

FIG. 1

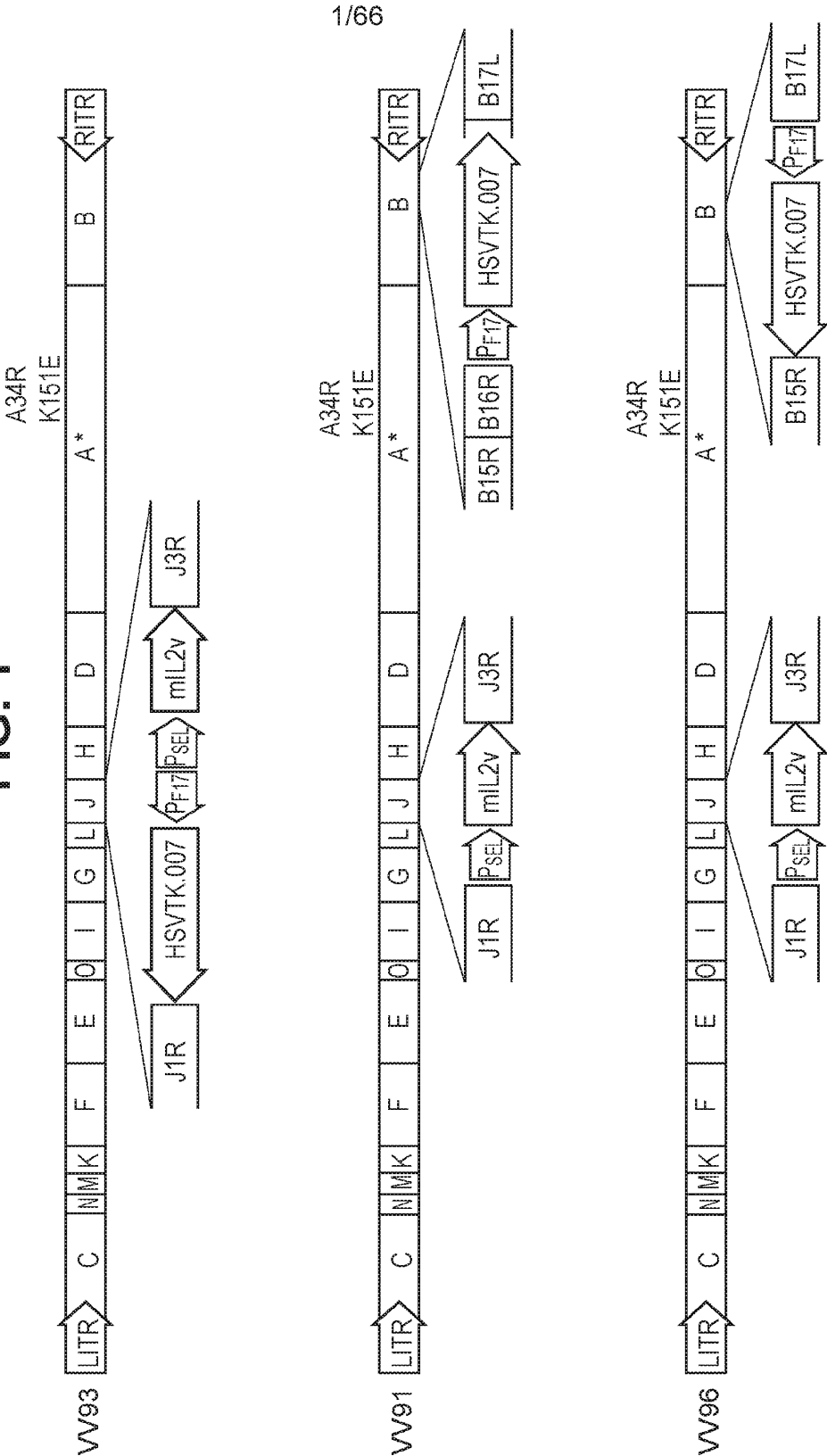


FIG. 2

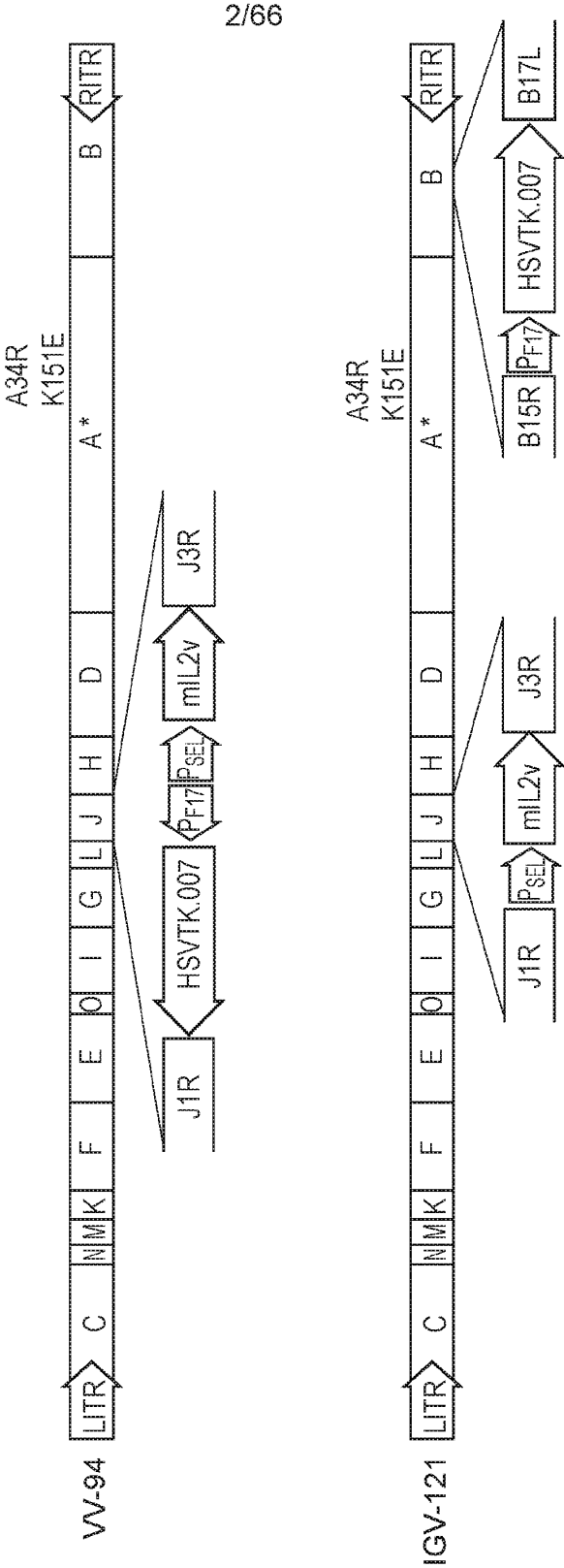
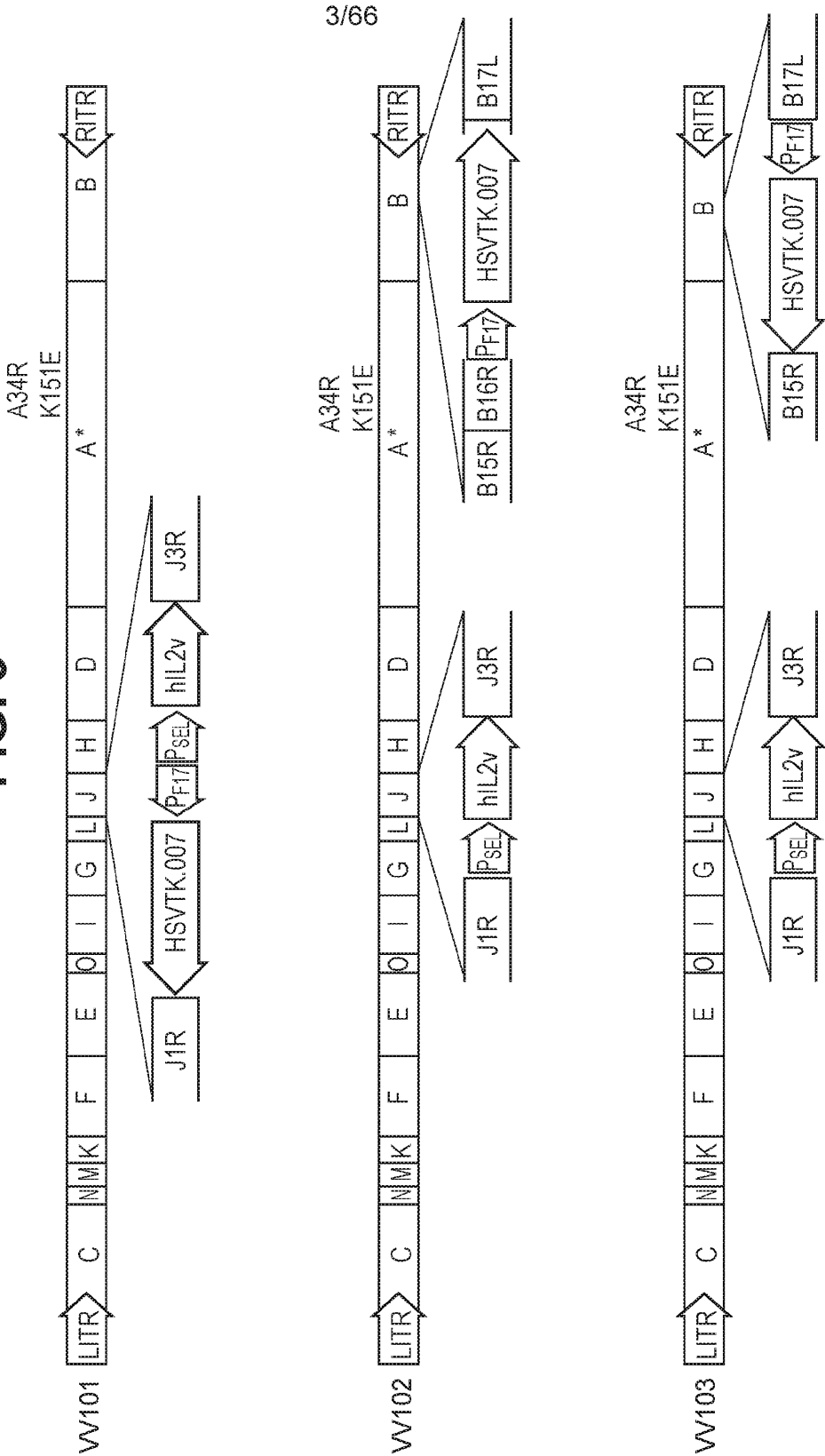


FIG. 3



4/66

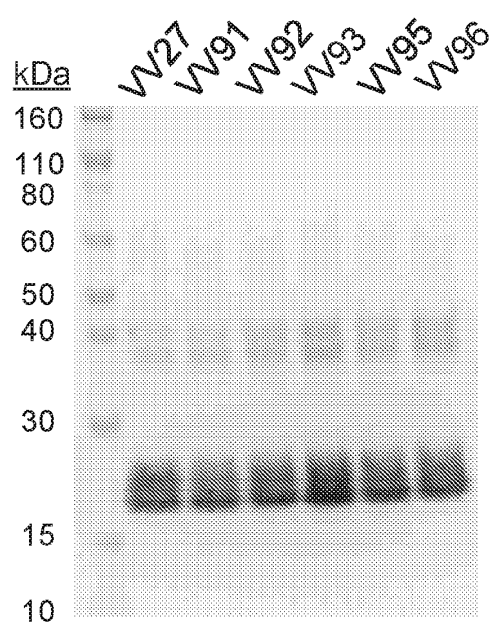
FIG. 4

FIG. 5

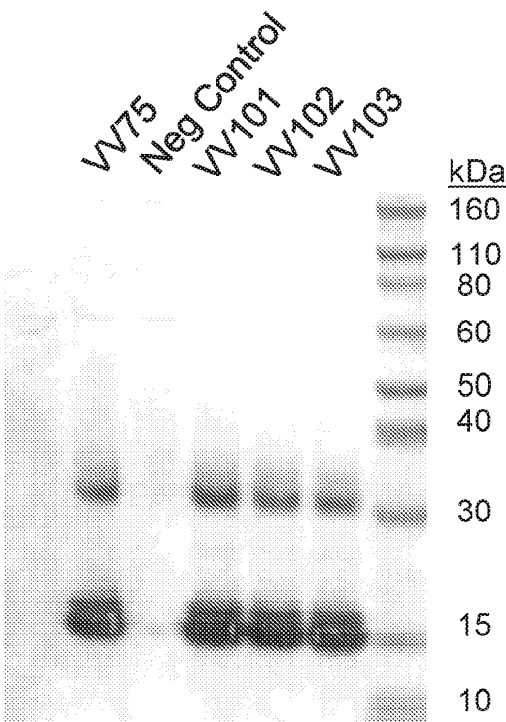
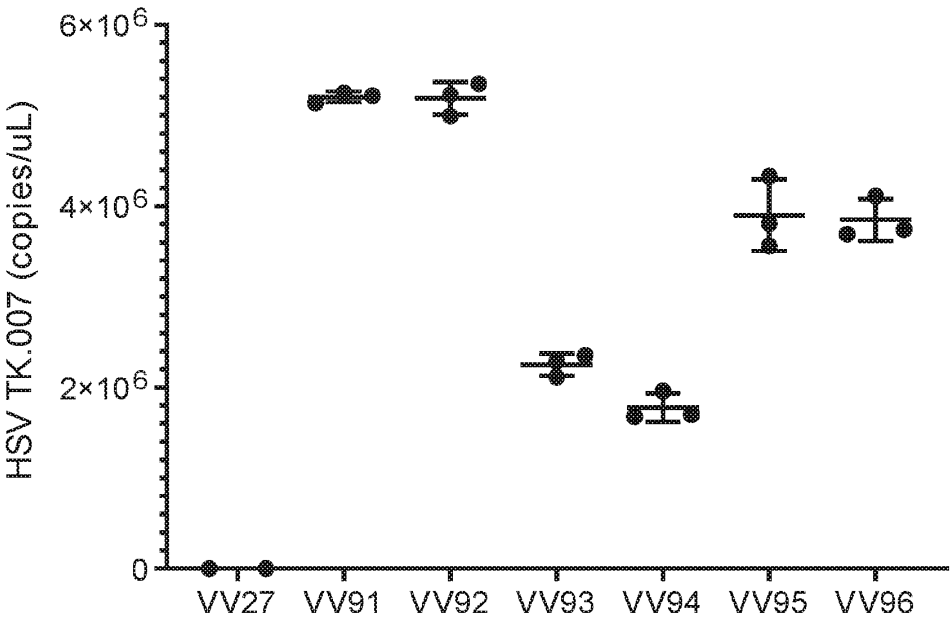


FIG. 6



7/66

FIG. 7A
Vehicle

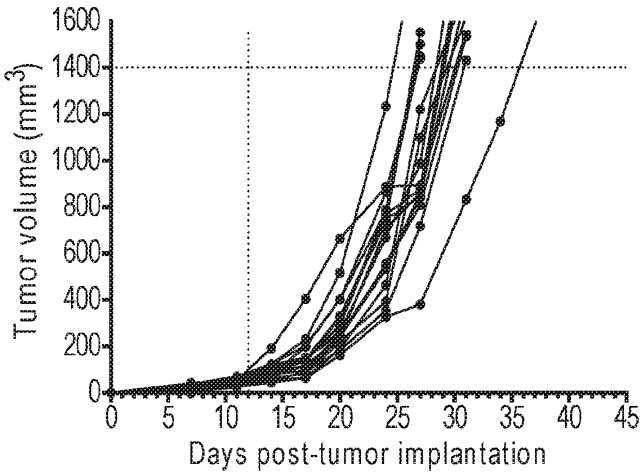


FIG. 7B
VV16

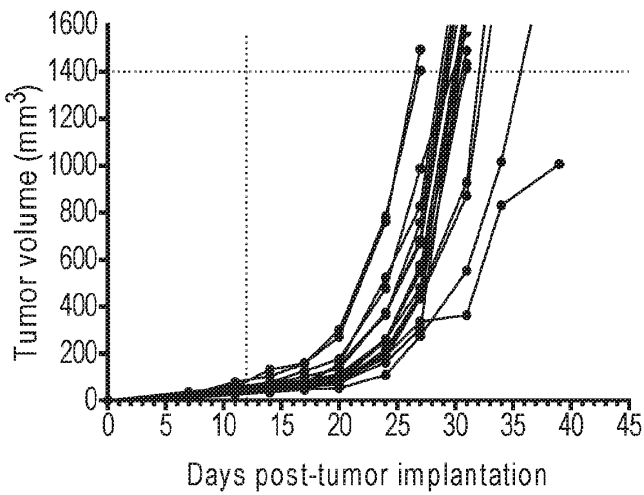
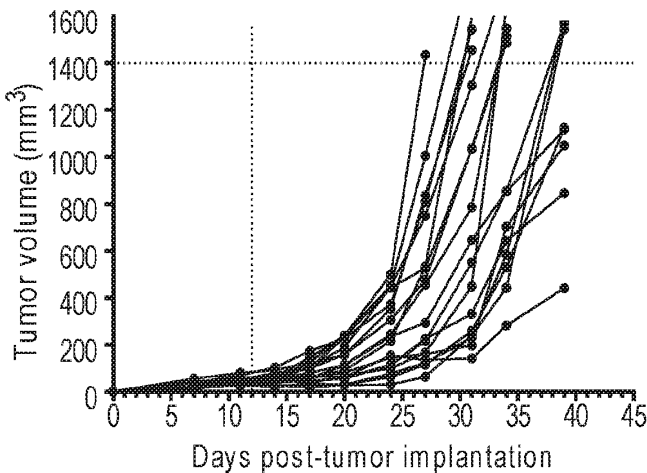


