

IL-2, a key regulator of the immune system

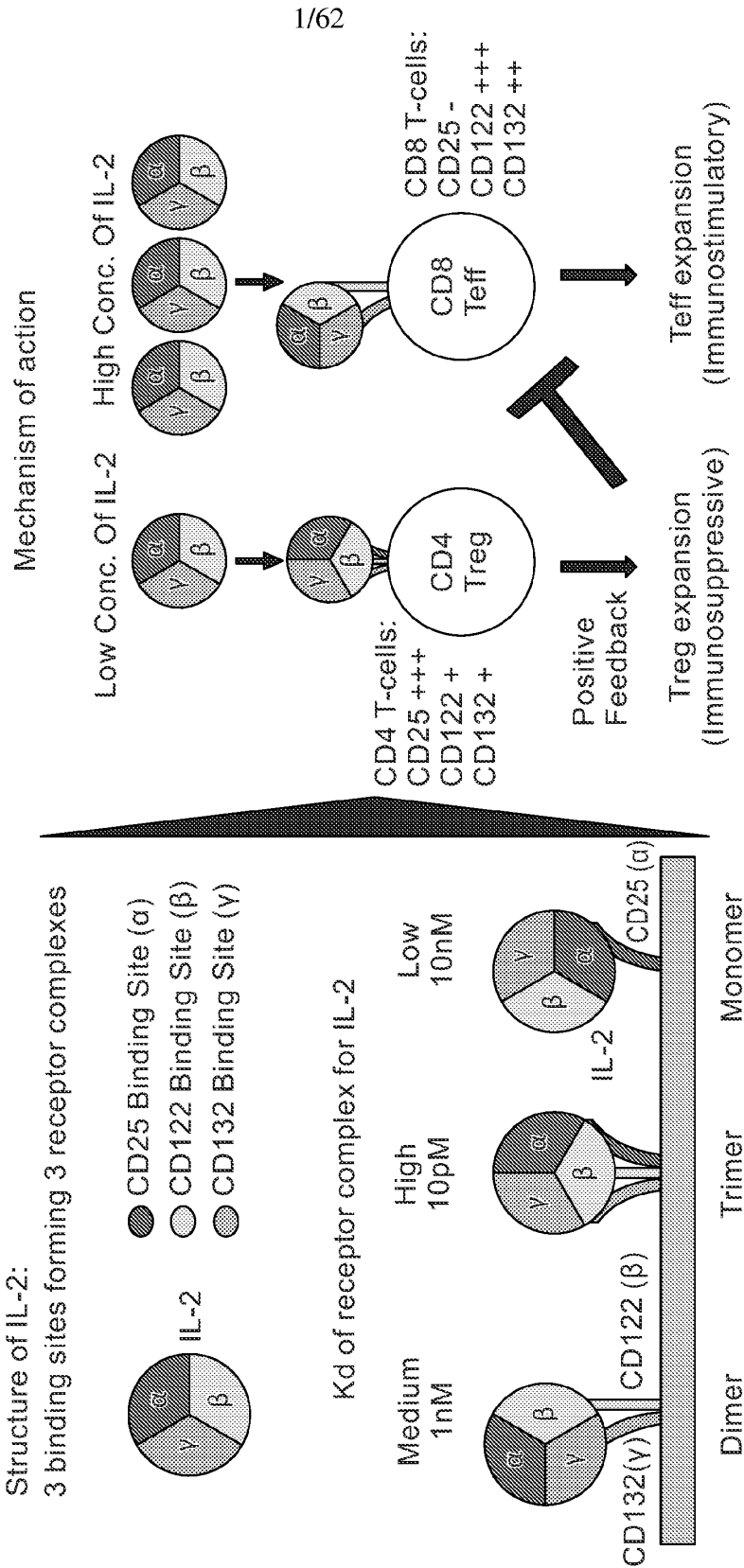
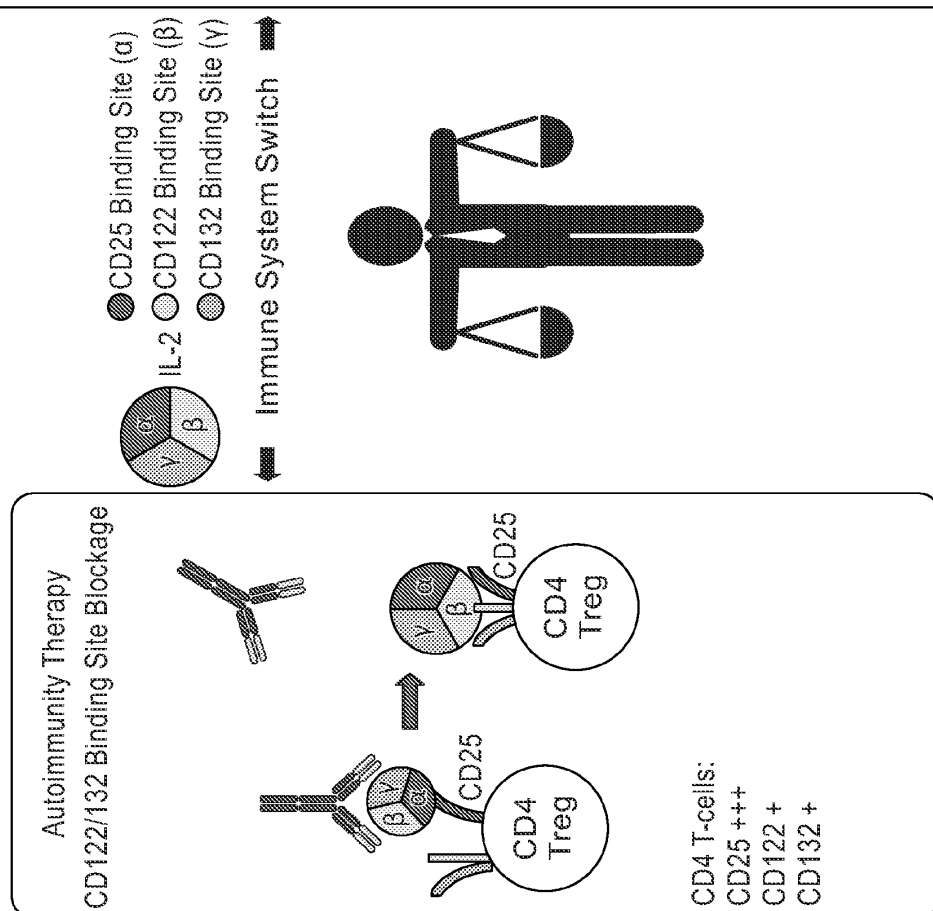
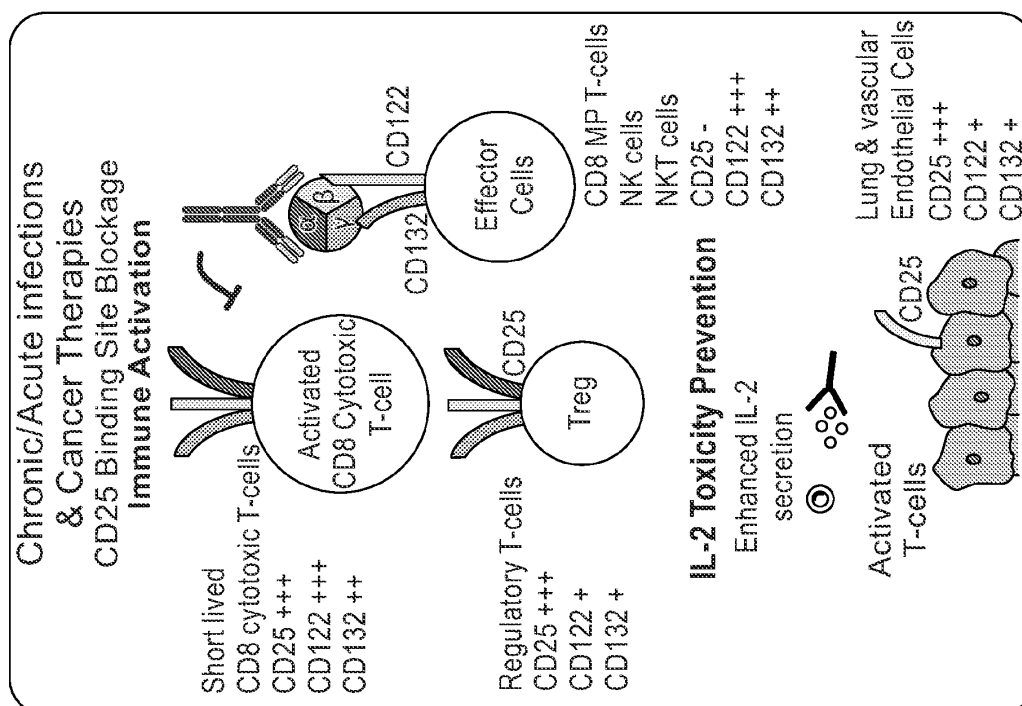
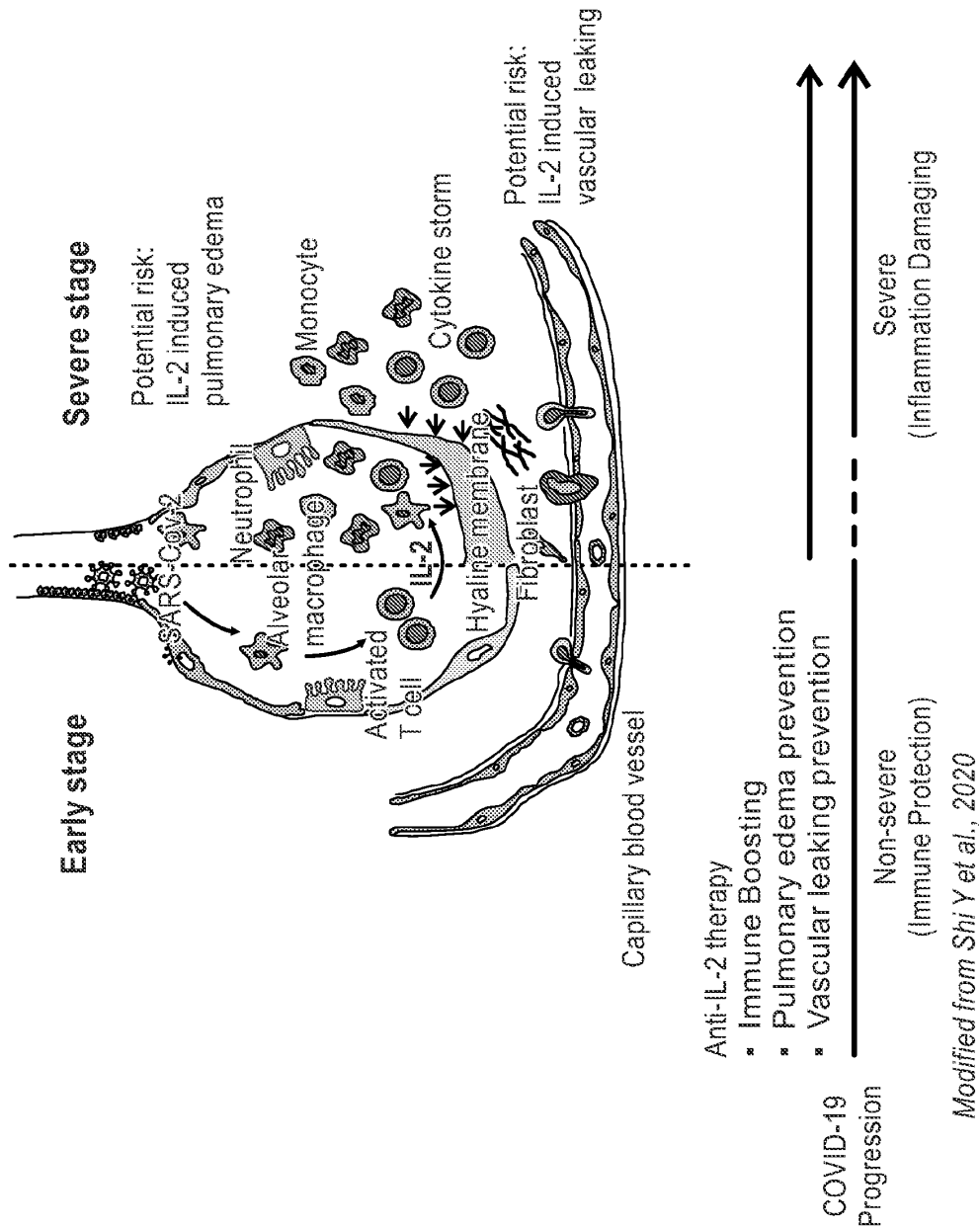


