CLAIMS

What is claimed is:

1. A composition for oral administration for forming a polymer *in situ* in a subject, comprising:

a polymer precursor;

an oxygen source; and

a permeation enhancer that enhances permeation of one or more active pharmaceutical ingredients:

optionally further comprising

one or more active pharmaceutical ingredient; and/or

a buffering agent; and/or

one or more additional permeation enhancers.

2. The composition of claim 2, wherein the composition comprises

(i) an amount of polymer precursor to (polymer precursor, oxygen source, and permeation enhancer) of 40% to 90%: and/or(ii) an amount of oxygen source to (polymer precursor, oxygen source, and permeation enhancer) of 1% to 15%: and/or

(iii) an amount of permeation enhancer to (polymer precursor, oxygen source, and permeation enhancer) of 0.1% to 60%; and/or

(iv) an amount of polymer precursor to (polymer precursor, oxygen source, permeation enhancer, and active pharmaceutical ingredient(s)) of 40% to 90%;

(v) an amount of oxygen source to (polymer precursor, oxygen source, permeation enhancer, and active pharmaceutical ingredient(s)) of 1% to 15%: and/or

(vi) an amount of permeation enhancer to (polymer precursor, oxygen source, permeation enhancer, and active pharmaceutical ingredient(s)) of 1% to 60%; and/or

(vii) an amount of active pharmaceutical ingredient(s) to (polymer precursor, oxygen source, permeation enhancer, and active pharmaceutical ingredient(s)) of 0.1% to 10%.

3. The composition of claim 1 or claim 2, wherein the active pharmaceutical ingredient is a macromolecule having a molecular weight between about 1 kD and about 160 kD; optionally wherein the macromolecule is a polypeptide or polynucleotide; optionally wherein the

polypeptide has a molecular weight of between about 1 kD and about 10 kD, or wherein the polypeptide comprises between about 8 and about 80 amino acids; optionallywherein the polypeptide comprises insulin, semaglutide, a GLP-1 receptor agonist, tirzepatide, liraglutide, desmopressin, octreotide, an analgesic peptide, difelikefalin, H-20, an antibiotic, cyclosporin, vancomycin, lactase, beta galactosidase, exenatide, teriparatide, nafarelin, buserelin, captopril, daptomycin, an antibody, caplacizumab, ozoralizumab, brolucizumab, ranibizumab, bevacizumab, trastuzumab, rituximab, adalimumab, an enzyme, lipase, a protease, phenylalanine hydroxylase, carbamoylphosphate synthetase I, glucose oxidase, or L-asparaginase.

4. The composition of claim 3, wherein the macromolecule is a polynucleotide, optionally wherein the polynucleotide has a molecular weight of between about 5 kD and about 1500 kD; optionally wherein the polynucleotide is single-stranded, optionally comprising between 10 and 5000 bases, or between 10 and 1000 bases or between 10 and 30 bases; or wherein the polynucleotide is double-stranded, optionally comprising between 5 and 2500 base pairs or between 5 and 500 base pairs or between 5 and 15 base pairs.

5. The composition of claim 4, wherein the polynucleotide comprises an antisense oligonucleotide, mipomersen, patisiran, exondys, an siRNA, or an inflammatory bowel disease (IBD) targeting siRNA.

6. The composition of claim 1, wherein the active pharmaceutical ingredient is a small molecule having a molecular weight of 1 kD or less, and/or wherein the polymer precursor comprises one or both of a monomer and an oligomer precursor to a polymer, and/or wherein the polymer precursor is selected from Table 1 or Table 2, or combinations thereof, optionally wherein the monomer is dopamine, levodopa, norepinephrine, methyldopa, levodopa methyl ester, levodopa ethyl ester, or combinations thereof; and/orwherein the oxygen source is a substrate for an endogenous catalyst, optionally wherein the oxygen source is urea hydrogen peroxide or hydrogen peroxide; and/or
wherein the composition is in an oral dosage form, optionally wherein the oral dosage form is a solution, a gel, a tablet, a powder, or a capsule; or wherein the oral dosage form comprises one or more solutions, gels, tablets, powders, or capsules; or wherein the oral

