

FIG. 1

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		Treatment Period			Post-Dose Follow-Up Period								LTFU ^p			
	Screen	Initial Dose	W0.5	W1	W2	W4	W6	W8	W8.5	W9	W10	W12	W16	W20	W36 ^r /ET	W52, 104, 156 Post initial Dose
Visit Week																
Visit Day (Visit Window) ^b	D-56 to D-1	D1 ^a	D4 (±2)	D8 (±2)	D15 (±2)	D29 (±3)	D43 (±3)	D57 ^a (±5)	D60 (±2)	D64 (±2)	D71 (±2)	D85 (±3)	D113 (±5)	D141 (±7)	D253 (±7)	
Informed consent	X															
Demography	X															
Medical history ^c	X															
Inclusion/exclusion criteria	X	X														
Randomization ^d		X														
Full physical examination ^e	X	X						X								
Symptom-directed physical examination ^f			X	X	X	X			X	X	X	X	X	X		
Body weight, height, & BMI	X															
Vital signs ^g	X	X	X	X	X	X		X	X	X	X	X	X	X	X	
Screening laboratory tests (CMV/HBV/HCV) ^h	X															

FIG. 2A

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		Treatment Period			Post-Dose Follow-Up Period								LTFU ^p			
	Screen	Initial Dose	W0.5	W1	W2	W4	W6	W8	W8.5	W9	W10	W12	W16	W20	W36/ ^r ET	W52, 104, 156 Post initial Dose
Visit Week			D4 (±2)	D8 (±2)	D15 (±2)	D29 (±3)	D43 (±3)	D57 ^a (±5)	D60 (±2)	D64 (±2)	D71 (±2)	D85 (±3)	D113 (±5)	D141 (±7)	D253 (±7)	(±30)
	X	X						X							X	X
HIV test ⁱ															X	
VISP assessment ^u															X	
Urine for drugs of abuse ^j	X															
FSH ^s	X															
Clinical laboratory assessments ^k	X	X	X	X	X	X		X		X	X	X	X	X	X	
Urinalysis	X															
Blood, urine, saliva for viremia/viral shedding ^q		X	X	X	X	X		X	X	X	X	X	X	X	X	
Blood sample for HLA Test		X														
Blood sample for immunogenicity (intracellular cytokine staining assay)		X		X	X	X		X			X	X	X	X	X	X
Serum sample for immunogenicity (antibody testing)		X		X				X			X				X ¹	X

FIG. 2B

			Treatment Period						Post-Dose Follow-Up Period						LTFU	
Visit Week	Screen	Initial Dose	W0.5	W1	W2	W4	W6	W8	W8.5	W9	W10	W12	W16	W20	W36 ^r / ET	W52, 104, 156 Post initial Dose
			D4 (±2)	D8 (±2)	D15 (±2)	D29 (±3)	D43 (±3)	D57 ^a (±5)	D60 (±2)	D64 (±2)	D71 (±2)	D85 (±3)	D113 (±5)	D141 (±7)	D253 (±7)	
Visit Day (Visit Window) ^b	D-56 to D-1	D1 ^a	X	X				X	X	X					D253 (±7)	(±30)
Blood sample for transcriptomics		X	X	X				X	X	X					X	
Leukapheresis ^m														- X -		
IP administration		X						X								
Reactogenicity assessments ⁿ		X	X	X	X			X	X	X	X					
Reactogenicity Telephone Call ^o							X									
Review/record AEs/NOCD ^s		X	X													X ^t
Review/record Concomitant medications	X	X	X													X ^t

