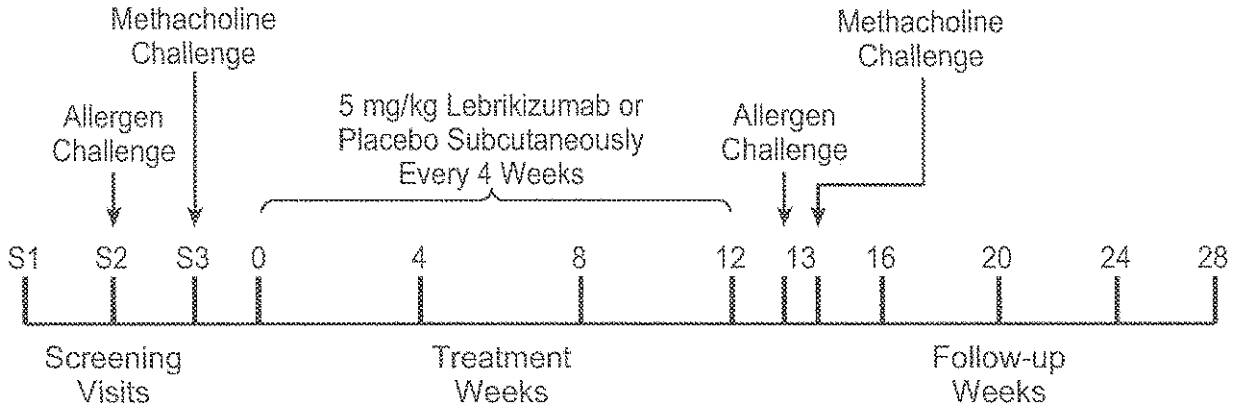

Methacholine Challenge
Allergen Challenge
5 mg/kg Lebrikizumab or Placebo Subcutaneously Every 4 Weeks
Allergen Challenge
Methacholine Challenge
S1
S2
S3
0
4
8
12
13
16
20
24
28
Screening Visits
Treatment Weeks
Follow-up Weeks

FIG. 1

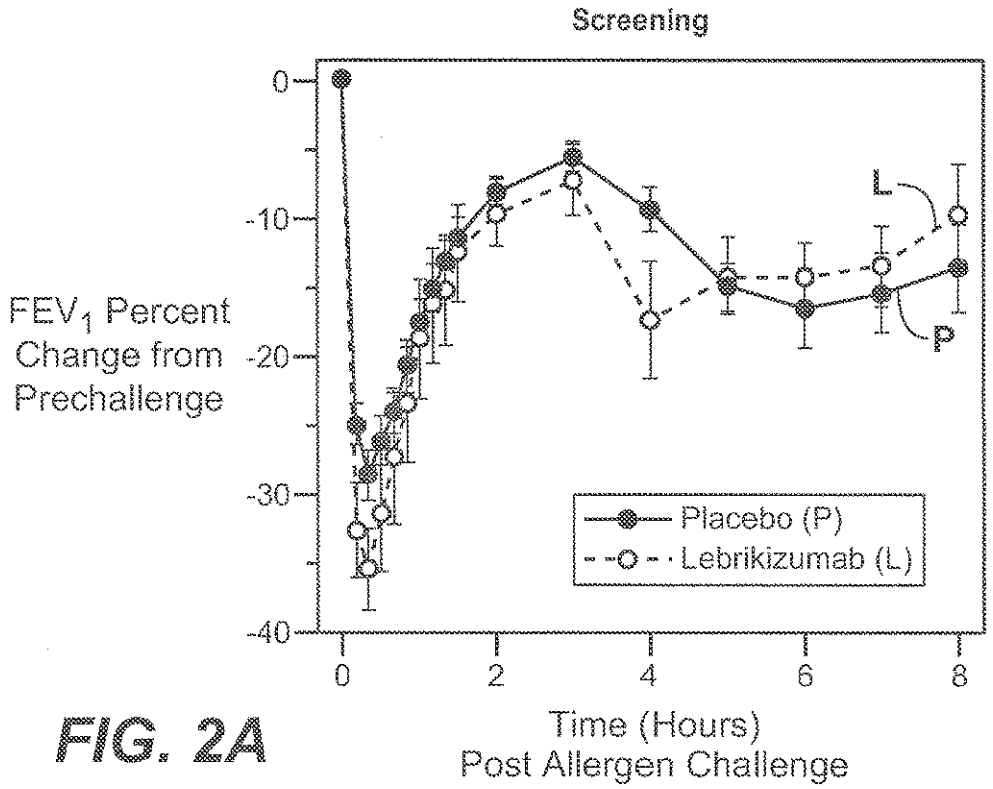

Screening
FEV1 Percent Change from Prechallenge
0
-10
-20
-30
-40
0
2
4
6
8
L
P
Placebo (P)
Lebrikizumab (L)
Time (Hours) Post Allergen Challenge

FIG. 2A

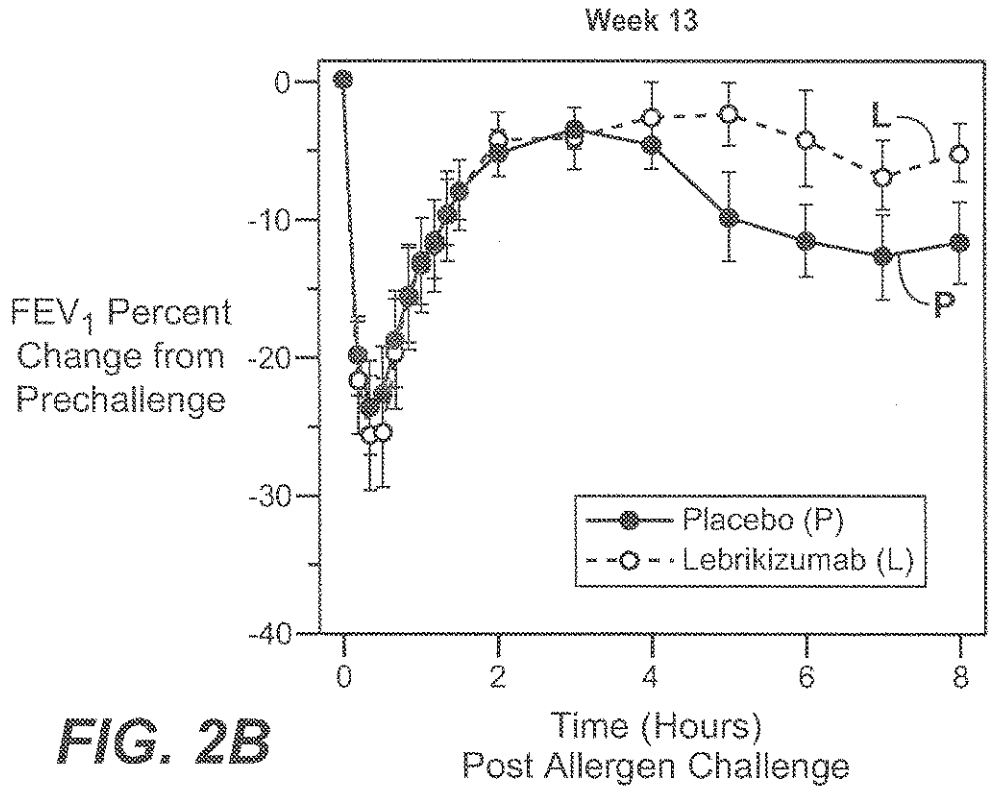

Week 13
FEV1 Percent Change from Prechallenge
0
-10
-20
-30
-40
0
2
4
6
8
L
P
Placebo (P)
Lebrikizumab (L)
Time (Hours) Post Allergen Challenge

