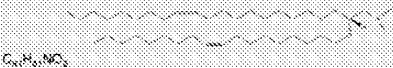


Figure 1

An Exemplary Composition of the LNP-1 Lipid Nanoparticle Platform: Structural Lipid Components

Lipid Components (LNP1)	Lipid Component & Formula	Mw (g/mol)	Exact Mass (g/mol)
DOOMA (18:1)	 <chem>C_{45}H_{81}NO_9</chem>	620.10	620.63
L1A (18:1)	 <chem>C_{45}H_{81}NO_{10}P</chem>	~2839.57 (Average)	~2837.79 (Average)
DSPE (18:0)	 <chem>C_{44}H_{80}NO_9P</chem>	790.16	789.62
Cholesterol	 <chem>C_{27}H_{46}O</chem>	386.65	386.35

Drug Product Formulation Buffer Solution pH 7.4 ± 0.2 , -18.7 ± 0.8 mV at 25°C (Exemplary):

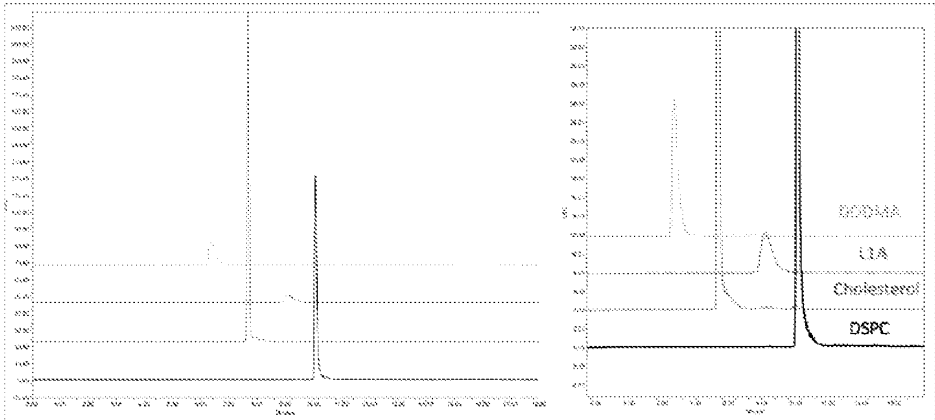
- Sodium Phosphate Dibasic: 10.14 mM
- Potassium Phosphate Monobasic: 1.76 mM
- Potassium Chloride: 2.7 mM
- Sodium Chloride: 137 mM
- Nuclease-Free Water, not DEPC-Treated

Figure 2

Lipid Composition of the LNP-1 Platform (Exemplary)

Sample	Lipid Name	Calculated Concentration (mg/ml)	LNP Total Mass (mg/ml)	MW	mmol in 1ml	Total Count (mmol)	Assay mmol%	Assay m/m%
eGFP mRNA/LNP-1 (Freshly-formulated)	DDMA	3.254	6.448	620.10	0.0005830	0.001256	46.41	50.46
	DSPC	1.024		790.15	0.0001440		11.46	15.88
	Cholesterol	1.802		385.65	0.0005191		41.33	27.94
	L1A	0.245		2841.00	0.0000956		6.76	3.80

Identity of LNP-1 Formulations: Four Lipid Components
Separation of Four Lipid Components of LNP-1 Formulations Obtained by UPLC-ELSD Method



Synthesis of PEGylated L1A (Exemplary)

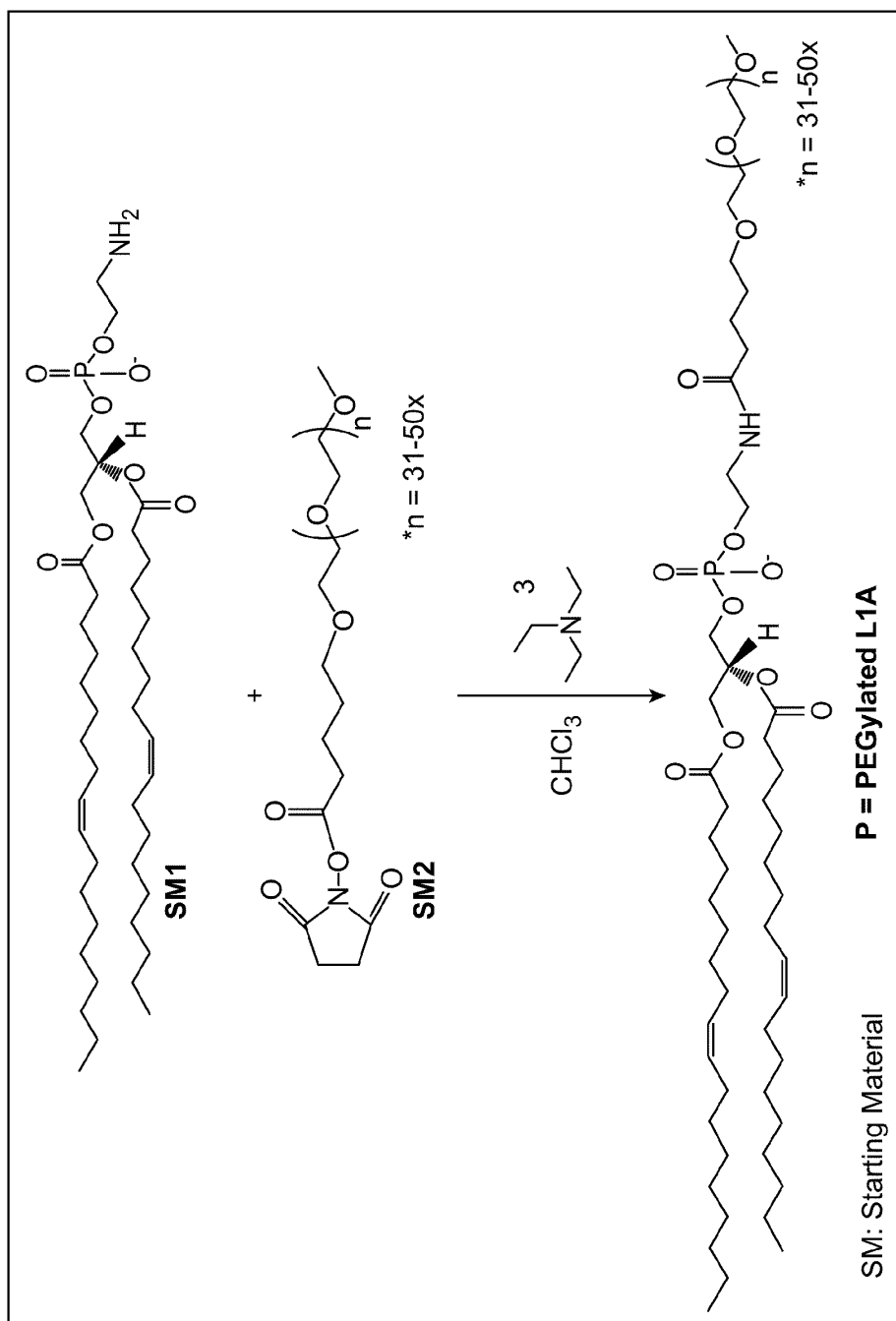


FIG. 3

Figure 3 (Cont.)

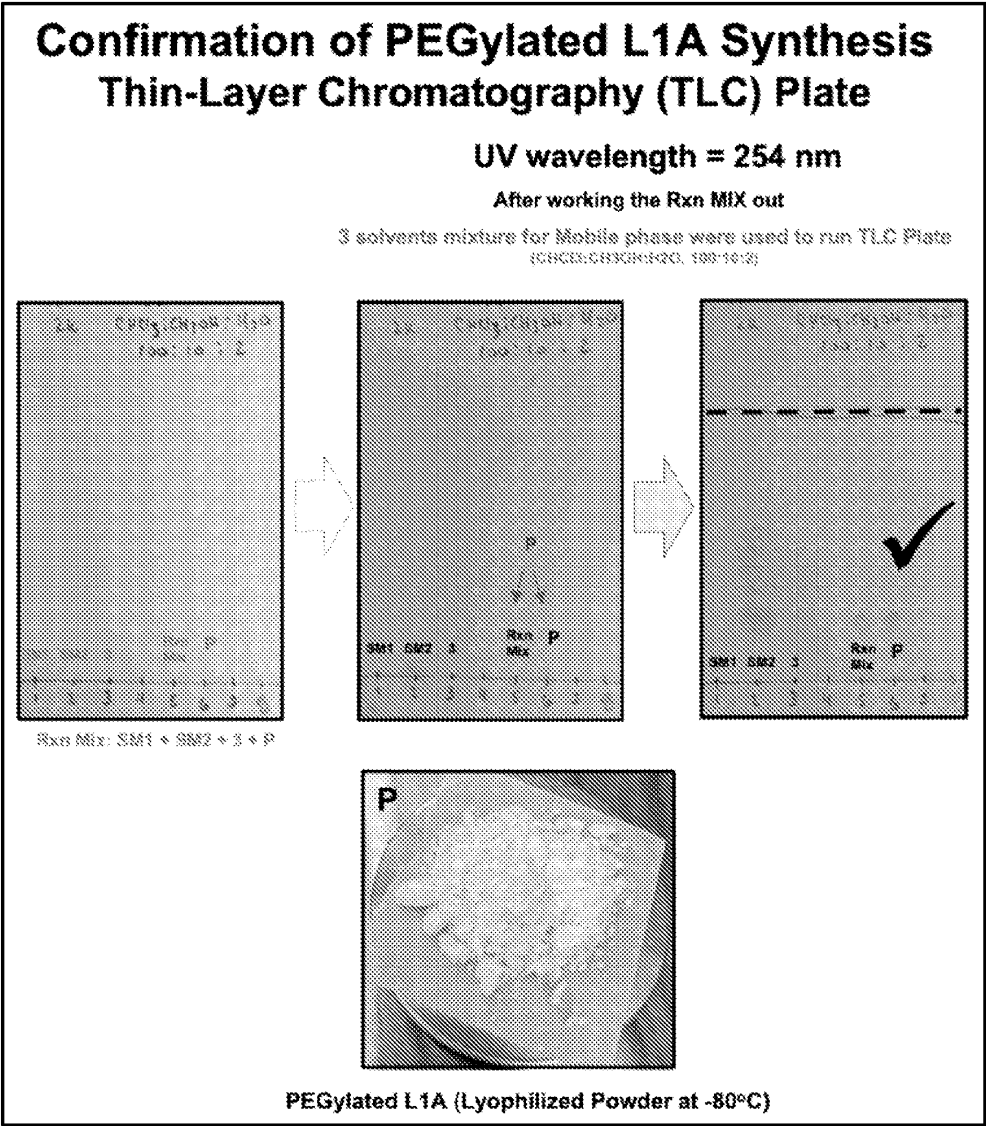


Figure 3 (Cont.)

Identity, Purity and Integrity Confirmation of PEGylated L1A
PEGylated L1A Successfully Identified, Integrity Confirmed with No Impurity
Identity of PEGylated L1A: Proton ^1H NMR

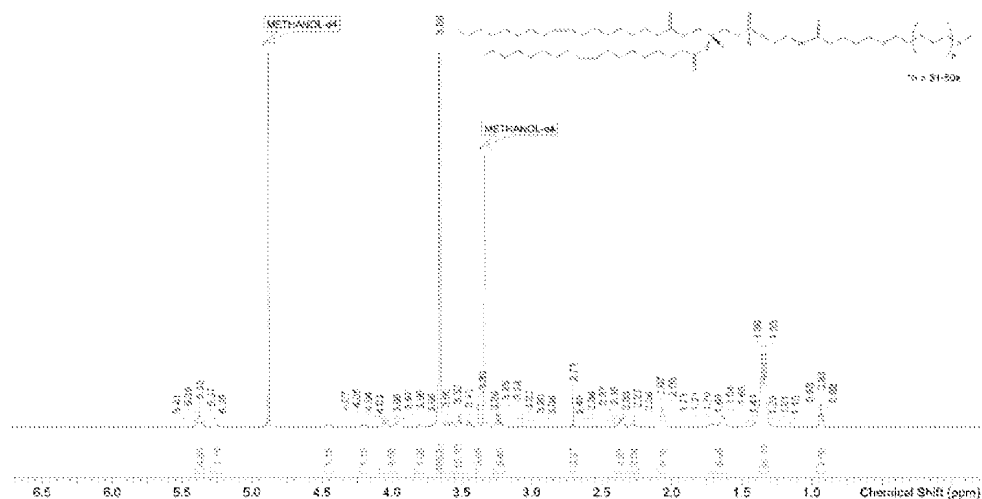


Figure 3 (Cont.)

