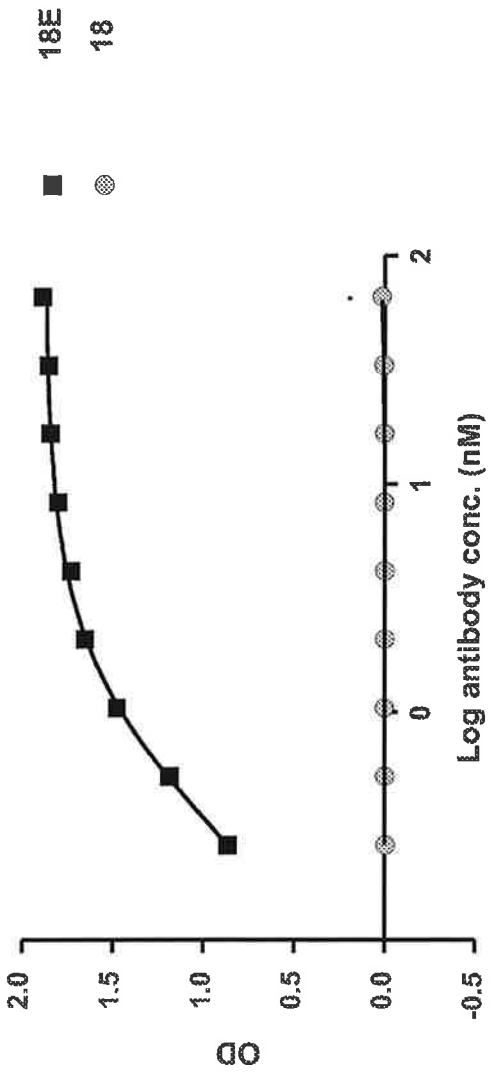
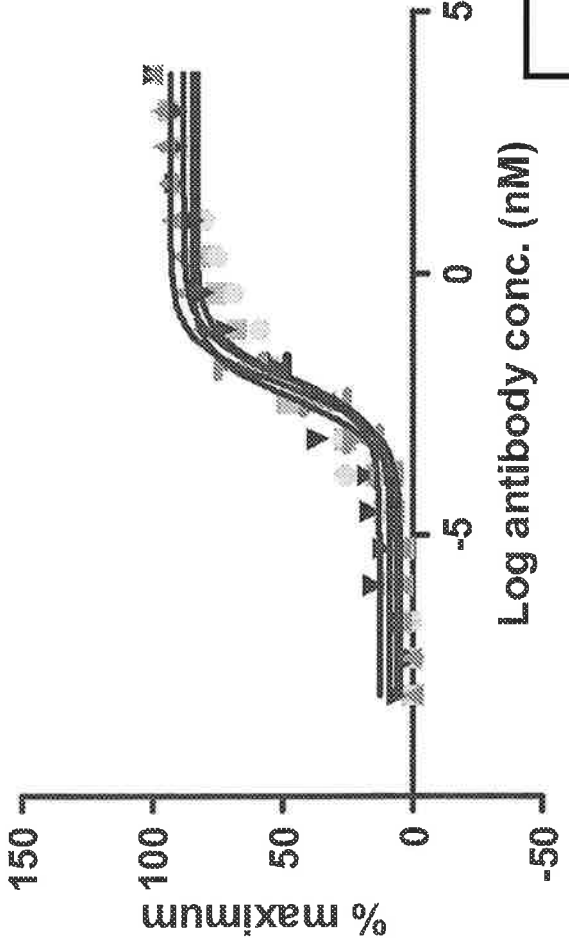
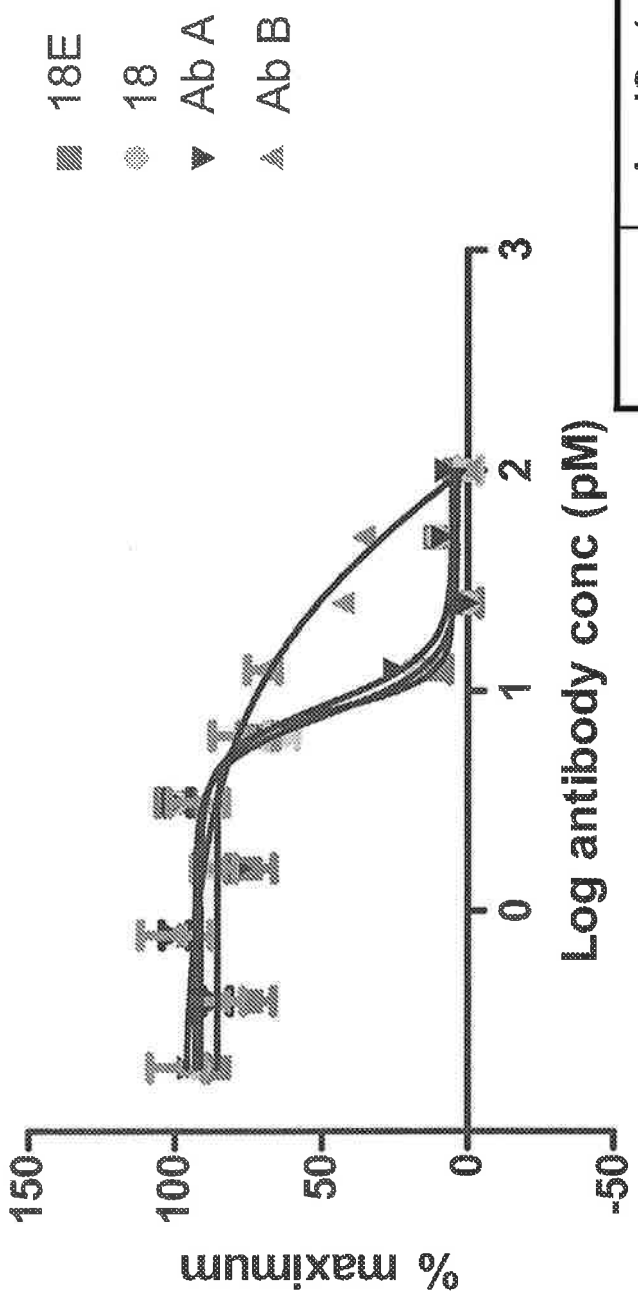


