

Compounds of drugs with an albumin binding moiety

The present application relates to compounds or pharmaceutically acceptable salts thereof, wherein the compounds comprise at least one polymeric moiety, to which at least two drug
5 moieties are covalently and reversibly conjugated, which drug moieties are conjugated to an albumin binding moiety. The application also relates to pharmaceutical composition comprising at least one such compound and their medical uses.

Whereas some classes of therapeutic proteins, including antibodies, have long inherent half-
10 lives, many other molecules, particularly protein or peptide hormones are often susceptible to enzymatic degradation, renal clearance and/or rapid receptor-mediated clearance, which leads to a short plasma elimination half-life. Furthermore, due to the challenges associated with oral delivery, most peptide- or protein-based drugs require parenteral administration, which combined with a short half-life necessitates frequent injections, resulting in discomfort and
15 inconvenience for the patient. This may negatively impact adherence and, ultimately, limit treatment efficacy and outcomes.

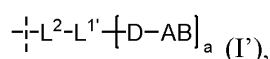
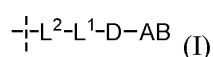
Injecting lipidated peptides has been demonstrated to have slower absorption from the subcutaneous tissue compared to the non-derivatized peptide as well as longer circulatory half-
20 life due to reversible binding to albumin. The half-life of endogenous albumin in the circulation is approximately 3 weeks. This long half-life can be attributed both to its large molecular size, which minimizes renal clearance, as well as to recycling via the neonatal Fc receptor (FcRn). In the circulation, the large molecular size protects the bound peptide from renal clearance and reduces the rate of distribution to the extravascular compartment.

25 The slower absorption is thought to be due to a reduced rate of diffusion in the tissue by a mechanism involving interaction of the fatty acid side chain with cell membranes and/or proteins such as albumin present at the injection site. The rate of diffusion in the tissue following injection and the passage over the capillary wall would expectedly be reduced due
30 to the large molecular size of the albumin-peptide complex. Molecules with a molecular size greater than approximately 16 kDa are preferentially alternatively be absorbed via a lymphatic route compared to direct absorption into blood across the capillary wall.

Thus, slower absorption and reversible albumin binding has enabled extension of dosing intervals for drugs, such as peptide drugs, to up to a week. However, an even further extension of the dosing intervals would be desirable.

- 5 It is an object of the present invention to overcome the shortcomings of current therapies at least partially.

This object is achieved with a compound or a pharmaceutically acceptable salt thereof, wherein the compound comprises at least one polymeric moiety, to which at least two moieties of
10 formula (I) are conjugated and/or to which at least one moiety of formula (I') is conjugated, wherein formula (I) and (I') are



wherein

- 15 each $\text{---} \text{L}^2 \text{---}$ is independently a spacer moiety or is absent;
each $\text{---} \text{L}^1 \text{---}$ is independently a linker moiety that is covalently and reversibly conjugated to $\text{---} \text{D} \text{---}$;
each $\text{---} \text{L}^{1'} \text{---}$ is independently a linker moiety that is covalently and reversibly conjugated to $\text{---} \text{D} \text{---}$;
20 each $\text{---} \text{D} \text{---}$ is independently a drug moiety;
each $\text{---} \text{AB} \text{---}$ is independently an albumin-binding moiety; and
each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

- 25 Applicant discovered that the compounds of the present invention are capable of further extending half-life and dosing frequency. It was surprisingly found that a compound of two or more drugs comprising an albumin binding moiety may coordinate more than one albumin molecule, resulting in a large molecular size of the albumin-drug complex.

- 30 This results in compounds exhibiting a further increased albumin binding and slowed absorption of the macromolecular drug-albumin complex. Such compounds also demonstrate a reduced absorption from the site of administration, such as from subcutaneous tissue,

compared to administration of the corresponding unconjugated drugs. Consequently, such compounds have a prolonged half-life compared to the corresponding unconjugated drugs.

Within the present invention the terms are used having the meaning as follows.

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As used herein, the term “GLP-1 receptor agonist” refers to agonists of the GLP-1 receptor (GLP1R) and optionally in addition agonists of one or more other receptors, such as for example a receptor for gastric inhibitory polypeptide (GIPR), a receptor for glucagon (GCGR), a receptor for amylin, a receptor for peptide YY (PYYR) or a receptor for glucagon-like peptide-2 (GLP2R). An “agonist” of a receptor, such as an agonist of the GLP-1 receptor, is a chemical compound that activates such receptor to produce a biological response. If a GLP-1 receptor agonist is in addition to being a GLP1R agonist also an agonist of one receptor other than GLP1R, such as an agonist of GIPR, GCGR, an amylin receptor, a PYYR or GLP2R, such GLP-1 receptor agonist is also referred to as being a “dual GLP-1 receptor agonist” or short “dual agonist”. Likewise, if a GLP-1 receptor agonist is in addition to being a GLP1R agonist also an agonist of two other receptors, which may be selected from the group consisting of GIPR, GCGR, an amylin receptor, a PYYR or GLP2R, such GLP-1 receptor agonist is also referred to as being a “triple GLP-1 receptor agonist” or short “triple agonist”.

20 As used herein, the term “peptide” as used herein refers to a chain of at least 2 and up to and including 50 amino acid monomer moieties, which may also be referred to as “amino acid residues”, linked by peptide (amide) linkages. The amino acid monomers may be selected from the group consisting of proteinogenic amino acids and non-proteinogenic amino acids and may be D- or L-amino acids. The term “peptide” also includes peptidomimetics, such as peptoids, beta-peptides, cyclic peptides and depsipeptides and covers such peptidomimetic chains with 25 up to and including 50 monomer moieties. The cyclic peptides may be mono-, bi-, tri- or tetracyclic peptides. The term “peptide” also includes lasso peptides.

As used herein, the term “protein” refers to a chain of more than 50 amino acid monomer moieties, which may also be referred to as “amino acid residues”, linked by peptide linkages, in which preferably no more than 12000 amino acid monomers are linked by peptide linkages, such as no more than 10000 amino acid monomer moieties, no more than 8000 amino acid monomer moieties, no more than 5000 amino acid monomer moieties or no more than 2000 amino acid monomer moieties.

As used herein, the term “small molecule drug” refers to drugs that are organic compounds with a molecular weight of less than 1000 Da, such as less than 900 Da or less than 800 Da. It is understood that nucleobase-based drug moieties, such as adenine or guanine analogues, may also be a type of small molecule drugs.

As used herein, the terms “medium molecule drug” or “medium size molecule drug” refer to drugs that are organic compounds which are not peptides and which are not proteins and have a molecular weight ranging from and including 1 kDa to 7.5 kDa.

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As used herein, the term “oligonucleotide” refers to double- or single-stranded RNA and DNA with preferably 2 to 1000 nucleotides and any modifications thereof. Modifications include, for example, those which provide other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the nucleic acid ligand bases or to the nucleic acid ligand as a whole. Such modifications include for example, to 2'-position sugar modifications, 5-position pyrimidine modifications, 8-position purine modifications, modifications at exocyclic amines, substitution of 4-thiouridines, substitution of 5-bromo or 5-iodo-uracil; backbone modifications, methylations, unusual base-pairing combinations such as the isobases isocytidine and isoguanidine. Modifications can also include 3' and 5' modifications such as capping and change of stereochemistry. The term also includes aptamers.

As used herein, the term “peptide nucleic acids” refers to organic polymers having a peptidic backbone, i.e., a backbone in which the monomers are connected to each other through peptide linkages, to which nucleobases such as adenine, cytosine, guanine, thymine and uracil, are attached. In certain embodiments, the peptide backbone comprises N-(2-aminoethyl)-glycine.

As used herein, the term “random coil” relates to any conformation of a polymeric molecule, including proteins, in which the individual monomeric elements that form said polymeric structure are essentially randomly oriented towards the adjacent monomeric elements while still being chemically bound to said adjacent monomeric elements. In particular, a polypeptide or protein having random coil conformation substantially lacks a defined secondary and tertiary structure. The nature of polypeptide random coils and their methods of experimental identification are known to the person skilled in the art. In particular, the lack of secondary and

tertiary structure of a protein may be determined by circular dichroism (CD) measurements. CD spectroscopy represents a light absorption spectroscopy method in which the difference in absorbance of right- and left-circularly polarized light by a substance is measured. The secondary structure of a protein can be determined by CD spectroscopy using far-ultraviolet spectra with a wavelength between approximately 190 and 250 nm. At these wavelengths the different secondary structures commonly found in conformations each give rise to a characteristic shape and magnitude of the CD spectrum. Accordingly, by using CD spectrometry the skilled artisan is readily capable of determining whether an amino acid polymer adopts random coil conformation at physiological conditions.

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When determining whether a peptide or protein adopts random coil conformation under experimental conditions using the methods as described herein, the biophysical parameters such as temperature, pH, osmolarity and protein content may be different to the physiological conditions normally found in vivo. Temperatures between 1 °C and 42 °C or preferably 4 °C to 25 °C may be considered useful to test and/or verify the biophysical properties and biological activity of a peptide or protein under physiological conditions in vitro.

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Several buffers, in particular in experimental settings (for example in the determination of protein structures, in particular in circular dichroism (CD) measurements and other methods that allow the person skilled in the art to determine the structural properties of a protein/polypeptide or peptide stretch) or in buffers, solvents and/or excipients for pharmaceutical compositions, are considered to represent "physiological solutions" or "physiological conditions" in vitro. Examples of such buffers are, e.g. phosphate-buffered saline (PBS: 115 mM NaCl, 4 mM KH_2PO_4 , 16 mM Na_2HPO_4 pH 7.4), Tris buffers, acetate buffers, citrate buffers or similar buffers such as those used in the appended examples. Generally, the pH of a buffer representing physiological conditions should lie in a range from 6.5 to 8.5, preferably in a range from 7.0 to 8.0, most preferably in a range from 7.2 to 7.7 and the osmolarity should lie in a range from 10 to 1000 mmol/kg H_2O , more preferably in a range from 50 to 500 mmol/kg H_2O and most preferably in a range from 200 to 350 mmol/kg H_2O . Optionally, the protein content of a buffer representing physiological conditions may lie in a range from 0 to 100 g/l, neglecting the protein with biological activity itself, whereby typical stabilizing proteins may be used, for example human or bovine serum albumin.

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Other established biophysical methods for determining random coil conformation include nuclear magnetic resonance (NMR) spectroscopy, absorption spectrometry, infrared and Raman spectroscopy, measurement of the hydrodynamic volume via size exclusion chromatography, analytical ultracentrifugation and dynamic/static light scattering as well as
5 measurements of the frictional coefficient or intrinsic viscosity.

As used herein the term “physiological conditions” refers to aqueous buffer at pH 7.4, 37°C.

As used herein the term “pharmaceutical composition” refers to a composition containing one
10 or more active ingredients, such as for example at least one compound of the present invention, and one or more excipients, as well as any product which results, directly or indirectly, from combination, complexation or aggregation of any two or more of the ingredients of the composition, or from dissociation of one or more of the ingredients, or from other types of reactions or interactions of one or more of the ingredients. Accordingly, a pharmaceutical
15 composition of the present invention encompasses any composition made by admixing one or more compound of the present invention and one or more pharmaceutically acceptable excipient.

As used herein, the term "excipient" refers to a diluent, adjuvant, or vehicle with which the
20 therapeutic, such as a drug or prodrug, is administered. Such pharmaceutical excipient may be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, including but not limited to peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is an example for an excipient when the pharmaceutical composition is administered orally. Saline and aqueous dextrose are examples of excipients when the
25 pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are in certain embodiments employed as liquid excipients for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, mannitol, trehalose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol,
30 water, ethanol and the like. The pharmaceutical composition, if desired, can also contain minor amounts of wetting or emulsifying agents, pH buffering agents, like, for example, acetate, succinate, tris, carbonate, phosphate, HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid), MES (2-(*N*-morpholino)ethanesulfonic acid), or can contain detergents, like Tween, poloxamers, poloxamines, CHAPS, Igepal, or amino acids like, for example, glycine, lysine,

or histidine. These pharmaceutical compositions can take the form of solutions, suspensions, emulsions, tablets, pills, capsules, powders, or sustained-release formulations. The pharmaceutical composition may be formulated as a suppository, with traditional binders and excipients such as triglycerides. Oral formulation can include standard excipients such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Such compositions will contain a therapeutically effective amount of the drug or drug moiety, together with a suitable amount of excipient so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

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As used herein the term “liquid composition” refers to a mixture comprising a water-soluble compound and one or more solvents, such as water.

