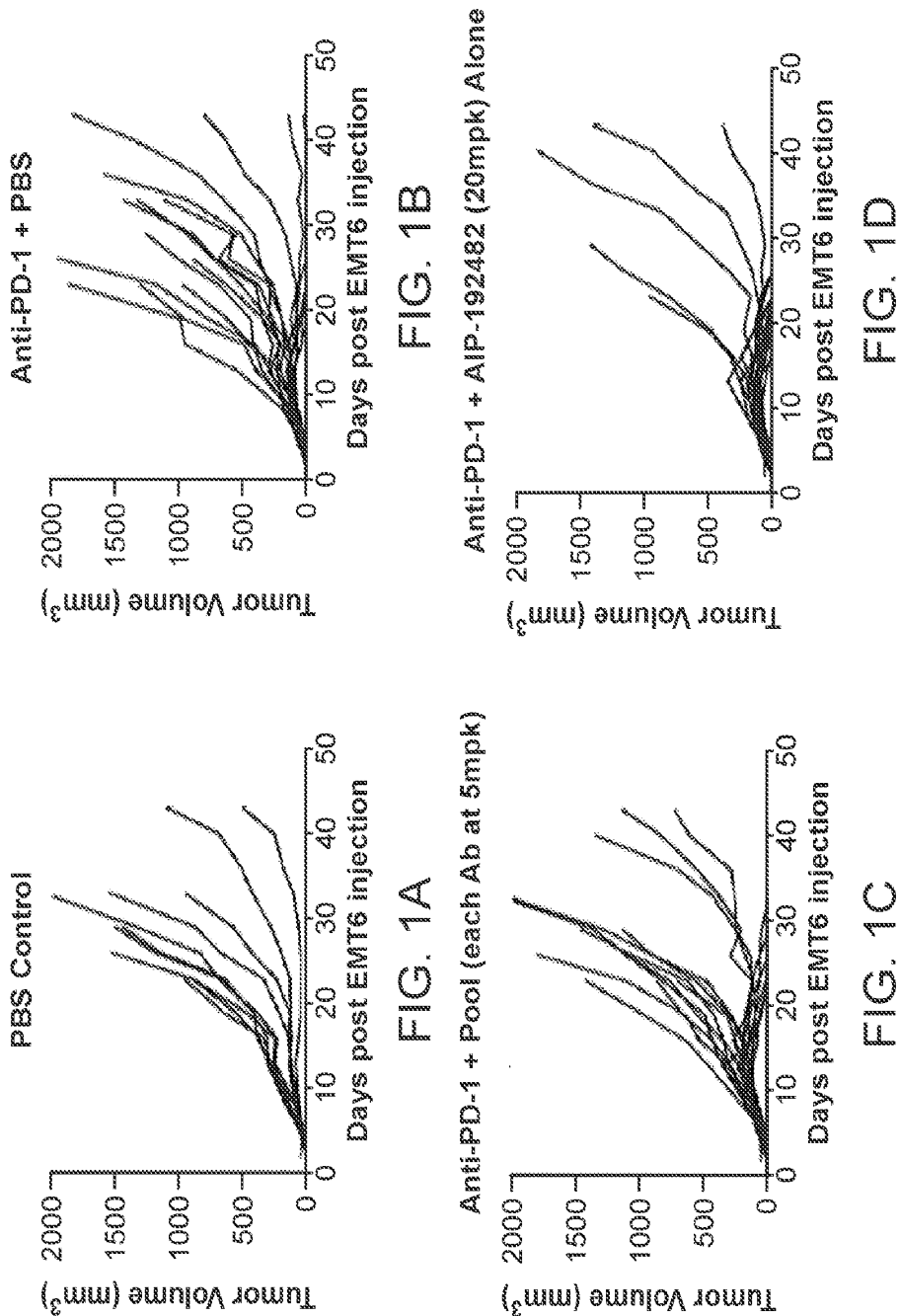


Identification of Lead Ab in Pool Screen with anti-PD1 Combination Therapy



First Generation Lead Variants in EMT6 Tumor Model-Tumor Growth

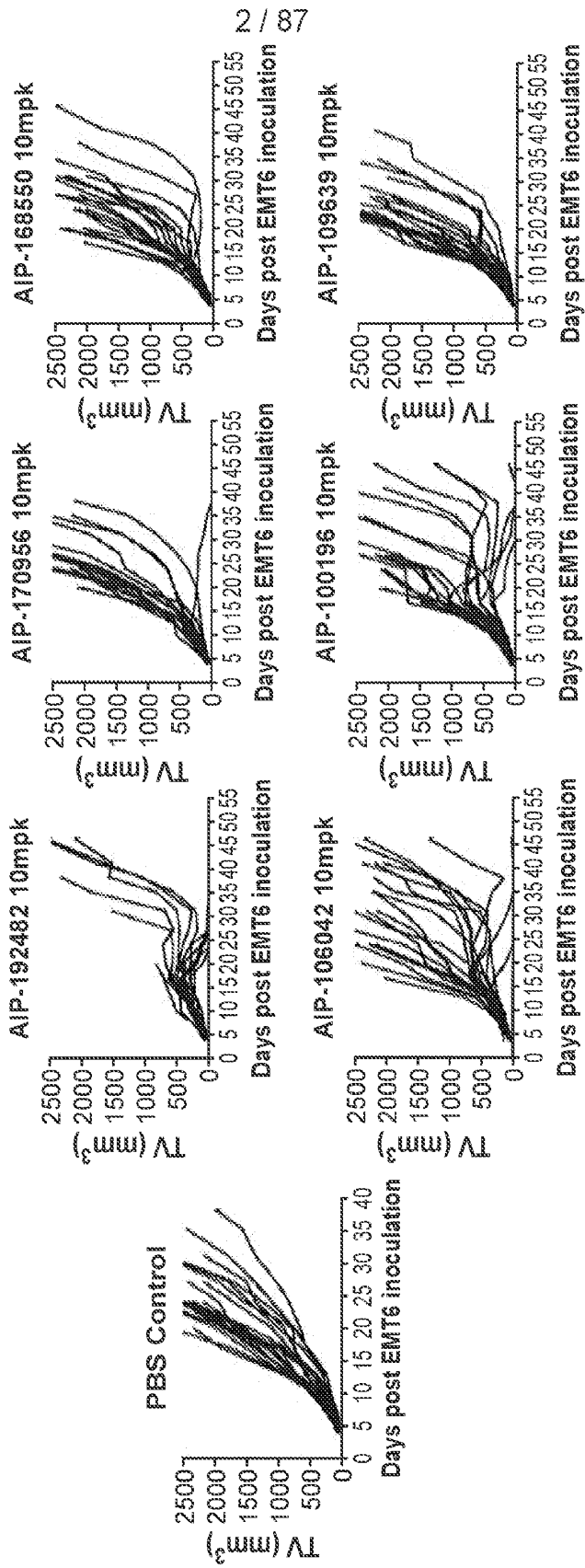


FIG. 2A

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First Generation Lead Variants in EMT6 Tumor Model-Tumor Growth

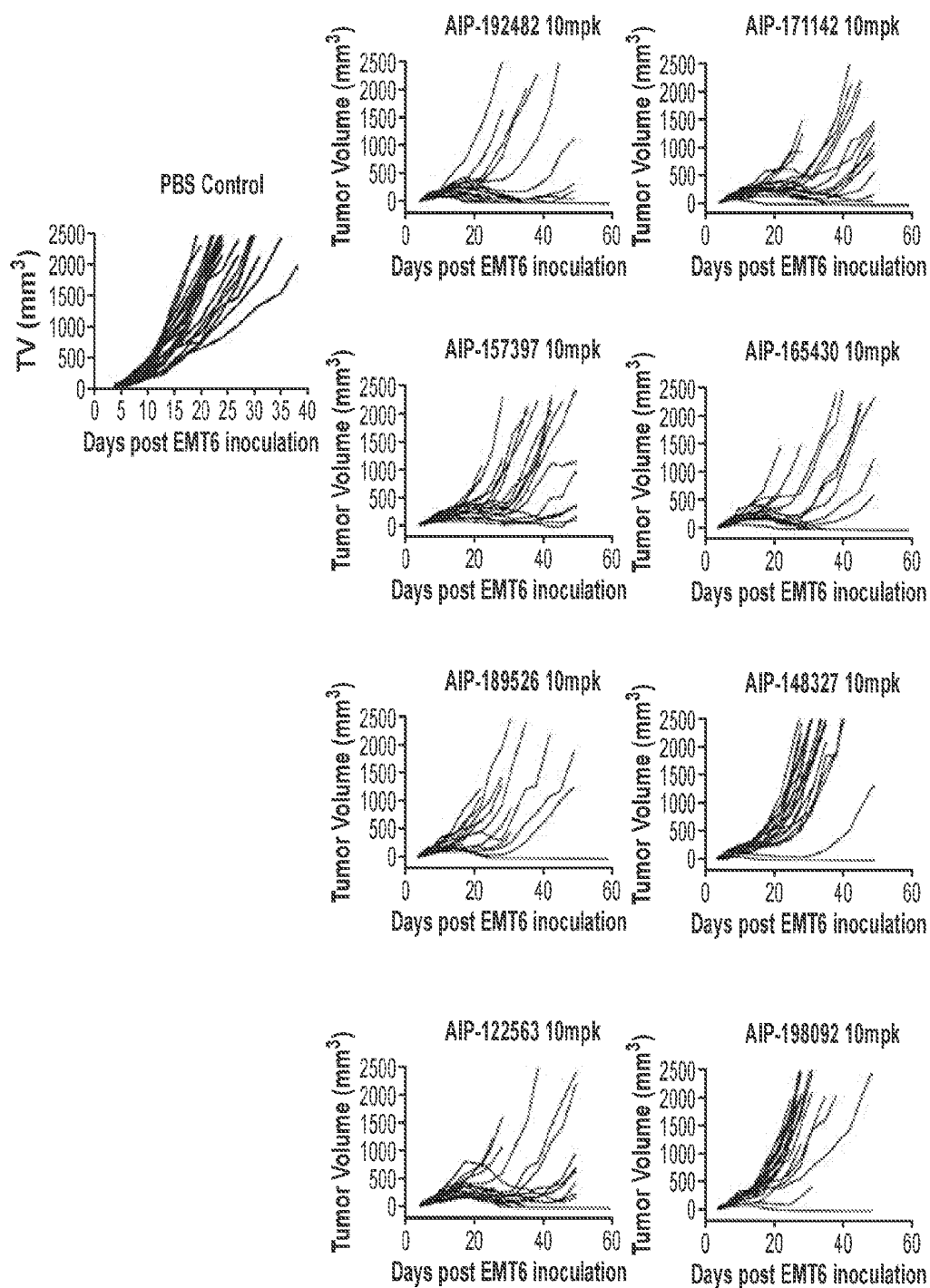


FIG. 2B

SUBSTITUTE SHEET (RULE 26)

Effect of Monotherapy Variant Dosing on Survival in EMT6 Tumor Model

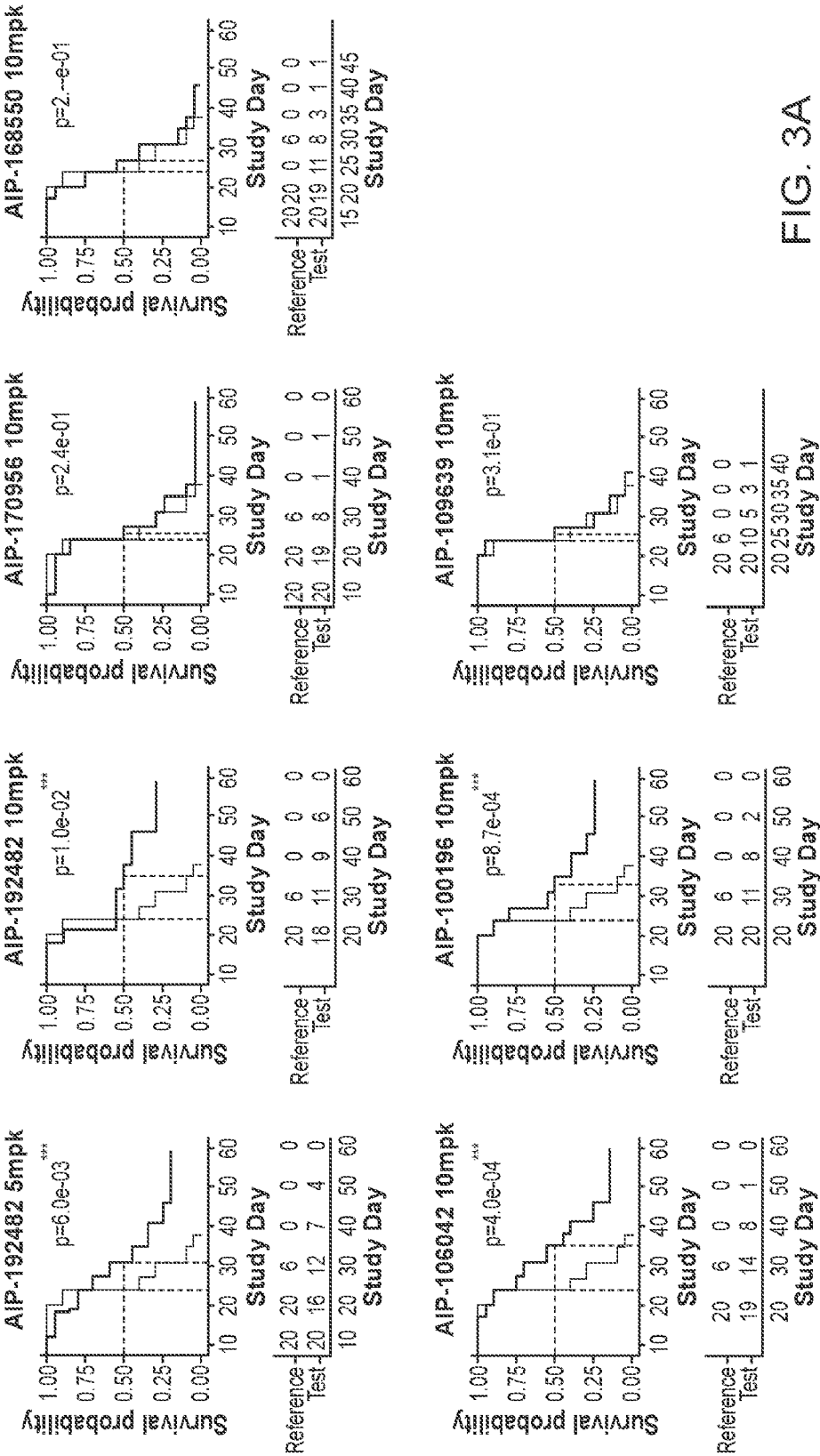


FIG. 3A

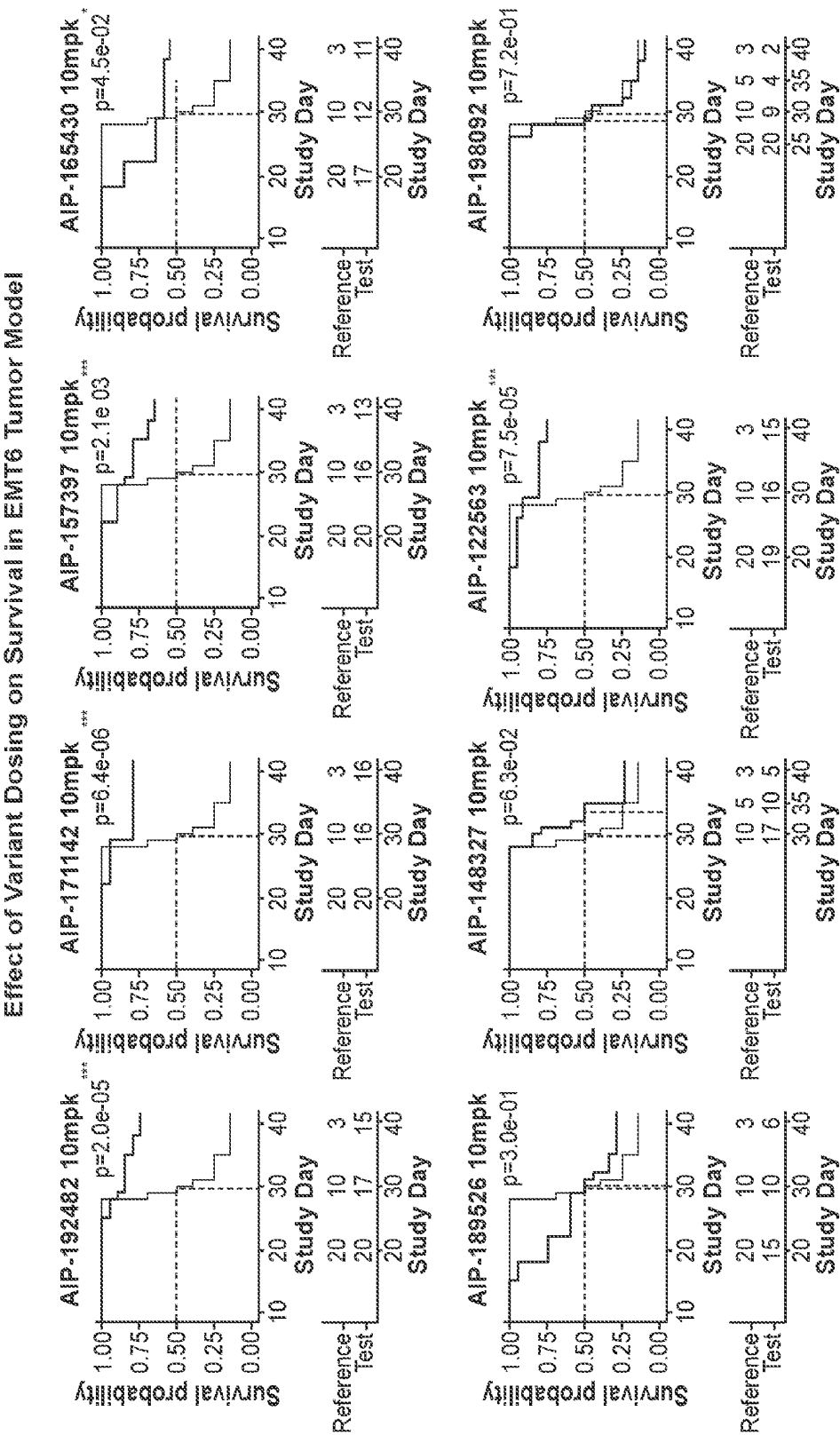


FIG. 3B

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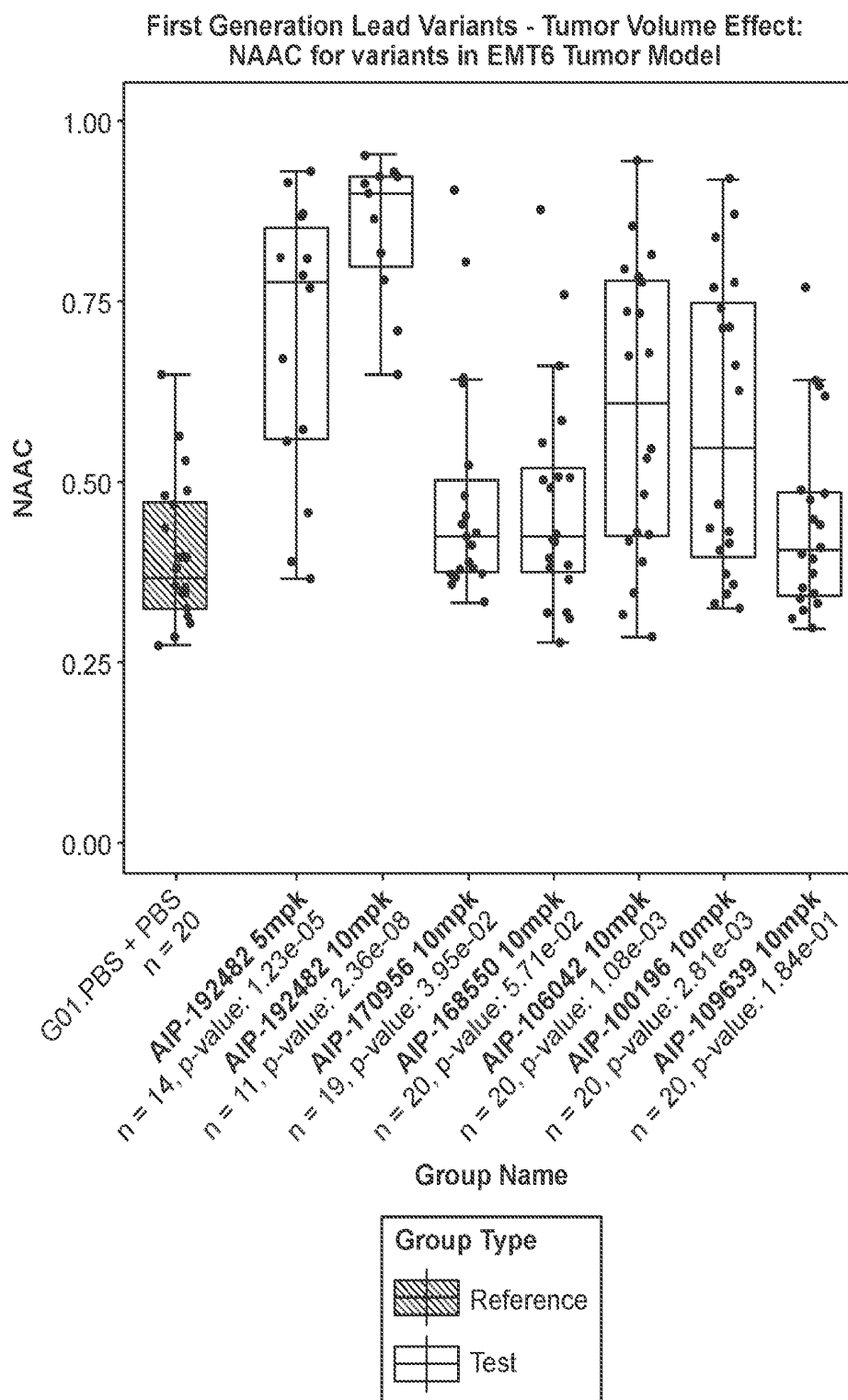


FIG. 4A

SUBSTITUTE SHEET (RULE 26)

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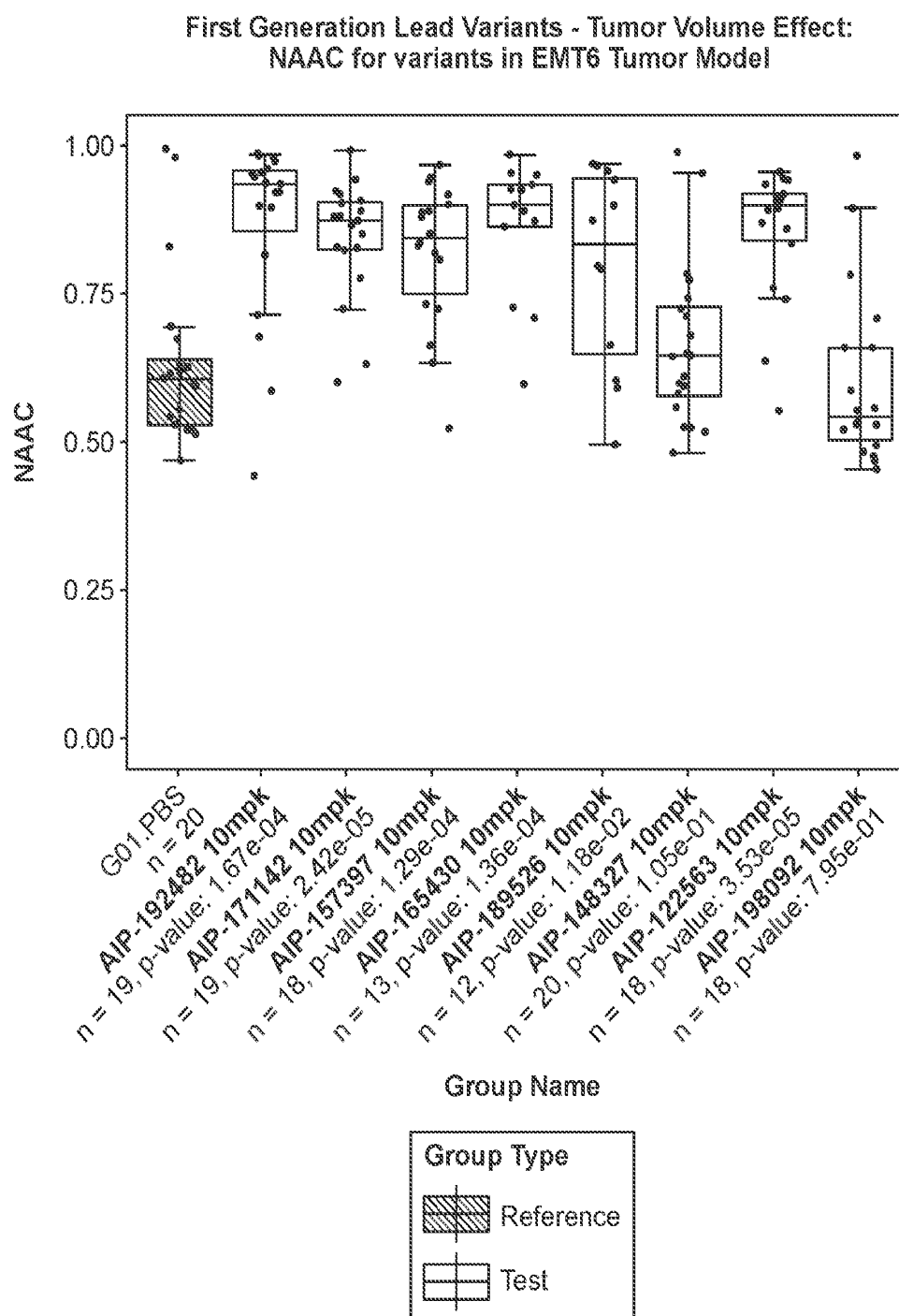


