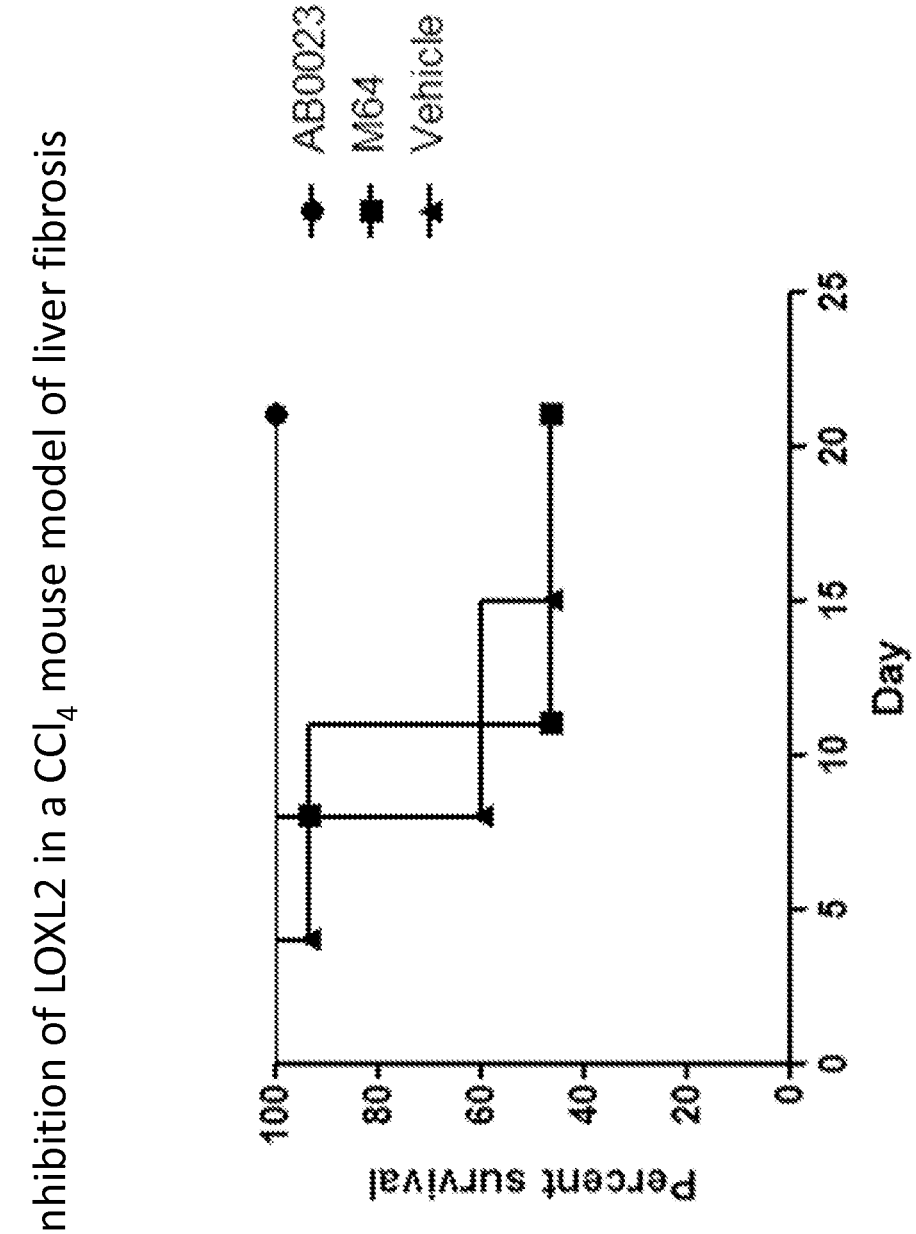

Inhibition of LOXL2 in a CCl_4 mouse model of liver fibrosis
AB0023
M64
Vehicle
Percent survival
100
80
60
40
20
0
0
5
10
15
20
25
Day

FIG. 1

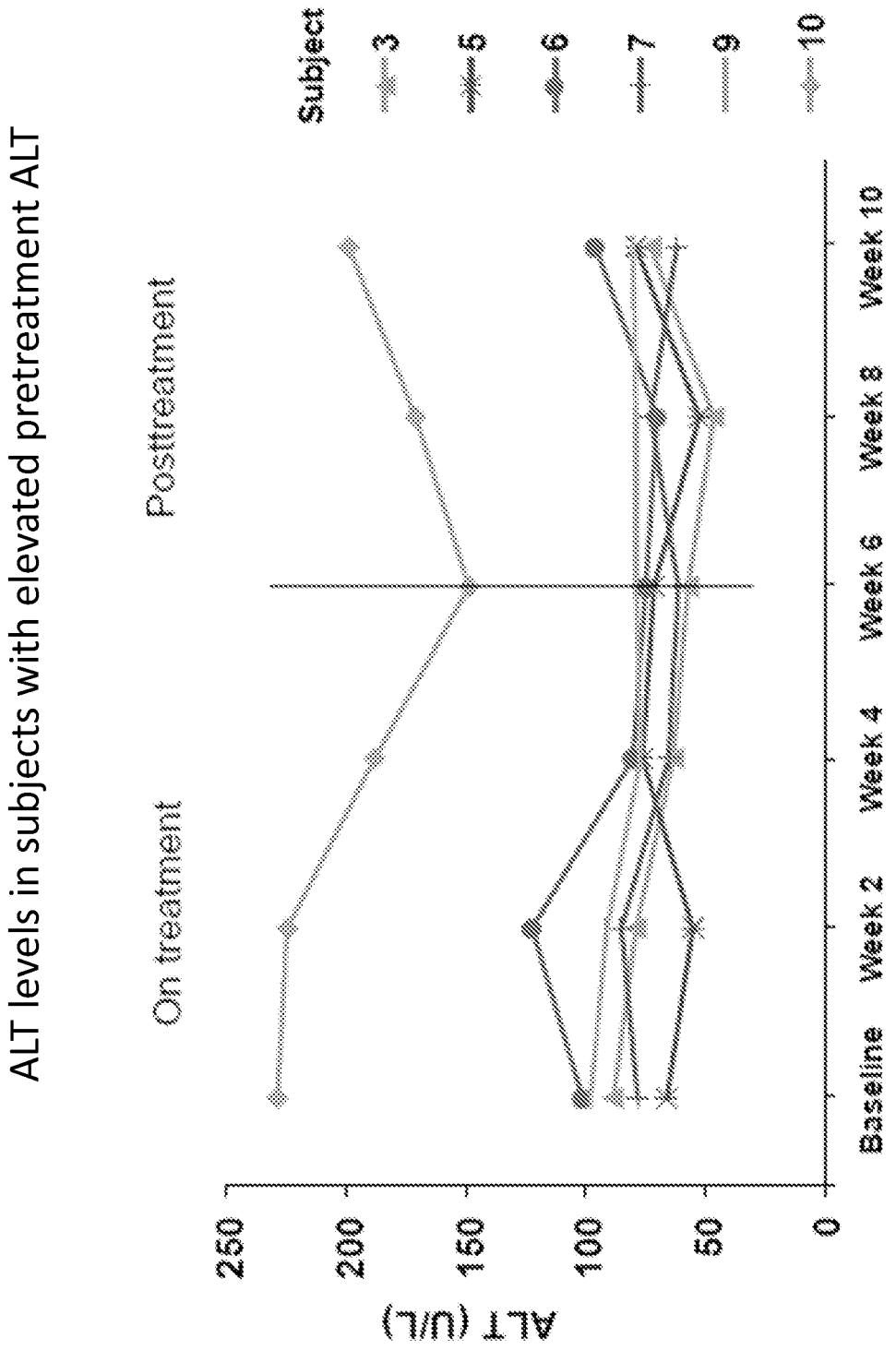

ALT levels in subjects with elevated pretreatment ALT
On treatment
Posttreatment
Subject
3
5
6
7
9
10
ALT (U/L)
250
200
150
100
50
0
Baseline
Week 2
Week 4
Week 6
Week 8
Week 10

FIG. 2

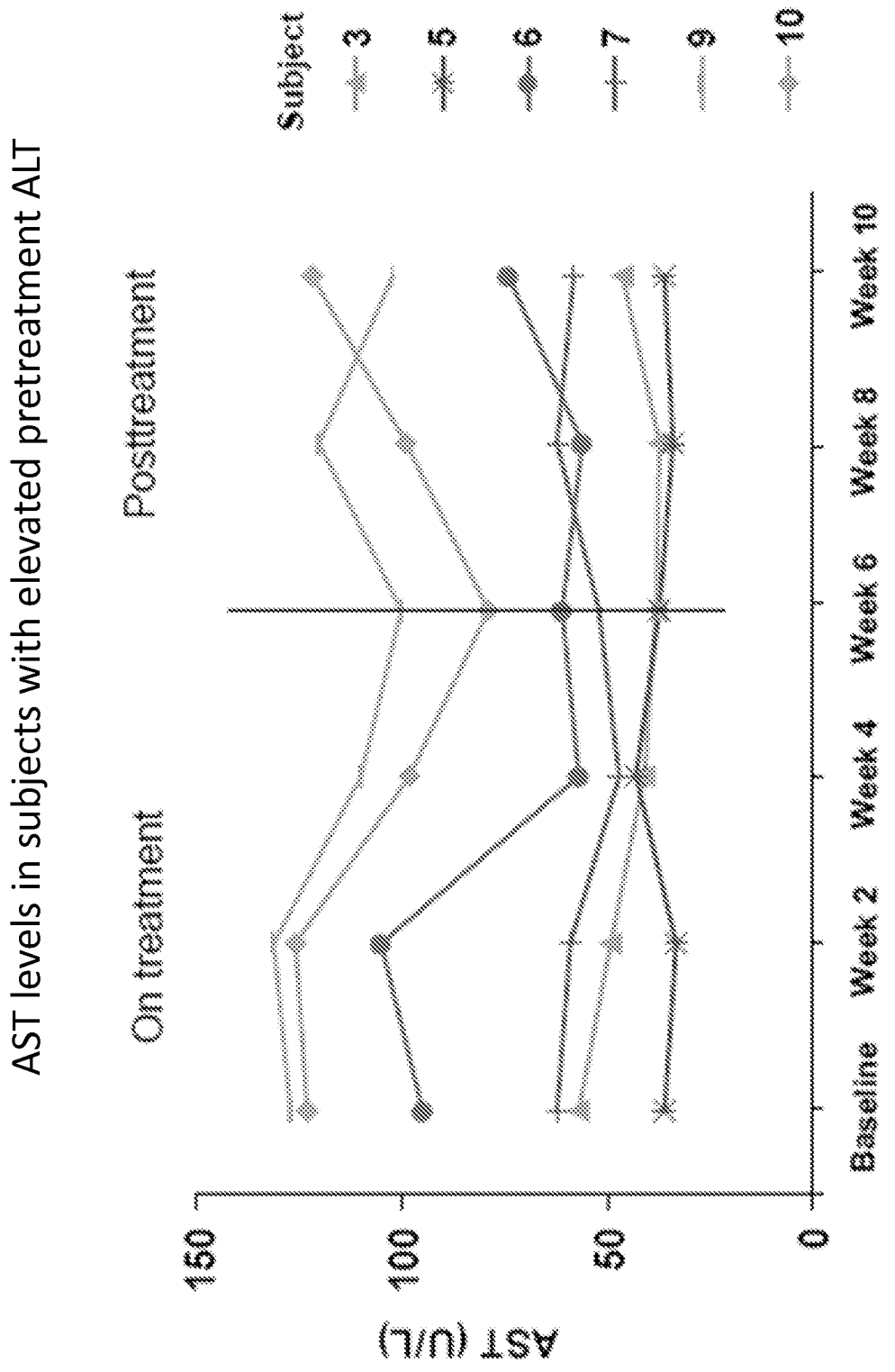

AST levels in subjects with elevated pretreatment ALT
On treatment
Posttreatment
Subject
3
5
6
7
9
10
AST (U/L)
150
100
50
0
Baseline
Week 2
Week 4
Week 6
Week 8
Week 10

FIG. 3

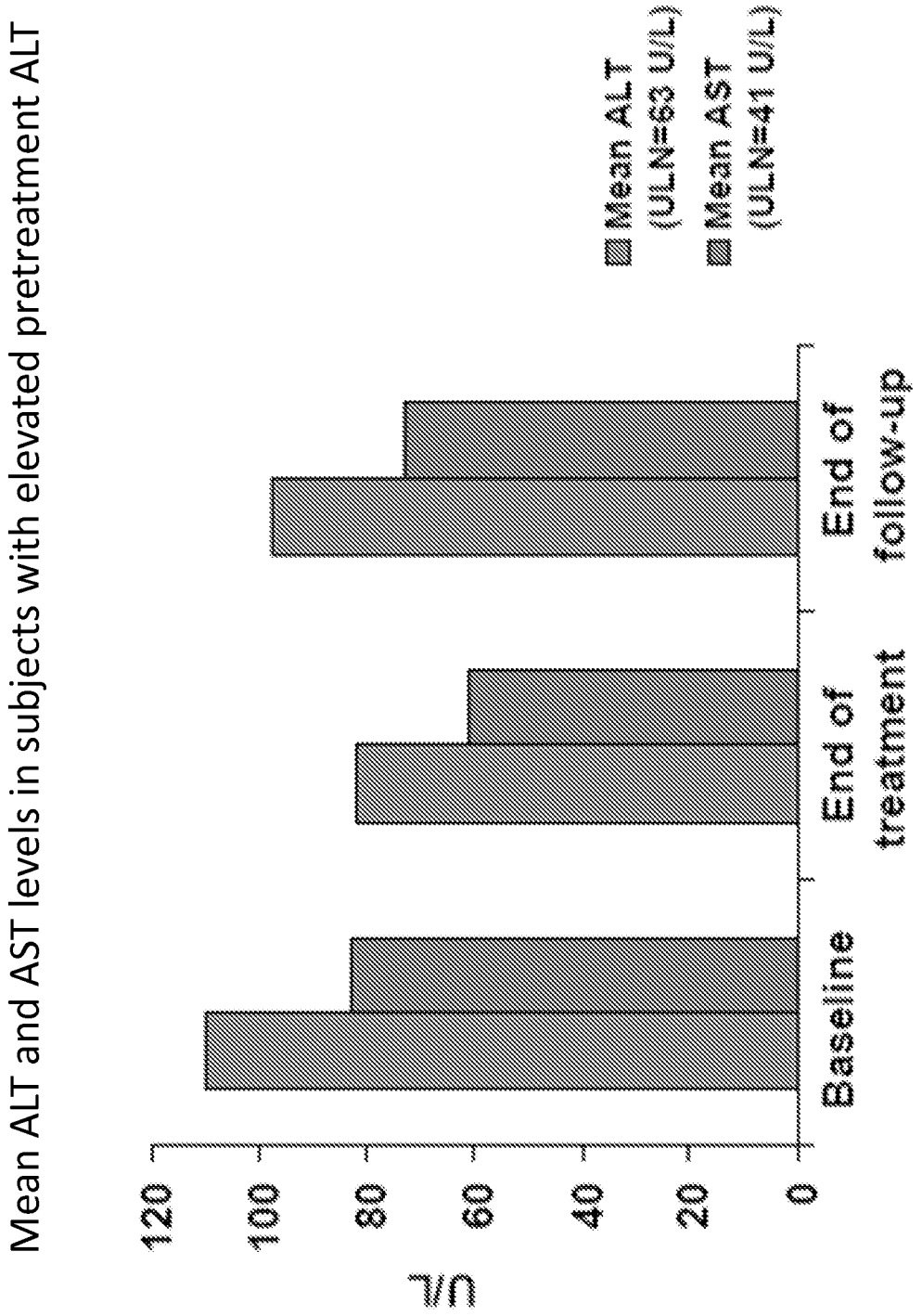

Mean ALT and AST levels in subjects with elevated pretreatment ALT
U/L
120
100
80
60
40
20
0
Baseline
End of treatment
End of follow-up
Mean ALT (ULN=63 U/L)
Mean AST (ULN=41 U/L)

FIG. 4

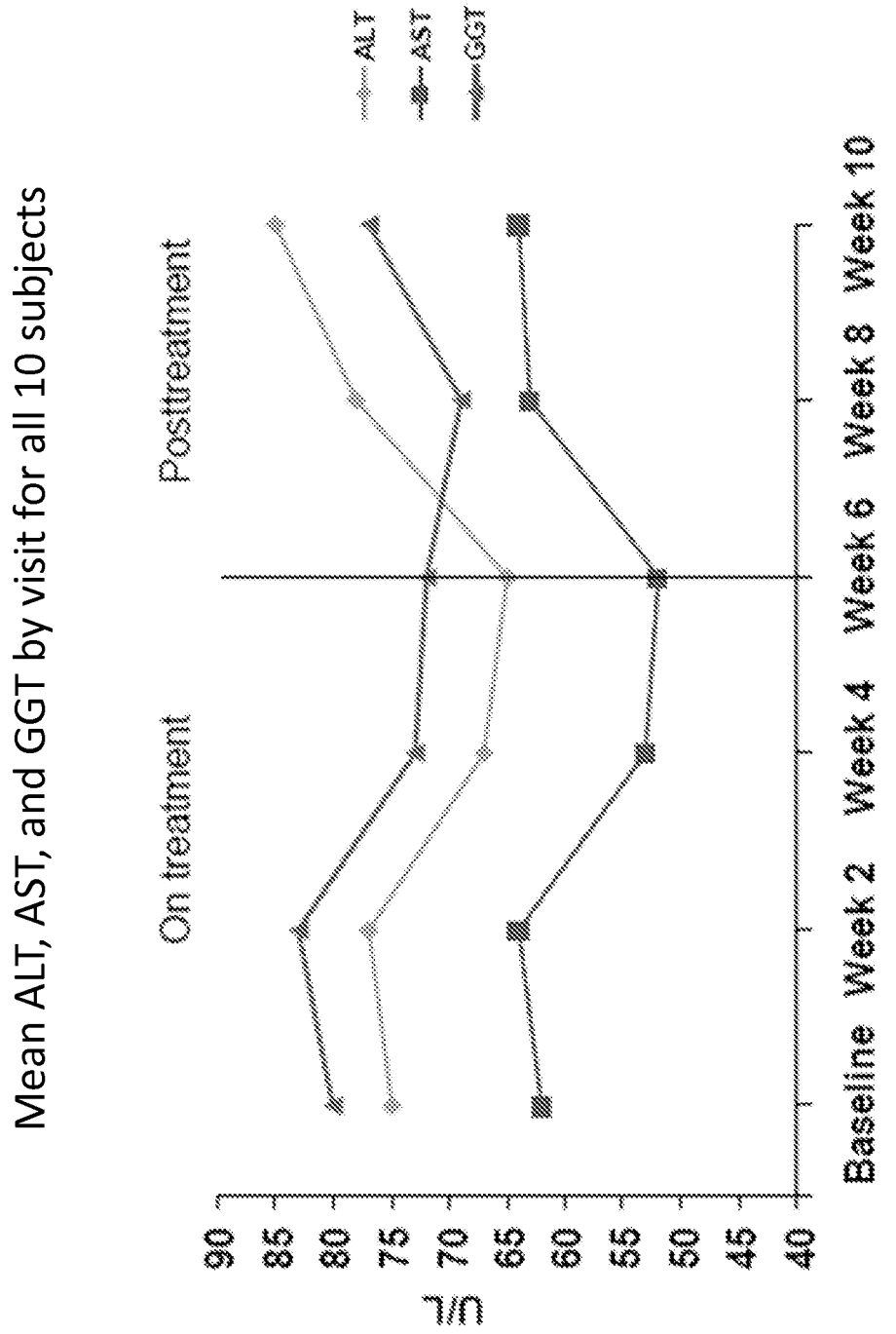

Mean ALT, AST, and GGT by visit for all 10 subjects
On treatment
Posttreatment
ALT
AST
GGT
U/L
90
85
80
75
70
65
60
55
50
45
40
Baseline
Week 2
Week 4
Week 6
Week 8
Week 10