FIG. 2C

KEY

a	Assessments performed pre-dose on Day 1 and Day 57. Day 1 assessments are considered separate from Screening labs.
b	Intervals between visit Days 4-43 are calculated post 1st dose (Day 1). Intervals between visit Days 60-253 are calculated post 2nd dose (Day 57). Week 52, 104, and 156 are calculated from Day 1.
c	Complete medical history will be taken at screening and any changes should be updated prior to dosing.
d	Randomization may occur within 48 hours prior to Day 1.
e	Full physical examination includes general appearance, head/neck, chest/respiratory, heart/cardiovascular, gastrointestinal/liver/spleen, extremities, skin, neurological assessments, as well as assessment of injection site and regional lymphatics.
f	Regional examination will be based on subject's symptoms and will include injection site and regional lymphatics.
g	Vital signs (blood pressure, pulse rate, respiratory rate, and temperature) should be measured after the subject has rested comfortably for approximately 10 minutes. On dosing days, vital signs should be measured and recorded within 30 minutes (+/- 10 minutes) pre- and post-dose. On all other visit days, vital signs are only required to be measured and recorded once.
h	HBV = HbsAg test
i	HIV pre-and post-test counseling to be provided. Given potential for VISP (<i>i.e.</i> , cross reactivity with vaccine induced anti-Gag antibodies), any positive antibody-based HIV testing obtained after study dosing will be reflexed to nucleic acid based testing to discriminate between false positive testing (VISP) and true infection.

FIG. 2D

KEY (continued)

j	Drugs of abuse included in the screen are described in the inclusion/exclusion criteria.
k	Clinical labs for safety evaluations will include a complete blood count (CBC) with differential and chemistry (ALT, AST, GGT, bilirubin (direct and total), alkaline phosphatase and creatinine).
l	Additional sample for vaccine induced seropositive antibodies to assess for reactivity in commercial HIV screening tests will be taken at Week 36 or ET.
m	A single leukapheresis procedure will be performed between Weeks 16 and 20.
n	Reactogenicity assessments post-dose (Dose 1: Day 1 through Day 15 and Dose 2: Day 57 through Day 71); subjects will record daily symptoms using a participant diary card for each dose period. Assessments include local signs and symptoms at injection site (pain/tenderness, swelling, redness, and induration) as well as systemic signs and symptoms (fever, headache, fatigue, arthralgia, myalgia, malaise, nausea, vomiting or chills). Additionally, reactogenicity assessments will be conducted by study staff during site visits on Days 1, 4, 8, 15, 57, 60, 64, and 71.
o	Reactogenicity telephone call at Week 6 (Day 43) to assess systemic signs and symptoms of reactogenicity (fever, chills, headache, fatigue, malaise, nausea, vomiting, myalgias, arthralgias). Subjects reporting systemic signs and symptoms during the reactogenicity telephone call will come into clinic for an unscheduled visit to assess AEs, complete a full physical examination with vitals, and clinical labs for safety evaluations, including blood, urine, and saliva samples for viral detection assays.

FIG. 2E

KEY (continued)

p	In-clinic visits for subjects who opt-in to long term immunogenicity follow-up and maintain eligibility for continued participation dependent on demonstration of a detectable immune response to the HIV Gag protein encoded in Vector 1.
q	If viral vector shedding is noted at the unblinding of Week 36, participants will continue to be monitored every 4 weeks (+/- 1 week) until 2 consecutive negative viral detection assays are documented. If a decreasing trend is observed but never reaches the lower limit of detection, monitoring should continue until results demonstrate that a plateau has been reached in at least 2 consecutive sampling timepoints (4 weeks +/- 1 week apart) at which time discontinuation of shedding assessments may be considered with Sponsor approval.
r	Following the Week 36 visit of the last subject in a cohort, sponsor, investigator, and subject will be unblinded to study treatment. A phone call or study visit will be conducted to unblind subjects and discuss any follow-up assessments that may be needed to continue to assess vector shedding and/or confirm VISP. Any ongoing study restrictions resulting from vector shedding and/or resources for VISP will be reviewed at this time. Subjects demonstrating a detectable immune response to the Gag protein encoded in Vector 1 will also meet eligibility for continued LTFU monitoring.
s	Optional testing in female participants to confirm postmenopausal status.
t	During the LTFU portion of the study, AEs associated with study procedures, additional SAEs that occur, and NOCD along with any associated new medications should be captured. Use of concomitant medications that are prohibited through Week 36 should also be recorded.
u	Serum sample will be collected at Week 36 for a comprehensive assessment of VISP using multiple commercial testing modalities as outlined in the VISP Monitoring Plan.

