Emibetuzumab (humanized IgG4)
(SEQ ID NO: 17 and 5 from US 8217148)

Amino Acid Sequence (10 AA per group, 5 groups per line)

Heavy Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 101):

```
QVQLVQSGAE VKKPGASVKV SCKASGYTFT DYYMHWVRQA PGQGLEWMGR 050
VNPNRRGTTY NQKFEGRVTM TTDTSTSTAY MELRSLRSDD TAVYYCARAN 100
WLDYWGQGTT VTVSS                                        115
```

Light Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 102):

```
DIQMTQSPSS LSASVGDRVT ITCSVSSSVS SIYLHWYQQK PGKAPKLLIY 050
STSNLASGVP SRFSGSGSGT DFTLTISSLQ PEDFATYYCQ VYSGYPLTFG 100
GGTKVEIKR                                               109
```

CDRs are underlined (CDR sequences disclosed as SEQ ID NOS 130-135, respectively, in order of appearance)

FIG. 1A

Onartuzumab (humanized IgG1/kappa, one-armed)
(SEQ ID NO: 14 and 12 from patent US 7476724)

Amino Acid Sequence (10 AA per group, 5 groups per line)

Heavy Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 103):

```
EVQLVESGGG LVQPGGSLRL SCAASGYTFT SYWLHWVRQA PGKGLEWVGM 050
IDPSNSDTRF NPNFKDRFTI SADTSKNTAY LQMNSLRAED TAVYYCATYR 100
SYVTPLDYWG QGTLVTVSS                                    119
```

Light Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 104):

```
DIQMTQSPSS LSASVGDRVT ITCKSSQSLL YTSSQKNYLA WYQQKPGKAP 050
KLLIYWASTR ESGVPSRFSG SGSGTDFTLT ISSLQPEDFA TYYCQQYYAY 100
PWTFGQGTKV EIKR                                         114
```

CDRs are underlined (CDR sequences disclosed as SEQ ID NOS 136-141, respectively, in order of appearance)

FIG. 1B

huAbF46-H4 (humanized IgG1/kappa)
(SEQ ID NO: 83 and 84 from US20130089557)

Amino Acid Sequence (10 AA per group, 5 groups per line)

Heavy Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 105):
EVQLVESGGG LVQPGGSLRL SCAASGFTFT DYYMSWVRQA PGKGLEWLGF 050
IRNKANGYTT EYSASVKGRF TISRDNSKNT LYLQMNSLRA EDTAVYYCAR 100
DNWFAYVVGQ GTLVTVSS 118

Light Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 106):
DIQMTQSPSS LSASVGDRVT ITCKSSQSLL ASGNQNNYLA WHQQKPGKAP 050
KMLIIWASTR VSGVPSRFSG SGSGTDFTLT ISSLQPEDFA TYYCQQSYSA 100
PLTFGQGTKV EIKR 114

CDRs are underlined (CDR sequences disclosed as SEQ ID NOS 142-147, respectively, in order of appearance)

FIG. 1C

ARGX-111 (36C4) (human IgG1/lambda)
(SEQ ID NO: 51 and 55 from US 8,637,027)

Amino Acid Sequence (10 AA per group, 5 groups per line)

Heavy Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 107):
QVQLVESGPG LVKPSQTLSL TCAVSGGSIT TNYYYWSWIR QSPGKGLEWM 050
GVIAYDGSTD YSPSLKSRTS ISRDTSKNQF SLQLSSVTPE DTAVYYCARD 100
VRVIATGWAT ANALDAWGQG TLVTVSS 127

Light Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 108):
QSVLTQPPSV SGSPGKTVTI SCAGTSSDVG YGNYVSWYQQ LPGTAPKLLI 050
FAVSYRASGI PDRFSGSKSG NTAFLTISGL QSEDEADYYC ASYRSSNNAA 100
VFGGGTHLTV L 111

CDRs are underlined (CDR sequences disclosed as SEQ ID NOS 148-153, respectively, in order of appearance)

FIG. 1D

SAIT-301

Amino Acid Sequence (10 AA per group, 5 groups per line)

Heavy Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 109):

```
EVQLVESGGG LVQPGGSLRL SCAASGFTFT DYYISWVRQA PGKGLEWVGF 050
IRNKANGYTT EYSASVKGRF TISRDDSKNS LYLQMNSLKT EDTAVYYCAR 100
DNWFAYWGQG TLVTVSS                                     117
```

Light Chain Variable Region (full-length sequence disclosed as SEQ ID NO: 110):

```
DIVMTQSPLS LPVTPGEPAS ISCKSSQSLL AWSNQNNYLA WYLQKPGQSP 050
QMLIIWAITR VGGVPDRFSG SGSGTDFTLK ISRVEAEDVG VYYCQQSYSR 100
PYTFGQGTKL EIKRT                                       115
```

CDRs are underlined (CDR sequences disclosed as SEQ ID NOS 154-158 and 111, respectively, in order of appearance)

FIG. 1E

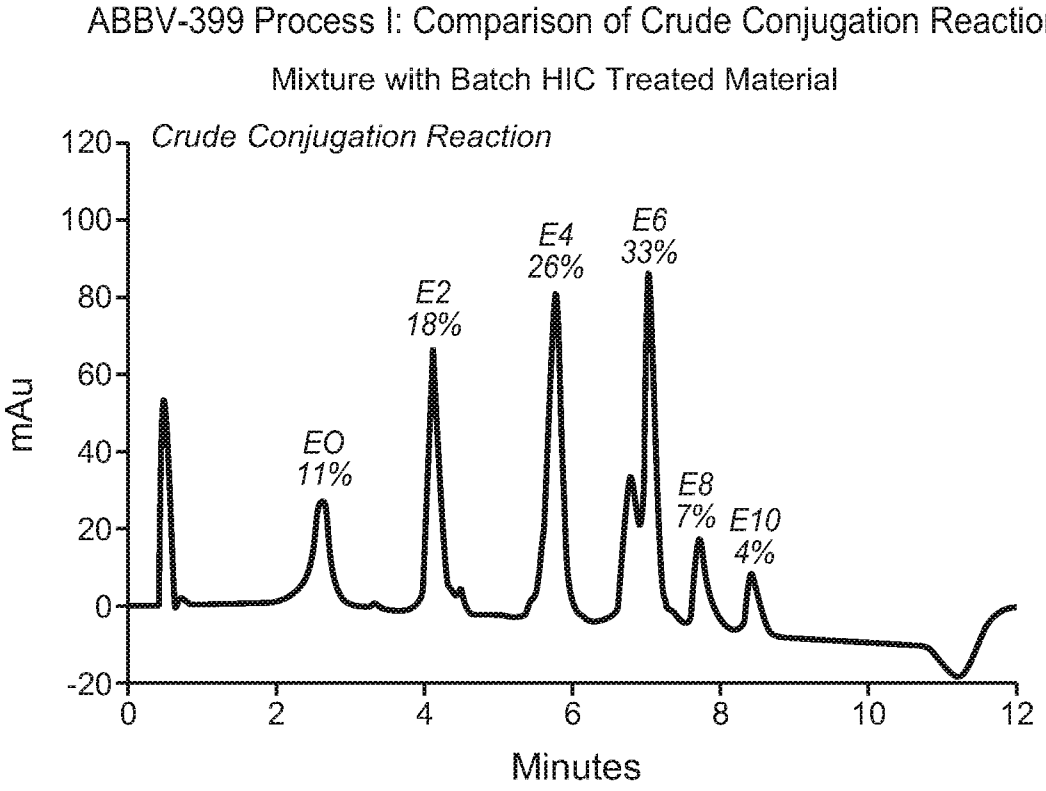

ABBV-399 Process I: Comparison of Crude Conjugation Reaction
Mixture with Batch HIC Treated Material
Crude Conjugation Reaction
mAu
Minutes
EO
11%
E2
18%
E4
26%
E6
33%
E8
7%
E10
4%

FIG. 2A

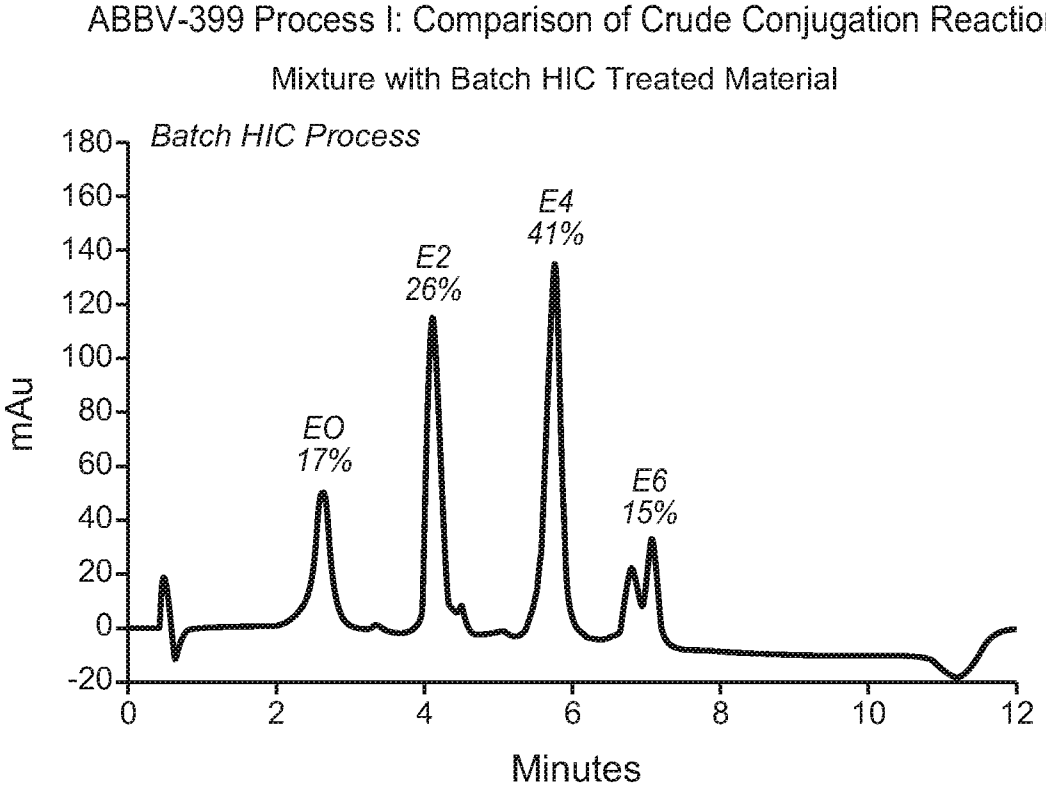

ABBV-399 Process I: Comparison of Crude Conjugation Reaction
Mixture with Batch HIC Treated Material
Batch HIC Process
mAu
Minutes
EO
17%
E2
26%
E4
41%
E6
15%

FIG. 2B

ABBV-399 Process II: Comparison of Crude Conjugation Reaction Mixture with Column HIC Treated Material

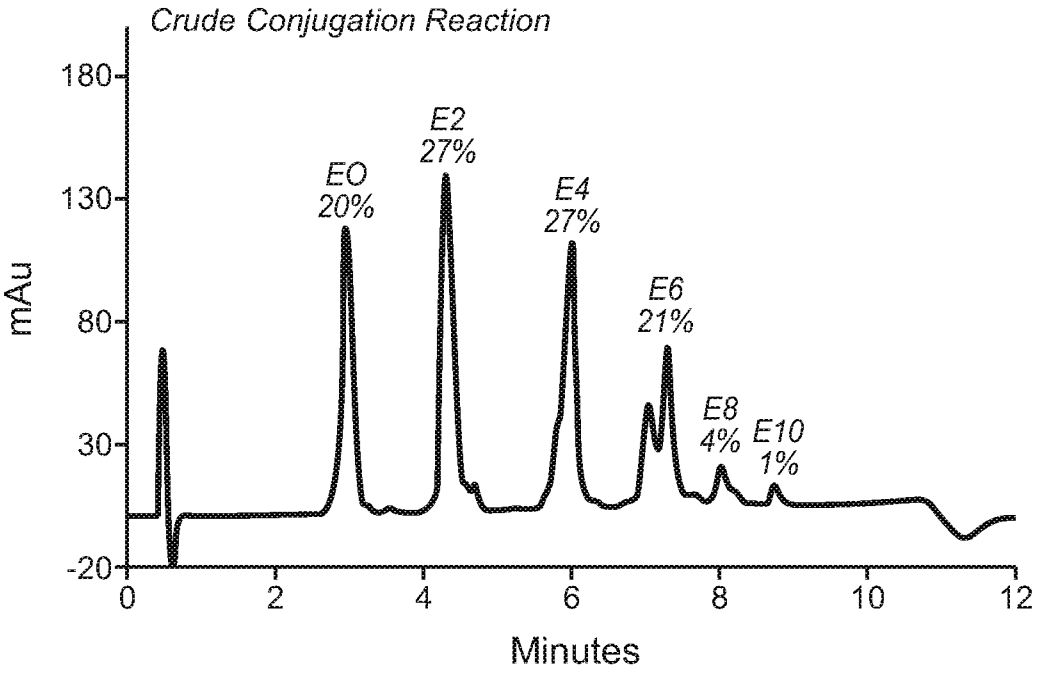


FIG. 3A

ABBV-399 Process II: Comparison of Crude Conjugation Reaction Mixture with Column HIC Treated Material