FIG. 5

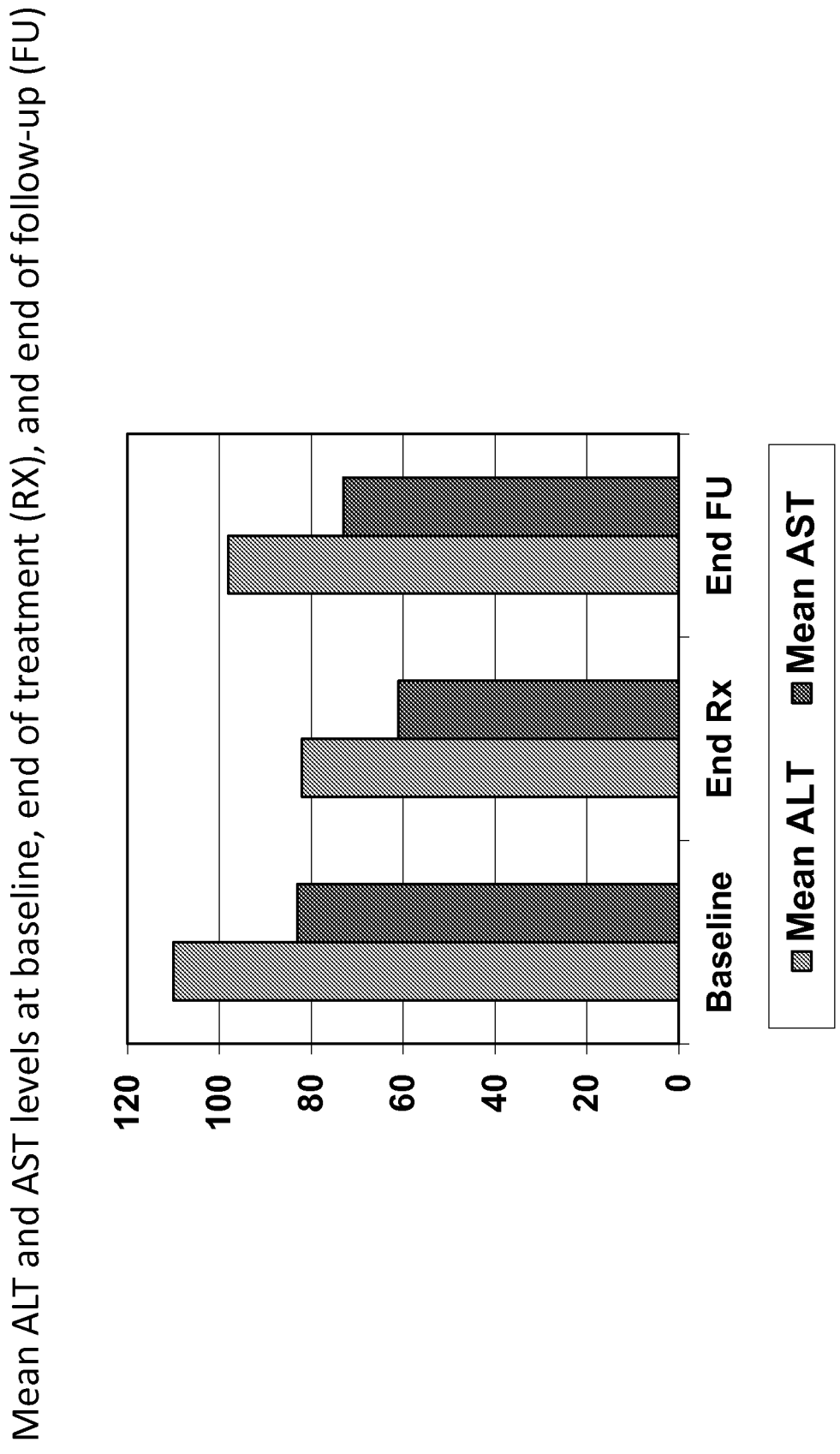

Mean ALT and AST levels at baseline, end of treatment (RX), and end of follow-up (FU)
120
100
80
60
40
20
0
Baseline
End Rx
End FU
Mean ALT
Mean AST

FIG. 6

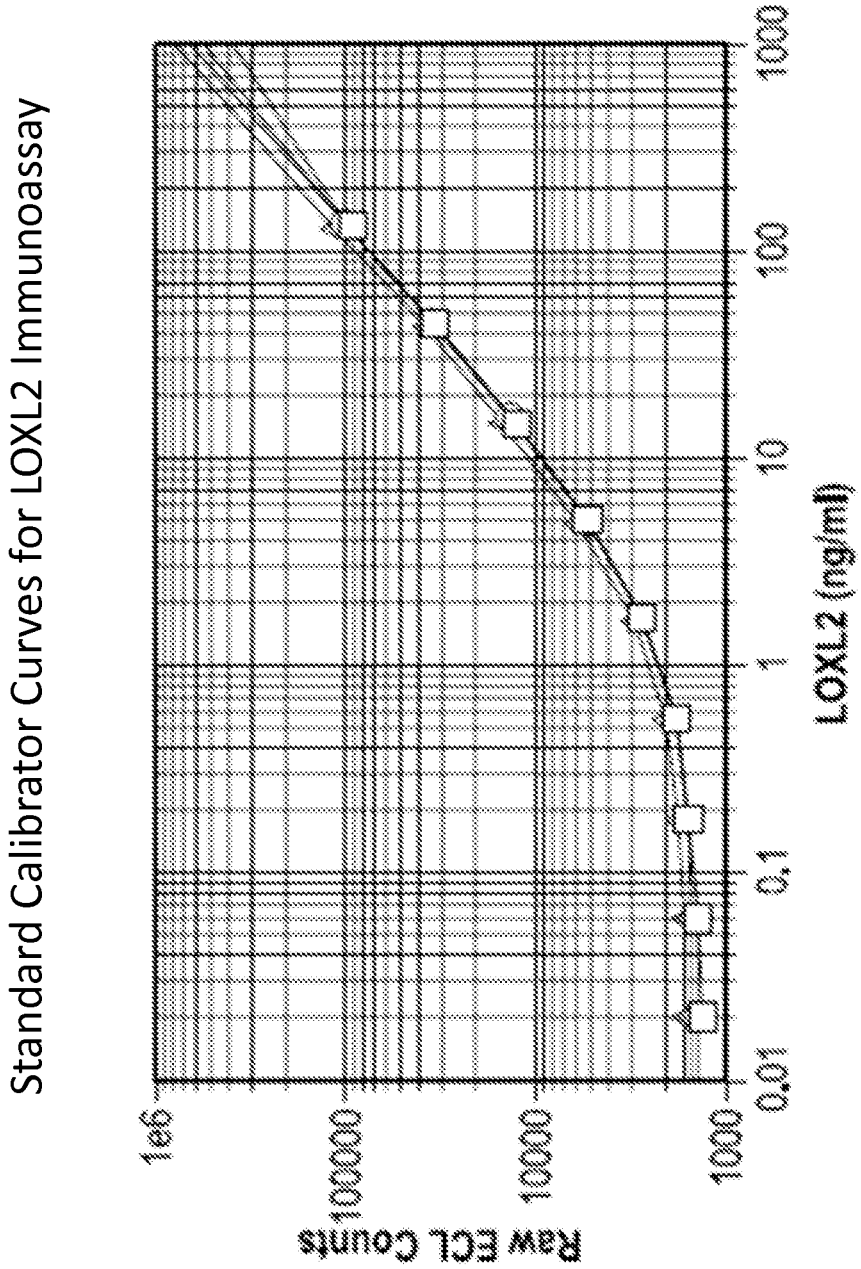

Standard Calibrator Curves for LOXL2 Immunoassay
Raw ECL Counts
1e6
100000
10000
1000
LOXL2 (ng/ml)
0,01
0,1
1
10
100
1000

FIG. 7

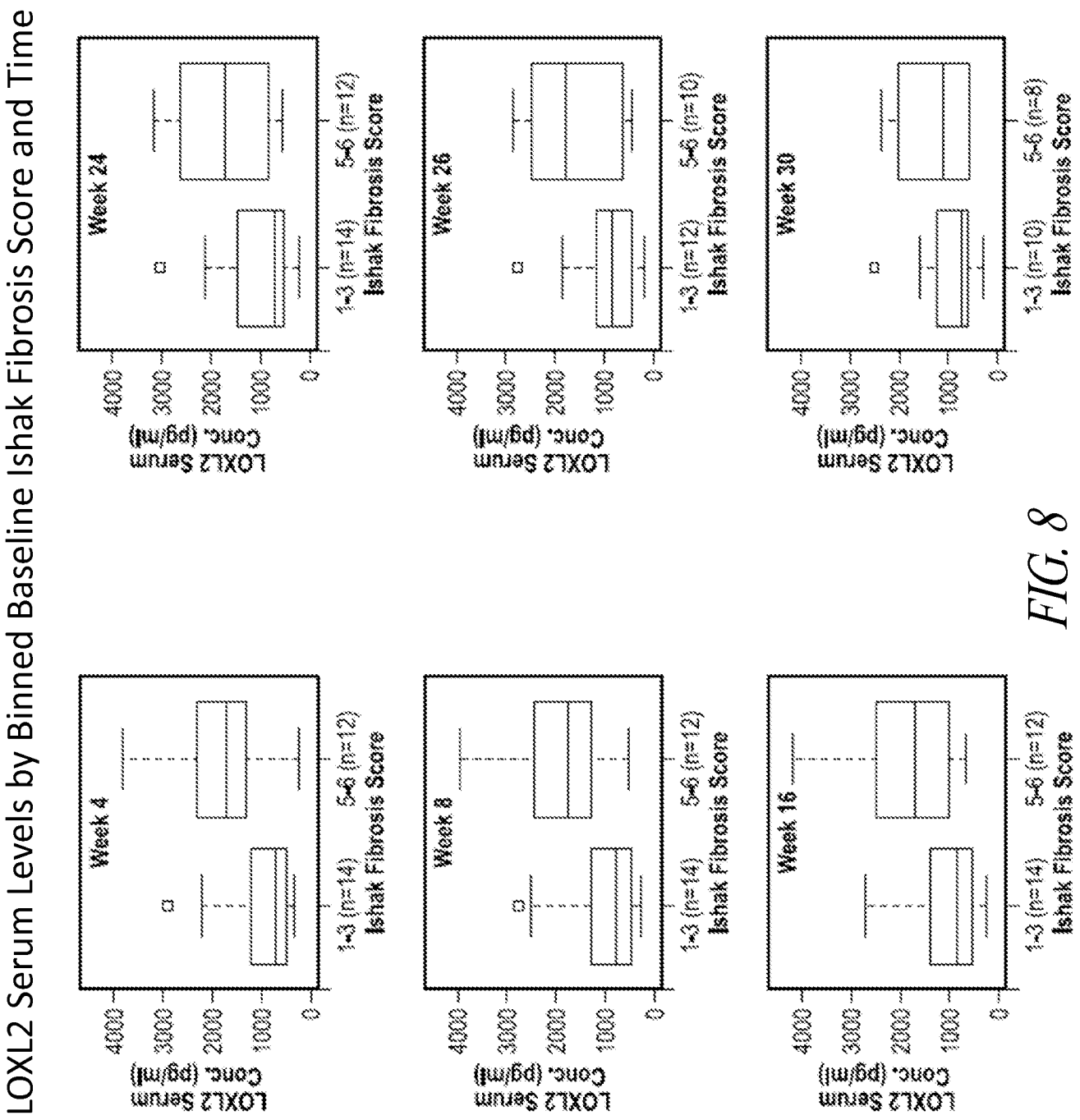

LOXL2 Serum Levels by Binned Baseline Ishak Fibrosis Score and Time
Week 4
Week 8
Week 16
Week 24
Week 26
Week 30
LOXL2 Serum Conc. (pg/ml)
4000
3000
2000
1000
0
1-3 (n=14)
5-6 (n=12)
Ishak Fibrosis Score

FIG. 8

Correlation between baseline LOXL2 levels and baseline measures of IPF Severity and functional status

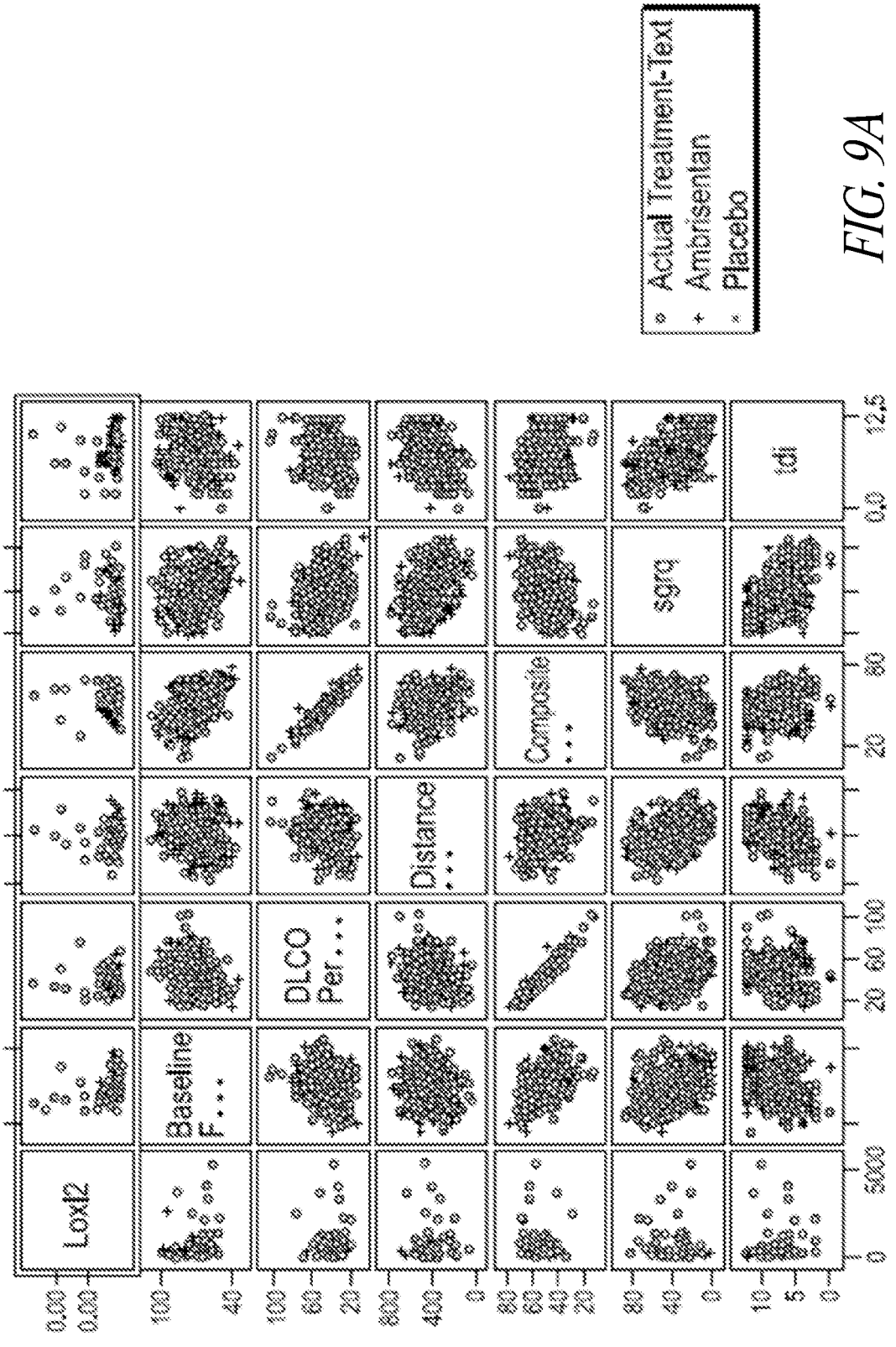


FIG. 9A

Correlation between baseline LOXL2 levels and baseline measures of IPF Severity and functional status

