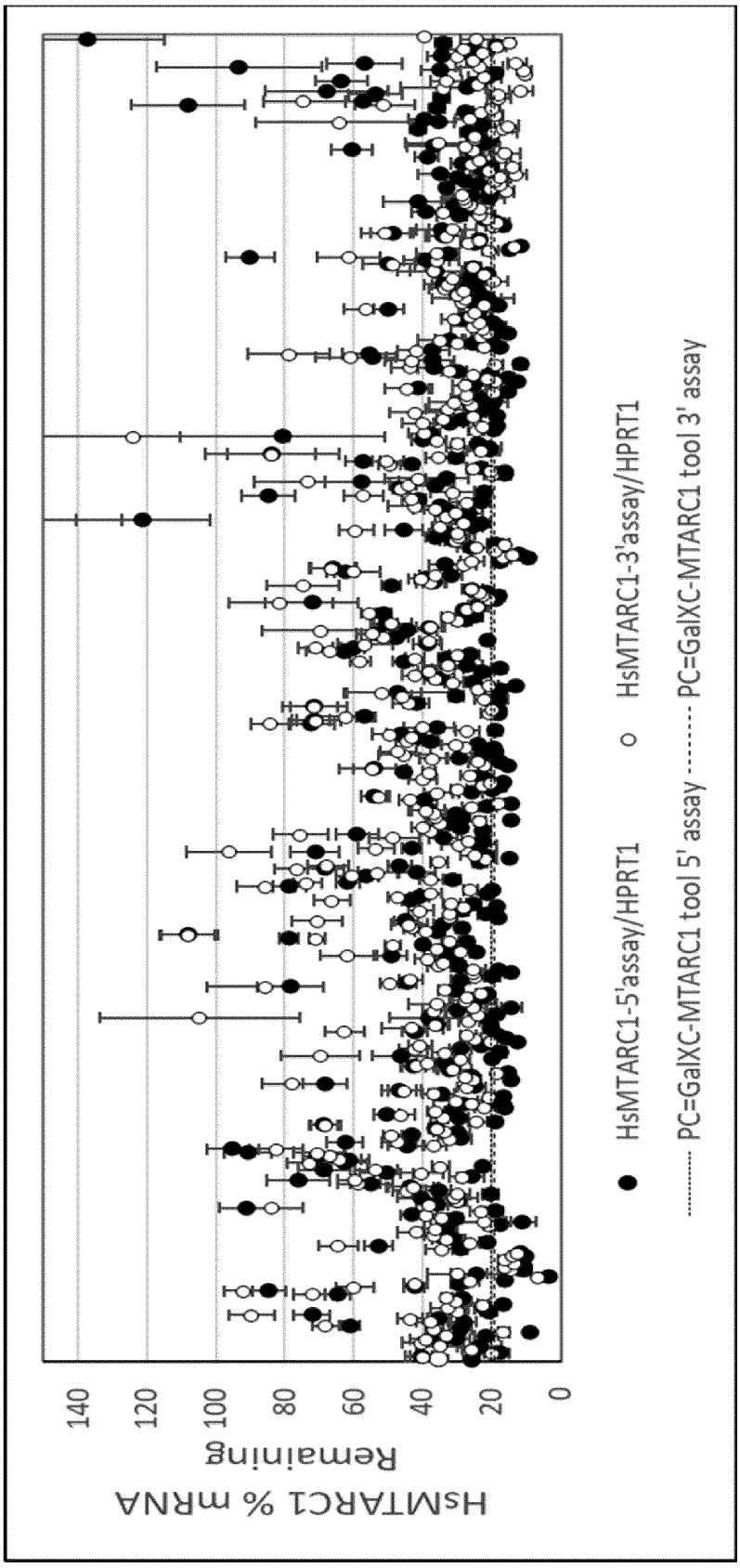
HsMTARC1 % mRNA Remaining
140
120
100
80
60
40
20
0
HsMTARC1-5'assay/HPRT1
HsMTARC1-3'assay/HPRT1
PC=GalXC-MTARC1 tool 5' assay
PC=GalXC-MTARC1 tool 3' assay