dosage form is an enteric dosage form; and/or wherein the permeation enhancer is a carnitine, optionally wherein the carnitine is an acyl carnitine and/or wherein the carnitine is selected from the group consisting of lauroylcarnitine, palmitoylcarnitine, and palmitoyl carnitine chloride (PCC); amd/prwherein the carnitine is lauroylcarnitine or palmitoylcarnitine; and/or

wherein the permeation enhancer is a choline, optionally wherein the choline is lysophosphatidyl choline; and/or

wherein the permeation enhancer is an aromatic alcohol, optionally wherein the aromatic alcohol is selected from the group consisting of propyl gallate, butylated hydroxytoluene, and butylated hydroxyanisole, optionally wherein the aromatic alcohol is benzyl alcohol, phenyl alcohol, or phenoxyethanol; and/or

wherein the permeation enhancer is a piperazine derivative, optionally wherein the piperazine derivative is selected from the group consisting of 1-phenylpiperazine, 1-methyl-4-phenylpiperazine, 1-(4-methylphenyl)piperazine, and 1-benzylpiperazine, optionallywherein the piperazine derivative is 1-phenylpiperazine or 1-methyl-4-piperazine; and/or

wherein the permeation enhancer is a mucoadhesive polymer, optionally wherein the mucoadhesive polymer is selected from the group consisting of chitosan, chitosan hydrochloride, trimethylated chitosan chloride, and N,N,N-trimethyl chitosan chloride, optionallywherein the mucoadhesive polymer is trimethylated chitosan chloride; and/or

wherein the permeation enhancer is a cell penetrating peptide, optionally wherein the cell penetrating peptide is selected from the group consisting of transportan and penetratin or wherein the cell penetrating peptide is selected from the group consisting of oligoarginines, polyarginines, oligolysines, polylysines, oligotryptophans, and polytryptophan; and/or

wherein the permeation enhancer is an amino acid, optionally wherein the amino acid is tryptophan; and/or

wherein the permeation enhancer is an ionic liquid, optionally wherein the ionic liquid is selected from the group consisting of choline geranate, nicotinic acid and trigonelline and/or wherein the ionic liquid is choline geranate; and/or

wherein the permeation enhancer is an organic solvent, optionally wherein the solvent is selected from the group consisting of ethanol, 2-propanol, 1-propanol, and 2-methyl-2-propanol and/or wherein the organic solvent is selected from the group consisting of dimethyl sulfoxide, ethyl acetate, and acetone; and/or wherein the permeation enhancer is an anionic surfactant, optionally wherein the anionic surfactant is sodium dodecyl sulphate, or an

