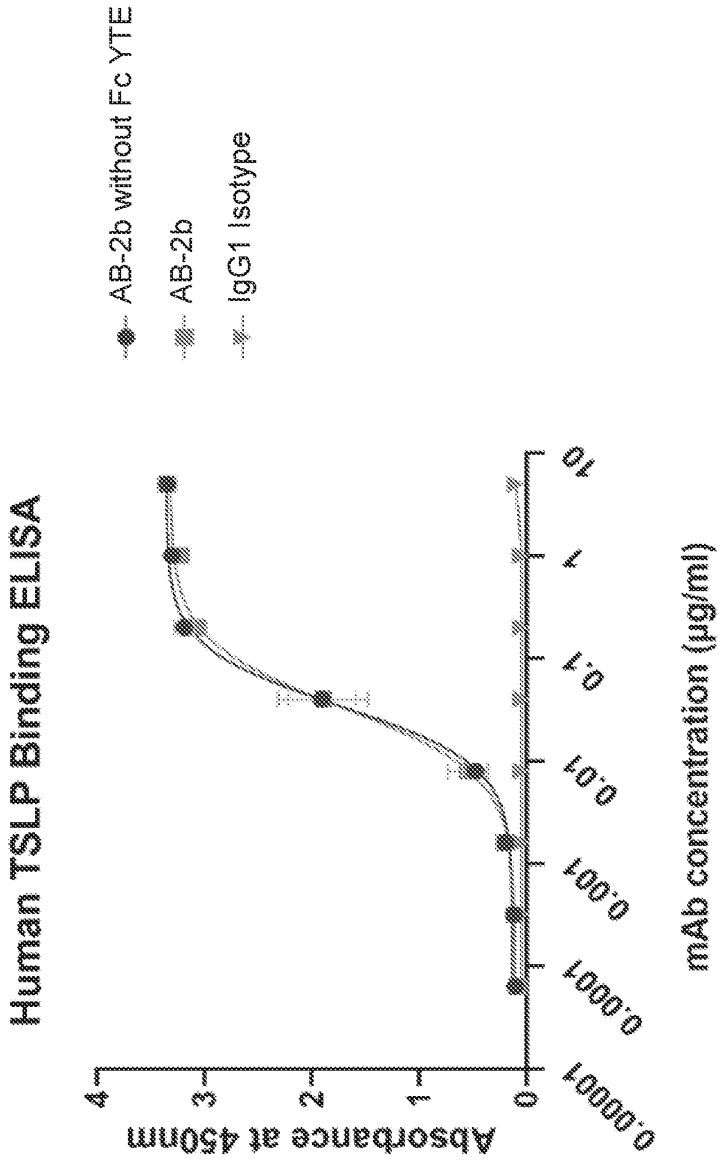
Human TSLP Binding ELISA
AB-2b without Fc YTE
AB-2b
IgG1 Isotype
Absorbance at 450nm
0
1
2
3
4
mAb concentration (µg/ml)
10
1
0.1
0.01
0.001
0.0001
0.00001

FIG. 1A

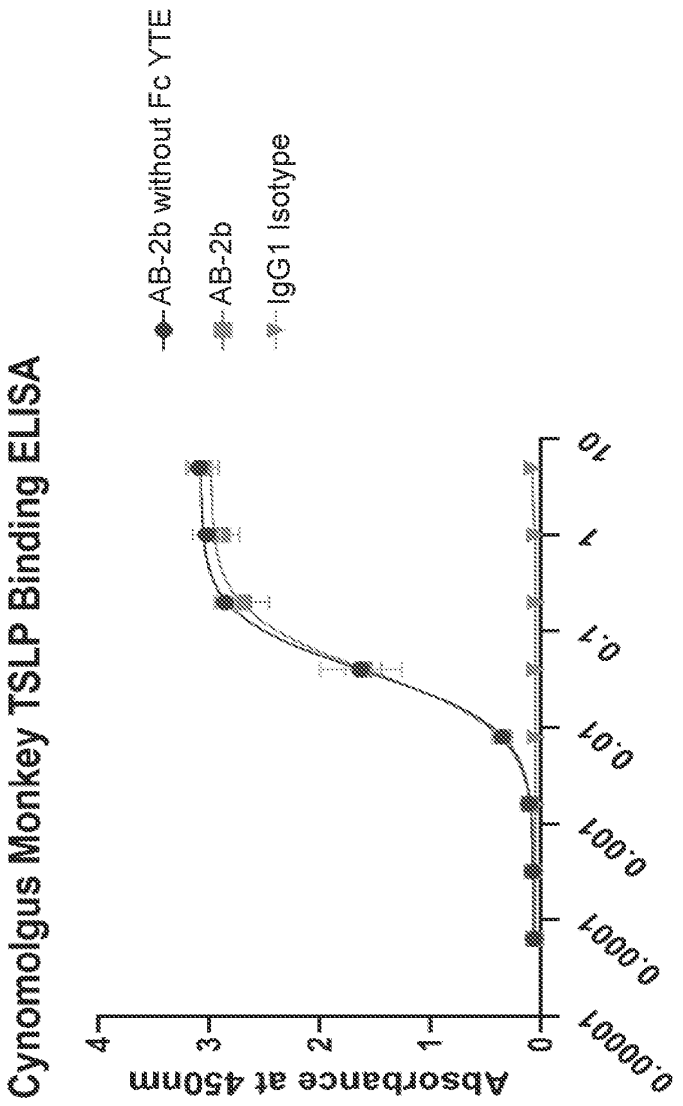
Cynomolgus Monkey TSLP Binding ELISA
AB-2b without Fc YTE
AB-2b
IgG1 Isotype
Absorbance at 450nm
0
1
2
3
4
0.00001
0.0001
0.001
0.01
0.1
1
10
mAb concentration (µg/ml)

FIG. 1B

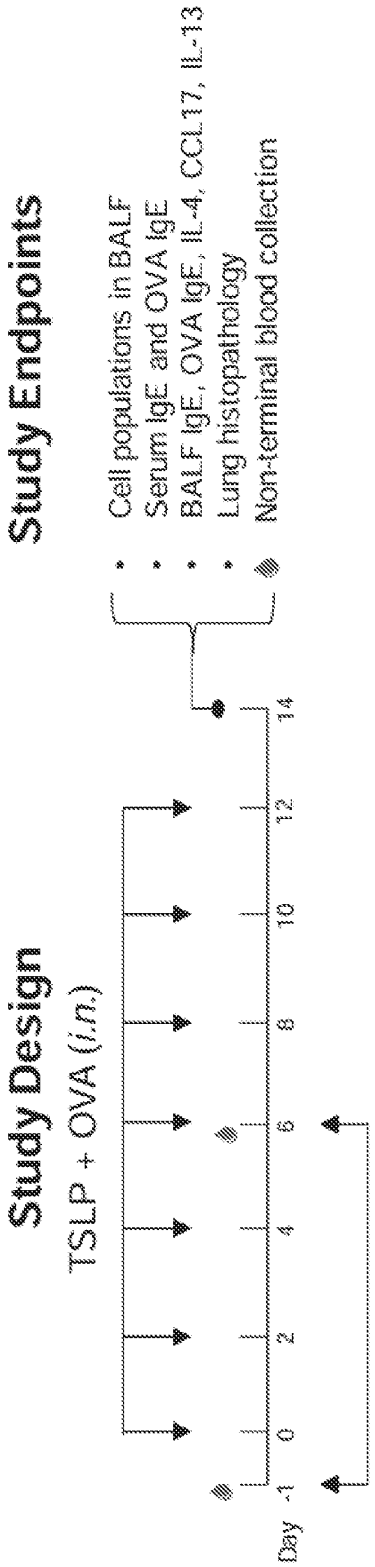
Study Endpoints
Cell populations in BALF
Serum IgE and OVA IgE
BALF IgE, OVA IgE, IL-4, CCL17, IL-13
Lung histopathology
Non-terminal blood collection
Study Design
TSLP + OVA (i.n.)
Day -1 0 2 4 6 8 10 12 14

FIG. 2A

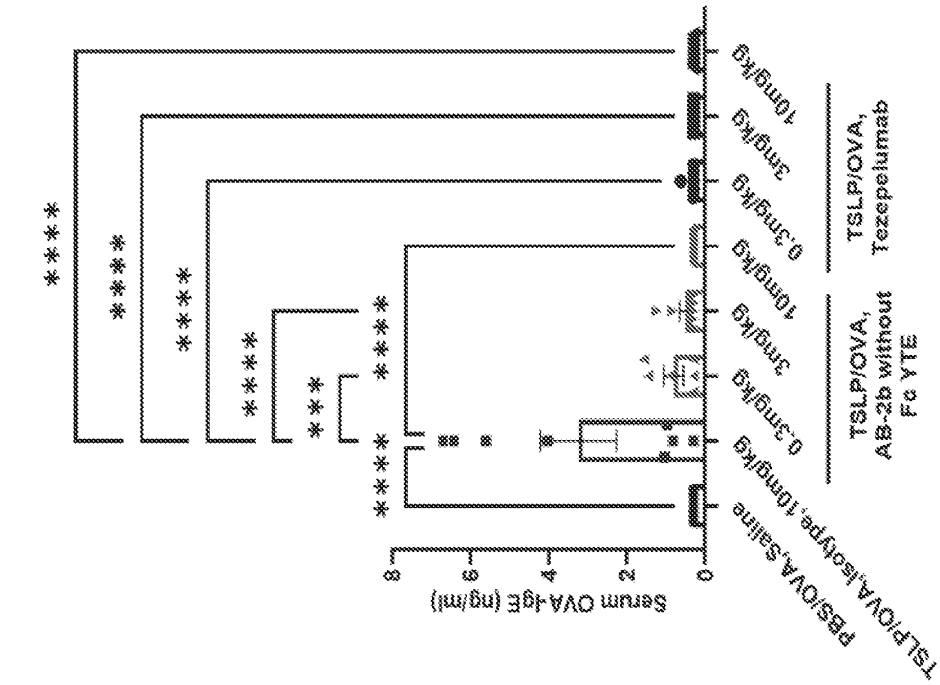
Serum OVA-IgE (ng/ml)
0
2
4
6
8
PBS/OVA,Saline
TSLP/OVA,Isotype, 10mg/kg
TSLP/OVA, AB-2b without Fc YTE
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, Tezepelumab
0.3mg/kg
3mg/kg
10mg/kg
****
****
****
***
****
****
****

FIG. 2C

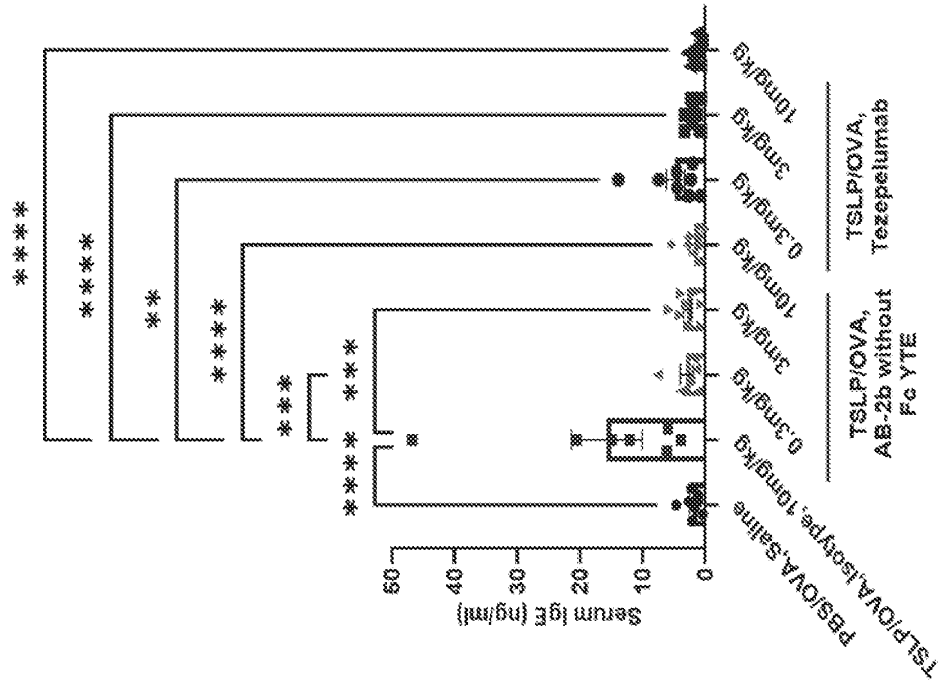
Serum IgE (ng/ml)
0
10
20
30
40
50
60
PBS/OVA,Saline
TSLP/OVA,Isotype, 10mg/kg
TSLP/OVA, AB-2b without Fc YTE
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, Tezepelumab
0.3mg/kg
3mg/kg
10mg/kg
****
****
**
****
***
****
****

FIG. 2B

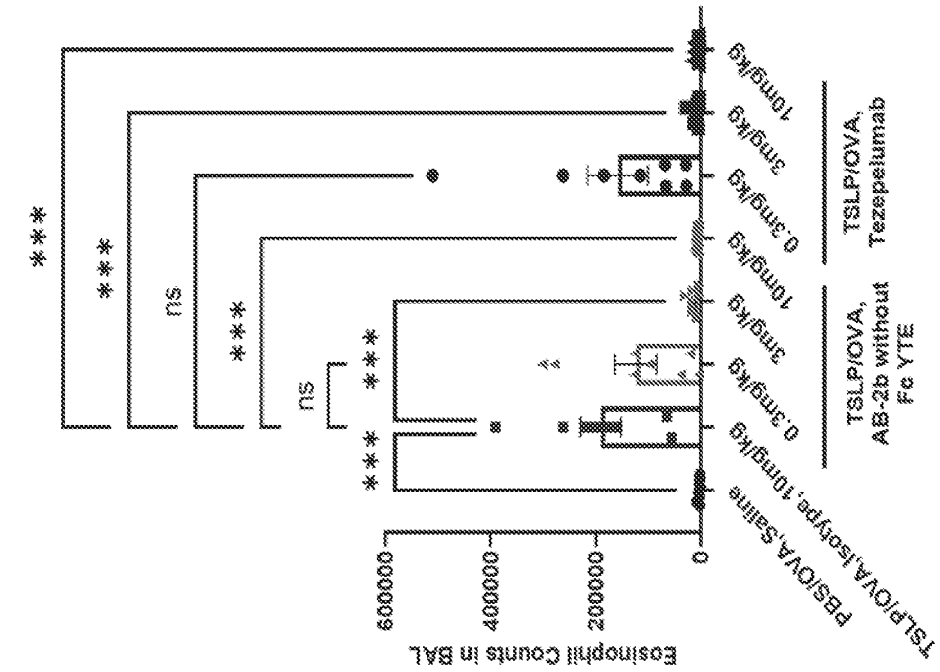
Eosinophil counts in BAL
600000
400000
200000
0
PBS/OVA,Saline
TSLP/OVA,Isotype, 10mg/kg
TSLP/OVA, AB-2b without Fc YTE
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, Tezepelumab
0.3mg/kg
3mg/kg
10mg/kg
***
***
ns
***
***
***
***