FIG. 4B

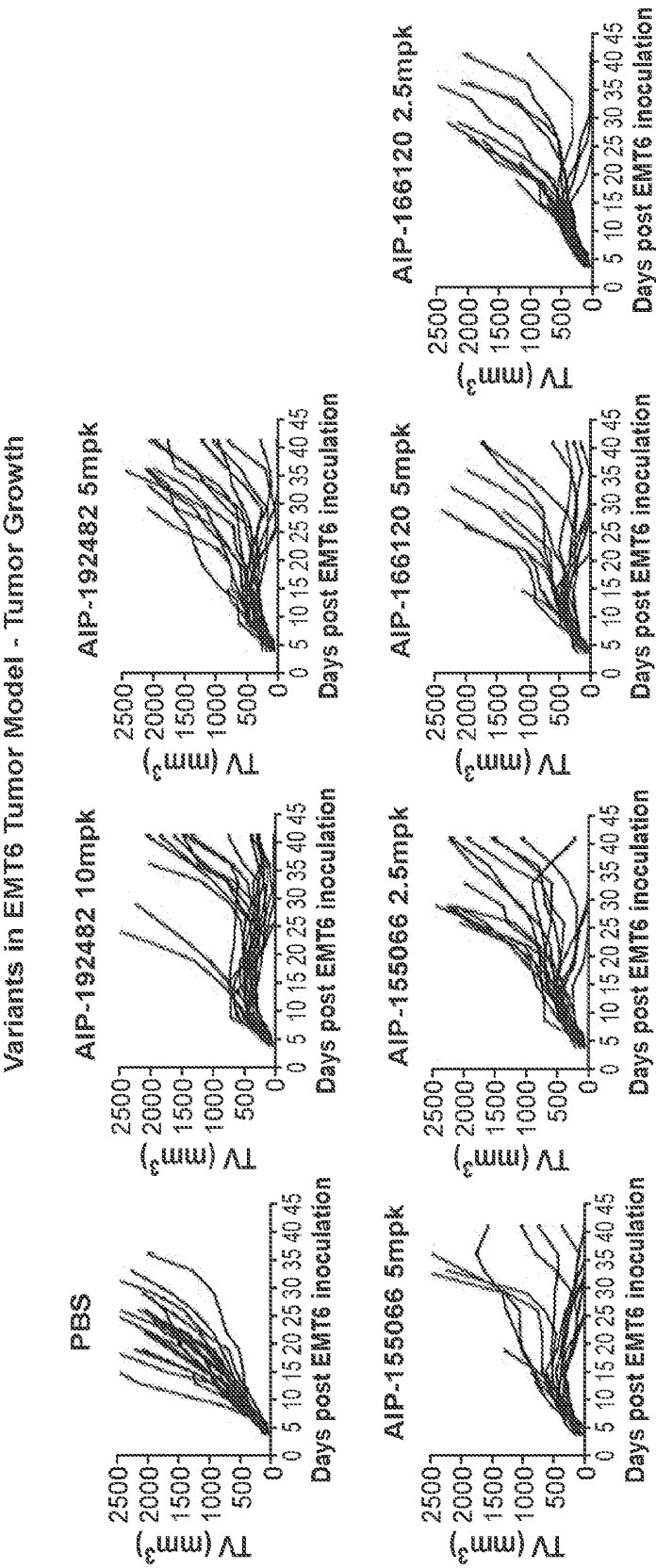


FIG. 5A

Variants in EMT6 Tumor Model - Tumor Growth

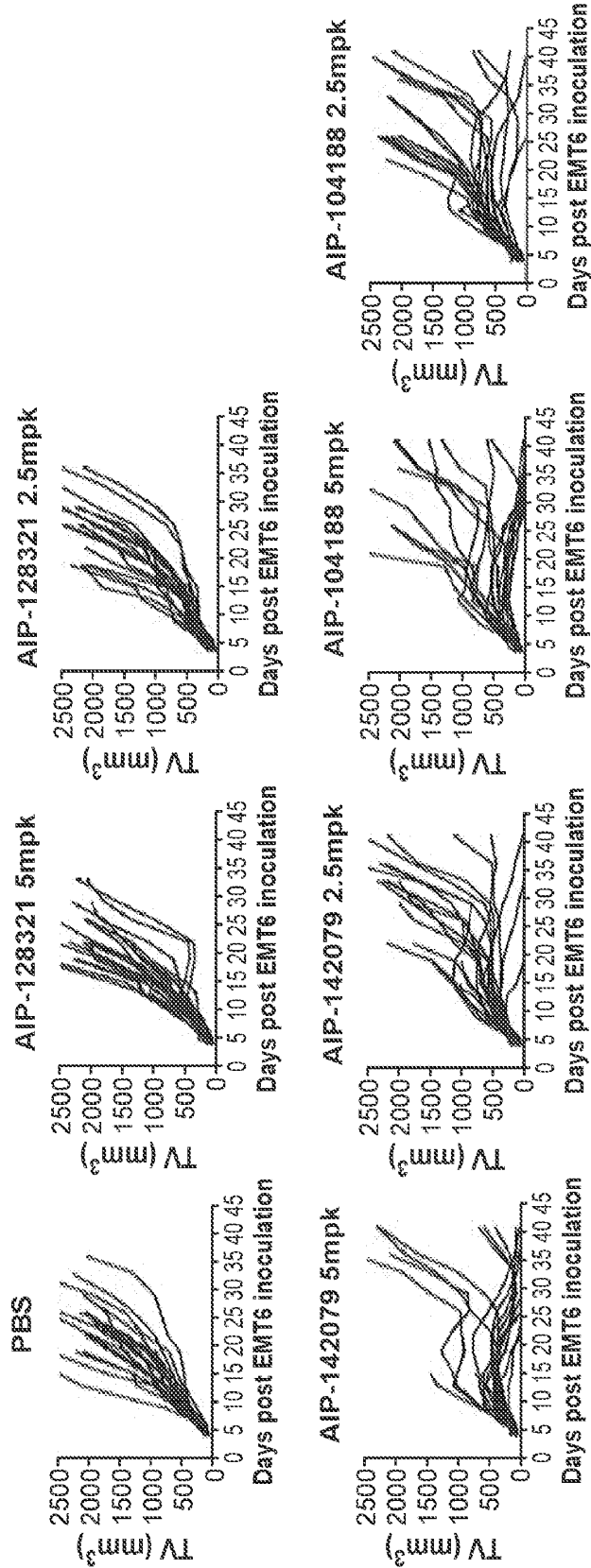


FIG. 5B

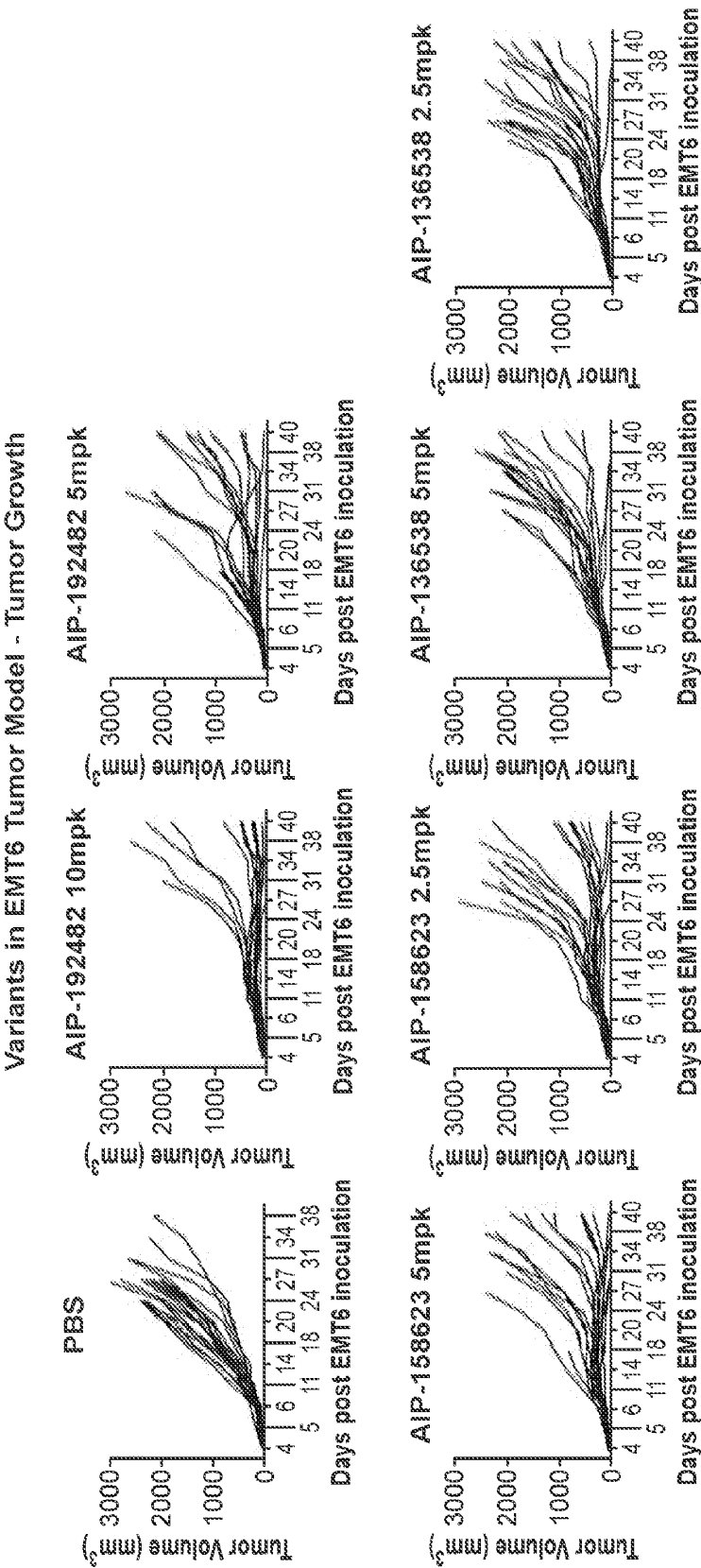


FIG. 5C

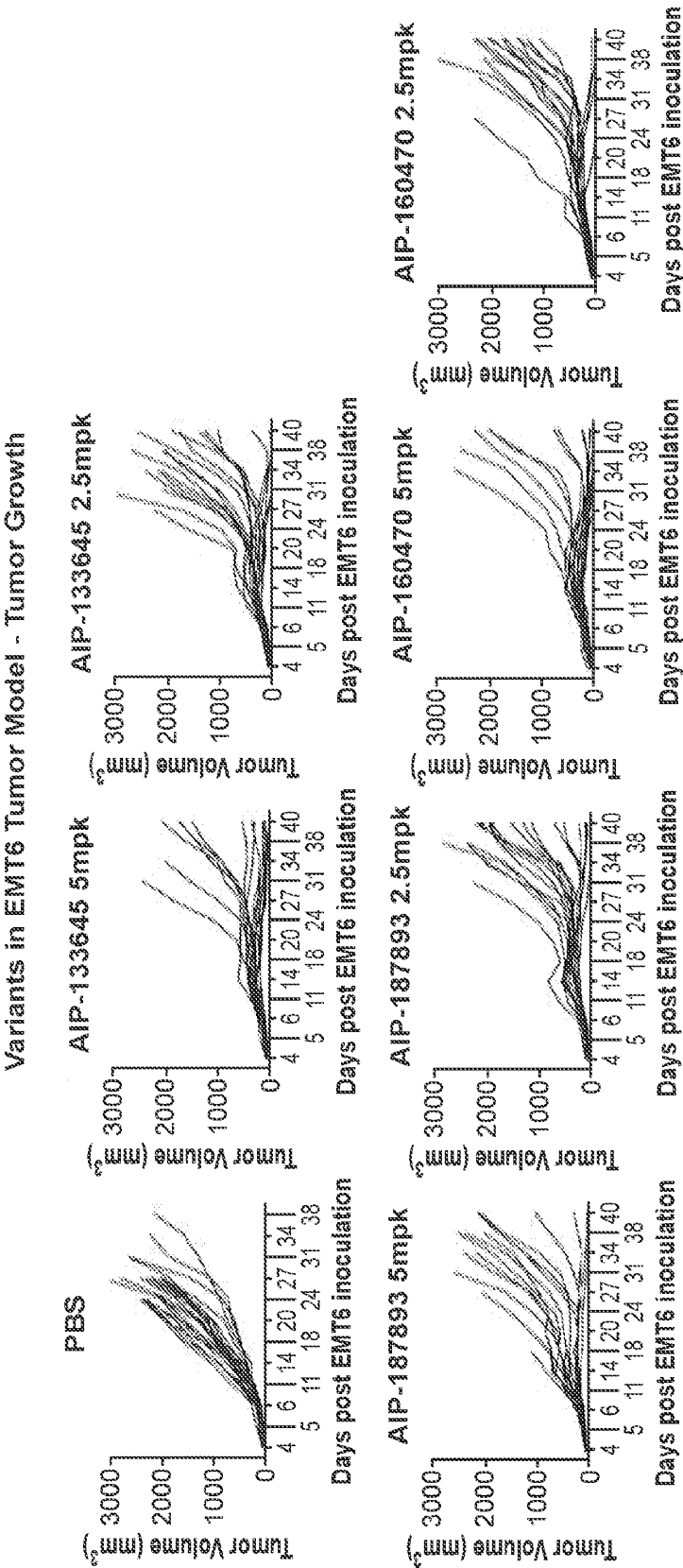


FIG. 5D

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Effect on Survival in EMT6 Tumor Model

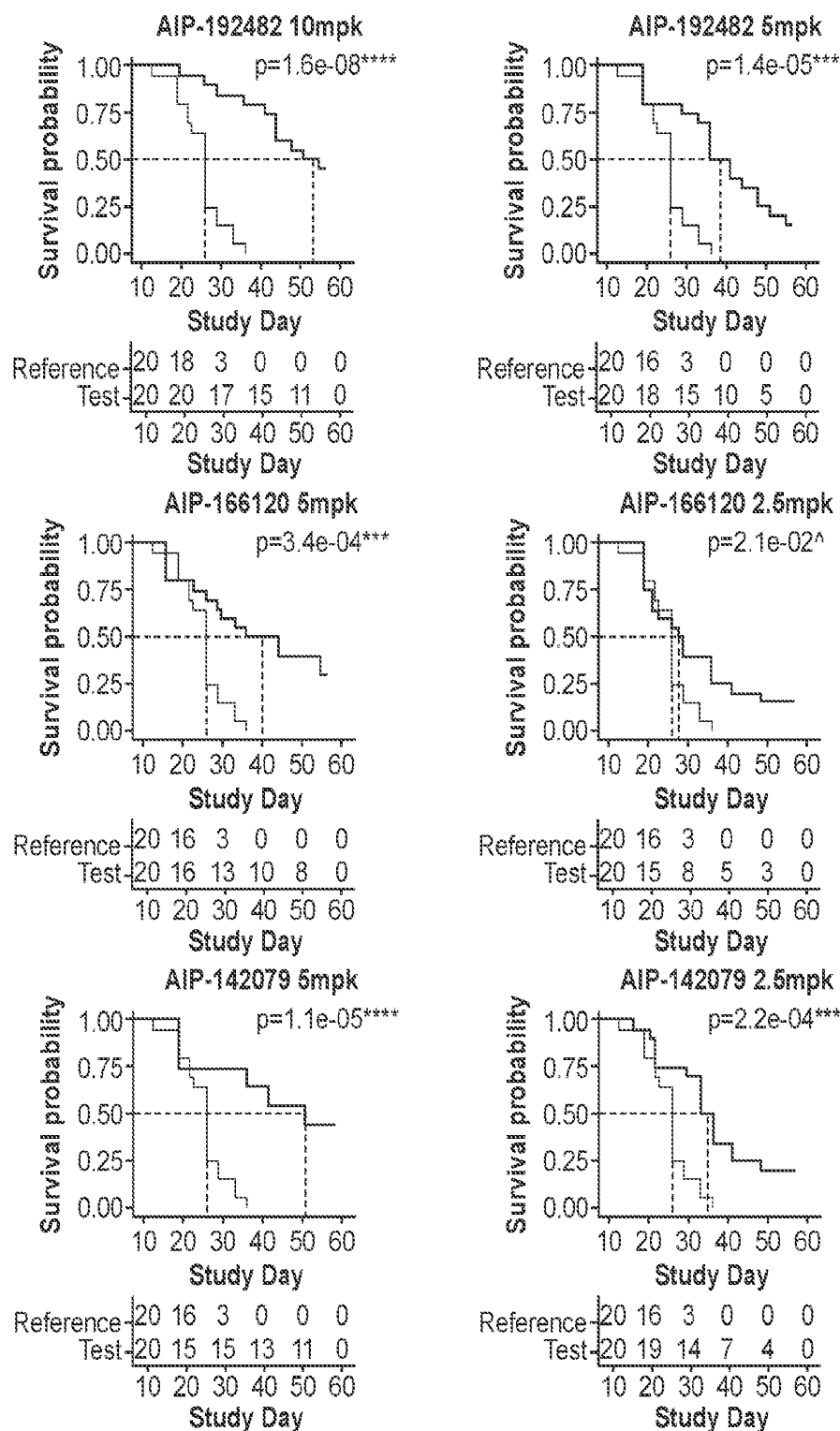


FIG. 6A

SUBSTITUTE SHEET (RULE 26)

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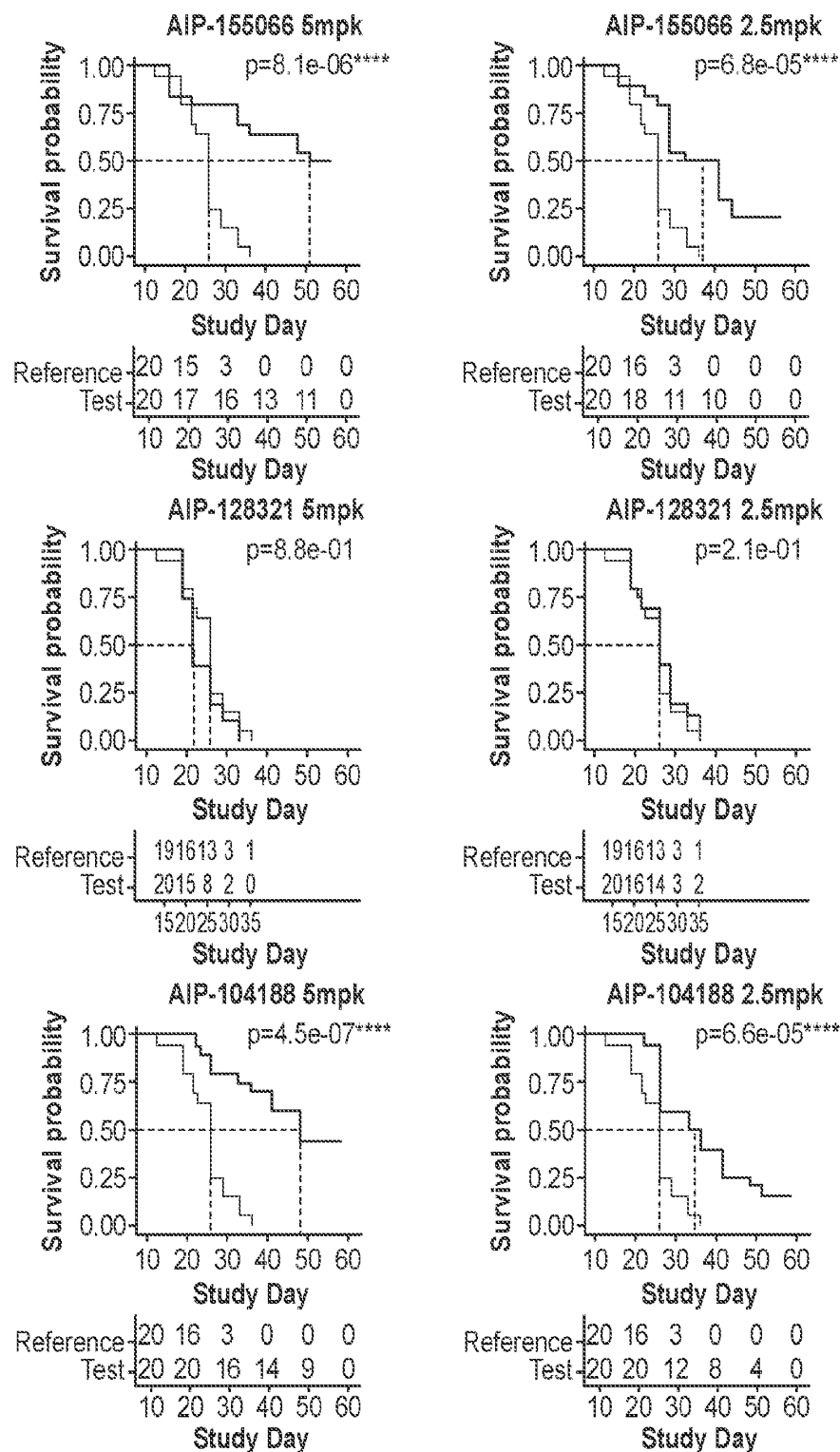


FIG. 6A (Cont.)

SUBSTITUTE SHEET (RULE 26)

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Effect on Survival in EMT6 Tumor Model

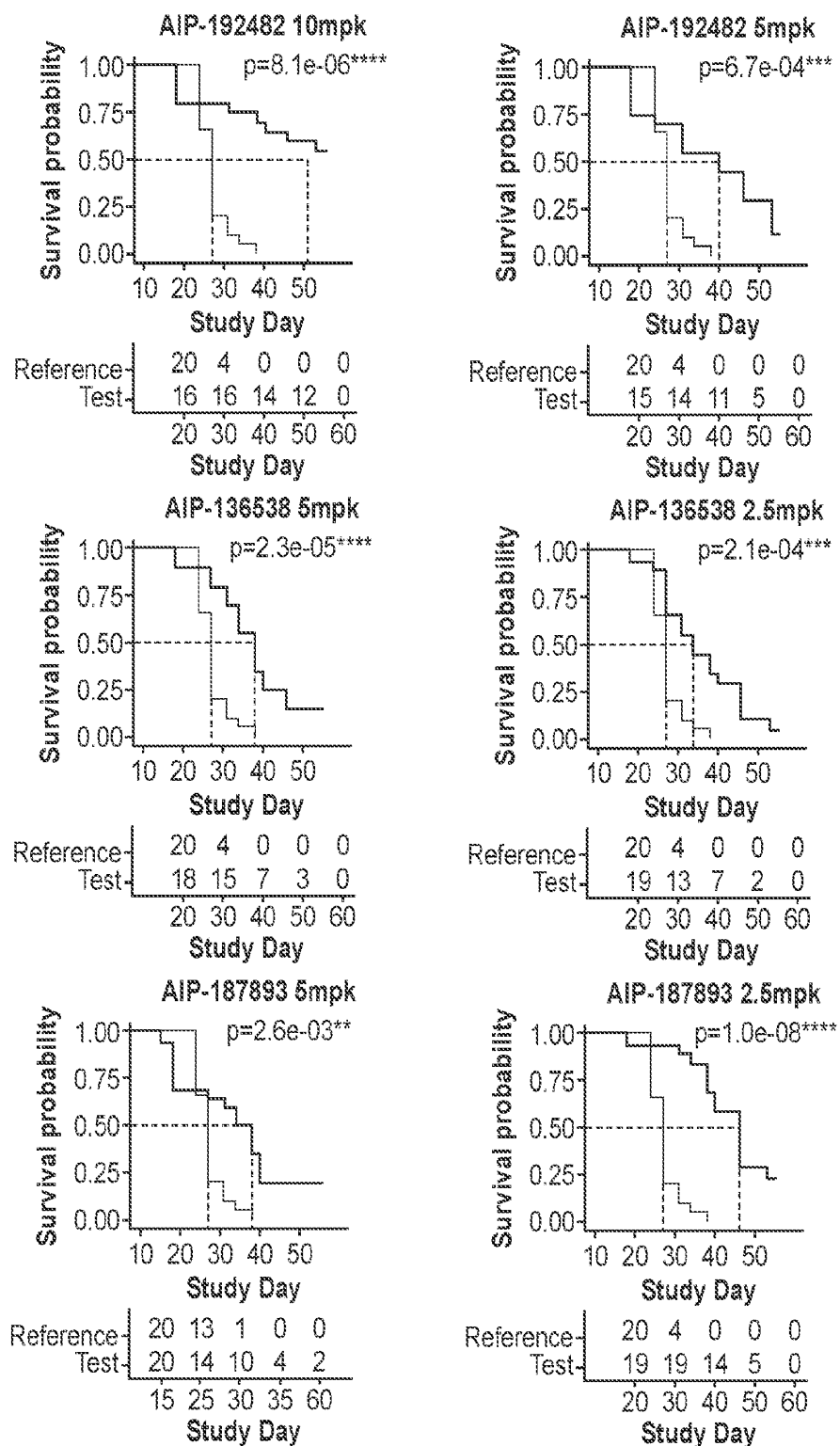


FIG. 6B

SUBSTITUTE SHEET (RULE 26)

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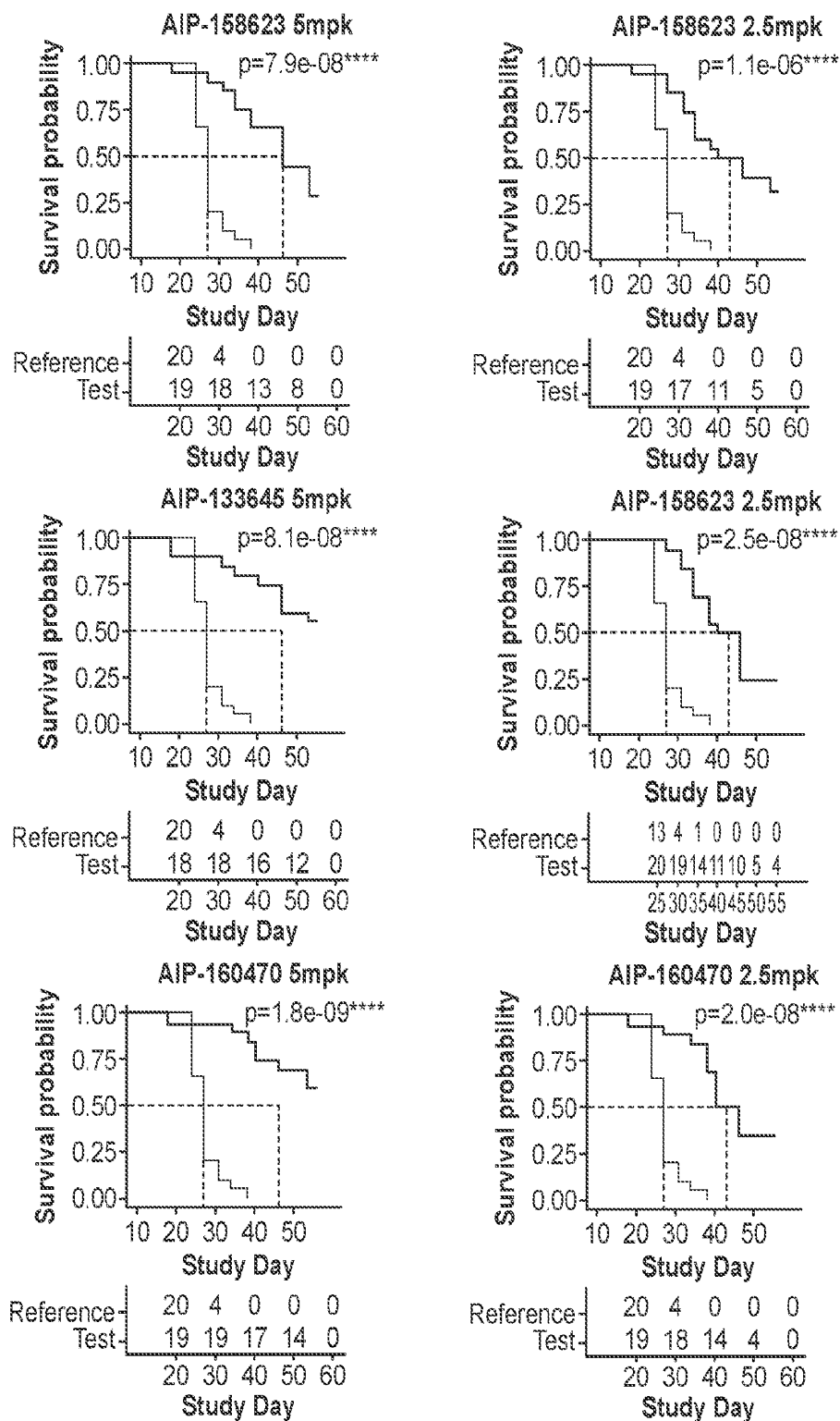


FIG. 6B (Cont.)

SUBSTITUTE SHEET (RULE 26)

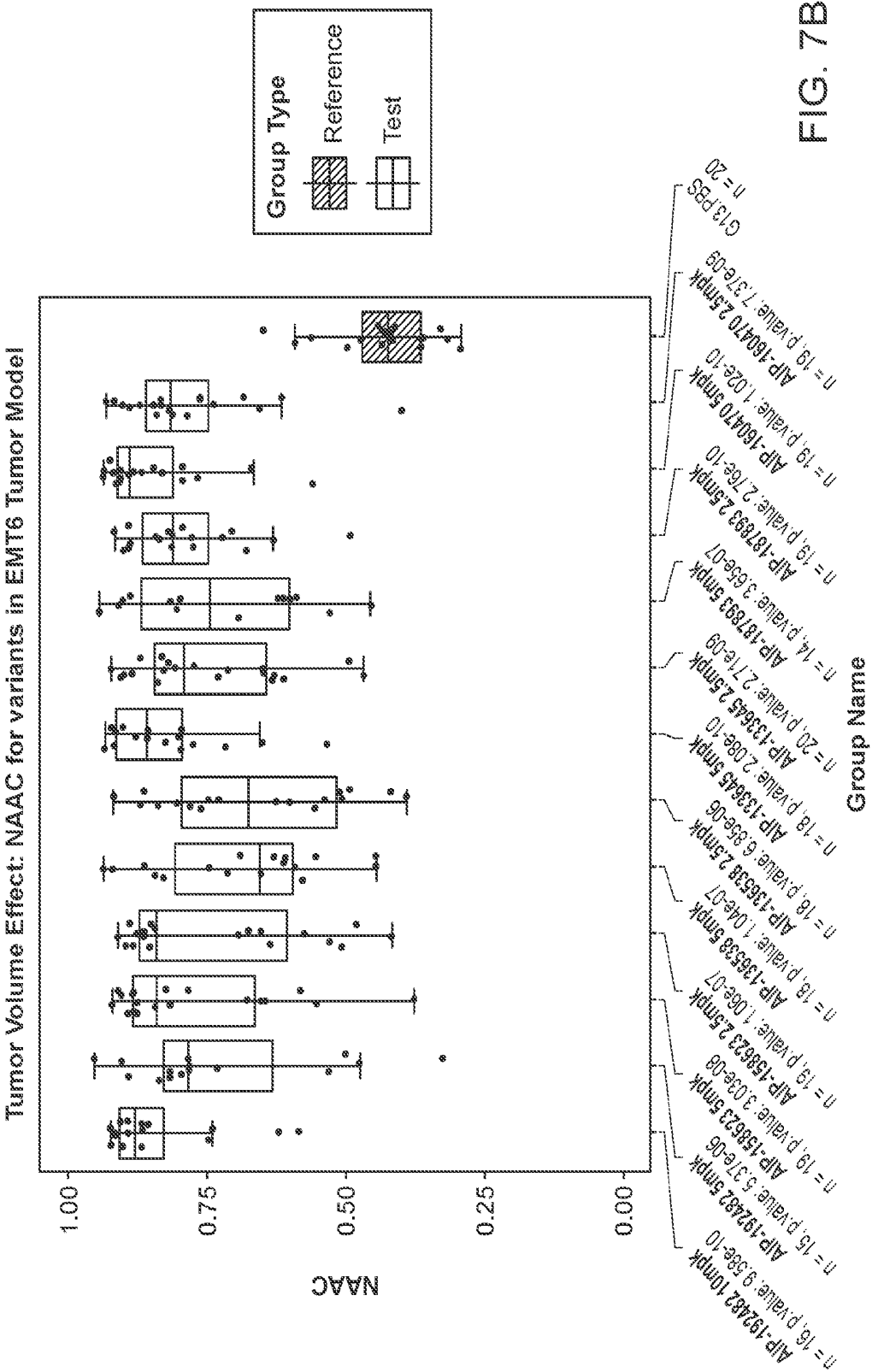


FIG. 7B

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Stay Design

Groups		#mice	Article 1				Article 2			
				mpk	Frequency	Route		mpk	Frequency	Route
1	PD1 + AIP-192482	20	PD-1 (RMP1-14)	10	TWx2	i.p.	AIP-192482	5	TWx3.5	i.p.
2	PD1 + AIP-192482	20	PD-1 (RMP1-14)	10	TWx2	i.p.	AIP-192482	10	TWx3.5	i.p.
3	PD1 + AIP-133645	20	PD-1 (RMP1-14)	10	TWx2	i.p.	AIP-133645	5	TWx3.5	i.p.
4	PD1 + AIP-133645	20	PD-1 (RMP1-14)	10	TWx2	i.p.	AIP-133645	2.5	TWx3.5	i.p.
5	PD1 + AIP-160470	20	PD-1 (RMP1-14)	10	TWx2	i.p.	AIP-160470	5	TWx3.5	i.p.
6	PD1 + AIP-160470	20	PD-1 (RMP1-14)	10	TWx2	i.p.	AIP-160470	2.5	TWx3.5	i.p.
7	PBS + AIP-192482	20	Vehicle	0	TWx2	i.p.	AIP-192482	5	TWx3.5	i.p.
8	PBS + AIP-192482	20	Vehicle	0	TWx2	i.p.	AIP-192482	10	TWx3.5	i.p.
9	PBS + AIP-133645	20	Vehicle	0	TWx2	i.p.	AIP-133645	5	TWx3.5	i.p.
10	PBS + AIP-133645	20	Vehicle	0	TWx2	i.p.	AIP-133645	2.5	TWx3.5	i.p.
11	PBS + AIP-160470	20	Vehicle	0	TWx2	i.p.	AIP-160470	5	TWx3.5	i.p.
12	PBS + AIP-160470	20	Vehicle	0	TWx2	i.p.	AIP-160470	2.5	TWx3.5	i.p.
13	AIP-192482 (CHO cells)	20	Vehicle	0	TWx2	i.p.	AIP-192482	10	TWx3.5	i.p.
14	PD1 + PBS	20	PD-1 (RMP1-14)	10	TWx2	i.p.	Vehicle	0	TWx3.5	i.p.
15	PBS + PBS	20	Vehicle	0	TWx2	i.p.	Vehicle	0	TWx3.5	i.p.

