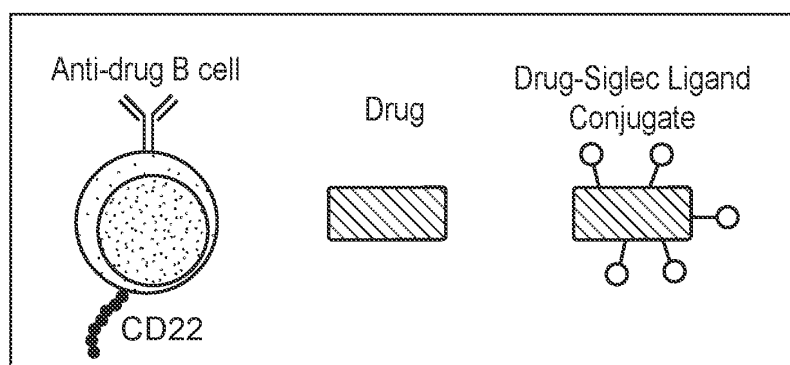
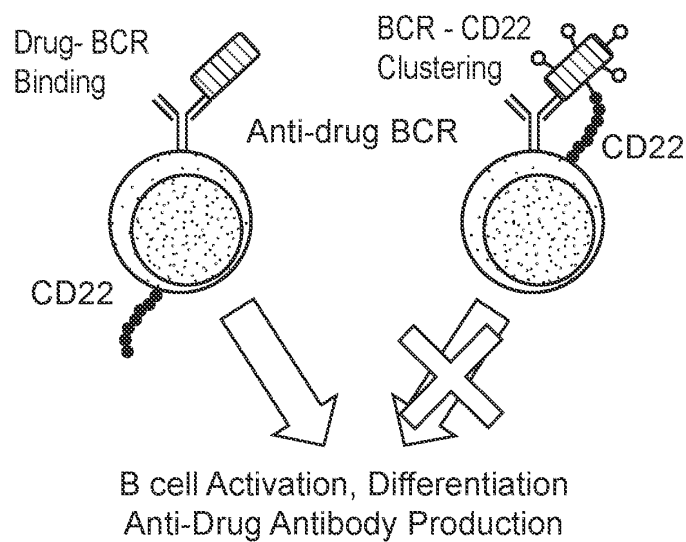


1/54

FIG. 1



- Drug-specific B cells are activated by standard drugs -> Anti-drug antibodies
- Drug-Siglec Ligand conjugates recruit CD22 to anti-Drug B cell receptors and suppress drug-specific B cell activation -> Anti-drug antibodies suppressed



2/54

FIG. 2

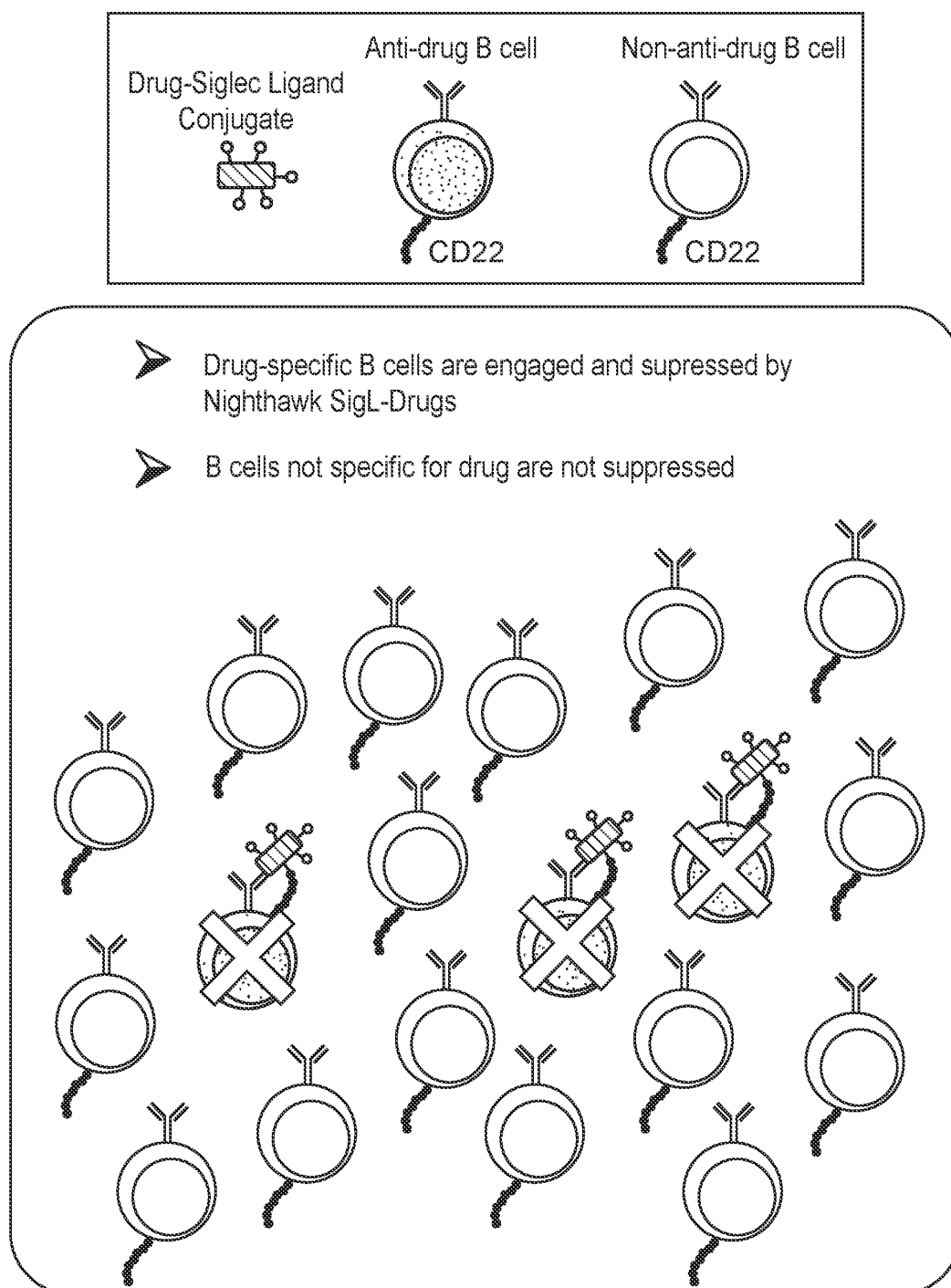
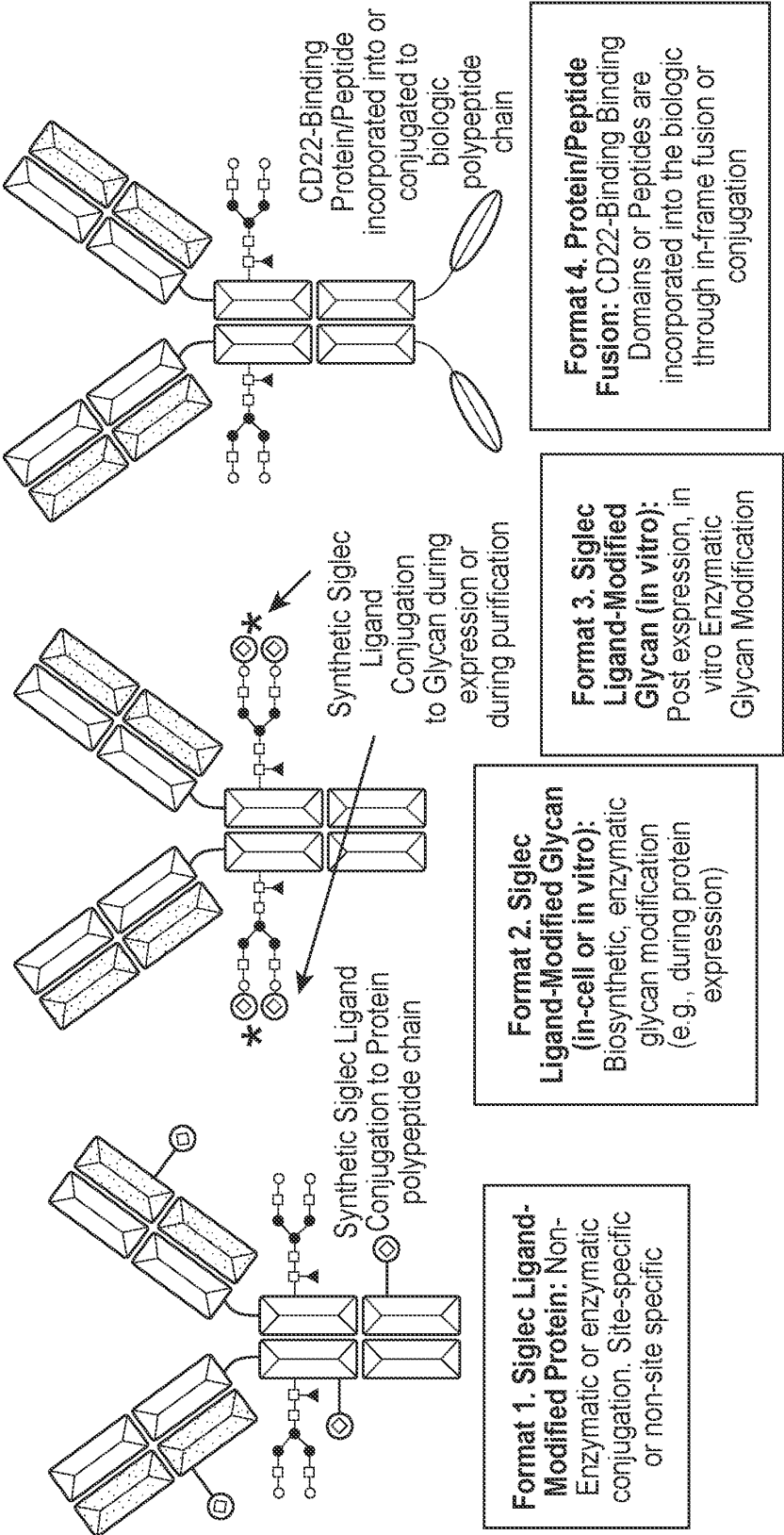
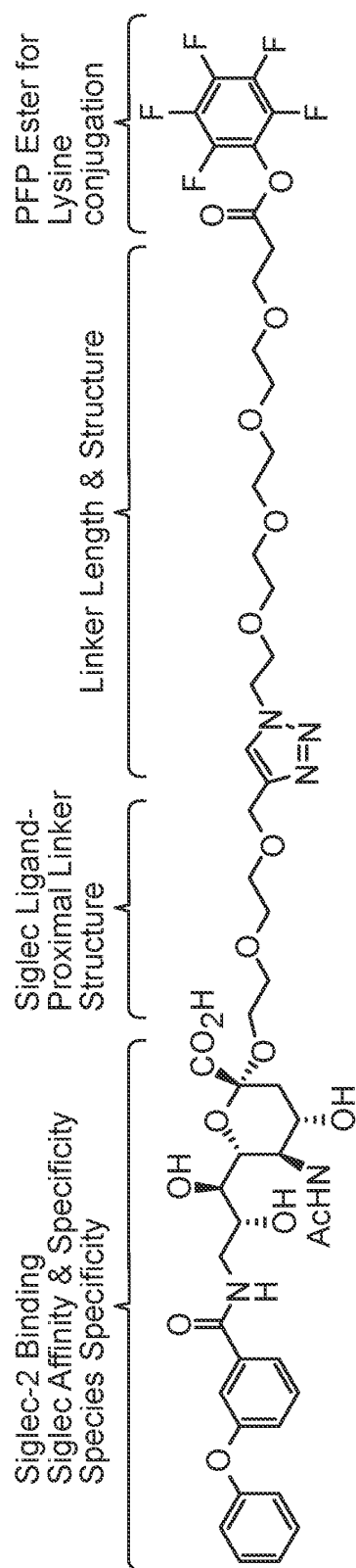


FIG. 3



4/54

FIG. 4



SUBSTITUTE SHEET (RULE 26)

5/54

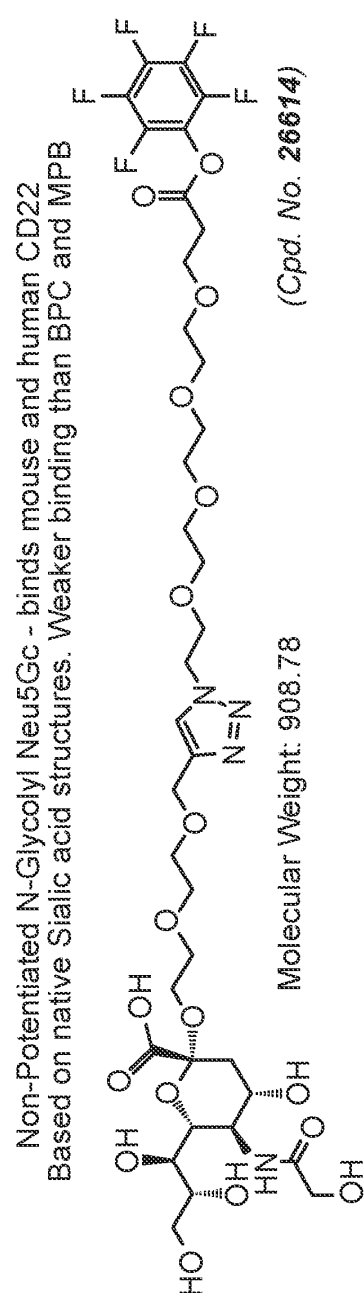
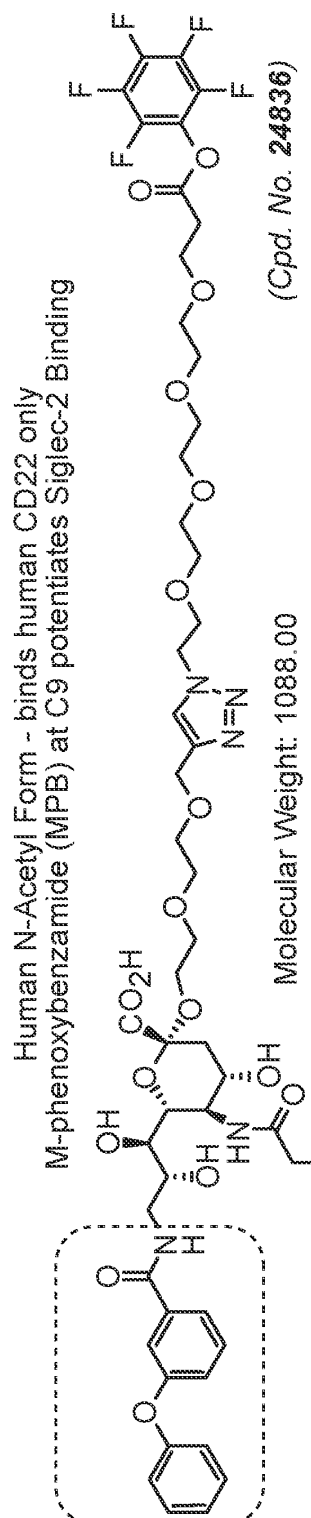
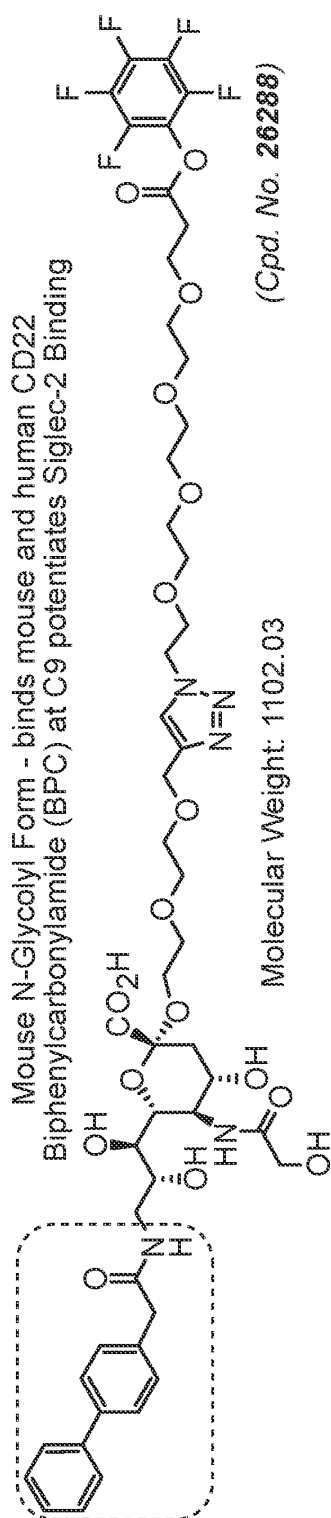
Siglec Affinity and Species Specificity**FIG. 5**

FIG. 6

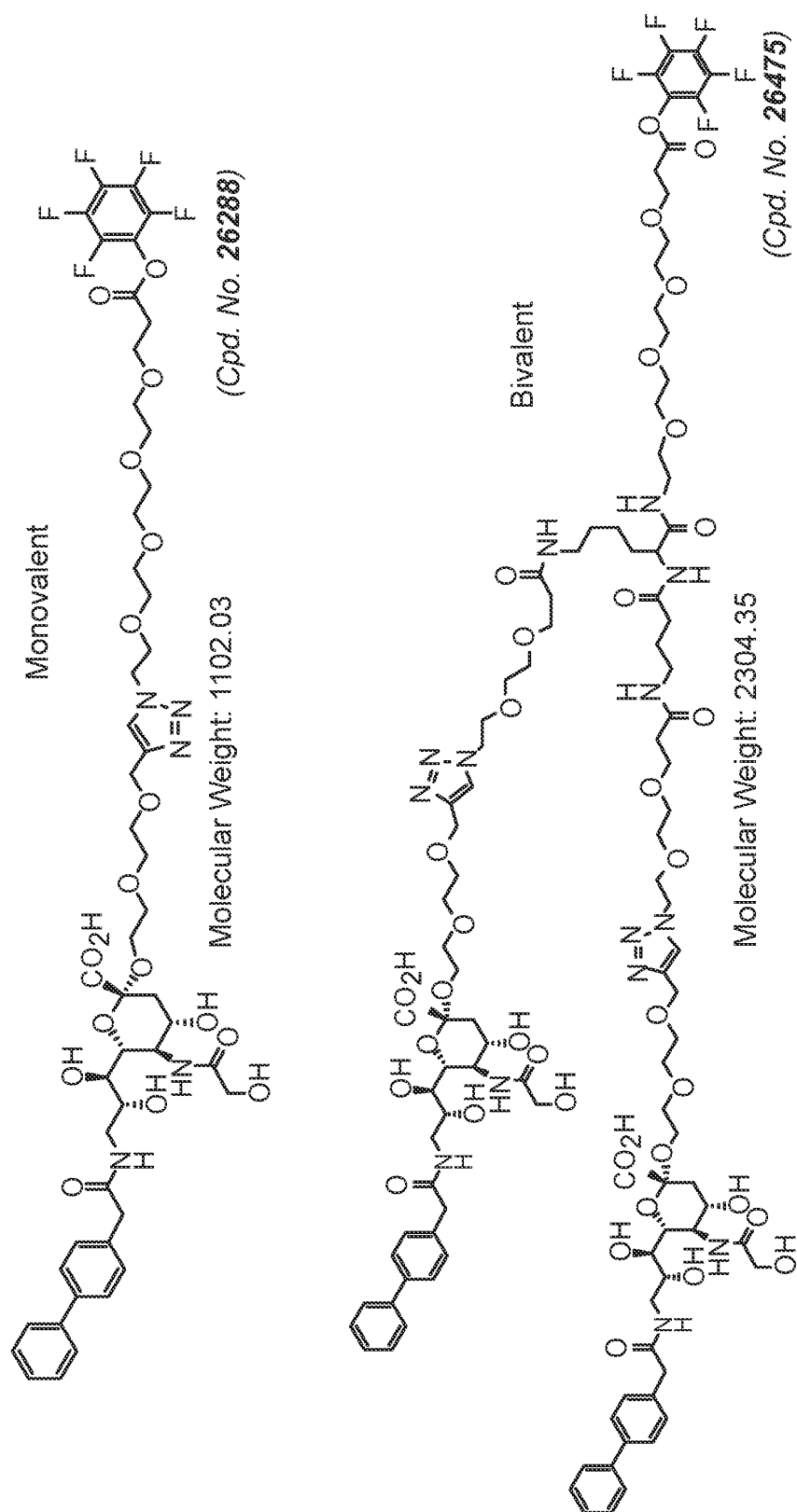
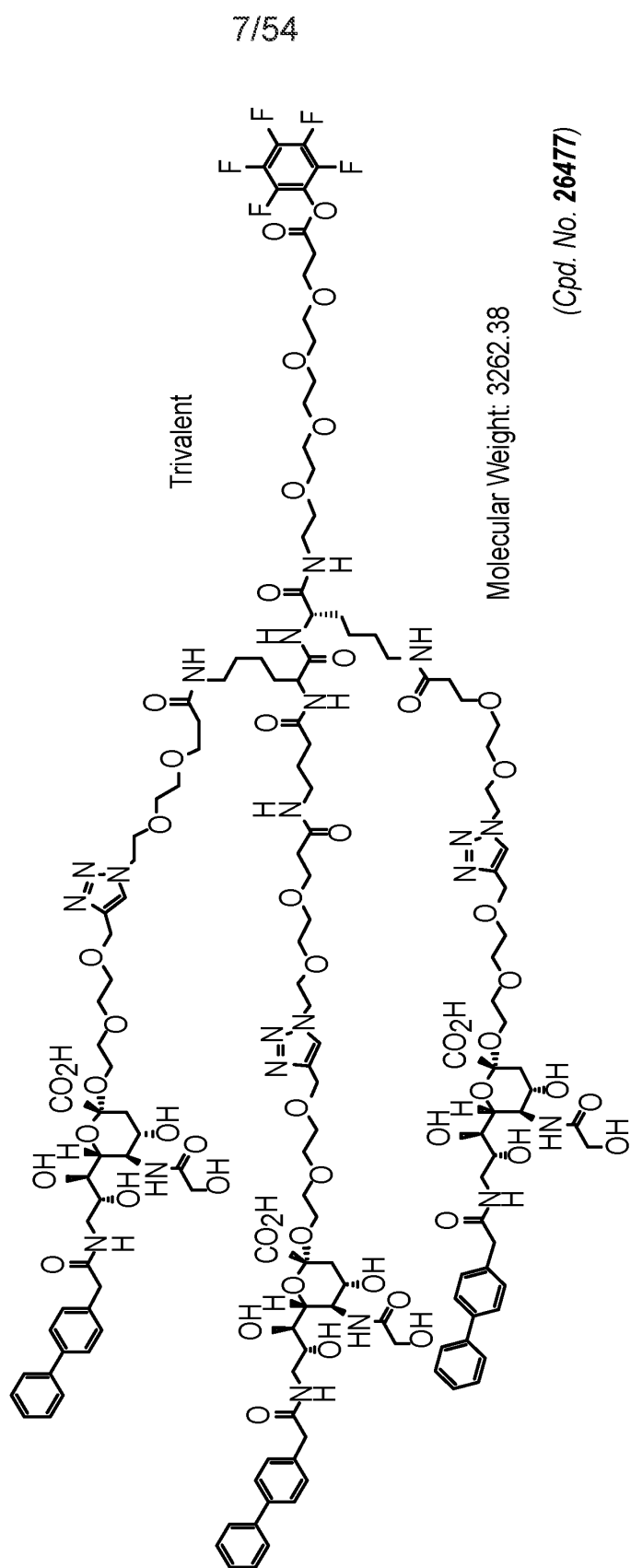
Siglec Ligand-Linker Valency

FIG. 6 (Cont.)

