

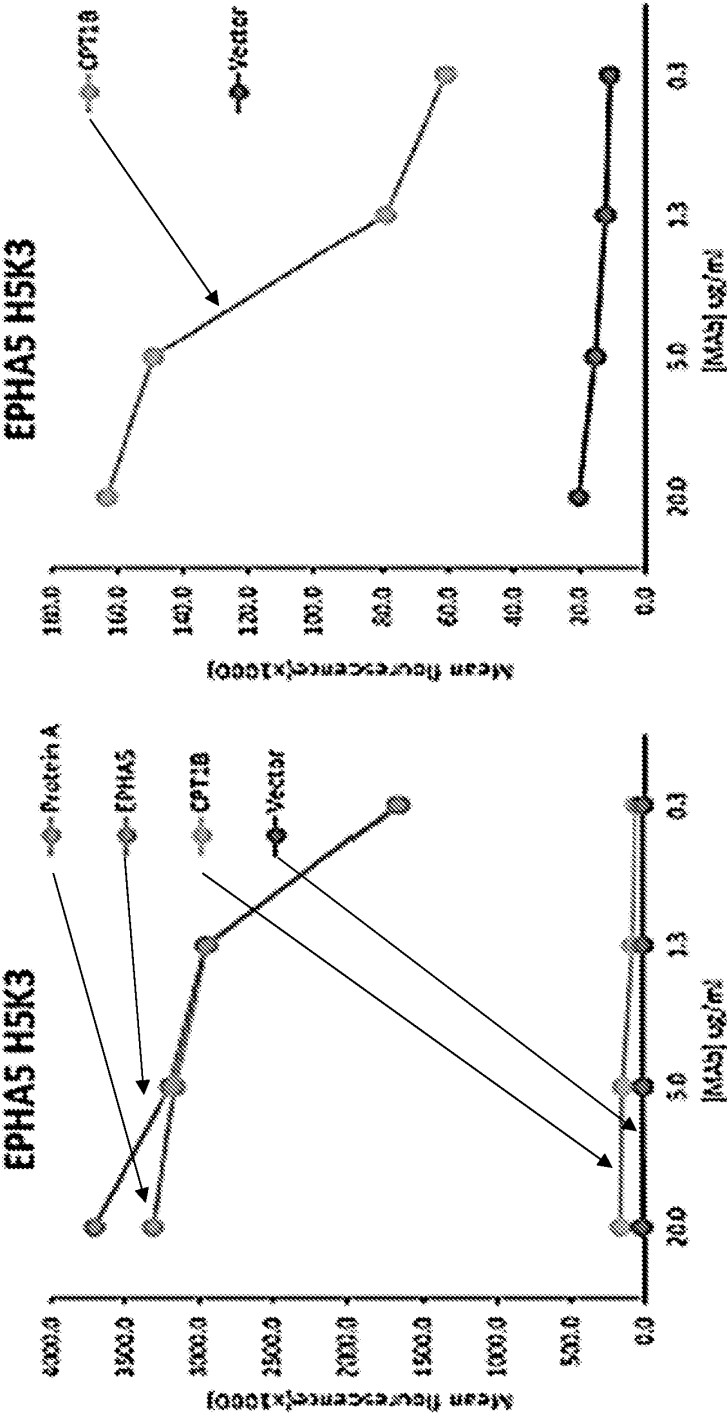


FIG. 1

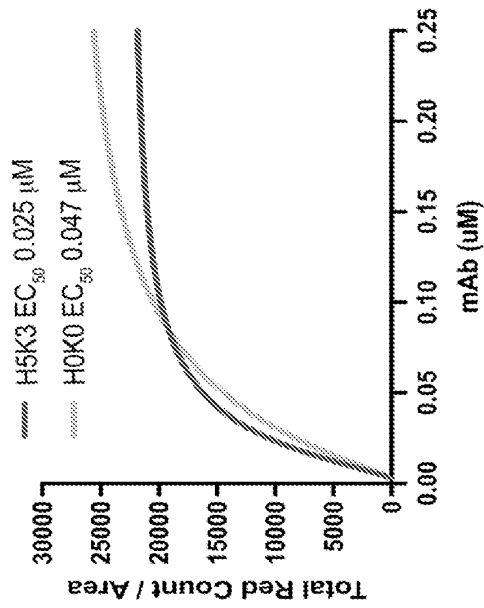


FIG. 2B

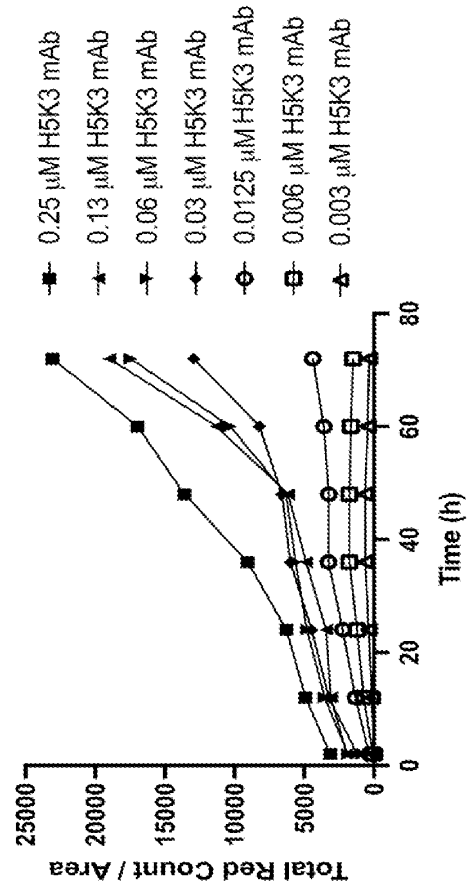


FIG. 2A

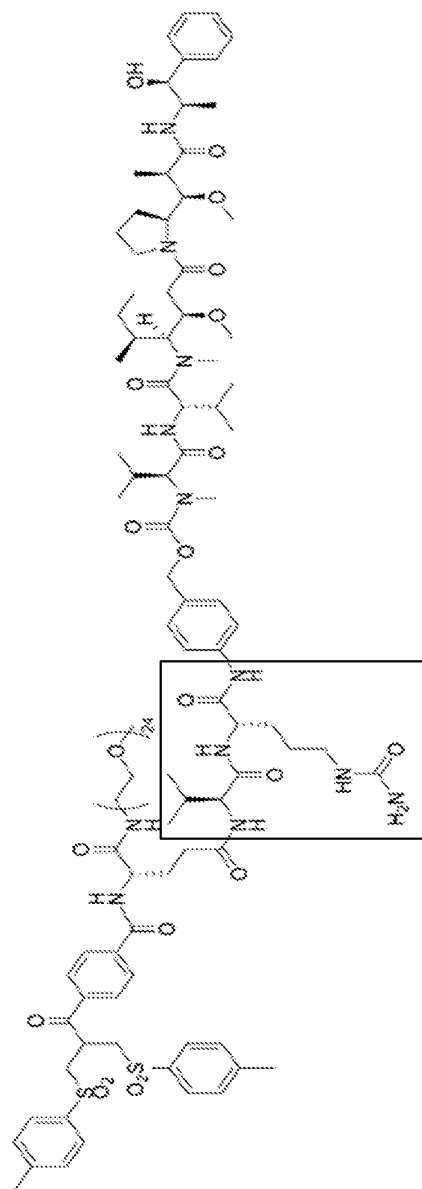


FIG. 3

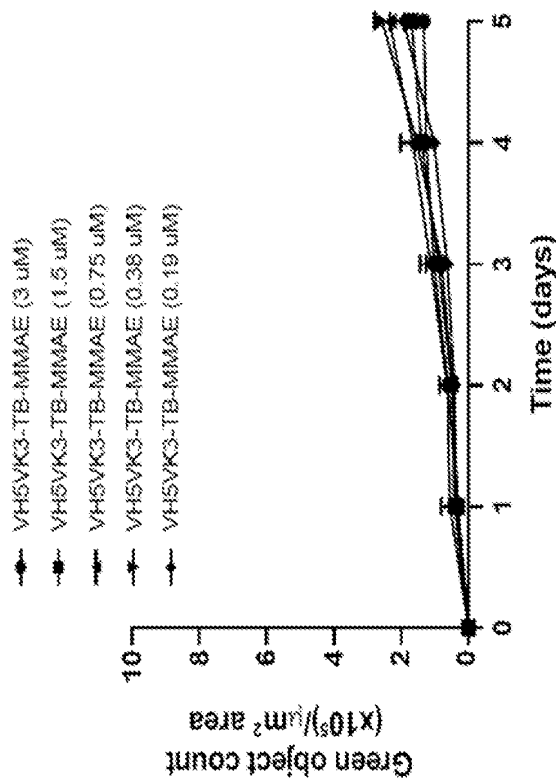


FIG. 4B

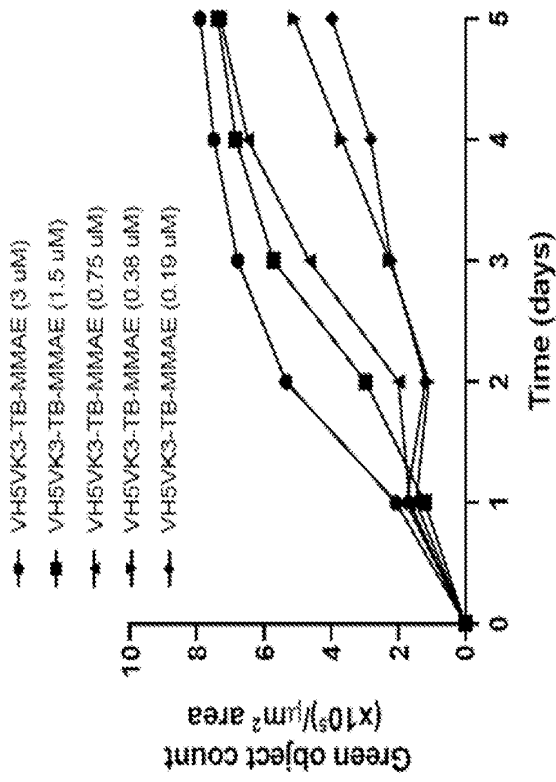


FIG. 4A

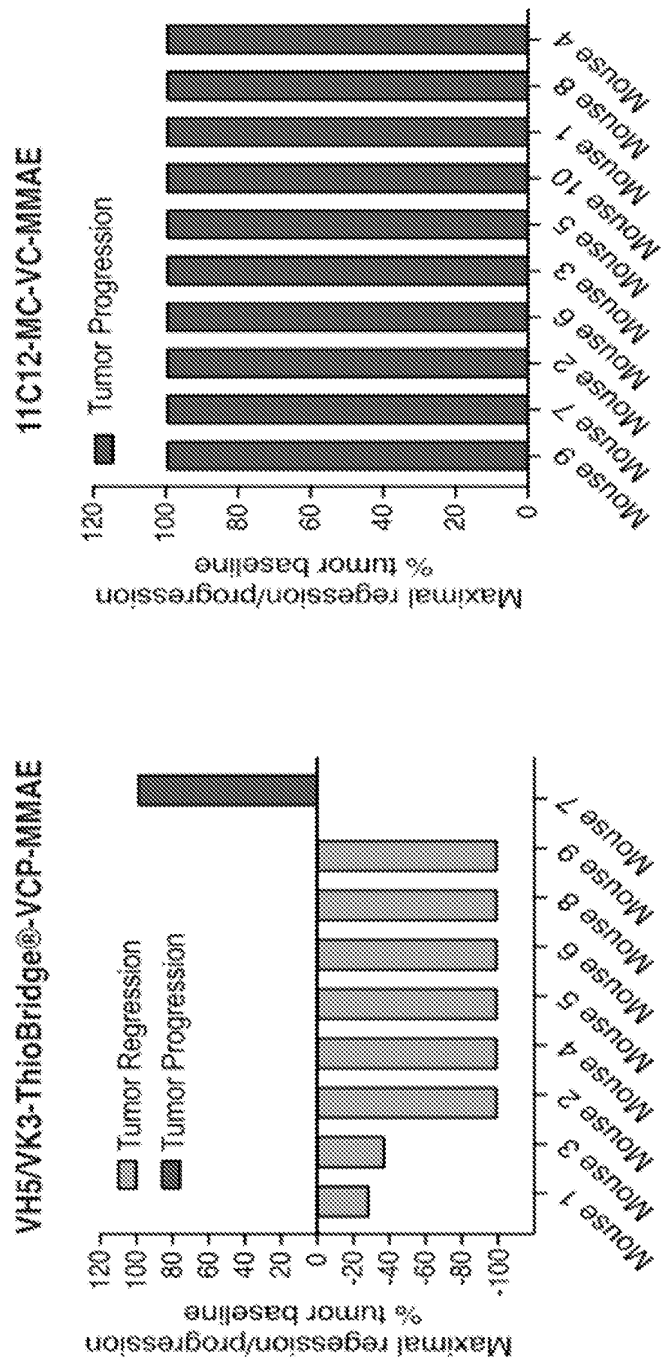


FIG. 5A

FIG. 5B

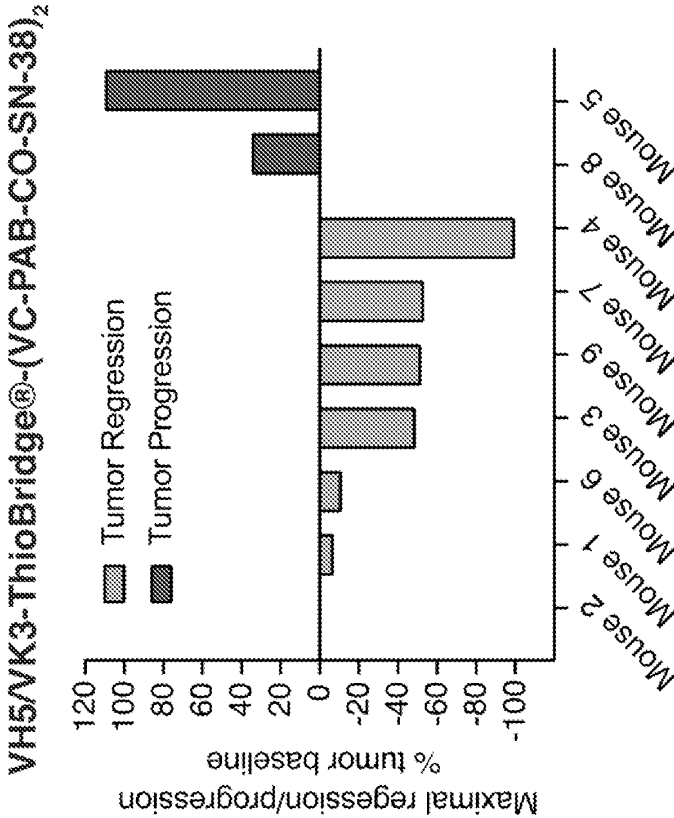


FIG. 6

11C12 Variants		IGHV3-48						IGHV3-66	
% Homology to closest Human Germline		VH0	VH1	VH2	VH3	VH4	VH5	VH6	
IGKV4-1	70.3	✓	✓						
	74.3	✓	✓	✓	✓	✓	✓	✓	
	75.2		✓	✓	✓	✓	✓	✓	
	76.2		✓	✓	✓	✓	✓	✓	
	76.2		✓	✓	✓	✓	✓	✓	
	77.2		✓	✓	✓	✓	✓	✓	

FIG. 7

Heavy Chain

Predicted affinity MHC class II	VH0	VH1	VH2	VH3	VH4	VH5	VH6
Number High	6	4	4	4	3	2	2
Number Moderate	3	3	3	3	2	2	1

Light chain

Predicted affinity MHC class II	VK0	VK1	VK2	VK3	VK4	VK5
Number High	6	3	2	2	2	2
Number Moderate	2	1	1	1	1	1

FIG. 8

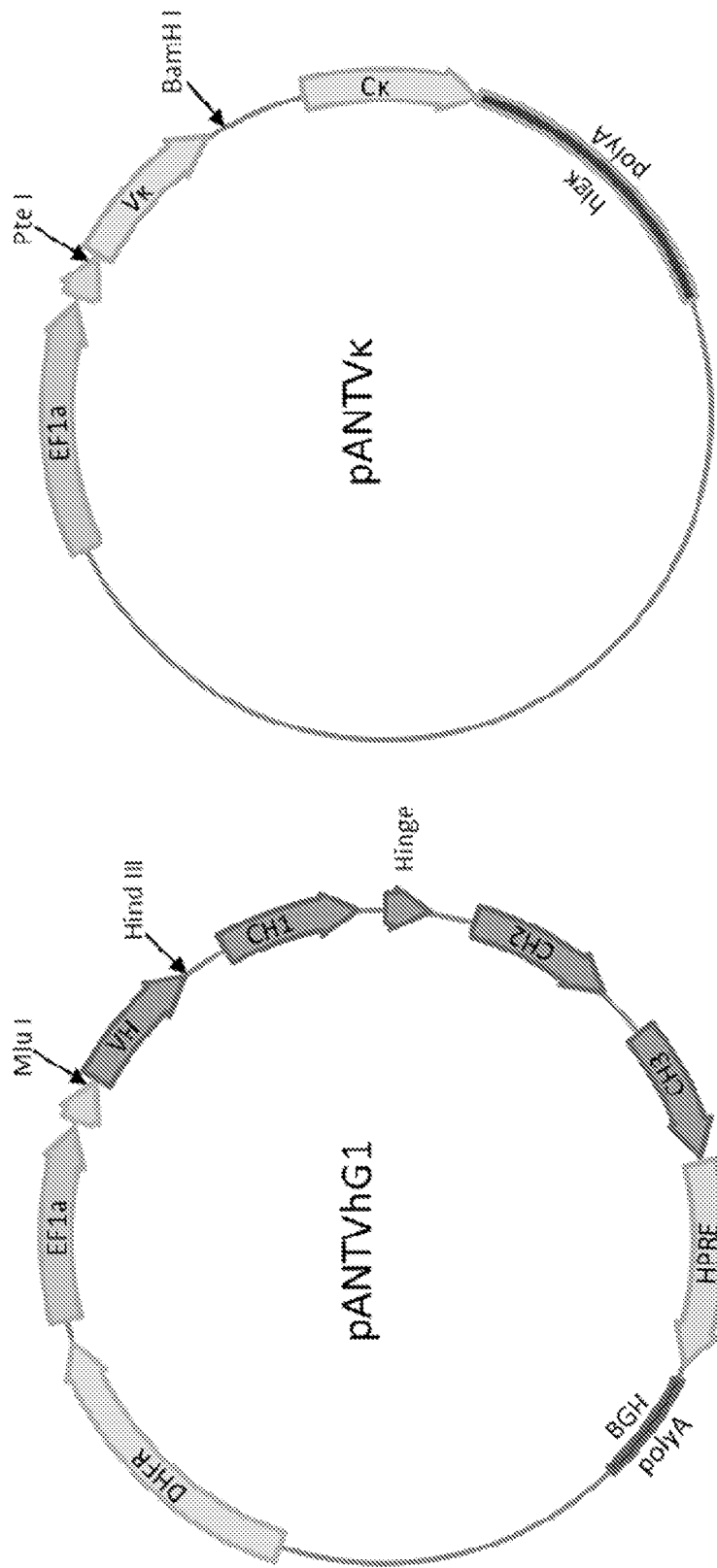


FIG. 9

		Heavy Chain						
Light Chain		VH0	VH1	VH2	VH3	VH4	VH5	VH6
	VK0	2.53	8.45					
	VK1	1.53	7.38	8.60	10.18	8.64	10.09	8.02
	VK2		9.65	9.49	10.12	8.79	8.40	9.80
	VK3		9.48	12.45	13.00	10.38	9.54	9.92
	VK4		8.56	9.60	12.90	8.31	9.31	7.71
	VK5		8.36	11.60	10.93	8.58	9.68	8.88

FIG. 10

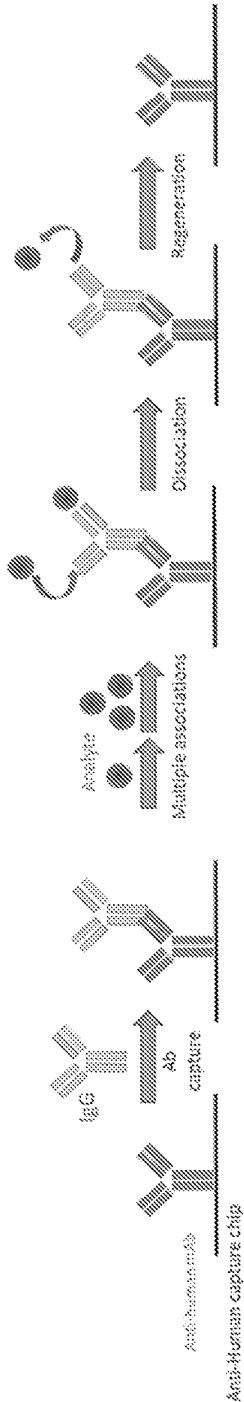


FIG. 11

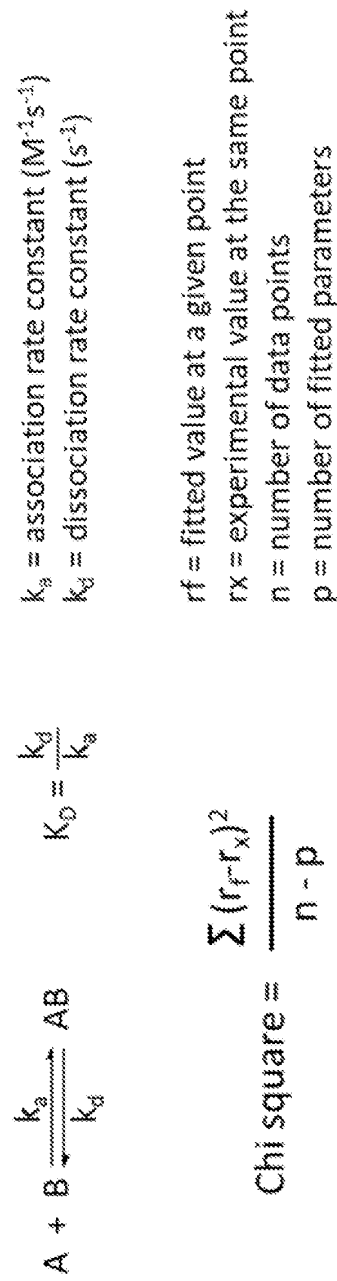


FIG. 12

Antibody	k_a (1/Ms)	k_d (1/s)	K_D (M)	Relative K_D	R_{MAX}	Chi ² (RU ²)
VH0/VK0	1.15×10^{-6}	1.53×10^{-3}	1.33×10^{-9}	1.00	33.0	0.0651
VH0/VK1	1.22×10^{-6}	1.37×10^{-3}	1.12×10^{-9}	0.84	29.1	0.0286
VH1/VK0	1.22×10^{-6}	1.27×10^{-3}	1.04×10^{-9}	0.78	32.1	0.0425
* VH1/VK1	1.25×10^{-6}	1.28×10^{-3}	1.02×10^{-9}	0.77	39.2	0.0125
* VH1/VK2	1.31×10^{-6}	1.26×10^{-3}	9.68×10^{-10}	0.73	24.3	0.0118
* VH1/VK3	1.32×10^{-6}	1.25×10^{-3}	9.48×10^{-10}	0.71	24.9	0.0120
* VH1/VK4	1.24×10^{-6}	1.37×10^{-3}	1.10×10^{-9}	0.83	23.4	0.0059
* VH1/VK5	1.24×10^{-6}	1.39×10^{-3}	1.12×10^{-9}	0.84	33.1	0.0121
* VH2/VK1	1.35×10^{-6}	1.20×10^{-3}	8.90×10^{-10}	0.67	30.3	0.0119
* VH2/VK2	1.30×10^{-6}	1.26×10^{-3}	9.71×10^{-10}	0.73	37.7	0.00878
* VH2/VK3	1.34×10^{-6}	1.32×10^{-3}	9.85×10^{-10}	0.74	25.2	0.0066
* VH2/VK4	1.37×10^{-6}	1.26×10^{-3}	9.17×10^{-10}	0.69	22.6	0.0063
* VH2/VK5	1.34×10^{-6}	1.40×10^{-3}	1.05×10^{-9}	0.79	28.1	0.0076
* VH3/VK1	1.39×10^{-6}	1.23×10^{-3}	8.84×10^{-10}	0.66	23.4	0.0072
* VH3/VK2	1.34×10^{-6}	1.30×10^{-3}	9.68×10^{-10}	0.73	26.1	0.0049
* VH3/VK3	1.32×10^{-6}	1.33×10^{-3}	1.01×10^{-9}	0.76	34.0	0.0068
# VH3/VK4	1.33×10^{-6}	1.28×10^{-3}	9.56×10^{-10}	0.72	34.2	0.0119
* VH3/VK5	1.29×10^{-6}	1.43×10^{-3}	1.10×10^{-9}	0.83	27.1	0.0060
* VH4/VK1	1.32×10^{-6}	1.29×10^{-3}	9.75×10^{-10}	0.73	33.8	0.0074
* VH4/VK2	1.34×10^{-6}	1.14×10^{-3}	8.54×10^{-10}	0.64	24.0	0.0044
# VH4/VK3	1.31×10^{-6}	1.37×10^{-3}	1.04×10^{-9}	0.78	28.6	0.0055
# VH4/VK4	1.33×10^{-6}	1.40×10^{-3}	1.05×10^{-9}	0.79	24.9	0.0045
* VH4/VK5	1.37×10^{-6}	1.37×10^{-3}	9.96×10^{-10}	0.75	22.0	0.0066
* VH5/VK1	1.34×10^{-6}	1.27×10^{-3}	9.47×10^{-10}	0.71	28.6	0.0085
# VH5/VK2	1.38×10^{-6}	1.23×10^{-3}	8.92×10^{-10}	0.67	31.2	0.0169
# VH5/VK3	1.36×10^{-6}	1.40×10^{-3}	1.03×10^{-9}	0.77	26.9	0.0093
# VH5/VK4	1.35×10^{-6}	1.41×10^{-3}	1.04×10^{-9}	0.78	26.4	0.0096
* VH5/VK5	1.37×10^{-6}	1.40×10^{-3}	1.03×10^{-9}	0.77	25.1	0.0092
VH6/VK1	1.65×10^{-9}	1.65×10^{-1}	1.00×10^{-8}	7.52	21.3	0.0525
VH6/VK2	1.74×10^{-9}	1.65×10^{-1}	9.49×10^{-9}	7.14	17.7	0.0349
VH6/VK3	5.22×10^{-9}	3.41×10^{-1}	6.52×10^{-9}	4.90	14.1	0.0651
VH6/VK4	2.15×10^{-9}	2.09×10^{-1}	9.76×10^{-9}	7.34	12.8	0.0544
VH6/VK5	4.01×10^{-9}	2.85×10^{-1}	7.10×10^{-9}	5.34	18.1	0.1130

FIG. 13

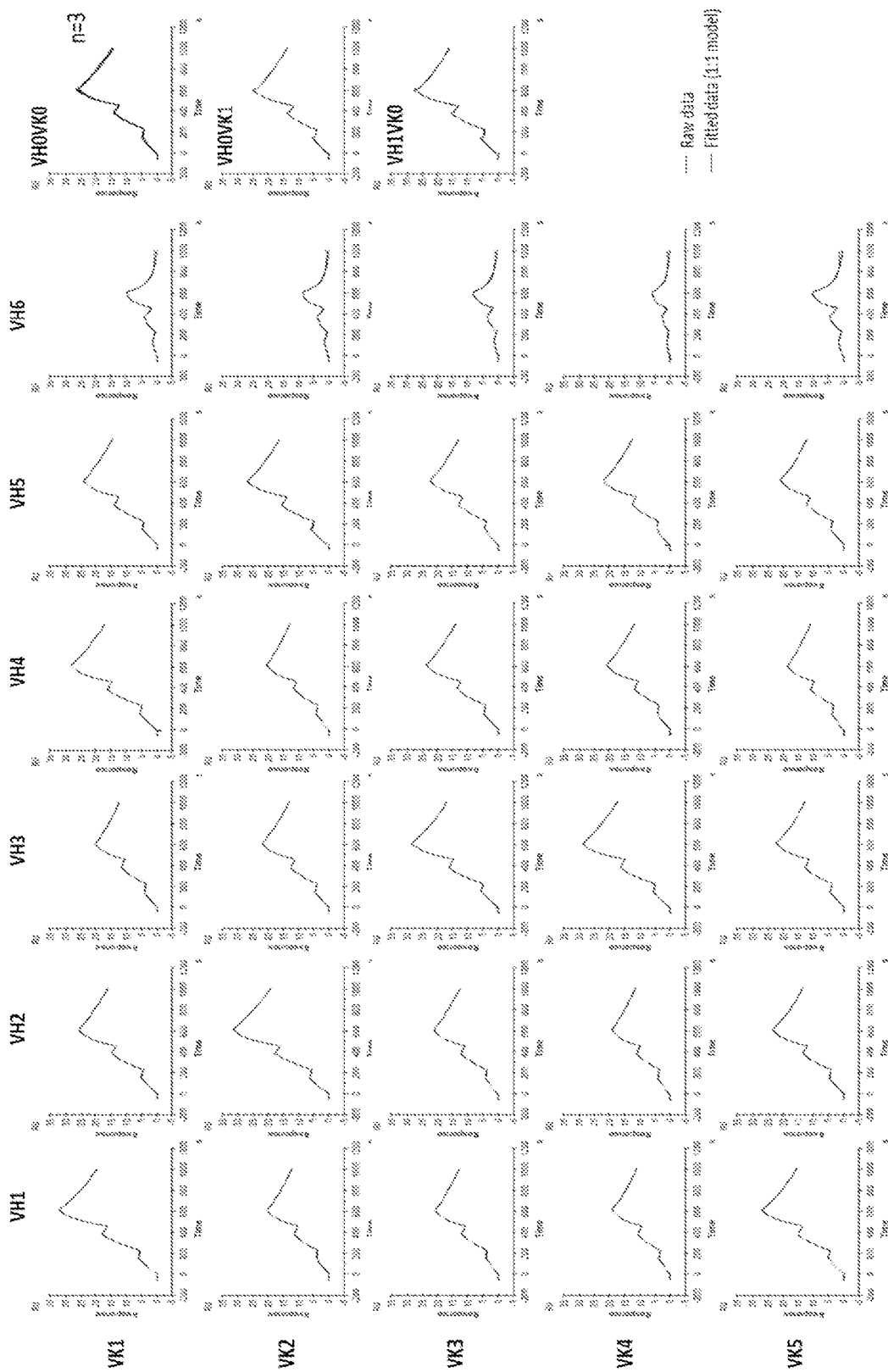


FIG. 14

Heavy Chain		Light Chain			
		VH0	VH3	VH4	VH5
VK0	61.0				
VK3			-	122.6	106.6
VK4			150.4	112.3	143.1
VK5			-	-	144.9

FIG. 15

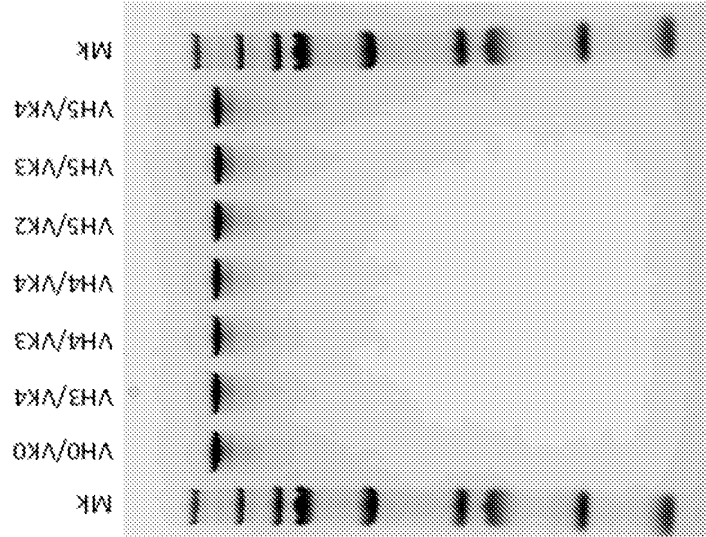


FIG. 16B

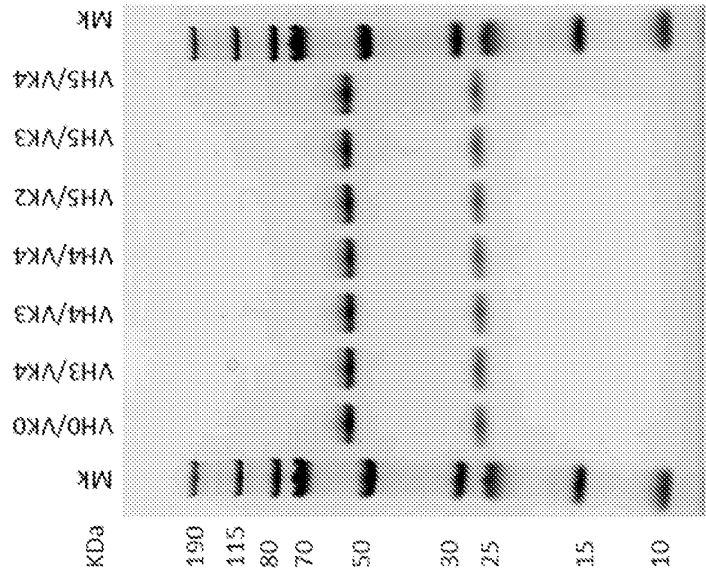


FIG. 16A

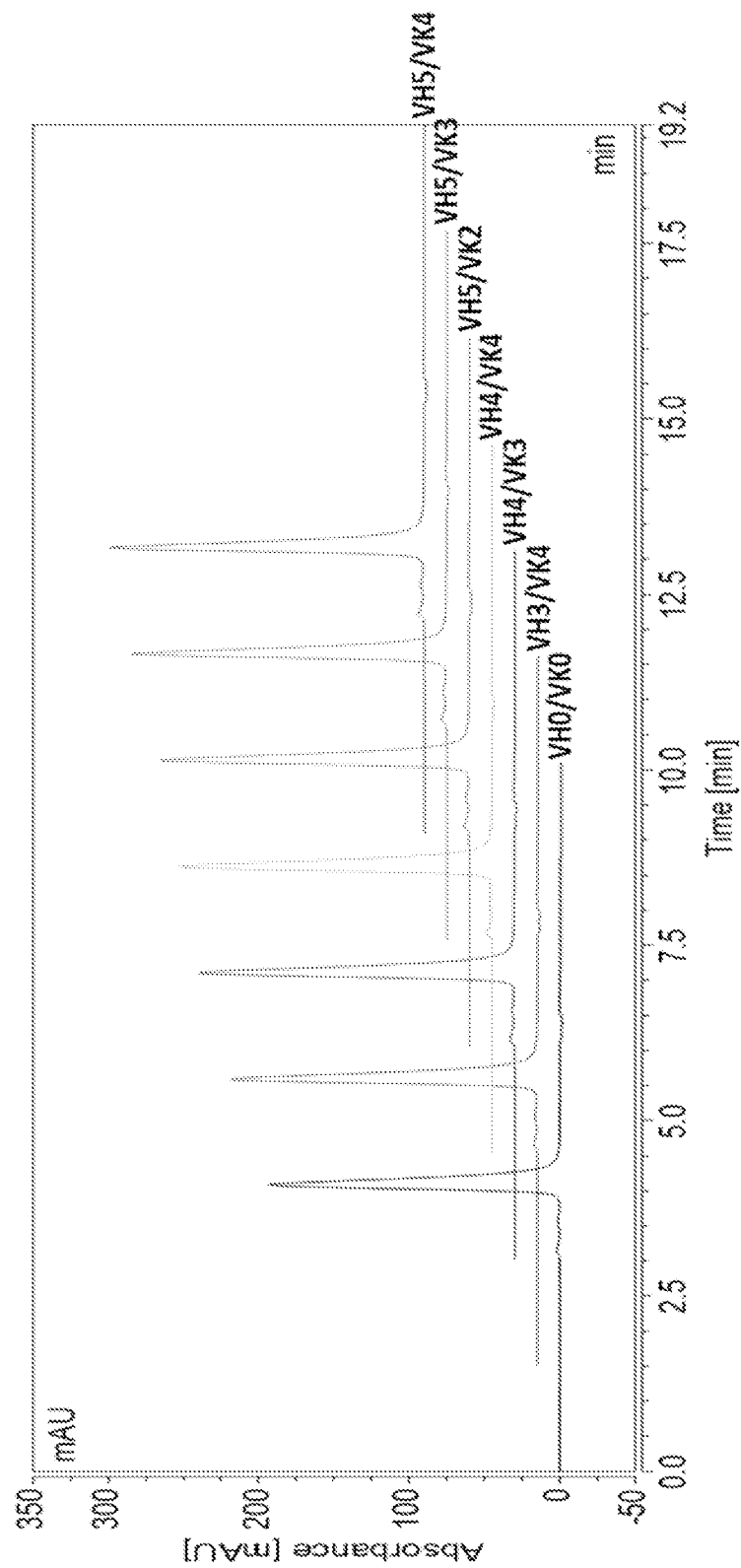


FIG. 17

Antibody	Monomer %
VH0/VK0	98.0
VH3/VK4	98.0
VH4/VK3	97.7
VH4/VK4	97.7
VH5/VK2	97.0
VH5/VK3	97.0
VH5/VK4	97.0

FIG. 18

Antibody	k_a (1/Ms)	k_d (1/s)	K_D (M)	Relative K_D	R_{MAX}	χ^2 (RU ²)
VH0/VK0	9.65×10^{-5}	1.50×10^{-3}	1.56×10^{-9}	1.00	47.8	1.23
VH3/VK4	1.31×10^{-6}	1.42×10^{-3}	1.08×10^{-9}	0.69	42.8	0.65
VH4/VK3	1.49×10^{-6}	1.39×10^{-3}	9.37×10^{-10}	0.60	46.3	0.776
VH4/VK4	1.27×10^{-6}	1.32×10^{-3}	1.04×10^{-9}	0.67	32.2	0.352
VH5/VK2	1.34×10^{-6}	1.25×10^{-3}	9.34×10^{-10}	0.60	48.6	0.892
VH5/VK3	1.21×10^{-6}	1.35×10^{-3}	1.11×10^{-9}	0.71	35.3	0.429
VH5/VK4	1.23×10^{-6}	1.28×10^{-3}	1.04×10^{-9}	0.67	43.3	0.605

FIG. 19

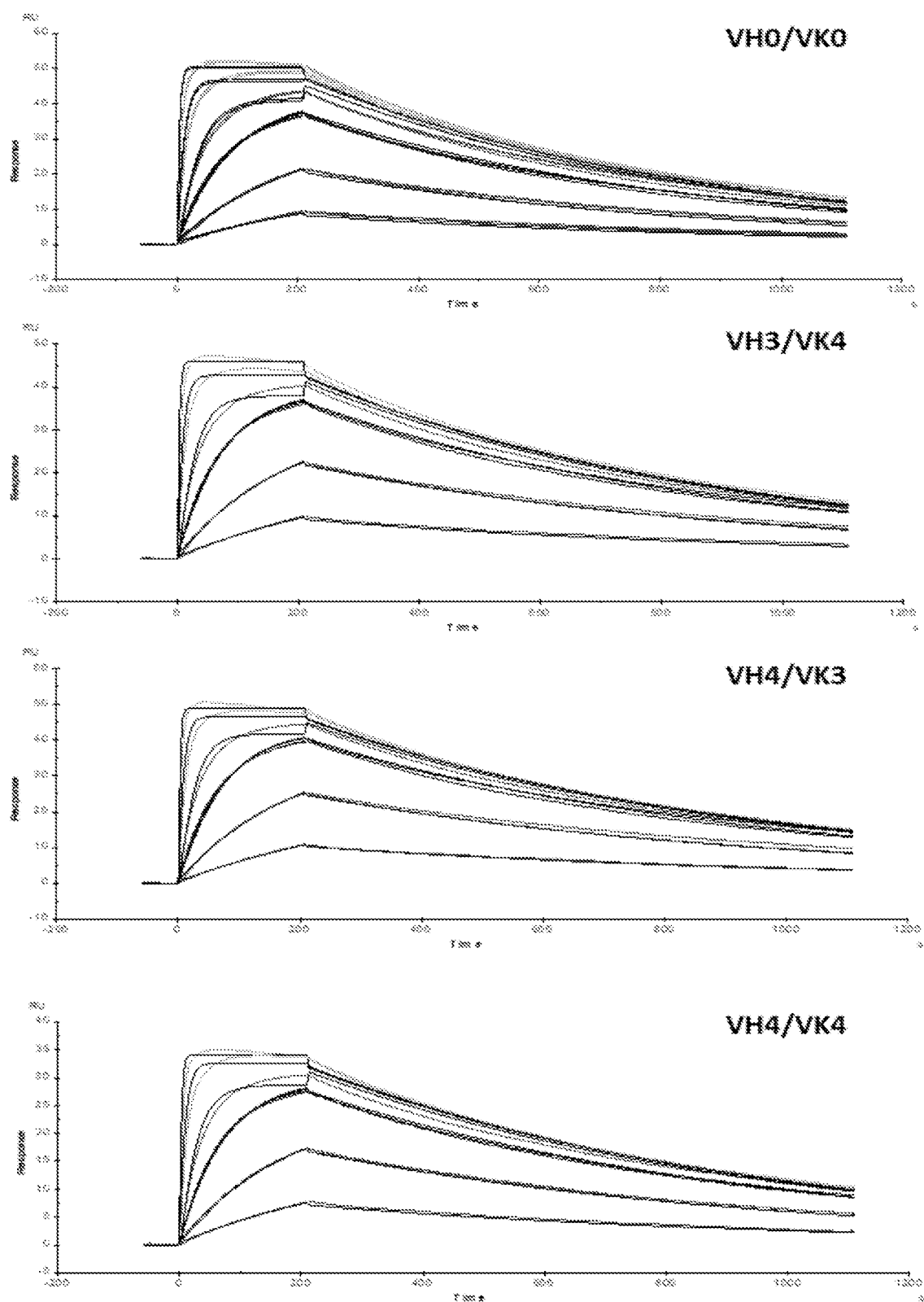


FIG. 20

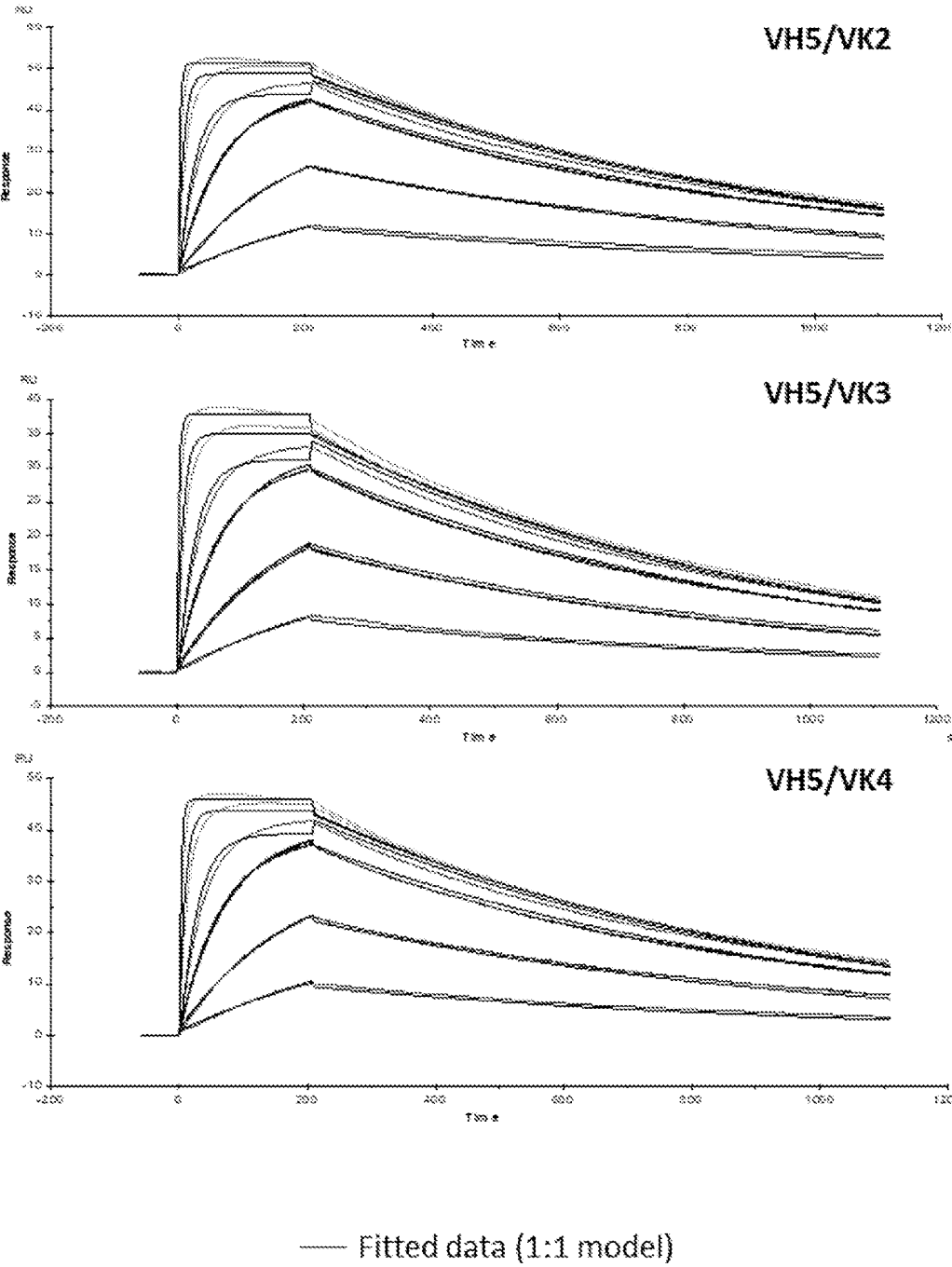


FIG. 20, continued

Sample	Tm1 (°C)	Average Tm1 (°C)	Tm2 (°C)	Average Tm2 (°C)	Tonset (°C)	Average Tonset (°C)	Tagg 473 (°C)	Average Tagg 473 (°C)
VH0/VK0	57.83	57.9	65.83	65.83	54.92	55.1	65.72	65.6
VH3/VK4	67.64	67.6			62.54	61.2	67.77	67.7
	67.48				59.94		67.63	
VH4/VK3	69.14	69.6			65.69	65.2	69.82	69.8
	69.99				64.80		69.69	
VH4/VK4	66.69	66.8			60.14	60.1	67.18	67.2
	66.93				60.00		67.25	
VH5/VK2	*	67.5			*	60.9	*	68.1
	67.54				60.95		68.08	
VH5/VK3	*	69.0			*	63.6	*	70.2
	68.99				63.59		70.17	
VH5/VK4	66.00	66.2			61.33	60.9	68.05	68.1
	66.46				60.52		68.25	

