(SEQ ID NO:1).

>gi|11184232|ref|NM_017545.2| Homo sapiens hydroxyacid oxidase (glycolate oxidase) 1 (HAO1), mRNA

CTGGGATAGCAATAACCTGTGAAAATGCTCCCCCGGCTAATTTGTATCAATGATTATGAACAACATGCTA
AATCAGTACTTCCAAAGTCTATATATGACTATTACAGGTCTGGGGCAAATGATGAAGAAACTTTGGCTGA
TAATATTGCAGCATTTTCCAGATGGAAGCTGTATCCAAGGATGCTCCGGAATGTTGCTGAAACAGATCTG
TCGACTTCTGTTTTAGGACAGAGGGTCAGCATGCCAATATGTGTGGGGGCTACGGCCATGCAGCGCATGG
CTCATGTGGACGGCGAGCTTGCCACTGTGAGAGCCTGTCAGTCCCTGGGAACGGGCATGATGTTGAGTTC
CTGGGCCACCTCCTCAATTGAAGAAGTGGCGGAAGCTGGTCCTGAGGCACTTCGTTGGCTGCAACTGTAT
ATCTACAAGGACCGAGAAGTCACCAAGAAGCTAGTGCGGCAGGCAGAGAAGATGGGCTACAAGGCCATAT
TTGTGACAGTGGACACACCTTACCTGGGCAACCGTCTGGATGATGTGCGTAACAGATTCAAACTGCCGCC
ACAACTCAGGATGAAAAATTTTGAAACCAGTACTTTATCATTTTCTCCTGAGGAAAATTTTGGAGACGAC
AGTGGACTTGCTGCATATGTGGCTAAAGCAATAGACCCATCTATCAGCTGGGAAGATATCAAATGGCTGA
GAAGACTGACATCATTGCCAATTGTTGCAAAGGGCATTTTGAGAGGTGATGATGCCAGGGAGGCTGTTAA
ACATGGCTTGAATGGGATCTTGGTGTCGAATCATGGGGCTCGACAACTCGATGGGGTGCCAGCCACTATT
GATGTTCTGCCAGAAATTGTGGAGGCTGTGGAAGGGAAGGTGGAAGTCTTCCTGGACGGGGGTGTGCGGA
AAGGCACTGATGTTCTGAAAGCTCTGGCTCTTGGCGCCAAGGCTGTGTTTGTGGGGAGACCAATCGTTTG
GGGCTTAGCTTTCCAGGGGGAGAAAGGTGTTCAAGATGTCCTCGAGATACTAAAGGAAGAATTCCGGTTG
GCCATGGCTCTGAGTGGGTGCCAGAATGTGAAAGTCATCGACAAGACATTGGTGAGGAAAAATCCTTTGG
CCGTTTCCAAGATCTGACAGTGCACAATATTTTCCCATCTGTATTATTTTTTTTCAGCATGTATTACTTG
ACAAAGAGACACTGTGCAGAGGGTGACCACAGTCTGTAATTCCCCACTTCAATACAAAGGGTGTCGTTCT
TTTCCAACAAAATAGCAATCCCTTTTATTTCATTGCTTTTGACTTTTCAATGGGTGTCCTAGGAACCTTT
TAGAAAGAAATGGACTTTCATCCTGGAAATATATTAACTGTTAAAAAGAAAACATTGAAAATGTGTTTAG
ACAACGTCATCCCCTGGCAGGCTAAAGTGCTGTATCCTTTAGTAAAATTGGAGGTAGCAAACACTAAGGT
GAAAAGATAATGATCTCATTGTTTATTAACCTGTATTCTGTTTACATGTCTTTAAAACAGTGGTTCTTAA
ATTGTAAGCTCAGGTTCAAAGTGTTGGTAATGCCTGATTCACAACTTTGAGAAGGTAGCACTGGAGAGAA
TTGGAATGGGTGGCGGTAATTGGTGATACTTCTTTGAATGTAGATTTCCAATCACATCTTTAGTGTCTGA
ATATATCCAAATGTTTTAGGATGTATGTTACTTCTTAGAGAGAAATAAAGCATTTTTGGGAAGAAT

FIG. 1

(SEQ ID NO:2)
>gi|133893166|ref|NM_010403.2| Mus musculus hydroxyacid oxidase 1, liver (Hao1), mRNA
GGTTGCCCTACCCTGCCACAATGTTGCCTCGACTGGTCTGCATCAGTGATTATGAACAGCATGTCCGATC
AGTGCTTCAGAAGTCAGTGTATGACTATTACAGGTCTGGGGCAAATGATCAGGAGACGTTAGCTGATAAC
ATCCAAGCATTTTCTAGATGGAAGCTCTATCCACGGATGCTTCGCAACGTTGCTGATATCGATCTGTCAA
CTTCTGTTTTAGGACAGAGAGTCAGCATGCCAATATGTGTTGGGGCTACTGCCATGCAGTGCATGGCTCA
CGTGGACGGGGAGCTGGCCACTGTGCGAGCCTGTCAGACCATGGGAACTGGCATGATGCTGAGTTCTTGG
GCTACCTCCTCAATAGAAGAAGTGGCAGAAGCTGGCCCAGAGGCACTTCGCTGGATGCAACTGTACATCT
ACAAAGACCGTGAGATCAGCAGACAGATAGTGAAGCGAGCTGAGAAGCAGGGTTACAAGGCCATATTTGT
GACTGTGGACACCCCTTACCTGGGCAACCGCATTGATGACGTGCGGAACAGGTTCAAGCTGCCACCACAA
CTCAGGATGAAAAACTTTGAAACCAATGATTTGGCATTTTCTCCTAAGGGAAATTTTGGAGACAACAGTG
GACTTGCTGAATATGTGGCACAAGCTATAGACCCATCTCTCAGCTGGGATGATATTACATGGCTCAGACG
ATTGACATCACTGCCTATTGTTGTAAAGGGCATTTTGAGAGGTGATGATGCCAAGGAAGCTGTTAAACAT
GGTGTGGATGGGATCTTGGTGTCGAATCATGGGGCGCGACAACTGGATGGGGTGCCAGCTACTATTGATG
TCCTGCCAGAGATTGTTGAGGCTGTGGAAGGGAAGGTAGAAGTCTTCCTGGATGGGGGAGTAAGGAAAGG
TACTGATGTTCTCAAAGCTCTGGCCCTAGGAGCCAAGGCCGTTTTTGTGGGAAGACCCATCATCTGGGGC
TTGGCTTTCCAGGGGGAGAAAGGTTTCAAGATGTCCTCGAGATATTGAAGGAAGAATTCCGACTGGCCA
TGGCTCTGAGTGGGTGCCAGAATGTGGAAAGTCATCGACAAGACATTGGTGAGGAAAAATCCTTTGGCTGT
TTCCAAGATCTGACAGTGCACAATATTTTCCCATCTGTATTATTTTTTTTCCAGCGTGGATTACTTGACA
AAGAGACACTGTGCAGAGGGTGACCACAGACTGTAACTCCCCACTTCTATACAAAGGGTGTCGTTCTTTT
CCAACAAAATAGCCACCCCTTTTCCTTCATTGCTTTTGACTTTTCAATGGGTGTCCTAGGAACCTTCTAG
AAAGAAATGGACTTGCATCCTGGAAATATATTAACTGTTAAAAAGAAAACATTGAAAATGTGTTTGGGCA
ACGTCATCCCCTGGCAGGCTAAAGTGCTGGGGAACAAAAGATATCCTCTGGTGAGATTGCAGGTAGCATG
CTGAAGTGAAAGATACTGACCTCACTGTTCATTAACCTGTCTTCTGTTTAGATTTCCTTAAGACAGTGGC
TCTTACAGTTTGCACTTGGCTTTGAAATGCTGGAAATGCCCAGAGAAACATGAGGTTTGGATTTGCCATG
TTGAGAAAATAGCACCAGGTAGAATTGAAATGGATGGTGGTAATTTGTGATTTTTTTTCTAGAAACTTTT
CATTTTTTAACACCCTATTTTTTTGAAGGTAGATTTTTAGCTATATATCACACGTCTGAATATGTCTGGA
TGTTTTGTGGCACTCATTGCATTTGAAAGGGATGTGTCTAGTCCAGTTGGGACCACATGGAGCTATTTTT
ACTTTTGAACTTTGTCTCCTCATTCTCATTTTAAAATAAGTGTTGACTTCCTAATTCCTCTTGAATCTTT
TTTGATTTTCTCACTTTTCCTCATTTATAGTCACATTCAGTGTAAAGTACATATTTTGTGGGGTCCGTGA
TGAATAAAGATTTGAAATTCTTGTTCAGAAGGAAGGCAAAAAAAAAAAAAAAGTCTTTCCTTTTATCACA

FIG. 2

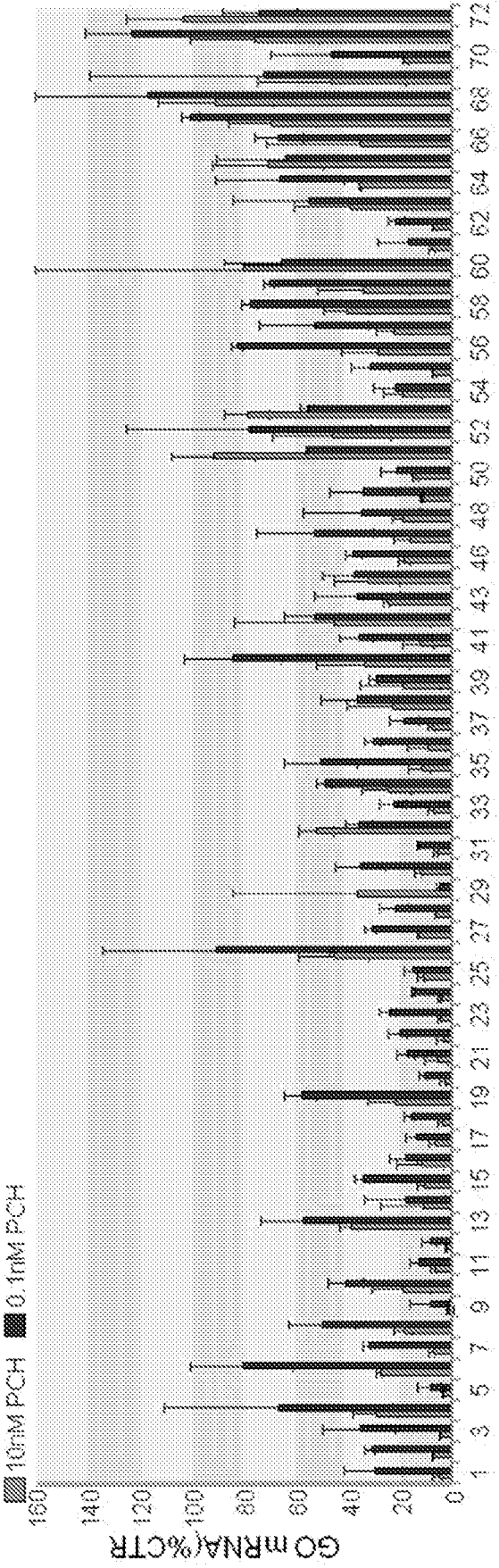

10nM PCH
0.1nM PCH
GO mRNA/%CTR
0
20
40
60
80
100
120
140
160
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43 46 48 50 52 54 56 58 60 62 64 66 68 70 72

FIG. 3A

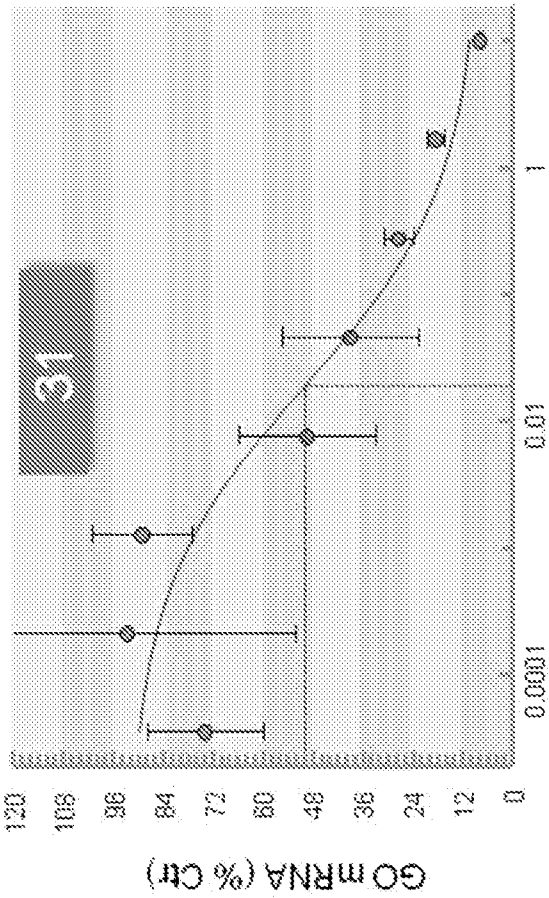

31
GO mRNA (% Ctr)
0
12
24
36
48
60
72
84
96
108
120
0.0001
0.01
1

FIG. 3B

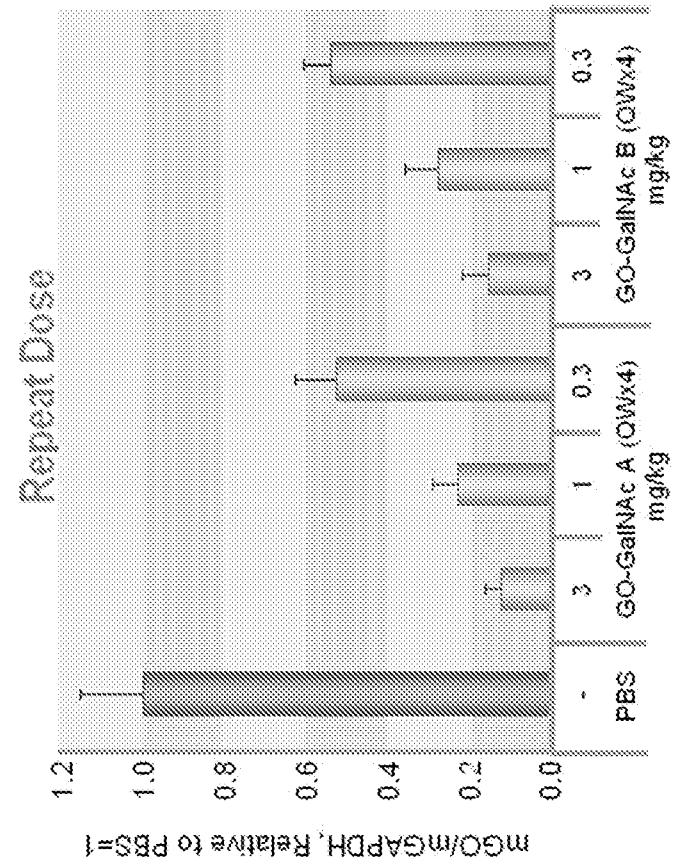

Repeat Dose
mGO/mGAPDH, Relative to PBS=1
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-
PBS
3
1
0.3
GO-GalNAc A (QWx4)
mg/kg
3
1
0.3
GO-GalNAc B (QWx4)
mg/kg

