

FIG. 1

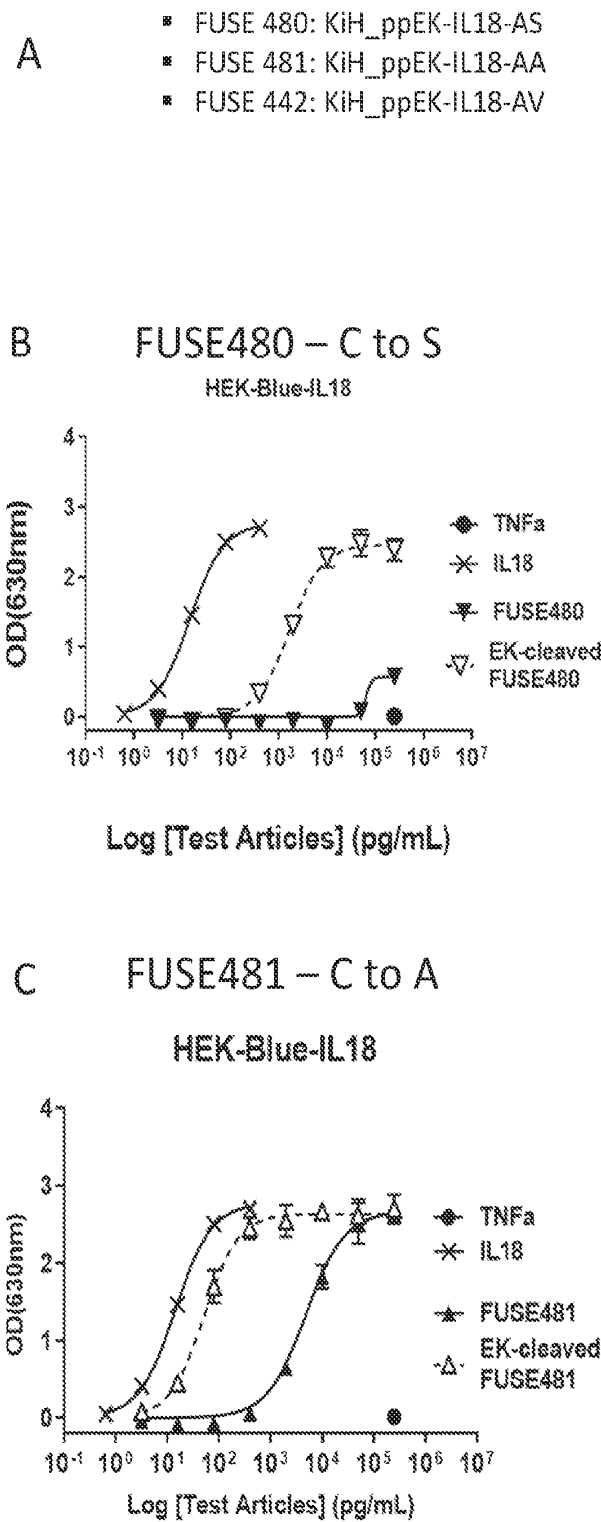
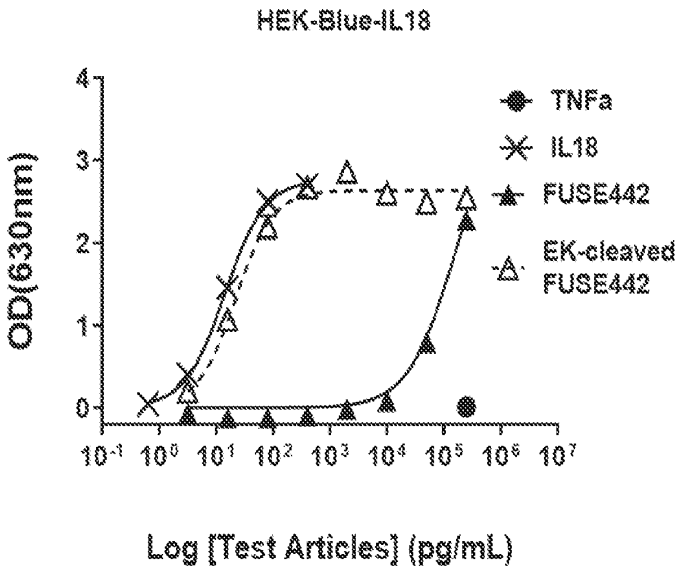


FIG. 1

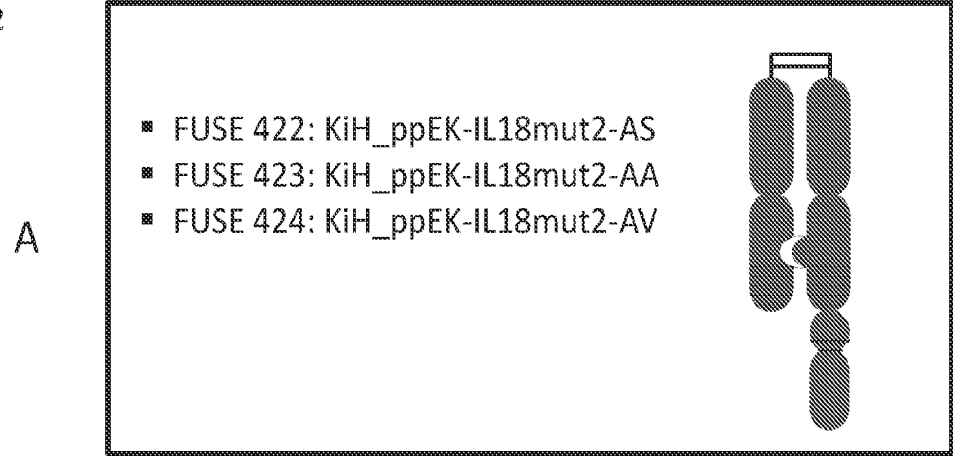
D FUSE442 – C to V



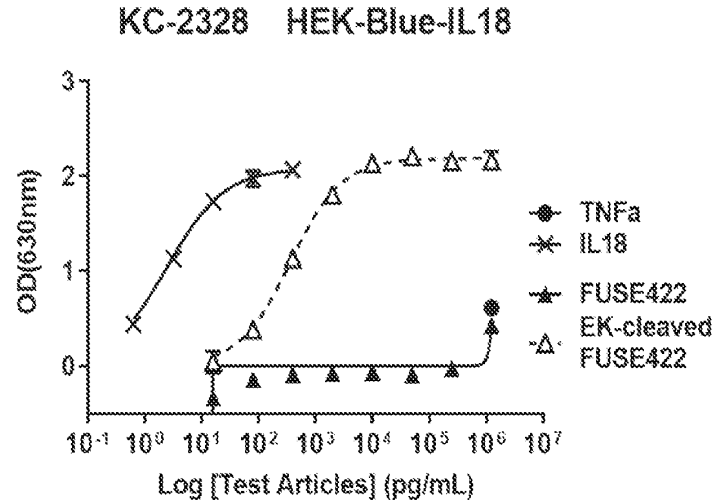
E

Compound	EC50-SEAP
Human rIL-18	0.014 ng/ml
Human rTNFα	N/A
FUSE480	>200 ng/ml
FUSE480 +EK	1.6 ng/ml
FUSE481	4.9 ng/ml
FUSE481 +EK	0.052 ng.ml
FUSE442	>200 ng/ml
FUSE442 + EK	0.022 ng/ml

FIG. 2



B
FUSE422 – C to S



C
FUSE423 – C to A

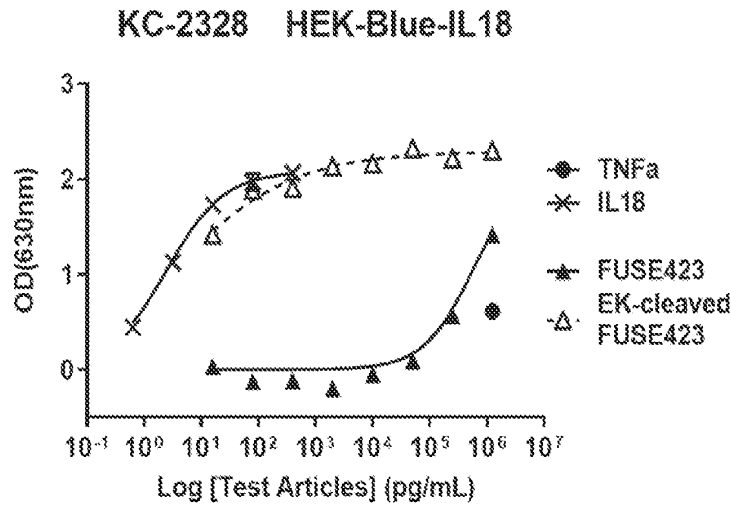
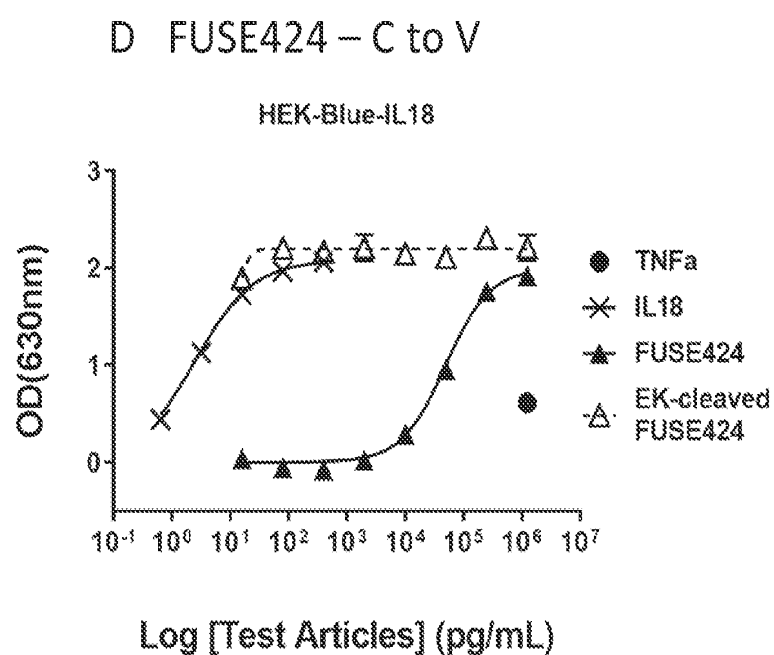


FIG. 2



E

Compound	EC50-SEAP
Human rIL-18	0.0025 ng/ml
Human rTNF α	N/A
FUSE422	> 1 ug/ml
FUSE422+EK	0.36 ng/ml
FUSE423	583.86 ng/ml
FUSE423+EK	0.0046 ng/ml
FUSE424	49.44 ng/ml
FUSE424+EK	<0.005 ng/ml