FIG. 8

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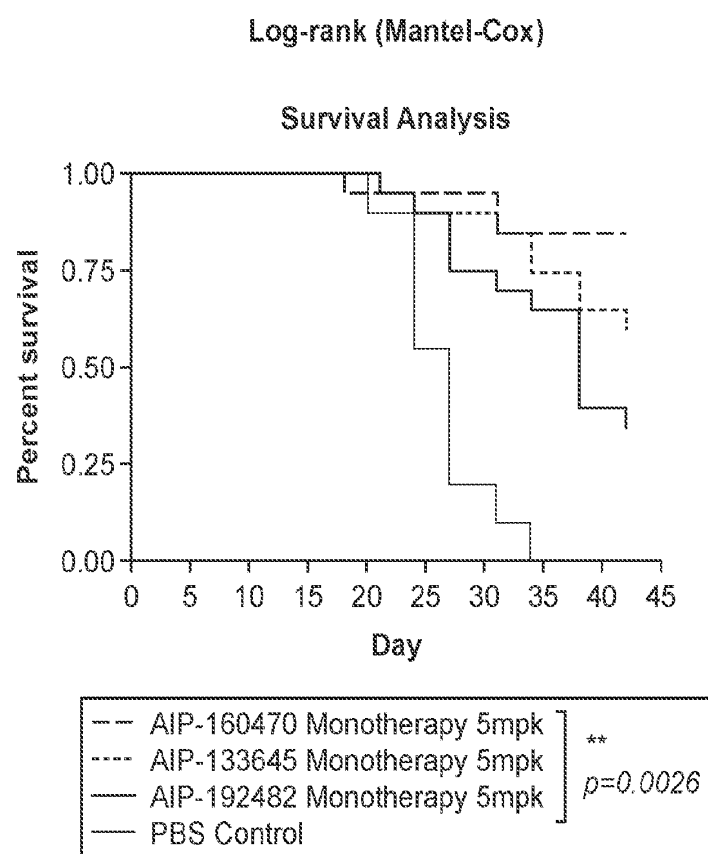


FIG. 9

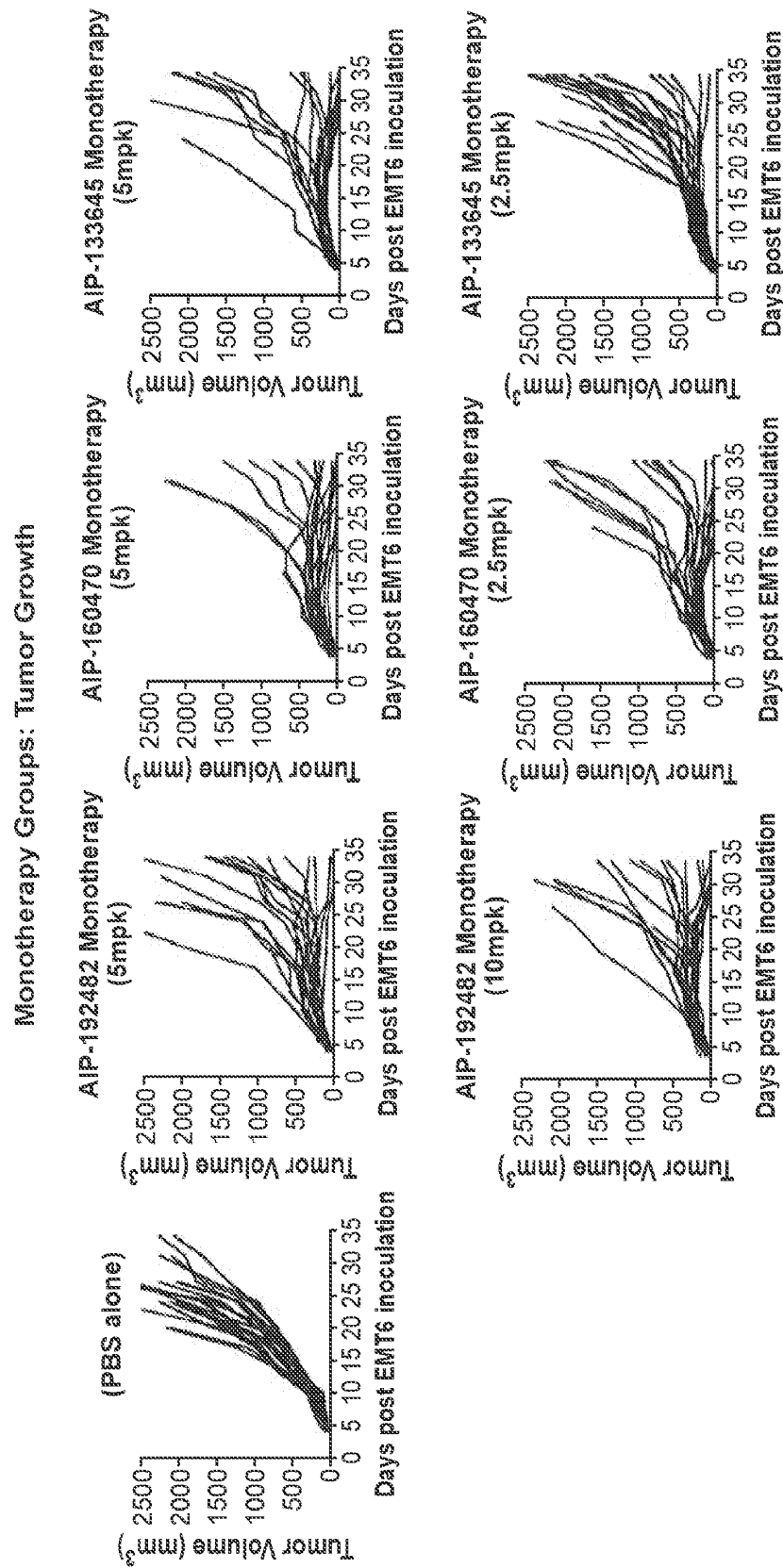


FIG. 10

Monotherapy Groups: Survival Analysis

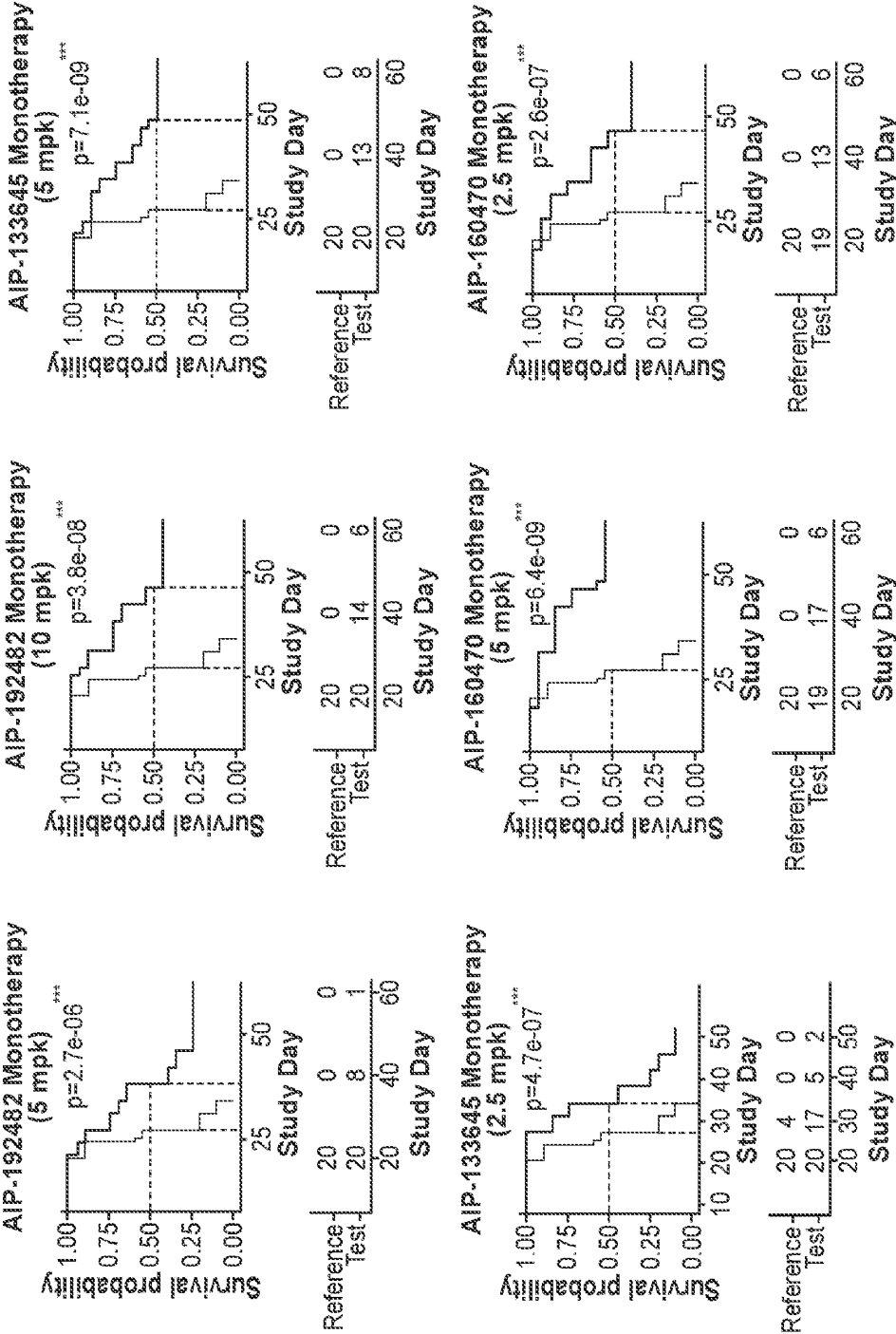


FIG. 11

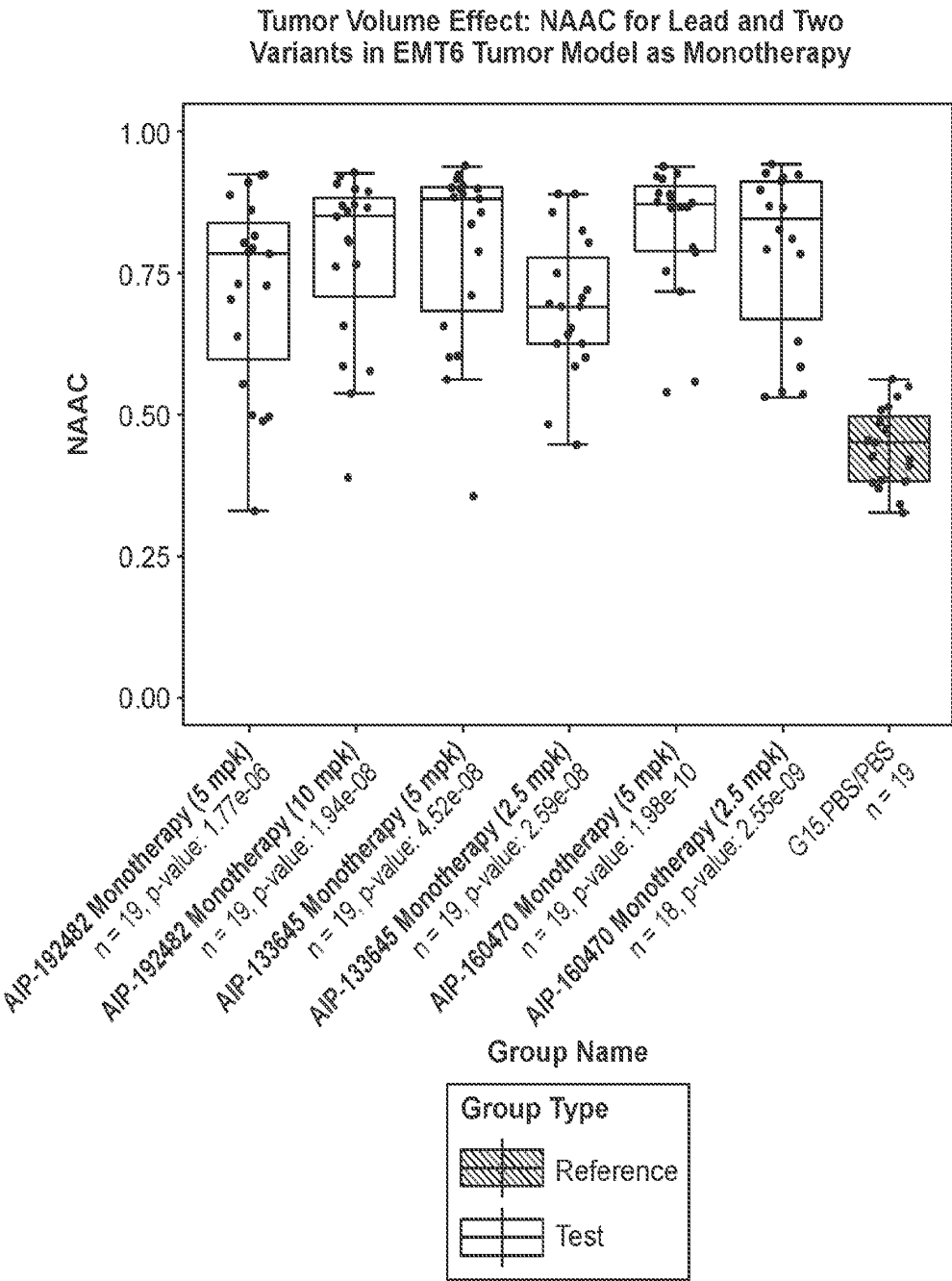


FIG. 12

Anti-PD1+ Lead or Variant. Combination Therapy in EMT6 Tumor Model-Tumor Growth

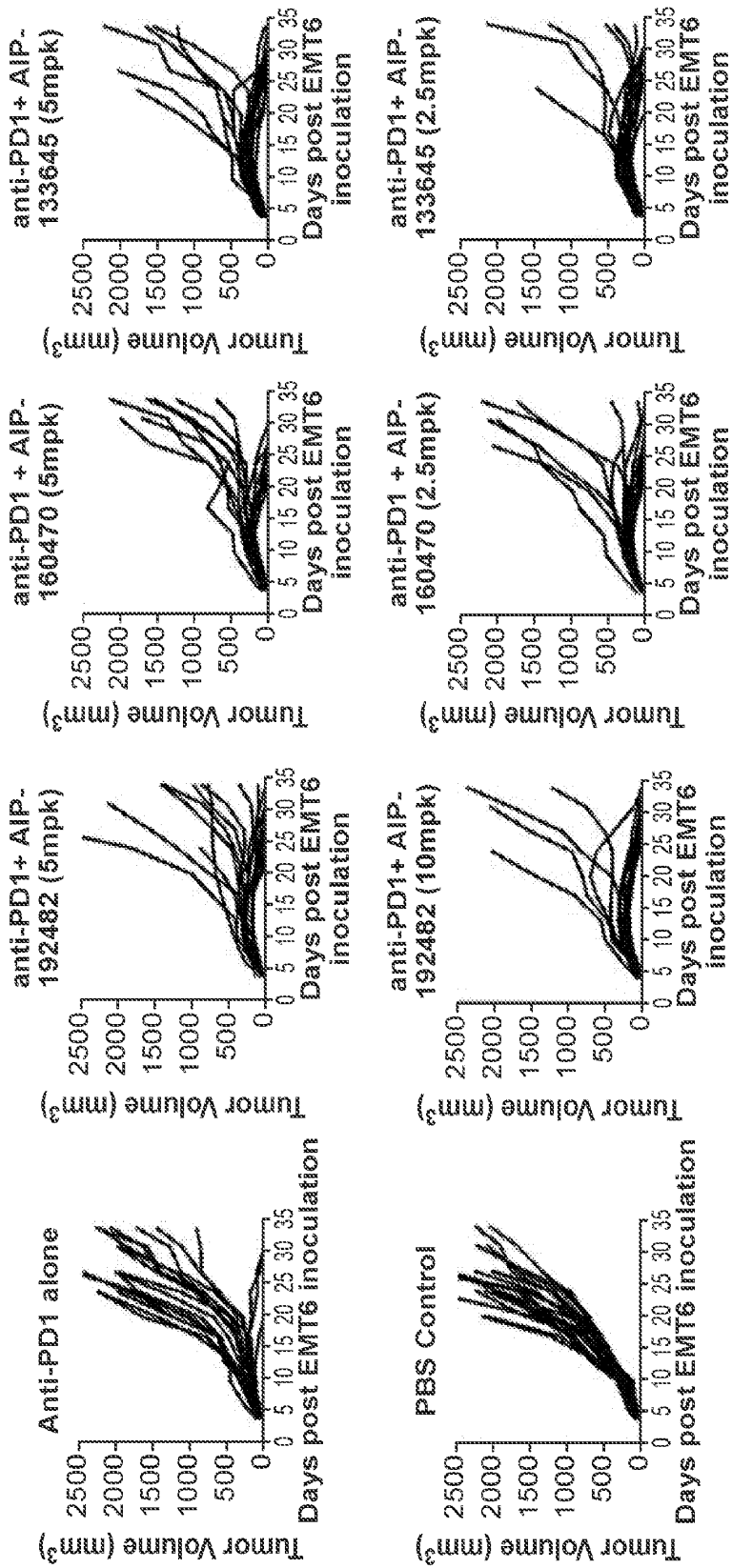


FIG. 13

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Anti-PD1+ Lead or Variant Combination Therapy in EMT6 Tumor Model-Survival

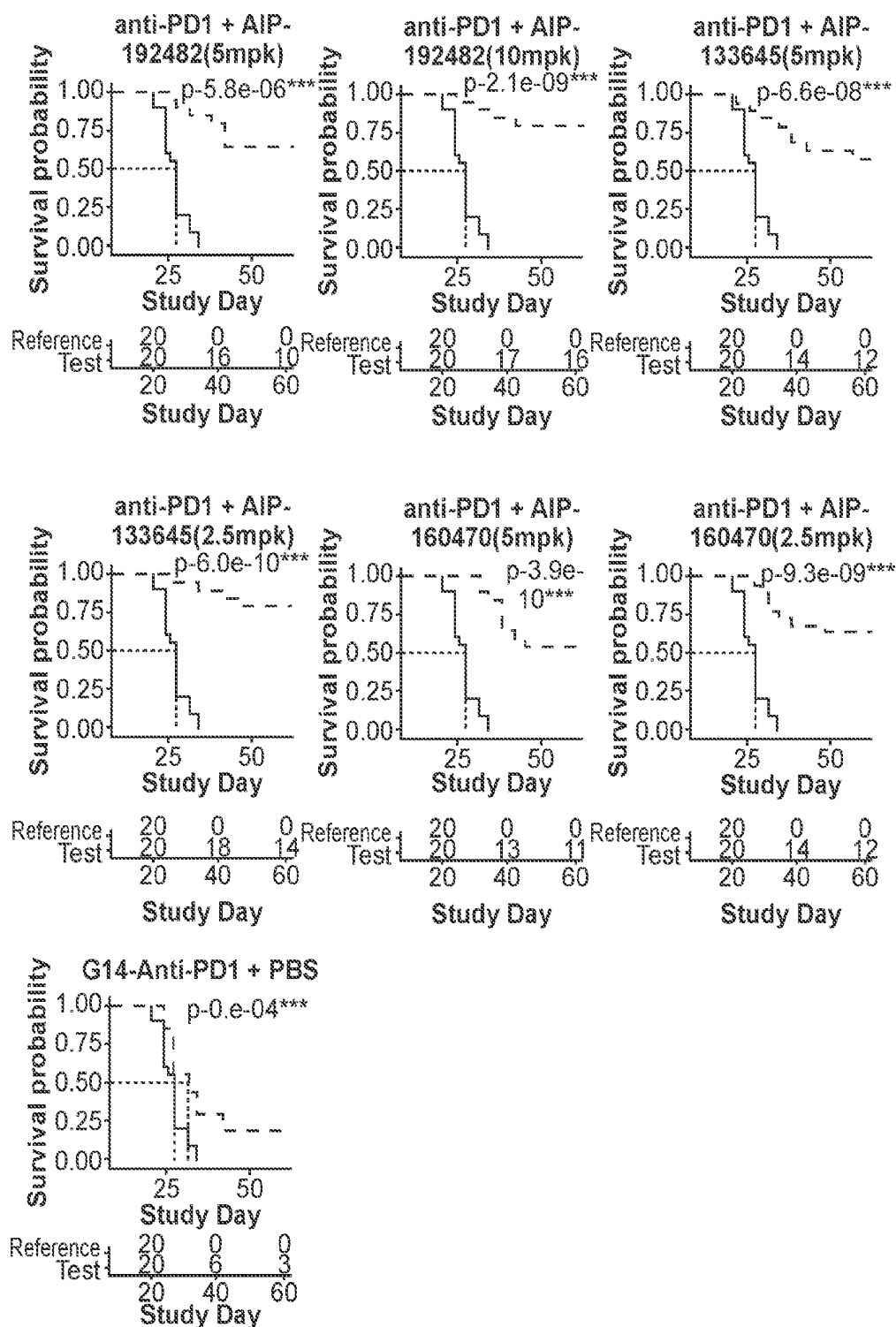


FIG. 14

SUBSTITUTE SHEET (RULE 26)

Tumor Volume Effect: NAAC for Lead/Variants in EMT6 Tumor Model in Combination with Anti-PD-1 Antibody.

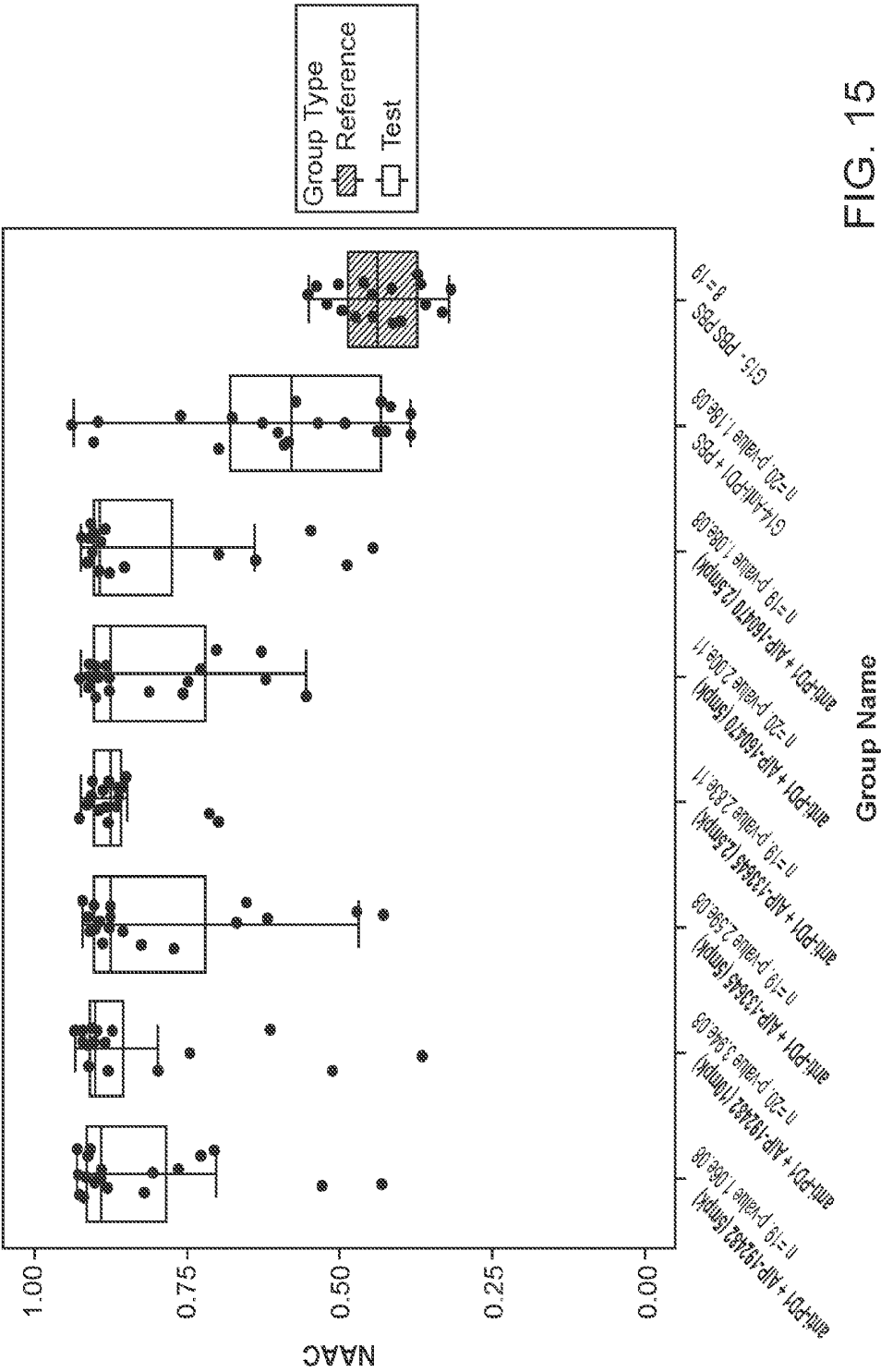


FIG. 15

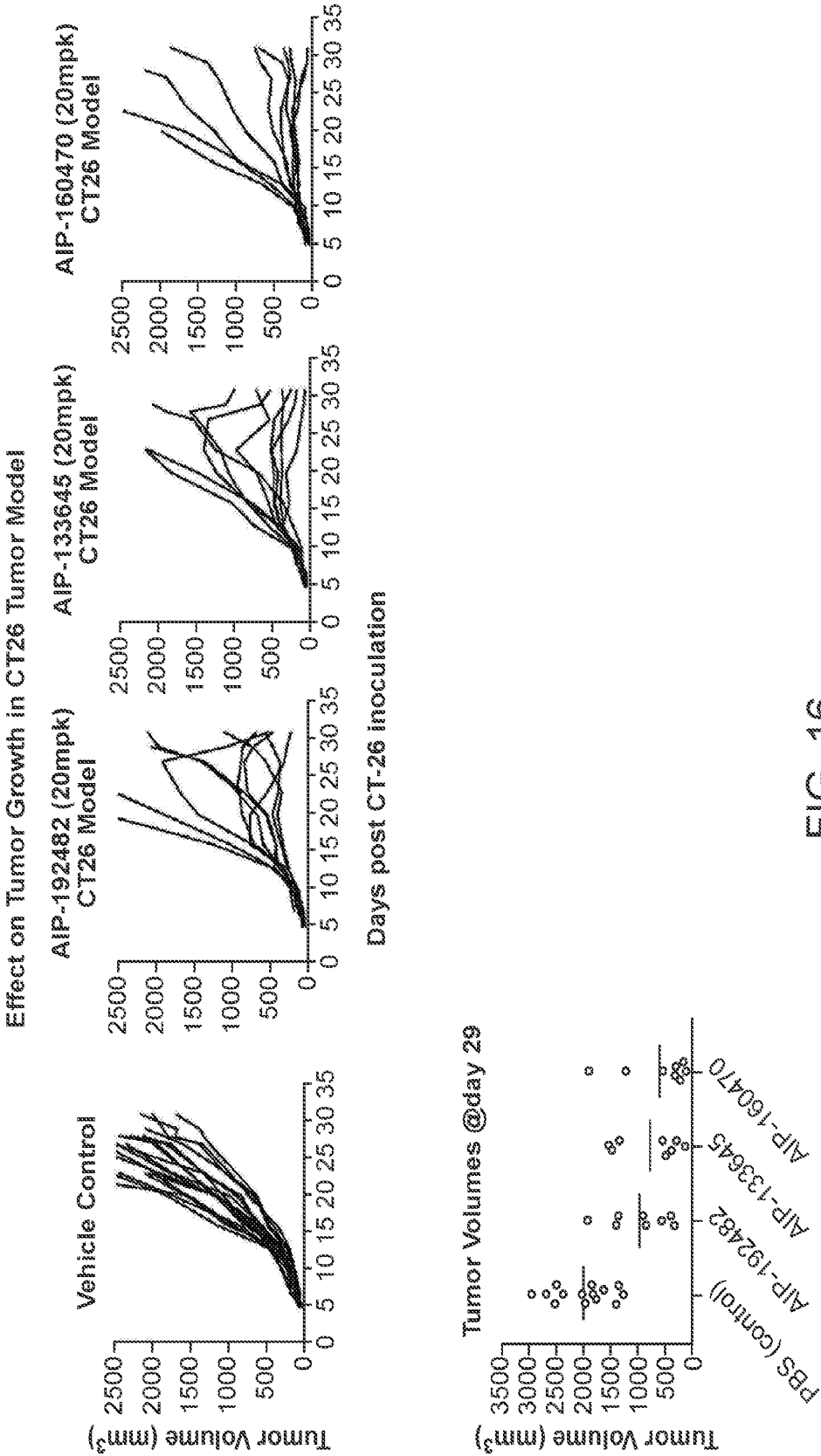


FIG. 16

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Effect on Survival in CT26 Tumor Model

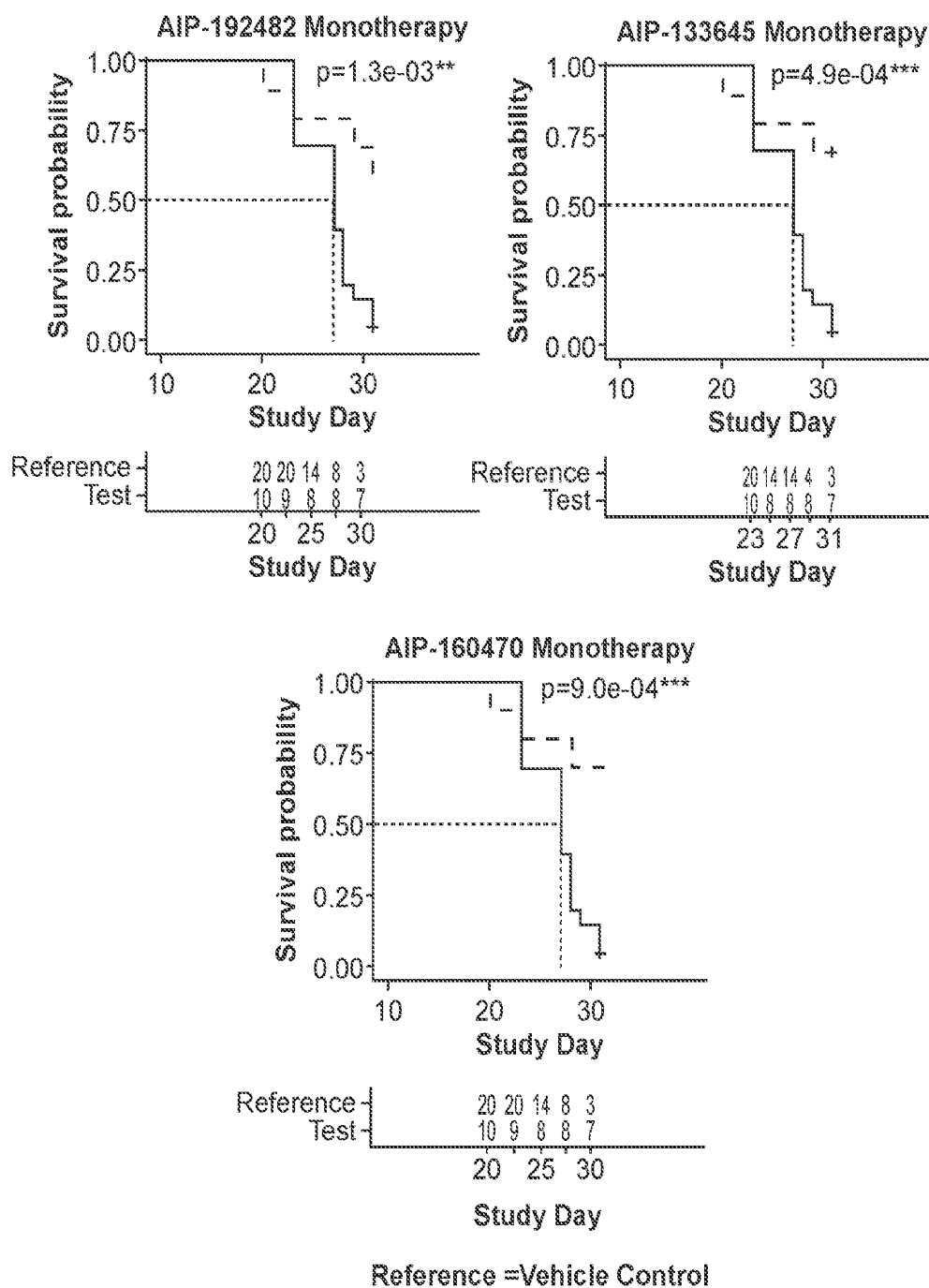


FIG. 17

SUBSTITUTE SHEET (RULE 26)