FIG. 7C
VV27



8/66

FIG. 7D
VV91

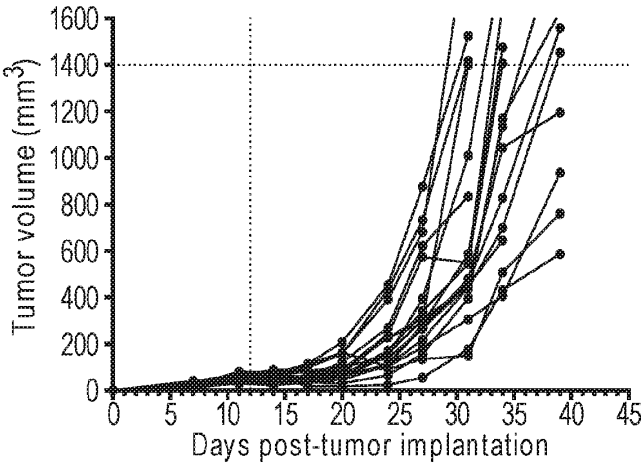


FIG. 7E
VV93

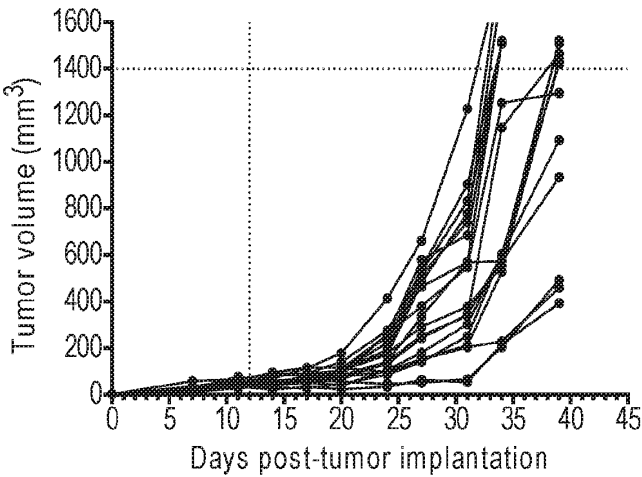
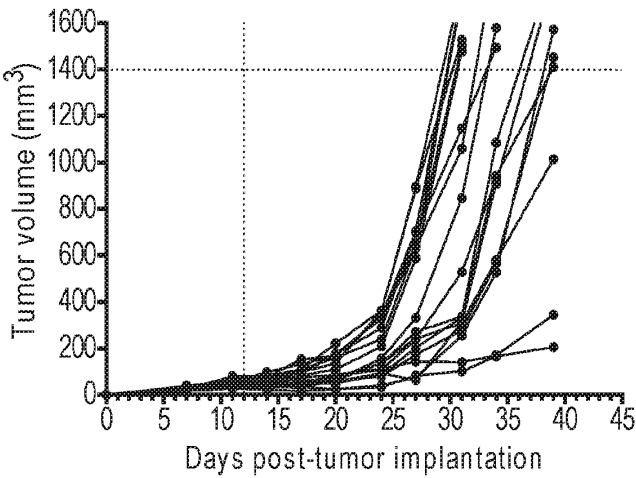
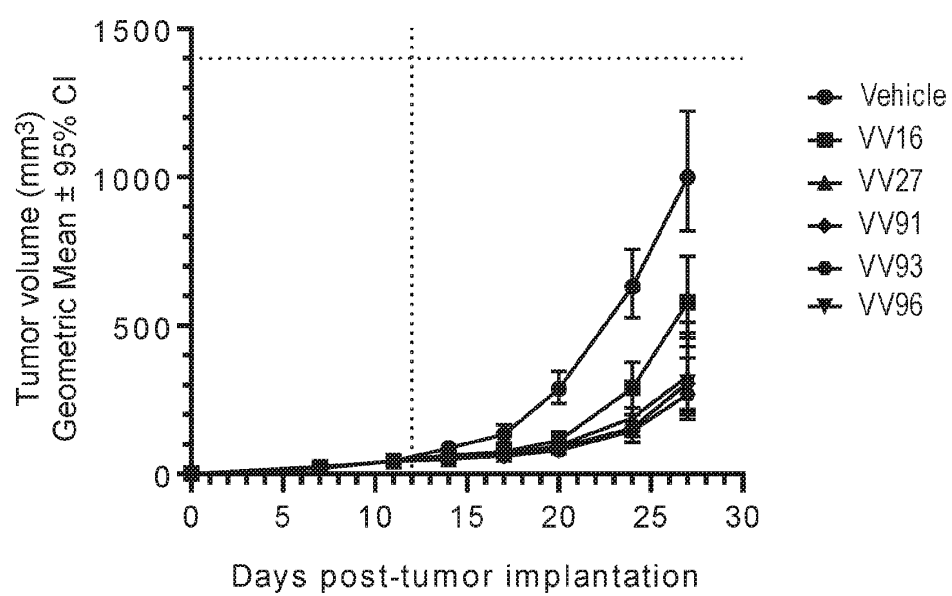


FIG. 7F
VV96



9/66

FIG. 7G

10/66

FIG. 8

	ANCOVA results (p-values for designated group comparisons)								
Day post-tumor implant	VV16 vs. vehicle	VV27 vs. vehicle	VV91 vs. vehicle	VV93 vs. vehicle	VV96 vs. vehicle	VV27 vs. VV16	VV91 vs. VV16	VV93 vs. VV16	VV96 vs. VV16
14	<0.001	<0.001	<0.001	<0.001	<0.001	0.004	0.025	0.007	0.018
17	<0.001	<0.001	<0.001	<0.001	<0.001	0.128	0.021	0.063	0.074
20	<0.001	<0.001	<0.001	<0.001	<0.001	0.136	0.010	0.013	0.054
24	<0.001	<0.001	<0.001	<0.001	<0.001	0.013	<0.001	<0.001	<0.001
27	0.008	<0.001	<0.001	<0.001	<0.001	0.007	0.003	<0.001	0.003

11/66

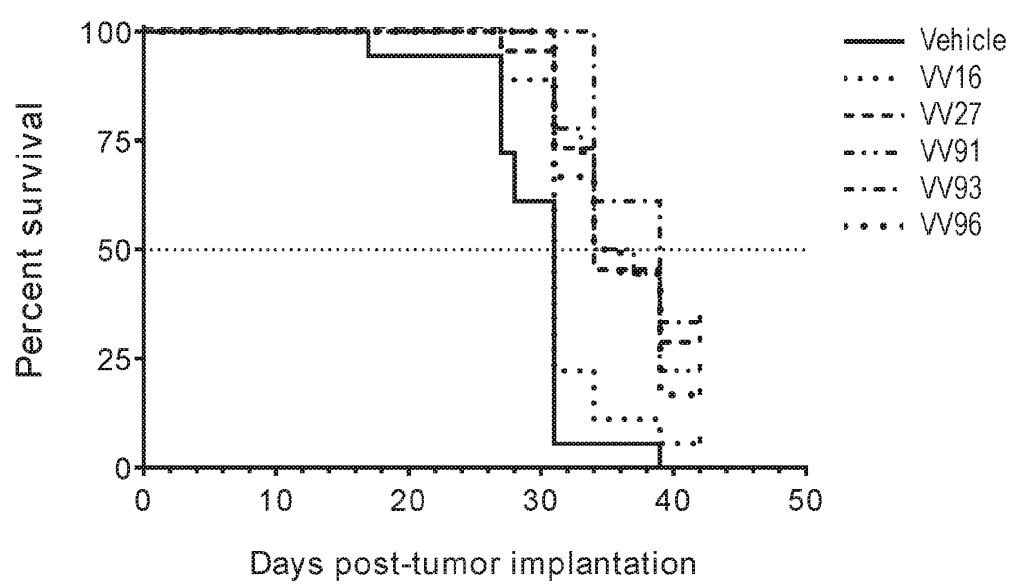
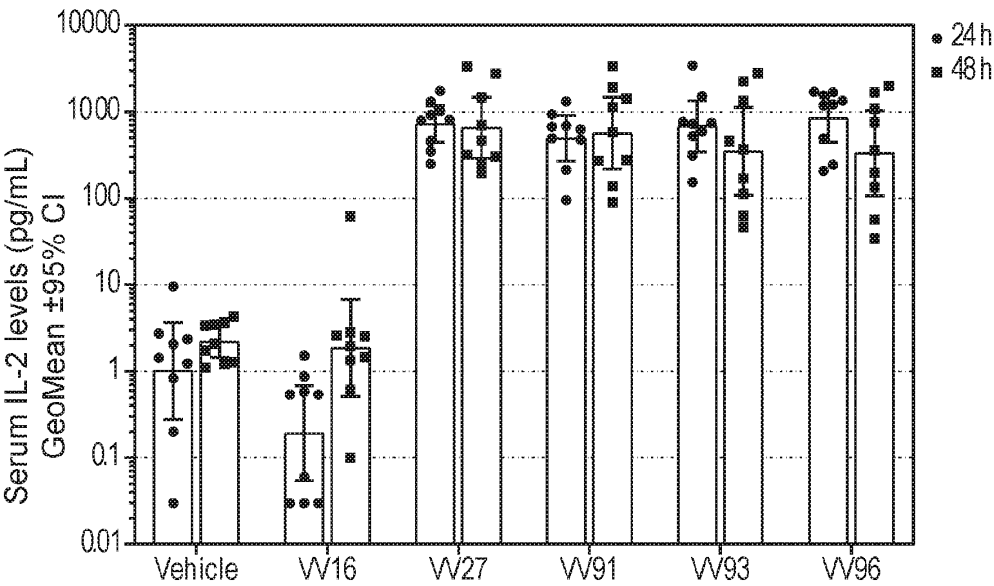
FIG. 9

FIG. 10



13/66

FIG. 11A
Vehicle

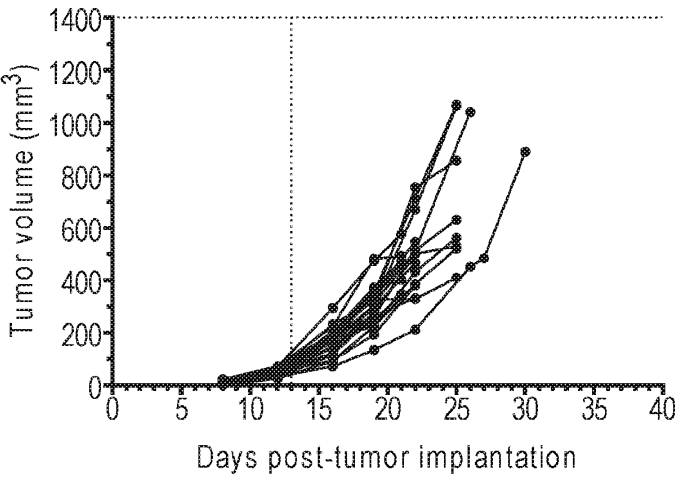


FIG. 11B
VV16

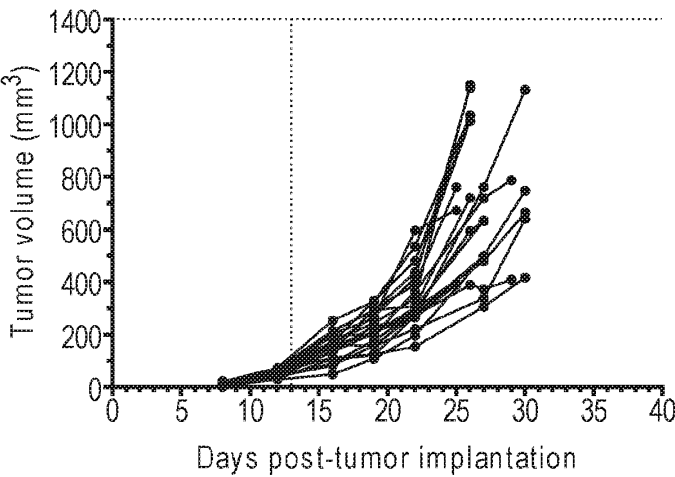


FIG. 11C
VV27

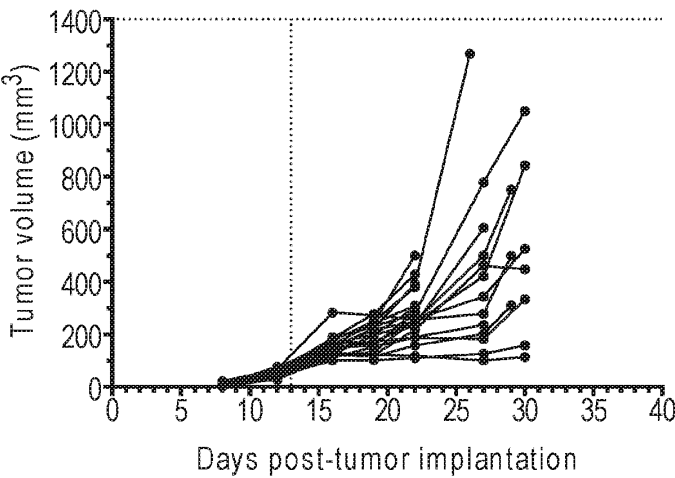


FIG. 11D
VV91

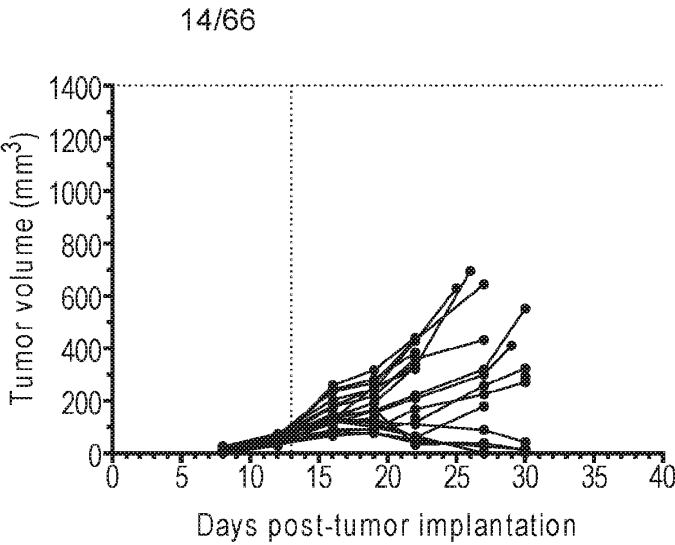


FIG. 11E
VV93

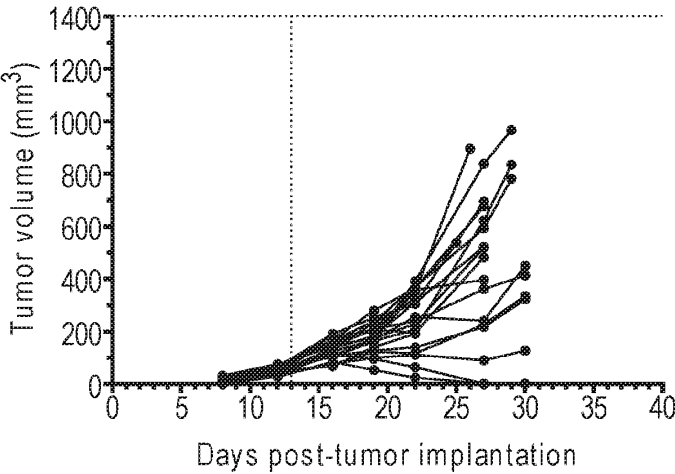


FIG. 11F
VV96

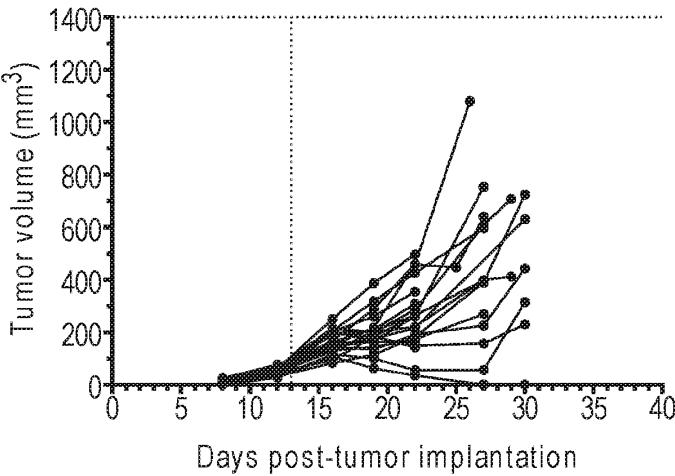


FIG. 12

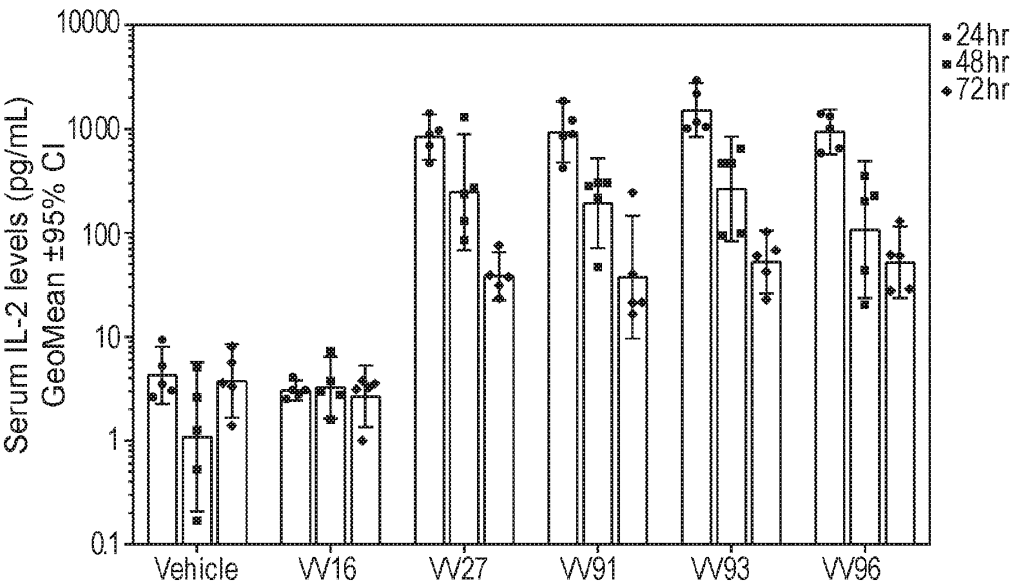


FIG. 13A

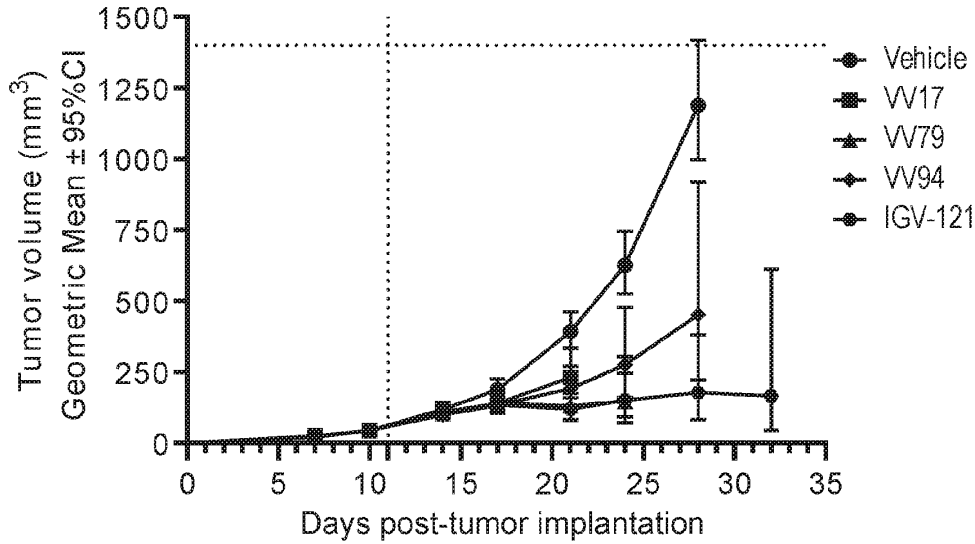


FIG. 13B
Vehicle

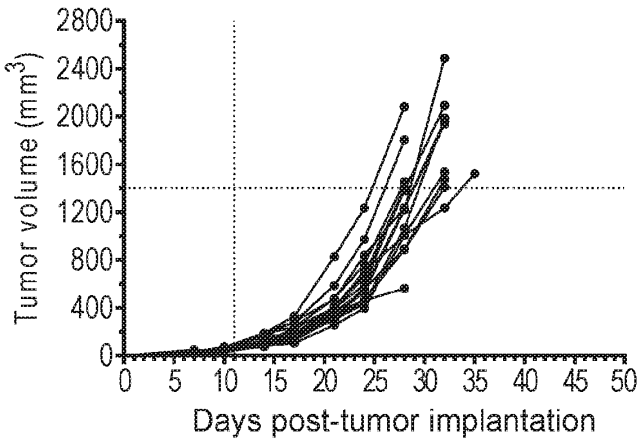
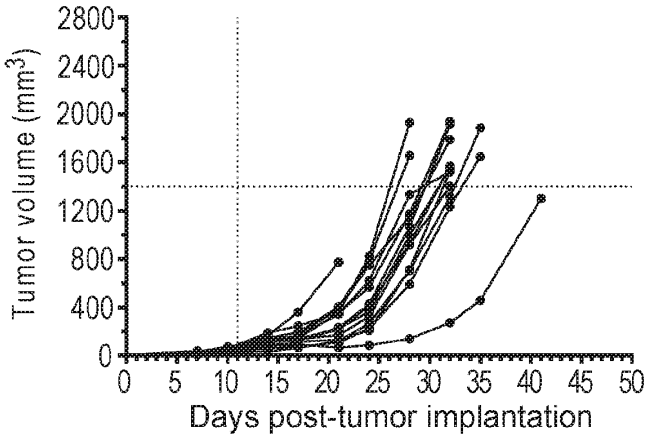