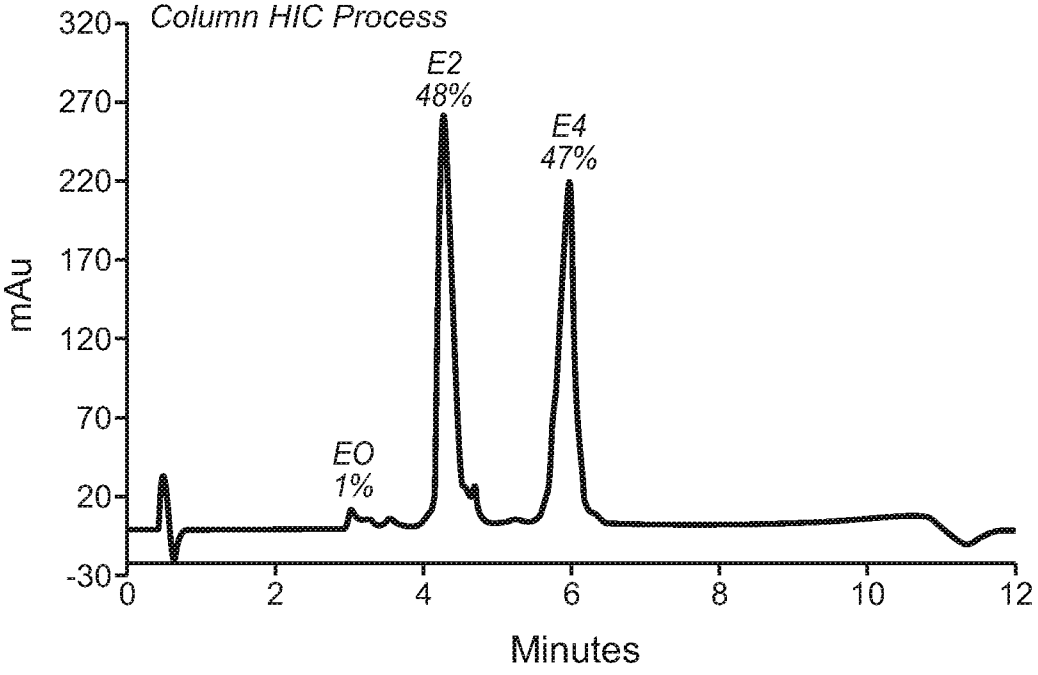


FIG. 3B

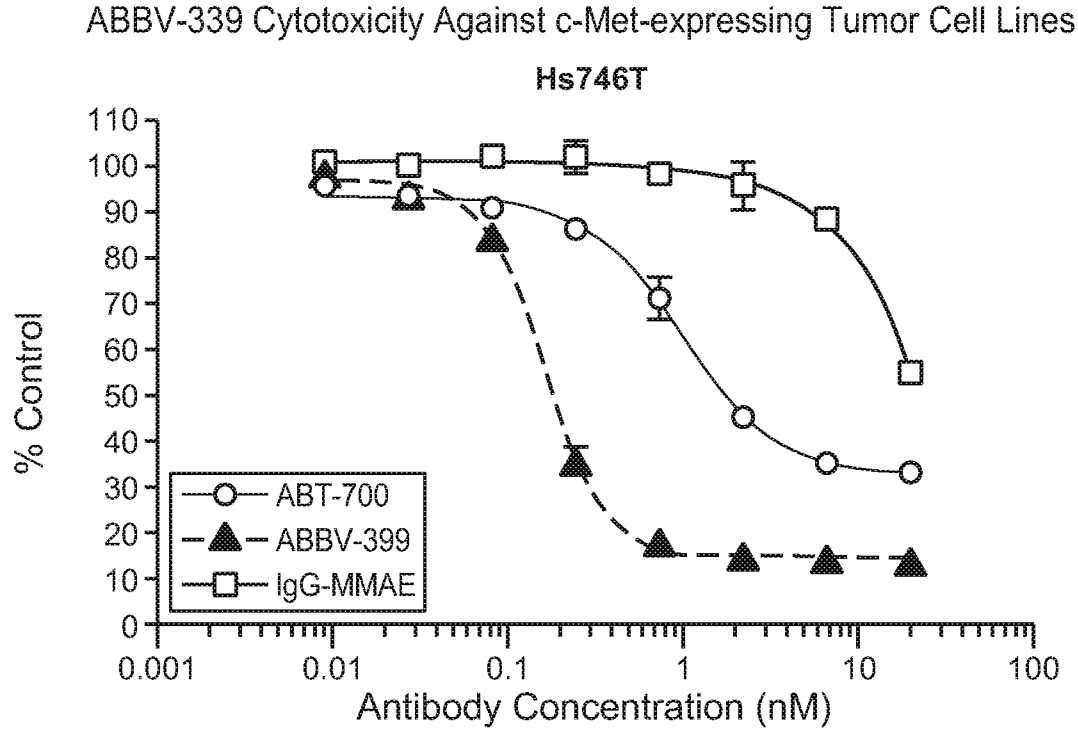

ABBV-339 Cytotoxicity Against c-Met-expressing Tumor Cell Lines
Hs746T
% Control
110
100
90
80
70
60
50
40
30
20
10
0
ABT-700
ABBV-399
IgG-MMAE
0.001
0.01
0.1
1
10
100
Antibody Concentration (nM)

FIG. 4A

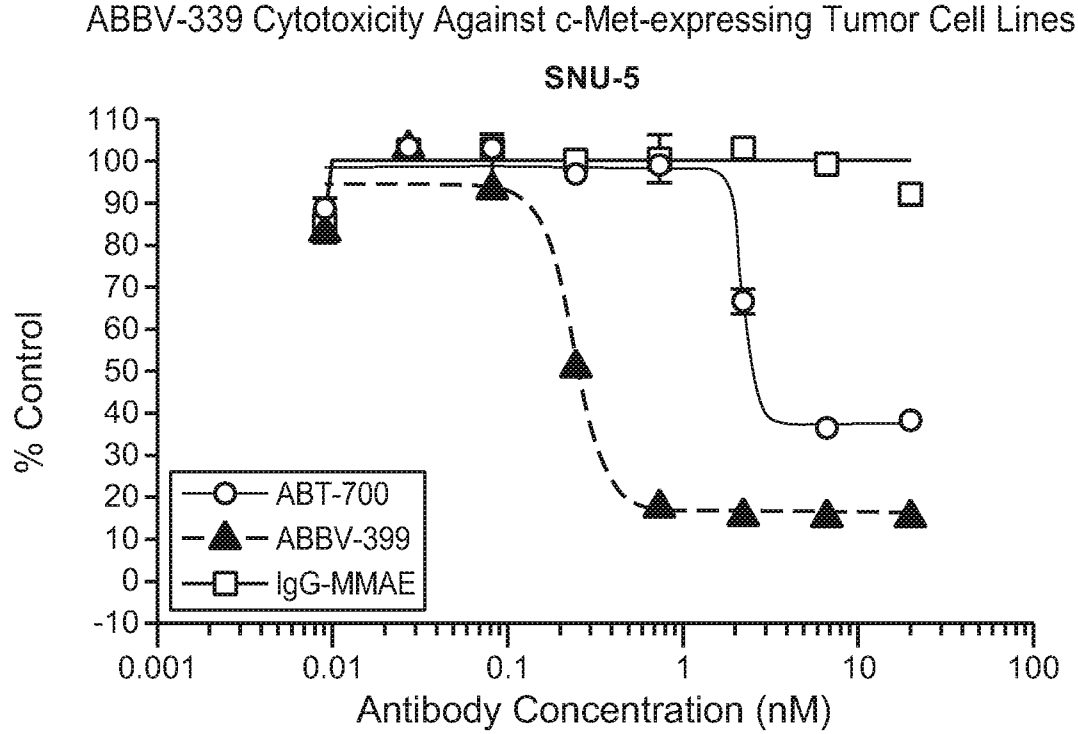

ABBV-339 Cytotoxicity Against c-Met-expressing Tumor Cell Lines
SNU-5
% Control
110
100
90
80
70
60
50
40
30
20
10
0
-10
ABT-700
ABBV-399
IgG-MMAE
0.001
0.01
0.1
1
10
100
Antibody Concentration (nM)

FIG. 4B

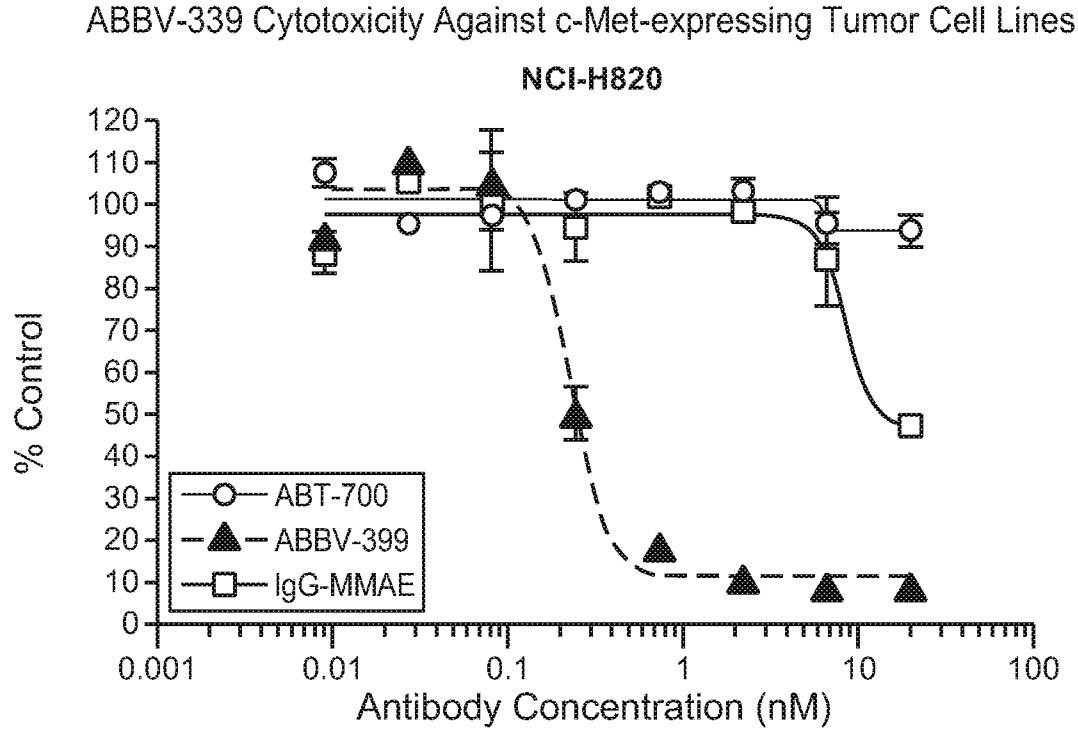

ABBV-339 Cytotoxicity Against c-Met-expressing Tumor Cell Lines
NCI-H820
% Control
120
110
100
90
80
70
60
50
40
30
20
10
0
ABT-700
ABBV-399
IgG-MMAE
0.001
0.01
0.1
1
10
100
Antibody Concentration (nM)

FIG. 4C

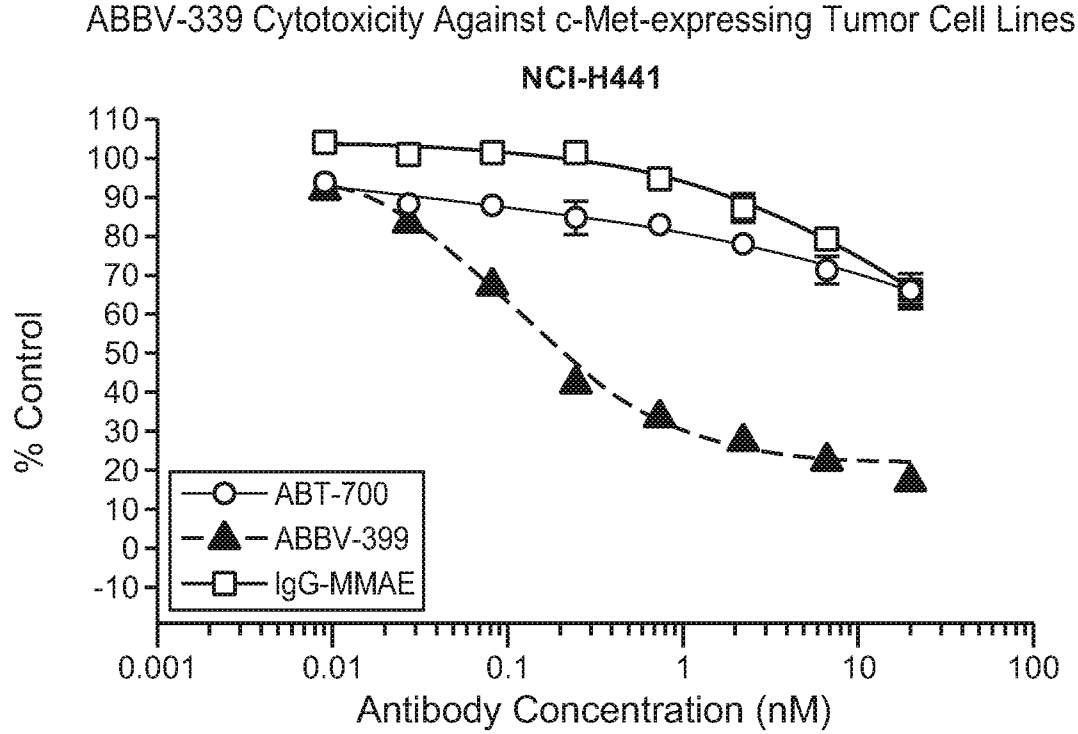

ABBV-339 Cytotoxicity Against c-Met-expressing Tumor Cell Lines
NCI-H441
% Control
110
100
90
80
70
60
50
40
30
20
10
0
-10
ABT-700
ABBV-399
IgG-MMAE
0.001
0.01
0.1
1
10
100
Antibody Concentration (nM)

FIG. 4D

Proliferation Inhibition Results with ABT-700-PBD

	Cytotoxicity IC_{50} (nM)		
Cell line	**ABBV-399**	**ABT-700-PBD**	**MMAE/PBD**
Hs746T (Ga, amp, high)	0.073	0.018	4.1
EBC -1 (Lu, amp, high)	**0.079**	0.095	0.8
H441 (Lu, high)	0.09	**0.01**	9
BT-20 (Br, low)	**0.23**	0.1	2.3
A549 (Lu, low)	1.36	**0.1**	13.6
U87MG (GBM, low)	18.76	**0.21**	89.3
M059J (GBM, low)	3.6	**0.02**	180
U118MG (GBM, low)	0.54	0.2	2.7
KP4 (Pa, low)	3.84	**0.02**	192
SW48 (CRC, low)	>20	**0.0029**	>1000
NHEK (keratinocytes)	none	none	n/a

