FIG. 1A

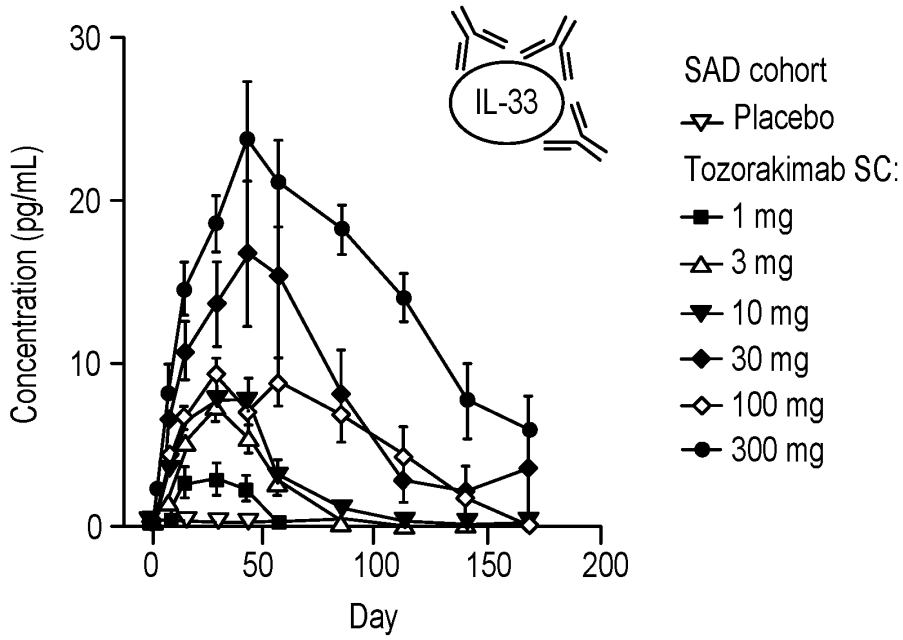

IL-33
Concentration (pg/mL)
30
20
10
0
0
50
100
150
200
Day
SAD cohort
Placebo
Tozorakimab SC:
1 mg
3 mg
10 mg
30 mg
100 mg
300 mg

FIG. 1B

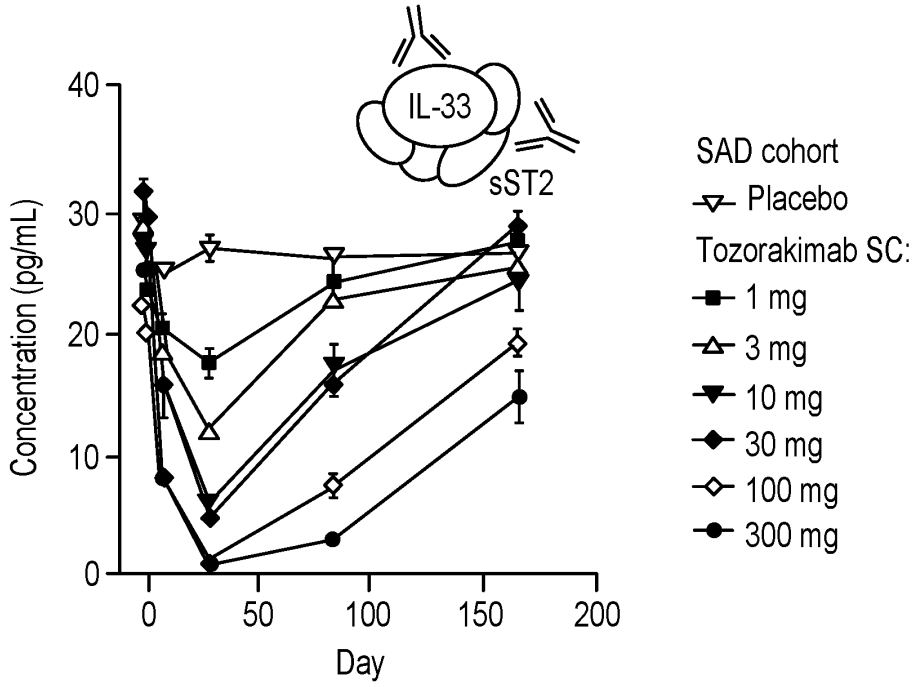

IL-33
sST2
Concentration (pg/mL)
40
30
20
10
0
0
50
100
150
200
Day
SAD cohort
Placebo
Tozorakimab SC:
1 mg
3 mg
10 mg
30 mg
100 mg
300 mg

FIG. 1C

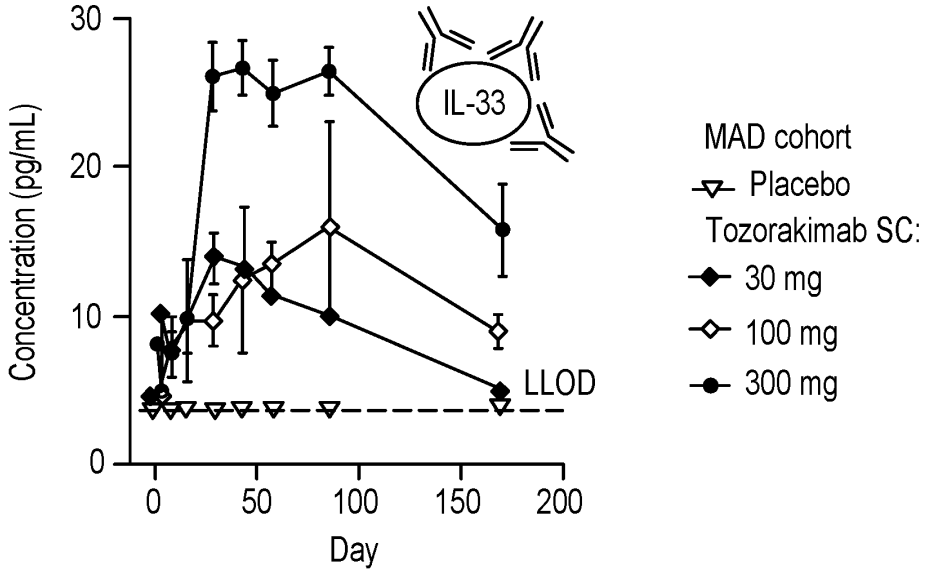

30
20
10
0
Concentration (pg/mL)
0
50
100
150
200
Day
IL-33
LLOD
MAD cohort
Placebo
Tozorakimab SC:
30 mg
100 mg
300 mg

FIG. 1D

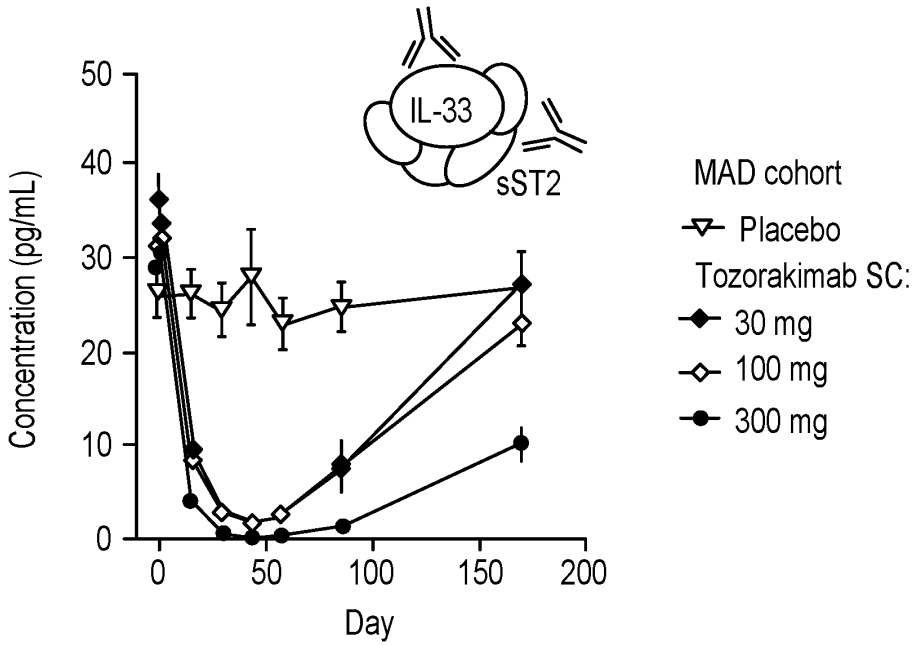

50
40
30
20
10
0
Concentration (pg/mL)
0
50
100
150
200
Day
IL-33
sST2
MAD cohort
Placebo
Tozorakimab SC:
30 mg
100 mg
300 mg