FIG. 1

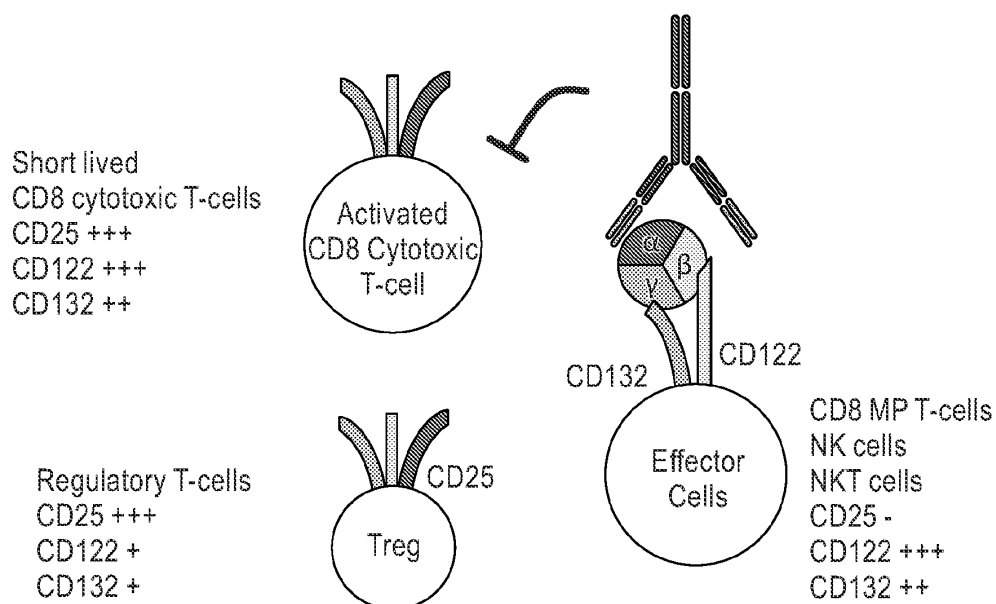
2
G
L



4/62

CD25 Binding Site Blockage

Immune Activation



IL-2 Toxicity Prevention

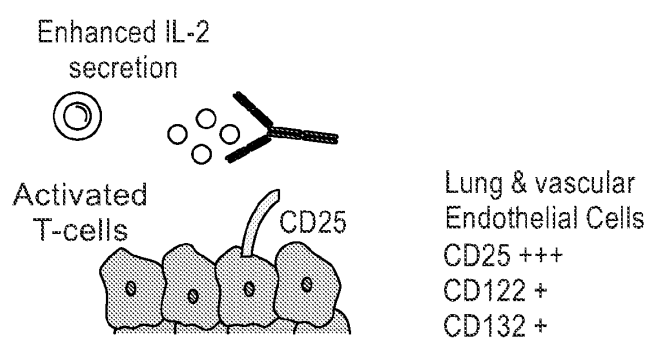


FIG. 3B

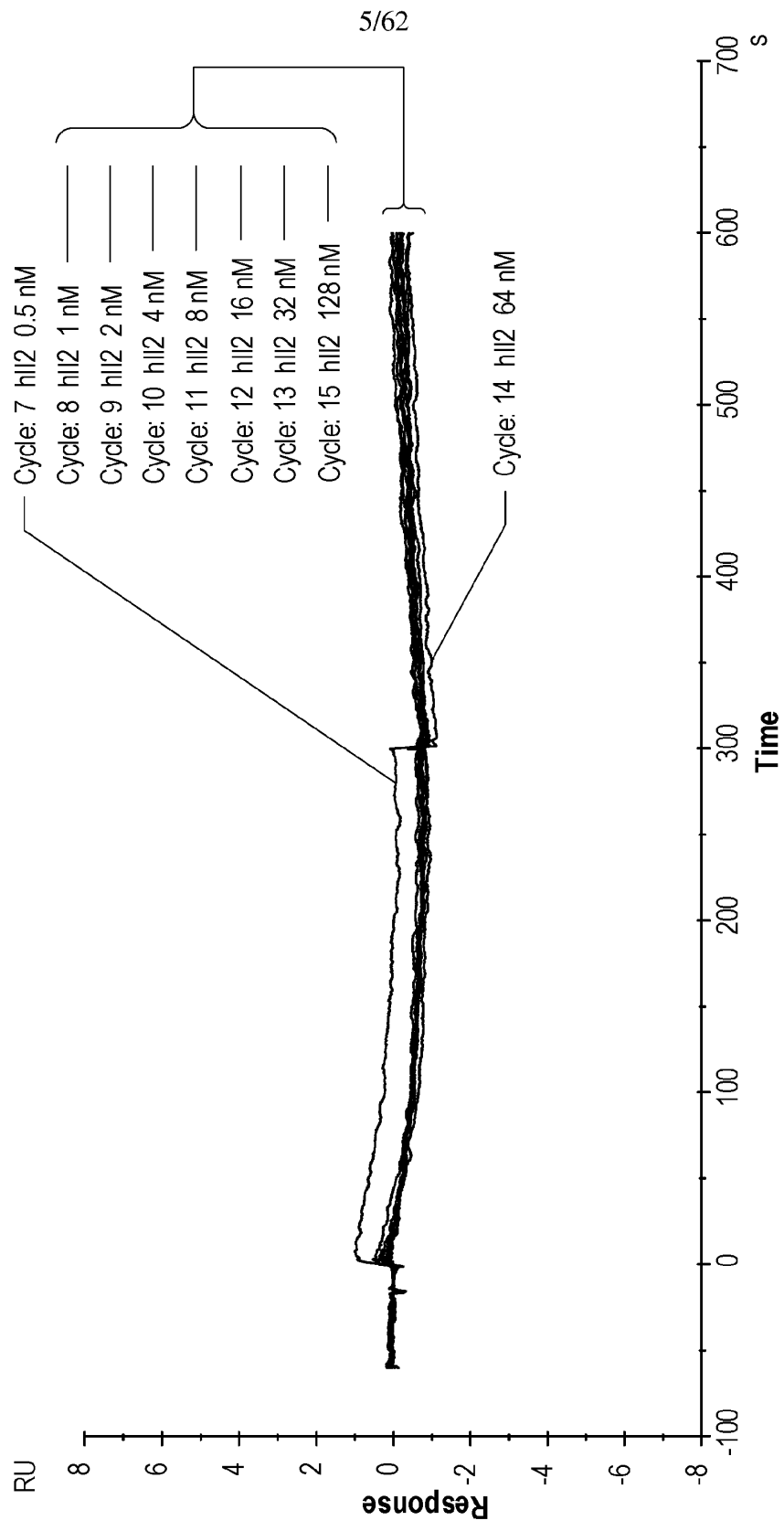


FIG. 4A



FIG. 4B

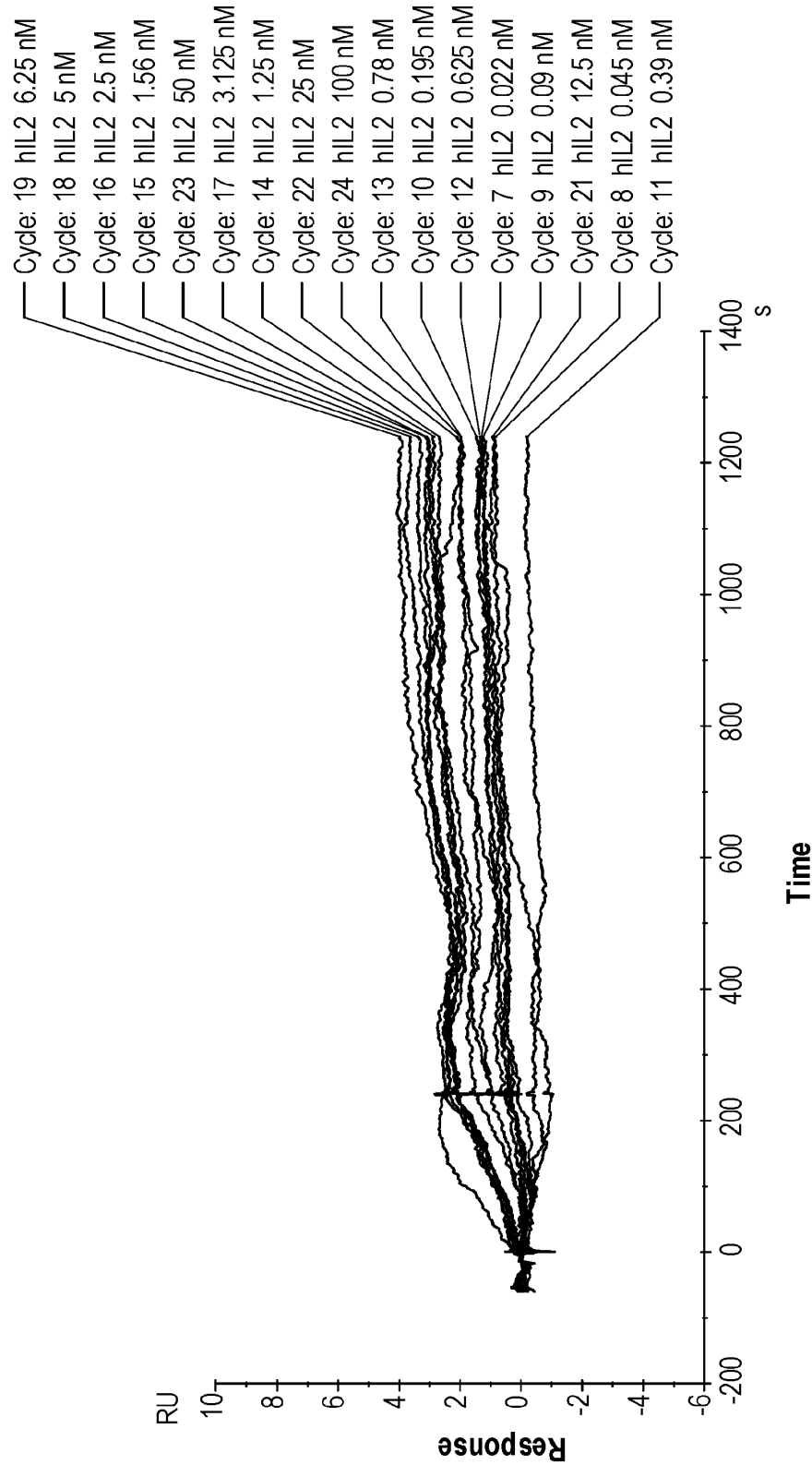


FIG. 4C

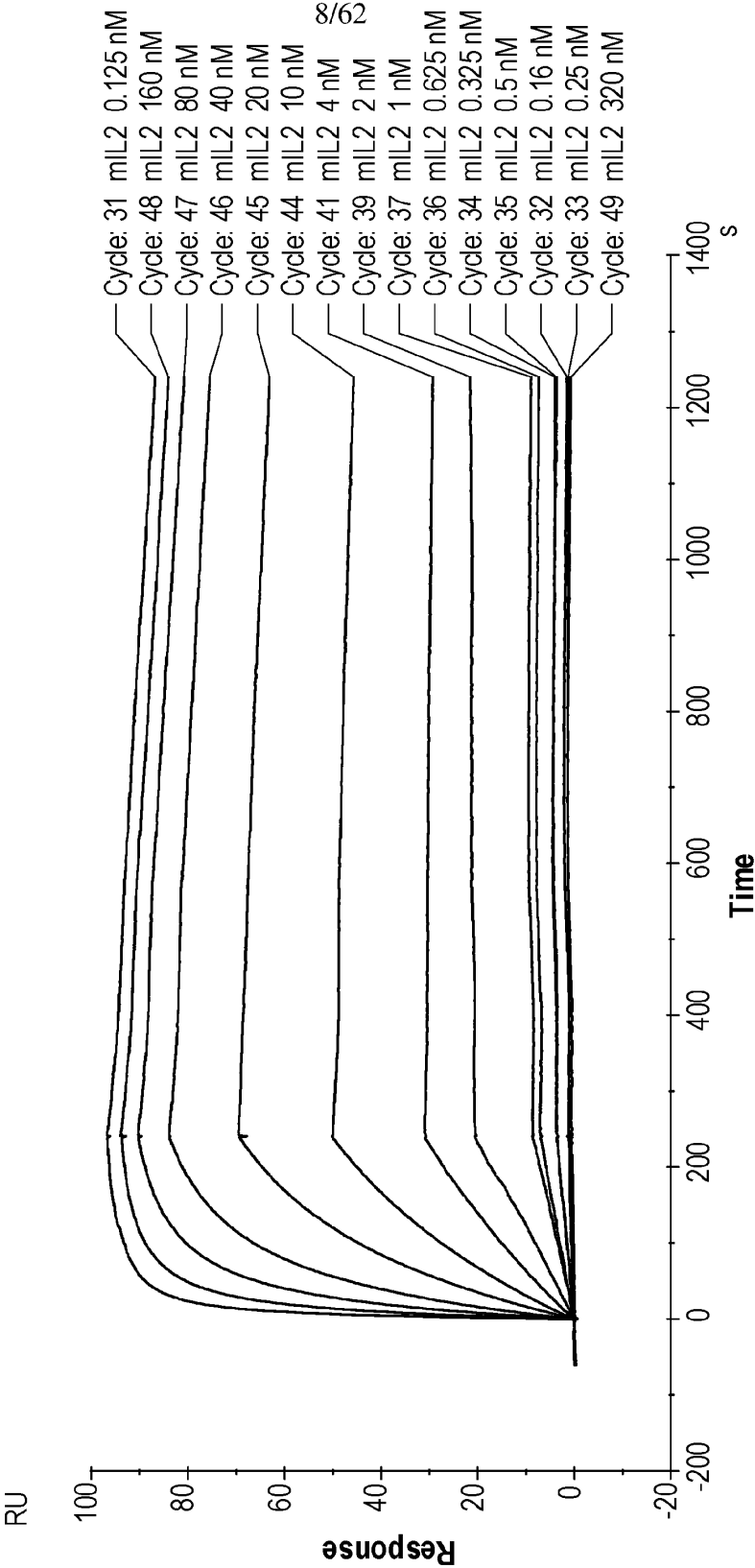
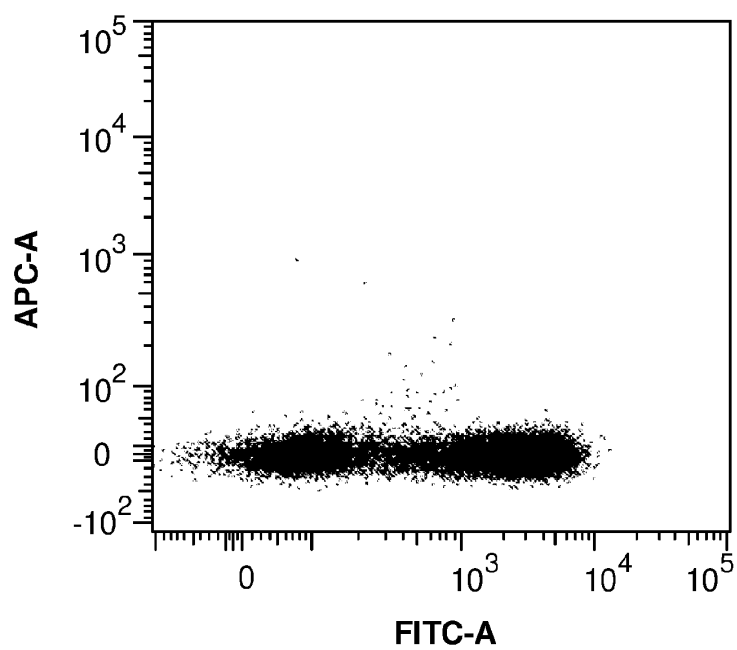
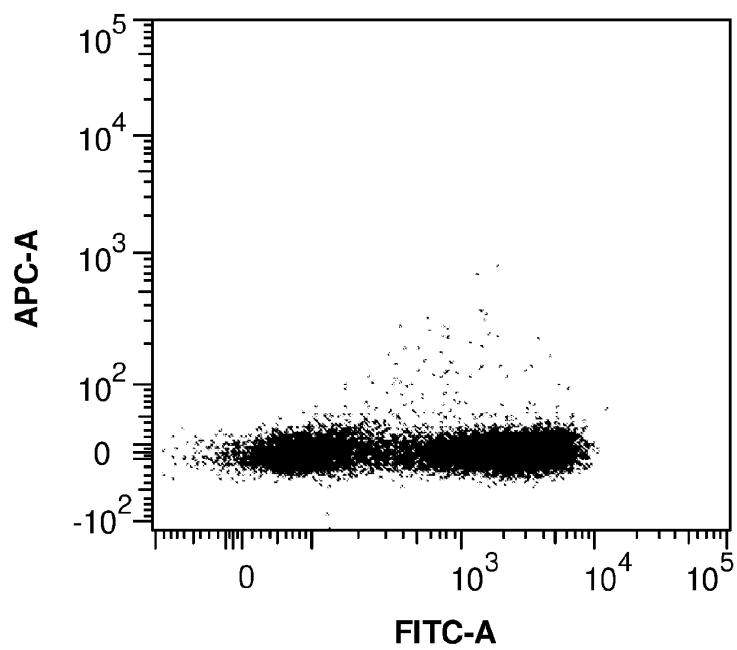
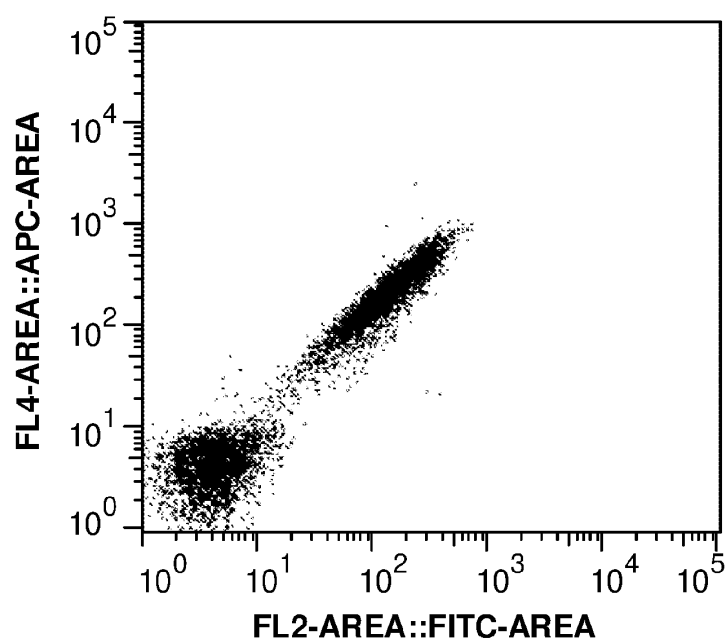


FIG. 4D

9/62

**FIG. 5A****FIG. 5B**

10/62

**FIG. 5C**

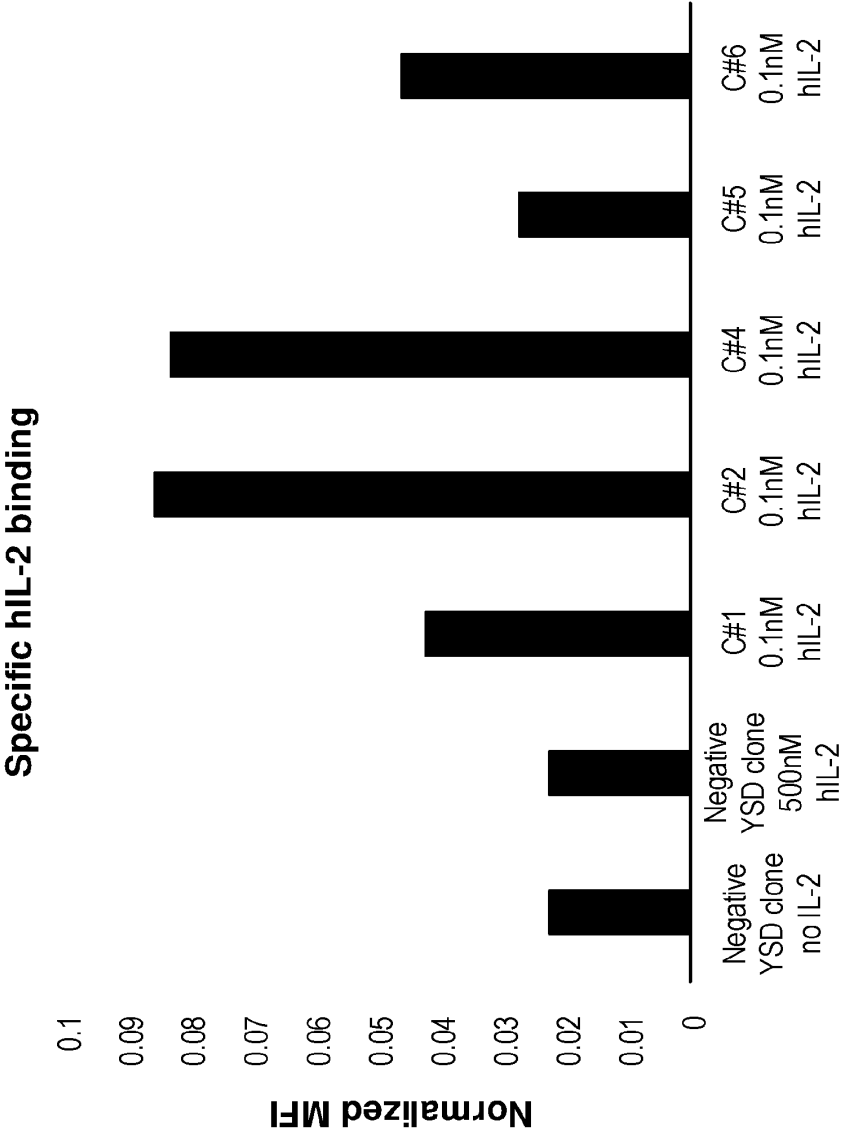


FIG. 6A

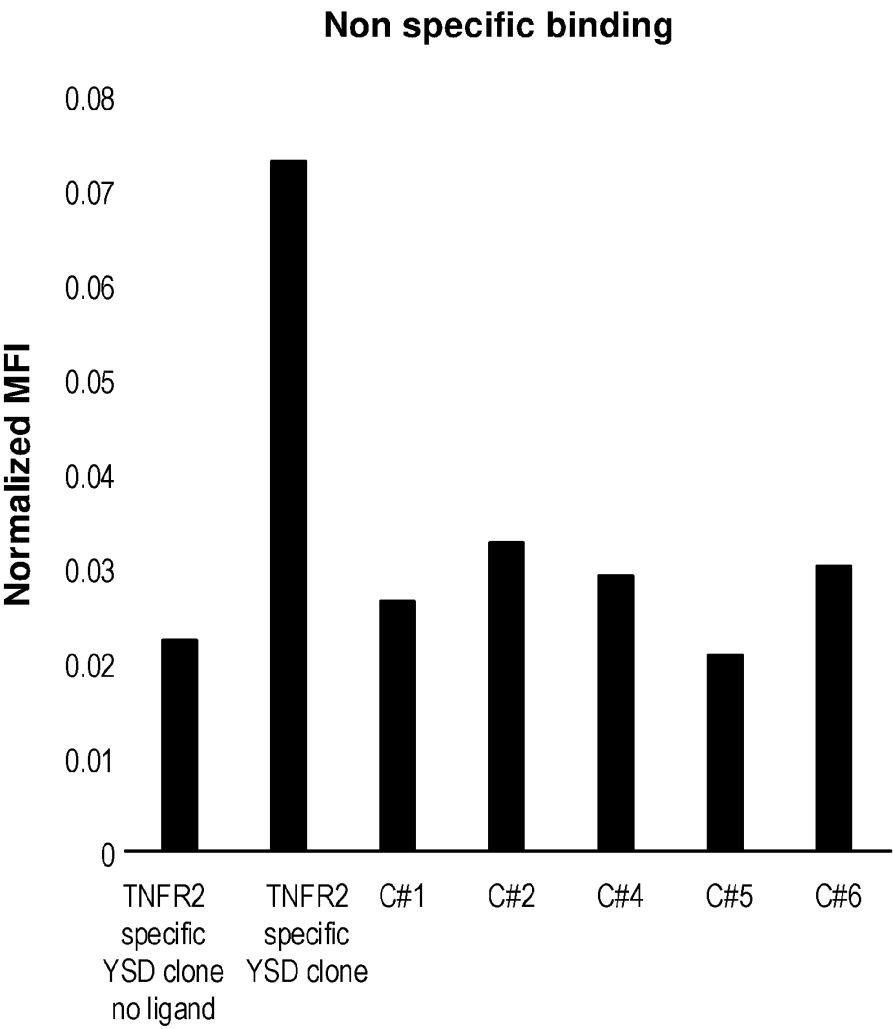
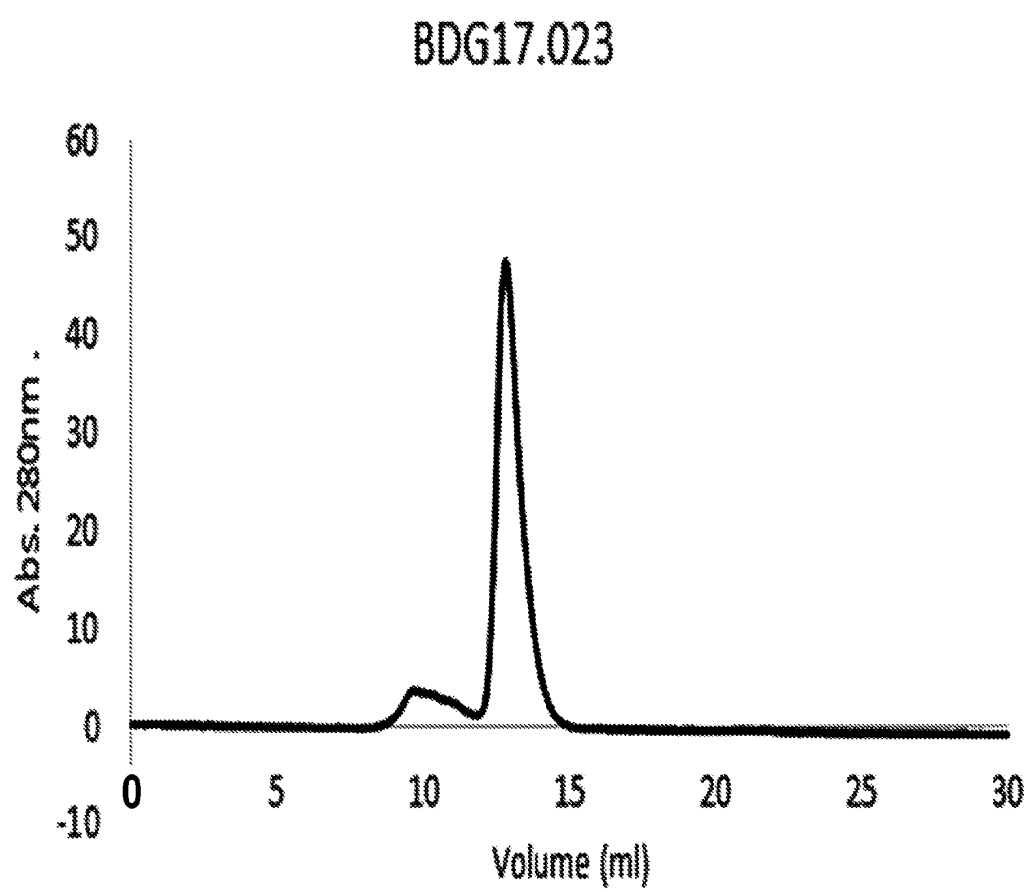


