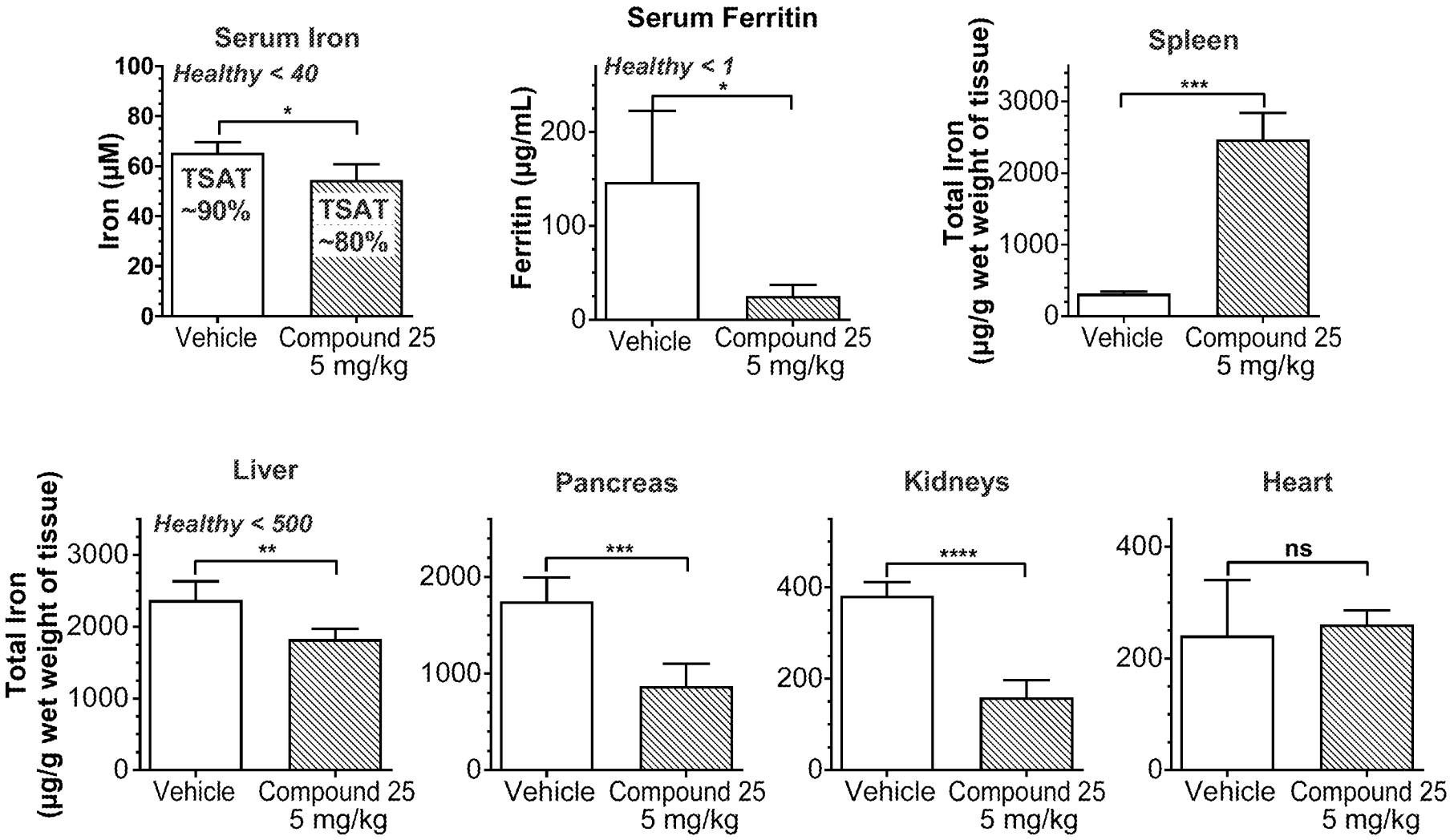

Serum Iron
Healthy < 40
Iron (µM)
100
80
60
40
20
0
*
TSAT ~90%
TSAT ~80%
Vehicle
Compound 25 5 mg/kg
Serum Ferritin
Healthy < 1
Ferritin (µg/mL)
200
100
0
*
Vehicle
Compound 25 5 mg/kg
Spleen
Total Iron (µg/g wet weight of tissue)
3000
2000
1000
0
***
Vehicle
Compound 25 5 mg/kg
Liver
Healthy < 500
Total Iron (µg/g wet weight of tissue)
3000
2000
1000
0
**
Vehicle
Compound 25 5 mg/kg
Pancreas
2000
1000
0
***
Vehicle
Compound 25 5 mg/kg
Kidneys
400
200
0
****
Vehicle
Compound 25 5 mg/kg
Heart
400
200
0
ns
Vehicle
Compound 25 5 mg/kg