FIG. 21

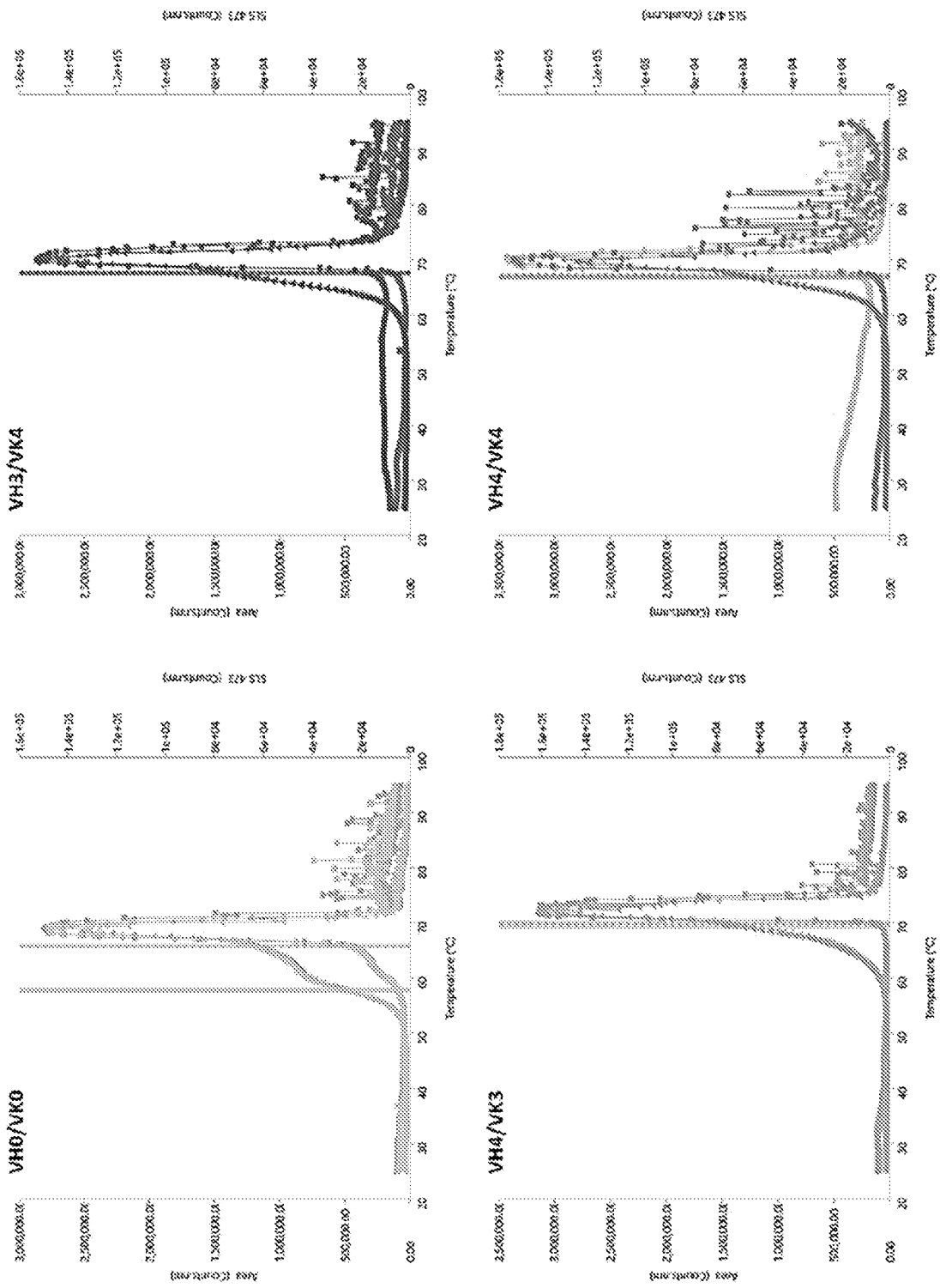


FIG. 22A

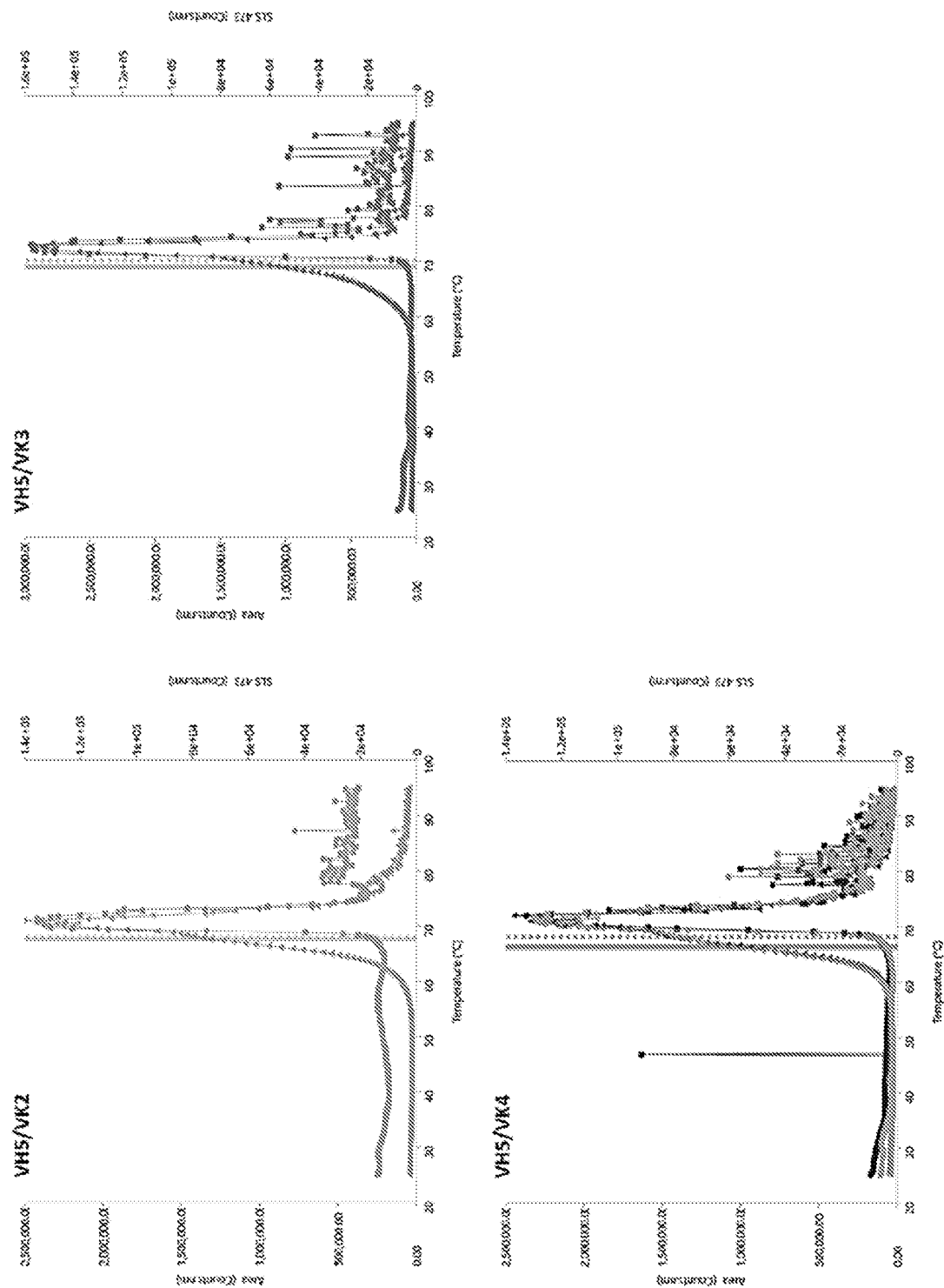


FIG. 22A, continued

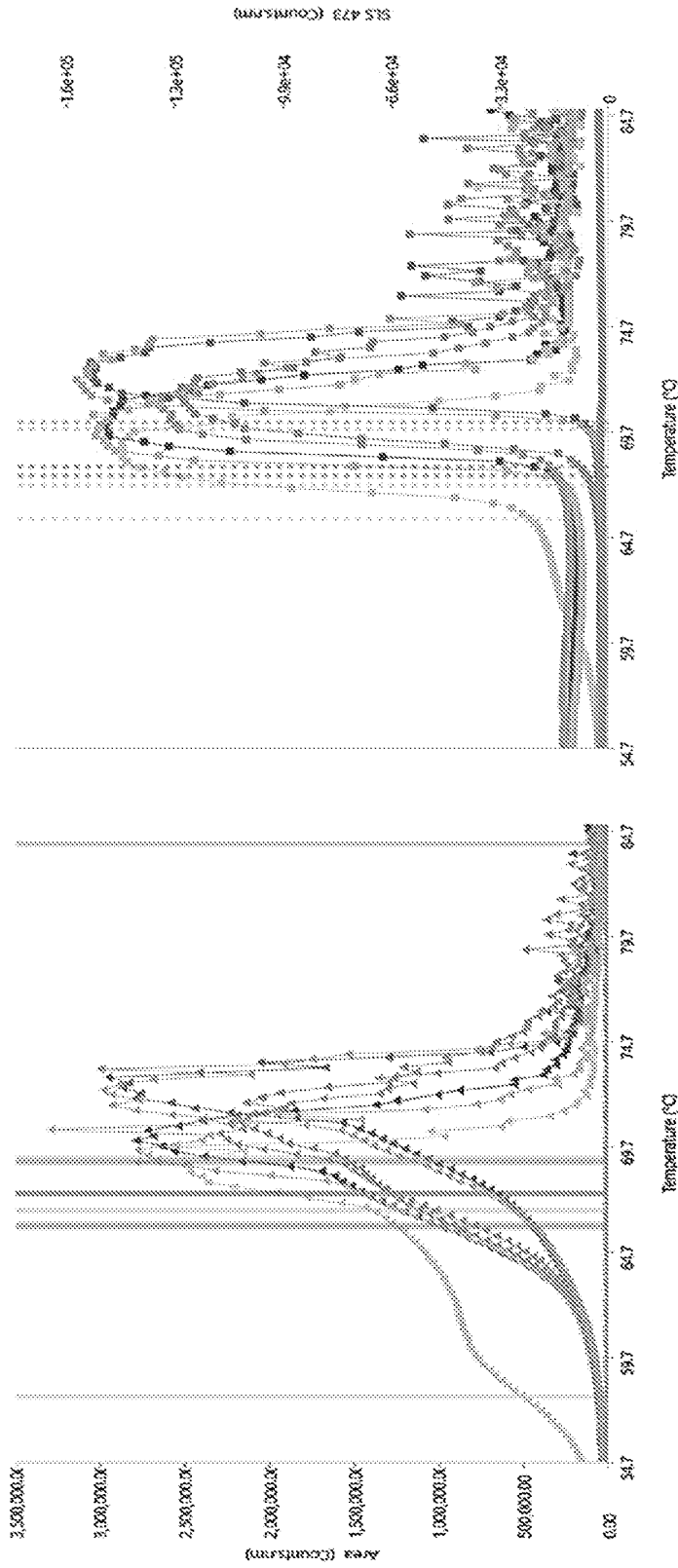


FIG. 22B

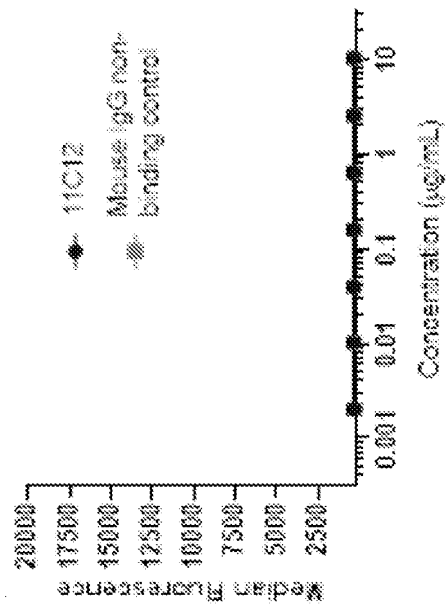


FIG. 23B

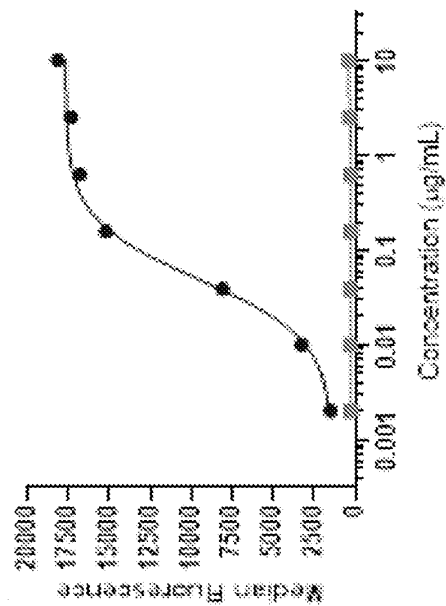


FIG. 23A

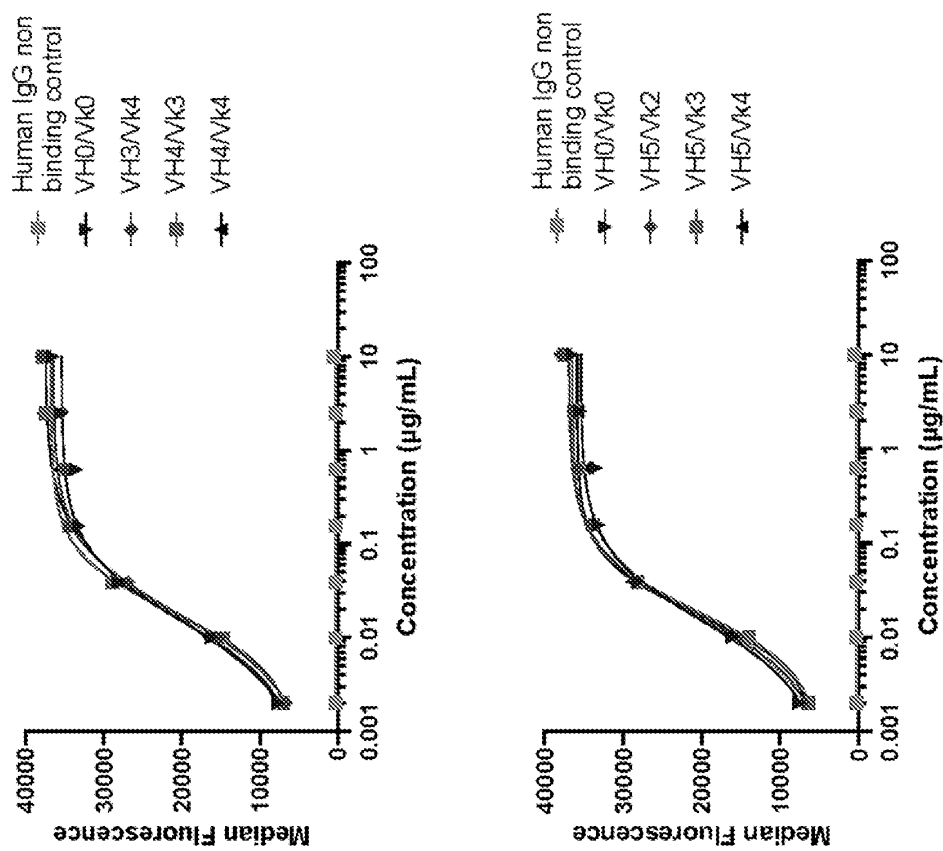


FIG. 24

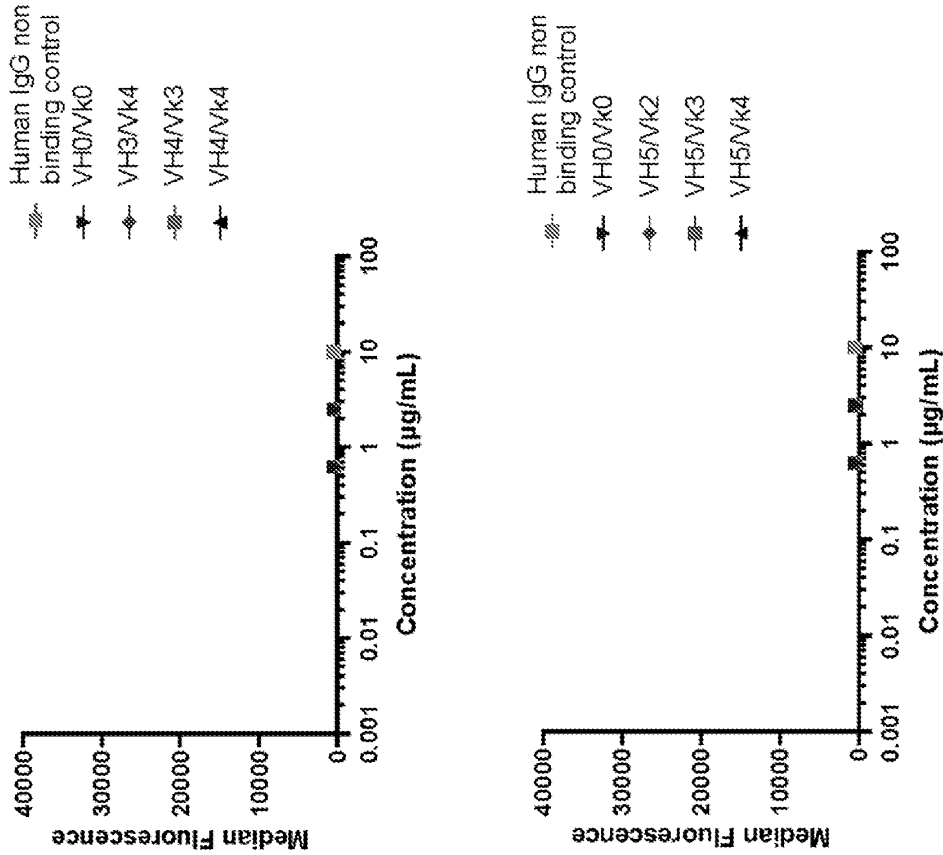
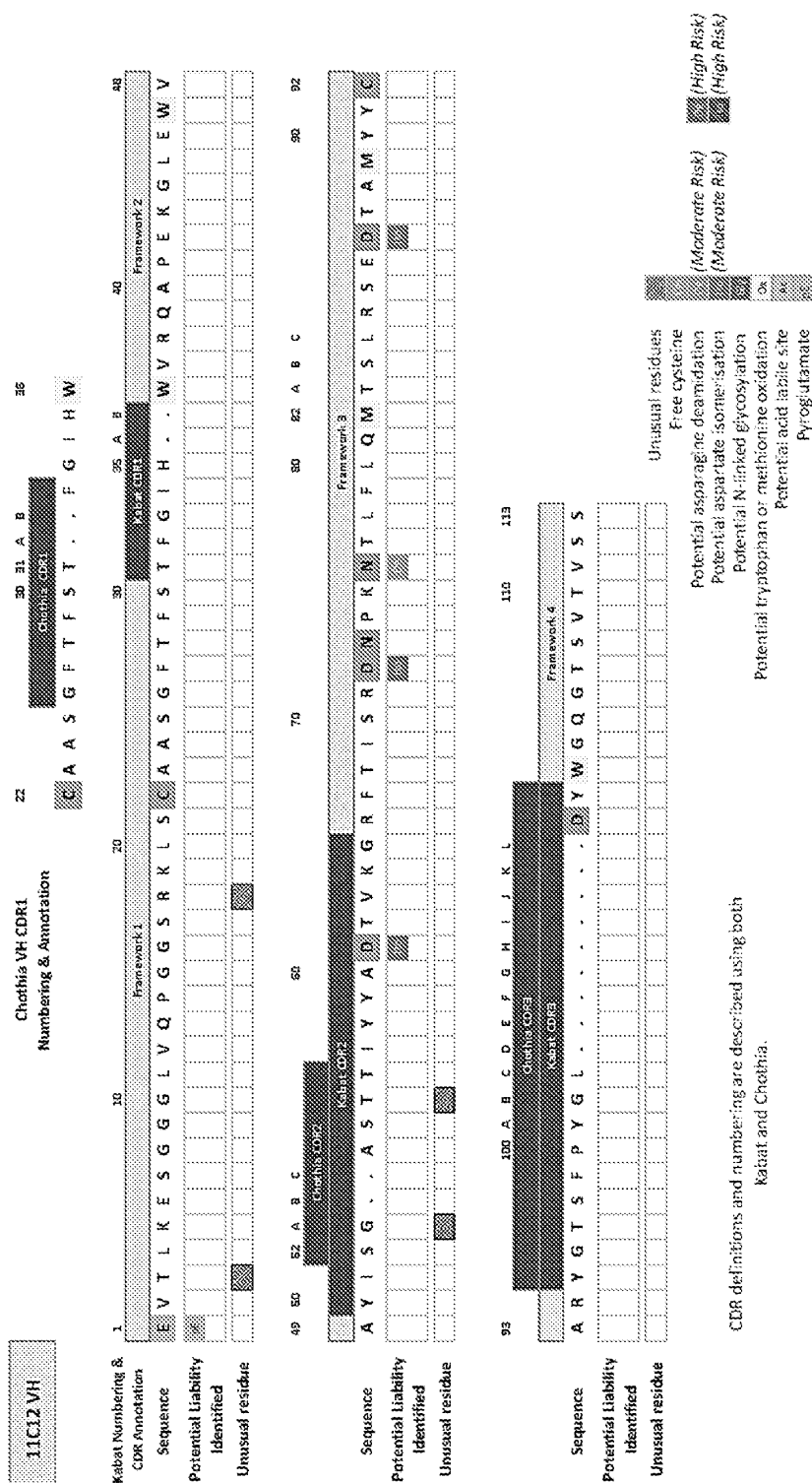


FIG. 25

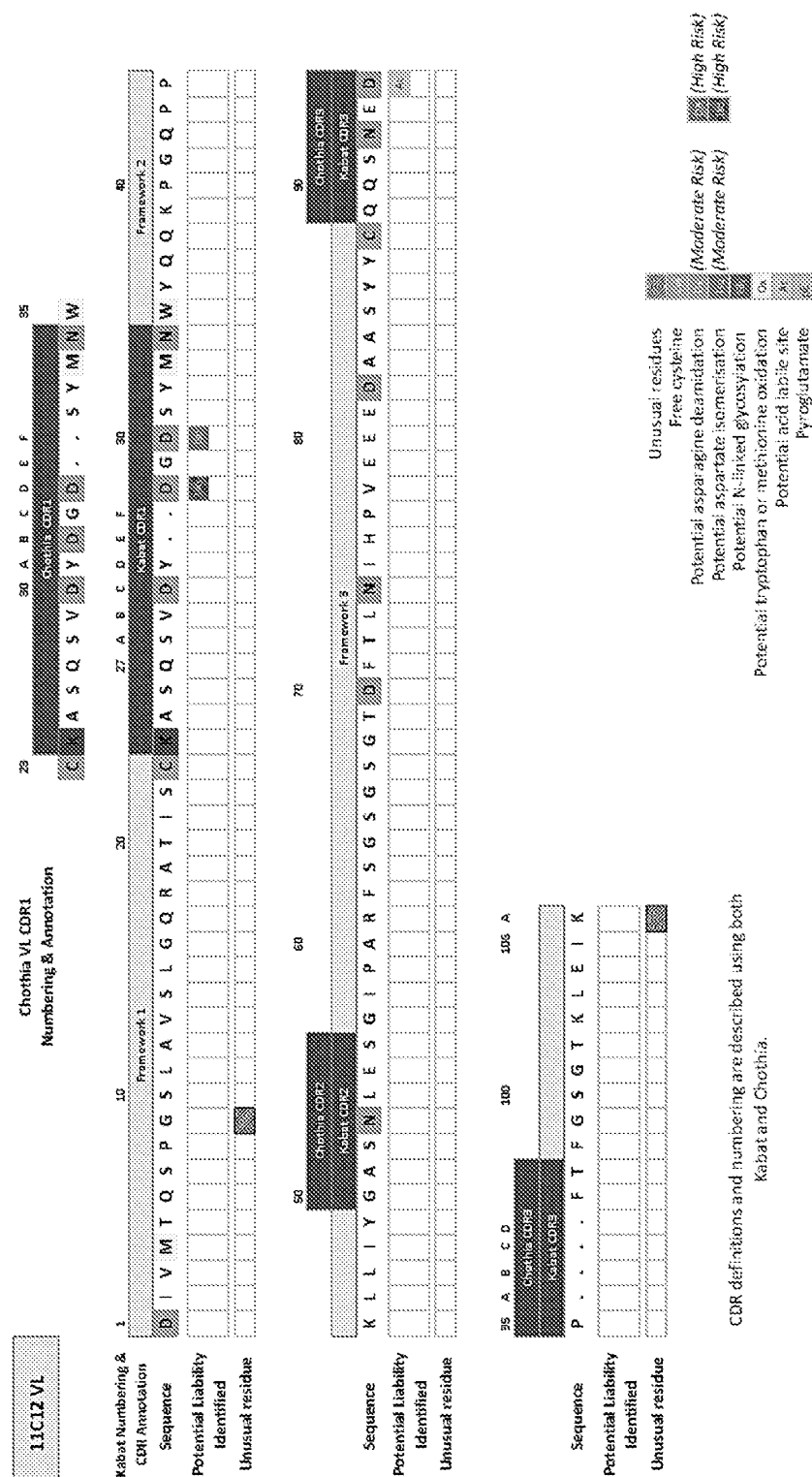
Sample Details				H460 Cell Line		H226 Cell Line
Variant	Stock Concentration (mg/mL)	Starting Assay Concentration (μg/mL)	EC ₅₀ (μg/mL)	Max. Binding (MFI)	EC ₅₀ (μg/mL)	Max. Binding (MFI)
Mouse Anti-EphA5	1	10	0.025	27334	N/A	N/A
Mouse IgG1 non-binding	0.5	10	N/A	N/A	N/A	N/A
Human IgG1 non-binding	0.5	10	N/A	N/A	N/A	N/A
VH0/VK0	3.06	10	0.015	35401	N/A	N/A
VH3/VK4	3.15	10	0.018	36481	N/A	N/A
VH4/VK3	3.67	10	0.018	36745	N/A	N/A
VH4/VK4	3.02	10	0.017	37500	N/A	N/A
VH5/VK2	3.31	10	0.017	36901	N/A	N/A
VH5/VK3	3.44	10	0.019	36475	N/A	N/A
VH5/VK4	2.92	10	0.018	35882	N/A	N/A

FIG. 26

Heavy Chain



Light Chain



Heavy chain

VH0 Protein Sequence	EVTLKESGGGLVQPGGSRKLSCAASGFTFSFGIHWROAPEKGLEWAVISGASTIIYYADTVKGRFTISRDNPKNITLF	10	20	30	40	50	52A	60	70
VH1 Protein Sequence	EVTLVESGGGLVQPGGSRKLSCAASGFTFSFGIHWROAPGKGLEWAVISGASTIIYYADTVKGRFTISRDNSKNTLY								
VH2 Protein Sequence	EVTLVESGGGLVQPGGSLKLSCAASGFTFSFGIHWROAPGKGLEWAVISGASTIIYYADTVKGRFTISRDNSKNTLY								
VH3 Protein Sequence	EVQLVESGGGLVQPGGSLKLSCAASGFTFSFGIHWROAPGKGLEWAVISGASTIIYYADTVKGRFTISRDNSKNTLY								
VH4 Protein Sequence	EVQLVESGGGLVQPGGSLKLSCAASGFTFSFGIHWROAPGKGLEWAVISGASTIIYYADTVKGRFTISRDNSKNTLY								
VH5 Protein Sequence	EVQLVESGGGLVQPGGSLKLSCAASGFTFSFGIHWROAPGKGLEWAVISGASTIIYYADSVKGRFTISRDNSKNTLY								
VH6 Protein Sequence	EVQLVESGGGLVQPGGSLKLSCAASGFTFSFGIHWROAPGKGLEWAEISGASTIIYYADSVKGRFTISRDNSKNTLY								

CDR1

CDR2

VH0 Protein Sequence	LOMTSLRSEDTAMYYCARYGTSFPYGLDYMGOGTSVTVSS	80	82ABC	90	100ABC	110
VH1 Protein Sequence	LOMNSLRSEDTAMYYCARYGTSFPYGLDYMGOGTSVTVSS					
VH2 Protein Sequence	LOMNSLRSEDTAMYYCARYGTSFPYGLDYMGOGTLVTVSS					
VH3 Protein Sequence	LOMNSLRSEDTAMYYCARYGTSFPYGLDYMGOGTLVTVSS					
VH4 Protein Sequence	LOMNSLRAEDTAVYYCARYGTSFPYGLDYMGOGTLVTVSS					
VH5 Protein Sequence	LOMNSLRAEDTAVYYCARYGTSFPYGLDYMGOGTLVTVSS					
VH6 Protein Sequence	LOMNSLRAEDTAVYYCARYGISEPYGLDYMGOGTLVTVSS					

CDR3

Light chain

VH0 Protein Sequence	DI VMTQSPGSLAVSLGQRATISCKASQSVQYDGDSDYMMWQOKPGKAPKLLIYGASNLESIGIPARFSGSGSGTDFTLNIH	10	20	27ABC	30	40	50	60	70
VK1 Protein Sequence	DI VMTQSPGSLAVSLGERATINCKASQSVQYDGDSDYMMWQOKPGKAPKLLIYGASNLESIGIPARFSGSGSGTDFTLTIIS								
VK2 Protein Sequence	DI VMTQSPDLSAVSLGERATINCKASQSVQYDGDSDYMMWQOKPGKAPKLLIYGASNLESIGIPARFSGSGSGTDFTLTIIS								
VK3 Protein Sequence	DI VMTQSPDLSAVSLGERATINCKASQSVQYDGDSDYMMWQOKPGKAPKLLIYGASNLESIGIPARFSGSGSGTDFTLTIIS								
VK4 Protein Sequence	DI VMTQSPDLSAVSLGERATINCKSSQSVQYDGDSDYMMWQOKPGKAPKLLIYGASNLESIGIPARFSGSGSGTDFTLTIIS								
VK5 Protein Sequence	DI VMTQSPDLSAVSLGERATINCKSSQSVQYDGDSDYMMWQOKPGKAPKLLIYGASNLESIGIPARFSGSGSGTDFTLTIIS								

CDR1

CDR2

VH0 Protein Sequence	PVEEEDAASYCQQSNEDPFTIFGSGTKLEIK	80	90	100	106A
VK1 Protein Sequence	RLEEEEDAASYCQQSNEDPFTIFGSGTKLEIK				
VK2 Protein Sequence	RLEPEEDAASYCQQSNEDPFTIFGSGTKLEIK				
VK3 Protein Sequence	RLEPEEDAASYCQQSNEDPFTIFGSGTKLEIK				
VK4 Protein Sequence	RLEPEEDAASYCQQSNEDPFTIFGSGTKLEIK				
VK5 Protein Sequence	RLEPEEDAASYCQQSNEDPFTIFGSGTKLEIK				

CDR3

FIG. 28

Chimeric		Variant 1		Variant 2		Variant 3		Variant 4		Variant 5		Variant 6	
CDR	Kabat Residue number	Promiscuous Moderate	Promiscuous High	Promiscuous Moderate	Promiscuous High	Promiscuous Moderate	Promiscuous High	Promiscuous Moderate	Promiscuous High	Promiscuous Moderate	Promiscuous High	Promiscuous Moderate	Promiscuous High
	1		E		E		E		E		E		E
	2		V		V		V		V		V		V
	3		T		T		T		T		T		T
	4		L		L		L		L		L		L
	5		K		K		K		K		K		K
	6												
	7												
	8												
	9												
	10		G		G		G		G		G		G
	11		L		L		L		L		L		L
	12		V		V		V		V		V		V
	13		Q		Q		Q		Q		Q		Q
	14		P		P		P		P		P		P
	15		G		G		G		G		G		G
	16		G		G		G		G		G		G
	17		S		S		S		S		S		S
	18		R		R		R		R		R		R
	19												
	20												
	21												
	22												
	23		A		A		A		A		A		A
	24		A		A		A		A		A		A
	25		S		S		S		S		S		S
	26		G		G		G		G		G		G
	27		F		F		F		F		F		F
	28		T		T		T		T		T		T
	29		F		F		F		F		F		F
	30		S		S		S		S		S		S
	31		T		T		T		T		T		T
	32	*	F		F		F		F		F		F
	33		G		G		G		G		G		G
	34		I		I		I		I		I		I
	35		H		H		H		H		H		H
	36	*	W		W		W		W		W		W
	37		V		V		V		V		V		V
	38		R		R		R		R		R		R
	39		Q		Q		Q		Q		Q		Q
	40		A		A		A		A		A		A
	41		P		P		P		P		P		P
	42		E		E		E		E		E		E
	43		K		K		K		K		K		K
	44		G		G		G		G		G		G
	45		L		L		L		L		L		L
	46		E		E		E		E		E		E
	47	*	W		W		W		W		W		W
	48		V		V		V		V		V		V
	49		A		A		A		A		A		A
	50	#	Y		Y		Y		Y		Y		Y
	51		I		I		I		I		I		I
	52		S		S		S		S		S		S
	53		G		G		G		G		G		G
	54		A		A		A		A		A		A
	55		S		S		S		S		S		S
	56		T		T		T		T		T		T
	57		T		T		T		T		T		T
	58	*	I		I		I		I		I		I
	59		Y		Y		Y		Y		Y		Y
	60		A		A		A		A		A		A
	61		D		D		D		D		D		D
	62		T		T		T		T		T		T
	63												
	64												
	65												
	66												

FIG. 29

CDR	Chimeric				Variant 1				Variant 2				Variant 3				Variant 4				Variant 5				Variant 6						
	Kabat Residue number	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity
CDR3	67			R					R					R					R						R				R		
	68			F	4	3			F	4	3			F	4	3			F	4	3			F	4	3			F	4	3
	69			T					T					T					T						T				T		
	70			I	6	1			I	3	2			I	3	2			I	3	2			I	3	2			I	3	2
	71			S					S					S					S						S				S		
	72			R					R					R					R						R				R		
	73			D					D					D					D						D				D		
	74			N					N					N					N						N				N		
	75			P					P					P					P						P				P		
	76			K					K					K					K						K				K		
	77			N					N					N					N						N				N		
	78			T					T					T					T						T				T		
	79		*	L	25	20			L	15	11			L	15	11			L	15	11			L	15	11			L	15	11
	80		*	F	20	20			F	20	20			F	20	20			F	19	18			F	19	18			F	19	18
	81	#	pt	L	20	13			L	24	16			L	24	16			L	24	16			L	24	16			L	24	16
	82	#		Q					Q					Q					Q						Q				Q		
	83			M	8	2			M	11	7			M	11	7			M	10	2			M	10	2			M	10	2
	84			T					T					T					T						T				T		
	85			S					S					S					S						S				S		
	86			L	31	23			L	31	23			L	31	23			L	30	21			L	30	21			L	30	21
87			A					A					A					A						A				A			
88			S					S					S					S						S				S			
89			E					E					E					E						E				E			
90			D					D					D					D						D				D			
91			T					T					T					T						T				T			
92			A					A					A					A						A				A			
93	#	pt	M	21	12			M	21	12			M	21	12			M	21	12			M	21	12			M	21	12	
94	#		Y	7	1			Y	7	1			Y	7	1			Y	7	1			Y	7	1			Y	7	1	
95			Y	1				Y	1				Y	1				Y	1					Y	1			Y	1		
96			C					C					C					C						C				C			
97			A					A					A					A						A				A			
98			R					R					R					R						R				R			
99			Y	6	3			Y	6	3			Y	6	3			Y	6	3			Y	6	3			Y	6	3	
100			G					G					G					G						G				G			
101			T					T					T					T						T				T			
102			S					S					S					S						S				S			
103			F	1				F	1				F	1				F	1					F	1			F	1		
104			P					P					P					P						P				P			
105			Y	3	1			Y	3	1			Y	3	1			Y	3	1				Y	3	1			Y	3	1
106			G					G					G					G						G				G			
107			L	2				L	2				L					L						L				L			
108			D					D					D					D						D				D			
109			Y	5	5			Y	5	5			Y	12	9			Y	12	9				Y	12	9			Y	12	9
110			W	6	4			W	6	3			W	6	3			W	6	3				W	6	3			W	6	3
111			G					G					G					G						G				G			
112			Q					Q					Q					Q						Q				Q			
113			G					G					G					G						G				G			
114			T					T					T					T						T				T			
115			S					S					S					S						S				S			
116			V					V					V					V						V				V			
117			T					T					T					T						T				T			
118			V					V					V					V						V				V			
119			S					S					S					S						S				S			
120			S					S					S					S						S				S			

FIG. 29, continued

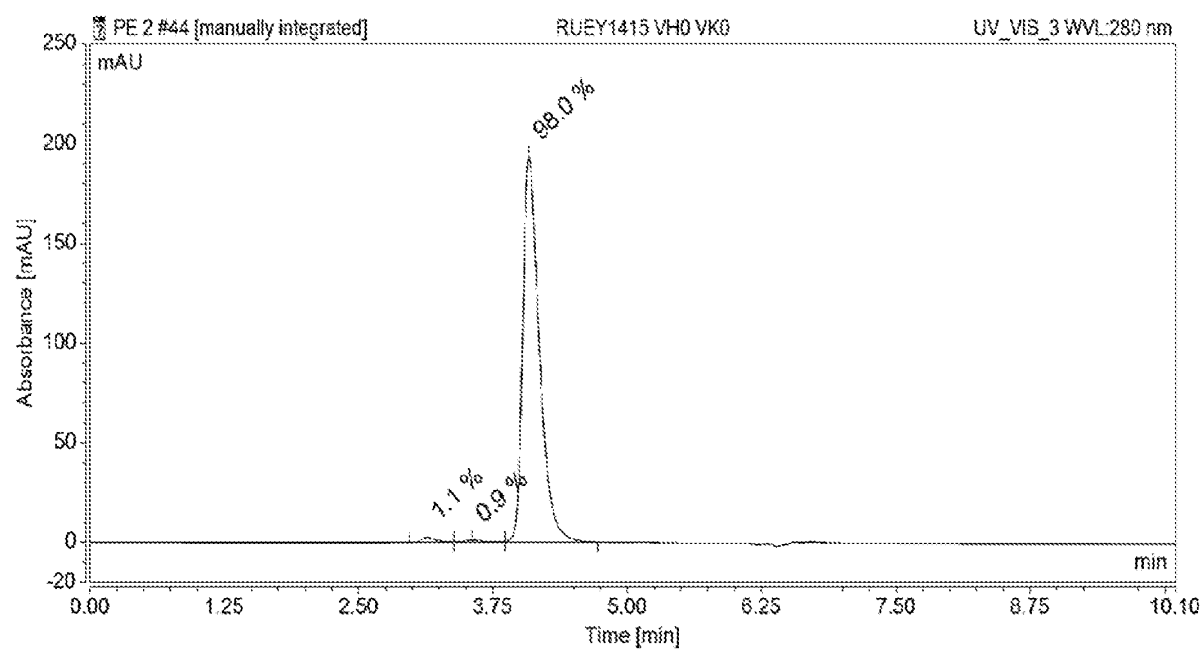
CDR	>Chimeric				>Variant 1				>Variant 2				>Variant 3				>Variant 4				>Variant 5			
	Kabat Residue number				Kabat Residue number				Kabat Residue number				Kabat Residue number				Kabat Residue number				Kabat Residue number			
CDR1	Promiscuous Moderate				Promiscuous Moderate				Promiscuous Moderate				Promiscuous Moderate				Promiscuous Moderate				Promiscuous Moderate			
	Promiscuous High				Promiscuous High				Promiscuous High				Promiscuous High				Promiscuous High				Promiscuous High			
CDR2	Sequence				Sequence				Sequence				Sequence				Sequence				Sequence			
	Total Alleles Binding				Total Alleles Binding				Total Alleles Binding				Total Alleles Binding				Total Alleles Binding				Total Alleles Binding			
CDR3	High Affinity				High Affinity				High Affinity				High Affinity				High Affinity				High Affinity			
	High Affinity				High Affinity				High Affinity				High Affinity				High Affinity				High Affinity			
1																								
2	*																							
3																								
4																								
5																								
6																								
7																								
8																								
9																								
10																								
11																								
12	#																							
13	p1																							
14																								
15	*																							
16																								
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43																								
44																								
45																								
46																								
47																								
48																								
49	*																							
50	#																							
51	p1																							
52																								
53	*																							
54																								
55																								
56																								
57																								
58																								
59																								
60																								
61																								
62																								