FIG. 13C
VV17



17/66

FIG. 13D
VV79

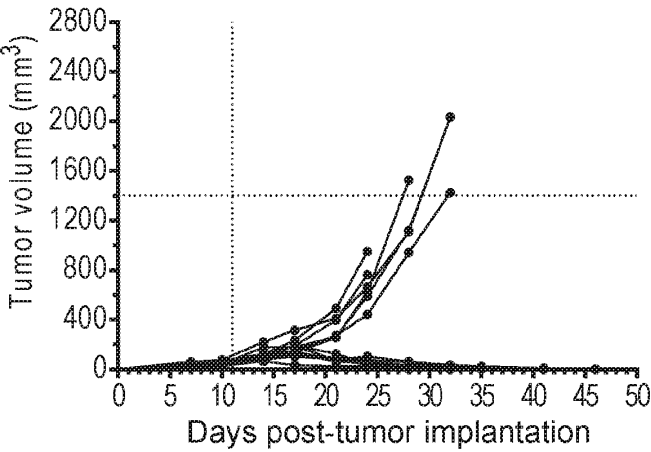


FIG. 13E
VV94

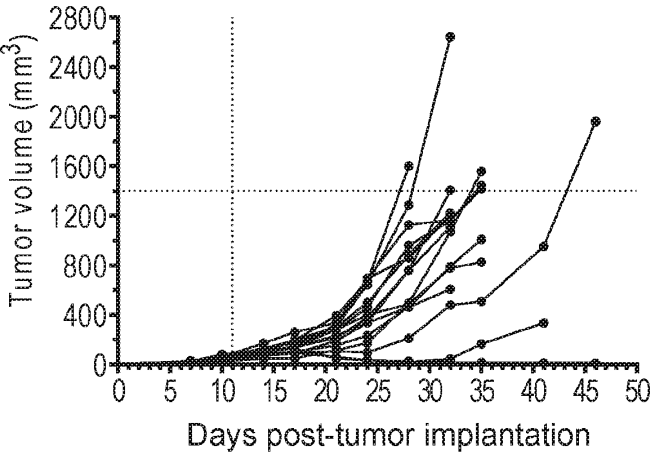
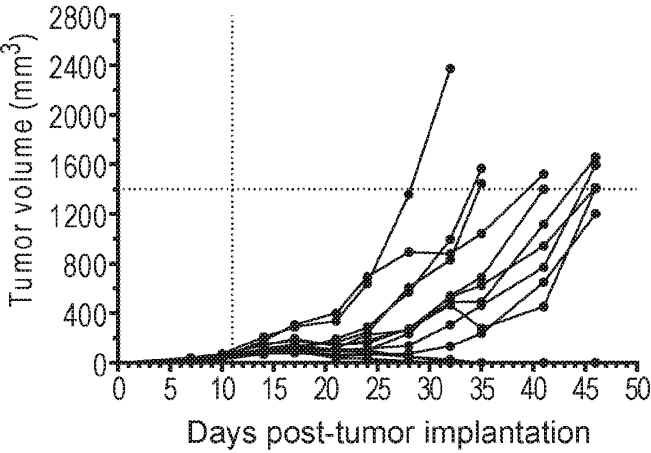


FIG. 13F
IGV-121

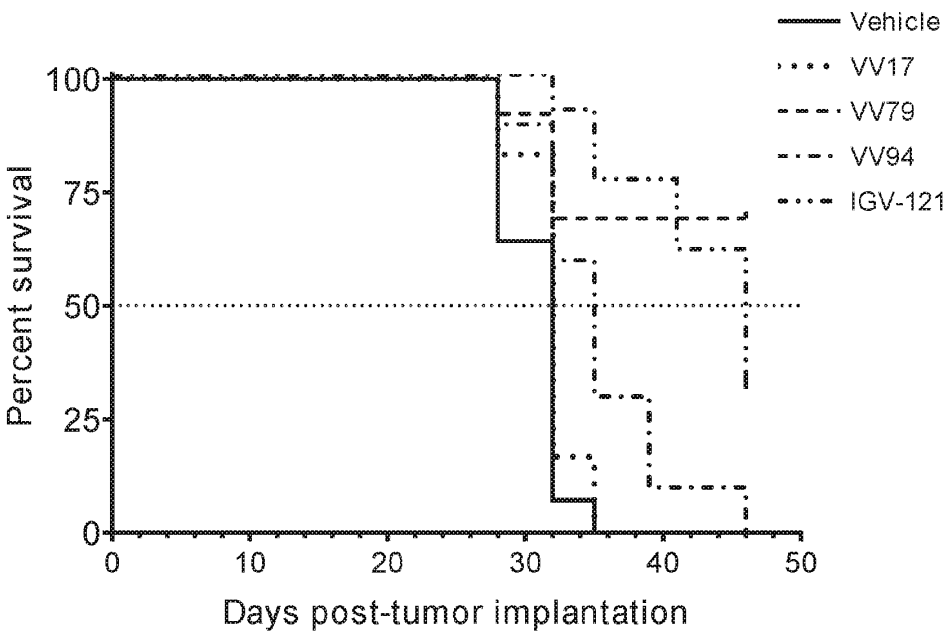


18/66

FIG. 14

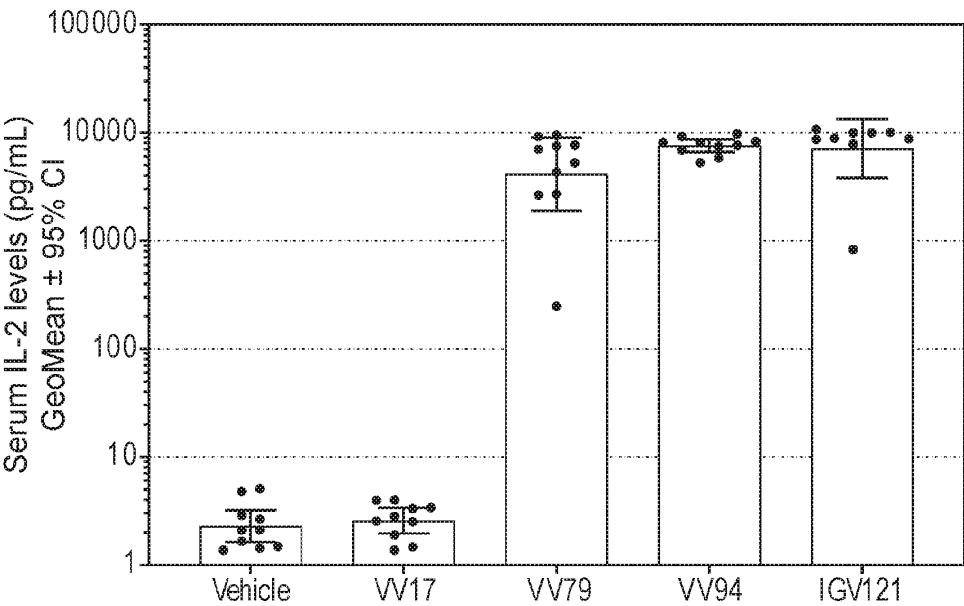
	ANCOVA results (p-values for designated group comparisons)								
Day post tumor implant	VV17 vs. vehicle	VV79 vs. vehicle	VV94 vs. vehicle	IGV-121 vs. vehicle	VV79 vs. VV17	VV94 vs. VV17	IGV-121 vs. VV17	VV94 vs. VV79	IGV-121 vs. VV79
14	0.201	0.073	0.031	0.178	0.268	0.149	0.460	0.5655	0.694
17	0.005	0.012	0.003	0.005	0.622	0.434	0.464	0.8209	0.346
21	0.005	<0.001	<0.001	<0.001	0.004	0.201	0.001	0.0110	0.332
24		<0.001	0.003	<0.001				0.0039	0.531
28				<0.001					

FIG. 15

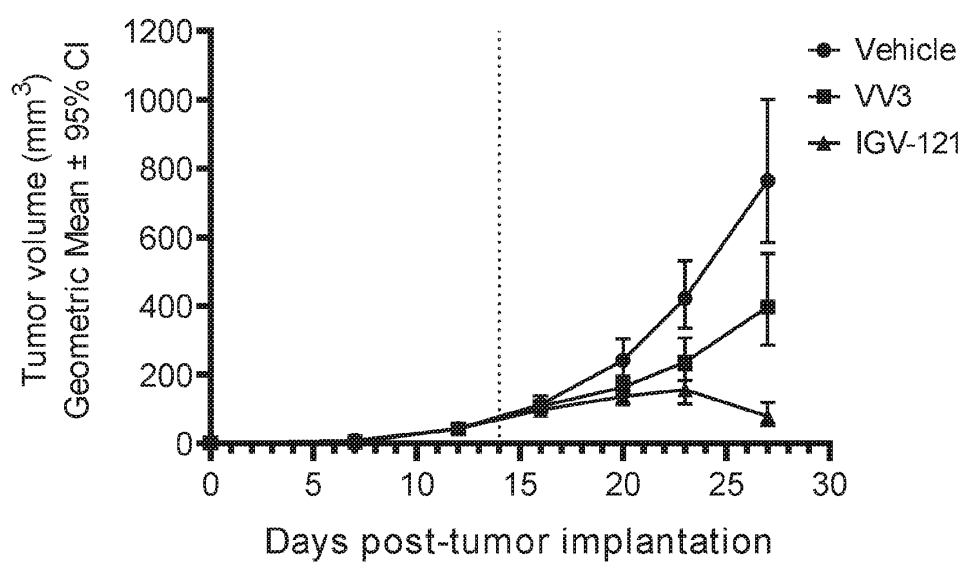


Log-rank (Mantel-Cox) survival curve test (p-values for paired group comparisons)					
	Vehicle	VV17	VV79	VV94	IGV-121
Vehicle		NS	0.0002	0.0053	<0.0001
VV17			0.0008	0.0282	<0.0001
VV79				0.0033	NS
VV94					0.0019
IGV-121					

FIG. 16



21/66

FIG. 17A

22/66

FIG. 17B
Vehicle

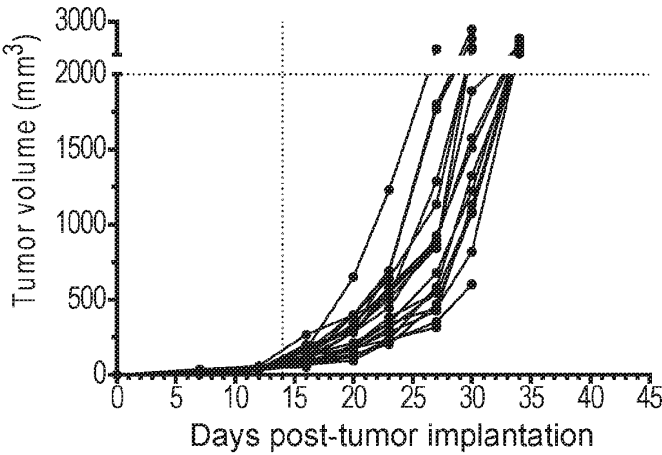


FIG. 17C
VV3

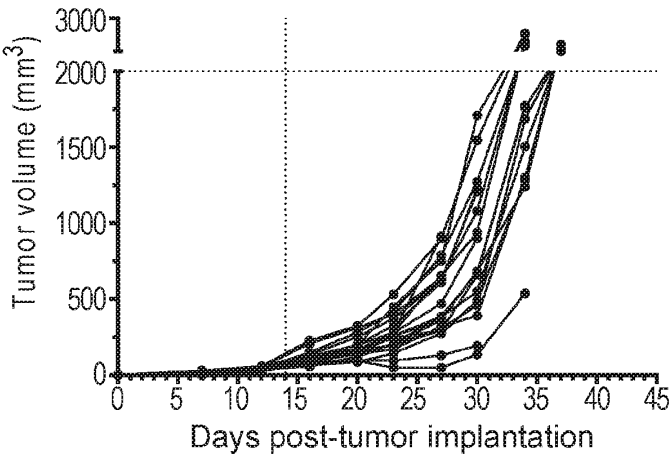
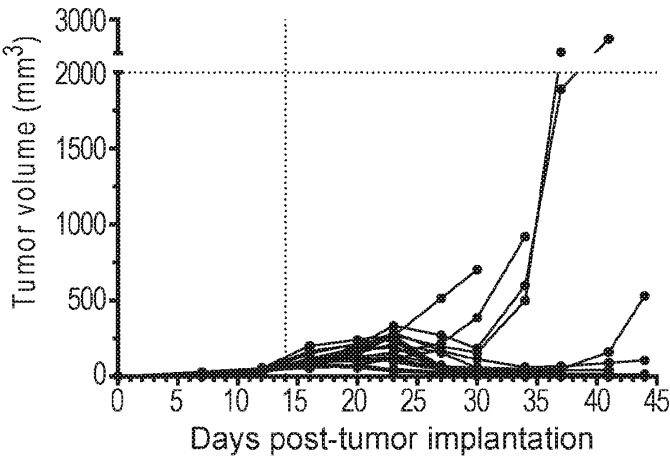


FIG. 17D
IGV-121

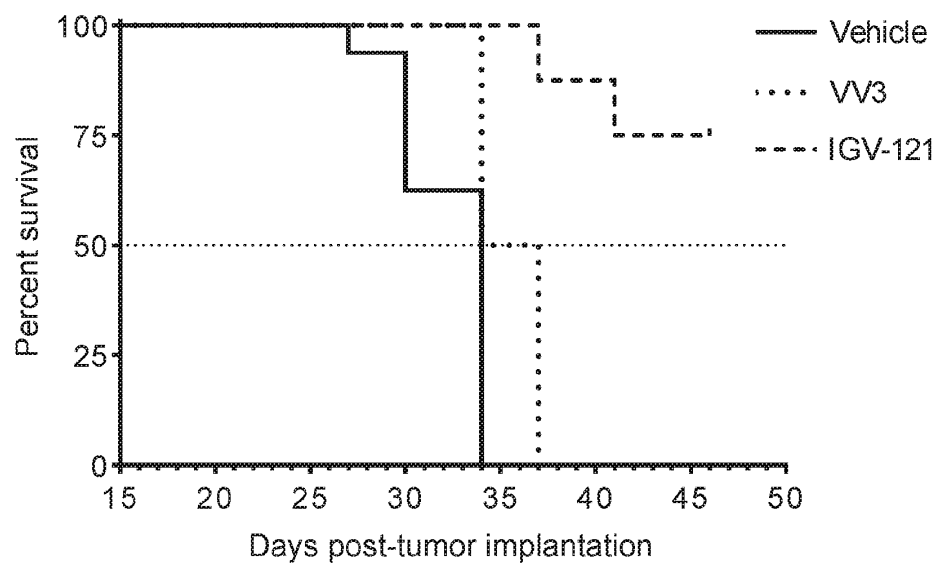


23/66

FIG. 18

	ANCOVA results (p-values for designated group comparisons)		
Day post-tumor implant	VV3 vs. vehicle	IGV -121 vs. vehicle	IGV -121 vs. VV3
16	0.4781	<0.0001	<0.0001
20	0.0015	<0.0001	<0.0001
24	0.0002	<0.0001	<0.0001
27	0.0013	<0.0001	<0.0001
30			<0.0001

FIG. 19



Log-rank (Mantel-Cox) survival curve test (p-values for paired group comparisons)			
	Vehicle	VV3	IGV121
Vehicle		0.0011	<0.0001
VV3			0.0002

25/66

FIG. 20A
Vehicle

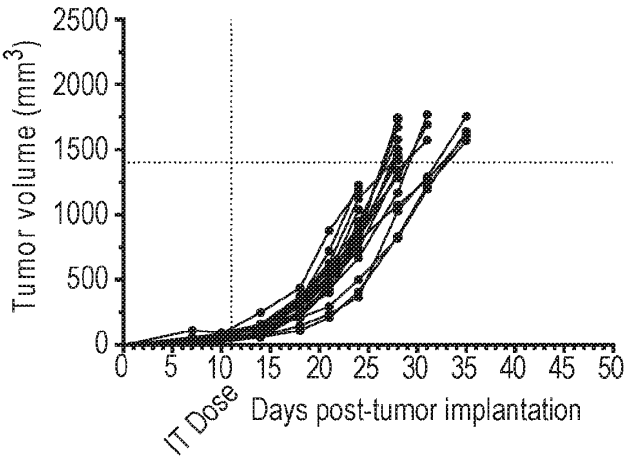


FIG. 20B
VV91 5E7

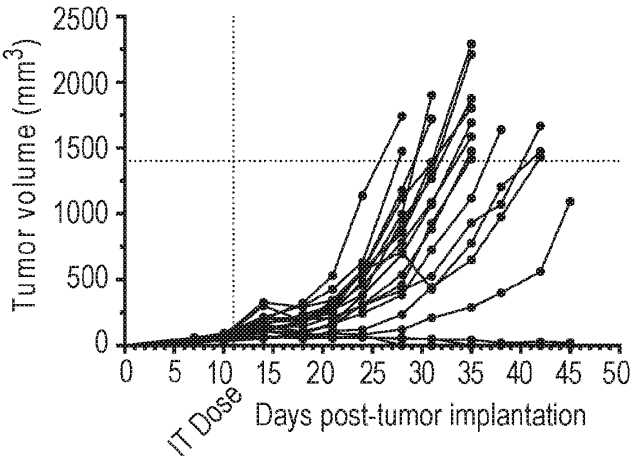
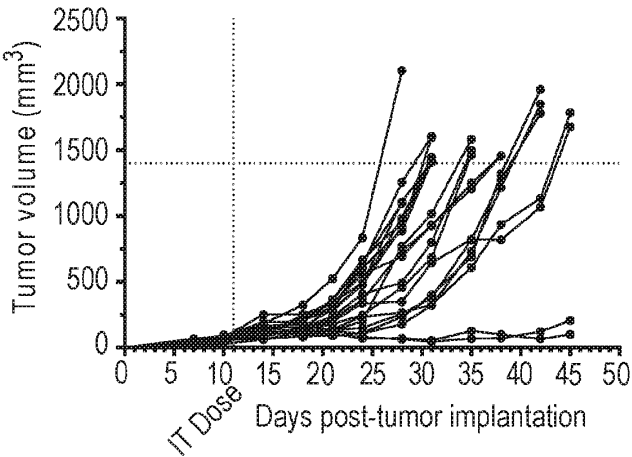