FIG. 5

In Vitro Activity of ABT-700 PBD in Colorectal Tumor Lines

	ADC and Free Drug IC_{50}s (nM)					ABBV-399 Results		
CRC Line	ABT-700 PBD	Ab095 PBD	Ab095 MMAF	PBD	MMAE	Max Inhib (20 nM)	IC_{50} (nM)	Receptors/Cell
SW1116	0.03	37.4	> 133	0.78	9.92			
HCT-116	0.005	42.6	> 133	0.49	4.81	same as control		~75K
LoVo	0.074	41.2	> 133	0.09	2.25	same as control		68K
SK-CO-1	~0.001	9.85	> 133	0.02	0.54			
SW620	0.005	21.3	> 133	*~ 0.008*	0.92	same as control		~100K
CaCO2	ambig	41.1	> 133	0.42	2.64			
DLD-1	0.004	21.3	> 133	0.14	46.2	same as control		43K
Colo 201	0.007	19	> 133	*~ 0.12*	1.4			
HCT-15	> 67 (ambig)	> 133	> 133	0.12	> 100	same as control		105K
RKO	0.01	28.1	> 133	*~ 0.006*	0.67	same as control		4k
HT-29	0.004	26.2	> 133	~ 0.01	1.1	70%	9	161K
Colo 205	0.02	27.4	> 133	< 0.001	1.18			
T84	0.1	53	> 133	0.037	7.64			
SW403	0.006	11.4	> 133	< 0.001	0.65			
SW1463	0.013	10.3	> 133	0.011	1.1			
LS1034	0.04	43.6	> 133	0.32	~ 32			
Colo320 DM	0.02	58.1	> 133	0.029	33.9			
Colo320 HSR	0.04	> 133	> 133	0.05	33			
LS174T	0.001	4.6	> 133	1.15	3			
SW48	< 0.001	1.9	~ 46	< 0.001	0.24	same as control		24K
SW480	26	56.4	> 133	0.02	2			
WiDr	0.01	34.8	> 133	0.012	0.5			

FIG. 6A

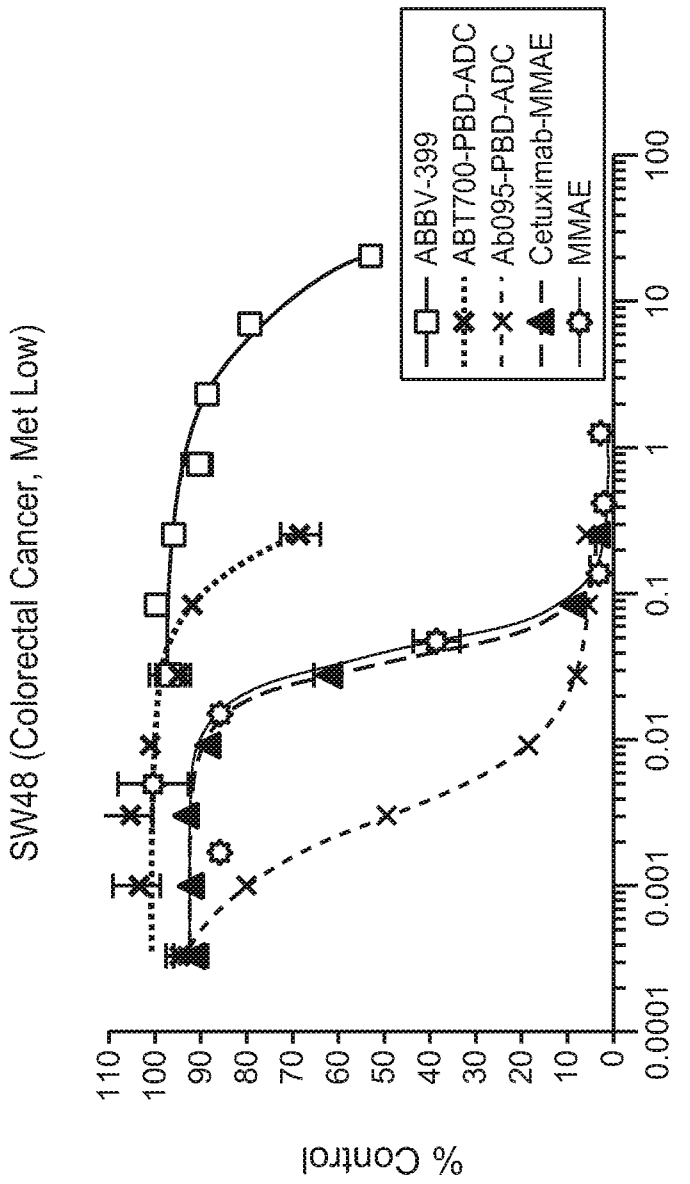

SW48 (Colorectal Cancer, Met Low)
% Control
nM
ABBV-399
ABT700-PBD-ADC
Ab095-PBD-ADC
Cetuximab-MMAE
MMAE
110
100
90
80
70
60
50
40
30
20
10
0
0.0001
0.001
0.01
0.1
1
10
100

FIG. 6B

In Vitro Activity of ABT-700 PBD in Brain Tumor Lines

	ADC and Free Drug IC_{50}s (nM)					ABBV-399 Results		
Brain Cancer Line	ABT-700 PBD	PBD	MMAE	Ab095 PBD	Ab095 MMAF	Max Inhib (20 nM)	IC_{50} (nM)	Receptors/Cell
U87MG	0.08	0.13	1.2	32.9	54.4	60%	18	21K
U138MG	< 0.001	0.18	0.54	23.3	22.8	90%	0.1	31K
T98G	141	0.34	2.1	> 133	> 133	same as control		
U251	< 0.007	< 0.002	1.47	9.2	> 133	same as control		
MO59J	< 0.001	0.05	2.3	26	> 133	60%	3.6	87K
MO59K	< 0.001	0.072	3.5	12.2	> 133	same as control		
A172	> 67 (ambig)	0.41	2.1	36.4	49.7	same as control		
PFSK-1	2.45	0.2	0.68	4.64	48.7			
DBTRG-05MG	< 0.001	0.21	2.1	26	> 133	same as control		
SNB-19	0.006	0.017	1.5	39.2	59.3	65%	8	66K
SNB-75	28.2	0.015	1.8	42.6	91.9	same as control		
SF-539	0.035	0.015	3.8	50	> 133	same as control		
SF-264	0.005	0.023	3	24.3	103			
CHLA-03-AA	0.97	0.045	2.8	14.8	51.5			

FIG. 7

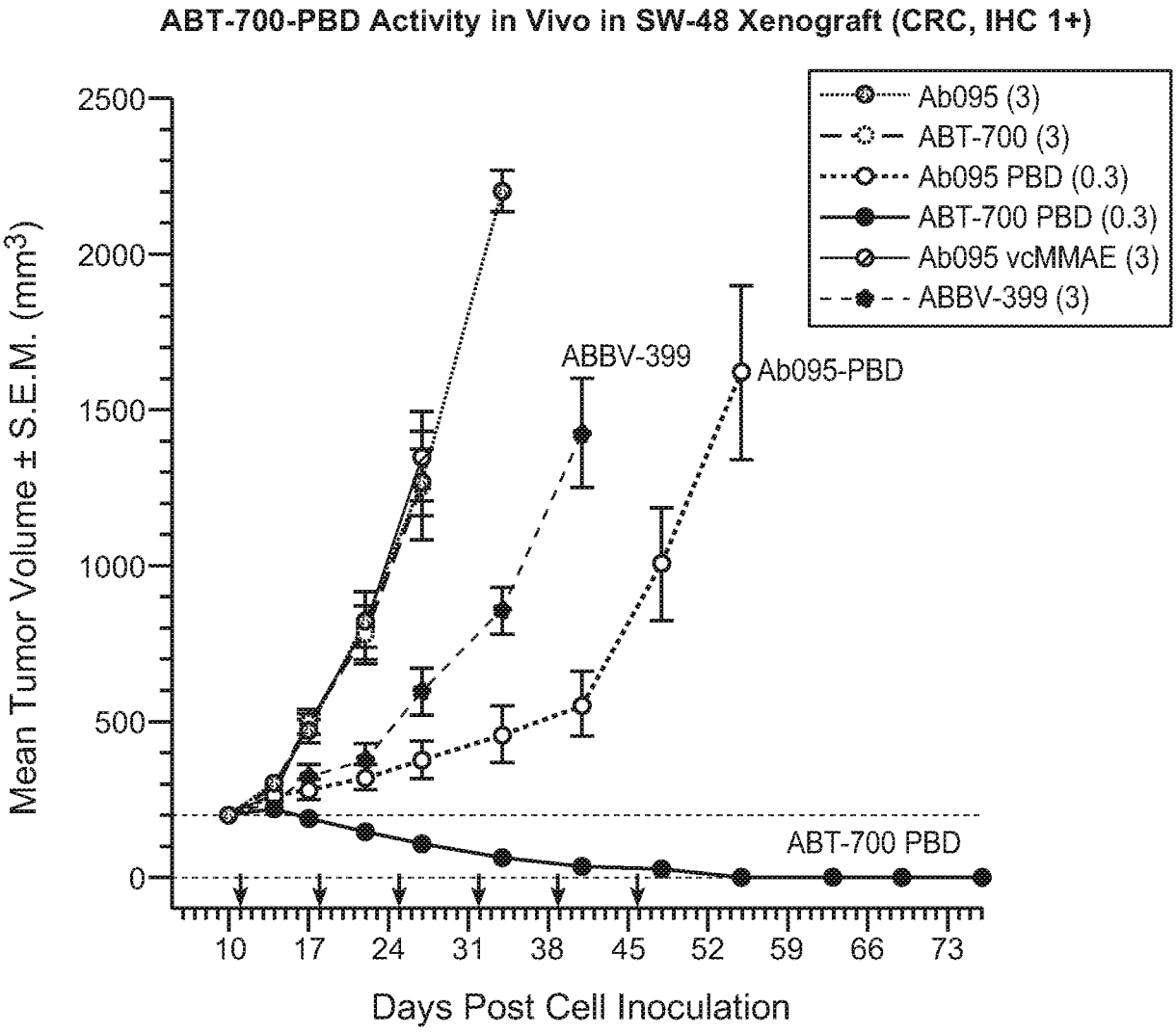

ABT-700-PBD Activity in Vivo in SW-48 Xenograft (CRC, IHC 1+)
Ab095 (3)
ABT-700 (3)
Ab095 PBD (0.3)
ABT-700 PBD (0.3)
Ab095 vcMMAE (3)
ABBV-399 (3)
Mean Tumor Volume ± S.E.M. (mm3)
2500
2000
1500
1000
500
0
ABBV-399
Ab095-PBD
ABT-700 PBD
10
17
24
31
38
45
52
59
66
73
Days Post Cell Inoculation

FIG. 8

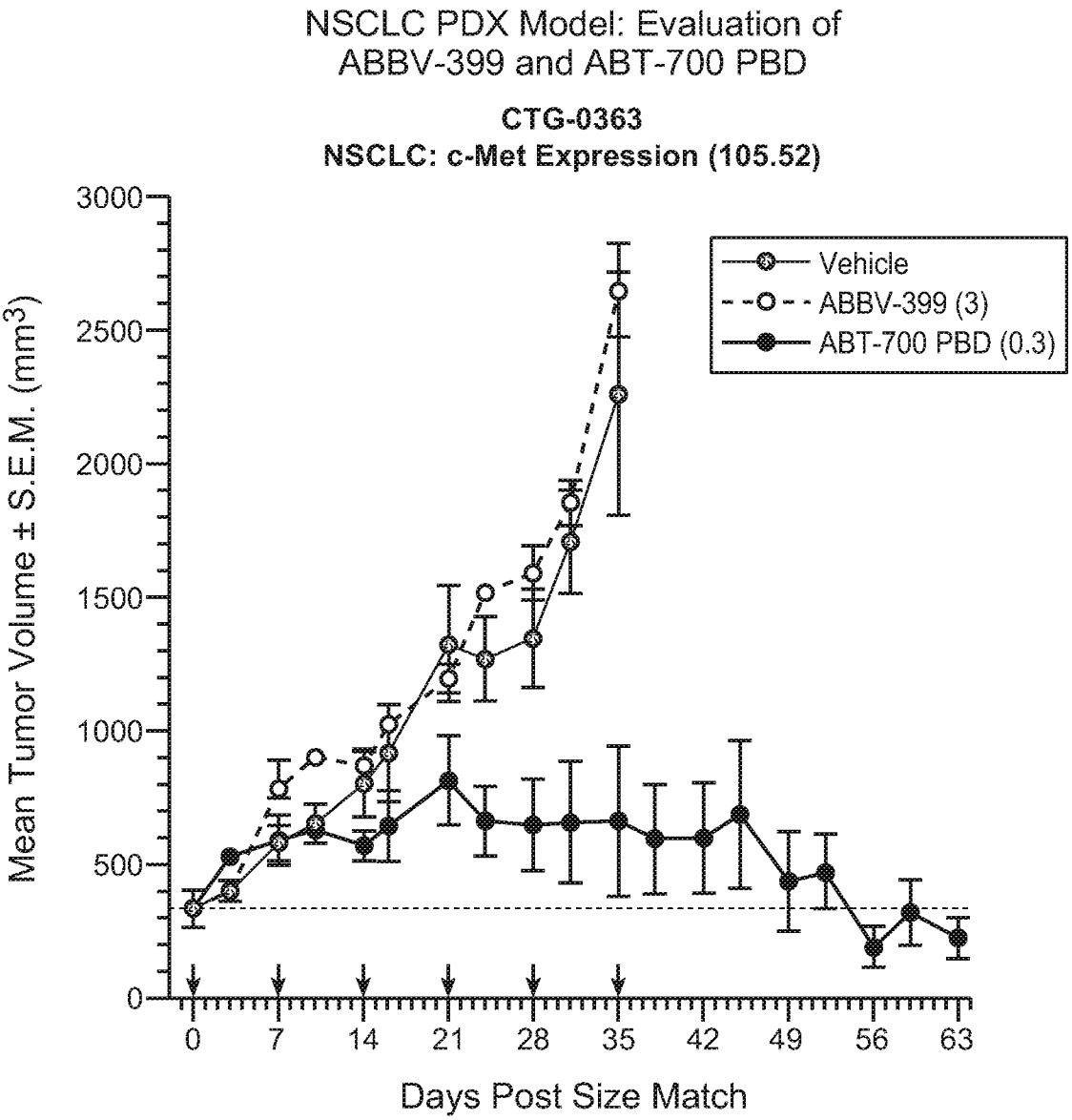

NSCLC PDX Model: Evaluation of
ABBV-399 and ABT-700 PBD
CTG-0363
NSCLC: c-Met Expression (105.52)
Mean Tumor Volume ± S.E.M. (mm3)
3000
2500
2000
1500
1000
500
0
0
7
14
21
28
35
42
49
56
63
Days Post Size Match
Vehicle
ABBV-399 (3)
ABT-700 PBD (0.3)

