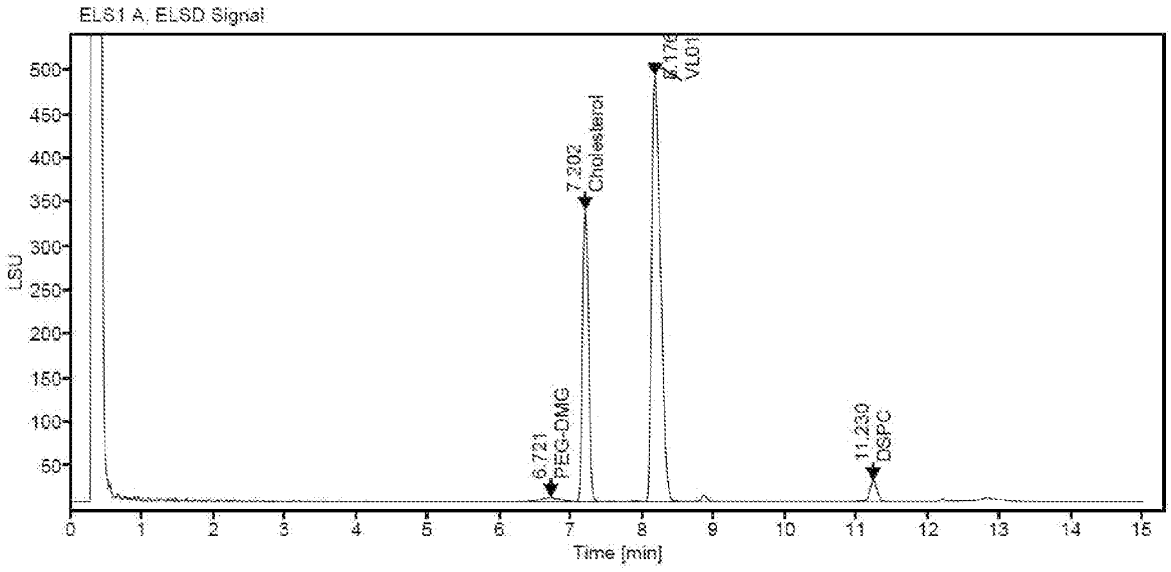

ELS1 A, ELSD Signal
LSU
Time [min]
6.721
PEG-DMG
7.302
Cholesterol
8.176
VL01
11.230
DSPC

FIG. 1A

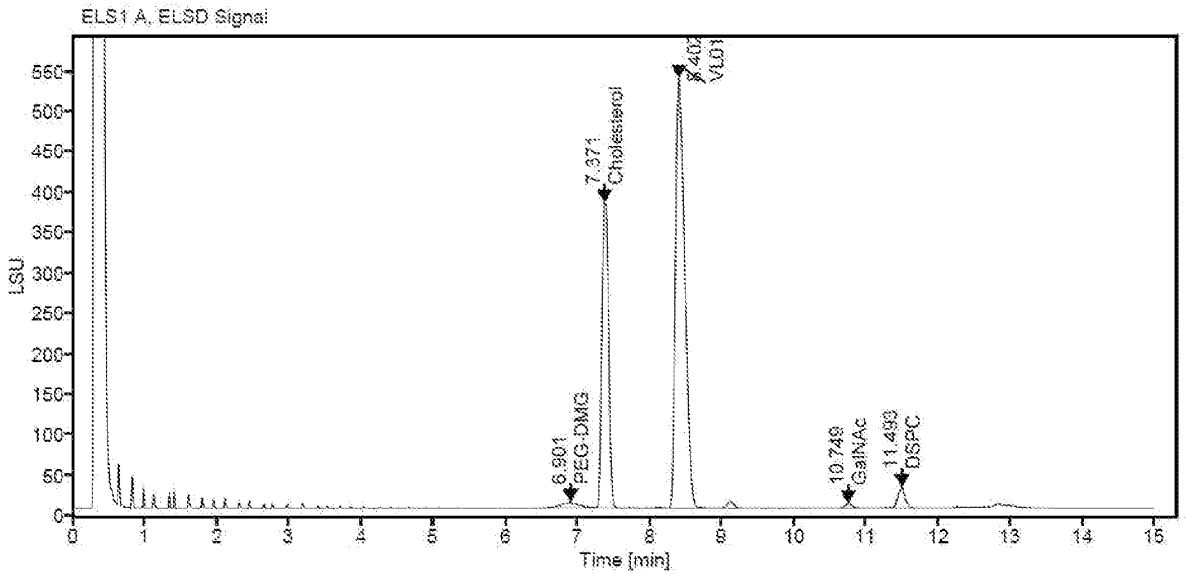

ELS1 A, ELSD Signal
LSU
Time [min]
6.901
PEG-DMG
7.371
Cholesterol
8.402
VL01
10.749
GalNAc
11.499
DSPC

FIG. 1B

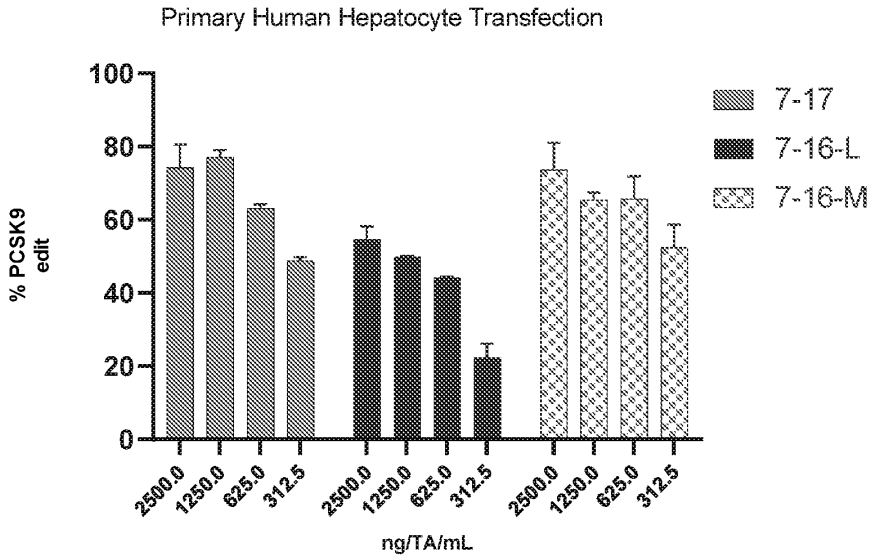

Primary Human Hepatocyte Transfection
% PCSK9 edit
100
80
60
40
20
0
7-17
7-16-L
7-16-M
2500.0
1250.0
625.0
312.5
ng/TA/mL

