

ROR1 mAbs										
V_H	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4			
1	23	35	49	57	88	98	107			
EBR1-324	EVVLQTPSPVSAVQVITMC	QASQSVYGNHEA	WYQRPGLAPGLIY	RASLTS	GVPSFSGSGSTFLLTISWQREDAIYTC	LGQVSSVRA	FGGCTQLVTC			
EBR1-TOP40	EVVLQTPSPVSAVQVITMC	QASQVLSY--LA	WYQRPGLAPGLIY	QASHLAS	GVPSFSGSGSTFLLTISWQREDAIYTC	LGQVSSVRA	FGGCTQLVTC			
V_L	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4			
1	23	35	49	57	88	98	107			
EBR1-402	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-301	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-306	QVVLQSPSPVSAALCAKALITC	TLSAHKTYTID-	WYQRPGLAPGLIY	LKNGSYTKAT	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-316	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-403	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-409	QVVLQSPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP4	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP15	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP22	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP43	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP54	SYELQLPSPVSVSLGQTARITC	GGNSIGSKAVH---	WYQRPGLAPGLIY	DDDERPS-----	GVPSFSGSGSGSTFLLTISWQREDAIYTC	QVHSSSAVY---	FGGCTQLVTC			
V_H	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4			
1	30	36	49	56	94	103	113			
EBR1-402	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-301	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-306	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-316	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-324	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-403	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-409	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP4	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP15	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP22	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP40	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP43	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			
EBR1-TOP54	QVQLVDSGGLVTPGGLLITCTASGFLS	SYTMS	WYQRPGLAPGLIY	ALGDSGSAIYASNAAS-	RSTTHTKMLT-ATLAKTSLTADATATPCAR	QVHSSSAVY---	FGGCTQLVTC			