FIG. 1

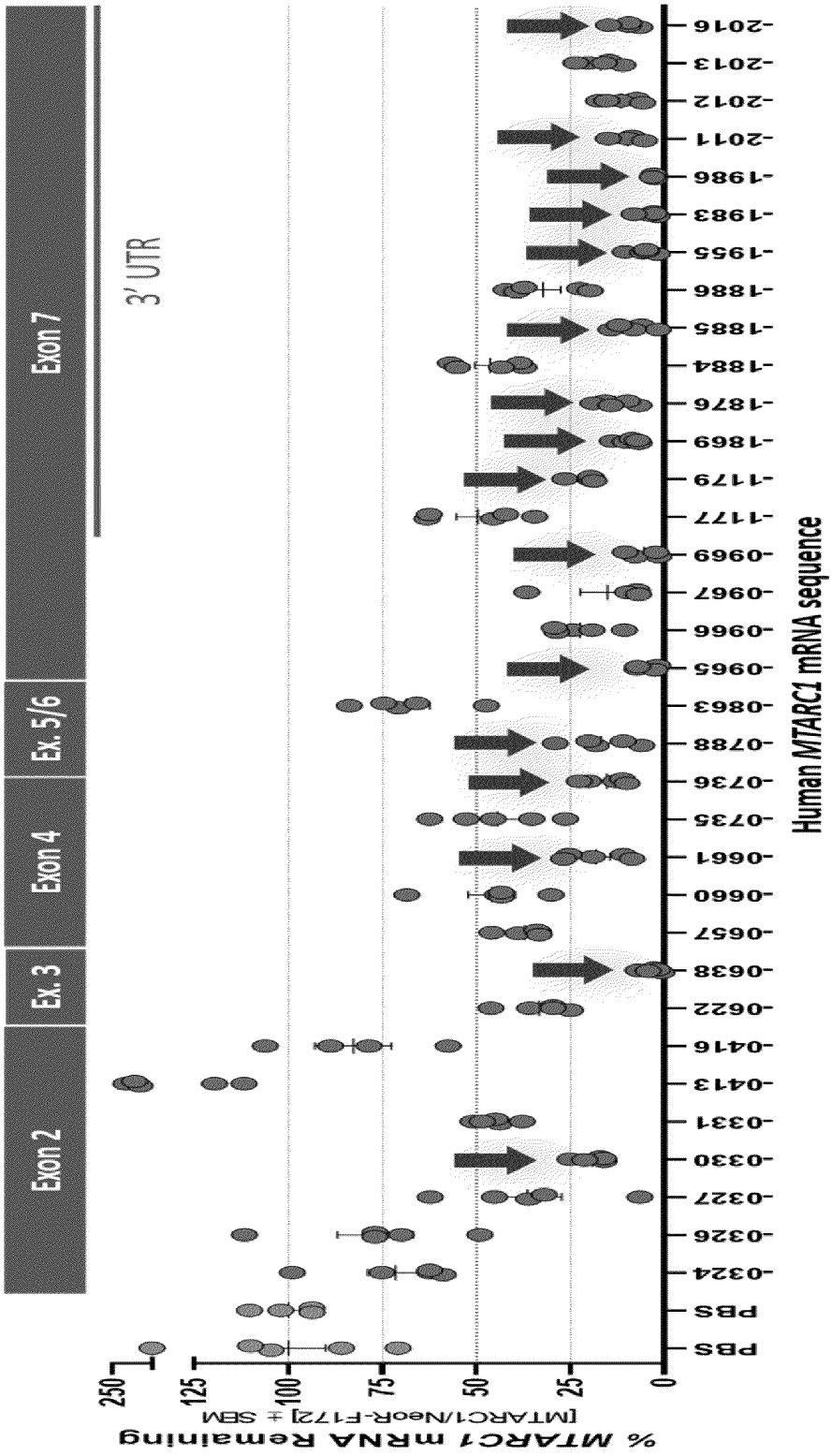
Exon 2
Ex. 3
Exon 4
Ex. 5/6
Exon 7
3' UTR
% MTARC1 mRNA Remaining
[MTARC1/NeoR-F172] ± SEM
250
125
100
75
50
25
0
Human MTARC1 mRNA sequence
PBS
PBS
-0324
-0326
-0327
-0330
-0331
-0413
-0416
-0622
-0638
-0657
-0660
-0661
-0735
-0736
-0788
-0863
-0965
-0966
-0967
-0969
-1177
-1179
-1869
-1876
-1884
-1885
-1886
-1955
-1983
-1986
-2011
-2012
-2013
-2016