FIG. 2A

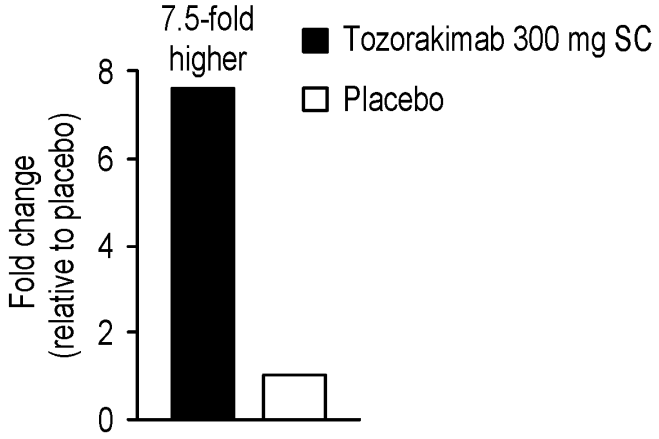


FIG. 2B

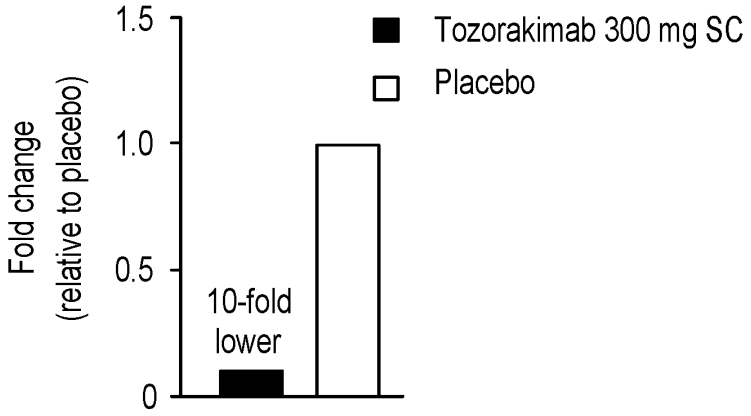


FIG. 2C

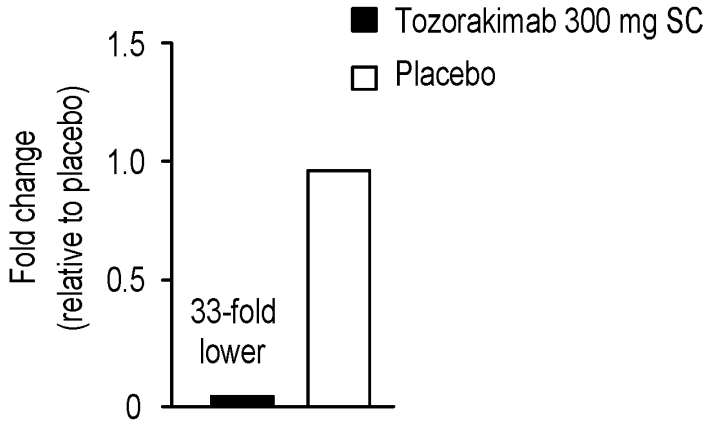


FIG. 3

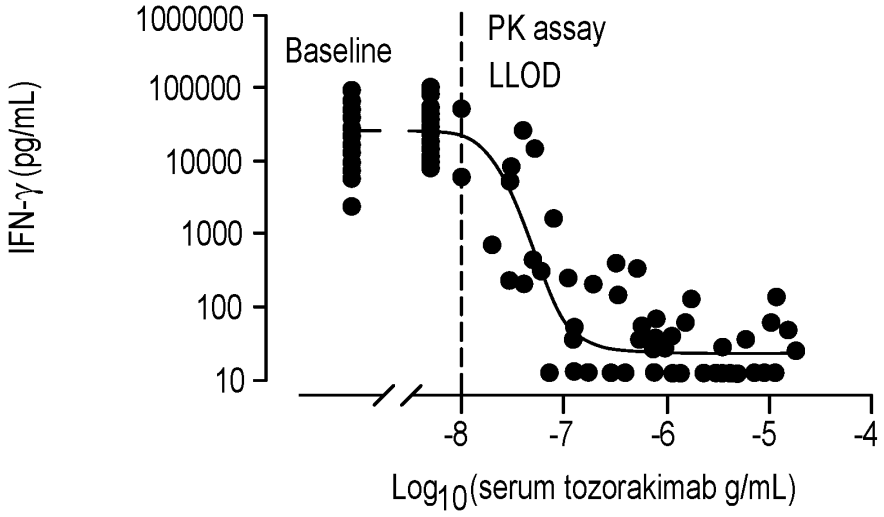

1000000
100000
10000
1000
100
10
IFN-γ (pg/mL)
Baseline
PK assay
LLOD
-8
-7
-6
-5
-4
Log10(serum tozorakimab g/mL)

FIG. 4A

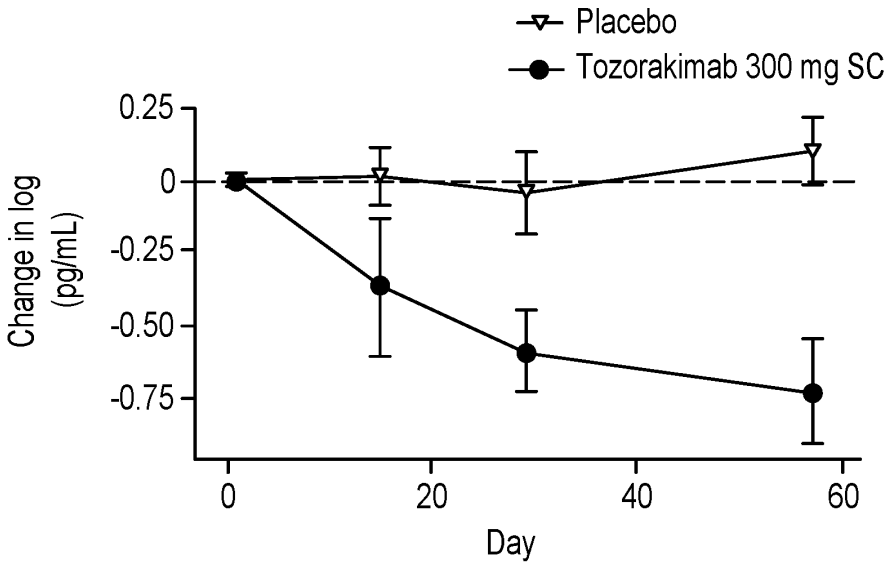

Placebo
Tozorakimab 300 mg SC
0.25
0
-0.25
-0.50
-0.75
Change in log (pg/mL)
0
20
40
60
Day

