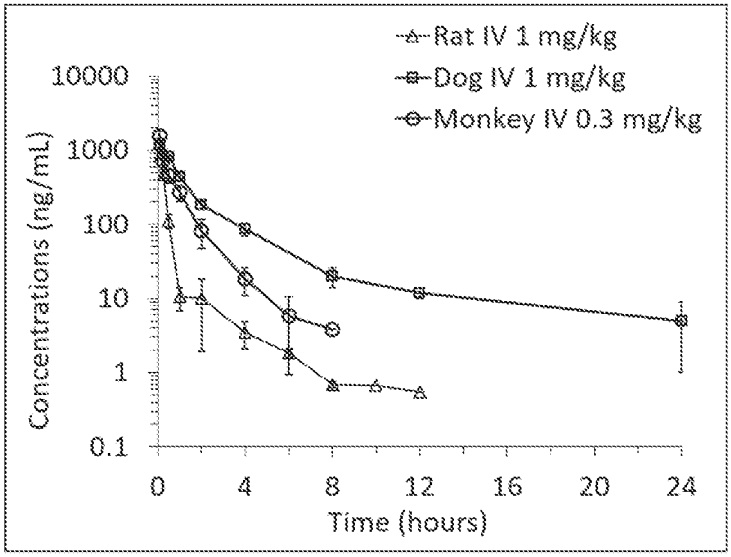

Rat IV 1 mg/kg
Dog IV 1 mg/kg
Monkey IV 0.3 mg/kg
Concentrations (ng/mL)
10000
1000
100
10
1
0.1
0
4
8
12
16
20
24
Time (hours)

FIG. 1A

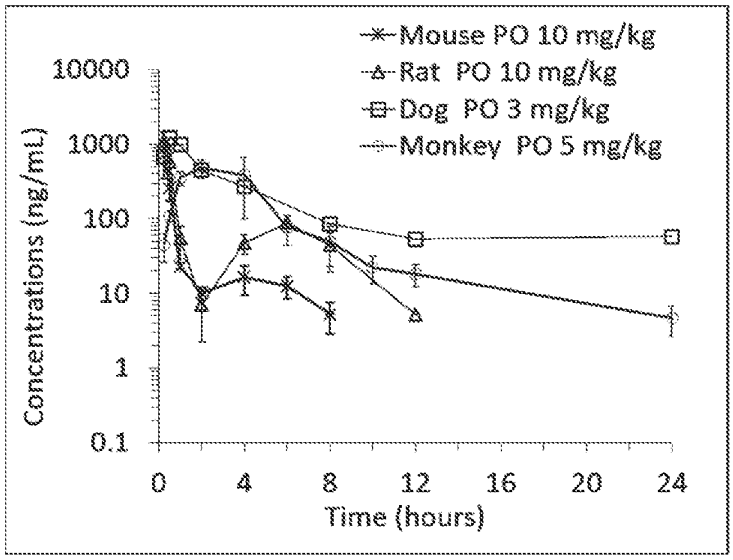

Mouse PO 10 mg/kg
Rat PO 10 mg/kg
Dog PO 3 mg/kg
Monkey PO 5 mg/kg
Concentrations (ng/mL)
10000
1000
100
10
1
0.1
0
4
8
12
16
20
24
Time (hours)

FIG. 1B

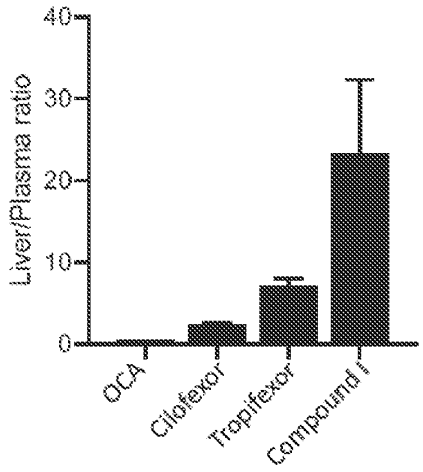

Liver/Plasma ratio
40
30
20
10
0
OCA
Clofexor
Tropifexor
Compound I

FIG. 2A

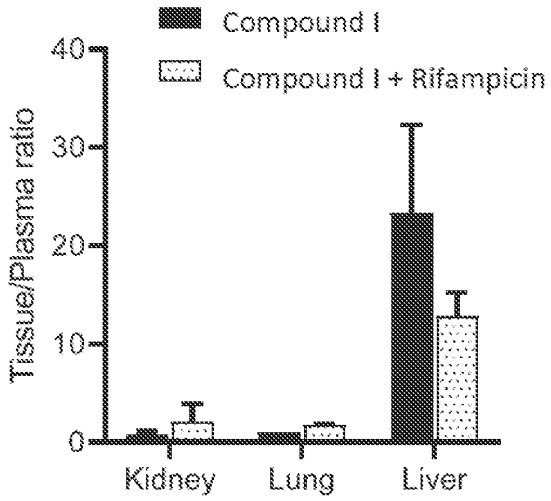

Compound I
Compound I + Rifampicin
Tissue/Plasma ratio
40
30
20
10
0
Kidney
Lung
Liver

FIG. 2B

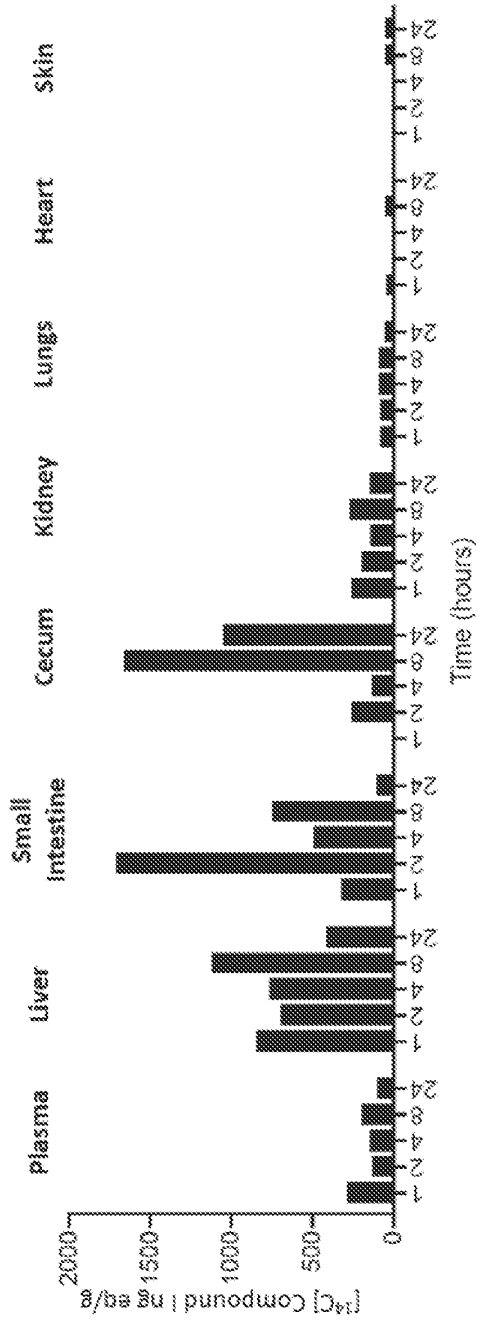

Plasma
Liver
Small Intestine
Cecum
Kidney
Lungs
Heart
Skin
Time (hours)
[14C] Compound ng eq/g
2000
1500
1000
500
0

