

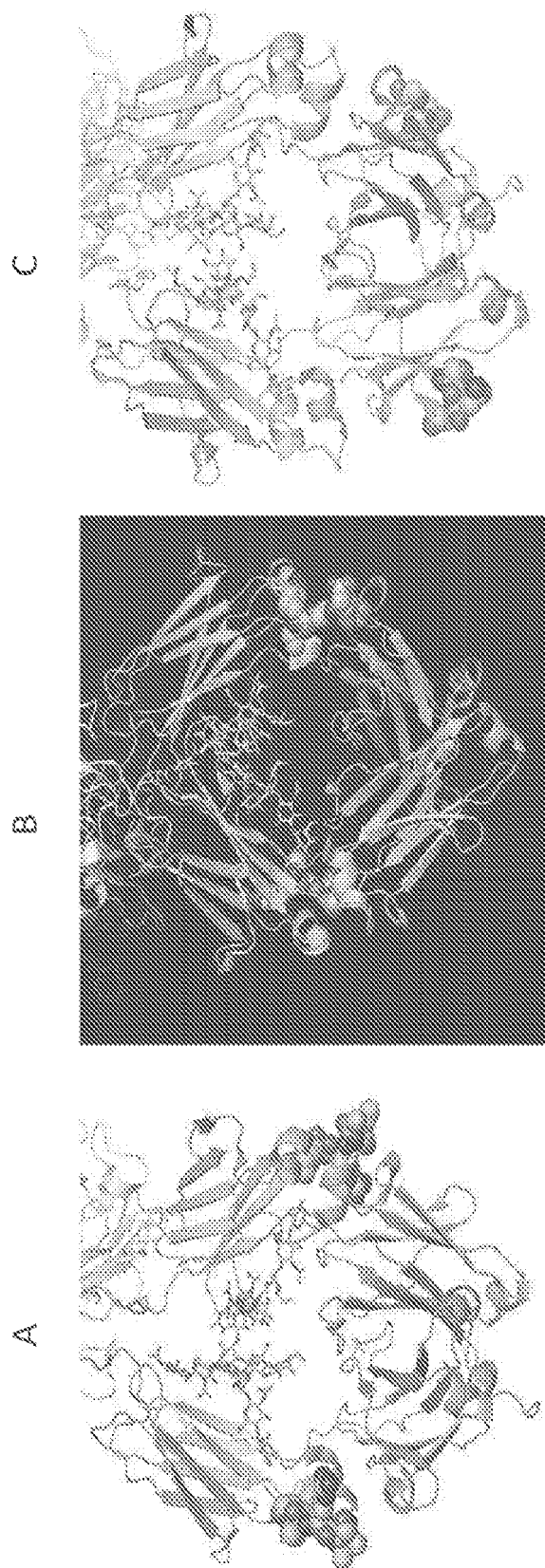


FIGURE 1

FIGURE 1D

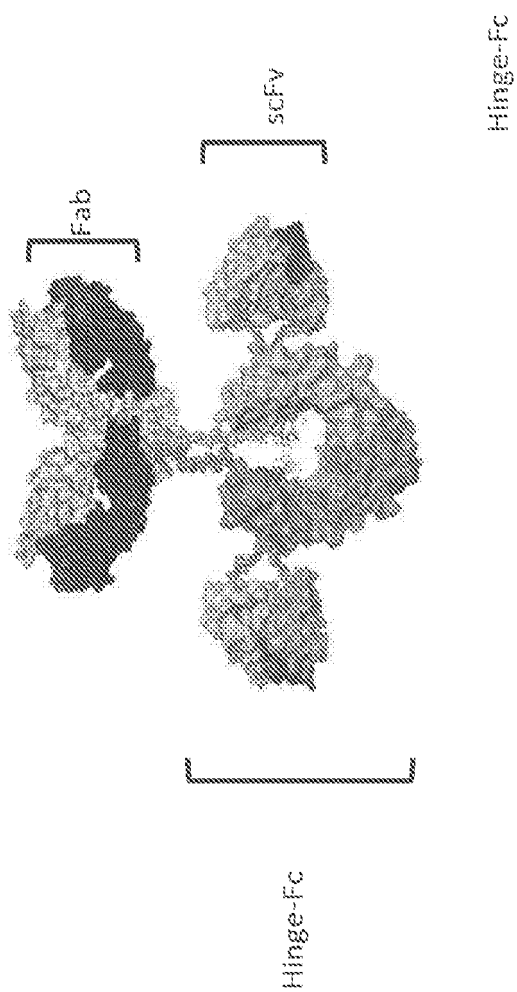


FIGURE 1E

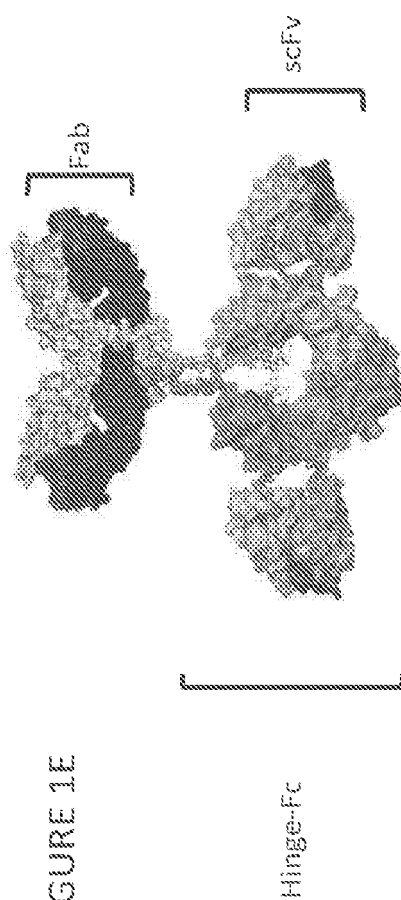


FIGURE 1F

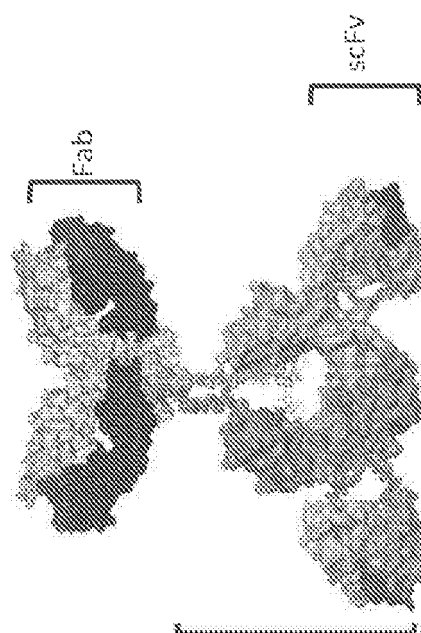


FIGURE 2A

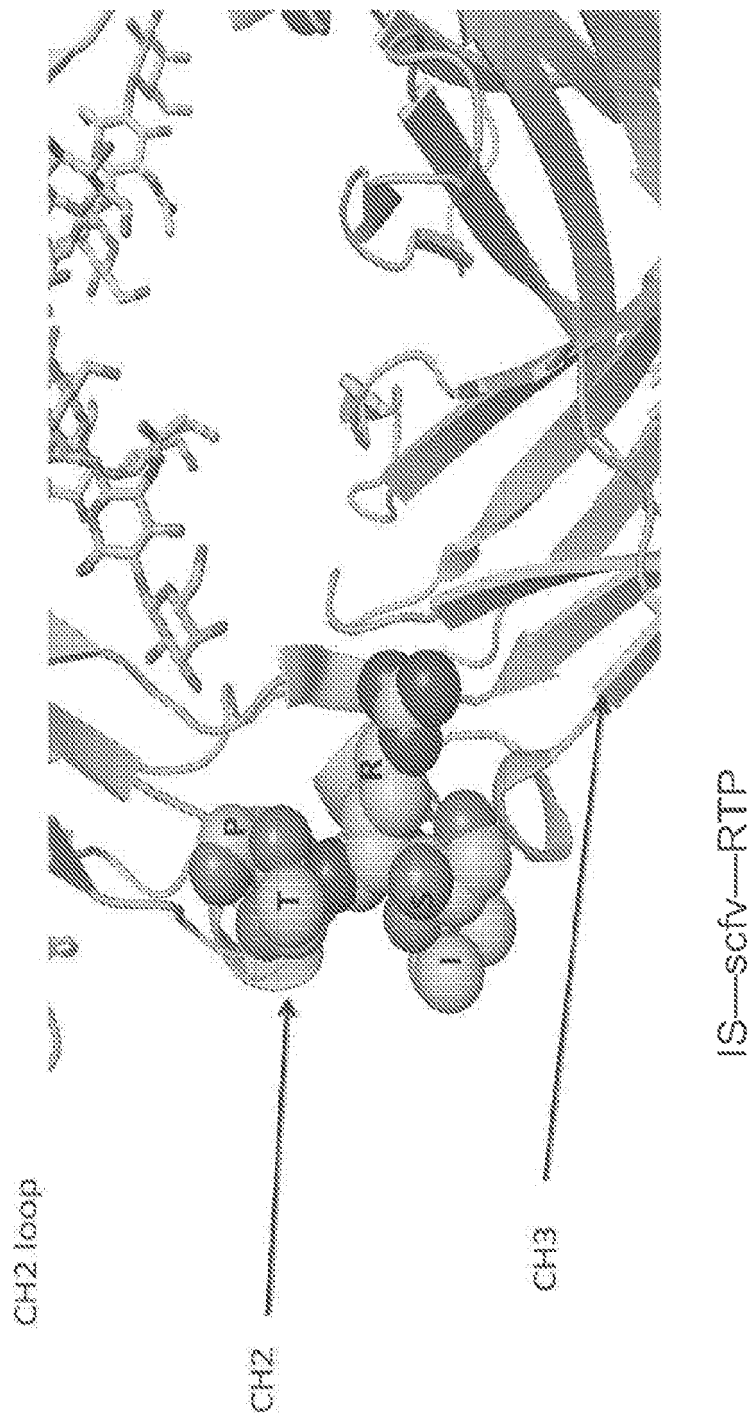


FIGURE 2B

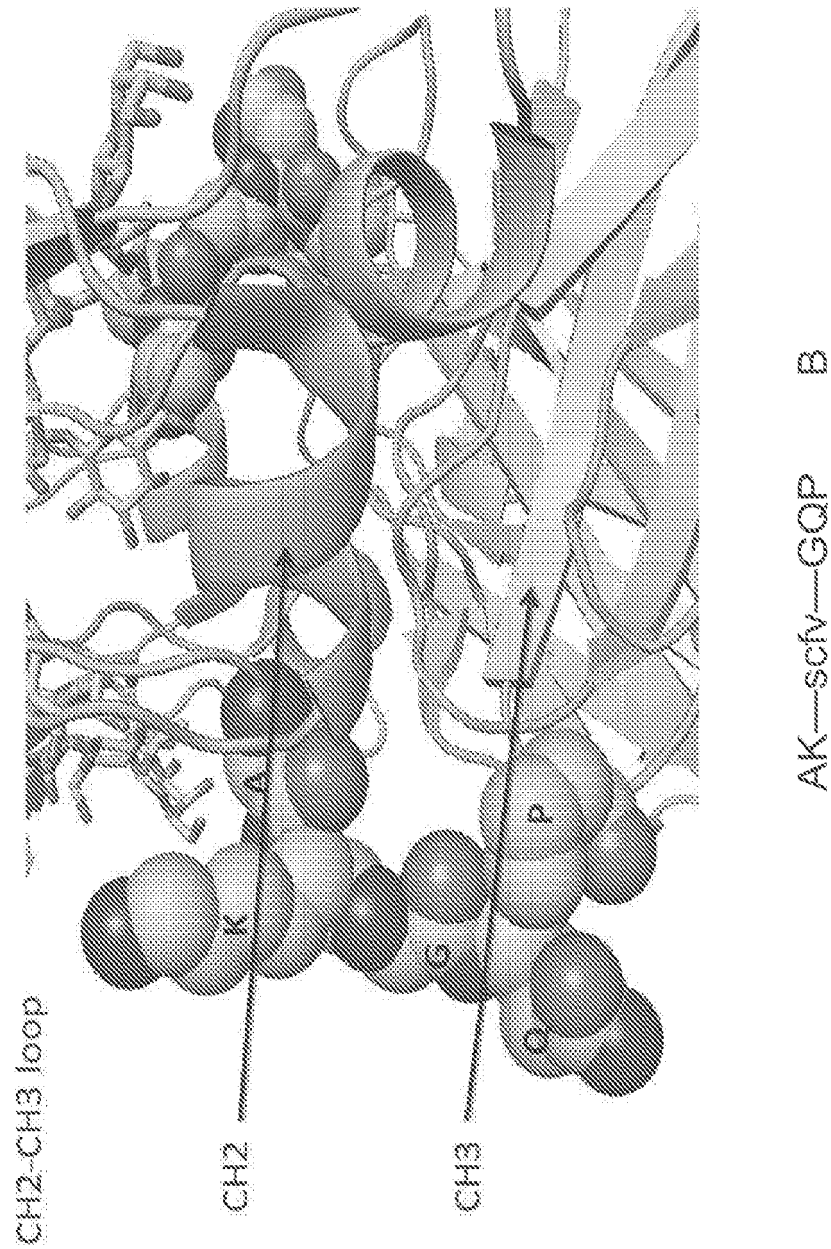
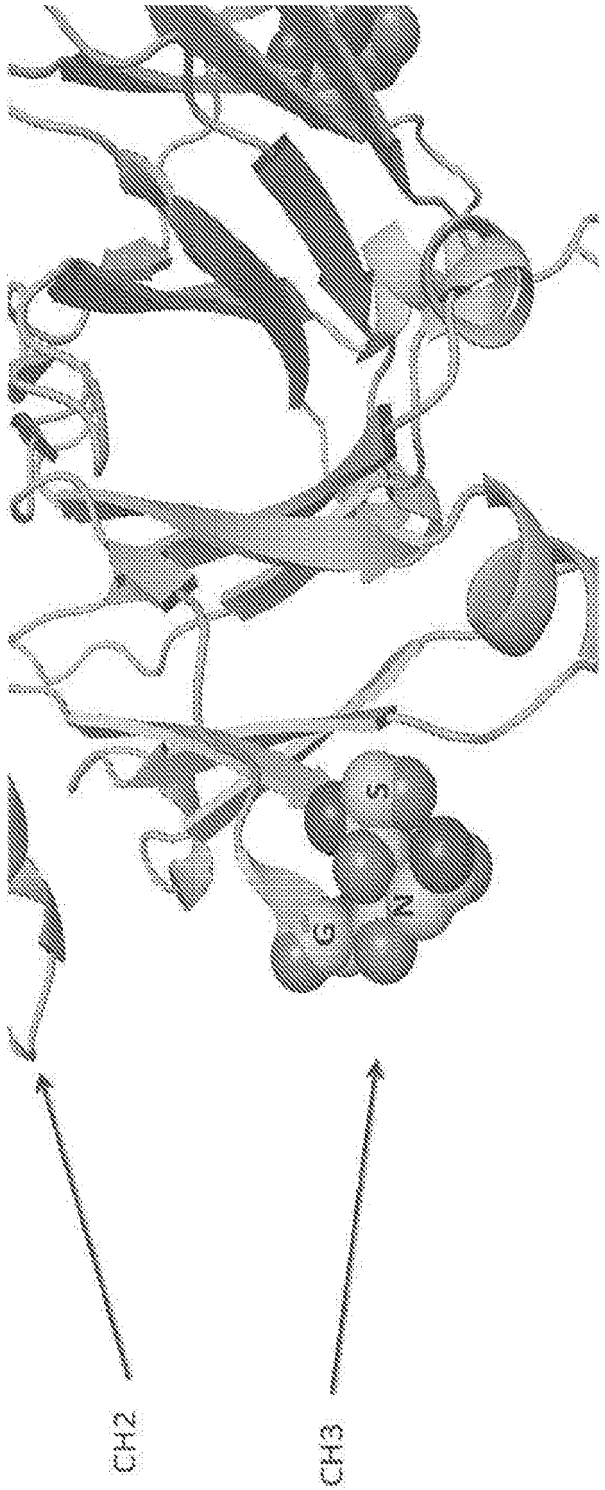


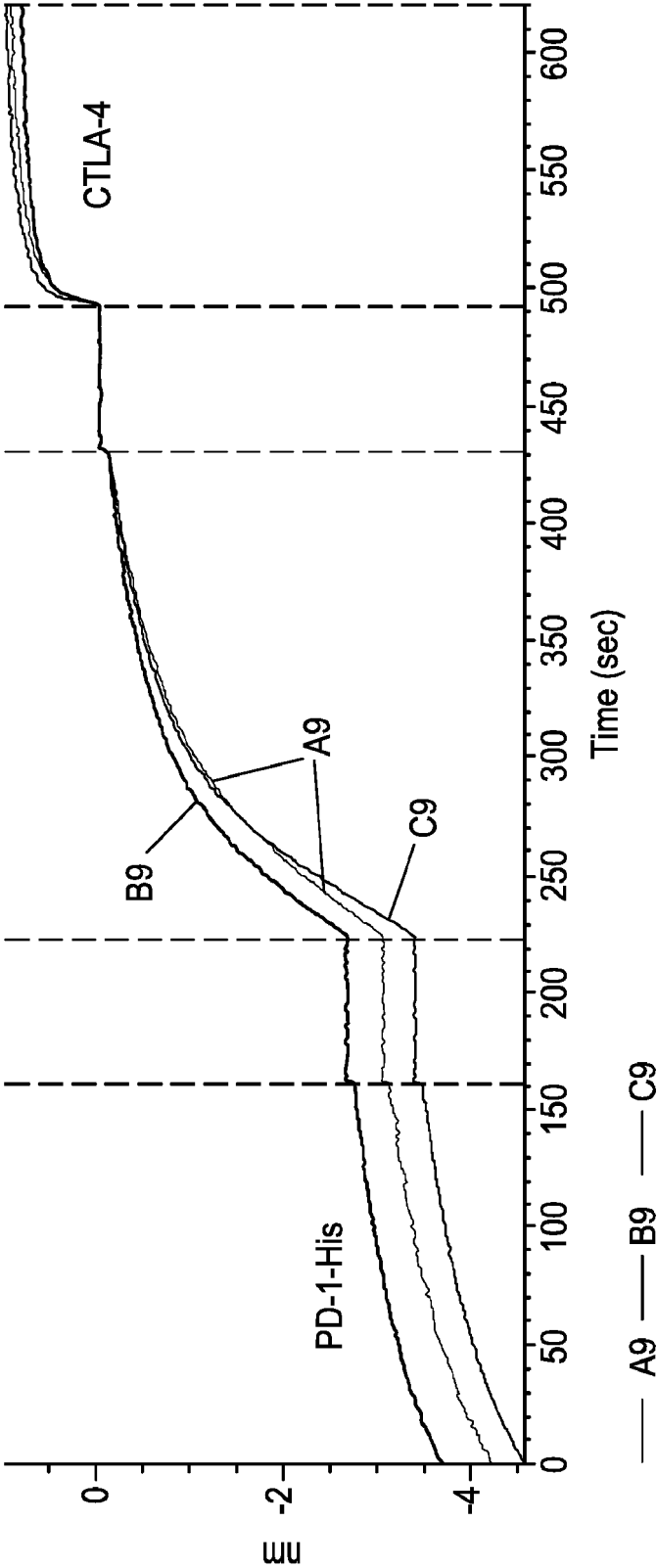
FIGURE 2C

CH3 loop



C S—scFv—NG
D SN—scFv—G

FIGURE 3



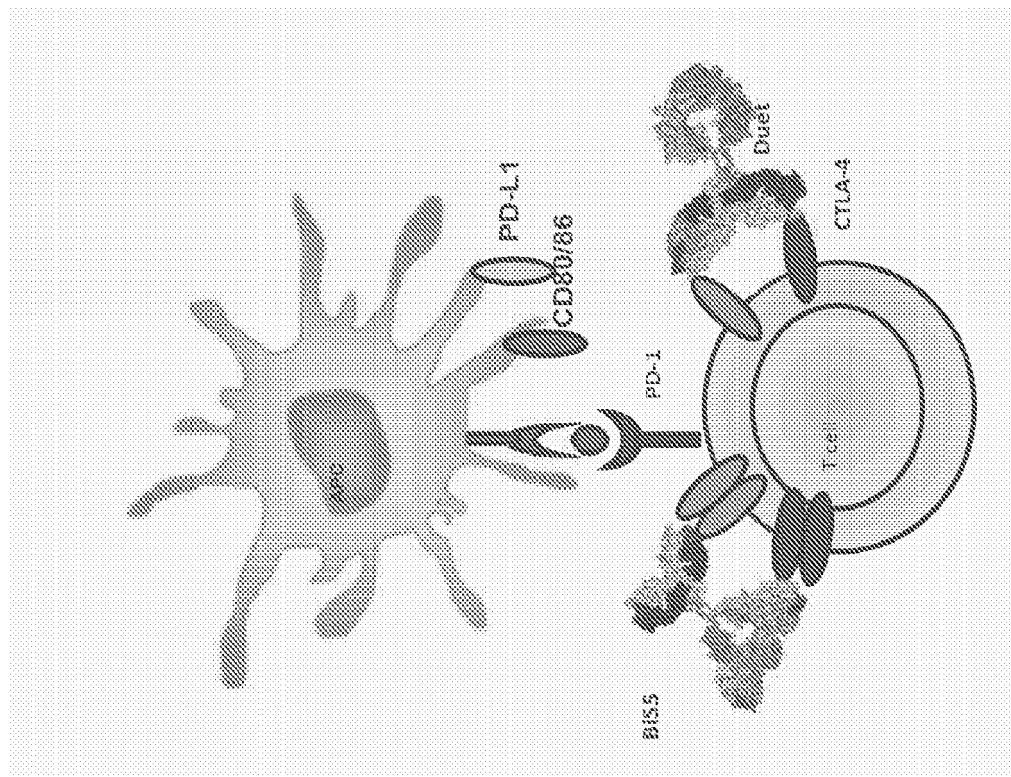


FIGURE 4

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FIGURE 5

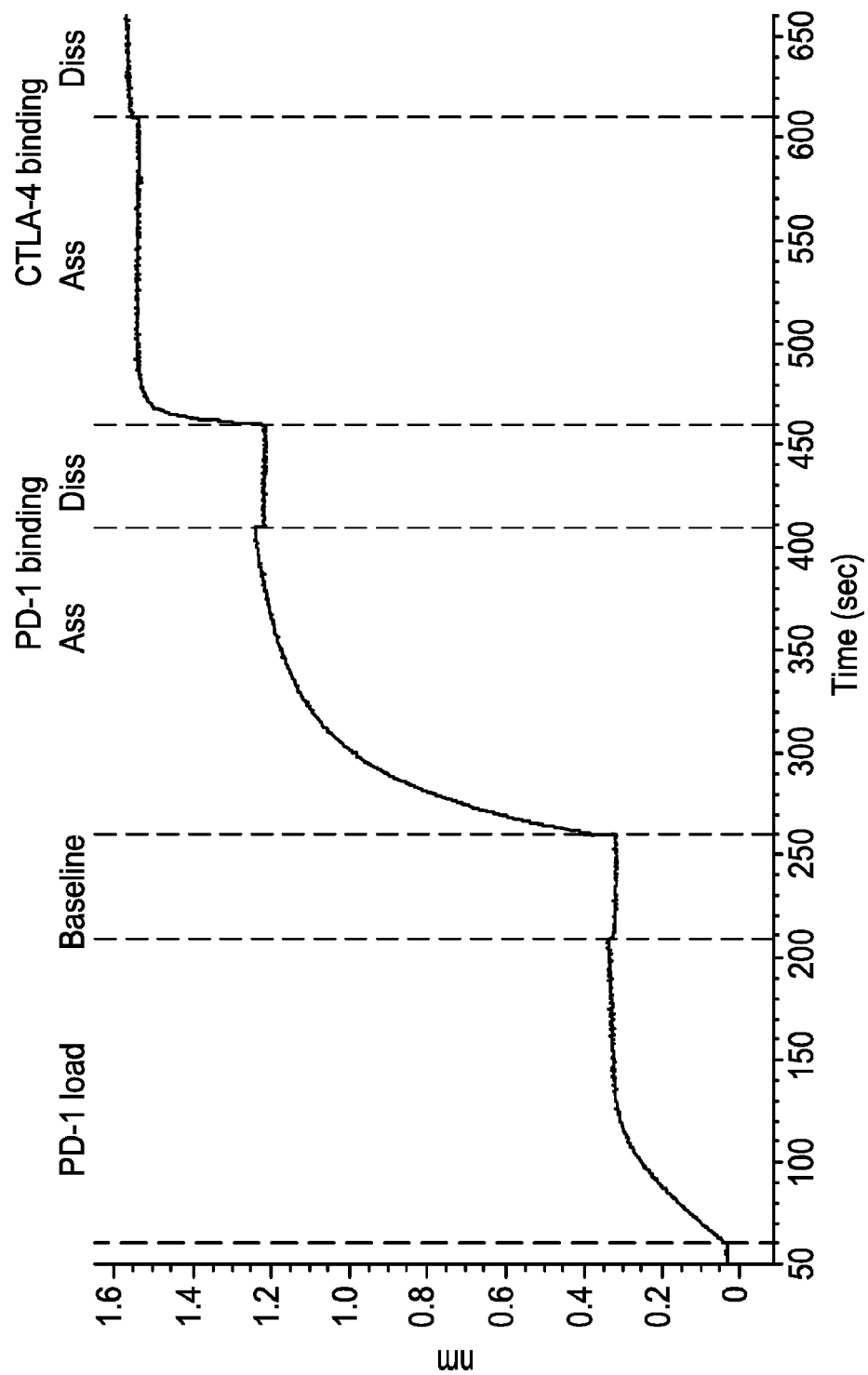


FIGURE 6 Cont'd

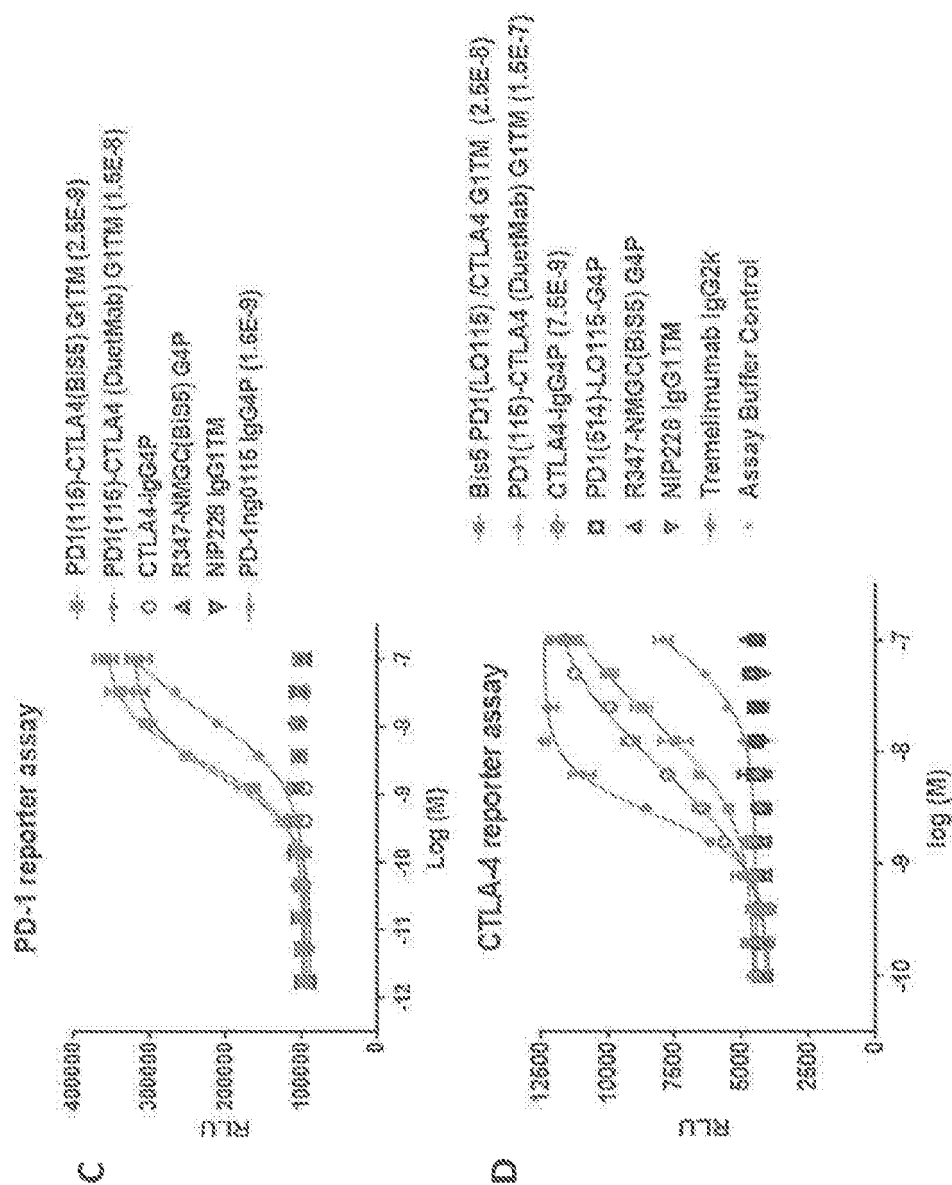


FIGURE 7

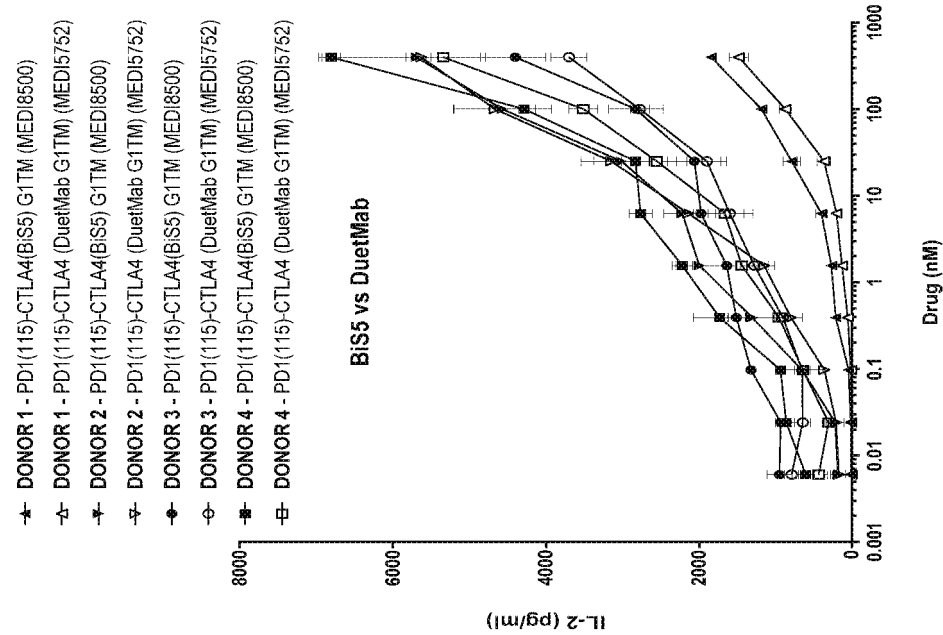


FIGURE 8

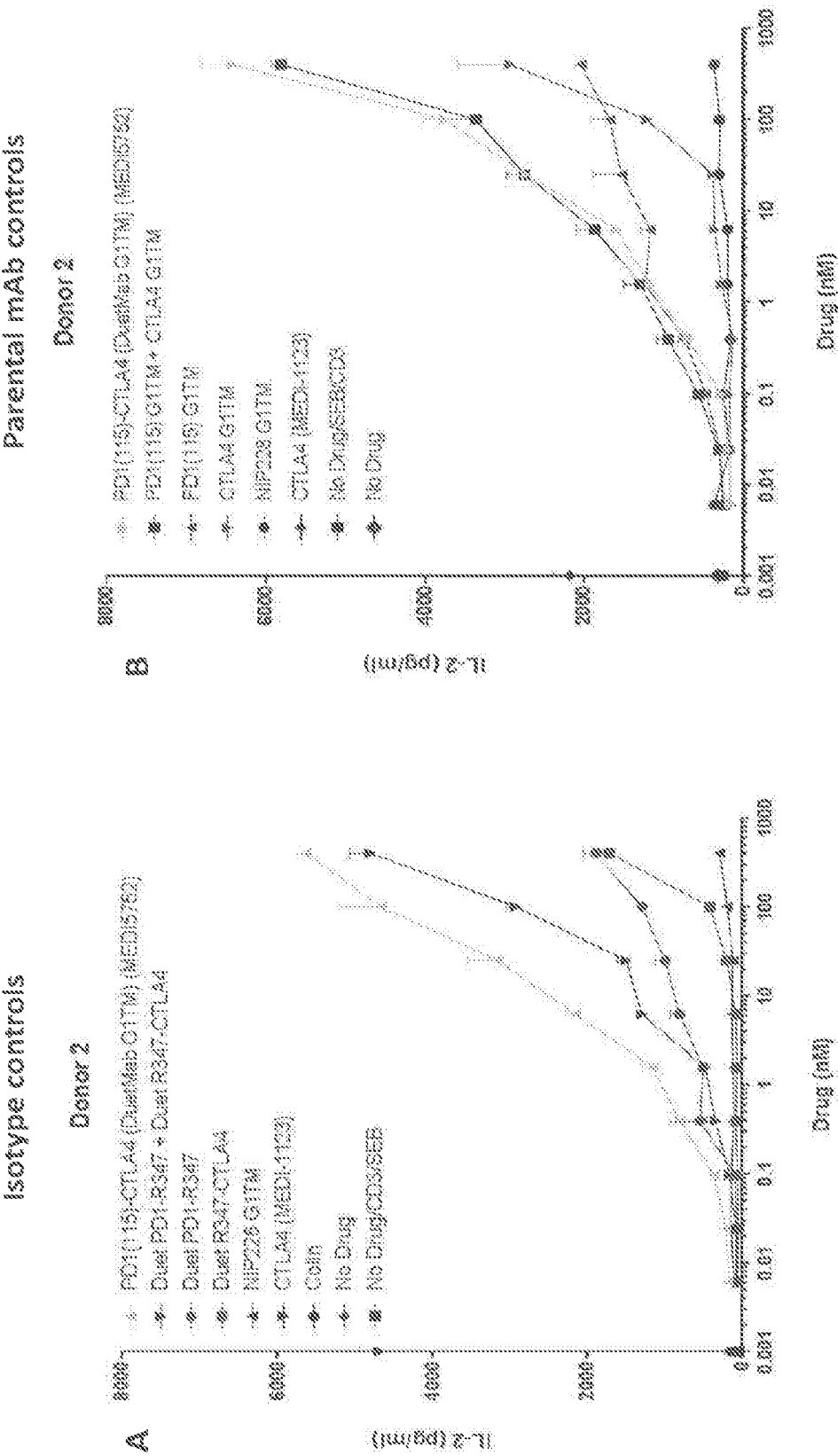


FIGURE 9

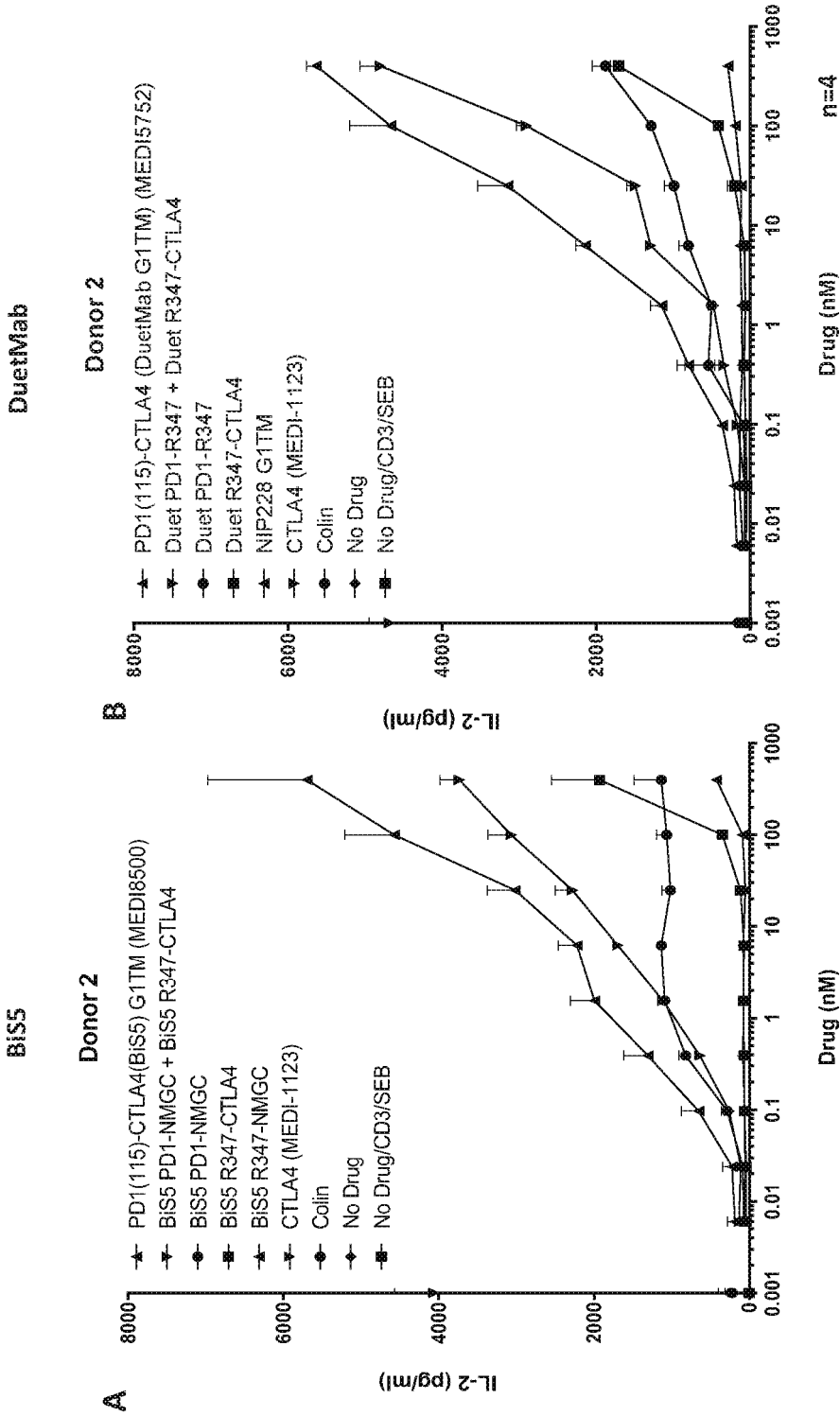


FIGURE 10

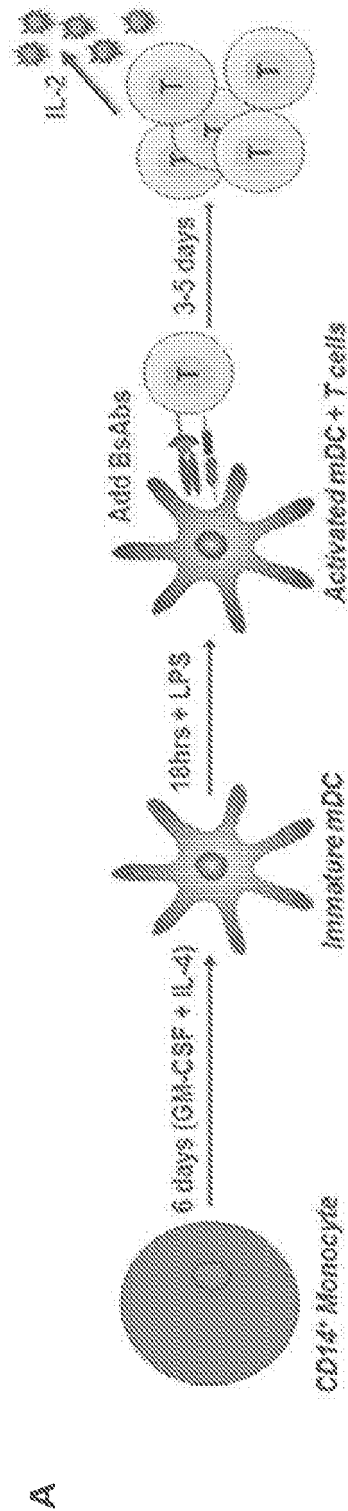


FIGURE 10 cont'd.