FIG. 6B

13/62

**FIG. 7**

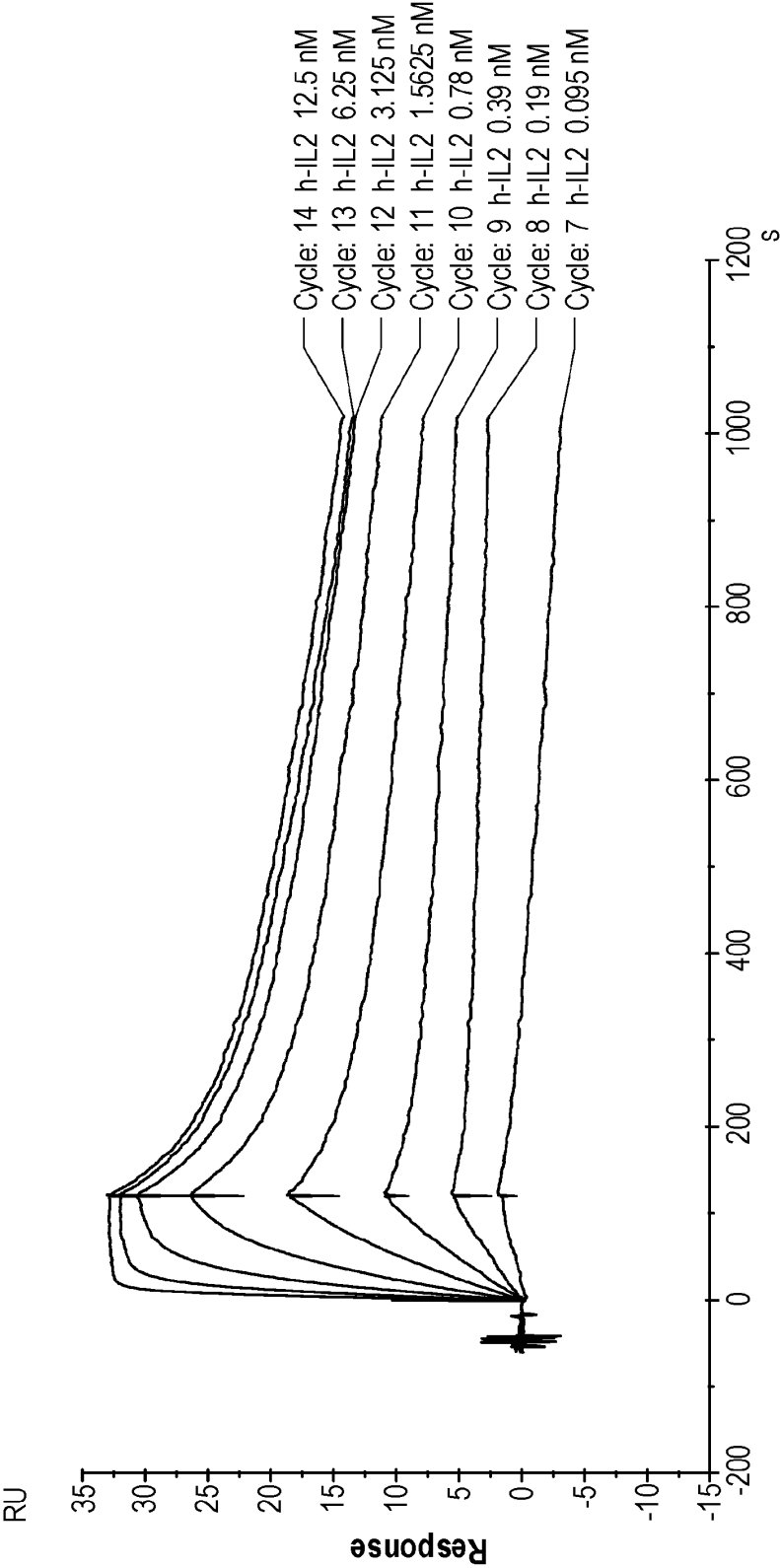


FIG. 8A

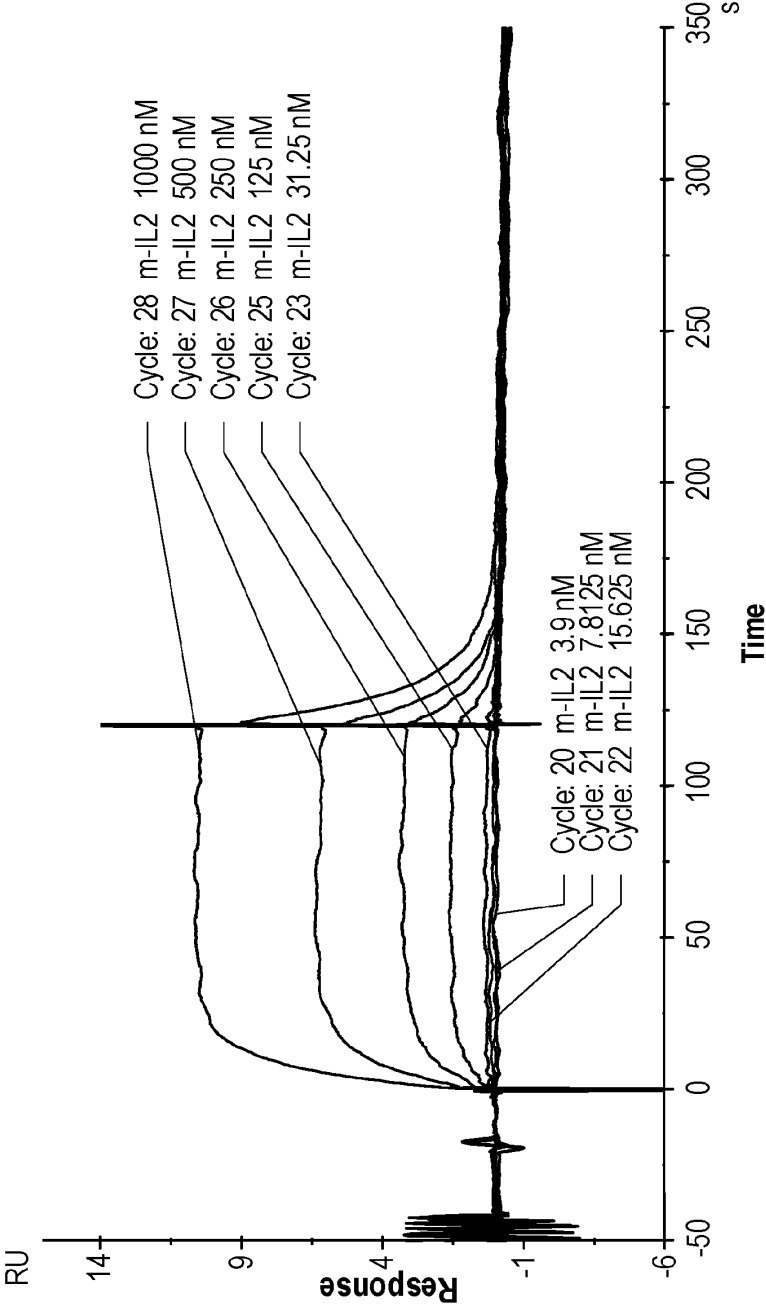


FIG. 8B

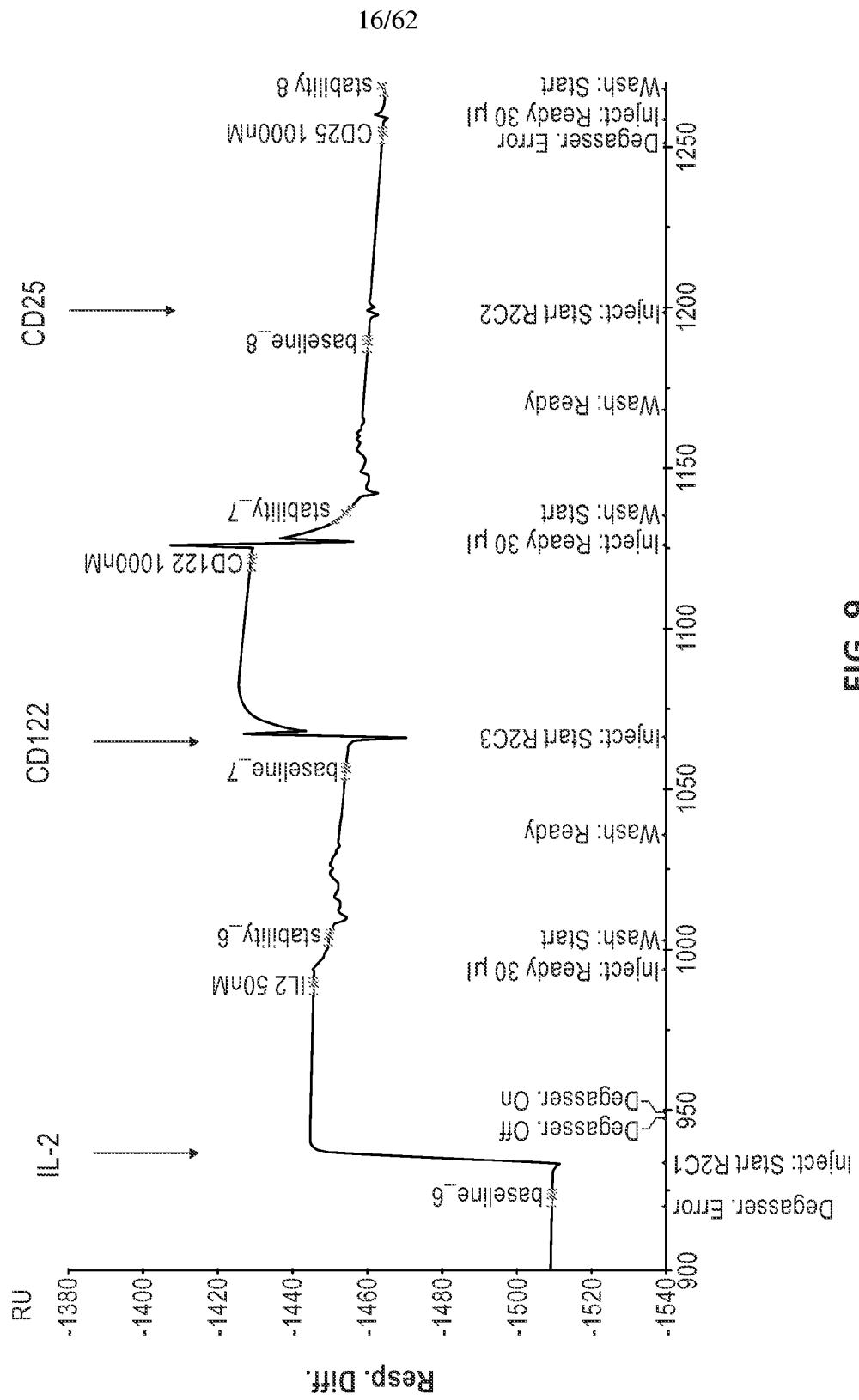


FIG. 9

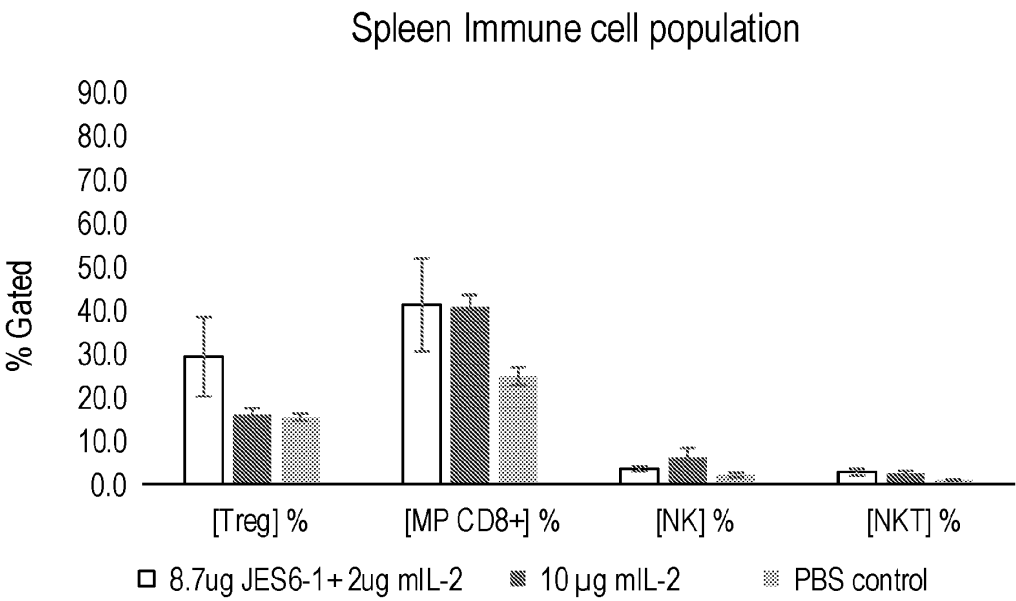


FIG. 10A

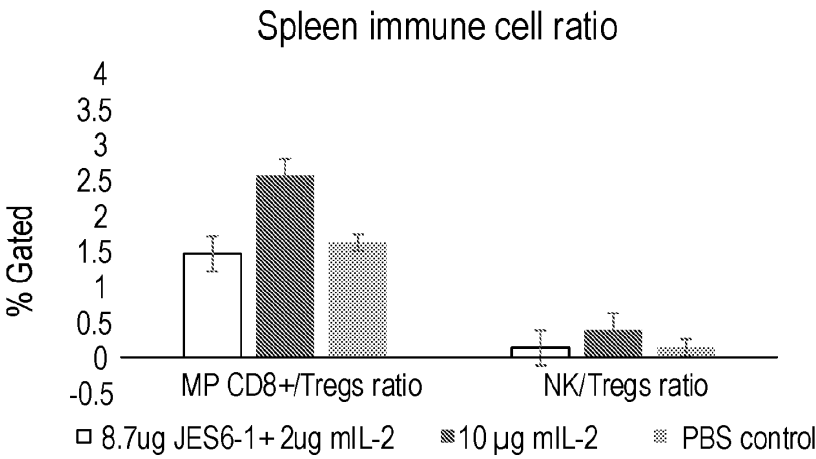
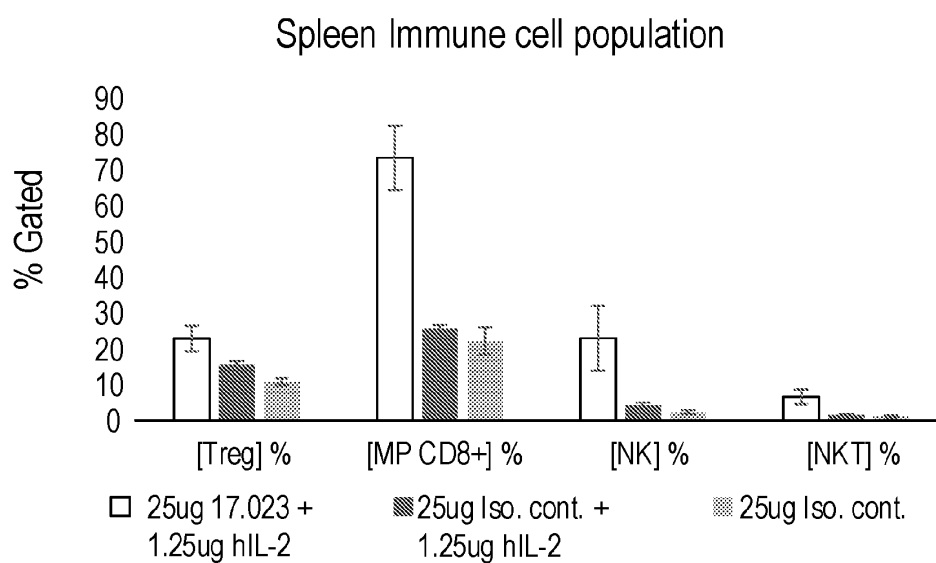
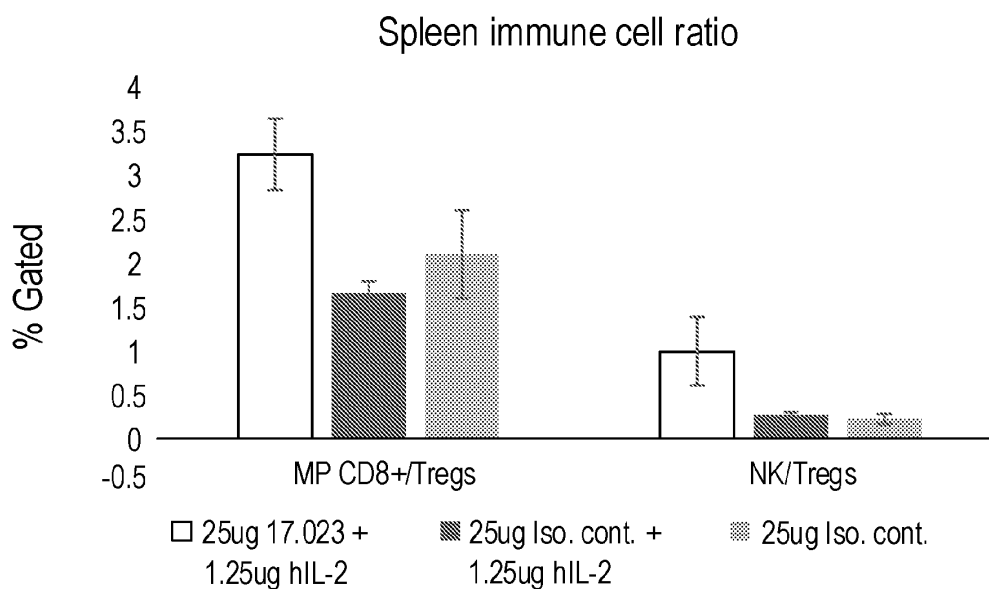


FIG. 10B

18/62

**FIG. 10C****FIG. 10D**

JES6_1_VH	EIQLQSGPELRPCSSVKLSCAKSYNTDYLHHWRHPHEGLEWICWDPEDGEIRYAOKEFQSKATITADISSNAAYMQLSLTPTEDATVFCARSLDSIIYIPFAYNGOGLTVTSS
17.021_VH	N.
17.022_VH	.
17.023_VH	.
17.030_VH	.
17.035_VH	.

19/62

JES6_1_VH = SEQ ID NO:6
17.021_VH = SEQ ID NO:10
17.022_VH = SEQ ID NO:12
17.023_VH = SEQ ID NO:14
17.030_VH = SEQ ID NO:16
17.035_VH = SEQ ID NO:18

E.G.E.

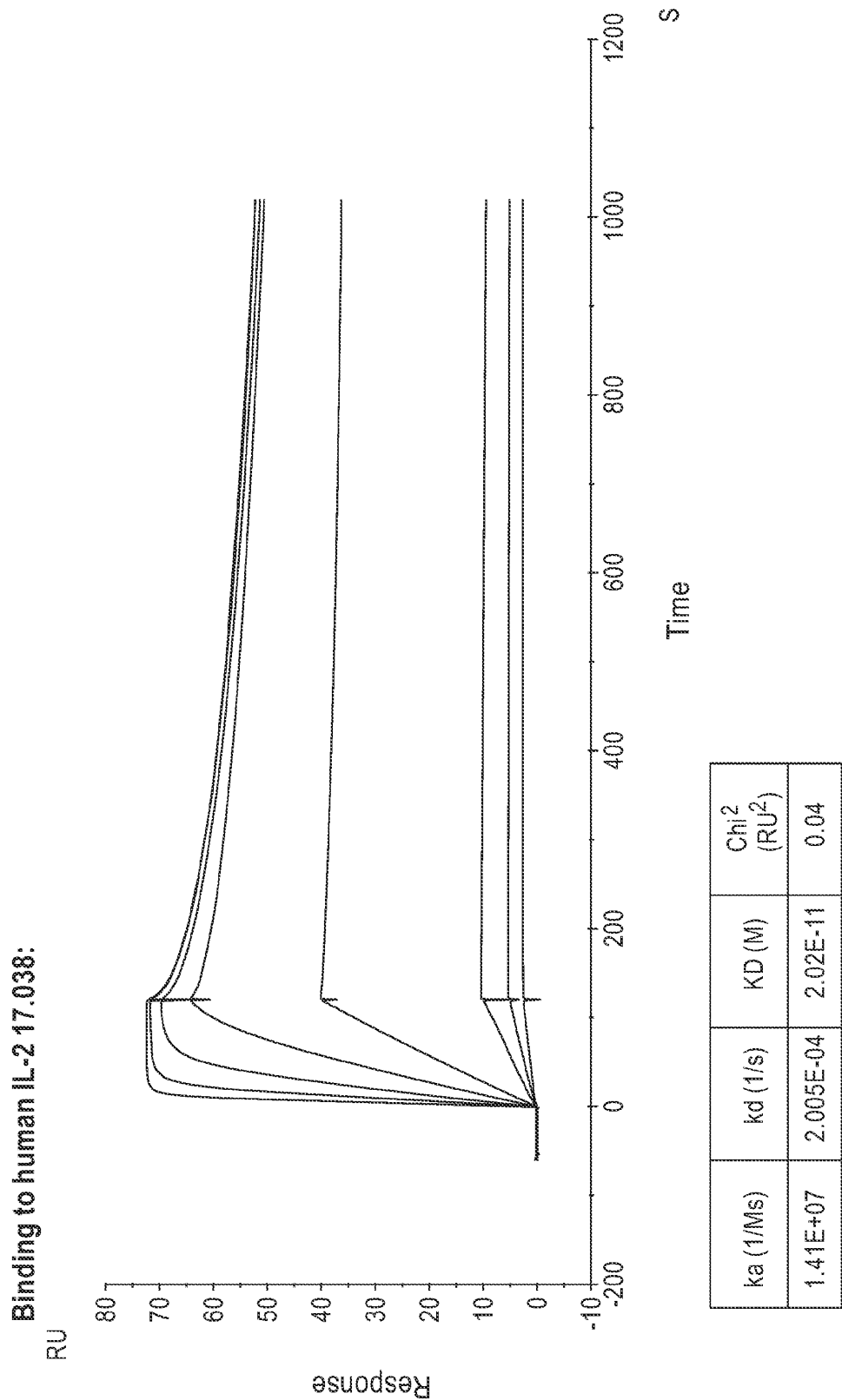


FIG. 14A

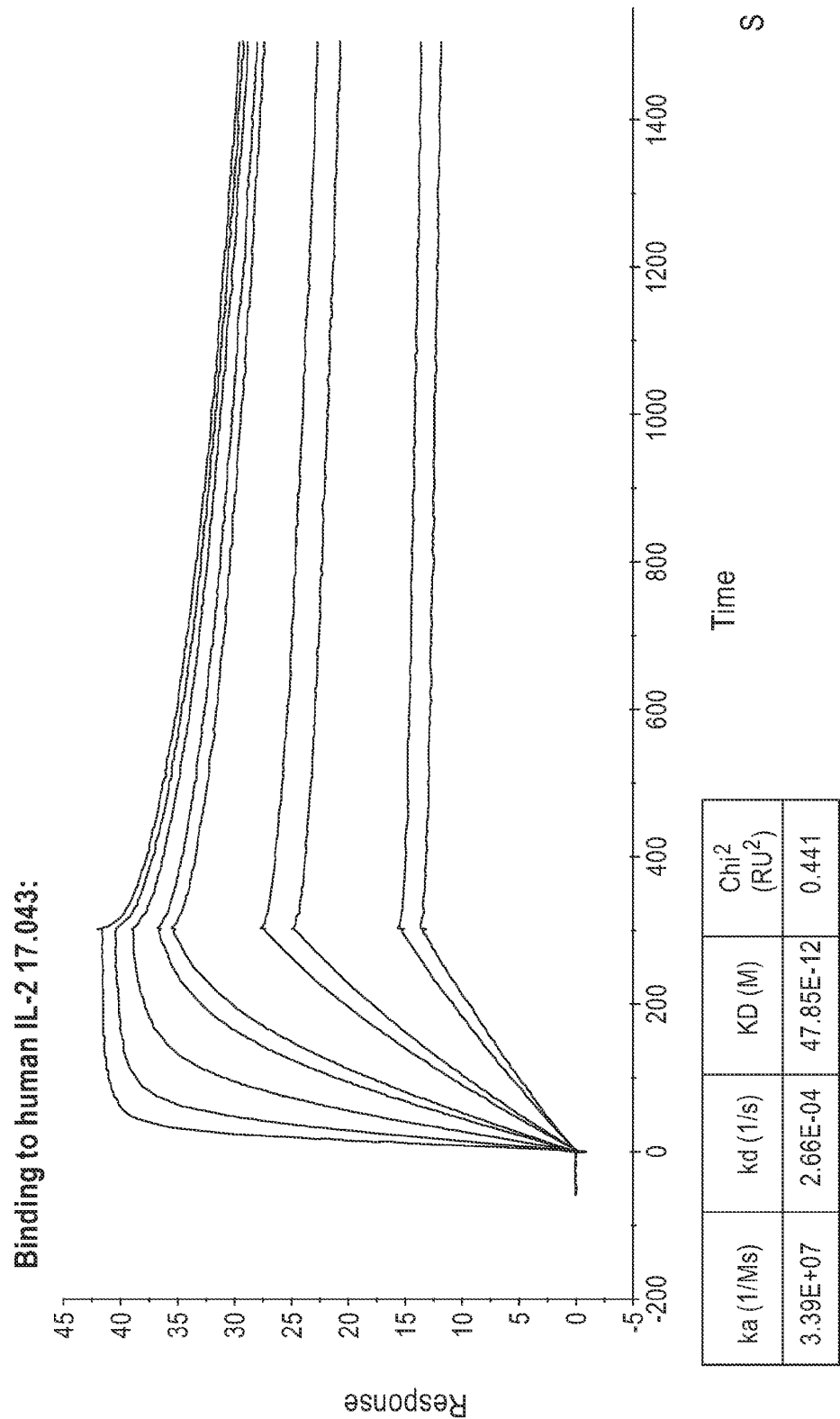


FIG. 14B

Binding to human IL-2 17.053:

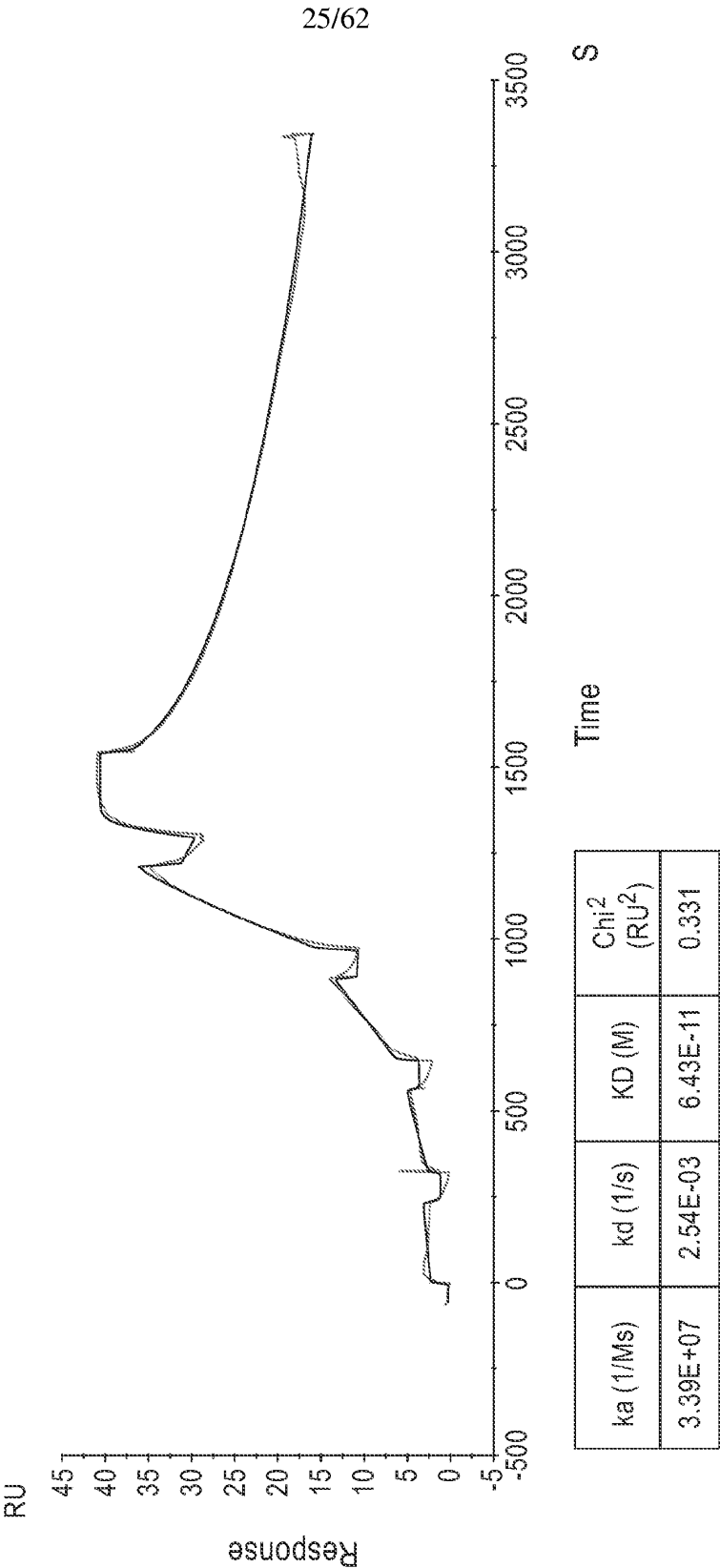


FIG. 14C

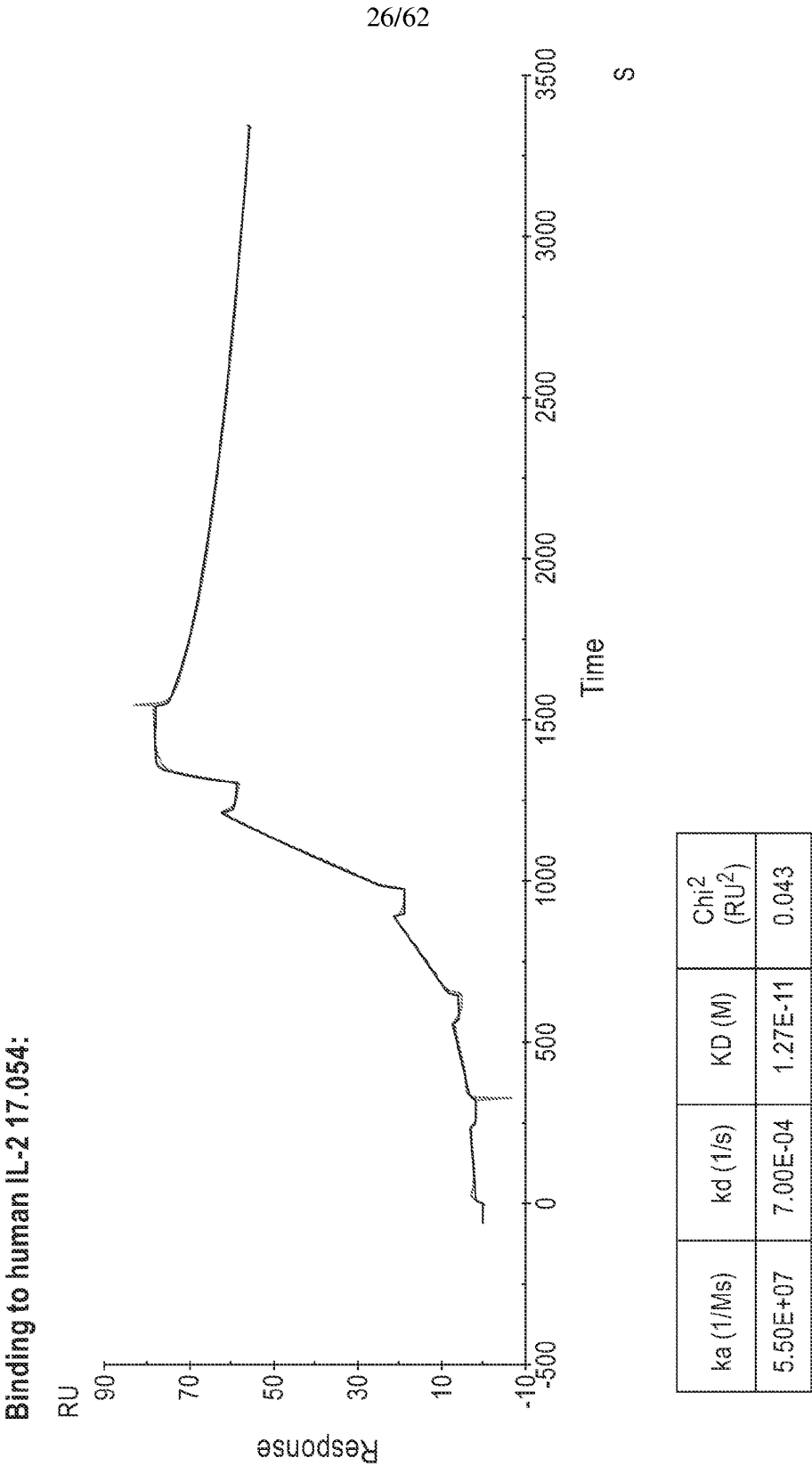


FIG. 14D

27/62

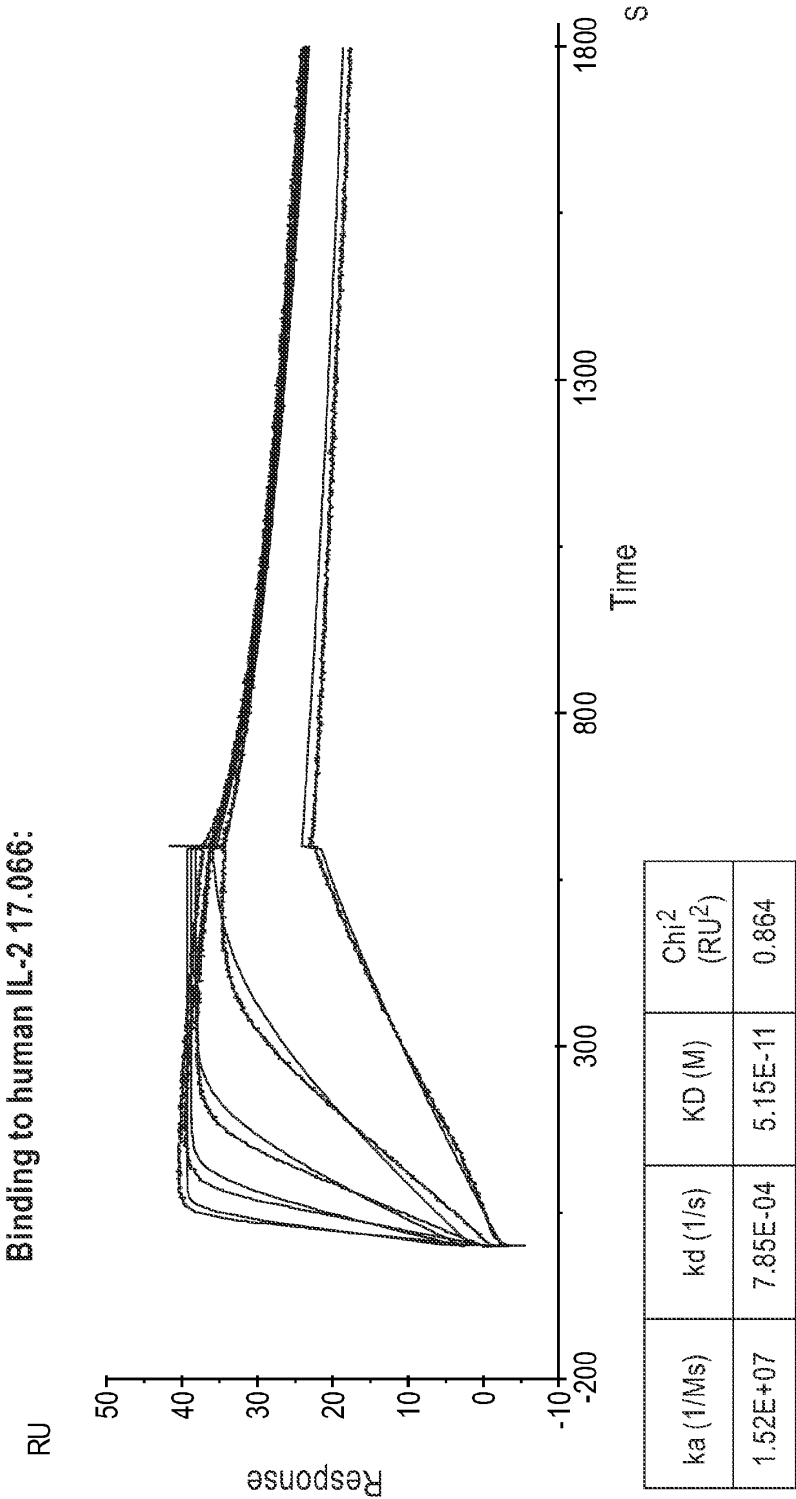


FIG. 14E

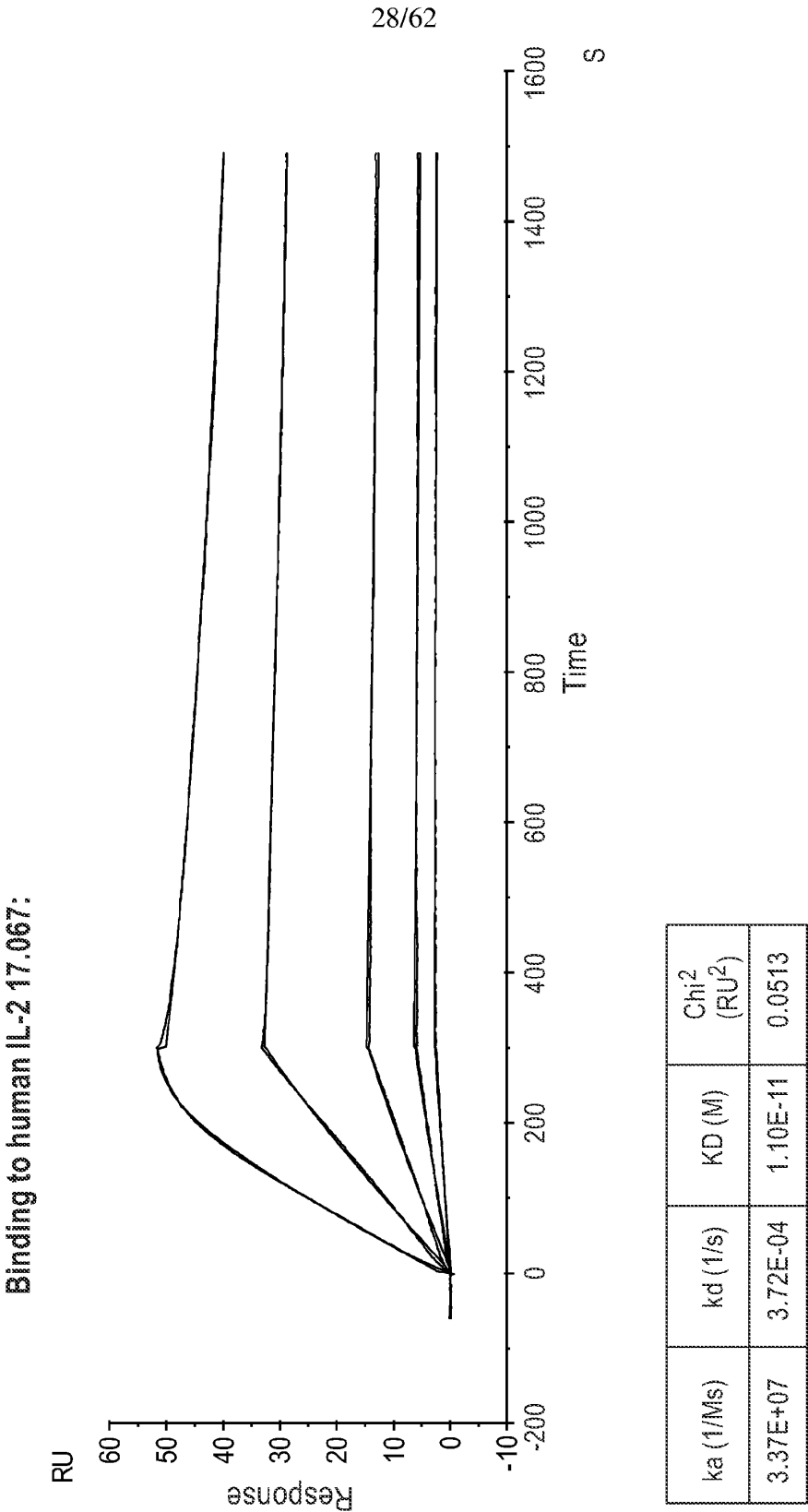


FIG. 14F

Binding to human IL-2 17.069:

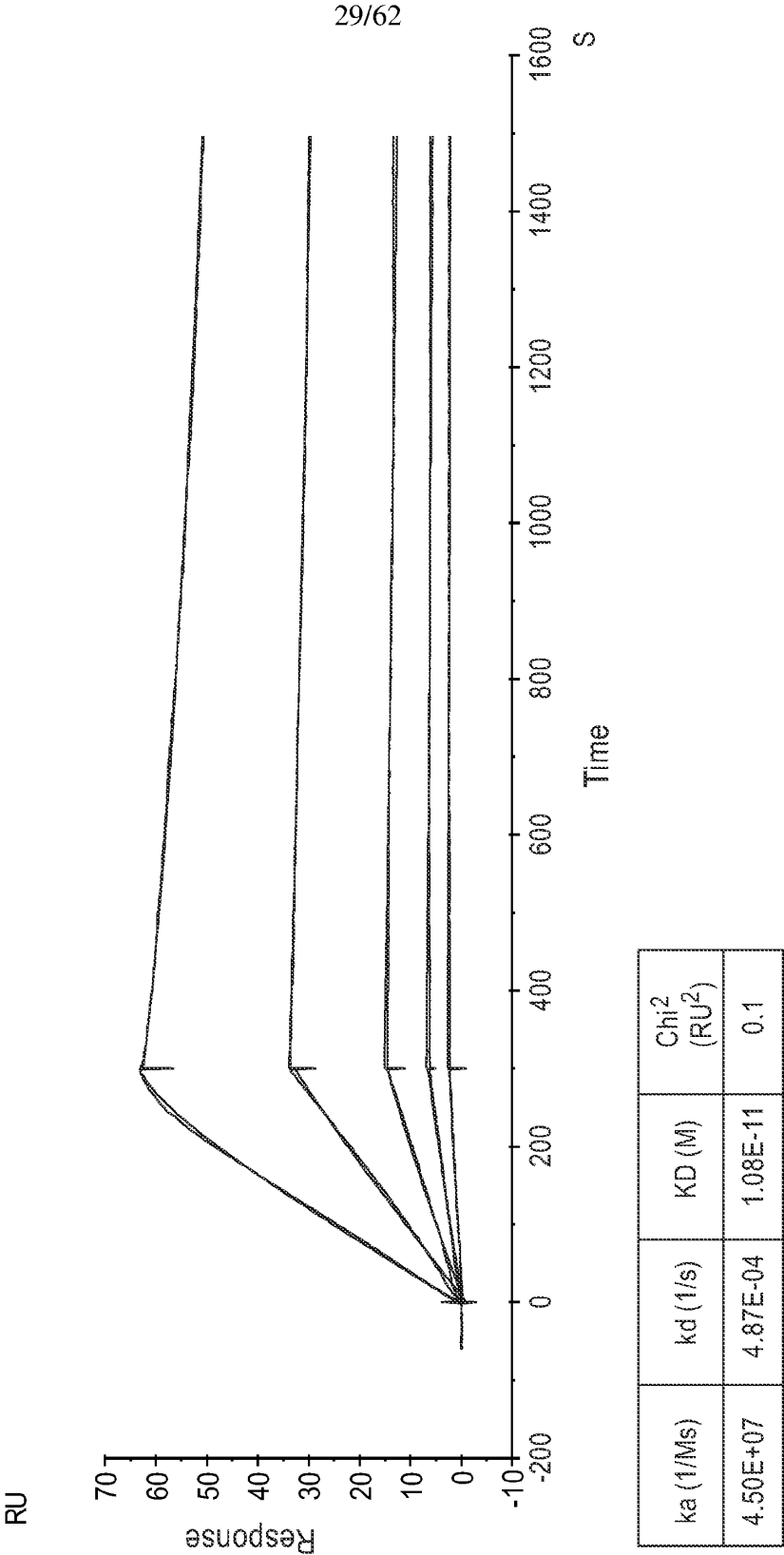


FIG. 14G

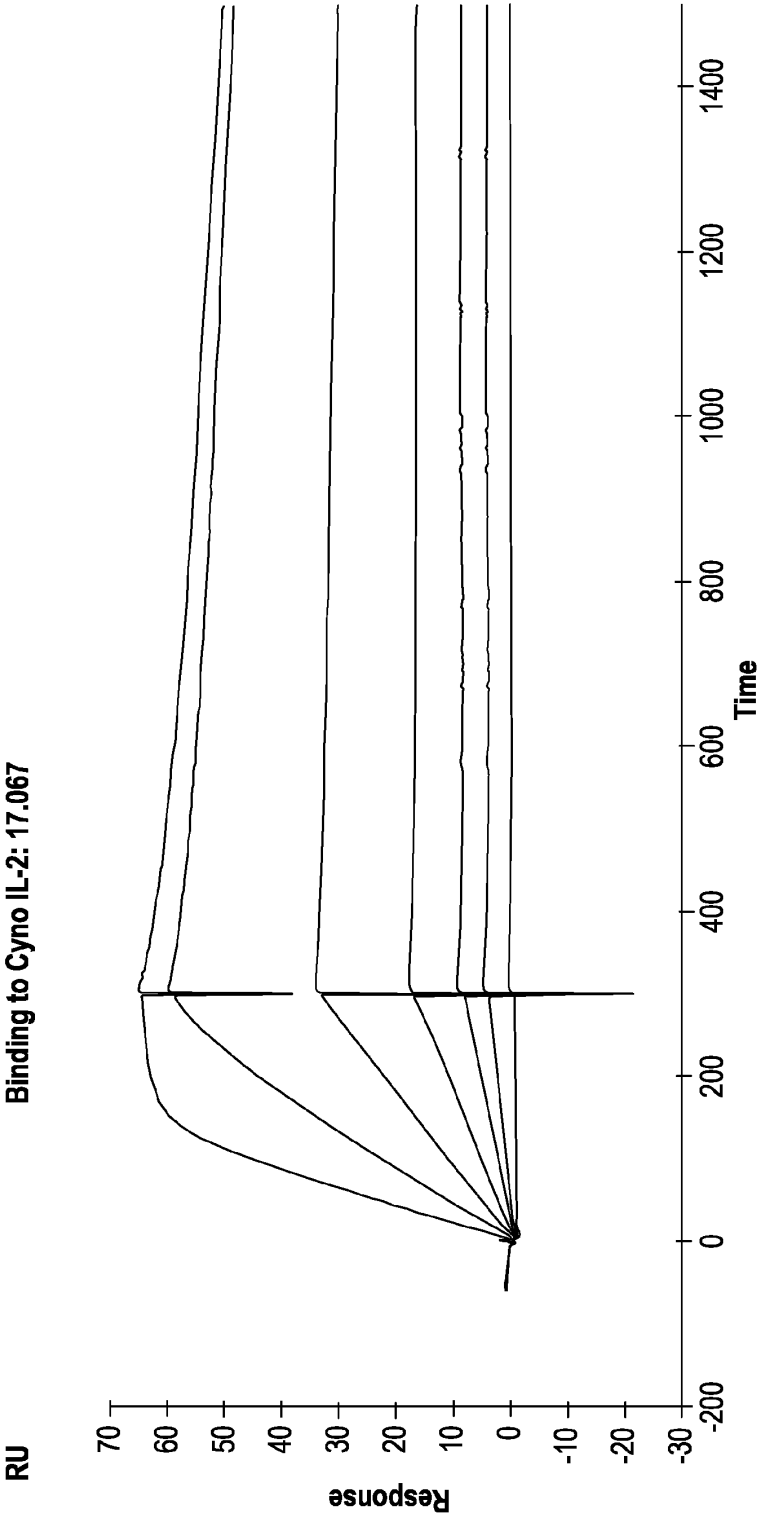


FIG. 15A

31/62

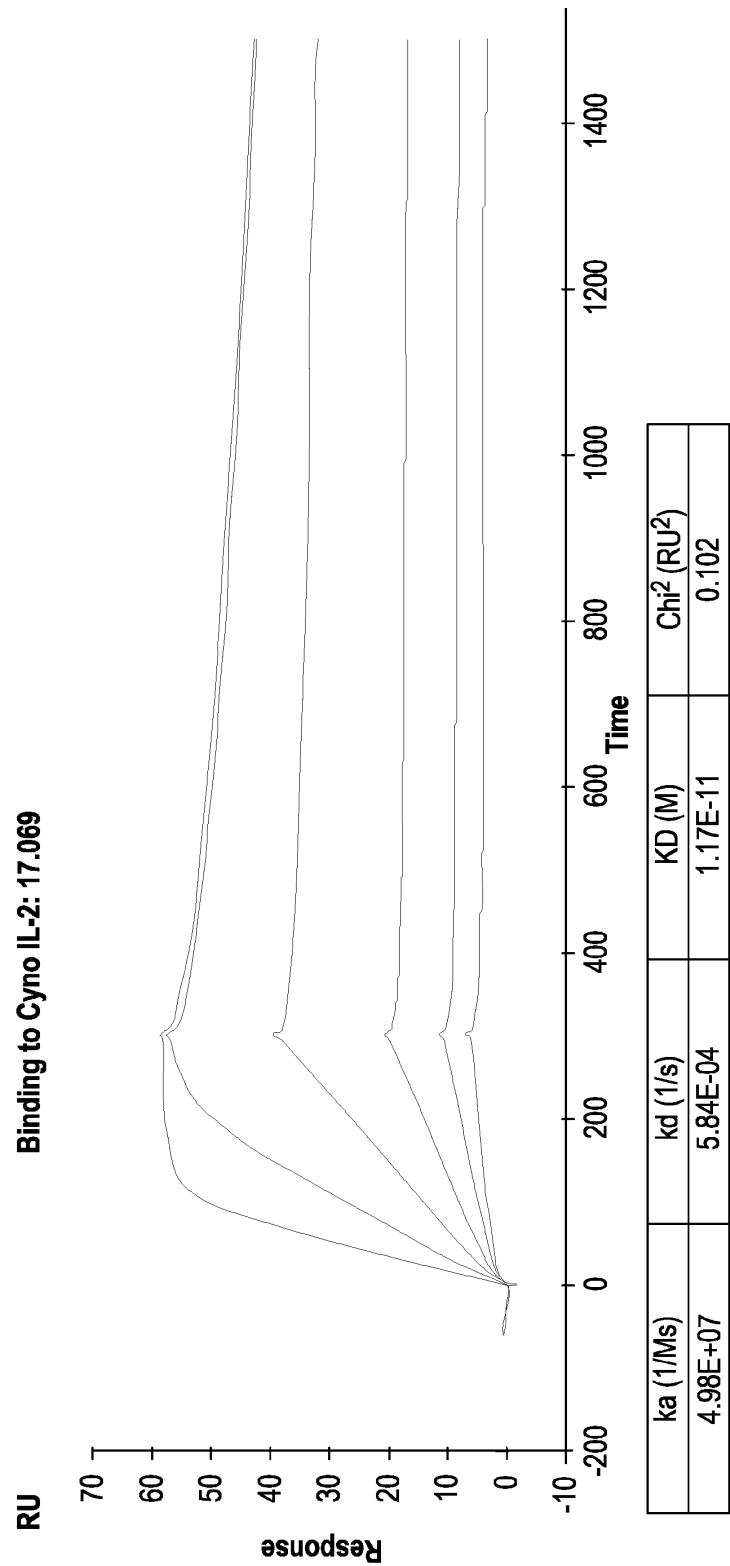
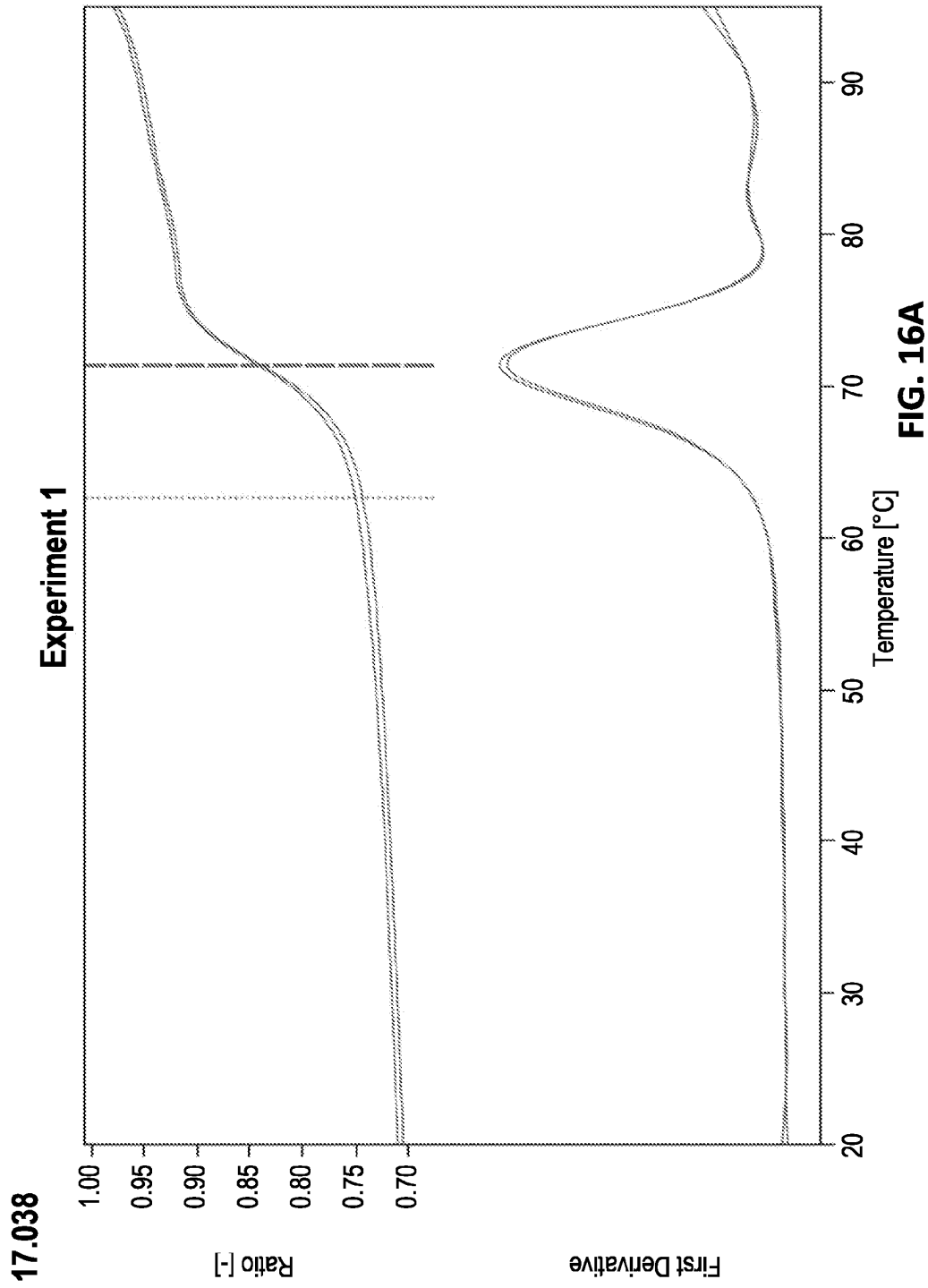