FIG. 1

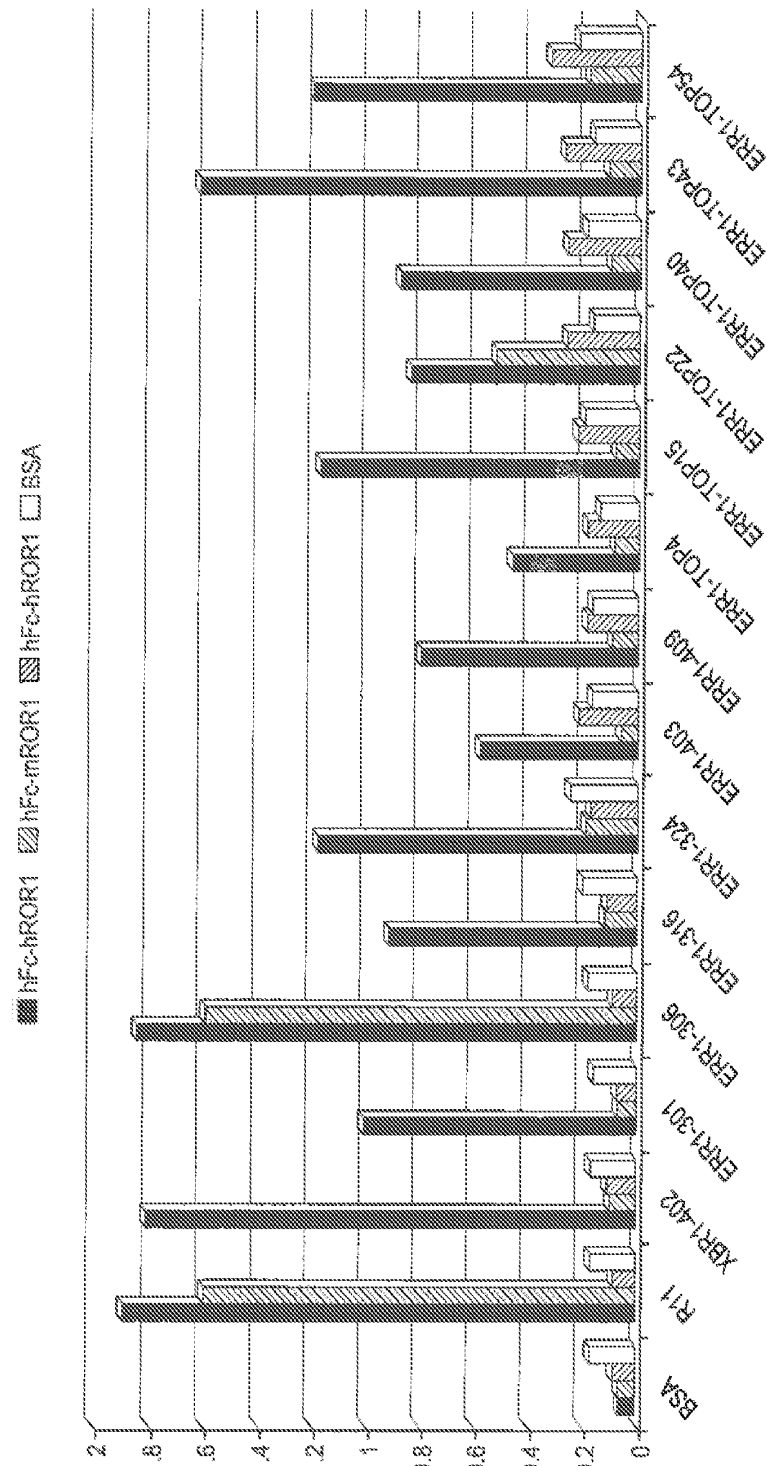


FIG. 2

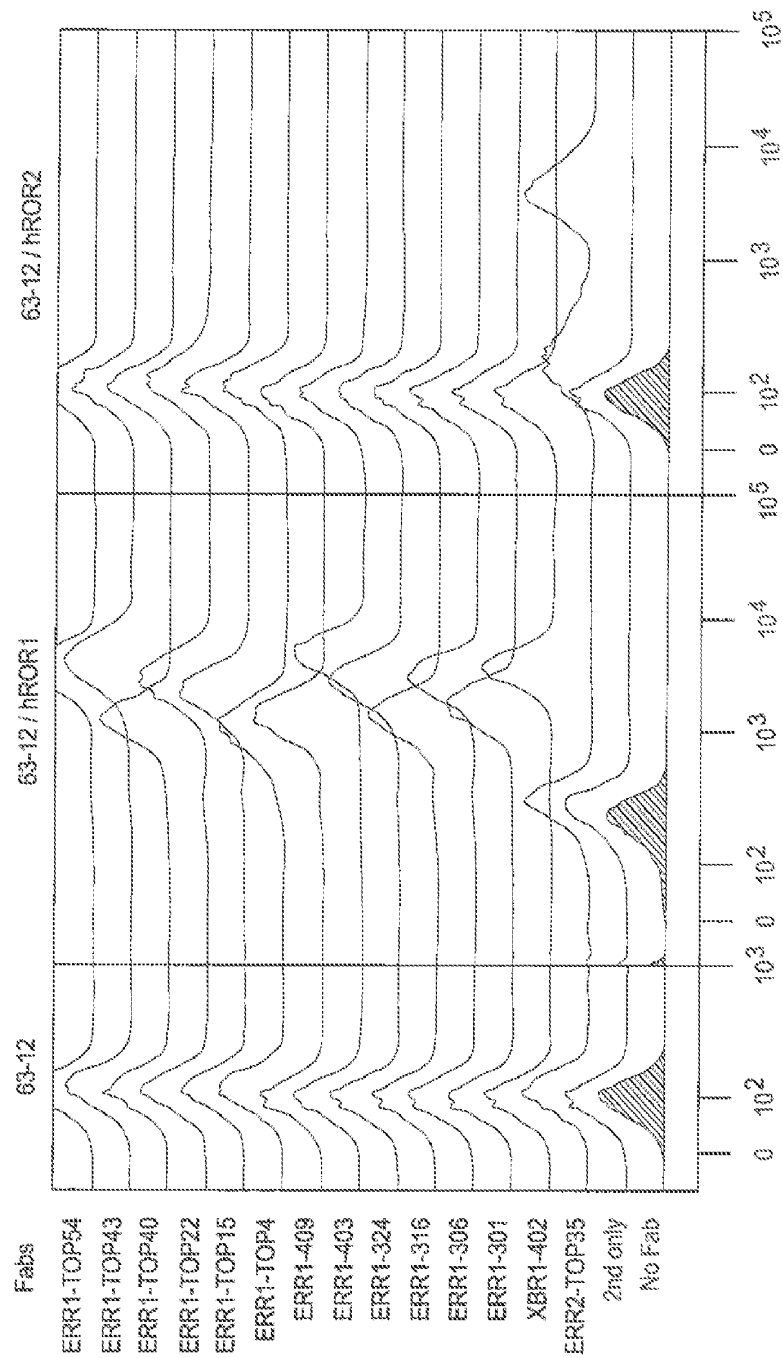


FIG. 3

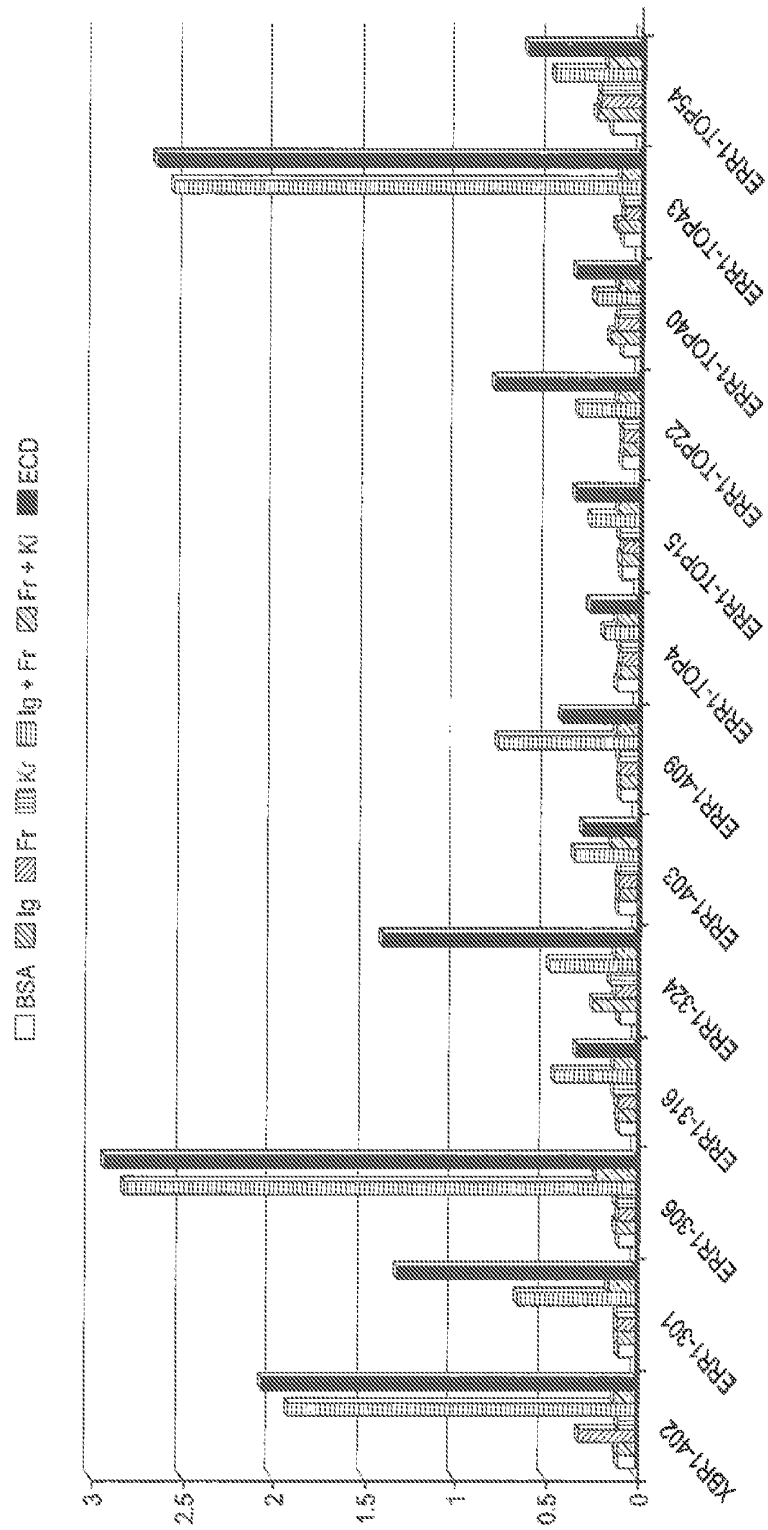


FIG. 4

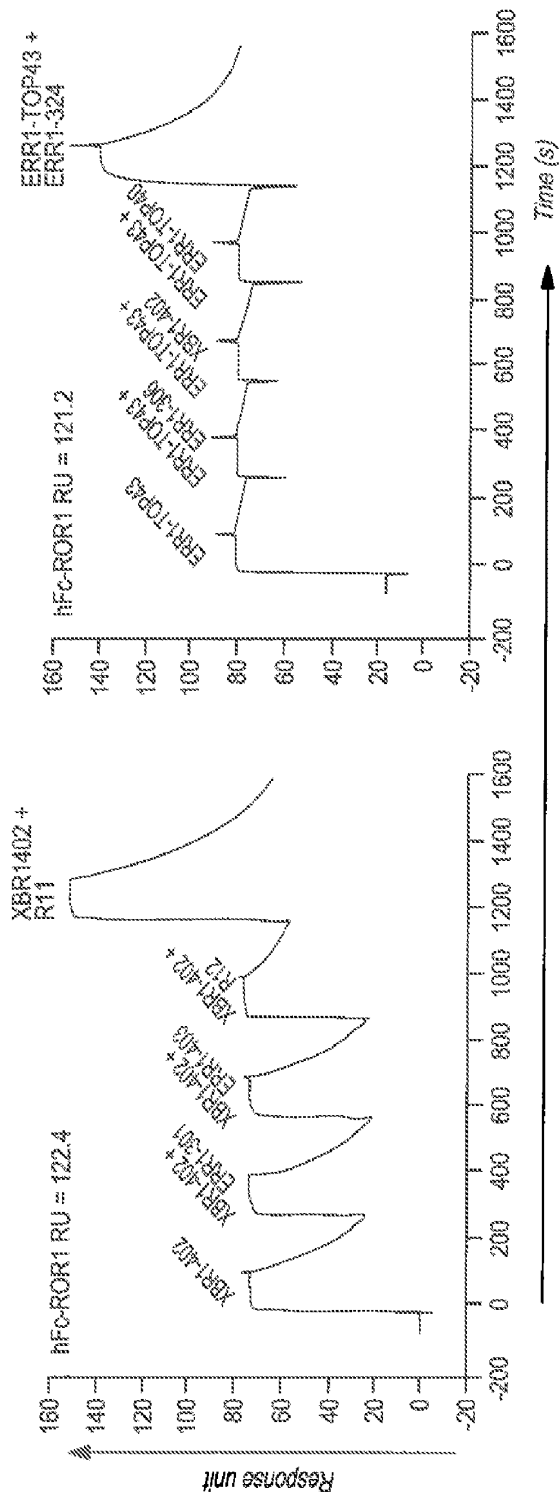
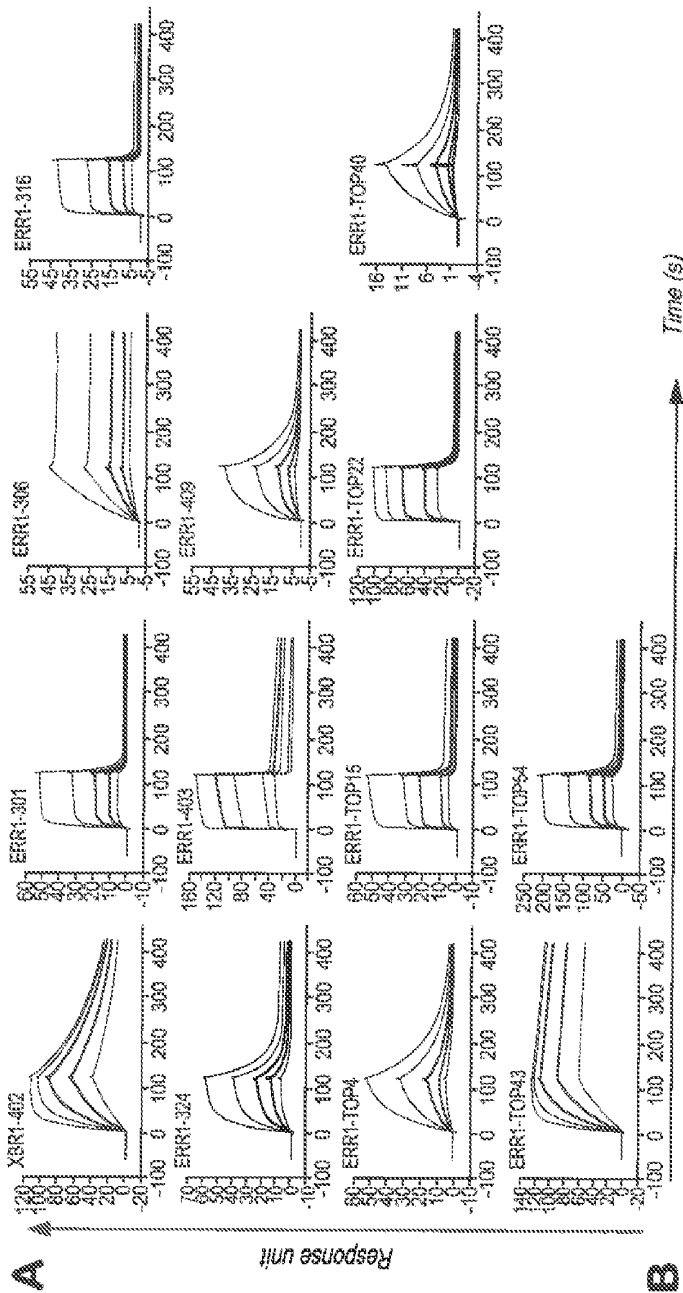


FIG. 5



clone	XBR1-402	ERR1-301	ERR1-306	ERR1-403	ERR1-408	ERR1-316	ERR1-324	ERR1-404	ERR1-405	ERR1-406	ERR1-407	ERR1-408
immobilization RU	402	301	306	5000	5000	5000	5000	5000	5000	5000	5000	5000
hfc-ROR1 RU	203.8	203	189.4	198.7	178.3	326.4	326.4	1000	200	200	172.2	167.9
Fab. Con. h (nM)	100	100	500	100	200	1000	1000	1000	200	200	200	200
$k_{on}(10^4 M^{-1} s^{-1})$	111	84.9	1.51	110	11.5	3.08	5.75	24.7	46.9	73.7	3.18	45.1
$k_{off}(10^{-3} s^{-1})$	6.43	100	0.146	132.5	12.51	1.28	16.16	59.24	65.36	81.26	20.19	0.501
K_d (nM)	5.91	118	9.66	121	106	41.5	281	240	139	110	636	1.11
Chi ²	0.616	0.922	0.137	1.95	4.64	16.7	0.302	0.403	9	14.9	0.14	1.17

