Kabat Numbering	VH Sequences																									
	CDR 2																	CDR 3								
	50	51	52	52a	53	54	55	56	57	58	59	60	61	62	63	64	65	95	96	97	98	99	100	101	102
ParB0067	T	I	S	Y	S	G	S	L	I	S	Y	A	D	S	V	K	G	I	N	N	D	P	M	D	V
PaB670129					H			H				H				H	H		H	H					
PaB670010										H															
PaB670020																				H					
PaB670034																									
PaB670045																			H	H					
PaB670048																			H	H					H
PaB670064																									
PaB670066																									
PaB670067																									
PaB670068																									
PaB670070																									
PaB670071																									
PaB670073																									
PaB670075																									
PaB670076																									
PaB670077																									
PaB670078																									
PaB670079																									
PaB670080																									
PaB670081				H			H	H			H	H			H	H									
PaB670082				H		H							H			H									
PaB670083			H	H			H		H		H			H											
PaB670084				H			H			H	H				H										
PaB670085					H			H				H	H		H										
PaB670087					H			H						H	H		H								
PaB670088							H			H				H	H	H									
PaB670089					H			H			H			H		H									
PaB670090					H		H	H			H			H			H								
PaB670091				H			H			H	H	H	H												
PaB670092					H			H				H			H	H									
PaB670093					H	H	H				H														
PaB670094					H		H	H			H			H	H										
PaB670095					H		H	H							H	H	H								
PaB670097			H	H			H		H			H	H	H											
PaB670098				H			H		H	H					H		H								
PaB670099					H			H				H				H	H								
PaB670100					H		H	H			H		H	H		H									
PaB670101																			H	H	H		H		H
PaB670102																				H					H
PaB670103																									

Figure 1A

Kabat Numbering	VH Sequences																									
	CDR 2																	CDR 3								
	50	51	52	52a	53	54	55	56	57	58	59	60	61	62	63	64	65	95	96	97	98	99	100	101	102
ParB0067	T	I	S	Y	S	G	S	L	I	S	Y	A	D	S	V	K	G	I	N	N	D	P	M	D	V
PaB670104																									
PaB670105																									
PaB670106																									
PaB670107																									
PaB670108																									
PaB670114										H										H					
PaB670115				H			H	H			H	H			H	H				H					
PaB670116				H			H			H	H				H					H					
PaB670117							H			H				H	H	H				H					
PaB670118					H			H			H			H		H				H					
PaB670119					H			H				H			H	H				H					
PaB670120					H		H	H							H	H	H			H					
PaB670121					H			H				H				H	H			H					
PaB670122										H									H	H					
PaB670123				H			H	H			H	H			H	H			H	H					
PaB670125							H			H				H	H	H			H	H					
PaB670126					H			H			H			H		H			H	H					
PaB670127					H			H				H			H	H			H	H					
PaB670128					H		H	H							H	H	H		H	H					
PaB670136					H		H	H							H	H	H		H	H					H
PaB670137					H			H				H				H	H		H	H					H
PaB670141																				H					
PaB670142																			H	H					
PaB670143					H		H	H							H	H	H								
PaB670144					H		H	H							H	H	H			H					
PaB670146																				H					
PaB670148					H		H	H							H	H	H								
PaB670149					H		H	H							H	H	H			H					
PaB670151																				H					
PaB670152																			H	H					
PaB670153					H		H	H							H	H	H								
PaB670156																				H					
PaB670157																			H	H					
PaB670158					H		H	H							H	H	H								
PaB670159					H		H	H							H	H	H			H					
PaB670160																				H					
PaB670161																			H	H					
PaB670162					H		H	H							H	H	H								
PaB670163					H		H	H							H	H	H			H					

