CLAIMS

We claim:

1. A composition comprising a messenger RNA (mRNA) that encodes a protein or a peptide and is encapsulated within a lipid nanoparticle for use in the treatment of a disease in a subject in need thereof, wherein the composition is to be administered to the subject by mucosal delivery and wherein the composition administered results in expression of the protein or peptide encoded by the mRNA that is detectable in the subject at least about 24 hours, about 48 hours, about 72 hours, or about 96 hours after administration.

2. The composition for use according to claim 1, wherein the mucosal delivery is
    a. rectal,
    b. vaginal,
    c. ocular,
    d. oral, optionally wherein the oral delivery is buccal or sublingual, or
    e. gastrointestinal;
    optionally wherein the mucosal delivery is the rectal delivery.

3. The composition for use according to claim 1 or 2, wherein the protein or peptide is expressed in the subject's circulation, liver, kidney, colon and/or rectum.

4. The composition for use according to any one of claims 1-3, wherein the lipid nanoparticle comprises:
    a. one or more cationic lipids, one or more non-cationic lipids and one or more PEG- modified lipids and/ or
    b. cholesterol.

5. The composition for use according to any one of claims 1-4, wherein the rectal delivery is by suppository, enema, catheter or a bulb syringe.

6. The composition for use according to claim 5, wherein the rectal delivery is by suppository, wherein the composition does not comprise a lipid-based suppository

component, optionally wherein the lipid-based suppository component is cocoa butter, theobroma oil, synthetic fats or synthetic bases.

7. The composition for use according to any one of claims 1-6, wherein the composition comprises a permeability enhancer, optionally wherein the permeability enhancer
    a. is selected from:
        i. bile salts,
        ii. surfactants,
        iii. fatty acids and derivatives, optionally selected from sorbitan laurate, sodium caprate, sucrose, palitate, lauroyl choline, sodium myristate, or palmitoyl carnitine,
        iv. glycerides,
        v. chelators,
        vi. salicylates, or
        vii. polymers; or
    b. is a form of caprate, optionally wherein the caprate-based permeability enhancer is sodium caprate; or
    c. is Labrasol®.

8. The composition for use according to any one of claims 1-7, wherein the composition comprises a water-based suppository component, optionally wherein the water-based suppository component is selected from glycerin, gelatin or polyethylene glycol (PEG), or combinations thereof, optionally wherein the only water-based suppository component is gelatin, optionally wherein the composition comprises about 5% or more gelatin in water, 10% or more gelatin in water, 20% or more gelatin in water, 30% or more gelatin in water, or 50% or more gelatin in water.

9. The composition for use according to any one of claims 1-8, wherein the composition comprises 0.25 mg/mL or greater mRNA, 0.5 mg/mL or greater mRNA, 0.75 mg/mL or greater mRNA, or 1 mg/mL or greater mRNA;
optionally wherein the composition comprises 0.5 mg or greater mRNA, 0.75 mg or greater mRNA, 1 mg or greater mRNA, 1.25 mg or greater mRNA, 1.5 mg or greater mRNA, or 1.75 mg or greater mRNA.

10. The composition for use according to any one of claims 1-9, wherein the composition is formulated for a suppository of about 3 grams, about 2 grams, or about 1 gram, and/or having a volume of about 2.0 mL, about 3.5 mL, about 7.5 mL, or about 10.0 mL.

11. The composition for use according to any one of claims 1-10, wherein the suppository is refrigerated prior to administration.

12. The composition for use according to any one of claims 1-11, wherein the subject is first to be administered a permeability enhancer prior to the administration of the composition comprising mRNA, optionally wherein the permeability enhancer is to be administered to the subject about 30 minutes, about 1 hour, about 2.5 hours, about 5 hours, or about 12 hours prior to the administration of the composition comprising mRNA, optionally wherein the permeability enhancer is to be administered about 30 minutes prior to the administration of the composition comprising mRNA.

13. A suppository for rectal administration of mRNA, the suppository comprising:
    a. mRNA encapsulated within a lipid nanoparticle, wherein the mRNA encodes a protein or peptide; and
    b. gelatin.

14. The suppository of claim 13, comprising about 5% or more gelatin in water, 10% or more gelatin in water, 20% or more gelatin in water, 30% or more gelatin in water, or 50% or more gelatin in water.

15. The suppository of claim 13 or 14, wherein the suppository does not comprise a lipid-based suppository component, optionally wherein the lipid-based suppository component is cocoa butter, theobroma oil, synthetic fats or synthetic bases.

16. The suppository of any one of claims 13-15, further comprising a permeability enhancer, glycerin and/or PEG, optionally wherein the permeability enhancer
    a. is selected from
        i. bile salts,
        ii. surfactants,

iii. fatty acids and derivatives, optionally wherein the fatty acids and derivatives are selected from sorbitan laurate, sodium caprate, sucrose, palitate, lauroyl choline, sodium myristate, or palmitoyl carnitine,

iv. glycerides,

v. chelators,

vi. salicylates, or

vii. polymers; or

b. is a form of caprate, optionally wherein the caprate-based permeability enhancer is sodium caprate; or

c. is Labrasol®.

17. The suppository of any one of claims 13-16, wherein the suppository softens or melts at about between 36 and 37°C.