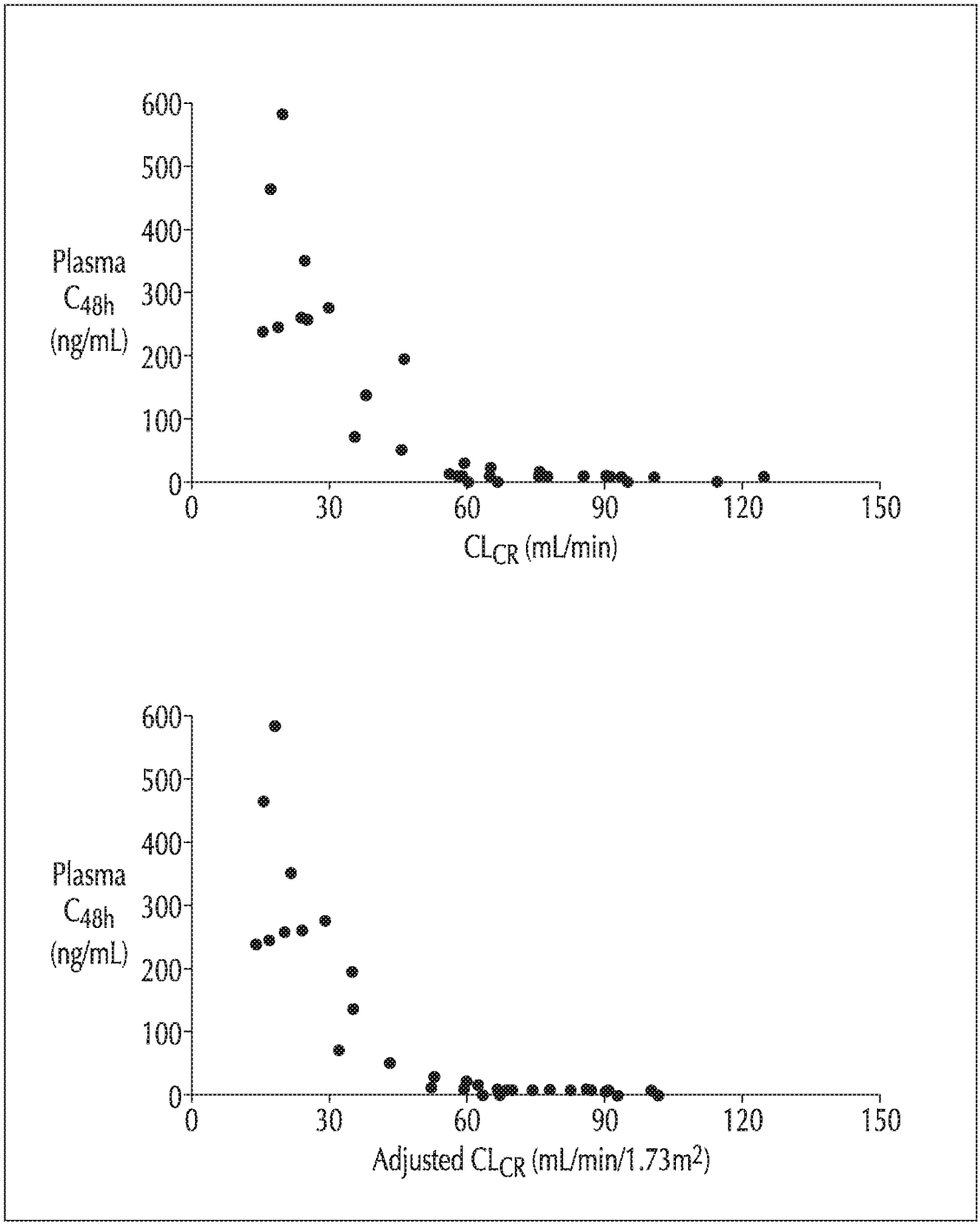

Plasma C_{48h} (ng/mL)
600
500
400
300
200
100
0
0
30
60
90
120
150
CL_{CR} (mL/min)
Plasma C_{48h} (ng/mL)
600
500
400
300
200
100
0
0
30
60
90
120
150
Adjusted CL_{CR} (mL/min/1.73m^2)

FIG. 1A

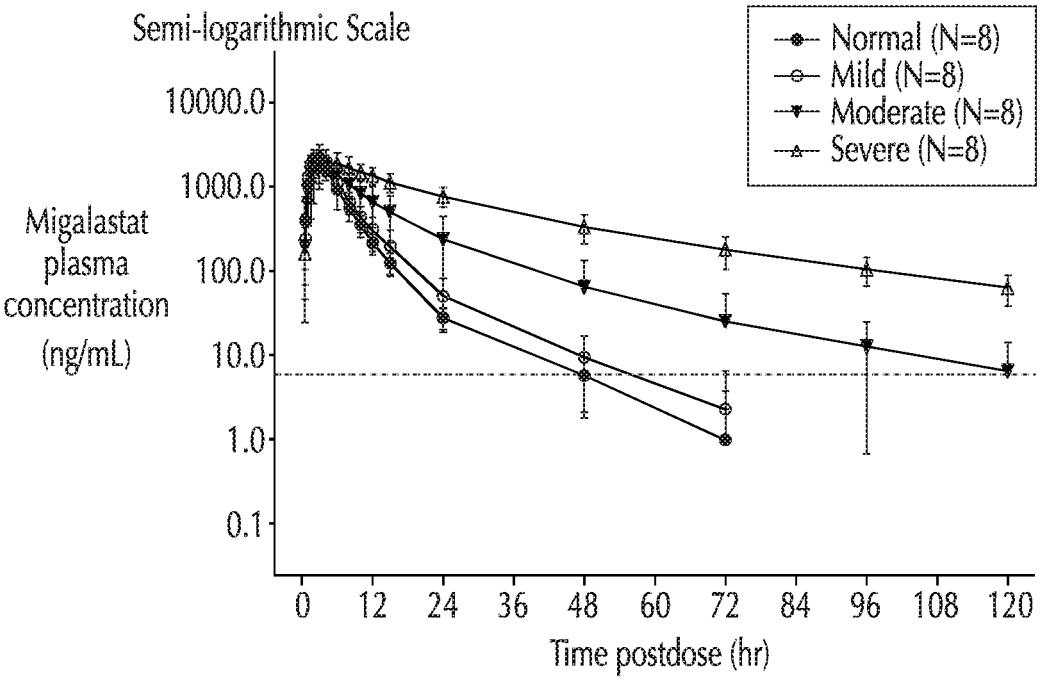

Semi-logarithmic Scale
Normal (N=8)
Mild (N=8)
Moderate (N=8)
Severe (N=8)
Migalastat plasma concentration (ng/mL)
10000.0
1000.0
100.0
10.0
1.0
0.1
0
12
24
36
48
60
72
84
96
108
120
Time postdose (hr)

FIG. 1B

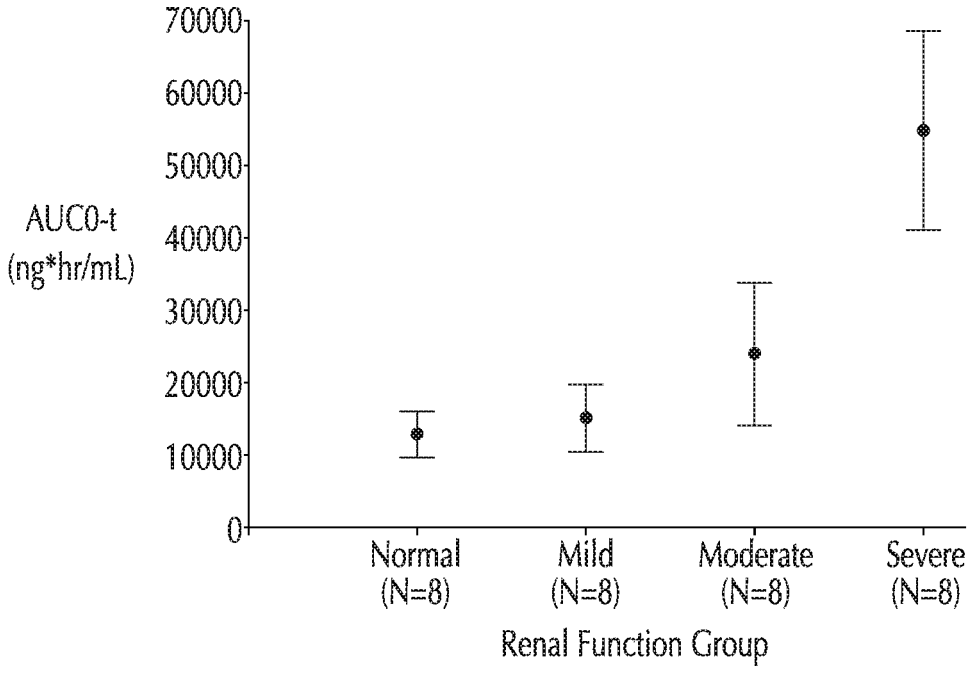

AUC0-t (ng*hr/mL)
70000
60000
50000
40000
30000
20000
10000
0
Normal (N=8)
Mild (N=8)
Moderate (N=8)
Severe (N=8)
Renal Function Group