FIG. 3

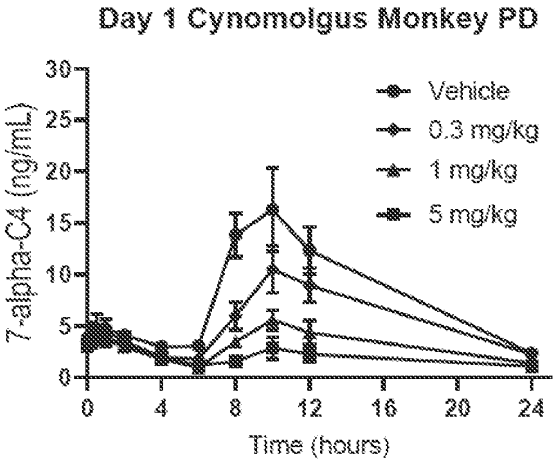


FIG. 4

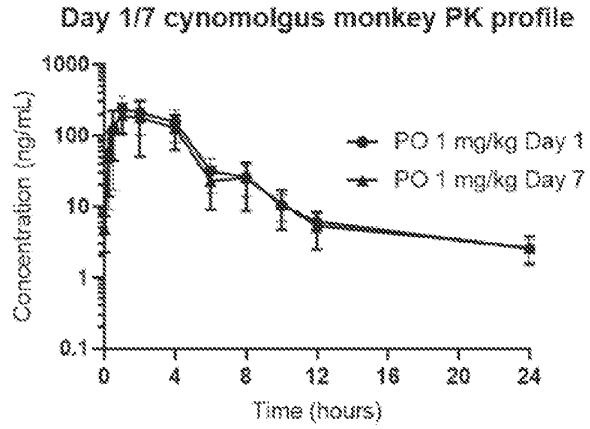


FIG. 5A

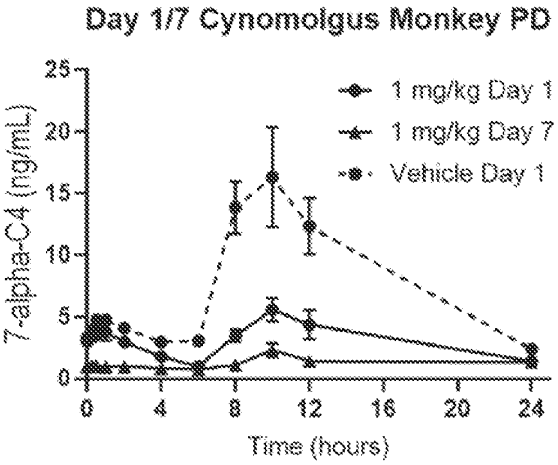


FIG. 5B

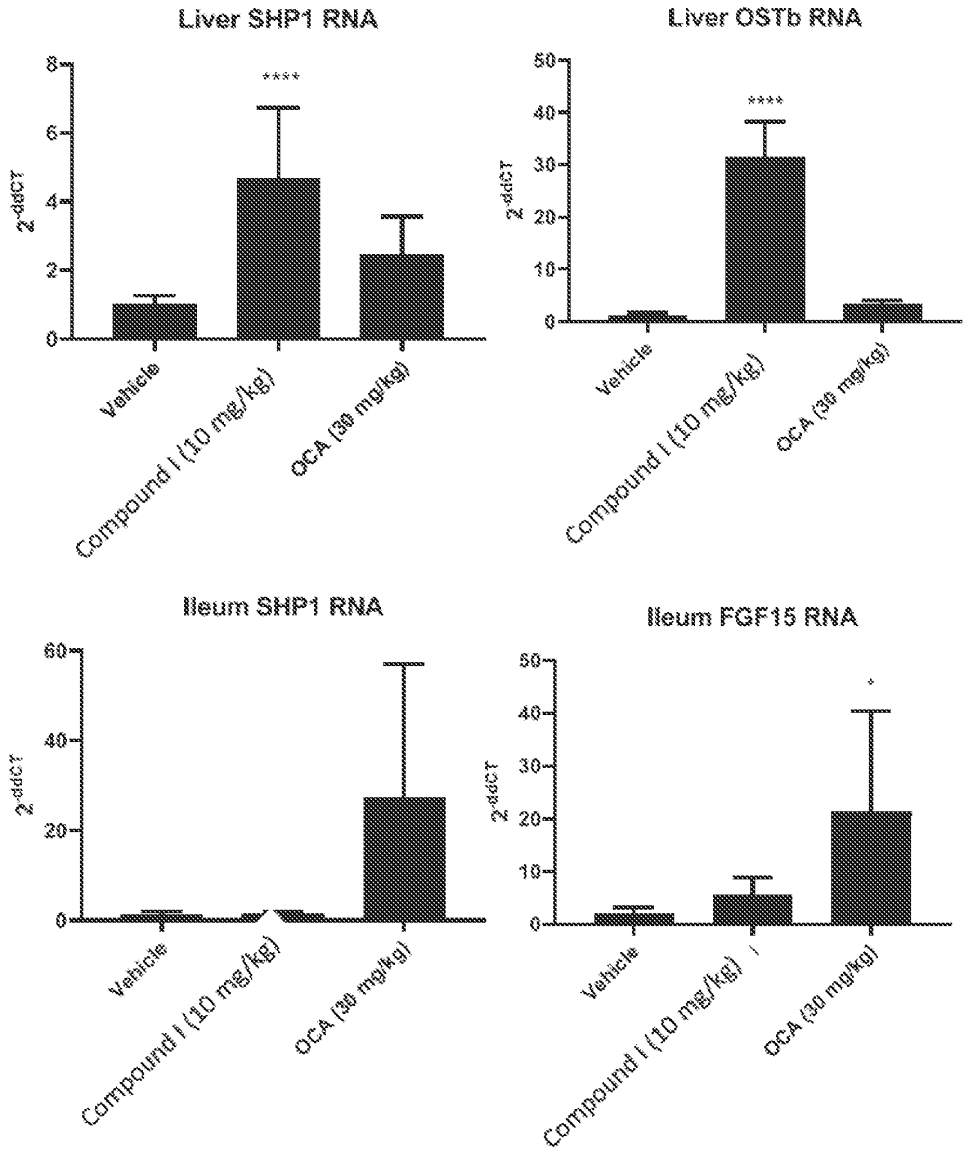

Liver SHP1 RNA
Liver OSTb RNA
Ileum SHP1 RNA
Ileum FGF15 RNA
2-ddCT
****
*
Vehicle
Compound I (10 mg/kg)
OCA (30 mg/kg)