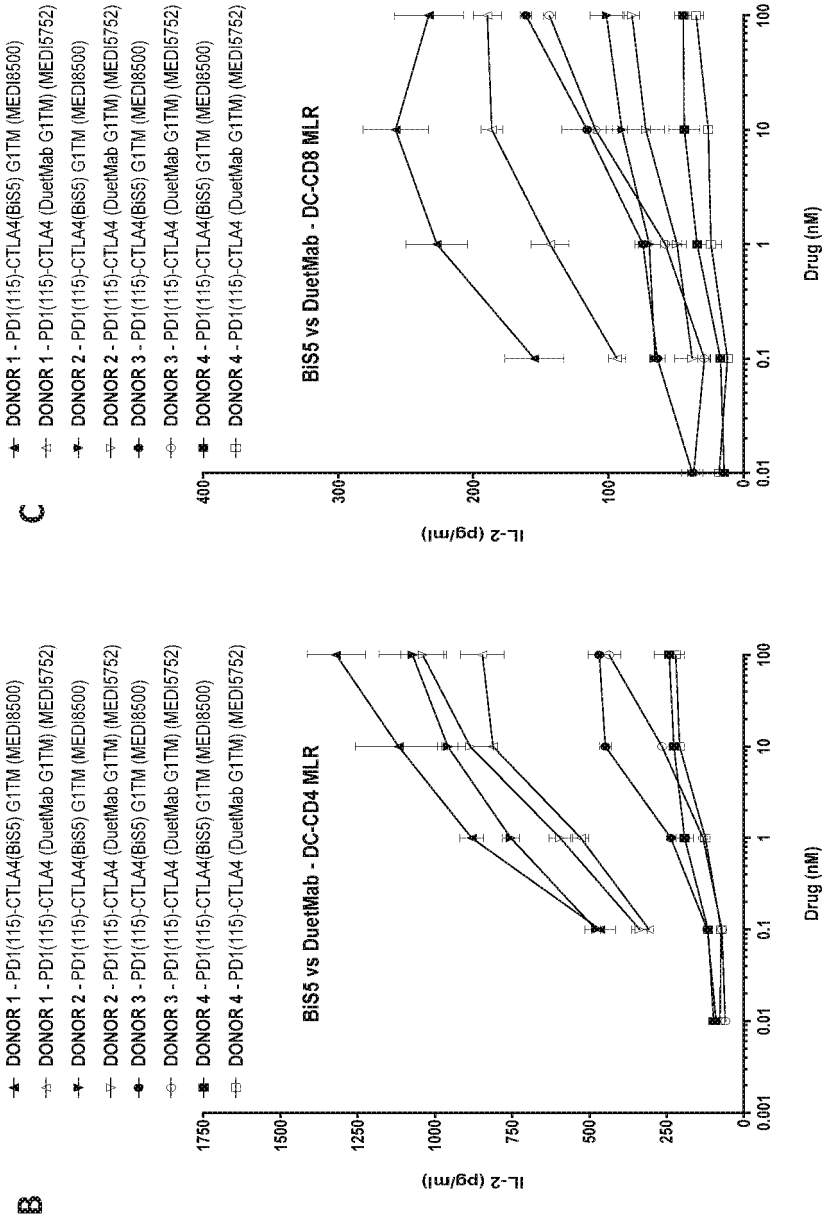


FIGURE 11

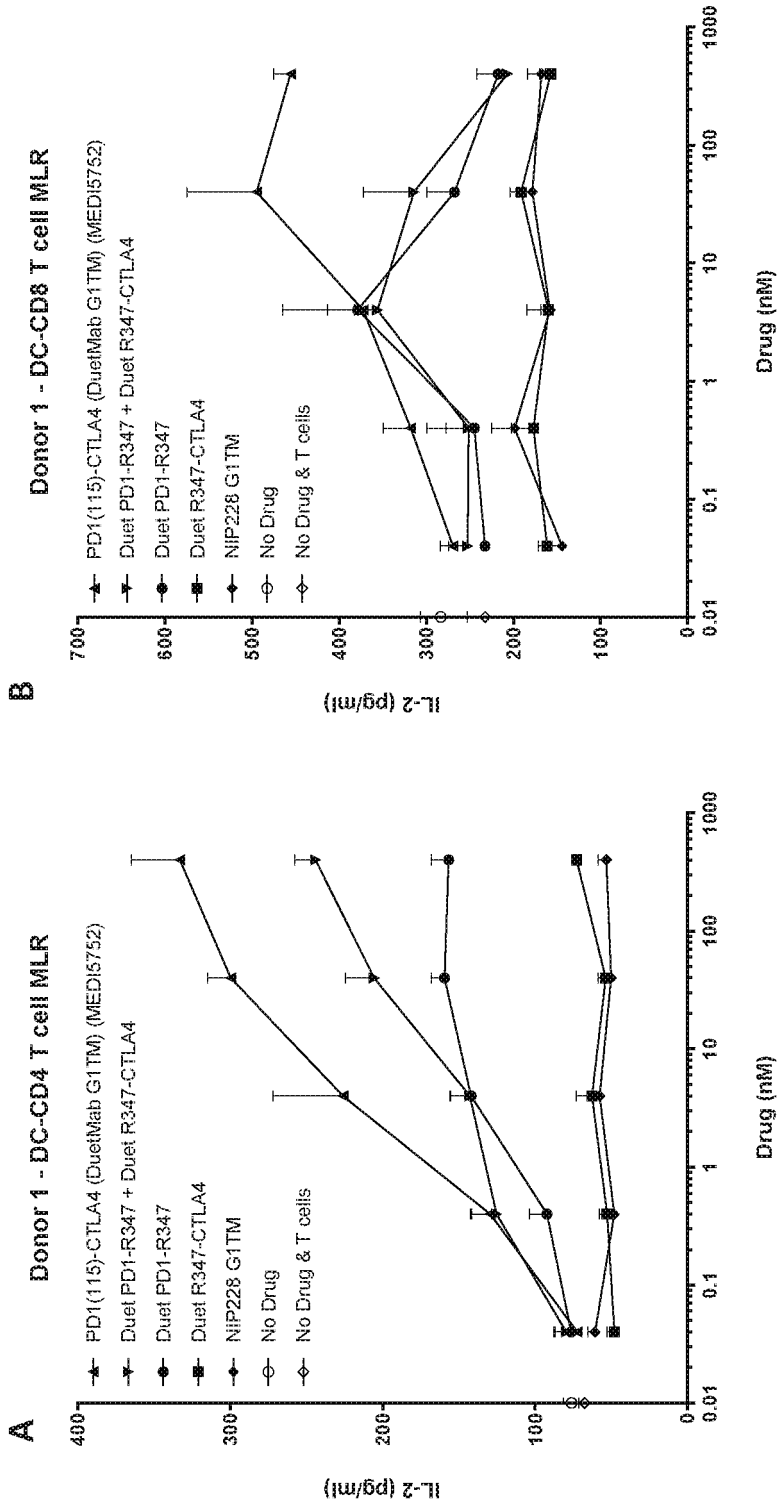


FIGURE 11 cont'd.

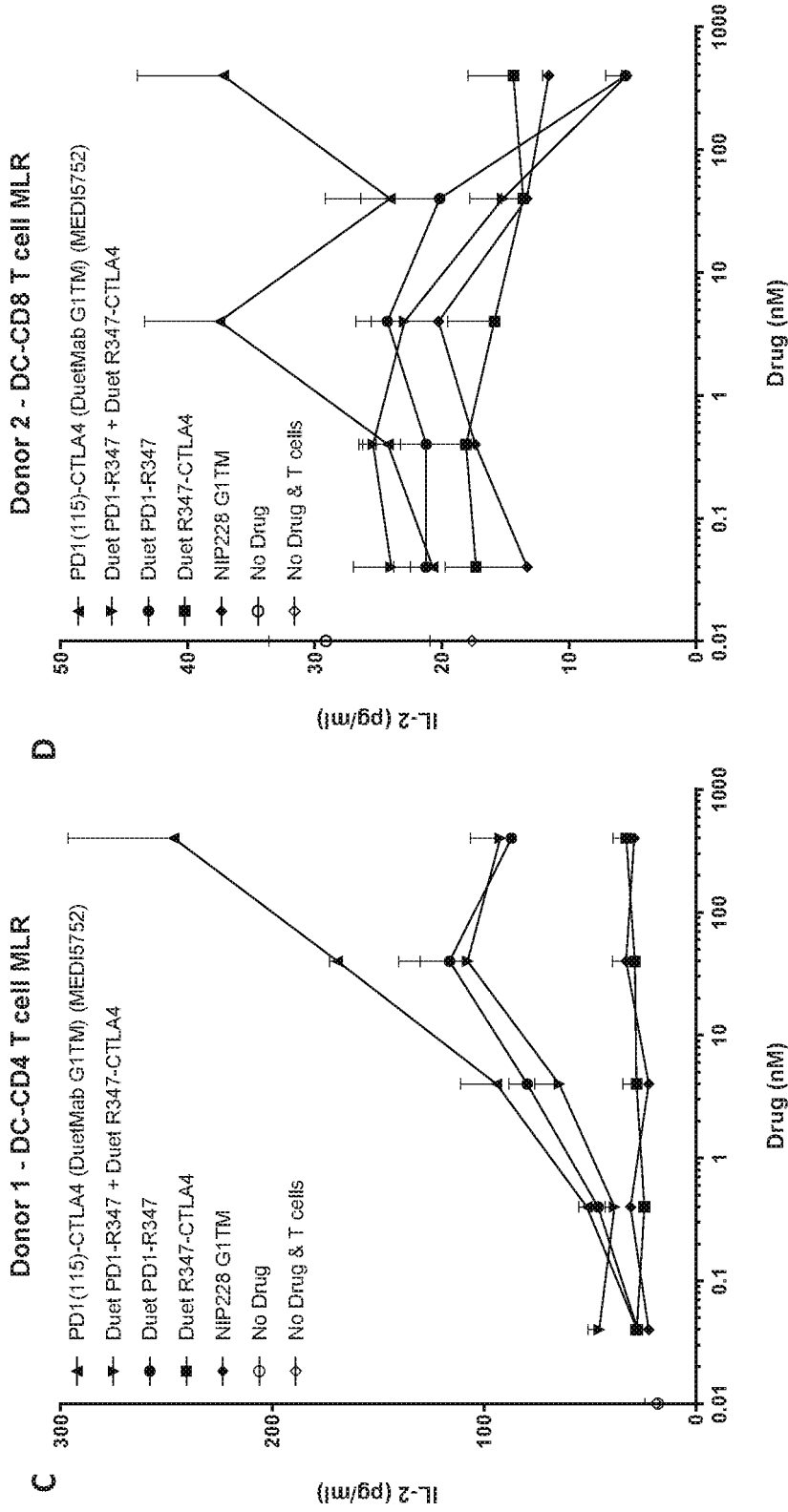


FIGURE 12

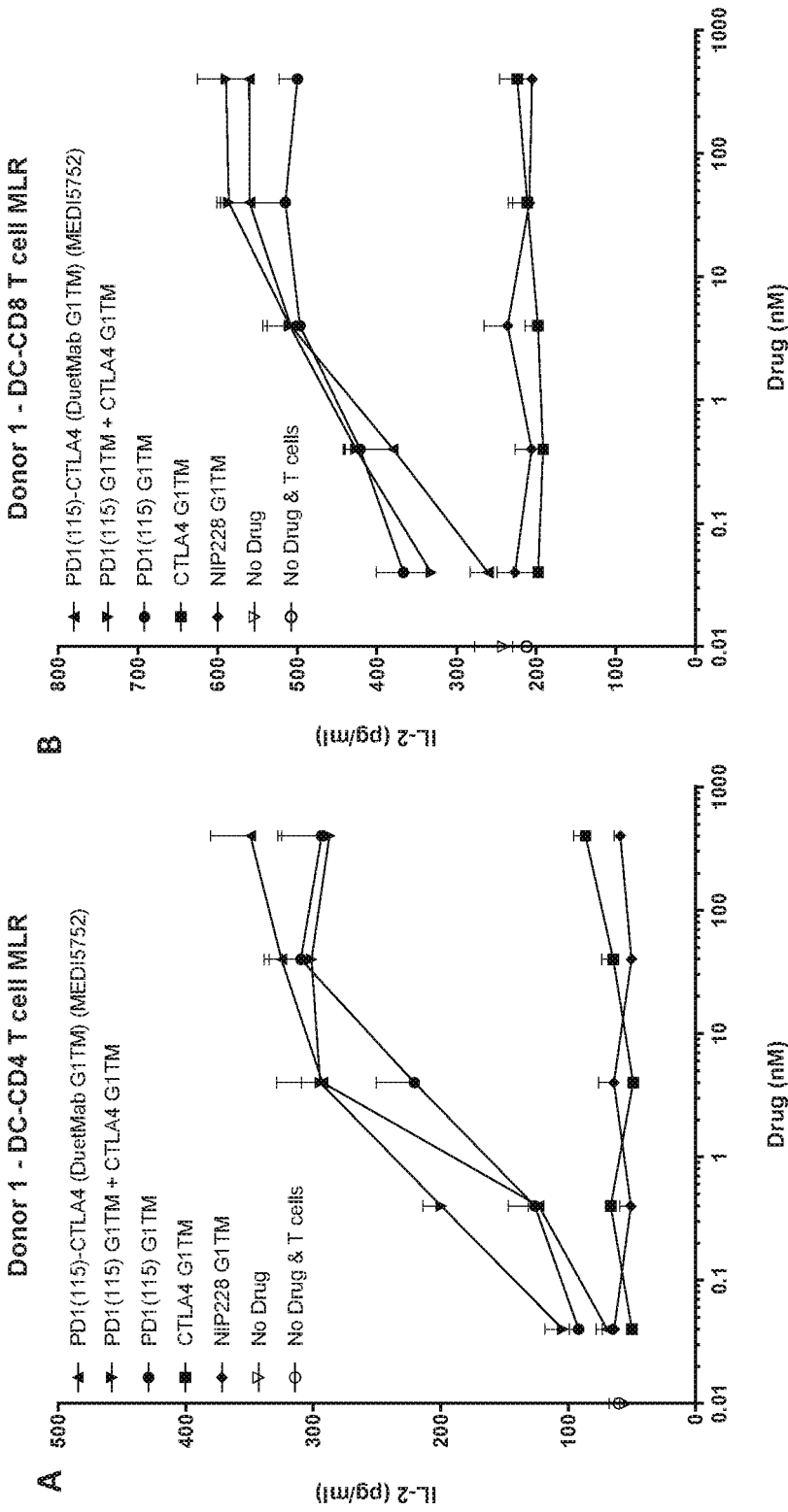


FIGURE 12 cont'd.

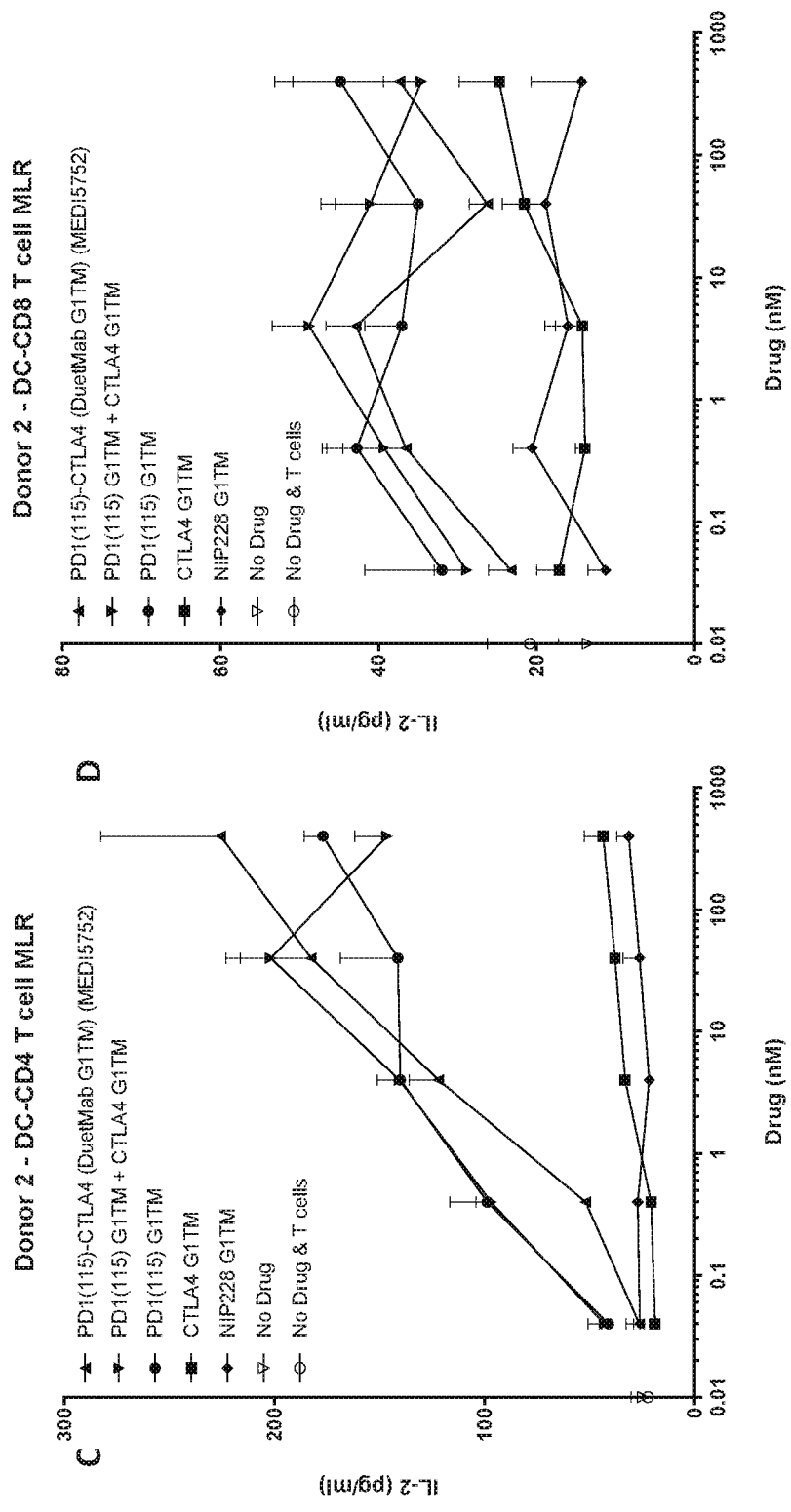


FIGURE 13

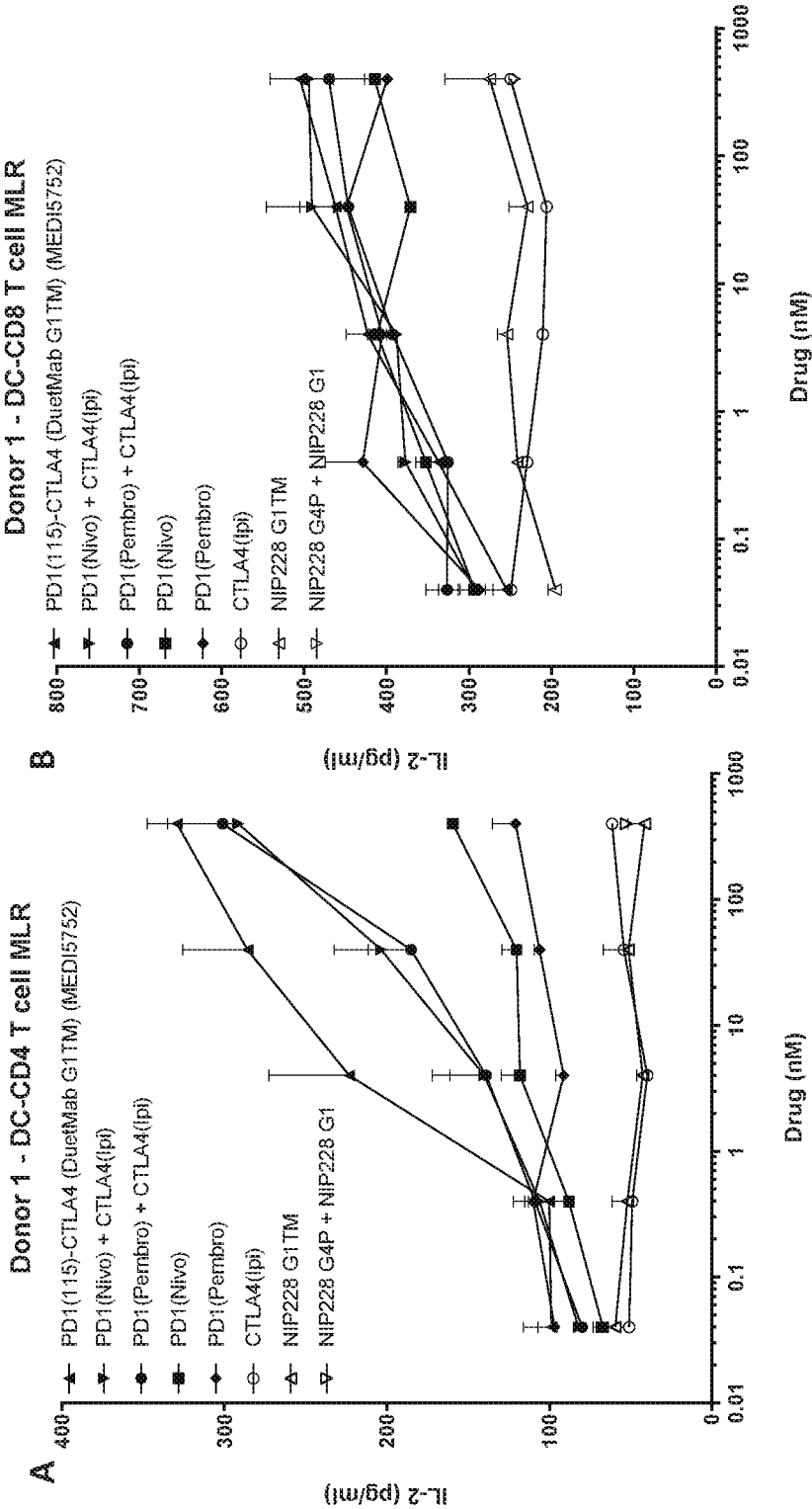


FIGURE 13 Cont'd.

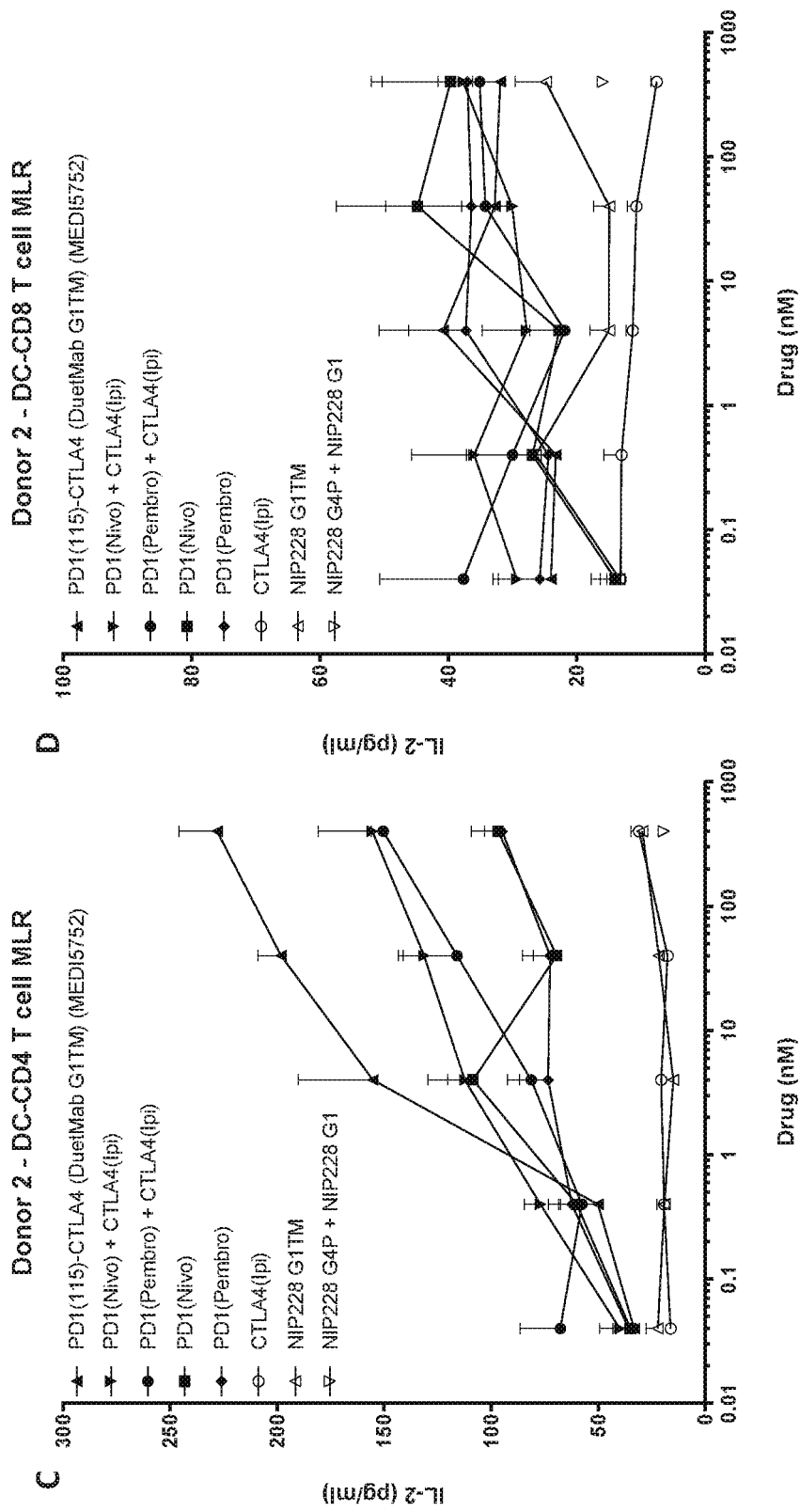


FIGURE 14

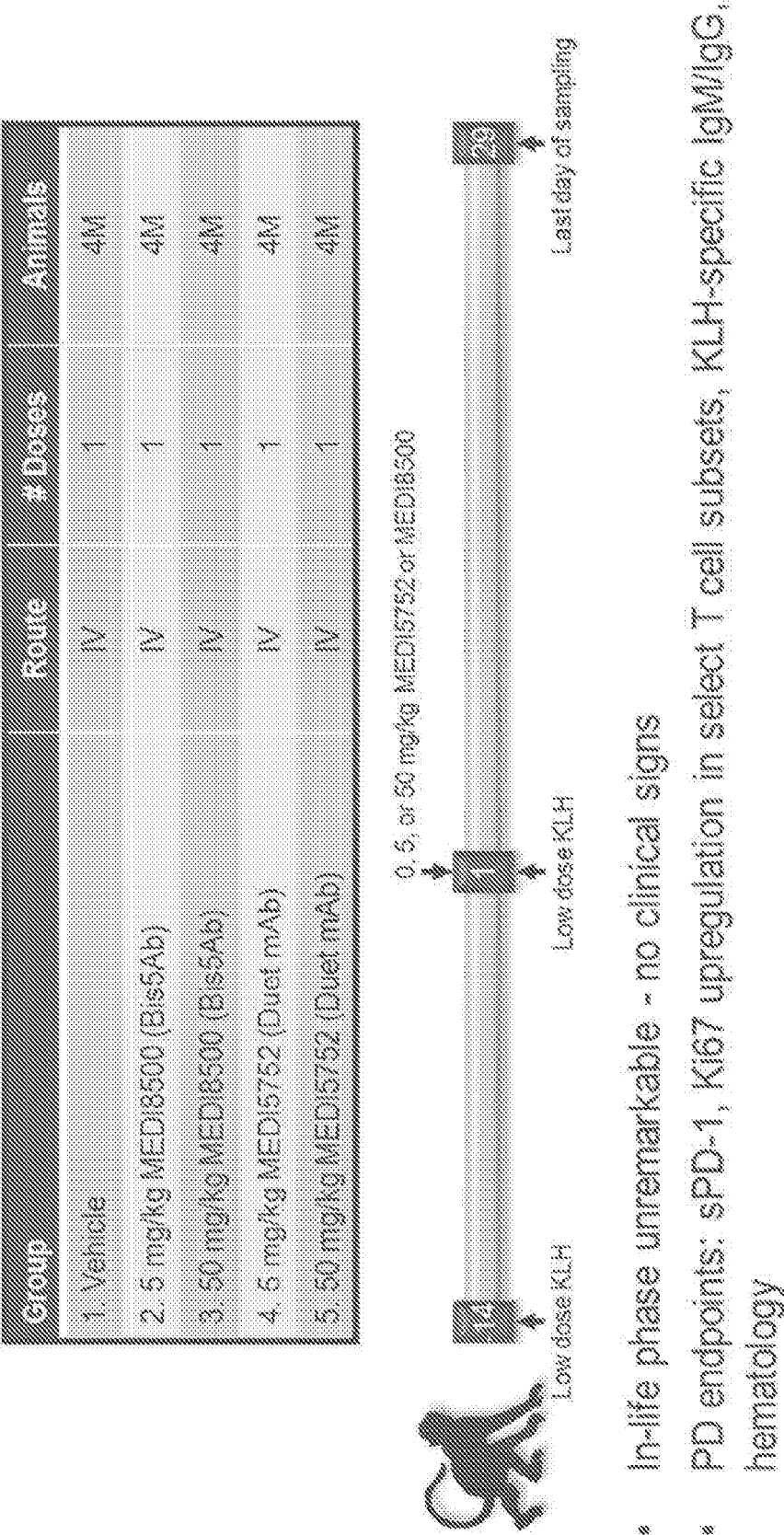


FIGURE 15

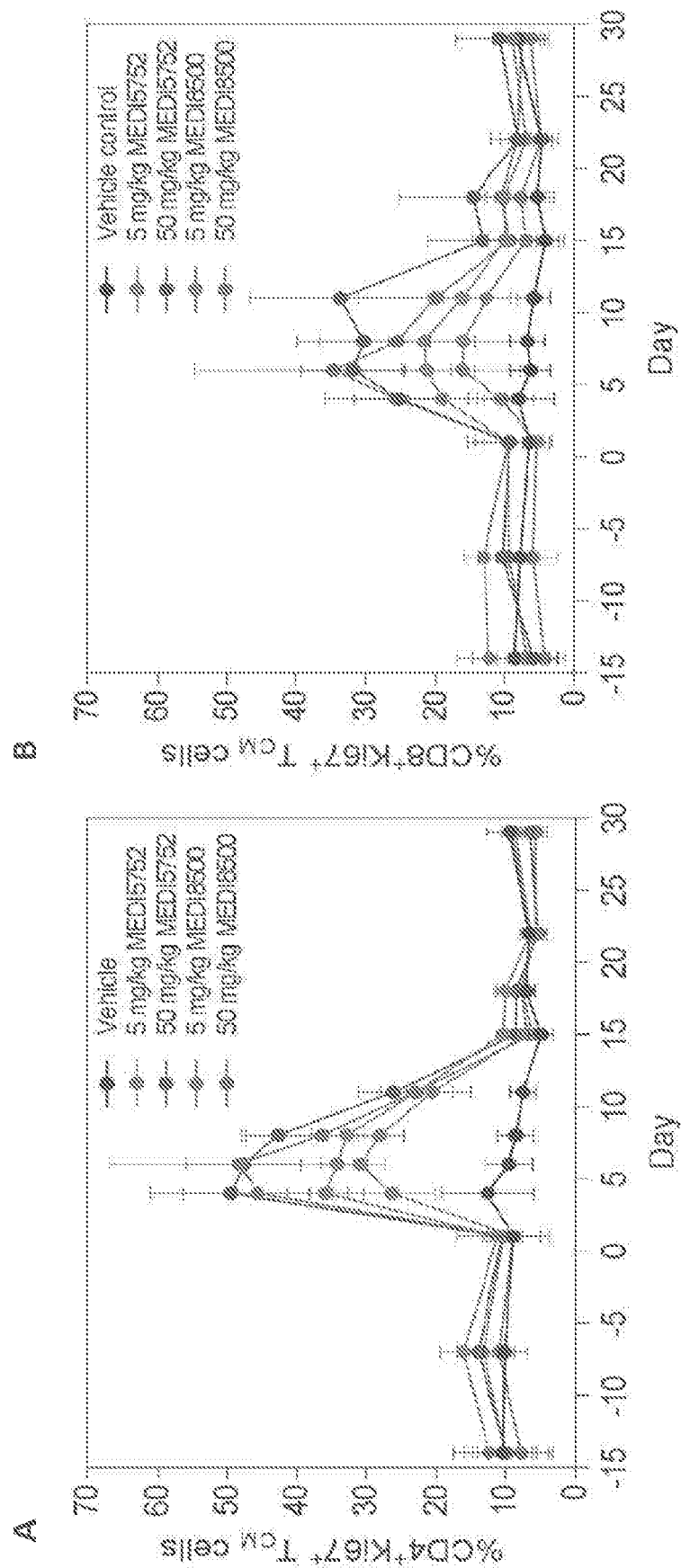


FIGURE 16

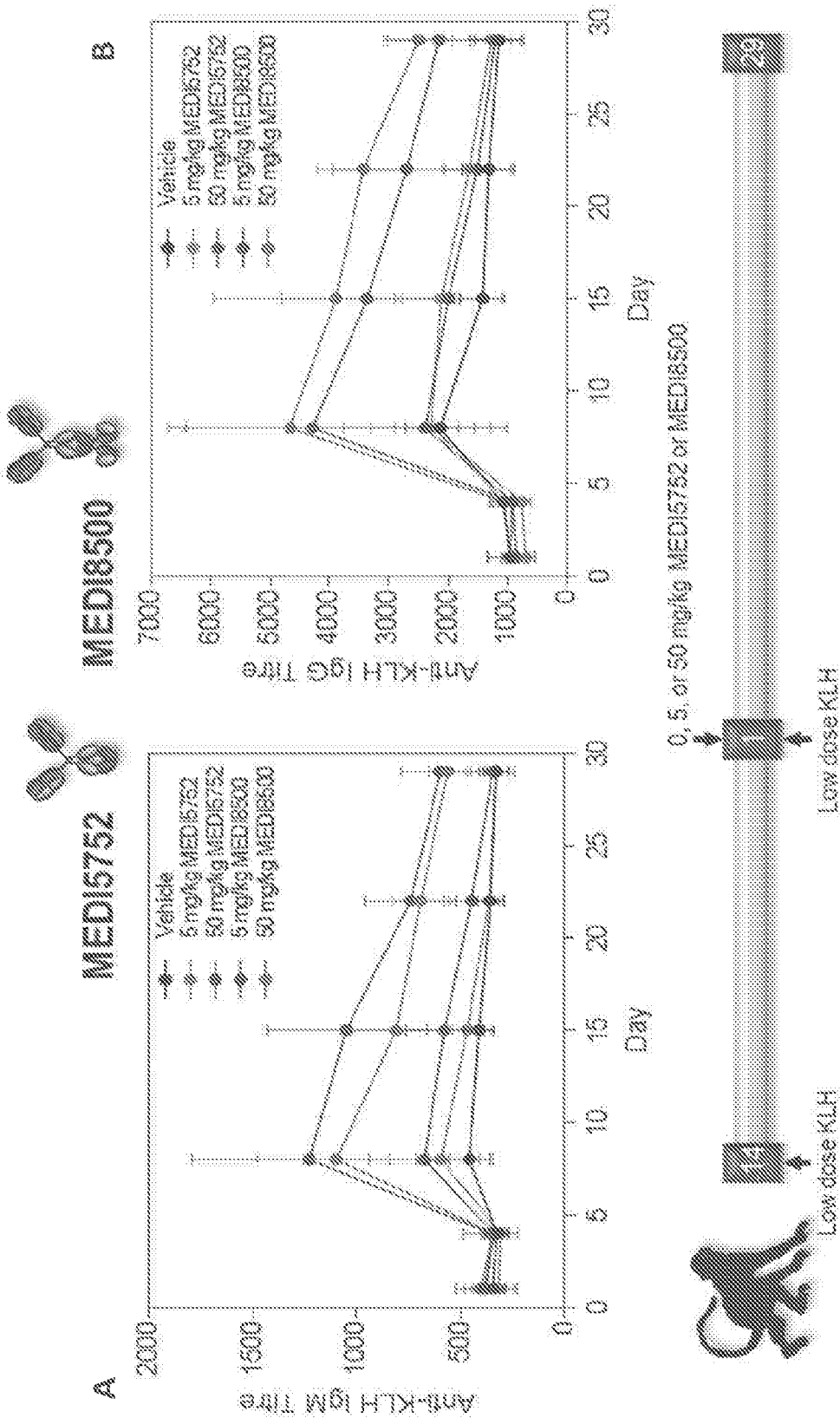


FIGURE 17

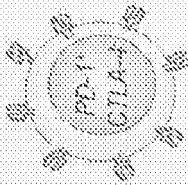
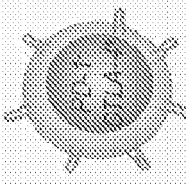
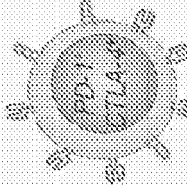
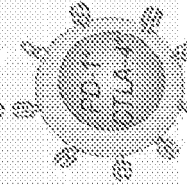
CHO cell	PD-1 receptor density	CTLA-4 receptor density	PD-1/CTLA-4 ratio
	2.4×10^6	-	-
	-	7.3×10^4	-
	7.3×10^5	5.5×10^4	$\sim 10:1$
	1.4×10^6	3.9×10^4	$\sim 40:1$