FIG. 6

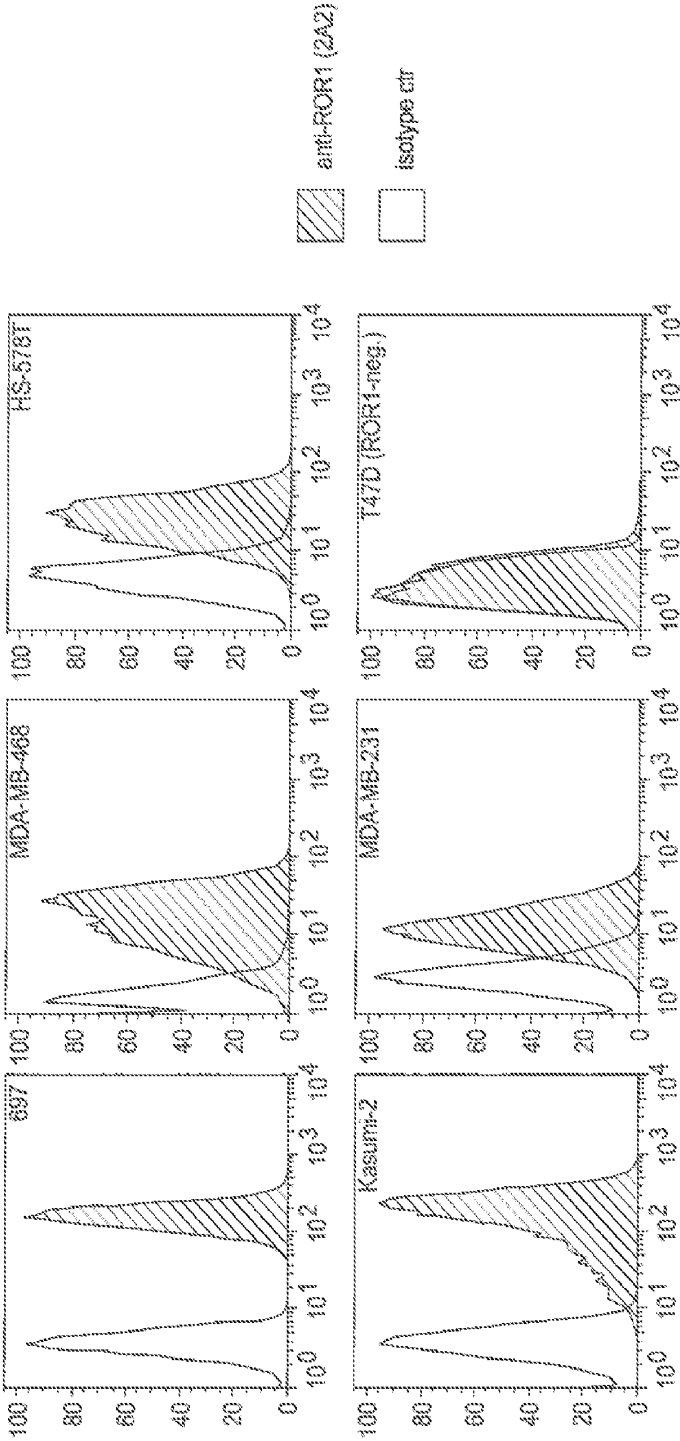


FIG. 7

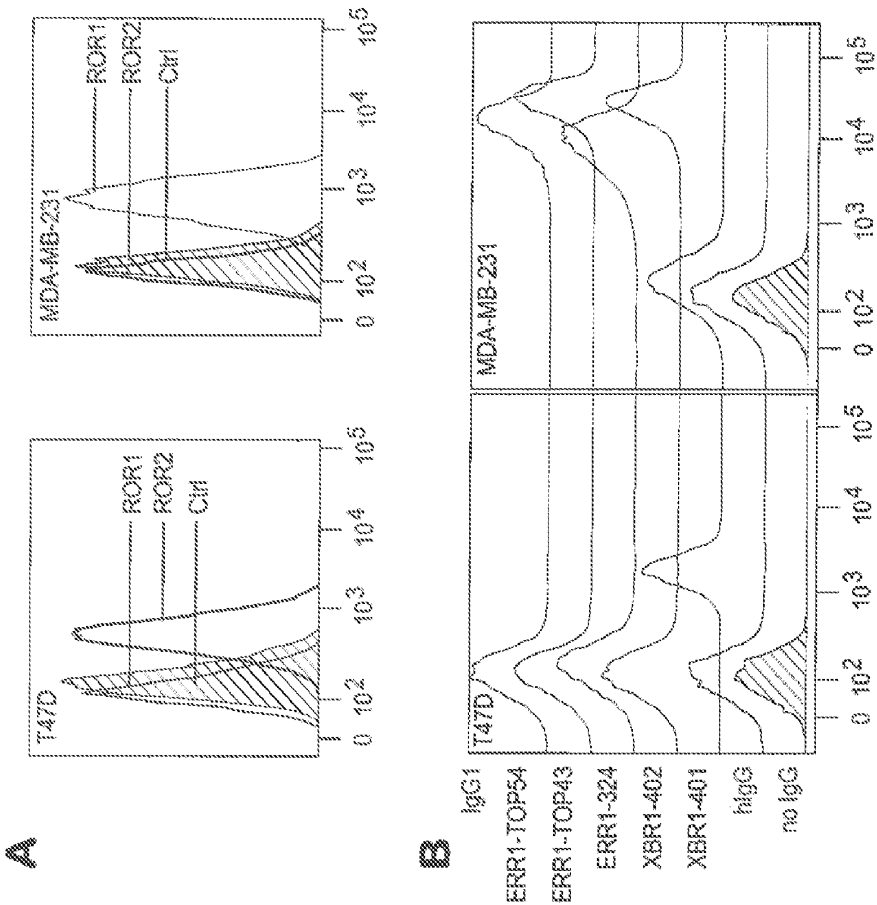


FIG. 8

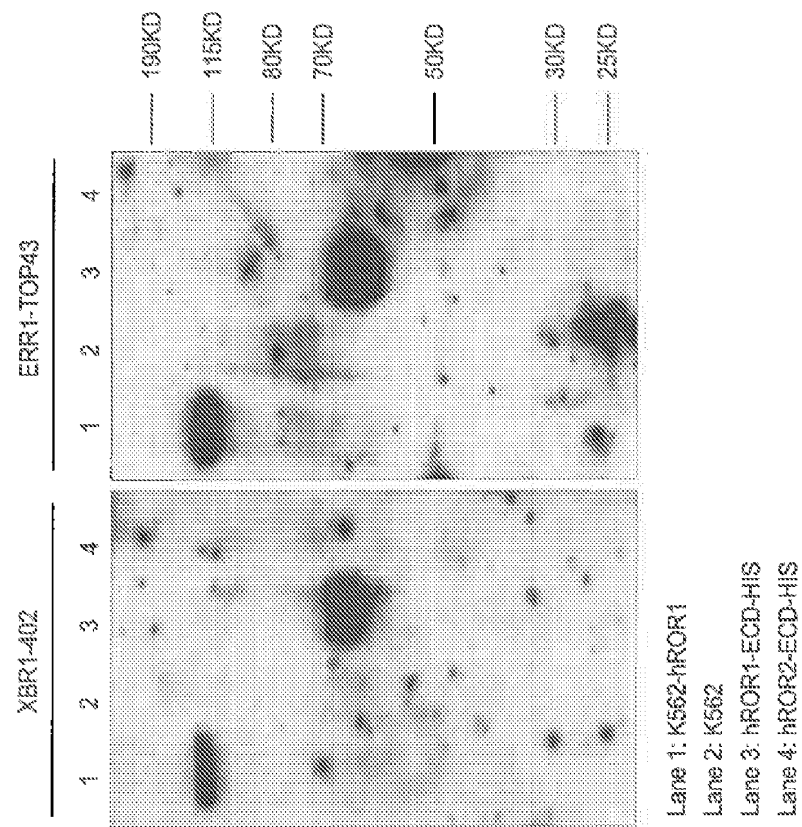


FIG. 9

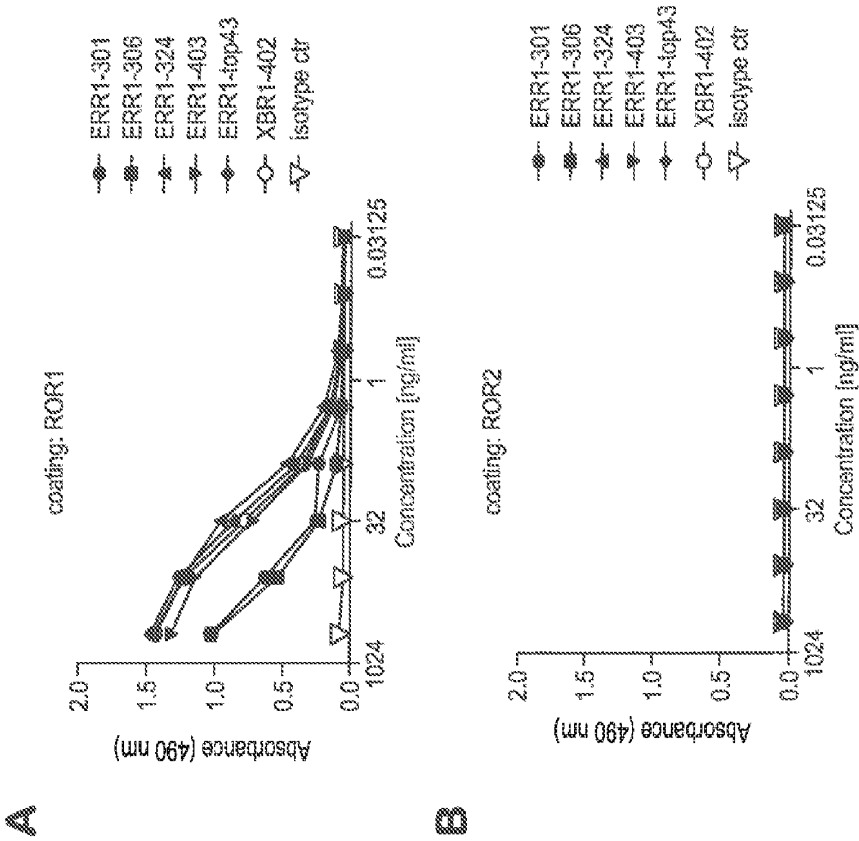


FIG. 10

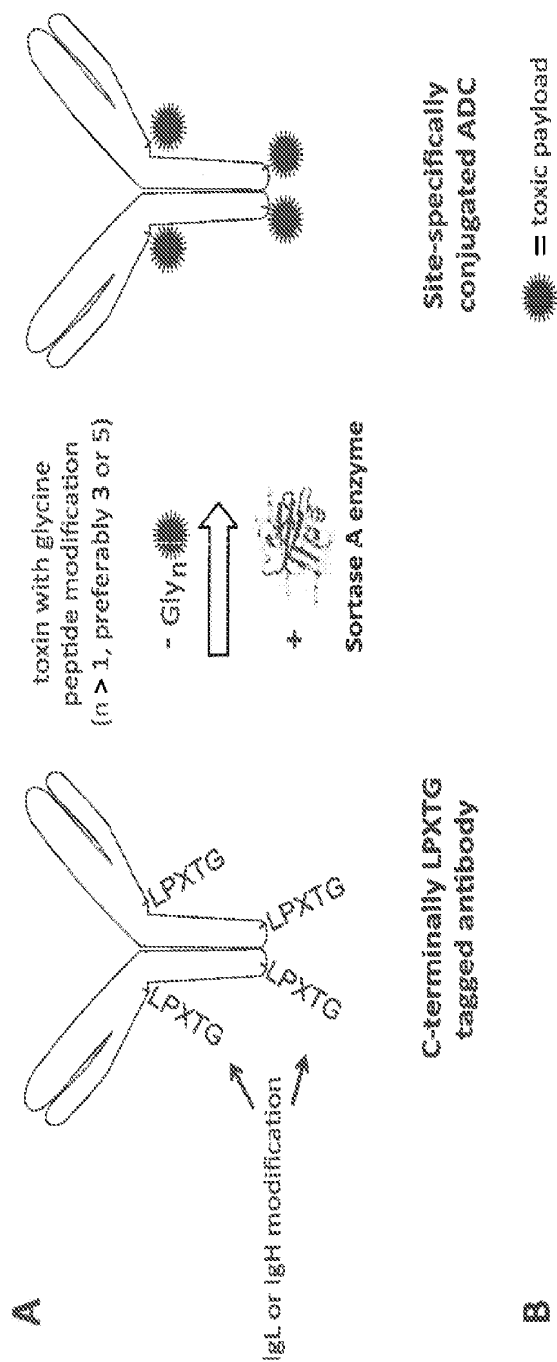
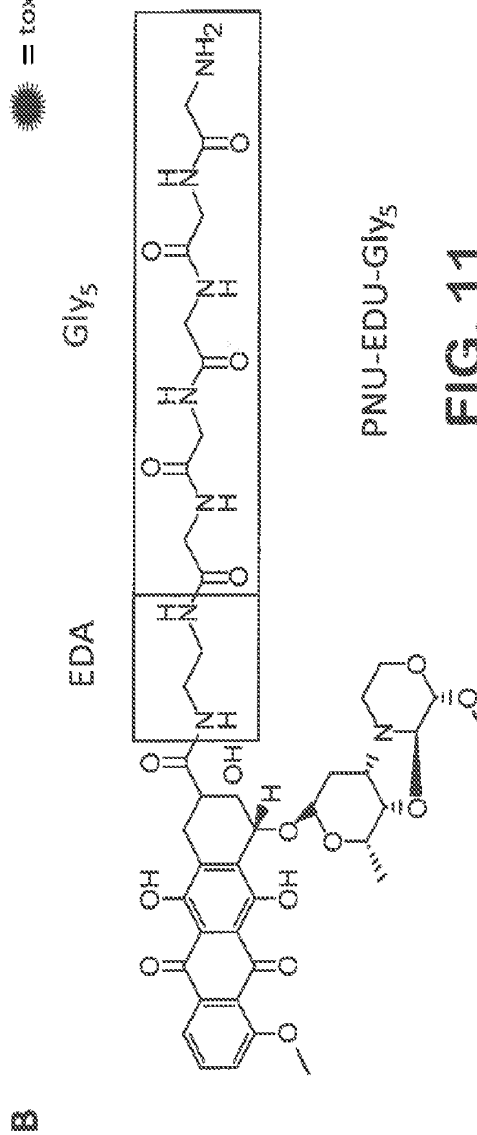