FIG. 6

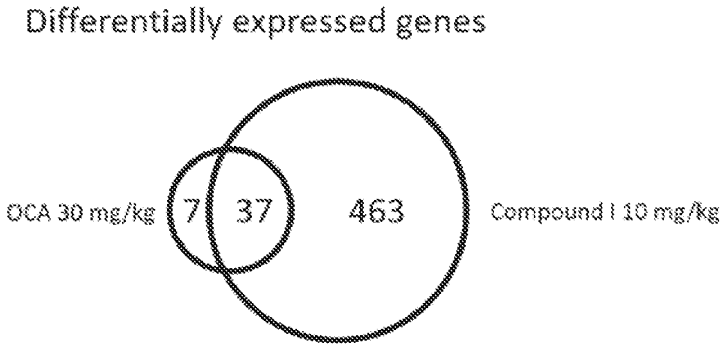

Differentially expressed genes
OCA 30 mg/kg
7
37
463
Compound I 10 mg/kg

FIG. 7A

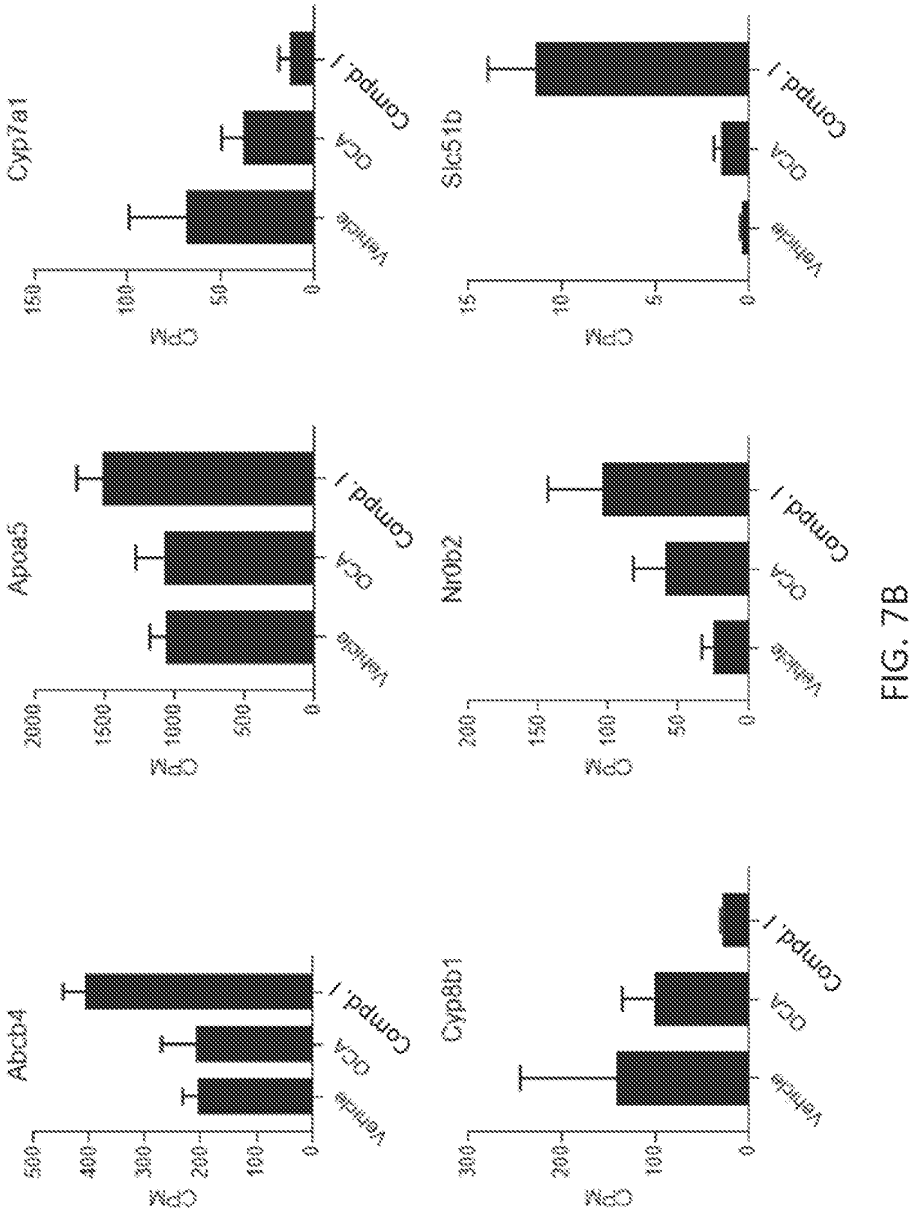

Cyp7a1
Slc51b
Apoa5
Nr0b2
Abcb4
Cyp8b1
CPM
Vehicle
OCA
Compd. I

FIG. 7B

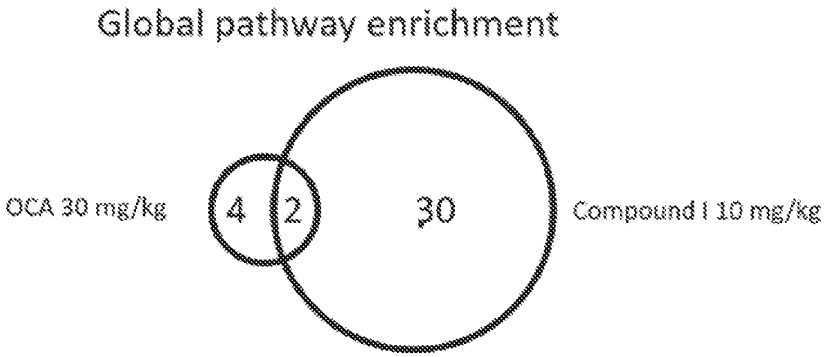

Global pathway enrichment
OCA 30 mg/kg
4
2
30
Compound I 10 mg/kg

FIG. 7C

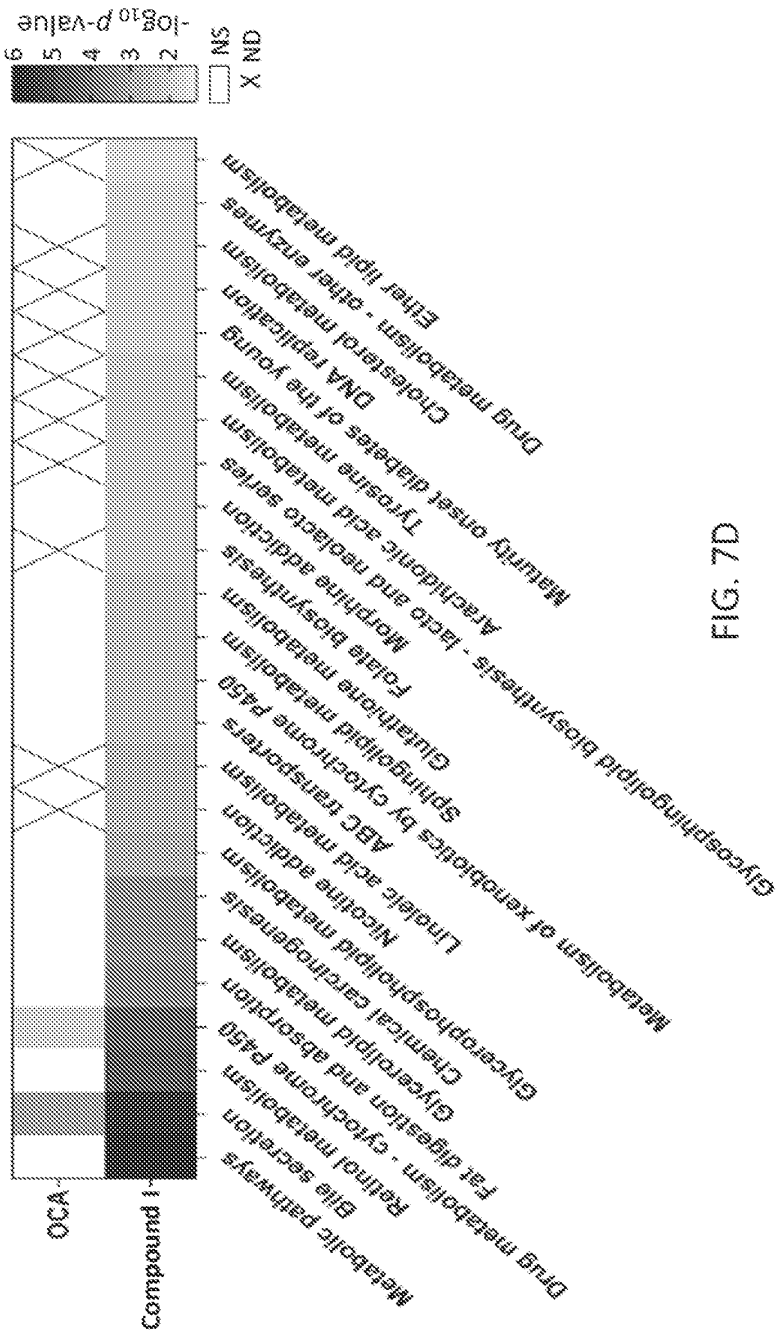

-log10 p-value
9 5 4 3 2
NS
NA
OCA
Compound 1
Metabolic pathways
Bile secretion
Retinol metabolism
Drug metabolism - cytochrome P450
Fat digestion and absorption
Chemical carcinogenesis
Glycerophospholipid metabolism
Nicotine addiction
Linoleic acid metabolism
ABC transporters
Sphingolipid metabolism
Metabolism of xenobiotics by cytochrome P450
Glutathione metabolism
Folate biosynthesis
Morphine addiction
Glycosphingolipid biosynthesis - lacto and neolacto series
Arachidonic acid metabolism
Tyrosine metabolism
Maturity onset diabetes of the young
DNA replication
Cholesterol metabolism
Drug metabolism - other enzymes
Ether lipid metabolism