FIG. 15B



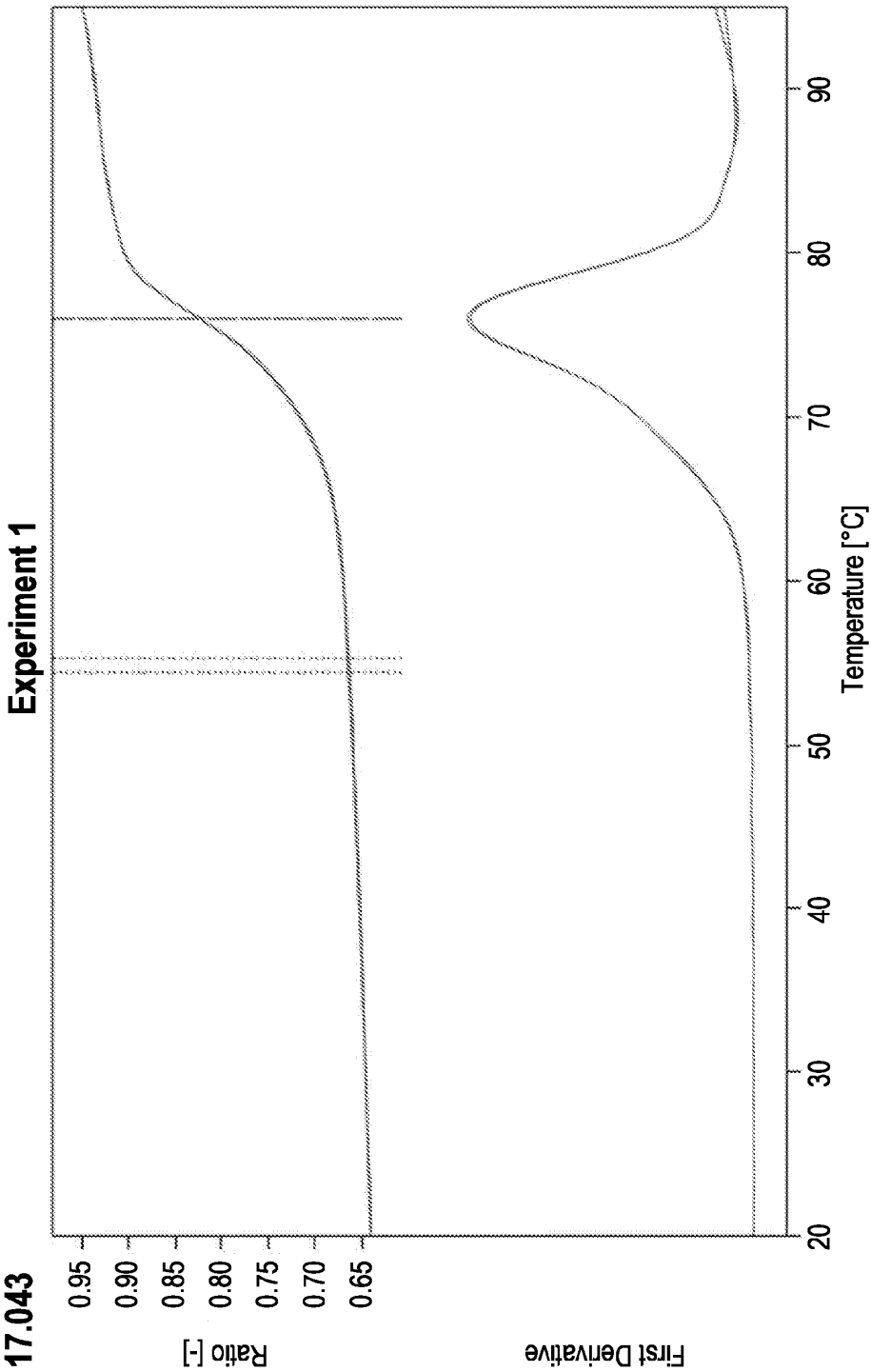


FIG. 16B

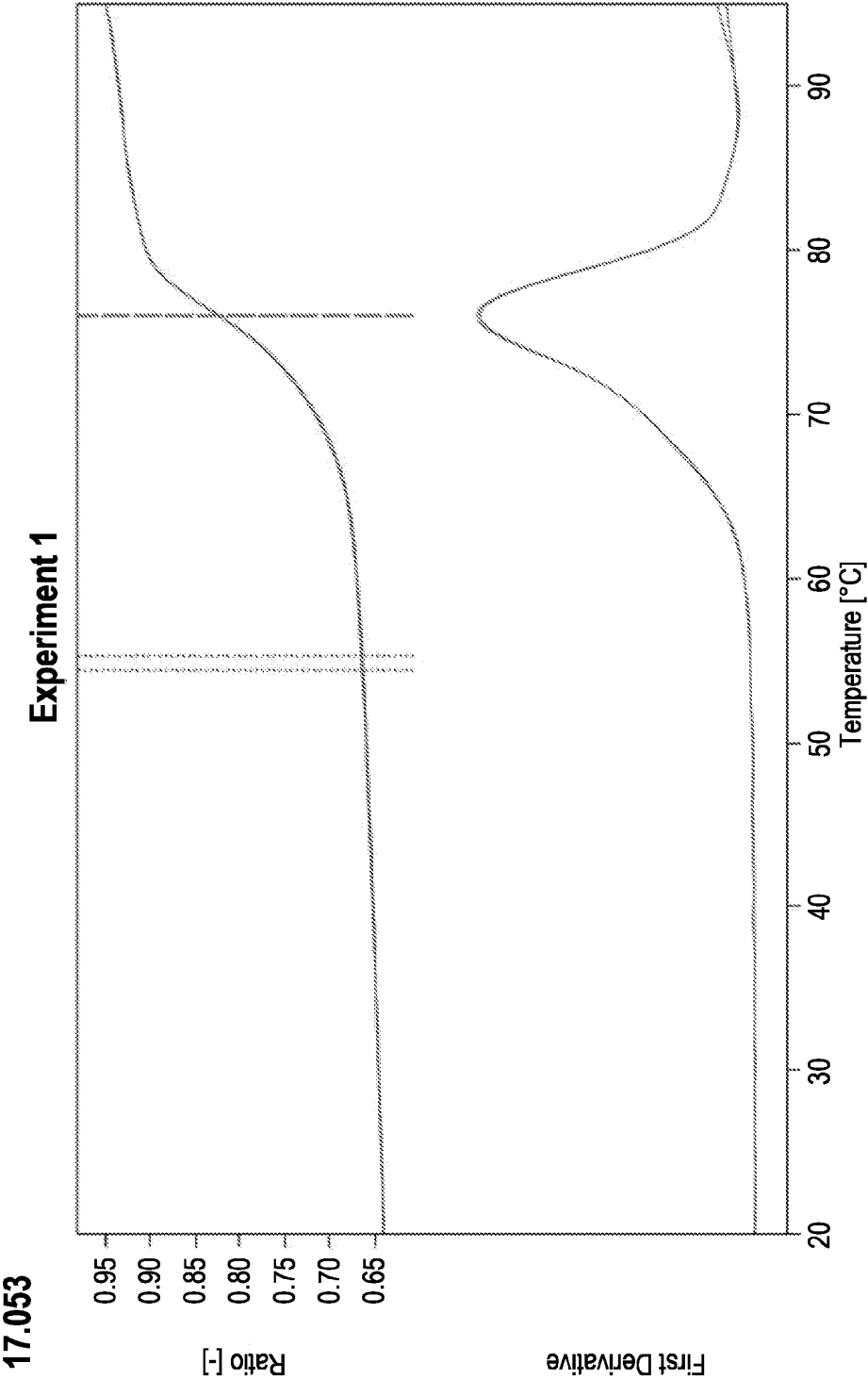


FIG. 16C

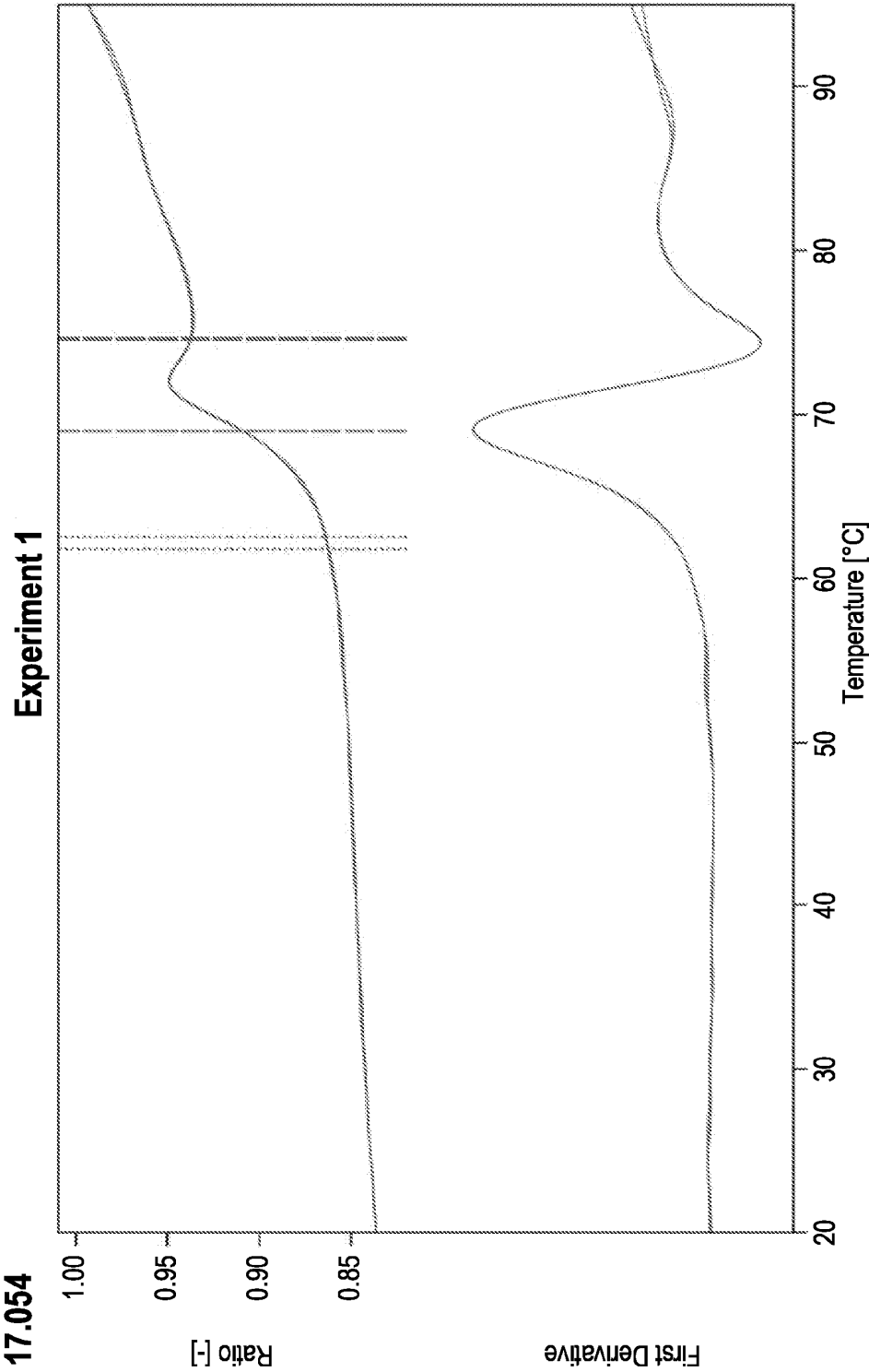


FIG. 16D

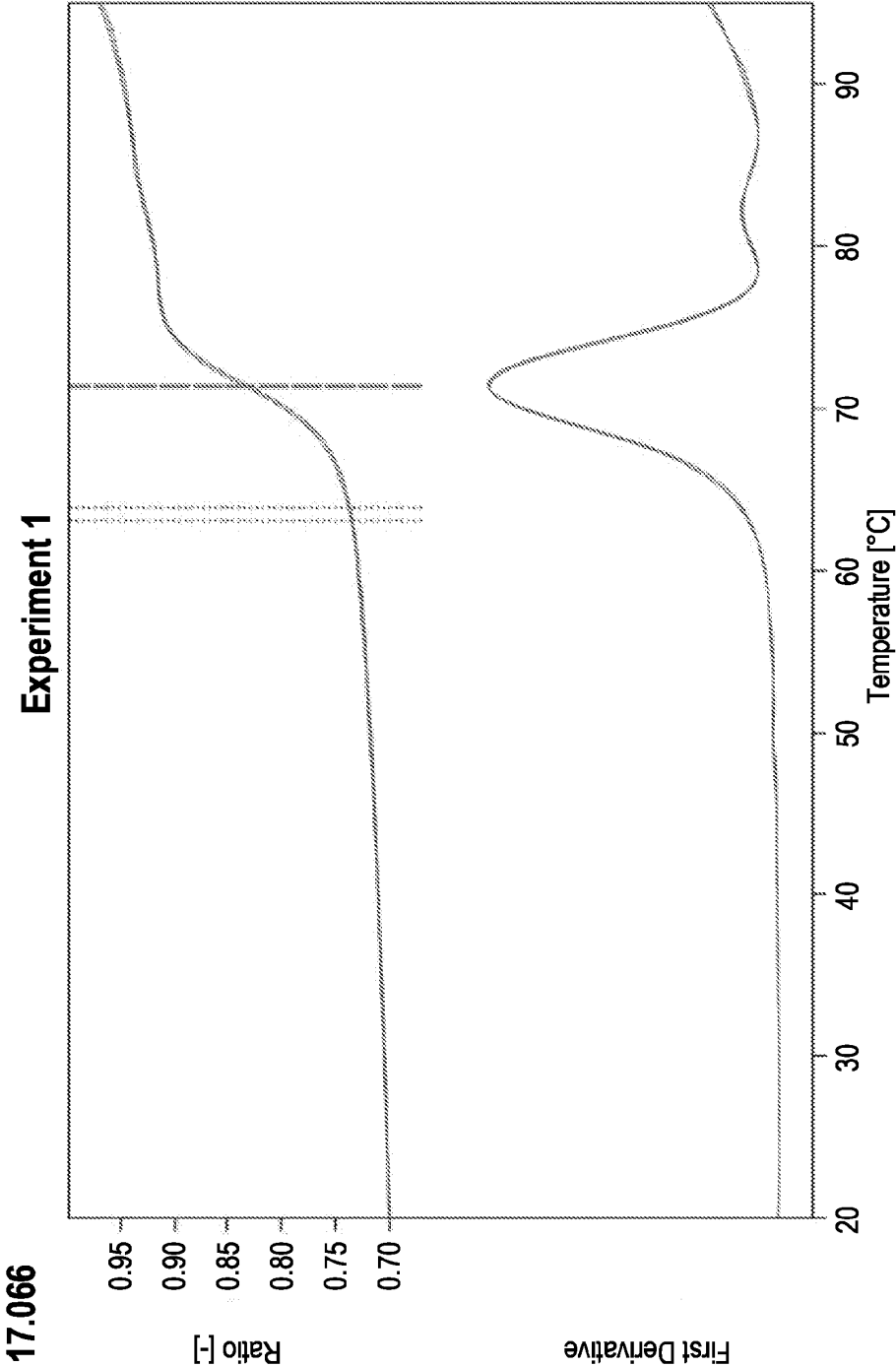


FIG. 16E

17.067

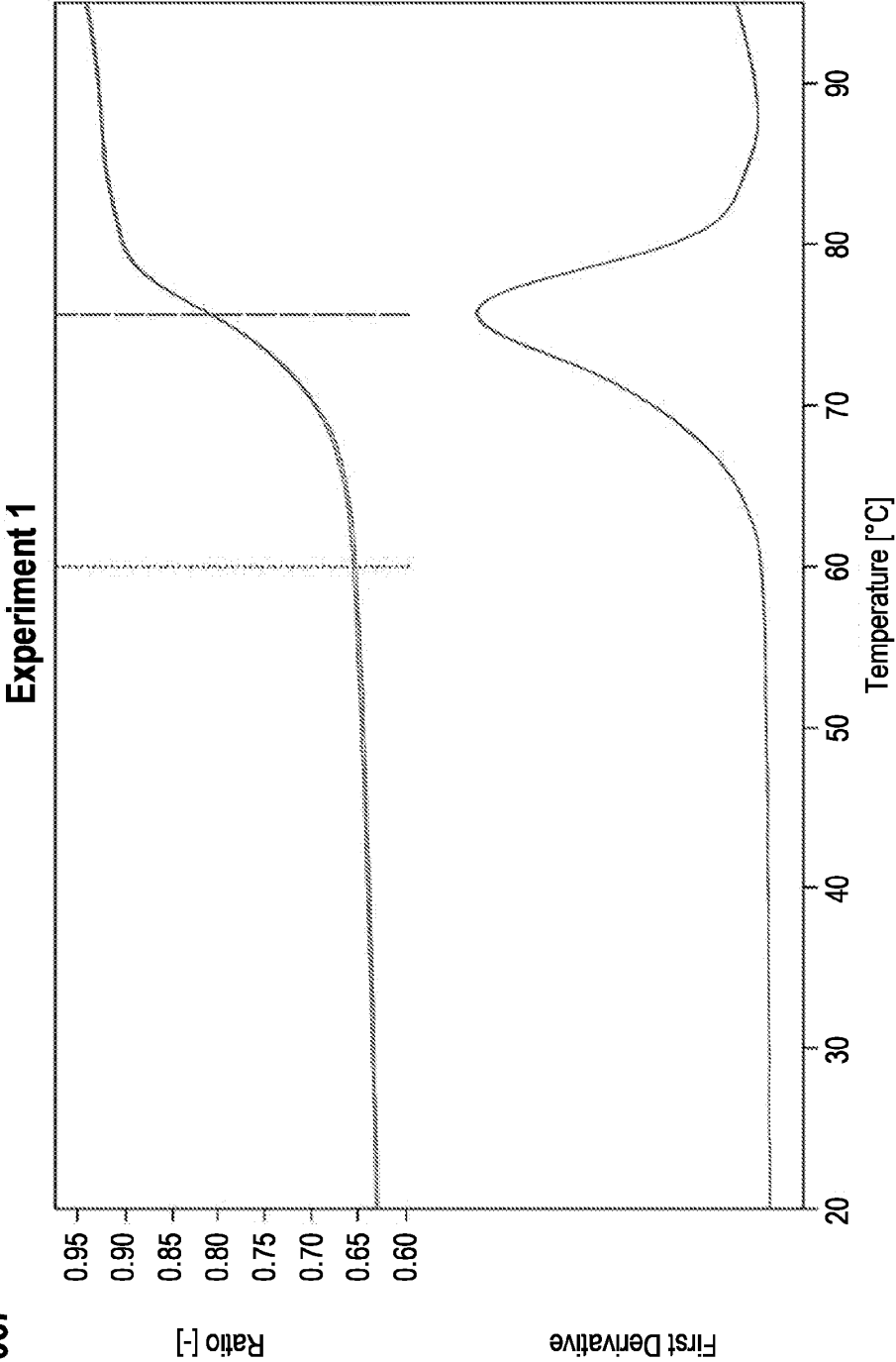


FIG. 16F

17.069

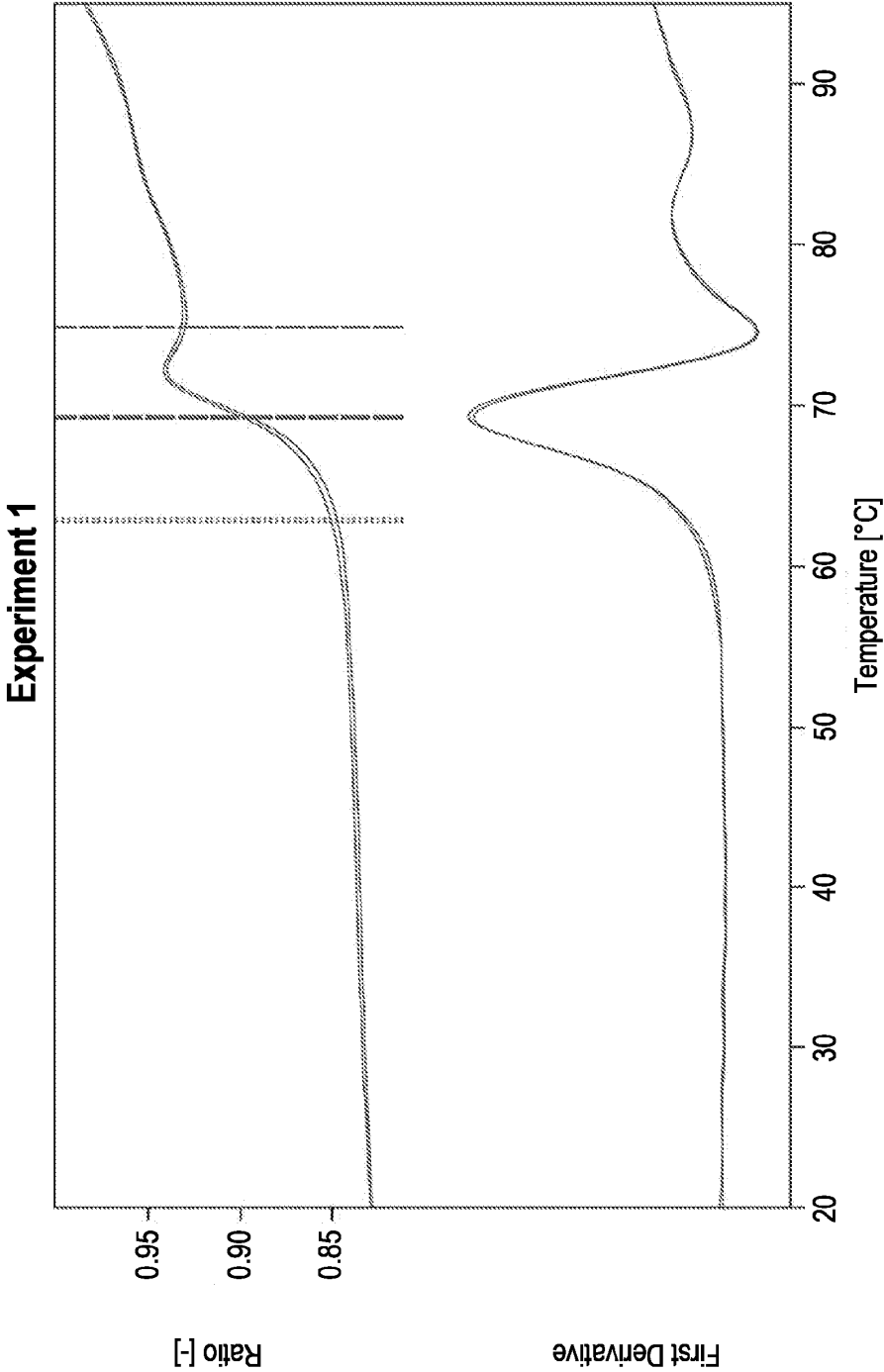
