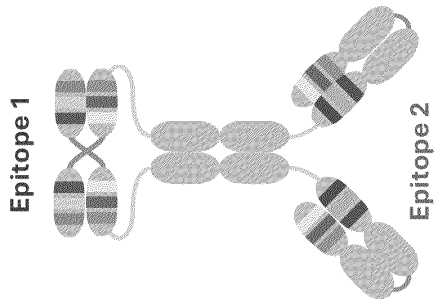
FIG. 4D



Bi-specific

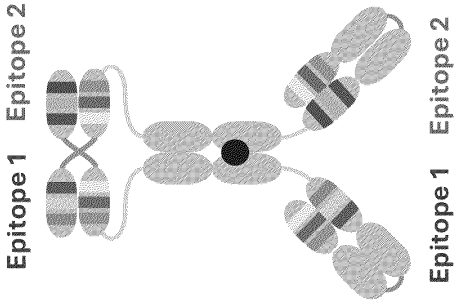
FIG. 5B





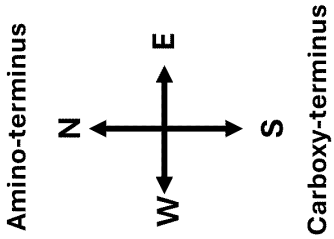
Bi-specific

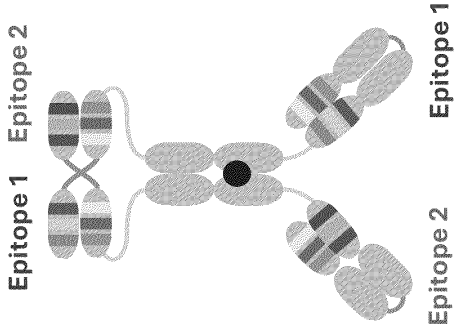
FIG. 5A



Bi-specific

FIG. 5D





Bi-specific

FIG. 5C

FIG. 6A


AB301-MMAE
DAR4
Lifastuzumab
NaPi-2b

FIG. 6B

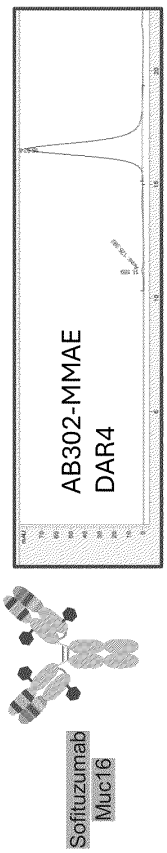

AB302-MMAE
DAR4
Sofituzumab
Muc16

FIG. 7A

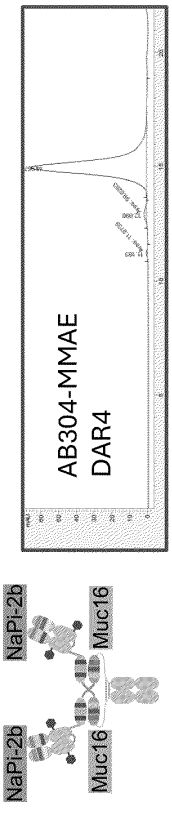


FIG. 7B

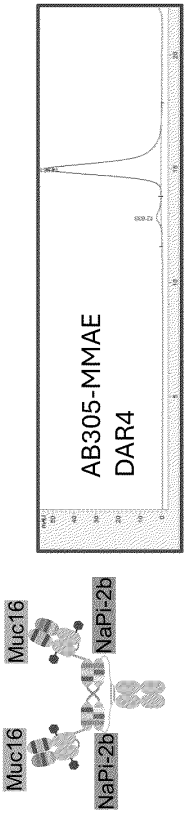


FIG. 7C

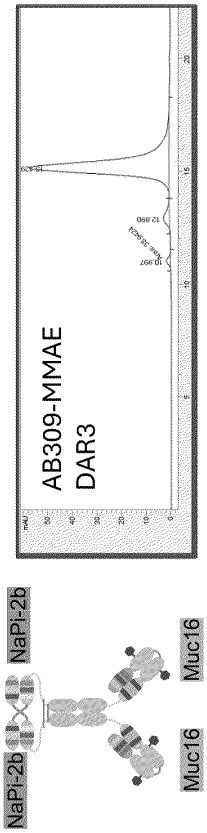
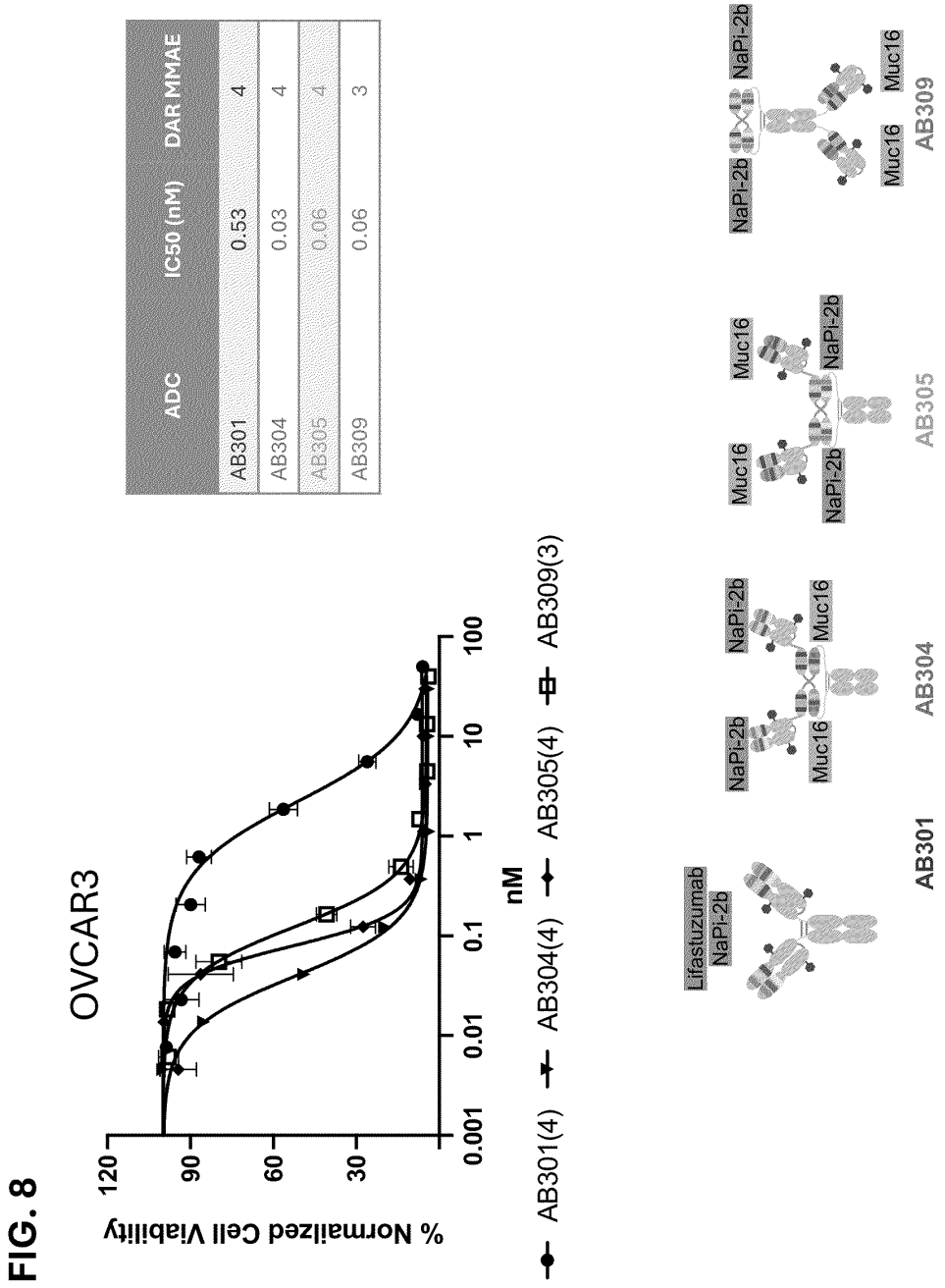


