

FIG. 1A

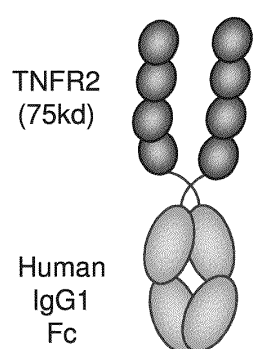


FIG. 1B

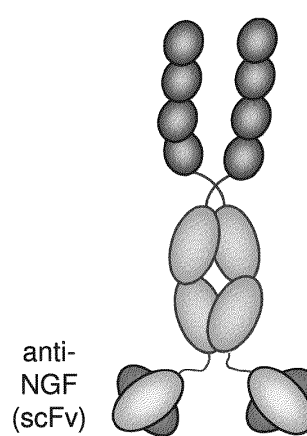


FIG. 2A

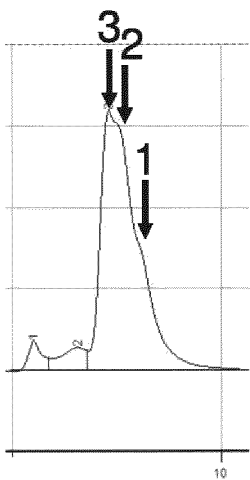


FIG. 2B

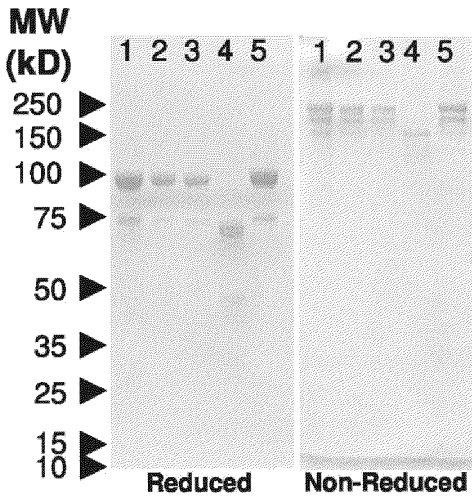


FIG. 3A

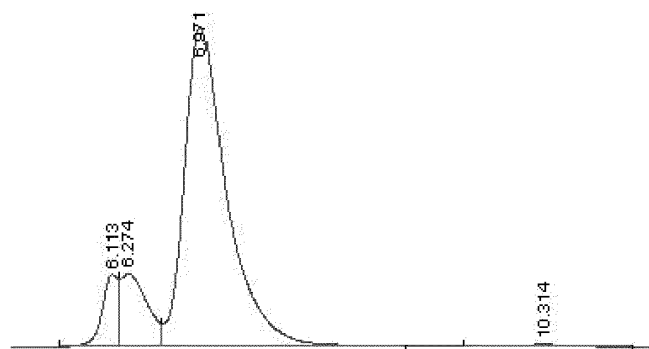


FIG. 3B

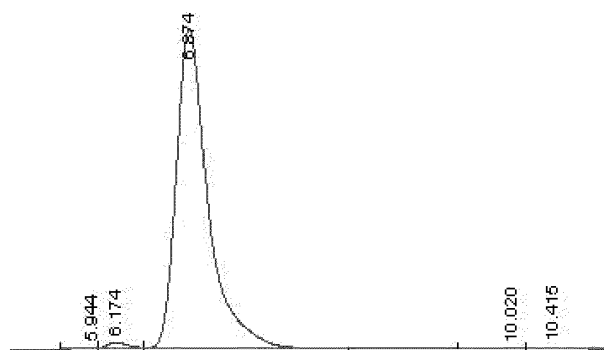
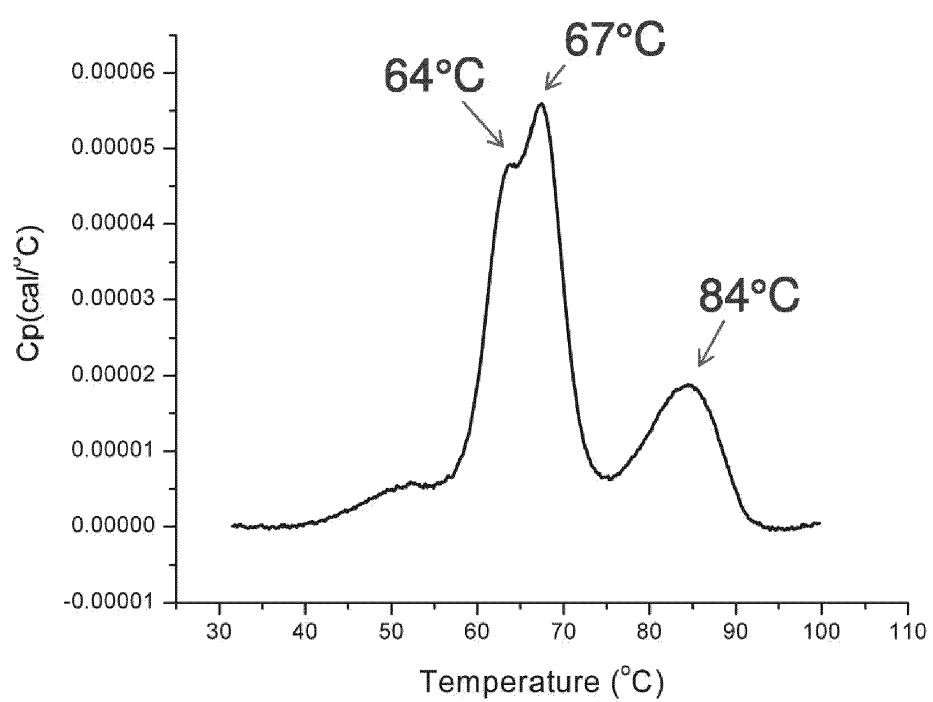


FIG. 4

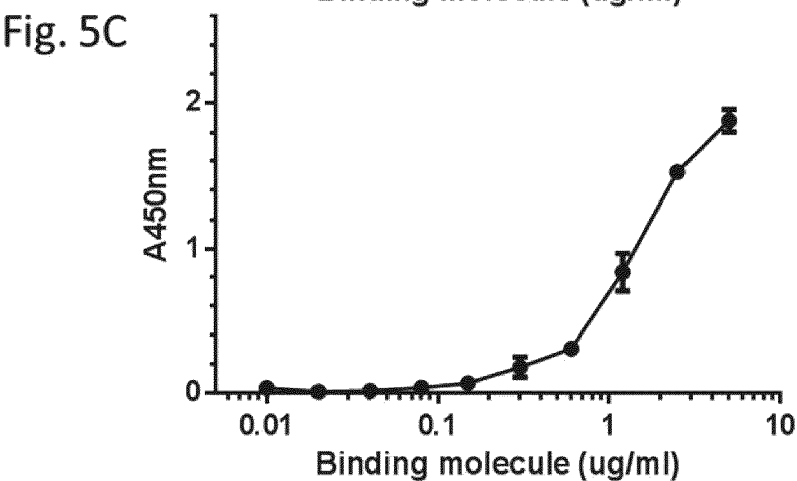
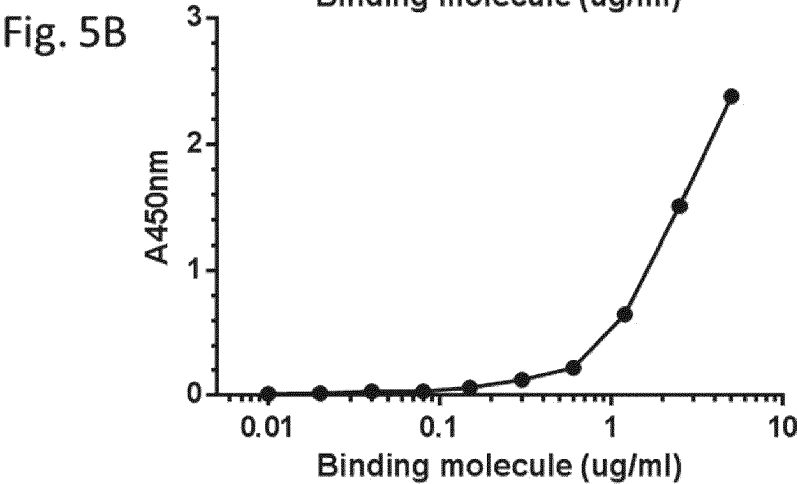
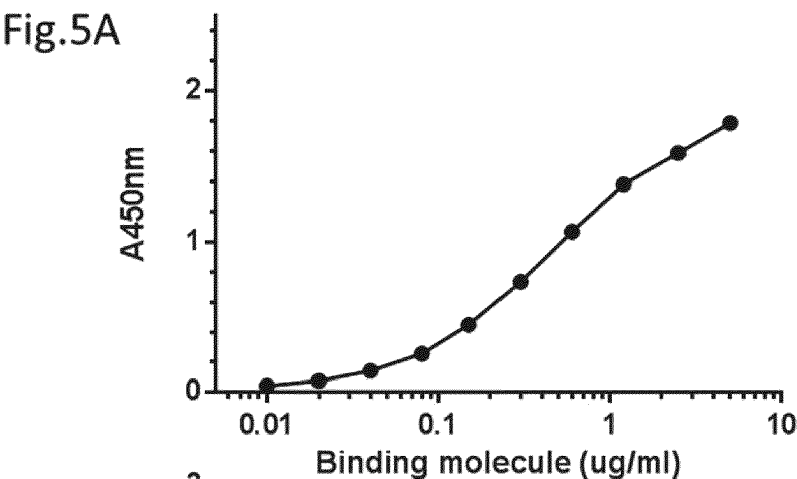