FIG. 1C

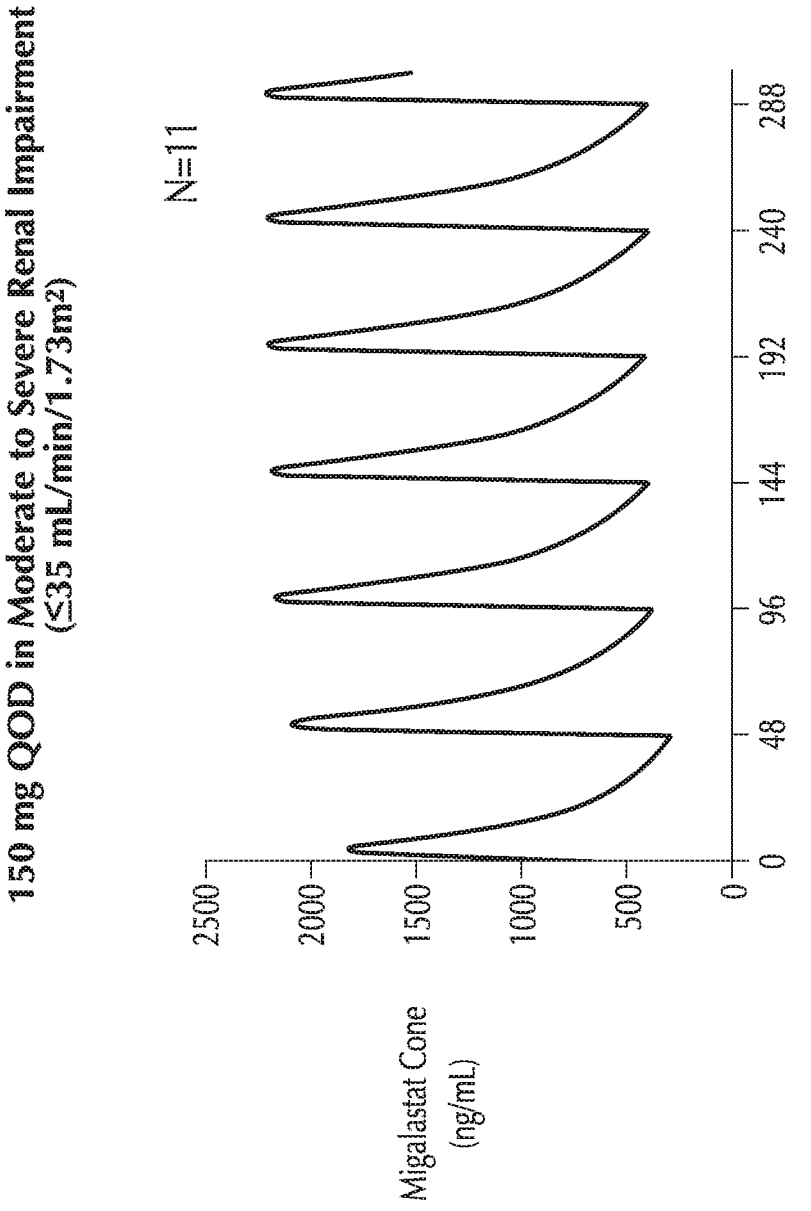

150 mg QOD in Moderate to Severe Renal Impairment
(≤35 mL/min/1.73m²)
N=11
Migalastat Conc
(ng/mL)
2500
2000
1500
1000
500
0
0
48
96
144
192
240
288
Time(hr)

FIG. 2

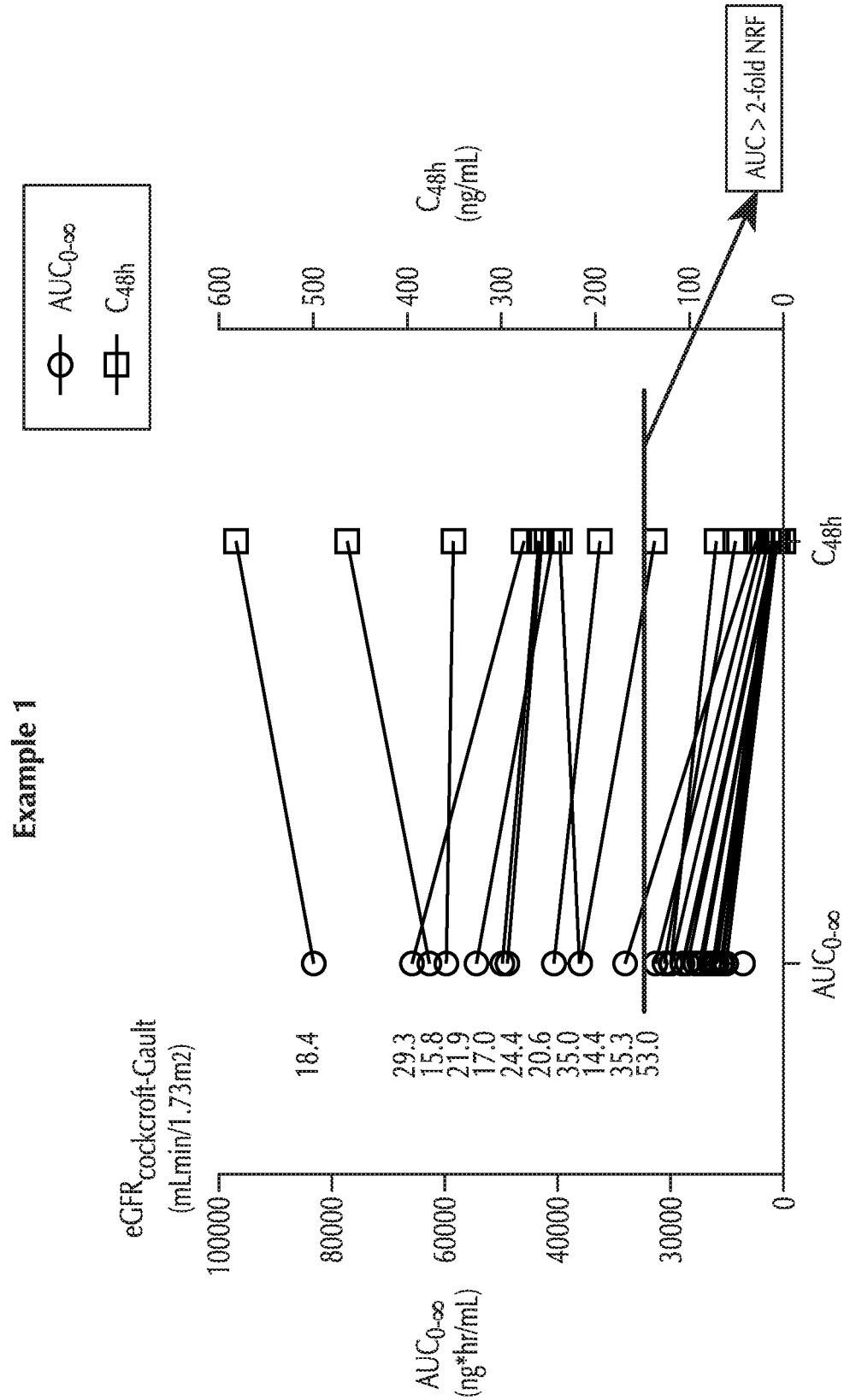

Example 1
AUC0-∞
C48h
C48h (ng/mL)
600
500
400
300
200
100
0
AUC > 2-fold NRF
C48h
AUC0-∞
eGFRcockcroft-Gault (mLmin/1.73m2)
18.4
29.3
15.8
21.9
17.0
24.4
20.6
35.0
14.4
35.3
53.0
100000
80000
60000
40000
30000
0
AUC0-∞ (ng*hr/mL)

