Figure 1A

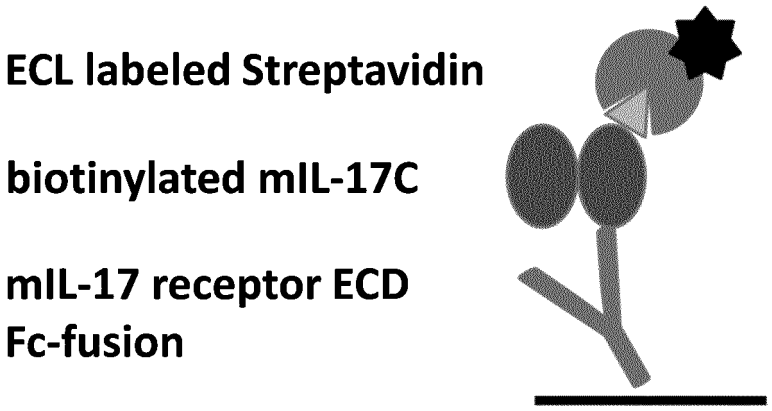

ECL labeled Streptavidin
biotinylated mIL-17C
mIL-17 receptor ECD
Fc-fusion

Figure 1B

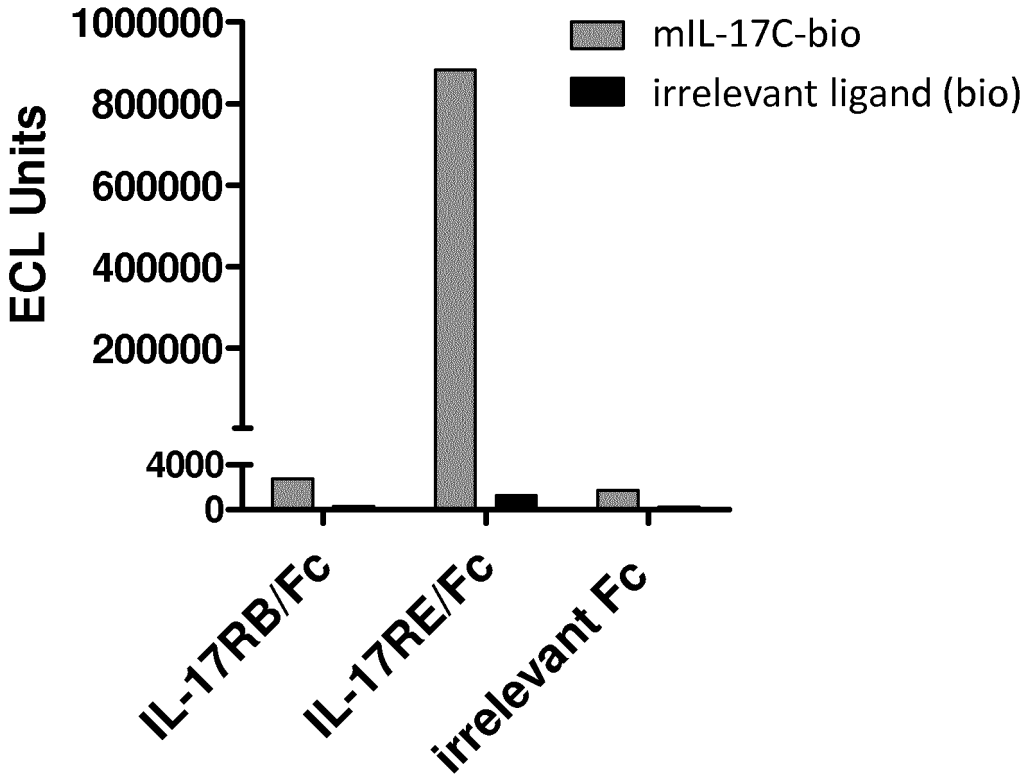

ECL Units
1000000
800000
600000
400000
200000
4000
0
mIL-17C-bio
irrelevant ligand (bio)
IL-17RB/Fc
IL-17RE/Fc
irrelevant Fc