FIG. 20C
VV102 5E7



26/66

FIG. 20D
VV10 5E7

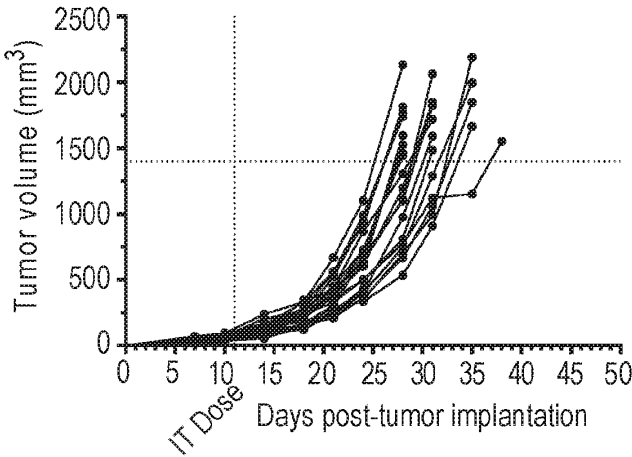


FIG. 20E
VV7 2E8

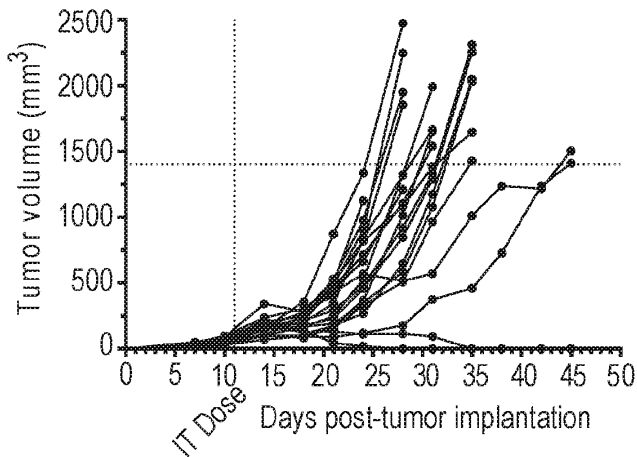
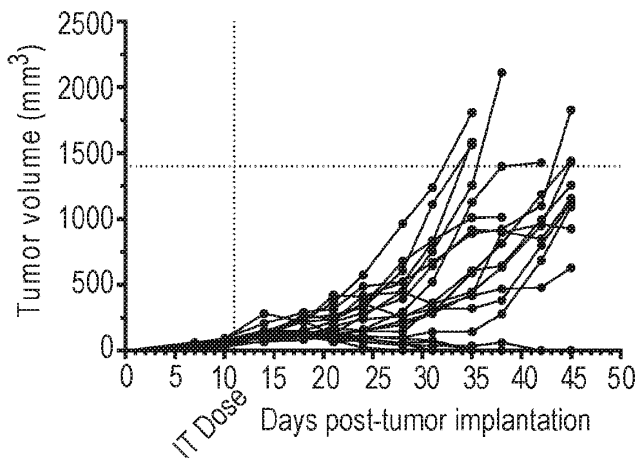


FIG. 20F
VV91 2E8



27/66

FIG. 20G
VV102 2E8

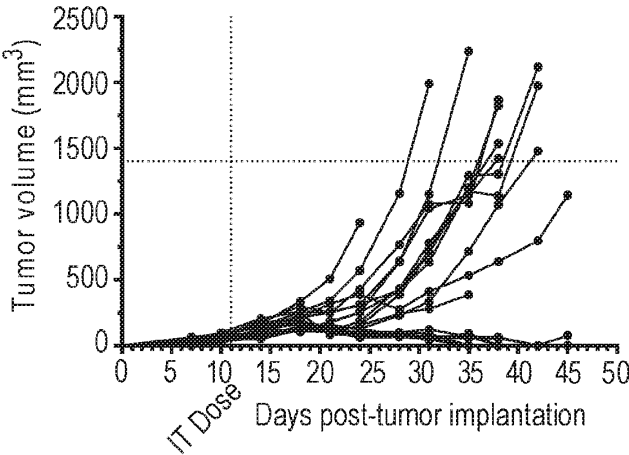


FIG. 20H
VV10 2E8

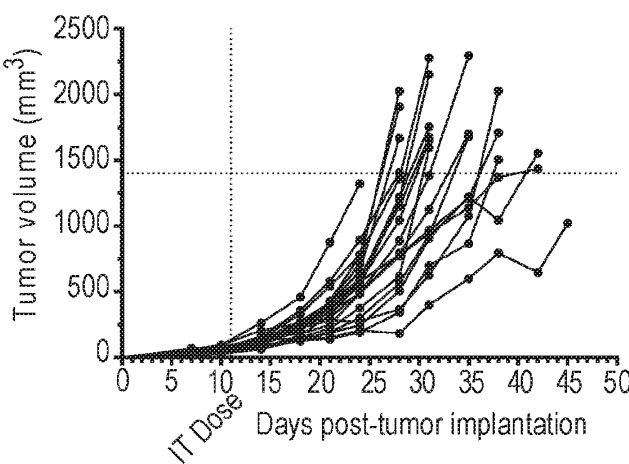


FIG. 20I

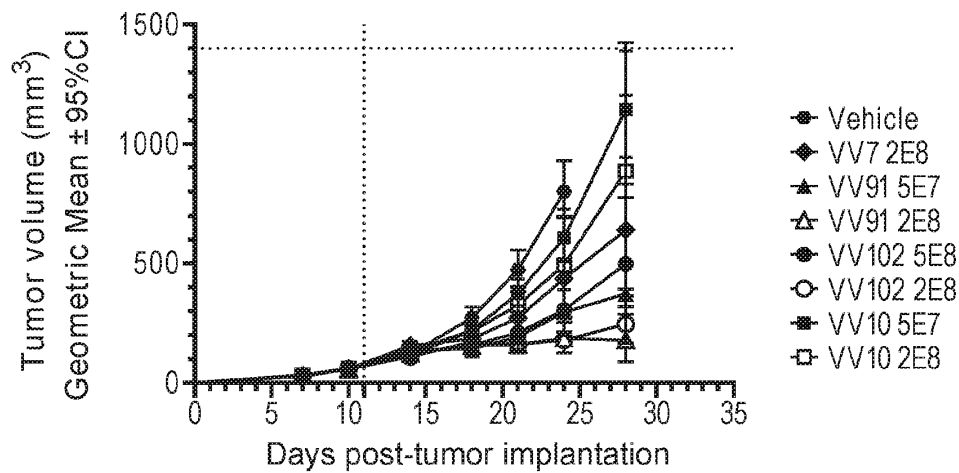
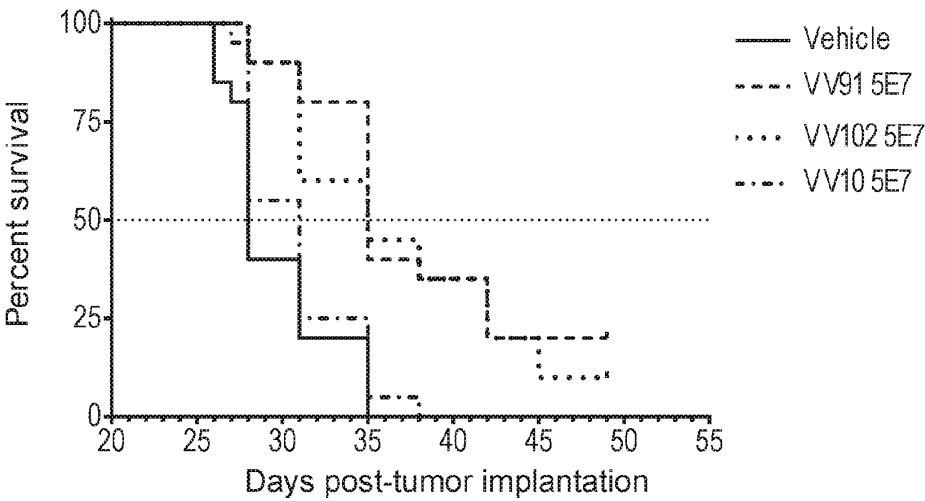


FIG. 21

	ANCOVA results (p-values for designated group comparisons)								
Day post-tumor implant	VV91 (5e7 pfu) vs. vehicle	VV102 (5e7 pfu) vs. vehicle	VV10 (5e7 pfu) vs. vehicle	VV7 (2e8 pfu) vs. vehicle	VV91 (2e8 pfu) vs. vehicle	VV102 (2e8 pfu) vs. vehicle	VV10 (2e8 pfu) vs. vehicle	VV91 (5e7 pfu) vs. VV10	VV102 (5e7 pfu) vs. VV10
18	<0.001	<0.001	0.011	<0.001	<0.001	<0.001	0.011	<0.001	0.001
21	<0.001	<0.001	0.035	<0.001	<0.001	<0.001	0.004	<0.001	<0.001
25	<0.001	<0.001	0.070	0.0015	<0.001	<0.001	0.008	<0.001	<0.001
28								0.0014	<0.001

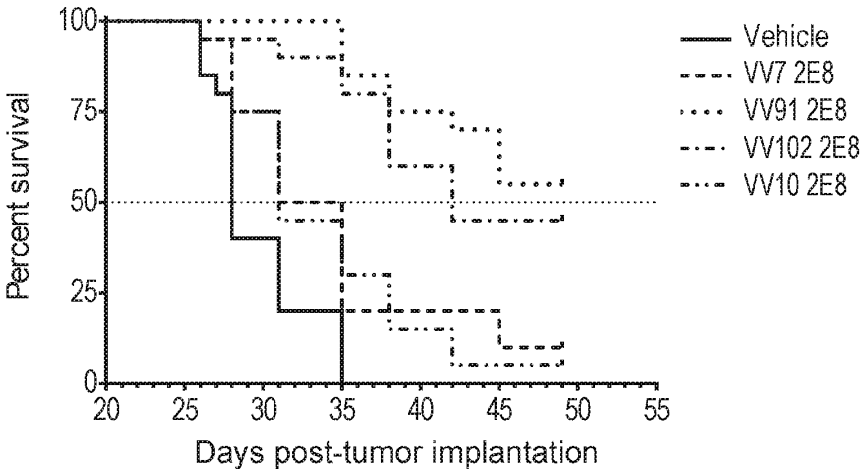
29/66

FIG. 22A



Log-rank (Mantel-Cox) survival curve test (p-values for paired group comparisons)					
	Vehicle	VV7	VV91	VV102	VV10
Vehicle			<0.0001	<0.0001	0.2576
VV91				0.4629	<0.0001
VV102					0.0006

FIG. 22B



Log-rank (Mantel-Cox) survival curve test (p-values for paired group comparisons)					
	Vehicle	VV7	VV91	VV102	VV10
Vehicle		0.0074	<0.0001	<0.0001	0.0052
VV7			<0.0001	0.0017	0.2186
VV91				0.7231	<0.0001
VV102					0.0003

FIG. 23

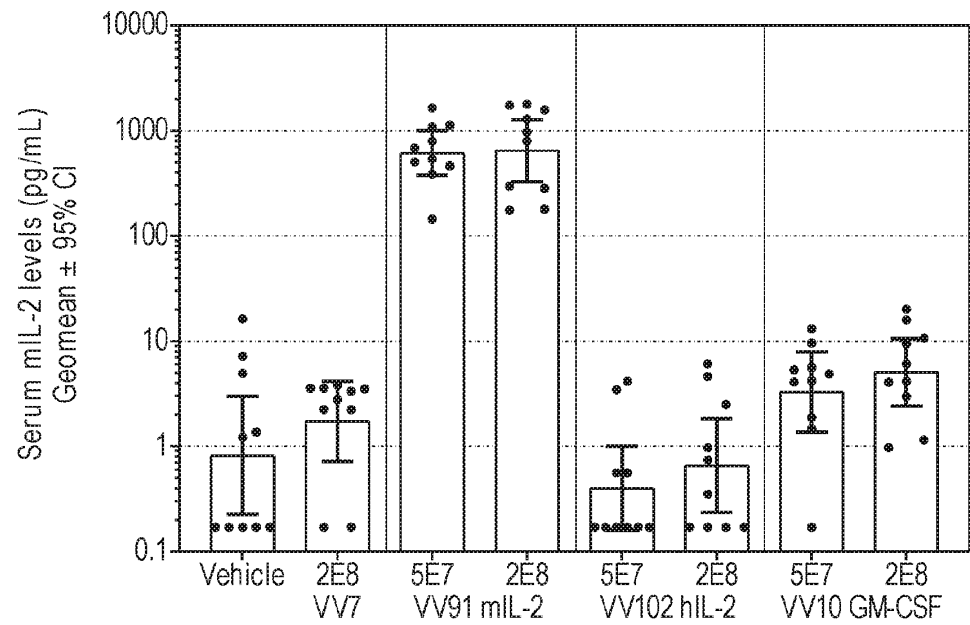
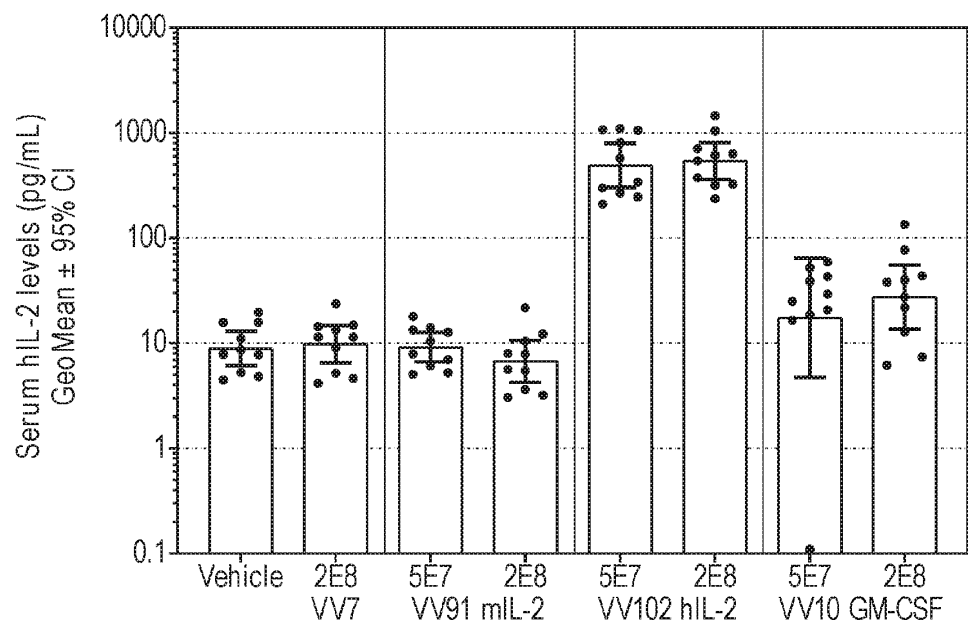