FIG. 8



ADC	IC50 (nM)	DAR MMAE
AB301	0.53	4
AB304	0.03	4
AB305	0.06	4
AB309	0.06	3

FIG. 9

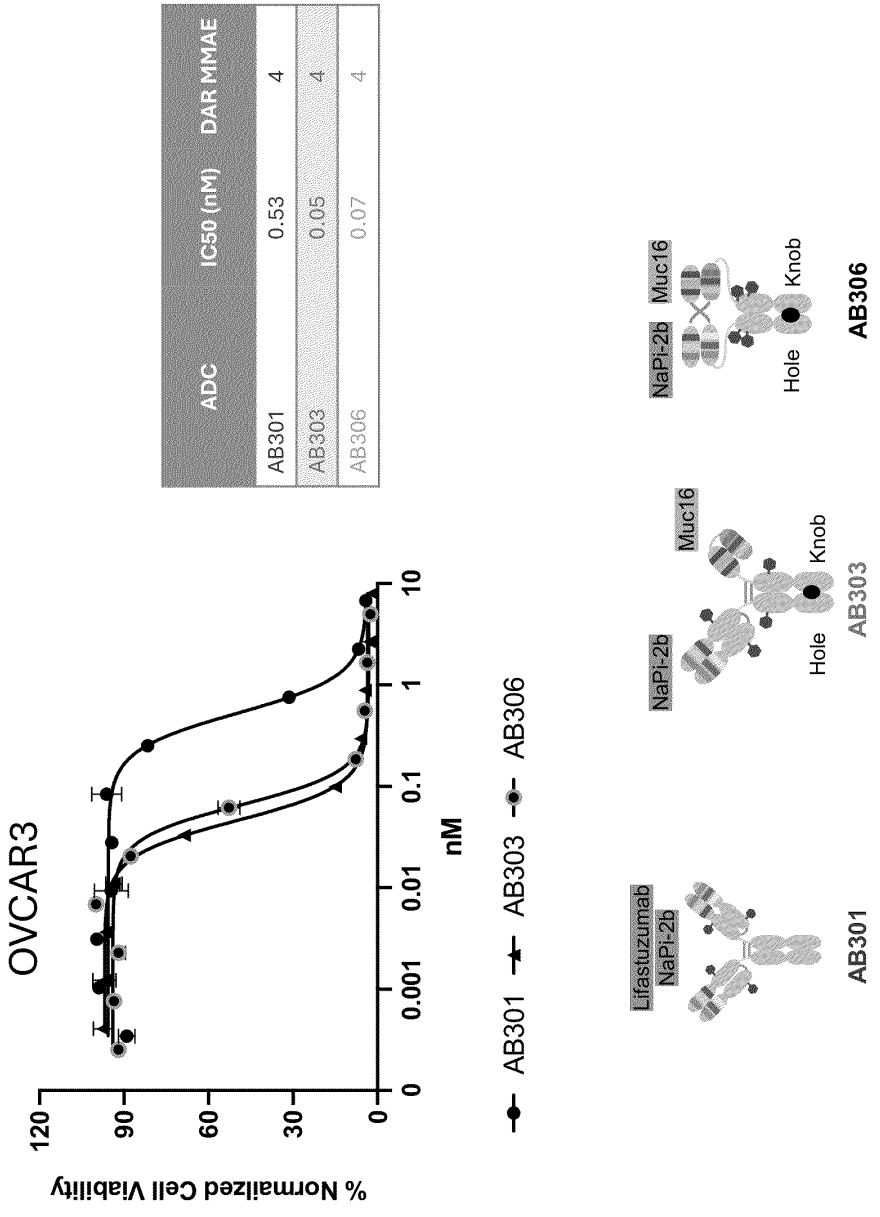
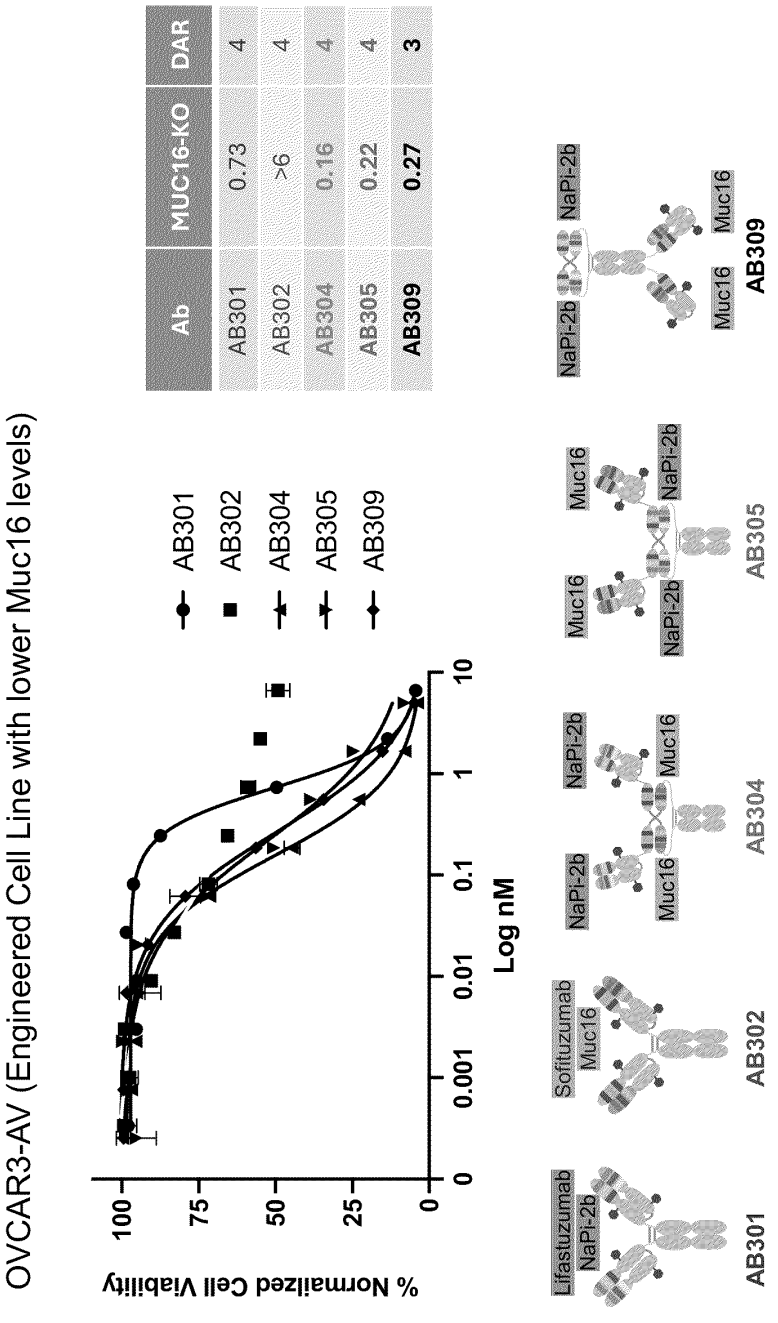

OVCAR3
% Normalized Cell Viability
120
90
60
30
0
0
0.001
0.01
0.1
1
10
nM
AB301
AB303
AB306
ADC
IC50 (nM)
DAR MMAE
AB301
0.53
4
AB303
0.05
4
AB306
0.07
4
Lifastuzumab
NaPi-2b
AB301
NaPi-2b
Muc16
Hole
Knob
AB303
NaPi-2b
Muc16
Hole
Knob
AB306