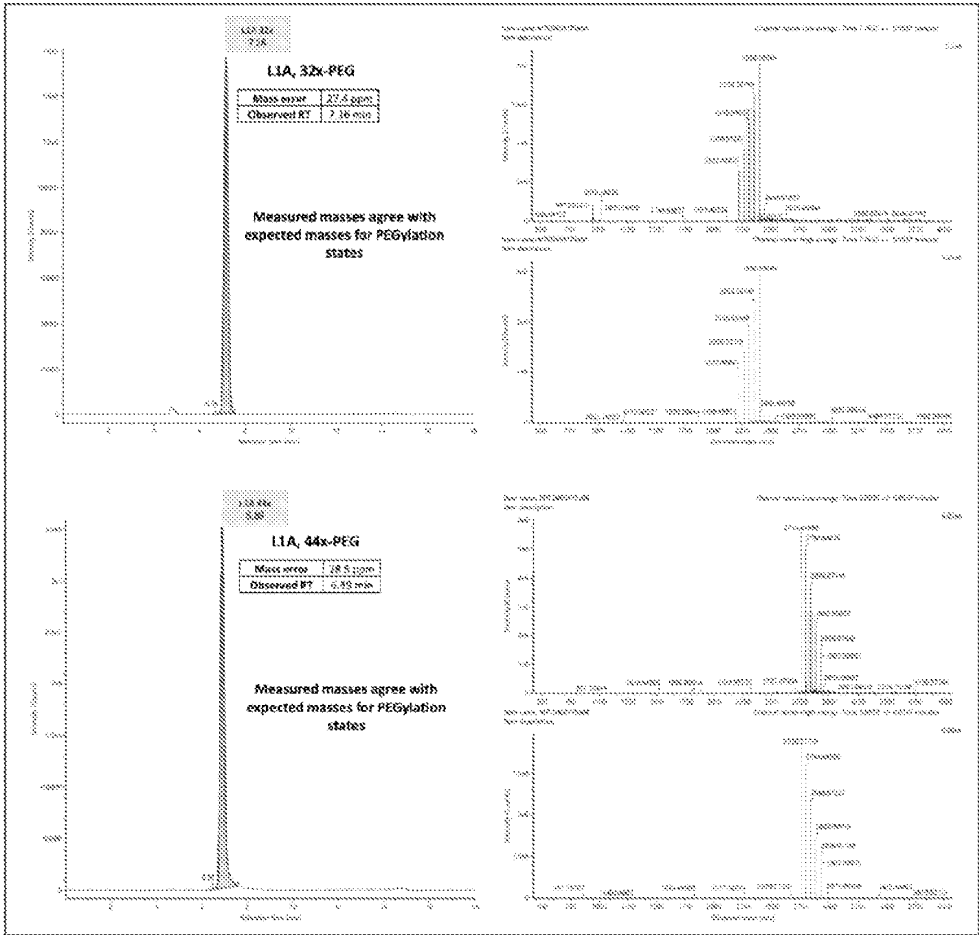


Figure 3 (Cont.)

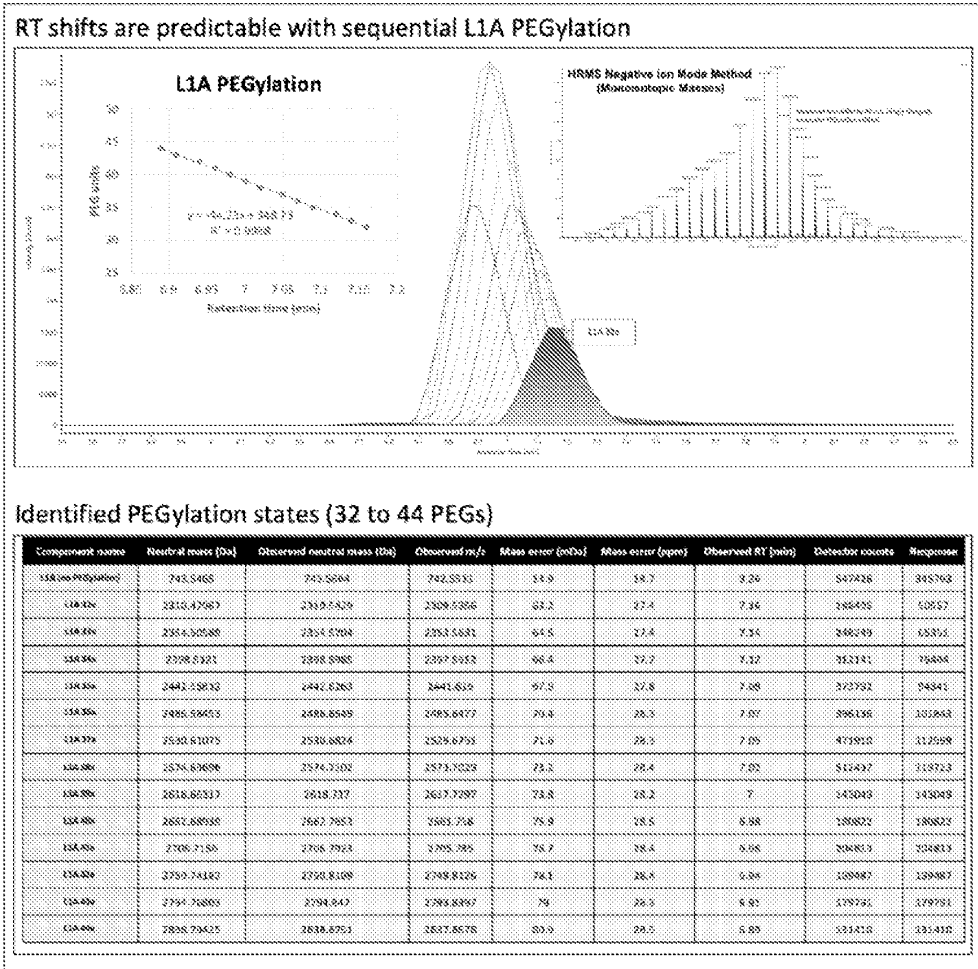


Figure 4

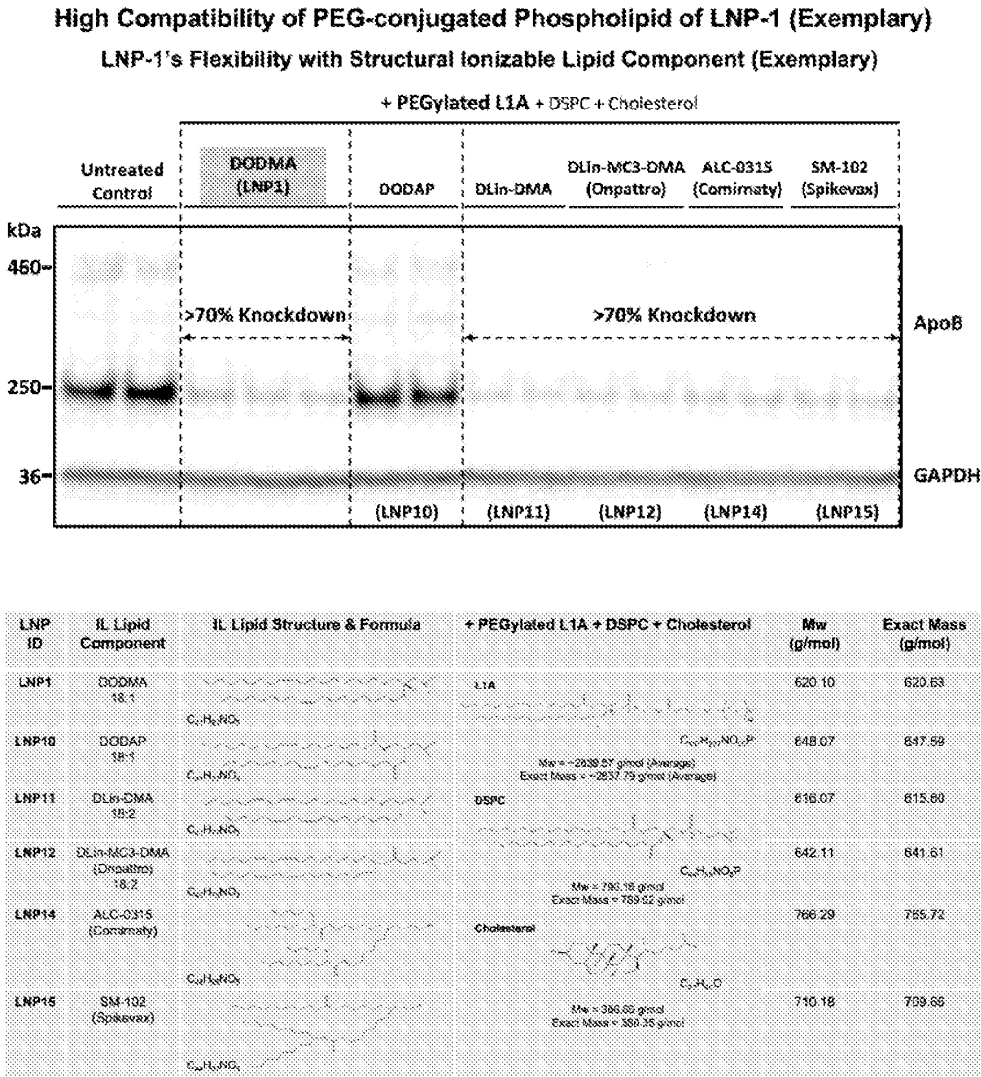


Figure 4 (Cont.)

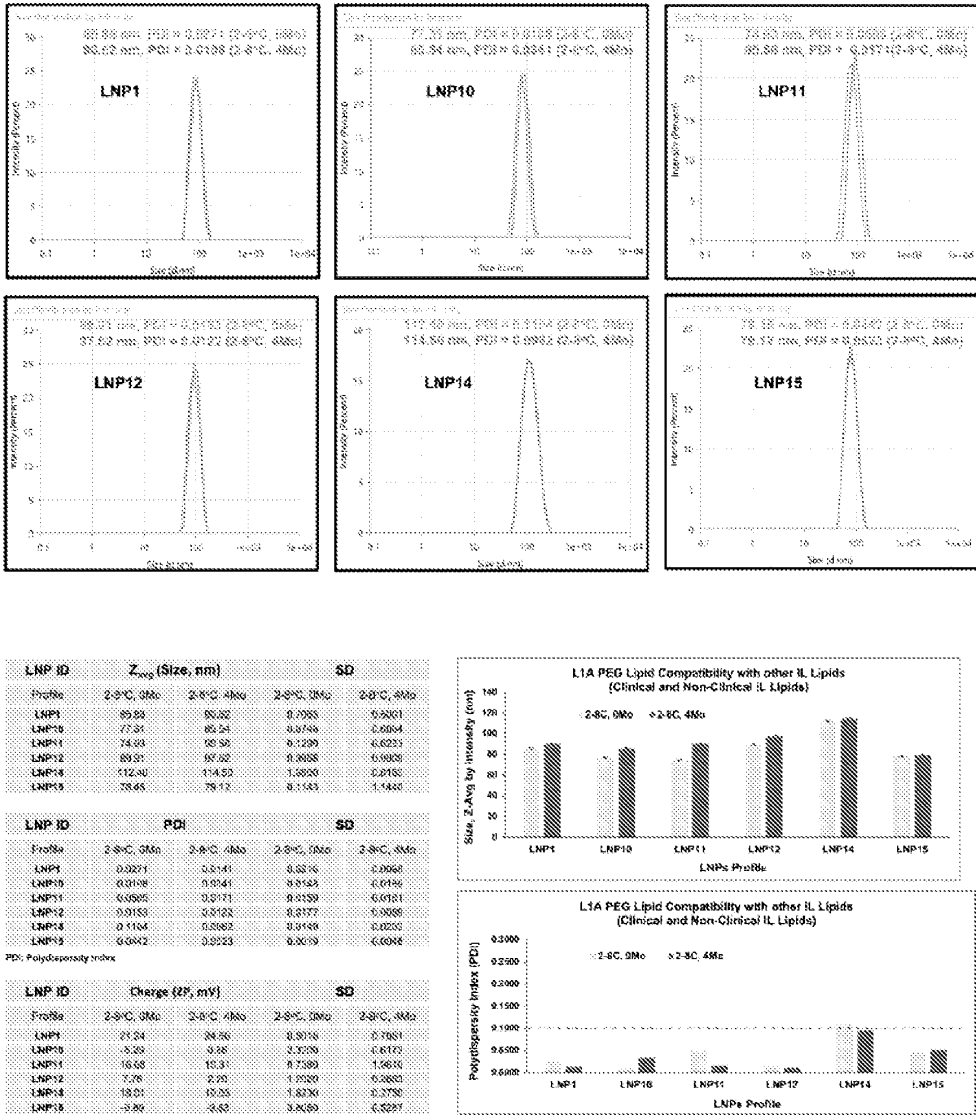
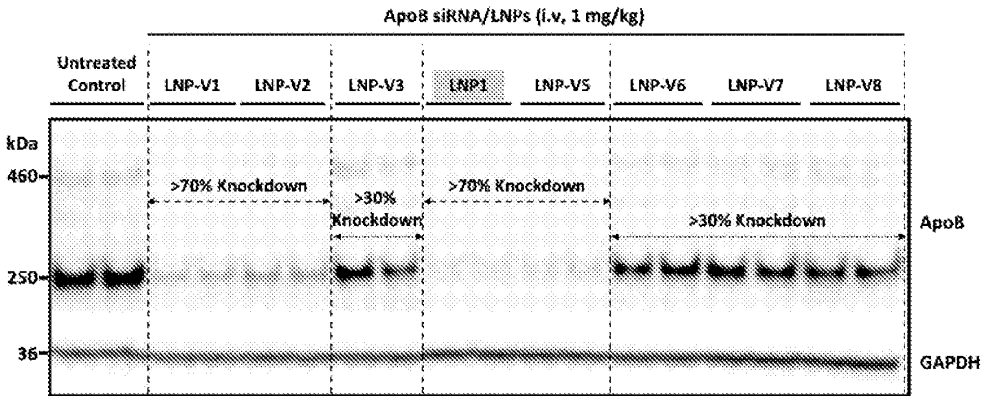
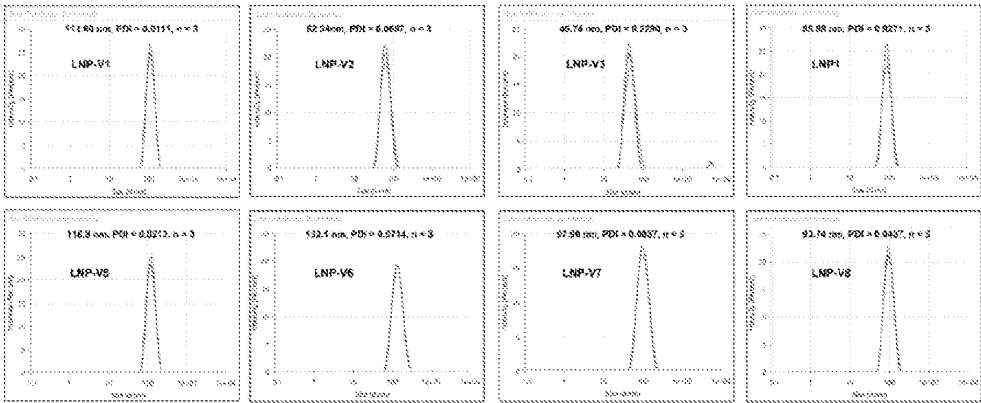


Figure 5
Flexibility with Four Lipid Component Molar Ratios of LNP-1 (Exemplary)



Varied Molar Ratios of Four Lipid Components of LNP-1 (Exemplary)				
LNP ID	DODMA	DSPC	Cholesterol	PEGylated L1A
LNP-V1	59.25	10	30	0.75
LNP-V2	50	10	38	2
LNP-V3	50	10	35	5
LNP1	50	10	39.25	0.75
LNP-V5	55	5	39.25	0.75
LNP-V6	10	50	39.25	0.75
LNP-V7	5	55	39.25	0.75
LNP-V8	30	10	59.25	0.75

Figure 5 (Cont.)