FIG. 11

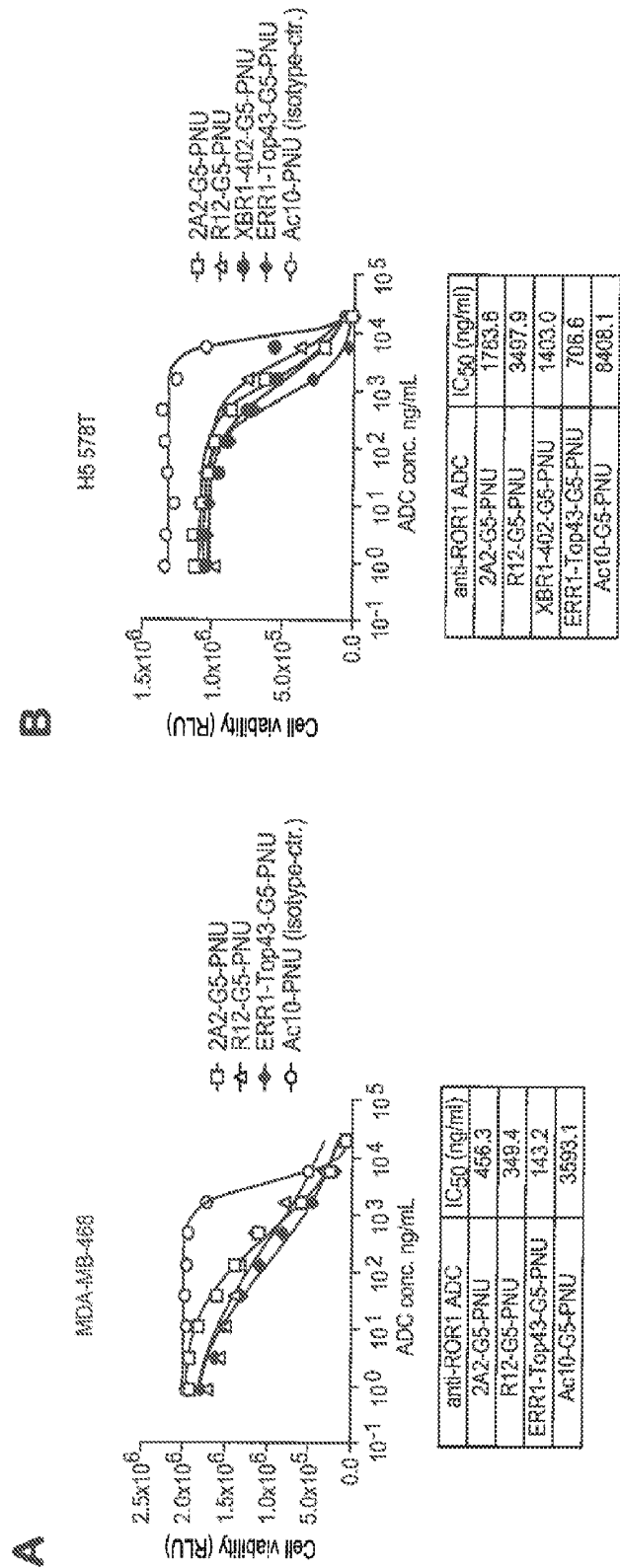


FIG. 12

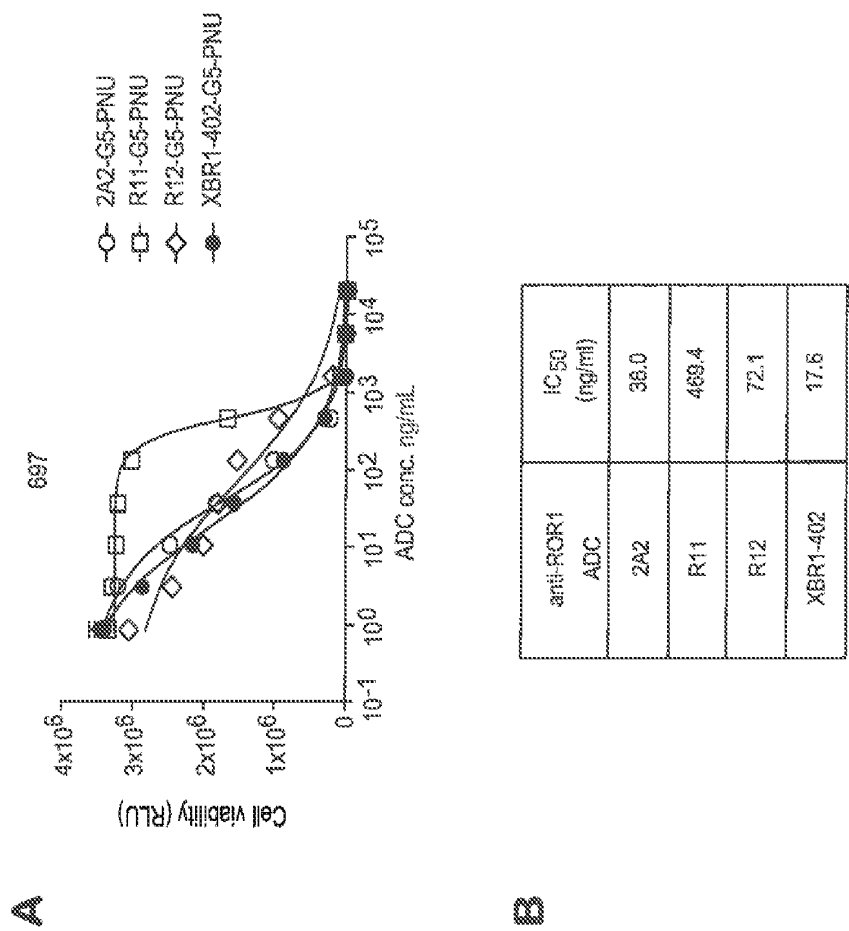


FIG. 13

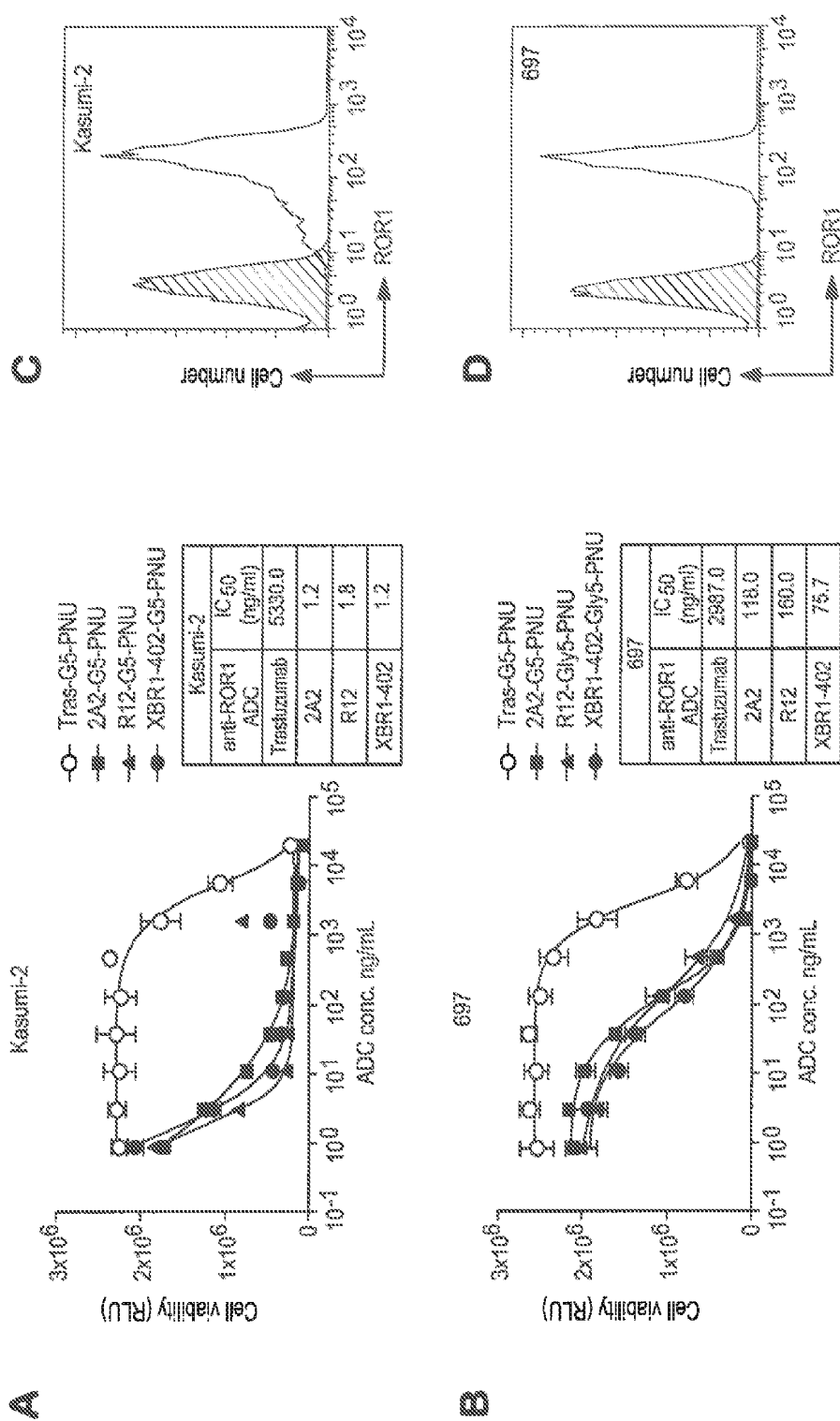


FIG. 14

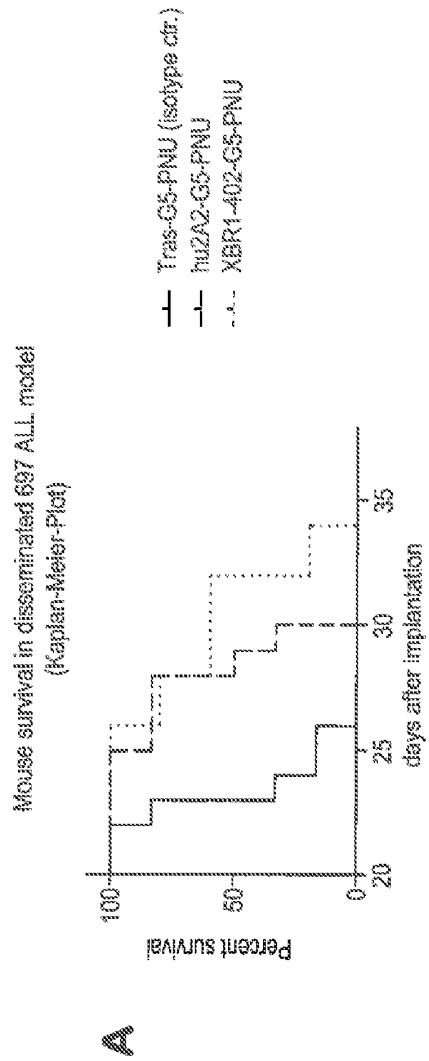