Figure 1



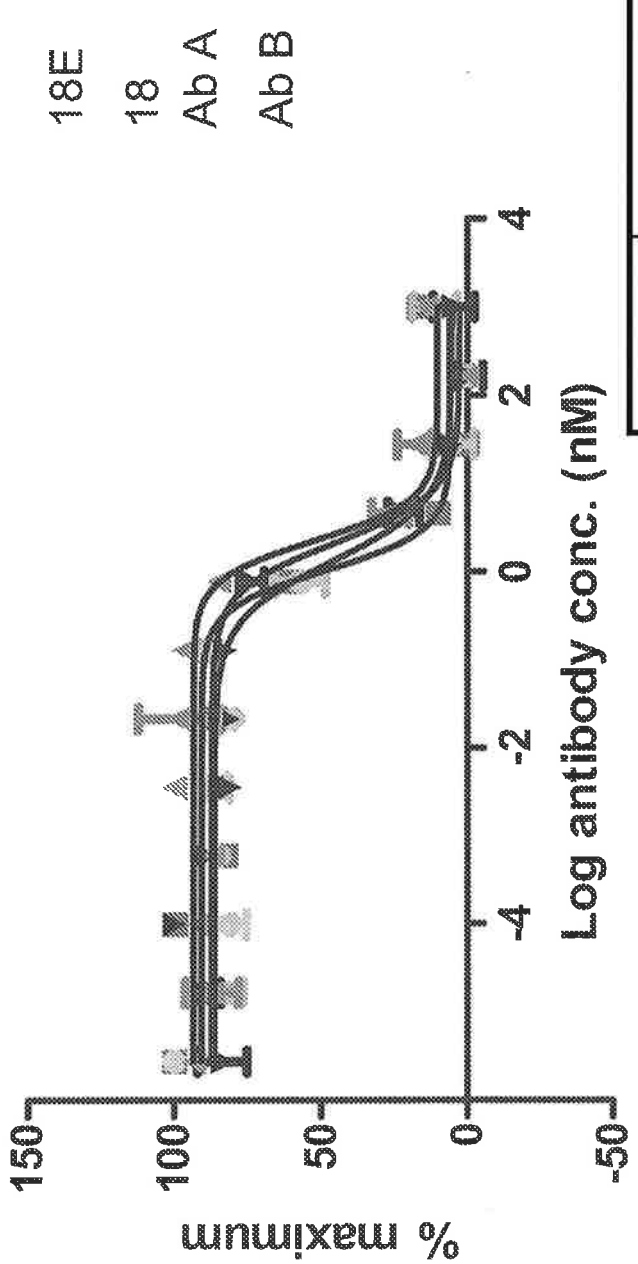
	Avg EC_{50} (pM)	n
18E	6.5	4
18	6.1	3
Ab A	7.8	4
Ab B	14.1	4

Figure 2



	Avg IC_{50} (pM)	n
18E	5.2	3
18	4.5	3
Ab A	5.9	3
Ab B	78.1	3

Figure 3



	Avg IC_{50} (nM)	n
18E	1.2	3
18	1.3	3
Ab A	2.8	3
Ab B	2.2	3

Figure 4

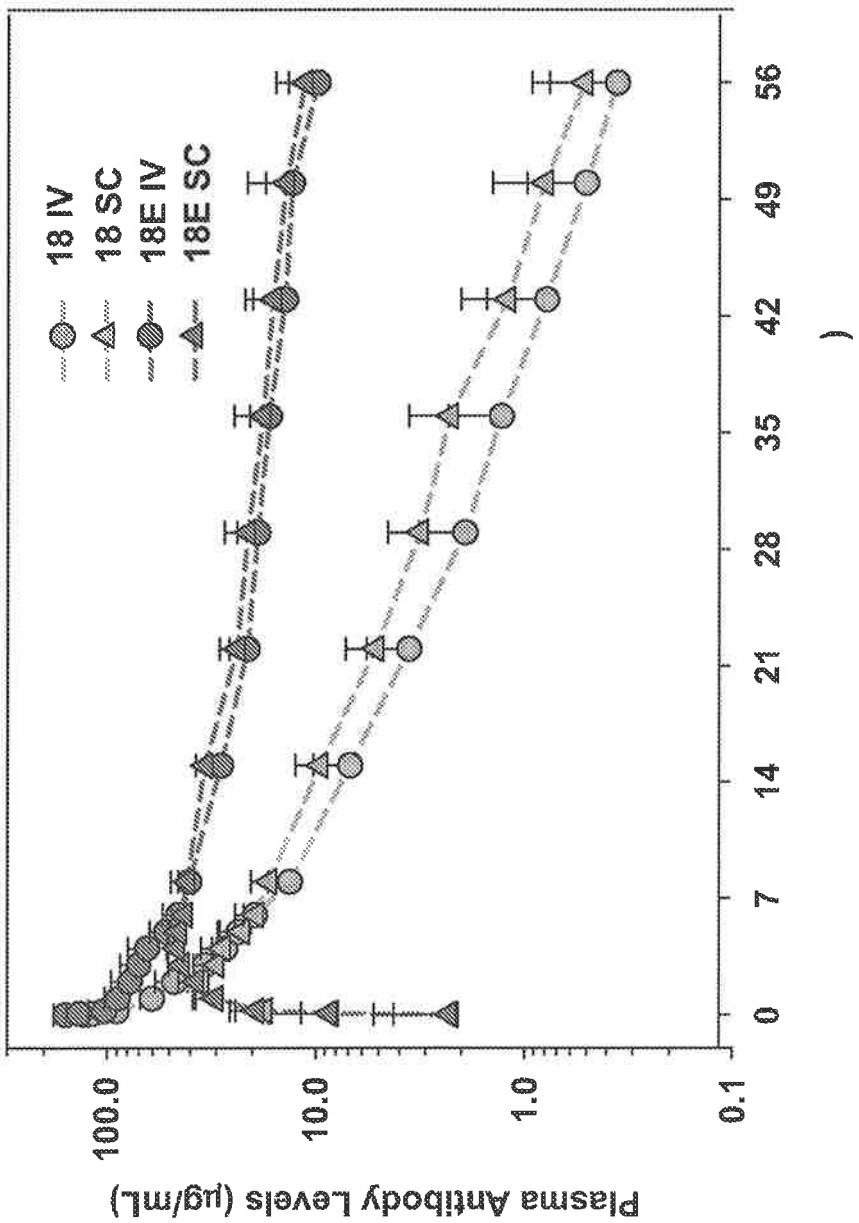

Plasma Antibody Levels (µg/mL)
100.0
10.0
1.0
0.1
0
7
14
21
28
35
42
49
56
)
18 IV
18 SC
18E IV
18E SC