Figure 1C

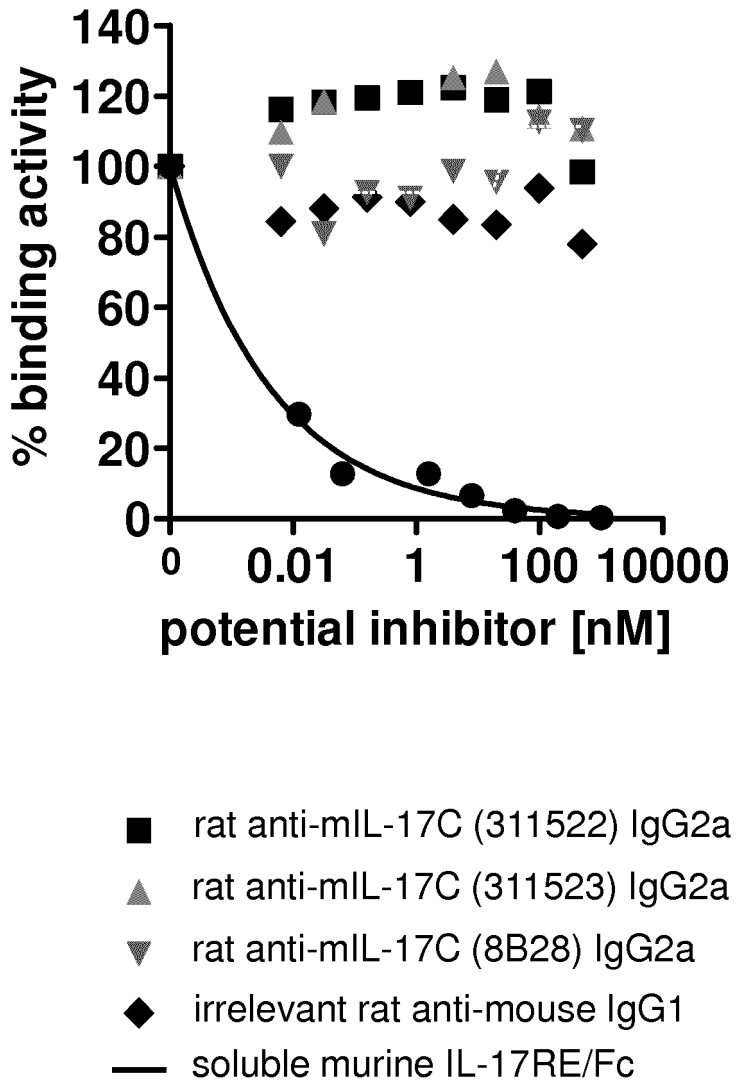

140
120
100
80
60
40
20
0
% binding activity
0
0.01
1
100
10000
potential inhibitor [nM]
rat anti-mIL-17C (311522) IgG2a
rat anti-mIL-17C (311523) IgG2a
rat anti-mIL-17C (8B28) IgG2a
irrelevant rat anti-mouse IgG1
soluble murine IL-17RE/Fc

Figure 2

			h/m IgG2a		
HCDR3 family	MOR	VL	SEC monomer portion [%]	yield culture purified [mg/l]	Comments
1	**12740**	lambda	93	9	low concentration
2	**12741**	lambda	95	23	
3	**12742**	lambda	8	10	failed in SEC
4	**12743**	lambda	98	23	
4	**12744**	lambda	98	16	
4	**12745**	lambda	94	28	
4	**12746**	lambda	99	18	
5	**12751**	lambda	96	19	
6	**12753**	lambda	92	3	low concentration
7	**12754**	kappa	93	28	
8	**12755**	lambda	96	26	
9	**12756**	lambda	92	25	
10	**12757**	kappa	98	22	
11	**12758**	lambda	93	29	
12	**12759**	kappa	97	18	
12	**12760**	kappa	91	17	
12	**12761**	kappa	97	24	
12	**12762**	kappa	97	28	

Figure 3

			Binding (ELISA)			
HCDR3 family	MOR	VL	mIL-17C EC_{50} [nM] n=1-2	huIL-17C	mslL-17B	lysozyme
1	**12740**	lambda	1.14 ± 0.11	No binding	No binding	No binding
2	**12741**	lambda	0.47 ± 0.1			
4	**12743**	lambda	0.3			
4	**12744**	lambda	0.28 ± 0.1			
4	**12745**	lambda	0.4			
4	**12746**	lambda	0.38 ±0.25			
5	**12751**	lambda	0.39 ± 0.0			
8	**12754**	kappa	0.40 ± 0.01			
13	**12759**	kappa	0.29± 0.18			
13	**12760**	kappa	0.27 ± 0.1			
13	**12761**	kappa	0.36 ± 0.15			
13	**12762**	kappa	0.4			

Figure 4

			Affinity (Fab)
HCDR3 family	**MOR**	**VL**	**KD [pM]**
1	**12740**	lambda	170
2	**12741**	lambda	*
3	**12742**	lambda	* (not available as IgG2a)
4	**12743**	lambda	48
4	**12744**	lambda	53
4	**12745**	lambda	75
4	**12746**	lambda	56
5	**12751**	lambda	*
6	**12753**	lambda	62 (not available as IgG2a)
7	**12754**	kappa	4100
8	**12755**	lambda	no signal
9	**12756**	lambda	no signal
10	**12757**	kappa	no signal
11	**12758**	lambda	no signal
12	**12759**	kappa	220
12	**12760**	kappa	**
12	**12761**	kappa	85
12	**12762**	kappa	96