FIG. 4B

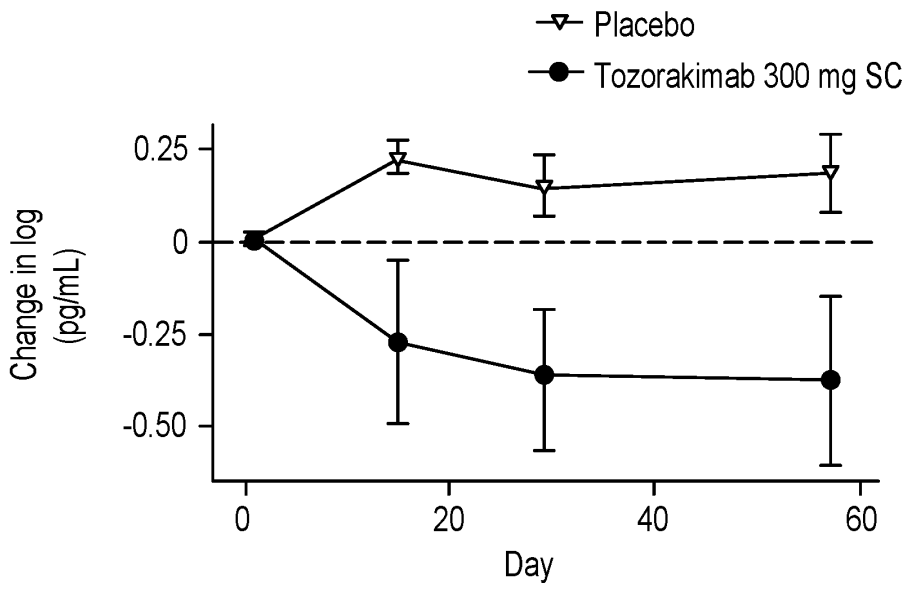

Placebo
Tozorakimab 300 mg SC
Change in log (pg/mL)
0.25
0
-0.25
-0.50
0
20
40
60
Day

FIG. 4C

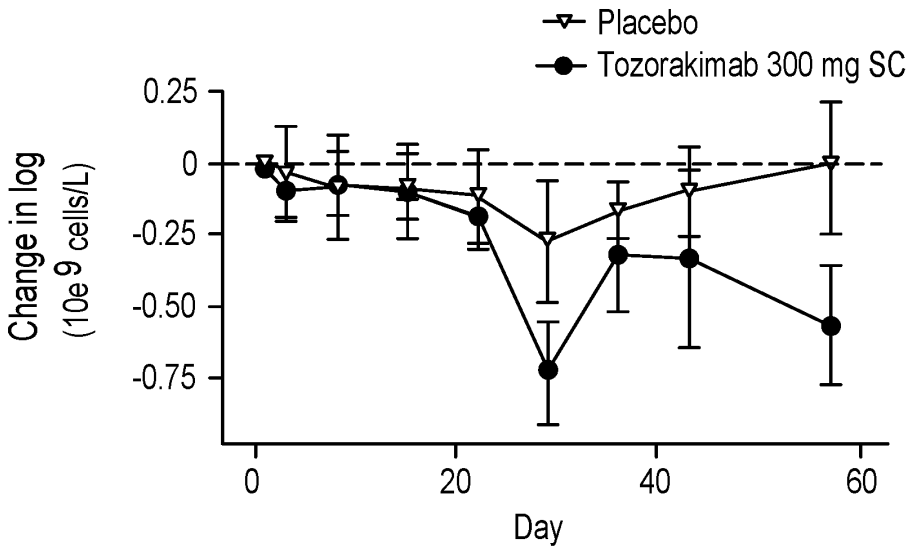

Placebo
Tozorakimab 300 mg SC
Change in log (10e9 cells/L)
0.25
0
-0.25
-0.50
-0.75
0
20
40
60
Day

FIG. 5

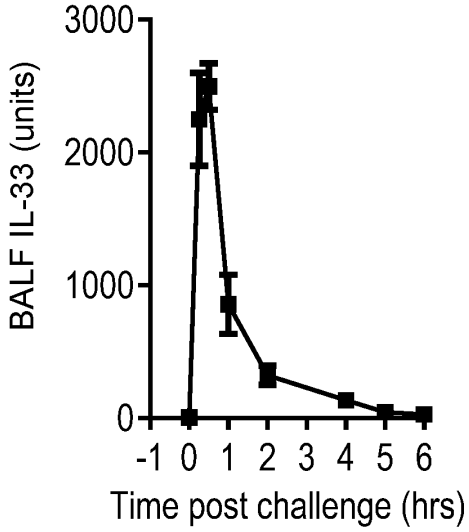

3000
2000
1000
0
BALF IL-33 (units)
-1 0 1 2 3 4 5 6
Time post challenge (hrs)

FIG. 6

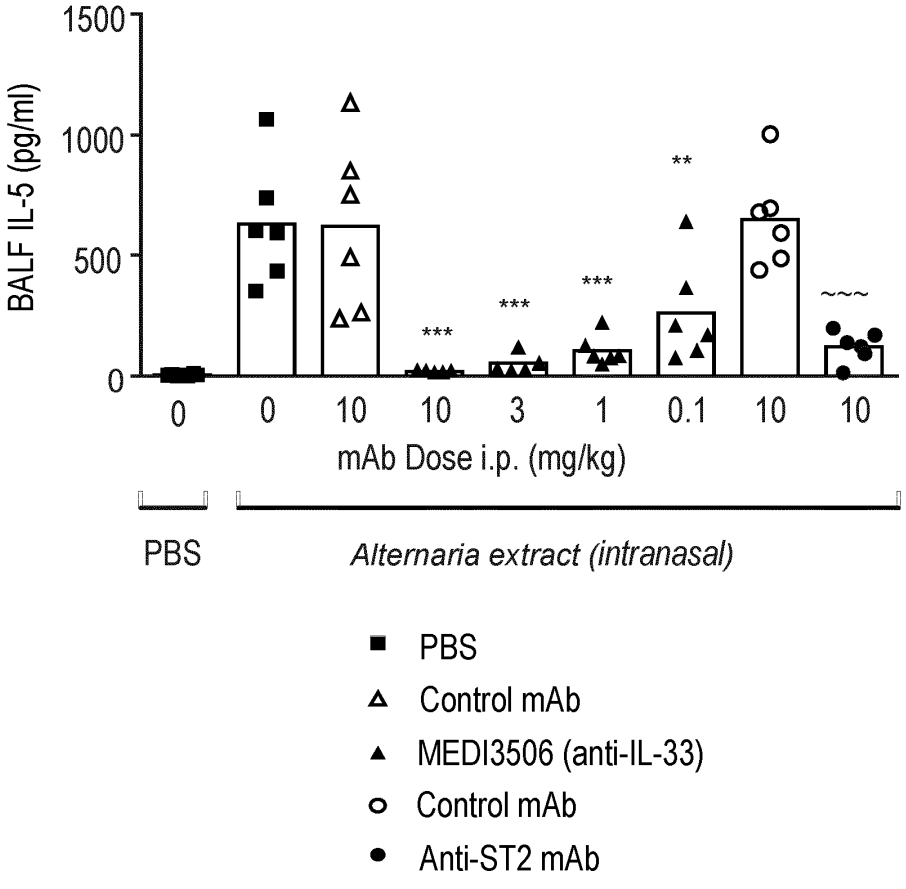

1500
1000
500
0
BALF IL-5 (pg/ml)
***
***
***
**
~~~
0 0 10 10 3 1 0.1 10 10
mAb Dose i.p. (mg/kg)
PBS
Alternaria extract (intranasal)
PBS
Control mAb
MEDI3506 (anti-IL-33)
Control mAb
Anti-ST2 mAb
~~~

