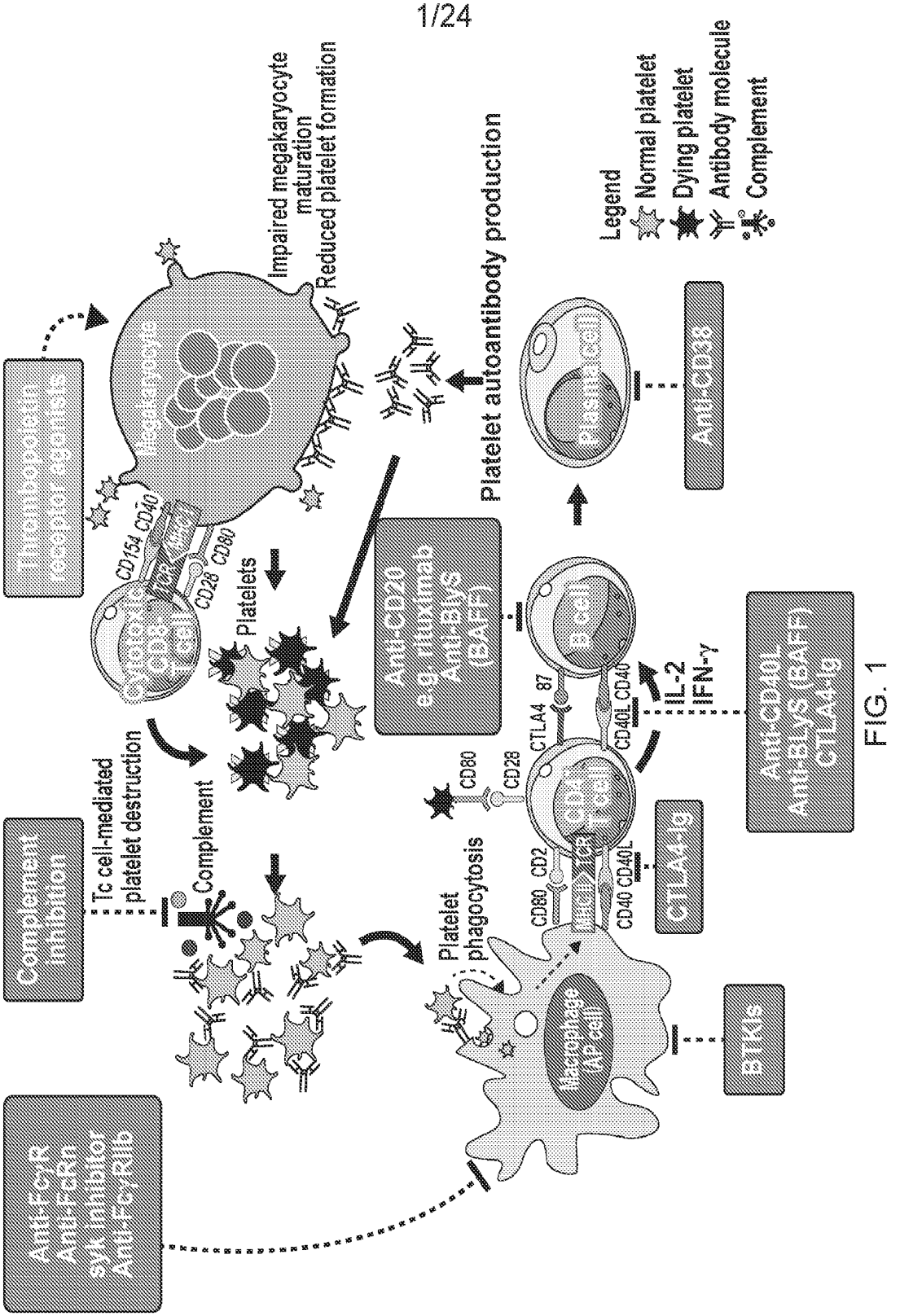

Thrombopoietin (receptor agonists)
Megakaryocyte
Impaired megakaryocyte maturation
Reduced platelet formation
Platelet autoantibody production
Legend
Normal platelet
Dying platelet
Antibody molecule
Complement
Anti-CD38
Plasma cell
Anti-CD20 e.g. rituximab Anti-BLyS (BAFF)
B cell
CD154 CD40
CD28 CD80
CD80
CD28
CTLA4
87
CD40L CD40
IL-2
IFN-γ
Platelets
Tc cell-mediated platelet destruction
Complement
Complement inhibition
Platelet phagocytosis
CD80 CD2
CD40 CD40L
CTLA4-Ig
Anti-CD40L Anti-BLyS (BAFF) CTLA4-Ig
Anti-FcγR Anti-FcRn SYK inhibitor Anti-FcγRIIb
BTKIs

FIG. 1

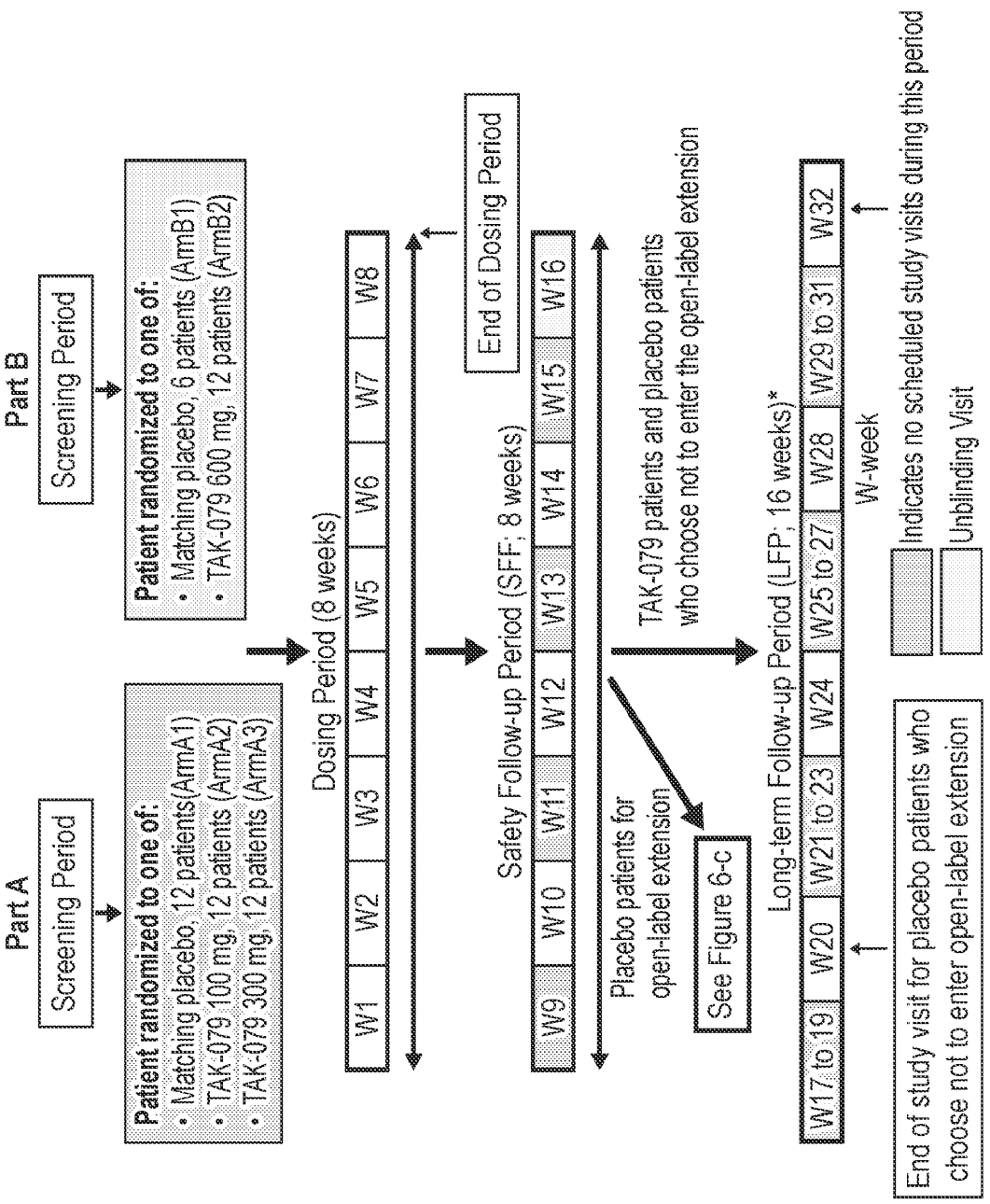

Part A
Screening Period
Patient randomized to one of:
• Matching placebo, 12 patients(ArmA1)
• TAK-079 100 mg, 12 patients (ArmA2)
• TAK-079 300 mg, 12 patients (ArmA3)
Part B
Screening Period
Patient randomized to one of:
• Matching placebo, 6 patients (ArmB1)
• TAK-079 600 mg, 12 patients (ArmB2)
Dosing Period (8 weeks)
W1 W2 W3 W4 W5 W6 W7 W8
End of Dosing Period
Safety Follow-up Period (SFF; 8 weeks)
W9 W10 W11 W12 W13 W14 W15 W16
Placebo patients for open-label extension
See Figure 6-c
TAK-079 patients and placebo patients who choose not to enter the open-label extension
Long-term Follow-up Period (LFP; 16 weeks)*
W17 to 19 W20 W21 to 23 W24 W25 to 27 W28 W29 to 31 W32
W-week
End of study visit for placebo patients who choose not to enter open-label extension
Indicates no scheduled study visits during this period
Unblinding Visit

FIG. 2A

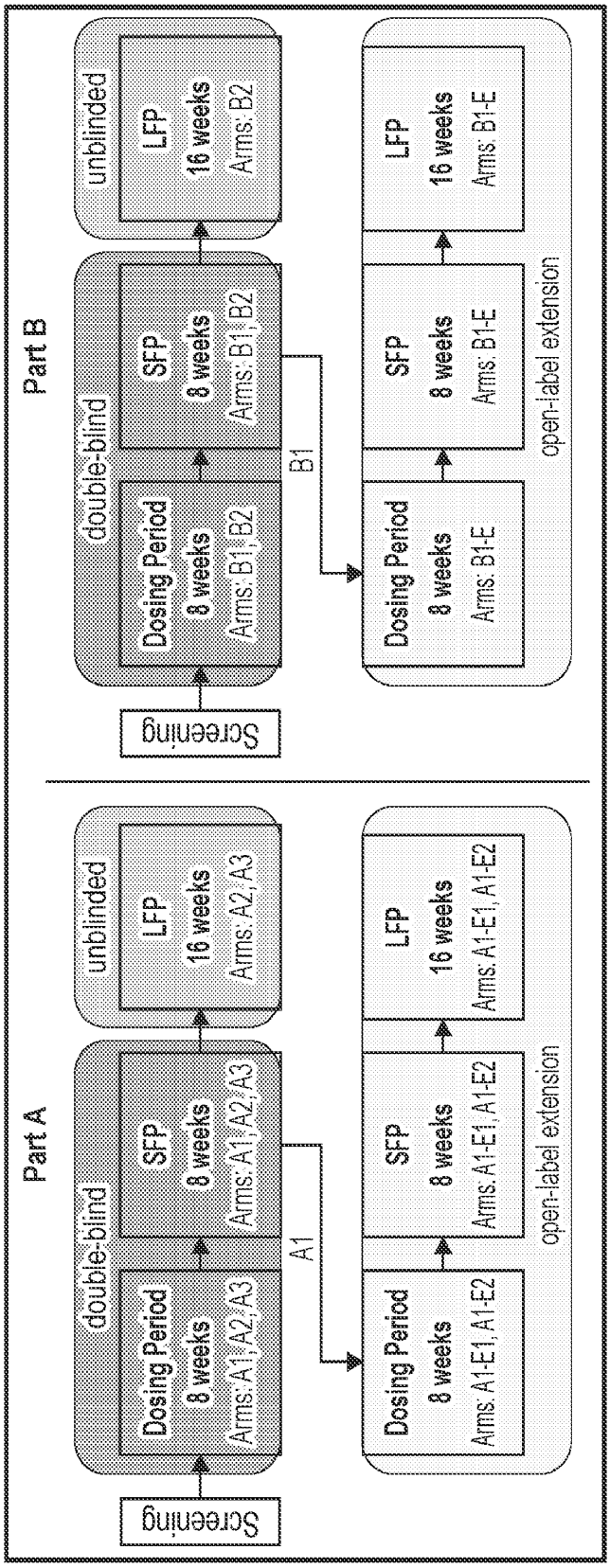

Part A
Screening
double-blind
Dosing Period
8 weeks
Arms: A1, A2, A3
SFP
8 weeks
Arms: A1, A2, A3
unblinded
LFP
16 weeks
Arms: A2, A3
A1
Dosing Period
8 weeks
Arms: A1-E1, A1-E2
SFP
8 weeks
Arms: A1-E1, A1-E2
LFP
16 weeks
Arms: A1-E1, A1-E2
open-label extension
Part B
Screening
double-blind
Dosing Period
8 weeks
Arms: B1, B2
SFP
8 weeks
Arms: B1, B2
unblinded
LFP
16 weeks
Arms: B2
B1
Dosing Period
8 weeks
Arms: B1-E
SFP
8 weeks
Arms: B1-E
LFP
16 weeks
Arms: B1-E
open-label extension