Figure 5

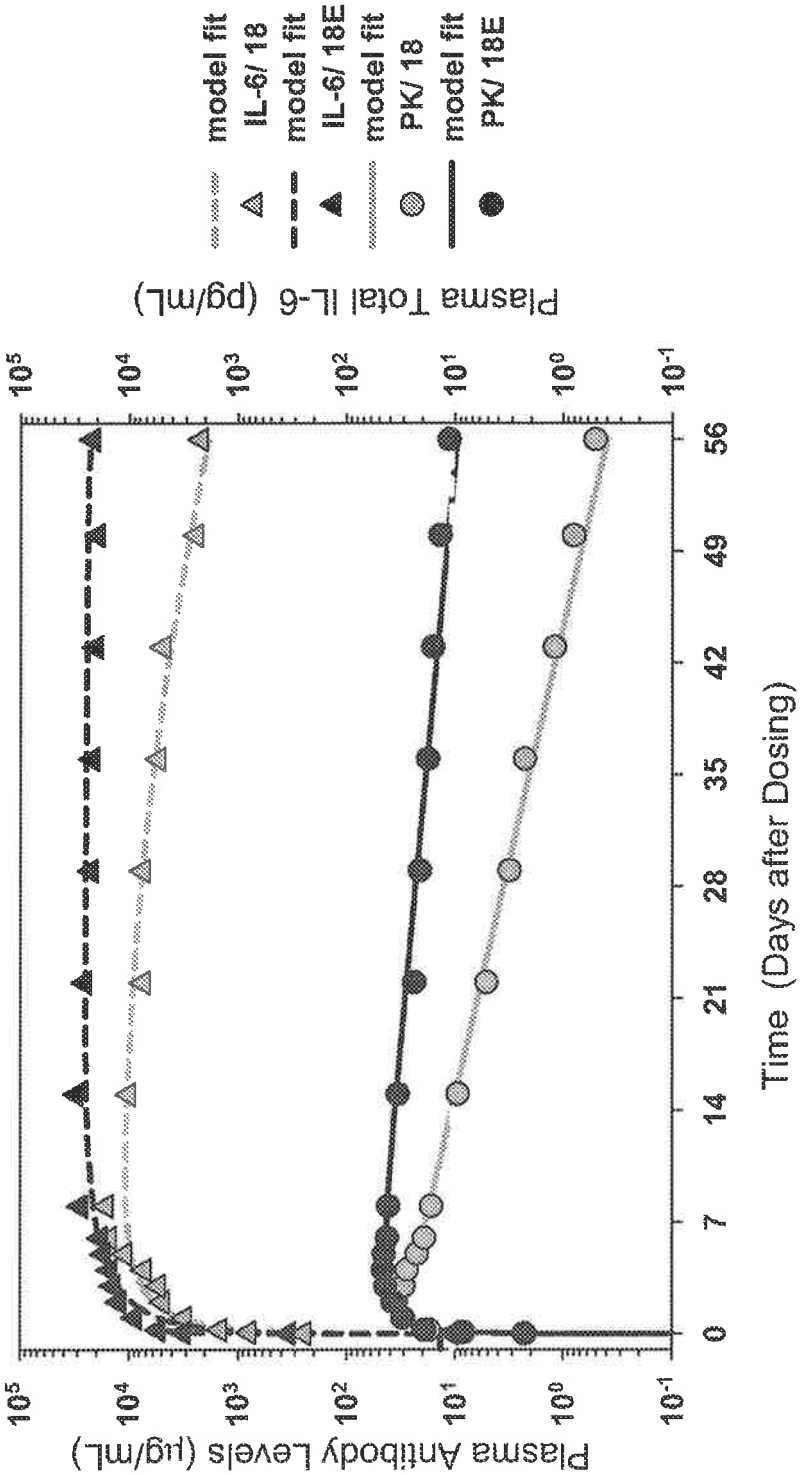

Plasma Antibody Levels (µg/mL)
Plasma Total IL-6 (pg/mL)
Time (Days after Dosing)
model fit
IL-6/ 18
model fit
IL-6/ 18E
model fit
PK/ 18
model fit
PK/ 18E

Figure 6

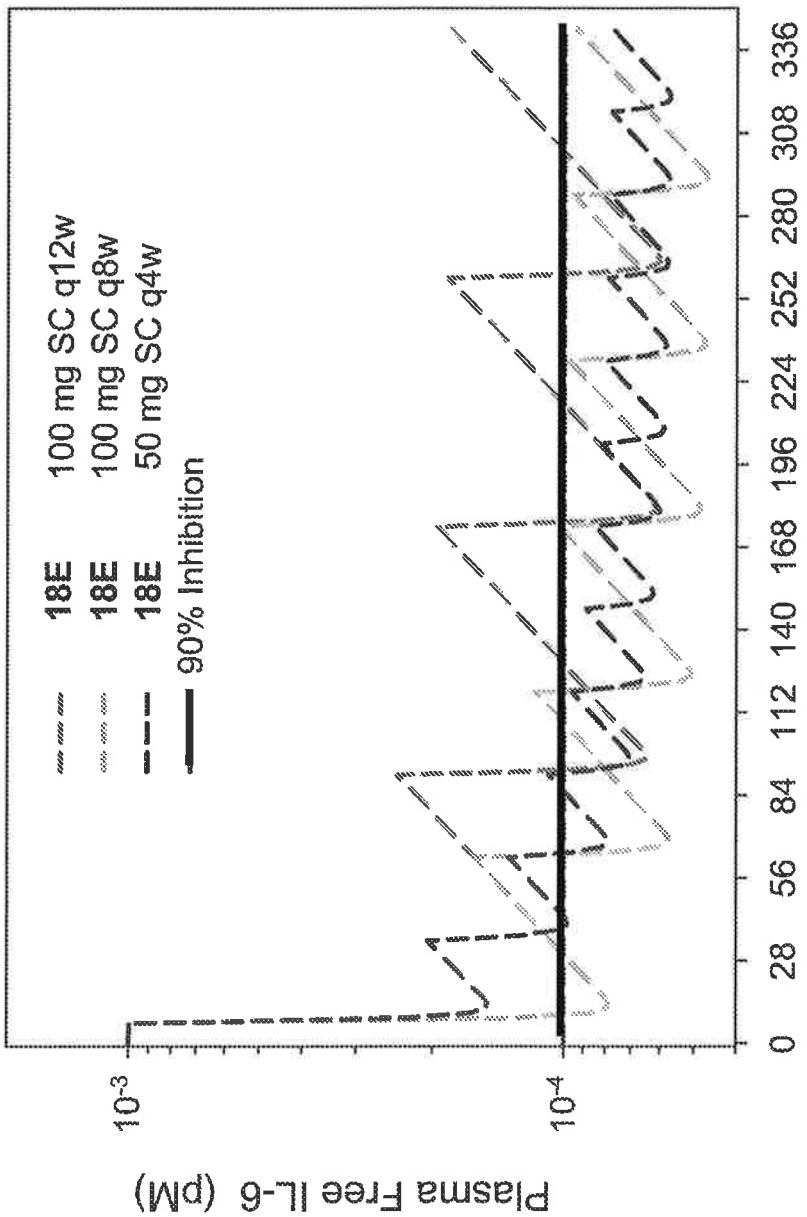

18E 100 mg SC q12w
18E 100 mg SC q8w
18E 50 mg SC q4w
90% Inhibition
Plasma Free IL-6 (pM)
10-3
10-4
0 28 56 84 112 140 168 196 224 252 280 308 336
Time (Days after Dosing)