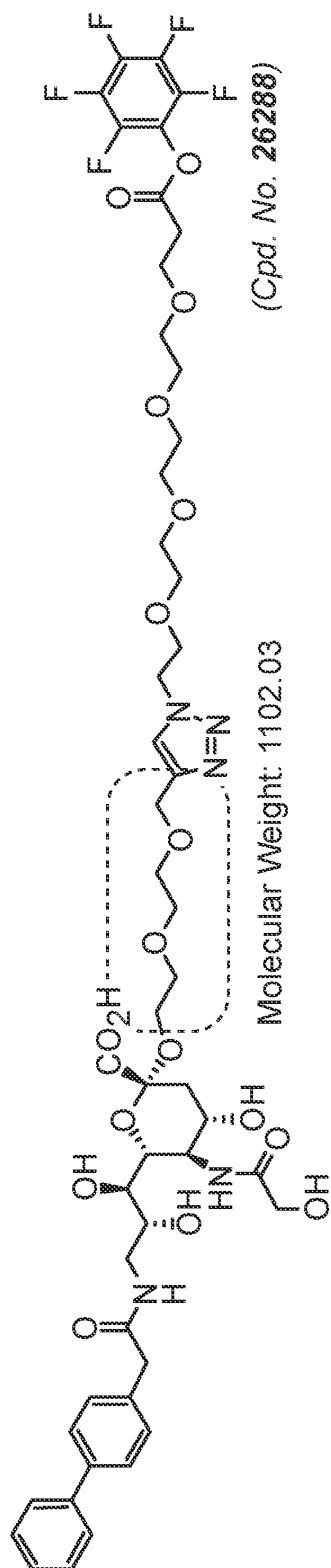


8/54

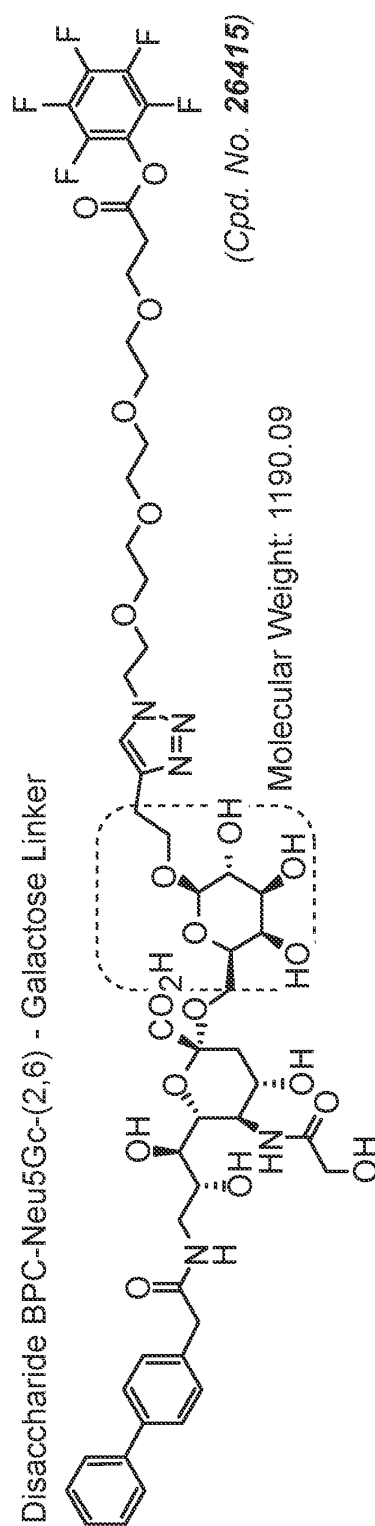
FIG. 7

Linker Structure

Monosaccharide BPC-Neu5Gc - PEG Linker

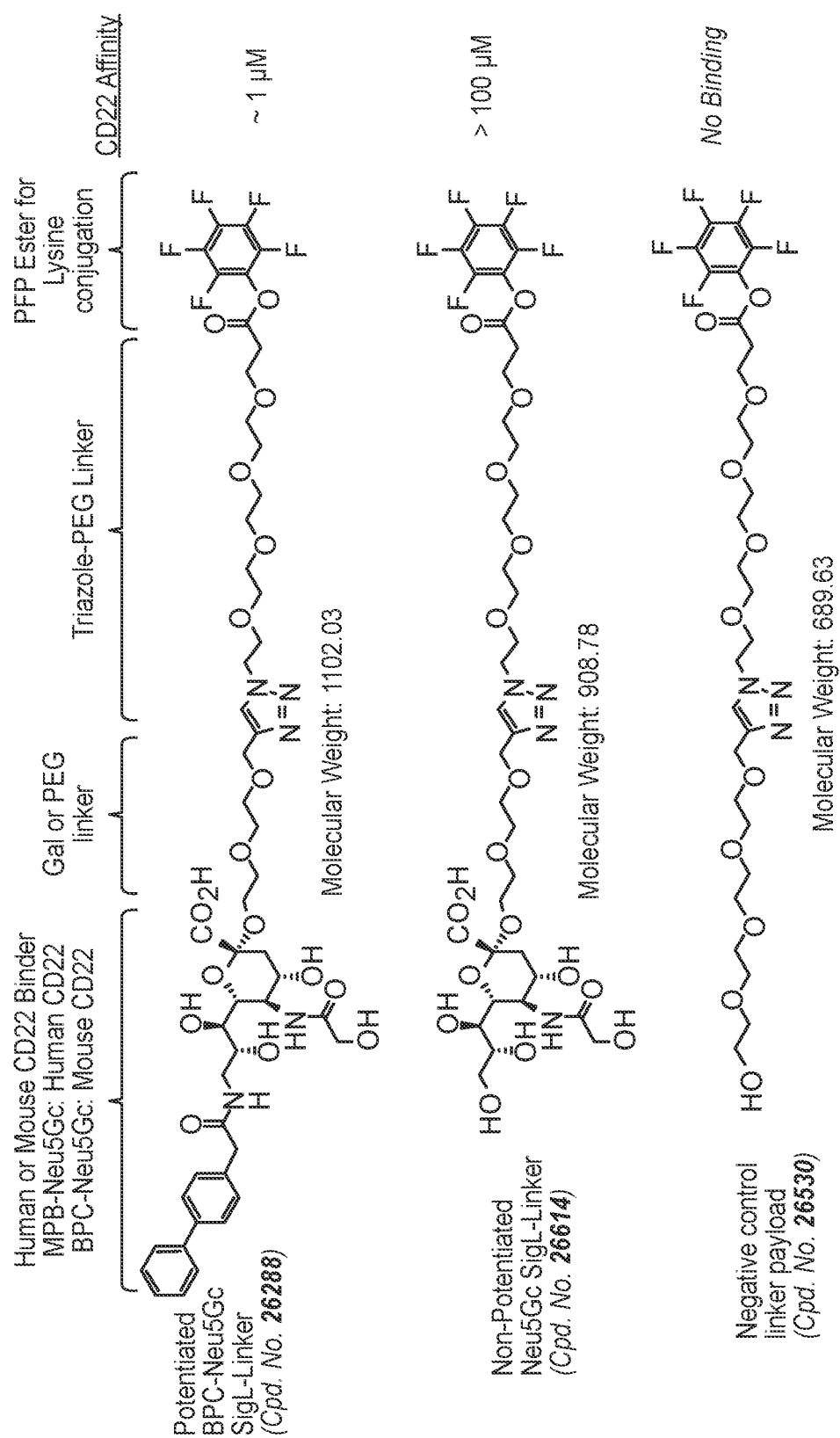


Disaccharide BPC-Neu5Gc-(2,6) - Galactose Linker



9/54

FIG. 8



Adalimumab-Siglec Ligand Conjugates: Capillary Gel Electrophoresis

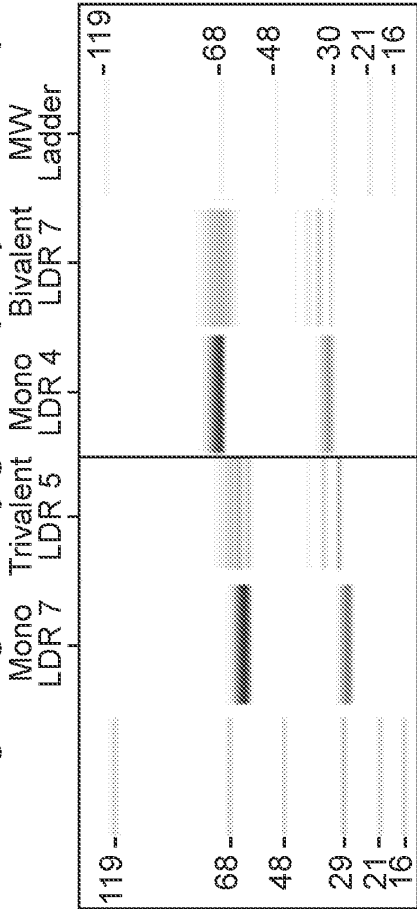


FIG. 9A

FIG. 9B

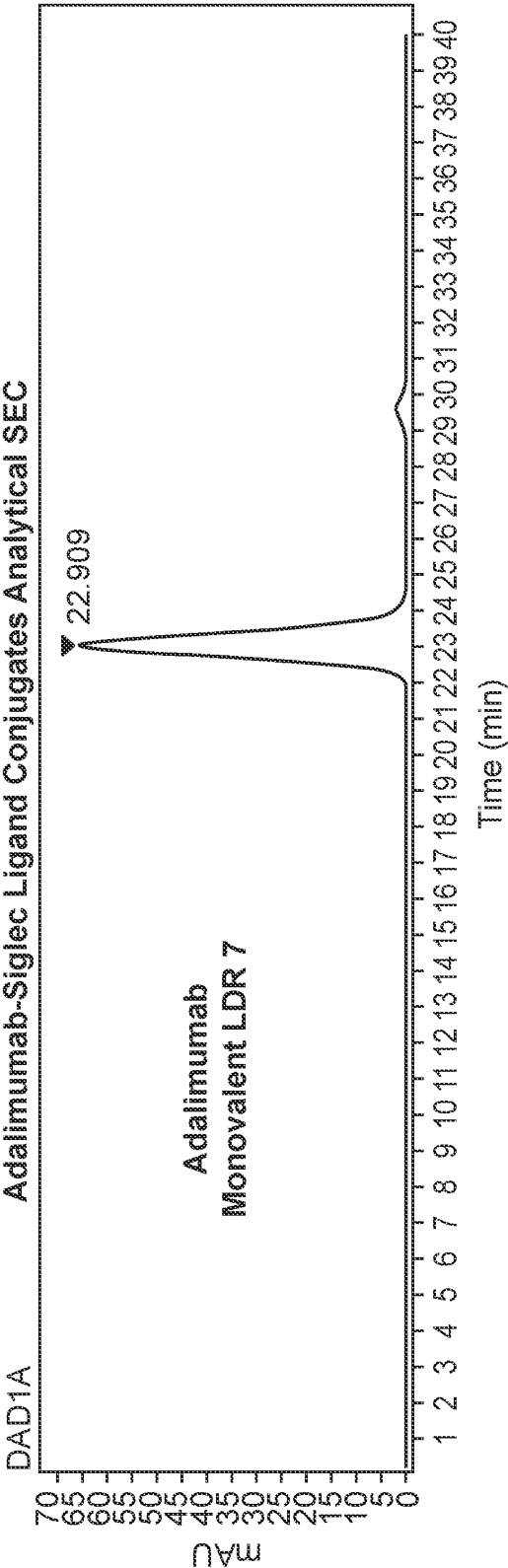


FIG. 9B (Cont.)

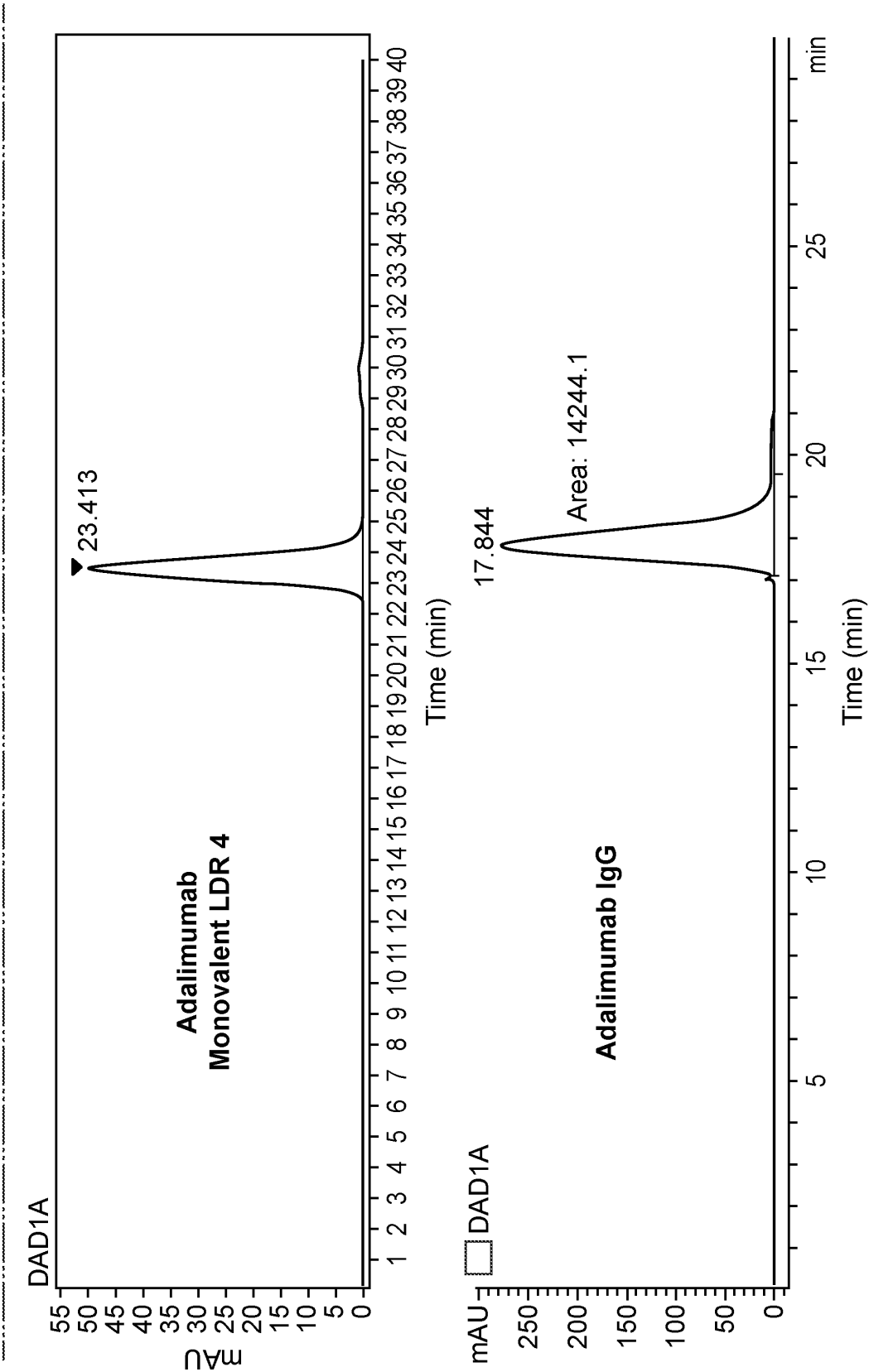
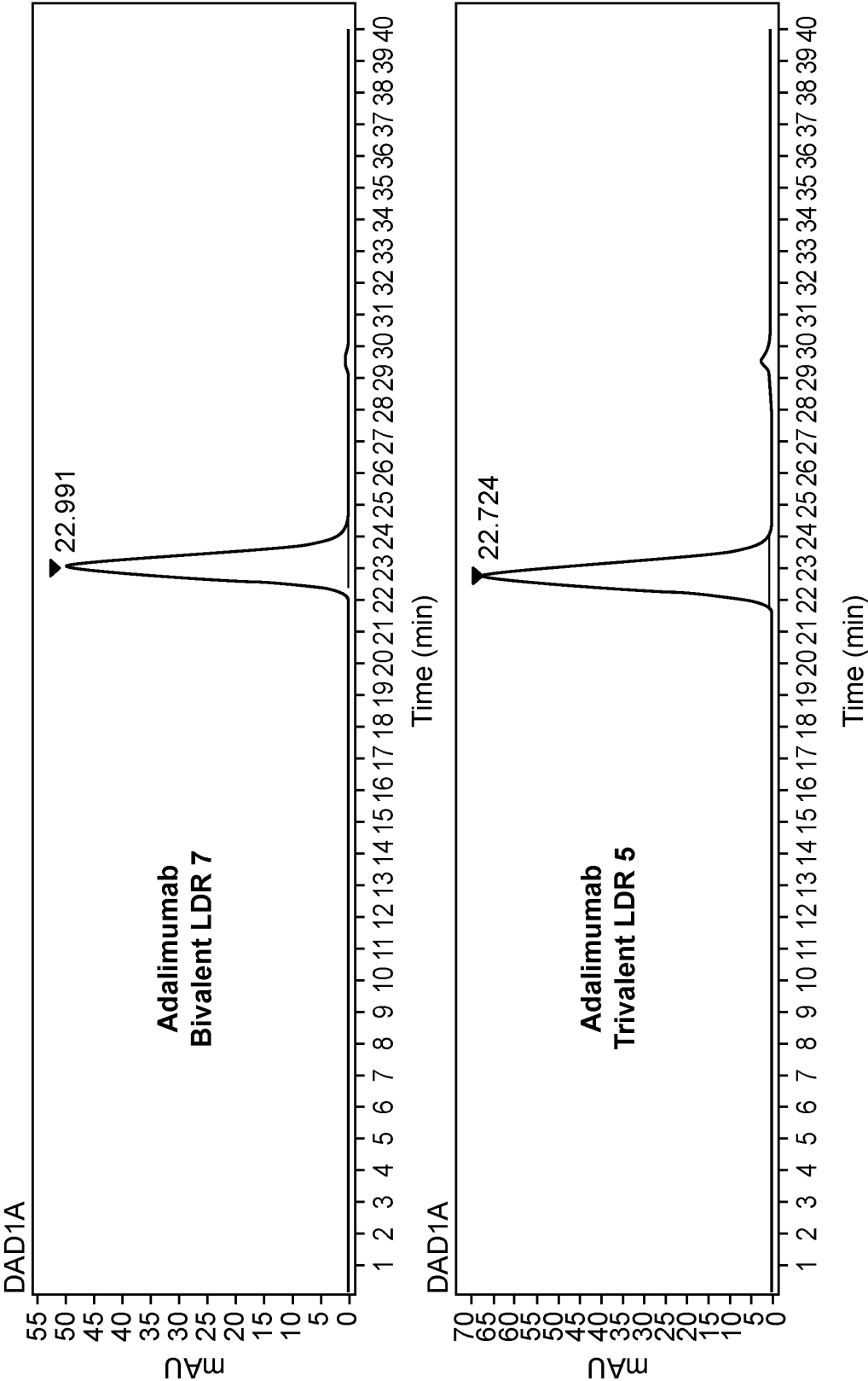


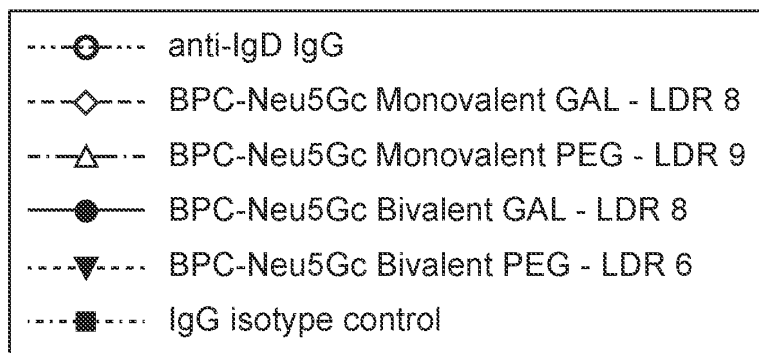
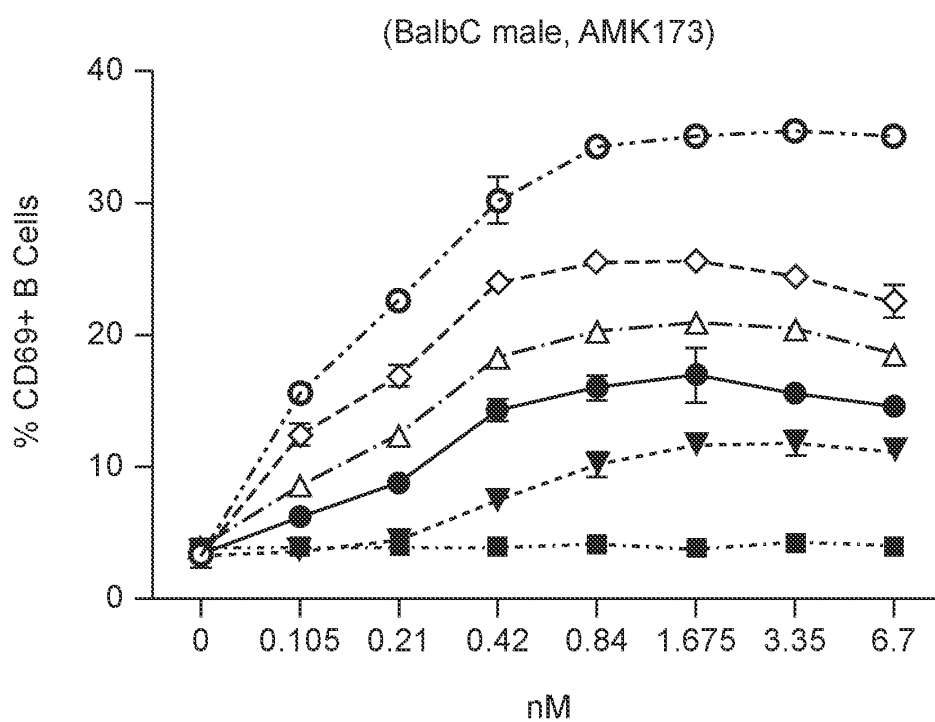
FIG. 9B (Cont.)