*= no sigmoidal binding
**= Fab precipitates

Figure 5

HCDR3 family	MOR	VL	mIL17C - mIL-17RE inhibition assay IC_{50} [pM]
1	**12740**	lambda	3493 ± 142
2	**12741**	lambda	incomplete inhibition
4	**12743**	lambda	16 ± 5.4
4	**12744**	lambda	12 ± 3.7
4	**12745**	lambda	13 ± 7.3
4	**12746**	lambda	23 ± 13
5	**12751**	lambda	160 ± 93.6
8	**12754**	kappa	8442 ± 1494
13	**12759**	kappa	28 ± 2.7
13	**12760**	kappa	122 ± 43.9
13	**12761**	kappa	24 ± 6
13	**12762**	kappa	9 ± 1.8

Figure 6

HCDR3 family	MOR	VL	Mouse Serum Stability Assay 24h/37°C Coefficient of variation
1	**12740**	lambda	n.d.
2	**12741**	lambda	13.01%
3	**12743**	lambda	2.88%
3	**12744**	lambda	11.78%
3	**12745**	lambda	15.94%
3	**12746**	lambda	7.36%
4	**12751**	lambda	3.75%
5	**12754**	kappa	17.00%
6	**12759**	kappa	8.80%
6	**12760**	kappa	35.31%
6	**12761**	kappa	1.23%
6	**12762**	kappa	2.43%