Figure 7

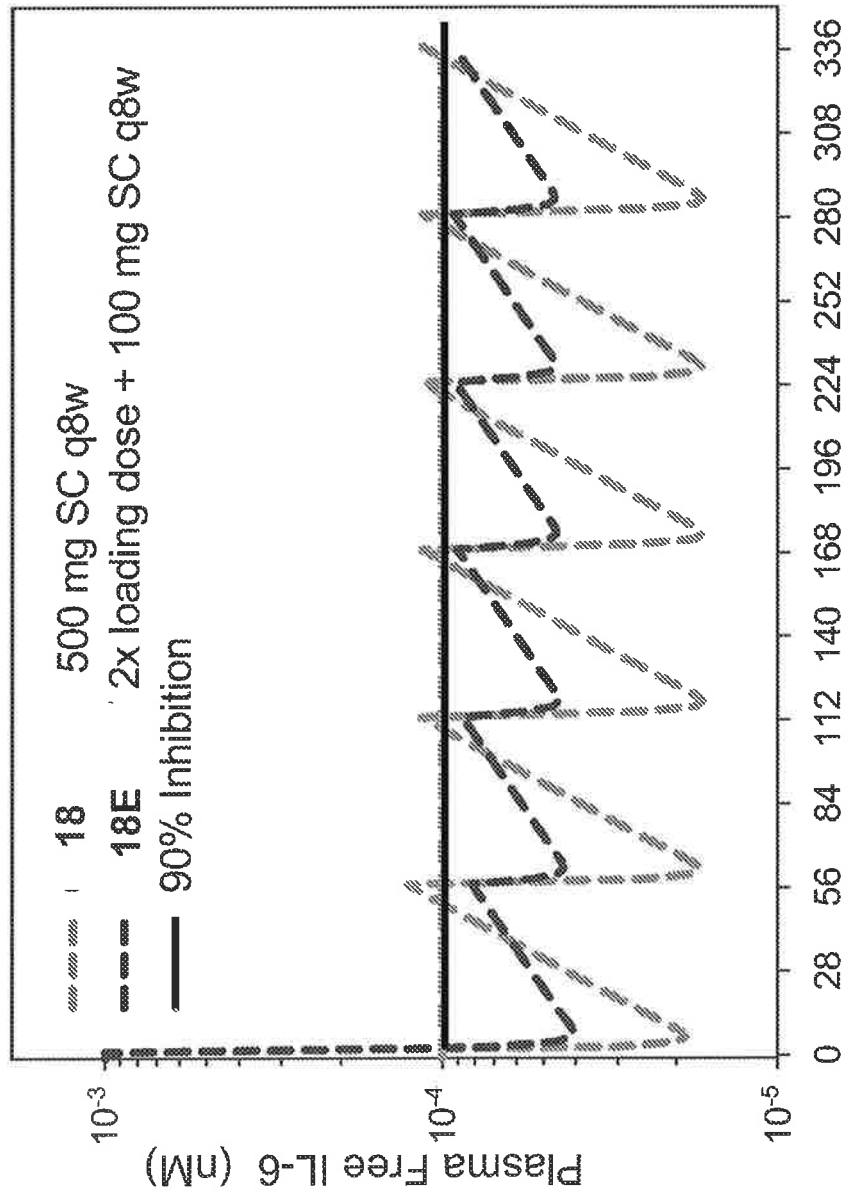

18
18E
90% Inhibition
500 mg SC q8w
2x loading dose + 100 mg SC q8w
Plasma Free IL-6 (nM)
10^{-3}
10^{-4}
10^{-5}
0
28
56
84
112
140
168
196
224
252
280
308
336
Time (Days after Dosing)