FIG. 1

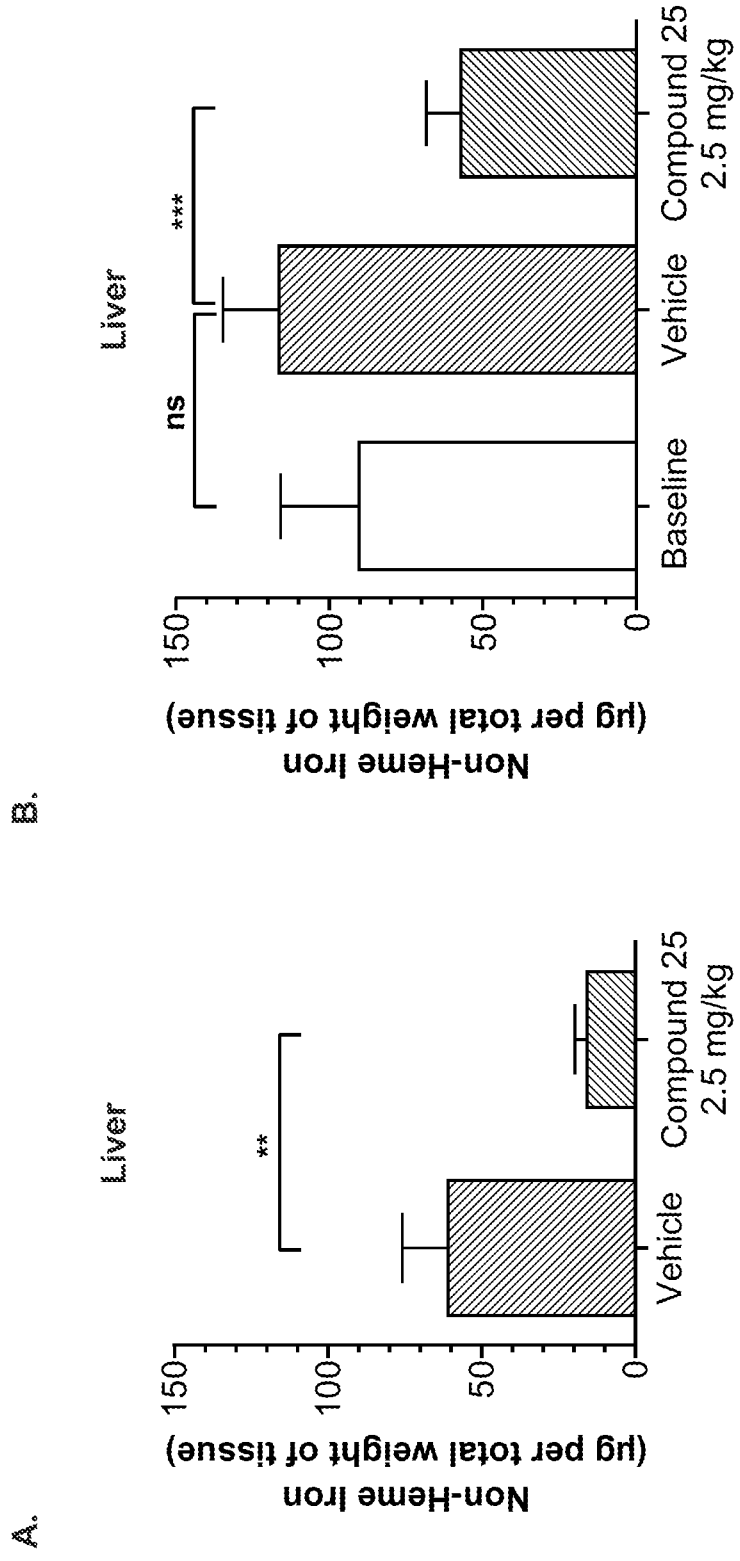
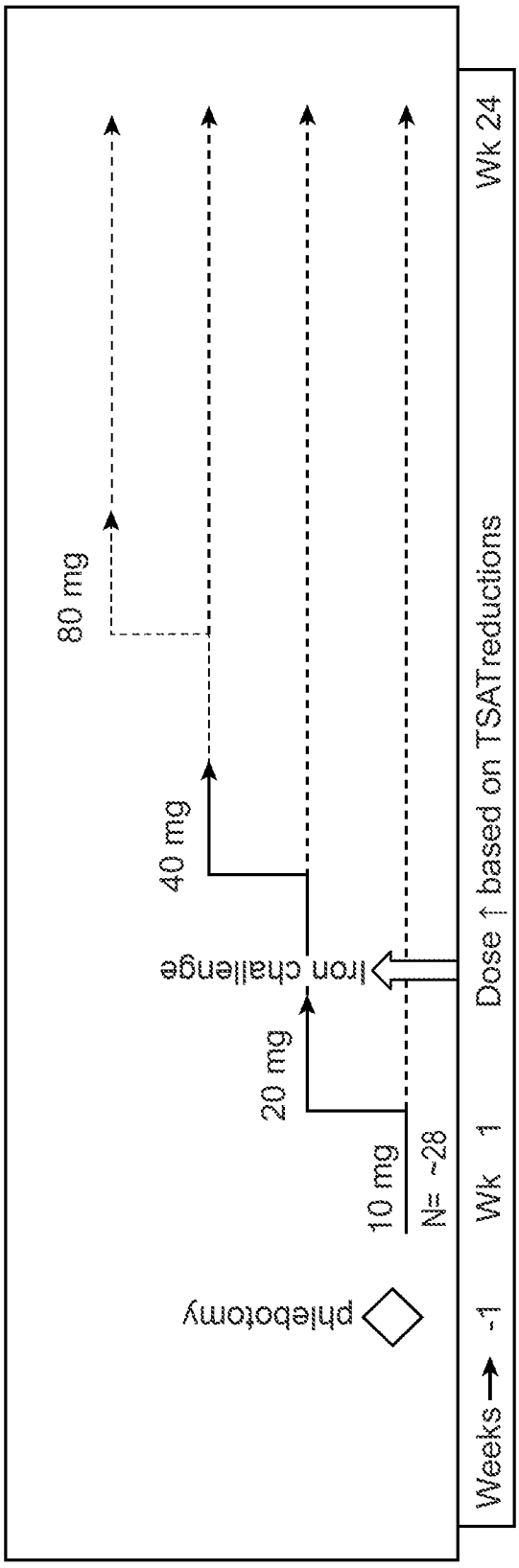

A.
Liver
Non-Heme Iron
(µg per total weight of tissue)
150
100
50
0
**
Vehicle
Compound 25
2.5 mg/kg
B.
Liver
Non-Heme Iron
(µg per total weight of tissue)
150
100
50
0
ns
***
Baseline
Vehicle
Compound 25
2.5 mg/kg

FIG. 2



- ~28 patient study
- Efficacy measures
  - Reduction in serum Iron, transferrin,ferritin
  - Phlebotomy reduction
  - TSAT
  - Liver iron content (LIC) by MRI
- Quality of Life (QOL) effects
  - SF-36
  - PGI-C