Figure 7

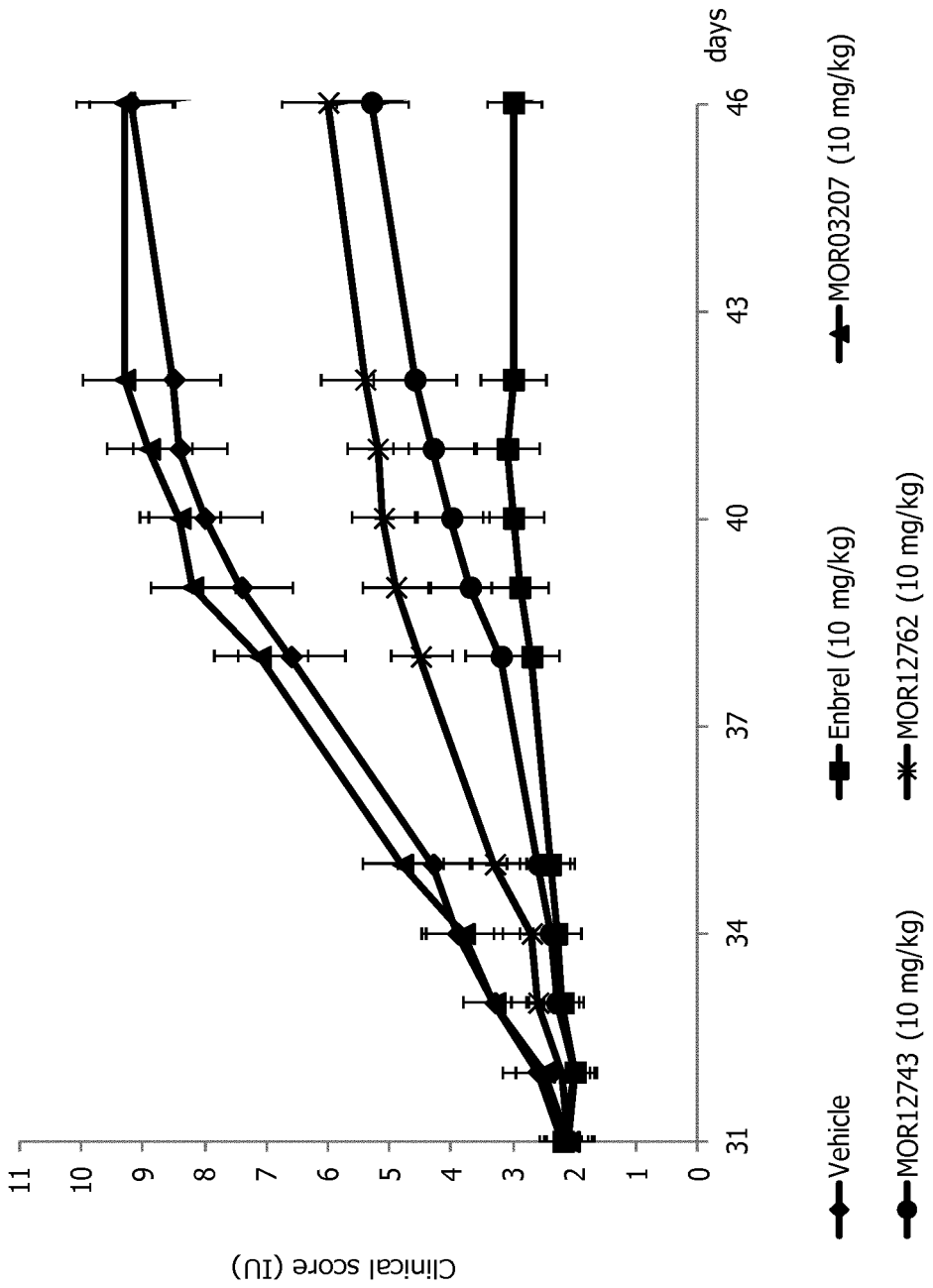

Clinical score (IU)
0
1
2
3
4
5
6
7
8
9
10
11
31
34
37
40
43
46
days
Vehicle
Enbrel (10 mg/kg)
MOR03207 (10 mg/kg)
MOR12743 (10 mg/kg)
MOR12762 (10 mg/kg)

Figure 8

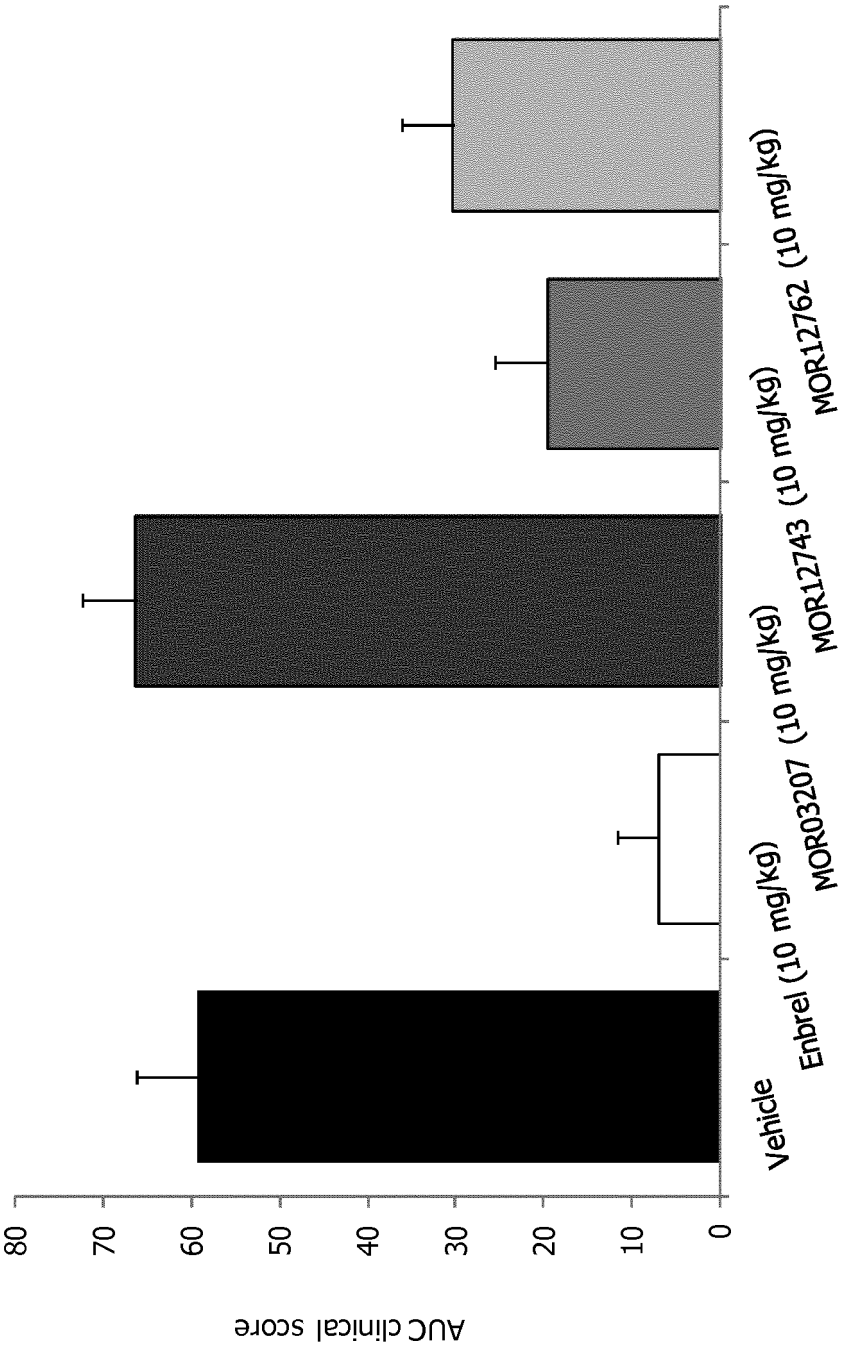

AUC clinical score
0
10
20
30
40
50
60
70
80
Vehicle
Enbrel (10 mg/kg)
MOR03207 (10 mg/kg)
MOR12743 (10 mg/kg)
MOR12762 (10 mg/kg)