FIG. 7A

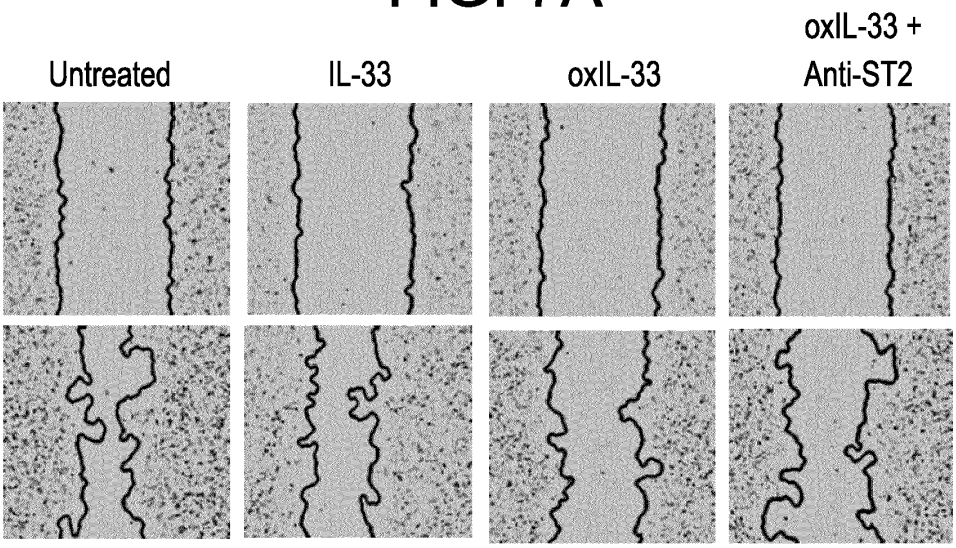

Untreated
IL-33
oxIL-33
oxIL-33 +
Anti-ST2
Normal human bronchial epithelial cells-24h

FIG. 7B

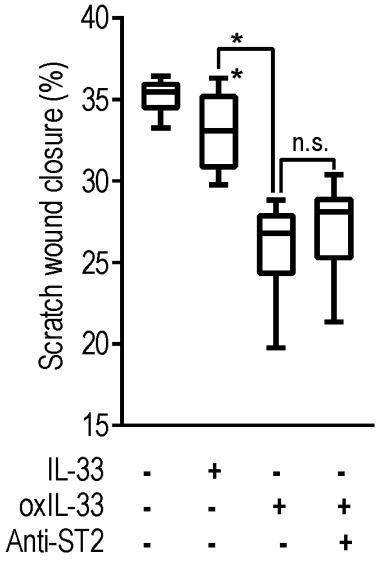

Scratch wound closure (%)
40
35
30
25
20
15
*
*
n.s.
IL-33 - + - -
oxIL-33 - - + +
Anti-ST2 - - - +

FIG. 8

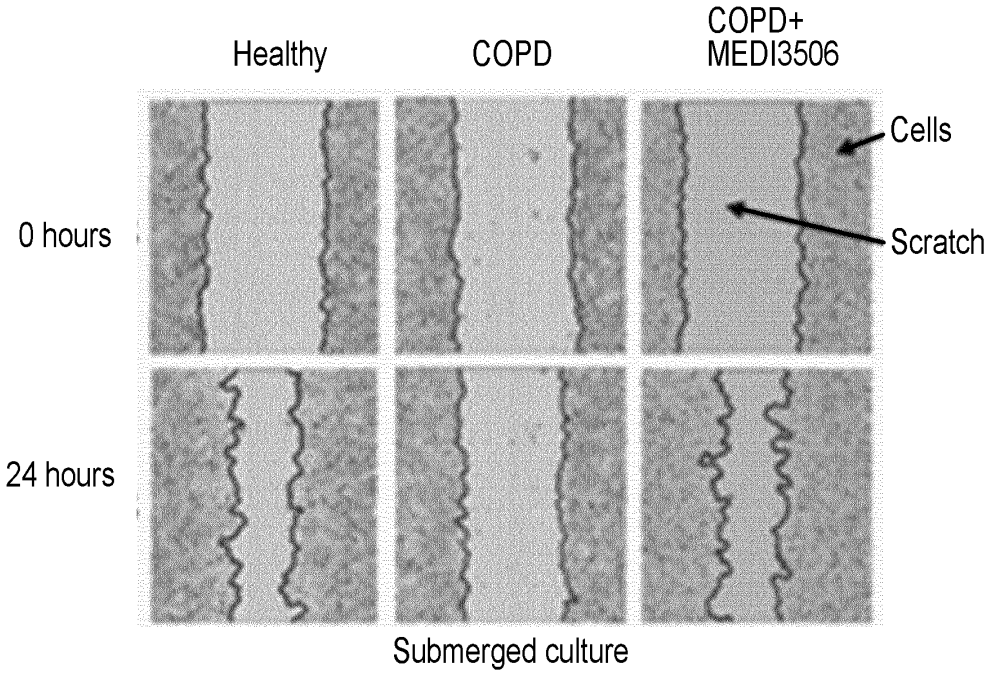

Healthy
COPD
COPD+
MEDI3506
Cells
Scratch
0 hours
24 hours
Submerged culture

FIG. 9

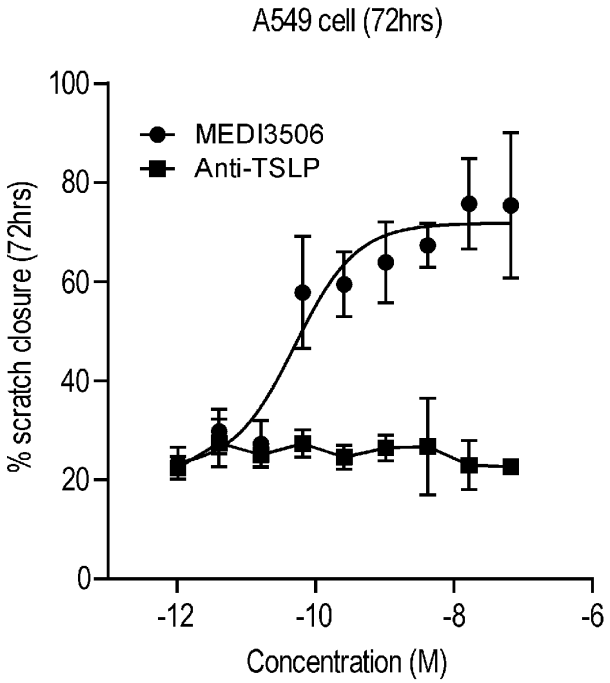

A549 cell (72hrs)
MEDI3506
Anti-TSLP
% scratch closure (72hrs)
100
80
60
40
20
0
-12
-10
-8
-6
Concentration (M)

FIG. 10

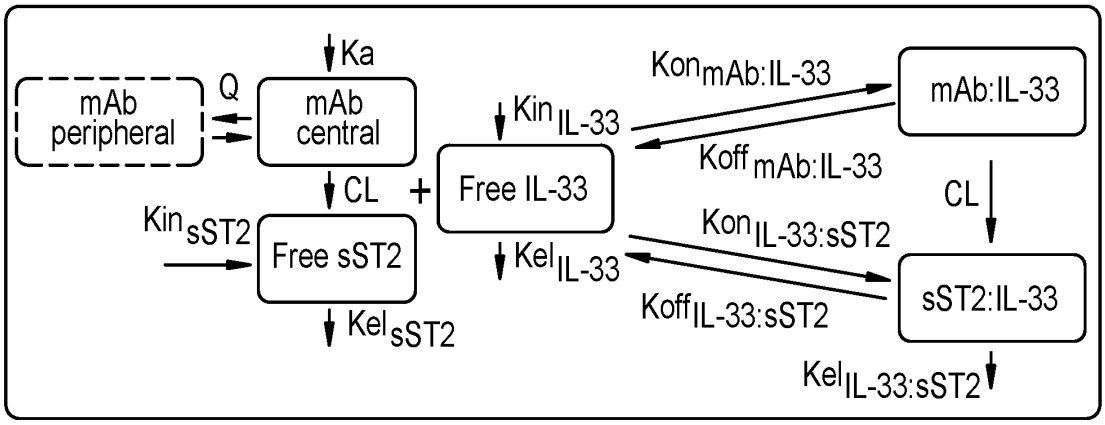

Ka
mAb peripheral
Q
mAb central
CL
Kin sST2
Free sST2
Kel sST2
Kin IL-33
Free IL-33
Kel IL-33
Kon mAb:IL-33
Koff mAb:IL-33
mAb:IL-33
CL
Kon IL-33:sST2
Koff IL-33:sST2
sST2:IL-33
Kel IL-33:sST2