FIG. 6

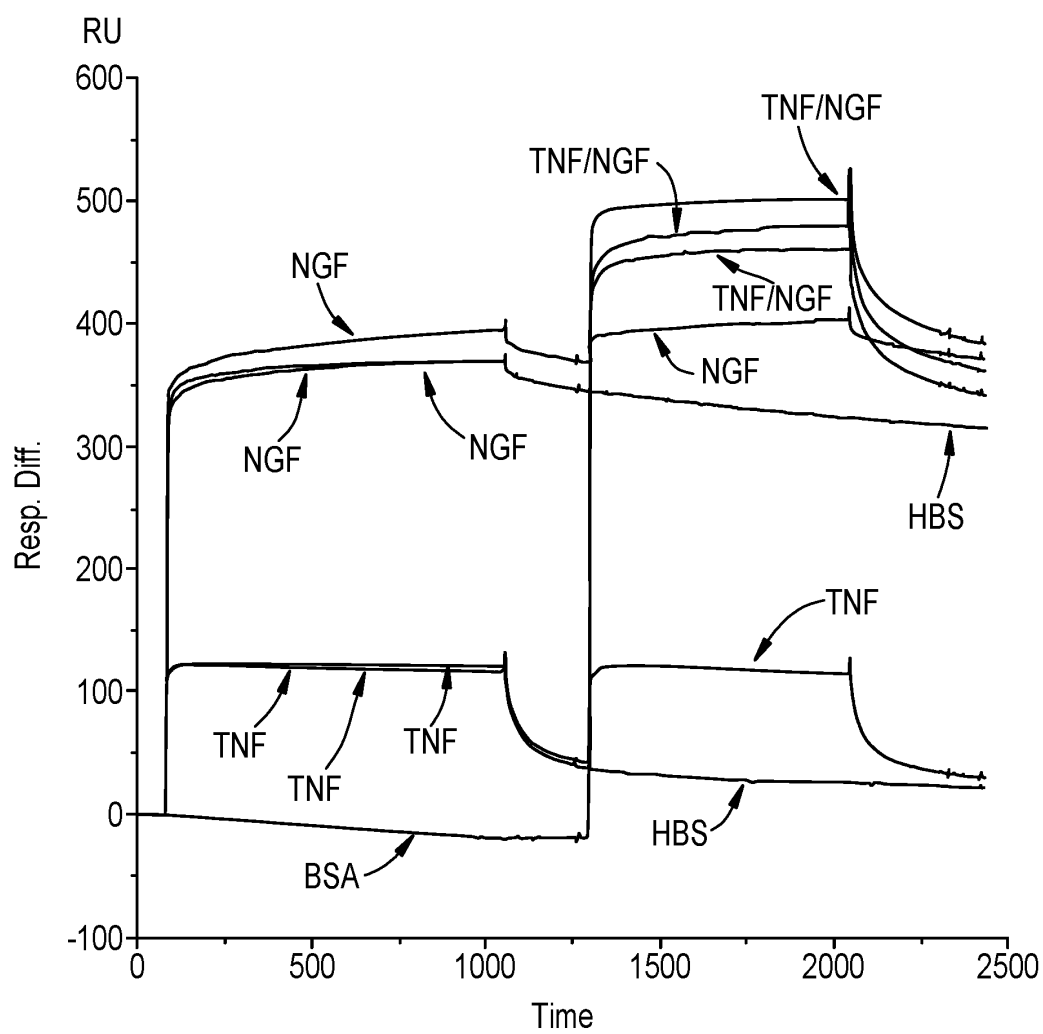


FIG. 7A

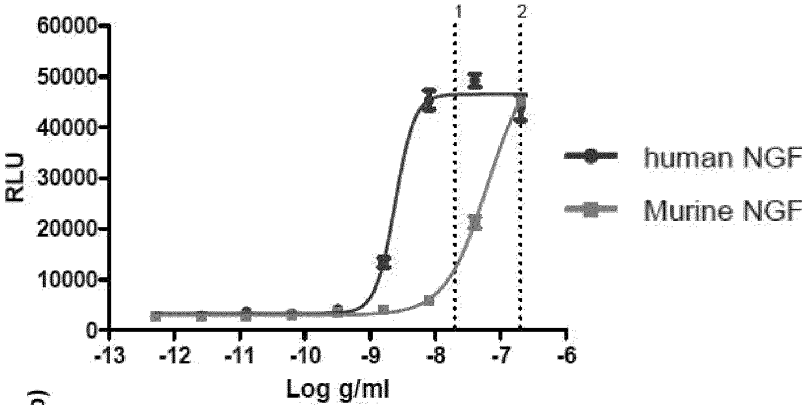


FIG. 7B

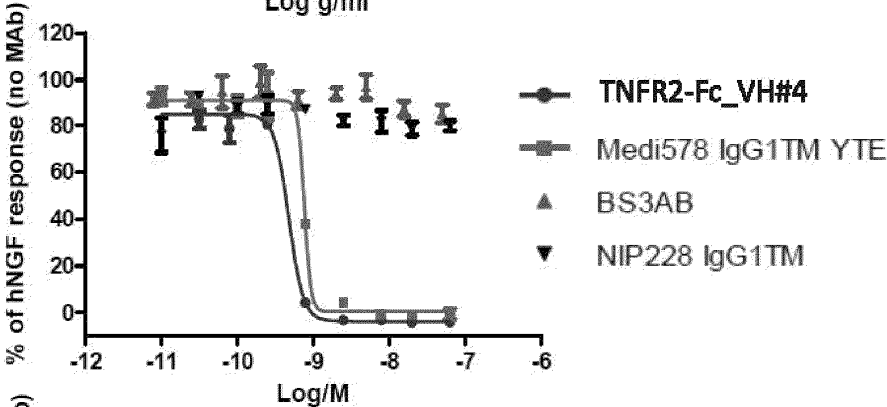


FIG. 7C

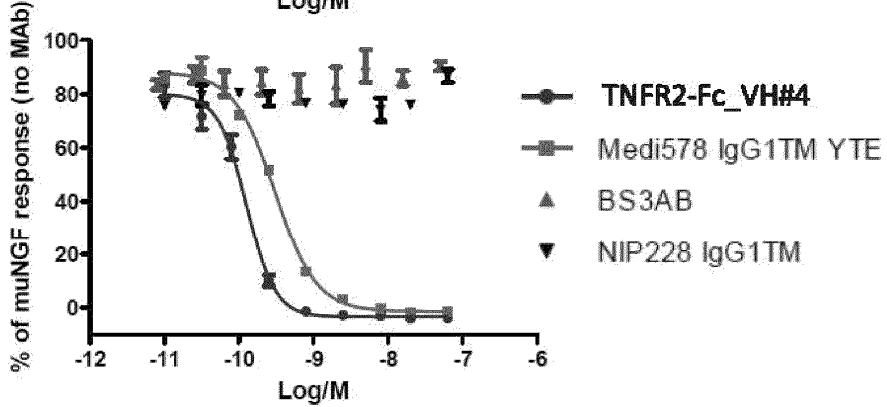
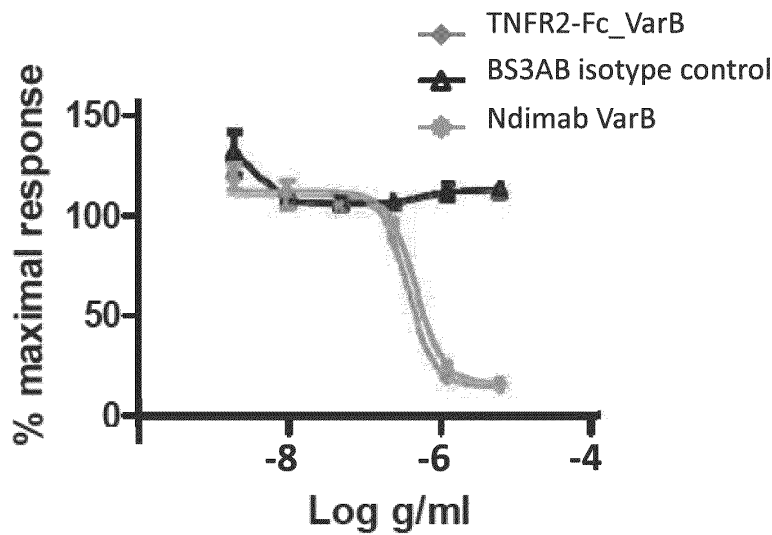
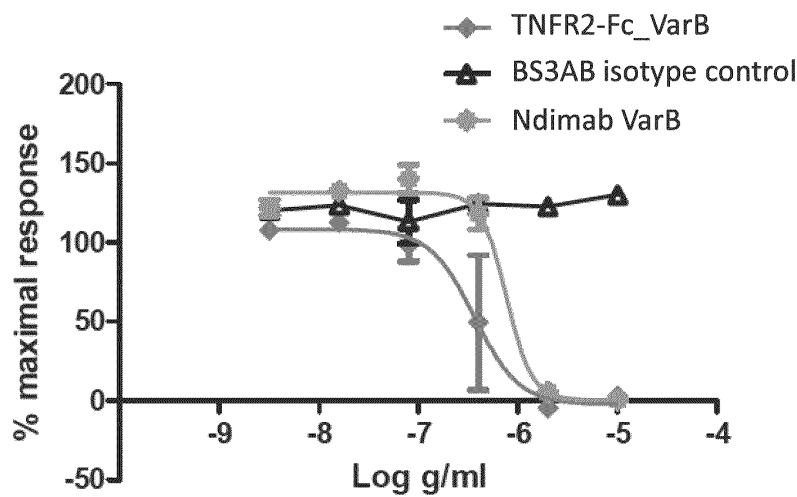


FIG. 7D



	TNFR2-Fc_VarB	ndimab VarB
IC50	3.134e-007	3.934e-007

FIG. 7E



	TNFR2-Fc_VarB	ndimab VarB
IC50	3.642e-007	7.602e-007

FIG. 8A

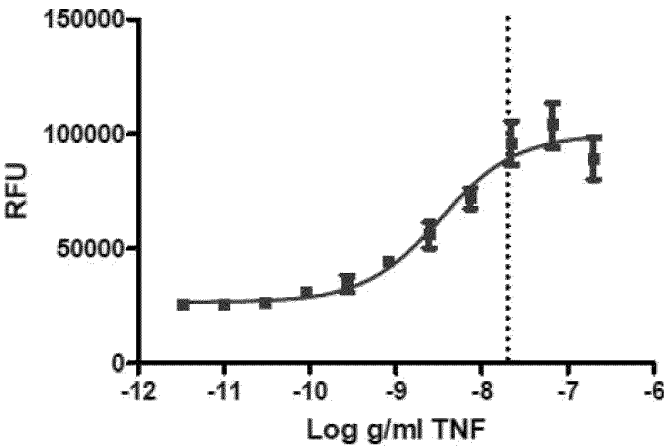


FIG. 8B

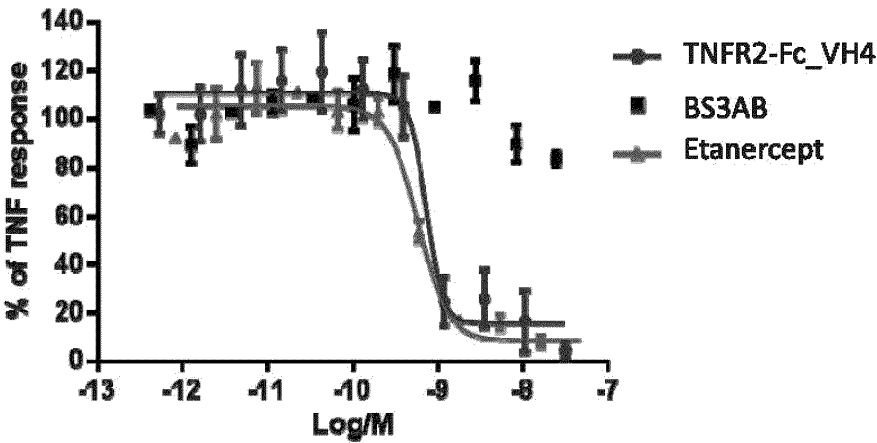
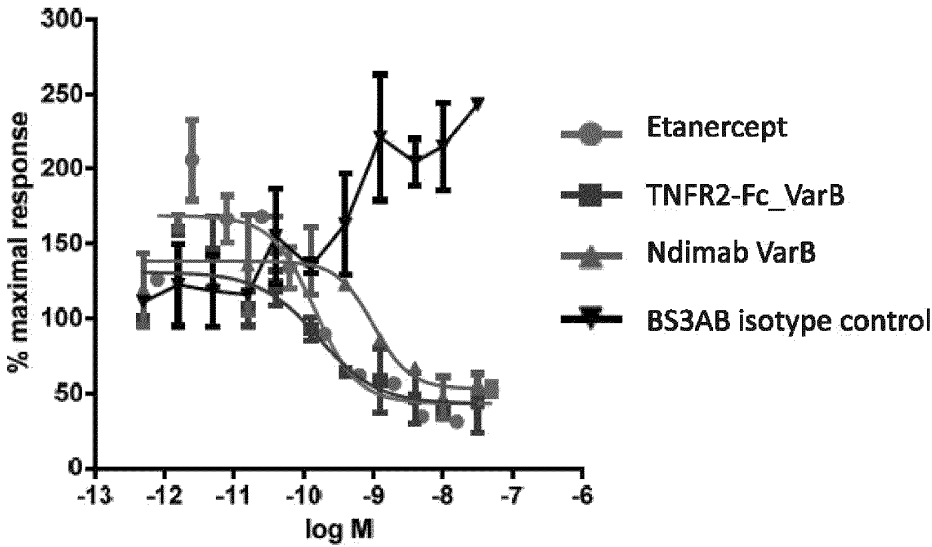
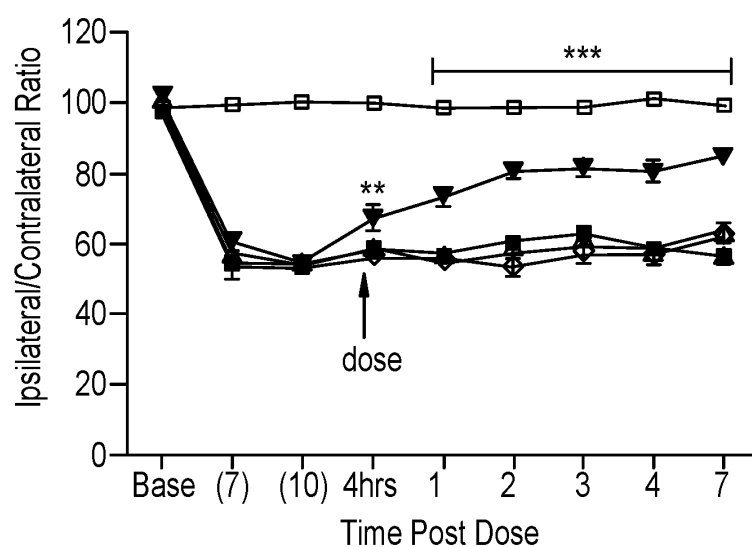


FIG. 8C



	Etanercept	TNFR2-Fc_VarB	ndimab VarB
IC50	1.444e-010	1.652e-010	1.004e-009

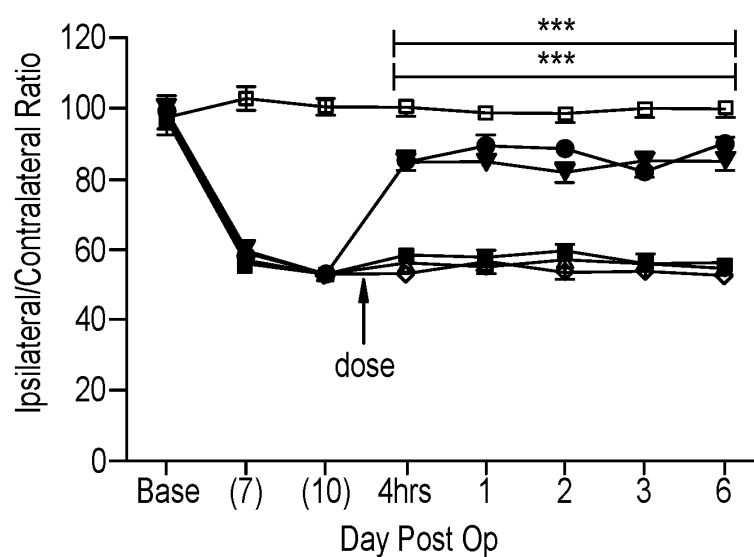
FIG. 9



—□— Sham + CAT251 0.03mg/kg s.c. —◇— Op + CAT251 0.03mg/kg s.g.
 —■— Op + Etanercept 0.01mg/kg s.g. —▲— Op + MEDI578 0.03mg/kg s.g.
 —▼— Op + Etanercept + MEDI578

N=9-10 per group. Data analysed using 2 way ANOVA with time and treatment as dependant factors. Subsequent statistical significance obtained using Bonferroni's Post Hoc test
 *** $p < 0.001$ to Op + CAT251 control

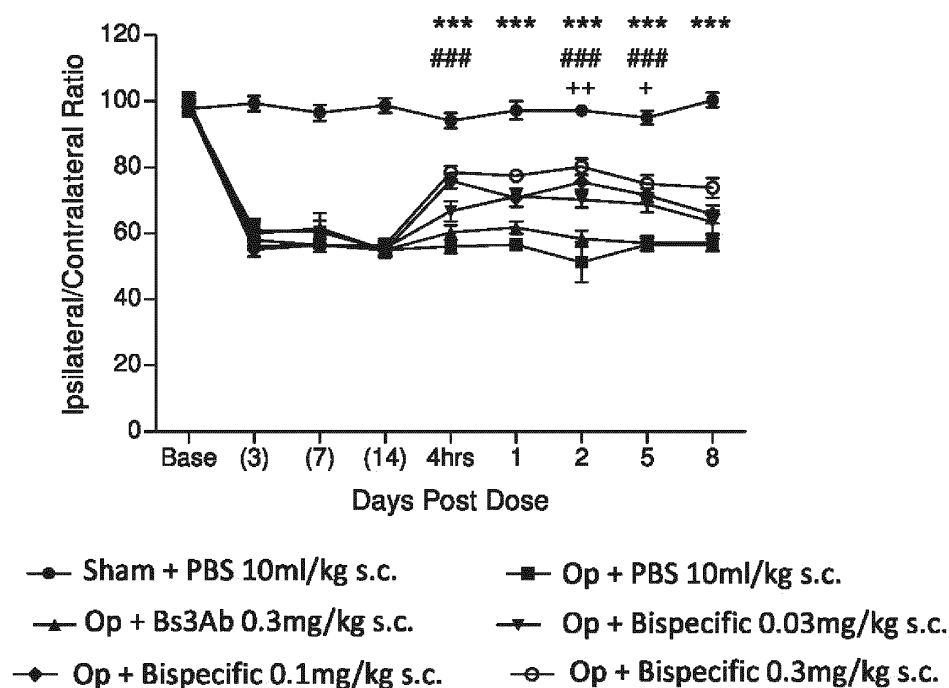
FIG. 10A



- Sham + Iso 0.03mg/kg s.c.
- Op + Etanercept 0.01mg/kg s.c.
- ▼— Op + BiSpecific 0.01mg/kg s.c.
- ◇— Op + Iso 0.03mg/kg s.c.
- ▲— Op + MEDI578 0.03mg/kg s.c.
- Op + BiSpecific 0.03mg/kg s.c.

N=10 per group. Data analysed using 2 way ANOVA with time and treatment as dependant factors. Subsequent statistical significance obtained using Bonferroni's Post Hoc test.