Figure 9

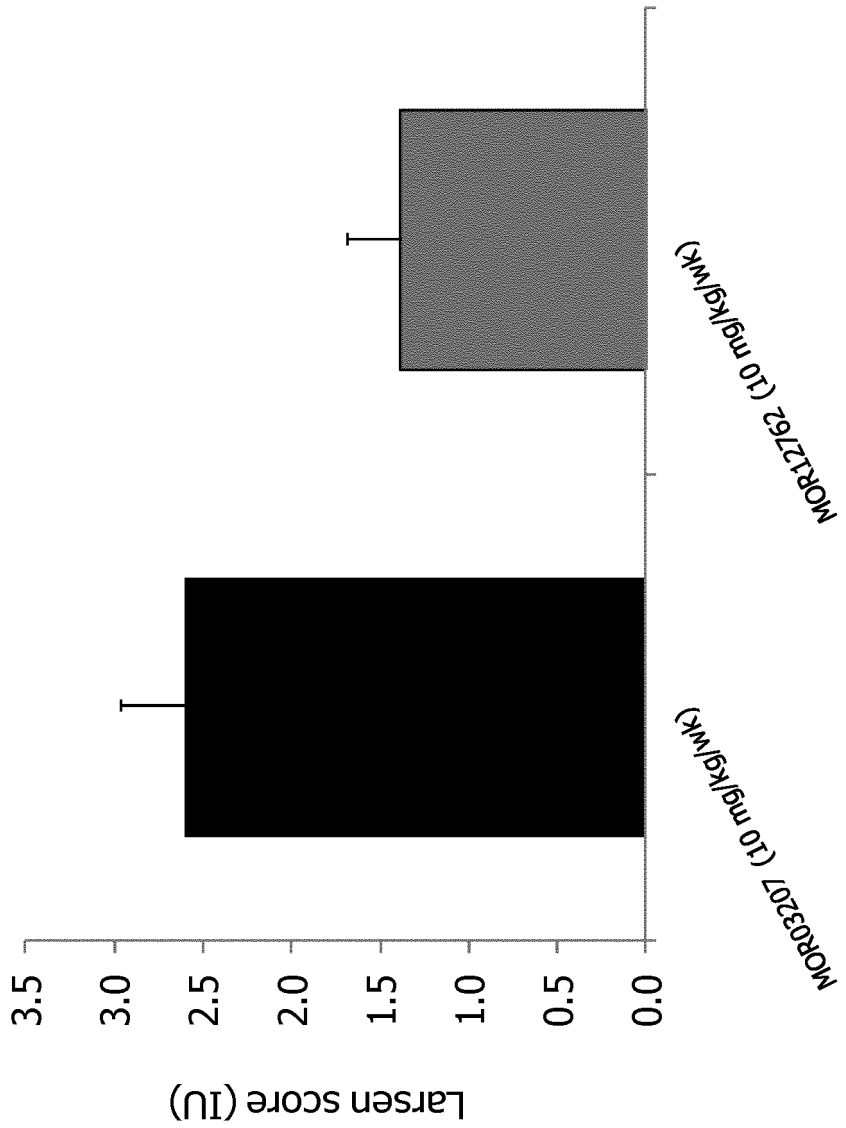

Larsen score (IU)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
MOR03207 (10 mg/kg/wk)
MOR12762 (10 mg/kg/wk)