FIG. 3

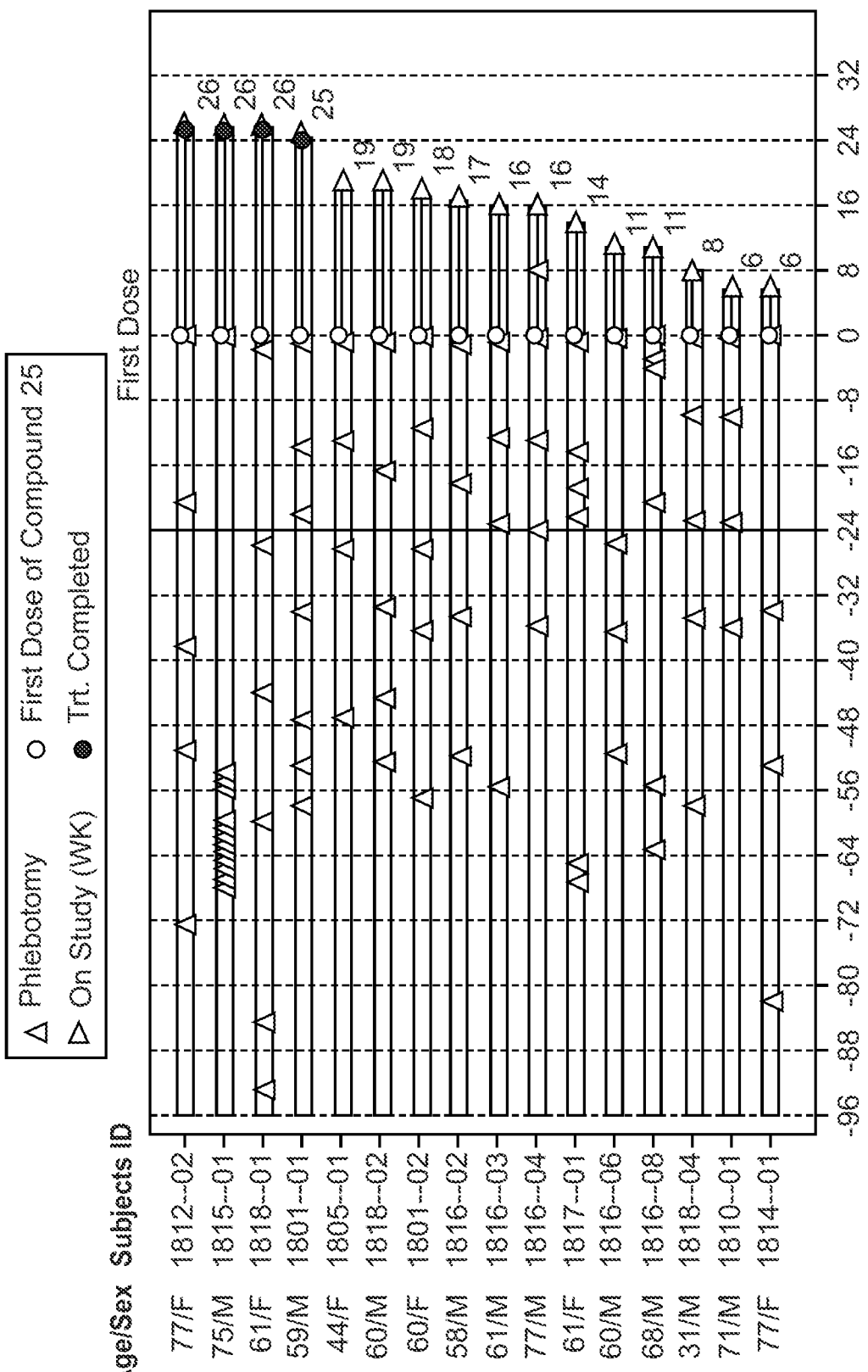

Phlebotomy
First Dose of Compound 25
On Study (WK)
Trt. Completed
Age/Sex
Subjects ID
77/F 1812--02
75/M 1815--01
61/F 1818--01
59/M 1801--01
44/F 1805--01
60/M 1818--02
60/F 1801--02
58/M 1816--02
61/M 1816--03
77/M 1816--04
61/F 1817--01
60/M 1816--06
68/M 1816--08
31/M 1818--04
71/M 1810--01
77/F 1814--01
First Dose
26
26
26
25
19
19
18
17
16
16
14
11
11
8
6
6
-96 -88 -80 -72 -64 -56 -48 -40 -32 -24 -16 -8 0 8 16 24 32
Weeks

FIG. 4A

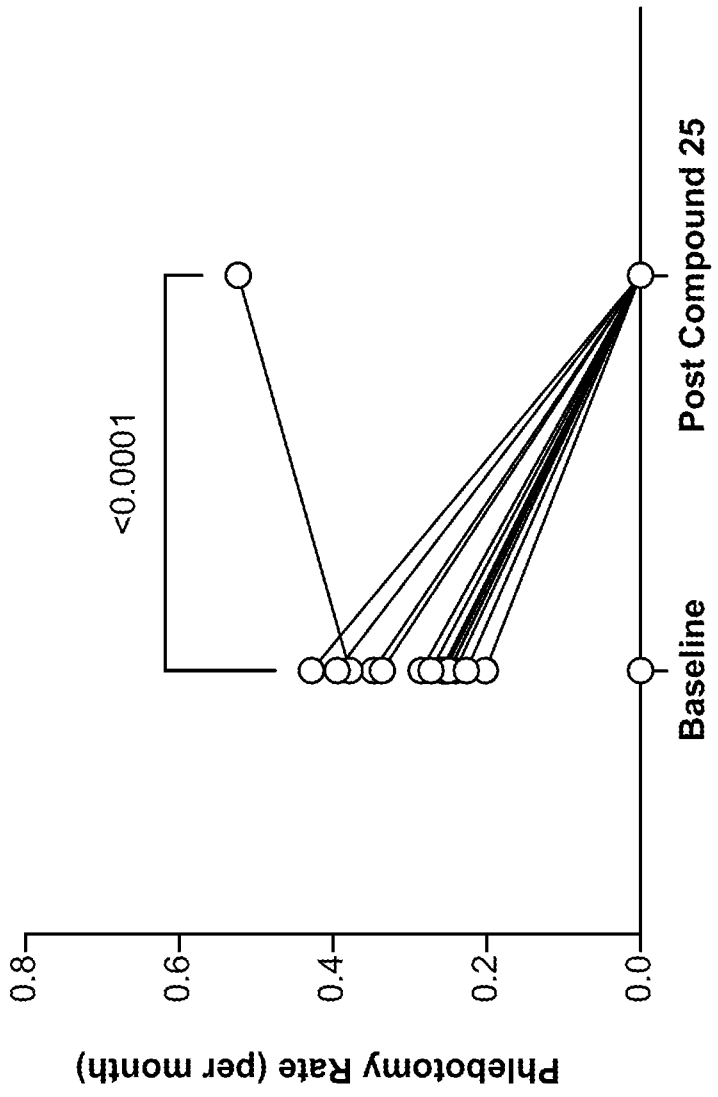

Phlebotomy Rate (per month)
0.0
0.2
0.4
0.6
0.8
Baseline
Post Compound 25
<0.0001

FIG. 4B

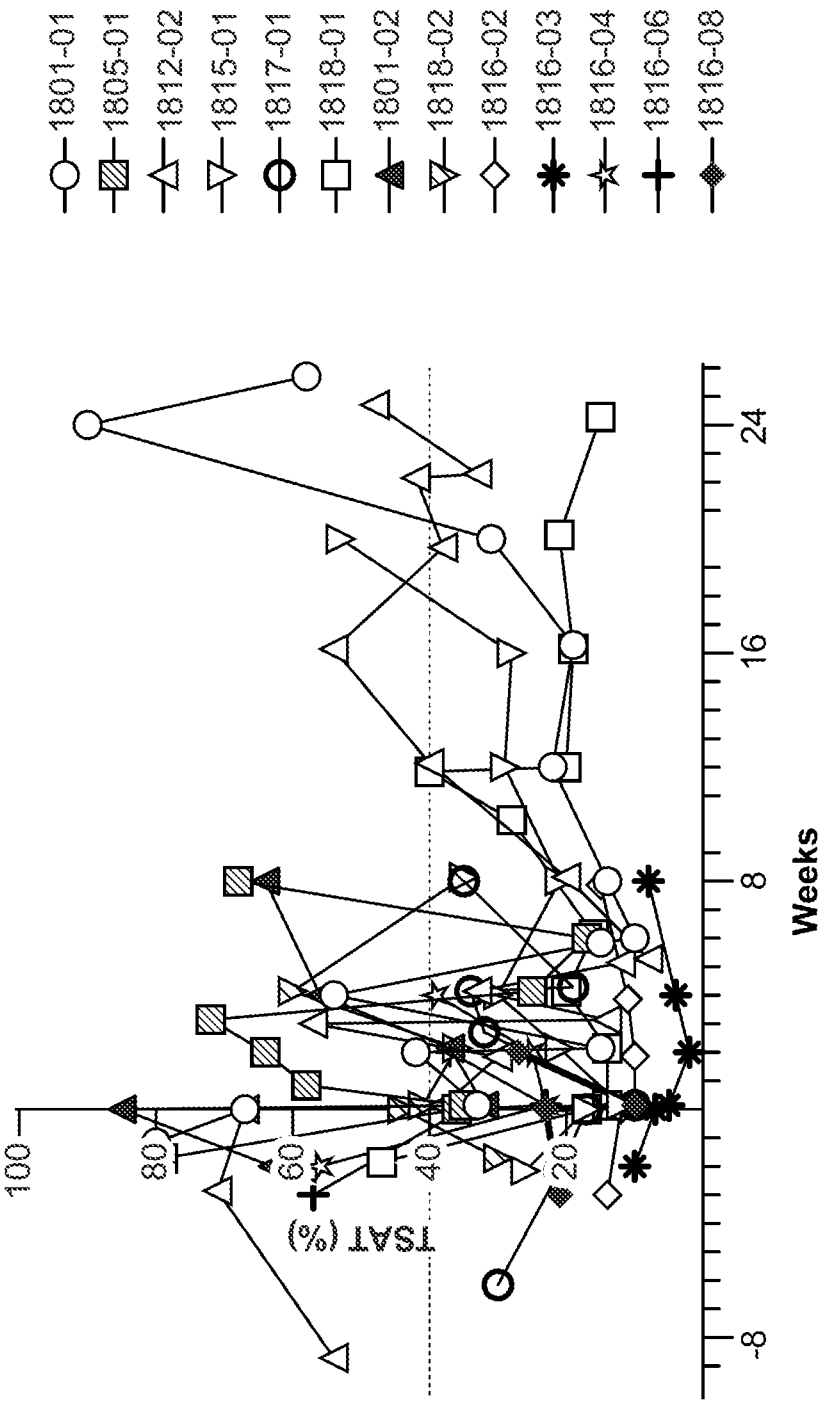
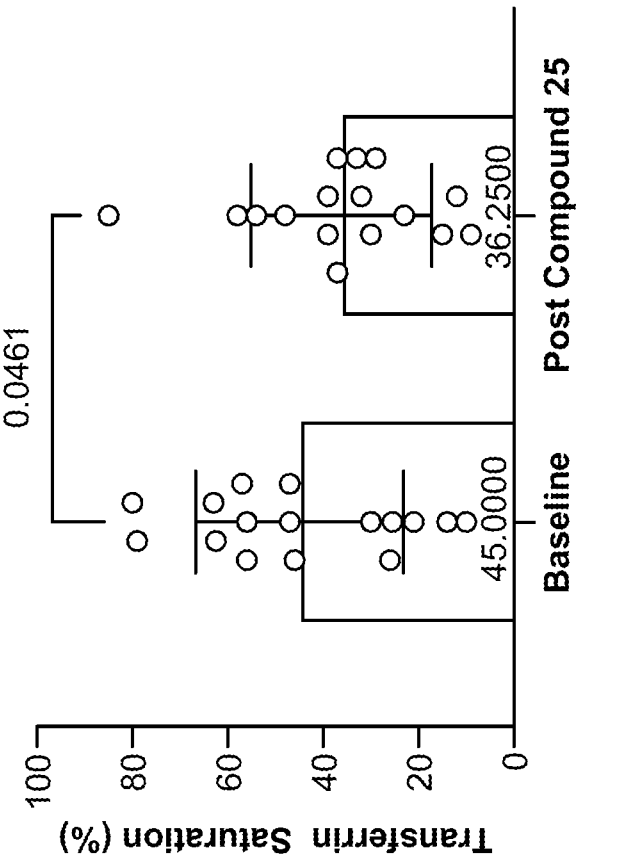