FIG. 3

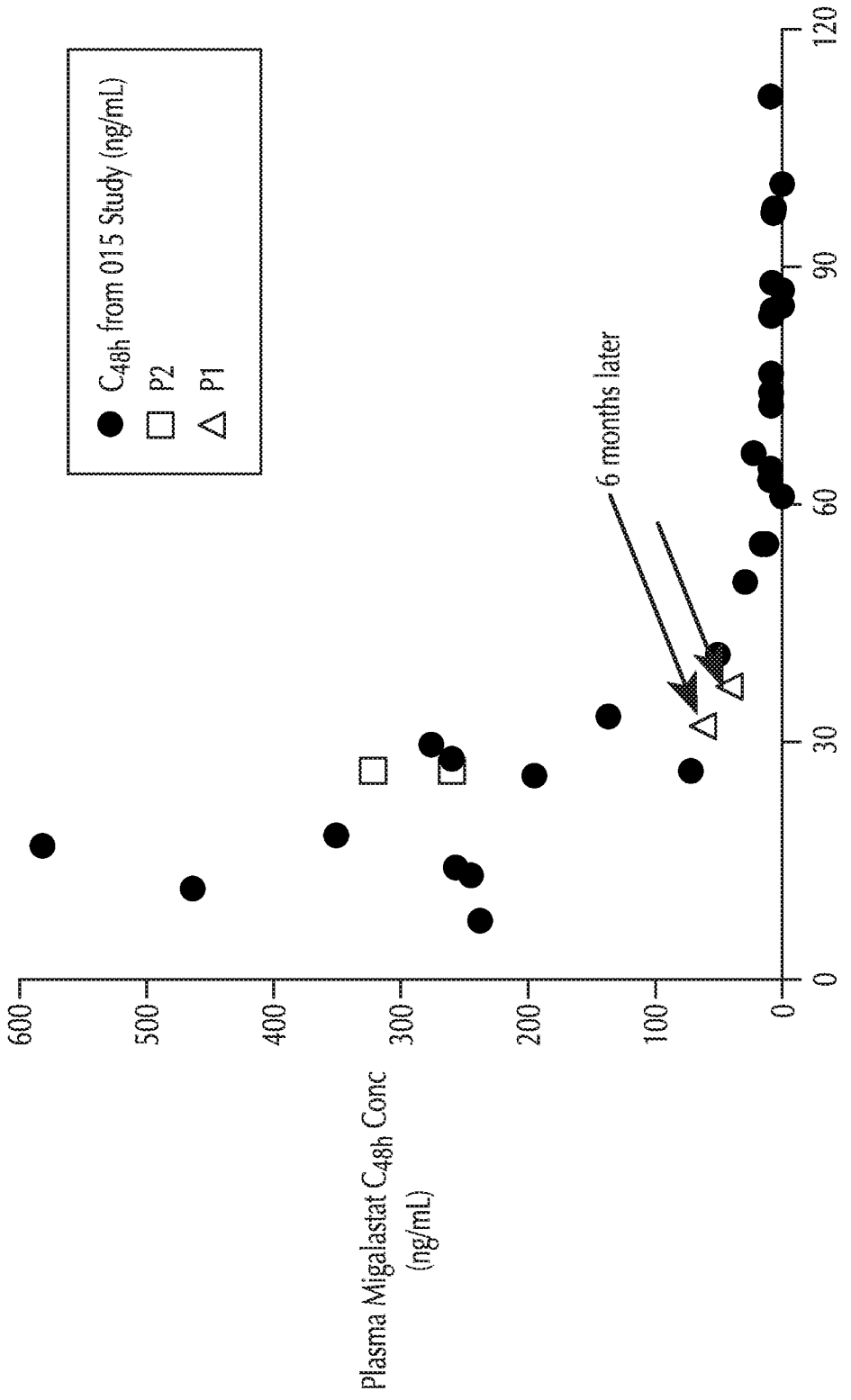

C_{48h} from 015 Study (ng/mL)
P2
P1
6 months later
Plasma Migalastat C_{48h} Conc (ng/mL)
600
500
400
300
200
100
0
0
30
60
90
120
$eGFR_{MDRD}$

FIG. 4

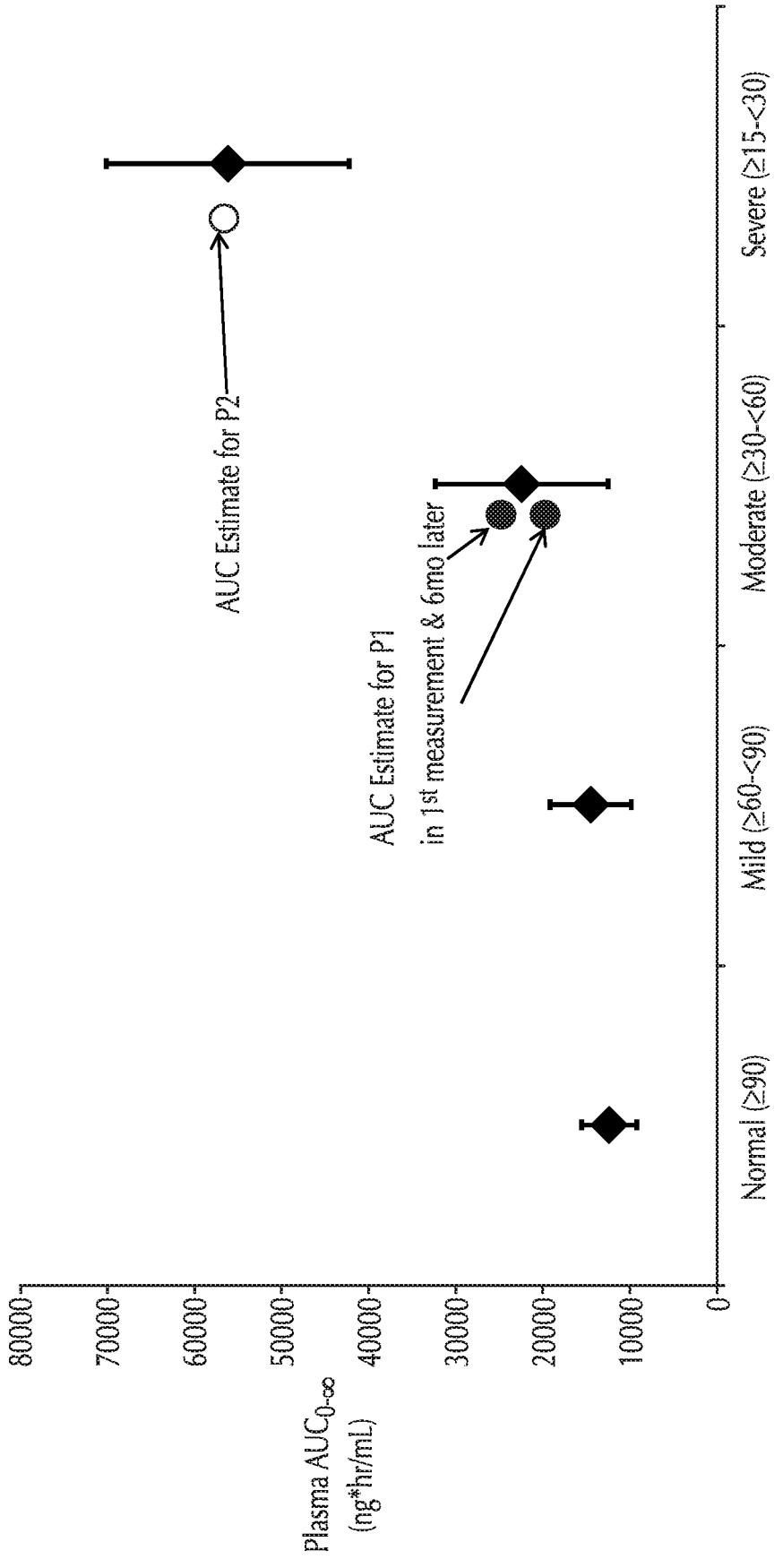

AUC Estimate for P2
AUC Estimate for P1
in 1st measurement & 6mo later
Plasma AUC0-∞
(ng*hr/mL)
80000
70000
60000
50000
40000
30000
20000
10000
0
Normal (≥90)
Mild (≥60-<90)
Moderate (≥30-<60)
Severe (≥15-<30)
Renal Function Group (range mL/min)