FIG. 2B

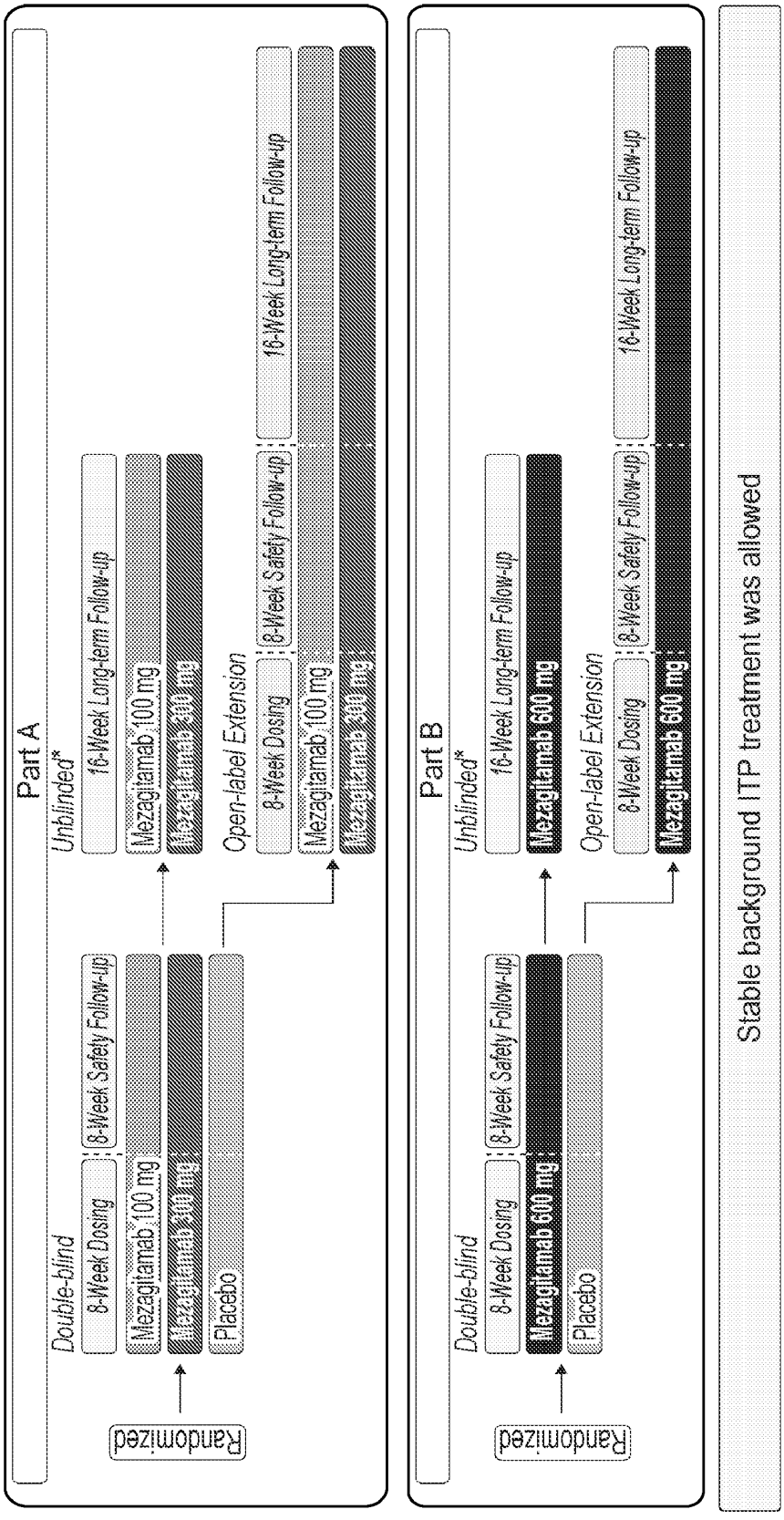

Part A
Double-blind
8-Week Dosing
8-Week Safety Follow-up
Mezagitamab 100 mg
Mezagitamab 600 mg
Placebo
Randomized
Unblinded*
16-Week Long-term Follow-up
Mezagitamab 100 mg
Mezagitamab 600 mg
Open-label Extension
8-Week Dosing
8-Week Safety Follow-up
16-Week Long-term Follow-up
Mezagitamab 100 mg
Mezagitamab 600 mg
Part B
Double-blind
8-Week Dosing
8-Week Safety Follow-up
Mezagitamab 600 mg
Placebo
Randomized
Unblinded*
16-Week Long-term Follow-up
Mezagitamab 600 mg
Open-label Extension
8-Week Dosing
8-Week Safety Follow-up
16-Week Long-term Follow-up
Mezagitamab 600 mg
Stable background ITP treatment was allowed

FIG. 2C

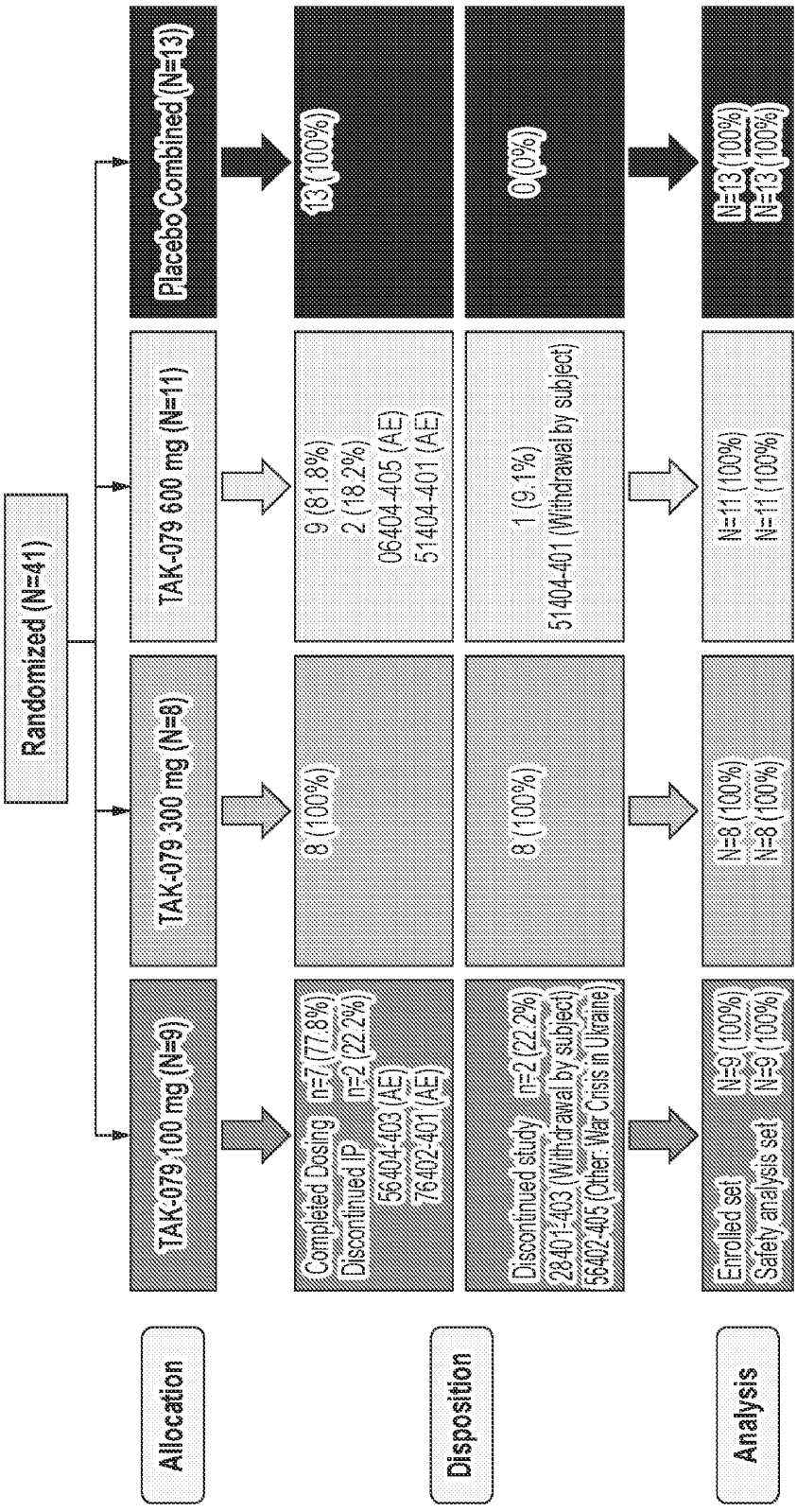

Randomized (N=41)
TAK-079 100 mg (N=9)
TAK-079 300 mg (N=8)
TAK-079 600 mg (N=11)
Placebo Combined (N=13)
Allocation
Completed Dosing n=7 (77.8%)
Discontinued IP n=2 (22.2%)
56404-403 (AE)
76402-401 (AE)
8 (100%)
9 (81.8%)
2 (18.2%)
06404-405 (AE)
51404-401 (AE)
13 (100%)
Disposition
Discontinued study n=2 (22.2%)
28401-403 (Withdrawal by subject)
56402-405 (Other: War Crisis in Ukraine)
8 (100%)
1 (9.1%)
51404-401 (Withdrawal by subject)
0 (0%)
Analysis
Enrolled set N=9 (100%)
Safety analysis set N=9 (100%)
N=8 (100%)
N=8 (100%)
N=11 (100%)
N=11 (100%)
N=13 (100%)
N=13 (100%)
TAK-079 600 mg: 7/11 completed w20, 4/11 completed w24 and 2/11 completed w32
Enrolled set: All randomized subjects.
Safety analysis set: Participants who received at least 1 dose of study drug.
IP - Investigational Prodect