FIG. 9A

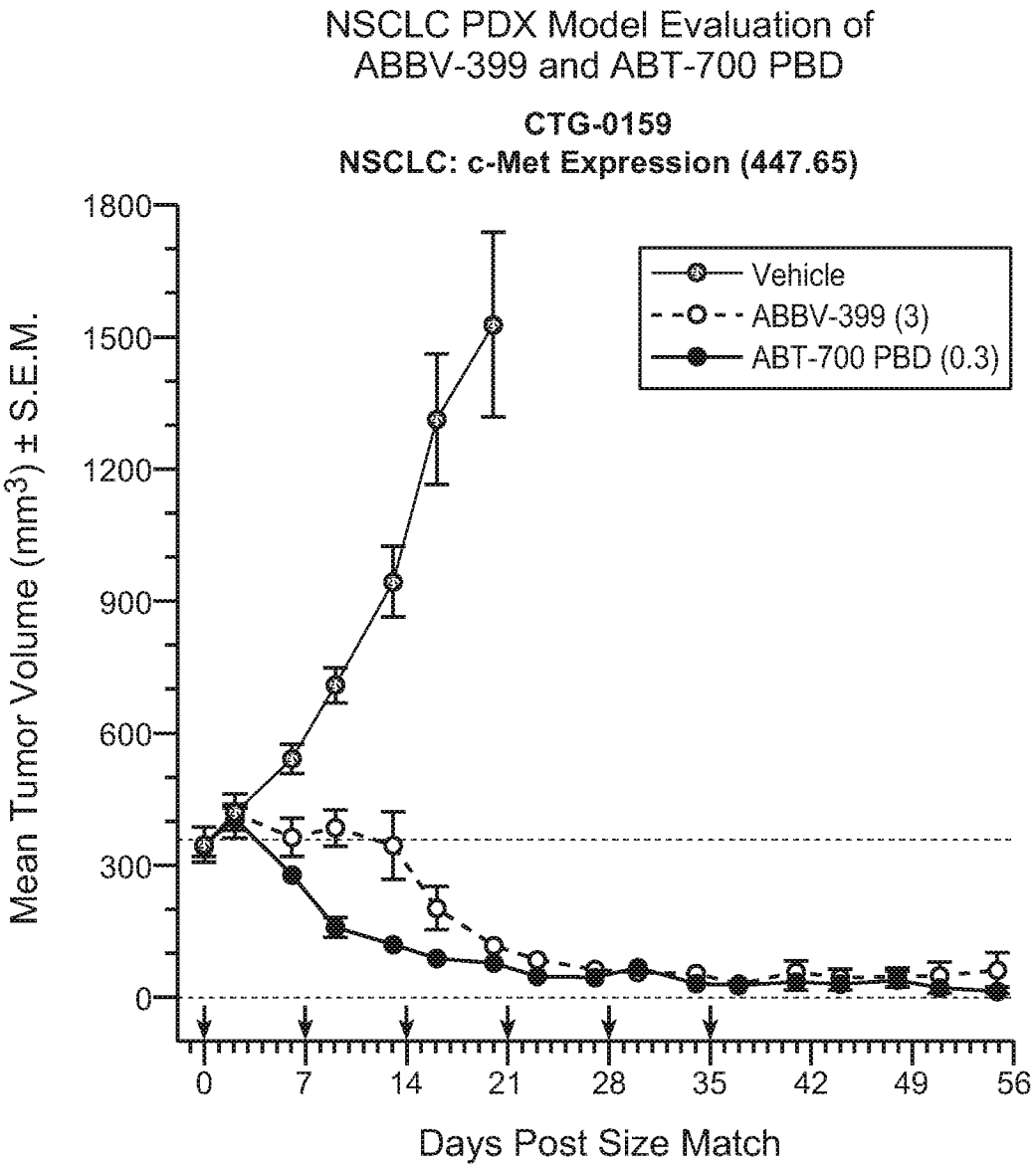

NSCLC PDX Model Evaluation of
ABBV-399 and ABT-700 PBD
CTG-0159
NSCLC: c-Met Expression (447.65)
Mean Tumor Volume (mm3) ± S.E.M.
1800
1500
1200
900
600
300
0
Vehicle
ABBV-399 (3)
ABT-700 PBD (0.3)
0
7
14
21
28
35
42
49
56
Days Post Size Match

FIG. 9B

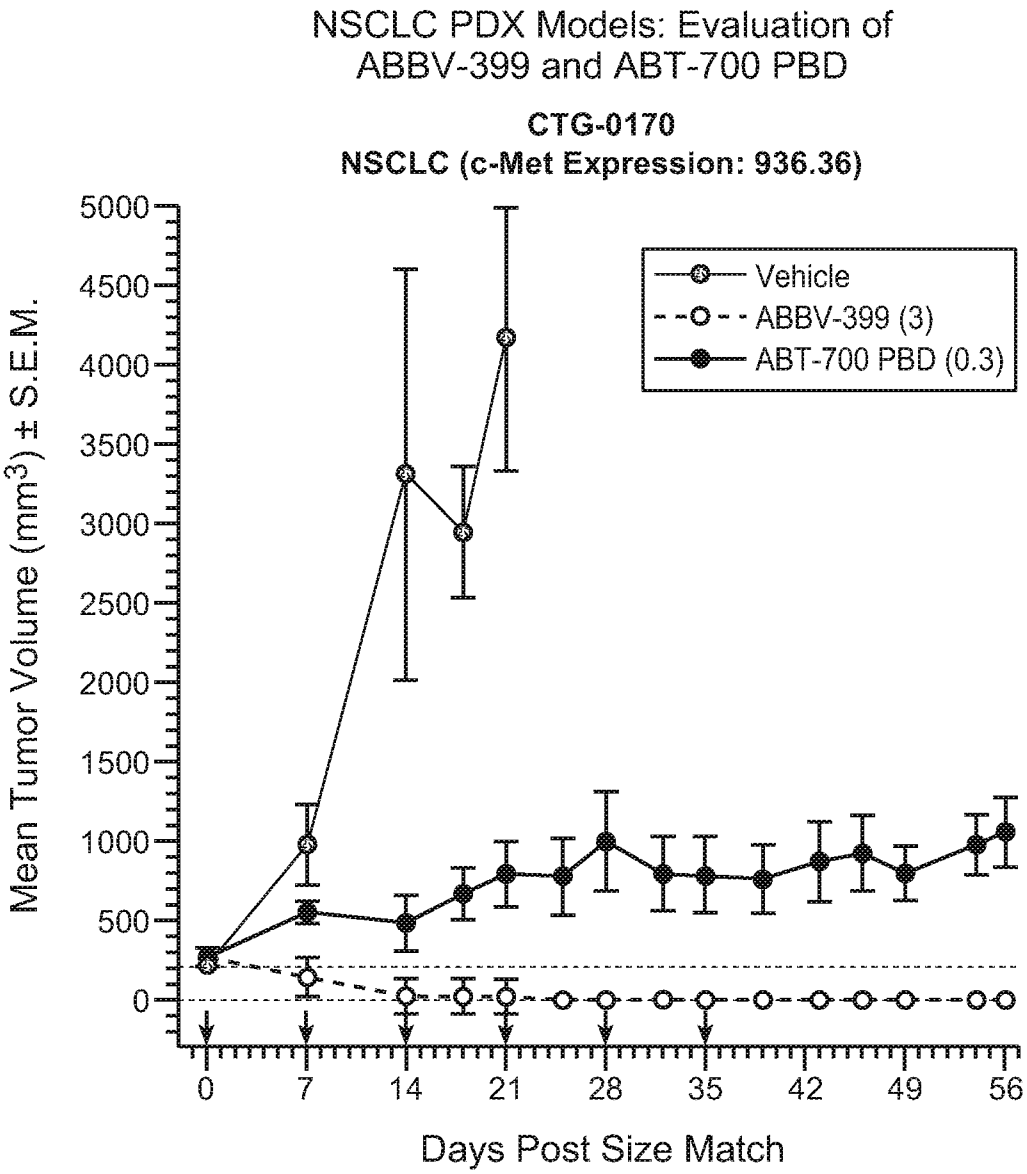

NSCLC PDX Models: Evaluation of
ABBV-399 and ABT-700 PBD
CTG-0170
NSCLC (c-Met Expression: 936.36)
Mean Tumor Volume (mm3) ± S.E.M.
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Vehicle
ABBV-399 (3)
ABT-700 PBD (0.3)
0
7
14
21
28
35
42
49
56
Days Post Size Match