FIGURE 18

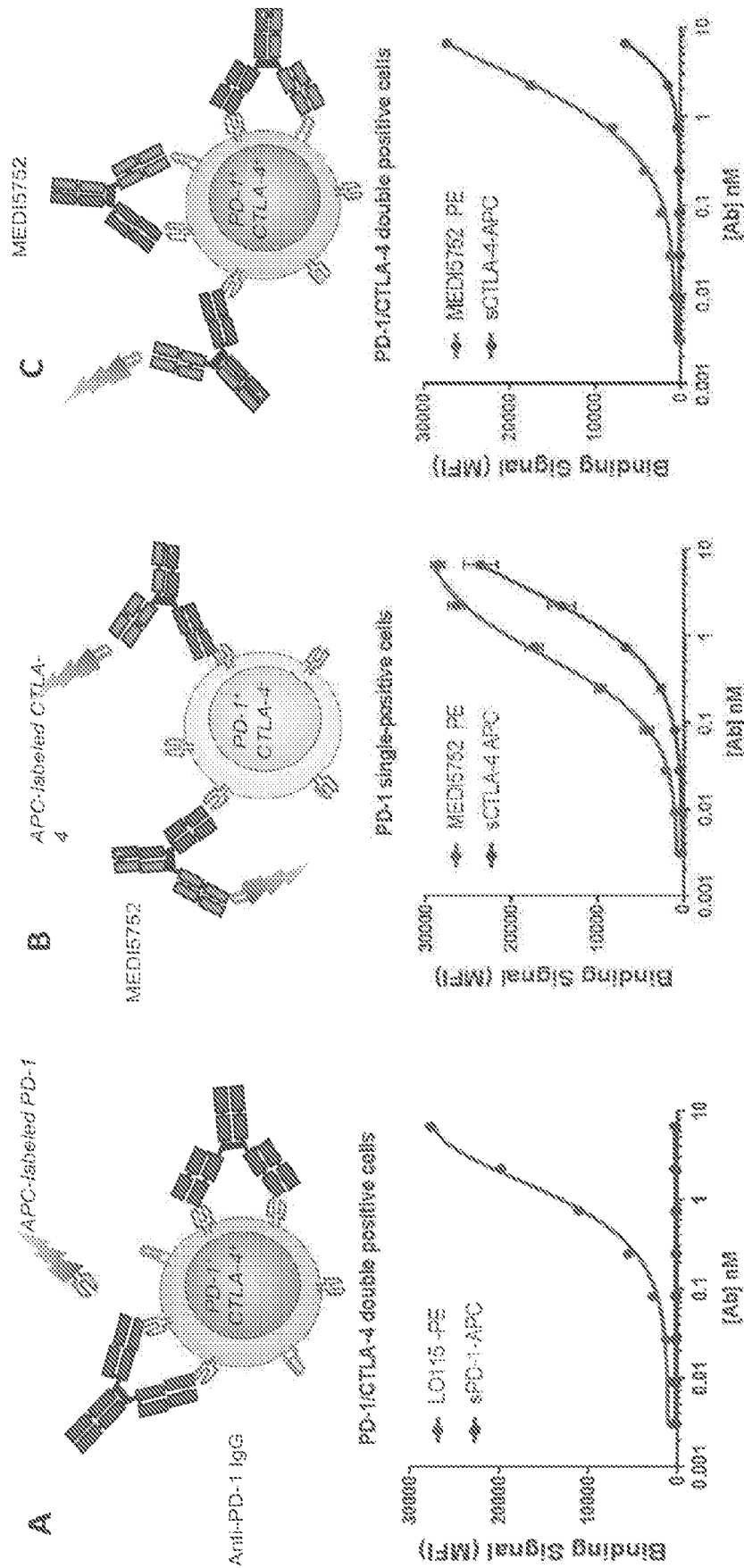


FIGURE 19

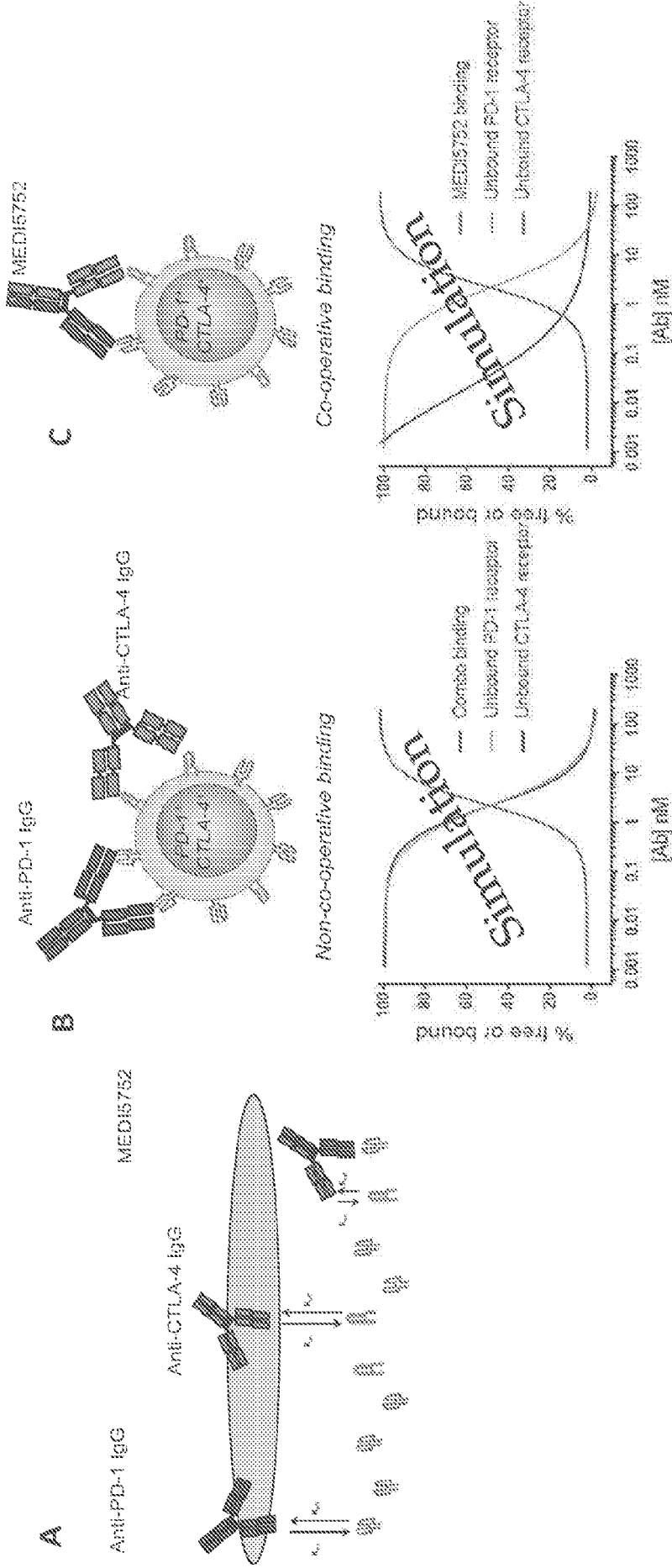


FIGURE 20

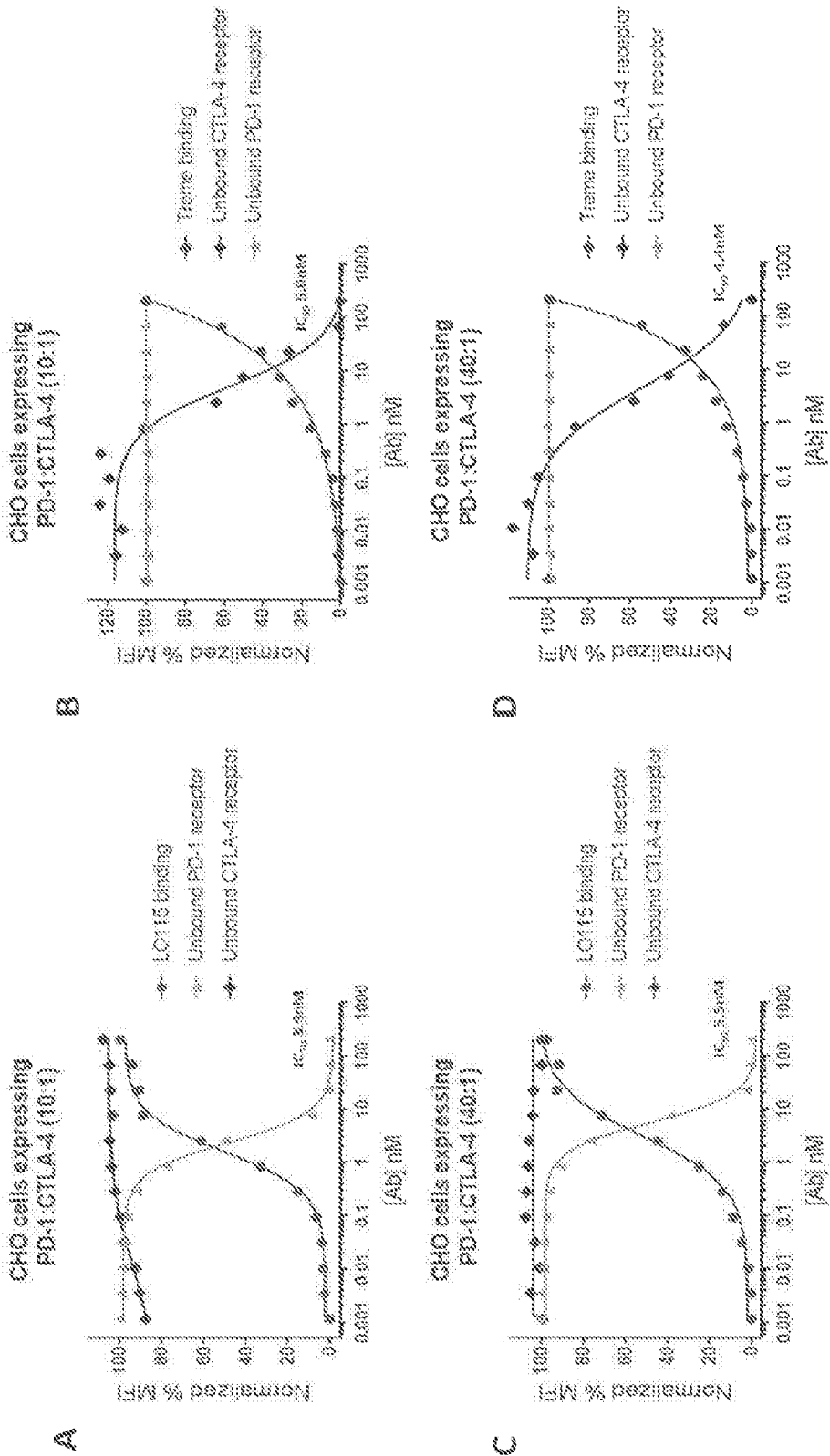


FIGURE 21

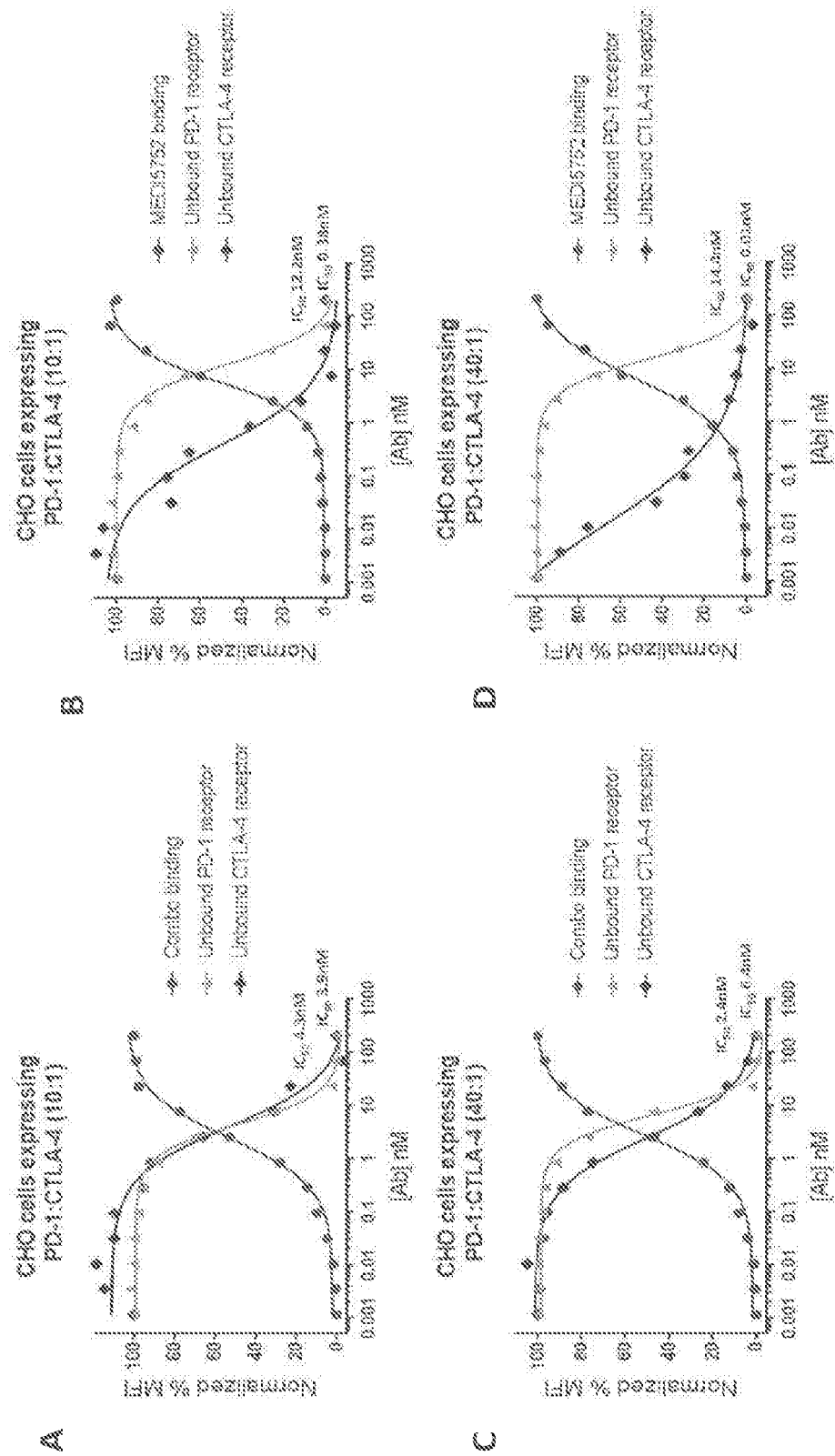


FIGURE 22

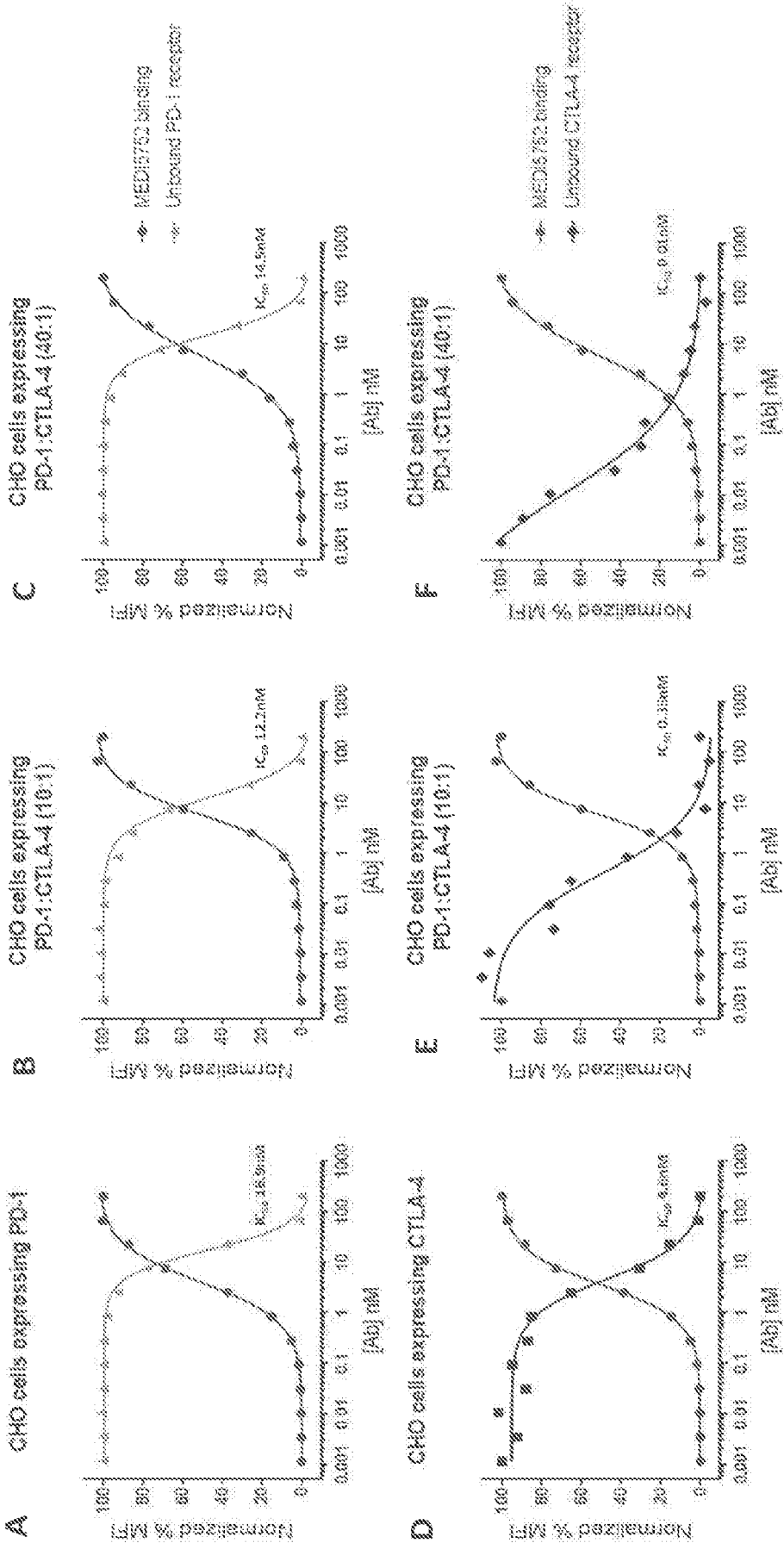
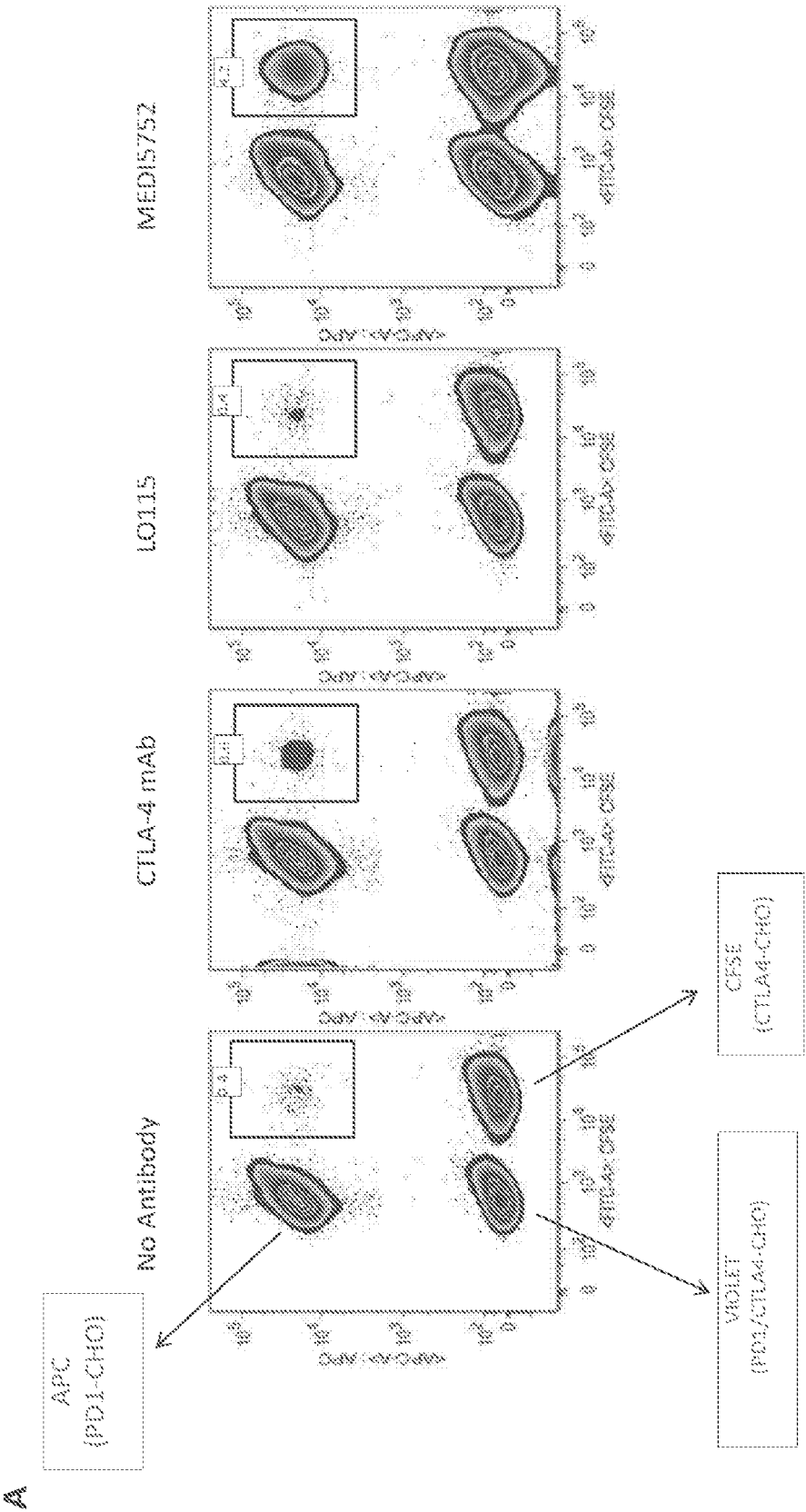


FIGURE 23



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FIGURE 23 cont'd.

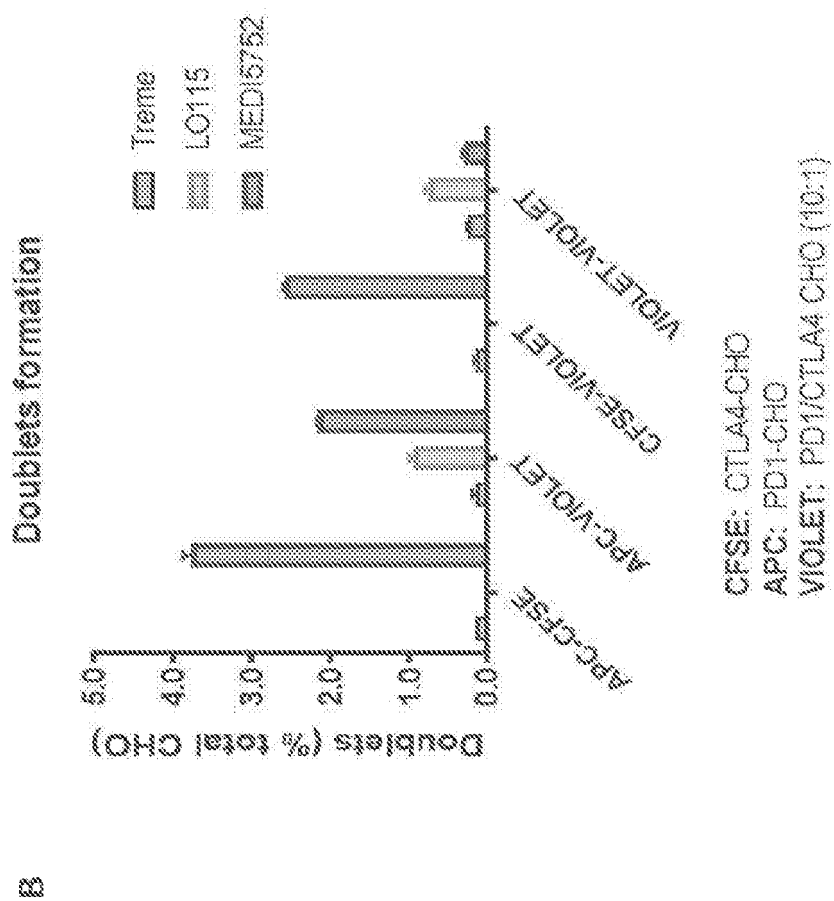


FIGURE 24

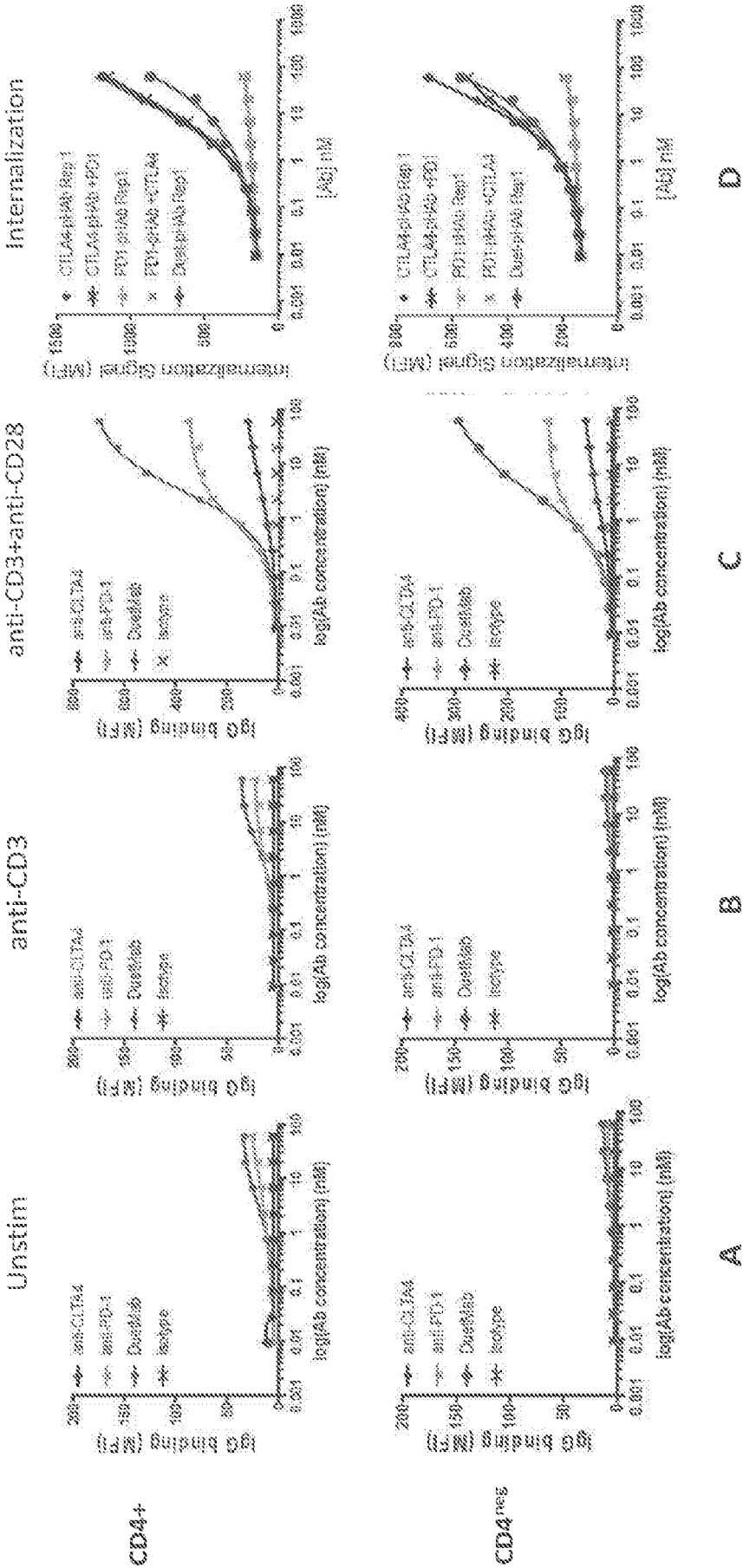


FIGURE 26

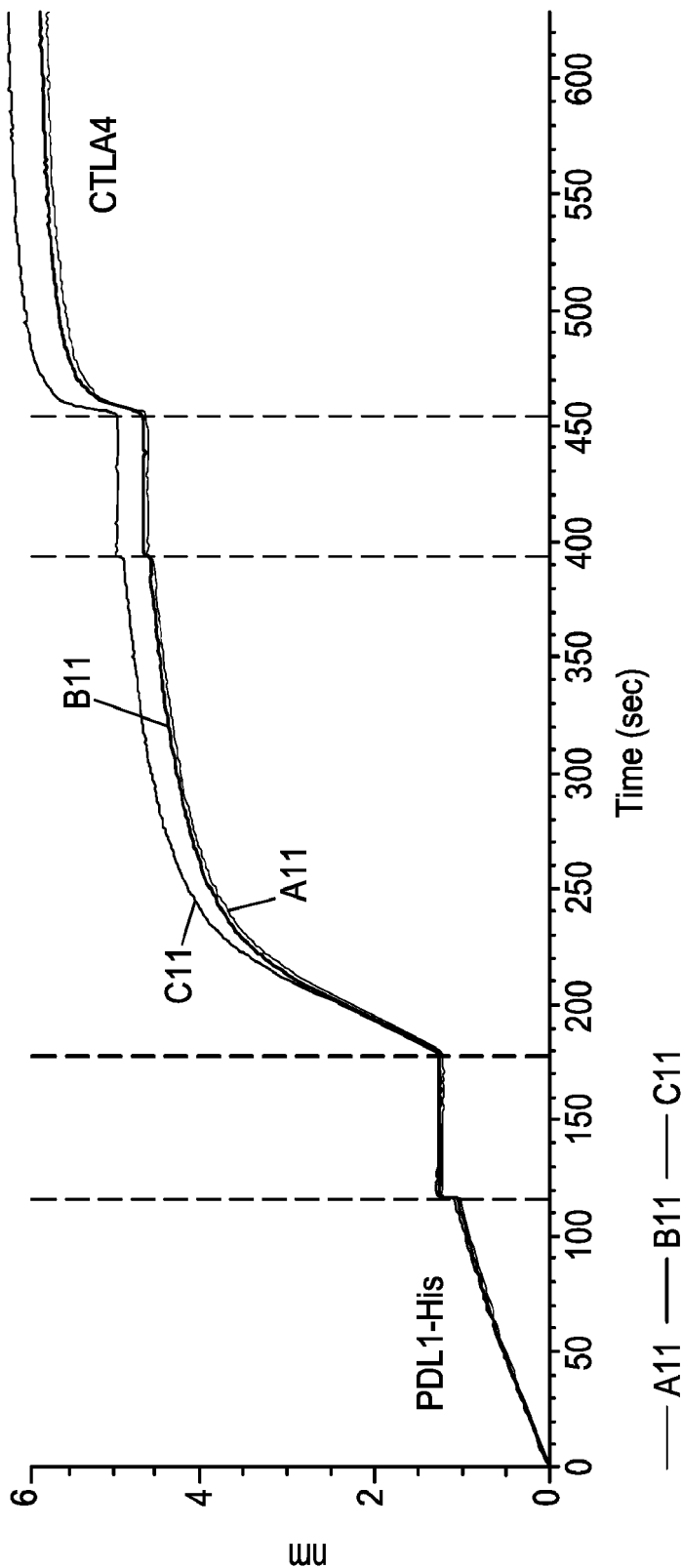
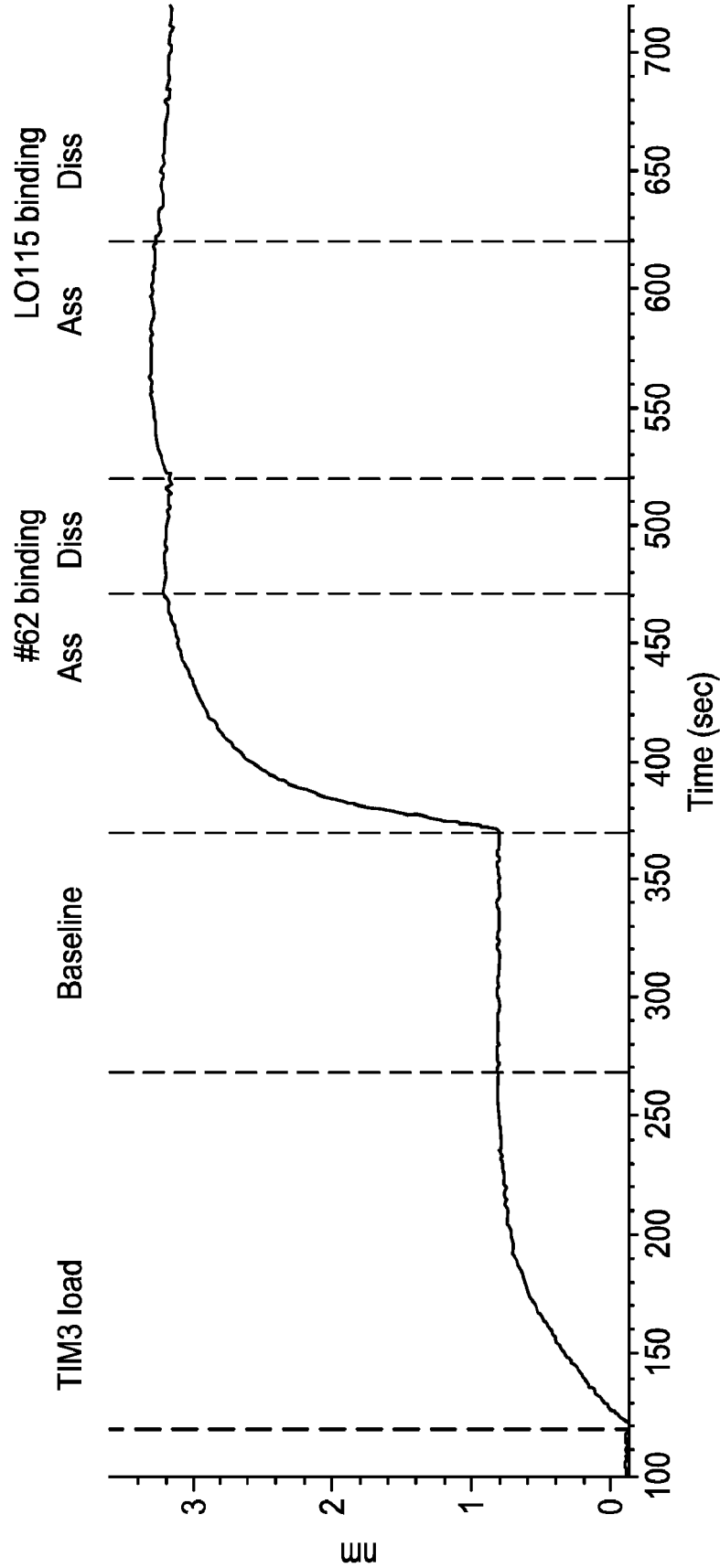


FIGURE 27A



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FIGURE 27B

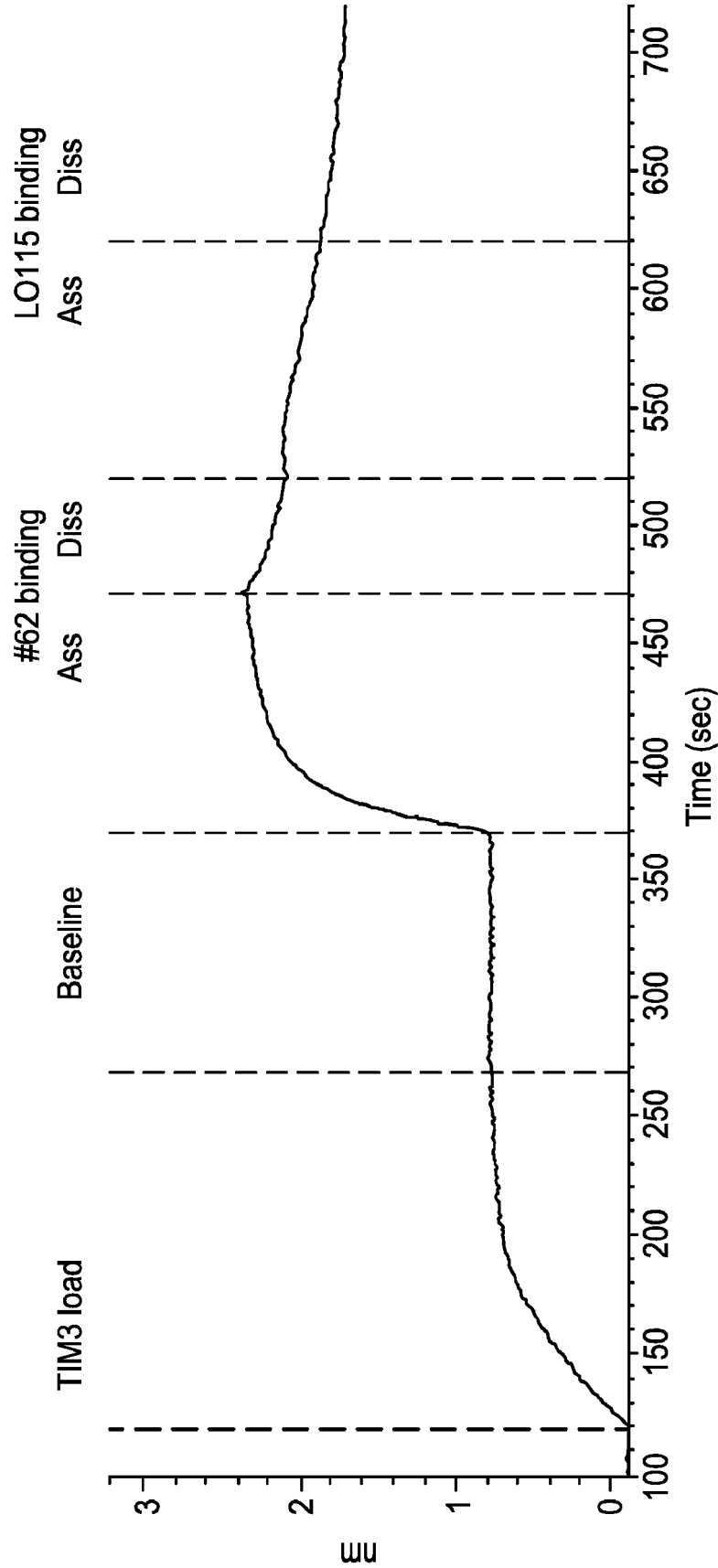
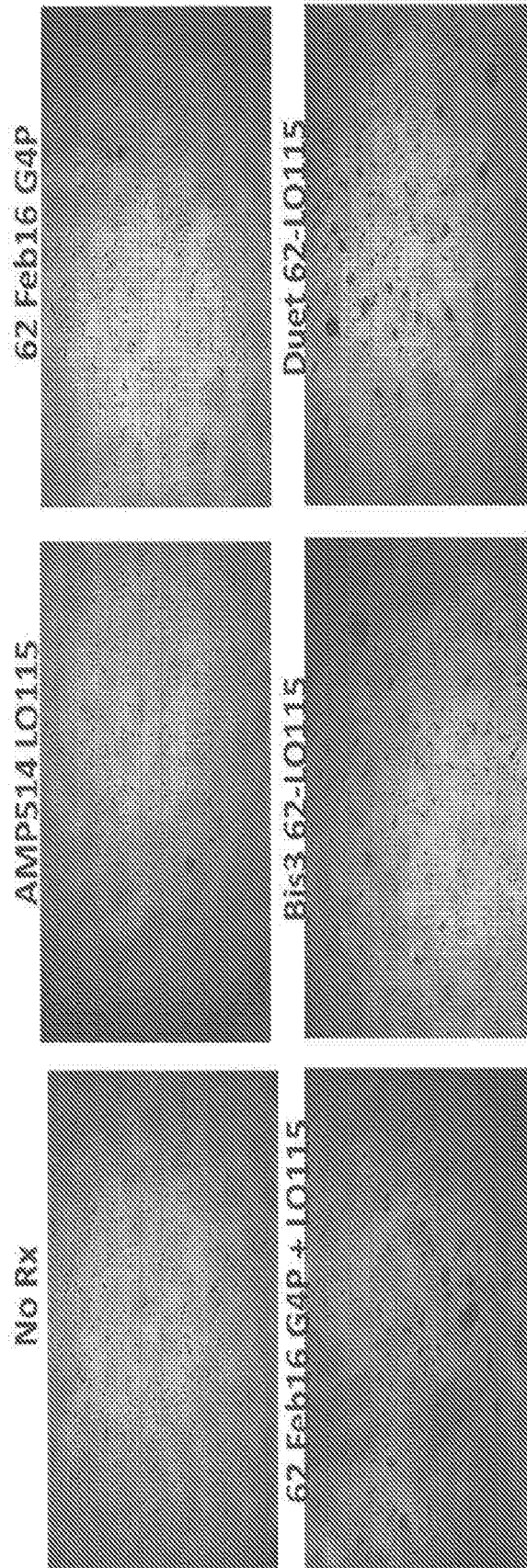


