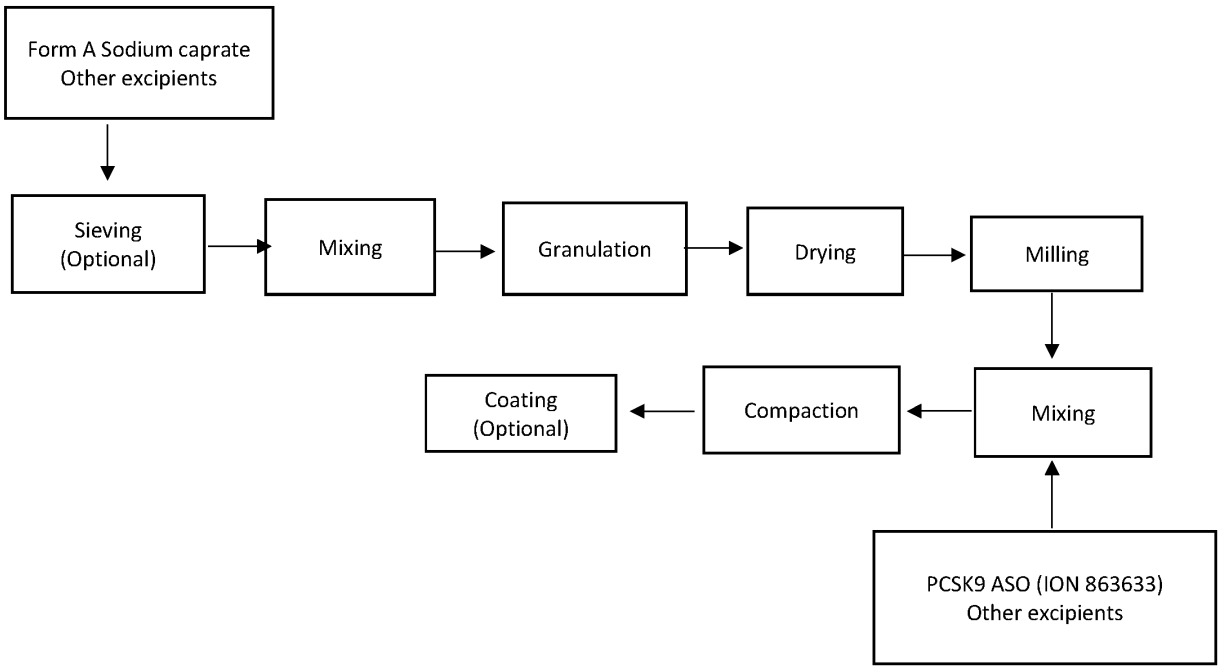

Form A Sodium caprate
Other excipients
Sieving
(Optional)
Mixing
Granulation
Drying
Milling
Mixing
Compaction
Coating
(Optional)
PCSK9 ASO (ION 863633)
Other excipients