FIG. 3A

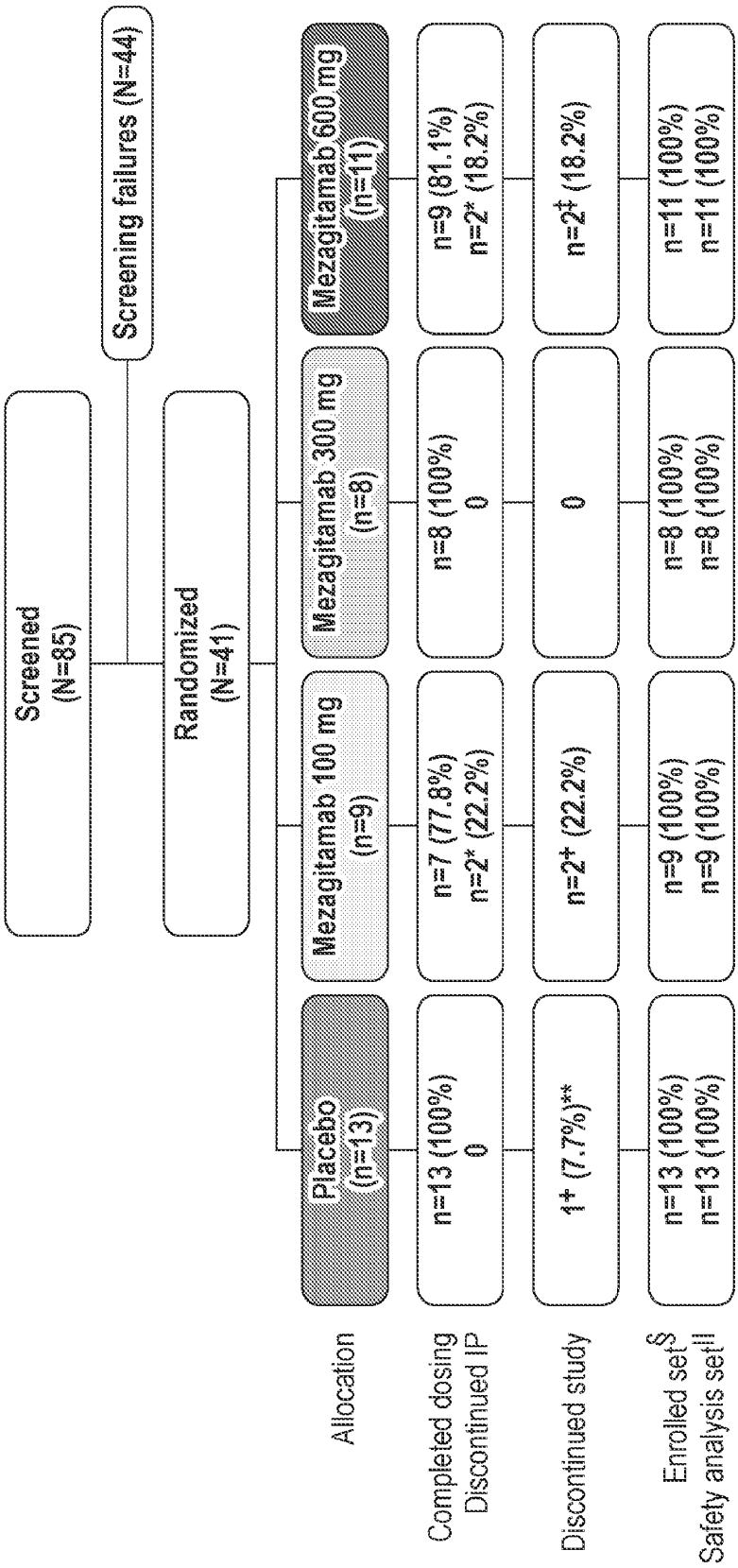

Screened (N=85)
Screening failures (N=44)
Randomized (N=41)
Placebo (n=13)
Mezagitamab 100 mg (n=9)
Mezagitamab 300 mg (n=8)
Mezagitamab 600 mg (n=11)
Allocation
n=13 (100%) 0
n=7 (77.8%) n=2* (22.2%)
n=8 (100%) 0
n=9 (81.1%) n=2* (18.2%)
Completed dosing Discontinued IP
1† (7.7%)**
n=2† (22.2%)
0
n=2‡ (18.2%)
Discontinued study
n=13 (100%) n=13 (100%)
n=9 (100%) n=9 (100%)
n=8 (100%) n=8 (100%)
n=11 (100%) n=11 (100%)
Enrolled set§ Safety analysis set¶

FIG. 3B

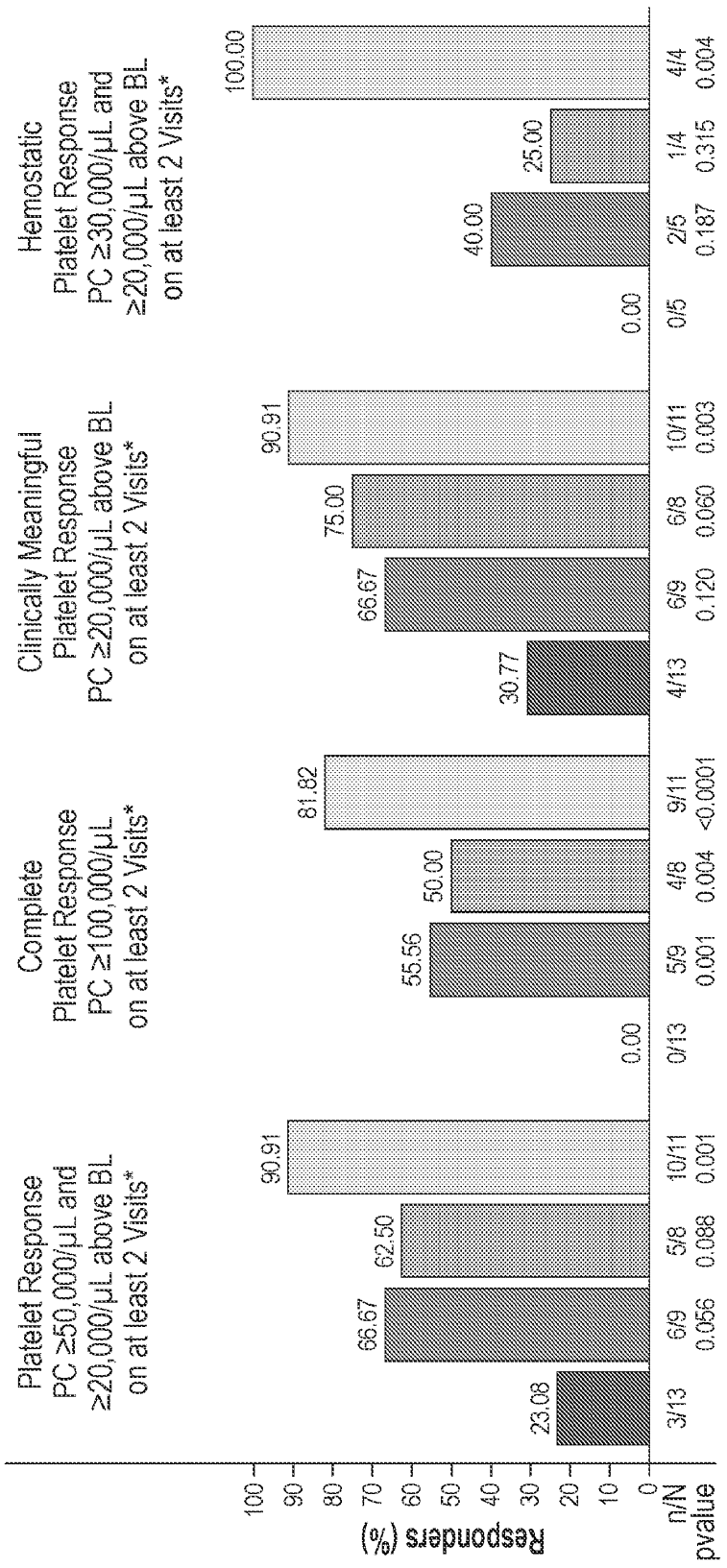

Placebo combined
TAK-079 100 mg
TAK-079 300 mg
TAK-079 600 mg
Platelet Response PC ≥50,000/µL and ≥20,000/µL above BL on at least 2 Visits*
Complete Platelet Response PC ≥100,000/µL on at least 2 Visits*
Clinically Meaningful Platelet Response PC ≥20,000/µL above BL on at least 2 Visits*
Hemostatic Platelet Response PC ≥30,000/µL and ≥20,000/µL above BL on at least 2 Visits*
Responders (%)
n/N
pvalue
3/13 6/9 0.056 5/8 0.088 10/11 0.001
0/13 5/9 0.001 4/8 0.004 9/11 <0.0001
4/13 6/9 0.120 6/8 0.060 10/11 0.003
0/5 2/5 0.187 1/4 0.315 4/4 0.004
23.08 66.67 62.50 90.91
0.00 55.56 50.00 81.82
30.77 66.67 75.00 90.91
0.00 40.00 25.00 100.00

FIG. 4A

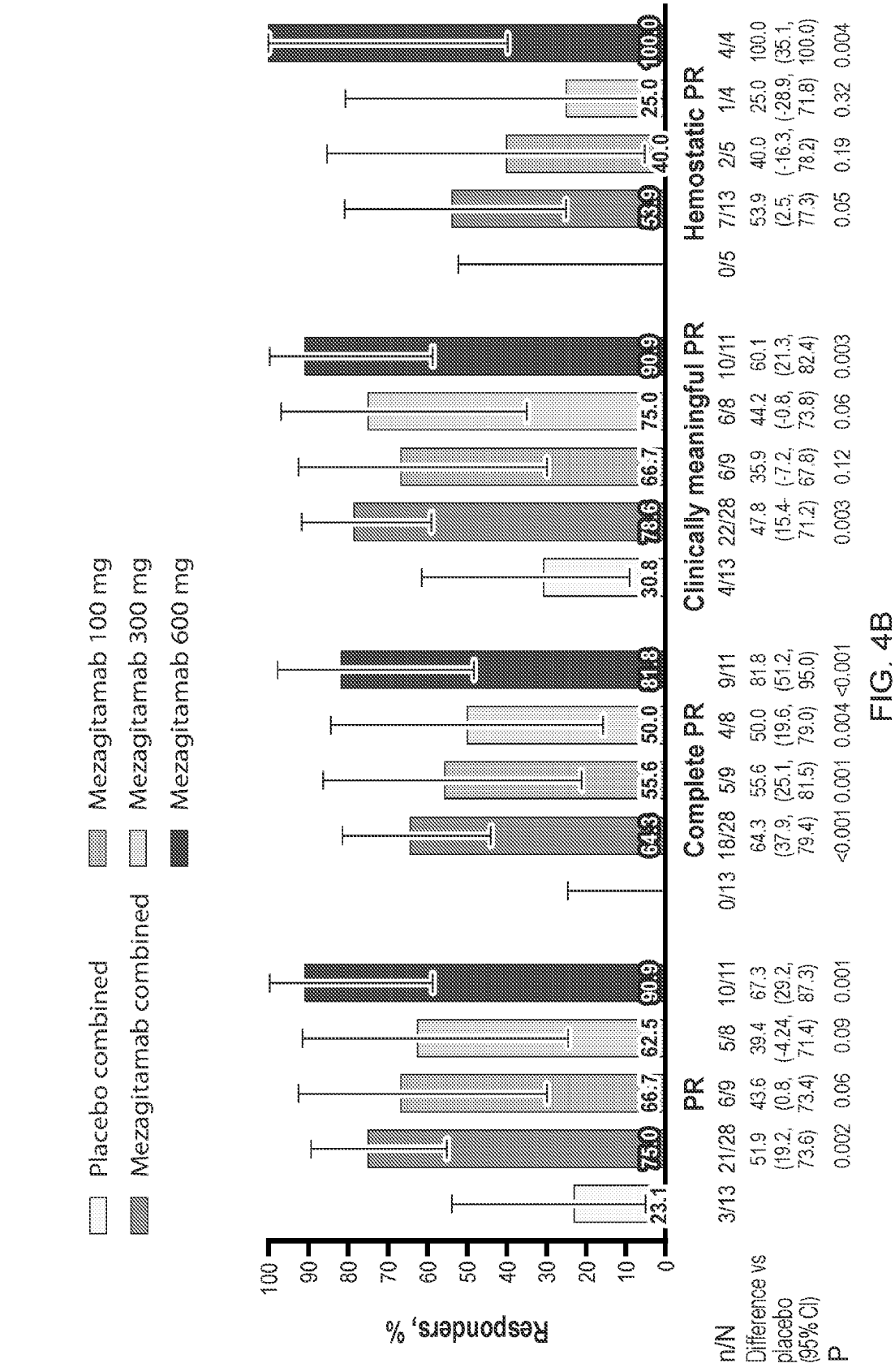

Placebo combined
Mezagitamab 100 mg
Mezagitamab combined
Mezagitamab 300 mg
Mezagitamab 600 mg
Responders, %
100
90
80
70
60
50
40
30
20
10
0
23.1
75.0
66.7
62.5
90.9
30.8
78.3
66.7
75.0
90.9
25.0
100.0
PR
Complete PR
Clinically meaningful PR
Hemostatic PR
n/N
3/13 21/28 6/9 5/8 10/11 0/13 18/28 5/9 4/8 9/11 4/13 22/28 6/9 6/8 10/11 0/5 7/13 2/5 1/4 4/4
Difference vs placebo (95% CI)
51.9 (19.2, 73.6) 43.6 (0.8, 73.4) 39.4 (-4.24, 71.4) 67.3 (29.2, 87.3)
64.3 (37.9, 79.4) 55.6 (25.1, 81.5) 50.0 (19.6, 79.0) 81.8 (51.2, 95.0)
47.8 (15.4- 71.2) 35.9 (-7.2, 67.8) 44.2 (-0.8, 73.8) 60.1 (21.3, 82.4)
53.9 (2.5, 77.3) 40.0 (-16.3, 78.2) 25.0 (-28.9, 71.8) 100.0 (35.1, 100.0)
P
0.002 0.06 0.09 0.001
<0.001 0.001 0.004 <0.001
0.003 0.12 0.06 0.003
0.05 0.19 0.32 0.004