Figure 1B

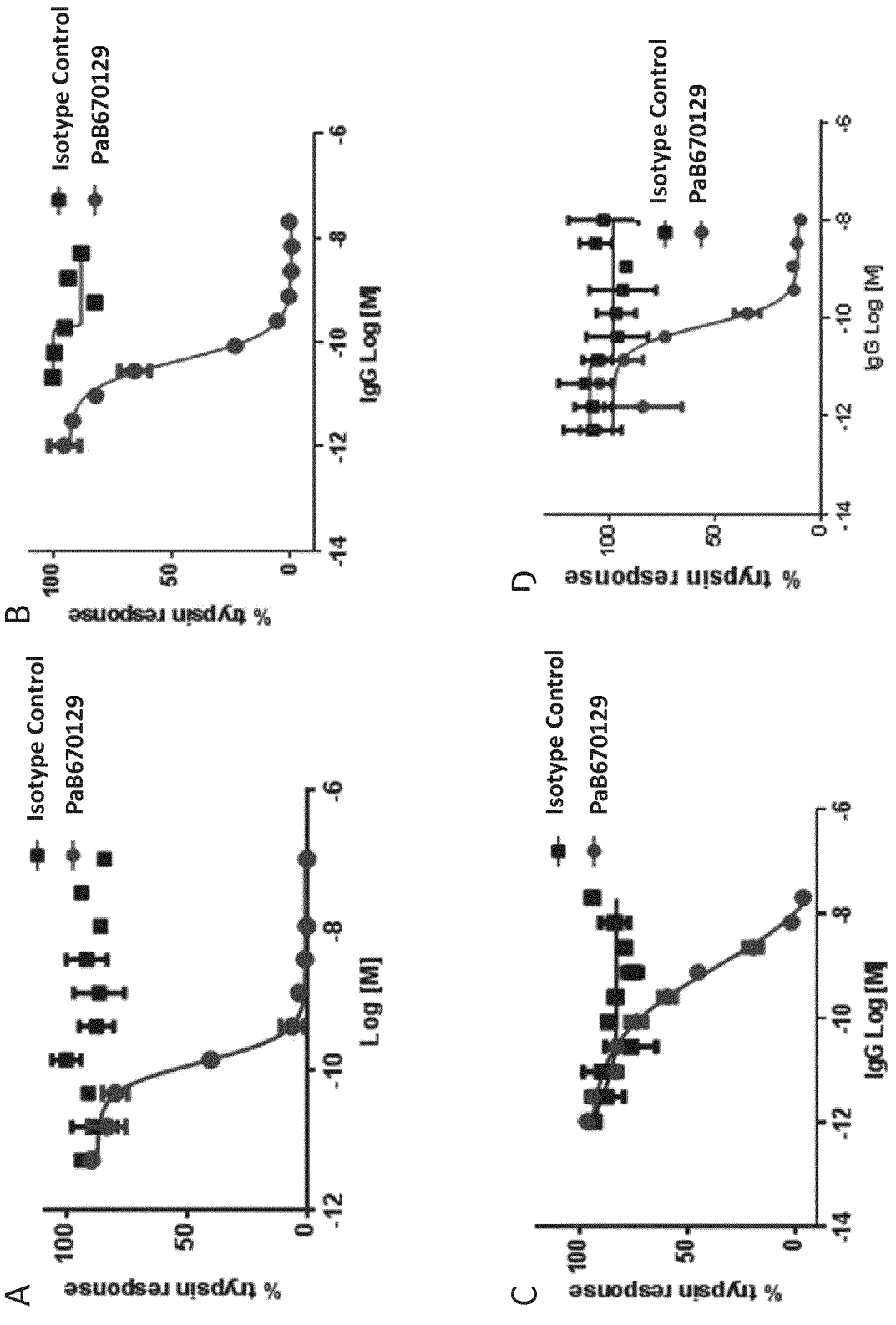
Kabat Numbering	VL Sequences													
	CDR 3													
	89	90	91	92	93	94	95	95a	95b	95c	95d	95e	96	97
ParB0067	Q	T	W	D	G	N	P	T	T	G	E	T	N	V
PaB670129														
PaB670010														
PaB670020														
PaB670034									H					
PaB670045														
PaB670048														
PaB670064	H			H	H			H						H
PaB670066	H	H		H			H	H						H
PaB670067	H			H	H	H			H			H		
PaB670068						H	H		H			H	H	
PaB670070					H		H	H			H			
PaB670071	H			H	H	H	H	H				H		H
PaB670073		H		H		H		H	H			H		
PaB670075		H					H	H	H					H
PaB670076	H				H	H	H					H		
PaB670077	H	H		H		H	H							H
PaB670078	H	H		H		H		H				H		
PaB670079		H				H	H							H
PaB670080						H	H	H						H
PaB670081														
PaB670082														
PaB670083														
PaB670084														
PaB670085														
PaB670087														
PaB670088														
PaB670089														
PaB670090														
PaB670091														
PaB670092														
PaB670093														
PaB670094														
PaB670095														
PaB670097														
PaB670098														
PaB670099														
PaB670100														
PaB670101														
PaB670102														
PaB670103	H					H	H							H

Figure 2A

Kabat Numbering	VL Sequences													
	CDR 3													
	89	90	91	92	93	94	95	95a	95b	95c	95d	95e	96	97
ParB0067	Q	T	W	D	G	N	P	T	T	G	E	T	N	V
PaB670104		H				H	H	H						
PaB670105		H		H				H				H		H
PaB670106	H				H			H	H	H	H			H
PaB670107	H	H		H	H				H	H				
PaB670108		H		H		H	H	H						
PaB670114														
PaB670115														
PaB670116														
PaB670117														
PaB670118														
PaB670119														
PaB670120														
PaB670121														
PaB670122														
PaB670123														
PaB670125														
PaB670126														
PaB670127														
PaB670128														
PaB670136														
PaB670137														
PaB670141									H					
PaB670142									H					
PaB670143									H					
PaB670144									H					
PaB670146	H			H	H	H			H			H		
PaB670148	H			H	H	H			H			H		
PaB670149	H			H	H	H			H			H		
PaB670151	H				H	H	H					H		
PaB670152	H				H	H	H					H		
PaB670153	H				H	H	H					H		
PaB670156						H	H	H						H
PaB670157						H	H	H						H
PaB670158						H	H	H						H
PaB670159						H	H	H						H
PaB670160	H					H	H							H
PaB670161	H					H	H							H
PaB670162	H					H	H							H
PaB670163	H					H	H							H