FIG. 1

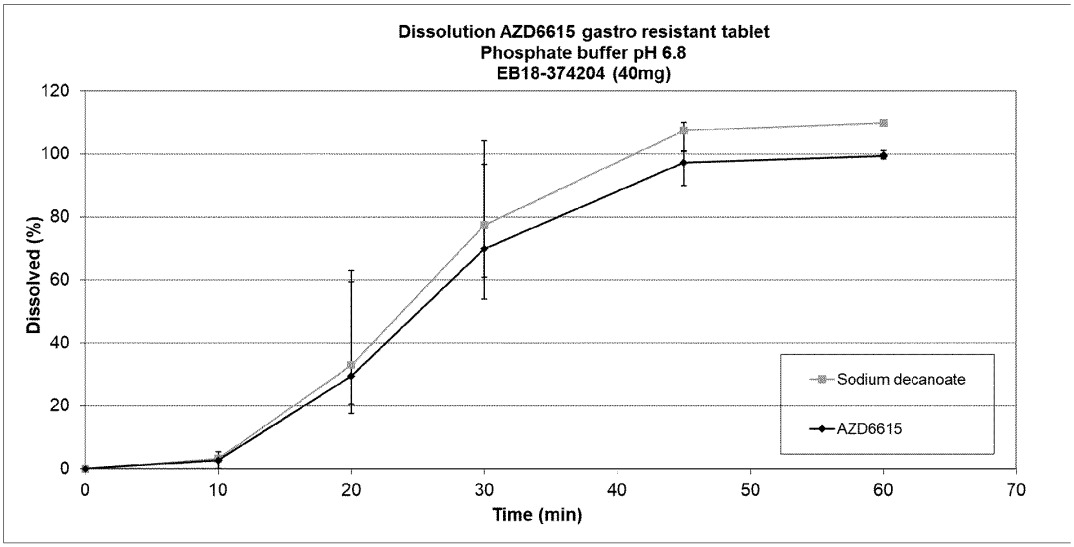

Dissolution AZD6615 gastro resistant tablet
Phosphate buffer pH 6.8
EB18-374204 (40mg)
Dissolved (%)
Time (min)
0
20
40
60
80
100
120
0
10
20
30
40
50
60
70
Sodium decanoate
AZD6615

FIG. 2

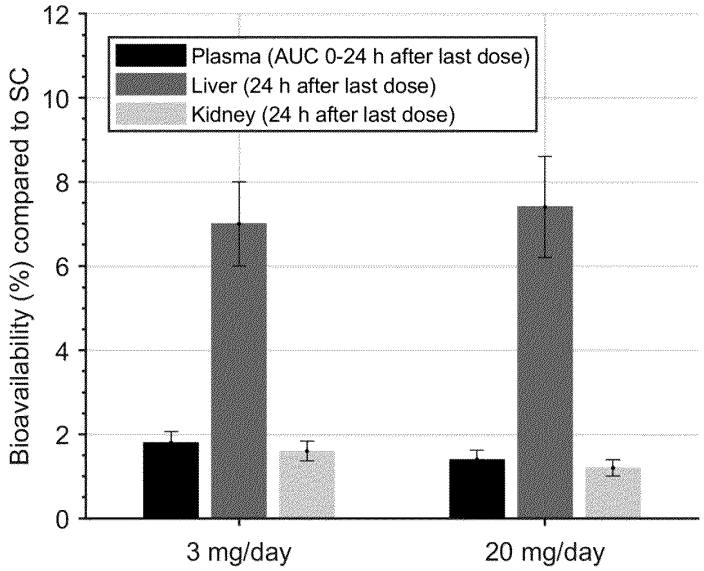

Plasma (AUC 0-24 h after last dose)
Liver (24 h after last dose)
Kidney (24 h after last dose)
Bioavailability (%) compared to SC
0
2
4
6
8
10
12
3 mg/day
20 mg/day