FIG. 11

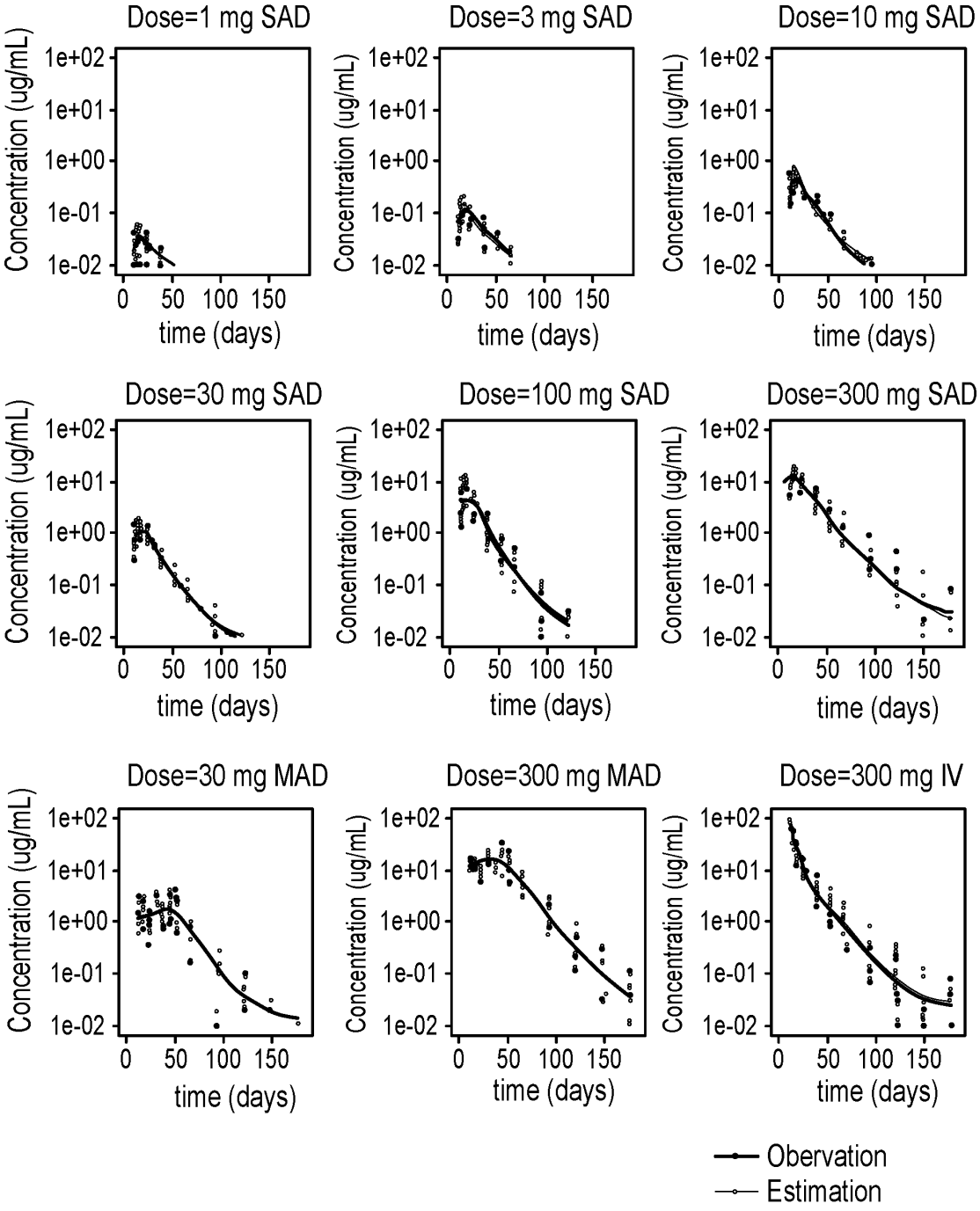

Prediction of mAb concentration
Dose=1 mg SAD
Dose=3 mg SAD
Dose=10 mg SAD
Dose=30 mg SAD
Dose=100 mg SAD
Dose=300 mg SAD
Dose=30 mg MAD
Dose=300 mg MAD
Dose=300 mg IV
Concentration (ug/mL)
1e+02
1e+01
1e+00
1e-01
1e-02
0 50 100 150
time (days)
Obervation
Estimation