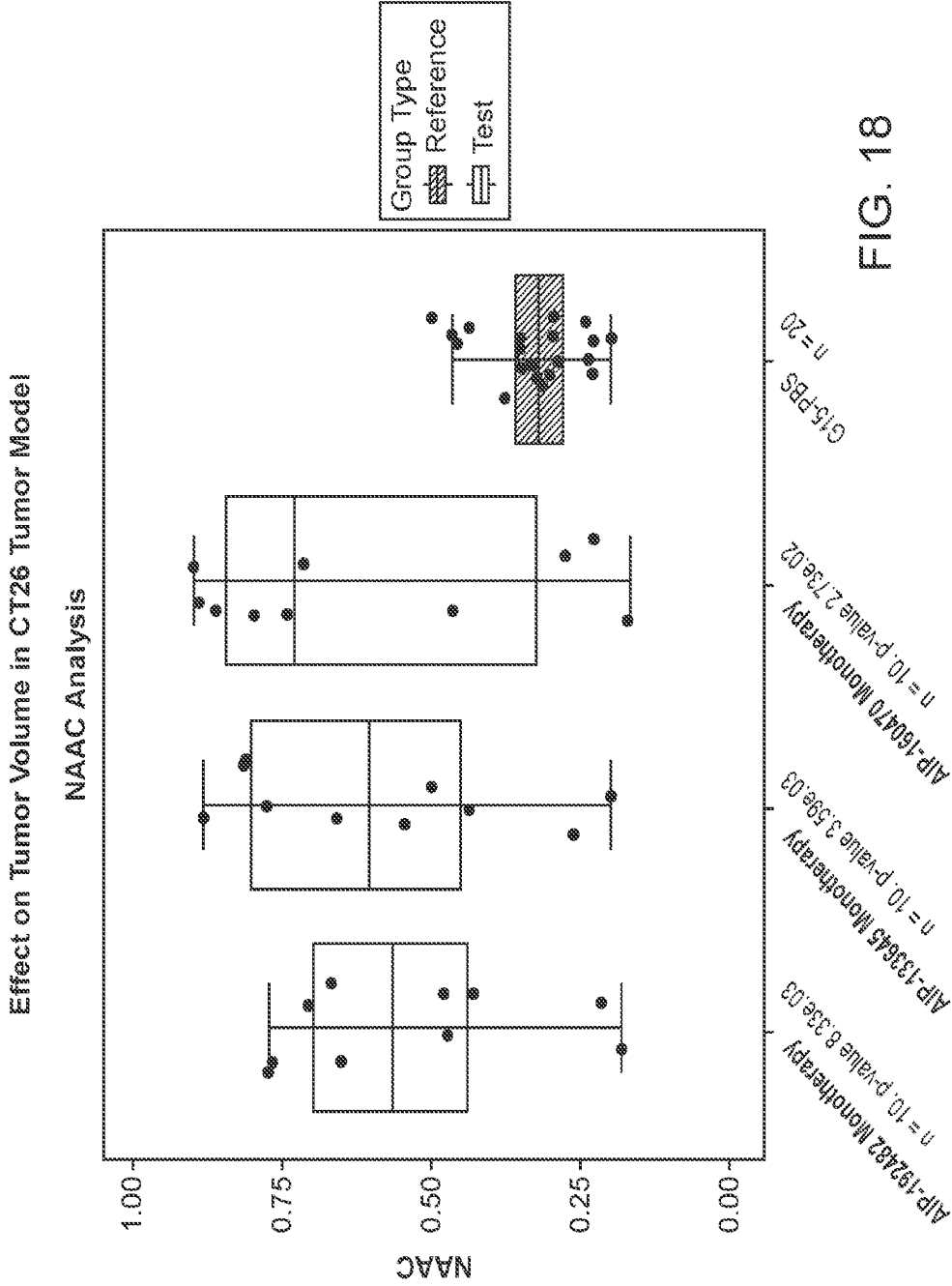


FIG. 18

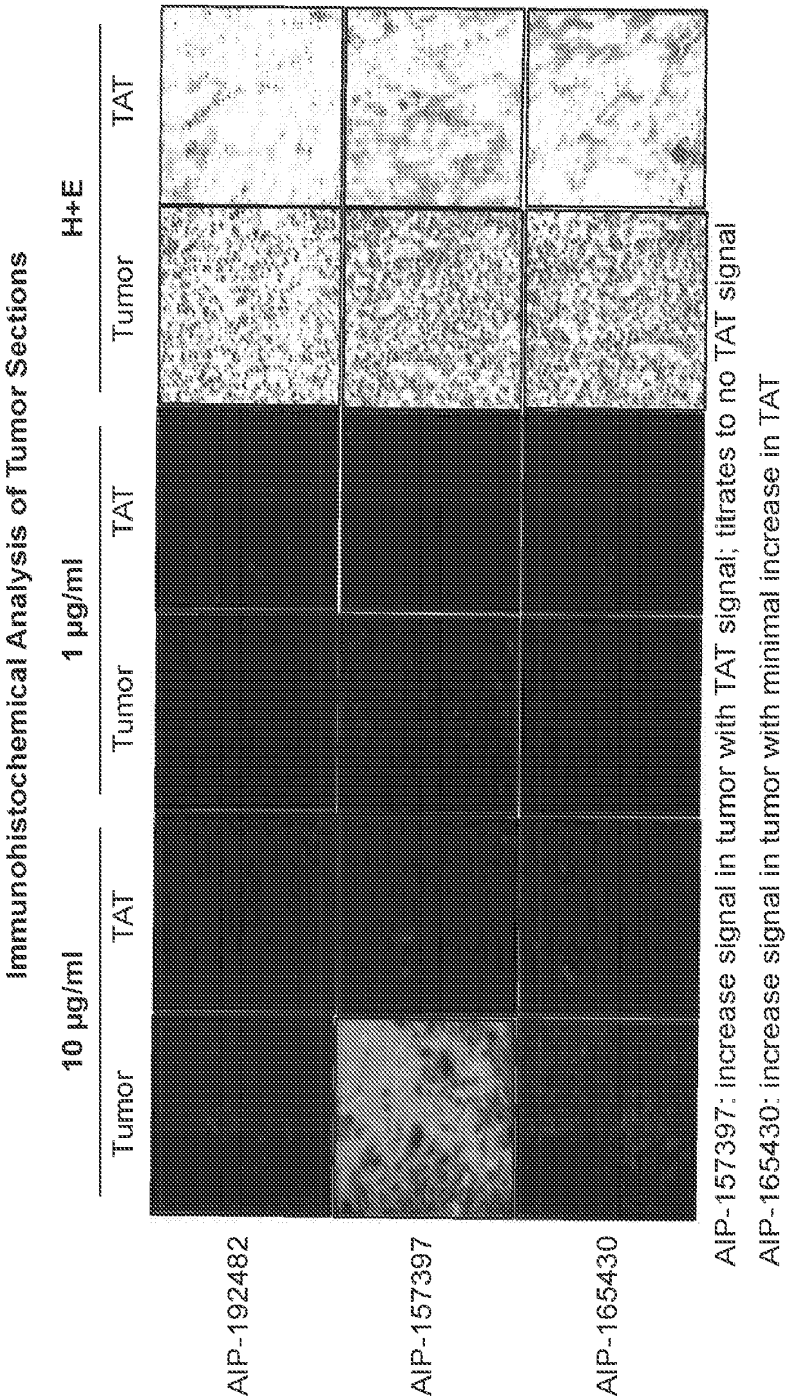


FIG. 19

Immunohistochemical Analysis of Tumor Sections - Variant AIP-106042

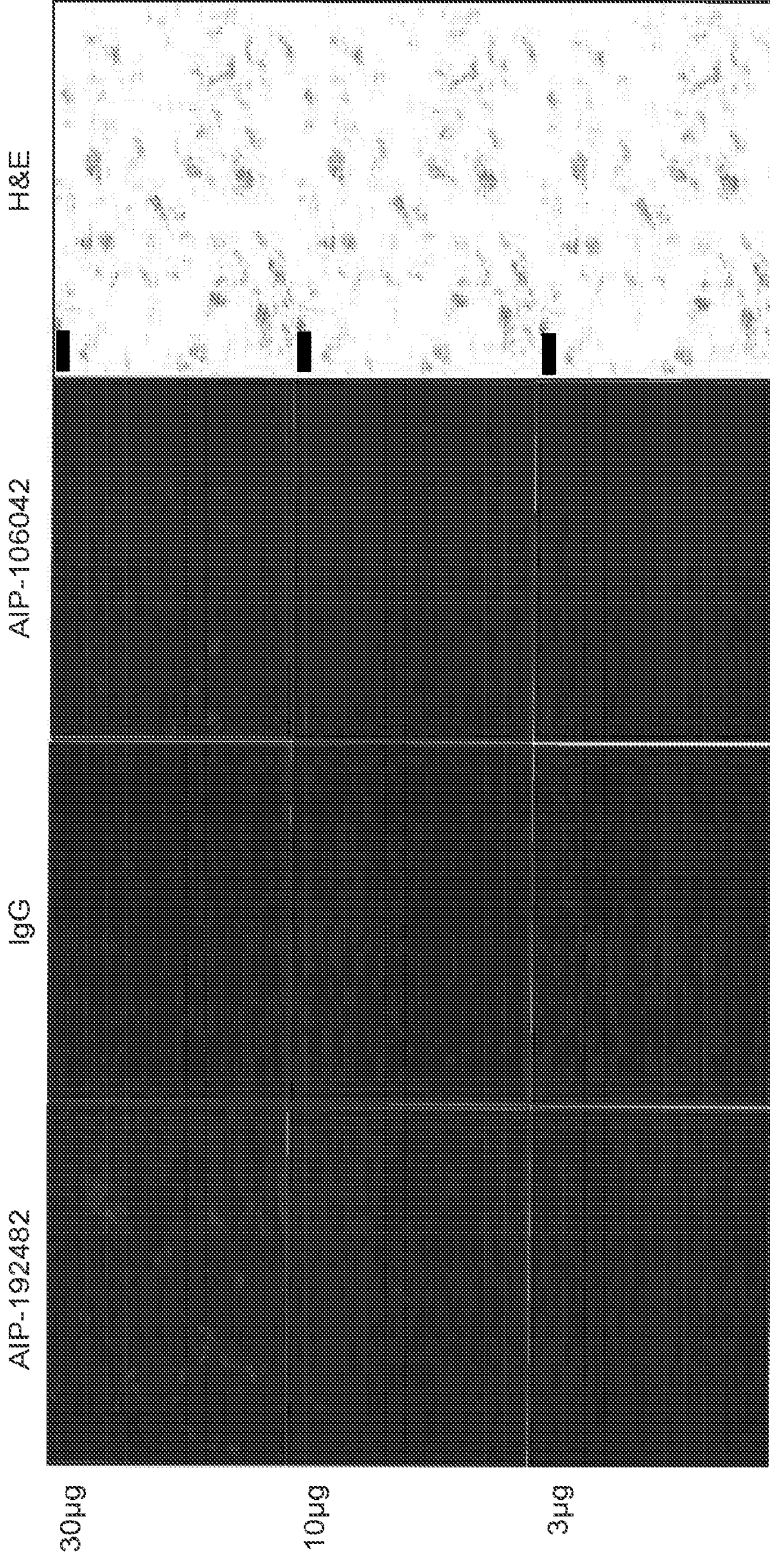


FIG. 20

Immunohistochemical Analysis of Tumor Sections- Variant AIP-100196

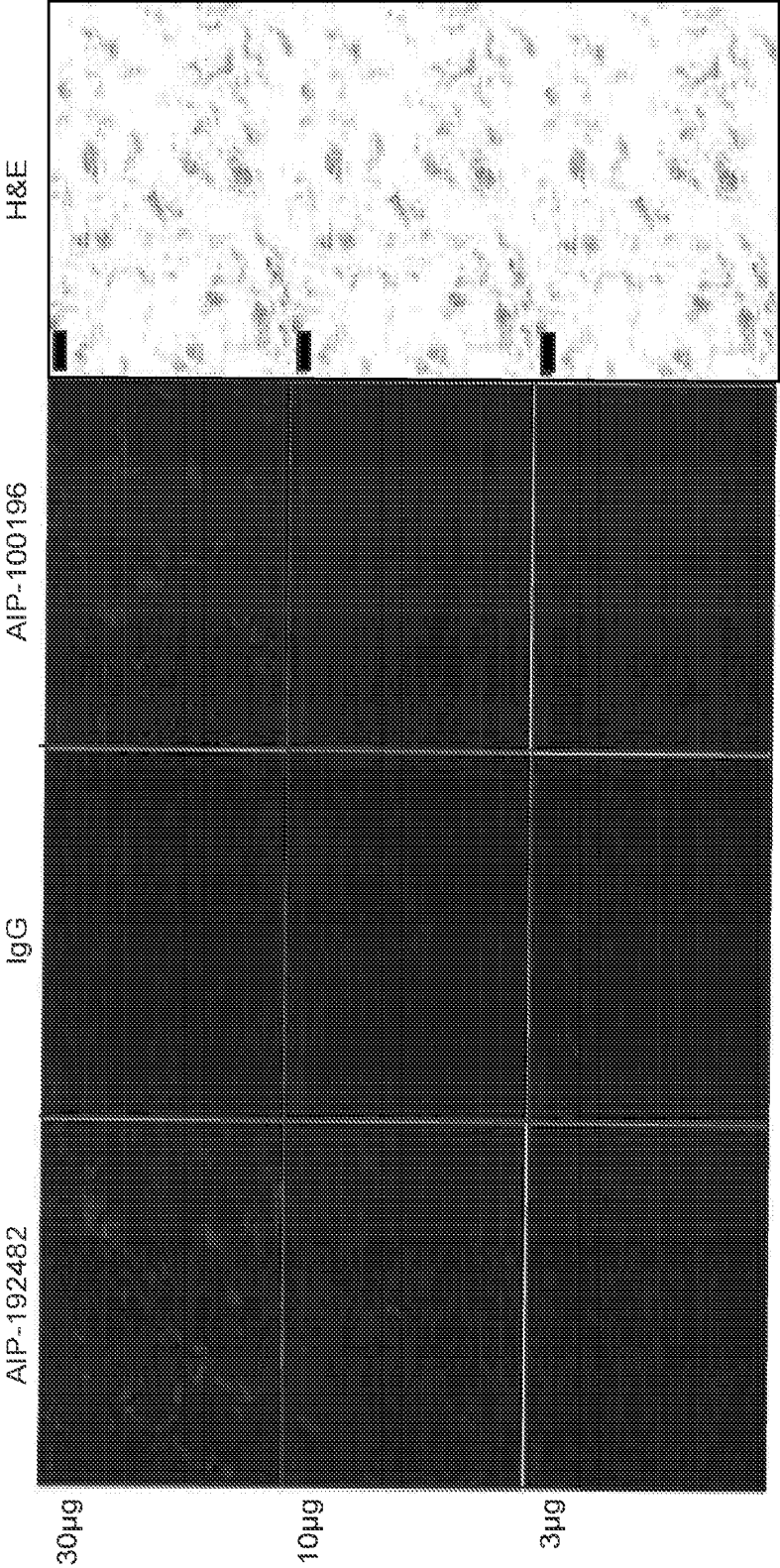


FIG. 21

Immunohistochemical Analysis of Tumor Tissue with Lead and Variant Abs

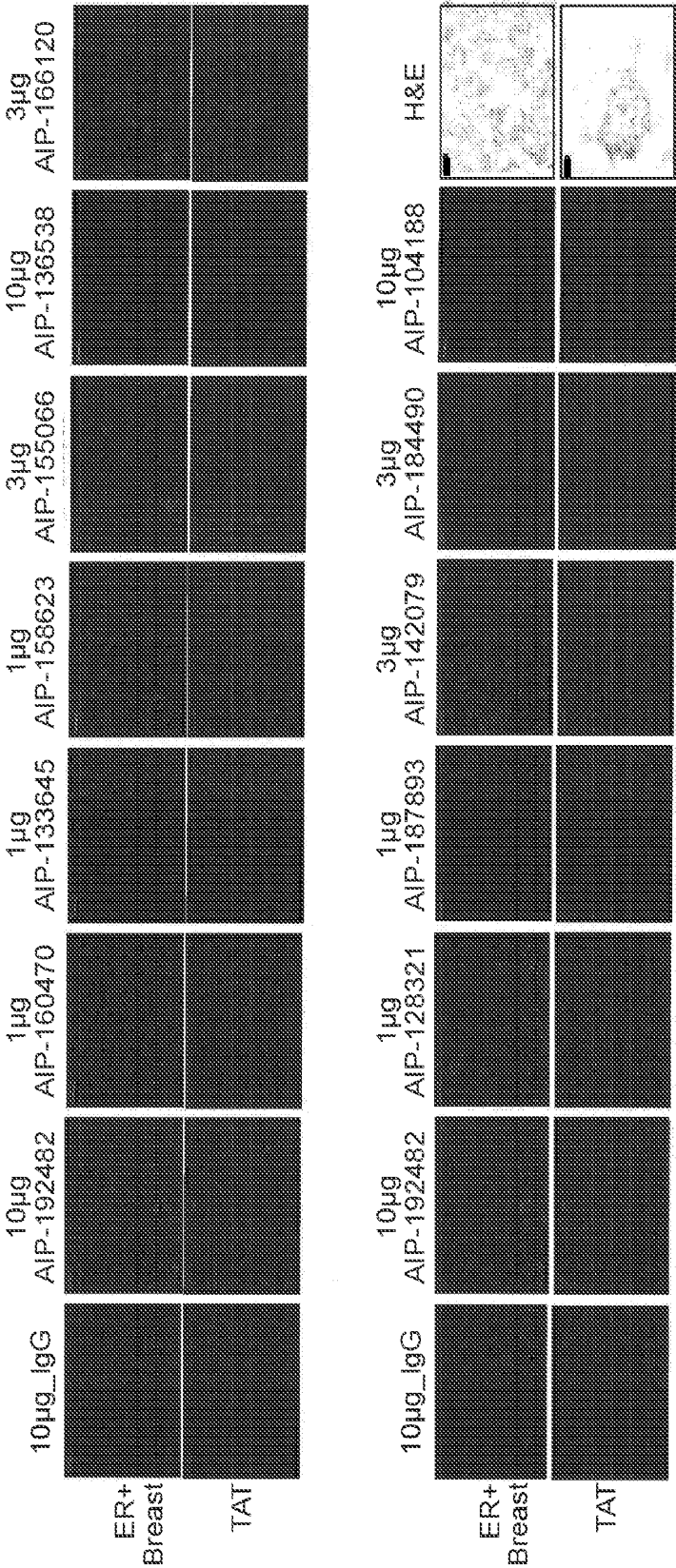


FIG. 22

Immunohistochemical Analysis of Tumor Sections with AIP-192482

MODEL: TISSUE:	Human						Mouse			
	A549 LUNG	BXPC3 PANCREAS	COLO205 COLON	JMT1 HER2 ⁺ BREAST	PC3 PROSTATE	CT26 COLON	E0771 TN BREAST	EMT6 ER ⁺ BREAST	LLC1 LUNG	RENCA KIDNEY
Ab:										
IgG:										
H&E:										

FIG. 23A

Immunohistochemical Analysis of Tumor Sections with AIP-133645

MODEL: TISSUE:	Human					Mouse			
	A549 LUNG	BXPC3 PANCREAS	COLO205 COLON	JIMT1 HER2+ BREAST	PC3 PROSTATE	CT26 COLON	E0771 TN BREAST	EMT6 ER+ BREAST	RENCA KIDNEY
Ab:									
IgG:									
H&E:									

FIG. 23B

Immunohistochemical Analysis of Tumor Sections with AIP-160470

MODEL: TISSUE:	Human						Mouse			
	A549 LUNG	BXPC3 PANCREAS	COLO205 COLON	JIMT1 HER2+ BREAST	PC3 PROSTATE	CT26 COLON	E0771 TN BREAST	EMT6 ER+ BREAST	LLC1 LUNG	RENCA KIDNEY
Ab:										
IgG:										
H&E:										

FIG. 23C

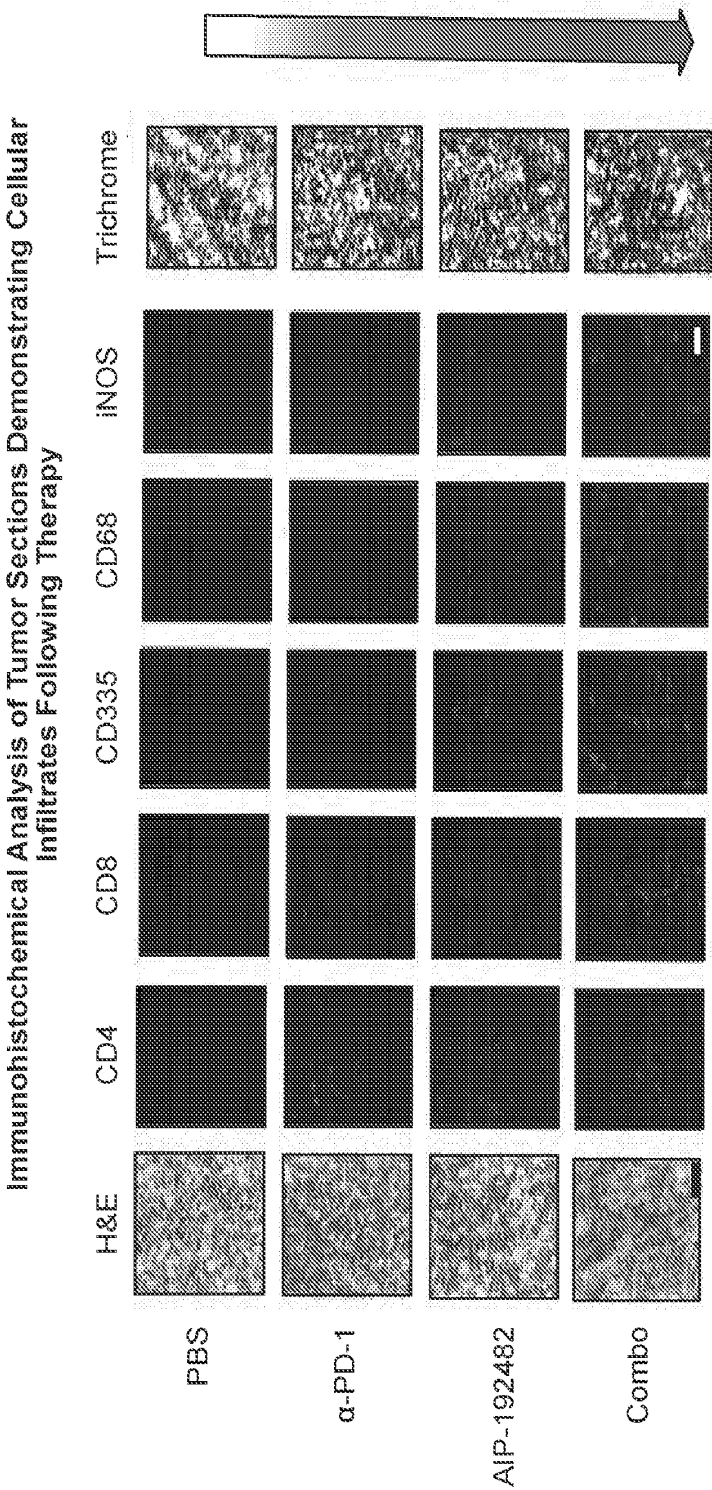


FIG. 24

Schematic of the ex vivo Binding Assay

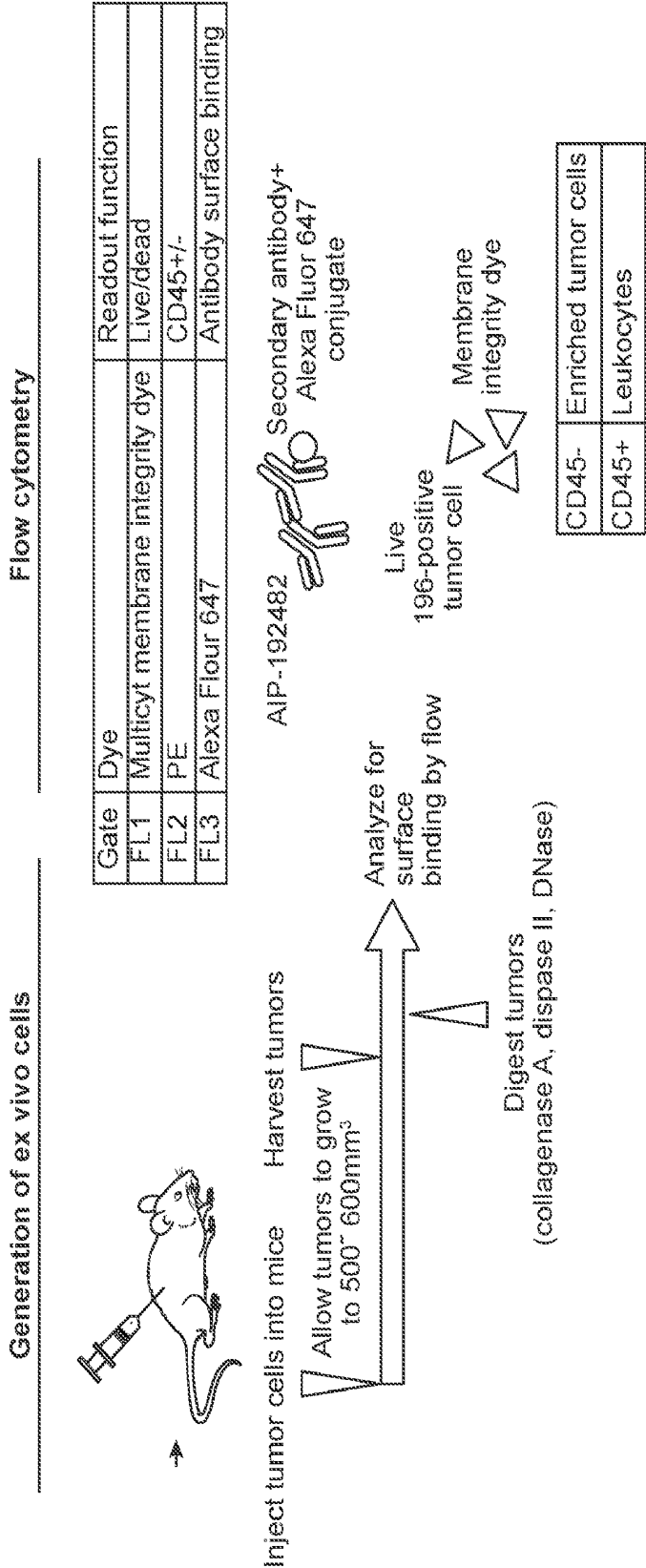


FIG. 25

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Binding of Variants to EMT6 ex vivo Cells Correlates with in vivo Data