FIG. 2B

FIG. 3A

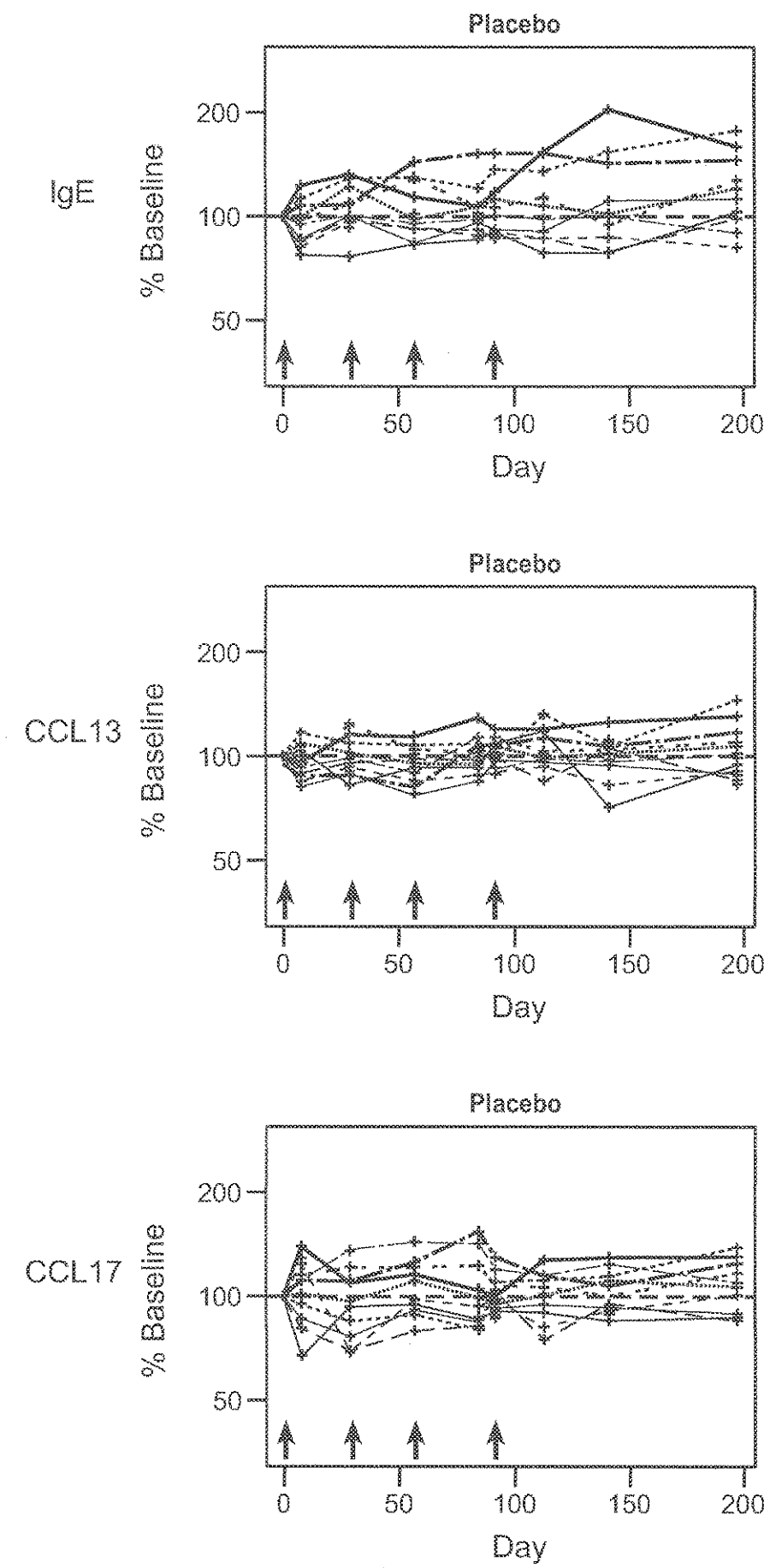

IgE
CCL13
CCL17
% Baseline
Placebo
200
100
50
0
50
100
150
200
Day

FIG. 3B

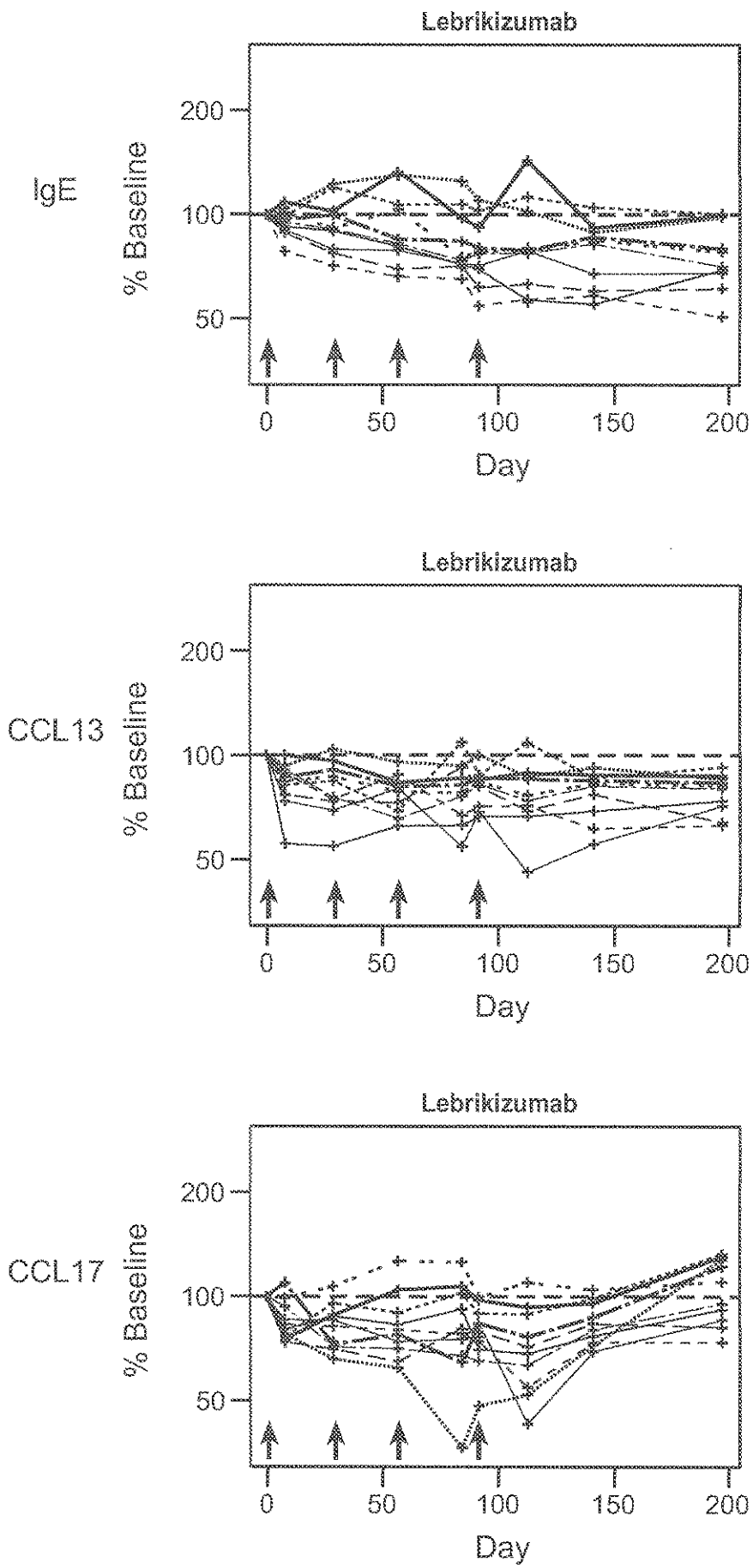
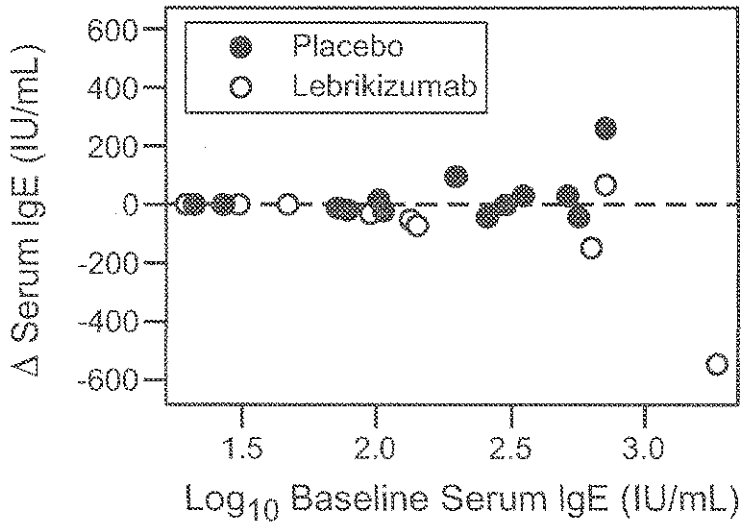
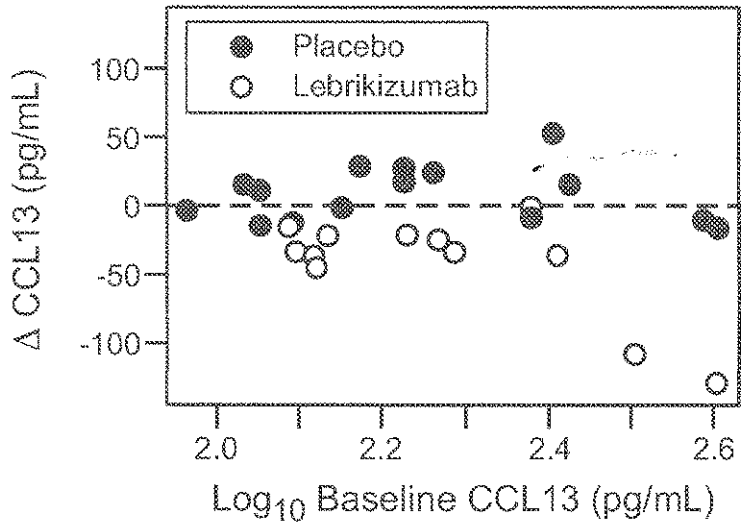

IgE
Lebrikizumab
% Baseline
200
100
50
0
50
100
150
200
Day
CCL13
Lebrikizumab
% Baseline
200
100
50
0
50
100
150
200
Day
CCL17
Lebrikizumab
% Baseline
200
100
50
0
50
100
150
200
Day

FIG. 3C

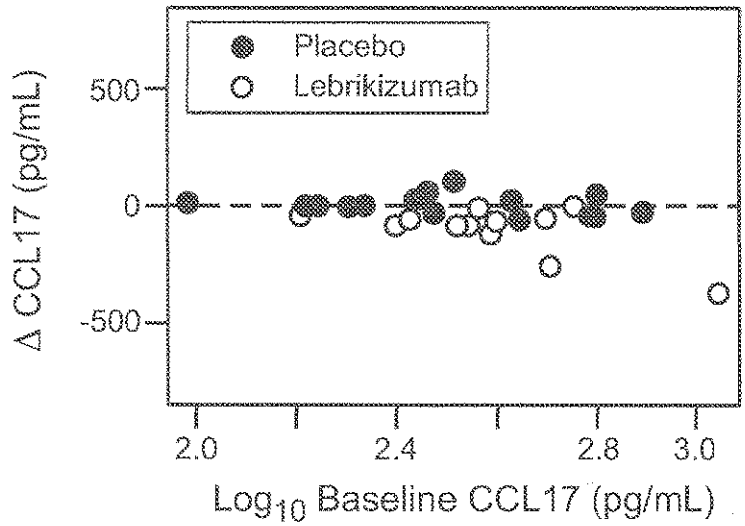
IgE



CCL13



CCL17



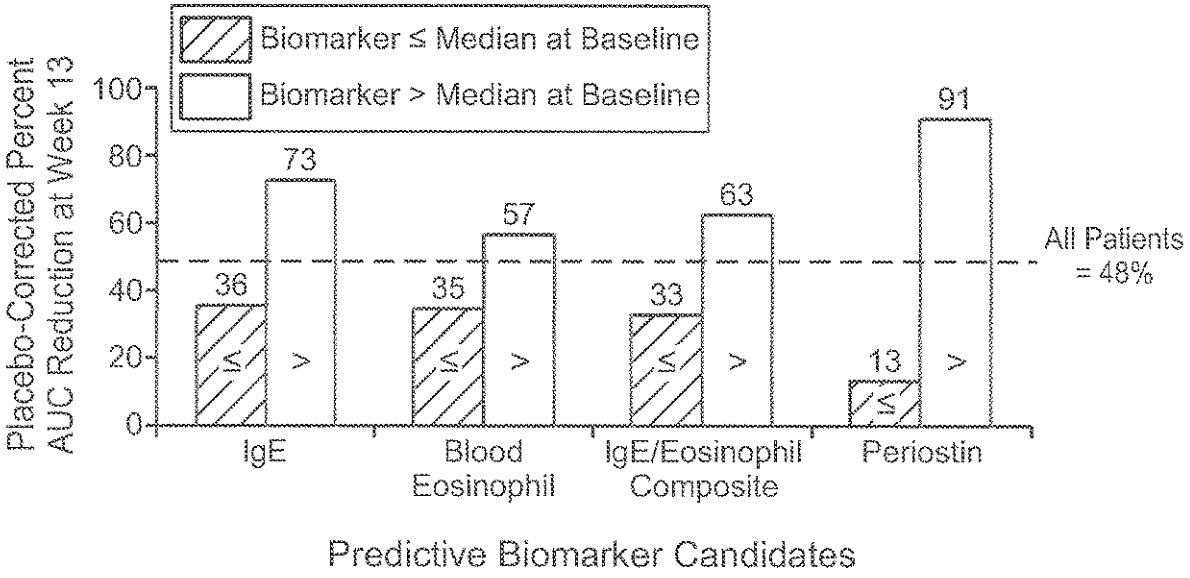

Biomarker ≤ Median at Baseline
Biomarker > Median at Baseline
Placebo-Corrected Percent AUC Reduction at Week 13
100
80
60
40
20
0
36
73
35
57
33
63
13
91
≤
>
All Patients = 48%
IgE
Blood Eosinophil
IgE/Eosinophil Composite
Periostin
Predictive Biomarker Candidates

FIG. 4

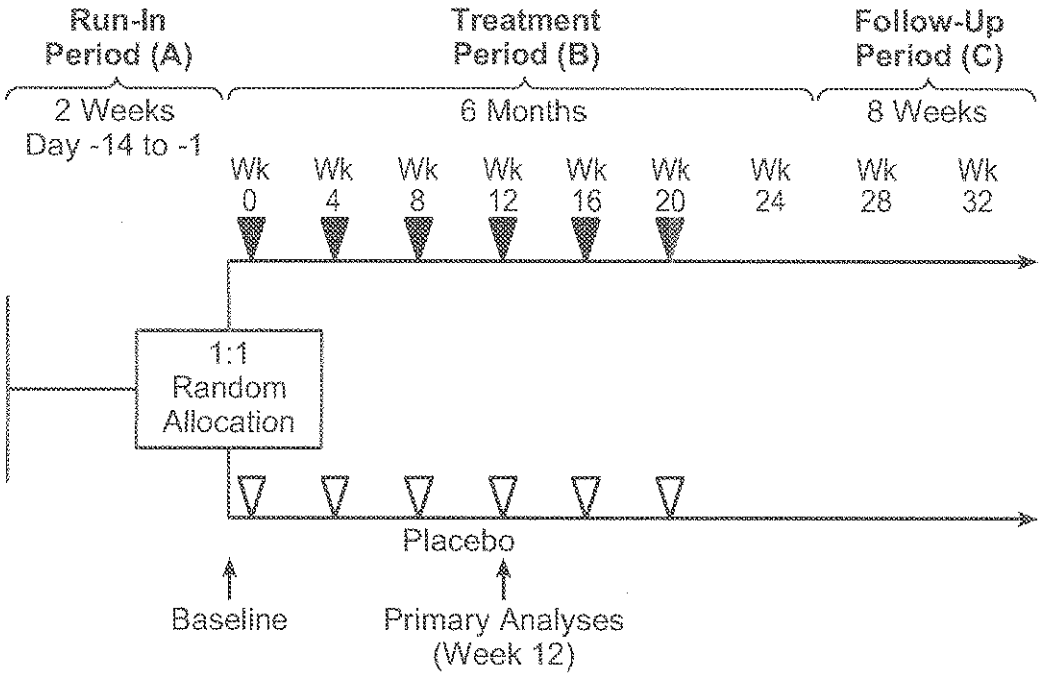

Run-In Period (A)
2 Weeks
Day -14 to -1
Treatment Period (B)
6 Months
Follow-Up Period (C)
8 Weeks
Wk 0
Wk 4
Wk 8
Wk 12
Wk 16
Wk 20
Wk 24
Wk 28
Wk 32
1:1 Random Allocation
Placebo
Baseline
Primary Analyses (Week 12)