FIG. 2E

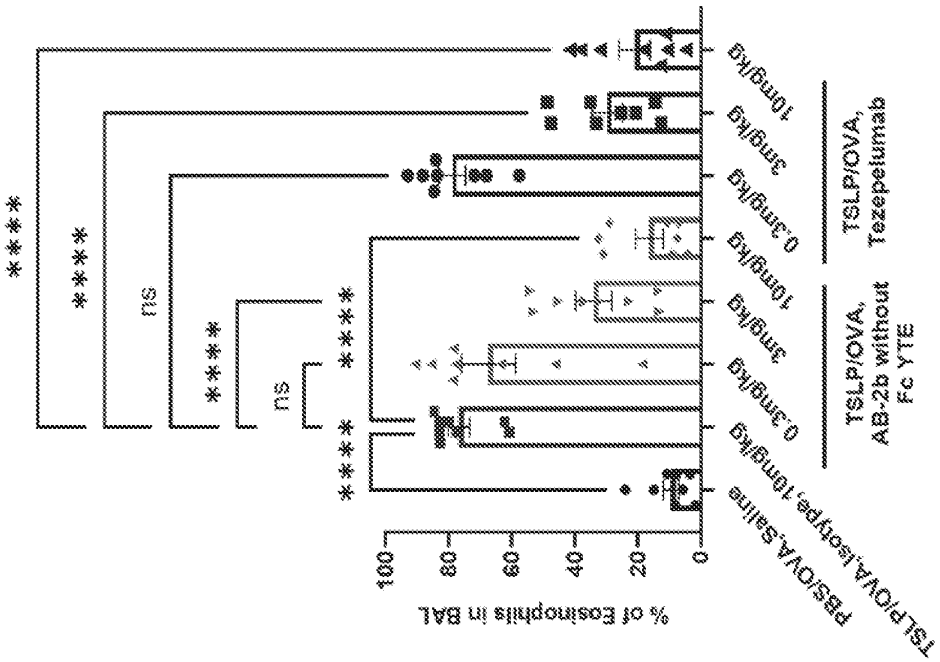
% of Eosinophils in BAL
100
80
60
40
20
0
PBS/OVA,Saline
TSLP/OVA,Isotype, 10mg/kg
TSLP/OVA, AB-2b without Fc YTE
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, Tezepelumab
0.3mg/kg
3mg/kg
10mg/kg
****
****
ns
****
****
****
****

FIG. 2D

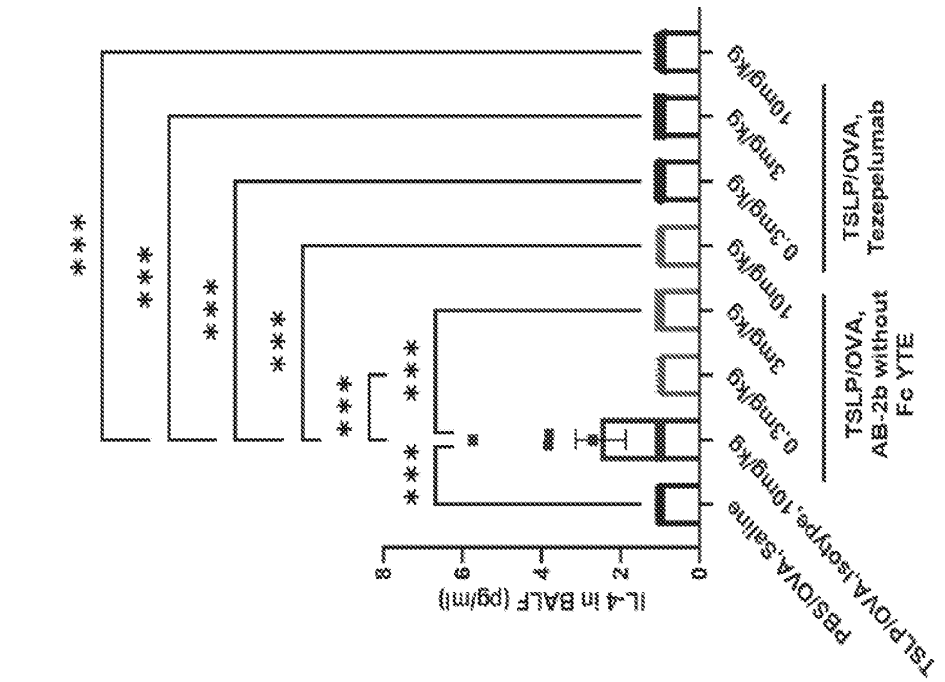
IL-4 in BALF (pg/ml)
0
2
4
6
8
PBS/OVA,Saline
TSLP/OVA,Isotype,10mg/kg
TSLP/OVA, AB-2b without Fc YTE
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, Tezepelumab
0.3mg/kg
3mg/kg
10mg/kg
****
****
****
****
****

FIG. 2G

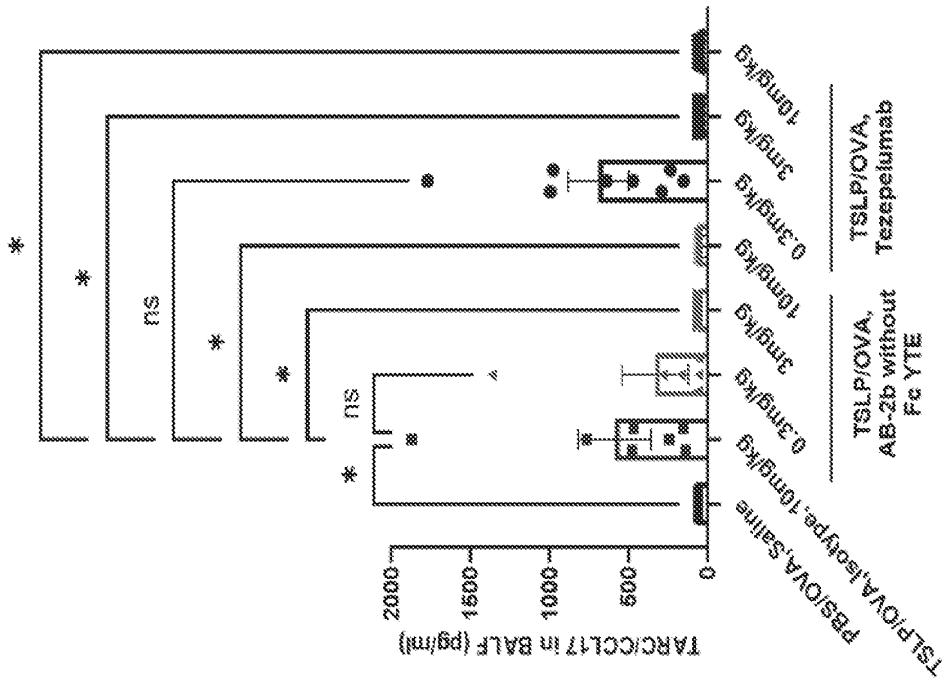
TARC/CCL17 in BALF (pg/ml)
0
600
1000
1600
2000
PBS/OVA,Saline
TSLP/OVA,Isotype,10mg/kg
TSLP/OVA, AB-2b without Fc YTE
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, Tezepelumab
0.3mg/kg
3mg/kg
10mg/kg
*
*
ns
*
*
ns
*
*

FIG. 2F

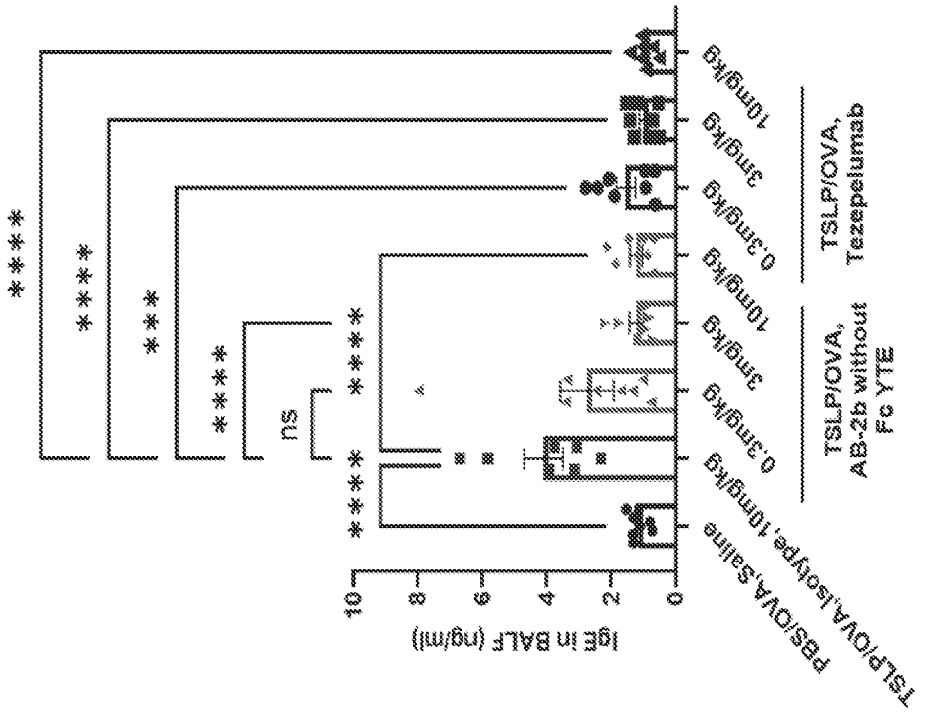
IgE in BALF (ng/ml)
0
2
4
6
8
10
PBS/OVA,Saline
TSLP/OVA,Isotype, 10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, AB-2b without Fc YTE
TSLP/OVA, Tezepelumab
ns
****
****
***
****
****
****

FIG. 2I

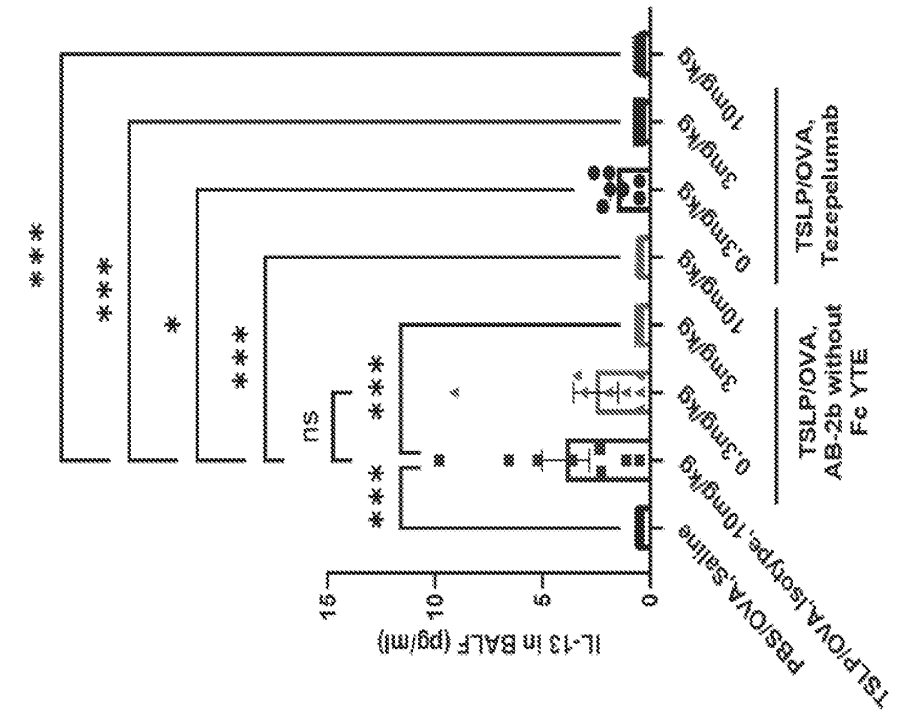
IL-13 in BALF (pg/ml)
0
5
10
15
PBS/OVA,Saline
TSLP/OVA,Isotype, 10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, AB-2b without Fc YTE
TSLP/OVA, Tezepelumab
ns
***
***
*
***
***
***

FIG. 2H

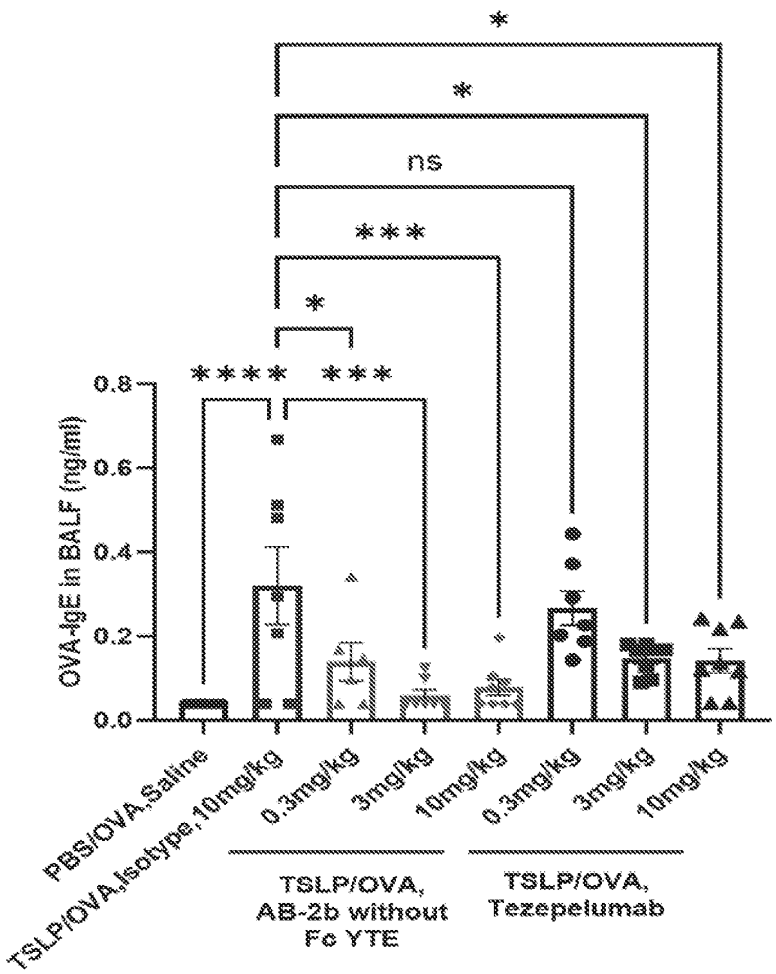
*
*
ns
***
*
****
***
OVA-IgE in BALF (ng/ml)
0.8
0.6
0.4
0.2
0.0
PBS/OVA,Saline
TSLP/OVA,Isotype,10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, AB-2b without Fc YTE
TSLP/OVA, Tezepelumab