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The term “suspension composition” relates to a mixture comprising at least one water-insoluble compound and one or more solvents, such as water.

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As used herein, the term “dry composition” means that a pharmaceutical composition is provided in a dry form. Suitable methods for drying are spray-drying and lyophilization, i.e., freeze-drying. Such dry composition has a residual water content of a maximum of 10%, such as less than 5% or less than 2%, determined according to Karl Fischer. In certain embodiments such dry pharmaceutical composition is dried by lyophilization.

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The term “drug” as used herein refers to a substance used in the treatment, cure, prevention, or diagnosis of a disease or used to otherwise enhance physical or mental well-being. If a drug is conjugated to another moiety, the moiety of the resulting product that originated from the drug is referred to as “drug moiety”.

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As used herein the term “prodrug” refers to a covalent conjugate in which a drug moiety is reversibly and covalently connected to a specialized protective group through a reversible linker moiety, also referred to as “reversible prodrug linker moiety” or “reversible linker moiety”, which is conjugated through a reversible linkage to the drug moiety and wherein the specialized protective group alters or eliminates undesirable properties in the parent molecule. This also includes the enhancement of desirable properties in the drug and the suppression of undesirable properties. The specialized non-toxic protective group is referred to as “carrier”. A

prodrug releases the reversibly and covalently bound drug moiety in the form of its corresponding drug. In other words, a prodrug is a compound comprising a drug moiety which is covalently and reversibly conjugated to a carrier moiety via a reversible linker moiety, which covalent and reversible conjugation of the carrier to the reversible linker moiety is either
5 directly or through a spacer. Such compound releases the formerly conjugated drug moiety in the form of a free unmodified drug.

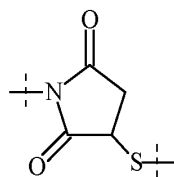
A “reversible linkage” is a linkage that is degradable, i.e., cleavable, in the absence of enzymes under physiological conditions (aqueous buffer at pH 7.4, 37°C) with a half-life ranging from
10 1 hour to three months. A “stable linkage” is a linkage having a half-life under physiological conditions (aqueous buffer at pH 7.4, 37°C) in the absence of enzymes of more than three months.

As used herein, the terms “traceless prodrug linker” or “traceless linker” means a reversible
15 prodrug linker, i.e., a linker moiety reversibly and covalently connecting a drug moiety with a carrier, which upon cleavage releases the drug in its free form. As used herein, the term “free form” of a drug means the drug in its unmodified, pharmacologically active form.

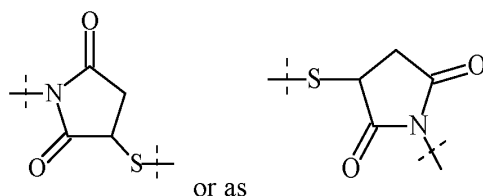
As used herein, the term “reagent” means a chemical compound which comprises at least one
20 functional group for reaction with the functional group of another chemical compound or drug. It is understood that a drug comprising a functional group, such as a primary or secondary amine or hydroxyl functional group, is also a reagent.

As used herein, the term “moiety” means a part of a molecule, which lacks one or more atom(s)
25 compared to the corresponding reagent. If, for example, a reagent of the formula “H-X-H” reacts with another reagent and becomes part of the reaction product, the corresponding moiety of the reaction product has the structure “H-X-” or “-X-”, whereas each “-” indicates attachment to another moiety. Accordingly, a drug moiety is released from a prodrug as a drug.

30 If a chemical structure of a group of atoms is provided, which group of atoms is attached to at least one other moiety, said chemical structure may be attached to the at least one other moiety in either orientation, unless explicitly stated otherwise. For example, a moiety “-C(O)N(R¹)-” may be attached to two moieties either as “-C(O)N(R¹)-” or as “-N(R¹)C(O)-”. Similarly, a moiety



may be attached to two moieties either as



- 5 As used herein, the term “functional group” means a group of atoms which can react with other groups of atoms. Functional groups are for example selected from the group consisting of carboxylic acid, primary or secondary amine, maleimide, thiol, sulfonic acid, carbonate, carbamate, hydroxyl, aldehyde, ketone, hydrazine, isocyanate, isothiocyanate, phosphoric acid, phosphonic acid, haloacetyl, alkyl halide, acryloyl, aryl fluoride, hydroxylamine, disulfide,
- 10 sulfonamides, sulfuric acid, vinyl sulfone, vinyl ketone, diazoalkane, oxirane and aziridine.

As used herein, the term “pharmaceutically acceptable salt(s) thereof” refers to salts that retain the biological effectiveness or properties of the compound and that typically are not biologically or otherwise undesirable. In certain embodiments, the compound is capable of

15 forming acid/or base salts by virtue of the presence of amino and/or carboxylic functional groups or groups similar thereto. Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids, e.g., acetate, aspartate, benzoate, besylate, bromide/hydrobromide, bicarbonate/carbonate, bisulfate/sulfate, camphorsulfonate, chloride/hydrochloride, chlorthephyllinate, citrate, ethanedisulfonate, fumarate, gluceptate,

20 gluconate, glucuronate, hippurate, hydroiodide/iodide, isethionate, lactate, lactobionate, laurylsulfate, malate, maleate, malonate, mandelate, mesylate, methylsulfate, naphthoate, napsylate, nicotinate, nitrate, octadecanoate, oleate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, polygalacturonate, propionate, stearate, succinate, subsalicylate, tartrate, tosylate and trifluoroacetate salts. Inorganic acids from which

25 salts can be derived include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like. Organic acids from which salts can be derived include,

for example, acetic acid, propionic acid, glycolic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, toluenesulfonic acid, sulfosalicylic acid, and the like. Pharmaceutically acceptable base addition salts can be formed with inorganic and organic
5 bases. Inorganic bases from which salts can be derived include, for example, ammonium salts and metals from columns I to XII of the periodic table. In certain embodiments, the salts are derived from sodium, potassium, ammonium, calcium, magnesium, iron, silver, zinc, and copper; particularly suitable salts include ammonium, potassium, sodium, calcium and magnesium salts. Organic bases from which salts can be derived include, for example, primary,
10 secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like. Certain organic amines include isopropylamine, benzathine, choline, diethanolamine, diethylamine, lysine, meglumine, piperazine, or tromethamine. The pharmaceutically acceptable salts can be synthesized from a parent compound, a basic or acidic moiety, by conventional chemical methods.

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The term "pharmaceutically acceptable" means a substance that does not cause harm when administered to a patient and in certain embodiments means approved by a regulatory agency, such as the EMA (Europe) and/or the FDA (US) and/or any other national regulatory agency for use in animals, in particular for use in humans.

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As used herein the terms "about" or "approx." in combination with a numerical value is used to indicate a range ranging from and including the numerical value plus and minus no more than 10% of said numerical value. For example, the phrases "about 200" or "approx. 200" is used to mean a range ranging from and including 200 +/- 10%, i.e. ranging from and including
25 180 to 220. It is understood that a percentage given as "about 20%" or "approx. 20%" does not mean "20% +/- 10%", i.e. ranging from and including 10 to 30%, but "about 20%" or "approx. 20%" means ranging from and including 18 to 22%, i.e. plus and minus 10% of the numerical value which is 20.

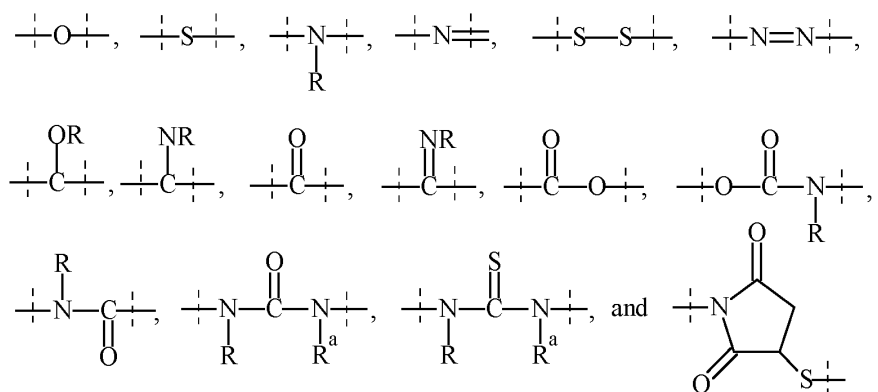
30 As used herein, the term "polymer" means a molecule comprising repeating structural units, i.e., the monomers, connected by chemical bonds in a linear, circular, branched, crosslinked or dendrimeric way or a combination thereof, which may be of synthetic or biological origin or a combination of both. It is understood that a polymer may also comprise one or more other chemical groups and/or moieties, such as, for example, one or more functional groups. In

certain embodiments a soluble polymer has a molecular weight of at least 0.5 kDa, e.g., a molecular weight of at least 1 kDa, a molecular weight of at least 2 kDa, a molecular weight of at least 3 kDa or a molecular weight of at least 5 kDa. If the polymer is soluble, it in certain embodiments has a molecular weight of at most 1000 kDa, such as at most 750 kDa, such as at most 500 kDa, such as at most 300 kDa, such as at most 200 kDa, or such as at most 100 kDa. It is understood that for water-insoluble polymers, such as hydrogels, no meaningful molecular weight ranges can be provided. It is understood that also a peptide or protein is a polymer in which the amino acids are the repeating structural units, even though the side chains of each amino acid may be different.

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As used herein, the term “polymeric” means a reagent or a moiety comprising one or more polymers or polymer moieties. A polymeric reagent or moiety may optionally also comprise one or more other moiety/moieties, which are in certain embodiments selected from the group consisting of:

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- C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, C₂₋₅₀ alkynyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, phenyl, naphthyl, indenyl, indanyl, and tetralinyl; and
 - linkages selected from the group comprising



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wherein

dashed lines indicate attachment to the remainder of the moiety or reagent, and -R and -R^a are independently of each other selected from the group consisting of -H, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl.

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The person skilled in the art understands that the polymerization products obtained from a polymerization reaction do not all have the same molecular weight, but rather exhibit a molecular weight distribution. Consequently, the molecular weight ranges, molecular weights, ranges of numbers of monomers in a polymer and numbers of monomers in a polymer as used
5 herein, refer to the number average molecular weight and number average of monomers, i.e., to the arithmetic mean of the molecular weight of the polymer or polymeric moiety and the arithmetic mean of the number of monomers of the polymer or polymeric moiety.

Accordingly, in a polymeric moiety comprising “x” monomer units any integer given for “x”
10 therefore corresponds to the arithmetic mean number of monomers. Any range of integers given for “x” provides the range of integers in which the arithmetic mean numbers of monomers lie. An integer for “x” given as “about x” means that the arithmetic mean numbers of monomers lie in a range of integers of $x \pm 10\%$, in certain embodiments $x \pm 8\%$, in certain embodiments $x \pm 5\%$ and in certain embodiments $x \pm 2\%$.

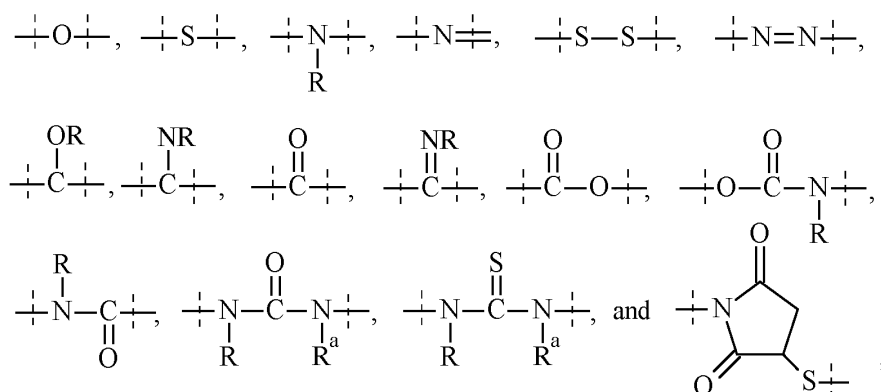
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As used herein, the term “number average molecular weight” means the ordinary arithmetic mean of the molecular weights of the individual polymers.