1801-01
1805-01
1812-02
1815-01
1817-01
1818-01
1801-02
1818-02
1816-02
1816-03
1816-04
1816-06
1816-08
TSAT (%)
100
80
60
40
20
-8
8
16
24
Weeks

FIG. 5A


Transferrin Saturation (%)
100
80
60
40
20
0
0.0461
45.0000
36.2500
Baseline
Post Compound 25

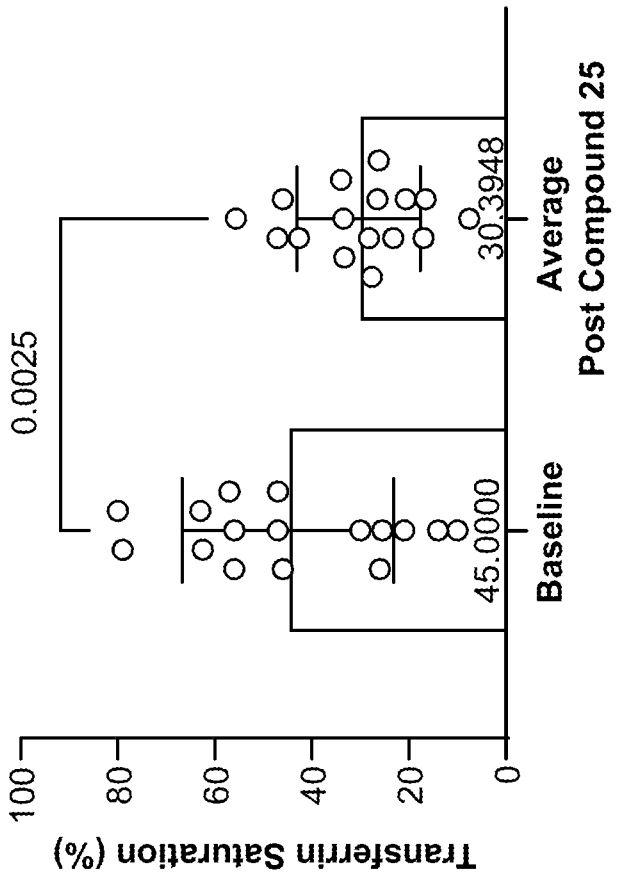

Transferrin Saturation (%)
100
80
60
40
20
0
0.0025
45.0000
30.3948
Baseline
Average
Post Compound 25

FIG. 5B

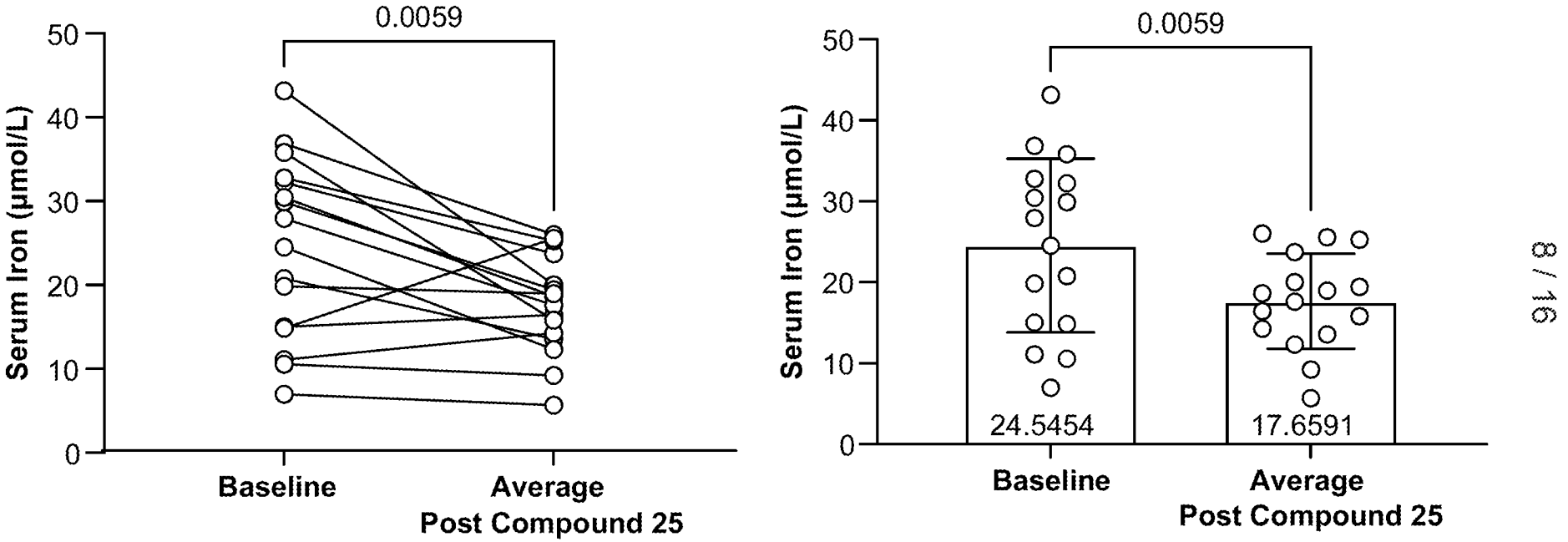

0.0059
50
40
30
20
10
0
Serum Iron (µmol/L)
Baseline
Average
Post Compound 25
0.0059
50
40
30
20
10
0
Serum Iron (µmol/L)
24.5454
17.6591
Baseline
Average
Post Compound 25

