	Sample	H75 concentration (mg/mL) Turbidity (A330) *Visual appearance** pH														
		t=0	−70°C		2–8°C				25°C				45°C		F/T	2–8°C
			t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	5 cycle	Shake 3 day
10mM Histidine	150mM Arginine, 150mM Glutamic acid, 0.01% PS20, pH 6.1	159 0.703 C,Y,NP 6.13	151 0.785 C,Y,NP 6.14	154 0.694 C,Y,NP 6.15	160 0.704 C,Y,NP 6.12	159 0.700 C,Y,NP 6.16	148 0.745 C,Y,NP 6.16	141 0.709 C,Y,NP 6.15	159 0.763 C,Y,NP 6.12	150 0.763 C,Y,NP 6.15	149 0.838 C,Y,NP 6.16	142 0.833 C,Y,NP 6.14	156 0.837 C,Y,NP 6.13	157 0.920 C,Y,NP 6.14	150 0.684 C,Y,NP 6.14	147 0.655 C,Y,NP 6.13
	55mM Arginine, 55mM Glutamic acid, 3% Sorbitol, 0.01% PS20, pH 6.3	162 0.708 C,Y,NP 6.34	145 0.729 C,Y,NP 6.35	146 0.720 C,Y,NP 6.34	151 0.739 C,Y,NP 6.31	158 0.733 C,Y,NP 6.34	155 0.725 C,Y,NP 6.34	148 0.731 C,Y,NP 6.33	167 0.721 C,Y,NP 6.33	158 0.840 C,Y,NP 6.31	155 0.834 C,Y,NP 6.33	150 0.842 C,Y,NP 6.31	156 0.854 C,Y,NP 6.3	147 0.969 C,Y,P 6.33	153 0.699 C,Y,NP 6.32	144 0.678 C,Y,NP 6.34
	150mM Arginine, 150mM Glutamic acid, 0.01% PS20, pH 6.3	162 0.753 C,Y,NP 6.36	154 0.778 C,Y,NP 6.32	150 0.758 C,Y,NP 6.34	157 0.759 C,Y,NP 6.31	163 0.756 C,Y,NP 6.34	155 0.790 C,Y,NP 6.34	149 0.758 C,Y,NP 6.34	165 0.768 C,Y,NP 6.32	168 0.797 C,Y,NP 6.31	154 0.867 C,Y,NP 6.35	149 0.936 C,Y,NP 6.34	166 0.891 C,Y,NP 6.32	152 1.081 C,Y,P 6.33	163 0.746 C,Y,NP 6.32	158 0.707 C,Y,NP 6.35
	75mM Arginine, 3% Sorbitol, 0.01% PS20, pH 6.1	165 0.753 C,Y,NP 6.14	152 0.795 C,Y,NP 6.15	154 0.763 C,Y,NP 6.14	171 0.758 C,Y,NP 6.12	169 0.763 C,Y,NP 6.15	156 0.793 C,Y,NP 6.13	148 0.763 C,Y,NP 6.13	167 0.750 C,Y,NP 6.11	174 0.847 C,Y,NP 6.11	157 0.843 C,Y,NP 6.12	156 0.838 C,Y,NP 6.12	160 0.961 C,Y,NP 6.09	159 1.024 C,Y,NP 6.13	160 0.735 C,Y,NP 6.13	158 0.702 C,Y,NP 6.14

FIG. 1

SE-UPLC (% Purity) *HMW* Main Peak LMW																
Sample Composition		t=0	−70°C		2–8°C			25°C				45°C		F/T 5 cycles	2–8°C Shake 3 day
			t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	t=6 weeks	t=12 weeks	t=1 week	t=3 weeks		
150mM Arginine, 150mM Glutamic acid, 0.01% PS20, pH 6.1		3.0	3.2	3.3	3.3	3.4	3.4	3.4	3.3	3.3	3.6	3.7	3.7	4.4	3.2	3.1
		96.8	96.7	96.6	96.6	96.5	96.6	96.5	96.6	96.5	96.3	96.2	96.2	95.4	96.7	96.5
		0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.1	0.2	0.1	0.4
10mM Histidine	55mM Arginine, 55mM Glutamic acid, 3% Sorbitol, 0.01% PS20, pH 6.3	3.0	3.2	3.3	3.3	3.4	3.4	3.6	3.5	3.6	3.7	3.9	4.0	4.6	3.2	3.2
		96.8	96.7	96.6	96.7	96.6	96.5	96.4	96.4	96.2	96.2	96.0	96.0	95.2	96.7	96.6
		0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1
	150mM Arginine, 150mM Glutamic acid, 0.01% PS20, pH 6.3	2.9	3.1	3.3	3.3	3.4	3.4	3.5	3.4	3.4	3.5	3.9	3.8	4.3	3.2	3.2
		96.7	96.8	96.6	96.6	96.6	96.6	96.5	96.5	96.5	96.4	96.0	96.1	95.3	96.7	96.7
		0.3	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.5	0.1	0.2
	75mM Arginine, 3% Sorbitol, 0.01% PS20, pH 6.1	3.0	3.2	3.4	3.3	3.3	3.5	3.4	3.5	3.5	3.7	4.0	4.1	4.3	3.3	3.2
		96.8	96.7	96.5	96.6	96.6	96.5	96.5	96.4	96.4	96.2	95.9	95.8	95.4	96.7	96.7
		0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.1	0.3	0.1	0.1

FIG.2

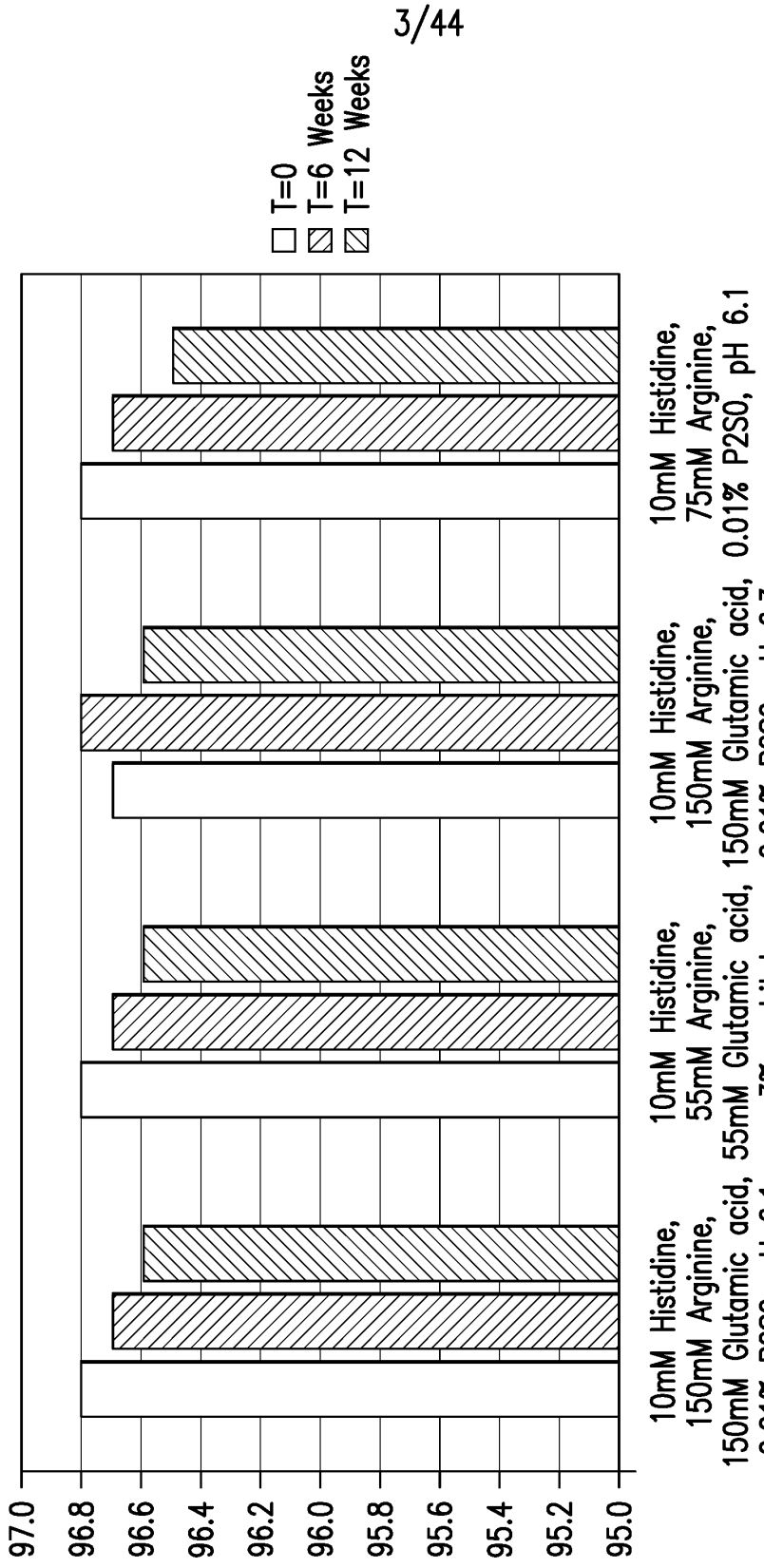

T=0
T=6 Weeks
T=12 Weeks
97.0
96.8
96.6
96.4
96.2
96.0
95.8
95.6
95.4
95.2
95.0
10mM Histidine, 150mM Arginine, 150mM Glutamic acid, 0.01% P2S0, pH 6.1
10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 3% sorbitol, 0.01% PS20, pH 6.3
10mM Histidine, 150mM Arginine, 150mM Glutamic acid, 0.01% P2S0, pH 6.3
10mM Histidine, 75mM Arginine, 0.01% P2S0, pH 6.1

FIG.3

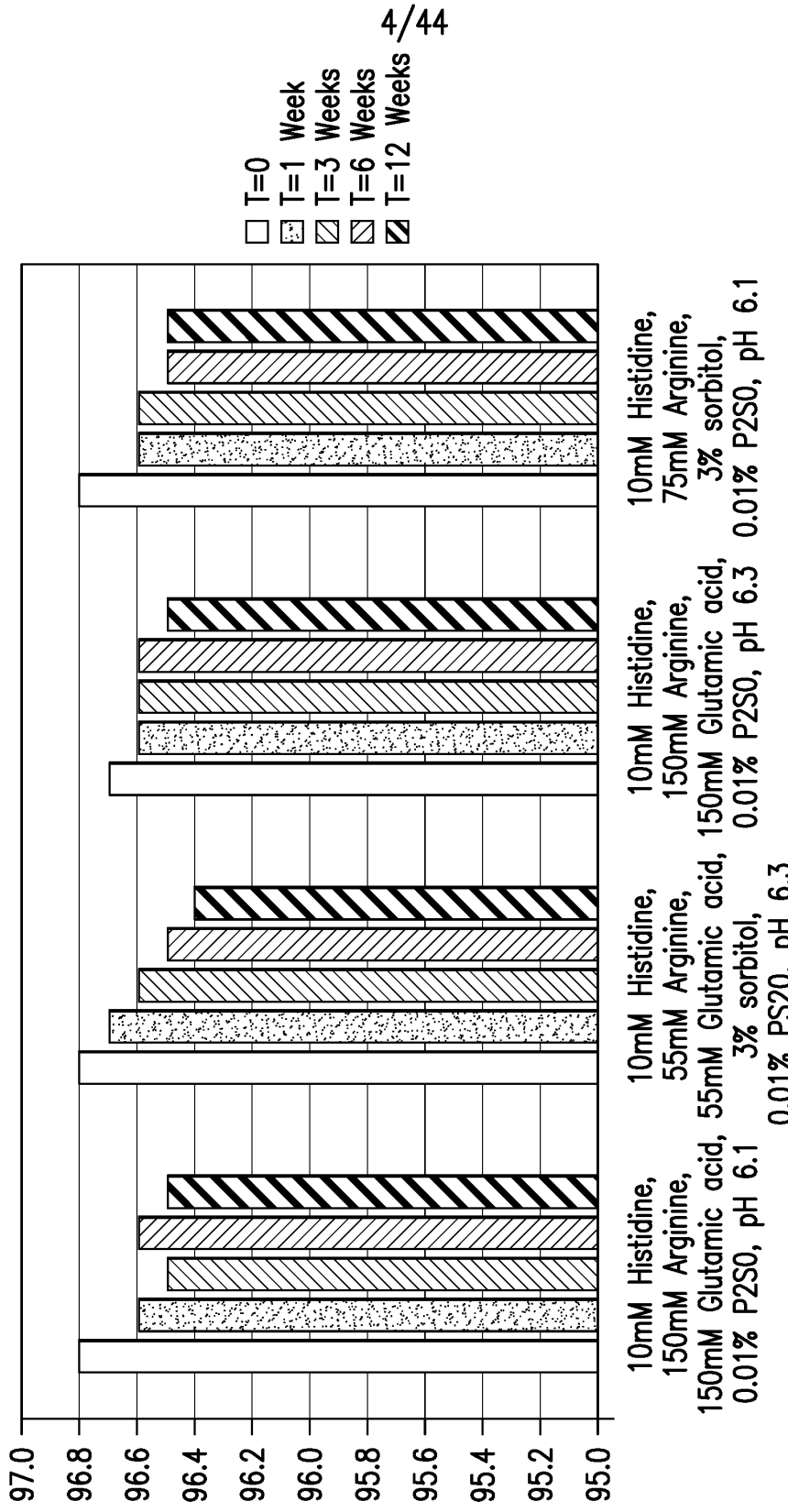

T=0
T=1 Week
T=3 Weeks
T=6 Weeks
T=12 Weeks
97.0
96.8
96.6
96.4
96.2
96.0
95.8
95.6
95.4
95.2
95.0
10mM Histidine, 150mM Arginine, 150mM Glutamic acid, 0.01% P2S0, pH 6.1
10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 3% sorbitol, 0.01% PS20, pH 6.3
10mM Histidine, 150mM Arginine, 150mM Glutamic acid, 0.01% P2S0, pH 6.3
10mM Histidine, 75mM Arginine, 3% sorbitol, 0.01% P2S0, pH 6.1

FIG.4

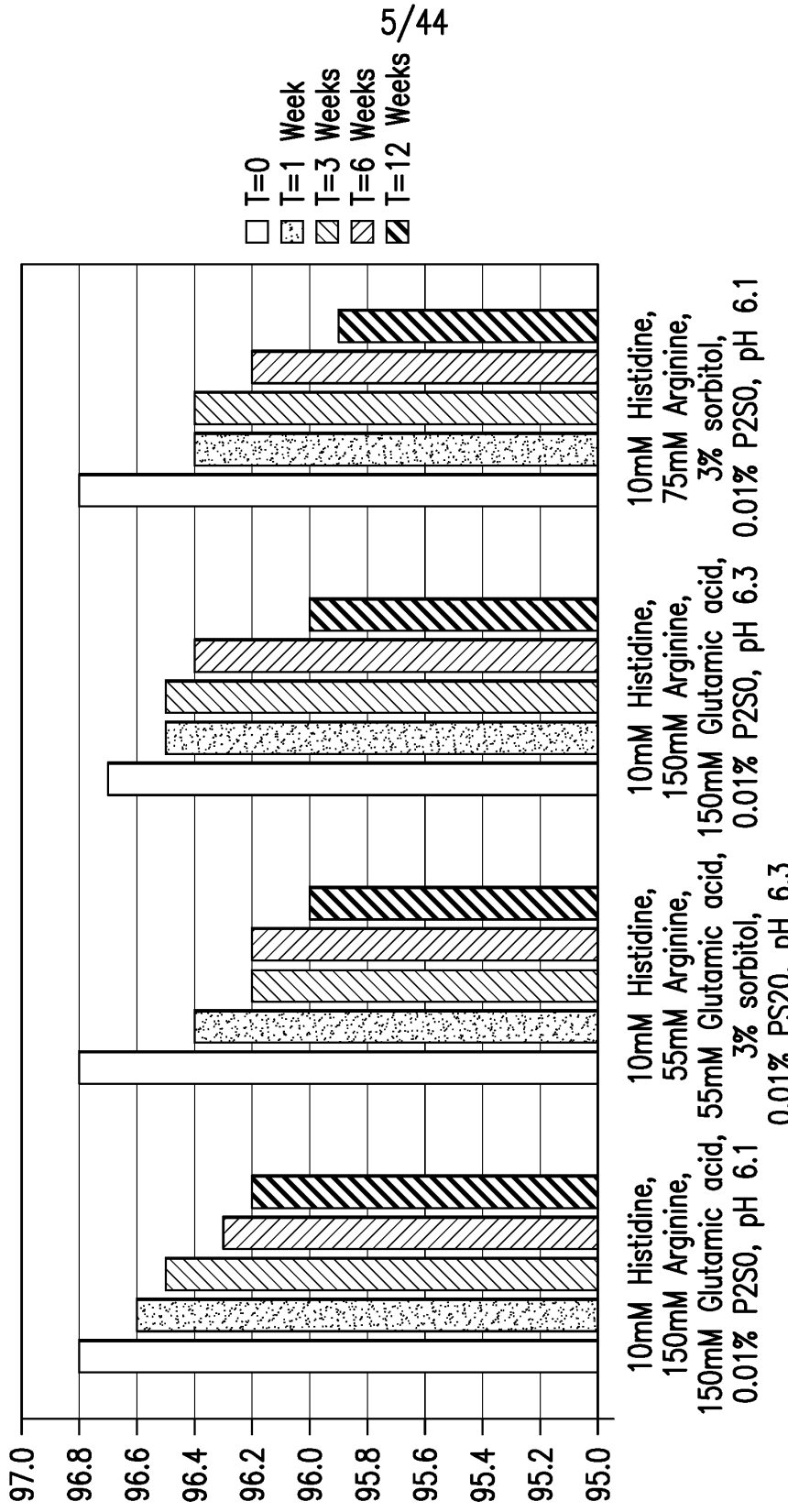

T=0
T=1 Week
T=3 Weeks
T=6 Weeks
T=12 Weeks
97.0
96.8
96.6
96.4
96.2
96.0
95.8
95.6
95.4
95.2
95.0
10mM Histidine, 150mM Arginine, 150mM Glutamic acid, 0.01% P2S0, pH 6.1
10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 3% sorbitol, 0.01% PS20, pH 6.3
10mM Histidine, 150mM Arginine, 150mM Glutamic acid, 0.01% P2S0, pH 6.3
10mM Histidine, 75mM Arginine, 3% sorbitol, 0.01% P2S0, pH 6.1