FIG. 2

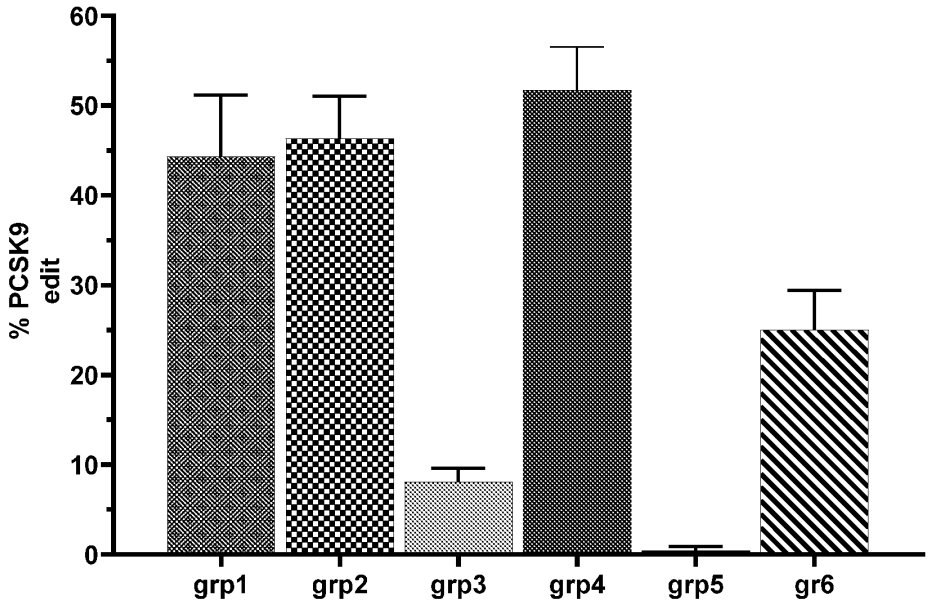

% PCSK9 edit
60
50
40
30
20
10
0
grp1
grp2
grp3
grp4
grp5
gr6

FIG. 3

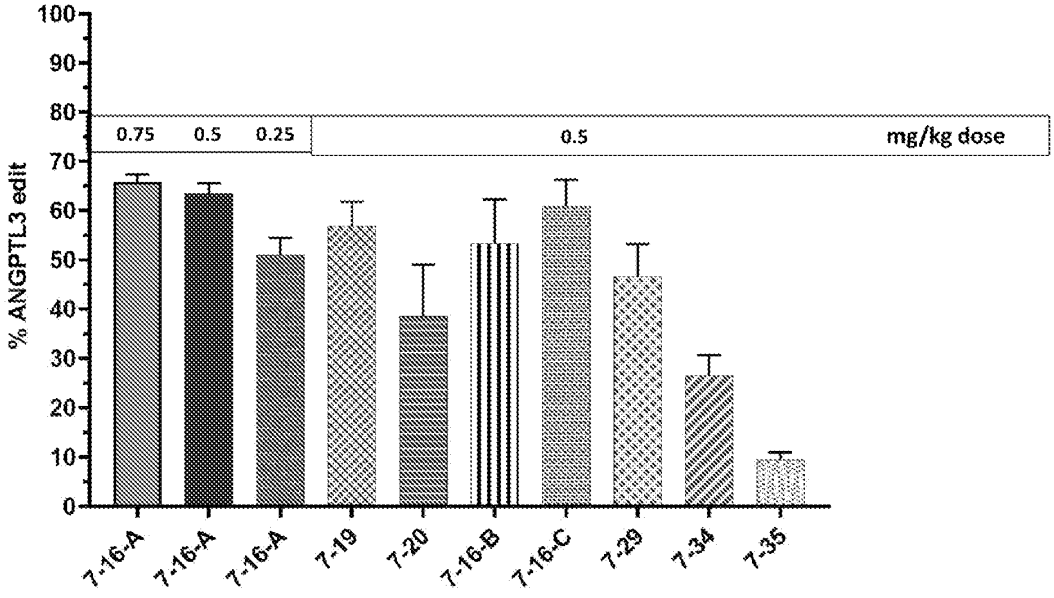

% ANGPTL3 edit
100
90
80
70
60
50
40
30
20
10
0
0.75
0.5
0.25
0.5
mg/kg dose
7-16-A
7-16-A
7-16-A
7-19
7-20
7-16-B
7-16-C
7-29
7-34
7-35