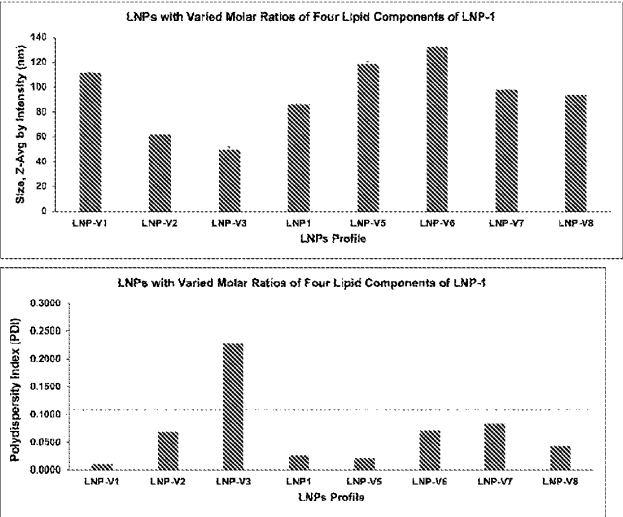


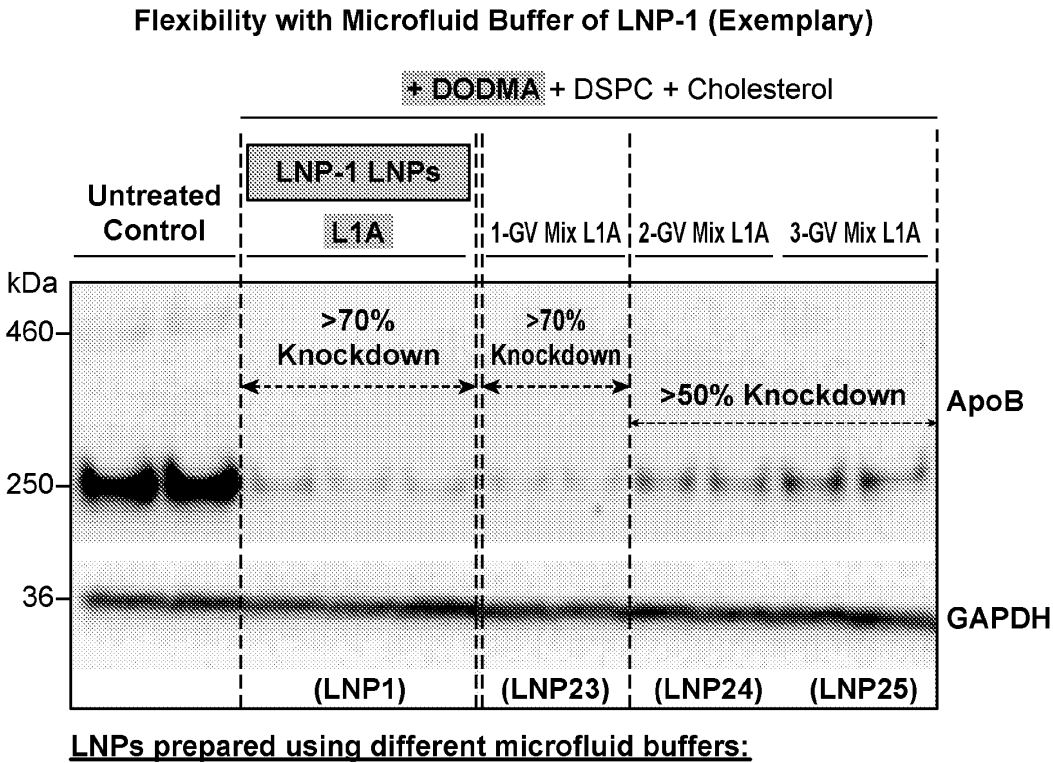
LNP ID	Z _{avg} (Size, nm)	SD
Profile	Freshly-formulated	
LNP-V1	111.6	0.466
LNP-V2	82.54	0.4446
LNP-V3	66.74	2.277
LNP1	65.88	3.7063
LNP-V5	116.3	1.76
LNP-V6	132.1	3.0865
LNP-V7	97.98	3.3531
LNP-V8	93.74	3.183

LNP ID	PDI	SD
Profile	Freshly-formulated	
LNP-V1	0.0111	0.3655
LNP-V2	0.0687	0.0900
LNP-V3	0.2295	3.0439
LNP1	0.0271	0.3216
LNP-V5	0.0213	0.3156
LNP-V6	0.0714	0.3125
LNP-V7	0.0837	0.3105
LNP-V8	0.0437	0.3153

PDI: Polydispersity Index

LNP ID	Charge (ZP, mV)	SD
Profile	Freshly-formulated	
LNP-V1	35.77	3.70
LNP-V2	24.82	6.79
LNP-V3	17.15	7.71
LNP1	21.54	0.50
LNP-V5	3.62	0.79
LNP-V6	25.92	5.61
LNP-V7	23.37	4.71
LNP-V8	8.48	0.82



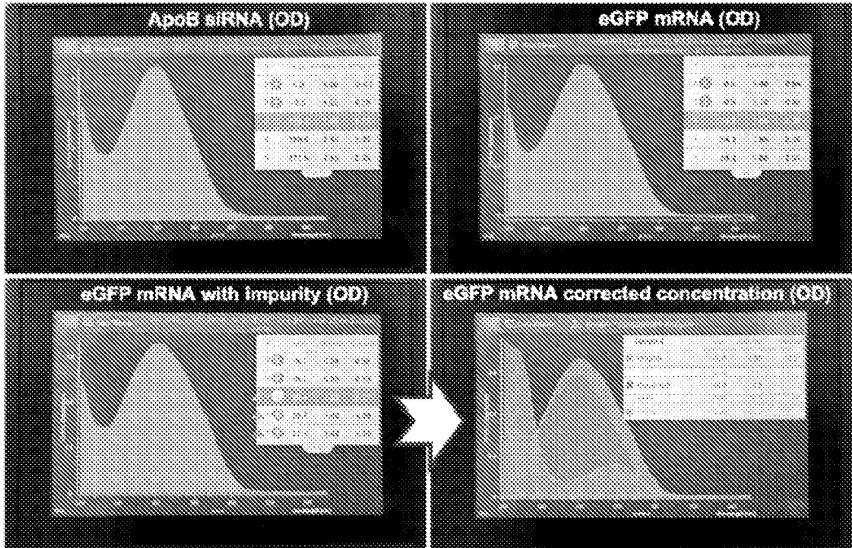


L1A 18:1 (LNP1): 25 mM Citrate Buffer, 0.210 mg/mL ApoB siRNA
1-GV Mix L1A (LNP23): 25 mM Acetate Buffer, 0.210 mg/mL ApoB siRNA
2-GV Mix L1A (LNP24): 50 mM Acetate Buffer, 0.210 mg/mL ApoB siRNA
3-GV Mix L1A (LNP25): 100mM Acetate Buffer, 0.210 mg/mL ApoB siRNA

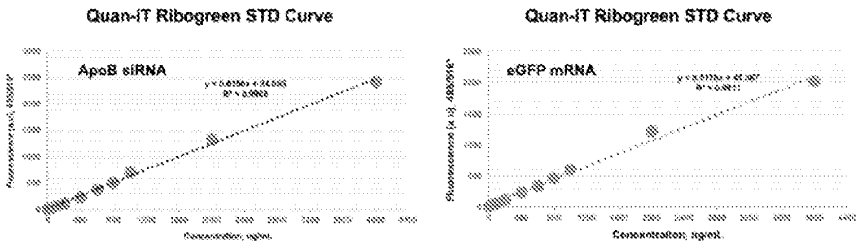
FIG. 6

Figure 7

RNA Payload Assay for LNP-1 LNPs Formulations
Fluorescent Quant-iT RNA RiboGreen Quantification Method (Exemplary)



OD measurements by NanoDrop One from Thermo Fisher Scientific (Exemplary)

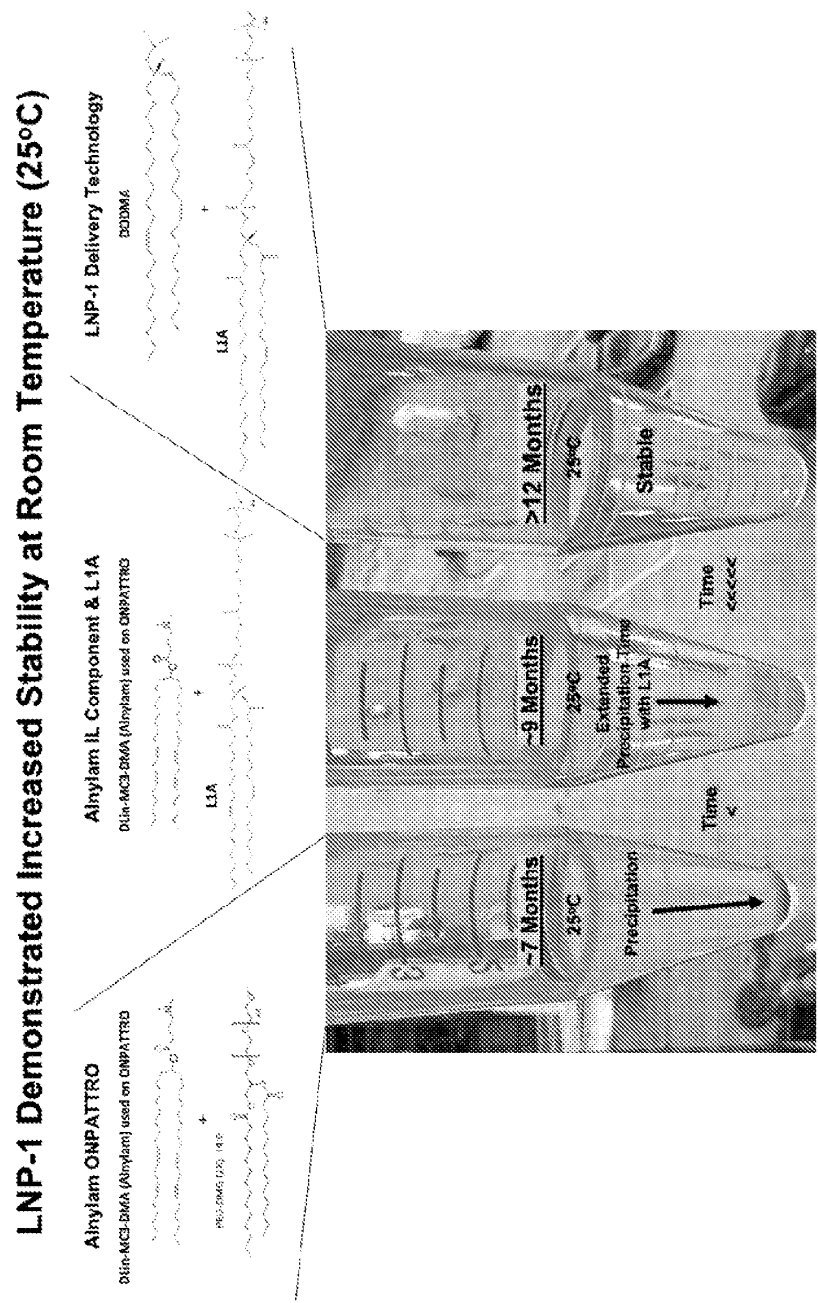


Fluorescent Quant-iT RNA RiboGreen Quantification Method STD Curve (Exemplary)