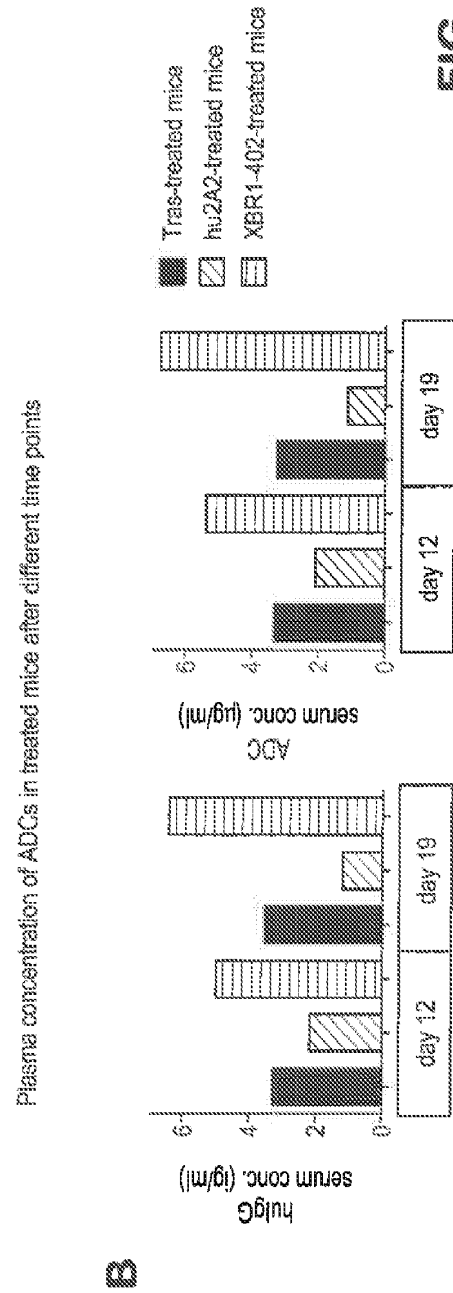


FIG. 15

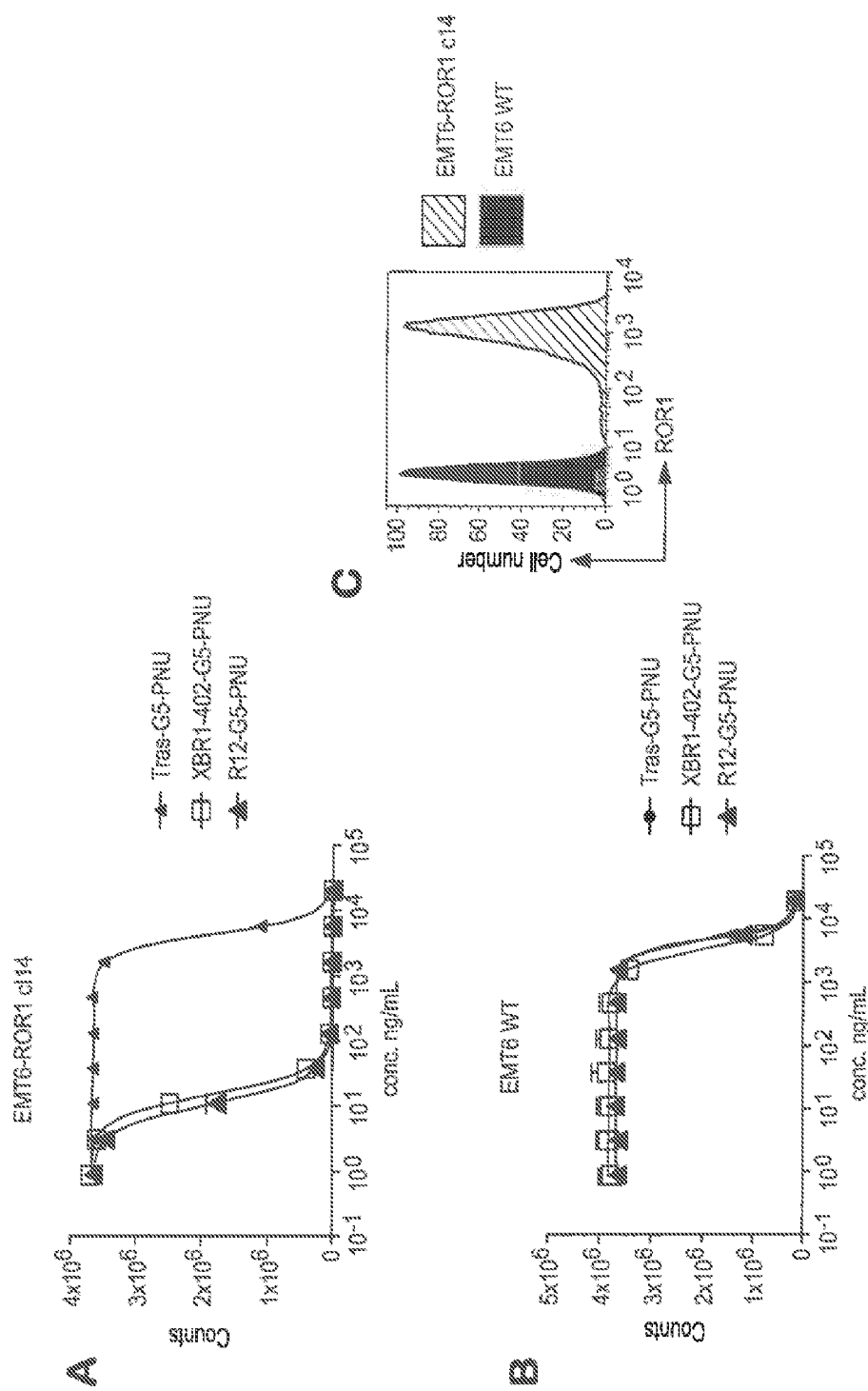


FIG. 16

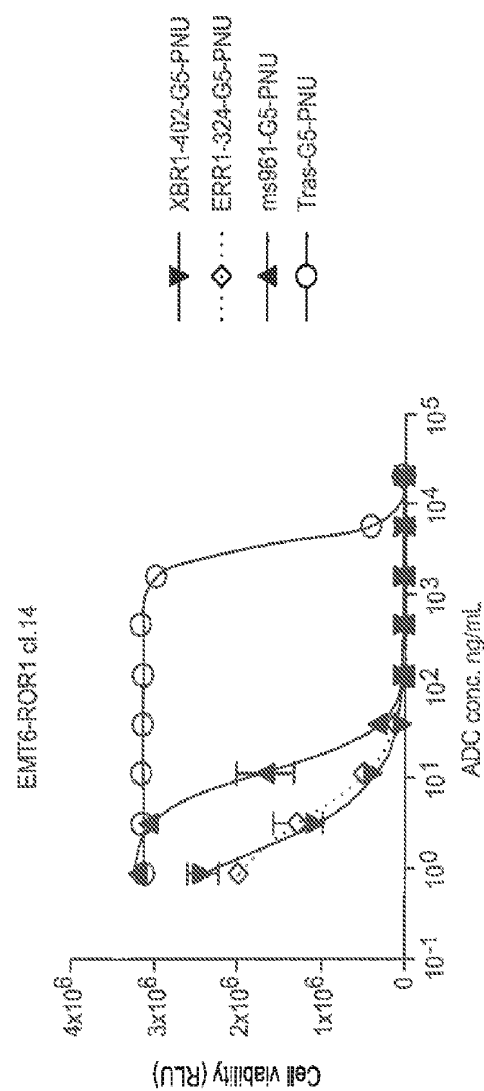
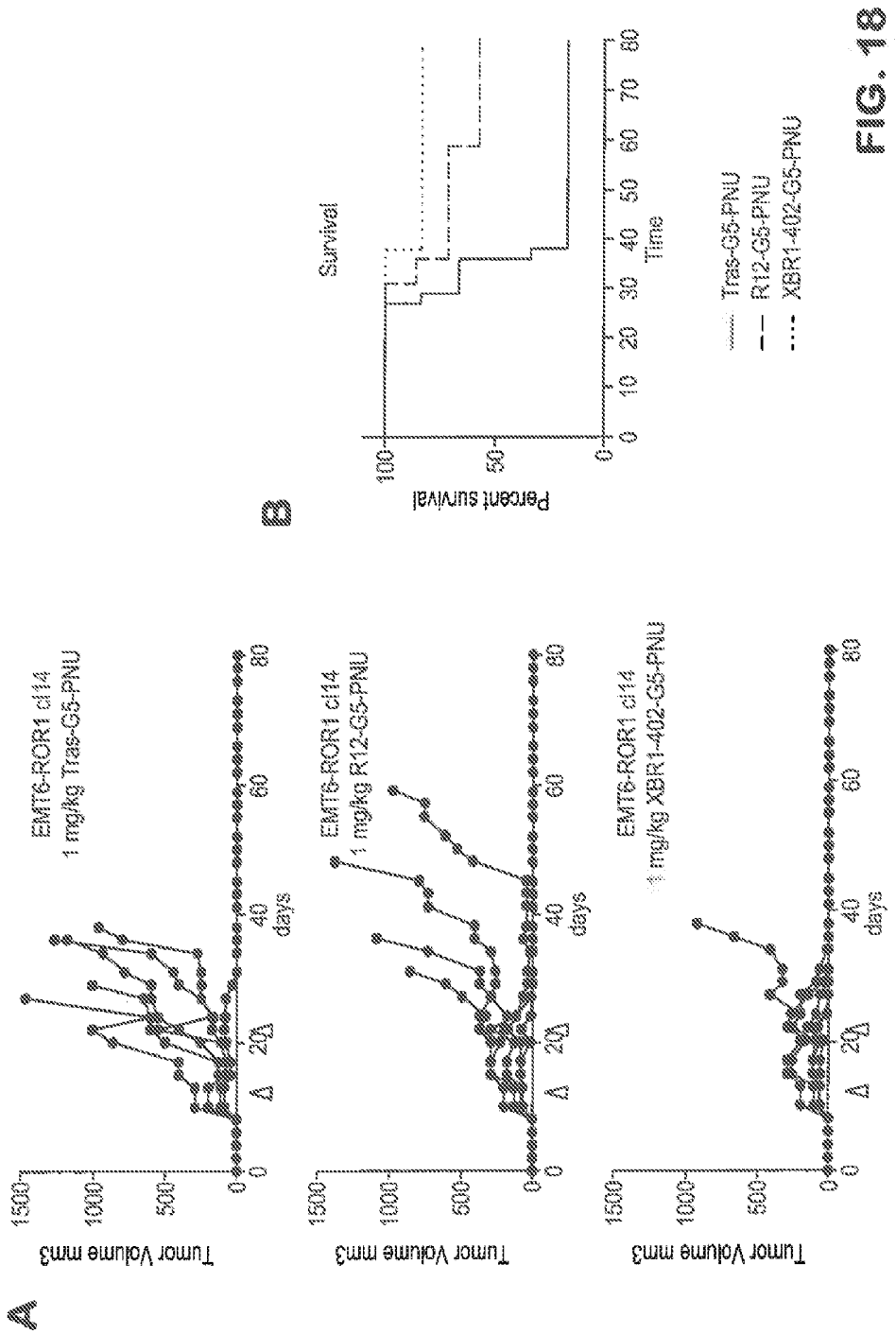