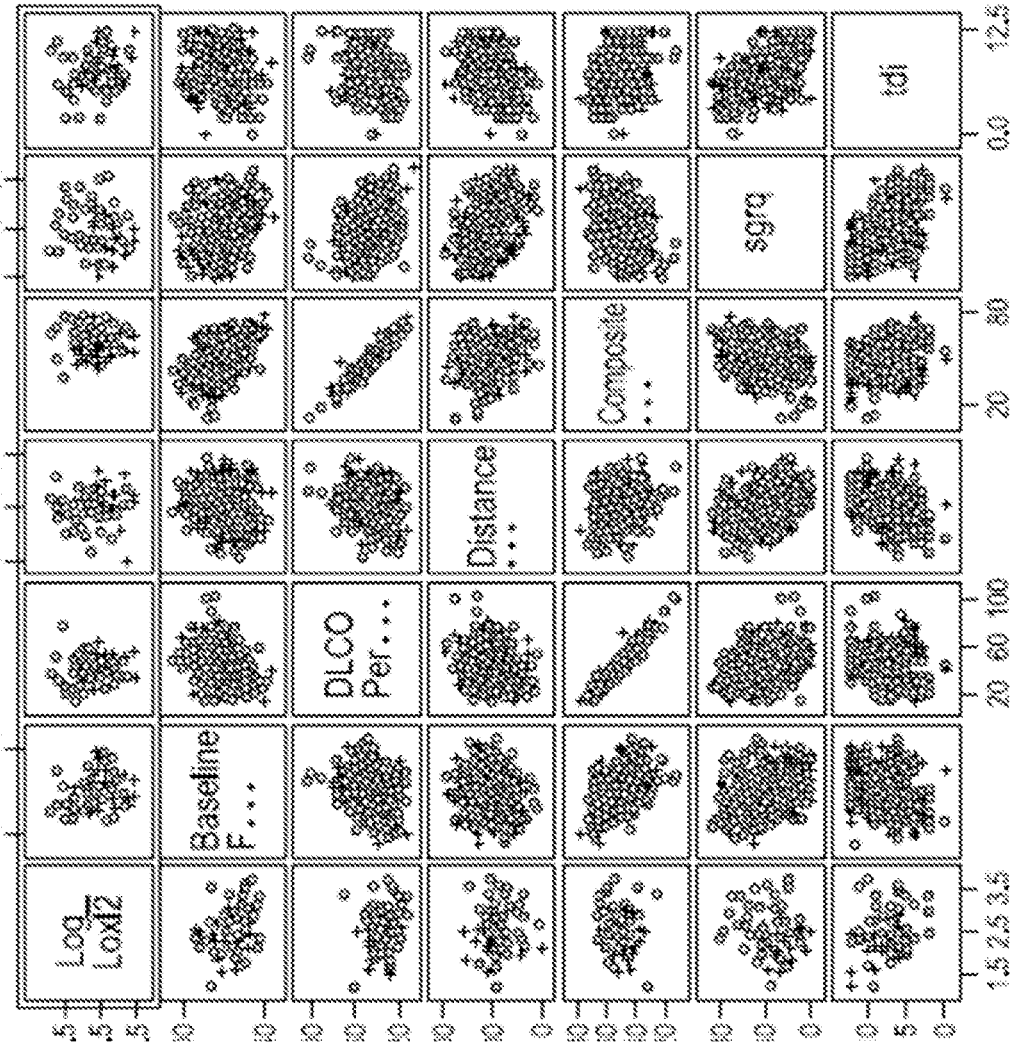


FIG. 9B

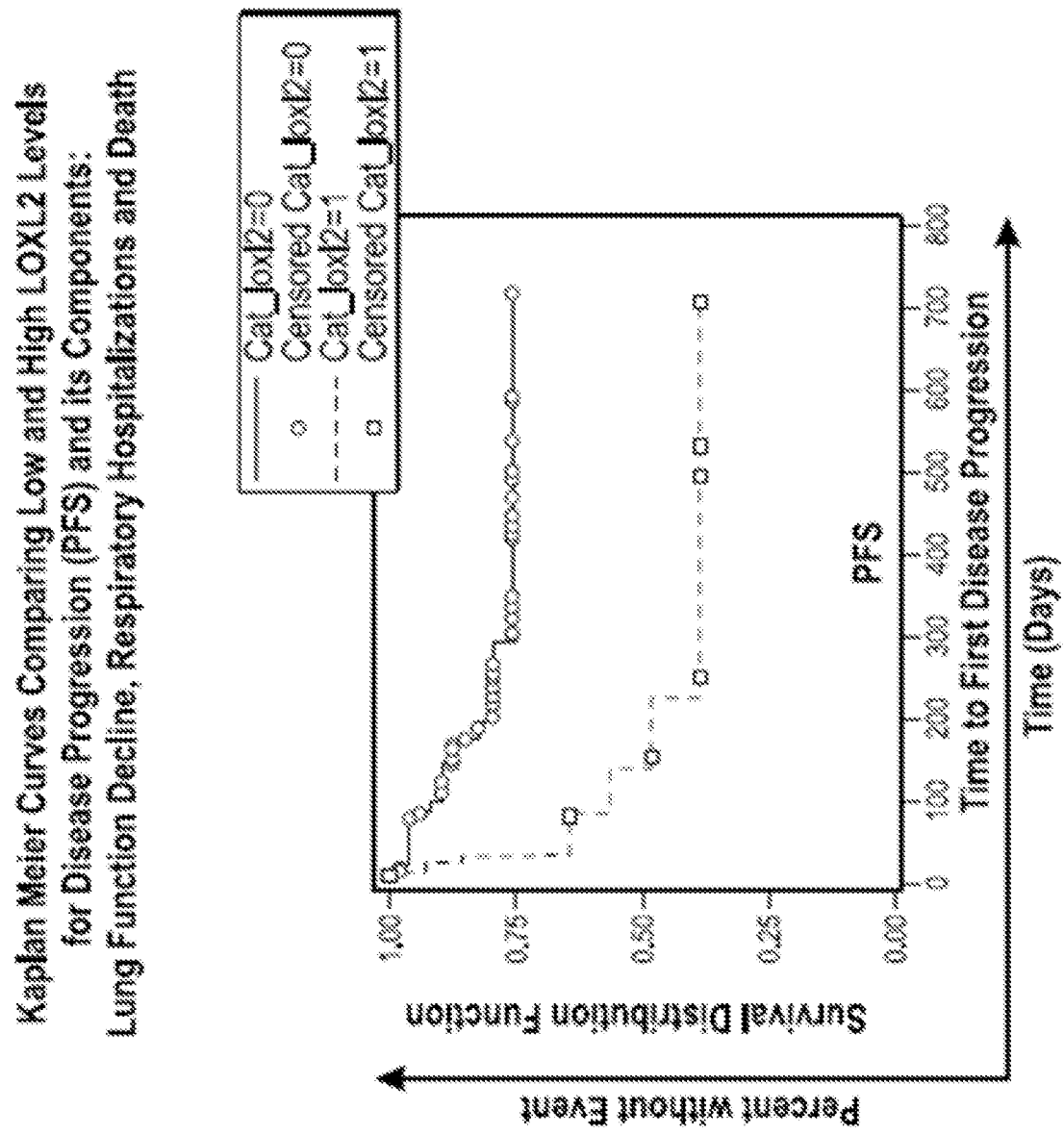

Kaplan Meier Curves Comparing Low and High LOXL2 Levels
for Disease Progression (PFS) and its Components:
Lung Function Decline, Respiratory Hospitalizations and Death
CatLoxl2=0
Censored CatLoxl2=0
CatLoxl2=1
Censored CatLoxl2=1
PFS
Survival Distribution Function
1.00
0.75
0.50
0.25
0.00
Percent without Event
0
100
200
300
400
500
600
700
800
Time to First Disease Progression
Time (Days)

FIG. 10A

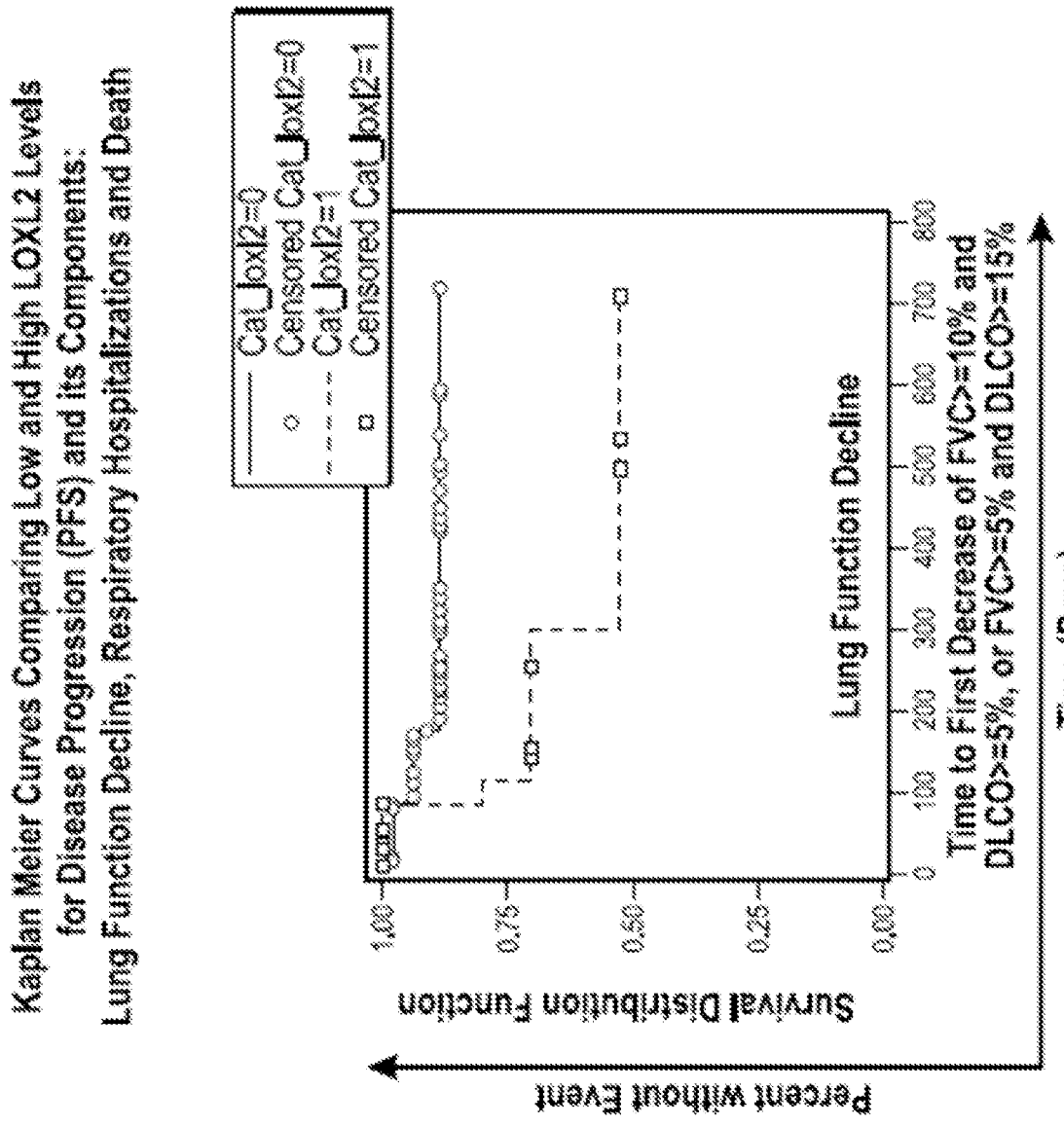

Kaplan Meier Curves Comparing Low and High LOXL2 Levels
for Disease Progression (PFS) and its Components:
Lung Function Decline, Respiratory Hospitalizations and Death
CatLoxl2=0
Censored CatLoxl2=0
CatLoxl2=1
Censored CatLoxl2=1
Percent without Event
Survival Distribution Function
1.00
0.75
0.50
0.25
0.00
0
100
200
300
400
500
600
700
800
Lung Function Decline
Time to First Decrease of FVC>=10% and
DLCO>=5%, or FVC>=5% and DLCO>=15%
Time (Days)

FIG. 10B

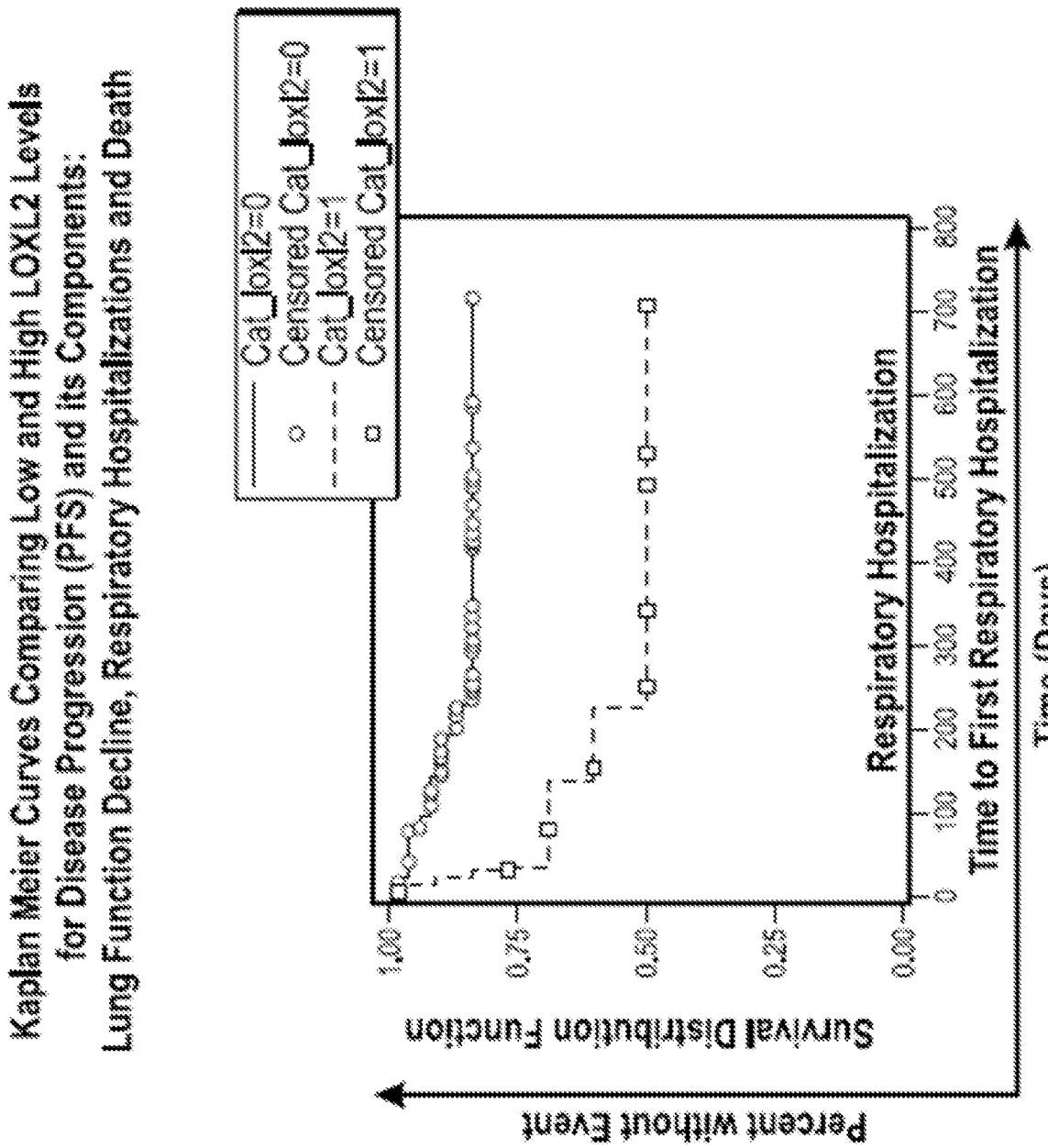

Kaplan Meier Curves Comparing Low and High LOXL2 Levels
for Disease Progression (PFS) and its Components:
Lung Function Decline, Respiratory Hospitalizations and Death
Cat_loxl2=0
Censored Cat_loxl2=0
Cat_loxl2=1
Censored Cat_loxl2=1
Percent without Event
Survival Distribution Function
1.00
0.75
0.50
0.25
0.00
0
100
200
300
400
500
600
700
800
Time (Days)
Time to First Respiratory Hospitalization
Respiratory Hospitalization

FIG. 10C

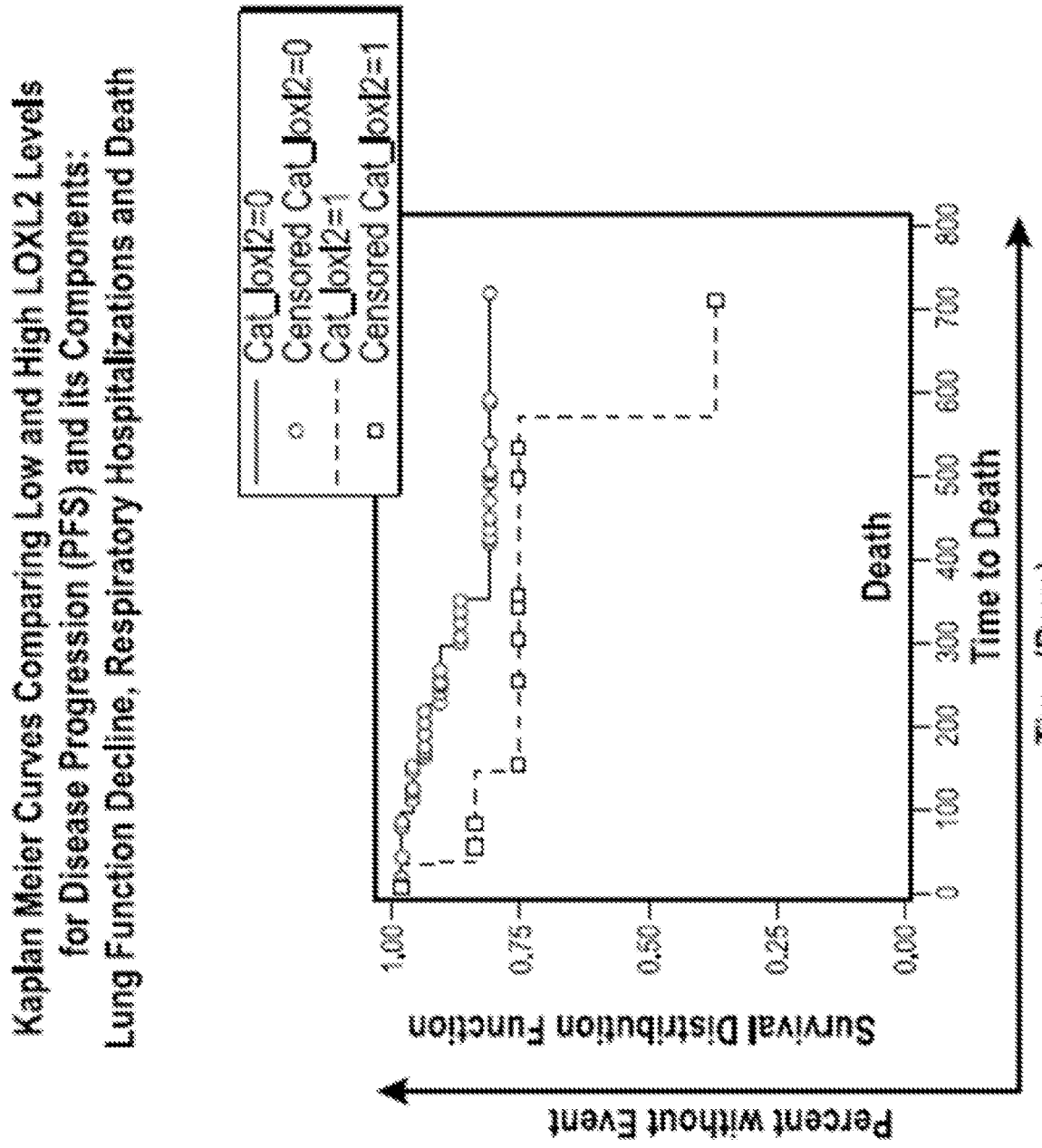

Kaplan Meier Curves Comparing Low and High LOXL2 Levels
for Disease Progression (PFS) and its Components:
Lung Function Decline, Respiratory Hospitalizations and Death
CatLoxl2=0
Censored CatLoxl2=0
CatLoxl2=1
Censored CatLoxl2=1
Percent without Event
Survival Distribution Function
1,00
0,75
0,50
0,25
0,00
Death
0
100
200
300
400
500
600
700
800
Time to Death
Time (Days)

FIG. 10D

Comparison of baseline LOXL2 distribution among ARTEMIS-IPF (placebo and Ambrisentan-treated subjects combined) and GAP Cohort subjects

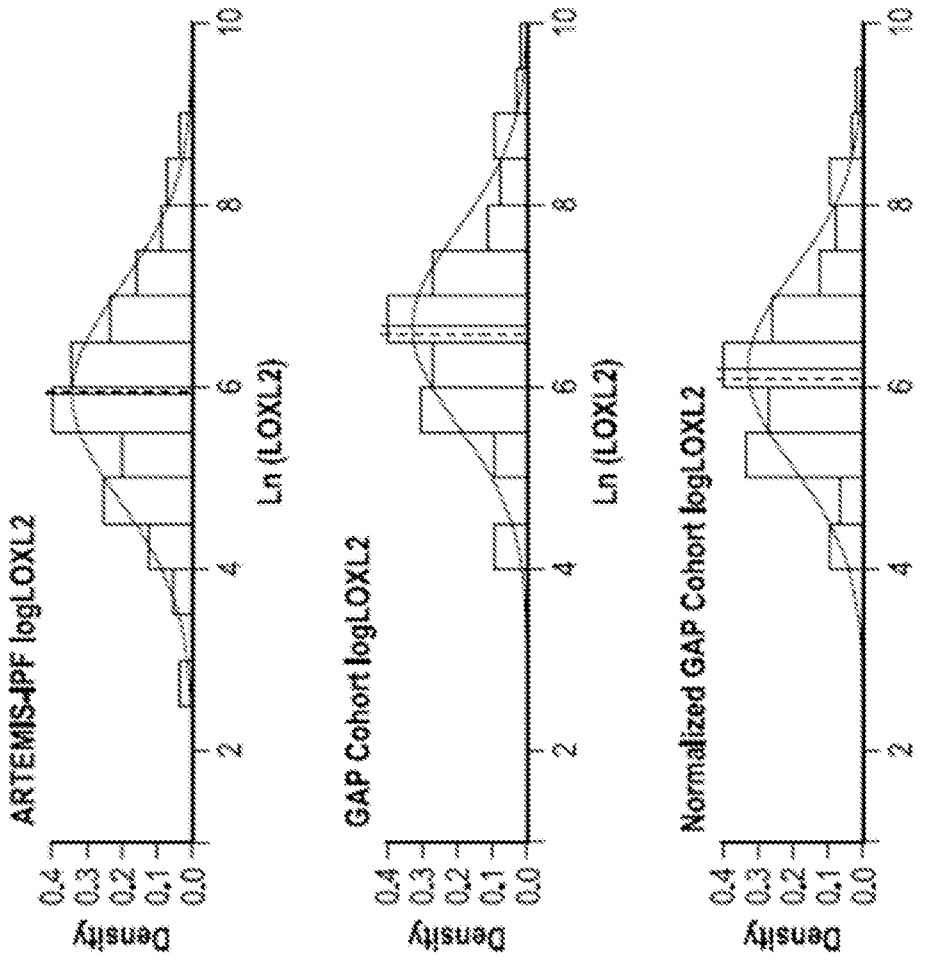


FIG. 11A

Comparison of baseline LOXL2 distribution among ARTEMIS-IPF (Ambrisentan-treated subjects) and GAP Cohort subjects