FIG. 2J

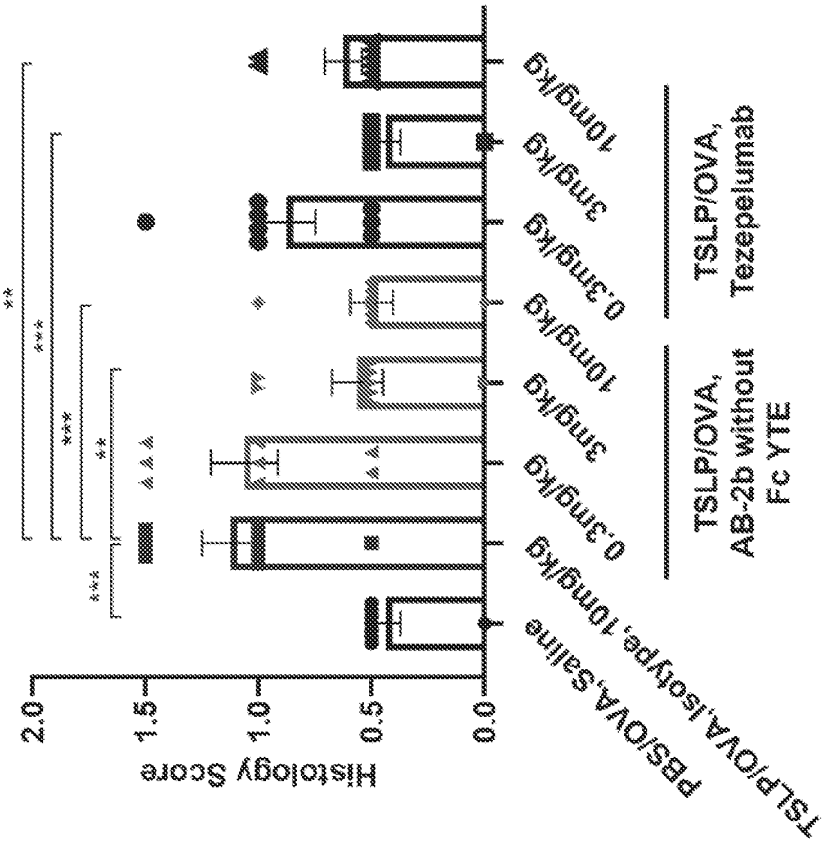
Histology Score
2.0
1.5
1.0
0.5
0.0
PBS/OVA, Saline
TSLP/OVA, isotype, 10mg/kg
TSLP/OVA, AB-2b without Fc YTE
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, Tezepelumab
0.3mg/kg
3mg/kg
10mg/kg
**
***
***
**
***

FIG. 3A

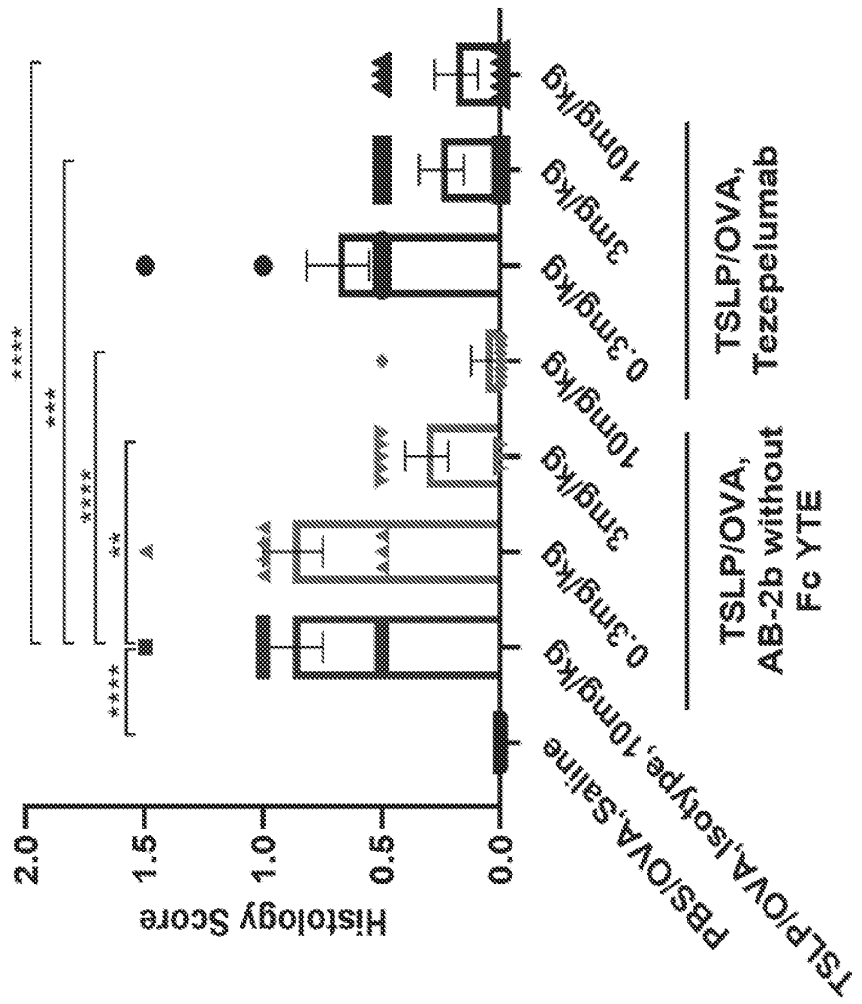
Histology Score
2.0
1.5
1.0
0.5
0.0
****
***
****
**
****
PBS/OVA,Saline
TSLP/OVA,isotype, 10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, AB-2b without Fc YTE
TSLP/OVA, Tezepelumab

FIG. 3B

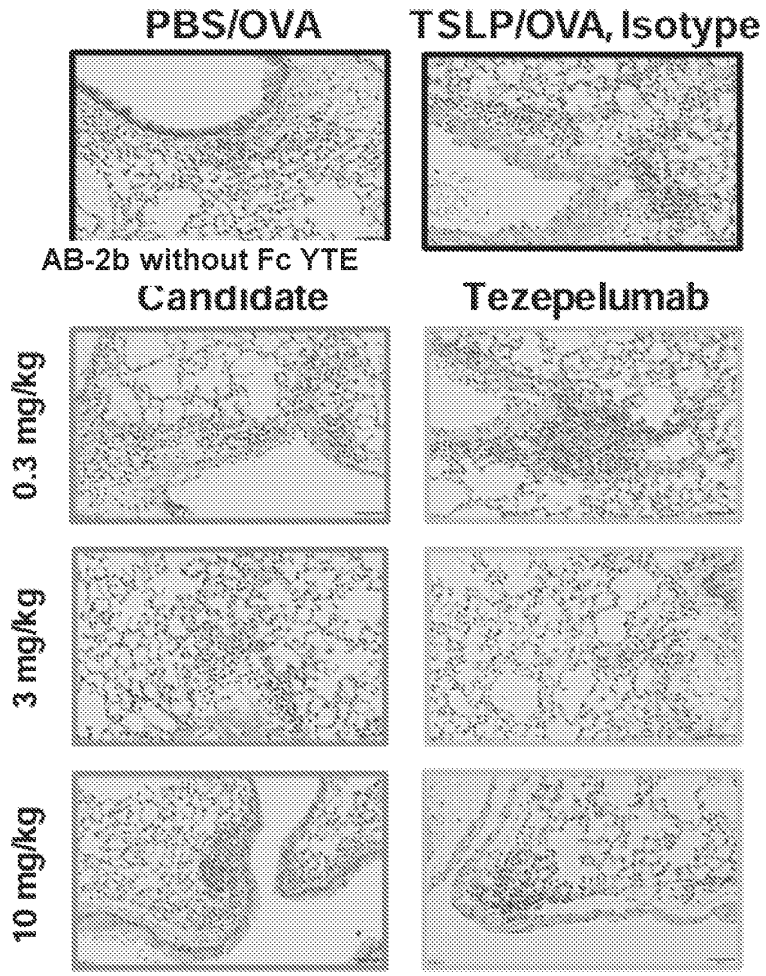
PBS/OVA
TSLP/OVA, Isotype
AB-2b without Fc YTE Candidate
Tezepelumab
0.3 mg/kg
3 mg/kg
10 mg/kg

FIG. 3C

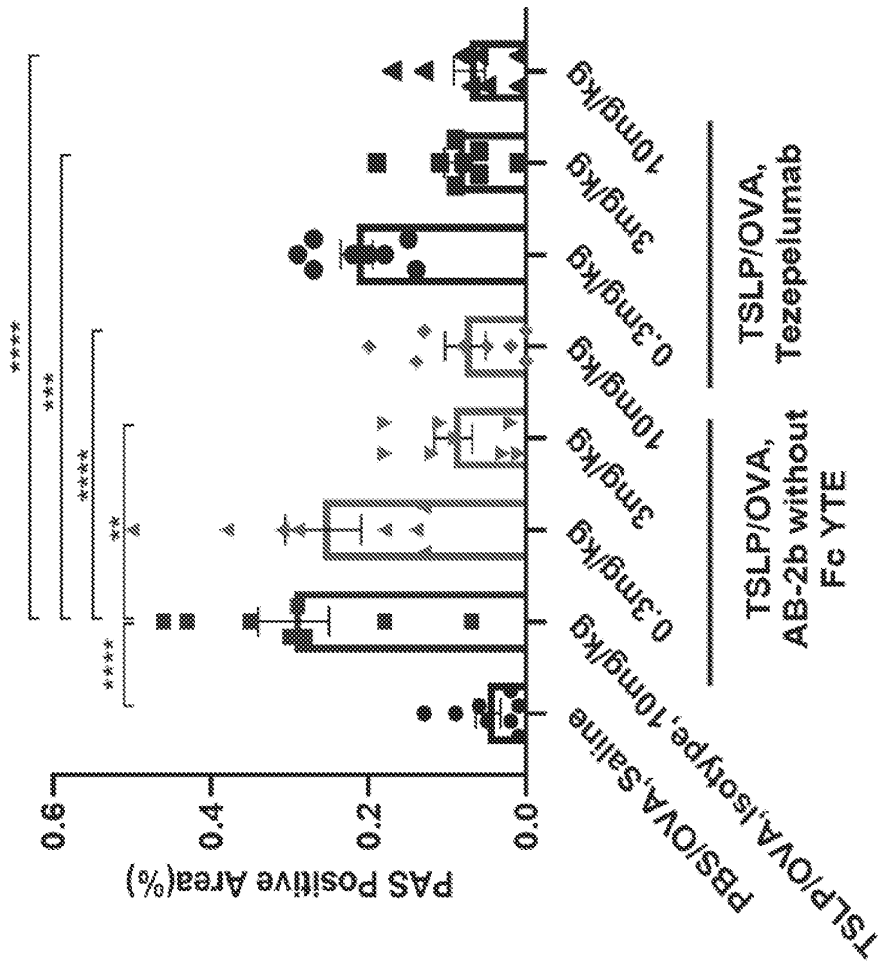
PAS Positive Area(%)
0.0
0.2
0.4
0.6
PBS/OVA,Saline
TSLP/OVA,Isotype, 10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
0.3mg/kg
3mg/kg
10mg/kg
TSLP/OVA, AB-2b without Fc YTE
TSLP/OVA, Tezepelumab
****
***
****
**
****

FIG. 3D

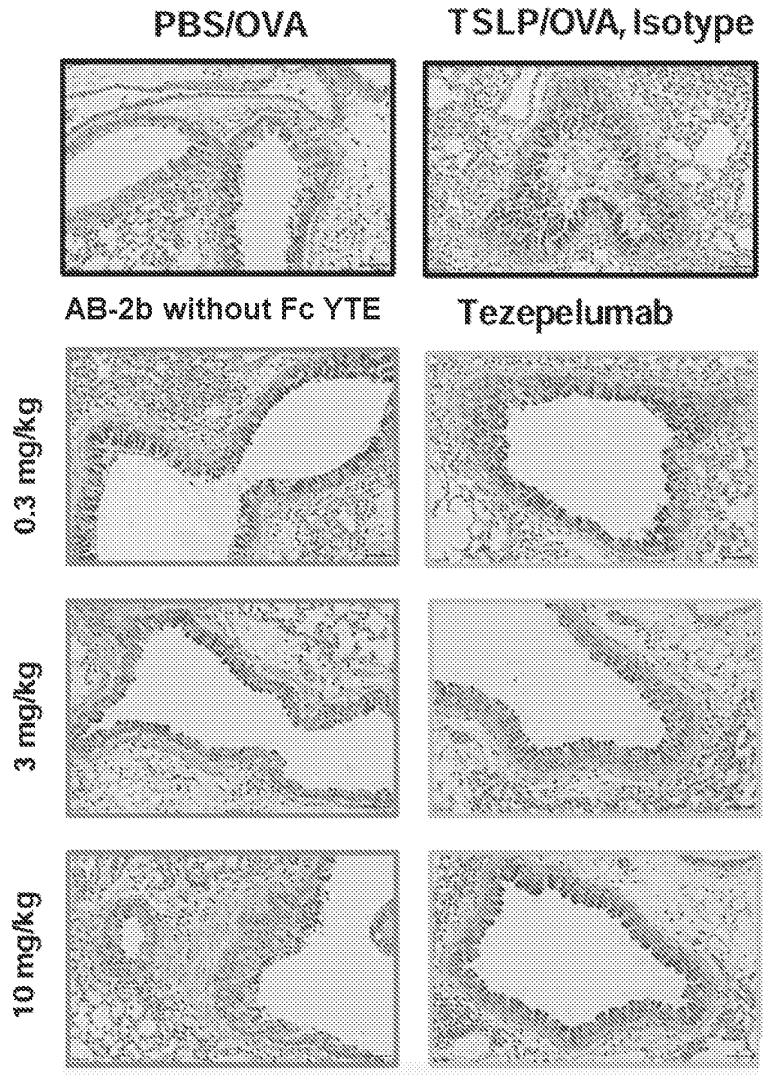
PBS/OVA
TSLP/OVA, Isotype
AB-2b without Fc YTE
Tezepelumab
0.3 mg/kg
3 mg/kg
10 mg/kg