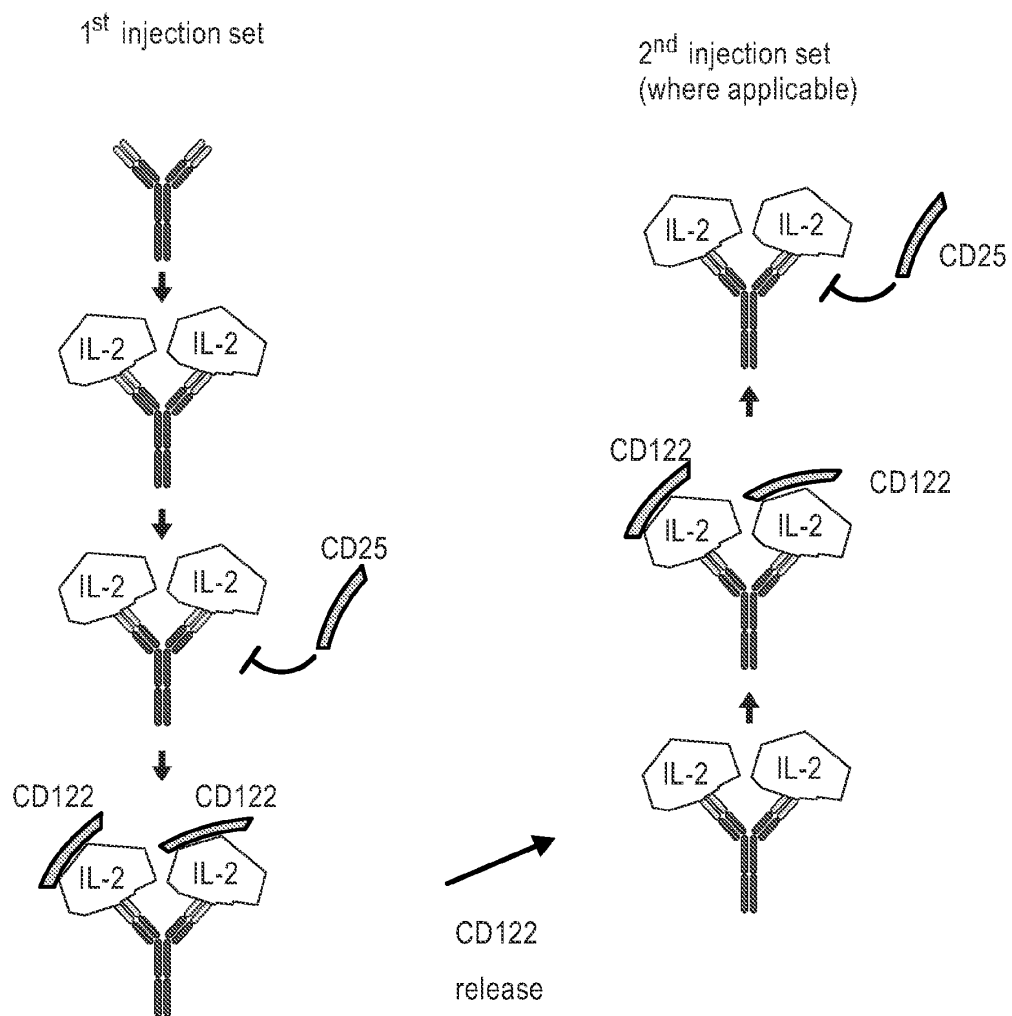


FIG. 16G

39/62

**FIG. 17A**

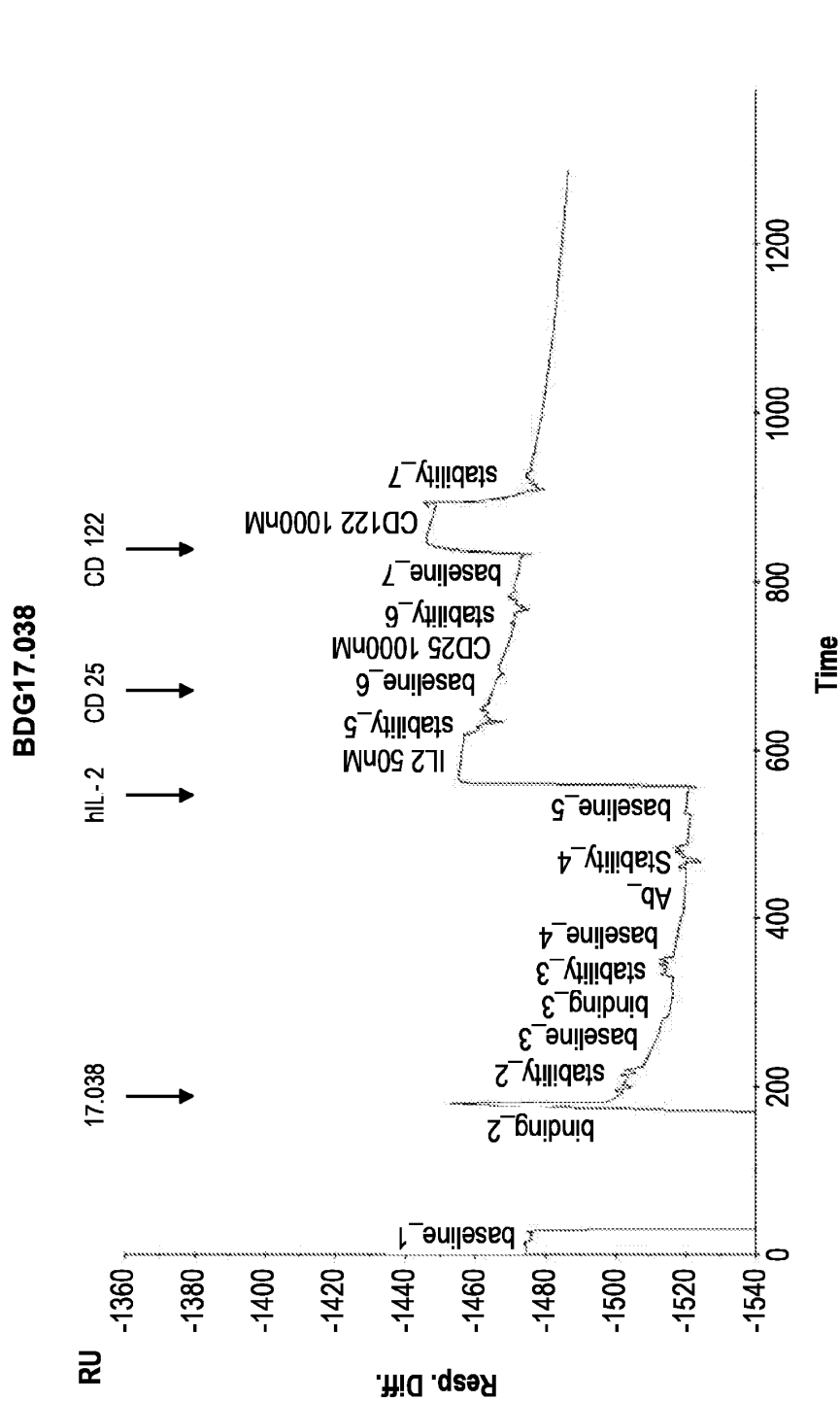


FIG. 17B

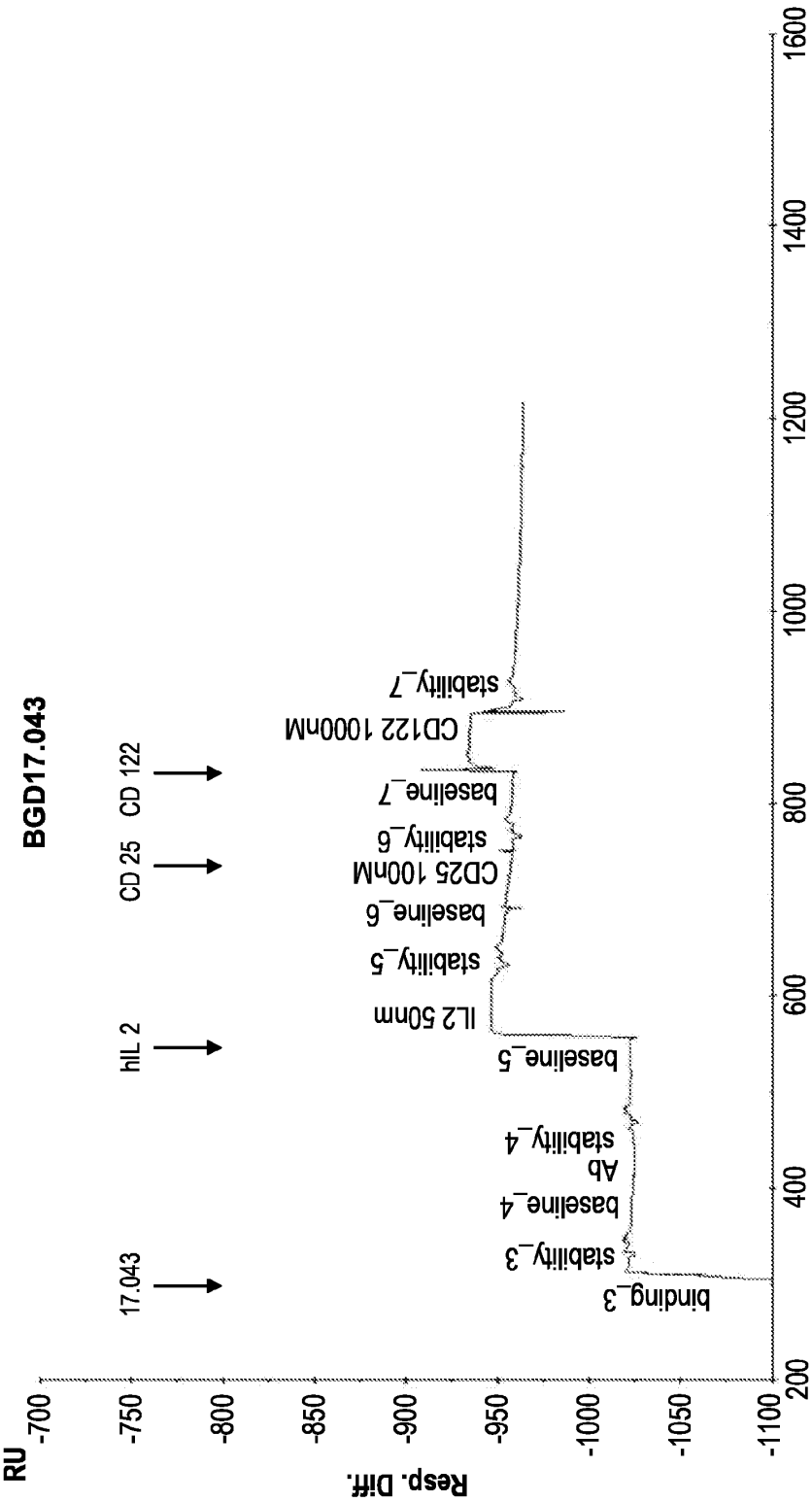


FIG. 17C

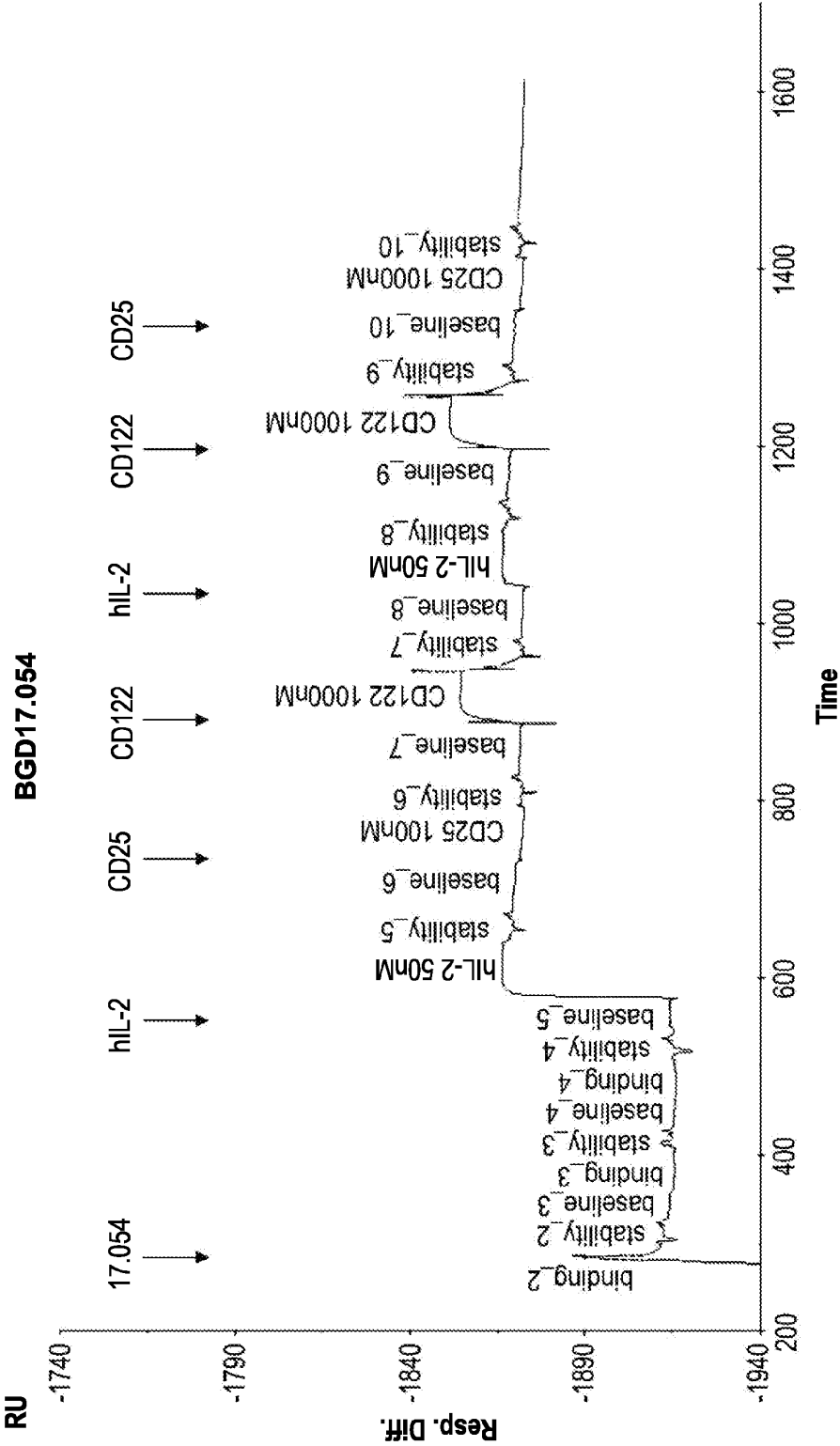
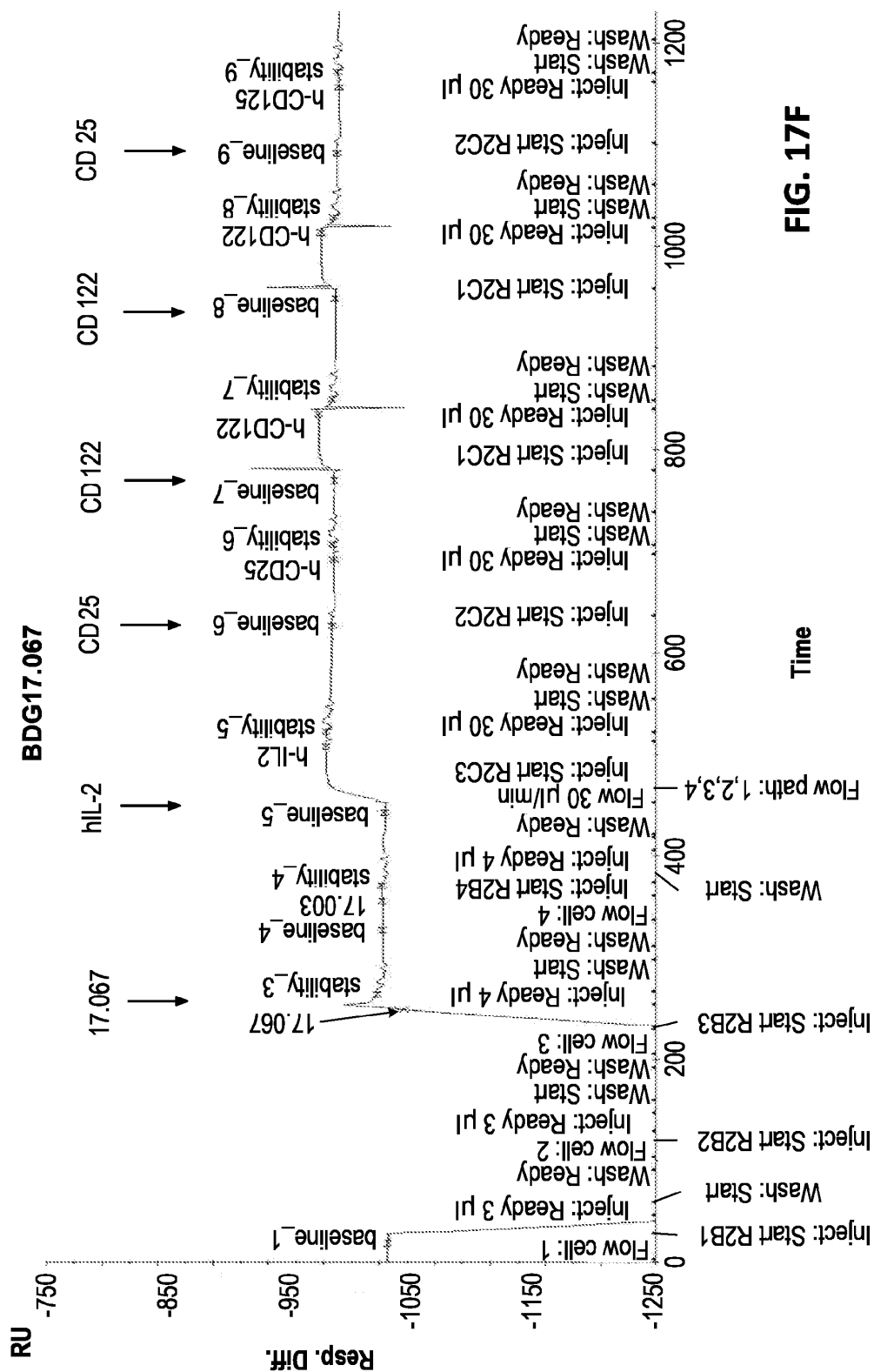
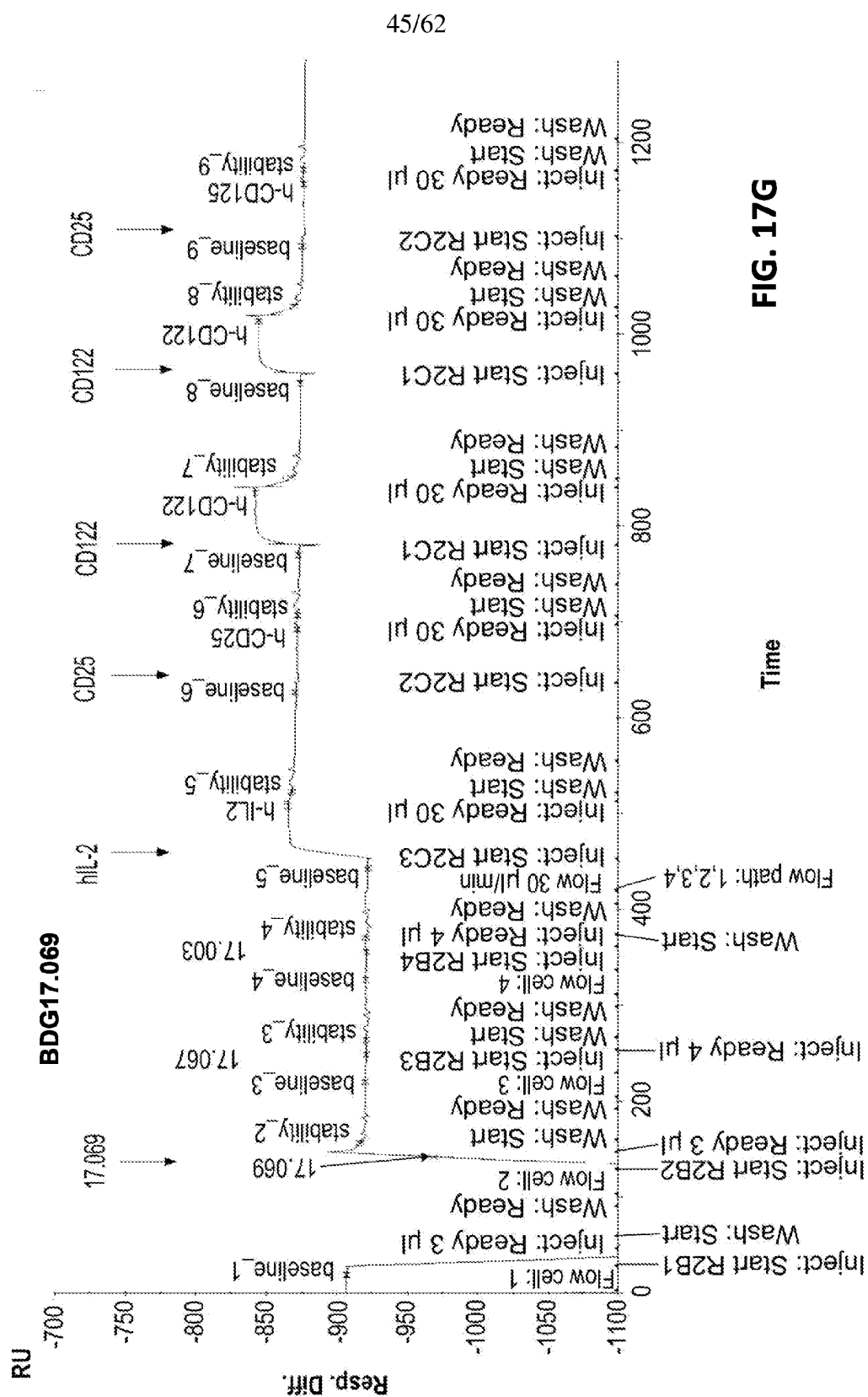