As used herein the term “water-soluble” with reference to the compound of the present
20 invention means that at least 1 g of the compound may be dissolved in one liter of water at 20°C to form a homogeneous solution. Accordingly, the term “water-insoluble” with reference to the compound means that less than 1 g of the compound may be dissolved in one liter of water at 20°C to form a homogeneous solution.

25 As used herein, the term “PEG-based” in relation to a moiety or reagent means that said moiety or reagent comprises PEG. In certain embodiments a PEG-based moiety or reagent comprises at least 10% (w/w) PEG, such as at least 20% (w/w) PEG, such as at least 30% (w/w) PEG, such as at least 40% (w/w) PEG, such as at least 50% (w/w), such as at least 60 (w/w) PEG, such as at least 70% (w/w) PEG, such as at least 80% (w/w) PEG, such as at least 90% (w/w)
30 PEG, such as at least 95%. The remaining weight percentage of the PEG-based moiety or reagent are other moieties that in certain embodiments are selected from the following moieties and linkages:

- C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, C₂₋₅₀ alkynyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, phenyl, naphthyl, indenyl, indanyl, and tetralinyl; and
- linkages selected from the group comprising



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wherein

dashed lines indicate attachment to the remainder of the moiety or reagent, and

- R and -R^a are independently of each other selected from the group consisting of -H, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl.

The term “substituted” as used herein means that one or more -H atom(s) of a molecule or moiety are replaced by a different atom or a group of atoms, which are referred to as “substituent”.

In certain embodiments the one or more further optional substituents are independently of each other selected from the group consisting of halogen, -CN, -COOR^{x1}, -OR^{x1}, -C(O)R^{x1}, -C(O)N(R^{x1}R^{x1a}), -S(O)₂N(R^{x1}R^{x1a}), -S(O)N(R^{x1}R^{x1a}), -S(O)₂R^{x1}, -S(O)R^{x1}, -N(R^{x1})S(O)₂N(R^{x1a}R^{x1b}), -SR^{x1}, -N(R^{x1}R^{x1a}), -NO₂, -OC(O)R^{x1}, -N(R^{x1})C(O)R^{x1a}, -N(R^{x1})S(O)₂R^{x1a}, -N(R^{x1})S(O)R^{x1a}, -N(R^{x1})C(O)OR^{x1a}, -N(R^{x1})C(O)N(R^{x1a}R^{x1b}), -OC(O)N(R^{x1}R^{x1a}), -T⁰, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T⁰, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{x2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T⁰-, -C(O)O-, -O-,

- C(O)-, -C(O)N(R^{x3})-, -S(O)₂N(R^{x3})-, -S(O)N(R^{x3})-, -S(O)₂-, -S(O)-, -N(R^{x3})S(O)₂N(R^{x3a})-, -S-, -N(R^{x3})-, -OC(OR^{x3})(R^{x3a})-, -N(R^{x3})C(O)N(R^{x3a})-, and -OC(O)N(R^{x3})-;
- R^{x1}, -R^{x1a}, -R^{x1b} are independently of each other selected from the group consisting of -H, -T⁰, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T⁰, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{x2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T⁰-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{x3})-, -S(O)₂N(R^{x3})-, -S(O)N(R^{x3})-; -S(O)₂-, -S(O)-, -N(R^{x3})S(O)₂N(R^{x3a})-, -S-, -N(R^{x3})-, -OC(OR^{x3})(R^{x3a})-, -N(R^{x3})C(O)N(R^{x3a})-, and -OC(O)N(R^{x3})-;
- each T⁰ is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, and 8- to 11-membered heterobicycyl; wherein each T⁰ is independently optionally substituted with one or more -R^{x2}, which are the same or different;
- each -R^{x2} is independently selected from the group consisting of halogen, -CN, oxo (=O), -COOR^{x4}, -OR^{x4}, -C(O)R^{x4}, -C(O)N(R^{x4}R^{x4a}), -S(O)₂N(R^{x4}R^{x4a}), -S(O)N(R^{x4}R^{x4a}), -S(O)₂R^{x4}, -S(O)R^{x4}, -N(R^{x4})S(O)₂N(R^{x4a}R^{x4b}), -SR^{x4}, -N(R^{x4}R^{x4a}), -NO₂, -OC(O)R^{x4}, -N(R^{x4})C(O)R^{x4a}, -N(R^{x4})S(O)₂R^{x4a}, -N(R^{x4})S(O)R^{x4a}, -N(R^{x4})C(O)OR^{x4a}, -N(R^{x4})C(O)N(R^{x4a}R^{x4b}), -OC(O)N(R^{x4}R^{x4a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different;
- each -R^{x3}, -R^{x3a}, -R^{x4}, -R^{x4a}, -R^{x4b} is independently selected from the group consisting of -H and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.

- In certain embodiments the one or more further optional substituents are independently of each other selected from the group consisting of halogen, -CN, -COOR^{x1}, -OR^{x1}, -C(O)R^{x1}, -C(O)N(R^{x1}R^{x1a}), -S(O)₂N(R^{x1}R^{x1a}), -S(O)N(R^{x1}R^{x1a}), -S(O)₂R^{x1}, -S(O)R^{x1}, -N(R^{x1})S(O)₂N(R^{x1a}R^{x1b}), -SR^{x1}, -N(R^{x1}R^{x1a}), -NO₂, -OC(O)R^{x1}, -N(R^{x1})C(O)R^{x1a}, -N(R^{x1})S(O)₂R^{x1a}, -N(R^{x1})S(O)R^{x1a}, -N(R^{x1})C(O)OR^{x1a}, -N(R^{x1})C(O)N(R^{x1a}R^{x1b}), -OC(O)N(R^{x1}R^{x1a}), -T⁰, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl; wherein -T⁰, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally substituted with one or more -R^{x2}, which are the same or different and wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T⁰-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{x3})-, -S(O)₂N(R^{x3})-, -S(O)N(R^{x3})-, -S(O)₂-, -S(O)-,

$-\text{N}(\text{R}^{\text{x}3})\text{S}(\text{O})_2\text{N}(\text{R}^{\text{x}3\text{a}})-$, $-\text{S}-$, $-\text{N}(\text{R}^{\text{x}3})-$, $-\text{OC}(\text{OR}^{\text{x}3})(\text{R}^{\text{x}3\text{a}})-$, $-\text{N}(\text{R}^{\text{x}3})\text{C}(\text{O})\text{N}(\text{R}^{\text{x}3\text{a}})-$, and $-\text{OC}(\text{O})\text{N}(\text{R}^{\text{x}3})-$;

each $-\text{R}^{\text{x}1}$, $-\text{R}^{\text{x}1\text{a}}$, $-\text{R}^{\text{x}1\text{b}}$, $-\text{R}^{\text{x}3}$, $-\text{R}^{\text{x}3\text{a}}$ is independently selected from the group consisting of $-\text{H}$, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

- 5 each T^0 is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, and 8- to 11-membered heterobicyclyl; wherein each T^0 is independently optionally substituted with one or more $-\text{R}^{\text{x}2}$, which are the same or different;

- each $-\text{R}^{\text{x}2}$ is independently selected from the group consisting of halogen, $-\text{CN}$, oxo
 10 $(=\text{O})$, $-\text{COOR}^{\text{x}4}$, $-\text{OR}^{\text{x}4}$, $-\text{C}(\text{O})\text{R}^{\text{x}4}$, $-\text{C}(\text{O})\text{N}(\text{R}^{\text{x}4}\text{R}^{\text{x}4\text{a}})$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{\text{x}4}\text{R}^{\text{x}4\text{a}})$, $-\text{S}(\text{O})\text{N}(\text{R}^{\text{x}4}\text{R}^{\text{x}4\text{a}})$, $-\text{S}(\text{O})_2\text{R}^{\text{x}4}$, $-\text{S}(\text{O})\text{R}^{\text{x}4}$, $-\text{N}(\text{R}^{\text{x}4})\text{S}(\text{O})_2\text{N}(\text{R}^{\text{x}4\text{a}}\text{R}^{\text{x}4\text{b}})$, $-\text{SR}^{\text{x}4}$, $-\text{N}(\text{R}^{\text{x}4}\text{R}^{\text{x}4\text{a}})$, $-\text{NO}_2$, $-\text{OC}(\text{O})\text{R}^{\text{x}4}$, $-\text{N}(\text{R}^{\text{x}4})\text{C}(\text{O})\text{R}^{\text{x}4\text{a}}$, $-\text{N}(\text{R}^{\text{x}4})\text{S}(\text{O})_2\text{R}^{\text{x}4\text{a}}$, $-\text{N}(\text{R}^{\text{x}4})\text{S}(\text{O})\text{R}^{\text{x}4\text{a}}$, $-\text{N}(\text{R}^{\text{x}4})\text{C}(\text{O})\text{OR}^{\text{x}4\text{a}}$, $-\text{N}(\text{R}^{\text{x}4})\text{C}(\text{O})\text{N}(\text{R}^{\text{x}4\text{a}}\text{R}^{\text{x}4\text{b}})$, $-\text{OC}(\text{O})\text{N}(\text{R}^{\text{x}4}\text{R}^{\text{x}4\text{a}})$, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

- 15 each $-\text{R}^{\text{x}4}$, $-\text{R}^{\text{x}4\text{a}}$, $-\text{R}^{\text{x}4\text{b}}$ is independently selected from the group consisting of $-\text{H}$, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

- In certain embodiments the one or more further optional substituents are independently of each other selected from the group consisting of halogen, $-\text{CN}$, $-\text{COOR}^{\text{x}1}$, $-\text{OR}^{\text{x}1}$, $-\text{C}(\text{O})\text{R}^{\text{x}1}$,
 20 $-\text{C}(\text{O})\text{N}(\text{R}^{\text{x}1}\text{R}^{\text{x}1\text{a}})$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{\text{x}1}\text{R}^{\text{x}1\text{a}})$, $-\text{S}(\text{O})\text{N}(\text{R}^{\text{x}1}\text{R}^{\text{x}1\text{a}})$, $-\text{S}(\text{O})_2\text{R}^{\text{x}1}$, $-\text{S}(\text{O})\text{R}^{\text{x}1}$, $-\text{N}(\text{R}^{\text{x}1})\text{S}(\text{O})_2\text{N}(\text{R}^{\text{x}1\text{a}}\text{R}^{\text{x}1\text{b}})$, $-\text{SR}^{\text{x}1}$, $-\text{N}(\text{R}^{\text{x}1}\text{R}^{\text{x}1\text{a}})$, $-\text{NO}_2$, $-\text{OC}(\text{O})\text{R}^{\text{x}1}$, $-\text{N}(\text{R}^{\text{x}1})\text{C}(\text{O})\text{R}^{\text{x}1\text{a}}$, $-\text{N}(\text{R}^{\text{x}1})\text{S}(\text{O})_2\text{R}^{\text{x}1\text{a}}$, $-\text{N}(\text{R}^{\text{x}1})\text{S}(\text{O})\text{R}^{\text{x}1\text{a}}$, $-\text{N}(\text{R}^{\text{x}1})\text{C}(\text{O})\text{OR}^{\text{x}1\text{a}}$, $-\text{N}(\text{R}^{\text{x}1})\text{C}(\text{O})\text{N}(\text{R}^{\text{x}1\text{a}}\text{R}^{\text{x}1\text{b}})$, $-\text{OC}(\text{O})\text{N}(\text{R}^{\text{x}1}\text{R}^{\text{x}1\text{a}})$, $-\text{T}^0$, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; wherein $-\text{T}^0$, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more $-\text{R}^{\text{x}2}$, which are the same
 25 or different and wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-\text{T}^0-$, $-\text{C}(\text{O})\text{O}-$, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{N}(\text{R}^{\text{x}3})-$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{\text{x}3})-$, $-\text{S}(\text{O})\text{N}(\text{R}^{\text{x}3})-$, $-\text{S}(\text{O})_2-$, $-\text{S}(\text{O})-$, $-\text{N}(\text{R}^{\text{x}3})\text{S}(\text{O})_2\text{N}(\text{R}^{\text{x}3\text{a}})-$, $-\text{S}-$, $-\text{N}(\text{R}^{\text{x}3})-$, $-\text{OC}(\text{OR}^{\text{x}3})(\text{R}^{\text{x}3\text{a}})-$, $-\text{N}(\text{R}^{\text{x}3})\text{C}(\text{O})\text{N}(\text{R}^{\text{x}3\text{a}})-$, and $-\text{OC}(\text{O})\text{N}(\text{R}^{\text{x}3})-$;

- each $-\text{R}^{\text{x}1}$, $-\text{R}^{\text{x}1\text{a}}$, $-\text{R}^{\text{x}1\text{b}}$, $-\text{R}^{\text{x}2}$, $-\text{R}^{\text{x}3}$, $-\text{R}^{\text{x}3\text{a}}$ is independently selected from the group consisting
 30 of $-\text{H}$, halogen, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

each T^0 is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, and 8- to 11-membered heterobicyclyl; wherein each T^0 is independently optionally substituted with one or more $-\text{R}^{\text{x}2}$, which are the same or different.