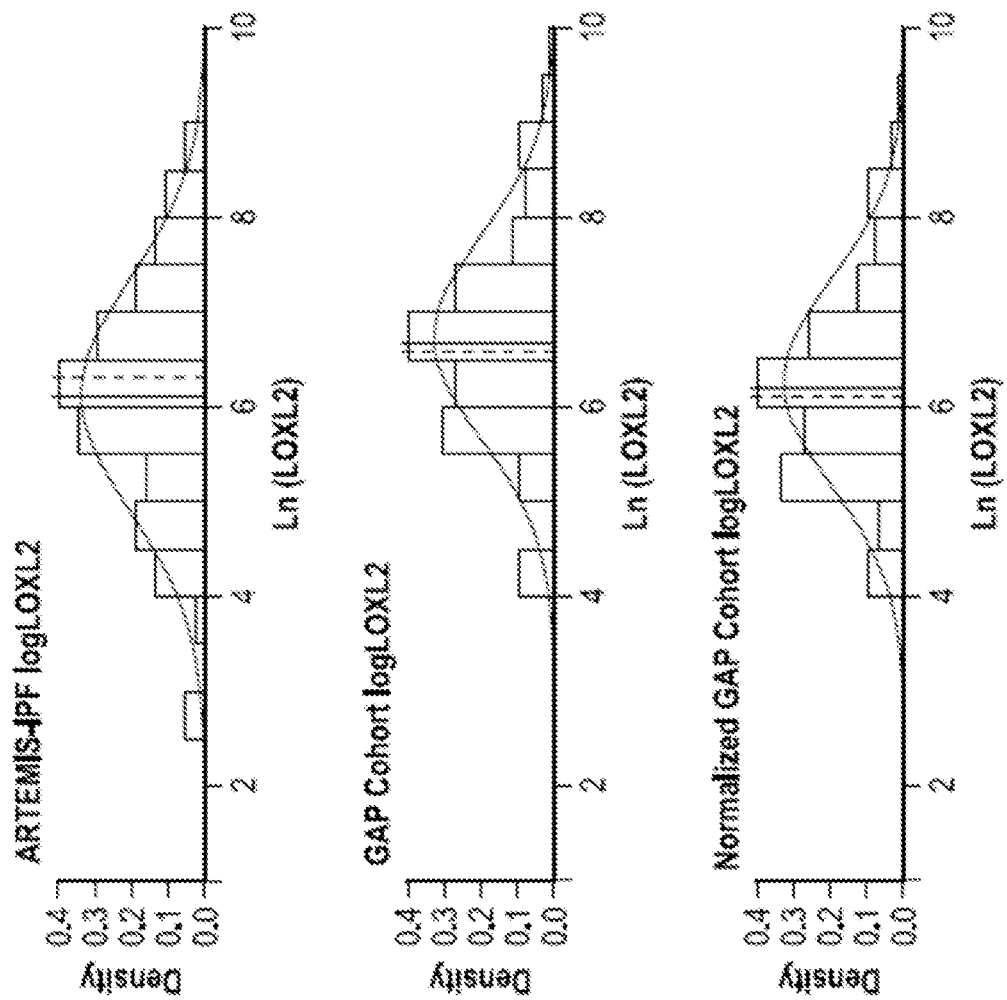


FIG. 11B

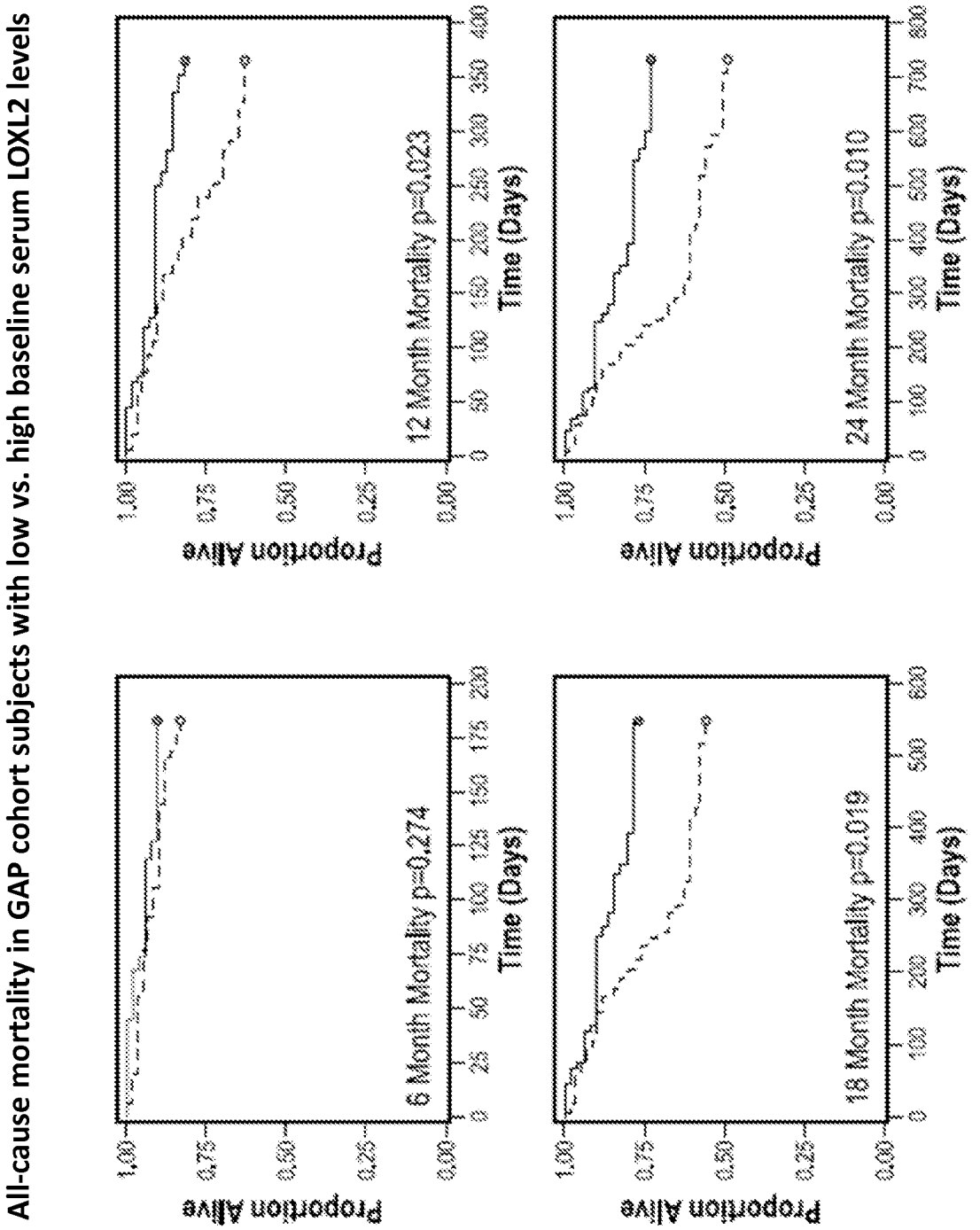

All-cause mortality in GAP cohort subjects with low vs. high baseline serum LOXL2 levels
6 Month Mortality p=0.274
12 Month Mortality p=0.023
18 Month Mortality p=0.019
24 Month Mortality p=0.010
Proportion Alive
Time (Days)

FIG. 12A

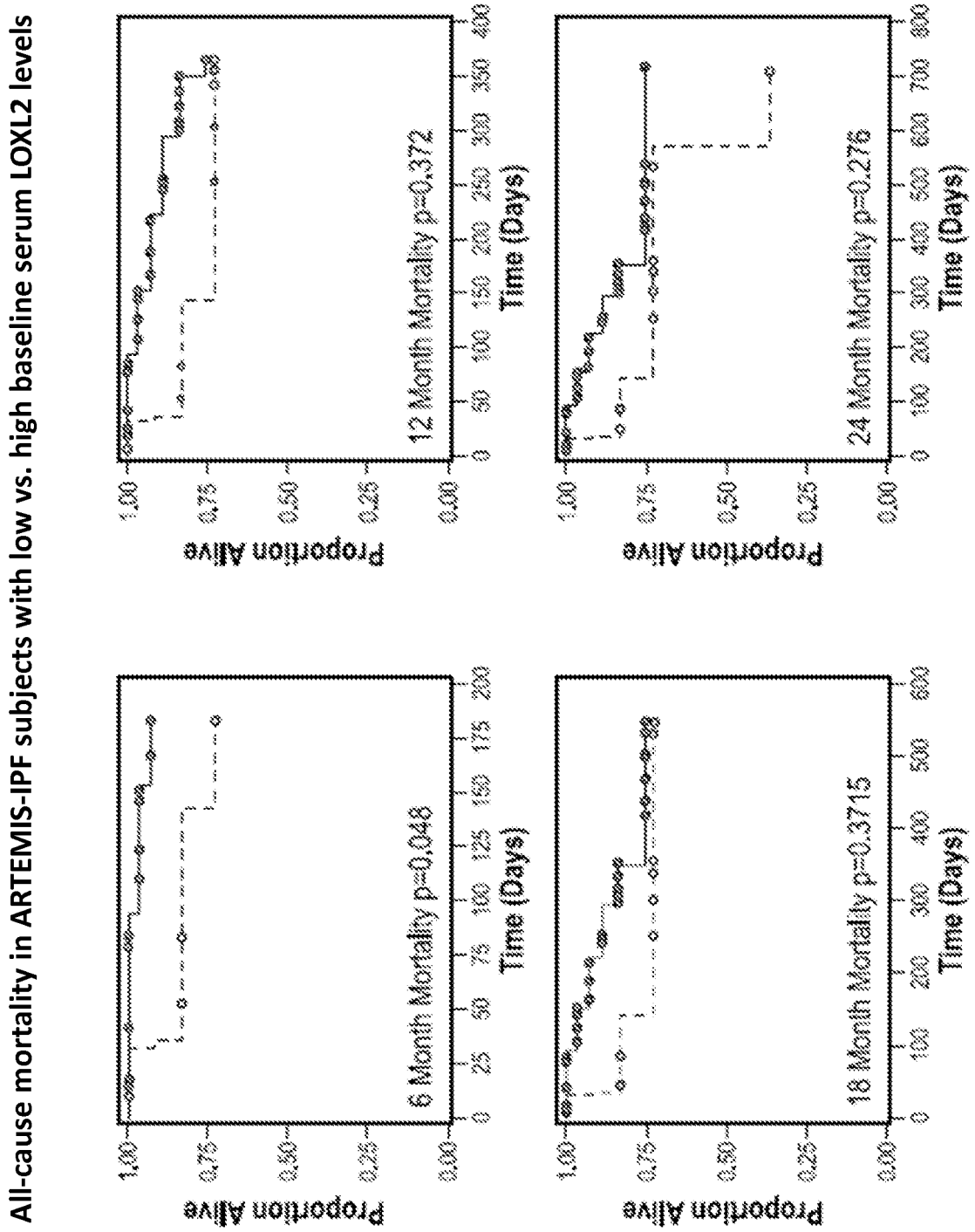

All-cause mortality in ARTEMIS-IPF subjects with low vs. high baseline serum LOXL2 levels
6 Month Mortality p=0.048
12 Month Mortality p=0.372
18 Month Mortality p=0.3715
24 Month Mortality p=0.276
Proportion Alive
Time (Days)

FIG. 12B

Disease progression and Mortality in ARTEMIS-IPF and GAP Cohort subjects with low vs. high serum LOXL2 levels