FIG. 3E

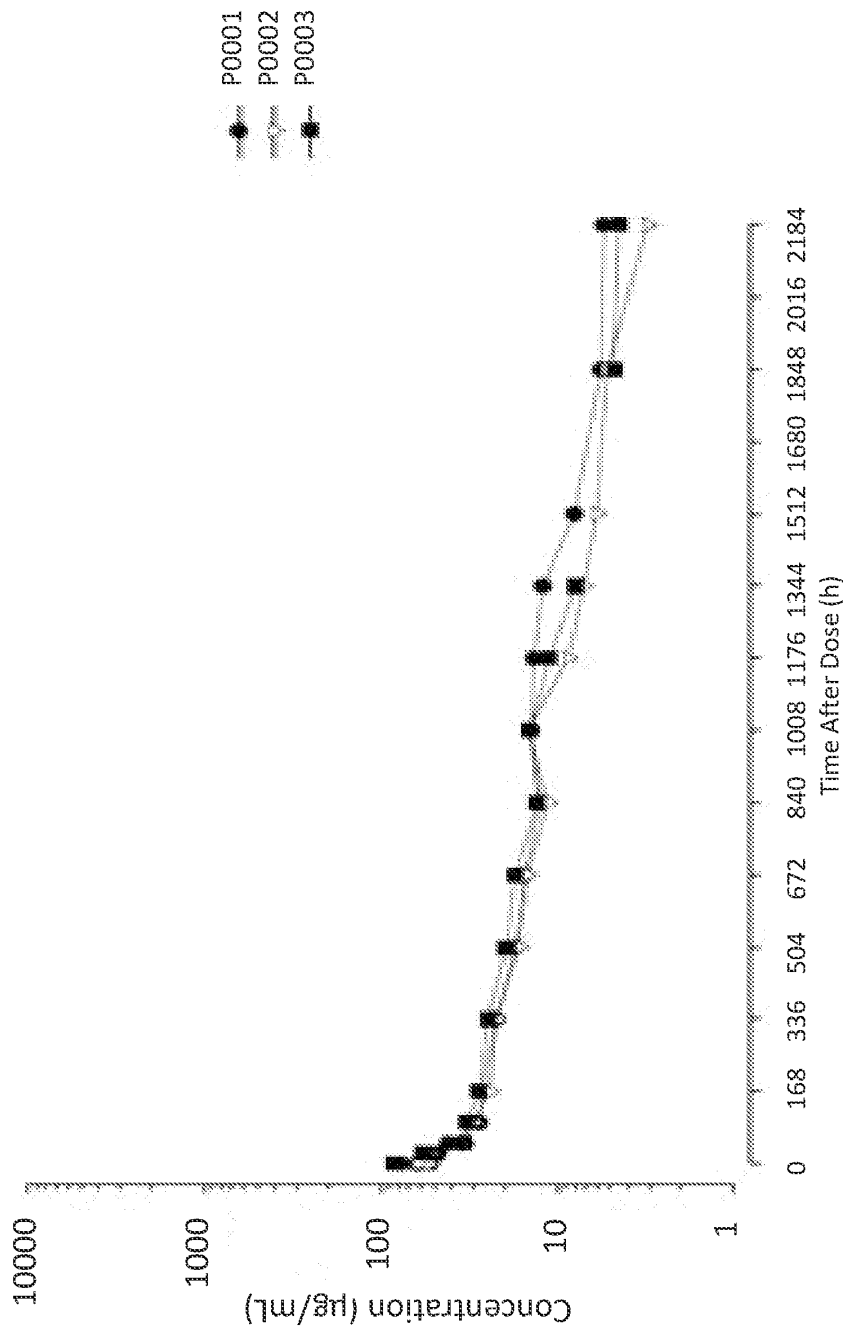
P0001
P0002
P0003
Concentration (µg/mL)
10000
1000
100
10
1
0
168
336
504
672
840
1008
1176
1344
1512
1680
1848
2016
2184
Time After Dose (h)

FIG. 4A

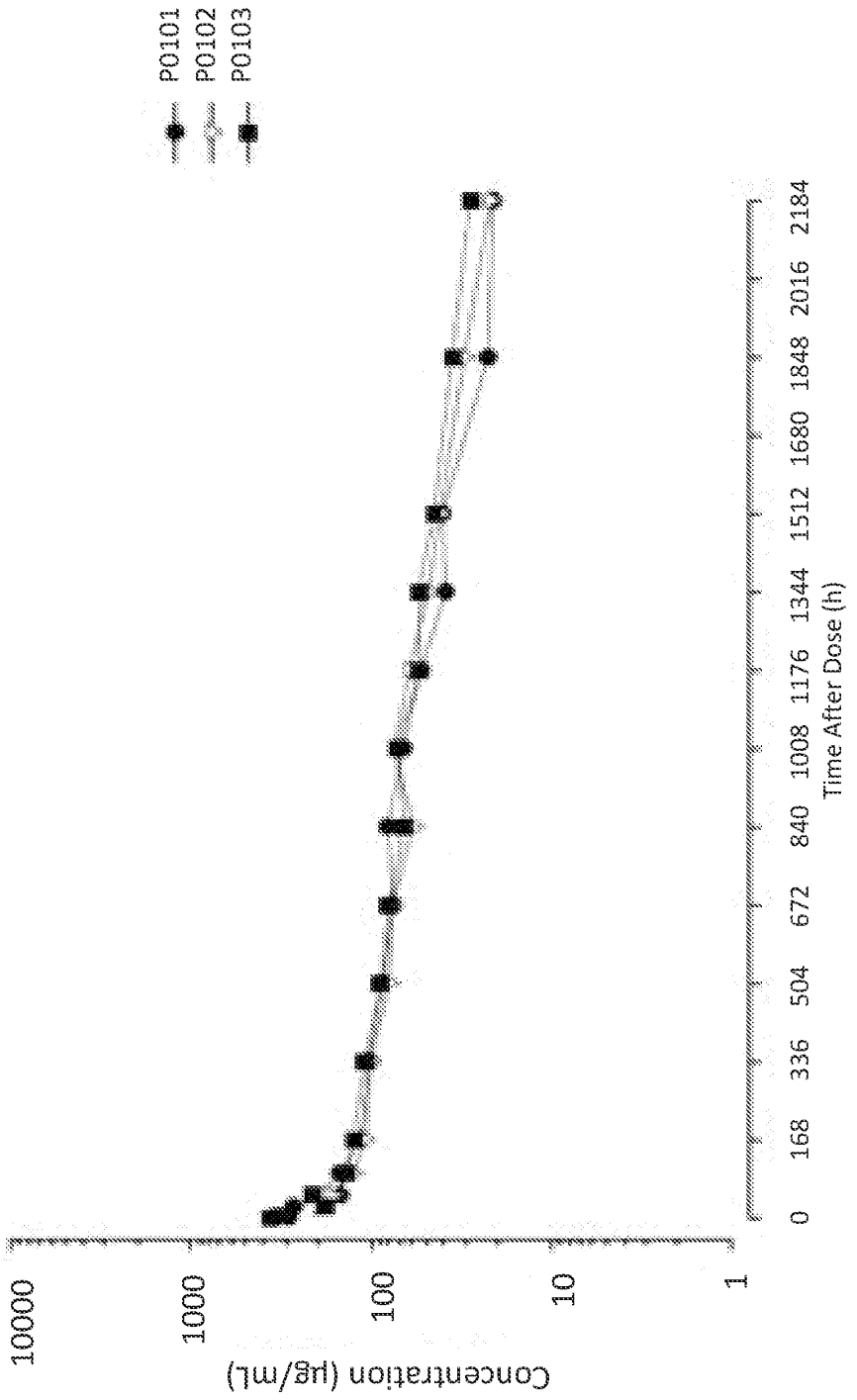
P0101
P0102
P0103
Concentration (µg/mL)
10000
1000
100
10
1
0
168
336
504
672
840
1008
1176
1344
1512
1680
1848
2016
2184
Time After Dose (h)

FIG. 4B

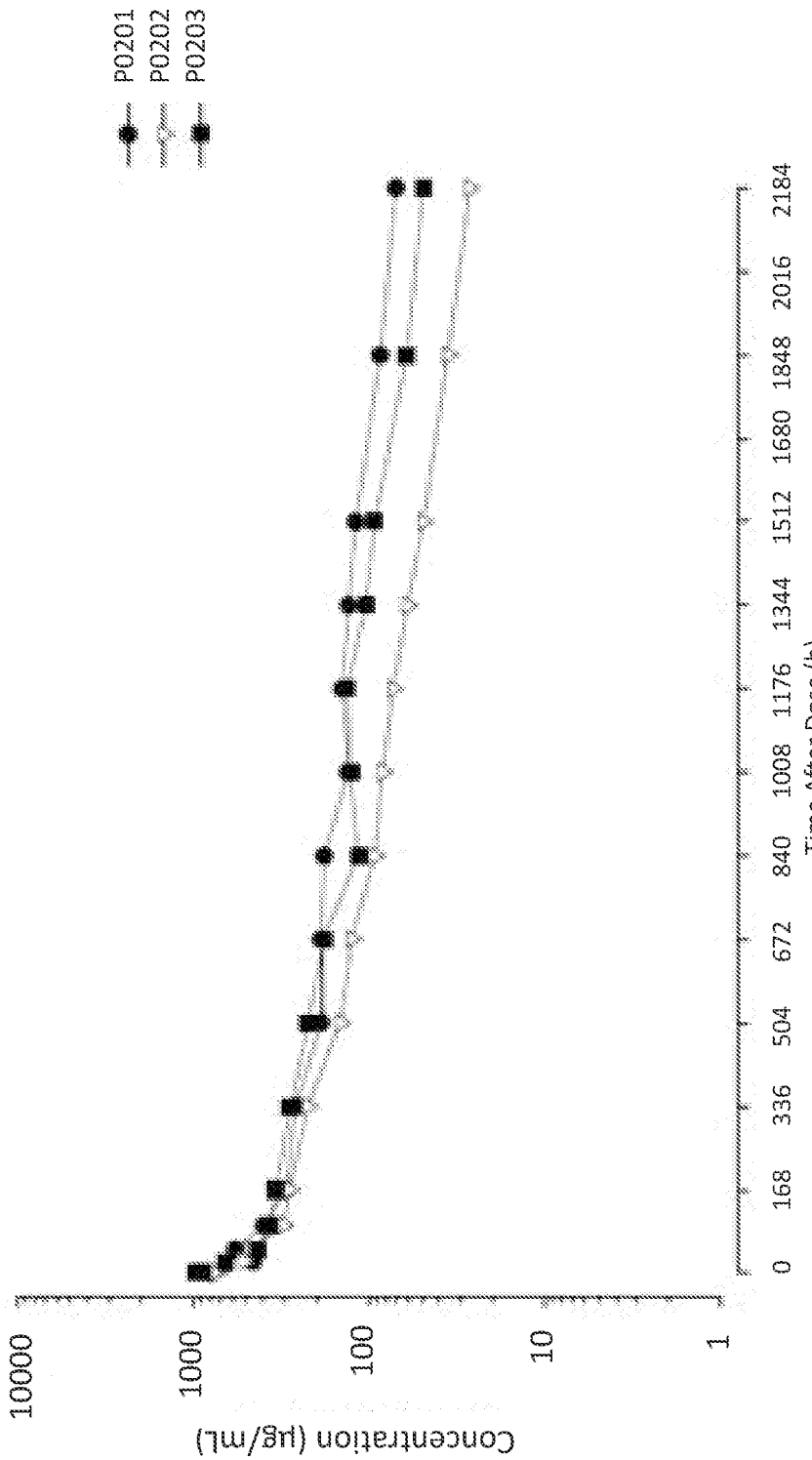
P0201
P0202
P0203
Concentration (µg/mL)
10000
1000
100
10
1
0
168
336
504
672
840
1008
1176
1344
1512
1680
1848
2016
2184
Time After Dose (h)

FIG. 4C

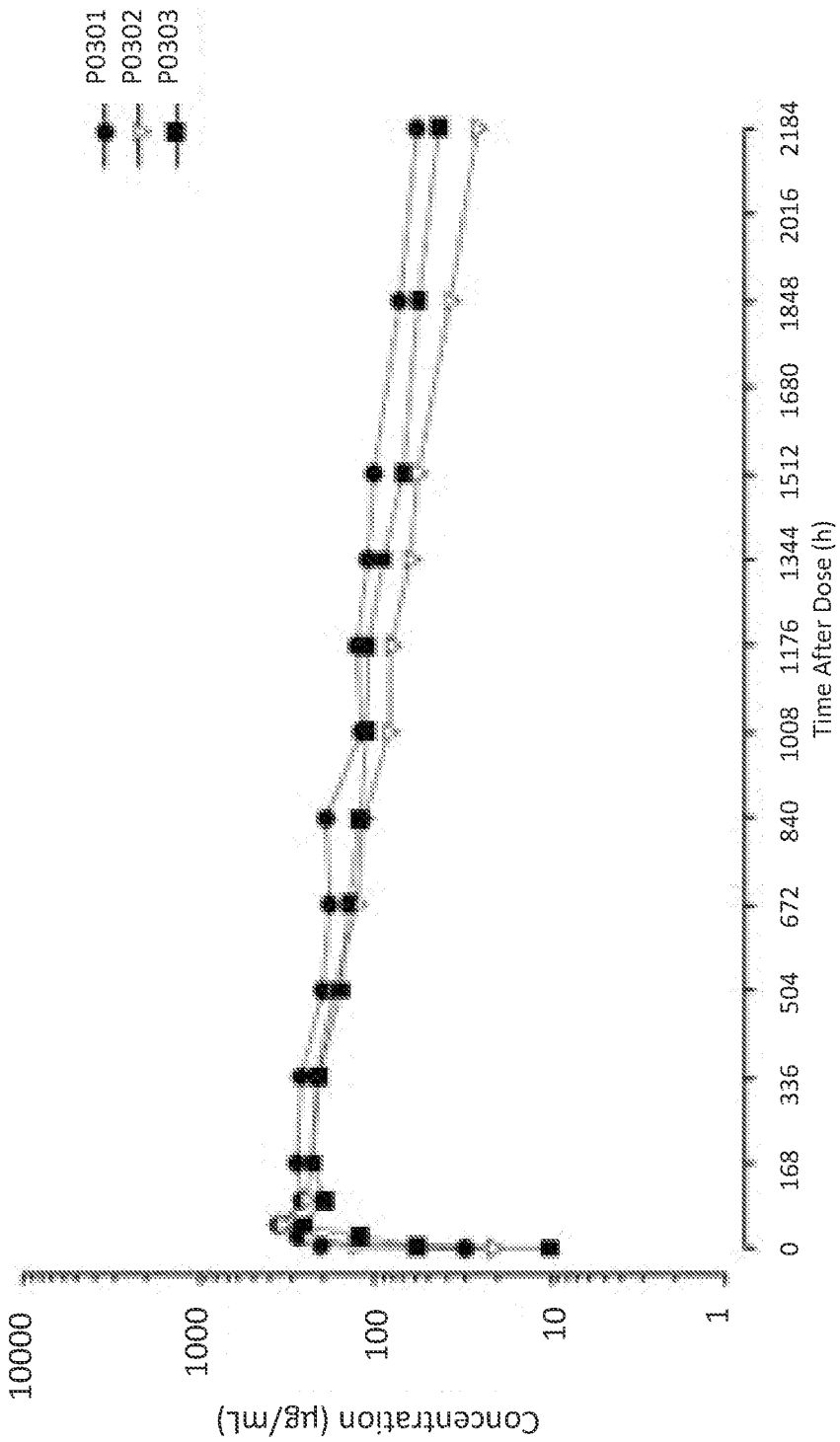
P0301
P0302
P0303
Concentration (µg/mL)
10000
1000
100
10
1
0
168
336
504
672
840
1008
1176
1344
1512
1680
1848
2016
2184
Time After Dose (h)