FIG.5

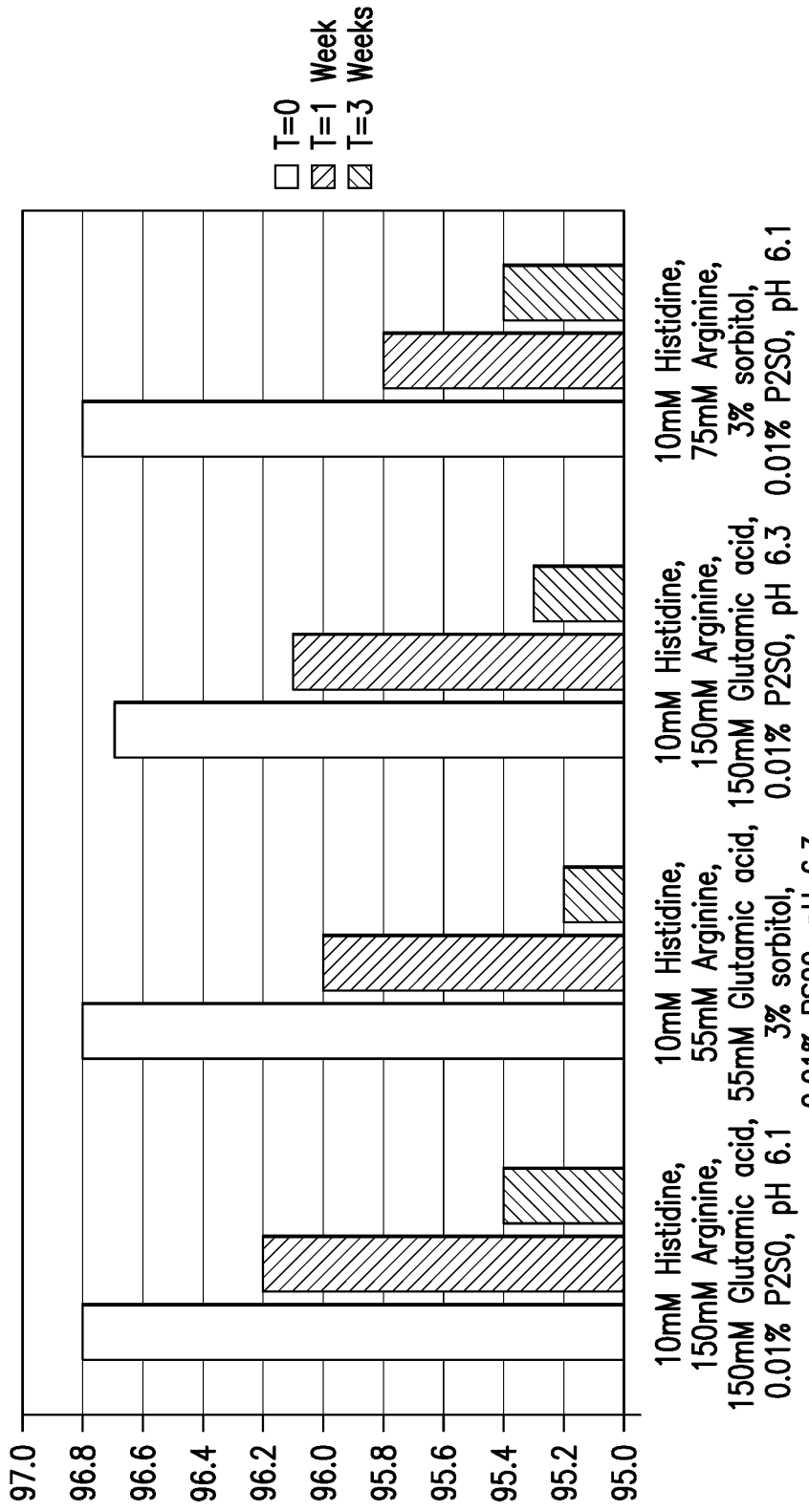

T=0
T=1 Week
T=3 Weeks
97.0
96.8
96.6
96.4
96.2
96.0
95.8
95.6
95.4
95.2
95.0
10mM Histidine, 150mM Arginine, 150mM Glutamic acid, 0.01% P2S0, pH 6.1
10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 3% sorbitol, 0.01% PS20, pH 6.3
10mM Histidine, 150mM Arginine, 150mM Glutamic acid, 0.01% P2S0, pH 6.3
10mM Histidine, 75mM Arginine, 3% sorbitol, 0.01% P2S0, pH 6.1

FIG.6

Sample Composition		(% Purity) *Acidic* Main Peak Basic													
		t=0	−70°C		2–8°C			25°C				45°C		F/T 5 cycle	2–8°C Shake 3 day
			t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	
150mM Arginine, 150mM Glutamic acid, 0.01% PS20, pH 6.1		21.7	21.8	21.8	21.8	22.0	21.9	22.1	22.0	22.8	24.5	28.3	26.7	37.4	21.7	21.6
		63.3	63.3	63.3	63.2	63.1	63.2	63.3	63.2	62.6	61.4	58.5	59.1	49.8	63.3	63.5
		15.1	14.9	14.9	15.0	14.9	14.9	14.7	14.9	14.6	14.0	13.2	14.3	12.8	15.0	14.9
10mM Histidine	55mM Arginine, 55mM Glutamic acid, 3% Sorbitol, 0.01% PS20, pH 6.3	21.9	21.9	21.9	21.9	22.0	22.2	22.3	22.1	23.2	25.1	29.0	27.4	38.9	21.8	21.7
		63.2	63.2	63.3	63.2	63.1	63.1	63.3	63.0	62.5	61.1	58.3	58.6	49.0	63.3	63.4
		14.9	14.9	14.8	14.9	14.9	14.7	14.5	14.8	14.3	13.8	12.7	14.0	12.1	14.9	14.8
	150mM Arginine, 150mM Glutamic acid, 0.01% PS20, pH 6.3	21.6	21.7	21.8	21.9	22.0	22.2	22.3	22.3	23.4	25.3	29.9	27.9	39.8	21.9	21.7
		63.4	63.3	63.3	63.1	63.0	63.1	63.1	62.8	62.2	60.7	57.2	58.1	48.0	63.2	63.4
		15.0	14.9	14.9	15.0	15.0	14.8	14.6	14.8	14.4	13.9	13.0	13.9	12.2	14.9	14.8
	75mM Arginine, 3% Sorbitol, 0.01% PS20, pH 6.1	21.7	21.8	21.8	22.0	22.1	22.1	22.2	21.9	22.8	24.2	27.2	26.0	35.6	21.8	21.8
		63.3	63.3	63.4	63.0	63.0	63.1	63.3	63.1	62.7	61.8	59.5	59.2	51.2	63.2	63.3
		15.1	14.9	14.8	15.0	14.9	14.8	14.5	15.0	14.5	14.0	13.3	14.8	13.2	15.0	14.9

FIG. 7

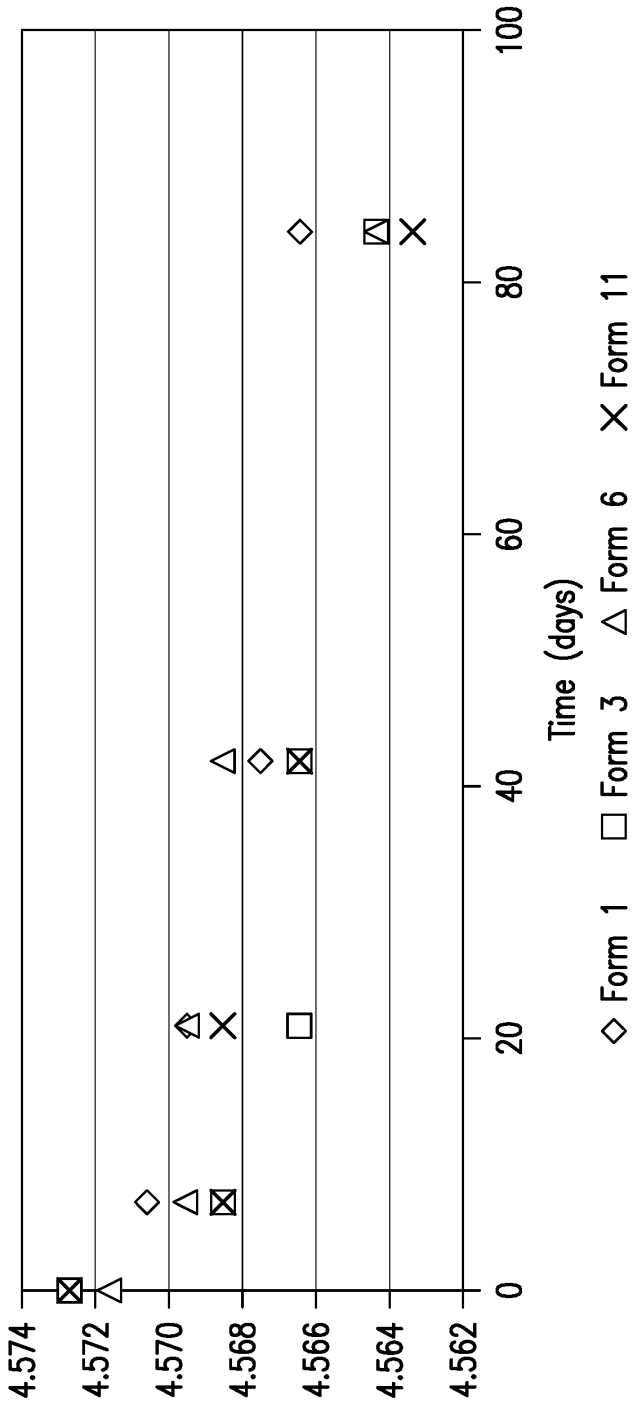

4.574
4.572
4.570
4.568
4.566
4.564
4.562
0
20
40
60
80
100
Time (days)
◇ Form 1
□ Form 3
△ Form 6
× Form 11

FIG.8

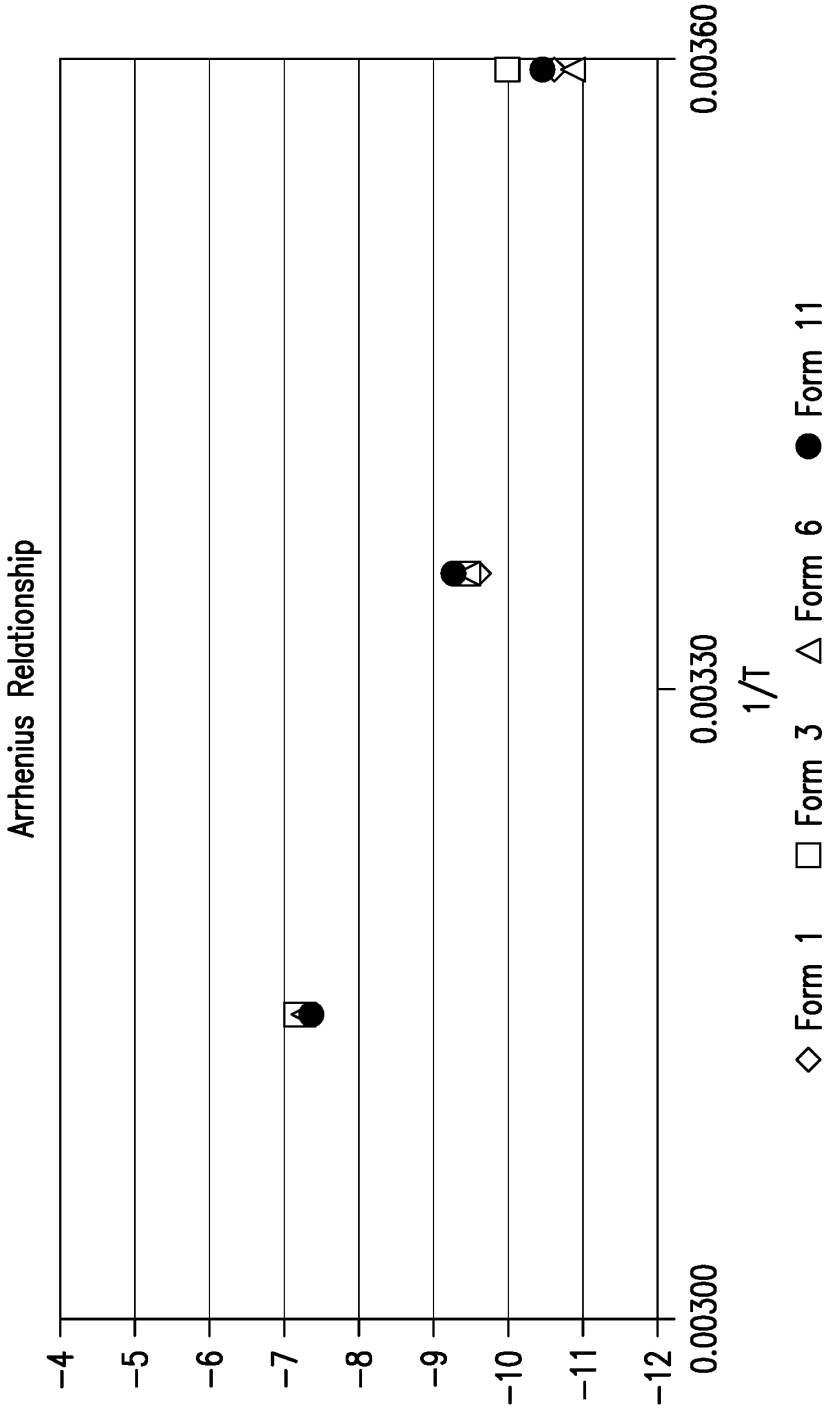

Arrhenius Relationship
−4
−5
−6
−7
−8
−9
−10
−11
−12
0.00300
0.00330
0.00360
1/T
◇ Form 1
□ Form 3
△ Form 6
● Form 11

FIG.9

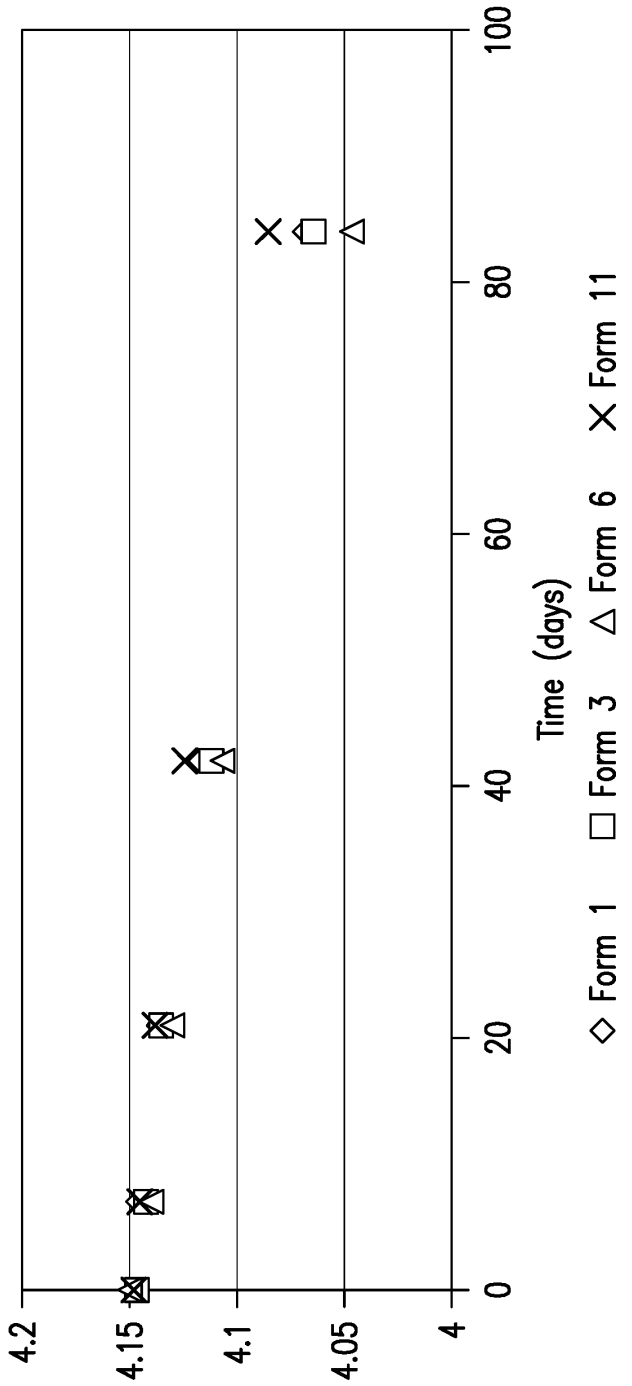

4.2
4.15
4.1
4.05
4
0
20
40
60
80
100
Time (days)
◇ Form 1
□ Form 3
△ Form 6
× Form 11