FIG. 24



33/66

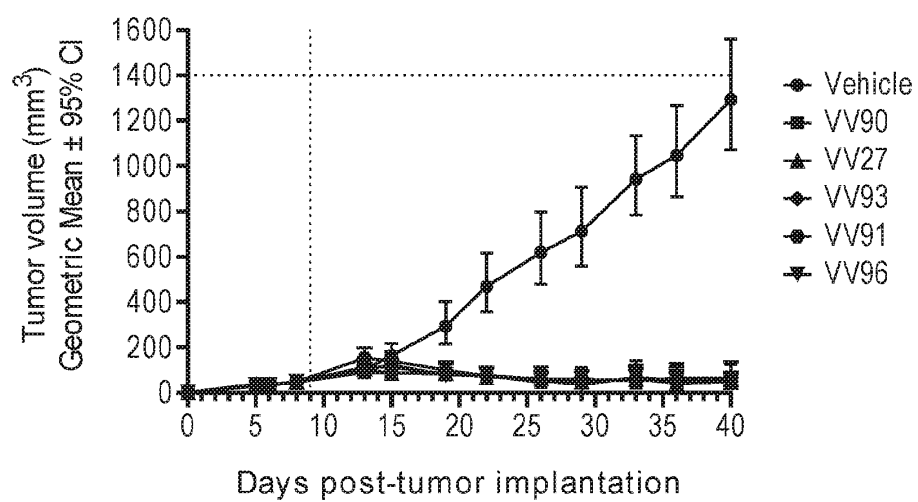
FIG. 25

FIG. 26

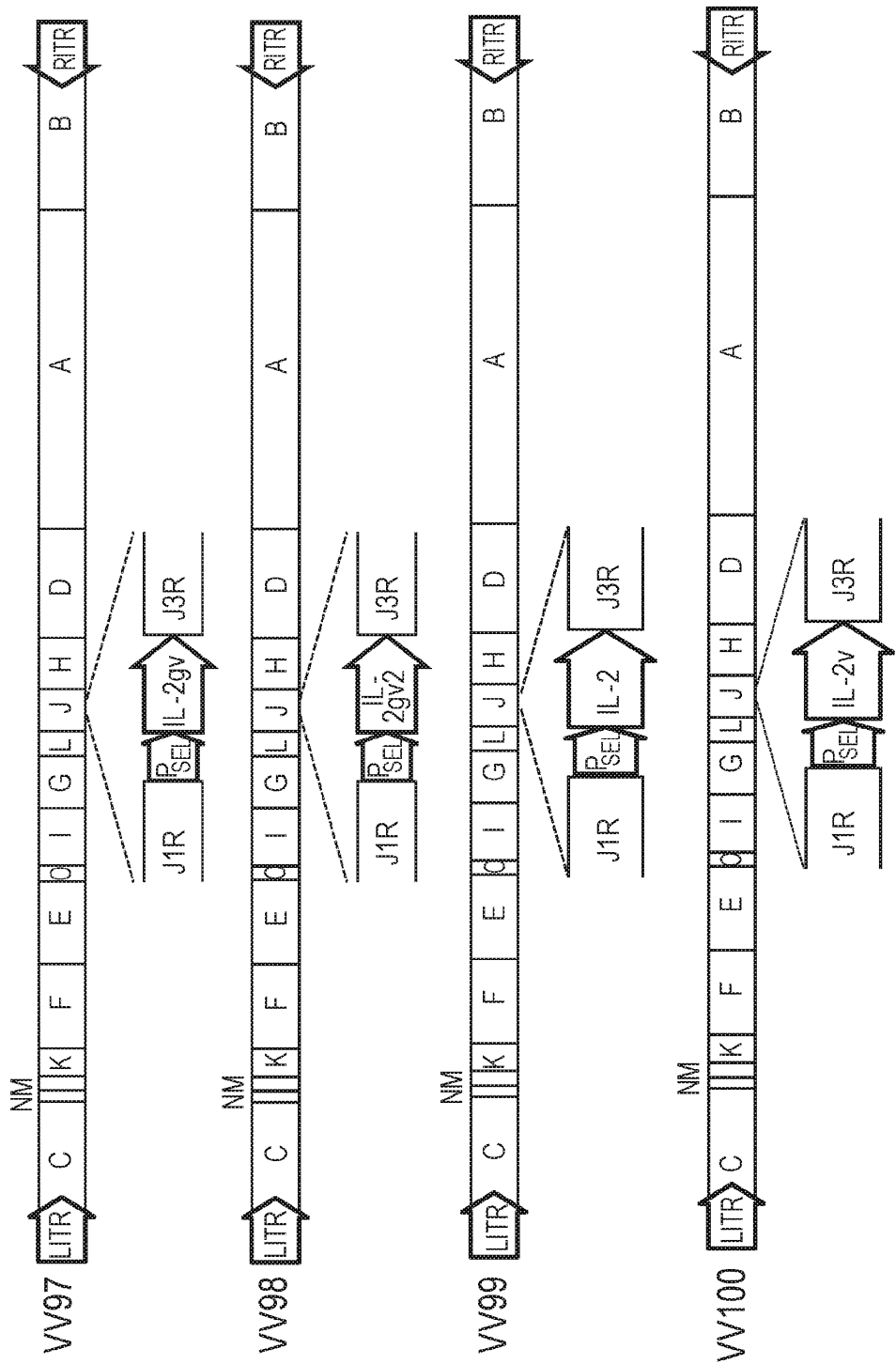


FIG. 27

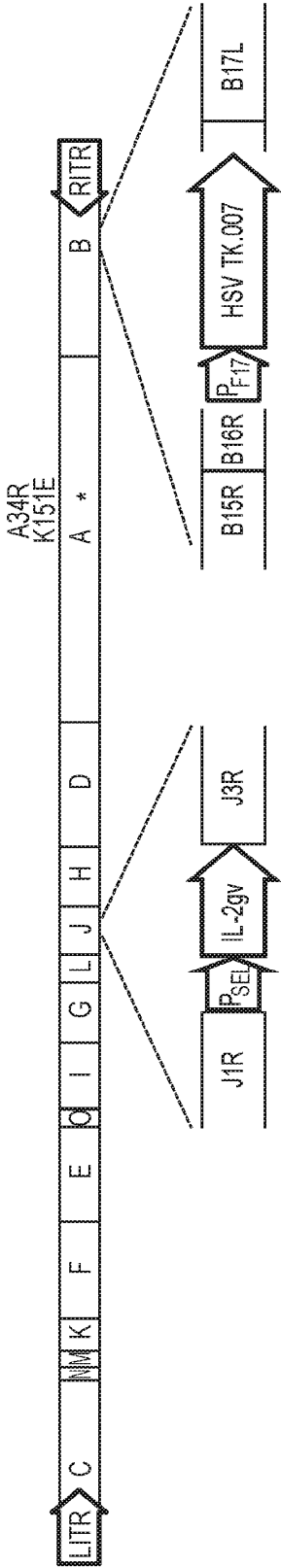
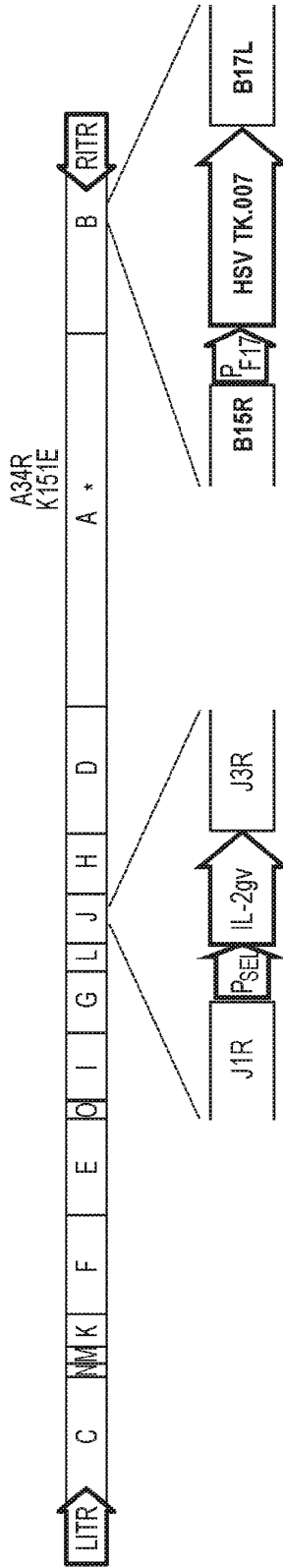


FIG. 28



36/66

FIG. 29A

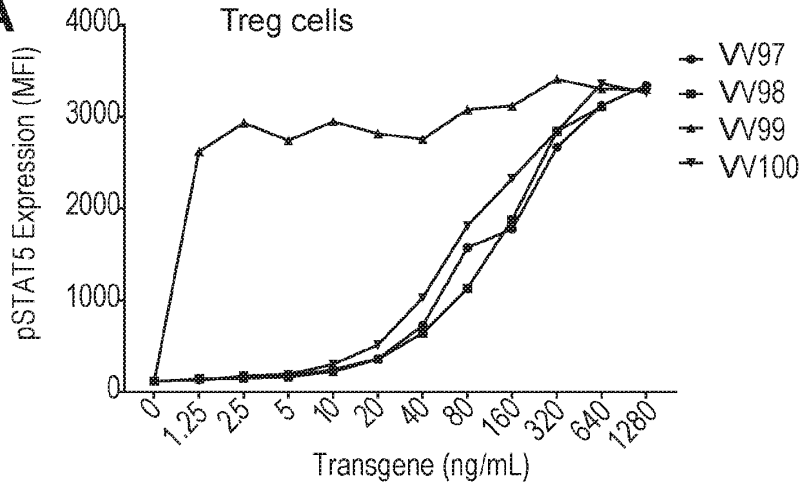


FIG. 29B

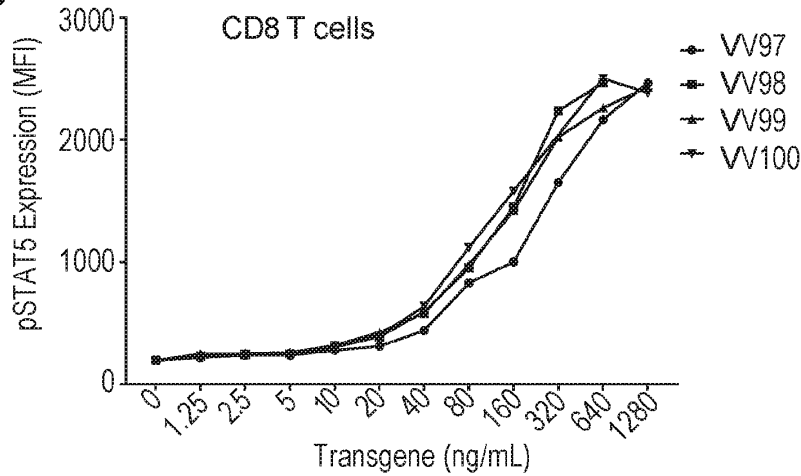
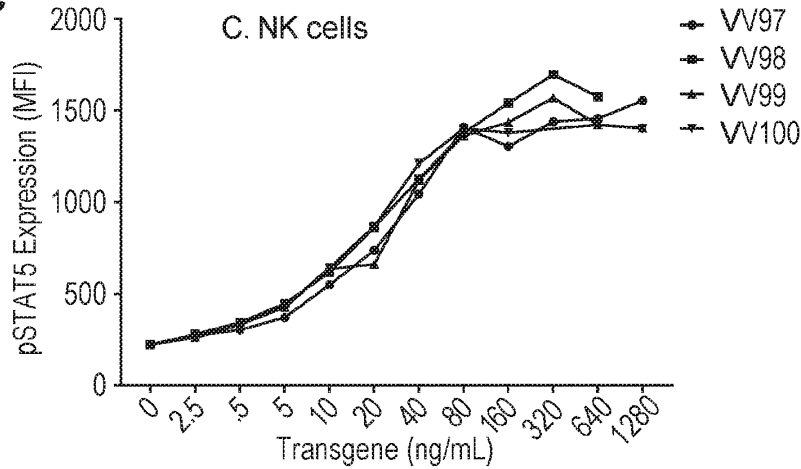


FIG. 29C



37/66

FIG. 30

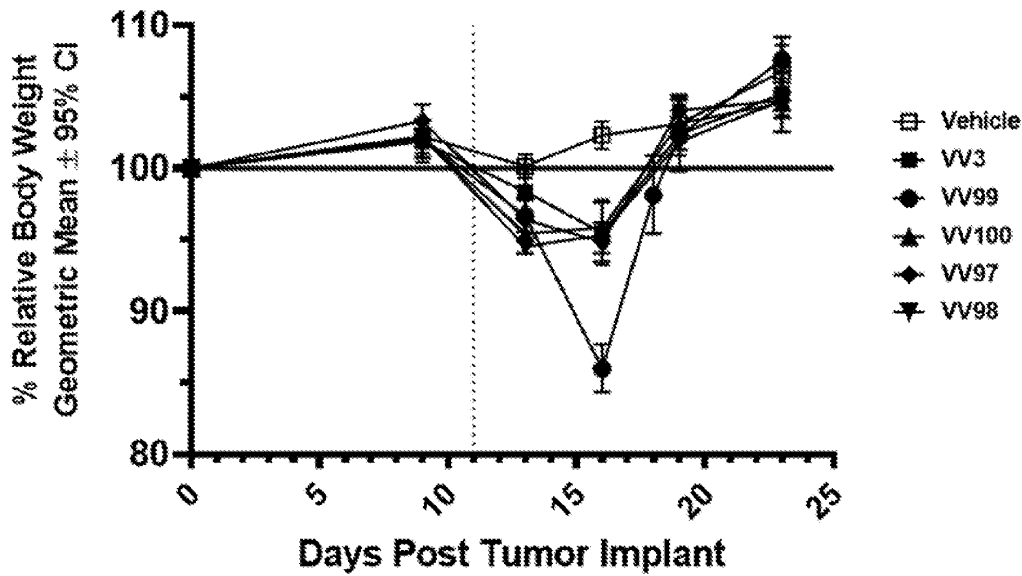


FIG. 31

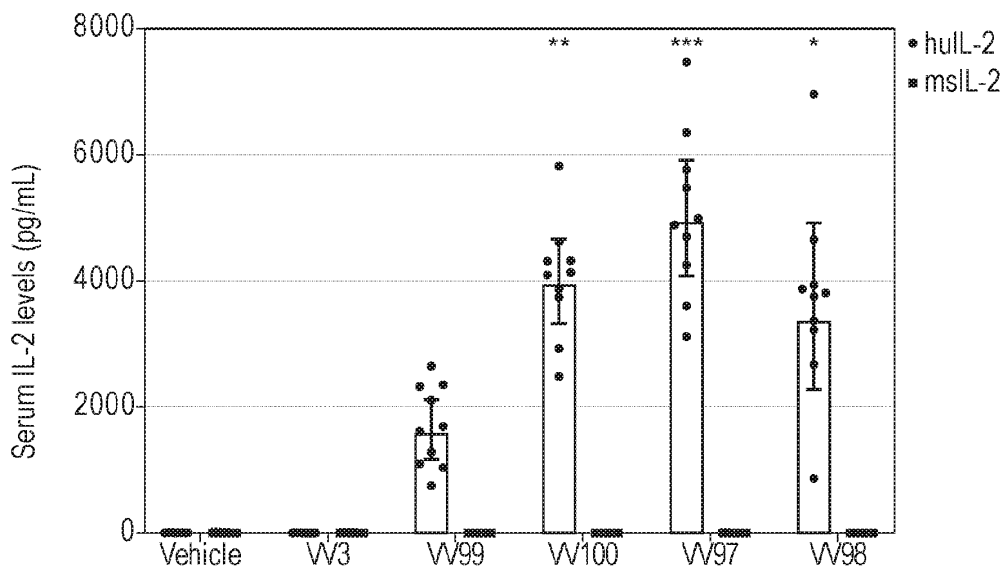


FIG. 32

Treatment (5E7 IV)	Cytokine / Chemokine (pg/mL) Geomean											
	hIL-2	mIL-2	IFN γ	IFN α	IL-10	IL-12p70	IL-1 β	IL-4	IL-5	IL-6	KC/ GRO	TNF α
Vehicle	6.1	5.4	0.9	452	9.1	56	1.3	0.3	6.9	20	88	11
VV3	2.6	5.1	171	226	42	346	7.4	3.5	59	520	329	45
VV99	1573	1.8	725	153	298	2586	57	79	2107	735	273	110
VV100	3936**	1.6	223 ⁺	244	44 [^]	346 [^]	7.0 [^]	3.9 [^]	67 [^]	419	205	43 [^]
VV97	4913 ⁺	2.3	336	217	44 [^]	342 [^]	10 [^]	4.6 [^]	60 [^]	445	220	41 [^]
VV98	3350 ⁺	1.2	316 ⁺	198	45 [^]	316 [^]	8.8 [^]	4.5 [^]	45 [^]	404	191	38 [^]

FIG. 33

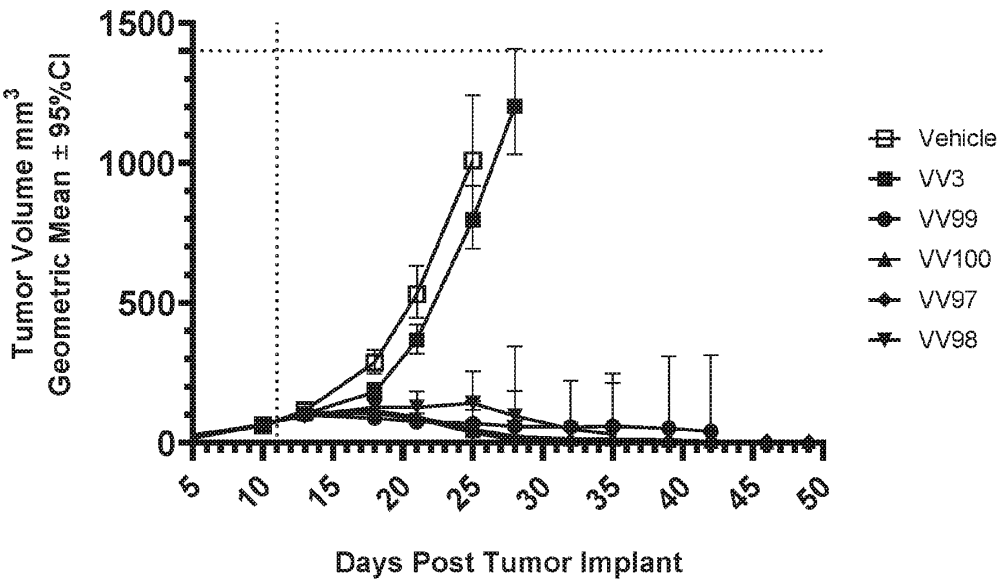


FIG. 35

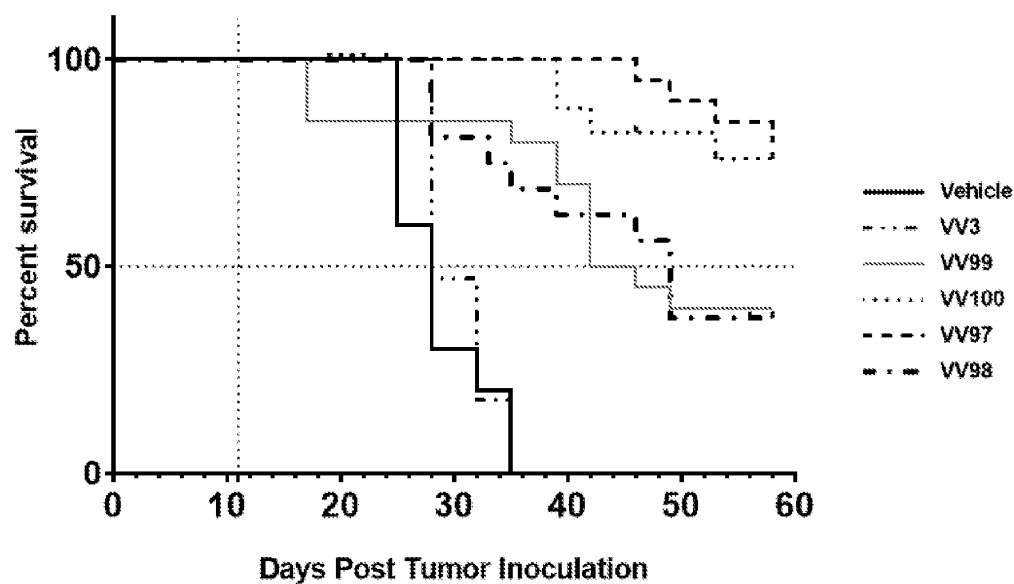


FIG. 36

Log-rank (Mantel-Cox) survival curve test (p-values for paired group comparisons)						
	Vehicle	VV3	VV99	VV100	VV97	VV98
Vehicle		NS	<0.001	<0.001	<0.001	<0.001
VV3			<0.001	<0.001	<0.001	<0.001
VV99				0.020	0.003	NS
VV100					NS	0.020
VV97						0.003
VV98						