FIG. 5

	Lebrikizumab (N = 88)	Placebo (N = 92)
Age (Years)	45 (11)	44 (13)
Gender (Female)	61%	65%
Race (White)	86%	86%
IL-13 Signature Surrogate Positive	57%	50%
IgE Median	173	211
Eosinophils	0.2 (0.2)	0.3 (0.2)
Periostin High	41%	51%
Weight	87 (20)	85 (19)
FEV1 % Predicted	65 (11)	67 (10)
LABA Use (YES)	77.3%	80.4%
High Dose ICS (≥500 mcg FP)	51%	63%
Never Smokers	81%	86%
Skin Test (Positive)	86% (n=59)	88% (n=60)
ACQ	2.5 (0.9)	2.6 (0.9)
FeNO	30.0 (24.7)	29.3 (27.6)
Eczema (Yes)	6.8%	18.5%
Allergic Rhinitis (Yes)	76%	75%
%Reversibility	22.0 (18.3)	18.1 (11.7)

FIG. 6

Time	12 Weeks (95% CI)			24 Weeks (95% CI)		
Treatment Group	Lebrikizumab	Placebo	Lebrikizumab-Placebo	Lebrikizumab	Placebo	Lebrikizumab-Placebo
All Subjects N = 180	9.1%	3.2%	5.9% (0.9%, 10.9%)	8.2%	3.5%	4.8% (0.3%, 9.3%)
IL-13 Signature + N = 96	9.0%	2.8%	6.2% (-0.2%, 12.6%)	9.2%	2.4%	6.8% (0.5%, 13.1%)
IL-13 Signature - N = 84	9.1%	3.5%	5.6% (-2.4%, 13.5%)	7.0%	4.5%	2.5% (-4.4%, 9.3%)
Periostin High (≥ Median) N = 83	11.8%	1.8%	10.0% (2.5%, 17.5%)	8.2%	2.2%	6.1% (-1.4%, 13.6%)
Periostin Low (< Median) N = 97	7.2%	4.6%	2.5% (-4.1%, 9.2%)	8.3%	4.8%	3.5% (-2.2%, 9.1%)

FIG. 7

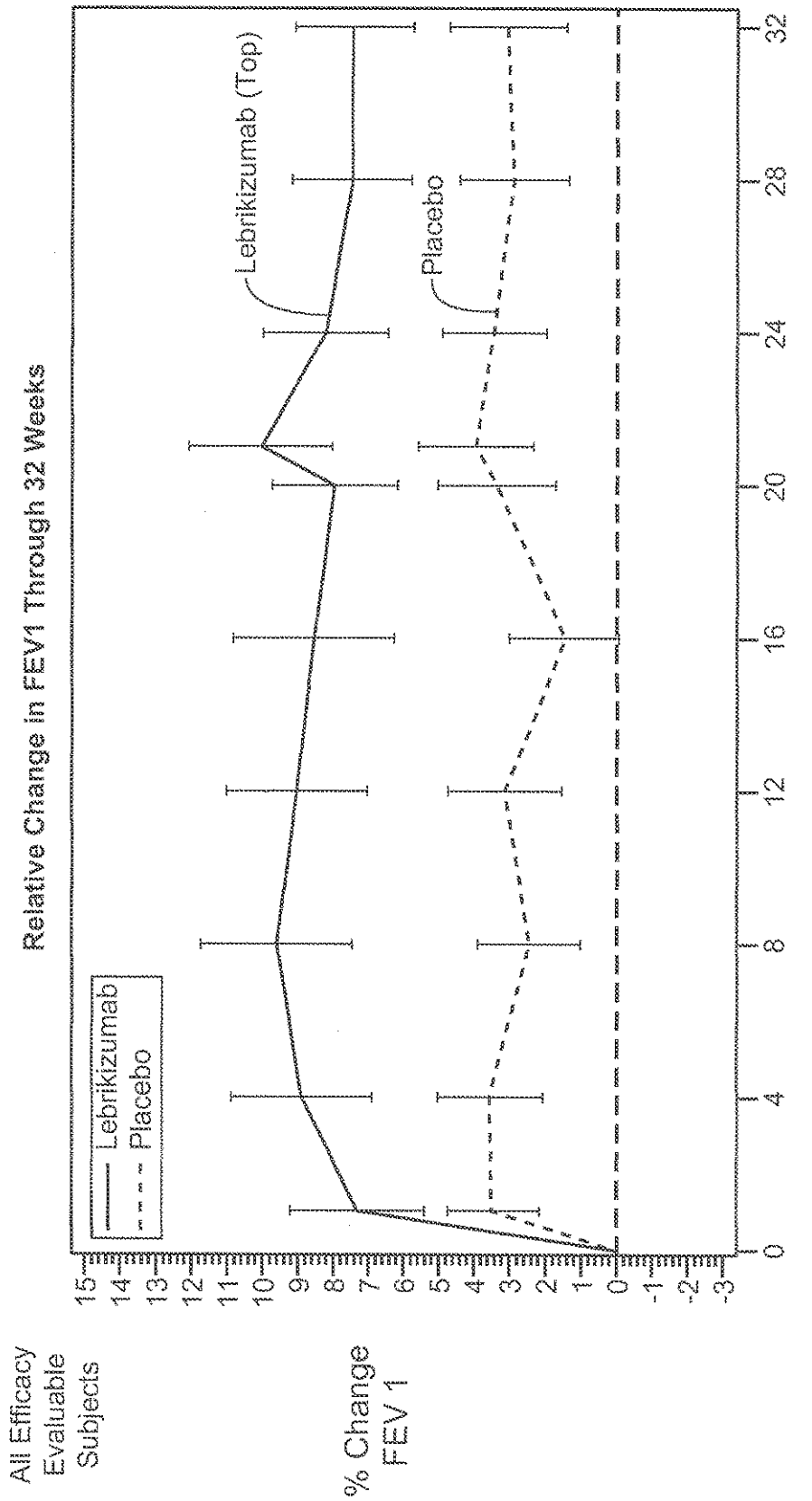

Relative Change in FEV1 Through 32 Weeks
All Efficacy Evaluable Subjects
% Change FEV1
Time (Weeks)
Lebrikizumab
Placebo
Lebrikizumab (Top)
Placebo
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
0
4
8
12
16
20
24
28
32

FIG. 8A

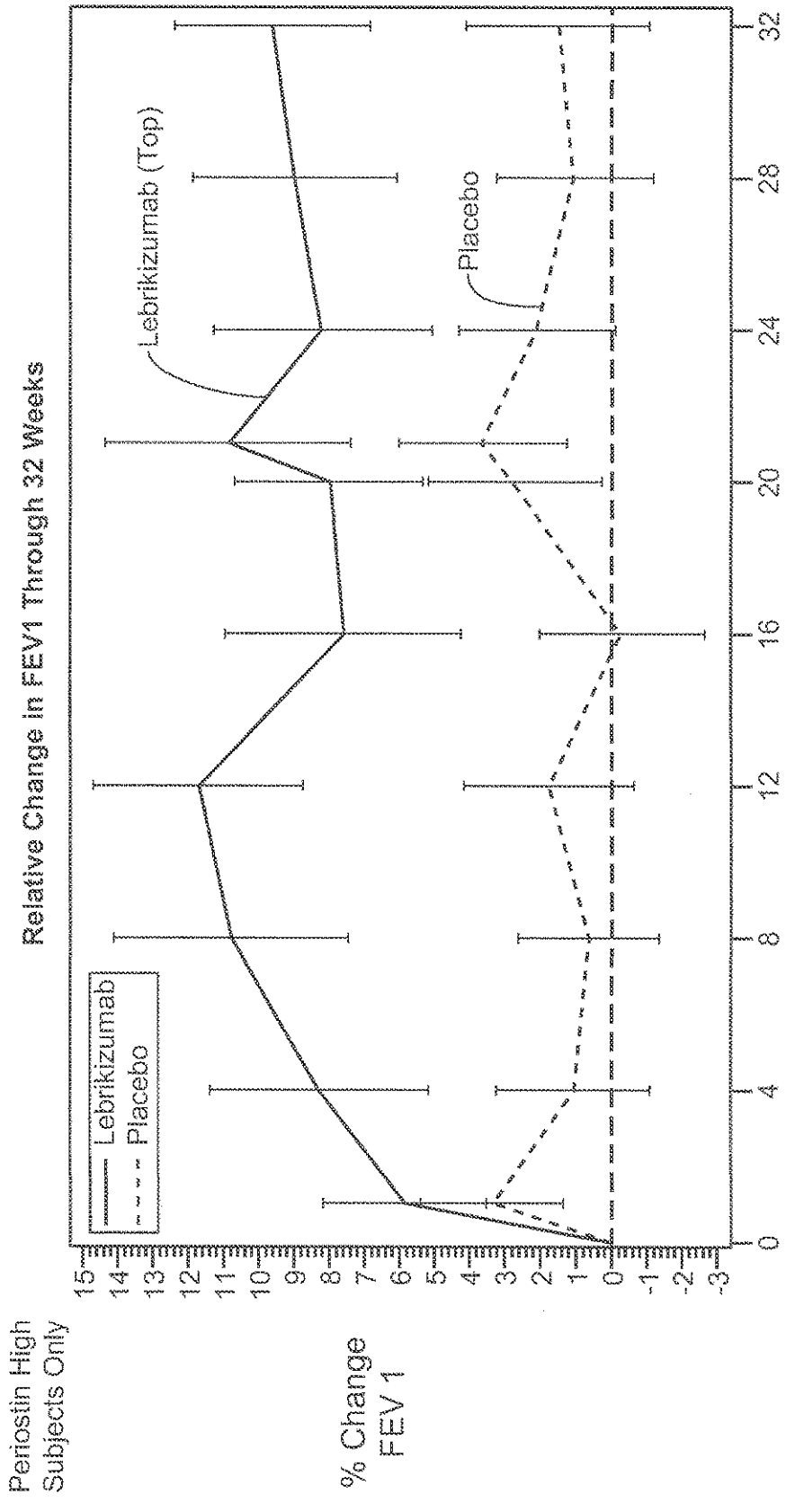

Relative Change in FEV1 Through 32 Weeks
Periostin High Subjects Only
% Change FEV 1
Time (Weeks)
Lebrikizumab
Placebo
Lebrikizumab (Top)
Placebo
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
0
4
8
12
16
20
24
28
32