13/54

FIG. 10A

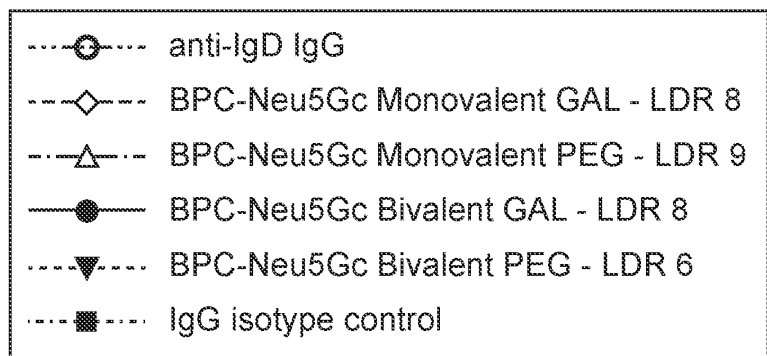
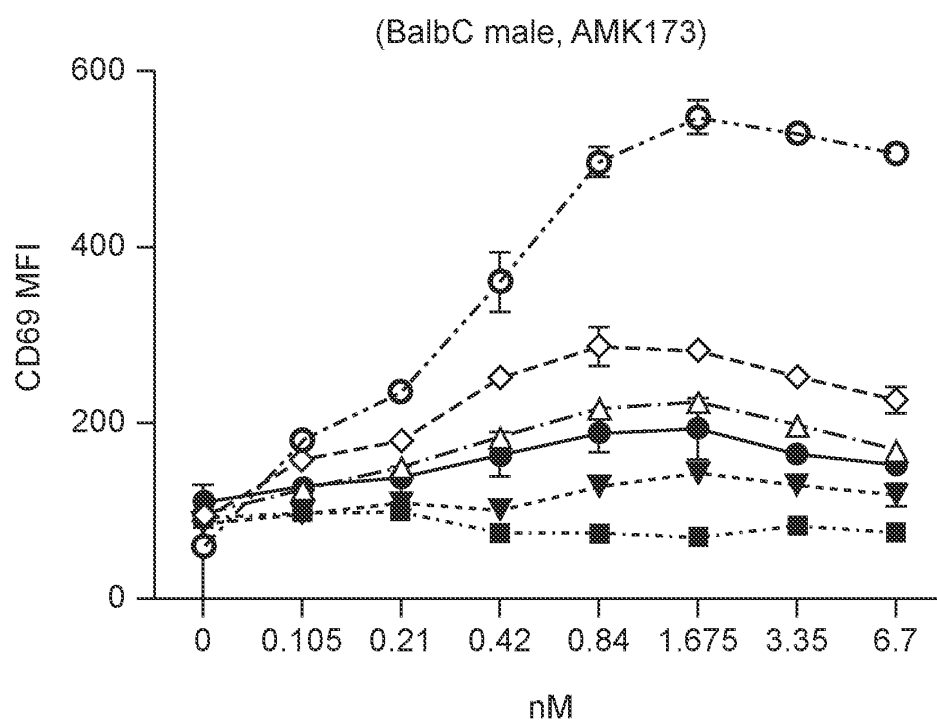
Monovalent and Bivalent PEG vs GAL



14/54

FIG. 10B

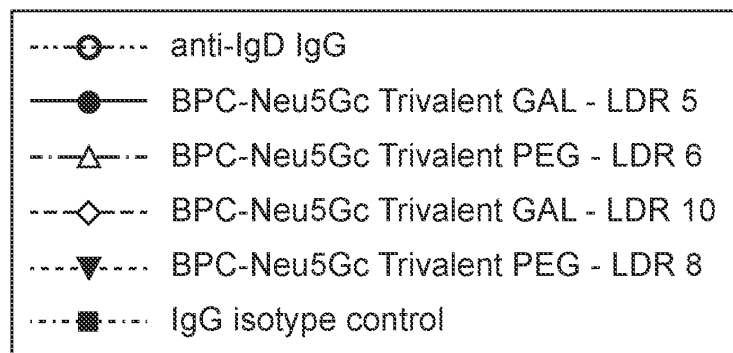
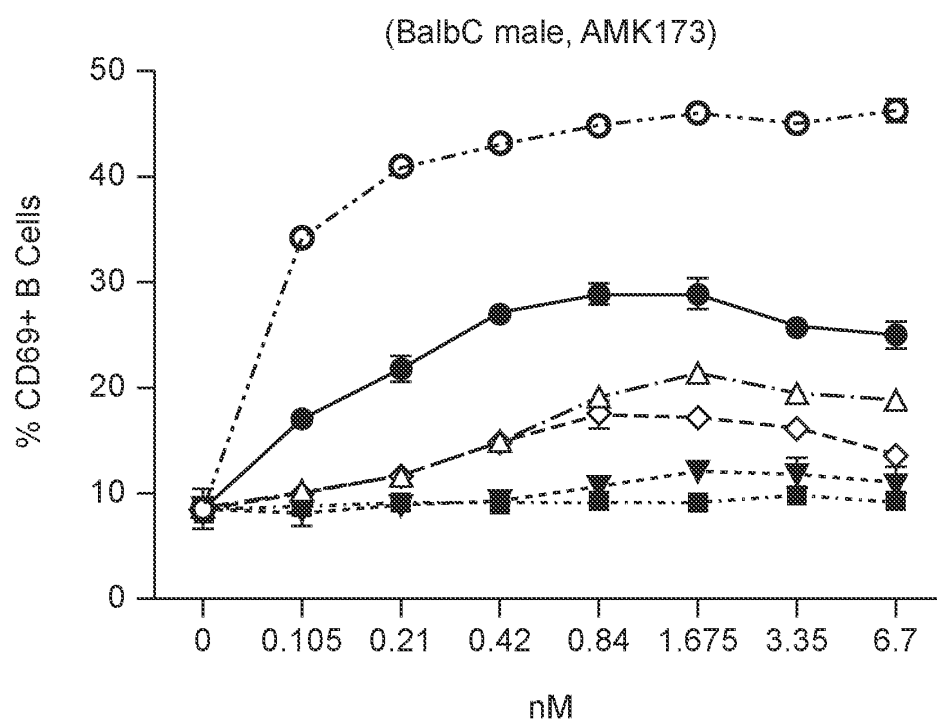
Monovalent and Bivalent PEG vs GAL



15/54

FIG. 11A

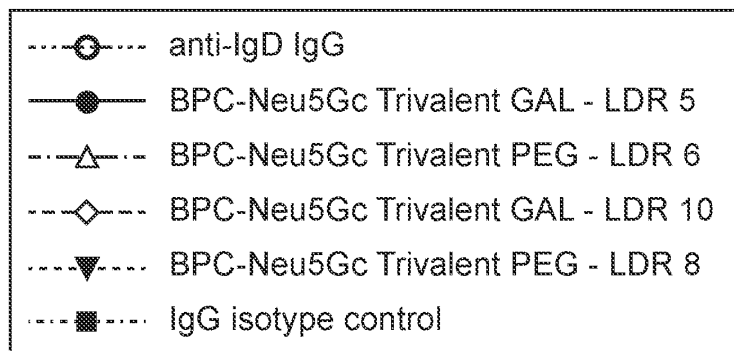
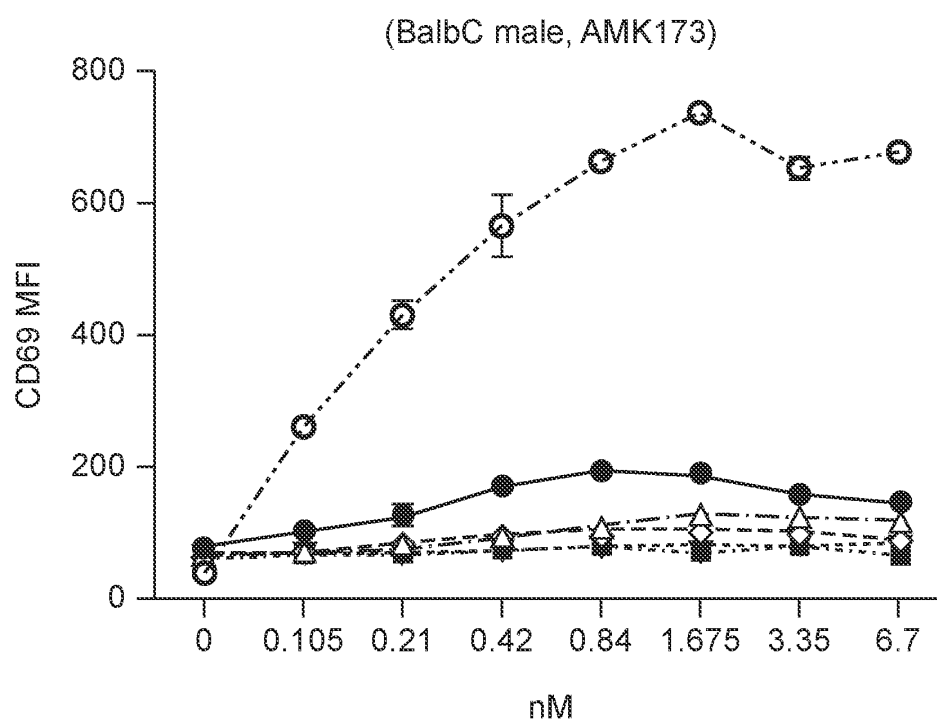
Trivalent PEG vs GAL



16/54

FIG. 11B

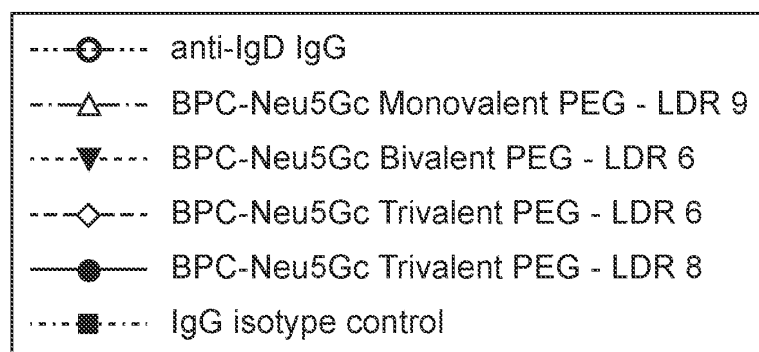
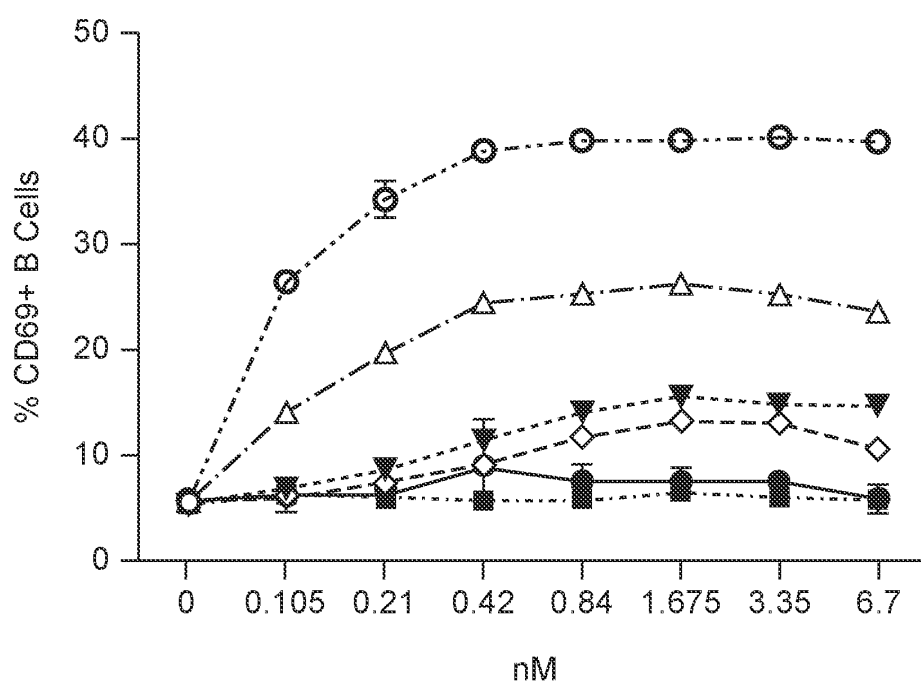
Trivalent PEG vs GAL



17/54

FIG. 12A

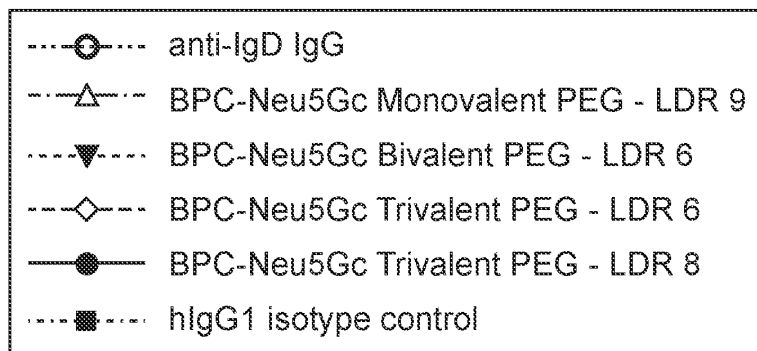
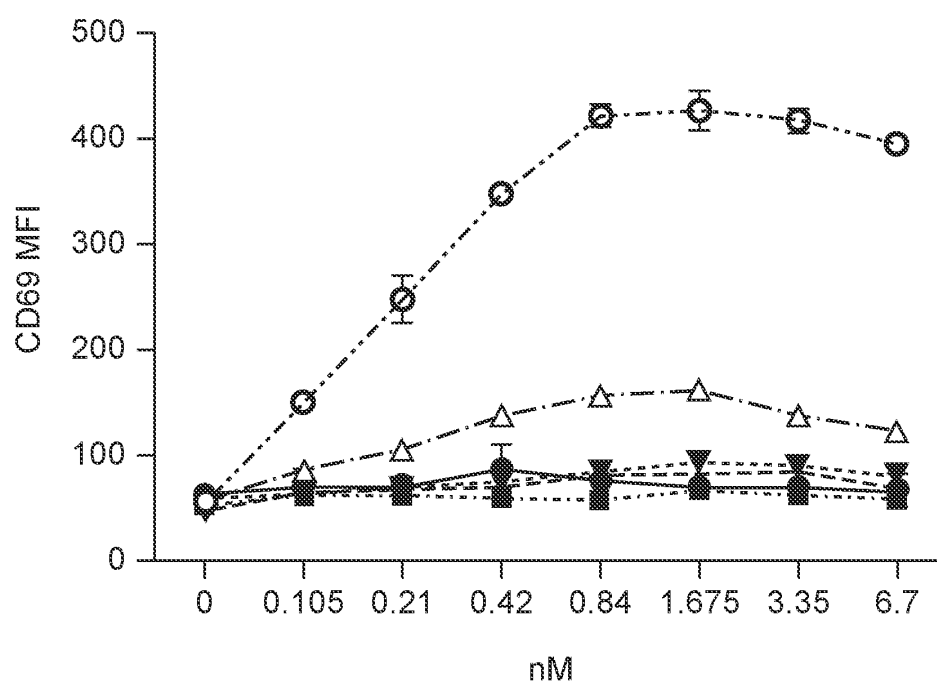
Percent CD69+ B cells