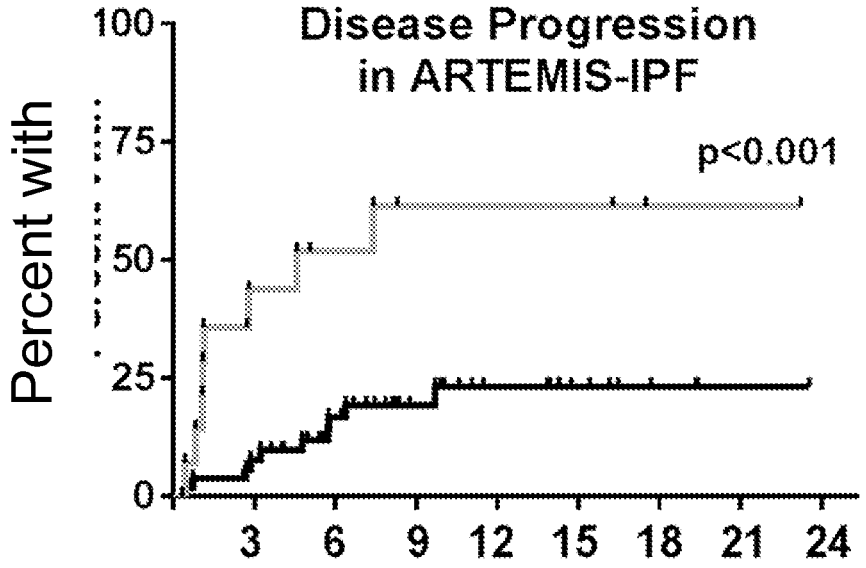


FIG. 13A

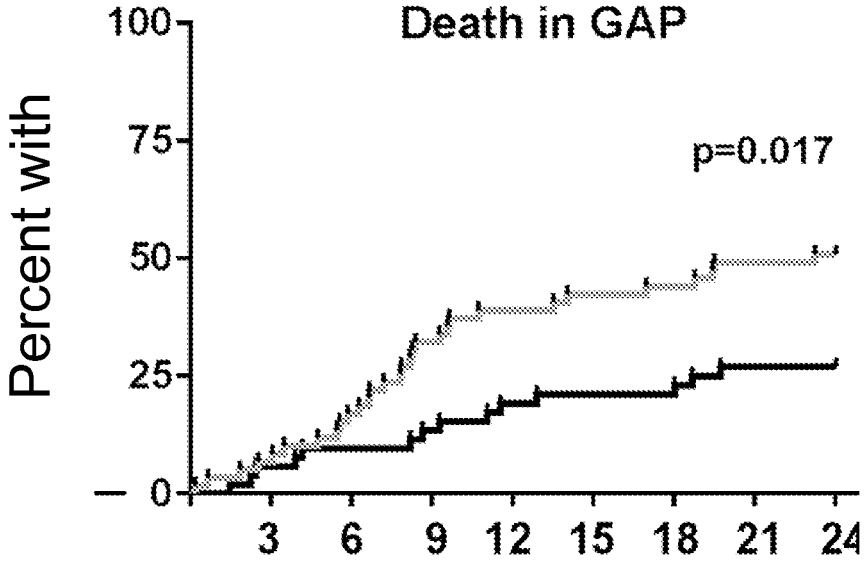


FIG. 13B

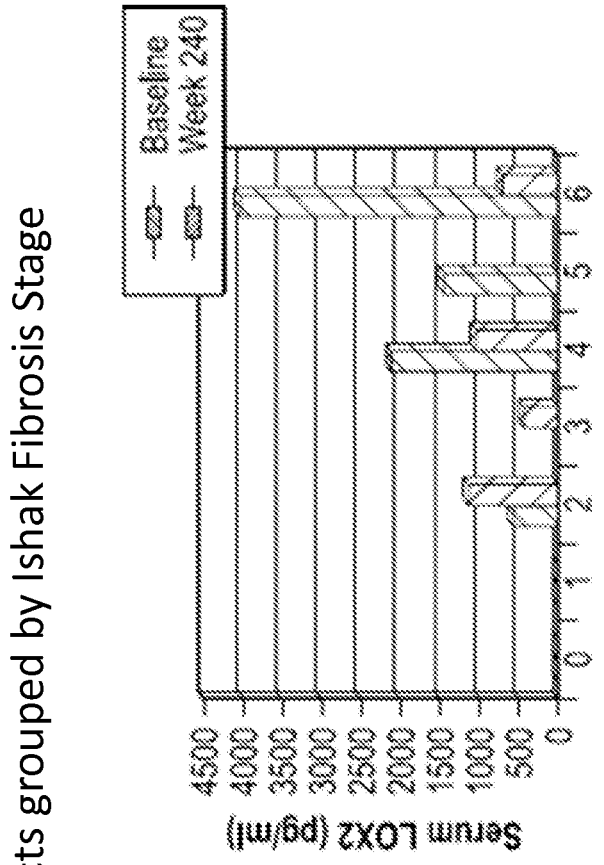


FIG. 14B

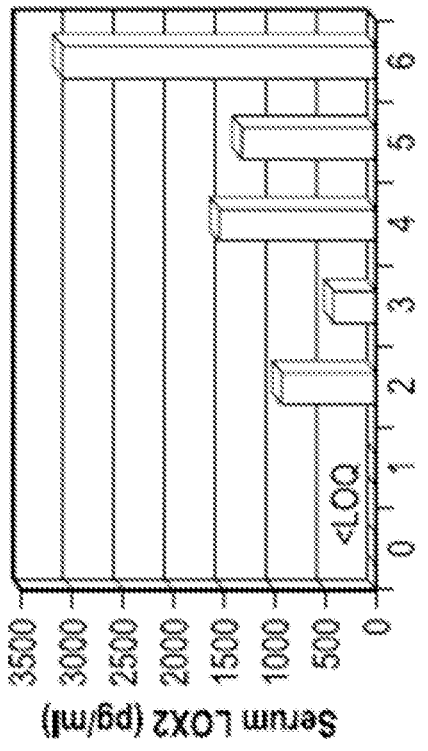


FIG. 14A

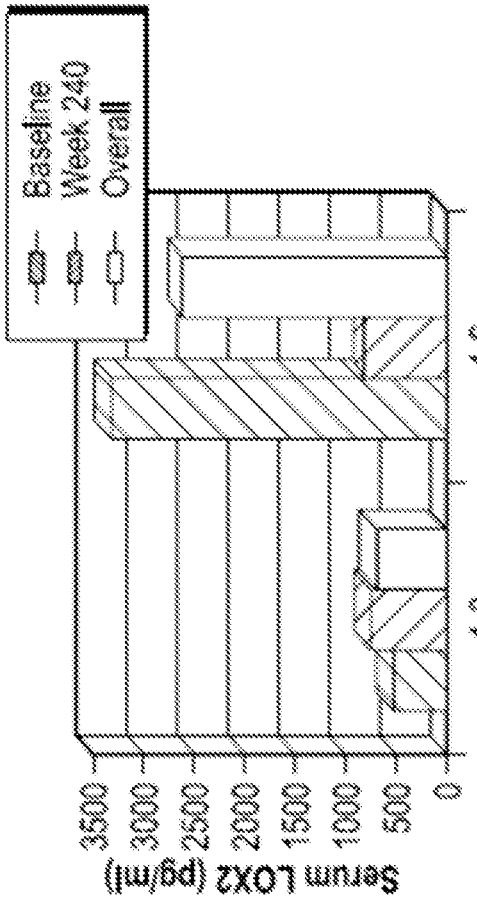


FIG. 14C

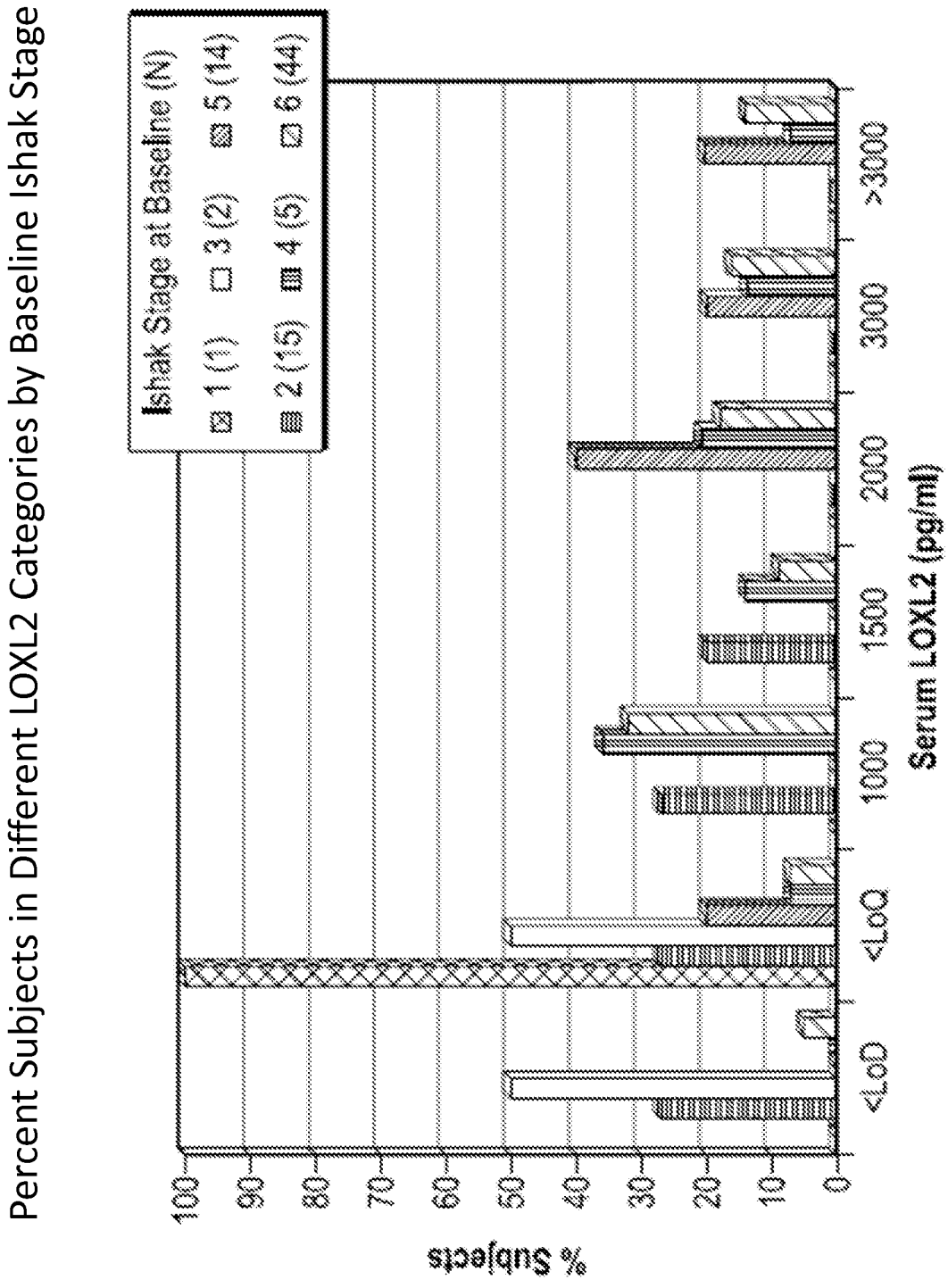

Percent Subjects in Different LOXL2 Categories by Baseline Ishak Stage
Ishak Stage at Baseline (N)
1 (1)
2 (15)
3 (2)
4 (5)
5 (14)
6 (44)
% Subjects
0
10
20
30
40
50
60
70
80
90
100
<LoD
<LoQ
1000
1500
2000
3000
>3000
Serum LOXL2 (pg/ml)

FIG. 15

Baseline (BL) and week-240 (WK 240) Serum LOXL2 levels in CHB subjects

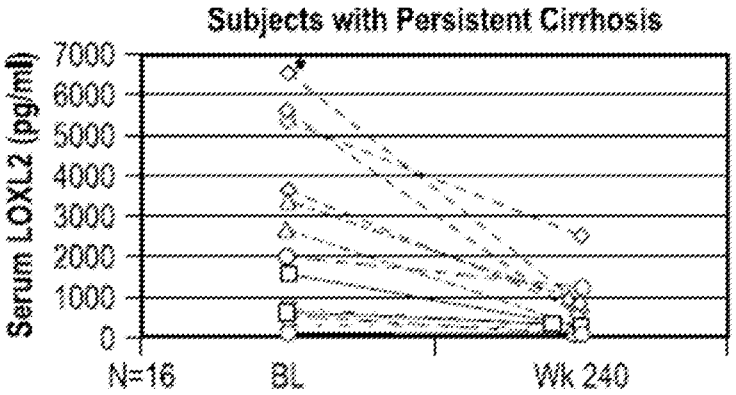


FIG. 16A

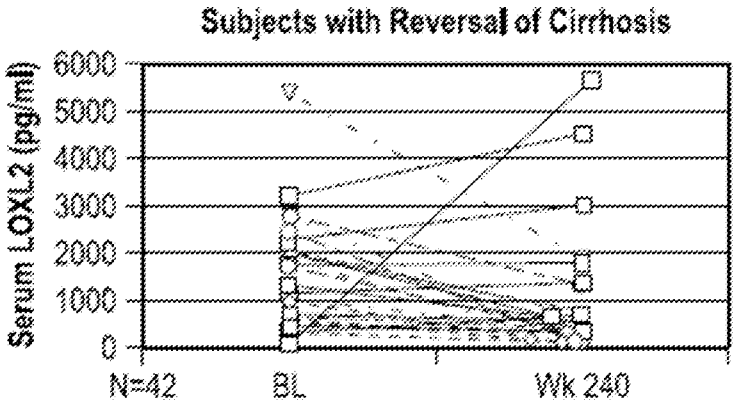


FIG. 16B

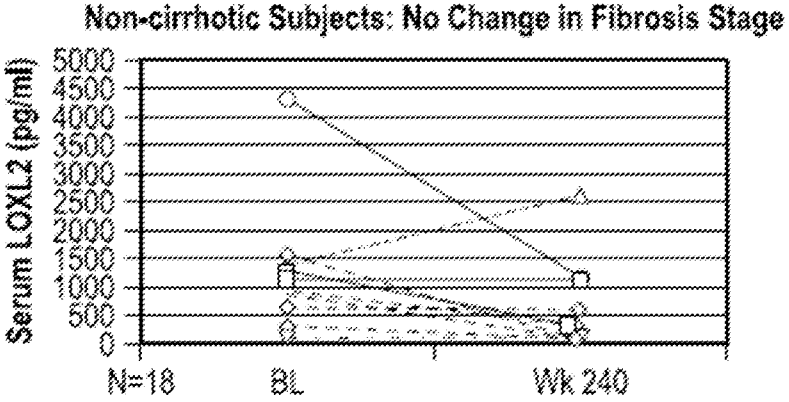


FIG. 16C

Baseline (BL) and week-240 (WK 240) Serum LOXL2 levels in CHB subjects

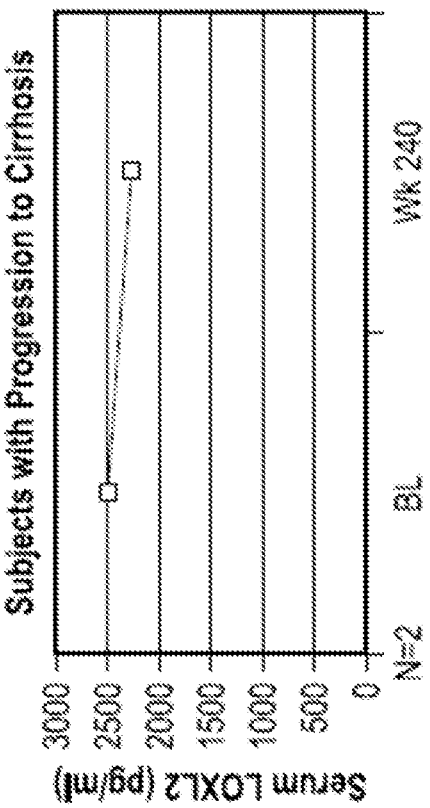


FIG. 16D

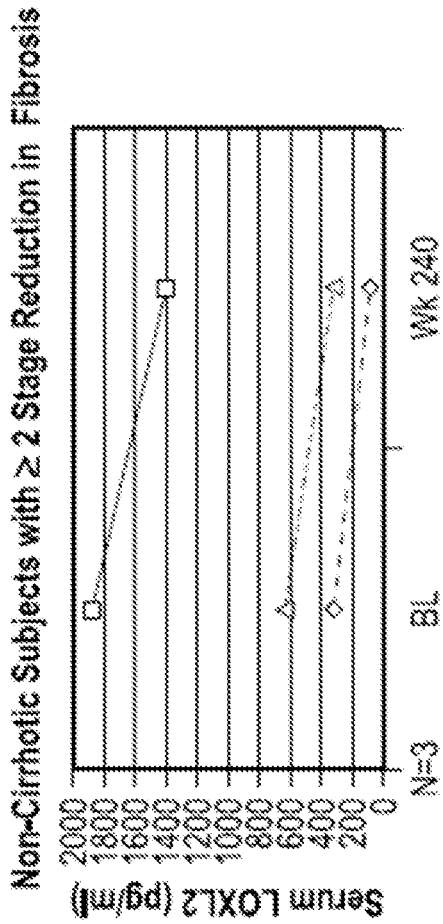


FIG. 16E

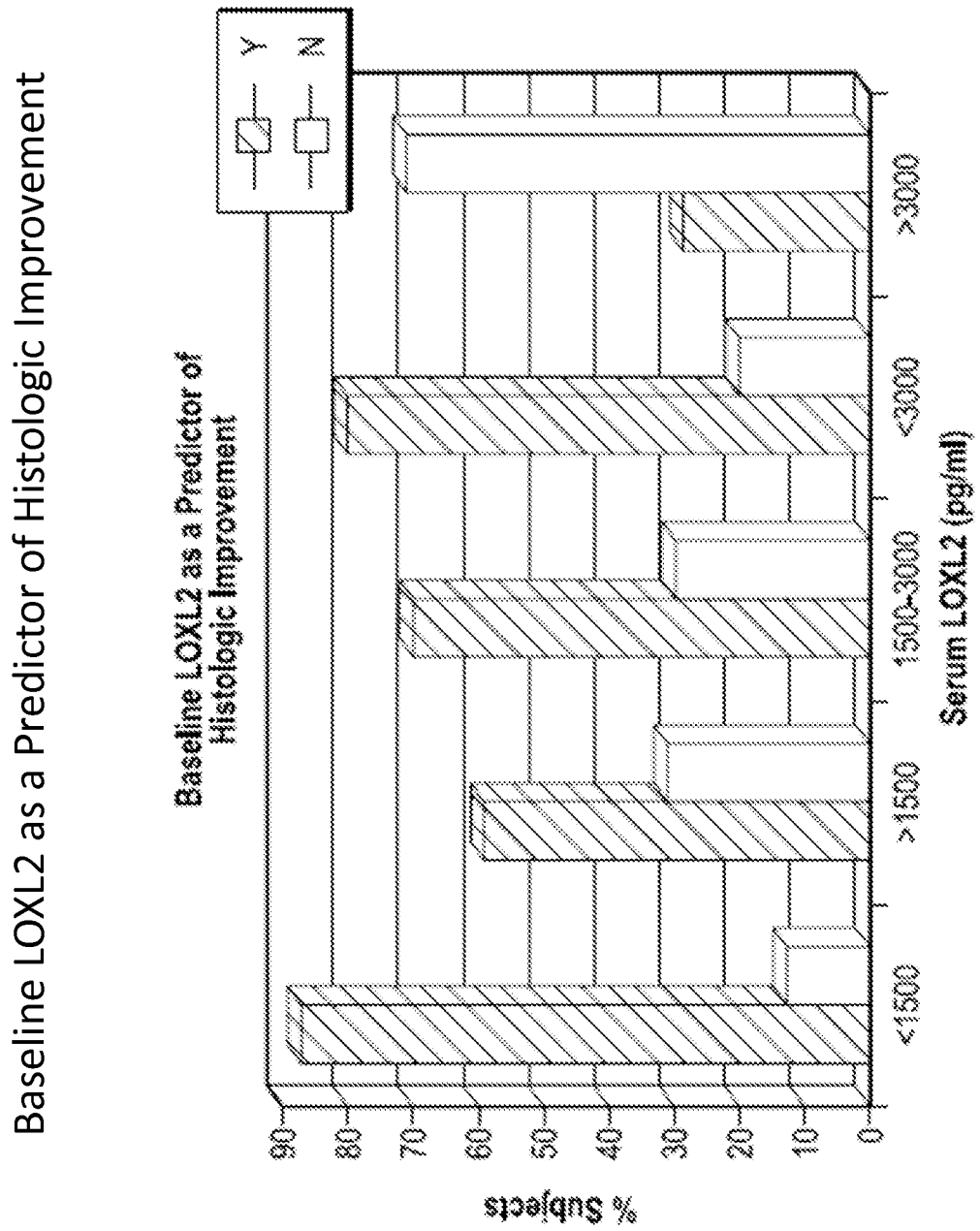

Baseline LOXL2 as a Predictor of Histologic Improvement
Baseline LOXL2 as a Predictor of Histologic Improvement
Y
N
% Subjects
0
10
20
30
40
50
60
70
80
90
<1500
>1500
1500-3000
<3000
>3000
Serum LOXL2 (pg/ml)

FIG. 17

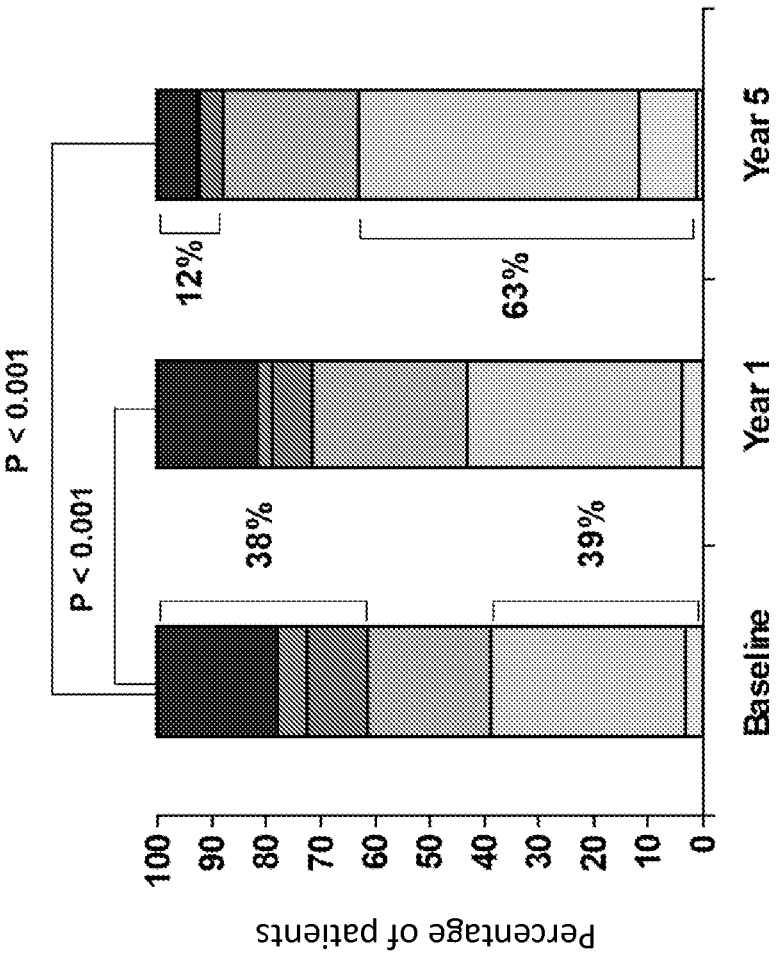

Percentage of patients
100
90
80
70
60
50
40
30
20
10
0
Baseline
Year 1
Year 5
38%
39%
12%
63%
P < 0.001
P < 0.001

FIG. 18

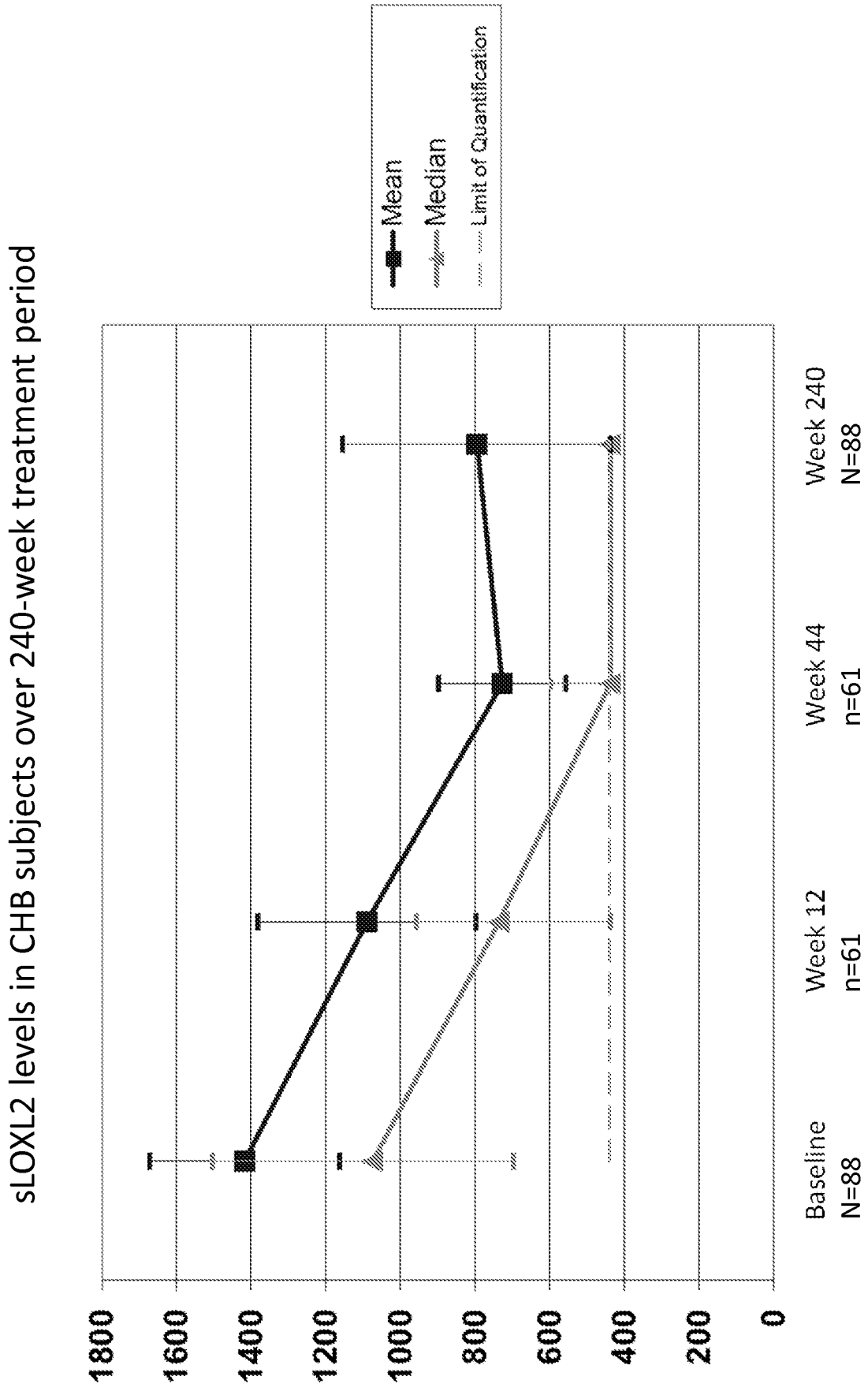

sLOXL2 levels in CHB subjects over 240-week treatment period
Mean
Median
Limit of Quantification
1800
1600
1400
1200
1000
800
600
400
200
0
Baseline
N=88
Week 12
n=61
Week 44
n=61
Week 240
N=88

