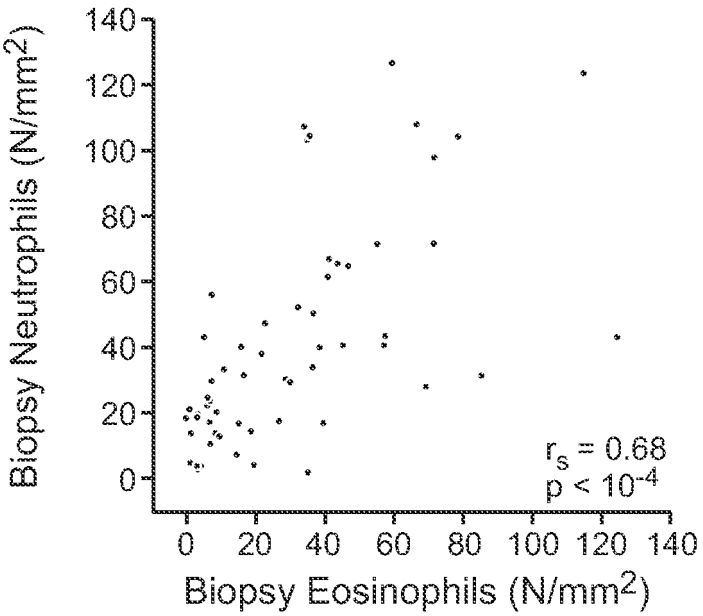


FIG. 1A

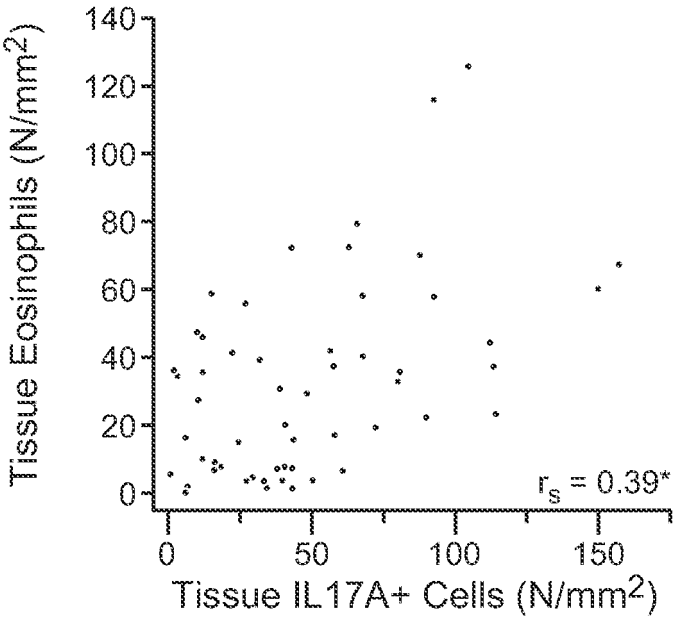


FIG. 1B

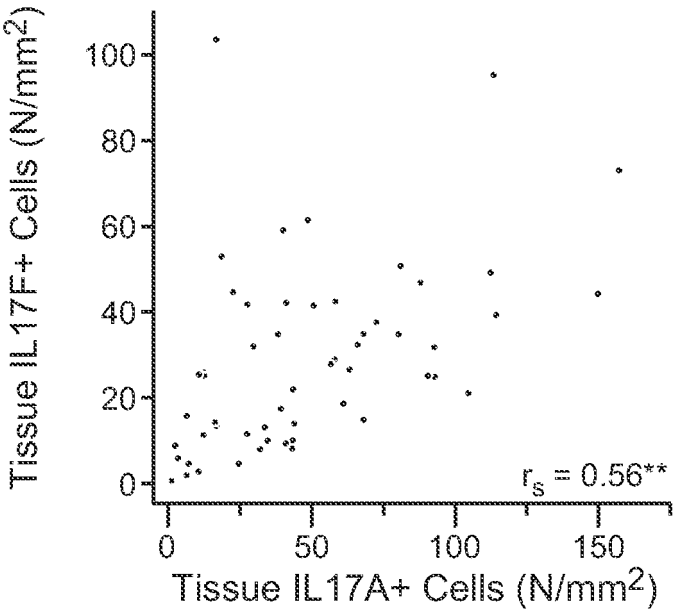


FIG. 1C

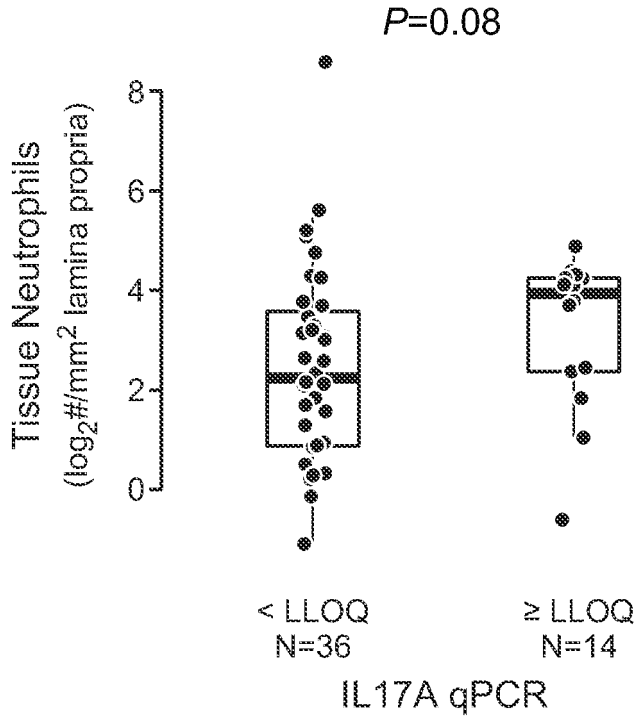

P=0.08
Tissue Neutrophils
(log2#/mm2 lamina propria)
0
2
4
6
8
< LLOQ
N=36
≥ LLOQ
N=14
IL17A qPCR

FIG. 2A

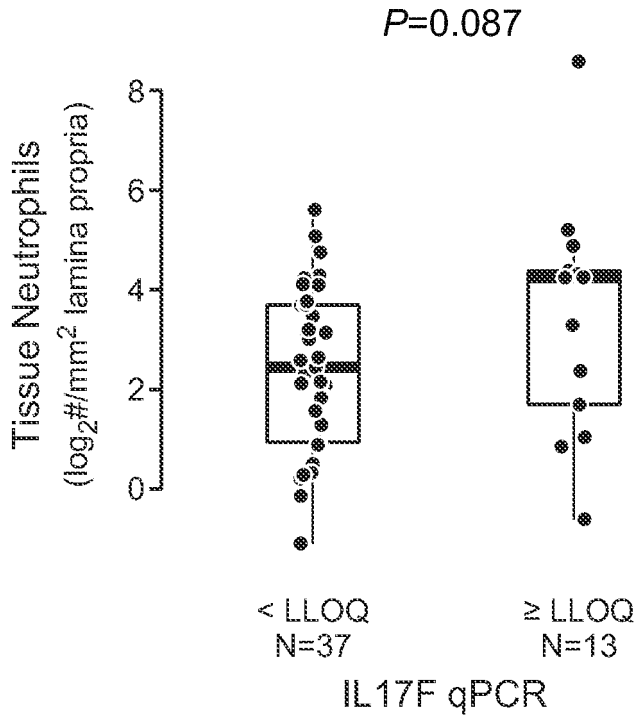

P=0.087
Tissue Neutrophils
(log2#/mm2 lamina propria)
0
2
4
6
8
< LLOQ
N=37
≥ LLOQ
N=13
IL17F qPCR