Figure 10

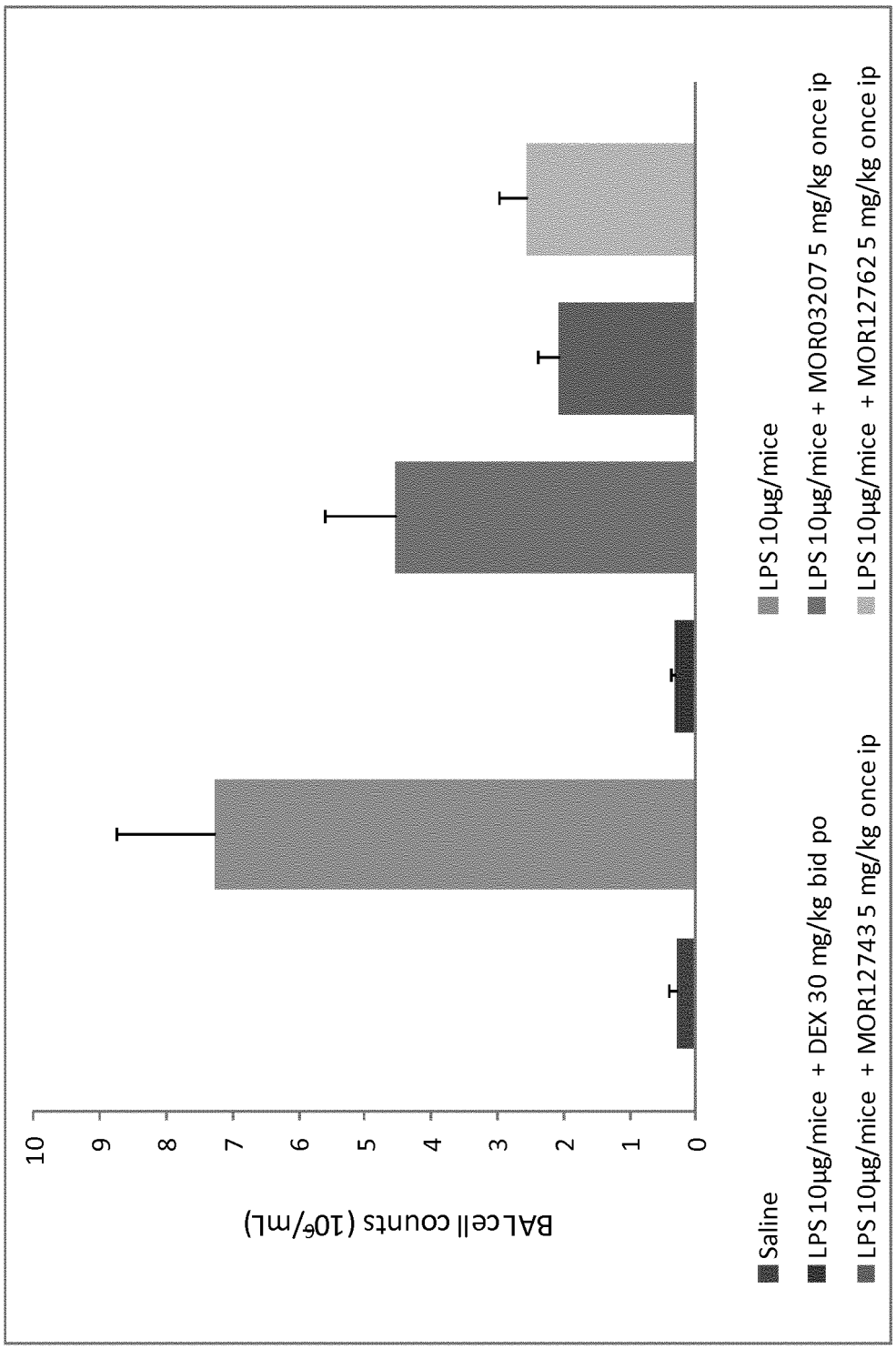

BAL cell counts (10⁶/mL)
10
9
8
7
6
5
4
3
2
1
0
Saline
LPS 10µg/mice + DEX 30 mg/kg bid po
LPS 10µg/mice + MOR12743 5 mg/kg once ip
LPS 10µg/mice
LPS 10µg/mice + MOR03207 5 mg/kg once ip
LPS 10µg/mice + MOR12762 5 mg/kg once ip

