Figure 1

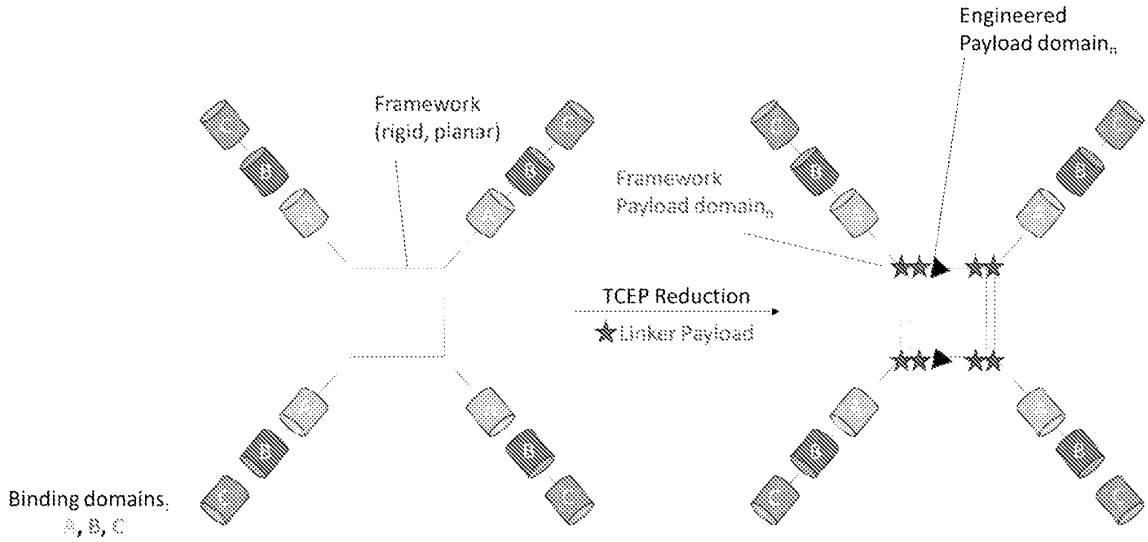


Figure 2

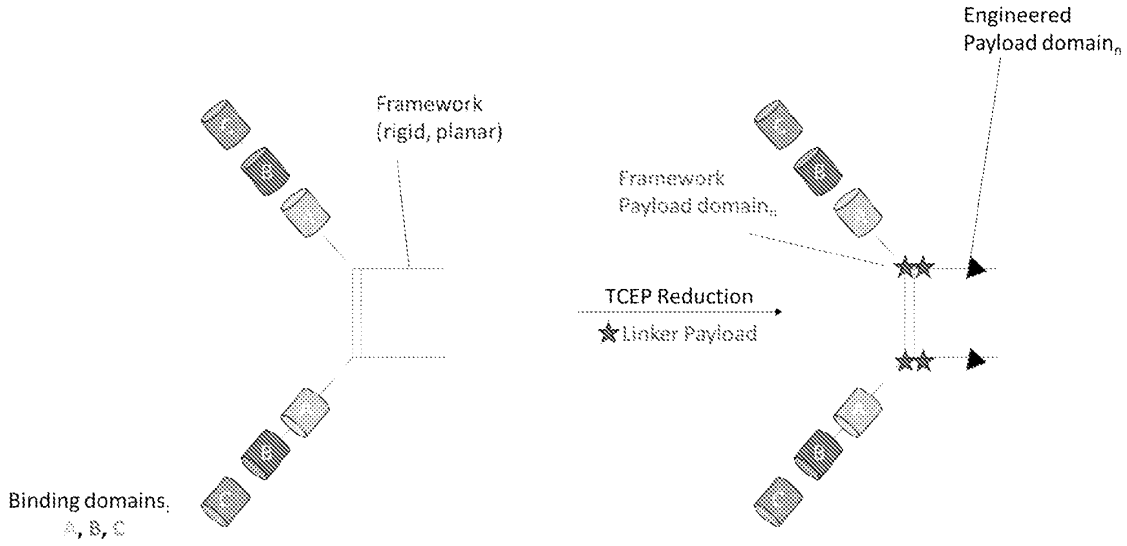


Figure 3

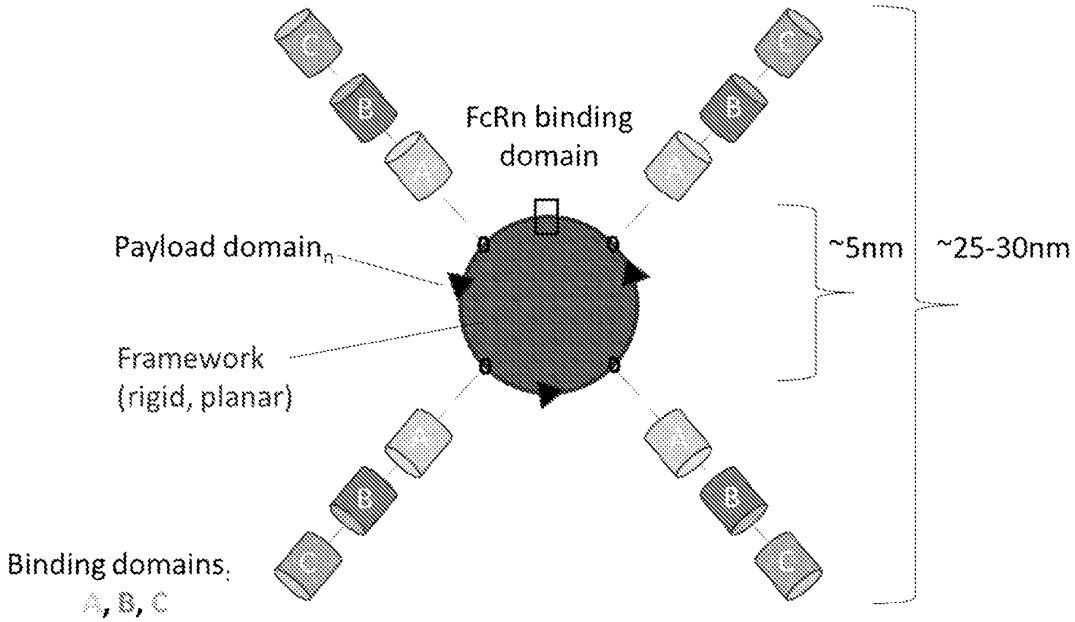


Figure 4

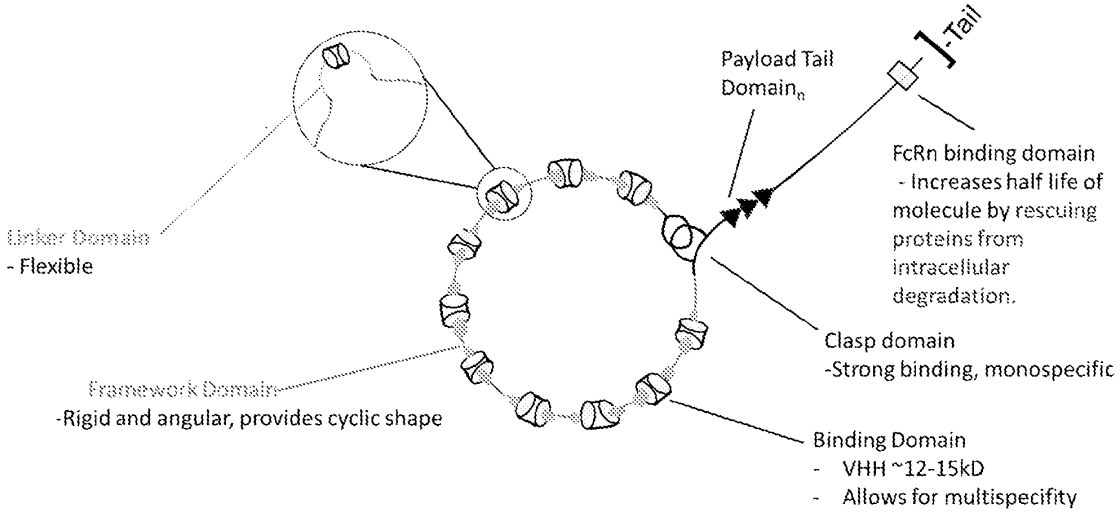
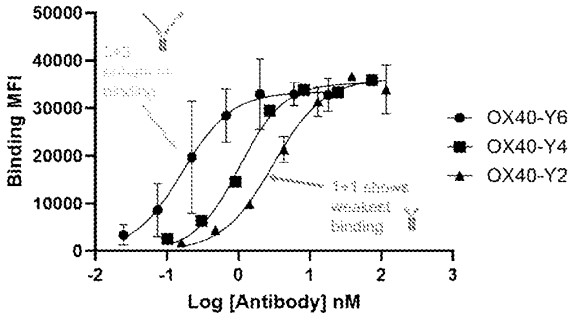


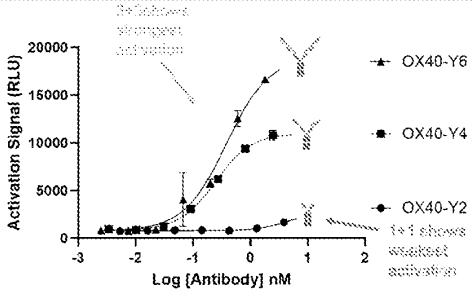
Figure 5A

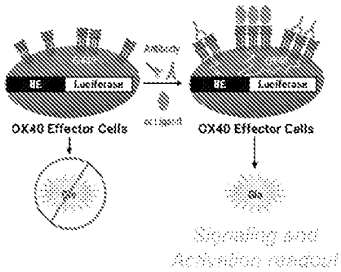
OX40 Monospecific Multivalent Cell Binding Data



Antibody	Binding EC50 (nM)	Max MFI
OX40-Y6	0.16	33452
OX40-Y4	1.03	35336