FIG. 10

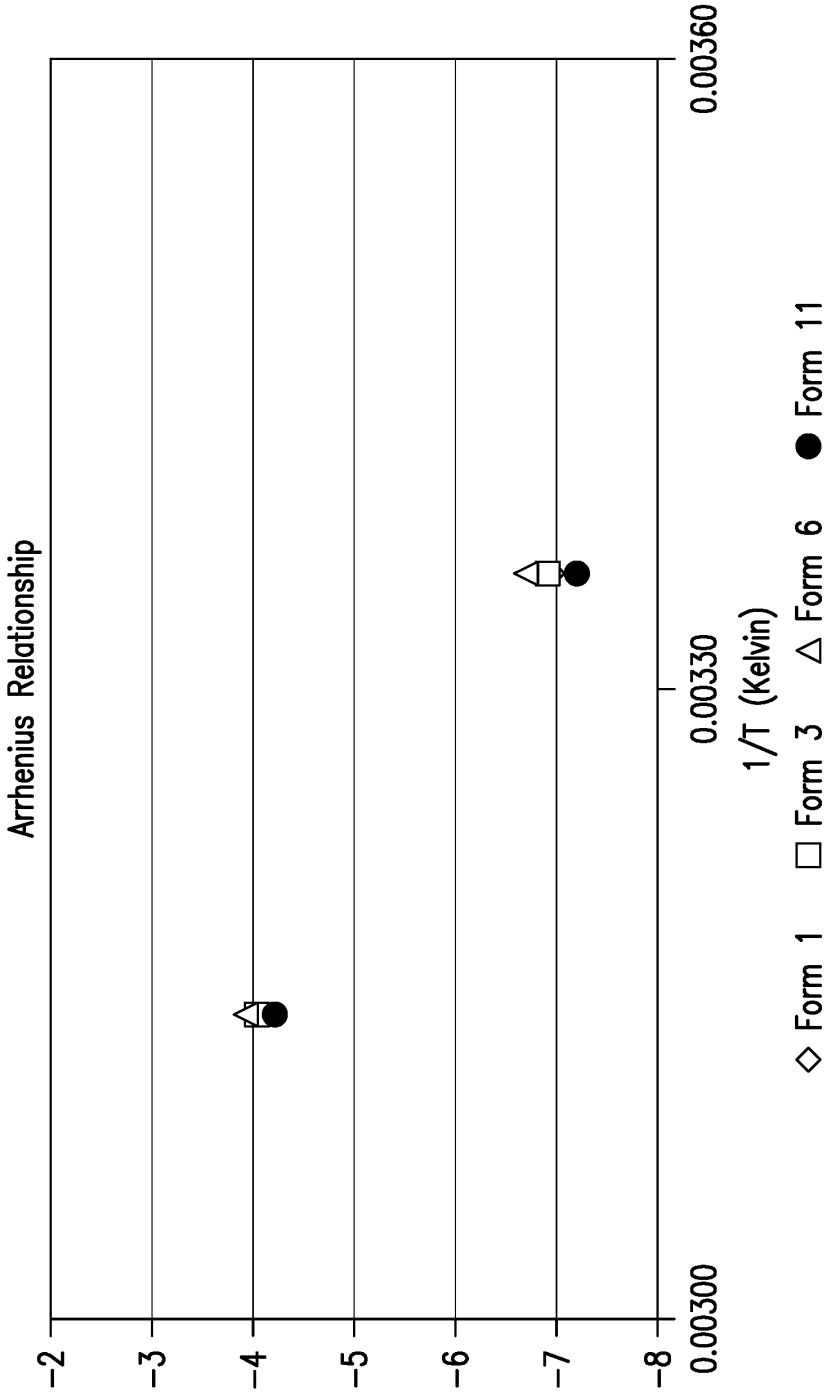

Arrhenius Relationship
-2
-3
-4
-5
-6
-7
-8
0.00300
0.00330
0.00360
1/T (Kelvin)
◇ Form 1
□ Form 3
△ Form 6
● Form 11

FIG.11

Sample Composition		Hydrodynamic radius (nm)/% Ms															
		t=0	−70°C		2–8°C				25°C				45°C		F/T 5 cycle	2–8°C Shake 3 day
			t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	t=6 weeks	t=12 weeks	t=1 week	t=3 weeks	t=6 weeks	t=12 weeks	t=1 week	t=3 weeks		
10mM Histidine	150mM Arginine, 150mM Glutamic acid, 0.01% PS20, pH 6.1	6.8/ 99.7 387.5/ 0.3	6.9/ 99.8 382.6/ 0.2	7.0/ 99.7 291.3/ 0.3	6.9/ 99.6 709.6/ 0.4	6.9/ 99.1 634/ 0.9	6.9/ 99.3 526.0/ 0.3 2659.2/ 0.4	6.6/ 99.8 346.5/ 0.2	7.0/ 99.8 68.1/ 0.0 587.8/ 0.2	6.6/ 99.6 585.4/ 0.4	7.1/ 99.8 498.1/ 0.2	6.9/ 99.8 355.3 0.2	6.9/ 99.6 370.7/ 0.4	6.4/ 99.6 344.5/ 0.4	6.6/ 99.7 381/ 0.3	6.7/ 99.4 601.0/ 0.6
	55mM Arginine, 55mM Glutamic acid, 3% Sorbitol, 0.01% PS20, pH 6.3	7.3/ 99.7 736.6/ 0.3	7.4/ 99.8 422.3/ 0.2	7.2/ 99.6 678.2/ 0.4	7.2/ 99.6 1244.5/ 0.4	7.0/ 99.7 755.4/ 0.3	7.4/ 99.8 382.5/ 0.2	7.0/ 99.6 986.9/ 0.4	7.6/ 99.9 608.5/ 0.1	6.7/ 99.8 583.4/ 0.2	6.9/ 99.7 743.4/ 0.3	7.3/ 99.3 1521.3/ 0.7	7.1/ 99.5 639.1/ 0.5	7.1/ 99.5 451.2/ 0.5	7.1/ 99.8 572.7/ 0.2	6.9/ 99.7 479.9/ 0.3
	150mM Arginine, 150mM Glutamic acid, 0.01% PS20, pH 6.3	6.9/ 99.6 426.7/ 0.4	7.6/ 99.5 471.0/ 0.5	7.4/ 99.4 796.7/ 0.6	7.3/ 99.3 766.1/ 0.7	7.0/ 99.5 765.0/ 0.5	7.4/ 99.5 644.2/ 0.5	7.4/ 99.5 765.3/ 0.5	7.2/ 99.6 585.4/ 0.4	7.0/ 99.1 1643.9/ 0.9	7.5/ 99.5 722.3/ 0.5	7.4/ 99.2 956.0/ 0.8	7.4/ 99.0 618.1/ 1.0	7.5/ 99.1 475.0/ 0.9	7.3/ 99.5 517.0/ 0.5	7.3/ 99.3 635.9/ 0.7
	75mM Arginine, 3% Sorbitol, 0.01% PS20, pH 6.1	7.9/ 99.3 777.0/ 0.7	7.8/ 99.3 829.7/ 0.7	8.1/ 99.1 698.9/ 0.9	8.0/ 99.6 479.8/ 0.4	7.5/ 99.6 328.2/ 0.4	7.7/ 99.6 392.04/ 0.4	7.9/ 99.5 519.7/ 0.5	7.8/ 99.4 638.5/ 0.6	7.3/ 99.8 264.1/ 0.2	7.6/ 99.2 214.8/ 0.2 4344.7/ 0.6	8.2/ 99.2 877.7/ 0.8	7.8/ 98.9 522.4/ 1.1	7.8/ 99.0 424.6/ 1.0	6.9/ 99.4 675.8/ 0.6	7.8/ 98.9 1187.8/ 1.1

FIG.12

Sample Composition	VH14_1G.VL15 concentration (mg/mL) Turbidity (A330) *Visual appearance** Measured pH															
	t=0	−70°C			2–8°C			25°C				45°C				
		t=4 weeks	t=8 weeks	t=12 weeks	t=2 weeks	t=4 weeks	t=8 weeks	t=12 week	t=2 weeks	t=4 weeks	t=8 weeks	t=12 weeks	t=1 week	t=2 weeks	t=4 weeks
10mM Histidine, 110mM Arginine, 1.5% Sorbitol, 0.01% (w/v) PS20, pH 6.0 20mg/mL	20.2 0.099 C,NC,NP 6.1	20.1 0.098 C,NC,NP 6.1	20.2 0.100 C,NC,NP 6.1	19.6 0.099 C,NC,NP 6.1	20.0 0.100 C,NC,NP 6.0	20.7 0.101 C,NC,NP 6.1	20.4 0.104 C,NC,NP 6.1	20.4 0.107 C,NC,NP 6.1	20.5 0.103 C,NC,NP 6.0	20.5 0.091 C,NC,NP 6.1	20.0 0.172 C,NC,NP 6.1	19.9 0.177 C,NC,NP 6.1	20.5 0.168 C,NC,NP 6.1	20.3 0.191 C,NC,NP 6.0	19.8 0.203 C,NC,NP 6.1
10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	20.2 0.102 C,NC,NP 6.4	20.3 0.102 C,NC,NP 6.4	19.6 0.105 C,NC,NP 6.4	19.6 0.106 C,NC,NP 6.4	20.3 0.067 C,NC,NP 6.3	20.5 0.103 C,NC,NP 6.4	19.9 0.109 C,NC,NP 6.4	20.5 0.111 C,NC,NP 6.4	19.8 0.119 C,NC,NP 6.3	20.6 0.135 C,NC,NP 6.4	20.4 0.174 C,NC,NP 6.3	20.4 0.186 C,NC,NP 6.4	20.0 0.165 C,NC,NP 6.3	20.7 0.182 C,NC,NP 6.3	20.0 0.160 C,NC,NP 6.3
10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 50mg/mL	47.8 0.226 C,NC,NP 6.6	47.6 0.221 C,NC,NP 6.6	48.6 0.232 C,NC,NP 6.6	50.3 0.225 C,NC,NP 6.6	49.9 0.219 C,NC,NP 6.5	47.0 0.223 C,NC,NP 6.6	48.6 0.232 C,NC,NP 6.5	50.1 0.238 C,NC,NP 6.6	48.0 0.267 C,NC,NP 6.5	47.7 0.310 C,NC,NP 6.6	50.0 0.348 C,NC,NP 6.5	49.2 0.362 C,NC,NP 6.6	47.0 0.332 C,NC,NP 6.5	45.6 0.352 C,NC,NP 6.5	47.2 0.376 C,NC,NP 6.5

Cont'd on Fig.13B

FIG.13A

Cont'd from Fig.13A

10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	20.1 0.112 C,NC,NP 6.6	19.9 0.106 C,NC,NP 6.6	19.8 0.115 C,NC,NP 6.6	20.0 0.116 C,NC,NP 6.6	19.9 0.083 C,NC,NP 6.5	19.9 0.107 C,NC,NP 6.6	19.8 0.113 C,NC,NP 6.6	20.4 0.115 C,NC,NP 6.6	20.1 0.127 C,NC,NP 6.5	20.1 0.158 C,NC,NP 6.6	20.2 0.204 C,NC,NP 6.5	20.4 0.219 C,NC,NP 6.6	19.7 0.180 C,NC,NP 6.6	20.0 0.192 C,NC,NP 6.5	20.2 0.217 C,NC,NP 6.5					
10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	20.4 0.101 C,NC,NP 6.5	19.9 0.098 C,NC,NP 6.6	20.3 0.105 C,NC,NP 6.5	20.5 0.099 C,NC,NP 6.6	20.4 0.094 C,NC,NP 6.5	20.2 0.072 C,NC,NP 6.5	20.3 0.111 C,NC,NP 6.5	20.5 0.108 C,NC,NP 6.5	20.1 0.111 C,NC,NP 6.5	20.0 0.123 C,NC,NP 6.5	20.4 0.175 C,NC,NP 6.5	20.5 0.203 C,NC,NP 6.5	20.4 0.156 C,NC,NP 6.5	19.9 0.180 C,NC,NP 6.5	20.1 0.196 C,NC,NP 6.5					

FIG.13B

Sample Composition	Counts/mL (Diameter) 2μm 3μm 5μm ≥10μm ≥25μm														
	t=0	−70°C			2–8°C			25°C				45°C			
		t=4 weeks	t=8 weeks	t=12 weeks	t=2 weeks	t=4 weeks	t=8 weeks	t=12 week	t=2 weeks	t=4 weeks	t=8 weeks	t=12 weeks	t=1 week	t=2 weeks	t=4 weeks
10mM Histidine, 110mM Arginine, 1.5% Sorbitol, 0.01% (w/v) PS20, pH 6.0 20mg/mL	183±29	80±26	97±21	17±15	67±23	70±26	47±23	33±6	83±45	60±36	47±12	77±23	207±42	173±68	77±47
	133±29	60±10	63±21	7±6	40±17	43±21	37±25	27±15	60±35	20±10	37±15	37±6	137±55	110±62	57±29
	70±26	27±15	37±6	7±6	17±6	20±20	20±26	13±15	20±20	7±6	17±21	13±6	80±26	33±25	10±10
	23±15	13±6	13±6	3±6	7±6	7±6	13±15	0±0	10±10	0±0	10±10	0±0	20±0	10±10	0±0
	3±6	0±0	3±6	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.3 20mg/mL	63±35	113±67	117±23	50±0	43±12	70±10	83±15	43±6	83±25	53±6	93±60	50±35	117±15	170±56	120±40
	40±20	67±42	73±12	30±10	27±12	40±10	63±6	23±6	60±10	33±6	83±60	37±31	87±25	120±26	77±15
	20±17	20±10	30±17	7±6	17±6	20±10	33±23	17±15	37±15	20±0	37±25	10±10	40±10	50±20	27±15
	10±10	7±6	7 ±2	0±0	10±0	3±6	20 ±10	3±6	17±21	7±6	7±12	3±6	20±10	23±15	10±0
	0±0	0±0	3±6	0±0	3±6	0±0	3±6	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 50mg/mL	130±62	180±46	137±47	173±90	167±83	160±53	139±93	137±51	127±45	137±91	130±46	90±26	223±45	233±40	130±82
	73±25	113±67	103±35	113±55	123±25	113±45	93±65	100±53	93±23	93±51	107±40	57±15	163±40	153±29	113±72
	43±25	40±52	57±29	47±40	67±6	63±51	53±31	40±26	57±21	27±21	43±21	17±6	80±46	63±6	57±47
	10±10	3±6	27±15	10±10	30±10	17±15	20±17	13±12	13±6	7±6	17±12	7±6	13±6	20±10	10±0
	0±0	0±0	10±10	3±6	3±6	0±0	0±0	3±6	0±0	0±0	0±0	0±0	0±0	0±0	0±0

Cont'd on Fig.14B

FIG.14A

Cont'd from Fig.14A

10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	37±15	33±21	140±46	53±6	90±26	53±15	80±20	43±25	140±46	50±10	37±23	57±38	117±32	127±15	73±21
	30±10	37±23	100±26	30±10	70±20	30±20	67±25	17±12	127±47	17±15	23±15	47±31	77±23	77±15	47±15
	13±6	7±12	30±0	0±0	33±12	10±10	43±12	7±6	67±38	7±12	10±0	20±20	50±17	40±10	30±17
	3±6	0±0	7±6	0±0	13±15	3±6	17±12	0±0	27±6	3±6	7±6	3±6	17±12	17±15	7±6
	0±0	0±0	3±6	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	3±6	0±0	0±0	0±0
10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	67±29	120±69	153±64	293±64	83±31	93±45	30±0	60±30	60±20	47±40	77±25	67±6	93±50	113±35	97±50
	37±15	83±67	83±31	213±91	33±15	60±30	17±6	50±20	50±10	40±30	70±20	60±10	70±40	77±35	67±31
	23±15	47±64	27±6	97±32	20±10	20±10	3±6	20±20	33±6	20±26	47±25	37±6	33±15	40±26	27±15
	7±12	17±21	7±6	37±15	10±10	3±6	0±0	3±6	10±10	10±10	37±21	7±6	17±12	13±6	7±6
	0±0	7±6	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	7±6	0±0

FIG.14B

Sample Composition	SE-HPLC (% Purity) HMW *Main Peak* LMW															
	t=0	−70°C			2–8°C			25°C				45°C				
		t=4 weeks	t=8 weeks	t=12 weeks	t=2 weeks	t=4 weeks	t=8 weeks	t=12 week	t=2 weeks	t=4 weeks	t=8 weeks	t=12 weeks	t=1 week	t=2 weeks	t=4 weeks
10mM Histidine, 110mM Arginine, 1.5% Sorbitol, 0.01% (w/v) PS20, pH 6.0 20mg/mL	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.2	1.1	1.3	1.5	1.8	2.2
	98.8	98.8	98.8	98.8	98.8	98.8	98.8	98.9	98.8	98.8	98.6	98.6	98.1	97.8	97.2
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.3	0.1	0.4	0.5	0.6
10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.3 20mg/mL	1.1	1.1	1.1	1.0	1.1	1.1	1.1	1.1	1.2	1.1	1.2	1.3	1.4	1.6	1.7
	98.8	98.8	98.8	98.8	98.8	98.8	98.8	98.9	98.8	98.8	98.6	98.6	98.3	98.0	97.7
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.4	0.4	0.6
10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 50mg/mL	1.2	1.2	1.1	1.1	1.2	1.2	1.2	1.2	1.3	1.5	1.6	1.7	1.7	1.8	2.0
	98.8	98.8	98.8	98.8	98.8	98.7	98.7	98.8	98.6	98.4	98.2	98.2	98.0	97.8	97.4
	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.4	0.4	0.6

Cont'd on Fig.14B

FIG.15A

Cont'd from Fig.15A

10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	1.1 98.8 0.1	1.1 98.8 0.1	1.2 98.8 0.1	1.1 98.8 0.1	1.1 98.8 0.1	1.1 98.8 0.1	1.1 98.8 0.1	1.2 98.8 0.1	1.2 98.8 0.1	1.2 98.5 0.3	1.5 98.4 0.1	1.4 98.3 0.3	1.5 98.2 0.3	1.7 97.7 0.6
10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	1.1 98.8 0.1	1.1 98.8 0.1	1.1 98.8 0.1	1.1 98.8 0.1	1.1 98.8 0.1	1.1 98.8 0.1	1.1 98.8 0.1	1.2 98.8 0.1	1.1 98.8 0.0	1.1 98.7 0.2	1.3 98.6 0.1	1.2 98.4 0.3	1.5 98.2 0.4	1.6 97.9 0.5