FIG. 3

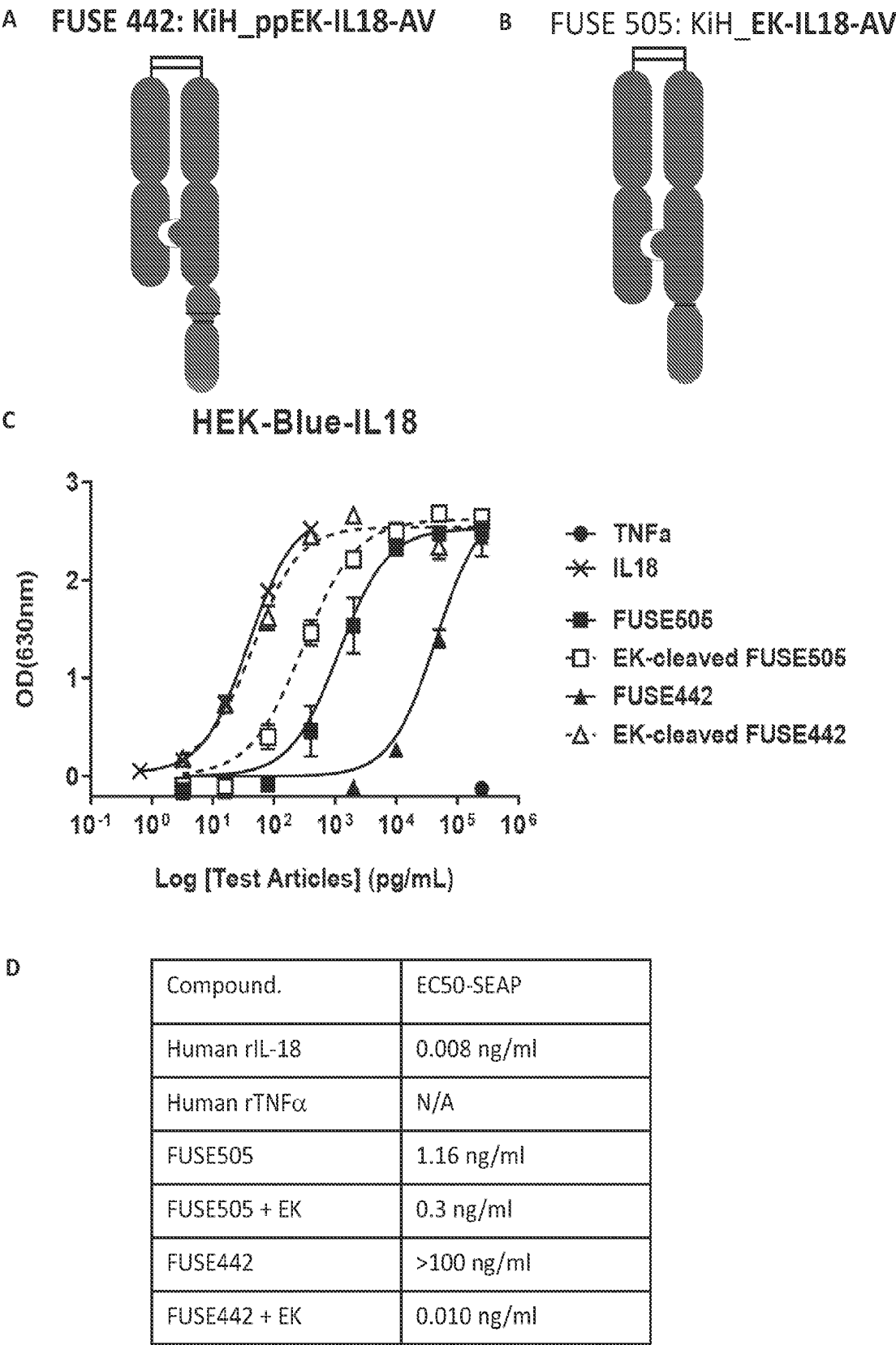
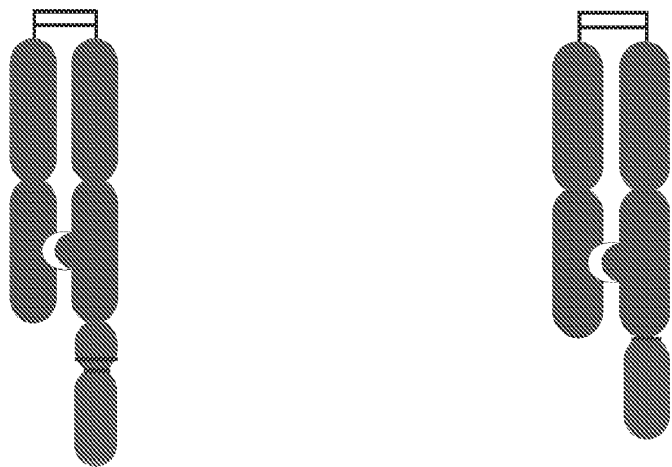
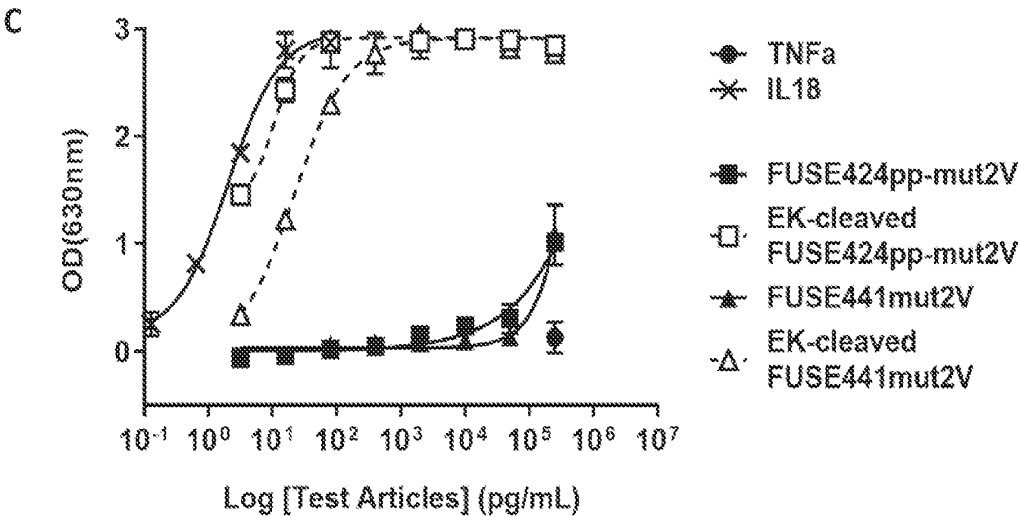


FIG. 4

A FUSE 424: KiH_ppEK-IL18mut2-AV **B** FUSE 441: KiH_EK-matIL18mut2-AV



KC-2328 HEK-Blue-IL18



D

Compound	EC50-SEAP
Human rIL-18	0.0020 ng/ml
Human rTNFα	N/A
FUSE424	> 1000 ng/ml
FUSE424+EK	0.0011 ng/ml
FUSE441	> 1000 ng/ml
FUSE441+EK	0.022 ng/ml