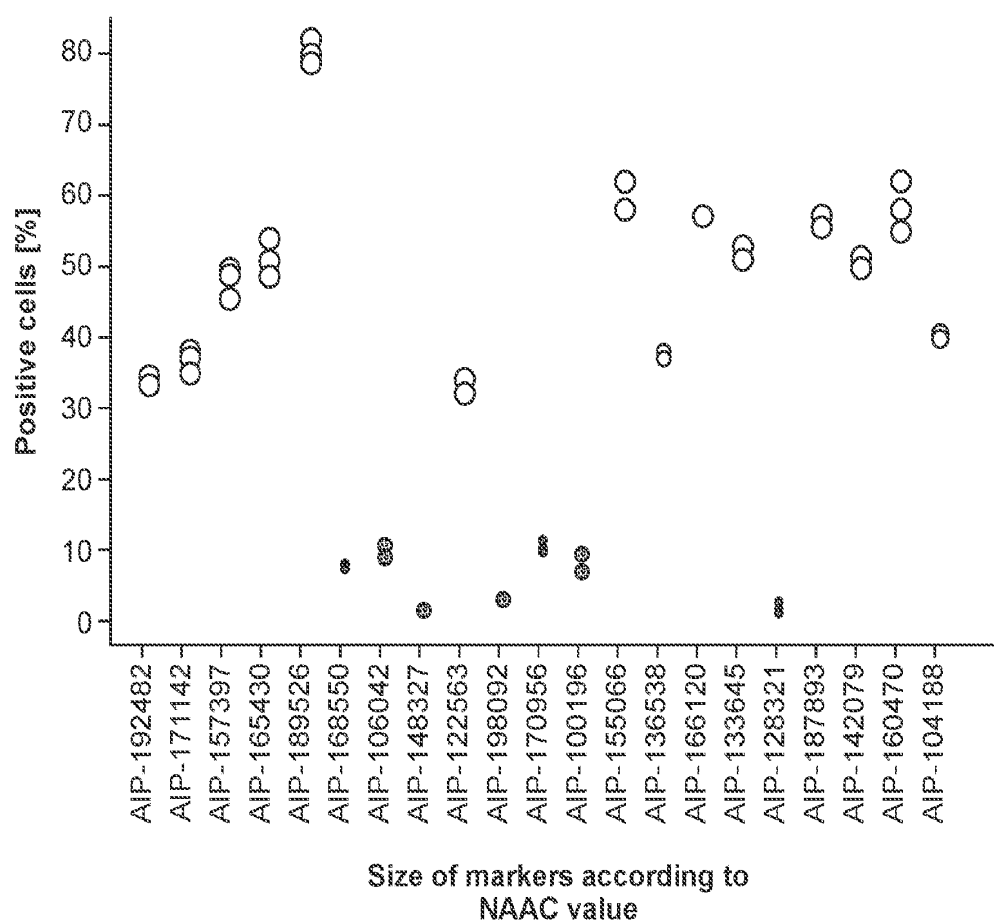


FIG. 26

Binding of Variants to ex vivo EMT6 Cells Correlates with in vivo Data

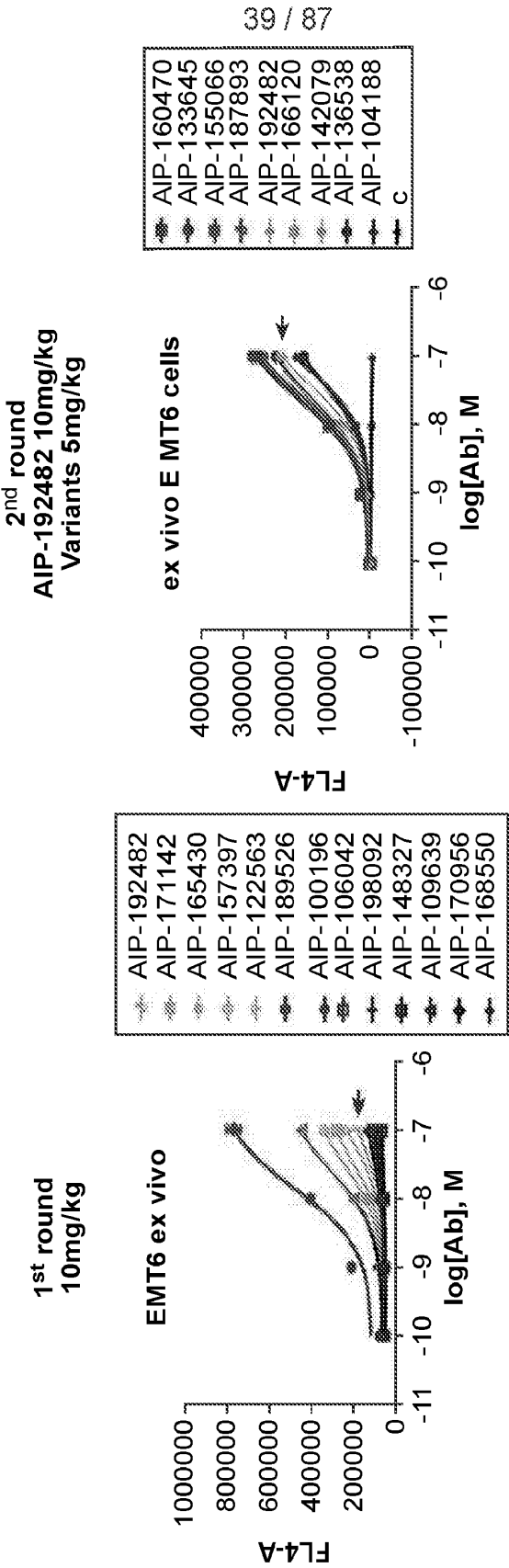


FIG. 27

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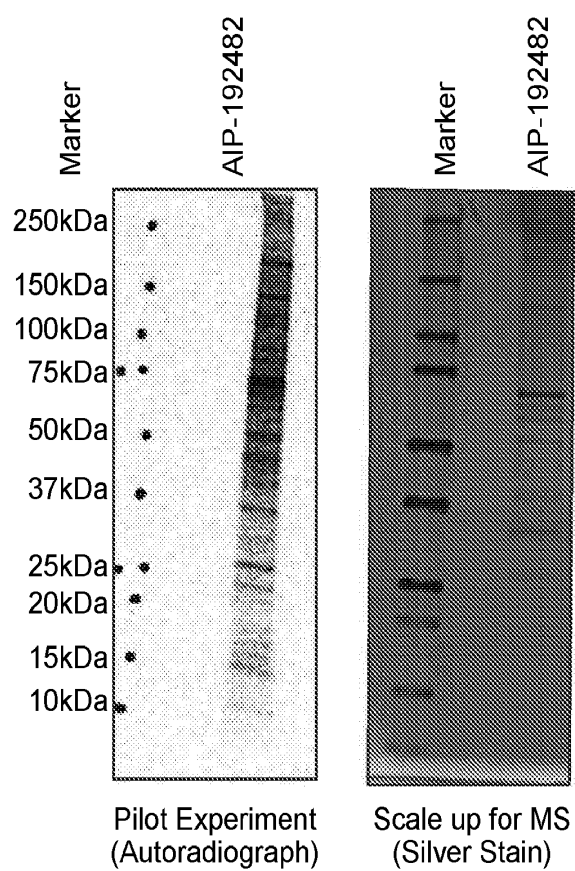


FIG. 28

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Treatment of Immunoprecipitates with RNase or DNase

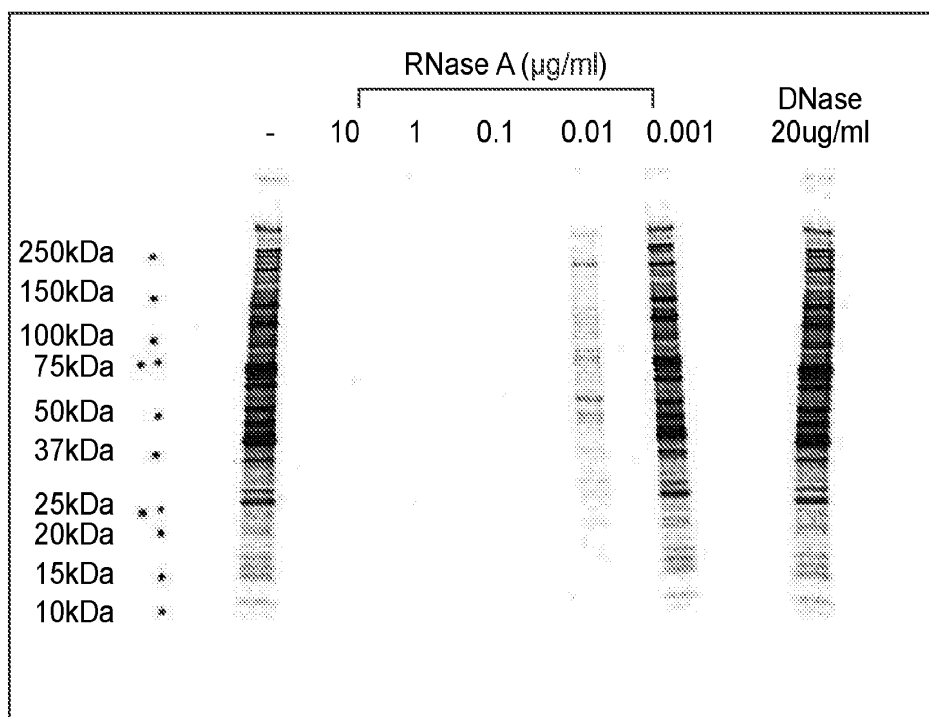


FIG. 29

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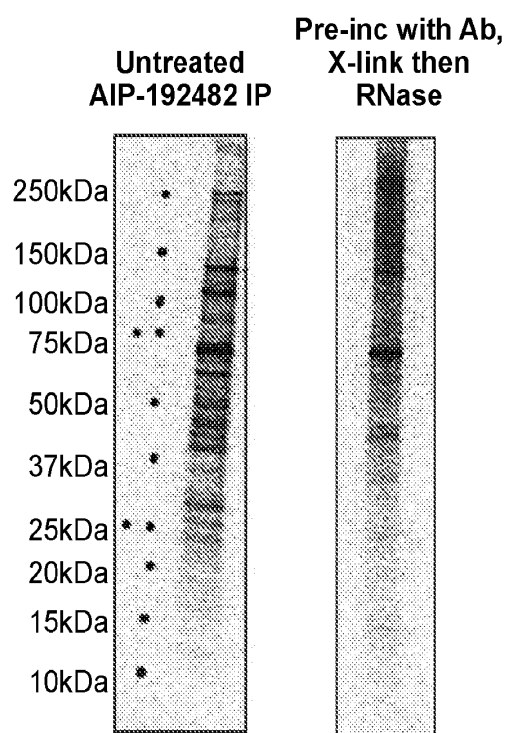


FIG. 30

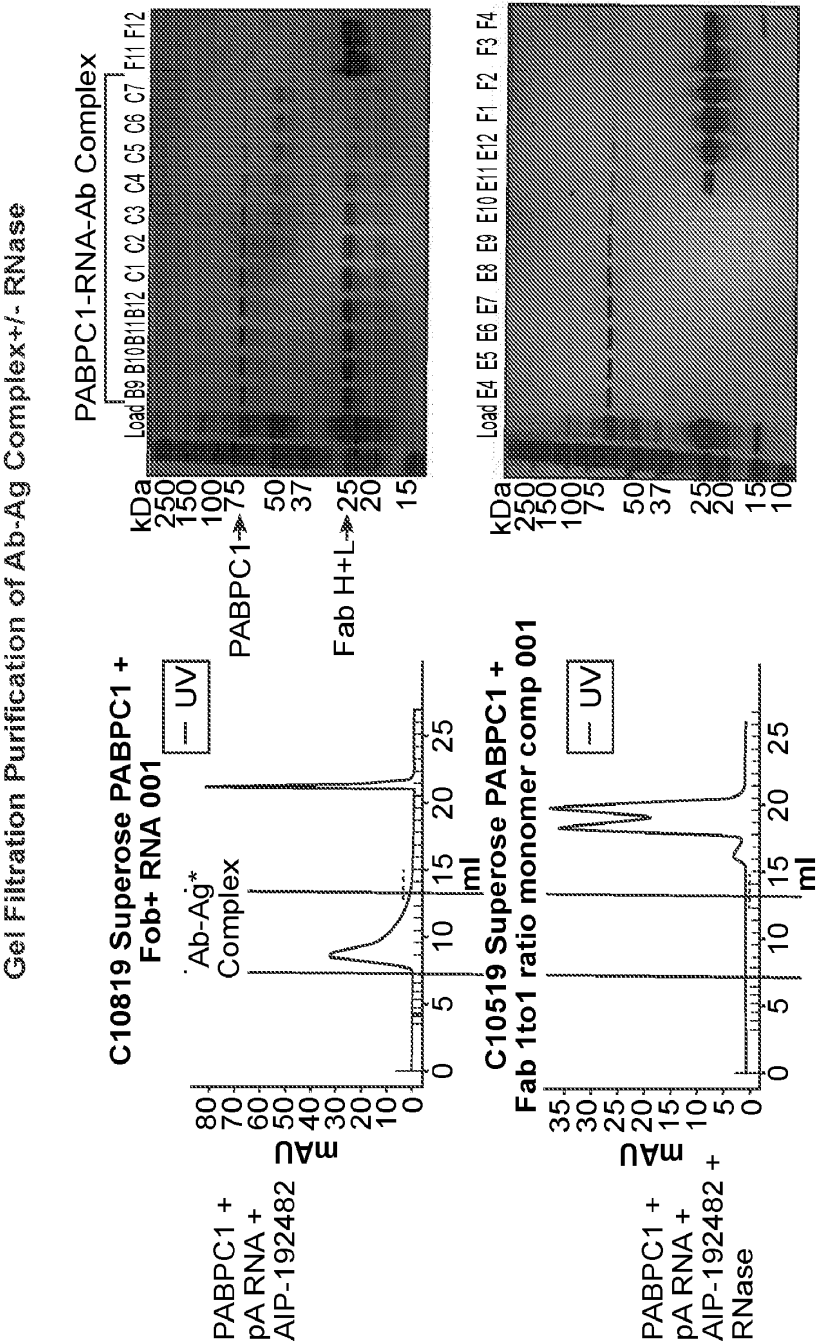


FIG. 31

AIP-192482 Co-locates with a Subpopulation of G3BP-Positive Structures within EMT6 Tumors

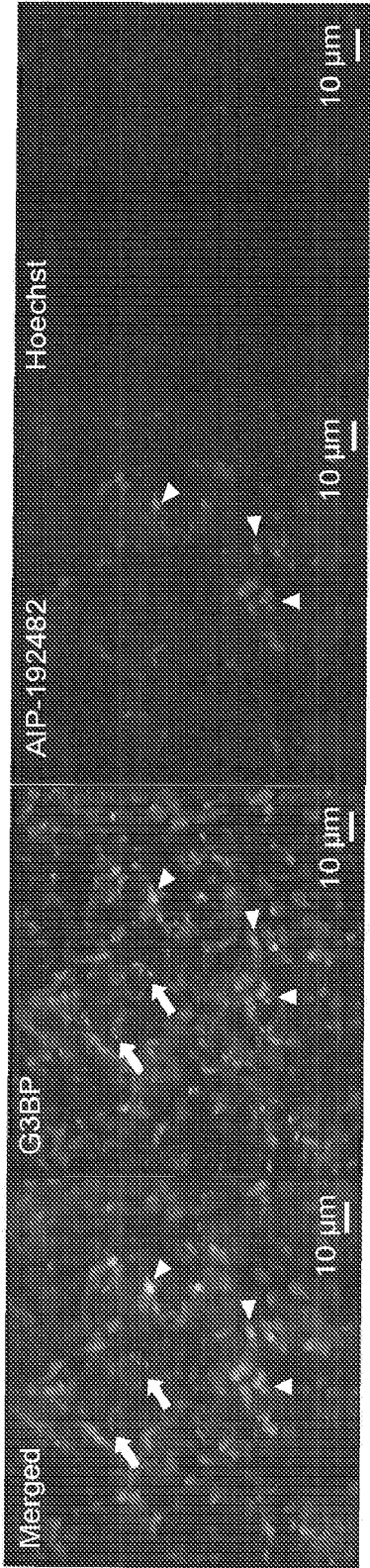


FIG. 32A

FIG. 32B

FIG. 32C

FIG. 32D

Co-distribution of AIP-160470 and CD9 Immunoreactivities in EMT6 Tumor

CD9/AIP-160470/ HOECHST



FIG. 33A



FIG. 33B

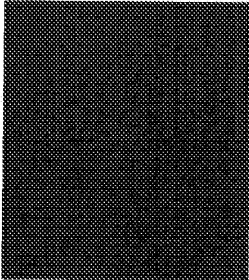


FIG. 33C

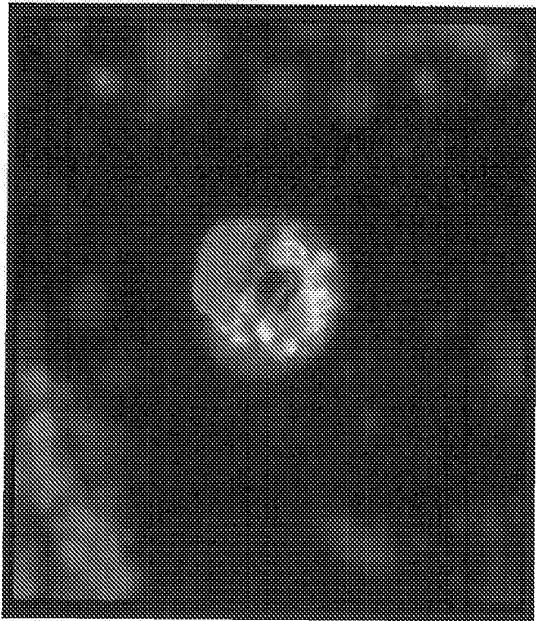


FIG. 33D

Co-distribution of AIP-160470 and CD9 Immunoreactivities in Human Breast Carcinoma

CD9/ AIP-160470/ HOECHST

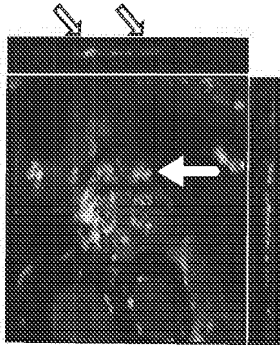


FIG. 34B

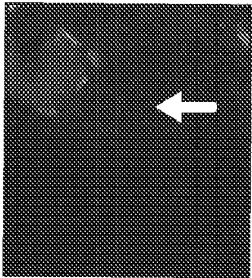


FIG. 34C

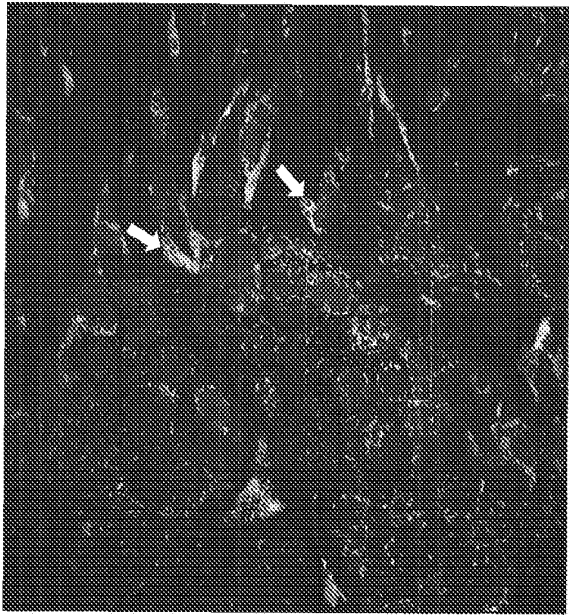


FIG. 34A

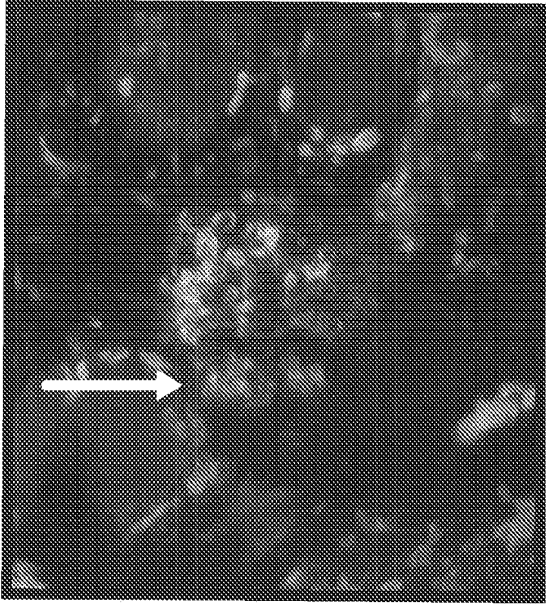


FIG. 34D

Doxorubicin (DOX) Increases Cell Surface Binding of AIP-192482 and AIP-160470 on EMT6 Cells *in Vitro*

Flow cytometry

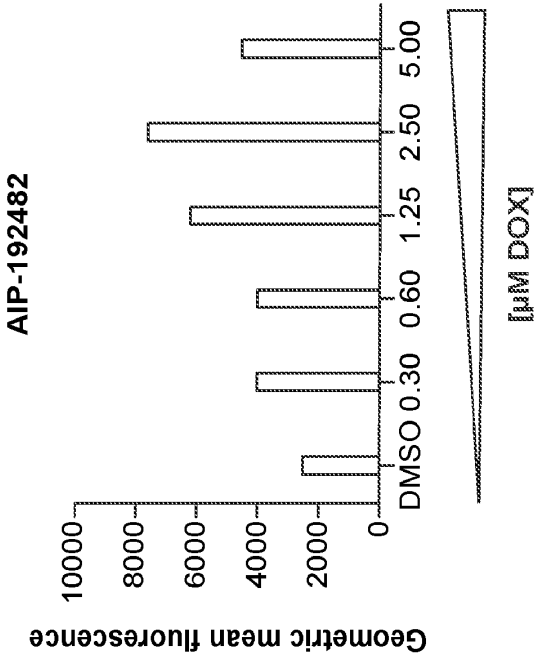


FIG. 35A

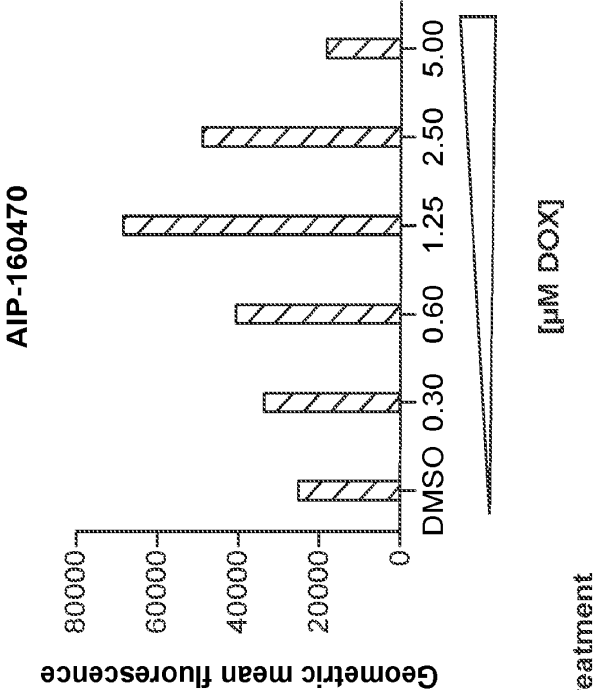


FIG. 35B

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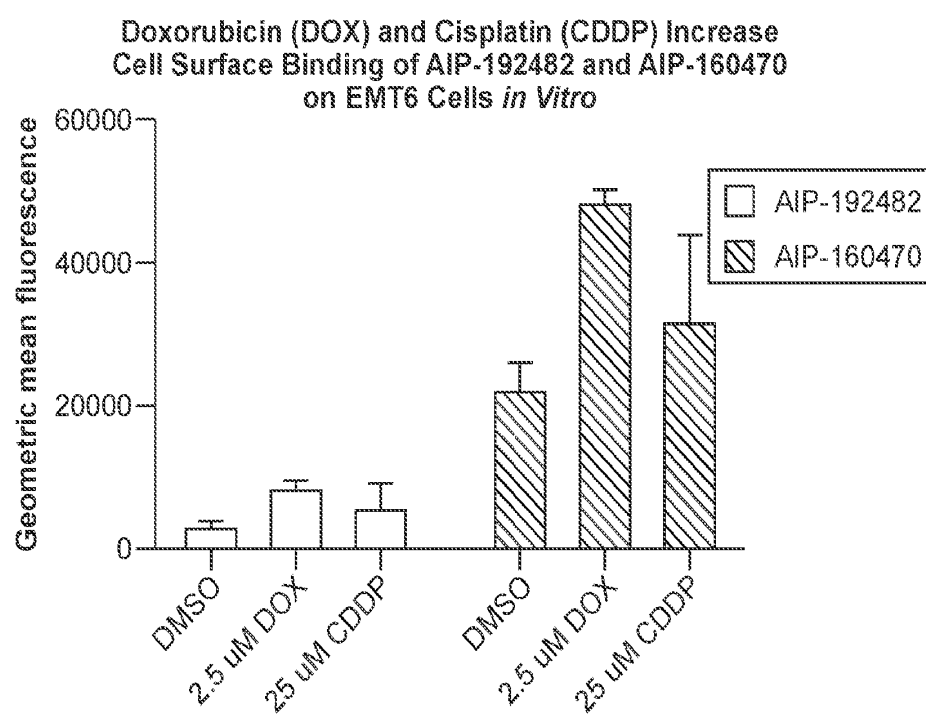


FIG. 36

Kabat Chothia IMGT Numbering of AIP-160470 V_H

Kabat:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Chothia:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
IMGT:	1	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	19	20	21
AIP-160470	E	V	Q	L	V	E	S	G	G	A	L	V	K	P	G	G	S	L	R	L

5

Kabat:	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
Chothia:	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
IMGT:	22	23	24	25	26	27	28	29	30	35	36	37	38	39	40	41	42	43	44	45
AIP-160470	S	C	A	A	S	G	F	T	F	S	K	A	W	M	S	W	V	R	Q	A

Kabat:	41	42	43	44	45	46	47	48	49	50	51	52	52a	52b	52c	53	54	55	56	57
Chothia:	41	42	43	44	45	46	47	48	49	50	51	52	52a	52b	52c	53	54	55	56	57
IMGT:	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65
AIP-160470	P	G	K	G	L	E	W	V	G	R	I	K	S	V	T	D	G	E	T	T

Kabat:	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77
Chothia:	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77
IMGT:	66	67	68	69	70	71	72	74	75	76	77	78	79	80	81	82	83	84	85	86
AIP-160470	D	Y	A	A	P	V	K	G	R	F	T	I	S	R	D	D	S	K	S	T

Kabat:	78	79	80	81	82	82a	82b	82c	83	84	85	86	87	88	89	90	91	92	93	94
Chothia:	78	79	80	81	82	82a	82b	82c	83	84	85	86	87	88	89	90	91	92	93	94
IMGT:	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106
AIP-160470	L	Y	L	Q	M	N	S	L	K	T	E	D	T	A	V	Y	Y	C	T	S

FIG. 37A

Kabat:	95	96	97	98	99	100	100a	100b	100c	100d	100e	100f	100g	100h	100i	100j
Choithia:	95	96	97	98	99	100	100a	100b	100c	100d	100e	100f	100g	100h	100i	100j
IMGT:	107	108	109	110	111	111.1	111.2	111.3	111.4	111.5	111.6	111.7	111.8	111.9	112.8	
AIP-160470	S	F	C	C	R	G	G	S	C	P	S	H	D	T	S	Y

Kabat:	100k	100l	100m	100n	100o	100p	100q	100r	100s	100t	100u	101	102	103	104	105
Choithia:	100k	100l	100m	100n	100o	100p	100q	100r	100s	100t	100u	101	102	103	104	105
IMGT:	112.7	112.6	112.5	112.4	112.3	112.2	112.1	112	113	114	115	116	117	118	119	120
AIP-160470	C	G	G	Q	Y	K	S	Y	Y	Y	M	D	V	W	G	K

Kabat:	106	107	108	109	110	111	112	113	
Choithia:	106	107	108	109	110	111	112	113	
IMGT:	121	122	123	124	125	126	127	128	
AIP-160470	G	T	T	V	T	V	S	S	

FIG. 37A (Cont.)

Kabat Choithia IMGT Numbering of AIP-160470 V_L

Kabat:	1	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	19	20	21
Choithia:	1	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	19	20	21
IMGT:	1	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	19	20	21
AIP-160470	Q	S	V	L	T	Q	P	P	S	A	S	G	T	P	G	Q	R	V	T	I

Kabat:	22	23	24	25	26	27	27a	27b	28	29	30	31	32	33	34	35	36	37	38	39
Choithia:	22	23	24	25	26	27	28	29	30	30a	30b	31	32	33	34	35	36	37	38	39
IMGT:	22	23	24	25	26	27	28	29	30	35	36	37	38	39	40	41	42	43	44	45
AIP-160470	S	C	S	G	S	S	S	N	I	G	S	S	S	S	V	S	W	Y	Q	L

Kabat:	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59
Choithia:	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59
IMGT:	46	47	48	49	50	51	52	53	54	55	56	57	65	66	67	68	69	70	71	72
AIP-160470	P	G	T	A	P	K	L	L	I	Y	K	N	N	Q	R	P	S	G	V	P

Kabat:	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79
Choithia:	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79
IMGT:	74	75	76	77	78	79	80	83	84	85	86	87	88	89	90	91	92	93	94	95
AIP-160470	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R

FIG. 37B

Kabat:	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	95a	95b	96	97
Choithia:	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	95a	95b	96	97
IMGT:	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	113	114	115	116	117
AIP-160470	S	E	D	E	A	D	Y	Y	C	S	T	W	D	D	S	L	S	V	R	V

Kabat:	98	99	100	101	102	103	104	105	106	107
Choithia:	98	99	100	101	102	103	104	105	106	107
IMGT:	118	119	120	121	122	123	124	125	126	127
AIP-160470	F	G	G	G	T	K	L	T	V	L

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FIG. 37B (Cont.)