FIG. 17



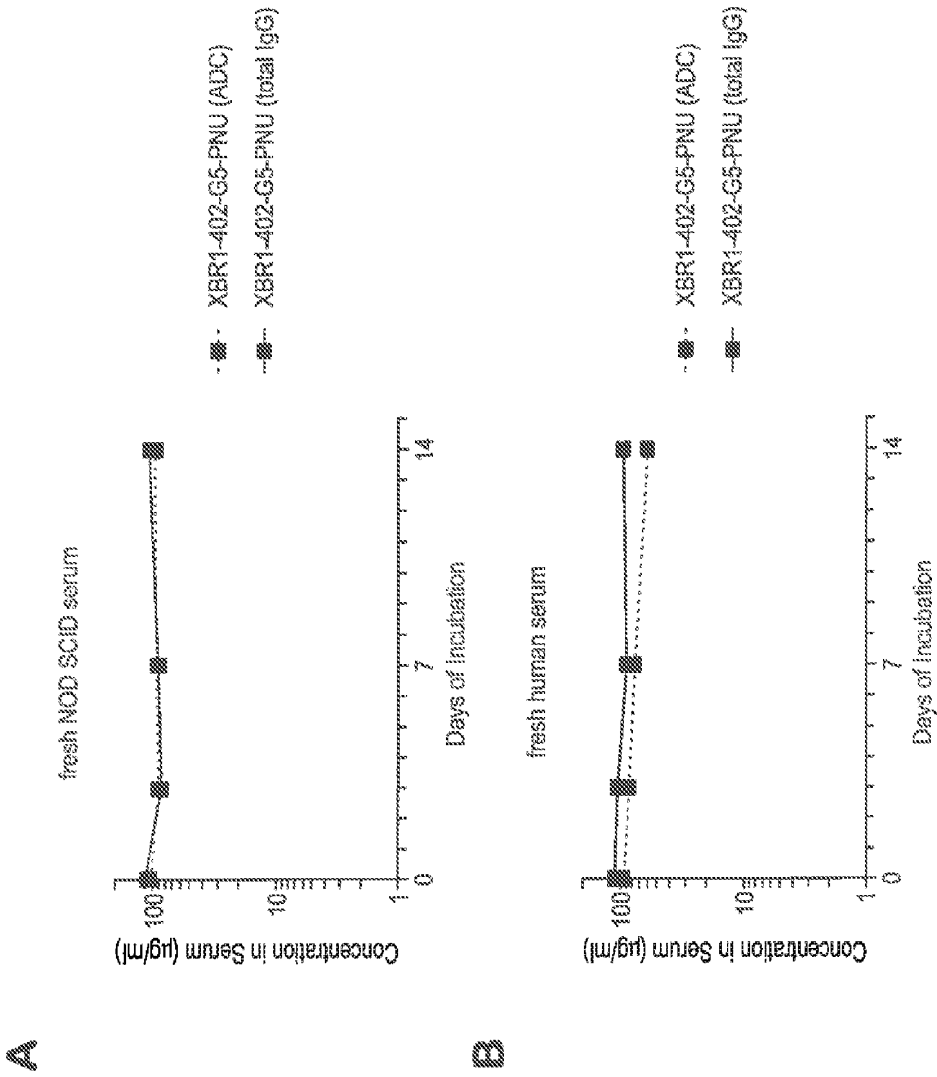


FIG. 19

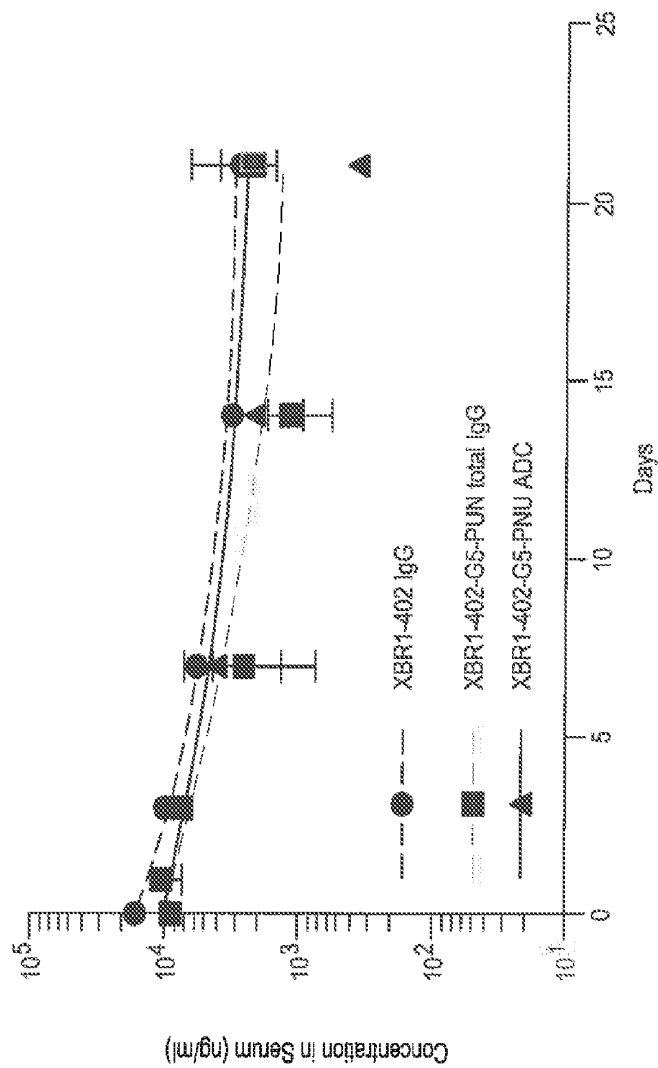


FIG. 20

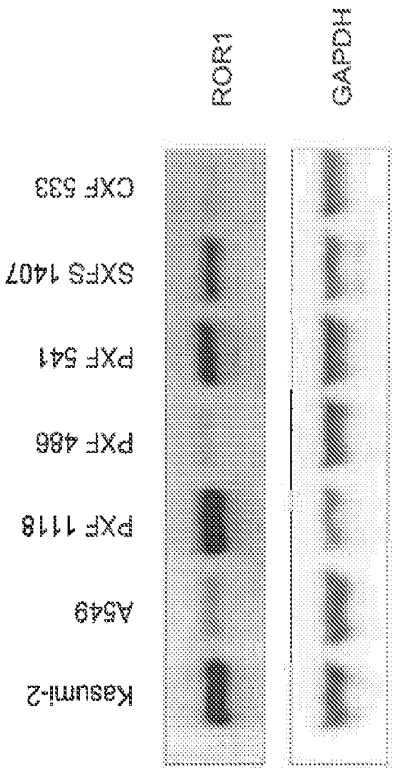


FIG. 21

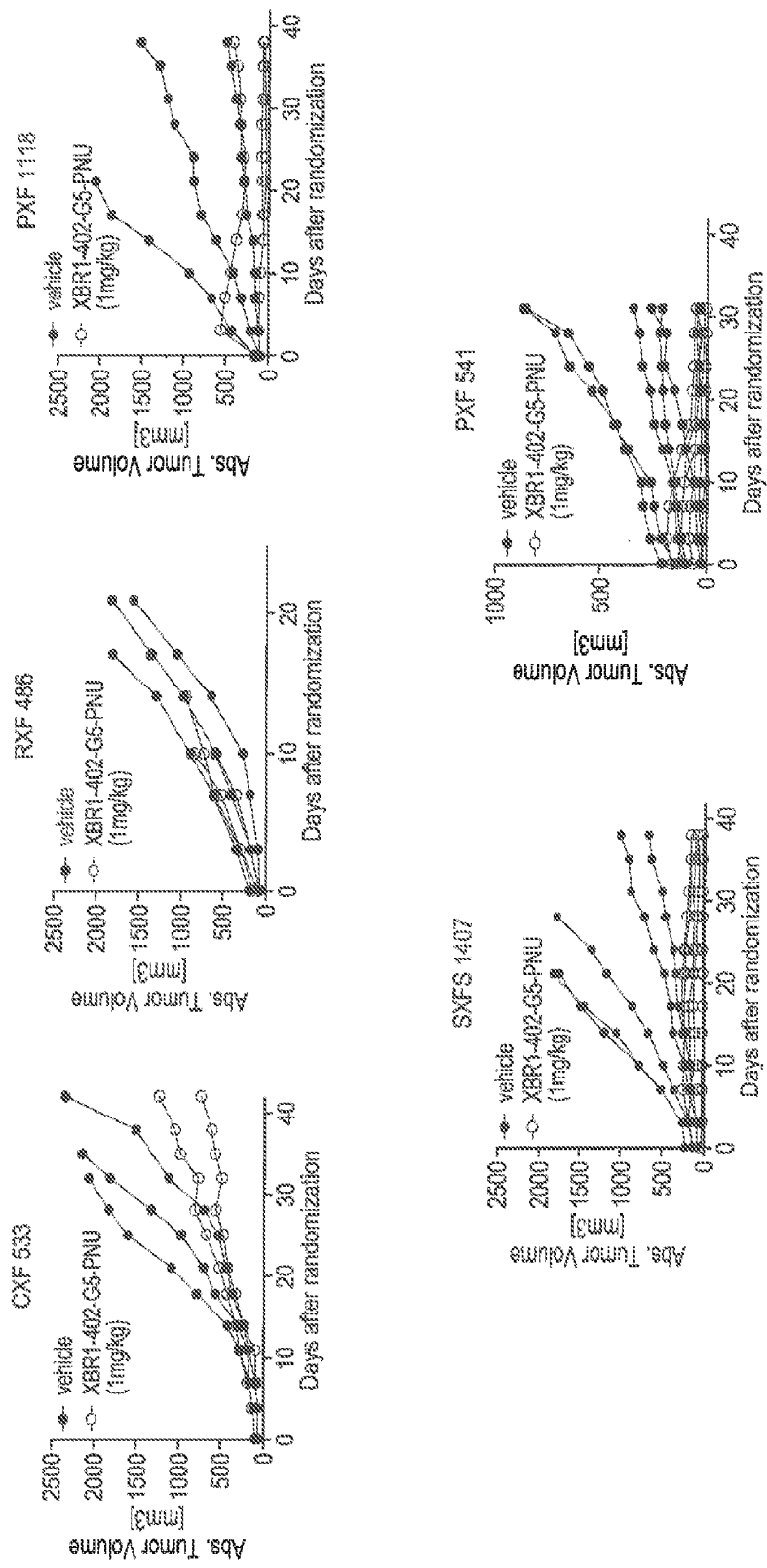


FIG. 22

ROR1 mAbs

V_{λ}	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
XBR1-402	1	22	34	48	56	97	107
huXR1-402-3	SYELTQPLSVSVSLGQTARITC	EQMIGSKAVH	WYQKPELAPLVII	EDDERPS	GYPDFSGNSGNTATLTISRAGACHEADNYC	QVWDSAYV	FGGCTQLTFTIC
huXR1-402-8	SYELTQPLSVSVSLGQTARITC	EQMIGSKAVH	WYQKPELAPLVII	EDDERPS	GYPDFSGNSGNTATLTISRAGACHEADNYC	QVWDSAYV	FGGCTQLTFTIC
huXR1-402-15	SYELTQPLSVSVSLGQTARITC	EQMIGSKAVH	WYQKPELAPLVII	EDDERPS	GYPDFSGNSGNTATLTISRAGACHEADNYC	QVWDSAYV	FGGCTQLTFTIC
huXR1-402-17	SYELTQPLSVSVSLGQTARITC	EQMIGSKAVH	WYQKPELAPLVII	EDDERPS	GYPDFSGNSGNTATLTISRAGACHEADNYC	QVWDSAYV	FGGCTQLTFTIC
huXR1-402-19	SYELTQPLSVSVSLGQTARITC	EQMIGSKAVH	WYQKPELAPLVII	EDDERPS	GYPDFSGNSGNTATLTISRAGACHEADNYC	QVWDSAYV	FGGCTQLTFTIC
huXR1-402-26	SYELTQPLSVSVSLGQTARITC	EQMIGSKAVH	WYQKPELAPLVII	EDDERPS	GYPDFSGNSGNTATLTISRAGACHEADNYC	QVWDSAYV	FGGCTQLTFTIC

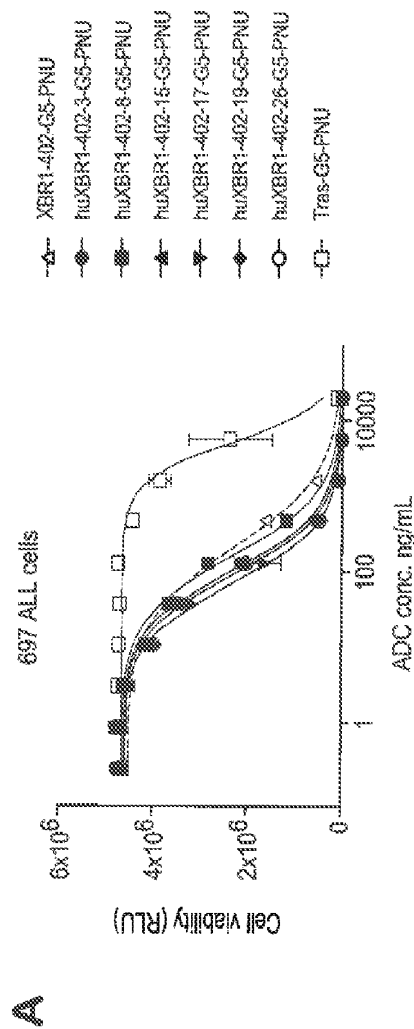
V_{H}	FR1	CDR1	FR2	CDR2	FR3	CDR3	FR4
XBR1-402	1	30	36	49	66	97	117
huXR1-402-3	QVQLRSGCLVKEPSTLSLTCTVSGPHIS	SYTMS	WVRQPPKGLNEMIG	AIGISGAYYASNAKS	RSTITPTNTLTNTVTLKNTSLTAAADNTVTCAR	DHPTVGMOL	WGPGTILVTYSS
huXR1-402-8	QVQLRSGCLVKEPSTLSLTCTVSGPHIS	SYTMS	WVRQPPKGLNEMIG	AIGISGAYYASNAKS	RVTISRTGKNDPSIKLSVTHAADTAVYTCAR	DHPTVGMOL	WGPGTILVTYSS