FIG. 5

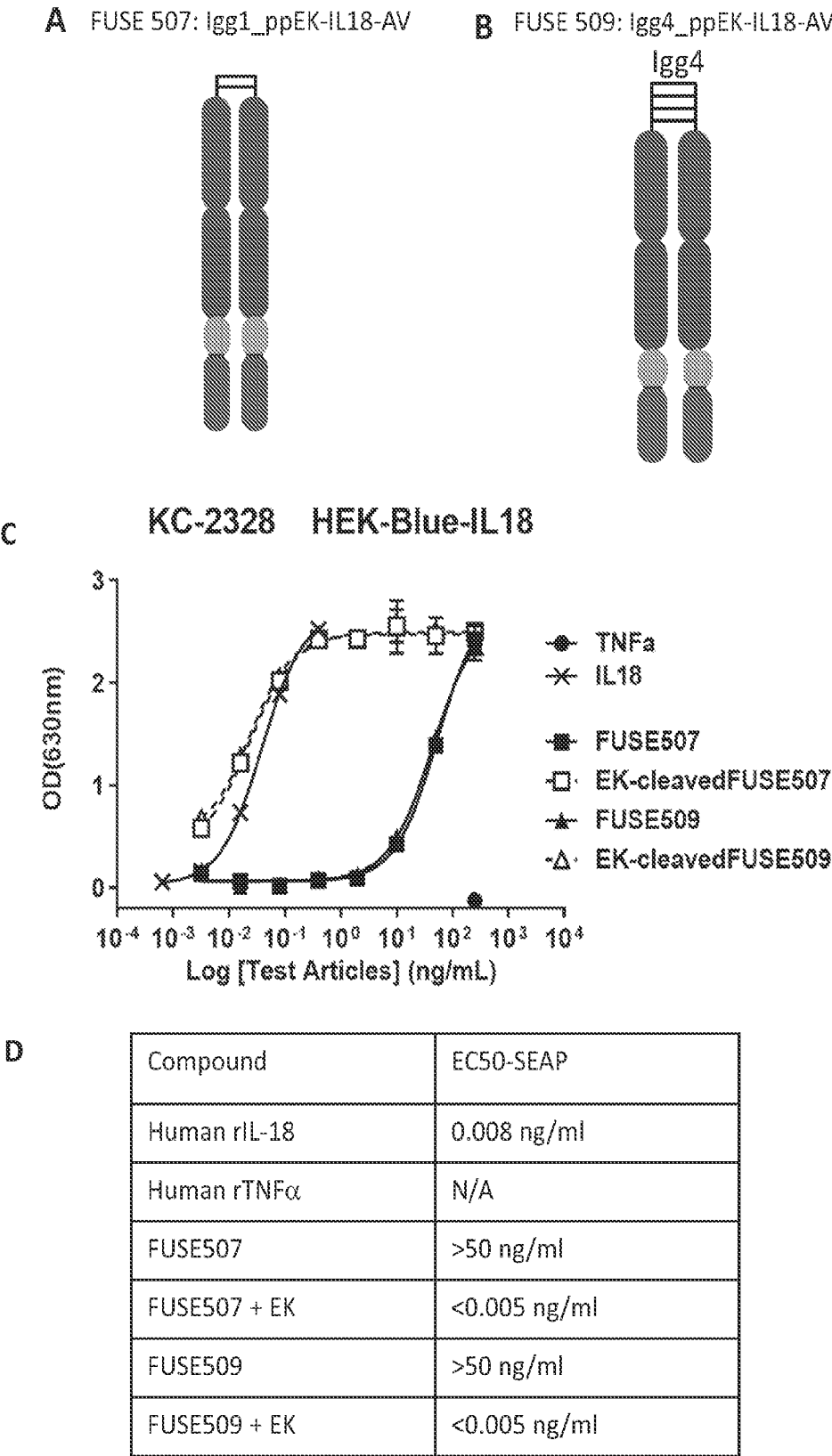


FIG. 6

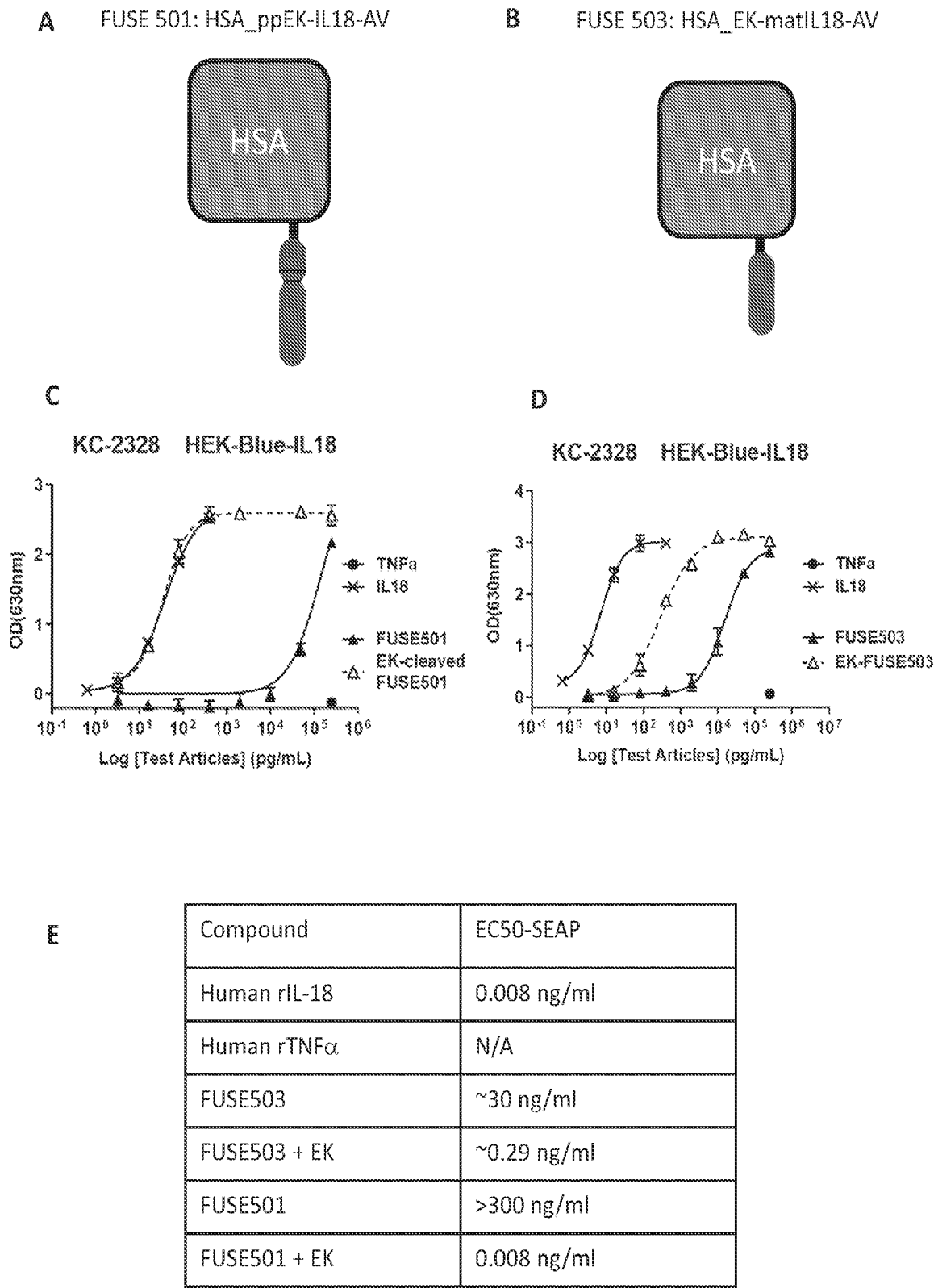
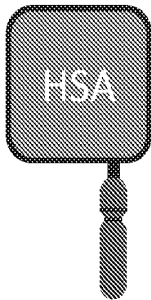
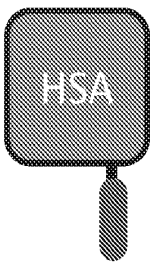


FIG. 7

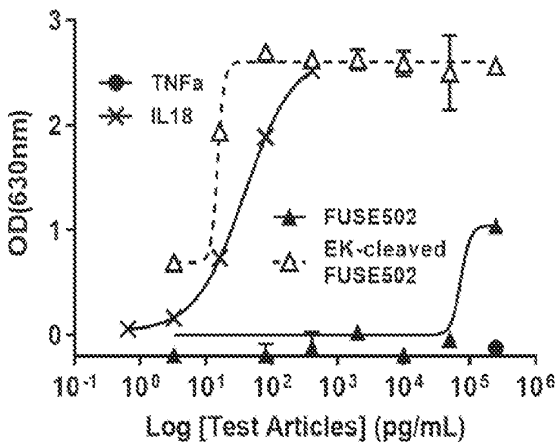
A FUSE 502: HSA_ppEK-IL18mut2-AV



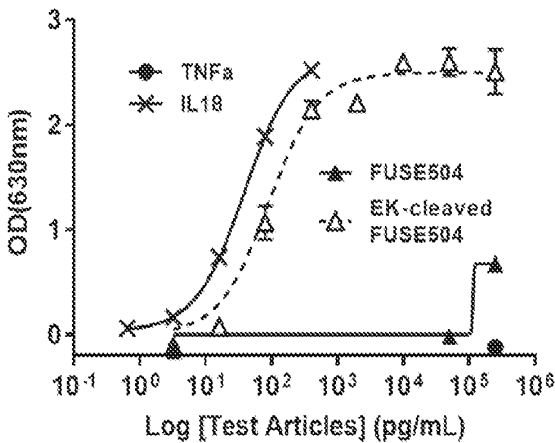
B FUSE 504: HSA_EK-matIL18mut2-AV



C KC-2328 HEK-Blue-IL18



D KC-2328 HEK-Blue-IL18



E

Compound	EC50-SEAP
Human rIL-18	0.008 ng/ml
Human rTNFα	N/A
FUSE504	>500 ng/ml
FUSE504 + EK	0.089 ng/ml
FUSE502	>500 ng/ml
FUSE502 + EK	<0.005 ng/ml

FIG. 8

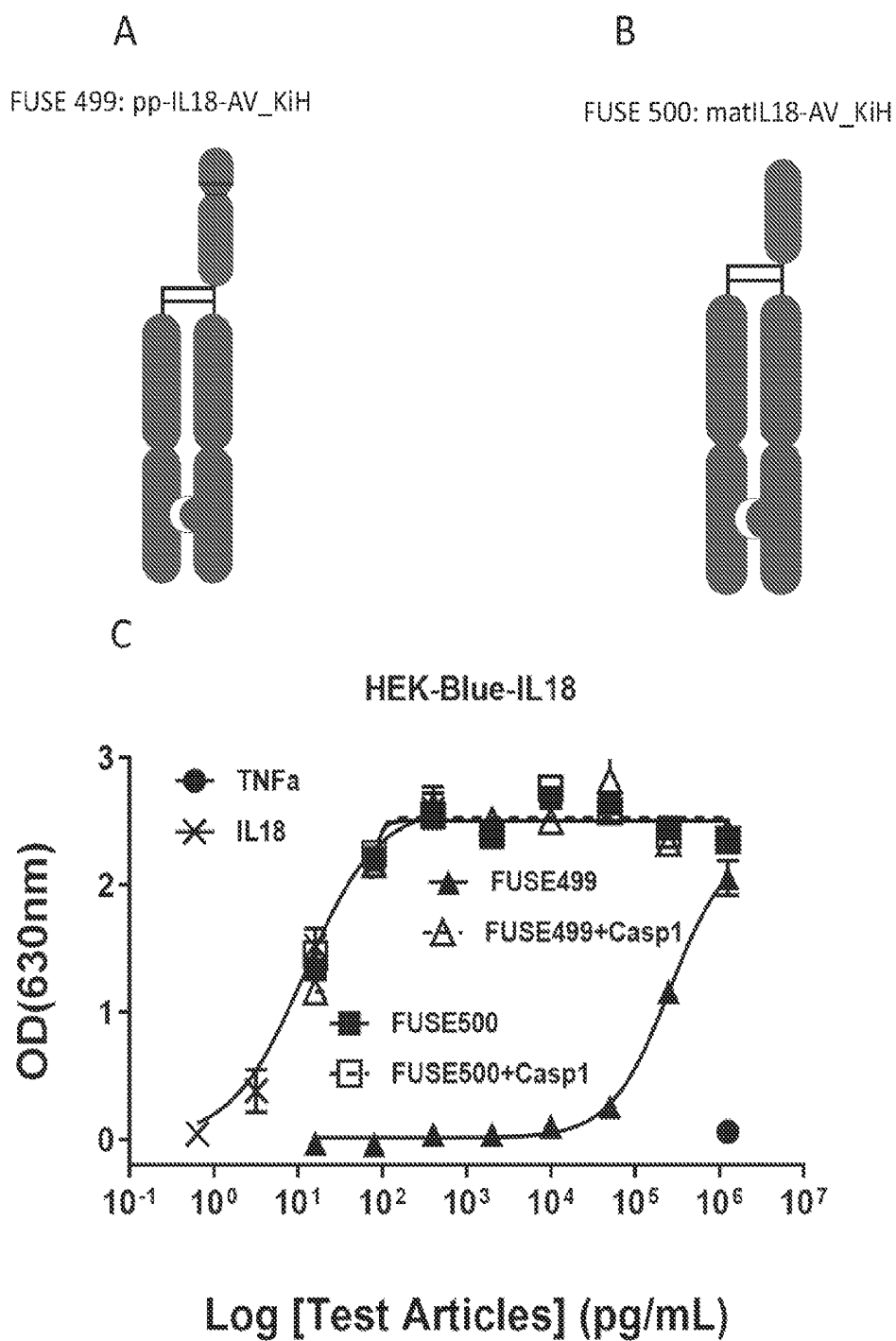


FIG. 8

D

Compound	EC50-SEAP
Human rIL-18	0.01 ng/ml
Human rTNF α	N/A
FUSE499	>500 ng/ml
FUSE499 + Casp1	~0.01 ng/ml
FUSE500	~0.01 ng/ml
FUSE500 + Casp1	~0.01 ng/ml

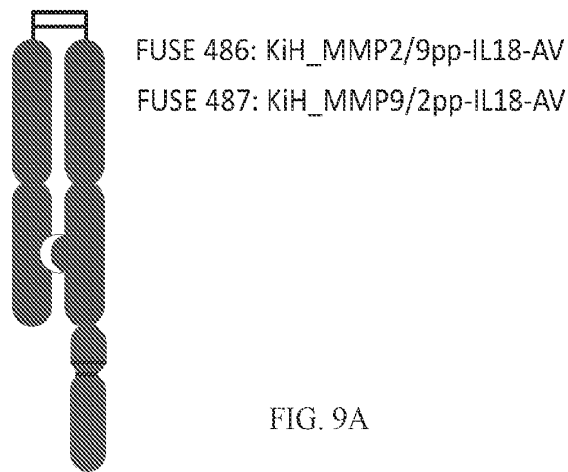
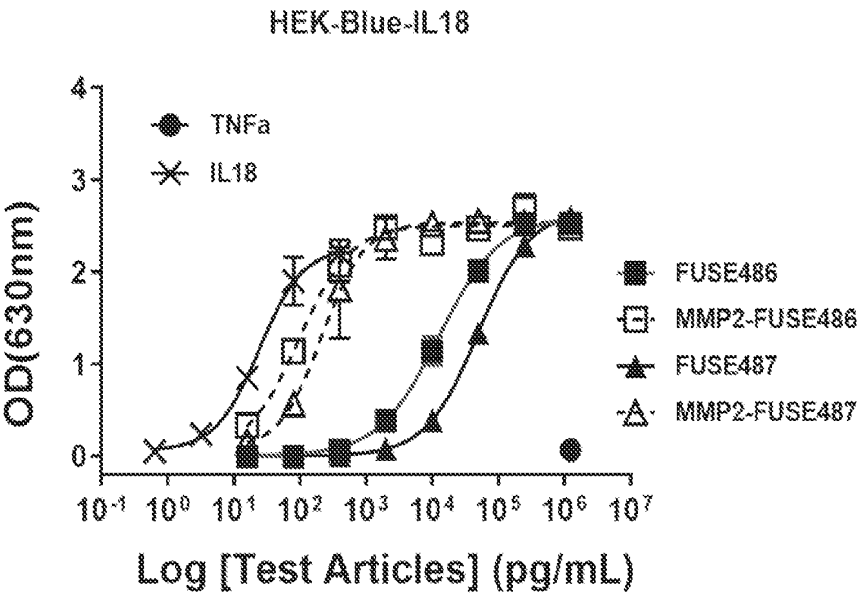


