FIGURE 1:

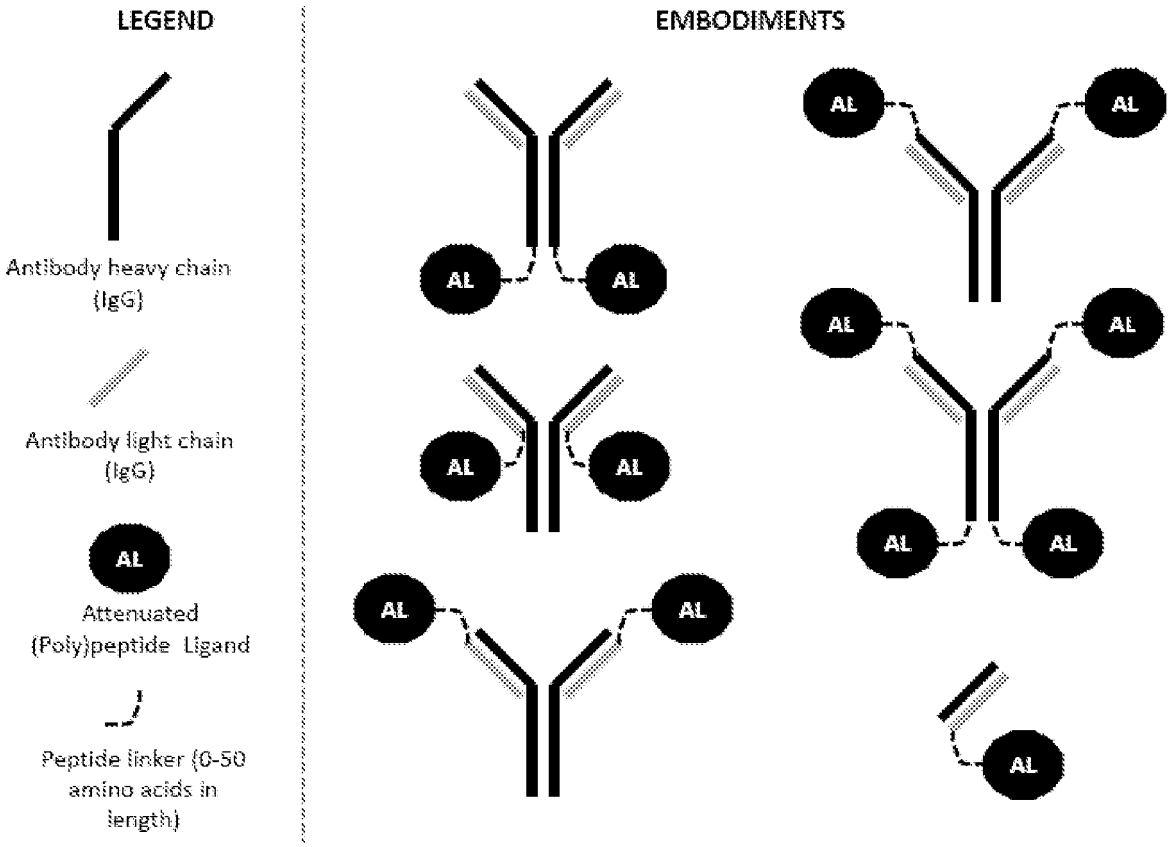

LEGEND
Antibody heavy chain (IgG)
Antibody light chain (IgG)
AL
Attenuated (Poly)peptide Ligand
Peptide linker (0-50 amino acids in length)
EMBODIMENTS
AL
AL
AL
AL
AL
AL
AL
AL
AL
AL
AL
AL
AL

FIGURE 2:

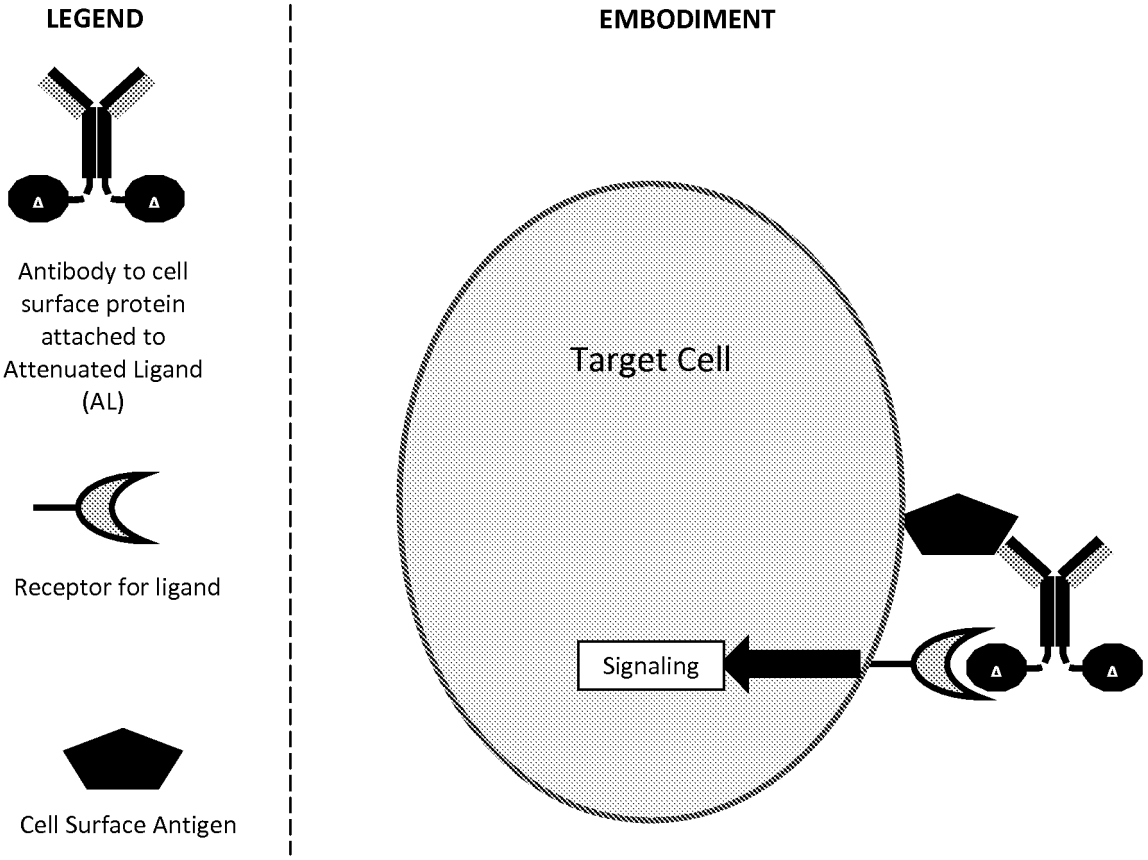

LEGEND
Antibody to cell surface protein attached to Attenuated Ligand (AL)
Receptor for ligand
Cell Surface Antigen
EMBODIMENT
Target Cell
Signaling

FIGURE 3:

Human CD38 (SEQ ID NO:131):

```
  1 MANCEFSPVSGDKPCCRLSRRAQLCLGVSILVLILVVVLAVVVPRWRQQWSGPGTTKRFP  60
 61 ETVLARCVKYTEIHPEMRHVDCQSVWDAFKGAFISKHPCNITEEDYQPLMKLGTQTVPCN 120
121 KILLWSRIKDLAHQFTQVQRDMFTLEDTLLGYLADDLTWCGEFNTSKINYQSCPDWRKDC 180
181 SNNPVSVFWKTVSRRFAEAACDVVHVMLNGSRSKIFDKNSTFGSVEVHNLQPEKVQTLEA 240
241 WVIHGGREDSRDLCQDPTIKELESIISKRNIQFSCKNIYRPDKFLQCVKNPEDSSCTSEI 300
```

underlined: extracellular domain
italic: transmembrane domain

FIGURE 4a:

Sequence of IFNα2b (SEQ ID NO:3)

human IFNα2b (SEQ ID NO:3)

```
  1 CDLPQTHSLG SRRTLMLLAQ MRRISLFSCL KDRHDFGFPQ EEFGNQFQKA ETIPVLHEMI QQIFNLFSTK DSSAAWDETL  80
 81 LDKFYTELYQ QLNDLEACVI QGVGVTETPL MKEDSILAVR KYFQRITLYL KEKKYSPCAW EVVRAEIMRS FSLSTNLQES 160
161 LRSKE                                                                                   165
```

Sequence of IFNβ1 (SEQ ID NO:91)

human IFNβ1 (SEQ ID NO:91)

```
  1 MSYNLLGFLQ RSSNFQCQKL LWQLNGRLEY CLKDRMNFDI PEEIKQLQQF QKEDAALTIY EMLQNIFAIF RQDSSSTGWN  80
 81 ETIVENLLAN VYHQINHLKT VLEEKLEKED FTRGKLMSSL HLKRYYGRIL HYLKAKEYSH CAWTIVRVEI LRNFYFINRL 160
161 TGYLRN                                                                                  166
```

Sequence of IFNβ1b (SEQ ID NO:103)

human IFNβ1b (SEQ ID NO:103)

```
  1 MSYNLLGFLQ RSSNFQSQKL LWQLNGRLEY CLKDRMNFDI PEEIKQLQQF QKEDAALTIY EMLQNIFAIF RQDSSSTGWN  80
 81 ETIVENLLAN VYHQINHLKT VLEEKLEKED FTRGKLMSSL HLKRYYGRIL HYLKAKEYSH CAWTIVRVEI LRNFYFINRL 160
161 TGYLRN                                                                                  166
```

Sequence of IFNγ (SEQ ID NO:106)

human IFNγ (SEQ ID NO:106)

```
  1 QDPYVKEAEN LKKYFNAGHS DVADNGTLFL GILKNWKEES DRKIMQSQIV SFYFKLFKNF KDDQSIQKSV ETIKEDMNVK  80
 81 FFNSNKKKRD DFEKLTNYSV TDLNVQRKAI HELIQVMAEL SPAAKTGKRK RSQMLFRGRR ASQ                   143
```

FIGURE 4b:

Sequence of IL-4 (SEQ ID NO:119)

human IL-4 (SEQ ID NO:119)

```
  1 HKCDITLQEI IKTLNSLTEQ KTLCTELTVT DIFAASKNTT EKETFCRAAT VLRQFYSHHE KDTRCLGATA QQFHRHKQLI  80
 81 RFLKRLDRNL WGLAGLNSCP VKEANQSTLE NFLERLKTIM REKYSKCSS                                   129
```

Sequence of IL-6 (SEQ ID NO:123)

human IL-6 (SEQ ID NO:123)

```
  1 PVPPGEDSKD VAAPHRQPLT SSERIDKQIR YILDGISALR KETCNKSNMC ESSKEALAEN NLNLPKMAEK DGCFQSGFNE  80
 81 ETCLVKIITG LLEFEVYLEY LQNRFESSEE QARAVQMSTK VLIQFLQKKA KNLDAITTPD PTTNASLLTK LQAQNQWLQD 160
161 MTTHLILRSF KEFLQSSLRA LRQM                                                              184
```

FIGURE 5a:

Heavy chain (SEQ ID NO:180):

```
  1 EVQLLESGGGLVQPGGSLRLSCAVSGFTFNSFAMSWVRQAPGKGLEWVSAISGSGGGTYY  60
 61 ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYFCAKDKILWFGEPVFDYWGQGTLVTV 120
121 SSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ 180
181 SSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP 240
241 SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS 300
301 TYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM 360
361 TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQ 420
421 EGNVFSCSVMHEALHNHYTQKSLSLSLGKCDLPQTHSLGSRRTLMLLAQMRRISLFSCLK 480
481 DRHDFGFPQEEFGNQFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQ 540
541 LNDLEACVIQGVGVTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRDEIMRSF 600
601 SLSTNLQESLRSKE                                                 614
```

Light chain (SEQ ID NO:134):

```
  1 EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA  60
 61 RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPPTFGQGTKVEIKRTVAAPSVFIFPP 120
121 SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT 180
181 LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC                             214
```

double underlined: antibody heavy and light chains
single underlined: cytokine
single underlined & bold: attenuating mutation

G005-HC-L0-IFNα(A145D) IgG4

FIGURE 5b:

Heavy chain (SEQ ID NO:330):

```
  1 QVQLQQSGSELMMPGASVKISCKATGYTFSNYWIEWVKQRPGHGLEWIGEILPGTGRTIY  60
 61 NEKFKGKATFTADISSNTVQMQLSSLTSEDSAVYYCARRDYYGNFYYAMDYWGQGTSVTV 120
121 SSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ 180
181 SSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP 240
241 SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS 300
301 TYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM 360
361 TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQ 420
421 EGNVFSCSVMHEALHNHYTQKSLSLSLGKCDLPQTHSLGSRRTLMLLAQMRRISLFSCLK 480
481 DRHDFGFPQEEFGNQFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQ 540
541 LNDLEACVIQGVGVTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRDEIMRSF 600
601 SLSTNLQESLRSKE                                                 614
```

Light chain (SEQ ID NO:326):

```
  1 DIQMTQSTSSLSASLGDRVTISCSASQGINNYLNWYQQKPDGTVELLIYYTSTLQSGVPS  60
 61 RFSGSGSGTDYSLTISNLEPEDIGTYYCQQYSKLPRTFGGGTKLEIKRTVAAPSVFIFPP 120
121 SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT 180
181 LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC                             214
```

double underlined: antibody heavy and light chains
single underlined: cytokine
single underlined & bold: attenuating mutation

nBT062-HC-L0-IFNα(A145D) IgG4

FIGURE 5c:

Heavy chain (SEQ ID NO:214):

```
  1 EVQLLESGGGLVQPGGSLRLSCAVSGFTFNSFAMSWVRQAPGKGLEWVSAISGSGGGTYY  60
 61 ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYFCAKDKILWFGEPVFDYWGQGTLVTV 120
121 SSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ 180
181 SSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGP 240
241 SVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS 300
301 TYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEM 360
361 TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQ 420
421 EGNVFSCSVMHEALHNHYTQKSLSLSLGKMSYNLLGFLQRSSNFQSQKLLWQLNGRLEYC 480
481 LKDAMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANV 540
541 YHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEIL 600
601 RNFYFINRLTGYLRN                                               615
```