OX40-Y6	3.05	36315

Figure 5B





Antibody	Signaling EC50 (nM)	Max Activation
OX40-Y6	0.38	18261
OX40-Y4	0.66	11667
OX40-Y2	4.0	2610

Figure 6A

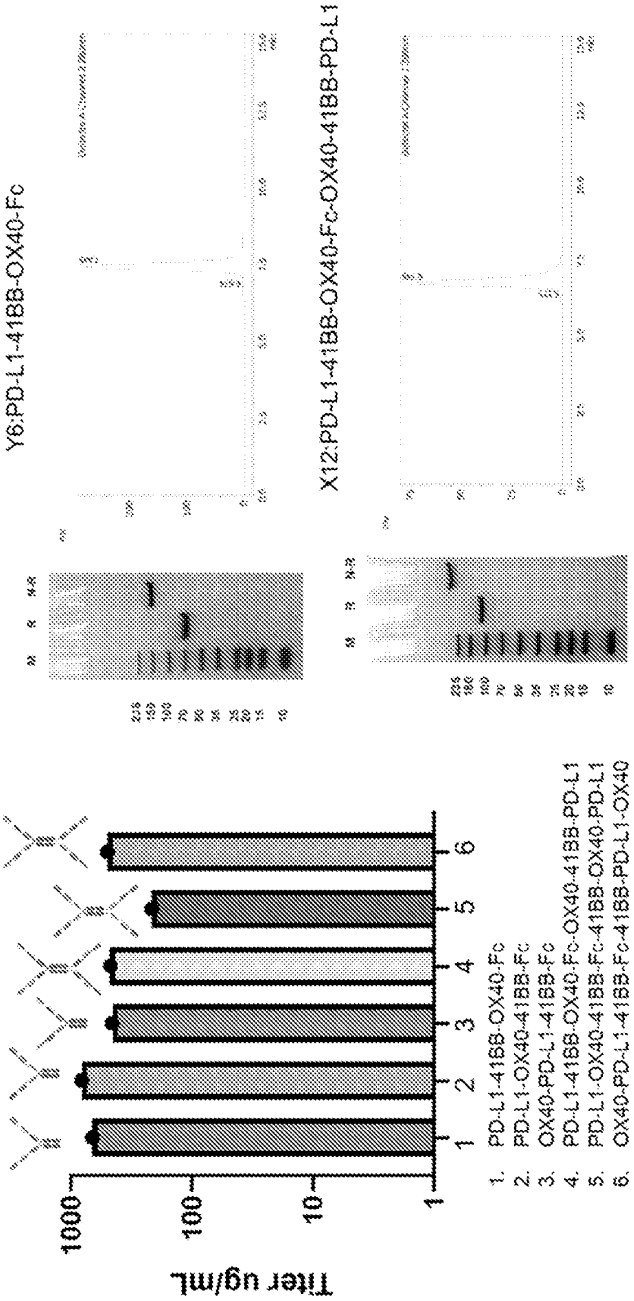

Y6:PD-L1-41BB-OX40-Fc
X12:PD-L1-41BB-OX40-Fc-OX40-41BB-PD-L1
Titer ug/mL
1000
100
10
1
1. PD-L1-41BB-OX40-Fc
2. PD-L1-OX40-41BB-Fc
3. OX40-PD-L1-41BB-Fc
4. PD-L1-41BB-OX40-Fc-OX40-41BB-PD-L1
5. PD-L1-OX40-41BB-Fc-41BB-OX40-PD-L1
6. OX40-PD-L1-41BB-Fc-41BB-PD-L1-OX40