Figure 2B

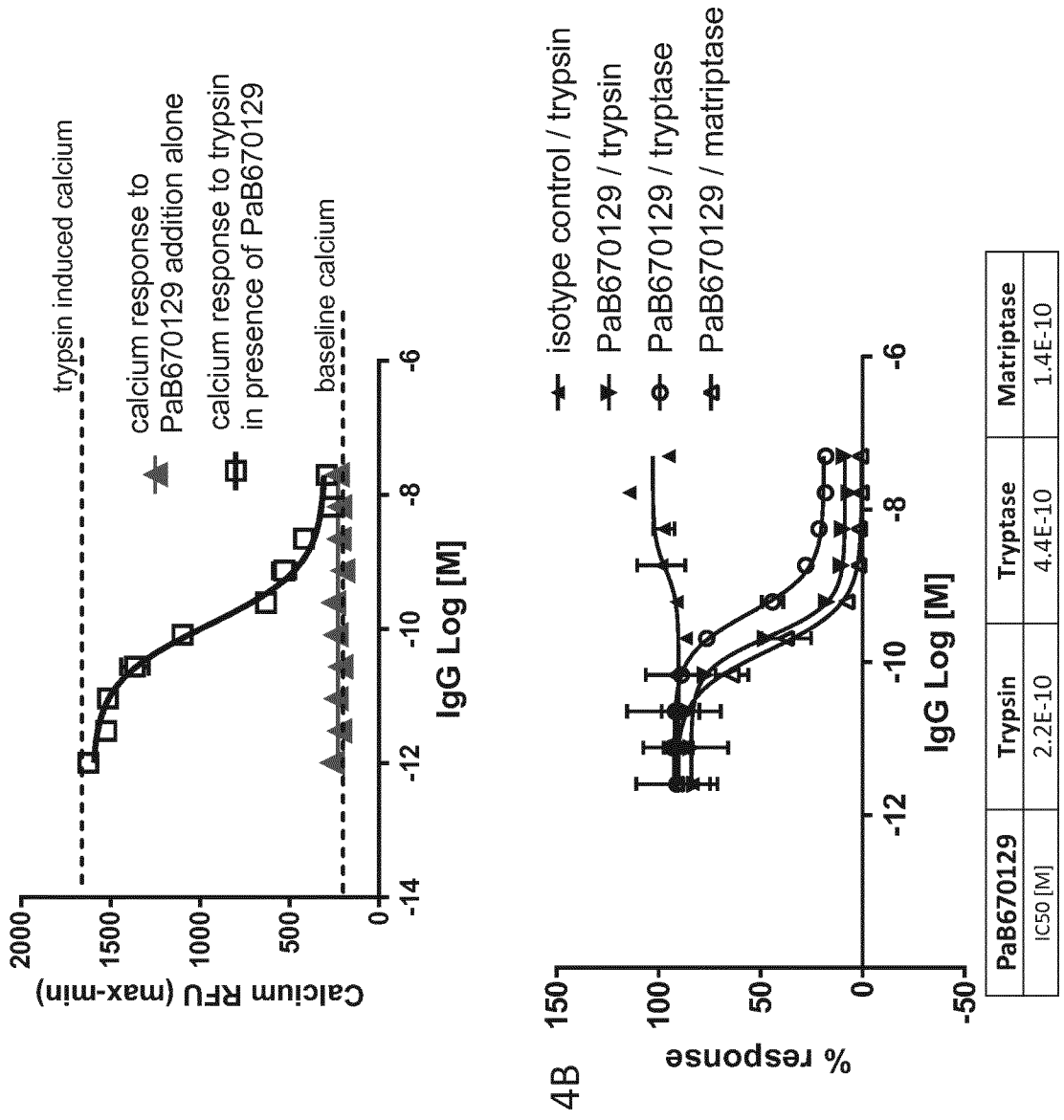
Figure 3


A
B
C
D
% trypsin response
Log [M]
IgG Log [M]
Isotype Control
PaB670129
100
50
0
-6
-8
-10
-12
-14