FIG. 4

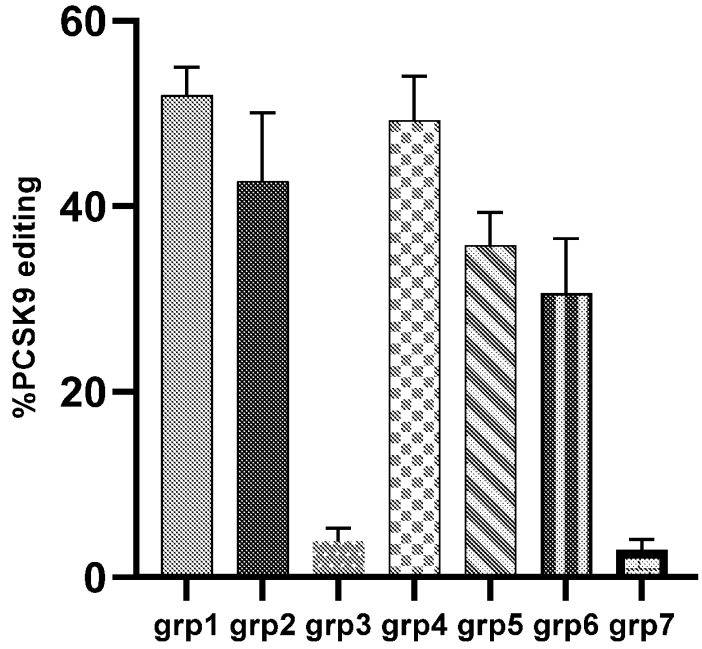

%PCSK9 editing
60
40
20
0
grp1 grp2 grp3 grp4 grp5 grp6 grp7

FIG. 5

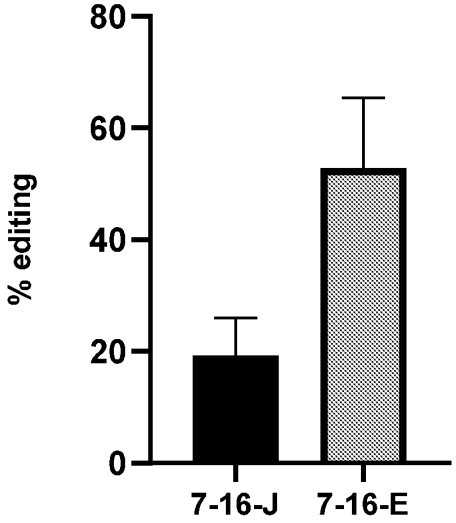

80
60
40
20
0
% editing
7-16-J
7-16-E

FIG. 6

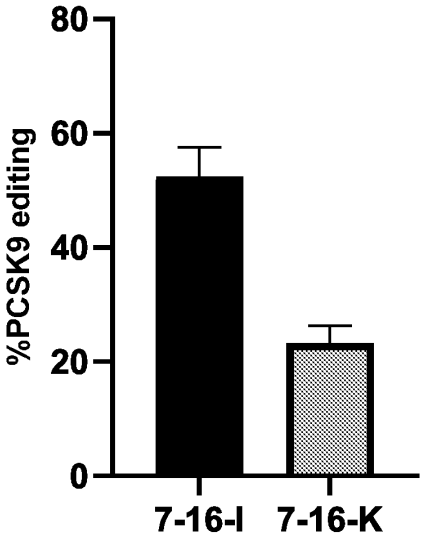

80
60
40
20
0
%PCSK9 editing
7-16-I
7-16-K

FIG. 7

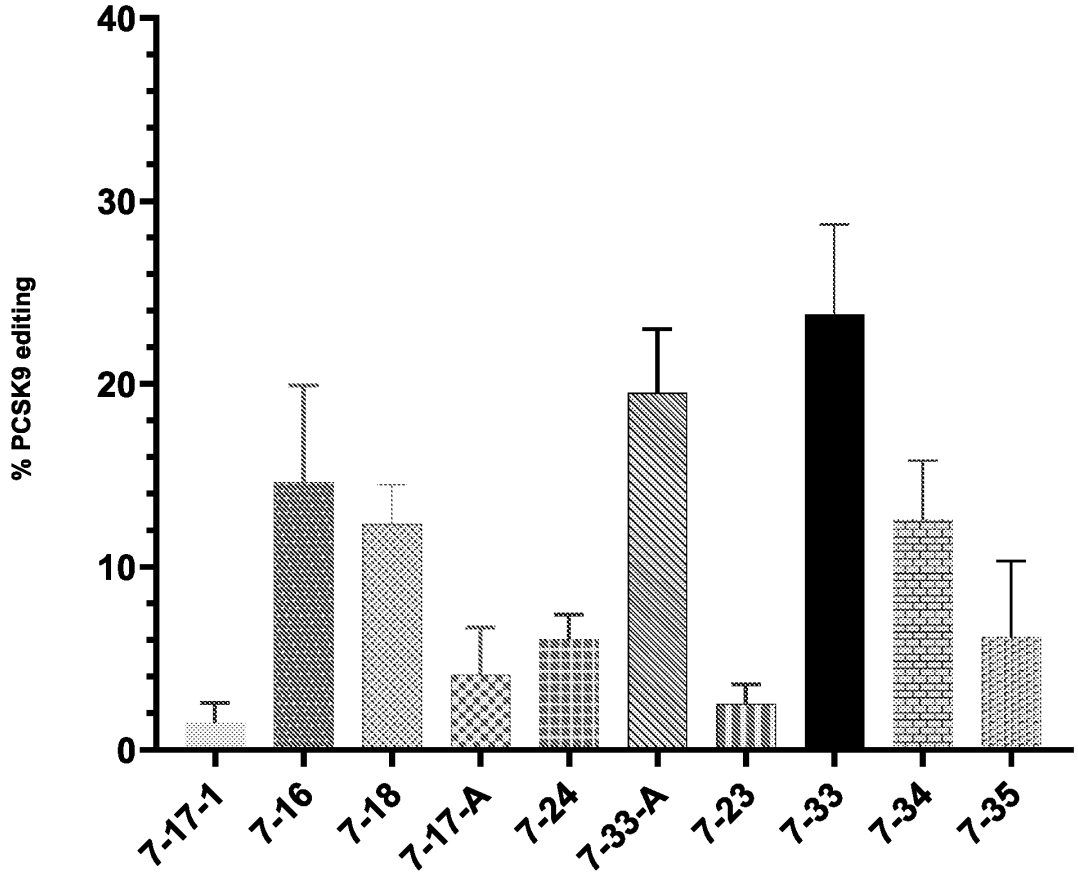

% PCSK9 editing
40
30
20
10
0
7-17-1
7-16
7-18
7-17-A
7-24
7-33-A
7-23
7-33
7-34
7-35