Figure 6B

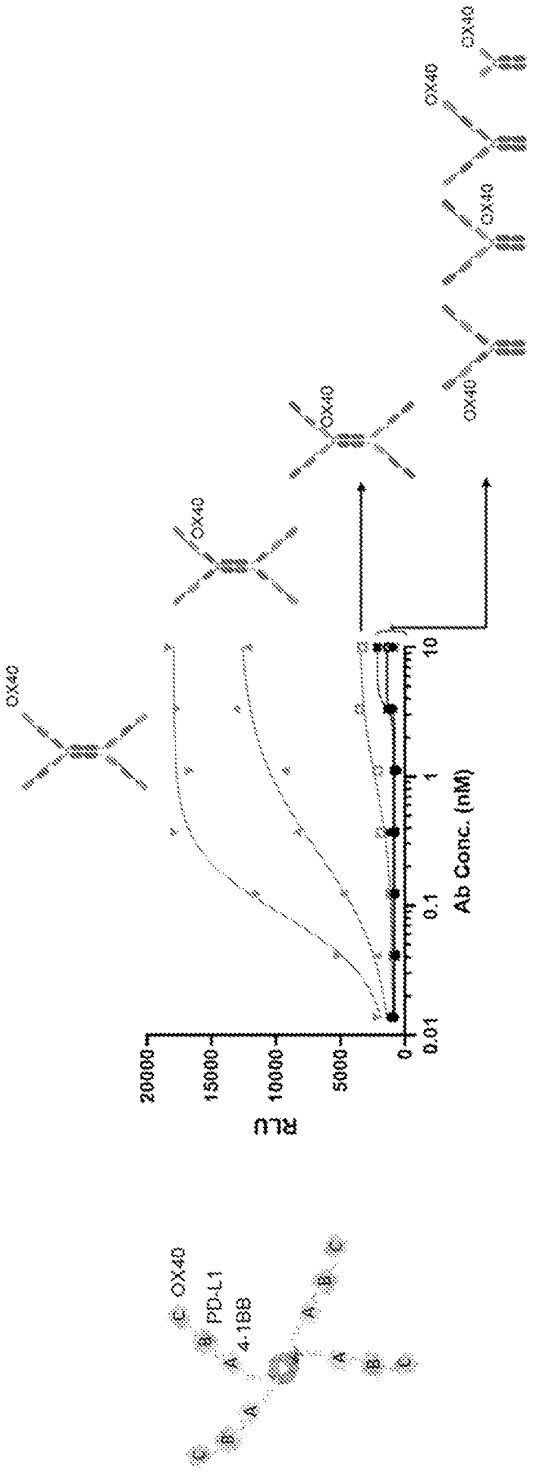

OX40
OX40
OX40
OX40
OX40
OX40
RLU
20000
15000
10000
5000
0
0.01
0.1
1
10
Ab Conc. (nM)
OX40
PD-L1
4-1BB
A
B
C

Figure 7

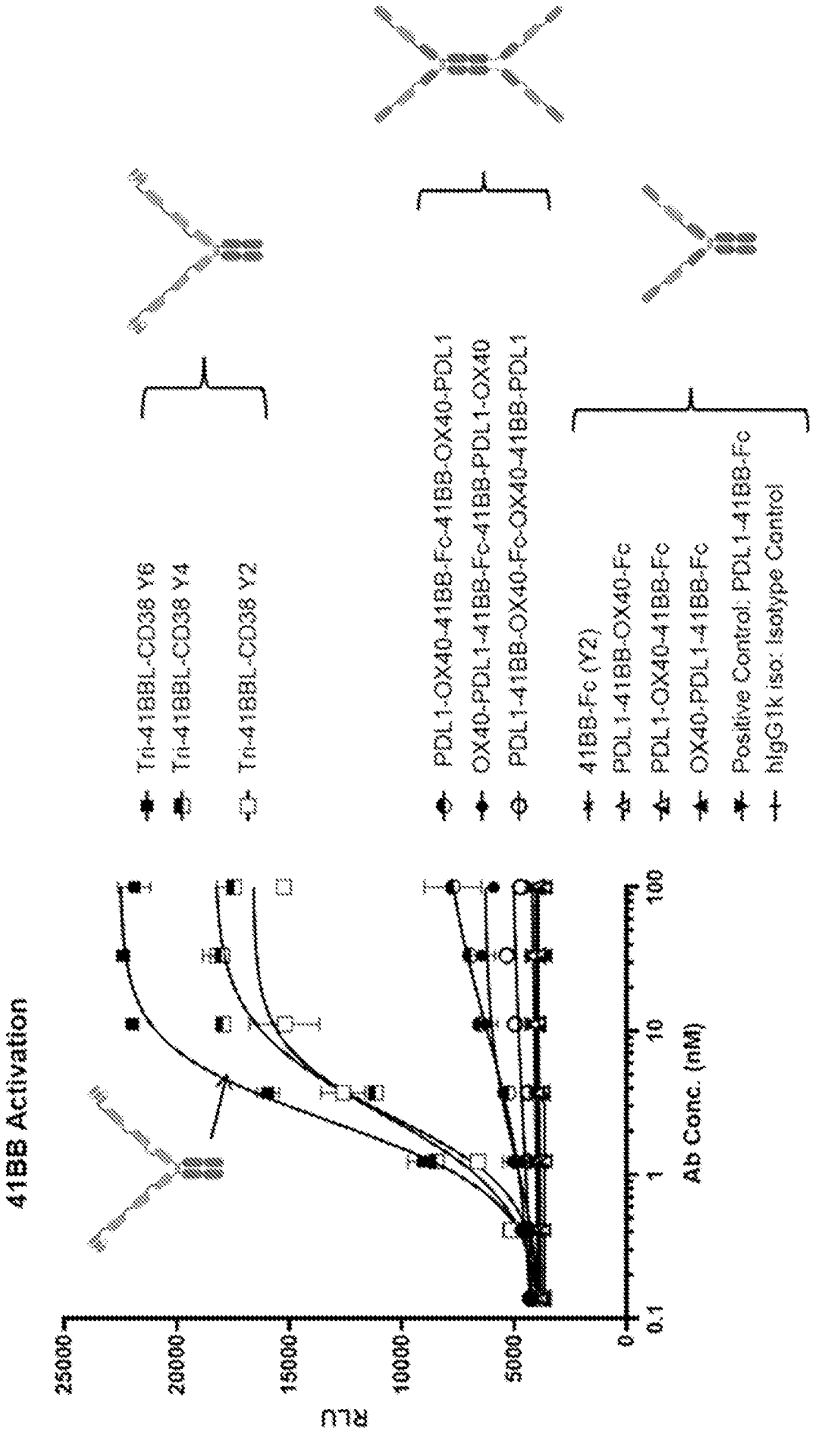

41BB Activation
RLU
25000
20000
15000
10000
5000
0
0.1
1
10
100
Ab Conc. (nM)
Tri-41BBL-CD38 Y6
Tri-41BBL-CD38 Y4
Tri-41BBL-CD38 Y2
PDL1-OX40-41BB-Fc-41BB-OX40-PDL1
OX40-PDL1-41BB-Fc-41BB-PDL1-OX40