18/54

FIG. 12B

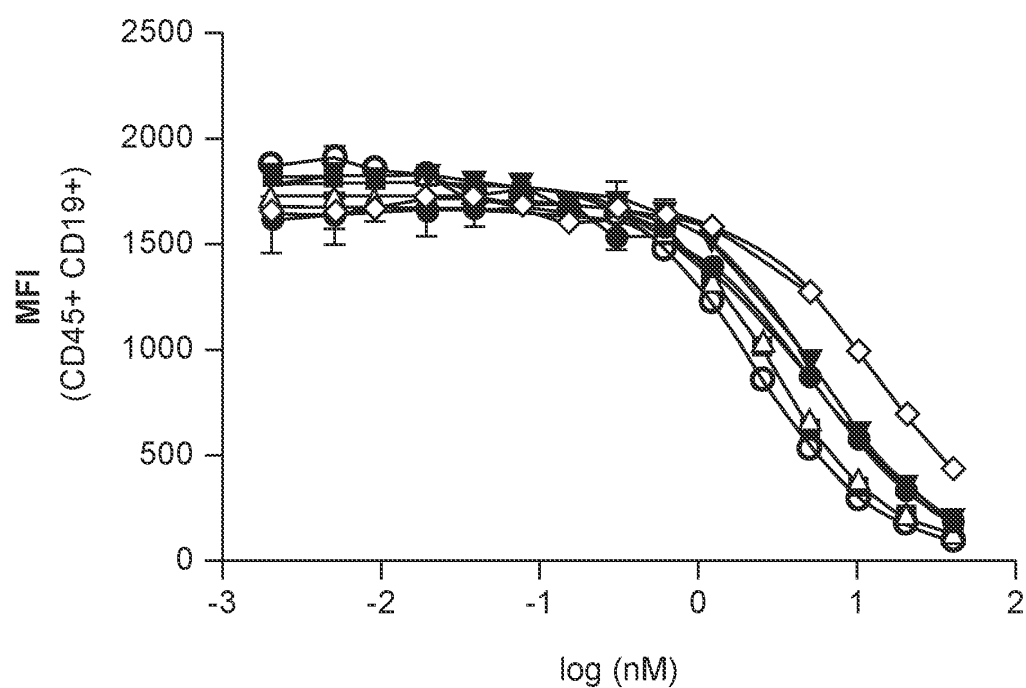
Levels of CD69 on B cells



19/54

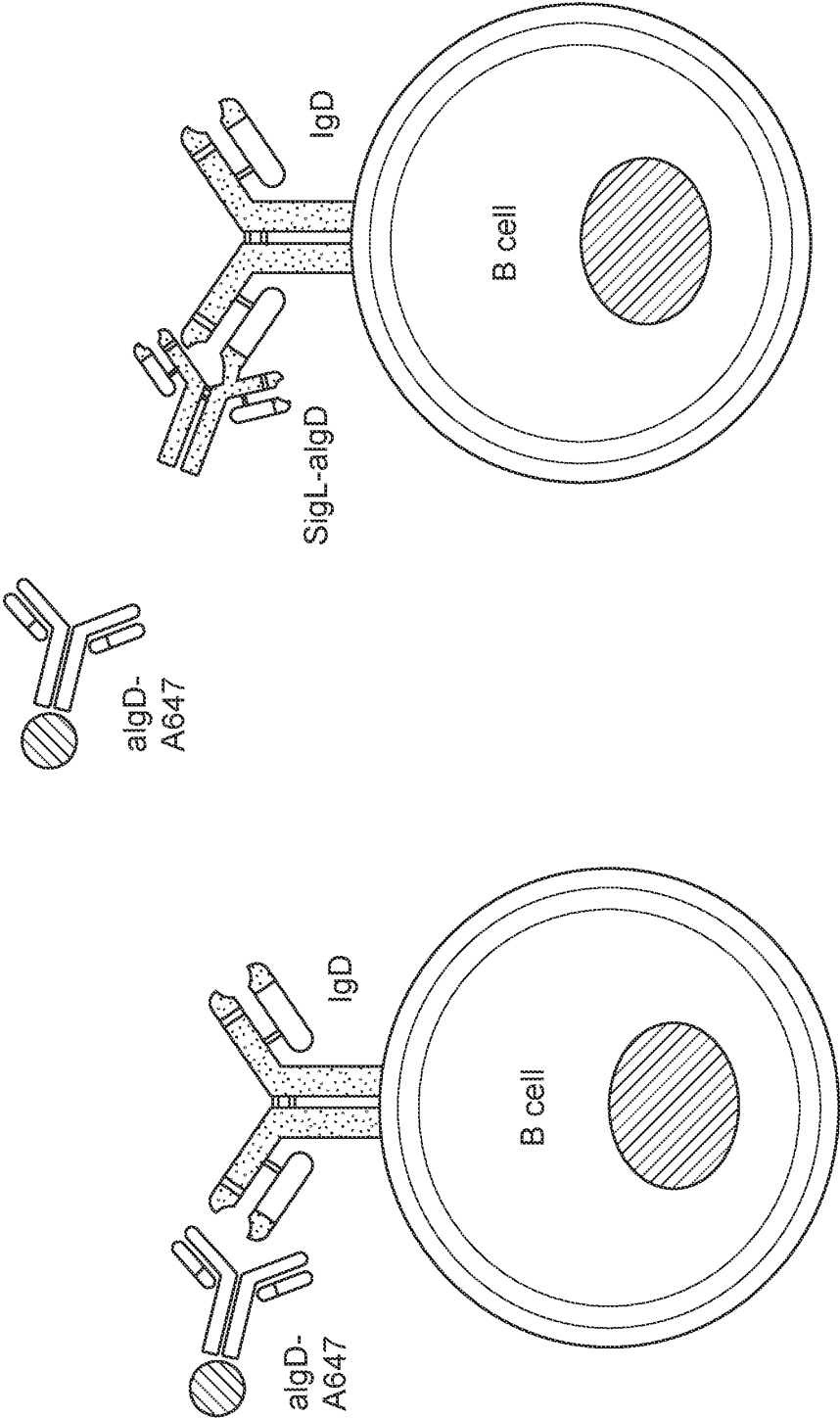
FIG. 13A

Cell Surface Competition Assay



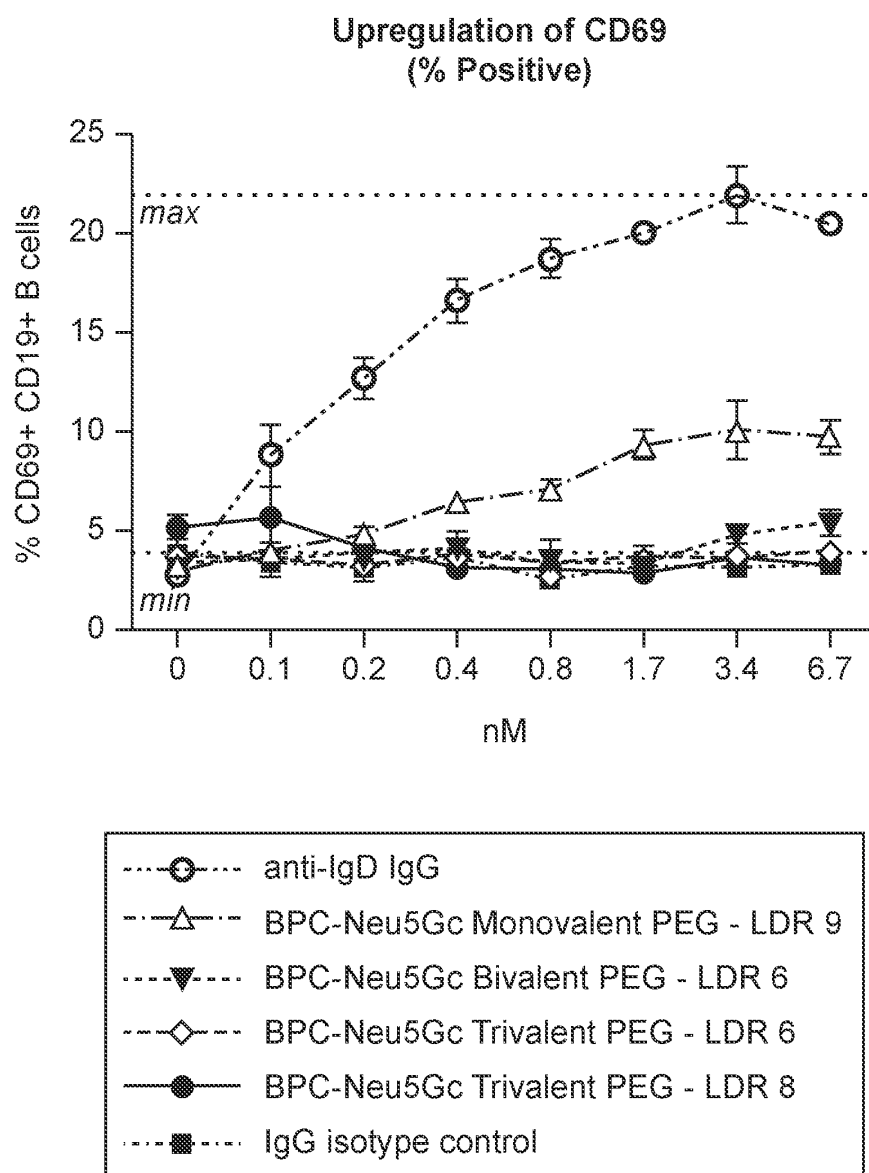
		IC50
—◇—	BPC-Neu5Gc Trivalent GAL - LDR 10	12.4
—●—	BPC-Neu5Gc Trivalent GAL - LDR 5	5.3
—▼—	BPC-Neu5Gc Bivalent GAL - LDR 8	5.5
—△—	BPC-Neu5Gc Monovalent GAL - LDR 8	3.3
—■—	BPC-Neu5Gc Monovalent GAL - LDR 5	2.8
—○—	anti-IgD IgG	2.2

FIG. 13B



21/54

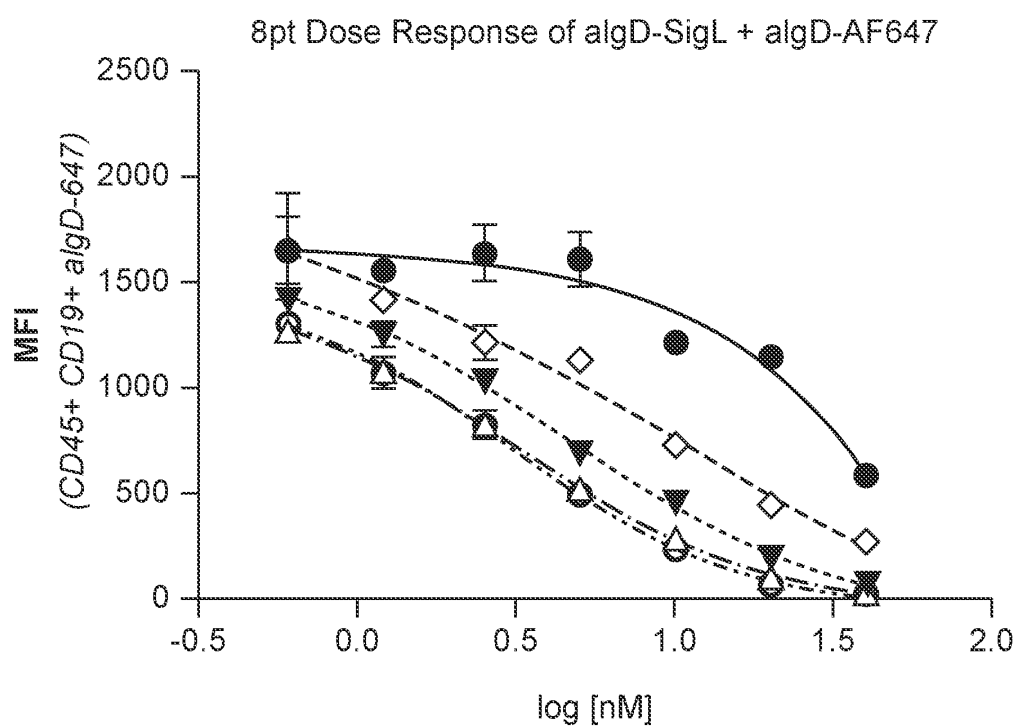
FIG. 14



22/54

FIG. 15

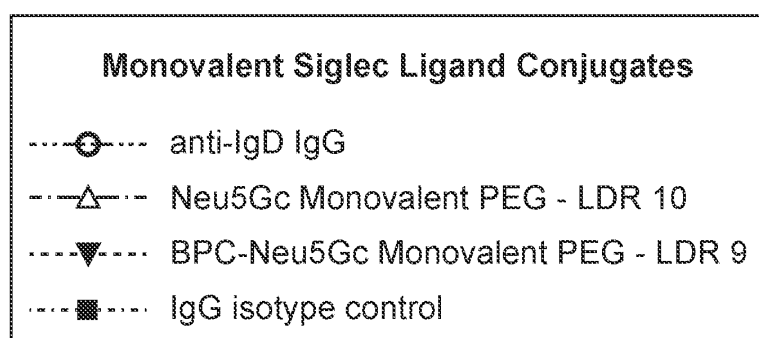
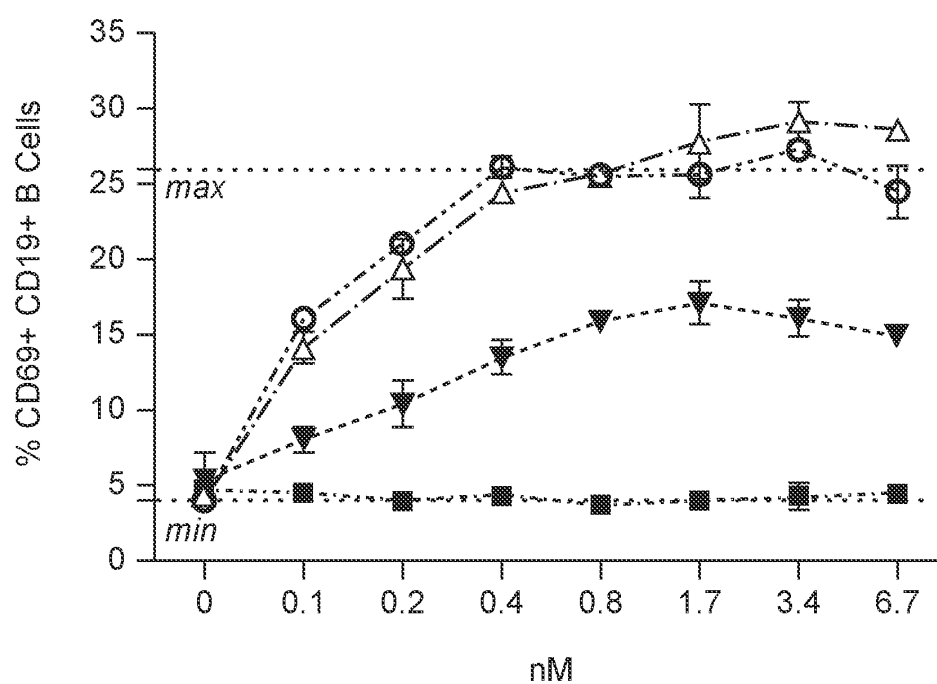
Cell Surface Competition Assay



		<u>IC50</u>
—●—	BPC-Neu5Gc Trivalent PEG - LDR 8	290
---◇---	BPC-Neu5Gc Trivalent PEG - LDR 6	11
.....▼.....	BPC-Neu5Gc Bivalent PEG - LDR 6	5
-·-·△-·-·	BPC-Neu5Gc Monovalent PEG - LDR 9	3
.....○.....	anti-IgD IgG	3

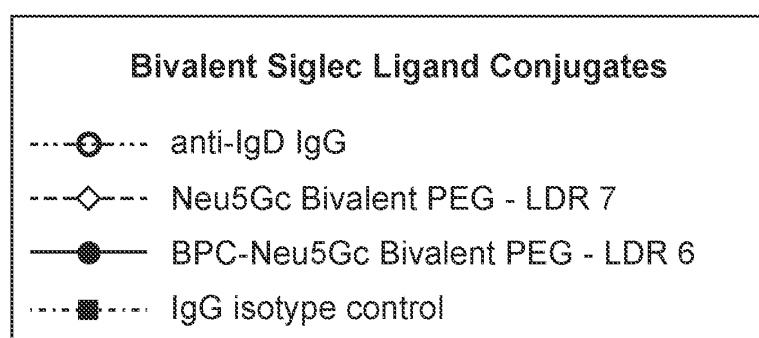
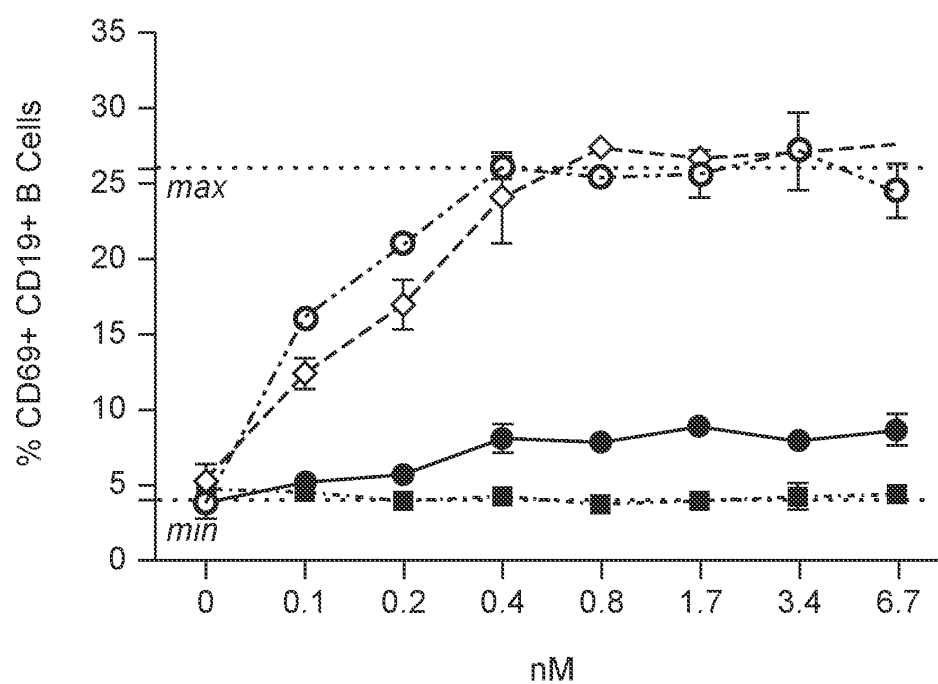
23/54

FIG. 16A

Upregulation of CD69
(% Positive)

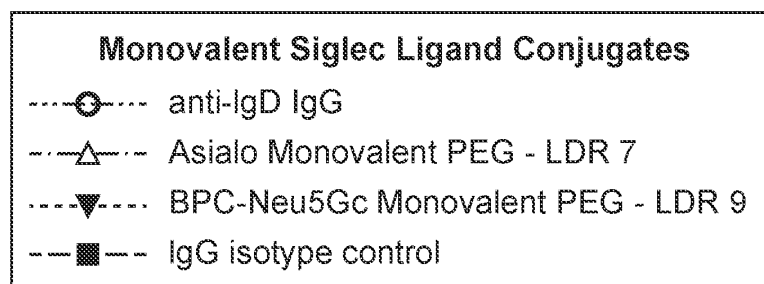
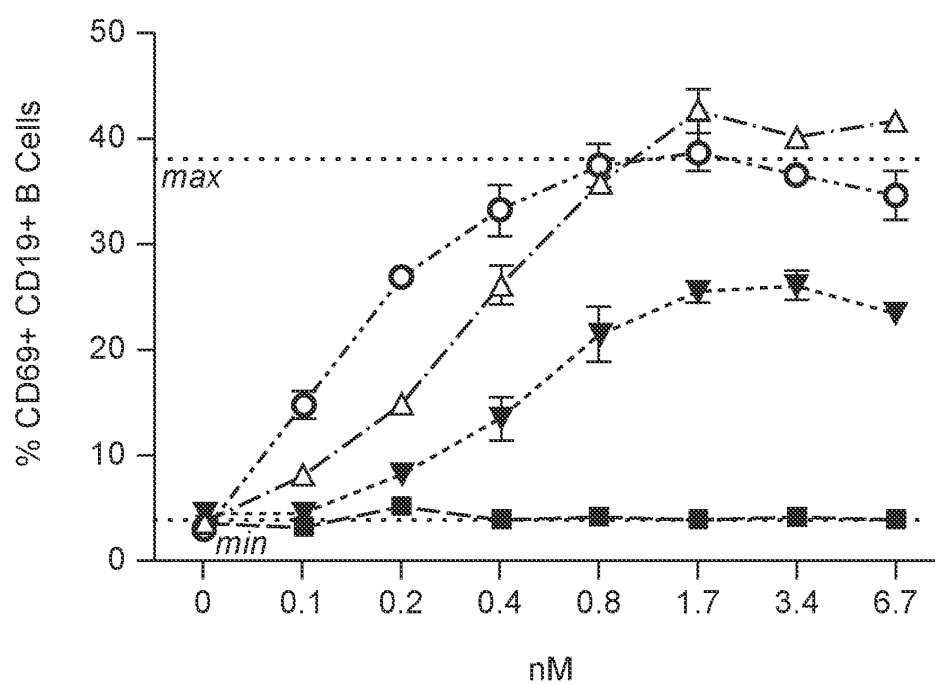
24/54

FIG. 16B

Upregulation of CD69
(% Positive)

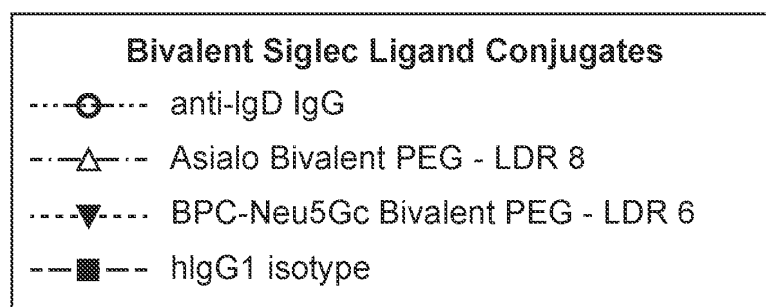
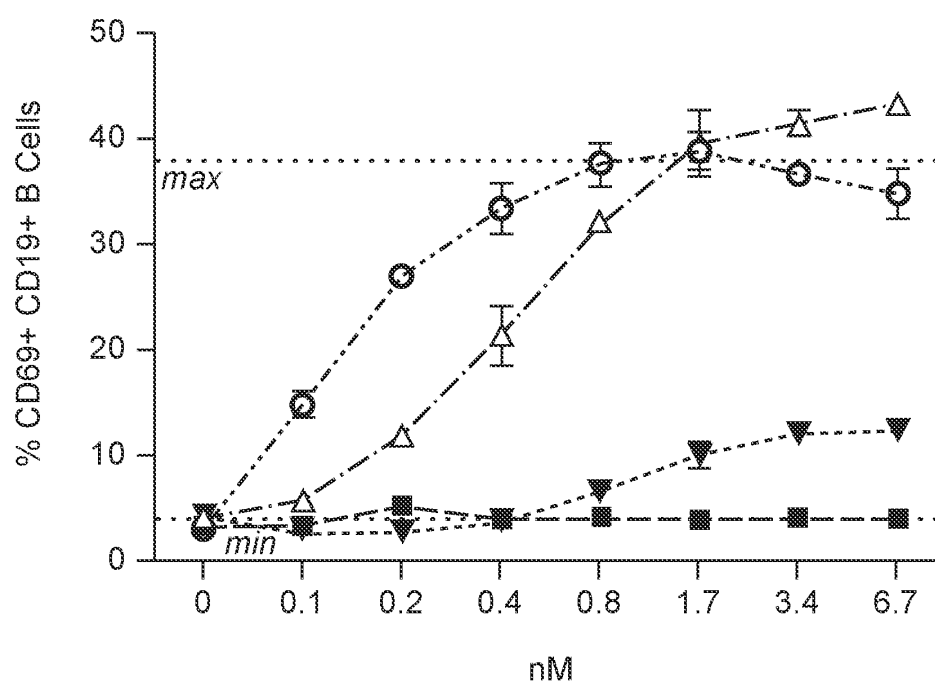
25/54

FIG. 17A

Upregulation of CD69
(% Positive)

26/54

FIG. 17B

Upregulation of CD69
(% Positive)

27/54

FIG. 17C

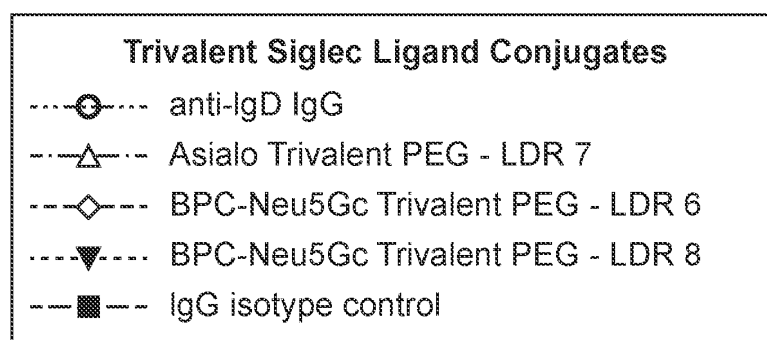
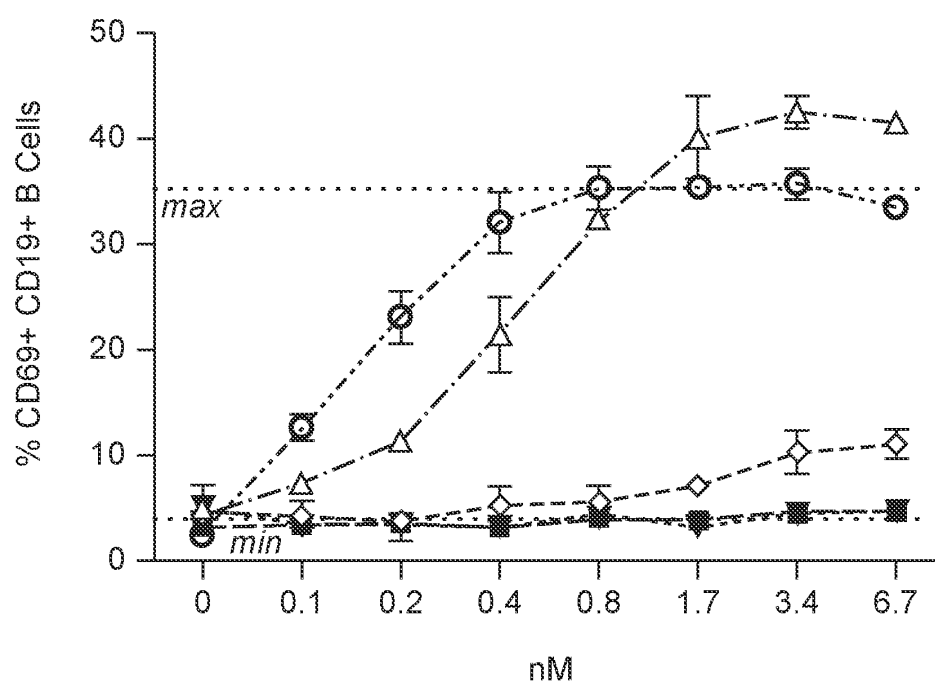
Upregulation of CD69
(% Positive)