FIG. 8

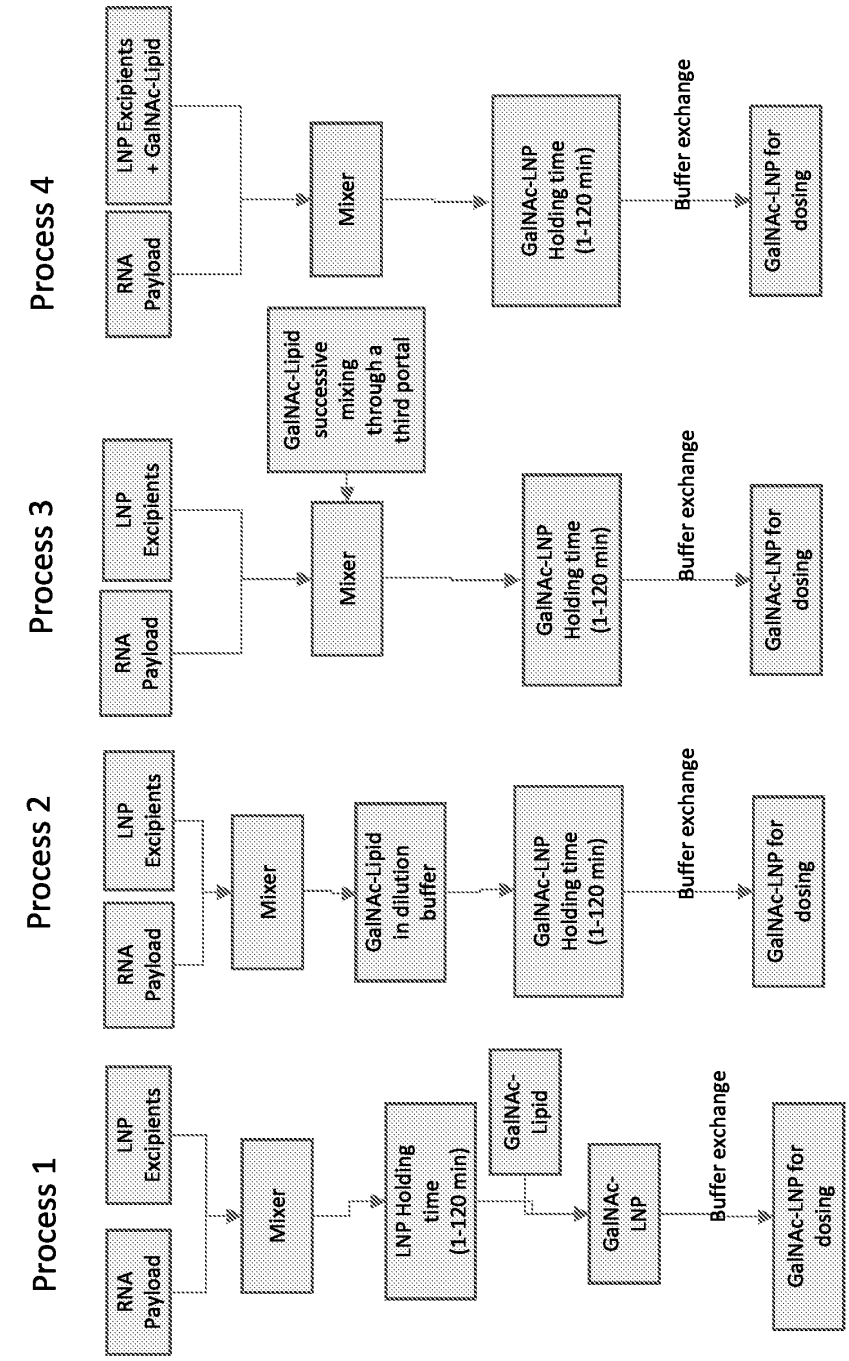

Process 1
RNA Payload
LNP Excipients
Mixer
LNP Holding time (1-120 min)
GalNAc-Lipid
GalNAc-LNP
Buffer exchange
GalNAc-LNP for dosing
Process 2
RNA Payload
LNP Excipients
Mixer
GalNAc-Lipid in dilution buffer
GalNAc-LNP Holding time (1-120 min)
Buffer exchange
GalNAc-LNP for dosing
Process 3
RNA Payload
LNP Excipients
Mixer
GalNAc-Lipid successive mixing through a third portal
GalNAc-LNP Holding time (1-120 min)
Buffer exchange
GalNAc-LNP for dosing
Process 4
RNA Payload
LNP Excipients + GalNAc-Lipid
Mixer
GalNAc-LNP Holding time (1-120 min)
Buffer exchange
GalNAc-LNP for dosing