Figure 8

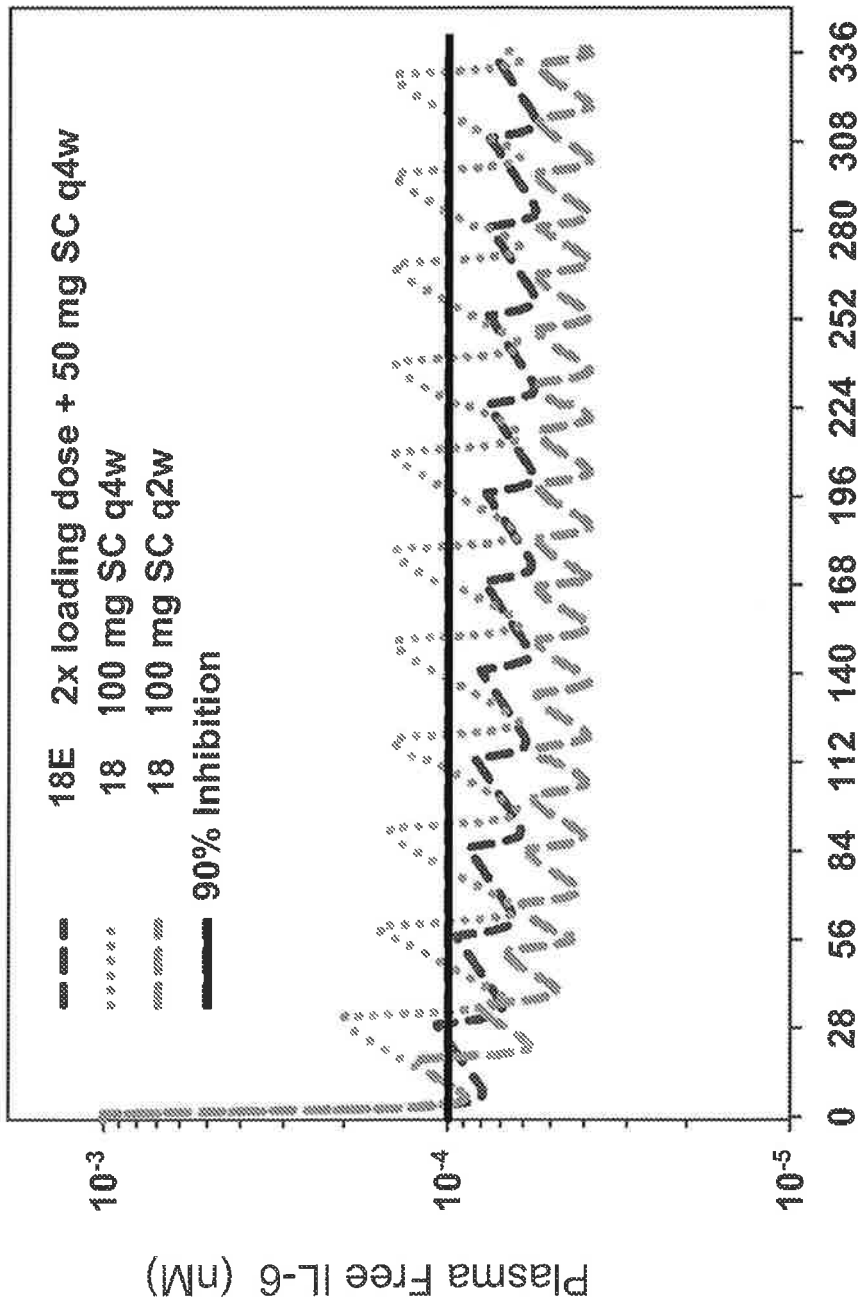

18E 2x loading dose + 50 mg SC q4w
18 100 mg SC q4w
18 100 mg SC q2w
90% Inhibition
Plasma Free IL-6 (nM)
10-3
10-4
10-5
0 28 56 84 112 140 168 196 224 252 280 308 336
Time (Days after Dosing)

Figure 9

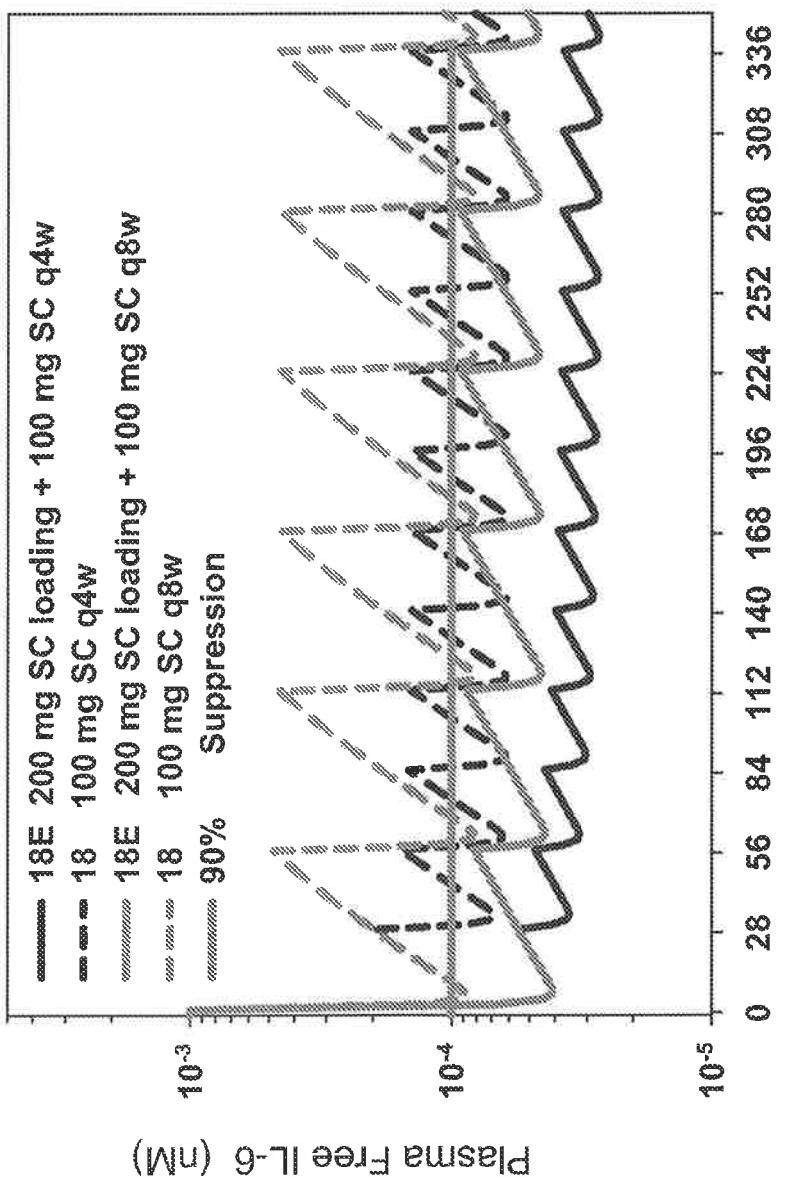

18E 200 mg SC loading + 100 mg SC q4w
18 100 mg SC q4w
18E 200 mg SC loading + 100 mg SC q8w
18 100 mg SC q8w
90% Suppression
Plasma Free IL-6 (nM)
10-3
10-4
10-5
0 28 56 84 112 140 168 196 224 252 280 308 336
Time (Days after Dosing)

Figure 10

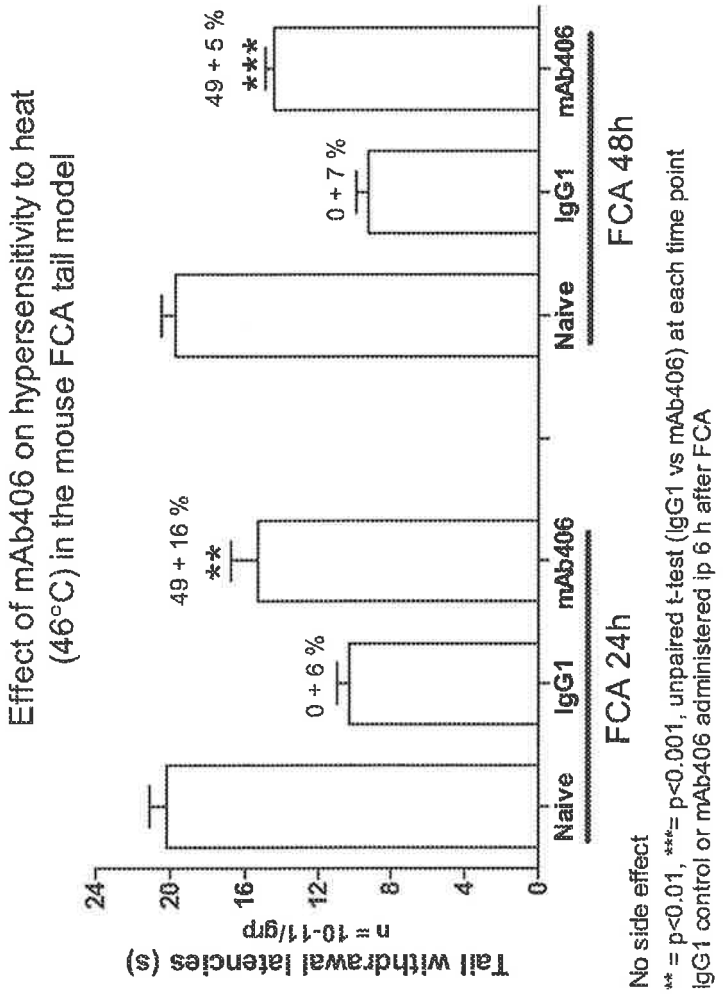

Effect of mAb406 on hypersensitivity to heat
(46°C) in the mouse FCA tail model
Tail withdrawal latencies (s)
n = 10-11/grp
24
20
16
12
8
4
0
0 + 6 %
49 + 16 %
**
0 + 7 %
49 + 5 %
***
Naive
IgG1
mAb406
Naive
IgG1
mAb406
FCA 24h
FCA 48h
No side effect
** = p<0.01, ***= p<0.001, unpaired t-test (IgG1 vs mAb406) at each time point
IgG1 control or mAb406 administered ip 6 h after FCA