FIG. 4B

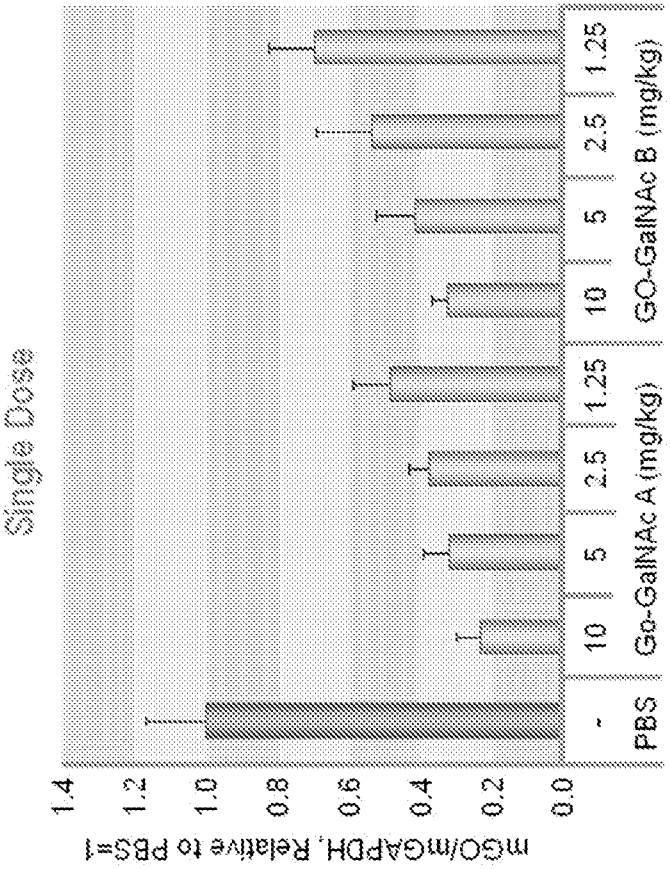

Single Dose
mGO/mGAPDH, Relative to PBS=1
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-
PBS
10
5
2.5
1.25
Go-GalNAc A (mg/kg)
10
5
2.5
1.25
GO-GalNAc B (mg/kg)

FIG. 4A

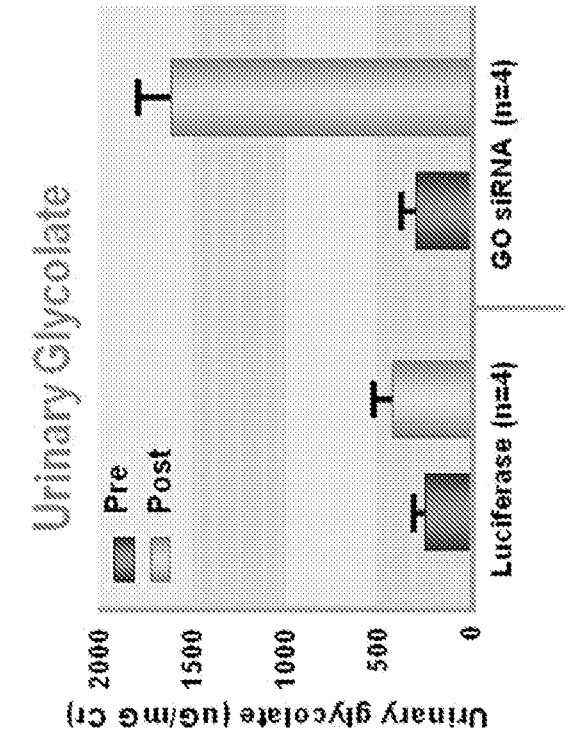

Urinary Glycolate
Pre
Post
Urinary glycolate (uG/mG cr)
2000
1500
1000
500
0
Luciferase (n=4)
GO siRNA (n=4)

FIG. 5B

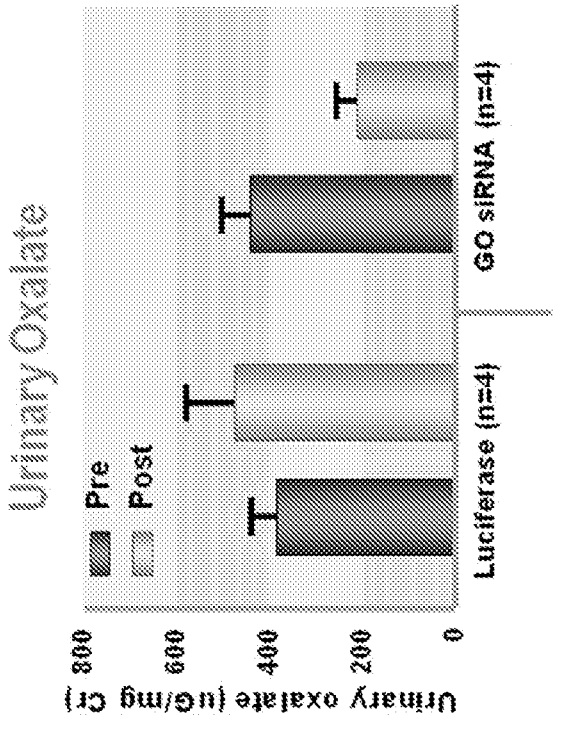

Urinary Oxalate
Pre
Post
Urinary oxalate (uG/mg cr)
800
600
400
200
0
Luciferase (n=4)
GO siRNA (n=4)

FIG. 5A

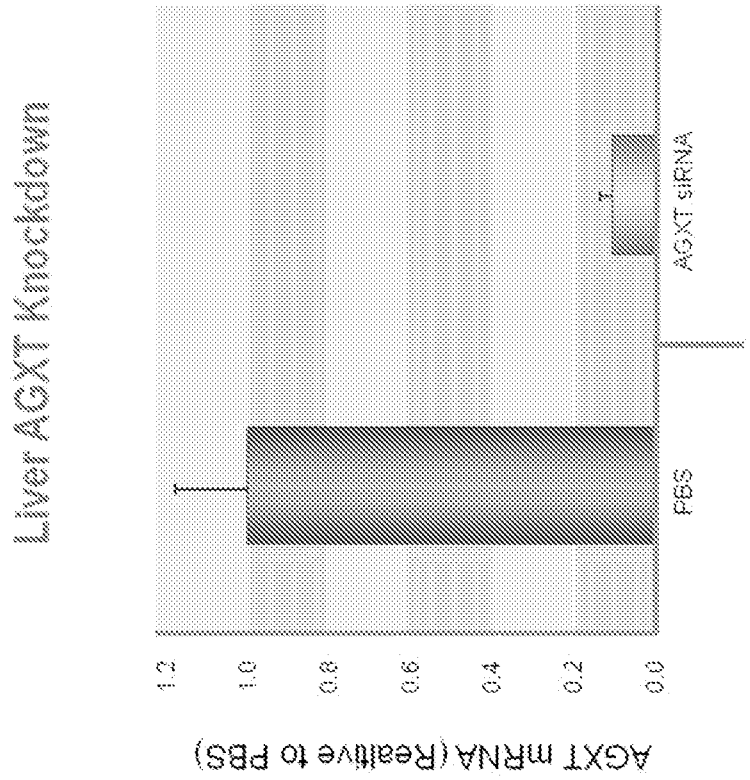

Liver AGXT Knockdown
AGXT mRNA (Relative to PBS)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
PBS
AGXT siRNA

FIG. 6A

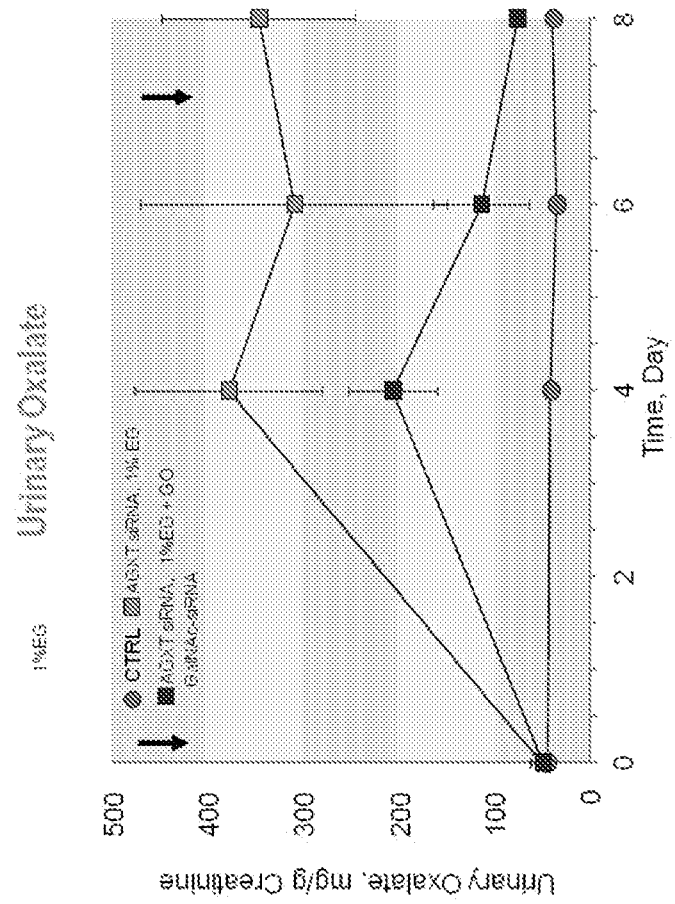

Urinary Oxalate
1%EG
CTRL
Urinary Oxalate, mg/g Creatinine
500
400
300
200
100
0
0
2
4
6
8
Time, Day

FIG. 6B

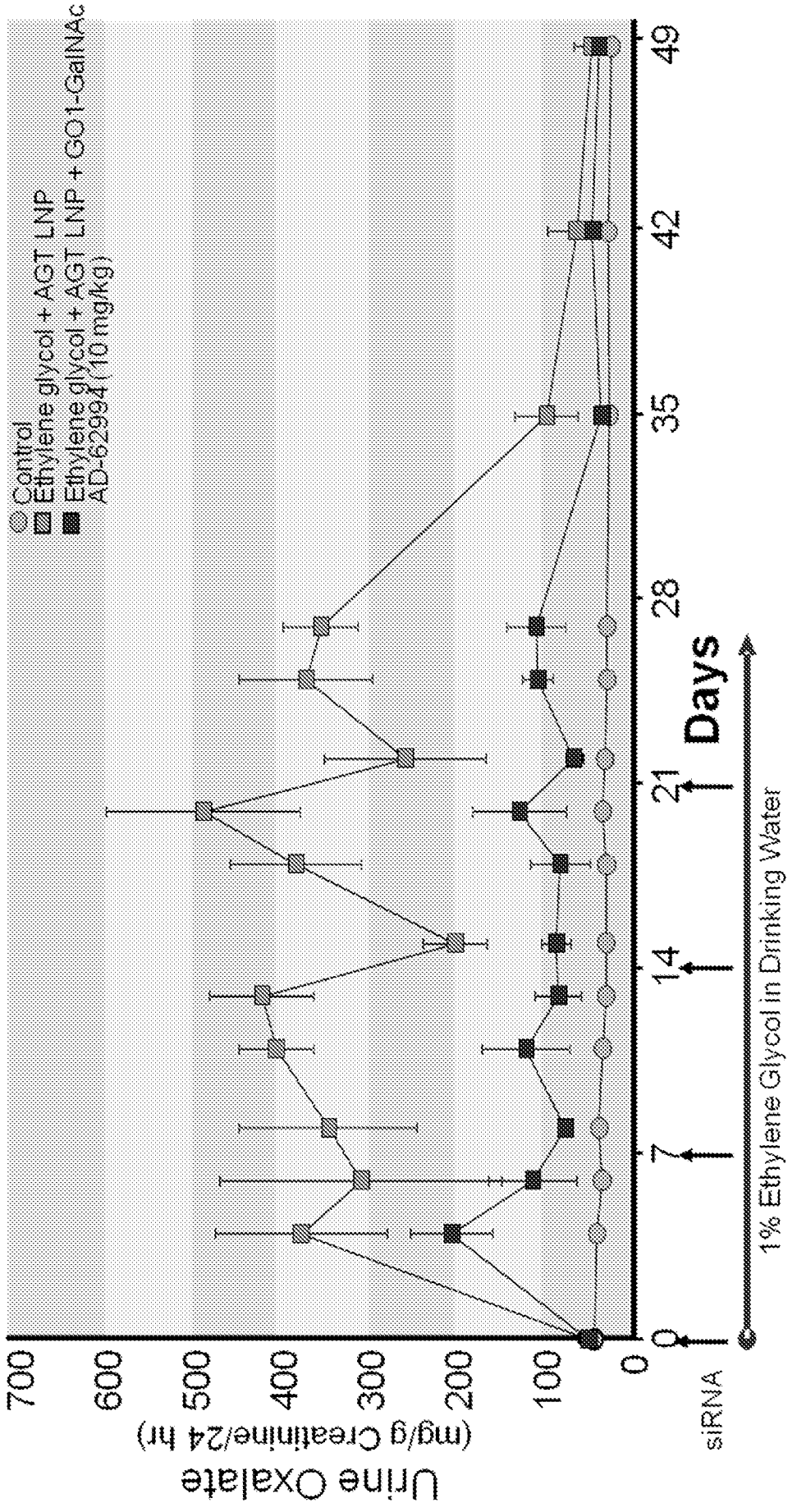

Control
Ethylene glycol + AGT LNP
Ethylene glycol + AGT LNP + GO1-GalNAc AD-62994 (10 mg/kg)
Urine Oxalate (mg/g Creatinine/24 hr)
700
600
500
400
300
200
100
0
siRNA
0
7
14
21
28
35
42
49
Days
1% Ethylene Glycol in Drinking Water

FIG. 6C

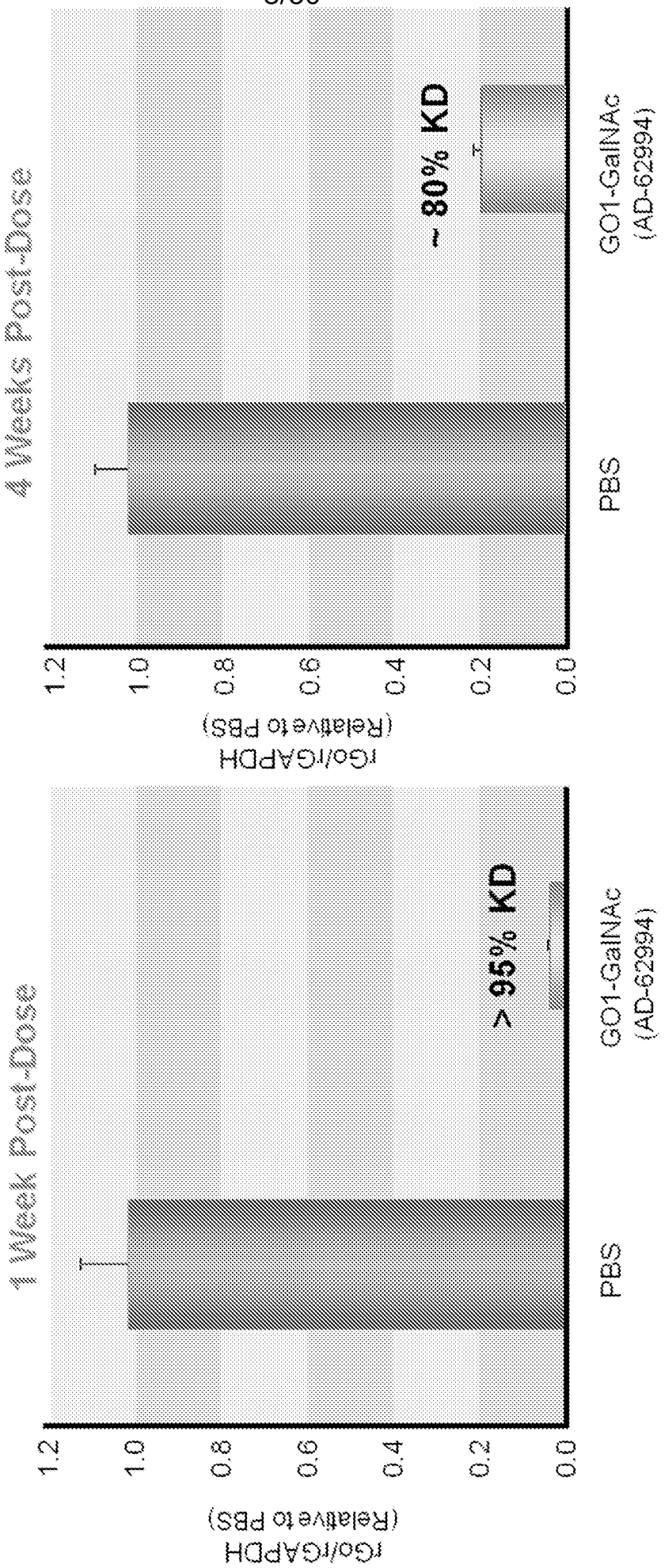

1 Week Post-Dose
4 Weeks Post-Dose
rGo/rGAPDH
(Relative to PBS)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
> 95% KD
~ 80% KD
PBS
GO1-GalNAc
(AD-62994)