1. Quantify a stock solution (e.g. 20-1000ng/uL) by OD (Optical Density) at A_{260} , A_{280} , A_{260}/A_{280} and A_{260}/A_{230} , see NanoDrop One exemplary spectra data images. Note: Apply a corrected RNA concentration if any impurity is present in the RNA samples, specifically for mRNAs, as shown on spectra data image.
2. Prepare in a fluorescent microplate assay (96-well plate) a series of diluted concentrations from the above RNA stock solution for building a Standard Curve (e.g. 0-2000+ng/mL). Add as well LNPs-RNAs stock solution as control, disassembled LNP-RNA samples from stock solution and/or other control samples in the black clear bottom microplate. Note: Disassembled LNP-RNA samples are incubated at 5% (v/v) TX-100 in TE Buffer (1x) at 50°C for 2h, then diluted at a final 0.1% (v/v) TX-100 concentration in TE Buffer (1x).
3. Ultrasensitive Fluorescent Quan-iT RNA Ribogreen Quantification Method is performed to all RNAs samples e.g. Standard Curve (STD as shown on plots images) vs LNPs-RNAs control vs disassembled LNP-RNA samples vs other control samples according to vendor protocol. Note: Take into consideration any effect of common contaminants for this ultrasensitive fluorescent assay, see link:
<https://assets.thermofisher.com/TFS-Assets/LSG/manuals/mp11490.pdf>

FIG. 7 (Cont. 3)

Figure 8



Structural & Functional Stable L1A PEG-lipid is Compatible with Other Ionizable Lipids Having Smaller Sizes

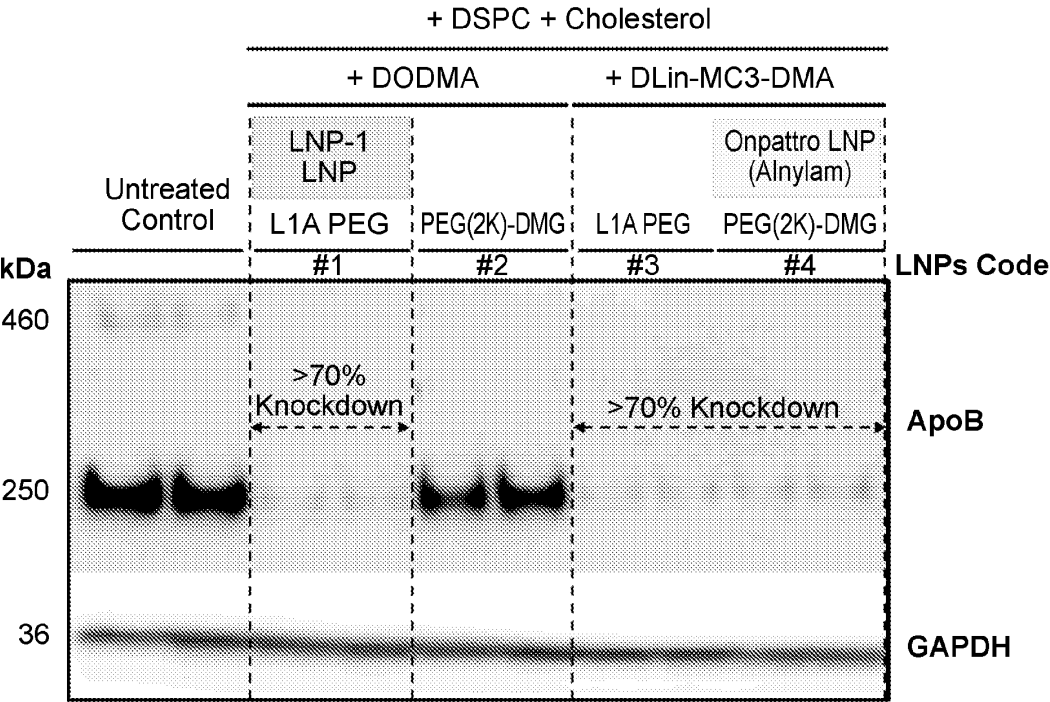


FIG. 9

Figure 9 (Cont.)

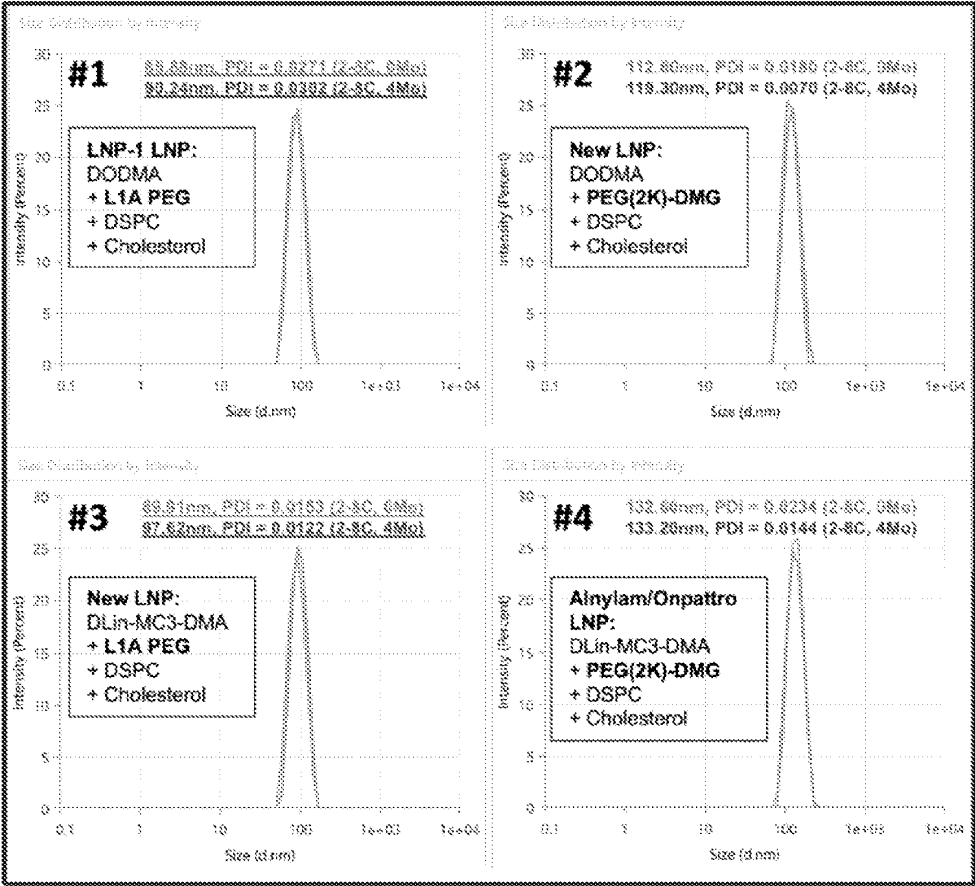


Figure 9 (Cont.)

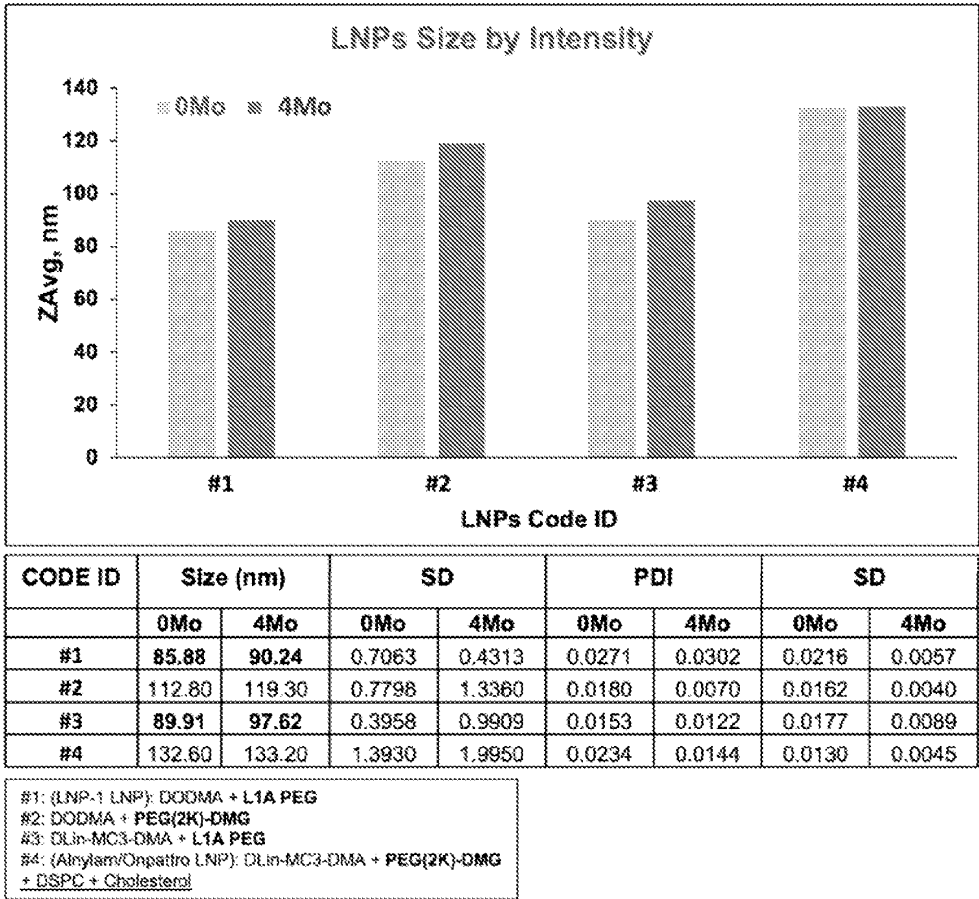


Figure 10

Long-term Structural Lipids Stability and Quantification
– Stable Lipid Composition of Aged eGFP mRNA/LNP-1

Sample	Lipid Name	Calculated Concentration (mg/ml)	LNP Total Mass (mg/ml)	MW	mmol in 1ml	Total Count (mmol)	Assay mmol%	Assay m/m%
eGFP mRNA/LNP-1 (Freshly-formulated)	DOXMA	3.254	8.448	620.10	0.0005230	6.001258	46.41	50.46
	DSPC	1.024		790.15	0.0001480		11.48	15.85
	Cholesterol	1.801		385.65	0.0005191		41.33	27.94
	LTA	0.245		2841.06	0.0000086		0.76	3.80
Sample	Lipid Name	Calculated Concentration (mg/ml)	LNP Total Mass (mg/ml)	MW	mmol in 1ml	Total Count (mmol)	Assay mmol%	Assay m/m%
eGFP mRNA/LNP-1 (2-8°C, 9 Months Storage)	DOXMA	2.775	5.547	620.10	0.0004874	6.001135	42.94	49.04
	DSPC	0.637		790.15	0.0000965		8.51	12.39
	Cholesterol	1.891		385.65	0.0005476		47.98	34.09
	LTA	0.137		2841.06	0.0000061		0.54	2.84

Figure 11
Long-term Physicochemical Stability of Aged LNP-1 with Different RNA Payloads

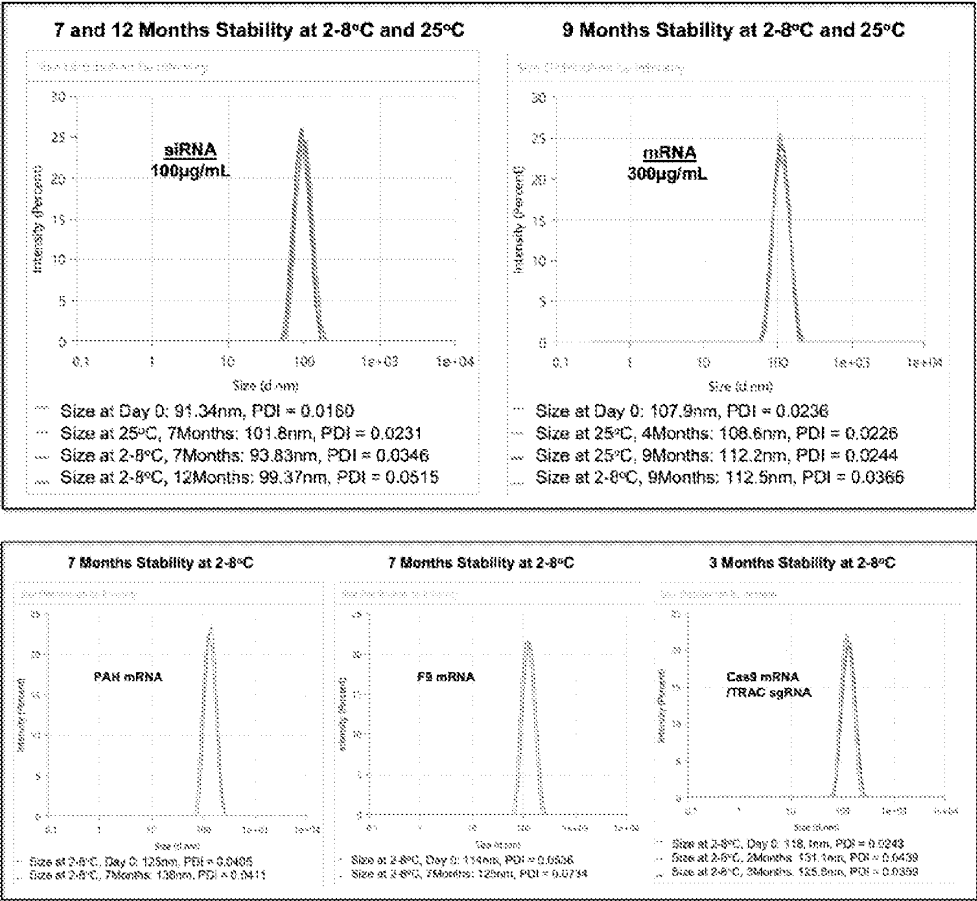
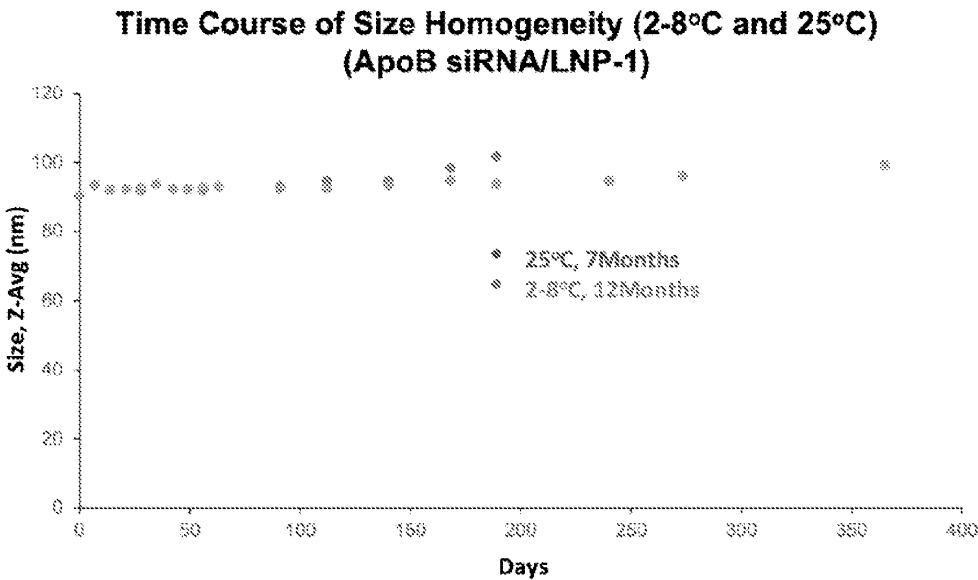