alternative pharmaceutically acceptable salt thereof or wherein the anionic surfactant is sodium cholate, or an alternative pharmaceutically acceptable salt thereof; and/or
wherein the permeation enhancer is a chelating agent, optionally wherein the chelating agent is selected from the group consisting of EDTA, EGTA, and DTPA and/or wherein the chelating agent is EDTA; and/or wherein the permeation enhancer is a non-ionic surfactant, optionally wherein the non-ionic surfactant is an ethoxylate or wherein the non-ionic surfactant is an alcohol ethoxylate (C_XE_Y, where X is the alcohol carbon number and Y is the ethylene oxide number) or wherein the non-ionic surfactant is a medium or long chain fatty acid sugar ester, or wherein the non-ionic surfactant is a medium or long chain fatty acid sucrose ester, or wherein the non-ionic surfactant is an ethoxylated fatty acid sugar ester or wherein the non-ionic surfactant is an ethoxylated sorbitan ester, or wherein the non-ionic surfactant is an ethoxylated glyceride, or wherein the non-ionic surfactant is selected from the group consisting of macrogol-8 glyceride, sucrose esters, sucrose laurate, ethoxylates, alkyl maltosides, dodecyl maltoside, short chain polyethylene glycol, Brij® series, polyoxyethylene(10) oleyl ether, polyoxyethylene (23) lauryl ether, polysorbates, polysorbate series PS 20, PS 40, PS 60, PS 65, PS 80, and Triton X-100, or wherein the non-ionic surfactant is caprylocaproyl polyoxyl-8 glyceride (LABRASOL®), poloxamers, polyoxylglycerides, or polyethylene monostearate; and/or
wherein the permeation enhancer is a non-ionic detergent, optionally wherein the non-ionic detergent is sucrose monolaurate or n-tetradecyl β-D-maltopyranoside (TDM) or wherein the non-ionic detergent is sucrose monolaurate; and/or
wherein the non-ionic detergent is n-tetradecyl β-D-maltopyranoside (TDM); and/or
wherein the permeation enhancer is a fatty acid, a fatty acid salt, an ethoxylated fatty acid ester, a sugar fatty acid ester, or an ethoxylated sugar fatty acid ester, optionally the fatty acid salt is sodium caprate (C_{10}), or an alternative pharmaceutically acceptable salt thereof or wherein the fatty acid salt is sodium caprylate (C_8), or an alternative pharmaceutically acceptable salt thereof, or sodium laurate (C_{12}), or alternative pharmaceutically acceptable salt thereof, or wherein the sugar fatty acid ester is a fatty acid ester of a monosaccharide or wherein the sugar fatty acid ester is an ethoxylated fatty acid ester of a monosaccharide, or wherein the sugar fatty acid ester is a fatty acid ester of sorbitan or glucose or wherein the sugar fatty acid ester is an ethoxylated fatty acid ester of sorbitan or glucose, or wherein the sugar fatty acid ester is a fatty acid ester of a disaccharide, or wherein the sugar fatty acid ester is an ethoxylated fatty acid ester of a disaccharide, or wherein the sugar fatty acid ester is a fatty acid ester of sucrose or maltose, or wherein the sugar fatty acid ester is an

ethoxylated fatty acid ester of sucrose or maltose or wherein the fatty acid, ethoxylated fatty acid ester, sugar fatty acid ester, or ethoxylated sugar fatty acid ester is selected from the group consisting of dodecylmaltoside, sodium dodecyl sulfate, nonaethylene glycol monododecyl ether ($C_{12}E_9$), sodium laurate (C_{12}), sodium nonanoate (C_9), sodium undecanoate (C_{11}), sodium undecylenate (C11:1), sodium oleate, linoleic acid, and sucrose monolaurate, and pharmaceutically acceptable salts thereof or alternative pharmaceutically acceptable salts thereof, or wherein the fatty acid, ethoxylated fatty acid ester, sugar fatty acid ester, or ethoxylated sugar fatty acid ester is nonaethylene glycol monododecyl ether ($C_{12}E_9$); and/or

wherein the permeation enhancer is an endogenous secretion, optionally wherein the endogenous secretion is a bile salt, optionally selected from the group consisting of sodium taurodeoxycholate, sodium taurocholate, sodium cholate, sodium deoxycholate, sodium glycodeoxycholate, sodium glycochenodeoxycholate, sodium glycocholiate, sodium chenodeoxycholate, sodium taurochenodeoxycholate, sodium lithocholate, and mixed sodium taurodihydrofusidate, or an alternative pharmaceutically acceptable salt thereof or wherein the bile salt is sodium cholate, or an alternative pharmaceutically acceptable salt thereof; and/or