FIG. 6D

(SEQ ID NO:3)

ATTCTTCCCAAAAATGCTTTATTTCTCTCTAAGAAGTAACATACATCCTAAAACATTTGGATATATTCAGACACTAAAGA
TGTGATTGGAAATCTACATTCAAAGAAGTATCACCAATTACCGCCACCCATTCCAATTCTCTCCAGTGCTACCTTCTCAA
AGTTGTGAATCAGGCATTACCAACACTTTGAACCTGAGCTTACAATTTAAGAACCACTGTTTTAAAGACATGTAAACAGA
ATACAGGTTAATAAACAATGAGATCATTATCTTTTCACCTTAGTGTTTGCTACCTCCAATTTTACTAAAGGATACAGCAC
TTTAGCCTGCCAGGGGATGACGTTGTCTAAACACATTTTCAATGTTTTCTTTTTAACAGTTAATATATTTCCAGGATGAA
AGTCCATTTCTTTCTAAAAGGTTCCTAGGACACCCATTGAAAAGTCAAAAGCAATGAAATAAAAGGGATTGCTATTTTGT
TGGAAAAGAACGACACCCTTTGTATTGAAGTGGGGAATTACAGACTGTGGTCACCCTCTGCACAGTGTCTCTTTGTCAAG
TAATACATGCTGAAAAAAAATAATACAGATGGGAAAATATTGTGCACTGTCAGATCTTGGAAACGGCCAAAGGATTTTTC
CTCACCAATGTCTTGTCGATGACTTTCACATTCTGGCACCCACTCAGAGCCATGGCCAACCGGAATTCTTCCTTTAGTAT
CTCGAGGACATCTTGAACACCTTTCTCCCCCTGGAAAGCTAAGCCCCAAACGATTGGTCTCCCCACAAACACAGCCTTGG
CGCCAAGAGCCAGAGCTTTCAGAACATCAGTGCCTTTCCGCACACCCCCGTCCAGGAAGACTTCCACCTTCCCTTCCACA
GCCTCCACAATTTCTGGCAGAACATCAATAGTGGCTGGCACCCCATCGAGTTGTCGAGCCCCATGATTCGACACCAAGAT
CCCATTCAAGCCATGTTTAACAGCCTCCCTGGCATCATCACCTCTCAAAATGCCCTTTGCAACAATTGGCAATGATGTCA
GTCTTCTCAGCCATTTGATATCTTCCCAGCTGATAGATGGGTCTATTGCTTTAGCCACATATGCAGCAAGTCCACTGTCG
TCTCCAAAATTTTCCTCAGGAGAAAATGATAAAGTACTGGTTTCAAAATTTTTCATCCTGAGTTGTGGCGGCAGTTTGAA
TCTGTTACGCACATCATCCAGACGGTTGCCCAGGTAAGGTGTGTCCACTGTCACAAATATGGCCTTGTAGCCCATCTTCT
CTGCCTGCCGCACTAGCTTCTTGGTGACTTCTCGGTCCTTGTAGATATACAGTTGCAGCCAACGAAGTGCCTCAGGACCA
GCTTCCGCCACTTCTTCAATTGAGGAGGTGGCCCAGGAACTCAACATCATGCCCGTTCCCAGGGACTGACAGGCTCTCAC
AGTGGCAAGCTCGCCGTCCACATGAGCCATGCGCTGCATGGCCGTAGCCCCCACACATATTGGCATGCTGACCCTCTGTC
CTAAAACAGAAGTCGACAGATCTGTTTCAGCAACATTCCGGAGCATCCTTGGATACAGCTTCCATCTGGAAAATGCTGCA
ATATTATCAGCCAAAGTTTCTTCATCATTTGCCCCAGACCTGTAATAGTCATATATAGACTTTGGAAGTACTGATTTAGC
ATGTTGTTCATAATCATTGATACAAATTAGCCGGGGGAGCATTTTCACAGGTTATTGCTATCCCAG

FIG. 7

(SEQ ID NO:4)
TGTGATAAAAGGAAAGACTTTTTTTTTTTGCCTTCCTTCTGAACAAGAATTTCAAATCTTTATTCATCACGGACCCCACAAAATATGTACTTTAC
ACTGAATGTGACTATATAAATGAGGAAAAGTGAGAAAATCAAAAAAAGATTCAAGAGGAATTAGGAAGTCAACACTTATTTTAAAATGAGAATGAGGAGAC
AAAGTTCAAAAGTAAAAATAGCTCCATGTGGTCCCAACTGGACTAGACACATCCCTTTCAAATGCAATGAGTGCCACAAAACATCCAGACATATTCAG
ACGTGTGATATATAGCTAAAAAATCTACCTTCAAAAAAATAGGGTGTTAAAAAAATGAAAAGTTTCTAGAAAAAAAATCACAAATTACCACCATCCATTT
CAATTCTACCTGGTGCTATTTTTCTCAACATGGCAAATCCAACCTCATGTTTCTCTGGGCATTTCCAGCATTTCAAAGCCAAGTGCAAACTGTAAGAG
CCACTGTCTTAAGGAAATCTAAACAGAAGACAGGTTAATGAACAGTGAGGTCAGTATCTTTCACTTCAGCATGCTACCTGCAATCTCACCAGAGGATA
TCTTTTGTTCCCCAGCACTTTAGCCTGCCAGGGGATGACGTTGCCCAAACACATTTTCAATGTTTTCTTTTTAACAGTTAATATATTTCCAGGATGCA
AGTCCATTTCTTTCTAGAAGGTTCCTAGGACACCCATTGAAAAGTCAAAAGCAATGAAGGAAAAGGGGTGGCTATTTTGTTGGAAAAGAACGACACCC
TTTGTATAGAAGTGGGGAGTTACAGTCTGTGGTCACCCTCTGCACAGTGTCTCTTTGTCAAGTAATCCACGCTGGAAAAAAATAATACAGATGGGAA
AATATTGTGCACTGTCAGATCTTGGAAACAGCCAAAGGATTTTTCCTCACCAATGTCTTGTCGATGACTTTCACATTCTGGCACCCACTCAGAGCCAT
GGCCAGTCGGAATTCTTCCTTCAATATCTCGAGGACATCTTGAACACCTTTCTCCCCCTGGAAAGCCAAGCCCCAGATGATGGGTCTTCCCACAAAAA
CGGCCTTGGCTCCTAGGGCCAGAGCTTTGAGAACATCAGTACCTTTCCTTACTCCCCCATCCAGGAAGACTTCTACCTTCCCTTCCACAGCCTCAACA
ATCTCTGGCAGGACATCAATAGTAGCTGGCACCCCATCCAGTTGTCGCGCCCCATGATTCGACACCAAGATCCCATCCACACCATGTTTAACAGCTTC
CTTGGCATCATCACCCTCTCAAAATGCCCTTTACAACAATAGGCAGTGATGTCAATCGTCTGAGCCATGTAATATCATCCCAGCTGAGAGATGGGTCTA
TAGCTTGTGCCACATATTCAGCAAGTCCACTGTTGTCTCCAAAATTTCCCTTAGGAGAAAATGCCAAATCATTGGTTTCAAAGTTTTTCATCCTGAGT
TGTGGTGGCAGCTTGAACCTGTTCCGCACGTCATCAATGCGGTTGCCCAGGTAAGGGGTGTCCACAGTCACACAAATATGGCCTTGTAACCCTGCTTCTC
AGCTCGCTTCACTATCTGTCTGCTGATCTCACGGTCTTTGTAGATGTACAGTTGCATCCAGCGAAGTGCCTCTGGGCCAGCTTCTGCCACTTCTTCTA
TTGAGGAGGTAGCCCAAGAACTCAGCATCATGCCAGTTCCCACATGGTCTGACAGGCTCGCACAGTGGCCAGCTCCCCGTCCACGTGAGCCATGCACTGC
ATGGCAGTAGCCCCAACACATATTGGCATGCTGACTCTCTGTCCTAAAACAGAAGTTGACAGATCGATATCAGCAACGTTGCGAAGCATCCGTGGATA
GAGCTTCCATCTAGAAAATGCTTGGATGTTATCAGCTAACGTCTCCTGATCATTTGCCCCCAGACCTGTAATAGTCATACACTGACTTCTGAAGCACTG
ATCGGACATGCTGTTCATAATCACTGATGCAGACCAGTCGAGGCAACATTGTGGCAGGGTAGGGCAACC

FIG. 8

(SEQ ID NO:5).
>gi|544464345|ref|XM_005568381.1| PREDICTED: Macaca fascicularis hydroxyacid oxidase (glycolate oxidase) 1 (HAO1), mRNA

GTGAGGATGTAGAAAGCAATACATTAAAAAAAACCCAAAAAACTCCATCTGGGATAACAATAACCTGTGA
AAATGCTCCCCCGGCTAATTTGTATCAATGATTATGAACAACATGCTAAATCAGTACTTCCAAAGTCTAT
ATATGACTATTATAGGTCTGGAGCAAATGATGAAGAAACTTTGGCCGATAATGTTGCAGCATTTTCCAGA
TGGAAGCTGTATCCAAGGATGCTCCGGAATGTTGCTGAAACAGATCTGTCGACTTCTGTTTTAGGACAGA
GGGTCAGCATGCCAATATGCGTGGGGGCCACGGCCATGCAGCGCATGGCTCATGTGGATGGCGAGCTTGC
CACTGTGCGAGCCTGTCAGTCCCTGGGAACGGGCATGATGTTGAGTTCCTGGGCCACCTCCTCAATTGAA
GAAGTGGCAGAAGCTGGTCCTGAGGCACTTCGTTGGTTGTAACTGTATATCTATAAGGACCGAGAAGTCA
CCAAGAAGCTGGTGCAGCAGGCAGAGAAGACGGGCTACAAGGCCATATTTGTGACAGTGGACACACCTTA
CCTGGGCAACCGTCTTGATGATGTACGTAACAGATTCAAGCTGCCACCACAACTCAGGATGAAAAATTTT
GAAACCAGTACTTTATCATTTTCTCCTGAGGAAAATTTTGGAGATGACAGTGGACTTGCTGCATATGTGG
CTAAAGCGATAGACCCATCTATCAGCTGGGAAGATATCAAATGGCTGAGAAGACTGACGTCATTGCCAAT
TGTTGCAAAGGGCATTTTGAGAGGTGATGATGCCAGGGAGGCTGTTAAACATGGCTTGAATGGGATCTTG
GTGTCGAATCATGGGGCTCGACAACTCGATGGGGTGCCAGCCACTATTGATGTTCTGCCAGAAATTGTGG
AGGCCGTGGAAGGGAAGGTGGAAGTCTTCCTGGACGGGGGTGTGCGGAAAGGCACTGATGTTCTGAAAGC
TCTGGCTCTTGGCGCCAAGGCTGTGTTTGTGGGGAGACCAATCATTTGGGGCTTAGCTTTCCAGGGGGAG
AAAGGTGTTCAAGATGTCCTTGAGATACTAAAGGAAGAATTCCGGTTGGCCATGGCTTTGAGTGGGTGCC
AGAATGTGAAAGTCATCGACAAGACATTGGTGAGGAAAAATCCTTTGGCCGTTTCCAAGATCTGACAGTG
CACAATATTTTCCCATCTGTATTATTTTTTTTTCAGCATGTATTACTTGACAAAGAGACACTGTGCAGAG
GGTGACCACAGTCTGTAATTCCCCACTTCAATACAAAGGATGTCGTTCTTTTCCAACAAAATAGCAATCC
CTTTTAGTTCATTGCTTTTGACTTTTCAATGGGTGTCCTAGGAACCTTTTAGAAAGAAATGGACTTTCAT
CCTGGAAATATATTAACTGTTAAAAAGAAAACATTGAAAATGTGTTTAGACAACGTCATCCTCTGGCAGG
CTAAAGTACTGTATCCTTTAGTAAAATTGGAGGTAGCAAACACTAAGGTGAAAAGATAATGATCTCATTG
TTTATTAACCTGTATTCTGTTTAGATGTCTTTAAAACAGTGGTTCTTAAATTGTAAGCTCAGGTTCAAAG
CATTGGAAATGCCTGATTGACAACATTGAGAAGGTAGCCCTGGATAGAATTGGAATGGATGGCAGTAACT
GGTGATACTTCTTTGAATGCAGCTTTCCAATCACATCTTTAGTGTCTGAATATATCCAAATGTTTTAGGA
TATATGTTACTTCTTAATCAGAGAGAAATAAAGCATTTTTTGGGAAGGATA

FIG. 9

(SEQ ID NO:6).