FIG. 3

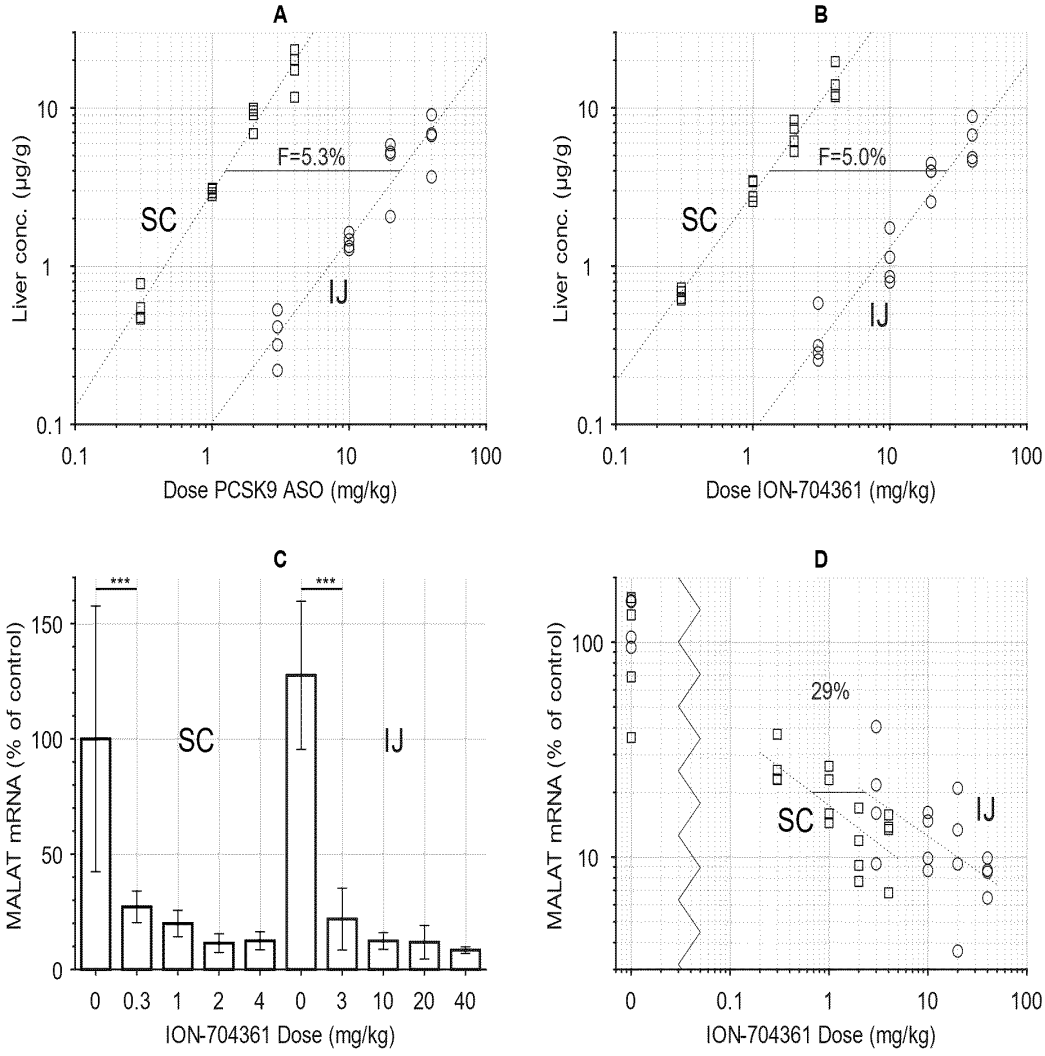

A
Liver conc. (µg/g)
10
1
0.1
F=5.3%
SC
IJ
0.1
1
10
100
Dose PCSK9 ASO (mg/kg)
B
Liver conc. (µg/g)
10
1
0.1
F=5.0%
SC
IJ
0.1
1
10
100
Dose ION-704361 (mg/kg)
C
MALAT mRNA (% of control)
150
100
50
0
***
***
SC
IJ
0 0.3 1 2 4 0 3 10 20 40
ION-704361 Dose (mg/kg)
D
MALAT mRNA (% of control)
100
10
29%
SC
IJ
0 0.1 1 10 100
ION-704361 Dose (mg/kg)