FIG. 7D

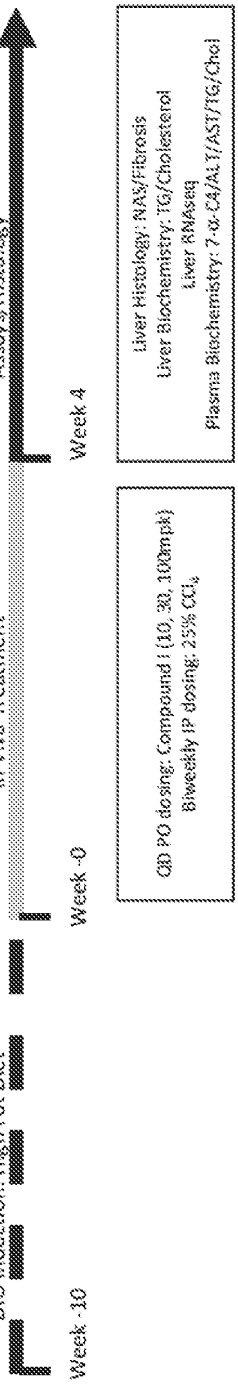

DIO Induction: High Fat Diet
Week -10
Week -0
In Vivo Treatment
Week 4
Assays/Histology
QD PO dosing: Compound I (10, 30, 100mpk)
Biweekly IP dosing: 25% CCl_4
Liver Histology: NAS/Fibrosis
Liver Biochemistry: TG/Cholesterol
Liver RNAseq
Plasma Biochemistry: 7-α-C4/ALT/AST/TG/Chol

FIG. 8

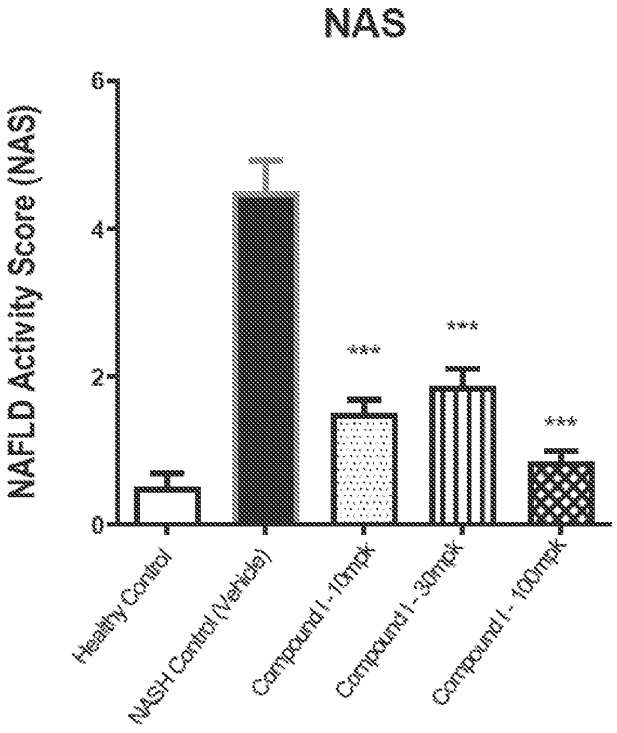

NAS
NAFLD Activity Score (NAS)
0
2
4
6
***
***
***
Healthy Control
NASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 9

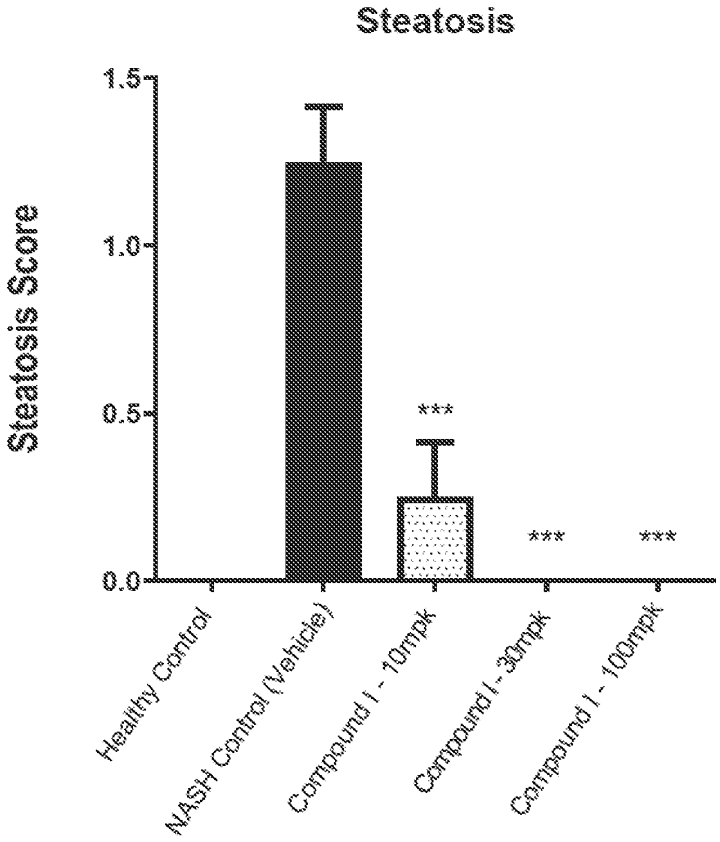

Steatosis
Steatosis Score
1.5
1.0
0.5
0.0
***
***
***
Healthy Control
NASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 10A

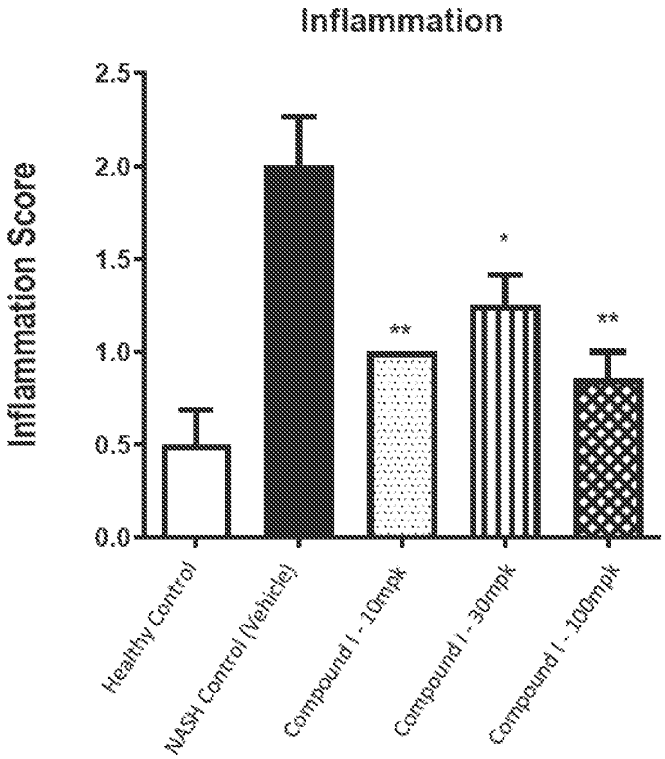

Inflammation
Inflammation Score
2.5
2.0
1.5
1.0
0.5
0.0
**
*
**
Healthy Control
NASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 10B

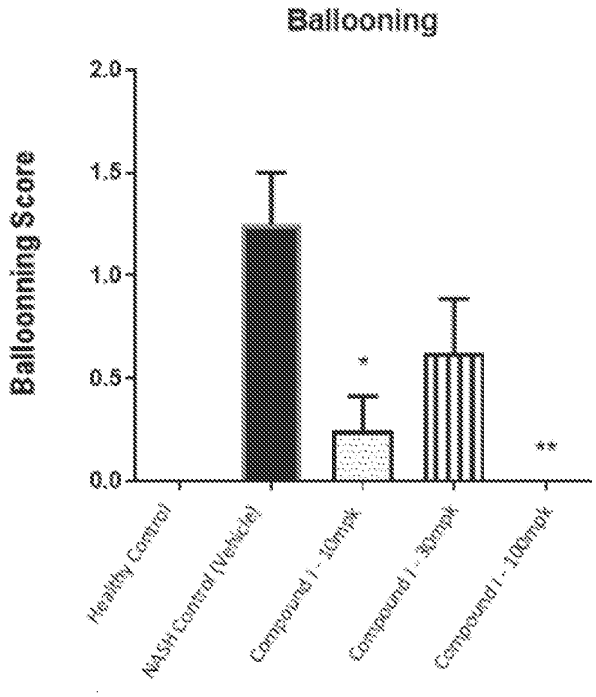

Ballooning
Ballooning Score
2.0
1.5
1.0
0.5
0.0
*
**
Healthy Control
NASH Control (Vehicle)
Compound 1 - 30mpk
Compound 1 - 30mpk
Compound 1 - 10mpk