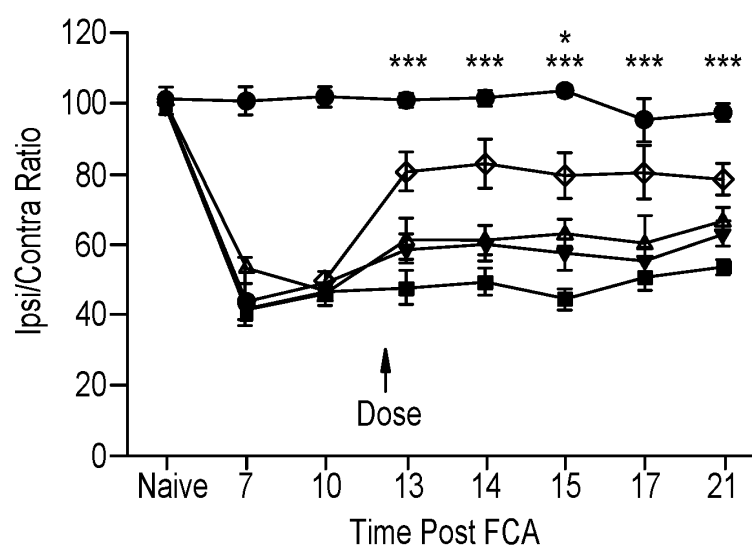
*** $p < 0.001$ vs BiSpec Isotype (0.03mg/kg s.c.)

FIG. 10B

Data analyzed using 2-way analysis of variance followed by Bonferonni's post hoc test where appropriate.

+ P<0.05; ++ P<0.01 PNL + Bispecific (0.03mg/kg sc); ### P<0.01 PNL + Bispecific (0.1mg/kg sc); *** P<0.001 PNL + Bispecific (0.3mg/kg sc) all vs PNL + R347

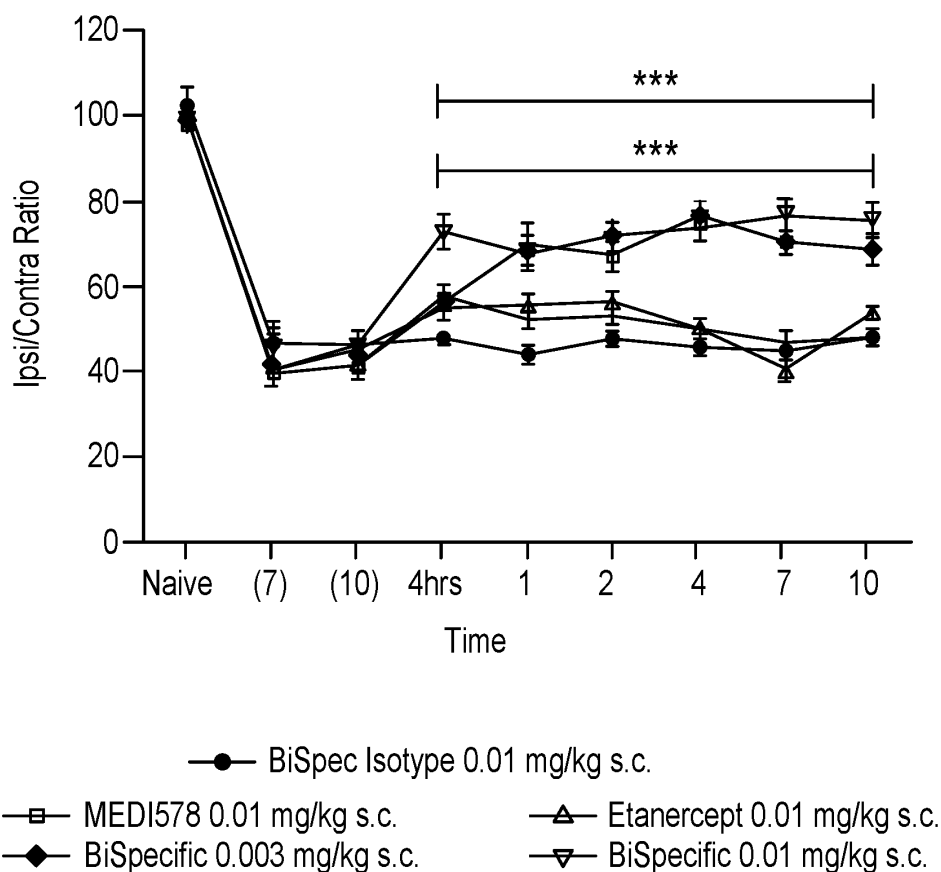
FIG. 11



- Veh - CAT251 (0.03 mg/kg i.v.) + PBS (10 ml/kg i.p.)
- ▲ FCA - MEDI 578 (0.03 mg/kg i.v.) + PBS (10 ml/kg i.p.)
- FCA - CAT251 (0.03 mg/kg i.v.) + PBS (10 ml/kg i.p.)
- ▼ FCA - CAT251 (0.03 mg/kg i.v.) + Etanercept (0.01 mg/kg i.p.)
- ◆ FCA - MEDI 578 (0.03 mg/kg i.v.) + Etanercept (0.01 mg/kg i.p.)

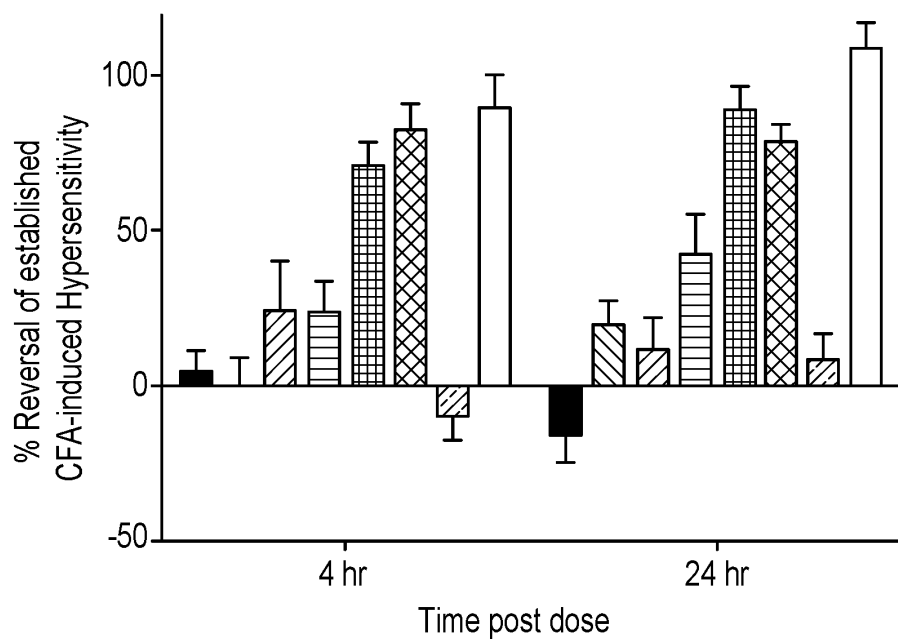
N=9/10 per group. Data analysed using 2 way ANOVA followed by Bonferroni post-hoc test. * $P > 0.05$, *** $P < 0.001$ vs Veh-CAT-251 (0.03 mg/kg i.v.) + PBS (10ml/kg i.p.)

FIG. 12



Data analysed using 2 way ANOVA with time and treatment as dependant factors. Subsequent statistical significance obtained using Bonferroni's Post Hoc test
 *** P<0.001 vs BiSpec Isotype (0.01 mg/kg s.c.) n=9-10

FIG. 13



Statistical analysis - Repeated measures ANOVA, followed by a planned comparison test, using invivostat.

*P<0.05, **P<0.01, ***P<0.001 Significant reversal of hyperalgesia when compared to vehicle at each time point.

- Vehicle
- ▨ 0.003mg/kg Bispecific
- ▧ 0.01mg/kg Bispecific
- ▩ 0.03mg/kg Bispecific
- 0.3mg/kg Bispecific
- 3mg/kg Bispecific
- ▬ 3mg/kg NIP228
- Indomethacin 10mg/kg

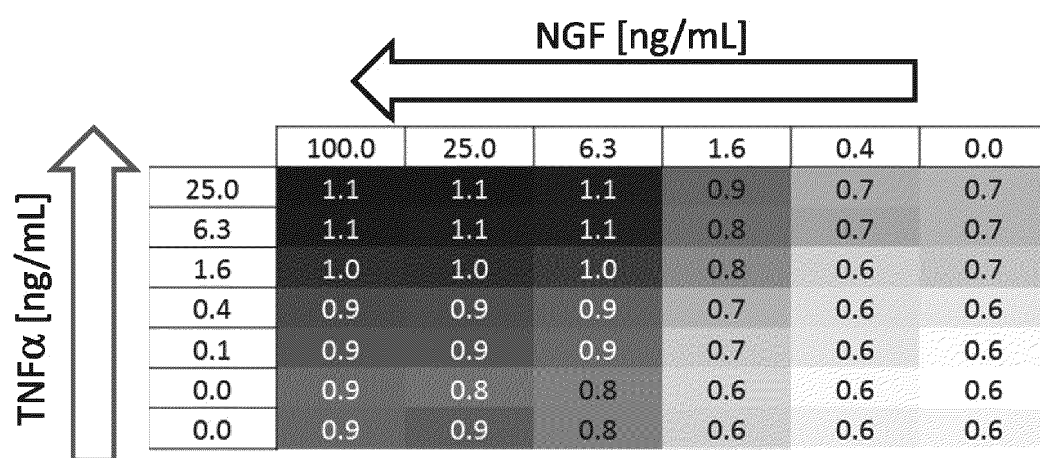
FIG. 14

FIG. 15

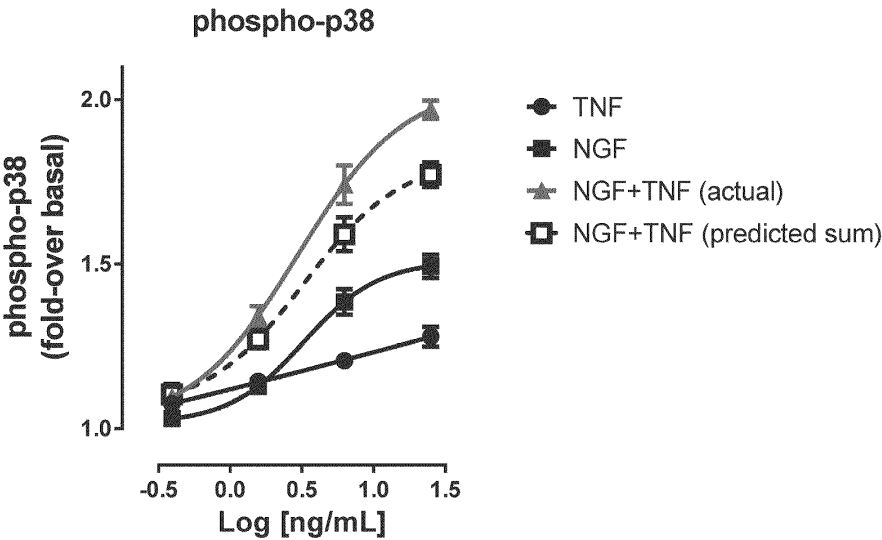


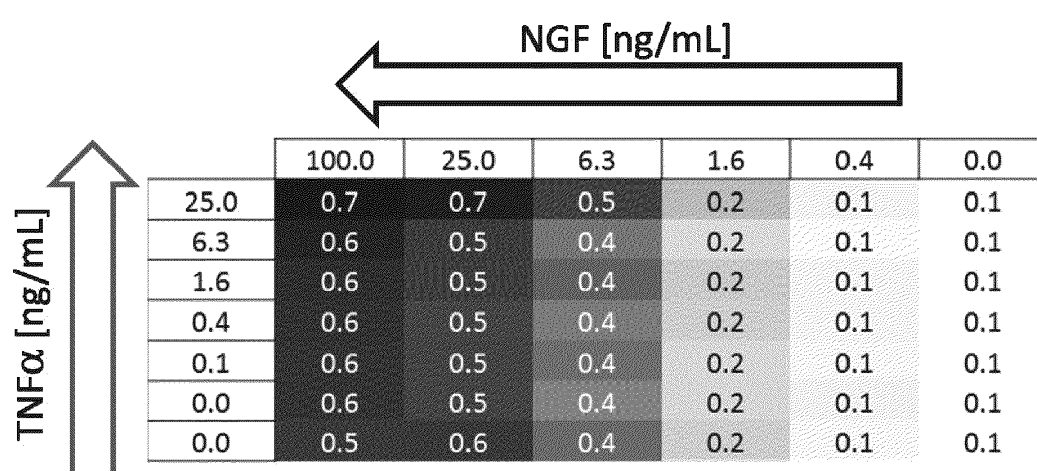
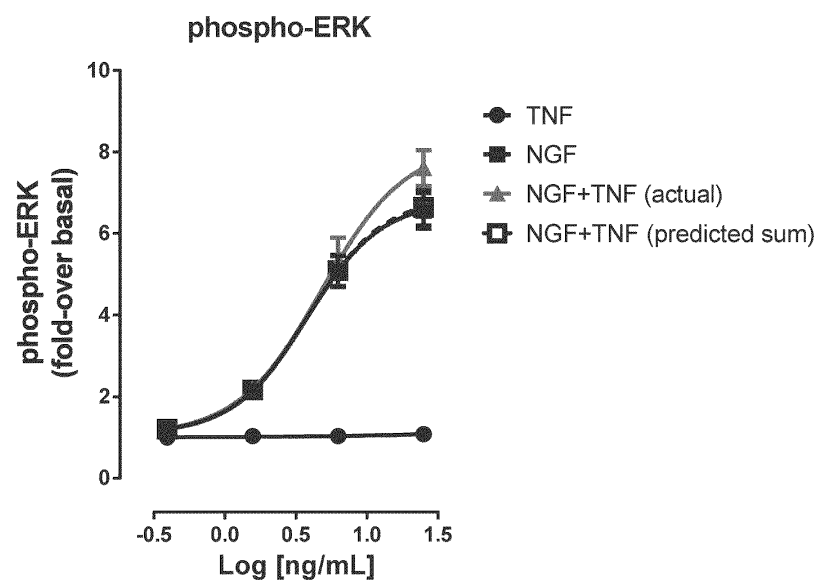
FIG. 16