FIG. 4B

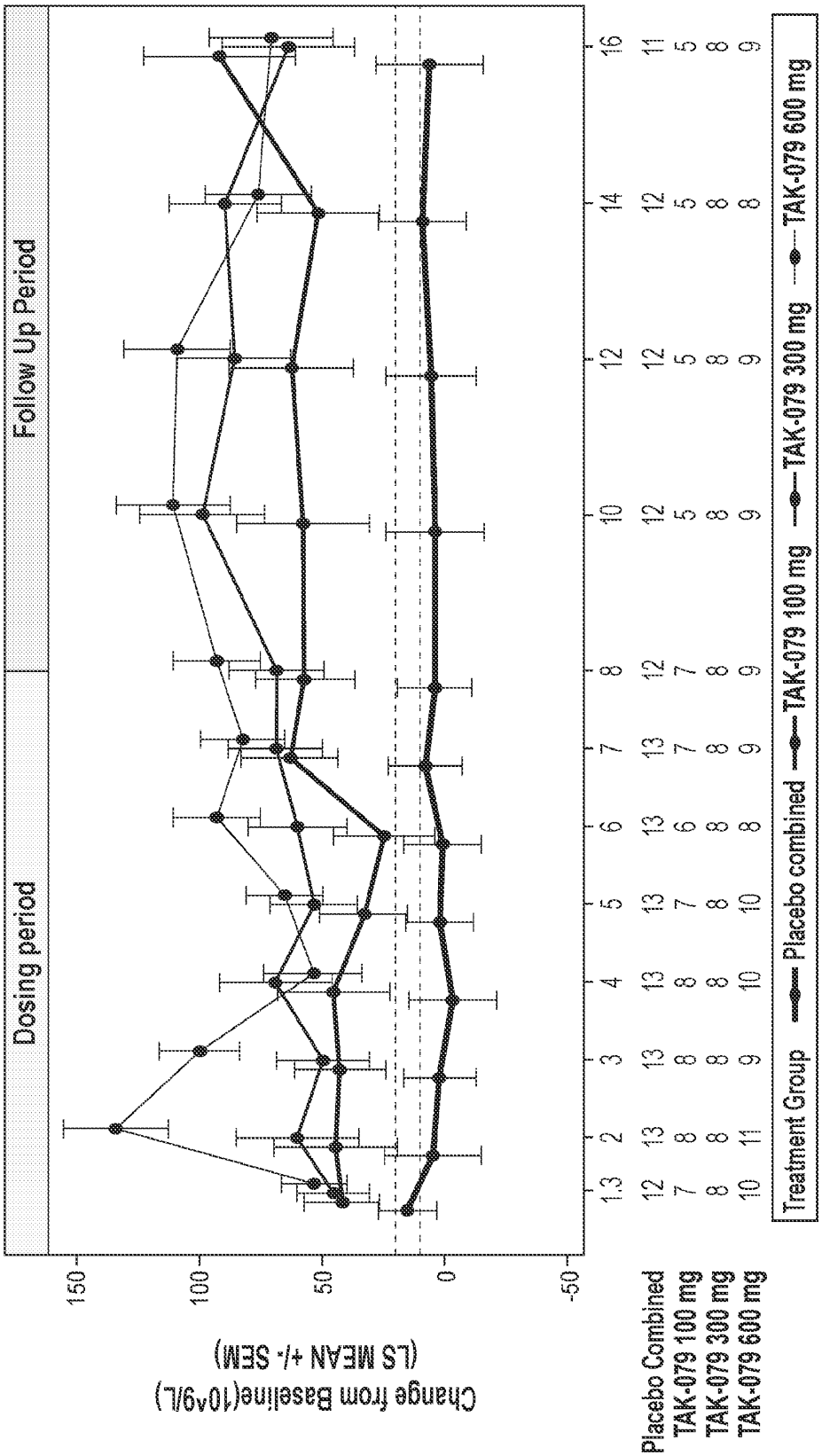

Dosing period
Follow Up Period
Change from Baseline(10^9/L)
(LS MEAN +/- SEM)
150
100
50
0
-50
1.3 2 3 4 5 6 7 8 10 12 14 16
Placebo Combined 12 13 13 13 13 13 13 12 12 12 11
TAK-079 100 mg 7 8 8 8 8 8 7 7 5 5 5
TAK-079 300 mg 8 8 8 8 8 8 8 8 8 8 8
TAK-079 600 mg 10 11 9 10 10 8 9 9 9 8 9
Treatment Group
Placebo combined
TAK-079 100 mg
TAK-079 300 mg
TAK-079 600 mg

FIG. 5

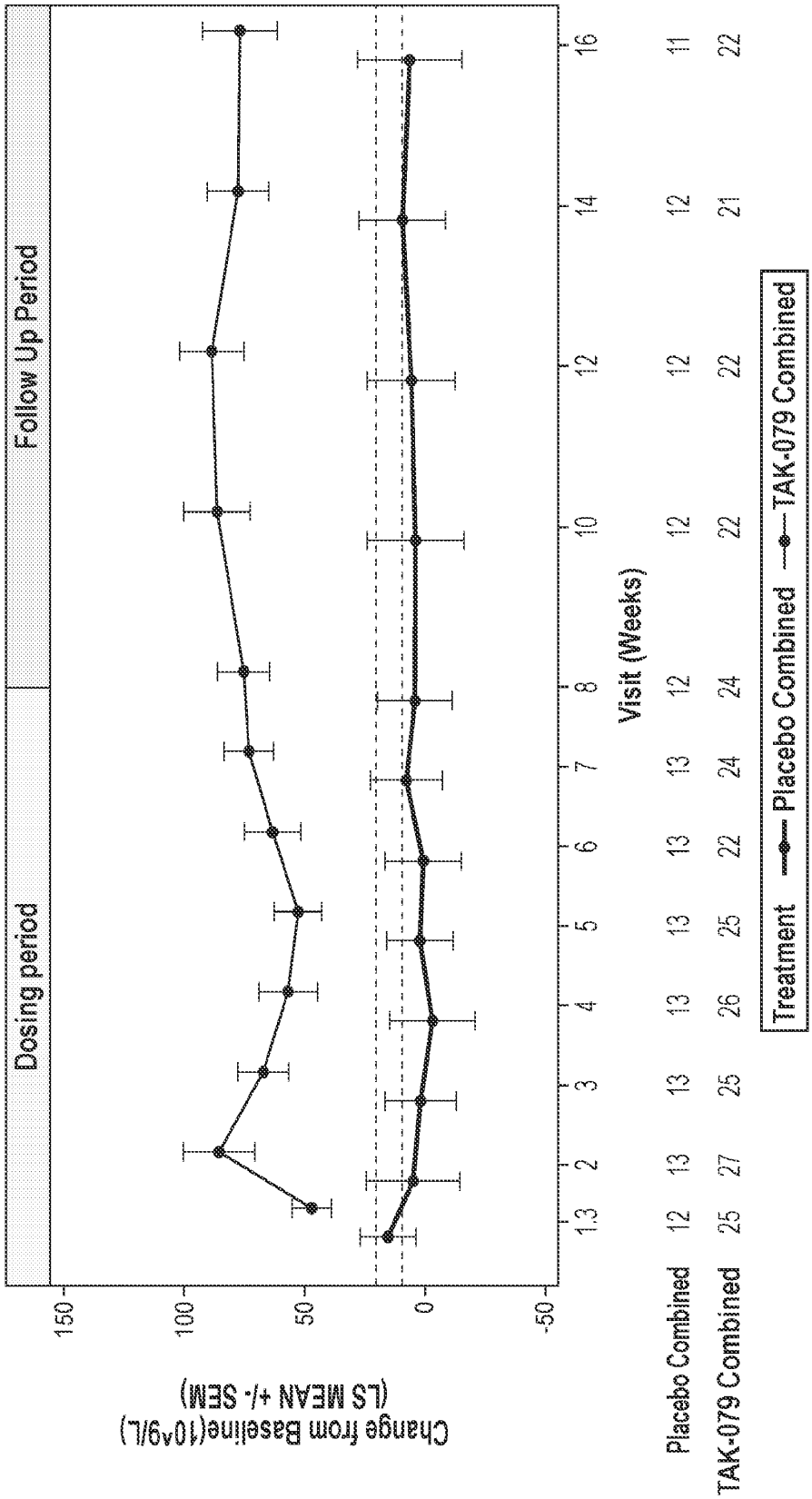

Dosing period
Follow Up Period
Change from Baseline(10^9/L)
(LS MEAN +/- SEM)
150
100
50
0
-50
1.3
2
3
4
5
6
7
8
10
12
14
16
Visit (Weeks)
Placebo Combined 12 13 13 13 13 13 13 12 12 12 12 11
TAK-079 Combined 25 27 25 26 25 22 24 24 22 22 21 22
Treatment
Placebo Combined
TAK-079 Combined

FIG. 6

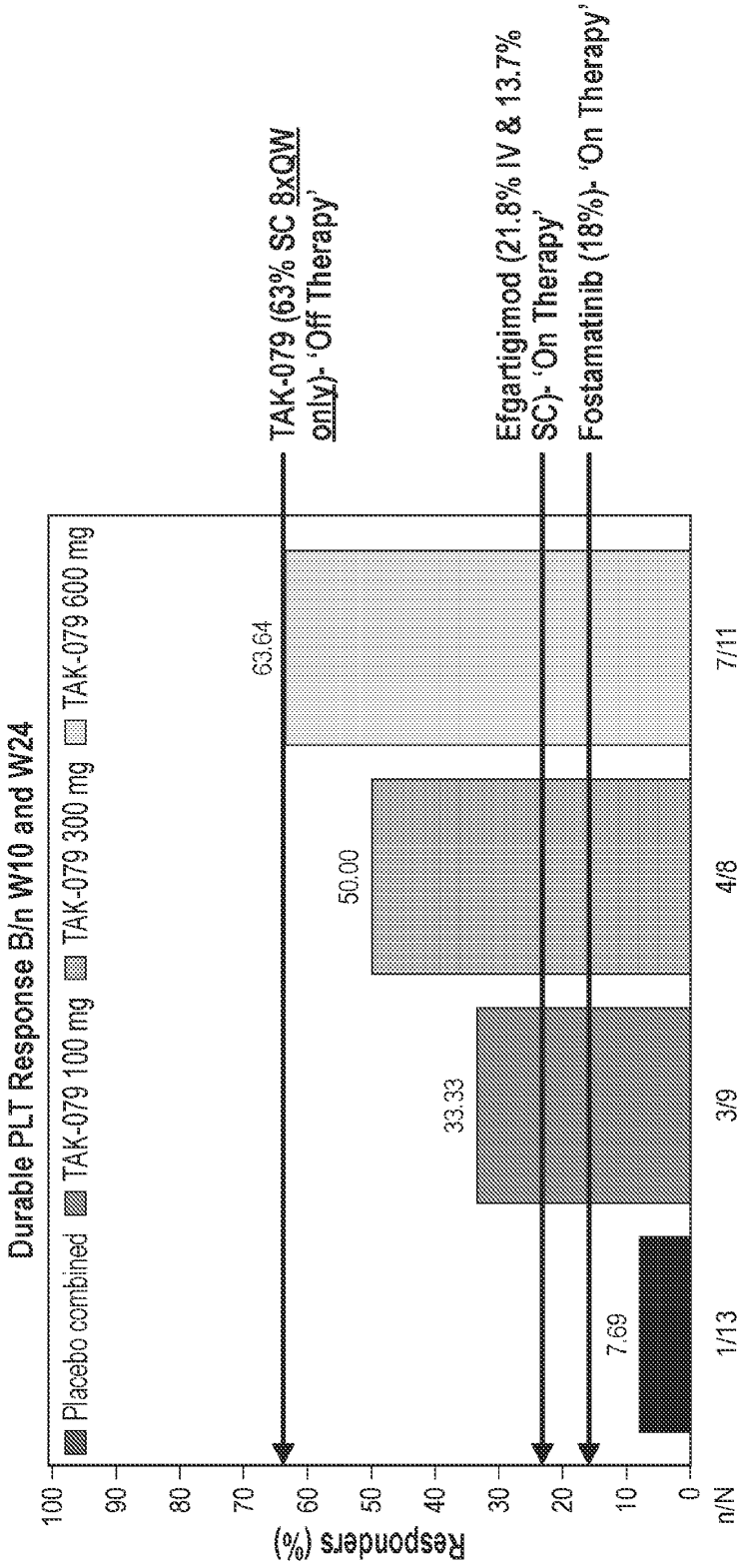

Durable PLT Response B/n W10 and W24
Placebo combined
TAK-079 100 mg
TAK-079 300 mg
TAK-079 600 mg
TAK-079 (63% SC 8xQW only)- 'Off Therapy'
Efgartigimod (21.8% IV & 13.7% SC)- 'On Therapy'
Fostamatinib (18%)- 'On Therapy'
63.64
50.00
33.33
7.69
7/11
4/8
3/9
1/13
n/N
Responders (%)
100
90
80
70
60
50
40
30
20
10
0