FIG. 5

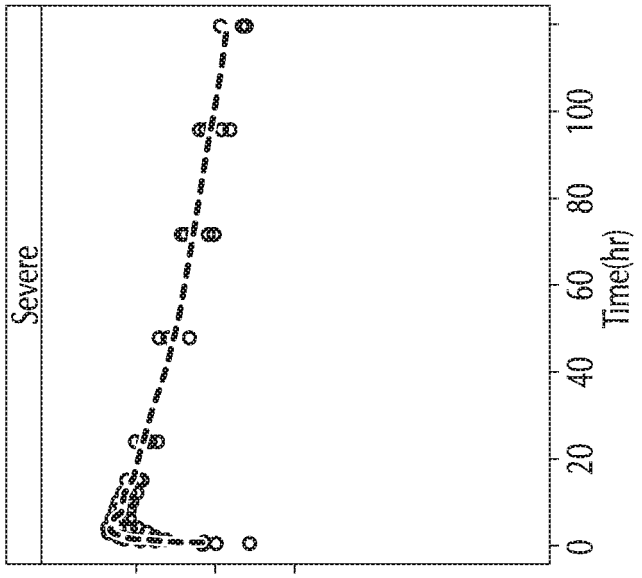


FIG. 6B

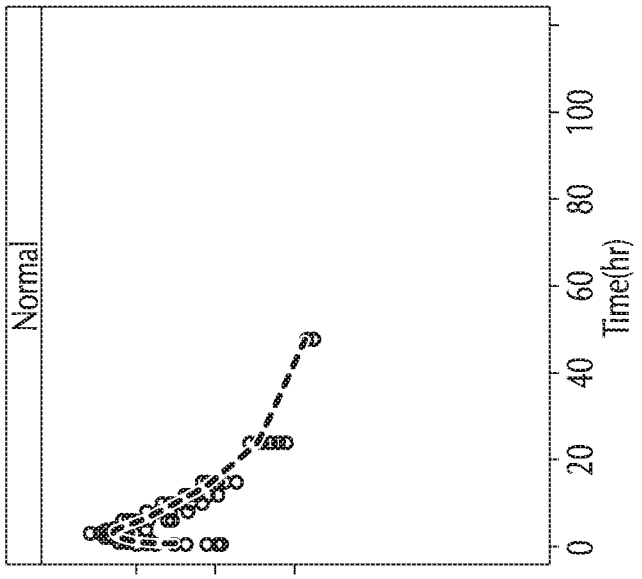


FIG. 6A

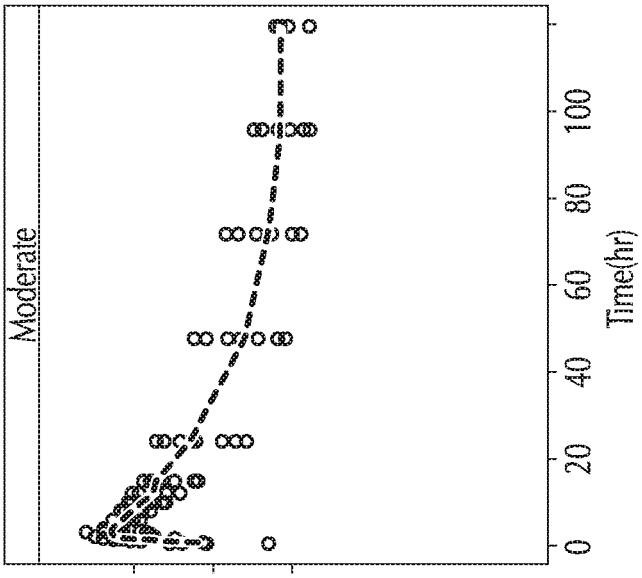


FIG. 6D

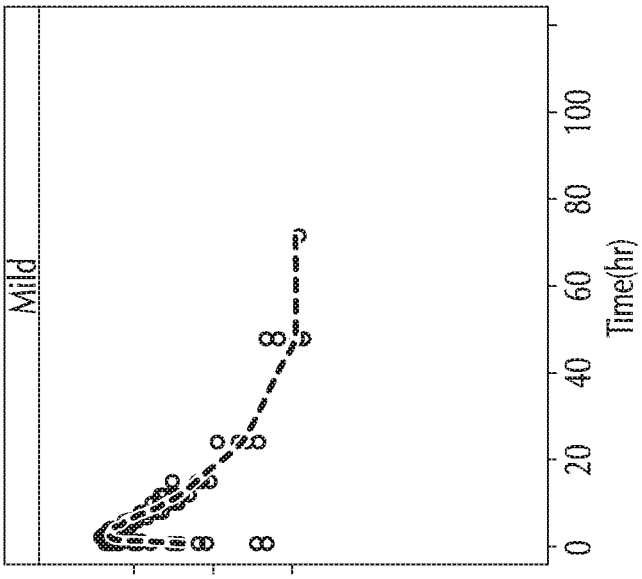


FIG. 6C

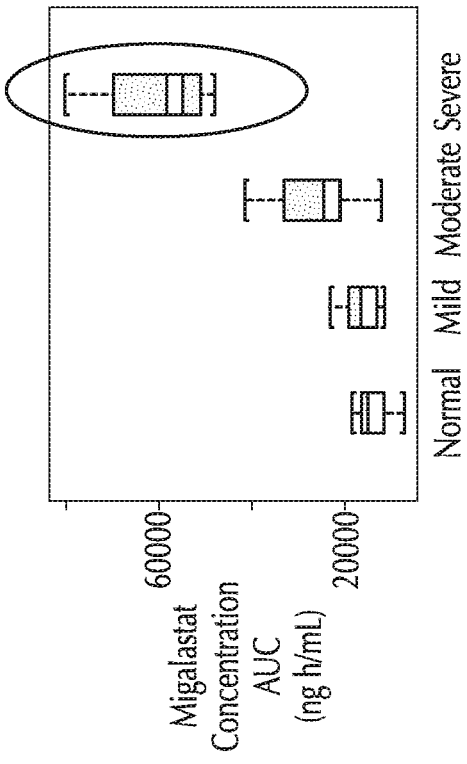


FIG. 7A

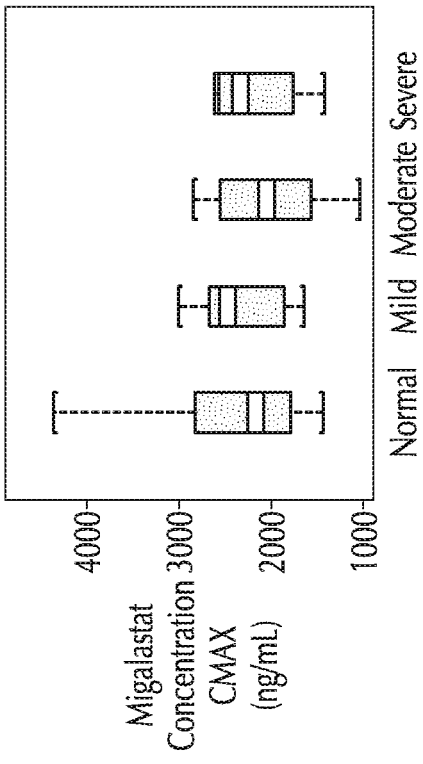


FIG. 7B

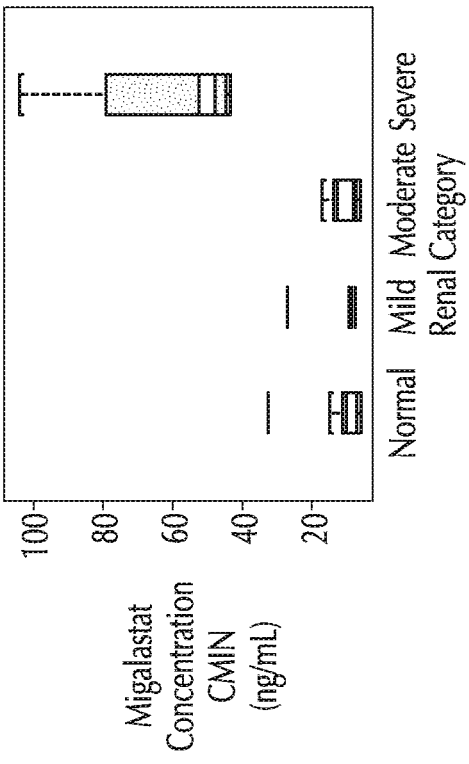


FIG. 7C

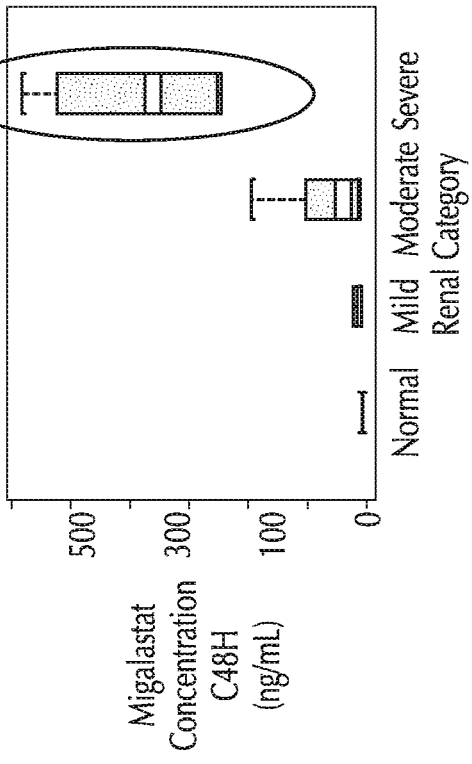


FIG. 7D