FIG. 9

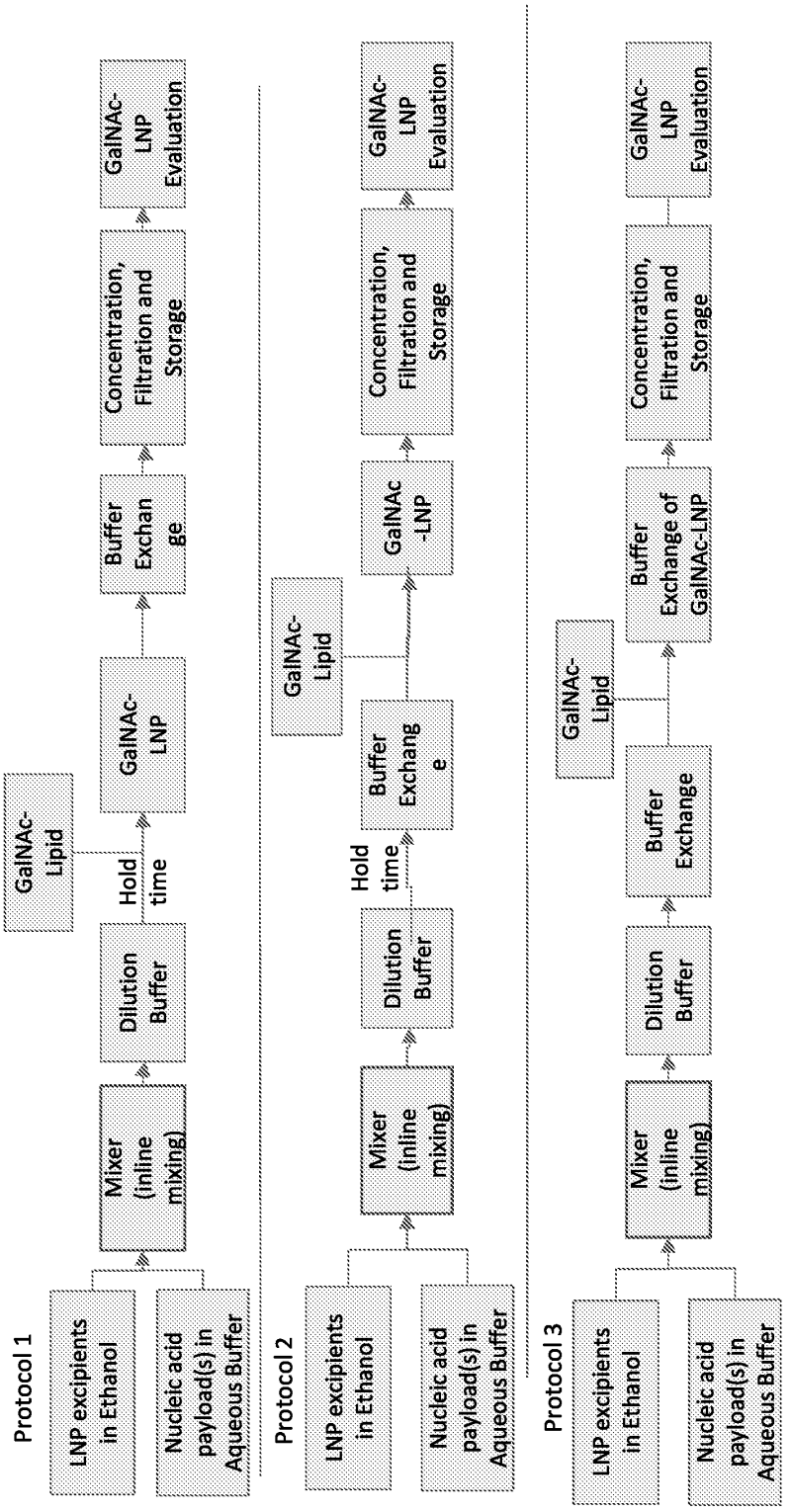

Protocol 1
LNP excipients in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Dilution Buffer
Hold time
GalNAc-Lipid
GalNAc-LNP
Buffer Exchange
Concentration, Filtration and Storage
GalNAc-LNP Evaluation
Protocol 2
LNP excipients in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Dilution Buffer
Hold time
Buffer Exchange
GalNAc-Lipid
GalNAc-LNP
Concentration, Filtration and Storage
GalNAc-LNP Evaluation
Protocol 3
LNP excipients in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Dilution Buffer
Buffer Exchange
GalNAc-Lipid
Buffer Exchange of GalNAc-LNP
Concentration, Filtration and Storage
GalNAc-LNP Evaluation