Figure 12



**Physical Characterization of Critical Quality Attributes Summary (25°C)
(ApoB siRNA/LNP-1)**

Days	Size Zavg ± SD (nm)	PDI ± SD	Average Charge Zeta Potential ± SD (mV)	Average Conductivity
0	91.34 ± 0.2126	0.0160 ± 0.0012	-26.9097 ± 7.1642	0.3802 ± 0.1530
7	90.73 ± 0.8719	0.0363 ± 0.0132		
28	90.65 ± 0.5808	0.0121 ± 0.0114		
56	93.45 ± 0.1841	0.0313 ± 0.0140		
84	96.65 ± 1.218	0.0589 ± 0.0107		
112	98.55 ± 0.2878	0.0716 ± 0.0183		
140	102.9 ± 0.9965	0.0793 ± 0.0440		
168	101.5 ± 0.6061	0.0693 ± 0.0096		
189	103.2 ± 0.6685	0.0836 ± 0.0111		

Figure 13

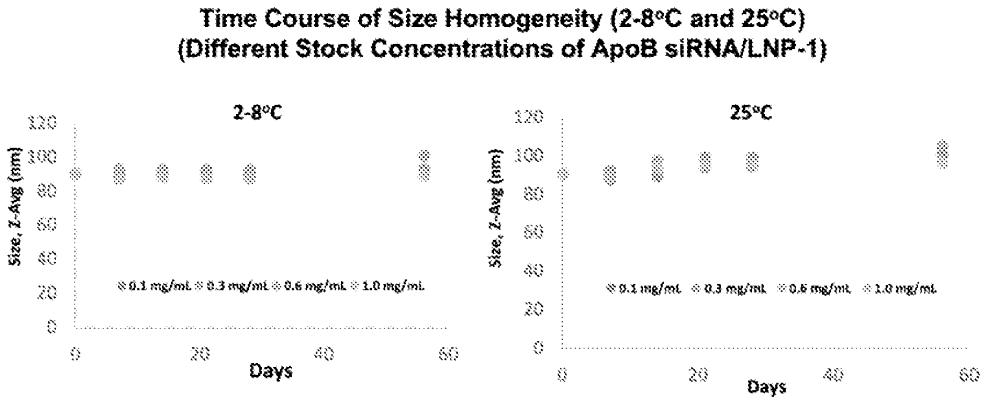
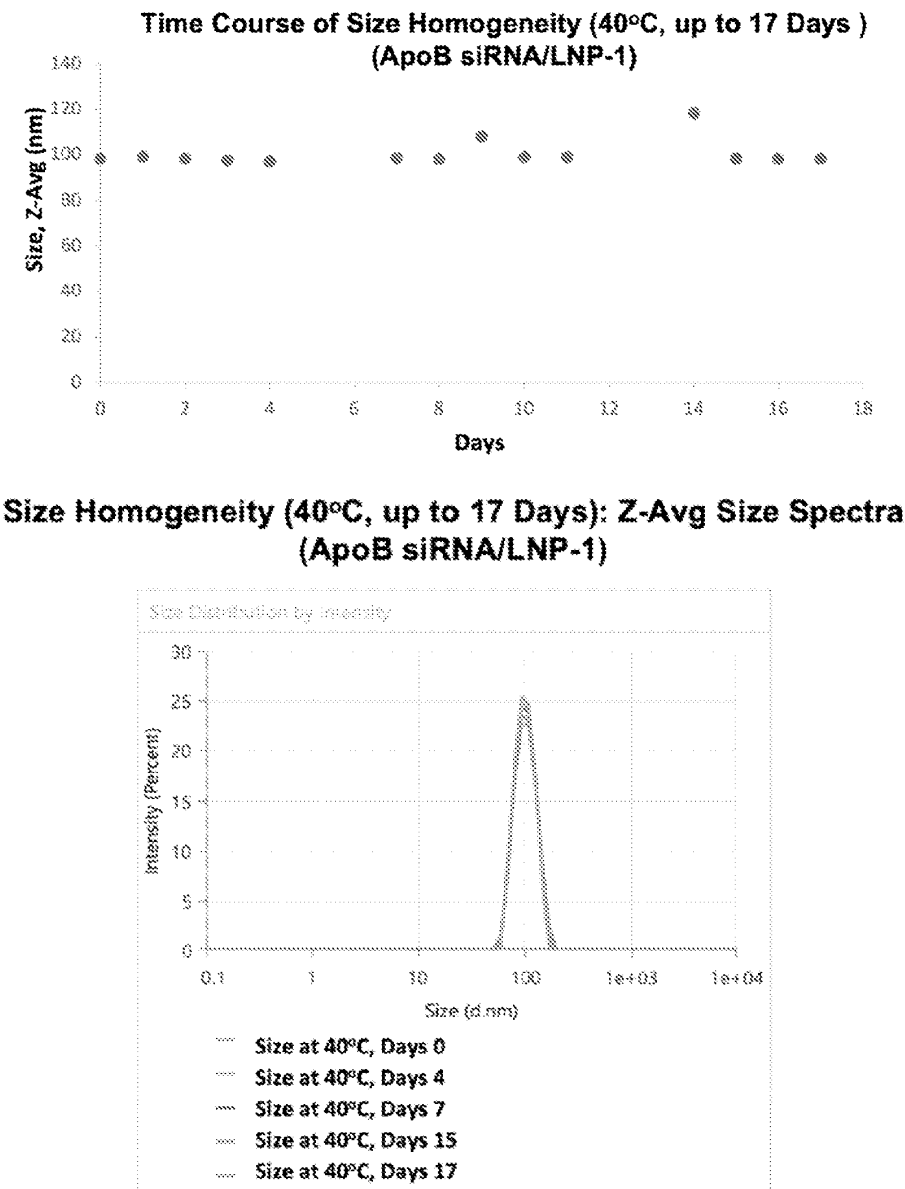


Figure 14

Long-term Stability of ApoB siRNA/LNP-1 at 40°C



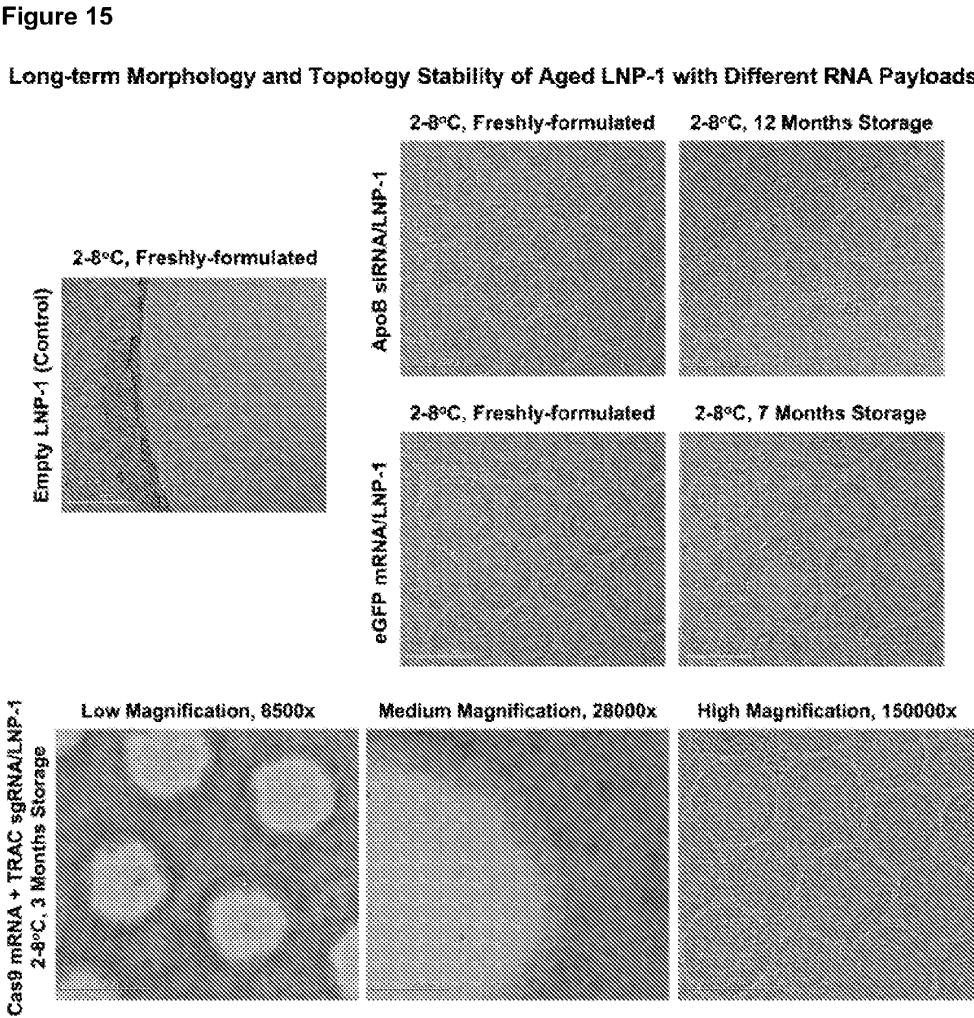


Figure 16

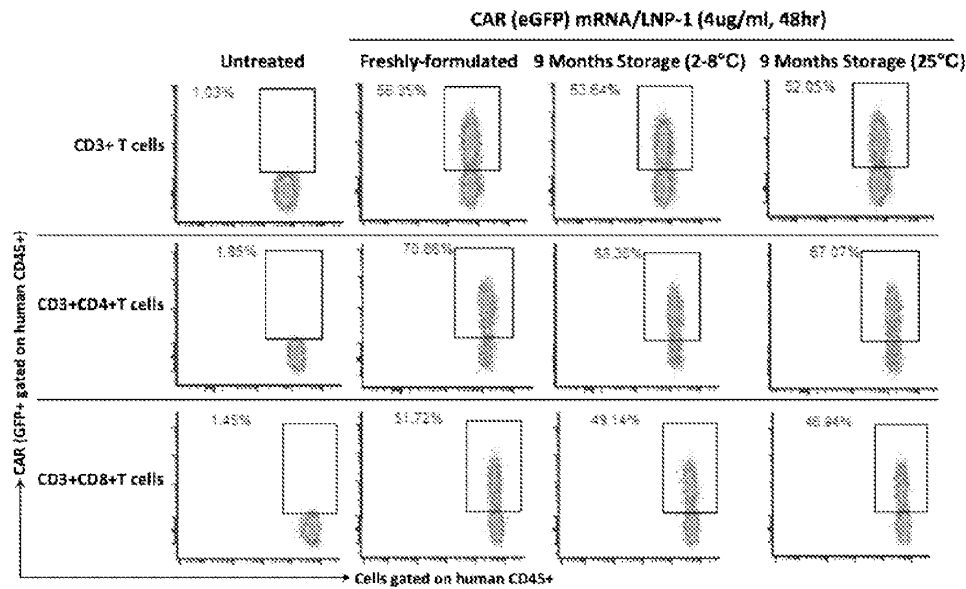
LNP-1 Platform Characterization Summary:
Payloads Versatility and Long-term Stability

Payload Type	Payload Size (nt)	Encapsulation Efficiency	RNA/LNP-1 Size (nm)	Long-term Stability (2-8°C)		
ApoB siRNA	21 (ds)	>94%	90 ± 10	12Months	PDI	0.0515
					Zeta Potential (mV)	35.02 ± 0.6746
eGFP mRNA	980 (ss)	>87%	117 ± 10	9Months	PDI	0.0366
					Zeta Potential (mV)	32.66 ± 1.234
PAH mRNA	1619 (ss)	>69%	129 ± 10	7Months	PDI	0.0411
					Zeta Potential (mV)	32.89 ± 1.743
P9 mRNA	1646 (ss)	>65%	125 ± 10	7Months	PDI	0.0734
					Zeta Potential (mV)	34.75 ± 1.065
Cas9 mRNA/sgRNA	4471/100 (ss/ss)	>80%/>90%	125 ± 10	3Months	PDI	0.0359
					Zeta Potential (mV)	36.32 ± 0.5906

ds: Double-Stranded
ss: Single-Stranded

Figure 17

Long-term Function Stability – Stable CAR-T Generation Potency of Aged eGFP mRNA/LNP-1