Light chain (SEQ ID NO:134):

```
  1 EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA  60
 61 RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPPTFGQGTKVEIKRTVAAPSVFIFPP 120
121 SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT 180
181 LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC                            214
```

double underlined: antibody heavy and light chains
single underlined: cytokine
single underlined & bold: attenuating mutation

G005-HC-L0-IFNβ(R35A) IgG4

FIGURE 5d:

Heavy chain (SEQ ID NO:324):

```
  1 QVQLKQSGPGLVQPSQSLSLTCTVSGFSLTSYGVHWVRQPPGKGLEWLGVIWSGGSTDYN  60
 61 AAFISRLSIRKDNSKSQVFFKMNSLQADDTAIYYCARTFTTSTSAWFAYWGQGTLVTVSA 120
121 ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS 180
181 GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG 240
241 PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN 300
301 STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE 360
361 LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW 420
421 QQGNVFSCSVMHEALHNHYTQKSLSLSPGK*SGGGGSGGGGSGGGGS*PVPPGEDSKDVAAP 480
481 HRQPLTSSERIDKQIRYILDGISALRKETCNKSNMCESSKEALAENNLNLPKMAEKDGCF 540
541 QSGFNEETCLVKIITGLLEFEVYLEYLQNRFESSEEQARAVQMSTKVLIQFLQKKAKNLD 600
601 AITTPDPTTNASLLTKLQAQNQWLQDMTTHLILRSFKEFLQSSL<b>E</b>ALRQM        650
```

Light chain (SEQ ID NO:312):

```
  1 SIVMTQTPKFLLVSAGDRVTITCKASQSVSNDVAWYQQKPGQSPKLLIYYASNRYTGVPD  60
 61 RFTGSGYGTDFTFTISTVQAEDLAVYFCQQDYSSPPWTFGGGTKLEIRRTVAAPSVFIFP 120
121 PSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL 180
181 TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC                           215
```

double underlined: antibody heavy and light chains
single underlined: cytokine
single underlined & bold: attenuating mutation
italic: linker sequence

HB95-HC-L16-IL-6(R179E) IgG1

FIGURE 5e:

Heavy chain (SEQ ID NO:306):

```
  1 DVQLQESGPGLVKPSQSLSLTCTVTGHSITSDYAWNWIRQFPGDKLEWMGYISYSGYTTY  60
 61 NPSLKSRVSITRDTSKNQFFLQLNSVTTEDTATYFCARDLDYGPWFAYWGQGTLVTVSAA 120
121 STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG 180
181 LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP 240
241 SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS 300
301 TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL 360
361 TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ 420
421 QGNVFSCSVMHEALHNHYTQKSLSLSPGKSGGGGSHKCDITLQEIIKTLNSLTEQKTLCT 480
481 ELTVTDIFAASKNTTEKETFCRAATVLRQFYSHHEKDTRCLGATAQQFHRHKQLIRFLKR 540
541 LDQNLWGLAGLNSCPVKEANQSTLENFLERLKTIMREKYSKCSS                   584
```

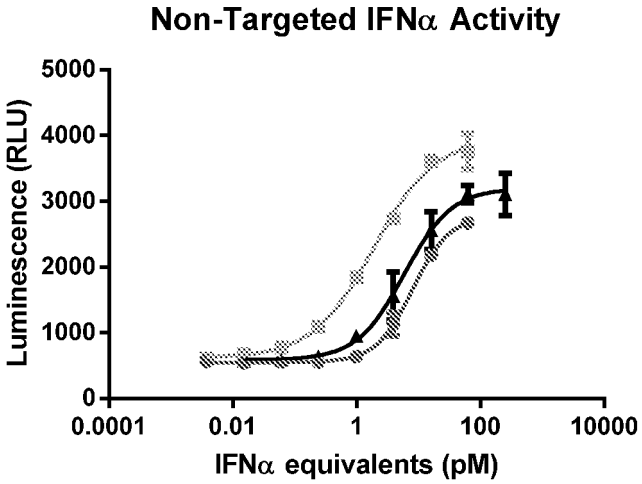
Light chain (SEQ ID NO:300):

```
  1 DIQMTQSPASLSASVGETVTLTCRASENIHNYLAWYQQKQGKSPQLLVYNVKTLADGVPS  60
 61 RFSGSGSGTQYSLKINSLQPEDFGSYYCQHFWSSPWTFGGGTKVEIKRTVAAPSVFIFPP 120
121 SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT 180
181 LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC                            214
```

double underlined: antibody heavy and light chains
single underlined: cytokine
single underlined & bold: attenuating mutation
italic: linker sequence

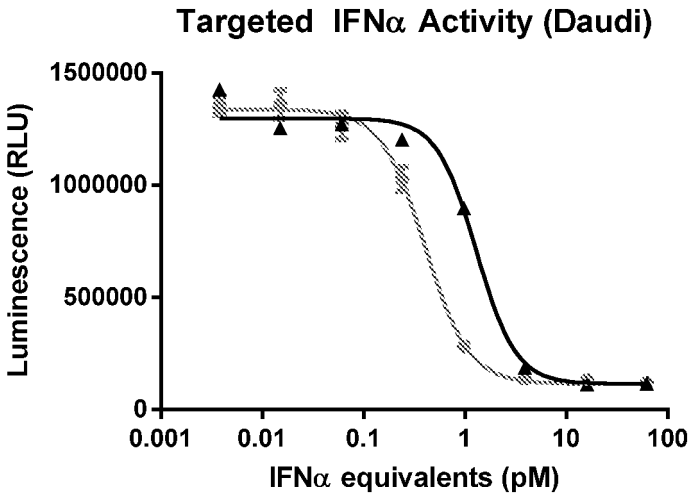
J110-HC-L6-IL-4(R88Q) IgG1

FIGURE 6:



Construct	EC50(pM)
IFNα	1.9
Rituximab-HC-L6-IFNα IgG1	5.9
Isotype-HC-L6-IFNα IgG1	8.0

FIGURE 7:



Construct	IC50(pM)
Rituximab-HC-L6-IFNα IgG1	0.40
IFNα	1.3

FIGURE 8:

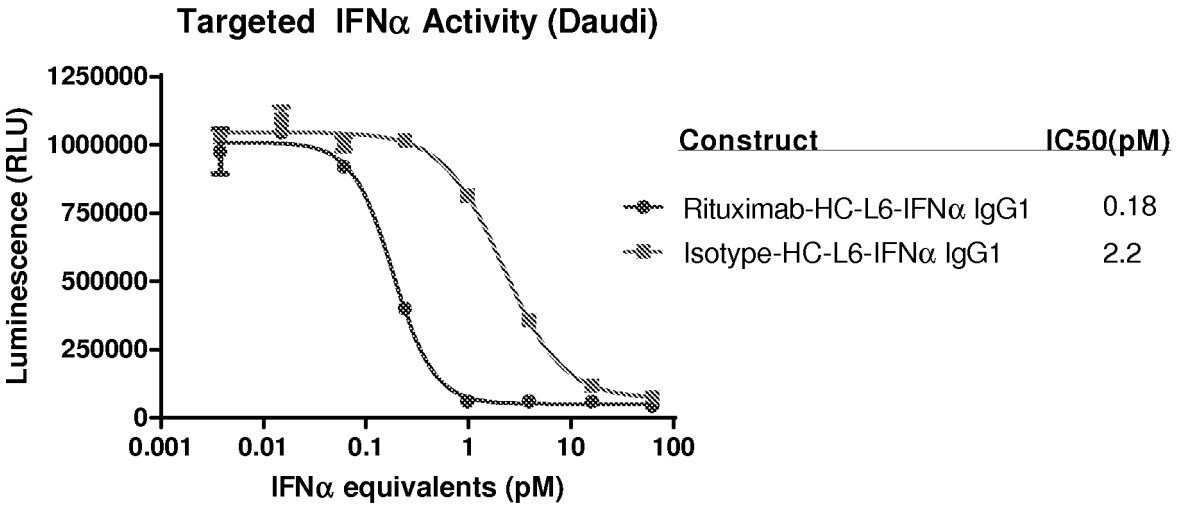
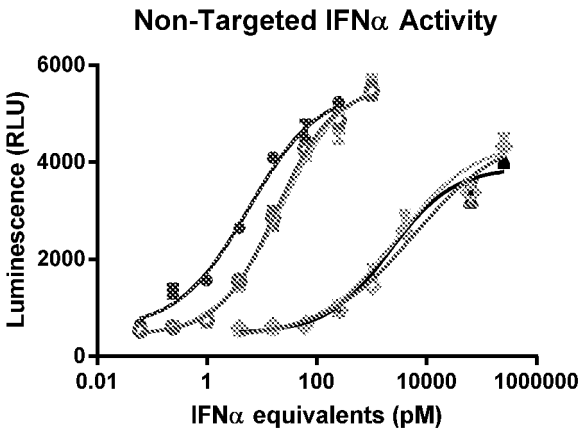
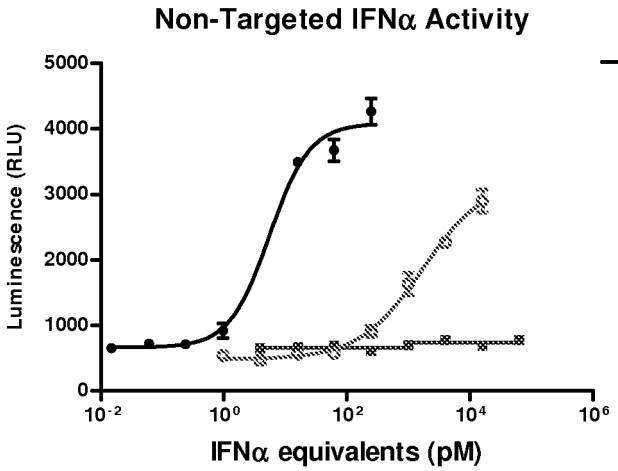

Targeted IFNα Activity (Daudi)
Luminescence (RLU)
1250000
1000000
750000
500000
250000
0
0.001
0.01
0.1
1
10
100
IFNα equivalents (pM)
Construct
IC50(pM)
Rituximab-HC-L6-IFNα IgG1
0.18
Isotype-HC-L6-IFNα IgG1
2.2

FIGURE 9:



Construct	EC50(pM)
IFNα	5.7
Rituximab-HC-L6-IFNα IgG1	22
Rituximab-HC-L6-IFNα (R144A) IgG1	2200
Rituximab-HC-L6-IFNα (A145G) IgG1	2800
Rituximab-HC-L6-IFNα (R33A+YNS) IgG1	6100
Isotype-HC-L6-IFNα IgG1	18

FIGURE 10:



Construct		EC50
●	Rituximab-HC-L6-IFNα IgG1	5.6
▩	Rituximab-HC-L6-IFNα (R33A) IgG1	ND
▨	Rituximab-HC-L6-IFNα (R144A + YNS) IgG1	1700

FIGURE 11:

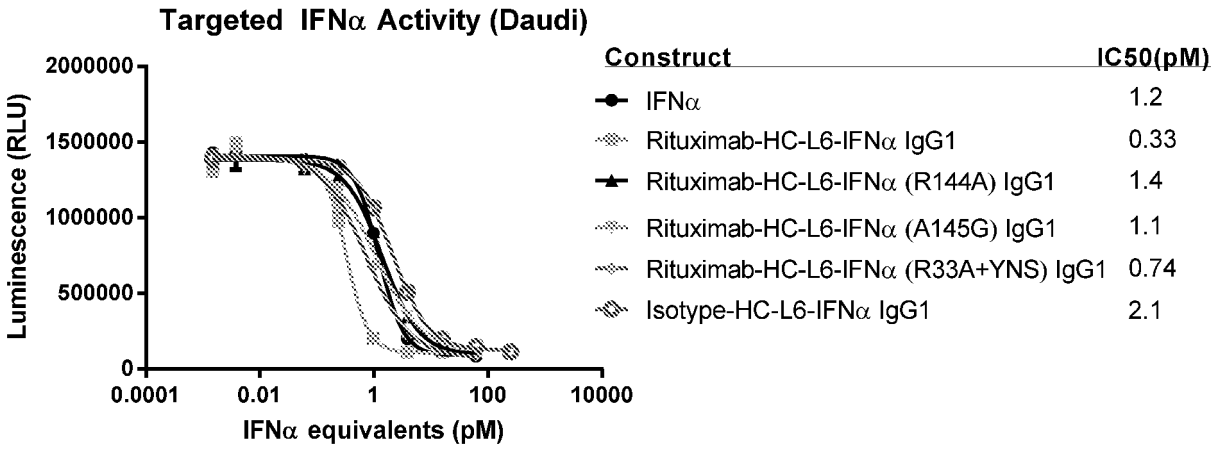
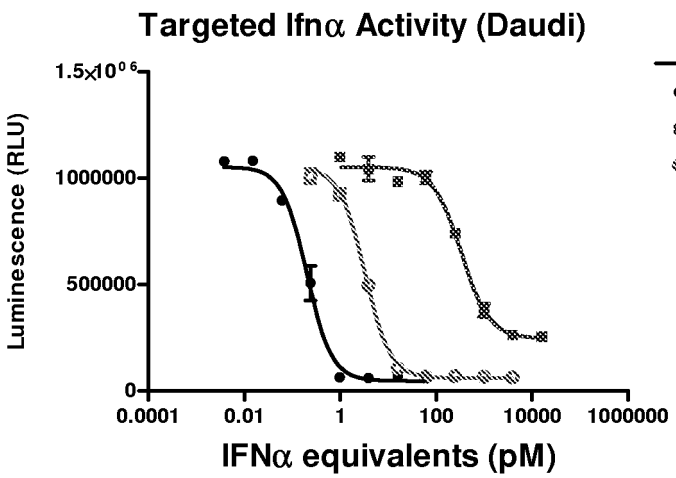

Targeted IFNα Activity (Daudi)
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.0001
0.01
1
100
10000
IFNα equivalents (pM)
Construct
IC50(pM)
IFNα
1.2
Rituximab-HC-L6-IFNα IgG1
0.33
Rituximab-HC-L6-IFNα (R144A) IgG1
1.4
Rituximab-HC-L6-IFNα (A145G) IgG1
1.1
Rituximab-HC-L6-IFNα (R33A+YNS) IgG1
0.74
Isotype-HC-L6-IFNα IgG1
2.1

FIGURE 12:



Construct	EC50
● Rituximab-HC-L6-IFNα IgG1	0.21
▩ Rituximab-HC-L6-IFNα (R33A) IgG1	340
⊘ Rituximab-HC-L6-IFNα (R144A + YNS) IgG1	3.3

FIGURE 13:

X355/02 VH (SEQ ID NO:391):

```
   1 QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWSWIRQHPGKGLEWIGYIYYSGSTN  60
  61 YNPSLKSRVTISVDTLKNQISLRLTSVTAADTAVYYCARVGGAGGWPMDVWGQGTTVTVS 120
 121 S                                                             121
```

X355/02 Vλ (SEQ ID NO:390):

```
   1 QAVLTQPASLSASPGESARLTCTLPSDINVRYYNIYWYQQKPGSPPRYLLYYYSDSHKGQ  60
  61 GSGVPSRFSGSKDVSTNSGILLISGLQSEDEADYYCMTWSSNGSGVFGGGTQLTVL     116
```

X355/07 VH (SEQ ID NO:393):

```
   1 QVQLQESGPGLVKPSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWIGSIYHSGSTYYN  60
  61 PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDLYYYYGMDVWGQGTTVTVSS   118
```

X355/07 Vκ (SEQ ID NO:392):

```
   1 AIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS  60
  61 RFSGSGSGTDFTLTISSLQPEDFATYYCQQSYFTPLYTFGQGTKLEIK             108
```

X910/12 VH (SEQ ID NO:395):

```
   1 EVQLVQSGAEVKKSGASVKVSCKASGYTFTDYYIHWVRQAPGQGLEWMGWINPNNGGVTF  60
  61 AQKFQGRVTMTRDTSISTAYMDLSSLRSDDTAVYFCARDIRMSGWLAPFDYWGQGTLVTV 120
 121 SS                                                            122
```

X910/12 Vλ (SEQ ID NO:394):

```
   1 QAVLTQPASLSASPGESARLTCTLPSDINVRYYNIYWYQQKPGSPPRYLLYYYSDSHKDQ  60
  61 GSGVPSRFSGSKDTSANTGILLISGLQSEDEADYYCMIWASNGSGVLGGGTQLTVL     116
```

X913/15 VH (SEQ ID NO:397):

```
   1 QVQLVESGGGVVQGGGSLRLSCAASGFTVRSNYMSWVRQAPGKGLEWVSAISGSGDSTYY  60
  61 ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKVAVTTGWYFDLWGRGTLVTVSS 120
```

X913/15 Vλ (SEQ ID NO:396):

```
   1 QAVLTQPASLSASPGESARLTCTLPSDINVRYHNIYWYQEKPGSPPRYLLYYYSDSSKGQ  60
  61 GSGVPSRFSGSKDVSTNTGILVISGLQSEDEAEYYCMTWSSNGSGVFGGGTQLTVL     116
```

FIGURE 14:

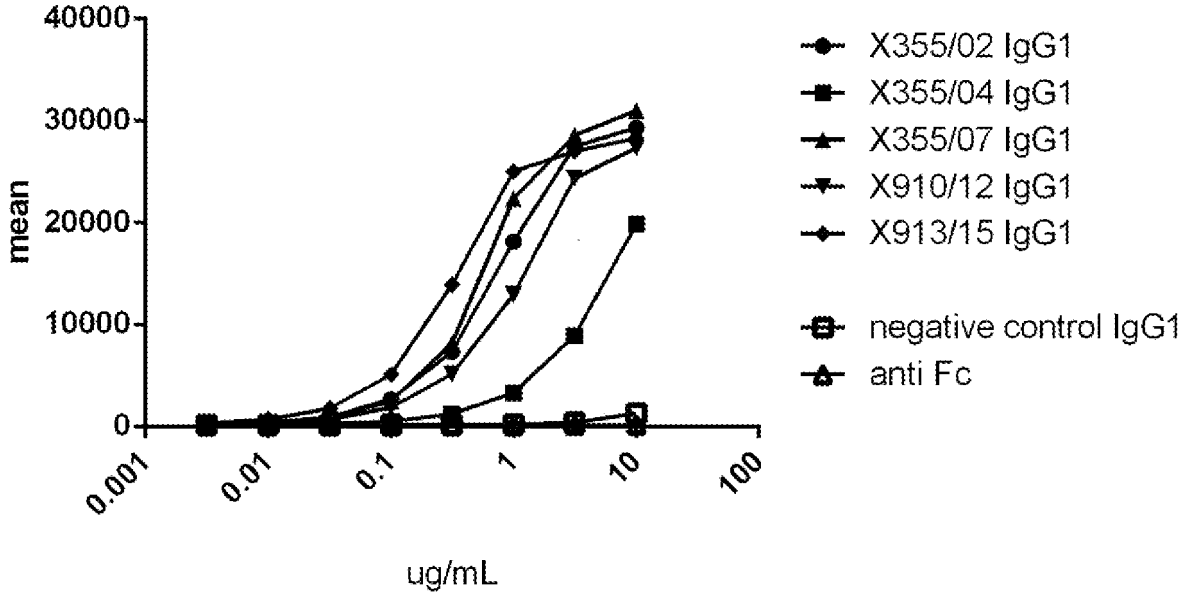
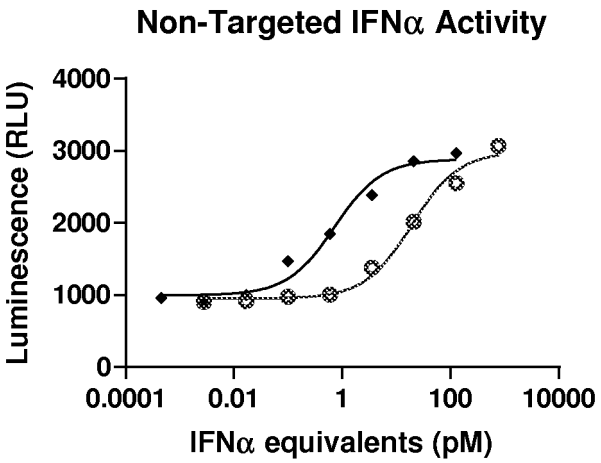
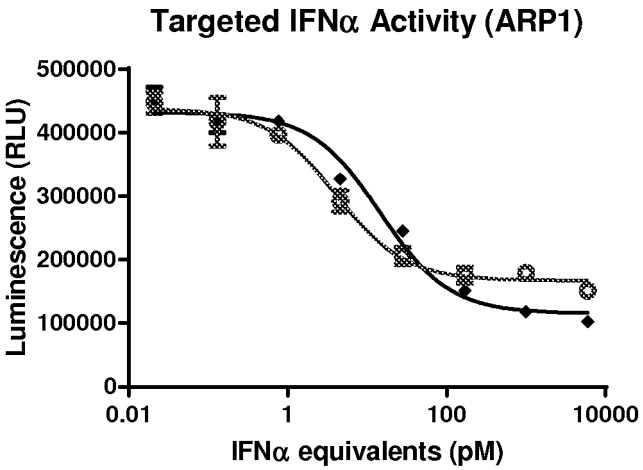

40000
30000
20000
10000
0
mean
0.001
0.01
0.1
1
10
100
ug/mL
X355/02 IgG1
X355/04 IgG1
X355/07 IgG1
X910/12 IgG1
X913/15 IgG1
negative control IgG1
anti Fc

FIGURE 15:



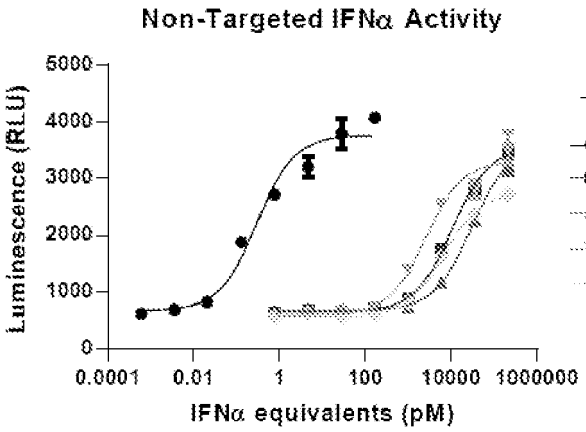
Construct	EC50 (pM)
IFNα	0.726
G005-HC-L0-IFNα IgG4	19.5

FIGURE 16:



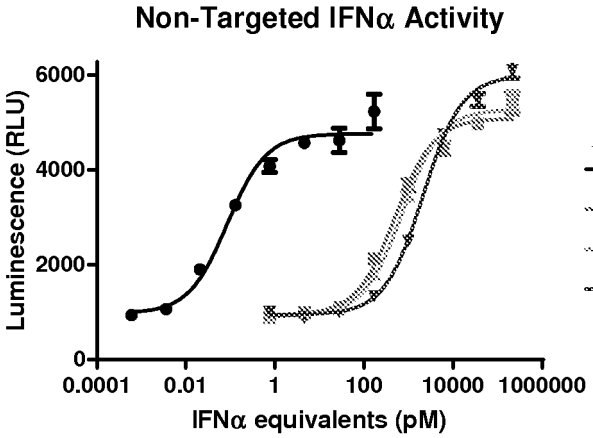
Construct	IC50
IFNα	14.70
G005-HC-L0-IFNα IgG4	4.079

FIGURE 17:



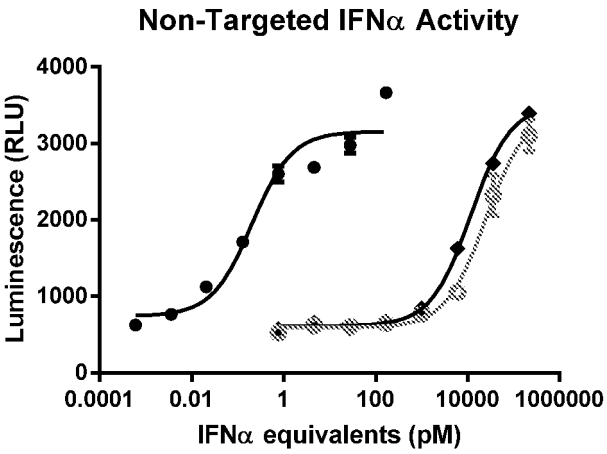
Construct	EC50
IFNα	0.30
G005-HC-L6-IFNα (R144A) IgG4	11.000
G005-HC-L0-IFNα (R144A) IgG4	30.000
G005-HC-L6-IFNα (R144A) IgG1	2600
G005-HC-L0-IFNα (R144A) IgG1	6800

FIGURE 18:



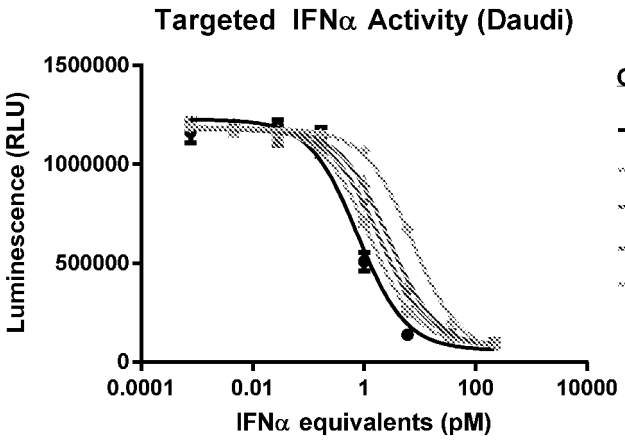
Construct	EC50(pM)
IFNα	0.087
G005-HC-L0-IFNα (A145G) IgG1	510
G005-HC-L6-IFNα (A145G) IgG1	730
G005-HC-L6-IFNα (A145G) IgG4	2200

FIGURE 19:



Construct	EC50(pM)
IFNα	0.21
G005-LC-L6-IFNα (A145G) IgG1	12000
G005-LC-L0-IFNα (A145G) IgG1	24000

FIGURE 20:



Construct	IC50(pM)
IFNα	0.77
G005-HC-L6-IFNα (R144A) IgG4	1.3
G005-HC-L0-IFNα (R144A) IgG4	2.7
G005-HC-L6-IFNα (R144A) IgG1	1.9
G005-HC-L0-IFNα (R144A) IgG1	7.3

FIGURE 21:

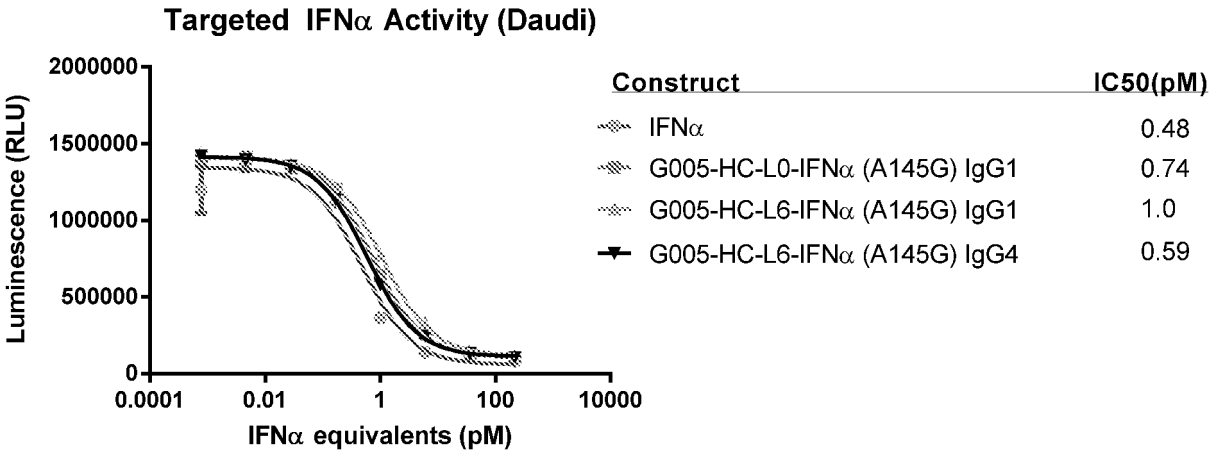
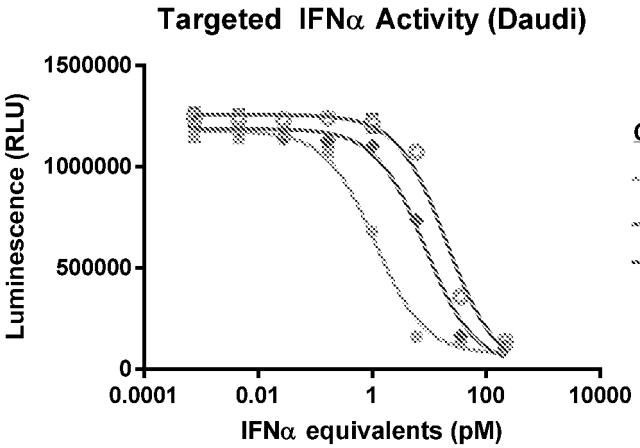
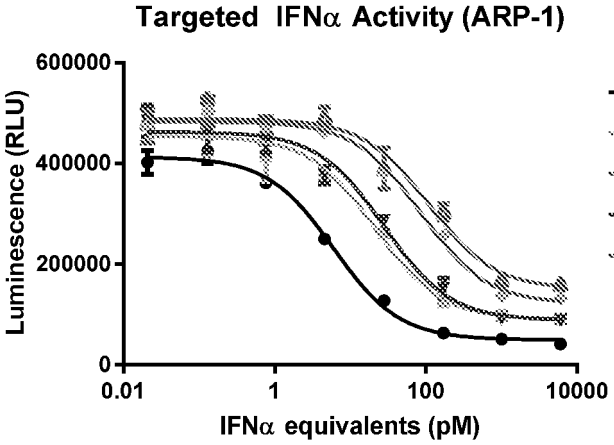