FIG. 12

Prediction of IL33/MEDI3506 complex

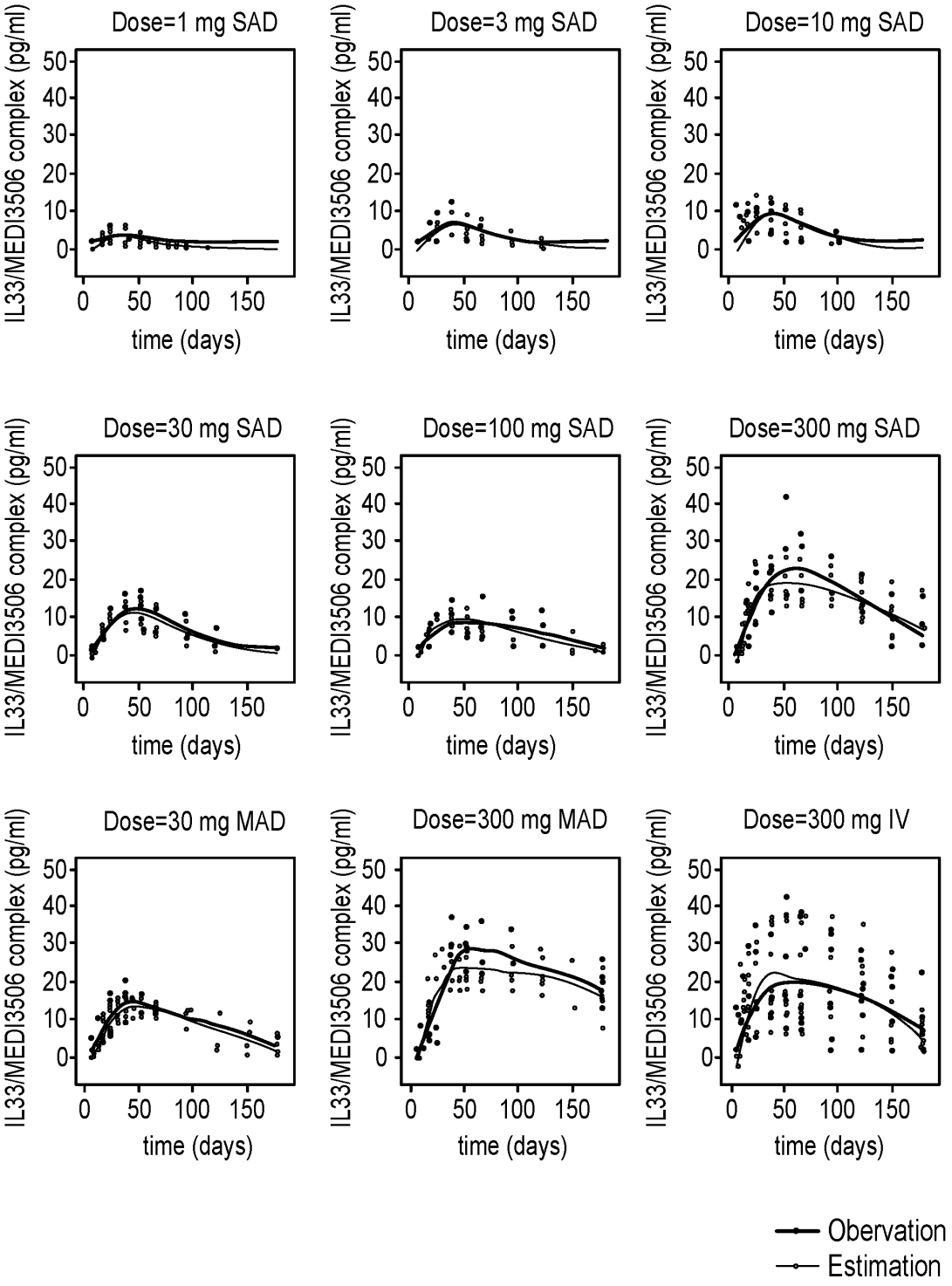


FIG. 13

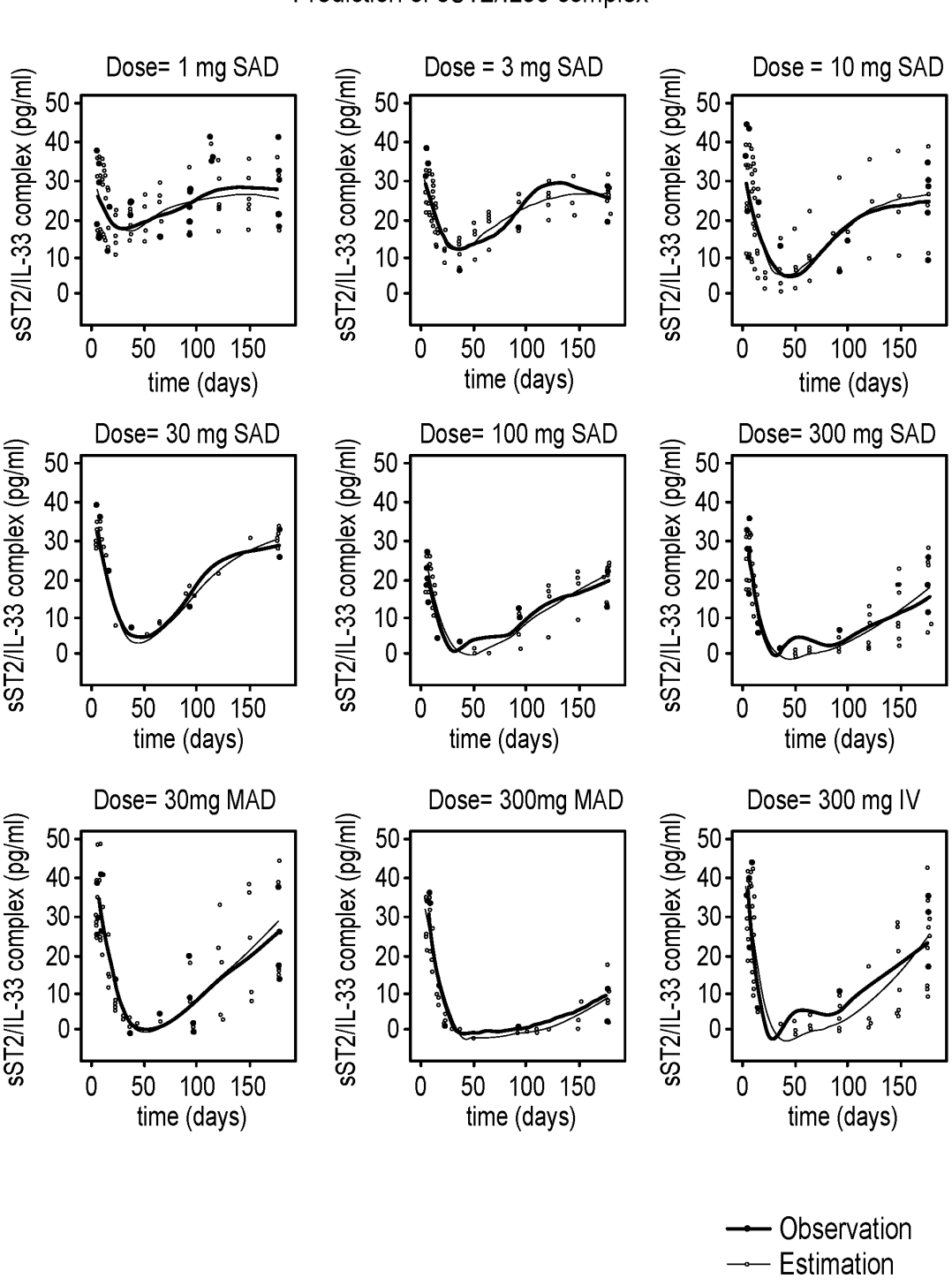

Prediction of sST2/IL33 complex
Dose= 1 mg SAD
Dose = 3 mg SAD
Dose = 10 mg SAD
Dose= 30 mg SAD
Dose= 100 mg SAD
Dose= 300 mg SAD
Dose= 30mg MAD
Dose= 300mg MAD
Dose= 300 mg IV
sST2/IL-33 complex (pg/ml)
time (days)
0 50 100 150
0 10 20 30 40 50
Observation
Estimation

FIG. 14

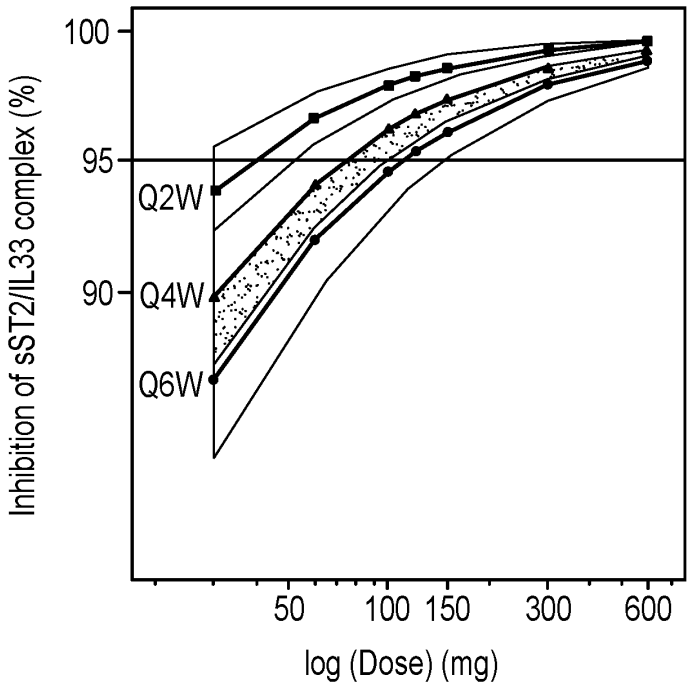

100
95
90
Q2W
Q4W
Q6W
Inhibition of sST2/IL33 complex (%)
50
100
150
300
600
log (Dose) (mg)