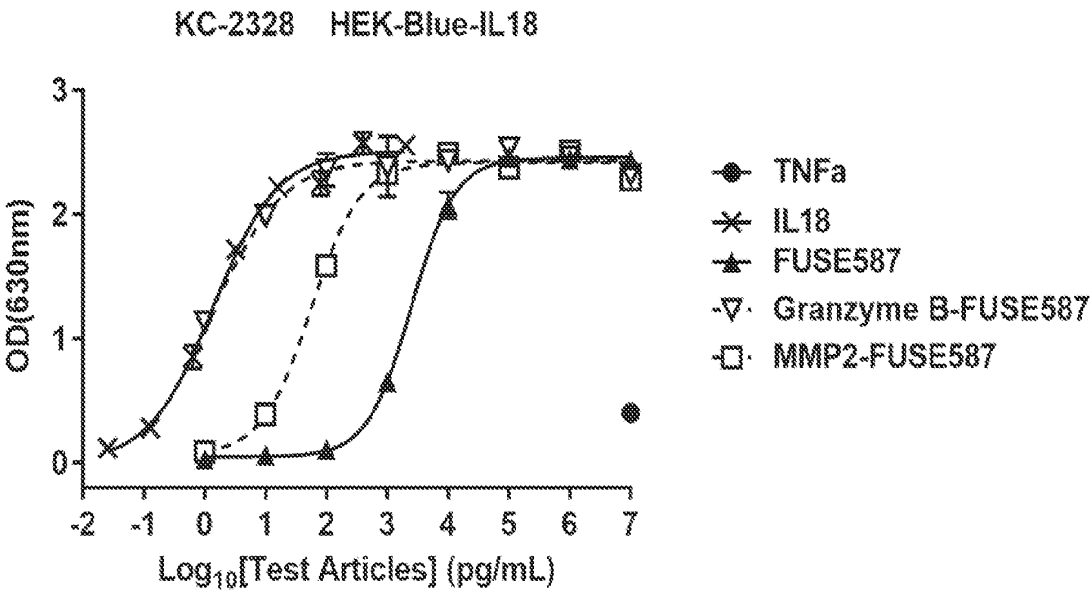
FIG. 9A



Compound	EC50-SEAP
Human rIL-18	0.02 ng/ml
Human rTNFα	N/A
FUSE486	~33 ng/ml
FUSE486 + MMP2	~0.06 ng/ml
FUSE487	~100 ng/ml
FUSE487 + MMP2	~0.12 ng/ml

FIG. 9B

FIG. 9C



Compound	EC50-SEAP
Human rIL-18	1.38
Human rTNFα	N/A
FUSE587	3483
FUSE587 + MMP2	2.23
FUSE587 + Granzyme B	56.24

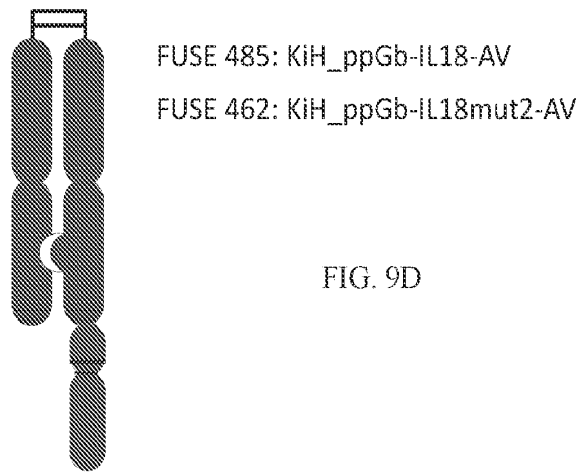


FIG. 9D

FIG. 9E

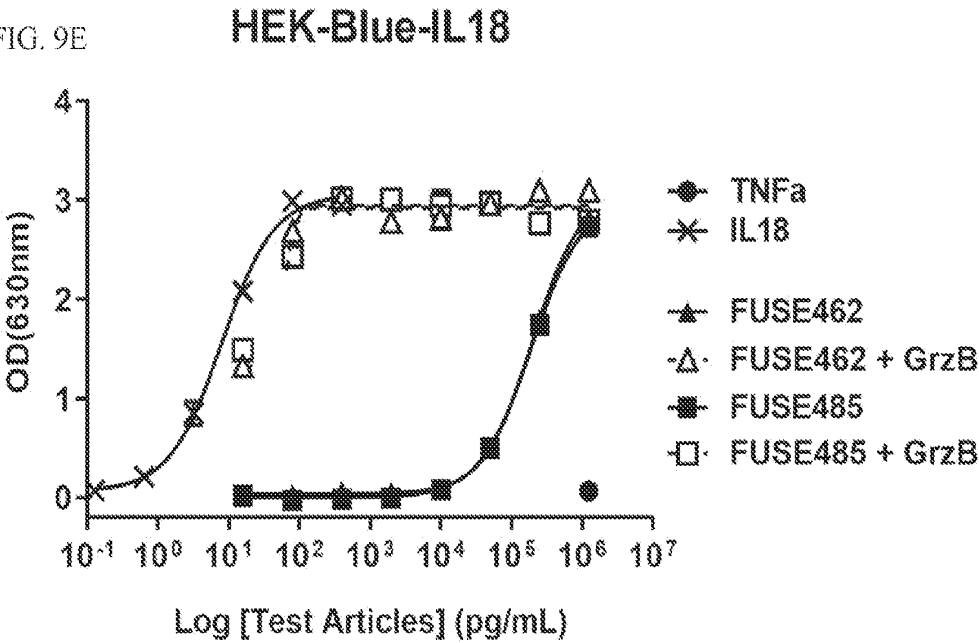


FIG. 9F

Compound.	EC50-SEAP
Human rIL-18	0.0020 ng/ml
Human rTNFα	N/A
FUSE462	>500 ng/ml
FUSE462 + GzmB	~0.03 ng/ml
FUSE485	>500 ng/ml
FUSE485 + GzmB	~0.03 ng/ml

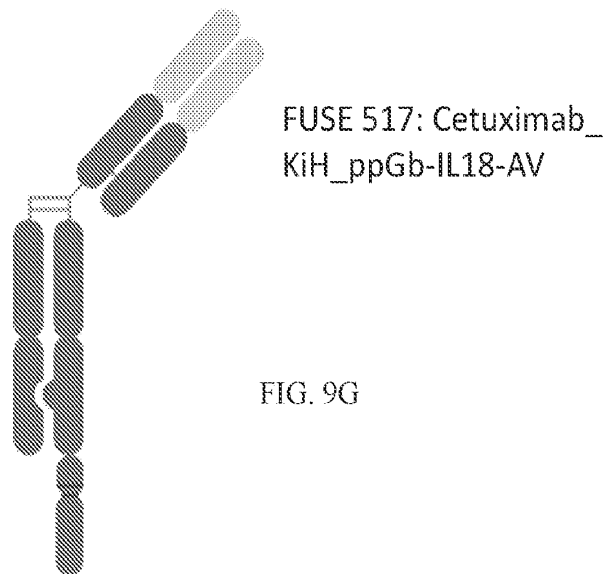


FIG. 9G

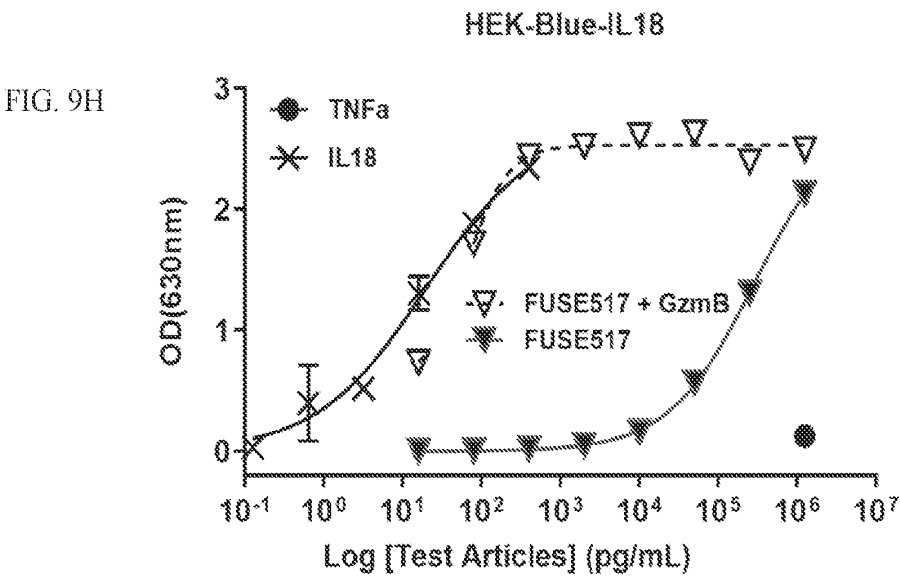


FIG. 9I

Compound	EC50-SEAP
Human rIL-18	0.002 ng/ml
Human rTNFα	N/A
FUSE517	>500 ng/ml
FUSE517 + GzmB	~0.03 ng/ml