FIG. 7

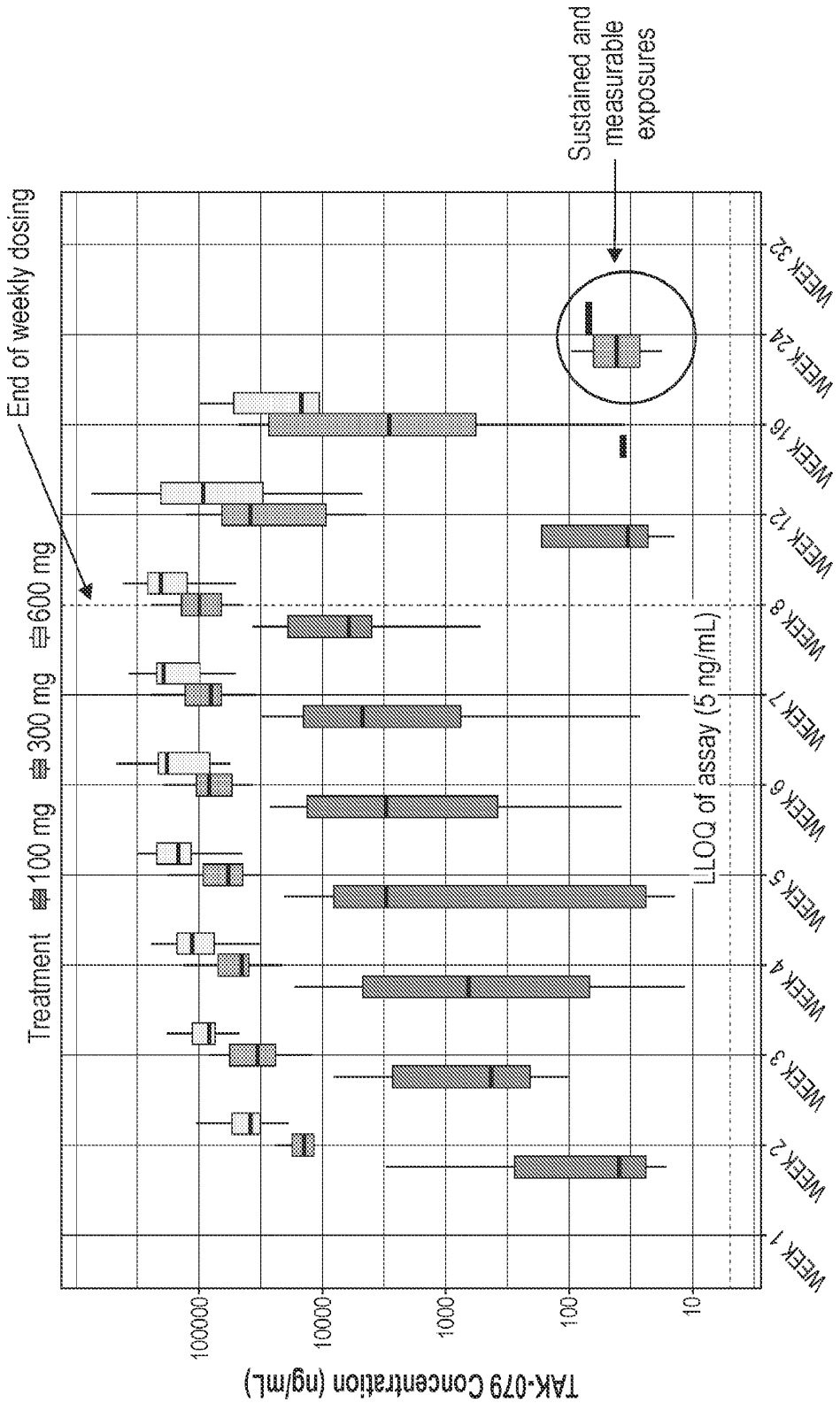

Sustained and measurable exposures
End of weekly dosing
Treatment
100 mg
300 mg
600 mg
LLOQ of assay (5 ng/mL)
TAK-079 Concentration (ng/mL)
100000
10000
1000
100
10
WEEK 1
WEEK 2
WEEK 3
WEEK 4
WEEK 5
WEEK 6
WEEK 7
WEEK 8
WEEK 12
WEEK 16
WEEK 24
WEEK 32
Visit

FIG. 8

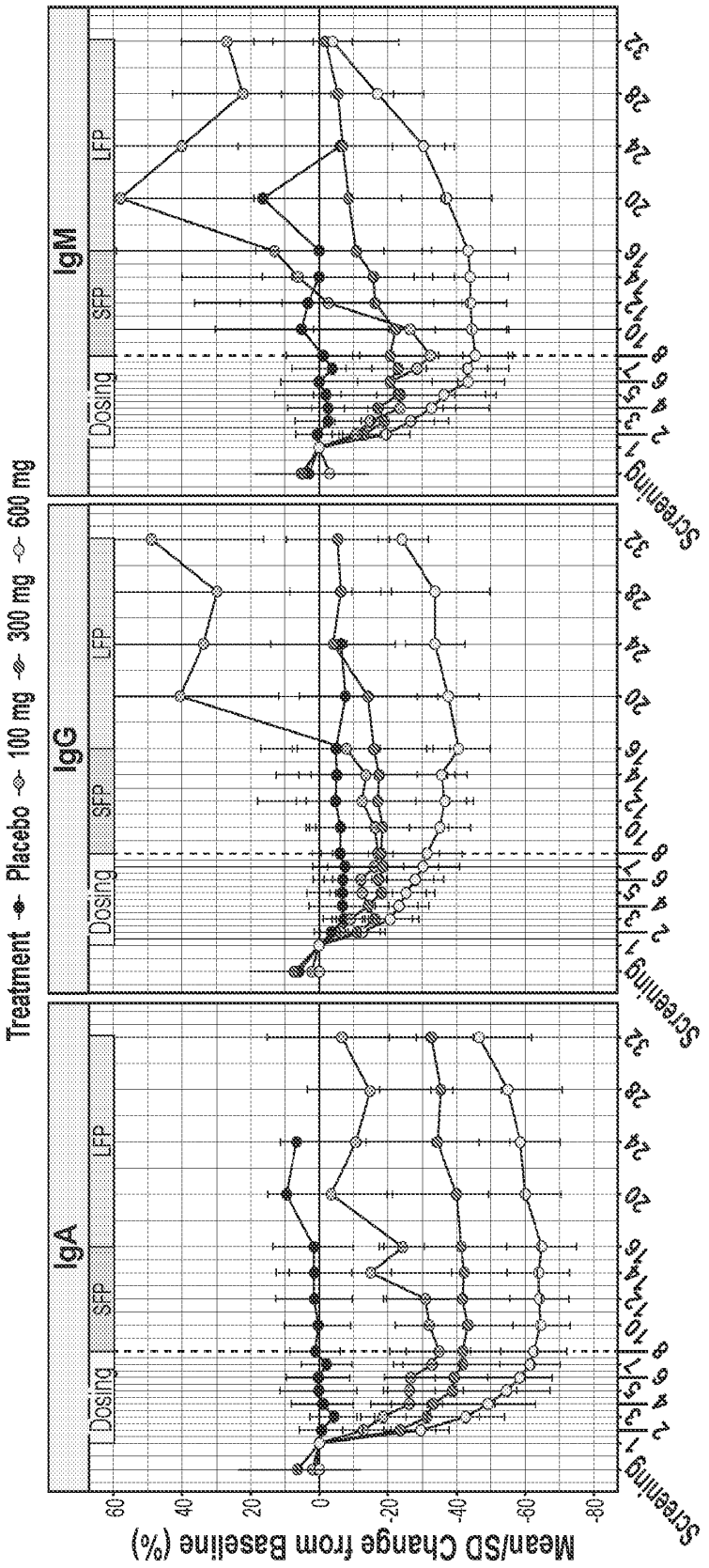

Treatment Placebo 100 mg 300 mg 600 mg
IgA
IgG
IgM
Dosing
SFP
LFP
Mean/SD Change from Baseline (%)
Visit (Week)
Screening 1
2
3
4
5
6
7
8
10
12
14
16
20
24
28
32

FIG. 9

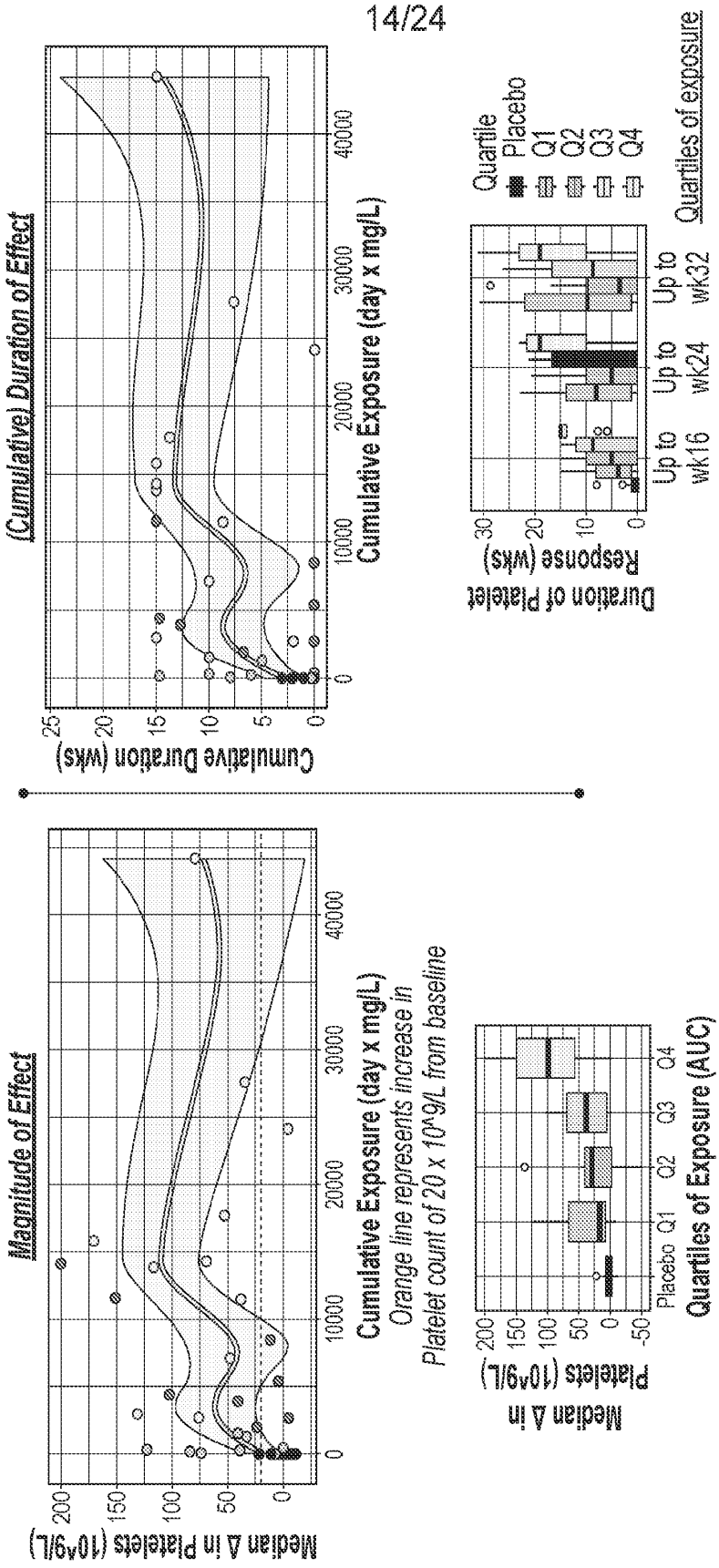

(Cumulative) Duration of Effect
Cumulative Duration (wks)
Cumulative Exposure (day x mg/L)
Quartile
Placebo
Q1
Q2
Q3
Q4
Duration of Platelet Response (wks)
Up to wk16
Up to wk24
Up to wk32
Quartiles of exposure
Magnitude of Effect
Median Δ in Platelets (10^9/L)
Cumulative Exposure (day x mg/L)
Orange line represents increase in Platelet count of 20 x 10^9/L from baseline
Median Δ in Platelets (10^9/L)
Placebo Q1 Q2 Q3 Q4
Quartiles of Exposure (AUC)