FIG. 10



Ab	MUC16-KO	DAR
AB301	0.73	4
AB302	>6	4
AB304	0.16	4
AB305	0.22	4
AB309	**0.27**	**3**

FIG. 11A

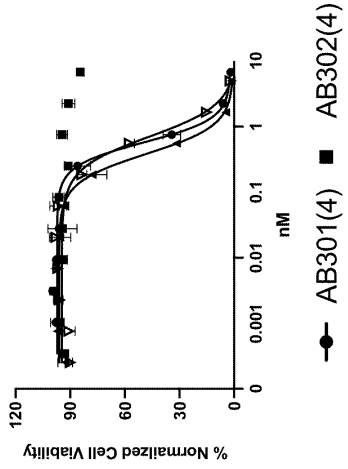
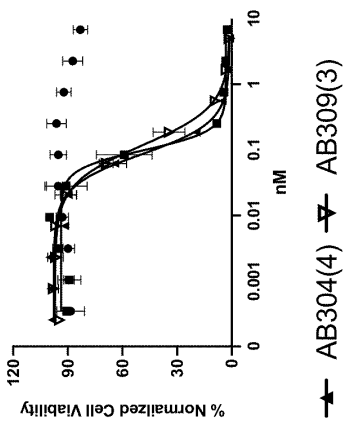
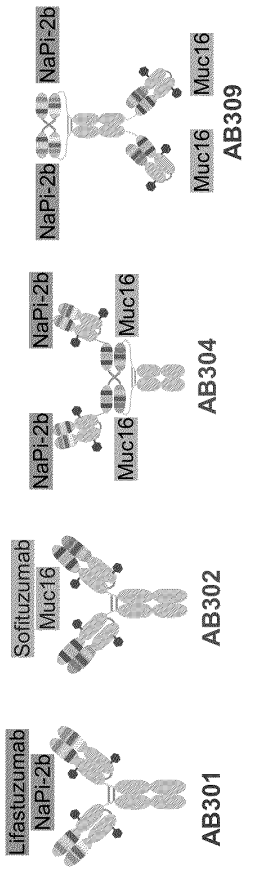


FIG. 11B





Ab	Muc16 KO IC50 (nM)	NaPi-2b KO IC50 (nM)	DAR
AB301	0.60	>10	4
AB302	>10	0.09	4
AB304	0.38	0.08	4
AB309	0.70	0.12	3

Ratio Muc16KO:OVCAR3

ADC	60:40 IC50 (nM)	70:30 IC50 (nM)	80:20 IC50 (nM)	90:10 IC50 (nM)
AB301	0.59	0.58	0.56	0.54
AB302	>5	>10	>10	>10
AB304	0.05	0.07	0.11	0.18

Cell viability assay with varying ratio of OVCAR3 WT and Muc16-KO cells

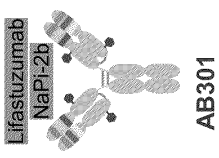


FIG. 12A
OVCAR3-AV1 (60:40)

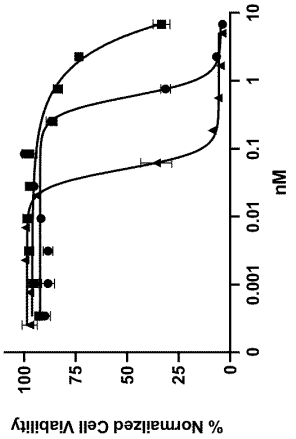


FIG. 12B
OVCAR3-AV2 (70:30)

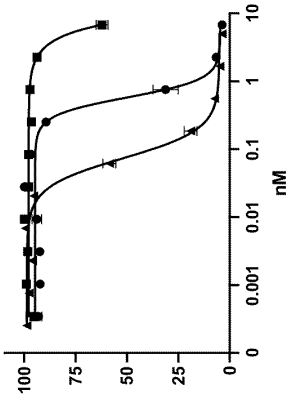


FIG. 12C
OVCAR3-AV3 (80:20)

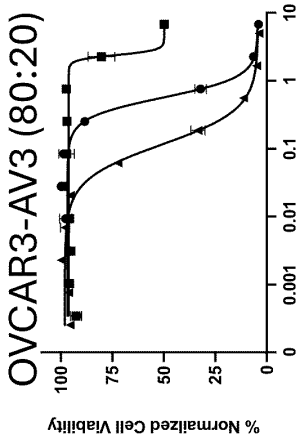
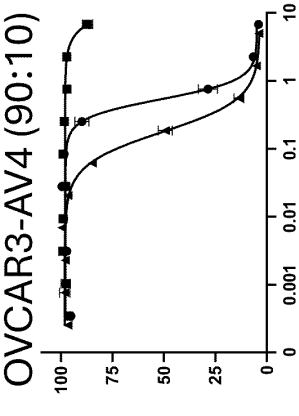


FIG. 12D
OVCAR3-AV4 (90:10)



Ab	OVCAR3-AV IC50 (nM)	DAR
AB001	>10	4
AB301	1.0	4
AB302	0.3	4
AB304	**0.07**	**4**
AB309	**0.10**	**4**
AB301+AB302	**0.36**	**4**

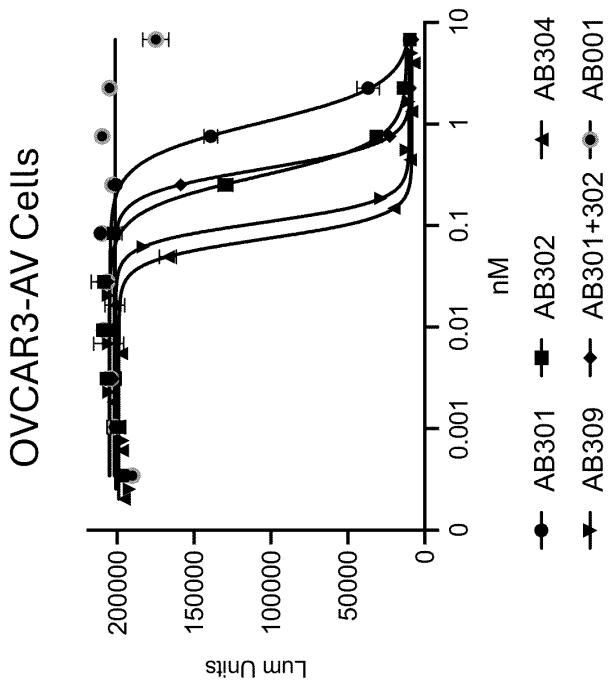


FIG. 13

Biologic	Format	Yield (mg/L)	HPLC-SEC	Valency
AB301	IgG	59	single peak	2
AB302	IgG	70	single peak	2
AB303 #	Fab1-scFv1-Fc	2	>80%	2
AB304	Fab-Diabody-Fc (MUTTA™ 4)	108	single peak	4
AB305	Fab-Diabody-Fc (MUTTA™ 4)	67	single peak	4
AB306	Diabody-Fc	82	>90%	2
AB307 #	Fab1-Diabody-Fc	1	single peak	3
AB308 #	IgG-scFv (Fab-Fc-scFv)	4	>90%	4
AB309	Diabody-Fc-Fab (MUTTA™ 2)	120	single peak	4

FIG. 14

FIG. 15A

Group	N	Agent	Active Dose	Route	Schedule
1	8	Vehicle	None	i.v.	qd x 1
2	8	AB301	2.25 mg/kg (15nmoles)	i.v.	qd x 1
3	8	AB302	2.25 mg/kg (15nmoles)	i.v.	qd x 1
4	8	AB304	3 mg/kg (15nmoles)	i.v.	qd x 1
5	8	AB309	3 mg/kg (15nmoles)	i.v.	qd x 1