PDL1-41BB-OX40-Fc-OX40-41BB-PDL1
41BB-Fc (Y2)
PDL1-41BB-OX40-Fc
PDL1-OX40-41BB-Fc
OX40-PDL1-41BB-Fc
Positive Control: PDL1-41BB-Fc
hIgG1k iso: Isotype Control

Figure 8A

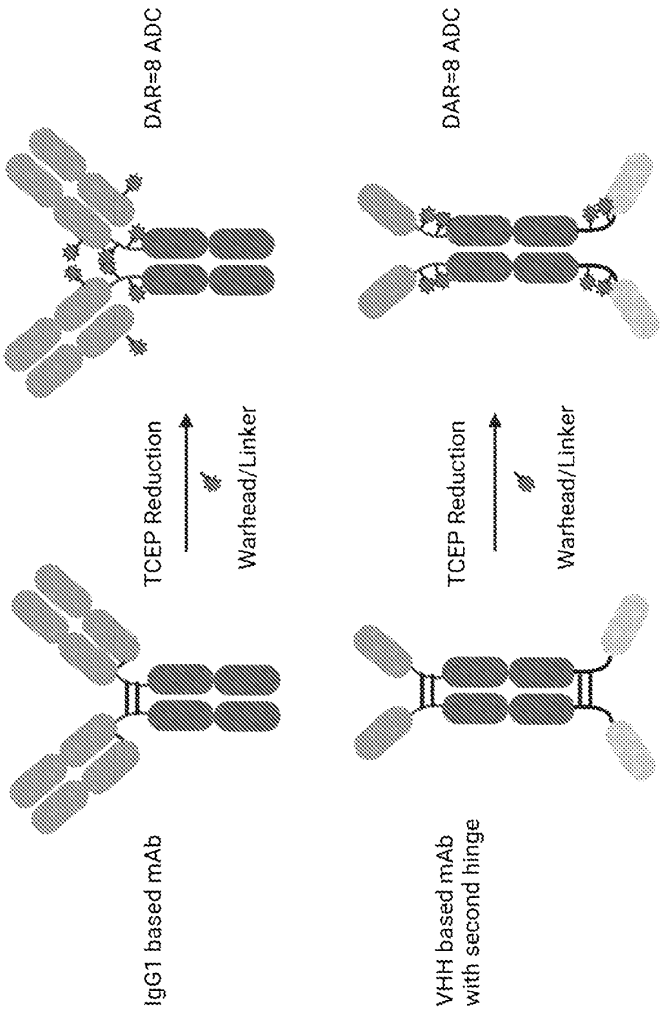
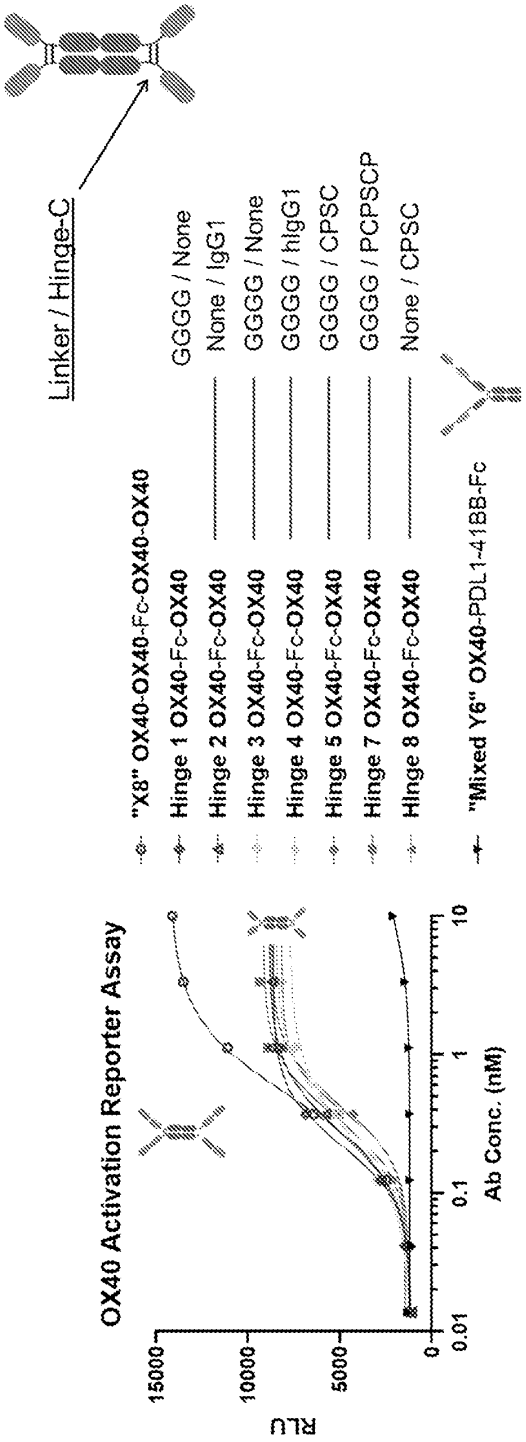

IgG1 based mAb
TCEP Reduction
Warhead/Linker
DAR=8 ADC
VHH based mAb
with second hinge
TCEP Reduction
Warhead/Linker
DAR=8 ADC