FIG. 10

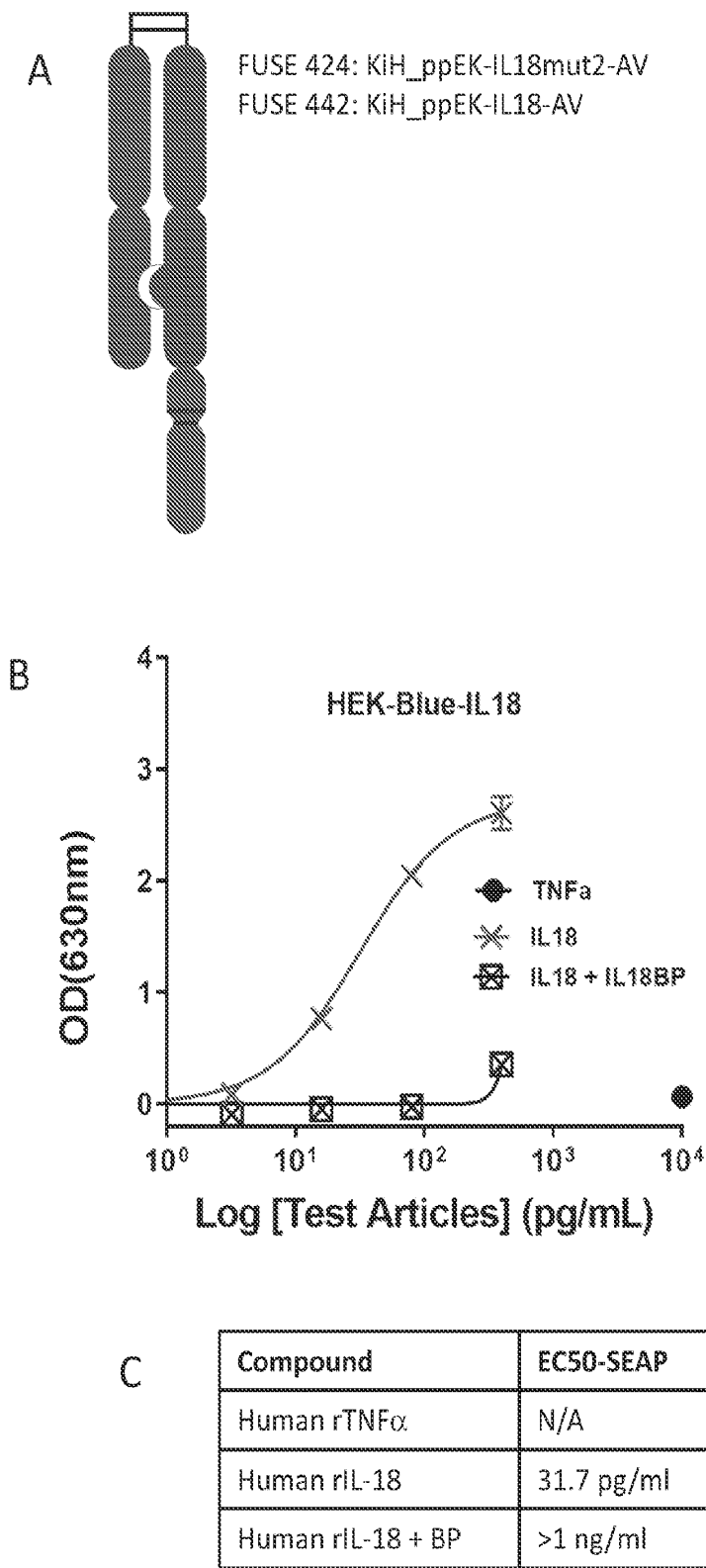
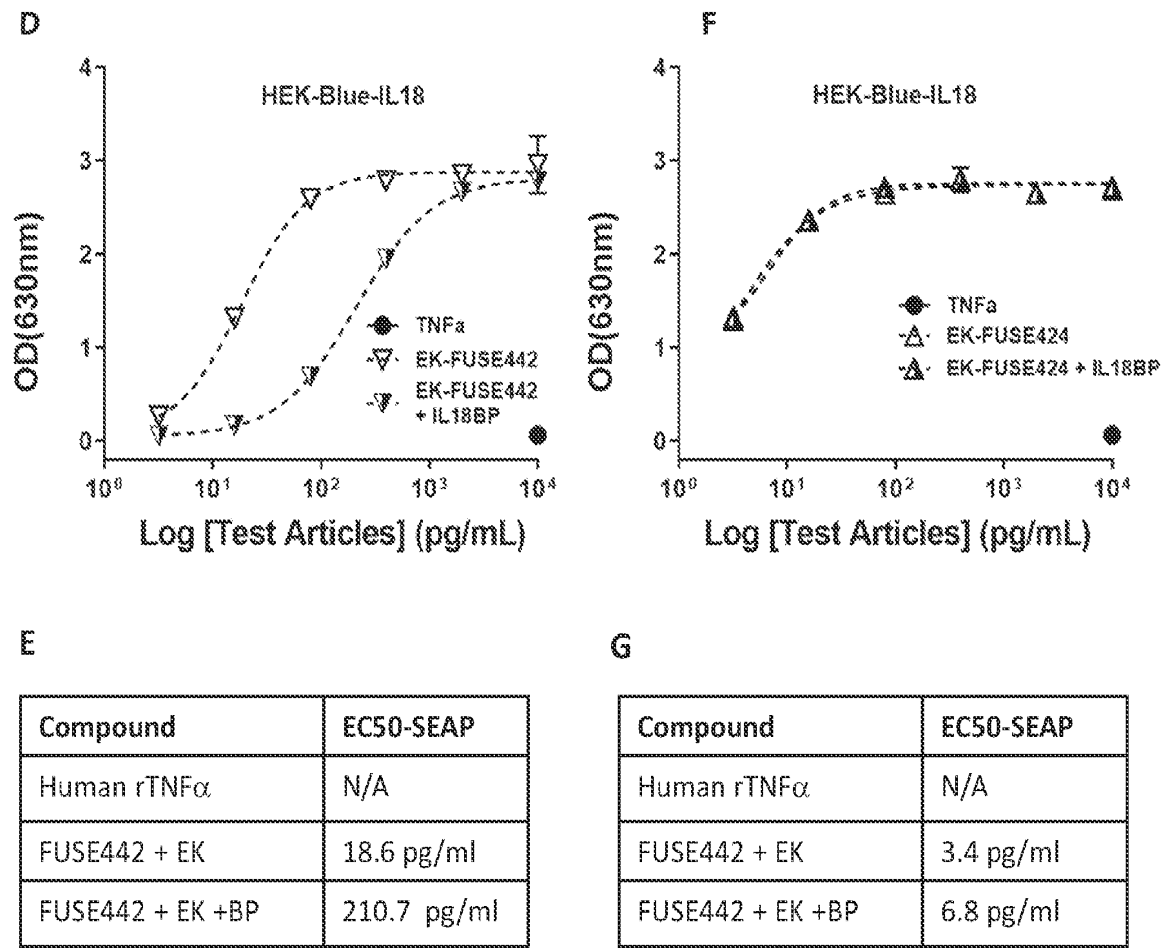


FIG. 10



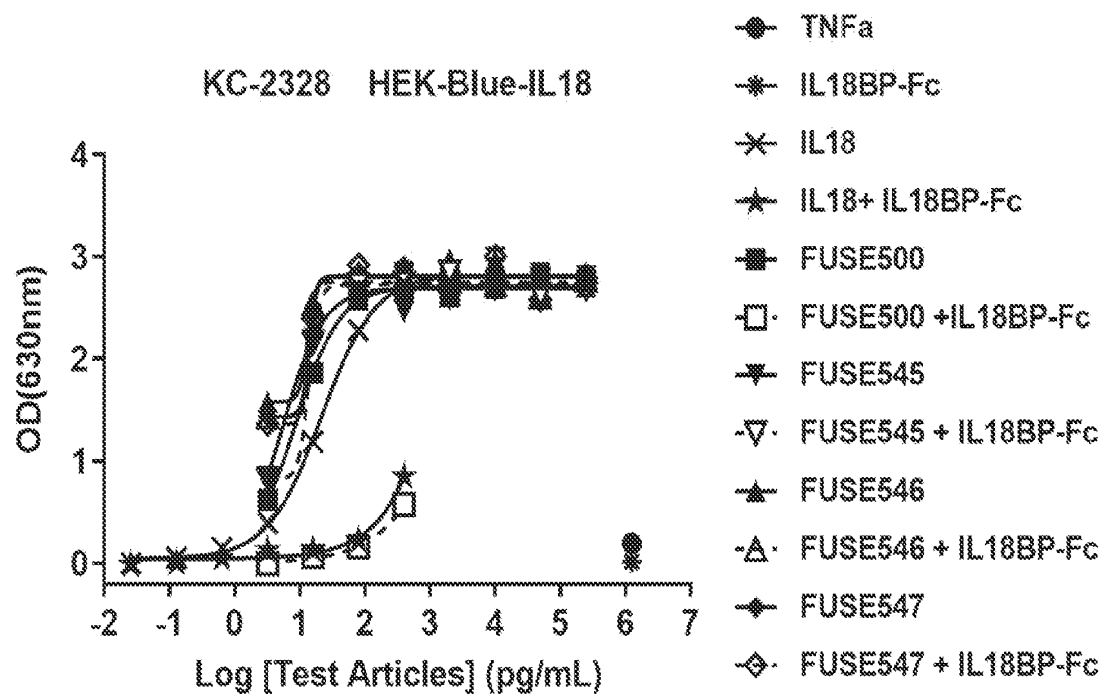
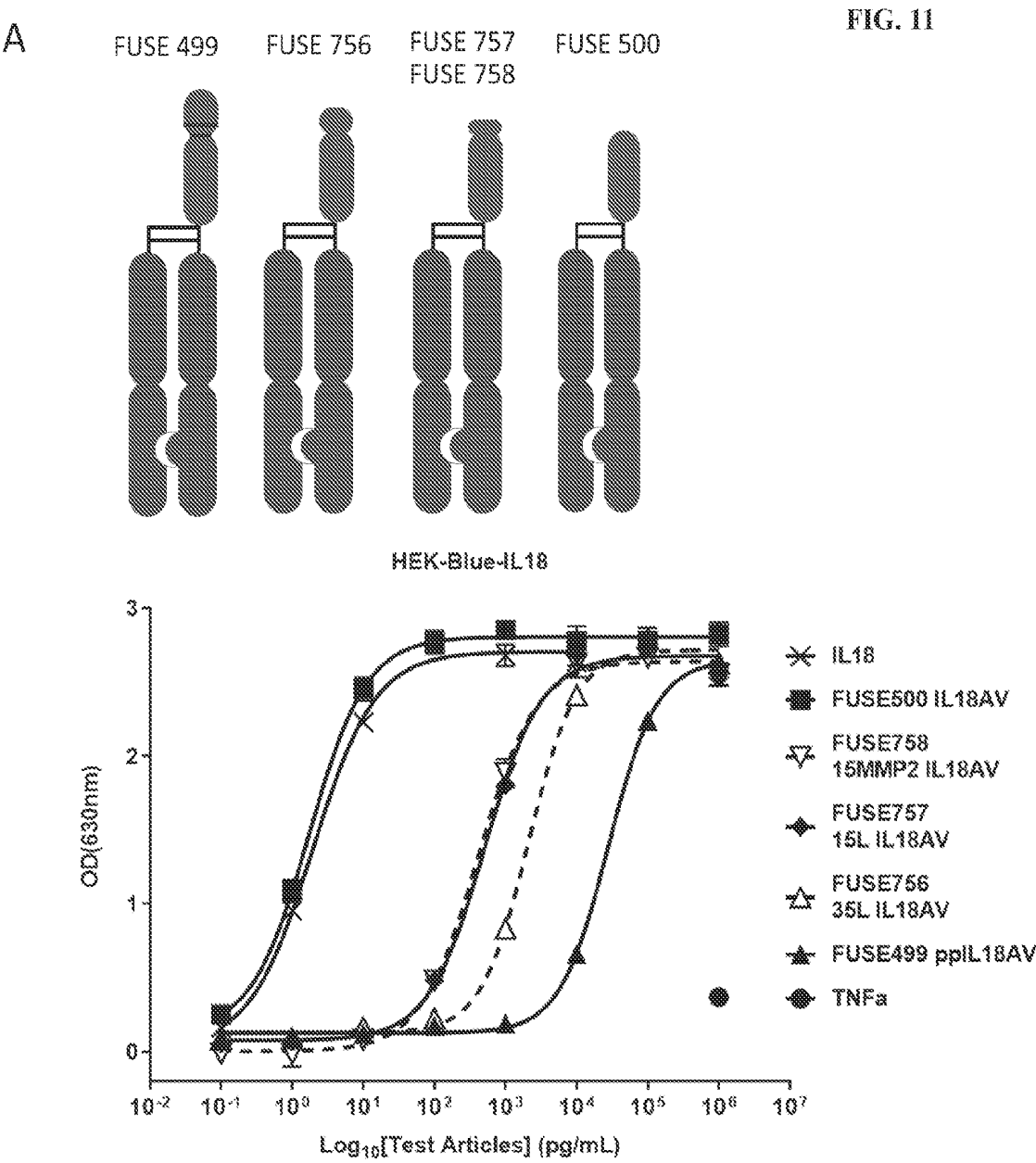