Sample	Qubit ng/uL
Control IP	63.2
AIP-192482 IP	>1000

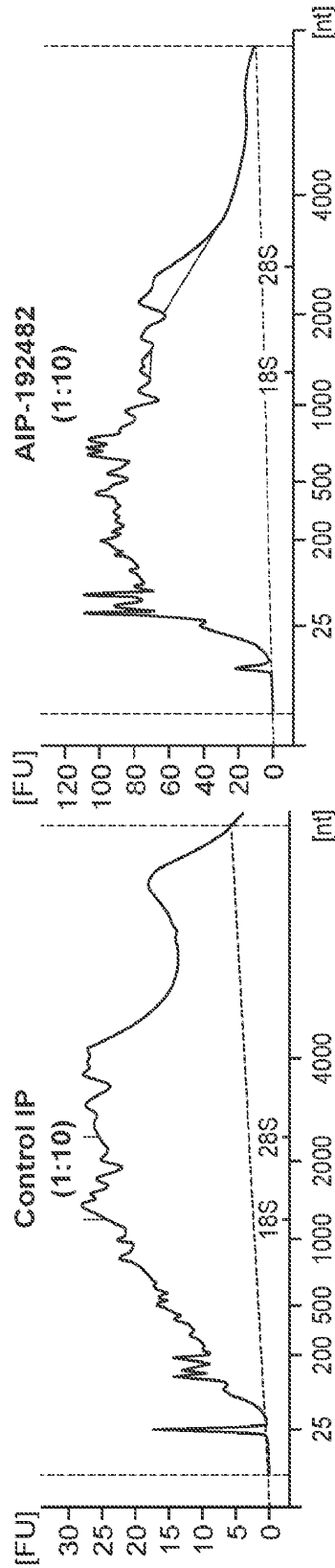


FIG. 38A

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Gene	Control Ab Rd 1	Control Ab Rd 2	AIP-192482 Exp 1	AIP-192482 Exp 2
CCDC125	0.00E+00	0.00E+00	2.53E-06	0.00E+00
PARP15	0.00E+00	0.00E+00	3.80E-06	0.00E+00
AC007620.3	0.00E+00	0.00E+00	1.27E-06	0.00E+00
TMEM182	0.00E+00	0.00E+00	5.06E-06	0.00E+00
F11R	0.00E+00	0.00E+00	1.27E-05	5.64E-05
SLC38A6	0.00E+00	0.00E+00	1.27E-06	0.00E+00
RPAIN	0.00E+00	0.00E+00	1.01E-05	2.82E-05
CTC-260E6.6	0.00E+00	0.00E+00	0.00E+00	2.82E-05
KTN1-AS1	0.00E+00	0.00E+00	0.00E+00	0.00E+00
MAB21L3	0.00E+00	0.00E+00	8.86E-06	0.00E+00

FIG. 38B

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EC50 Rank (Expressed as fold over AIP-160470)

0 = >500 nM; 1 = <0.5; 2 = 0.5 to 2; 3 = 2 to 4; 4 = >4

 Δ Activity Rank (relative to AIP-160470)

0 = <0.12; 1 = 0.12 to 0.3; 2 = 0.3 to 0.75; 3 = > 0.75

AIP Number	Number of Expts	EC ₅₀ (nM)	EC ₅₀ Rank	Δ Activity (relative to AIP-160470)	Δ Activity Rank
AIP-109729	1	13	4.0	0.57	2.0
AIP-128136	3	1	4.0	1.21	3.0
AIP-131972	1	2	4.0	0.79	3.0
AIP-153125	3	2	4.0	0.99	3.0
AIP-157045	2	21	4.0	1.21	3.0
AIP-160829	2	17	4.0	1.04	3.0
AIP-181273	3	9	4.0	1.12	3.0
AIP-189526	2	12	4.0	0.98	3.0
AIP-125062	2	21	3.5	1.03	3.0
AIP-125258	2	31	3.5	0.91	3.0
AIP-150199	2	26	3.5	1.00	3.0
AIP-166722	2	29	3.5	0.49	2.0
AIP-170105	2	28	3.5	0.88	3.0
AIP-180422	2	32	3.5	0.63	2.0
AIP-180675	2	17	3.5	0.78	2.5
AIP-184744	2	24	3.5	0.84	2.5
AIP-102624	1	50	3.0	0.47	2.0
AIP-115363	1	29	3.0	0.90	3.0
AIP-128147	2	32	3.0	0.84	2.5
AIP-154181	2	46	3.0	0.69	2.0
AIP-157078	1	51	3.0	0.67	2.0
AIP-174676	1	40	3.0	0.33	2.0
AIP-101601	2	42	2.5	0.67	2.5
AIP-109048	2	40	2.5	0.74	2.5
AIP-111240	2	50	2.5	0.89	3.0
AIP-114403	2	46	2.5	0.83	2.5
AIP-127782	2	76	2.5	1.05	3.0
AIP-129145	2	39	2.5	0.63	2.0
AIP-136060	2	51	2.5	0.85	2.5
AIP-148062	2	47	2.5	0.79	3.0
AIP-162041	2	47	2.5	0.84	3.0
AIP-167533	2	52	2.5	0.55	2.0
AIP-190051	2	43	2.5	0.79	3.0
AIP-100340	1	152	2.0	0.31	2.0
AIP-101235	2	51	2.0	0.95	3.0
AIP-102299	2	93	2.0	0.63	2.0
AIP-104086	2	104	2.0	0.87	3.0

FIG. 39

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AIP Number	Number of Expts	EC ₅₀ (nM)	EC ₅₀ Rank	ΔActivity (relative to AIP-160470)	ΔActivity Rank
AIP-104364	1	148	2.0	0.22	1.0
AIP-105241	1	86	2.0	0.43	2.0
AIP-106633	2	95	2.0	0.67	2.0
AIP-107759	2	111	2.0	0.68	2.0
AIP-109343	2	53	2.0	0.80	2.5
AIP-109484	1	134	2.0	0.59	2.0
AIP-109510	1	79	2.0	0.63	2.0
AIP-110143	1	111	2.0	0.83	3.0
AIP-112328	1	174	2.0	0.65	2.0
AIP-112580	2	84	2.0	0.77	2.5
AIP-113513	1	169	2.0	0.59	2.0
AIP-114196	1	102	2.0	0.64	2.0
AIP-116142	1	172	2.0	0.60	2.0
AIP-116579	3	143	2.0	0.64	2.0
AIP-119622	2	94	2.0	0.77	2.5
AIP-119664	2	96	2.0	0.71	2.5
AIP-124314	3	161	2.0	0.91	2.7
AIP-125984	2	80	2.0	0.72	2.5
AIP-126285	2	71	2.0	0.77	2.5
AIP-127108	1	68	2.0	0.49	2.0
AIP-128195	3	138	2.0	0.52	2.0
AIP-128243	1	111	2.0	0.70	2.0
AIP-130491	1	107	2.0	0.75	3.0
AIP-130915	2	60	2.0	0.84	2.5
AIP-133650	1	119	2.0	0.58	2.0
AIP-134312	1	179	2.0	0.78	3.0
AIP-134770	3	90	2.0	0.88	3.0
AIP-136628	1	126	2.0	0.50	2.0
AIP-137169	1	57	2.0	0.38	2.0
AIP-138776	1	97	2.0	0.66	2.0
AIP-141887	3	103	2.0	0.53	2.0
AIP-142489	3	177	2.0	0.75	2.3
AIP-143132	1	60	2.0	0.65	2.0
AIP-143155	1	68	2.0	0.54	2.0
AIP-143179	3	88	2.0	0.69	2.3
AIP-146871	1	185	2.0	0.50	2.0
AIP-147176	1	85	2.0	0.63	2.0
AIP-147389	1	97	2.0	0.56	2.0
AIP-150055	1	136	2.0	0.55	2.0
AIP-151167	1	83	2.0	0.48	2.0
AIP-151709	1	154	2.0	0.65	2.0
AIP-152283	1	75	2.0	0.34	2.0
AIP-153462	3	87	2.0	0.83	2.3
AIP-153475	1	116	2.0	1.00	3.0

FIG. 39 (Cont. 1)

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AIP Number	Number of Expts	EC ₅₀ (nM)	EC ₅₀ Rank	ΔActivity (relative to AIP-160470)	ΔActivity Rank
AIP-153888	2	67	2.0	0.71	2.0
AIP-154873	2	89	2.0	0.65	2.0
AIP-156514	2	81	2.0	0.64	2.0
AIP-156760	1	58	2.0	0.64	2.0
AIP-158623	1	90	2.0	0.71	2.0
AIP-159023	1	170	2.0	0.33	2.0
AIP-159037	2	67	2.0	0.72	2.5
AIP-159326	2	69	2.0	0.97	3.0
AIP-160470	54	107	2.0	1.00	3.0
AIP-161082	1	118	2.0	0.79	3.0
AIP-164754	1	89	2.0	0.36	2.0
AIP-166120	2	72	2.0	0.92	3.0
AIP-166832	2	42	2.0	0.61	2.0
AIP-166959	1	135	2.0	0.46	2.0
AIP-167246	1	57	2.0	0.70	2.0
AIP-167726	3	204	2.0	0.63	2.3
AIP-168083	1	115	2.0	0.81	3.0
AIP-168605	2	71	2.0	0.60	2.0
AIP-169636	1	99	2.0	0.61	2.0
AIP-170053	1	118	2.0	0.51	2.0
AIP-170569	2	76	2.0	0.68	2.0
AIP-172872	2	98	2.0	0.46	2.0
AIP-173276	1	98	2.0	0.54	2.0
AIP-175775	2	90	2.0	0.80	2.5
AIP-177584	1	137	2.0	0.34	2.0
AIP-179097	2	82	2.0	0.80	3.0
AIP-181246	2	161	2.0	0.74	2.0
AIP-183133	1	136	2.0	0.49	2.0
AIP-183190	1	68	2.0	0.57	2.0
AIP-183350	2	76	2.0	0.88	3.0
AIP-184151	1	191	2.0	0.46	2.0
AIP-185291	1	123	2.0	0.59	2.0
AIP-185304	1	174	2.0	0.70	2.0
AIP-186435	2	136	2.0	0.44	2.0
AIP-186826	2	108	2.0	0.62	2.0
AIP-188155	2	111	2.0	0.80	2.5
AIP-189338	3	120	2.0	0.81	3.0
AIP-189473	2	85	2.0	0.84	2.5
AIP-189475	2	147	2.0	0.62	2.0
AIP-190274	2	120	2.0	0.74	2.5
AIP-190362	1	99	2.0	0.39	2.0
AIP-190526	1	57	2.0	0.71	2.0
AIP-190761	2	104	2.0	0.77	2.5
AIP-190915	1	174	2.0	0.83	3.0

FIG. 39 (Cont. 2)

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AIP Number	Number of Expts	EC ₅₀ (nM)	EC ₅₀ Rank	ΔActivity (relative to AIP-160470)	ΔActivity Rank
AIP-191735	2	70	2.0	0.85	2.5
AIP-192216	2	155	2.0	0.54	2.0
AIP-192275	2	103	2.0	0.72	2.0
AIP-192571	2	110	2.0	0.66	2.0
AIP-193490	1	158	2.0	0.16	1.0
AIP-195587	3	99	2.0	0.81	3.0
AIP-195588	1	107	2.0	0.70	2.0
AIP-197886	1	106	2.0	0.40	2.0
AIP-198351	2	51	2.0	0.87	3.0
AIP-199834	3	114	2.0	0.77	2.3
AIP-102396	2	139	1.5	0.56	2.0
AIP-103817	2	177	1.5	0.79	2.5
AIP-106139	2	148	1.5	0.81	2.5
AIP-126080	2	191	1.5	0.65	2.5
AIP-143369	2	196	1.5	0.69	2.5
AIP-155066	2	165	1.5	0.82	2.5
AIP-160621	2	286	1.5	0.54	2.0
AIP-161571	2	122	1.5	0.58	2.0
AIP-187893	2	154	1.5	0.85	3.0
AIP-191470	2	118	1.5	0.71	2.5
AIP-197809	2	307	1.5	0.63	2.0
AIP-199483	2	179	1.5	0.60	2.0
AIP-135247	3	233	1.3	0.66	2.0
AIP-192329	3	221	1.3	0.56	2.0
AIP-102833	1	300	1.0	0.60	2.0
AIP-103803	1	198	1.0	0.71	2.0
AIP-104188	1	433	1.0	0.17	1.0
AIP-115388	2	319	1.0	0.92	3.0
AIP-118505	1	297	1.0	0.46	2.0
AIP-120546	1	327	1.0	0.54	2.0
AIP-122563	1	260	1.0	0.63	2.0
AIP-124013	1	263	1.0	0.57	2.0
AIP-126175	1	483	1.0	0.36	2.0
AIP-133645	1	154	1.0	0.64	2.0
AIP-136538	1	471	1.0	0.56	2.0
AIP-142079	1	148	1.0	0.75	3.0
AIP-145518	1	308	1.0	0.78	3.0
AIP-145722	1	310	1.0	0.69	2.0
AIP-147652	1	456	1.0	0.58	2.0
AIP-148327	1	452	1.0	0.03	0.0
AIP-150485	1	336	1.0	0.63	2.0
AIP-151090	1	231	1.0	0.87	3.0
AIP-152243	1	402	1.0	0.65	2.0
AIP-157122	2	174	1.0	0.71	2.0

FIG. 39 (Cont. 3)

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AIP Number	Number of Expts	EC ₅₀ (nM)	EC ₅₀ Rank	ΔActivity (relative to AIP-160470)	ΔActivity Rank
AIP-157397	1	283	1.0	0.42	2.0
AIP-161048	1	377	1.0	0.49	2.0
AIP-163039	2	223	1.0	0.76	2.5
AIP-165430	1	145	1.0	0.75	2.0
AIP-166847	2	239	1.0	0.60	2.5
AIP-167084	1	358	1.0	0.58	2.0
AIP-167400	1	338	1.0	0.59	2.0
AIP-167833	2	304	1.0	0.60	2.0
AIP-171074	1	237	1.0	0.48	2.0
AIP-171142	2	282	1.0	0.64	2.0
AIP-171912	1	294	1.0	0.72	2.0
AIP-172643	2	237	1.0	0.51	2.0
AIP-173396	1	225	1.0	0.37	2.0
AIP-182061	1	329	1.0	0.76	3.0
AIP-182722	1	488	1.0	0.35	2.0
AIP-184490	1	256	1.0	0.34	2.0
AIP-190749	1	294	1.0	0.52	2.0
AIP-192482	2	322	1.0	0.57	2.0
AIP-196203	3	299	1.0	0.57	2.0
AIP-100196	1	>500 nM	0.0	0.29	1.0
AIP-105092	1	>500 nM	0.0	0.32	2.0
AIP-106042	1	>500 nM	0.0	0.32	2.0
AIP-109364	1	>500 nM	0.0	0.55	2.0
AIP-115782	1	>500 nM	0.0	0.39	2.0
AIP-123438	1	>500 nM	0.0	0.56	2.0
AIP-124068	1	>500 nM	0.0	0.31	2.0
AIP-124301	1	>500 nM	0.0	0.38	2.0
AIP-126097	1	>500 nM	0.0	0.54	2.0
AIP-129967	1	>500 nM	0.0	0.22	1.0
AIP-132355	1	>500 nM	0.0	0.19	1.0
AIP-135679	1	>500 nM	0.0	0.44	2.0
AIP-138130	1	>500 nM	0.0	0.51	2.0
AIP-139782	1	>500 nM	0.0	0.26	1.0
AIP-140148	1	>500 nM	0.0	0.31	2.0
AIP-141706	1	>500 nM	0.0	0.40	2.0
AIP-144568	1	>500 nM	0.0	0.45	2.0
AIP-145212	1	>500 nM	0.0	0.30	2.0
AIP-147945	1	>500 nM	0.0	0.45	2.0
AIP-148102	1	>500 nM	0.0	0.46	2.0
AIP-148484	1	>500 nM	0.0	0.38	2.0
AIP-149787	1	>500 nM	0.0	0.39	2.0
AIP-150277	1	>500 nM	0.0	0.44	2.0
AIP-151315	1	>500 nM	0.0	0.28	1.0
AIP-151388	1	>500 nM	0.0	0.51	2.0

FIG. 39 (Cont. 4)

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AIP Number	Number of Expts	EC ₅₀ (nM)	EC ₅₀ Rank	ΔActivity (relative to AIP-160470)	ΔActivity Rank
AIP-152031	1	>500 nM	0.0	0.58	2.0
AIP-155587	1	>500 nM	0.0	0.62	2.0
AIP-156172	1	>500 nM	0.0	0.74	2.0
AIP-163319	1	>500 nM	0.0	0.35	2.0
AIP-165276	1	>500 nM	0.0	0.45	2.0
AIP-166629	1	>500 nM	0.0	0.60	2.0
AIP-167482	1	>500 nM	0.0	0.14	1.0
AIP-169676	1	>500 nM	0.0	0.37	2.0
AIP-170221	1	>500 nM	0.0	0.66	2.0
AIP-171348	1	>500 nM	0.0	0.31	2.0
AIP-171543	1	>500 nM	0.0	0.27	1.0
AIP-177193	1	>500 nM	0.0	0.72	2.0
AIP-178251	1	>500 nM	0.0	0.91	3.0
AIP-180905	1	>500 nM	0.0	0.15	1.0
AIP-181592	1	>500 nM	0.0	0.36	2.0
AIP-182087	1	>500 nM	0.0	0.35	2.0
AIP-186403	1	>500 nM	0.0	0.45	2.0
AIP-188293	1	>500 nM	0.0	0.35	2.0
AIP-189296	1	>500 nM	0.0	0.56	2.0
AIP-191805	1	>500 nM	0.0	0.40	2.0
AIP-193088	1	>500 nM	0.0	0.31	2.0
AIP-193106	1	>500 nM	0.0	0.44	2.0
AIP-197785	1	>500 nM	0.0	0.46	2.0
AIP-198092	1	>500 nM	0.0	0.18	1.0
AIP-199264	1	>500 nM	0.0	0.35	2.0
AIP-199616	1	>500 nM	0.0	0.24	1.0

FIG. 39 (Cont. 5)

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AIP-160470 Variants Selected for *In-vivo* Study Round 1

Antibody ID	Group	Mutations	EC50	EC50 Rank	dAct Rank
AIP-167533	HCDR2 Combination	H53SA, H54VA, H55TD, H58EK, H59TQ	52 nM	2.5	2.0
AIP-180675	HCDR3 Mutation	H126YF	17 nM	3.5	2.5
AIP-126080	HCDR3 Combination	H121YN, H123SQ	191 nM	1.5	2.5
AIP-186435	HCDR3 Combination	H103CA, H117CV	136 nM	2.0	2.0
AIP-161571	HCDR3 Combination	H108SN, H113DE, H119GN	122 nM	1.5	2.0
AIP-163039	HCDR3 Combination	H102F, H105RL, H120QS	223 nM	1.0	2.5
AIP-101235	HCDR3 Combination	H106GS, H112HS, H118GN	51 nM	2.0	3.0
AIP-172643	HCDR3 Combination	H101ST, H110PL, H126YW	237 nM	1.0	2.0
AIP-181246	HCDR3 Combination	H127MV, H128DN, H129VI	161 nM	2.0	2.0
AIP-192216	HCDR3 Combination	H100ST, H107GA, H118GA, H120QS	155 nM	2.0	2.0
AIP-112580	HCDR3 Combination	H99TI, H107GN, H112HS, H118GN	84 nM	2.0	2.5
AIP-170105	LCDR1 Mutation	L35SY	28 nM	3.5	3.0
AIP-136060	LCDR2 Combination	L53NS, L54QL, L57SQ	51 nM	2.5	2.5
AIP-172872	CDR Combination	H59TQ, L53NT, L97SN	98 nM	2.0	2.0
AIP-190051	CDR Combination	H35ST, L26SP, L95SA	43 nM	2.5	3.0
AIP-168605	CDR Combination	L28ND, L93DN, L95SA	71 nM	2.0	2.0

FIG. 40

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AIP-160470 Variants Selected for *In-vivo* Study Round 2

Antibody ID	Group	Comments	EC50	EC50 Rank	dAct Rank
AIP-101235	HCDR3 Combination	TSSFCCRSGSCPSSDTSYCNQGQYKSYYYMDV (3)	51 nM	2.0	3.0
AIP-189473	HCDR3 Combination	TTSFCCRGAACPSSDTSYAGSYKSYFVNI (9)	85 nM	2.0	2.5
AIP-192571	HCDR3 Combination	TSSFCCRGNQCPSSDTSYCGGQYPSYYMDP (5)	110 nM	2.0	2.0
AIP-125258	HCDR3 Combination	ISSFCCRGRKQCPSSDTSYCNNGYADYYFMDV (9)	31 nM	3.5	3.0
AIP-150199	HCDR3 Combination	ISSFCCRGRKQCPSSDTSYCGGQYKSYFMDV (6)	26 nM	3.5	3.0
AIP-115388	HCDR3 Combination	ISSFCCCHSNNCPSSDTSYCNNGYKQYFMDV (10)	319 nM	1.0	3.0
AIP-143369	CDR Combination	Mutations in H1, H2, L1, L2 (8)	196 nM	1.5	2.5
AIP-157045	CDR Combination	Mutations in H1, H2, L1, L2, L3 (9)	21 nM	4.0	3.0
AIP-175775	CDR Combination	Mutations in H1, H3, L1, L2, L3 (10)	90 nM	2.0	2.5
AIP-154181	CDR Combination	Mutations in H1, H2, H3, L1, L2, L3 (9)	46 nM	3.0	2.0
AIP-125984	CDR Combination	Mutations in H1, H2, L1, L2, L3 (9)	80 nM	2.0	2.5
AIP-160829	CDR Combination	Mutations in H1, H2, H3, L1, L2, L3 (12)	17 nM	4.0	3.0
AIP-184744	CDR Combination	Mutations in H1, H2, H3, L1, L2, L3 (11)	24 nM	3.5	2.5
AIP-127782	Framework Swap	IGHV3-72, IGLV1-51	76 nM	2.5	3.0
AIP-128136	Affinity Improvement	8 mutations	1 nM	4.0	3.0
AIP-181273	Affinity Improvement	Subset A from AIP-128136 (4)	9nM	4.0	3.0
AIP-153125	Affinity Improvement	Subset B from AIP-128136 + L33SY (5)	2 nM	4.0	3.0

FIG. 41

Study Design

Grp #	Test Art.1	ATUM Order No.	Lot#	dose level (mg/kg)	Dose Freq.	n=	# of Doses	Route	MODEL
1	AIP-127782	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
2	AIP-189473	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
3	AIP-192571	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
4	AIP-125258	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
5	AIP-150199	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
6	AIP-115388	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
7	AIP-143369	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
8	AIP-157045	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
9	AIP-175775	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
10	AIP-154181	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
11	AIP-125984	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
12	AIP-160829	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
13	AIP-184744	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
14	AIP-128136	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
15	AIP-181273	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
16	AIP-153125	113823	2	5	2xWk x 2	10	4	i.p.	EMT6
17	AIP-101235	113823	3	5	2xWk x 2	10	4	i.p.	EMT6
18	AIP-192482	113823	60	5	2xWk x 2	20	4	i.p.	EMT6
19	AIP-160470	113823	56	5	2xWk x 2	20	4	i.p.	EMT6
20	PES			0	2xWk x 2	20	4	i.p.	EMT6

Study Outline

- study tested 16 new variants + 1 (from round 1) + 2 in the EMT6 tumor model

- All antibodies tested at 5 mg/kg

- dosing plan was 2x/Wk for 4 doses

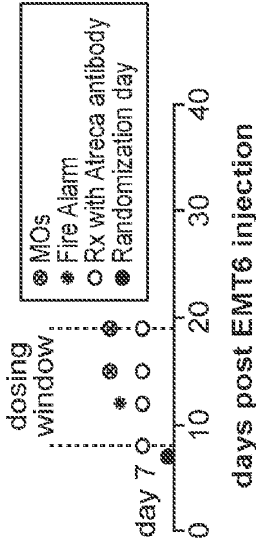


FIG. 42

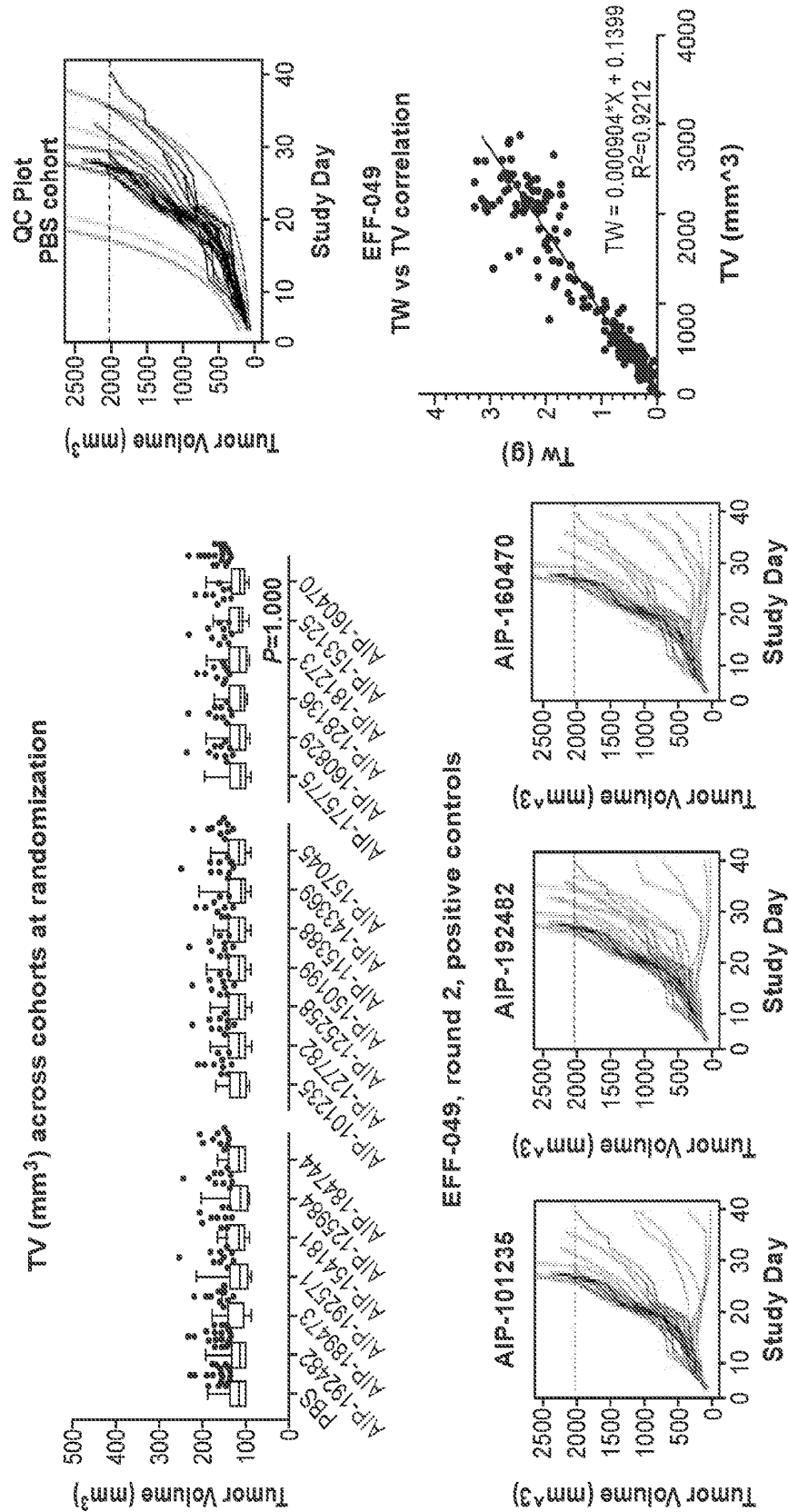


FIG. 43

Antibody Performance Metrics
antibodies sorted by median survival (days)

Antibody ID	Median Survival	Log-Rank p-value	Ref. Median Survival
AIP-192571		3.0E-05	28
AIP-101235		1.9E-02	28
AIP-189473	40	2.6E-03	28
AIP-125258	40	2.2E-03	28
AIP-160470	36	1.1E-02	28
AIP-150199	34	2.7E-02	28
AIP-157045	33.5	1.8E-02	28
AIP-127782	30	7.5E-02	28
AIP-181273	30	4.4E-02	28
AIP-125984	28	5.5E-01	28
AIP-128136	27	4.8E-01	28
AIP-175775	27	2.7E-01	28
AIP-192482	26	2.1E-01	28
AIP-115388	23	4.7E-01	28
AIP-160829	19	9.5E-01	28
AIP-143369	19	9.2E-01	28
AIP-184744	19	9.1E-01	28
AIP-153125	19	4.5E-01	28
AIP-154181	19	4.4E-01	28