FIG. 9C

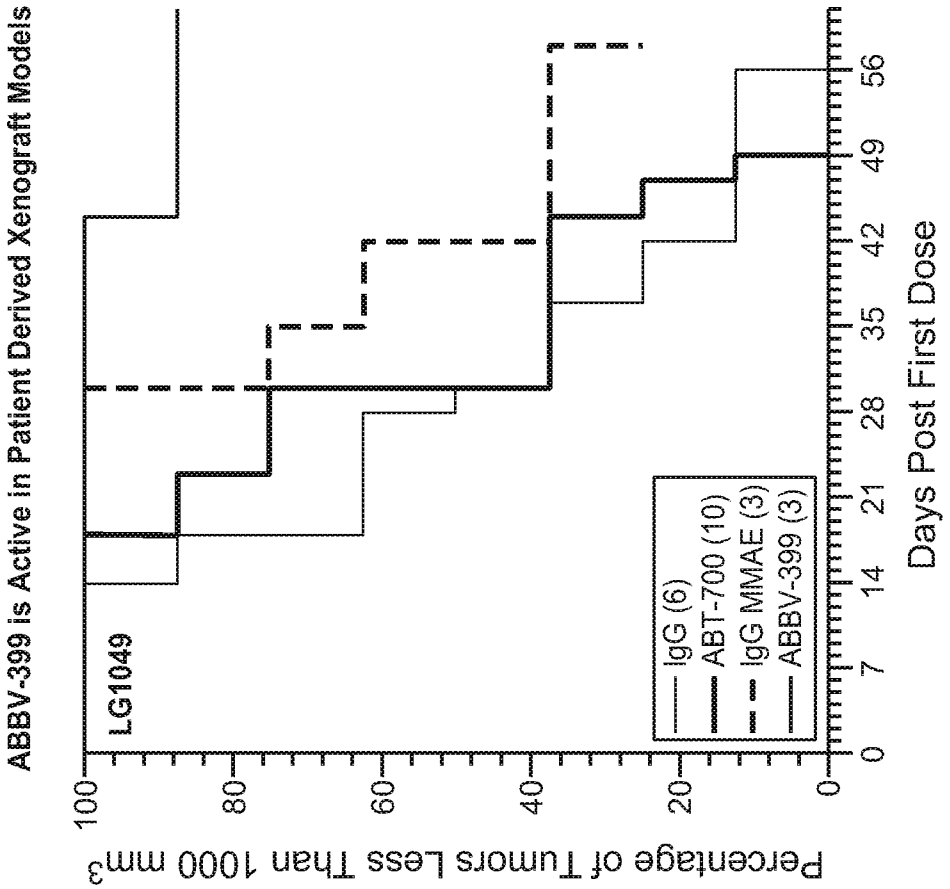


FIG. 10B

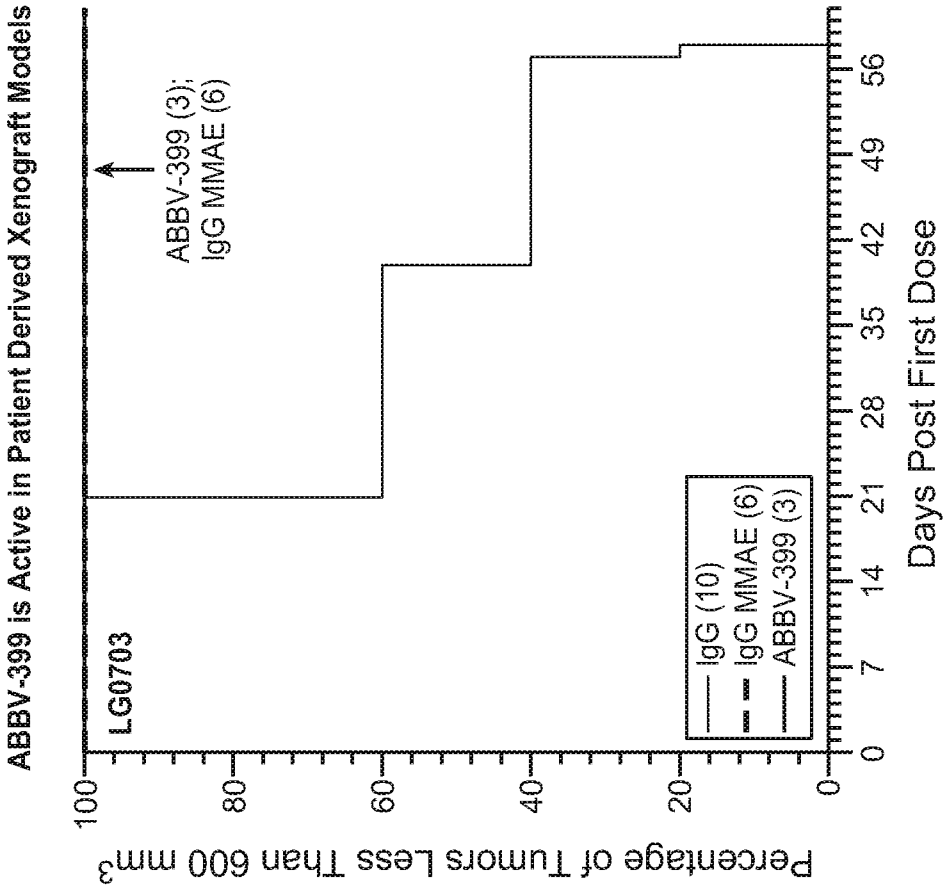


FIG. 10A

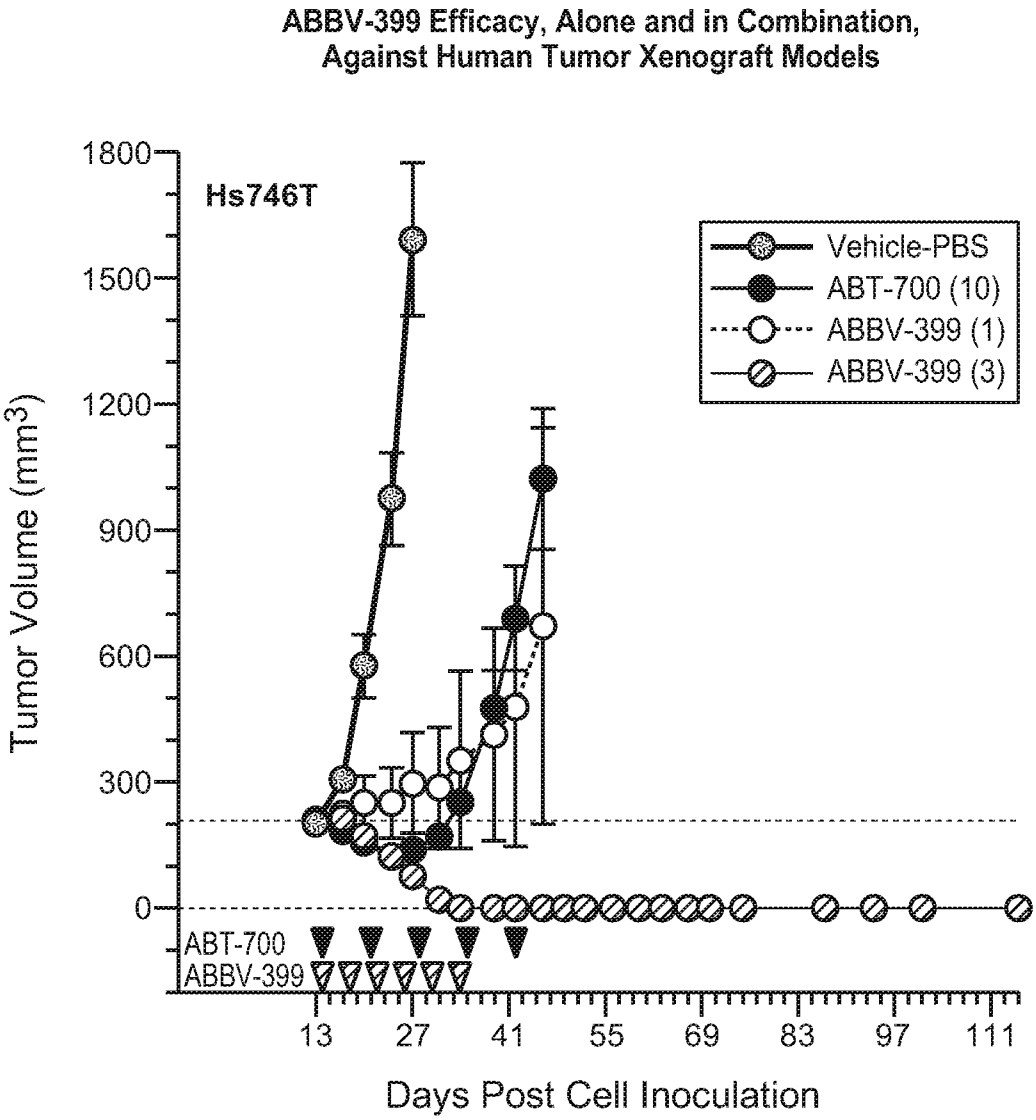

ABBV-399 Efficacy, Alone and in Combination,
Against Human Tumor Xenograft Models
Hs746T
Vehicle-PBS
ABT-700 (10)
ABBV-399 (1)
ABBV-399 (3)
Tumor Volume (mm3)
1800
1500
1200
900
600
300
0
ABT-700
ABBV-399
13
27
41
55
69
83
97
111
Days Post Cell Inoculation

FIG. 11A

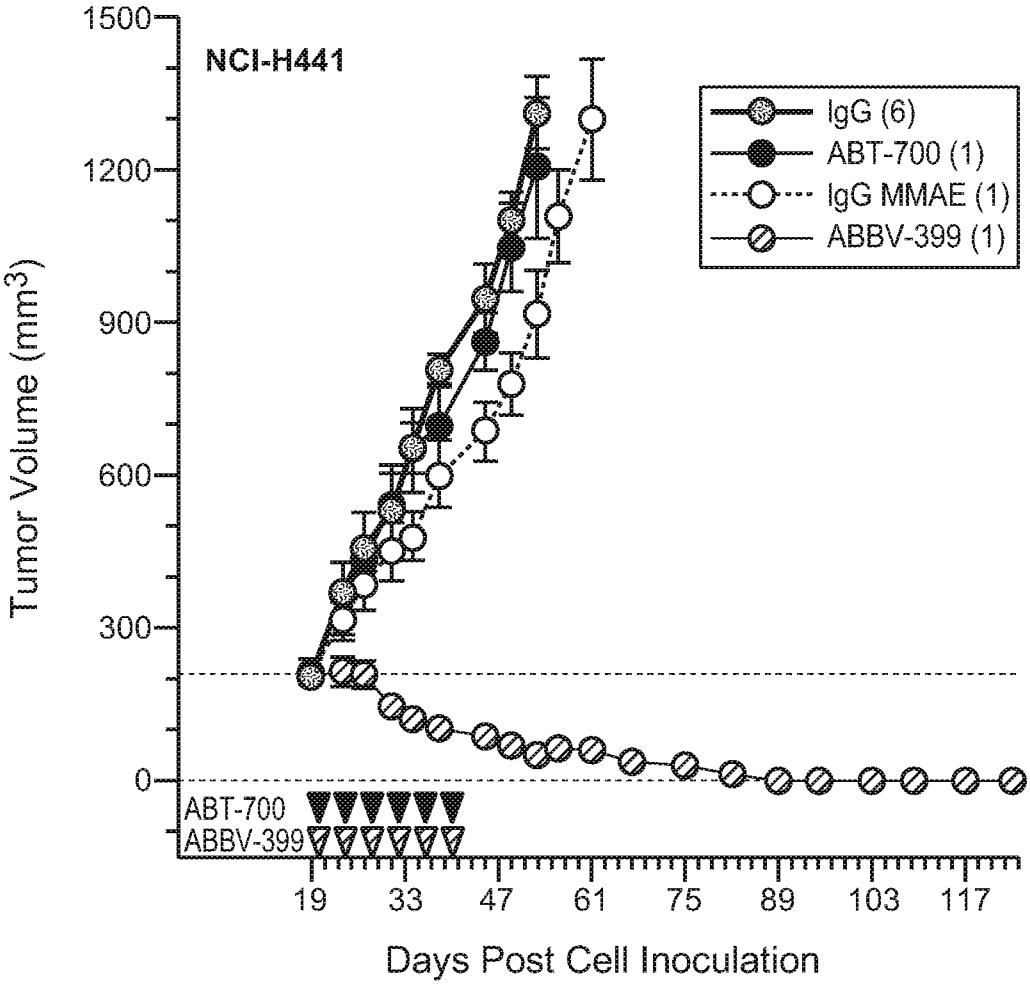

NCI-H441
IgG (6)
ABT-700 (1)
IgG MMAE (1)
ABBV-399 (1)
Tumor Volume (mm3)
1500
1200
900
600
300
0
ABT-700
ABBV-399
19
33
47
61
75
89
103
117
Days Post Cell Inoculation

FIG. 11B

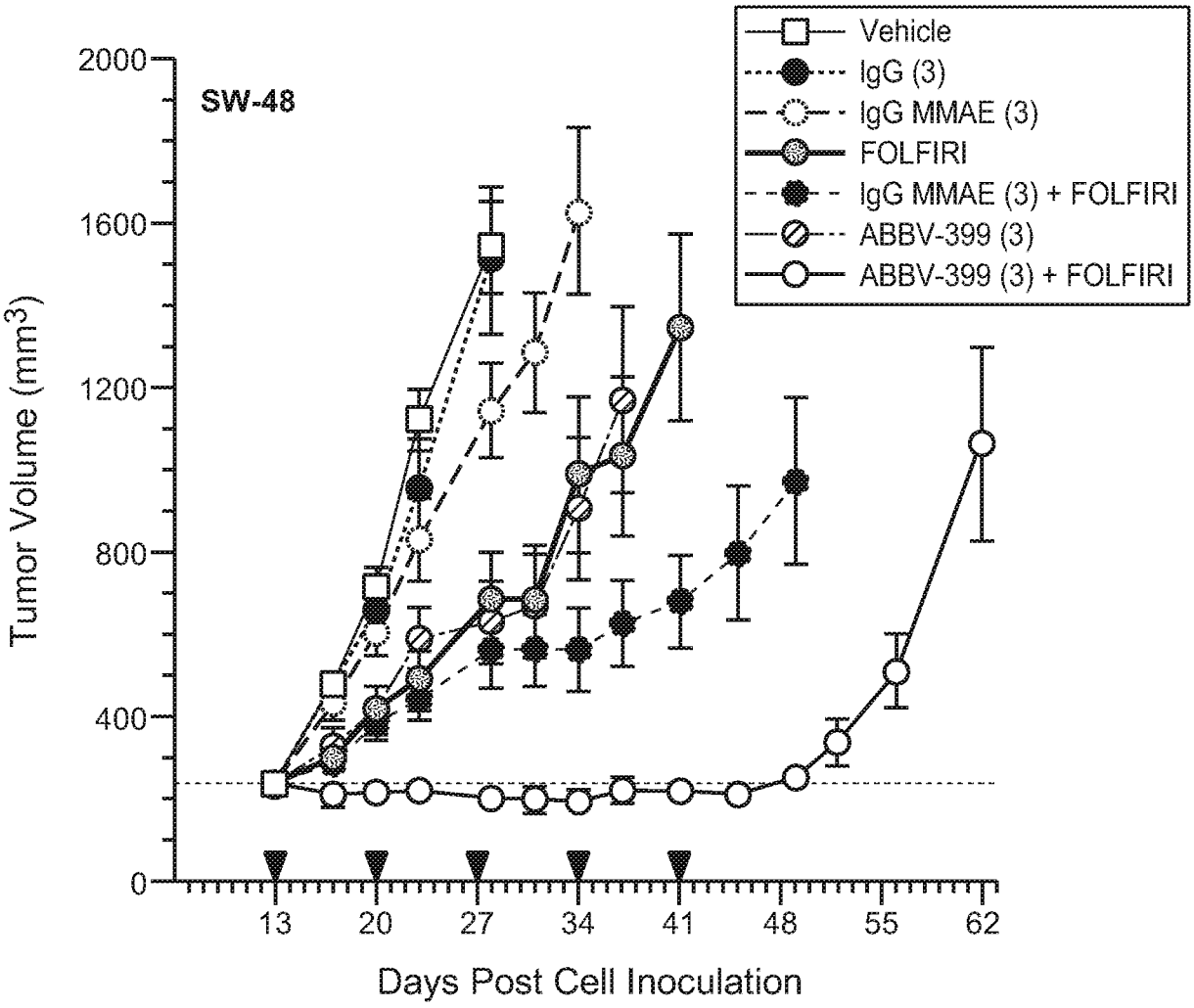

SW-48
Vehicle
IgG (3)
IgG MMAE (3)
FOLFIRI
IgG MMAE (3) + FOLFIRI
ABBV-399 (3)
ABBV-399 (3) + FOLFIRI
Tumor Volume (mm3)
2000
1600
1200
800
400
0
13
20
27
34
41
48
55
62
Days Post Cell Inoculation