FIG. 30

CDR	>Chimeric					>Variant 1					>Variant 2					>Variant 3					>Variant 4					>Variant 5						
	Kabat Residue number	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	Promiscuous Moderate	Promiscuous High	Sequence	Total Alleles Binding	High Affinity	
CDR3	63			T					T					T					T					T					T			
	64			S					S					S					S					S					S			
	65			H					H					H					H					H					H			
	66			T					T					T					T					T					T			
	67			G					G					G					G					G					G			
	68			G					G					G					G					G					G			
	69			S					S					S					S					S					S			
	70			G					G					G					G					G					G			
	71			G					G					G					G					G					G			
	72			G					G					G					G					G					G			
	73			T					T					T					T					T					T			
	74			D					D					D					D					D					D			
	75			F	6	3			F	9	4			F	9	4			F	9	4			F	9	4			F	9	4	
	76		*	T					T					T					T					T					T			
	77			L	24	17			L	6	1			L	6	1			L	6	1			L	6	1			L	6	1	
	78			N					N					N					N					N					N			
	79			I	1				I	2				I	16	5			I	16	5			I	16	5			I	16	5	
	80			H					H					H					H					H					H			
	81			P					P					P					P					P					P			
	82			V					V					V	4	3			V	4	3			V	4	3			V	4	3	
	83			E					E					E					E					E					E			
	84			E					E					E					E					E					E			
	85			E					E					E					E					E					E			
	86			D					D					D					D					D					D			
	87			A					A					A					A					A					A			
	88			A					A					A					A					A					A			
	89			S					S					S	7				S					S					S	7		
90			Y	8	5			Y	8	5			Y	8	5			Y	8	5			Y	8	5			Y	8	5		
91			Y	2	1			Y	2	1			Y	2	1			Y	2	1			Y	2	1			Y	2	1		
92			C					C					C					C					C					C				
93			Q					Q					Q					Q					Q					Q				
94			Q					Q					Q					Q					Q					Q				
95			S					S					S					S					S					S				
96			N					N					N					N					N					N				
97			E					E					E					E					E					E				
98			D					D					D					D					D					D				
99			P					P					P					P					P					P				
100			F	5	3			F	5	3			F	5	3			F	5	3			F	5	3			F	5	3		
101		*	T					T					T					T					T					T				
102			F	16	14			F	16	13			F	16	13			F	16	13			F	16	13			F	16	13		
103			G					G					G					G					G					G				
104			S					S					S					S					S					S				
105			G					G					G					G					G					G				
106			T					T					T					T					T					T				
107			K					K					K					K					K					K				
108			L					L					L					L					L					L				
109			E					E					E					E					E					E				
110			I					I					I					I					I					I				
111			K					K					K					K					K					K				

FIG. 30, continued

VH0/VK0



VH3/VK4

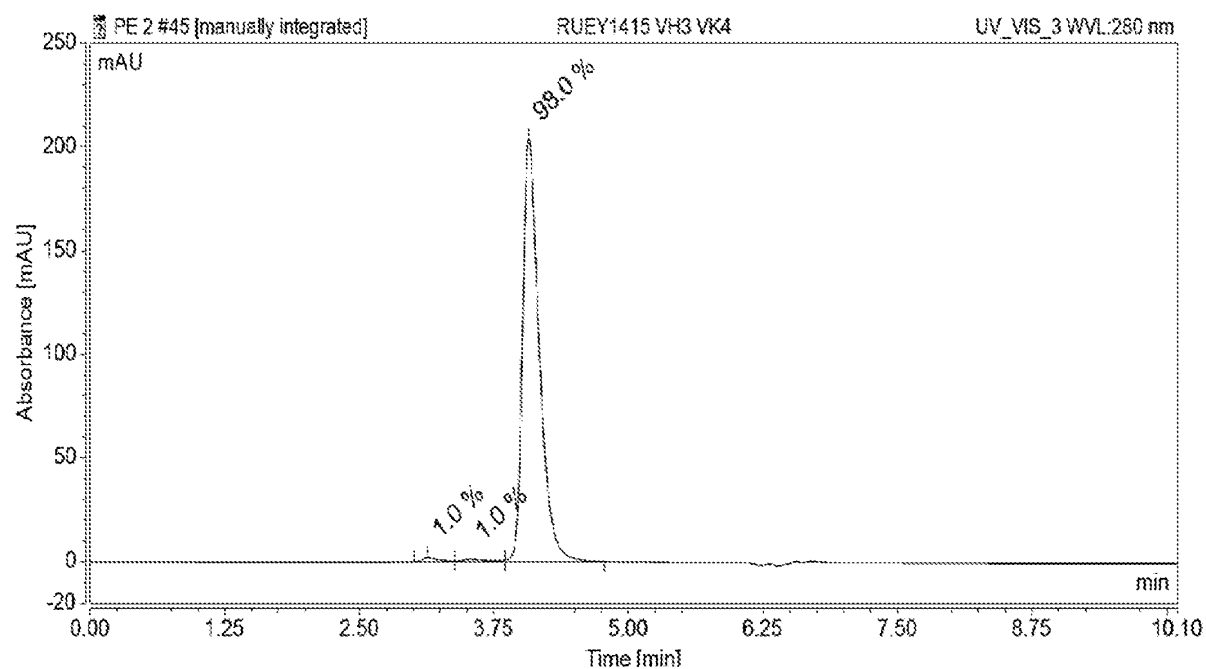
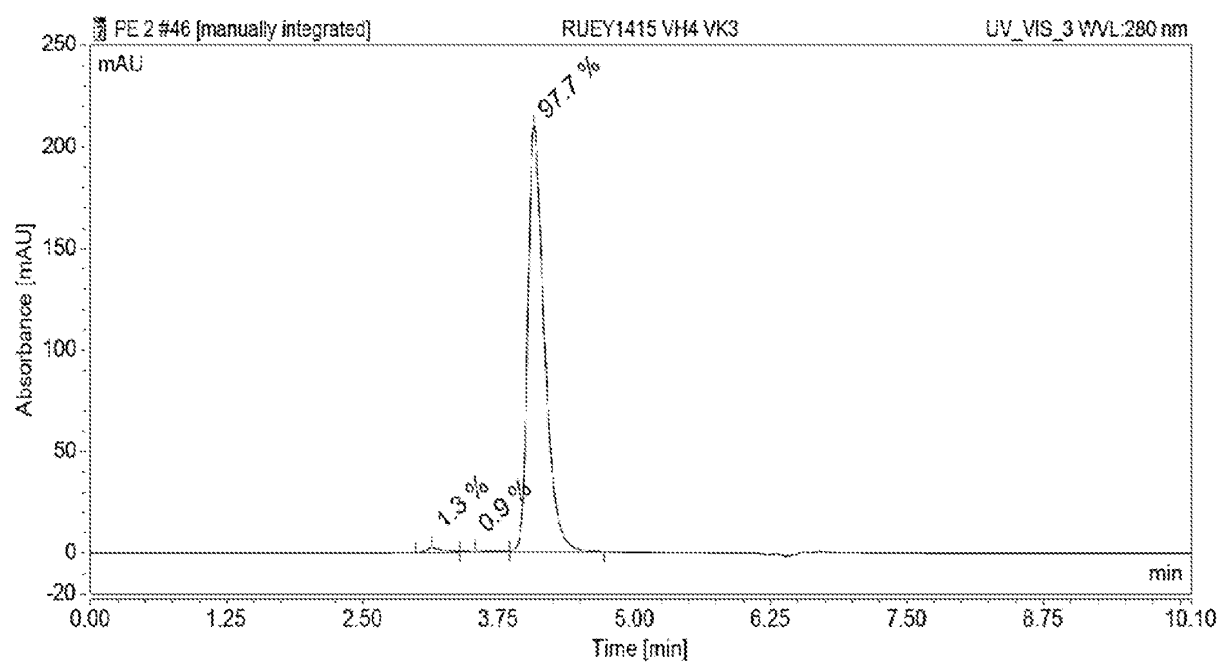


FIG. 31A

VH4/VK3



VH4/VK4

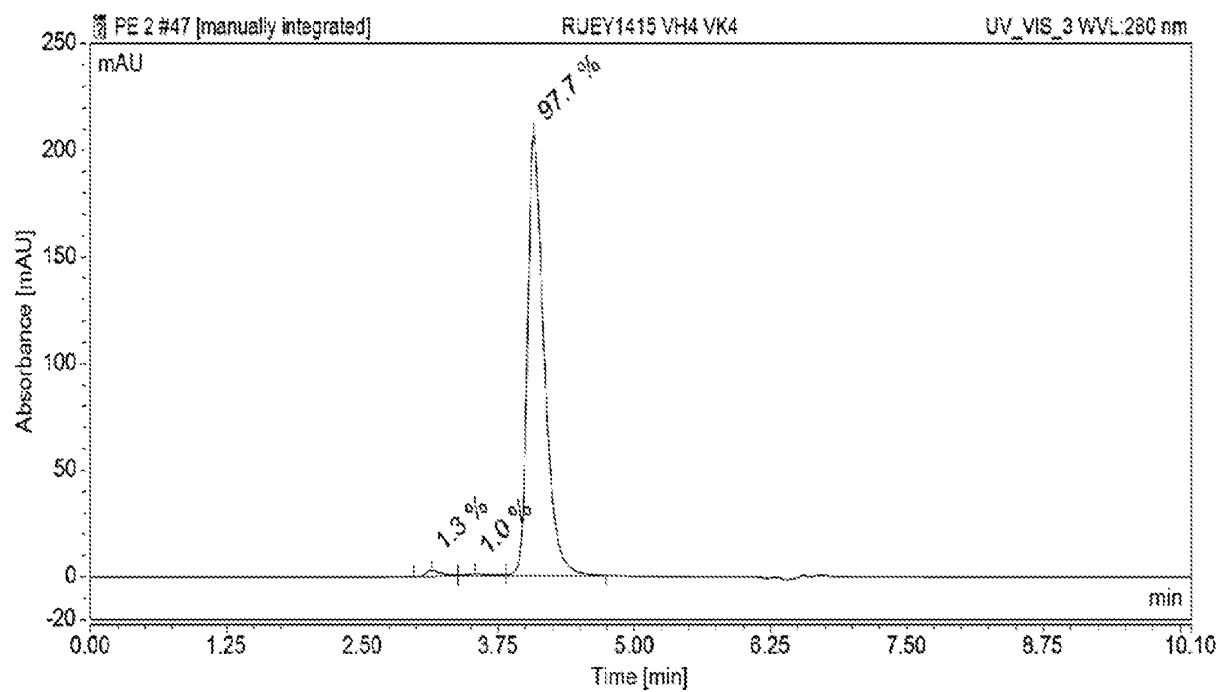
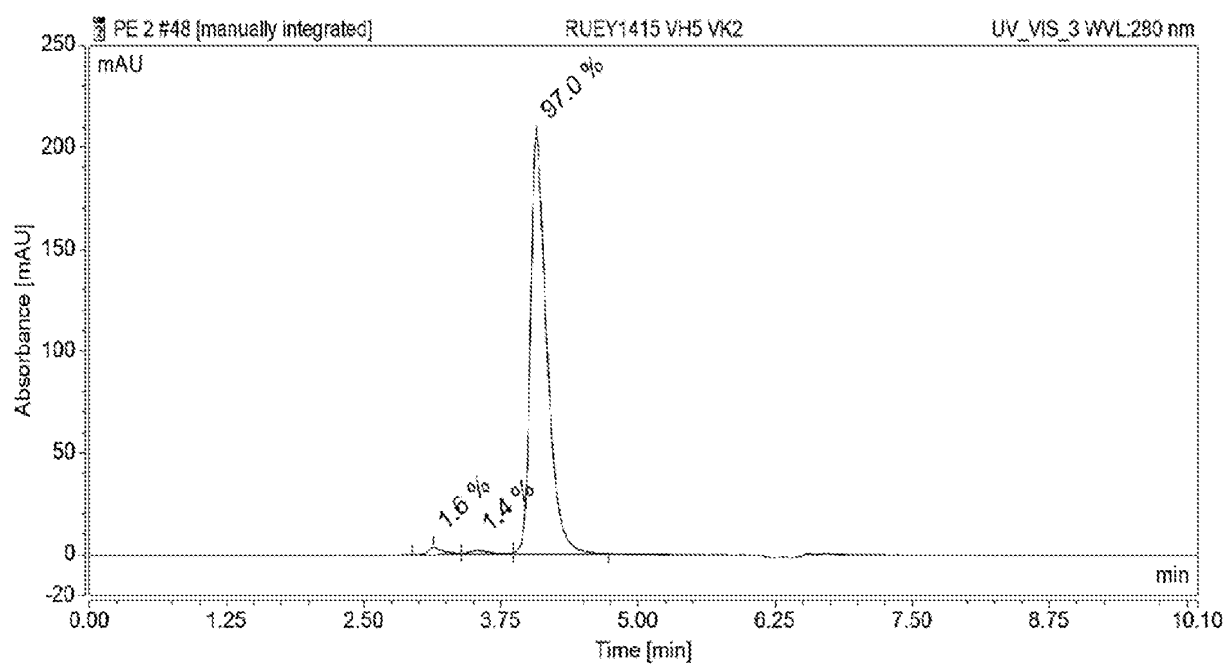


FIG. 31B

VH5/VK2



VH5/VK3

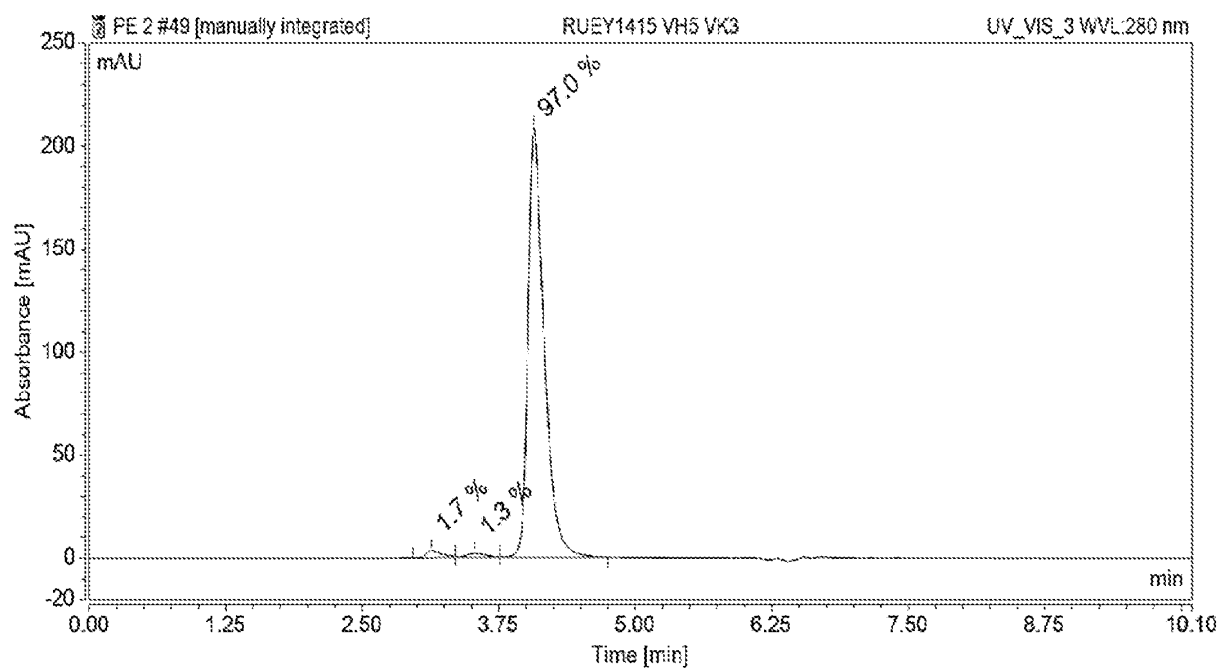
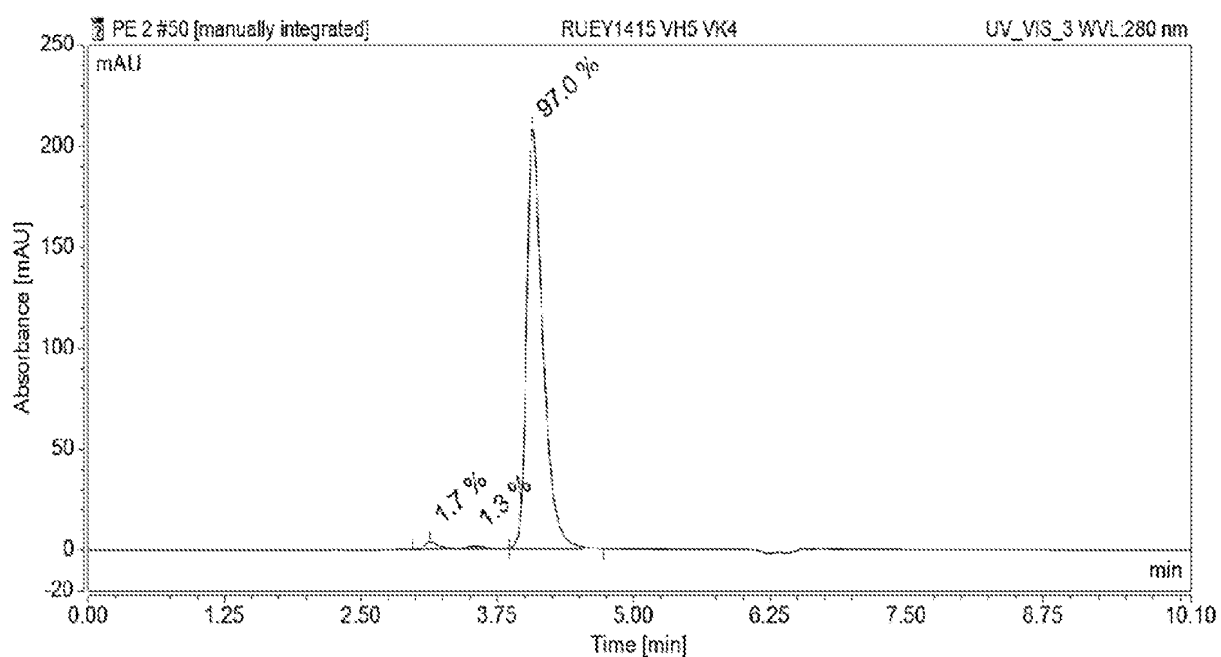