FIG. 6

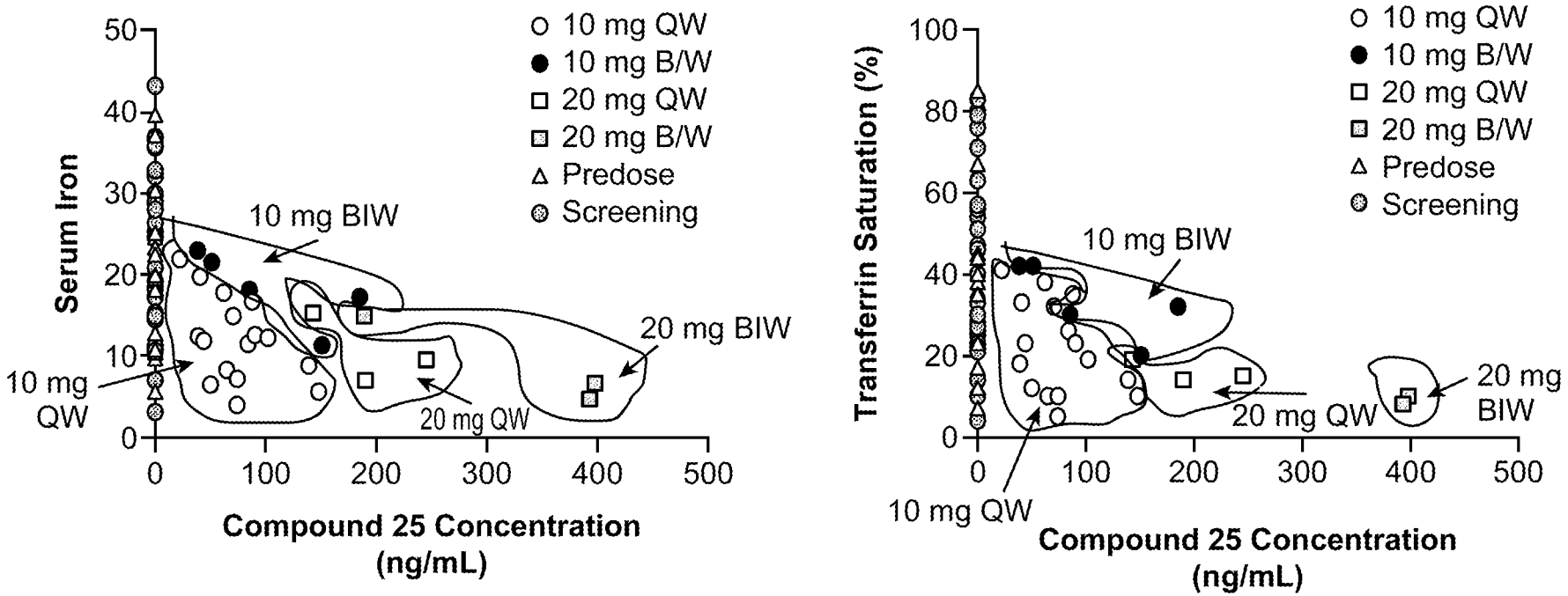

Serum Iron
50
40
30
20
10
0
0
100
200
300
400
500
Compound 25 Concentration (ng/mL)
10 mg QW
10 mg B/W
20 mg QW
20 mg B/W
Predose
Screening
10 mg BIW
20 mg BIW
10 mg QW
20 mg QW
Transferrin Saturation (%)
100
80
60
40
20
0
0
100
200
300
400
500
Compound 25 Concentration (ng/mL)
10 mg QW
10 mg B/W
20 mg QW
20 mg B/W
Predose
Screening
10 mg BIW
20 mg QW
20 mg BIW
10 mg QW

FIG. 7

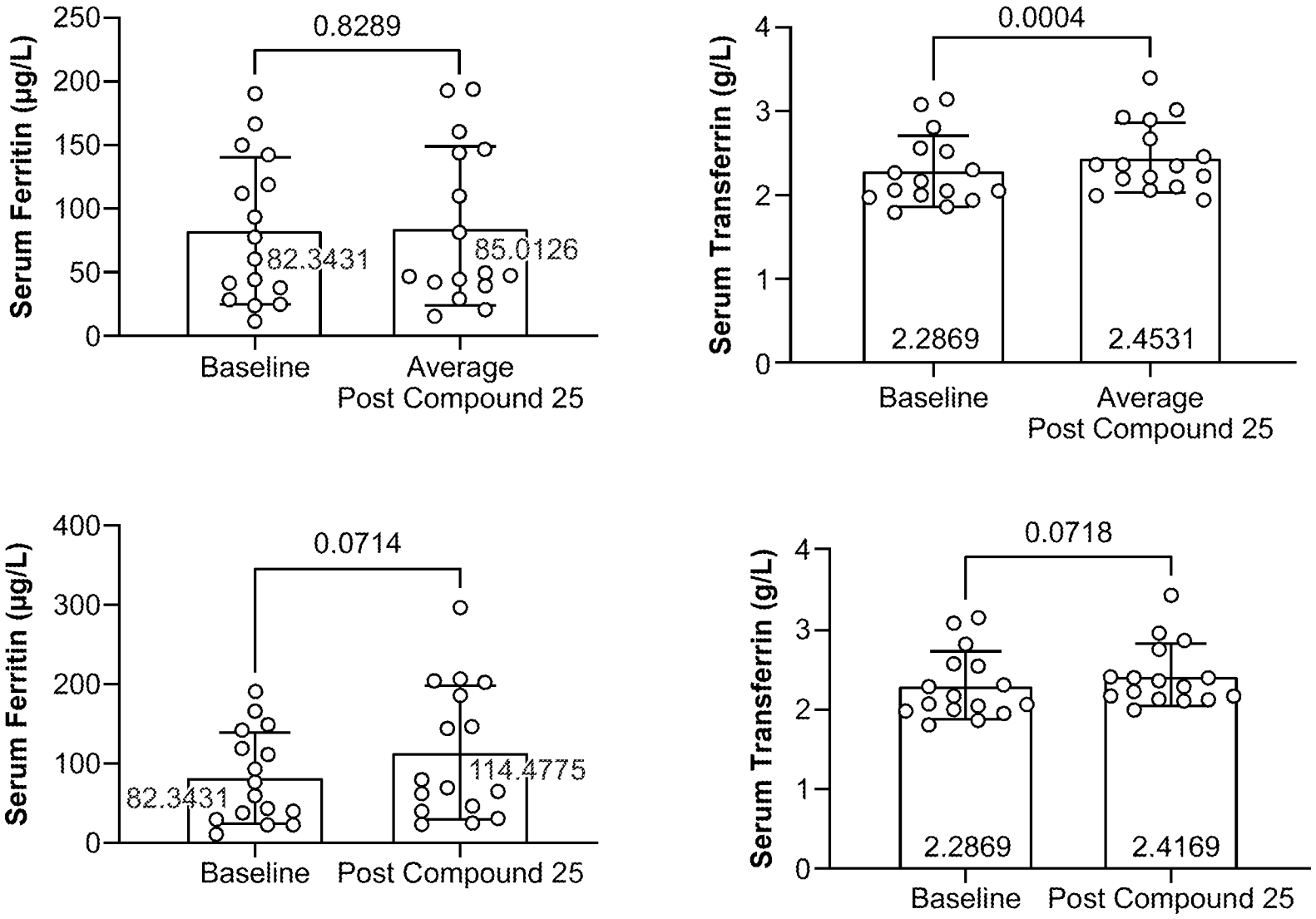

Serum Ferritin (µg/L)
250
200
150
100
50
0
0.8289
82.3431
85.0126
Baseline
Average
Post Compound 25
Serum Transferrin (g/L)
4
3
2
1
0
0.0004
2.2869
2.4531
Baseline
Average
Post Compound 25
Serum Ferritin (µg/L)
400
300
200
100
0
0.0714
82.3431
114.4775
Baseline
Post Compound 25
Serum Transferrin (g/L)
4
3
2
1
0
0.0718
2.2869
2.4169
Baseline
Post Compound 25