FIG. 2B

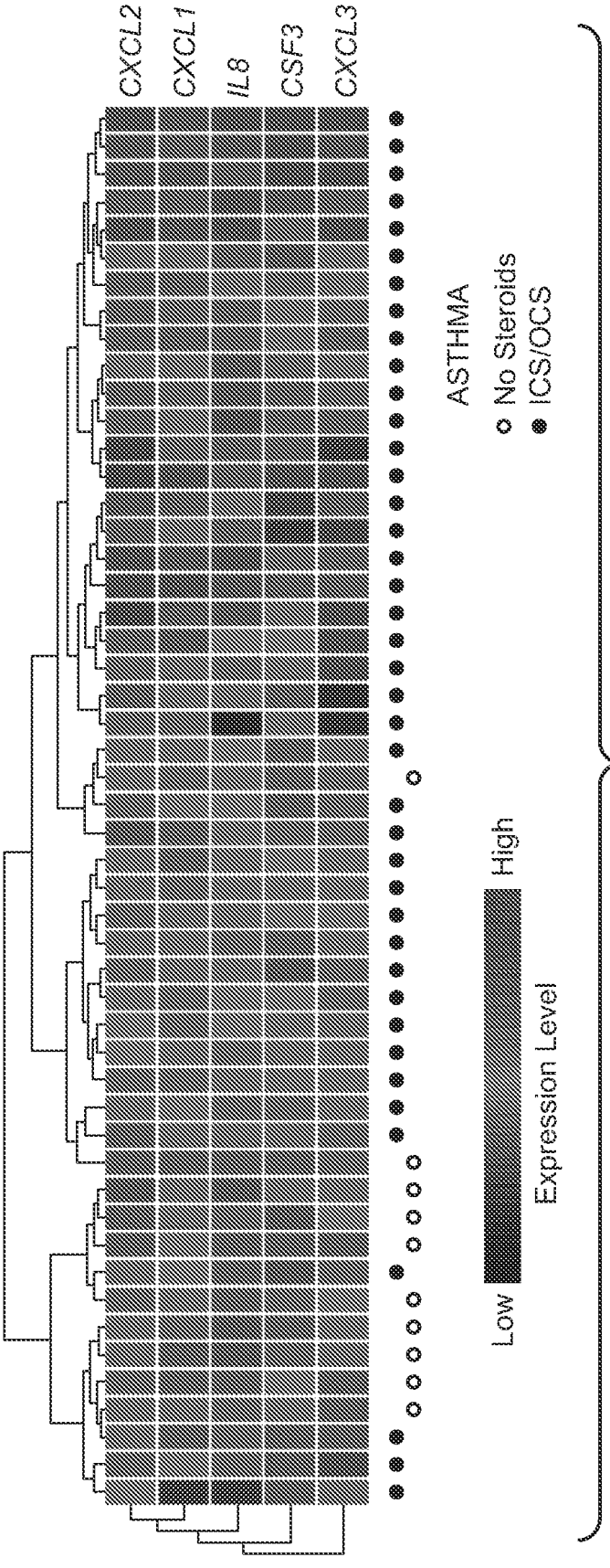

CXCL2
CXCL1
IL8
CSF3
CXCL3
ASTHMA
No Steroids
ICS/OCS
Low
High
Expression Level

FIG. 3

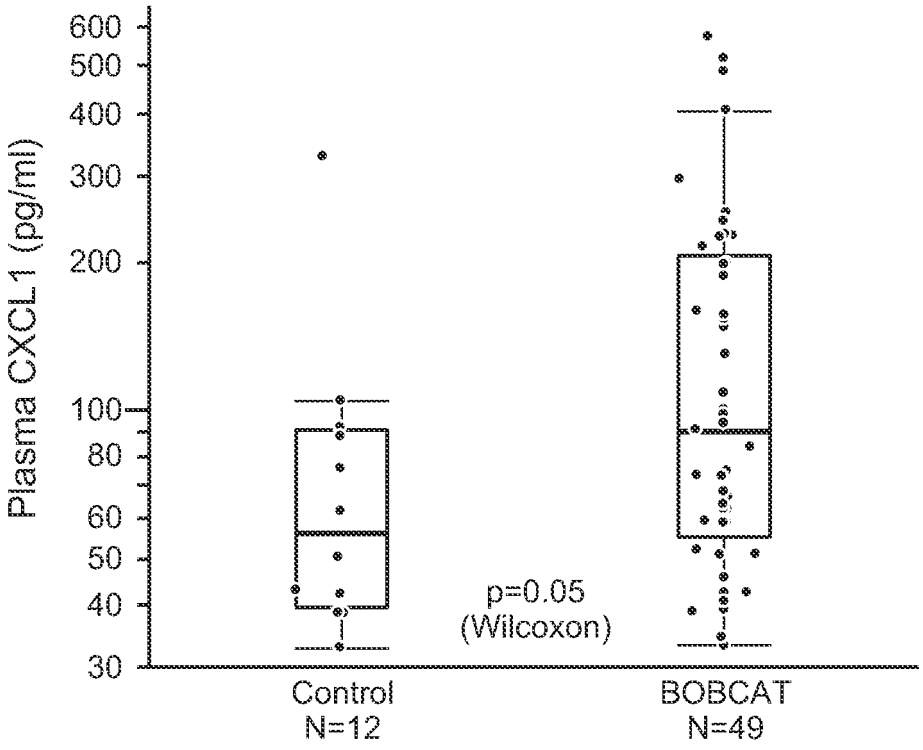

Plasma CXCL1 (pg/ml)
600
500
400
300
200
100
80
60
50
40
30
p=0.05
(Wilcoxon)
Control
N=12
BOBCAT
N=49

FIG. 4A

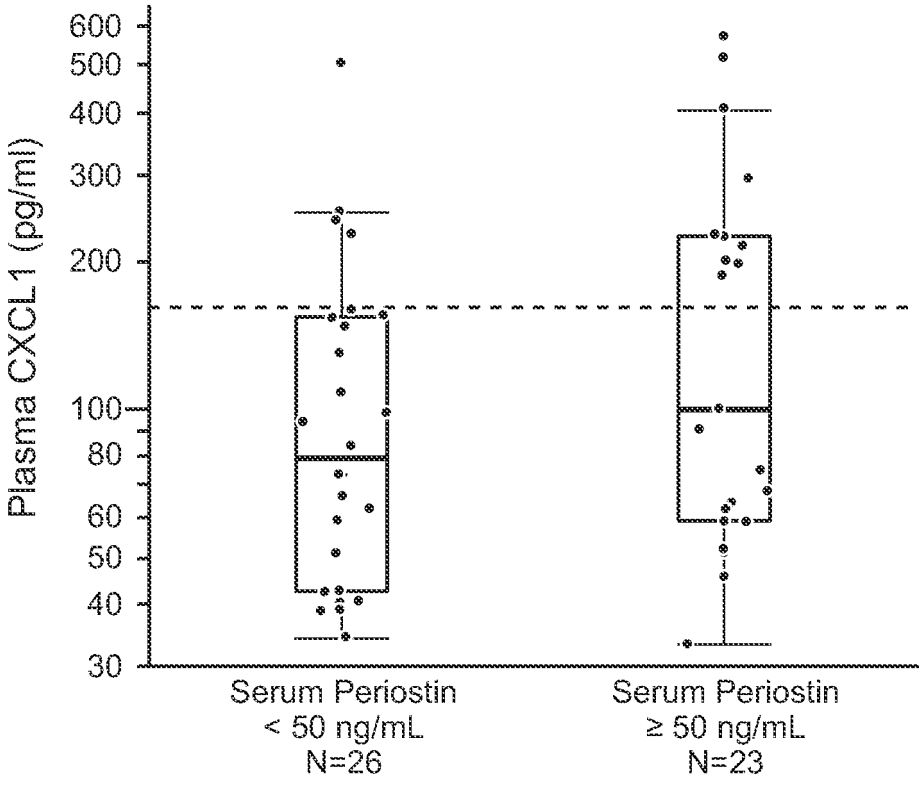

Plasma CXCL1 (pg/ml)
600
500
400
300
200
100
80
60
50
40
30
Serum Periostin
< 50 ng/mL
N=26
Serum Periostin
≥ 50 ng/mL
N=23

FIG. 4B

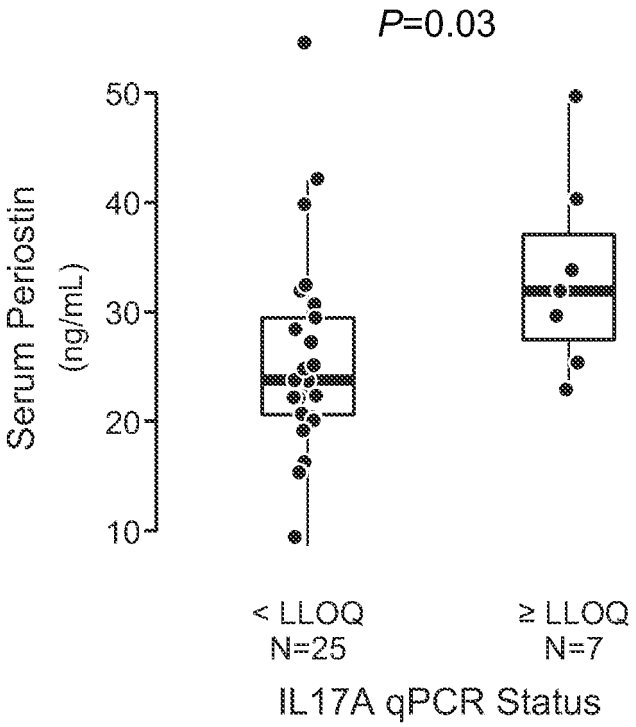

P=0.03
Serum Periostin (ng/mL)
50
40
30
20
10
< LLOQ
N=25
≥ LLOQ
N=7
IL17A qPCR Status