FIG. 15

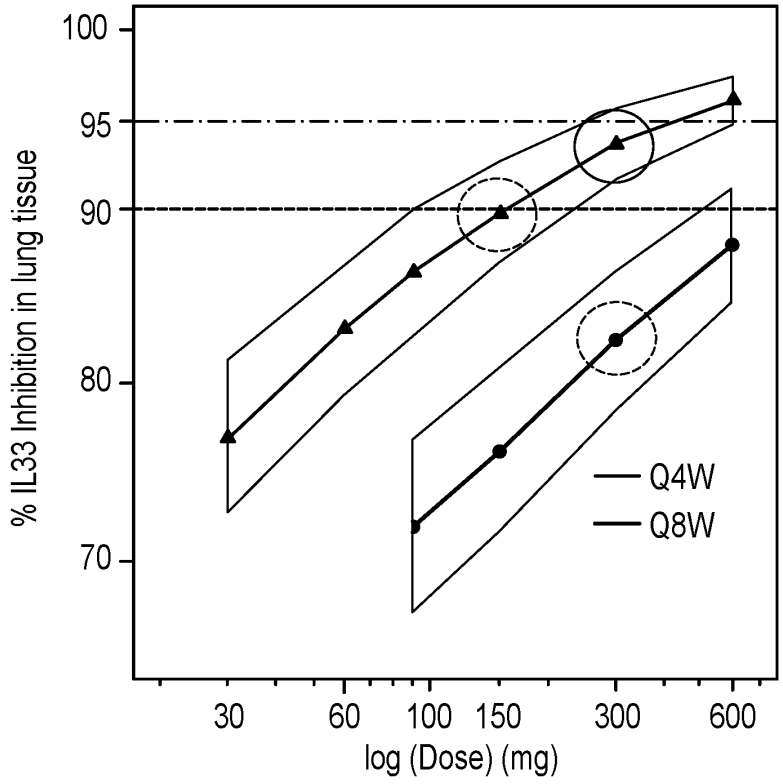

100
95
90
80
70
% IL33 Inhibition in lung tissue
Q4W
Q8W
30
60
100
150
300
600
log (Dose) (mg)

FIG. 16

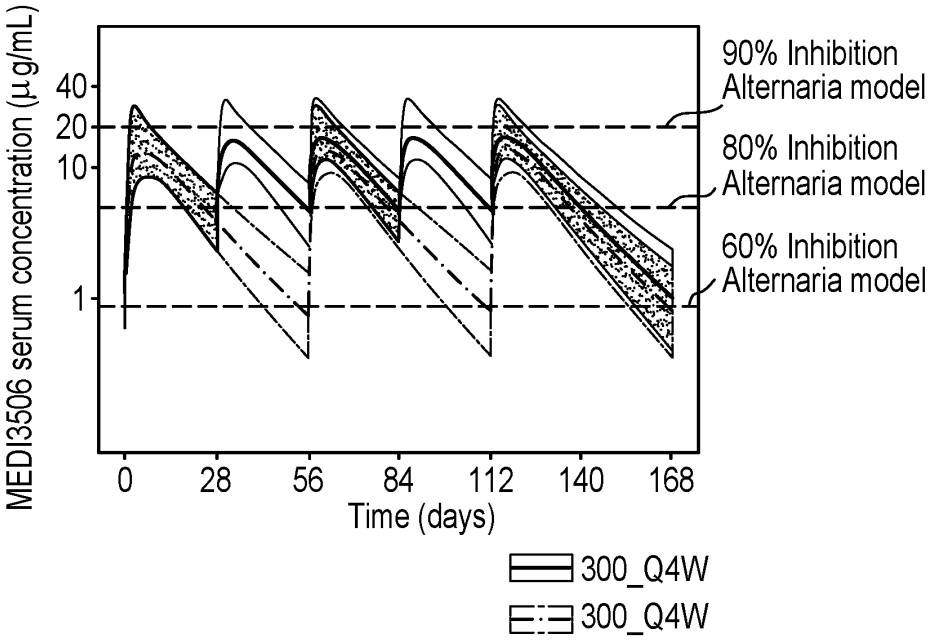

MEDI3506 serum concentration (µg/mL)
40
20
10
1
0
28
56
84
112
140
168
Time (days)
90% Inhibition Alternaria model
80% Inhibition Alternaria model
60% Inhibition Alternaria model
300_Q4W
300_Q4W

FIG. 17

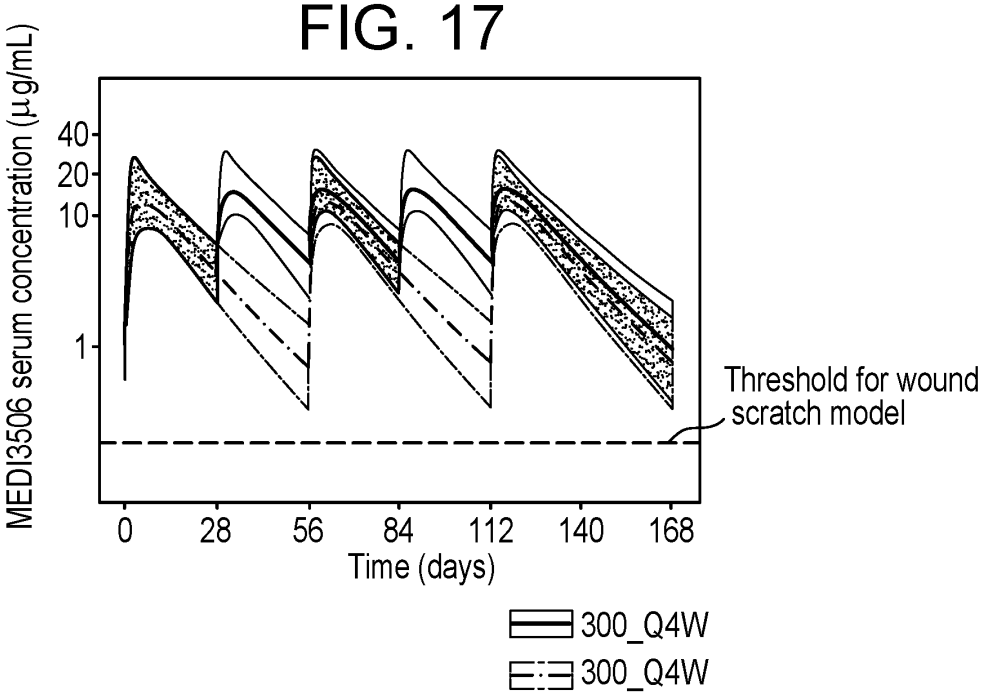

MEDI3506 serum concentration (µg/mL)
40
20
10
1
0
28
56
84
112
140
168
Time (days)
Threshold for wound scratch model
300_Q4W
300_Q4W