Figure 11

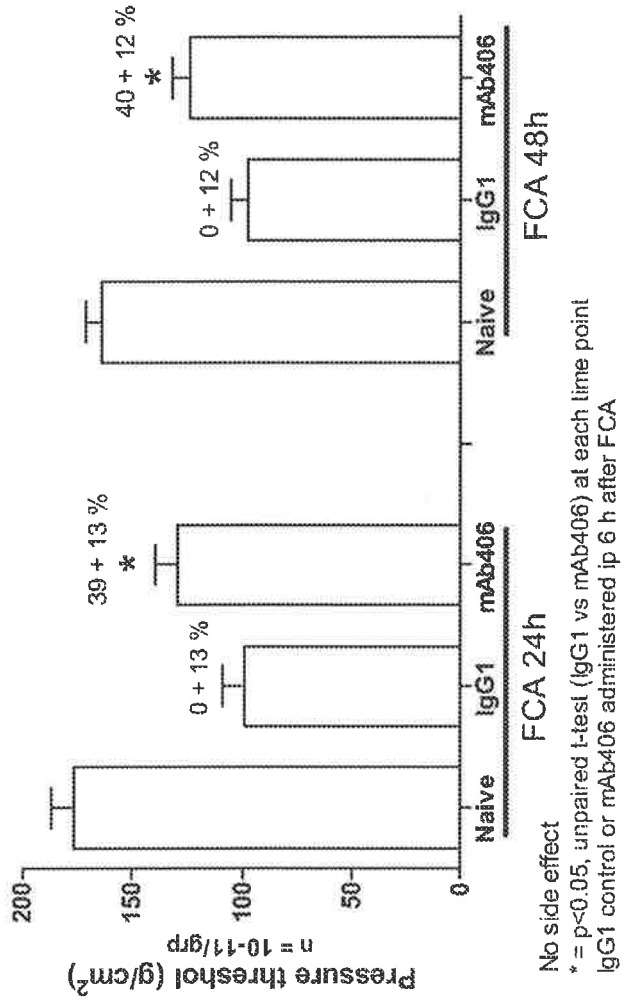
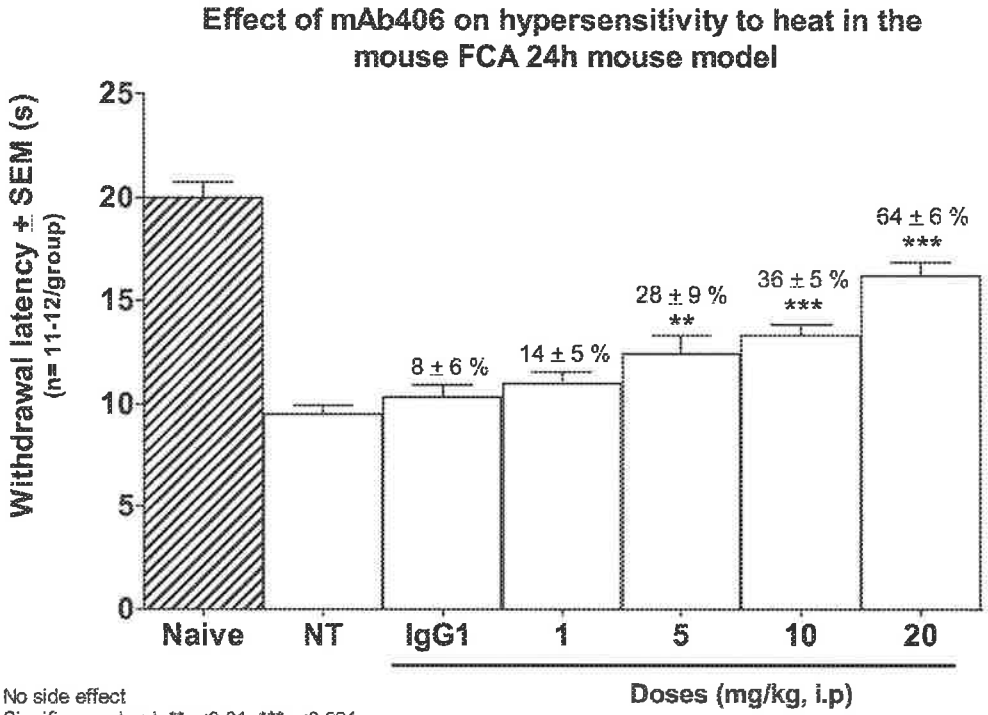

Effect of mAb406 on hypersensitivity to mechanical pressure in the mouse FCA tail model
Pressure threshold (g/cm²)
n = 10-11/grp
200
150
100
50
0
0 + 13 %
39 + 13 %
*
0 + 12 %
40 + 12 %
*
Naive
IgG1
mAb406
Naive
IgG1
mAb406
FCA 24h
FCA 48h
No side effect
* = p<0.05, unpaired t-test (IgG1 vs mAb406) at each time point
IgG1 control or mAb406 administered ip 6 h after FCA

Figure 12



No side effect
Significance level: **p<0.01, ***p<0.001
Statistics: One-way ANOVA, followed by a Holm Sidak post hoc test
IgG1 control isotype or mAb406 dosed ip 6 h after the FCA challenge. NT refers to "no treatment" mice.