Figure 8B


Linker / Hinge-C
"X8" OX40-OX40-Fc-OX40-OX40
Hinge 1 OX40-Fc-OX40 GGGG / None
Hinge 2 OX40-Fc-OX40 None / IgG1
Hinge 3 OX40-Fc-OX40 GGGG / None
Hinge 4 OX40-Fc-OX40 GGGG / hIgG1
Hinge 5 OX40-Fc-OX40 GGGG / CPSC
Hinge 7 OX40-Fc-OX40 GGGG / PCPSCP
Hinge 8 OX40-Fc-OX40 None / CPSC
"Mixed Y6" OX40-PDL1-41BB-Fc
OX40 Activation Reporter Assay
RLU
15000
10000
5000
0
0.01
0.1
1
10
Ab Conc. (nM)

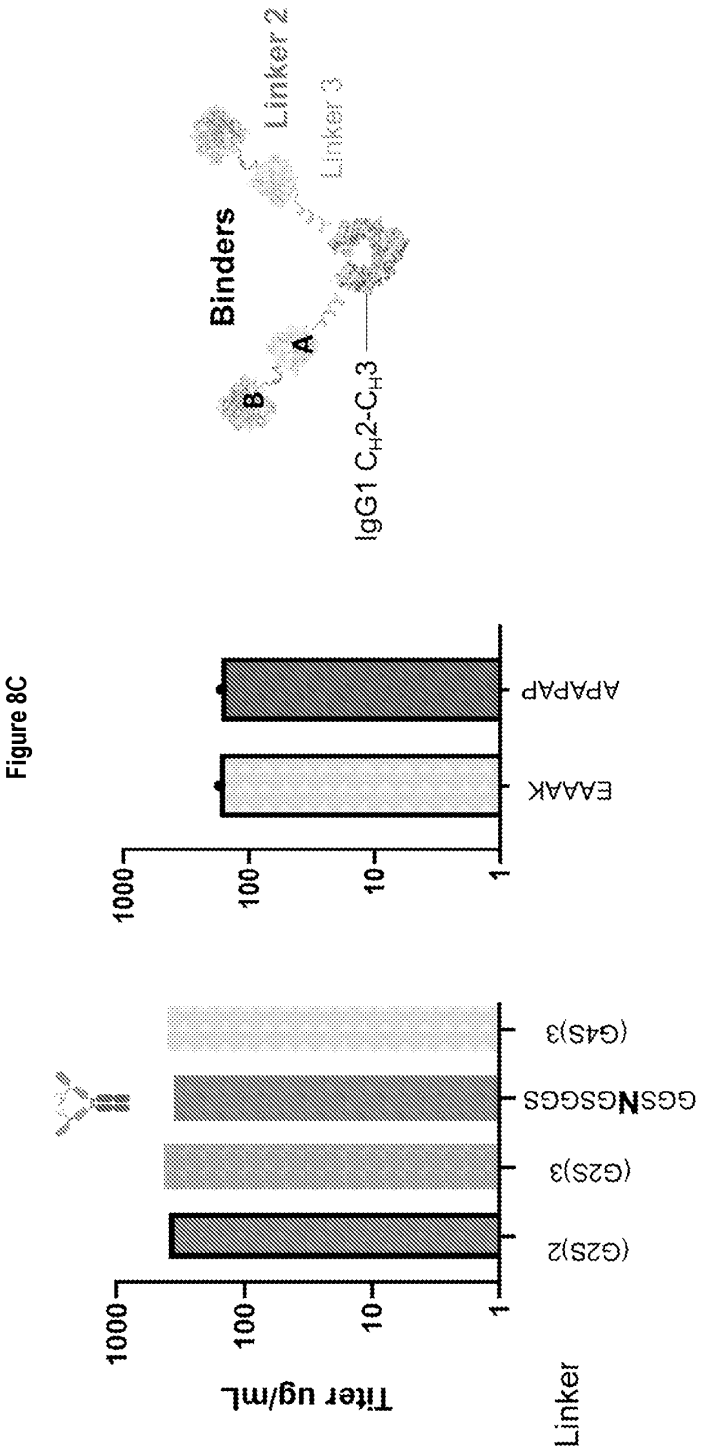

Figure 8C
Binders
Linker 2
Linker 3
A
B
IgG1 C_H2-C_H3
Titer ug/mL
1000
100
10
1
(G2S)2
(G2S)3
GGSNGSGGS
(G4S)3
Linker
EAAAK
APAPAP

Figure 9

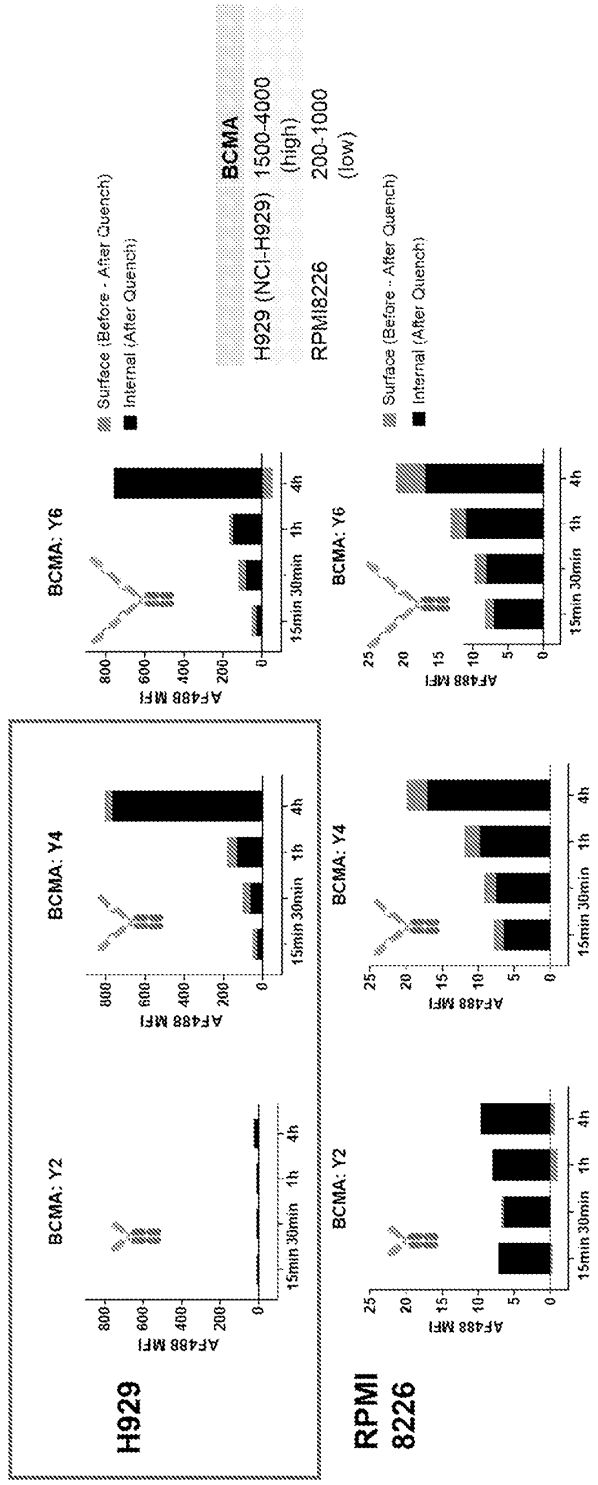

H929
RPMI 8226
BCMA: Y2
BCMA: Y4
BCMA: Y6
AF488 MFI
15min 30min 1h 4h
Surface (Before - After Quench)
Internal (After Quench)
BCMA
H929 (NCI-H929) 1500-4000 (high)
RPMI8226 200-1000 (low)