FIG. 8

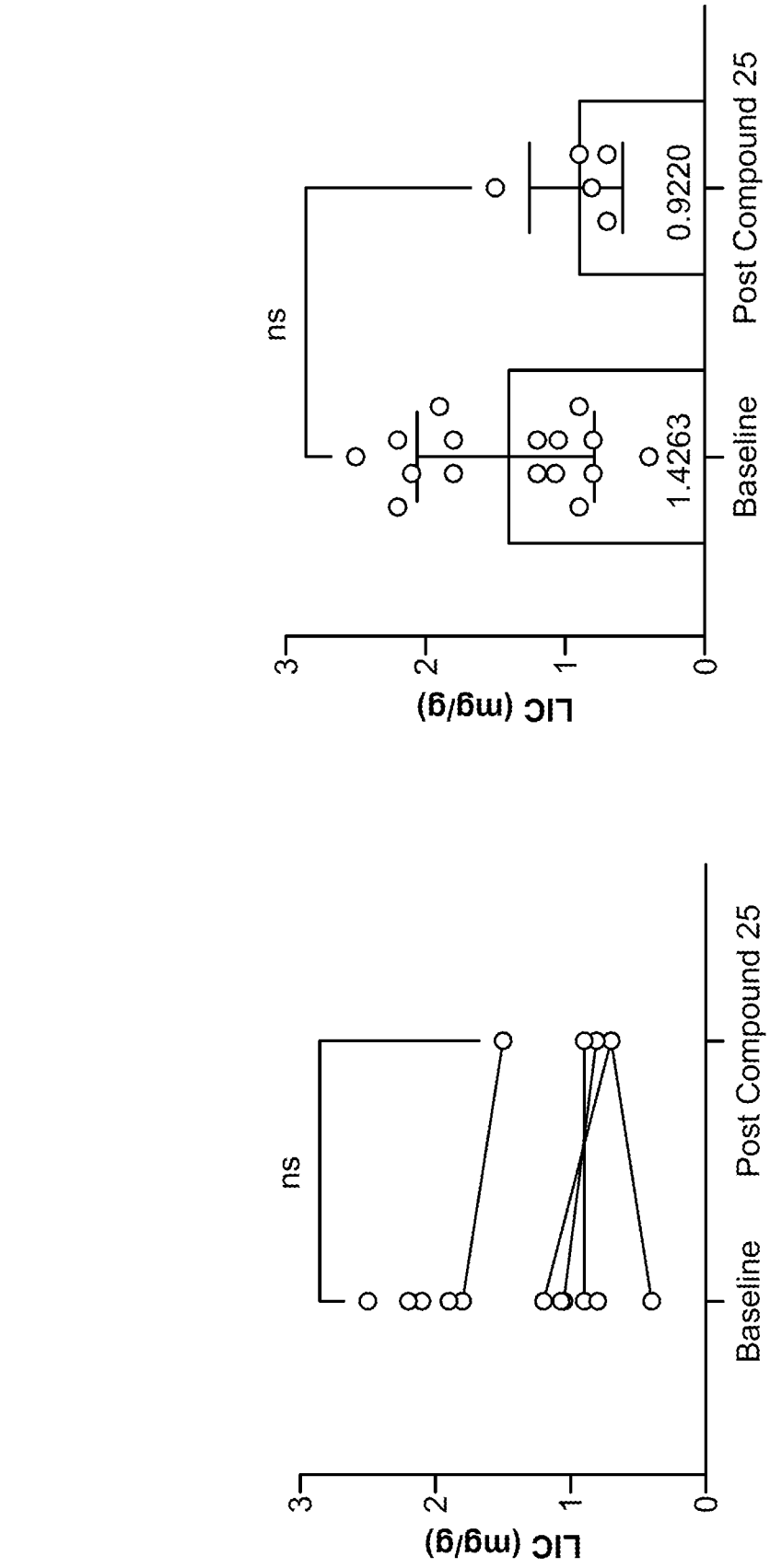
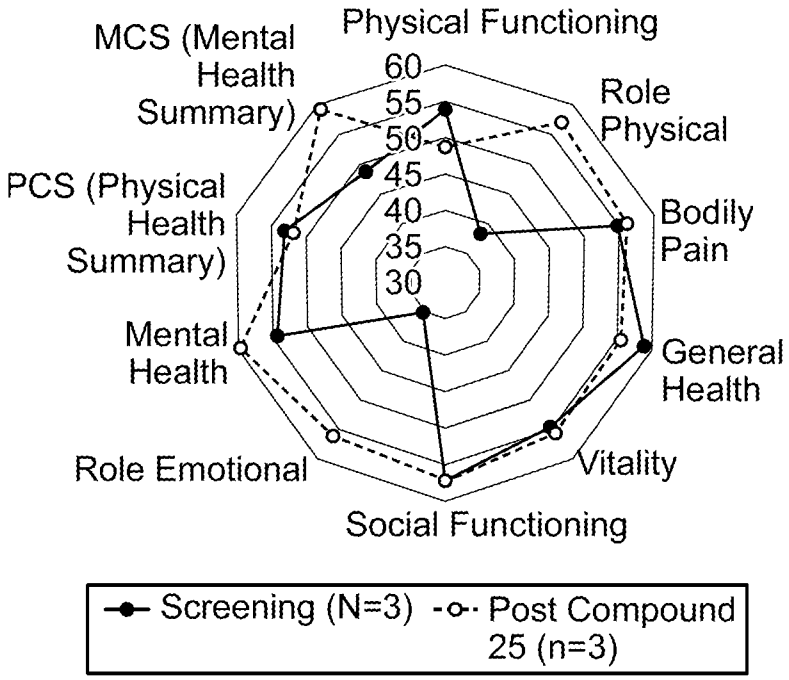
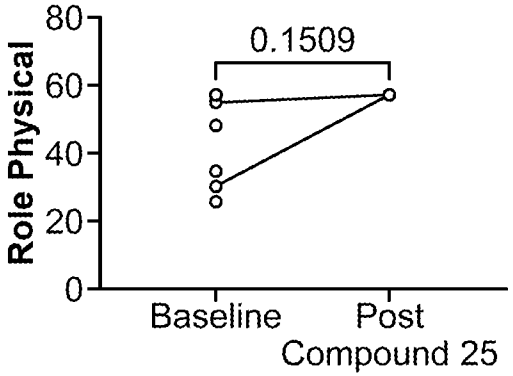
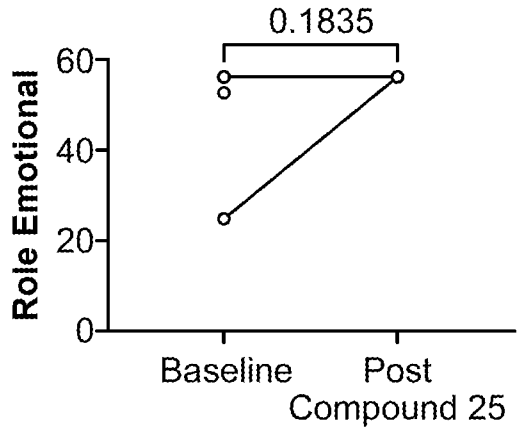