	PAR2 FLIPR ASSAY POTENCY DATA IC_{50}											
	Human A549 FLIPR IC_{50} (M)	SEM	n	Rat KNRK FLIPR IC_{50} (M)	SEM	n	Cyno CYNOM-K1 FLIPR IC_{50} (M)	SEM	n	Mouse LL/2 FLIPR IC_{50} (M)	SEM	n
ParB0067	1.16E-10	1.47E-11	5	7.23E-12	1.48E-12	6	5.87E-11		1	2.58E-11	2.66E-12	2
PaB670034	2.06E-10		1	7.92E-12		1						
PaB670045	1.42E-10		1	1.02E-11		1						
PaB670048	1.31E-10	6.15E-12	3	1.17E-11	2.41E-12	4						
PaB670061	NI		1	NI		1						
PaB670062	2.34E-09		1	7.89E-10		1						
PaB670066	7.22E-10		1	3.84E-09		1						
PaB670075	8.04E-10		1	NI		1						
PaB670076	1.15E-10	5.10E-12	2	7.89E-11	3.82E-11	2						
PaB670077	9.28E-10		1	1.56E-09		1						
PaB670078	5.88E-10		1	1.25E-09		1						
PaB670079	7.01E-10		1	4.64E-10		1						
PaB670080	2.61E-10		1	1.44E-11		1						
PaB670084	1.23E-10	3.64E-11	2	2.27E-11	7.73E-12	2						
PaB670103	2.38E-10		1	1.46E-11		1						
PaB670114	1.62E-10		1	1.35E-09		1						
PaB670115	1.28E-10		1	2.97E-10		1						
PaB670116	3.48E-10		1	2.60E-08		1						
PaB670117	1.64E-10		1	5.79E-10		1						
PaB670118	1.41E-10		1	1.04E-10		1						
PaB670119	1.08E-10		1	8.48E-11		1						
PaB670120	1.50E-10	8.95E-12	2	9.53E-11	2.02E-11	2						
PaB670121	1.13E-10		1	1.41E-10		1						
PaB670122	2.18E-10		1	NI		1						
PaB670123	2.55E-10		1	2.54E-09		1						
PaB670124	NI		1	NI		1						
PaB670125	2.27E-10		1	1.34E-09		1						
PaB670126	1.64E-10		1	3.95E-10		1						
PaB670127	1.13E-10		1	2.12E-10		1						
PaB670128	1.23E-10	4.05E-12	2	2.85E-10	8.33E-11	3	3.71E-11		1			
PaB670129	1.09E-10	1.41E-11	4	5.21E-10	7.47E-11	6	4.64E-11	3.87E-12	3	5.09E-11	1.92E-11	2
PaB670130	NI		1	NI		1						
PaB670131	NI		1	NI		1						
PaB670132	NI		1	NI		1						
PaB670133	NI		1	NI		1						
PaB670134	NI		1	7.04E-10		1						
PaB670135	NI		1	4.32E-10		1						
PaB670136	1.37E-10	2.43E-11	2	4.45E-10	3.12E-11	2						
PaB670137	1.57E-10		1	1.14E-09		1						
PaB670139	9.62E-11	7.73E-12	2	3.06E-11	7.38E-12	2						
PaB670140	NI		1	NI		1						
PaB670129 Fab	3.5E-09		1	3.44E-08		1						