Figure 10

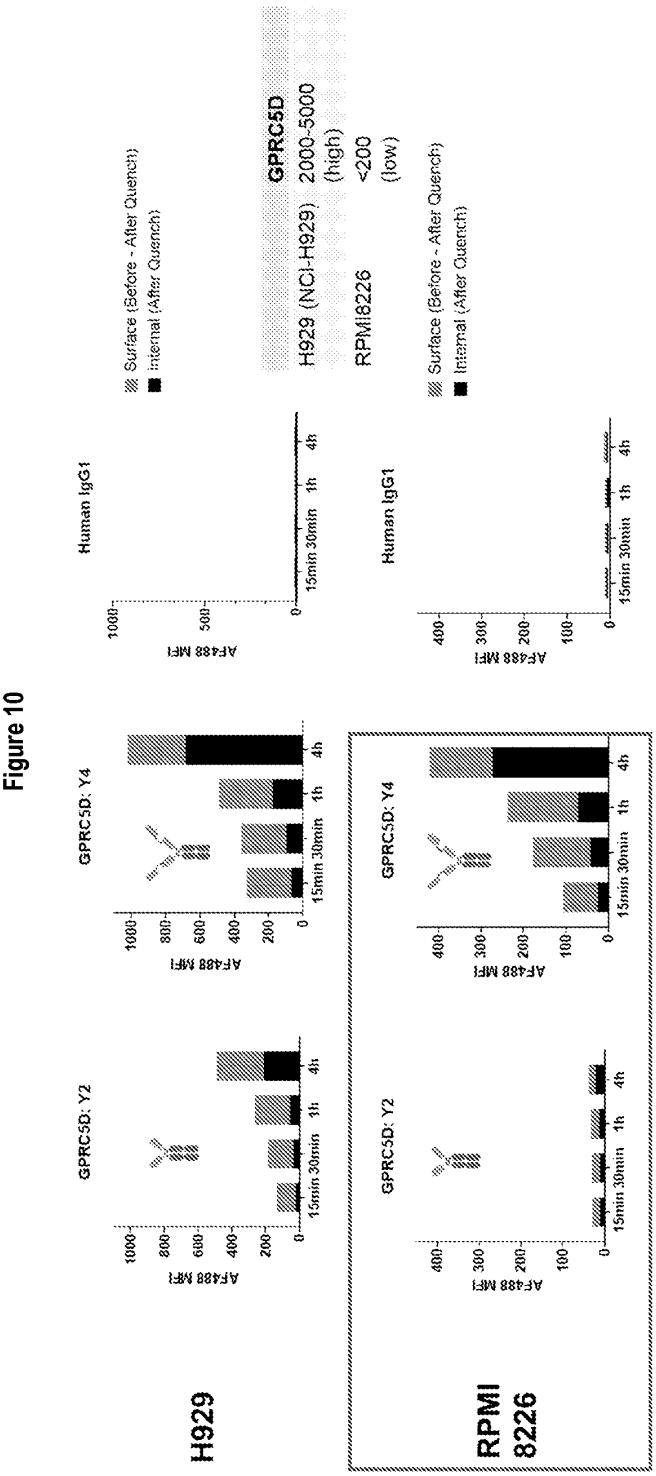

GPRC5D
H929 (NCI-H929) 2000-5000 (high)
RPMI8226 <200 (low)
Surface (Before - After Quench)
Internal (After Quench)
Human IgG1
GPRC5D: Y2
GPRC5D: Y4
AF488 MFI
15min 30min 1h 4h
H929
RPMI 8226