FIG. 4

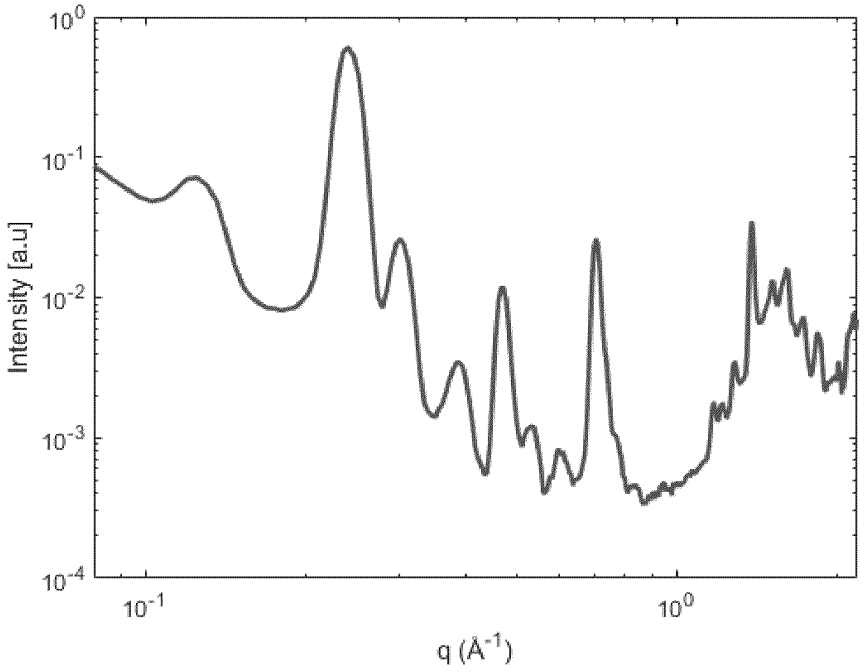


FIG. 5

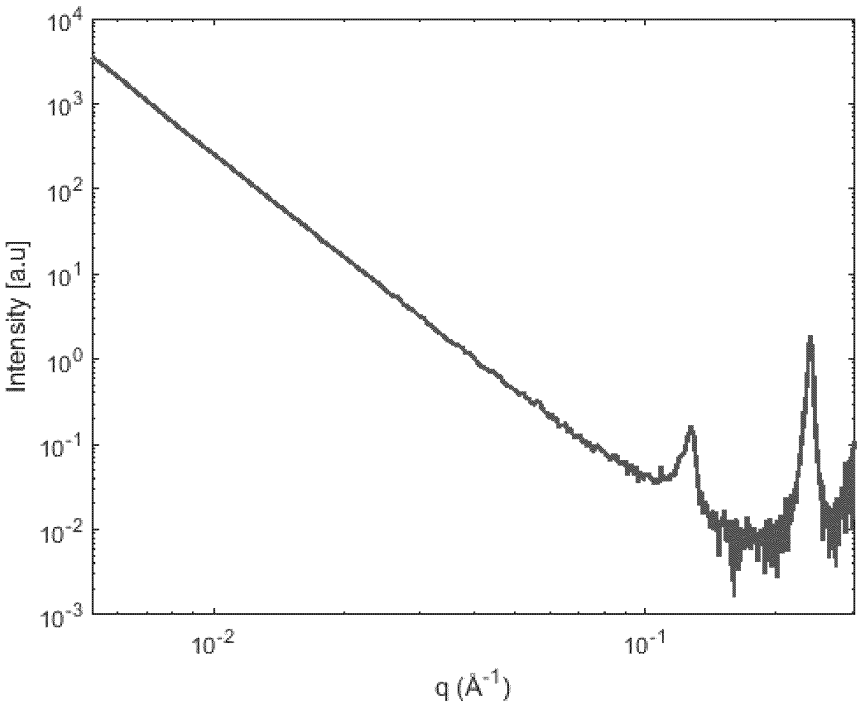


FIG. 6

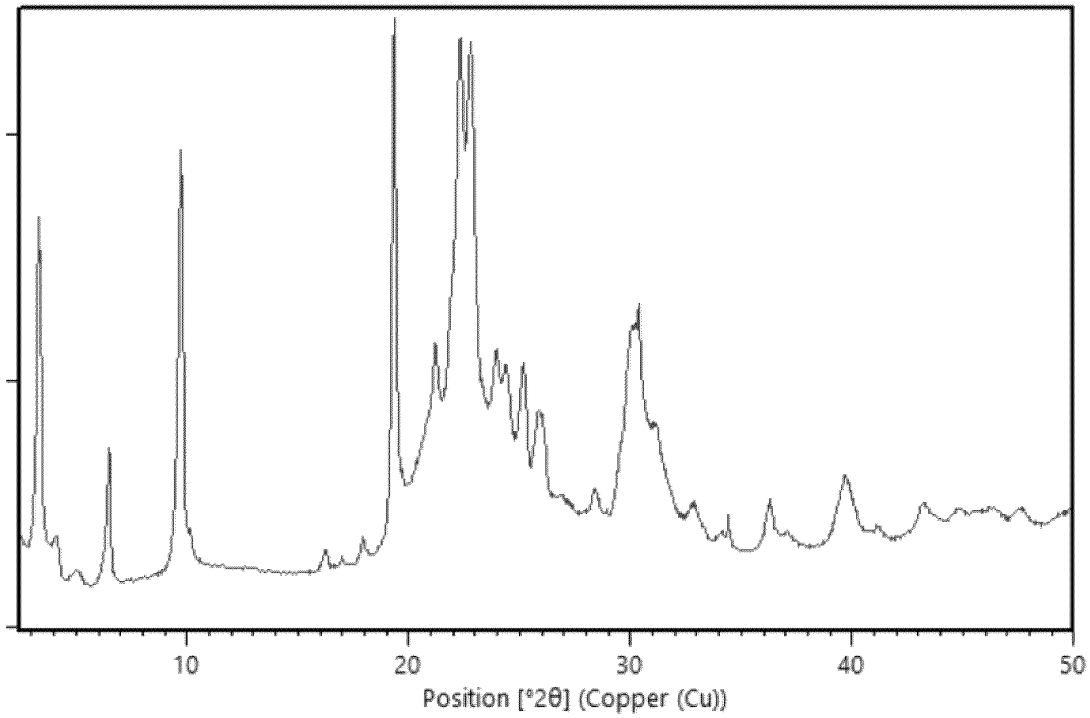


FIG. 7