FIGURE 3E

Figure 4



PaB670129	Trypsin	Tryptase	Matriptase
IC50 [M]	2.2E-10	4.4E-10	1.4E-10

Figure 5

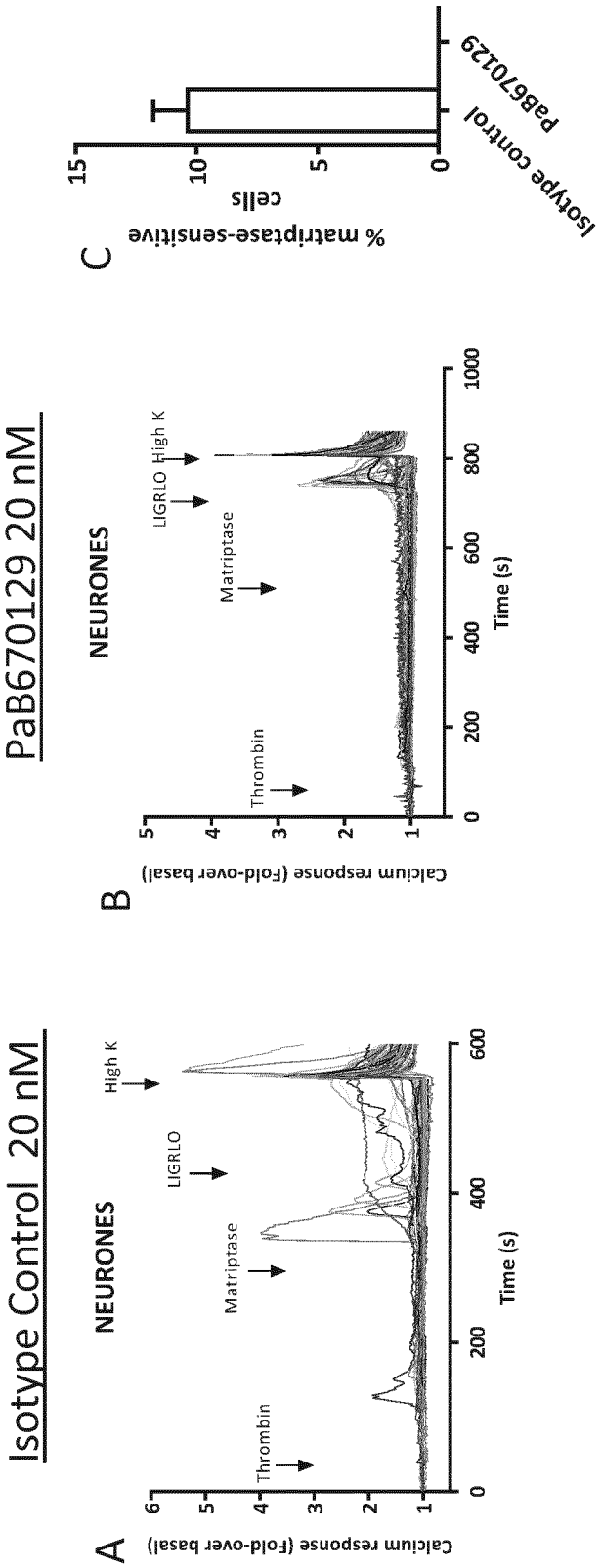

Isotype Control 20 nM
NEURONES
Thrombin
Matriptase
LIGRLO
High K
Calcium response (Fold-over basal)
Time (s)