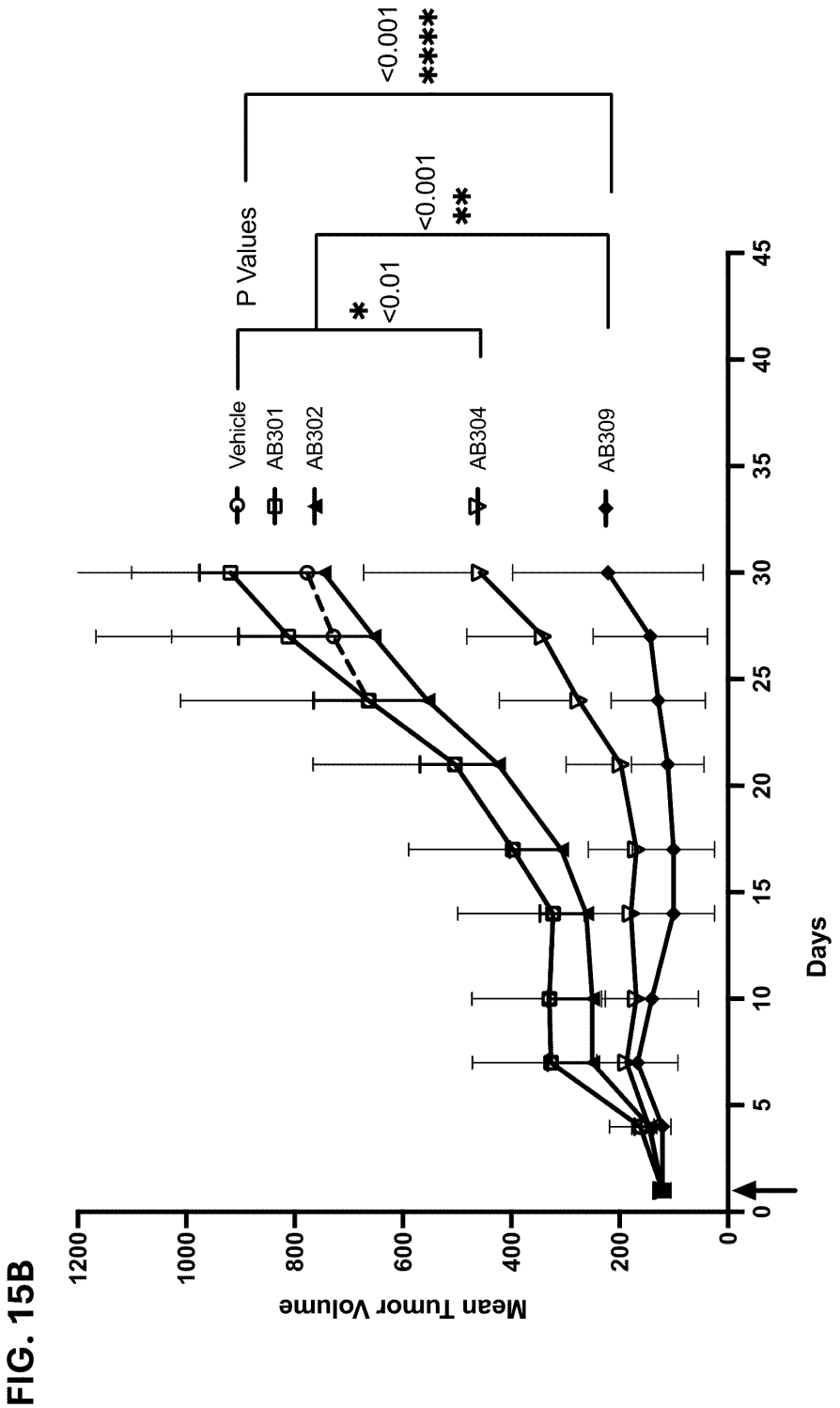

Mean Tumor Volume
1200
1000
800
600
400
200
0
0
5
10
15
20
25
30
35
40
45
Days
Vehicle
AB301
AB302
AB304
AB309
P Values
*
<0.01
**
<0.001
****
<0.001

FIG. 15B

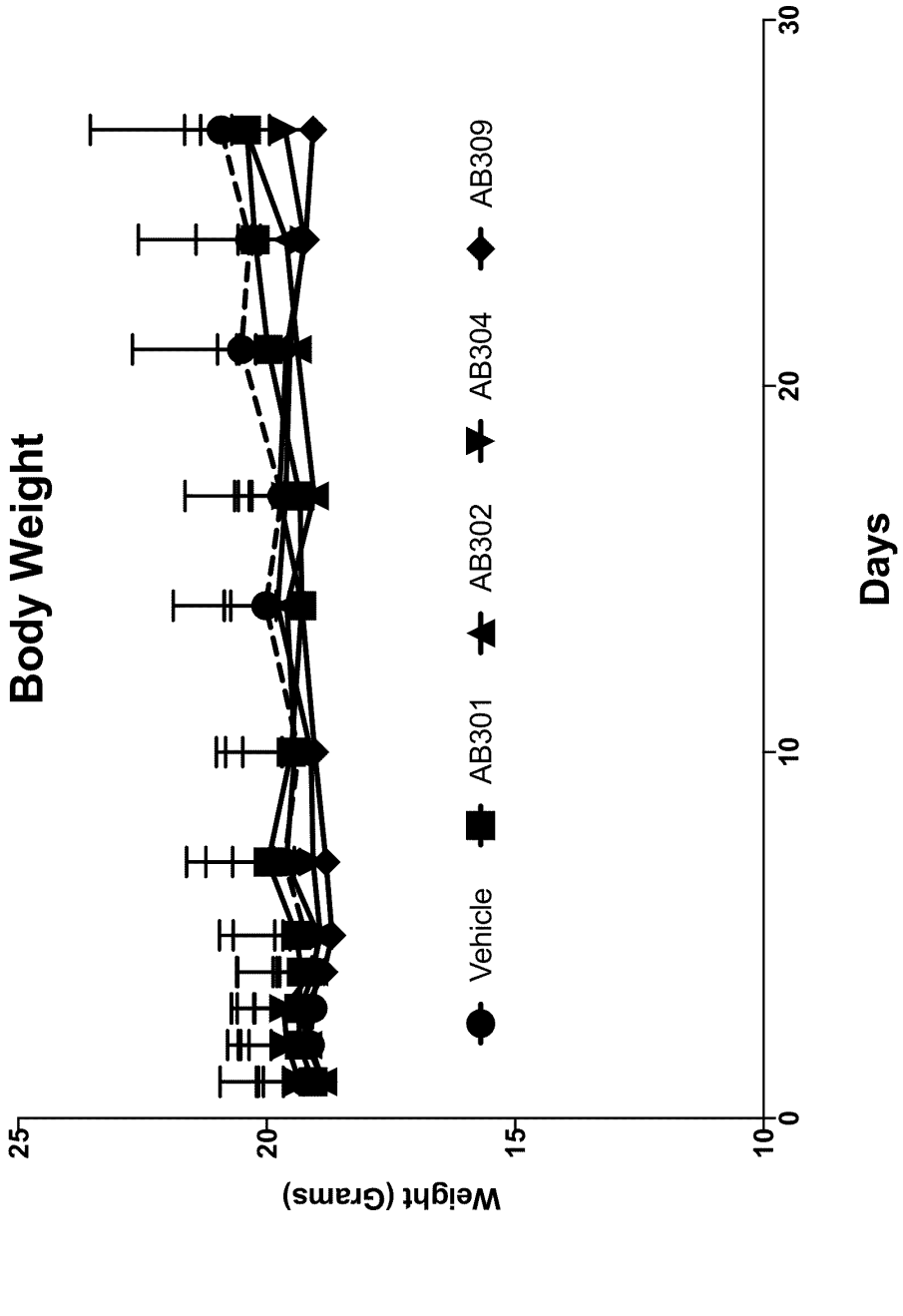

Body Weight
Weight (Grams)
25
20
15
10
0
10
20
30
Days
Vehicle
AB301
AB302
AB304
AB309