FIG. 18A

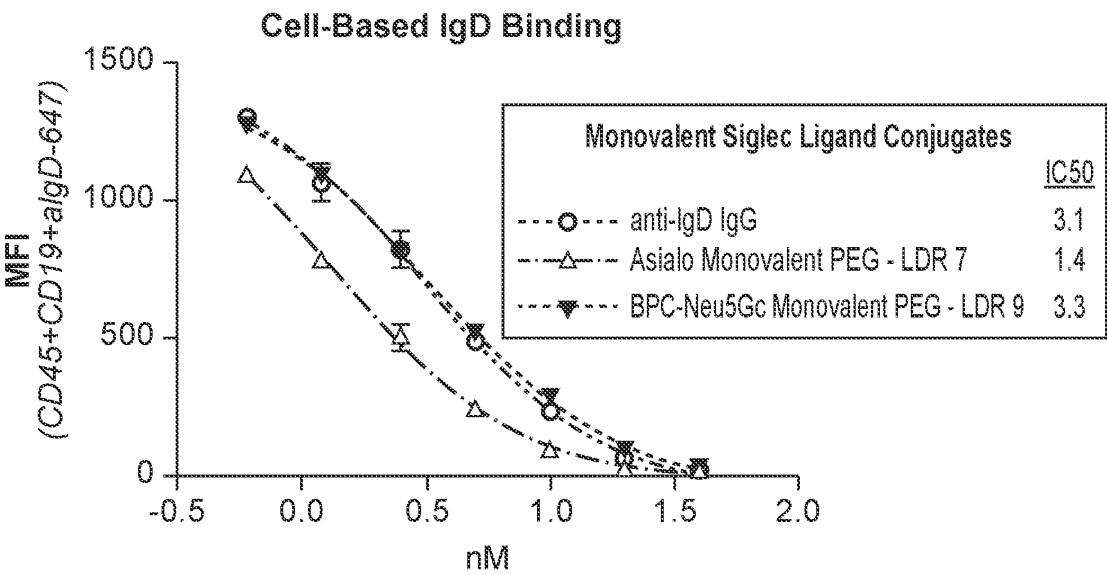
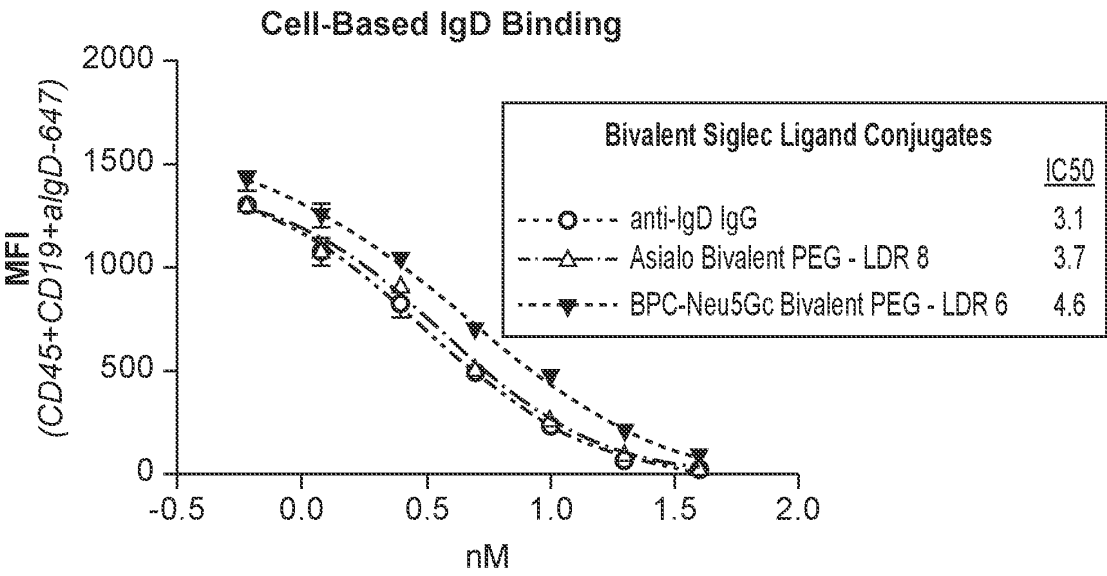


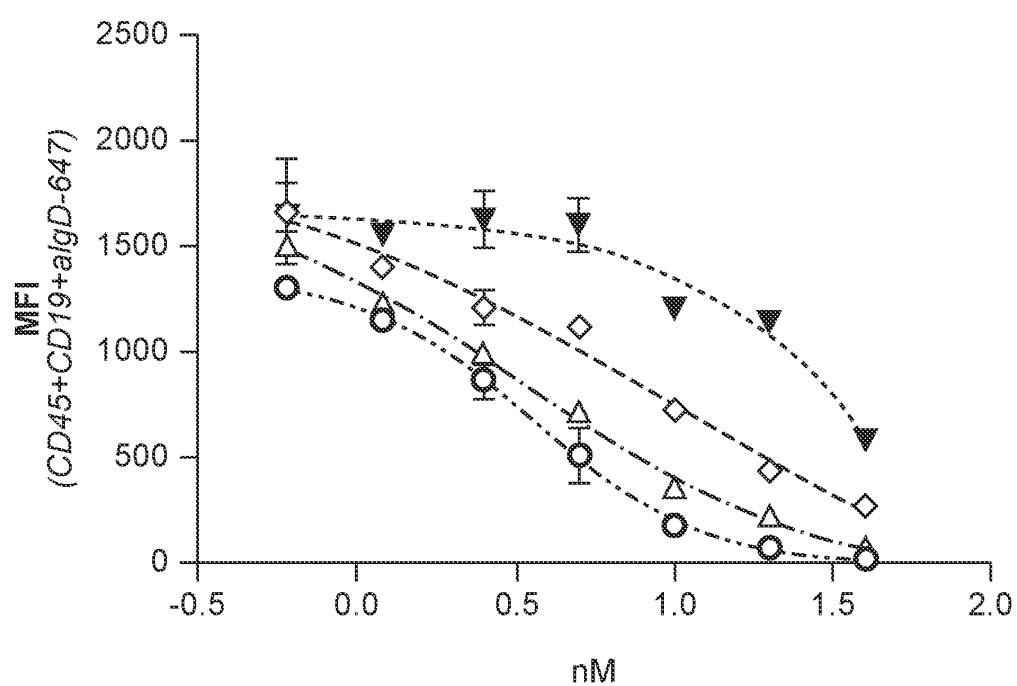
FIG. 18B



29/54

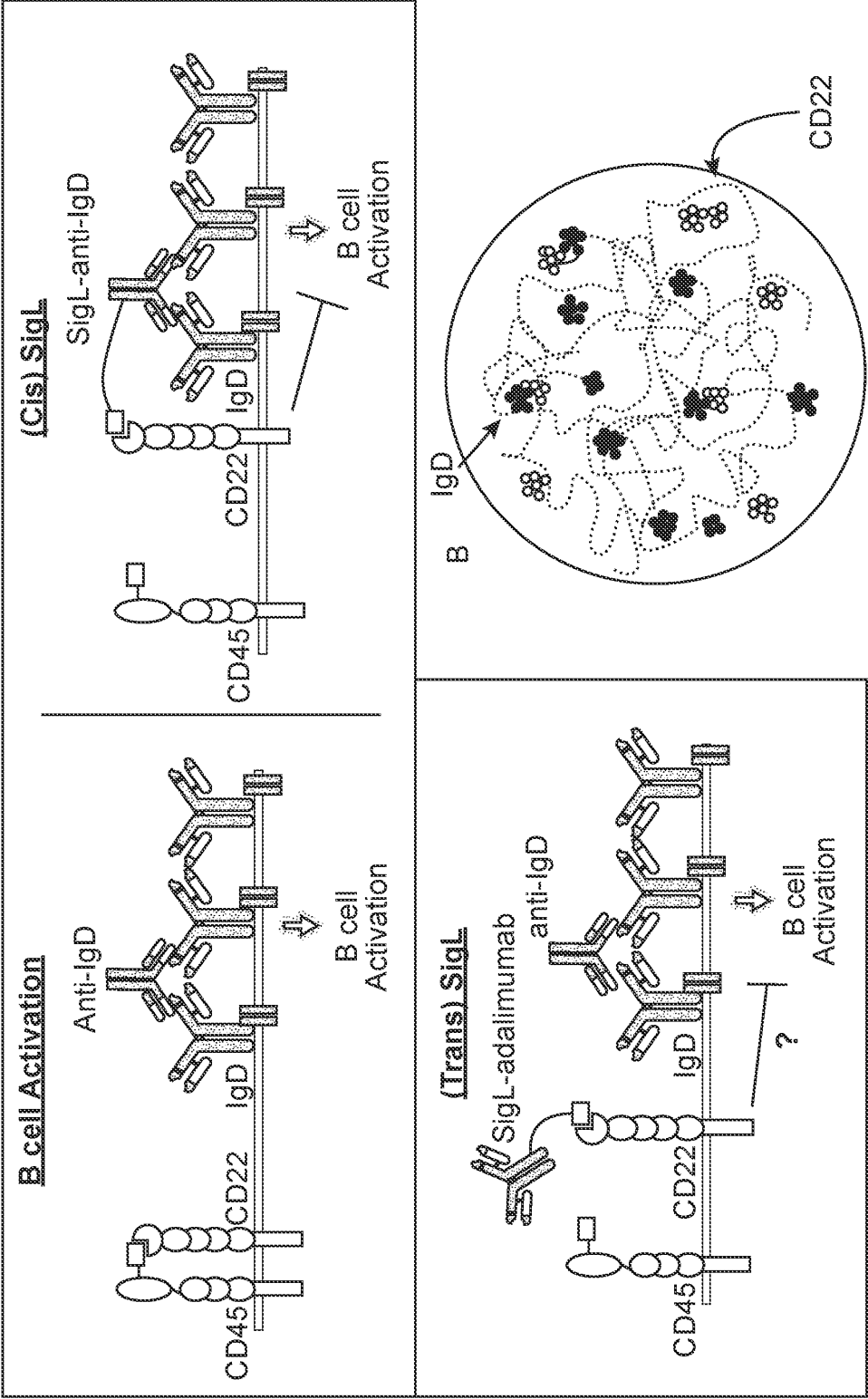
FIG. 18C

Cell-Based IgD Binding



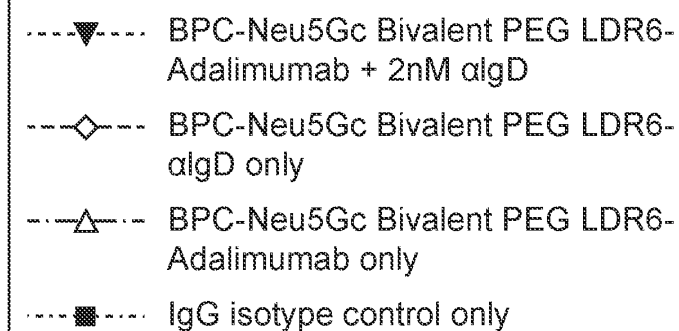
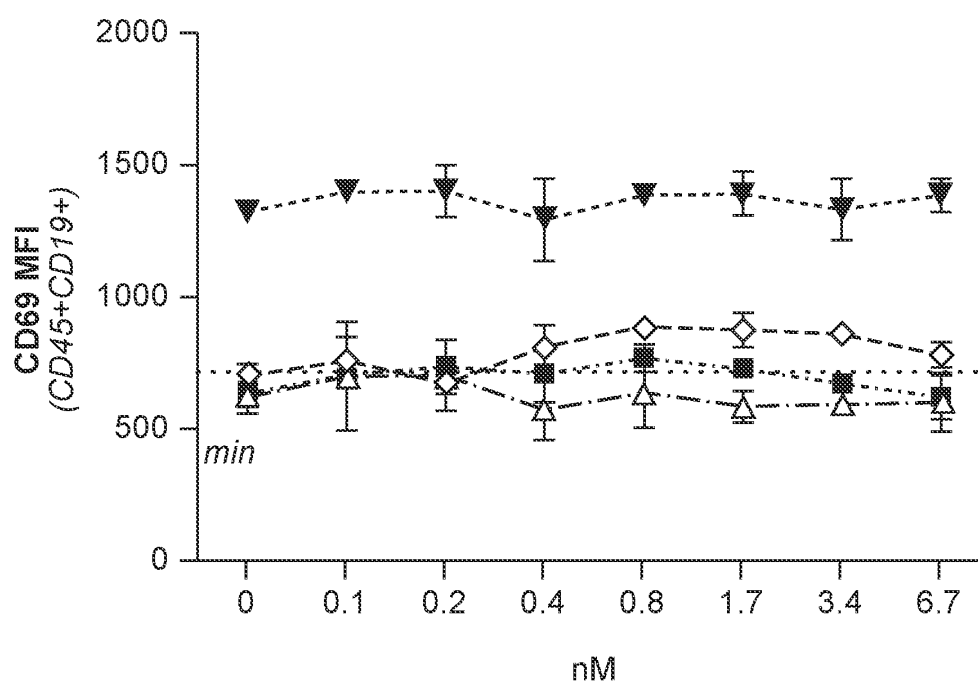
Trivalent Siglec Ligand Conjugates		IC50
---●---	anti-IgD IgG	4
---△---	Asialo Trivalent PEG - LDR 7	3
---◇---	BPC-Neu5Gc Trivalent PEG - LDR 6	11
---▼---	BPC-Neu5Gc Trivalent PEG - LDR 8	290

FIG. 19A



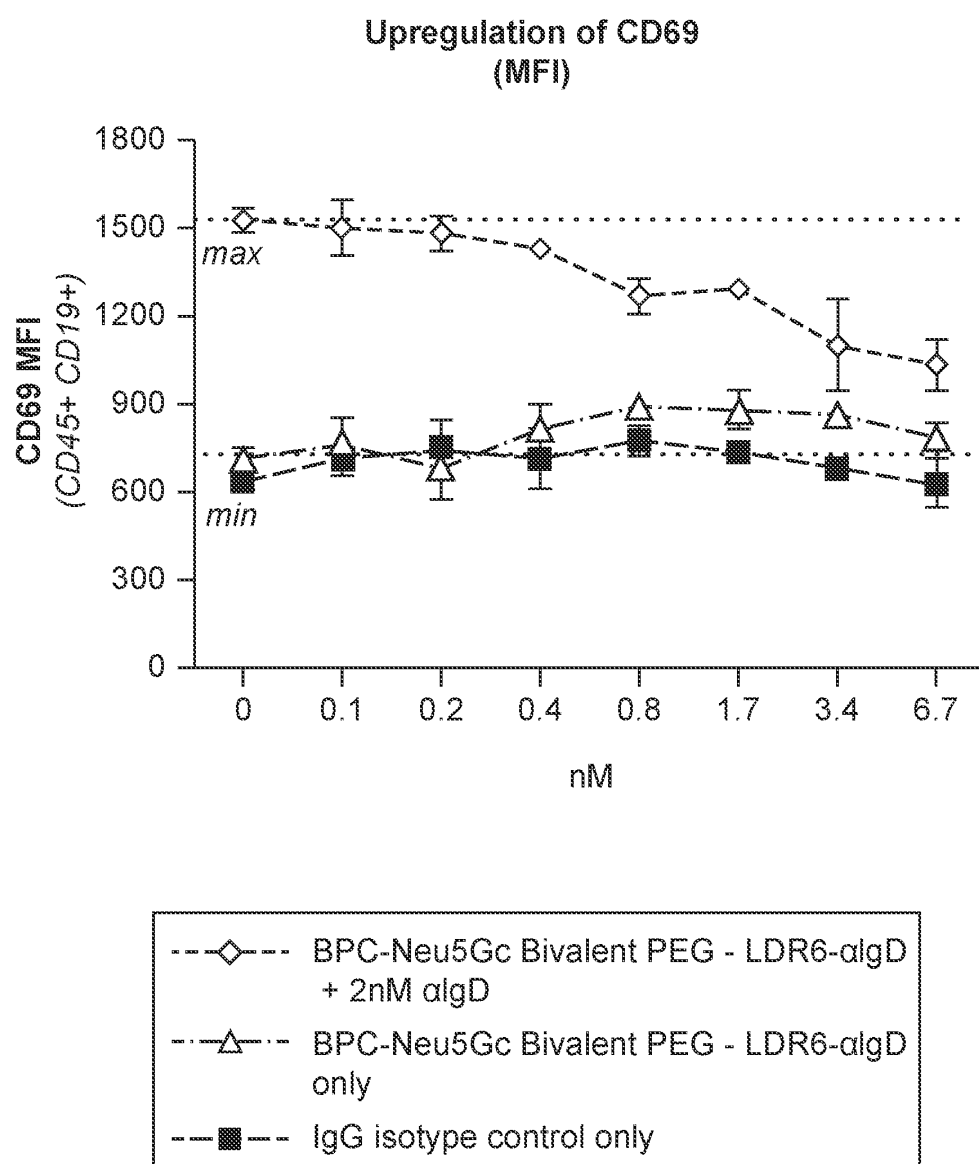
31/54

FIG. 19B

Upregulation of CD69
(MFI)

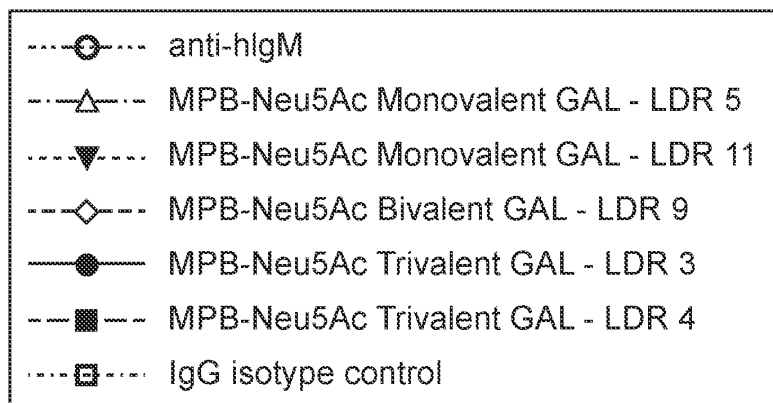
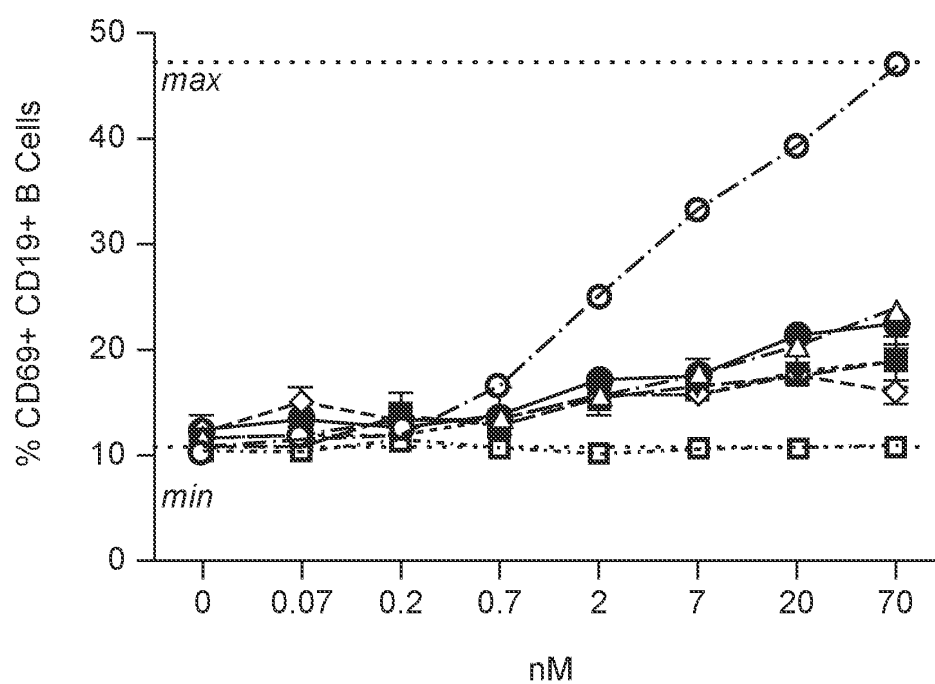
32/54