41/66

FIG. 37

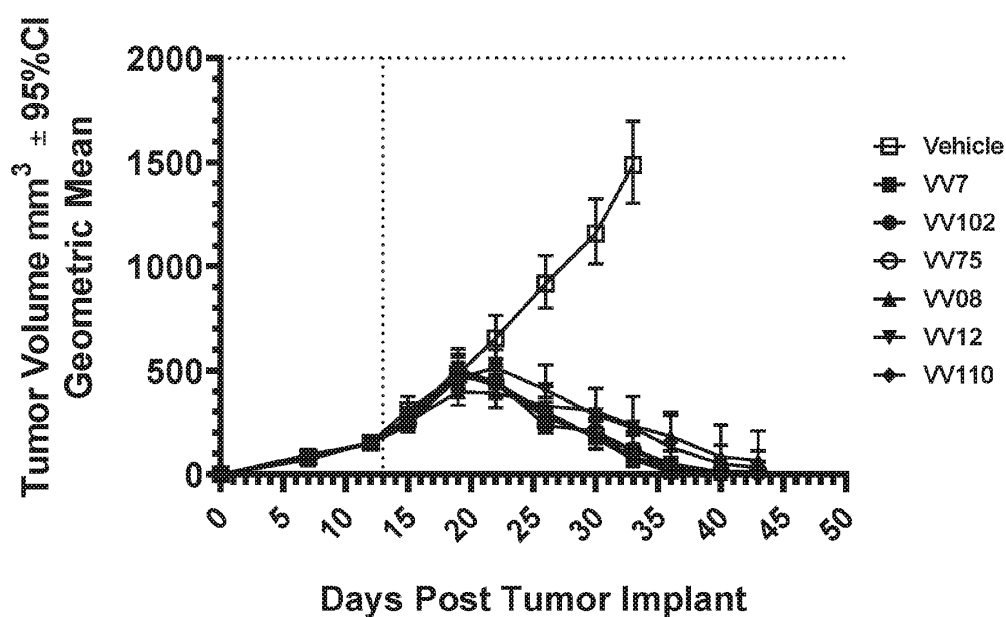


FIG. 38

ANCOVA results (p-values for designated group comparisons)																					
Days post tumor implant	VW7 vs Vehicle	VW102 vs Vehicle	VW75 vs Vehicle	VW8 vs Vehicle	VW12 vs Vehicle	VW110 vs Vehicle	VW102 vs VW7	VW75 vs VW7	VW8 vs VW7	VW12 vs VW7	VW110 vs VW7	VW75 vs VW102	VW8 vs VW102	VW12 vs VW102	VW110 vs VW102	VW8 vs VW75	VW12 vs VW75	VW110 vs VW75	VW12 vs VW8	VW110 vs VW8	VW110 vs VW12
15	0.004	0.031	<0.001	0.002	0.008	<0.001	0.392	0.358	0.844	0.776	0.145	0.077	0.293	0.567	0.022	0.469	0.229	0.588	0.630	0.207	0.082
19	0.500	0.713	0.361	0.016	0.343	0.476	0.574	0.722	0.032	0.685	0.952	0.360	0.007	0.334	0.534	0.073	0.960	0.767	0.081	0.037	0.730
22	<0.001	<0.001	<0.001	<0.001	0.010	<0.001	0.973	0.921	0.248	0.161	0.778	0.896	0.271	0.157	0.808	0.211	0.192	0.704	0.011	0.382	0.093
26	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.842	0.143	0.410	0.023	0.695	0.102	0.541	0.041	0.558	0.023	0.000	0.282	0.142	0.225	0.008
30	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.928	0.426	0.010	0.023	0.860	0.489	0.014	0.032	0.934	0.068	0.135	0.535	0.739	0.015	0.035
33	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.154	0.184	0.001	0.002	0.596	0.903	0.069	0.086	0.363	0.049	0.062	0.423	0.916	0.006	0.008
36	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.005	0.037	<0.001	<0.001	0.115	0.432	0.017	0.076	0.194	0.001	0.010	0.599	0.520	0.000	0.002
40	.	.	.	.	.	.	0.035	0.012	<0.001	<0.001	0.028	0.703	0.008	0.051	0.957	0.020	0.109	0.739	0.460	0.008	0.054
43	.	.	.	.	.	.	0.009	0.009	<0.001	<0.001	0.032	0.998	0.040	0.230	0.600	0.040	0.230	0.602	0.378	0.010	0.061

42/66

FIG. 39

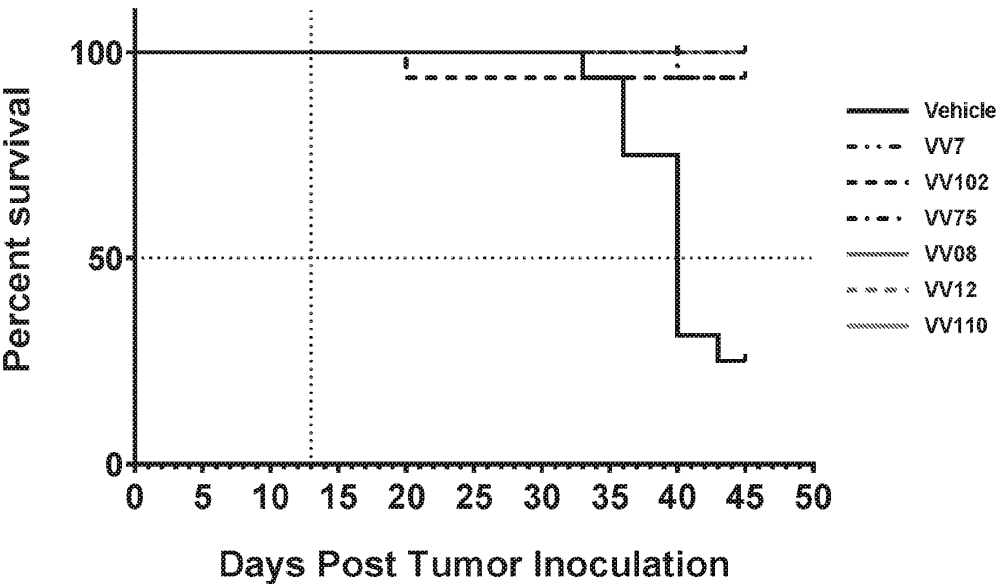


FIG. 40

Logrank (Mantel-Cox) survival curve test (p-values for paired group comparisons)							
	Vehicle	VV7	VV102	VV75	VV8	VV12	VV110
Vehicle		<0.0001	0.0002	<0.0001	<0.0001	<0.0001	<0.0001
VV7			NS	NS	<0.0001	NS	NS
VV102				NS	NS	NS	NS
VV75					NS	NS	NS
VV8						NS	NS
VV12							NS
VV110							

FIG. 41

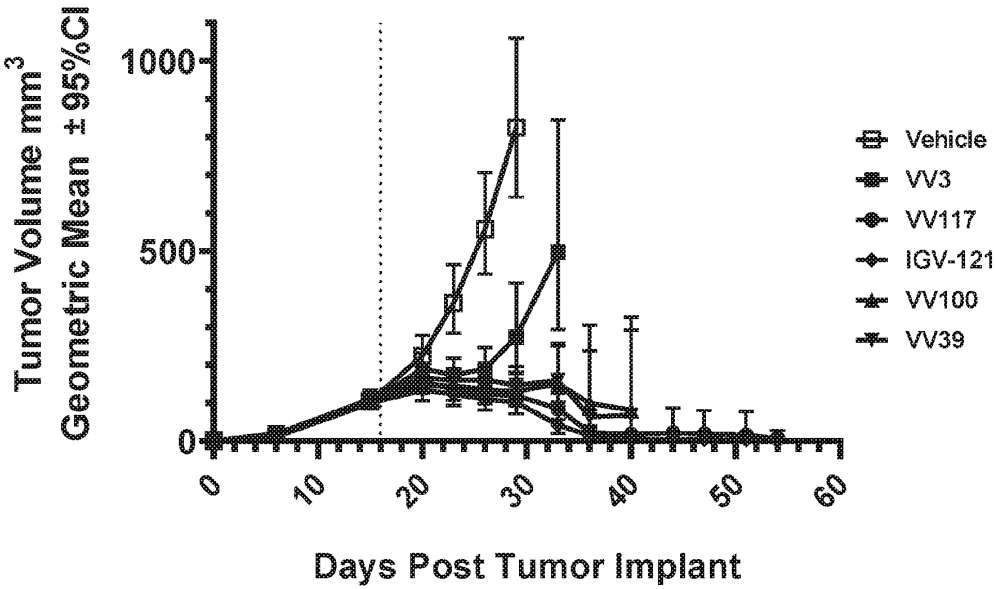


FIG. 42

ANCOVA results (p-values for designated group comparisons)														
Days post tumor implant	VV3 vs Vehicle	VV117 vs Vehicle	IGV-121 vs Vehicle	VV100 vs Vehicle	VV39 vs Vehicle	VV117 vs VV3	IGV-121 vs VV3	VV100 vs VV3	VV39 vs VV3	IGV-121 vs VV117	VV100 vs VV117	VV39 vs VV117	VV100 vs IGV-121	VV39 vs IGV-121
20	0.036	<0.001	<0.001	<0.001	<0.001	0.015	<0.001	<0.001	0.031	0.121	0.347	0.827	0.516	0.086
23	<0.001	<0.001	<0.001	<0.001	<0.001	0.006	0.002	0.045	0.146	0.664	0.422	0.214	0.219	0.101
26	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.005	0.081	0.595	0.390	0.070	0.167	0.022
29	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.555	0.646	0.378	0.295	0.151
33						<0.001	<0.001	<0.001	<0.001	0.109	0.056	0.056	<0.001	<0.001
36						<0.001	<0.001	0.003	<0.001	0.436	0.023	0.112	0.003	0.022
40										0.150	0.055	0.098	0.001	0.003

FIG. 43

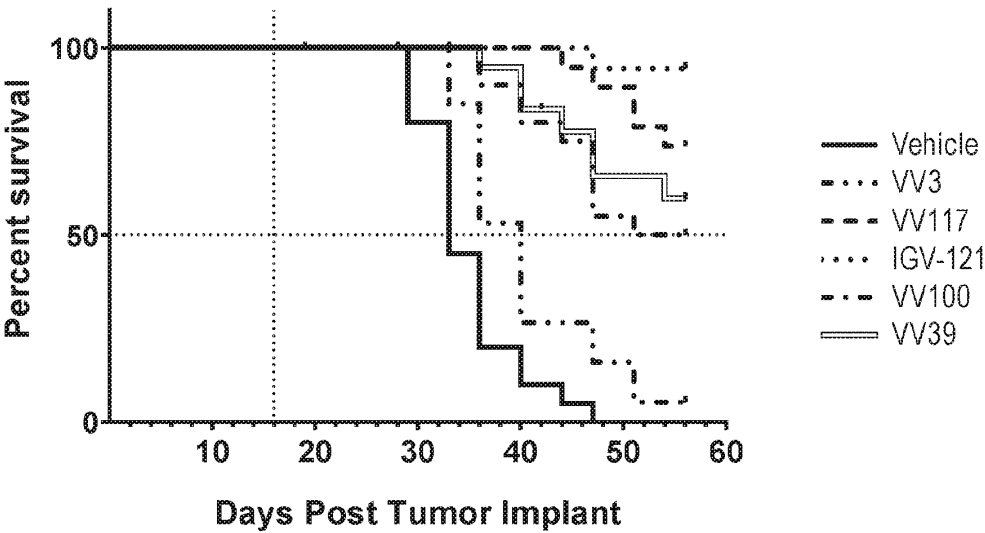


FIG. 44

Log-rank (Mantel-Cox) survival curve test (p-values for paired group comparisons)						
	Vehicle	VV3	VV117	IGV-121	VV100	VV39
Vehicle		0.0036	<0.0001	<0.0001	<0.0001	<0.0001
VV3			<0.0001	<0.0001	<0.0003	<0.0001
VV117				0.0960	0.0811	0.1141
IGV-121					0.0026	0.0039
VV100						0.9497
VV39						

FIG. 47

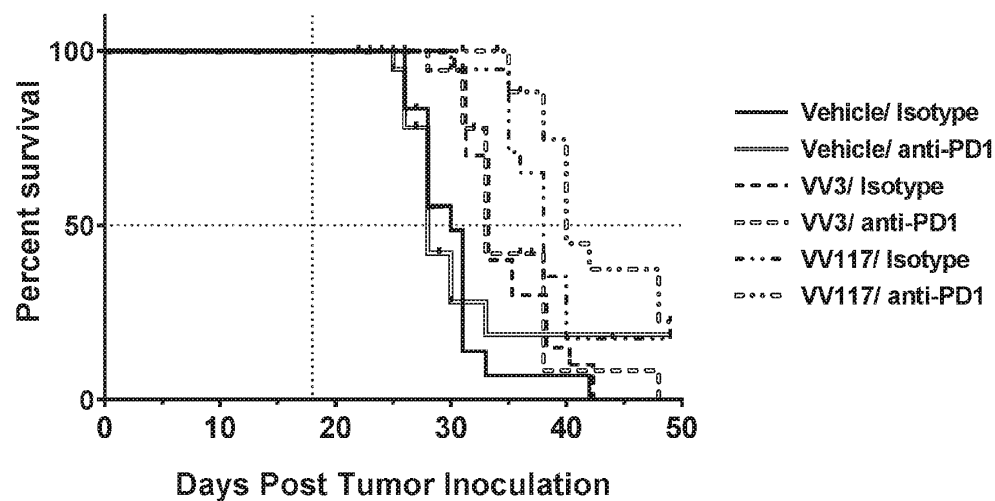
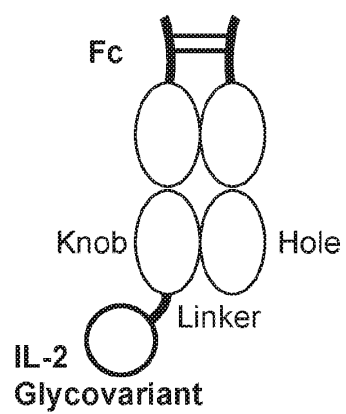


FIG. 48

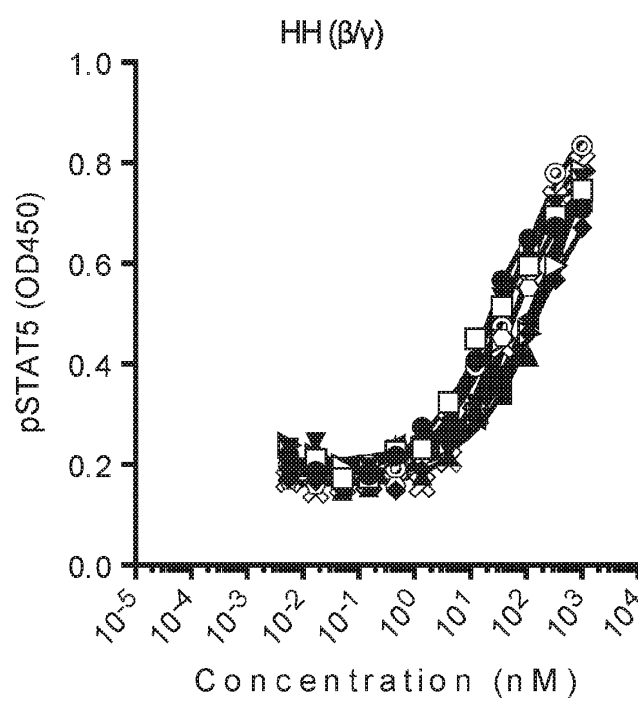
Log-rank (Mantel-Cox) survival curve test						
	Vehicle/ Isotype	Vehicle/ anti-PD1	VV3/ Isotype	VV3/ anti-PD1	VV117/ Isotype	VV117/ anti-PD1
Vehicle/Isotype		0.8990	0.0035		0.0001	
Vehicle/anti-PD1				0.0194		0.0005
VV3/Isotype				0.5607	0.0154	
VV3/anti-PD1						0.0004
VV117/Isotype						0.0483
VV117/anti-PD1						

47/66

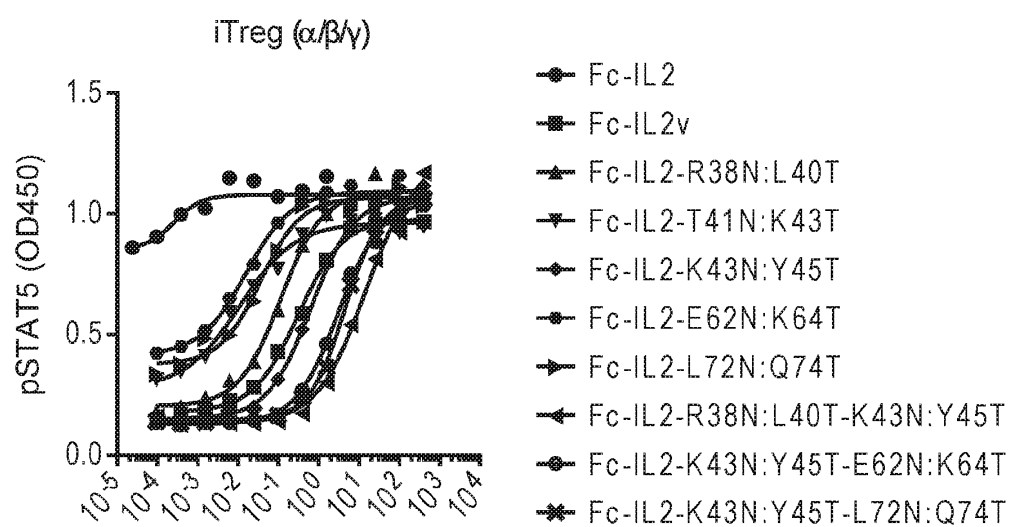
FIG. 49



48/66

FIG. 50A

49/66

FIG. 50B

50/66

FIG. 51A

CD8 T cells

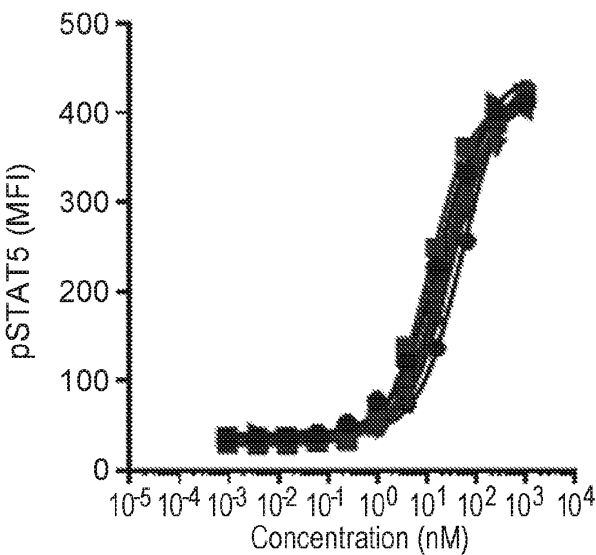


FIG. 51B

NK cells

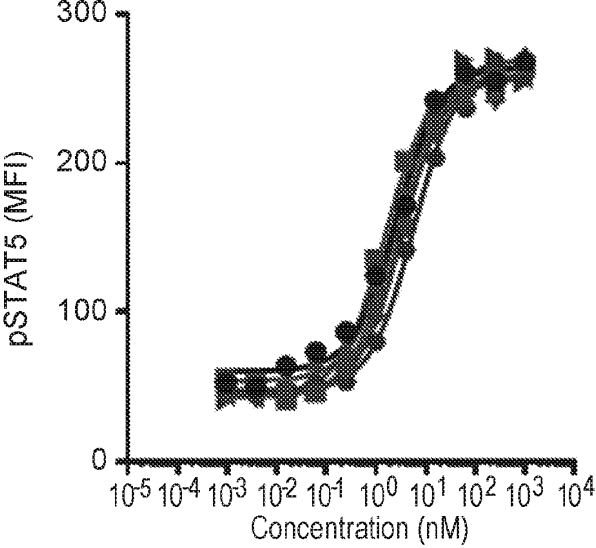
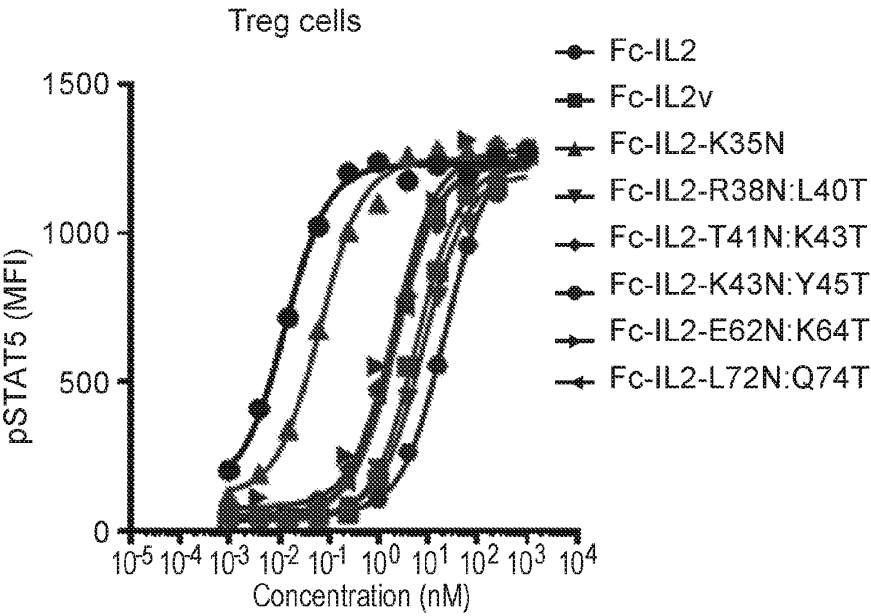