FIG. 10

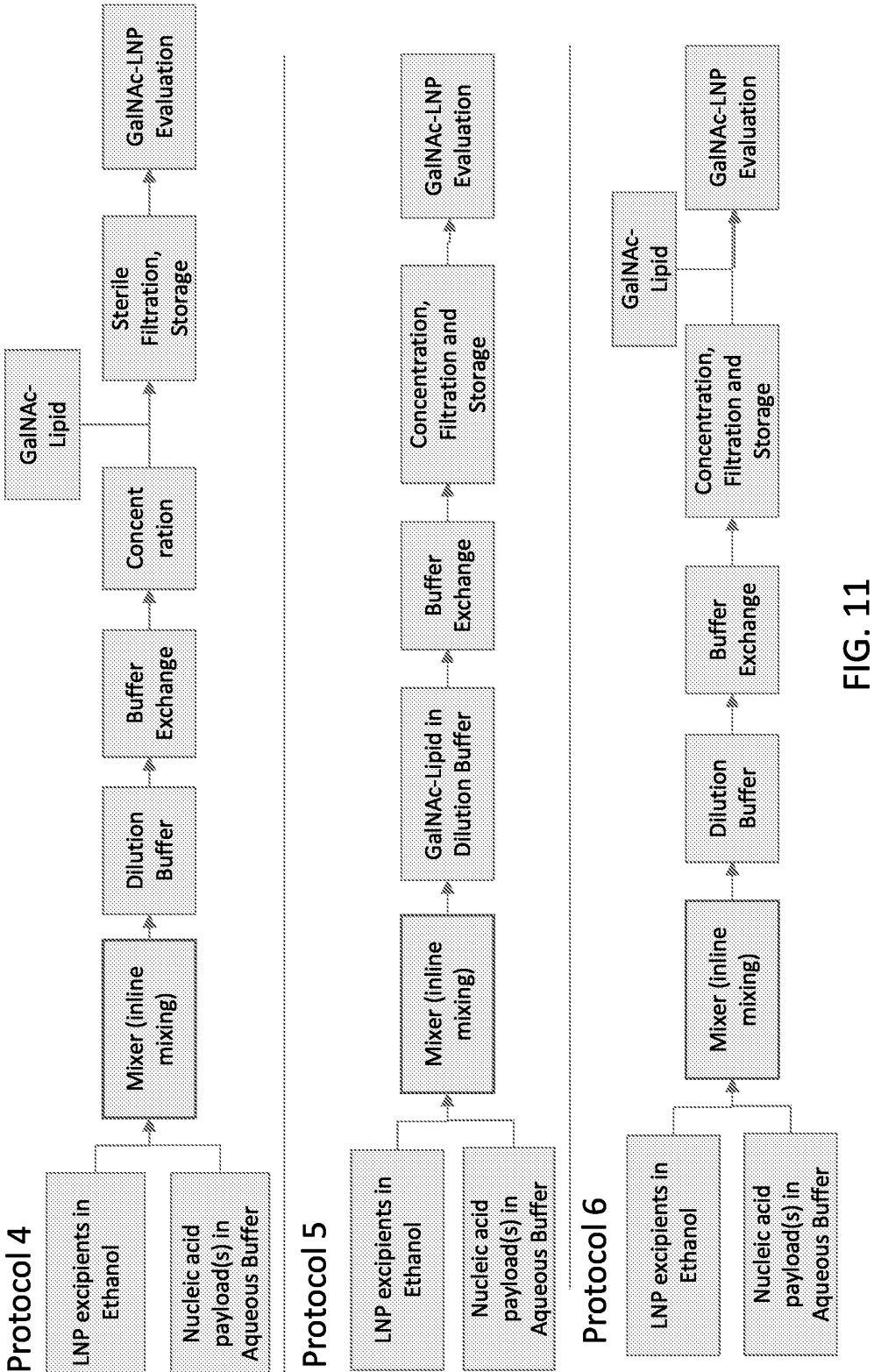

Protocol 4
LNP excipients in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Dilution Buffer
Buffer Exchange
Concent ration
GalNAc-Lipid
Sterile Filtration, Storage
GalNAc-LNP Evaluation
Protocol 5
LNP excipients in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
GalNAc-Lipid in Dilution Buffer
Buffer Exchange
Concentration, Filtration and Storage
GalNAc-LNP Evaluation
Protocol 6
LNP excipients in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Dilution Buffer
Buffer Exchange
Concentration, Filtration and Storage
GalNAc-Lipid
GalNAc-LNP Evaluation

FIG. 11

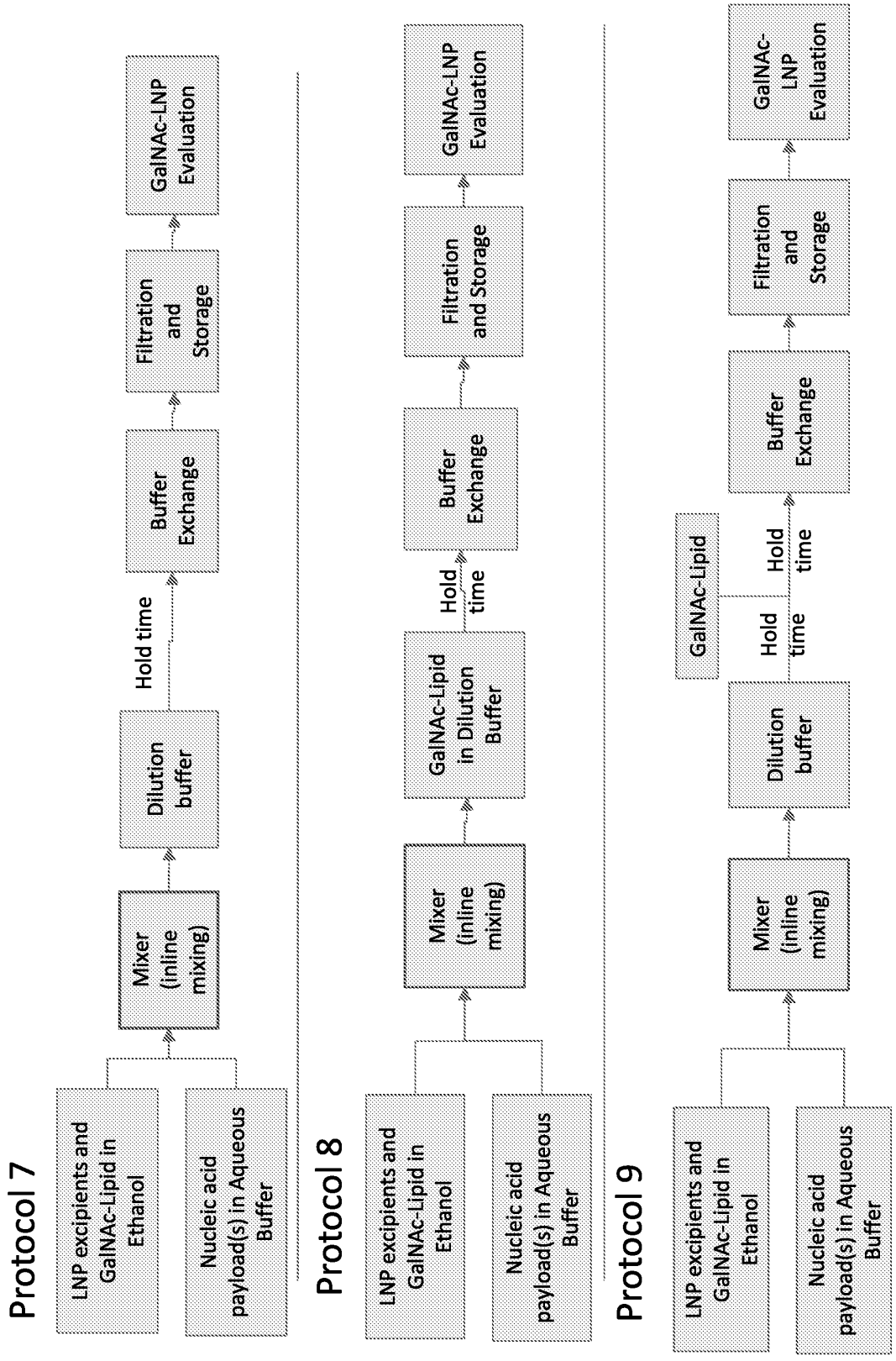

Protocol 7
LNP excipients and GalNAc-Lipid in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Dilution buffer
Hold time
Buffer Exchange
Filtration and Storage
GalNAc-LNP Evaluation
Protocol 8
LNP excipients and GalNAc-Lipid in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
GalNAc-Lipid in Dilution Buffer
Hold time
Buffer Exchange
Filtration and Storage
GalNAc-LNP Evaluation
Protocol 9
LNP excipients and GalNAc-Lipid in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Dilution buffer
GalNAc-Lipid
Hold time
Hold time
Buffer Exchange
Filtration and Storage
GalNAc-LNP Evaluation