FIG. 17



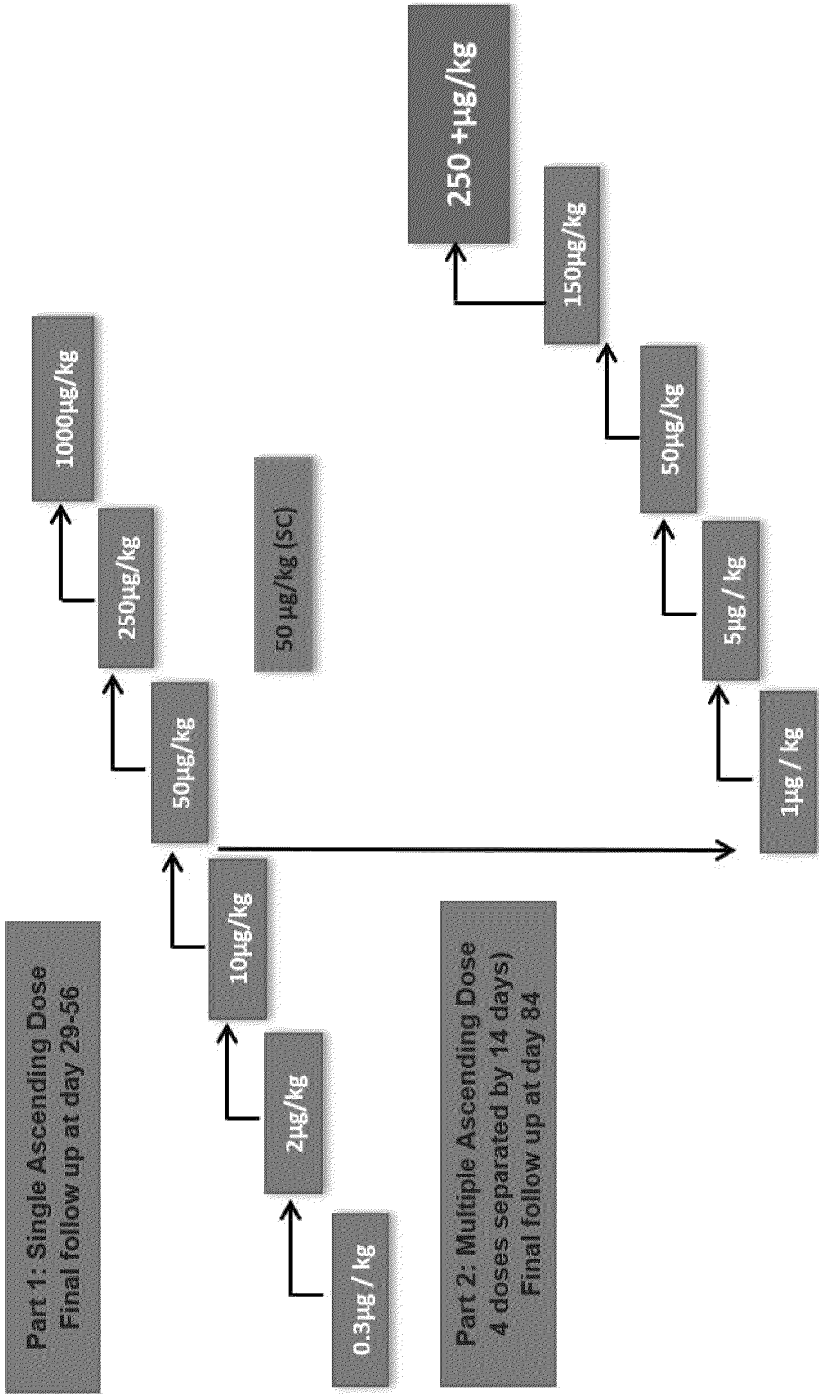


FIG. 18A

Cohort	RoA	Dose (µg/kg)	Predicted av %NGF suppre
Part I – SAD			
1	IV	0.3	10
2	IV	2	27
3	IV	10	38
4	IV	50	53
5	IV	250	71
6	IV	1000	82
7	SC	50	20
Part II – MAD			
8	IV	1	21
9	IV	5	34
10	IV	50	51
11	IV	150	69

FIG. 18B

Cohort	RoA	Dose (µg/kg)	Predicted average %NGF suppression
Part I – SAD			
1	IV	0.3	10
2	IV	2	27
3	IV	10	38
4	IV	50	53
5	IV	250	71
6	IV	1000	82
7	SC	50	20
Part II – MAD			
8	IV	1	21
9	IV	5	34
10	IV	50	51
11	IV	150	69

FIG. 18B

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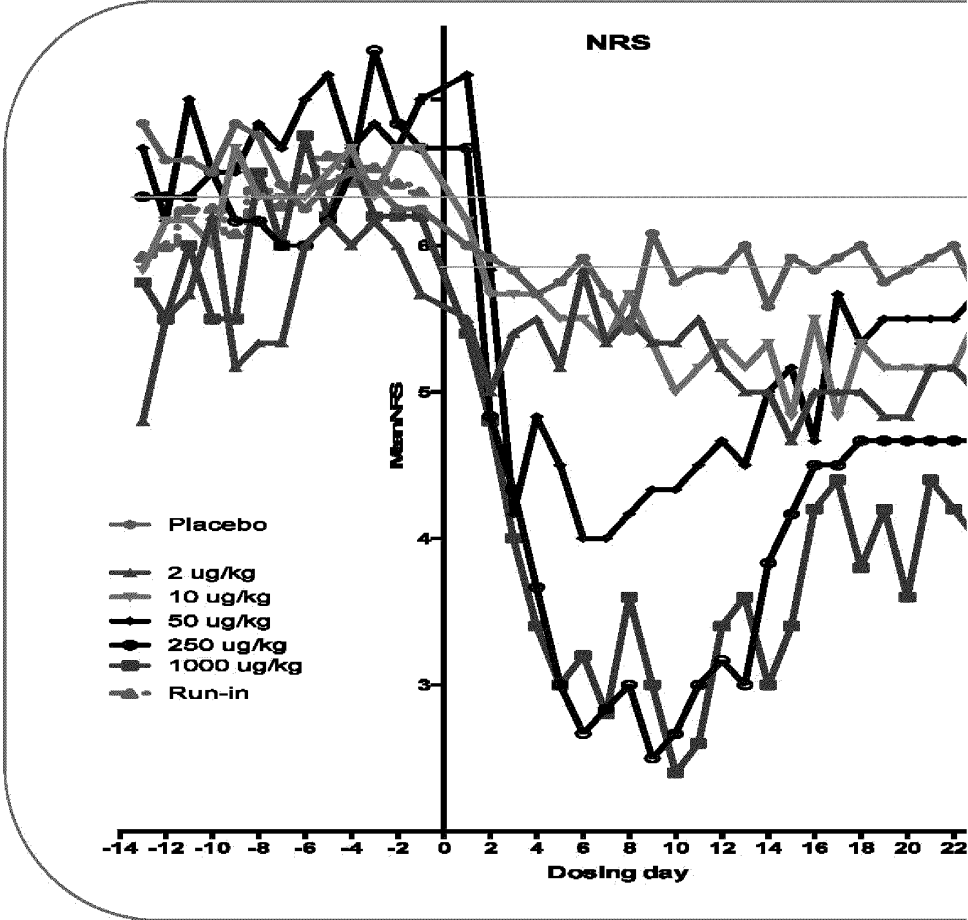


FIG. 19A

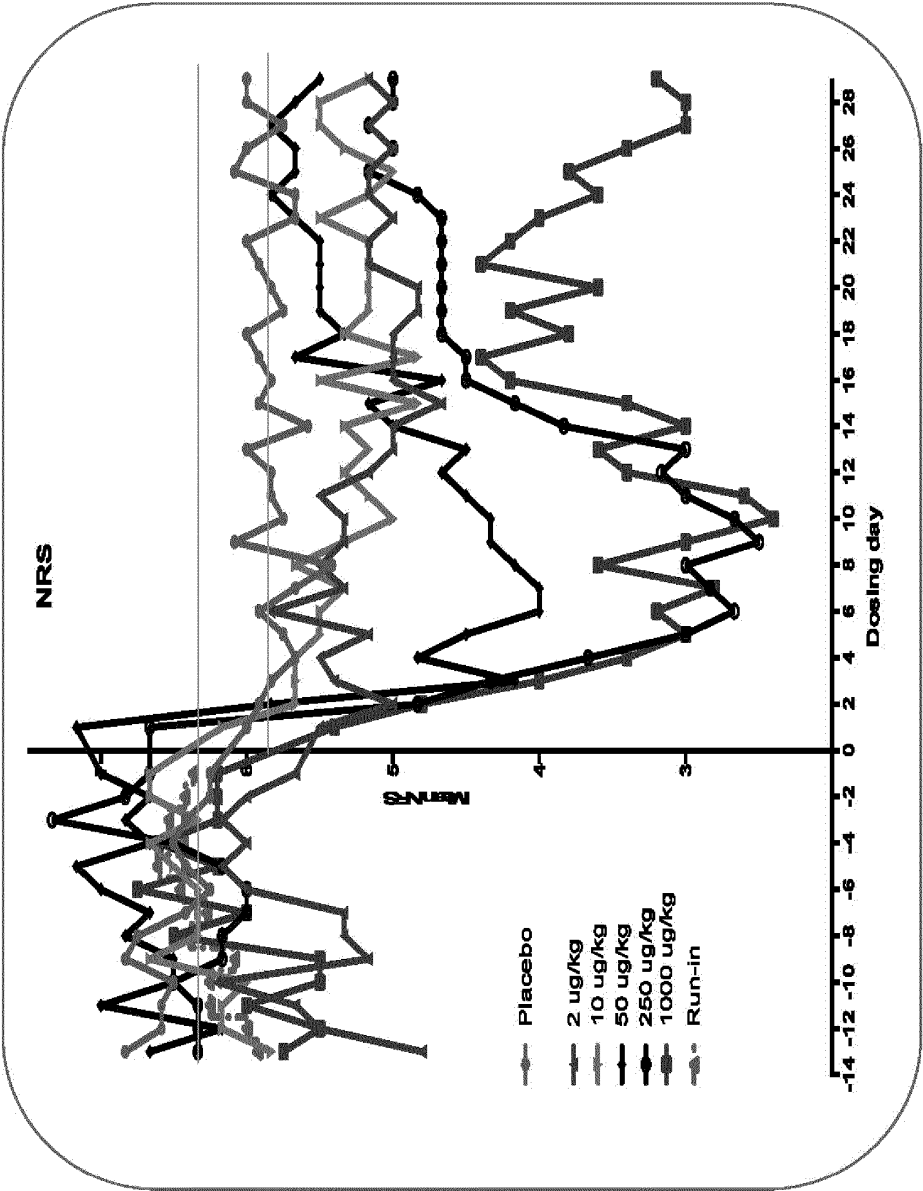


FIG. 19A

SAD cohort dose (µg per kg)	Predicted mean NGF suppression (%)	Peak NRS change vs. PBO
2	27	- 0.69
10	38	- 0.85
50	53	- 1.85
250	71	- 3.35
1000	83	- 3.45

FIG. 19B

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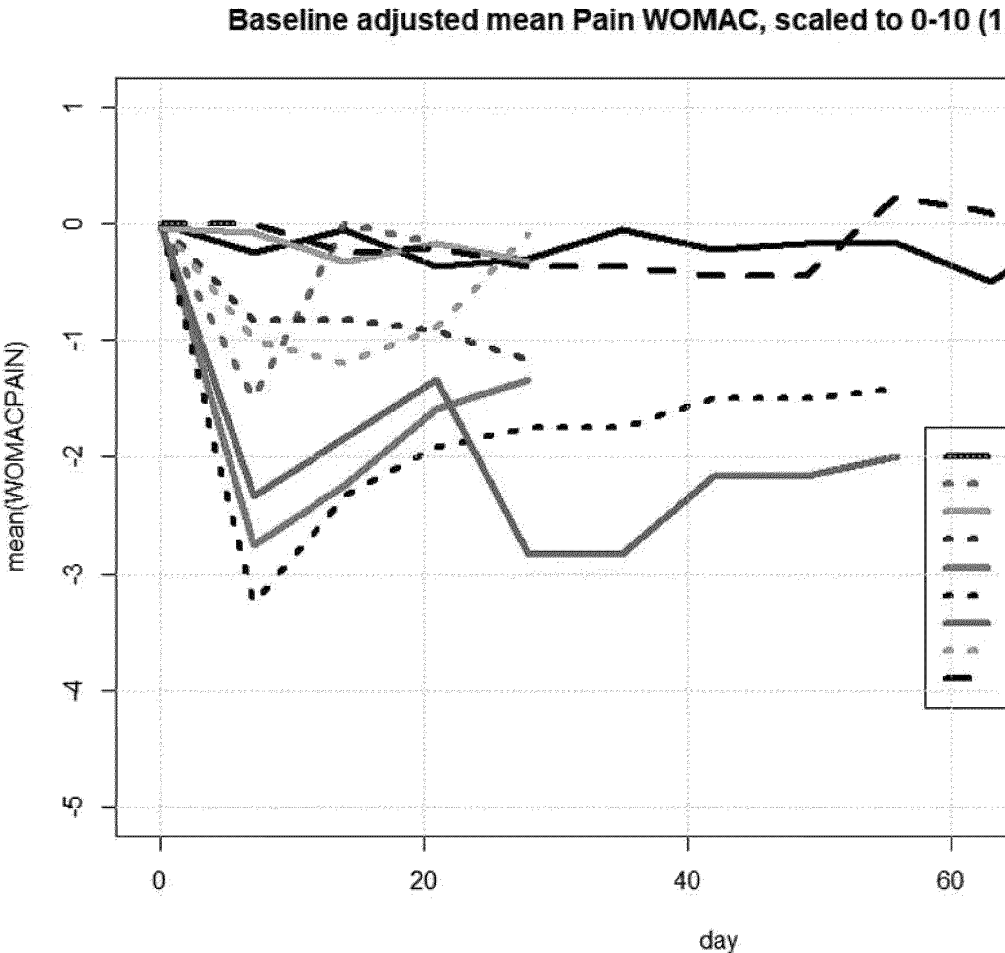
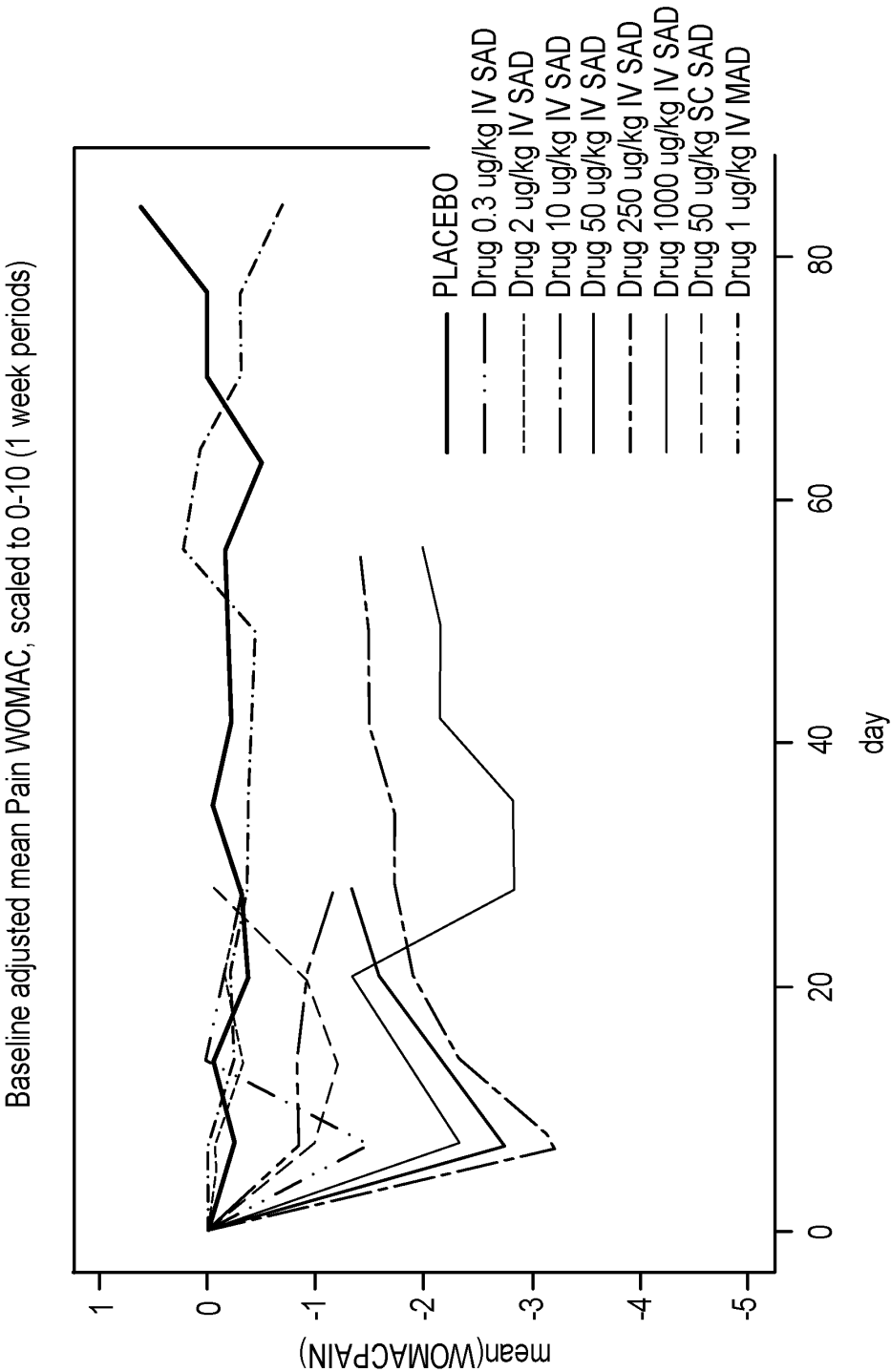