In certain embodiments a maximum of 6 -H atoms of an optionally substituted molecule are independently replaced by a substituent, e.g. 5 -H atoms are independently replaced by a substituent, 4 -H atoms are independently replaced by a substituent, 3 -H atoms are independently replaced by a substituent, 2 -H atoms are independently replaced by a substituent, or 1 -H atom is replaced by a substituent.

The term “interrupted” means that a moiety is inserted between two carbon atoms or – if the insertion is at one of the moiety’s ends – between a carbon or heteroatom and a hydrogen atom, in certain embodiments between a carbon and a hydrogen atom.

As used herein, the term “monocyclic or bicyclic aryl” means an aromatic hydrocarbon ring system which may be monocyclic or bicyclic, wherein the monocyclic aryl ring consists of at least 5 ring carbon atoms and may comprise up to 10 ring carbon atoms and wherein the bicyclic aryl ring consists of at least 8 ring carbon atoms and may comprise up to 12 ring carbon atoms. Each hydrogen atom of a monocyclic or bicyclic aryl may be replaced by a substituent as defined below.

As used herein, the term “monocyclic or bicyclic heteroaryl” means a monocyclic aromatic ring system that may comprise 2 to 6 ring carbon atoms and 1 to 3 ring heteroatoms or a bicyclic aromatic ring system that may comprise 3 to 9 ring carbon atoms and 1 to 5 ring heteroatoms, such as nitrogen, oxygen and sulfur. Examples for monocyclic or bicyclic heteroaryl groups include, but are not limited to, benzofuranyl, benzothiophenyl, furanyl, imidazolyl, indolyl, azaindolyl, azabenzimidazolyl, benzoxazolyl, benzthiazolyl, benzthiadiazolyl, benzotriazolyl, tetrazinyl, tetrazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridinyl, pyrimidinyl, pyrrolyl, quinolinyl, quinazolinyl, quinoxalinyl, triazolyl, thiazolyl and thiophenyl. Each hydrogen atom of a monocyclic or bicyclic heteroaryl may be replaced by a substituent as defined below.

As used herein, the term “cleavable triggering moiety (-Tr)” refers to a moiety that may undergo chemical or enzymatic cleavage under physiological conditions (aqueous buffer at pH 7.4, 37°C), wherein upon cleavage of said cleavable triggering moiety a compound will release at least two drug moieties comprising an albumin-binding moiety.

As used herein, the term “C₁₋₄ alkyl” alone or in combination means a straight-chain or branched alkyl moiety having 1 to 4 carbon atoms. If present at the end of a molecule, examples of straight-chain or branched C₁₋₄ alkyl are methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl and tert-butyl. When two moieties of a molecule are linked by the C₁₋₄ alkyl, then
5 examples for such C₁₋₄ alkyl groups are -CH₂-, -CH₂-CH₂-, -CH(CH₃)-, -CH₂-CH₂-CH₂-, -CH(C₂H₅)-, -C(CH₃)₂-. Each hydrogen of a C₁₋₄ alkyl carbon may optionally be replaced by a substituent as defined above. Optionally, a C₁₋₄ alkyl may be interrupted by one or more moieties as defined below.

10 As used herein, the term “nucleophile” refers to a reagent or functional group that forms a bond to its reaction partner, i.e., the electrophile by donating both bonding electrons.

As used herein, the term “C₁₋₆ alkyl” alone or in combination means a straight-chain or branched alkyl moiety having 1 to 6 carbon atoms. If present at the end of a molecule, examples
15 of straight-chain and branched C₁₋₆ alkyl groups are methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl. When two moieties of a molecule are linked by the C₁₋₆ alkyl group, then examples for such C₁₋₆ alkyl groups are -CH₂-, -CH₂-CH₂-, -CH(CH₃)-, -CH₂-CH₂-CH₂-,
20 -CH(C₂H₅)- and -C(CH₃)₂-. Each hydrogen atom of a C₁₋₆ carbon may optionally be replaced by a substituent as defined above. Optionally, a C₁₋₆ alkyl may be interrupted by one or more moieties as defined below.

Accordingly, “C₁₋₁₀ alkyl”, “C₁₋₂₀ alkyl” or “C₁₋₅₀ alkyl” means an alkyl chain having 1 to 10,
25 1 to 20 or 1 to 50 carbon atoms, respectively, wherein each hydrogen atom of the C₁₋₁₀, C₁₋₂₀ or C₁₋₅₀ carbon may optionally be replaced by a substituent as defined above. Optionally, a C₁₋₁₀ or C₁₋₅₀ alkyl may be interrupted by one or more moieties as defined below.

As used herein, the term “C₂₋₆ alkenyl” alone or in combination means a straight-chain or
30 branched hydrocarbon moiety comprising at least one carbon-carbon double bond having 2 to 6 carbon atoms. If present at the end of a molecule, examples are -CH=CH₂, -CH=CH-CH₃, -CH₂-CH=CH₂, -CH=CHCH₂-CH₃ and -CH=CH-CH=CH₂. When two moieties of a molecule are linked by the C₂₋₆ alkenyl group, then an example for such C₂₋₆ alkenyl is -CH=CH-. Each

hydrogen atom of a C₂₋₆ alkenyl moiety may optionally be replaced by a substituent as defined above. Optionally, a C₂₋₆ alkenyl may be interrupted by one or more moieties as defined below.

Accordingly, the term “C₂₋₁₀ alkenyl”, “C₂₋₂₀ alkenyl” or “C₂₋₅₀ alkenyl” alone or in combination means a straight-chain or branched hydrocarbon moiety comprising at least one carbon-carbon double bond having 2 to 10, 2 to 20 or 2 to 50 carbon atoms. Each hydrogen atom of a C₂₋₁₀ alkenyl, C₂₋₂₀ alkenyl or C₂₋₅₀ alkenyl group may optionally be replaced by a substituent as defined above. Optionally, a C₂₋₁₀ alkenyl, C₂₋₂₀ alkenyl or C₂₋₅₀ alkenyl may be interrupted by one or more moieties as defined below.

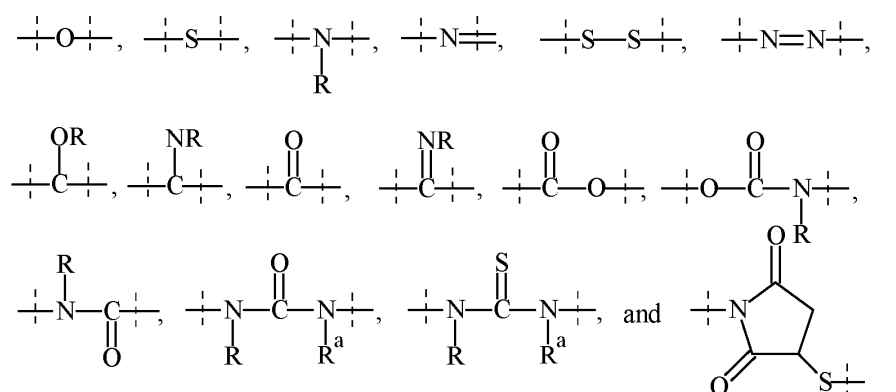
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As used herein, the term “C₂₋₆ alkynyl” alone or in combination means straight-chain or branched hydrocarbon moiety comprising at least one carbon-carbon triple bond having 2 to 6 carbon atoms. If present at the end of a molecule, examples are -C≡CH, -CH₂-C≡CH, CH₂-CH₂-C≡CH and CH₂-C≡C-CH₃. When two moieties of a molecule are linked by the alkynyl group, then an example is -C≡C-. Each hydrogen atom of a C₂₋₆ alkynyl group may optionally be replaced by a substituent as defined above. Optionally, one or more double bond(s) may occur. Optionally, a C₂₋₆ alkynyl may be interrupted by one or more moieties as defined below.

Accordingly, as used herein, the term “C₂₋₁₀ alkynyl”, “C₂₋₂₀ alkynyl” and “C₂₋₅₀ alkynyl” alone or in combination means a straight-chain or branched hydrocarbon moiety comprising at least one carbon-carbon triple bond having 2 to 10, 2 to 20 or 2 to 50 carbon atoms, respectively. Each hydrogen atom of a C₂₋₁₀ alkynyl, C₂₋₂₀ alkynyl or C₂₋₅₀ alkynyl group may optionally be replaced by a substituent as defined above. Optionally, one or more double bond(s) may occur. Optionally, a C₂₋₁₀ alkynyl, C₂₋₂₀ alkynyl or C₂₋₅₀ alkynyl may be interrupted by one or more moieties as defined below.

As mentioned above, a C₁₋₄ alkyl, C₁₋₆ alkyl, C₁₋₁₀ alkyl, C₁₋₂₀ alkyl, C₁₋₅₀ alkyl, C₂₋₆ alkenyl, C₂₋₁₀ alkenyl, C₂₋₂₀ alkenyl, C₂₋₅₀ alkenyl, C₂₋₆ alkynyl, C₂₋₁₀ alkynyl, C₂₋₂₀ alkynyl or C₂₋₅₀ alkynyl may optionally be interrupted by one or more moieties which in certain embodiments are selected from the group consisting of

30



wherein

dashed lines indicate attachment to the remainder of the moiety or reagent; and

- 5 -R and -R^a are independently of each other selected from the group consisting of -H, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl.

As used herein, the term "C₃₋₁₀ cycloalkyl" means a cyclic alkyl chain having 3 to 10 carbon atoms, which may be saturated or unsaturated, e.g. cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, cyclooctyl, cyclononyl or cyclodecyl. Each hydrogen atom of a C₃₋₁₀ cycloalkyl carbon may be replaced by a substituent as defined above. The term "C₃₋₁₀ cycloalkyl" also includes bridged bicycles like norbornane or norbornene.

- 15 The term "8- to 30-membered carbopolycyclyl" or "8- to 30-membered carbopolycycle" means a cyclic moiety of two or more rings with 8 to 30 ring atoms, where two neighboring rings share at least one ring atom and that may contain up to the maximum number of double bonds (aromatic or non-aromatic ring which is fully, partially or un-saturated). In certain embodiments an 8- to 30-membered carbopolycyclyl means a cyclic moiety of two, three, four
20 or five rings, in certain embodiments of two, three or four rings.

As used herein, the term "3- to 10-membered heterocyclyl" or "3- to 10-membered heterocycle" means a ring with 3, 4, 5, 6, 7, 8, 9 or 10 ring atoms that may contain up to the maximum number of double bonds (aromatic or non-aromatic ring which is fully, partially or un-saturated) wherein at least one ring atom up to 4 ring atoms are replaced by a heteroatom selected from the group consisting of sulfur (including -S(O)-, -S(O)₂-), oxygen and nitrogen

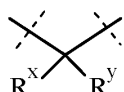
(including =N(O)-) and wherein the ring is linked to the rest of the molecule via a carbon or nitrogen atom. Examples for 3- to 10-membered heterocycles include but are not limited to aziridine, oxirane, thiirane, azirine, oxirene, thiirene, azetidine, oxetane, thietane, furan, thiophene, pyrrole, pyrroline, imidazole, imidazoline, pyrazole, pyrazoline, oxazole, oxazoline, isoxazole, isoxazoline, thiazole, thiazoline, isothiazole, isothiazoline, thiadiazole, thiadiazoline, tetrahydrofuran, tetrahydrothiophene, pyrrolidine, imidazolidine, pyrazolidine, oxazolidine, isoxazolidine, thiazolidine, isothiazolidine, thiadiazolidine, sulfolane, pyran, dihydropyran, tetrahydropyran, imidazolidine, pyridine, pyridazine, pyrazine, pyrimidine, piperazine, piperidine, morpholine, tetrazole, triazole, triazolidine, tetrazolidine, diazepane, azepine and homopiperazine. Each hydrogen atom of a 3- to 10-membered heterocyclyl or 3- to 10-membered heterocyclic group may be replaced by a substituent as defined below.