FIG. 20



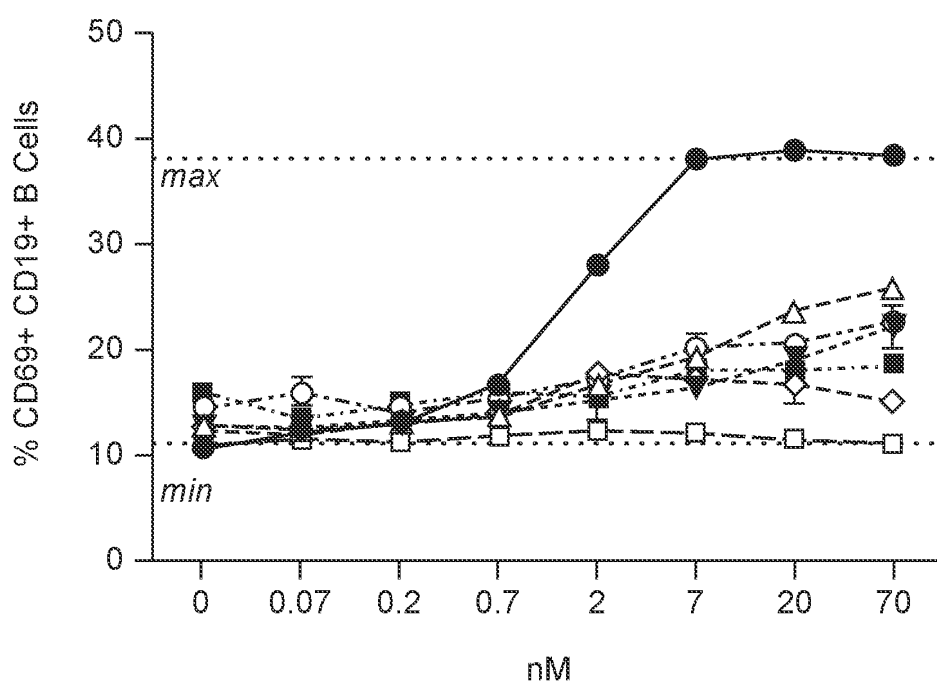
33/54

FIG. 21A

Upregulation of CD69
(% Positive)

34/54

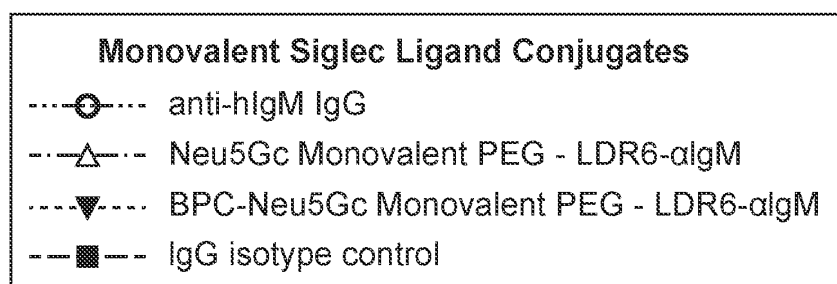
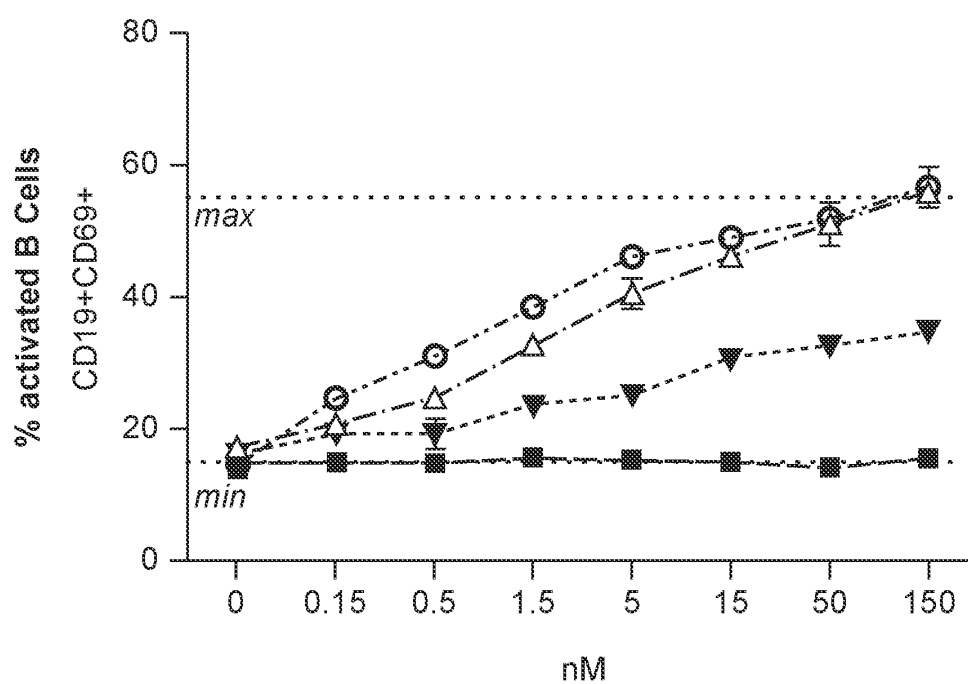
FIG. 21B

Upregulation of CD69
(% Positive)**PEG Linker Conjugates**

- anti-hIgM
- - -△- - - MPB-Neu5Ac Monovalent PEG - LDR 5
- - -▼- - - MPB-Neu5Ac Monovalent PEG - LDR 11
- - -◇- - - MPB-Neu5Ac Bivalent PEG - LDR 9
- - -○- - - MPB-Neu5Ac Trivalent PEG - LDR 3
- - -■- - - MPB-Neu5Ac Trivalent PEG - LDR 4
- - -□- - - IgG isotype control

35/54

FIG. 22A

Upregulation of CD69
(% Positive)

36/54

FIG. 22B

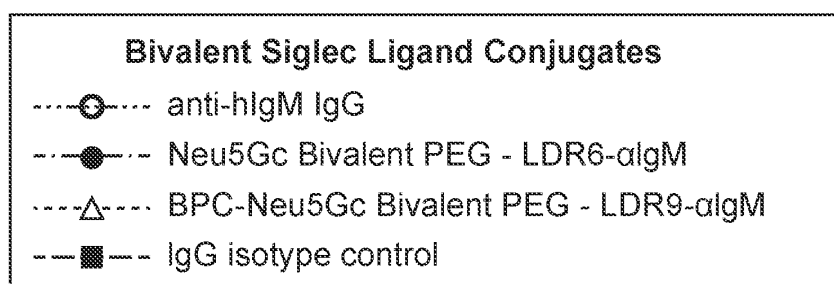
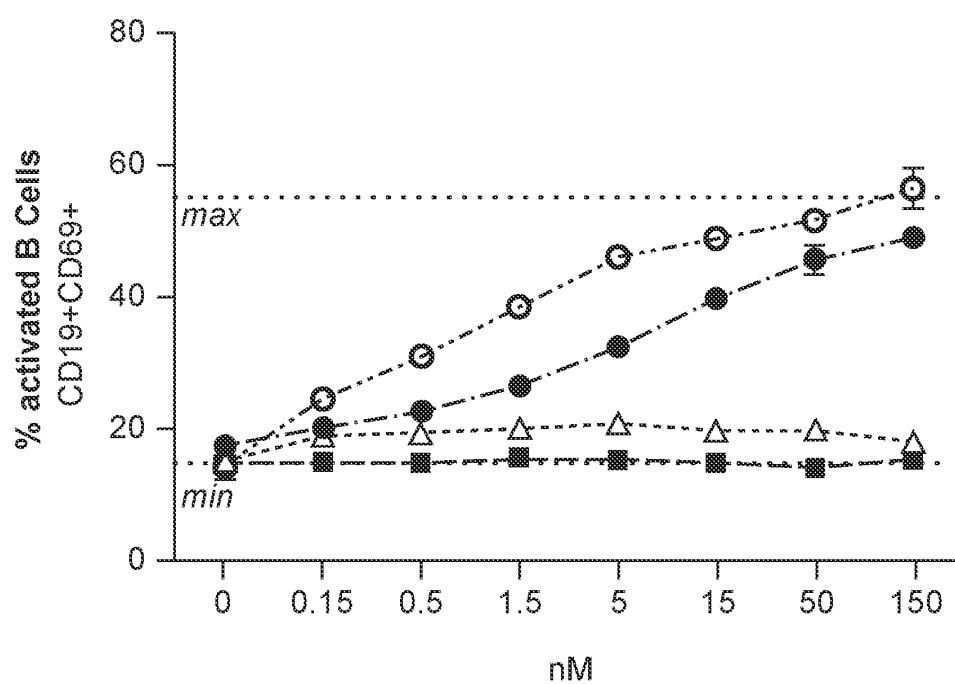
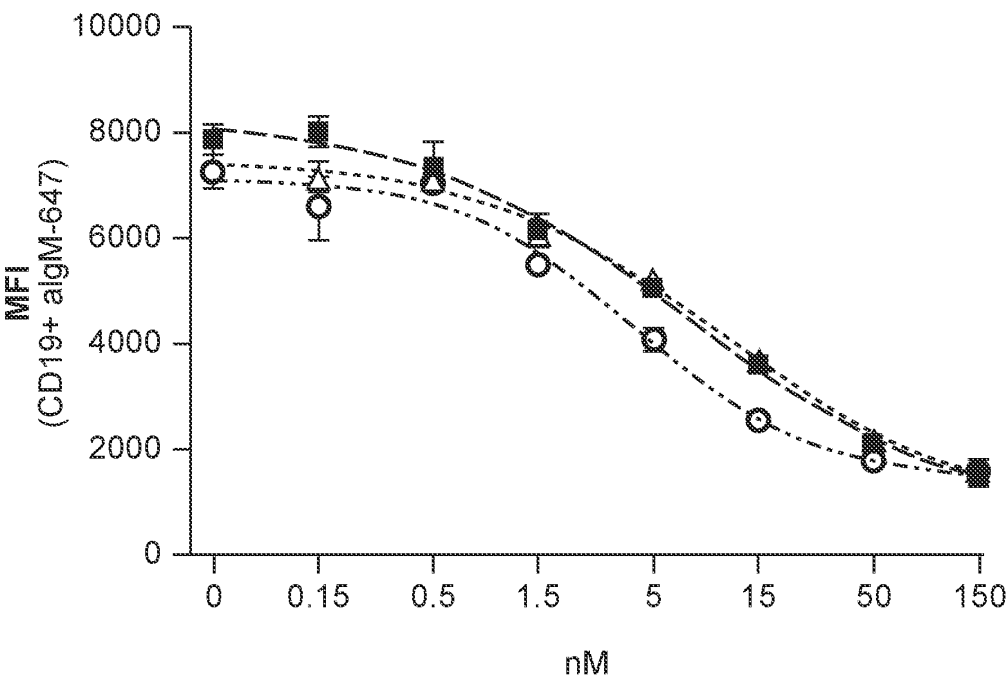
Upregulation of CD69
(% Positive)

FIG. 23A

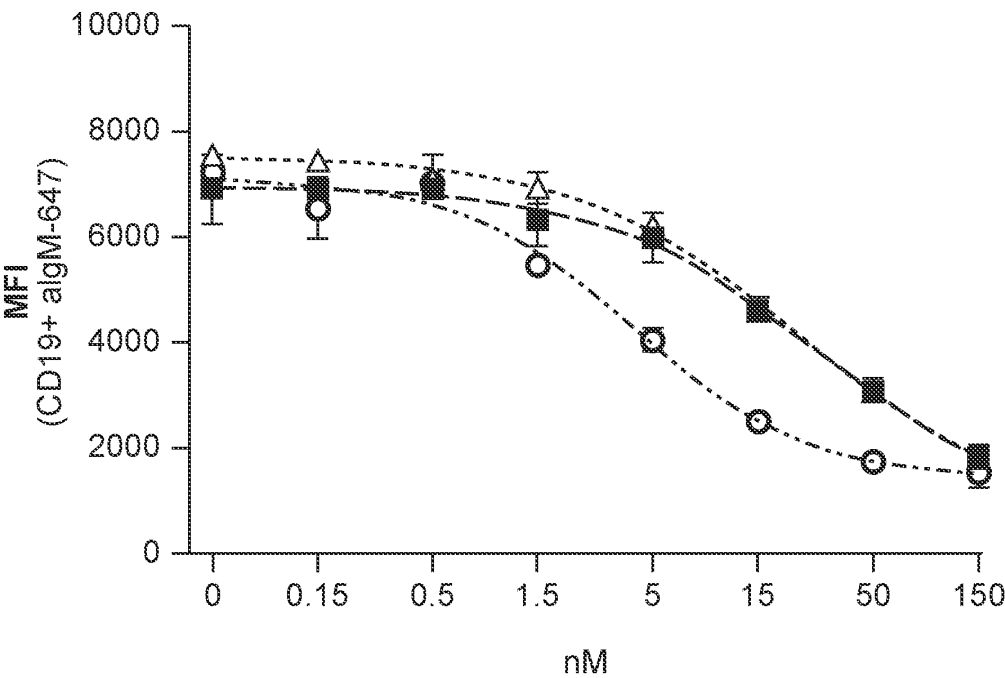
Cell-Based IgM Binding



Monovalent Siglec Ligand Conjugates		IC50 (nM)
---■---	BPC-Neu5Gc Monovalent PEG - LDR 5-algM	7
---△---	Neu5Gc Monovalent PEG - LDR6-algM	11
---○---	anti-hIgM	4

FIG. 23B

Cell-Based IgM Binding



Bivalent Siglec Ligand Conjugates		IC50 (nM)
---■---	BPC-Neu5Gc Bivalent PEG LDR9-algM	29
---△---	Neu5Gc Bivalent PEG LDR6-algM	23
---○---	anti-hlgM	4

39/54

FIG. 24A

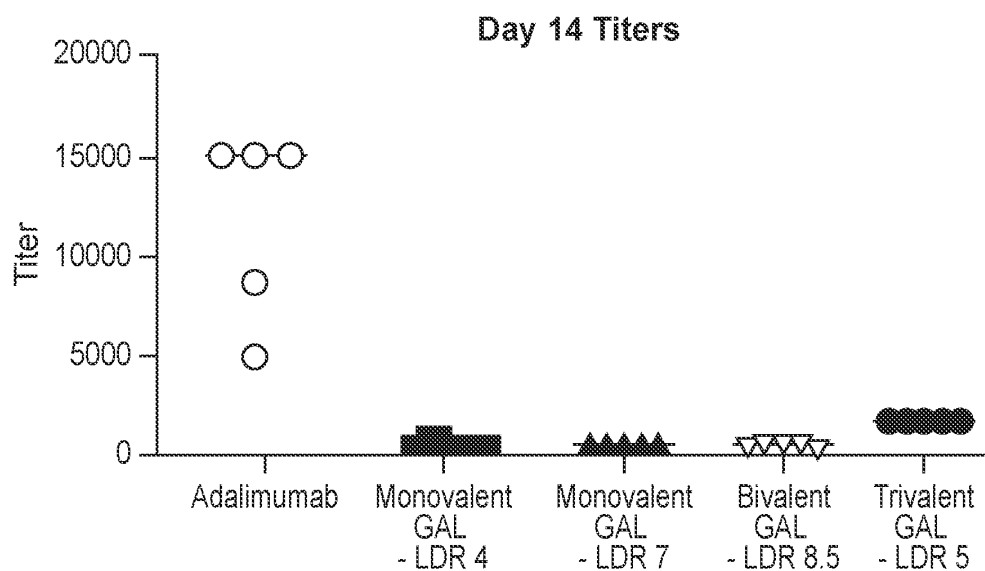
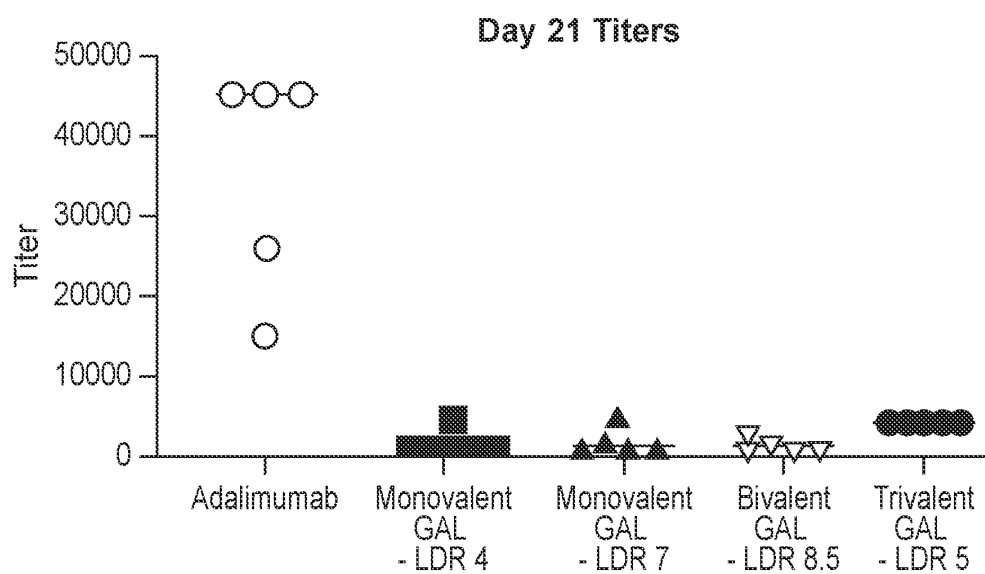


FIG. 24B



40/54

FIG. 24C

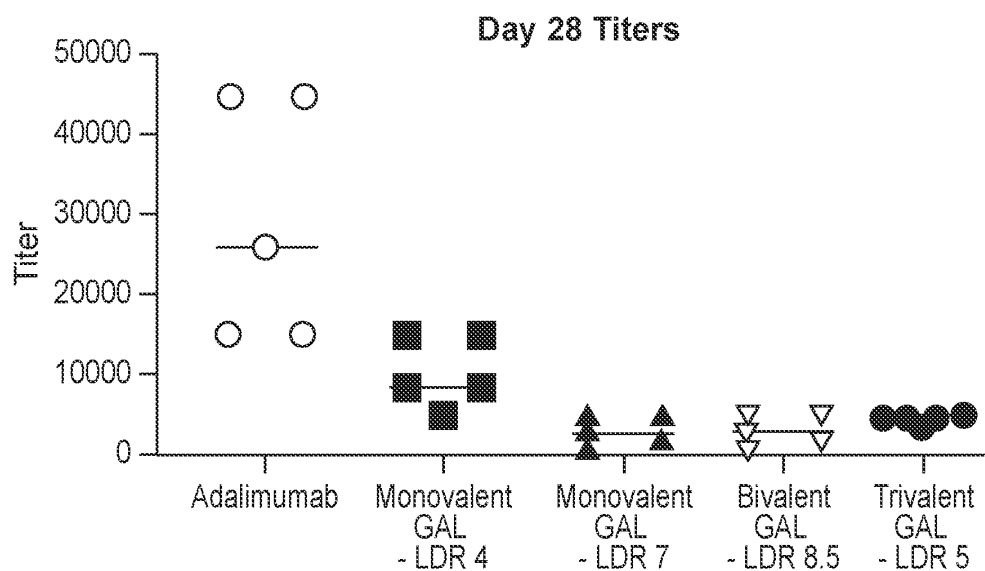
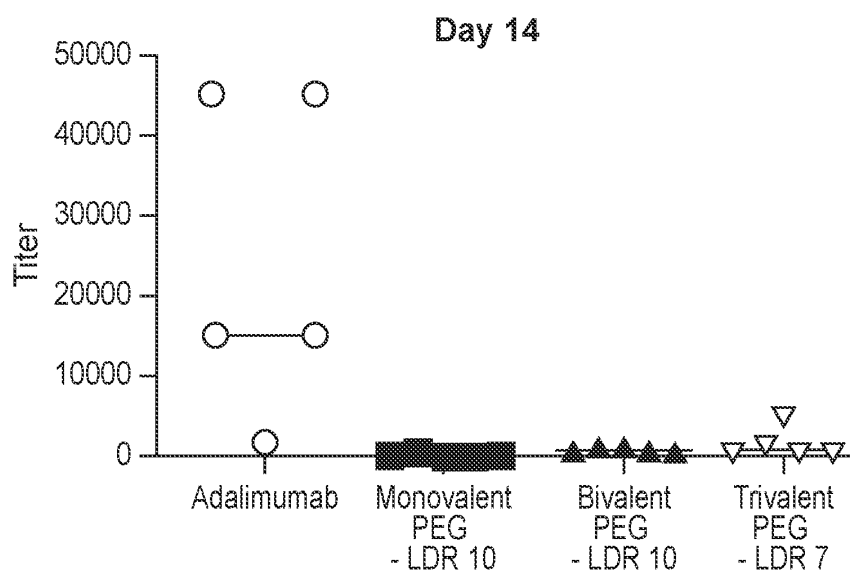


FIG. 25A



41/54

FIG. 25B

Day 21

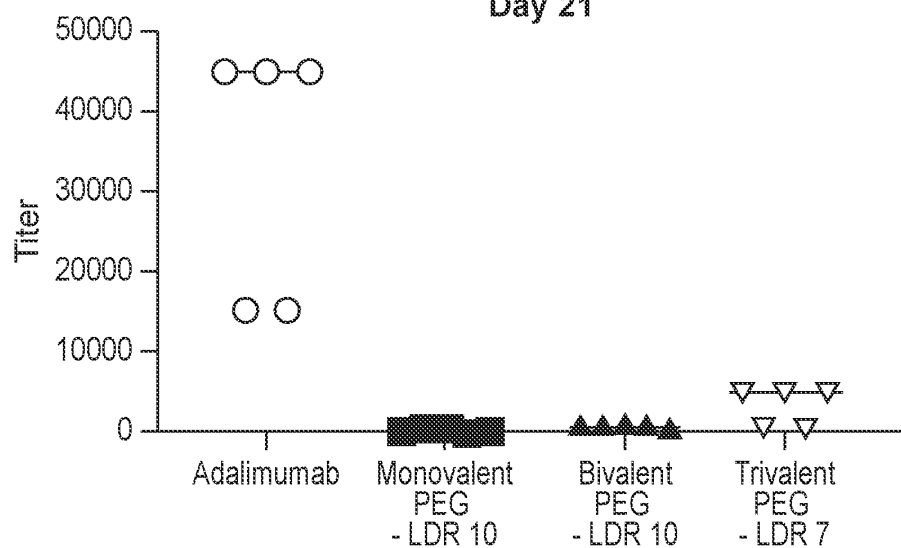
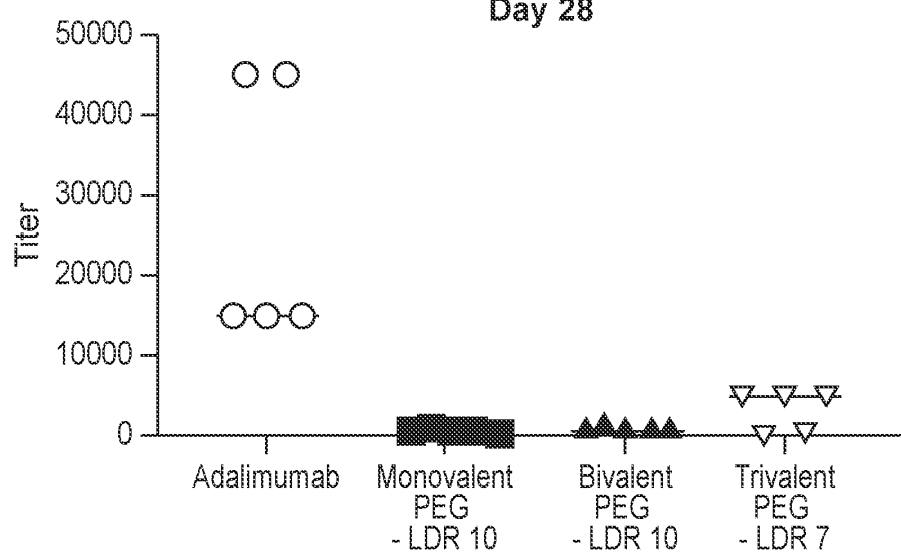