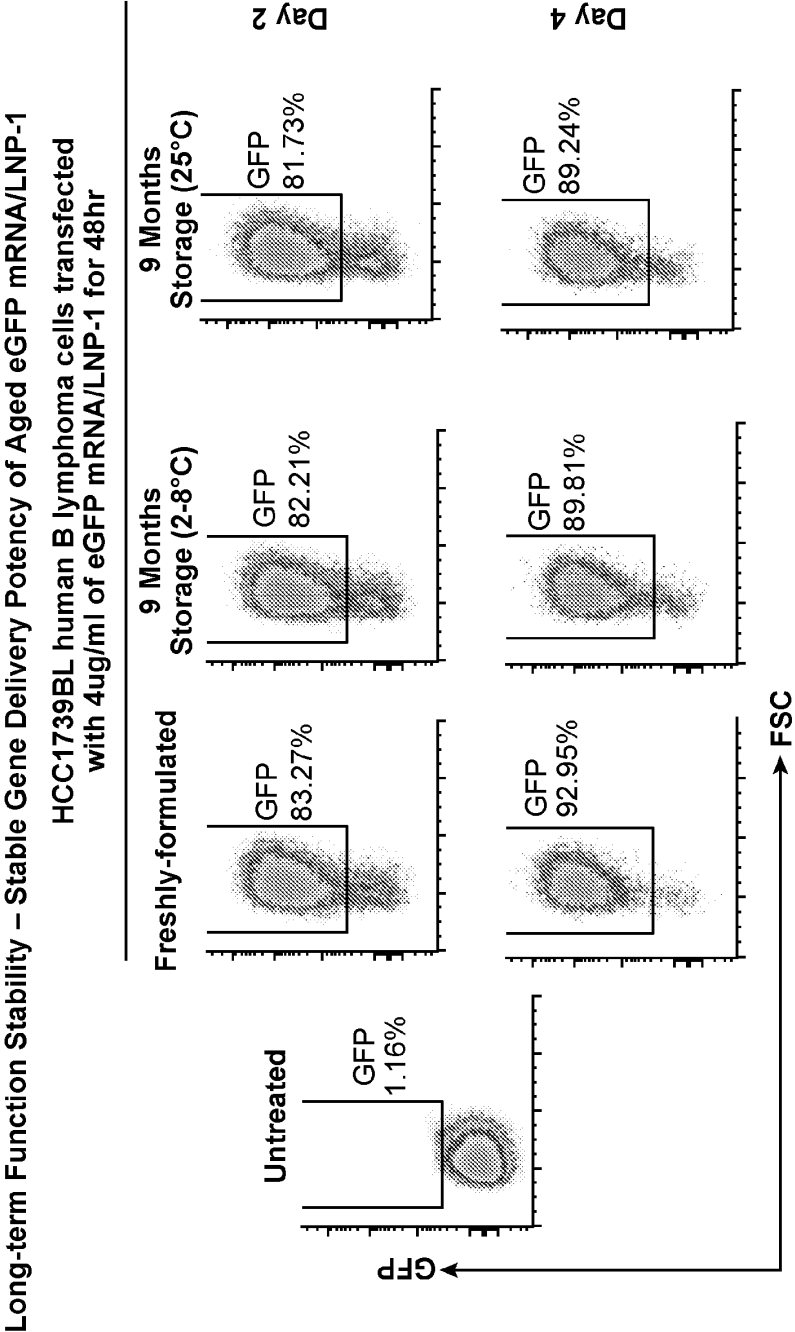


FIG. 18

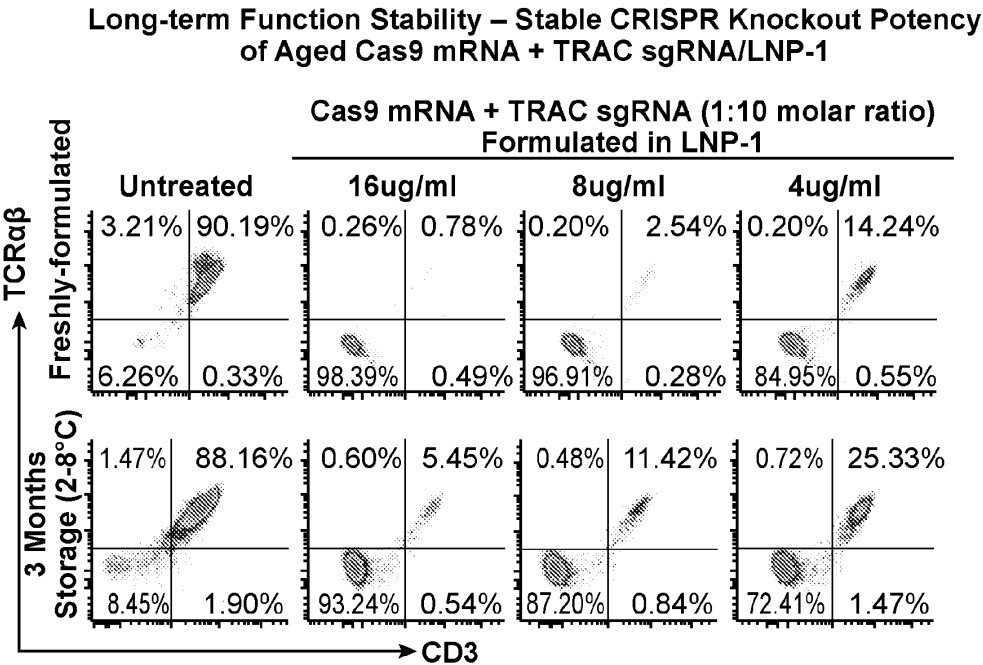


FIG. 19

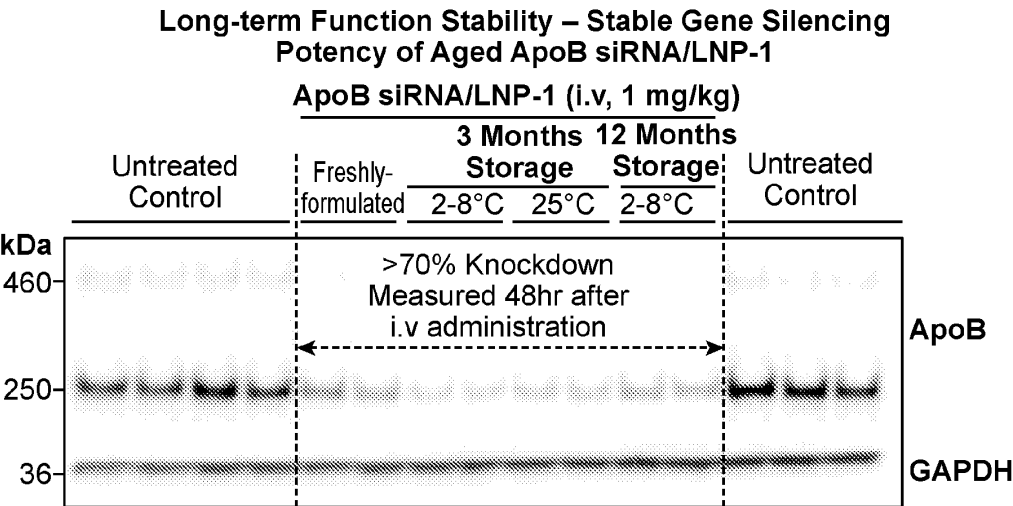
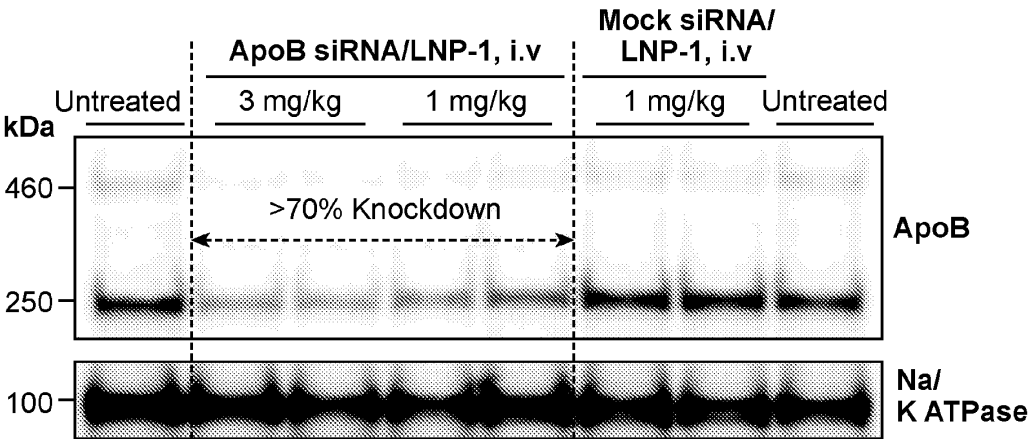
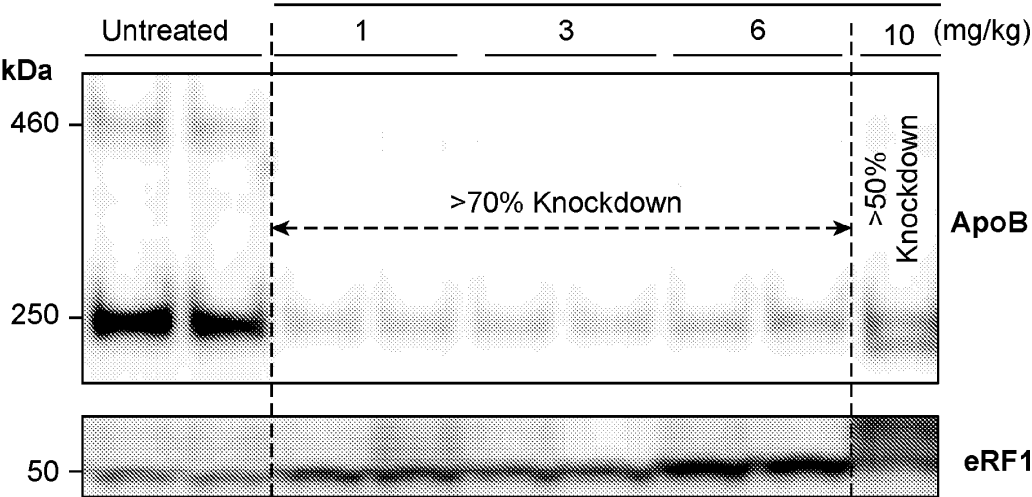


FIG. 20

LNP-1's Versatile Therapeutic Applications – Gene Silencing
In Vivo Knockdown Potency of ApoB siRNA/LNP-1 in Mouse Livers



ApoB siRNA/LNP-1 In Vivo Potency at Different Dosages
ApoB siRNA/LNP-1, i.v.



Note: No abnormality in biochemistry profiles was detected in 1-3 mg/kg treated mice.

FIG. 21

Figure 22

**Batch Consistency of Stable ApoB siRNA/LNP-1:
Western Blotting of Liver Tissues from Mice Received 1 mg/kg (i.v) ApoB siRNA/LNP-1**