FIGURE 28A



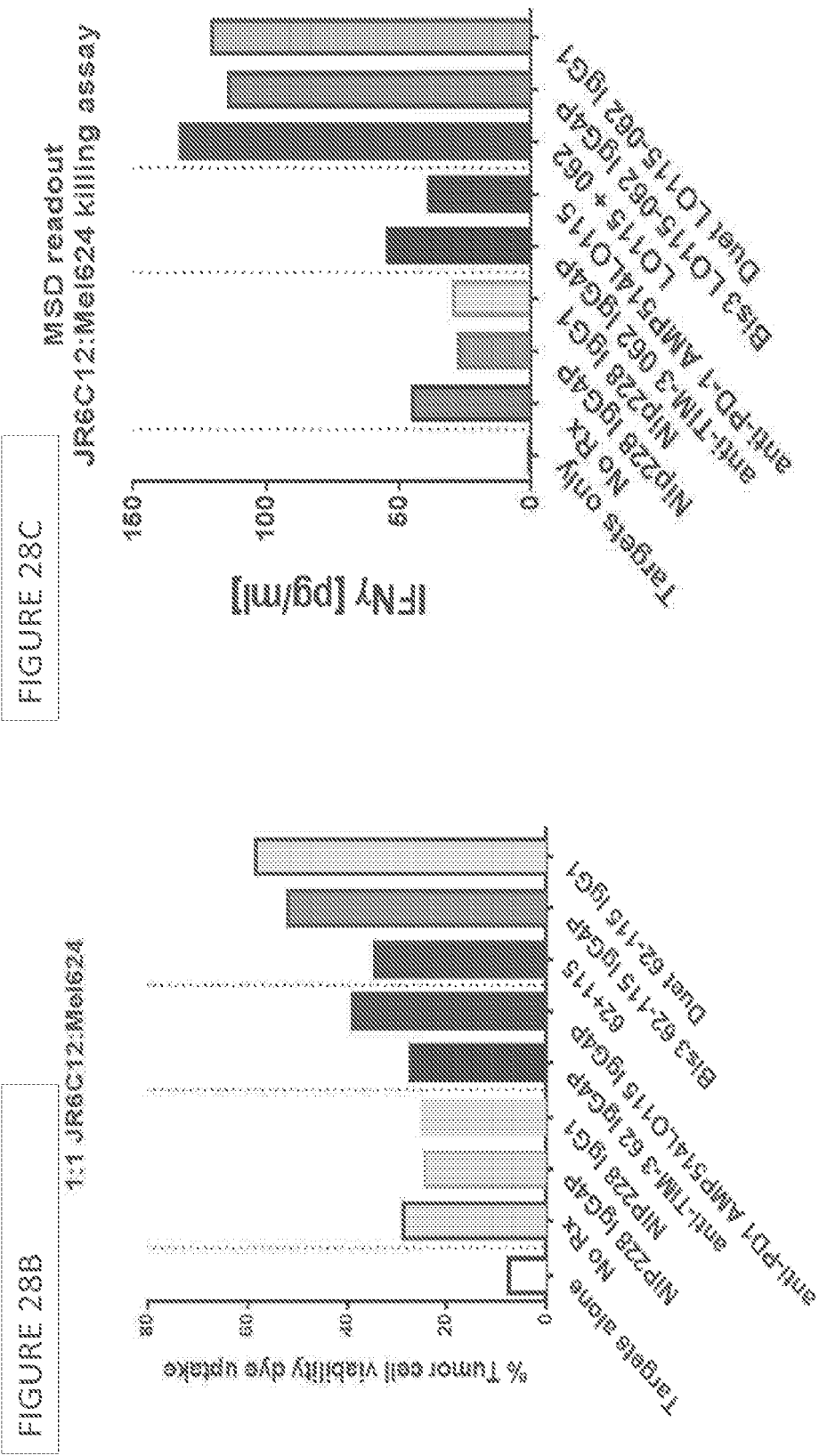


FIGURE 29

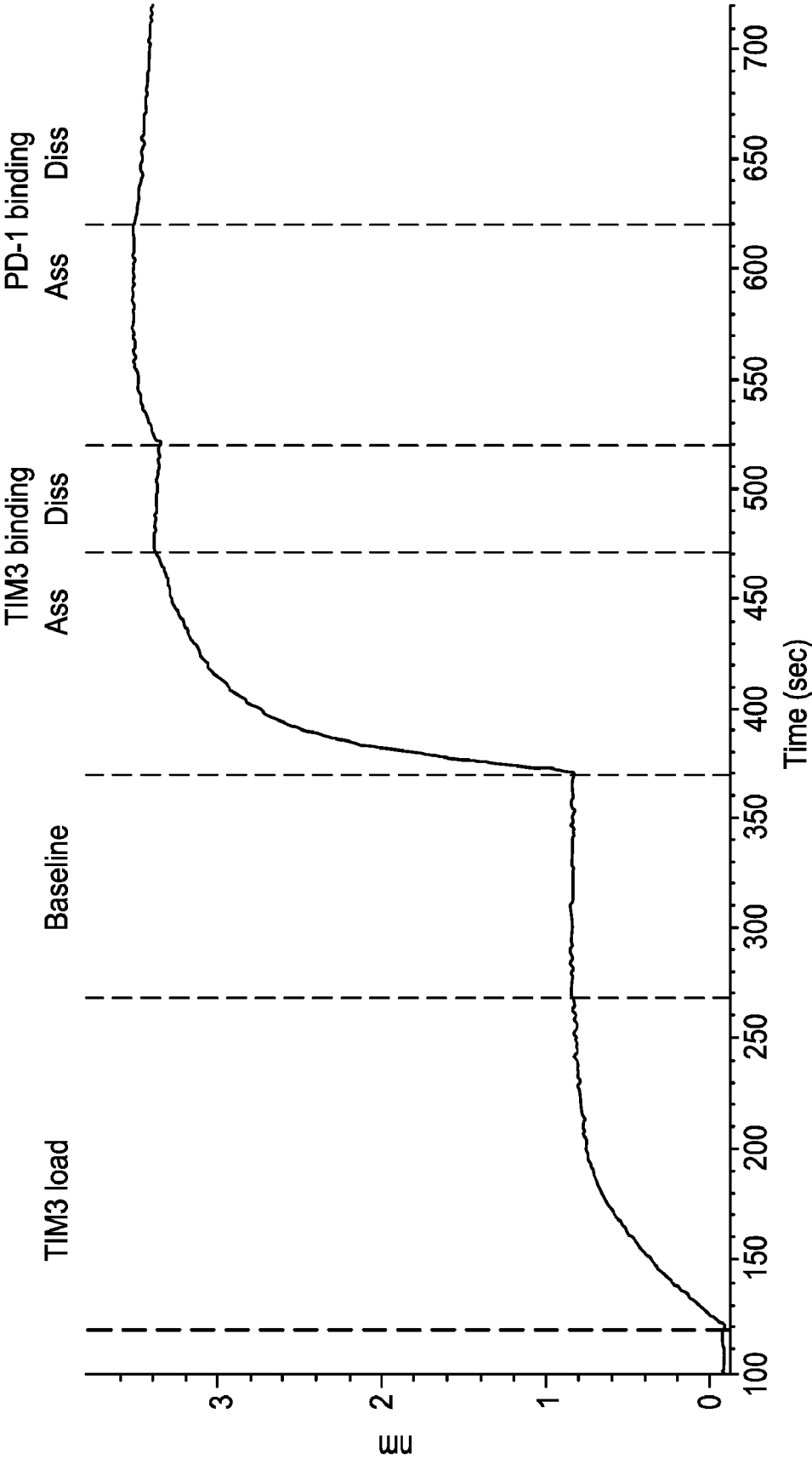


FIGURE 30

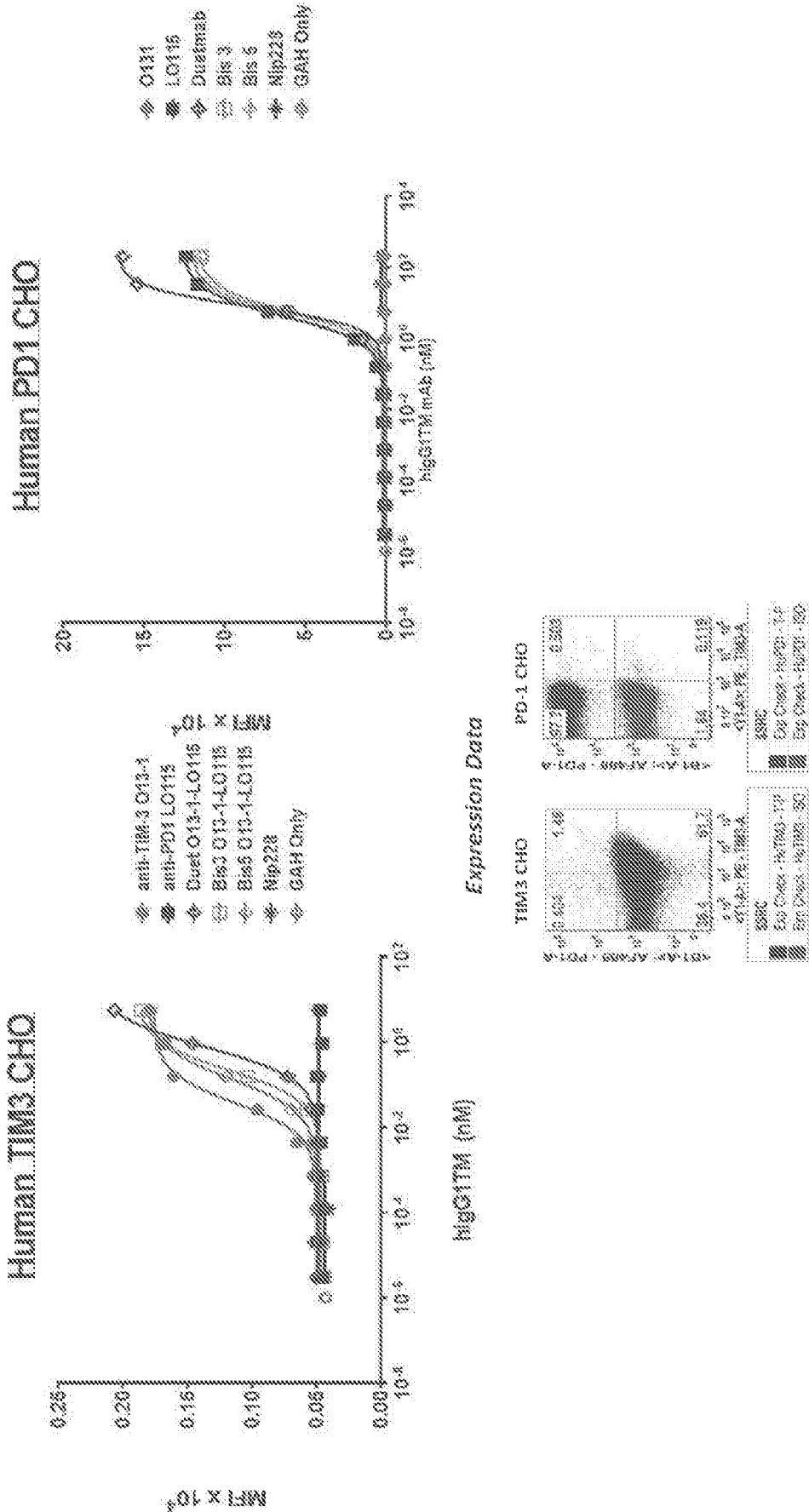


FIGURE 31

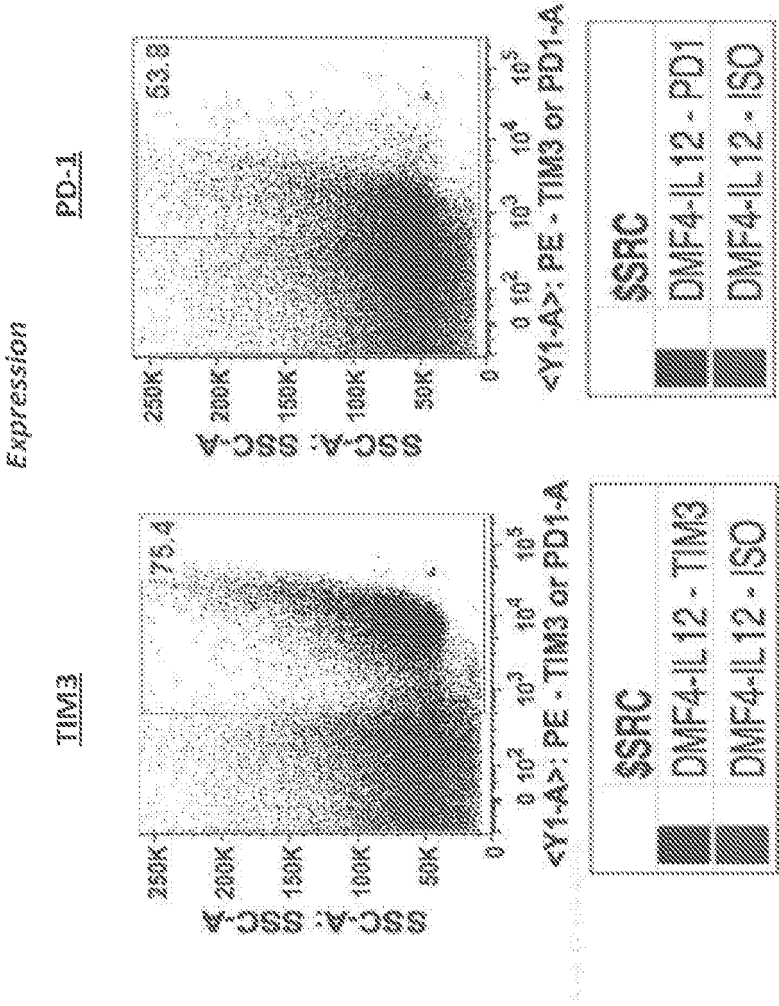


FIGURE 32

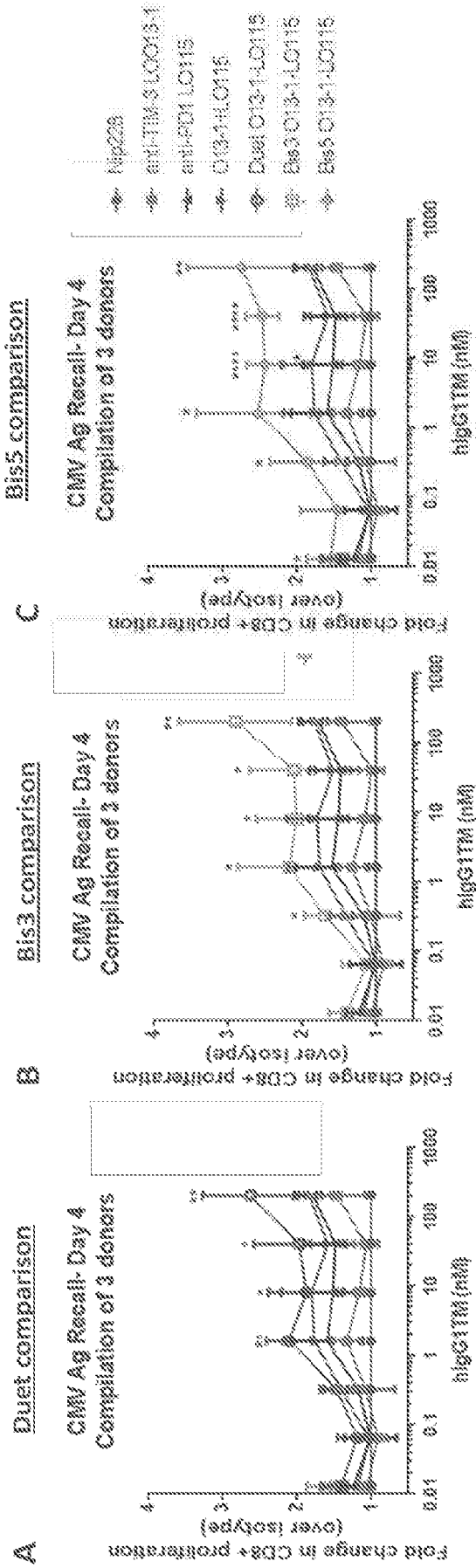


FIGURE 33

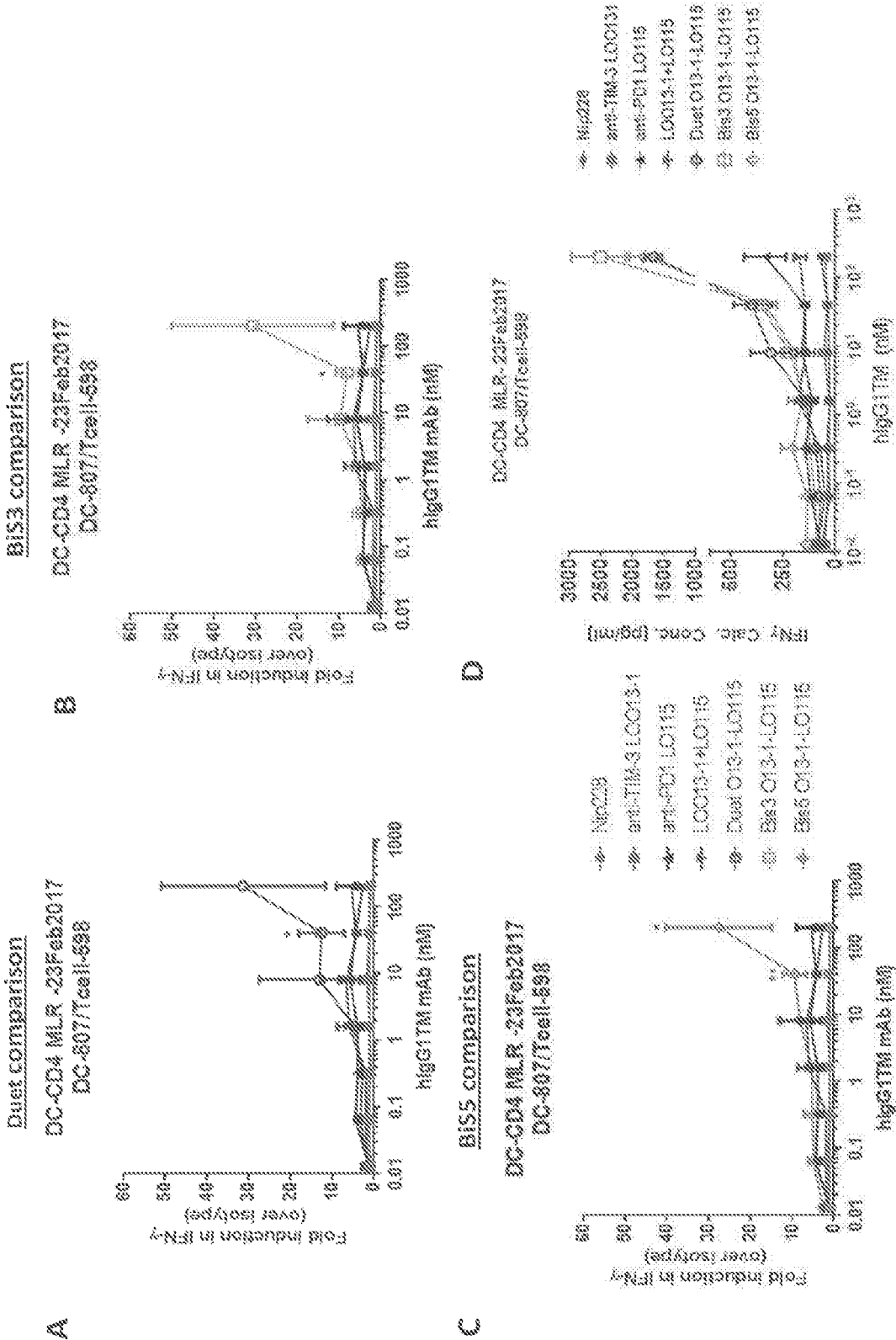


FIGURE 34

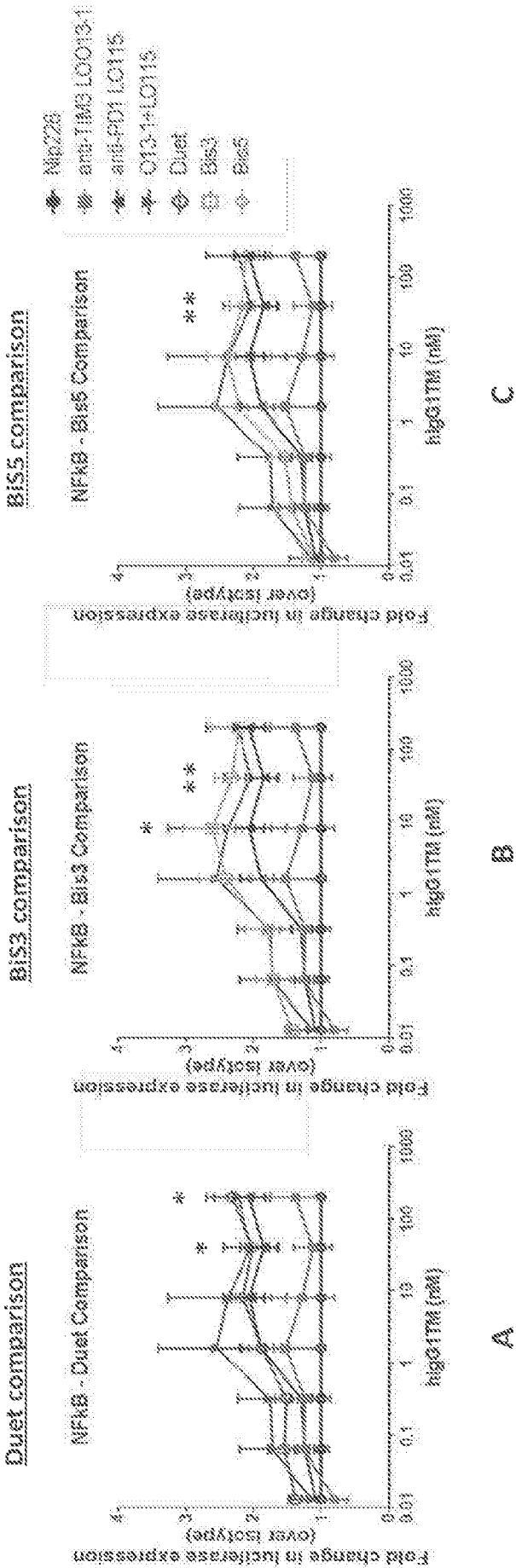


FIGURE 35

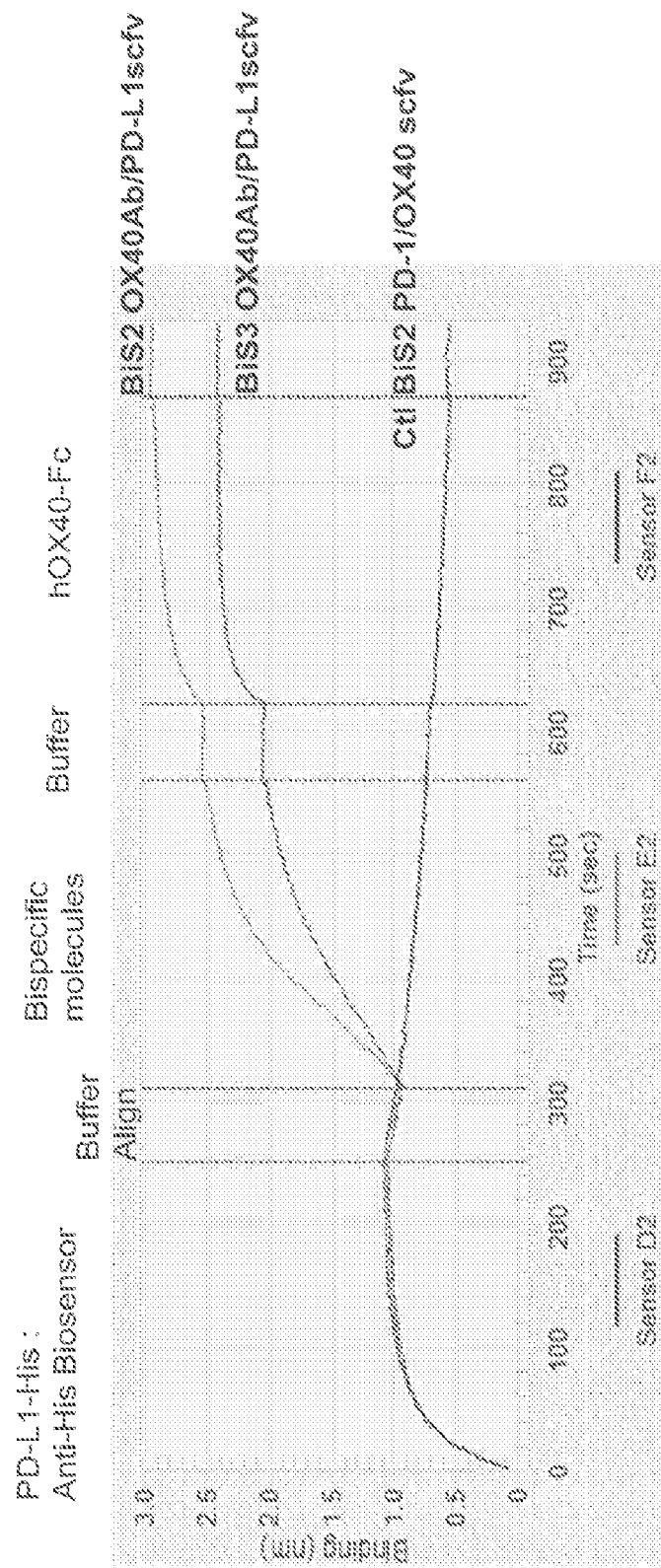


FIGURE 36

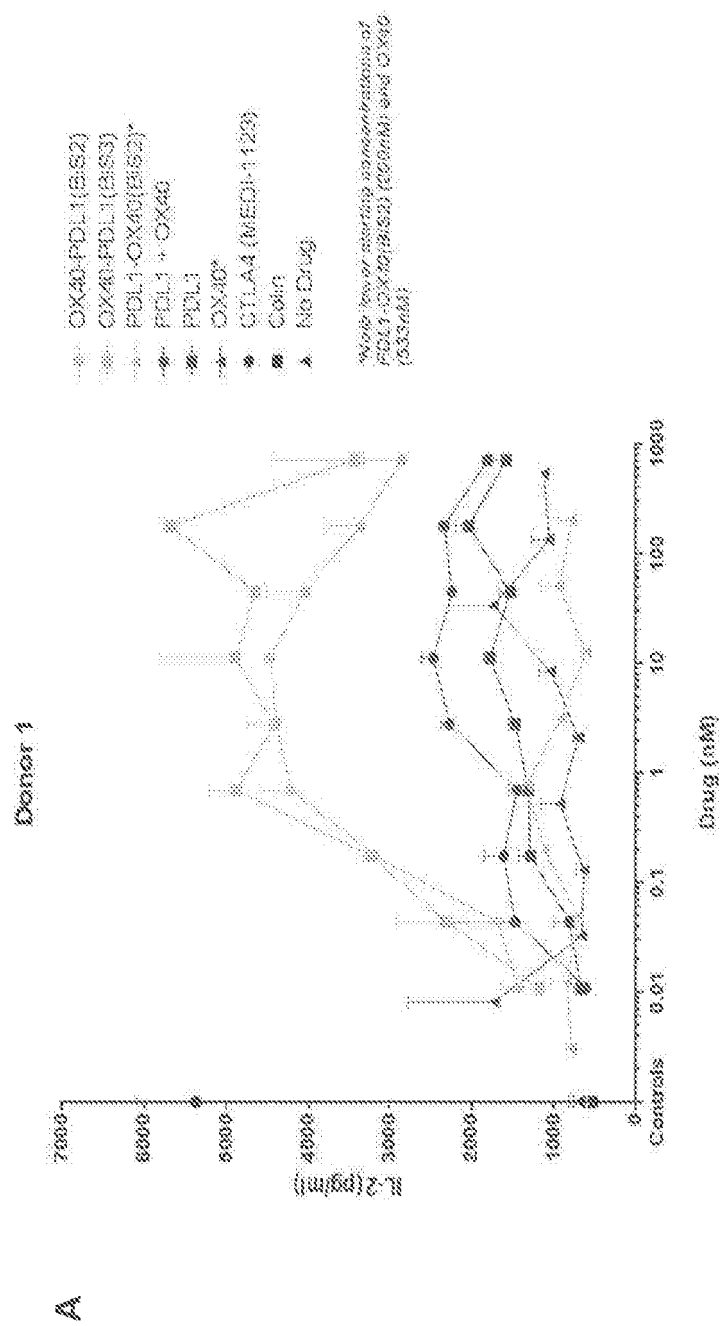
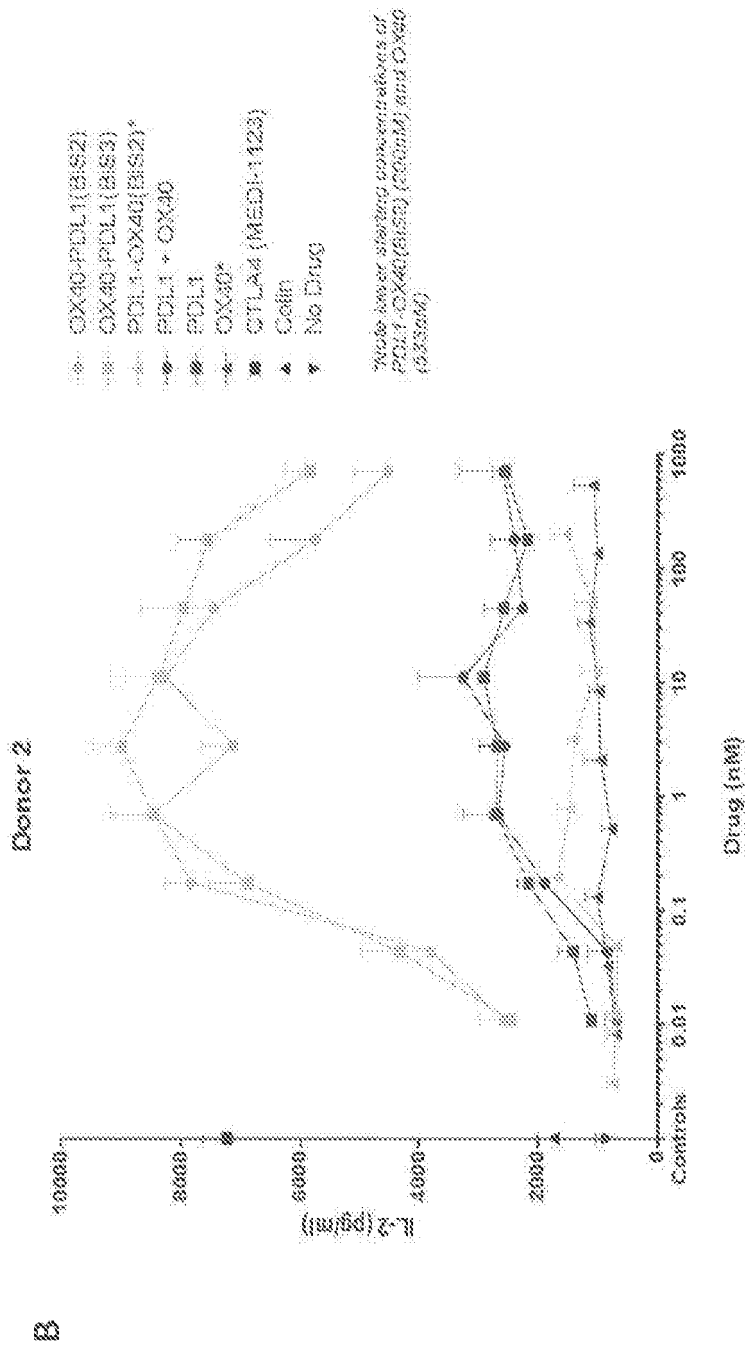
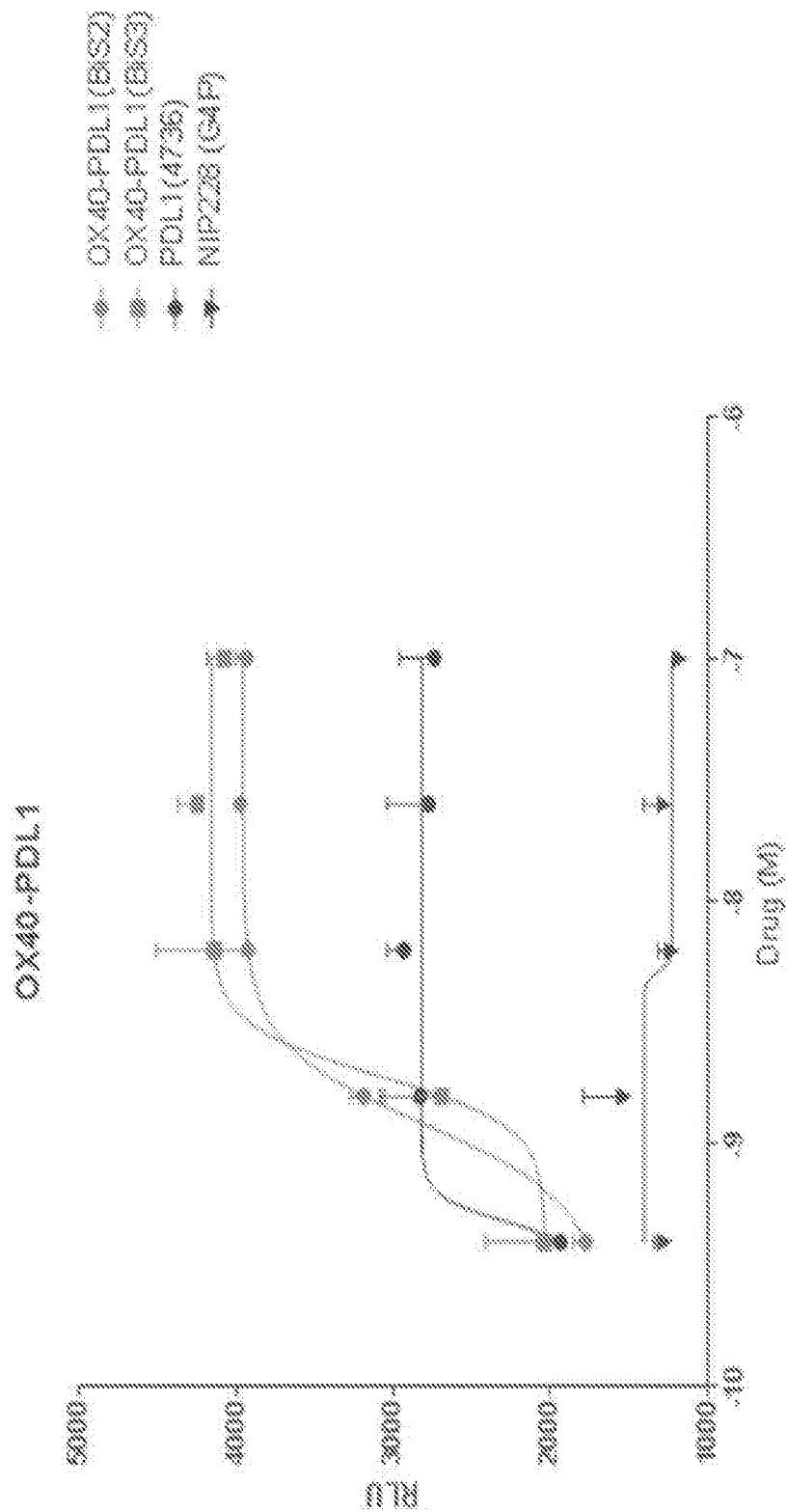


FIGURE 36 cont'd.



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FIGURE 37



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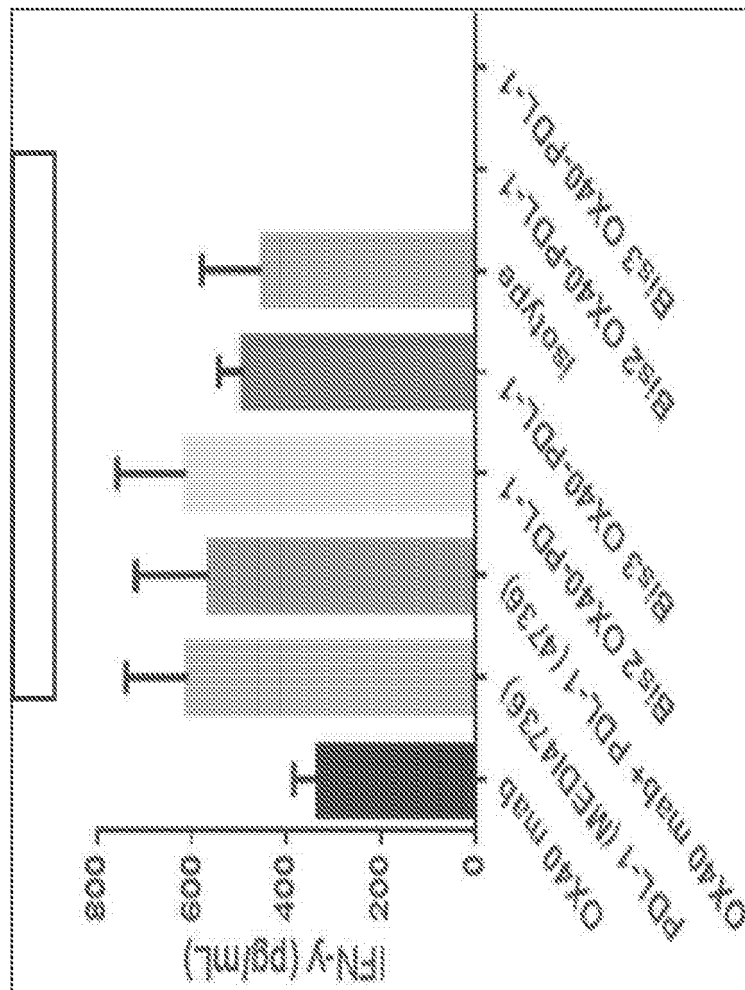
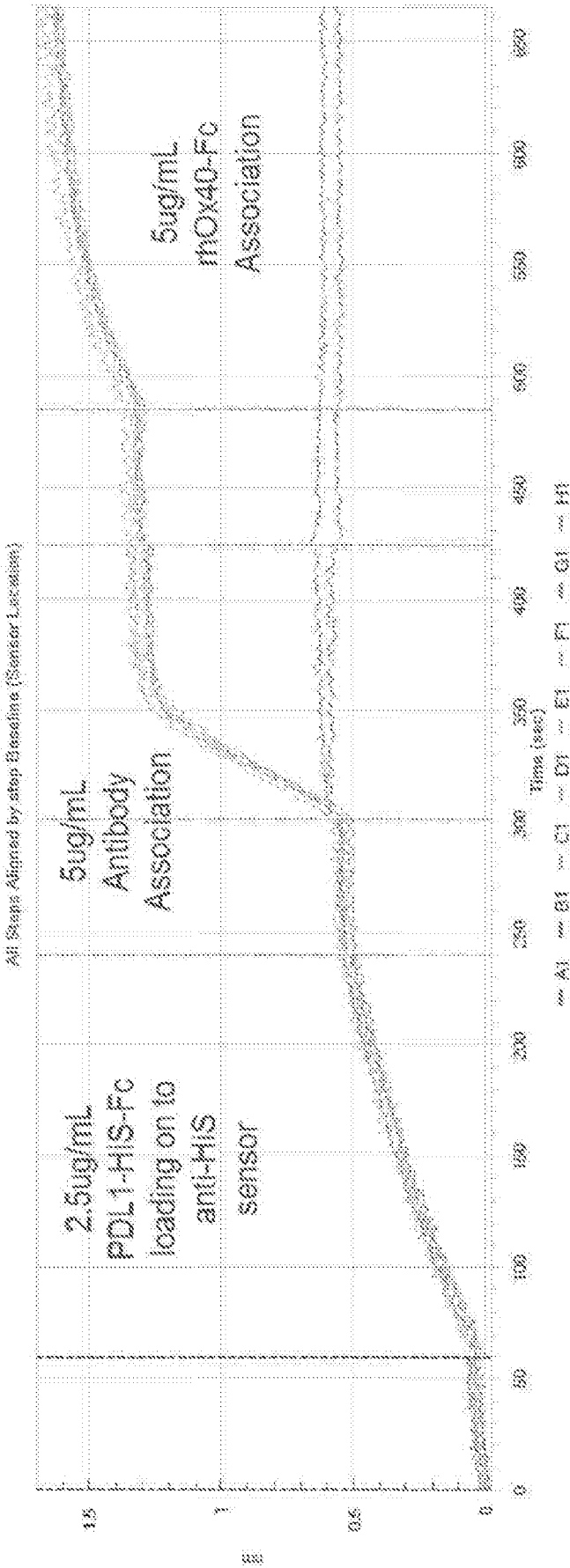


FIGURE 38

FIGURE 39



Step	G1	G2	G3	G4	G5	G6	G7	G8
B1S5	B1S2	B1S5	B1S5	B1S5	B1S5	B1S5	B1S5	B1S5
R347/nMGC	R347/OX40	VH-VL	VH-VL	VH-VL	VH-VL	VH-VL	VH-VL	VL-VH
G4P	G4P	YTE-G4P	N434A G1	N434A-G4P	G4P	G1	G1	G4P

FIGURE 40

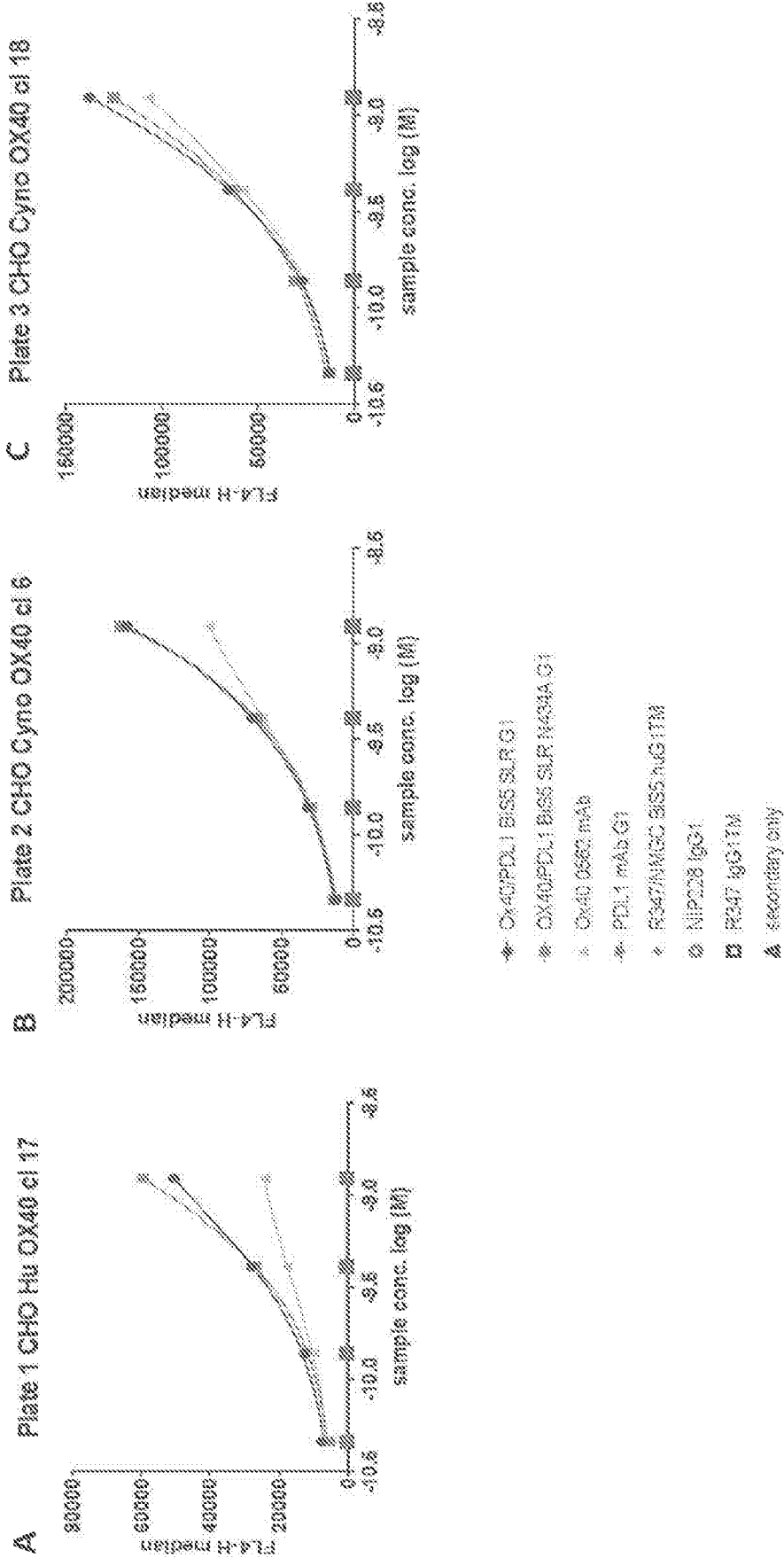
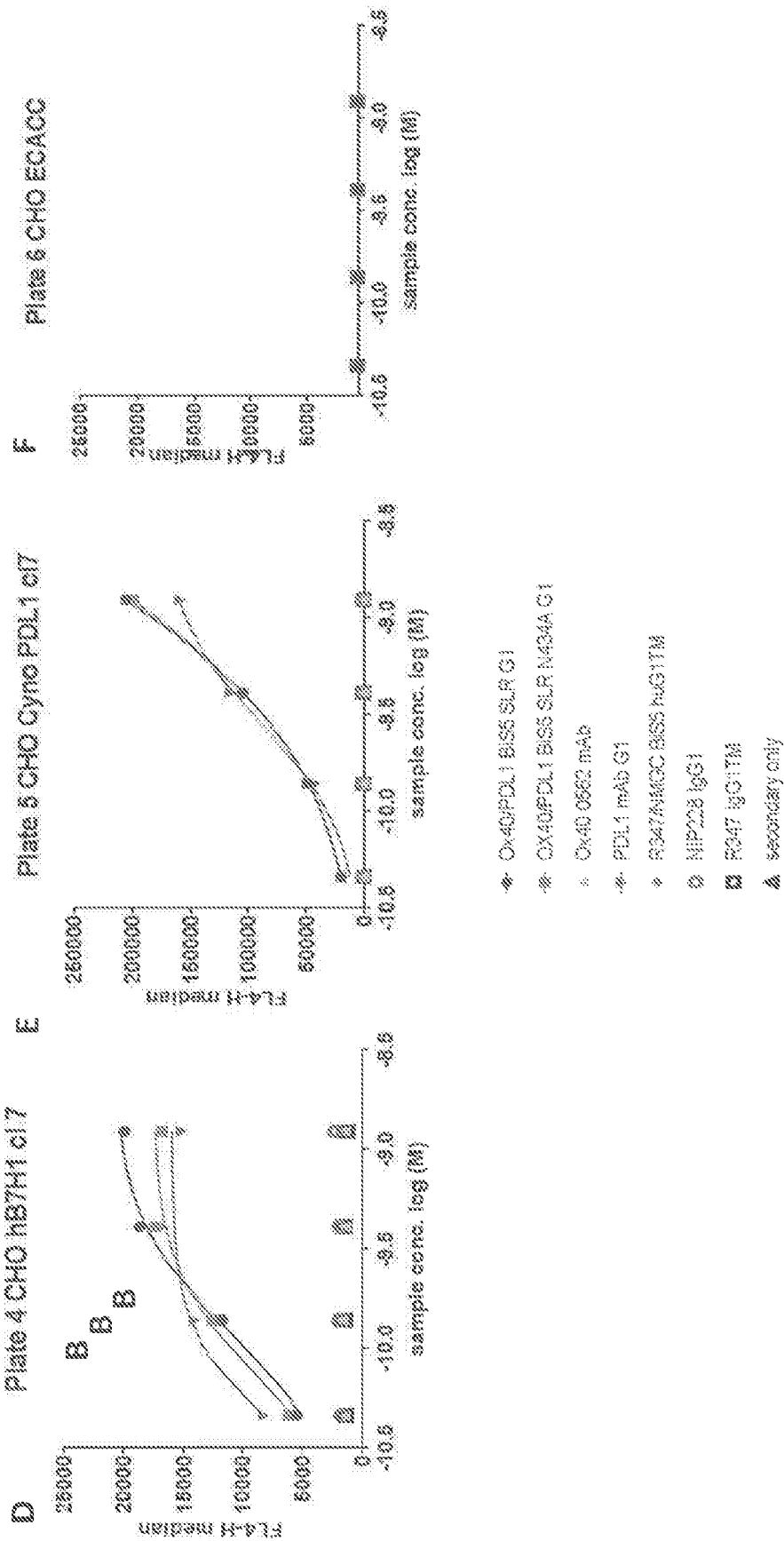


FIGURE 40 cont'd.