FIG. 31C

VH5/VK4



Overlays

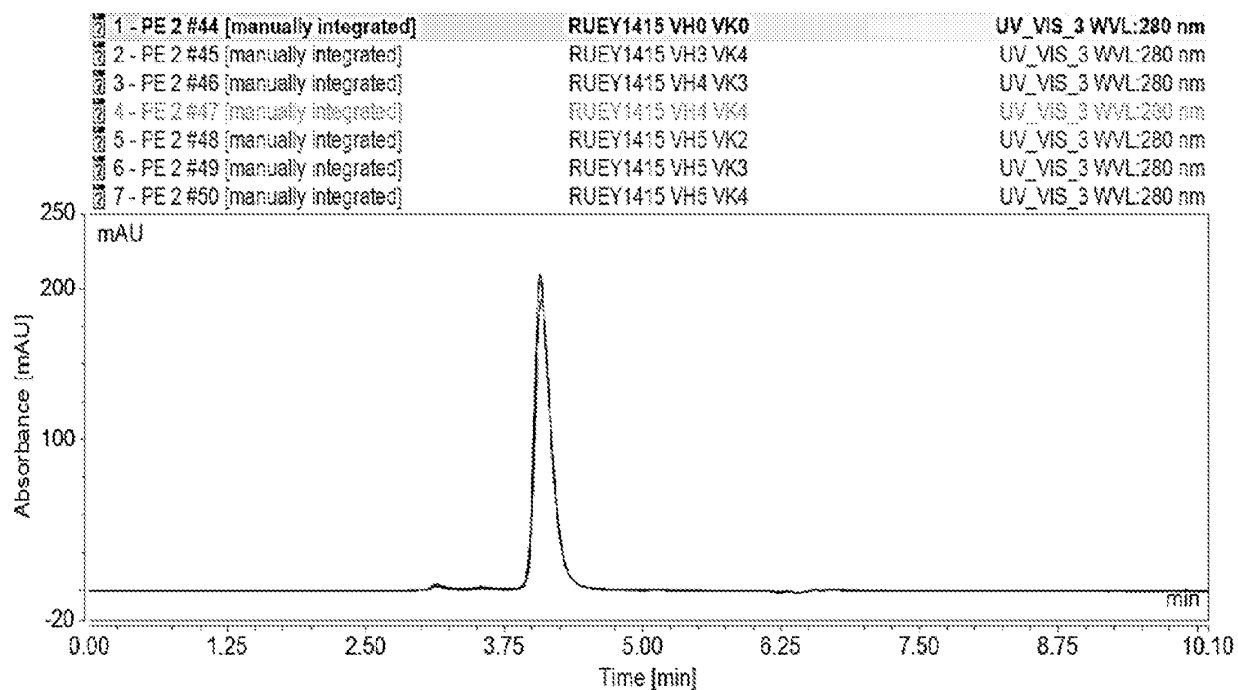


FIG. 31D

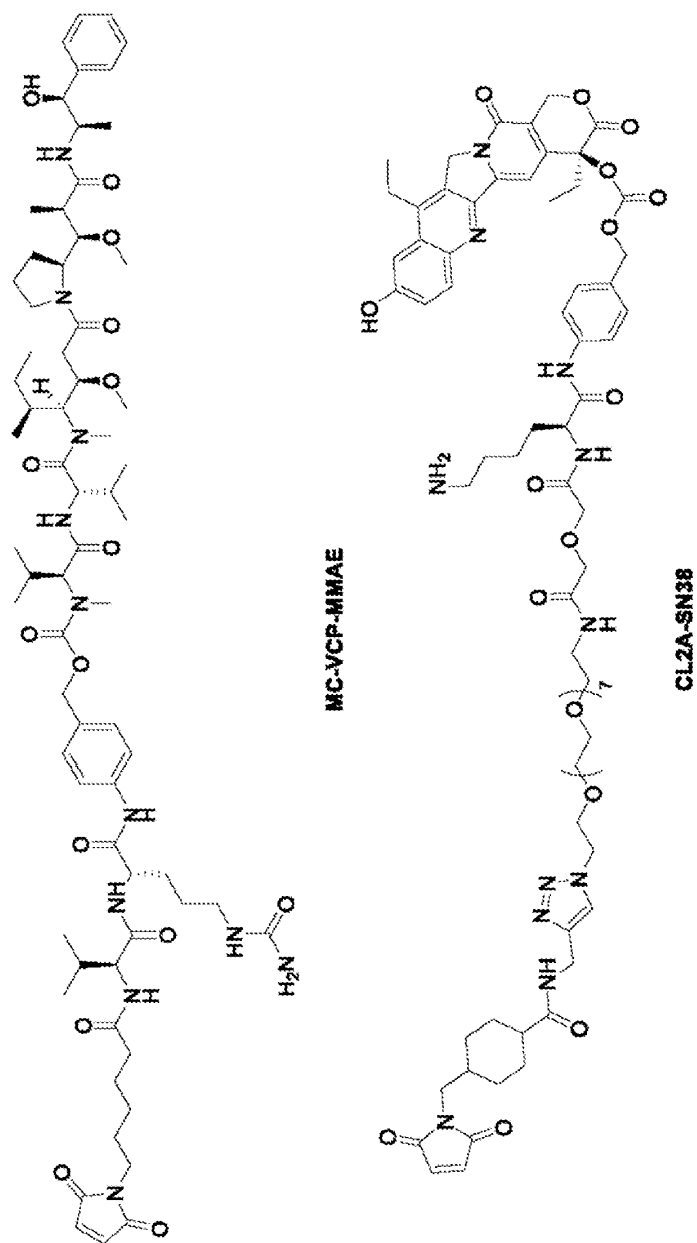


FIG. 32

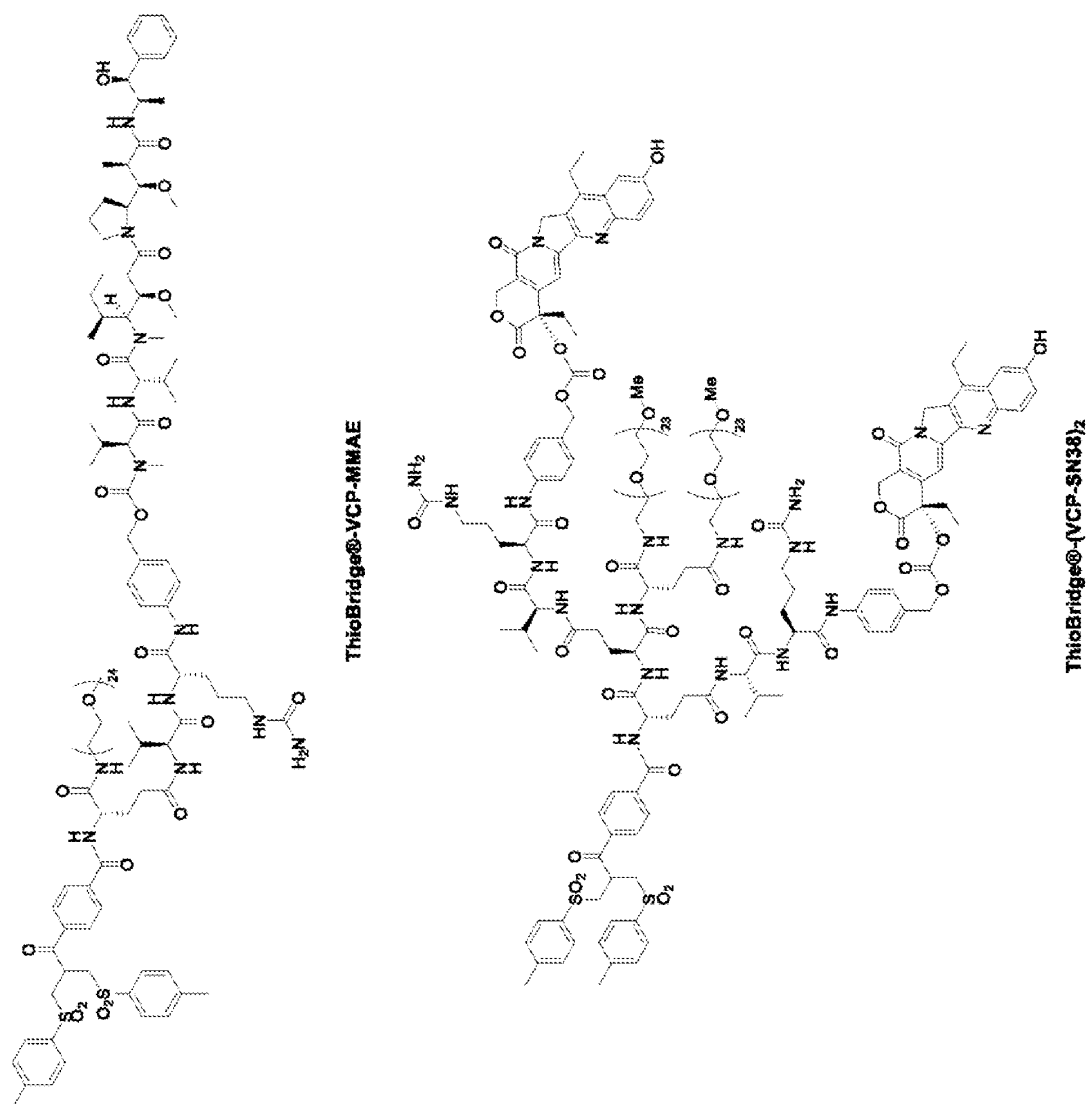


FIG. 33

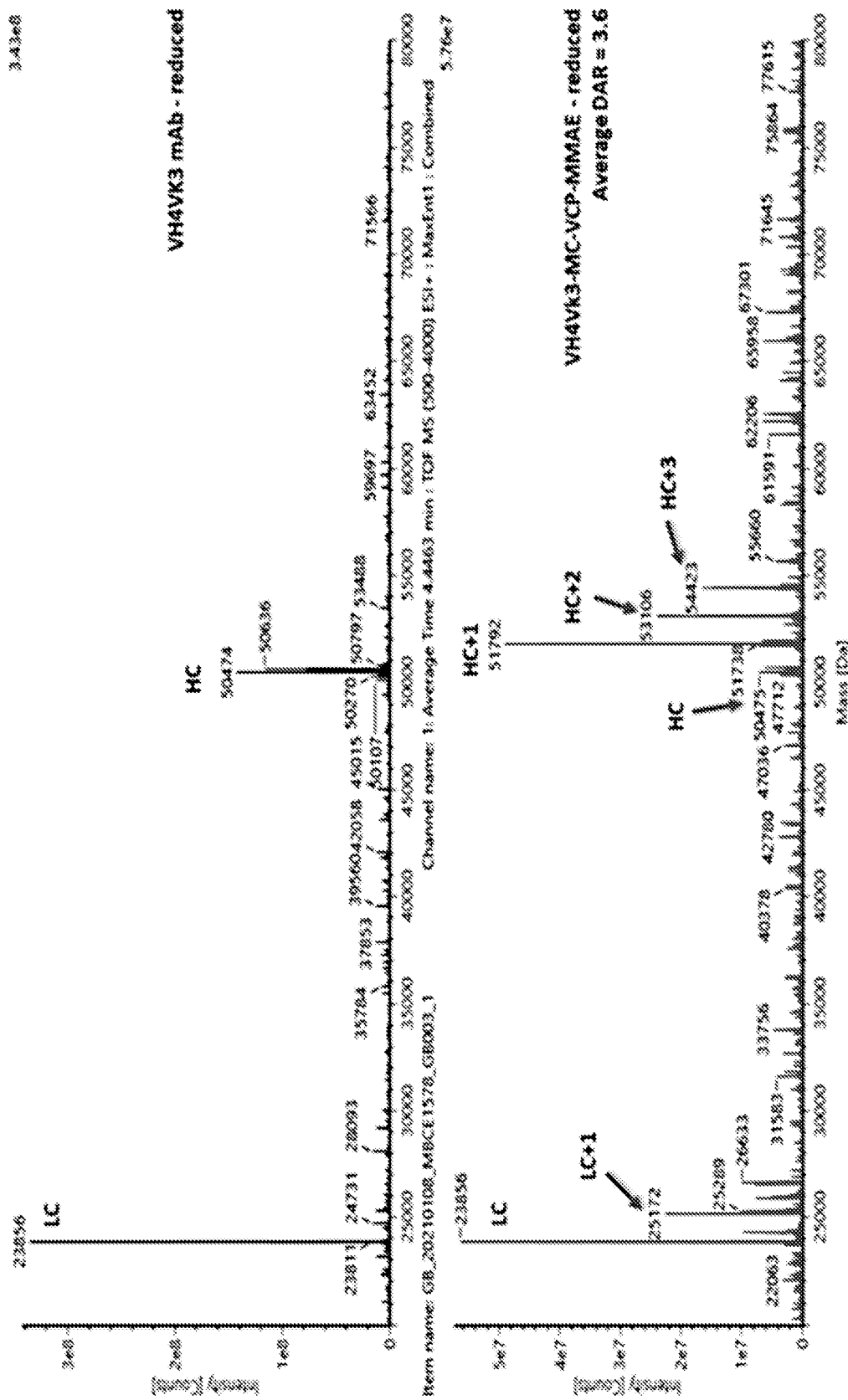


FIG. 34

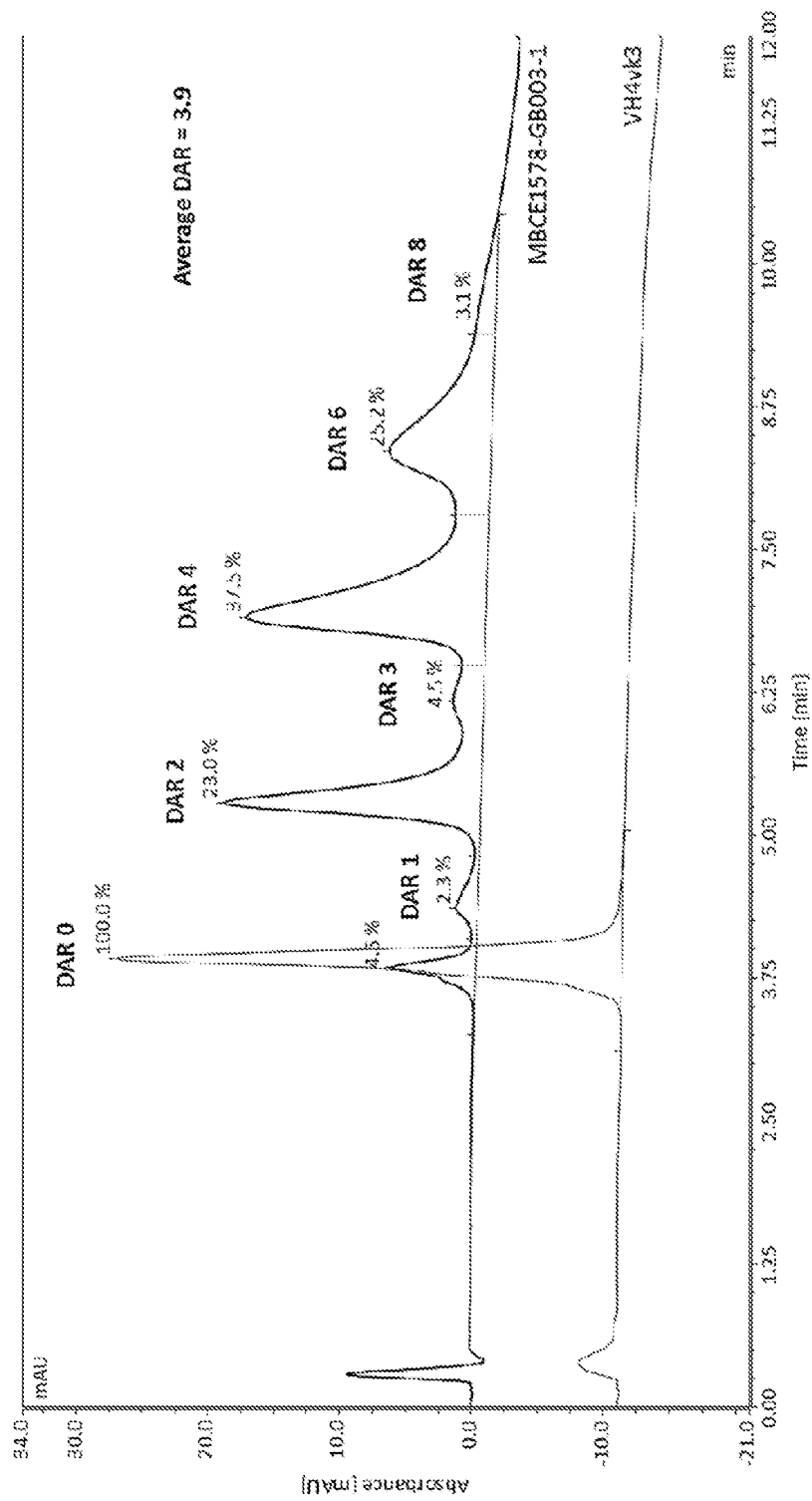


FIG. 35

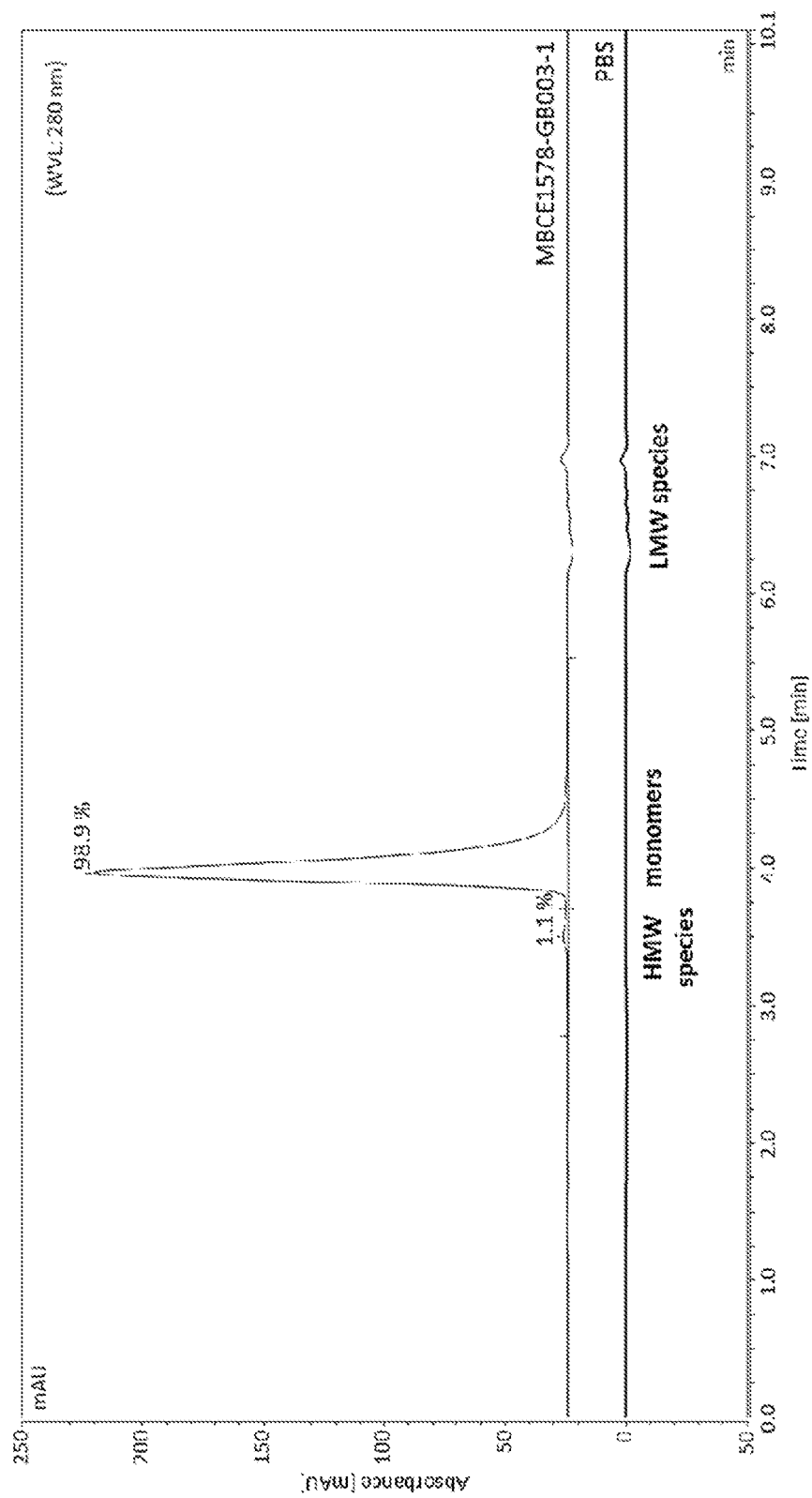


FIG. 36

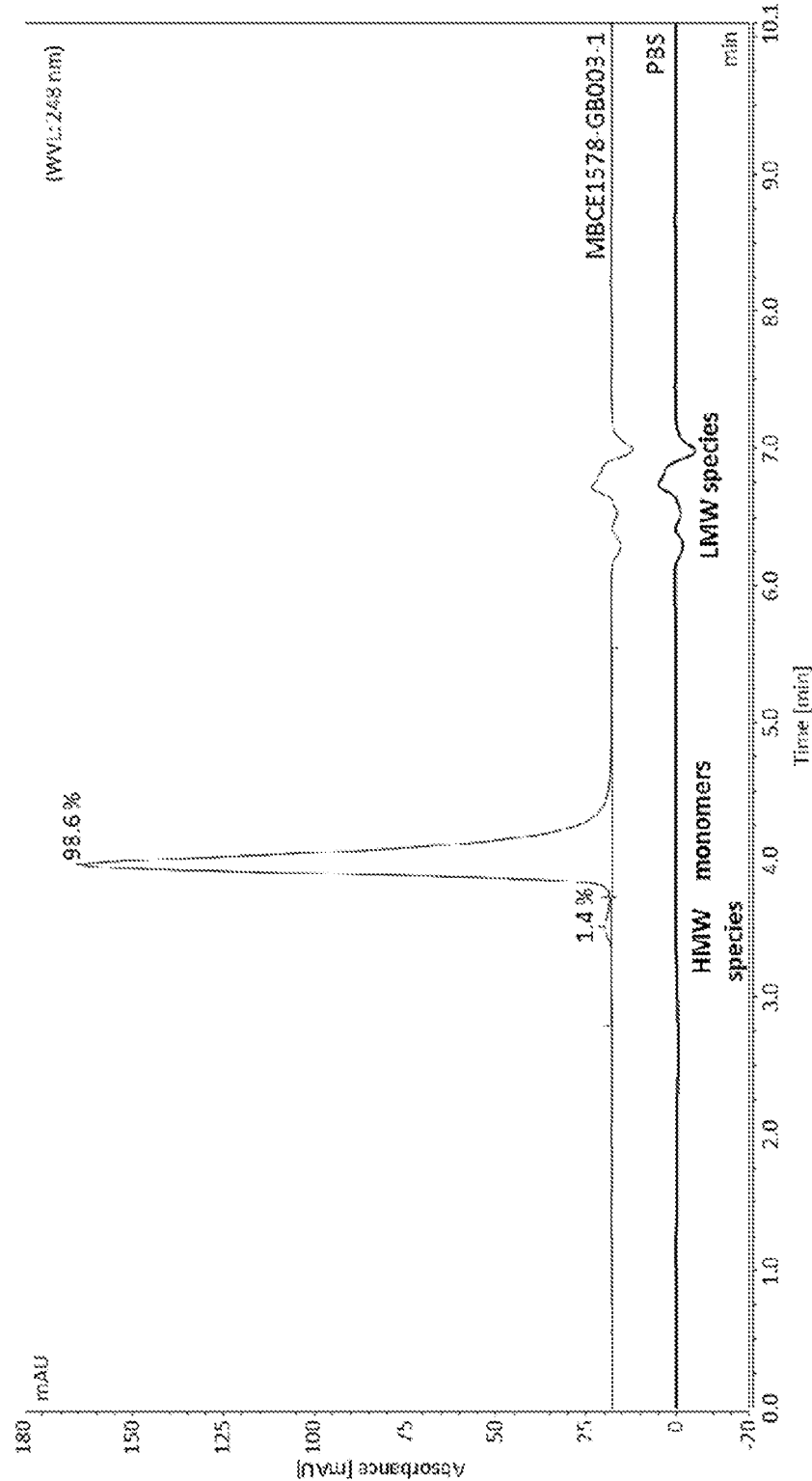


FIG. 37

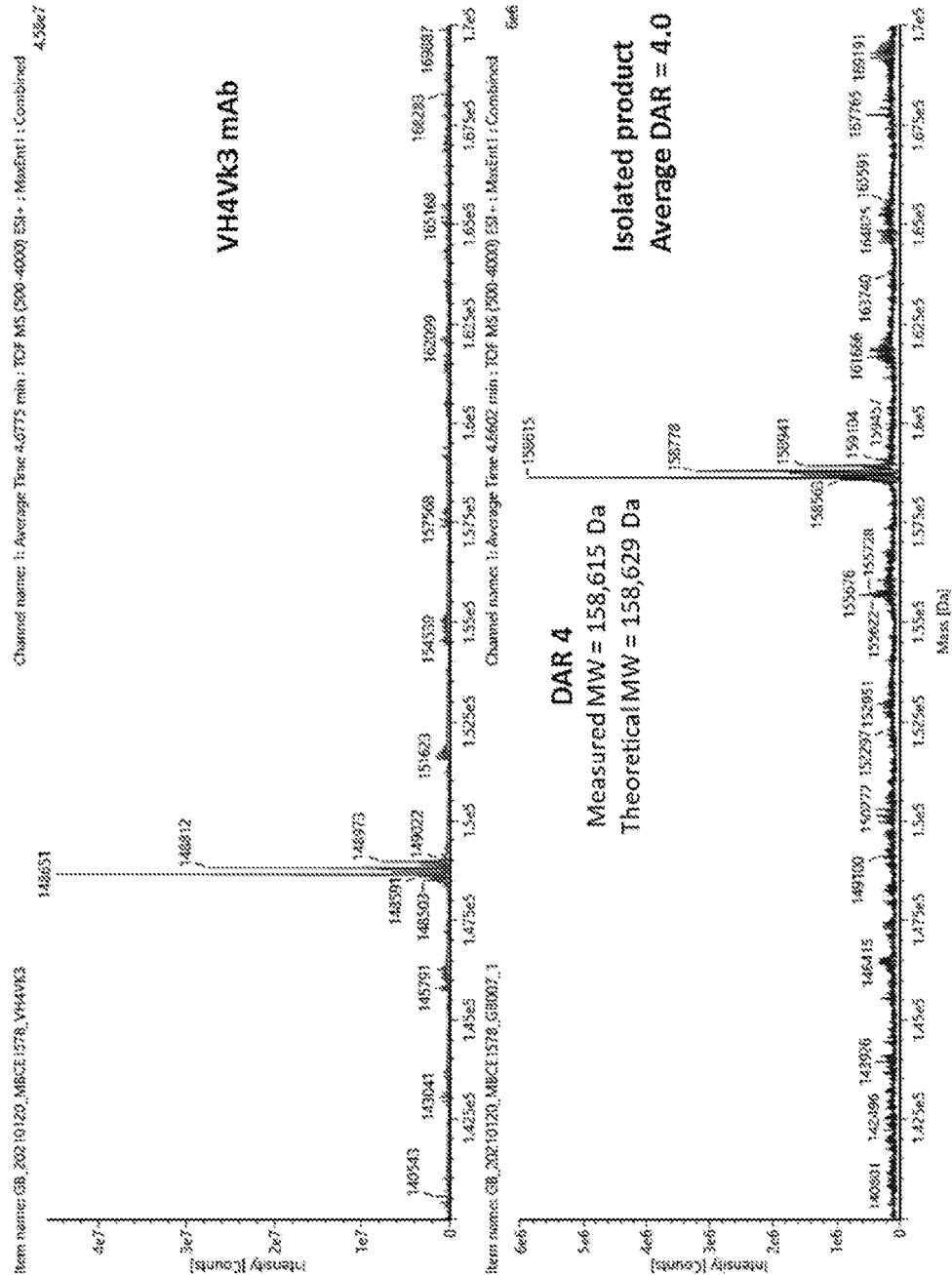


FIG. 38

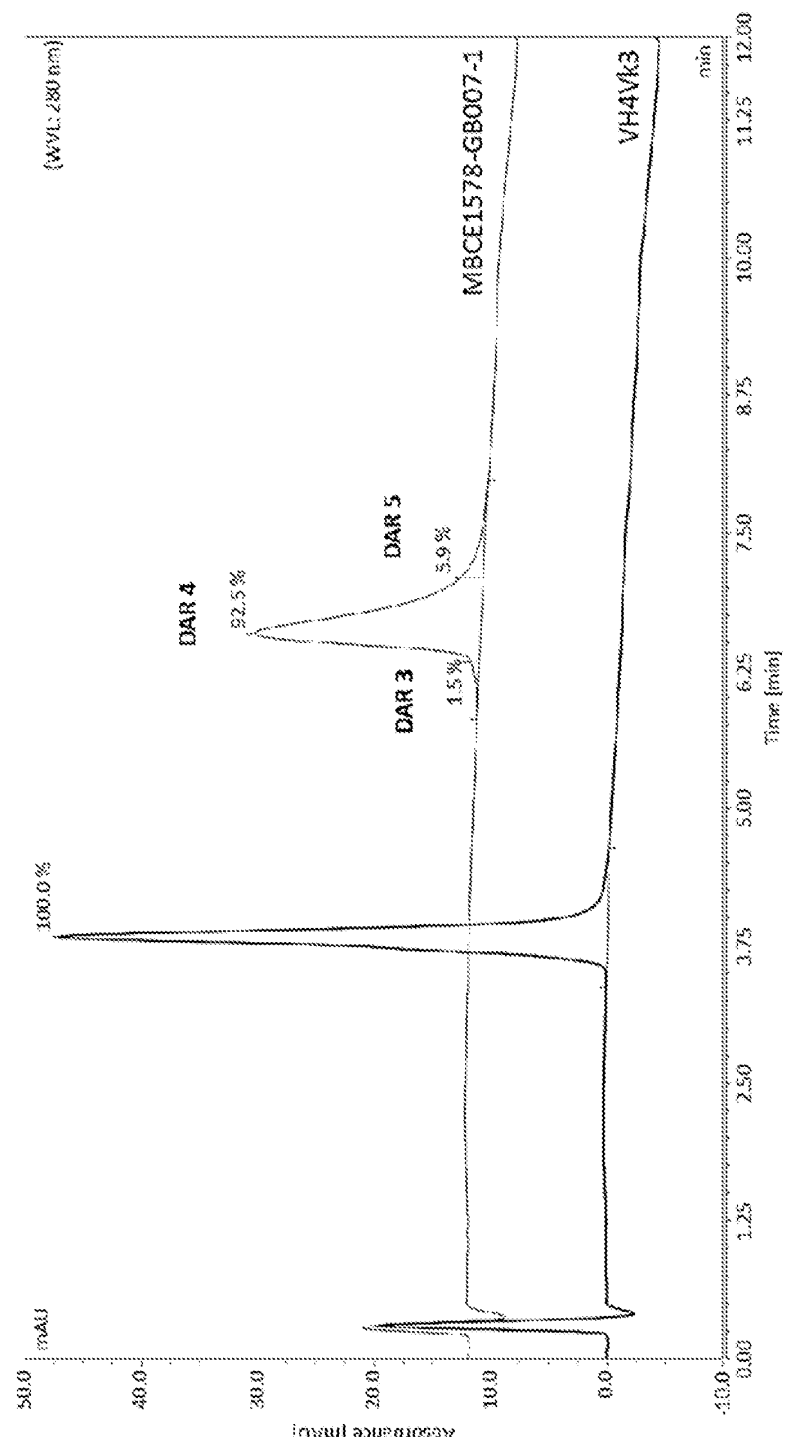


FIG. 39

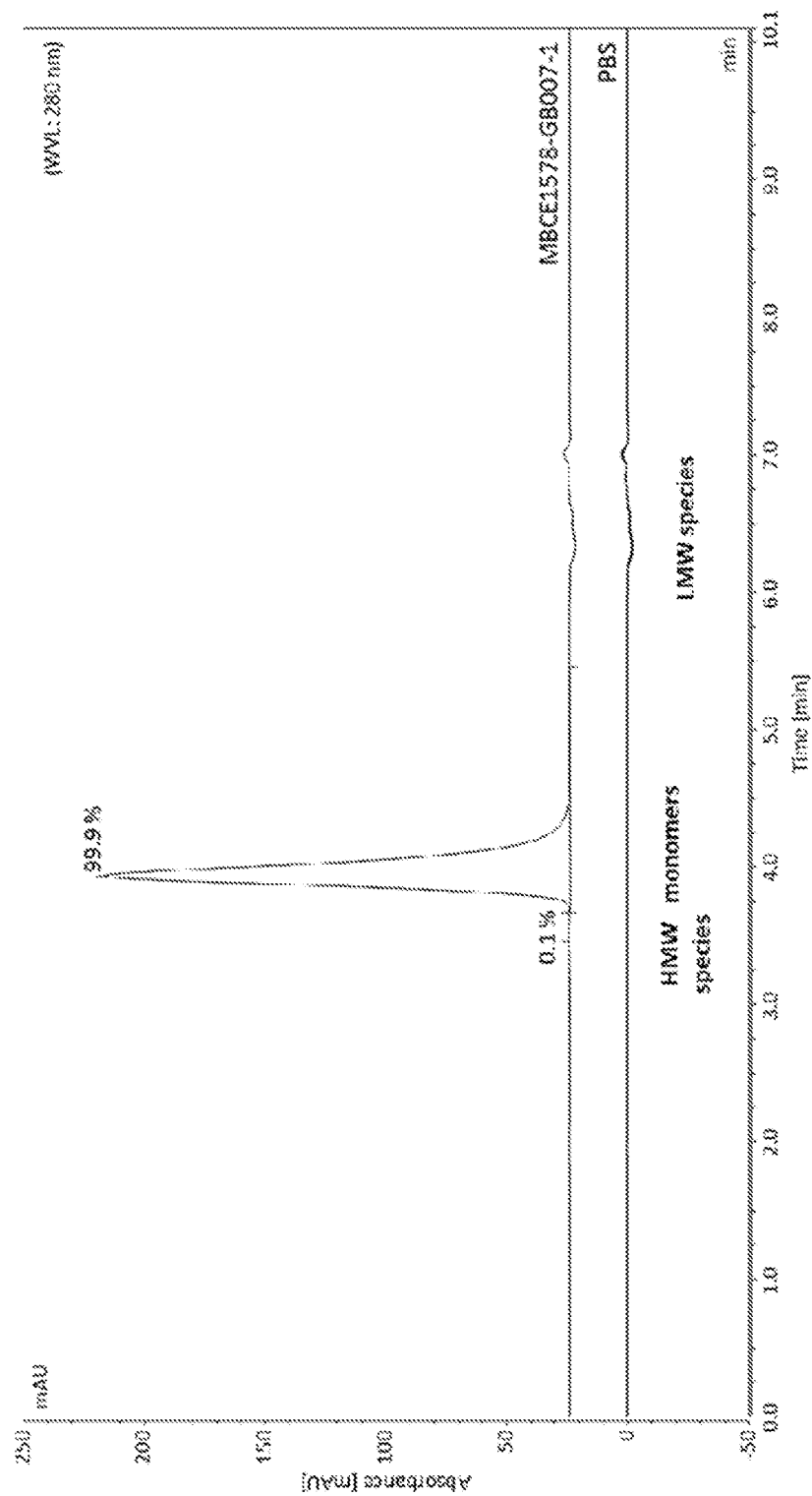


FIG. 40

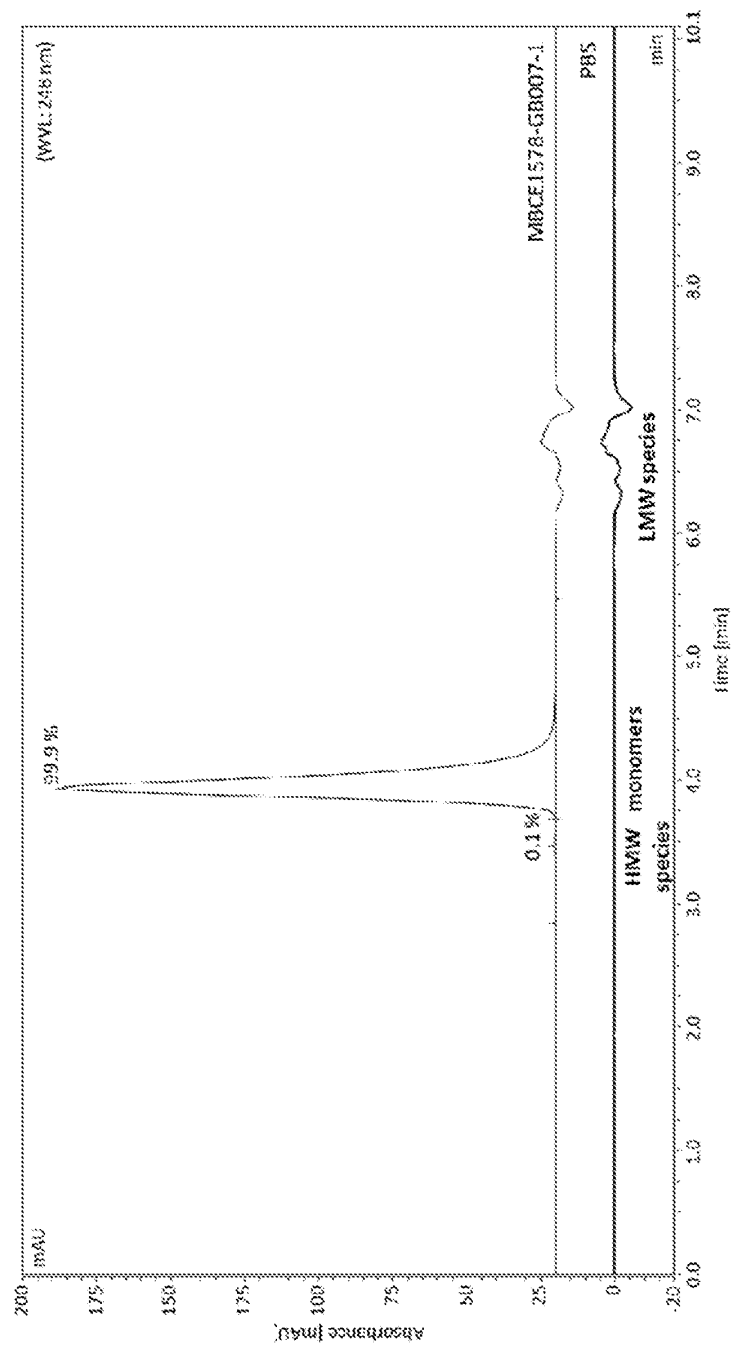


FIG. 41

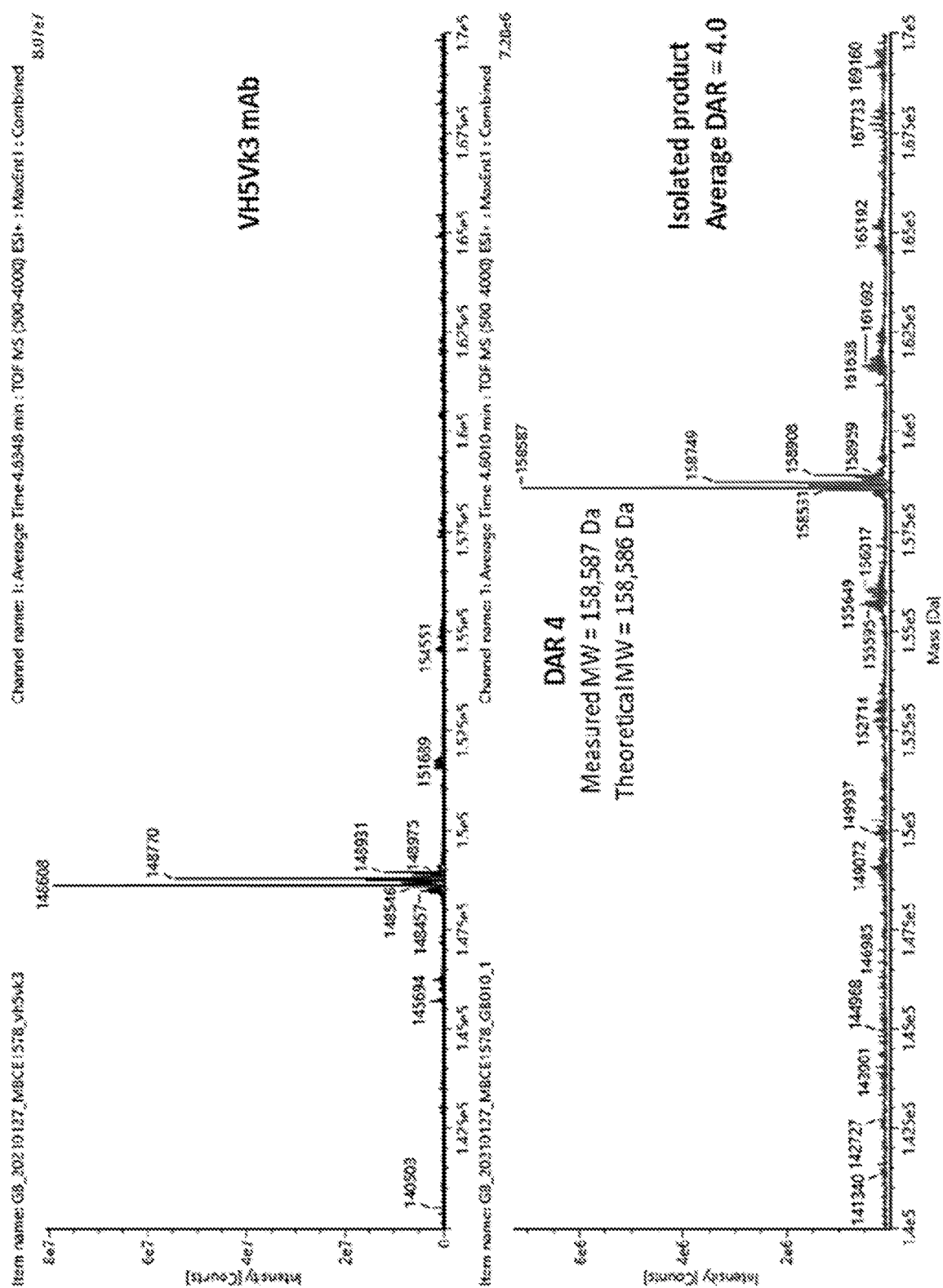


FIG. 42

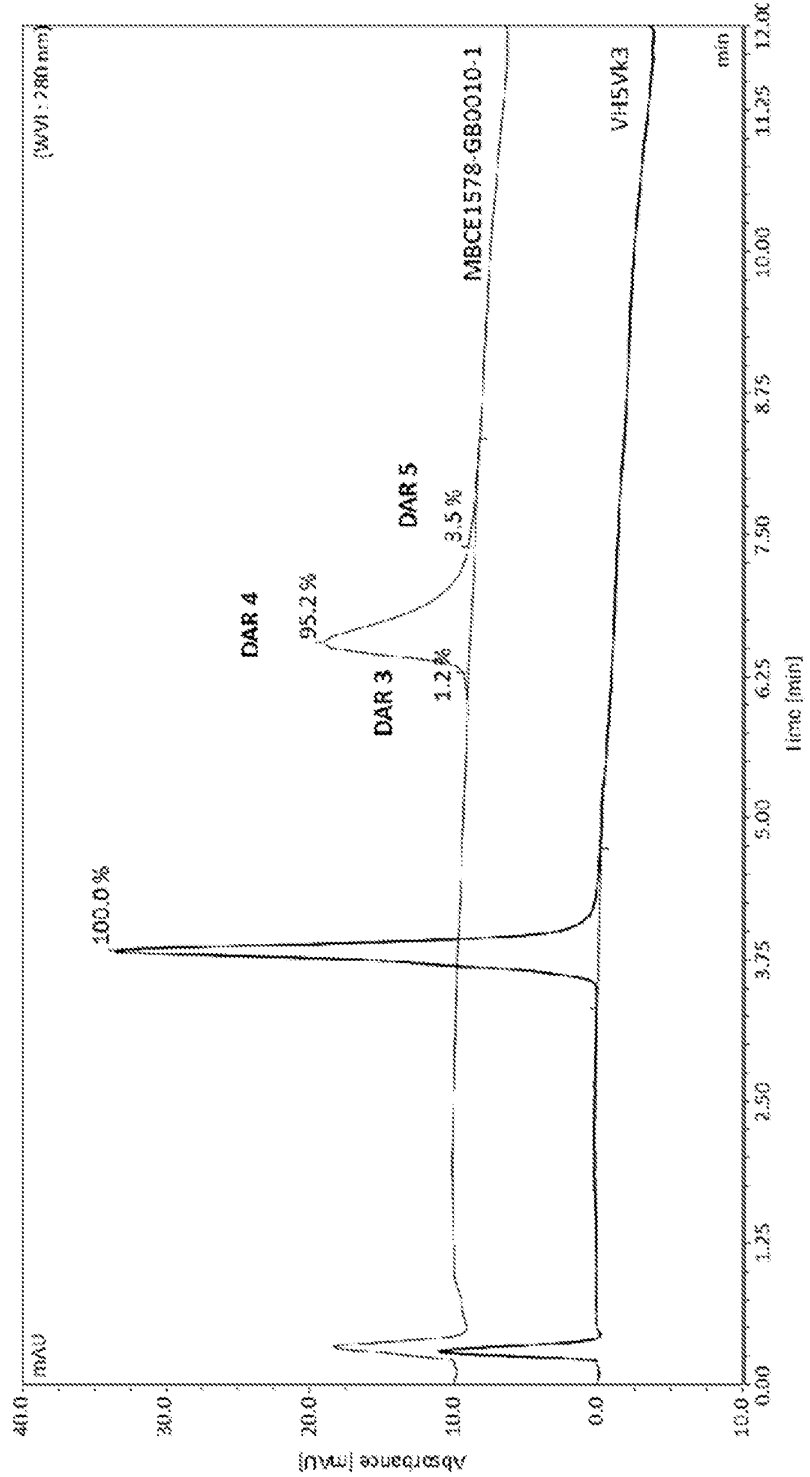


FIG. 43

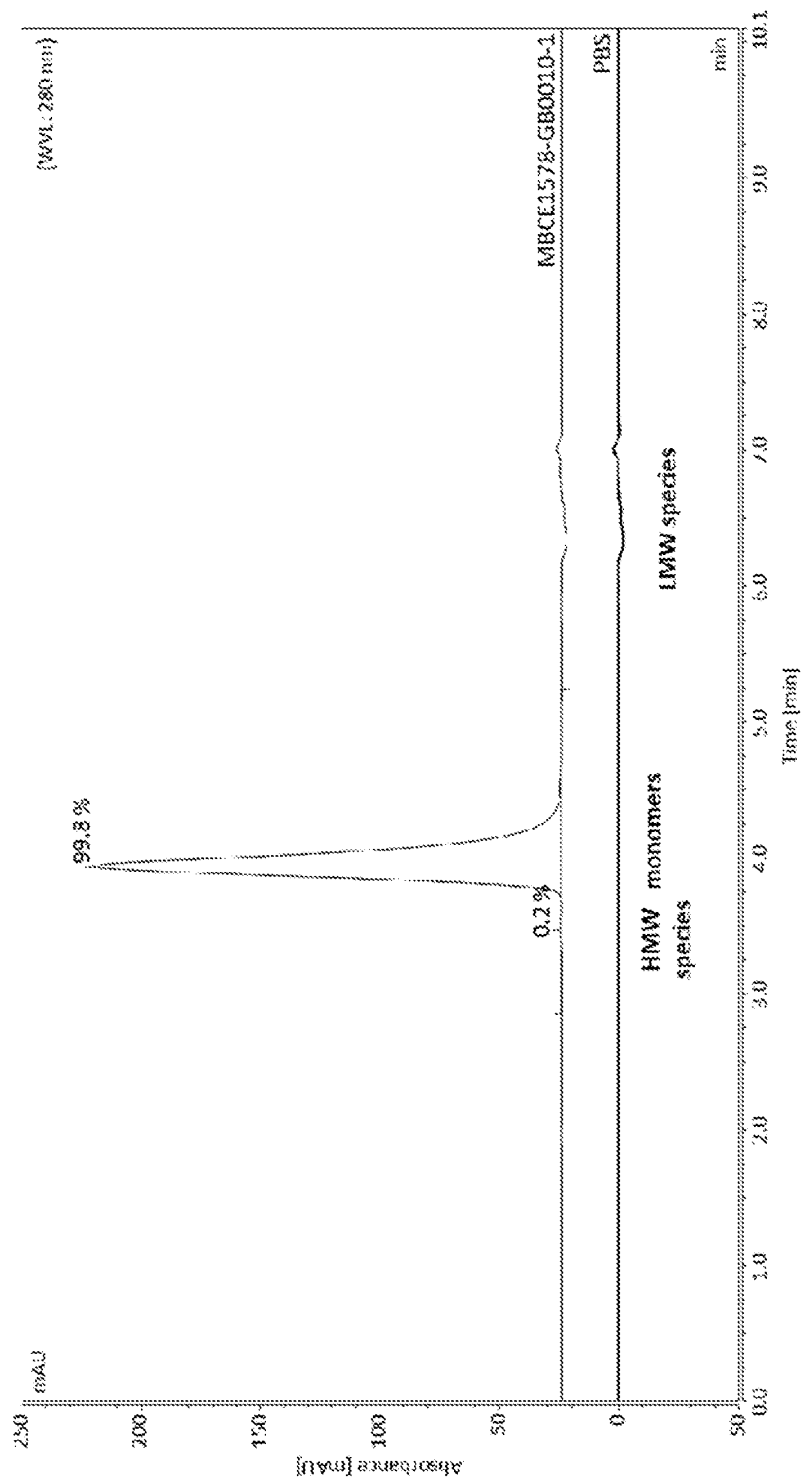


FIG. 44

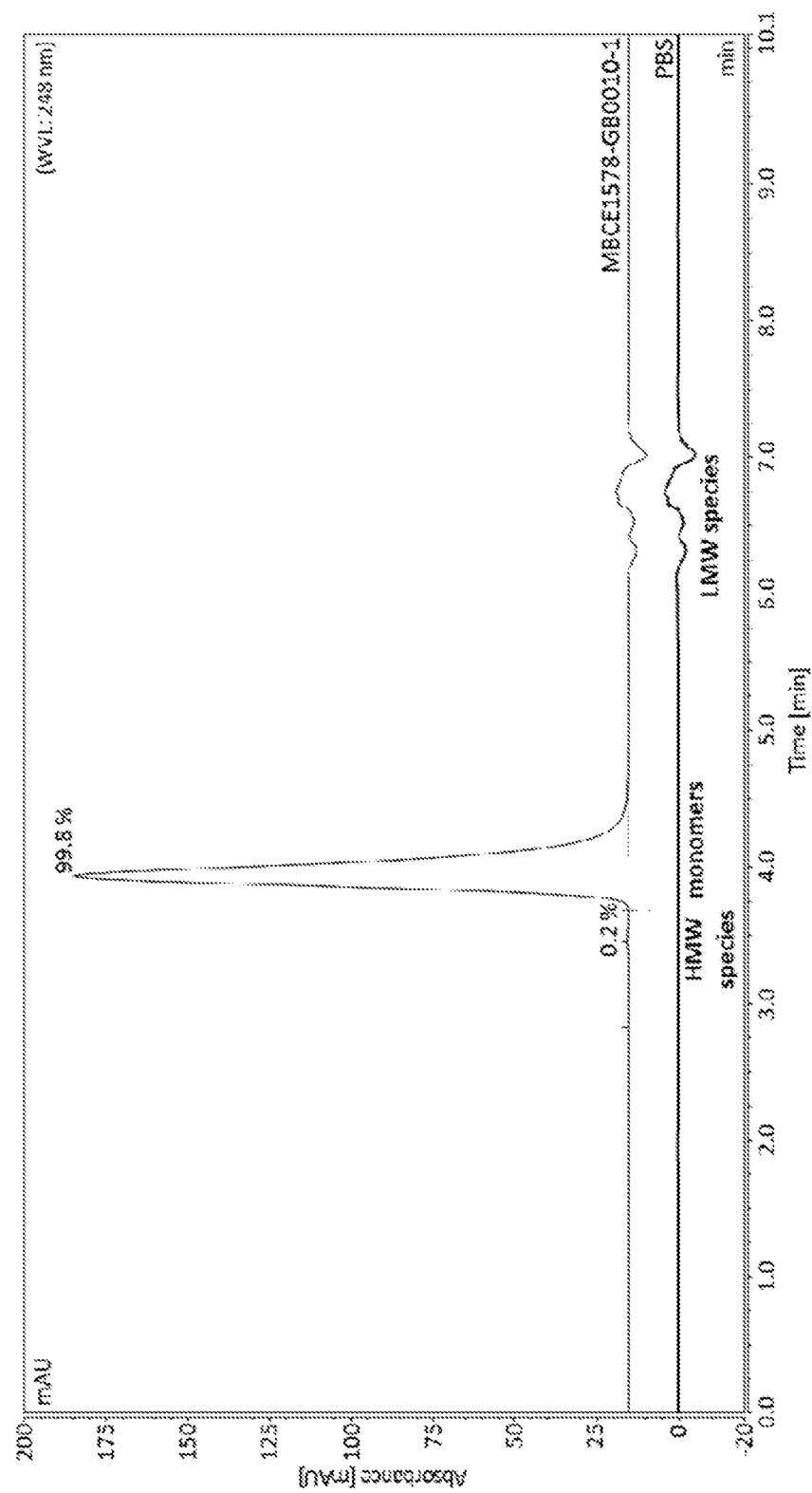


FIG. 45

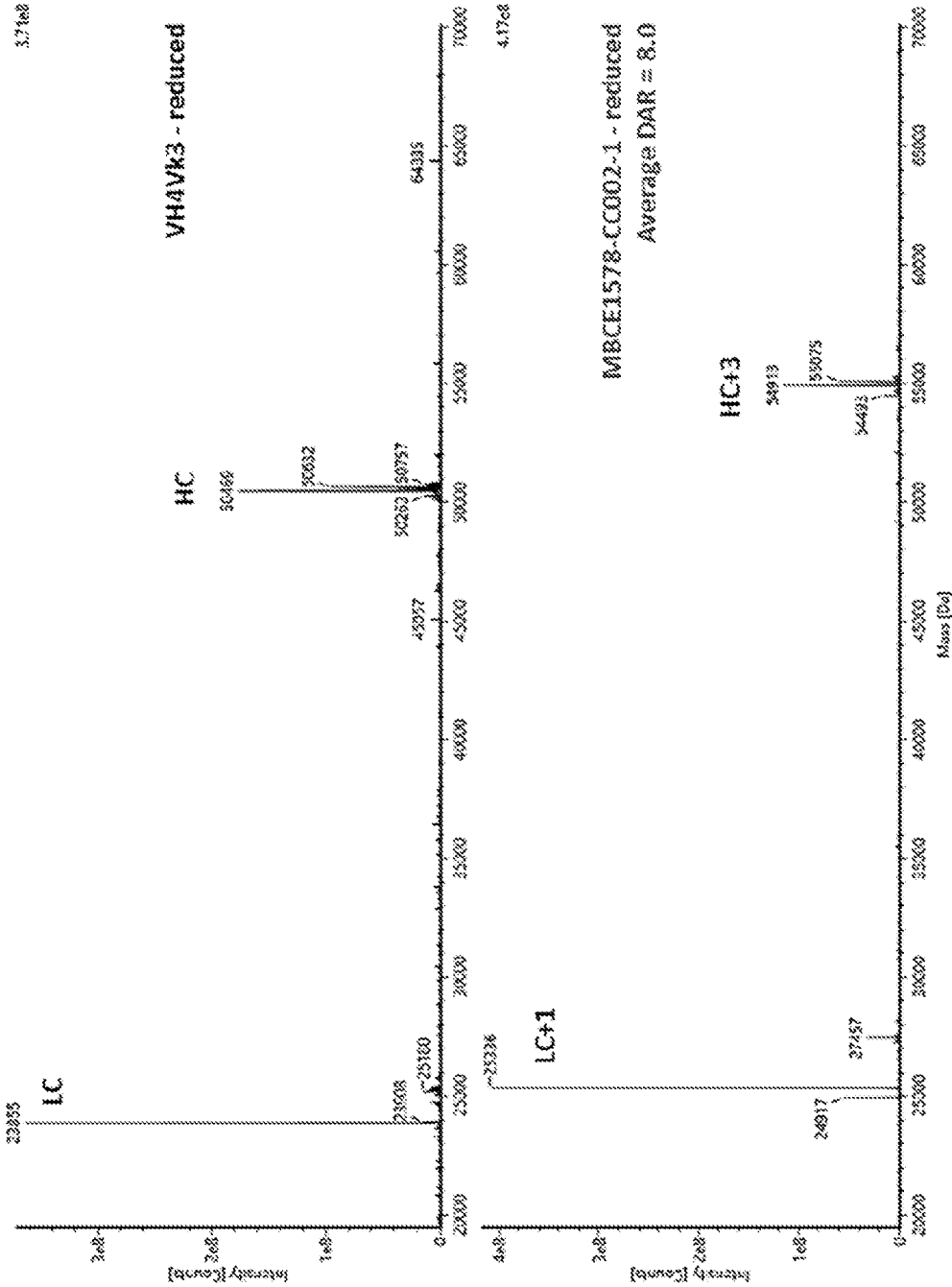


FIG. 46

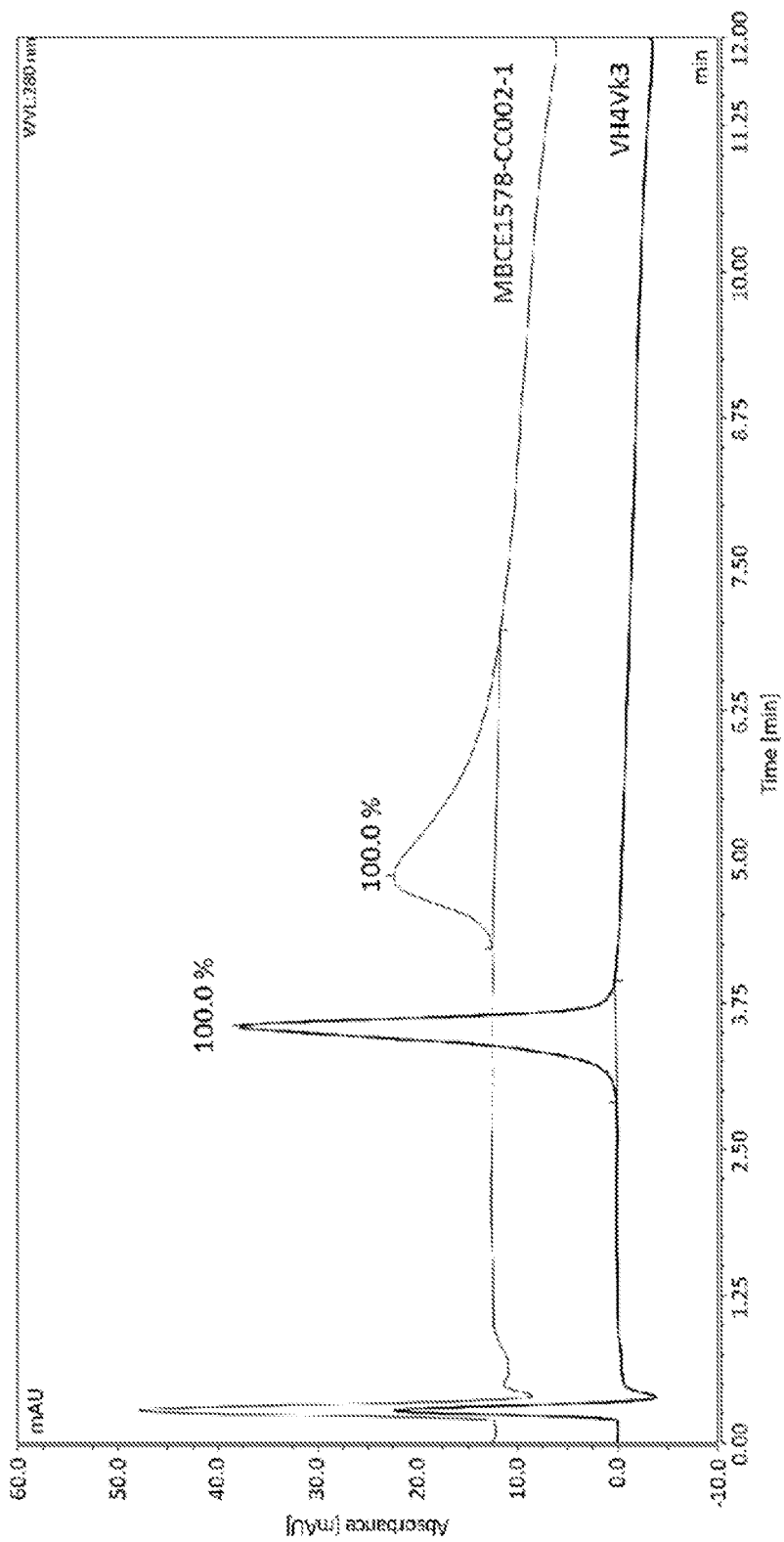


FIG. 47

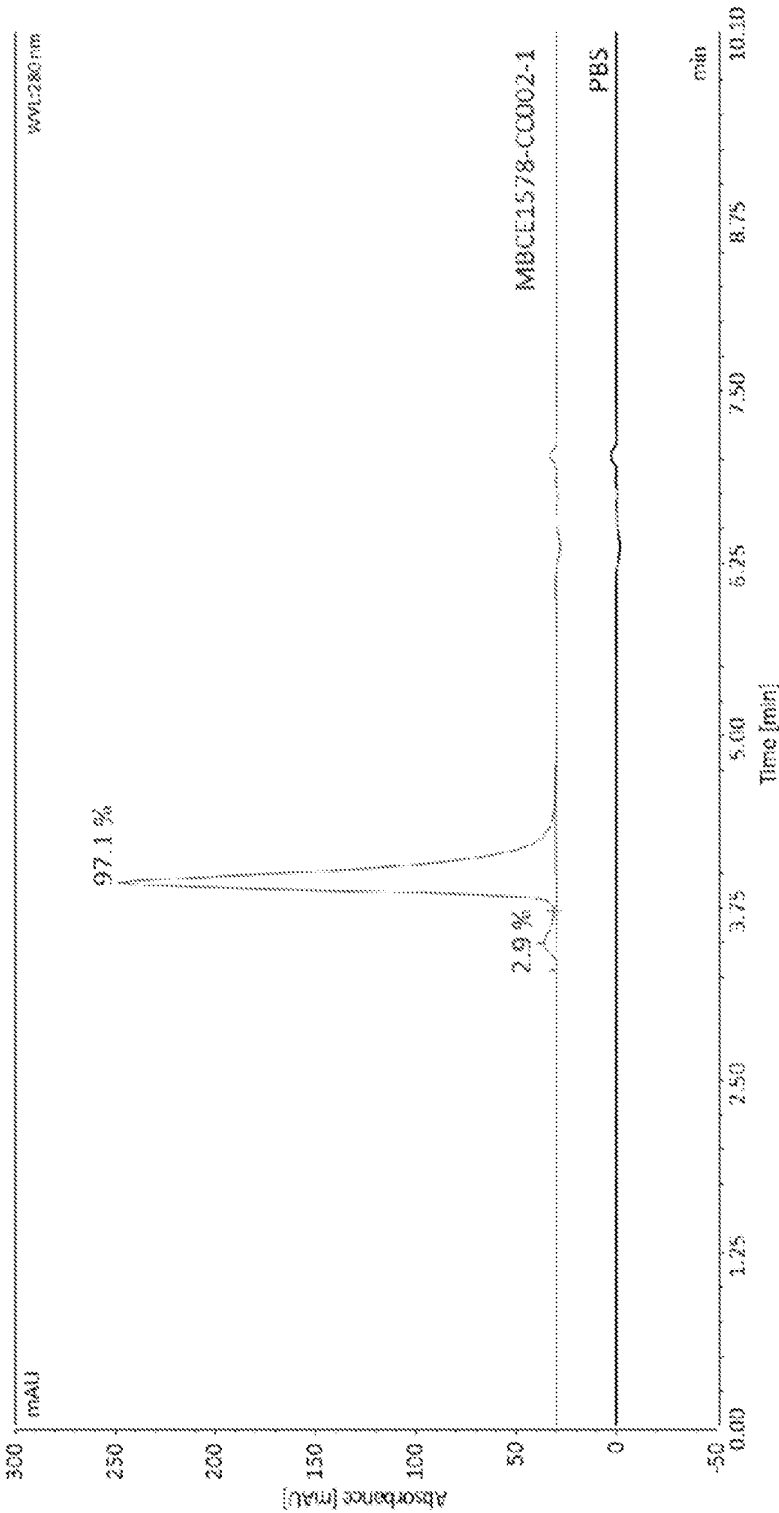


FIG. 48

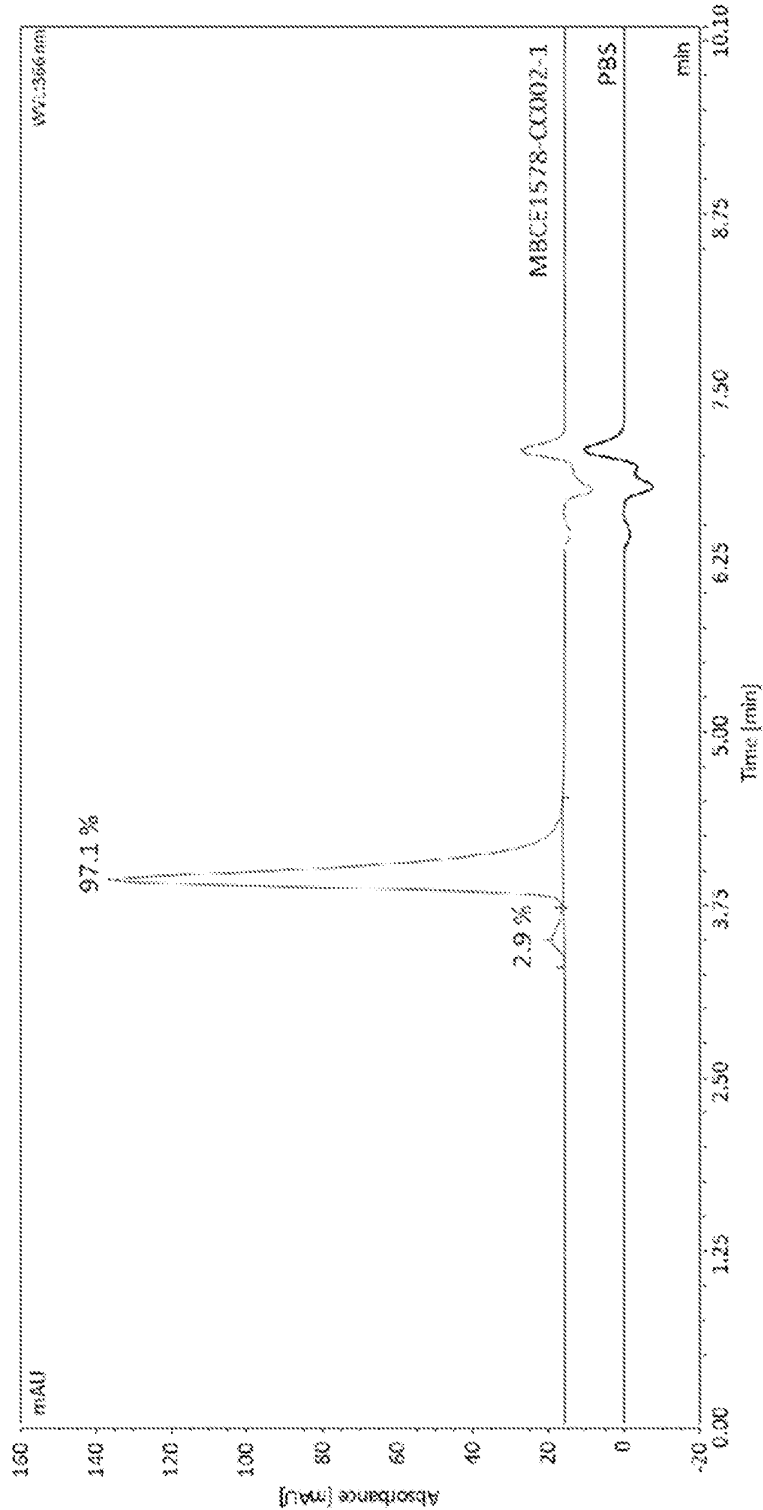


FIG. 49

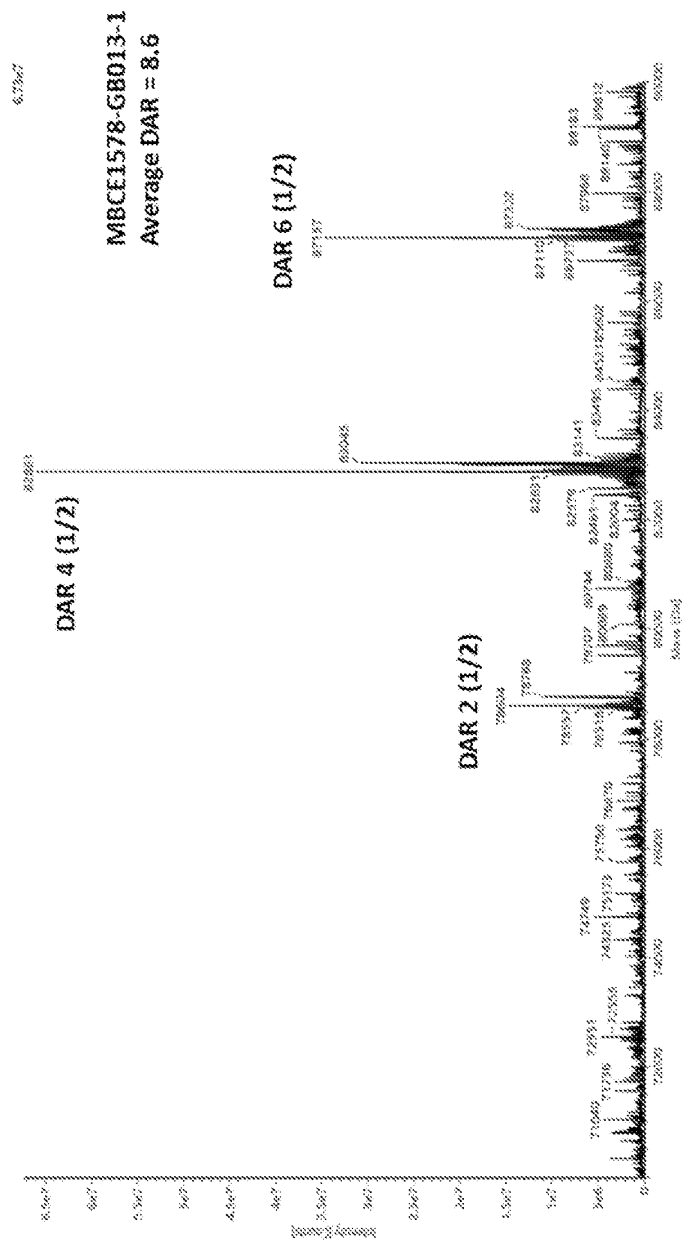


FIG. 50

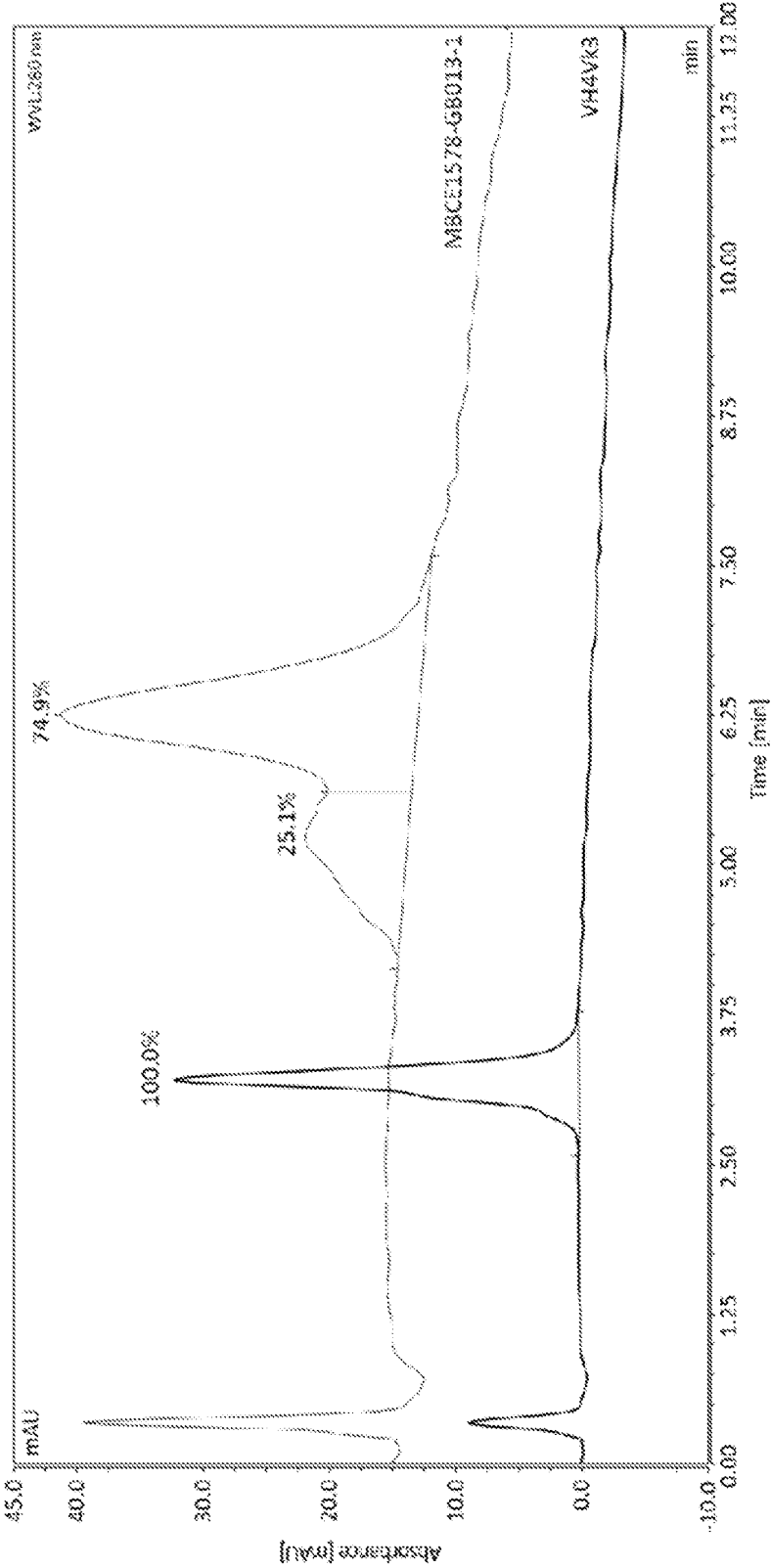


FIG. 51

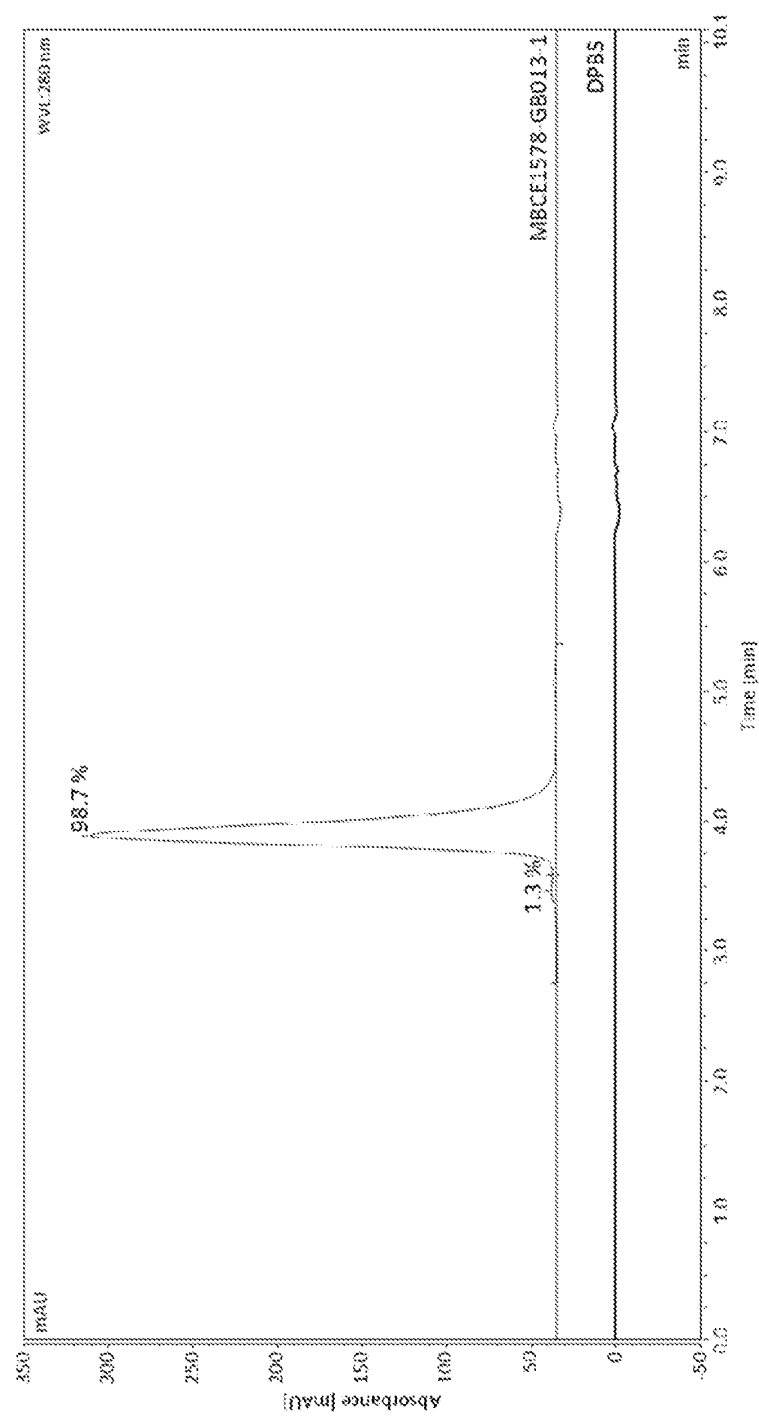


FIG. 52

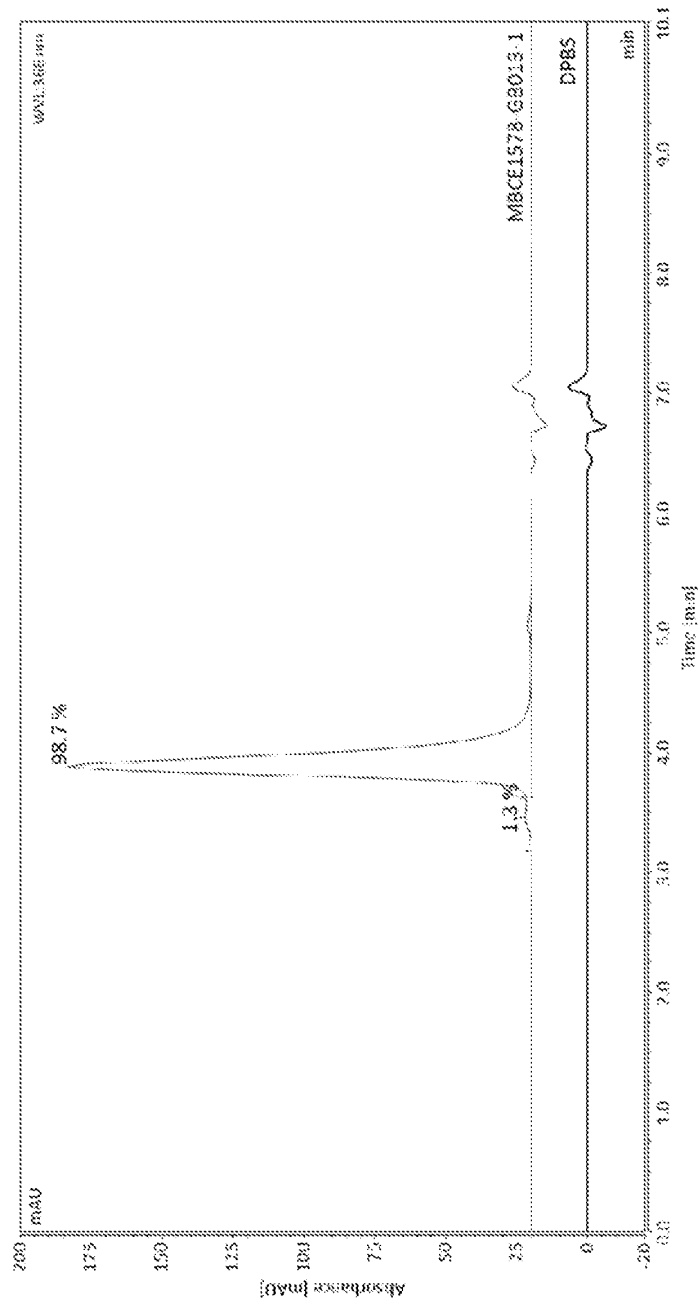


FIG. 53

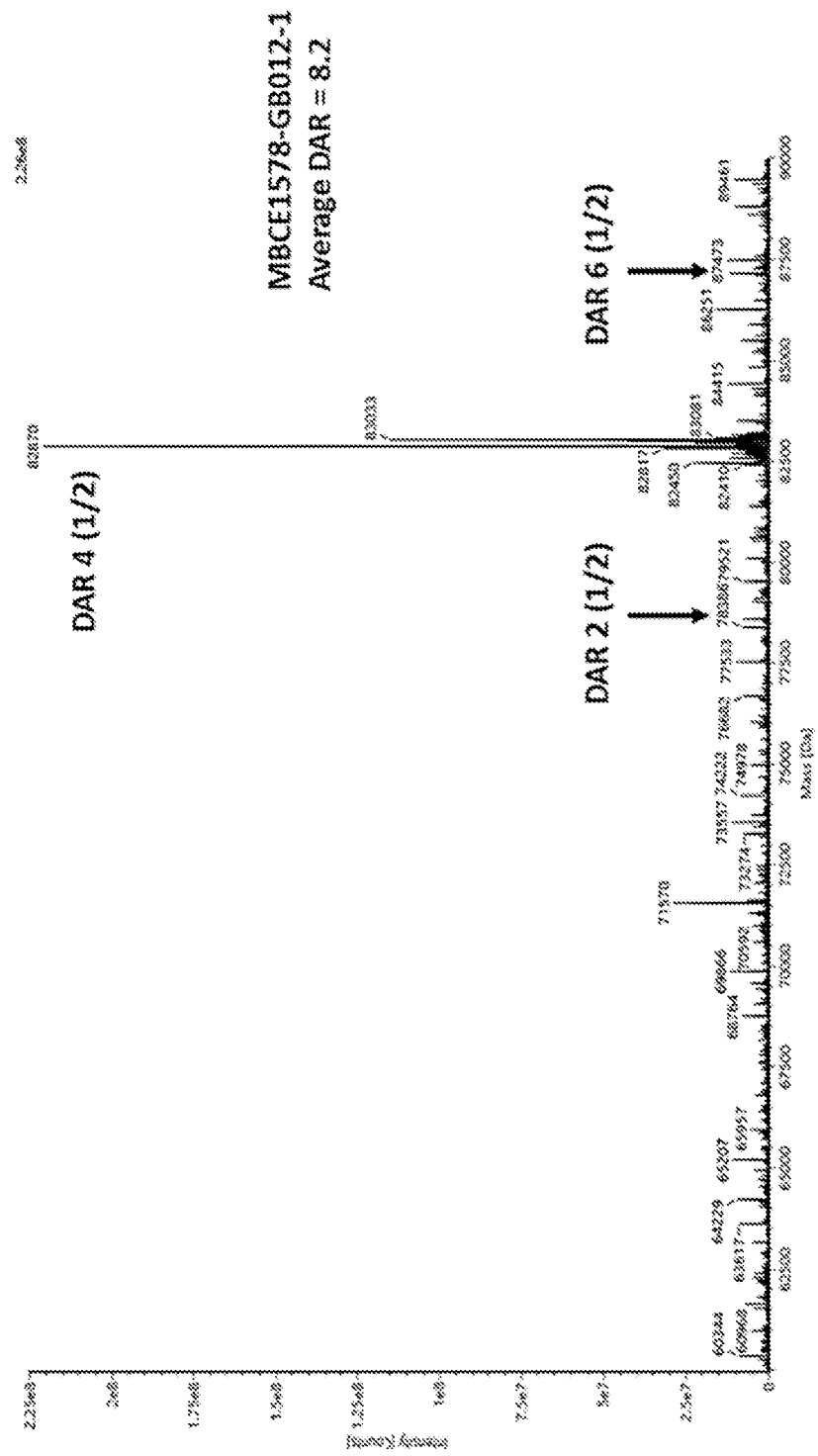