FIG.15B

Sample Composition	CE-HPLC (% Purity) Acidic Forms Main Peak Basic Forms														
		-70°C			2-8°C				25°C				45°C		
	t=0	t=4 weeks	t=8 weeks	t=12 weeks	t=2 weeks	t=4 weeks	t=8 weeks	t=12 week	t=2 weeks	t=4 weeks	t=8 weeks	t=12 weeks	t=1 week	t=2 weeks	t=4 weeks
10mM Histidine, 110mM Arginine, 1.5% Sorbitol, 0.01% (w/v) PS20, pH 6.0 20mg/mL	14.7 63.2 22.1	15.6 63.5 20.9	16.2 63.0 20.8	15.7 63.5 20.7	15.5 63.4 21.0	15.5 63.6 20.9	16.4 62.7 20.8	15.9 63.5 20.6	16.9 62.1 20.9	19.6 60.1 20.3	23.8 56.4 19.8	25.2 54.7 20.0	22.3 57.6 20.1	27.9 52.4 19.8	37.9 44.8 17.3
10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.3 20mg/mL	14.9 62.9 22.2	15.5 63.7 20.8	16.1 63.1 20.8	15.9 63.4 20.6	15.5 63.5 20.9	15.7 63.8 20.5	16.5 62.8 20.8	16.1 63.2 20.7	17.3 62.1 20.6	20.6 59.6 19.8	25.6 55.6 18.8	27.5 53.5 19.0	23.8 56.8 19.4	29.7 51.8 18.5	40.7 43.5 15.7
10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 50mg/mL	14.7 63.1 22.2	15.5 63.6 20.8	16.3 63.0 20.7	15.8 63.5 20.7	15.6 63.5 20.9	15.8 63.5 20.8	16.7 62.6 20.7	16.4 63.1 20.5	18.3 61.4 20.2	21.2 59.3 19.5	24.6 56.7 18.7	26.8 54.4 18.8	23.6 56.6 19.8	30.0 52.1 17.9	42.5 43.0 14.5

Cont'd on Fig.16B

FIG.16A

SUBSTITUTE SHEET (RULE 26)

Cont'd from Fig.16A

10mM Histidine, 75mM Arginine, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	15.0	15.5	16.3	15.8	15.7	15.6	16.9	16.5	18.1	22.8	28.8	31.3	26.1	32.3	44.7
	63.1	63.8	63.0	63.5	63.4	63.5	62.5	63.1	61.6	58.1	53.3	51.1	54.5	50.4	41.4
	21.9	20.7	20.8	20.7	20.9	20.9	20.7	20.4	20.4	19.1	17.9	17.6	19.4	17.3	13.9
10mM Histidine, 55mM Arginine, 55mM Glutamic acid, 3% Sorbitol, 0.01% (w/v) PS20, pH 6.5 20mg/mL	14.7	15.6	16.6	15.8	15.5	15.7	17.1	16.3	17.1	19.4	27.1	30.5	24.2	32.2	45.5
	63.4	63.6	62.7	63.6	63.7	63.5	62.3	63.2	62.4	60.9	55.0	52.0	56.4	50.9	41.2
	21.8	20.8	20.7	20.6	20.8	20.8	20.6	20.5	20.6	19.7	17.9	17.5	19.4	16.9	13.3

FIG.16B

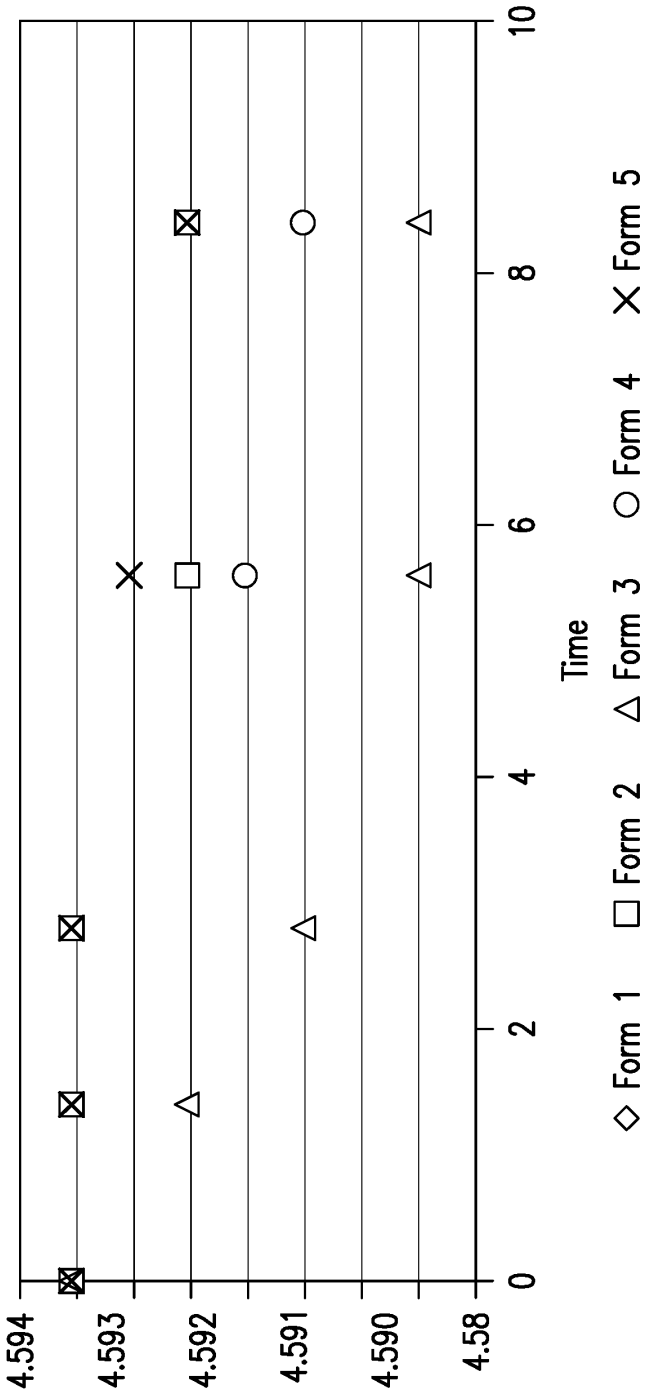

4.594
4.593
4.592
4.591
4.590
4.58
0
2
4
6
8
10
Time
◇ Form 1
□ Form 2
△ Form 3
○ Form 4
× Form 5

FIG.17

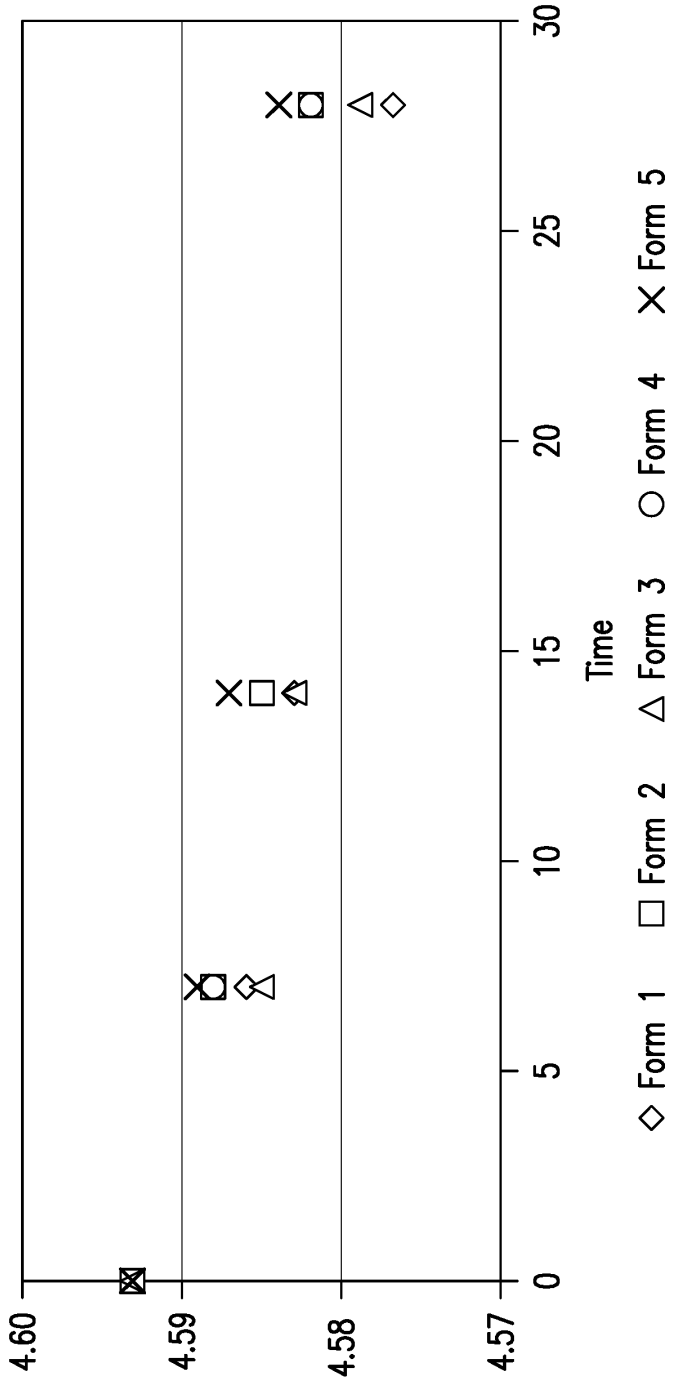

4.60
4.59
4.58
4.57
0
5
10
15
20
25
30
Time
◇ Form 1
□ Form 2
△ Form 3
○ Form 4
× Form 5

FIG.18

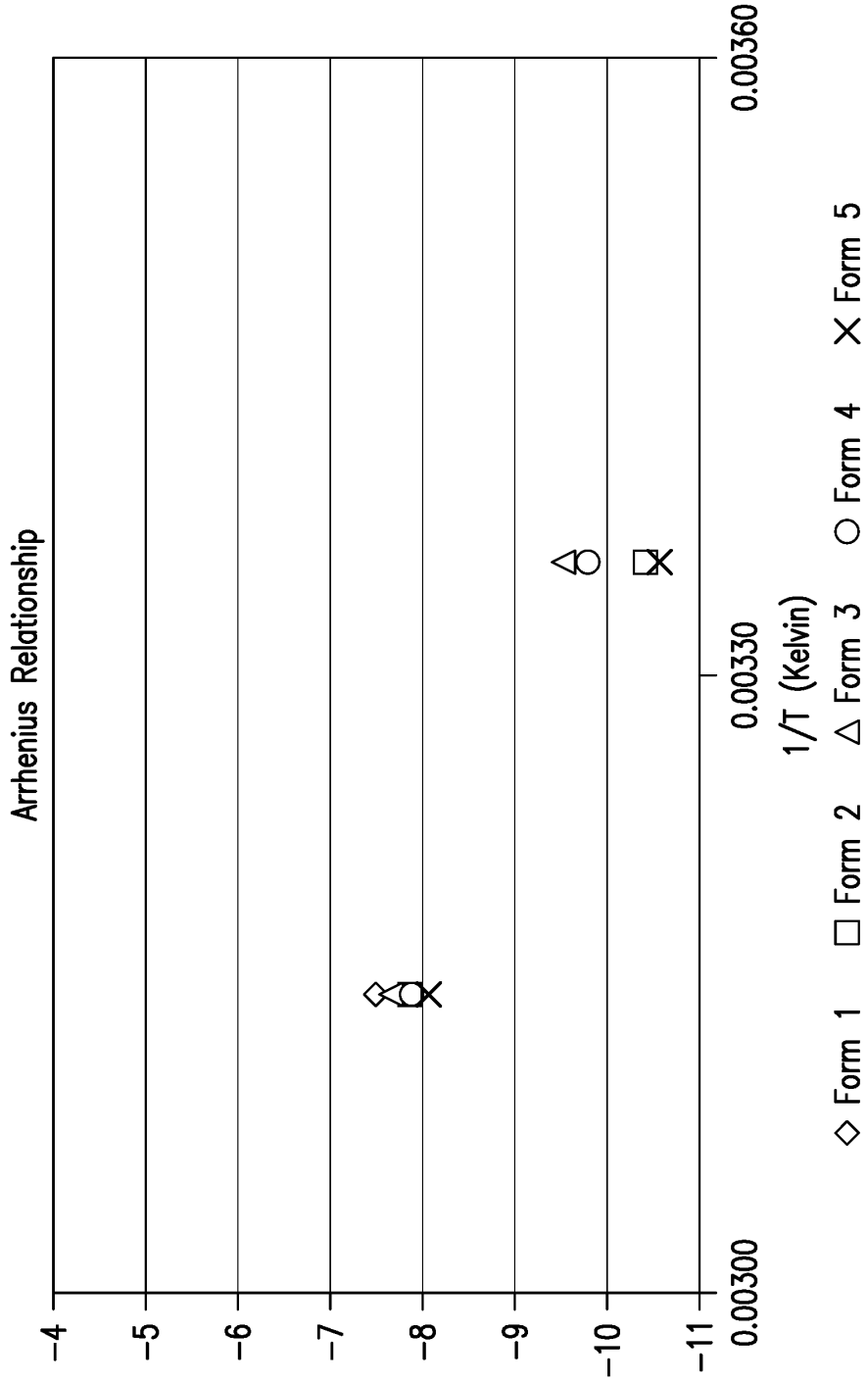

Arrhenius Relationship
−4
−5
−6
−7
−8
−9
−10
−11
0.00300
0.00330
0.00360
1/T (Kelvin)
◇ Form 1
□ Form 2
△ Form 3
○ Form 4
× Form 5

FIG.19

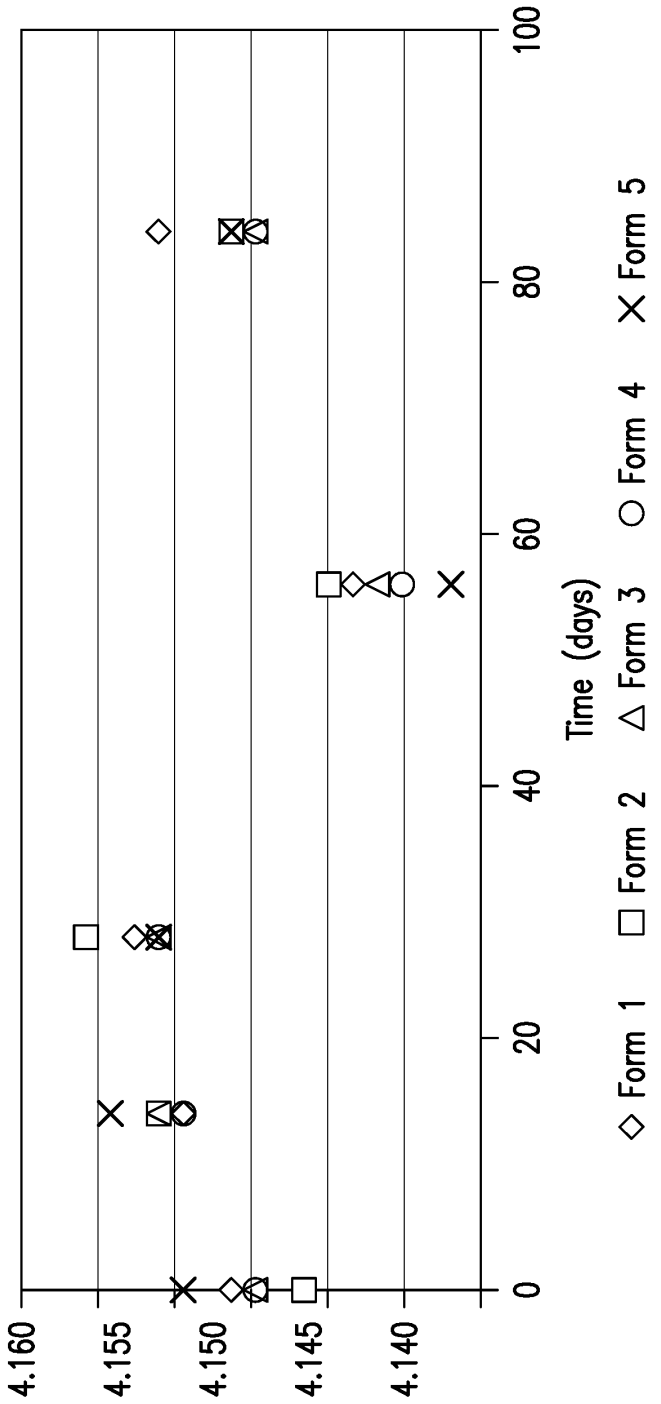

4.160
4.155
4.150
4.145
4.140
0
20
40
60
80
100
Time (days)
◇ Form 1
□ Form 2
△ Form 3
○ Form 4
× Form 5