FIG. 4D

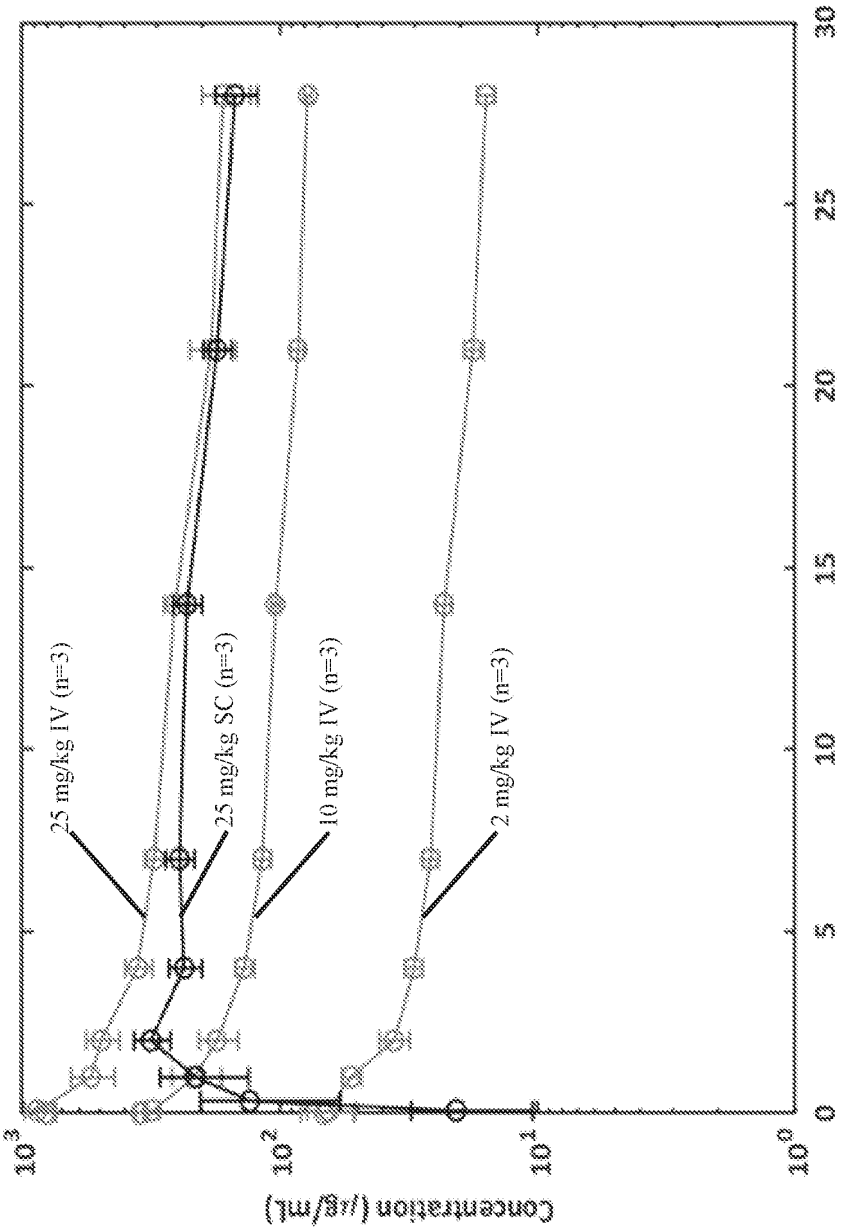
25 mg/kg IV (n=3)
25 mg/kg SC (n=3)
10 mg/kg IV (n=3)
2 mg/kg IV (n=3)
Concentration (μg/mL)
Time (days)
10^3
10^2
10^1
10^0
0
5
10
15
20
25
30

FIG. 5A

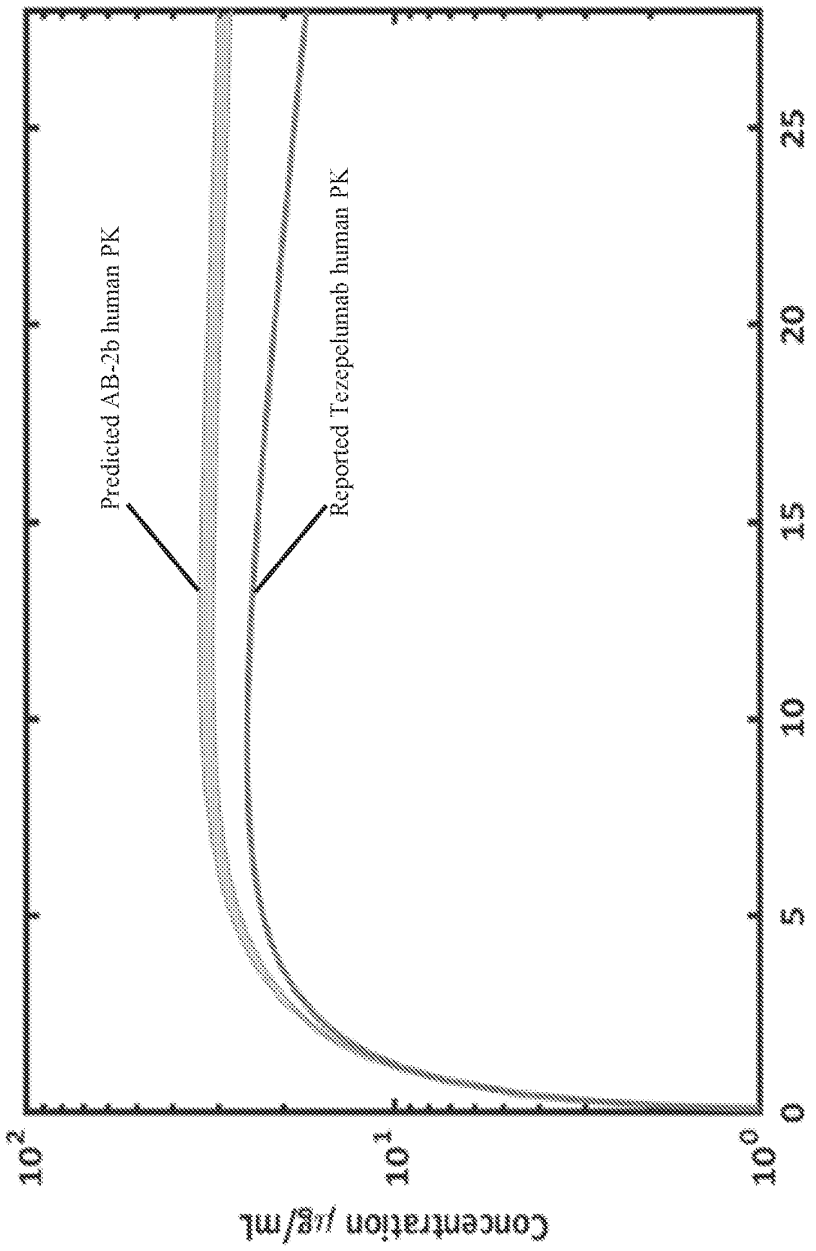
Predicted AB-2b human PK
Reported Tezepelumab human PK
Concentration µg/mL
10^2
10^1
10^0
0
5
10
15
20
25
Time (days)

FIG. 5B

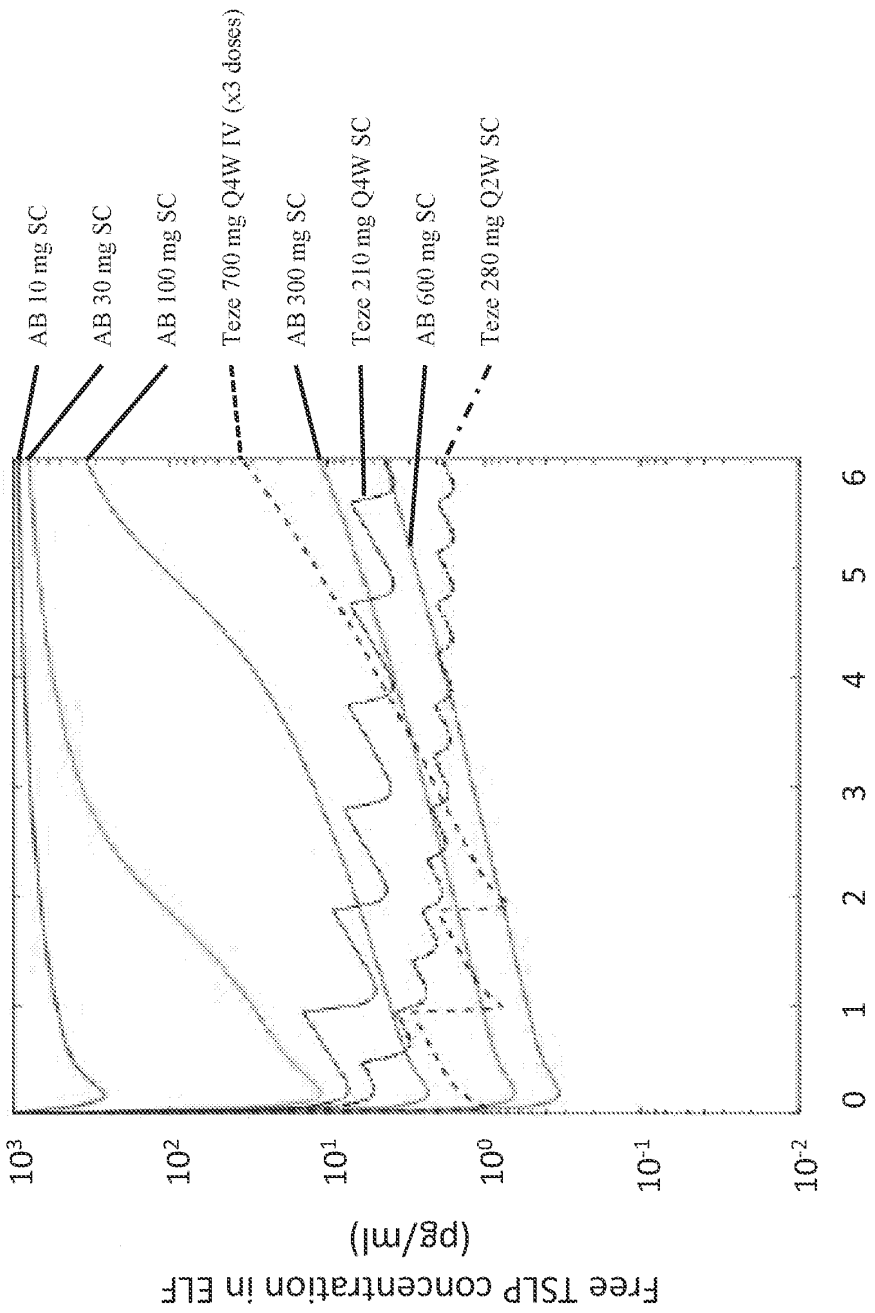
AB 10 mg SC
AB 30 mg SC
AB 100 mg SC
Teze 700 mg Q4W IV (x3 doses)
AB 300 mg SC
Teze 210 mg Q4W SC
AB 600 mg SC
Teze 280 mg Q2W SC
Free TSLP concentration in ELF
(pg/ml)
10^3
10^2
10^1
10^0
10^{-1}
10^{-2}
0 1 2 3 4 5 6
Time (months)

FIG. 5C

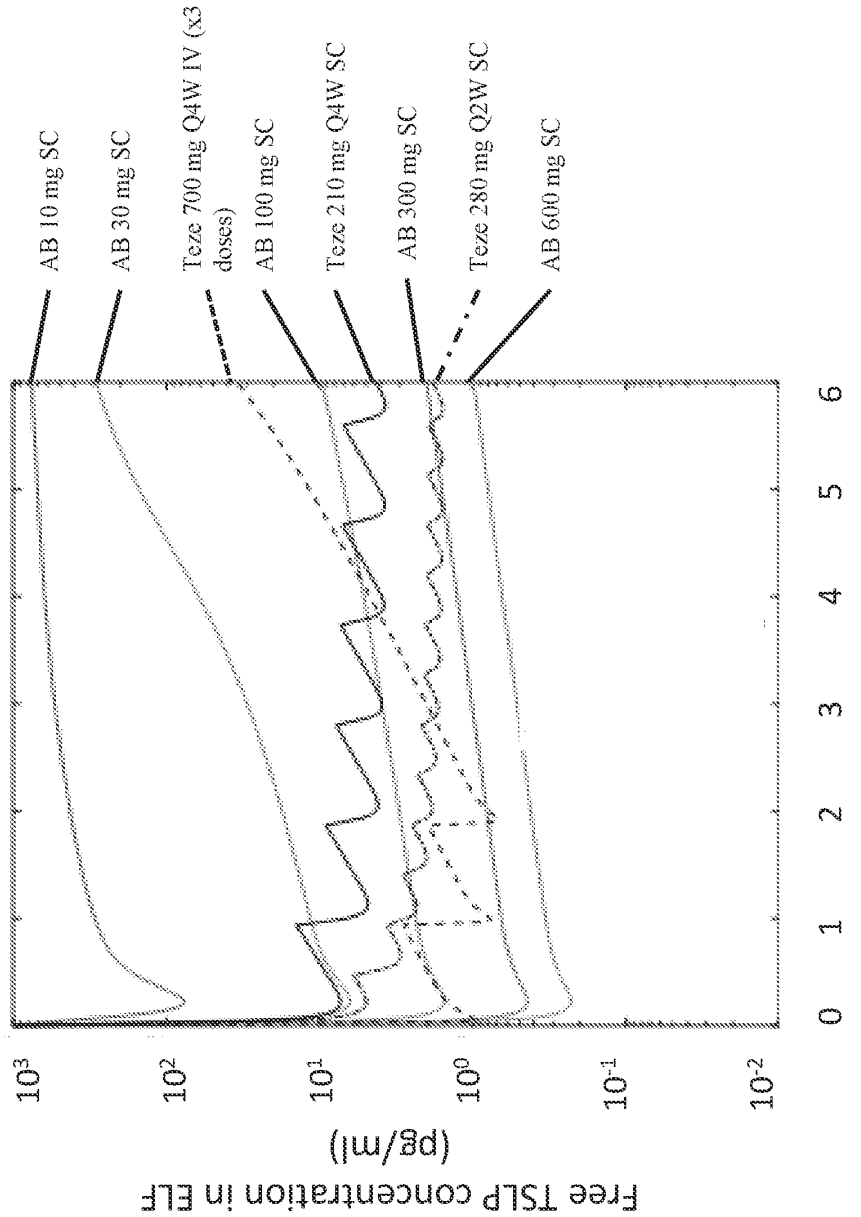
AB 10 mg SC
AB 30 mg SC
Teze 700 mg Q4W IV (x3 doses)
AB 100 mg SC
Teze 210 mg Q4W SC
AB 300 mg SC
Teze 280 mg Q2W SC
AB 600 mg SC
Free TSLP concentration in ELF
(pg/ml)
10^3
10^2
10^1
10^0
10^{-1}
10^{-2}
0 1 2 3 4 5 6
Time (months)