FIG. 20A

FIG. 20A



	Testing at one week
Placebo vs.	TNFR2-Fc_varB 0.3 ug/kg IV SAD
Placebo vs.	TNFR2-Fc_varB 2 ug/kg IV SAD
Placebo vs.	TNFR2-Fc_varB 10 ug/kg IV SAD
Placebo vs.	TNFR2-Fc_varB 50 ug/kg IV SAD
Placebo vs.	TNFR2-Fc_varB 250 ug/kg IV SAD
Placebo vs.	TNFR2-Fc_varB 1000 ug/kg IV SAD
Placebo vs.	TNFR2-Fc_varB 50 ug/kg SC SAD

FIG. 20B

	Testing at one week	p-value
Placebo vs.	TNFR2-Fc_varB 0.3 ug/kg IV SAD	0.95
Placebo vs.	TNFR2-Fc_varB 2 ug/kg IV SAD	0.97
Placebo vs.	TNFR2-Fc_varB 10 ug/kg IV SAD	0.43
Placebo vs.	TNFR2-Fc_varB 50 ug/kg IV SAD	0.06
Placebo vs.	TNFR2-Fc_varB 250 ug/kg IV SAD	0.03
Placebo vs.	TNFR2-Fc_varB 1000 ug/kg IV SAD	0.03
Placebo vs.	TNFR2-Fc_varB 50 ug/kg SC SAD	0.59

FIG. 20B

MEDI7352 dose (µg/kg)	Measured % NGF suppression (vs. predicted)		Peak WOMAC pain subscale change vs. placebo MEDI7352
	Peak	Average	
50 (SAD)	92 (99)	46 (53)	-2.4
250 (SAD)	90 (100)	55 (71)	-2.9
1000 (SAD)	tbd (100)	tbd (82)	-2.0

FIG. 21

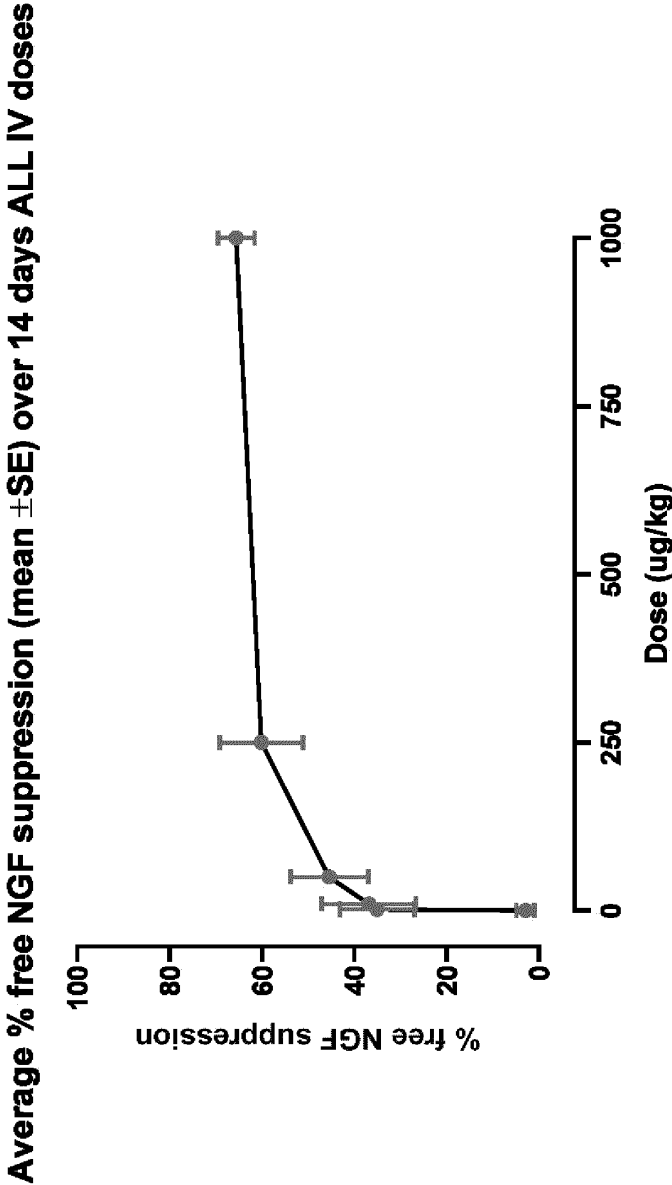


FIG. 22

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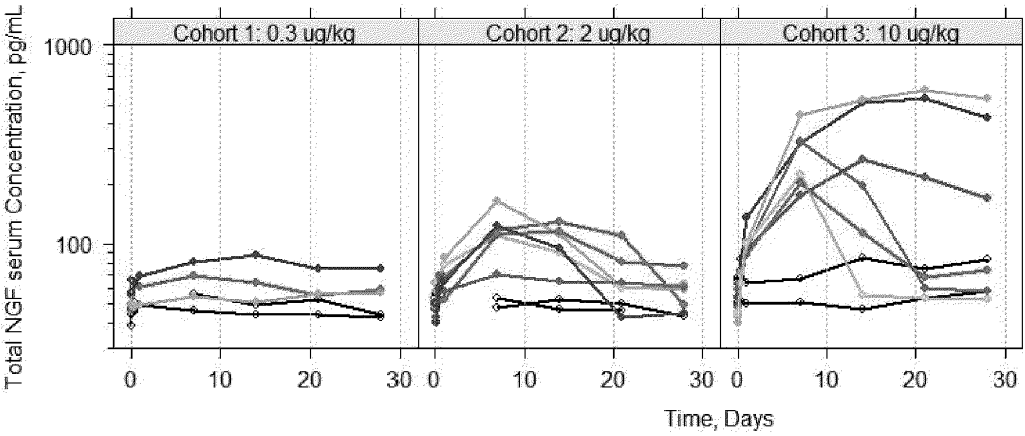
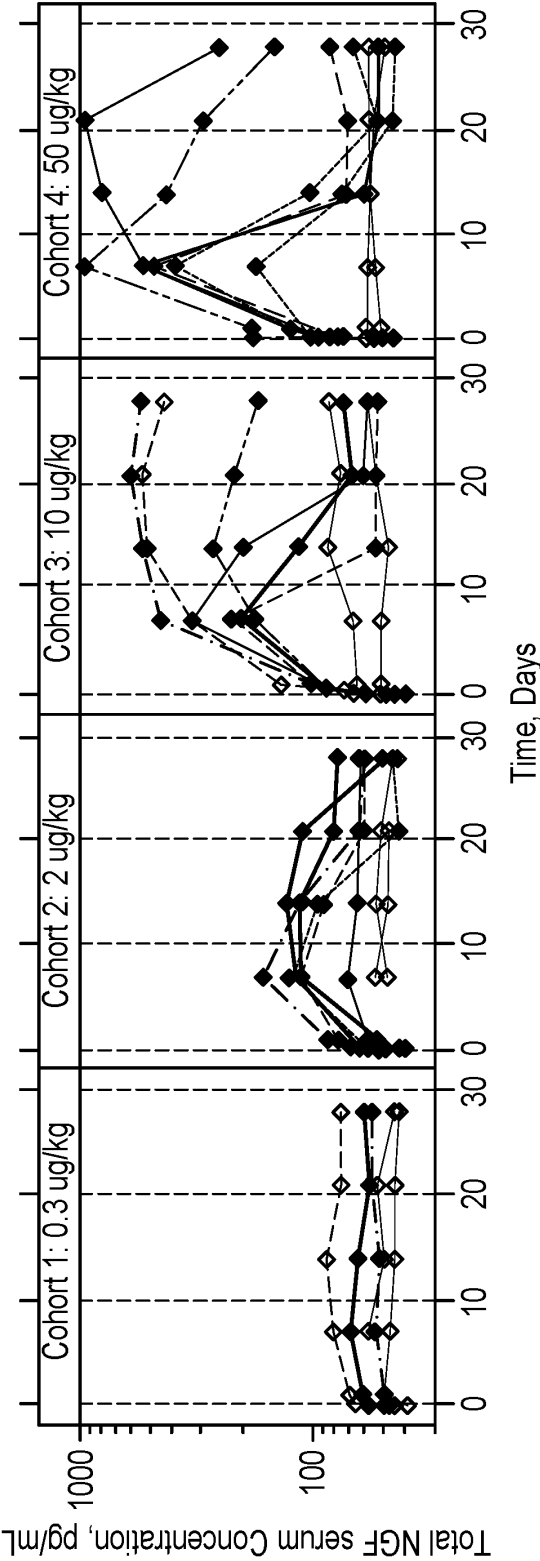


FIG. 23

FIG. 23



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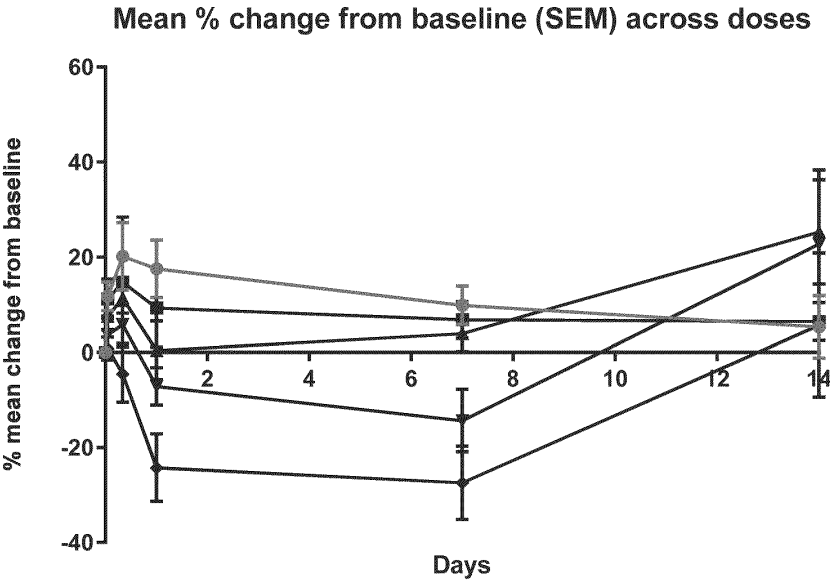