FIG. 2

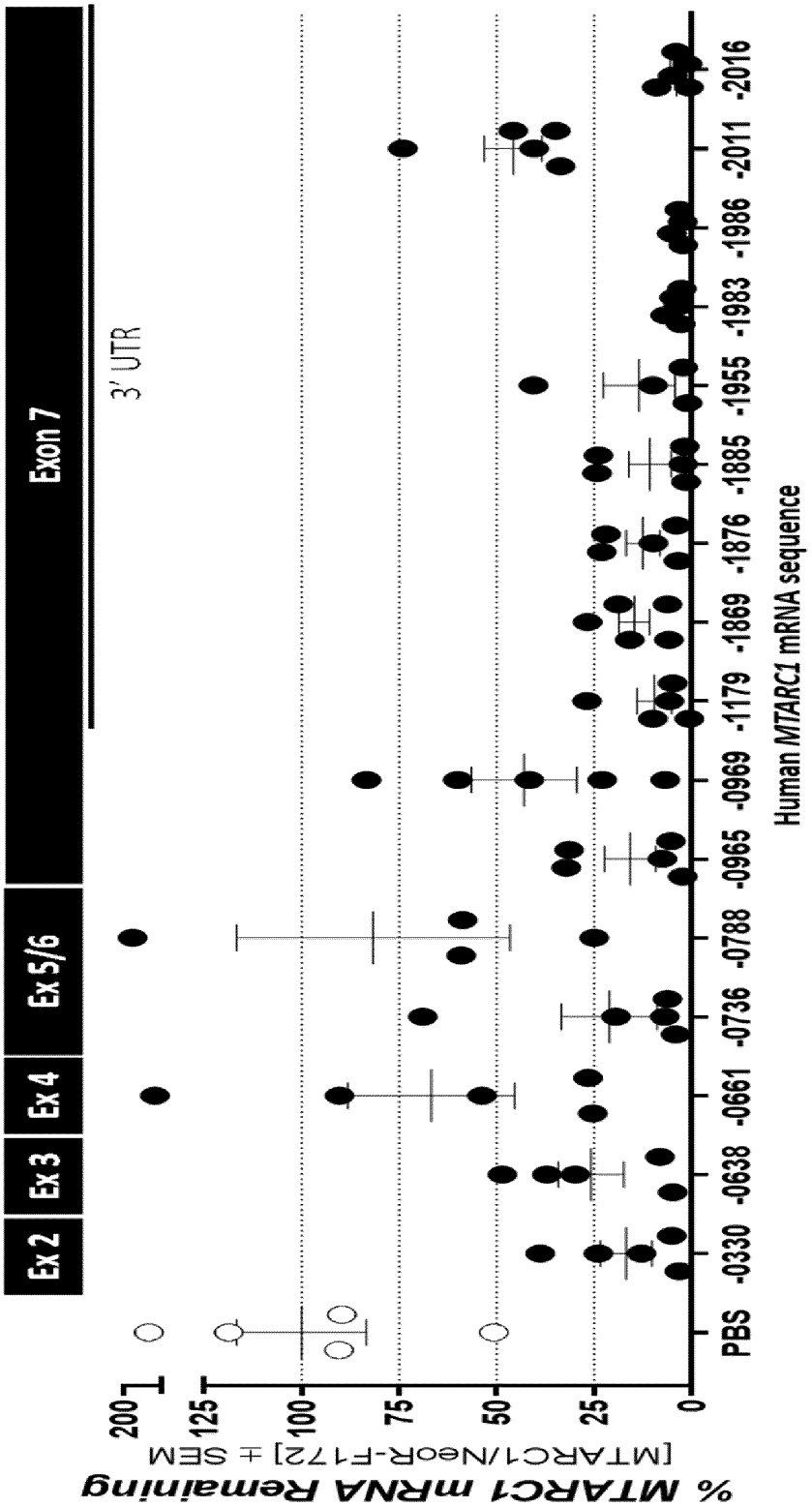
Ex 2
Ex 3
Ex 4
Ex 5/6
Exon 7
3' UTR
% MTARC1 mRNA Remaining
[MTARC1/NeoR-F172] ± SEM
200
125
100
75
50
25
0
PBS
-0330
-0638
-0661
-0736
-0788
-0965
-0969
-1179
-1869
-1876
-1885
-1955
-1983
-1986
-2011
-2016
Human MTARC1 mRNA sequence

FIG. 3

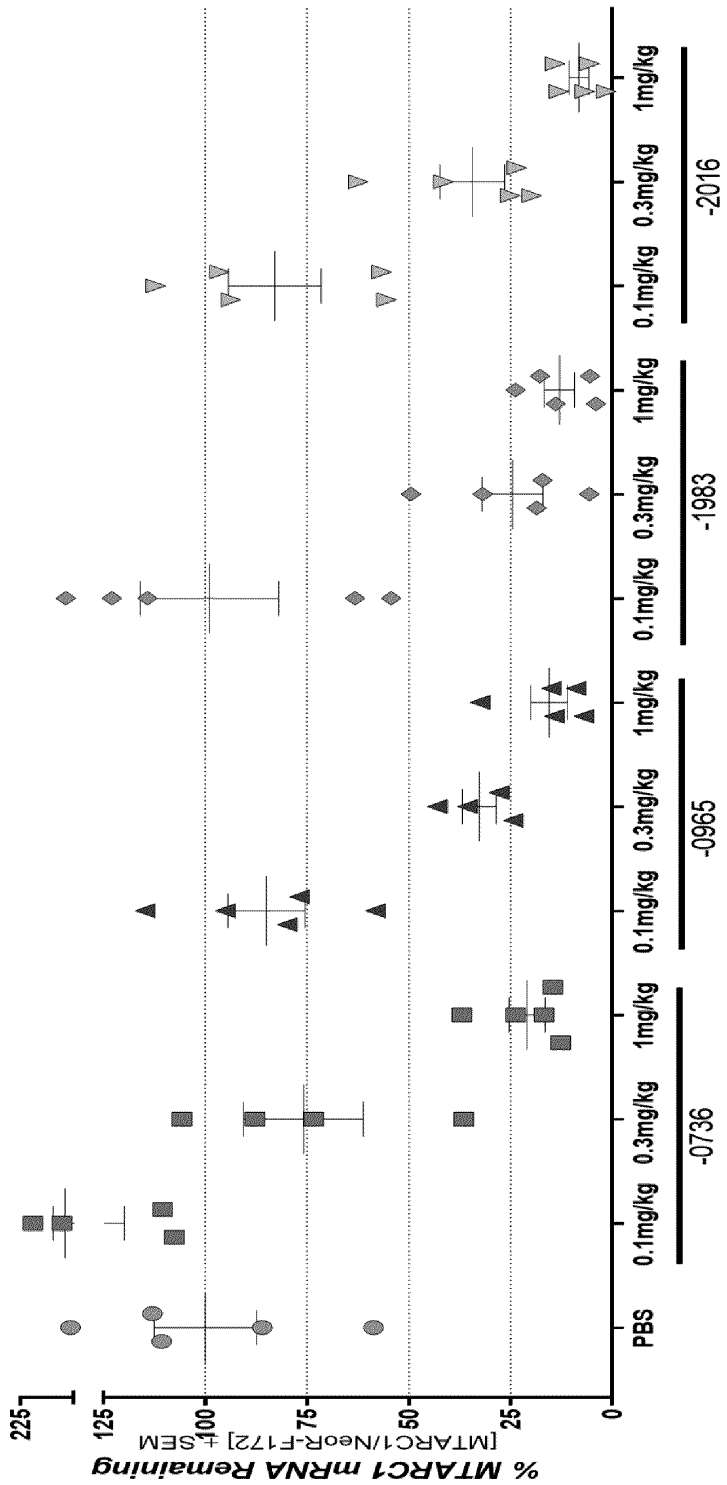
% MTARC1 mRNA Remaining
[MTARC1/NeoR-F172] ± SEM
225
125
100
75
50
25
0
PBS
0.1mg/kg
0.3mg/kg
1mg/kg
-0736
0.1mg/kg
0.3mg/kg
1mg/kg
-0965
0.1mg/kg
0.3mg/kg
1mg/kg
-1983
0.1mg/kg
0.3mg/kg
1mg/kg
-2016