FIG. 17D





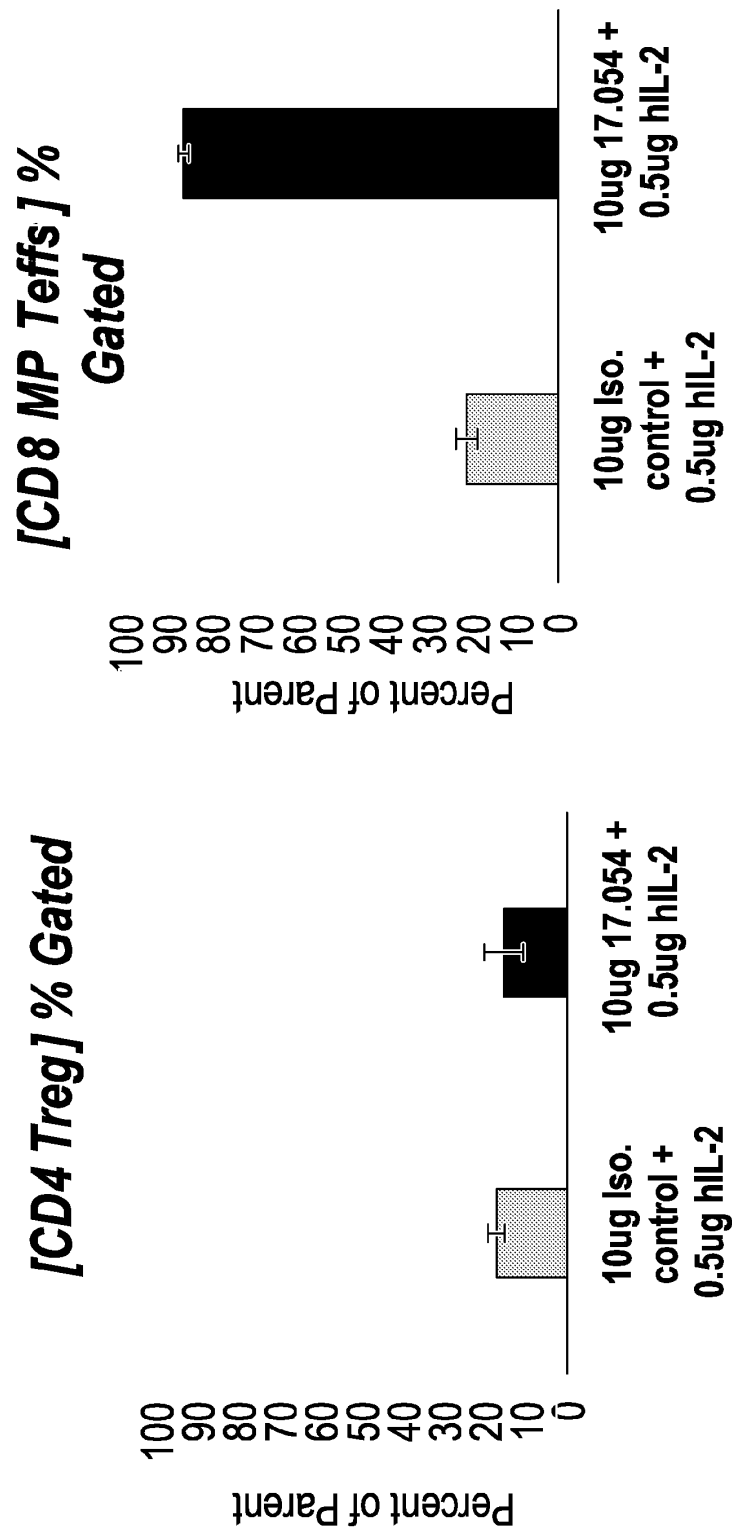


FIG. 18A

47/62

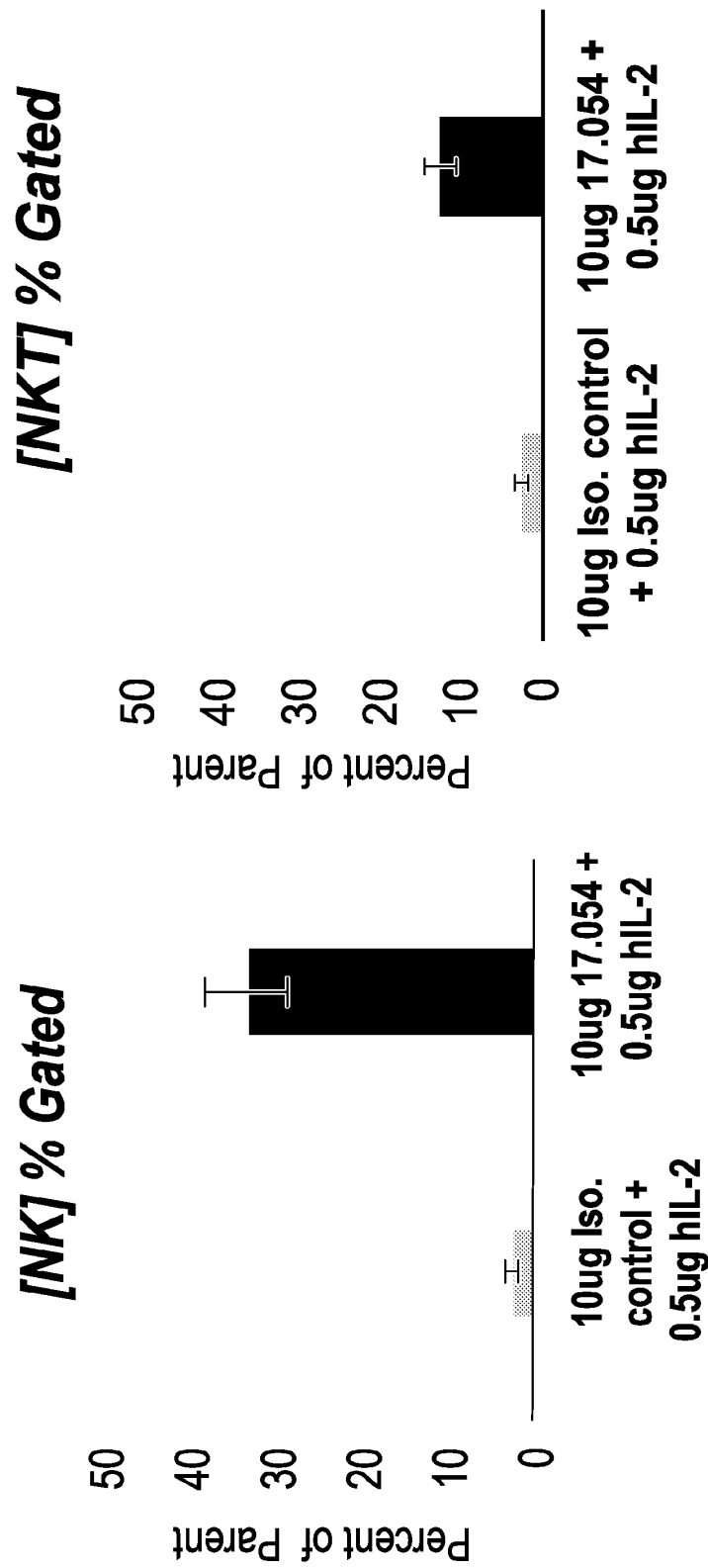


FIG. 18A continued

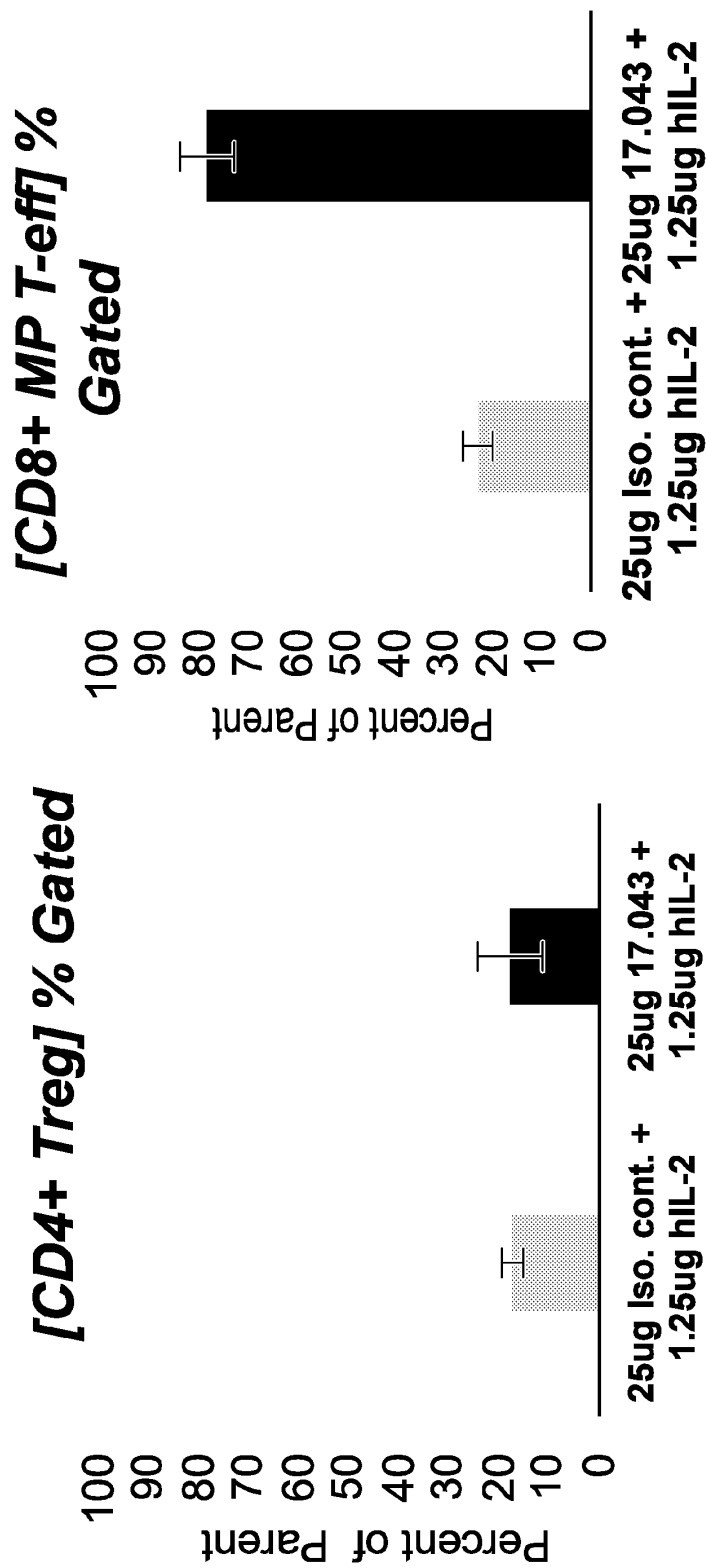


FIG. 18B

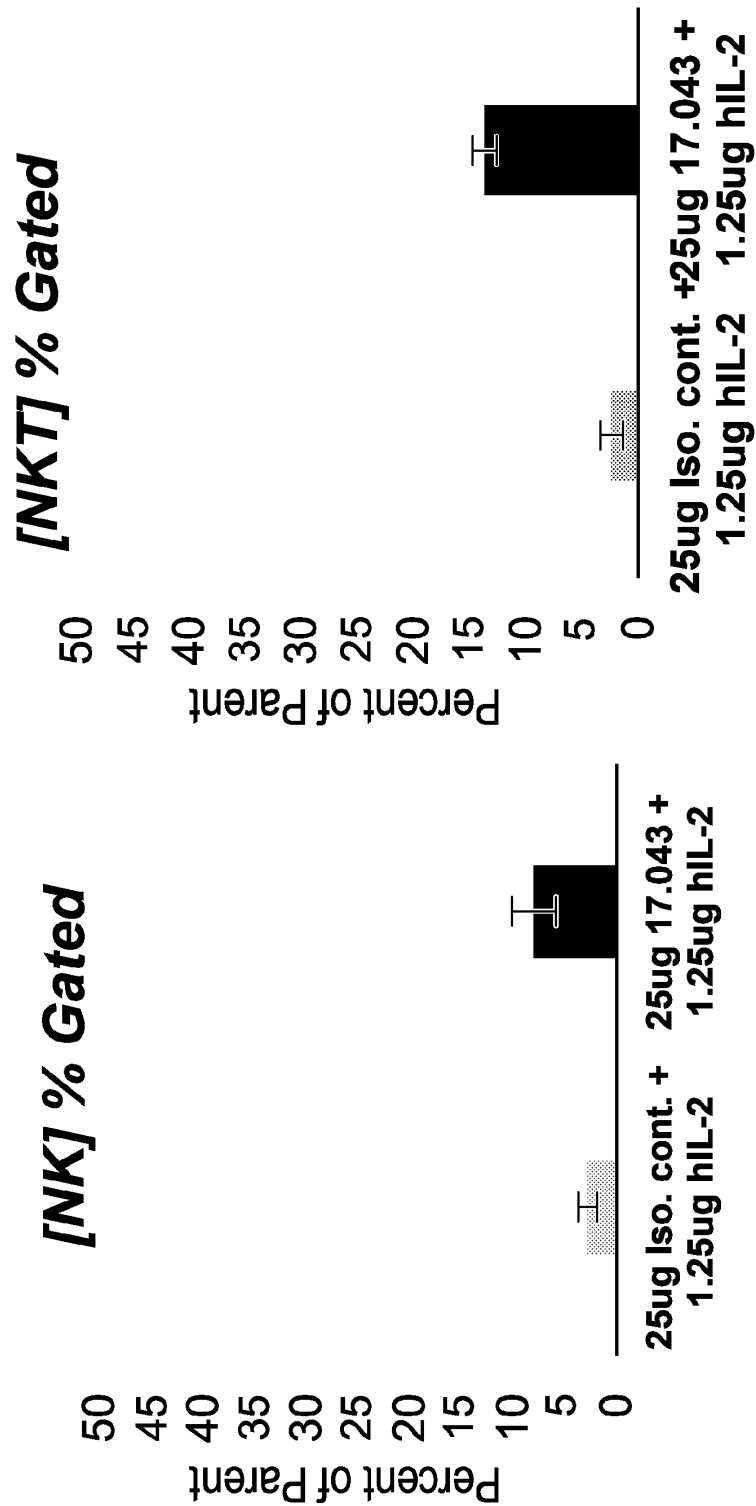
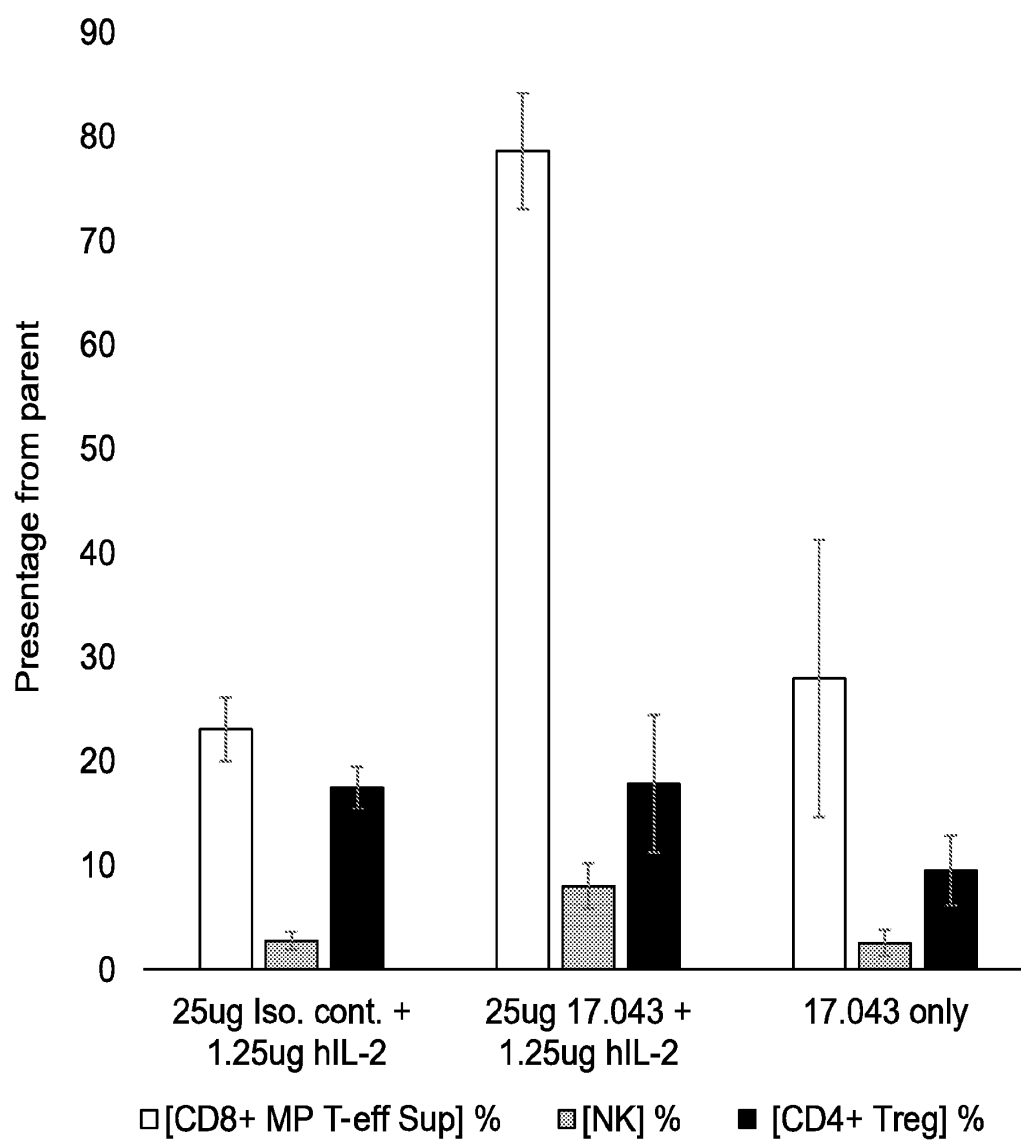
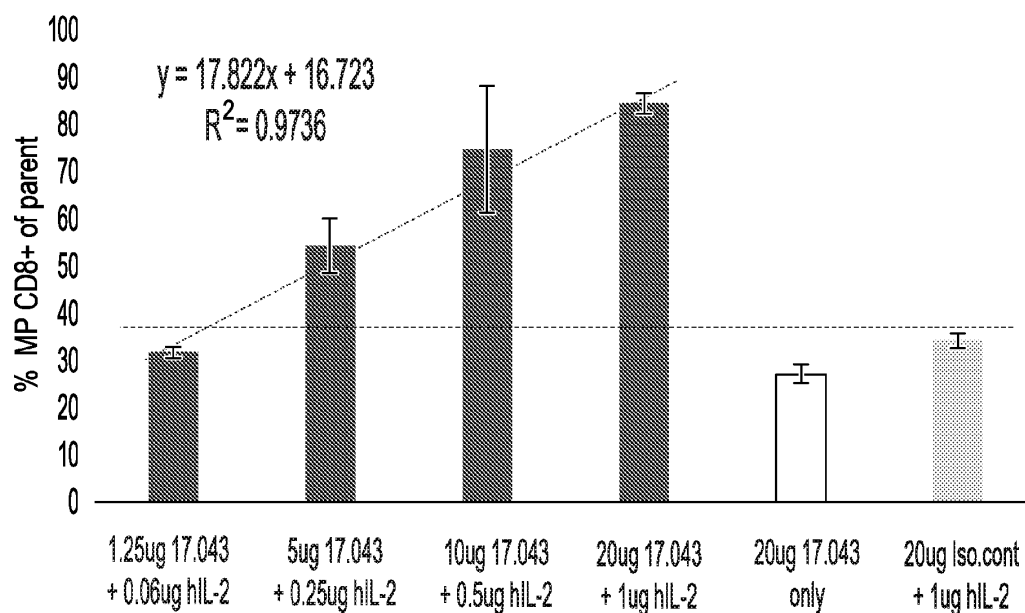
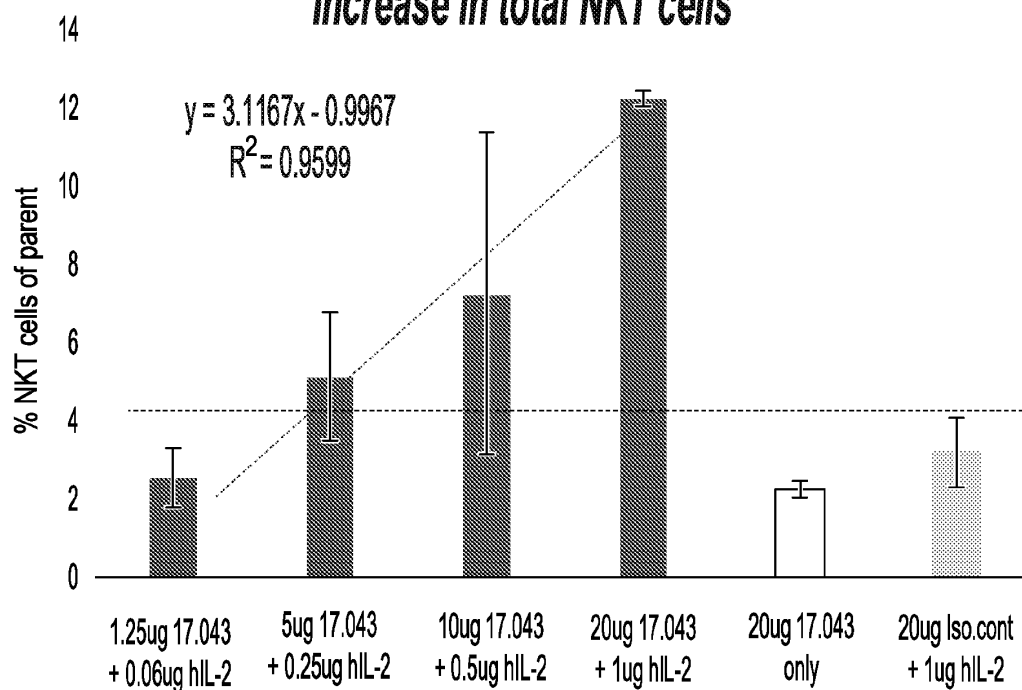


FIG. 18B continued

50/62

**FIG. 19A**

51/62

Increase in total MP CD8+ T cells (Teffs)***Increase in total NKT cells*****FIG. 19B**