As used herein, the term "8- to 11-membered heterobicycyl" or "8- to 11-membered heterobicycle" means a heterocyclic moiety of two rings with 8 to 11 ring atoms, where at least one ring atom is shared by both rings and that may contain up to the maximum number of double bonds (aromatic or non-aromatic ring which is fully, partially or un-saturated) wherein at least one ring atom up to 6 ring atoms are replaced by a heteroatom selected from the group consisting of sulfur (including -S(O)-, -S(O)₂-), oxygen and nitrogen (including =N(O)-) and wherein the ring is linked to the rest of the molecule via a carbon or nitrogen atom. Examples for an 8- to 11-membered heterobicycle are indole, indoline, benzofuran, benzothiophene, benzoxazole, benzisoxazole, benzothiazole, benzisothiazole, benzimidazole, benzimidazoline, quinoline, quinazoline, dihydroquinazoline, quinoline, dihydroquinoline, tetrahydroquinoline, decahydroquinoline, isoquinoline, decahydroisoquinoline, tetrahydroisoquinoline, dihydroisoquinoline, benzazepine, purine and pteridine. The term 8- to 11-membered heterobicycle also includes spiro structures of two rings like 1,4-dioxo-8-azaspiro[4.5]decane or bridged heterocycles like 8-aza-bicyclo[3.2.1]octane. Each hydrogen atom of an 8- to 11-membered heterobicycyl or 8- to 11-membered heterobicycle carbon may be replaced by a substituent as defined below.

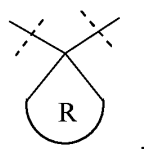
Similarly, the term "8- to 30-membered heteropolycyclyl" or "8- to 30-membered heteropolycycle" means a heterocyclic moiety of more than two rings with 8 to 30 ring atoms, in certain embodiments of three, four or five rings, where two neighboring rings share at least one ring atom and that may contain up to the maximum number of double bonds (aromatic or non-aromatic ring which is fully, partially or unsaturated), wherein at least one ring atom up to

10 ring atoms are replaced by a heteroatom selected from the group of sulfur (including -S(O)- and -S(O)₂-), oxygen and nitrogen (including =N(O)-) and wherein the ring is linked to the rest of a molecule via a carbon or nitrogen atom.

- 5 It is understood that the phrase “the pair R^x/R^y is joined together with the atom to which they are attached to form a C₃₋₁₀ cycloalkyl or a 3- to 10-membered heterocyclyl” in relation with a moiety of the structure



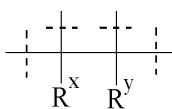
means that R^x and R^y form the following structure:



10

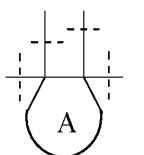
wherein R is C₃₋₁₀ cycloalkyl or 3- to 10-membered heterocyclyl.

It is also understood that the phrase “the pair R^x/R^y is joint together with the atoms to which they are attached to form a ring A” in relation with a moiety of the structure



15

means that R^x and R^y form the following structure:



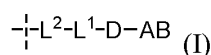
- 20 As used herein, "halogen" means fluoro, chloro, bromo or iodo. In certain embodiments halogen is fluoro or chloro.

In general, the term “comprise” or “comprising” also encompasses “consist of” or “consisting of”.

The compounds of the present invention release a compound H-D-AB upon cleavage of the linkage between -L¹- and -D-, wherein H- is hydrogen. If a compound of the present invention for example comprises semaglutide in bound form, such as conjugated to -L¹- or -L^{1'}-, the semaglutide moiety -D-AB may for simplification be referred to herein as semaglutide, even
 5 though it strictly speaking would be a “semaglutide moiety”.

The compounds release the corresponding free drug of the moiety -D-AB, which is H-D-AB, wherein H- is hydrogen.

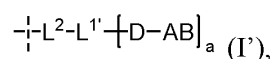
10 In certain embodiments the compound comprises at least one polymeric moiety, to which at least two moieties of formula (I) are conjugated, wherein formula (I) is



wherein

each -L²- is independently a spacer moiety or is absent;
 15 each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;
 each -D- is independently a drug moiety;
 each -AB is independently an albumin-binding moiety.

20 In certain embodiments the compound comprises at least one polymeric moiety, to which at least one moiety of formula (I') is conjugated, wherein formula (I') is



wherein

each -L²- is independently a spacer moiety or is absent;
 25 each -L^{1'}- is independently a linker moiety that is covalently and reversibly conjugated to -D-;
 each -D- is independently a drug moiety;
 each -AB is independently an albumin-binding moiety; and
 each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6,
 30 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

In certain embodiments the compound comprises two moieties of formula (I). In certain embodiments the compound comprises three moieties of formula (I). In certain embodiments

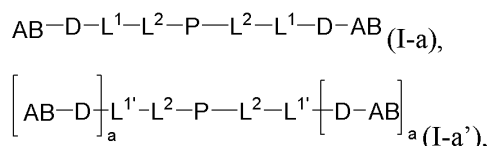
the compound comprises four moieties of formula (I). In certain embodiments the compound comprises five moieties of formula (I). In certain embodiments the compound comprises six moieties of formula (I). In certain embodiments the compound comprises seven moieties of formula (I). In certain embodiments the compound comprises eight moieties of formula (I).

5

In certain embodiments the at least one polymeric moiety of the compounds of the present invention is a linear polymeric moiety -P-.

10 In certain embodiments a moiety of formula (I) or (I') is conjugated to each of the two ends of such linear moiety -P-.

In certain embodiments the compound is of formula (I-a) or (I-a')



15

wherein

each -L²- is independently a spacer moiety or is absent;

each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

20

each -L^{1'}- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -D- is independently a drug moiety;

each -AB is independently an albumin-binding moiety;

-P- is a polymeric moiety; and

25

each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

In certain embodiments the compound is of formula (I-a). In certain embodiments the compound is of formula (I-a').

30 It is understood that a moiety -L^{1'}- is conjugated to more than one moiety -D- and that all linkages between -L^{1'}- and a moiety -D- are covalent and reversible.

In certain embodiments both a of formula (I-a') are the same integer. In certain embodiments both a of formula (I-a') are 2. In certain embodiments both a of formula (I-a') are 3. In certain embodiments both a of formula (I-a') are 4. In certain embodiments both a of formula (I-a') are 5. In certain embodiments both a of formula (I-a') are 6. In certain embodiments both a of formula (I-a') are 7. In certain embodiments both a of formula (I-a') are 8. In certain embodiments both a of formula (I-a') are 9. In certain embodiments both a of formula (I-a') are 10. In certain embodiments both a of formula (I-a') are 11. In certain embodiments both a of formula (I-a') are 12. In certain embodiments both a of formula (I-a') are 13. In certain embodiments both a of formula (I-a') are 14. In certain embodiments both a of formula (I-a') are 15. In certain embodiments both a of formula (I-a') are 16.

Optionally, further moieties of formula (I) or (I') are conjugated to -P- of formula (I-a) or (I-a').

In certain embodiments no further moieties of formula (I) or (I') are conjugated to -P- of formula (I-a) or (I-a').

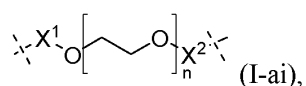
A moiety -P- of formula (I-a) or (I-a') comprises one or more polymer, such as a polymer selected from the group consisting of poly(2-methacryloyl-oxyethyl phosphoyl choline)s, poly(acrylic acids), poly(acrylates), poly(acrylamides), poly(alkoxy) polymers, poly(amides), poly(amidoamines), poly(amino acids), poly(anhydrides), poly(aspartamides), poly(hydroxybutyrate), poly(glycolic acids), poly(butylene terephthalates), poly(caprolactones), poly(carbonates), poly(cyanoacrylates), poly(dimethylacrylamides), poly(esters), poly(ethylenes), poly(ethyleneglycols), poly(ethylene oxides), poly(ethylene phosphates), poly(ethyloxazolines), poly(glycolic acids), poly(hydroxyethyl acrylates), poly(hydroxyethyl-oxazolines), poly(2-hydroxyethyl methacrylates), poly(N-(2-hydroxypropyl)methacrylamides), poly(hydroxypropyl methacrylates), poly(hydroxypropyloxazolines), poly(iminocarbonates), poly(lactic acids), poly(lactic-co-glycolic acids), poly(methacrylamides), poly(methacrylates), poly(methyloxazolines), poly(organophosphazenes), poly(ortho esters), poly(oxazolines), poly(propylene glycols), poly(siloxanes), poly(urethanes), poly(vinyl alcohols), poly(vinyl amines), poly(vinylmethylethers), poly(vinylpyrrolidones), celluloses, carboxymethyl celluloses, hydroxypropyl methylcelluloses, chitins, chitosans, dextrans, dextrins, gelatins, hyaluronic acids and derivatives, functionalized hyaluronic acids, mannans, pectins,

rhamnogalacturonans, starches, hydroxyalkyl starches, hydroxyethyl starches and other carbohydrate-based polymers, xylans, and copolymers thereof.

In certain embodiments -P- of formula (I-a) or (I-a') comprises one or more polymer selected from the group consisting of 2-methacryloyl-oxyethyl phosphoyl cholins, poly(acrylic acids), poly(acrylates), poly(acrylamides), poly(alkyloxy) polymers, poly(amides), poly(amidoamines), poly(amino acids), poly(anhydrides), poly(aspartamides), poly(butyric acids), poly(glycolic acids), polybutylene terephthalates, poly(caprolactones), poly(carbonates), poly(cyanoacrylates), poly(dimethylacrylamides), poly(esters), poly(ethylenes), poly(ethyleneglycols), poly(ethylene oxides), poly(ethyl phosphates), poly(ethyloxazolines), poly(glycolic acids), poly(hydroxyethyl acrylates), poly(hydroxyethyl-oxazolines), poly(hydroxymethacrylates), poly(hydroxypropylmethacrylamides), poly(hydroxypropyl methacrylates), poly(hydroxypropyloxazolines), poly(iminocarbonates), poly(lactic acids), poly(lactic-co-glycolic acids), poly(methacrylamides), poly(methacrylates), poly(methyloxazolines), poly(organophosphazenes), poly(ortho esters), poly(oxazolines), poly(propylene glycols), poly(siloxanes), poly(urethanes), poly(vinyl alcohols), poly(vinyl amines), poly(vinylmethylethers), poly(vinylpyrrolidones), silicones, celluloses, carbomethyl celluloses, hydroxypropyl methylcelluloses, chitins, chitosans, dextrans, dextrans, gelatins, hyaluronic acids and derivatives, functionalized hyaluronic acids, mannans, pectins, rhamnogalacturonans, starches, hydroxyalkyl starches, hydroxyethyl starches and other carbohydrate-based polymers, xylans, and copolymers thereof.

In certain embodiments -P- of formula (Ia) or (I-a') is a PEG-based or hyaluronic acid-based moiety. In certain embodiments -P- of formula (Ia) or (I-a') is a PEG-based moiety. In certain embodiments -P- of formula (Ia) or (I-a') is a hyaluronic acid-based moiety.