FIG. 4

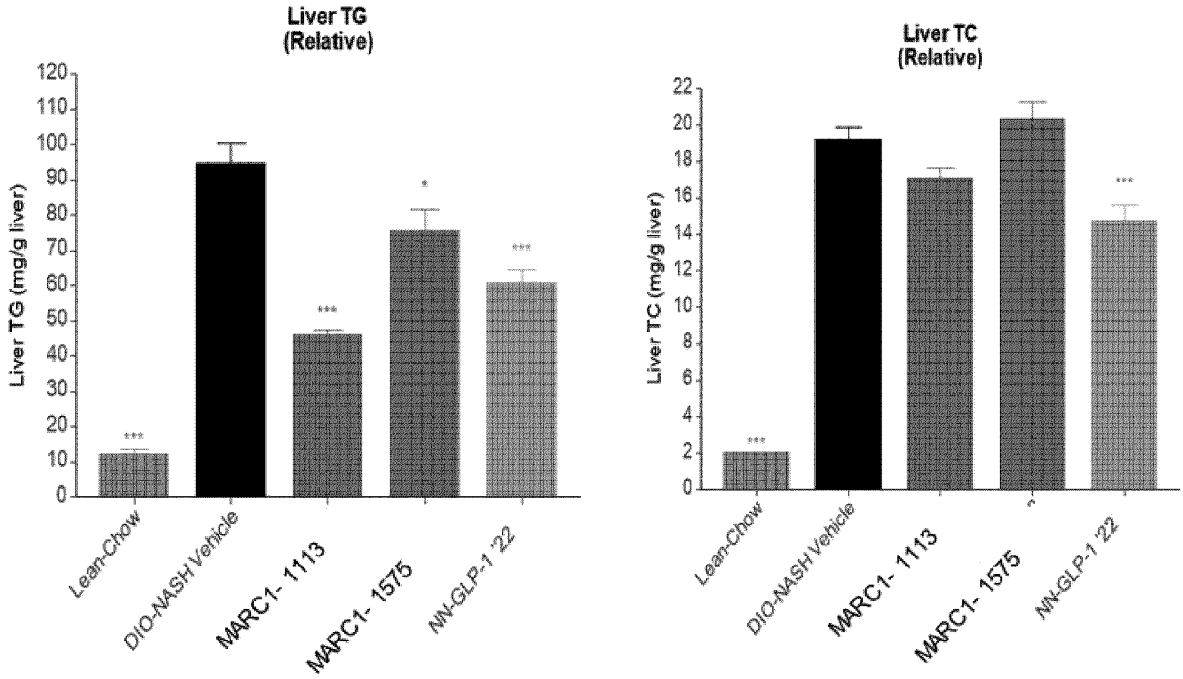
Liver TG
(Relative)
Liver TG (mg/g liver)
120
110
100
90
80
70
60
50
40
30
20
10
0
***
***
*
***
Lean-Chow
DIO-NASH Vehicle
MARC1- 1113
MARC1- 1575
NN-GLP-1 '22
Liver TC
(Relative)
Liver TC (mg/g liver)
22
20
18
16
14
12
10
8
6
4
2
0
***
***
Lean-Chow
DIO-NASH Vehicle
MARC1- 1113
MARC1- 1575
NN-GLP-1 '22