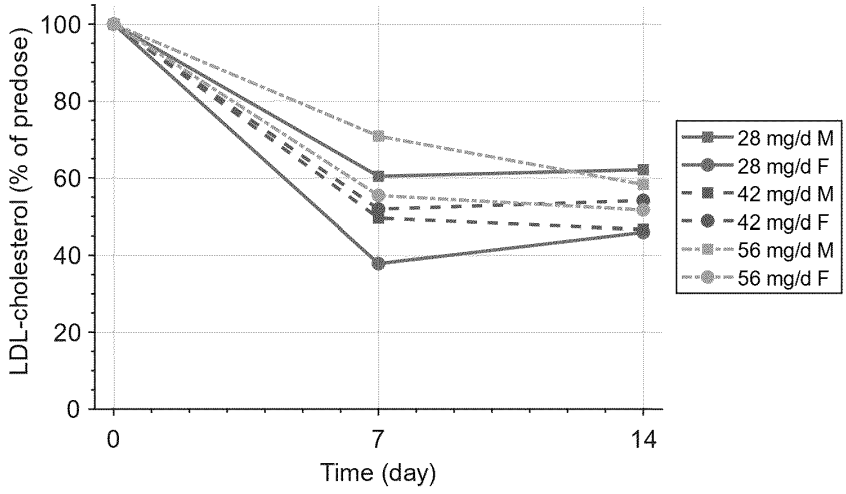

LDL-cholesterol (% of predose)
100
80
60
40
20
0
0
7
14
Time (day)
28 mg/d M
28 mg/d F
42 mg/d M
42 mg/d F
56 mg/d M
56 mg/d F