LIC (mg/g)
0
1
2
3
ns
1.4263
0.9220
Baseline
Post Compound 25
LIC (mg/g)
0
1
2
3
ns
Baseline
Post Compound 25

FIG. 9


Physical Functioning
Role Physical
Bodily Pain
General Health
Vitality
Social Functioning
Role Emotional
Mental Health
PCS (Physical Health Summary)
MCS (Mental Health Summary)
60
55
50
45
40
35
30
Screening (N=3)
Post Compound 25 (n=3)


Role Physical
80
60
40
20
0
0.1509
Baseline
Post Compound 25


Role Emotional
60
40
20
0
0.1835
Baseline
Post Compound 25

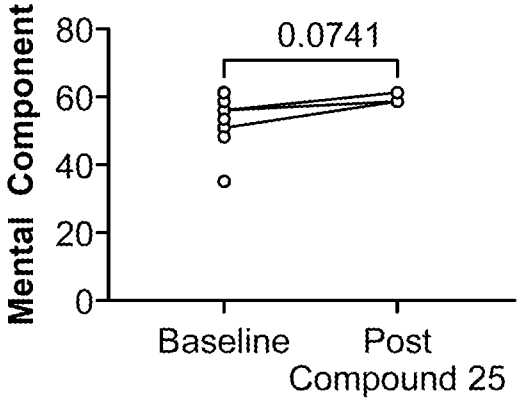

Mental Component
80
60
40
20
0
0.0741
Baseline
Post Compound 25

FIG. 10

	Compound 25 Dosing Regimens Administered				
Subject	10 mg once per week	10 mg twice per week	20 mg once per week	20 twice per week	40 mg once week
1801-01	✓		✓	✓	
1801-02	✓	✓			
1805-01	✓	✓	✓	✓	✓
1810-01	✓				
1812-02	✓	✓	✓	✓	
1814-01	✓				
1815-01	✓	✓			
1816-02	✓				
1816-03	✓				
1816-04	✓	✓			
1816-06	✓	✓			
1816-08	✓				
1817-01	✓		✓		
1818-01	✓	✓			
1818-02	✓				
1818-04	✓				

FIG. 11

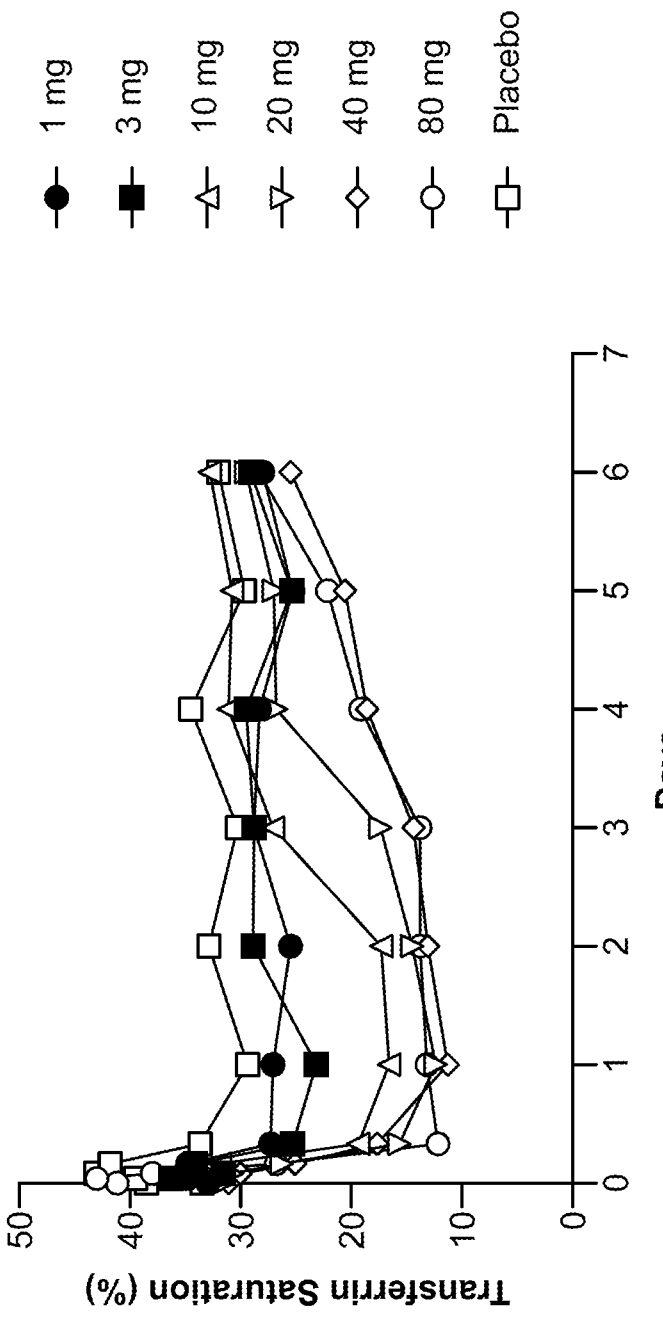

1 mg
3 mg
10 mg
20 mg
40 mg
80 mg
Placebo
Transferrin Saturation (%)
50
40
30
20
10
0
0
1
2
3
4
5
6
7
Days