FIG. 54

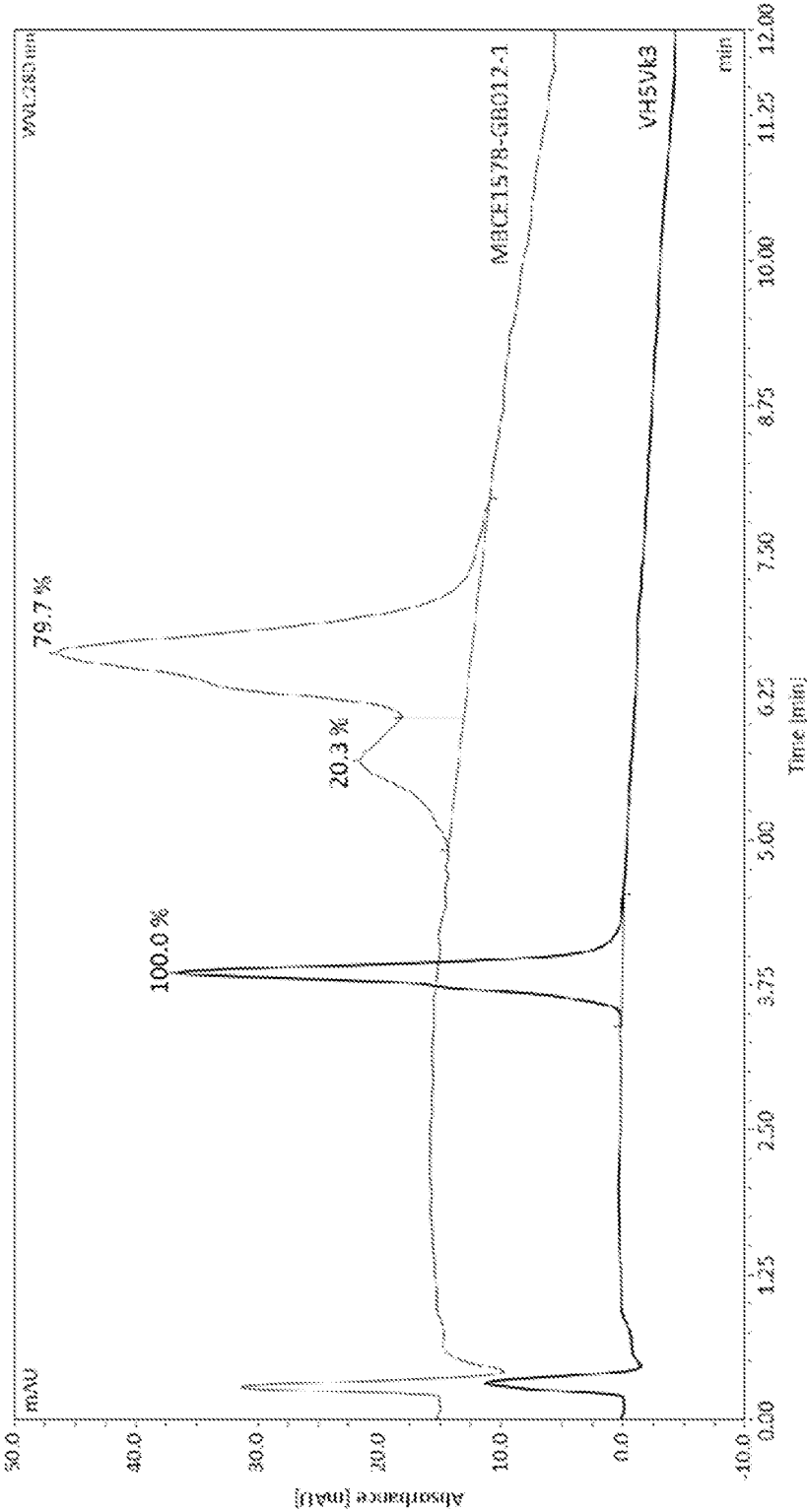


FIG. 55

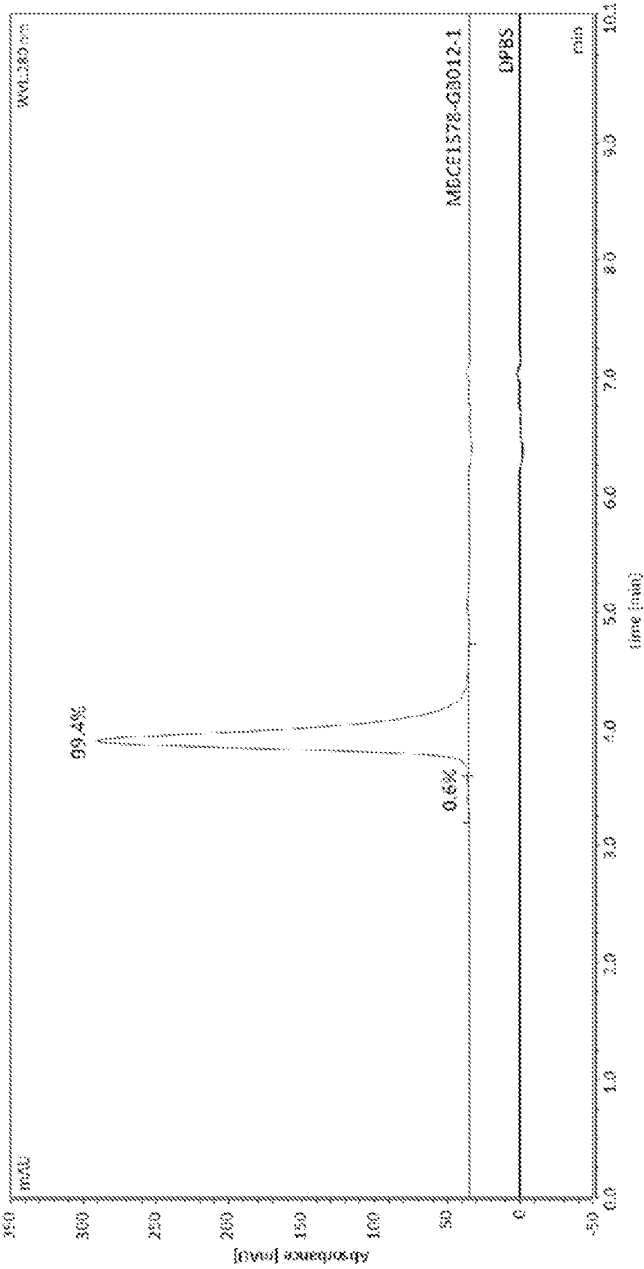


FIG. 56

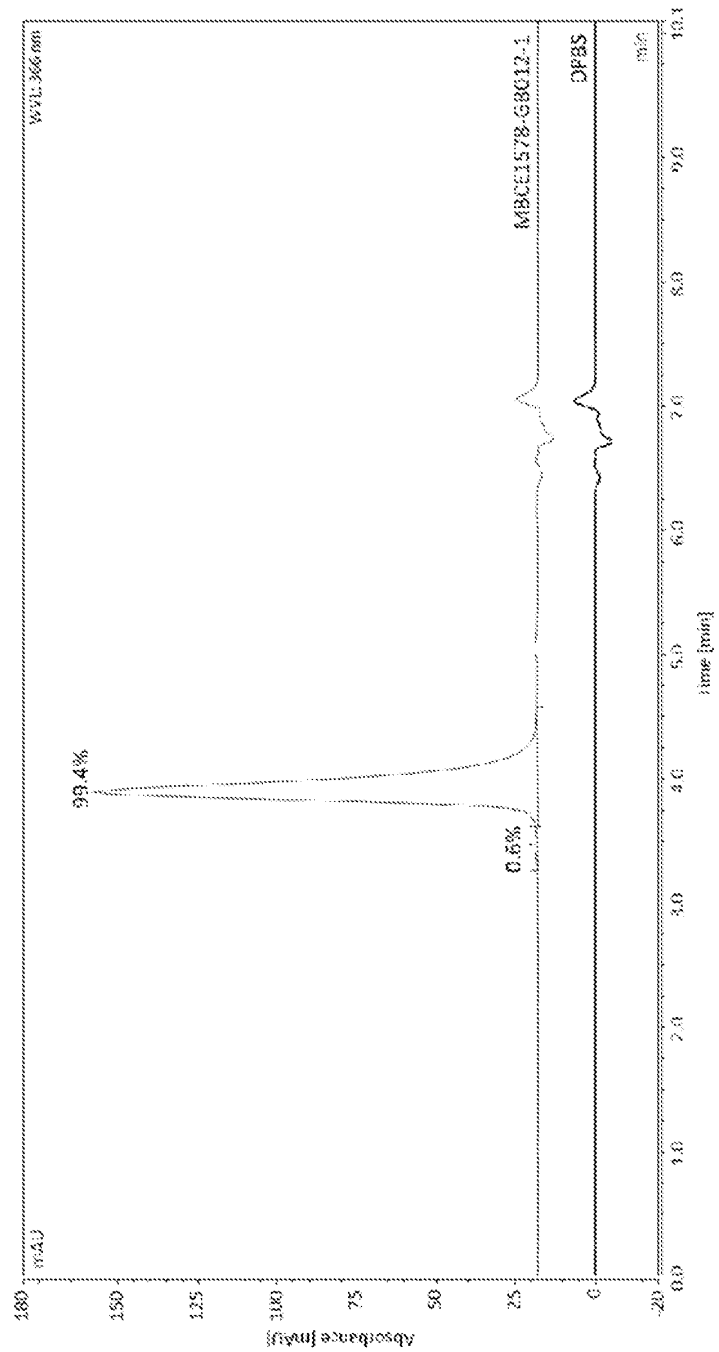


FIG. 57

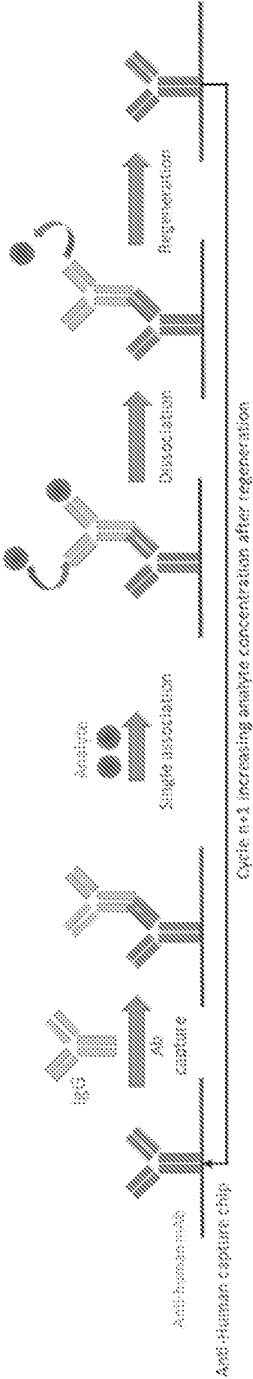


FIG. 58

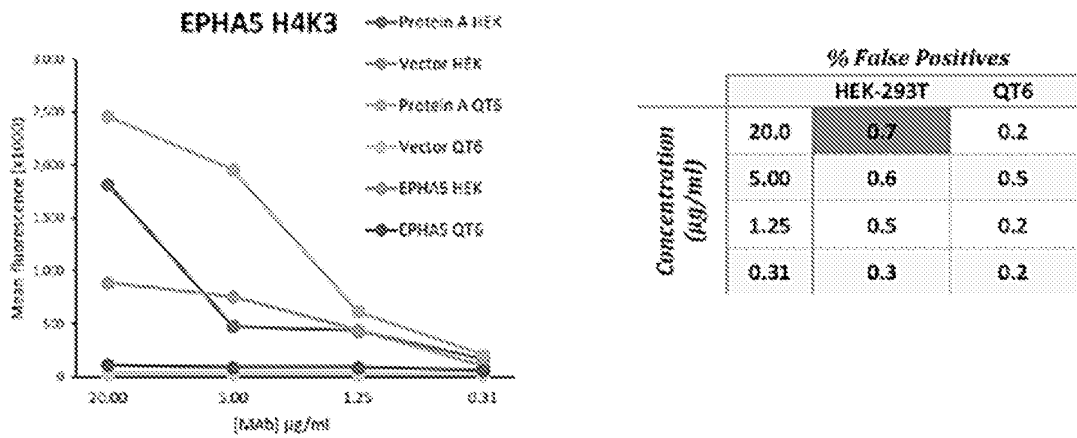
$$\begin{aligned} \text{Average } DAR_{\text{non-reduced sample}} &= \frac{\sum_{i=0}^n SI_i \times l}{\sum_{i=0}^n SI_i} \\ \text{Average } DAR_{\text{reduced sample}} &= 2 \times \frac{\sum_{i=0}^n LSI_i \times l}{\sum_{i=0}^n LSI_i} + 2 \times \frac{\sum_{i=0}^n HSI_i \times l}{\sum_{i=0}^n HSI_i} \end{aligned}$$

FIG. 59A

$$\begin{aligned} \text{Average } DAR &= \frac{\sum_{i=0}^n AUC_i \times l}{\sum_{i=0}^n AUC_i} \\ MW_{ADC} &= MW_{mAb} + DAR \times MW_{LP} \end{aligned}$$

FIG. 59B

Assay Setup



Membrane Proteome Array

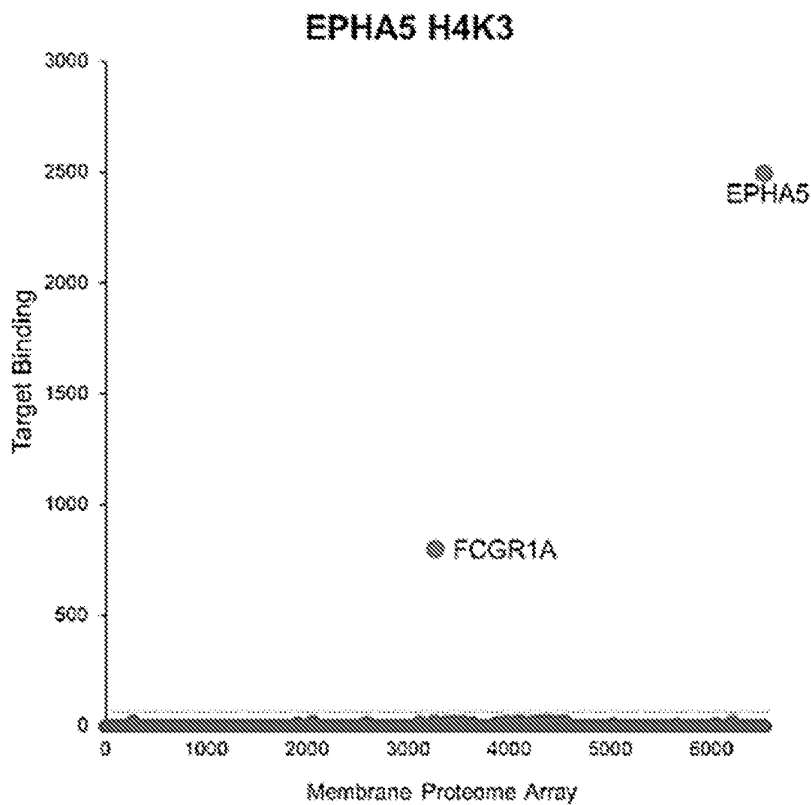
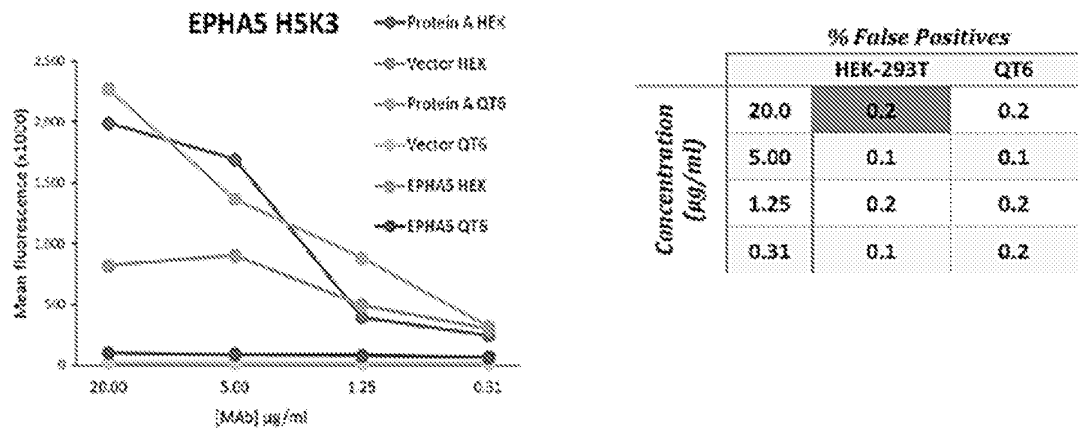


FIG. 60

Assay Setup



Membrane Proteome Array

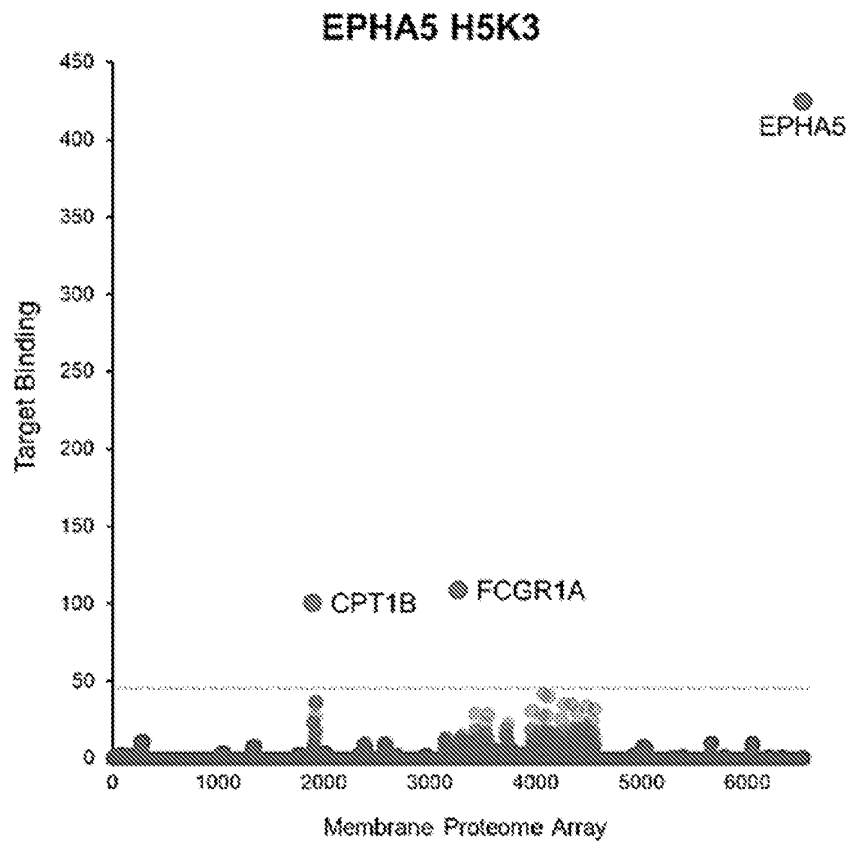


FIG. 61

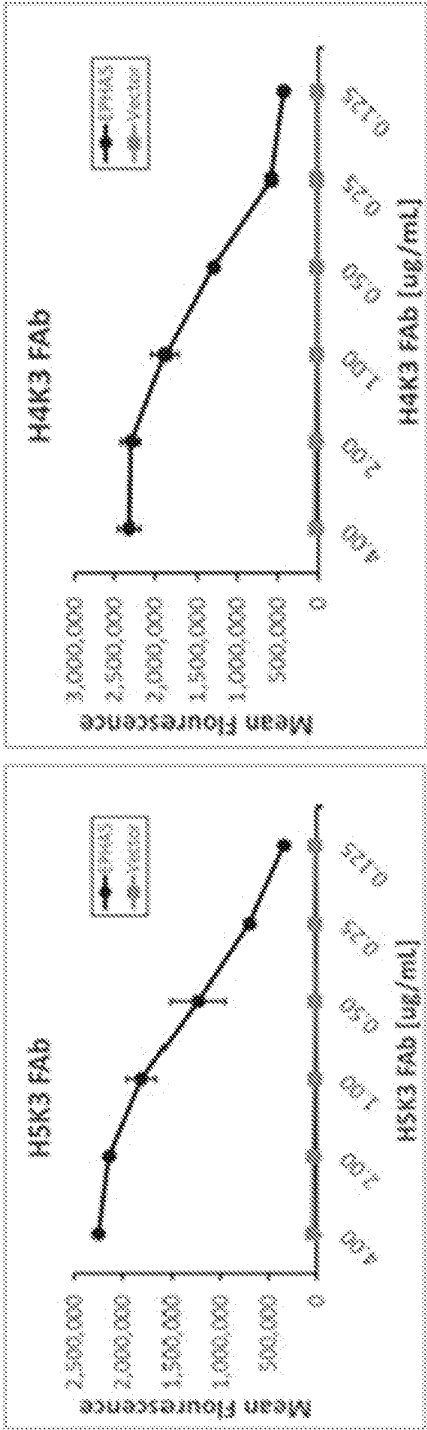


FIG. 62

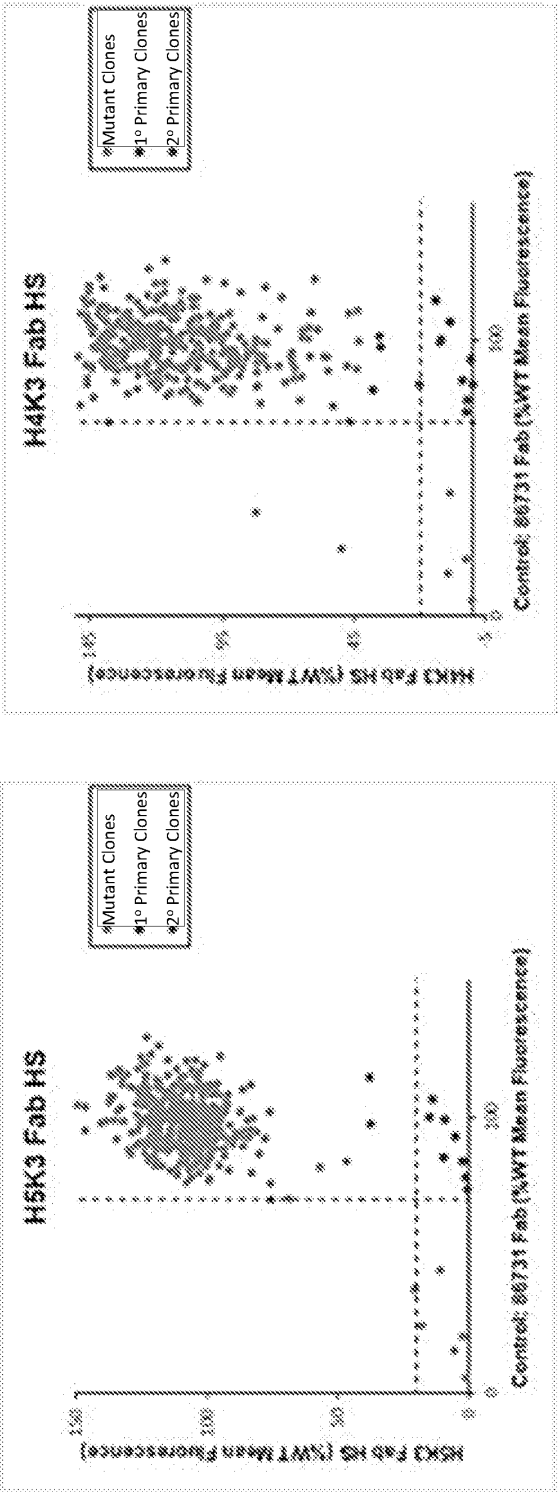
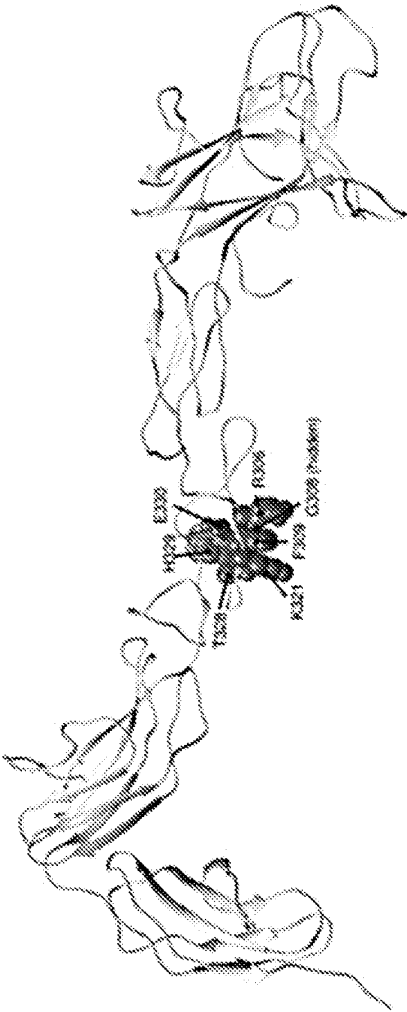


FIG. 63

H5K3 Fab HS



H4K3 Fab HS

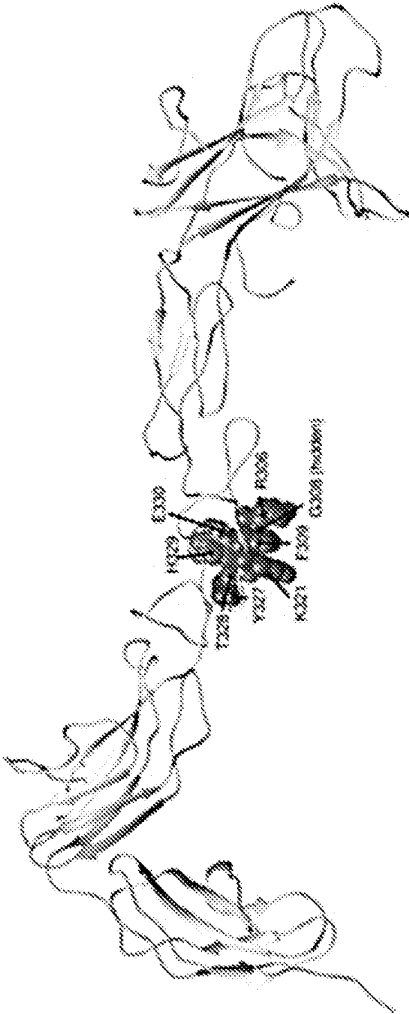
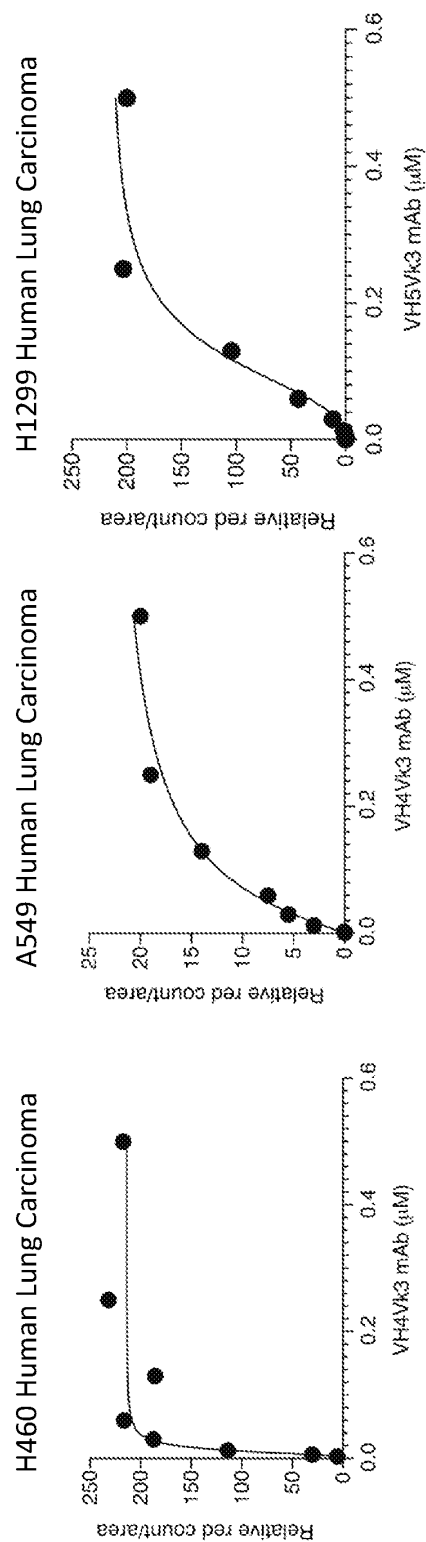