FIG. 5

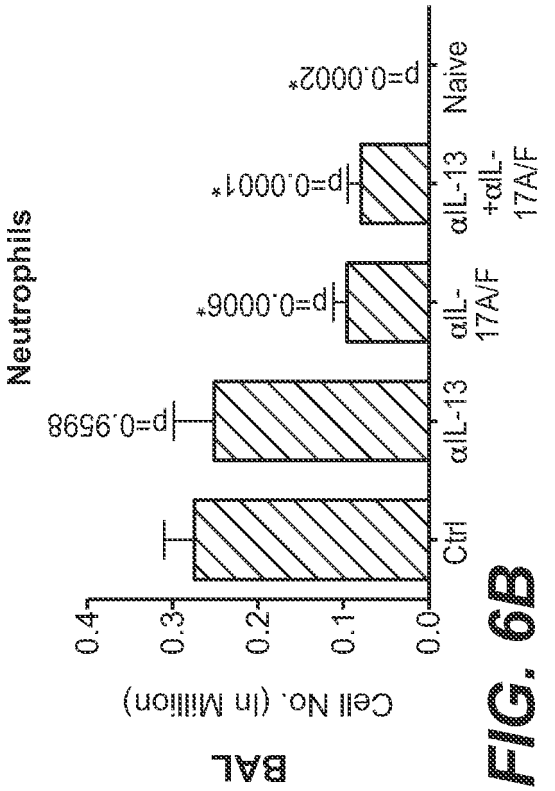


FIG. 6B

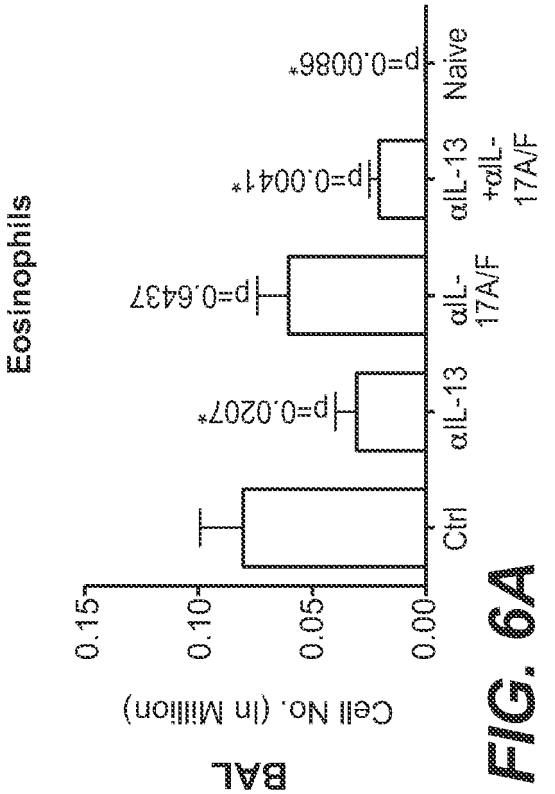


FIG. 6A

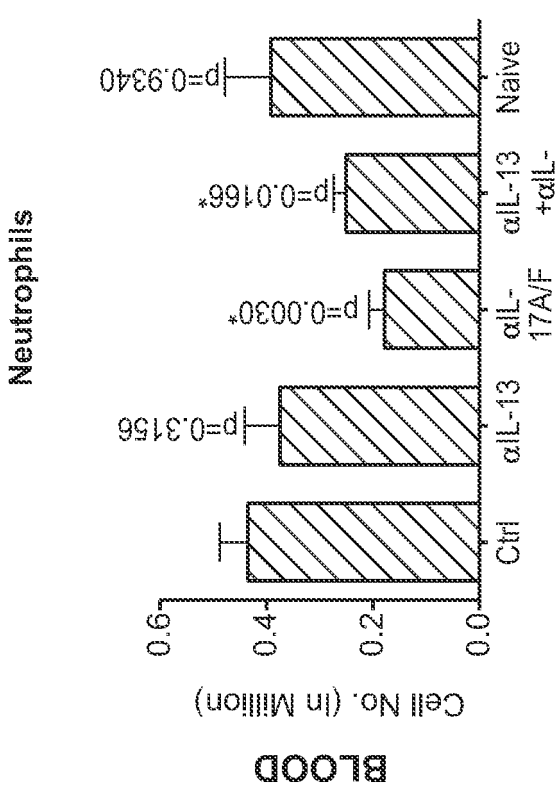


FIG. 6D

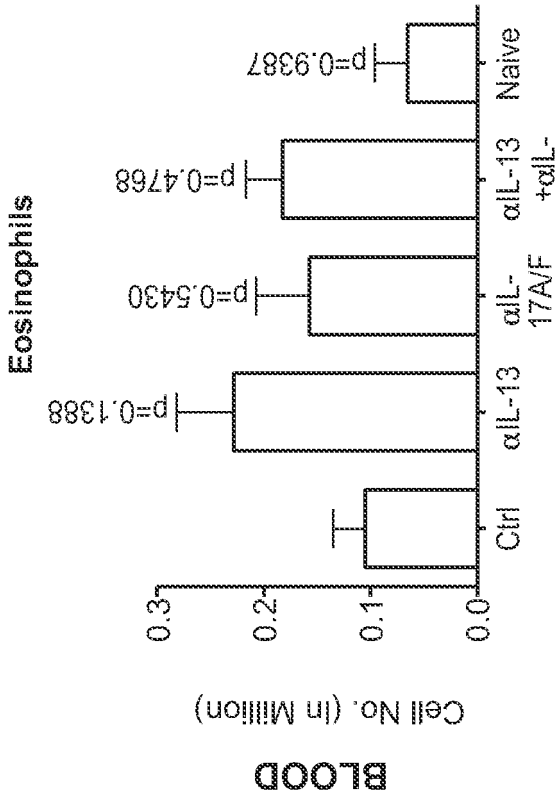


FIG. 6C

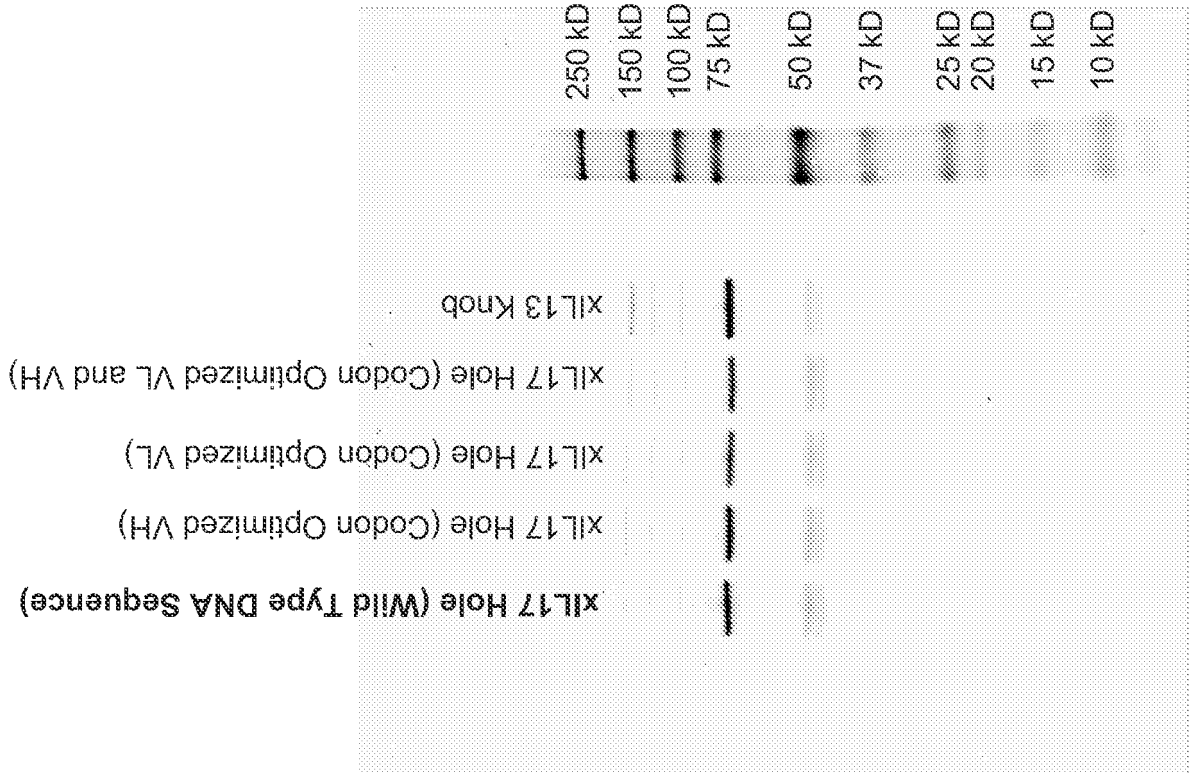

xIL17 Hole (Wild Type DNA Sequence)
xIL17 Hole (Codon Optimized VH)
xIL17 Hole (Codon Optimized VL)
xIL17 Hole (Codon Optimized VL and VH)
xIL13 Knob
250 kD
150 kD
100 kD
75 kD
50 kD
37 kD
25 kD
20 kD
15 kD
10 kD