FIG. 10

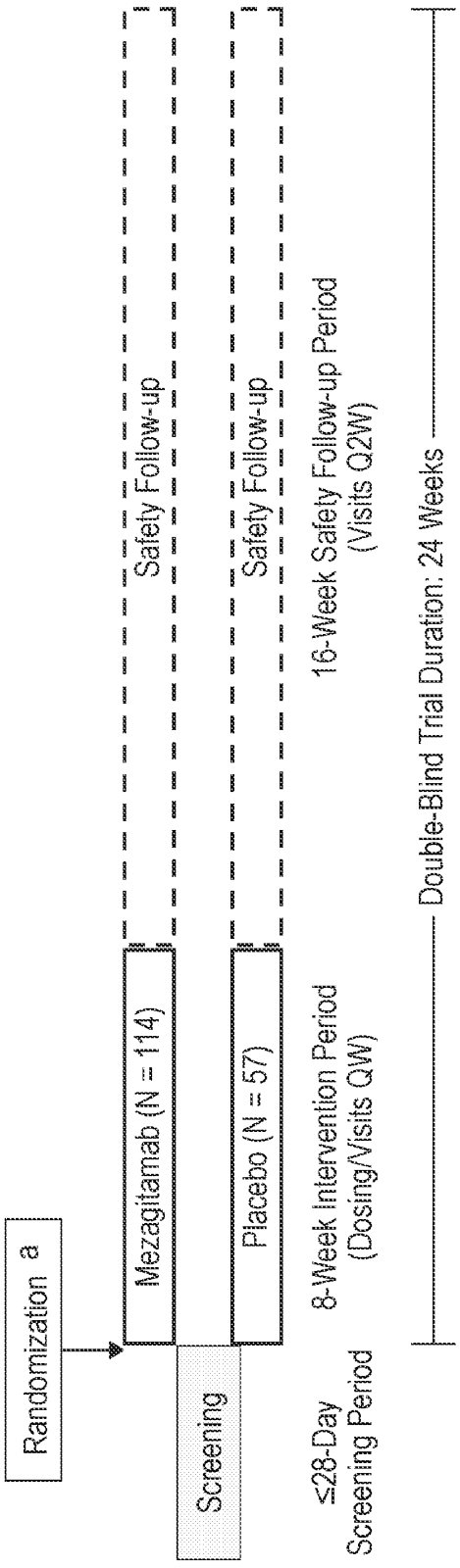

Randomization a
Screening
Mezagitamab (N = 114)
Placebo (N = 57)
Safety Follow-up
Safety Follow-up
≤28-Day Screening Period
8-Week Intervention Period (Dosing/Visits QW)
16-Week Safety Follow-up Period (Visits Q2W)
Double-Blind Trial Duration: 24 Weeks

FIG. 11

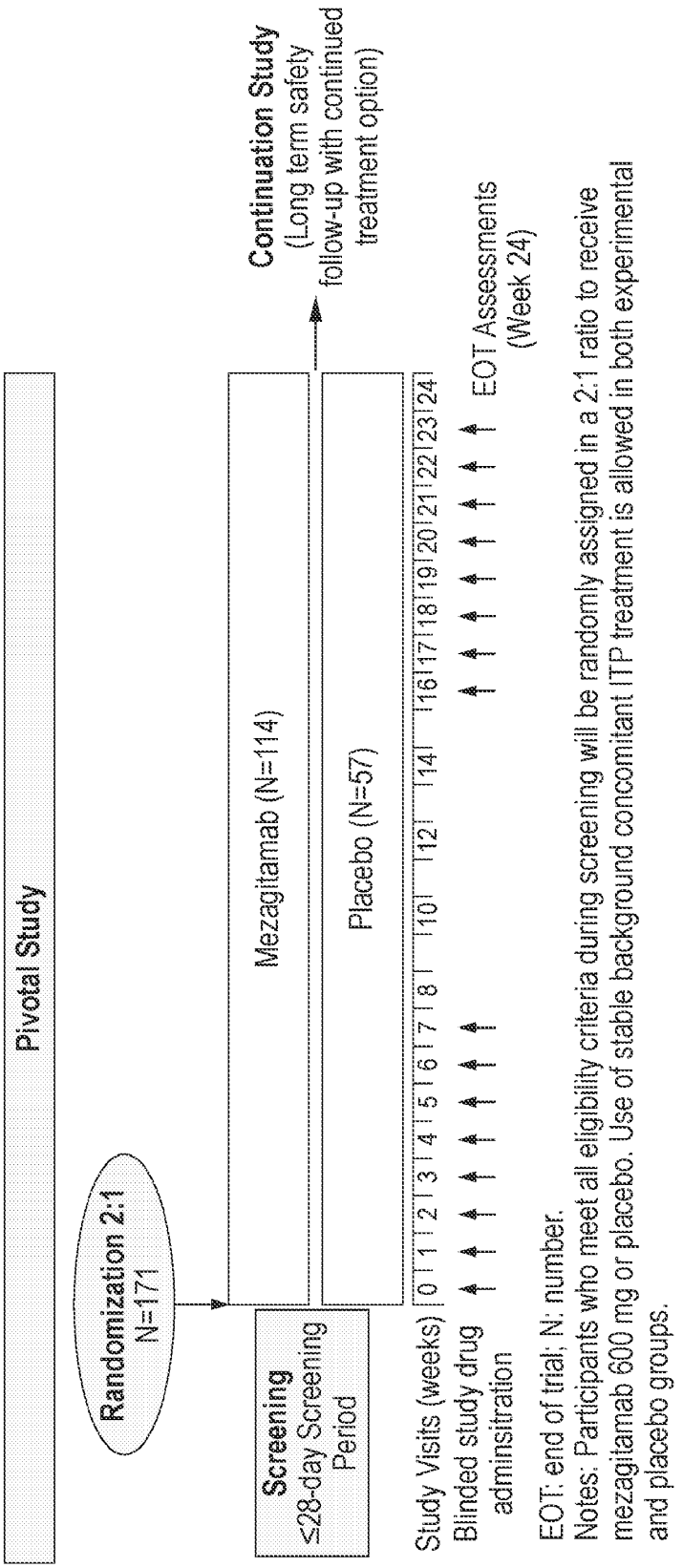

Pivotal Study
Randomization 2:1
N=171
Screening
≤28-day Screening Period
Mezagitamab (N=114)
Placebo (N=57)
Continuation Study
(Long term safety follow-up with continued treatment option)
Study Visits (weeks) 0 1 2 3 4 5 6 7 8 10 12 14 16 17 18 19 20 21 22 23 24
Blinded study drug adminsitration
EOT Assessments (Week 24)
EOT: end of trial; N: number.
Notes: Participants who meet all eligibility criteria during screening will be randomly assigned in a 2:1 ratio to receive mezagitamab 600 mg or placebo. Use of stable background concomitant ITP treatment is allowed in both experimental and placebo groups.

FIG. 12

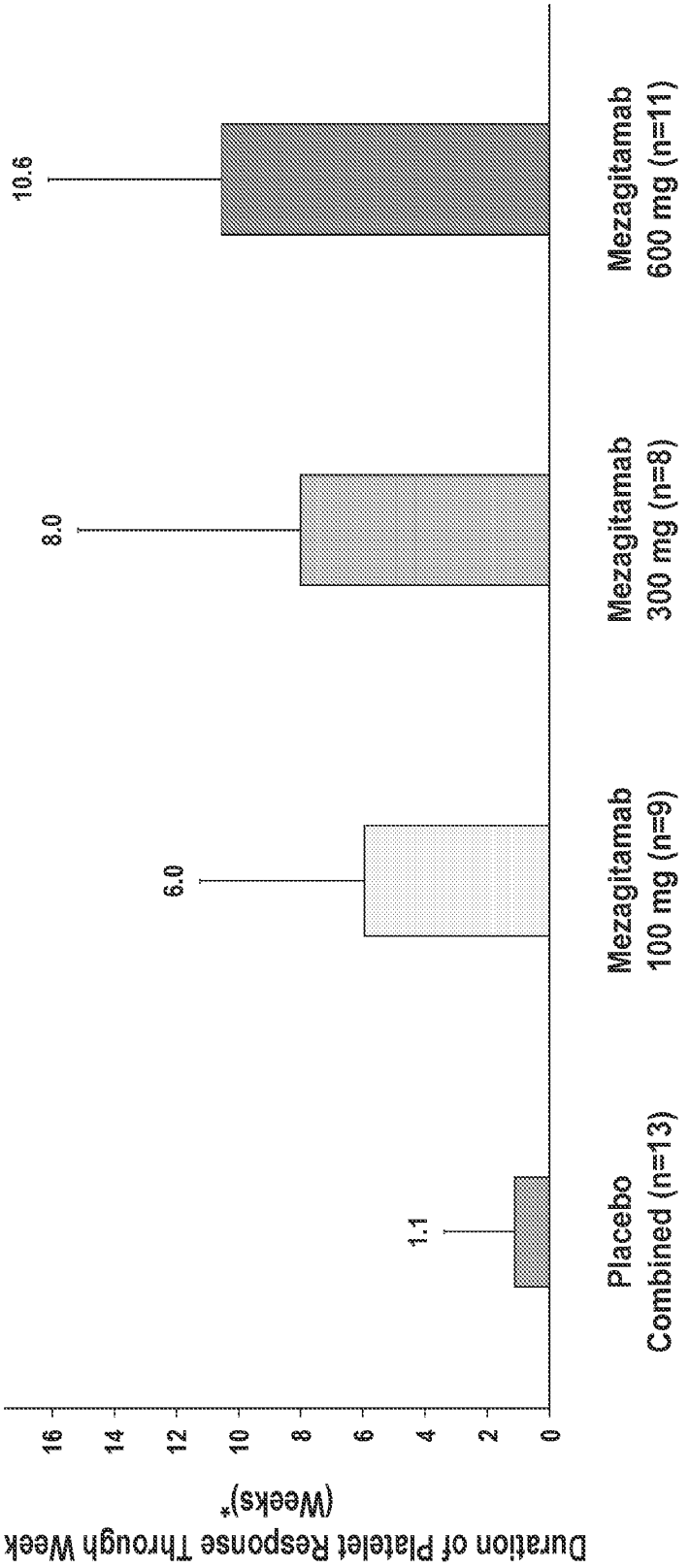
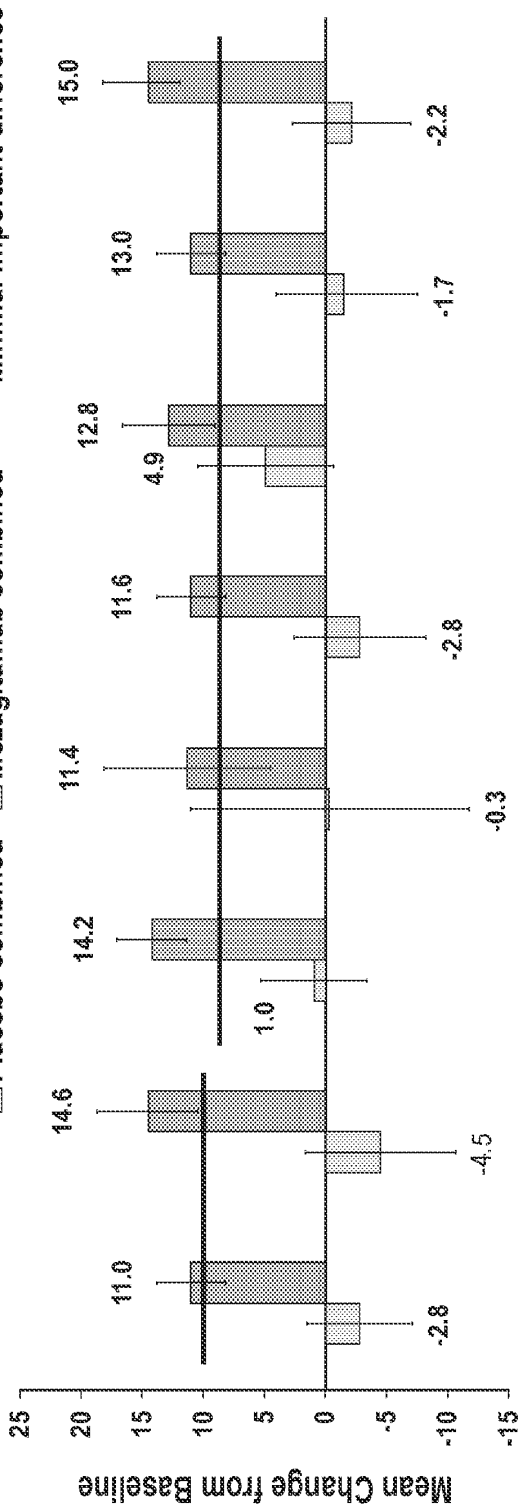