FIG. 15C

ADC	OVCAR3 IC50 (nM)	DAR
AB301	0.42	4
AB302	0.07	4
AB312	0.10	2
AB304	0.02	4
AB309	0.03	4
AB001	>10	4

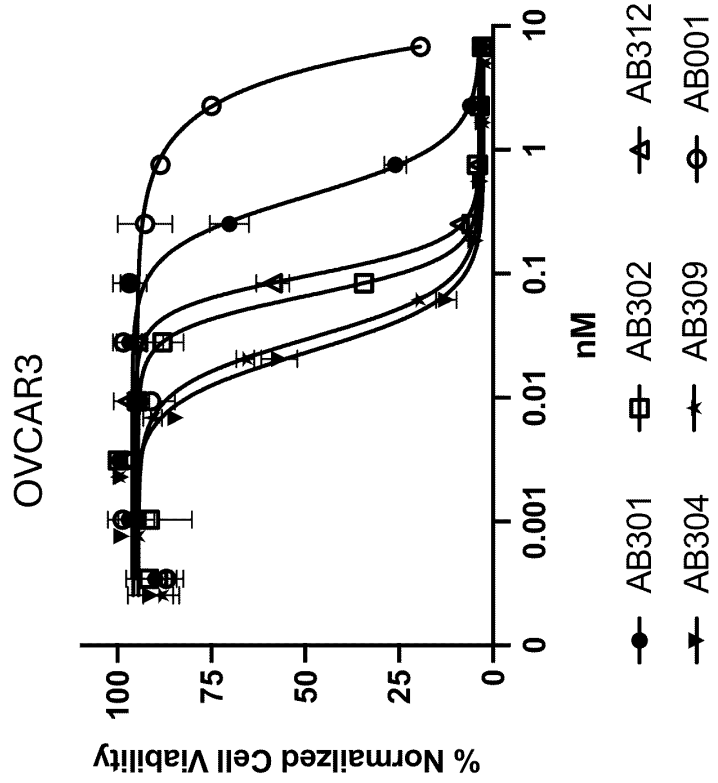


FIG. 16

FIG. 17A

Group	N	Agent	Active Dose (mg/kg)	Active Dose (nmoles/kg)	Route	Schedule
1	8	Vehicle	None	None	i.v.	qd x 1
2	8	AB301	6	40	i.v.	qd x 1
3	8	AB302	6	40	i.v.	qd x 1
4	8	AB301+AB302	3+3	20+20	i.v.	qd x 1
6	8	AB312	6	40	i.v.	qd x 1
8	8	AB304	8	40	i.v.	qd x 1
10	8	AB309	8	40	i.v.	qd x 1

FIG. 17B-17D

FIG. 17B

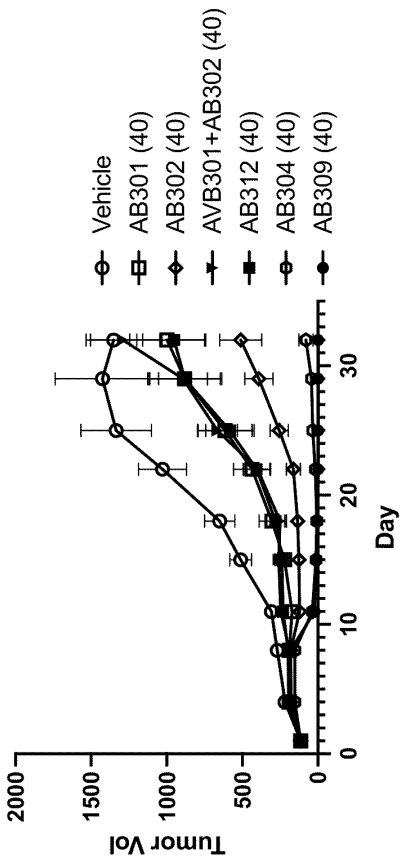


FIG. 17C

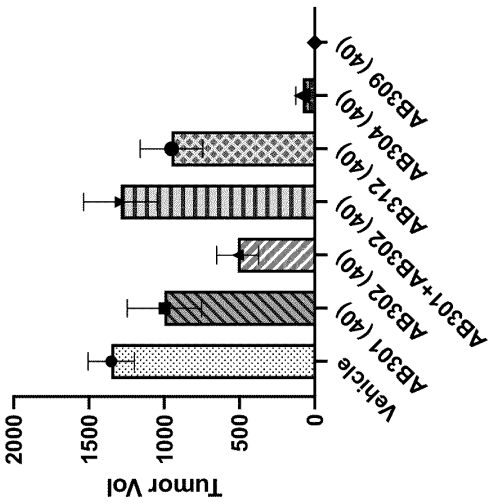


FIG. 17D

Efficacy Superiority	*	pValue
AB301 (40) < AB304 (40)		
AB301 (40) < AB309 (40)		
AB302 (40) < AB309 (40)	****	<0.0001
AB312 (40) < AB304 (40)		
AB312 (40) < AB309 (40)		
AB301+AB302 (40) < AB304 (40)		
AB301+AB302 (40) < AB309 (40)		
AB302 (40) < AB304 (40)	**	0.0092

FIG. 18A

Group	N	Agent	Active Dose (mg/kg)	Active Dose (nmoles/kg)	Route	Schedule
1	8	Vehicle	None	None	i.v.	qd x 1
2	8	AB301	6	40	i.v.	qd x 1
3	8	AB309	8	40	i.v.	qd x 1
4	8	AB309	4	20	i.v.	qd x 1
4	8	AB309	2	10	i.v.	qd x 1

FIG. 18B-18D

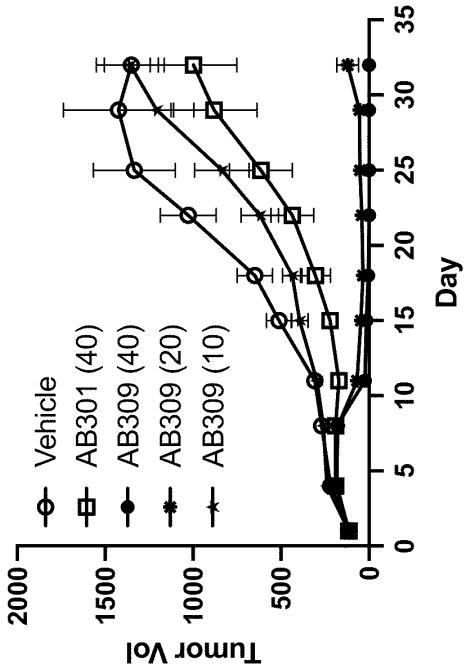


FIG. 18B

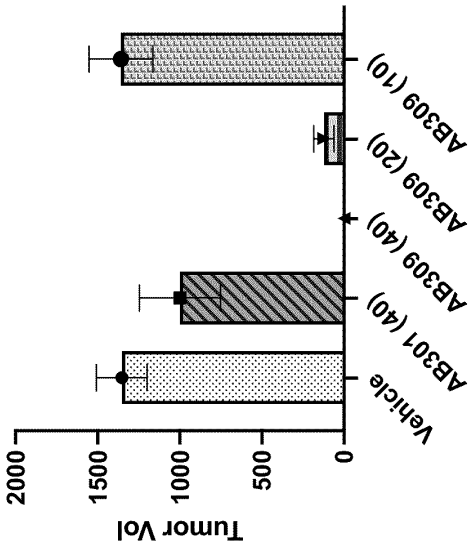


FIG. 18C

FIG. 18D

Efficacy Superiority	*	pValue
AB301 (40) < AB309 (20) AB301 (40) < AB309 (40)	****	<0.0001

FIG. 19A

Group	N	Agent	Active Dose (mg/kg)	Active Dose (nmoles/kg)	Route	Schedule
1	8	Vehicle	None	None	i.v.	qd x 1
2	8	AB312	12	80	i.v.	qd x 1
3	8	AB312	6	40	i.v.	qd x 1
4	8	AB312	3	20	i.v.	qd x 1
5	8	AB309	8	40	i.v.	qd x 1
6	8	AB309	4	20	i.v.	qd x 1
7	8	AB309	2	10	i.v.	qd x 1