wherein the permeation enhancer is an N-acylated acid, optionally wherein the N-acylated acid is acetylsalicylic acid, or a pharmaceutically acceptable salt thereof or wherein the N-acylated acid is sodium N-[8-(2-hydroxybenzoyl)amino]caprylate (SNAC), or an alternative pharmaceutically acceptable salt thereof, or the corresponding acid thereof or wherein the N-acylated acid is 8-(N-2-hydroxy-5-chloro-benzoyl)-amino-caprylic acid (5-CNAC), or an alternative pharmaceutically acceptable salt thereof, or the corresponding acid thereof or wherein the N-acylated acid is 4-[(4-chloro-2-hydroxy-benzoyl)amino]butanoic acid (4-CNAB), or an alternative pharmaceutically acceptable salt thereof, or the corresponding acid thereof or wherein the N-acylated acid is N-(10-[2-hydroxybenzoyl]-amino)decanoic acid (SNAD), or an alternative pharmaceutically acceptable salt thereof, or the corresponding acid thereof or wherein the N-acylated acid is monosodium N-(4-chlorosalicyloyl)-4-aminobutyrate (5-CNAB), or an alternative pharmaceutically acceptable salt thereof, or the corresponding acid thereof or wherein the N-acylated acid is N-[8-(2-hydroxy-4-methoxy)benzoyl]amino caprylic acid (4-MOAC), or a pharmaceutically acceptable salt thereof, or wherein the N-acylated acid is sodium N-[8-(2-hydroxybenzoyl)amino]caprylate (SNAC), or an alternative pharmaceutically acceptable salt thereof, or the corresponding acid thereof; and/or

wherein the permeation enhancer is a high molecular weight polymer, optionally wherein the high molecular weight polymer is a polysaccharide or wherein the high molecular weight polymer is an antibacterial toxin, optionally wherein the antibacterial toxin is selected from the group consisting of zonula occludens toxin analogs, viral protein 8 analogs, and clostridium perfringens enterotoxin analogs, or wherein the high molecular weight polymer is chitosan or carboxymethylcellulose; and/or

wherein the permeation enhancer is a caprylocaproyl PEG 8 glyceride; and/or

wherein the permeation enhancer is a sugar-based surfactant, optionally wherein the sugar-based surfactant is dodecyl-β-D-maltopyranoside (DDM); and/or wherein the permeation enhancer is glyceryl monocaprate; and/or

wherein the permeation enhancer is urea; and/or

wherein the permeation enhancer is sodium docusate, or an alternative pharmaceutically acceptable salt thereof, or the corresponding acid thereof; and/or

wherein the permeation enhancer is citric acid, or a pharmaceutically acceptable salt thereof.

7. The composition of any one of claims 1-6, wherein the permeation enhancer enhances paracellular transport, or wherein the permeation enhancer enhances transcellular transport or wherein the permeation enhancer enhances paracellular transport and transcellular transport.

8. The composition of any one of claims 1-7 for use in a method of forming a polymer coating in the small intestine of a subject, the method comprising administering to a subject the composition..

9. A composition comprising:

a polymer precursor;

an oxygen source; and

a permeation enhancer that enhances uptake of one or more active pharmaceutical ingredients;

for use in a method of forming a polymer coating in the small intestine of a subject, the method comprising orally administering the composition to the subject, wherein the polymer precursor and the oxygen source contact a catalyst endogenous to the subject and the catalyst polymerizes the polymer precursor.

10. The composition for use of claim 9, further comprising administering an active pharmaceutical ingredient to the subject or wherein the polymer precursor, the oxygen source and the permeation enhancer are administered as a single composition, optionally wherein the polymer precursor, the oxygen source, the permeation enhancer, and the active pharmaceutical ingredient are administered as a single composition.

11. The composition of claim 3, wherein the macromolecule is a polypeptide and wherein the polypeptide comprises semaglutide or tirzepatide.

12. The composition of claim 1 comprising at least two different permeation enhancers selected from the group comprising ammonium salts, carbonate salts, bicarbonate salts, an endogenous secretion, a bile salt, a bile acid, a mixture of a bile salt and a bile acid, a carnitine, an acyl carnitine, a choline, an aromatic alcohol, a piperazine derivative, a mucoadhesive polymer, a cell penetrating peptide, an amino acid, an ionic liquid, an organic solvent, an anionic surfactant, a chelating agent, a non-ionic surfactant, a non-ionic detergent, a fatty acid, a fatty acid salt, an ethoxylated fatty acid ester, a sugar fatty acid ester, an ethoxylated sugar fatty acid ester, an N-acylated acid, a high molecular weight polymer, a sugar-based surfactant, pharmaceutically acceptable salts of any of the foregoing acids or bases, alternative pharmaceutically acceptable salts of any of the foregoing salts, the free acids of any of the foregoing acid salts, and the free bases of any of the foregoing base salts.