FIG. 5

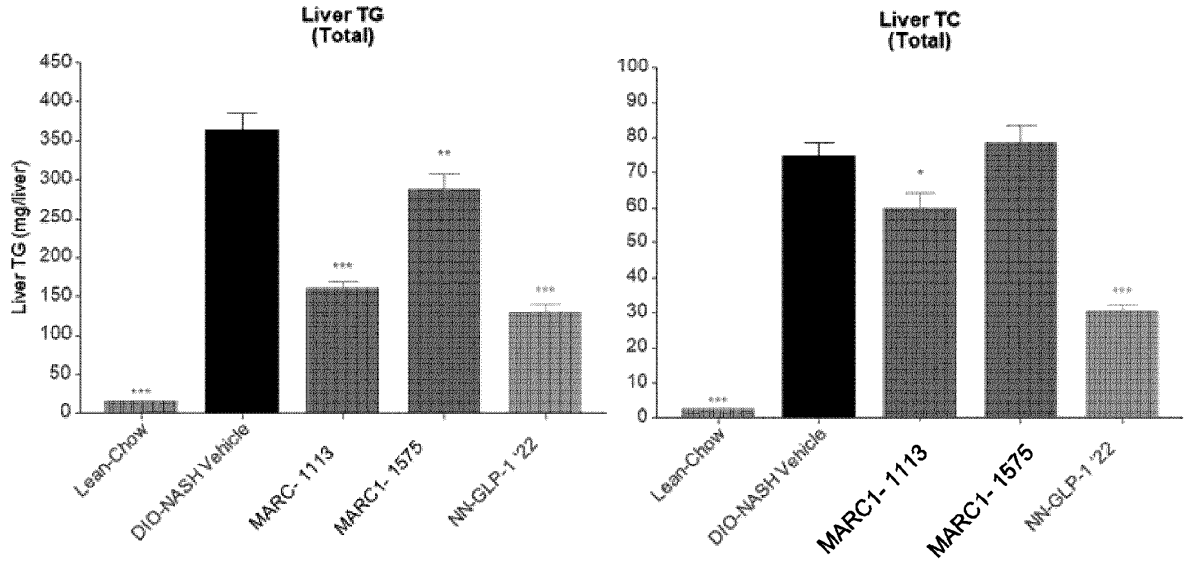
Liver TG
(Total)
Liver TG (mg/liver)
450
400
350
300
250
200
150
100
50
0
***
**
***
***
Lean-Chow
DIO-NASH Vehicle
MARC- 1113
MARC1- 1575
NN-GLP-1 '22
Liver TC
(Total)
100
90
80
70
60
50
40
30
20
10
0
***
*
***
Lean-Chow
DIO-NASH Vehicle
MARC1- 1113
MARC1- 1575
NN-GLP-1 '22

FIG. 6

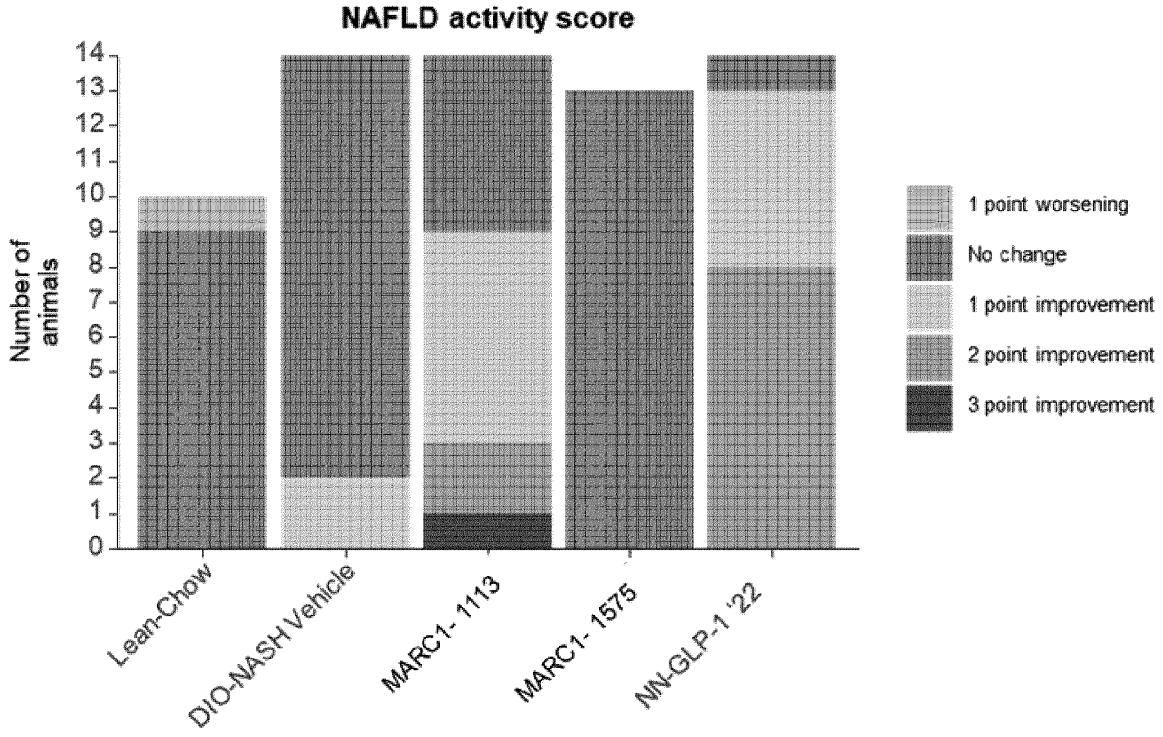
NAFLD activity score
Number of animals
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Lean-Chow
DIO-NASH Vehicle
MARC1- 1113
MARC1- 1575
NN-GLP-1 '22
1 point worsening
No change
1 point improvement
2 point improvement
3 point improvement