FIG. 19

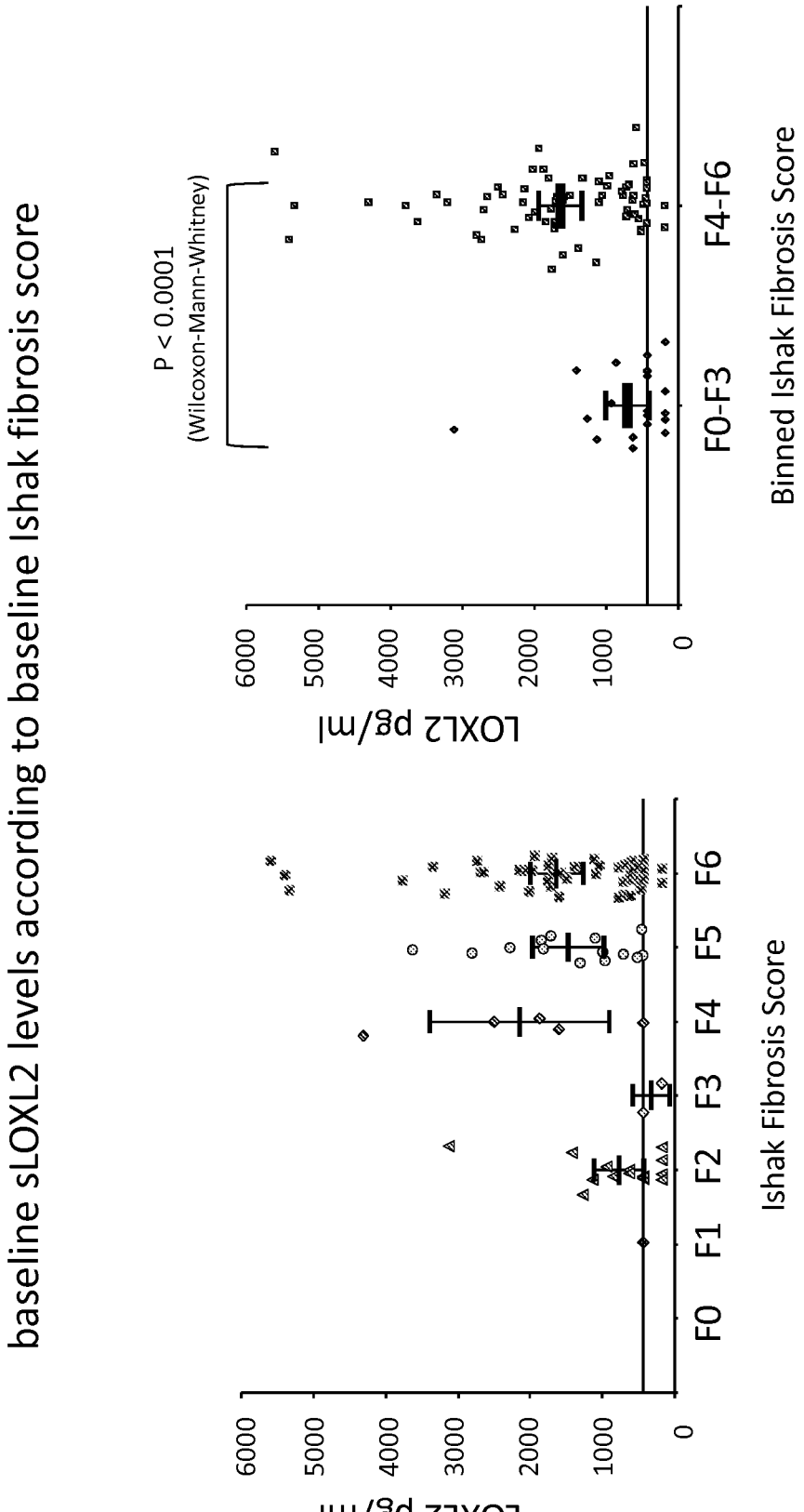


FIG. 20A

FIG. 20B

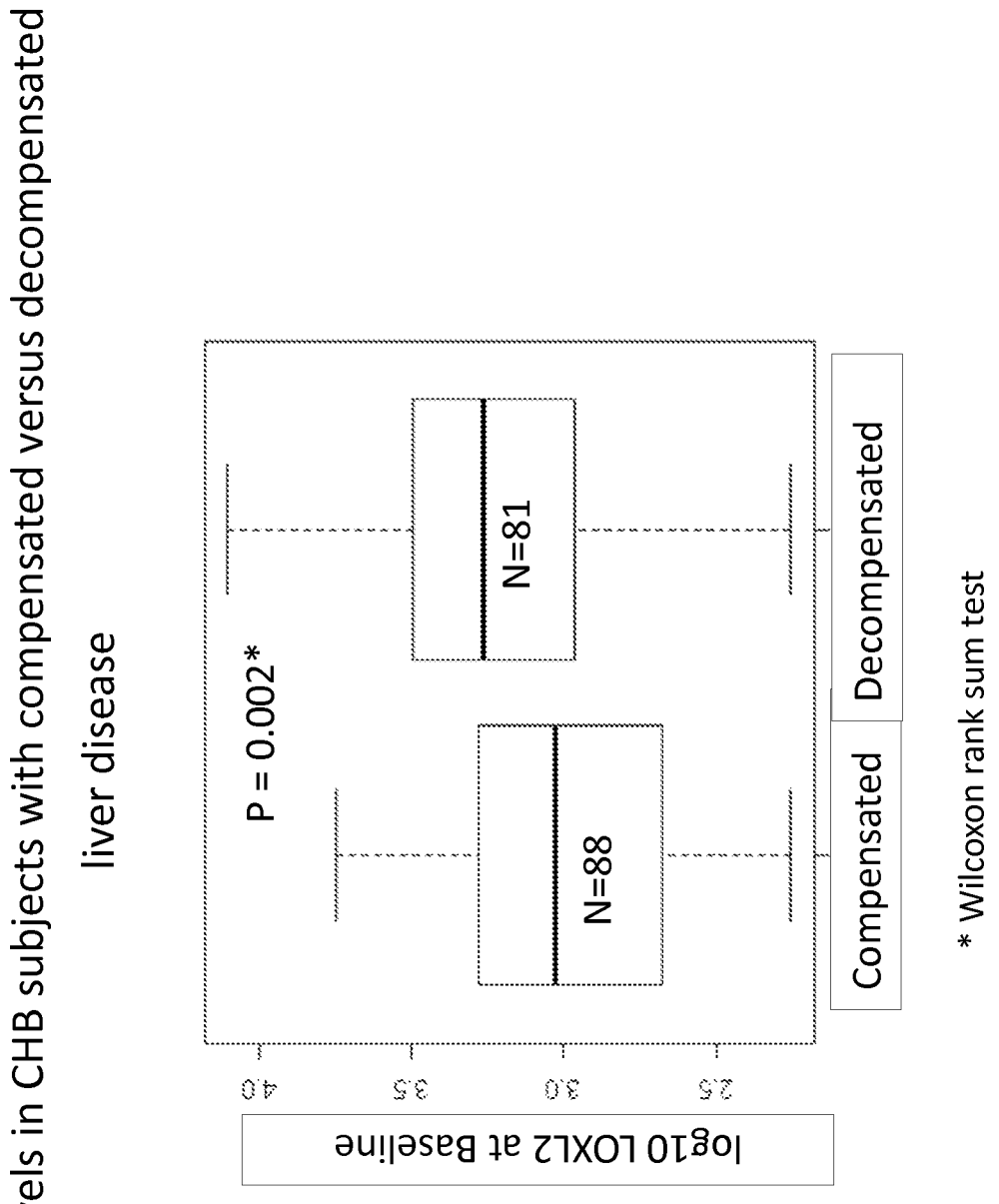

sLOXL2 levels in CHB subjects with compensated versus decompensated liver disease
log10 LOXL2 at Baseline
4.0
3.5
3.0
2.5
P = 0.002*
N=88
N=81
Compensated
Decompensated
* Wilcoxon rank sum test

FIG. 21

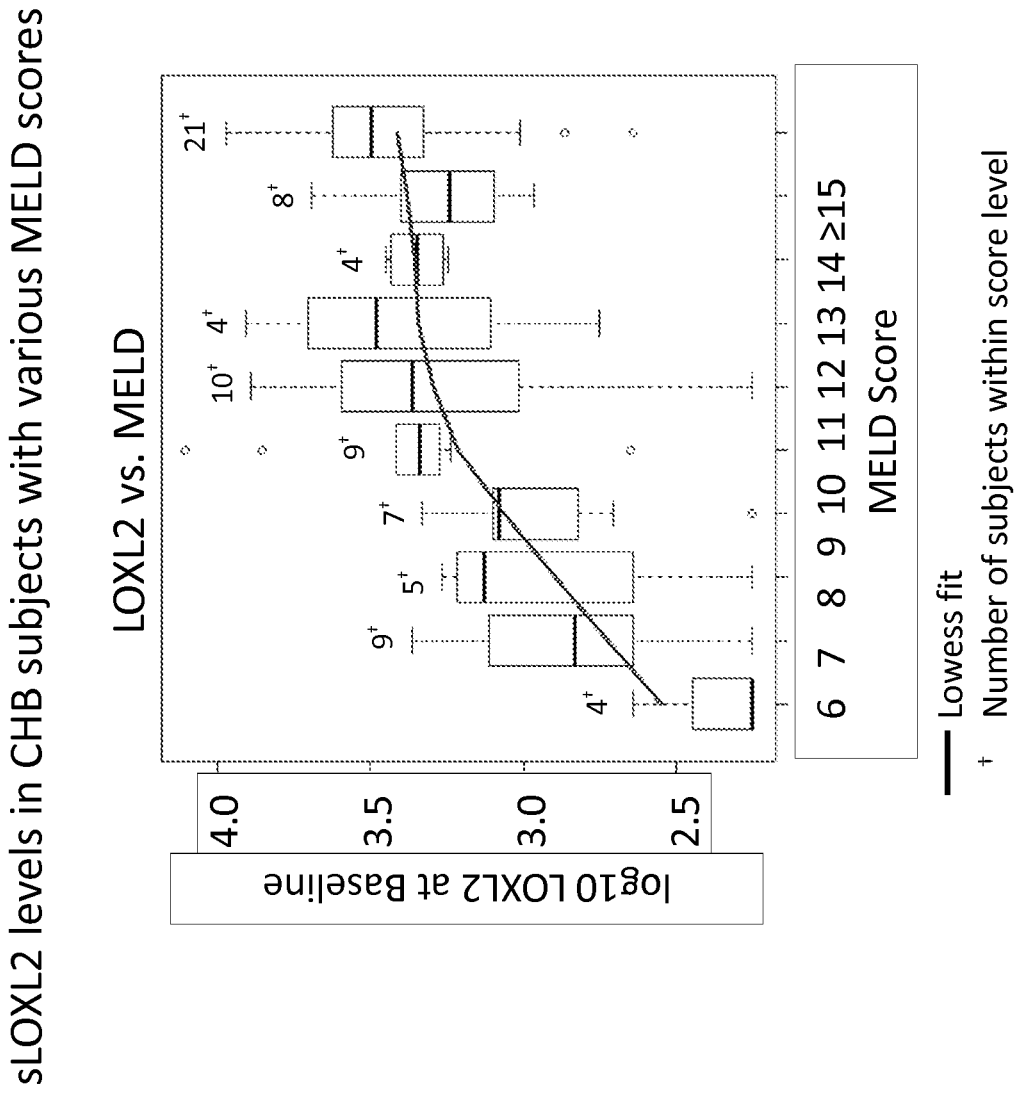

sLOXL2 levels in CHB subjects with various MELD scores
LOXL2 vs. MELD
log10 LOXL2 at Baseline
4.0
3.5
3.0
2.5
6 7 8 9 10 11 12 13 14 ≥15
MELD Score
Lowess fit
† Number of subjects within score level

FIG. 22

LOXL2 protein expression in cholestatic liver disease

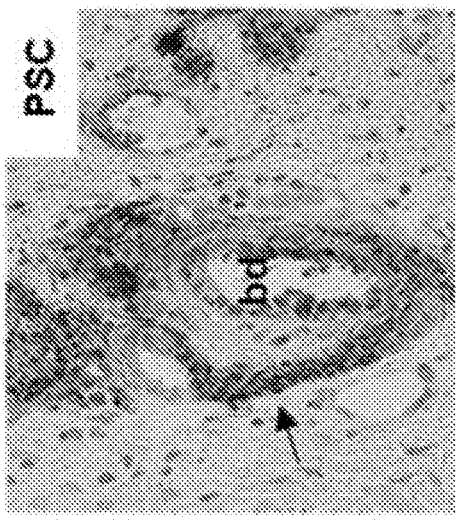


FIG. 23A

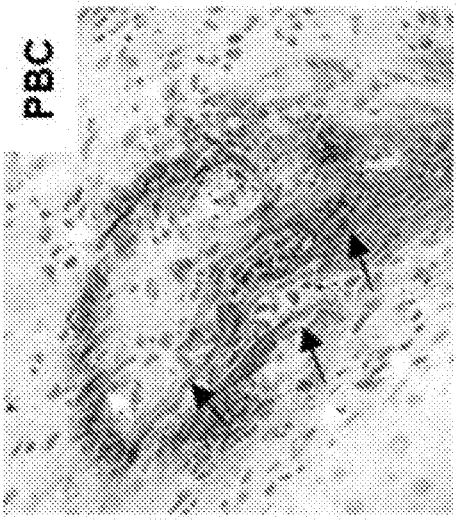


FIG. 23B

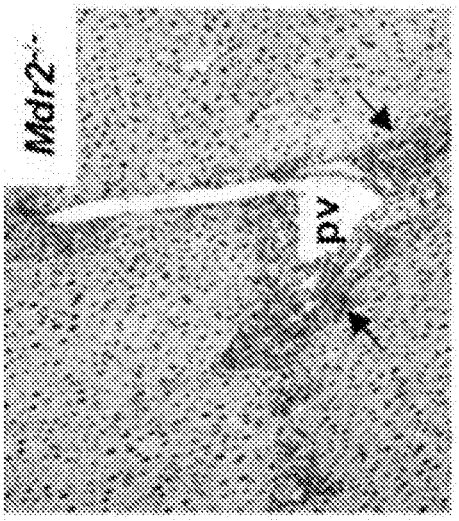


FIG. 23C

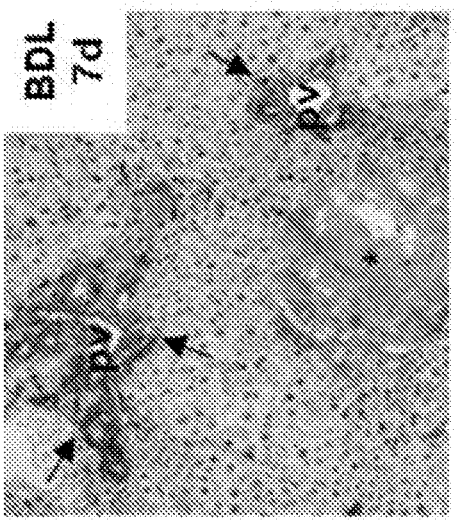


FIG. 23D

LOXL2 mRNA expression in animal cholestatic disease models

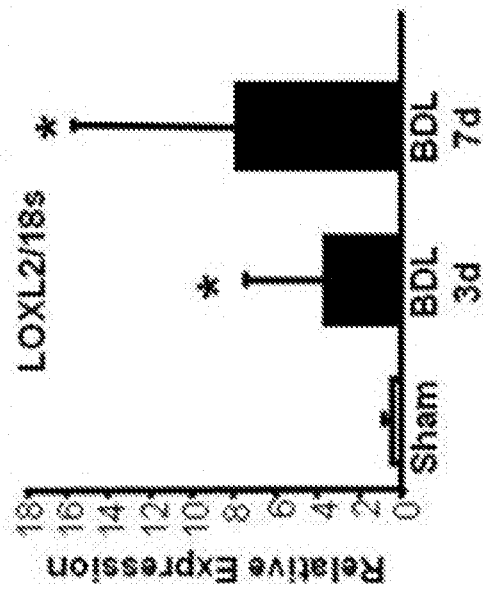


FIG. 24B

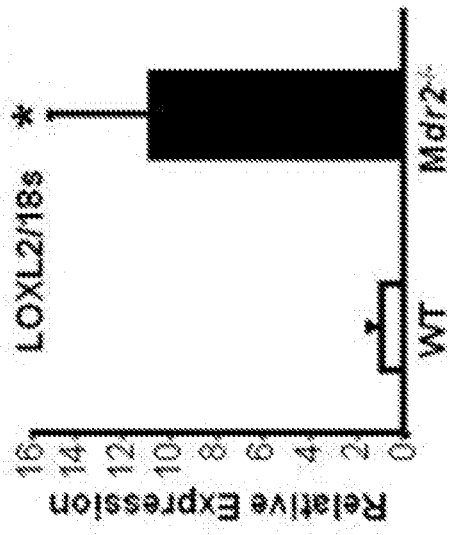
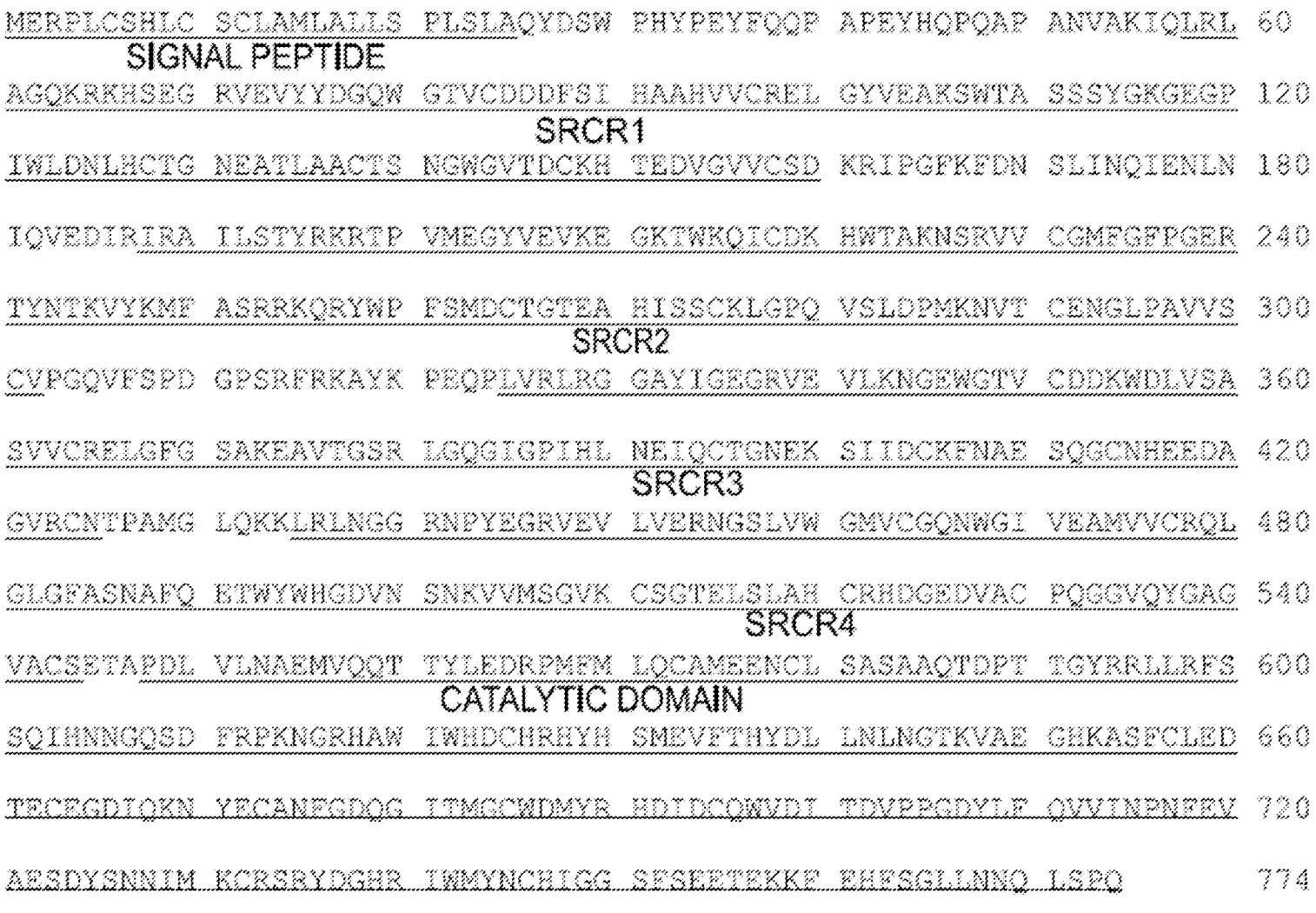