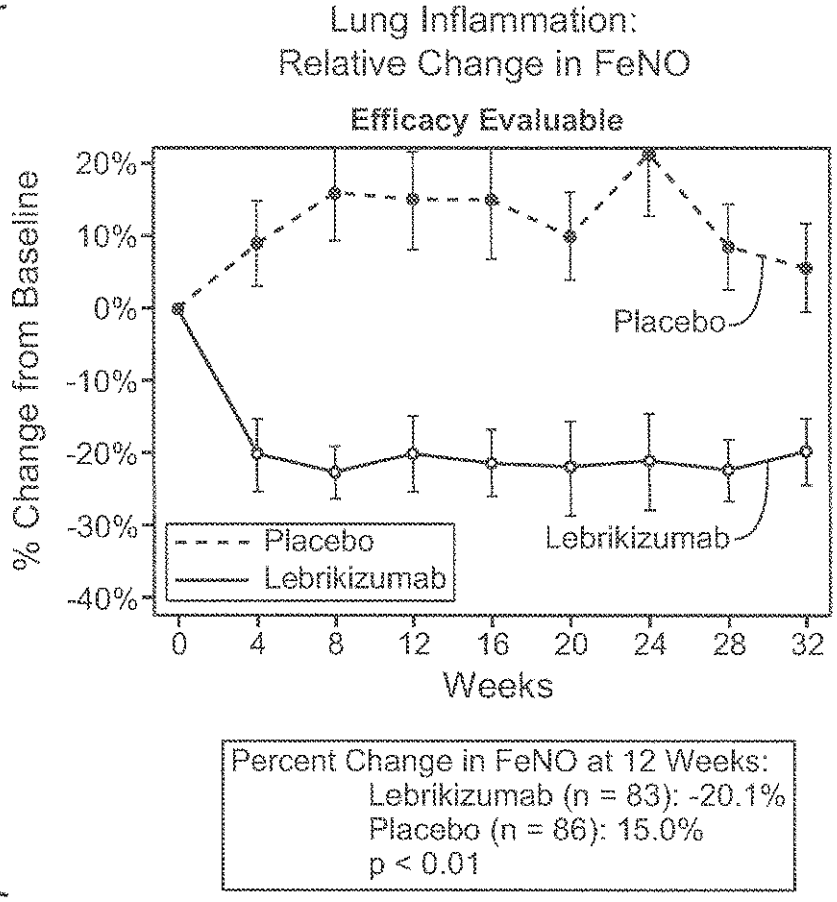
FIG. 8B

Group	Rate Reduction in Exacerbations Over 24 Weeks (95% CI) p Value	Rate Reduction in *Severe* Exacerbations Over 24 Weeks (95% CI) p Value
All Patients (n = 180)	37% (-22%, 67%) p = 0.17	51% (-33%, 82%) p = 0.16
Periostin High* (n = 83)	61% (-6%, 86%) p = 0.07	84% (14%, 97%) p = 0.03
Periostin Low* (n = 97)	25% (-73%, 68%) p = 0.50	9% (-228%, 75%) p = 0.89

*Defined by ≥ median periostin in all subjects.

FIG. 9

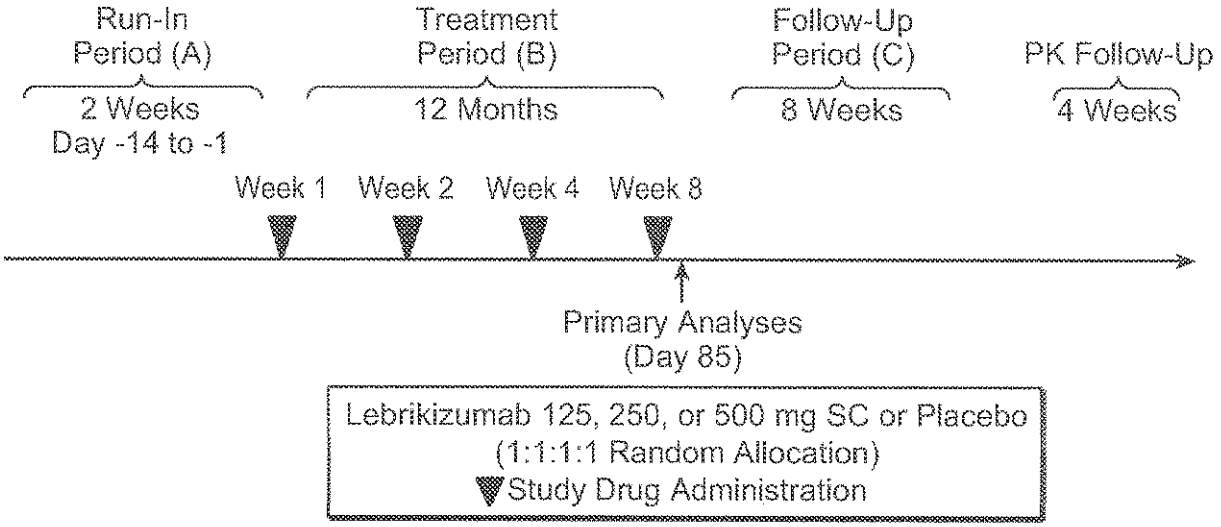
FIG. 10



	Lebrikizumab n = 106	Placebo n = 112	All n = 218
Any Adverse Event	79 (74.5%)	87 (77.7%)	166 (76.1%)
All SAEs	4 (3.8%)	6 (5.4%)	10 (4.6%)
SAEs Related to Study Drug	0	0	0
Discontinuations Due to AEs	5 (4.7%)	3 (2.7%)	8 (3.7%)
Mild AEs	58 (54.7%)	66 (58.9%)	124 (56.9%)
Mild Related AEs	12 (11.3%)	11 (9.8%)	23 (10.6%)
Moderate AEs	51 (48.1%)	58 (51.8%)	109 (50.0%)
Moderate Related AEs	9 (8.5%)	7 (6.3%)	16 (7.3%)
Severe AEs	15 (14.2%)	20 (17.9%)	35 (16.1%)
Severe Related AEs	5 (4.7%)	3 (2.7%)	8 (3.7%)
Deaths	0	0	0
Pregnancies	0	0	0
Malignancies	0	1	1

[1]n = Number of subjects with at least one event

FIG. 11



A) Run-in period (Day -14 to -1): Establish eligibility including FEV1 and bronchodilator reversibility. Characterize asthma including baseline peak expiratory flow, exhaled nitric oxide and asthma control questionnaire (ACQ) data.
B) Treatment period (Day 1 to 85): Four doses of study drug with efficacy and safety assessments throughout.
C) Follow-up period from Day 85 to Day 141

FIG. 12

Clinical Data
Demographics
Spirometry
Asthma Diary
ACQ
Biomarker Samples
Peripheral Blood Eosinophils
Serum
FeNO
Day -21 to -14
Visit 1
Screening
Continue ICS Dose (± LABA)
Clinical Data
Spirometry
Asthma Diary
ACQ
Day 0
Visit 2
Airway Samples
Sputum (Differential Cell Count)
Biomarker Samples
Peripheral Blood Eosinophils
Serum
FeNO
Continue ICS Dose (± LABA)
Clinical Data
Spirometry
Asthma Diary
Day +4 to +14
Visit 3
Airway Samples
Bronchoscopy
Biomarker Samples
Peripheral Blood Eosinophils
Serum