FIG. 7A

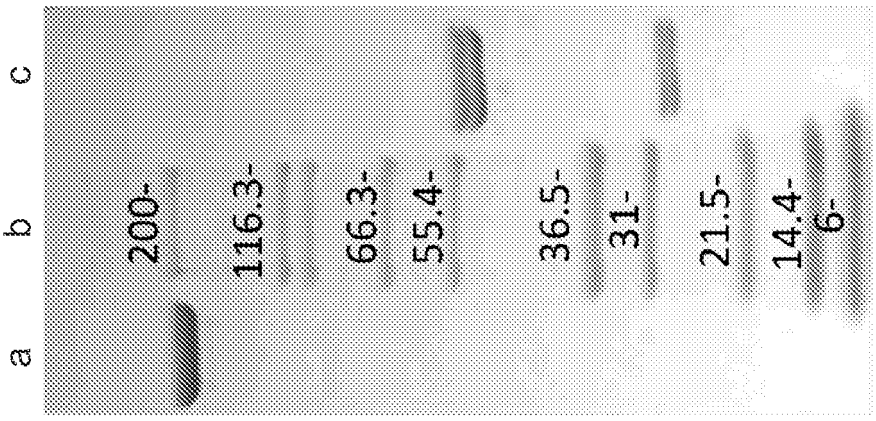

a
b
c
200-
116.3-
66.3-
55.4-
36.5-
31-
21.5-
14.4-
6-

FIG. 7C

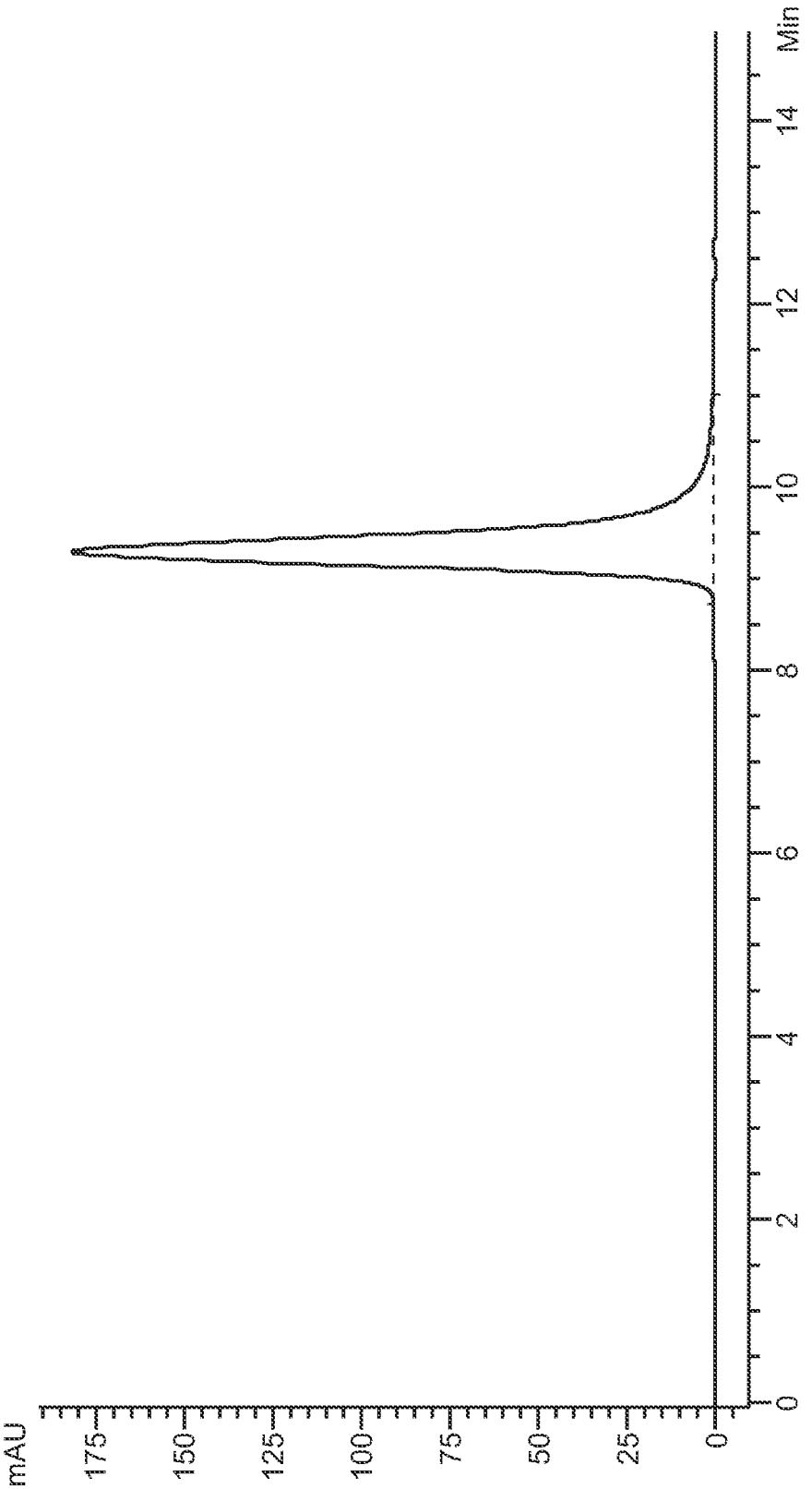
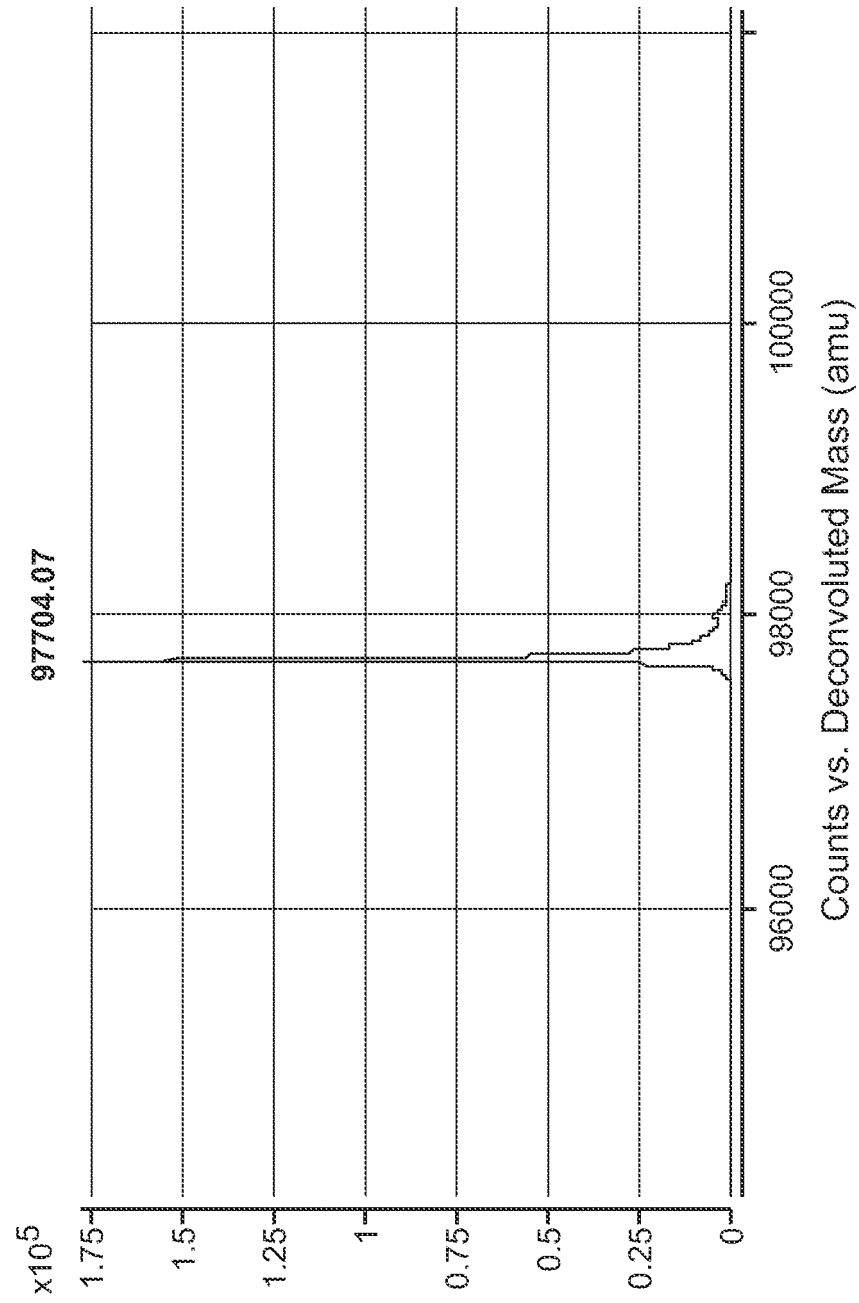


FIG. 7B



$F(ab')_2$ Mass ID	Theoretical MW (Da)
xIL17/xIL17	97,919.58
xIL13/xIL13	97,515.36
xIL17/xIL13	97,717.47

FIG. 7D

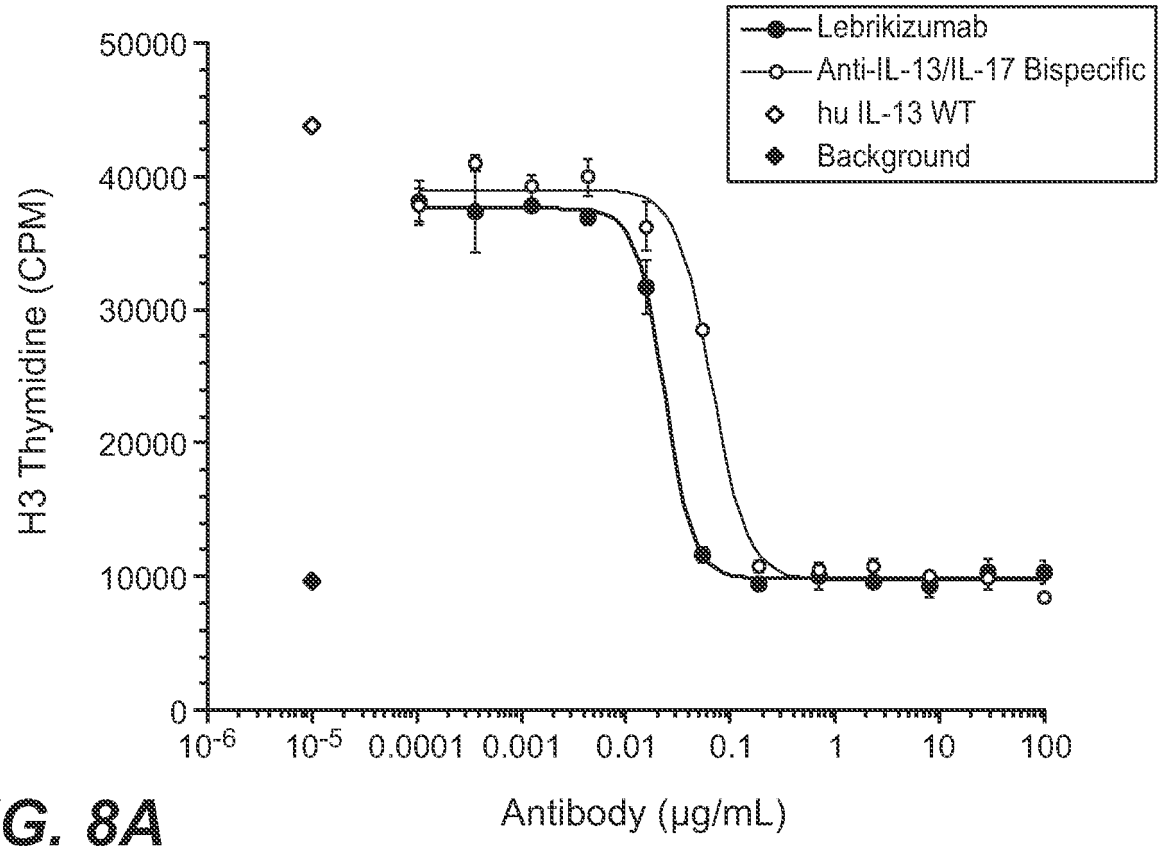

Lebrikizumab
Anti-IL-13/IL-17 Bispecific
hu IL-13 WT
Background
H3 Thymidine (CPM)
50000
40000
30000
20000
10000
0
10-6
10-5
0.0001
0.001
0.01
0.1
1
10
100
Antibody (µg/mL)