Figure 11

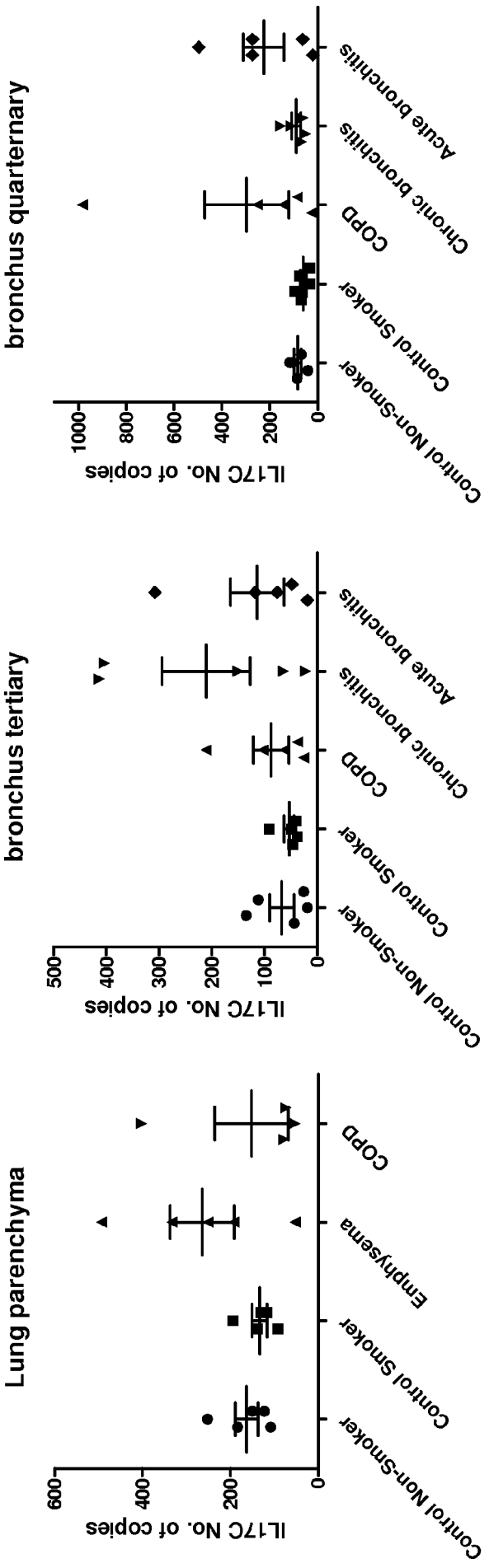
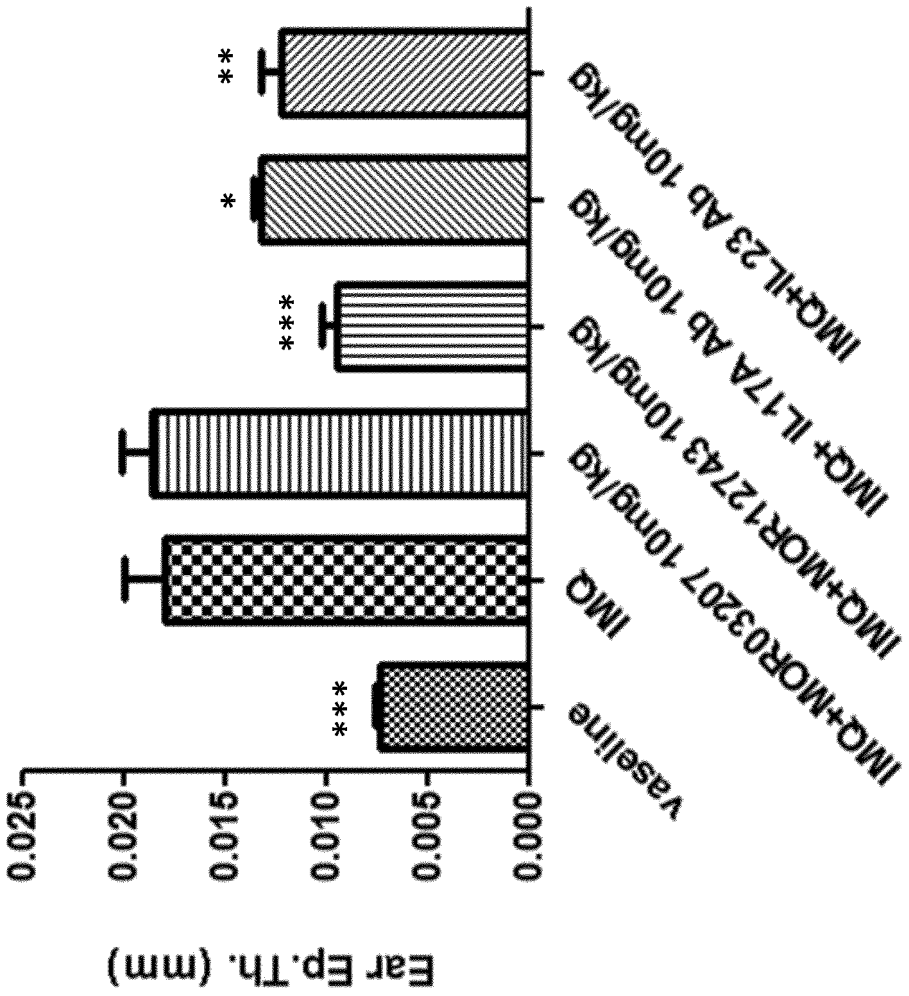

Lung parenchyma
IL17C No. of copies
0
200
400
600
Control Non-Smoker
Control Smoker
Emphysema
COPD
bronchus tertiary
IL17C No. of copies
0
100
200
300
400
500
Control Non-Smoker
Control Smoker
COPD
Chronic bronchitis
Acute bronchitis
bronchus quarternary
IL17C No. of copies
0
200
400
600
800
1000
Control Non-Smoker
Control Smoker
COPD
Chronic bronchitis
Acute bronchitis