FIG. 10C

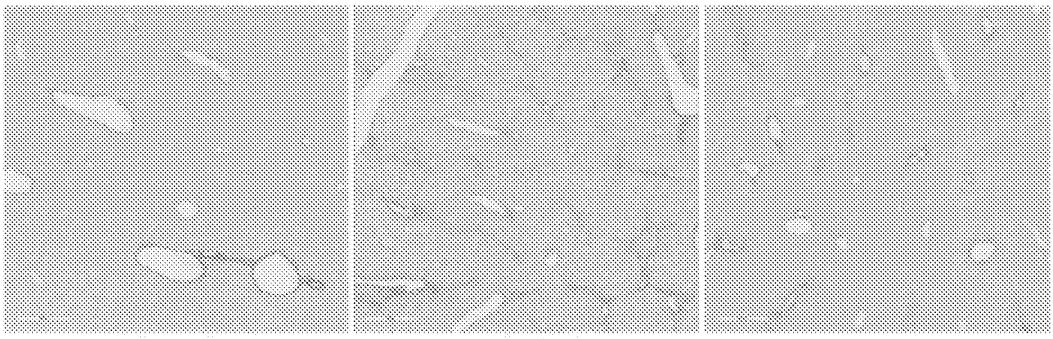


FIG. 11A

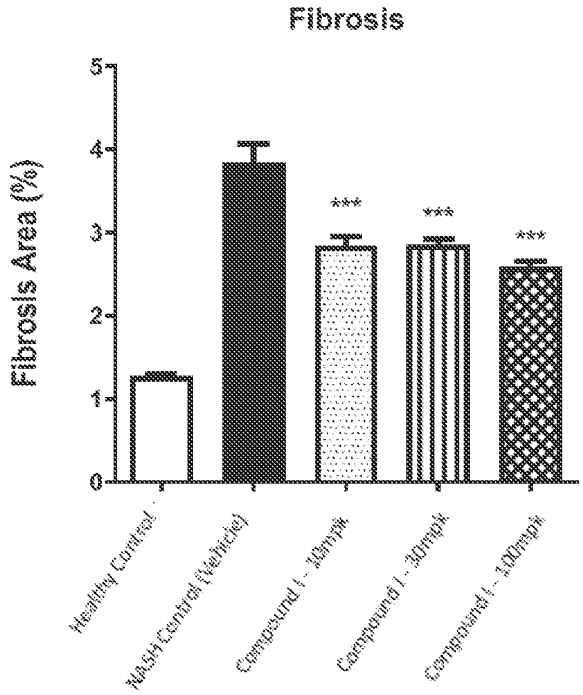

Fibrosis
Fibrosis Area (%)
0
1
2
3
4
5
***
***
***
Healthy Control
NASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 11B

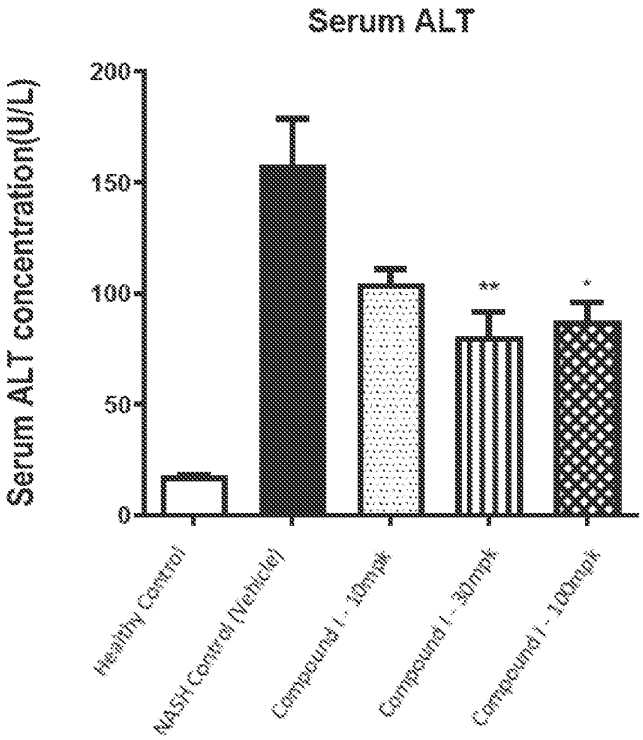

Serum ALT
Serum ALT concentration(U/L)
200
150
100
50
0
**
*
Healthy Control
MASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 12A

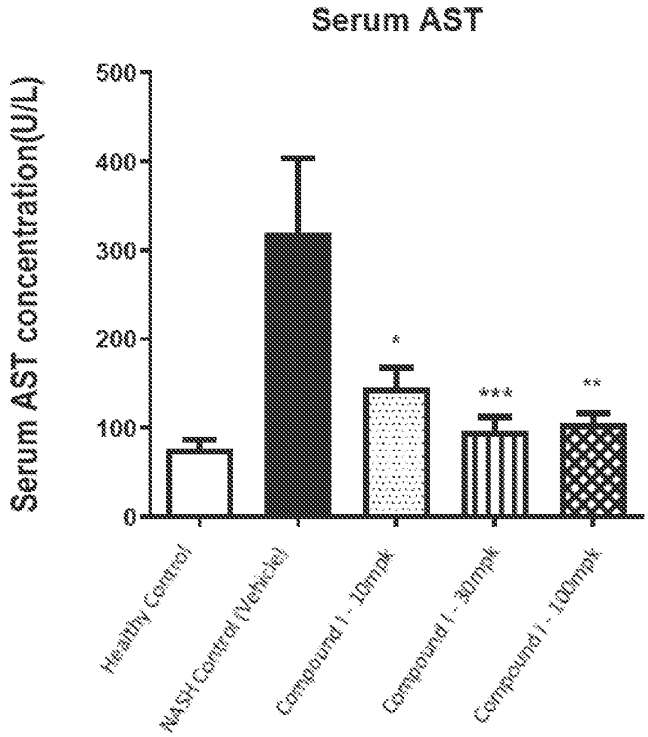

Serum AST
Serum AST concentration(U/L)
500
400
300
200
100
0
*
***
**
Healthy Control
NASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 12B

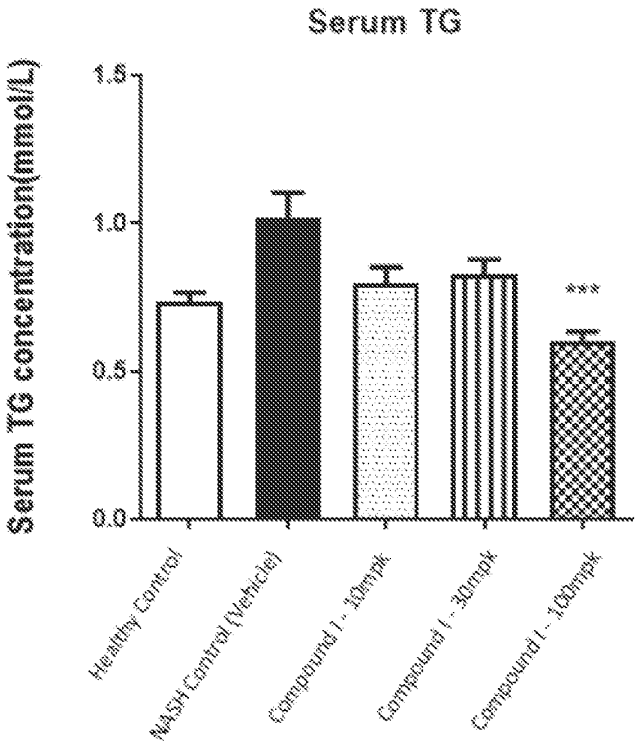

Serum TG
Serum TG concentration(mmol/L)
1.5
1.0
0.5
0.0
***
Healthy Control
NASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 12C