Duration of Platelet Response Through Week 16
(Weeks)*
0
2
4
6
8
10
12
14
16
1.1
6.0
8.0
10.6
Placebo
Combined (n=13)
Mezagitamab
100 mg (n=9)
Mezagitamab
300 mg (n=8)
Mezagitamab
600 mg (n=11)

FIG. 13



	Fatigue/Sleep	Physical activity	Symptoms	Women's reproductive health	Physical health - Bother	Psychological health	Overall quality of life	Social activity
	n=10 n=20	n=9 n=22	n=10 n=22	n=4 n=9	n=10 n=22	n=10 n=22	n=10 n=22	n=10 n=22
Differences in least squares mean (95% CI vs Placebo)	13.9 (3.6, 24.3)	19.2 (3.8, 34.7)	13.0 (2.4, 23.6)	10.3 (-17.7, 38.2)	14.4 (1.5, 27.4)	7.8 (-5.9, 21.6)	14.7 (0.4, 29.0)	17.2 (5.6, 28.8)
P value	0.01	0.02	0.02	0.44	0.03	0.25	0.04	<0.01

FIG. 14

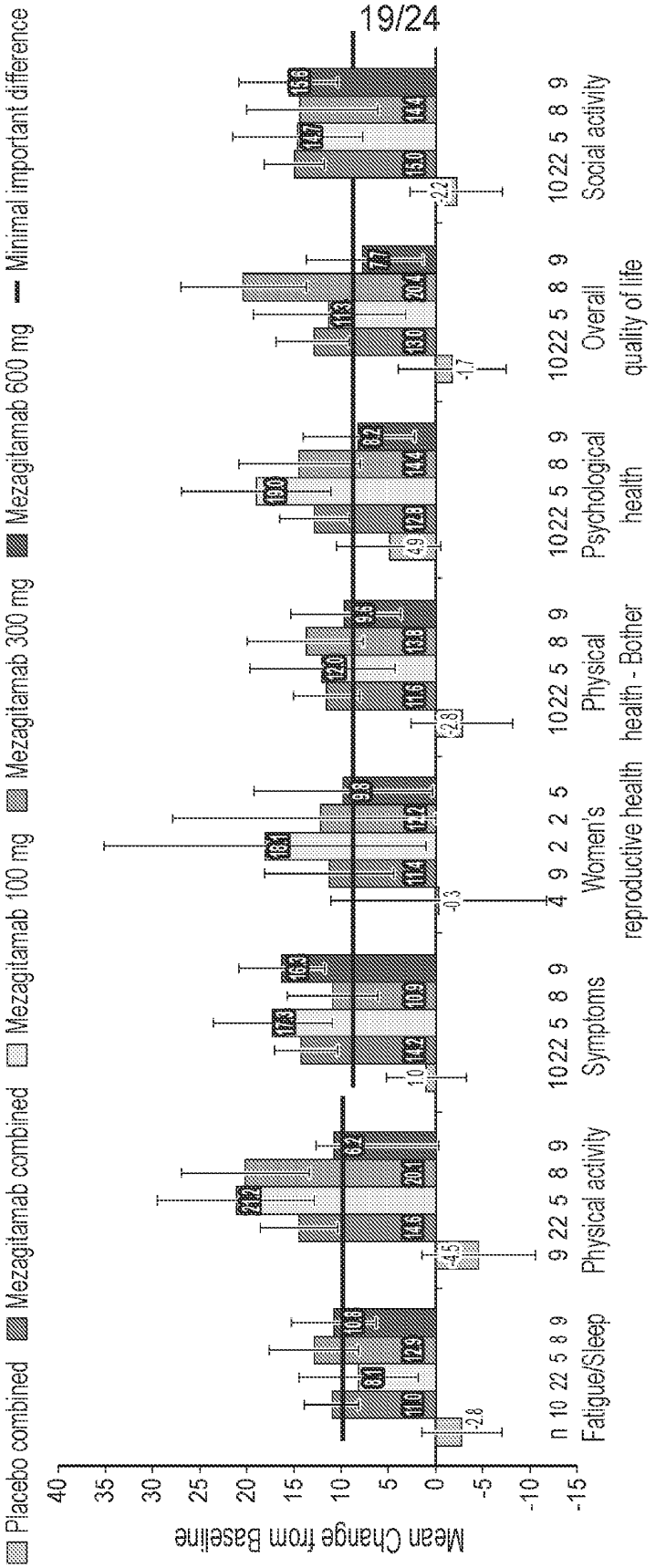

Placebo combined
Mezagitamab combined
Mezagitamab 100 mg
Mezagitamab 300 mg
Mezagitamab 600 mg
Minimal important difference
Mean Change from Baseline
40
35
30
25
20
15
10
5
0
-5
-10
-15
n 10 22 5 8 9
Fatigue/Sleep
9 22 5 8 9
Physical activity
10 22 5 8 9
Symptoms
4 9 2 2 5
Women's reproductive health
10 22 5 8 9
Physical health - Bother
10 22 5 8 9
Psychological health
10 22 5 8 9
Overall quality of life
10 22 5 8 9
Social activity

FIG. 15

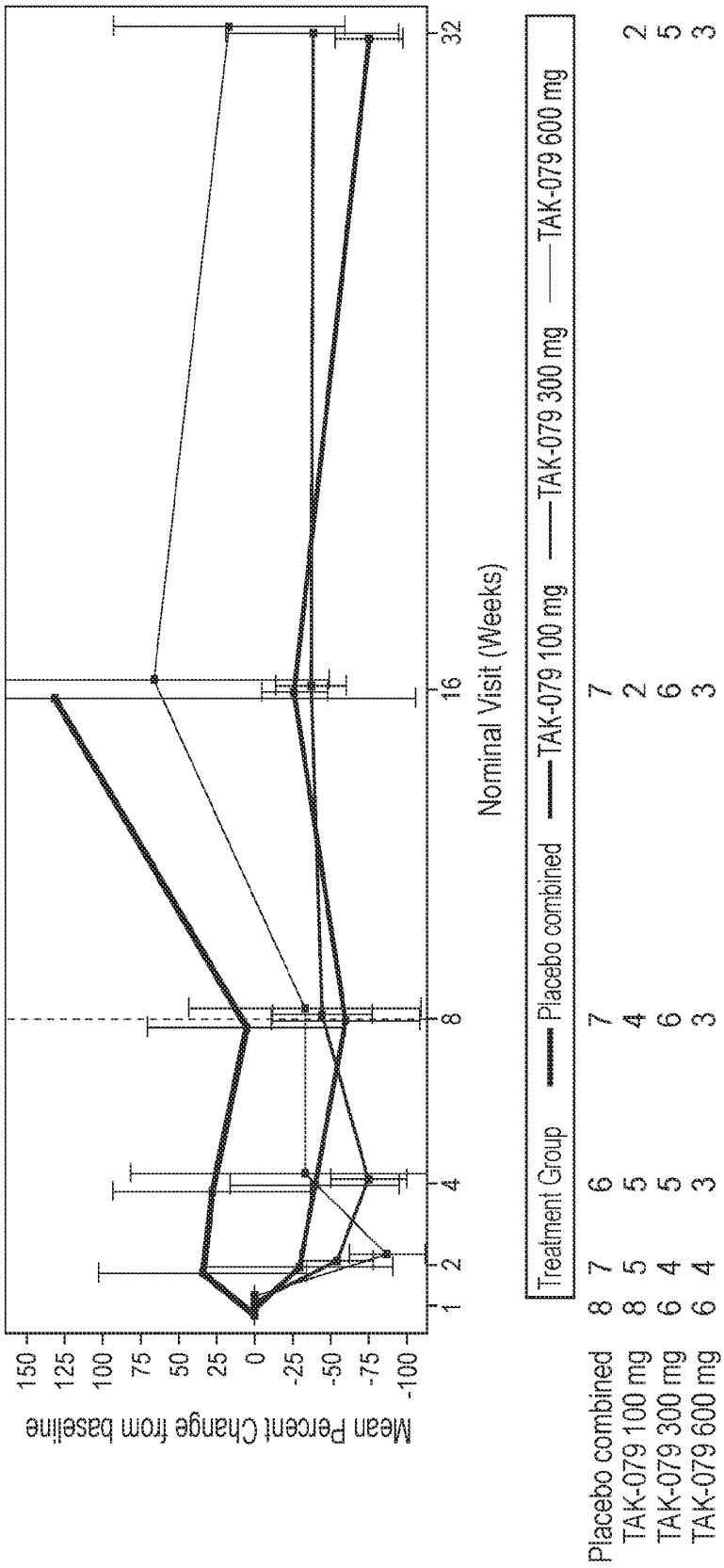

Mean Percent Change from baseline
150
125
100
75
50
25
0
-25
-50
-75
-100
1
2
4
8
16
32
Nominal Visit (Weeks)
Treatment Group
Placebo combined
TAK-079 100 mg
TAK-079 300 mg
TAK-079 600 mg
Placebo combined 8 7 6 7 7
TAK-079 100 mg 8 5 5 4 2
TAK-079 300 mg 6 4 5 6 5
TAK-079 600 mg 6 4 3 3 3
2
5
3

FIG. 16A

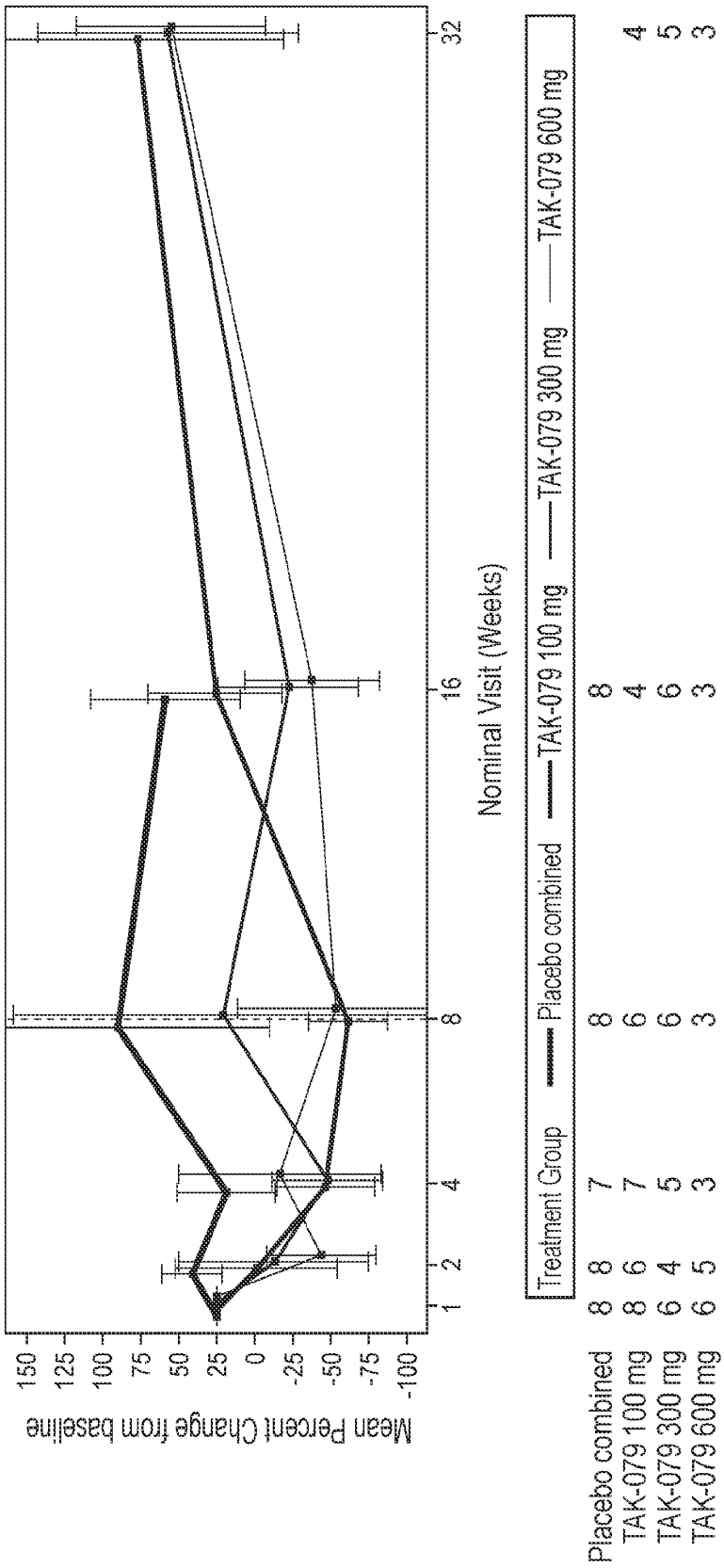

Mean Percent Change from baseline
150
125
100
75
50
25
0
-25
-50
-75
-100
1
2
4
8
16
32
Nominal Visit (Weeks)
Treatment Group
Placebo combined
TAK-079 100 mg
TAK-079 300 mg
TAK-079 600 mg
Placebo combined 8 8 7 8 8 4
TAK-079 100 mg 8 6 7 6 4 5
TAK-079 300 mg 6 4 5 6 6 3
TAK-079 600 mg 6 5 3 3 3