FIG. 13

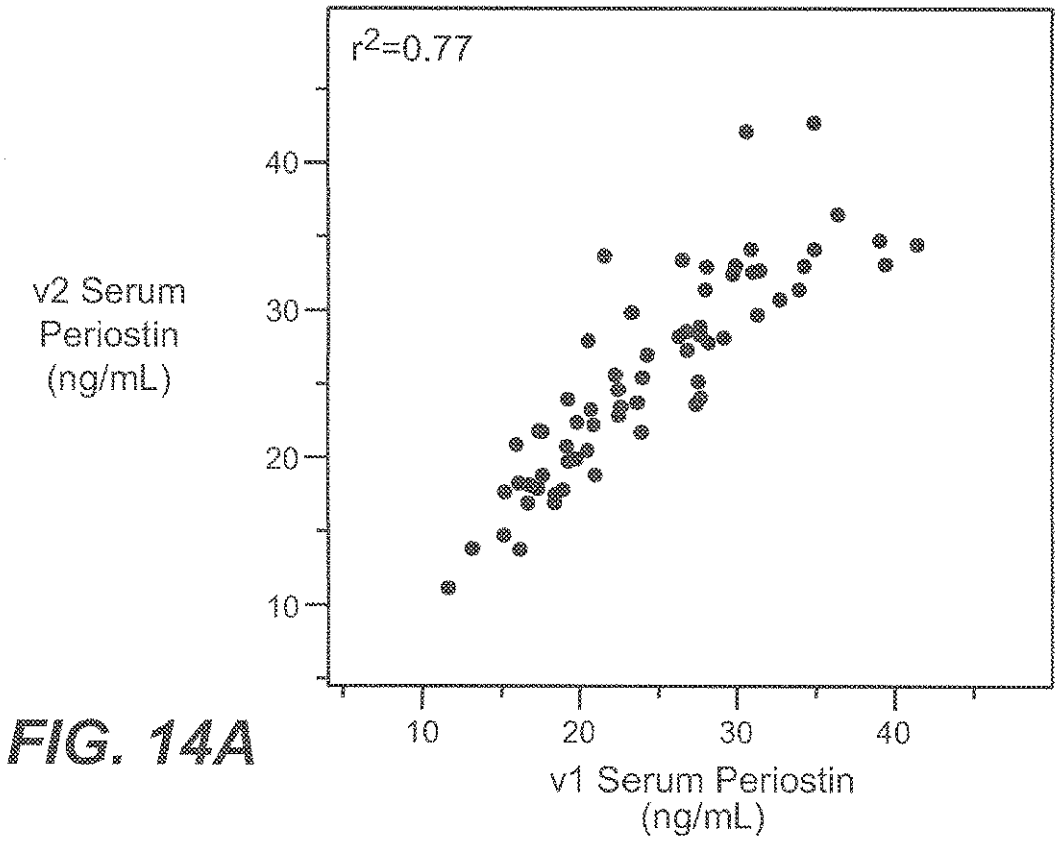


FIG. 14A

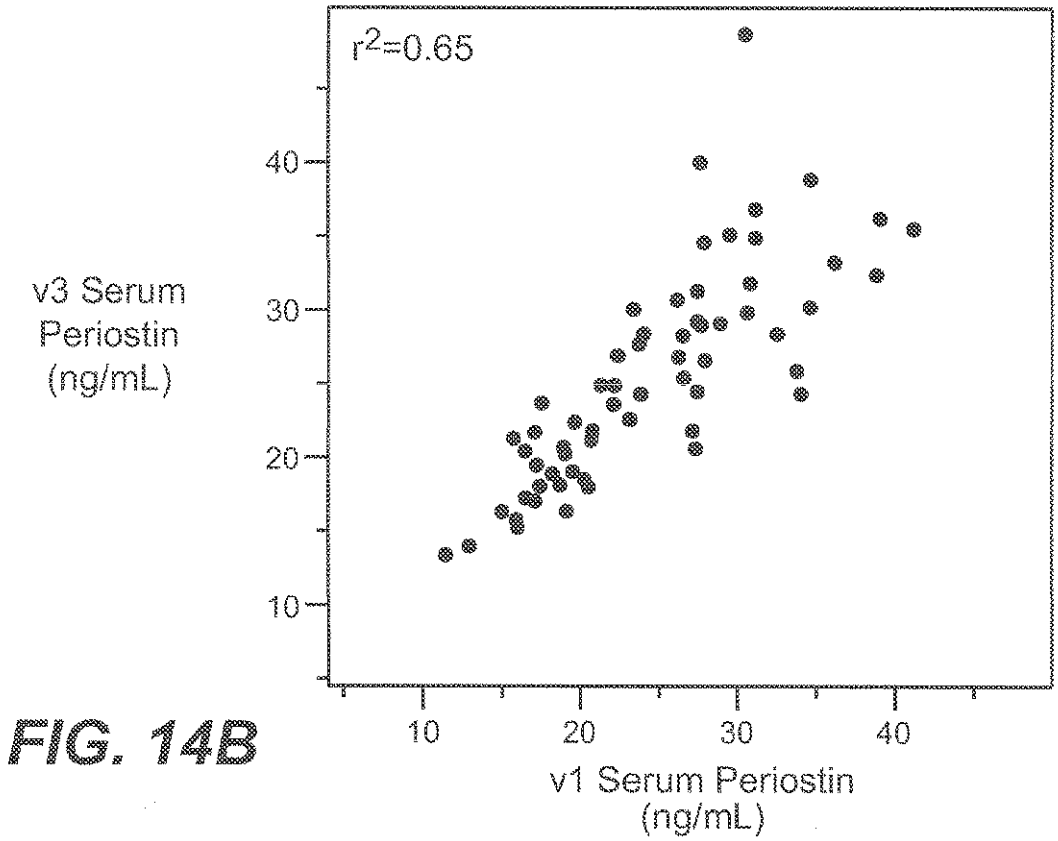


FIG. 14B

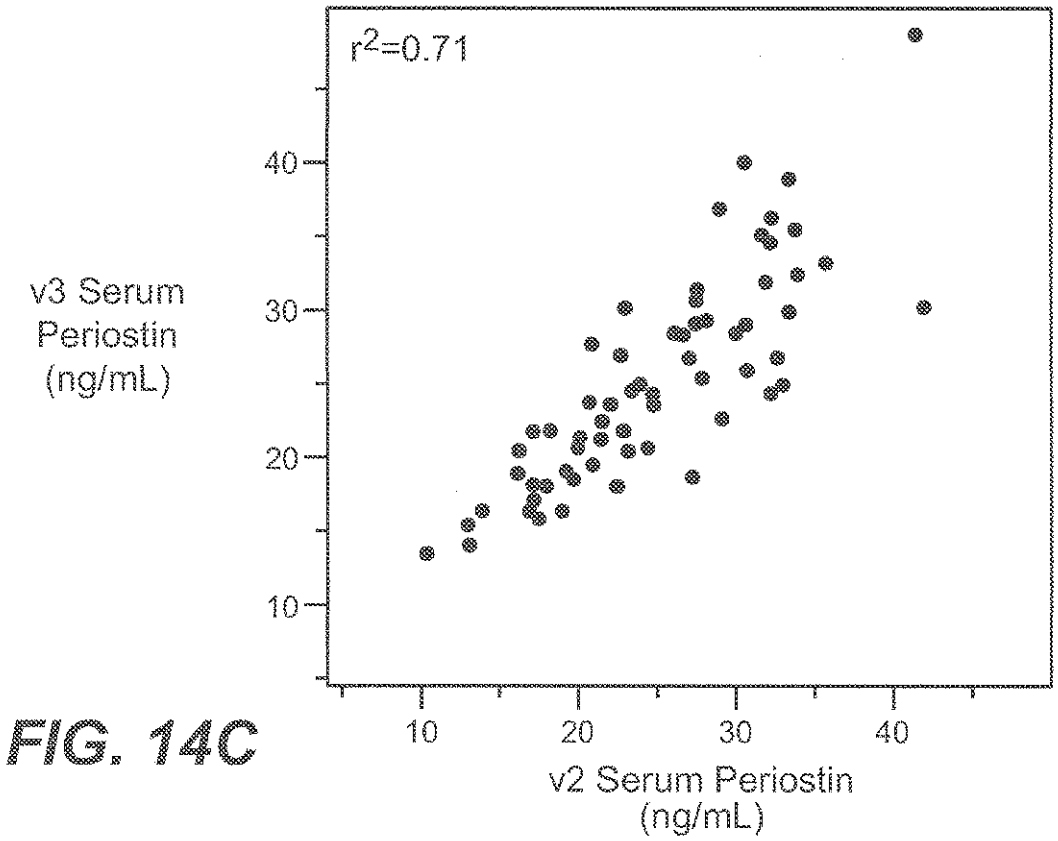


FIG. 14C

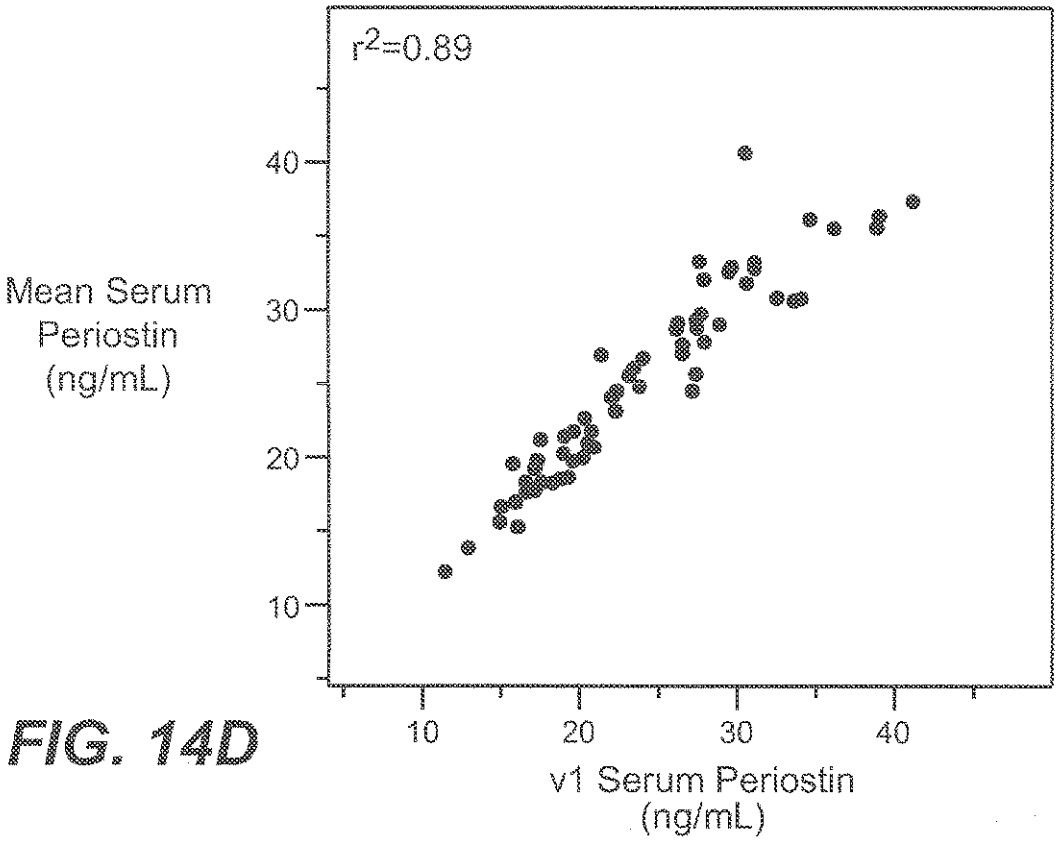


FIG. 14D

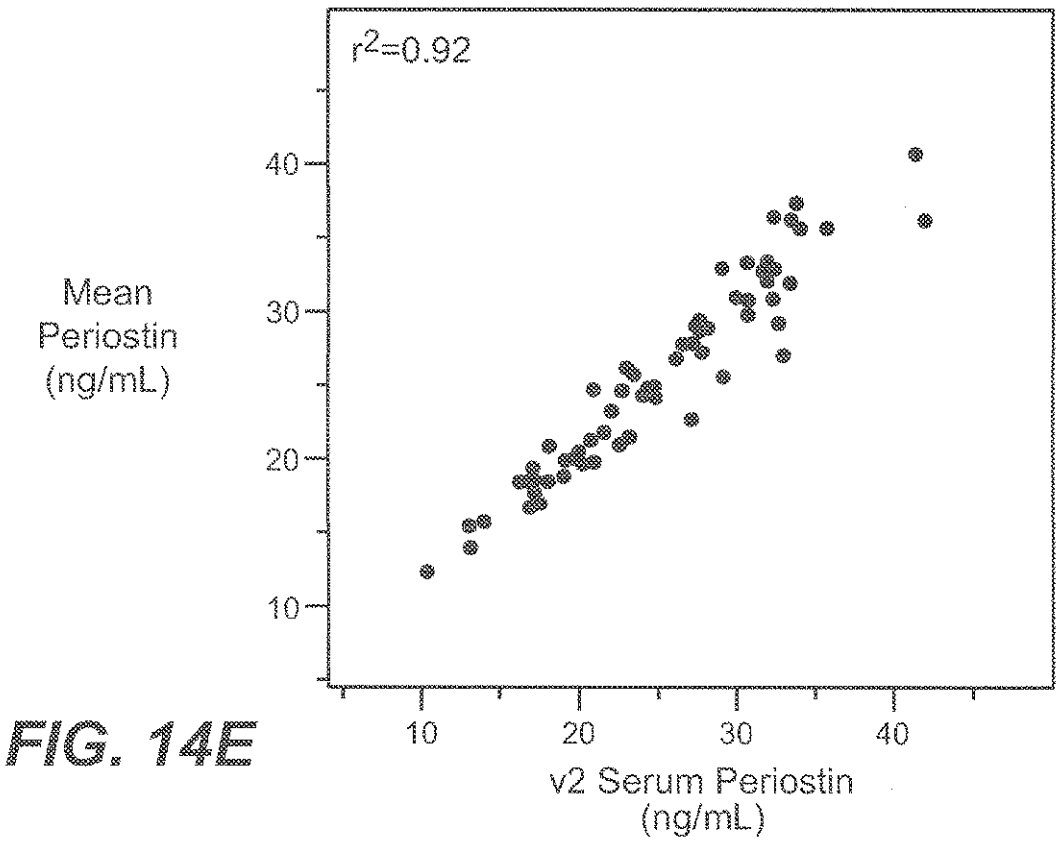


FIG. 14E

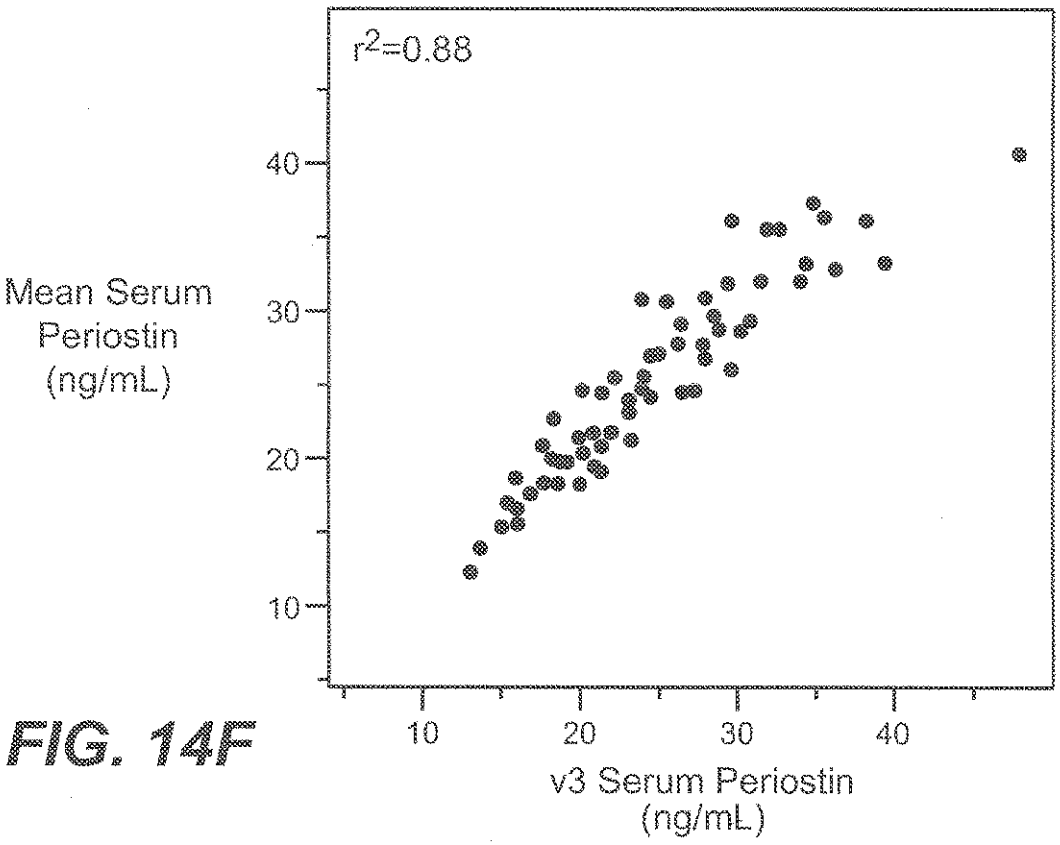


FIG. 14F

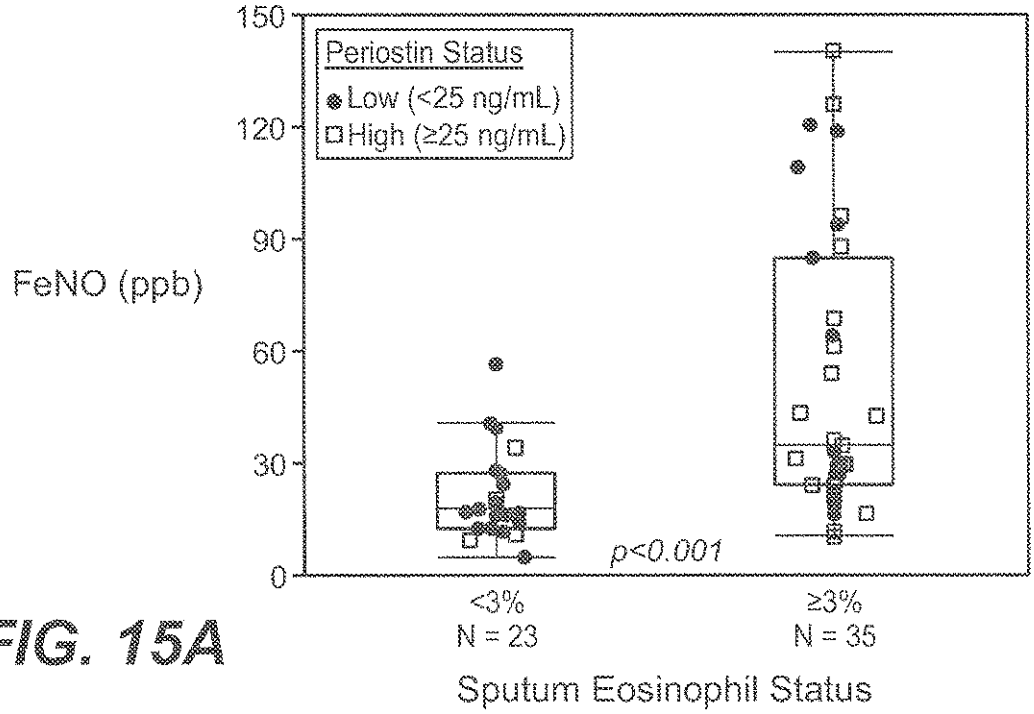


FIG. 15A

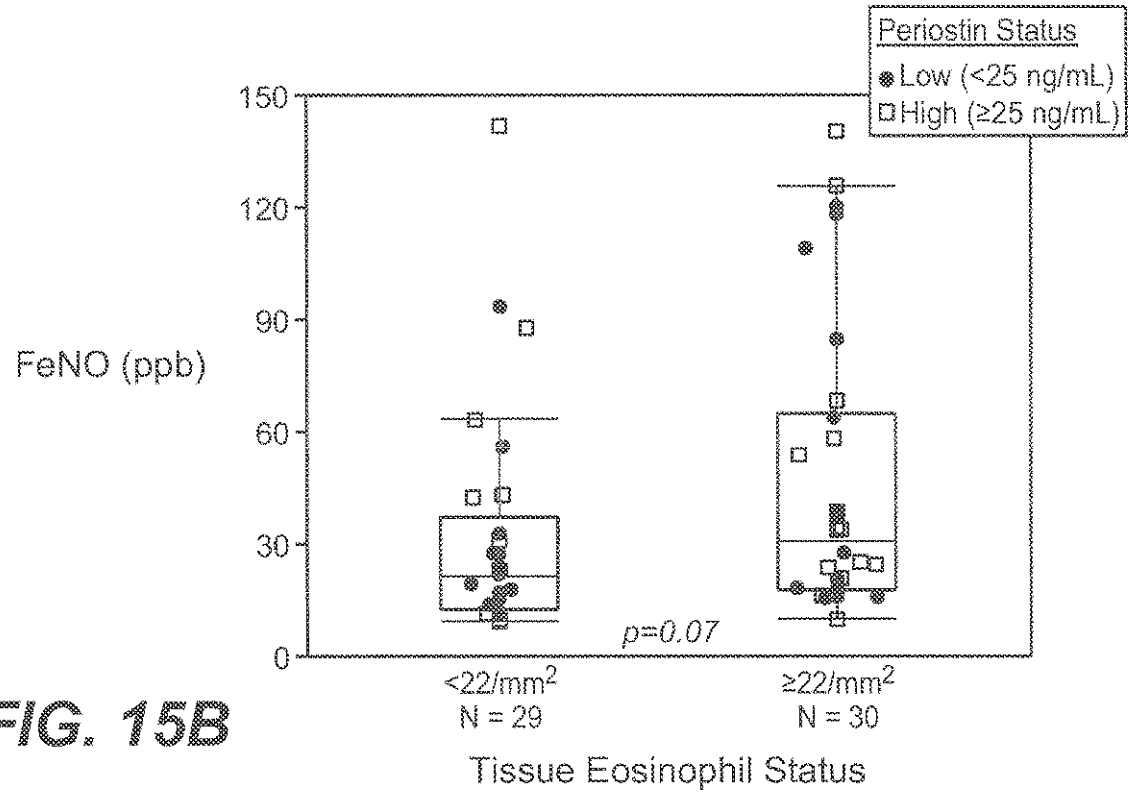


FIG. 15B

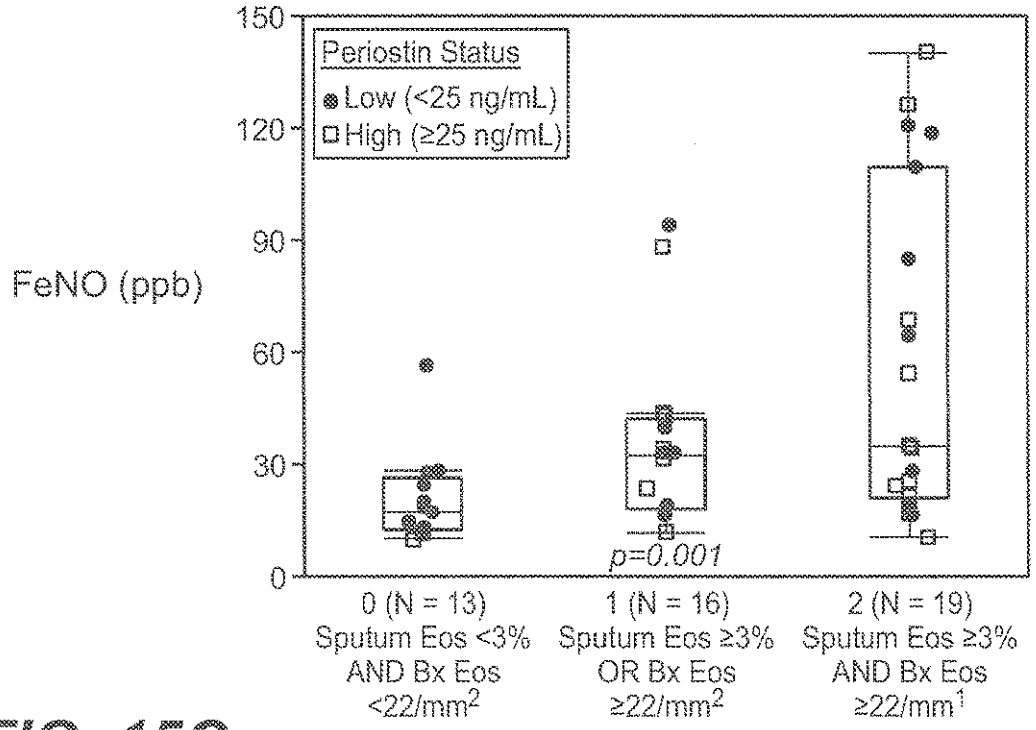


FIG. 15C

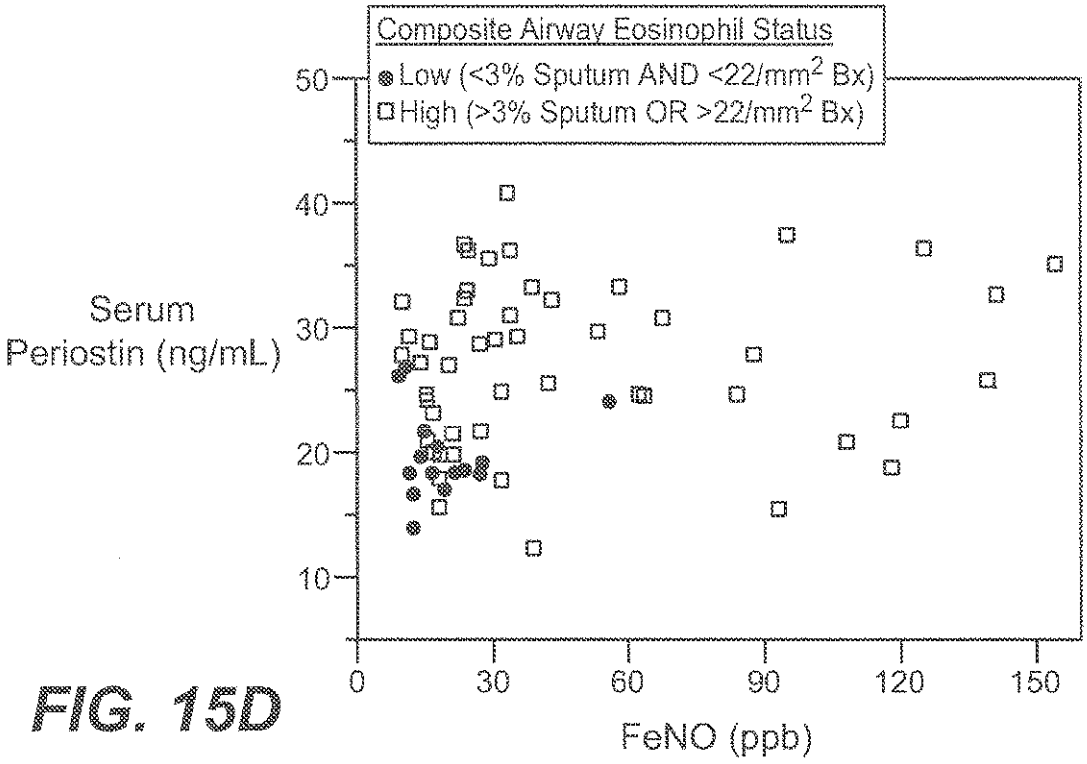