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FIGURE 41

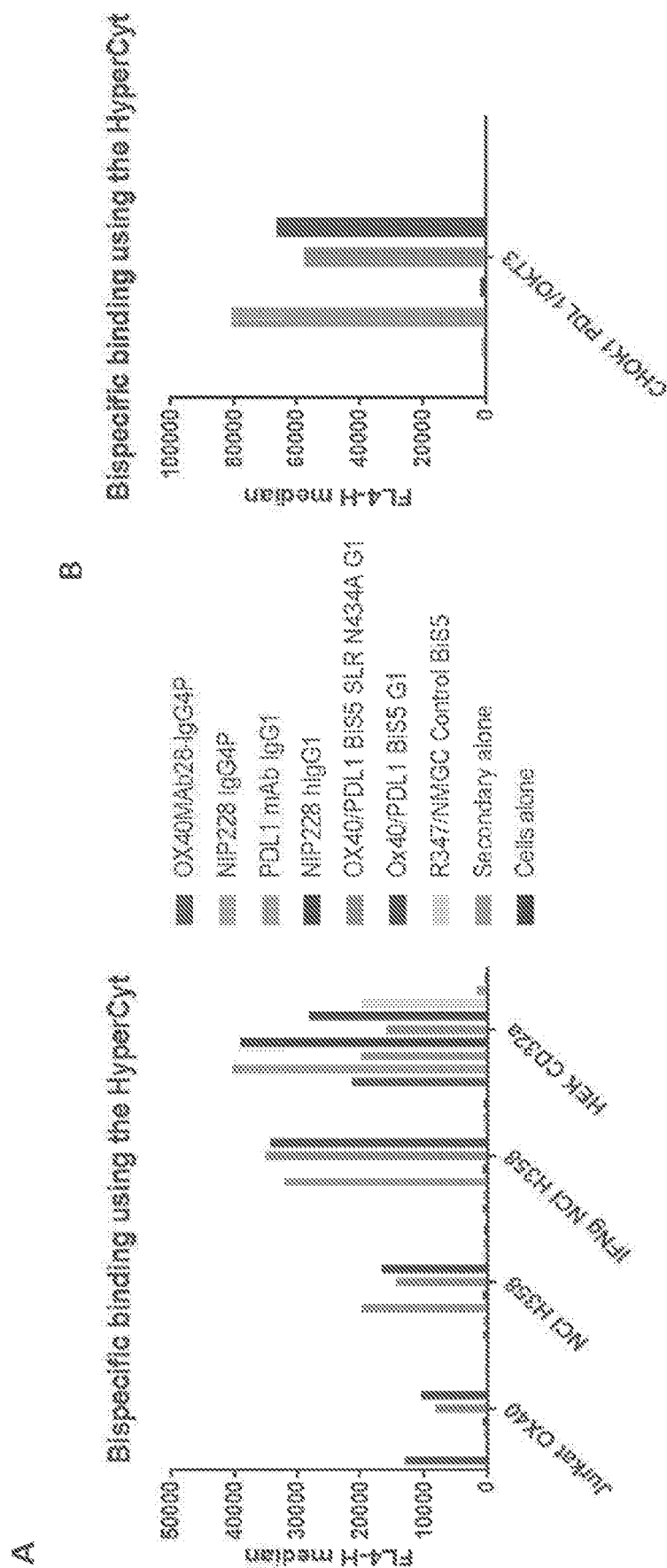


FIGURE 42

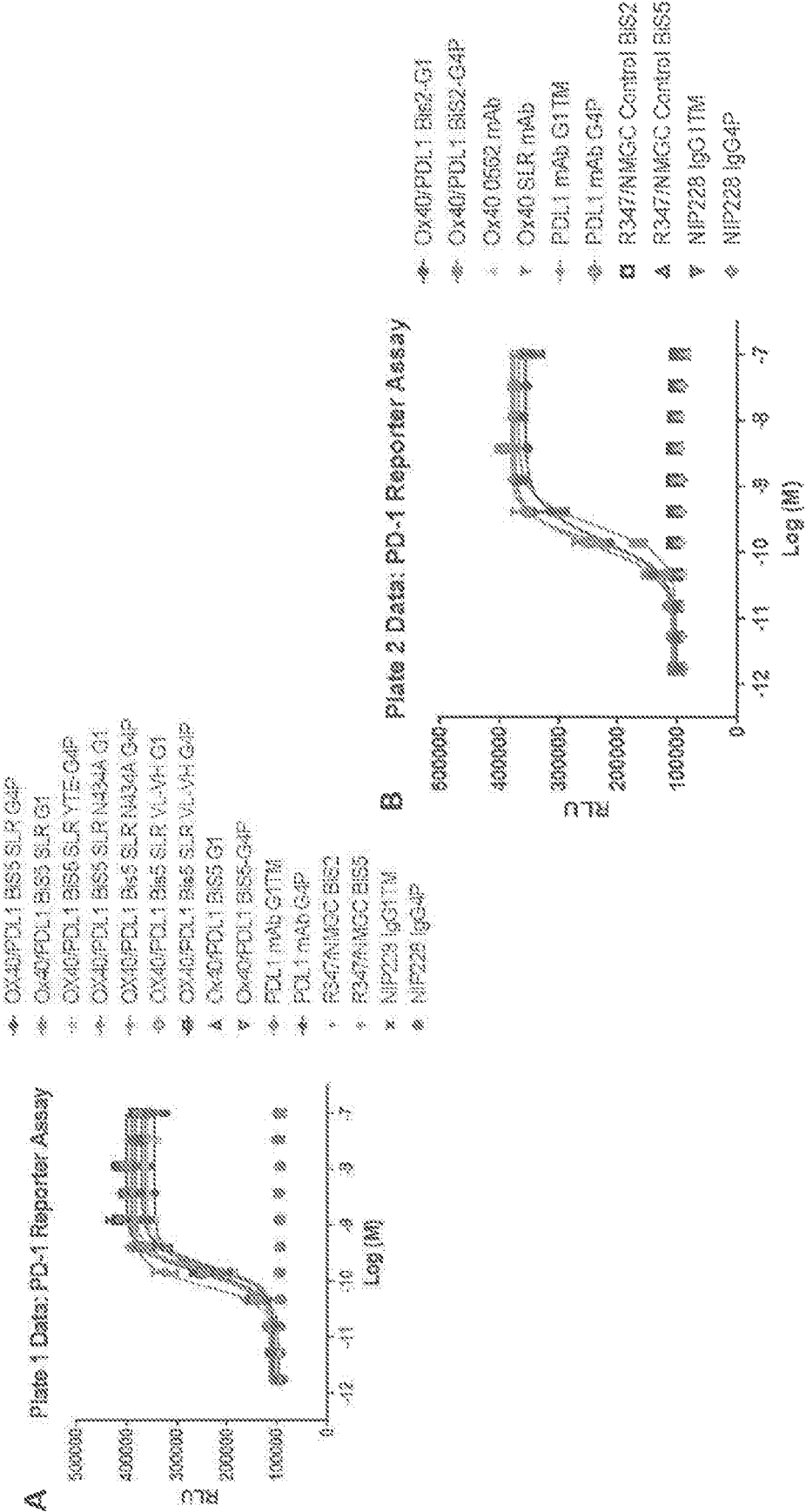


FIGURE 43

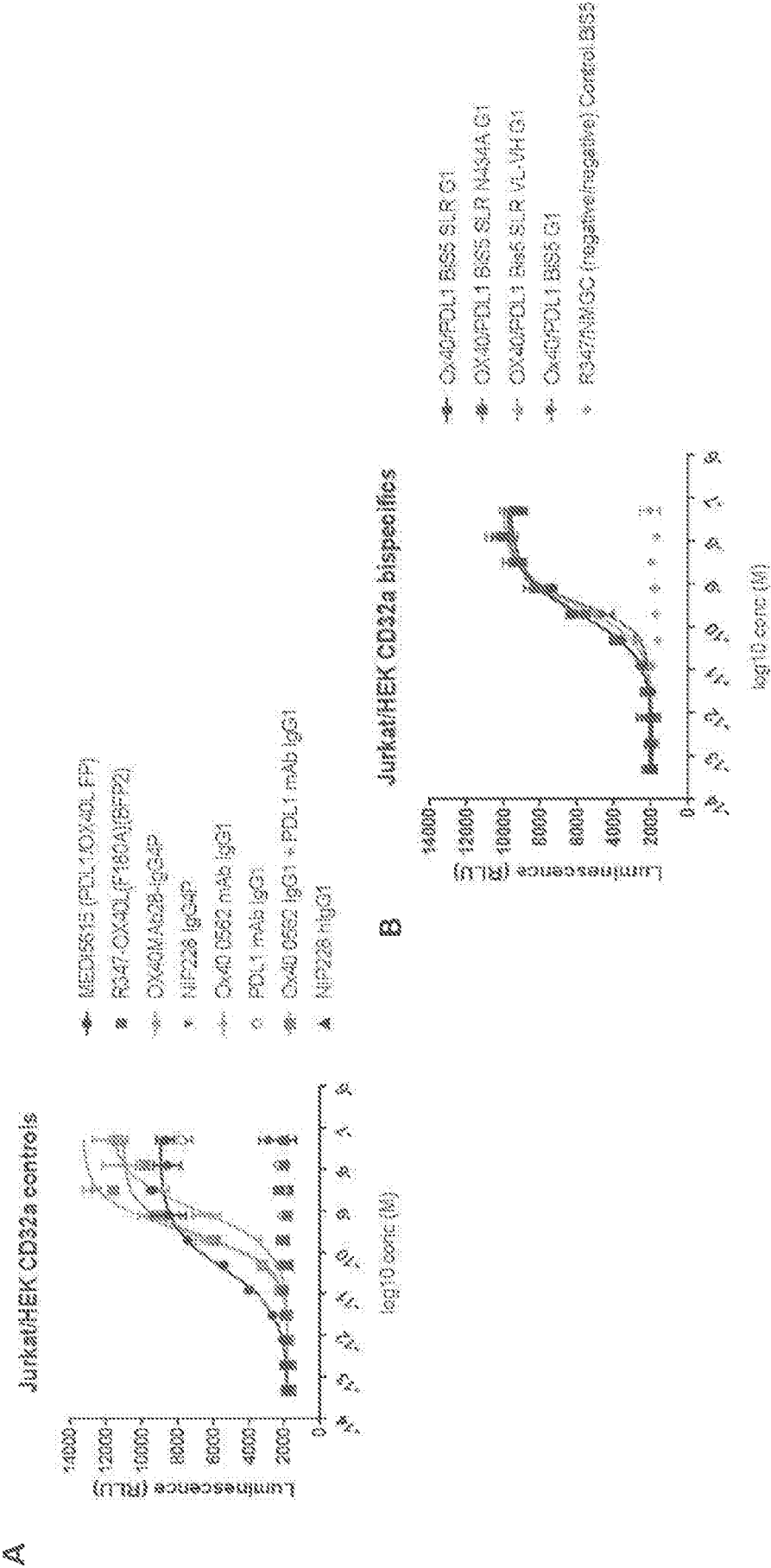


FIGURE 44

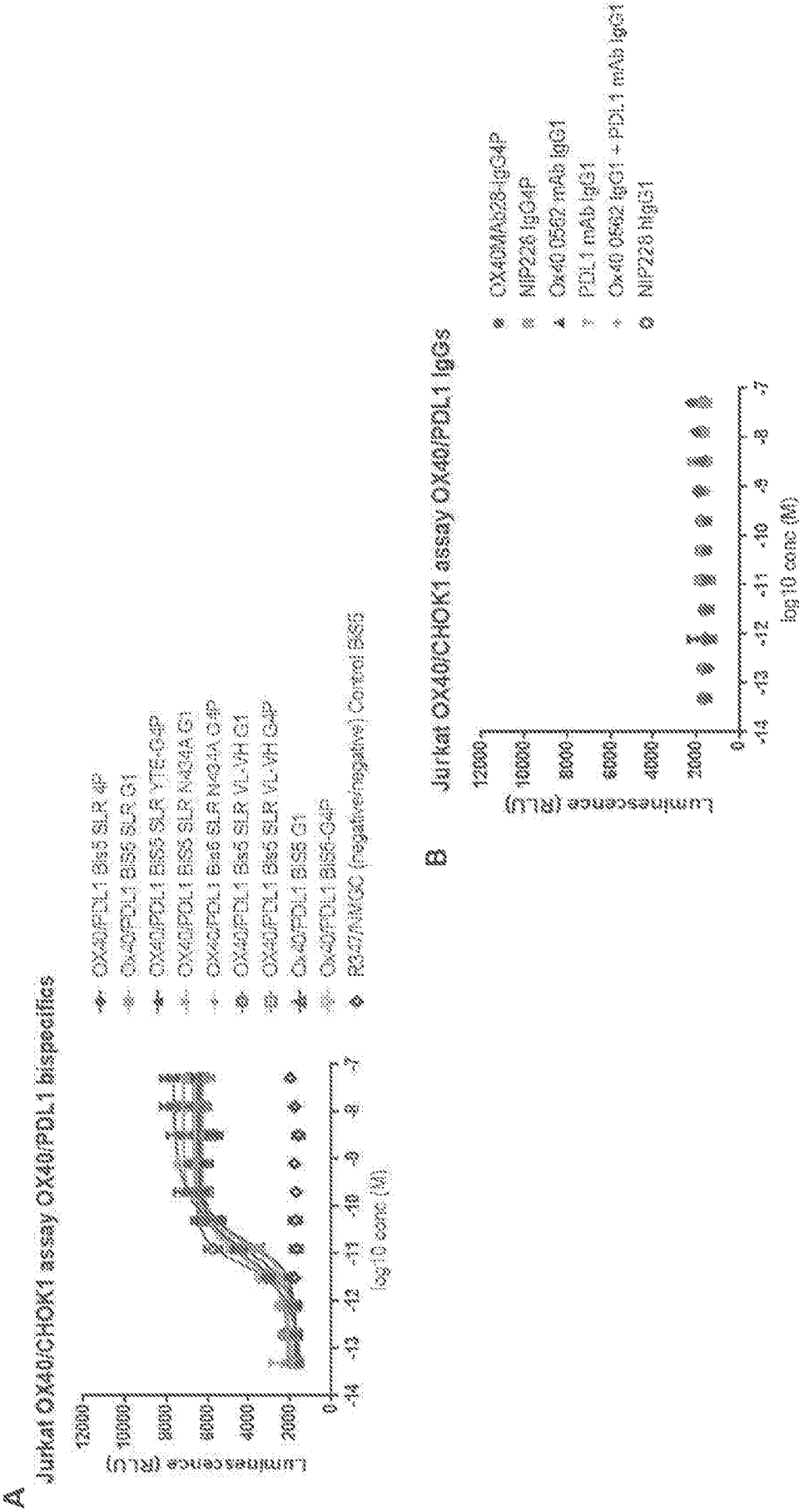


FIGURE 45

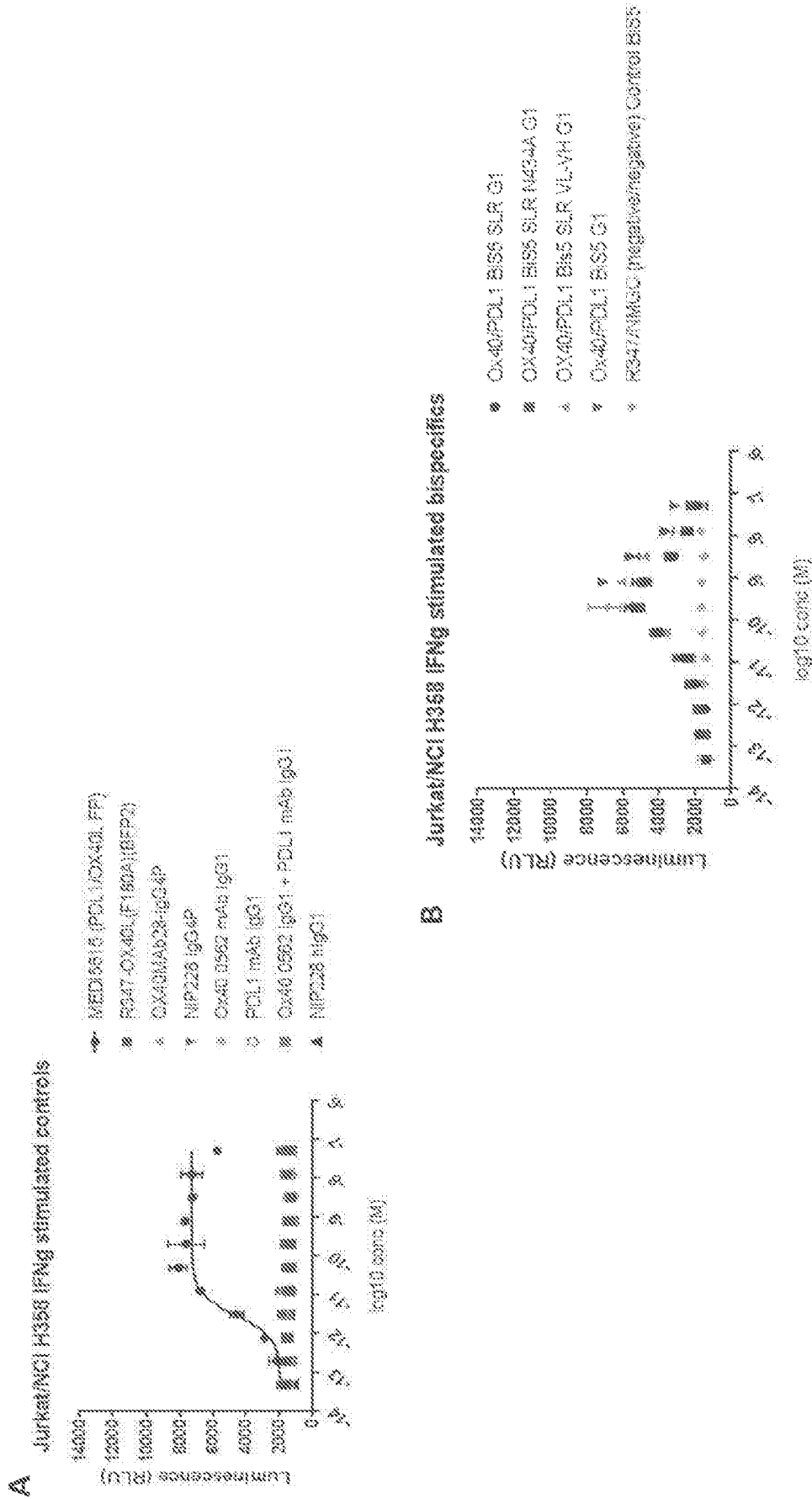


FIGURE 46

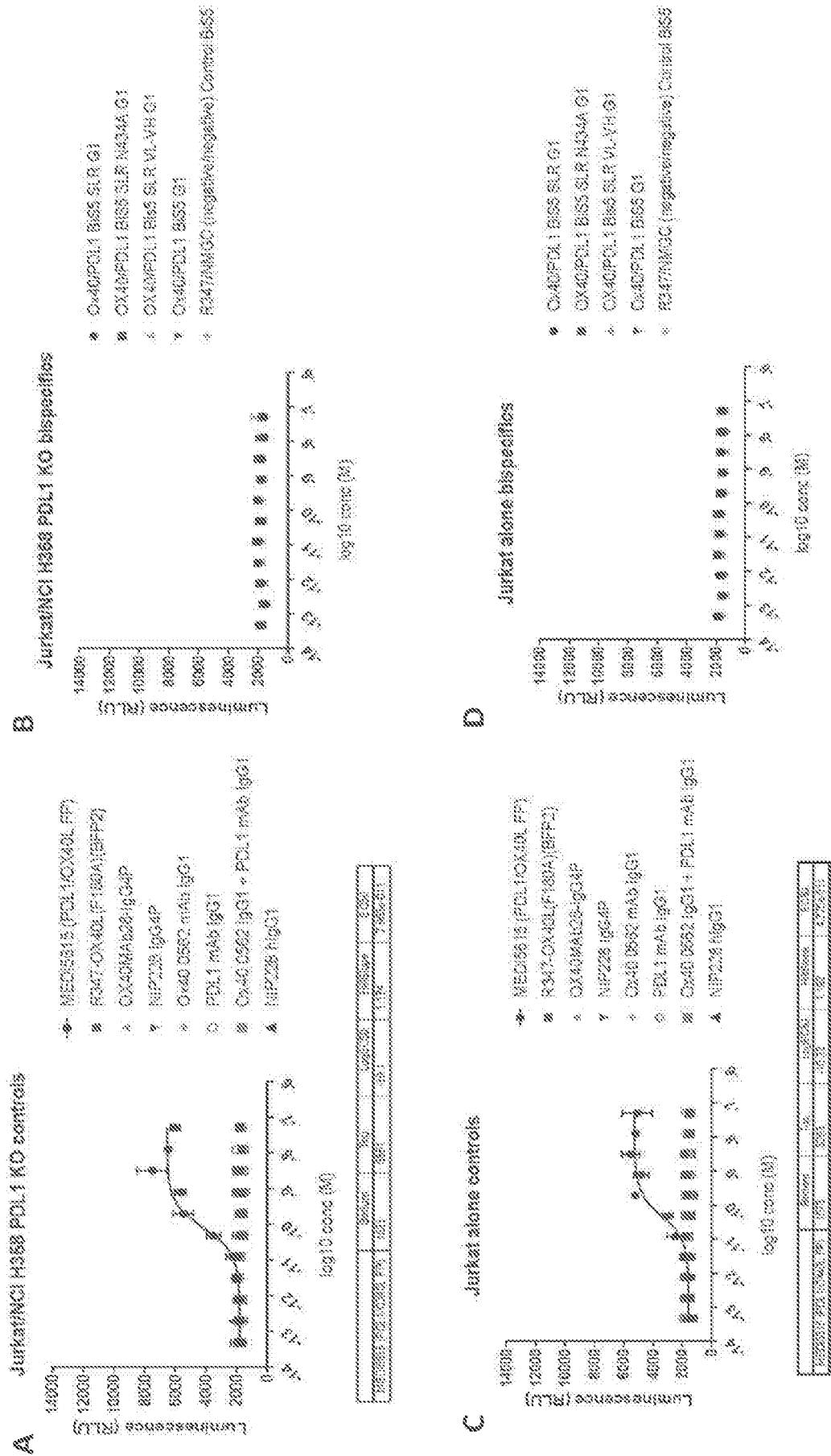


FIGURE 47

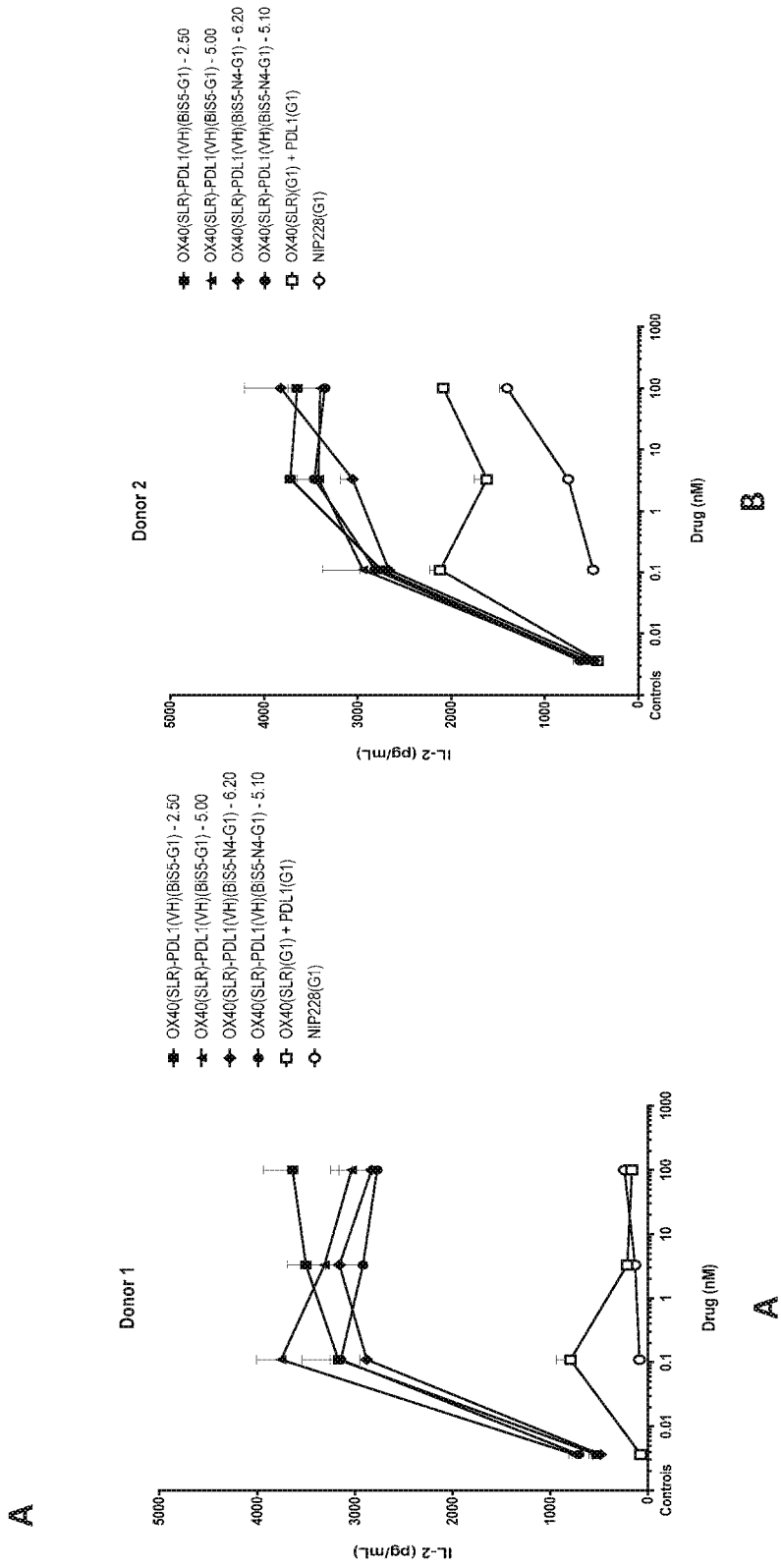


FIGURE 47 cont'd.

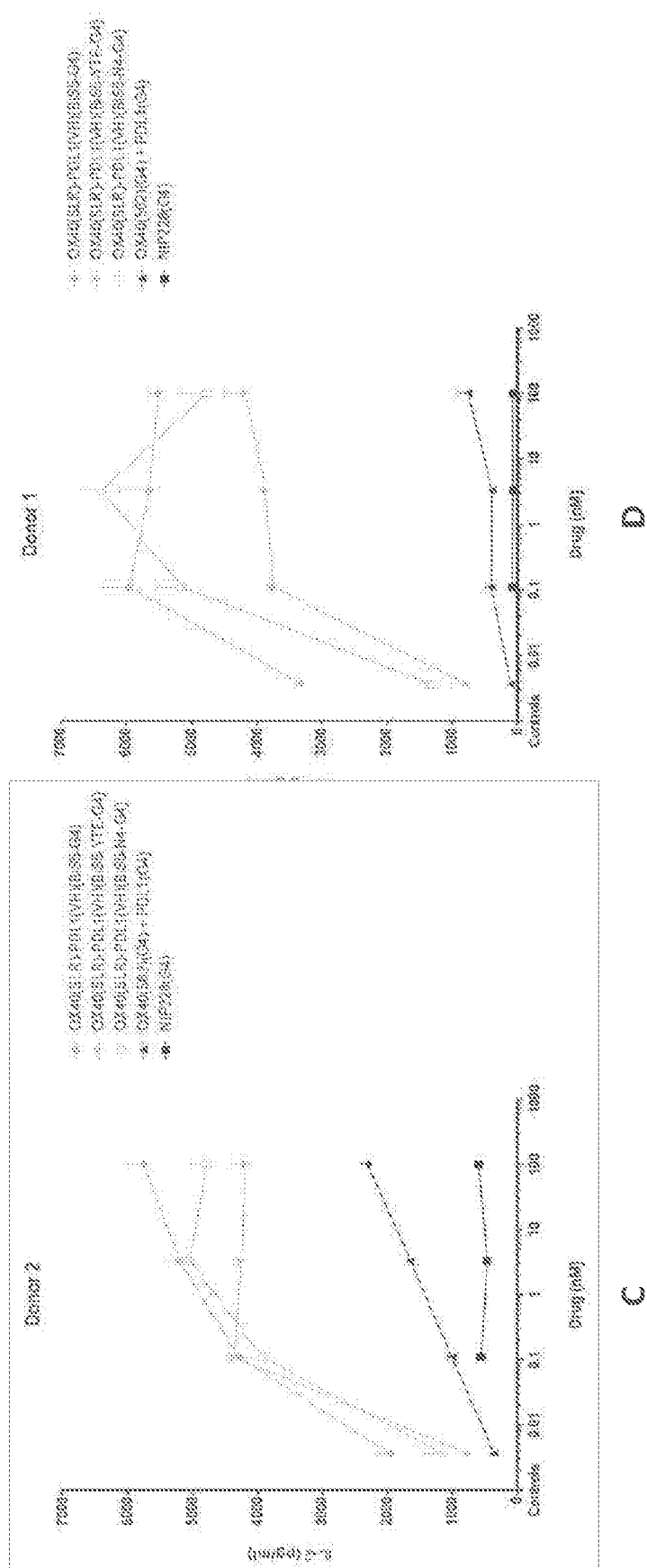


FIGURE 48

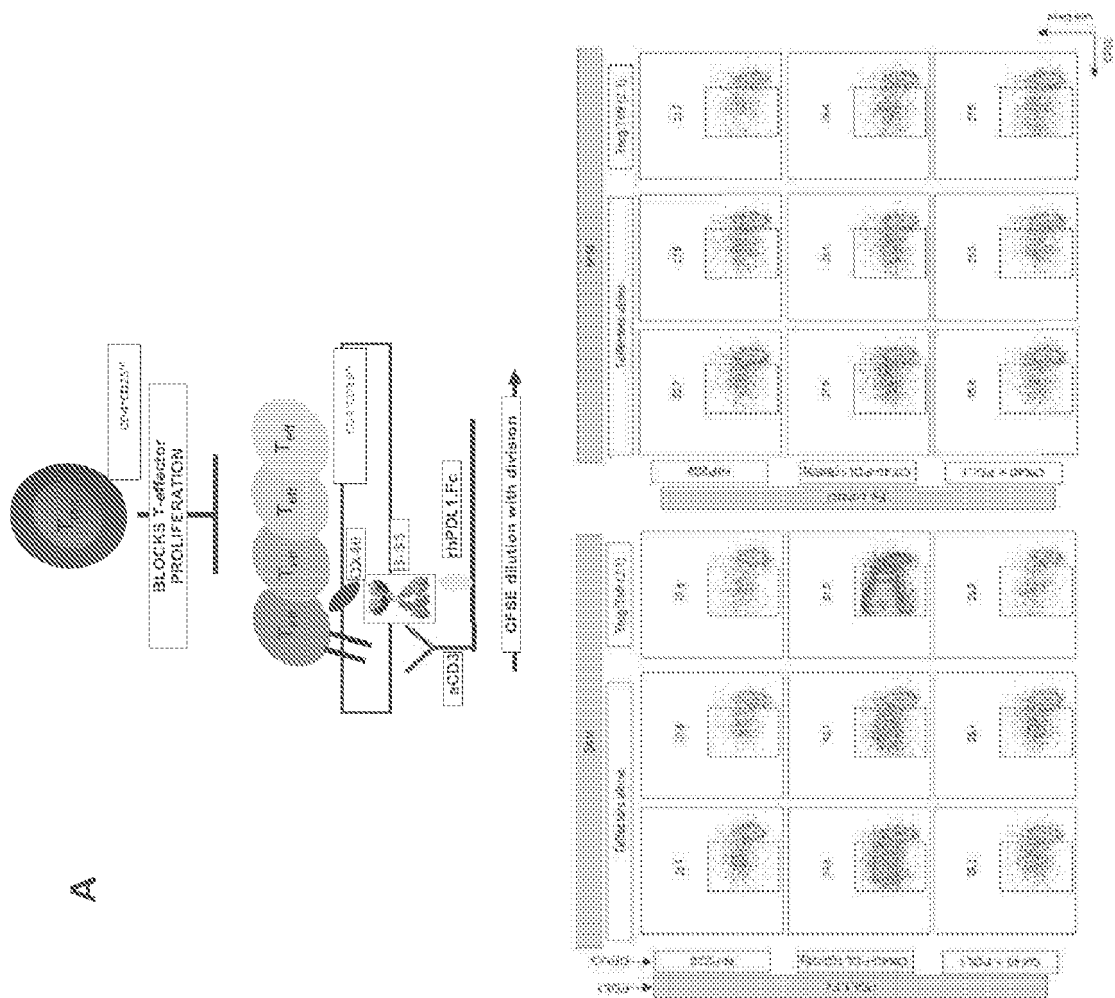
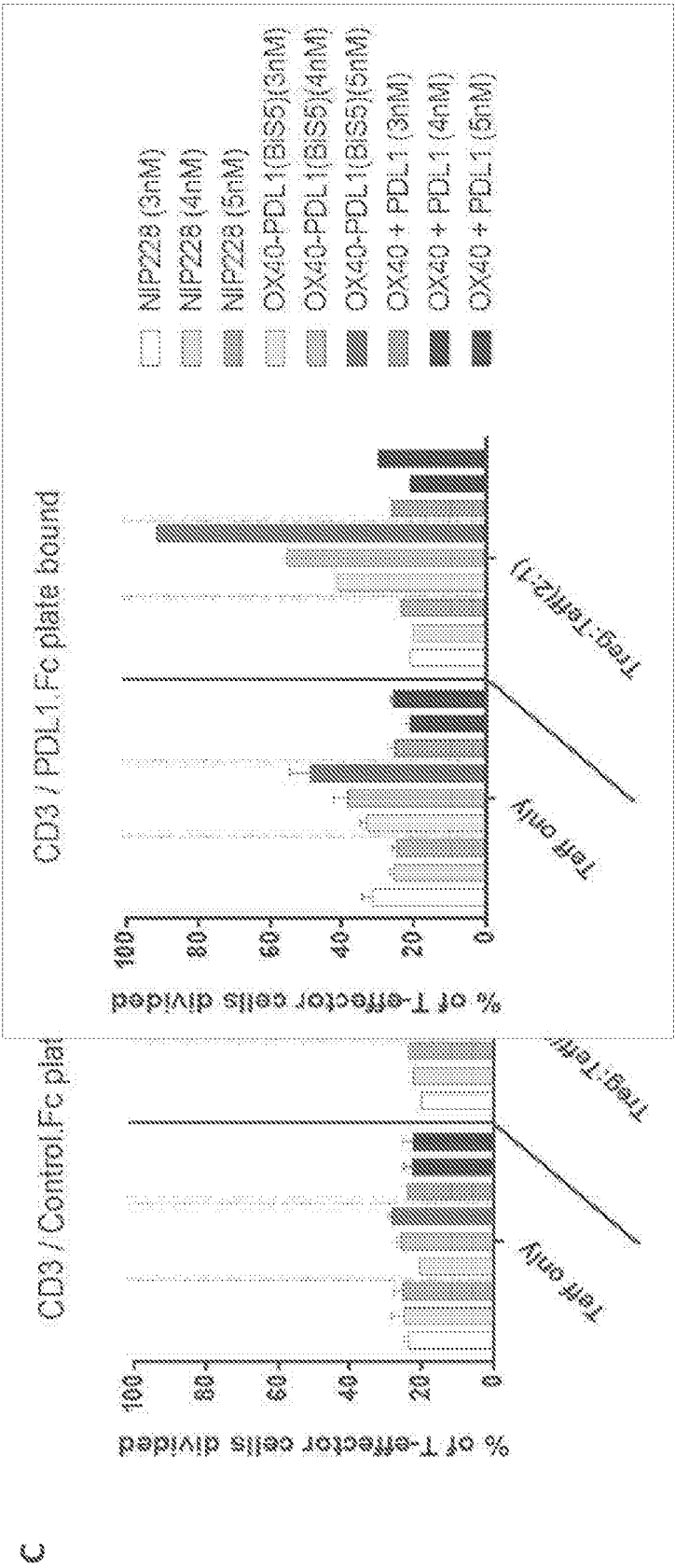
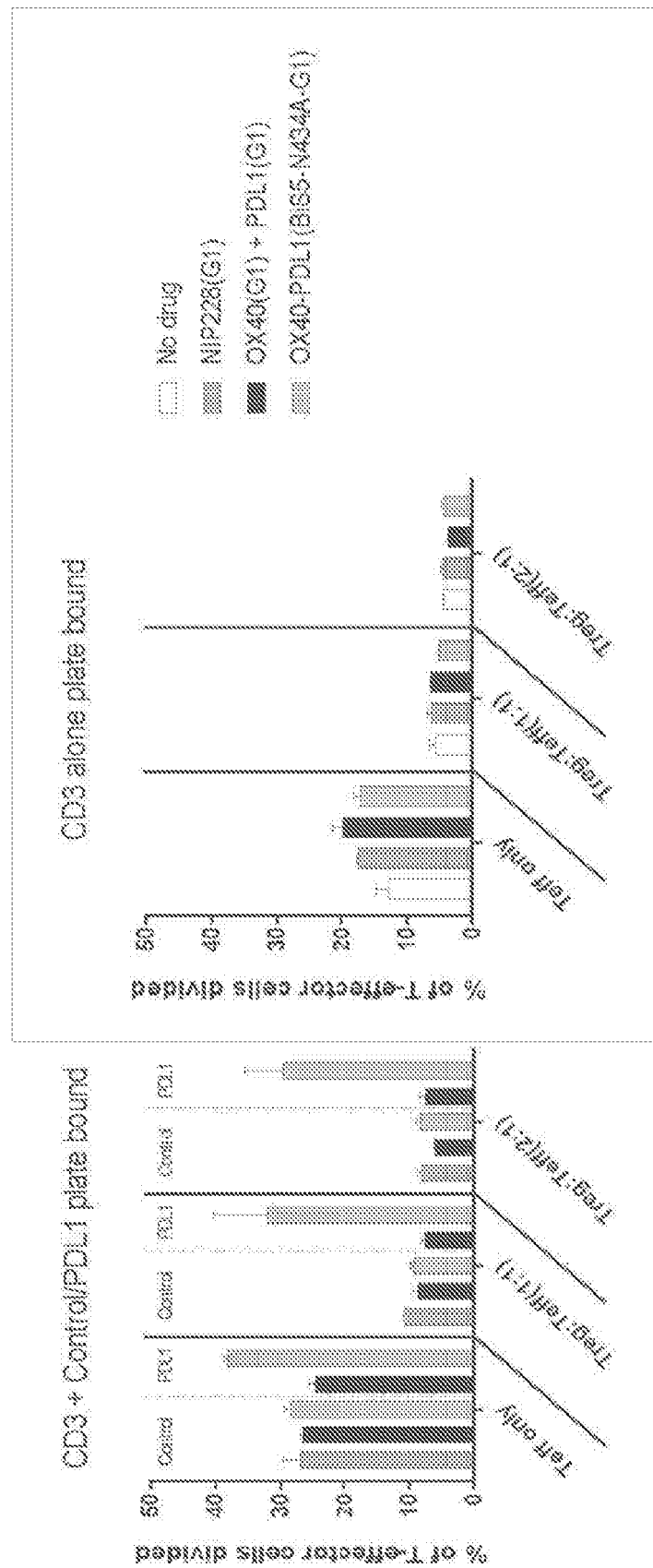


FIGURE 48 cont'd.