FIG. 25C

Day 28



42/54

FIG. 26A

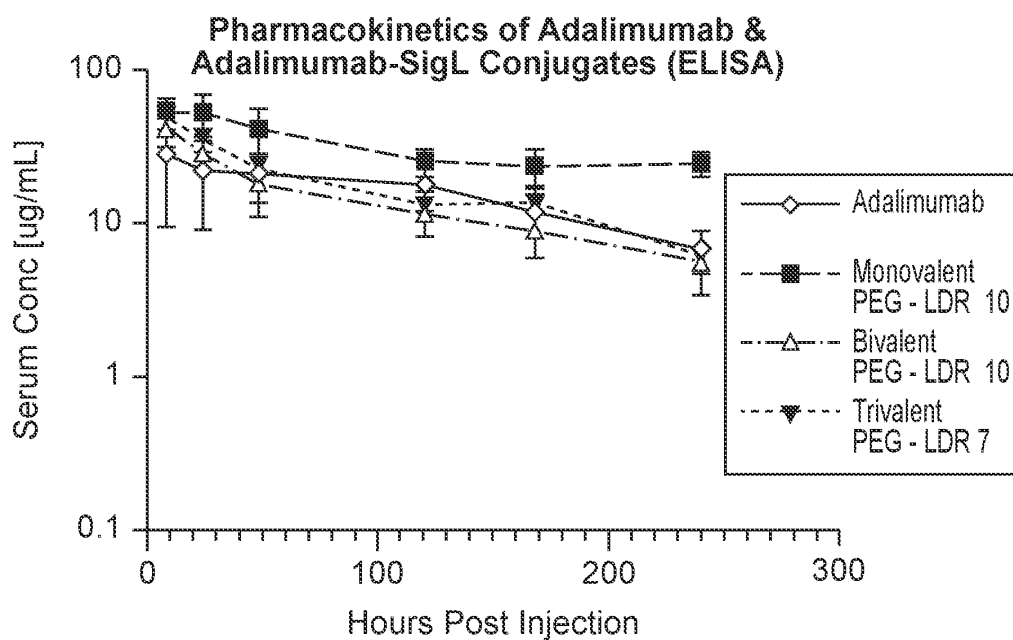
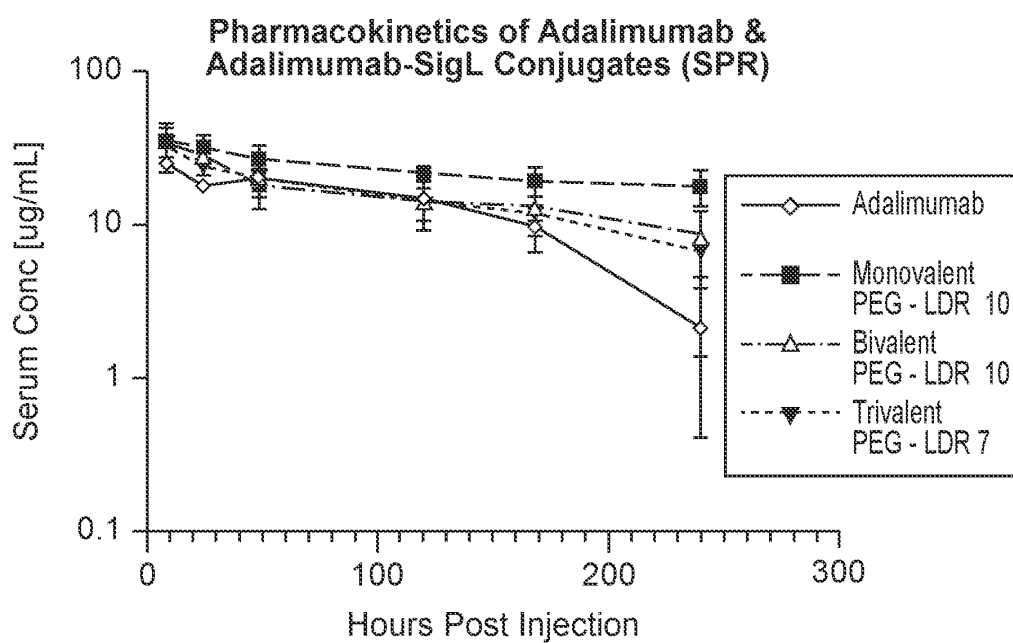
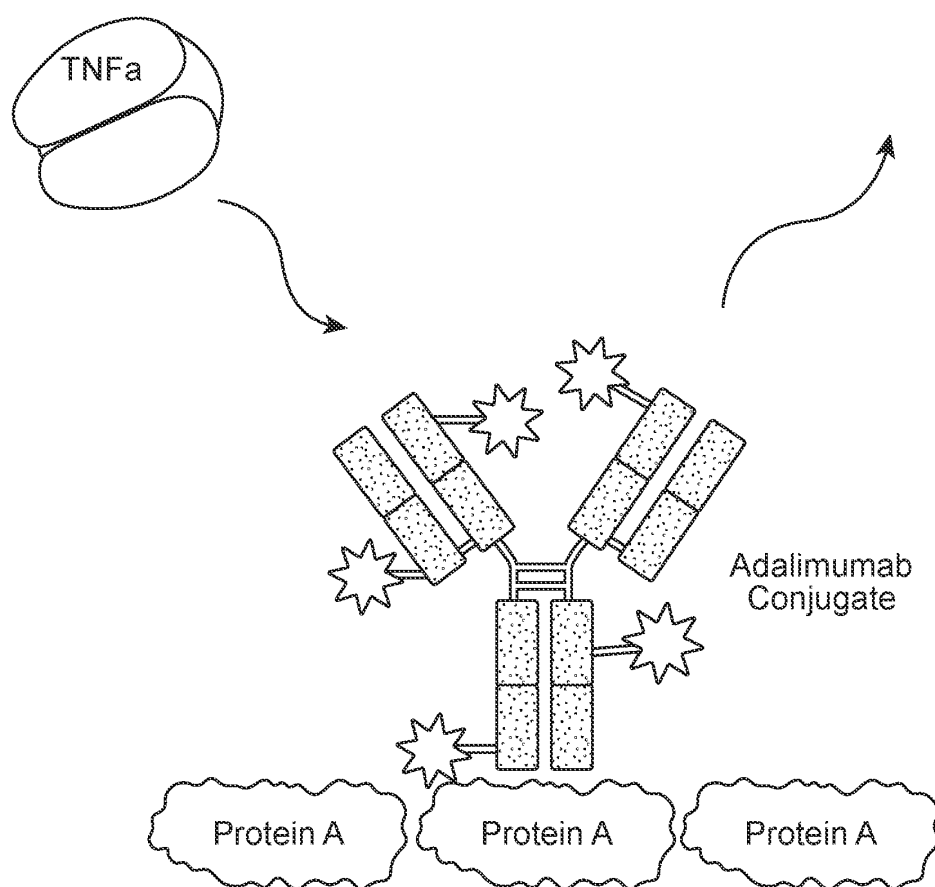


FIG. 26B



43/54

FIG. 27A



44/54

FIG. 27B

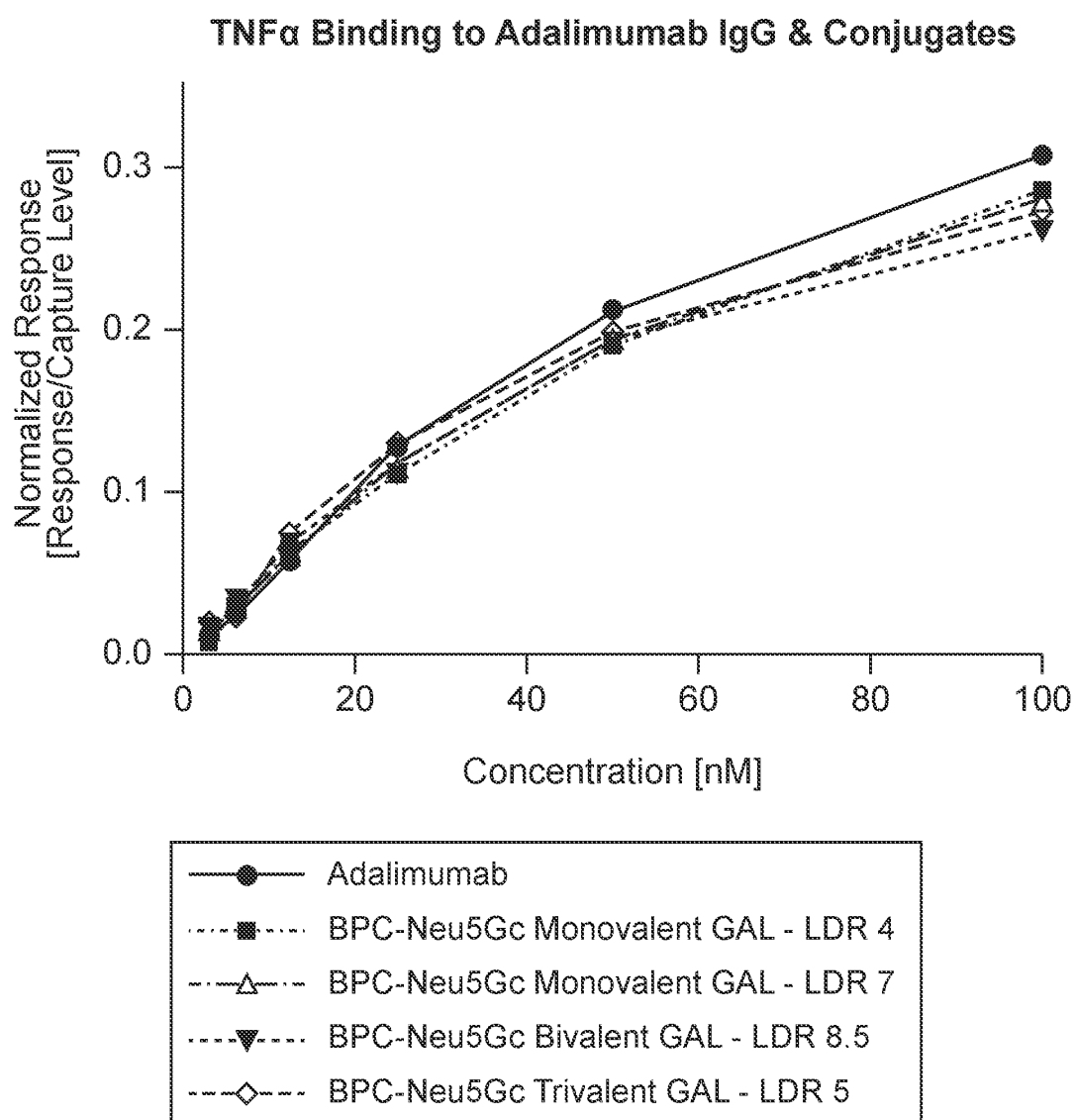


FIG. 27C

Adalimumab

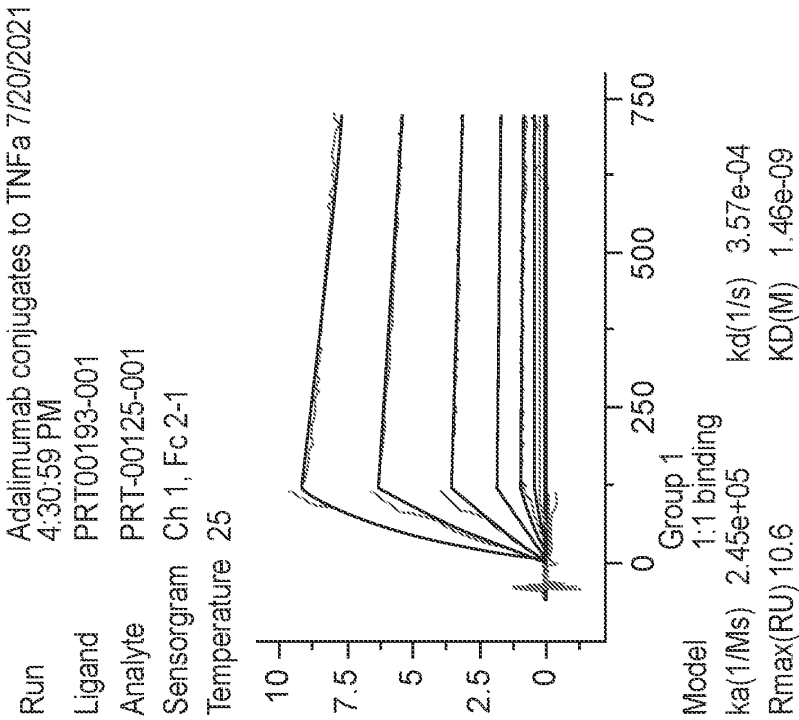


FIG. 27D

Adalimumab
BPC-Neu5Gc
Monovalent GAL LDR 4

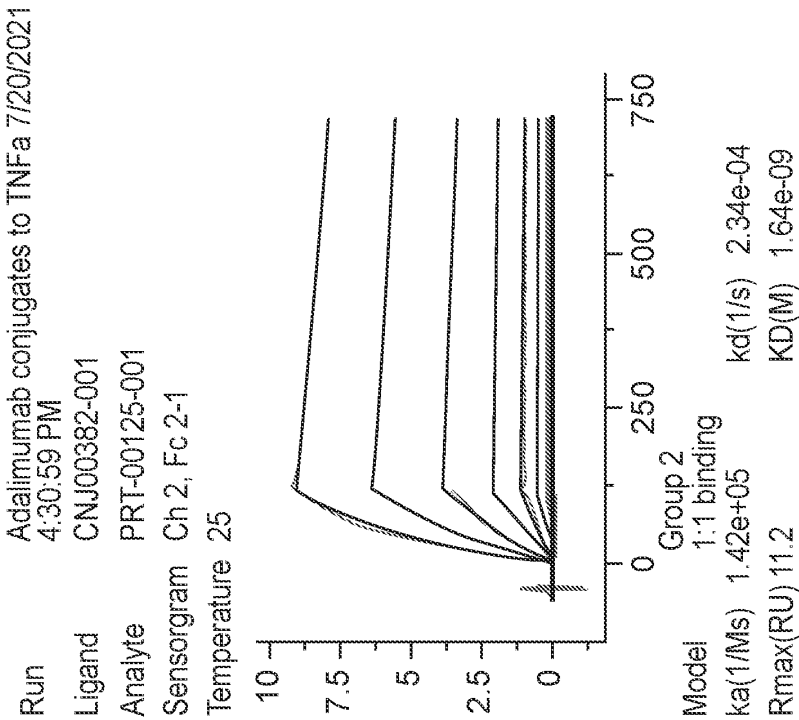


FIG. 27E

Adalimumab
BPC-Neu5Gc
Monovalent GAL LDR 7

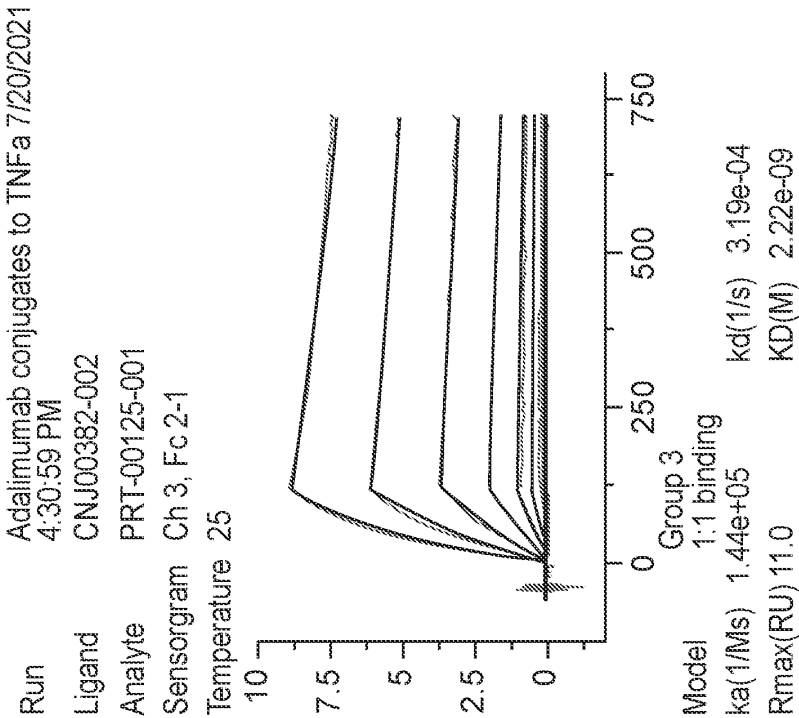
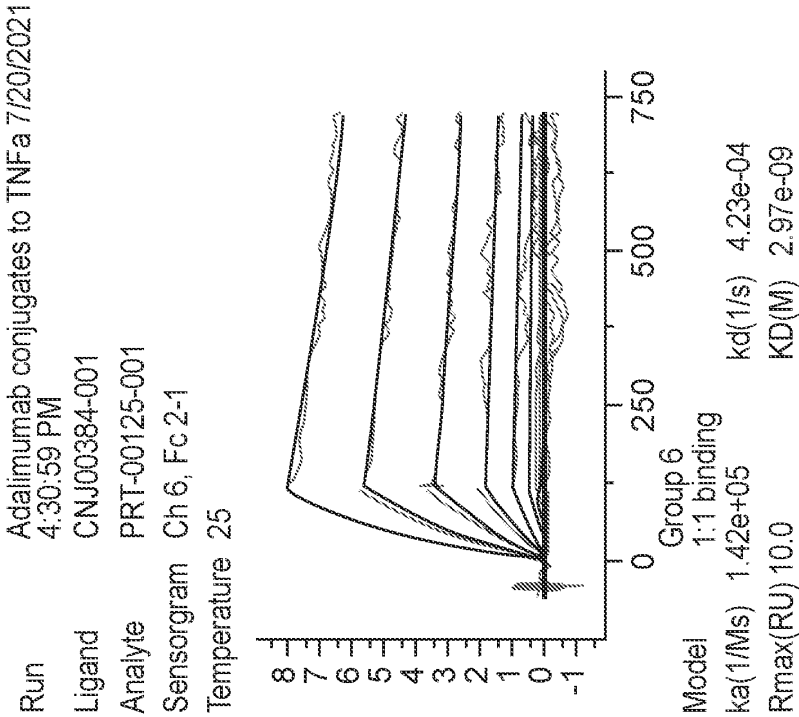


FIG. 27F

Adalimumab
BPC-Neu5Gc
Bivalent GAL LDR 8.5

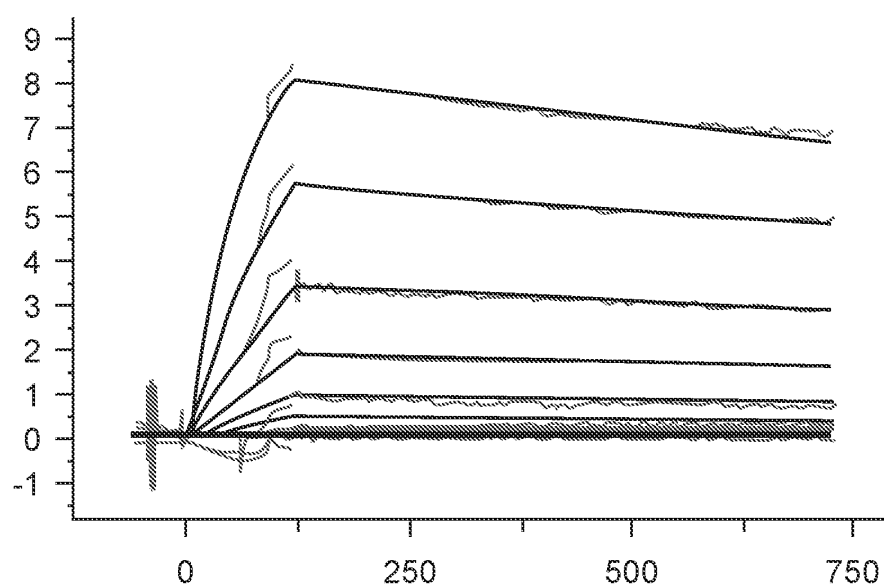


47/54

FIG. 27G

Adalimumab
BPC-Neu5Gc
Trivalent GAL LDR 5

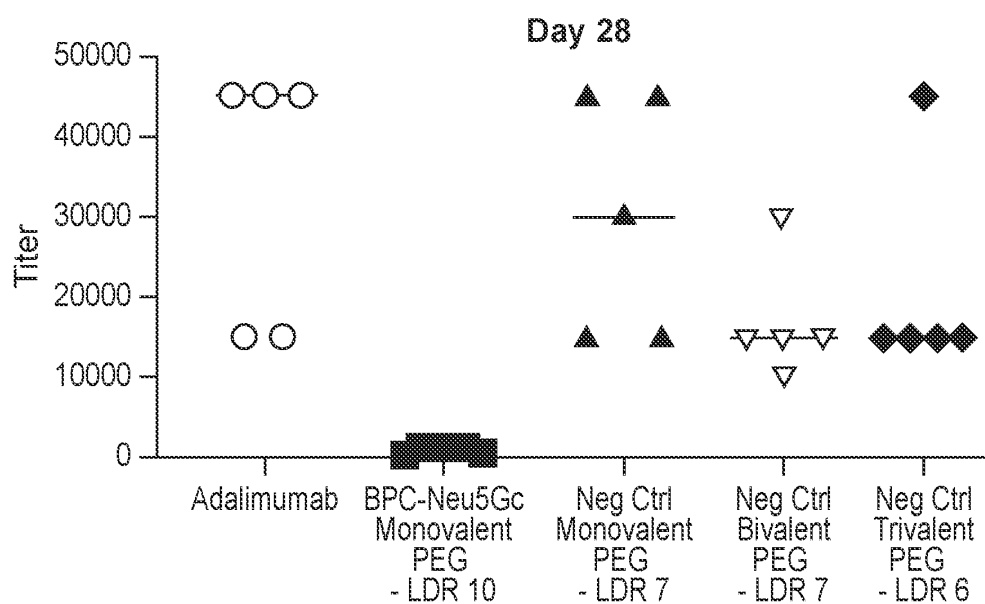
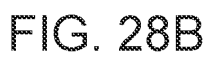
Run Adalimumab conjugates to TNFa 7/20/2021
4:30:59 PM
Ligand CNJ00390-001
Analyte PRT-00125-001
Sensorgram Ch 8, Fc 2-1
Temperature 25