FIG. 19B-19D

FIG. 19B

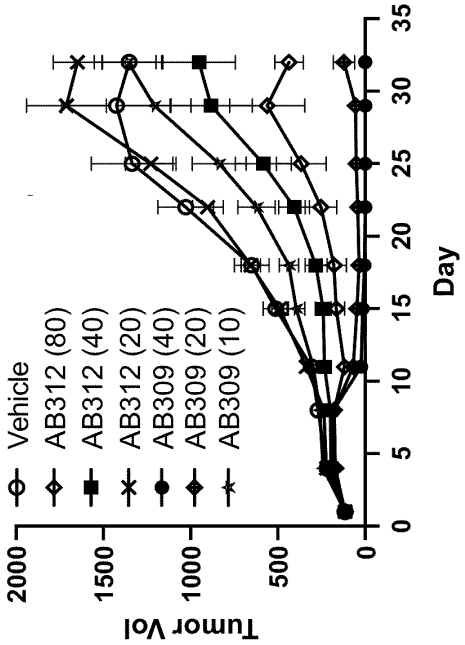


FIG. 19C

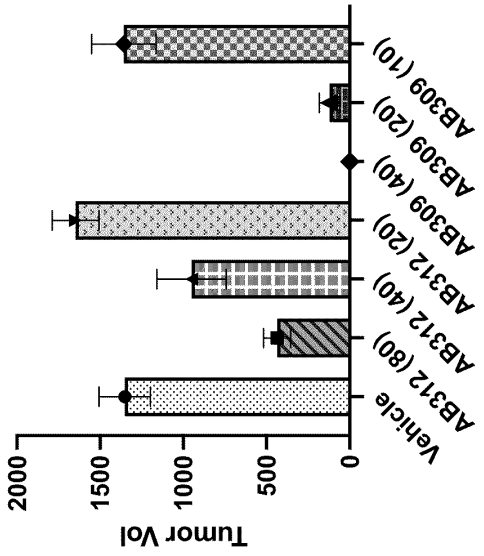


FIG. 19D

Group	*	pValue
AB312 (80) < AB309 (20)	**	0.0028
AB312 (80) < AB309 (40)		
AB312 (40) < AB309 (40)	****	<0.0001
AB312 (40) < AB309 (20)		

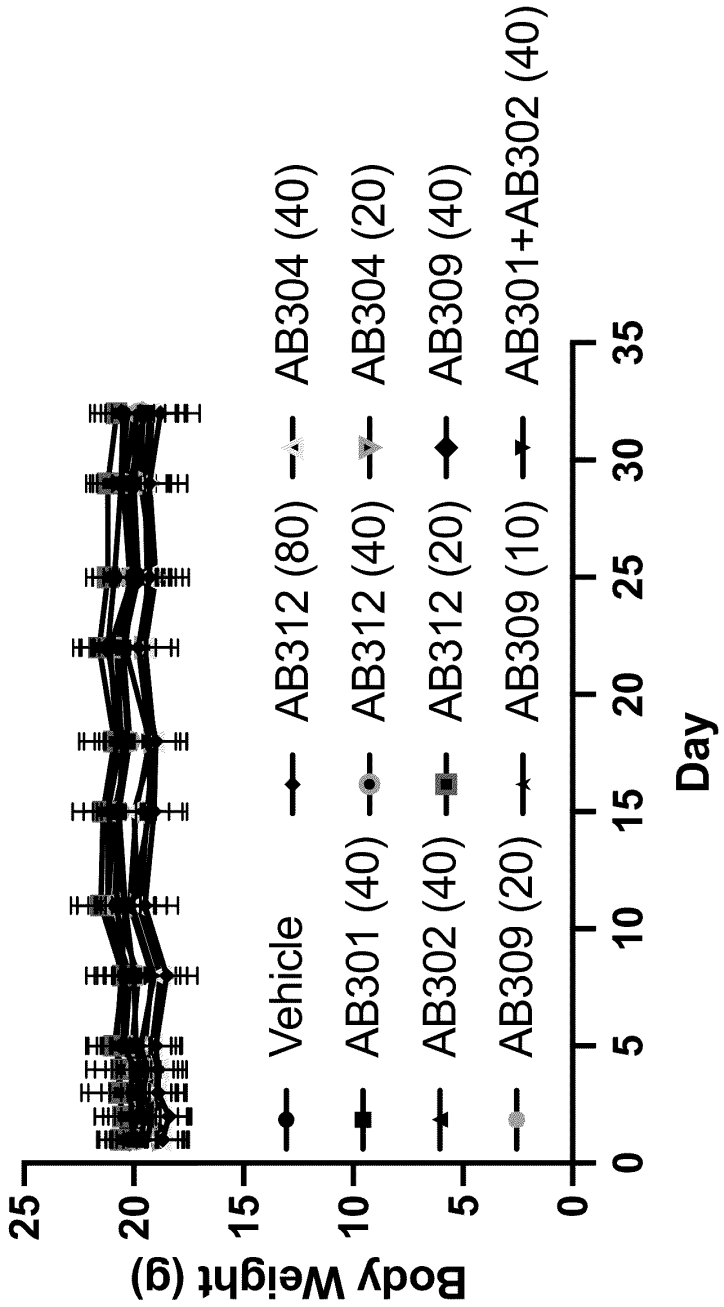

Body Weight (g)
25
20
15
10
5
0
0
5
10
15
20
25
30
35
Day
Vehicle
AB312 (80)
AB304 (40)
AB301 (40)
AB312 (40)
AB304 (20)
AB302 (40)
AB312 (20)
AB309 (40)
AB309 (20)
AB309 (10)
AB301+AB302 (40)

FIG. 20

Group	Clearance mL/Day/kg
AB304 (3mg/kg), n=2	19.84
AB309 (3mg/kg), n=2	13.37
*Anti-NaPi-2b mAb 1mg/kg, n=4	13.80

*Reported value in the publication
Clin Cancer Res. 2015;21(22):5139-5150

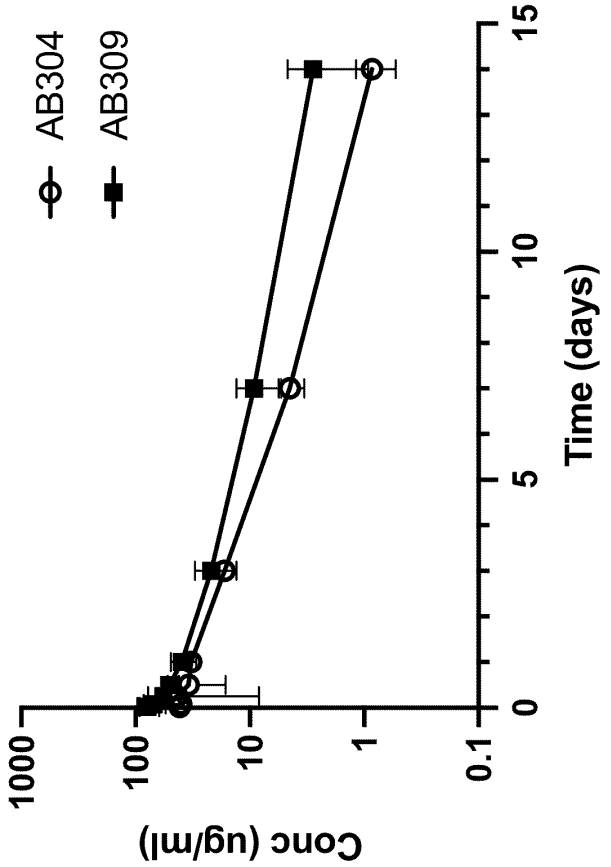
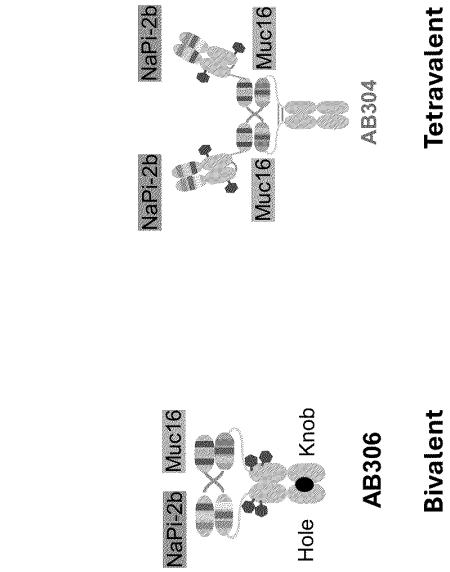