FIG. 2F

<u>Hematology</u> Complete blood cell count (white blood cells, red blood cells, hemoglobin, hematocrit, platelets) with differential (lymphocyte (including atypical), monocyte, segmented neutrophils, eosinophils, basophils)
<u>Chemistry</u> Serum creatinine
<u>Liver Function Tests</u> Aspartate aminotransferase (AST) Alanine aminotransferase (ALT) Alkaline phosphatase Gamma-glutamyl transpeptidase (GGT) Bilirubin (direct and total)
<u>Urinalysis (Screening only)</u> Bilirubin Glucose Ketones Leukocytes Nitrite Microscopy (if clinically indicated) pH (dipstick) Drugs of abuse (cocaine, methadone, opiates, benzodiazepines, barbiturates, amphetamine) Proteins Red blood cells (RBCs) Specific gravity Urobilinogen Visual inspection for appearance and color
<u>Immunology</u> Screening only: CMV serology (IgG) HBV (HBsAg) HCV (anti-HCV) with reflex RNA testing if positive HIV (4 th generation antigen/antibody testing) with reflex RNA testing if positive

FIG. 3

Severity	Definition
Grade 1	Mild symptoms causing no or minimal interference with usual social & functional activities with intervention not indicated.
Grade 2	Moderate symptoms causing greater than minimal interference with usual social & functional activities with intervention indicated.
Grade 3	Severe symptoms causing inability to perform usual social & functional activities with intervention or hospitalization indicated
Grade 4	Potentially life-threatening symptoms causing inability to perform basic self-care functions with intervention indicated to prevent permanent impairment, persistent disability, or death.