FIG. 5D

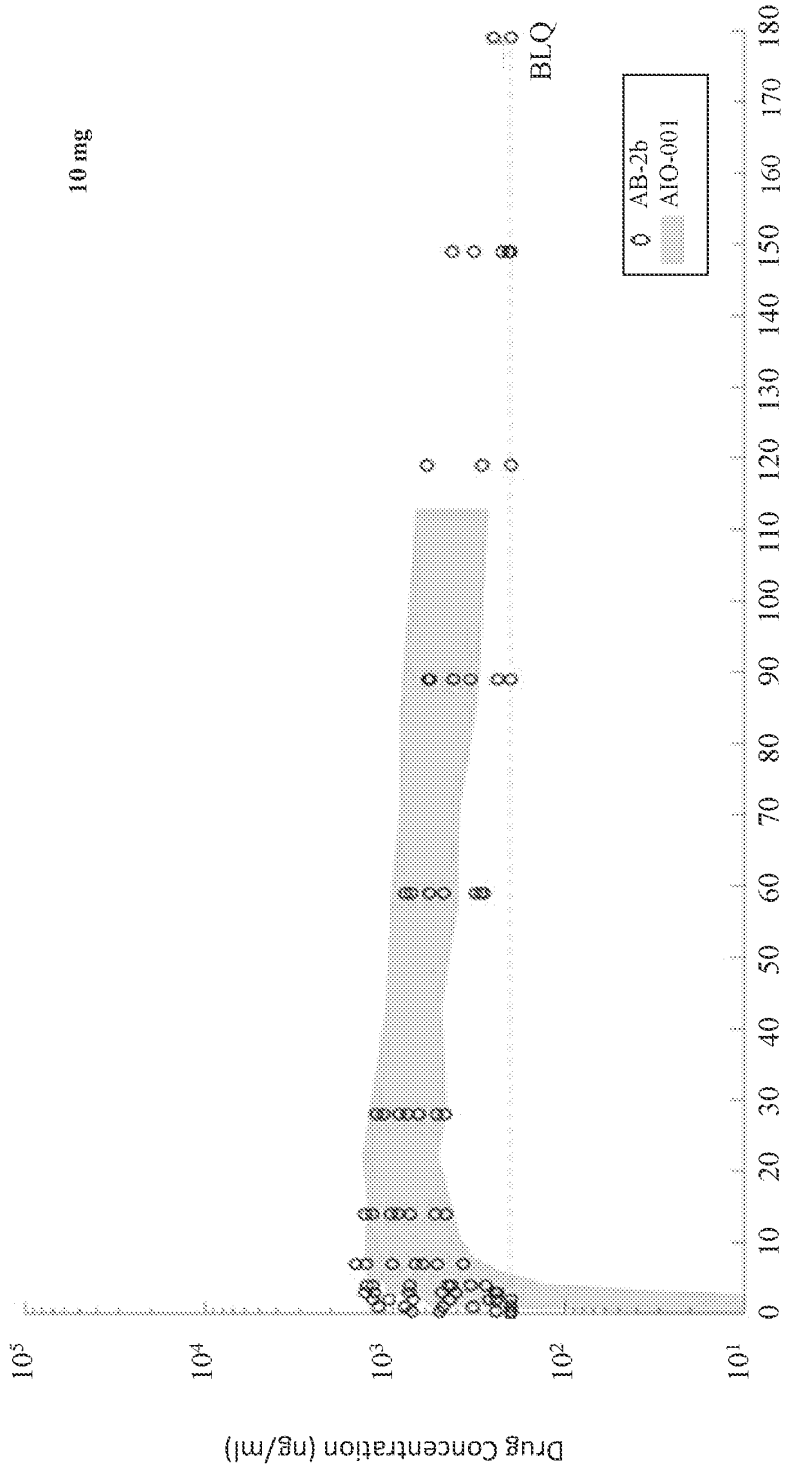
10 mg
BLQ
AB-2b
AIO-001
Drug Concentration (ng/ml)
10^5
10^4
10^3
10^2
10^1
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
Time (days)

FIG. 6A

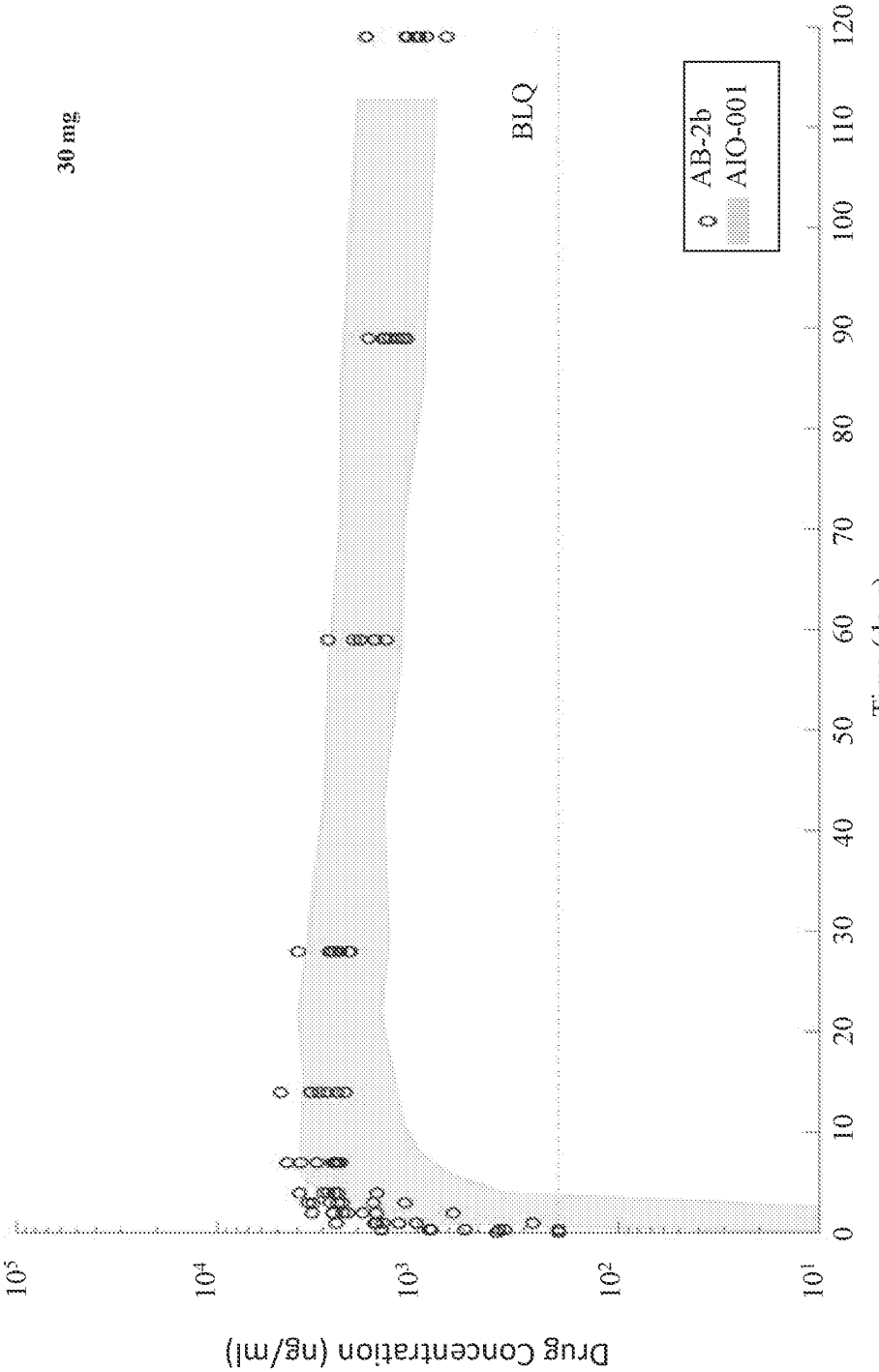
30 mg
BLQ
AB-2b
AIO-001
Drug Concentration (ng/ml)
Time (days)
10^5
10^4
10^3
10^2
10^1
0
10
20
30
40
50
60
70
80
90
100
110
120

FIG. 6B

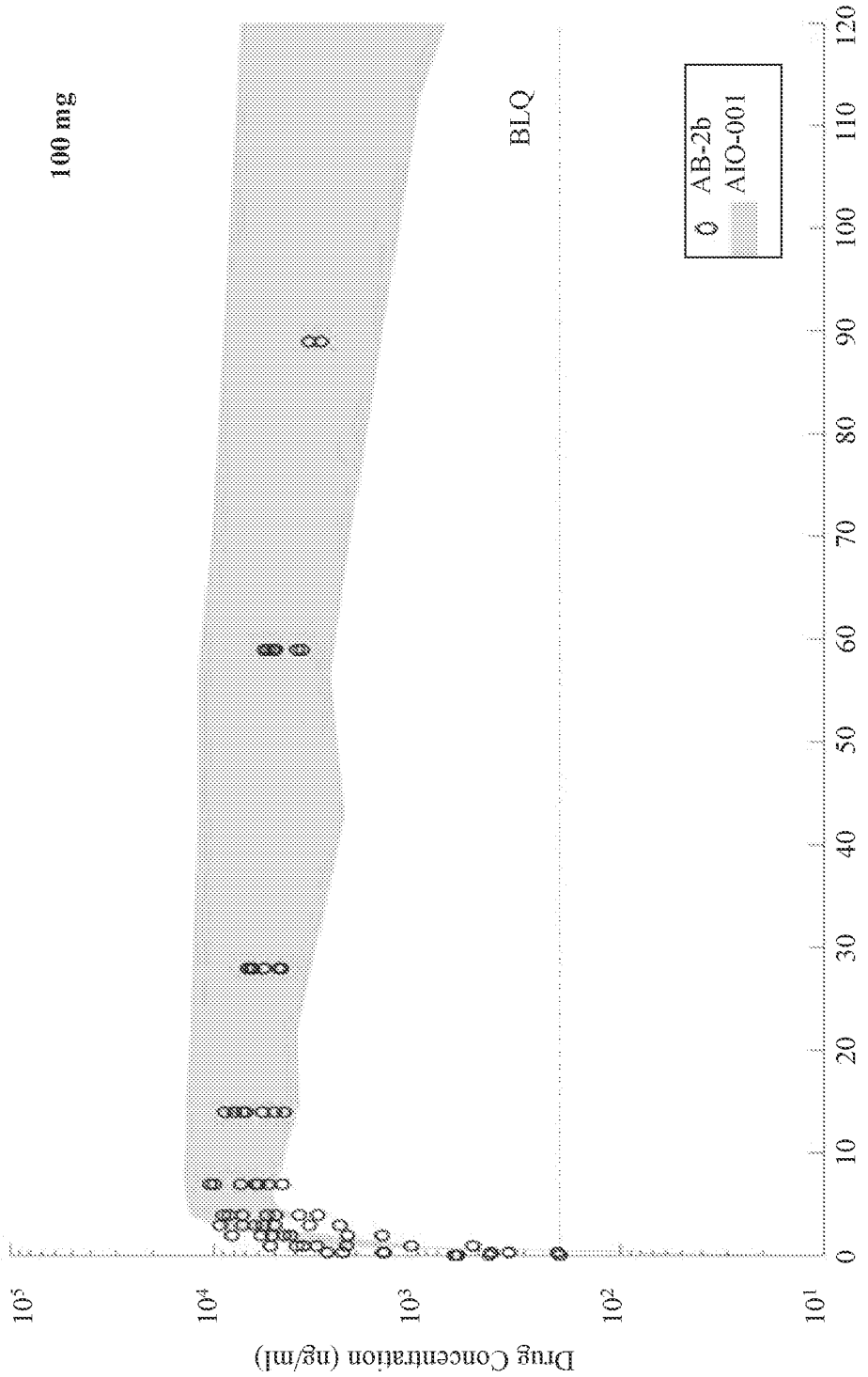
100 mg
BLQ
AB-2b
AIO-001
Drug Concentration (ng/ml)
10^5
10^4
10^3
10^2
10^1
0
10
20
30
40
50
60
70
80
90
100
110
120
Time (days)