FIG. 12

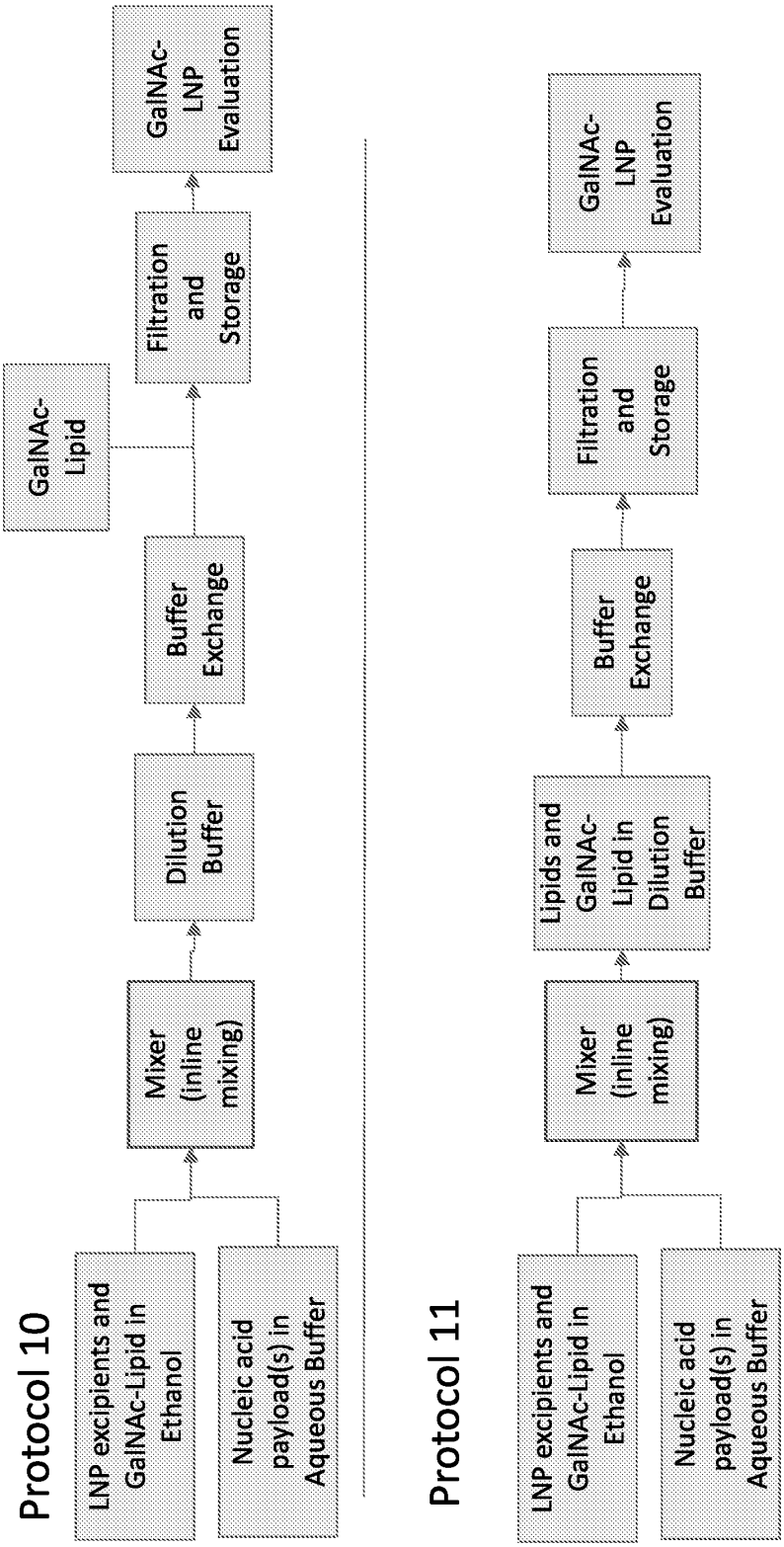

Protocol 10
LNP excipients and GalNAc-Lipid in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Dilution Buffer
Buffer Exchange
GalNAc-Lipid
Filtration and Storage
GalNAc-LNP Evaluation
Protocol 11
LNP excipients and GalNAc-Lipid in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
Mixer (inline mixing)
Lipids and GalNAc-Lipid in Dilution Buffer
Buffer Exchange
Filtration and Storage
GalNAc-LNP Evaluation