FIG. 11C

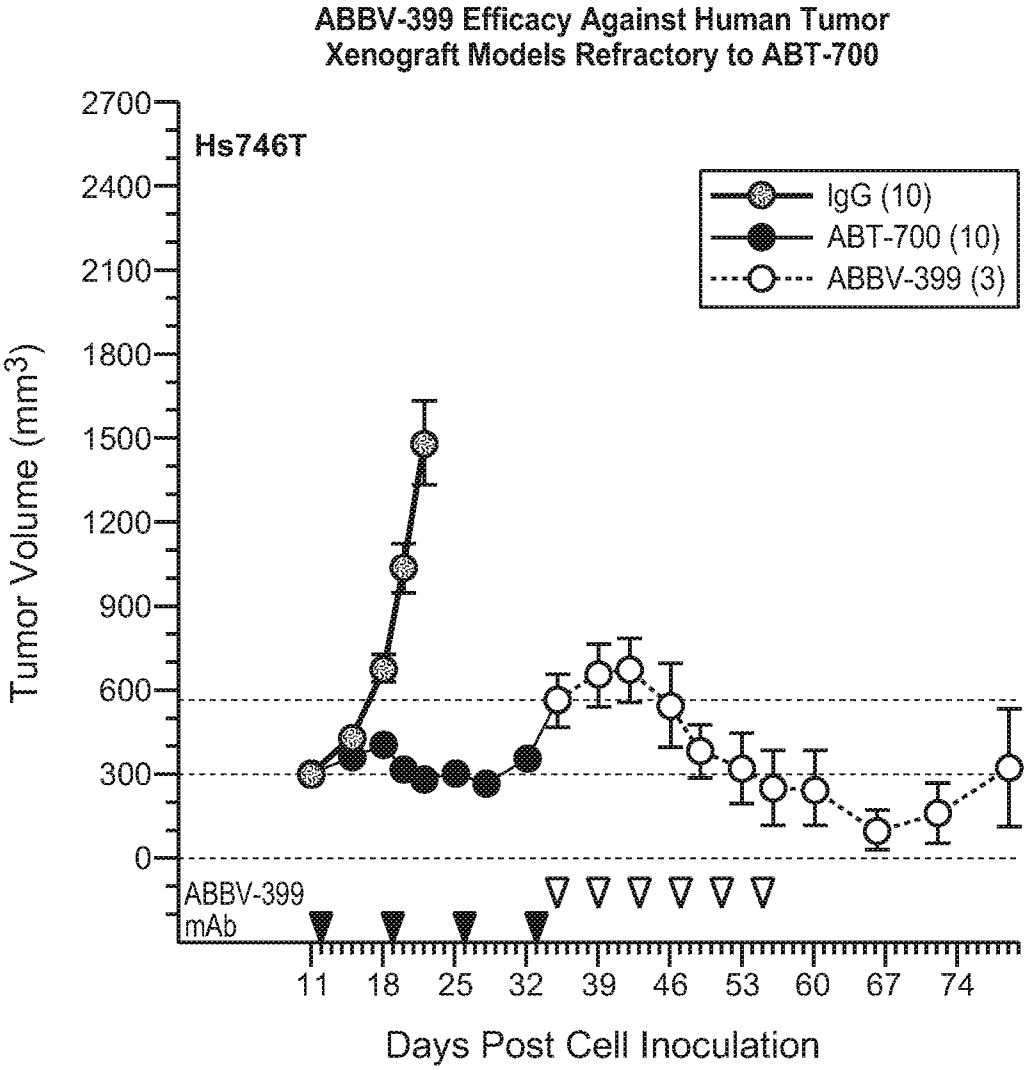

ABBV-399 Efficacy Against Human Tumor Xenograft Models Refractory to ABT-700
Hs746T
IgG (10)
ABT-700 (10)
ABBV-399 (3)
Tumor Volume (mm3)
2700
2400
2100
1800
1500
1200
900
600
300
0
ABBV-399 mAb
11
18
25
32
39
46
53
60
67
74
Days Post Cell Inoculation

FIG. 12A

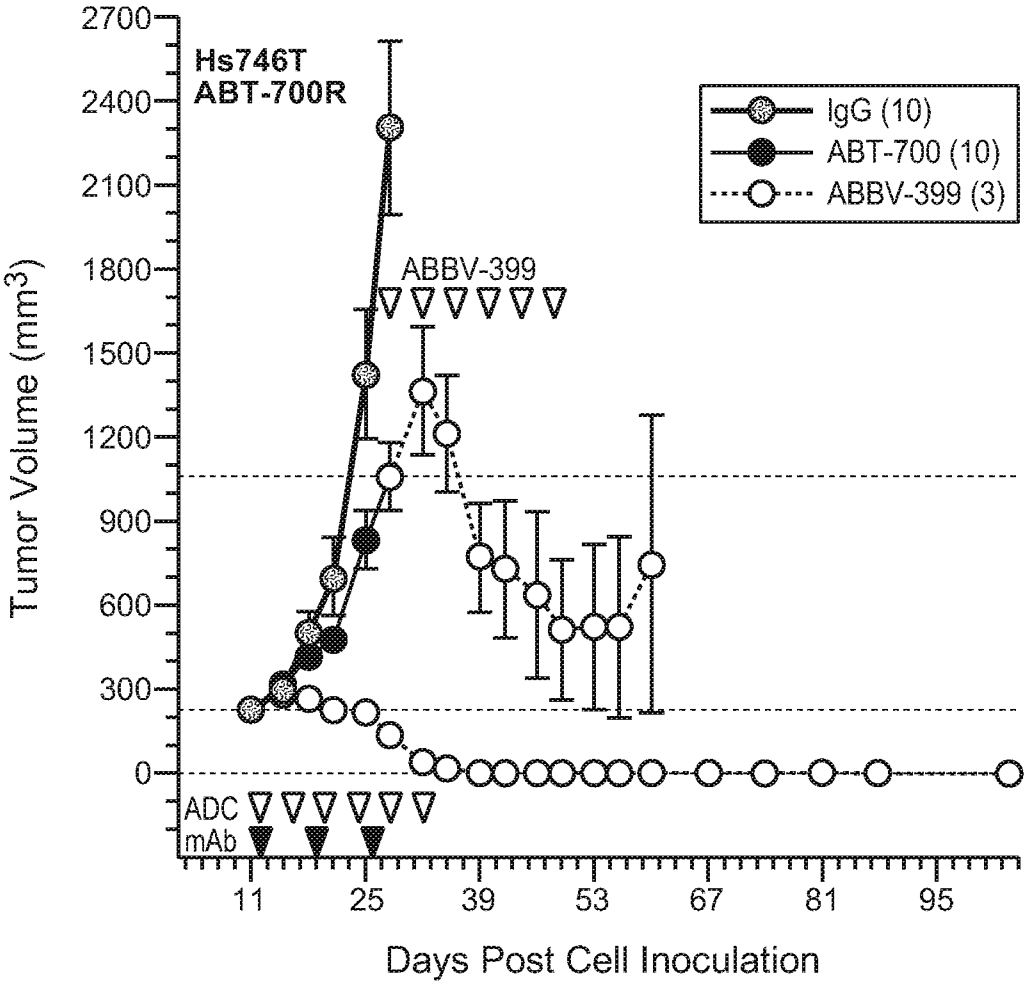

Hs746T
ABT-700R
IgG (10)
ABT-700 (10)
ABBV-399 (3)
ABBV-399
ADC
mAb
Tumor Volume (mm3)
2700
2400
2100
1800
1500
1200
900
600
300
0
11
25
39
53
67
81
95
Days Post Cell Inoculation

FIG. 12B

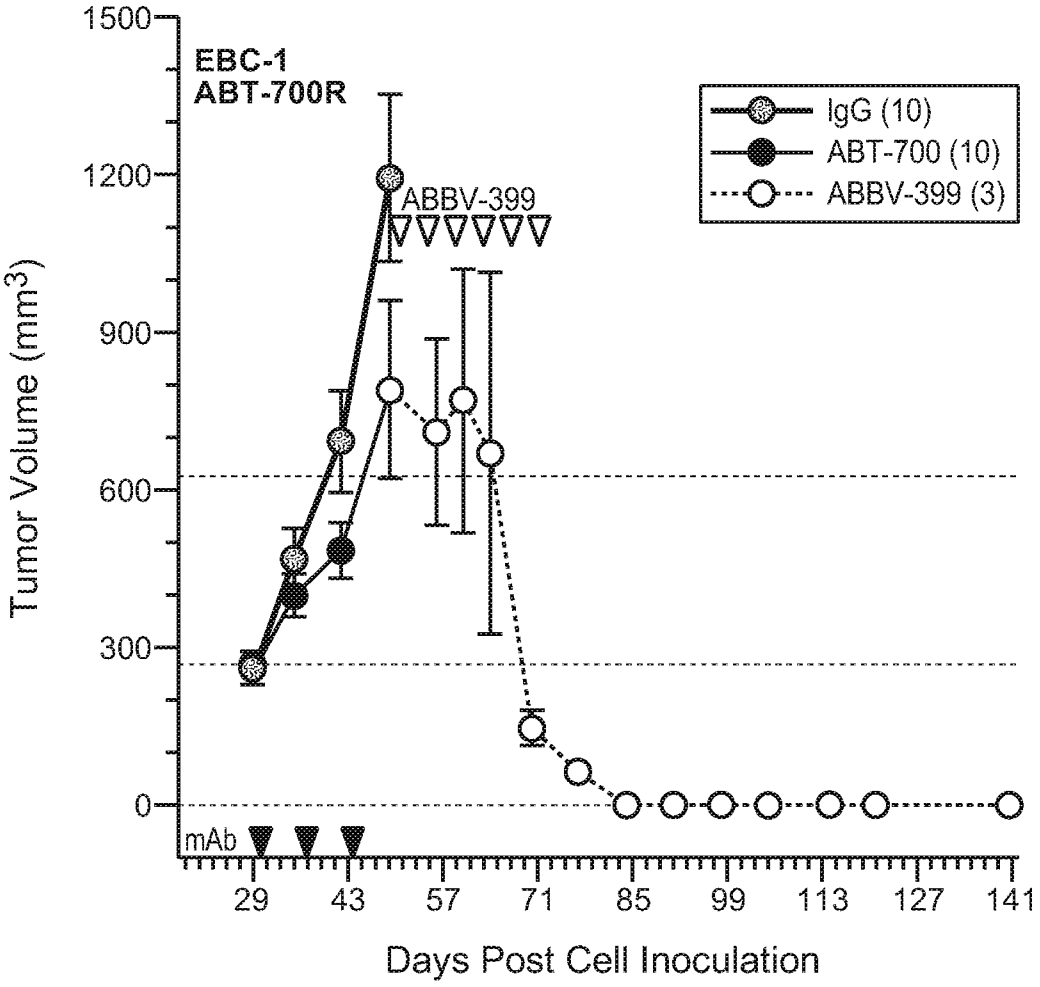

EBC-1
ABT-700R
IgG (10)
ABT-700 (10)
ABBV-399 (3)
ABBV-399
Tumor Volume (mm3)
1500
1200
900
600
300
0
mAb
29
43
57
71
85
99
113
127
141
Days Post Cell Inoculation

FIG. 12C

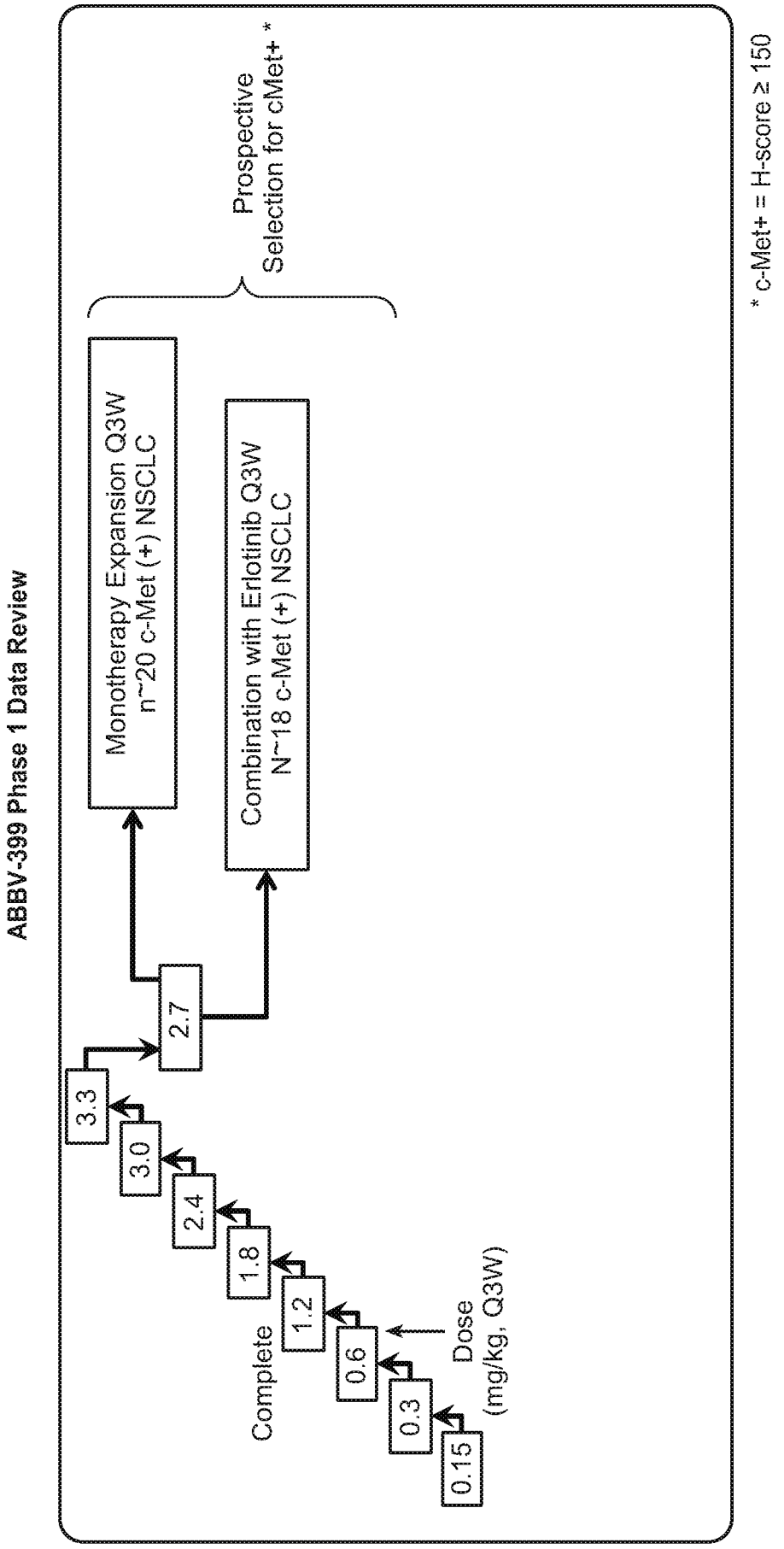

ABBV-399 Phase 1 Data Review
Dose (mg/kg, Q3W)
0.15
0.3
0.6
1.2
1.8
2.4
3.0
3.3
Complete
2.7
Monotherapy Expansion Q3W
n~20 c-Met (+) NSCLC
Combination with Erlotinib Q3W
N~18 c-Met (+) NSCLC
Prospective
Selection for cMet+ *
* c-Met+ = H-score ≥ 150