huXR1-402-15	QVQLRSGCLVKEPSTLSLTCTVSGPHIS	SYTMS	WVRQPPKGLNEMIG	AIGISGAYYASNAKS	RVTISRTGKNDPSIKLSVTHAADTAVYTCAR	DHPTVGMOL	WGPGTILVTYSS
huXR1-402-17	QVQLRSGCLVKEPSTLSLTCTVSGPHIS	SYTMS	WVRQPPKGLNEMIG	AIGISGAYYASNAKS	RVTISRTGKNDPSIKLSVTHAADTAVYTCAR	DHPTVGMOL	WGPGTILVTYSS
huXR1-402-19	QVQLRSGCLVKEPSTLSLTCTVSGPHIS	SYTMS	WVRQPPKGLNEMIG	AIGISGAYYASNAKS	RVTISRTGKNDPSIKLSVTHAADTAVYTCAR	DHPTVGMOL	WGPGTILVTYSS
huXR1-402-26	QVQLRSGCLVKEPSTLSLTCTVSGPHIS	SYTMS	WVRQPPKGLNEMIG	AIGISGAYYASNAKS	RVTISRTGKNDPSIKLSVTHAADTAVYTCAR	DHPTVGMOL	WGPGTILVTYSS

FIG. 23

ADC clone	T20 score HC	T20 score LC	K_{on} ($10^{-4} M^{-1} s^{-1}$)	K_{off} ($10^{-3} s^{-1}$)	K_D (nM)
XBR1-402*1	60.64	78.85	116	5.91	5.1
XBR1-402*1	60.64	78.85	110	5.56	5.1
huXBR1-402-3	80.34	88.26	119	3.75	3.2
huXBR1-402-8	81.20	82.75	129	2.76	2.1
huXBR1-402-15	81.20	91.15	111	3.94	3.5
huXBR1-402-17	80.34	91.15	96	3.22	3.4
huXBR1-402-19	80.30	91.15	111	3.32	3.0
huXBR1-402-26	80.30	86.56	105	3.28	3.1

*1: two independent measurements

FIG. 24



B

ADC clone	IC ₅₀
XBR1-402-G5-PNU	211.6
huXBR1-402-3-G5-PNU	98.1
huXBR1-402-8-G5-PNU	164.2
huXBR1-402-15-G5-PNU	105.6
huXBR1-402-17-G5-PNU	70.6
huXBR1-402-19-G5-PNU	81.7
huXBR1-402-26-G5-PNU	93.9
Trastuzumab-G5-PNU	5214

FIG. 25

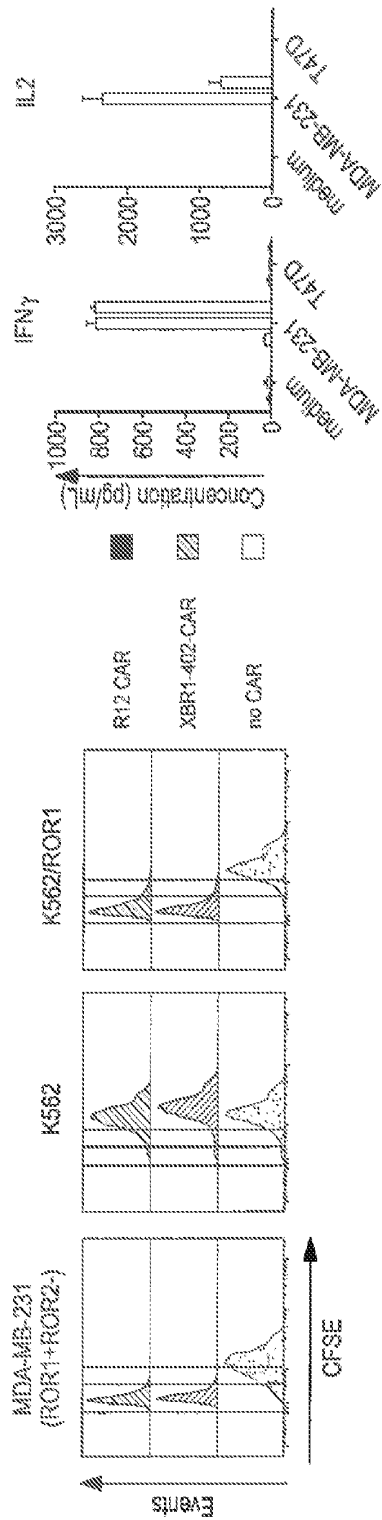
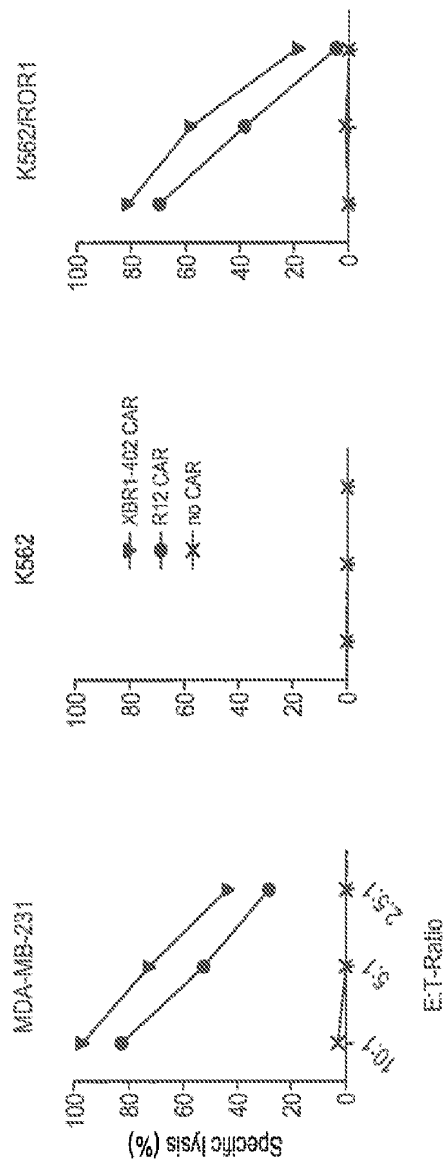