FIG. 4

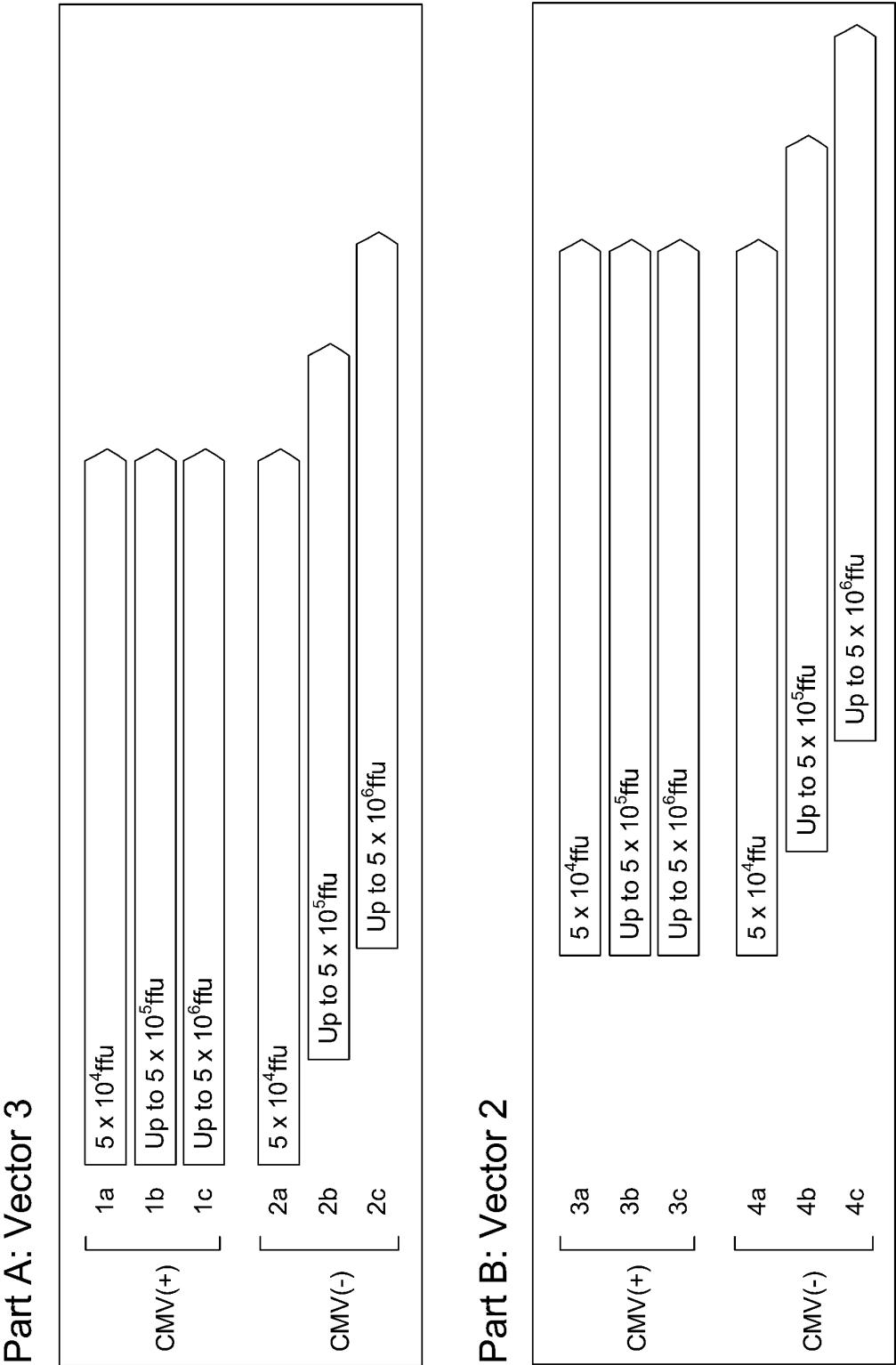


FIG. 5

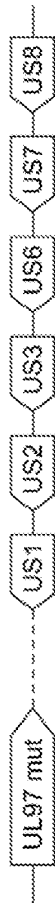


FIG. 6A

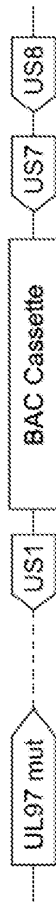


FIG. 6B

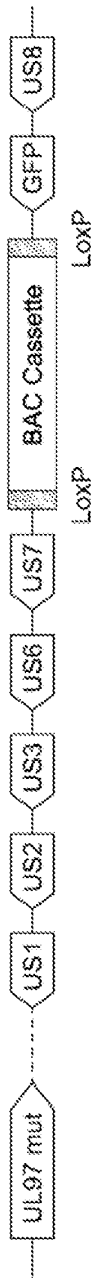


FIG. 6C

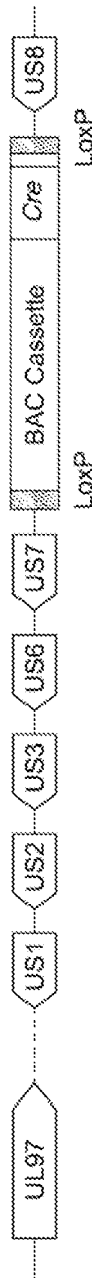