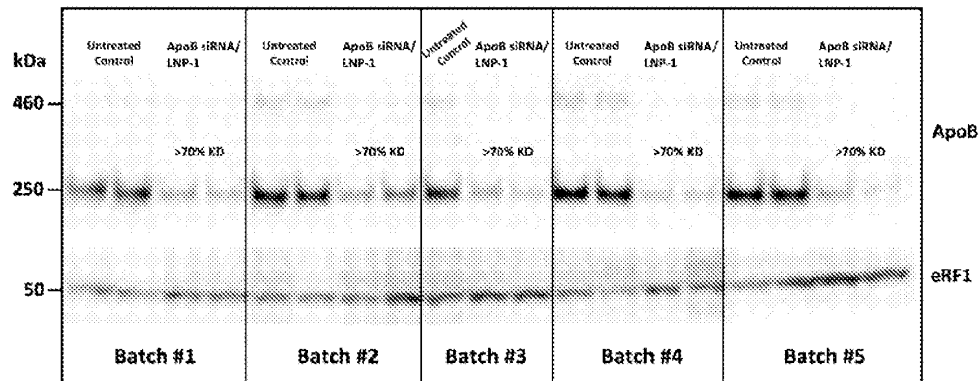


Figure 23

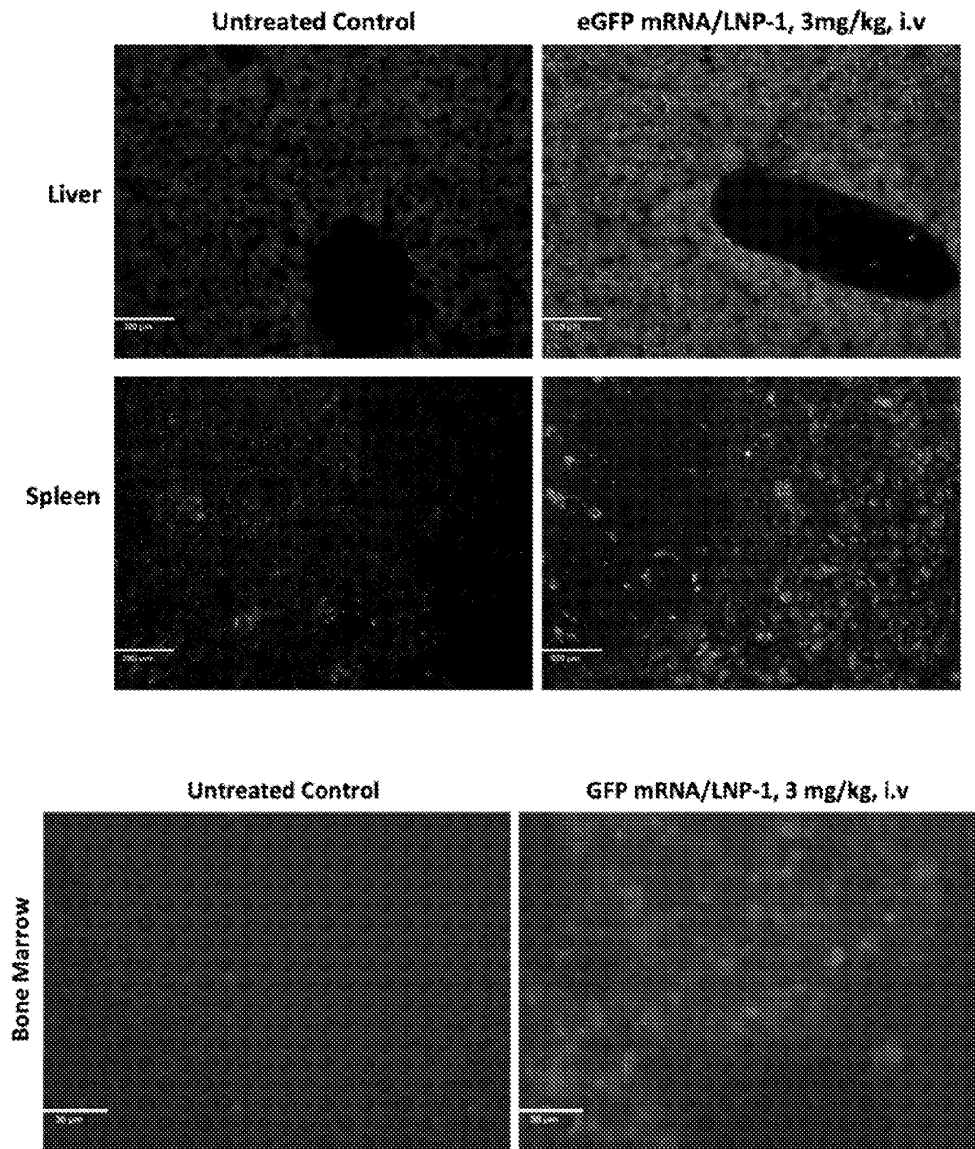
LNP-1's Versatile Therapeutic Applications – mRNA Therapy**In Vivo Gene Delivery Potency of LNP-1 (Exemplary)**

Figure 24

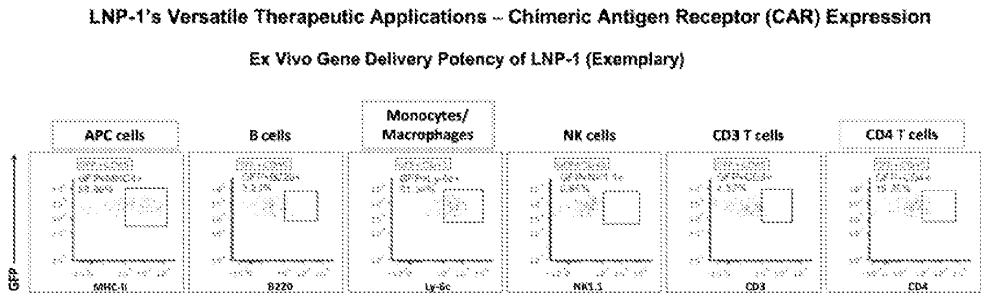


Figure 25

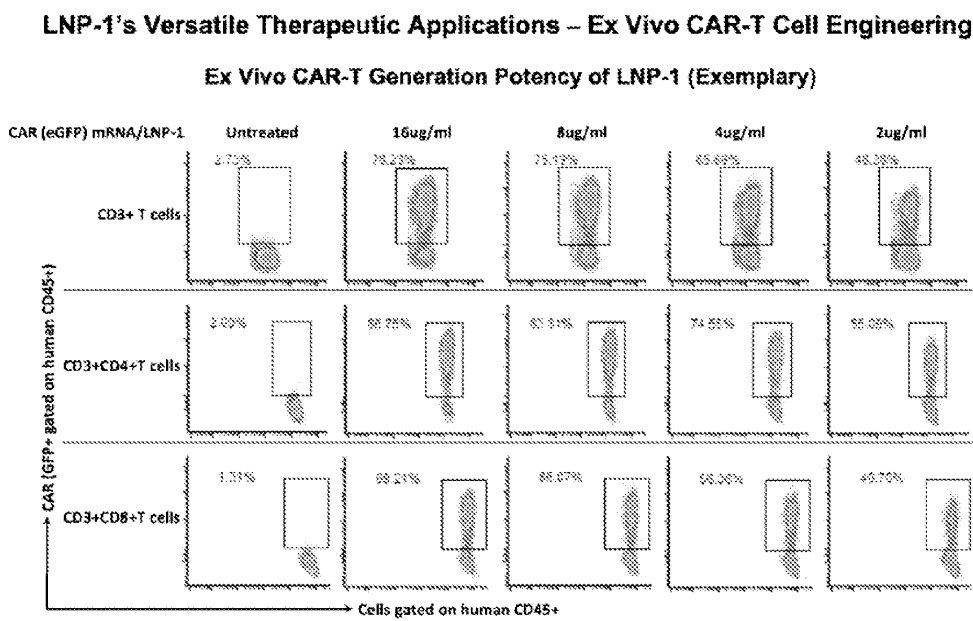


Figure 26

LNP-1's Versatile Therapeutic Applications – In Vivo CAR-T Cell Engineering

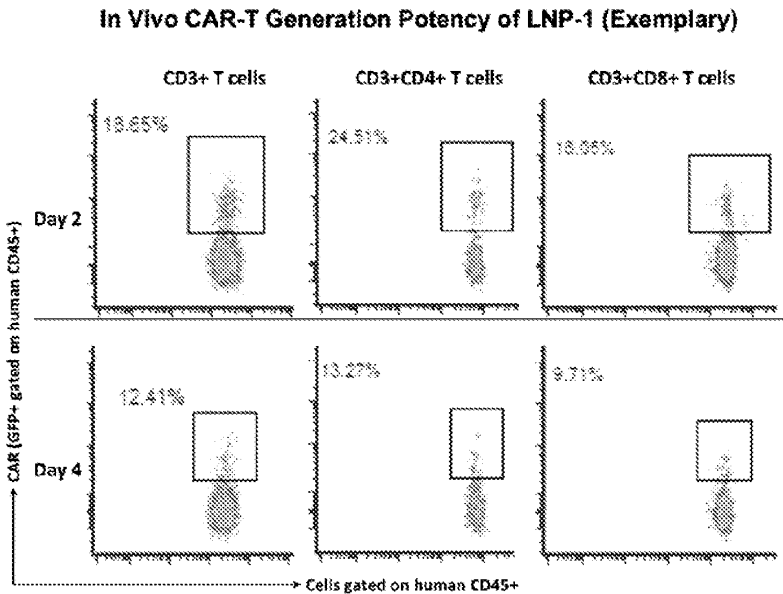
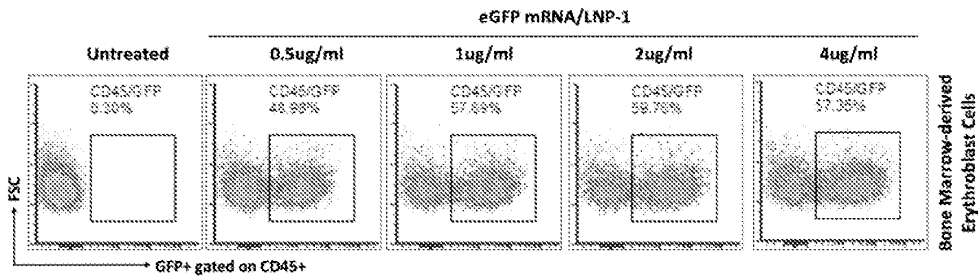


Figure 27

LNP-1's Versatile Therapeutic Applications – Stem Cell Engineering

Gene Delivery Potency of LNP-1 to Hematopoietic Stem Cells (Exemplary)



LNP-1's Versatile Therapeutic Applications - Gene Editing
CRISPR-Cas-mediated Gene Editing Potency of LNP-1 (Exemplary)
Cas9 mRNA + TRAC sgRNA (1:10 molar ratio) Formulated in LNP-1

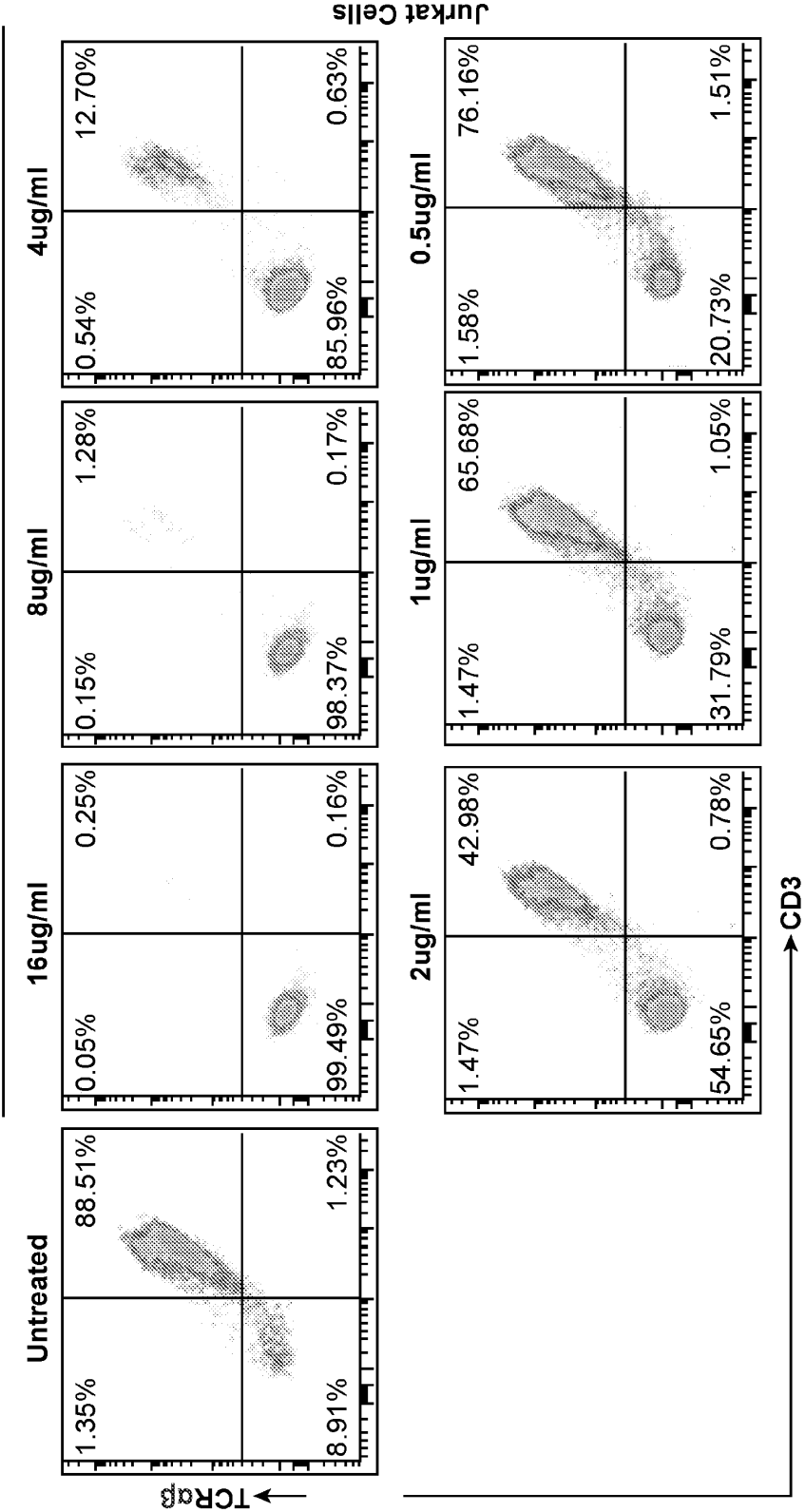


FIG. 28

Figure 29

LNP-1's Versatile Therapeutic Applications – Gene Therapy for Malignant Cells
Gene Delivery Potency of LNP-1 to Human Leukemia Cells (Exemplary)