FIG. 24

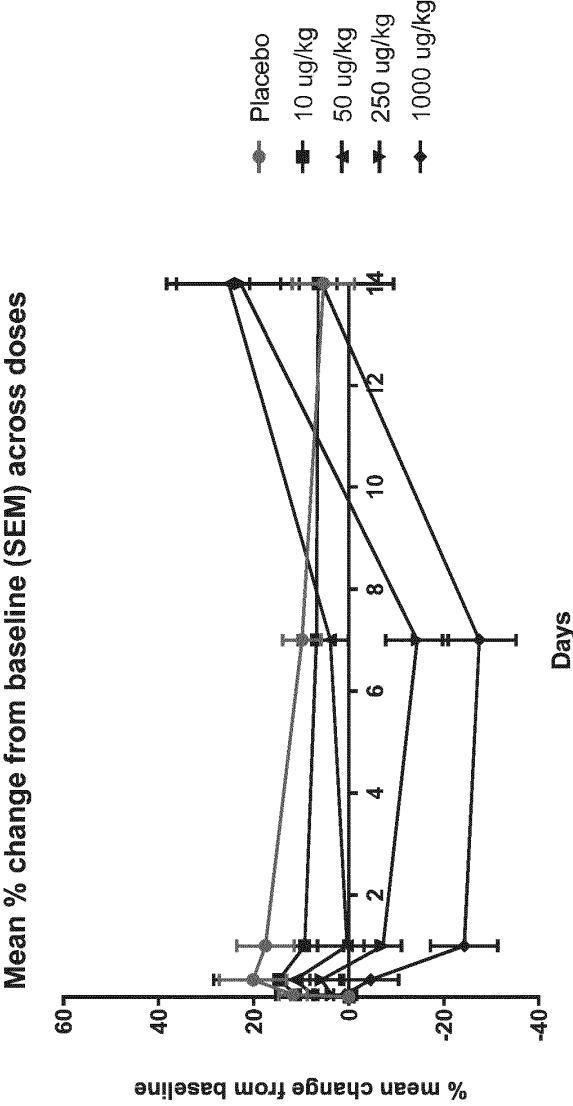
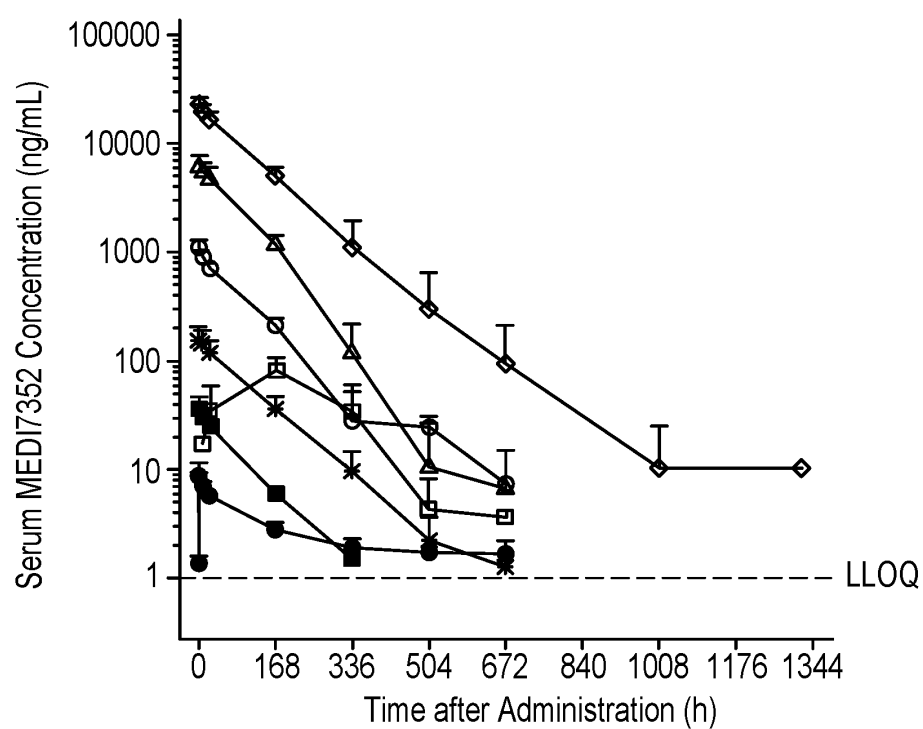


FIG. 24

FIG. 25



- Treatment
- MEDI7352 0.3 ug/kg IV (SAD)
 - MEDI7352 2 ug/kg IV (SAD)
 - * MEDI7352 10 ug/kg IV (SAD)
 - MEDI7352 50 ug/kg IV (SAD)
 - △ MEDI7352 250 ug/kg IV (SAD)
 - ◇ MEDI7352 1000 ug/kg IV (SAD)
 - MEDI7352 50 ug/kg SC (SAD)

FIG 26A

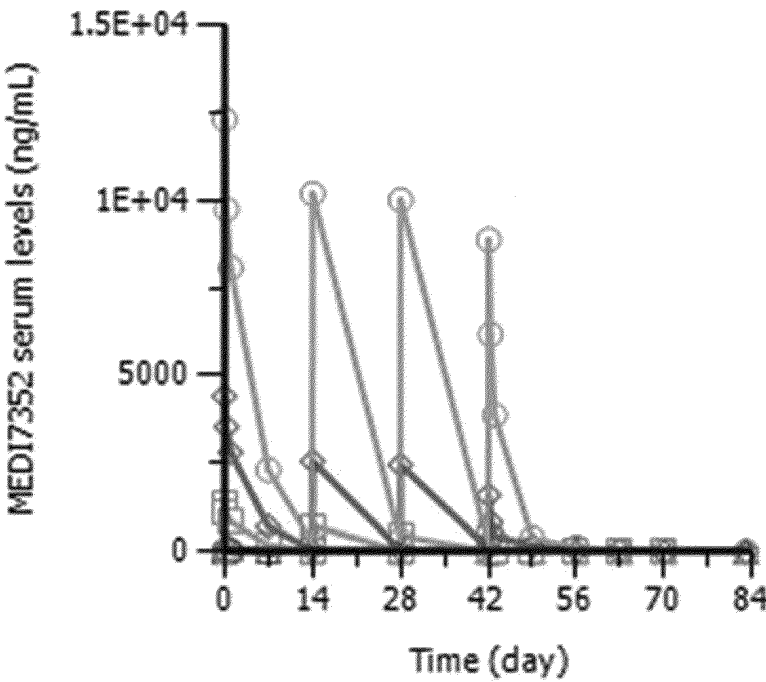


FIG 26B

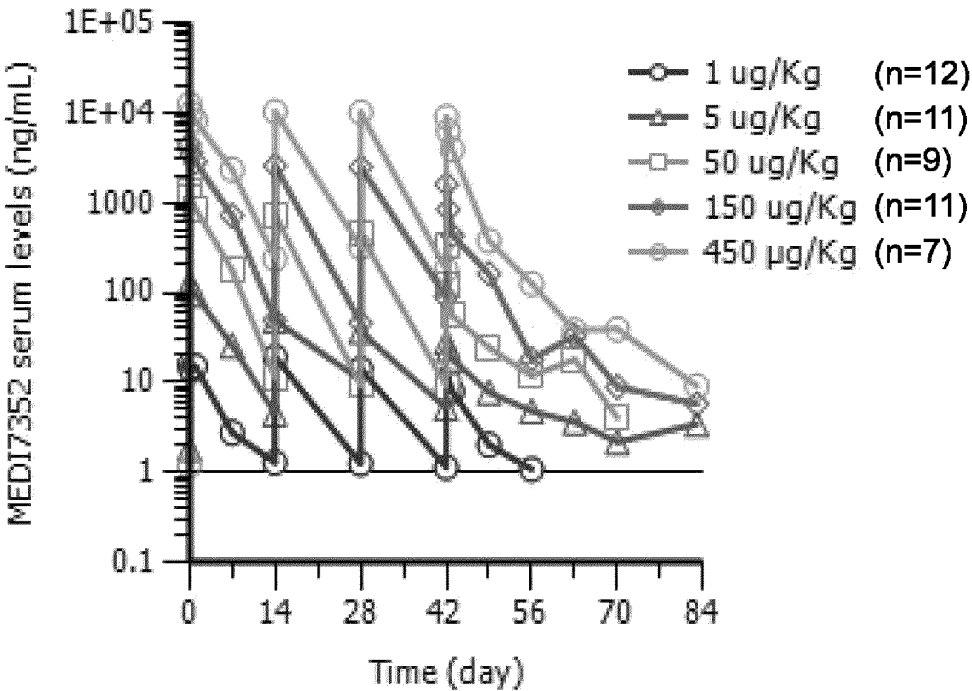
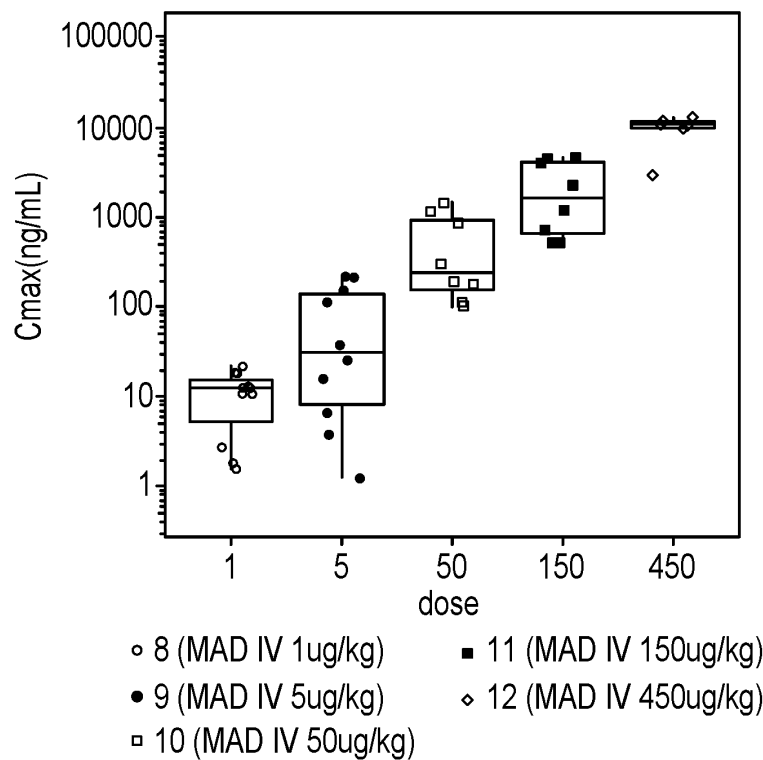


FIG. 27

C_{max} vs. Dose in MAD Cohorts (Day 43)



Change from Baseline at Week 8 (MAD Cohorts)

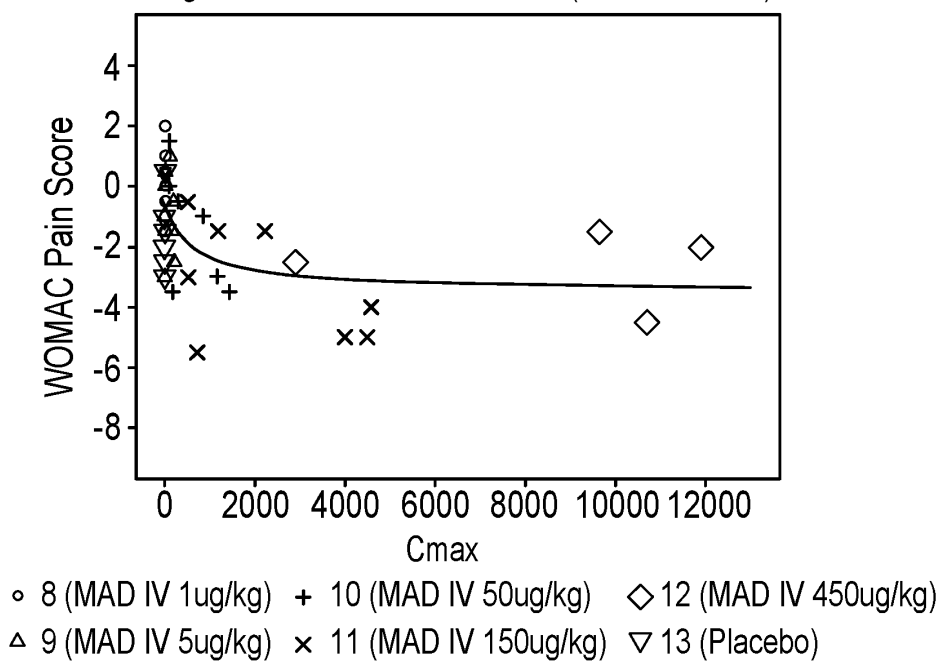
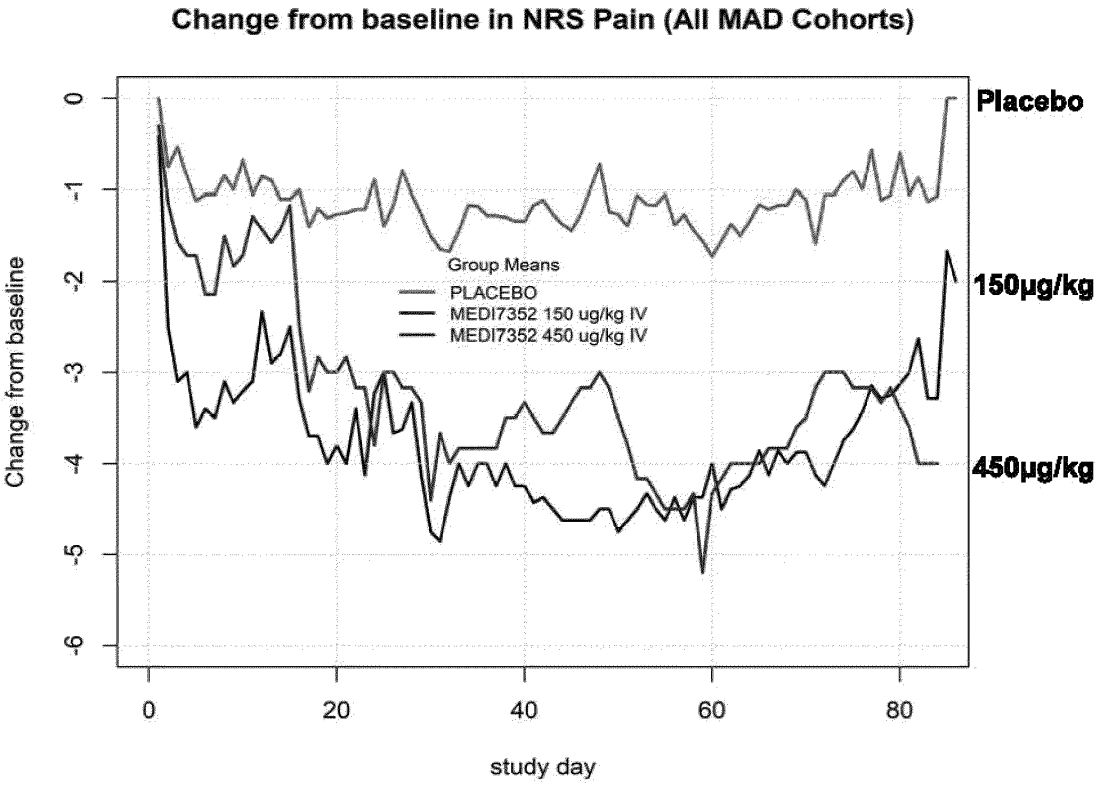