FIG. 26

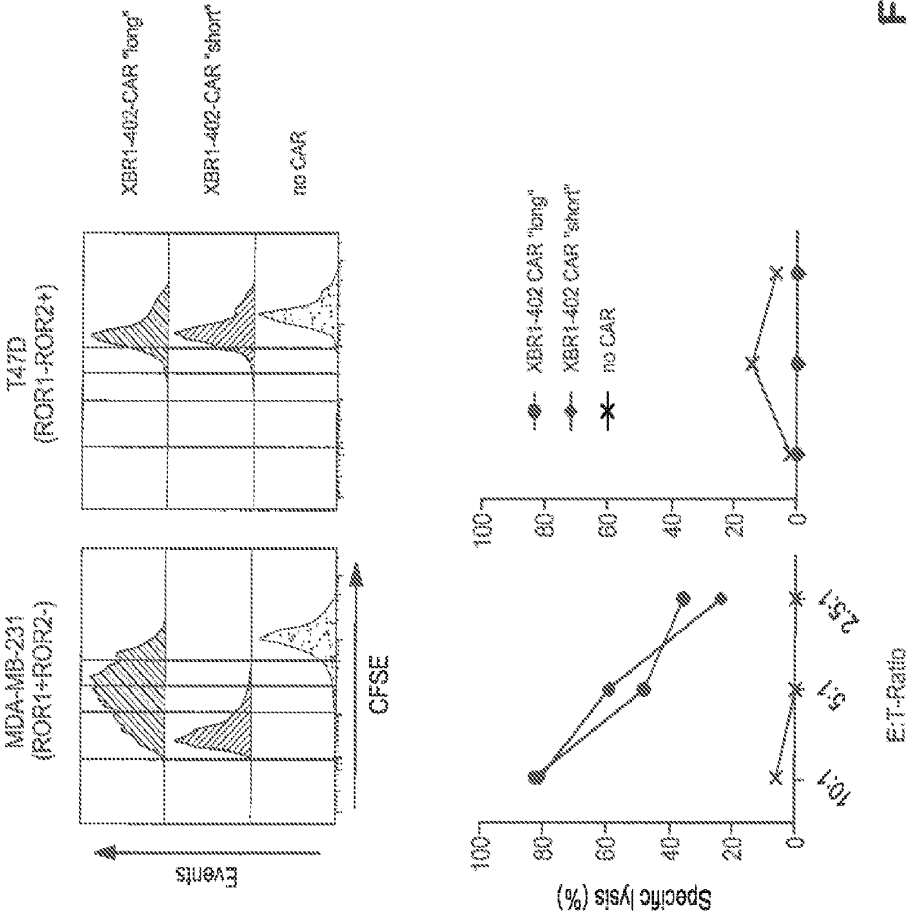


FIG. 27

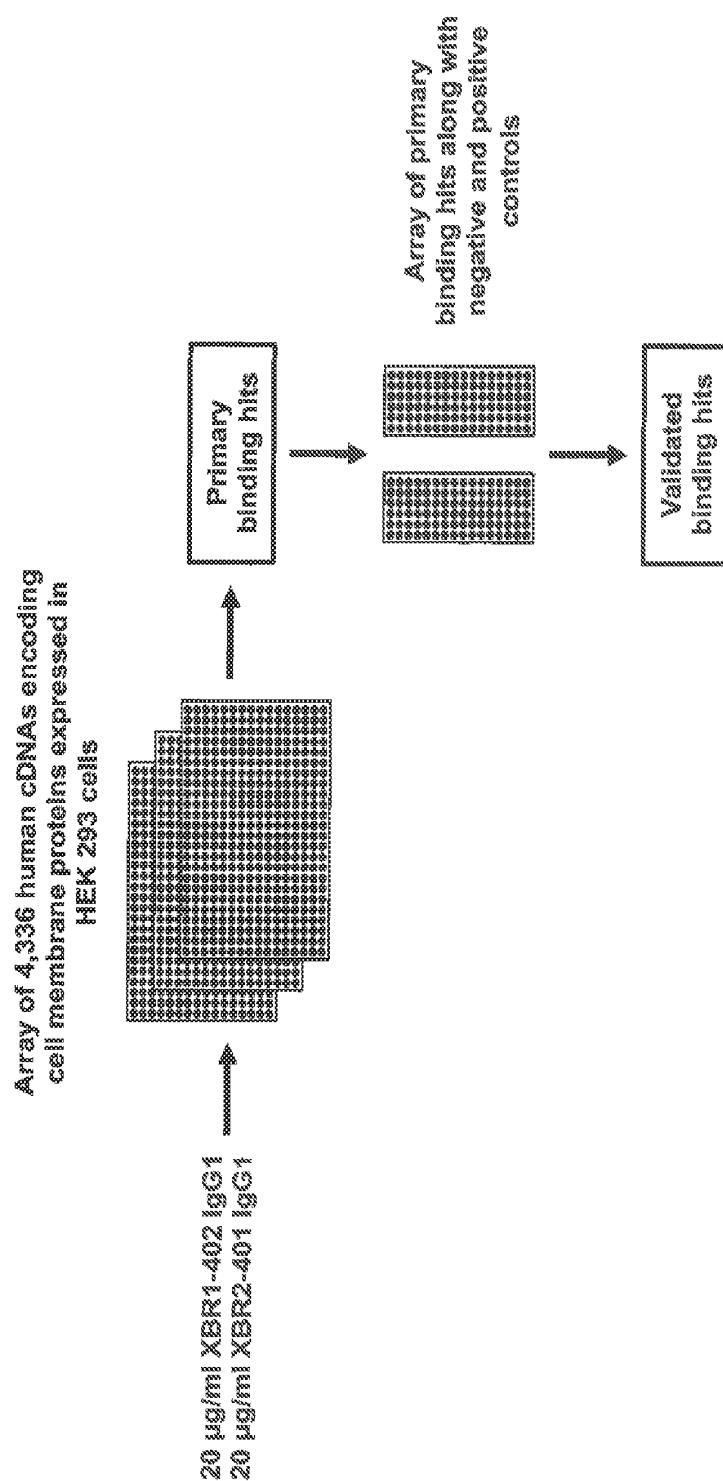


FIG. 28

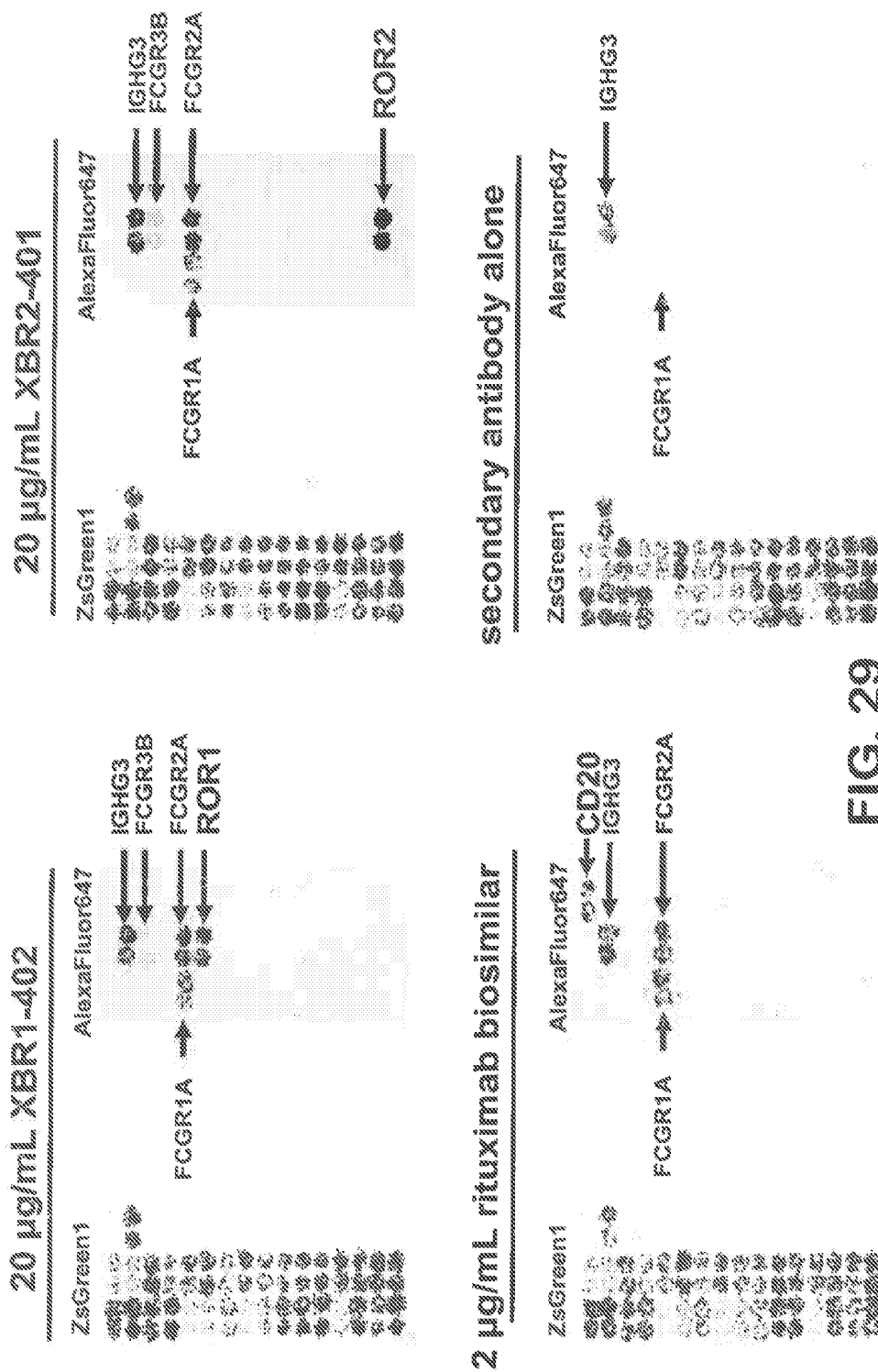


FIG. 29