>gi|564343200|ref|XM_006235096.1| PREDICTED: Rattus norvegicus hydroxyacid oxidase (glycolate oxidase) 1 (Hao1), transcript variant X1,

mRNAATACTGCCTTGCTGGCTTTGGAAATTCTAGAGTTTCTGAGGCATAGTAGACTTGGTGACCTCCAAGTTCTAACCGAGCAGAAAGAGTCTCATGG
CTTCTGTGACTACTATAGTGGAAGCTCTATCCACGGATGCTGCGCAACGTTGCTGATATCGACCTGTCGACTTCTGTTTTAGGACAGAGAGTGAGCAT
GCCAATATGCGTTGGGGCTACGGCTATGCAGTGCATGGCTCATGTGGATGGGGAGCTGGCCACTGTTCGAGCCTGTCAGACCATGGGAACTGGCATGA
TGTTGAGTTCCTGGGCCACTTCCTCAATAGAAGAGGTGGCAGAGGCTGGCCCGGAGGCACTTCGCTGGATGCAACTCTACATCTACAAAGATCGTGAG
GTCAGCAGTCAGCTAGTGAAGAGGGCTGAGCAGATGGGTTACAAGGCCATATTTGTGACTGTGGACACCCCTTACCTGGGAAATCGCTTCGATGATGT
GCGGAACAGGTTCAAGCTACCACCACAGCTCAGGATGAAAAACTTTGAAACCAACGATTTGGCATTTTCTCCTAAGGGGAATTTTGGAGACAACAGTG
GCCTTGCTGAATATGTGGCACAAGCCATAGACCCATCTCTCAGCTGGGATGATATTAAATGGCTCAGACGGTTGACCTCACTGCCCATTGTTGTAAAG
GGAATTTTGAGAGGTGATGATGCCCAGGAAGCTGTTAAACATGGTGTGGATGGGATCTTAGTGTCGAATCATGGGGCACGACAACTGGATGGGGTGCC
AGCTACTATTGATGCCCTGCCAGAGATCGTTGAGGCTGTGGAAGGGAAGGTAGAAGTCTTCCTGGATGGGGGAGTCAGGAAAGGCACCGATGTTCTCA
AAGCTCTGGCCCTGGGAGCCAGAGCTGTTTTTGTGGGGAGACCCATCATCTGGGGCTTGGCTTTCCAGGGGGAGAAAGGTGTTCAAGATGTCCTCGAG
ATACTGAAGGAAGAGTTCCGGCTGGCCATGGCTCTGAGTGGGTGCCAGAATGTGAAAGTCATCGACAAGACATTGGTGAGGAAAAATCCTTTGGCTGT
TTCCAAGATCTGACAGTGCACAATATTTTCCCATCTGTATTATTTTTTTCCAGCATGGATTACTTGACAAAGAGACACTGTGCAGAGGGTGACCACAG
ACTGTAACTCCCCACTTCAACACAAAGGGTGTCGTTCTTTTCCAACAAAATAGCCACCCCTTCTCCTTCATTGCTTTTGACTTTTCAATGGGTGTCCT
AGGAACCTTCTAGAAAGAAATGGACTTGCATCCTGGAAATATATTAACTGTTAAAAAGAAAACATTGAAAATGTGTTTGGGCAACGTCATCCCCTGGC
AGGCTAAAGTGAGGGGGAACAAAAGATATCCTCTGGTGAGATTGGAGGTAGCATGCCGAAGTAAAAGACACTGACCTCACTGTTTATTAACCTGTCTT
CTGTTTAGATTTCCTTAAGACAGTGGCTCTTACAGTGTGCGCTGGGCTTTGAAATGCCGGAAATGCCCAGAGAAACATGGGGTTTGGATTTGCCGTGT
TGAGAAAATAGCACCCGATAGAATTGAAACGGATGGTGGTAATTTGTGATTTTTCTAGAGACTTTTCATTTTTTAACACCCTATTTCTTTGAAGGTGG
ATTTCTAGCTATATATCGCATGTCTGAATATGTCTGGCTGTTTTGTGGCACTCACTGTGTTTGAAAGGAATGTGTCTAGTCCACTTGGGACCATGCAA
AGTTATTTTATTTTTGAACTCTGTCTCTTCATTCCCATTTTAAAGTAAGTGTTGACTTCCTAATTCCCCTTGAATCATTTTTATTTTCTCACTTCTCA
TTTATAGTCACATTCAGTGTCAAGTATATATTTTGTGGGGTCCATGGTGAATAAAGCTTTAAAATTCTTGTCCAGAAA

FIG. 10

(SEQ ID NO:7)

TATCCTTCCCAAAAAATGCTTTATTTCTCTCTGATTAAGAAGTAACATATATCCTAAAACATTTGGATATATTCAGACACTAAAGATGTGATTGGAA
AGCTGCATTCAAAGAAGTATCACCAGTTACTGCCATCCATTCCAATTCTATCCAGGGCTACCTTCTCAATGTTGTCAATCAGGCATTTCCAATGCTT
TGAACCTGAGCTTACAATTTAAGAACCACTGTTTTAAAGACATCTAAACAGAATACAGGTTAATAAACAATGAGATCATTATCTTTTCACCTTAGTG
TTTGCTACCTCCAATTTTACTAAAGGATACAGTACTTTAGCCTGCCAGAGGATGACGTTGTCTAAACACATTTTCAATGTTTTCTTTTTAACAGTTA
ATATATTTCCAGGATGAAAGTCCATTTCTTTCTAAAAGGTTCCTAGGACACCCATTGAAAAGTCAAAAGCAATGAACTAAAAGGGATTGCTATTTTG
TTGGAAAAGAACGACATCCTTTGTATTGAAGTGGGGAATTACAGACTGTGGTCACCCTCTGCACAGTGTCTCTTTGTCAAGTAATACATGCTGAAAA
AAAAATAATACAGATGGGAAAATATTGTGCACTGTCAGATCTTGGAAACGGCCAAAGGATTTTTCCTCACCAATGTCTTGTCGATGACTTTCACATT
CTGGCACCCACTCAAAGCCATGGCCAACCGGAATTCTTCCTTTAGTATCTCAAGGACATCTTGAACACCTTTCTCCCCCTGGAAAGCTAAGCCCCAA
ATGATTGGTCTCCCCACAAACACAGCCTTGGCGCCAAGAGCCAGAGCTTTCAGAACATCAGTGCCTTTCCGCACACCCCCGTCCAGGAAGACTTCCA
CCTTCCCTTCCACGGCCTCCACAATTTCTGGCAGAACATCAATAGTGGCTGGCACCCCATCGAGTTGTCGAGCCCCATGATTCGACACCAAGATCCC
ATTCAAGCCATGTTTAACAGCCTCCCTGGCATCATCACCTCTCAAAATGCCCTTTGCAACAATTGGCAATGACGTCAGTCTTCTCAGCCATTTGATA
TCTTCCCAGCTGATAGATGGGTCTATCGCTTTAGCCACATATGCAGCAAGTCCACTGTCATCTCCAAAATTTTCCTCAGGAGAAAATGATAAAGTAC
TGGTTTCAAAATTTTTCATCCTGAGTTGTGGTGGCAGCTTGAATCTGTTACGTACATCATCAAGACGGTTGCCCAGGTAAGGTGTGTCCACTGTCAC
AAATATGGCCTTGTAGCCCGTCTTCTCTGCCTGCTGCACCAGCTTCTTGGTGACTTCTCGGTCCTTATAGATATACAGTTACAACCAACGAAGTGCC
TCAGGACCAGCTTCTGCCACTTCTTCAATTGAGGAGGTGGCCCAGGAACTCAACATCATGCCCGTTCCCAGGGACTGACAGGCTCGCACAGTGGCAA
GCTCGCCATCCACATGAGCCATGCGCTGCATGGCCGTGGCCCCCACGCATATTGGCATGCTGACCCTCTGTCCTAAAACAGAAGTCGACAGATCTGT
TTCAGCAACATTCCGGAGCATCCTTGGATACAGCTTCCATCTGGAAAATGCTGCAACATTATCGGCCAAAGTTTCTTCATCATTTGCTCCAGACCTA
TAATAGTCATATATAGACTTTGGAAGTACTGATTTAGCATGTTGTTCATAATCATTGATACAAATTAGCCGGGGGAGCATTTTCACAGGTTATTGTT
ATCCCAGATGGAGTTTTTTGGGTTTTTTTTAATGTATTGCTTTCTACATCCTCAC

FIG. 11

(SEQ ID NO:8)

TTTCTGGACAAGAATTTTAAAGCTTTATTCACCATGGACCCCACAAAATATATACTTGACACTGAATGTGACTATAAATGAGAAGTGAGAAAATAA
AAATGATTCAAGGGGAATTAGGAAGTCAACACTTACTTTAAAATGGGAATGAAGAGACAGAGTTCAAAAATAAAATAACTTTGCATGGTCCCAAGT
GGACTAGACACATTCCTTTCAAACACAGTGAGTGCCACAAAACAGCCAGACATATTCAGACATGCGATATATAGCTAGAAATCCACCTTCAAAGAA
ATAGGGTGTTAAAAAATGAAAAGTCTCTAGAAAAATCACAAATTACCACCATCCGTTTCAATTCTATCGGGTGCTATTTTCTCAACACGGCAAATC
CAAACCCCATGTTTCTCTGGGCATTTCCGGCATTTCAAAGCCCAGCGCACACTGTAAGAGCCACTGTCTTAAGGAAATCTAAACAGAAGACAGGTT
AATAAACAGTGAGGTCAGTGTCTTTTACTTCGGCATGCTACCTCCAATCTCACCAGAGGATATCTTTTGTTCCCCCTCACTTTAGCCTGCCAGGGG
ATGACGTTGCCCAAACACATTTTCAATGTTTTCTTTTTAACAGTTAATATATTTCCAGGATGCAAGTCCATTTCTTTCTAGAAGGTTCCTAGGACA
CCCATTGAAAAGTCAAAAGCAATGAAGGAGAAGGGGTGGCTATTTTGTTGGAAAAGAACGACACCCTTTGTGTTGAAGTGGGGAGTTACAGTCTGT
GGTCACCCTCTGCACAGTGTCTCTTTGTCAAGTAATCCATGCTGGAAAAAAATAATACAGATGGGAAAATATTGTGCACTGTCAGATCTTGGAAAC
AGCCAAAGGATTTTTCCTCACCAATGTCTTGTCGATGACTTTCACATTCTGGCACCCACTCAGAGCCATGGCCAGCCGGAACTCTTCCTTCAGTAT
CTCGAGGACATCTTGAACACCTTTCTCCCCCTGGAAAGCCAAGCCCCAGATGATGGGTCTCCCCACAAAAACAGCTCTGGCTCCCAGGGCCAGAGC
TTTGAGAACATCGGTGCCTTTCCTGACTCCCCCATCCAGGAAGACTTCTACCTTCCCTTCCACAGCCTCAACGATCTCTGGCAGGGCATCAATAGT
AGCTGGCACCCCATCCAGTTGTCGTGCCCCATGATTCGACACTAAGATCCCATCCACACCATGTTTAACAGCTTCCTGGGCATCATCACCTCTCAA
AATTCCCTTTACAACAATGGGCAGTGAGGTCAACCGTCTGAGCCATTTAATATCATCCCAGCTGAGAGATGGGTCTATGGCTTGTGCCACATATTC
AGCAAGGCCACTGTTGTCTCCAAAATTCCCCTTAGGAGAAAATGCCAAATCGTTGGTTTCAAAGTTTTTCATCCTGAGCTGTGGTGGTAGCTTGAA
CCTGTTCCGCACATCATCGAAGCGATTTCCCAGGTAAGGGGTGTCCACAGTCACAAATATGGCCTTGTAACCCATCTGCTCAGCCCTCTTCACTAG
CTGACTGCTGACCTCACGATCTTTGTAGATGTAGAGTTGCATCCAGCGAAGTGCCTCCGGGCCAGCCTCTGCCACCTCTTCTATTGAGGAAGTGGC
CCAGGAACTCAACATCATGCCAGTTCCCATGGTCTGACAGGCTCGAACAGTGGCCAGCTCCCCATCCACATGAGCCATGCACTGCATAGCCGTAGC
CCCAACGCATATTGGCATGCTCACTCTCTGTCCTAAAACAGAAGTCGACAGGTCGATATCAGCAACGTTGCGCAGCATCCGTGGATAGAGCTTCCA
CTATAGTAGTCACAGAAGCCATGAGACTCTTTCTGCTCGGTTAGAACTTGGAGGTCACCAAGTCTACTATGCCTCAGAAACTCTAGAATTTCCAAA
GCCAGCAAGGCAGTAT

FIG. 12

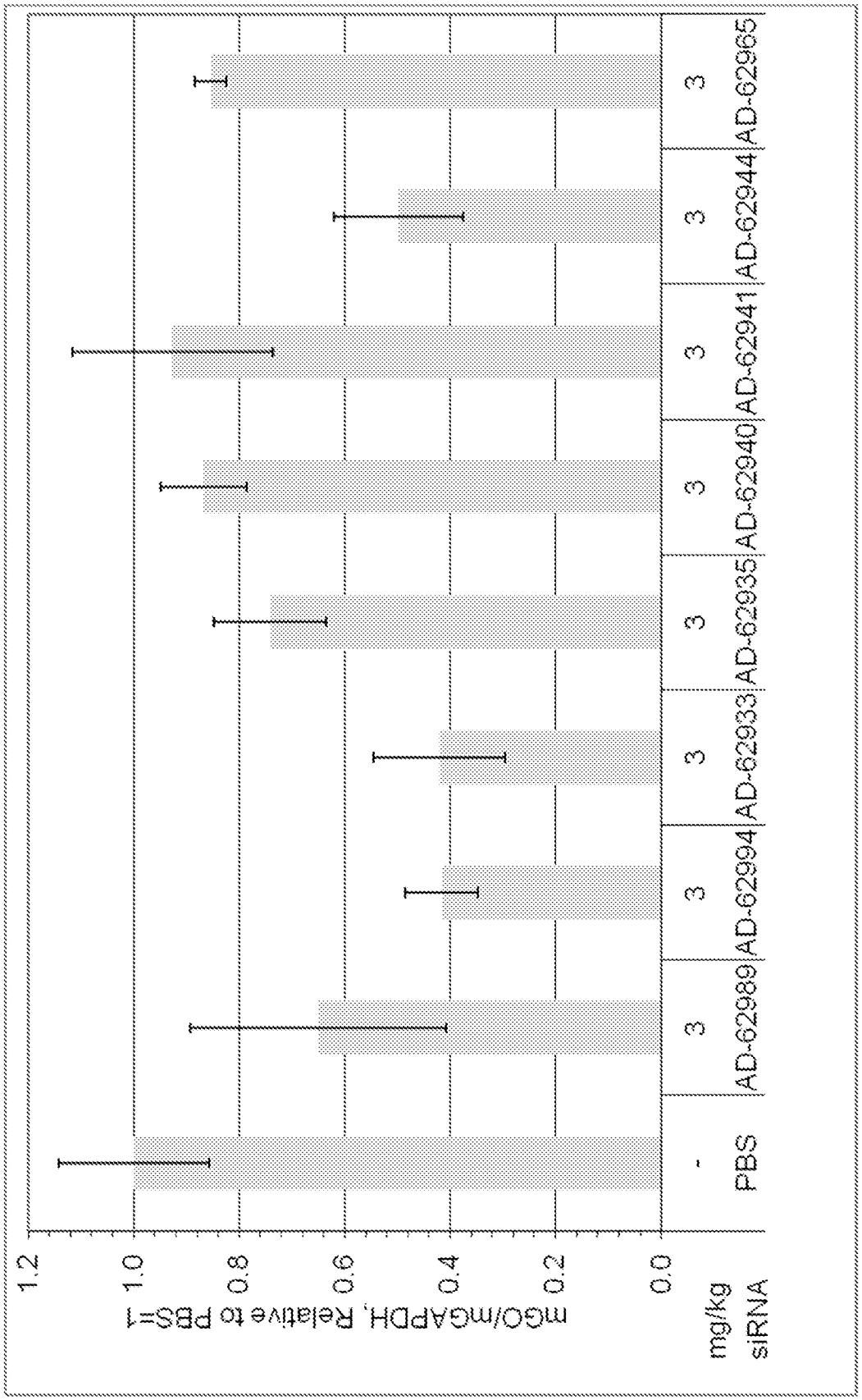

mGO/mGAPDH, Relative to PBS=1
1.2
1.0
0.8
0.6
0.4
0.2
0.0
mg/kg
siRNA
-
PBS
3
AD-62989
3
AD-62994
3
AD-62933
3
AD-62935
3
AD-62940
3
AD-62941
3
AD-62944
3
AD-62965