A
PaB670129 20 nM
NEURONES
Thrombin
Matriptase
LIGRLO High K
Calcium response (Fold-over basal)
Time (s)
B
% matriptase-sensitive cells
Isotype control
PaB670129
C

Figure 5

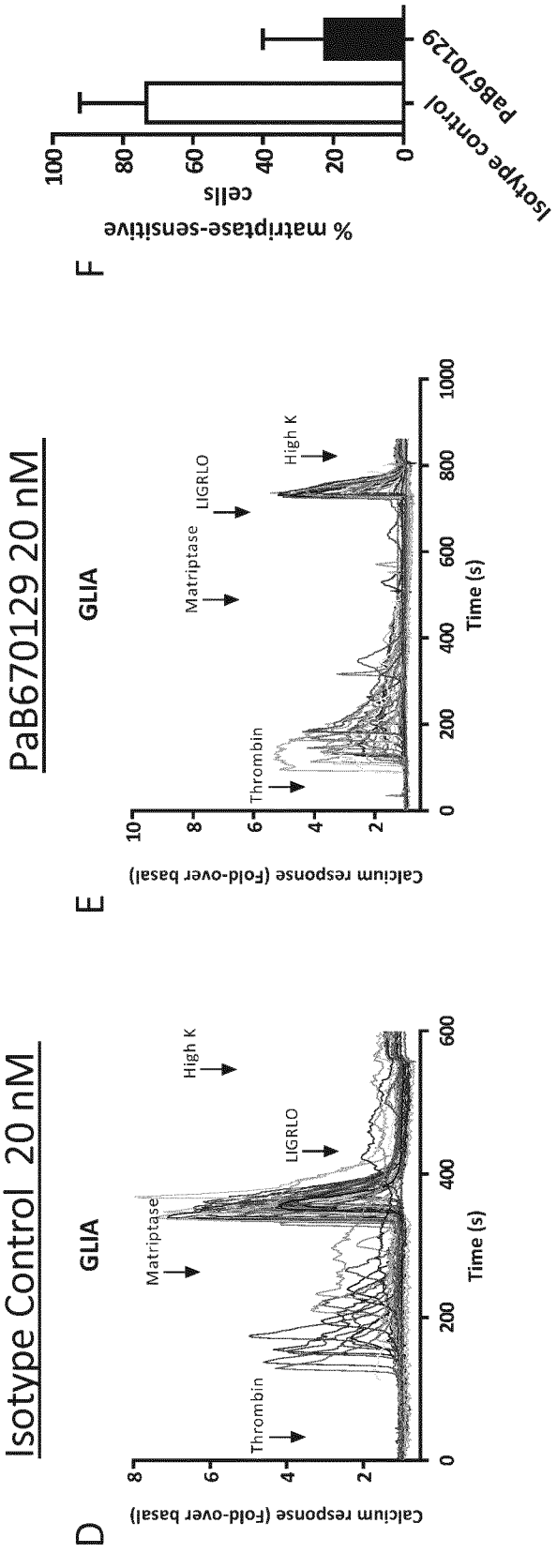
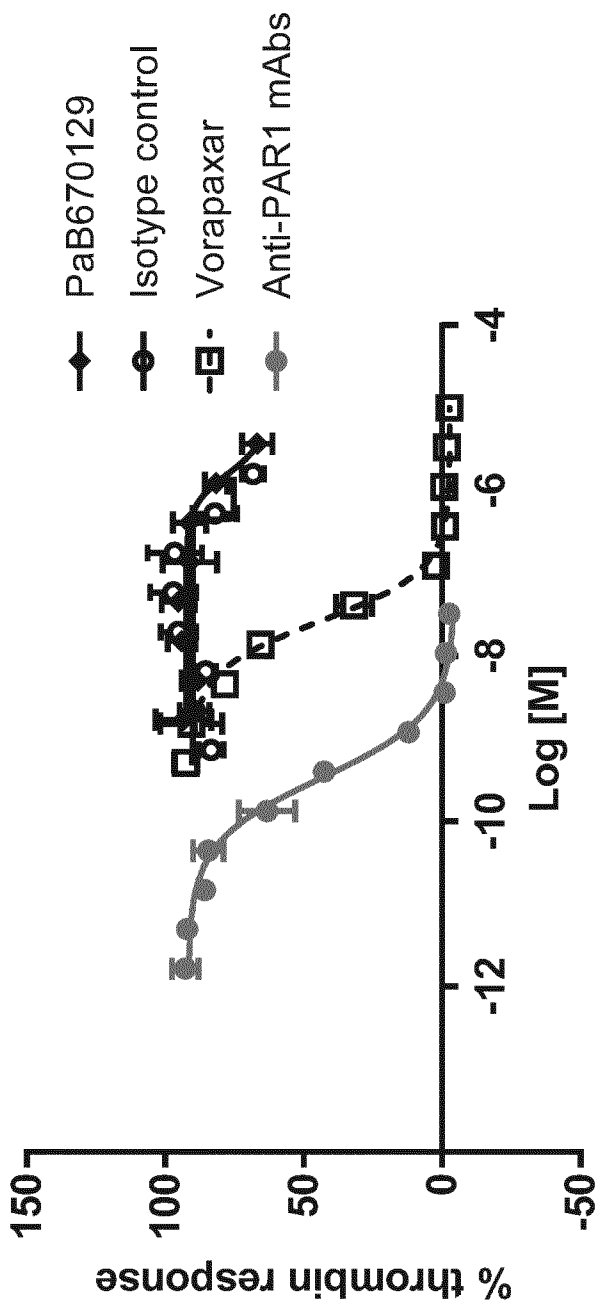