FIG. 13

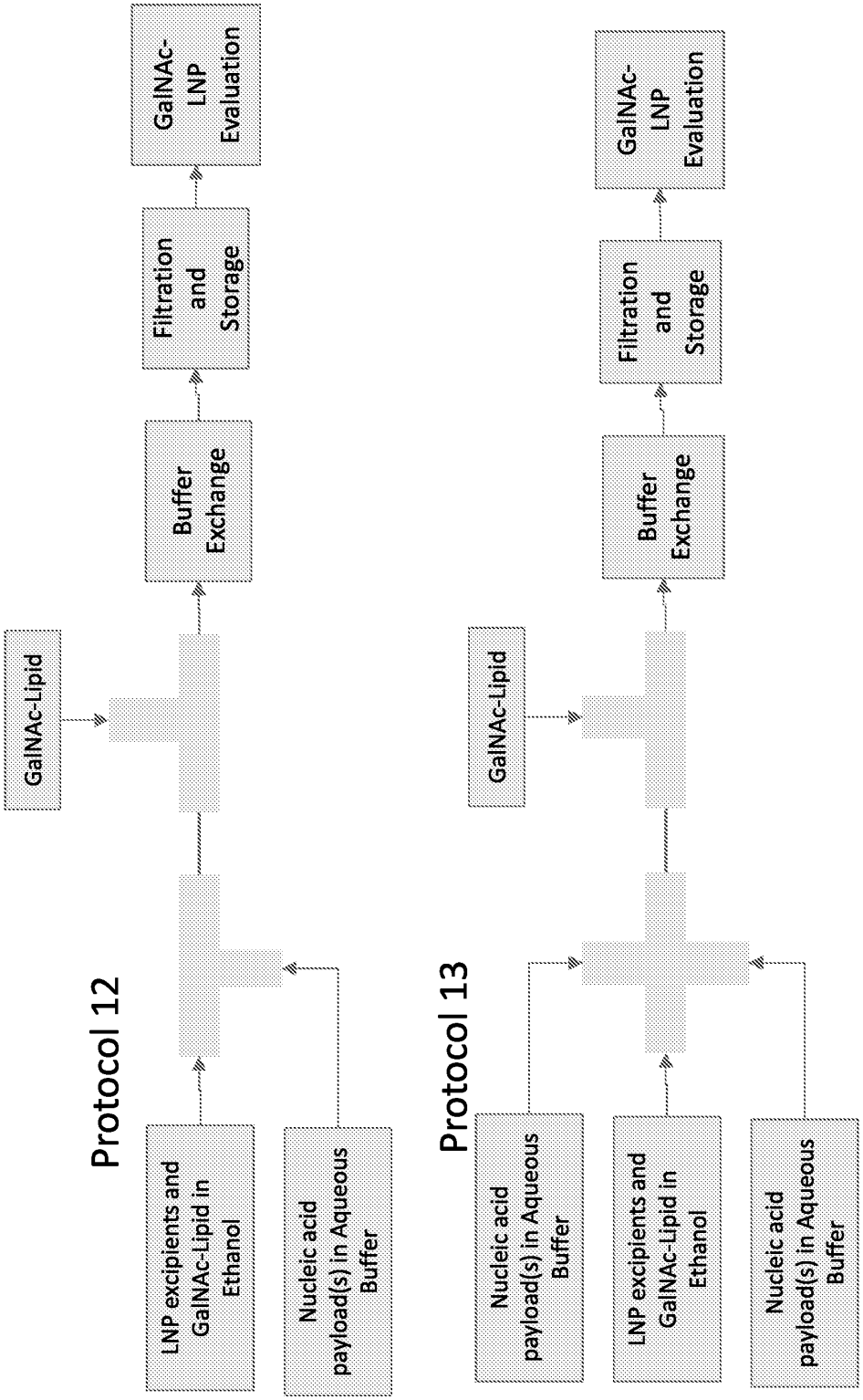

Protocol 12
LNP excipients and GalNAc-Lipid in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
GalNAc-Lipid
Buffer Exchange
Filtration and Storage
GalNAc-LNP Evaluation
Protocol 13
Nucleic acid payload(s) in Aqueous Buffer
LNP excipients and GalNAc-Lipid in Ethanol
Nucleic acid payload(s) in Aqueous Buffer
GalNAc-Lipid
Buffer Exchange
Filtration and Storage
GalNAc-LNP Evaluation

FIG. 14

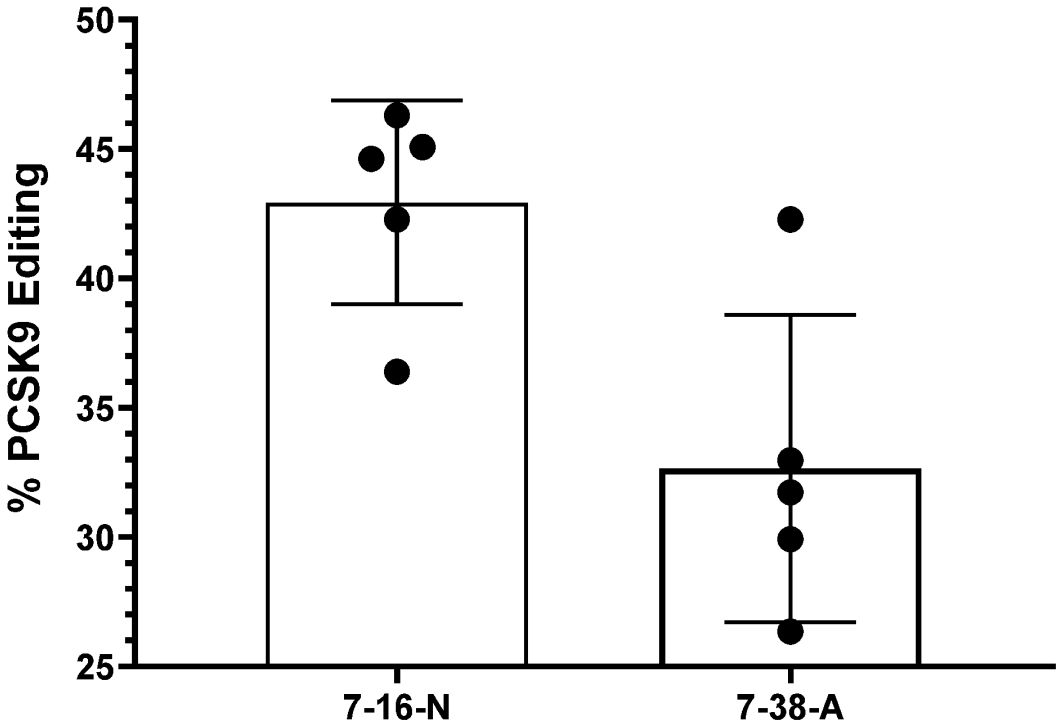


FIG. 15