13. The composition of claim 1 comprising at least two different permeation enhancers selected from the group consisting of: ammonium carbonate, ammonium sulfate, ammonium citrate, ammonium phosphate, diammonium phosphate, monoammonium phosphate, ammonium bicarbonate, ammonium chloride, ammonium lactate, ammonium acetate, ammonium sulfate, ammonium sulfite, triammonium citrate, ammonium propionate, ammonium sulfamate, sodium carbonate, potassium carbonate, sodium bicarbonate, potassium bicarbonate, cholic acid, glycocholic acid, deoxycholic acid, glychochenodeoxychlic acid, glycodeoxycholic acid, taurodeoxycholic acid, taurocholic acid, bovine bile, chenodeoxycholic acid, taurochenodeoxycholic acid, lithocholic acid, glycolithocholate, glycohyocholate, taurolithocholate, ursodeoxycholic acid, tauroursodeoxycholic acid, glycoursodeoxycholic acid, 12-monoketocholic acid (12-MKC), 7-monoketocholic acid (7-MKC), 7,12-diketocholic acid (7,12-DKC), 3,7,12-triketocholic acid (3,7,12-TKC), 12-monoketodeoxycholic acid (12-MKDC), taurodihydrofusidic acid, 3-

[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS), a salt of cholic acid, a salt of glycocholic acid, a salt of deoxycholic acid, a salt of glychochenodeoxychlic acid, a salt of glycodeoxycholic acid, a salt of taurodeoxycholic acid, a salt of taurocholic acid, a salt of bovine bile, a salt of chenodeoxycholic acid, a salt of taurochenodeoxycholic acid, a salt of lithocholic acid, a salt of glycolithocholate, a salt of glycohyocholate, a salt of taurolithocholate, a salt of ursodeoxycholic acid, a salt of tauroursodeoxycholic acid, a salt of glycoursodeoxycholic acid, a salt of 12-monoketocholic acid, a salt of 7-monoketocholic acid, a salt of 7,12-diketocholic acid, a salt of 3,7,12-triketocholic acid, a salt of 12-monoketodeoxycholic acid, a salt of taurodihydrofusidic acid, a salt of 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate, sodium cholate, sodium glycocholate, sodium deoxycholate, sodium glychochenodeoxychlate, sodium glycodeoxycholate, sodium taurodeoxycholate, sodium taurocholate, a sodium salt of bovine bile, sodium chenodeoxycholate, sodium taurochenodeoxycholate, sodium lithocholate, sodium glycolithocholate, sodium glycohyocholate, sodium taurolithocholate, sodium ursodeoxycholate, sodium tauroursodeoxycholate, sodium glycoursodeoxycholate, sodium 12-monoketocholate, sodium 7-monoketocholate, sodium 7,12-diketocholate, sodium 3,7,12-triketocholate, sodium 12-monoketodeoxycholate, sodium taurodihydrofusidate, sodium 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate, lauroylcarnitine, palmitoylcarnitine, palmitoyl carnitine chloride (PCC), lysophosphatidyl choline, benzyl alcohol, phenyl alcohol, phenoxyethanol, propyl gallate, butylated hydroxytoluene, butylated hydroxyanisole, 1-phenylpiperazine, 1-methyl-4-phenylpiperazine, 1-(4-methylphenyl)piperazine, chitosan, chitosan hydrochloride, trimethylated chitosan chloride, N,N,N-trimethyl chitosan chloride, transportan, penetratin, oligoarginines, polyarginines, oligolysines, polylysines, oligotryptophans, polytryptophans, tryptophan, choline geranate, nicotinic acid, trigonelline, ethanol, 2-propanol, 1-propanol, 2-methyl-2-propanol, dimethyl sulfoxide, ethyl acetate, acetone, sodium cholate, a pharmaceutically acceptable salt of cholic acid, cholic acid, a mixture of cholic acid and a pharmaceutically acceptable salt of cholic acid, sodium dodecyl sulphate, a pharmaceutically acceptable salt of dodecyl hydrogen sulphate, dodecyl hydrogen sulphate, a mixture of dodecyl hydrogen sulphate and sodium dodecyl sulphate, EDTA, EGTA, DTPA, an ethoxylate, an alcohol ethoxylate (C_XE_Y, where X is the alcohol carbon number and Y is the ethylene oxide number), a medium or long chain fatty acid sugar ester, sodium laurate, a medium or long chain fatty acid sucrose ester, an ethoxylated fatty acid sugar ester, an ethoxylated sorbitan ester, an ethoxylated glyceride, macrogol-8 glyceride, sucrose esters, sucrose laurate, alkyl maltosides, dodecyl maltoside,