Figure 13

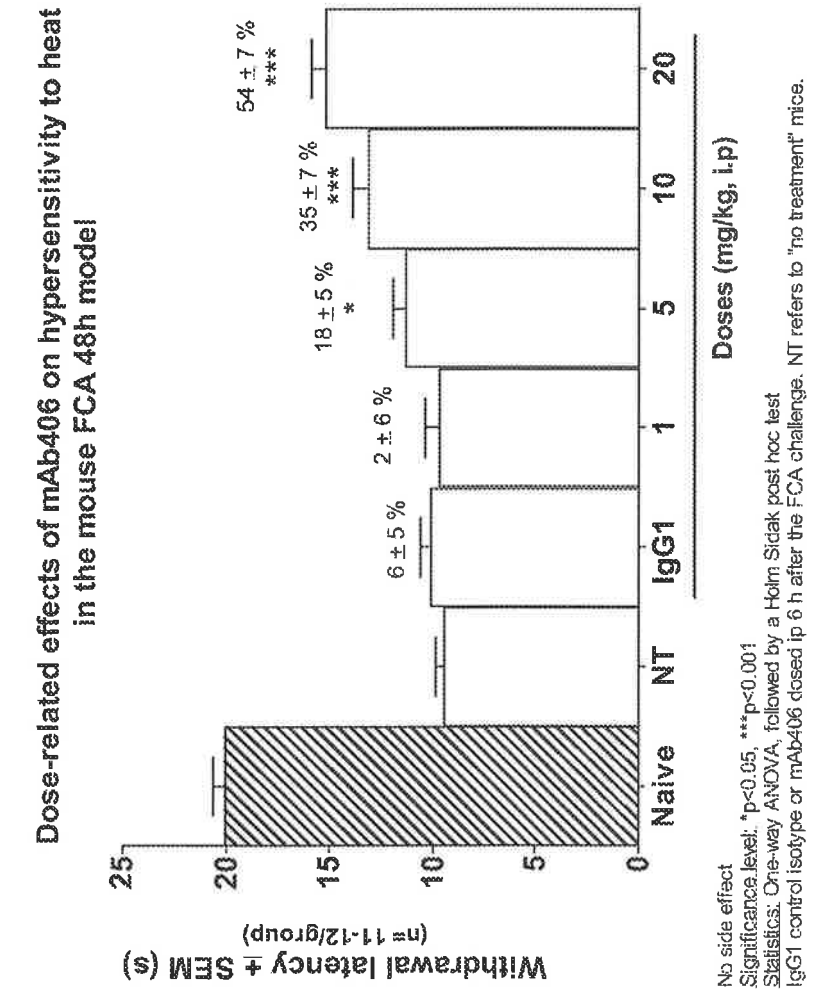
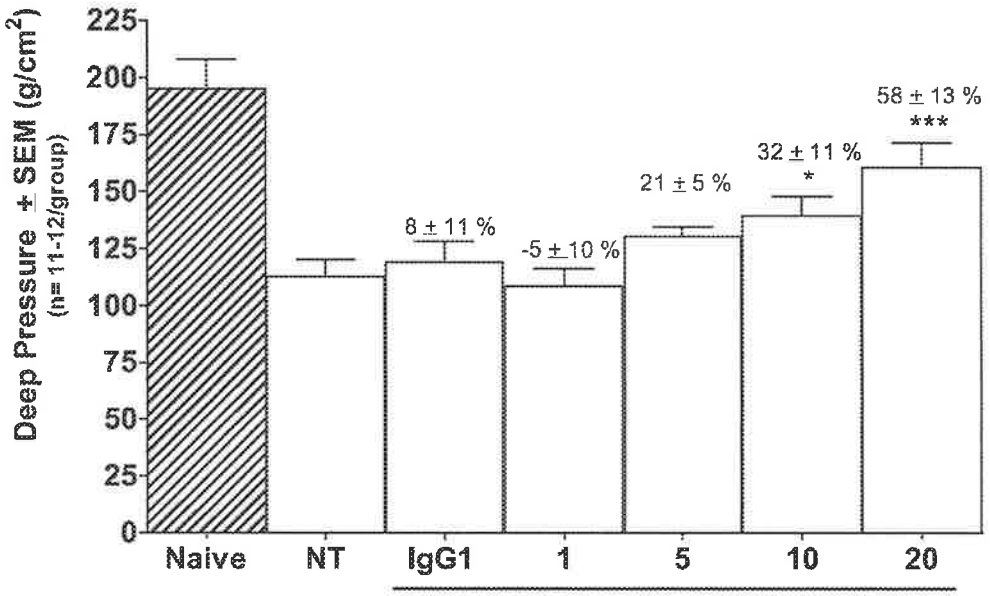

Dose-related effects of mAb406 on hypersensitivity to heat in the mouse FCA 48h model
Withdrawal latency ± SEM (s)
(n= 11-12/group)
25
20
15
10
5
0
Naive
NT
IgG1
1
5
10
20
Doses (mg/kg, i.p)
6 ± 5 %
2 ± 6 %
18 ± 5 %
*
35 ± 7 %
***
54 ± 7 %
***
No side effect
Significance level: *p<0.05, ***p<0.001
Statistics: One-way ANOVA, followed by a Holm Sidak post hoc test
IgG1 control isotype or mAb406 dosed ip 6 h after the FCA challenge. NT refers to "no treatment" mice.

Figure 14

Dose-related effects of mAb406 on hypersensitivity to mechanical pressure in the FCA mouse 24h model



No side effect observed
Significance level: *p<0.05, ***p<0.001
Statistics: One-way ANOVA, followed by a Holm Sidak post hoc test
IgG1 control isotype or mAb406 dosed ip 6 h after the FCA challenge. NT refers to "no treatment" mice.