FIG.20

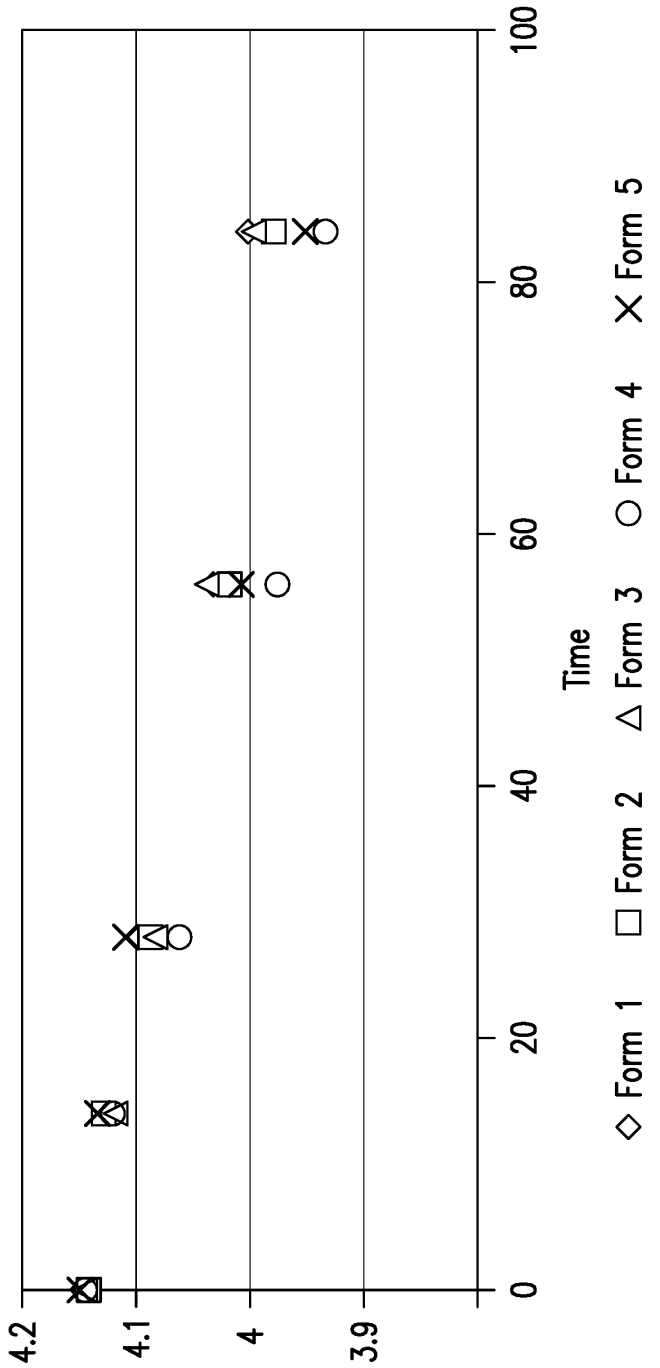


FIG.21

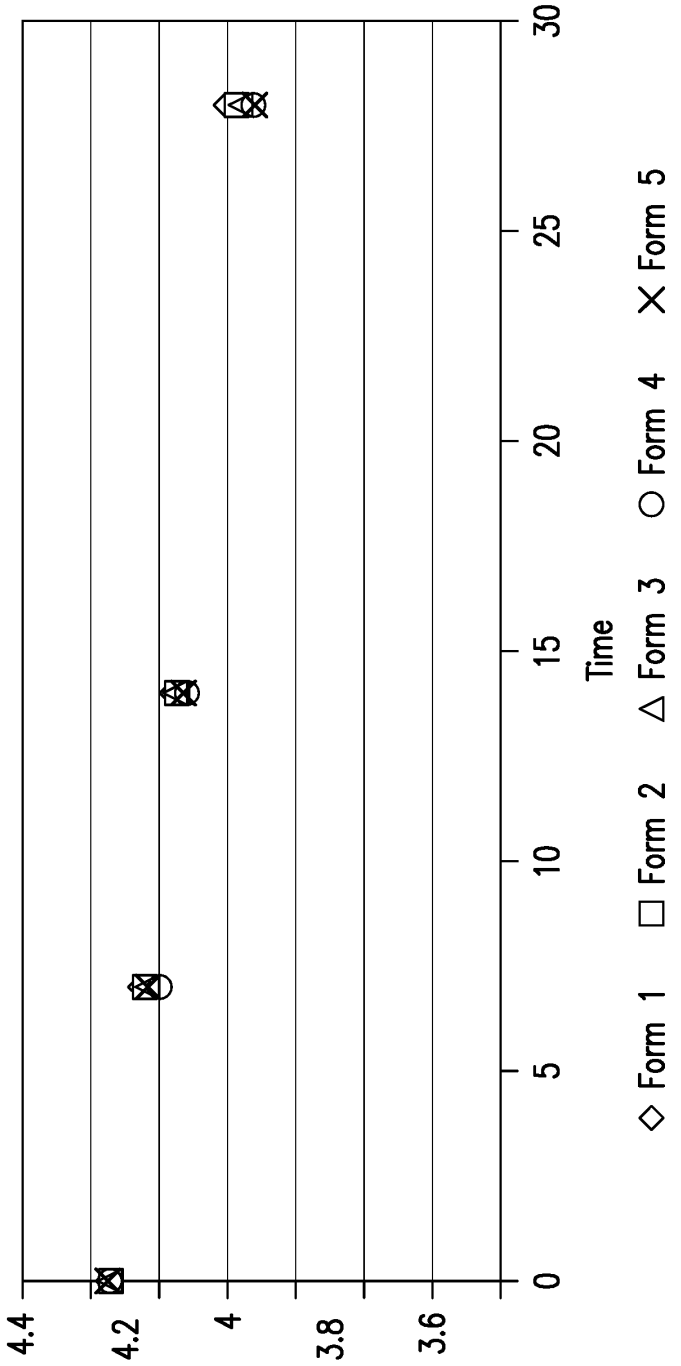

4.4
4.2
4
3.8
3.6
0
5
10
15
20
25
30
Time
◇ Form 1
□ Form 2
△ Form 3
○ Form 4
× Form 5

FIG.22


Arrhenius Relationship
-4
-5
-6
-7
-8
-9
-10
-11
-12
0.00300
0.00330
0.00360
0.00390
1/T (Kelvin)
◇ Form 1
□ Form 2
△ Form 3
○ Form 4
× Form 5

FIG.23

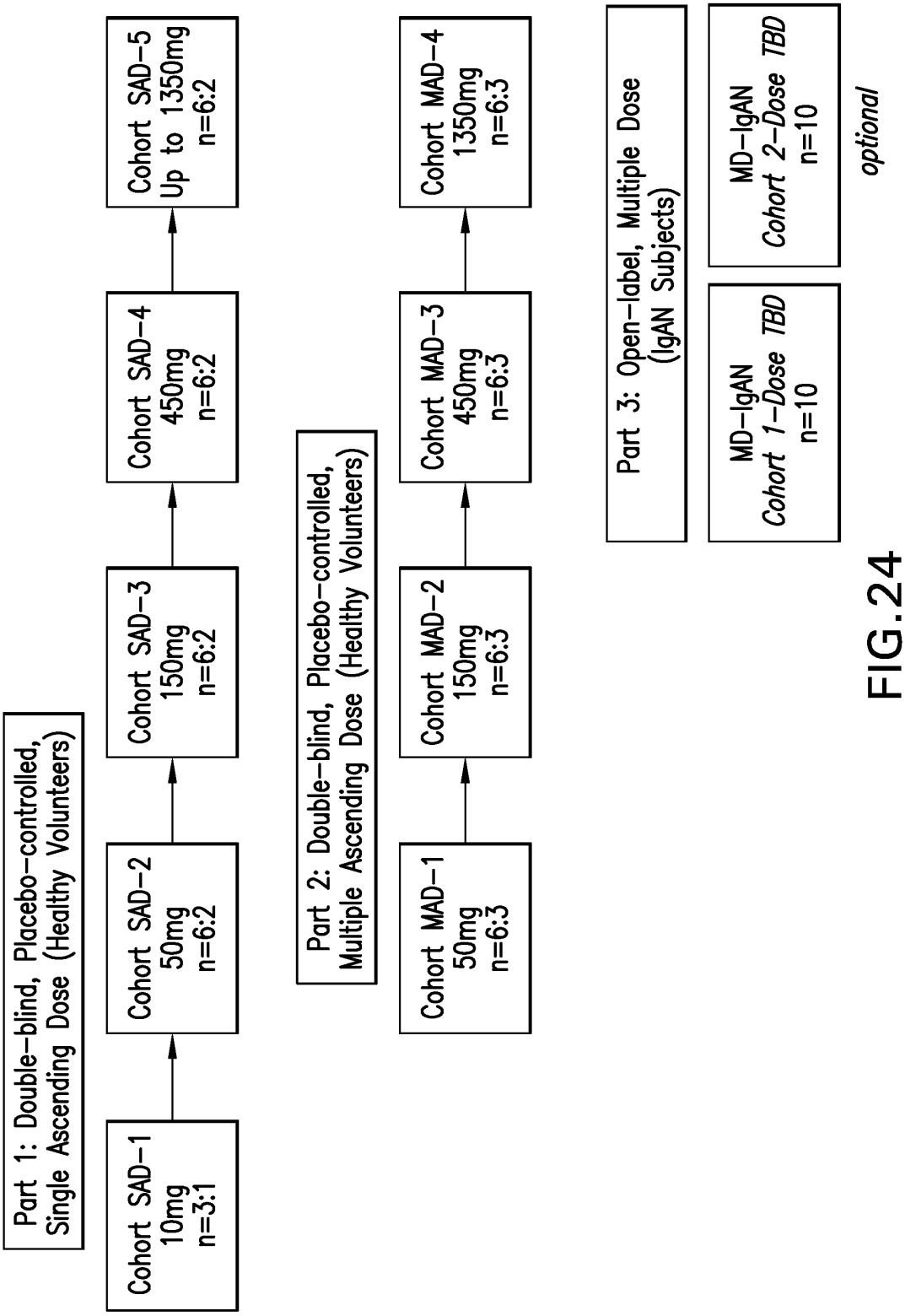

Part 1: Double-blind, Placebo-controlled, Single Ascending Dose (Healthy Volunteers)
Cohort SAD-1 10mg n=3:1
Cohort SAD-2 50mg n=6:2
Cohort SAD-3 150mg n=6:2
Cohort SAD-4 450mg n=6:2
Cohort SAD-5 Up to 1350mg n=6:2
Part 2: Double-blind, Placebo-controlled, Multiple Ascending Dose (Healthy Volunteers)
Cohort MAD-1 50mg n=6:3
Cohort MAD-2 150mg n=6:3
Cohort MAD-3 450mg n=6:3
Cohort MAD-4 1350mg n=6:3
Part 3: Open-label, Multiple Dose (IgAN Subjects)
MD-IgAN Cohort 1-Dose TBD n=10
MD-IgAN Cohort 2-Dose TBD n=10
optional

FIG.24

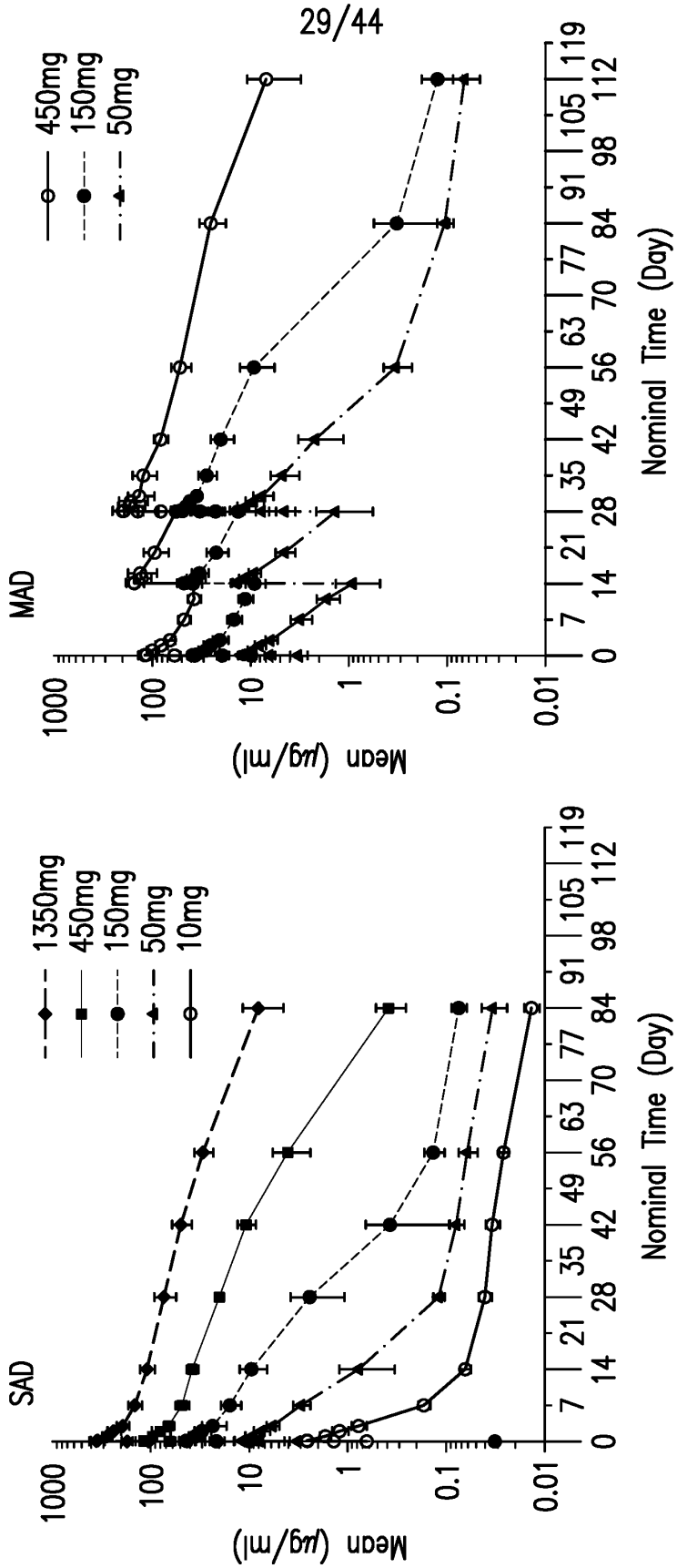

MAD
450mg
150mg
50mg
Mean (μg/ml)
1000
100
10
1
0.1
0.01
0
7
14
21
28
35
42
49
56
63
70
77
84
91
98
105
112
119
Nominal Time (Day)
SAD
1350mg
450mg
150mg
50mg
10mg
Mean (μg/ml)
Nominal Time (Day)

FIG.25

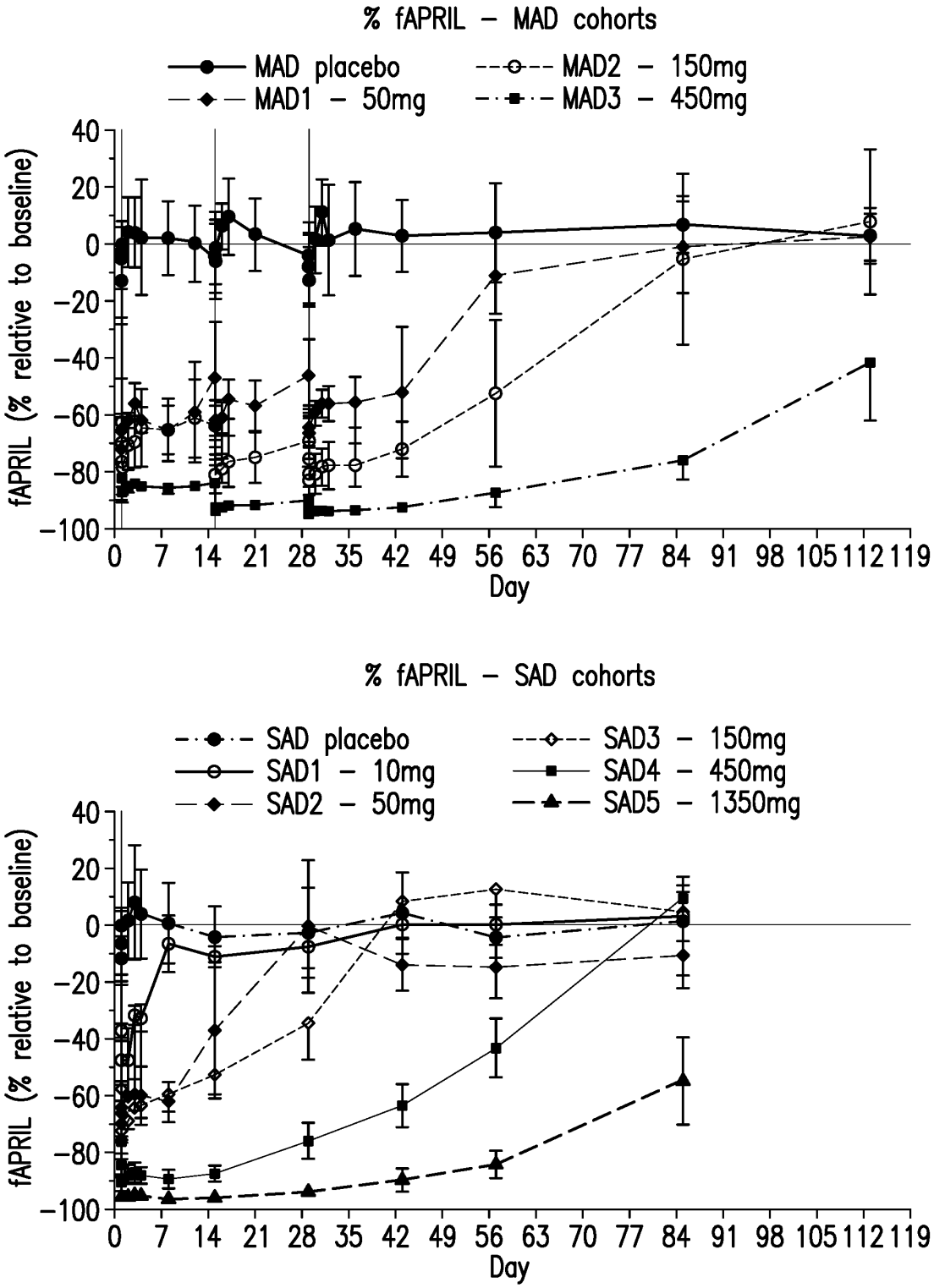

% fAPRIL – MAD cohorts
MAD placebo
MAD1 – 50mg
MAD2 – 150mg
MAD3 – 450mg
fAPRIL (% relative to baseline)
Day
% fAPRIL – SAD cohorts
SAD placebo
SAD1 – 10mg
SAD2 – 50mg
SAD3 – 150mg
SAD4 – 450mg
SAD5 – 1350mg
fAPRIL (% relative to baseline)
Day