FIG. 13

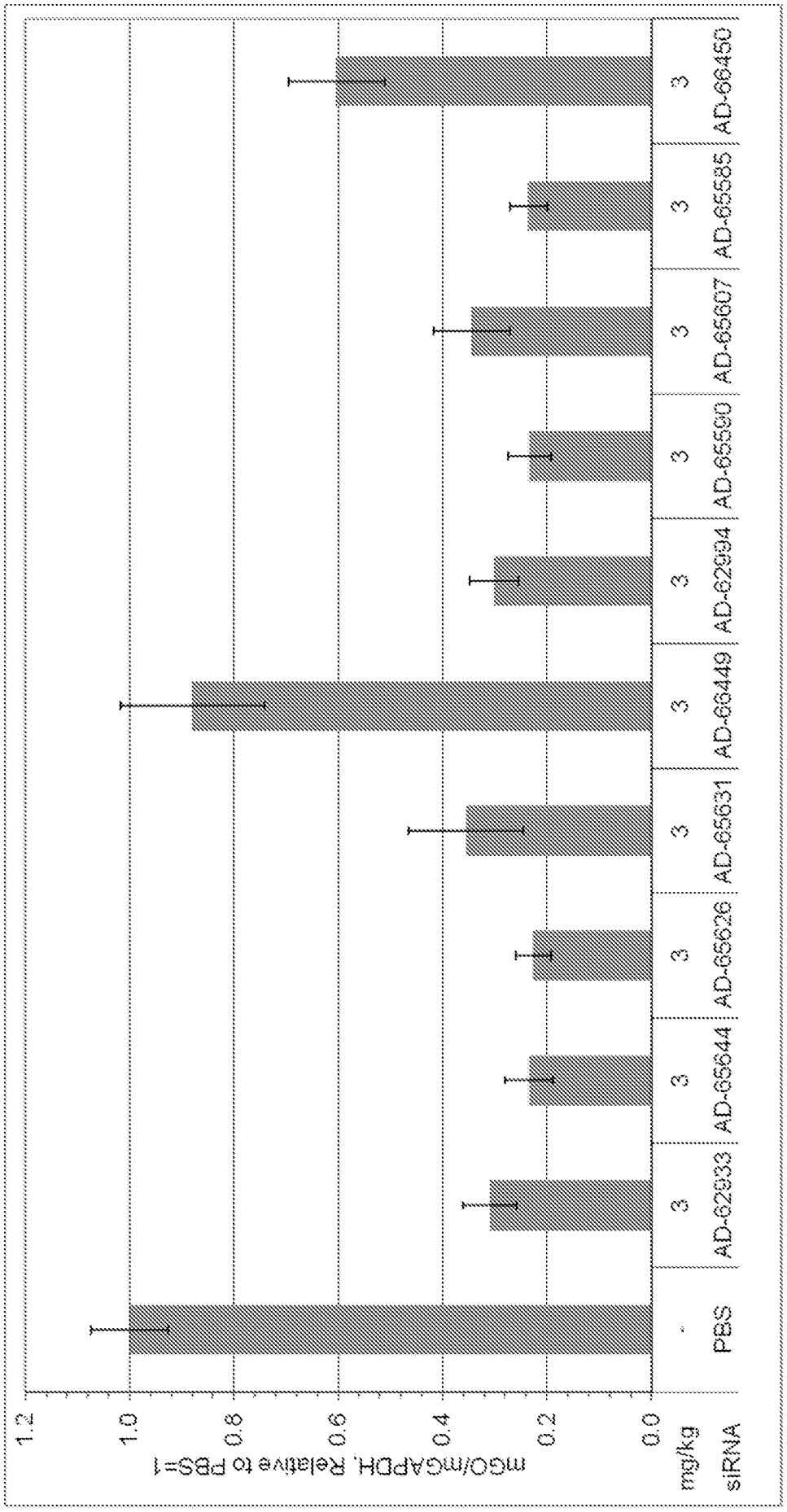

mGO/mGAPDH, Relative to PBS=1
1.2
1.0
0.8
0.6
0.4
0.2
0.0
siRNA
mg/kg
PBS
-
AD-62933
3
AD-65644
3
AD-65626
3
AD-65631
3
AD-66449
3
AD-62934
3
AD-65590
3
AD-65607
3
AD-65585
3
AD-66450
3

FIG. 14

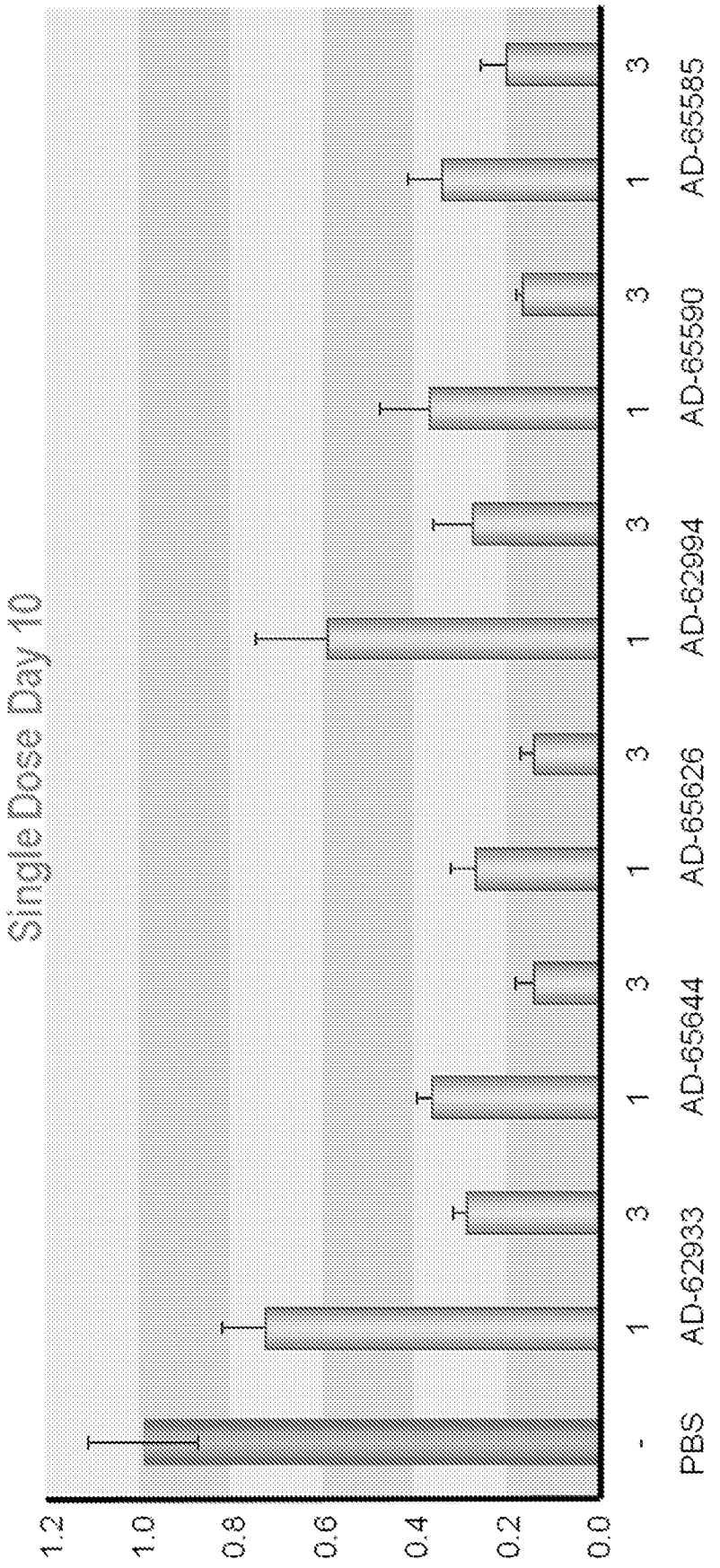

Single Dose Day 10
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-
PBS
1
AD-62933
3
1
AD-65644
3
1
AD-65626
3
1
AD-62994
3
1
AD-65590
3
1
AD-65585
3

FIG. 15

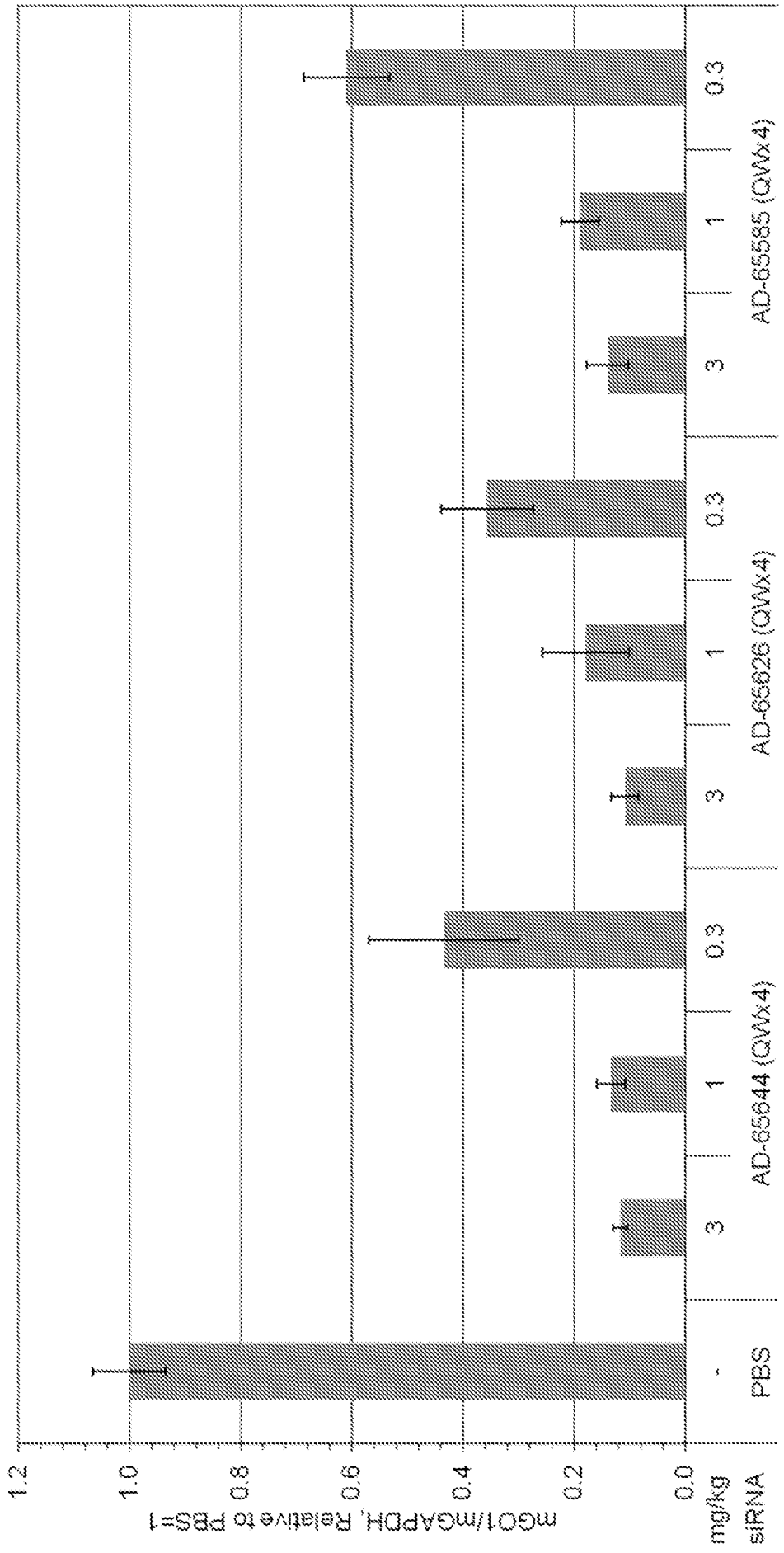

mGO1/mGAPDH, Relative to PBS=1
1.2
1.0
0.8
0.6
0.4
0.2
0.0
mg/kg
siRNA
-
PBS
3
1
0.3
AD-65644 (QWx4)
3
1
0.3
AD-65626 (QWx4)
3
1
0.3
AD-65585 (QWx4)

FIG. 16

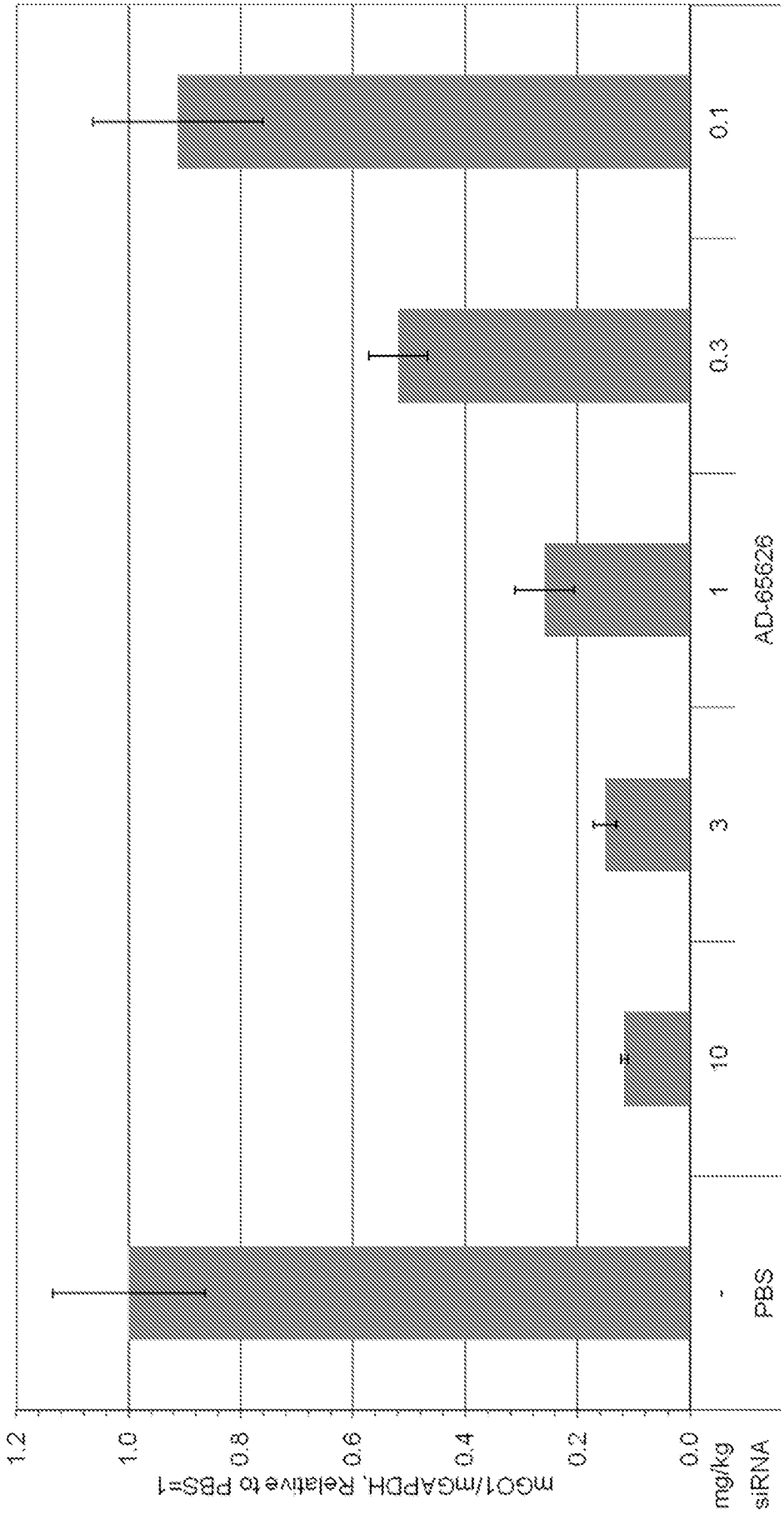
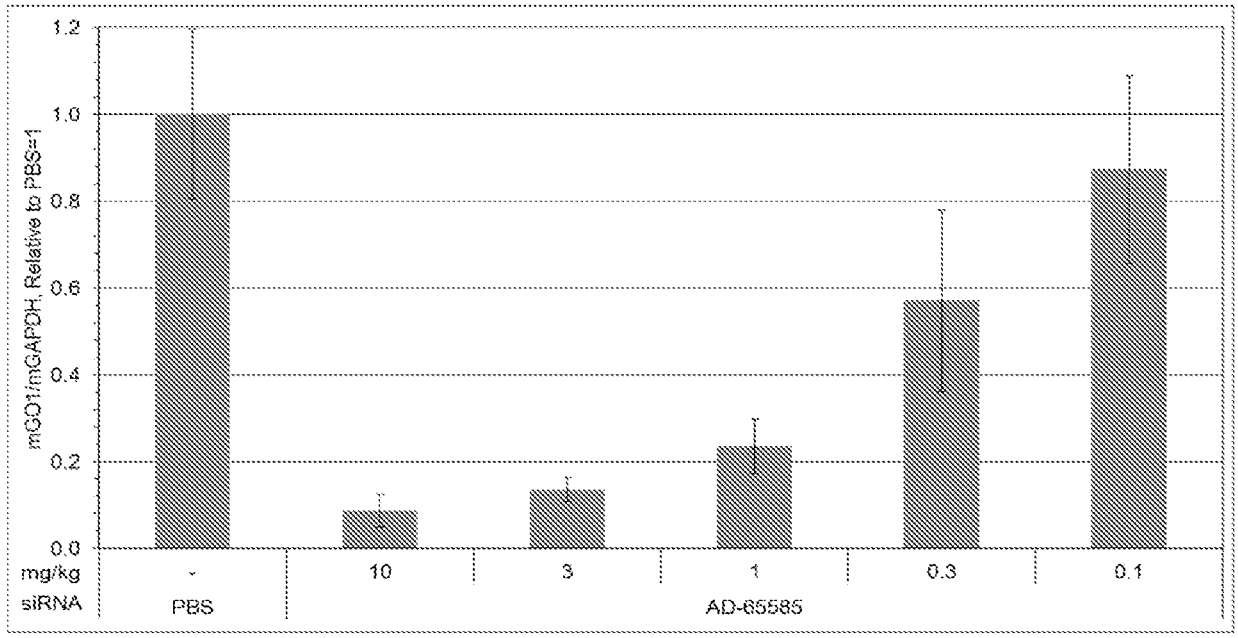