FIG. 16B

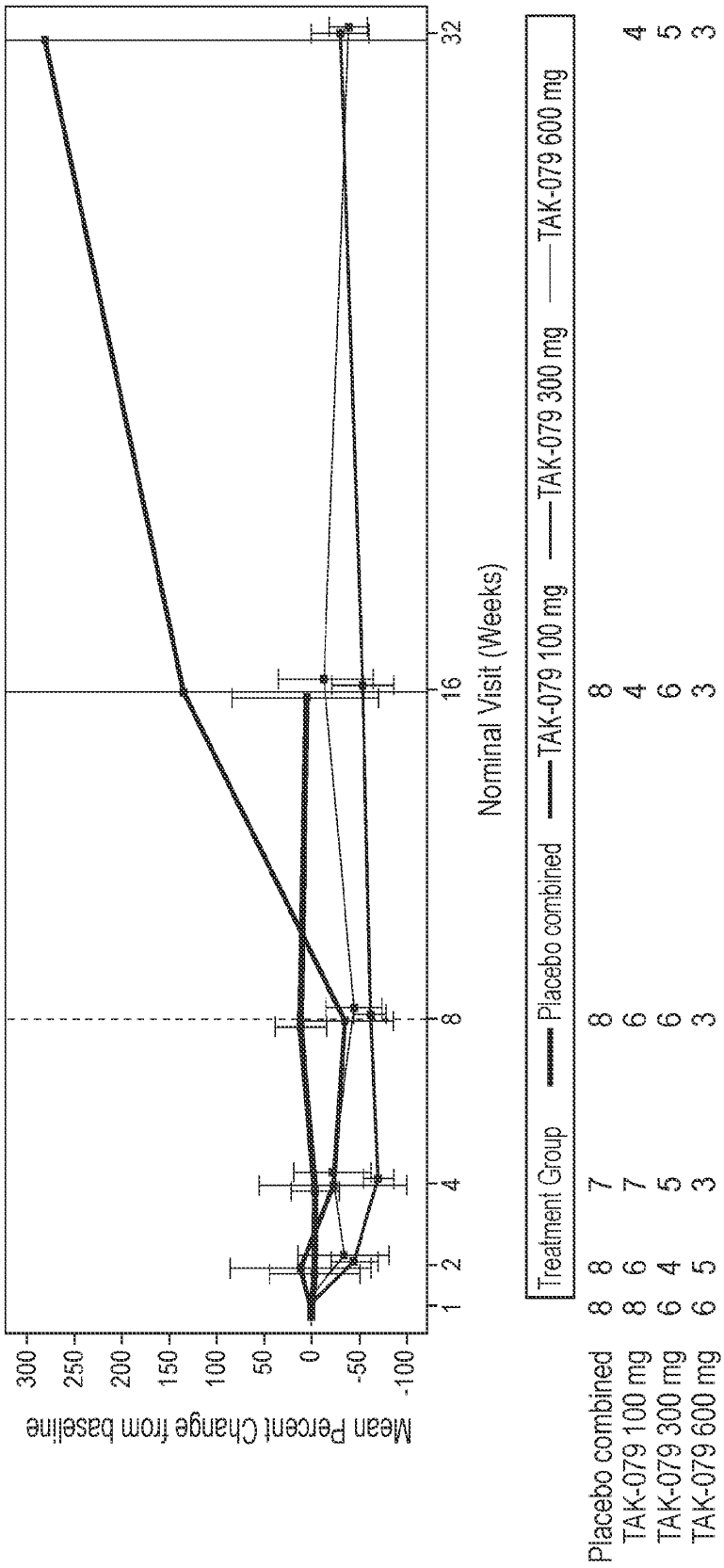

Mean Percent Change from baseline
300
250
200
150
100
50
0
-50
-100
1
2
4
8
16
32
Nominal Visit (Weeks)
Treatment Group
Placebo combined
TAK-079 100 mg
TAK-079 300 mg
TAK-079 600 mg
Placebo combined 8 8 7 8 8 4
TAK-079 100 mg 8 6 7 6 4 5
TAK-079 300 mg 6 4 5 6 6 3
TAK-079 600 mg 6 5 3 3 3

FIG. 16C

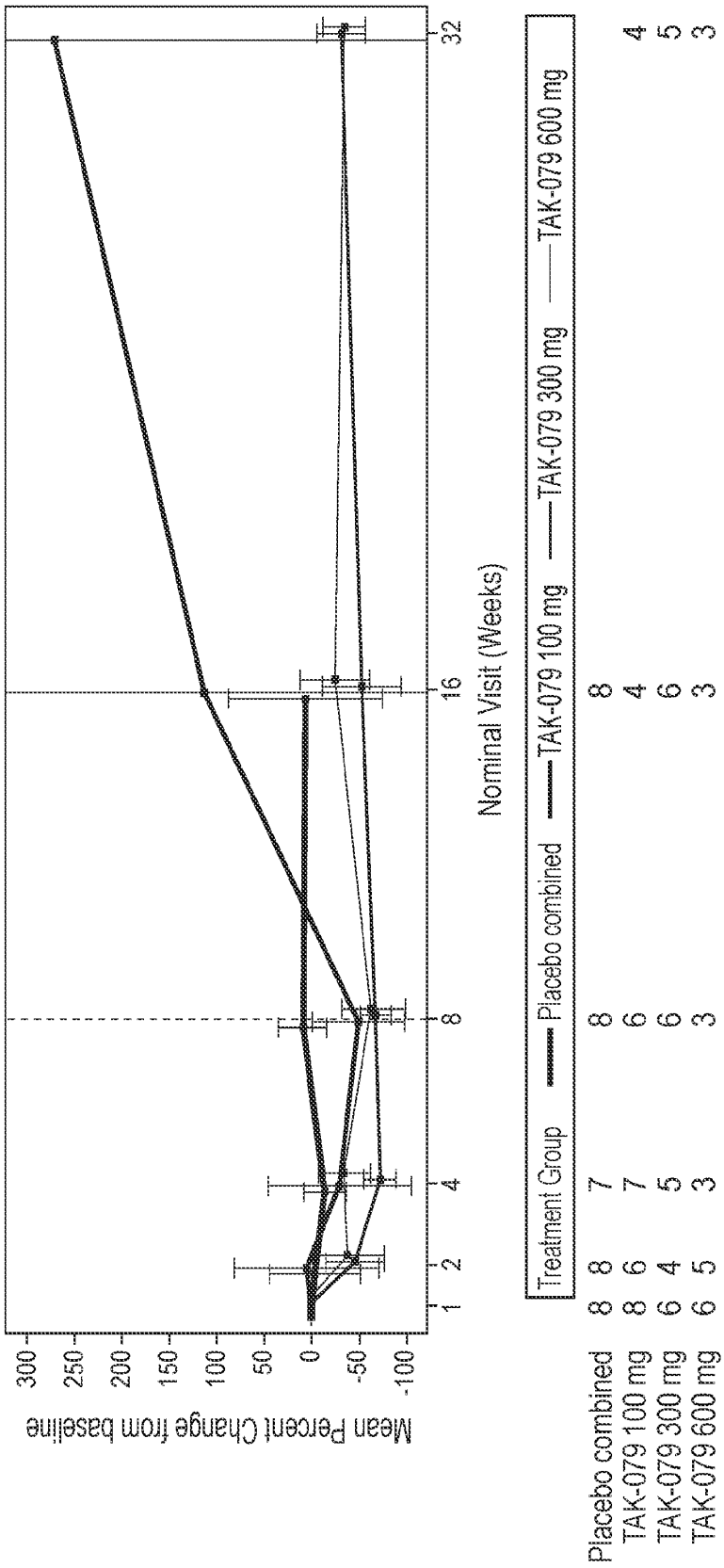

Mean Percent Change from baseline
300
250
200
150
100
50
0
-50
-100
1
2
4
8
16
32
Nominal Visit (Weeks)
Treatment Group
Placebo combined
TAK-079 100 mg
TAK-079 300 mg
TAK-079 600 mg
Placebo combined 8 8 7 8 8 4
TAK-079 100 mg 8 6 7 6 4 5
TAK-079 300 mg 6 4 5 6 6 3
TAK-079 600 mg 6 5 3 3 3

FIG. 16D

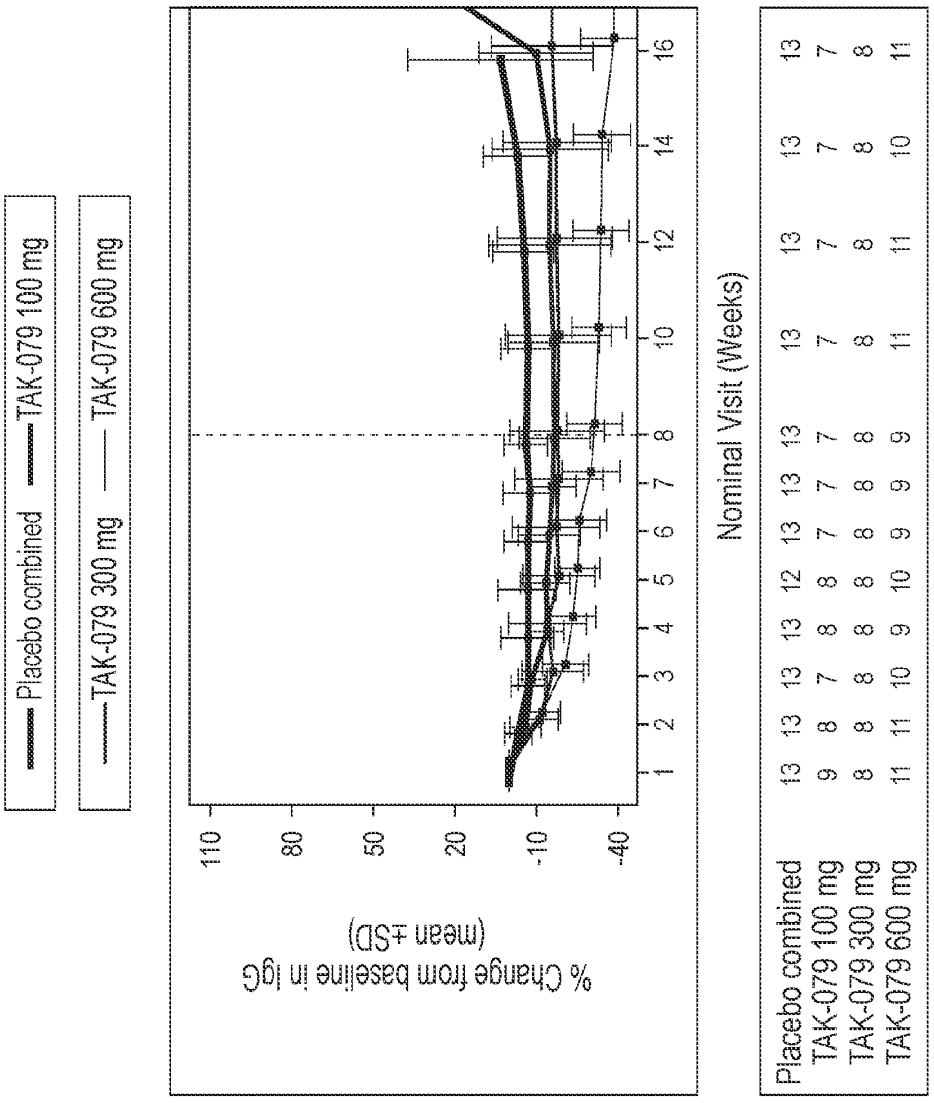

Placebo combined
TAK-079 100 mg
TAK-079 300 mg
TAK-079 600 mg
% Change from baseline in IgG
(mean ±SD)
110
80
50
20
-10
-40
1 2 3 4 5 6 7 8 10 12 14 16
Nominal Visit (Weeks)
Placebo combined 13 13 13 13 12 13 13 13 13 13 13 13
TAK-079 100 mg 9 8 7 8 8 7 7 7 7 7 7 7
TAK-079 300 mg 8 8 8 8 8 8 8 8 8 8 8 8
TAK-079 600 mg 11 11 10 9 10 9 9 9 11 11 10 11

FIG. 16E