Figure 12



*p<0.05, **p<0.01, ***p<0.0001 vs IMQ Control with Anova, Dunnett's-Test

Figure 13A

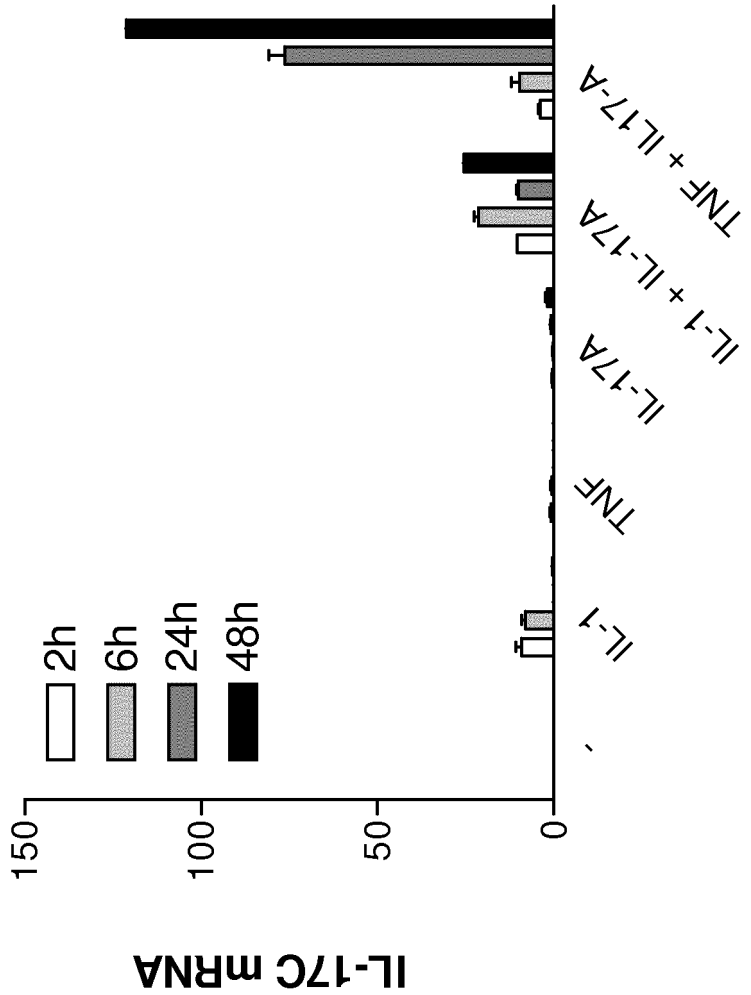
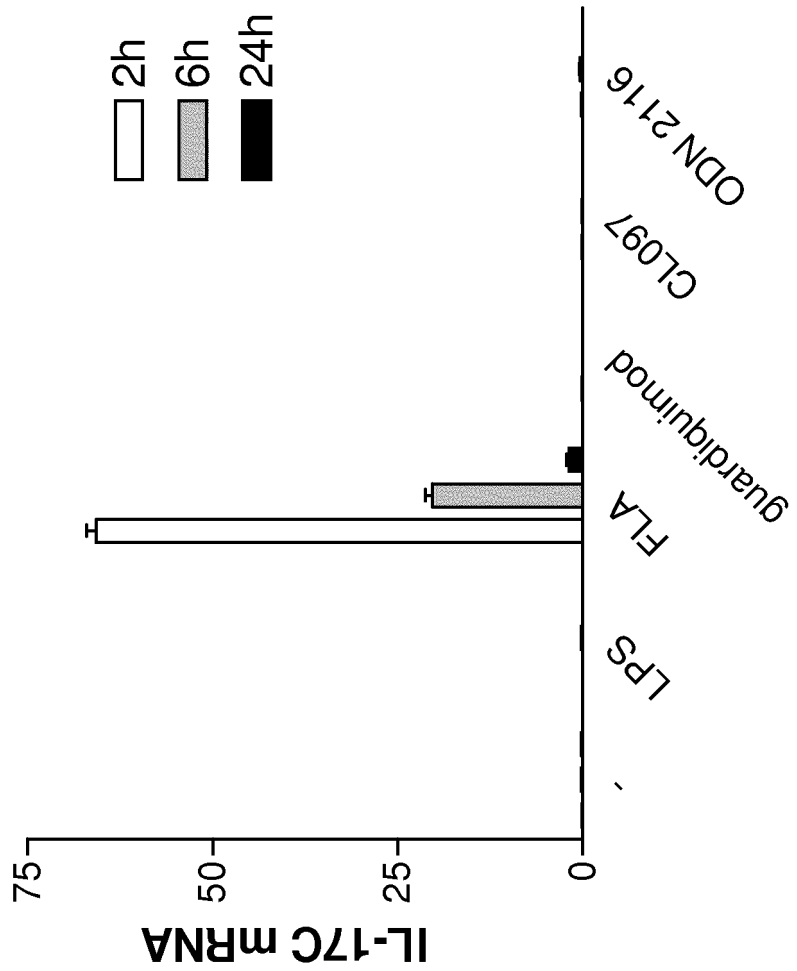

IL-17C mRNA
150
100
50
0
2h
6h
24h
48h
-
IL-1
TNF
IL-17A
IL-1 + IL-17A
TNF + IL17-A

Figure 13B


2h
6h
24h
IL-17C mRNA
75
50
25
0
-
LPS
FLA
guardiquimod
CL097
ODN 2116