Targeted IFNα Activity (Daudi)
Luminescence (RLU)
2000000
1500000
1000000
500000
0
0.0001
0.01
1
100
10000
IFNα equivalents (pM)
Construct
IC50(pM)
IFNα
0.48
G005-HC-L0-IFNα (A145G) IgG1
0.74
G005-HC-L6-IFNα (A145G) IgG1
1.0
G005-HC-L6-IFNα (A145G) IgG4
0.59

FIGURE 22:



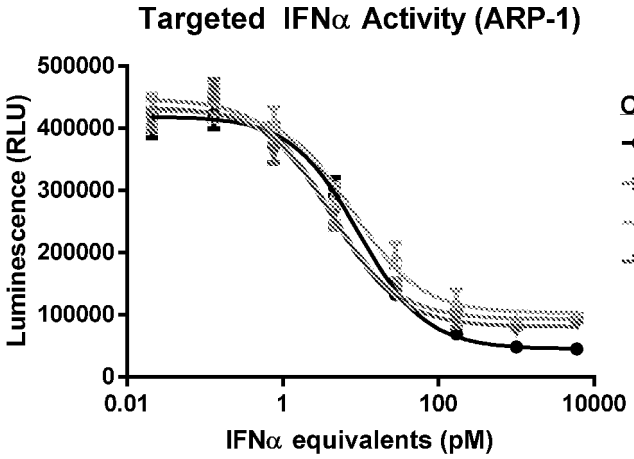
Construct	IC50(pM)
IFNα	1.1
G005-LC-L6-IFNα (A145G) IgG1	8.5
G005-LC-L0-IFNα (A145G) IgG1	21

FIGURE 23:



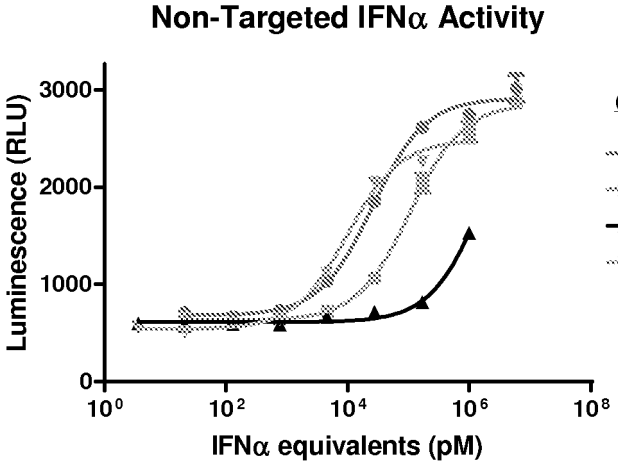
Construct	IC50(pM)
IFNα	6.0
G005-HC-L6-IFNα (R144A) IgG1	21
G005-HC-L0-IFNα (R144A) IgG1	110
G005-HC-L6-IFNα (R144A) IgG4	28
G005-HC-L0-IFNα (R144A) IgG4	85

FIGURE 24:



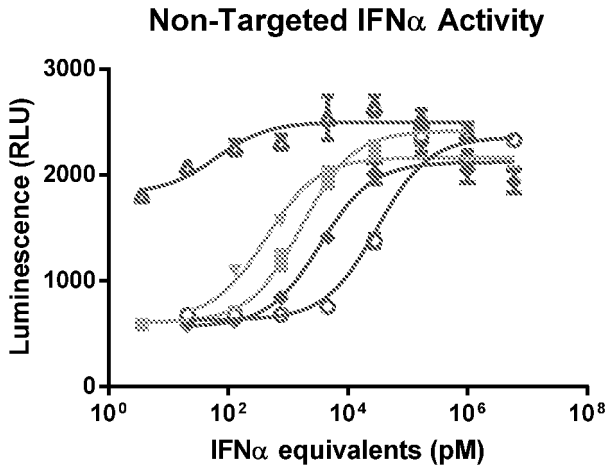
Construct	IC50(pM)
IFNα	9.5
G005-HC-L6-IFNα (A145G) IgG1	4.0
G005-HC-L0-IFNα (A145G) IgG1	8.0
G005-HC-L6-IFNα (A145G) IgG4	4.4

FIGURE 25:



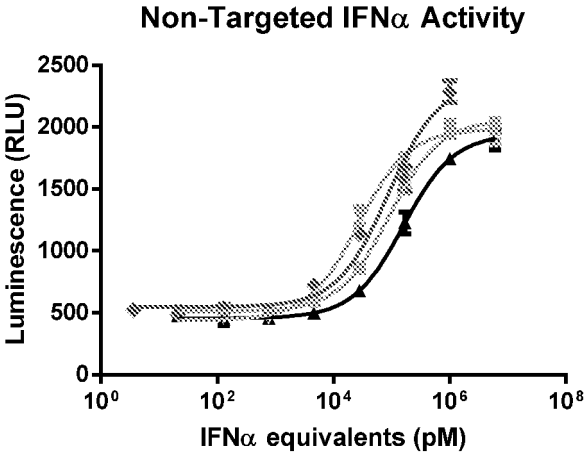
Construct	EC50(pM)
G005-HC-L0-IFNα (R144**A**) IgG4	25,800
G005-HC-L0-IFNα (R144**S**) IgG4	108,000
G005-HC-L0-IFNα (R144**E**) IgG4	$>10^5$
G005-HC-L0-IFNα (R144**G**) IgG4	9,970

FIGURE 26:



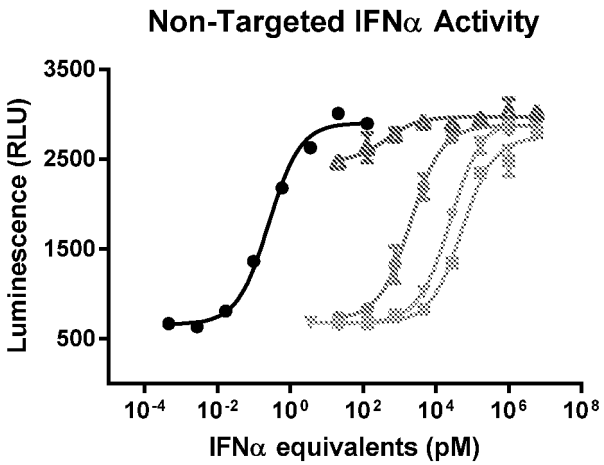
Construct	EC50(pM)
G005-HC-L0-IFNα (R144**H**) IgG4	1,690
G005-HC-L0-IFNα (R144**K**) IgG4	<100
G005-HC-L0-IFNα (R144**N**) IgG4	431
G005-HC-L0-IFNα (R144**Q**) IgG4	3,500
G005-HC-L0-IFNα (R144**T**) IgG4	30,800

FIGURE 27:



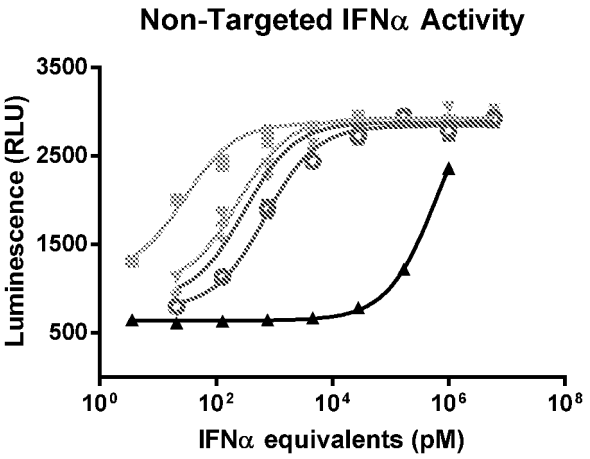
Construct	EC50(pM)
G005-HC-L0-IFNα (R144**Y**) IgG4	92,100
G005-HC-L0-IFNα (R144**I**) IgG4	159,000
G005-HC-L0-IFNα (R144**L**) IgG4	26,700
G005-HC-L0-IFNα (R144**V**) IgG4	86,900

FIGURE 28:



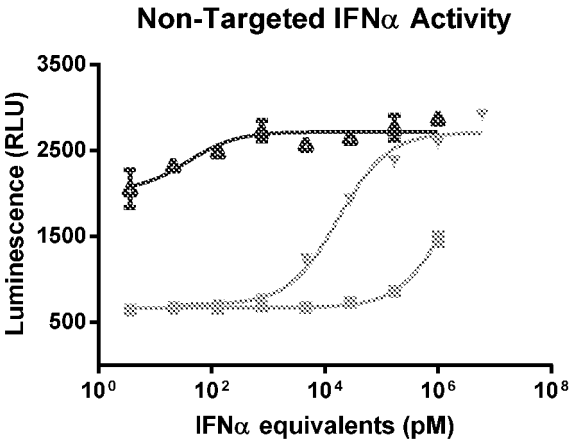
Construct	EC50(pM)
G005-HC-L0-IFNα (A145**G**) IgG4	2,040
G005-HC-L0-IFNα (A145**D**) IgG4	52,600
G005-HC-L0-IFNα (A145**E**) IgG4	<100
G005-HC-L0-IFNα (A145**H**) IgG4	24,900
IFNα	0.260

FIGURE 29:



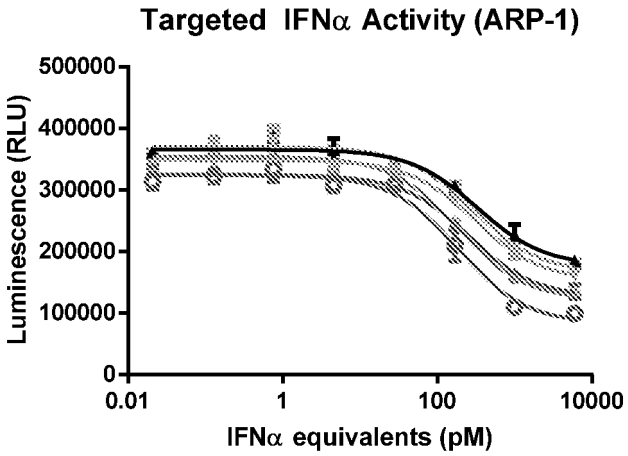
Construct	EC50(pM)
G005-HC-L0-IFNα (A145I) IgG4	28.9
G005-HC-L0-IFNα (A145**K**) IgG4	662,000
G005-HC-L0-IFNα (A145**L**) IgG4	239
G005-HC-L0-IFNα (A145**N**) IgG4	309
G005-HC-L0-IFNα (A145**Q**) IgG4	709

FIGURE 30:



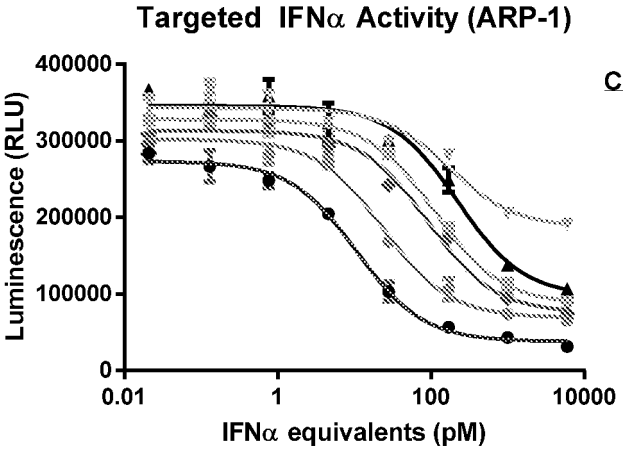
Construct	EC50(pM)
G005-HC-L0-IFNα(A145**R**) IgG4	$>3x10^5$
G005-HC-L0-IFNα(A145**T**) IgG4	<2
G005-HC-L0-IFNα(A145**Y**) IgG4	19,200

FIGURE 31:



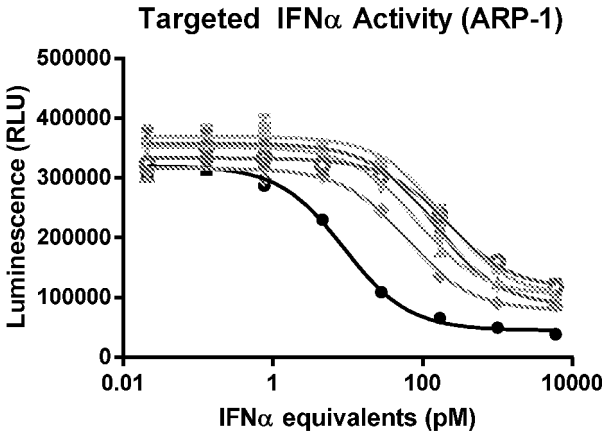
Construct	IC50(pM)
G005-HC-L0-IFNα (R144**A**) IgG4	186
G005-HC-L0-IFNα (R144**S**) IgG4	290
G005-HC-L0-IFNα (R144**T**) IgG4	333
G005-HC-L0-IFNα (R144**Y**) IgG4	306
G005-HC-L0-IFNα (R144**I**) IgG4	257
G005-HC-L0-IFNα (R144**L**) IgG4	191