FIG. 8A

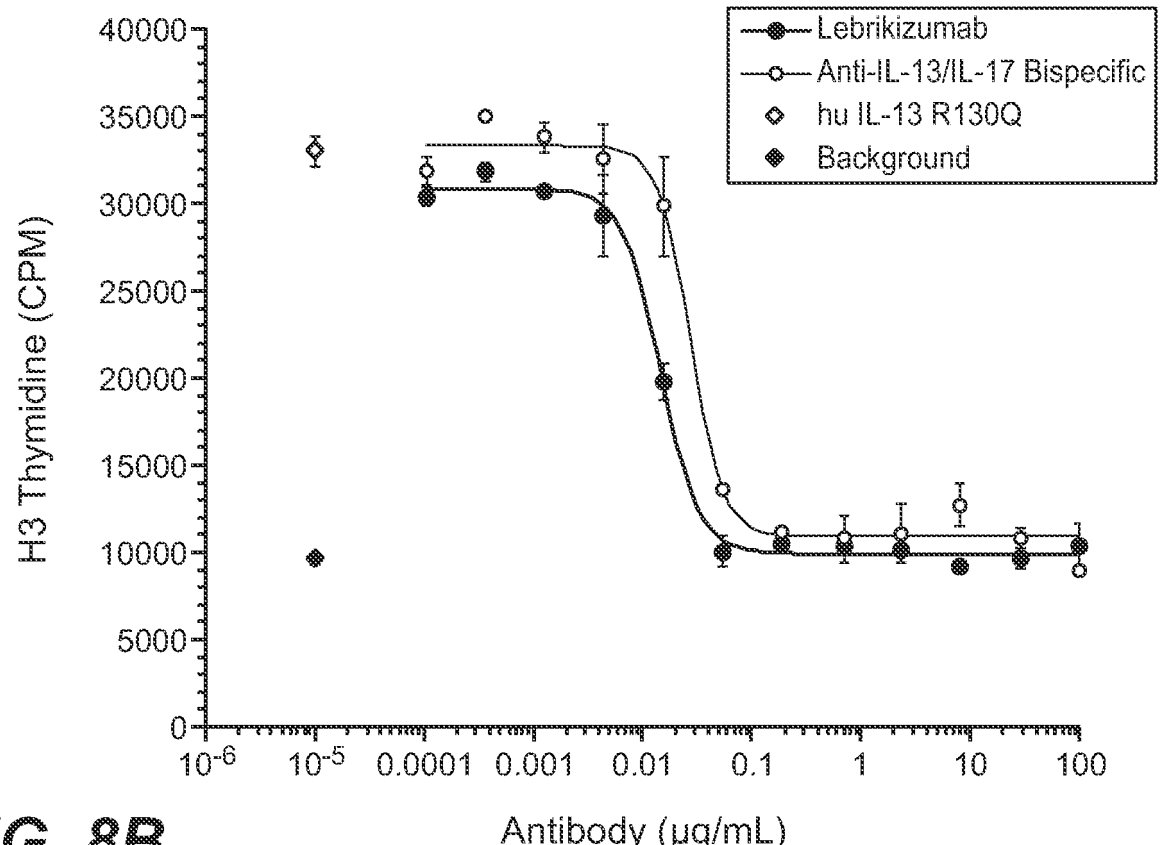

Lebrikizumab
Anti-IL-13/IL-17 Bispecific
hu IL-13 R130Q
Background
H3 Thymidine (CPM)
40000
35000
30000
25000
20000
15000
10000
5000
0
10-6
10-5
0.0001
0.001
0.01
0.1
1
10
100
Antibody (µg/mL)