FIG. 8

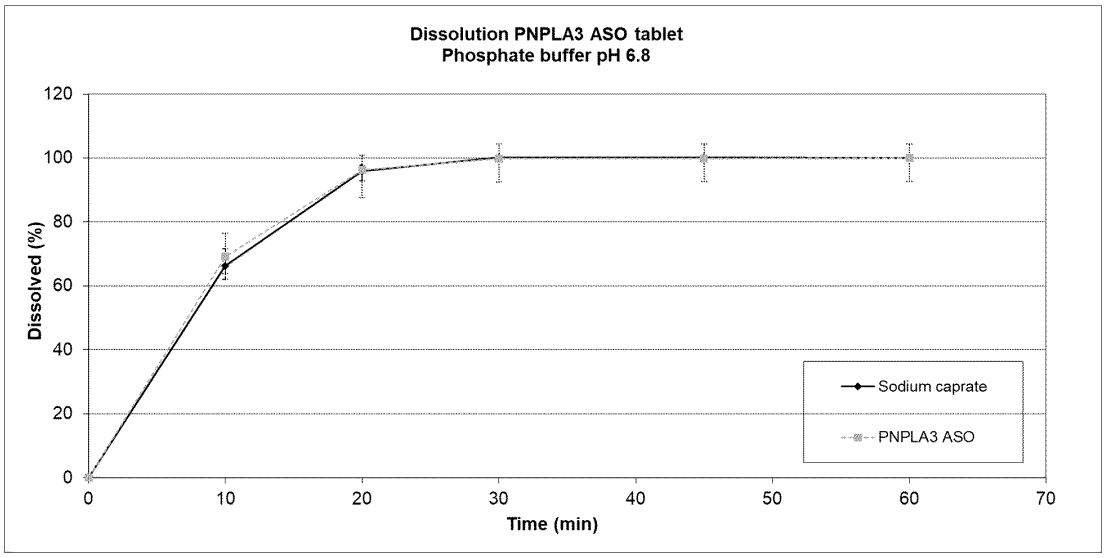


FIG. 9A

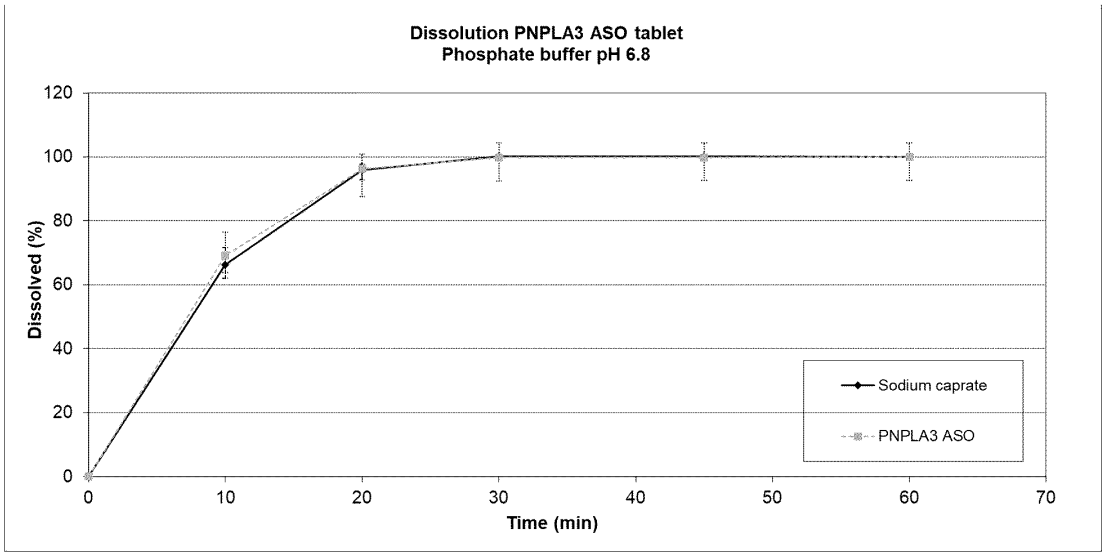


FIG. 9B

FIGS. 9A-B