mGO1/mGAPDH, Relative to PBS=1
1.2
1.0
0.8
0.6
0.4
0.2
0.0
mg/kg
siRNA
-
PBS
10
3
1
0.3
0.1
AD-65626

FIG. 17


mGO1/mGAPDH, Relative to PBS=1
1.2
1.0
0.8
0.6
0.4
0.2
0.0
mg/kg
siRNA
-
PBS
10
3
1
0.3
0.1
AD-65585

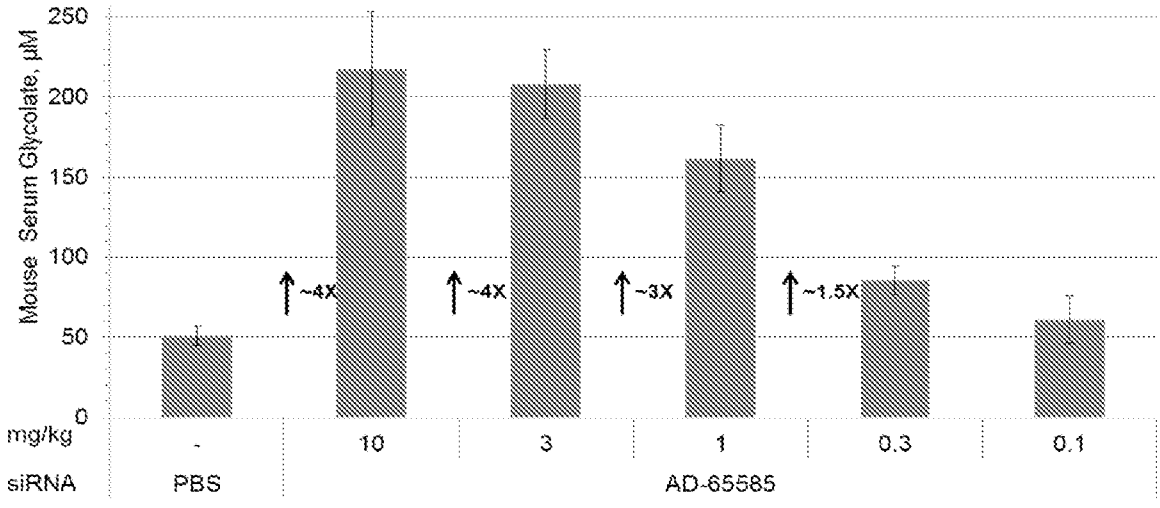
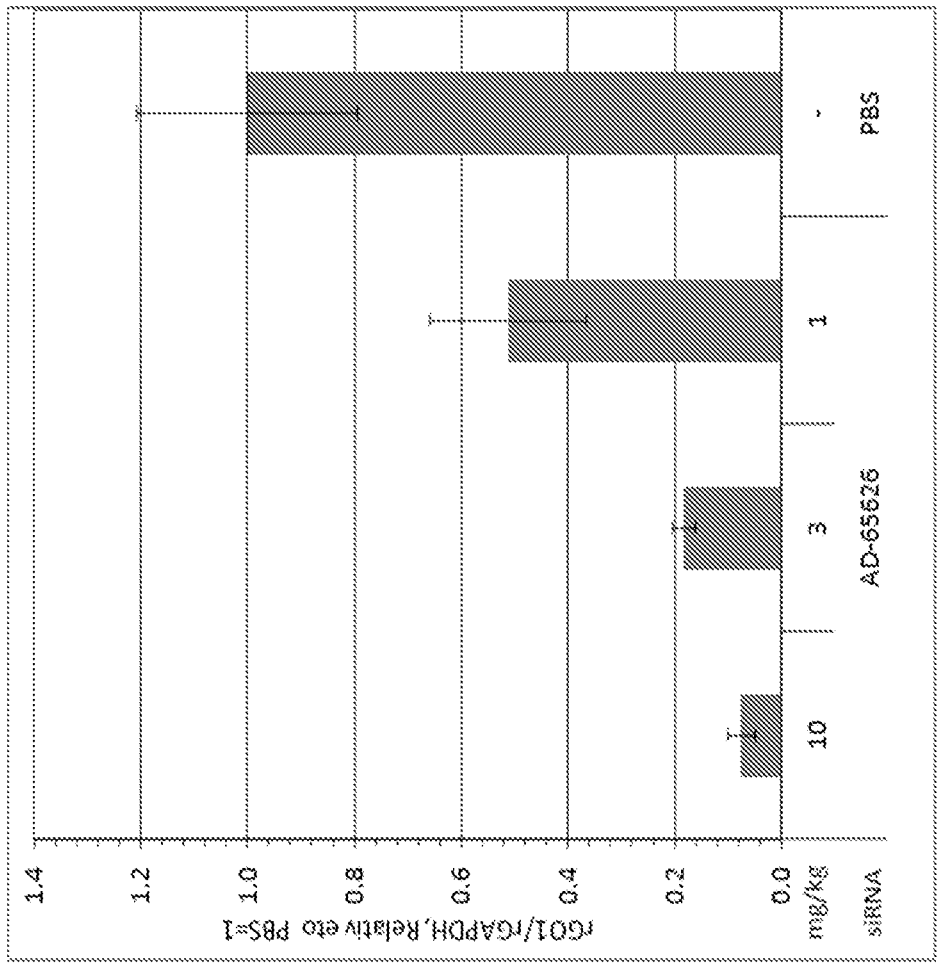

Mouse Serum Glycolate, µM
250
200
150
100
50
0
~4X
~4X
~3X
~1.5X
mg/kg
siRNA
-
PBS
10
3
1
0.3
0.1
AD-65585

FIG. 18


rGO1/rGAPDH, Relativ eto PBS=1
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
mg/kg
siRNA
10
3
1
-
AD-65626
PBS

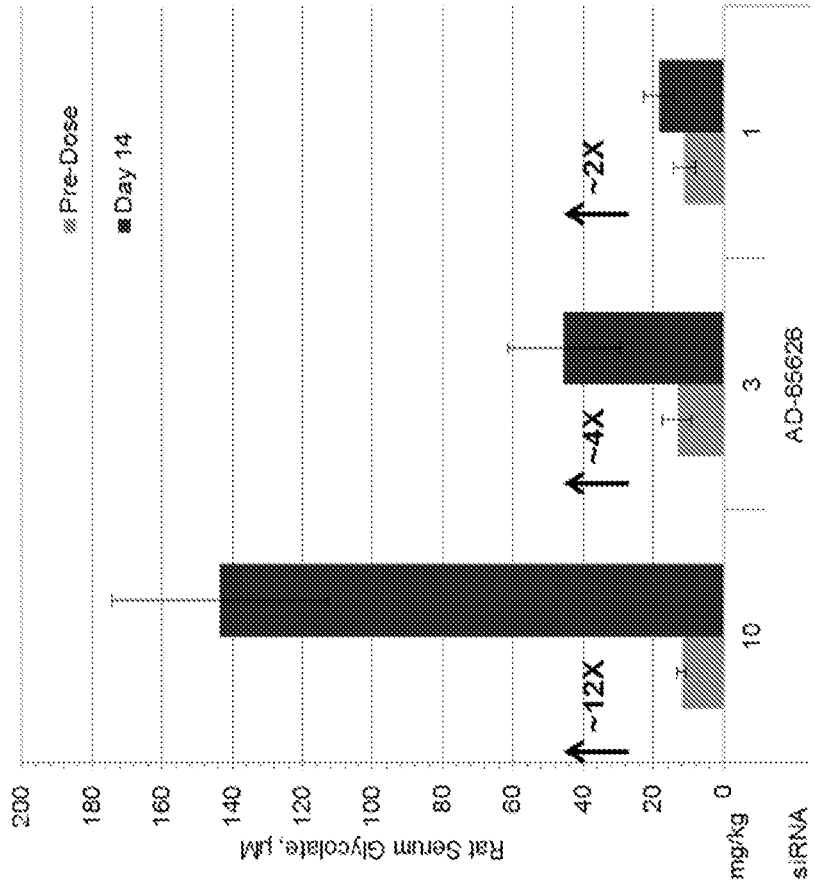

Rat Serum Glycolate, µM
200
180
160
140
120
100
80
60
40
20
0
mg/kg
siRNA
10
3
1
AD-65626
~12X
~4X
~2X
Pre-Dose
Day 14

FIG. 19

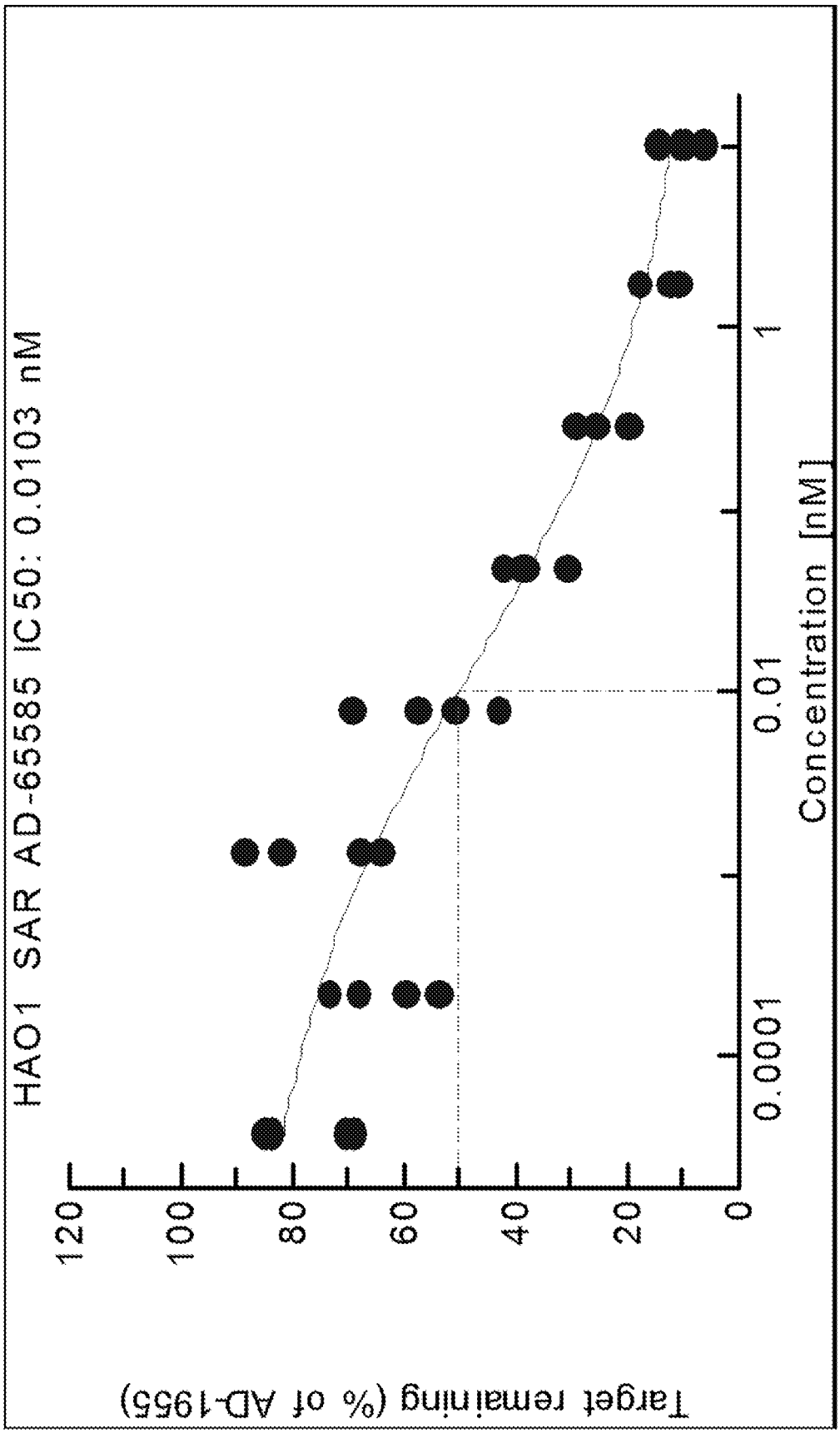

HAO1 SAR AD-65585 IC50: 0.0103 nM
Target remaining (% of AD-1955)
120
100
80
60
40
20
0
0.0001
0.01
1
Concentration [nM]