FIG. 21

Format	IC_{50} nM ADC exposure-short time
AB304	0.04
AB306	0.19



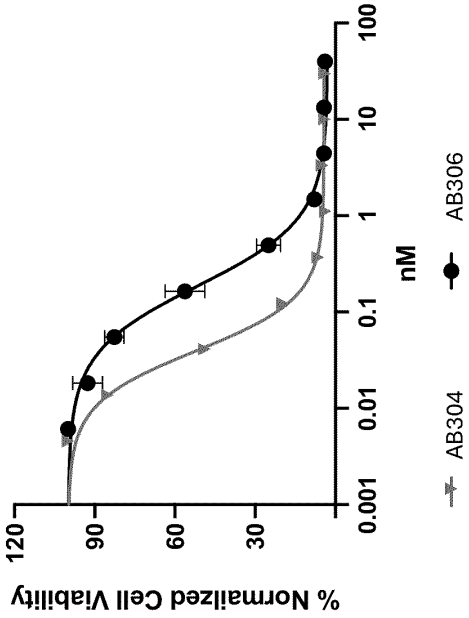


FIG. 22

FIG. 23A

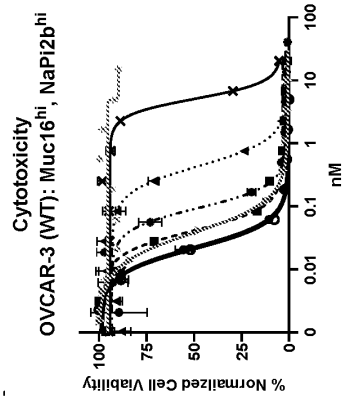


FIG. 23B

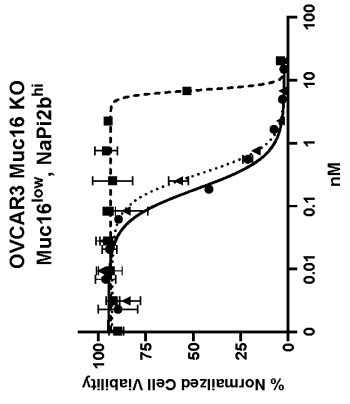
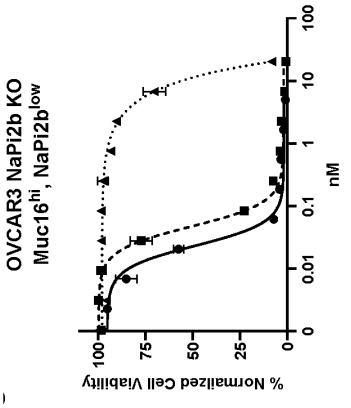


FIG. 23C



Test Article	OVCAR-3 WT IC50 (nM)	OVCAR-3 Muc16 KO IC50 (nM)	OVCAR-3 NaPi2b KO IC50 (nM)
AB301	0.44	0.32	>5
AB302	0.04	>5	0.04
AB301 + AB302	0.09		
AB311	0.04		
AB304	0.02		
AB309	0.02	0.52	0.02
AB001	>5		
AB309-Antibody	>20		

FIG. 24A

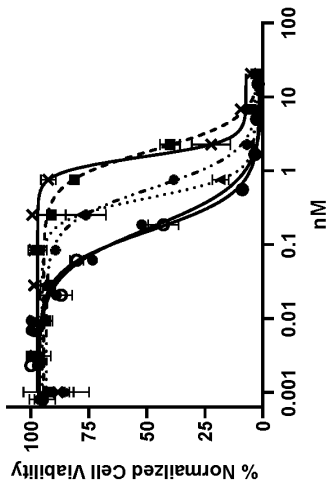
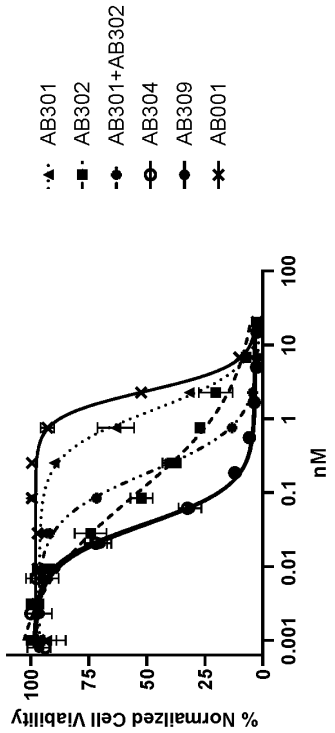


FIG. 24B



Test Article	High NaPi2b and Low Muc16 IC50 (nM)	Intermediate NaPi2b and Muc16 IC50 (nM)
AB301	0.44	1.30
AB302	~5.0	0.079
AB301 + AB302	0.58	0.19
AB304	0.15	0.038
AB309	0.17	0.036
AB001	1.53	~5.0