FIG. 51C



52/66

FIG. 52A

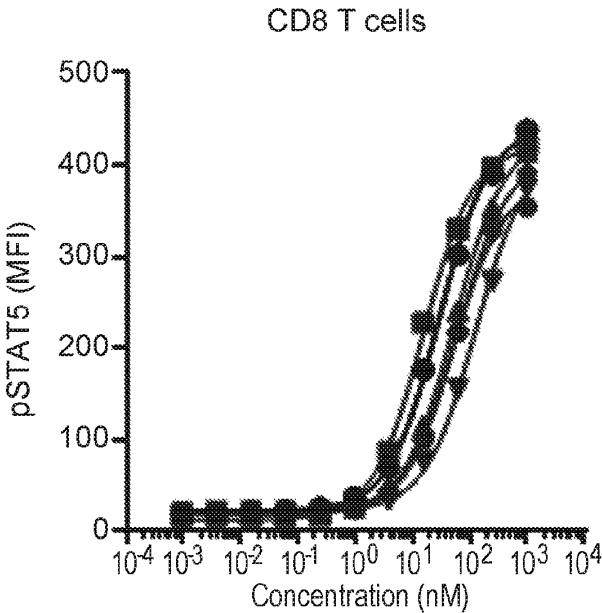
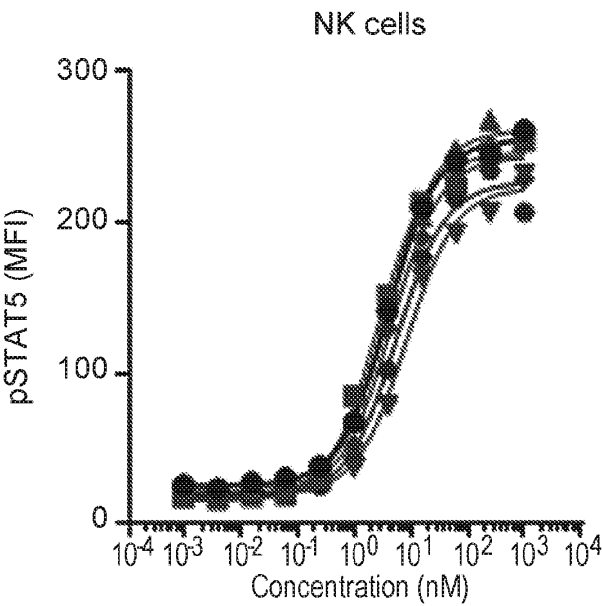
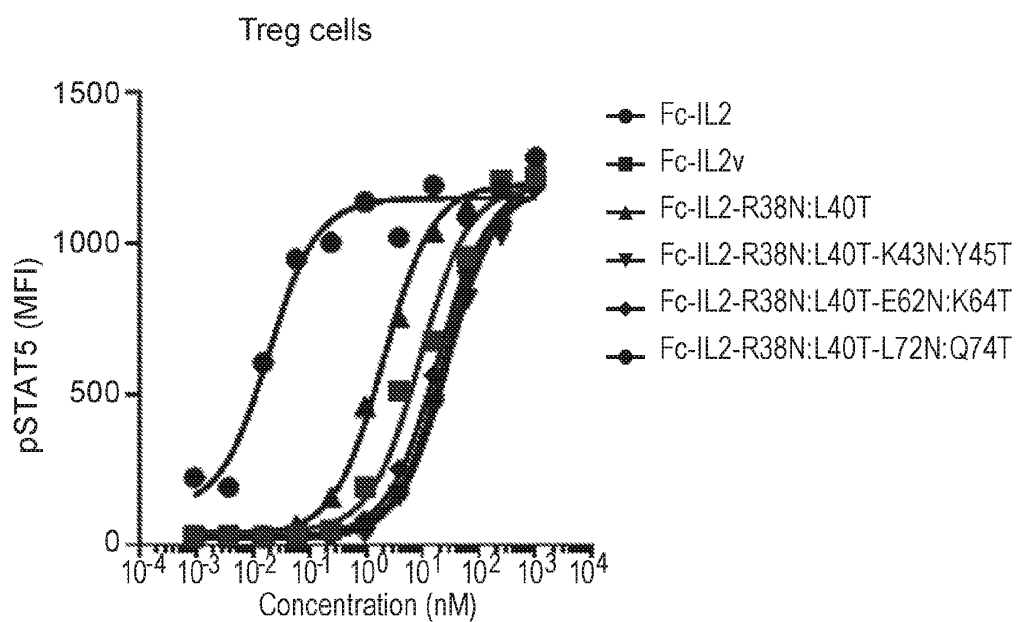


FIG. 52B



53/66

FIG. 52C

54/28

FIG. 53A

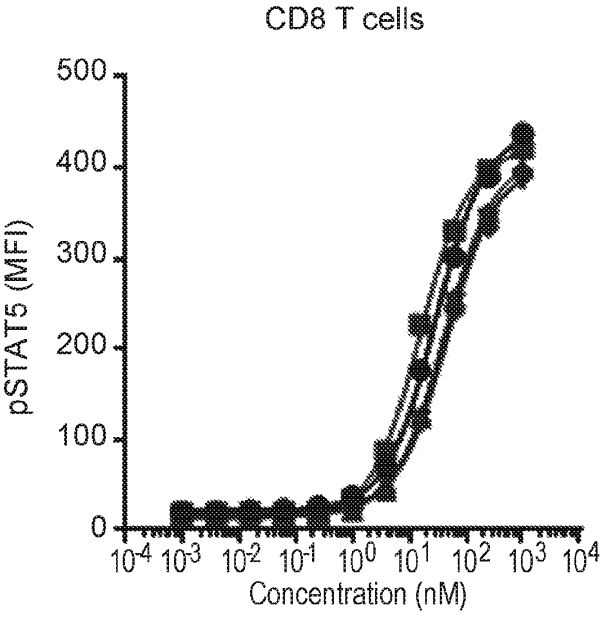
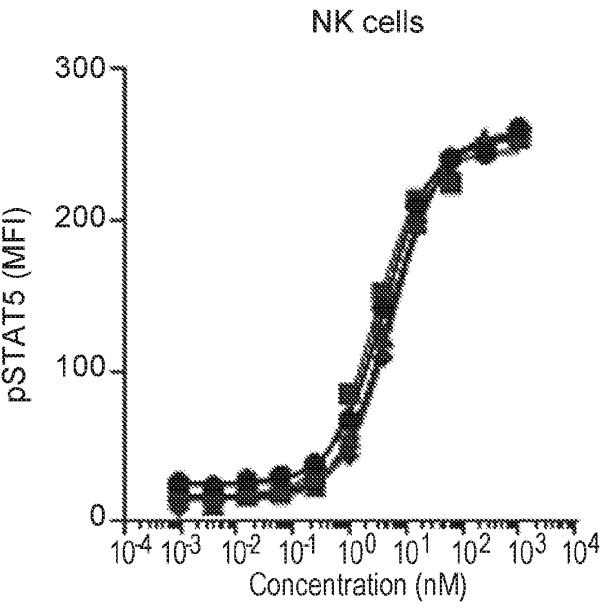
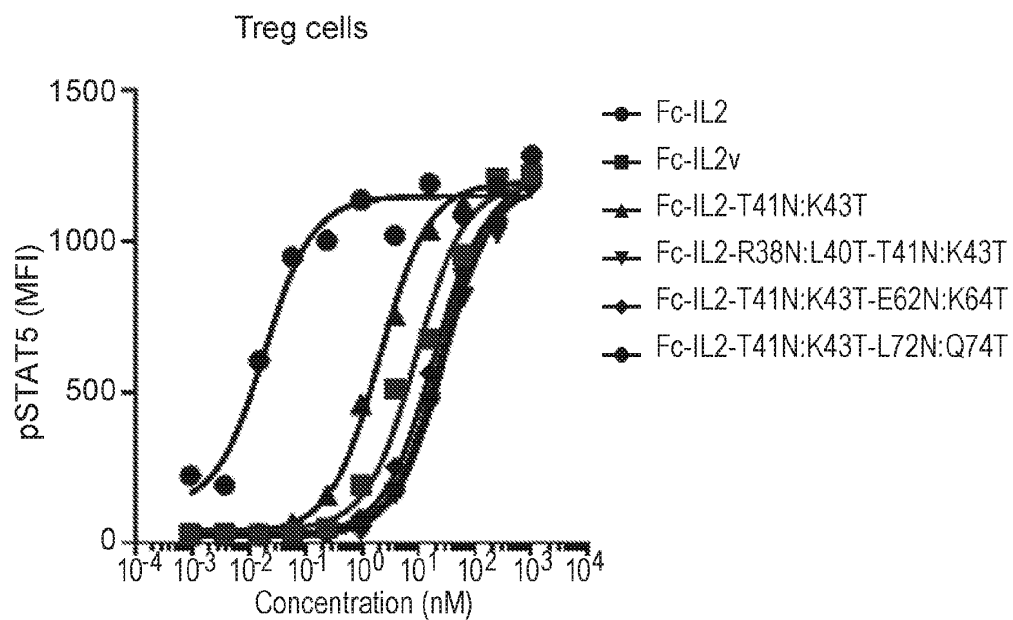


FIG. 53B



55/66

FIG. 53C

56/66

FIG. 54A

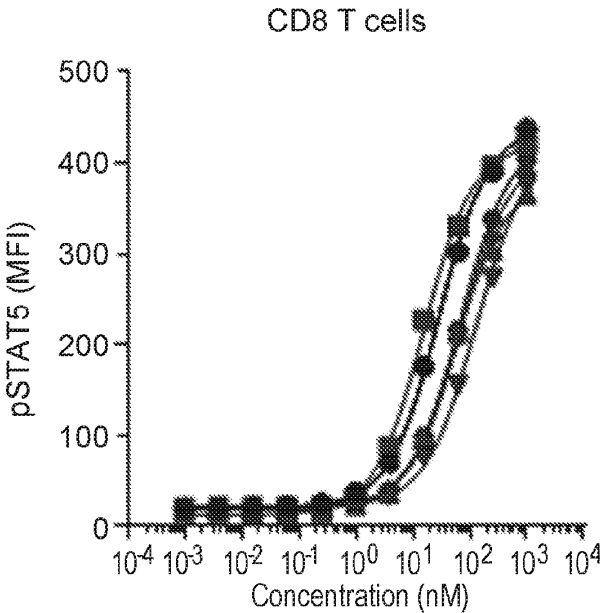
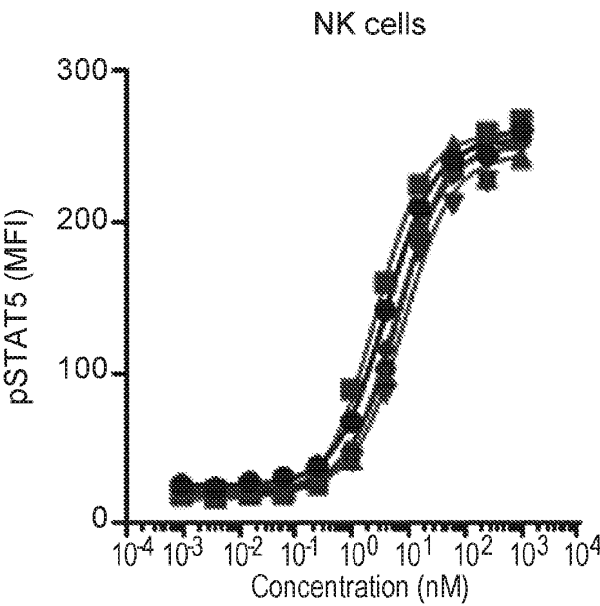
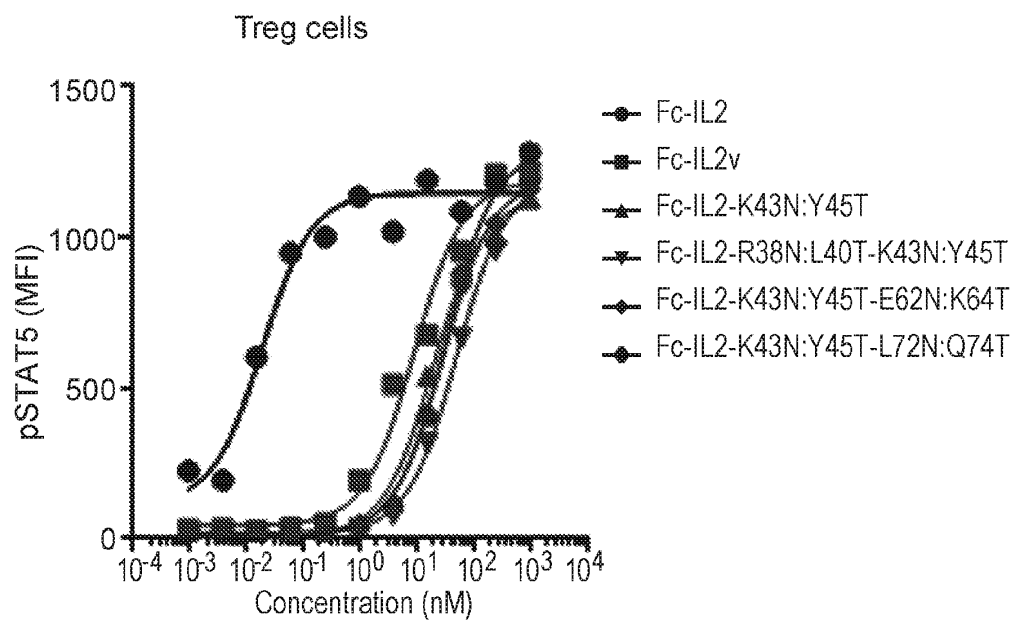