FIG. 8B

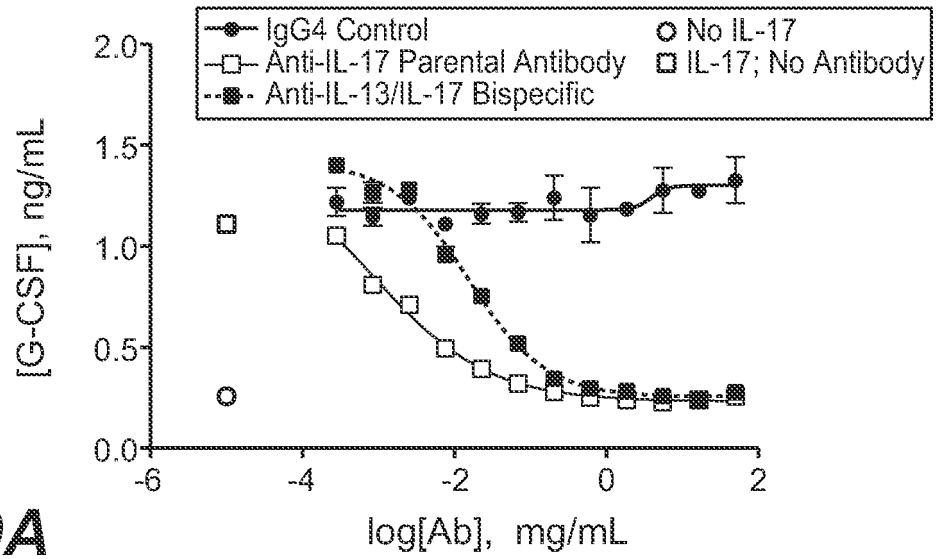


FIG. 9A

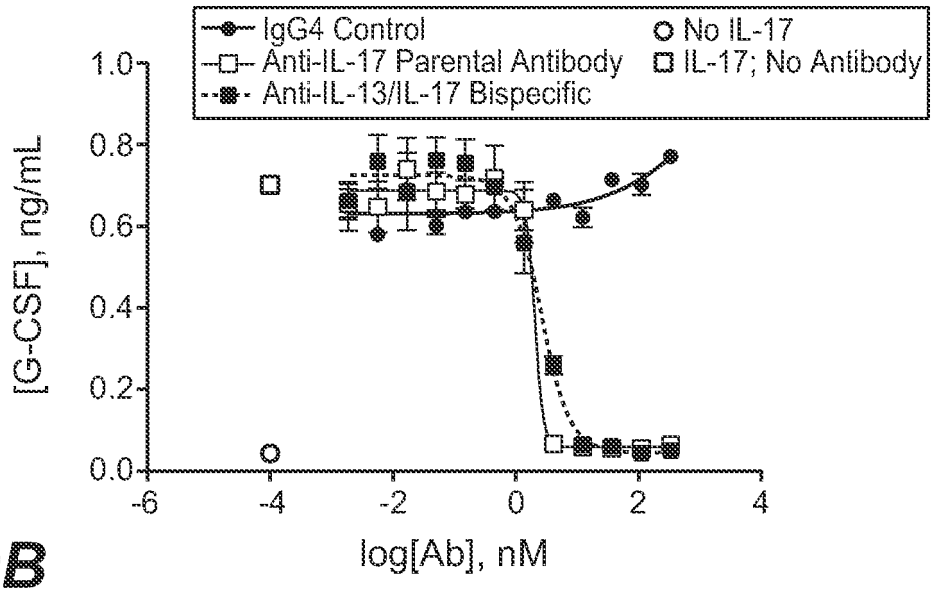


FIG. 9B

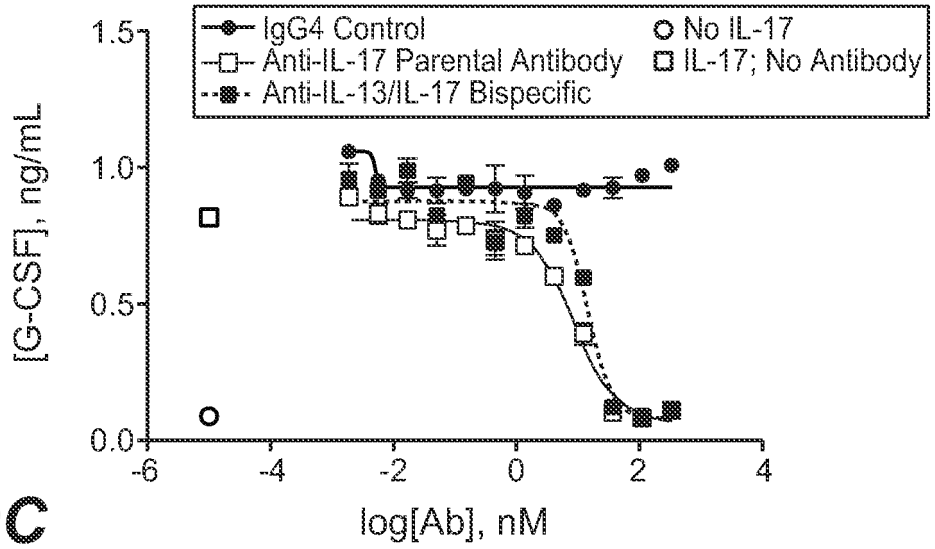


FIG. 9C

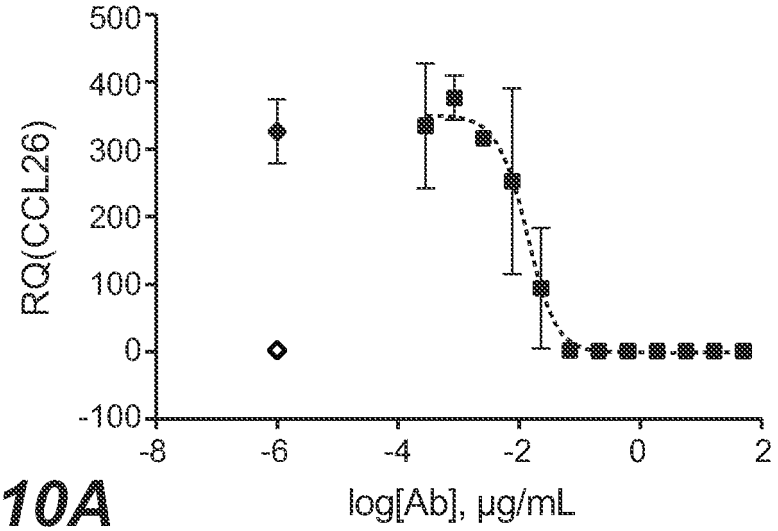


FIG. 10A

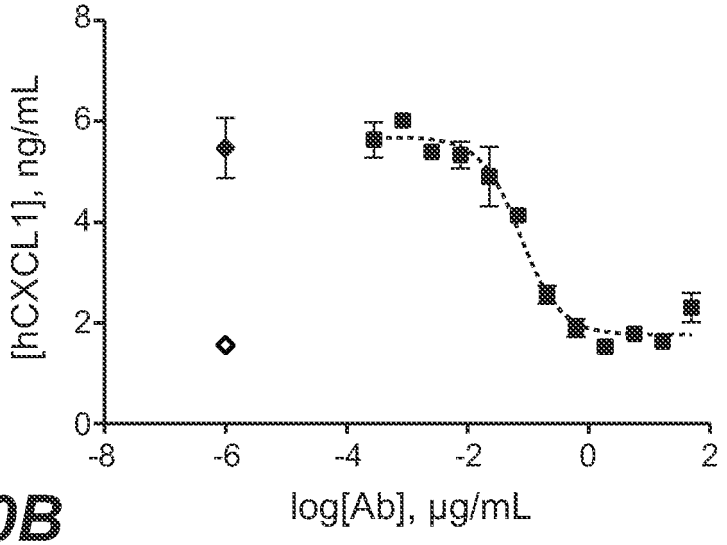


FIG. 10B

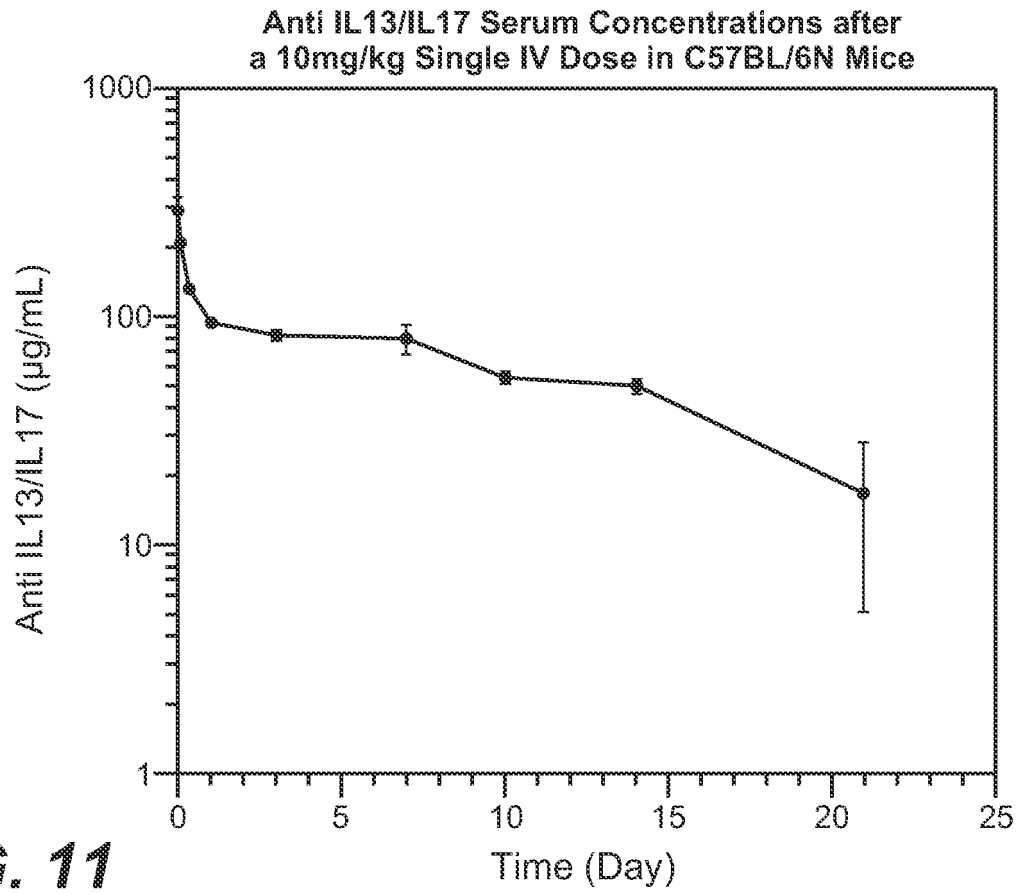

Anti IL13/IL17 Serum Concentrations after
a 10mg/kg Single IV Dose in C57BL/6N Mice
Anti IL13/IL17 (µg/mL)
1000
100
10
1
0
5
10
15
20
25
Time (Day)

FIG. 11

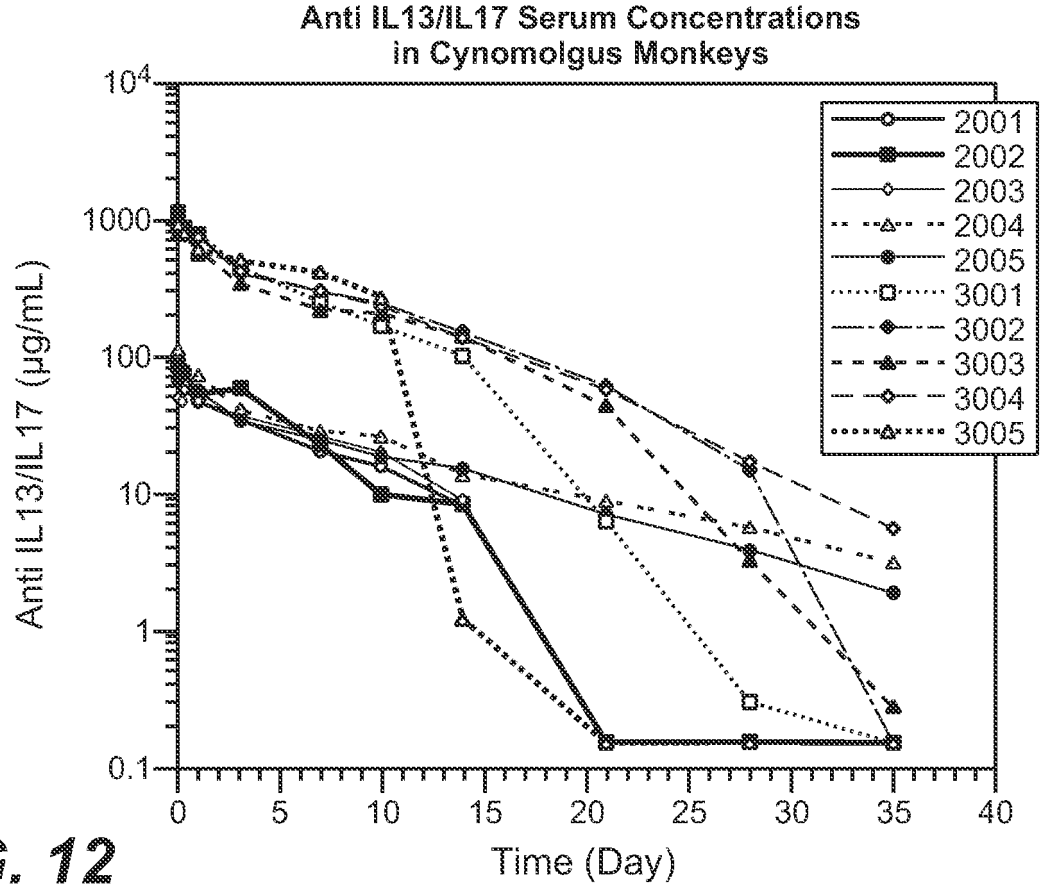

Anti IL13/IL17 Serum Concentrations
in Cynomolgus Monkeys
Anti IL13/IL17 (µg/mL)
10^4
1000
100
10
1
0.1
0
5
10
15
20
25
30
35
40
Time (Day)
2001
2002
2003
2004
2005
3001
3002
3003
3004
3005

FIG. 12

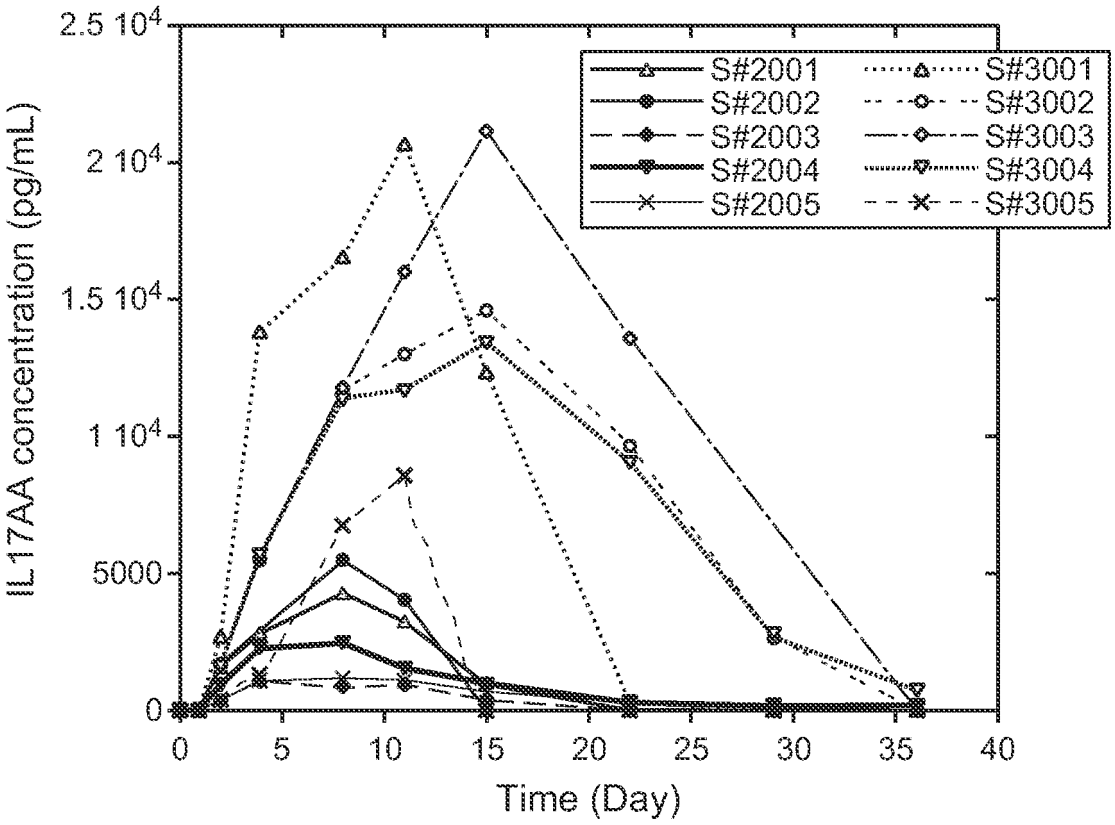

2.5 10^4
2 10^4
1.5 10^4
1 10^4
5000
0
IL17AA concentration (pg/mL)
0
5
10
15
20
25
30
35
40
Time (Day)
S#2001
S#2002
S#2003
S#2004
S#2005
S#3001
S#3002
S#3003
S#3004
S#3005