FIG. 13

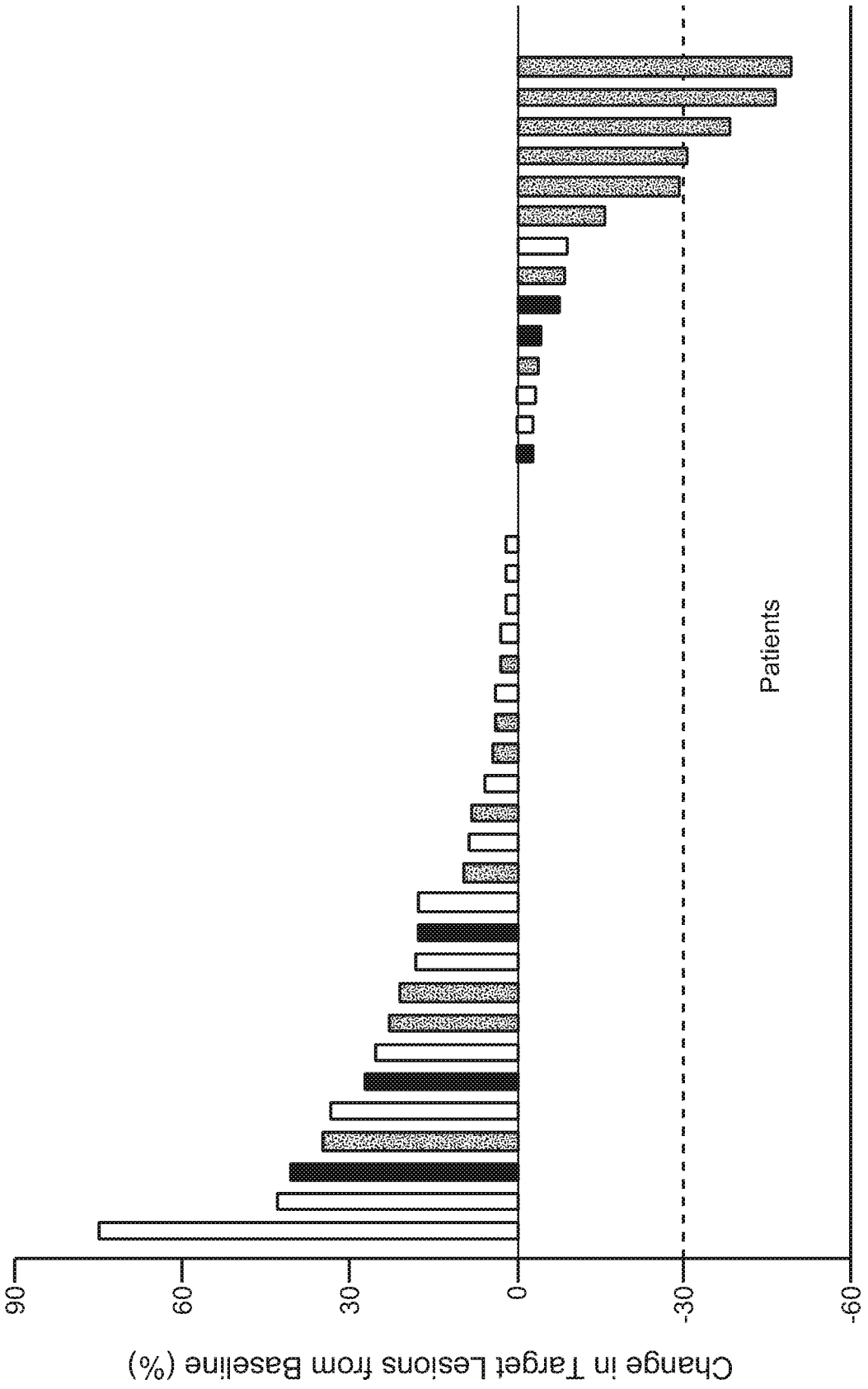

Change in Target Lesions from Baseline (%)
90
60
30
0
-30
-60
Patients

FIG. 14

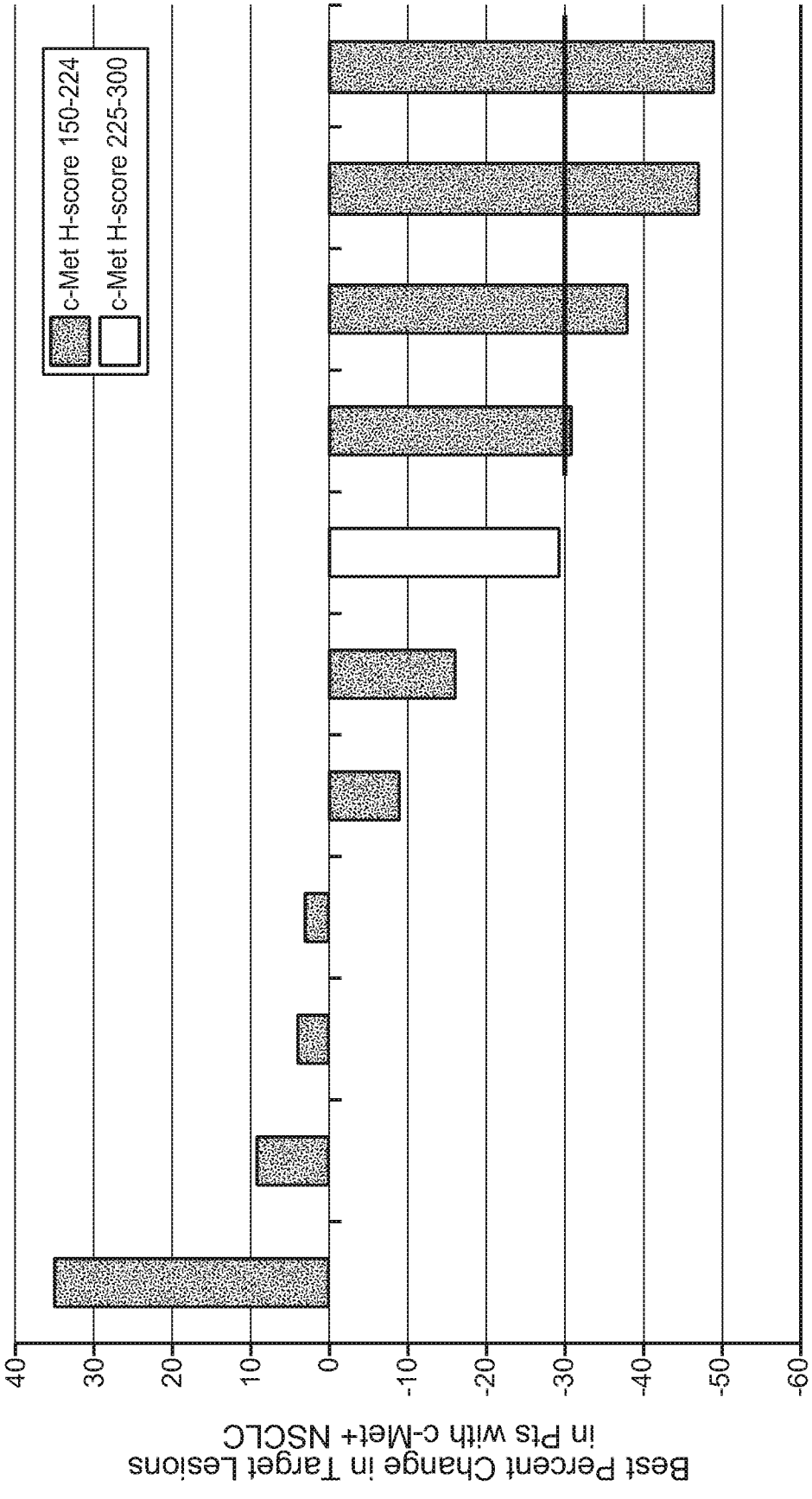

c-Met H-score 150-224
c-Met H-score 225-300
40
30
20
10
0
-10
-20
-30
-40
-50
-60
Best Percent Change in Target Lesions
in Pts with c-Met+ NSCLC

FIG. 15

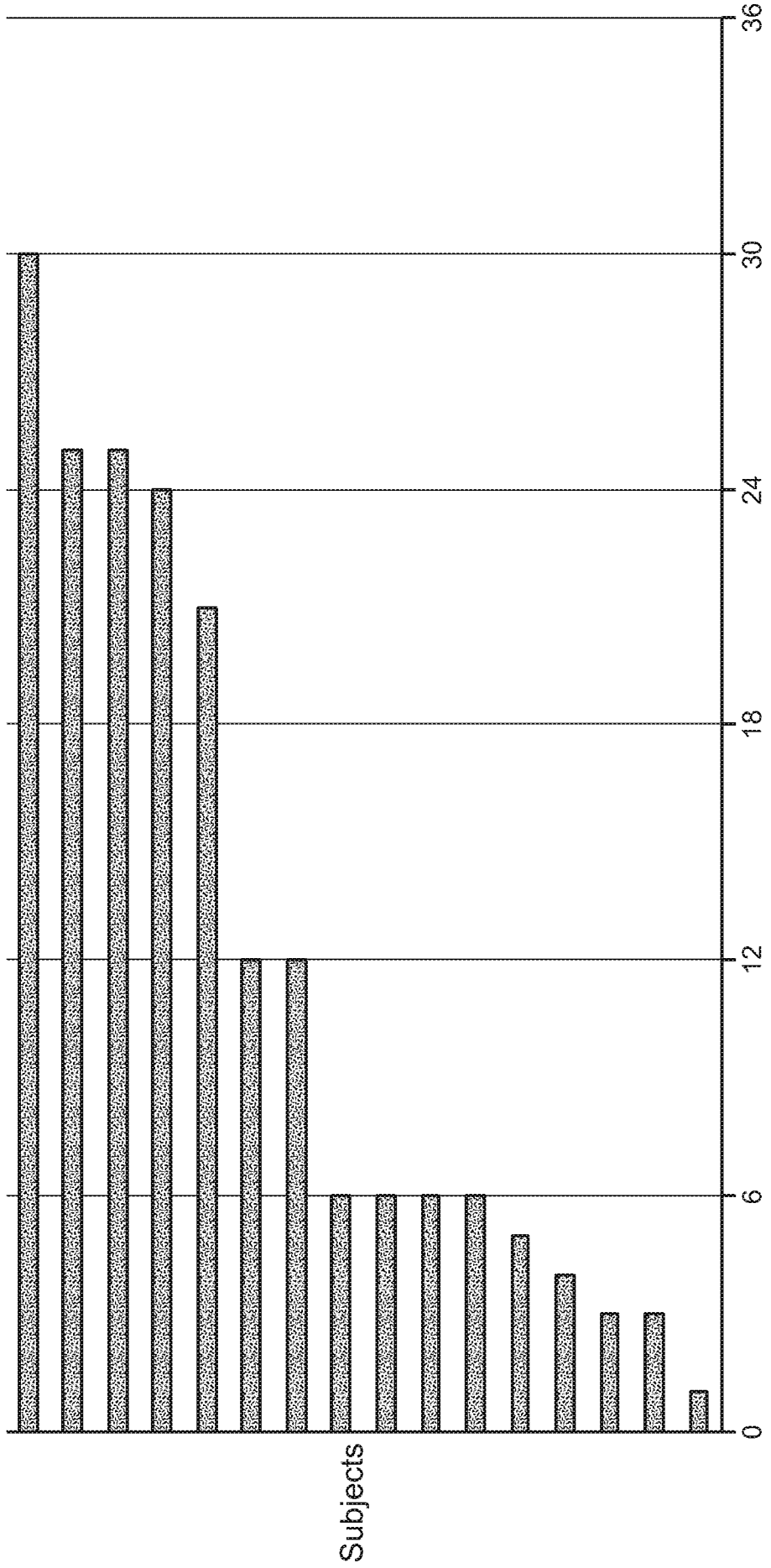


FIG. 16

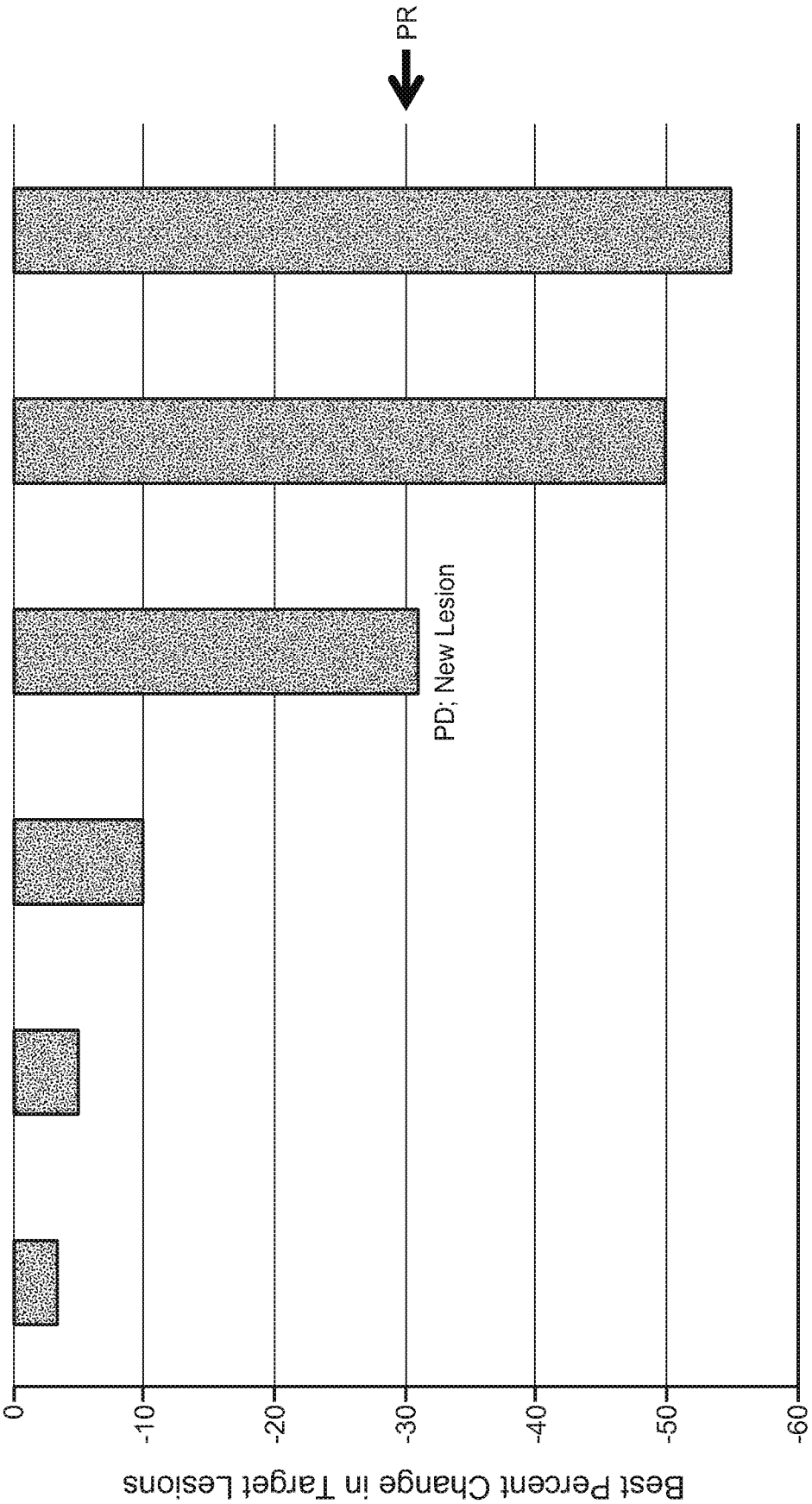

PR
PD; New Lesion
0
-10
-20
-30
-40
-50
-60
Best Percent Change in Target Lesions