FIG 28A



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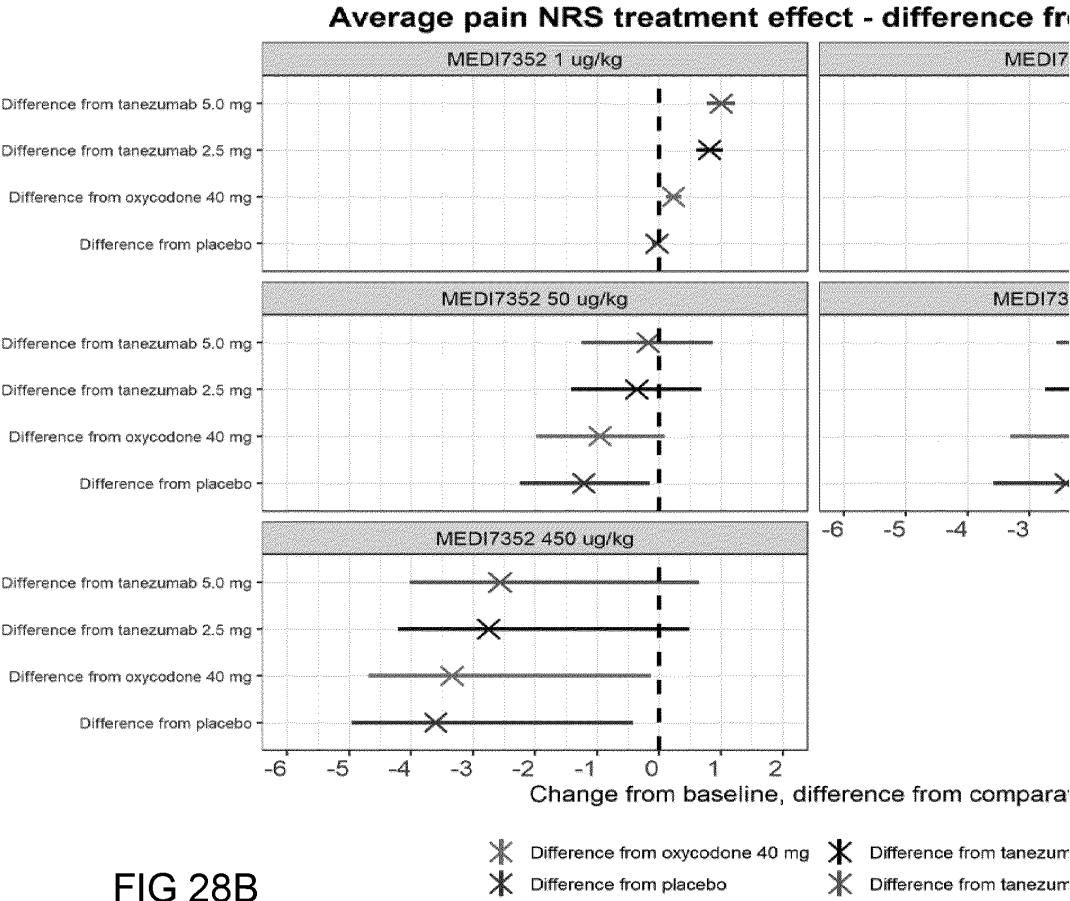


FIG 28B

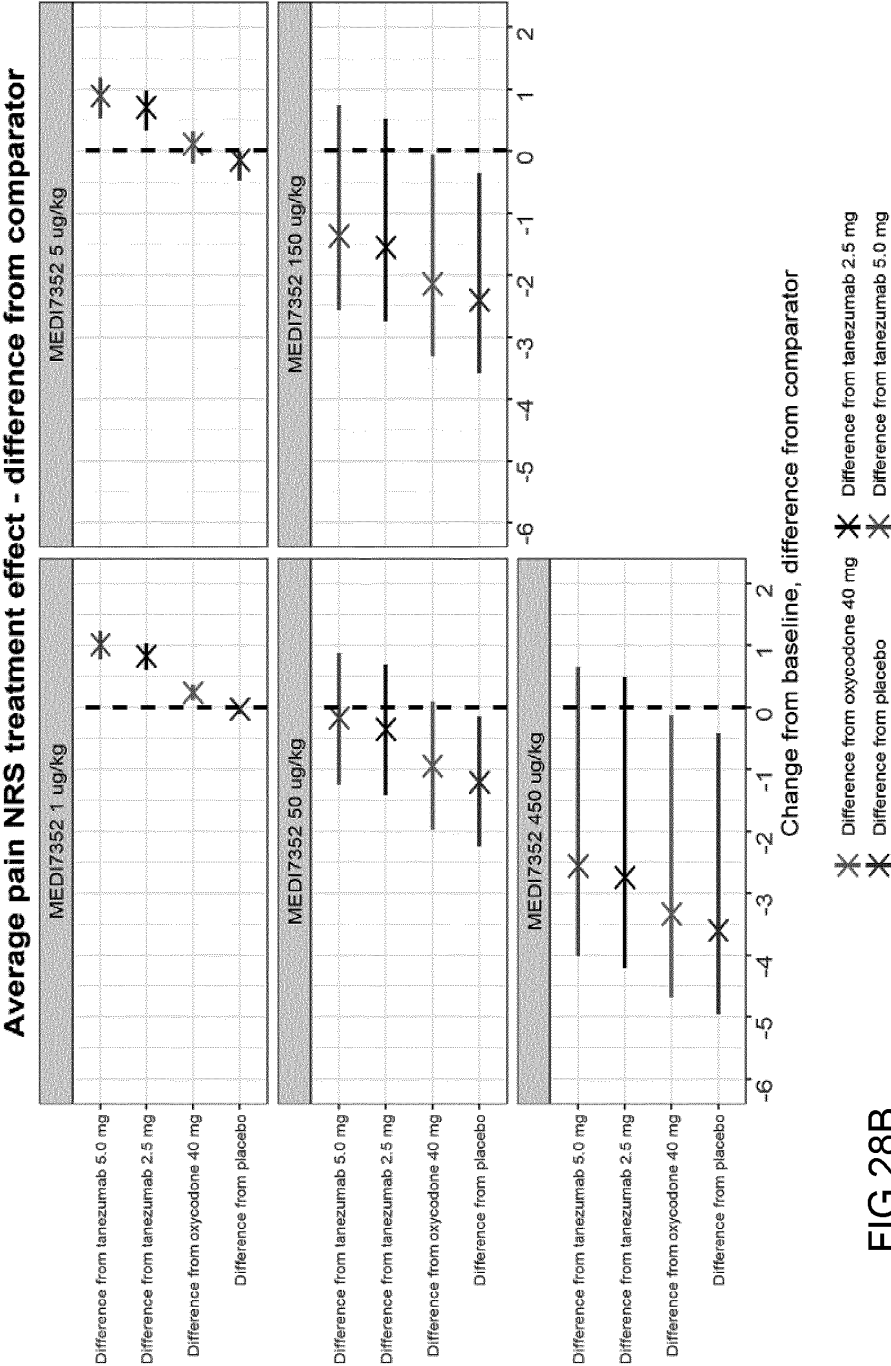


FIG 28B

FIG. 28C

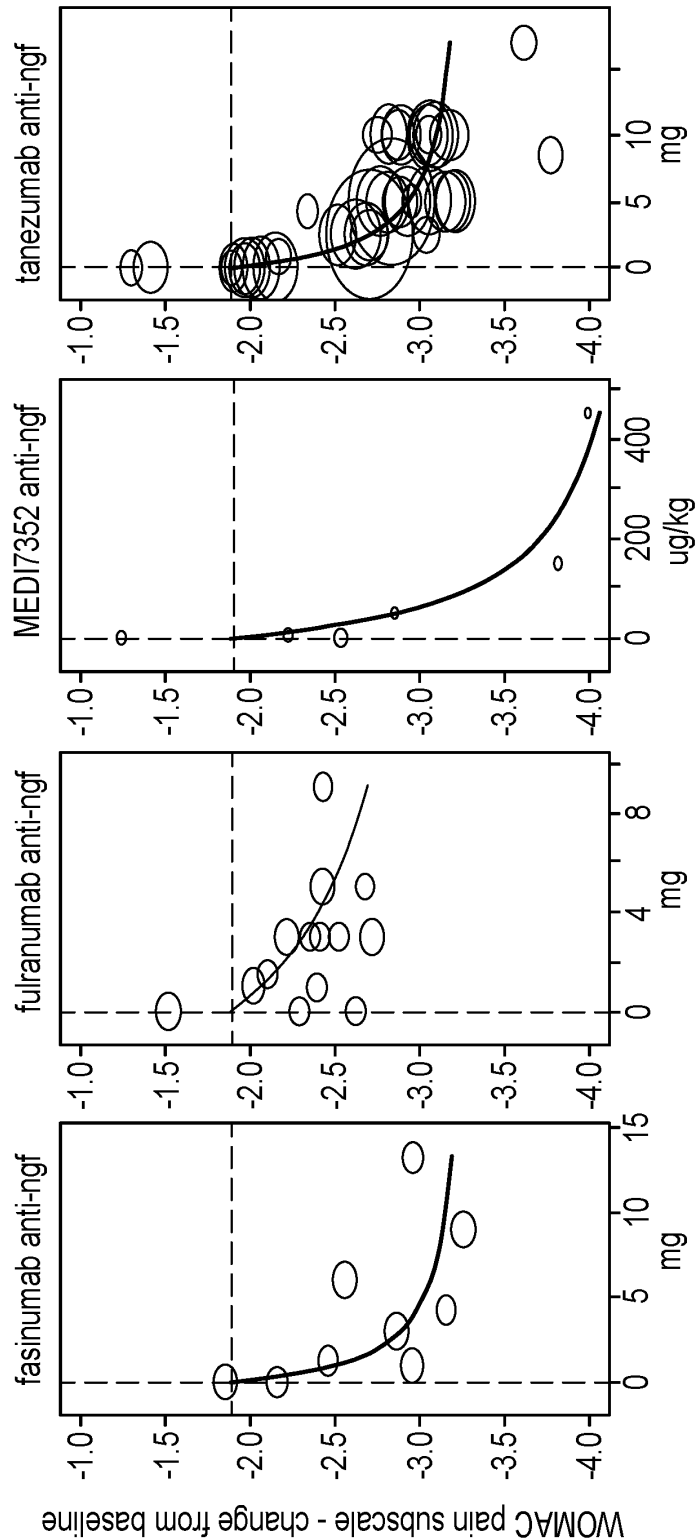
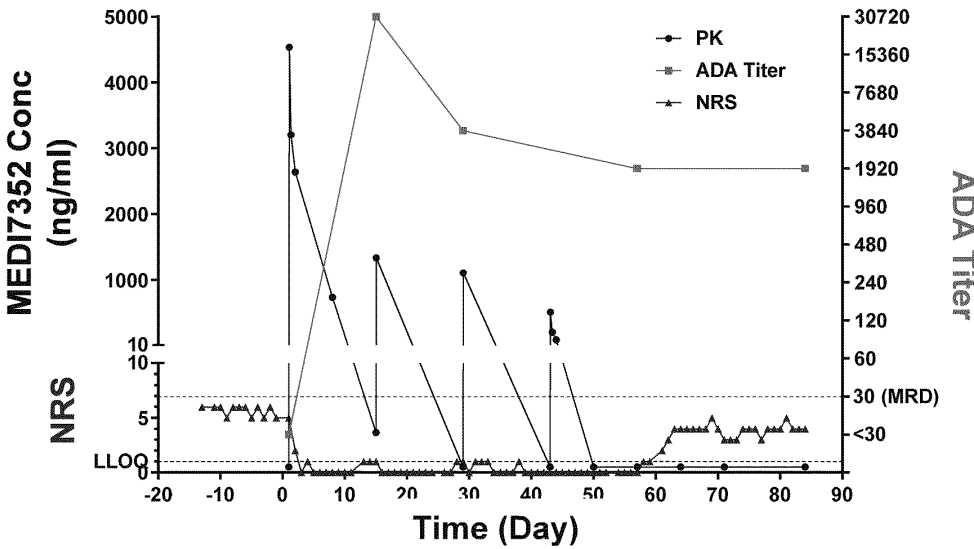
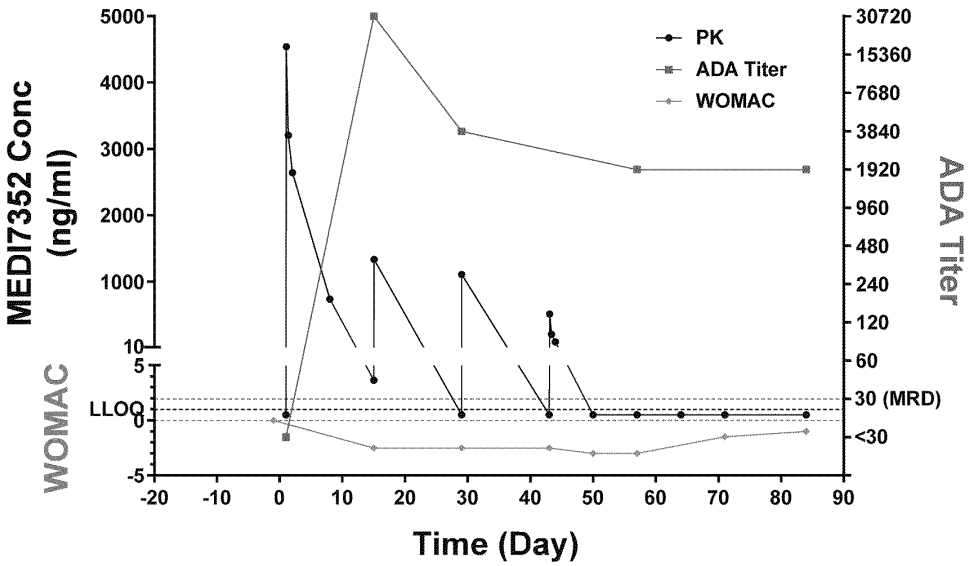