FIG.26

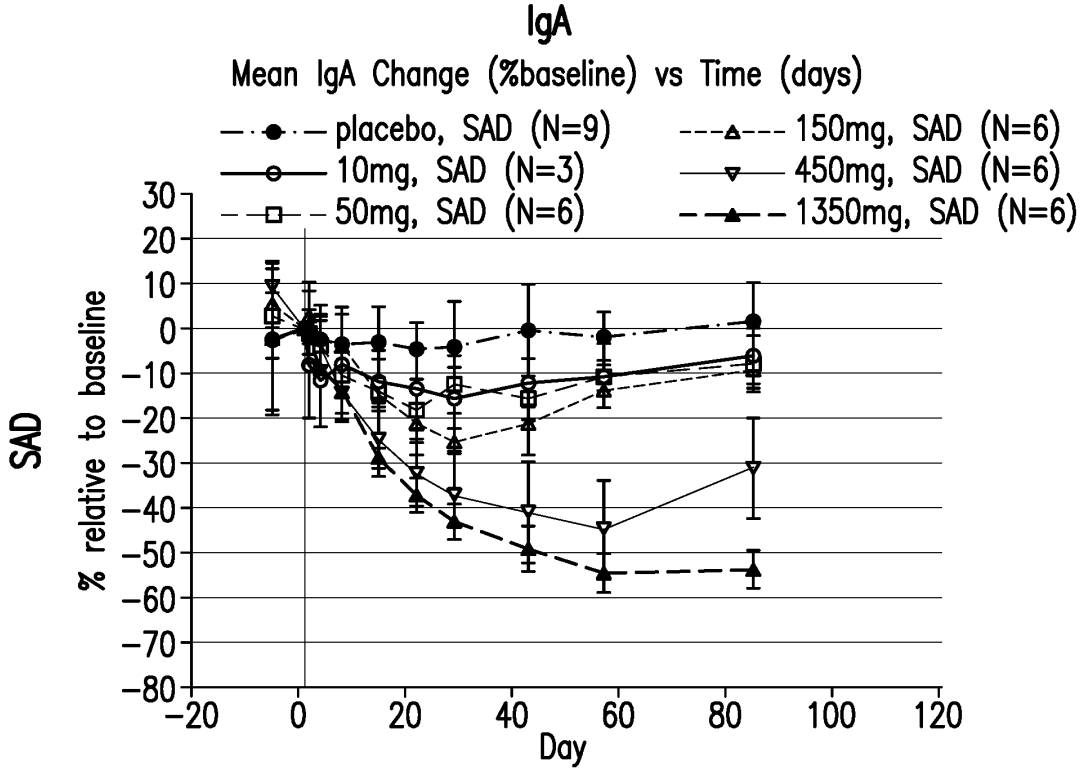


FIG.27A

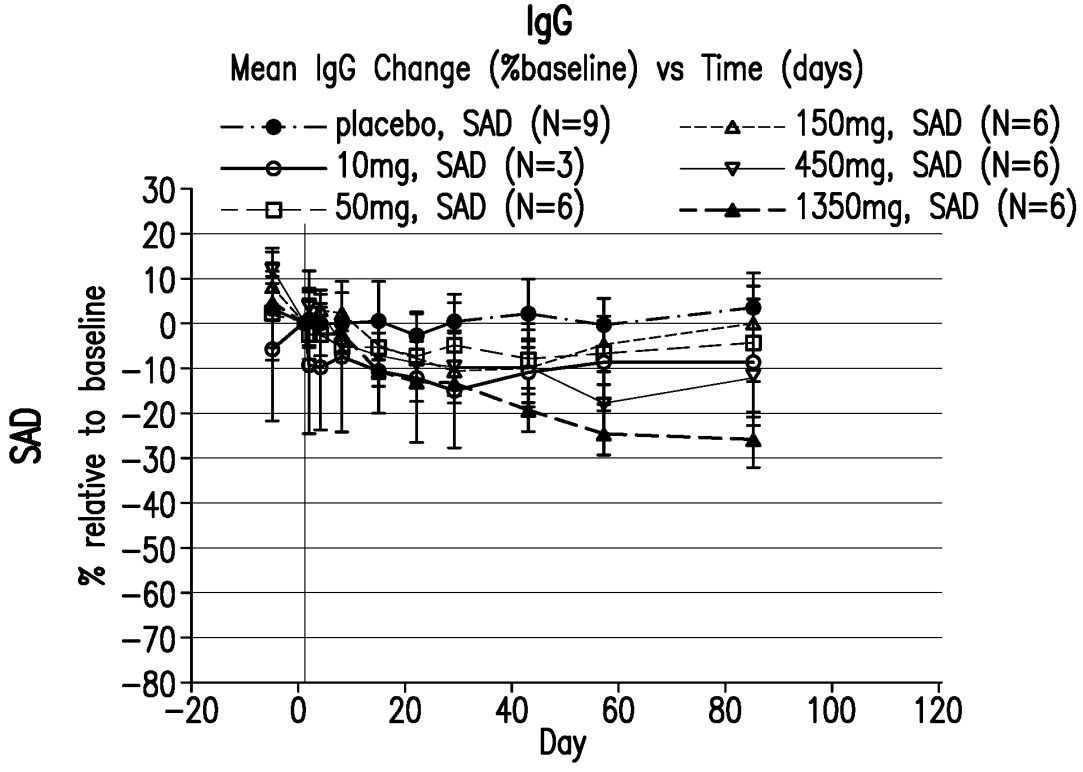


FIG.27B

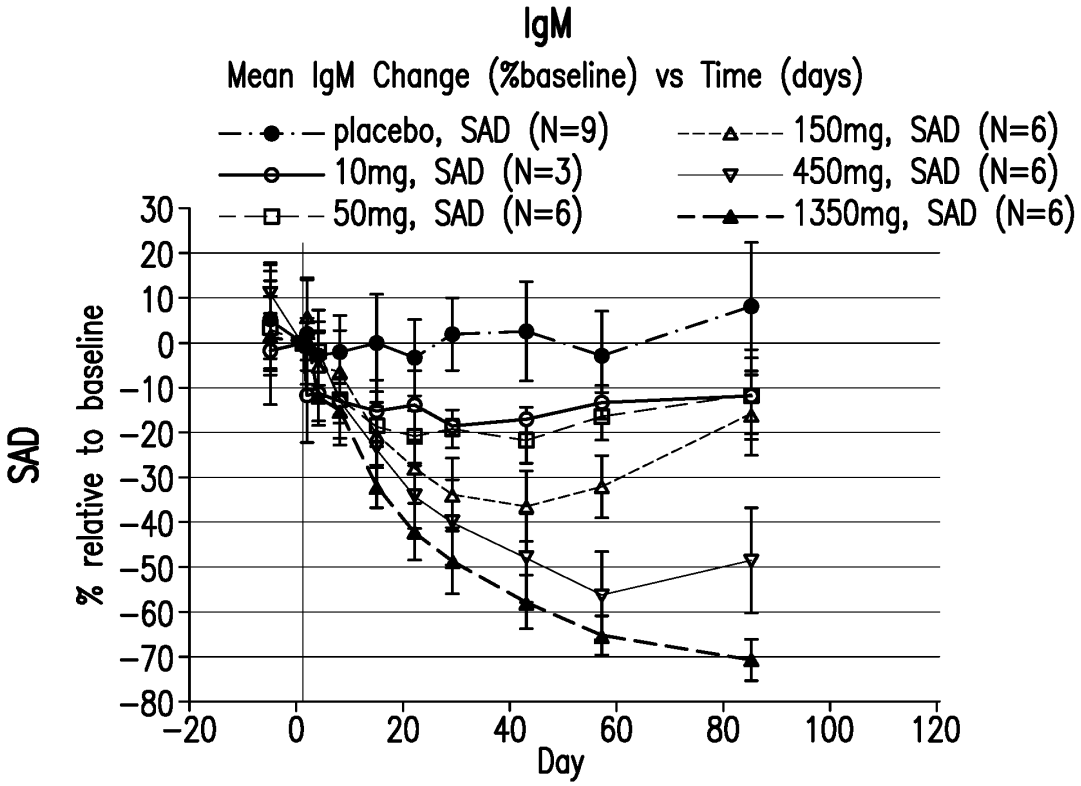


FIG.27C

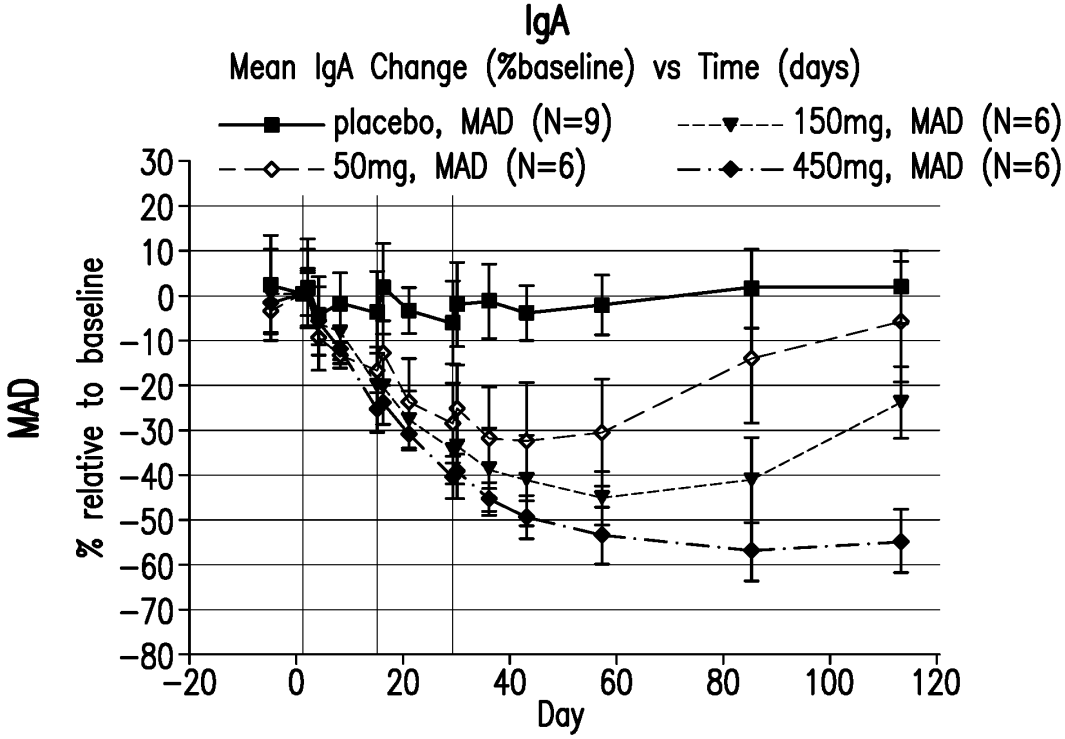


FIG.27D

IgG

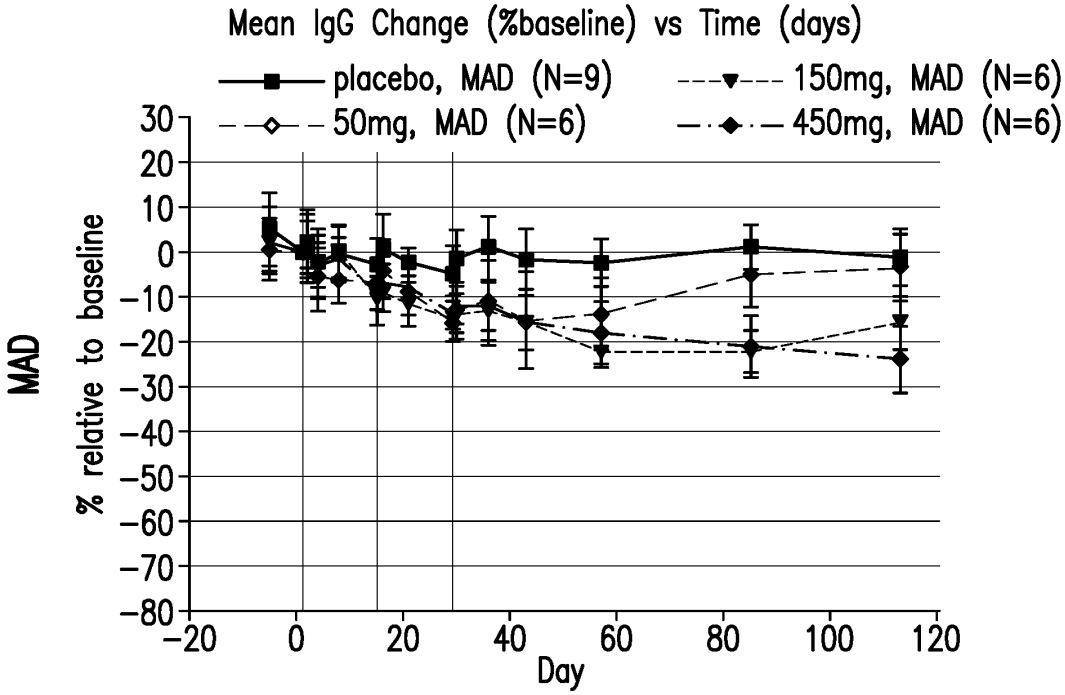


FIG.27E

IgM

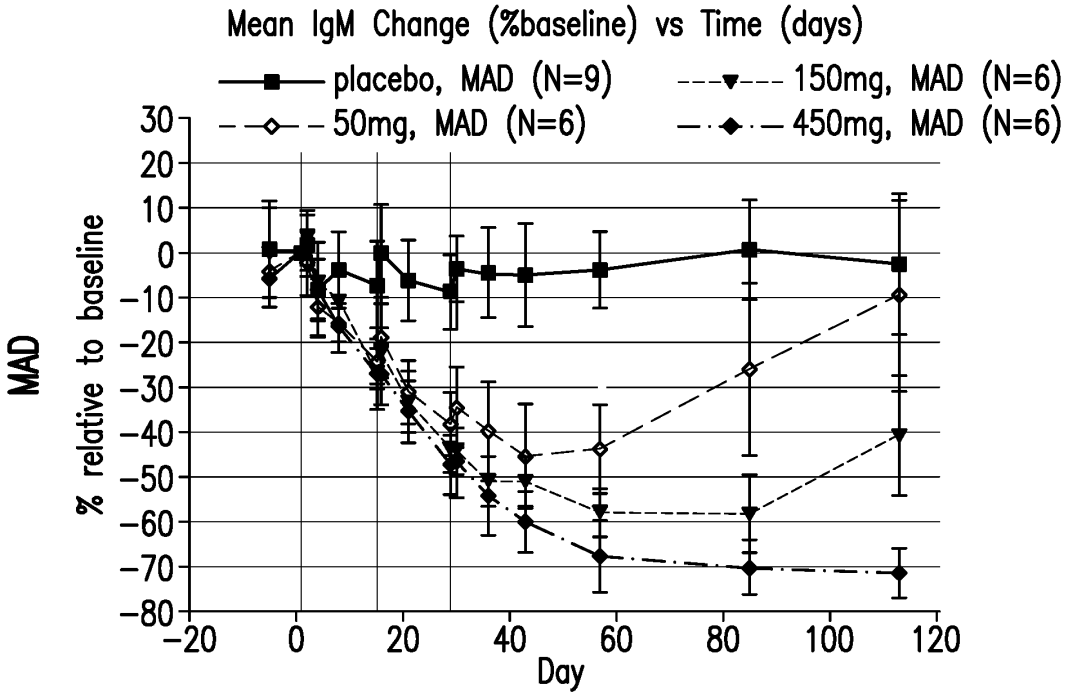


FIG.27F

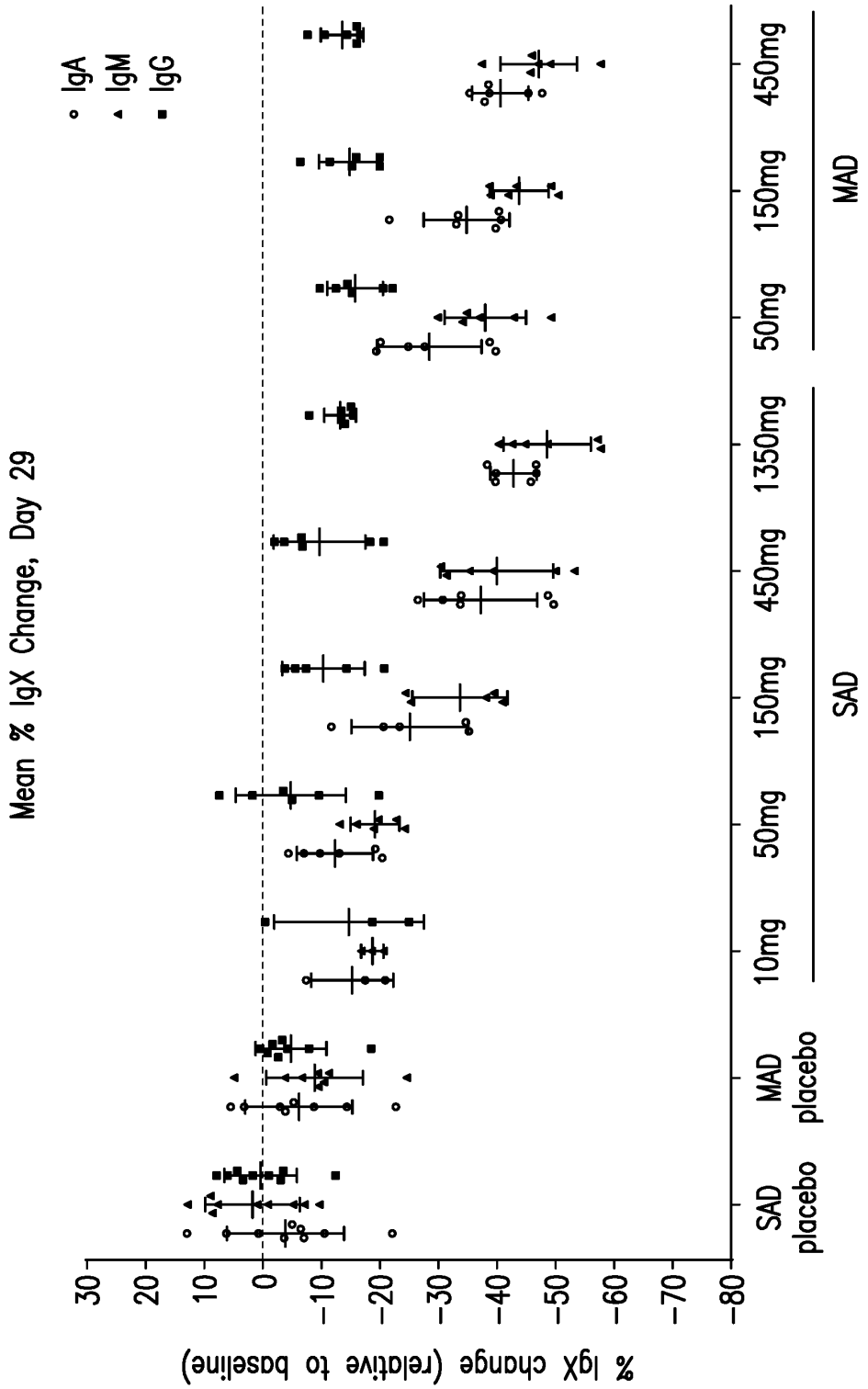

Mean % IgX Change, Day 29
IgA
IgM
IgG
% IgX change (relative to baseline)
30
20
10
0
−10
−20
−30
−40
−50
−60
−70
−80
SAD placebo
MAD placebo
10mg
50mg
150mg
450mg
1350mg
SAD
50mg
150mg
450mg
MAD