Figure 11

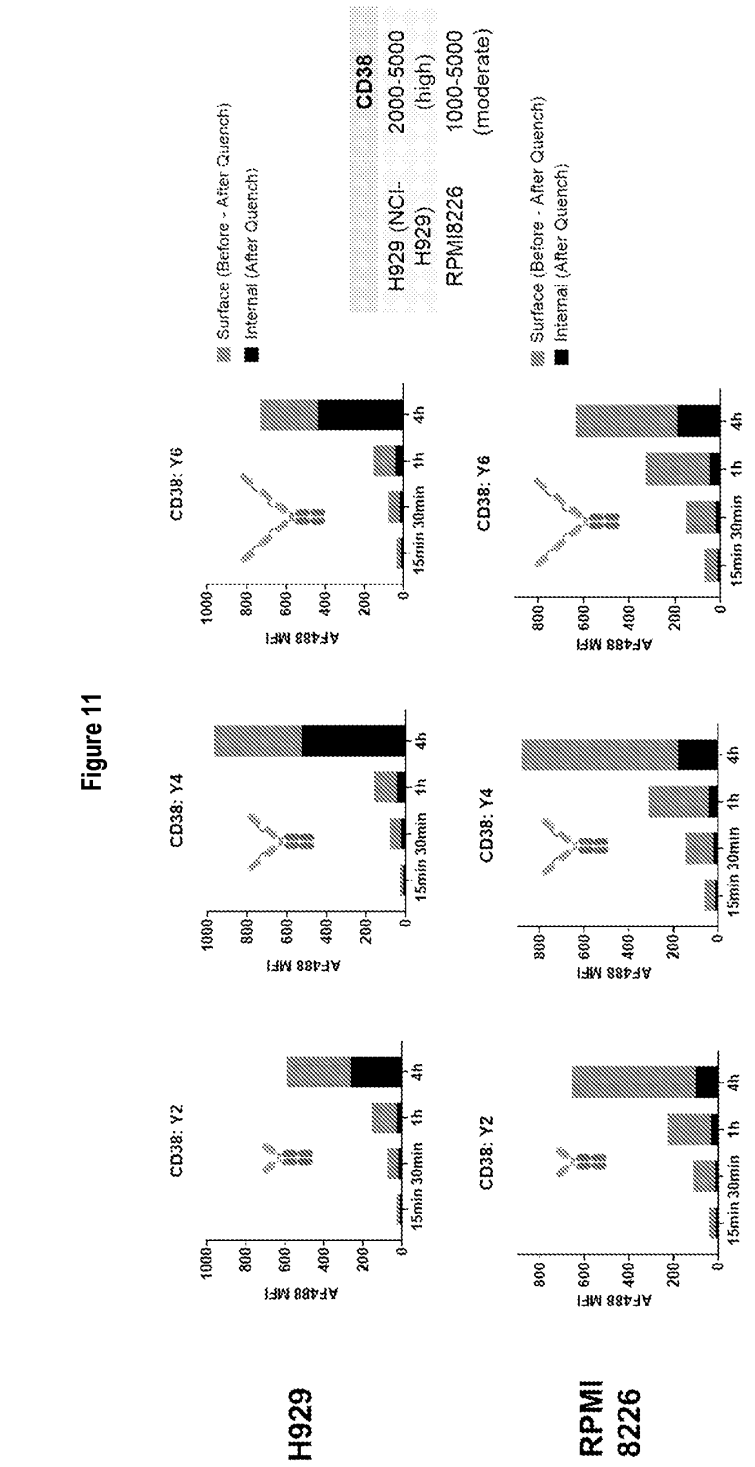

Surface (Before - After Quench)
Internal (After Quench)
CD38
H929 (NCI-H929) 2000-5000 (high)
RPMI8226 1000-5000 (moderate)
H929
RPMI 8226
CD38: Y2
CD38: Y4
CD38: Y6
AF488 MFI
15min 30min 1h 4h

Figure 12

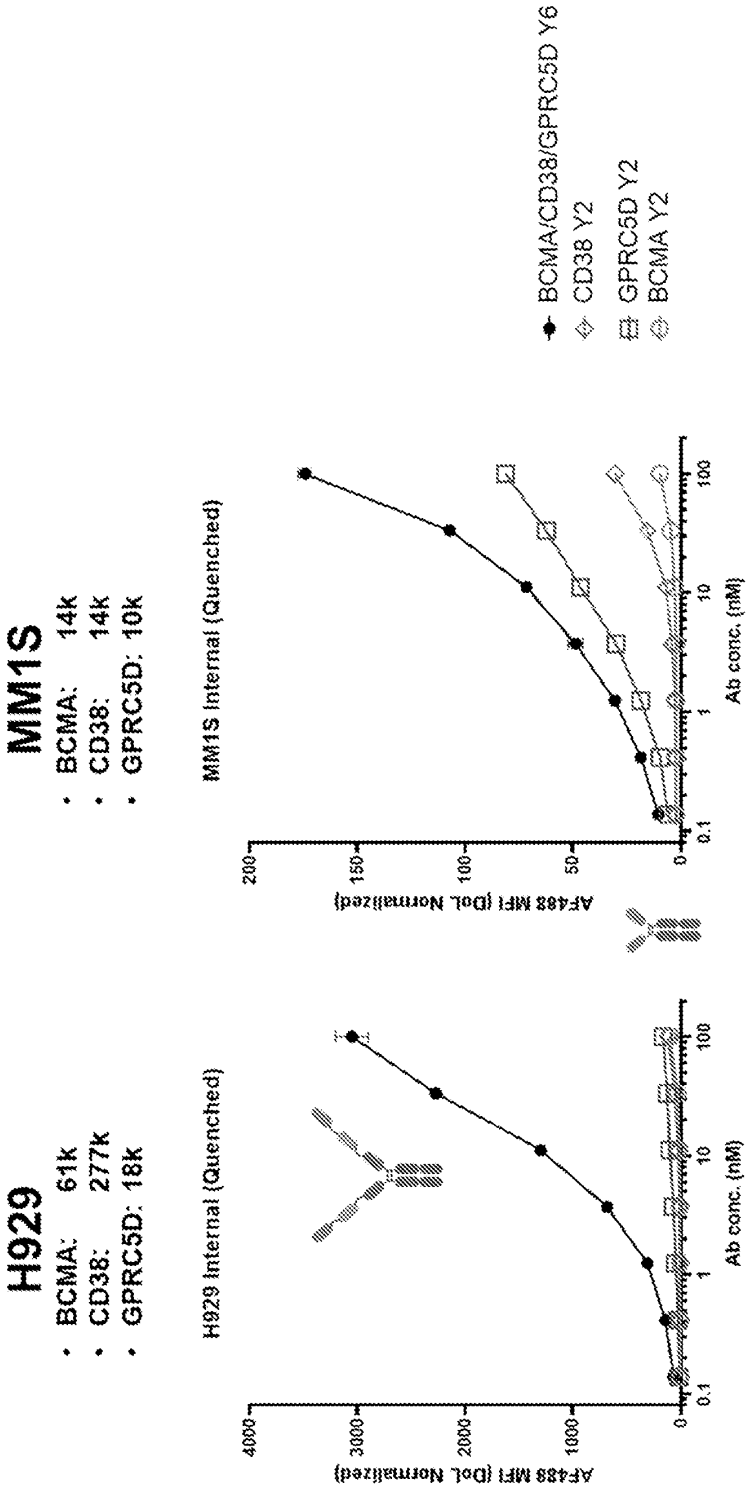

H929
• BCMA: 61k
• CD38: 277k
• GPRC5D: 18k
H929 Internal (Quenched)
AF488 MFI (DoL Normalized)
Ab conc. (nM)
MM1S
• BCMA: 14k
• CD38: 14k
• GPRC5D: 10k
MM1S Internal (Quenched)
AF488 MFI (DoL Normalized)
Ab conc. (nM)
BCMA/CD38/GPRC5D Y6
CD38 Y2
GPRC5D Y2
BCMA Y2