FIG. 6C

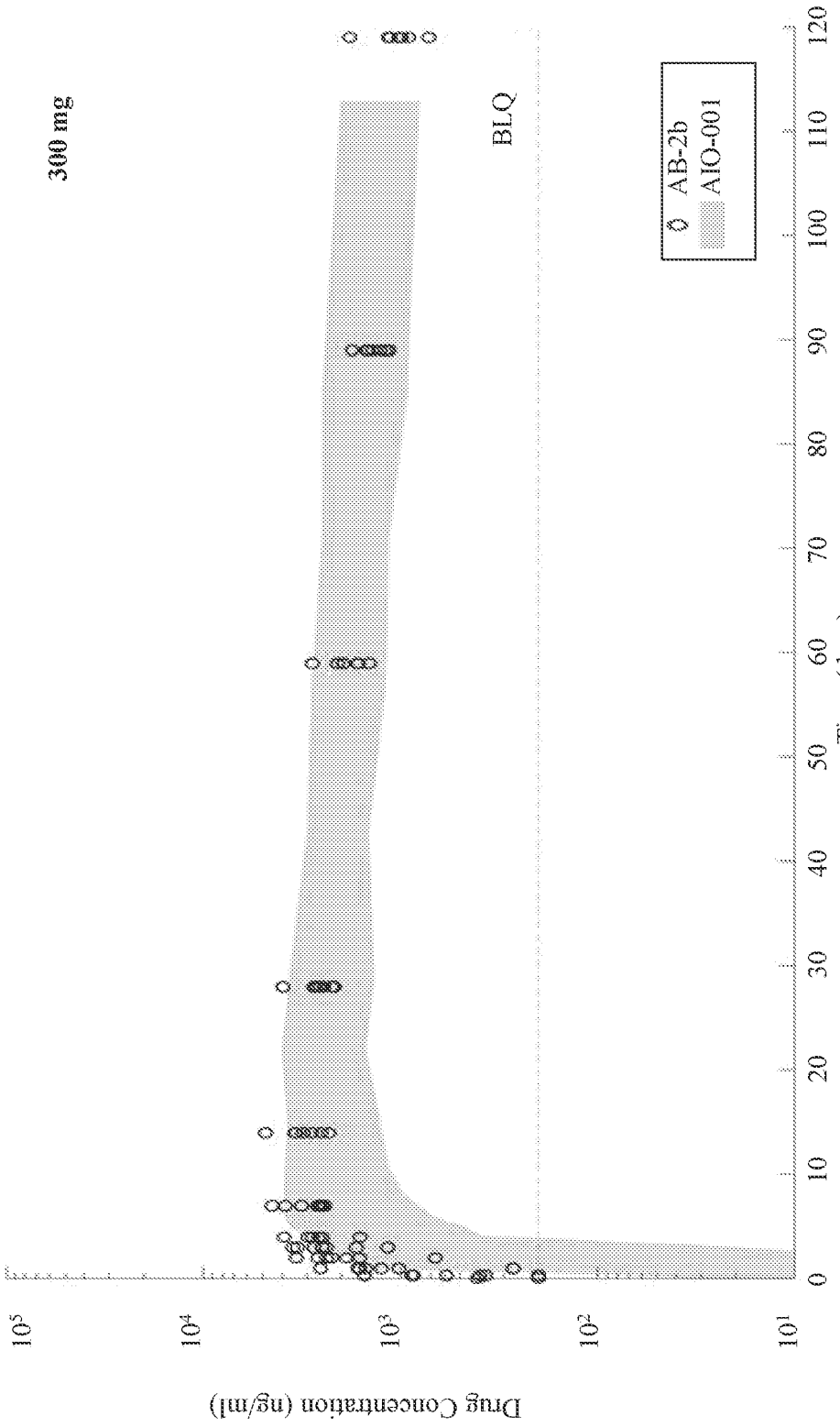
300 mg
BLQ
AB-2b
AIO-001
Drug Concentration (ng/ml)
10^5
10^4
10^3
10^2
10^1
0
10
20
30
40
50
60
70
80
90
100
110
120
Time (days)

FIG. 6D

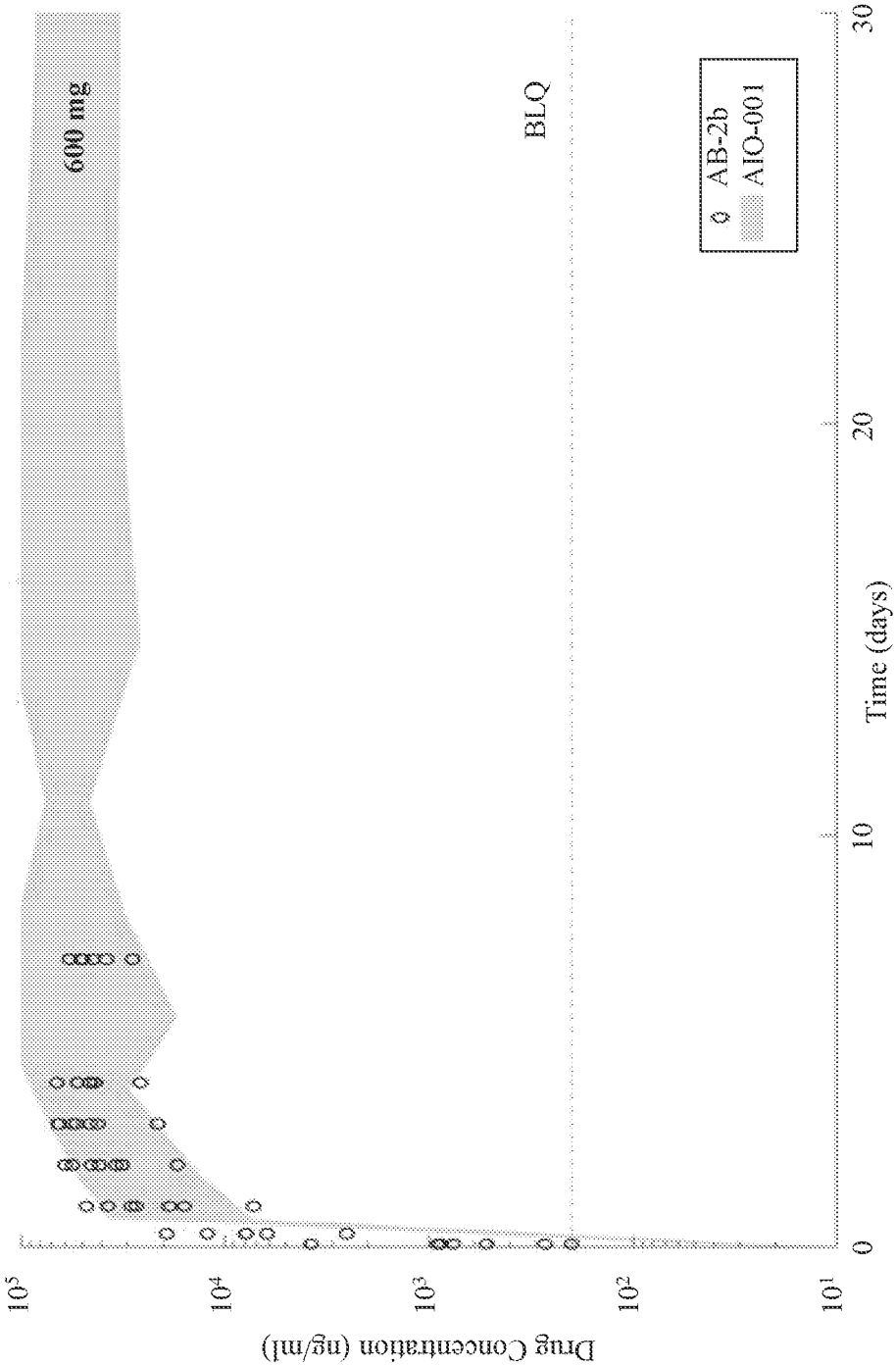
600 mg
BLQ
AB-2b
AIO-001
Drug Concentration (ng/ml)
10^5
10^4
10^3
10^2
10^1
0
10
20
30
Time (days)

FIG. 6E

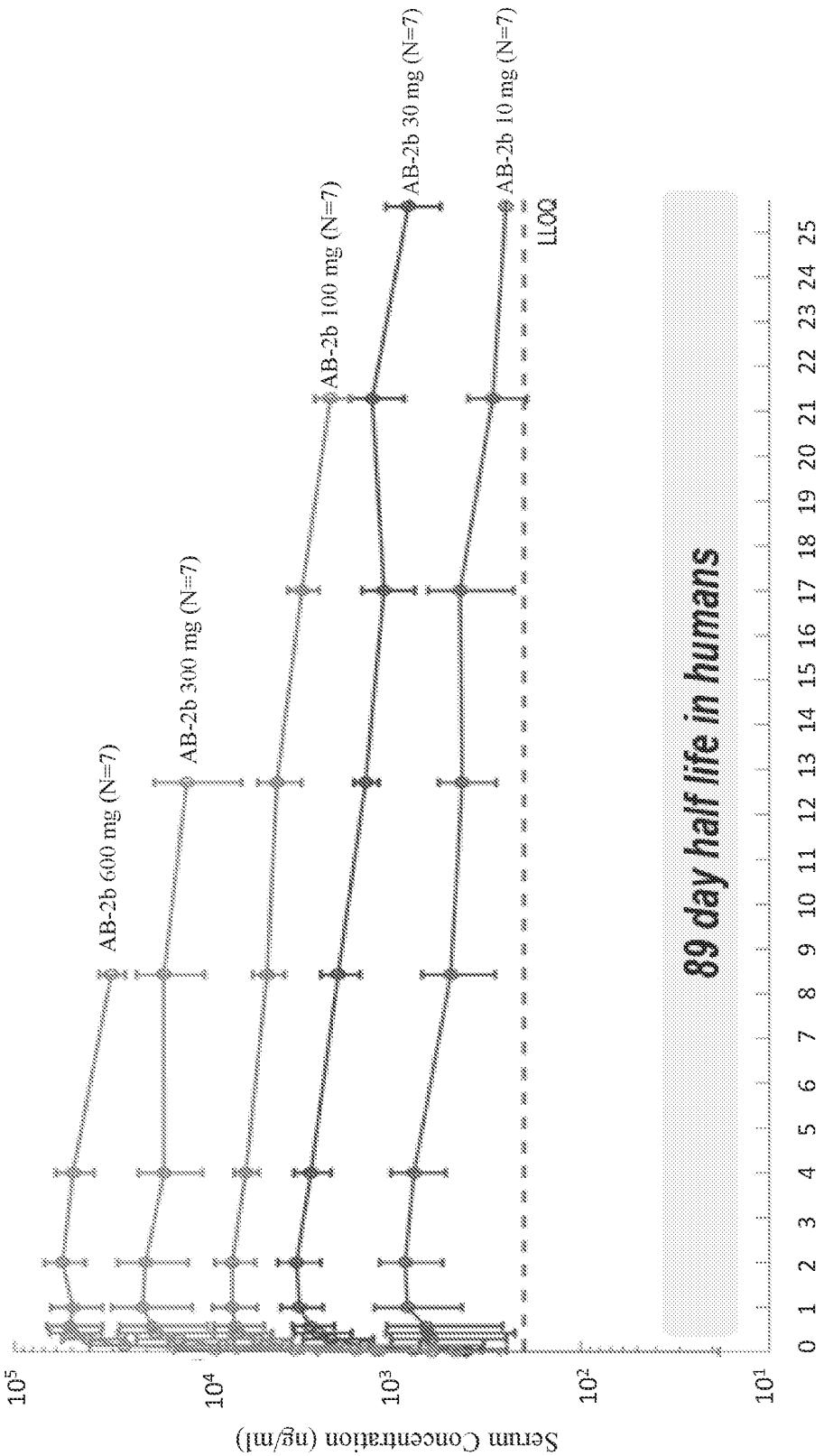
Serum Concentration (ng/ml)
10^5
10^4
10^3
10^2
10^1
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Weeks
AB-2b 600 mg (N=7)
AB-2b 300 mg (N=7)
AB-2b 100 mg (N=7)
AB-2b 30 mg (N=7)
AB-2b 10 mg (N=7)
LLOQ
89 day half life in humans

FIG. 6F

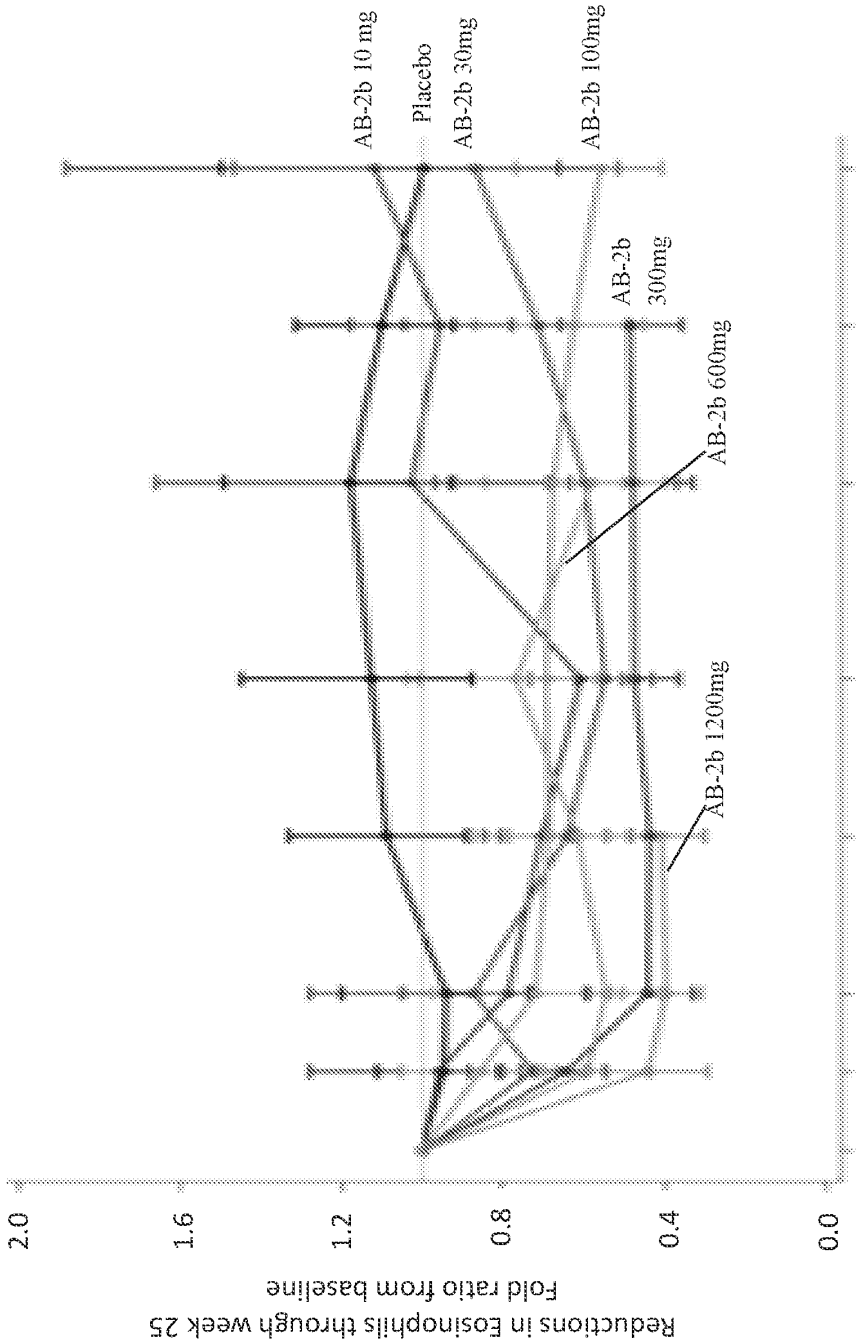
Reductions in Eosinophils through week 25
Fold ratio from baseline
2.0
1.6
1.2
0.8
0.4
0.0
Baseline
2
4
8
12
17
21
25
Weeks
AB-2b 10 mg
Placebo
AB-2b 30mg
AB-2b 100mg
AB-2b 300mg
AB-2b 600mg
AB-2b 1200mg