FIG. 64

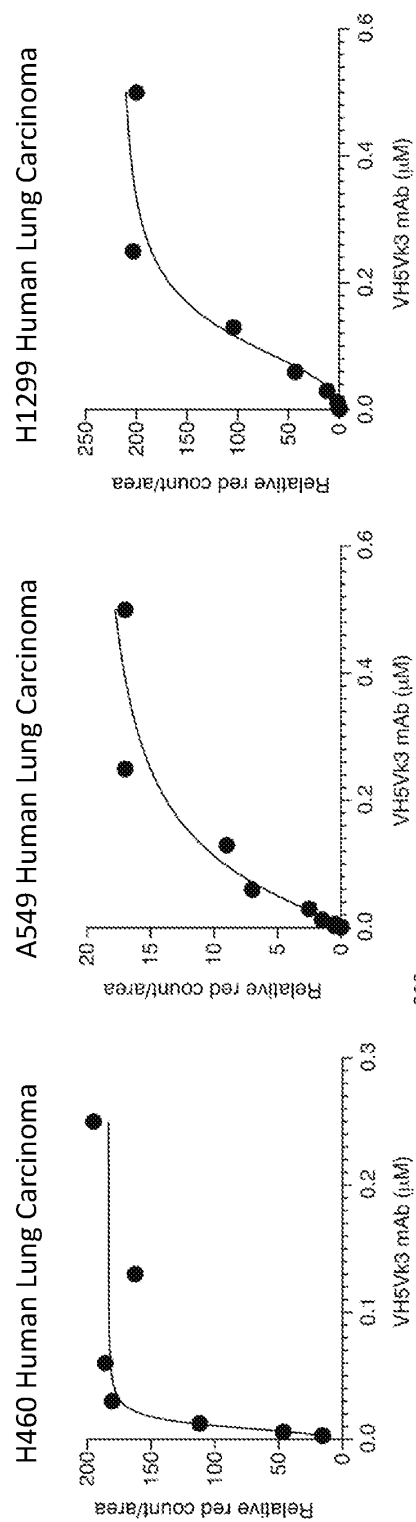
Antibody Name	Primary Residues
H5K3 Fab HS	<u>R306</u> , G308, F309, K321, <u>T328</u> , <u>H329</u> , E330
H4K3 Fab HS	R306, G308, <u>F309</u> , K321, Y327, <u>T328</u> , <u>H329</u> , E330

FIG. 65



Internalization of VH4Vk3 mAb		
Cell Line	EC50	
H460	12 nM	
A549	100 nM	
H1299	131 nM	

FIG. 66



Internalization of VH5Vk3 mAb		
Cell Line	EC50	
H460	10 nM	
A549	100 nM	
H1299	115 nM	

FIG. 67

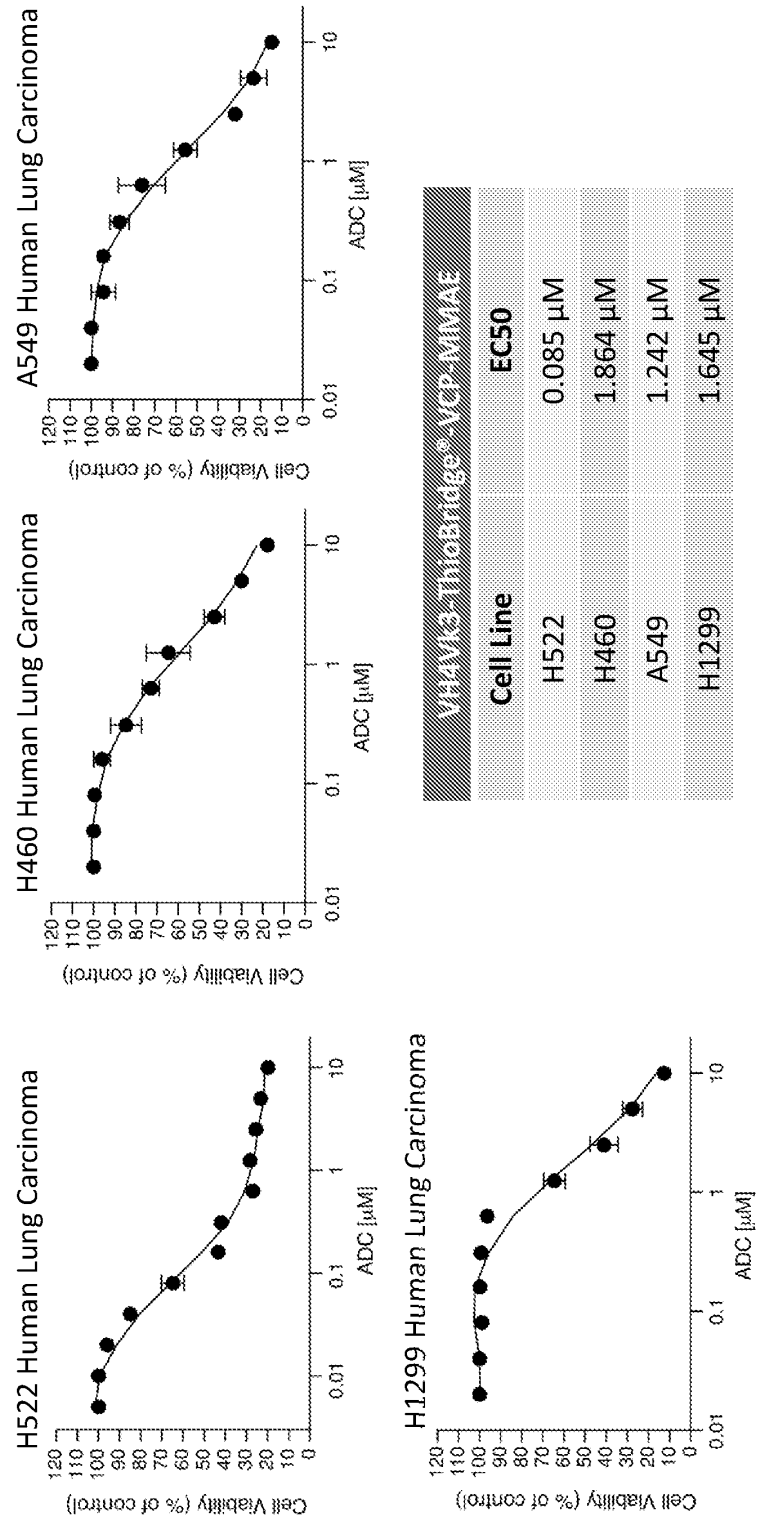


FIG. 68

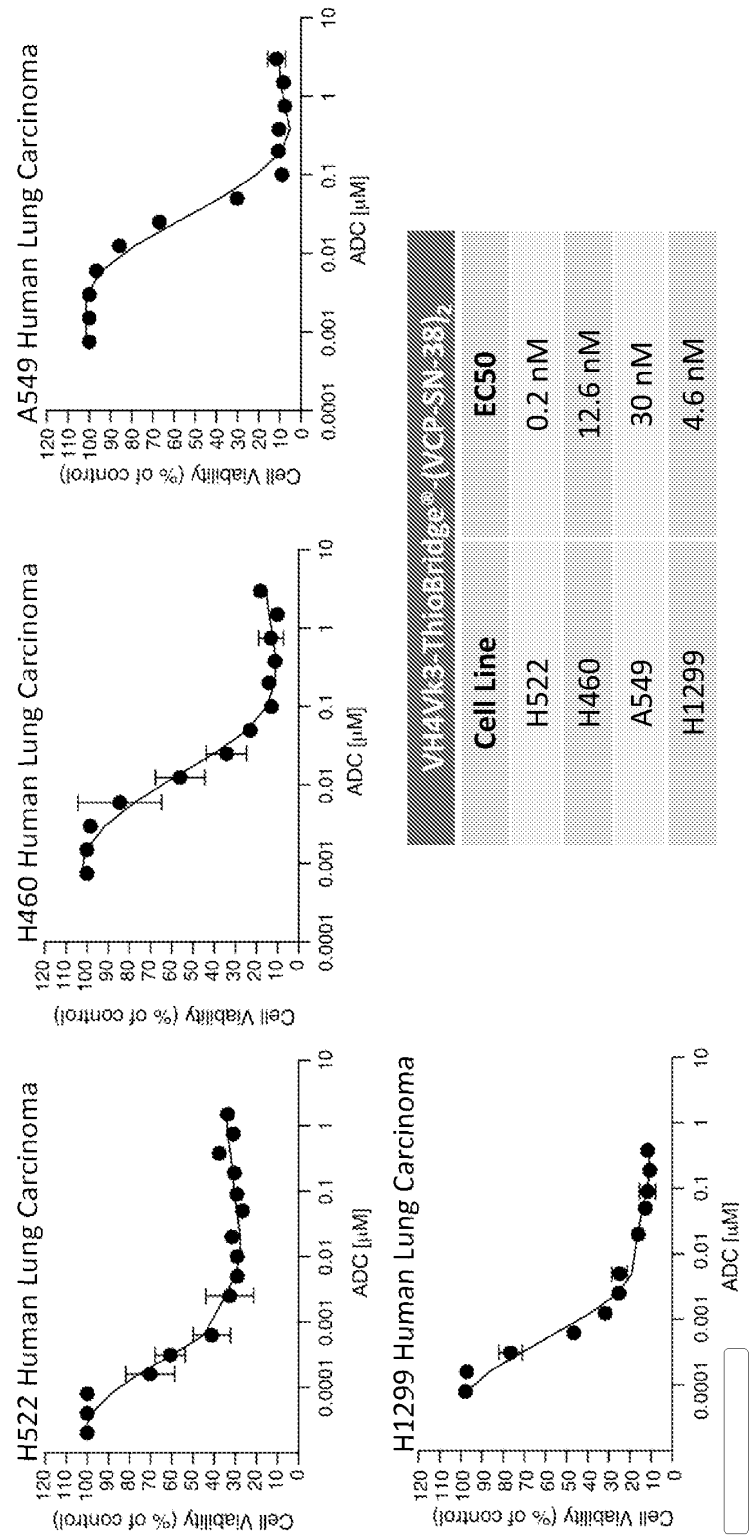


FIG. 69

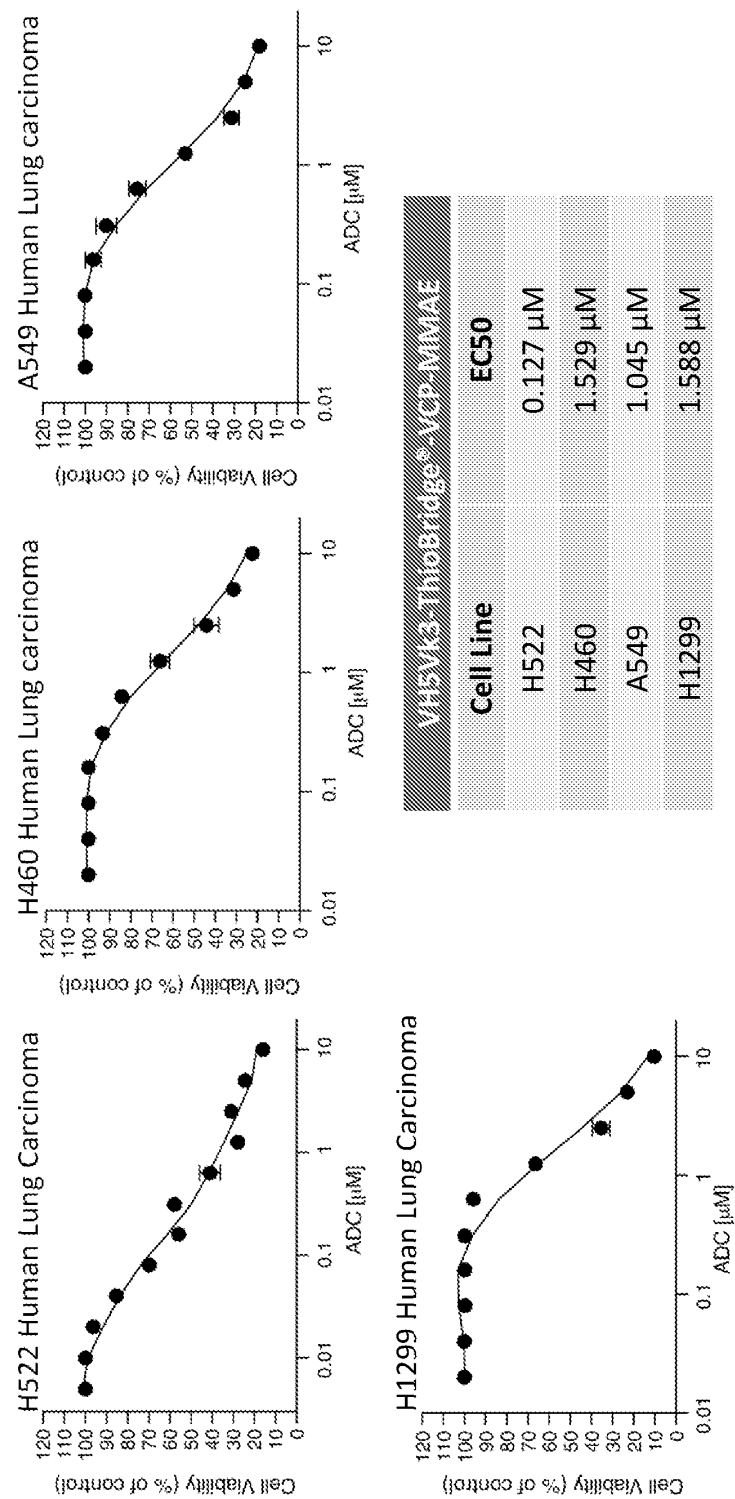


FIG. 70

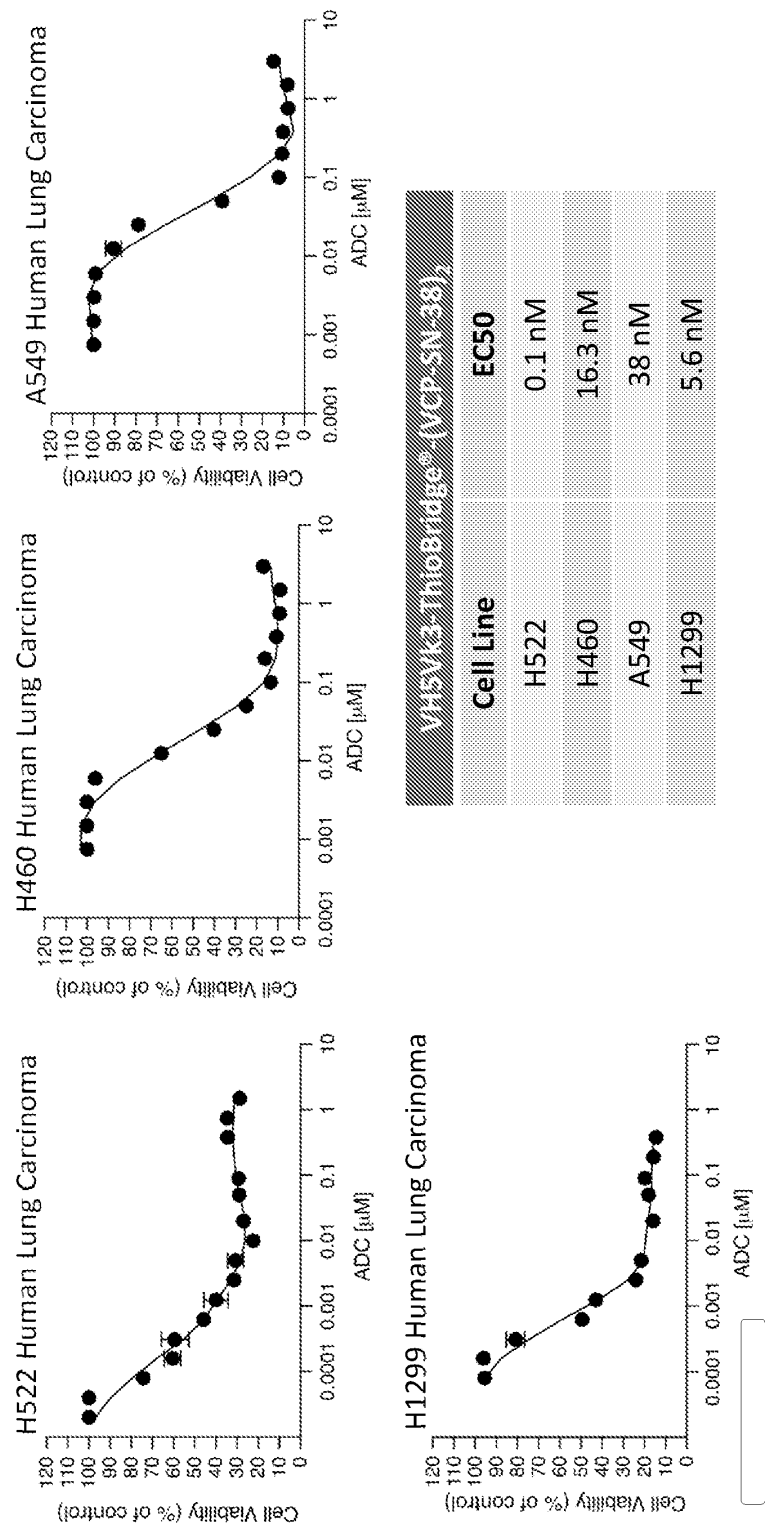


FIG. 71

EXPERIMENT 1

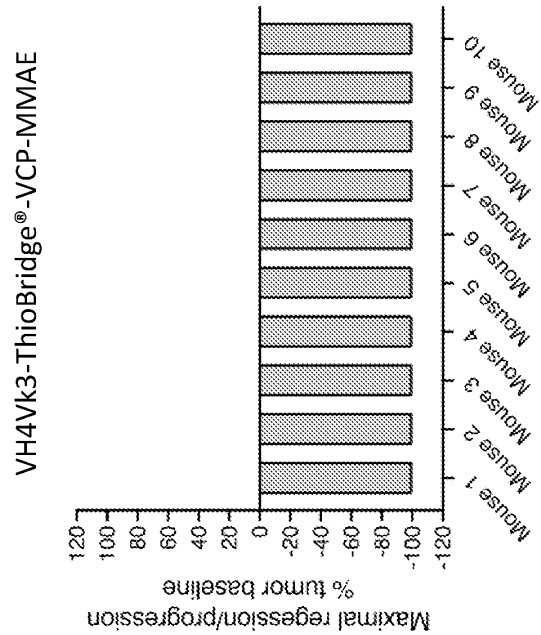
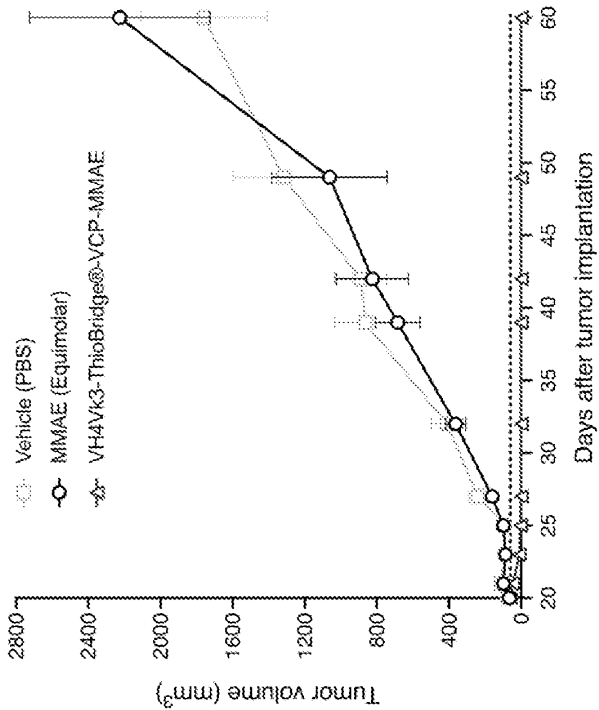