Figure 15

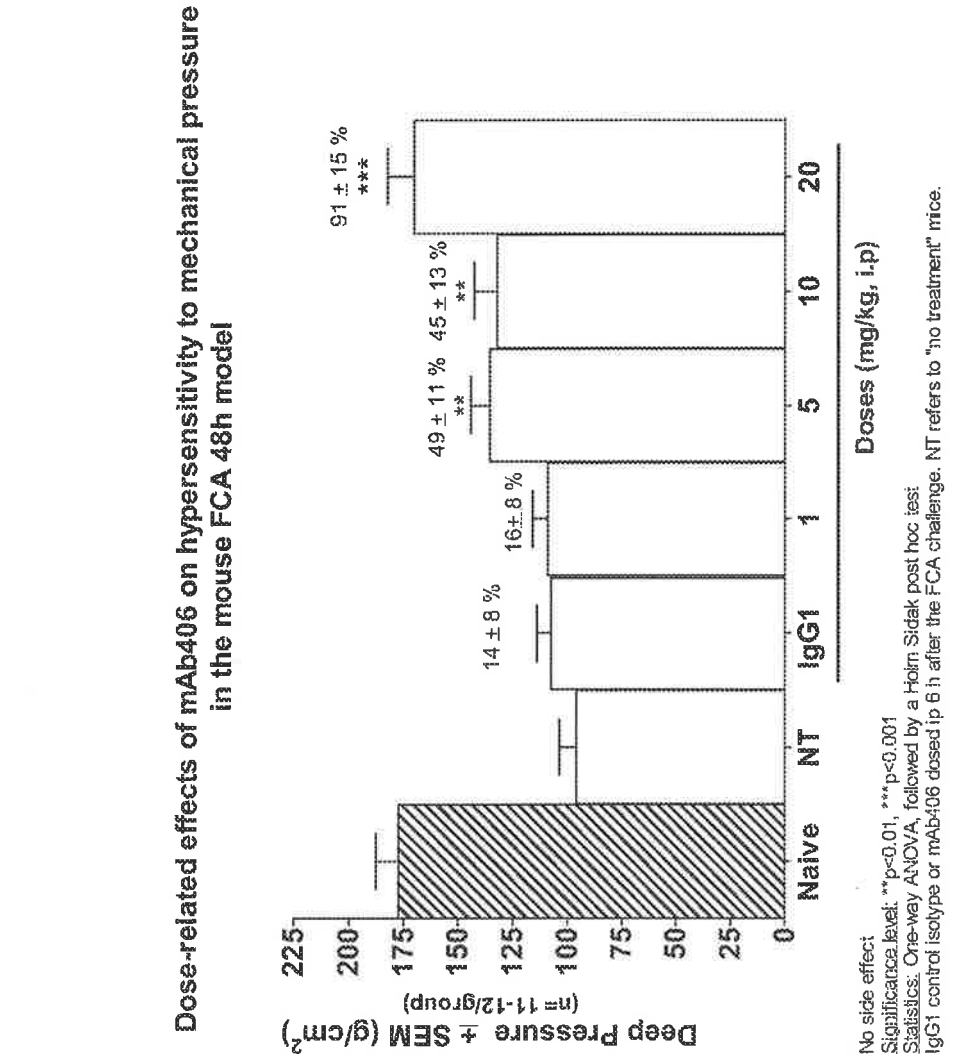

Dose-related effects of mAb406 on hypersensitivity to mechanical pressure in the mouse FCA 48h model
Deep Pressure + SEM (g/cm²)
(n= 11-12/group)
225
200
175
150
125
100
75
50
25
0
14 ± 8 %
16± 8 %
49 ± 11 %
**
45 ± 13 %
**
91 ± 15 %
***
Naive
NT
IgG1
1
5
10
20
Doses (mg/kg, i.p)
No side effect
Significance level: **p<0.01, ***p<0.001
Statistics: One-way ANOVA, followed by a Holm Sidak post hoc test
IgG1 control isotype or mAb406 dosed ip 6 h after the FCA challenge. NT refers to "no treatment" mice.

Figure 16

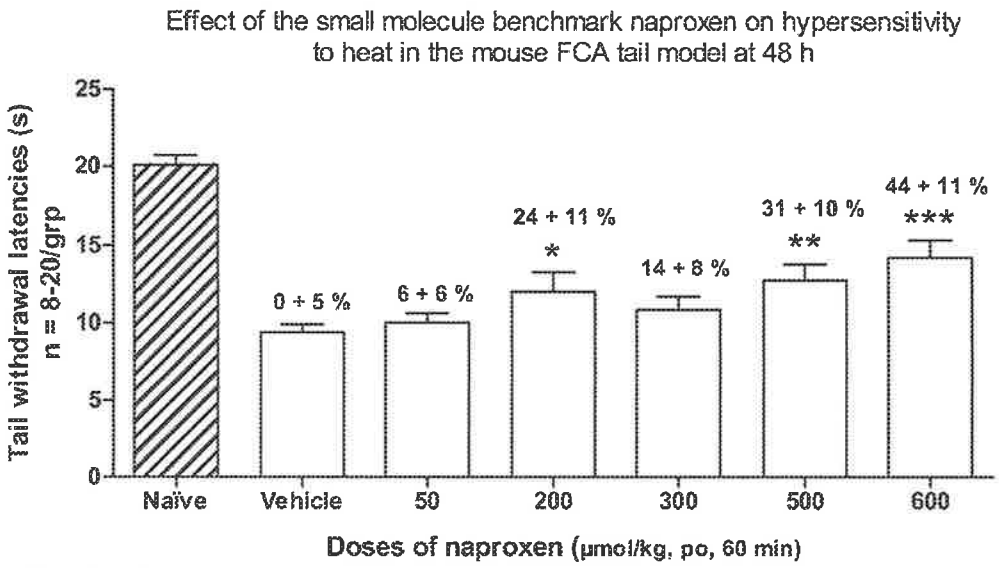
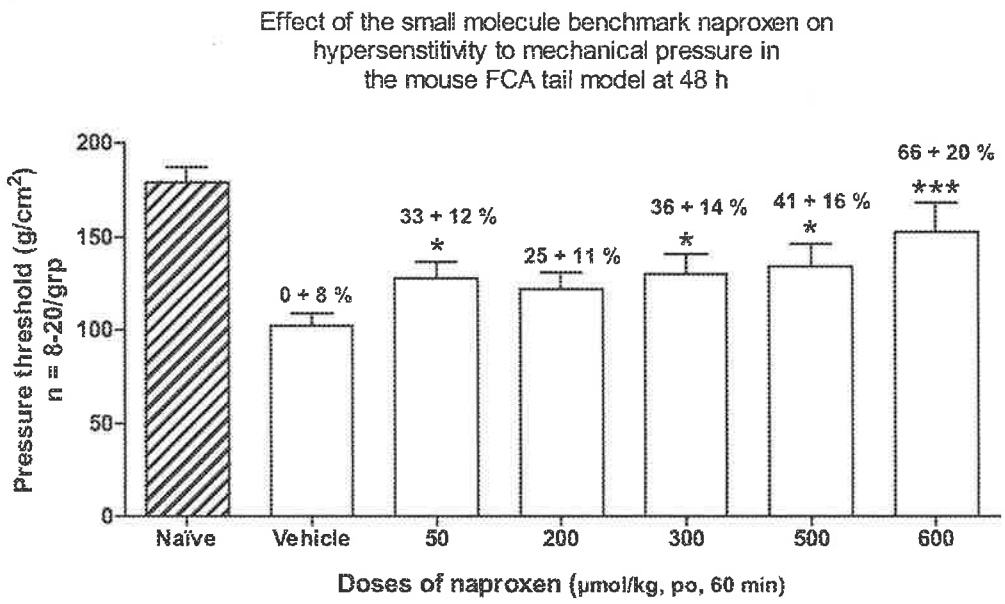

Effect of the small molecule benchmark naproxen on hypersensitivity to heat in the mouse FCA tail model at 48 h
Tail withdrawal latencies (s)
n = 8-20/grp
25
20
15
10
5
0
0 + 5 %
6 + 6 %
24 + 11 %
*
14 + 8 %
31 + 10 %
**
44 + 11 %
***
Naïve
Vehicle
50
200
300
500
600
Doses of naproxen (µmol/kg, po, 60 min)
Side effects: None
* = p<0.05, ** = p<0.01, ***p<0.001, one-way ANOVA, one sided Holm Sidak post hoc test

Figure 17



Side effects: None

* = p<0.05, ***p<0.001, one-way ANOVA, one sided Holm Sidak post hoc test

Figure 18