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FIGURE 49



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FIGURE 50

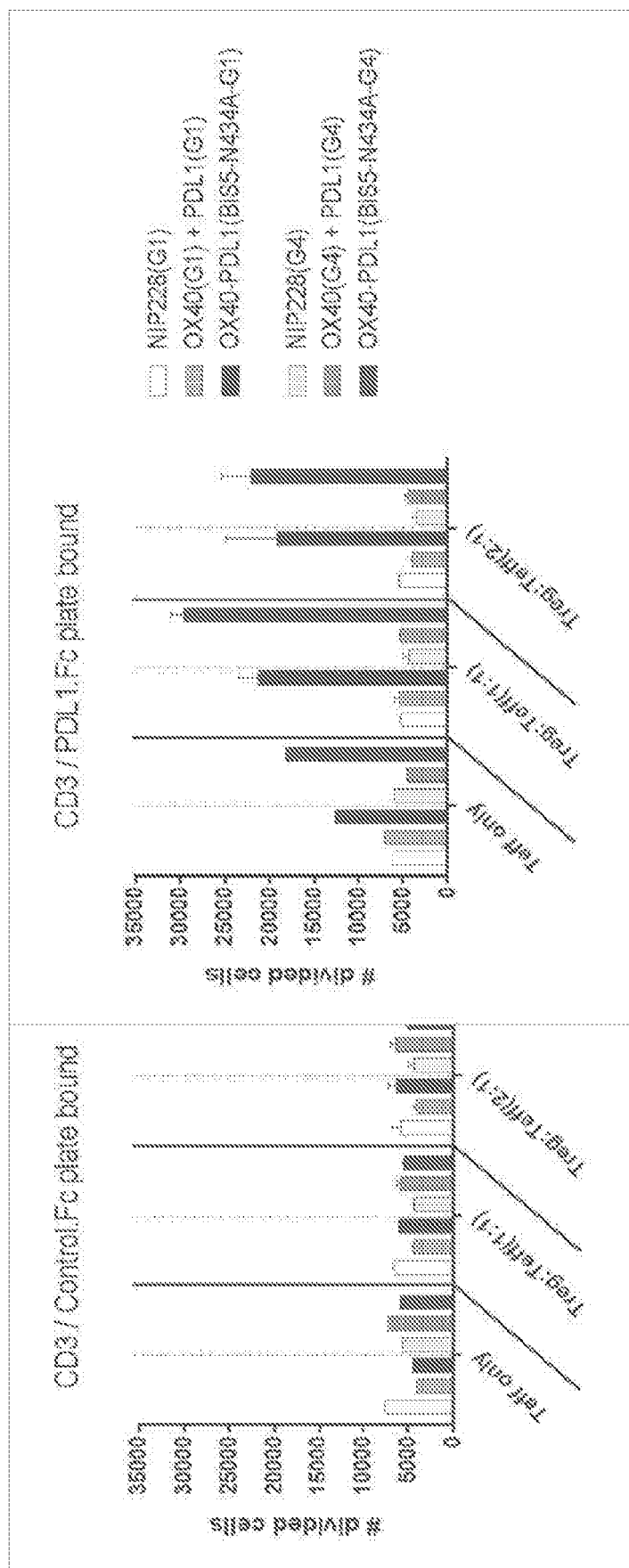
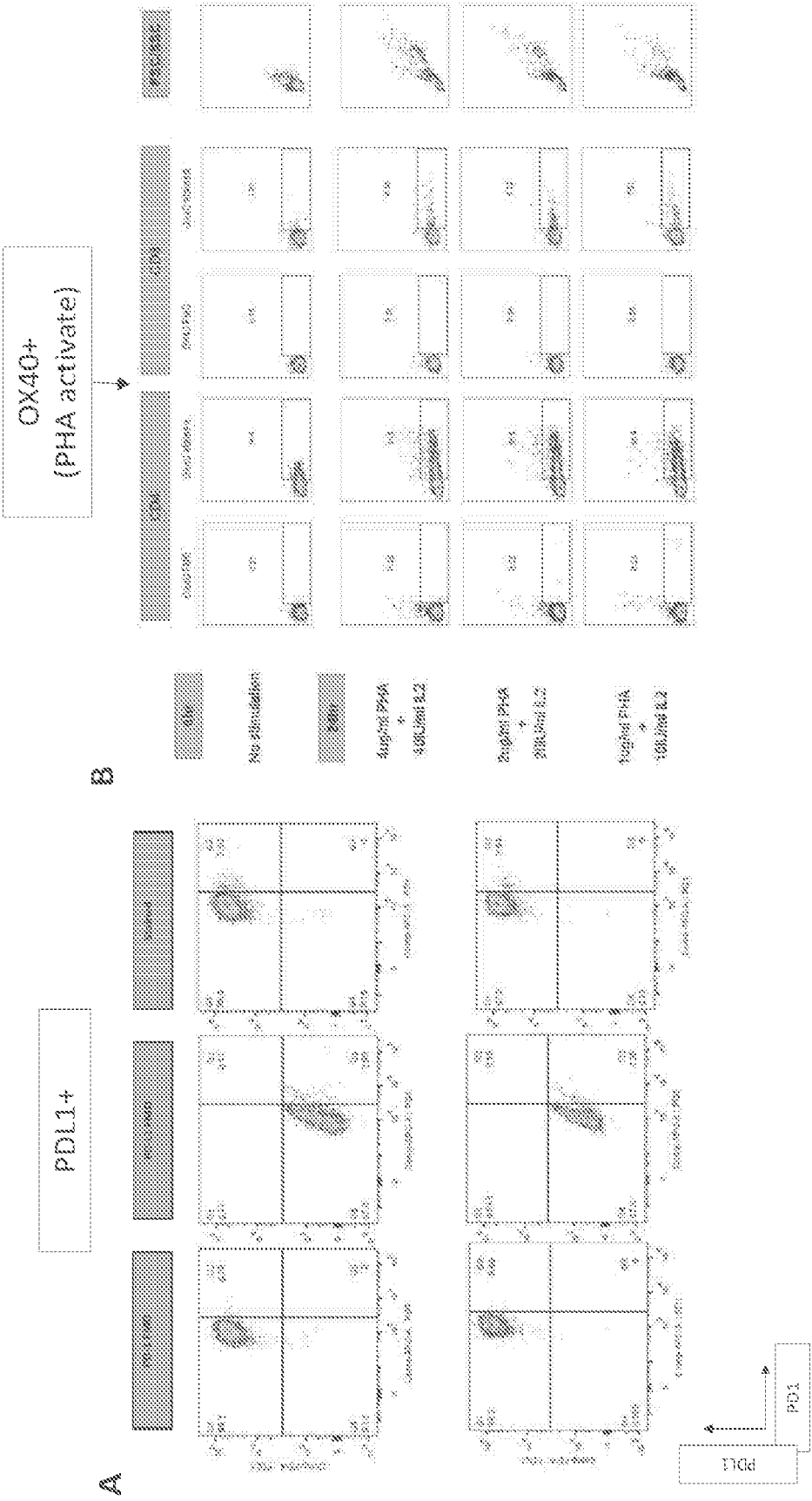
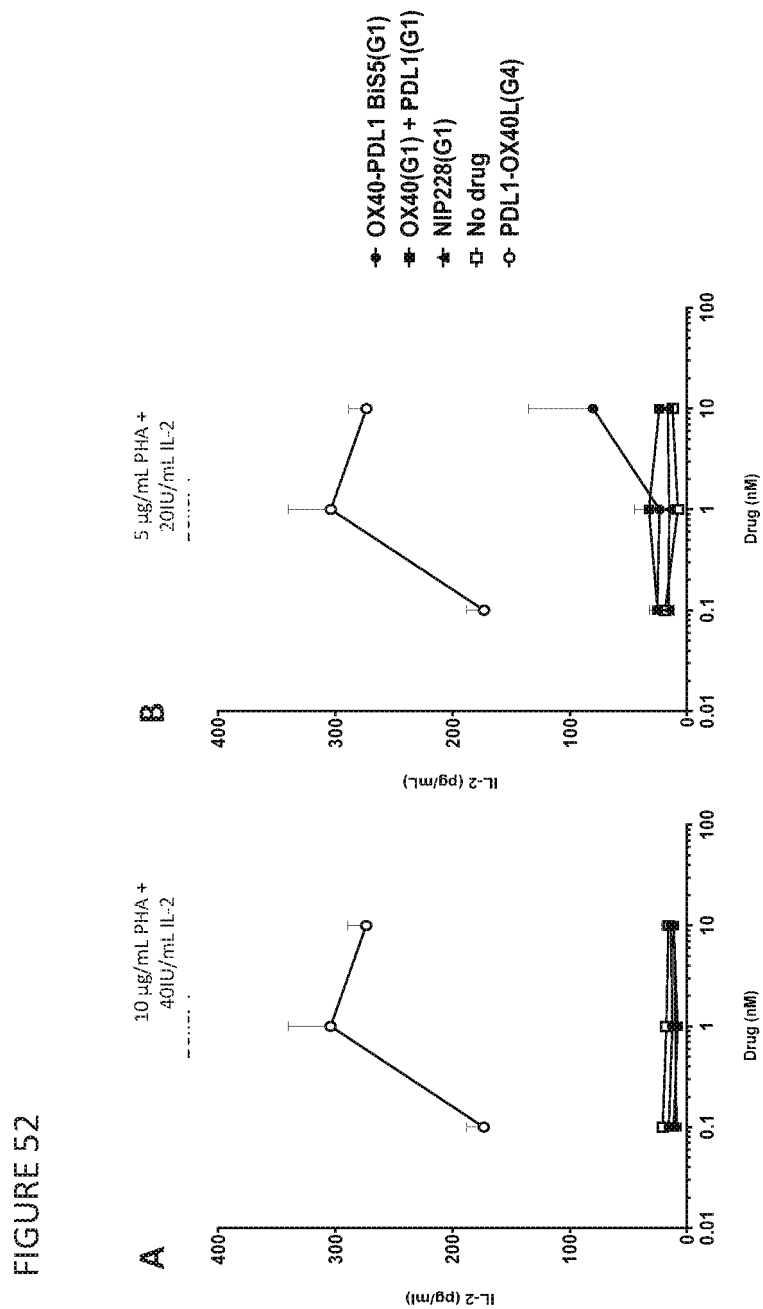


FIGURE 51



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FIGURE 52 cont'd.

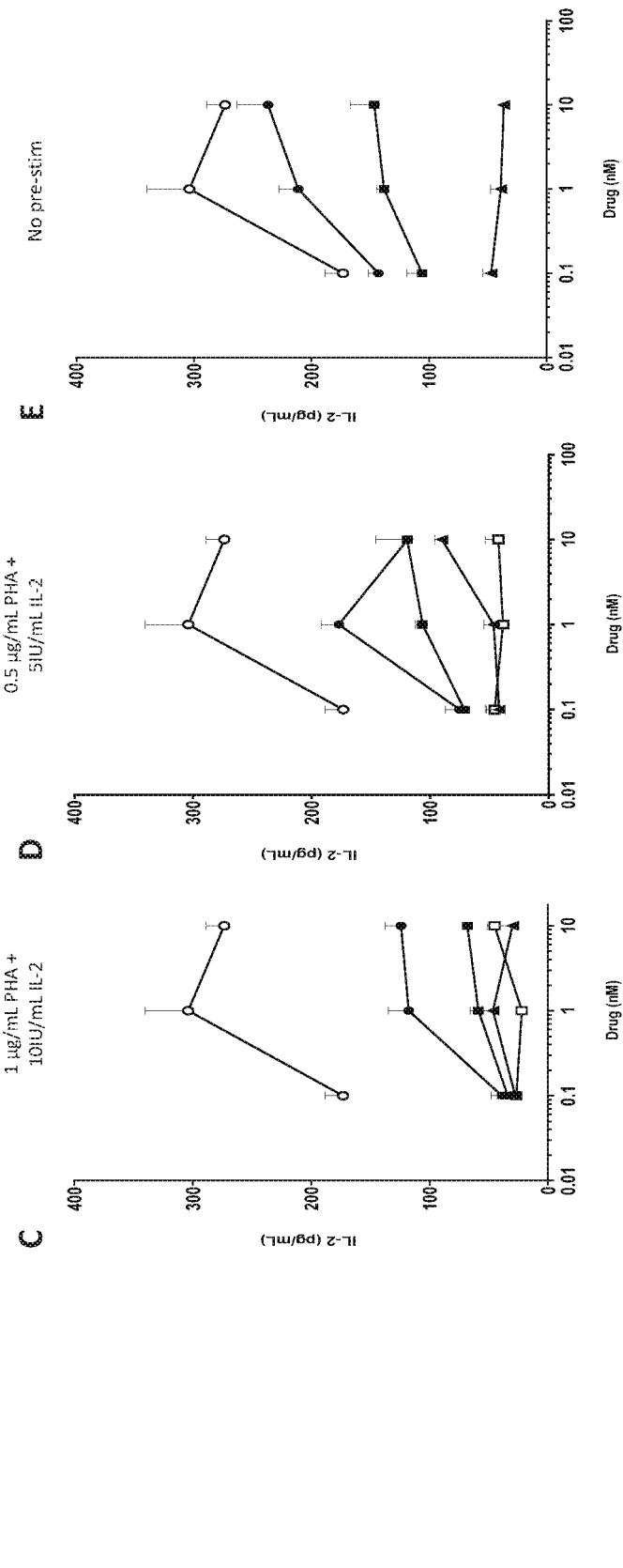


FIGURE 53

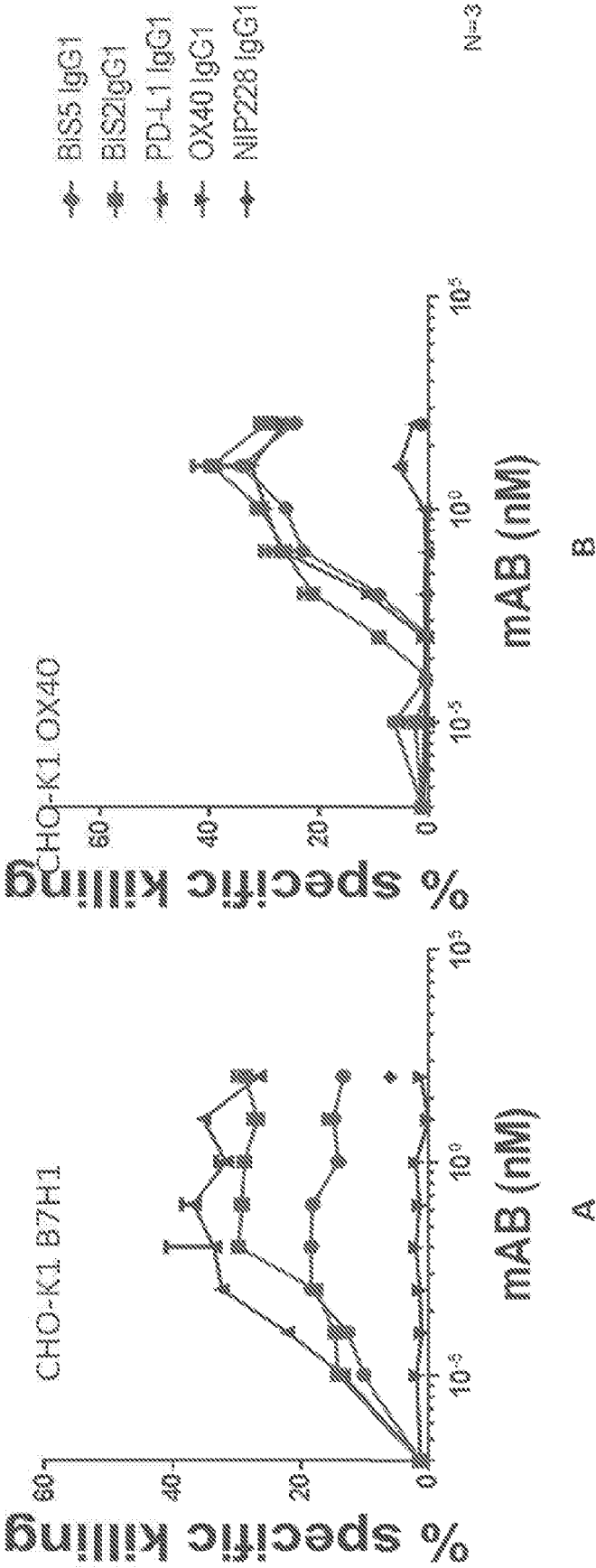
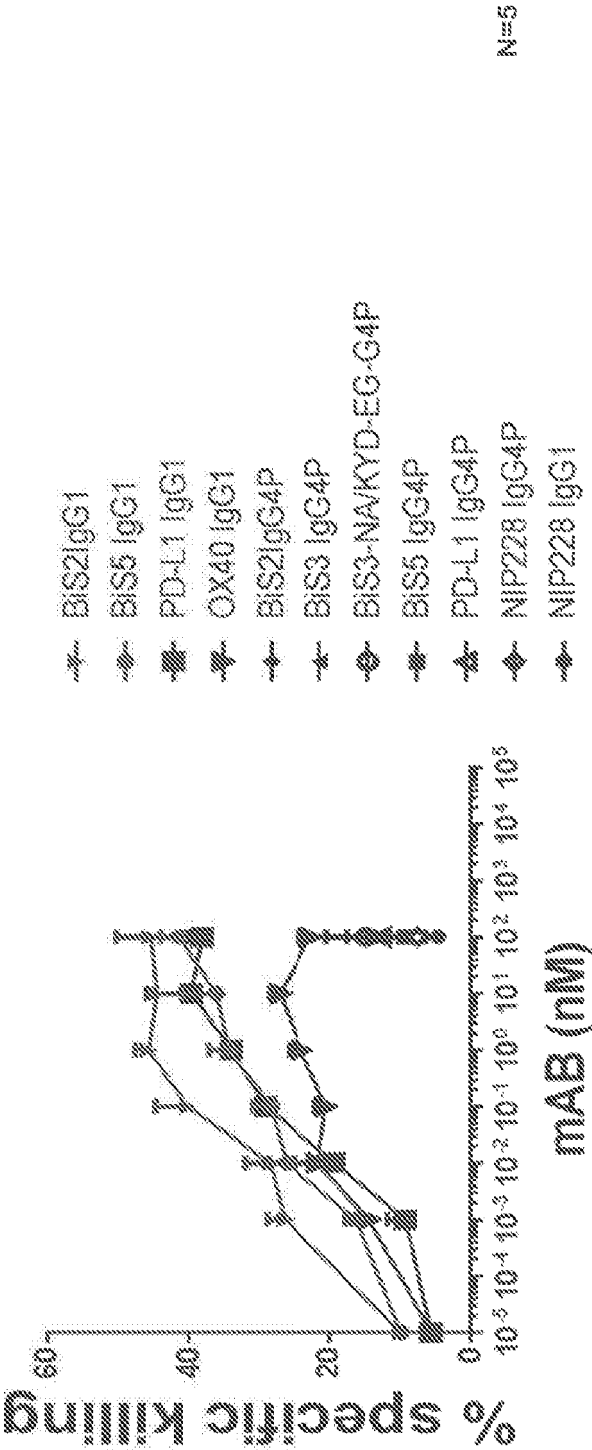
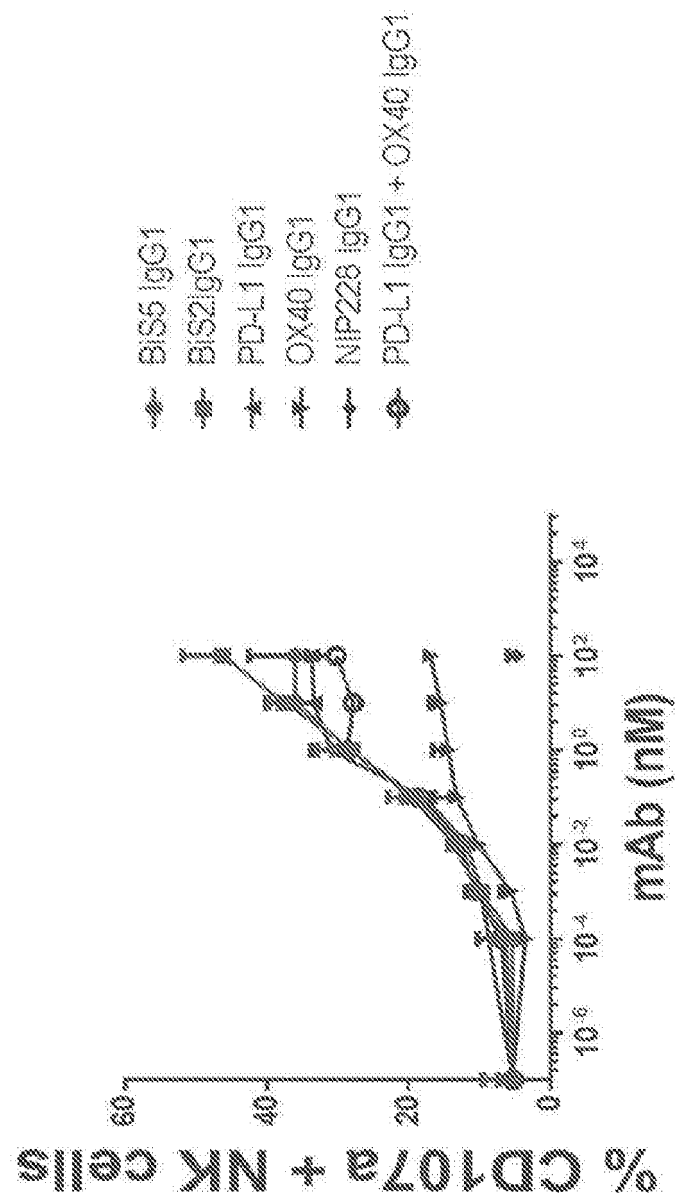


FIGURE 54



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FIGURE 55



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FIGURE 56

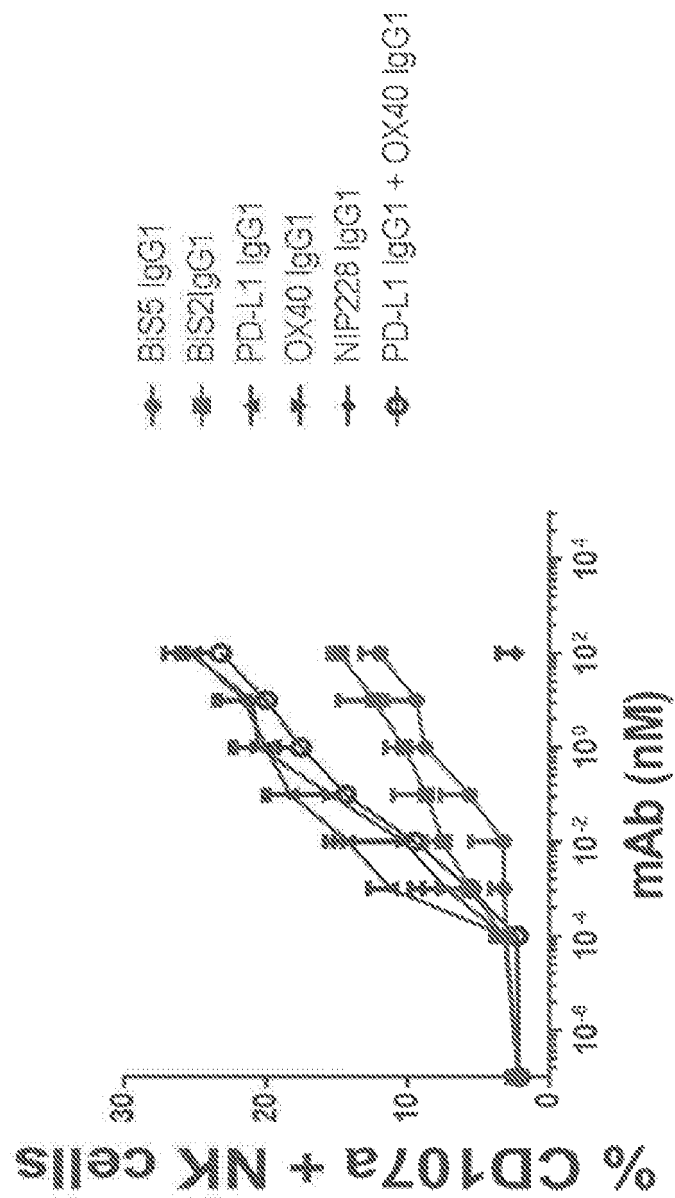


FIGURE 57

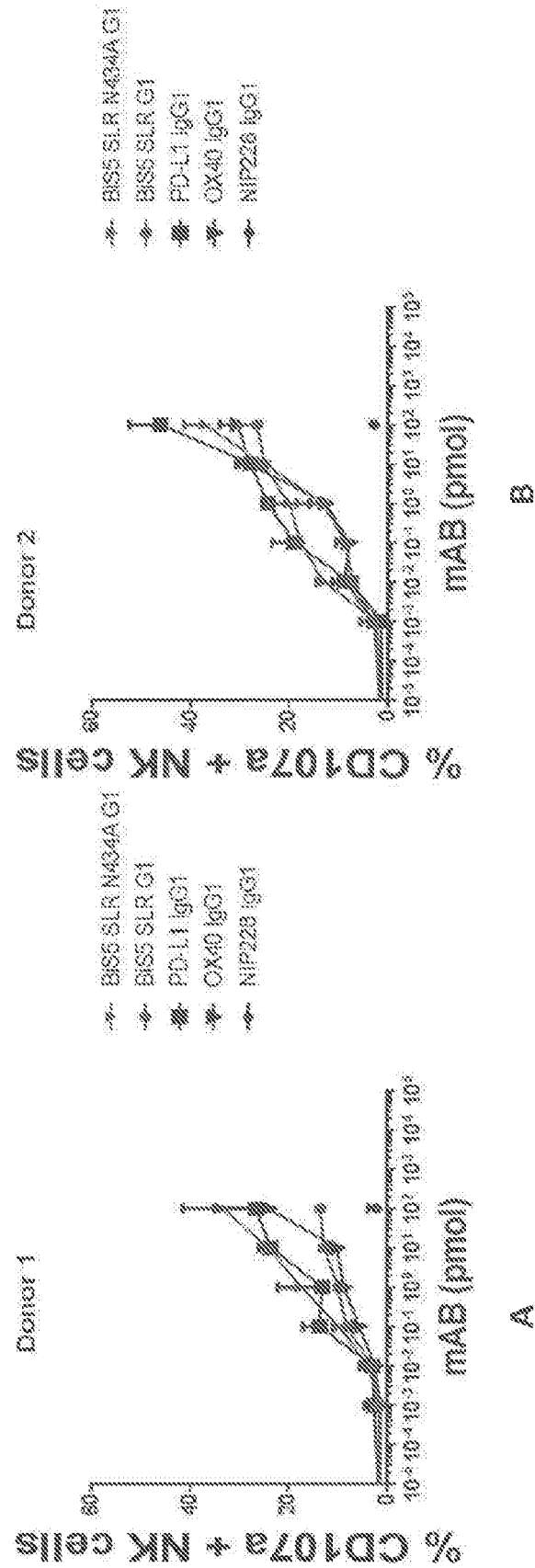
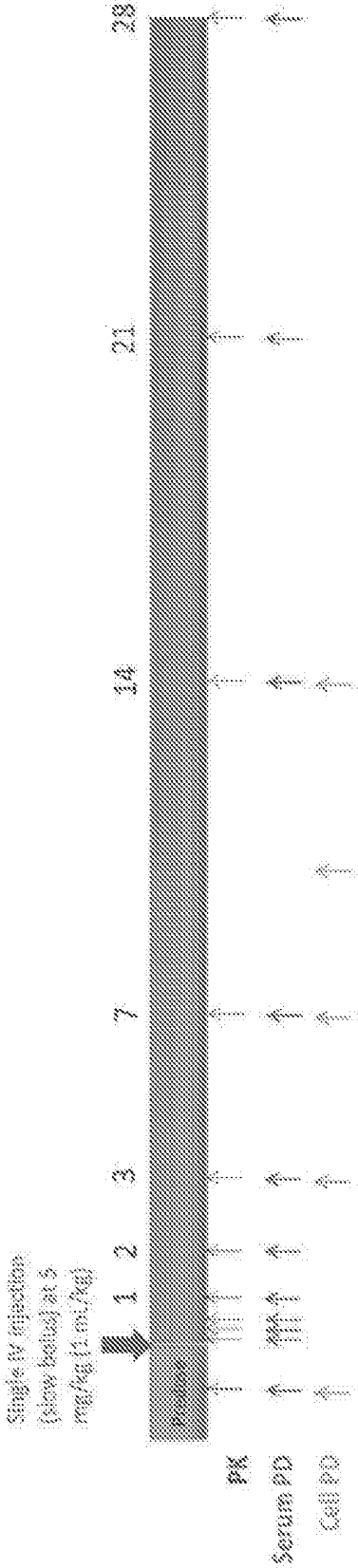


FIGURE 58

Study Design

Objective: to compare PK/PD of OX40/PD-L1 BisAbs:

- BISS-OX40/PD-L1-G1 N434A (with half-life extension mutation)
- BISS-OX40/PD-L1-G1 WT (IgG1)



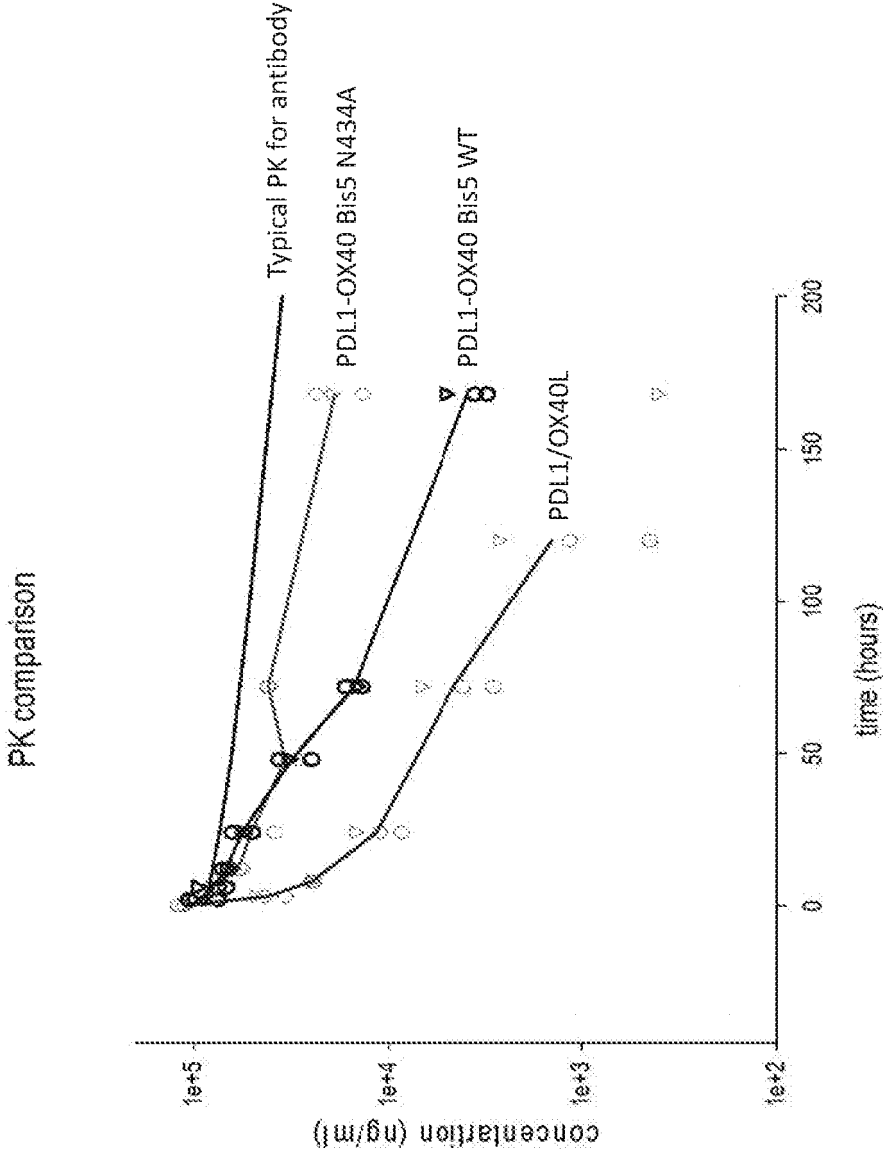
Evaluations (n=3):

- Viability, clinical observations, physical exams, injection sites, body weights, food consumption
- PK: predose, 2, 6, 12, 24, 48, 72 and 168 hours postdose, Days 14, 21, 28
- ADA
- Serum PD: soluble PD-L1 (duplicate PK samples)
- Cell PD: flow based evaluation of Ki67 staining

Execution:

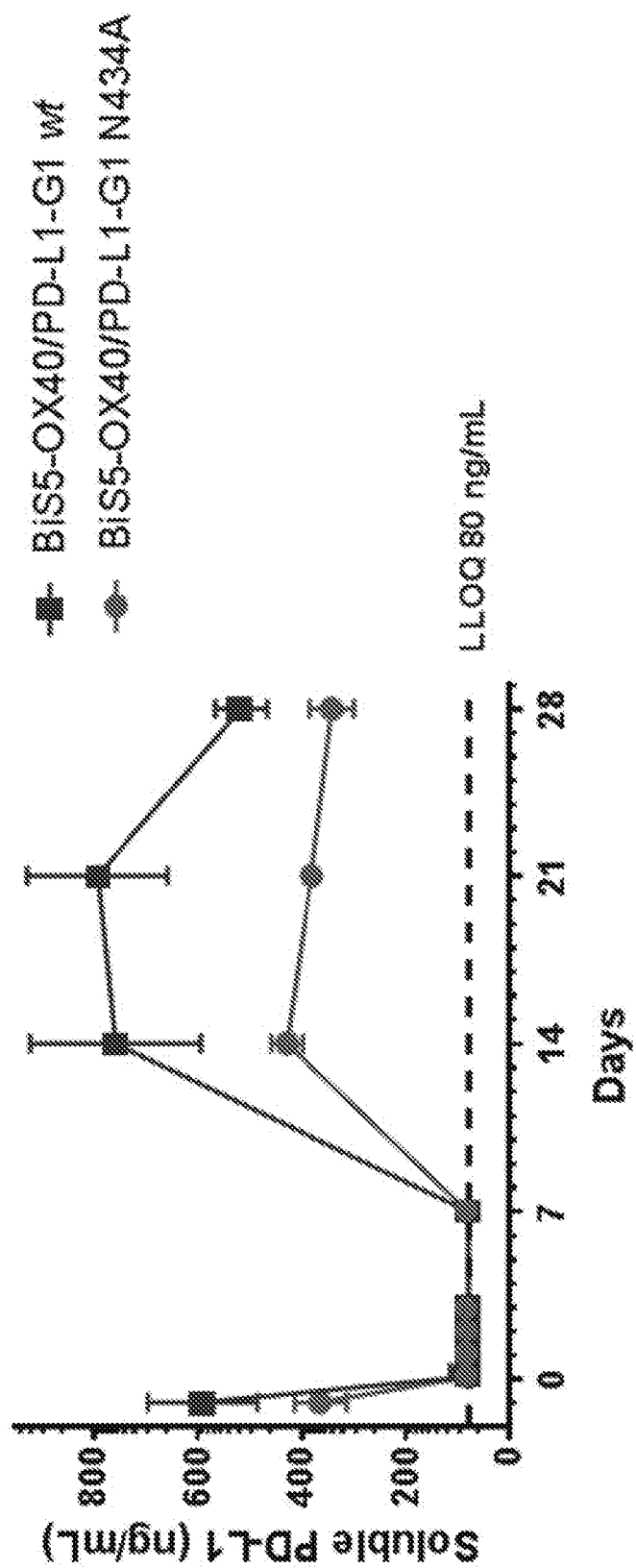
- 50 days from injection to PK summary

FIGURE 59



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FIGURE 60



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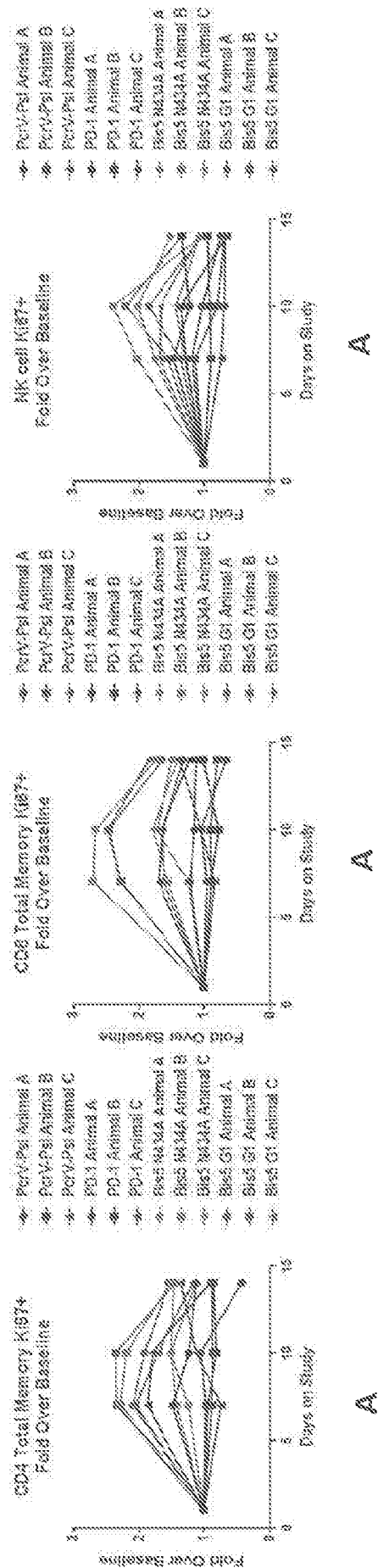
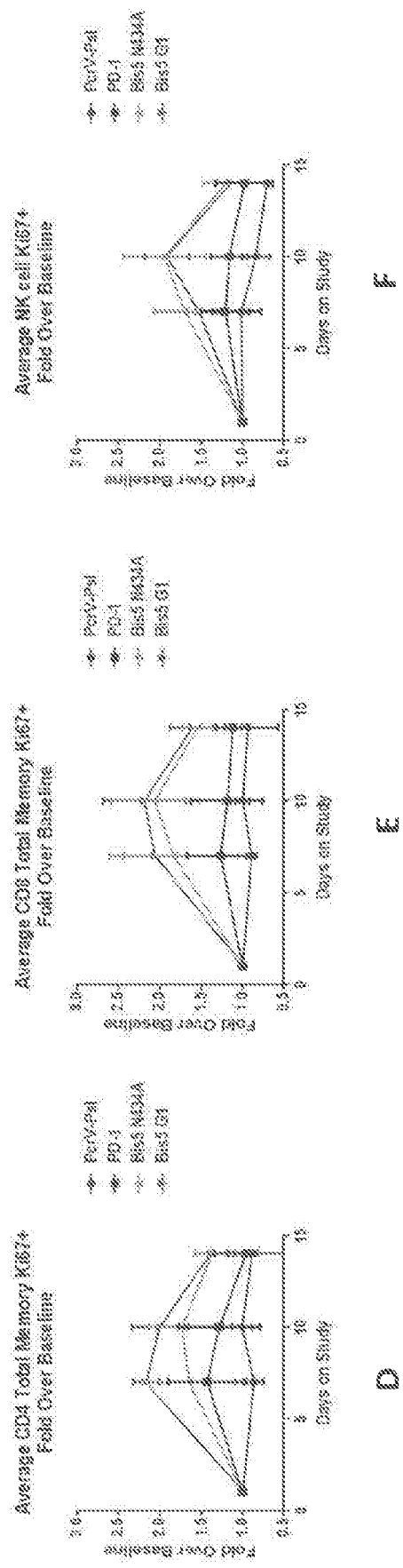


FIGURE 61 cont'd.