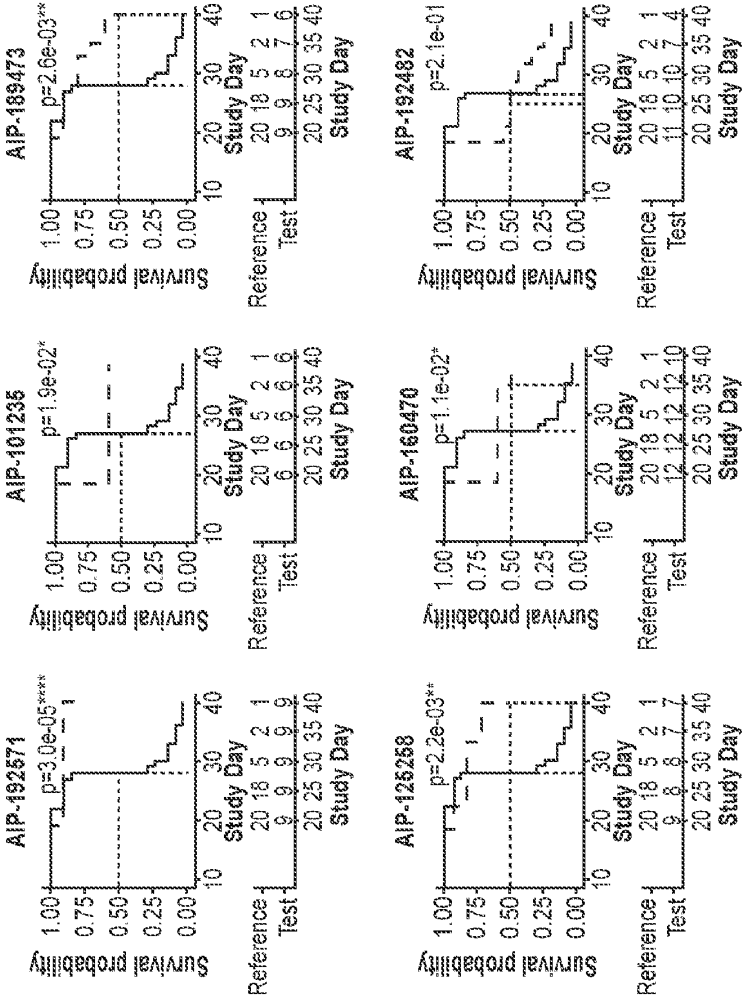


FIG. 44

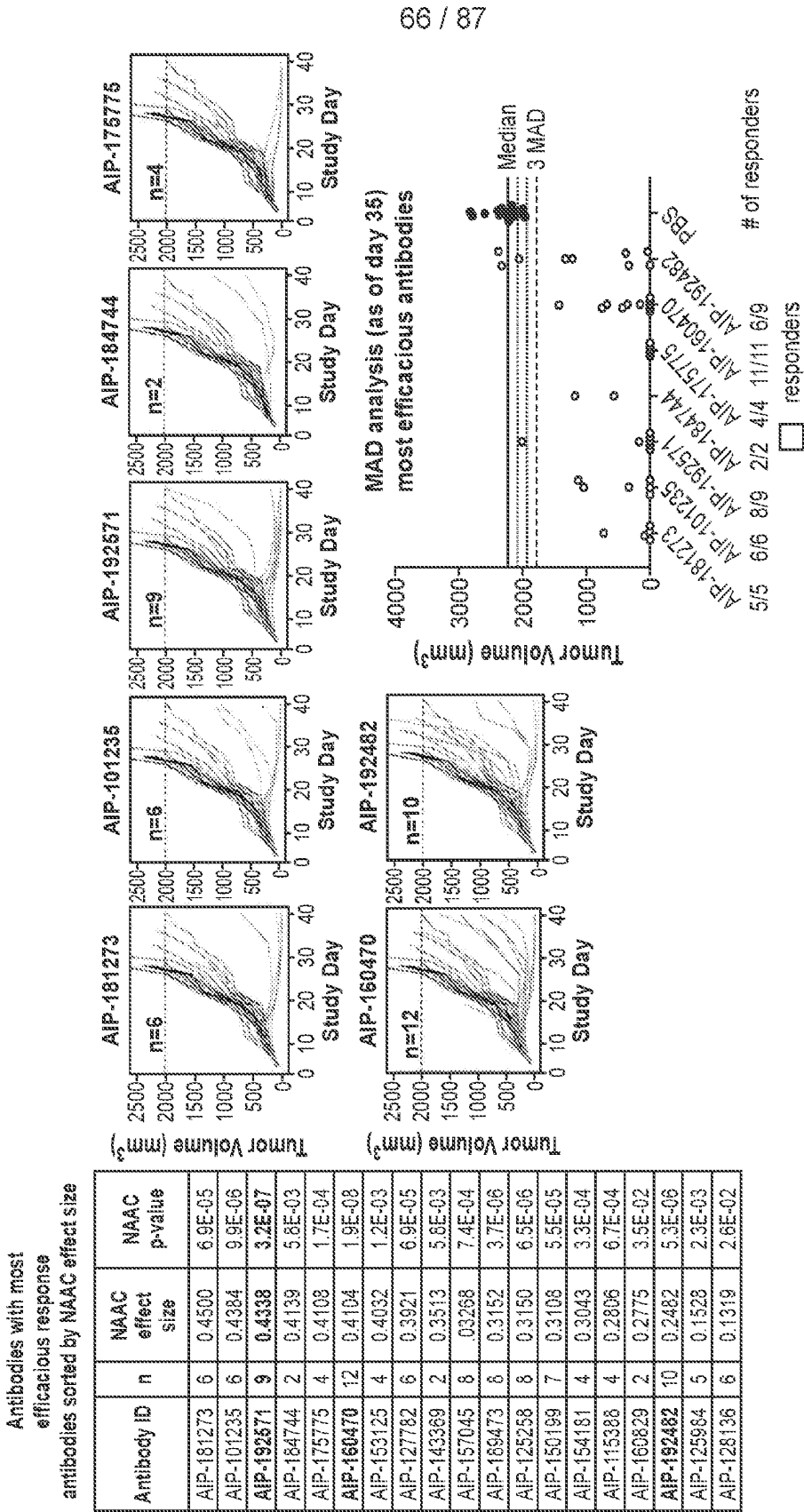
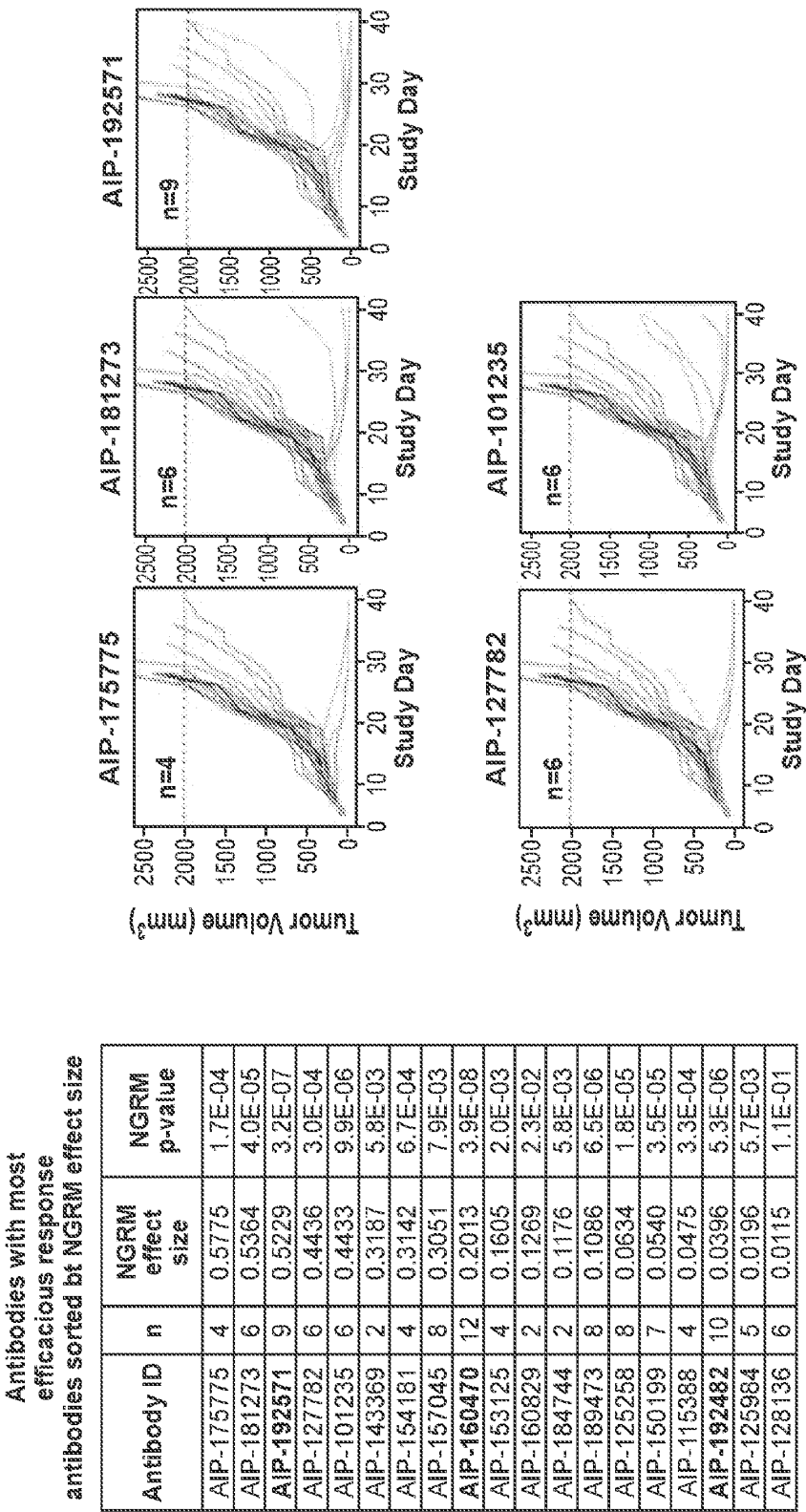
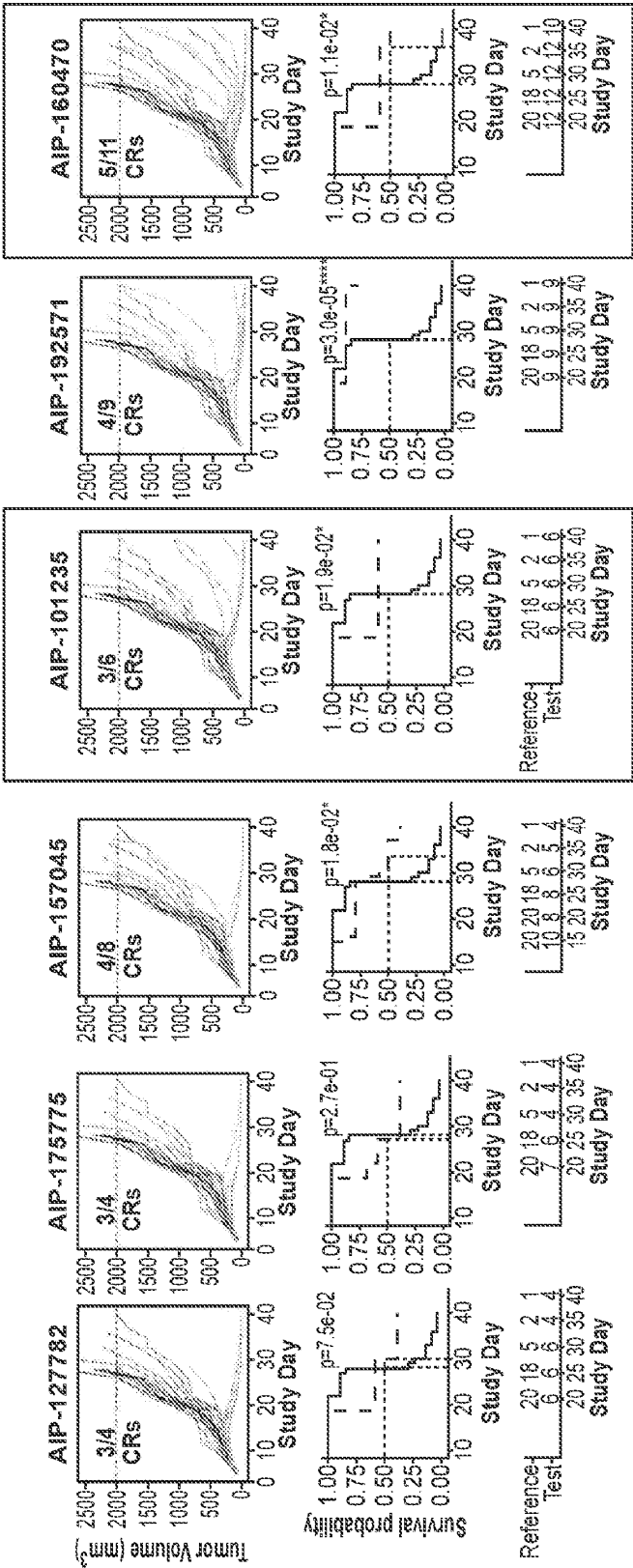


FIG. 45



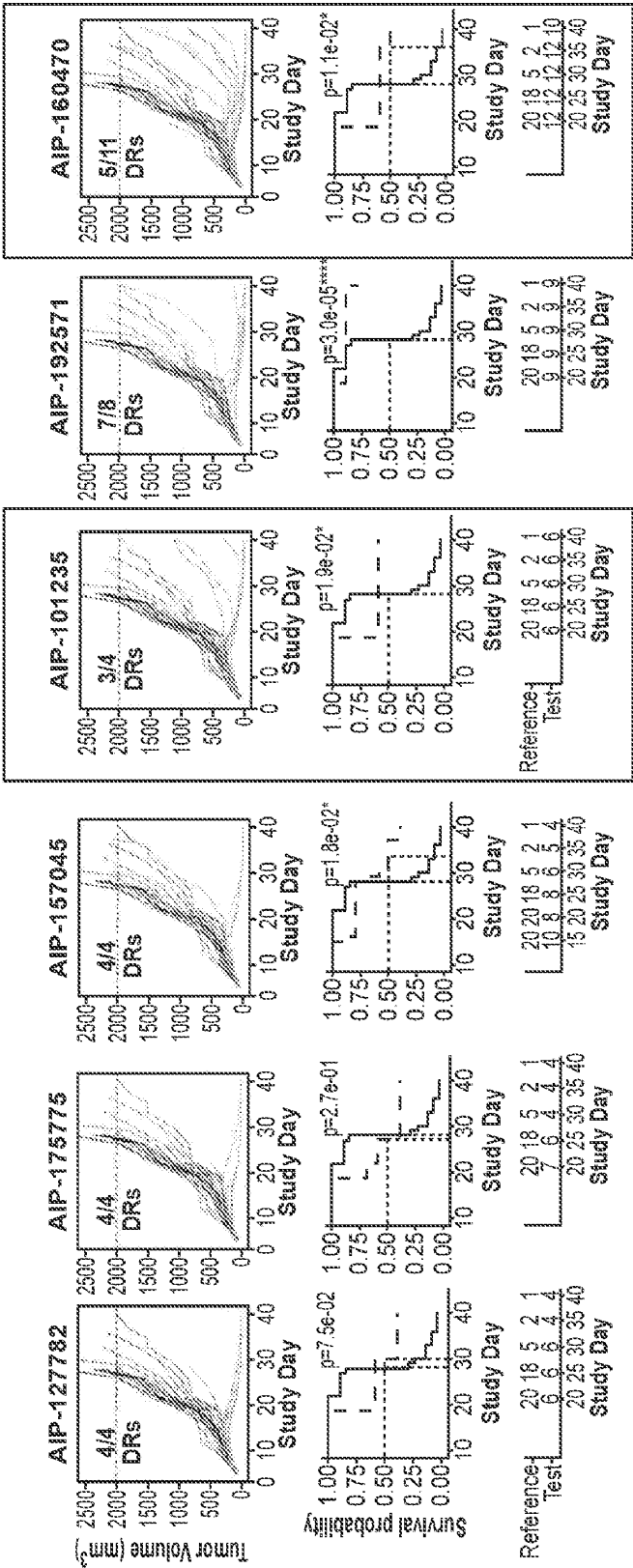
Antibodies with most Complete Responses



CR is when three consecutive TVMs are recorded as 0 mm³.
(Analysis at day 40)

FIG. 47

Antibodies with most durable response



Of the mice that showed a response to Rx, DR represents continued tumor regression post-dosing window (Analysis at day 40)

FIG. 48

AIP-192482 IP Variants summary- Round 1 + Round 2
EFF-046

Group	Mutations	Antibody ID	n	NAAC effect size	NGRM effect size
HCDR3 mutation	H106GS, H112HS, H118GN	AIP-101235	9	0.376	0.285
-	Wildtype	AIP-160470	17	0.366	0.317
Other CDRs	L28ND, L93DN, L95SA	AIP-168605	8	0.359	0.255
Other CDRs	H108SN, H113DE, H119GN	AIP-161571	9	0.348	0.194
Other CDRs	H35ST, L26SP, L95SA	AIP-190051	6	0.344	0.177
Computational design of LCDR2	L53NS, L54QL, L57SQ	AIP-136060	10	0.342	0.082

EFF-049

Group	Mutations	Antibody ID	n	NAAC effect size	NGRM effect size
Affinity Improvement	Conservative set from AIP-128136 (4)	AIP-181273	6	0.450	0.536
HCDR3 mutation	H106GS, H112HS, H118GN	AIP-101235	6	0.438	0.443
HCDR3 Combination	TSSFCRGNQCPSSDTSYCGGQYPSYYMDP (5)	AIP-192571	9	0.434	0.523
CDR Combination	Mutations in H1, H2, H3, L1, L2, L3 (11)	AIP-184744	2	0.414	0.118
CDR Combination	Mutations in H1, H3, L1, L2, L3 (10)	AIP-175775	4	0.411	0.578
-	Wildtype	AIP-160470	12	0.410	0.201

FIG. 49

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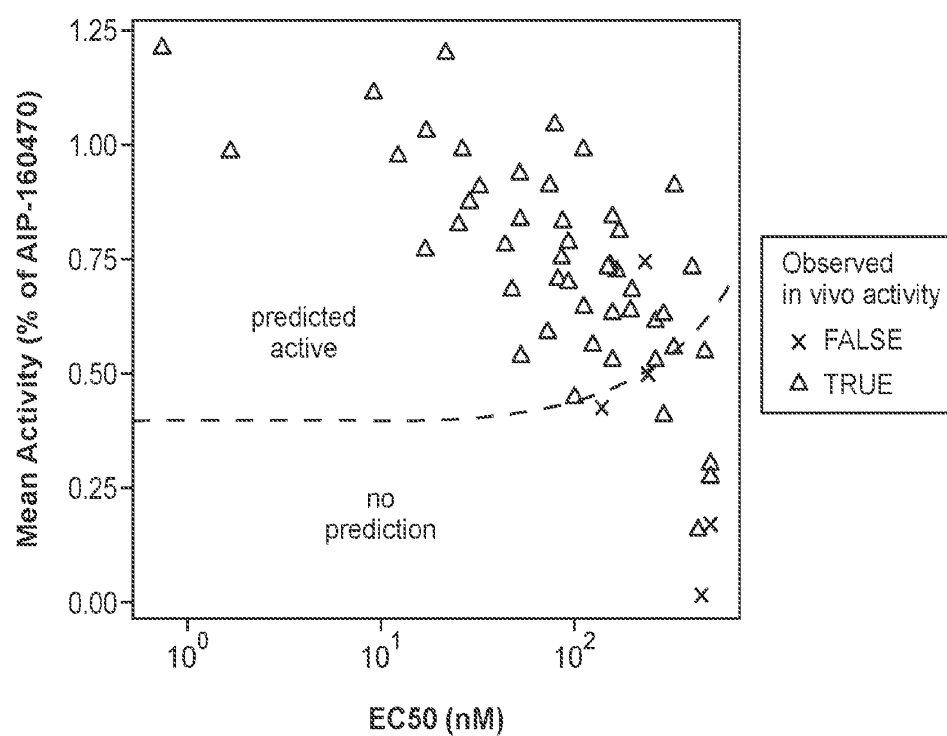


FIG. 50A

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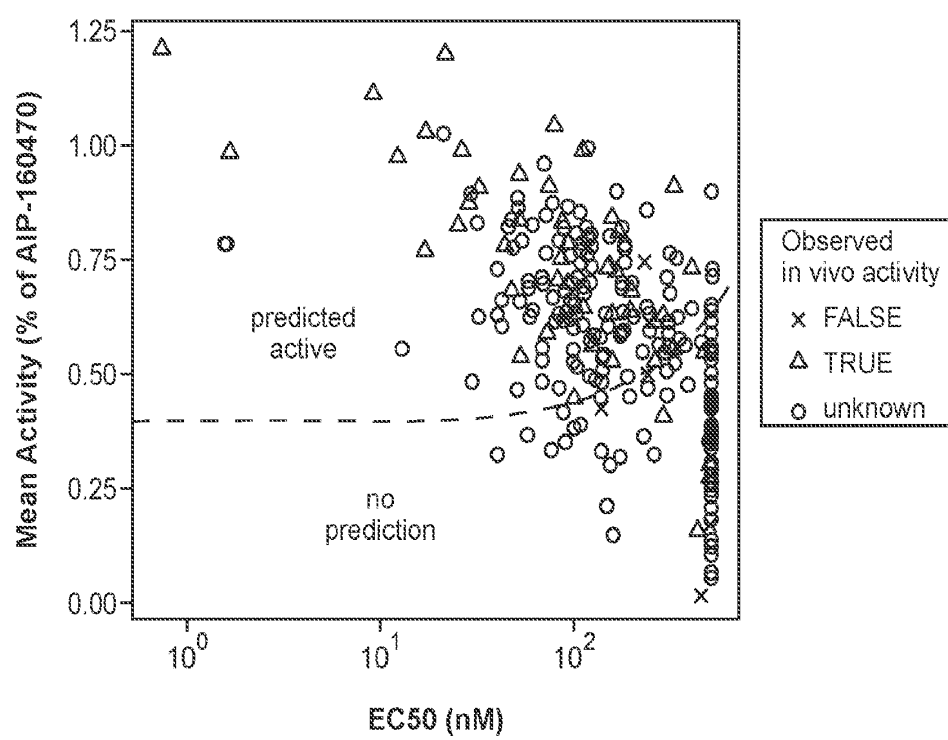


FIG. 50B

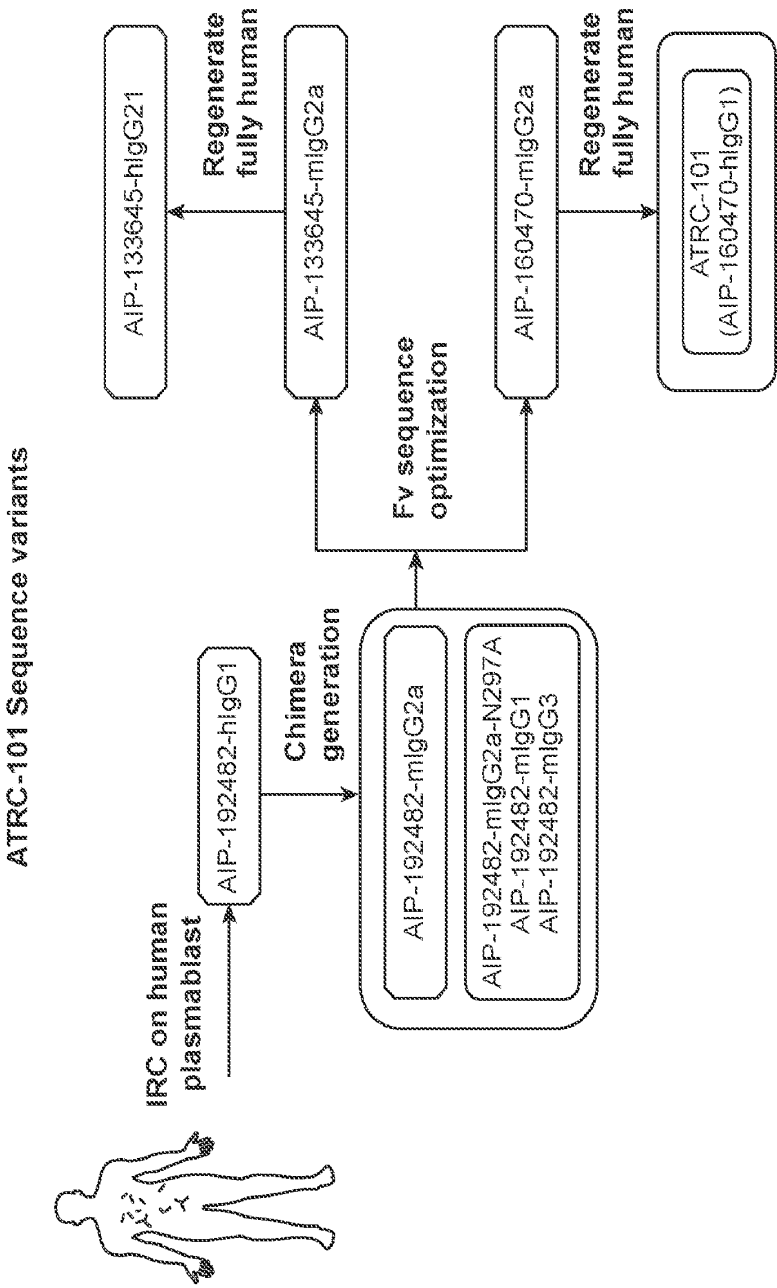


FIG. 51

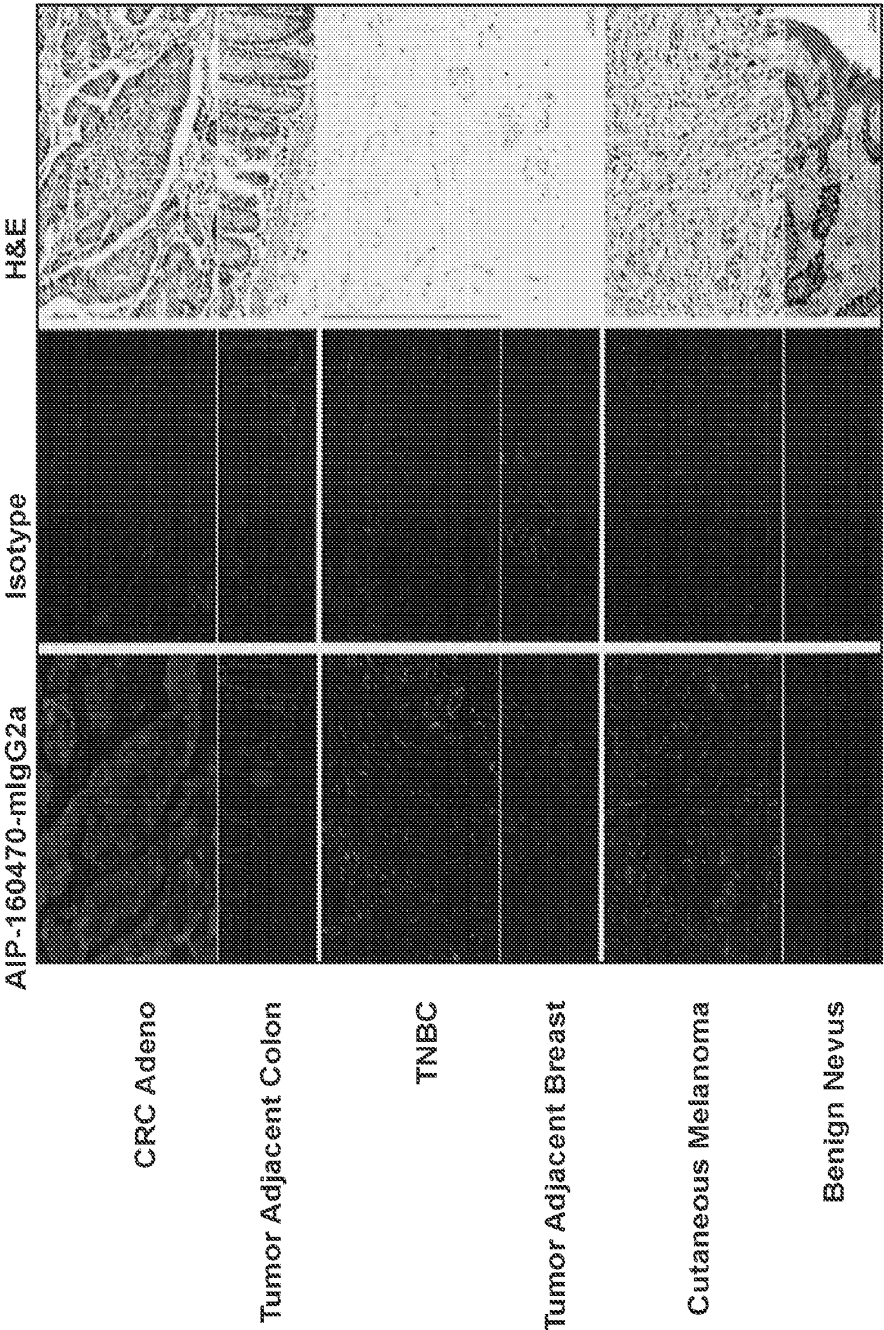


FIG. 52

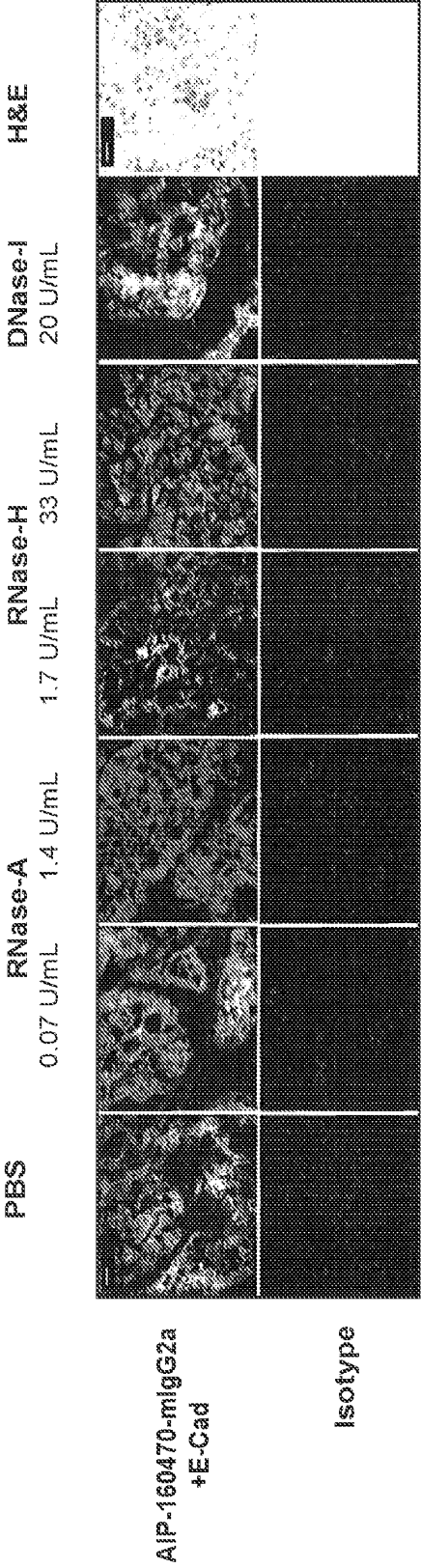


FIG. 53

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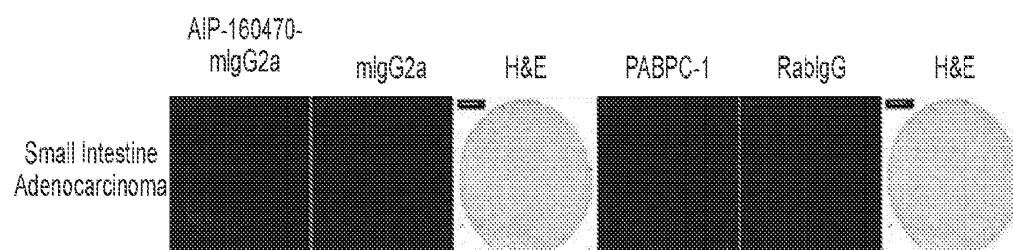


FIG. 54A

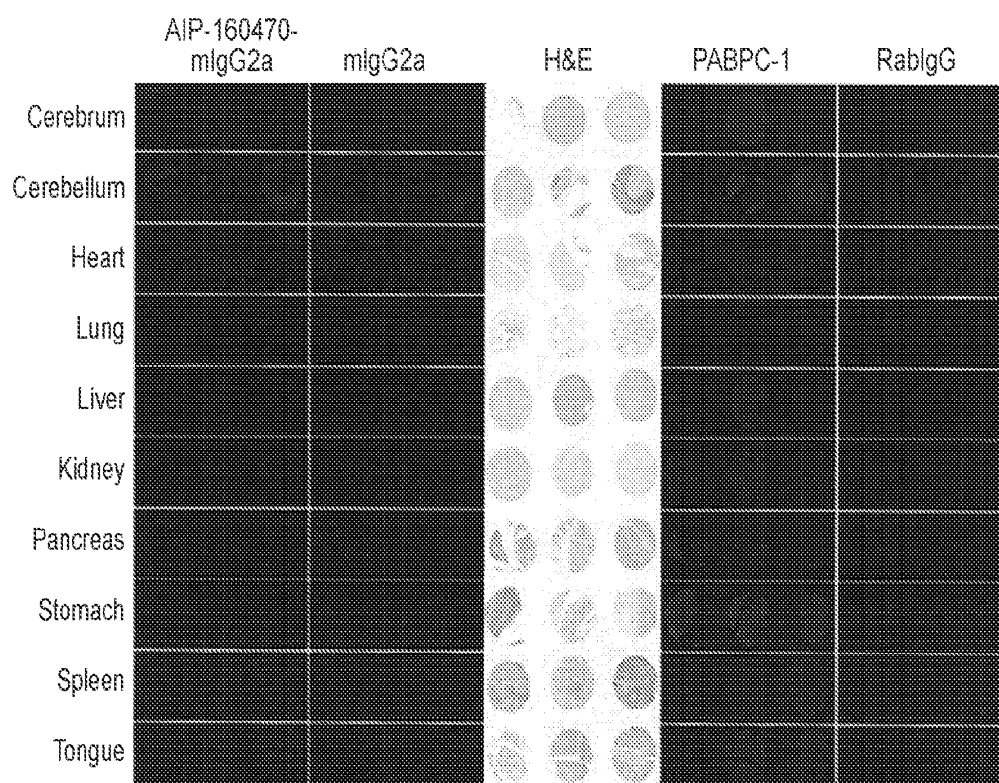


FIG. 54B

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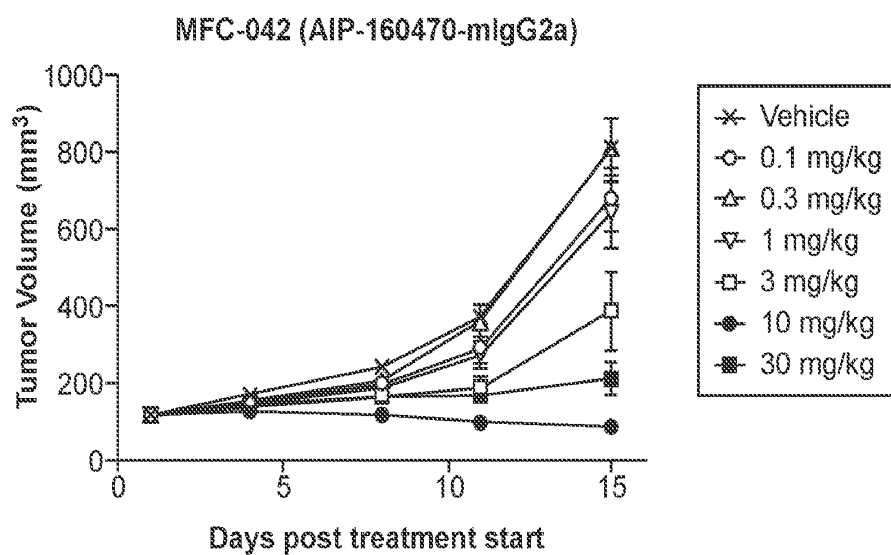