FIGURE 32:



Construct	IC50(pM)
G005-HC-L0-IFNα (A145**G**) IgG4	23.8
G005-HC-L0-IFNα (A145**H**) IgG4	113
G005-HC-L0-IFNα (A145**D**) IgG4	222
G005-HC-L0-IFNα (A145**K**) IgG4	174
G005-HC-L0-IFNα (A145**Y**) IgG4	91.4
IFNα	10.8

FIGURE 33:



Construct	IC50(pM)
IFNα	8.91
X910/12-HC-L0-IFNα (R144A) IgG4	191
X355/02-HC-L0-IFNα (R144A) IgG4	147
X913/15-HC-L0-IFNα (R144A) IgG4	84.1
X355/07-HC-L0-IFNα (R144A) IgG4	61.2
G005-HC-L0-IFNα (R144A) IgG4	220

FIGURE 34:

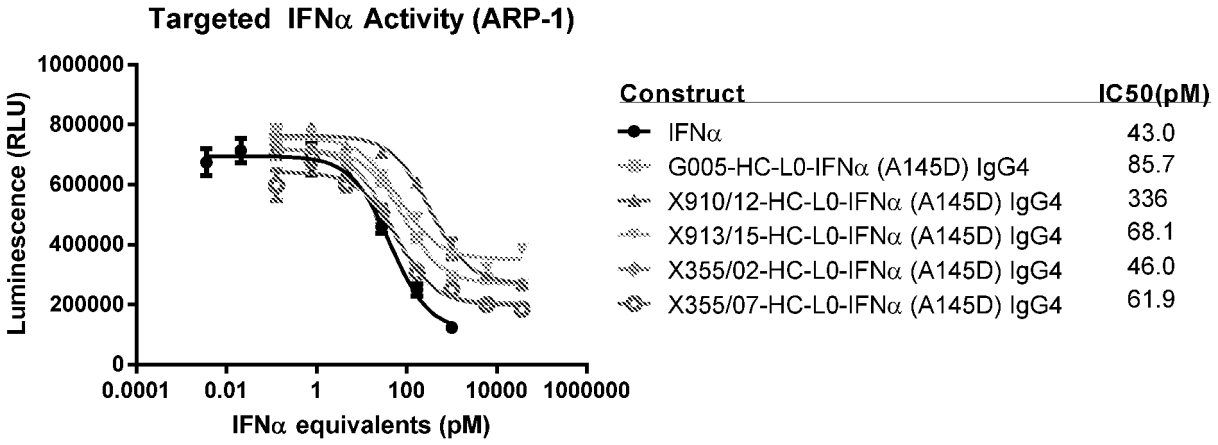
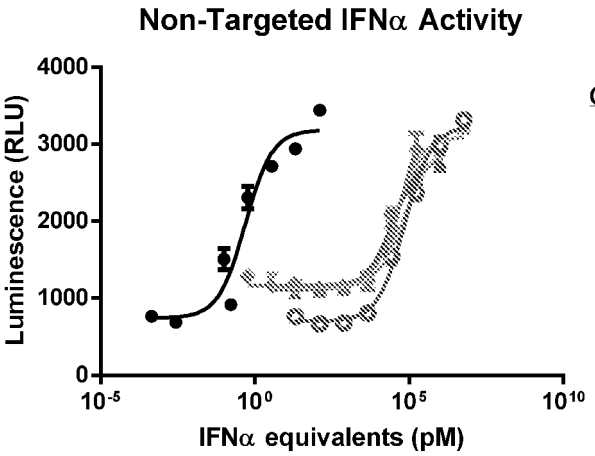
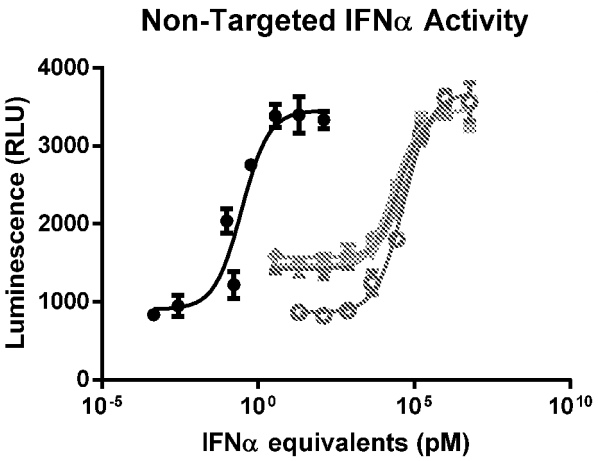

Targeted IFNα Activity (ARP-1)
Luminescence (RLU)
1000000
800000
600000
400000
200000
0
0.0001
0.01
1
100
10000
1000000
IFNα equivalents (pM)
Construct
IC50(pM)
IFNα
43.0
G005-HC-L0-IFNα (A145D) IgG4
85.7
X910/12-HC-L0-IFNα (A145D) IgG4
336
X913/15-HC-L0-IFNα (A145D) IgG4
68.1
X355/02-HC-L0-IFNα (A145D) IgG4
46.0
X355/07-HC-L0-IFNα (A145D) IgG4
61.9

FIGURE 35:



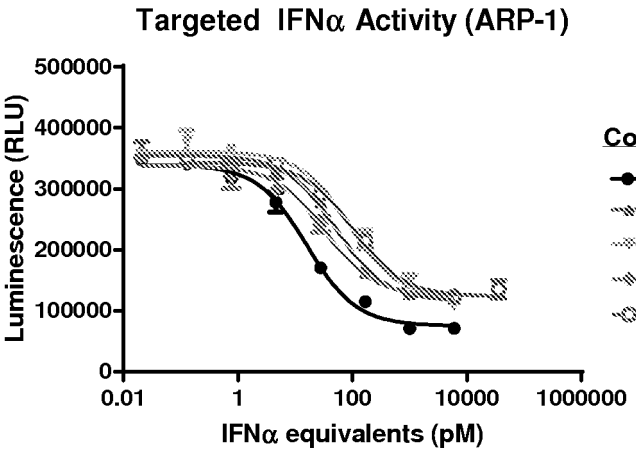
Construct	EC50(pM)
IFNα	0.499
X910/12-HC-L0-IFNα (R144A) IgG4	41,000
X913/15-HC-L0-IFNα (R144A) IgG4	29,600
X355/02-HC-L0-IFNα (R144A) IgG4	70,500
X355/07-HC-L0-IFNα (R144A) IgG4	70,300
G005-HC-L0-IFNα (R144A) IgG4	73,200

FIGURE 36:



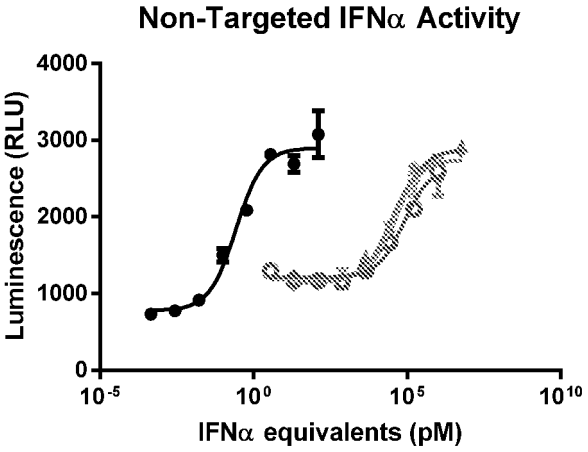
Construct	EC50(pM)
IFNα	0.304
X910/12-HC-L0-IFNα (A145D) IgG4	22,500
X913/15-HC-L0-IFNα (A145D) IgG4	31,800
X355/02-HC-L0-IFNα (A145D) IgG4	53,900
X355/07-HC-L0-IFNα (A145D) IgG4	61,800
G005-HC-L0-IFNα (A145D) IgG4	47,100

FIGURE 37:



Construct	IC50(pM)
IFNα	16.1
R5D1-HC-L0-IFNα (A145D) IgG4	51.3
R5E8-HC-L0-IFNα (A145D) IgG4	89.2
R10A2-HC-L0-IFNα (A145D) IgG4	32.7
X355/02-HC-L0-IFNα (A145D) IgG4	104

FIGURE 38:



Construct	EC50(pM)
IFNα	0.271
R5D1-HC-L0-IFNα (A145D) IgG4	49,500
R5E8-HC-L0-IFNα (A145D) IgG4	38,400
R10A2-HC-L0-IFNα (A145D) IgG4	29,600
X355/02-HC-L0-IFNα (A145D) IgG4	81,600

FIGURE 39:

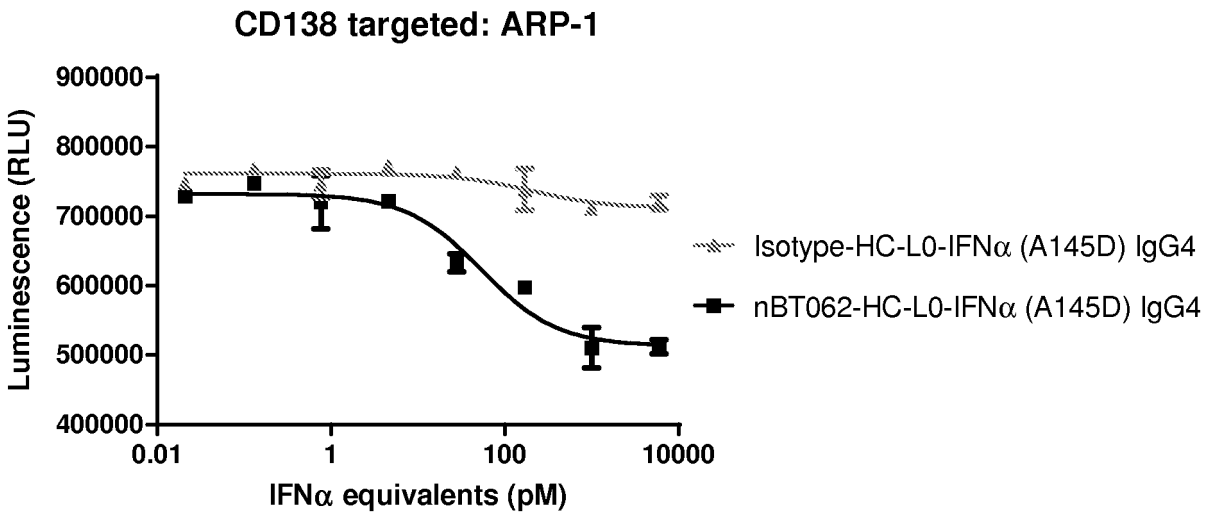
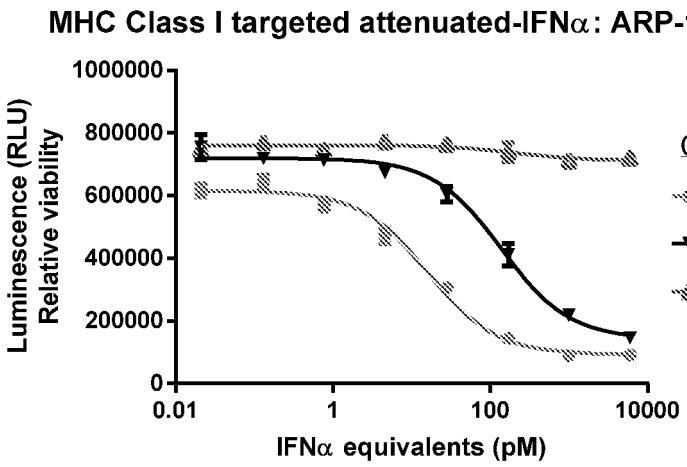

CD138 targeted: ARP-1
Luminescence (RLU)
900000
800000
700000
600000
500000
400000
0.01
1
100
10000
IFNα equivalents (pM)
Isotype-HC-L0-IFNα (A145D) IgG4
nBT062-HC-L0-IFNα (A145D) IgG4

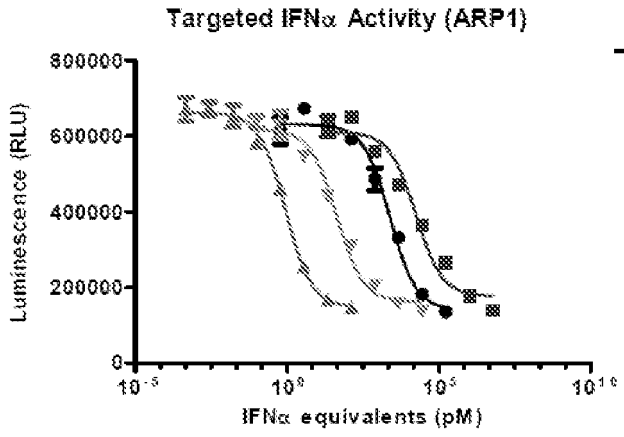
FIGURE 40:

(a)



Construct	IC50(pM)
IFNα	16
HB95-HC-L0-Ifnα(A145D) IgG4	139
Isotype-HC-L0-IFNα(A145D) IgG4	N/A

(b)



Construct	IC50
Palivizumab-HC-L6-IFNα (A145D) Fab	2419
2D12-HC-L6-IFNα (A145D) Fab	17,000
HB95-HC-L6-IFNα (A145D) Fab	0.874
IFNα	42.6

FIGURE 41:

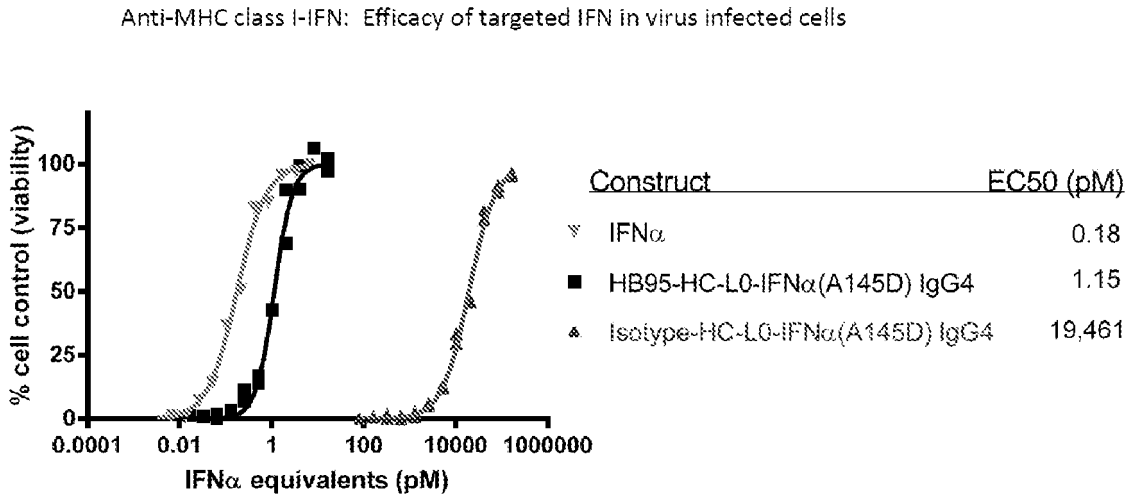
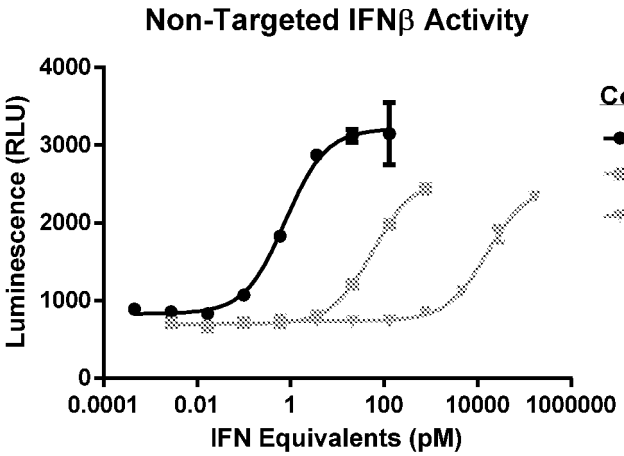
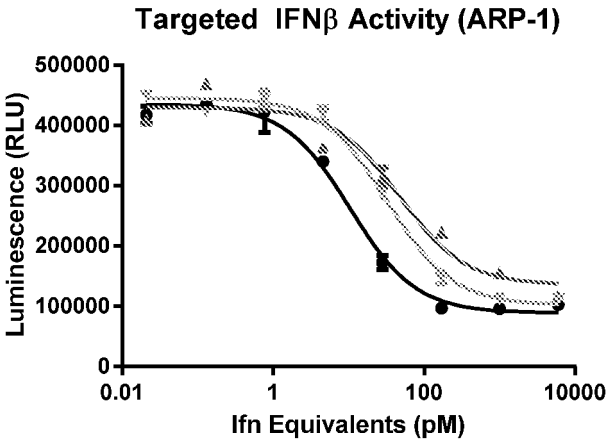

Anti-MHC class I-IFN: Efficacy of targeted IFN in virus infected cells
% cell control (viability)
100
75
50
25
0
0.0001
0.01
1
100
10000
1000000
IFNα equivalents (pM)
Construct
EC50 (pM)
IFNα
0.18
HB95-HC-L0-IFNα(A145D) IgG4
1.15
Isotype-HC-L0-IFNα(A145D) IgG4
19,461

FIGURE 42:



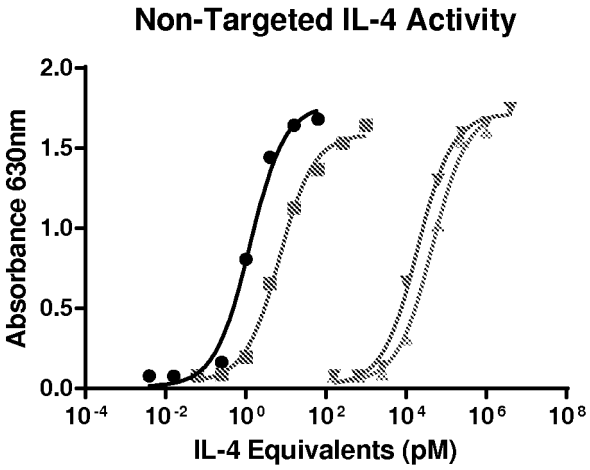
Construct	EC50(pM)
IFNβ1	0.799
G005-HC-L0-IFNβ IgG4	57.6
G005-HC-L0-IFNβ (R35A) IgG4	16,100

FIGURE 43:



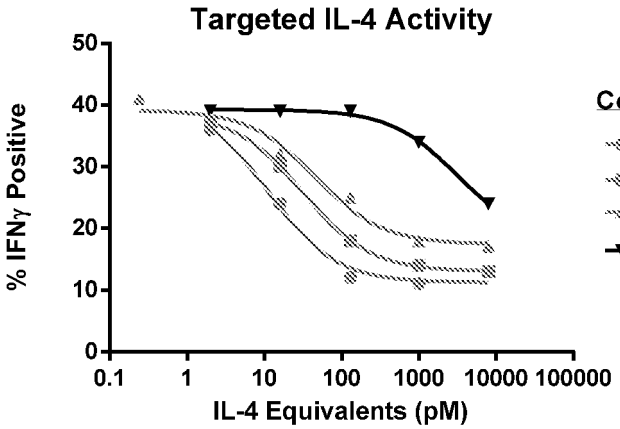
Construct	IC50(pM)
IFNβ1	10.5
G005-HC-L0-IFNβ (R35A) IgG4	46.9
G005-HC-L0-IFNβ IgG4	32.7

FIGURE 44:



Construct	EC50(pM)
IL-4	1.26
J110-HC-L6-IL-4 IgG1	6.88
Isotype-HC-L6-IL-4 (R88Q) IgG1	19,200
J110-HC-L6-IL-4 (R88Q) IgG1	44,800

FIGURE 45:



Construct	IC50(pM)
IL-4	11.4
J110-HC-L6-IL-4 IgG1	31.8
J110-HC-L6-IL-4 (R88Q) IgG1	46.1
Isotype-HC-L6-IL-4 (R88Q) IgG1	>1000

FIGURE 46:

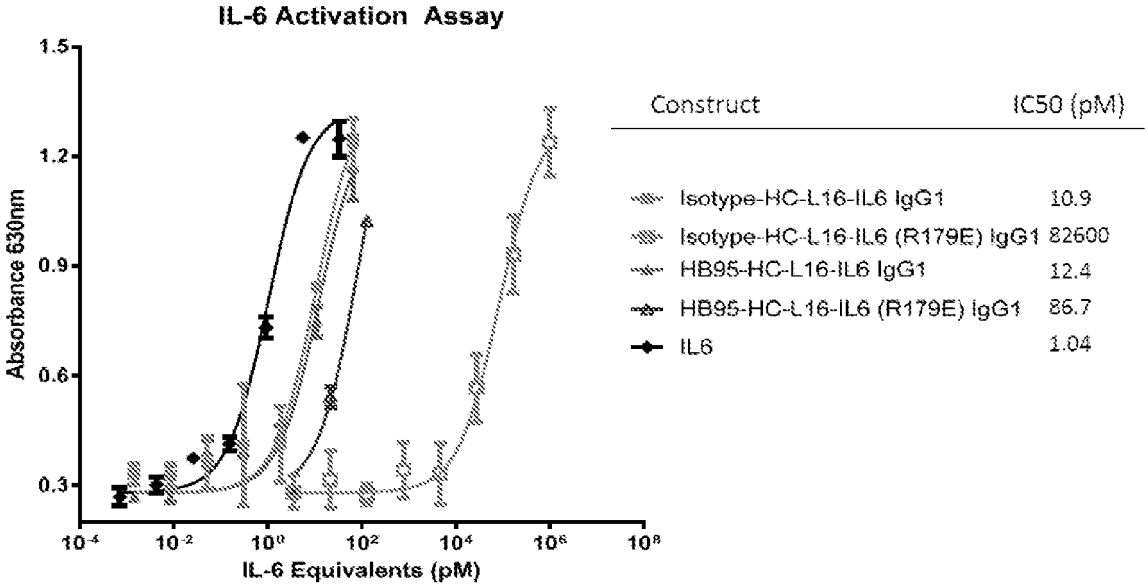

IL-6 Activation Assay
Absorbance 630nm
1.5
1.2
0.9
0.6
0.3
10⁻⁴
10⁻²
10⁰
10²
10⁴
10⁶
10⁸
IL-6 Equivalents (pM)
Construct
IC50 (pM)
Isotype-HC-L16-IL6 IgG1
10.9
Isotype-HC-L16-IL6 (R179E) IgG1
82600
HB95-HC-L16-IL6 IgG1
12.4
HB95-HC-L16-IL6 (R179E) IgG1
86.7
IL6
1.04

FIGURE 47:

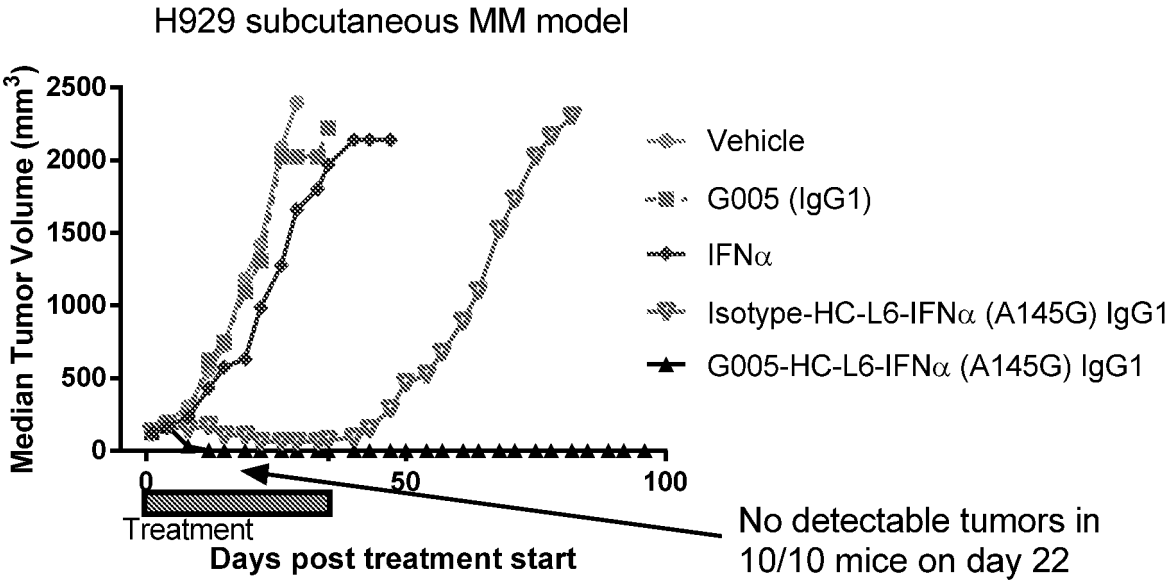

H929 subcutaneous MM model
Median Tumor Volume (mm3)
2500
2000
1500
1000
500
0
0
50
100
Treatment
Days post treatment start
Vehicle
G005 (IgG1)
IFNα
Isotype-HC-L6-IFNα (A145G) IgG1
G005-HC-L6-IFNα (A145G) IgG1
No detectable tumors in
10/10 mice on day 22

FIGURE 48:

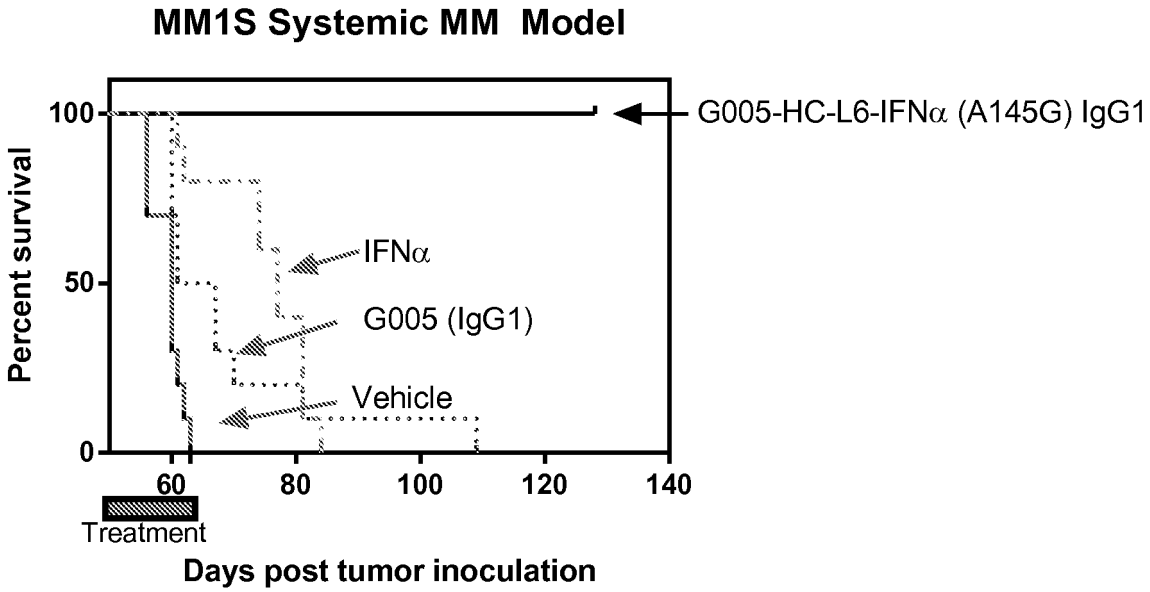

MM1S Systemic MM Model
Percent survival
100
50
0
60
80
100
120
140
Treatment
Days post tumor inoculation
G005-HC-L6-IFNα (A145G) IgG1
IFNα
G005 (IgG1)
Vehicle

FIGURE 49:

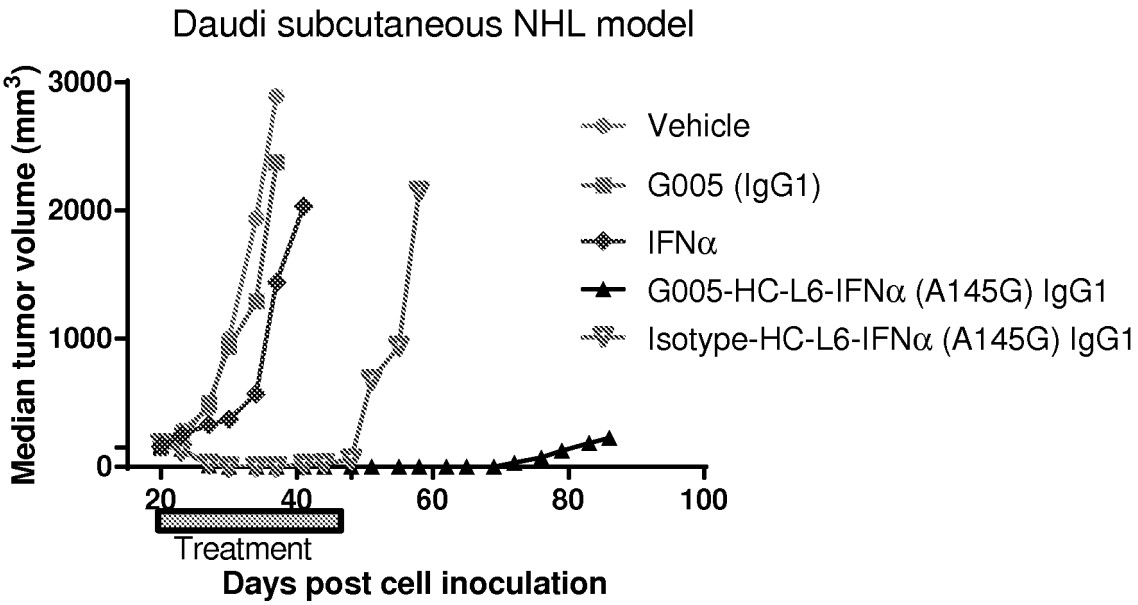

Daudi subcutaneous NHL model
Median tumor volume (mm3)
3000
2000
1000
0
20
40
60
80
100
Treatment
Days post cell inoculation
Vehicle
G005 (IgG1)
IFNα
G005-HC-L6-IFNα (A145G) IgG1
Isotype-HC-L6-IFNα (A145G) IgG1

FIGURE 50:

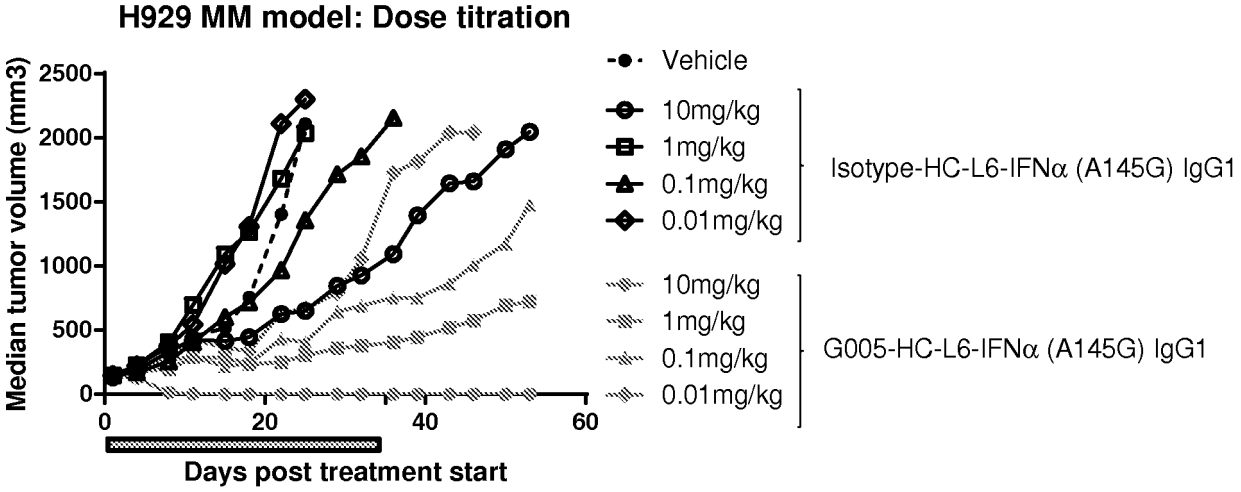

H929 MM model: Dose titration
Median tumor volume (mm3)
2500
2000
1500
1000
500
0
0
20
40
60
Days post treatment start
Vehicle
10mg/kg
1mg/kg
0.1mg/kg
0.01mg/kg
Isotype-HC-L6-IFNα (A145G) IgG1
10mg/kg
1mg/kg
0.1mg/kg
0.01mg/kg
G005-HC-L6-IFNα (A145G) IgG1

FIGURE 51:

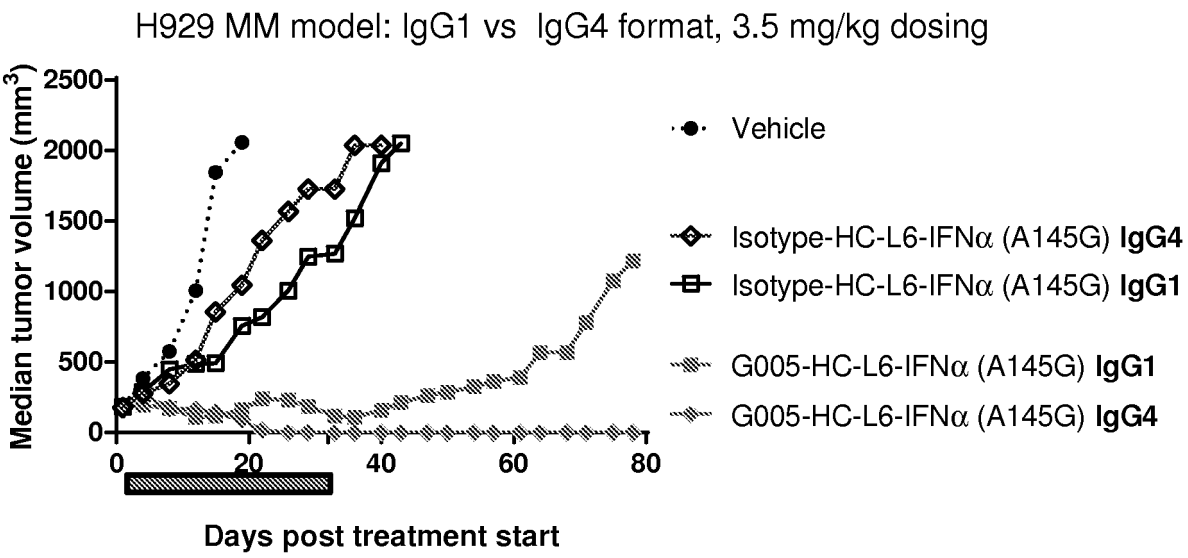

H929 MM model: IgG1 vs IgG4 format, 3.5 mg/kg dosing
Median tumor volume (mm3)
2500
2000
1500
1000
500
0
0
20
40
60
80
Days post treatment start
Vehicle
Isotype-HC-L6-IFNα (A145G) IgG4
Isotype-HC-L6-IFNα (A145G) IgG1
G005-HC-L6-IFNα (A145G) IgG1
G005-HC-L6-IFNα (A145G) IgG4

FIGURE 52:

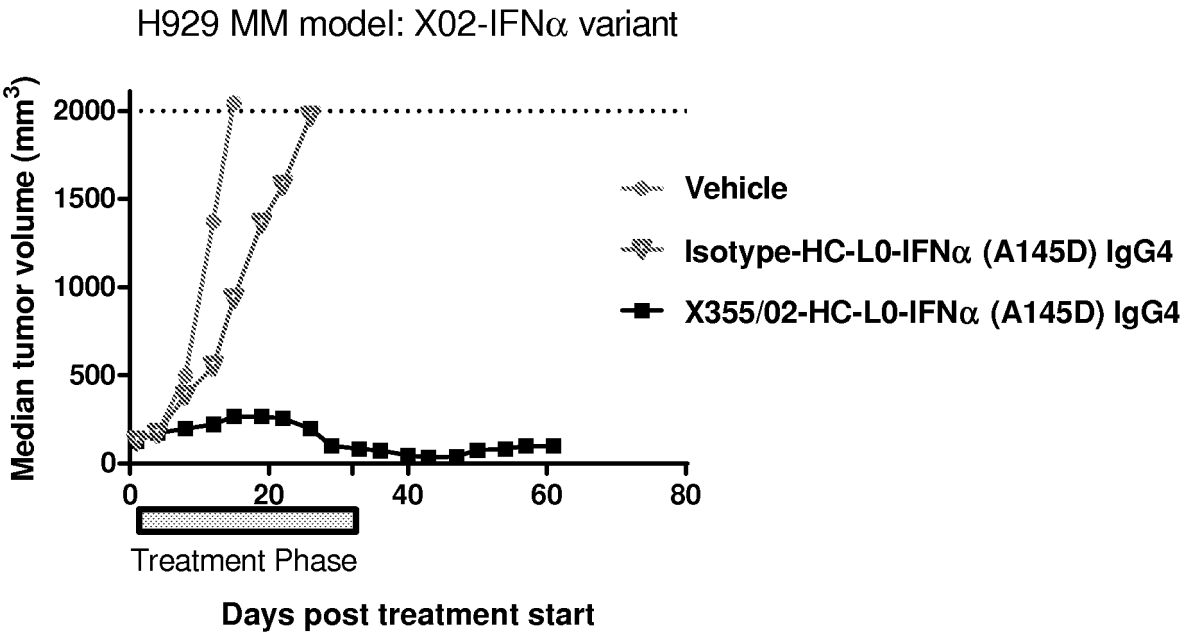

H929 MM model: X02-IFNα variant
Median tumor volume (mm3)
2000
1500
1000
500
0
0
20
40
60
80
Treatment Phase
Days post treatment start
Vehicle
Isotype-HC-L0-IFNα (A145D) IgG4
X355/02-HC-L0-IFNα (A145D) IgG4

FIGURE 53:

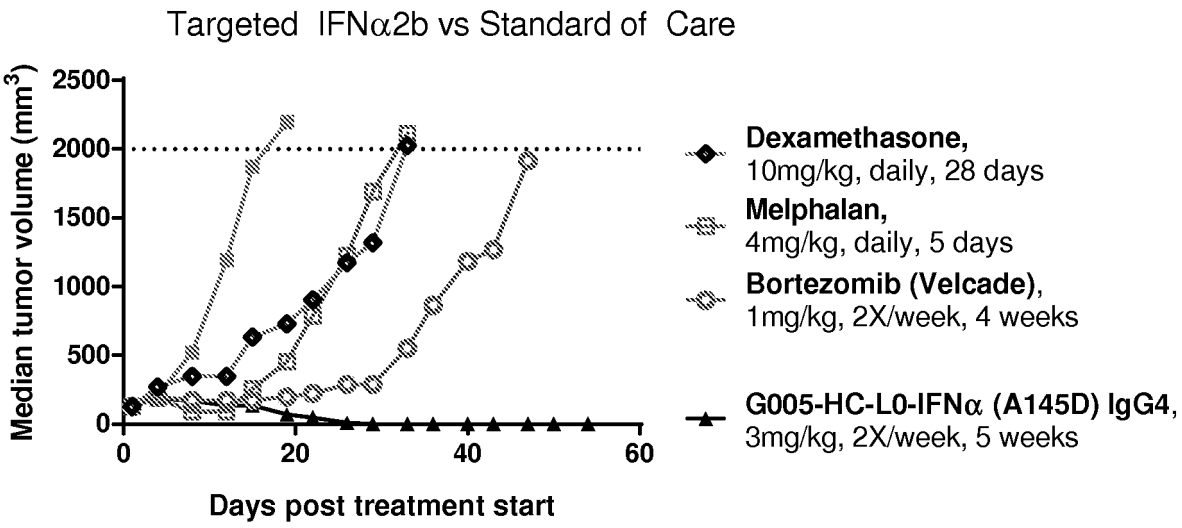

Targeted IFNα2b vs Standard of Care
Median tumor volume (mm3)
2500
2000
1500
1000
500
0
0
20
40
60
Days post treatment start
Dexamethasone, 10mg/kg, daily, 28 days
Melphalan, 4mg/kg, daily, 5 days
Bortezomib (Velcade), 1mg/kg, 2X/week, 4 weeks
G005-HC-L0-IFNα (A145D) IgG4, 3mg/kg, 2X/week, 5 weeks

FIGURE 54:

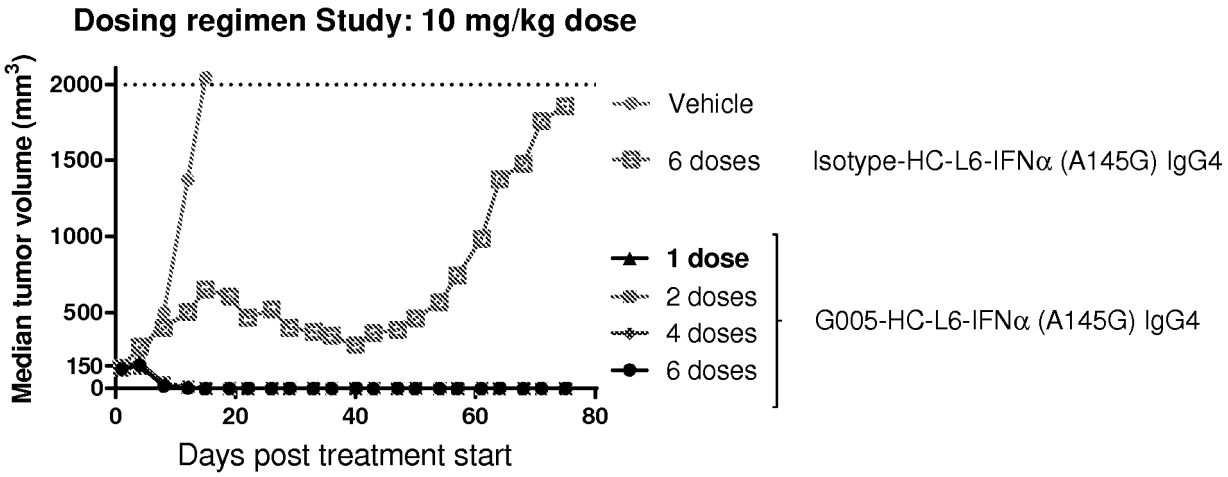

Dosing regimen Study: 10 mg/kg dose
Median tumor volume (mm3)
2000
1500
1000
500
150
0
0
20
40
60
80
Days post treatment start
Vehicle
6 doses
Isotype-HC-L6-IFNα (A145G) IgG4
1 dose
2 doses
4 doses
6 doses
G005-HC-L6-IFNα (A145G) IgG4