FIG. 7A

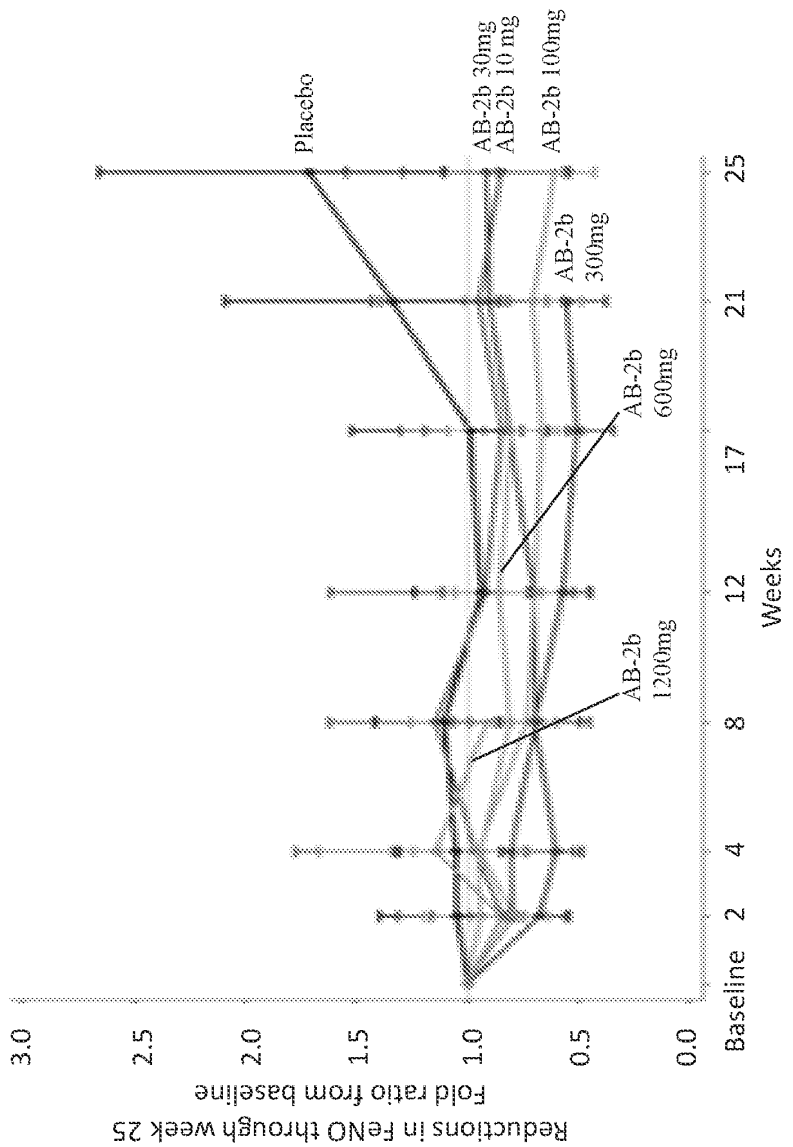
Reductions in FeNO through week 25
Fold ratio from baseline
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Baseline
2
4
8
12
17
21
25
Weeks
Placebo
AB-2b 30mg
AB-2b 10 mg
AB-2b 100mg
AB-2b 300mg
AB-2b 600mg
AB-2b 1200mg

FIG. 7B

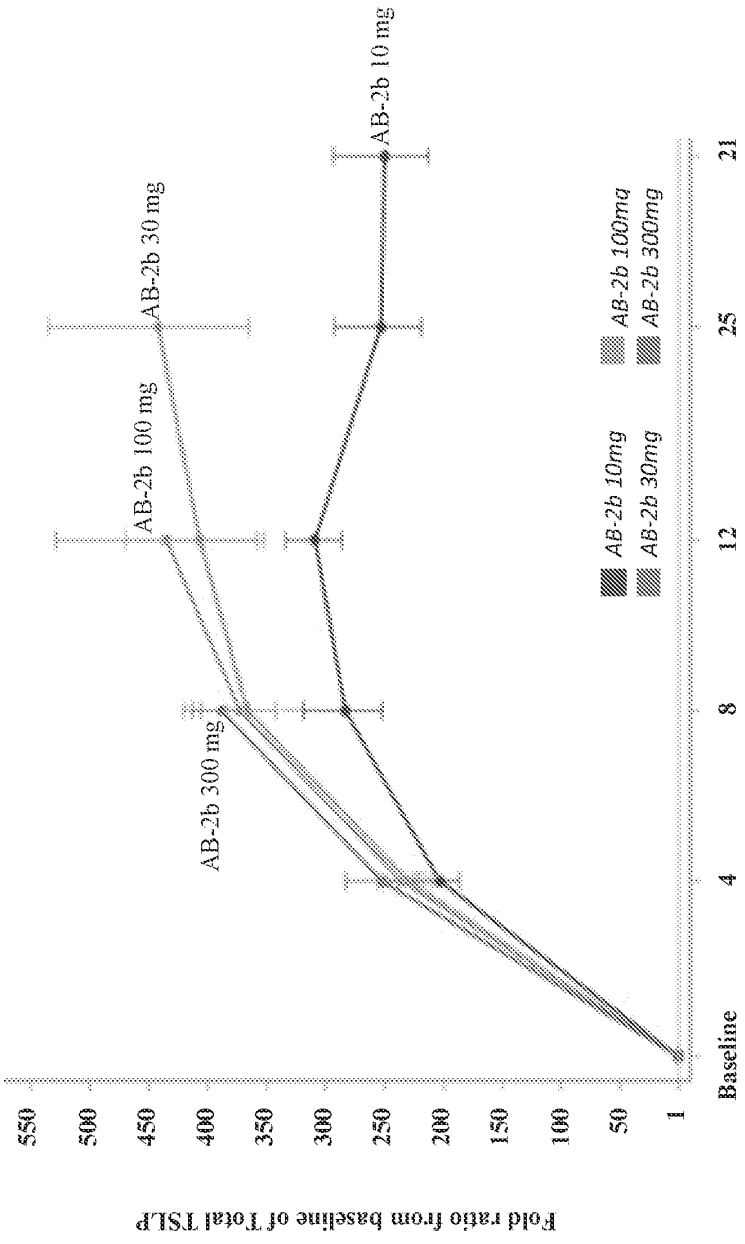
Fold ratio from baseline of Total TSLP
550
500
450
400
350
300
250
200
150
100
50
1
Baseline
4
8
12
25
21
AB-2b 10mg
AB-2b 30mg
AB-2b 100mg
AB-2b 300mg
AB-2b 300 mg
AB-2b 100 mg
AB-2b 30 mg
AB-2b 10 mg

FIG. 7C

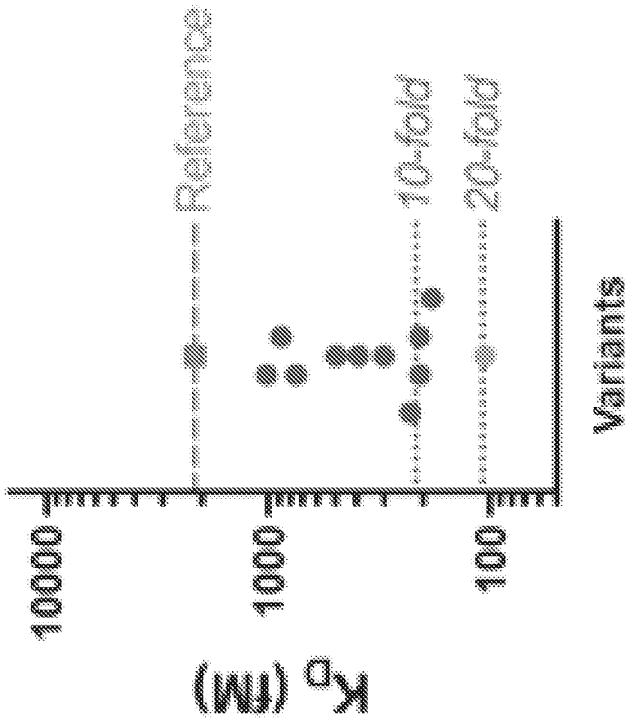

FIG. 7D

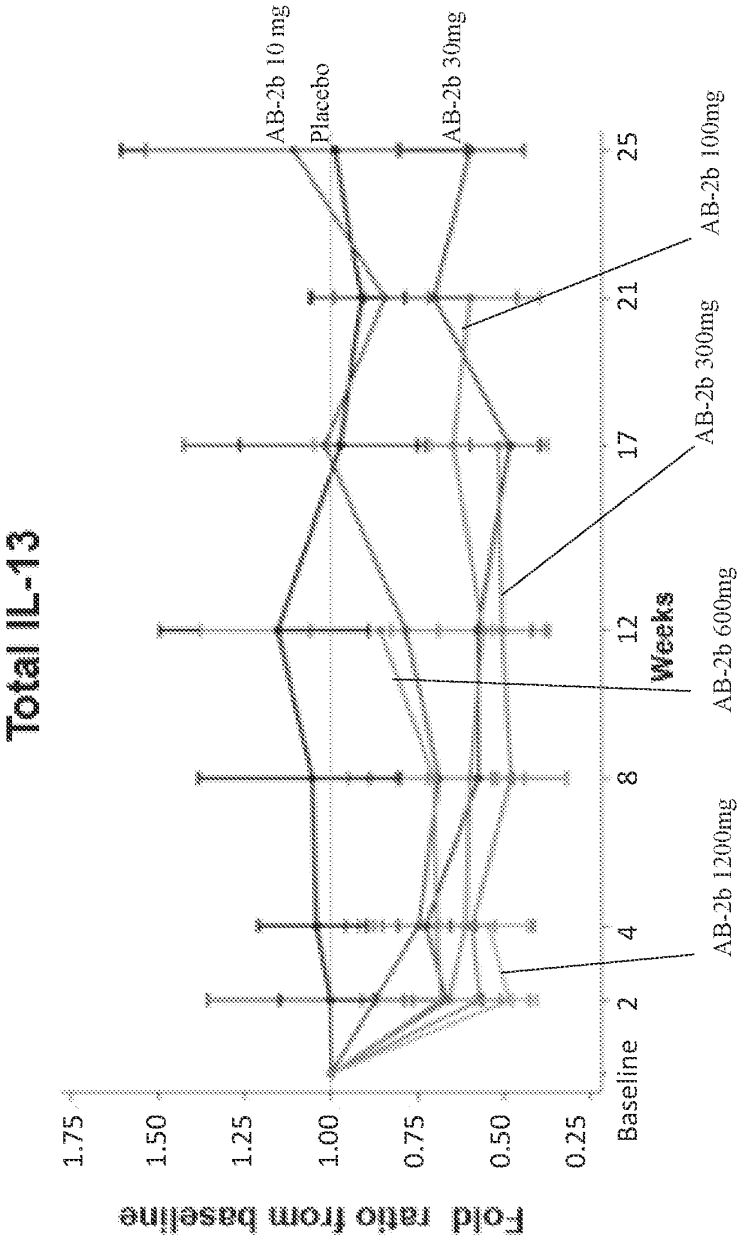
Total IL-13
Fold ratio from baseline
1.75
1.50
1.25
1.00
0.75
0.50
0.25
Baseline
2
4
8
12
17
21
25
Weeks
AB-2b 10 mg
Placebo
AB-2b 30mg
AB-2b 100mg
AB-2b 300mg
AB-2b 600mg
AB-2b 1200mg

FIG. 7E

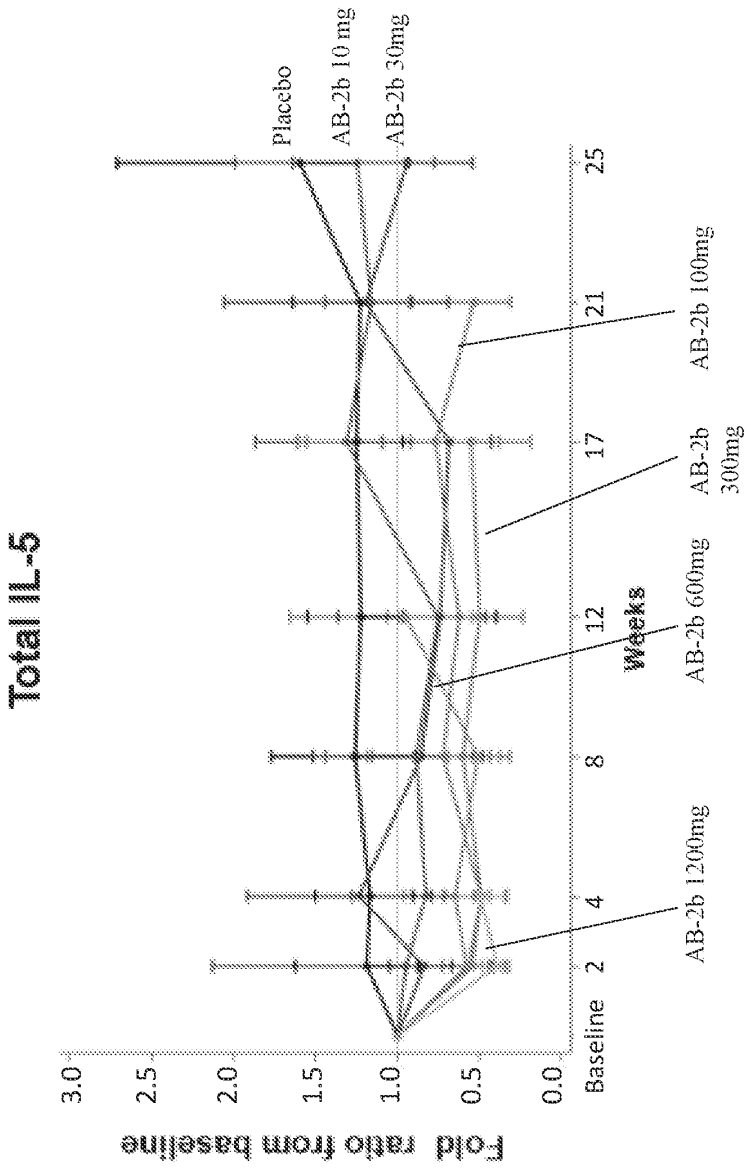
Total IL-5
Fold ratio from baseline
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Baseline
2
4
8
12
17
21
25
Weeks
Placebo
AB-2b 10 mg
AB-2b 30mg
AB-2b 100mg
AB-2b 300mg
AB-2b 600mg
AB-2b 1200mg

FIG. 7F