FIG.28A

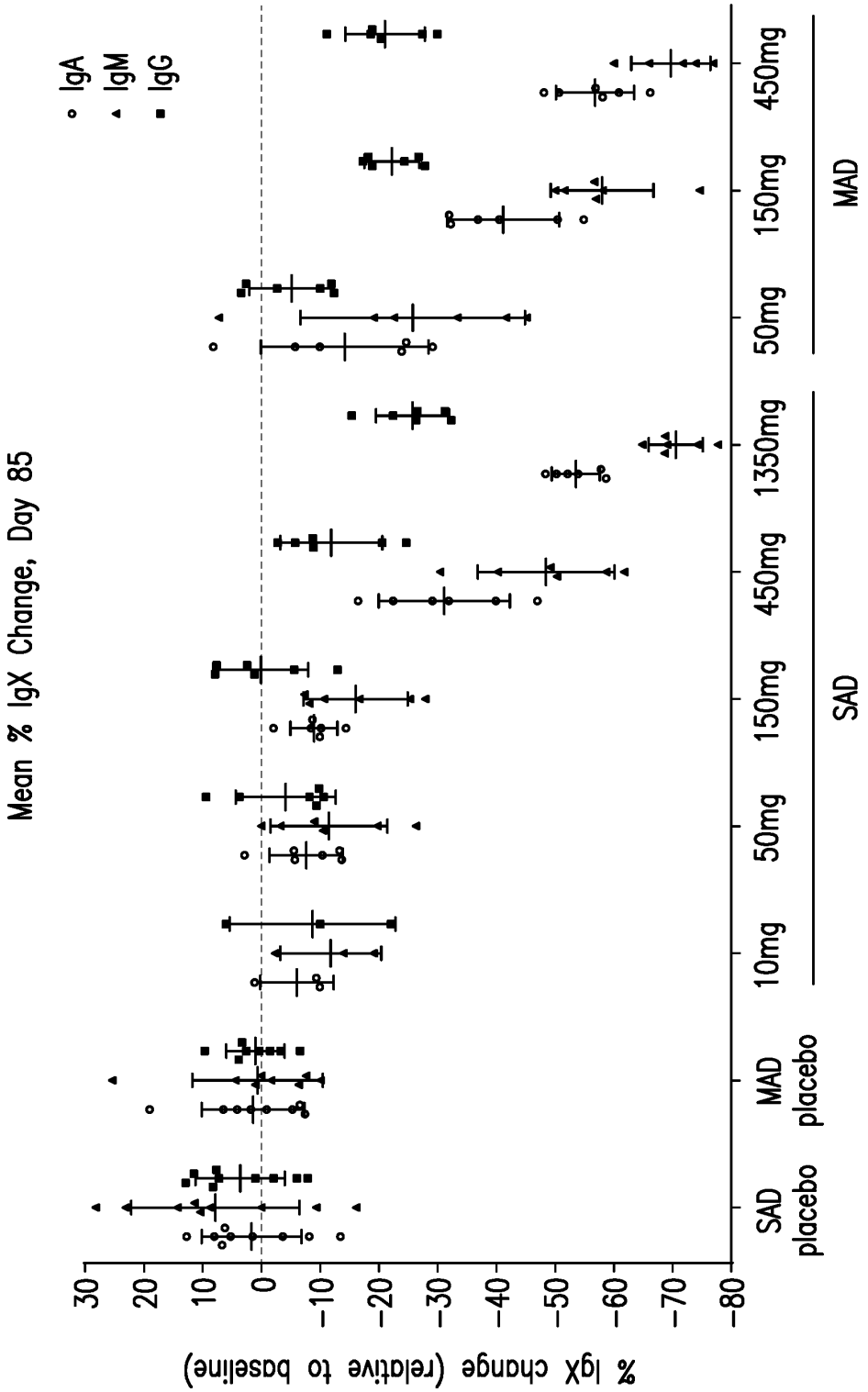

Mean % IgX Change, Day 85
IgA
IgM
IgG
% IgX change (relative to baseline)
30
20
10
0
−10
−20
−30
−40
−50
−60
−70
−80
SAD placebo
MAD placebo
10mg
50mg
150mg
450mg
1350mg
50mg
150mg
450mg
SAD
MAD

FIG.28B

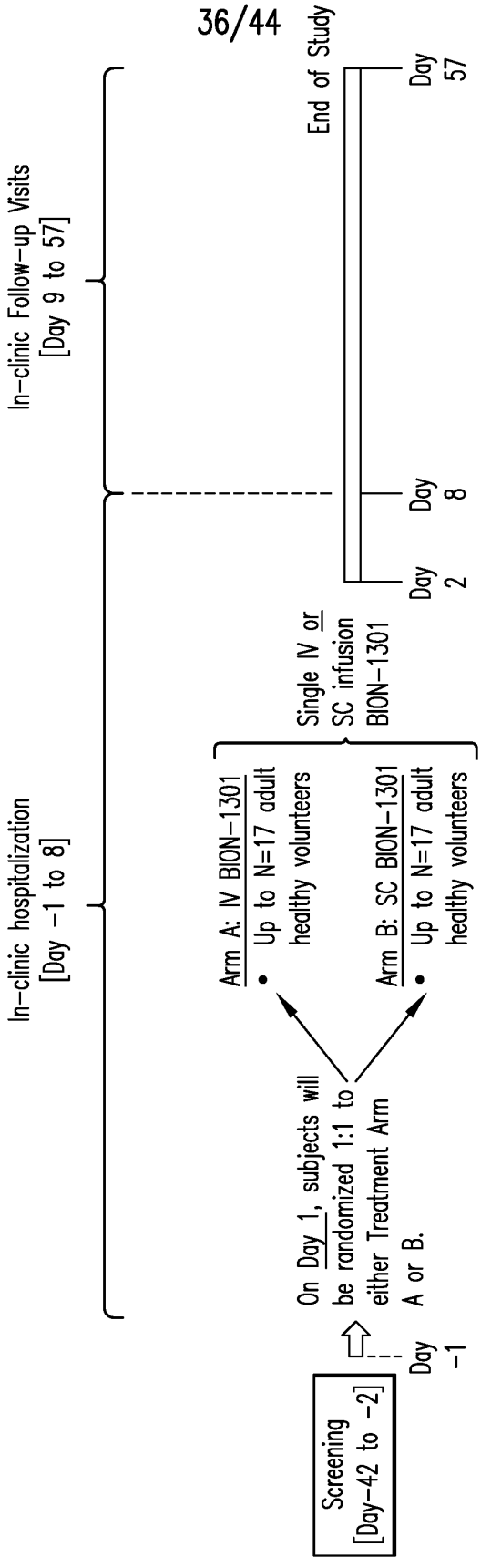

Screening
[Day-42 to -2]
Day -1
On Day 1, subjects will be randomized 1:1 to either Treatment Arm A or B.
Arm A: IV BION-1301
• Up to N=17 adult healthy volunteers
Arm B: SC BION-1301
• Up to N=17 adult healthy volunteers
Single IV or SC infusion BION-1301
Day 2
Day 8
End of Study
Day 57
In-clinic hospitalization
[Day -1 to 8]
In-clinic Follow-up Visits
[Day 9 to 57]

FIG.29

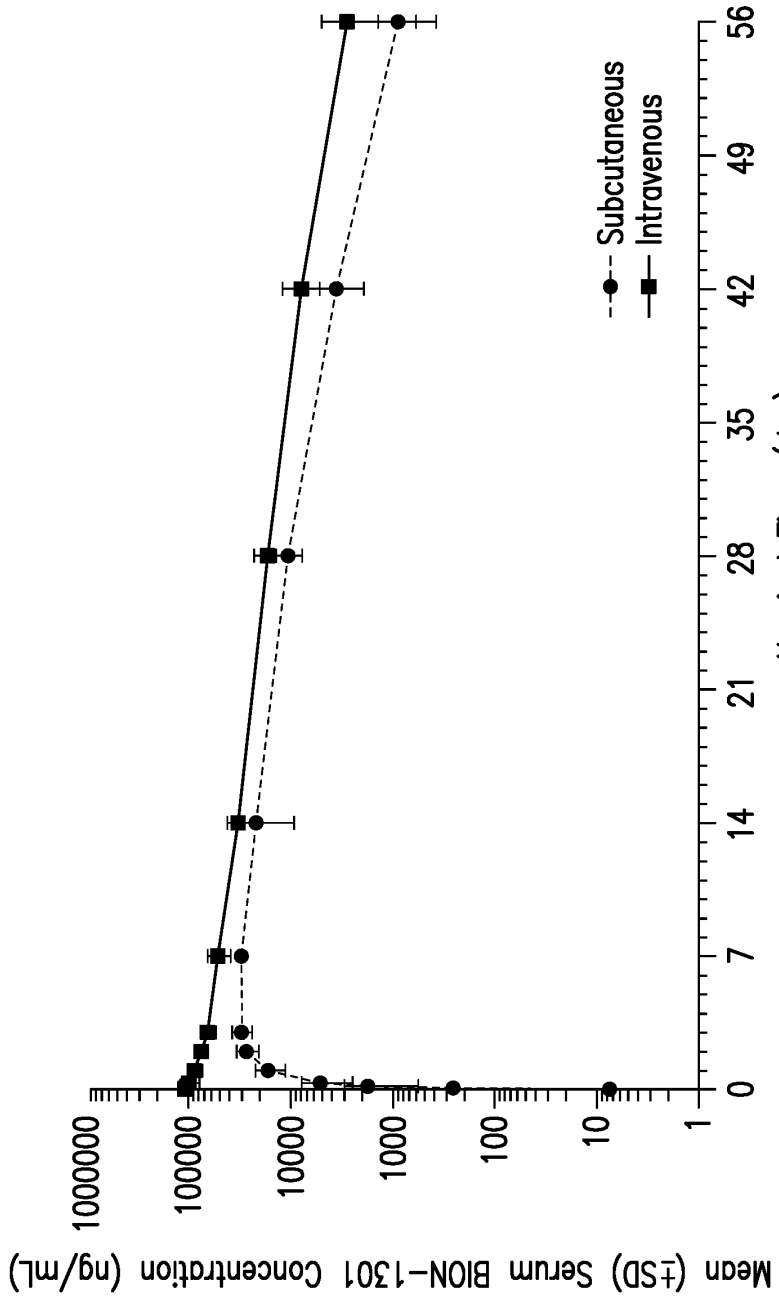

Mean (±SD) Serum BION-1301 Concentration (ng/mL)
1000000
100000
10000
1000
100
10
1
0
7
14
21
28
35
42
49
56
Nominal Time (day)
Subcutaneous
Intravenous

FIG.30

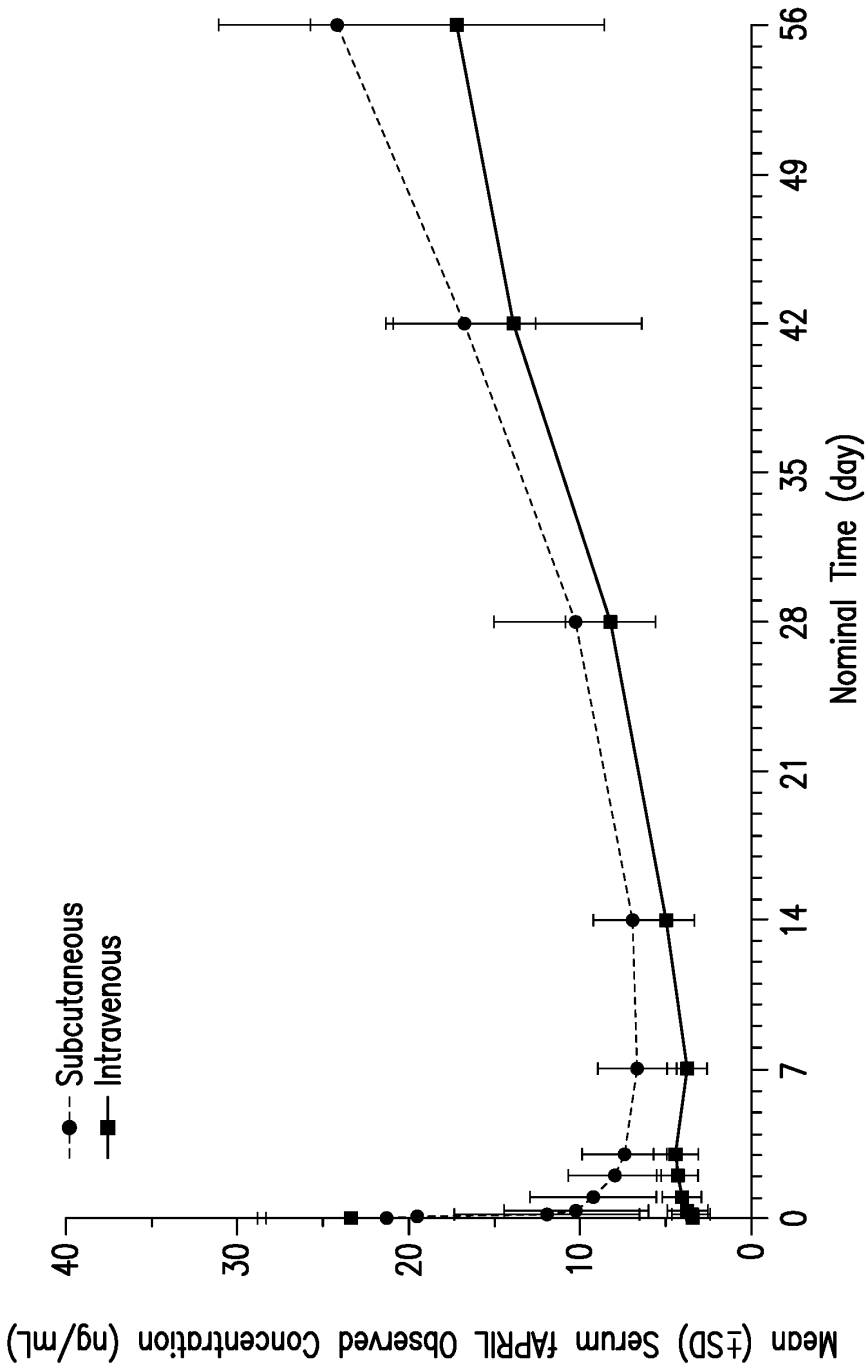

Mean (±SD) Serum fAPRIL Observed Concentration (ng/mL)
0
10
20
30
40
0
7
14
21
28
35
42
49
56
Nominal Time (day)
Subcutaneous
Intravenous

FIG.31A

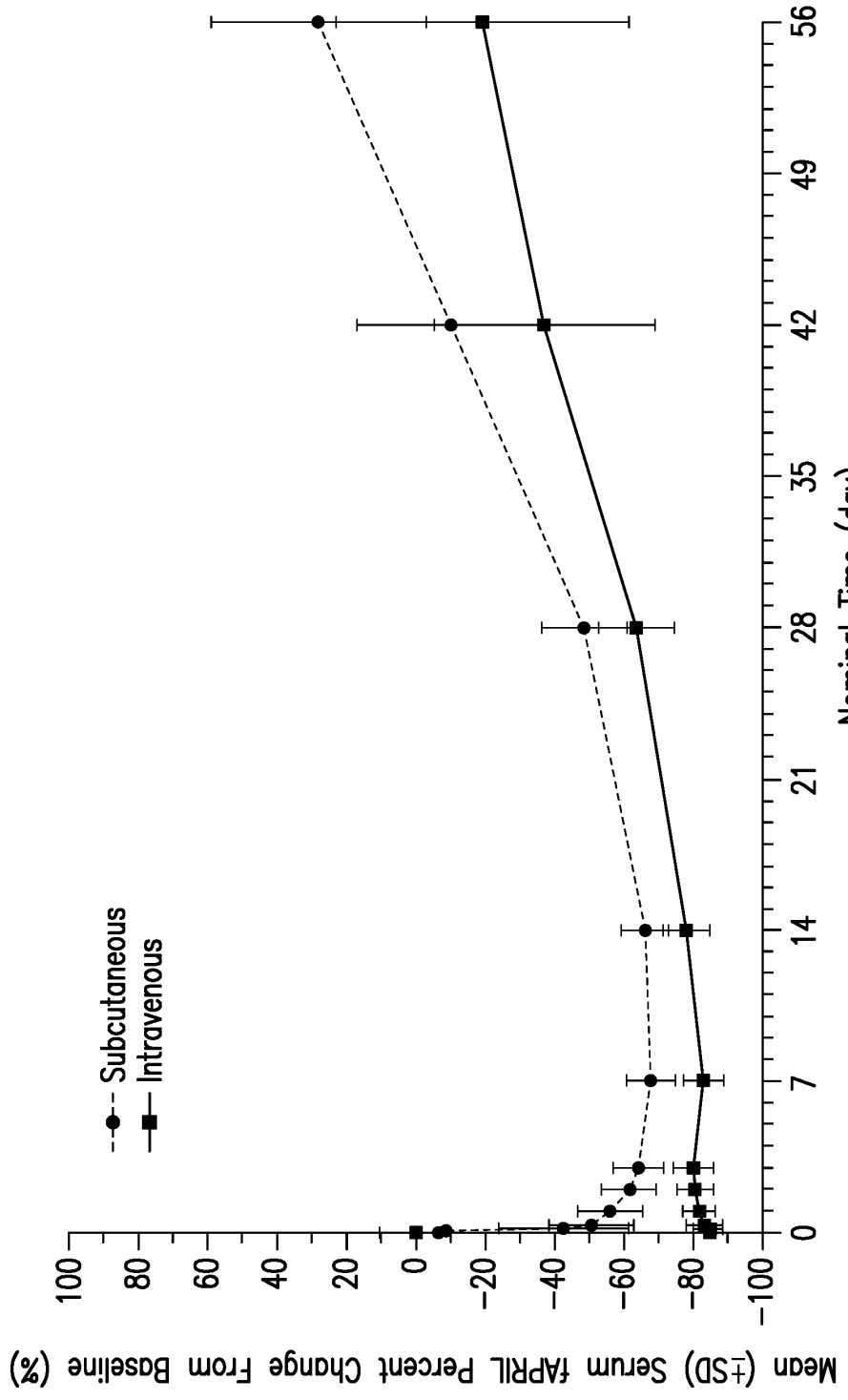

Mean (±SD) Serum fAPRIL Percent Change From Baseline (%)
100
80
60
40
20
0
−20
−40
−60
−80
−100
0
7
14
21
28
35
42
49
56
Nominal Time (day)
Subcutaneous
Intravenous