FIG. 10F

FIG. 10G

Compound	EC50-SEAP
Human rTNF α	N/A
Human rIL-18	0.0217 ng/mL
Human rIL-18 + IL18BP-Fc	>4,000 ng/mL
FUSE500	0.0090 ng/mL
FUSE500 + IL18BP-Fc	2,175.8 ng/mL
FUSE545	0.0056 ng/mL
FUSE545 + IL18BP-Fc	0.0138 ng/mL
FUSE546	0.0133 ng/mL
FUSE546 + IL18BP-Fc	0.0134 ng/mL
FUSE547	0.0140 ng/mL
FUSE547 + IL18BP-Fc	0.0143 ng/mL



	mut2	mut3	mut4	mut5	mut6	mut7	mut8	mut9	mut10	mut11	mut12
Fuse-500											
(wt-AV)	Fuse-545	Fuse-546	Fuse-547	Fuse-583	Fuse-584	Fuse-585	Fuse-586	Fuse-599	Fuse-600	Fuse-601	Fuse-602
E42	-	K	R	A	H	R	Q	K	K		
M87	K	-	-					H	K	H	K
K89	G	G	G	A	G	E	A	G	G	A	A
M96	L	-	-					-	-	I	I
M149	V	-	-					-	-	I	I

FIG. 12A

	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE
IL-18*	500	545	546	547	583	584	585	586	599	600	601
IL-18 BP	7.28E-										
Kd (nM)	4.00E-10	10*	1.40E-07	4.00E-08	3.20E-09	4.00E-08	1.50E-07	2.60E-09	-	-	-

*<https://www.pnas.org/doi/10.1073/pnas.97.3.1190>

FIG. 12C

	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE	FUSE
IL18*	500	545	546	547	583	584	585	586	599	600	601
IL-18RA	7.4E-										
Kd (nM)	2E-08*	09**	1.90E-08	1.80E-08	2.60E-08	1.20E-08	2.50E-08	2.00E-08	1.60E-08	3.00E-08	2.10E-08

*<https://arthritis-research.biomedcentral.com/articles/10.1186/ar3295>

FIG. 12E

FIG. 12B(i)

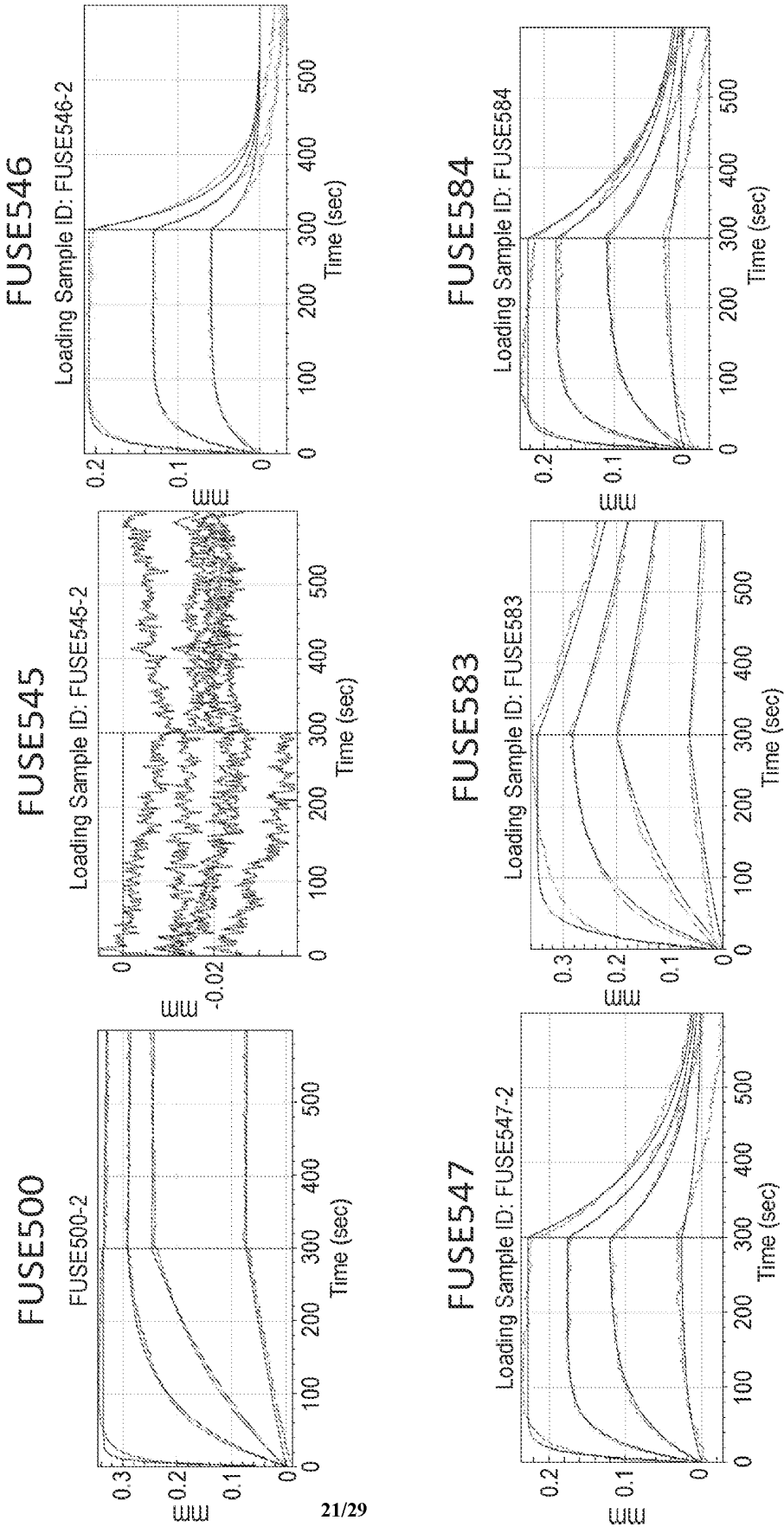


FIG. 12B(ii)

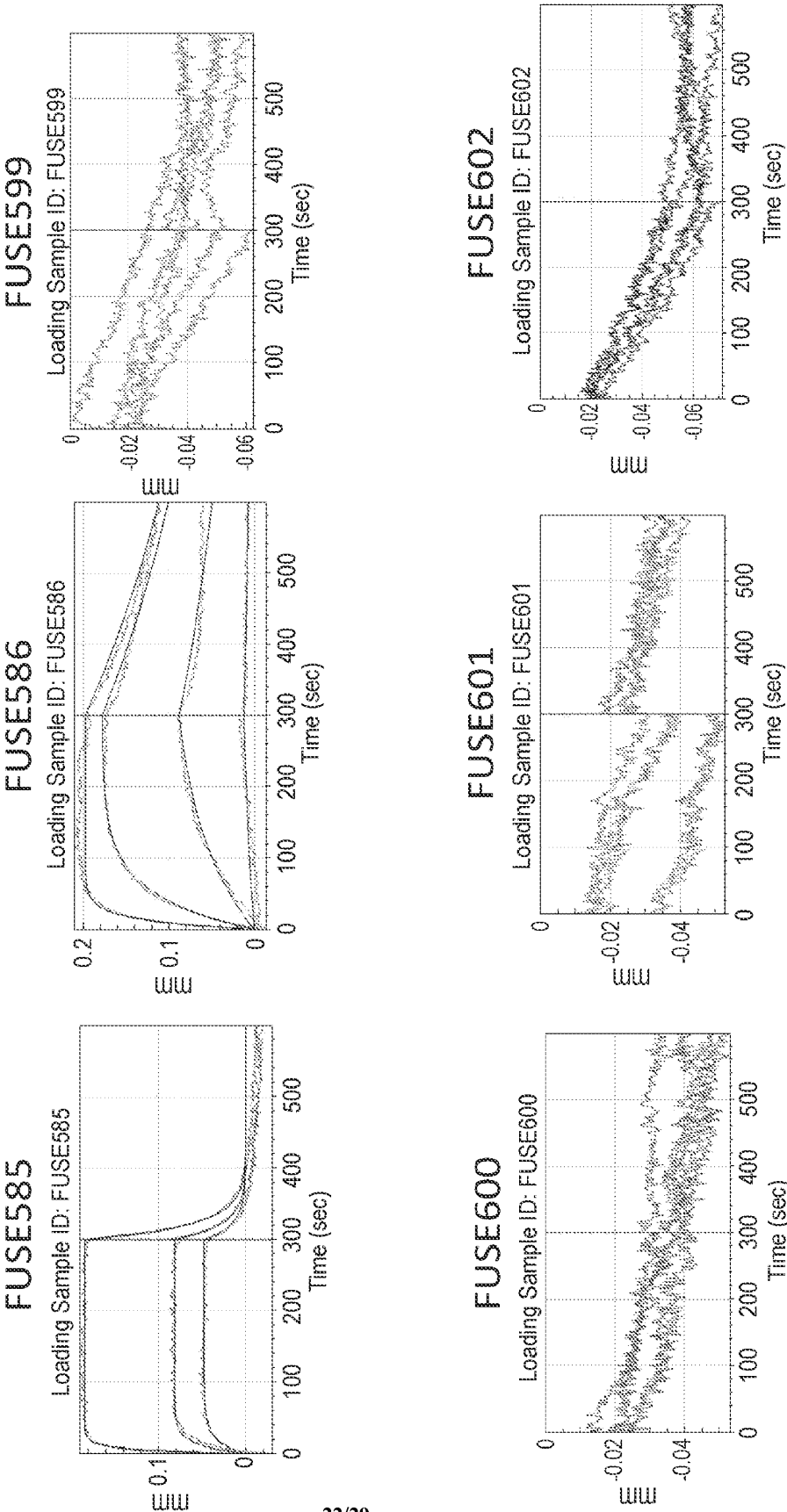


FIG.
12D(ii)