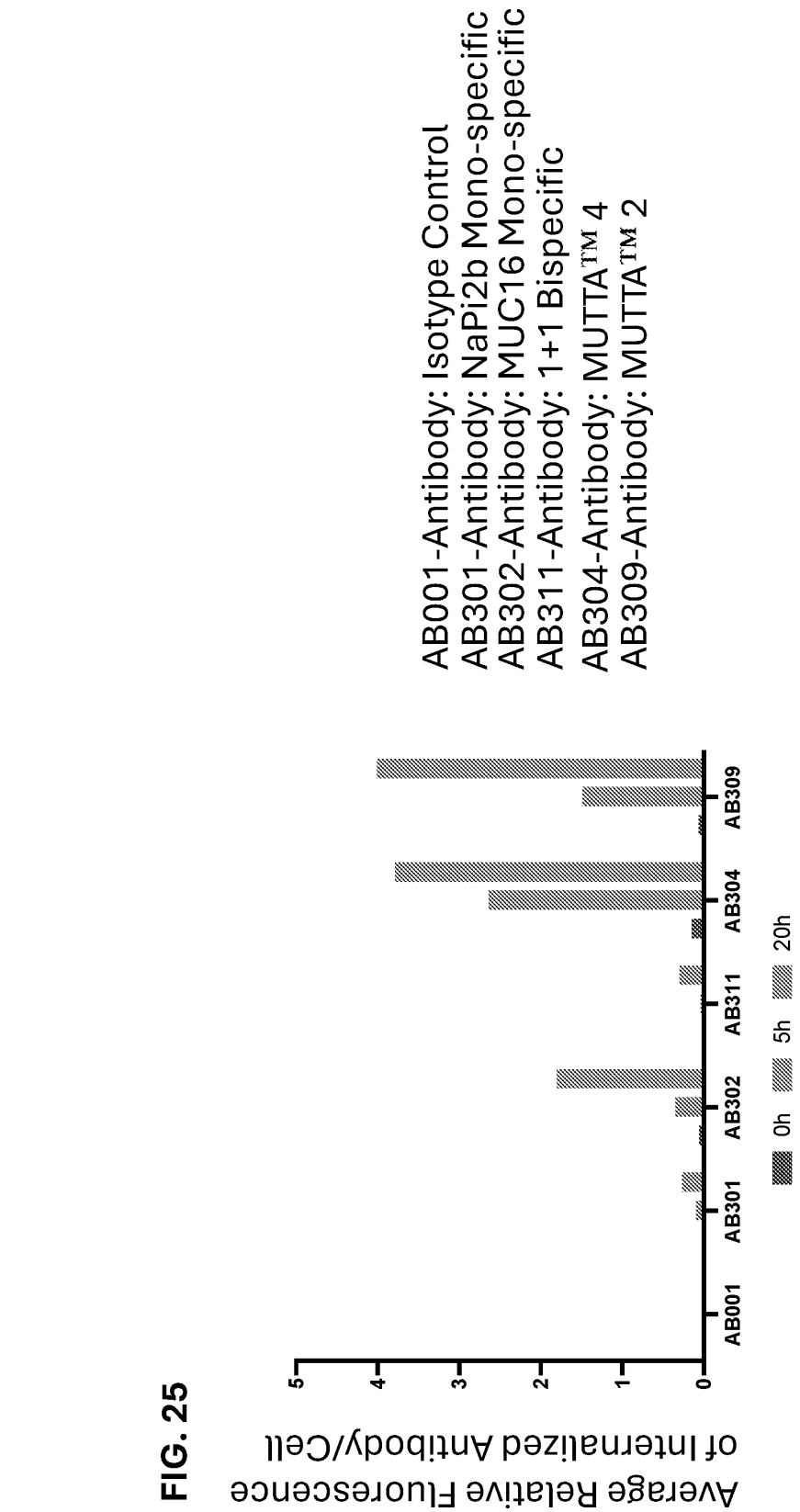

Average Relative Fluorescence of Internalized Antibody/Cell
0
1
2
3
4
5
AB001
AB301
AB302
AB311
AB304
AB309
0h
5h
20h
AB001-Antibody: Isotype Control
AB301-Antibody: NaPi2b Mono-specific
AB302-Antibody: MUC16 Mono-specific
AB311-Antibody: 1+1 Bispecific
AB304-Antibody: MUTTA™ 4
AB309-Antibody: MUTTA™ 2

FIG. 25

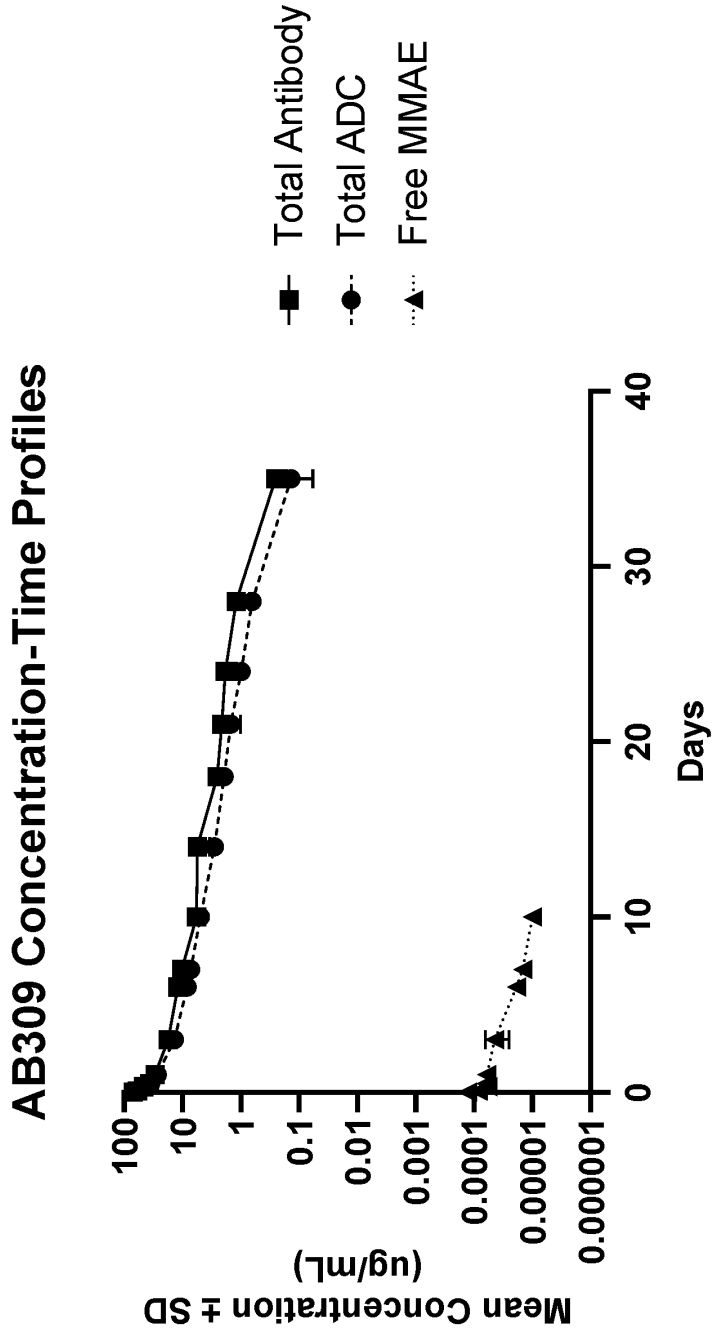
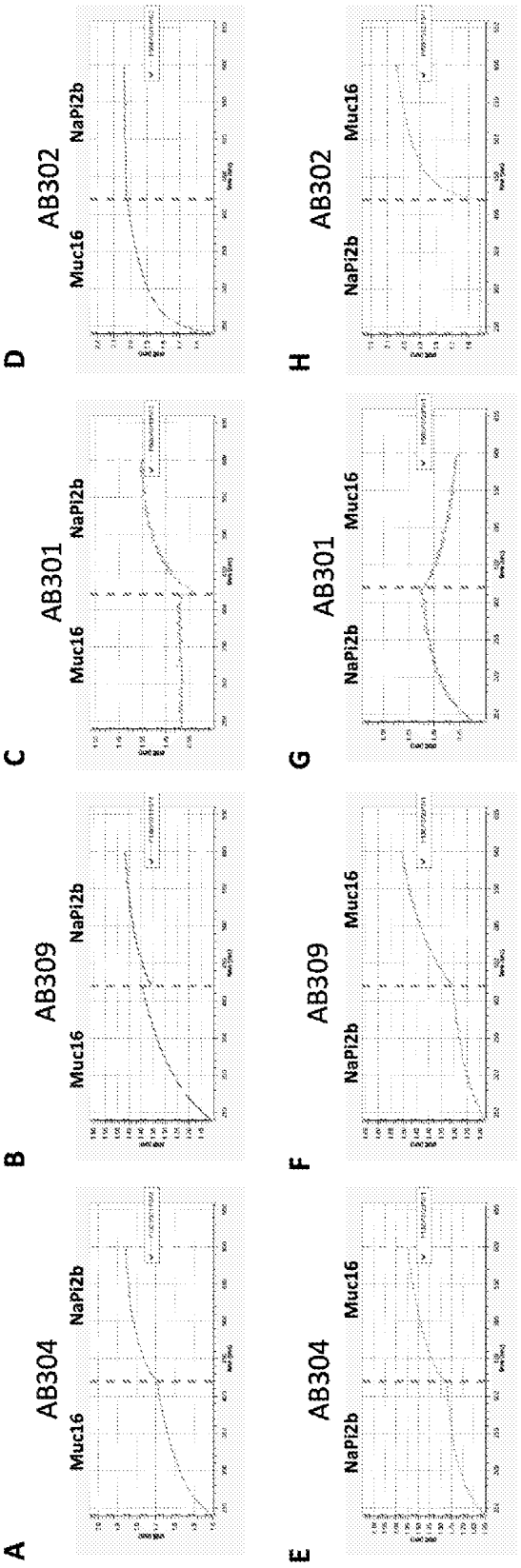

AB309 Concentration-Time Profiles
Total Antibody
Total ADC
Free MMAE
Mean Concentration ± SD
(ug/mL)
100
10
1
0.1
0.01
0.001
0.0001
0.00001
0.000001
0
10
20
30
40
Days

FIG. 26

FIG. 27


A
AB304
Muc16
NaPi2b
B
AB309
Muc16
NaPi2b
C
AB301
Muc16
NaPi2b
D
AB302
Muc16
NaPi2b
E
AB304
Muc16
NaPi2b
F
AB309
Muc16
NaPi2b
G
AB301
Muc16
NaPi2b
H
AB302
Muc16
NaPi2b