short chain polyethylene glycol, Brij® series (polyoxyethylene(10) oleyl ether, polyoxyethylene (23) lauryl ether, etc.), polysorbates, polysorbate series PS 20, PS 40, PS 60, PS 65, PS 80, Triton X-100, caprylocaproyl polyoxyl-8 glyceride, poloxamers, polyoxylglycerides, polyethylene monostearate, sucrose monolaurate, n-Tetradecyl β-D-maltopyranoside, sodium caprate, sodium caprylate, nonaethylene glycol monododecyl ether, a fatty acid ester of a monosaccharide, an ethoxylated fatty acid ester of a monosaccharide, a fatty acid ester of sorbitan, a fatty acid ester of glucose, an ethoxylated fatty acid ester of sorbitan, an ethoxylated fatty acid ester of glucose, a fatty acid ester of a disaccharide, an ethoxylated fatty acid ester of a disaccharide, a fatty acid ester of sucrose, a fatty acid ester of maltose, an ethoxylated fatty acid ester of sucrose, an ethoxylated fatty acid ester of maltose, dodecylmaltoside, sodium dodecyl sulfate, nonaethylene glycol monododecyl ether, sodium laurate, sodium nonanoate, sodium undecanoate, sodium undecylenate, sodium oleate, linoleic acid, sucrose monolaurate, acetylsalicylic acid, sodium N-[8-(2-hydroxybenzoyl)amino]caprylate (SNAC), 8-(N-2-hydroxy-5-chloro-benzoyl)-amino-caprylic acid (5-CNAC), 4-[(4-chloro-2-hydroxy-benzoyl)amino]butanoic acid (4-CNAB), N-(10-[2-hydroxybenzoyl]-amino)decanoic acid (SNAD), monosodium N-(4-chlorosalicyloyl)-4-aminobutyrate (5-CNAB), N-[8-(2-hydroxy-4-methoxy)benzoyl]amino caprylic acid (4-MOAC), a polysaccharide, an antibacterial toxin, zonula occludens toxin analogs, viral protein 8 analogs, clostridium perfringens enterotoxin analogs, chitosan, carboxymethylcellulose, a caprylocaproyl PEG 8 glyceride, dodecyl-β-D-maltopyranoside (DDM), glyceryl monocaproate, urea, sodium docusate, citric acid, pharmaceutically acceptable salts of any of the foregoing acids or bases, alternative pharmaceutically acceptable salts of any of the foregoing salts, the free acids of any of the foregoing acid salts, and the free bases of any of the foregoing base salts.

14. The composition of any one of claims 1-7 or the method of any one of claims 8-13, wherein the permeation enhancer is a bile salt.

15. The composition of any one of claims 1-7 or the method of any one of claims 8-13, wherein the permeation enhancer is selected from the group consisting of sodium taurodeoxycholate, sodium taurocholate, sodium cholate, sodium deoxycholate, sodium glycodeoxycholate, sodium glycochenodeoxycholate, sodium glycocholiate, sodium chenodeoxycholate, sodium taurochenodeoxycholate, sodium lithocholate, and mixed sodium

taurodihydrofusidate, the corresponding acids thereof, an alternative pharmaceutically acceptable salt thereof, and a mixture of a salt and an acid thereof.