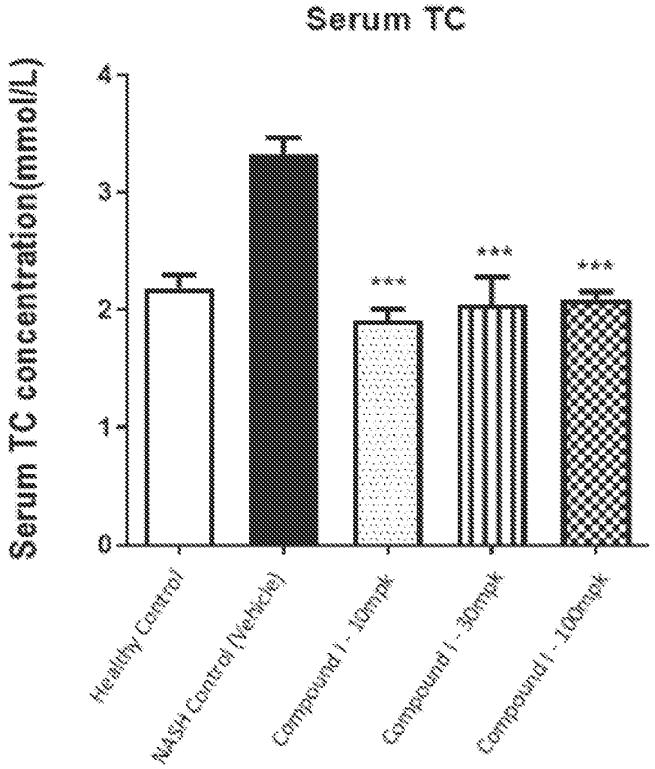

Serum TC
Serum TC concentration(mmol/L)
0
1
2
3
4
***
***
***
Healthy Control
NASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 12D

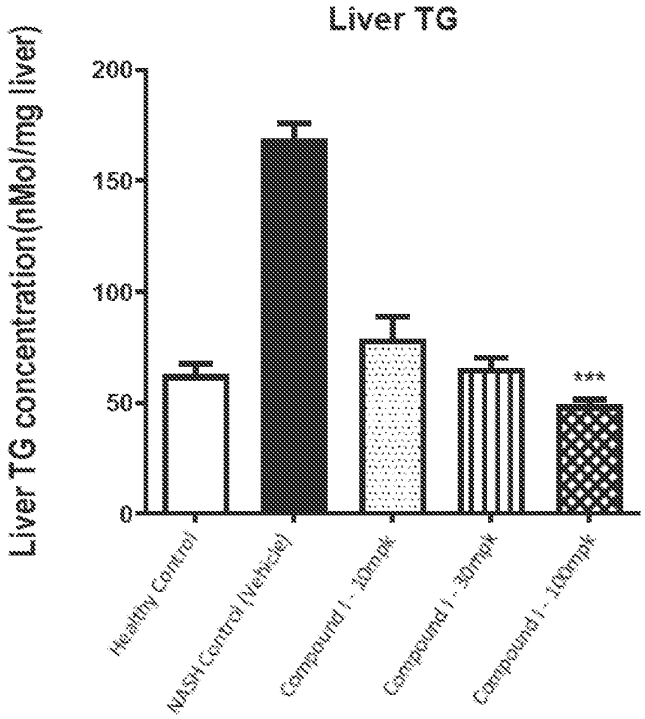

Liver TG
Liver TG concentration(nMol/mg liver)
200
150
100
50
0
***
Healthy Control
NASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 13A

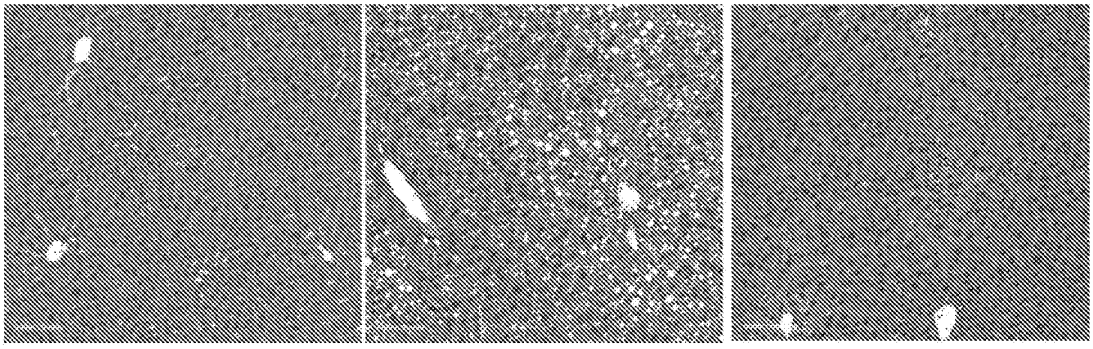


FIG. 13B

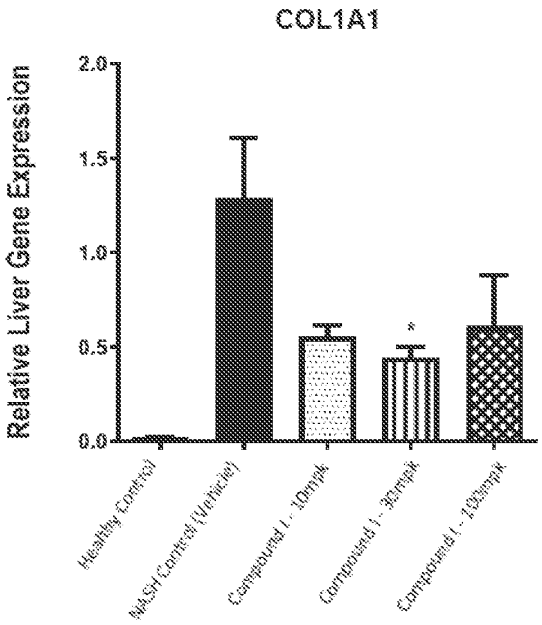

COL1A1
Relative Liver Gene Expression
2.0
1.5
1.0
0.5
0.0
*
Healthy Control
MASH Control (Vehicle)
Compound I - 10mpk
Compound I - 30mpk
Compound I - 100mpk

FIG. 14A

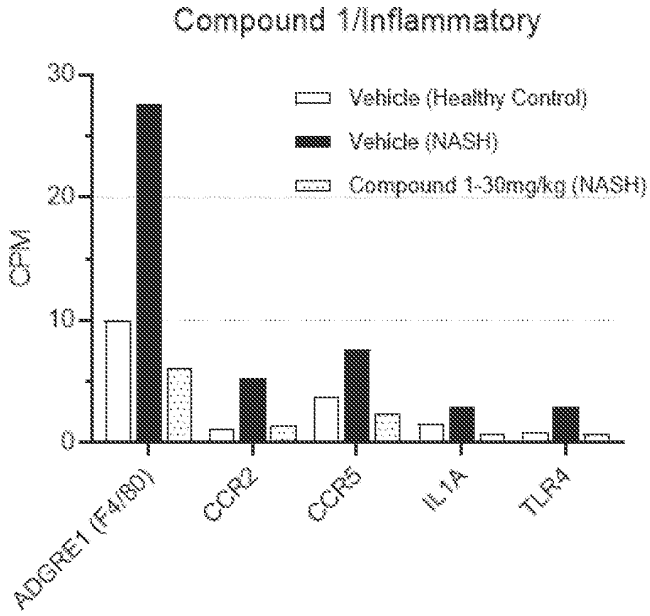

Compound 1/Inflammatory
Vehicle (Healthy Control)
Vehicle (NASH)
Compound 1-30mg/kg (NASH)
CPM
30
20
10
0
ADGRE1 (F4/80)
CCR2
CCR5
IL1A
TLR4