In certain embodiments -P- of formula (Ia) or (I-a') is of formula (I-ai)



wherein

dashed lines indicate attachment to -L²-;

n is an integer such that the molecular weight of the PEG moiety ranges from about 1 about 20 kDa;

$-X^1$ - and $-X^2$ - are independently of each other selected from the group consisting of $-T$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{y1})$ -, $-S(O)_2N(R^{y1})$ -, $-S(O)N(R^{y1})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{y1})S(O)_2N(R^{y1a})$ -, $-S$ -, $-N(R^{y1})$ -, $-OC(OR^{y1})(R^{y1a})$ -, $-N(R^{y1})C(O)N(R^{y1a})$ -, $-OC(O)N(R^{y1})$ -, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl;

5 wherein $-T$ -, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{y3})$ -, $-S(O)_2N(R^{y3})$ -, $-S(O)N(R^{y3})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{y3})S(O)_2N(R^{y3a})$ -, $-S$ -, $-N(R^{y3})$ -, $-OC(OR^{y3})(R^{y3a})$ -, $-N(R^{y3})C(O)N(R^{y3a})$ -, and $-OC(O)N(R^{y3})$ -;

10 $-R^{y1}$ and $-R^{y1a}$ are independently of each other selected from the group consisting of $-H$ -, $-T$ -, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T$ -, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different, and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{y4})$ -, $-S(O)_2N(R^{y4})$ -, $-S(O)N(R^{y4})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{y4})S(O)_2N(R^{y4a})$ -, $-S$ -, $-N(R^{y4})$ -, $-OC(OR^{y4})(R^{y4a})$ -, $-N(R^{y4})C(O)N(R^{y4a})$ -, and $-OC(O)N(R^{y4})$ -;

15 each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more $-R^{y2}$, which are the same or different;

20 each $-R^{y2}$ is independently selected from the group consisting of halogen, $-CN$, oxo ($=O$), $-COOR^{y5}$, $-OR^{y5}$, $-C(O)R^{y5}$, $-C(O)N(R^{y5}R^{y5a})$, $-S(O)_2N(R^{y5}R^{y5a})$, $-S(O)N(R^{y5}R^{y5a})$, $-S(O)_2R^{y5}$, $-S(O)R^{y5}$, $-N(R^{y5})S(O)_2N(R^{y5a}R^{y5b})$, $-SR^{y5}$, $-N(R^{y5}R^{y5a})$, $-NO_2$, $-OC(O)R^{y5}$, $-N(R^{y5})C(O)R^{y5a}$, $-N(R^{y5})S(O)_2R^{y5a}$, $-N(R^{y5})S(O)R^{y5a}$, $-N(R^{y5})C(O)OR^{y5a}$, $-N(R^{y5})C(O)N(R^{y5a}R^{y5b})$, $-OC(O)N(R^{y5}R^{y5a})$, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

25 each $-R^{y3}$, $-R^{y3a}$, $-R^{y4}$, $-R^{y4a}$, $-R^{y5}$, $-R^{y5a}$ and $-R^{y5b}$ is independently selected from the group consisting of $-H$, and C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

30

In certain embodiments n of formula (I-ai) ranges from 2 to 22.

- In certain embodiments $-X^1$ - and $-X^2$ - of formula (I-ai) are independently of each other selected from the group consisting of $-T$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{y1})$ -, $-S(O)_2N(R^{y1})$ -, $-S(O)N(R^{y1})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{y1})S(O)_2N(R^{y1a})$ -, $-S$ -, $-N(R^{y1})$ -, $-OC(OR^{y1})(R^{y1a})$ -, $-N(R^{y1})C(O)N(R^{y1a})$ -, $-OC(O)N(R^{y1})$ -, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T$ -, C_{1-20} alkyl, C_{2-20} alkenyl, and C_{2-20} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different and wherein C_{1-20} alkyl, C_{2-20} alkenyl, and C_{2-20} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{y3})$ -, $-S(O)_2N(R^{y3})$ -, $-S(O)N(R^{y3})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{y3})S(O)_2N(R^{y3a})$ -, $-S$ -, $-N(R^{y3})$ -, $-OC(OR^{y3})(R^{y3a})$ -, $-N(R^{y3})C(O)N(R^{y3a})$ -, and $-OC(O)N(R^{y3})$ -;
- $-R^{y1}$ and $-R^{y1a}$ are independently of each other selected from the group consisting of $-H$ -, $-T$ -, C_{1-10} alkyl, C_{2-10} alkenyl, and C_{2-10} alkynyl; wherein $-T$ -, C_{1-10} alkyl, C_{2-10} alkenyl, and C_{2-10} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different, and wherein C_{1-10} alkyl, C_{2-10} alkenyl, and C_{2-10} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{y4})$ -, $-S(O)_2N(R^{y4})$ -, $-S(O)N(R^{y4})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{y4})S(O)_2N(R^{y4a})$ -, $-S$ -, $-N(R^{y4})$ -, $-OC(OR^{y4})(R^{y4a})$ -, $-N(R^{y4})C(O)N(R^{y4a})$ -, and $-OC(O)N(R^{y4})$ -;
- each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more $-R^{y2}$, which are the same or different;
- $-R^{y2}$ is selected from the group consisting of halogen, $-CN$, oxo ($=O$), $-COOR^{y5}$ -, $-OR^{y5}$ -, $-C(O)R^{y5}$ -, $-C(O)N(R^{y5}R^{y5a})$ -, $-S(O)_2N(R^{y5}R^{y5a})$ -, $-S(O)N(R^{y5}R^{y5a})$ -, $-S(O)_2R^{y5}$ -, $-S(O)R^{y5}$ -, $-N(R^{y5})S(O)_2N(R^{y5a}R^{y5b})$ -, $-SR^{y5}$ -, $-N(R^{y5}R^{y5a})$ -, $-NO_2$ -, $-OC(O)R^{y5}$ -, $-N(R^{y5})C(O)R^{y5a}$ -, $-N(R^{y5})S(O)_2R^{y5a}$ -, $-N(R^{y5})S(O)R^{y5a}$ -, $-N(R^{y5})C(O)OR^{y5a}$ -, $-N(R^{y5})C(O)N(R^{y5a}R^{y5b})$ -, $-OC(O)N(R^{y5}R^{y5a})$ -, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different; and
- each $-R^{y3}$ -, $-R^{y3a}$ -, $-R^{y4}$ -, $-R^{y4a}$ -, $-R^{y5}$ -, $-R^{y5a}$ and $-R^{y5b}$ is independently of each other selected from the group consisting of $-H$ -, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

In certain embodiments $-X^1-$ and $-X^2-$ of formula (I-ai) are independently of each other selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{y1})-$, $-S(O)_2N(R^{y1})-$, $-S(O)N(R^{y1})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{y1})S(O)_2N(R^{y1a})-$, $-S-$, $-N(R^{y1})-$, $-OC(OR^{y1})(R^{y1a})-$, $-N(R^{y1})C(O)N(R^{y1a})-$, $-OC(O)N(R^{y1})-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{y3})-$, $-S(O)_2N(R^{y3})-$, $-S(O)N(R^{y3})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{y3})S(O)_2N(R^{y3a})-$, $-S-$, $-N(R^{y3})-$, $-OC(OR^{y3})(R^{y3a})-$, $-N(R^{y3})C(O)N(R^{y3a})-$, and $-OC(O)N(R^{y3})-$;

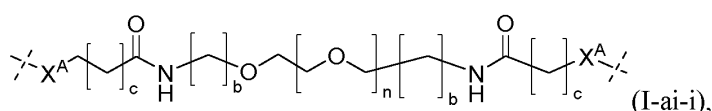
$-R^{y1}$ and $-R^{y1a}$ are independently selected from the group consisting of $-H$, $-T$, C_{1-10} alkyl, C_{2-10} alkenyl, and C_{2-10} alkynyl;

each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl;

each $-R^{y2}$ is independently selected from the group consisting of halogen, and C_{1-6} alkyl; and each $-R^{y3}$, $-R^{y3a}$, $-R^{y4}$, $-R^{y4a}$, $-R^{y5}$, $-R^{y5a}$ and $-R^{y5b}$ is independently of each other selected from the group consisting of $-H$, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

20

In certain embodiments $-P-$ of formula (I-a) or (I-a') is of formula (I-ai-i)