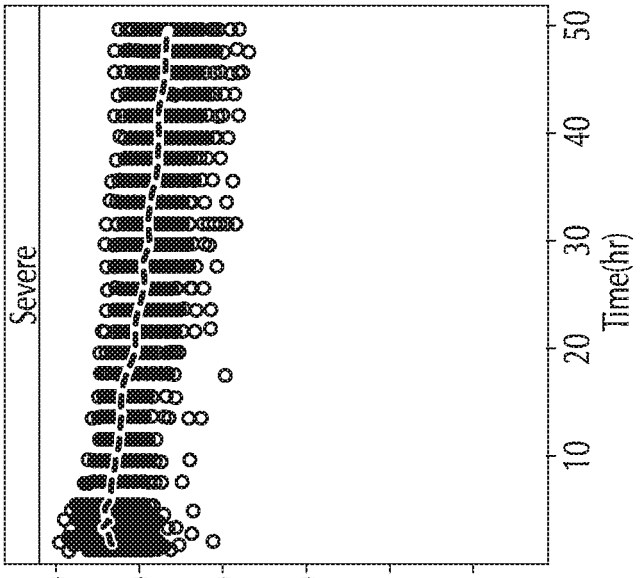


FIG. 8B

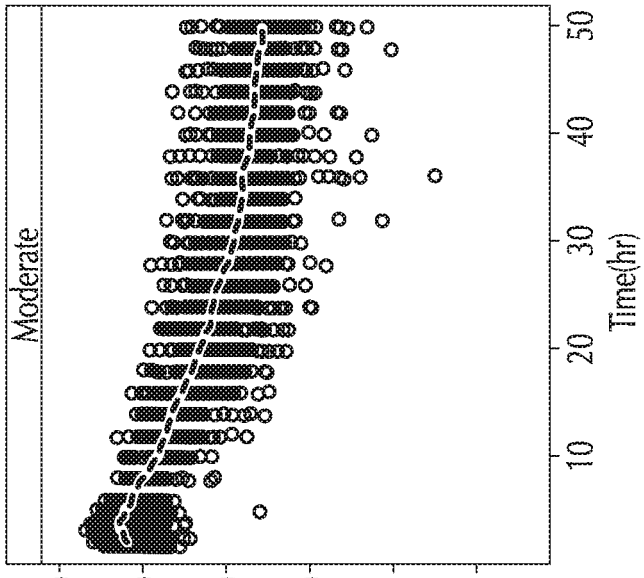


FIG. 8D

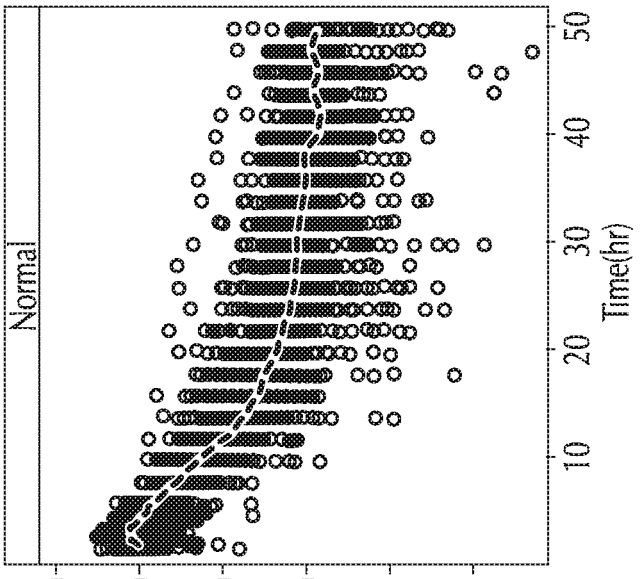


FIG. 8A

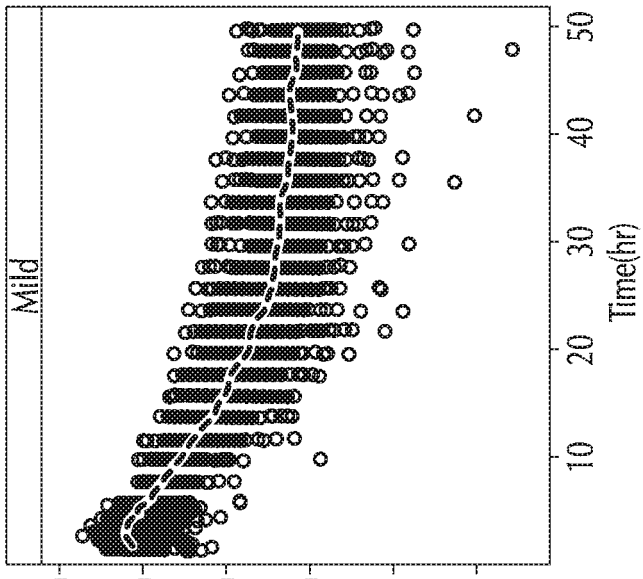


FIG. 8C

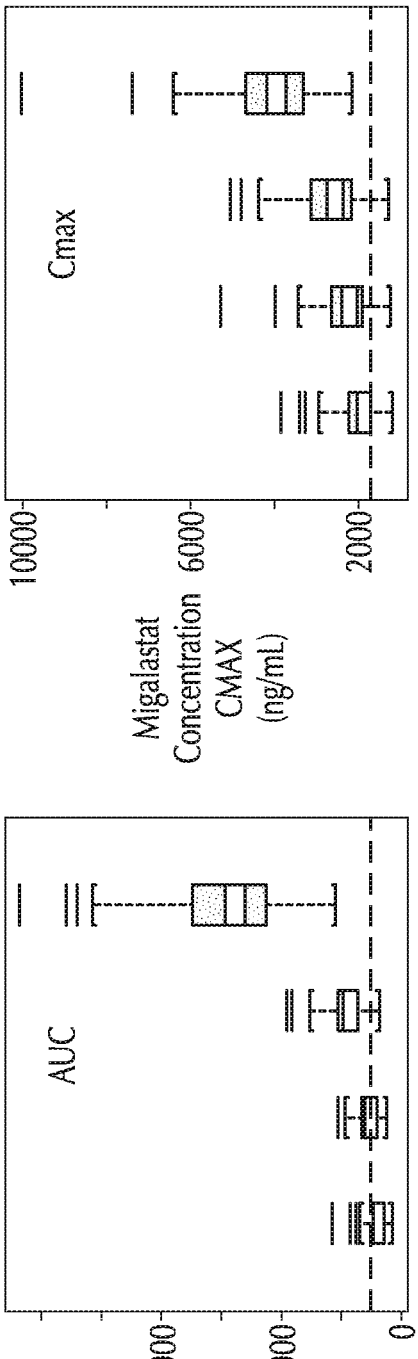


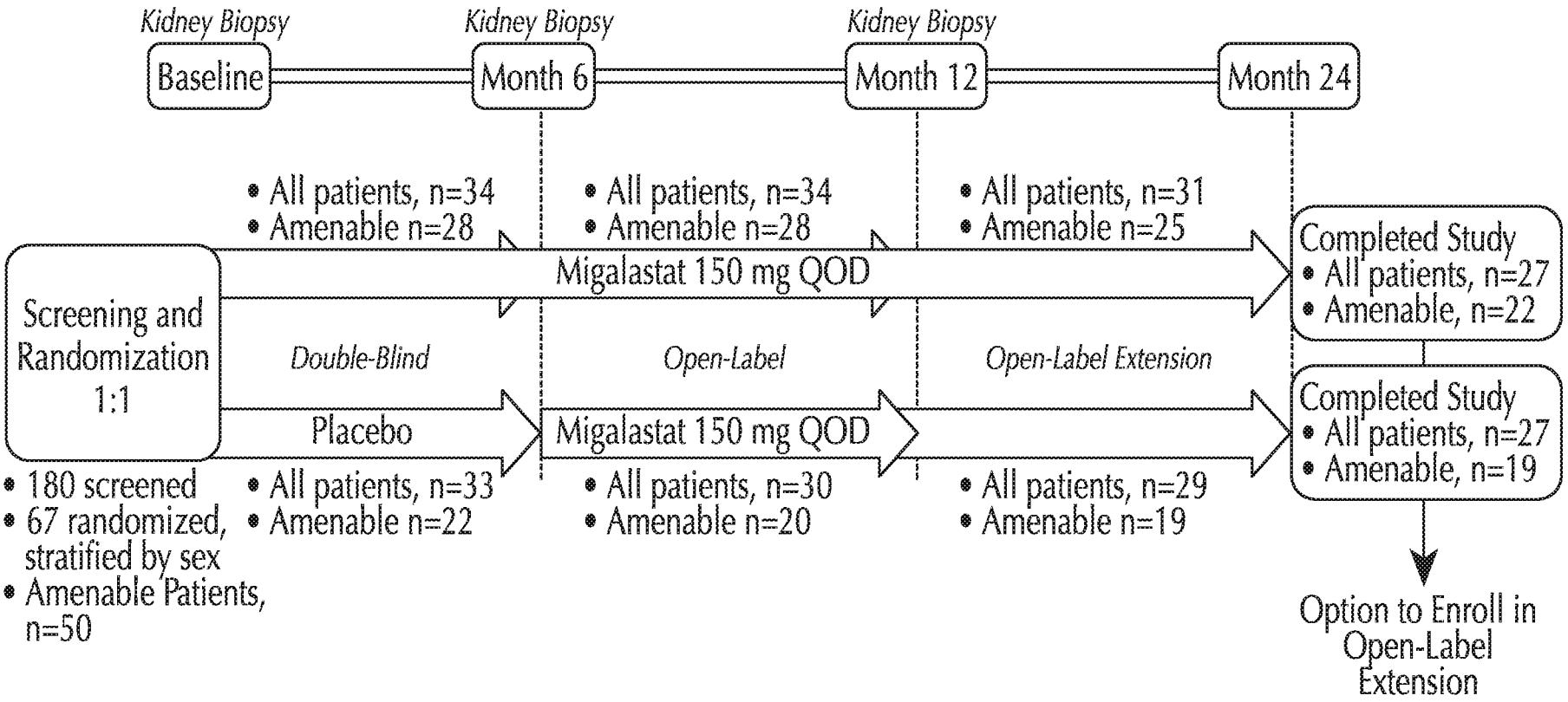
FIG. 9A

FIG. 9B

FIG. 9C

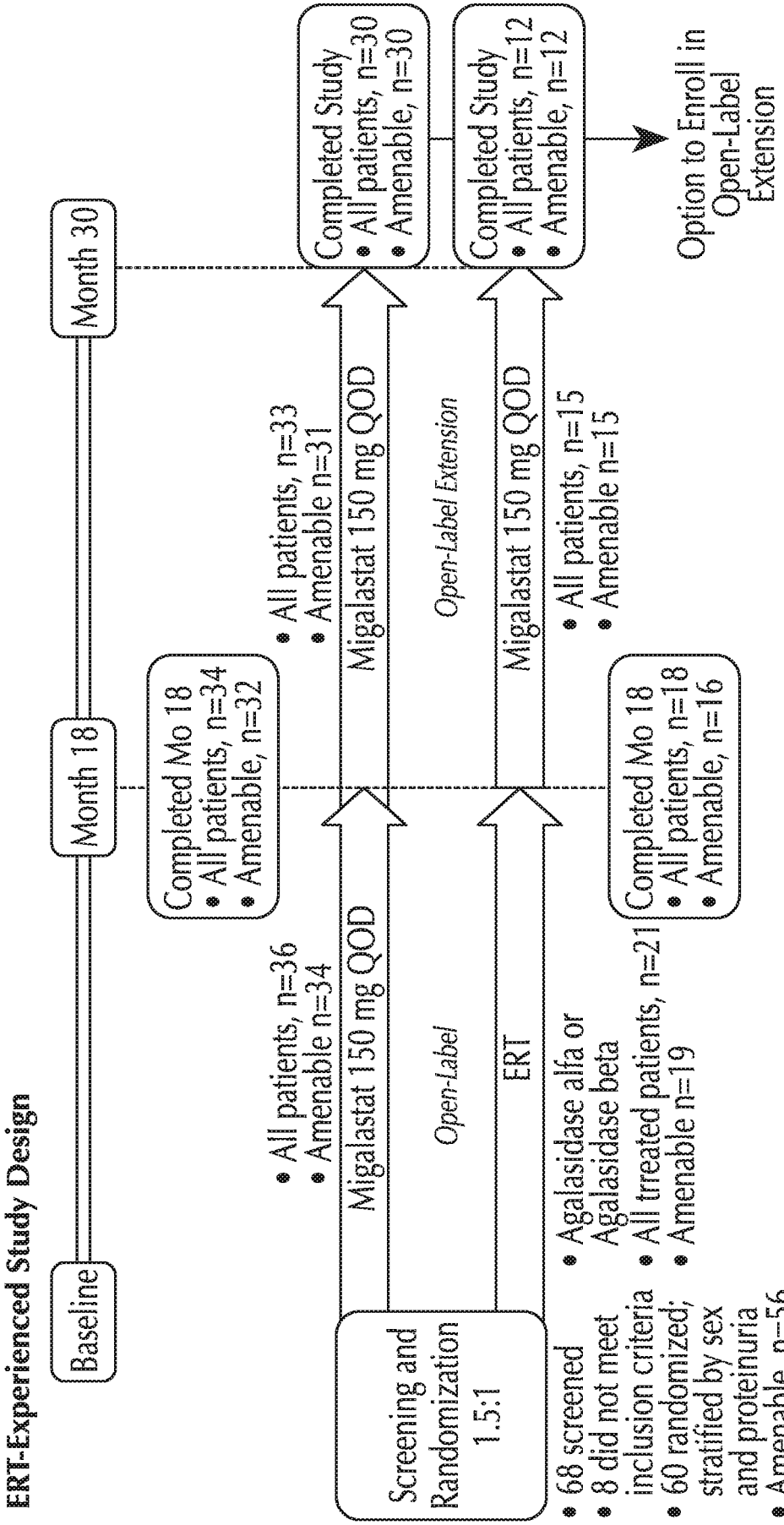
FIG. 9D

ERT-Naïve Study Design



Amenability was determined using the GLP-validated HEK assay, which became available during the phase 3 study, replacing a preliminary HEK assay used for enrolling patients.
Germain DP et al. *N Engl J Med*. 2016;375(6):545-555.

FIG. 10A



Amenability was determined using the GLP-validated HEK assay, which became available during the study, replacing a preliminary HEK assay used for enrolling patients.
Hughes DA et al. / *Med Genet.* 2017;54;288-296.