FIGURE 55:

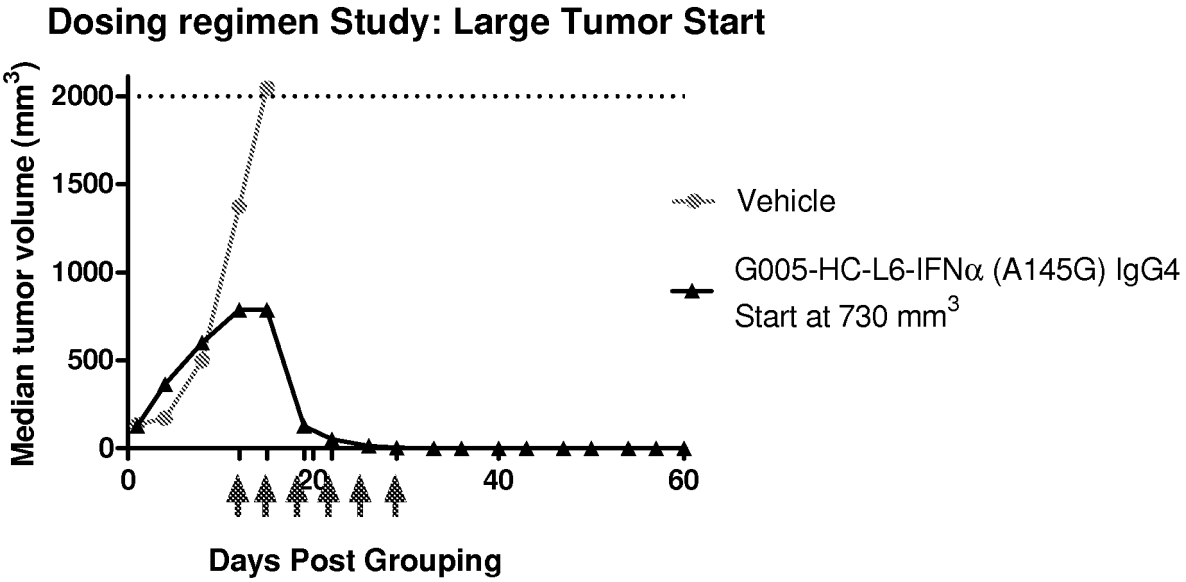

Dosing regimen Study: Large Tumor Start
Median tumor volume (mm3)
2000
1500
1000
500
0
0
20
40
60
Days Post Grouping
Vehicle
G005-HC-L6-IFNα (A145G) IgG4
Start at 730 mm3

FIGURE 56:

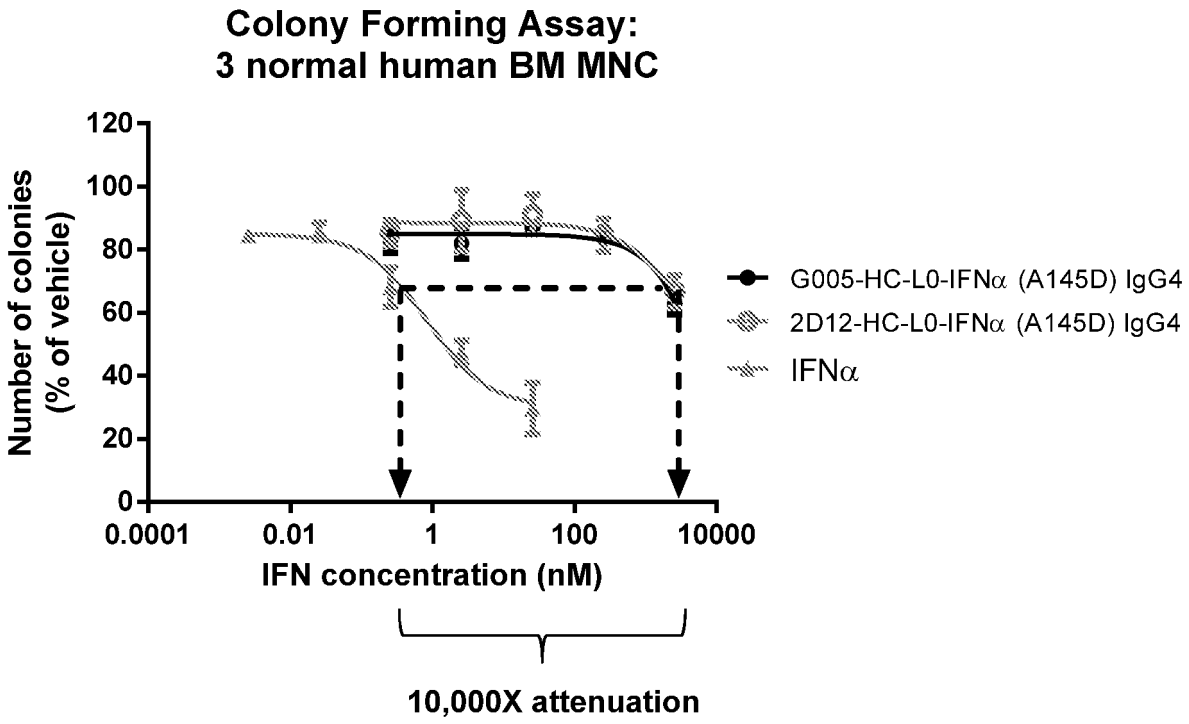

Colony Forming Assay:
3 normal human BM MNC
Number of colonies
(% of vehicle)
120
100
80
60
40
20
0
0.0001
0.01
1
100
10000
IFN concentration (nM)
10,000X attenuation
G005-HC-L0-IFNα (A145D) IgG4
2D12-HC-L0-IFNα (A145D) IgG4
IFNα

FIGURE 57a:

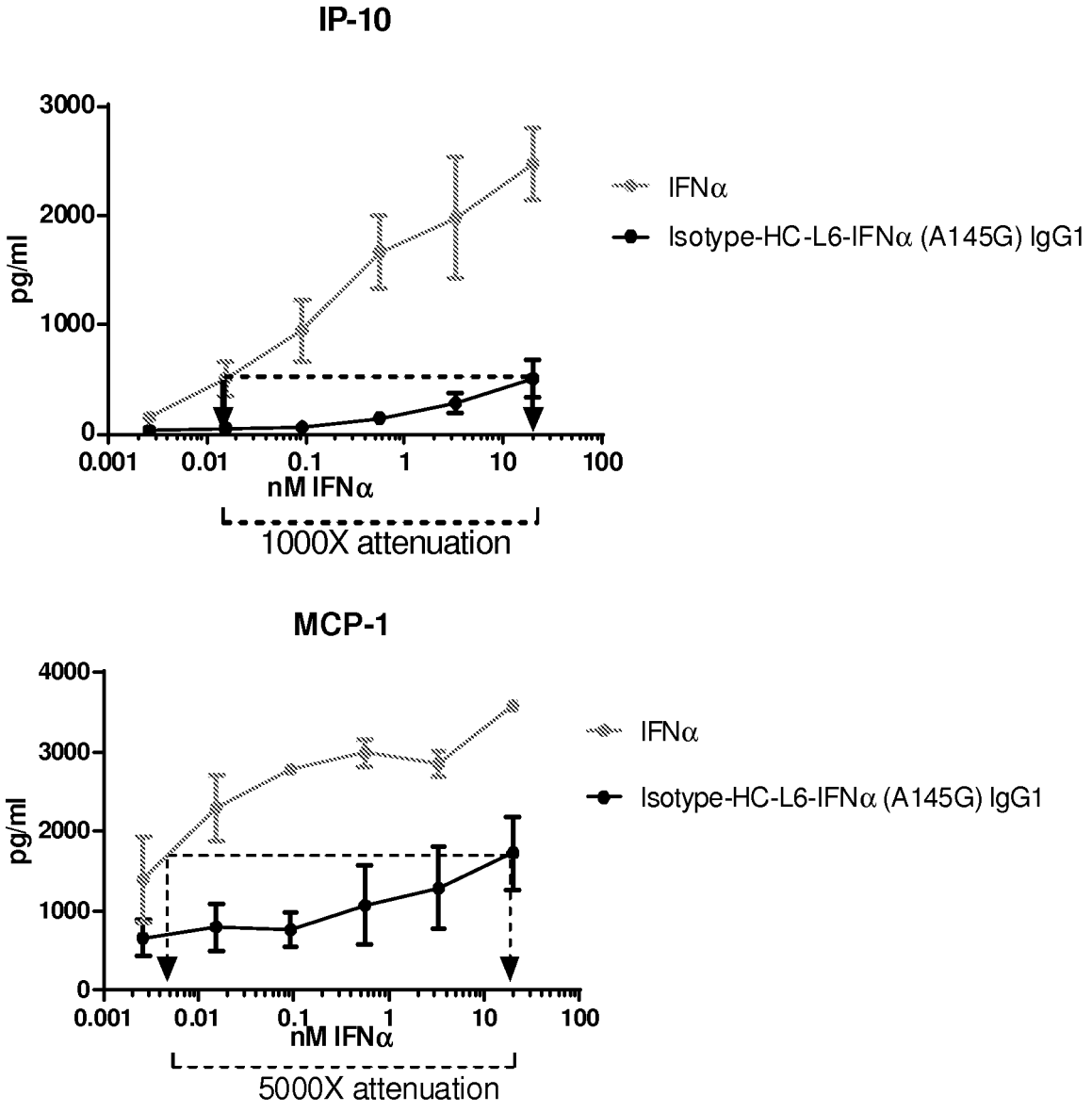
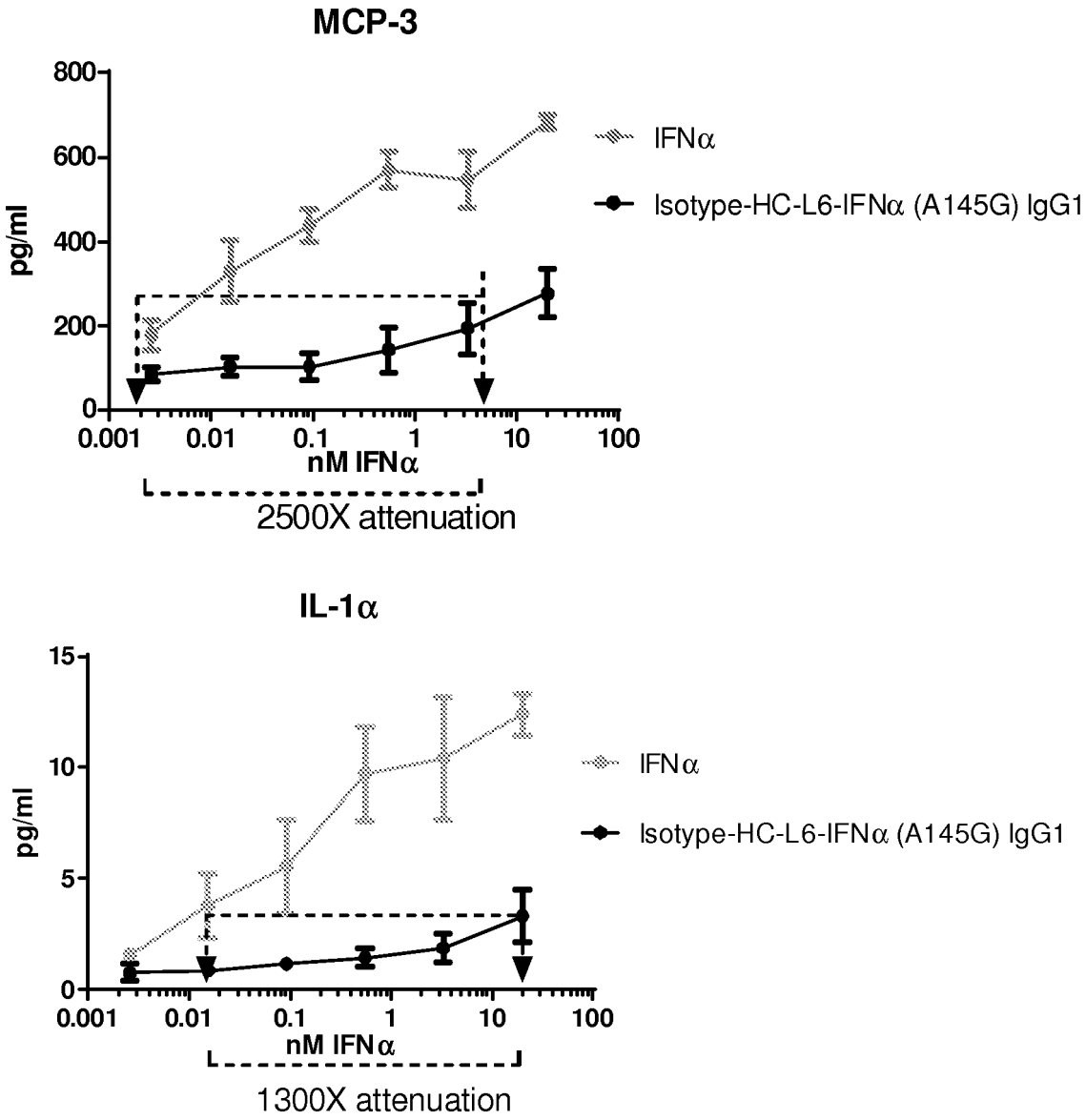

IP-10
3000
2000
1000
0
pg/ml
0.001
0.01
0.1
1
10
100
nM IFNα
1000X attenuation
IFNα
Isotype-HC-L6-IFNα (A145G) IgG1
MCP-1
4000
3000
2000
1000
0
pg/ml
0.001
0.01
0.1
1
10
100
nM IFNα
5000X attenuation
IFNα
Isotype-HC-L6-IFNα (A145G) IgG1

FIGURE 57b:


MCP-3
800
600
400
200
0
pg/ml
0.001
0.01
0.1
1
10
100
nM IFNα
2500X attenuation
IFNα
Isotype-HC-L6-IFNα (A145G) IgG1
IL-1α
15
10
5
0
pg/ml
0.001
0.01
0.1
1
10
100
nM IFNα
1300X attenuation
IFNα
Isotype-HC-L6-IFNα (A145G) IgG1