FIG. 24A

LOXL2 domains



SEQ ID NO:1

FIG. 25

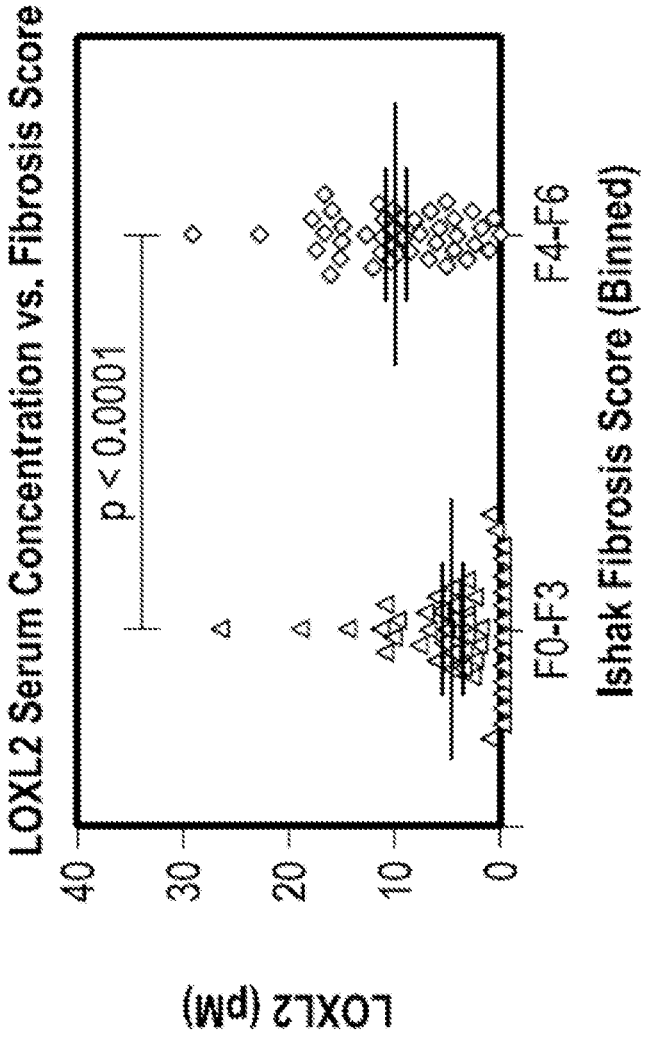

LOXL2 Serum Concentration vs. Fibrosis Score
p < 0.0001
LOXL2 (pM)
40
30
20
10
0
F0-F3
F4-F6
Ishak Fibrosis Score (Binned)

FIG. 26

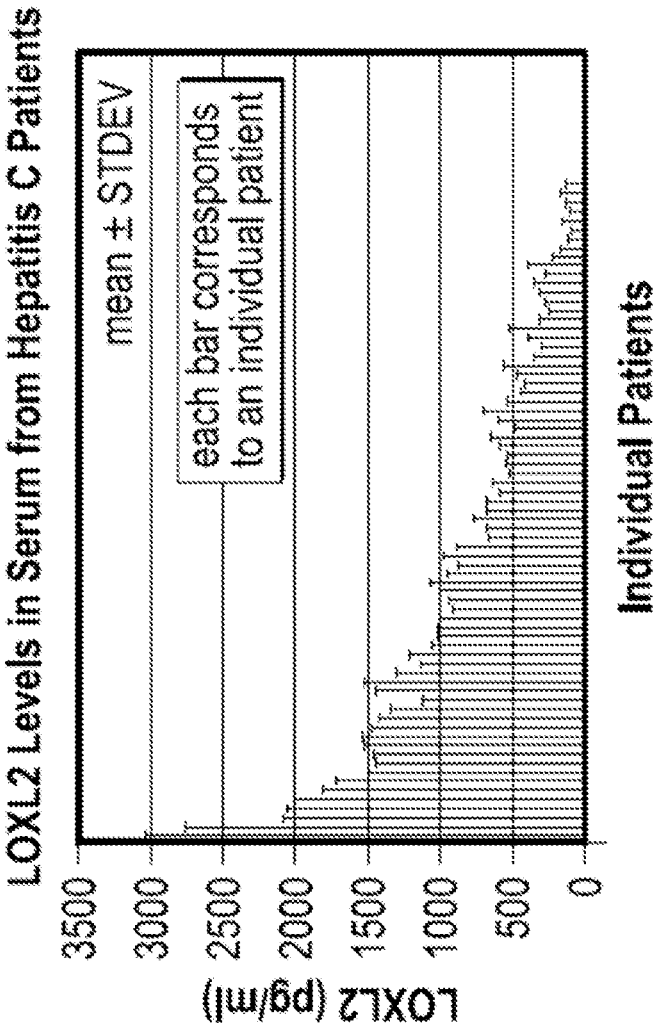

LOXL2 Levels in Serum from Hepatitis C Patients
mean ± STDEV
each bar corresponds to an individual patient
LOXL2 (pg/ml)
3500
3000
2500
2000
1500
1000
500
0
Individual Patients

FIG. 27

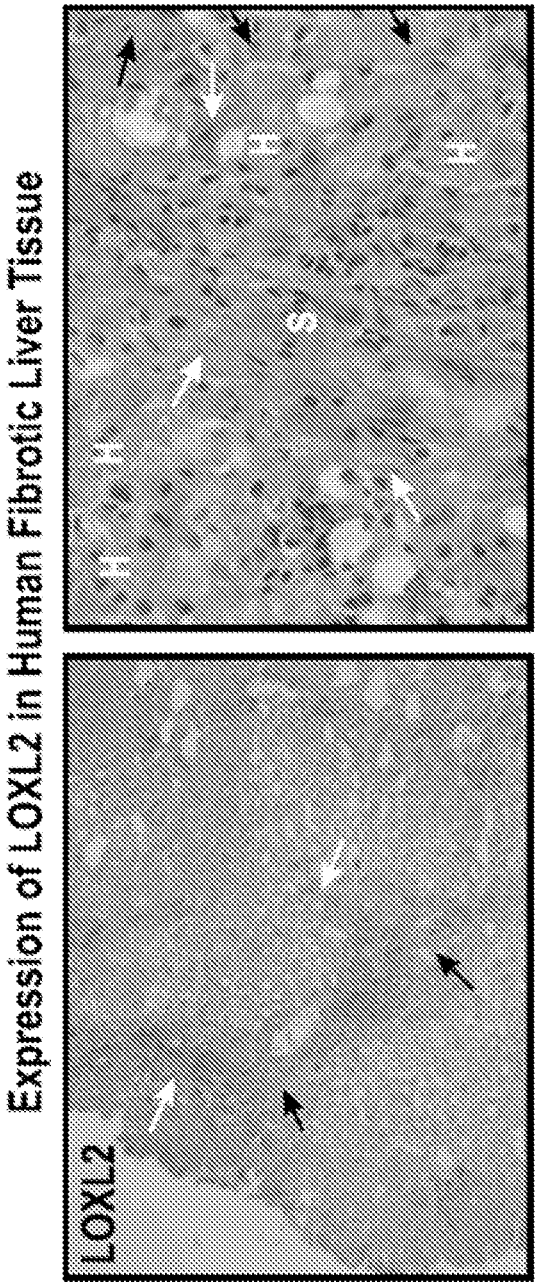

Expression of LOXL2 in Human Fibrotic Liver Tissue
LOXL2
H
S

FIG. 28

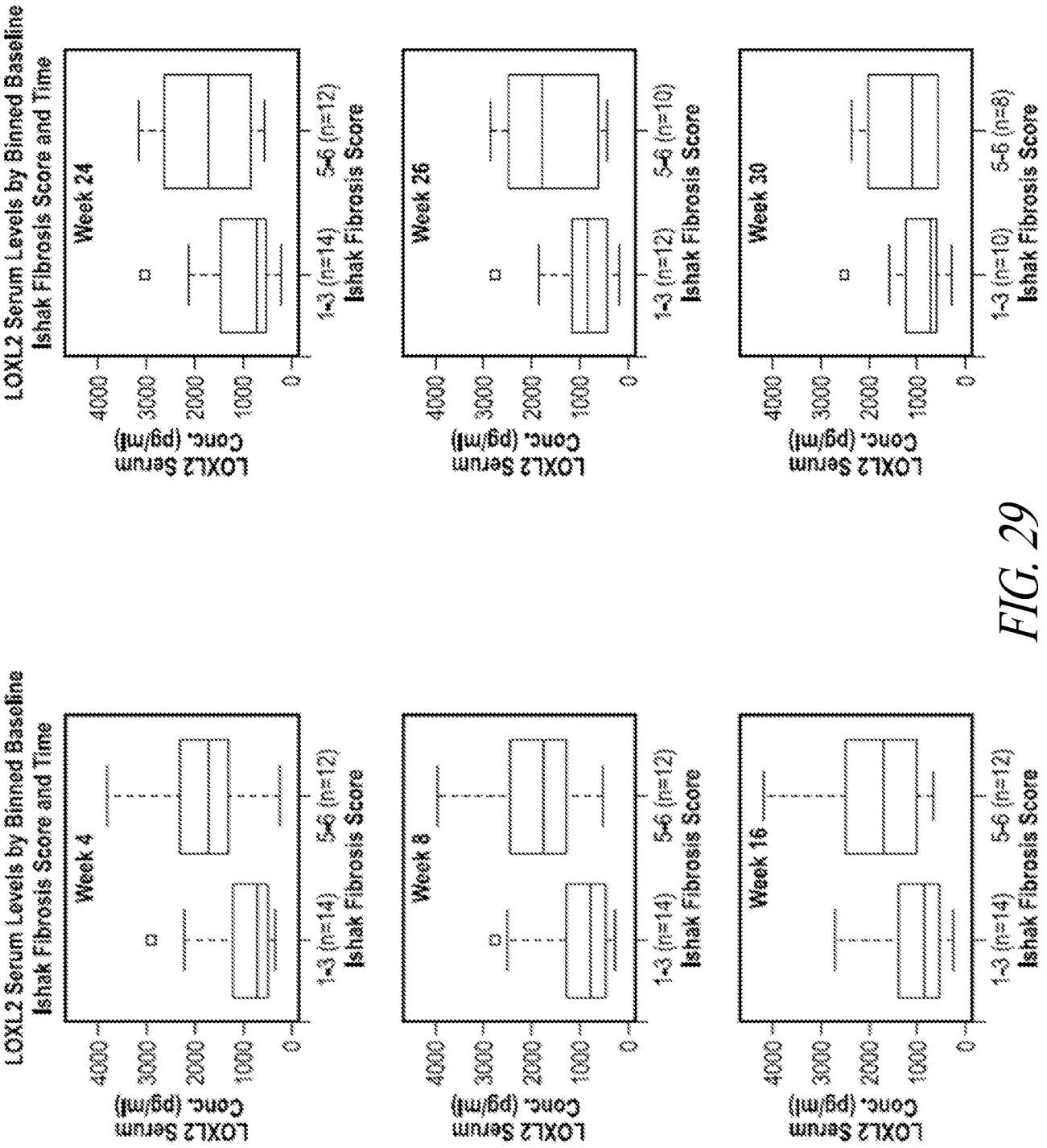

LOXL2 Serum Levels by Binned Baseline Ishak Fibrosis Score and Time
Week 4
Week 8
Week 16
Week 24
Week 26
Week 30
LOXL2 Serum Conc. (pg/ml)
0
1000
2000
3000
4000
1-3 (n=14)
5-6 (n=12)
1-3 (n=12)
5-6 (n=10)
1-3 (n=10)
5-6 (n=8)
Ishak Fibrosis Score

FIG. 29

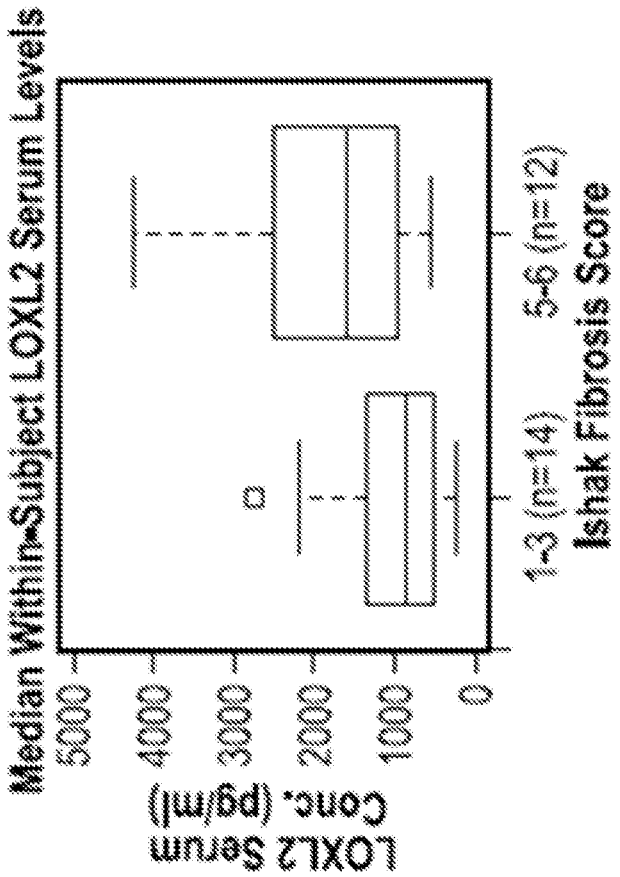

Median Within-Subject LOXL2 Serum Levels
LOXL2 Serum Conc. (pg/ml)
5000
4000
3000
2000
1000
0
1-3 (n=14)
5-6 (n=12)
Ishak Fibrosis Score

FIG. 30

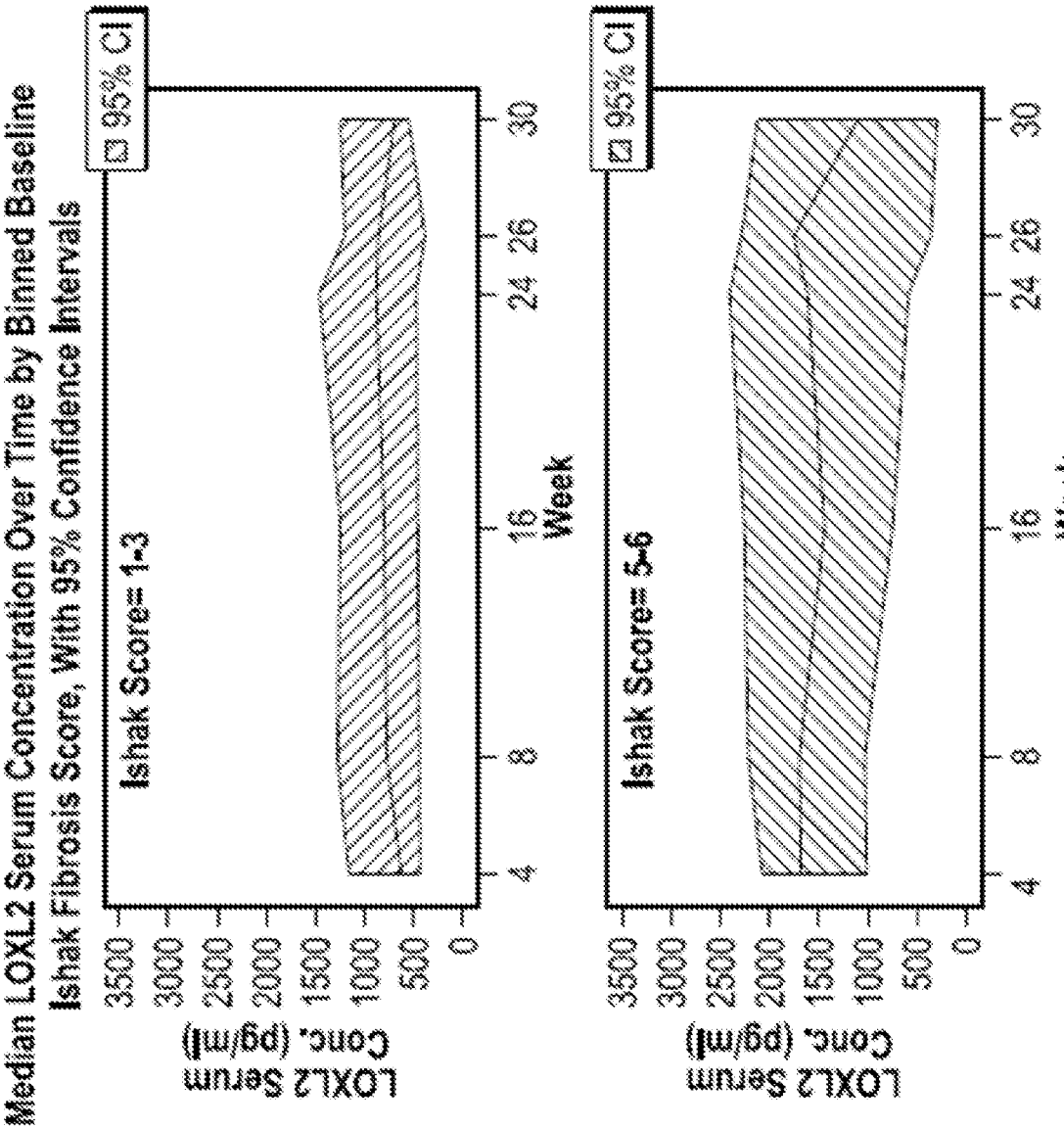

Median LOXL2 Serum Concentration Over Time by Binned Baseline Ishak Fibrosis Score, With 95% Confidence Intervals
95% CI
Ishak Score= 1-3
LOXL2 Serum Conc. (pg/ml)
3500
3000
2500
2000
1500
1000
500
0
4
8
16
24
26
30
Week
95% CI
Ishak Score= 5-6
LOXL2 Serum Conc. (pg/ml)
3500
3000
2500
2000
1500
1000
500
0
4
8
16
24
26
30
Week