Figure 13

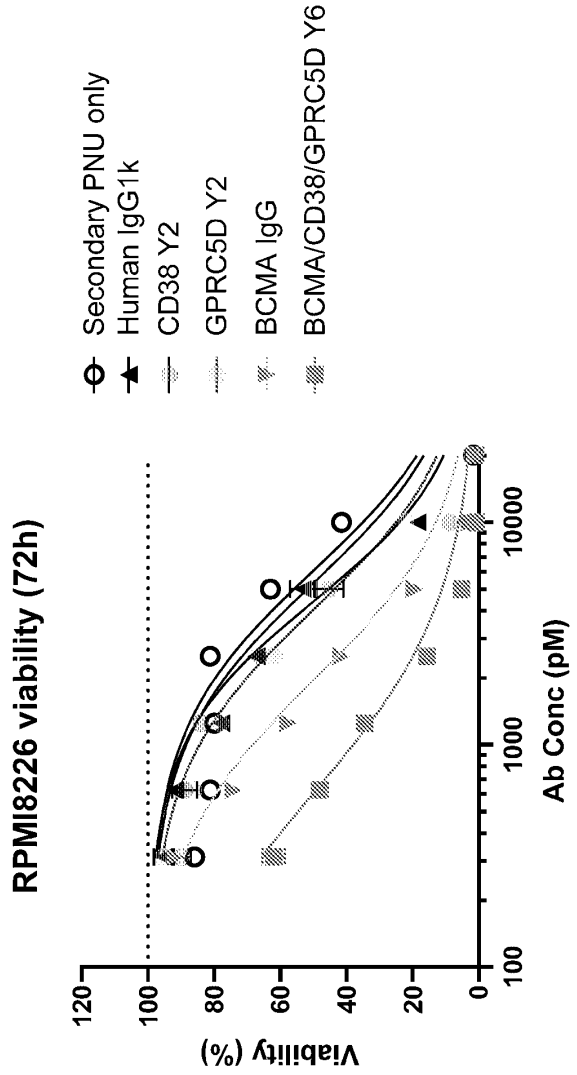

RPMI8226 viability (72h)
Secondary PNU only
Human IgG1k
CD38 Y2
GPRC5D Y2
BCMA IgG
BCMA/CD38/GPRC5D Y6
Viability (%)
120
100
80
60
40
20
0
100
1000
10000
Ab Conc (pM)

Figure 14

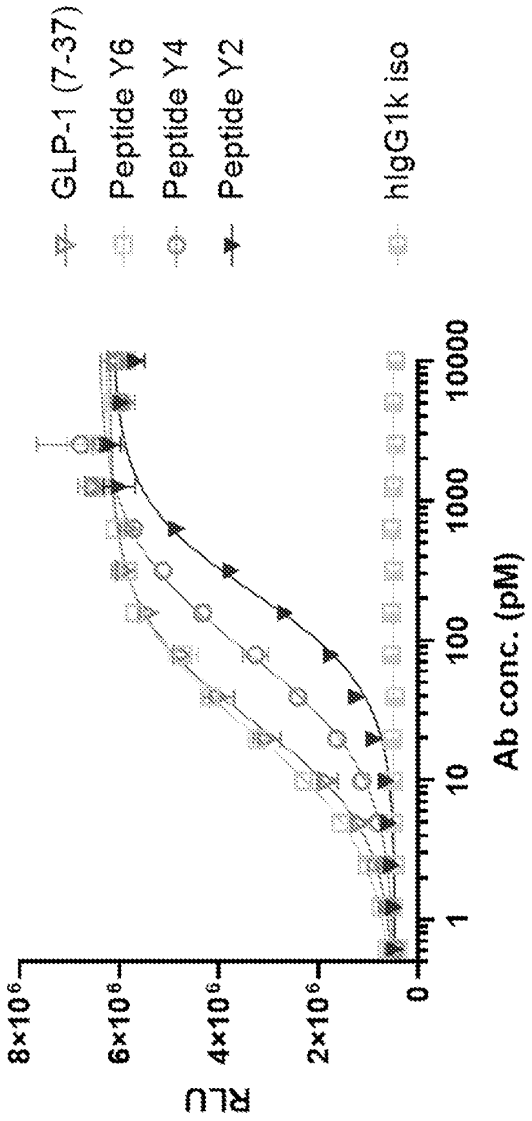
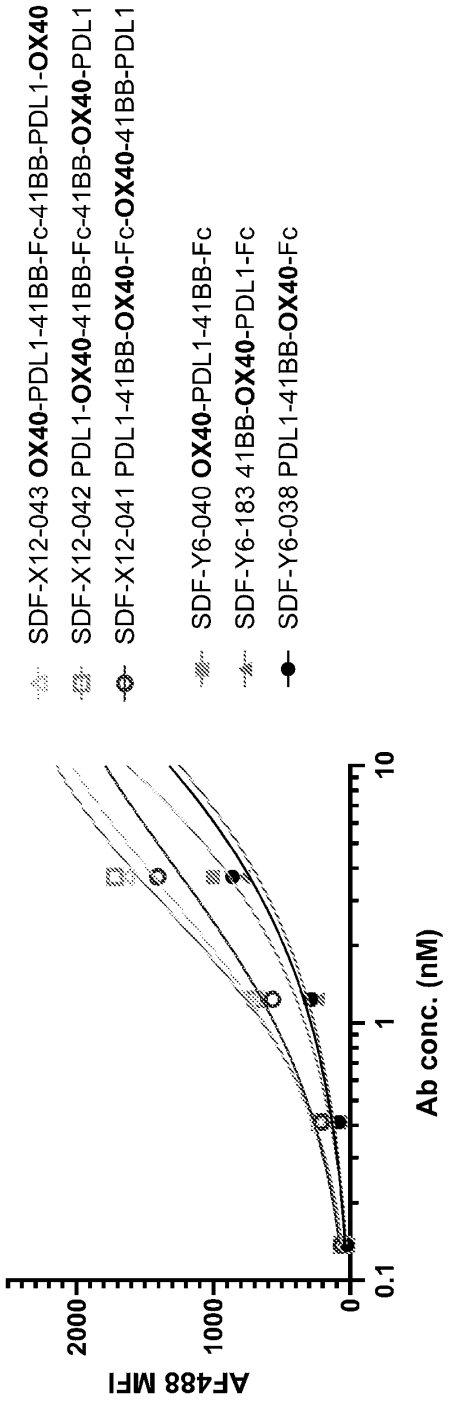

GLP-1 (7-37)
Peptide Y6
Peptide Y4
Peptide Y2
hIgG1k iso
RLU
8×10^6
6×10^6
4×10^6
2×10^6
0
1
10
100
1000
10000
Ab conc. (pM)

Figure 15


SDF-X12-043 OX40-PDL1-41BB-Fc-41BB-PDL1-OX40
SDF-X12-042 PDL1-OX40-41BB-Fc-41BB-OX40-PDL1
SDF-X12-041 PDL1-41BB-OX40-Fc-OX40-41BB-PDL1
SDF-Y6-040 OX40-PDL1-41BB-Fc
SDF-Y6-183 41BB-OX40-PDL1-Fc
SDF-Y6-038 PDL1-41BB-OX40-Fc
AF488 MFI
2000
1000
0
0.1
1
10
Ab conc. (nM)