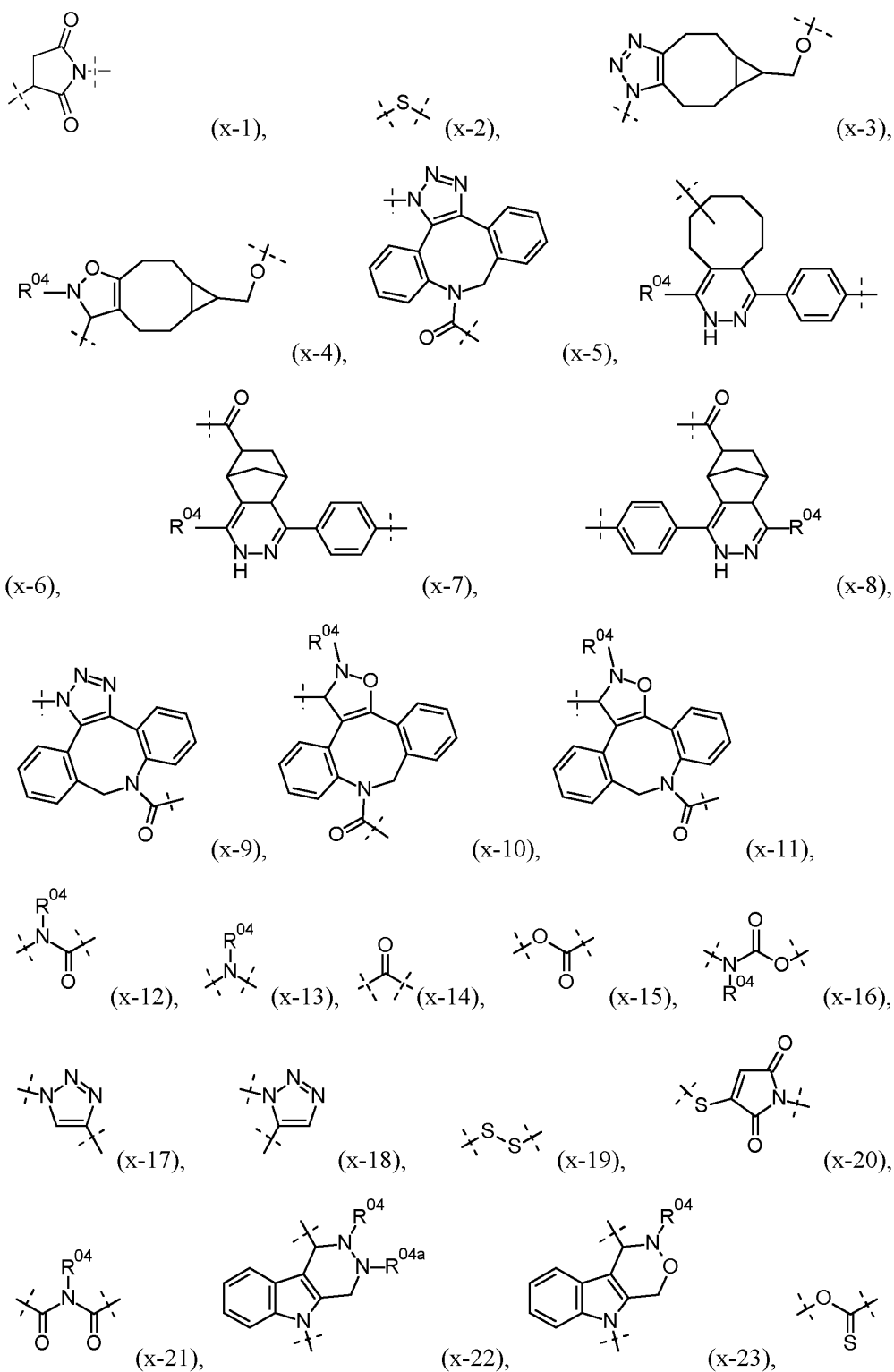


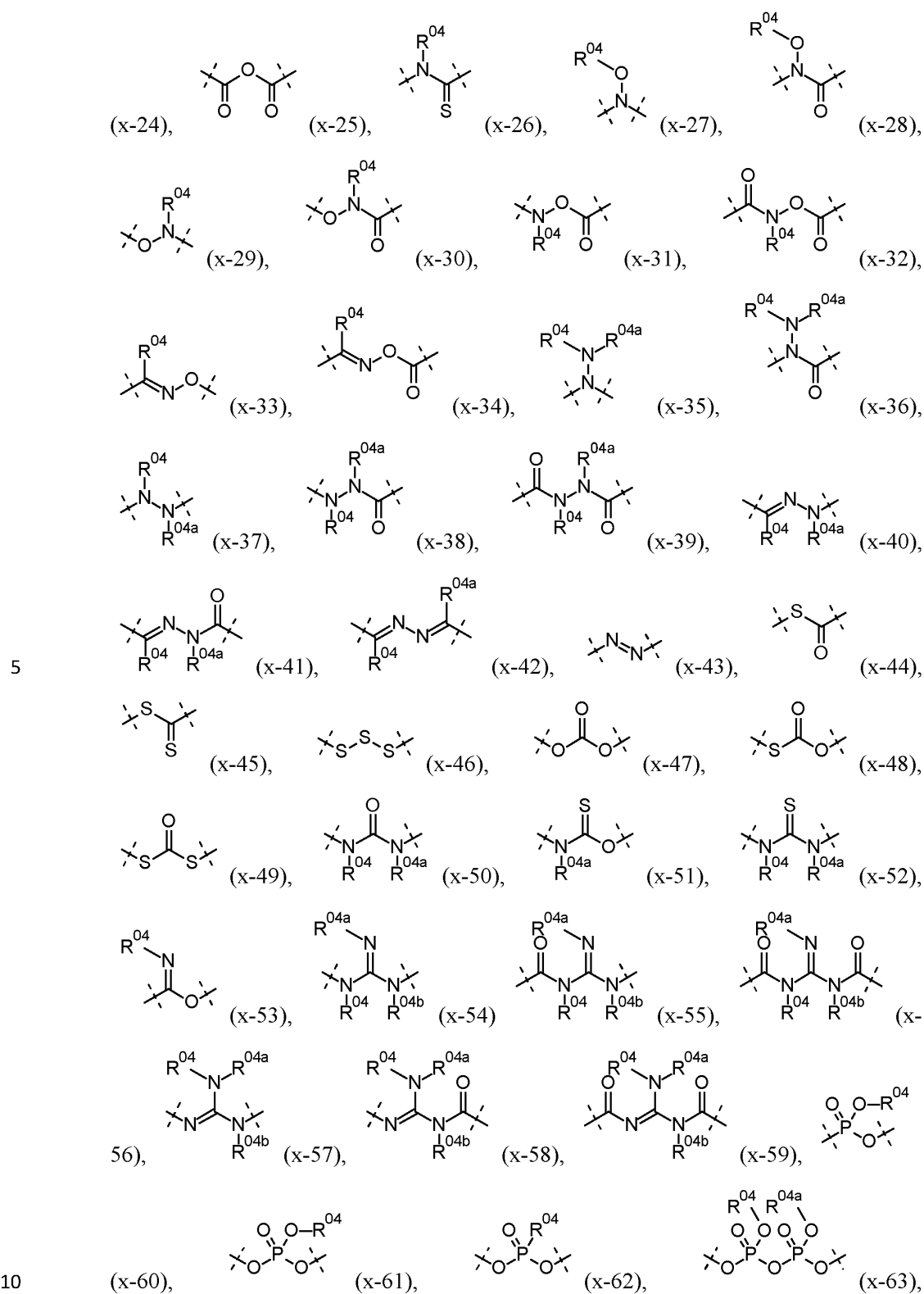
wherein

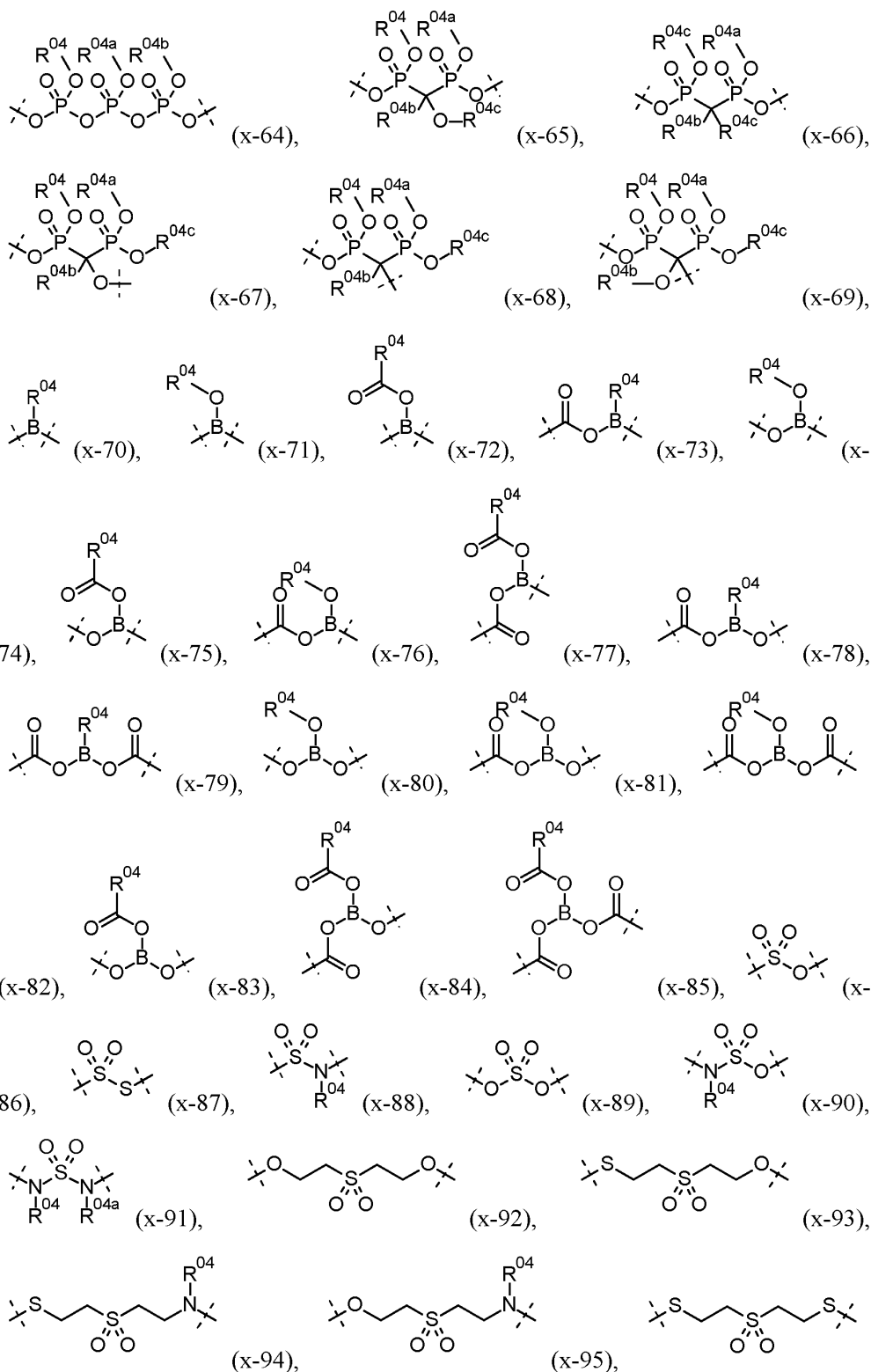
dashed lines indicate attachment to $-L^2-$;

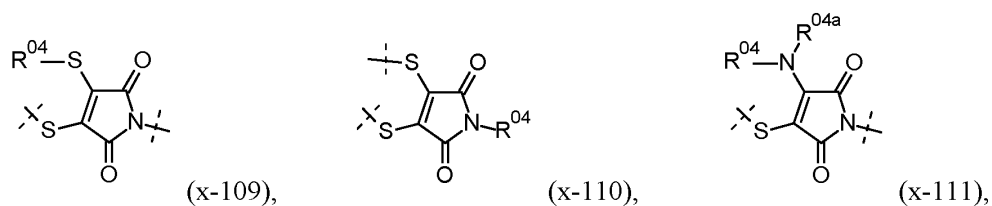
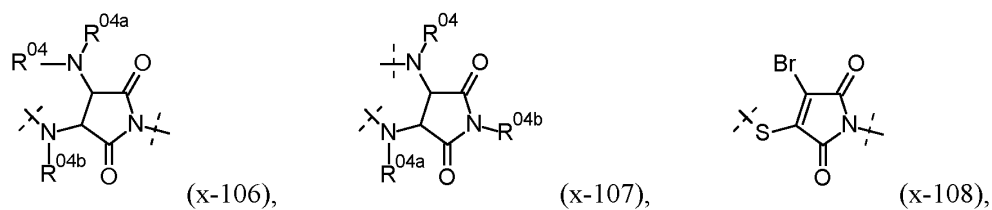
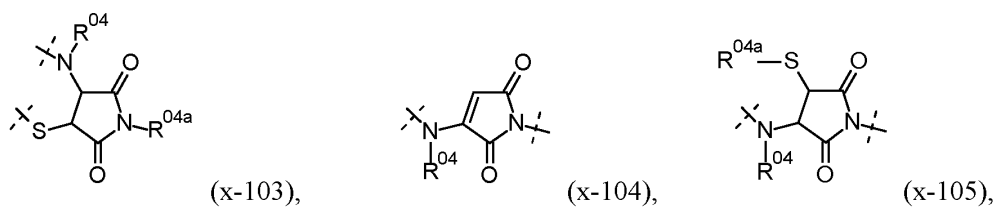
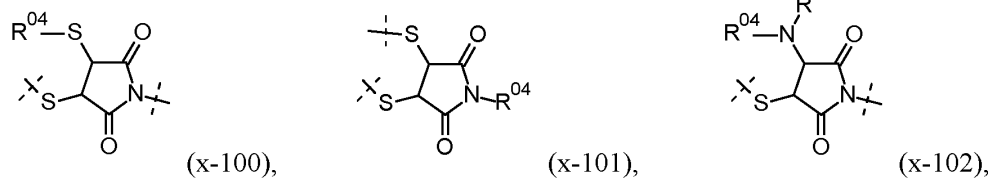
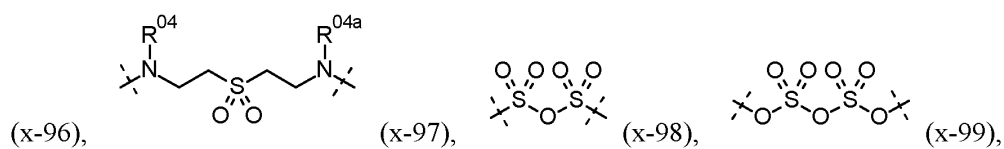
each $-X^A-$ is independently selected from the group consisting of

25

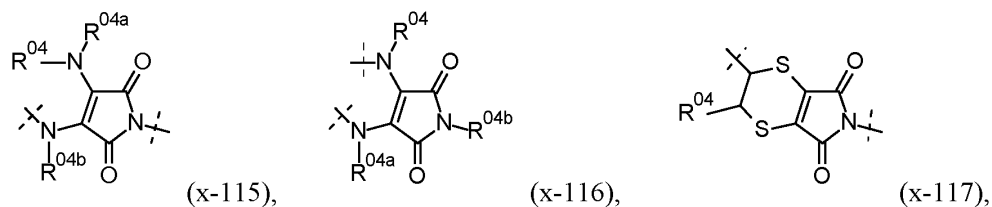
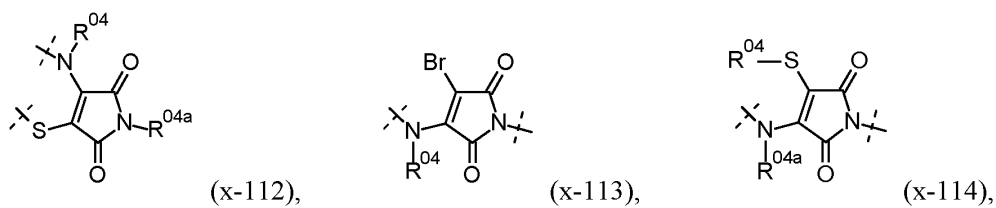