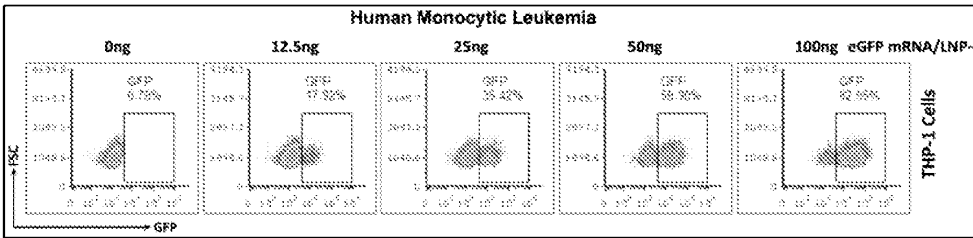
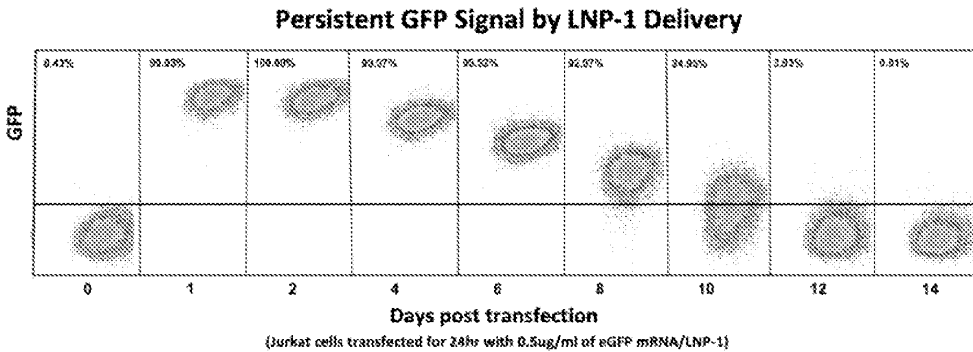
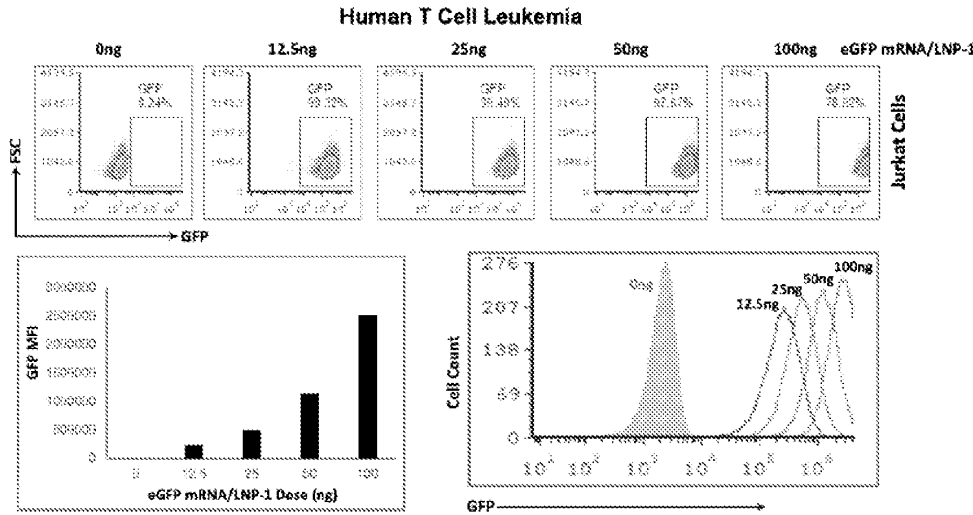


Figure 30

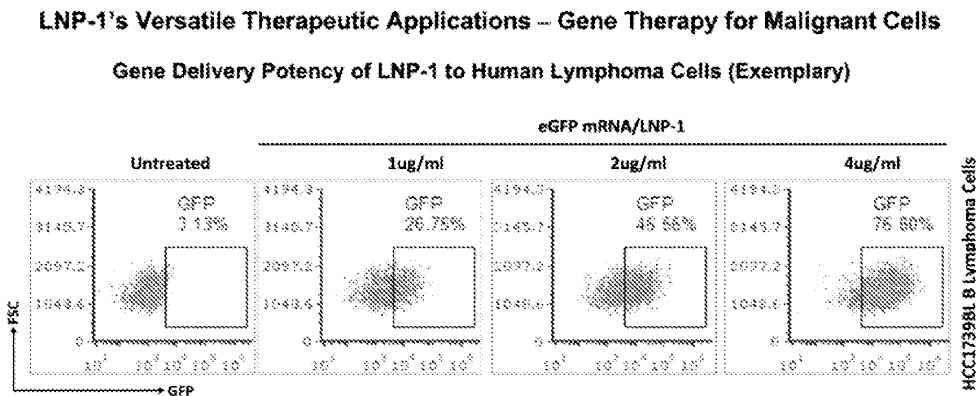
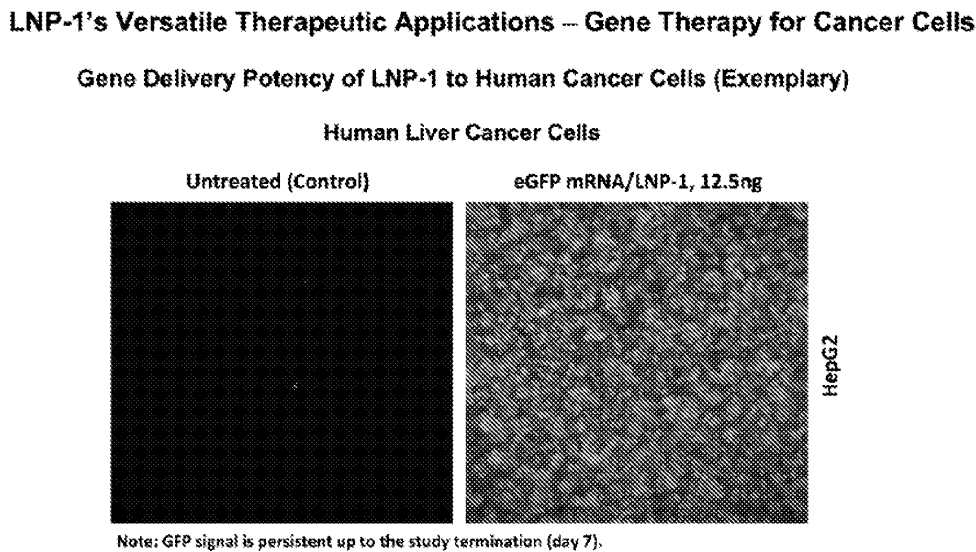


Figure 31



LNP-1's Versatile Therapeutic Applications - Vaccines
LNP-1's Potency as COVID-19 mRNA Vaccines (Exemplary)

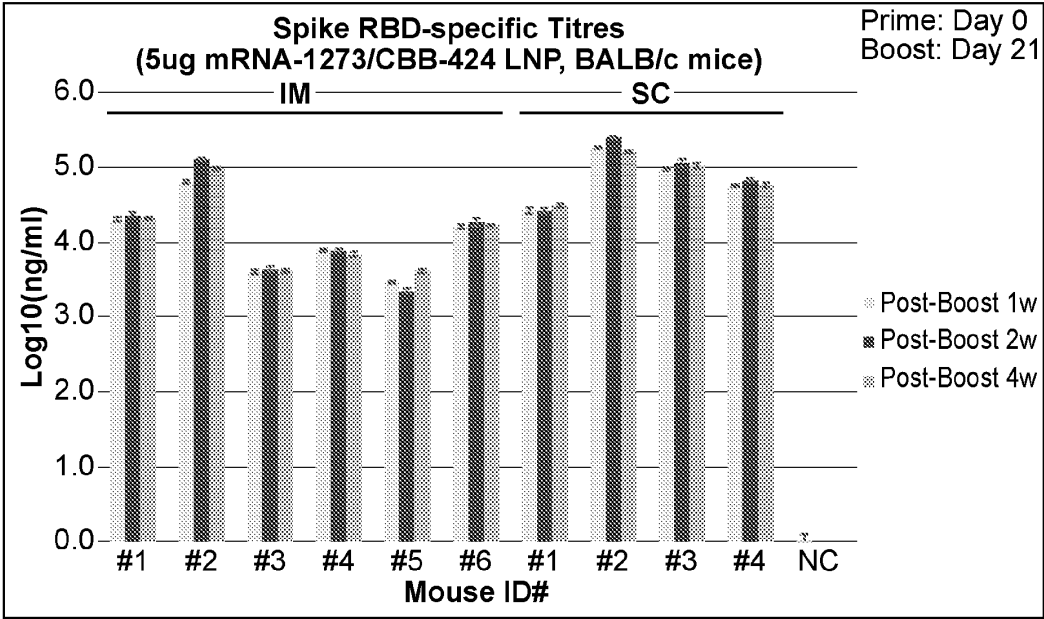
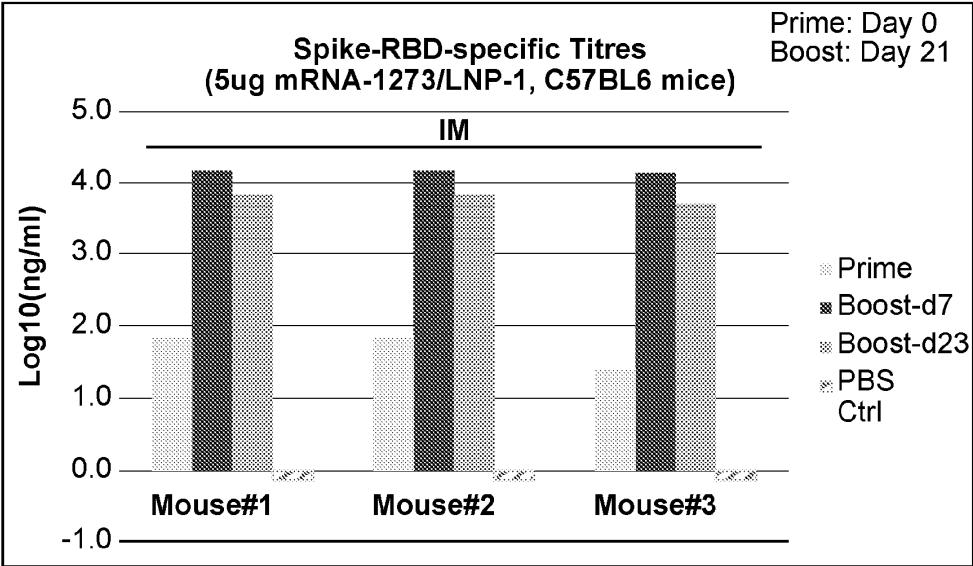


FIG. 32

Figure 33

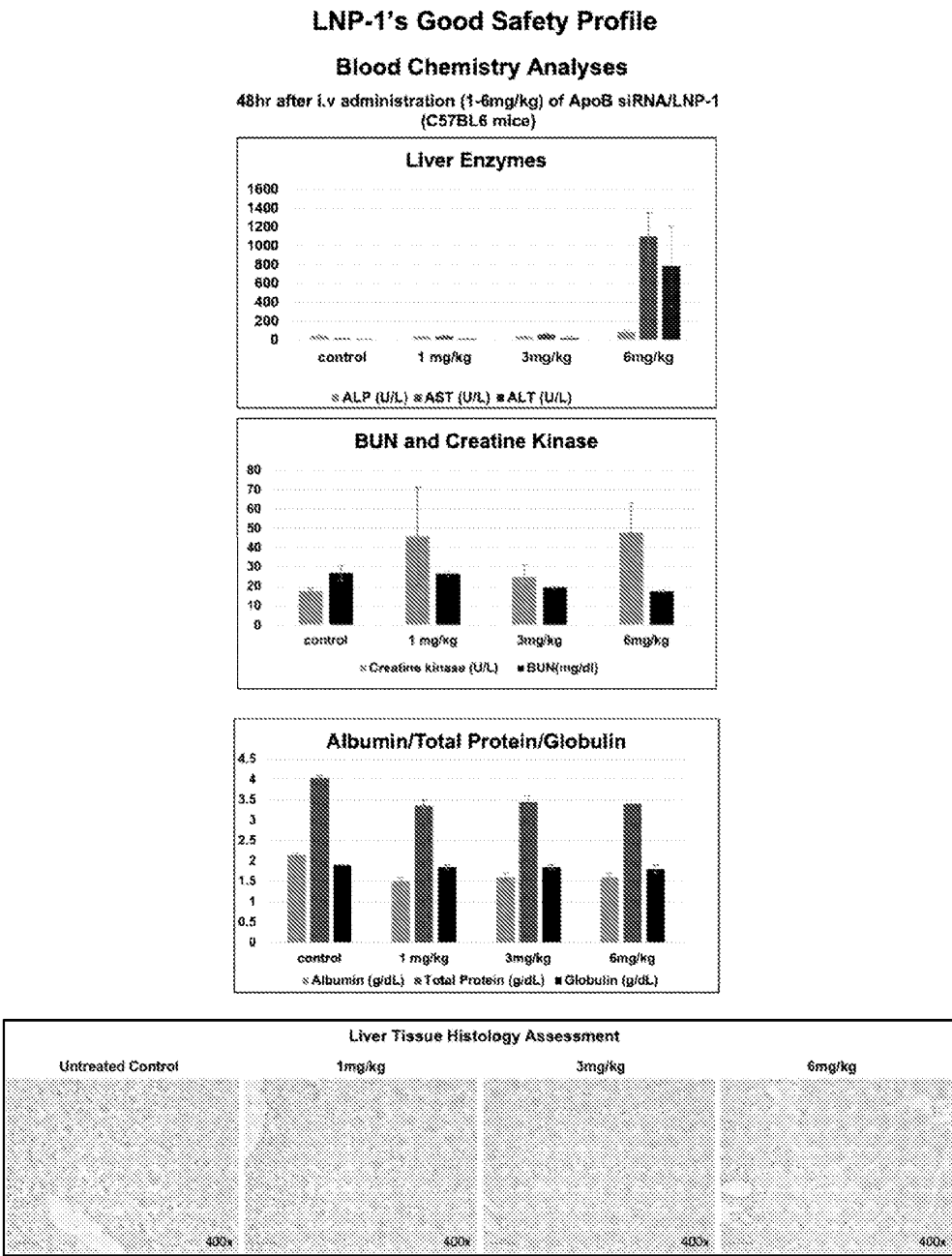


Figure 34