FIG. 14B

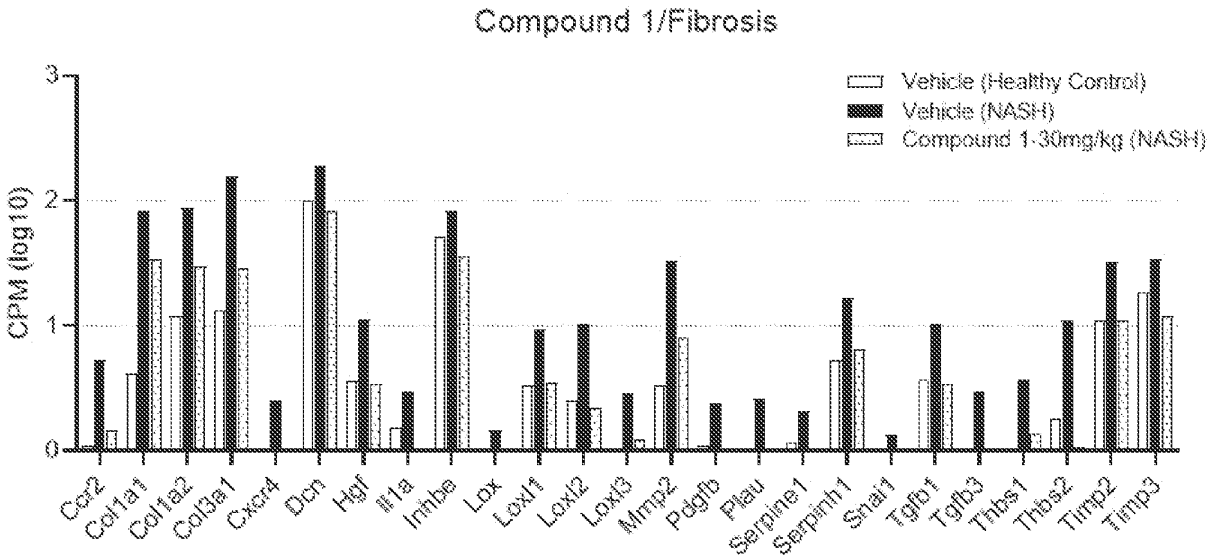

Compound 1/Fibrosis
Vehicle (Healthy Control)
Vehicle (NASH)
Compound 1-30mg/kg (NASH)
CPM (log10)
3
2
1
0
Ccr2
Col1a1
Col1a2
Col3a1
Cxcr4
Dcn
Hgf
Il1a
Inhbe
Lox
Loxl1
Loxl2
Loxl3
Mmp2
Pdgfb
Plau
Serpine1
Serpinh1
Snai1
Tgfb1
Tgfb3
Thbs1
Thbs2
Timp2
Timp3

FIG. 14C

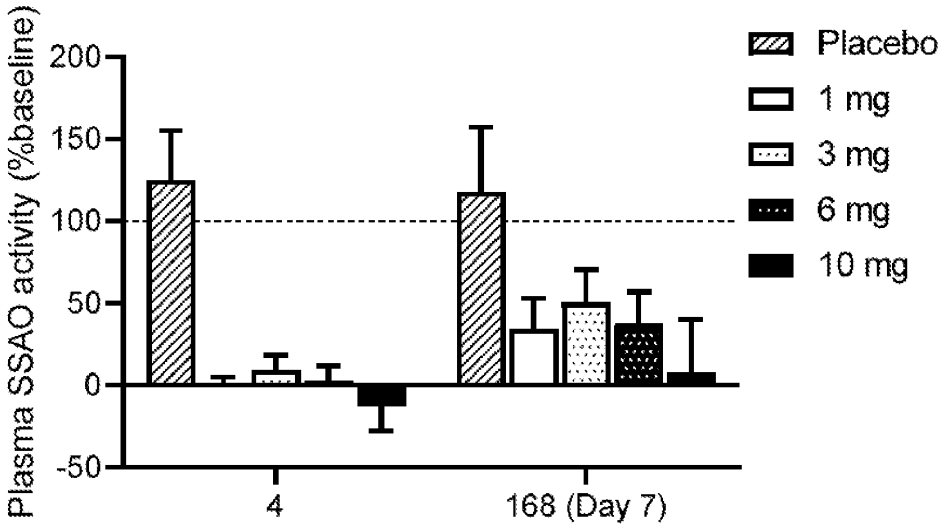

Plasma SSAO activity (%baseline)
200
150
100
50
0
-50
4
168 (Day 7)
Placebo
1 mg
3 mg
6 mg
10 mg

FIG. 15A

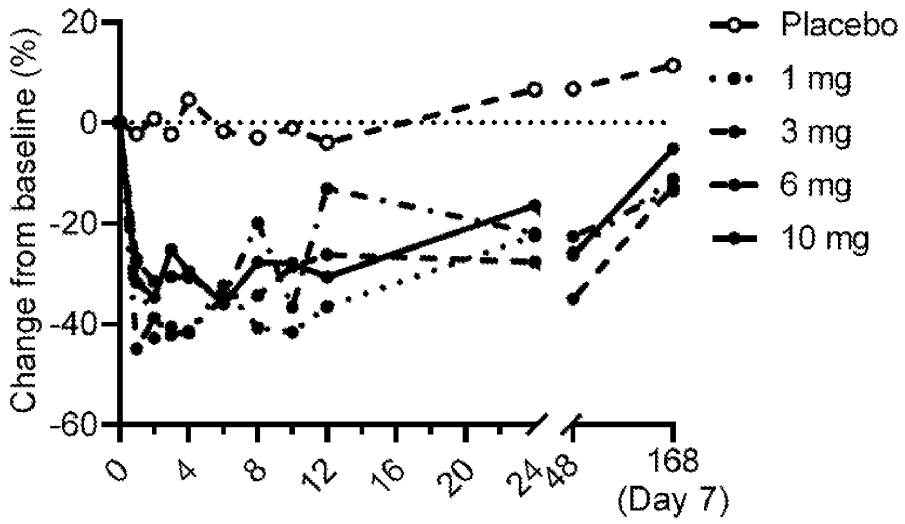

Change from baseline (%)
20
0
-20
-40
-60
0
4
8
12
16
20
24
48
168
(Day 7)
Placebo
1 mg
3 mg
6 mg
10 mg

FIG. 15B

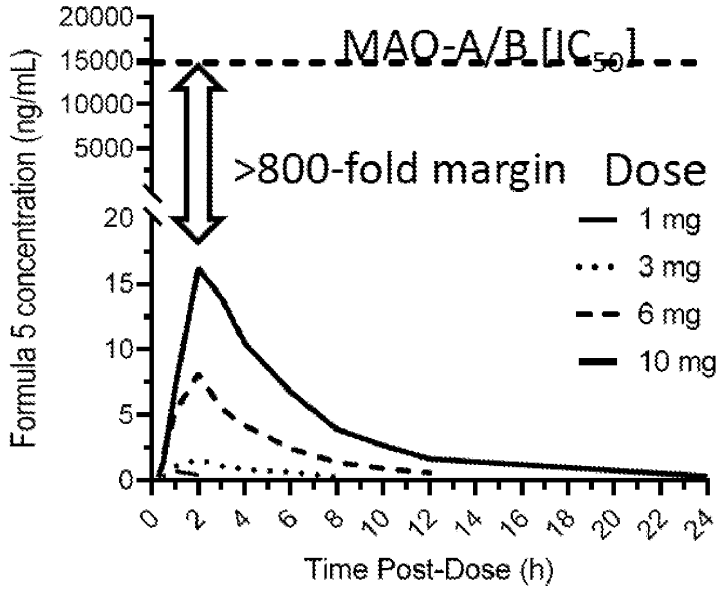

20000
15000
10000
5000
20
15
10
5
0
MAO-A/B [IC50]
>800-fold margin
Dose
1 mg
3 mg
6 mg
10 mg
Formula 5 concentration (ng/mL)
0 2 4 6 8 10 12 14 16 18 20 22 24
Time Post-Dose (h)