FIG. 6D

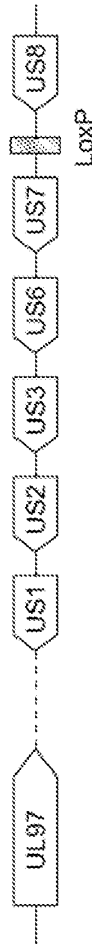
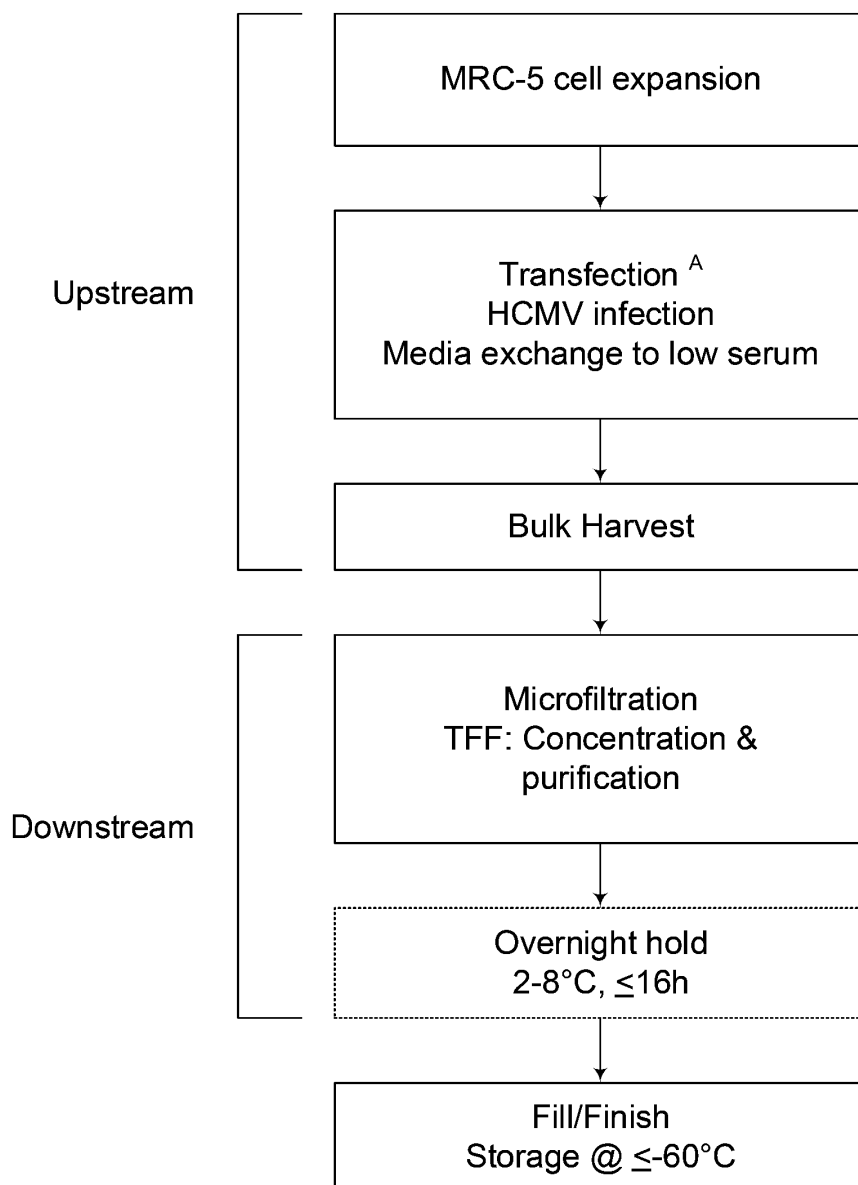


FIG. 6E

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^ATransfection is specific to the Vector 2 process (Vector 3 does not have a transfection step).