FIG. 10B

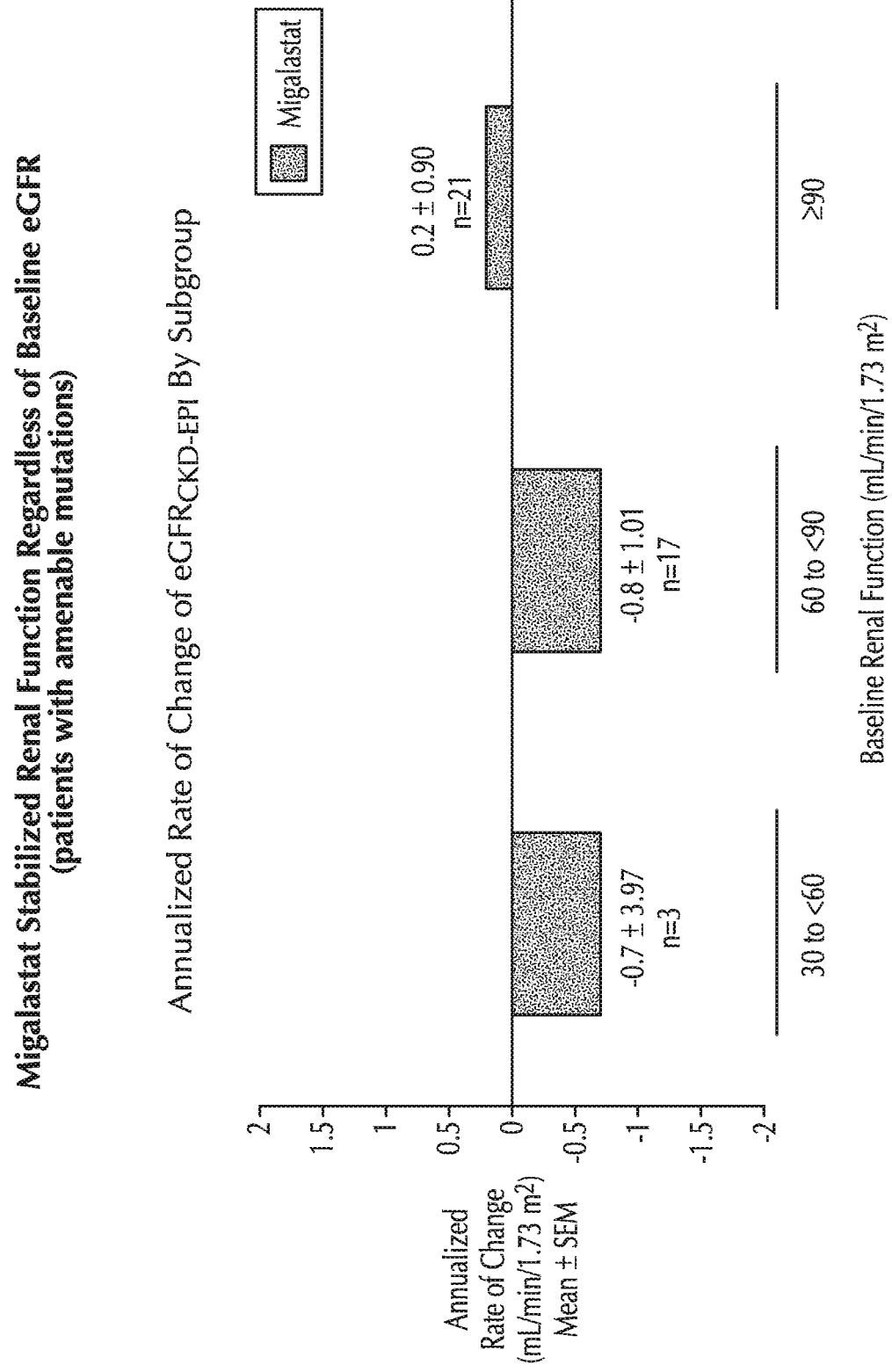
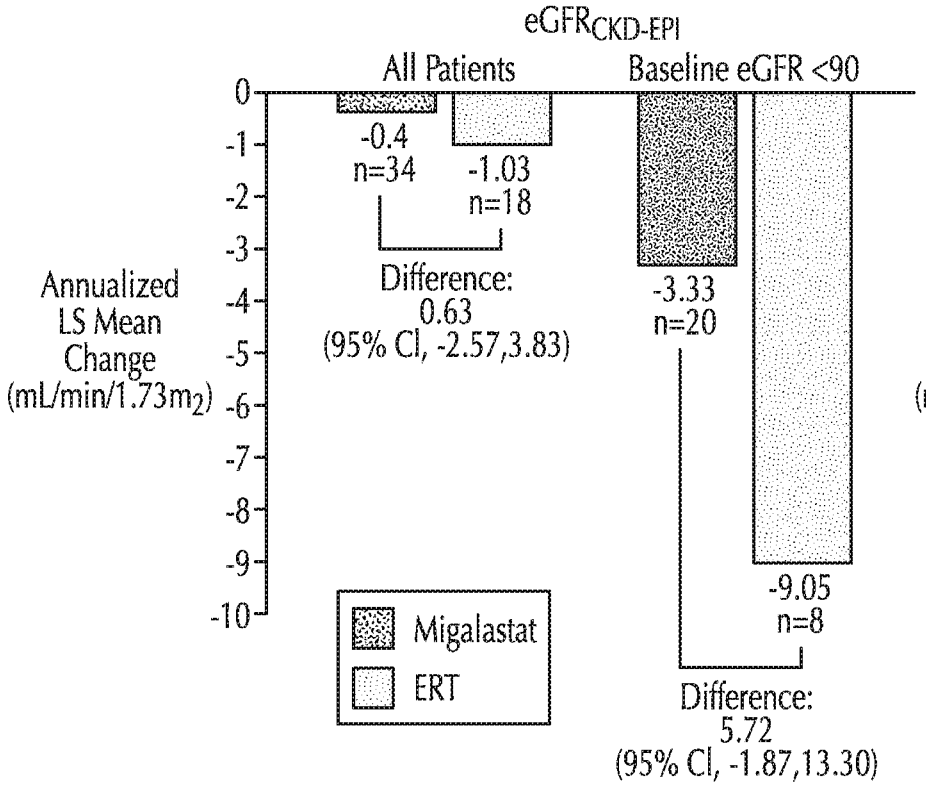

Migalastat Stabilized Renal Function Regardless of Baseline eGFR
(patients with amenable mutations)
Annualized Rate of Change of eGFRCKD-EPI By Subgroup
Migalastat
Annualized Rate of Change (mL/min/1.73 m2) Mean ± SEM
2
1.5
1
0.5
0
-0.5
-1
-1.5
-2
-0.7 ± 3.97
n=3
-0.8 ± 1.01
n=17
0.2 ± 0.90
n=21
30 to <60
60 to <90
≥90
Baseline Renal Function (mL/min/1.73 m2)

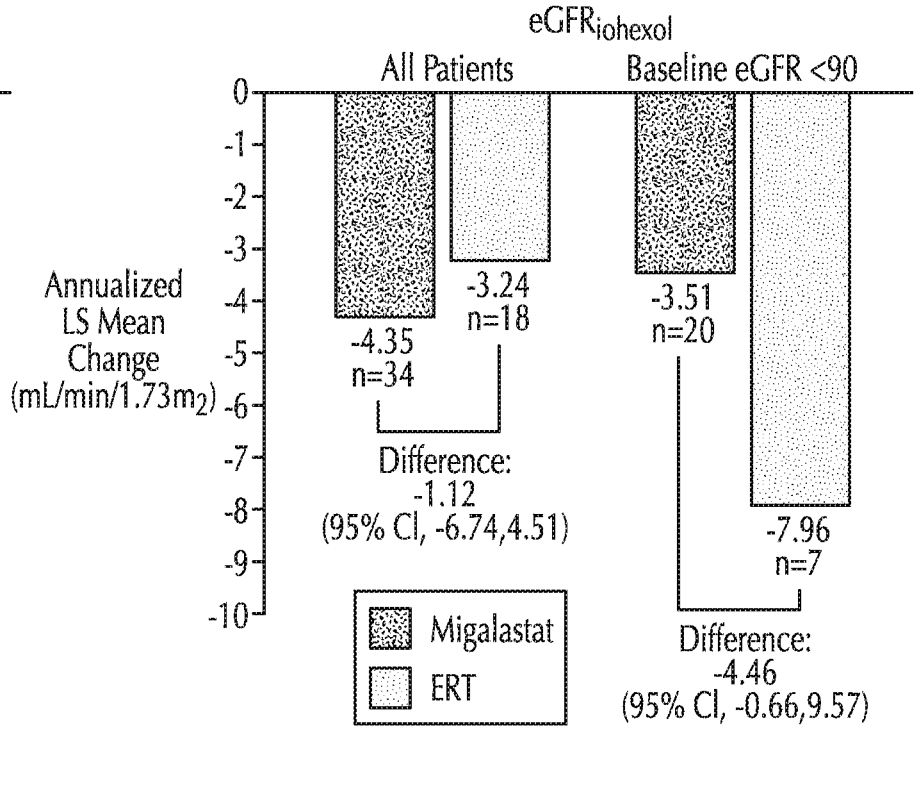
FIG. 11

At Month 18, Migalastat and ERT Had Comparable Favorable Effects on Renal Function using both GFR Methods (patients with amenable mutations)



LS mean and 95% CI based on ANCOVA that includes treatment, baseline GFR, sex, age,and 24-hour urine protein. LS = least-squares.