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FIGURE 62

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FIGURE 63

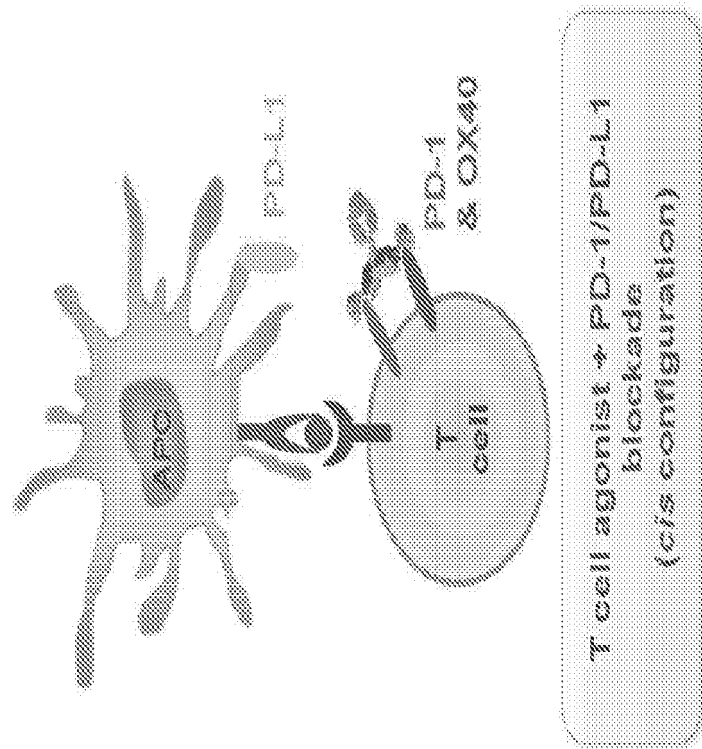


FIGURE 64

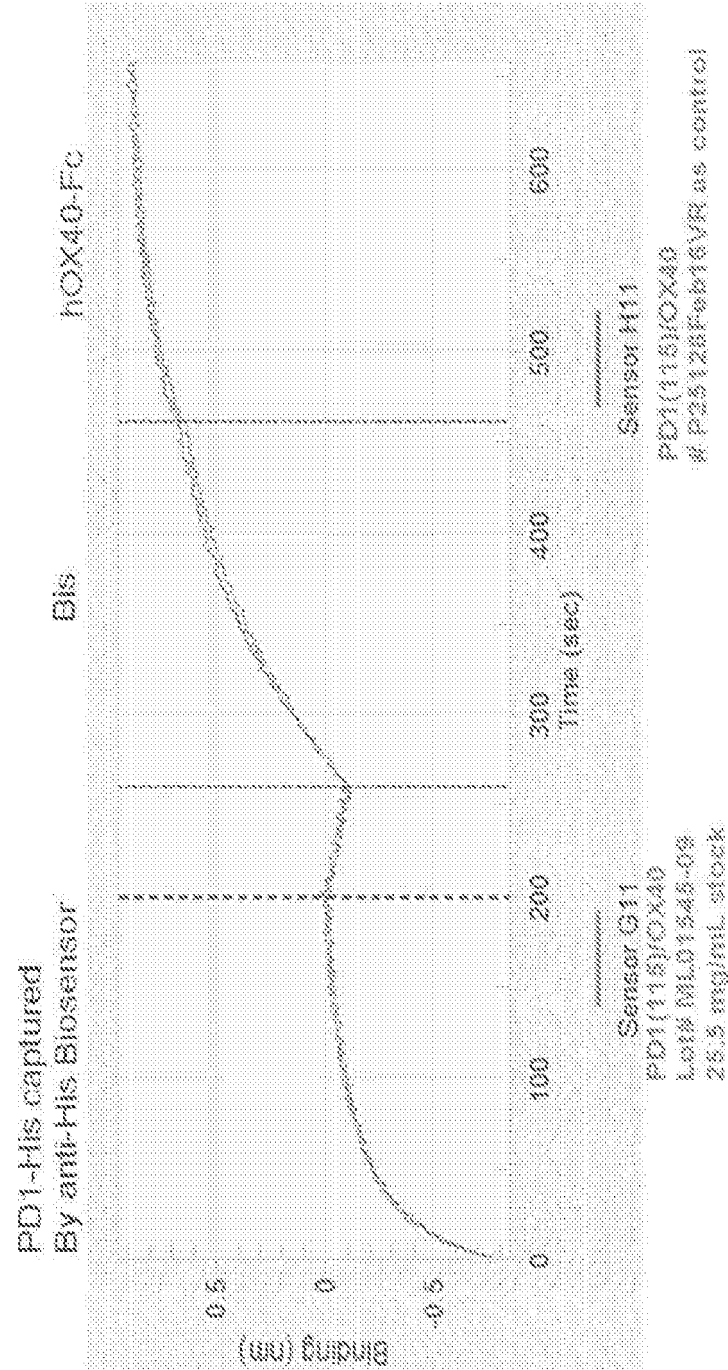


FIGURE 65

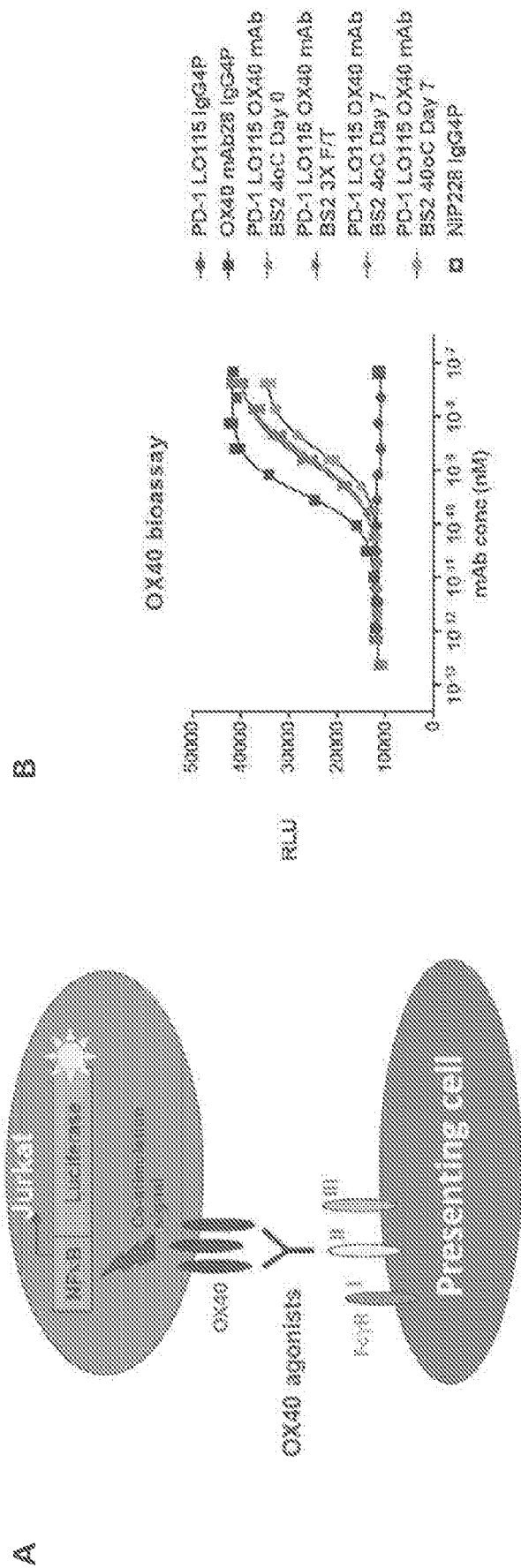
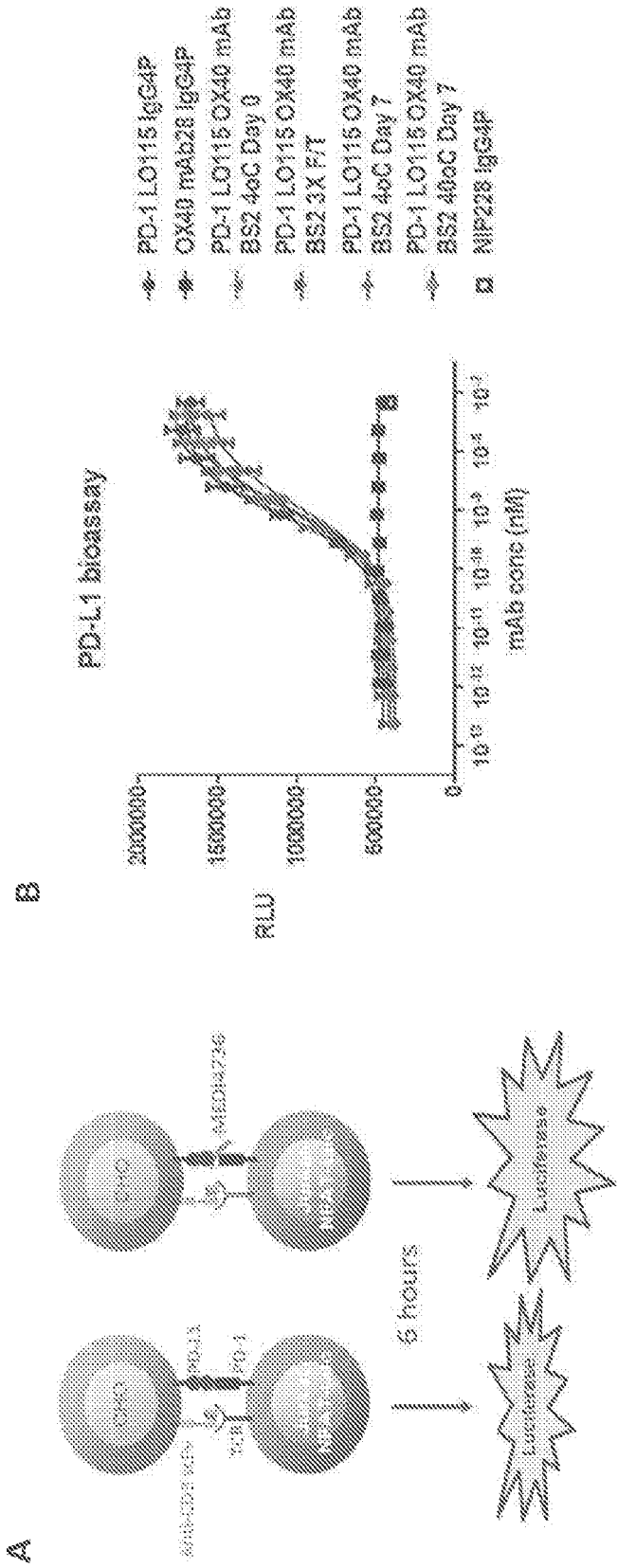


FIGURE 66



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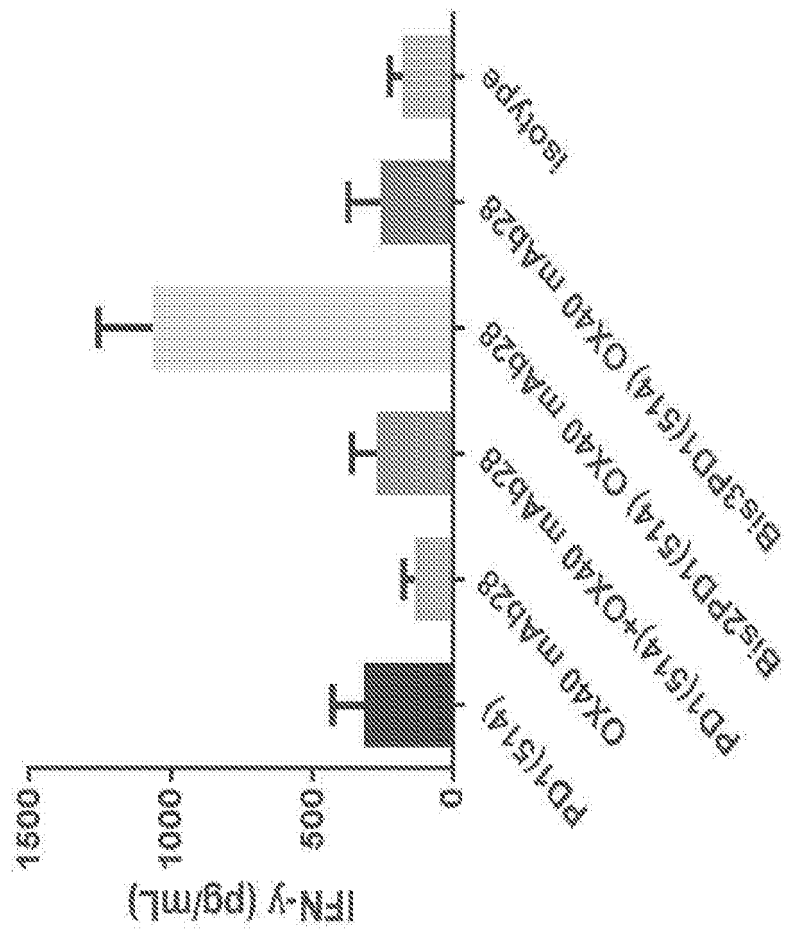


FIGURE 67

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FIGURE 68

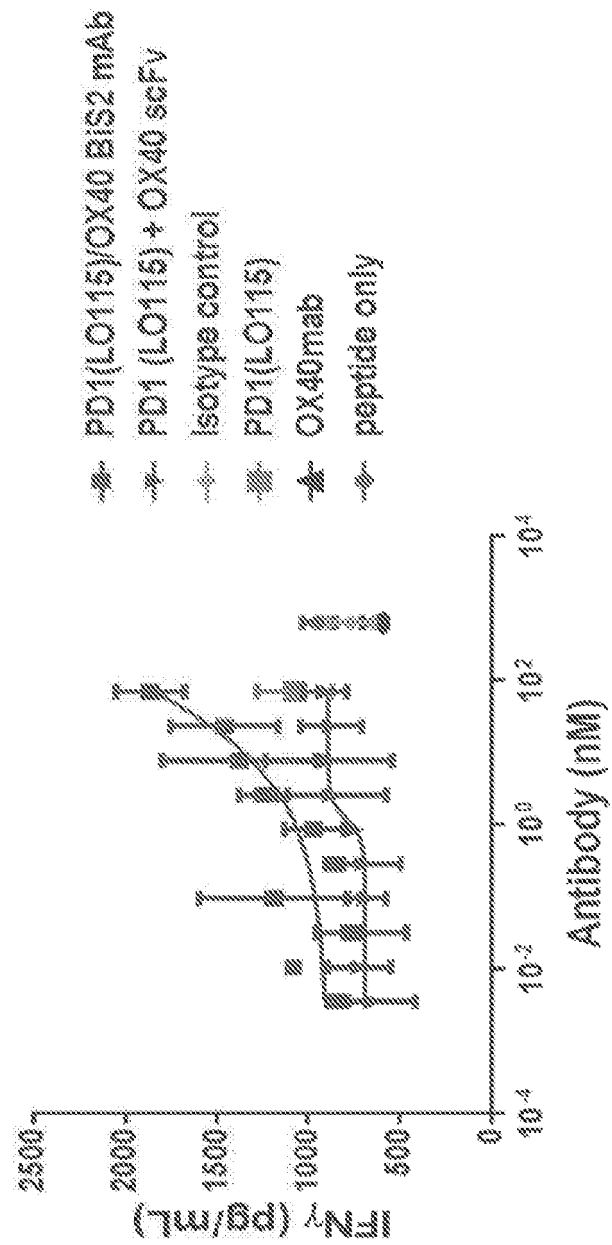
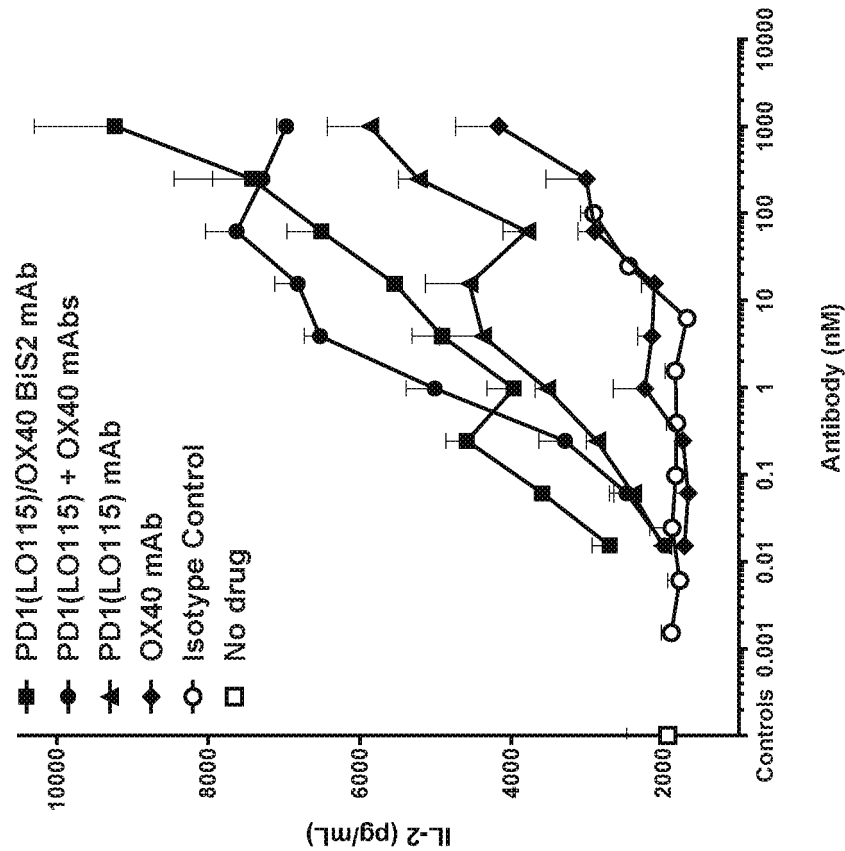


FIGURE 69



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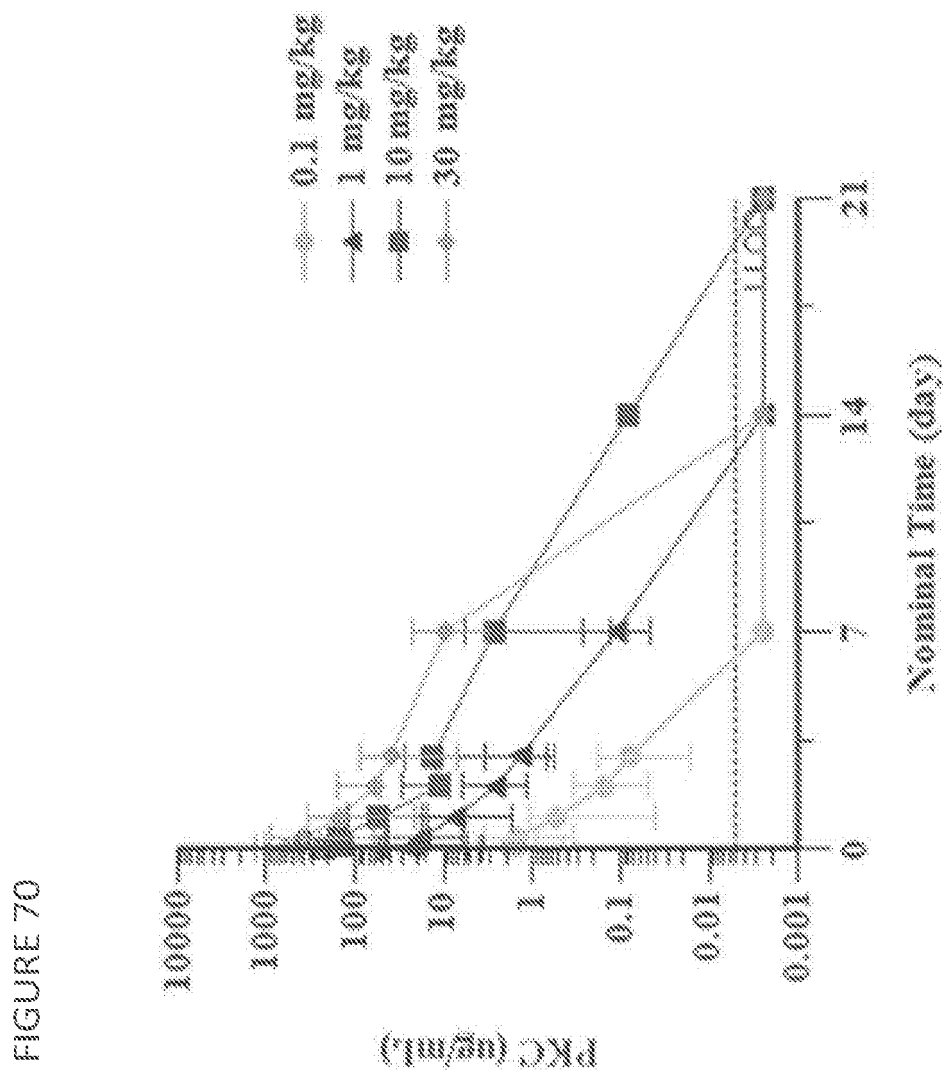


FIGURE 71

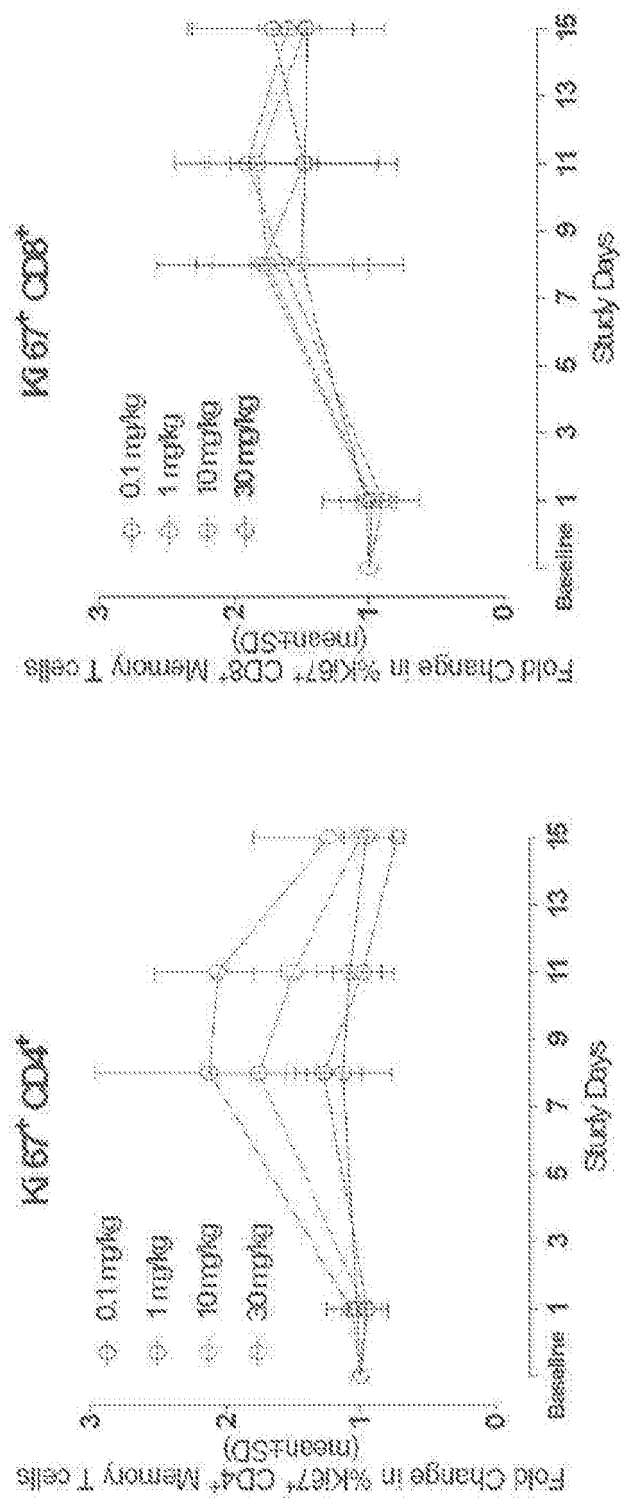
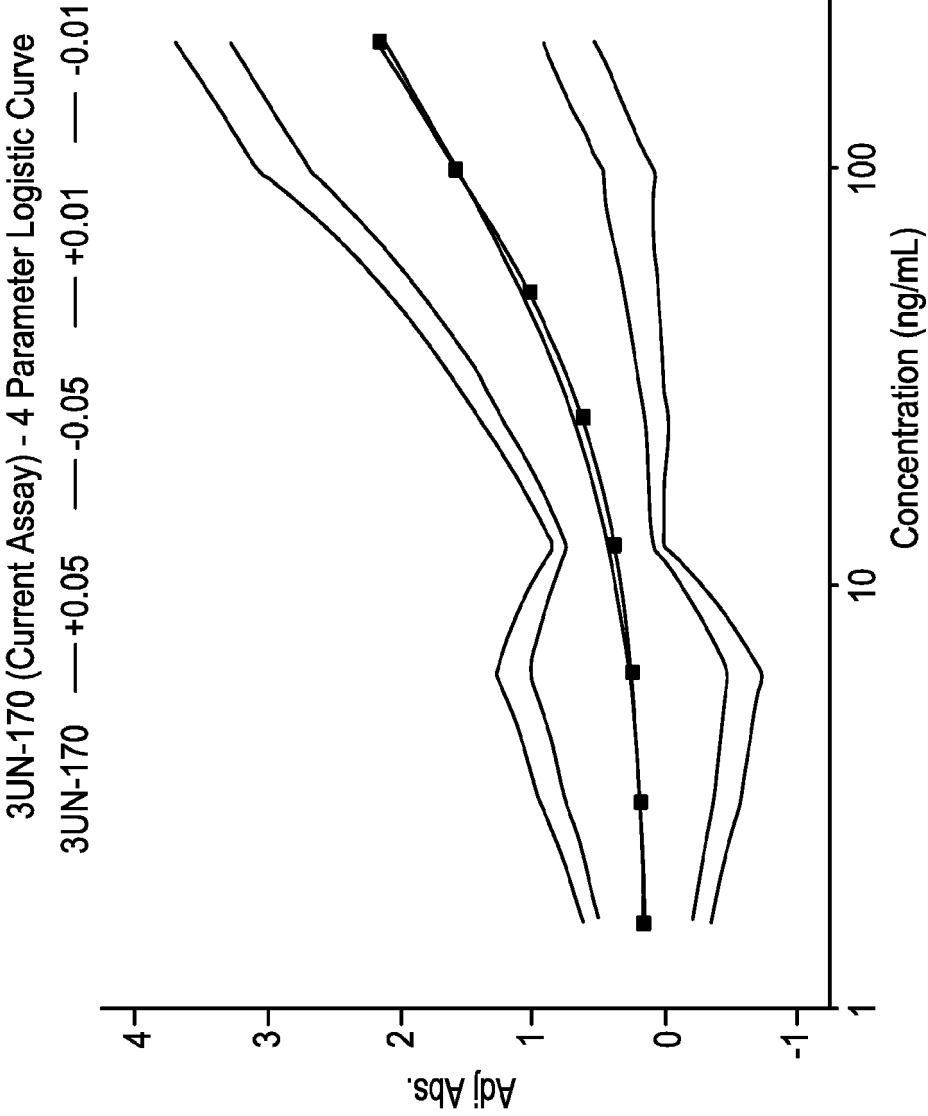


FIGURE 72



FIGURES 73A-73D

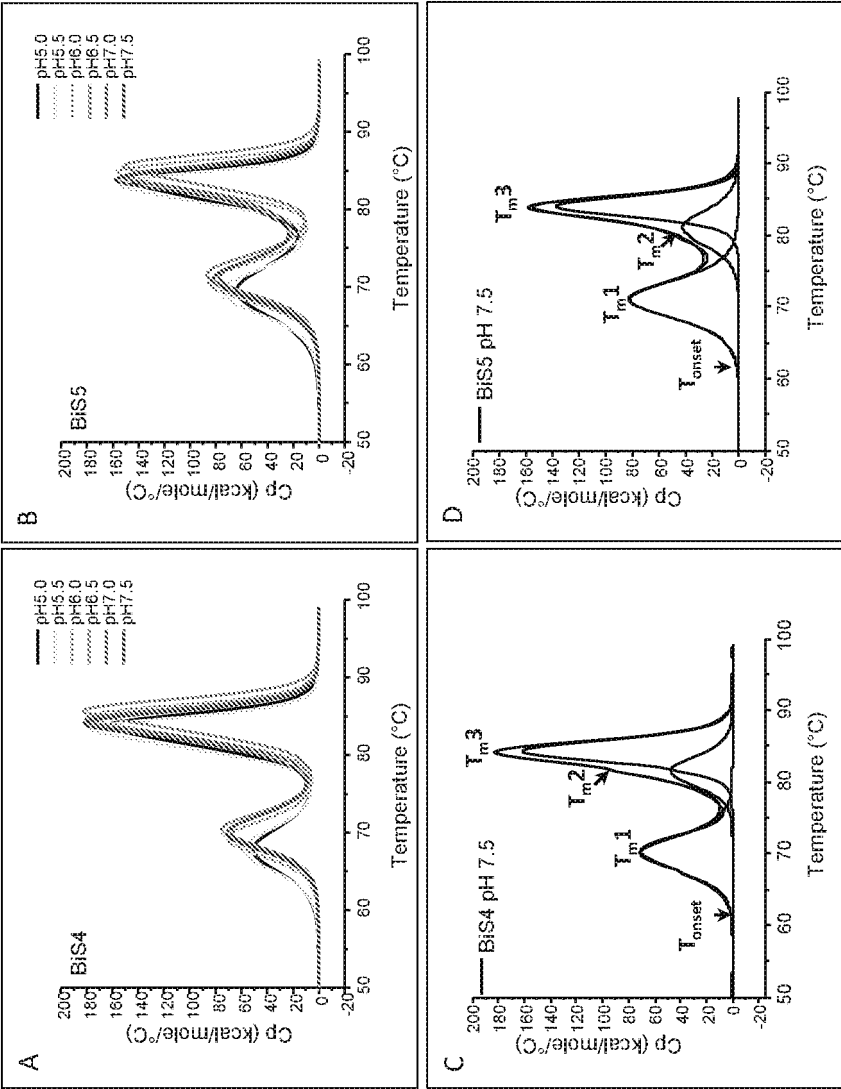


FIGURE 73E

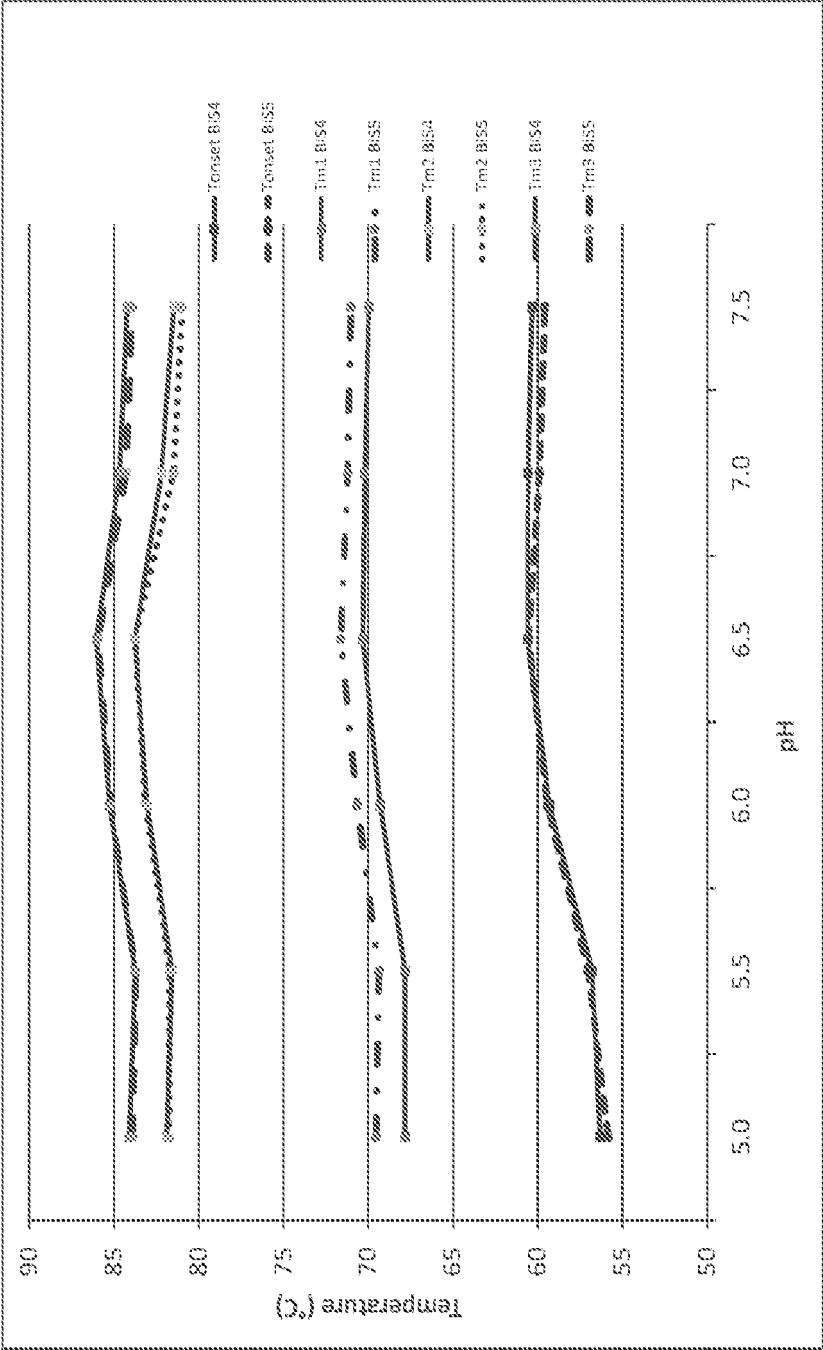
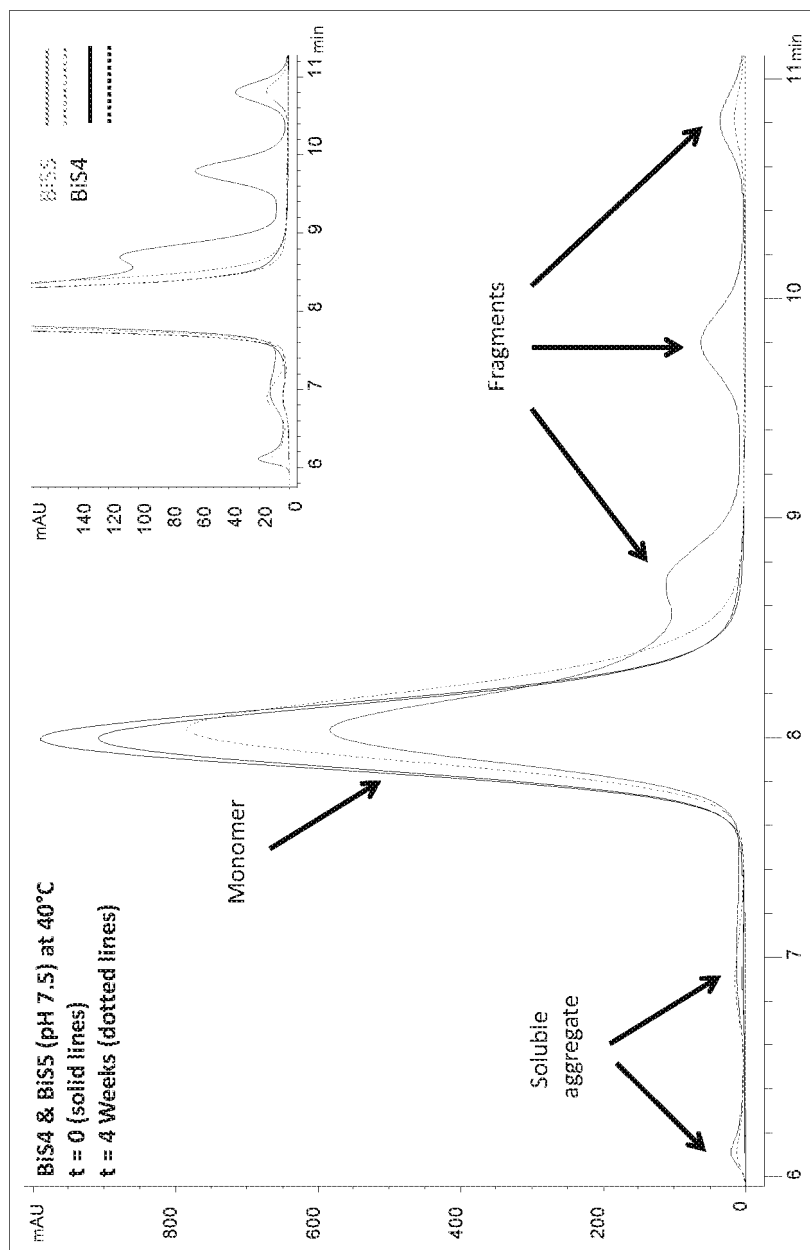


FIGURE 74A



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FIGURE 74B

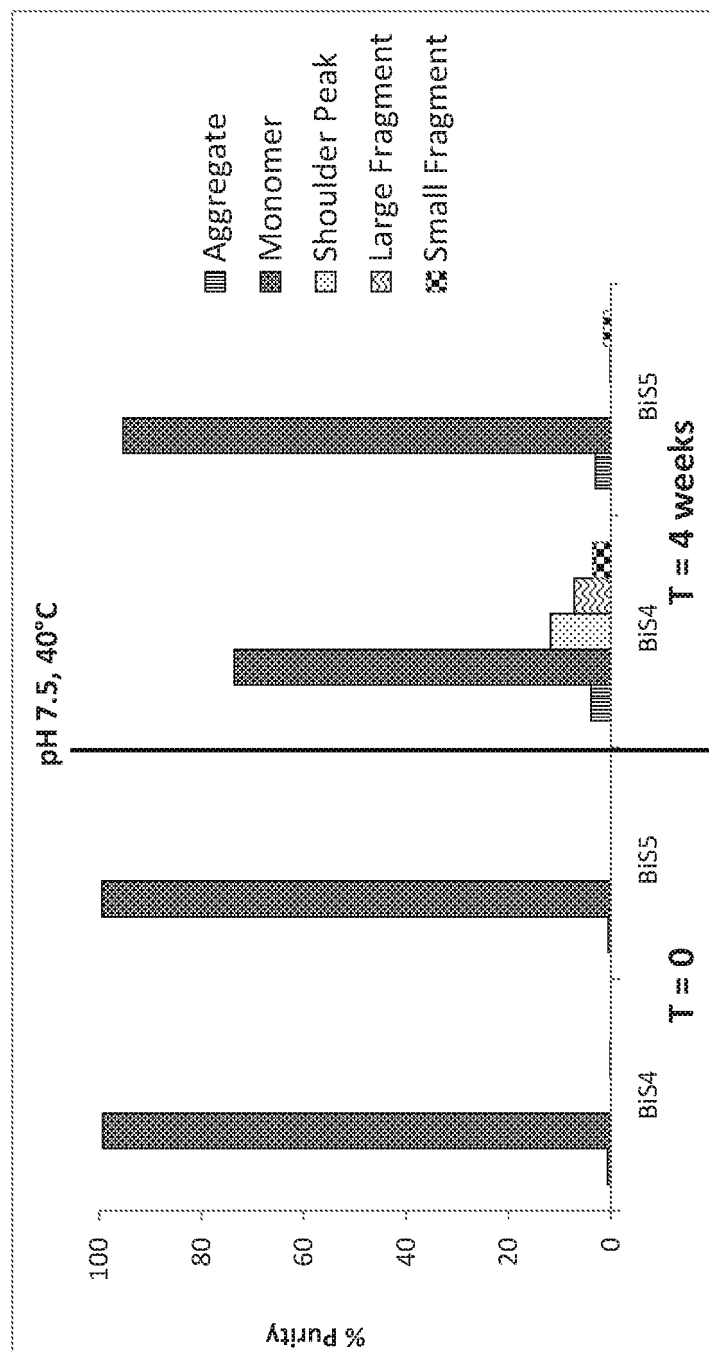


FIGURE 75A

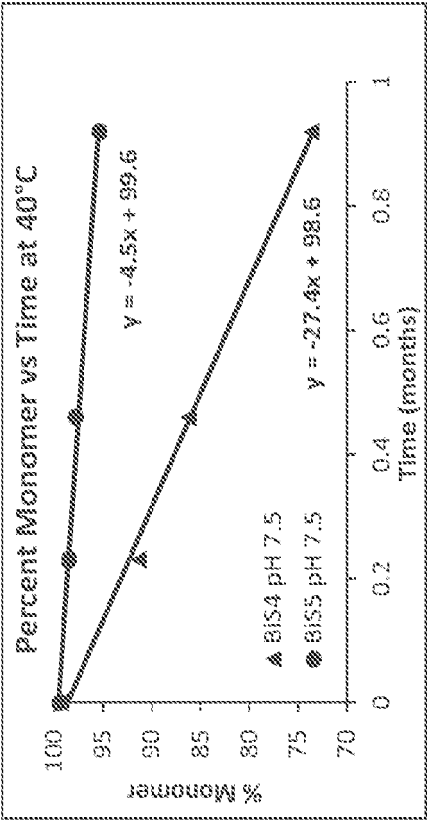


FIGURE 75B

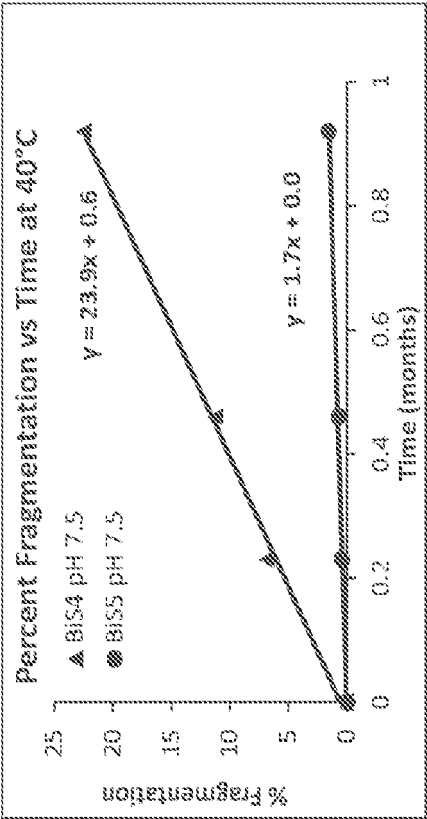


FIGURE 75C

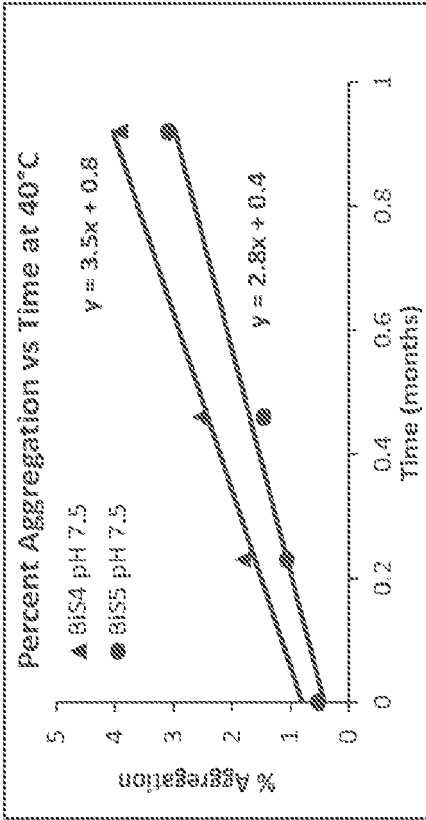


FIGURE 76A

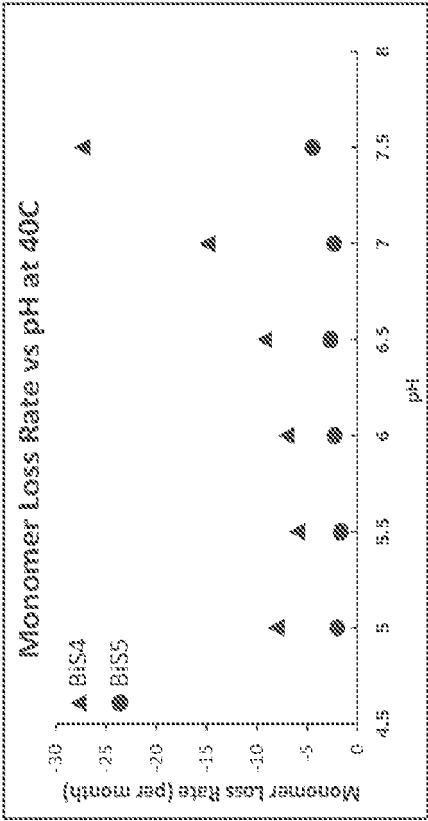


FIGURE 76B

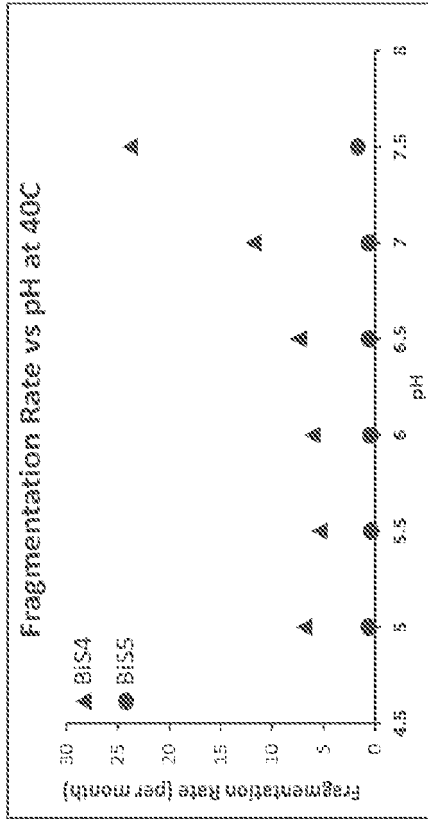


FIGURE 76C

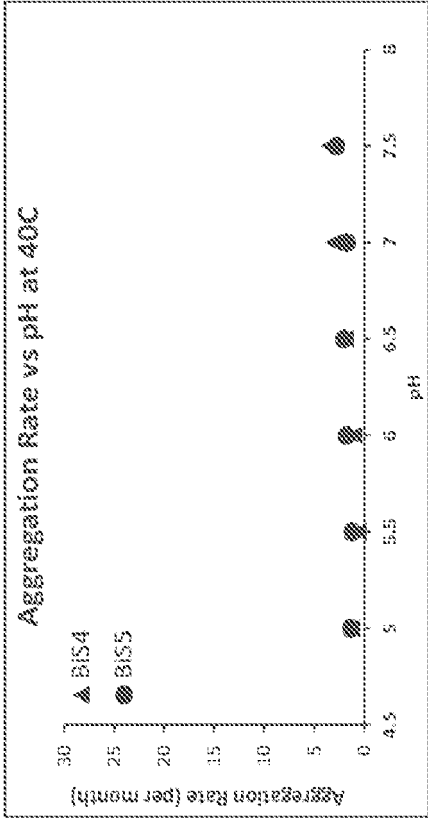


FIGURE 77A

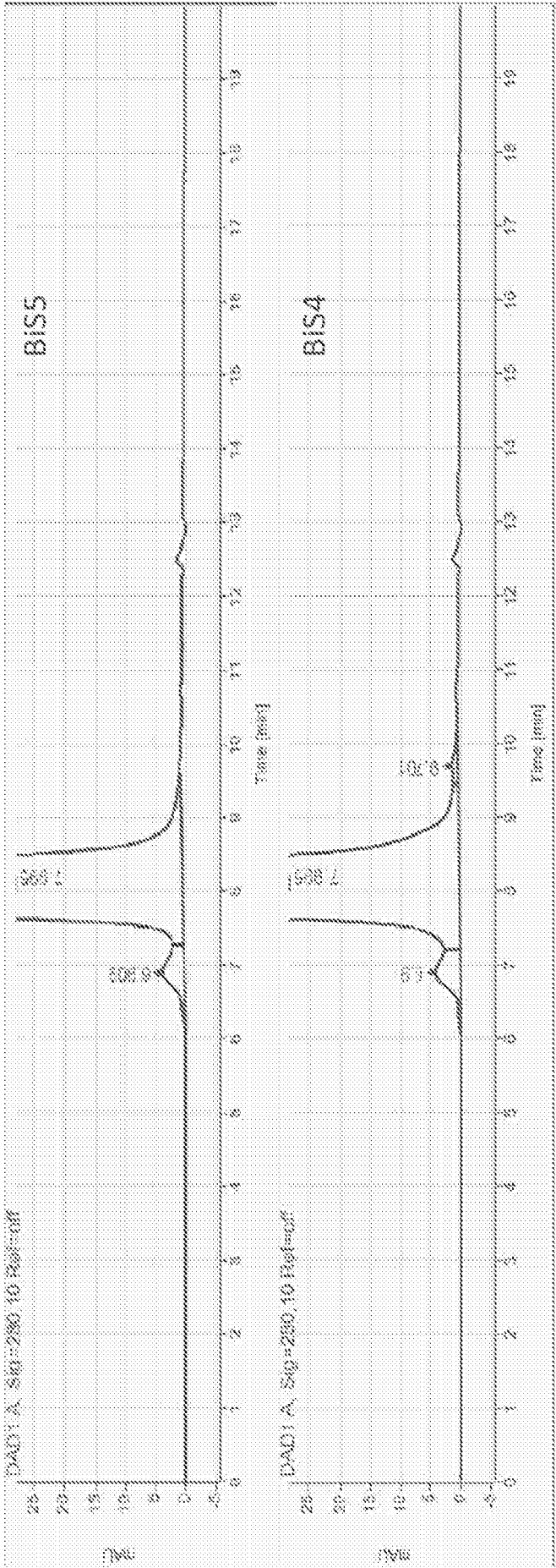
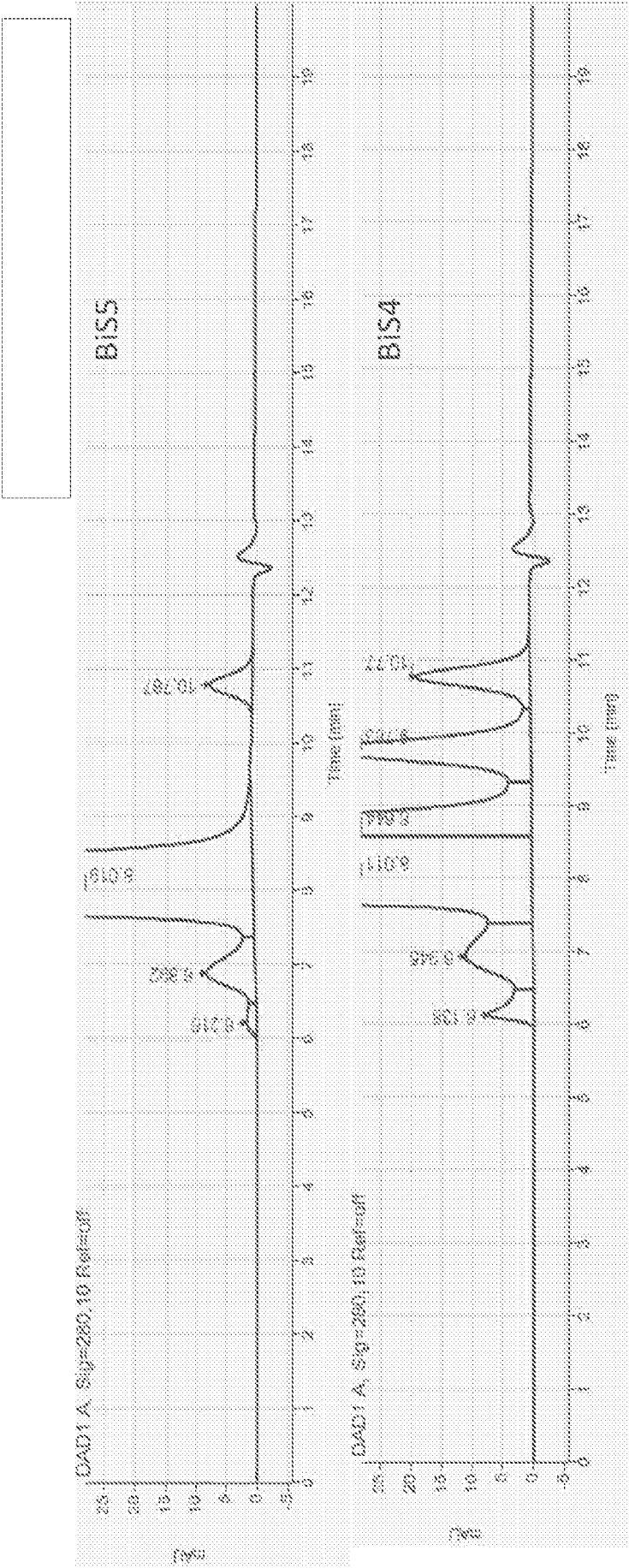