FIG. 31

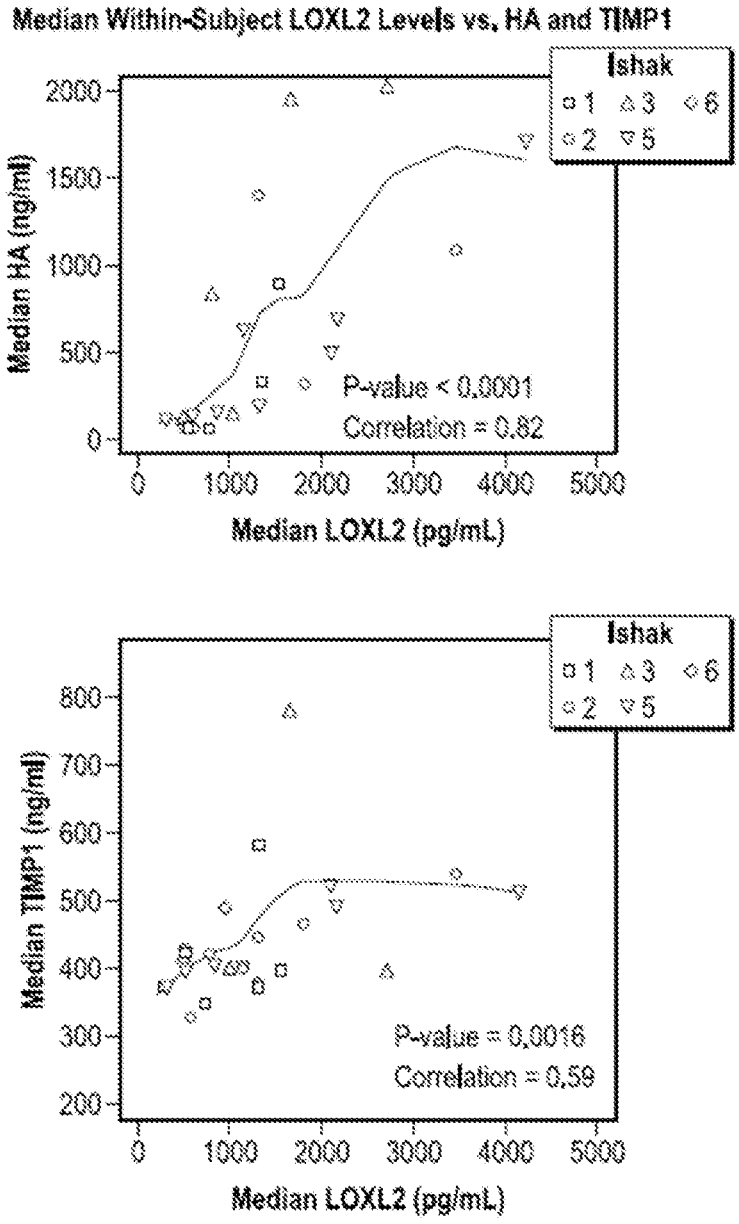

Median Within-Subject LOXL2 Levels vs. HA and TIMP1
Ishak
1 3 6
2 5
Median HA (ng/ml)
2000
1500
1000
500
0
P-value < 0.0001
Correlation = 0.82
0 1000 2000 3000 4000 5000
Median LOXL2 (pg/mL)
Ishak
1 3 6
2 5
Median TIMP1 (ng/ml)
800
700
600
500
400
300
200
P-value = 0.0016
Correlation = 0.59
0 1000 2000 3000 4000 5000
Median LOXL2 (pg/mL)

FIG. 32

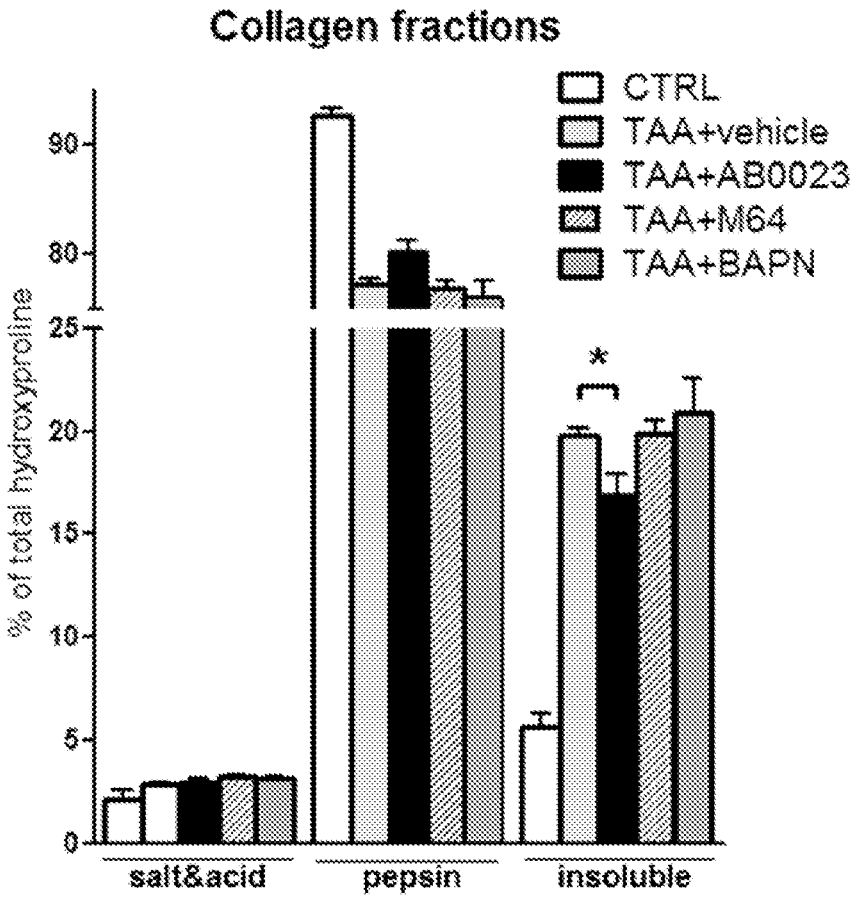


FIG. 33A

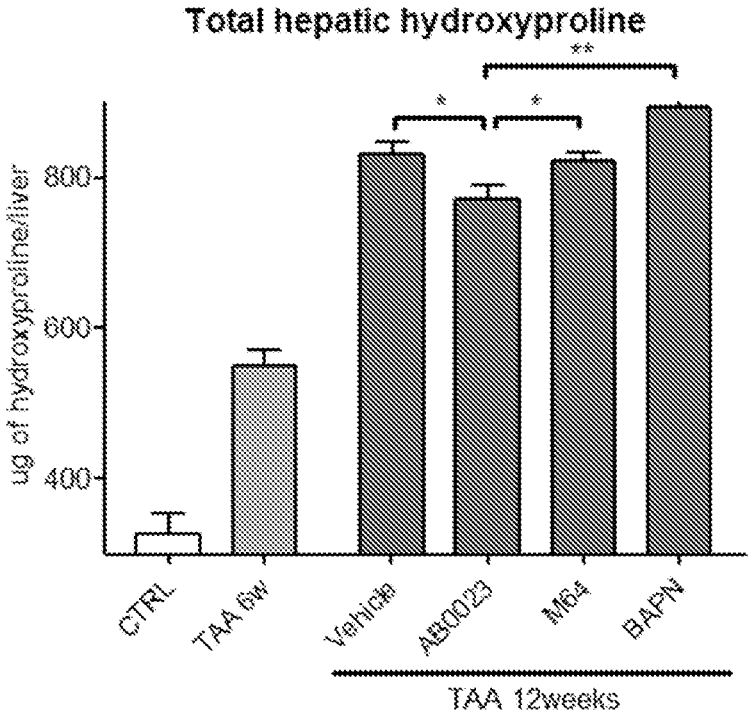


FIG. 33B

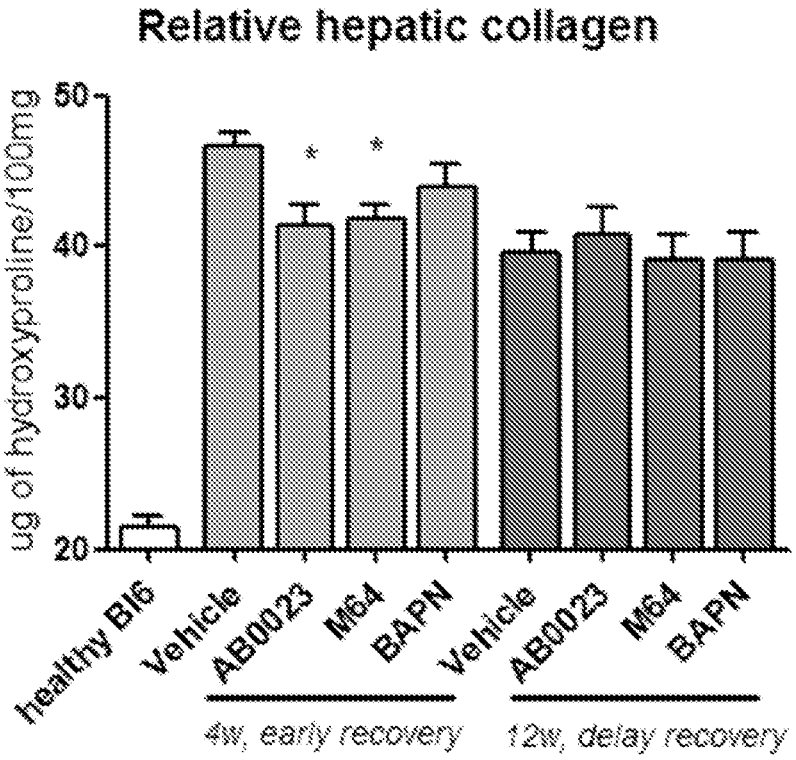


FIG. 33C

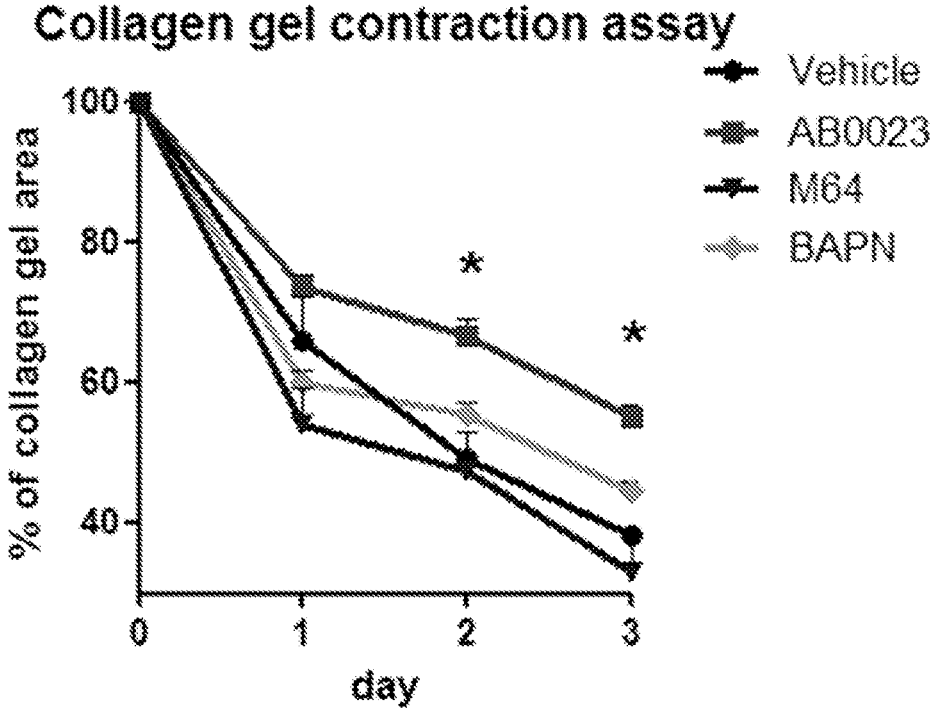


FIG. 33D

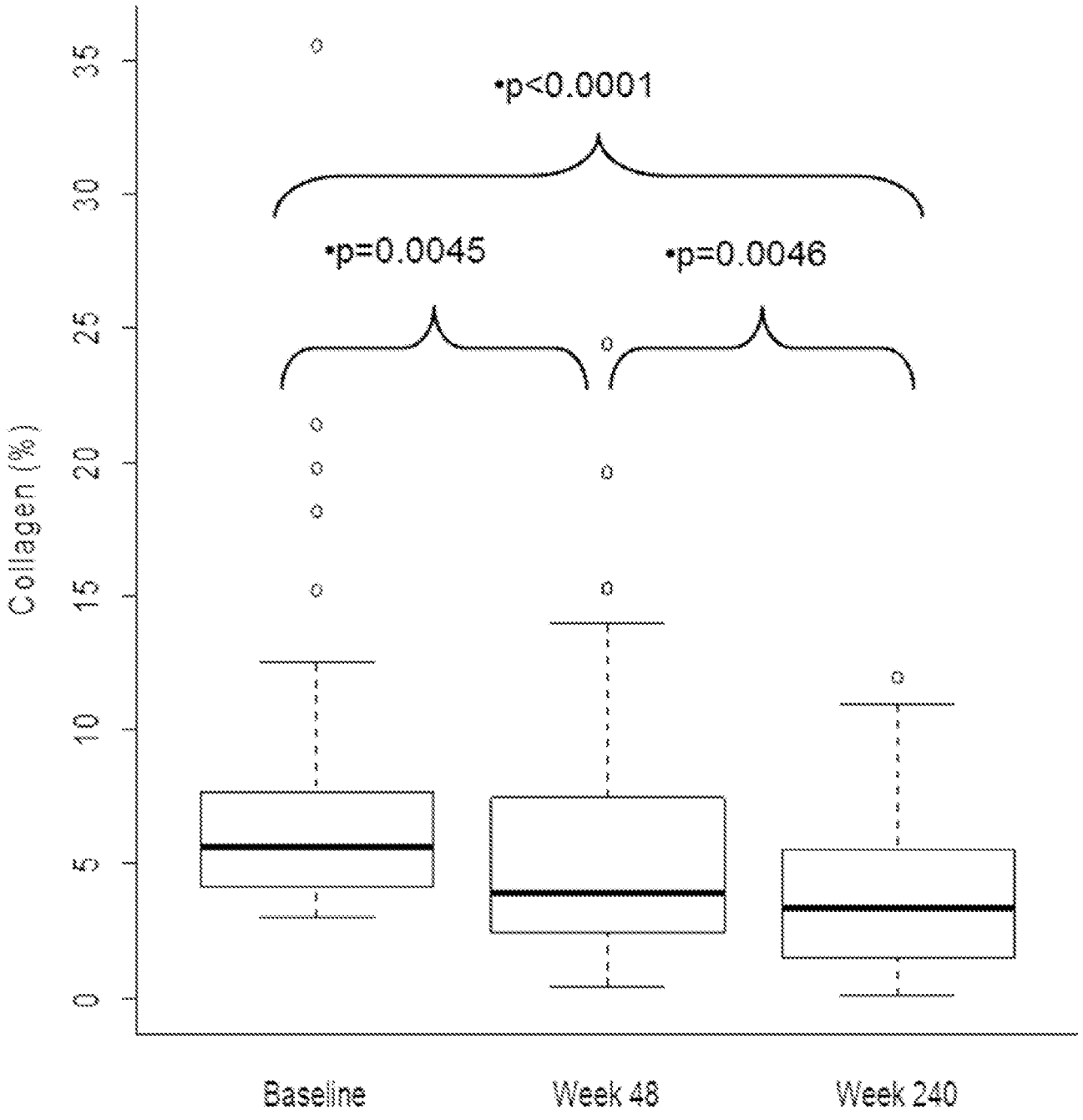

•p<0.0001
•p=0.0045
•p=0.0046
Collagen (%)
0
5
10
15
20
25
30
35
Baseline
Week 48
Week 240

FIG. 34A

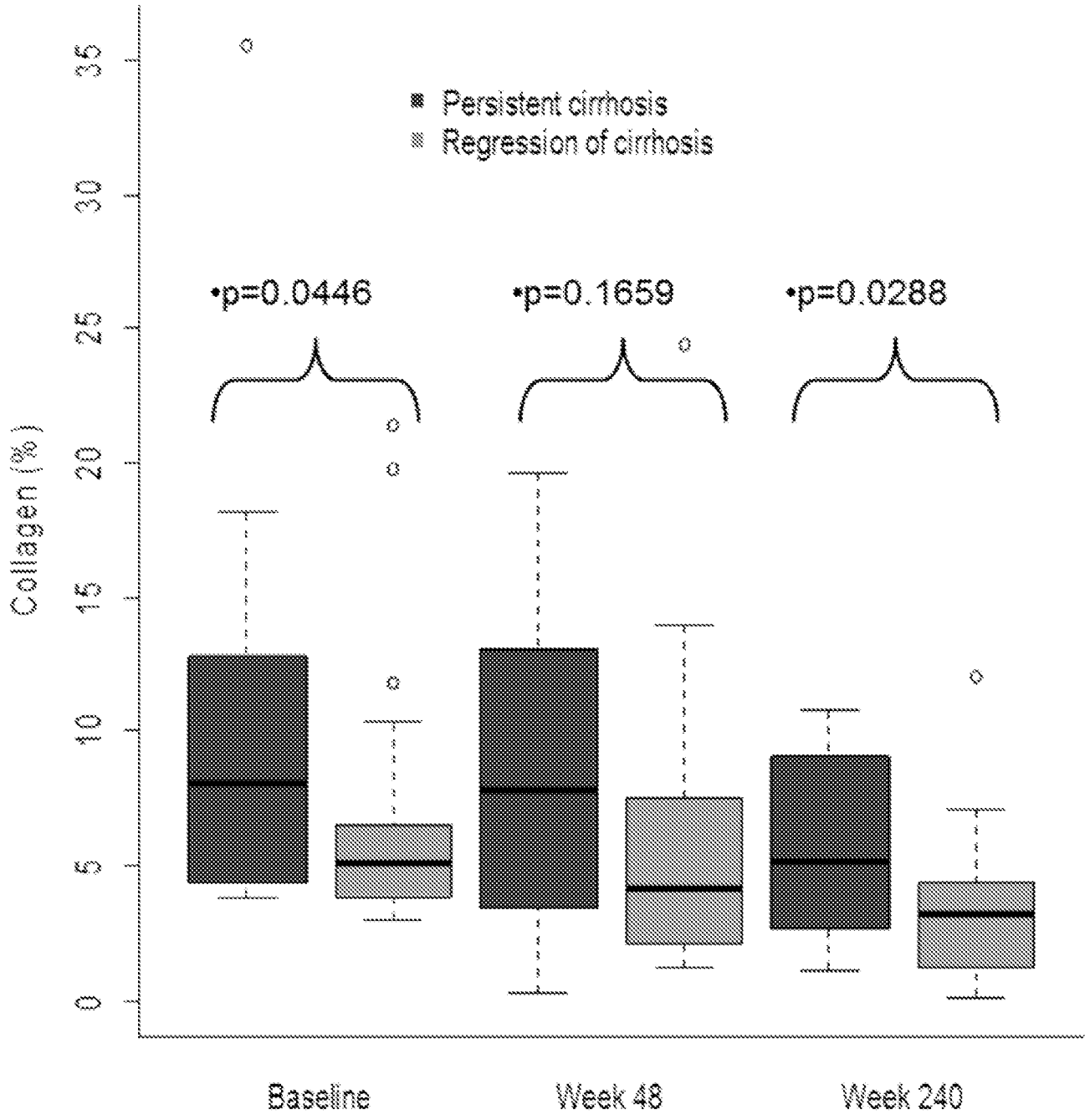

Persistent cirrhosis
Regression of cirrhosis
•p=0.0446
•p=0.1659
•p=0.0288
Collagen (%)
0
5
10
15
20
25
30
35
Baseline
Week 48
Week 240

FIG. 34B