Model Group 8
1:1 binding
ka(1/Ms) 1.95e+05 kd(1/s) 3.55e-04
Rmax(RU) 9.4 KD (M) 1.82e-09

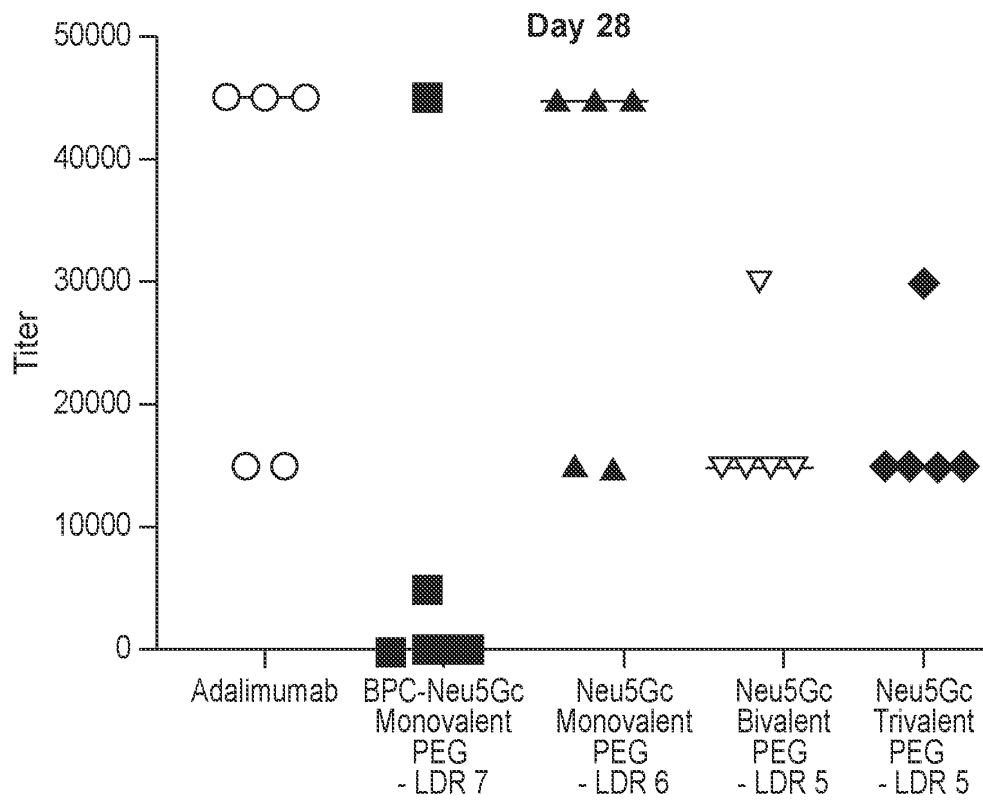
SUBSTITUTE SHEET (RULE 26)

FIG. 28A



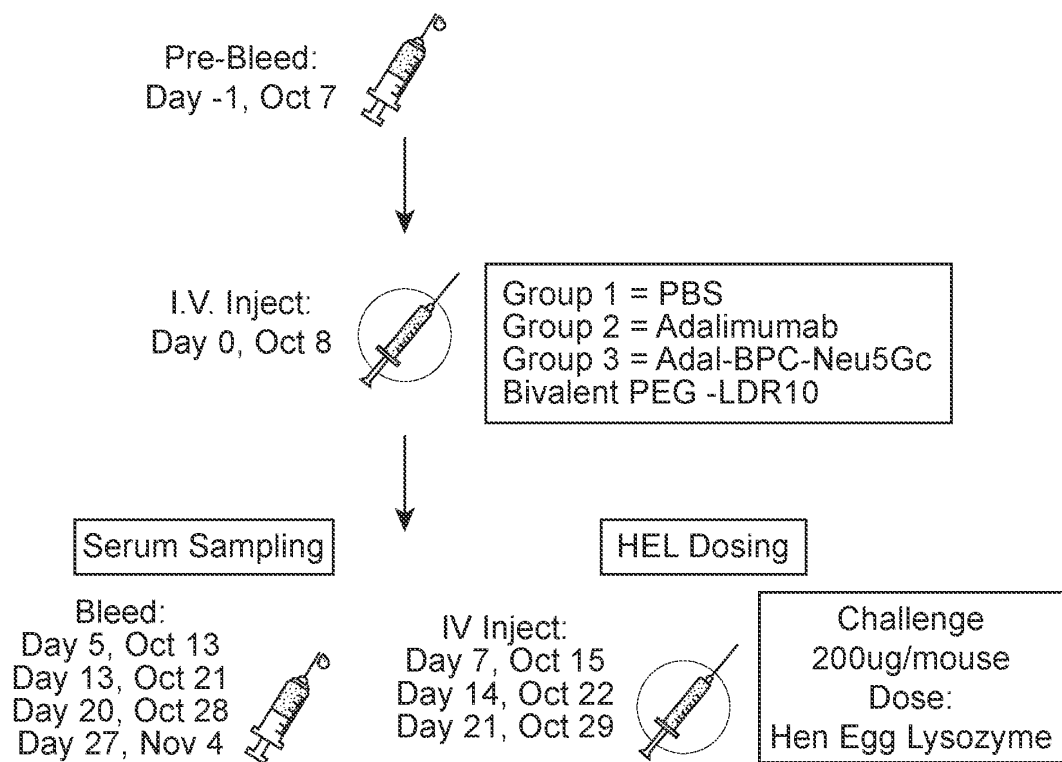
49/54

FIG. 29



50/54

FIG. 30A



51/54

FIG. 30B

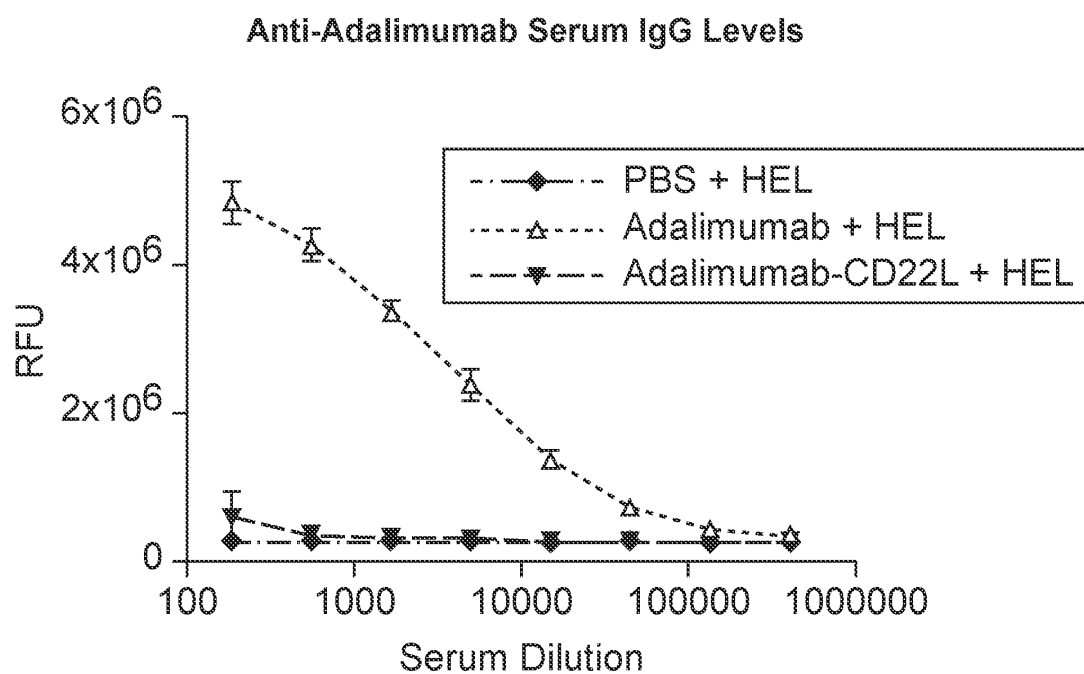
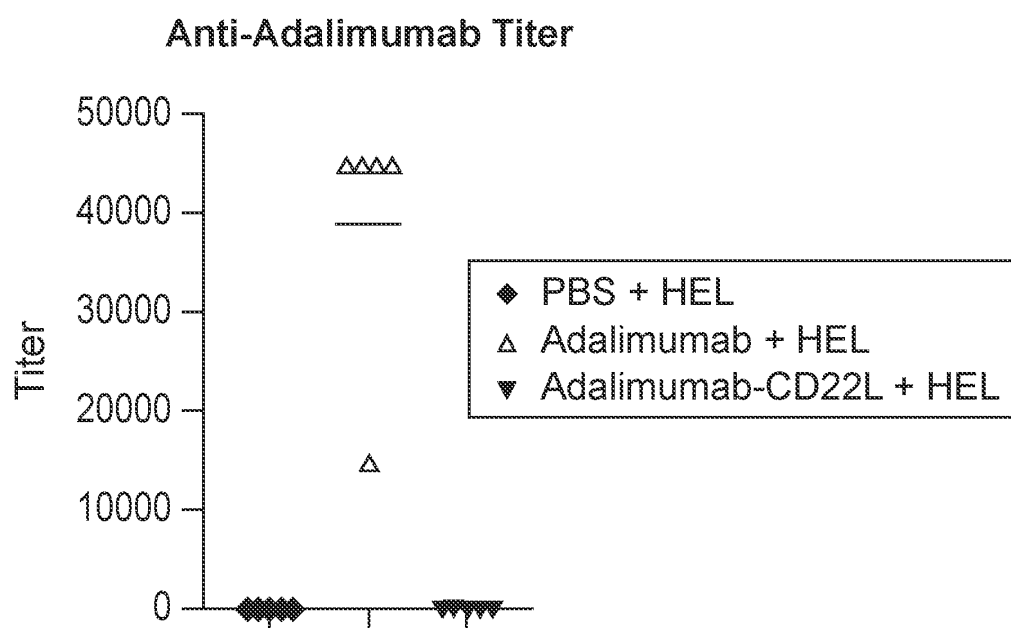


FIG. 30C



52/54

FIG. 30D

Anti-HEL Serum IgG Levels

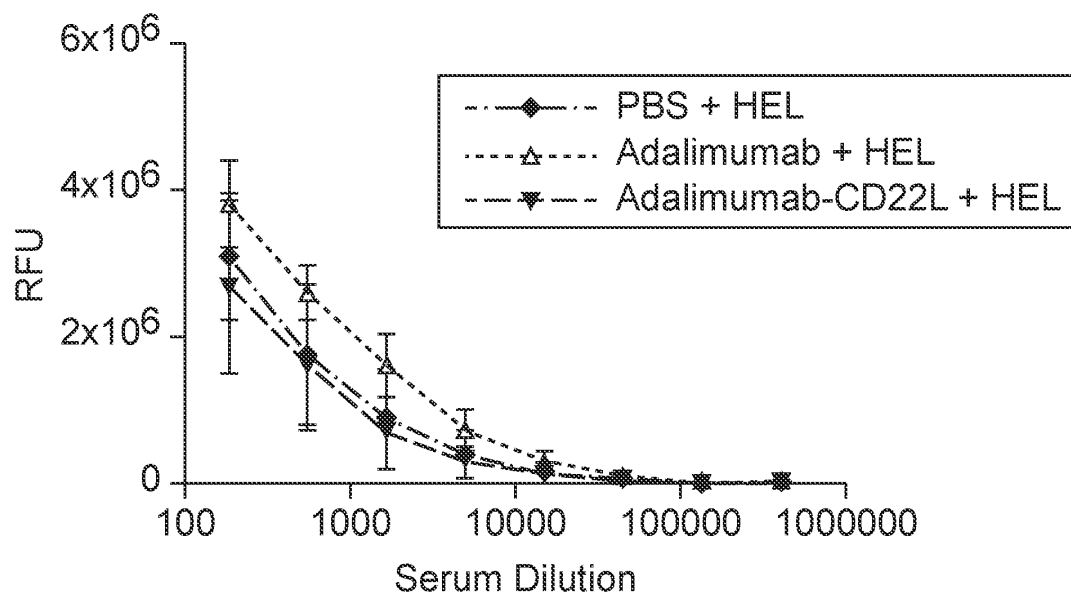


FIG. 30E

Anti-HEL Titer

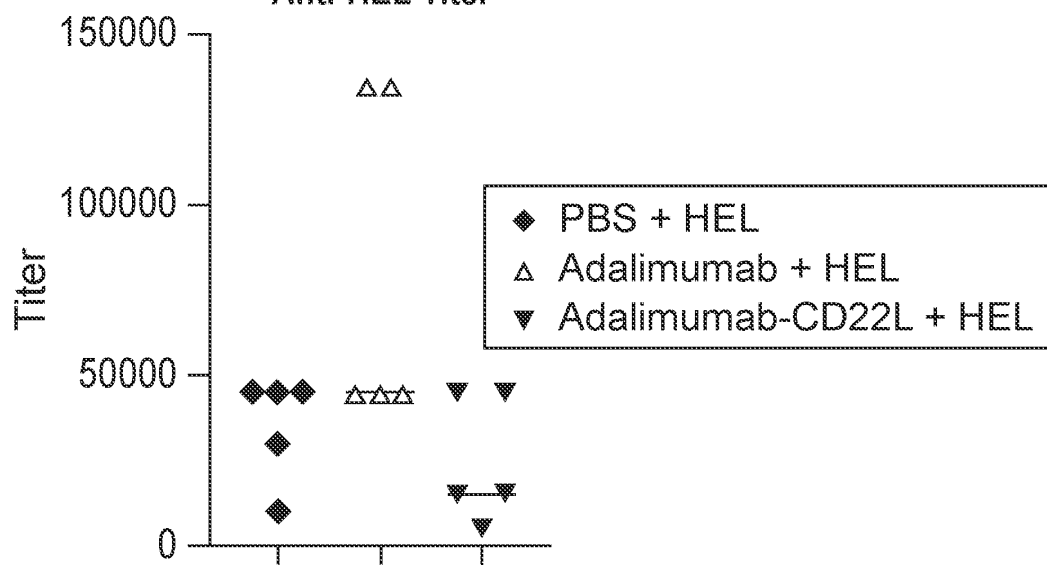


FIG. 31A

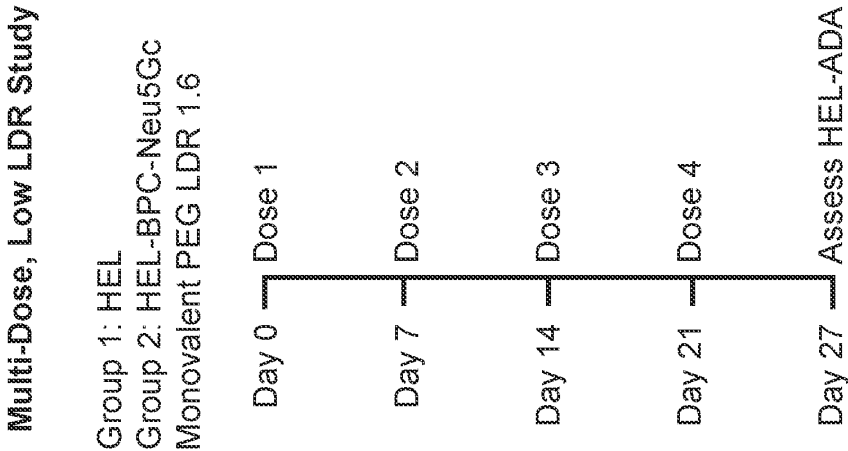
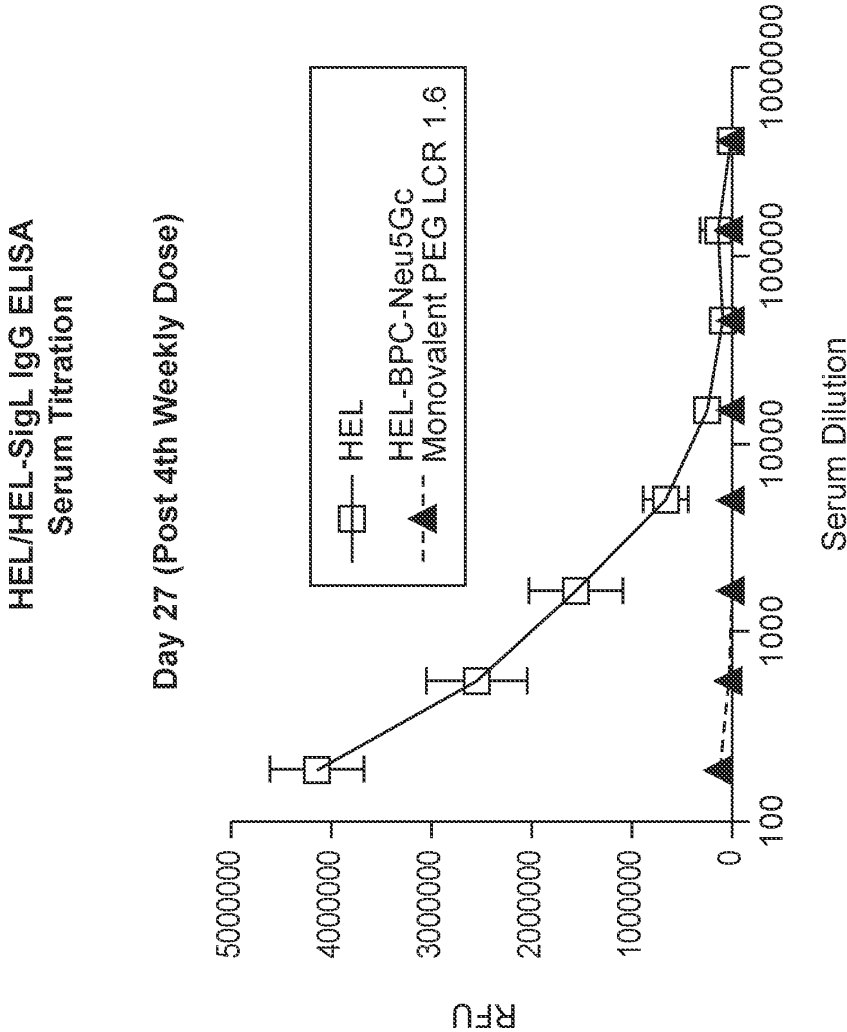


FIG. 31B



54/54

FIG. 31C

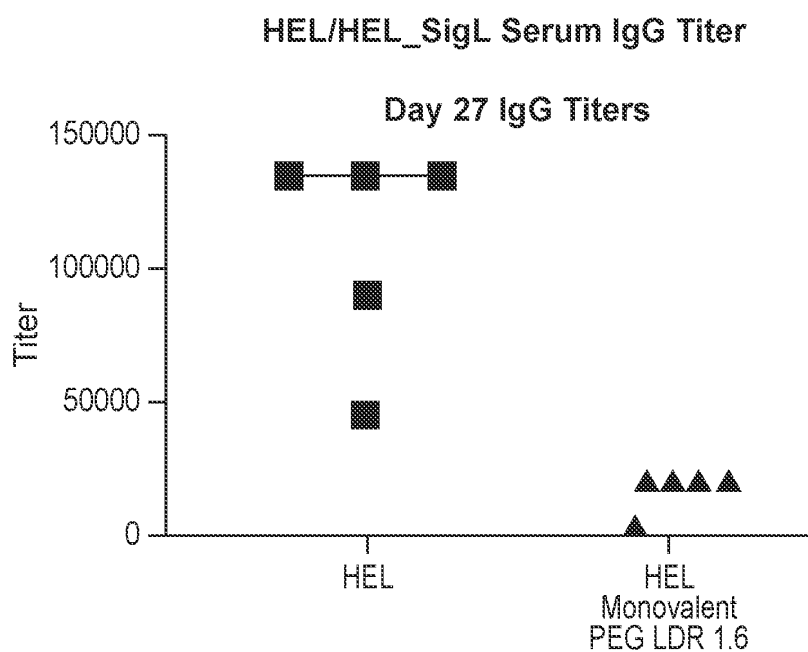


FIG. 32