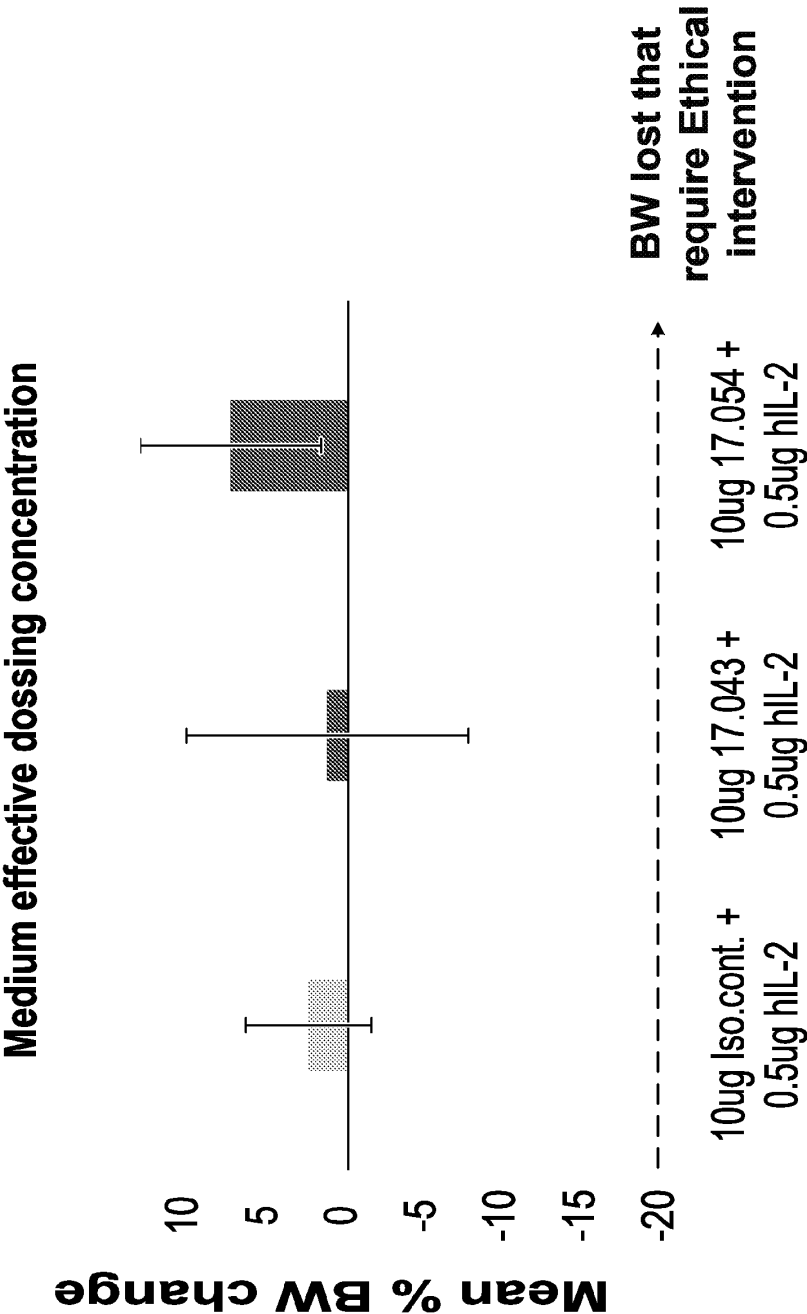


FIG. 20A

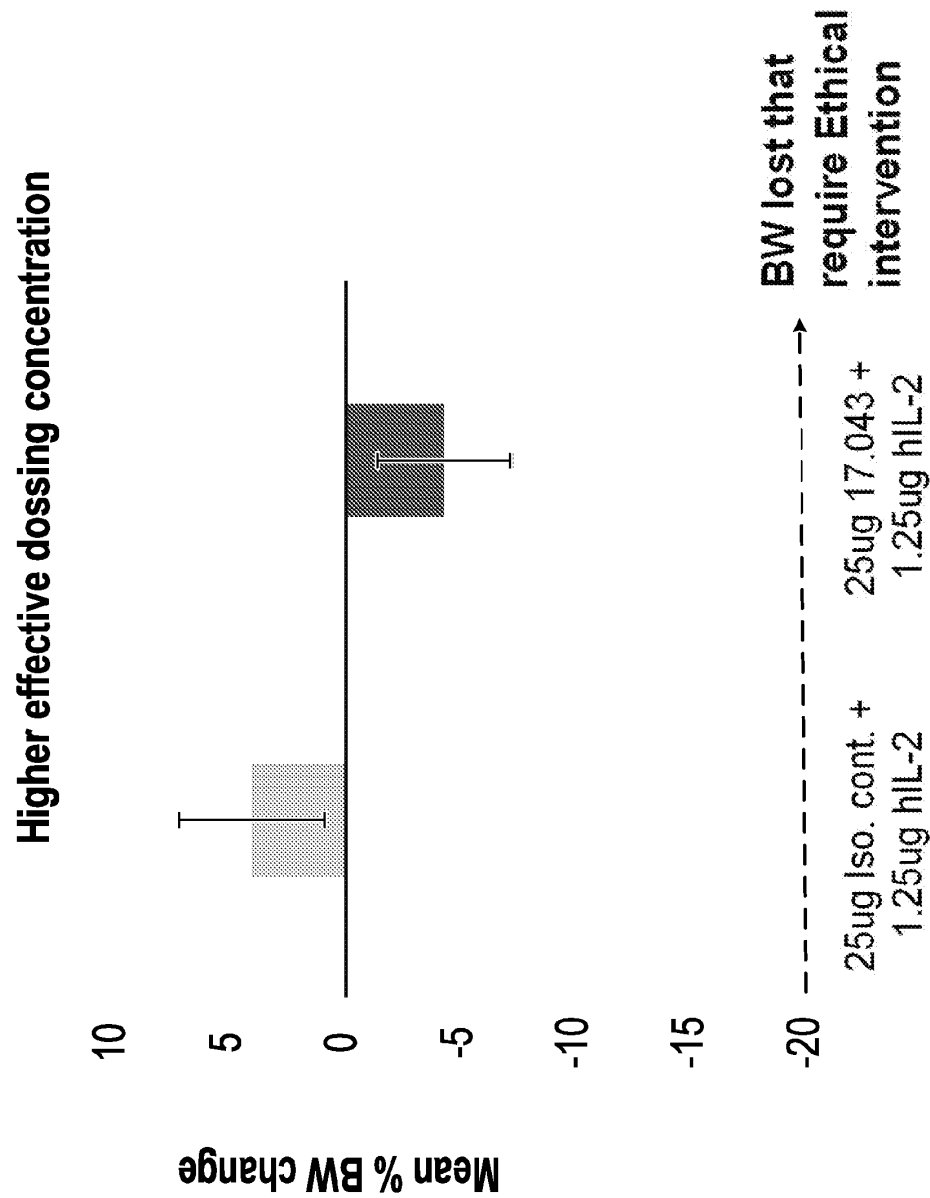


FIG. 20B

54/62

Biologic BD 8 clones - Mean Tumor Volume

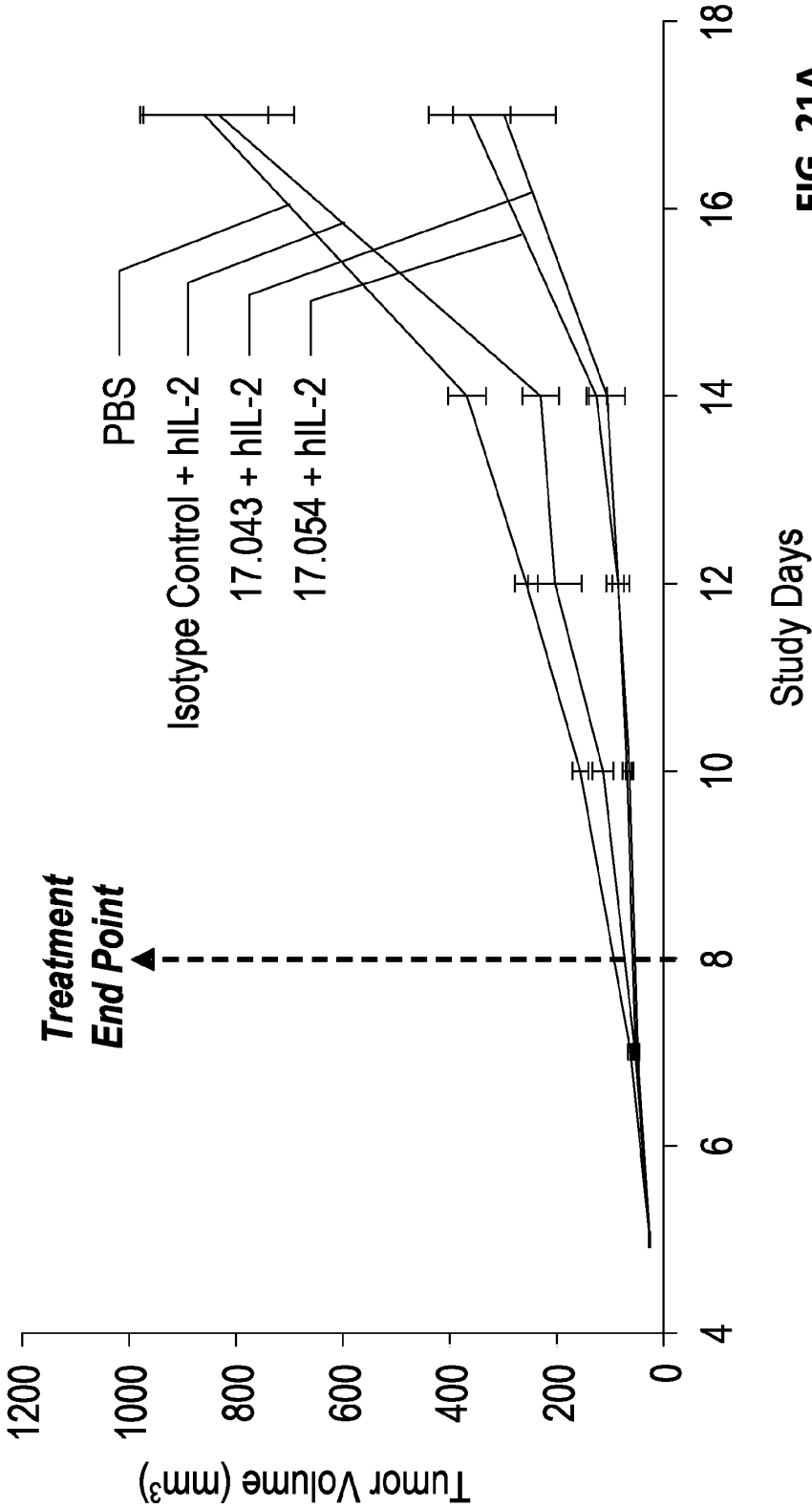


FIG. 21A

55/62

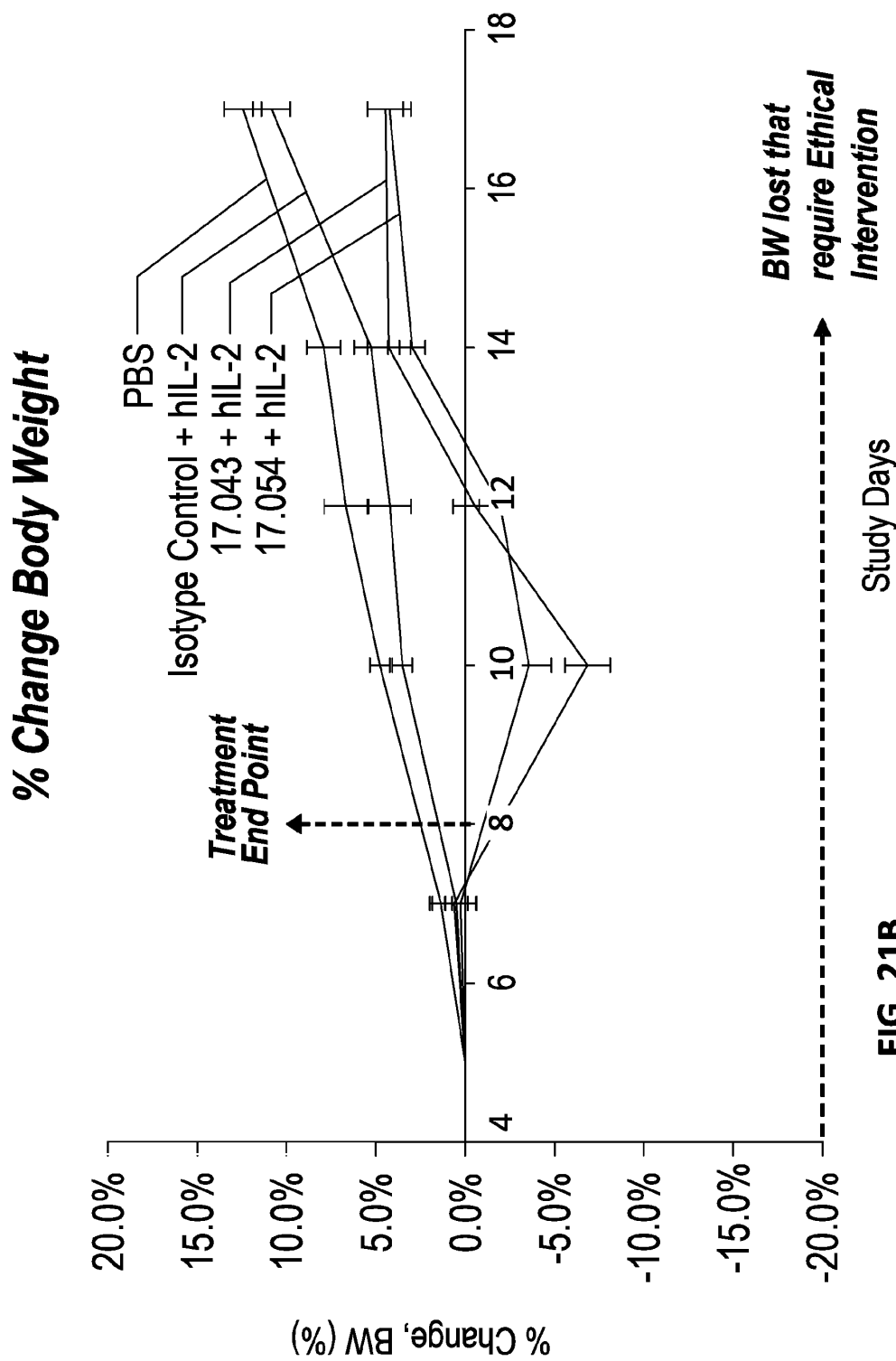


FIG. 21B

56/62

Candidates No.	Appearance	Protein concentration (mg/mL)	Osmolality (mOsm/kg)	T _g /°C	DSC				pH
					T _m onset (°C)	T _m 1 (°C)	T _m 2 (°C)	T _m 3 (°C)	
F1	SY, SO, PF	31.1	313	-29.80	59.88	68.09	73.83	84.07	5.5
F2	SY, SO, PF	30.8	325	-29.52	63.77	73.5	86.04	NA	6.0
F3	SY, SO, PF	31.2	335	-29.88	63.47	73.88	85.32	NA	5.5
F4	SY, SO, PF	30.9	349	-30.11	60.11	67.4	74.04	83.03	5.5
SY (slightly yellow); SO (slightly opalescent liquid); FP (free of visible particle)									

FIG. 22A

Candidates No.	Appearance			pH			Protein concentration (mg/mL)			
	T0	40°C-1W	40°C-2W	T0	40°C-1W	40°C-2W	T0	40°C-1W	40°C-2W	
F1	SY,SO,FP	SY,SO,FP	SY,SO,PO(5)	5.5	5.5	5.6	31.1	31.3	31.2	
F2	SY,SO,FP	SY,SO,FP	SY,SO,FP	6.0	6.0	6.1	30.8	30.9	30.8	
F3	SY,SO,FP	SY,SO,FP	SY,SO,FP	5.5	5.5	5.4	31.2	31.1	31.2	
F4	SY,SO,FP	SY,SO,FP	SY,SO,FP	5.5	5.5	5.6	30.9	30.9	30.9	

SY (slightly yellow); SO(slightly opalescent liquid); FP(free of visible particle), PO(particle observed)

Candidates No.	MFI																	
	T0						40°C-1W						40°C-2W					
	>=2 um	>=5 um	>=10 um	>=25 um	>=2 um	>=5 um	>=10 um	>=25 um	>=2 um	>=5 um	>=10 um	>=25 um	>=2 um	>=5 um	>=10 um	>=25 um		
F1	1532	190	20	4	1781	187	15	0	3507	482	58	10						
F2	561	76	23	2	3094	322	32	5	1717	118	19	0						
F3	587	84	22	4	818	115	17	0	1591	210	32	4						
F4	692	66	15	4	1560	171	10	0	2958	251	23	0						

58/62

Candidates No.	SEC-UPLC % (MPH/MW/LMW)			Caliper-SDS-NR % (Purity)		
	T0	40°C-1W	40°C-2W	T0	40°C-1W	40°C-2W
F1	99.1/0.9/ND	98.2/1.6/0.2	95.8(1.3)/2.2(1.3)/2.0(1.2.0)	97.6	98.0	95.4(1.2.2)
F2	99.1/0.9/ND	98.0/1.8/0.2	95.6(1.3.5)/2.4(1.5)/2.0(1.2.0)	97.6	98.1	95.8(1.1.8)
F3	99.1/0.9/ND	98.0/1.7/0.2	95.8(1.3.3)/2.2(1.3)/2.1(1.2.1)	97.6	98.2	95.4(1.2.2)
F4	99.1/0.9/ND	98.2/1.6/0.2	95.9(1.3.2)/2.0(1.1)/2.1(1.2.1)	97.7	98.4	95.8(1.1.9)
	NA			STD: 98.4	STD: 99.1	STD: 98.3
Candidates No.	Caliper-SDS-R % (Purity/LC/HC)			cIEF pl		
	T0	40°C-1W	40°C-2W	T0	40°C-1W	40°C-2W
F1	99.2/30.4/68.8	99.3/31.5/67.8	98.4(1.0.8)/29.5/68.8	7.5	7.6	7.5
F2	99.2/30.3/68.9	99.3/31.1/68.2	98.8(1.0.4)/29.7/69.1	7.5	7.6	7.5
F3	98.9/30.6/68.3	99.2/30.6/68.6	98.3(1.0.6)/29.8/68.4	7.6	7.6	7.6
F4	99.1/30.5/68.5	99.3/31.3/68.0	98.8(1.0.4)/29.9/68.9	7.6	7.6	7.6
				27.0/57.3/15.7	31.3/54.8/13.9	39.4(12.4)/48.2(19.1)/12.4(13.3)
				28.3/57.0/14.7	32.5/54.5/13.0	40.7(12.4)/48.6(18.4)/10.7(14.0)
				25.8/59.7/14.4	37.6/50.1/12.2	47.1(21.3)/42.1(17.6)/10.7(13.7)
				25.5/57.9/16.6	32.2/53.9/13.9	38.7(13.2)/49.0(18.9)/12.3(14.3)

FIG. 22C

Candidates No.	Appearance			pH		Protein concentration (mg/mL)		
	T0	A-1 Days	A-3 Days	T0	A-3 Days	T0	A-3 Days	
	F1	SY,SO,FP	SY,SO,FP	SY,SO,FP	5.5	5.5	31.1	31.2
F2	SY,SO,FP	SY,SO,FP	SY,SO,PO+	6.0	6.1	30.8	30.8	
F3	SY,SO,FP	SY,SO,FP	SY,SO,PO+	5.5	5.5	31.2	31.1	
F4	SY,SO,FP	SY,SO,FP	SY,SO,FP	5.5	5.5	30.9	31.1	
■ SY (slightly yellow); SO(slightly opalescent liquid); FP(free of visible particle), PO(particles observed)/(a few visible particles) ■ Few visible particles were observed in F2/F3 samples for agitation 3 days.								
Candidates No.	MFI							
	T0			A-3 Days				
	>=2 um	>=5 um	>=10 um	>=25 um	>=2 um	>=5 um	>=10 um	>=25 um
F1	1532	190	20	4	2077	110	12	2
F2	561	76	23	2	644	146	20	7
F3	587	84	22	4	313	55	9	2
F4	692	66	15	4	1856	77	4	0

FIG. 22D

60/62

Candidates No.	SEC-UPLC % (MP/HMW/LMW)		Caliper-SDS- NR % (Purity)		Caliper-SDS-R % (Purity/LC/HC)		pI		cIEF % Acidic/Main/Basic	
	T0	A-3 Days	T0	A-3 Days	T0	A-3 Days	T0	A-3 Days	T0	A-3 Days
F1	99.1/0.9/ND	99.0/1.0/ND	97.6	97.7	99.2/30.4/68.8	99.2/30.9/68.3	7.5	7.6	27.0/57.3/15.7	28.3/56.3/15.3
F2	99.1/0.9/ND	99.0/1.0/ND	97.6	97.6	99.2/30.3/68.9	99.2/31.1/68.1	7.6	7.6	28.3/57.0/14.7	27.2/57.4/15.4
F3	99.1/0.9/ND	99.0/1.0/ND	97.6	97.5	98.9/30.6/68.3	99.0/30.7/68.4	7.6	7.6	25.8/59.7/14.4	22.9/61.8/15.3
F4	99.1/0.9/ND	99.1/0.9/ND	97.7	97.5	99.1/30.5/68.5	99.2/30.8/68.4	7.6	7.6	25.5/57.9/16.6	24.5/60.1/15.5

FIG. 22E

Candidates No.	Appearance			pH		Protein concentration (mg/mL)		
	T0	FT-3C	FT-5C	T0	FT-5C	T0	FT-5C	
F1	SY,SO,FP	SY,SO,FP	SY,SO,FP	5.5	5.6	31.1	31.3	
F2	SY,SO,FP	SY,SO,FP	SY,SO,FP	6.0	6.1	30.8	30.9	
F3	SY,SO,FP	SY,SO,FP	SY,SO,FP	5.5	5.6	31.2	31.1	
F4	SY,SO,FP	SY,SO,FP	SY,SO,FP	5.5	5.6	30.9	31.0	
SY (slightly yellow); SO(slightly opalescent liquid); FP(free of visible particle)								
MFI								
Candidates No.	T0				FT-5C			
	>=2 um	>=5 um	>=10 um	>=25 um	>=2 um	>=5 um	>=10 um	>=25 um
F1	1532	190	20	4	770	76	4	0
F2	561	76	23	2	469	46	4	0
F3	587	84	22	4	439	30	9	0
F4	692	66	15	4	670	44	14	2

FIG. 22F

62/62

Candidates No.	SEC-UPLC % (MP/HMW/LMW)		Caliper-SDS-NR % (Purity)		Caliper-SDS-R % (Purity/LC/HC)		pI		cIEF % Acidic/Main/Basic	
	T0	FT-5C	T0	FT-5C	T0	FT-5C	T0	FT-5C	T0	FT-5C
F1	99.1/0.9/ND	99.1/0.9/ND	97.6	97.7	99.2/30.4/68.8	99.2/30.4/68.8	7.5	7.6	27.0/57.3/15.7	22.3/60.5/17.2
F2	99.1/0.9/ND	99.1/0.9/ND	97.6	97.6	99.2/30.3/68.9	99.2/30.9/68.4	7.6	7.6	28.3/57.0/14.7	20.7/63.5/15.8
F3	99.1/0.9/ND	99.1/0.9/ND	97.6	97.5	98.9/30.6/68.3	99.2/30.6/68.6	7.6	7.6	25.8/59.7/14.4	21.8/62.8/15.4
F4	99.1/0.9/ND	99.1/0.9/ND	97.7	97.6	99.1/30.5/68.5	99.1/30.3/68.8	7.6	7.6	25.5/57.9/16.6	24.4/60.1/15.5

FIG. 22G