FIG. 13

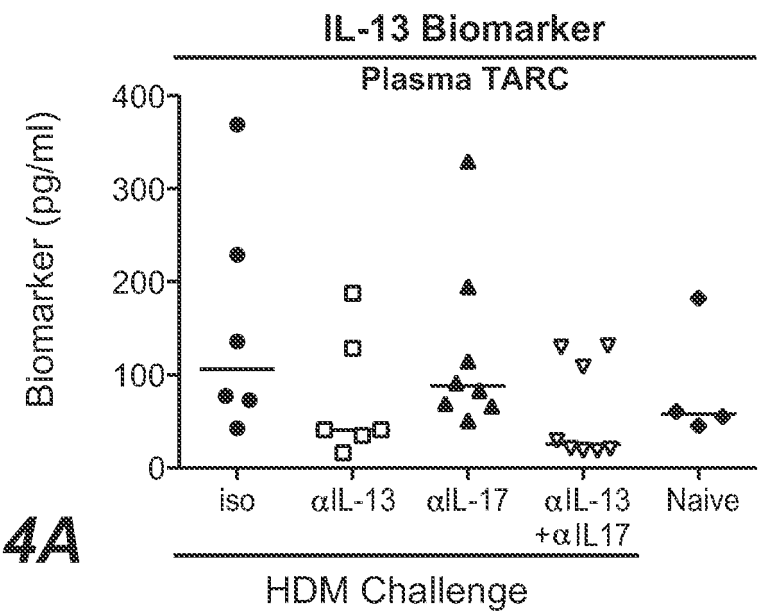


FIG. 14A

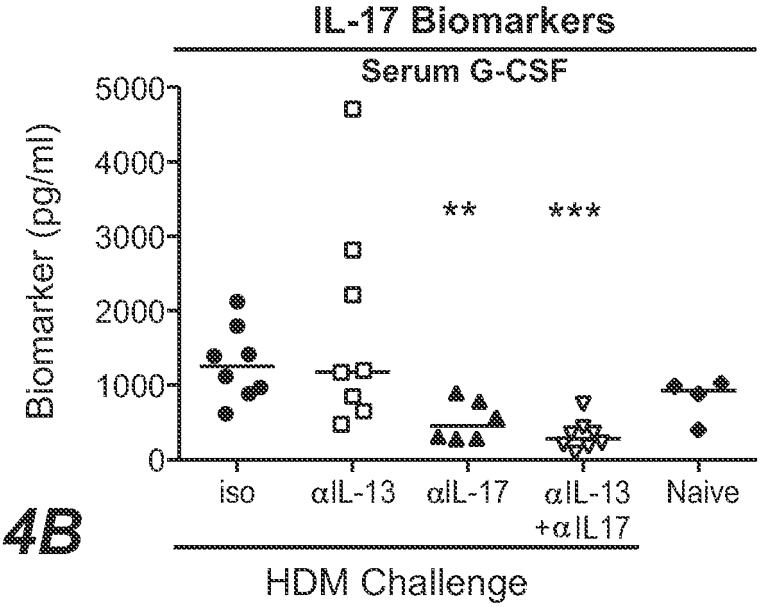


FIG. 14B

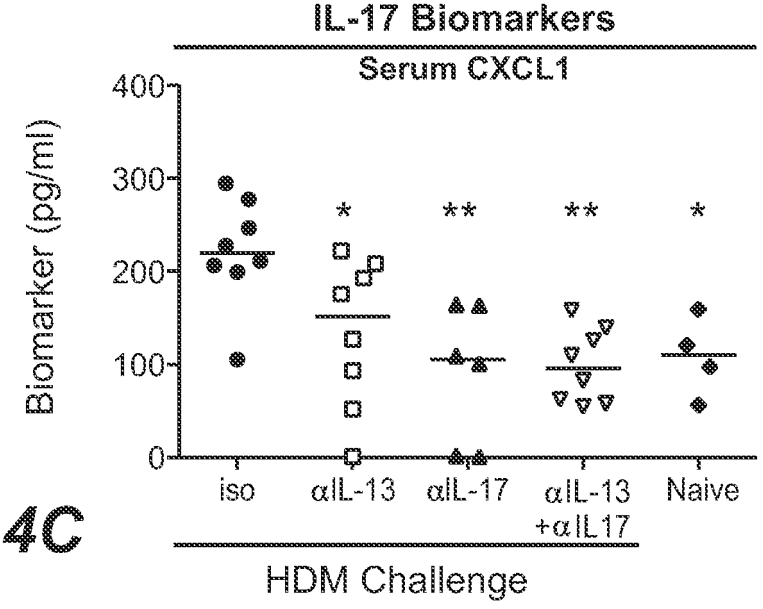


FIG. 14C