FIG. 20

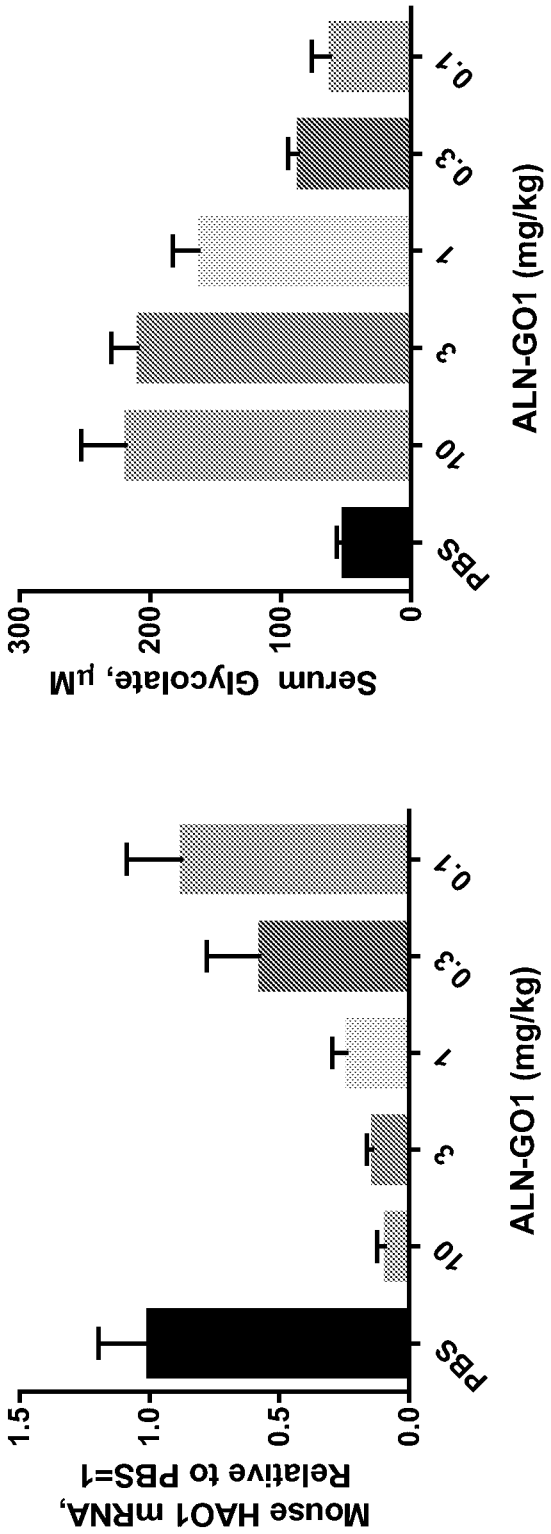

Serum Glycolate, μM
300
200
100
0
PBS
10
3
1
0.3
0.1
ALN-GO1 (mg/kg)
Mouse HAO1 mRNA,
Relative to PBS=1
1.5
1.0
0.5
0.0
PBS
10
3
1
0.3
0.1
ALN-GO1 (mg/kg)

FIG. 21

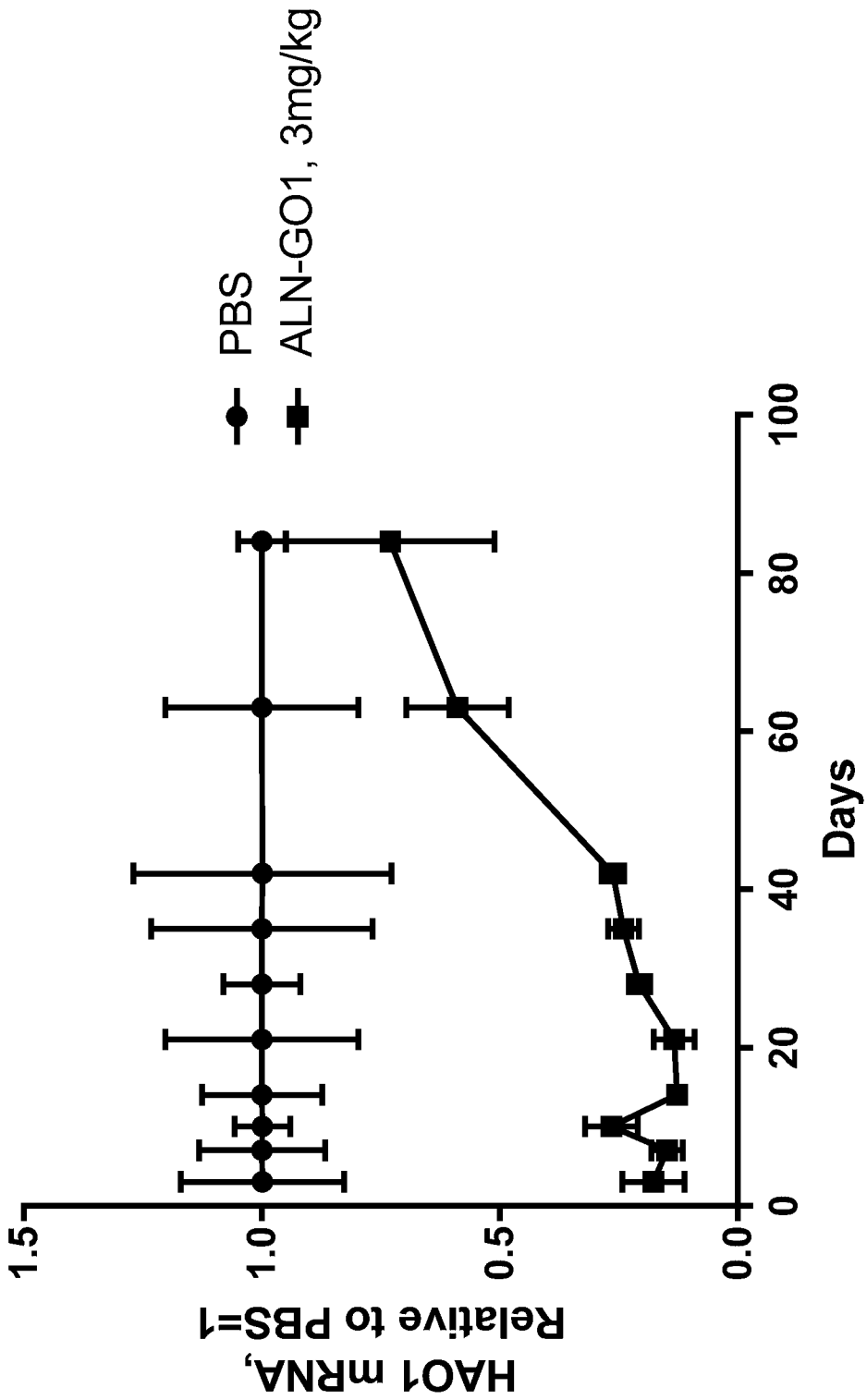

PBS
ALN-GO1, 3mg/kg
HAO1 mRNA,
Relative to PBS=1
1.5
1.0
0.5
0.0
0
20
40
60
80
100
Days

FIG. 22

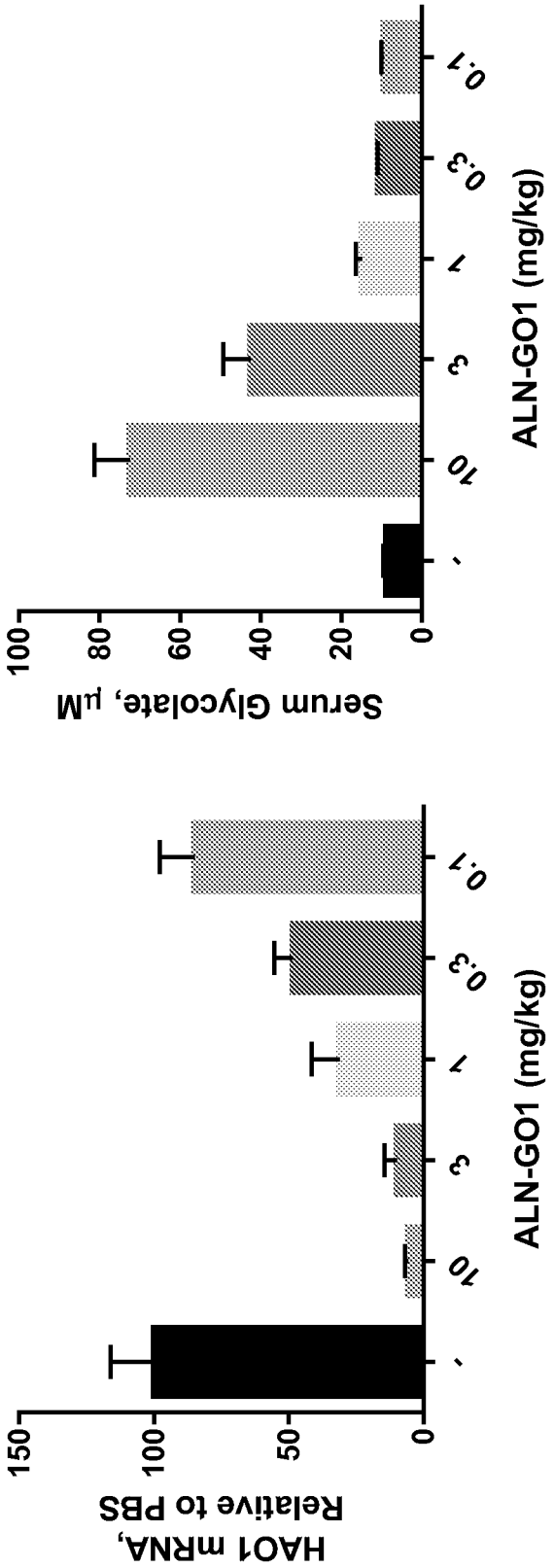

Serum Glycolate, μM
100
80
60
40
20
0
ALN-GO1 (mg/kg)
PBS
10
3
1
0.3
0.1
HAO1 mRNA, Relative to PBS
150
100
50
0
ALN-GO1 (mg/kg)
PBS
10
3
1
0.3
0.1

FIG. 23

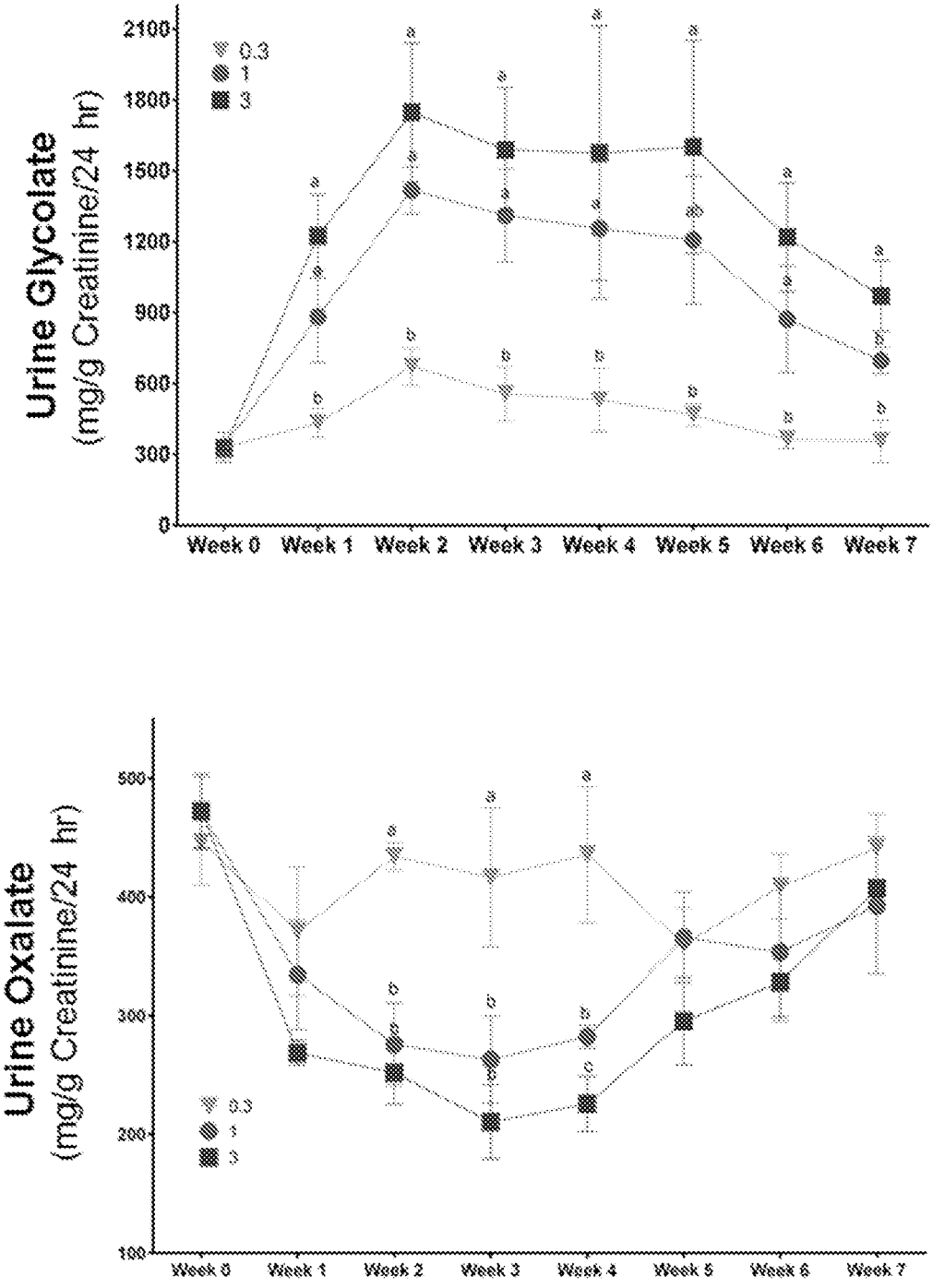

Urine Glycolate
(mg/g Creatinine/24 hr)
2100
1800
1500
1200
900
600
300
0
0.3
1
3
Week 0
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Urine Oxalate
(mg/g Creatinine/24 hr)
500
400
300
200
100
0.3
1
3
Week 0
Week 1
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7