FIG. 15D

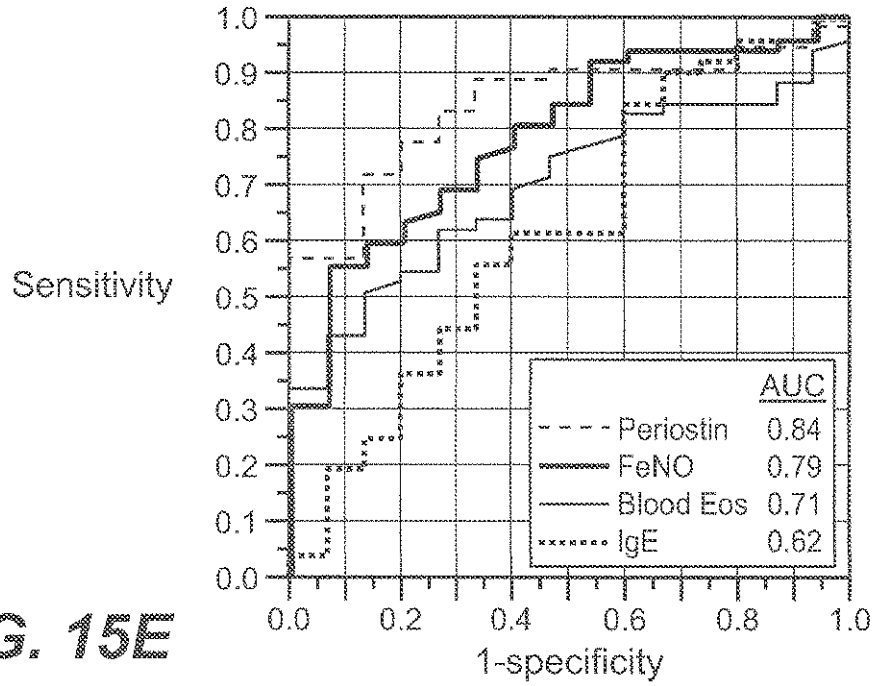


FIG. 15E

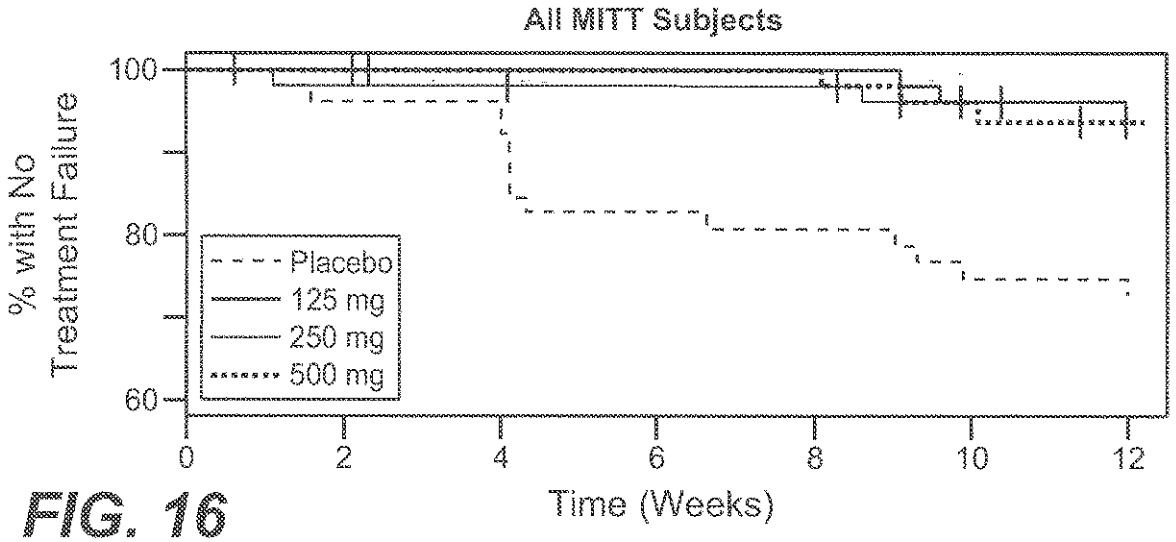


FIG. 16

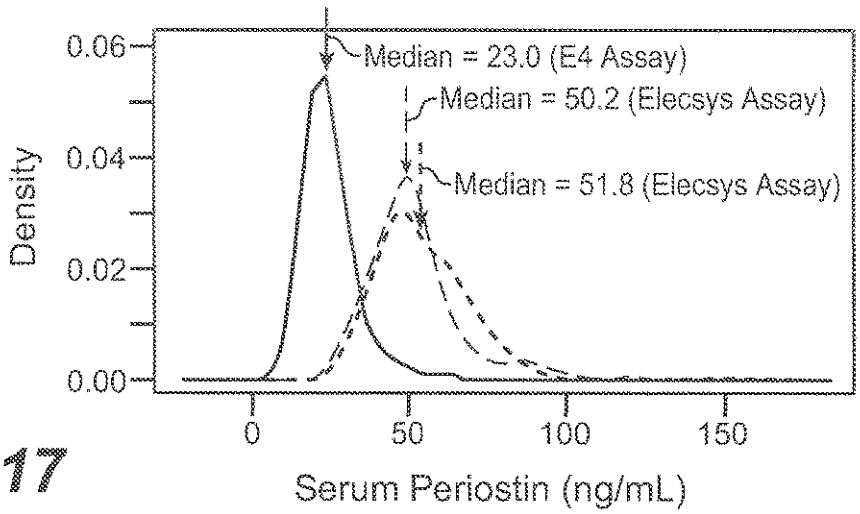


FIG. 17

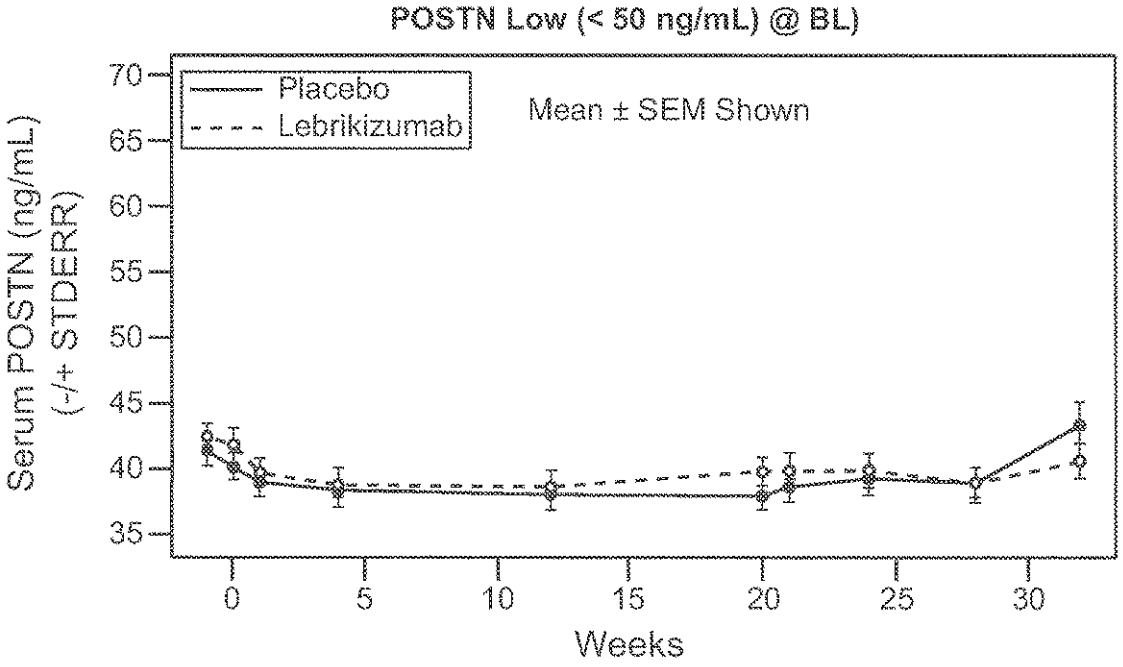


FIG. 18A

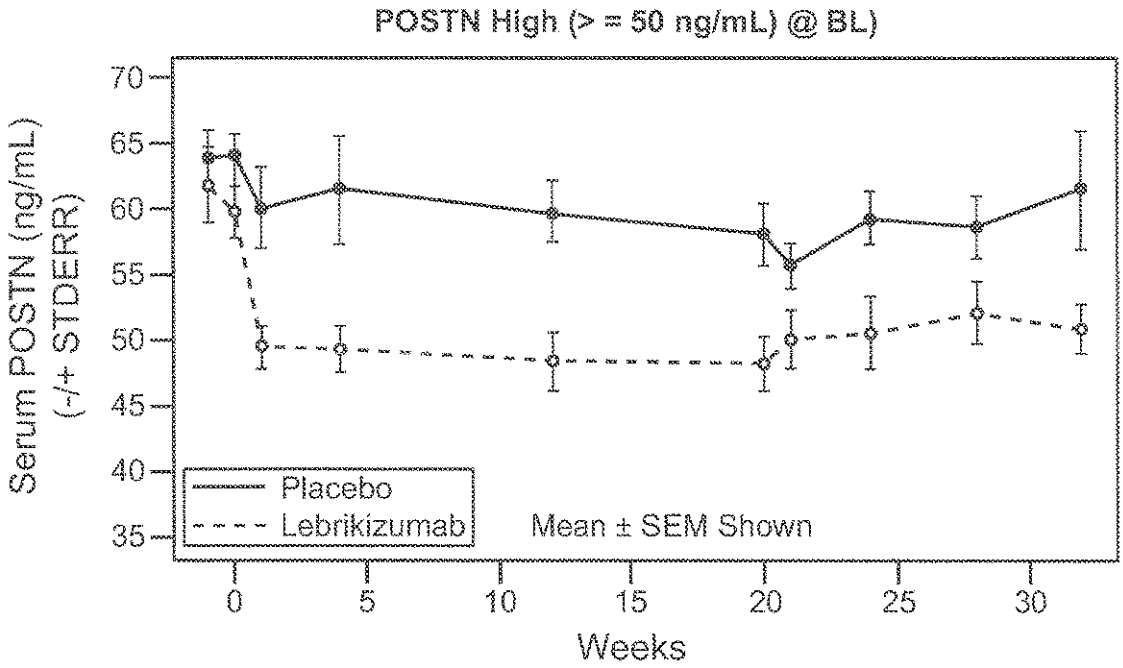


FIG. 18B

		Placebo	ebrikizumab	Δ	p-value
1 Week	Periostin-LOW	-2.3%	-5.9%	-3.6%	0.2
	Periostin-HIGH	-8.1%	-14.9%	-6.8%	0.0006
	TOTAL	-5.4%	-9.8%	-4.4%	0.003
		Placebo	**Lebrikizumab**	Δ	**p-value**
4 Weeks	Periostin-LOW	-4.0%	-6.5%	-2.5%	0.6
	Periostin-HIGH	-7.1%	-17.2%	-10.1%	<0.0001
	TOTAL	-4.9%	-10.5%	-5.6%	0.005
		Placebo	**Lebrikizumab**	Δ	**p-value**
12 Weeks	Periostin-LOW	-4.9%	-7.1%	-2.2%	0.6
	Periostin-HIGH	-3.9%	-19.2%	-15.3%	<0.0001
	TOTAL	-4.6%	-12.3%	-7.7%	0.0006
		Placebo	**Lebrikizumab**	Δ	**p-value**
24 Weeks	Periostin-LOW	-2.6%	-6.7%	-4.1%	0.2
	Periostin-HIGH	-6.0%	-16.5%	-10.5%	0.0003
	TOTAL	-4.6%	-10.7%	-6.1%	0.002
		Placebo	**Lebrikizumab**	Δ	**p-value**
32 Weeks	Periostin-LOW	+0.3%	-3.0%	-3.3%	0.02
	Periostin-HIGH	-7.4%	-14.1%	-6.7%	0.009
	TOTAL	-2.2%	-8.9%	-6.7%	0.005