FIG.31B

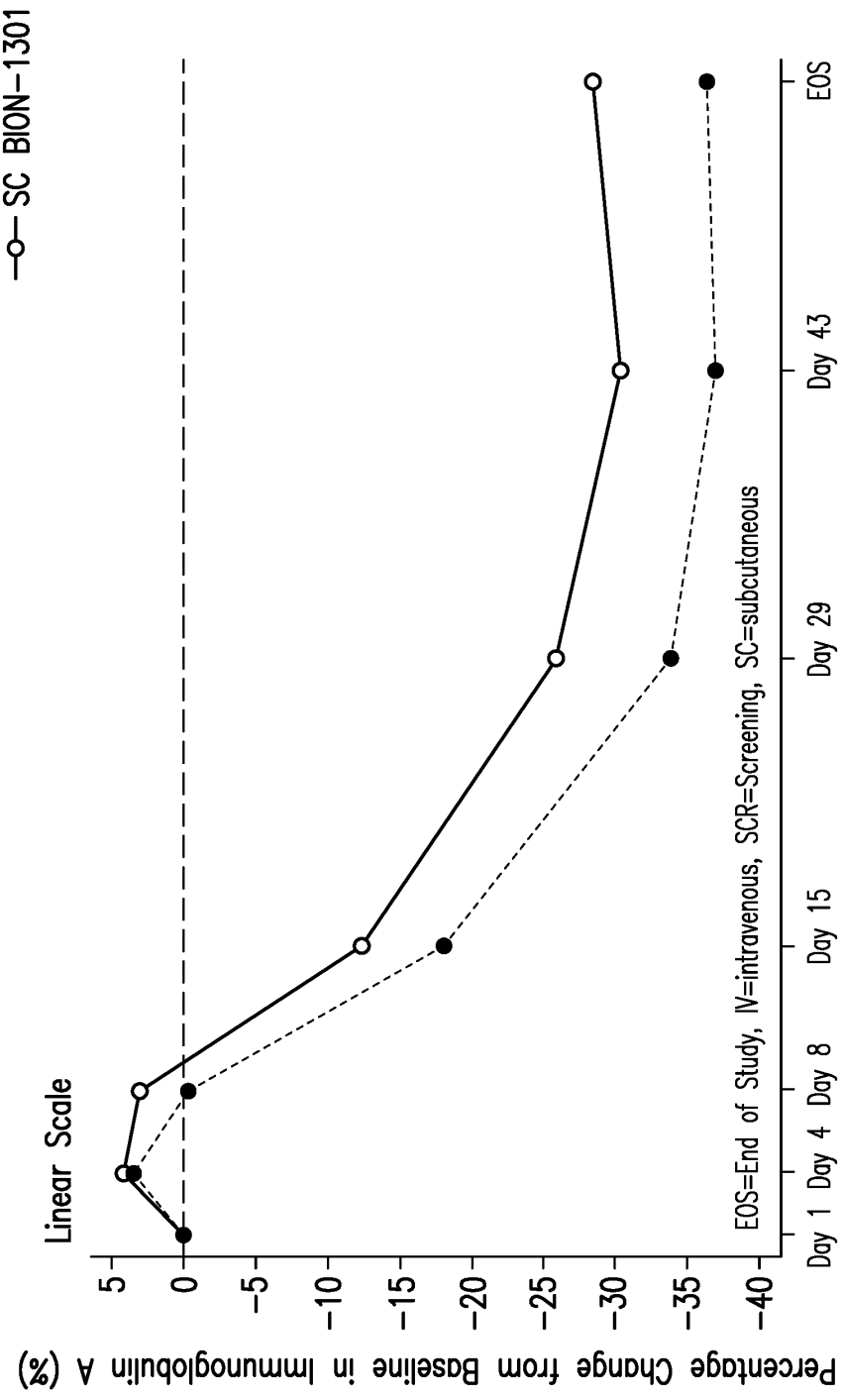

IV BION-1301
SC BION-1301
Linear Scale
Percentage Change from Baseline in Immunoglobulin A (%)
5
0
-5
-10
-15
-20
-25
-30
-35
-40
Day 1
Day 4
Day 8
Day 15
Day 29
Day 43
EOS
Timepoint
EOS=End of Study, IV=intravenous, SCR=Screening, SC=subcutaneous

FIG.32A

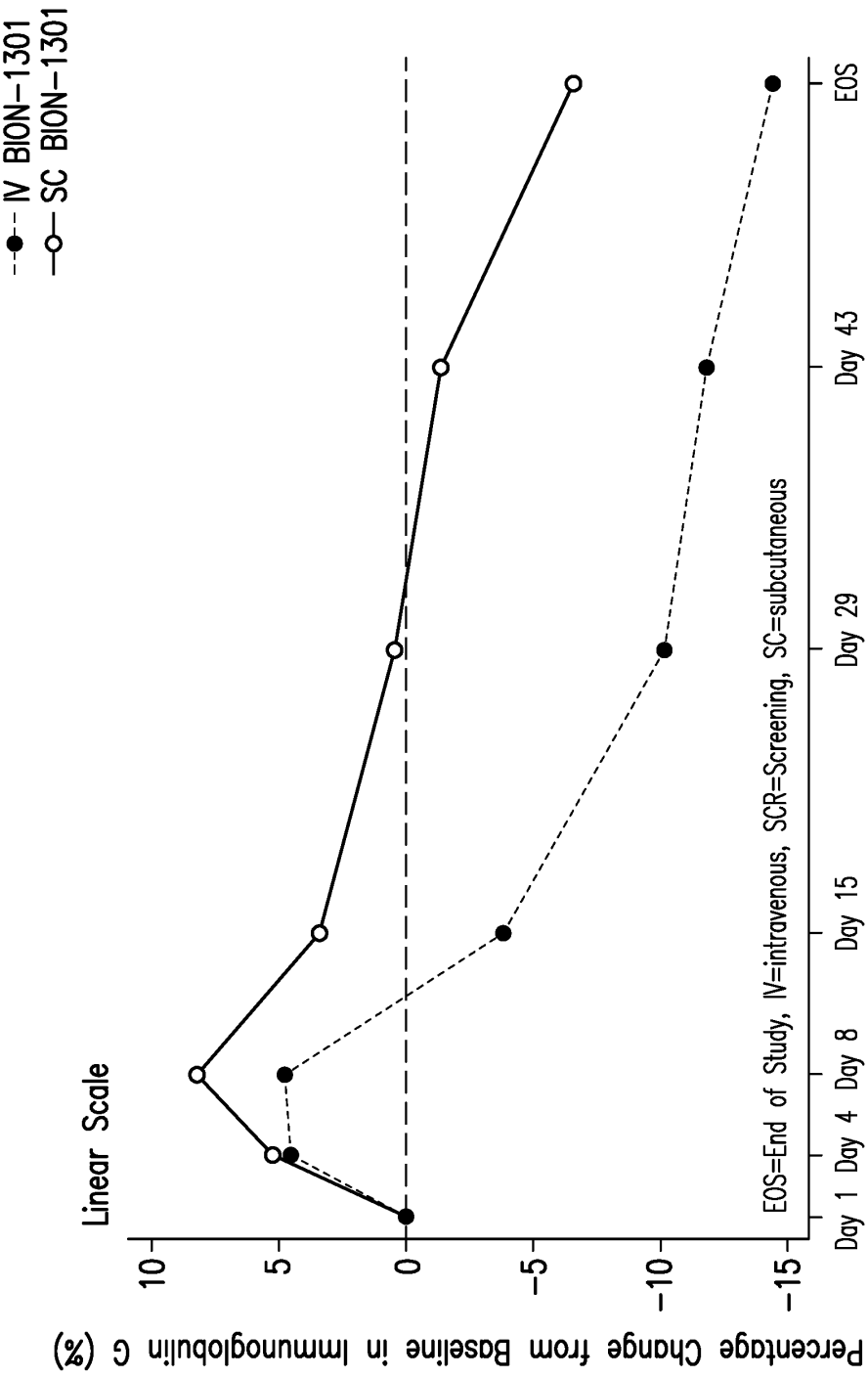

IV BION-1301
SC BION-1301
Linear Scale
Percentage Change from Baseline in Immunoglobulin G (%)
10
5
0
-5
-10
-15
Day 1
Day 4
Day 8
Day 15
Day 29
Day 43
EOS
EOS=End of Study, IV=intravenous, SCR=Screening, SC=subcutaneous
Timepoint

FIG.32B

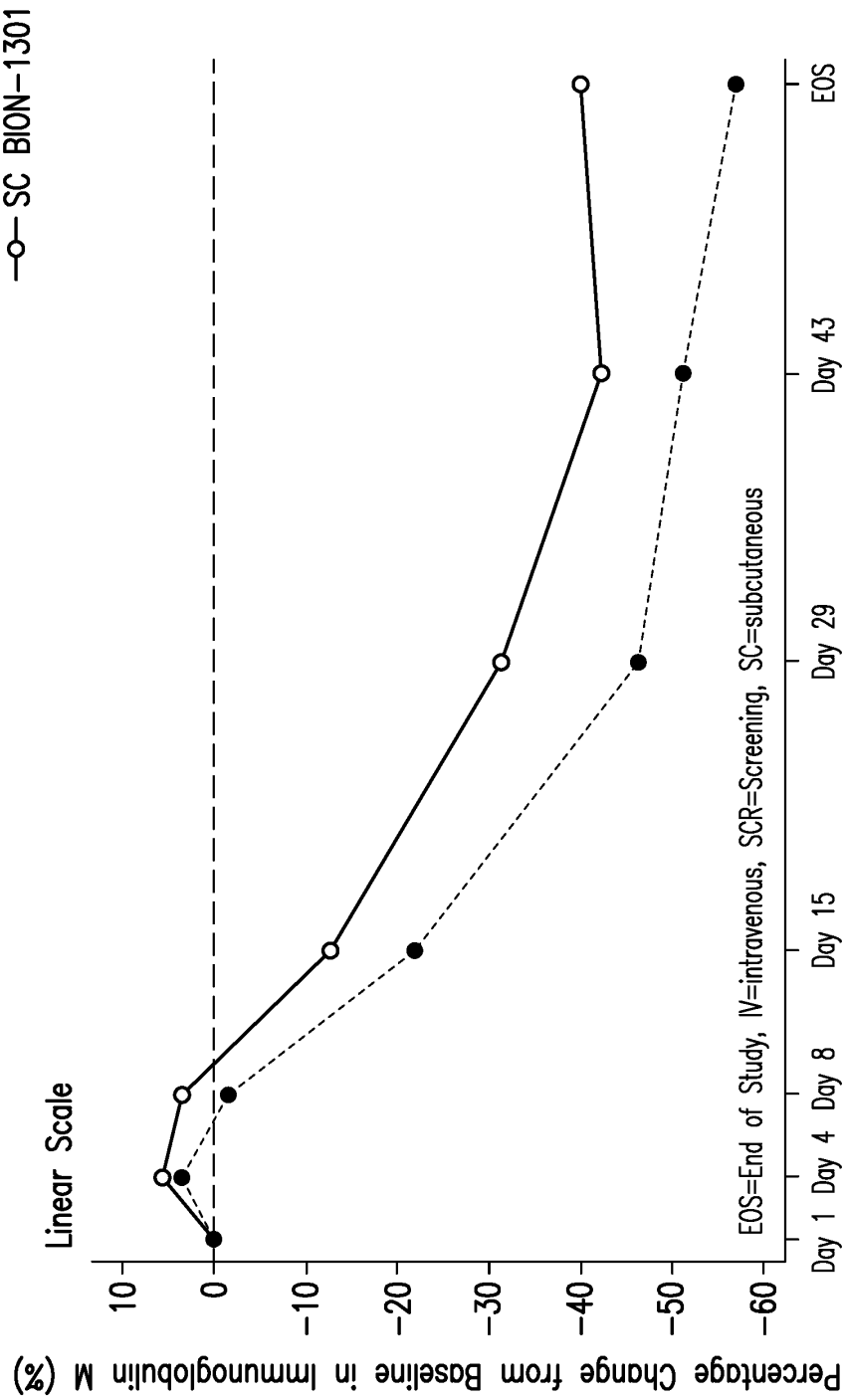

IV BION-1301
SC BION-1301
Linear Scale
Percentage Change from Baseline in Immunoglobulin M (%)
10
0
-10
-20
-30
-40
-50
-60
Day 1
Day 4
Day 8
Day 15
Day 29
Day 43
EOS
Timepoint
EOS=End of Study, IV=intravenous, SCR=Screening, SC=subcutaneous

FIG.32C

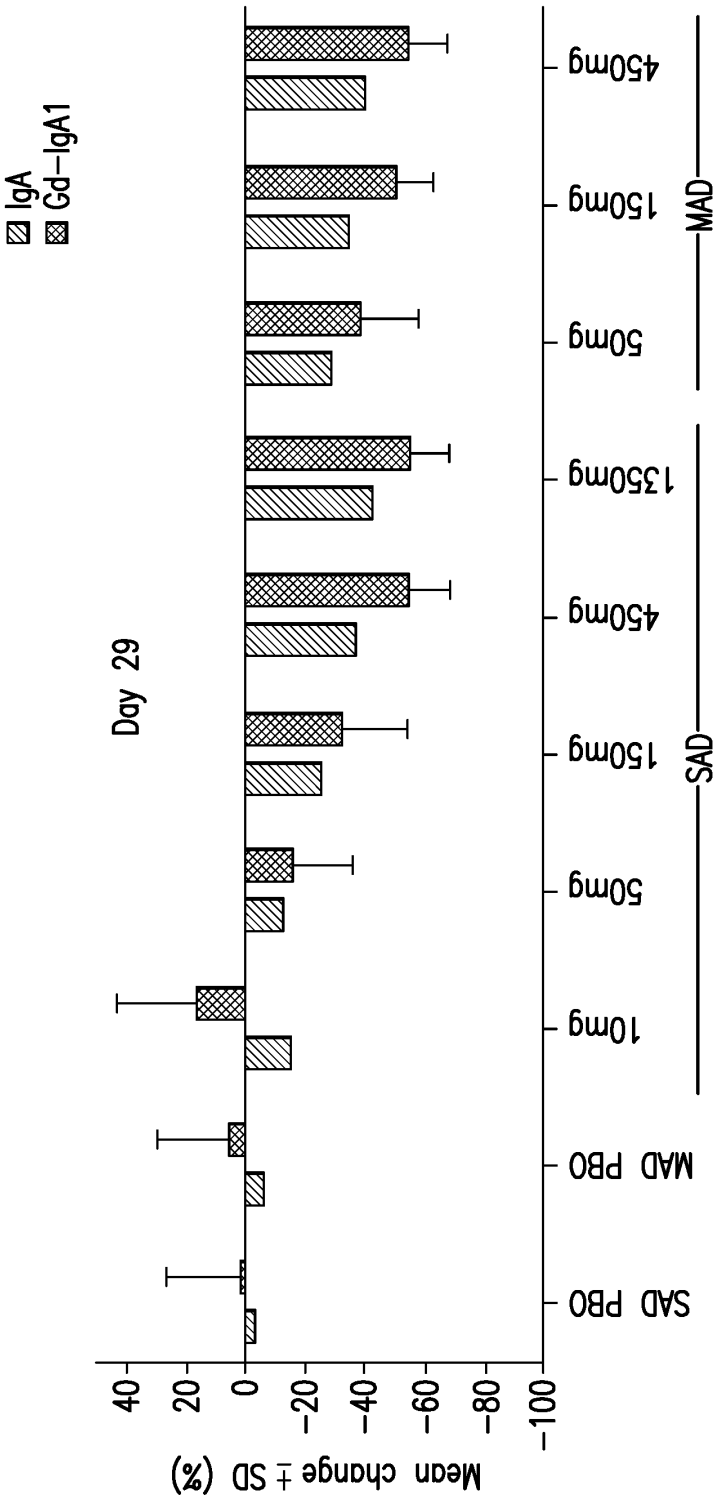

IgA
Gd-IgA1
Day 29
Mean change ± SD (%)
40
20
0
-20
-40
-60
-80
-100
SAD PBO
MAD PBO
10mg
50mg
150mg
450mg
1350mg
50mg
150mg
450mg
SAD
MAD

FIG.33

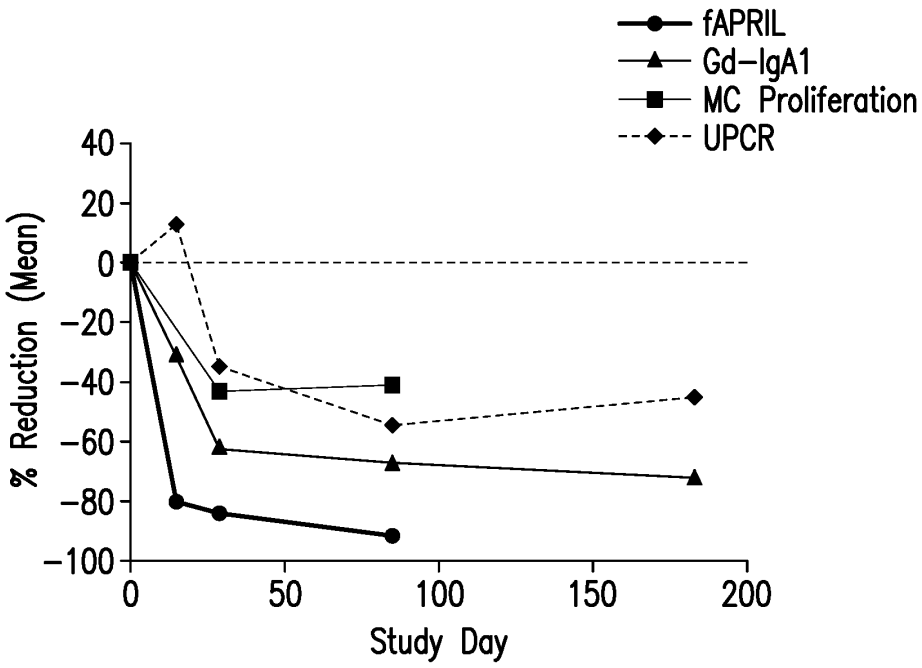

fAPRIL
Gd-IgA1
MC Proliferation
UPCR
% Reduction (Mean)
40
20
0
-20
-40
-60
-80
-100
0
50
100
150
200
Study Day

FIG.34