FIG. 12A



LS mean and 95% CI based on ANCOVA that includes treatment, baseline GFR, sex, age,and 24-hour urine protein. LS = least-squares.

FIG. 12B

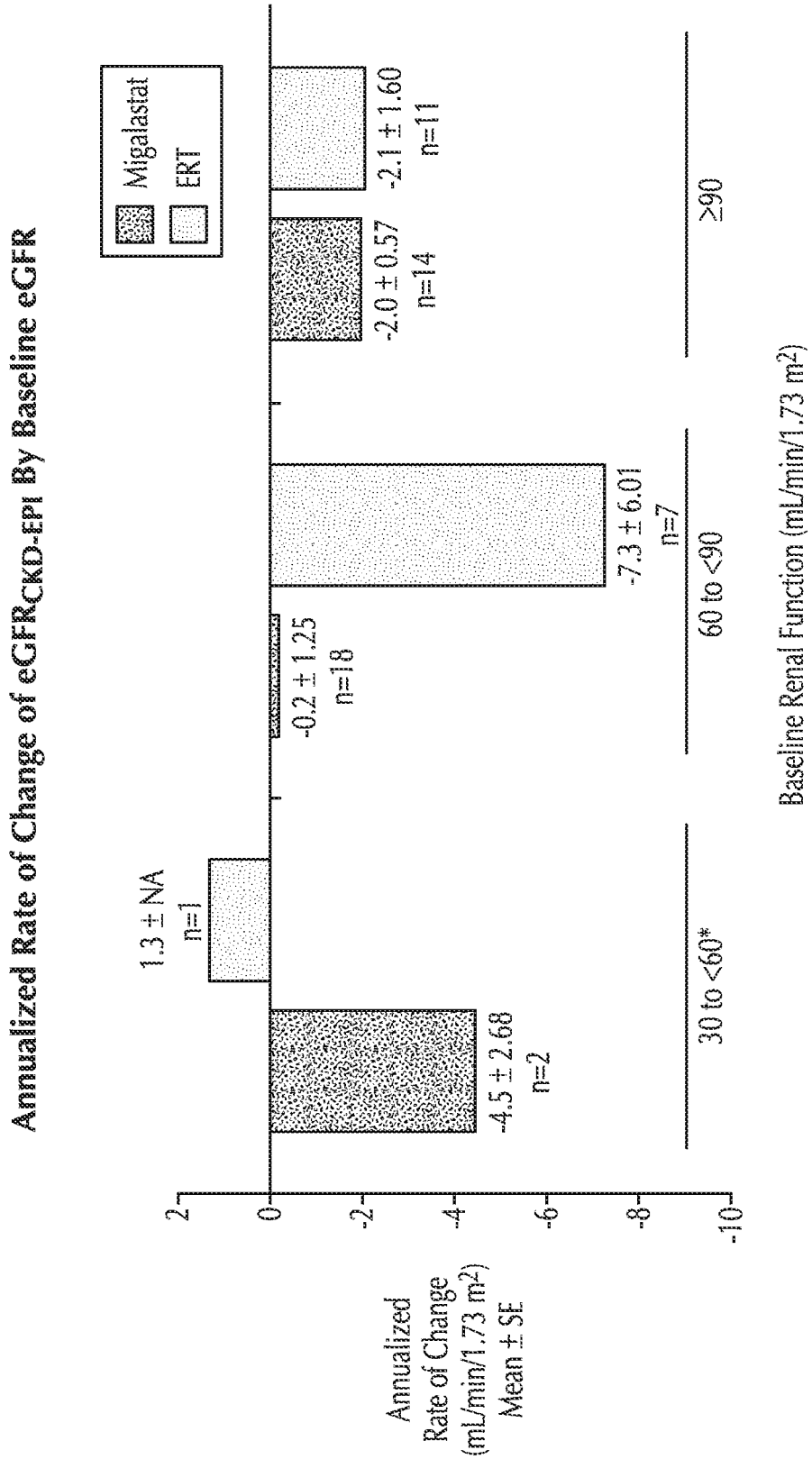

Annualized Rate of Change of eGFRCKD-EPI By Baseline eGFR
Migalastat
ERT
1.3 ± NA
n=1
-4.5 ± 2.68
n=2
-0.2 ± 1.25
n=18
-7.3 ± 6.01
n=7
-2.0 ± 0.57
n=14
-2.1 ± 1.60
n=11
2
0
-2
-4
-6
-8
-10
Annualized Rate of Change (mL/min/1.73 m2) Mean ± SE
30 to <60*
60 to <90
≥90
Baseline Renal Function (mL/min/1.73 m2)
*Inconclusive due to low n

FIG. 13

ccttctgtaggggcagagaggttctacttcattactgcgtctcctgggaaggccatcag 60
gactgctggctaaagtgggaaccaggactctttgtgagttaagaatttgtgtatttatat 120
gtgtgttatacacatttttaaaaaactgtaacgacatcaggttgagcagtcgtctccgg 180
gtggtgaattatgtgtatttttaaattttatactatattgttatttttcaaatgttcgaa 240
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gataaaattcacttggggcctcccttacagacaatcaggcagtggagactgagtgcctg 420
aatggatagaccagcactcagaccactattttcagtatctgtttttcttaactcagggcc 480
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FIG. 14A

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aaaacaaggaaaaaaagaaacagccctcatgacacttagaaagtagaatagctggctgtt 5700
atctgaacattgaattgtaaggcttatcaggtggactttgcattccatcagcagacaatt 5760

FIG. 14B

```
ttttttttttttttttttgagatggagtctcattctgtctcccaggctggagggcagtg      5820
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ccatctctcccaggttccaaccacttctcaccatccccactgctgtaattatagcctaag      8580
ctaccatcacctggaaagtcatccttgtgtcttcccctttatttcaccattcatgtcctg      8640
```

FIG. 14C

tctatcaacagtccttccaccagtatctctaaaatatctcctgaatcagcccacttcctt 8700
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tcgggactttgagacccgcctggacaacatggtgaaaccccatttctaataaaaatataa 11460
aaattagccaggtgtggtggcgcacctgtggtcccagctactctgggggctgaggcatga 11520

FIG. 14D

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gaatcgcttgaacccgggagtggaggttgcattgagctgagatcatgccacctcactcca      11580
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agaccagcctggctaacatagtaaagccctgtctctactaaaaatacaaaaattagccag      11760
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acctgggaggcagaggctgcagtgagctgaggttgtaccaattgcactccagcctaggta      12360
acgagcaacactccatctcaaaaaaagaaaaaaaaaaagatgtataatttggaactgtta      12420
agaggcattttaaaga                                                  12436
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FIG. 14E

```
MQLRNPELHL GCALALRFLA LVSWDIPGAR ALDNGLARTP TMGWLHWERF MCNLDCQEEP   60
DSCISEKLFM EMAELMVSEG WKDAGYEYLC IDDCWMAPQR DSEGRLQADP QRFPHGIRQL  120
ANYVHSKGLK LGIYADVGNK TCAGFPGSFG YYDIDAQTFA DWGVDLLKFD GCYCDSLENL  180
ADGYKHMSLA LNRTGRSIVY SCEWPLYMWP FQKPNYTEIR QYCNHWRNFA DIDDSWKSIK  240
SILDWTSFNQ ERIVDVAGPG GWNDPDMLVI GNFGLSWNQQ VTQMALWAIM AAPLFMSNDL  300
RHISPQAKAL LQDKDVIAIN QDPLGKQGYQ LRQGDNFEVW ERPLSGLAWA VAMINRQEIG  360
GPRSYTIAVA SLGKGVACNP ACFITQLLPV KRKLGFYEWT SRLRSHINPT GTVLLQLENT  420
MQMSLKDLL                                                          429
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FIG. 15