FIG. 54B



57/66

FIG. 54C

58/66

FIG. 55A

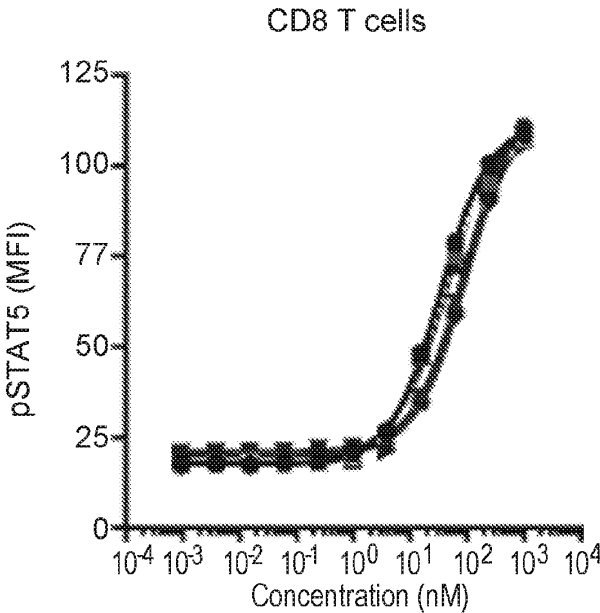


FIG. 55B

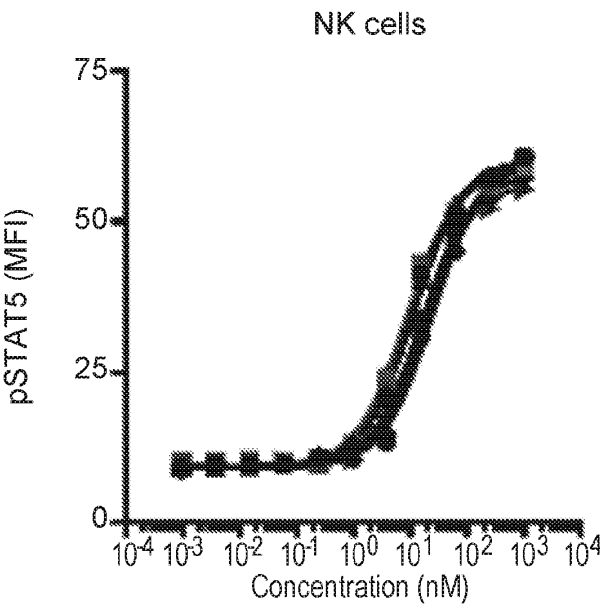


FIG. 55C

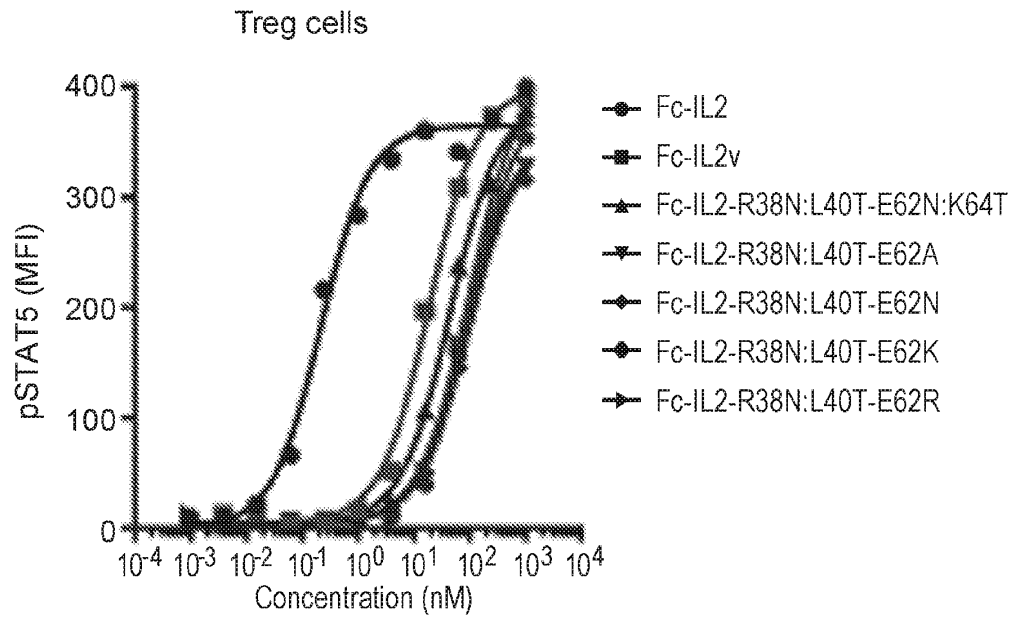


FIG. 56A

CD8 T cells

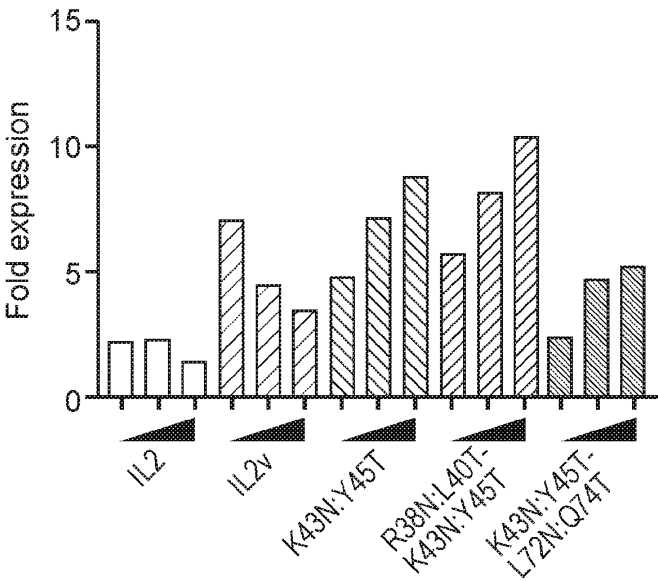
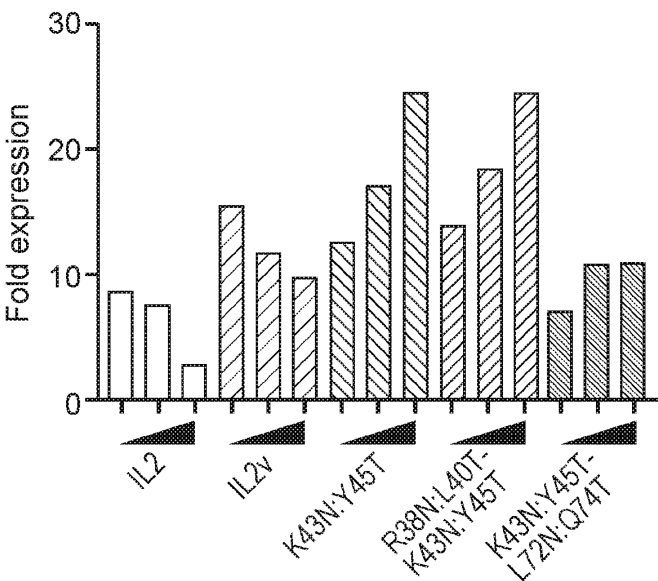


FIG. 56B

NK cells



61/66

FIG. 56C

Treg cells

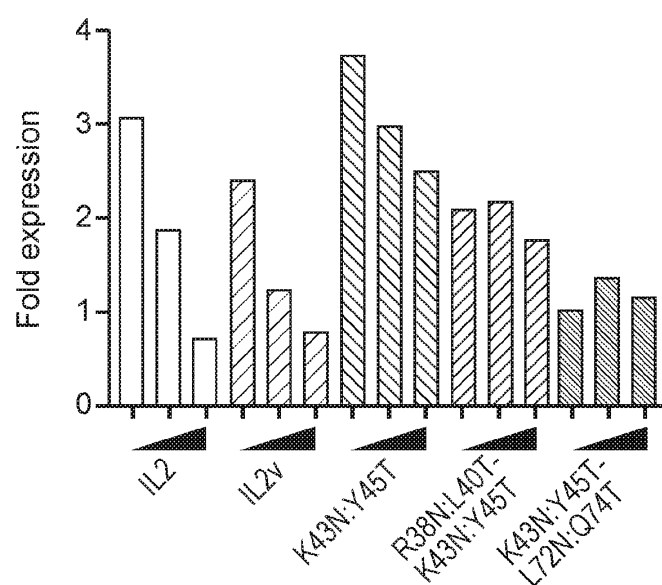


FIG. 57A

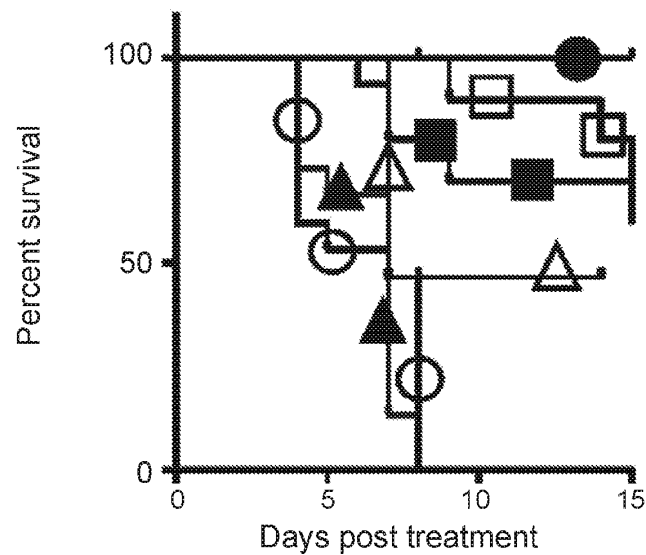


FIG. 57B

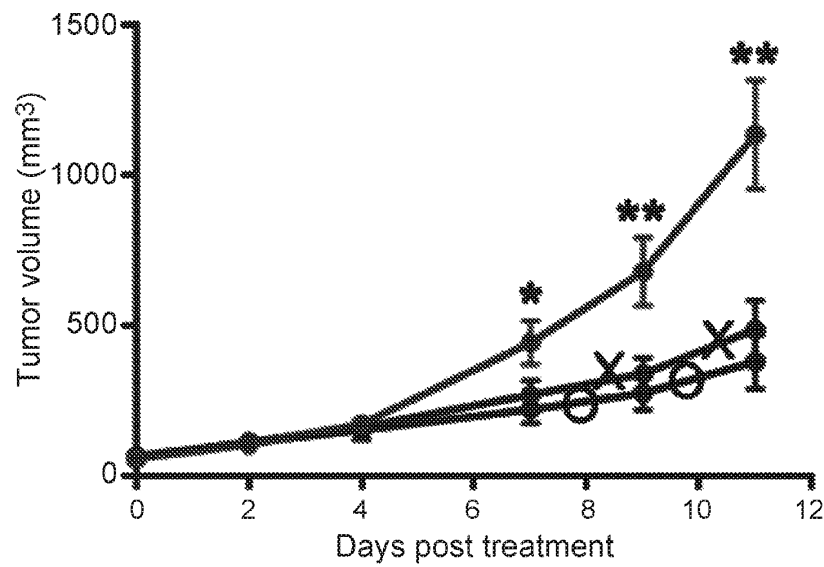


FIG. 58

Indication	Cell Line	VV110 (%)			VV12 (JX-594) (%)			
		48 hr	72 hr	96 hr	48 hr	72 hr	96 hr	96 hr
NSCLC	A549	28	92 ± 3	99 ± 3	29*	97 ± 1	101 ± 2	
	Hop-62	8	77 ± 12	93 ± 1	27*	94 ± 2	97 ± 0.3	
	EKVX	8	92 ± 3	99 ± 1	83*	96 ± 1	100 ± 1	
Melanoma	SK-MEL-2	52 ± 7	72 ± 5	94 ± 2	46 ± 15	61 ± 12	87 ± 5	
	SK-MEL-5	31 ± 14	92 ± 9	97 ± 4	34 ± 34	85 ± 20	96 ± 7	
	SK-MEL-28	69 ± 5	79 ± 0.1	94 ± 0.05	63 ± 1	83 ± 2	93 ± 0.3	
RCC	Malme-3M	n.t.	74 ± 3	91 ± 2	n.t.	82 ± 3	95 ± 1	
	A-498	6 ± 0.4	73 ± 24	105 ± 0.5	3 ± 3	70 ± 38	97 ± 0.4	
	786-O	96 ± 1	97 ± 1	n.t.	93 ± 5	98 ± 1	n.t.	
	A-704	55 ± 14	93 ± 1	n.t.	51 ± 23	82 ± 2	n.t.	
CRC	769-P	89 ± 12	97 ± 4	n.t.	88 ± 10	99 ± 3	n.t.	
	HT-29	n.t.	63 ± 10	107 ± 2	n.t.	102 ± 7	116 ± 4	
	SW-620	8	93 ± 1	100 ± 0.09	99*	97 ± 5	106 ± 0.01	
HCC	HCT-116	106 ± 8	123 ± 4	n.t.	107 ± 10	122 ± 3	n.t.	
	HepG2	97 ± 1	98 ± 0.1	n.t.	87 ± 4	97 ± 1	n.t.	

n.d.: not determined ; n.t.:not tested. n = 2, 3 or 4 replicates per cell line, except n = 1 only experiment
Data is expressed as mean ± SD

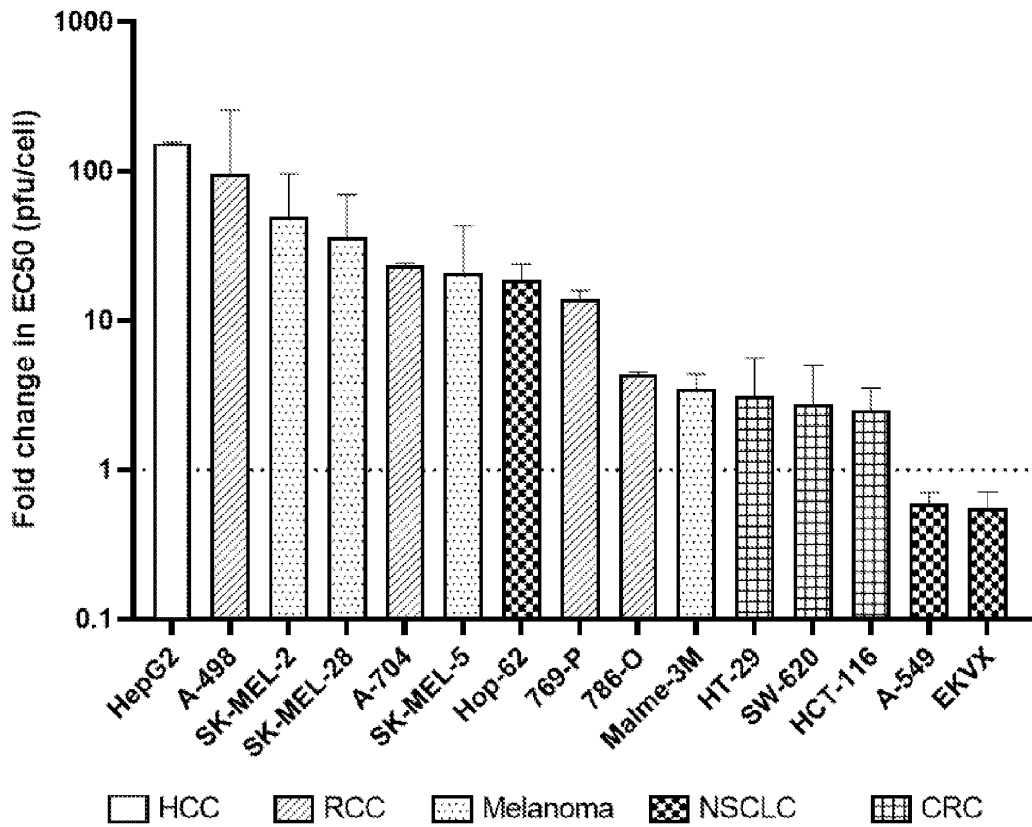
FIG. 59

Indication	Cell Line	VV110 (PFU/cell)			VV12 (JX-594) (PFU/cell)		
		48 hr	72 hr	96 hr	48 hr	72 hr	96 hr
NSCLC	A549	8.79×10^4 *	$3.10 \times 10^2 \pm 2.17 \times 10^2$	$2.05 \times 10^3 \pm 8.01 \times 10^4$	1.02×10^4 *	$1.75 \times 10^3 \pm 9.84 \times 10^3$	$2.37 \times 10^3 \pm 3.51 \times 10^4$
	Hop-62	n.d.	$1.92 \times 10^3 \pm 4.03 \times 10^4$	$3.70 \times 10^4 \pm 4.80 \times 10^5$	n.d.	$3.46 \times 10^2 \pm 4.24 \times 10^3$	$3.54 \times 10^3 \pm 1.68 \times 10^3$
	EKVX	2.88×10^{-4} *	$9.35 \times 10^3 \pm 4.10 \times 10^4$	$1.24 \times 10^3 \pm 1.41 \times 10^4$	2.77×10^{-4} *	$5.16 \times 10^3 \pm 1.25 \times 10^3$	$1.02 \times 10^3 \pm 6.91 \times 10^3$
Melanoma	SK-MEL-2	$7.66 \times 10^1 \pm 5.39 \times 10^1$	$5.52 \times 10^2 \pm 6.47 \times 10^2$	$1.85 \times 10^3 \pm 7.82 \times 10^4$	$1.59 \times 10^1 \pm 2.27 \times 10^1$	$2.07 \times 10^0 \pm 1.84 \times 10^0$	$4.12 \times 10^1 \pm 3.42 \times 10^1$
	SK-MEL-5	n.d.	$7.08 \times 10^1 \pm 7.16 \times 10^1$	$1.51 \times 10^3 \pm 1.59 \times 10^3$	n.d.	$6.00 \times 10^0 \pm 6.76 \times 10^0$	$6.84 \times 10^2 \pm 4.11 \times 10^2$
	SK-MEL-28	$2.63 \times 10^2 \pm 1.45 \times 10^2$	$2.56 \times 10^3 \pm 1.81 \times 10^3$	$1.81 \times 10^3 \pm 6.01 \times 10^3$	$8.77 \times 10^2 \pm 4.78 \times 10^2$	$6.27 \times 10^2 \pm 1.96 \times 10^2$	$5.95 \times 10^2 \pm 1.44 \times 10^2$
RCC	Malme-3M	n.L.	$1.22 \times 10^1 \pm 5.40 \times 10^2$	$1.12 \times 10^3 \pm 9.68 \times 10^3$	n.L.	$4.00 \times 10^1 \pm 7.75 \times 10^2$	$3.78 \times 10^3 \pm 2.69 \times 10^2$
	A-498	n.d.	$1.69 \times 10^1 \pm 8.88 \times 10^2$	$3.55 \times 10^3 \pm 3.18 \times 10^3$	n.d.	$9.54 \times 10^0 \pm 1.52 \times 10^1$	$1.24 \times 10^2 \pm 3.64 \times 10^3$
	786-O	$4.80 \times 10^1 \pm 4.48 \times 10^1$	$4.50 \times 10^2 \pm 5.76 \times 10^2$	n.L.	$1.06 \times 10^0 \pm 3.33 \times 10^1$	$1.91 \times 10^1 \pm 2.43 \times 10^1$	n.L.
CRC	A-704	$2.54 \times 10^0 \pm 6.13 \times 10^1$	$1.07 \times 10^2 \pm 1.59 \times 10^3$	n.L.	$1.33 \times 10^1 \pm 1.46 \times 10^1$	$2.52 \times 10^1 \pm 4.47 \times 10^2$	n.L.
	769-P	$3.68 \times 10^2 \pm 4.86 \times 10^2$	$2.52 \times 10^4 \pm 1.35 \times 10^4$	n.L.	$2.61 \times 10^1 \pm 3.12 \times 10^1$	$3.62 \times 10^3 \pm 2.39 \times 10^3$	n.L.
	HT-29	n.L.	$8.54 \times 10^2 \pm 4.35 \times 10^2$	$2.68 \times 10^3 \pm 1.69 \times 10^3$	n.L.	$2.24 \times 10^1 \pm 1.18 \times 10^1$	$2.33 \times 10^2 \pm 1.72 \times 10^2$
HCC	SW-620	8.45×10^{-1} *	$9.66 \times 10^2 \pm 7.82 \times 10^2$	$1.69 \times 10^3 \pm 1.07 \times 10^2$	4.97×10^0 *	$1.61 \times 10^1 \pm 1.63 \times 10^1$	$4.18 \times 10^2 \pm 1.47 \times 10^2$
	HCT-116	$2.03 \times 10^2 \pm 1.16 \times 10^2$	$5.37 \times 10^3 \pm 3.59 \times 10^3$	n.L.	$1.20 \times 10^1 \pm 4.99 \times 10^2$	$1.17 \times 10^2 \pm 3.59 \times 10^3$	n.L.
	HepG2	$2.15 \times 10^2 \pm 1.15 \times 10^2$	$1.11 \times 10^3 \pm 4.36 \times 10^4$	n.L.	$9.54 \times 10^1 \pm 2.46 \times 10^1$	$1.72 \times 10^1 \pm 6.97 \times 10^2$	n.L.

n.d.: not determined; n.L.: not tested n = 2, 3 or 4 replicates per cell line, except * n = 1 only experiment

Data is expressed as mean $\pm$ SD

FIG. 60



66/66

FIG. 61

Group	Animal	ACV	Lesion	D5	D7	D9
1	101	Non-treated	1	85.7	<2.86	<2.86
			2	71.4	22.9	<2.86
			3	171	14.3	<2.86
	151	Non-treated	1	614	28.6	<2.86
			2	1060	10100	<2.86
			3	786	73000	<2.86
2	201	Treated	1	714	2.86	<2.86
			2	14.3	2.86	<2.86
			3	100	54.3	<2.86
	251	Treated	1	9710	<2.86	<2.86
			2	8.57	42.9	<2.86
			3	1100	34.3	<2.86