FIG. 7

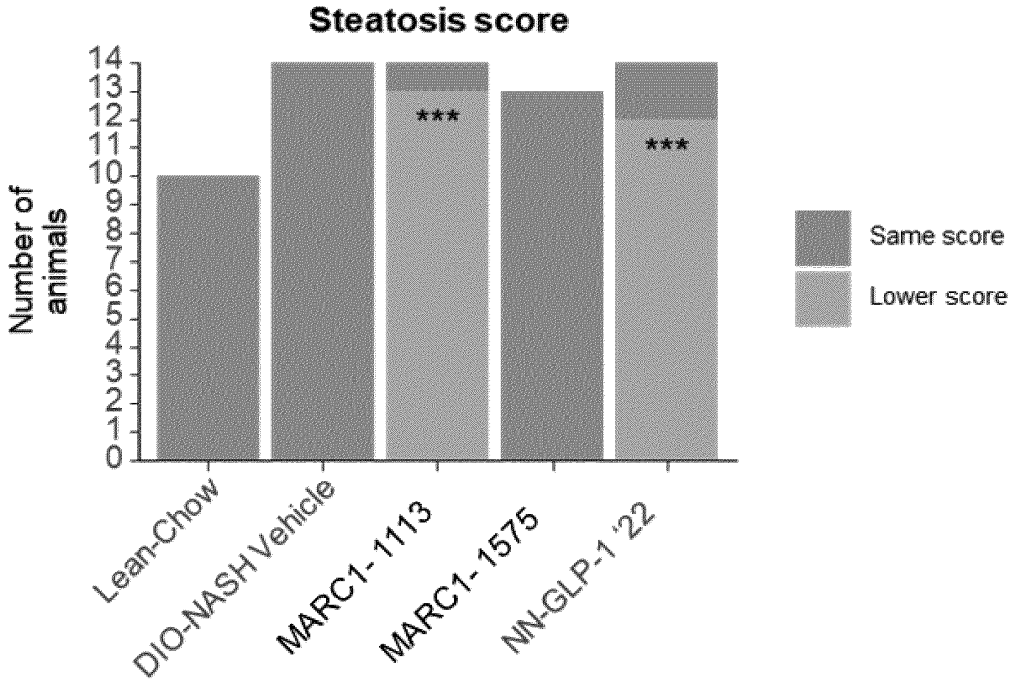
Steatosis score
Number of animals
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
***
***
Lean-Chow
DIO-NASH Vehicle
MARC1-1113
MARC1-1575
NN-GLP-1 '22
Same score
Lower score

FIG. 8

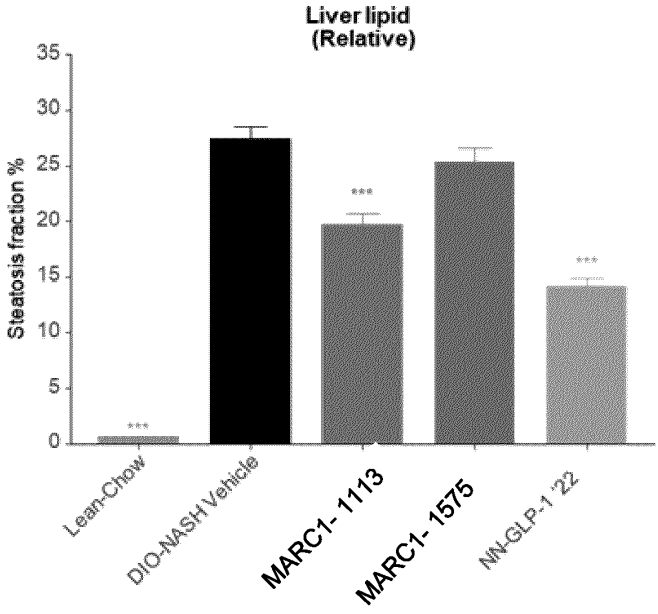
Liver lipid
(Relative)
Steatosis fraction %
35
30
25
20
15
10
5
0
***
***
***
Lean-Chow
DIO-NASH Vehicle
MARC1- 1113
MARC1- 1575
NN-GLP-1 '22