FIG. 12

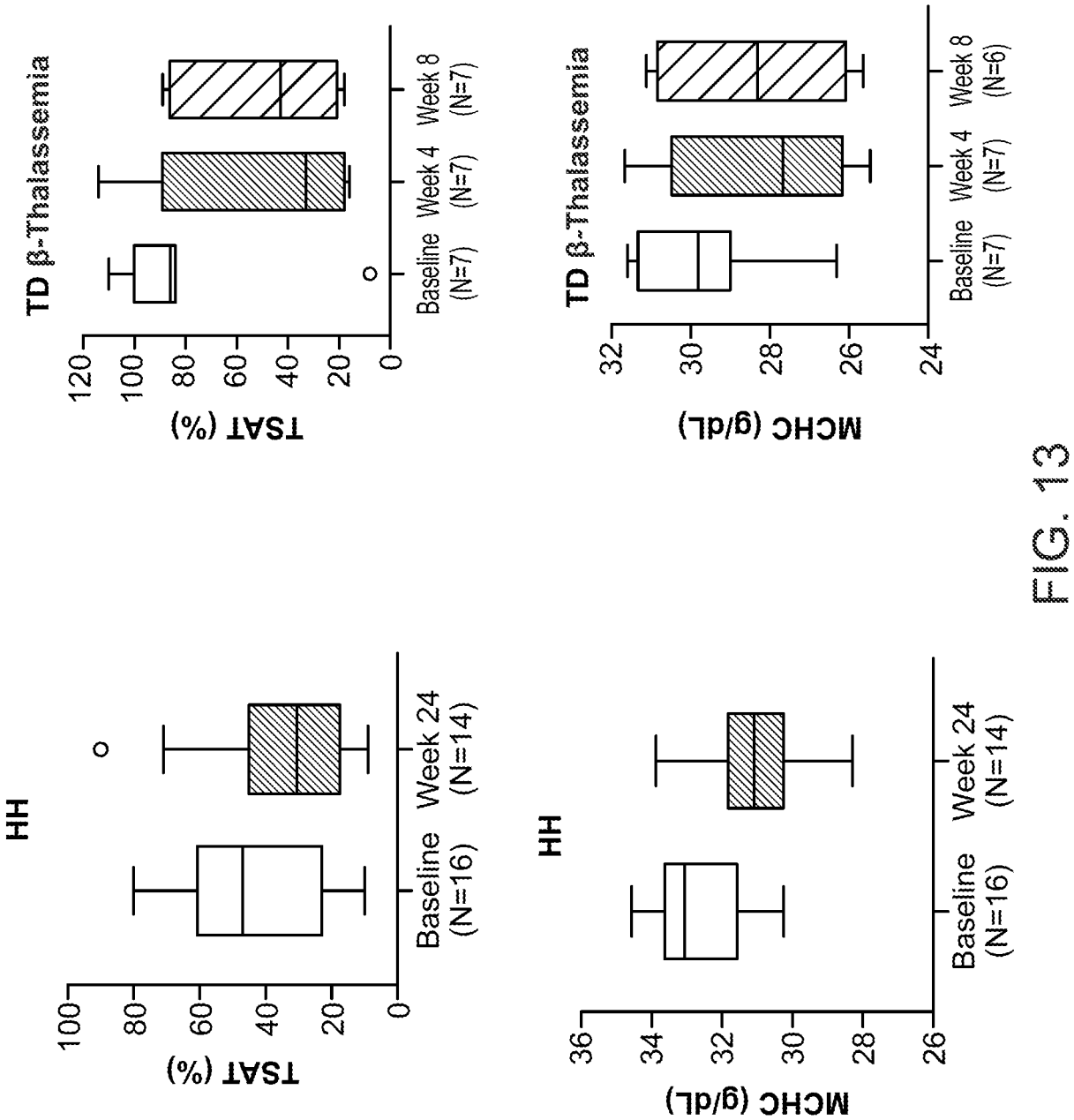

TD β-Thalassemia
TSAT (%)
120
100
80
60
40
20
0
Baseline (N=7)
Week 4 (N=7)
Week 8 (N=7)
TD β-Thalassemia
MCHC (g/dL)
32
30
28
26
24
Baseline (N=7)
Week 4 (N=7)
Week 8 (N=6)
HH
TSAT (%)
100
80
60
40
20
0
Baseline (N=16)
Week 24 (N=14)
HH
MCHC (g/dL)
36
34
32
30
28
26
Baseline (N=16)
Week 24 (N=14)

FIG. 13

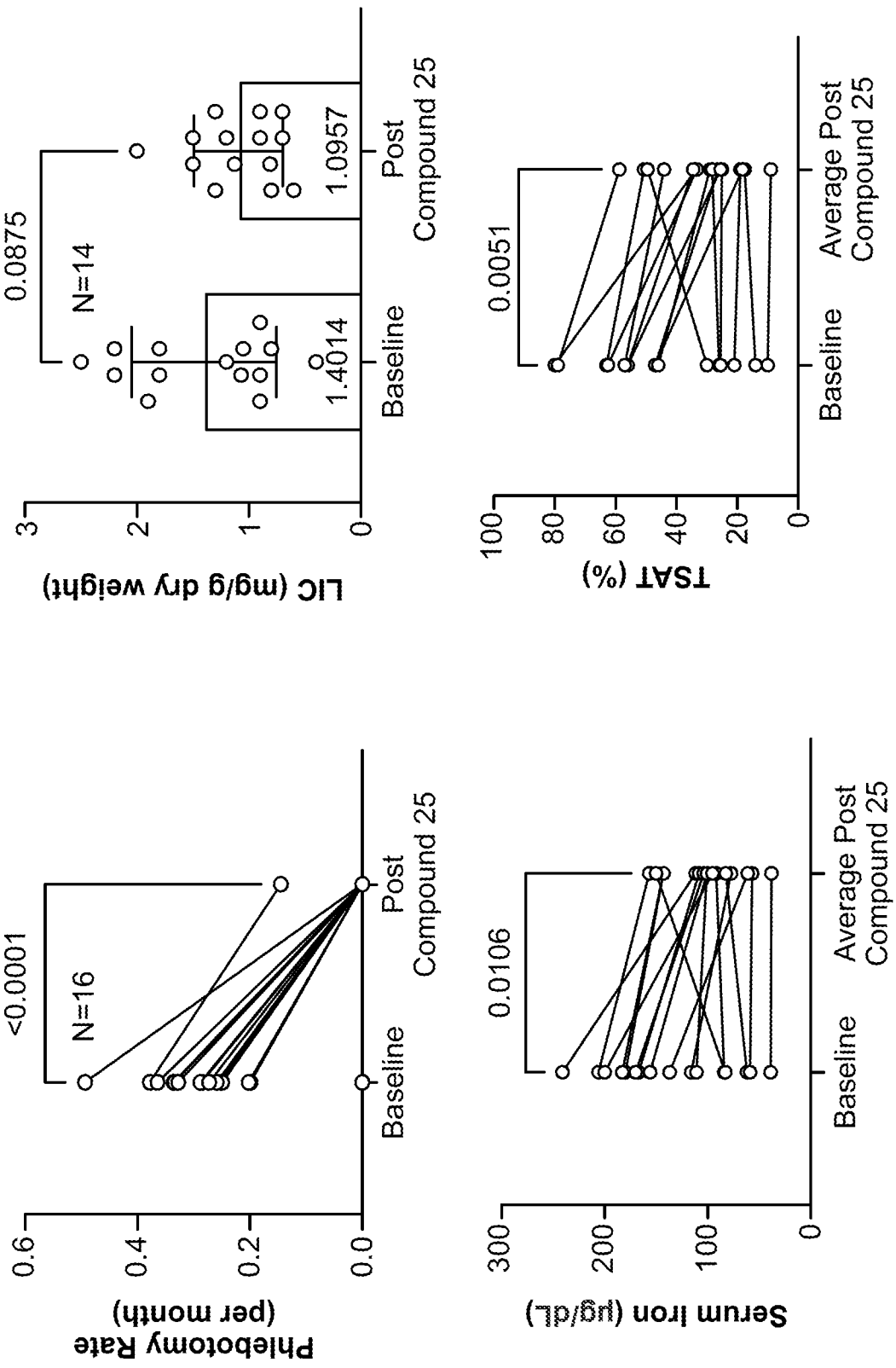

Phlebotomy Rate (per month)
<0.0001
N=16
0.6
0.4
0.2
0.0
Baseline
Post Compound 25
LIC (mg/g dry weight)
0.0875
N=14
1.4014
1.0957
3
2
1
0
Baseline
Post Compound 25
TSAT (%)
0.0051
100
80
60
40
20
0
Baseline
Average Post Compound 25
Serum Iron (µg/dL)
0.0106
300
200
100
0
Baseline
Average Post Compound 25

FIG. 14