FIG. 72

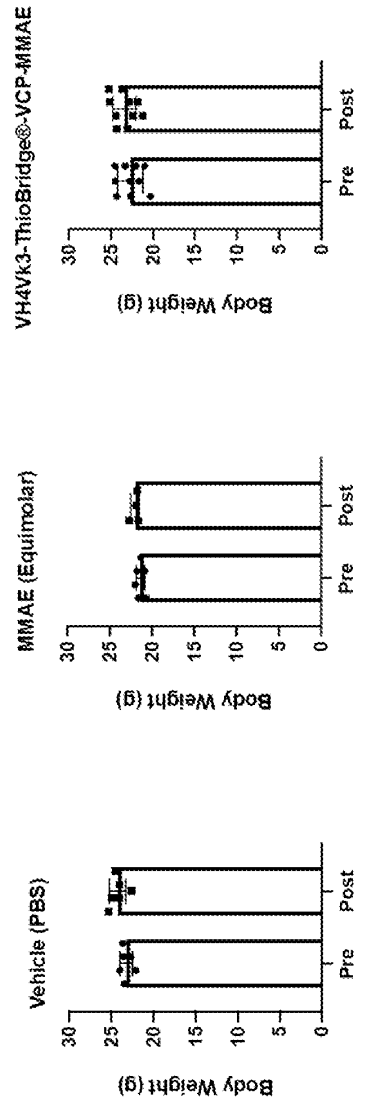


FIG. 73

EXPERIMENT 2

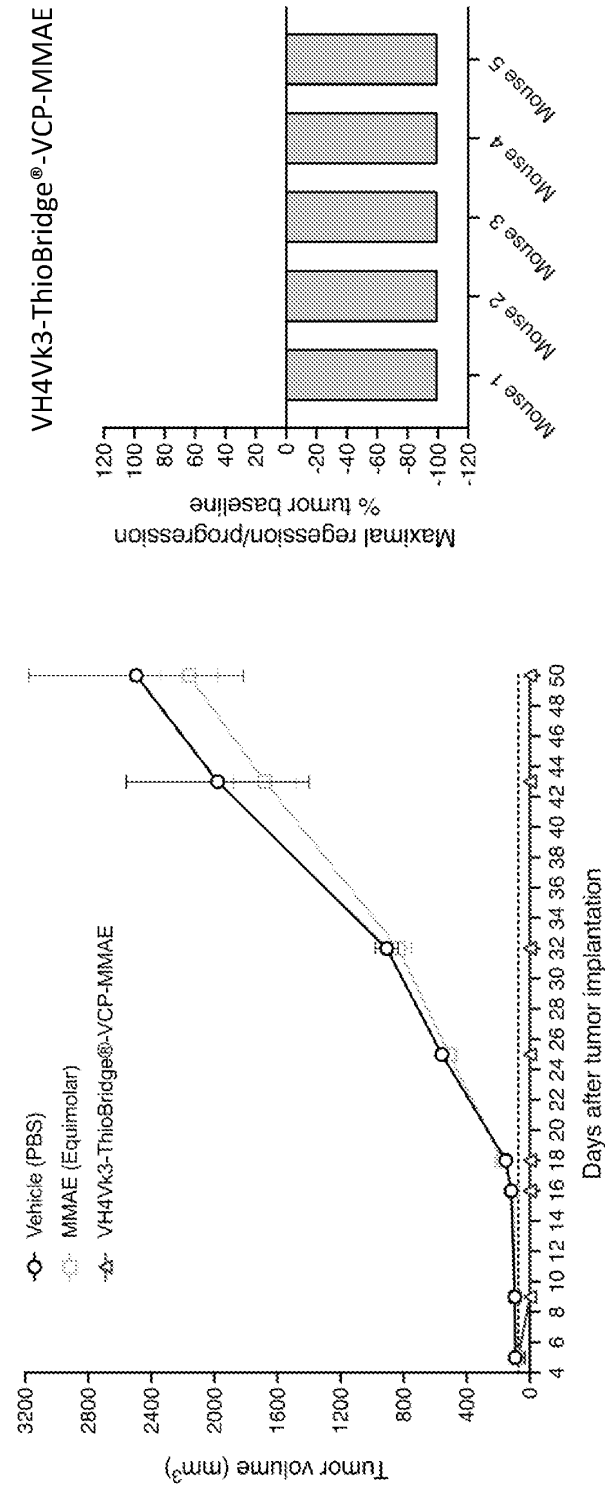


FIG. 74

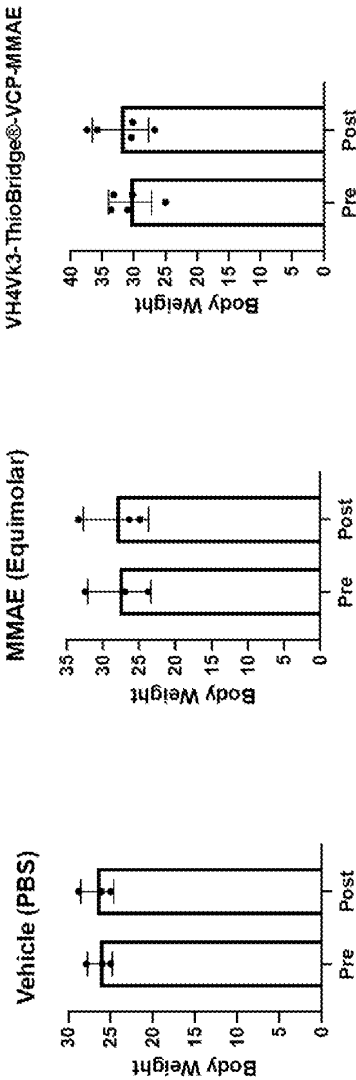


FIG. 75

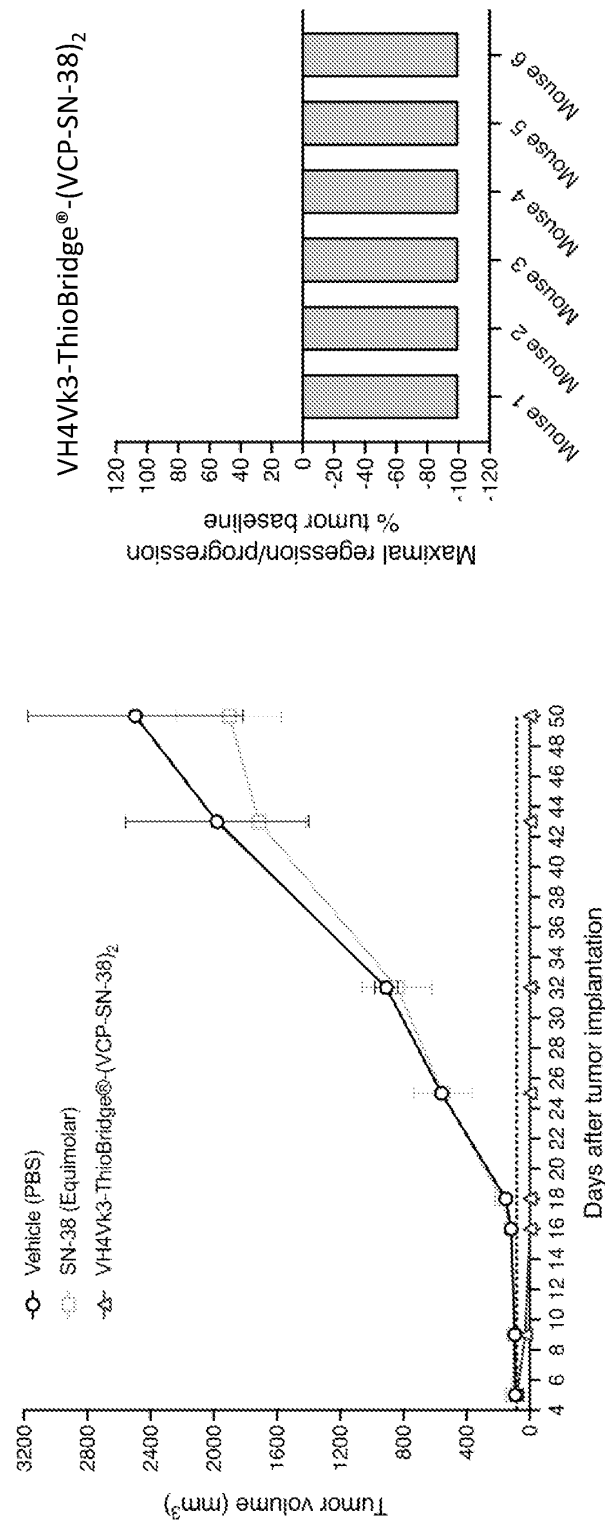


FIG. 76

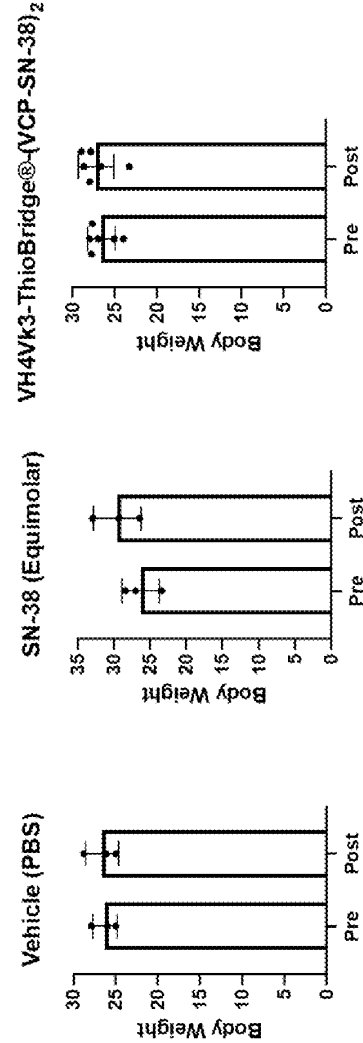


FIG. 77

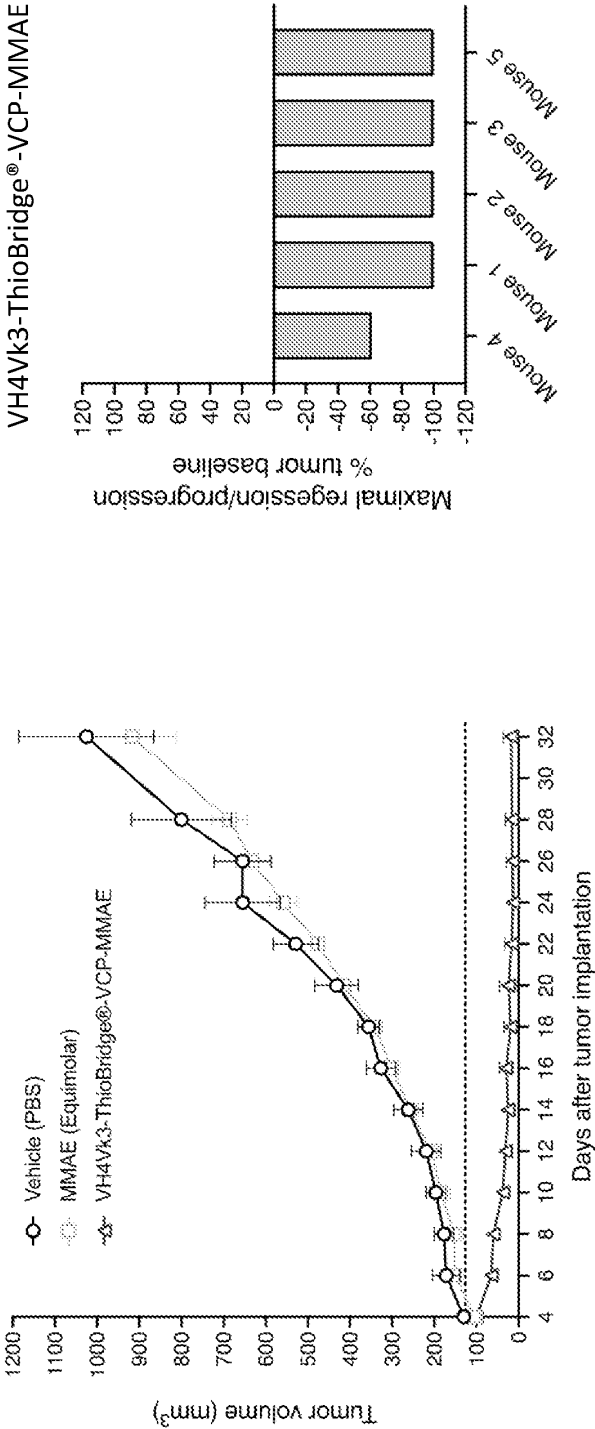


FIG. 78

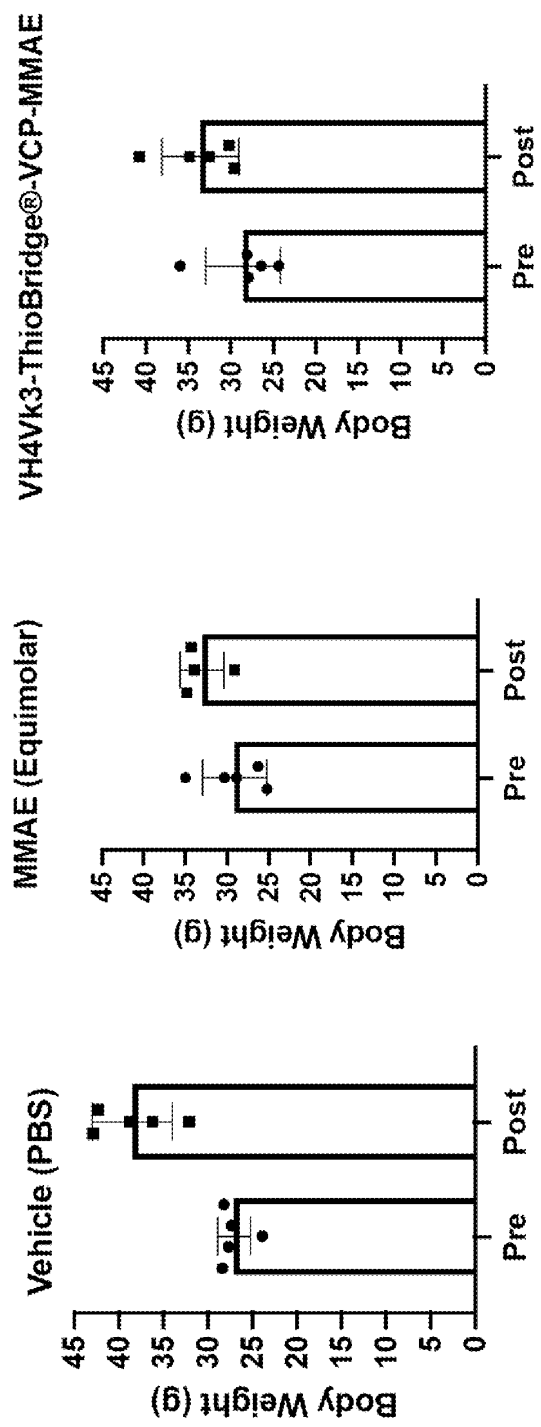


FIG. 79

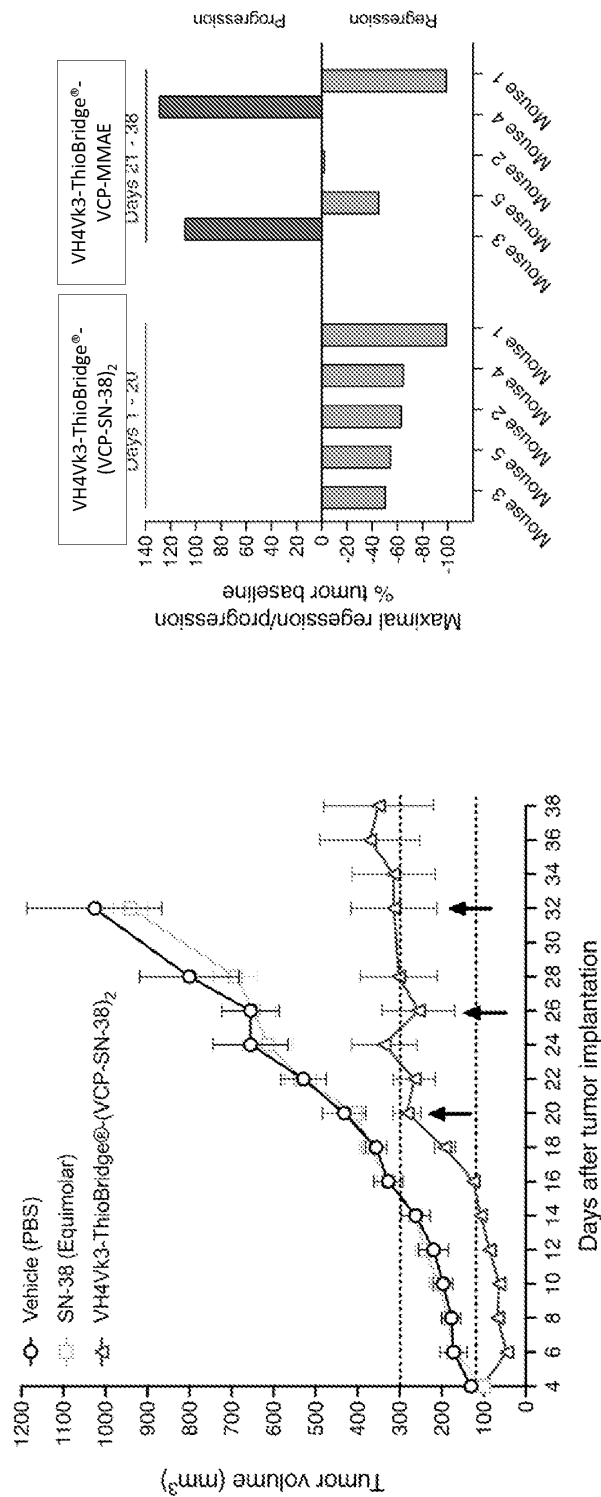


FIG. 80

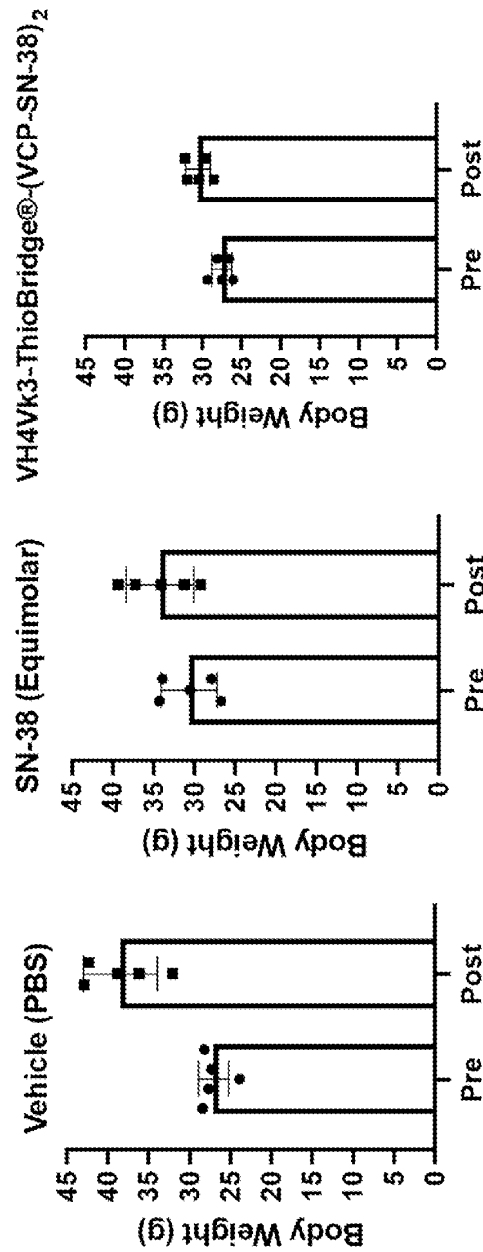


FIG. 81

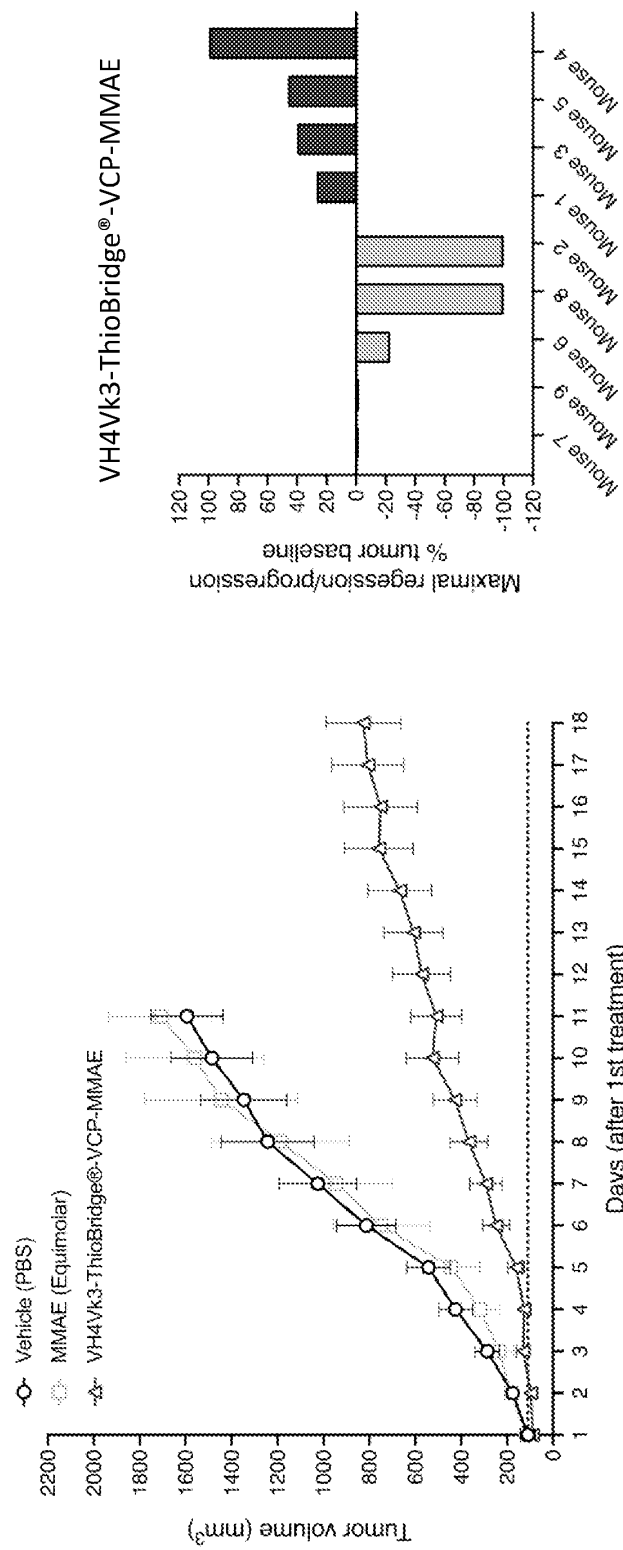


FIG. 82

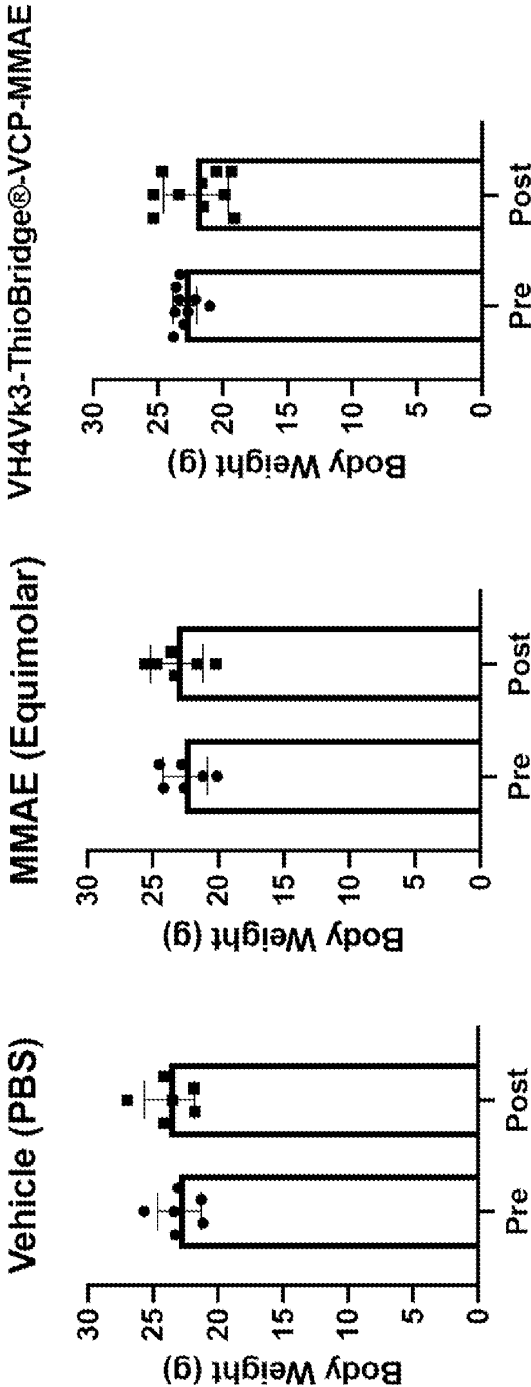


FIG. 83

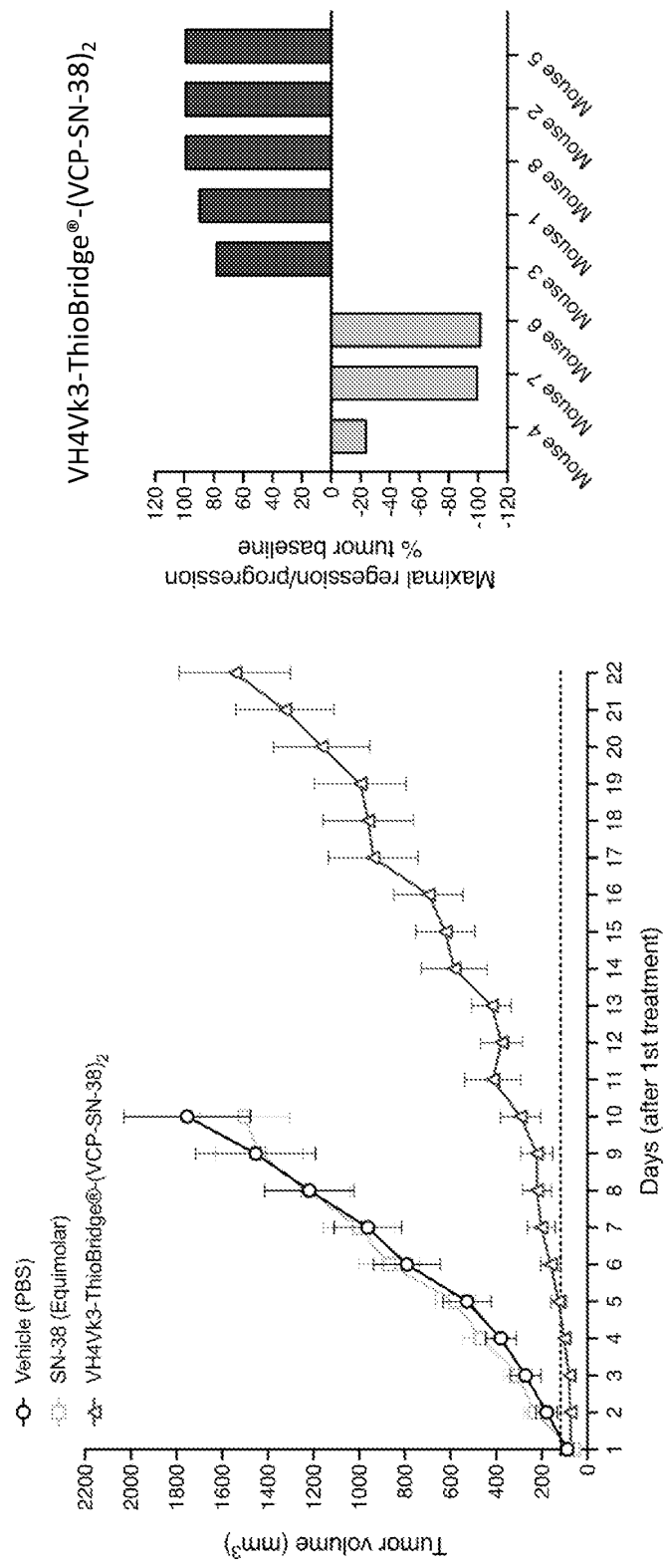


FIG. 84

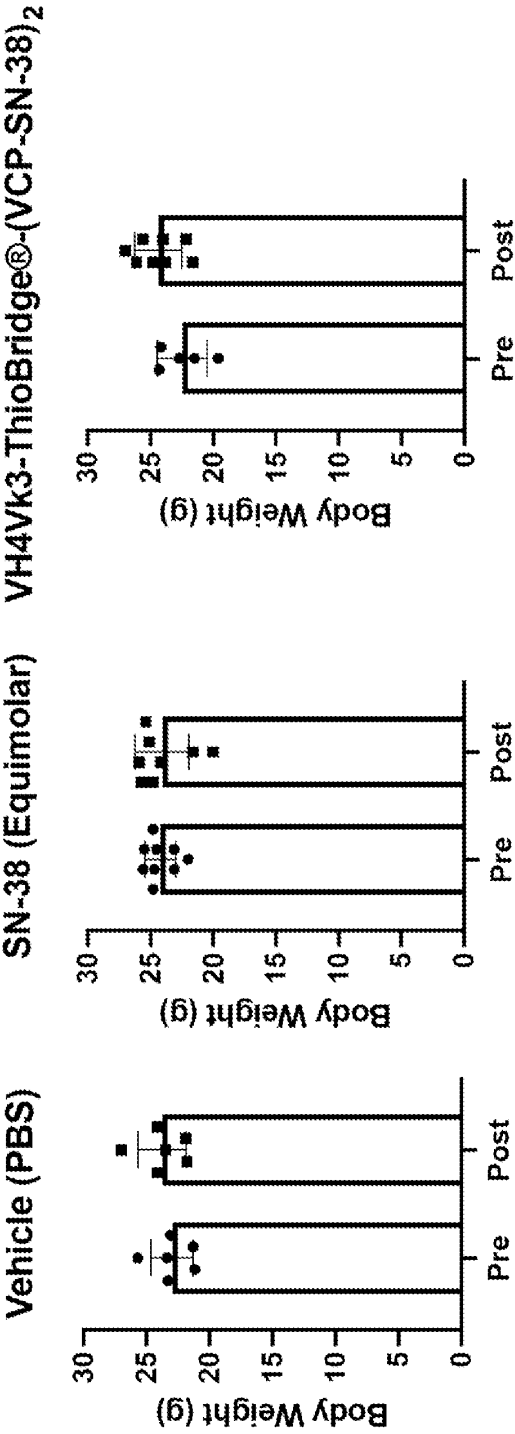


FIG. 85

EXPERIMENT 1

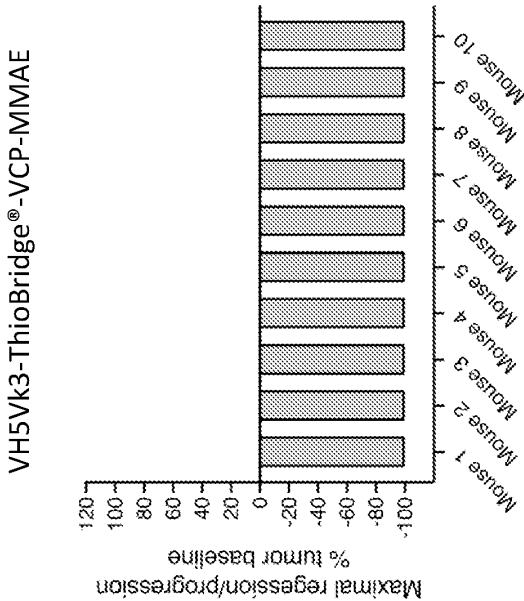
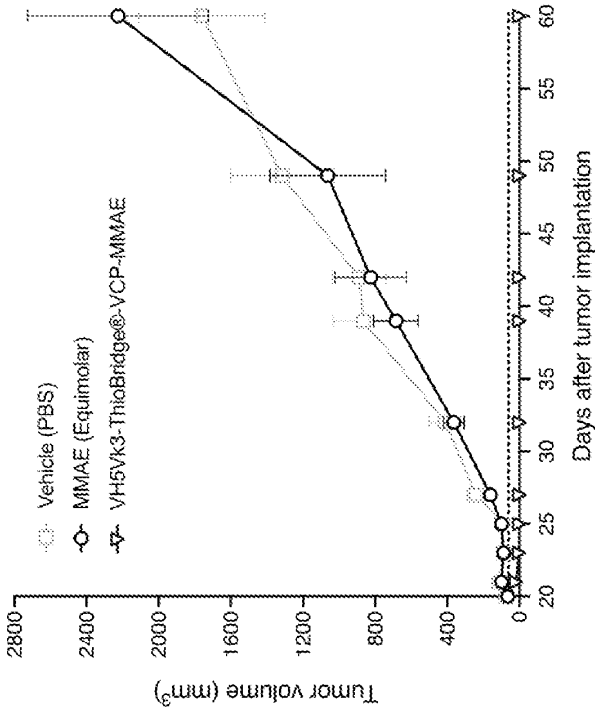


FIG. 86

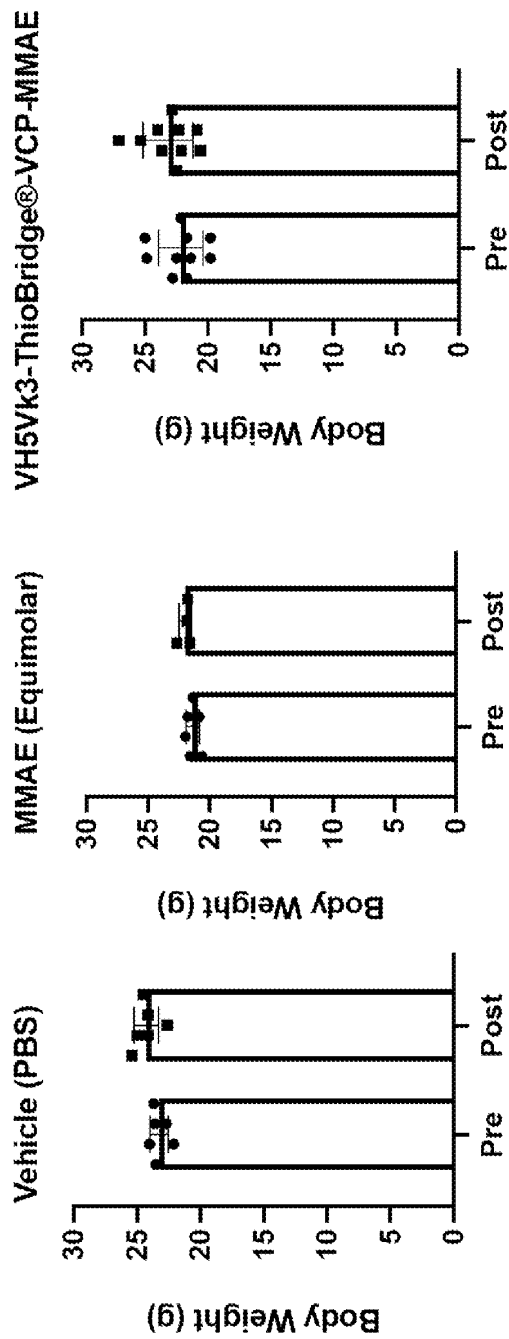


FIG. 87

EXPERIMENT 2

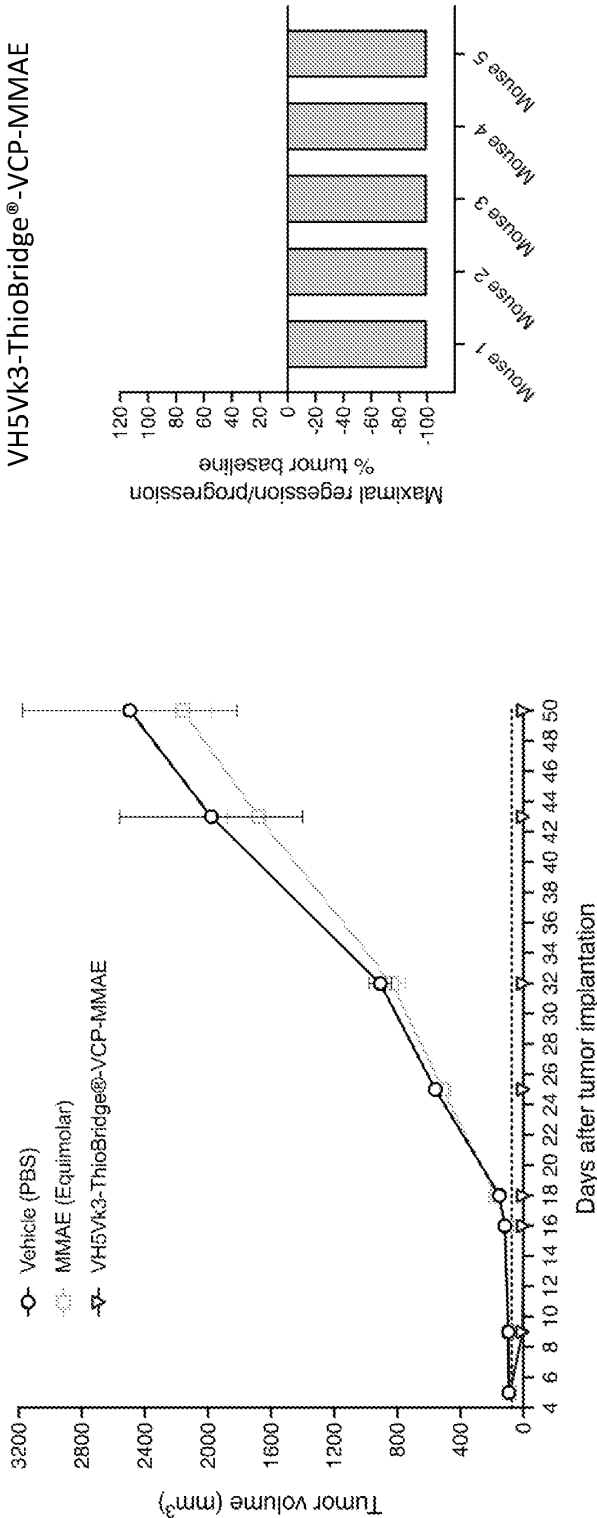


FIG. 88

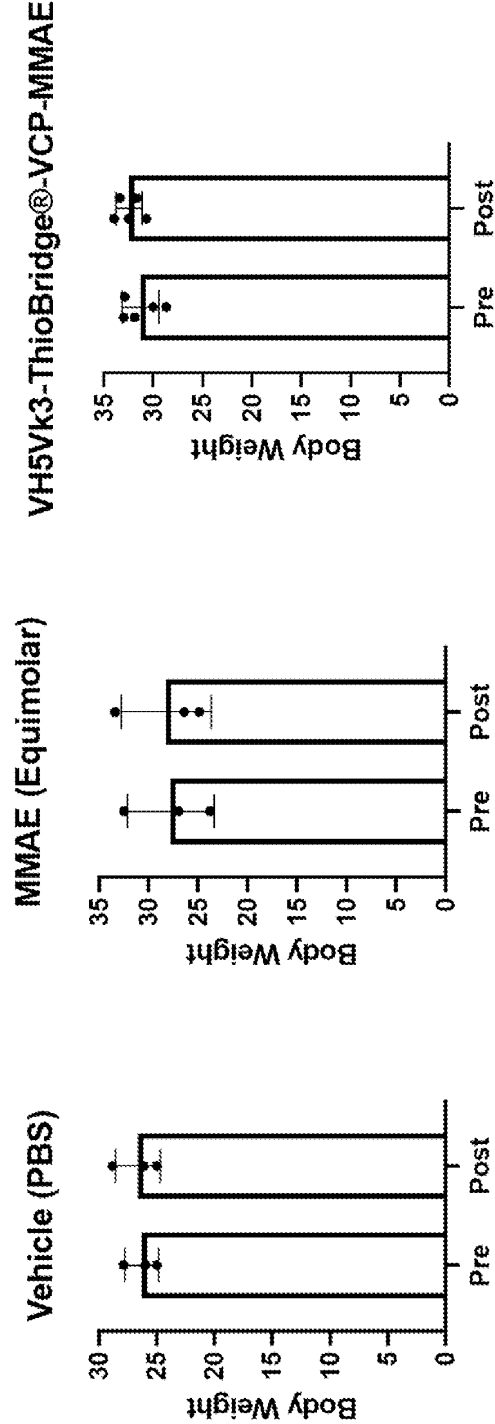


FIG. 89

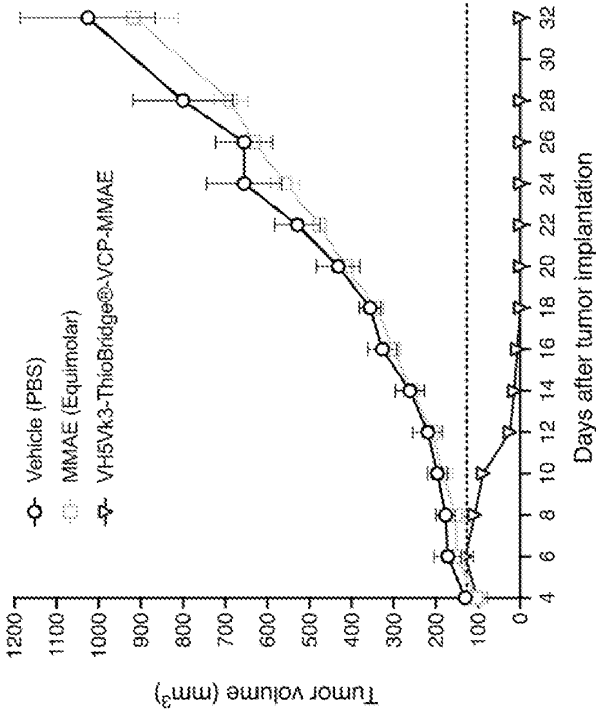
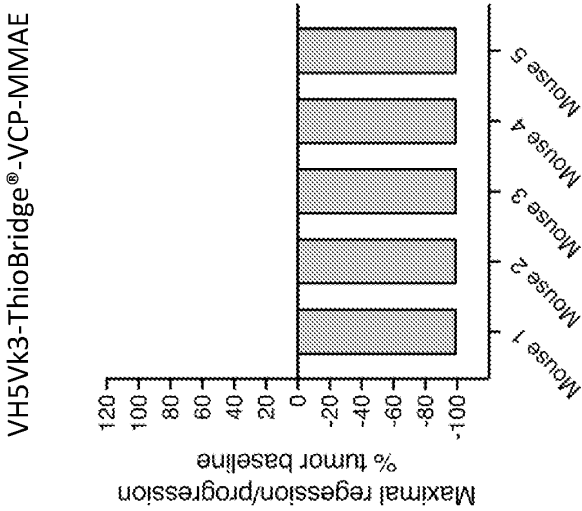


FIG. 90

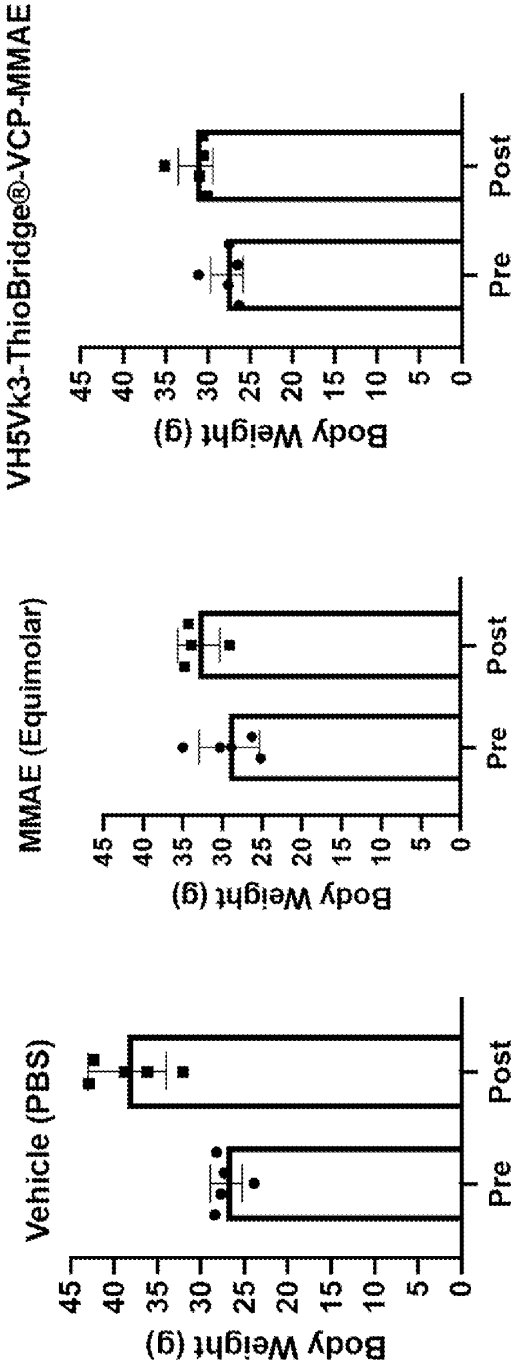


FIG. 91

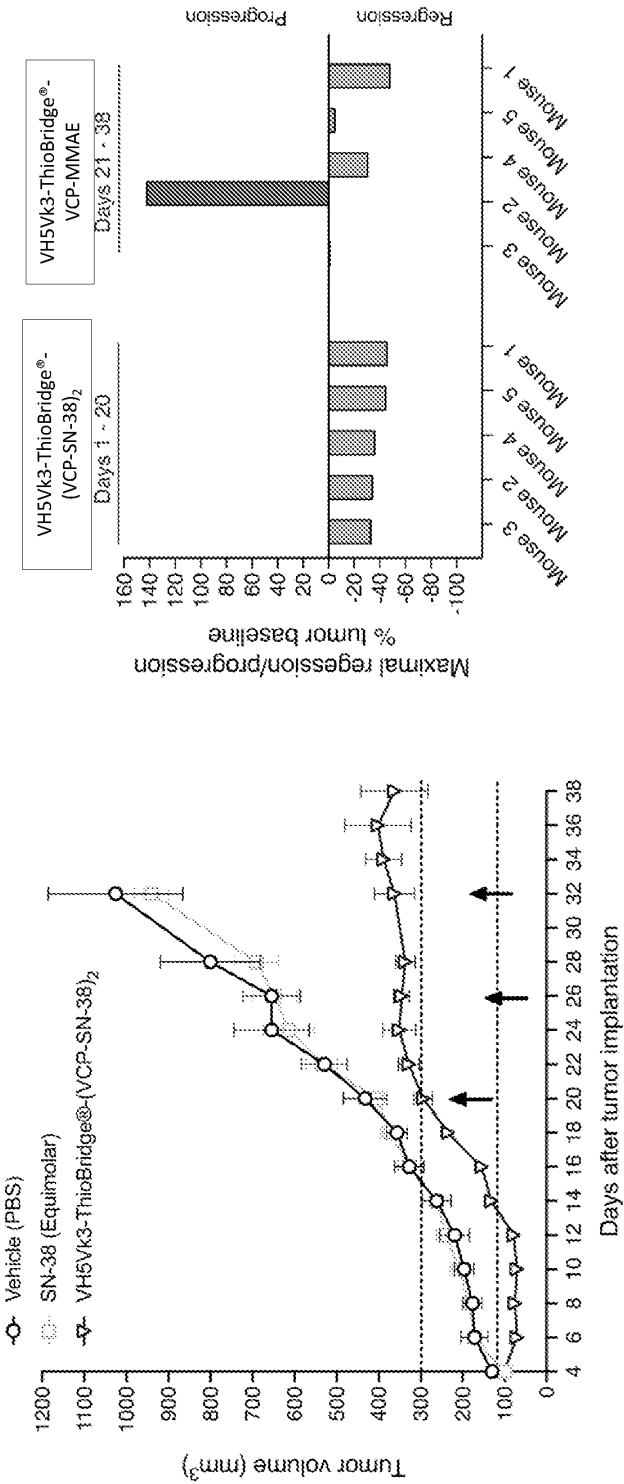


FIG. 92

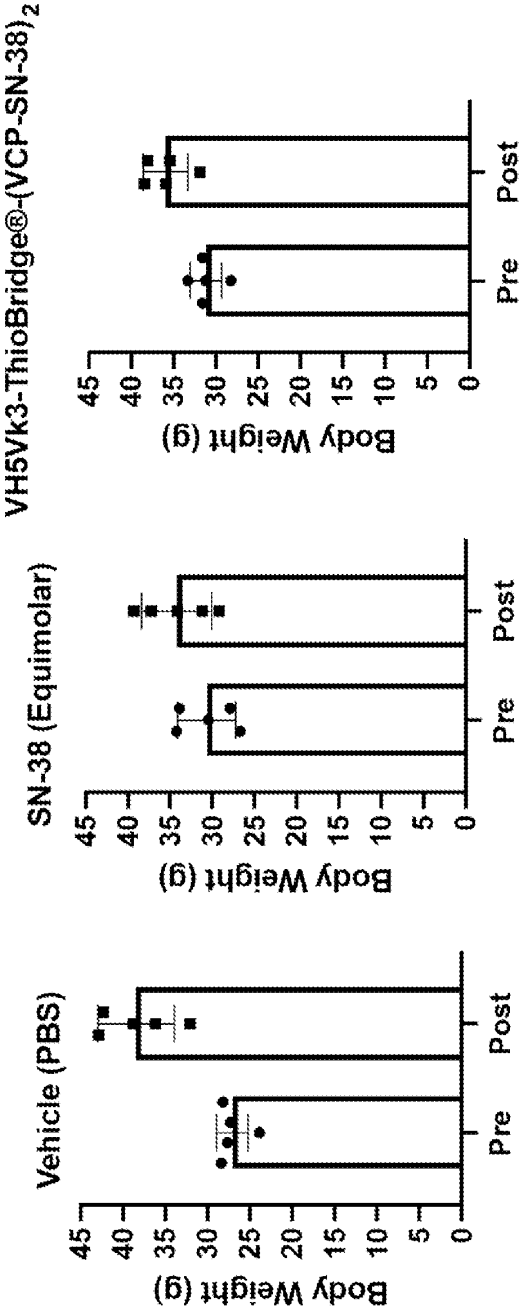


FIG. 93

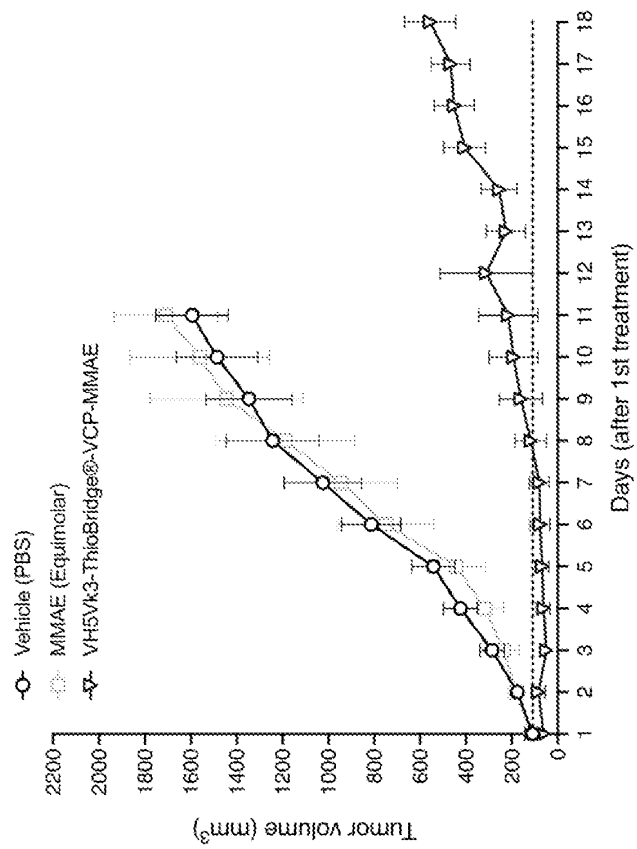


FIG. 94

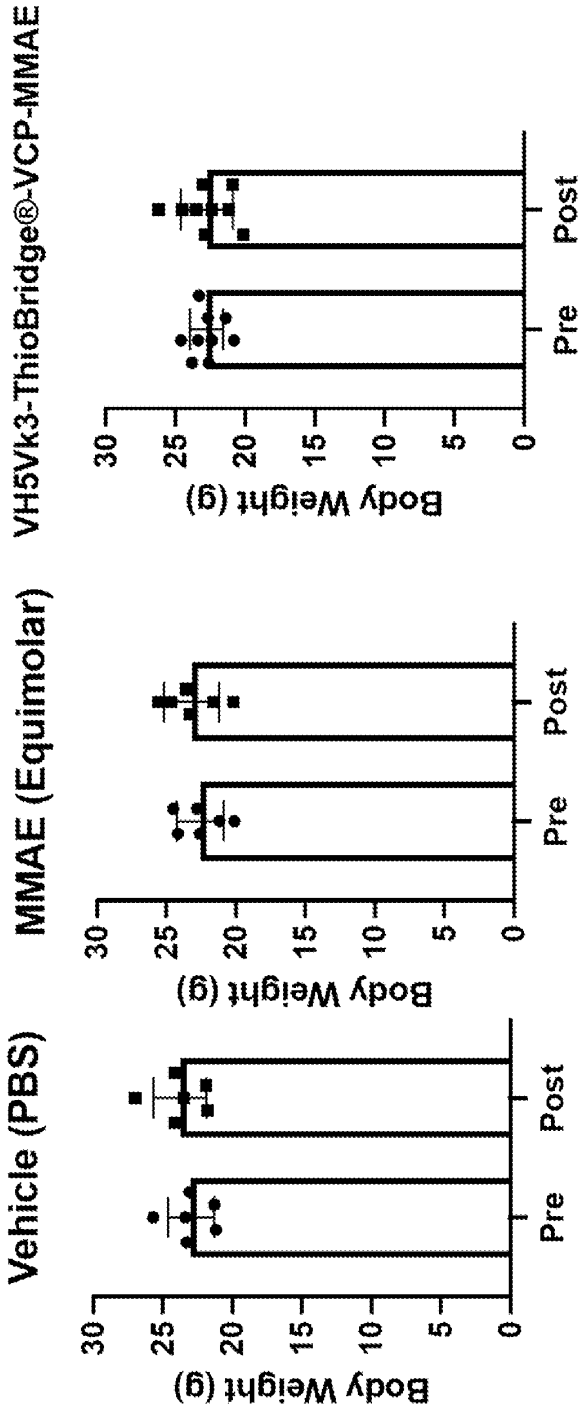


FIG. 95

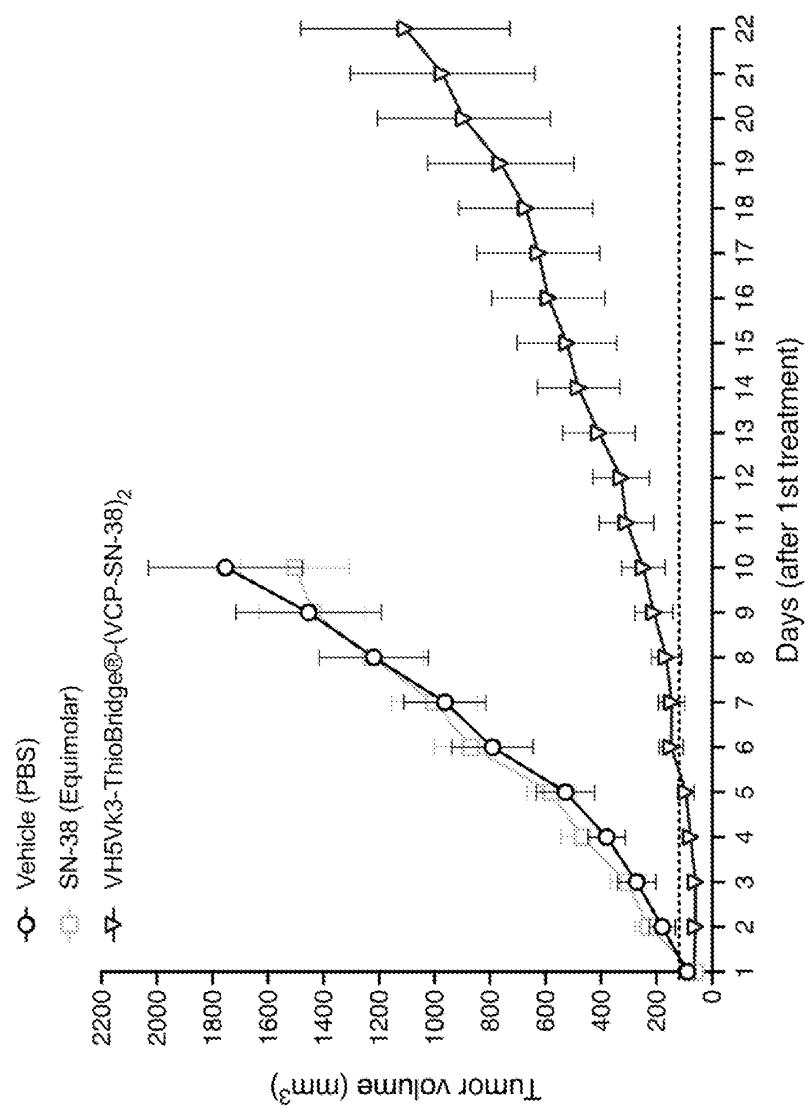


FIG. 96

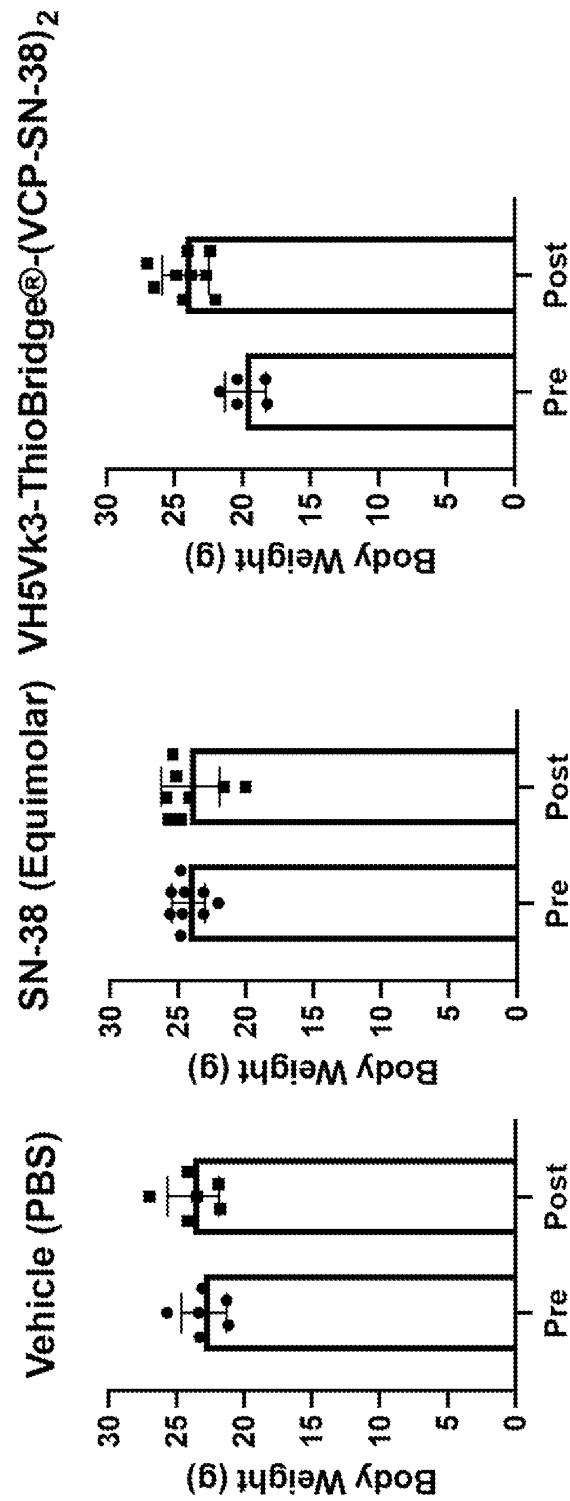
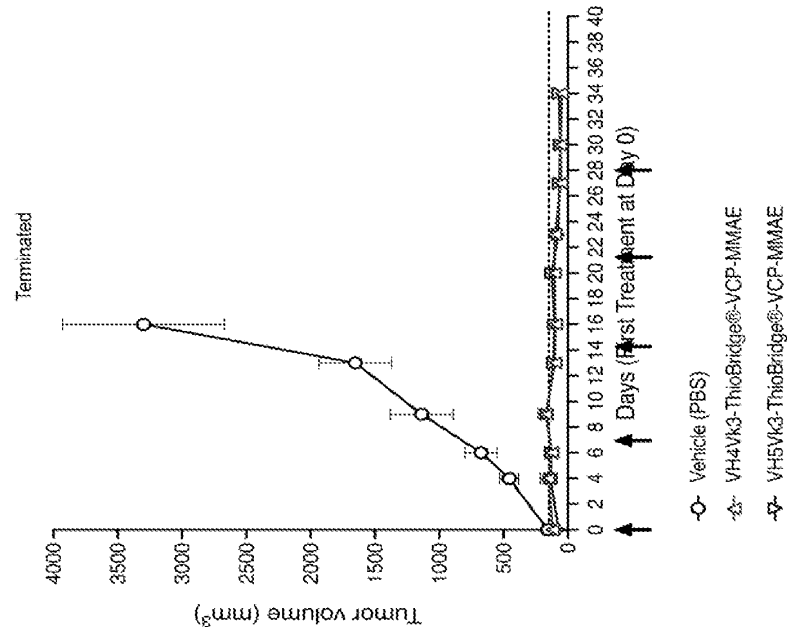


FIG. 97

5 doses (10mg/kg) of MMAE-conjugates
(1 dose/week)