FIG. 9A

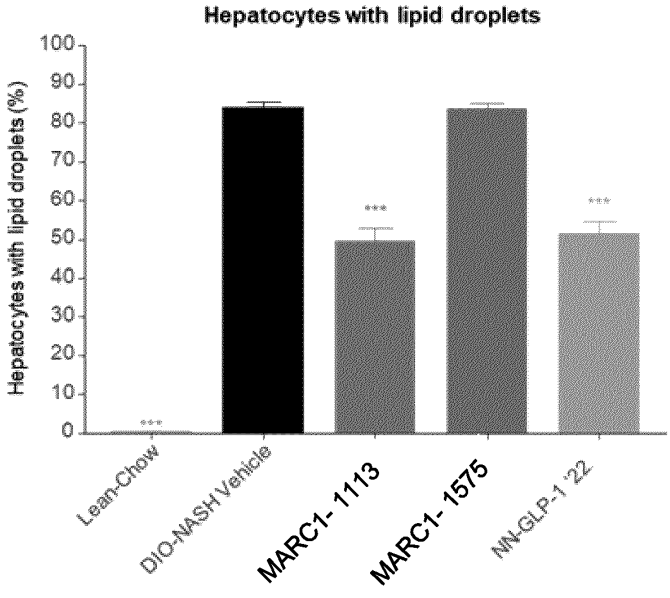
Hepatocytes with lipid droplets
Hepatocytes with lipid droplets (%)
100
90
80
70
60
50
40
30
20
10
0
***
***
***
Lean-Chow
DIO-NASH Vehicle
MARC1- 1113
MARC1- 1575
NN-GLP-1 '22

FIG. 9B

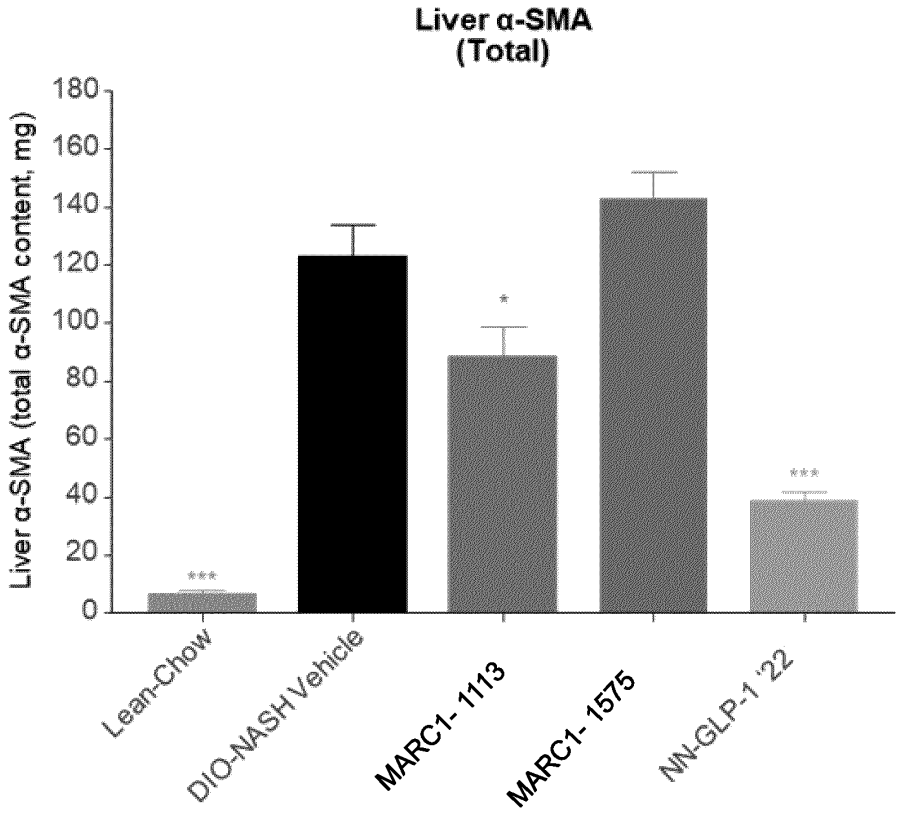
Liver α-SMA
(Total)
Liver α-SMA (total α-SMA content, mg)
180
160
140
120
100
80
60
40
20
0
***
*
***
Lean-Chow
DIO-NASH Vehicle
MARC1- 1113
MARC1- 1575
NN-GLP-1 '22