FIG. 7

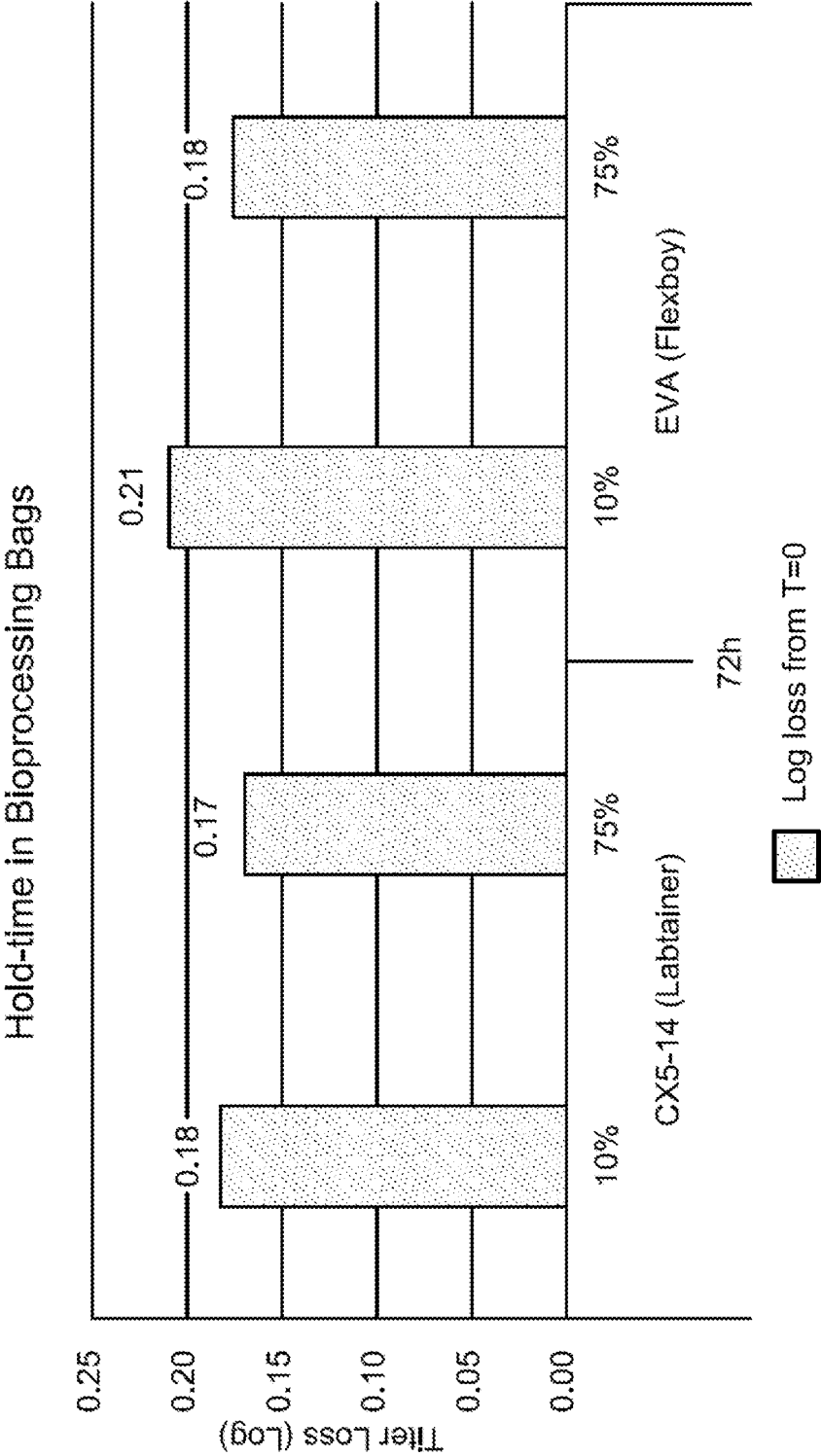


FIG. 8

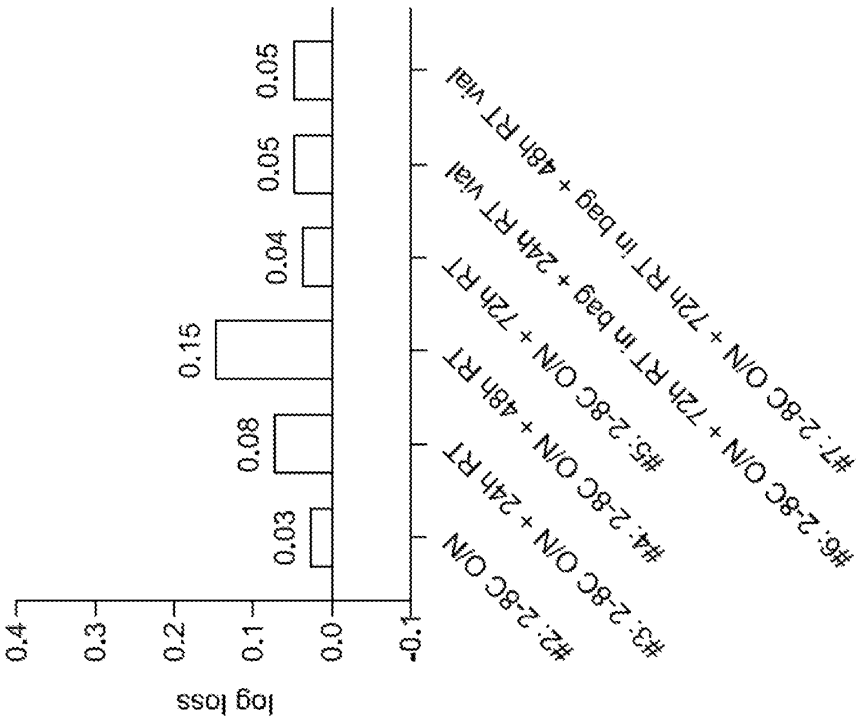


FIG. 9