D
Isotype Control 20 nM
GLIA
Calcium response (Fold-over basal)
Thrombin
Matriptase
LIGRLO
High K
Time (s)
E
PaB670129 20 nM
GLIA
Calcium response (Fold-over basal)
Thrombin
Matriptase
LIGRLO
High K
Time (s)
F
% matriptase-sensitive cells
Isotype control
PaB670129

Figure 6



	PaB670129	Anti-PAR-1 WEDE15/ATAP2	Vorapaxar
PAR-1 IC50 [nM]	Non-Inhibitory Tested up to 4 µM (0.6 mg/mL)	0.33	30.3 (± 3.8)

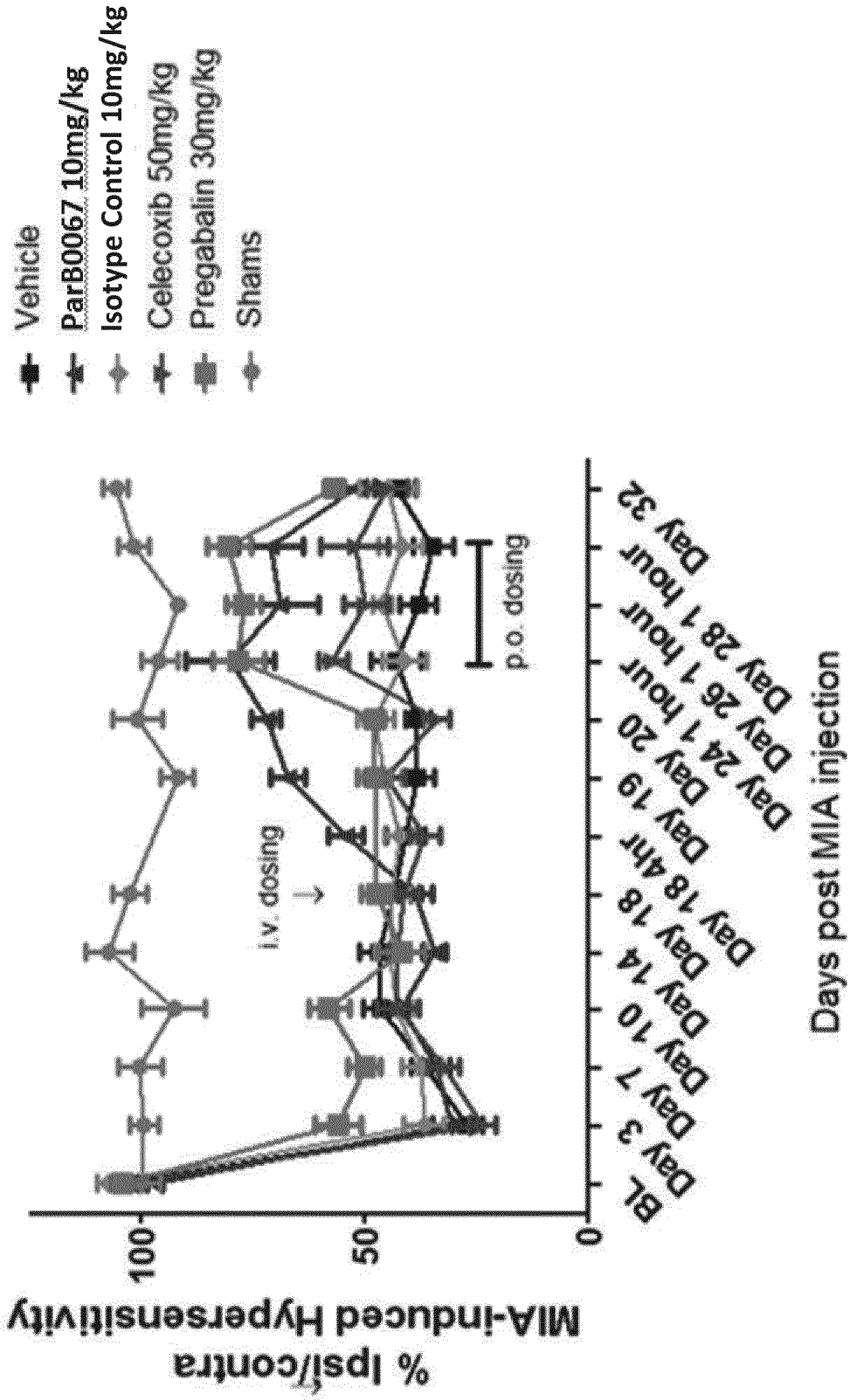

Vehicle
ParB0067 10mg/kg
Isotype Control 10mg/kg
Celecoxib 50mg/kg
Pregabalin 30mg/kg
Shams
% Ipsi/contra
MIA-induced Hypersensitivity
100
50
0
i.v. dosing
p.o. dosing
BL
Day 3
Day 7
Day 10
Day 14
Day 18
Day 18 4hr
Day 19
Day 20
Day 24 1 hour
Day 26 1 hour
Day 28 1 hour
Day 32
Days post MIA injection

Figure 7A

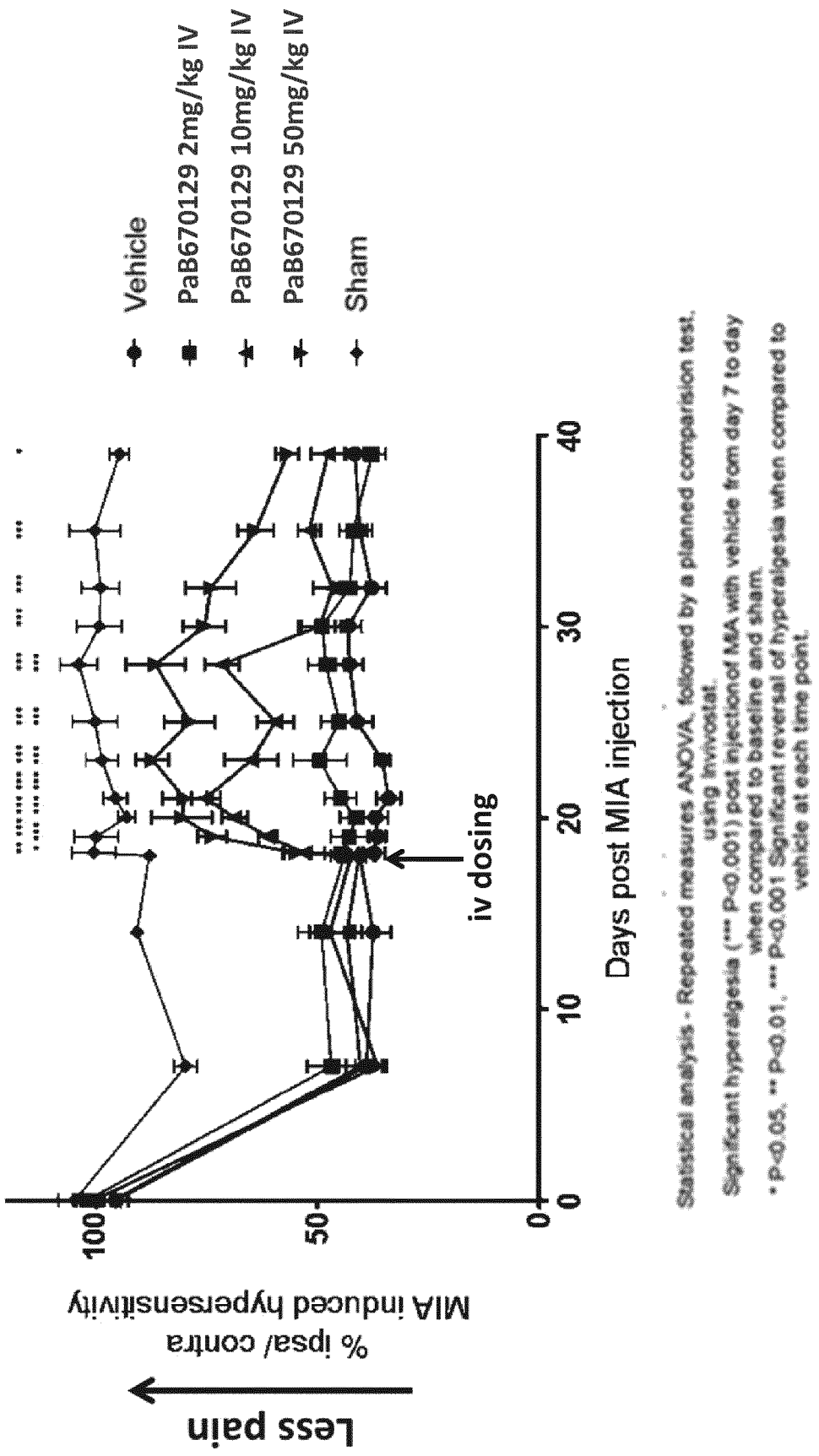
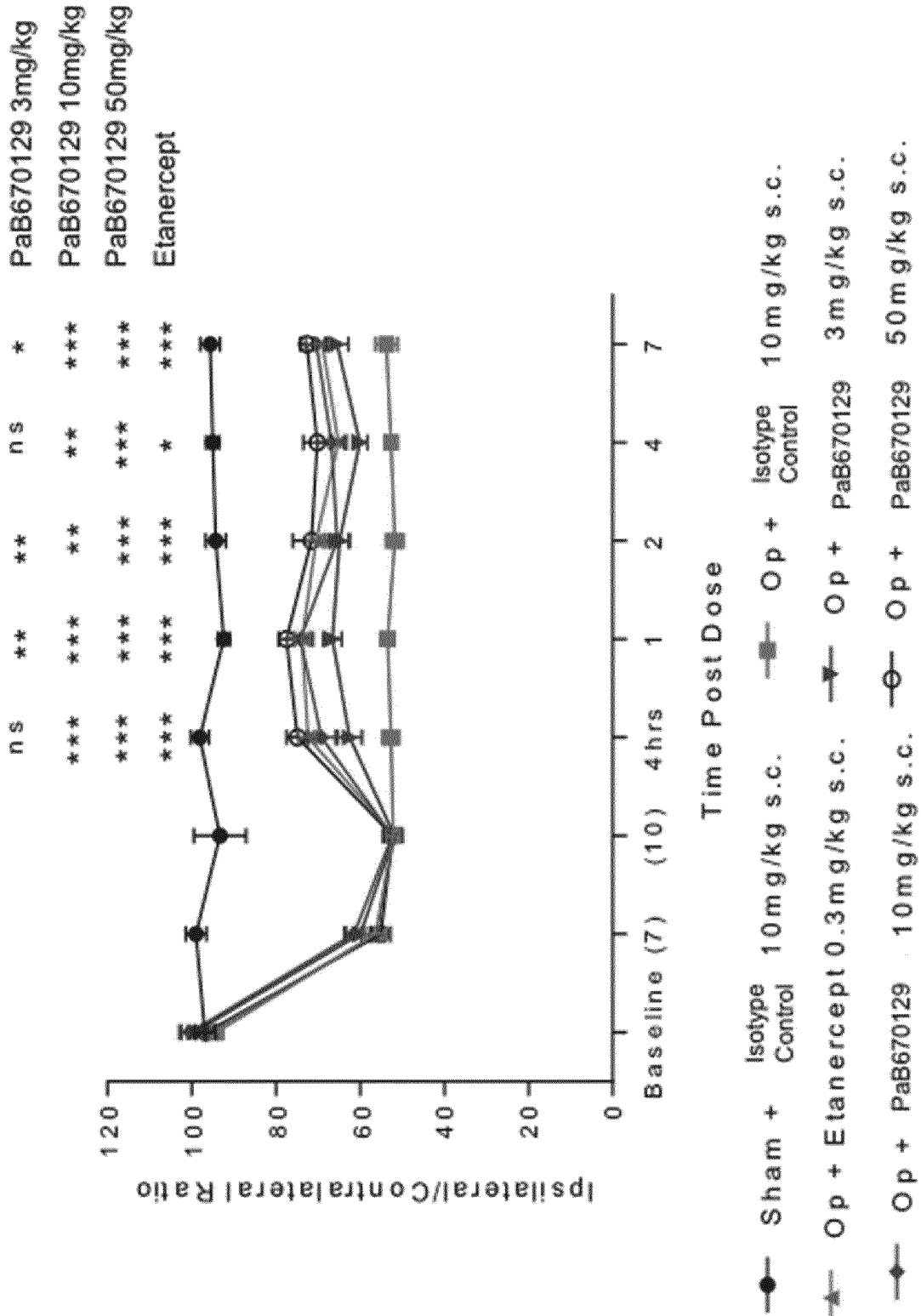

Vehicle
PaB670129 2mg/kg IV
PaB670129 10mg/kg IV
PaB670129 50mg/kg IV
Sham
Less pain
% ipsa/ contra
MIA induced hypersensitivity
100
50
0
0
10
20
30
40
Days post MIA injection
iv dosing
Statistical analysis - Repeated measures ANOVA, followed by a planned comparision test, using Invivostat.
Significant hyperalgesia (*** P<0.001) post injection of MIA with vehicle from day 7 to day when compared to baseline and sham.
* P<0.05, ** P<0.01, *** P<0.001 Significant reversal of hyperalgesia when compared to vehicle at each time point.

Fig 7B

Fig 8


ns
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ns
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***
PaB670129 3mg/kg
PaB670129 10mg/kg
PaB670129 50mg/kg
Etanercept
Ipsilateral/Contralateral Ratio
120
100
80
60
40
20
0
Baseline (7)
(10)
4hrs
1
2
4
7
Time Post Dose
Sham + Isotype Control 10mg/kg s.c.
Op + Isotype Control 10mg/kg s.c.
Op + Etanercept 0.3mg/kg s.c.
Op + PaB670129 3mg/kg s.c.
Op + PaB670129 10mg/kg s.c.
Op + PaB670129 50mg/kg s.c.