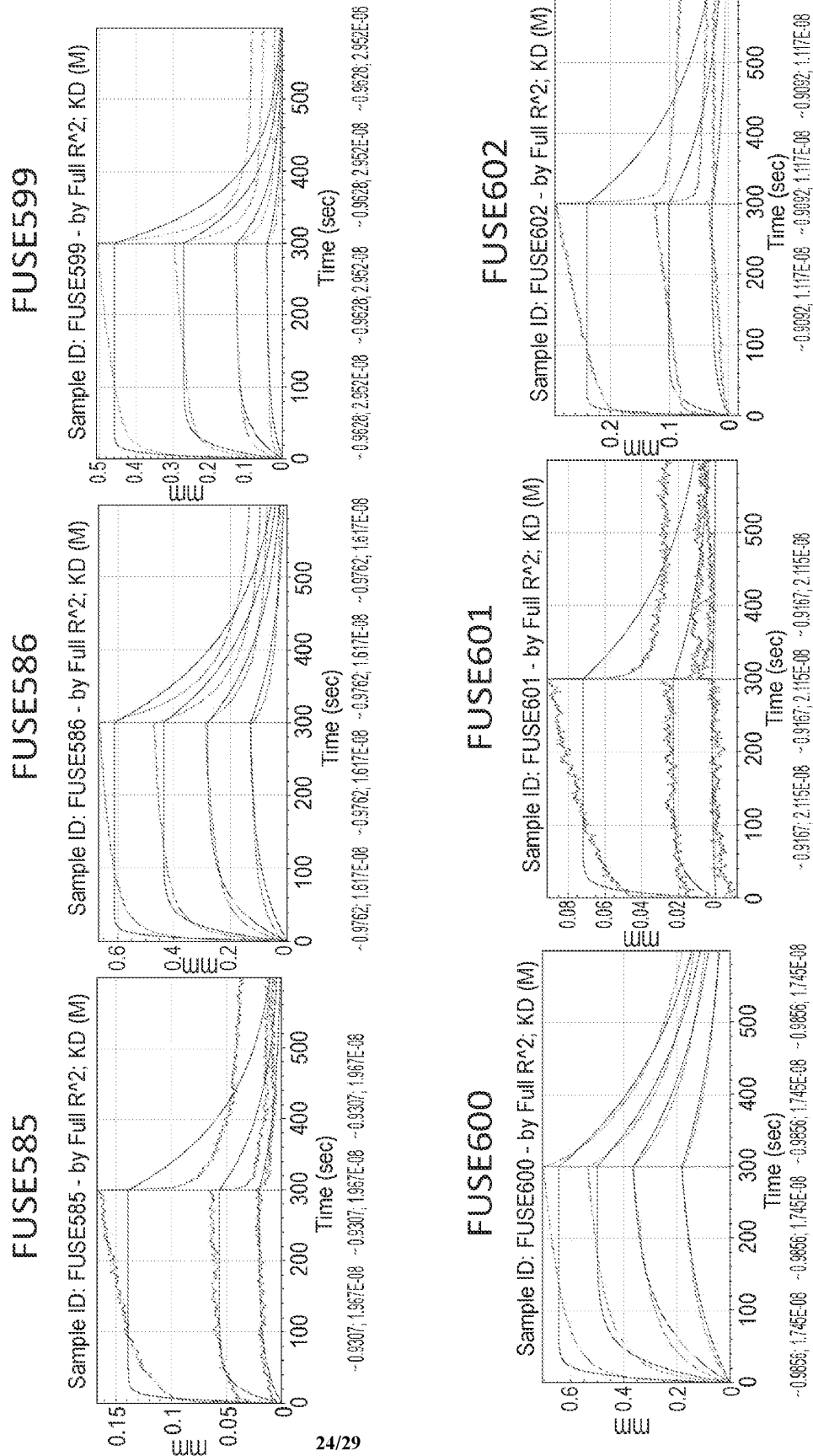
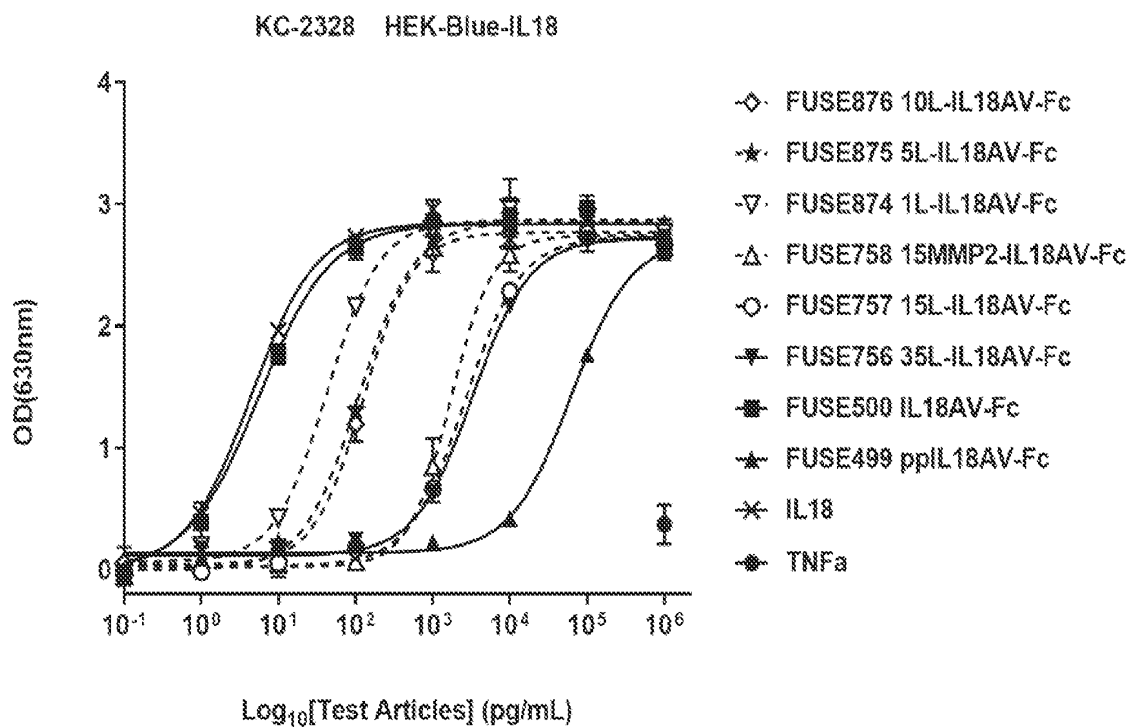
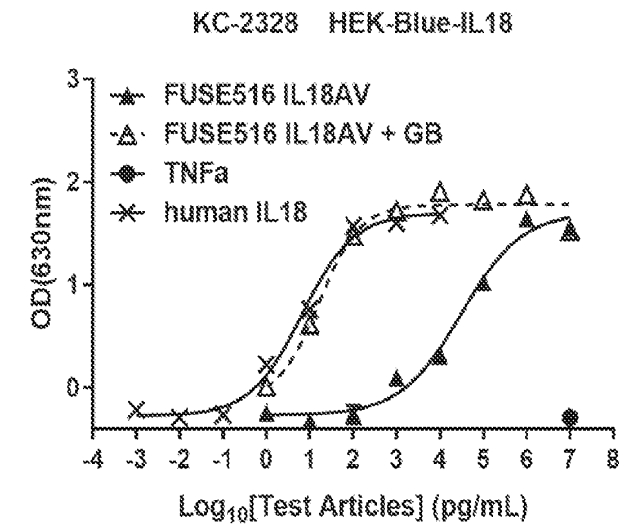


FIG. 13

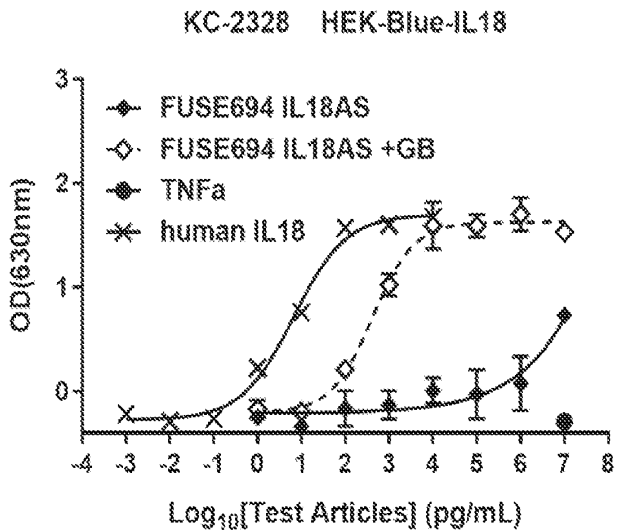


Compound	EC50-SEAP
Human rIL-18	0.0044 ng/mL
FUSE500	0.0056 ng/mL
Human rTNFα	N/A
FUSE874 (L)	0.053 ng/mL
FUSE875 (5L)	0.1103 ng/mL
FUSE876 (10L)	0.1258 ng/mL
FUSE758 (15MM)	1.689 ng/mL
FUSE756 (35L)	3.257 ng/mL
FUSE499 (pp)	62.14 ng/mL



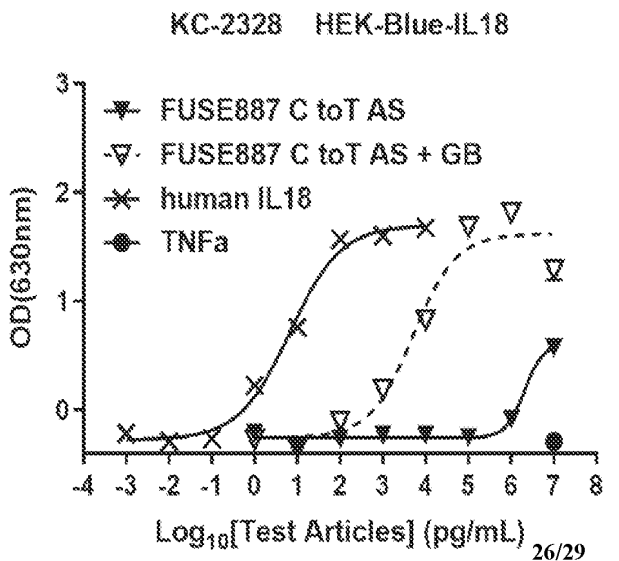
Compound	EC50-SEAP
Human rIL-18	6.67 pg/mL
Human rTNFα	N/A
FUSE516	31000 pg/ml
FUSE516 + GB	16.4 pg/ml

FIG. 14A



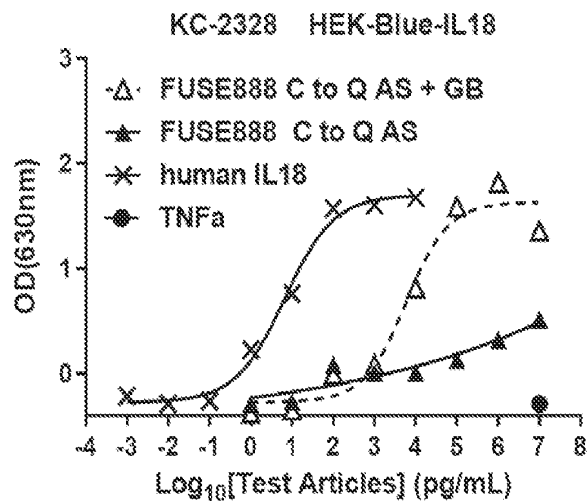
Compound	EC50-SEAP
Human rIL-18	6.66 pg/ml
Human rTNFα	N/A
FUSE694	>1,000,000 pg/ml
FUSE695 + GB	421.1 pg/ml