FIG. 24

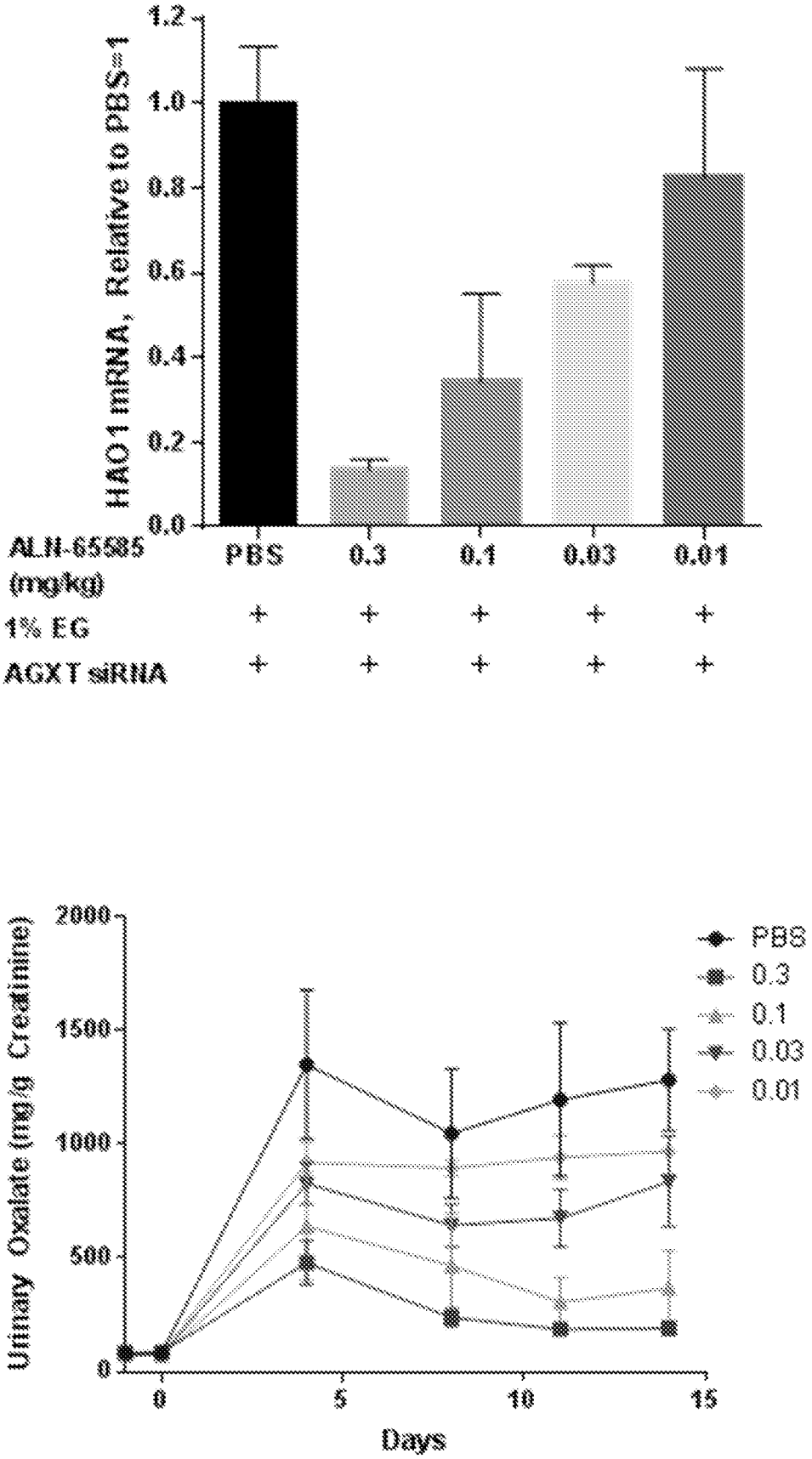

HAO1 mRNA, Relative to PBS=1
1.2
1.0
0.8
0.6
0.4
0.2
0.0
ALN-65585 (mg/kg)
PBS
0.3
0.1
0.03
0.01
1% EG
AGXT siRNA
Urinary Oxalate (mg/g Creatinine)
2000
1500
1000
500
0
0
5
10
15
Days
PBS
0.3
0.1
0.03
0.01

FIG. 25A

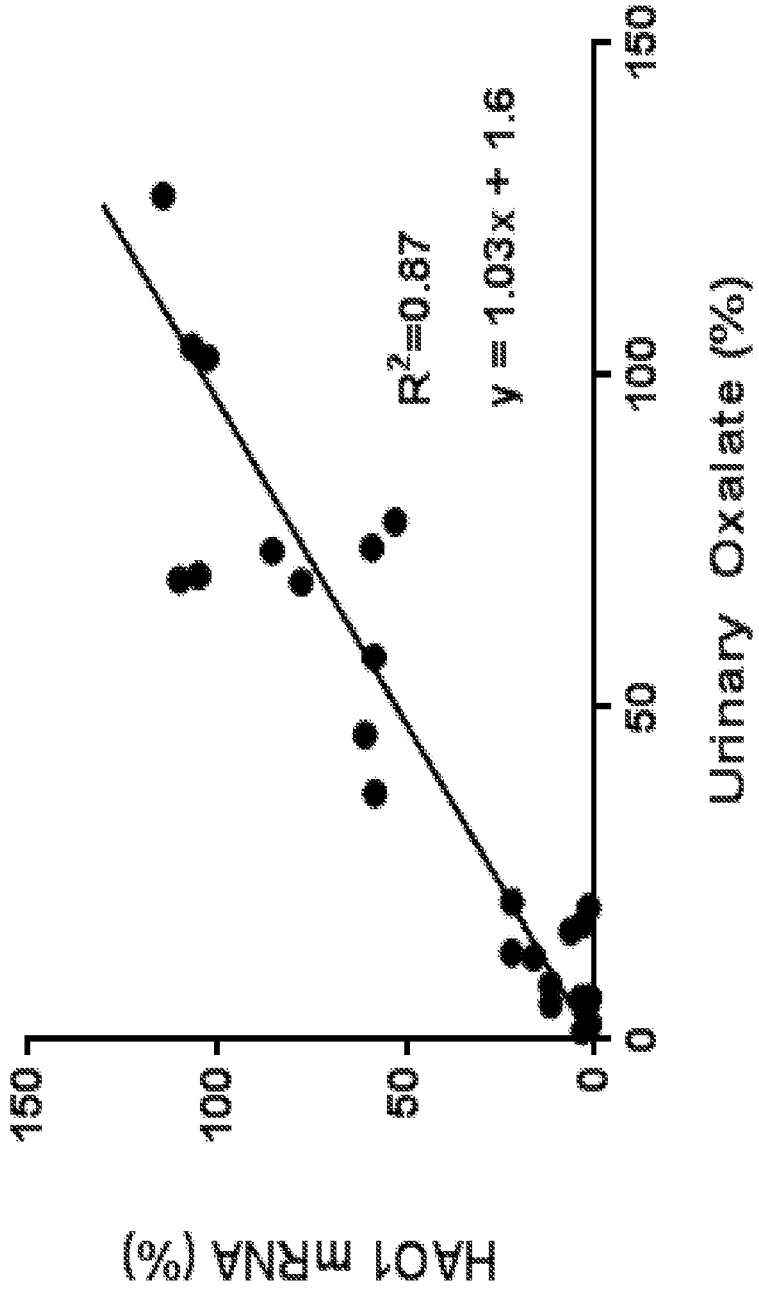

HAO1 mRNA (%)
150
100
50
0
0
50
100
150
Urinary Oxalate (%)
R^2=0.87
y = 1.03x + 1.6

FIG. 25B

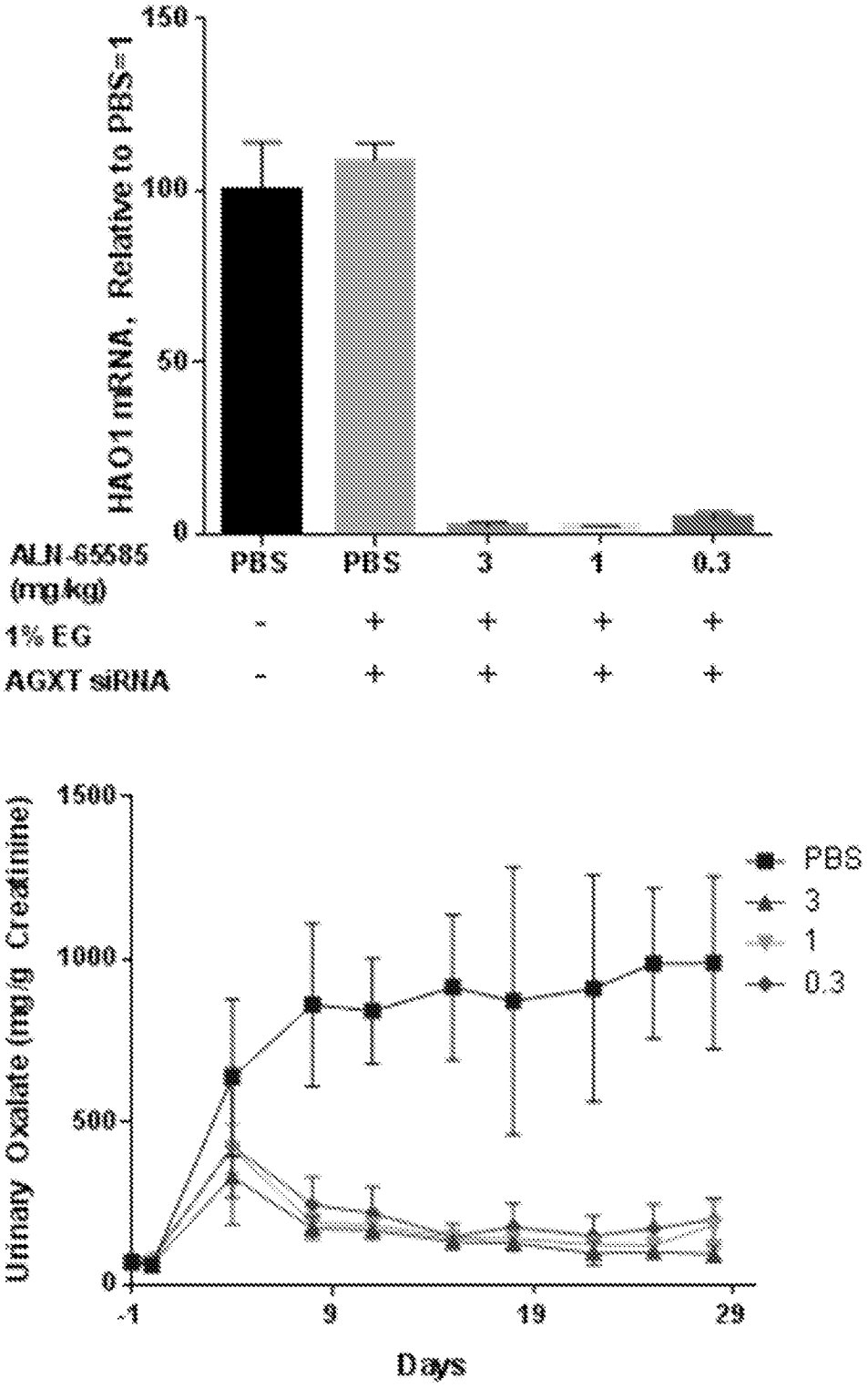
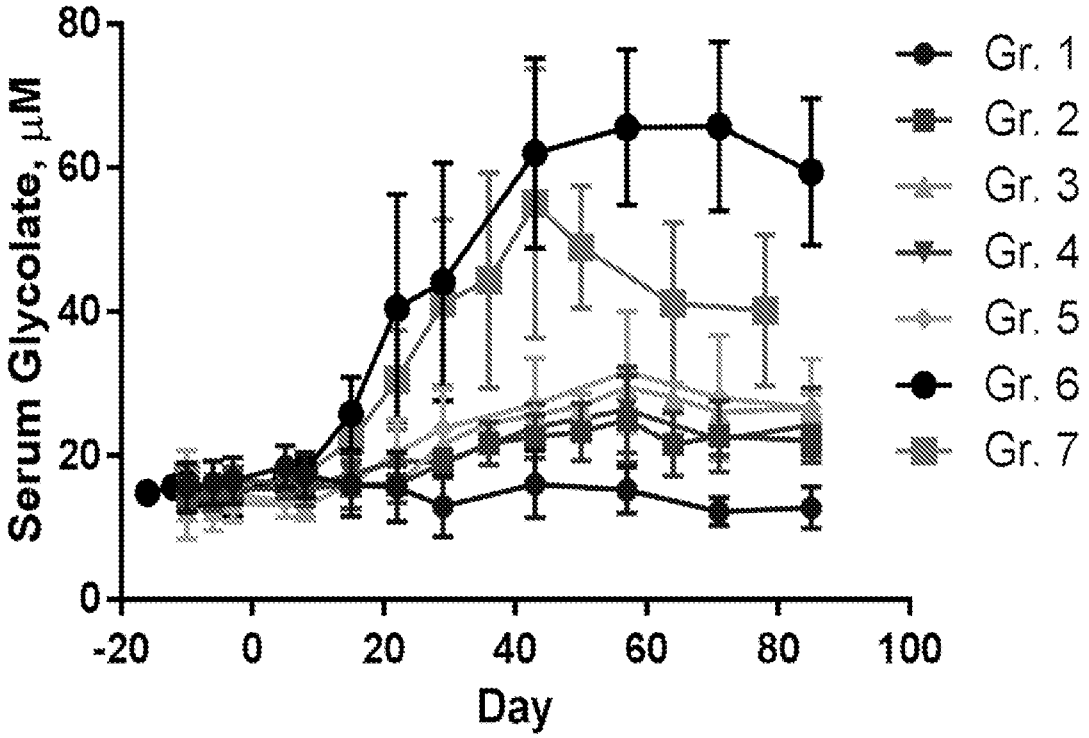

HAO1 mRNA, Relative to PBS=1
150
100
50
0
ALN-65585 (mg/kg)
PBS
PBS
3
1
0.3
1% EG
-
+
+
+
+
AGXT siRNA
-
+
+
+
+
Urinary Oxalate (mg/g Creatinine)
1500
1000
500
0
-1
9
19
29
Days
PBS
3
1
0.3

FIG. 26


Serum Glycolate, μM
80
60
40
20
0
-20
0
20
40
60
80
100
Day
Gr. 1
Gr. 2
Gr. 3
Gr. 4
Gr. 5
Gr. 6
Gr. 7

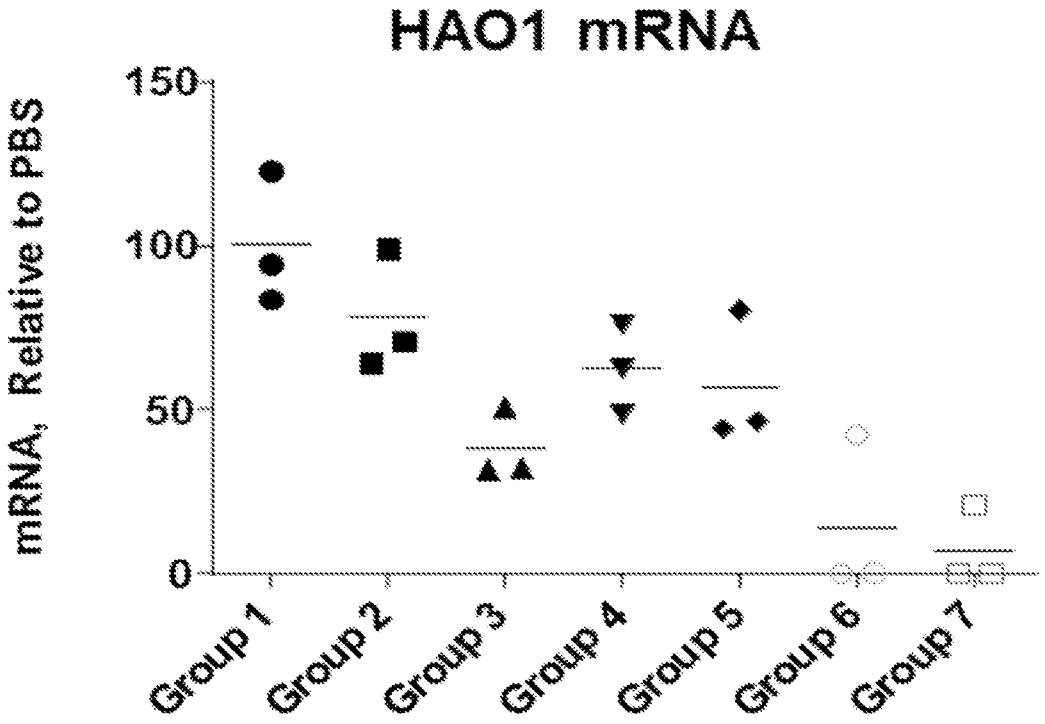

HAO1 mRNA
mRNA, Relative to PBS
150
100
50
0
Group 1
Group 2
Group 3
Group 4
Group 5
Group 6
Group 7

FIG. 27