FIG. 15C

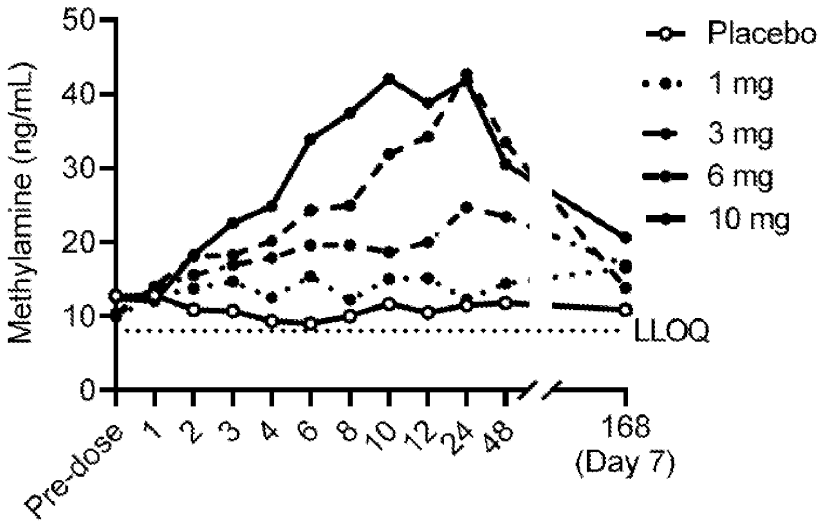

Methylamine (ng/mL)
50
40
30
20
10
0
Pre-dose
1
2
3
4
6
8
10
12
24
48
168
(Day 7)
LLOQ
Placebo
1 mg
3 mg
6 mg
10 mg

FIG. 15D

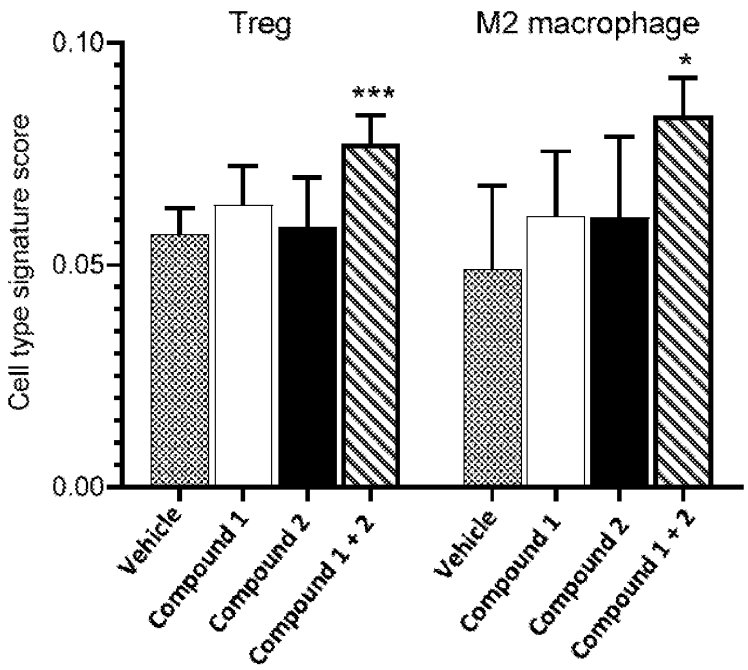

Treg
M2 macrophage
0.10
0.05
0.00
Cell type signature score
***
*
Vehicle
Compound 1
Compound 2
Compound 1 + 2
Vehicle
Compound 1
Compound 2
Compound 1 + 2

FIG. 16

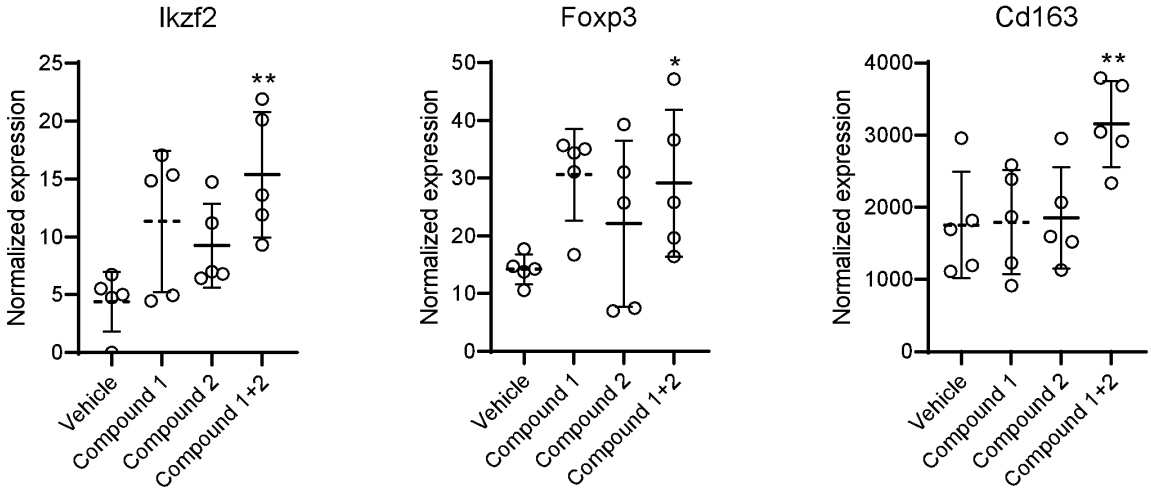

Ikzf2
Normalized expression
25
20
15
10
5
0
**
Vehicle
Compound 1
Compound 2
Compound 1+2
Foxp3
Normalized expression
50
40
30
20
10
0
*
Vehicle
Compound 1
Compound 2
Compound 1+2
Cd163
Normalized expression
4000
3000
2000
1000
0
**
Vehicle
Compound 1
Compound 2
Compound 1+2

FIG. 17

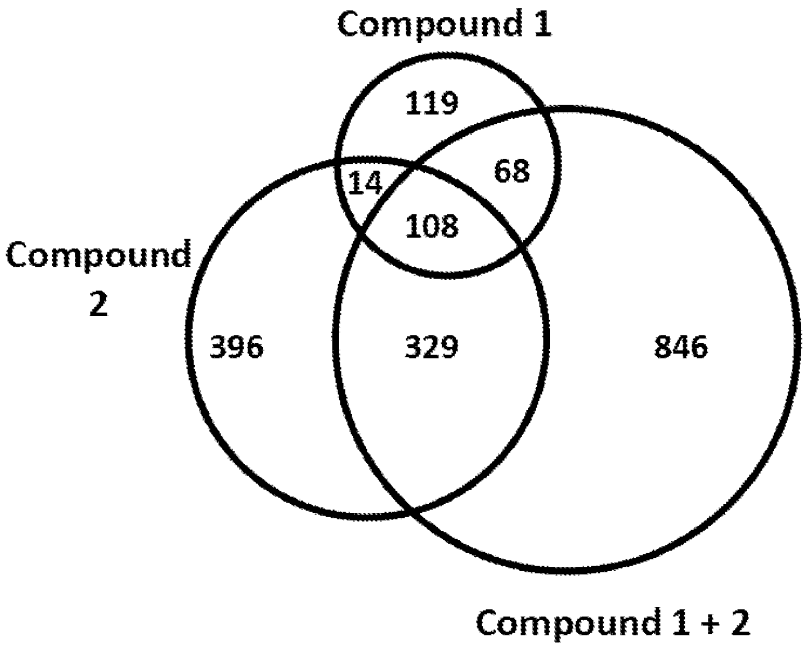


FIG. 18