FIG 29



ADA titer: negative <30; median = 1920; Q3 = 7680

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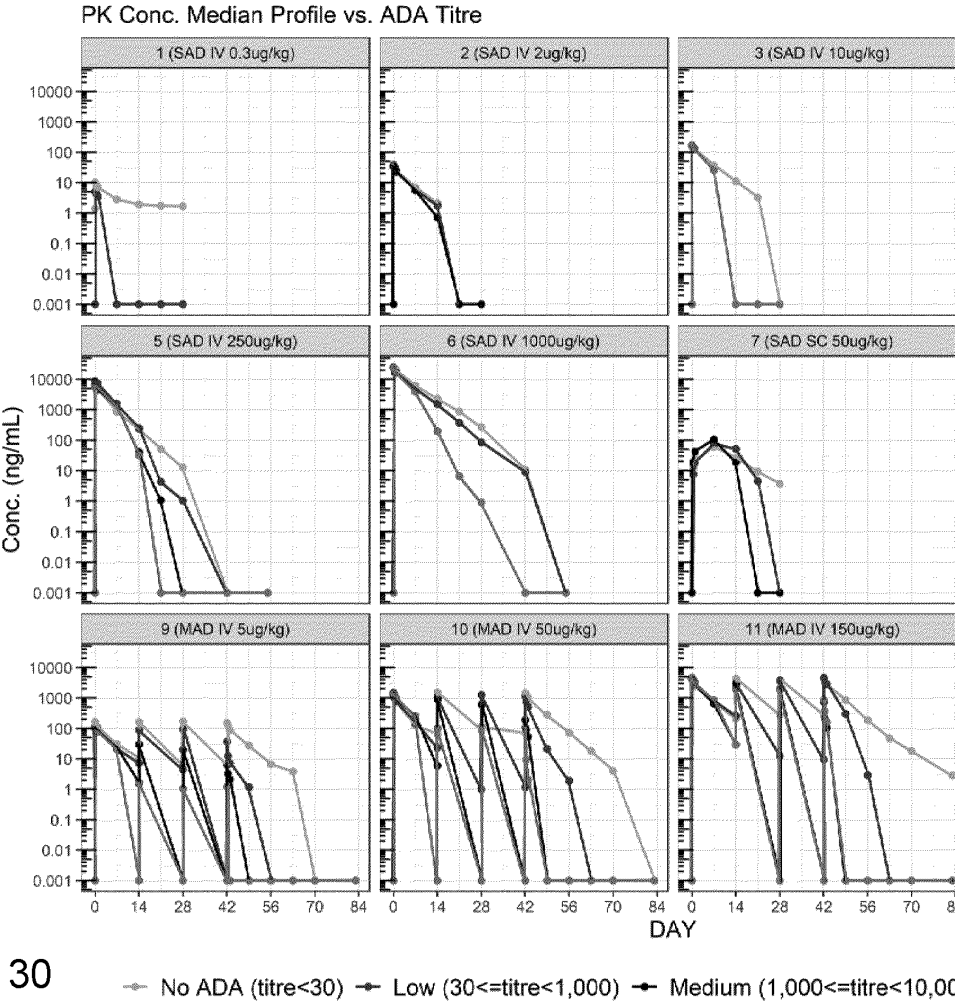


FIG 30

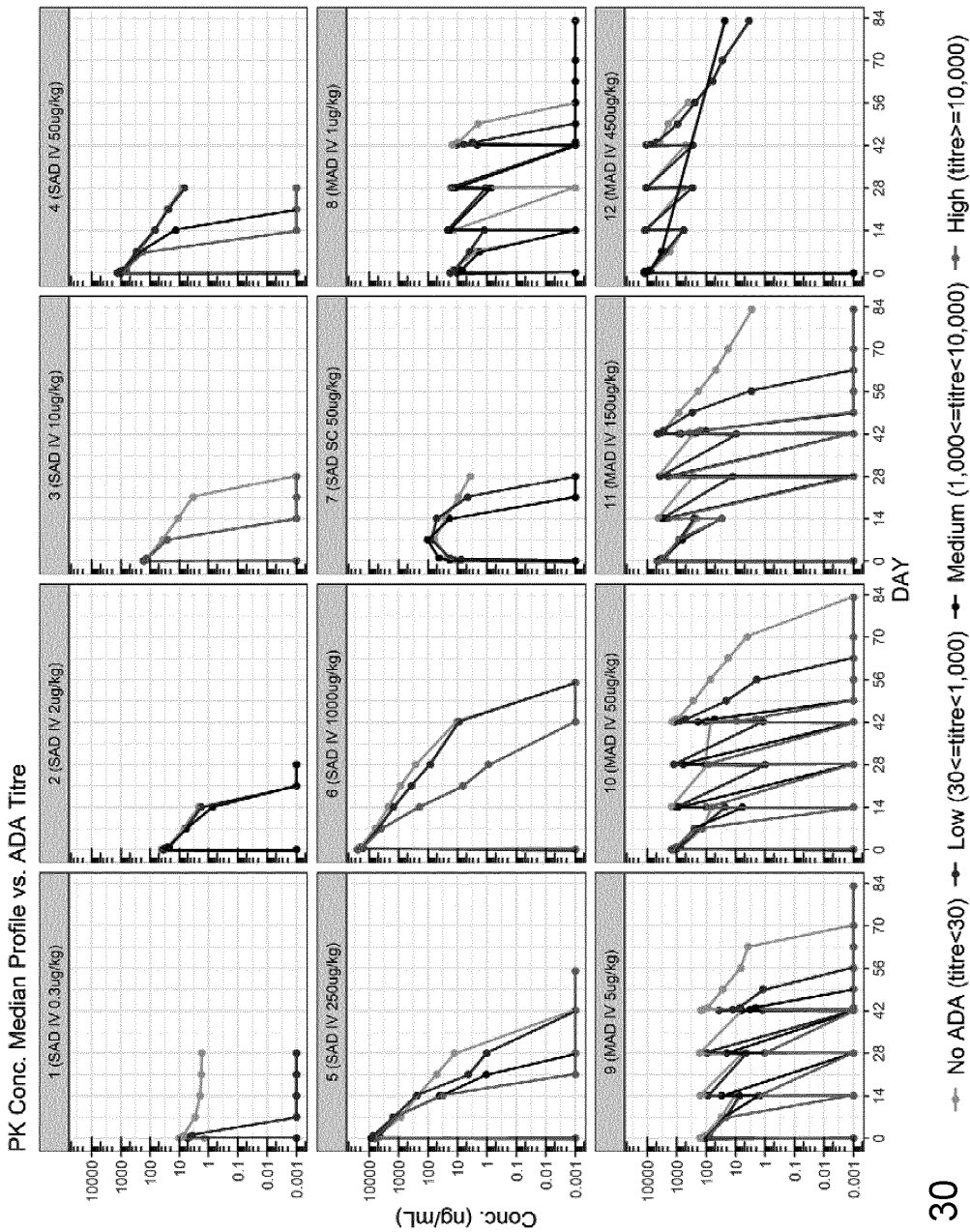
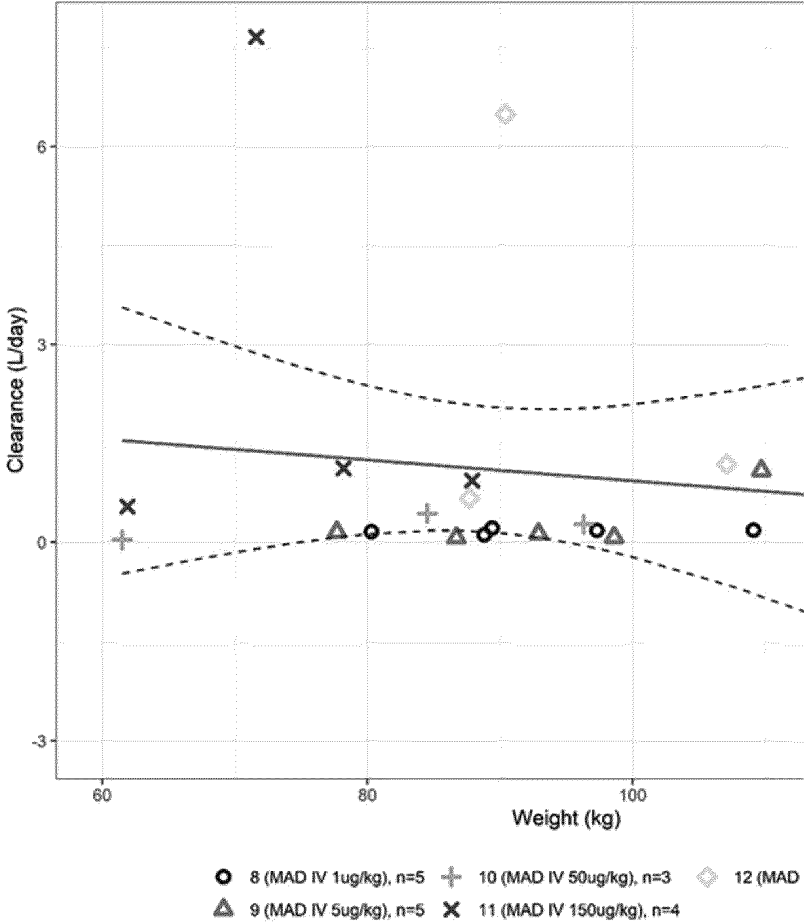


FIG 30



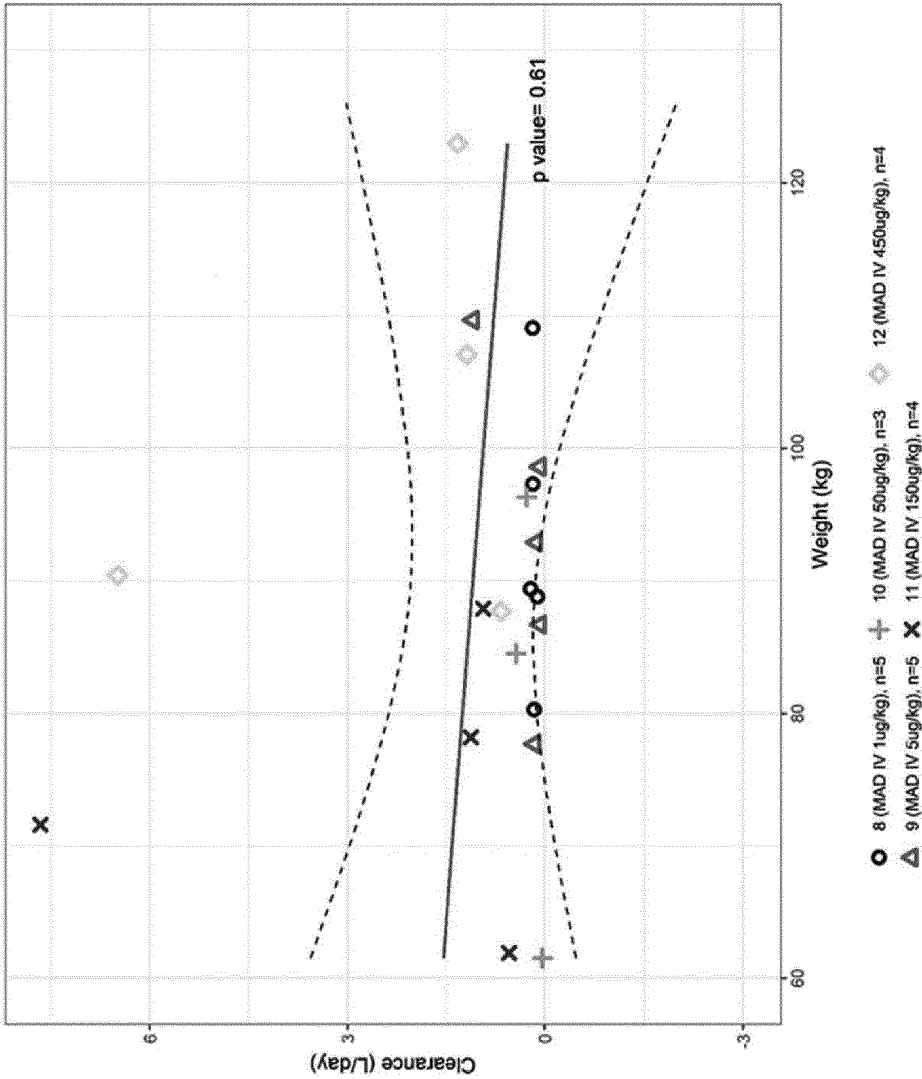


FIG 31

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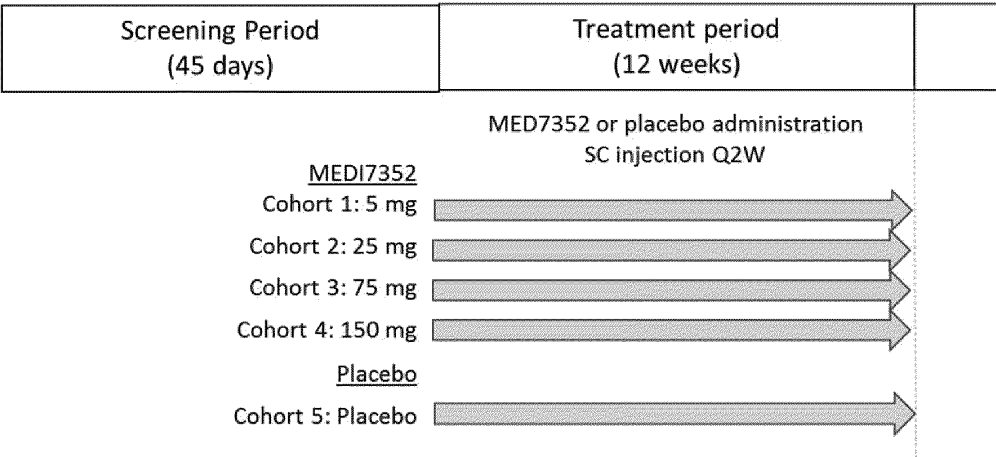


FIG 32

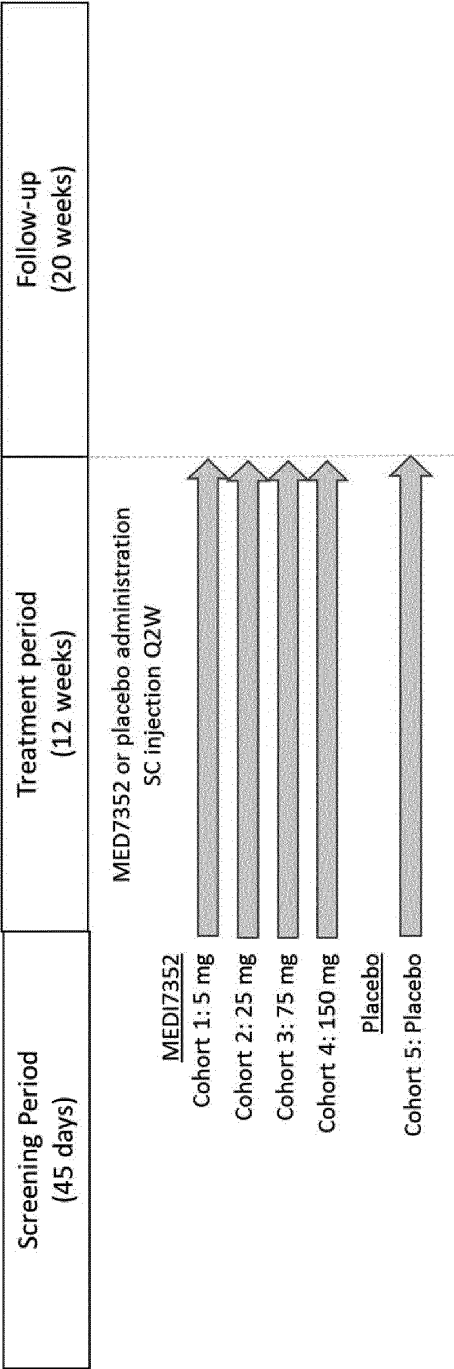


FIG 32