FIG. 19

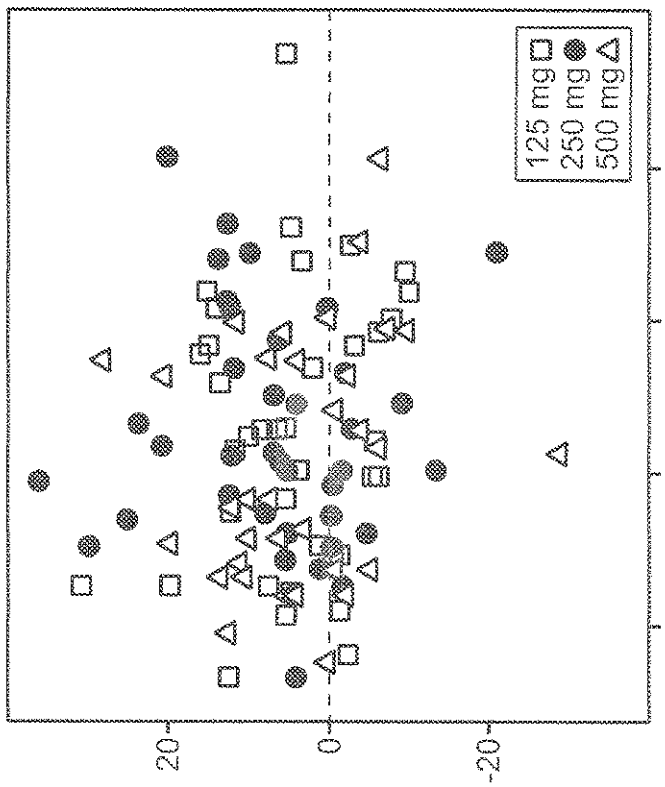


FIG. 20B

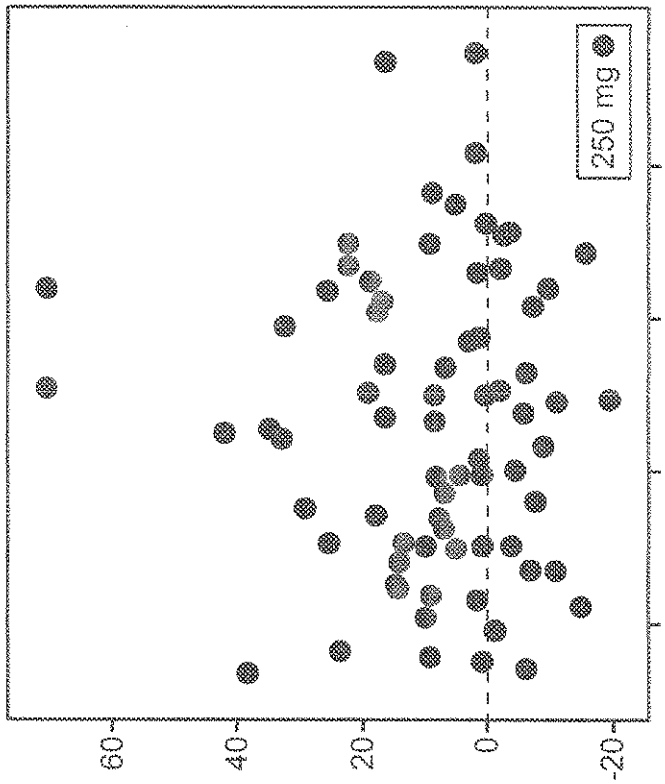


FIG. 20A

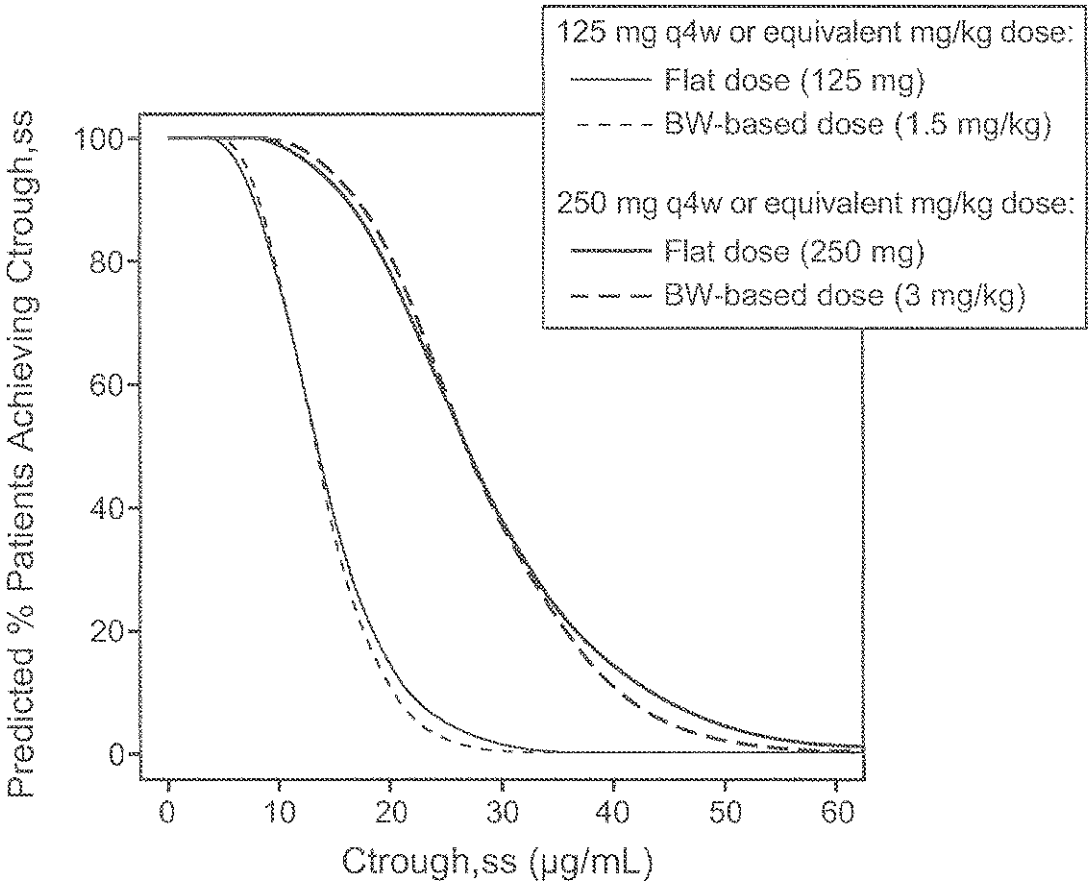

125 mg q4w or equivalent mg/kg dose:
Flat dose (125 mg)
BW-based dose (1.5 mg/kg)
250 mg q4w or equivalent mg/kg dose:
Flat dose (250 mg)
BW-based dose (3 mg/kg)
Predicted % Patients Achieving Ctrough,ss
100
80
60
40
20
0
0
10
20
30
40
50
60
Ctrough,ss (µg/mL)

FIG. 21

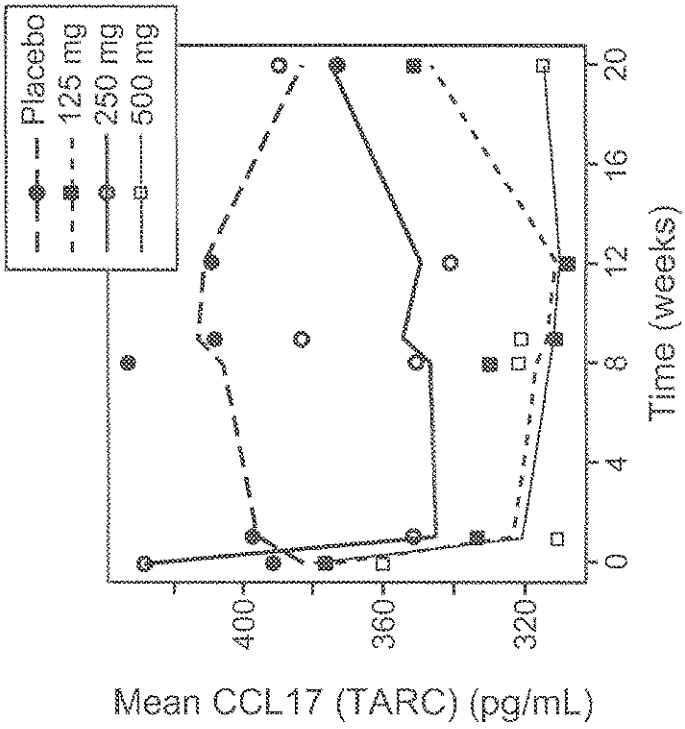


FIG. 22B

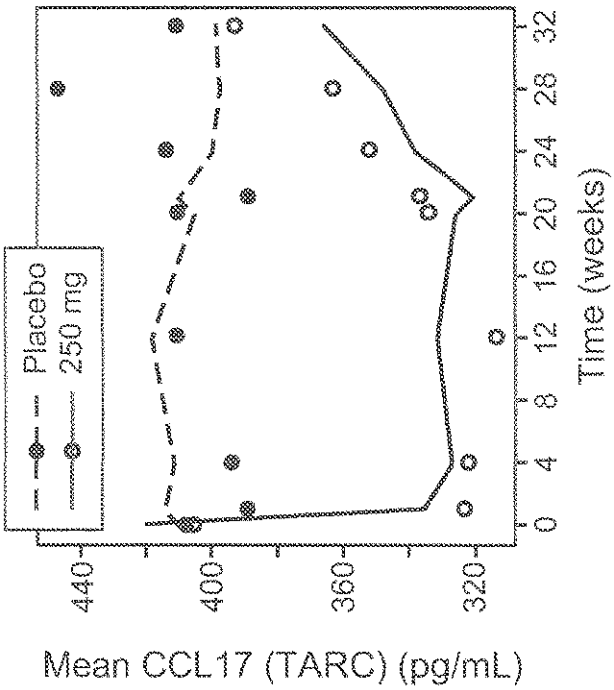


FIG. 22A

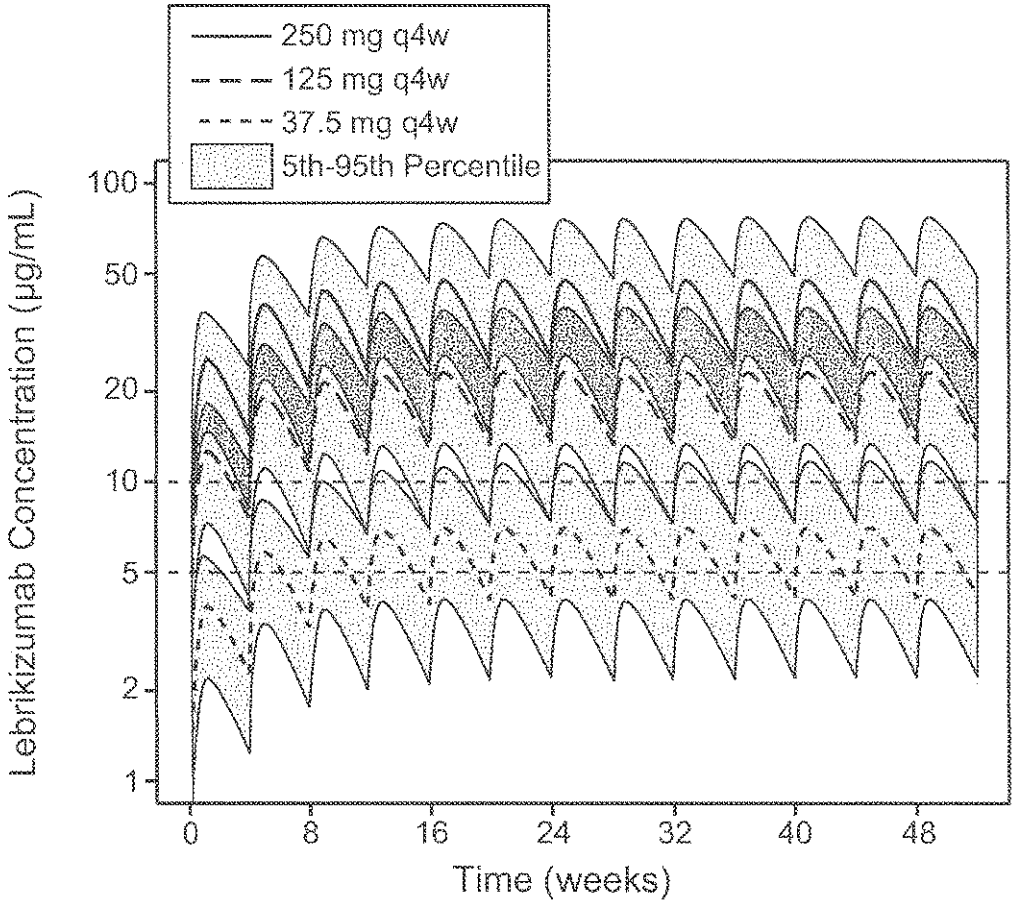

250 mg q4w
125 mg q4w
37.5 mg q4w
5th-95th Percentile
Lebrikizumab Concentration (µg/mL)
100
50
20
10
5
2
1
0
8
16
24
32
40
48
Time (weeks)

FIG. 23