FIG. 10

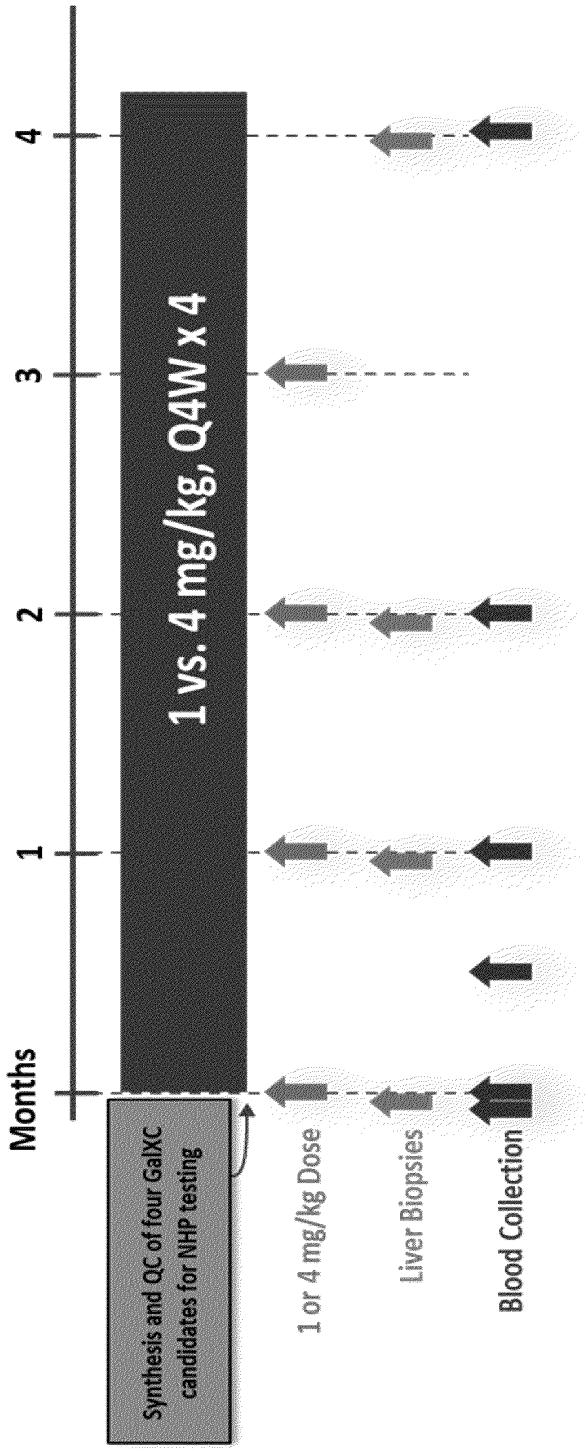
Months
1
2
3
4
1 vs. 4 mg/kg, Q4W x 4
Synthesis and QC of four GalXC candidates for NHP testing
1 or 4 mg/kg Dose
Liver Biopsies
Blood Collection

FIG. 11

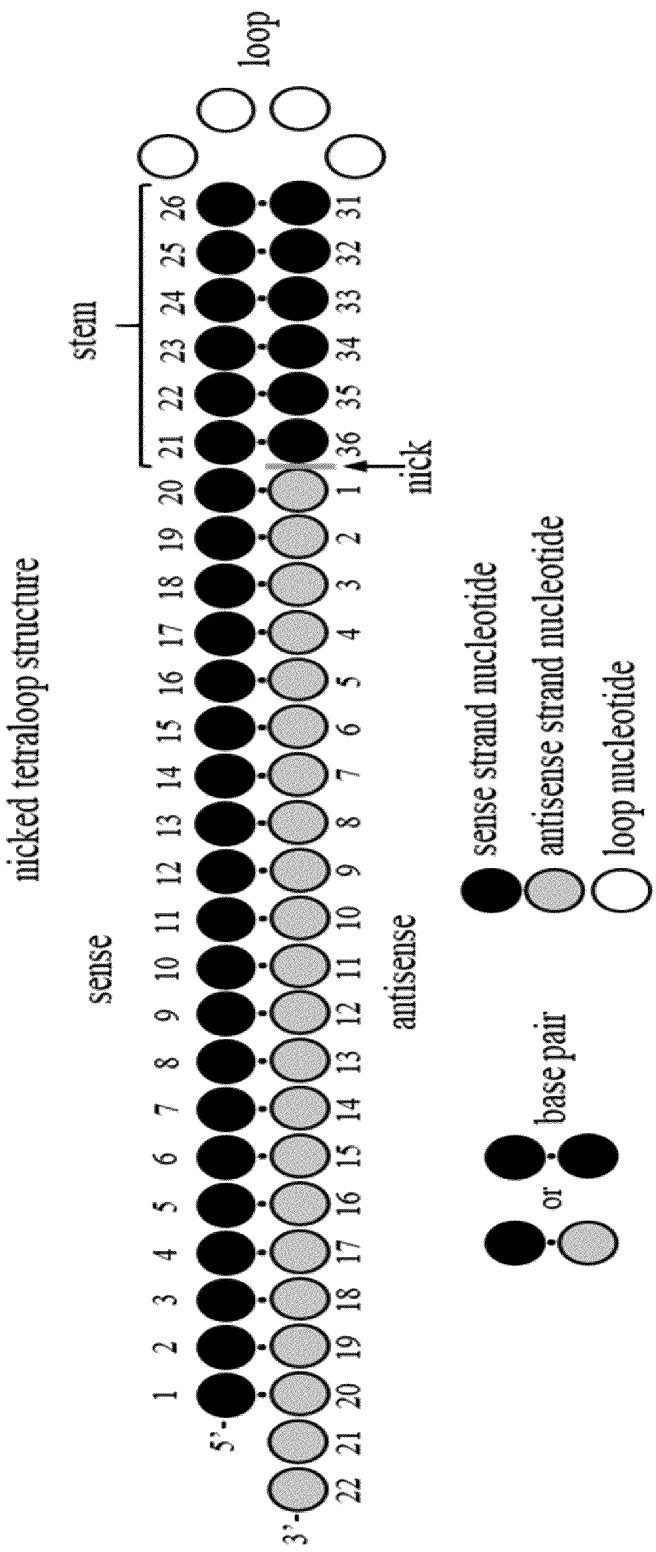
nicked tetraloop structure
stem
loop
nick
sense
antisense
5'-
3'-
sense strand nucleotide
antisense strand nucleotide
loop nucleotide
base pair
or

FIG. 12