FIG. 55A

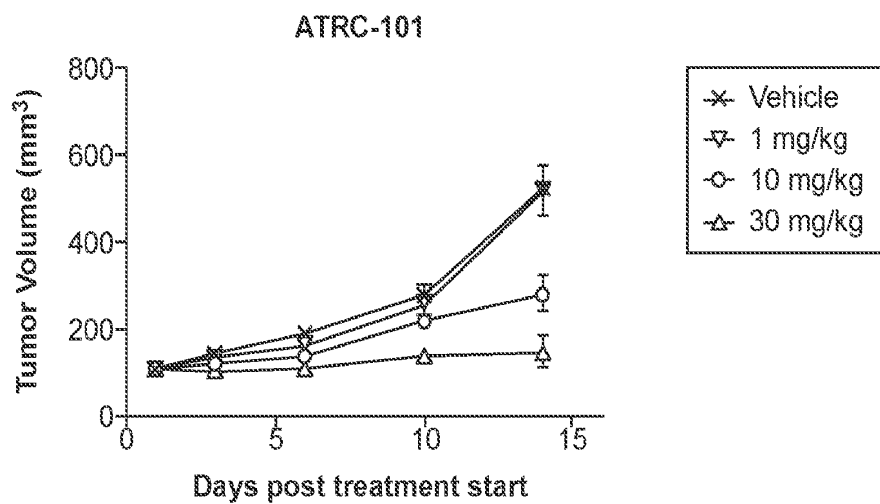


FIG. 55B

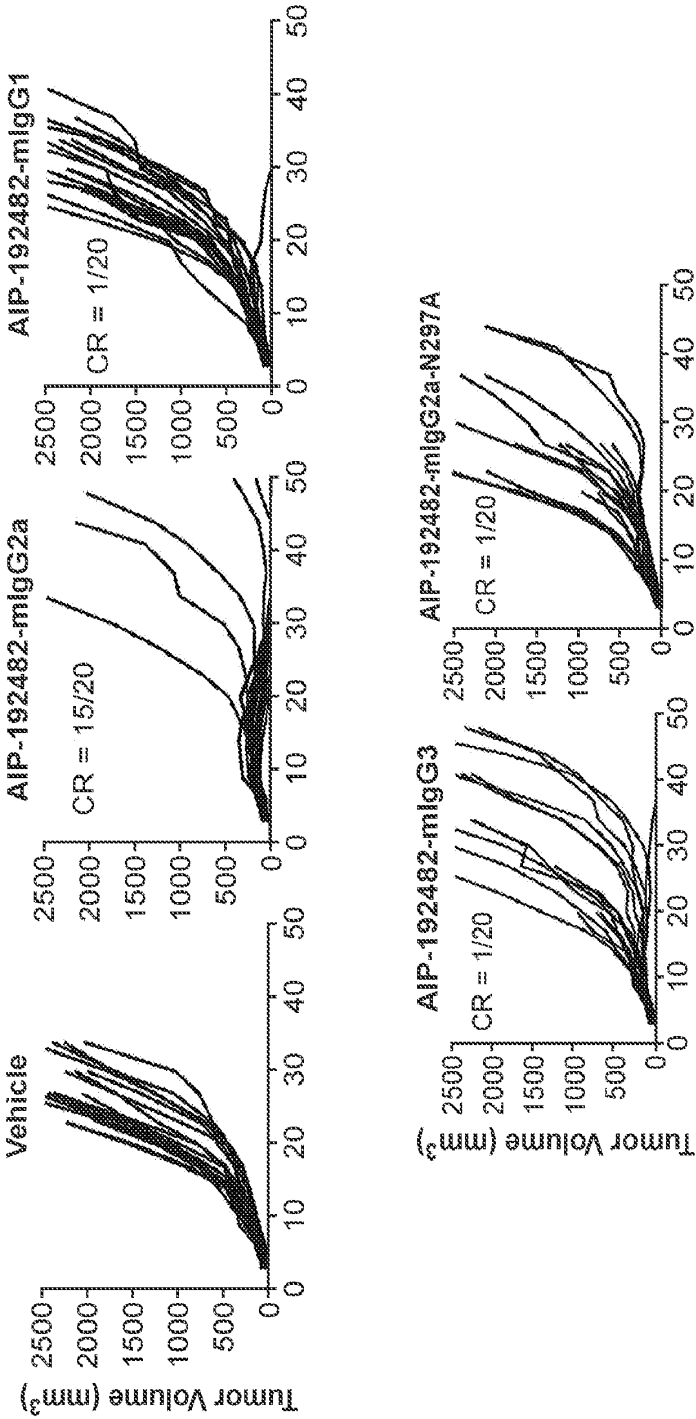


FIG. 56

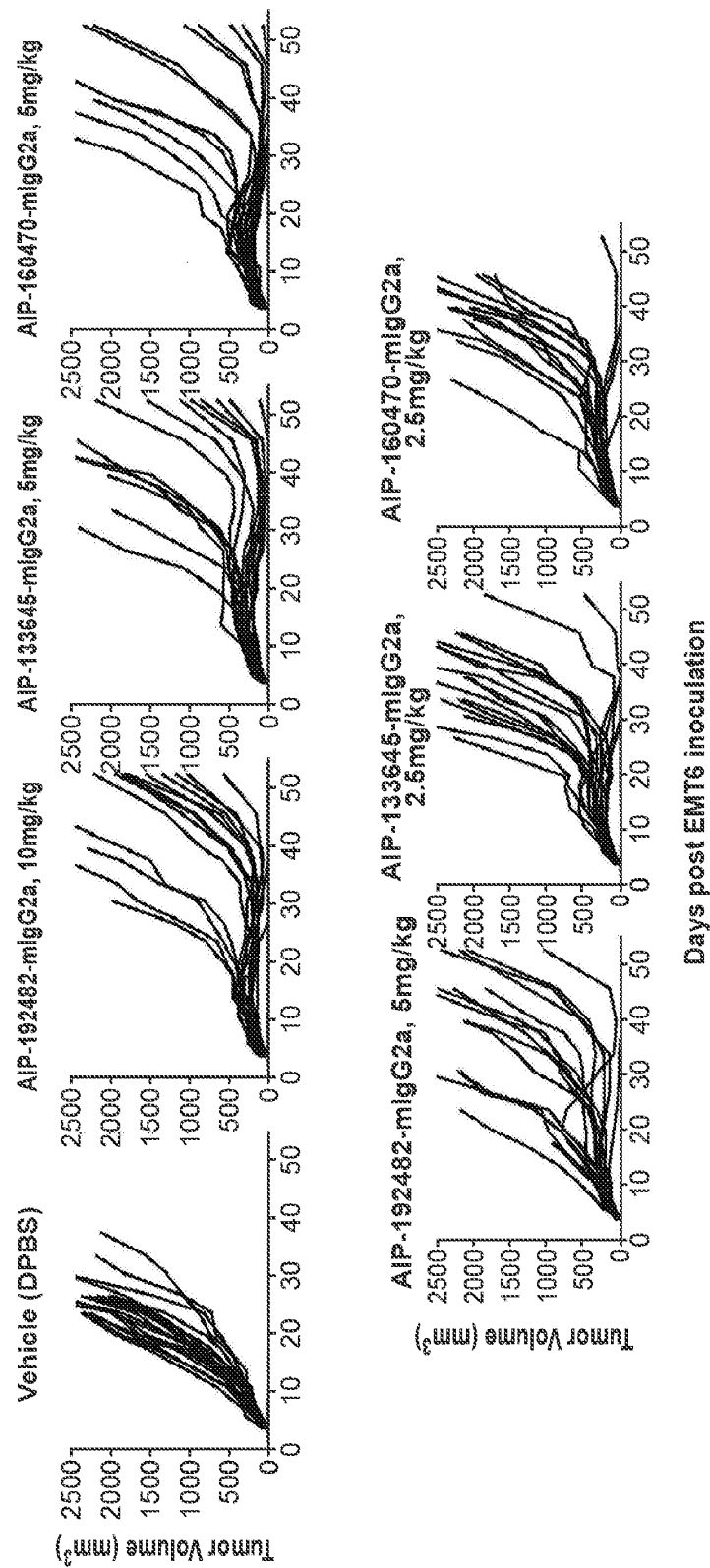
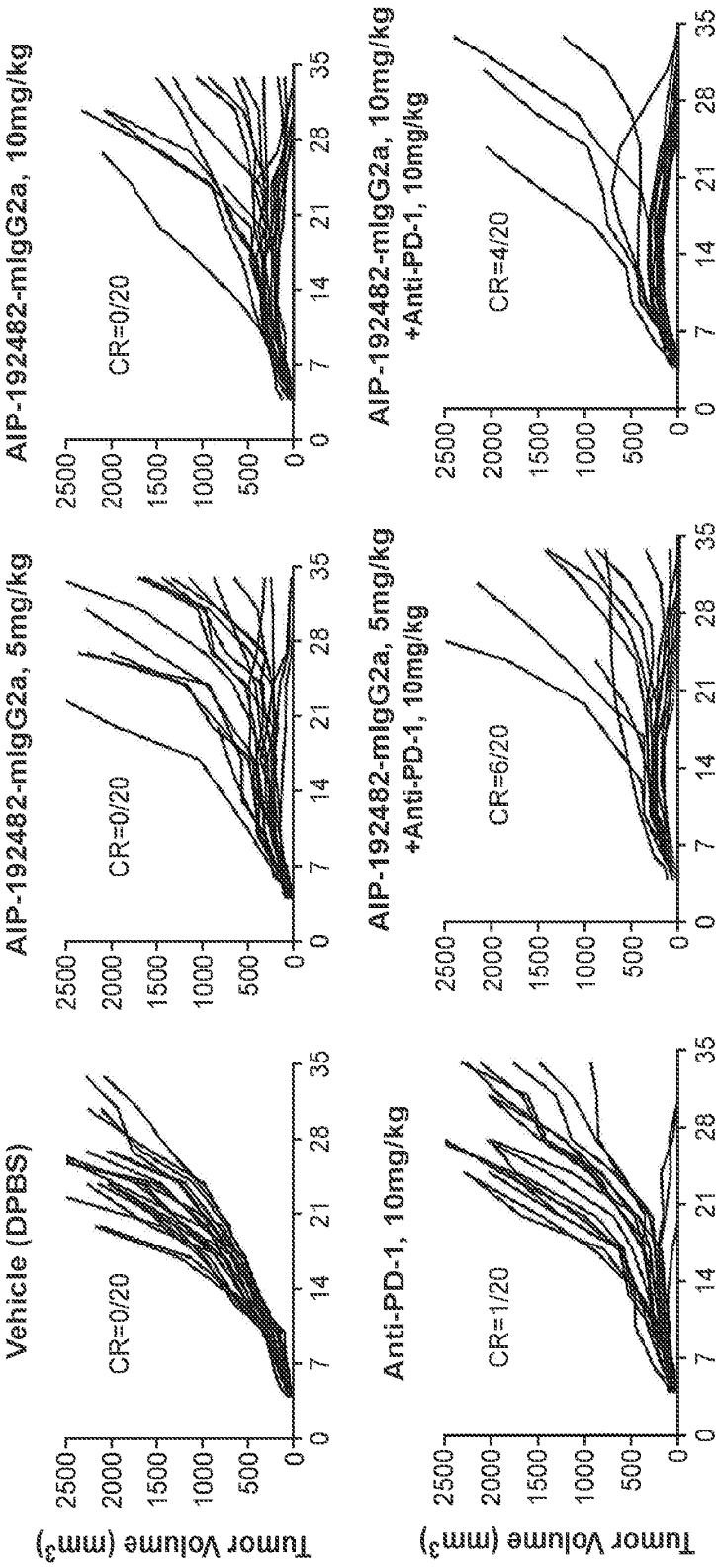


FIG. 57



Days post EMT6 injection

FIG. 58A

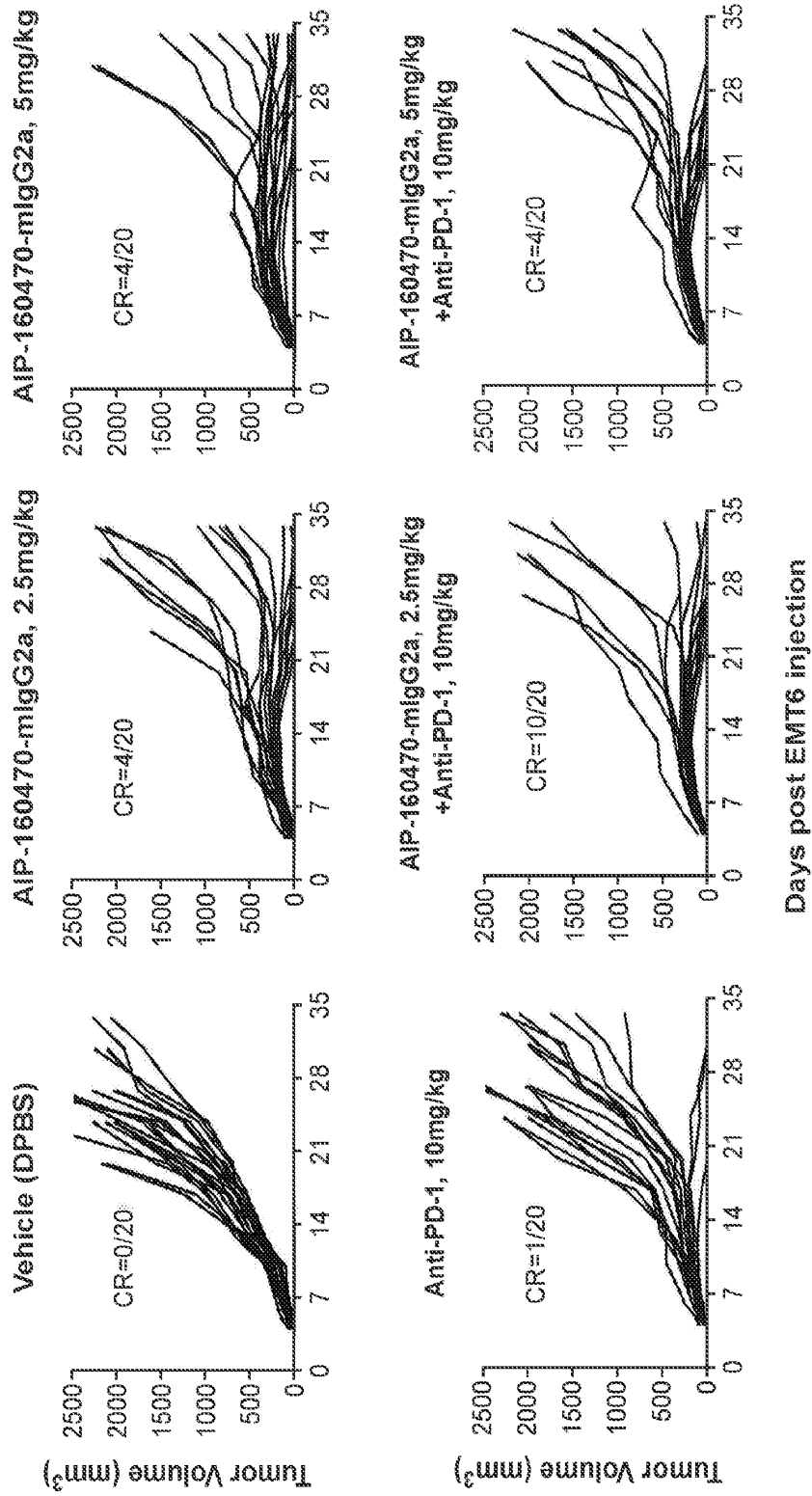


FIG. 58B

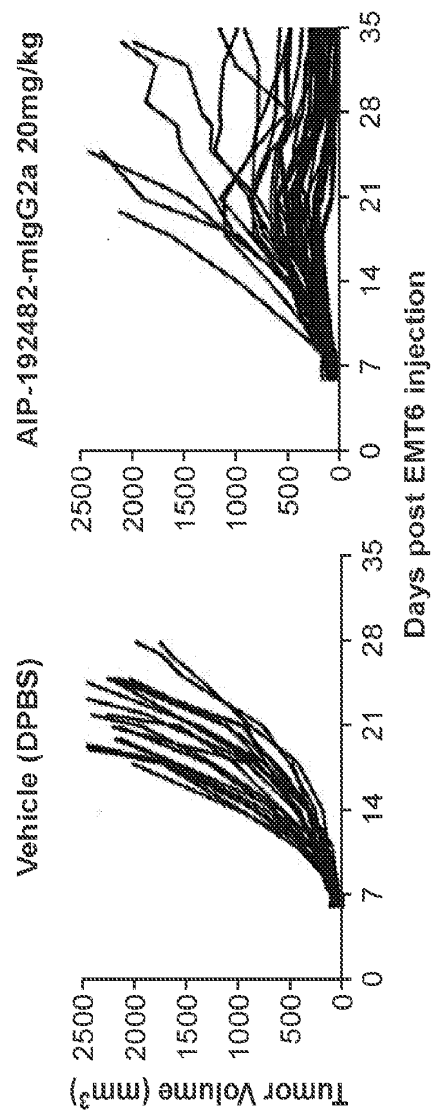


FIG. 59A

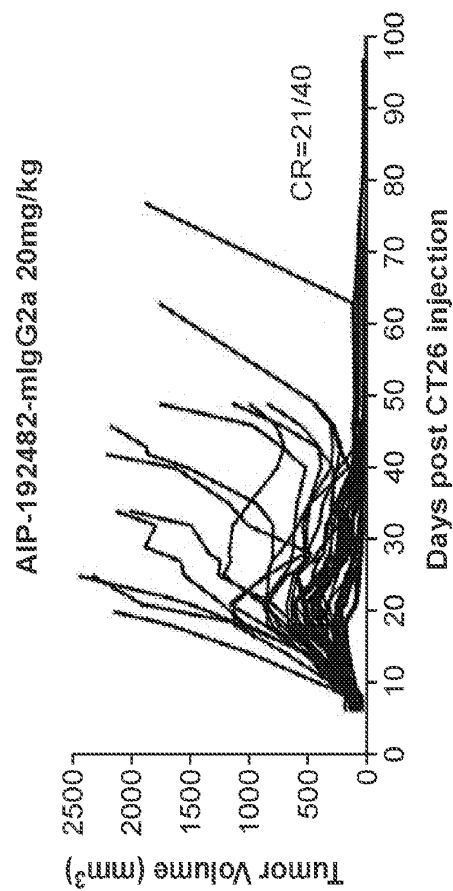


FIG. 59B

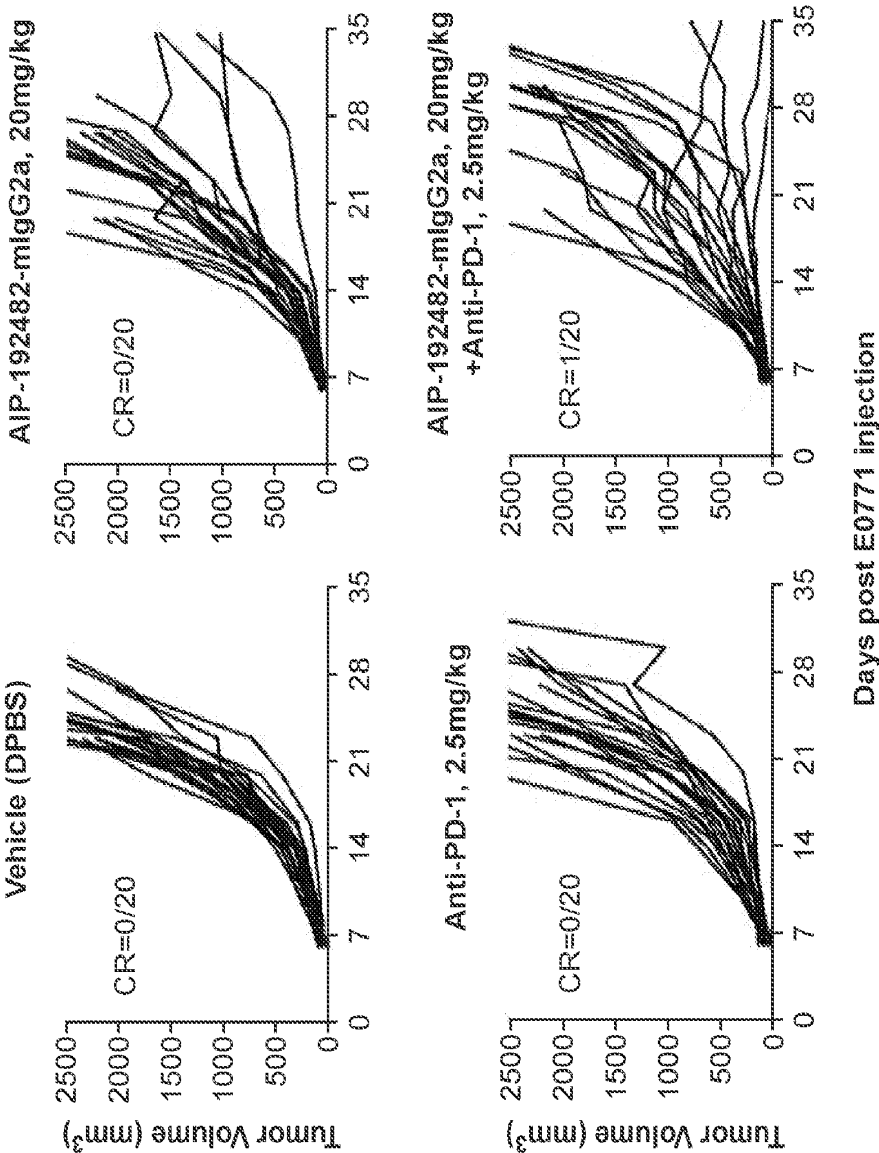


FIG. 60

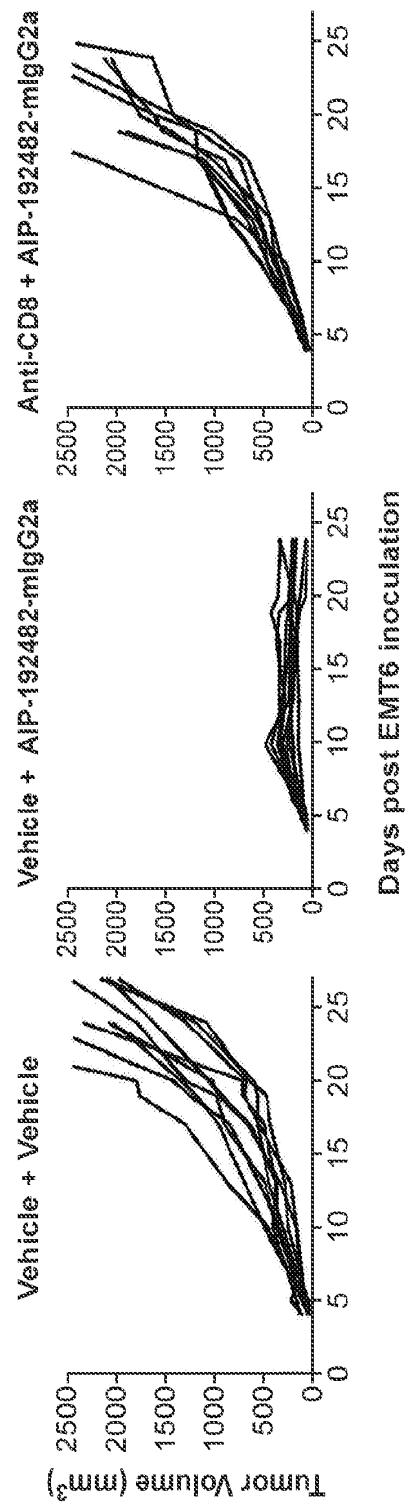
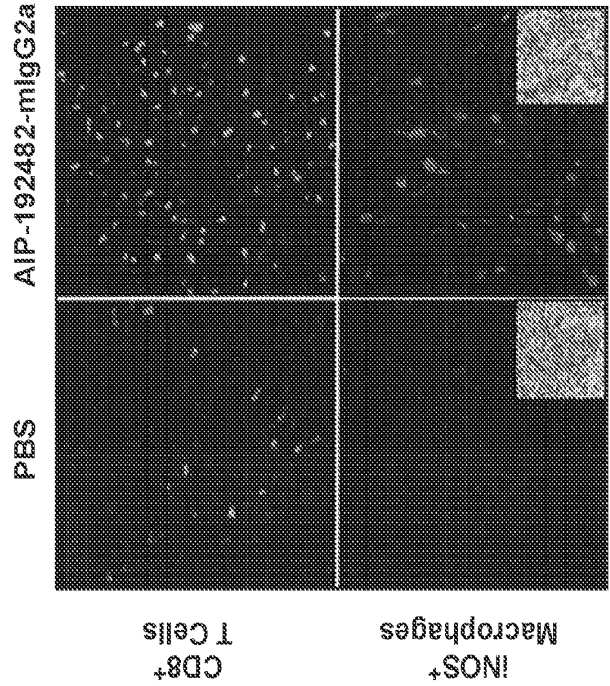
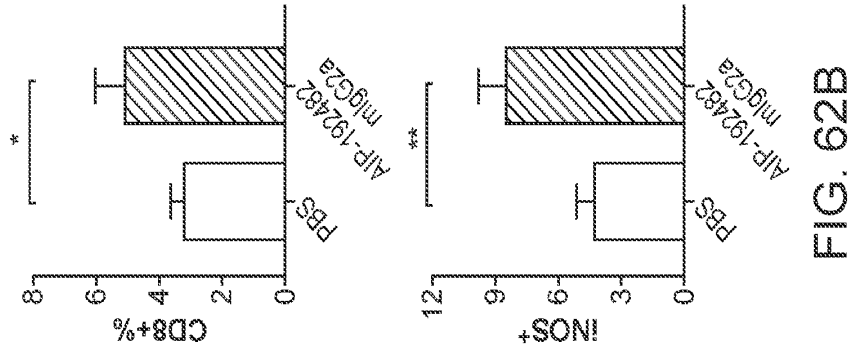


FIG. 61



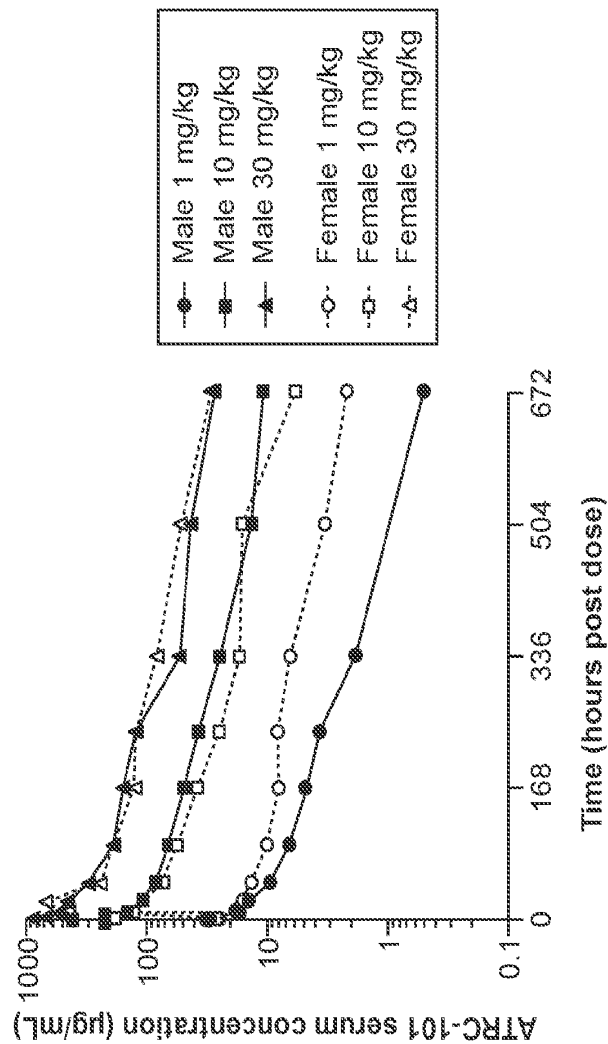


FIG. 63

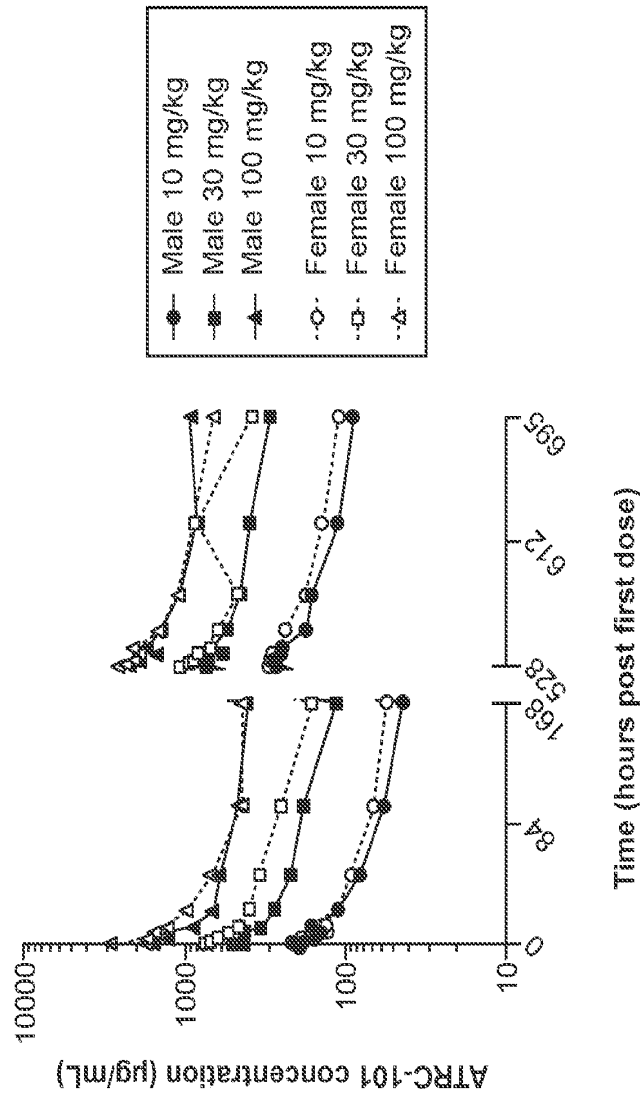


FIG. 64