FIG. 14B



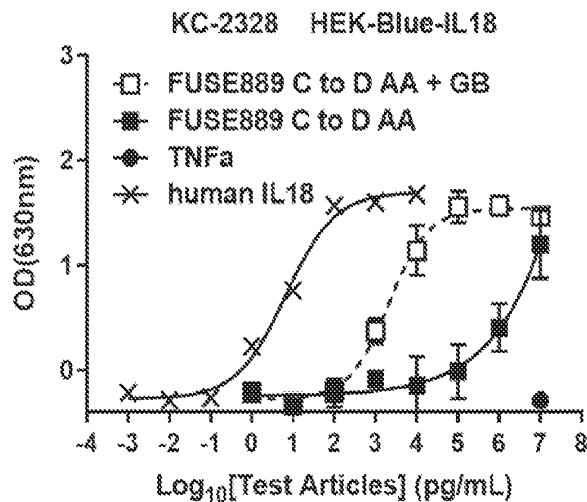
Compound	EC50-SEAP
Human rIL-18	6.7 pg/mL
Human rTNFα	N/A
FUSE887	>2000000 pg/ml
FUSE887 + GB	5000 pg/ml

FIG. 14C



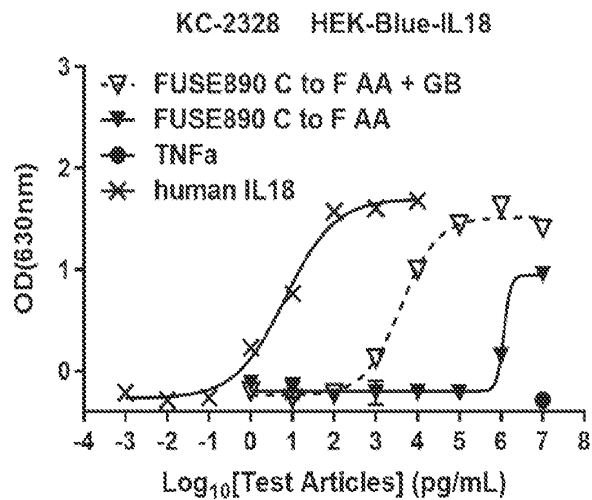
Compound	EC50-SEAP
Human rIL-18	6.7 pg/mL
Human rTNFα	N/A
FUSE888	>1000000 pg/ml
FUSE888+ GB	5900 pg/ml

FIG. 14D



Compound	EC50-SEAP
Human rIL-18	6.7 pg/mL
Human rTNFα	N/A
FUSE889	>1000000 pg/ml
FUSE889 + GB	2083 pg/ml

FIG. 14E



Compound	EC50-SEAP
Human rIL-18	6.7 pg/mL
Human rTNFα	N/A
FUSE890	>1000000 pg/ml
FUSE890 + GB	4000 pg/ml

FIG. 14F

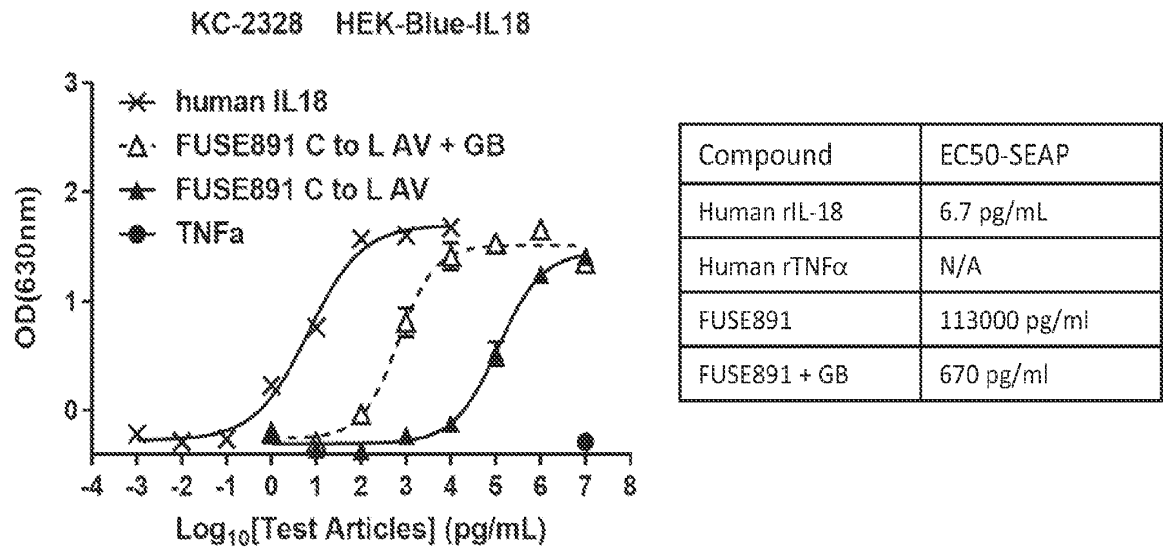


FIG. 14G

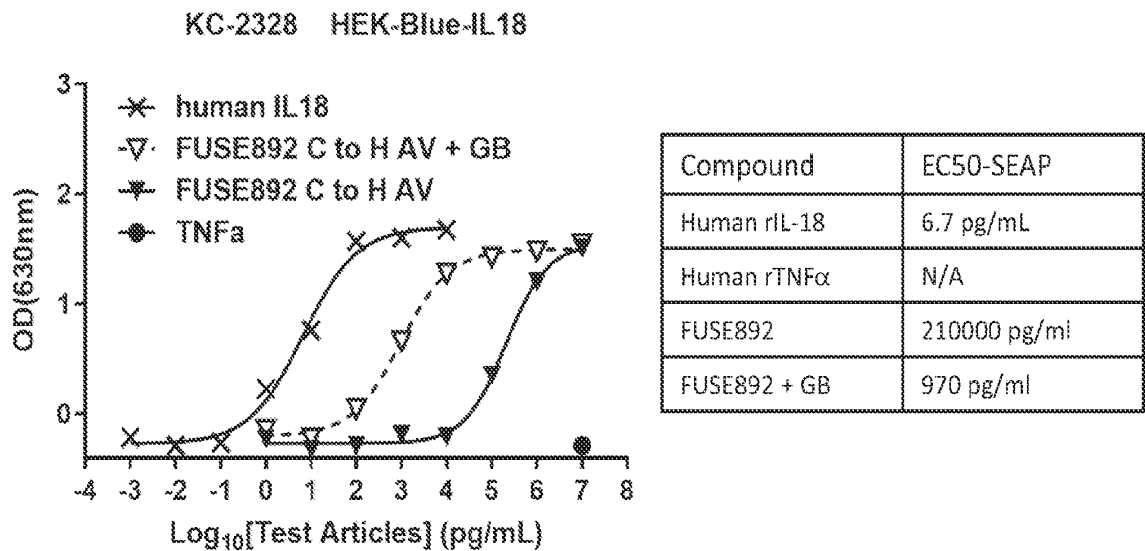


FIG. 14H

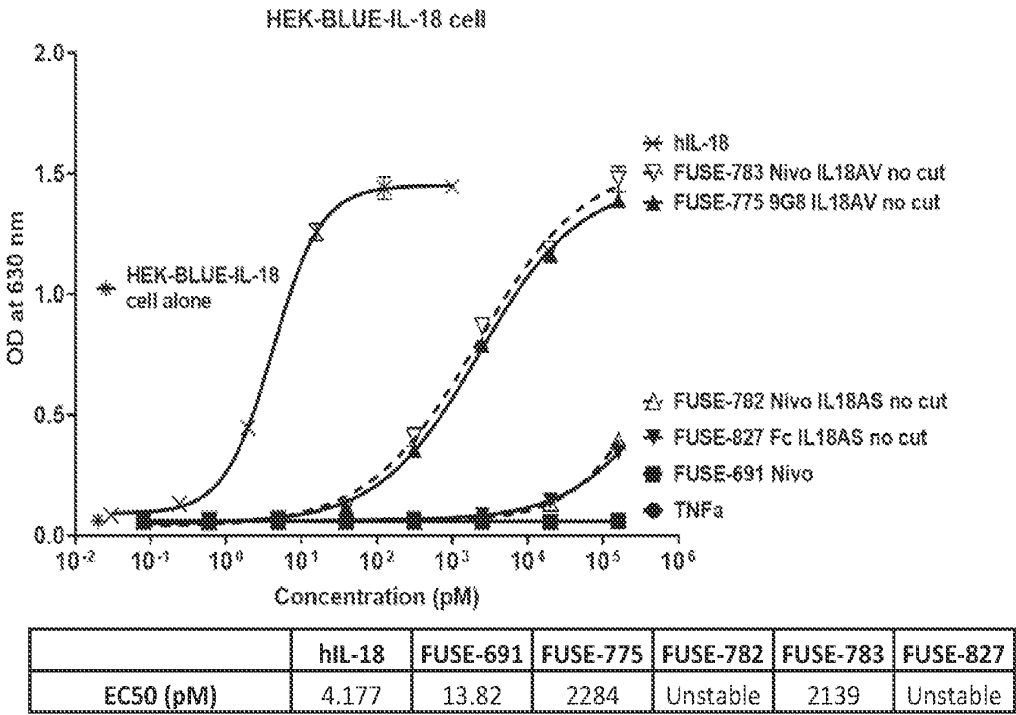


FIG. 15A

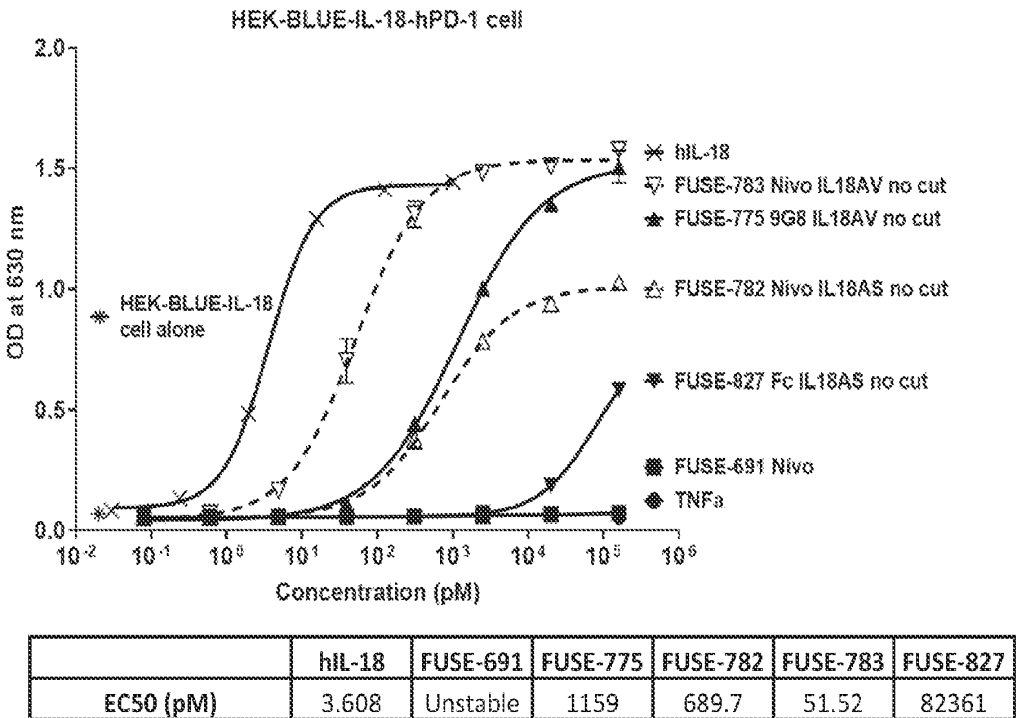


FIG. 15B