FIG. 18

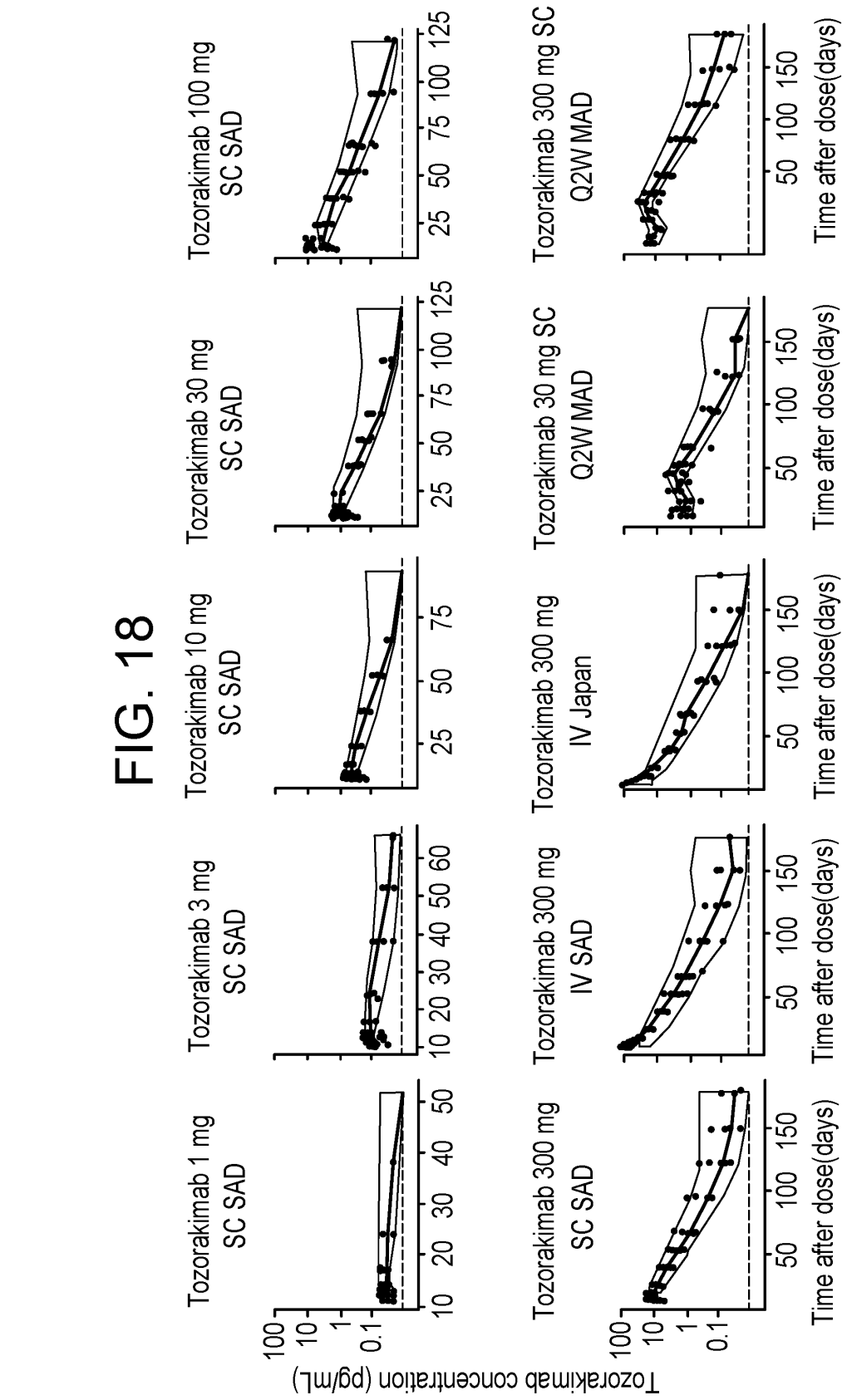
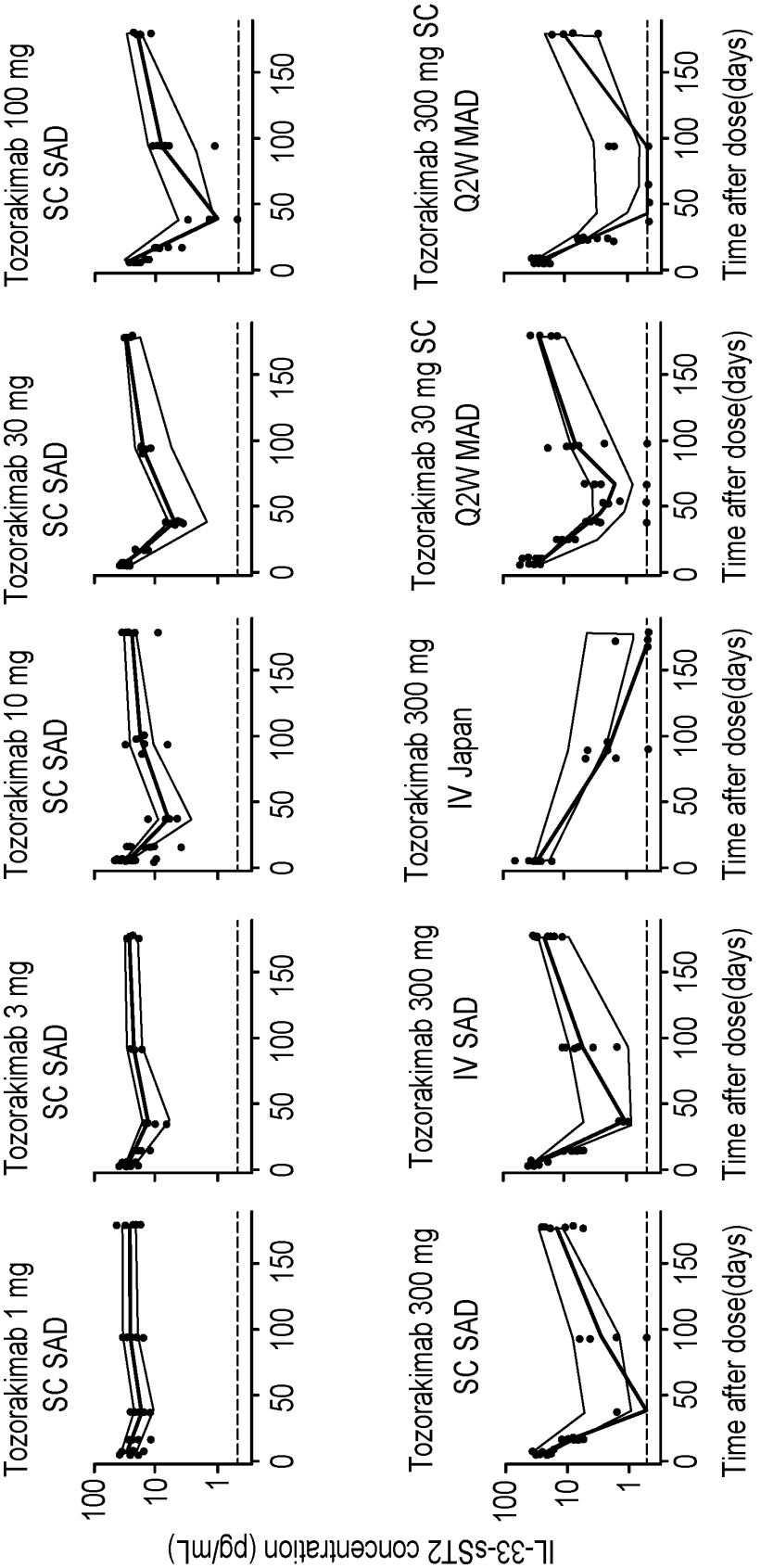

Tozorakimab concentration (pg/mL)
100
10
1
0.1
Tozorakimab 1 mg SC SAD
Tozorakimab 3 mg SC SAD
Tozorakimab 10 mg SC SAD
Tozorakimab 30 mg SC SAD
Tozorakimab 100 mg SC SAD
Tozorakimab 300 mg SC SAD
Tozorakimab 300 mg IV SAD
Tozorakimab 300 mg IV Japan
Tozorakimab 30 mg SC Q2W MAD
Tozorakimab 300 mg SC Q2W MAD
Time after dose(days)
10 20 30 40 50
10 20 30 40 50 60
25 50 75
25 50 75 100 125
50 100 150

FIG. 19


Tozorakimab 1 mg SC SAD
Tozorakimab 3 mg SC SAD
Tozorakimab 10 mg SC SAD
Tozorakimab 30 mg SC SAD
Tozorakimab 100 mg SC SAD
Tozorakimab 300 mg IV SAD
Tozorakimab 300 mg IV Japan
Tozorakimab 30 mg SC Q2W MAD
Tozorakimab 300 mg SC Q2W MAD
IL-33-sST2 concentration (pg/mL)
100
10
1
0 50 100 150
Time after dose(days)