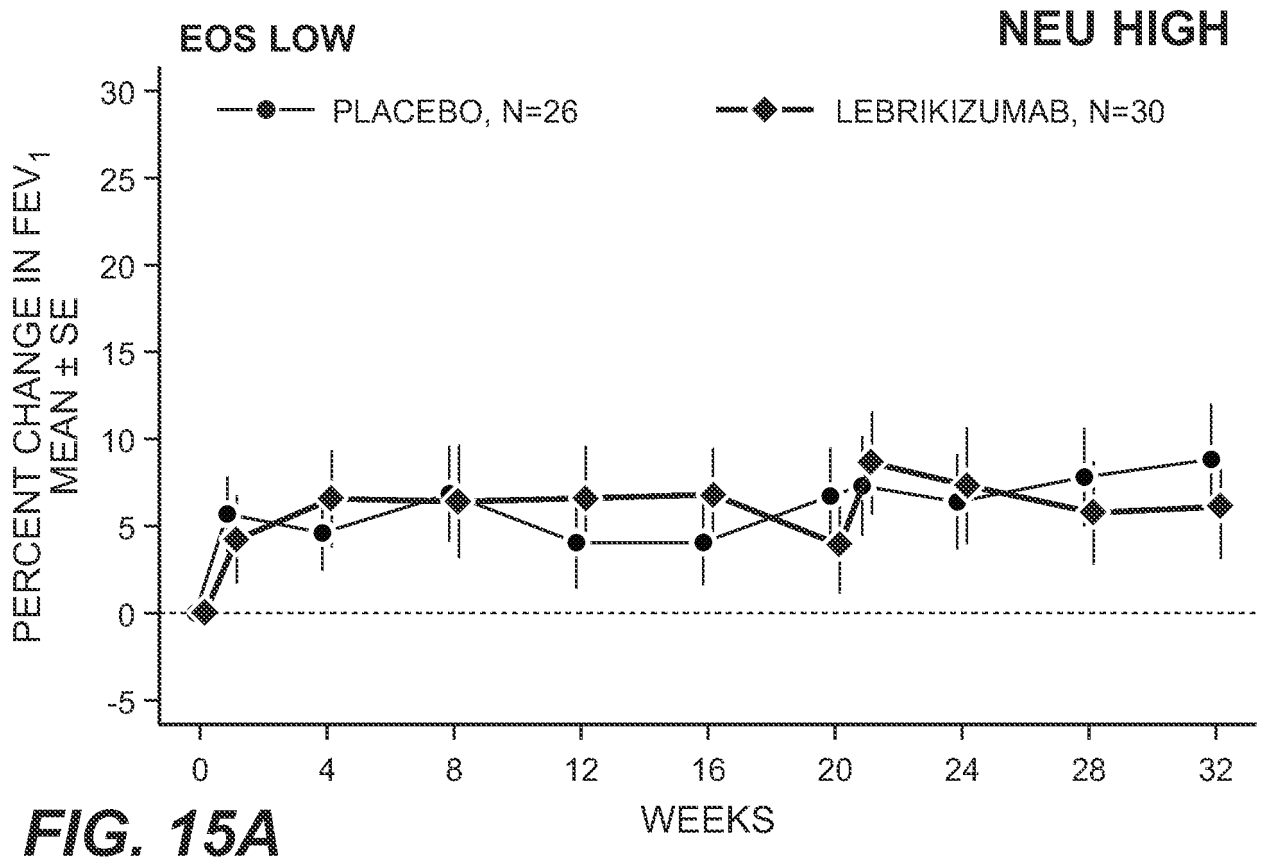


FIG. 15A

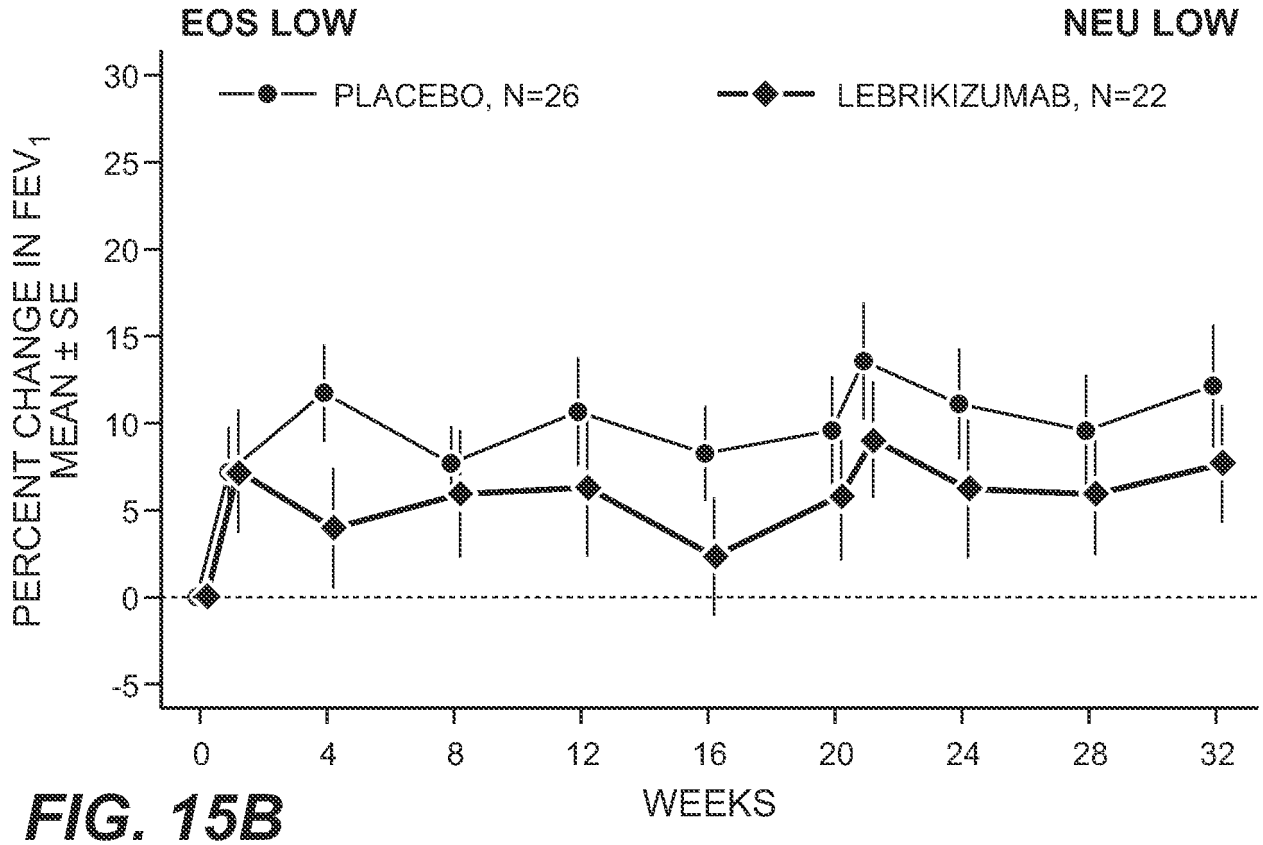


FIG. 15B

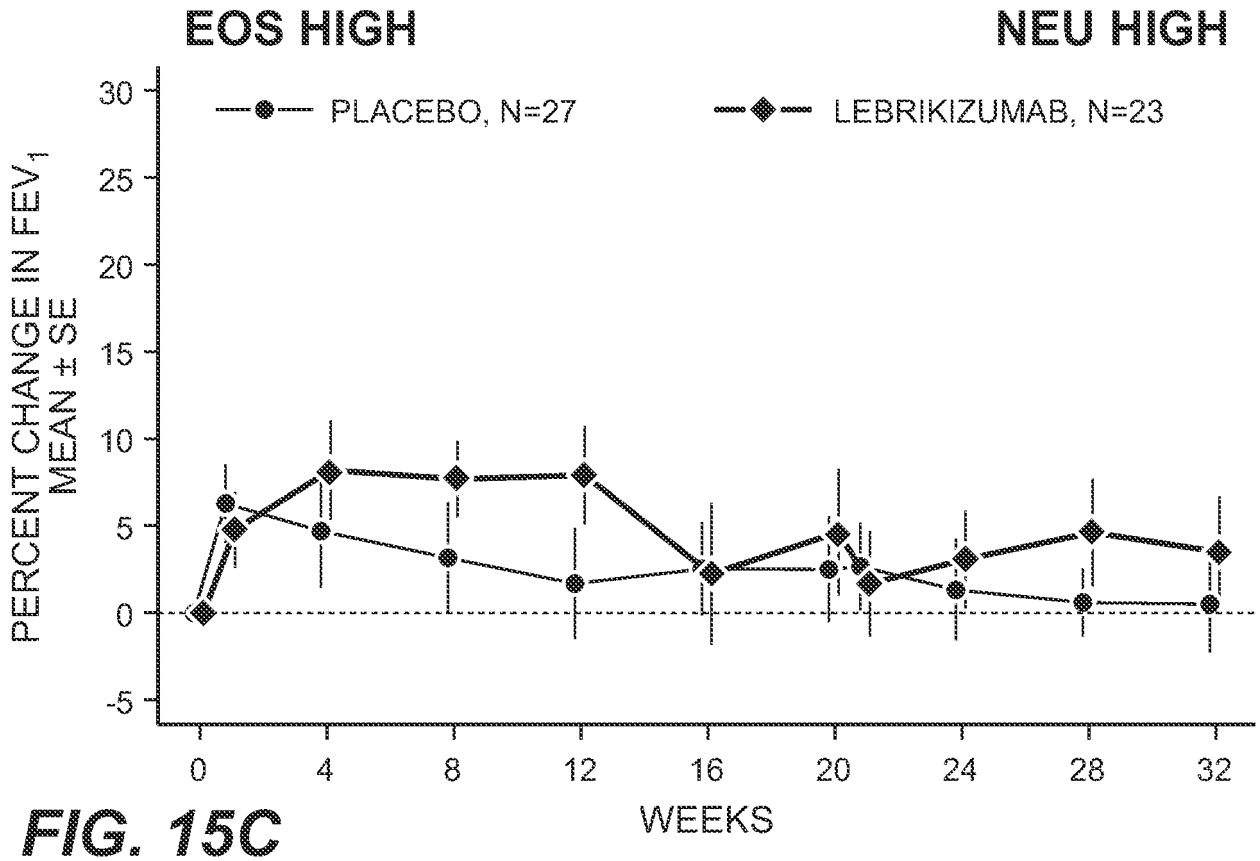


FIG. 15C

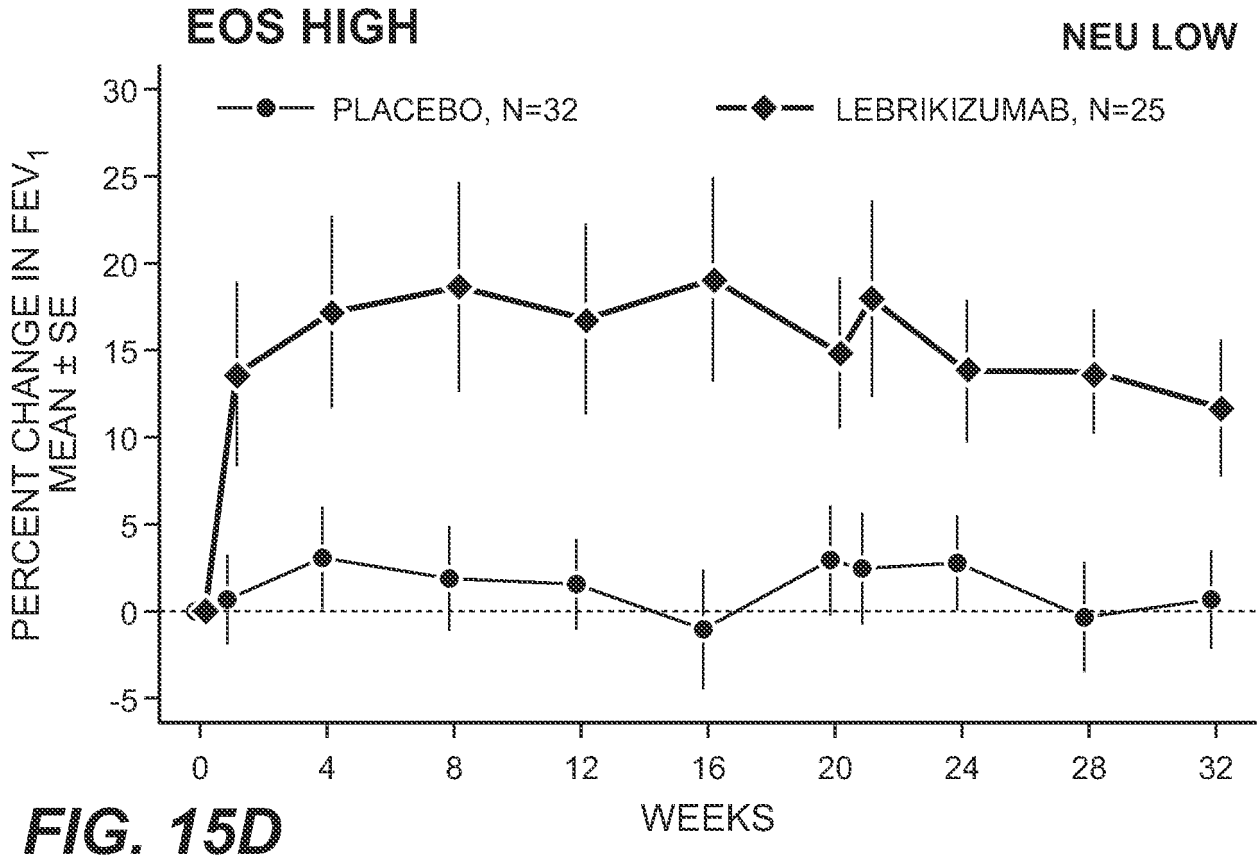


FIG. 15D