FIGURE 77B



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FIGURE 78

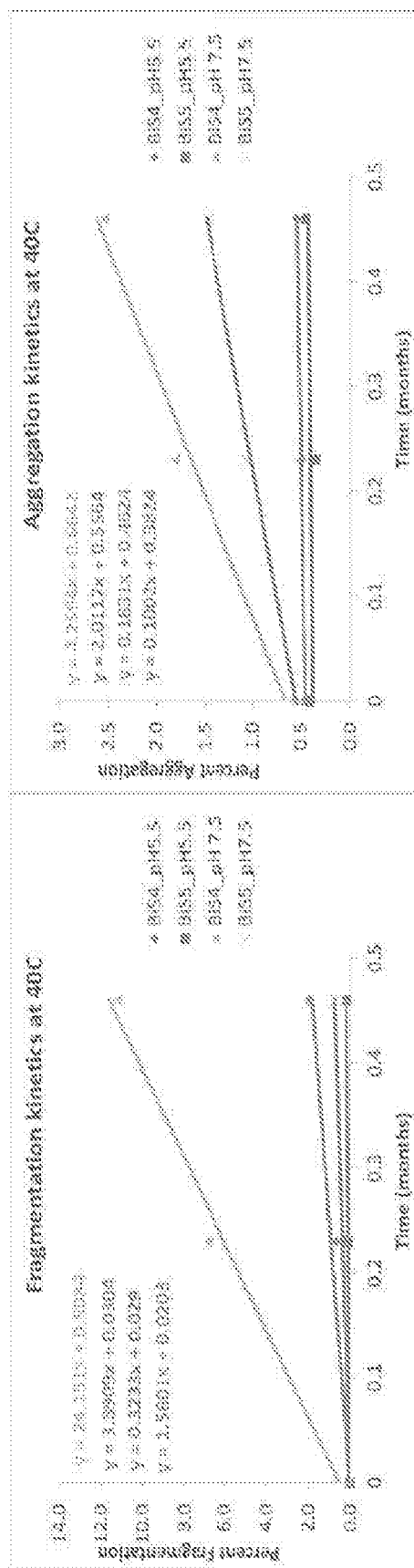
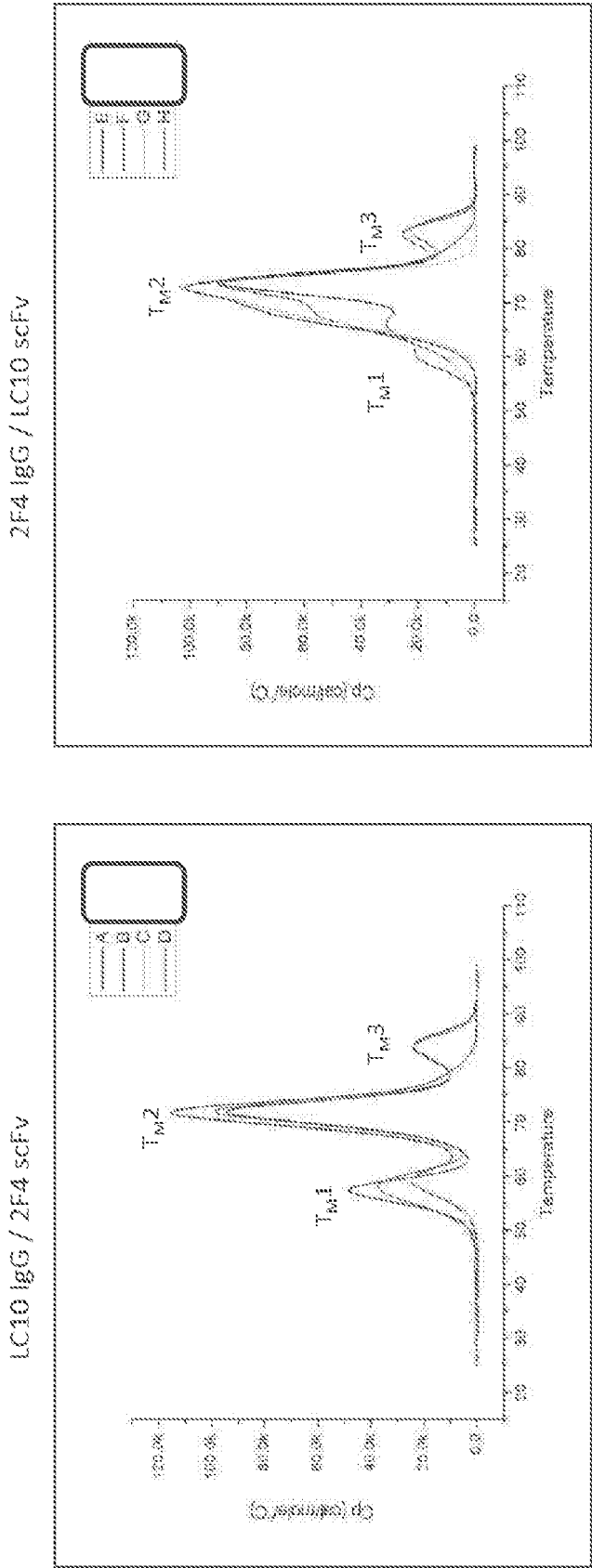


Figure 79



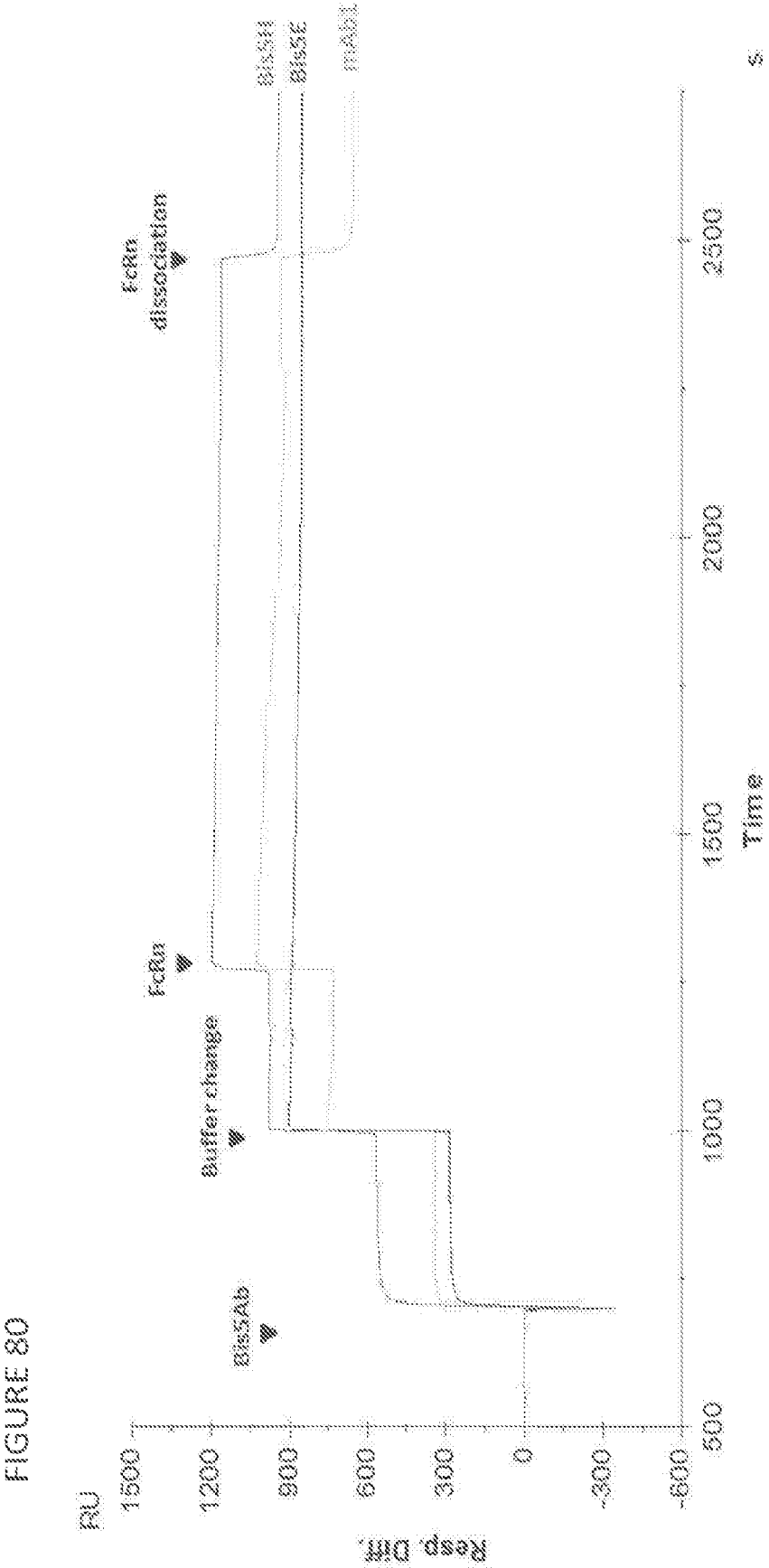


FIGURE 81

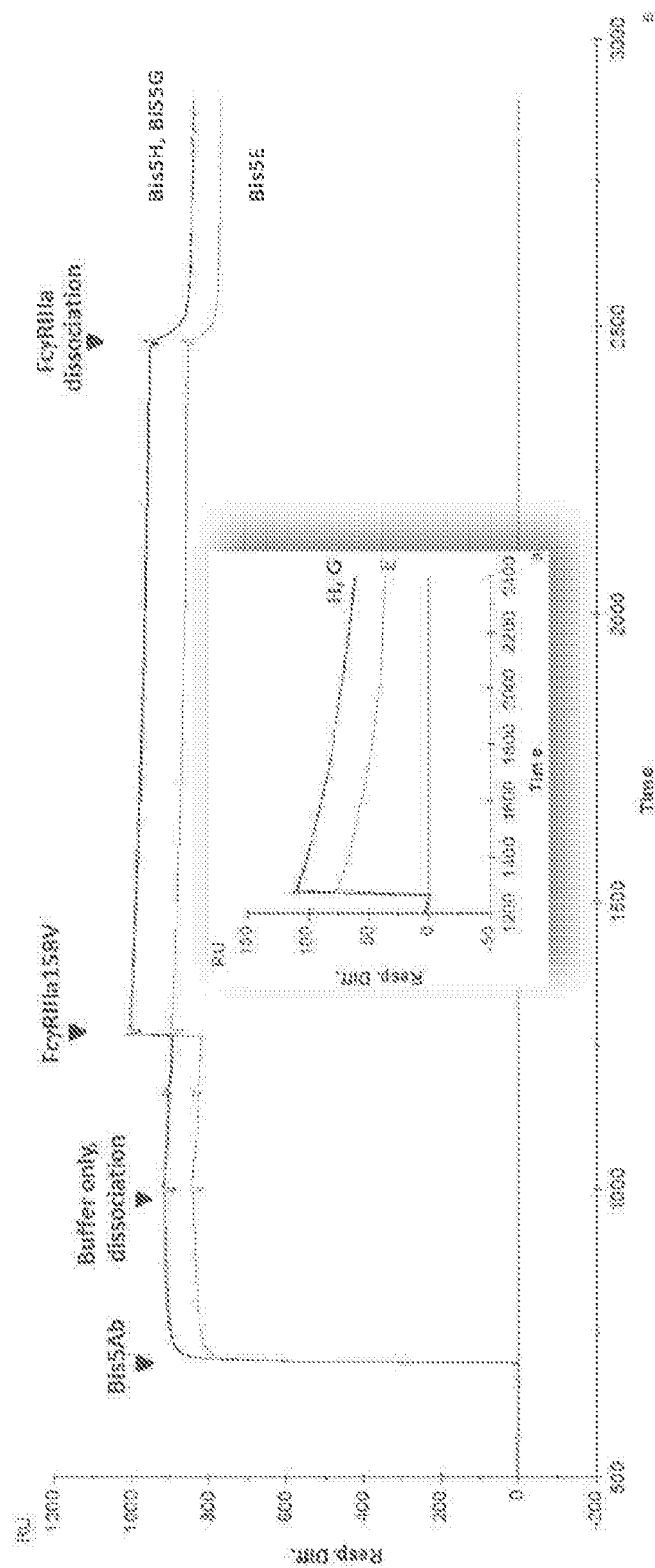


FIGURE 82

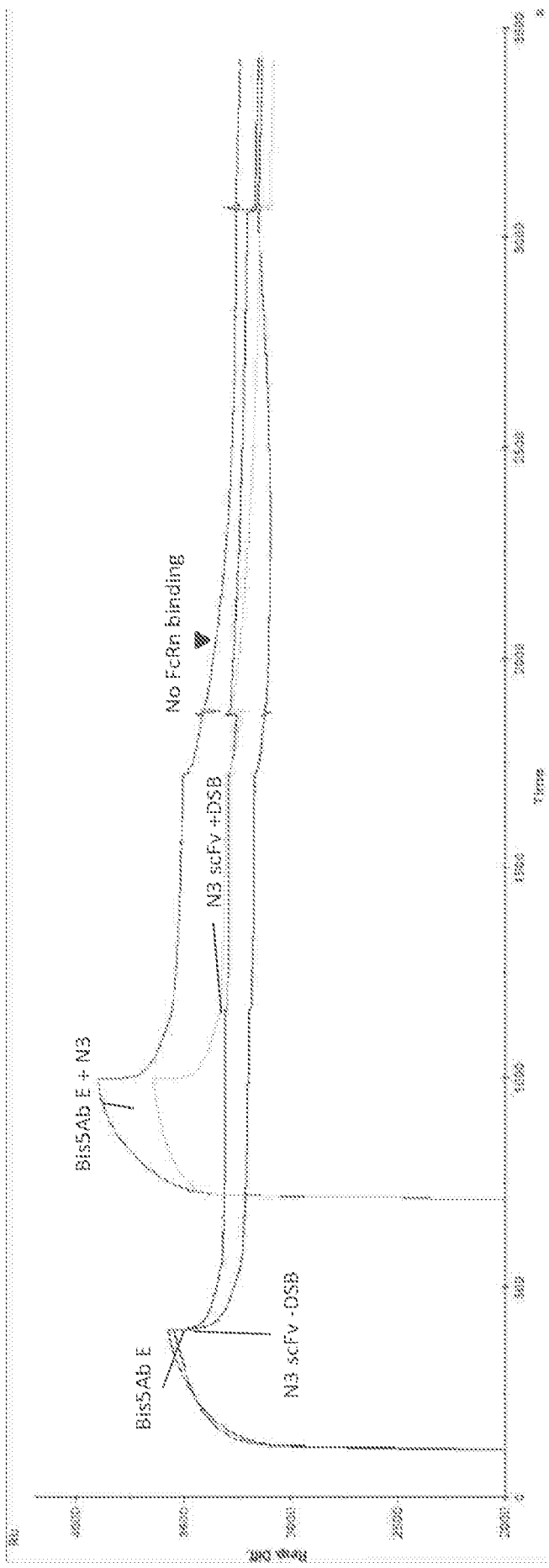


FIGURE 83

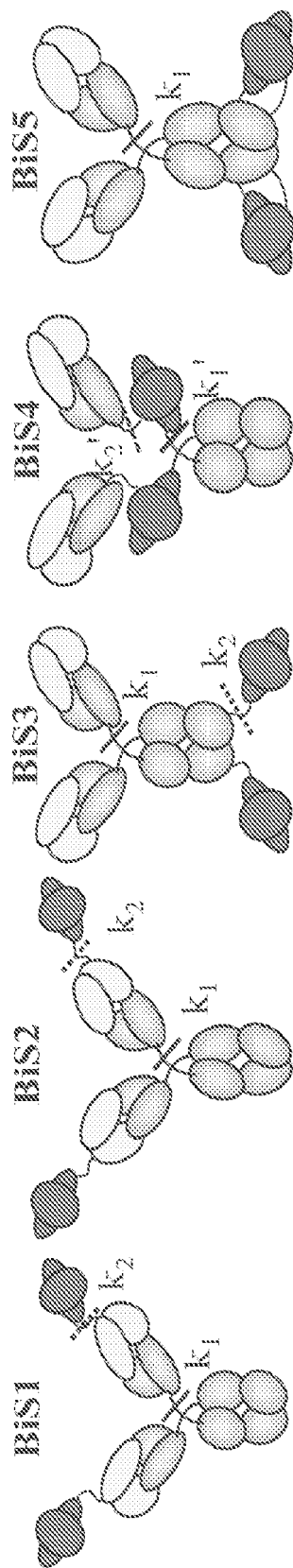


FIGURE 84

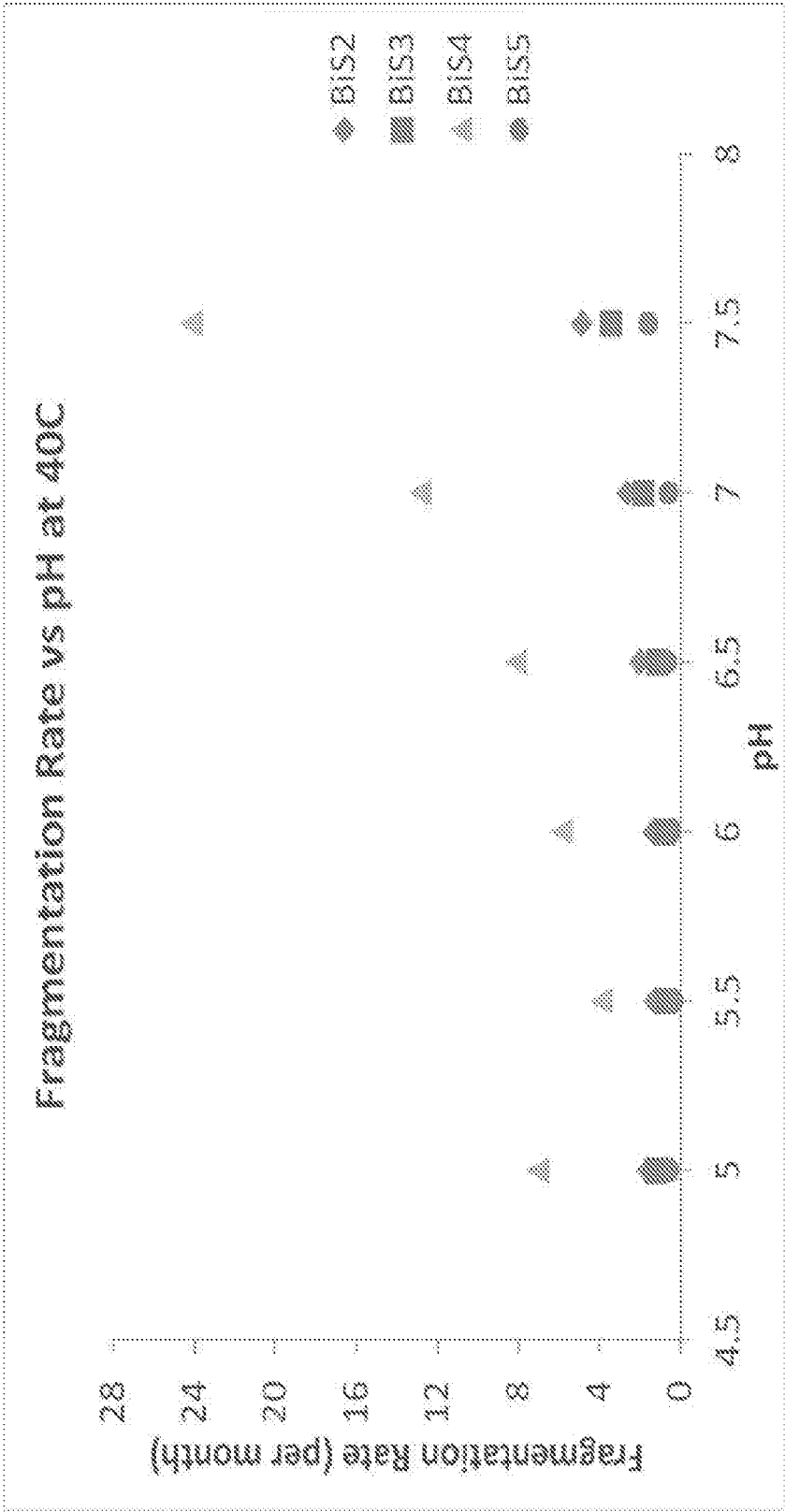


FIGURE 85

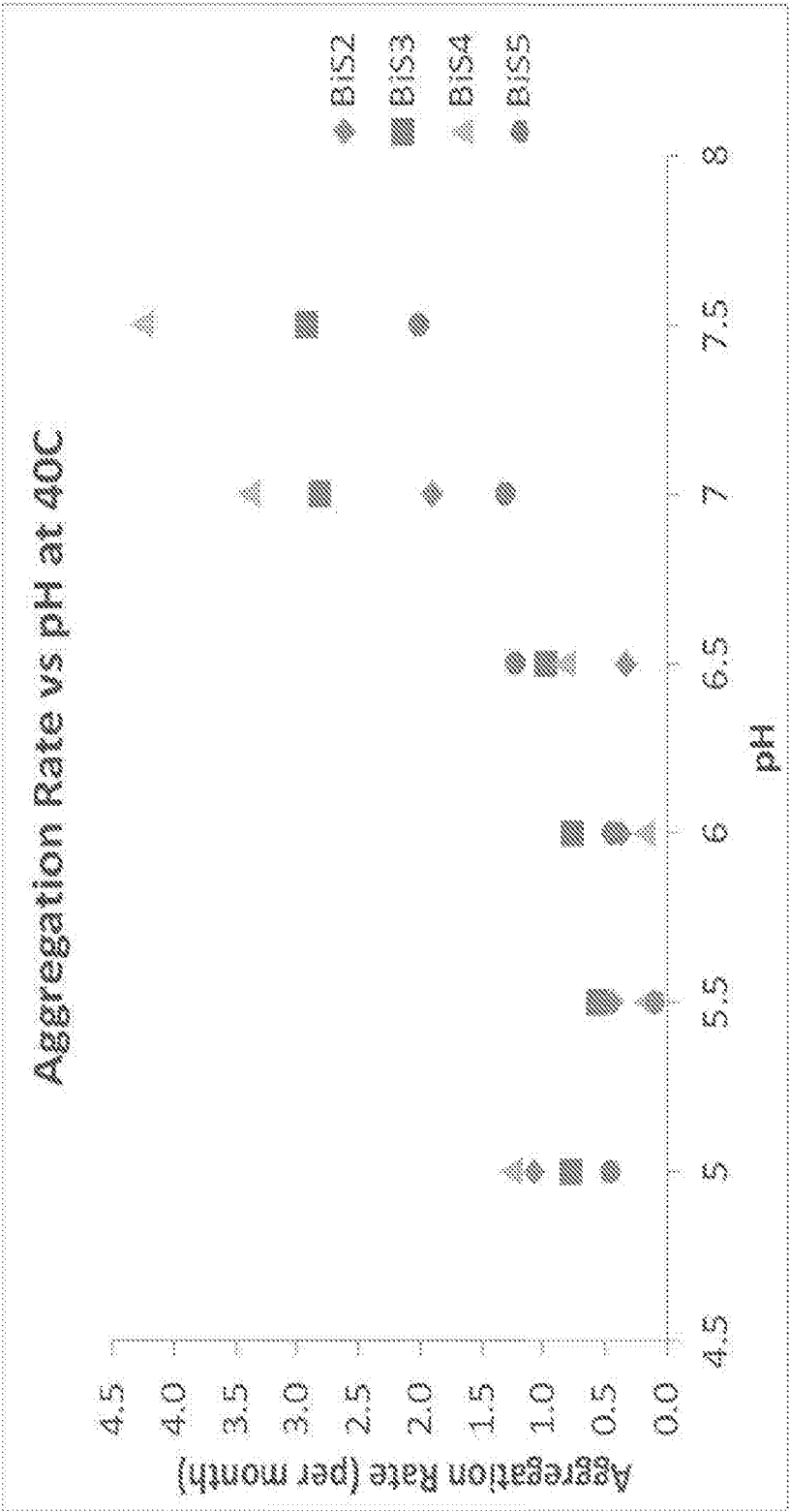
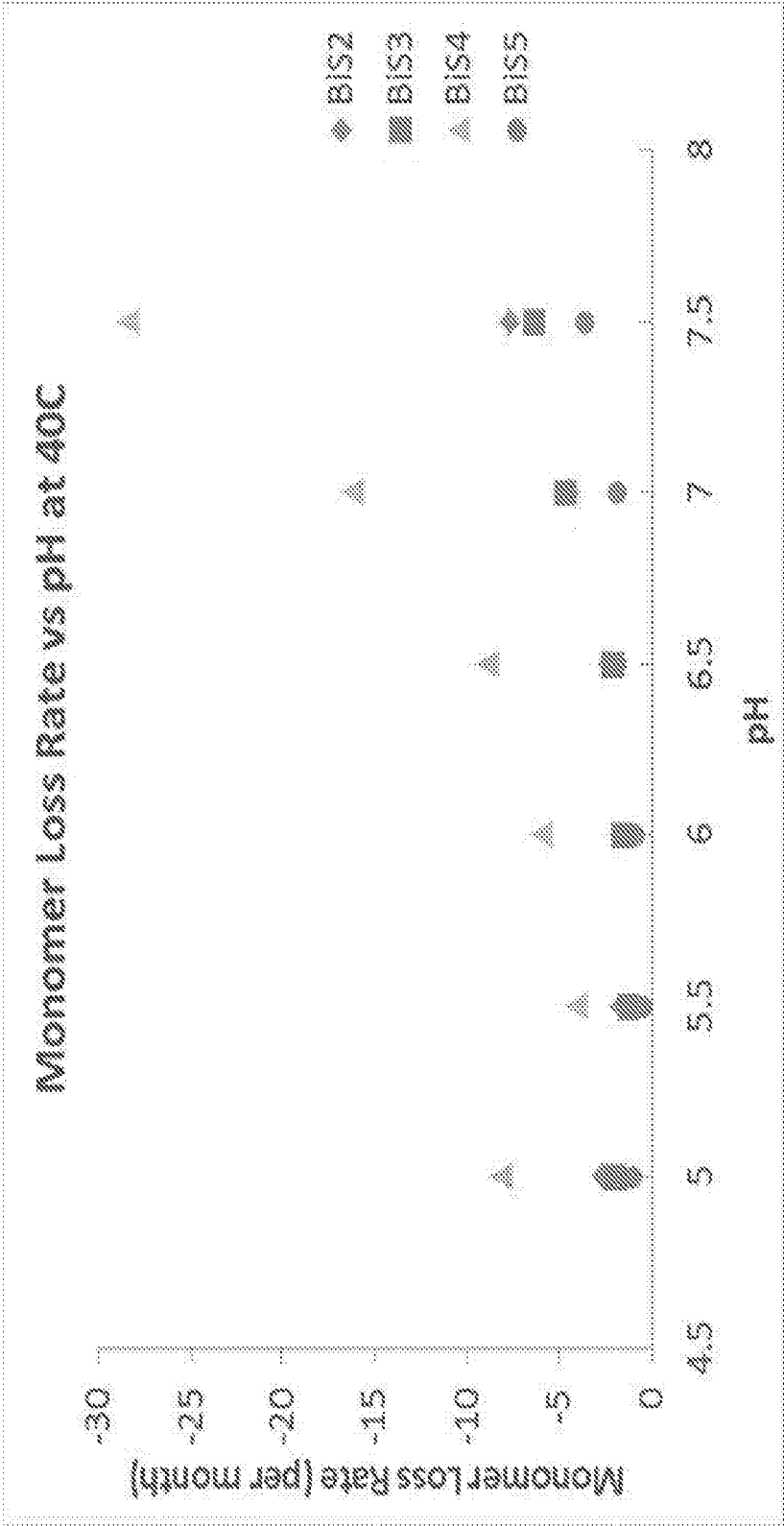


FIGURE 86



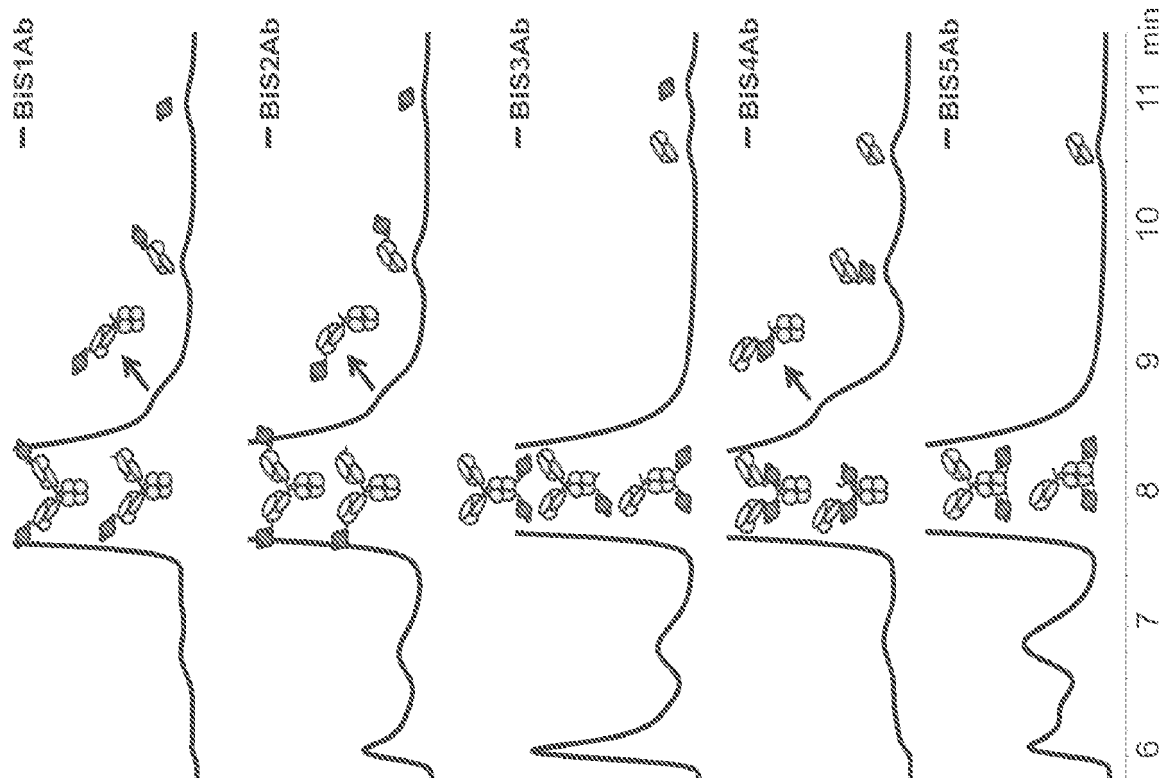


FIGURE 87

FIGURE 88

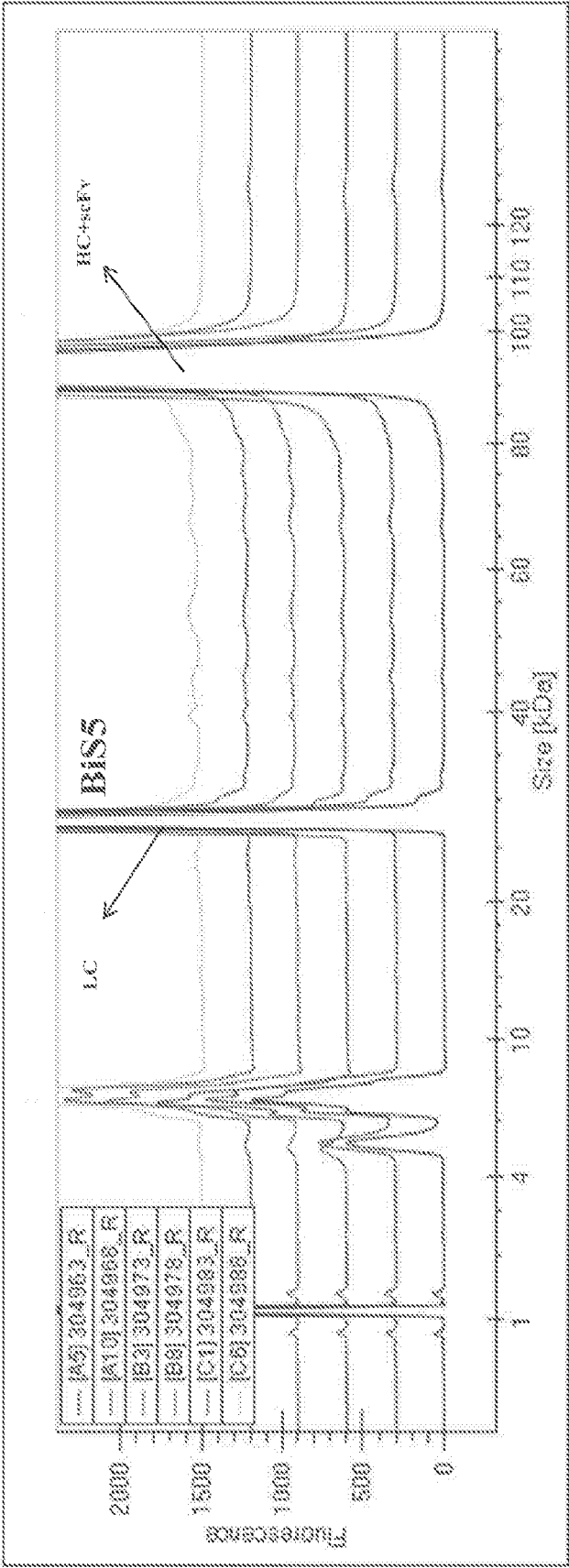


FIGURE 89

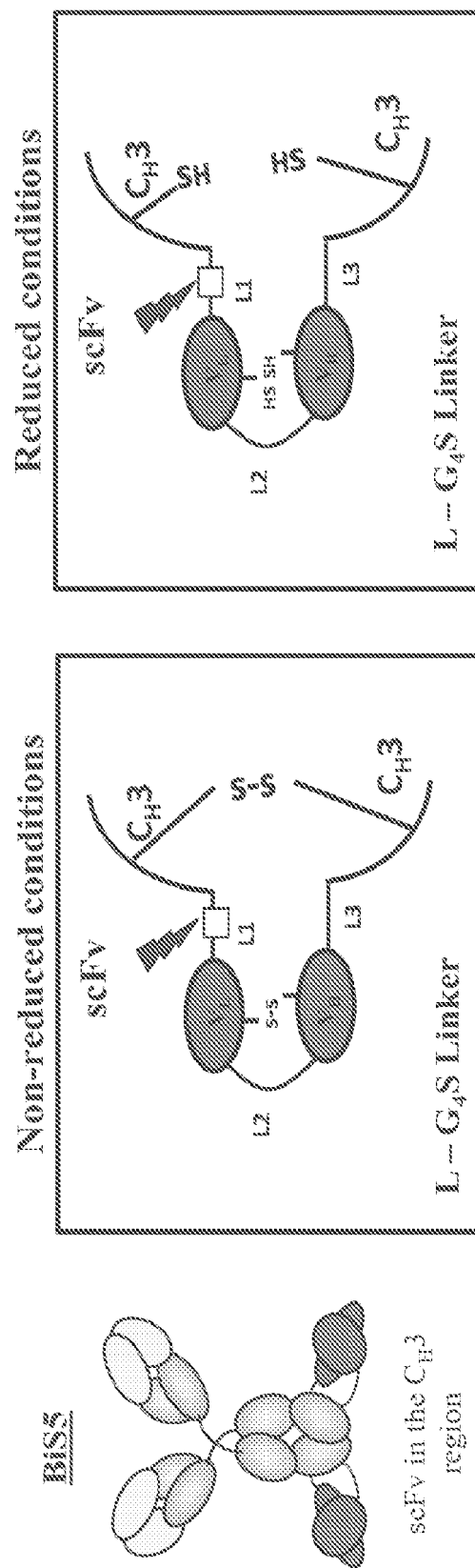


FIGURE 90

SEB Assay Format