FIG. 17

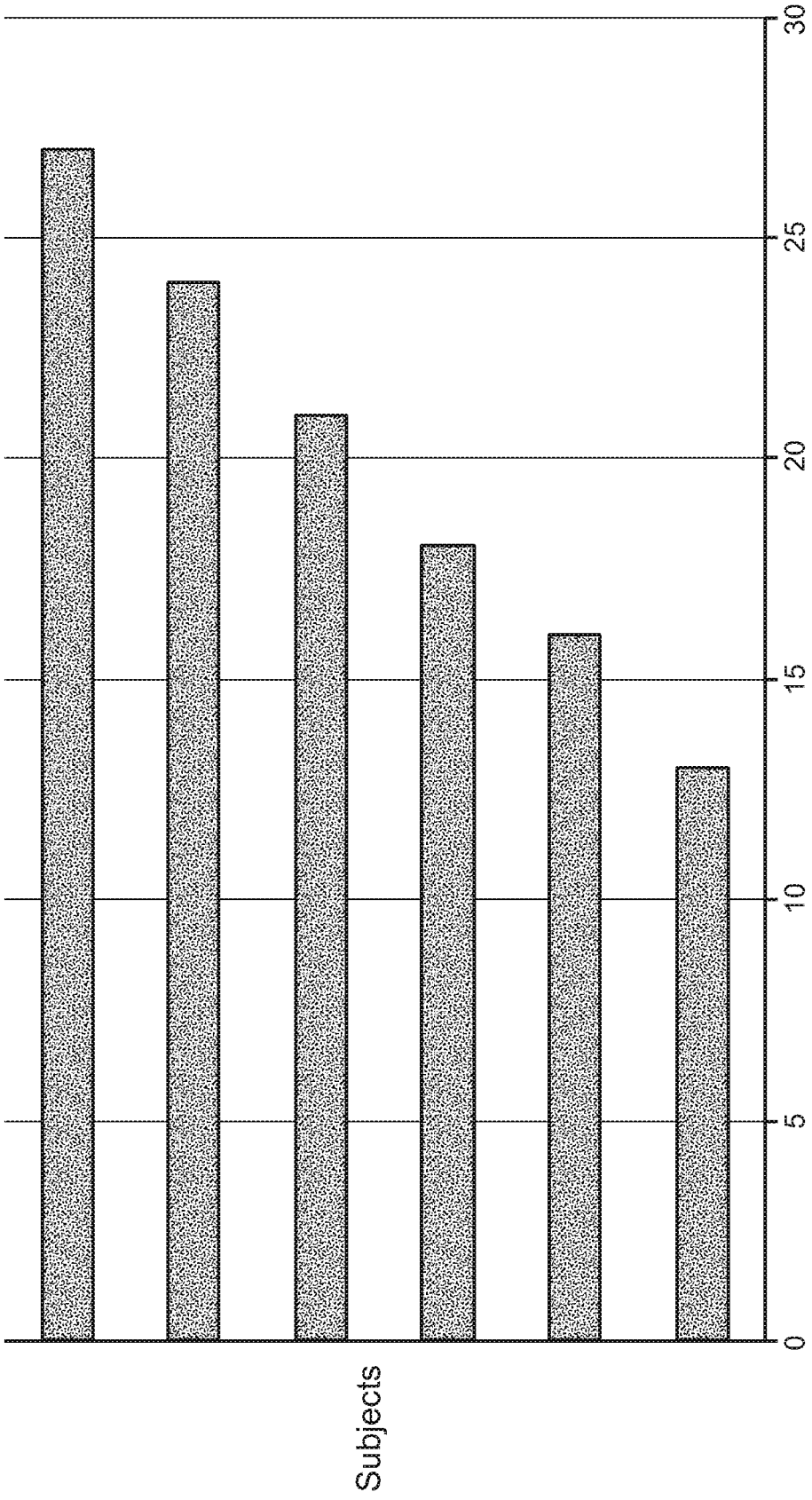


FIG. 18

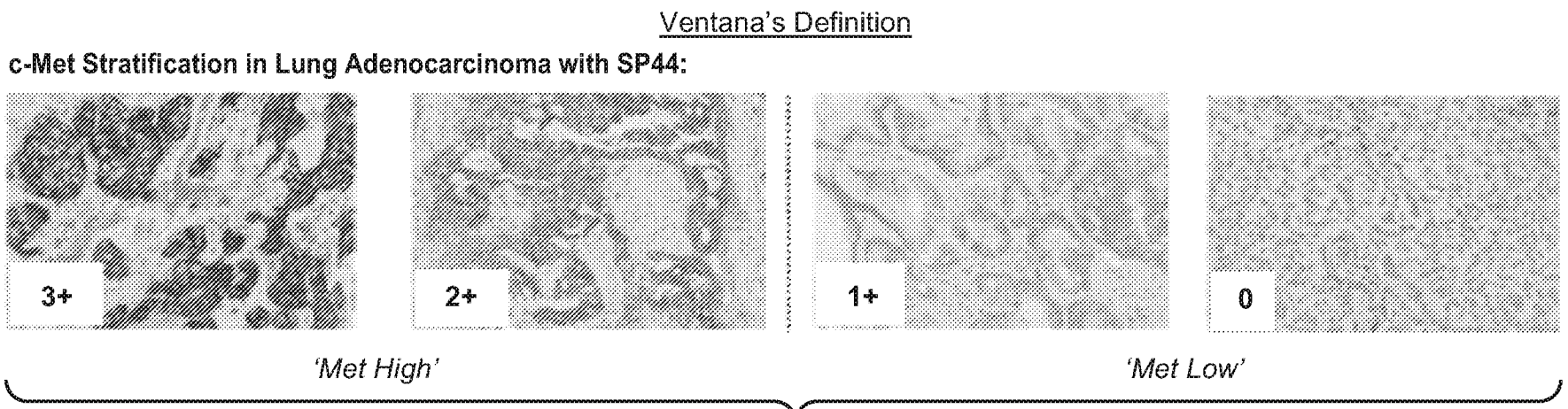

Ventana's Definition
c-Met Stratification in Lung Adenocarcinoma with SP44:
3+
2+
1+
0
'Met High'
'Met Low'

FIG. 19

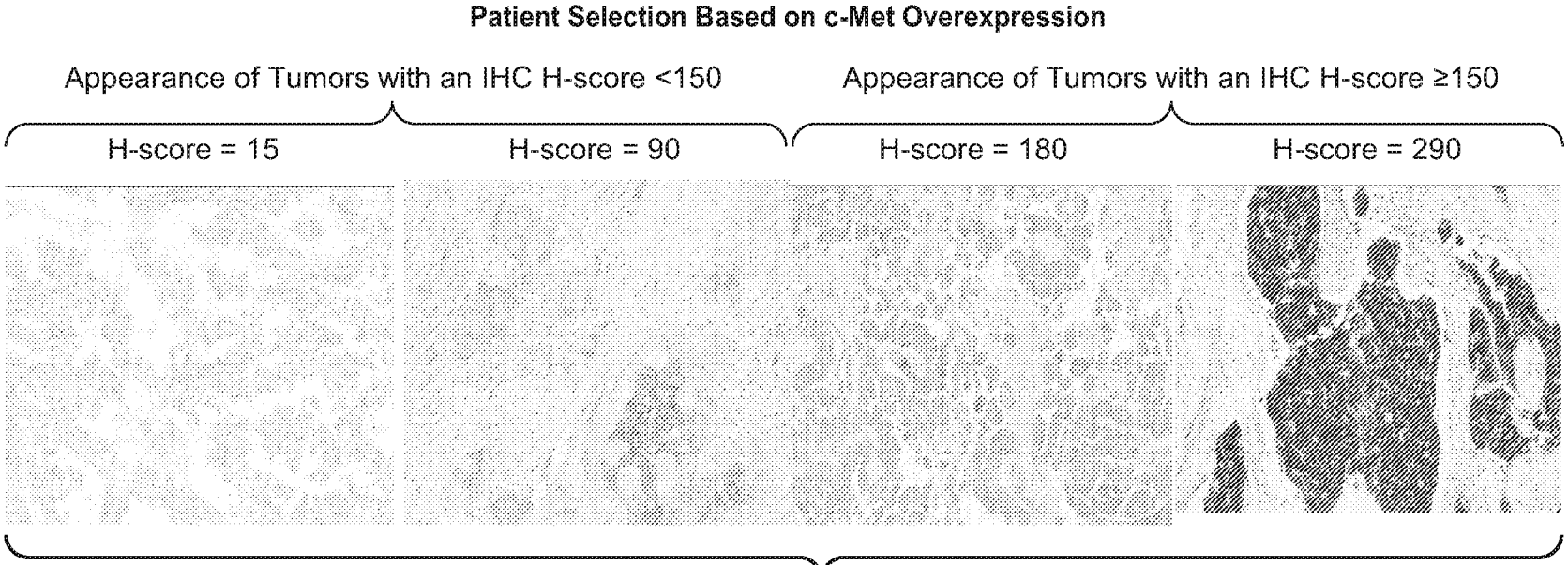
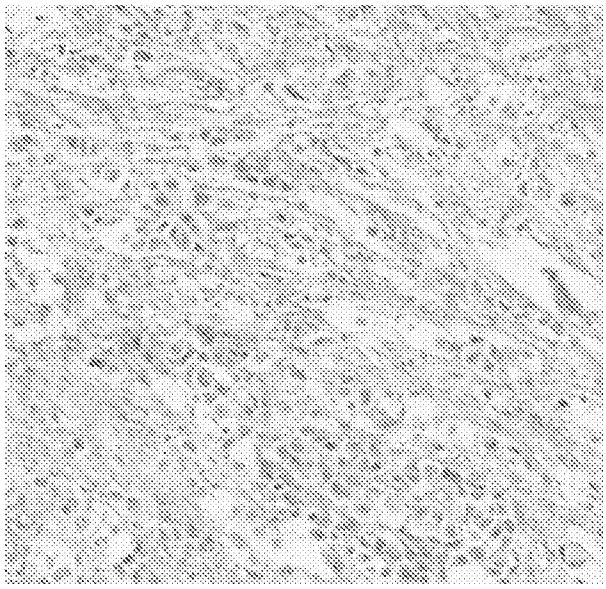

Patient Selection Based on c-Met Overexpression
Appearance of Tumors with an IHC H-score <150
Appearance of Tumors with an IHC H-score ≥150
H-score = 15
H-score = 90
H-score = 180
H-score = 290

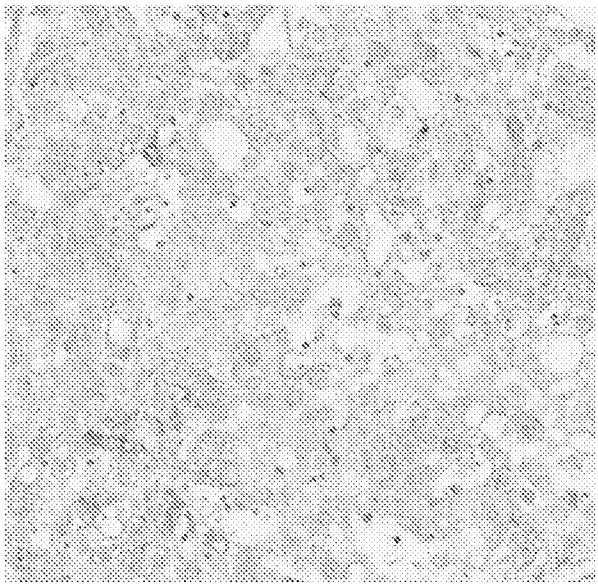
FIG. 20

Representative IHC Scores Obtained with the "cMet ABBV-ADC Staining Protocol."

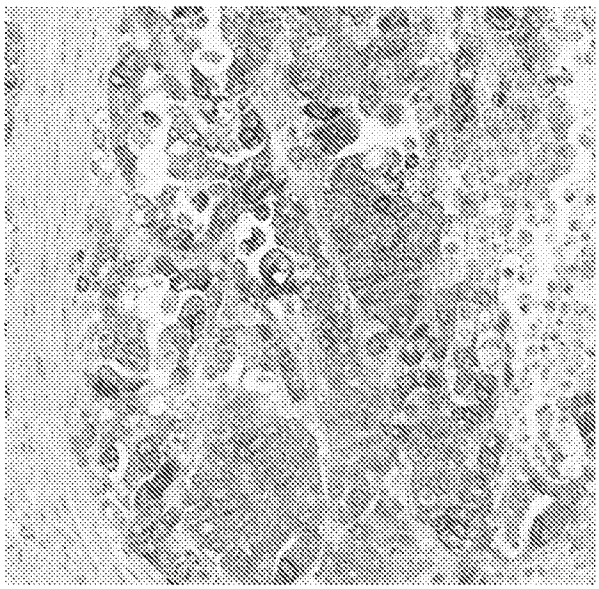
IHC 0+ Score



IHC 1+ Score



IHC 2+ Score



IHC 3+ Score



FIG. 21