EphA5 expression 2+

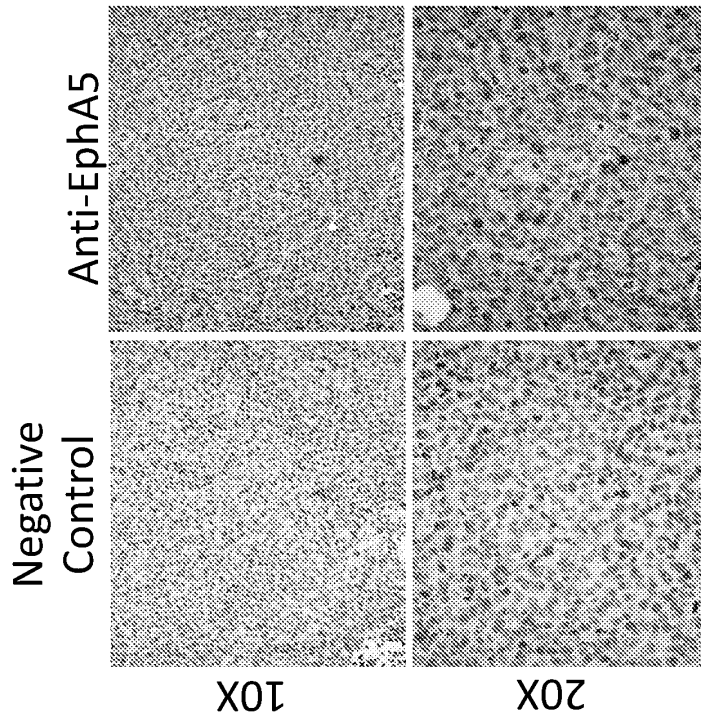


FIG. 98

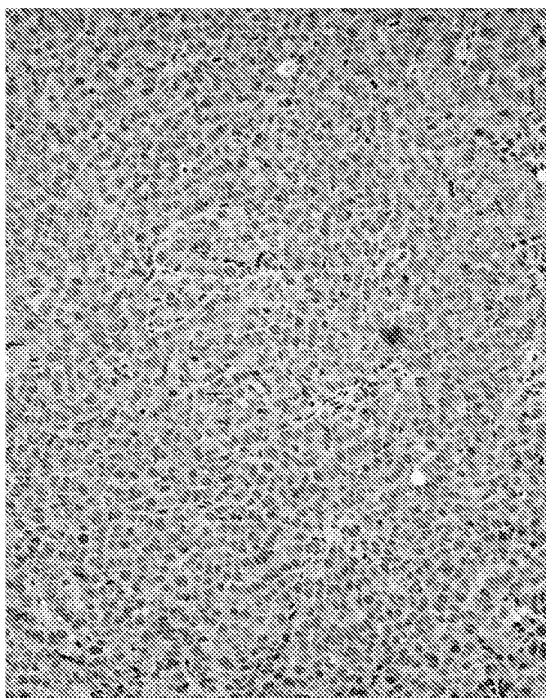


FIG. 99B



FIG. 99A

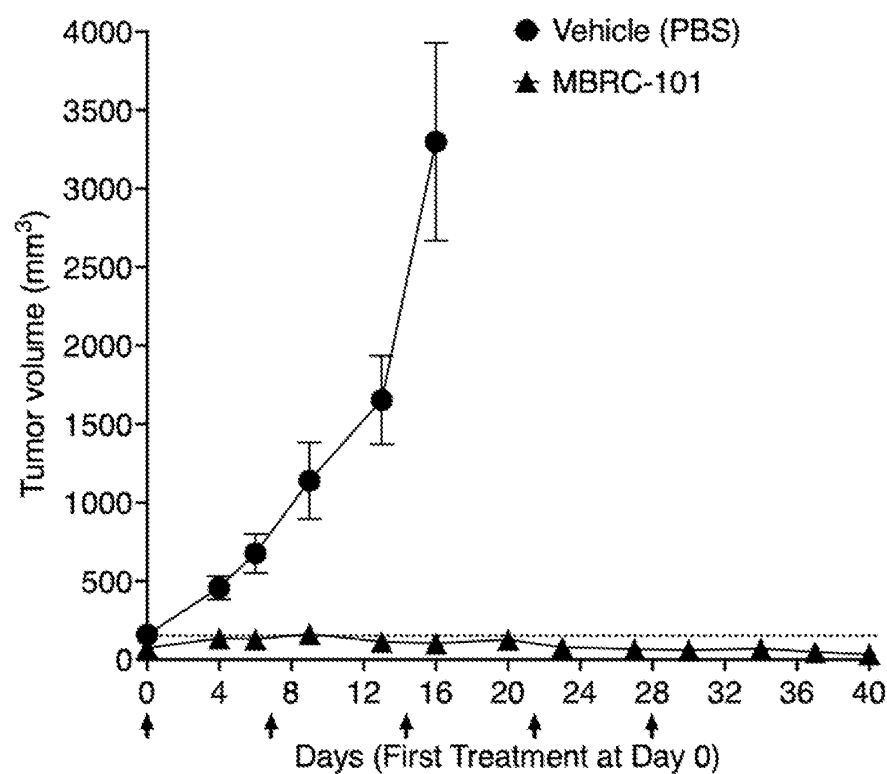


FIG. 100

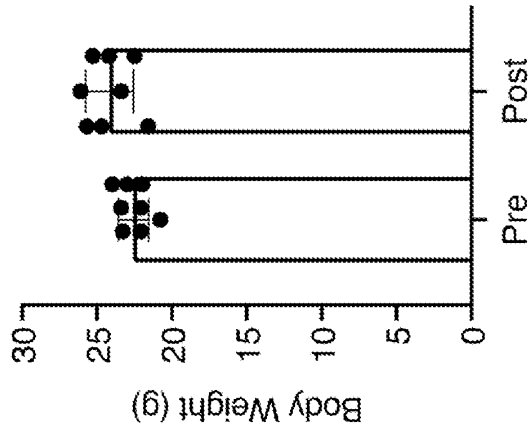


FIG. 101B

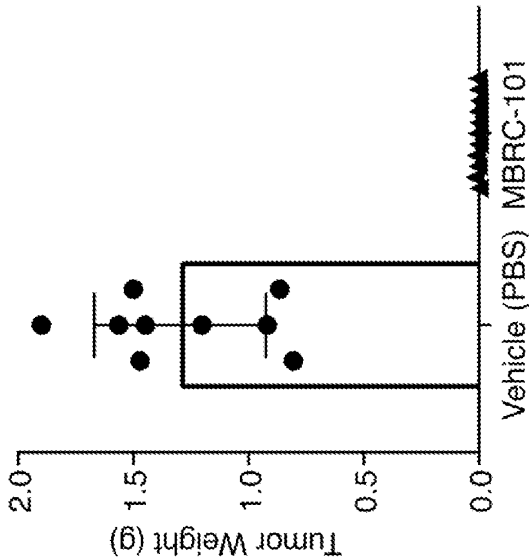


FIG. 101A

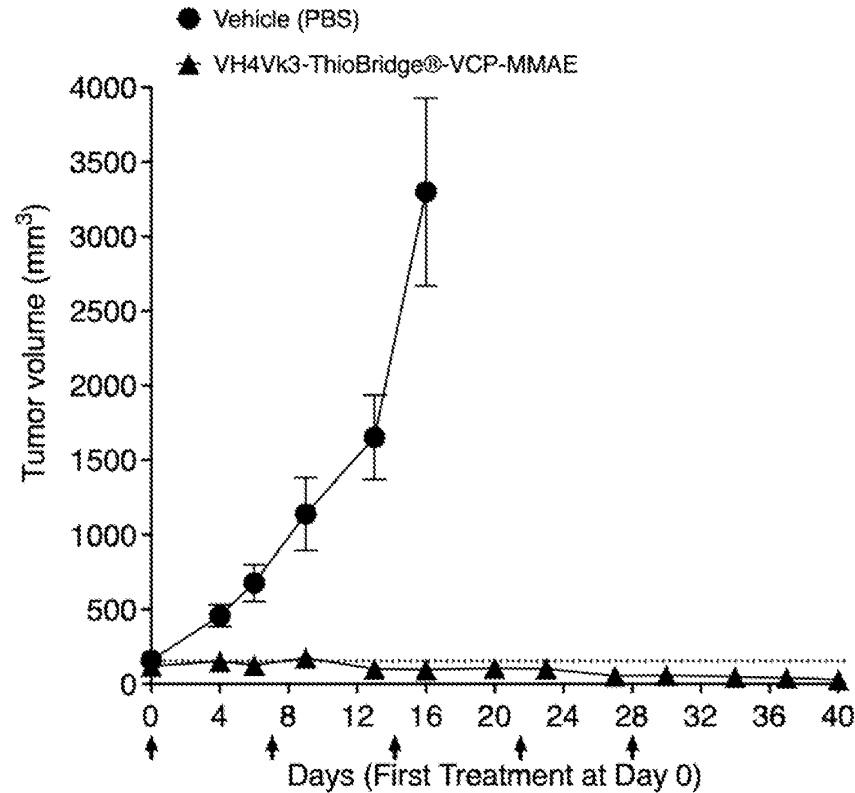


FIG. 102

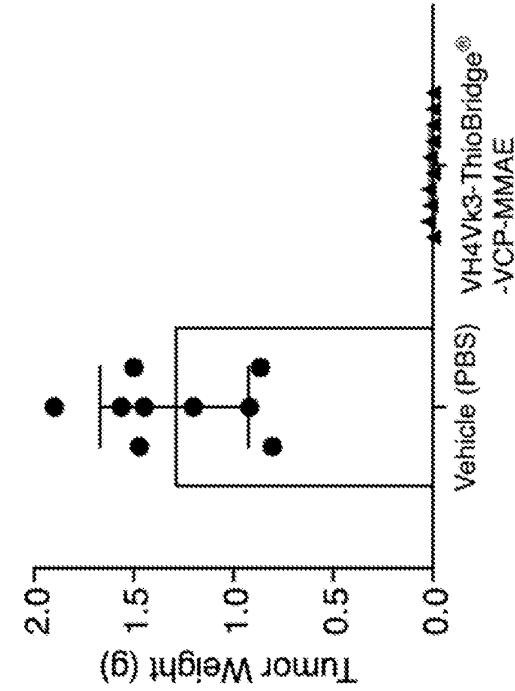


FIG. 103A

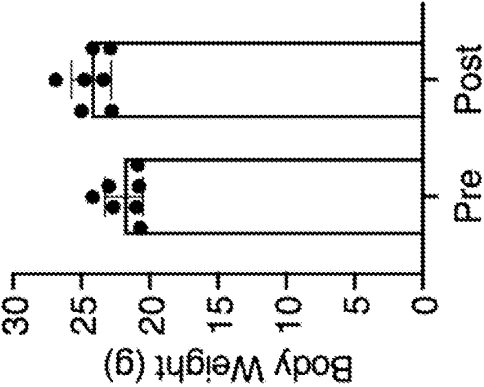


FIG. 103B

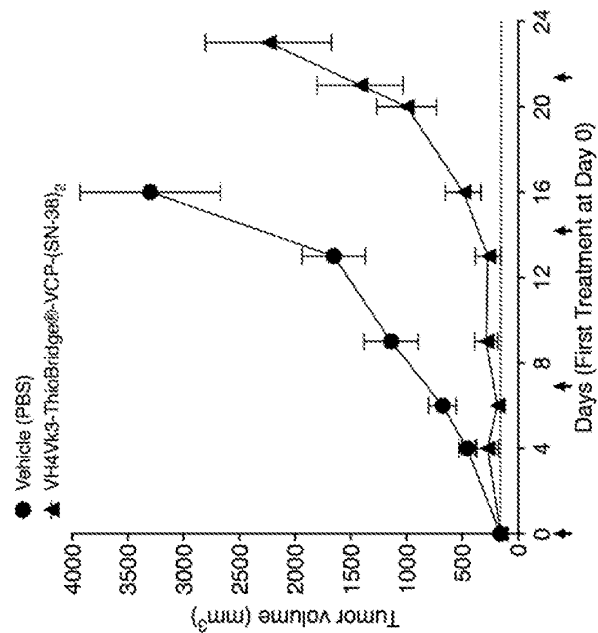


FIG. 104B

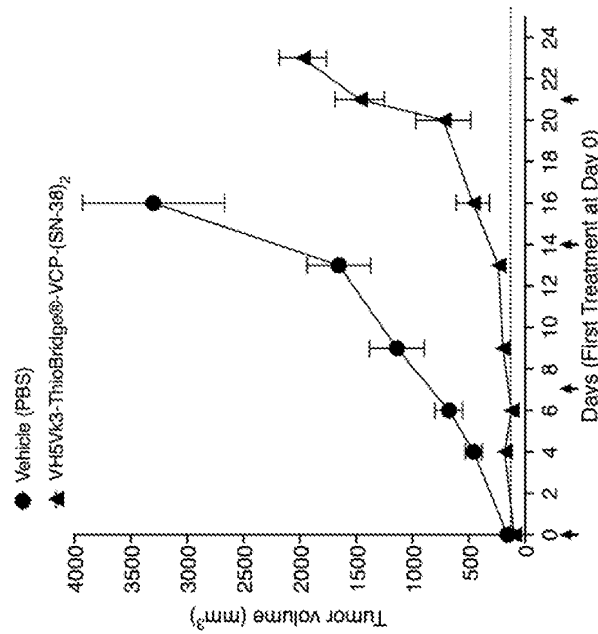


FIG. 104A

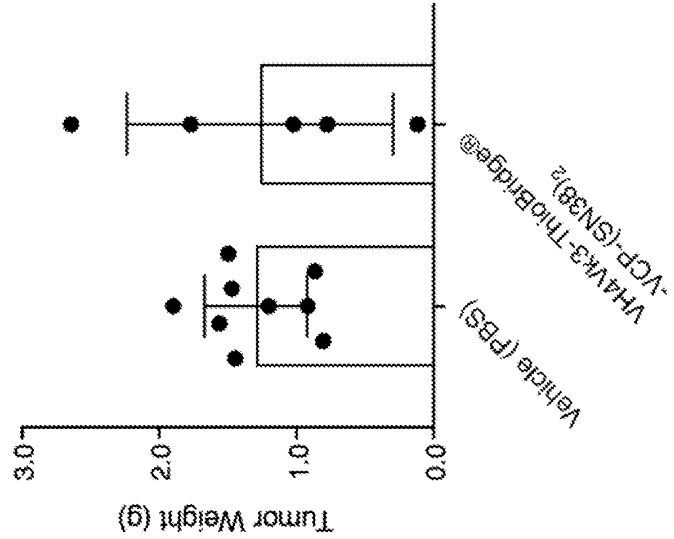


FIG. 105B

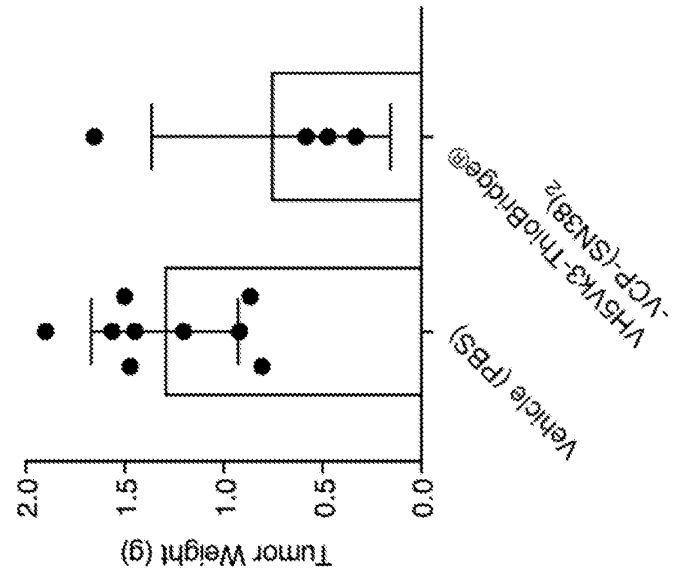


FIG. 105A

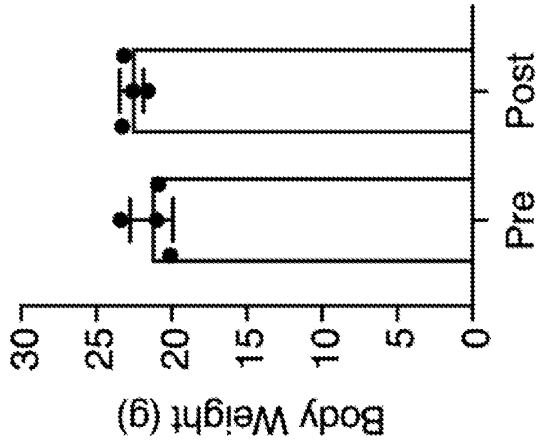


FIG. 106A

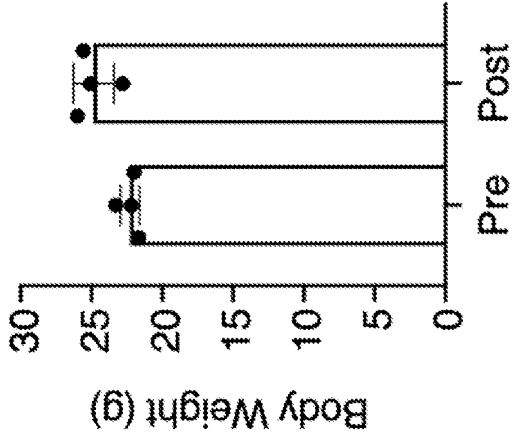


FIG. 106B



FIG. 107B

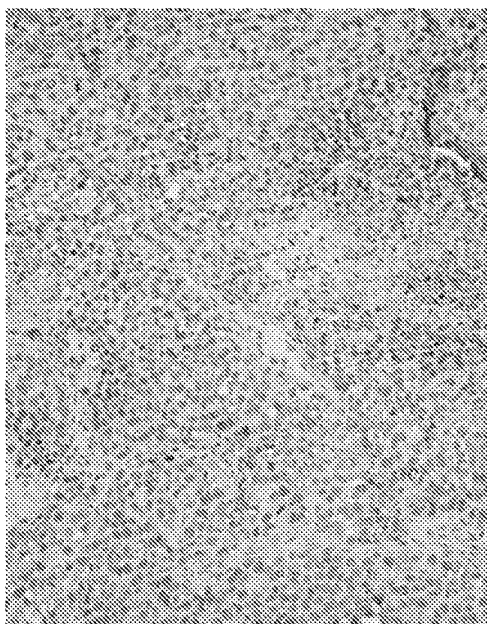


FIG. 107A

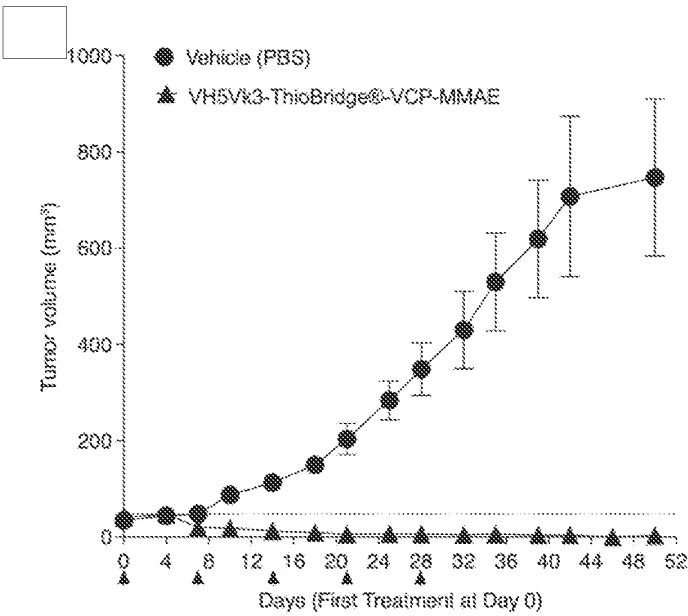


FIG. 108A

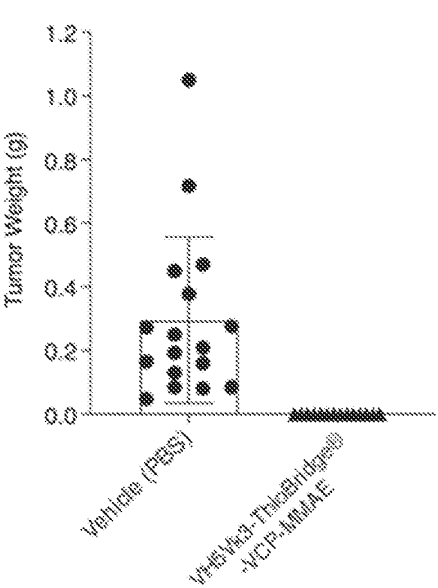


FIG. 108B

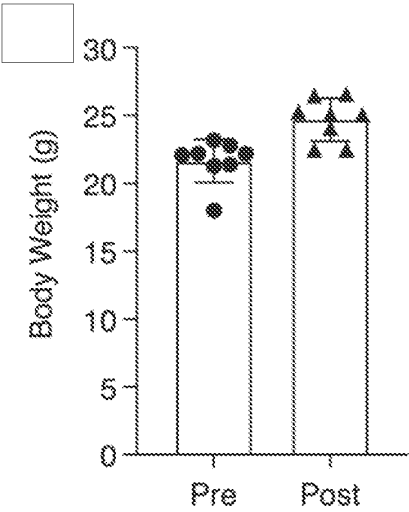


FIG. 108C

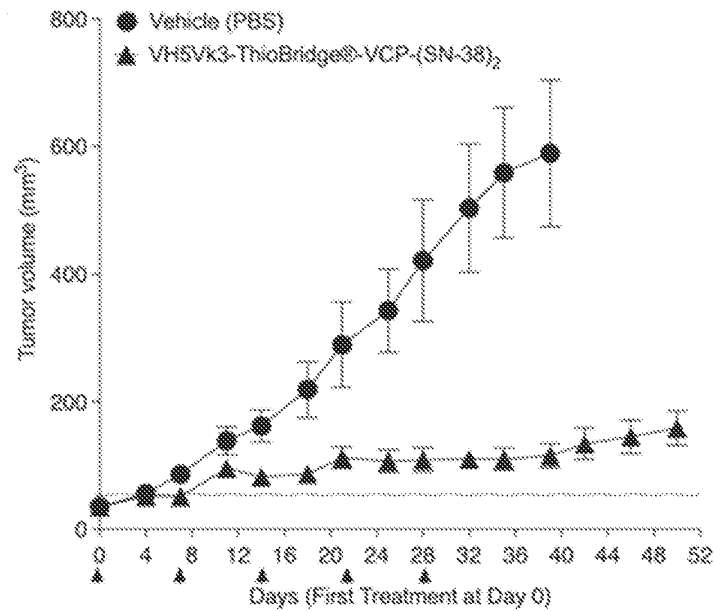


FIG. 109A

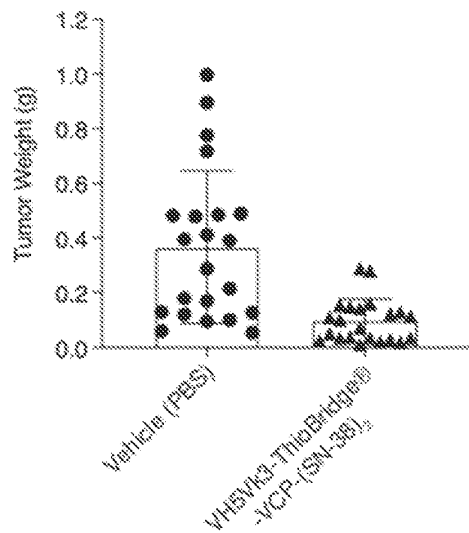


FIG. 109B

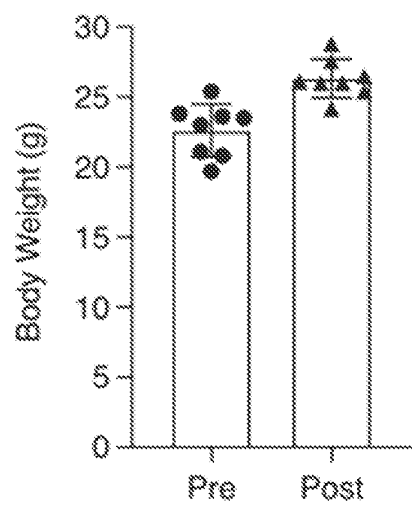


FIG. 109C

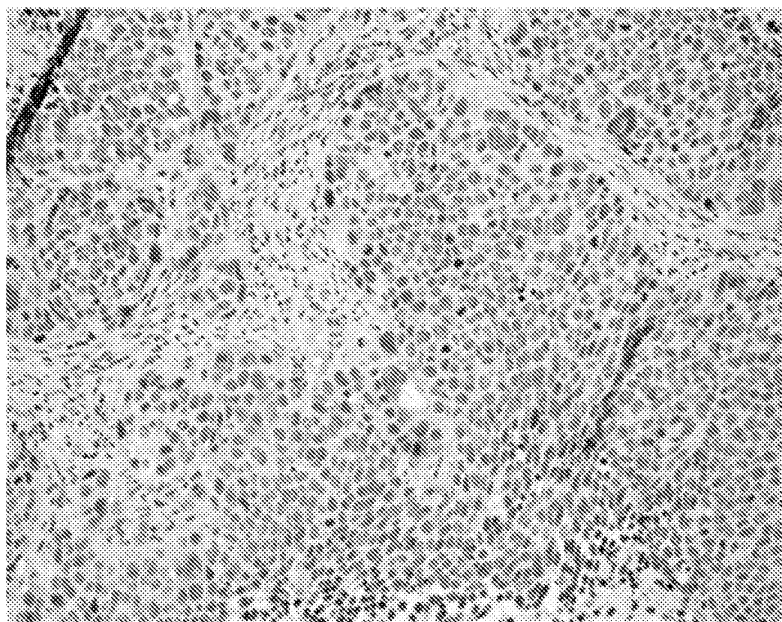


FIG. 110A

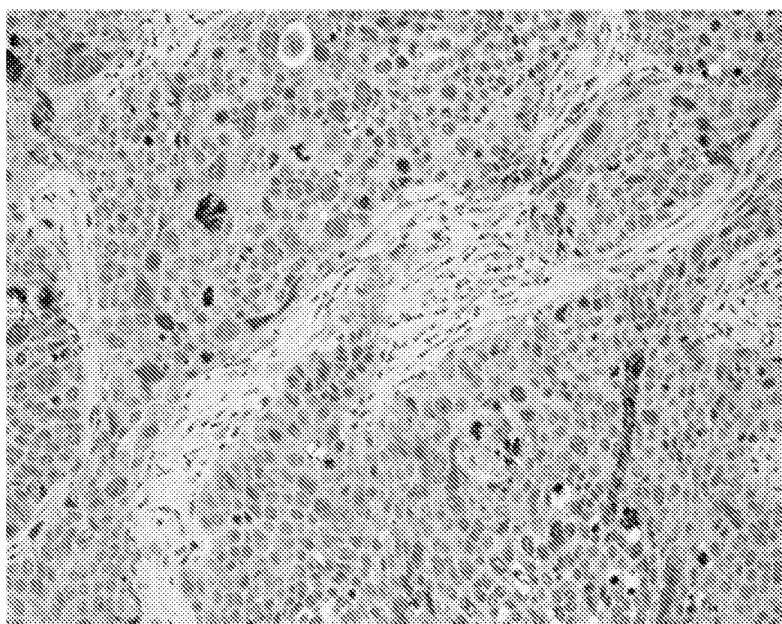


FIG. 110B

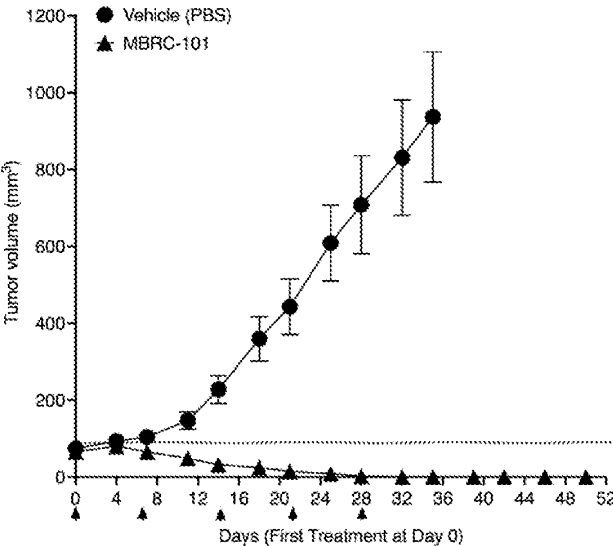


FIG. 111A

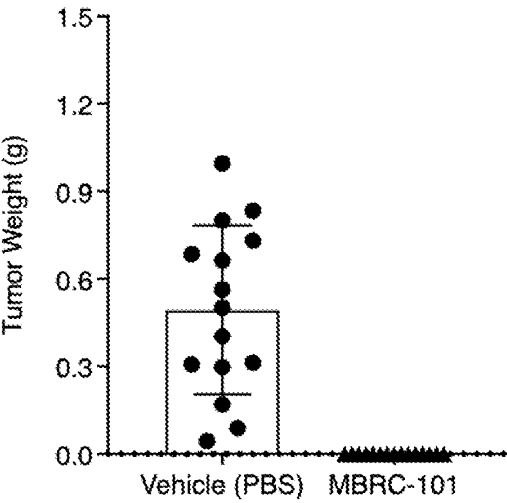


FIG. 111B

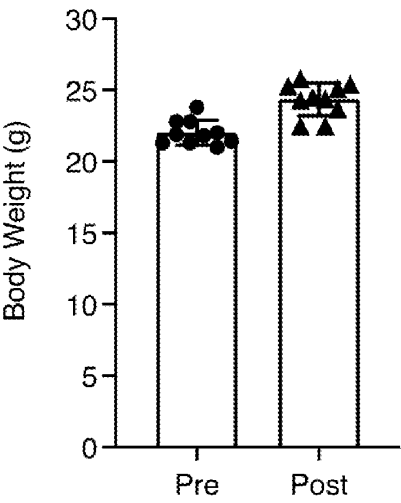


FIG. 111C

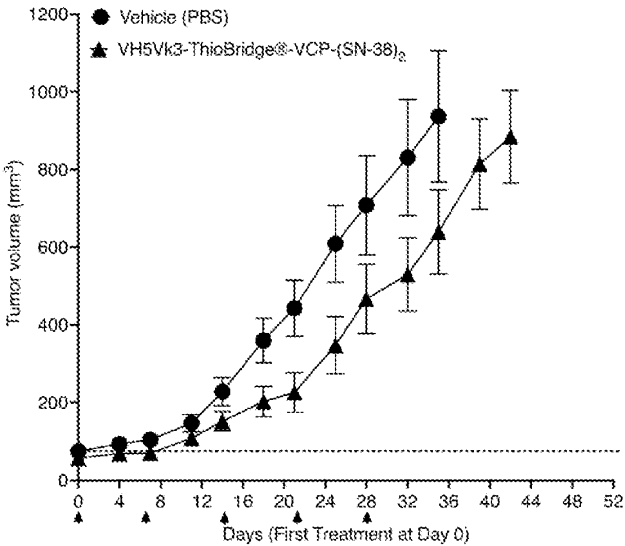


FIG. 112A

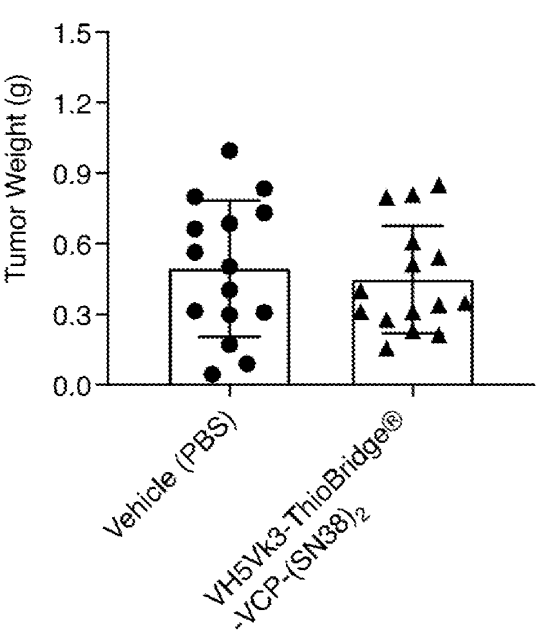


FIG. 112B

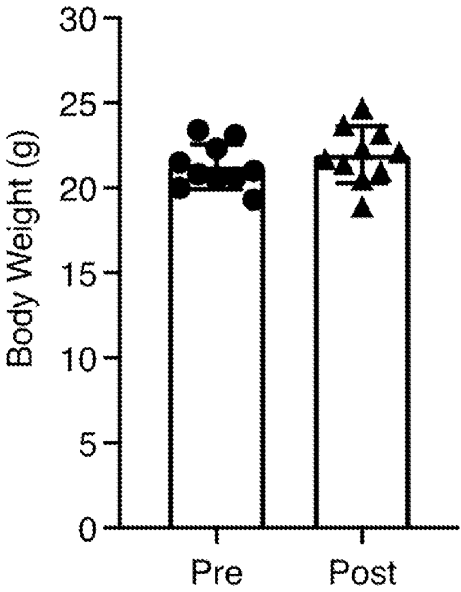


FIG. 112C

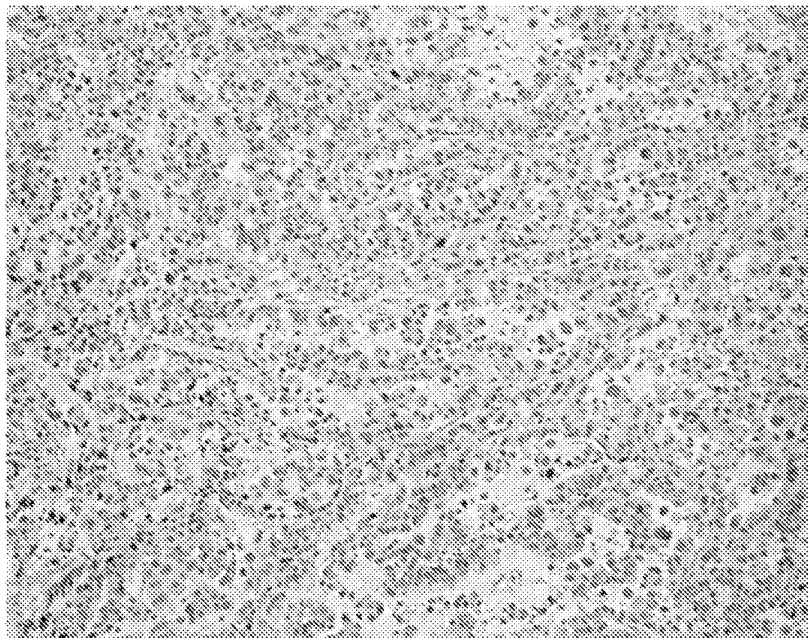


FIG. 113A

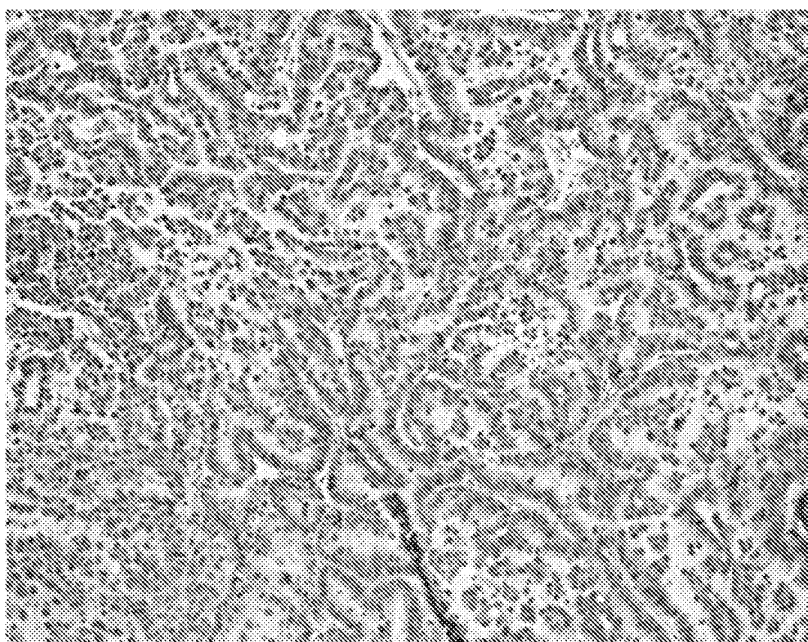


FIG. 113B

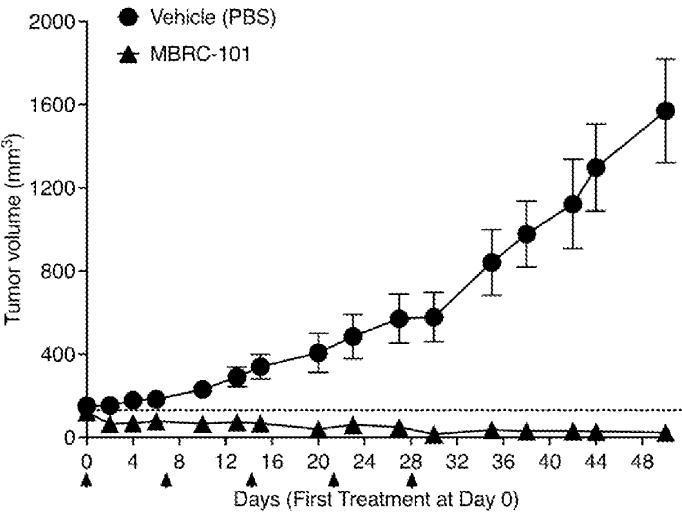


FIG. 114A

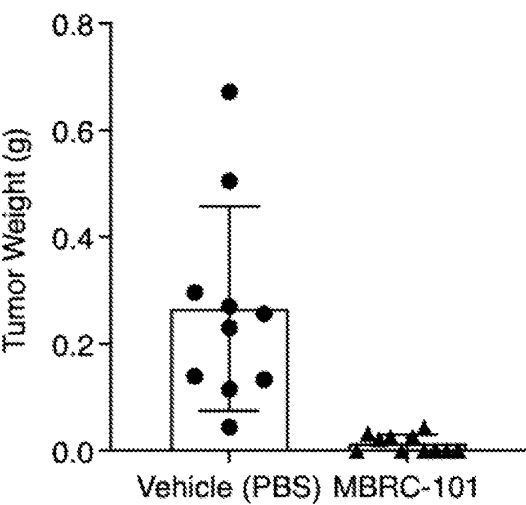


FIG. 114B

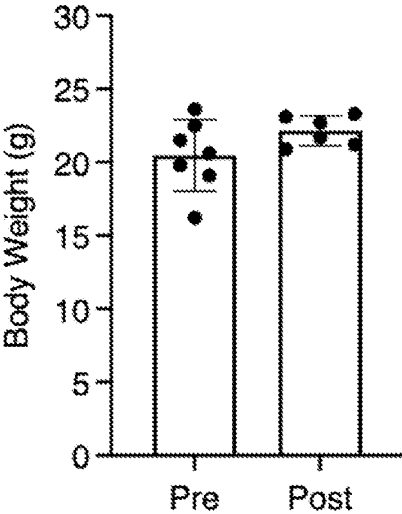


FIG. 114C

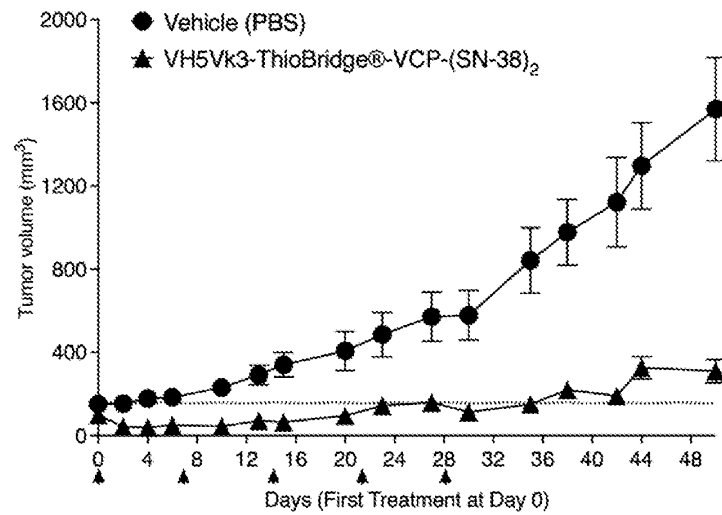


FIG. 115A

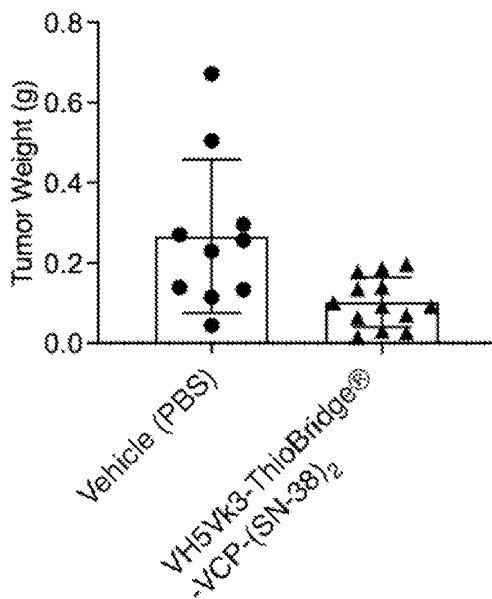


FIG. 115B

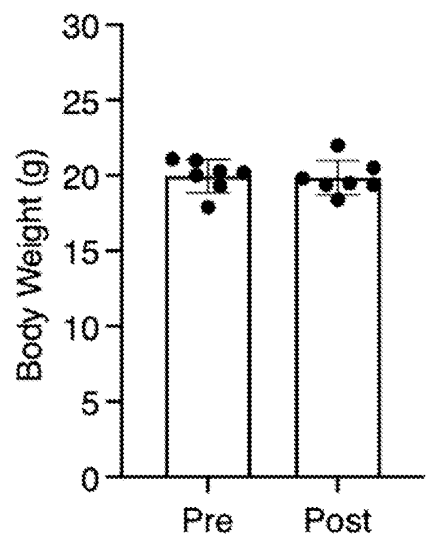


FIG. 115C

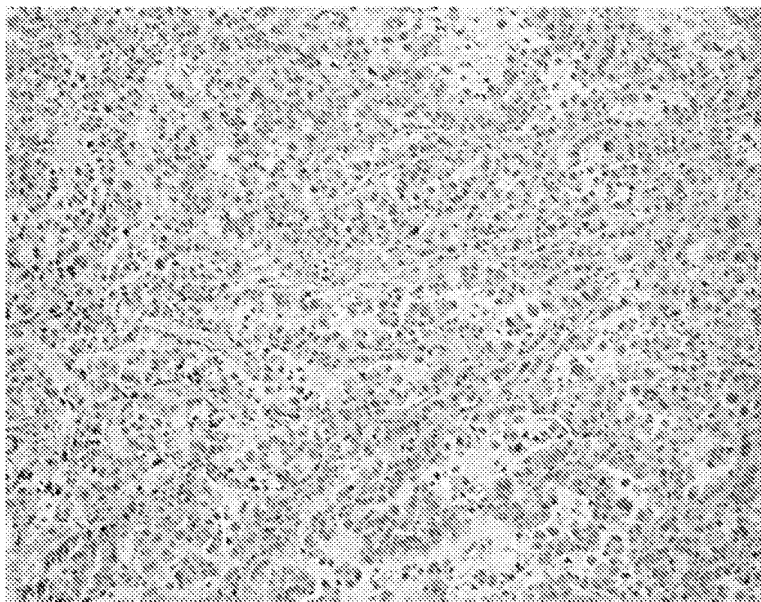


FIG. 116A

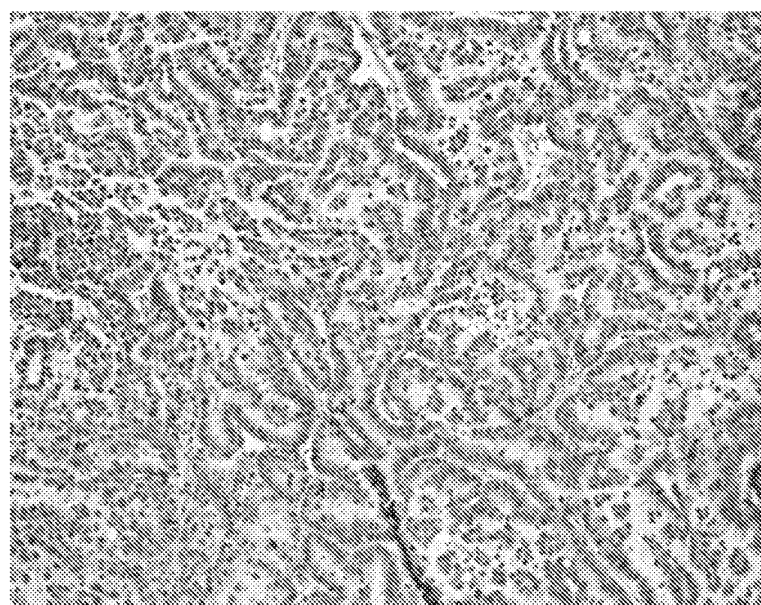


FIG. 116B

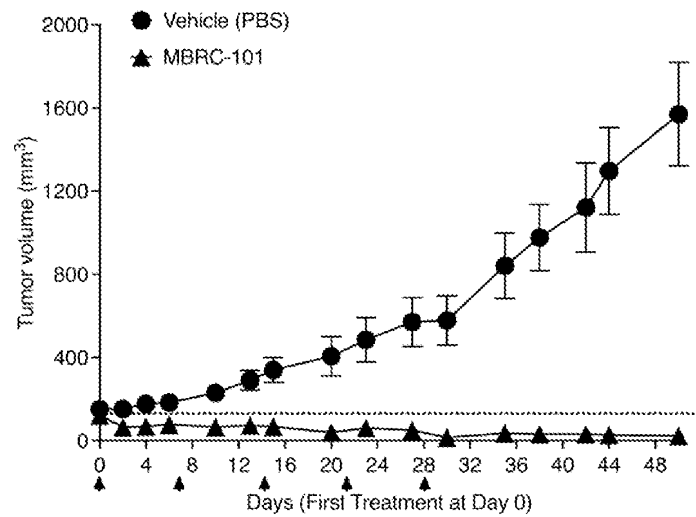


FIG. 117A

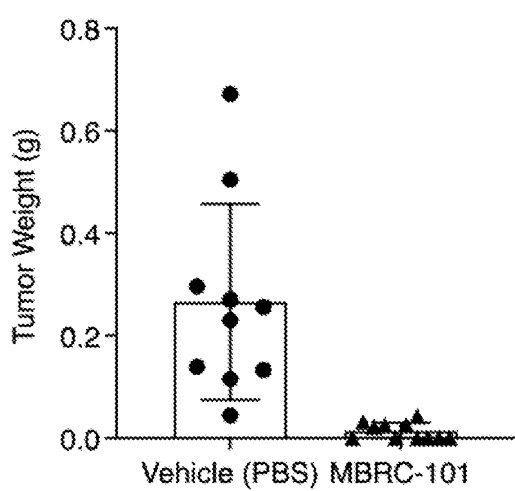


FIG. 117B

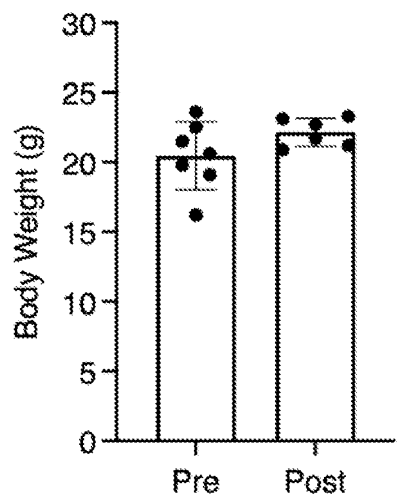


FIG. 117C

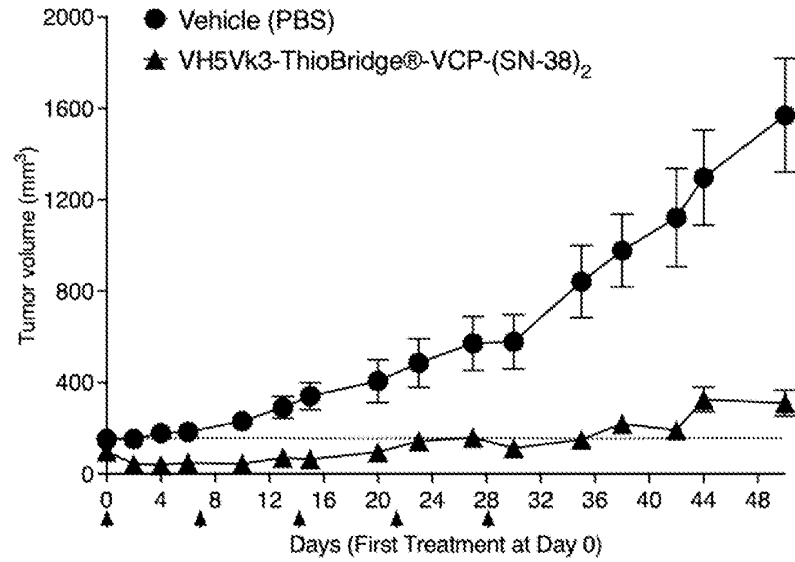


FIG. 118A

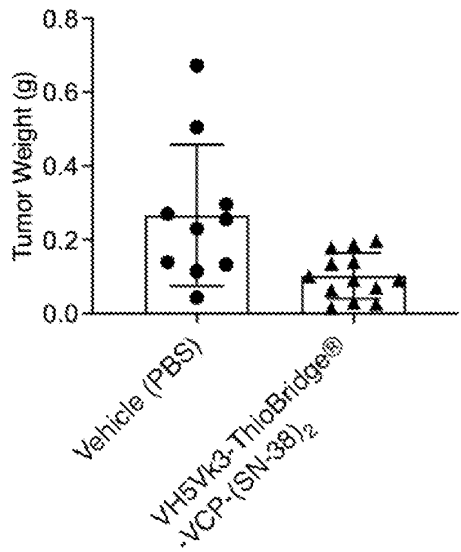


FIG. 118B

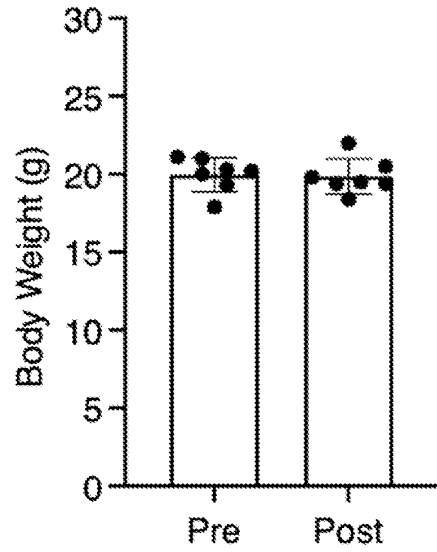


FIG. 118C