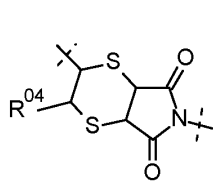




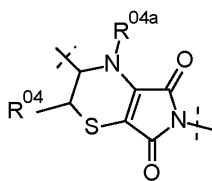


5

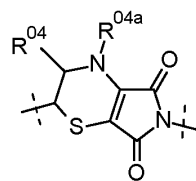




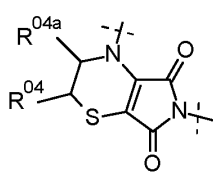
(x-118),



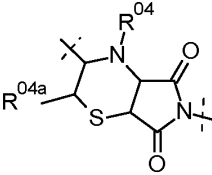
(x-119),



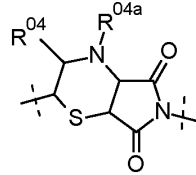
(x-120),



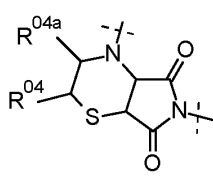
(x-121),



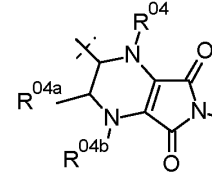
(x-122),



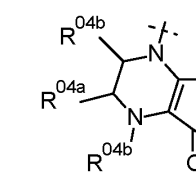
(x-123),



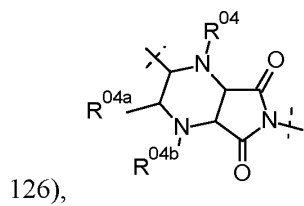
(x-124),



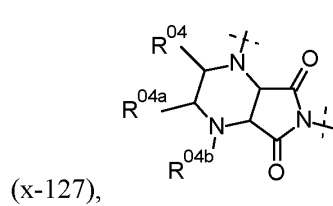
(x-125),



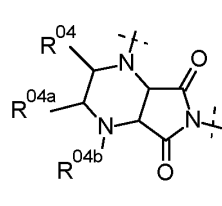
(x-



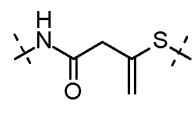
126),



(x-127),

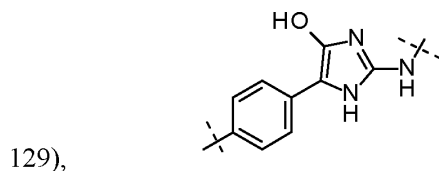


(x-128),



(x-

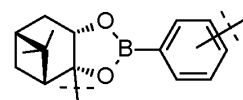
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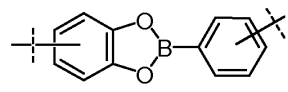
129),



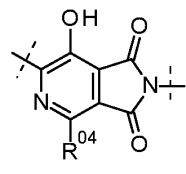
(x-130),



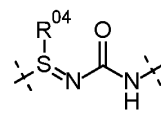
(x-131),



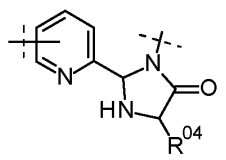
(x-132),



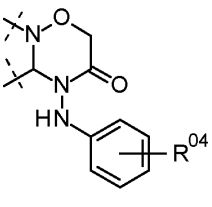
(x-133),



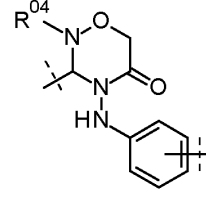
(x-134),



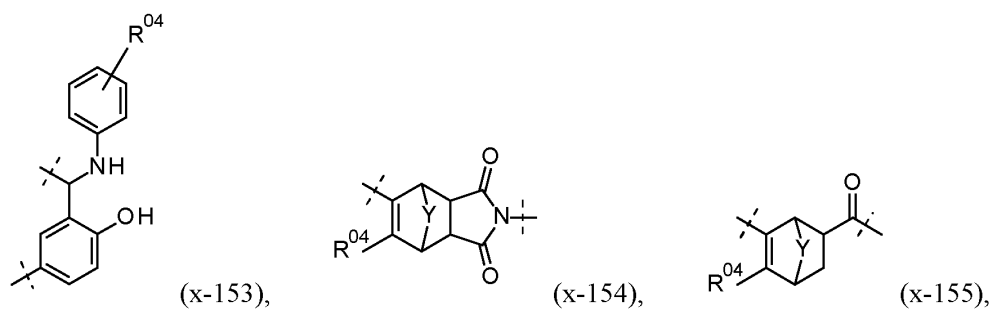
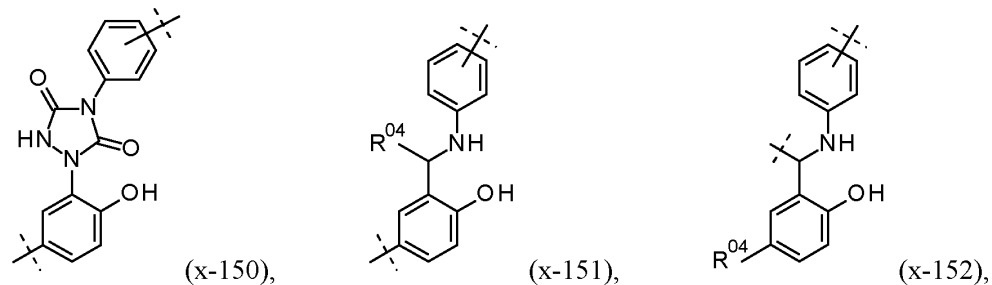
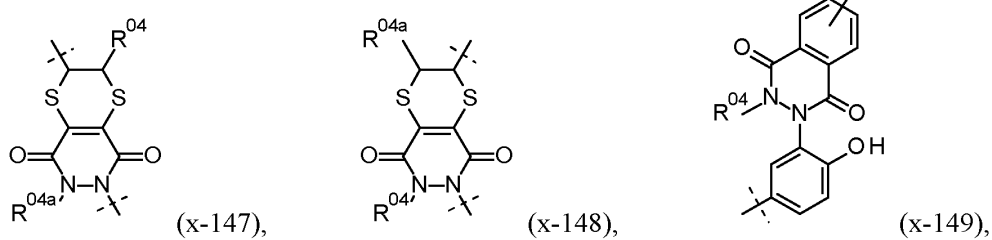
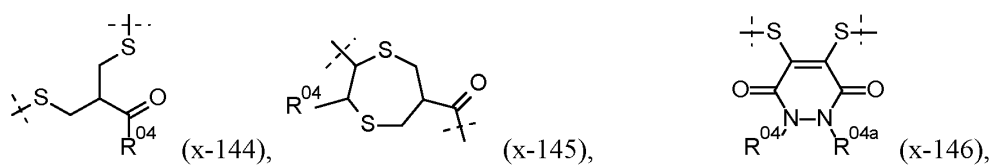
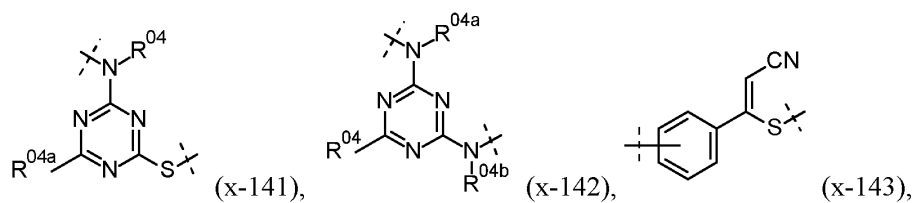
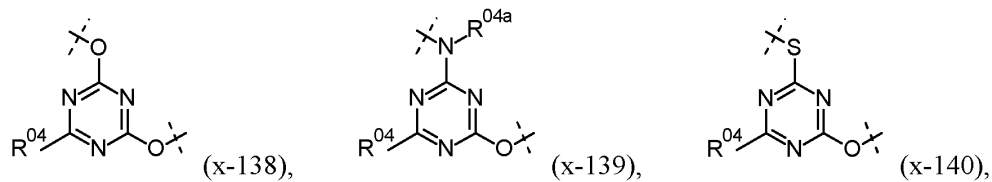
(x-135),

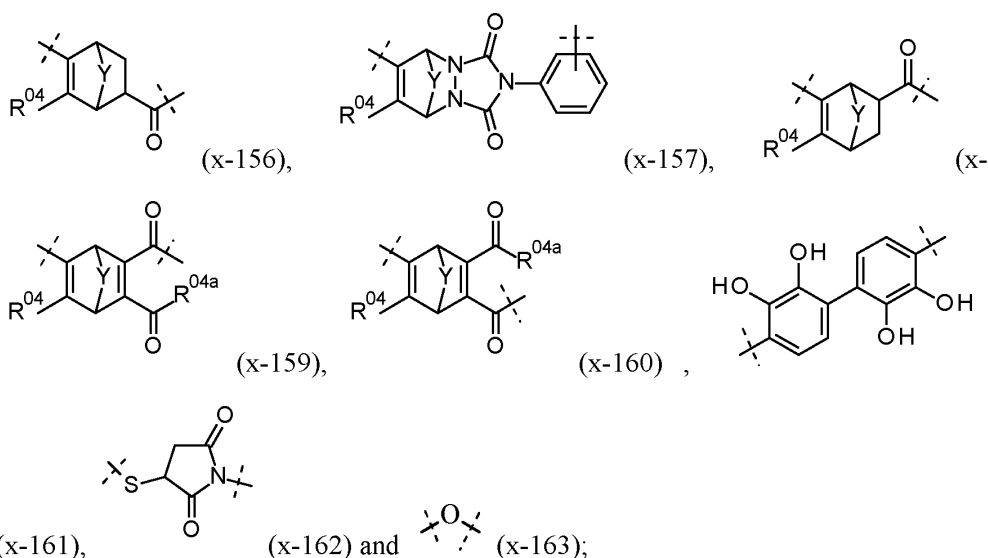


(x-136),



(x-137),





wherein

a dashed line indicates attachment to $-L^2-$ or the remainder of the moiety of formula (I-ai-i);

each $-R^{04}$, $-R^{04a}$, $-R^{04b}$ and $-R^{04c}$ is independently selected from the group consisting of halogen, $-H$, $-CN$, $-T^0$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T^0$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{06}$, which are the same or different, and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T^0-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{07})-$, $-S(O)_2N(R^{07})-$, $-S(O)N(R^{07})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{07})S(O)_2N(R^{07a})-$, $-S-$, $-N(R^{07})-$, $-OC(OR^{07})(R^{07a})-$, $-N(R^{07})C(O)N(R^{07a})-$, and $-OC(O)N(R^{07})-$;

each T^0 is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, and 8- to 11-membered heterobicyclyl; wherein each T^0 is independently optionally substituted with one or more $-R^{06}$, which are the same or different; and

each $-R^{06}$, $-R^{07}$ and $-R^{07a}$ is independently selected from the group consisting of $-H$ and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different

each b is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16;

each c is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and

n is an integer such that the molecular weight of the PEG moiety ranges from about 1 kDa to about 20 kDa.

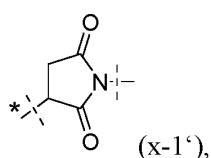
In certain embodiments n of formula (I-ai-i) ranges from 2 to 22, i.e., n is in certain
5 embodiments selected from the group consisting of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 and 22. In general, based on the number of ethylene glycol units the molecular weight of a PEG moiety can be calculated by multiplying the number of ethylene glycol units with 0.044 kDa.

10 In certain embodiments both moieties $-X^A-$ are identical. In certain embodiments the moieties $-X^A-$ are different from each other.

In certain embodiments a moiety $-X^A-$ is selected from the group consisting of formula (x-1), (x-2), (x-3), (x-4), (x-5), (x-6), (x-7), (x-8), (x-9), (x-10), (x-11), (x-12), (x-13), (x-14), (x-15),
15 (x-16), (x-17), (x-18), (x-19), (x-20), (x-21), (x-22) and (x-23). In certain embodiments a moiety $-X^A-$ is selected from the group consisting of formula (x-1), (x-2), (x-3), (x-5), (x-6), (x-7), (x-8), (x-12), (x-13), (x-14), (x-15), (x-16), (x-17), (x-18), (x-19), (x-20), (x-21), (x-22) and (x-23). In certain embodiments a moiety $-X^A-$ is selected from the group consisting of formula (x-1), (x-2), (x-3), (x-5), (x-6), (x-7), (x-8), (x-12), (x-13), (x-14), (x-15), (x-16), (x-17), (x-18), (x-19), (x-20) and (x-21). In certain embodiments a moiety $-X^A-$ is selected from the group consisting of formula (x-1), (x-2), (x-3), (x-5), (x-12), (x-13), (x-14), (x-15), (x-16), (x-17) and (x-18).

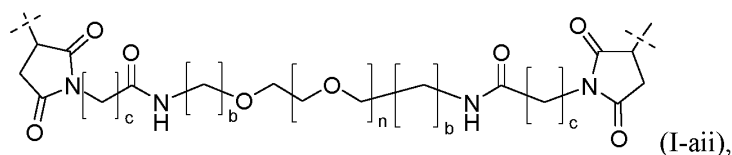
In certain embodiments $-R^{04}$ of formula is -H. In certain embodiments $-R^{04a}$ is -H. In certain
25 embodiments $-R^{04b}$ is -H. In certain embodiments $-R^{04c}$ is -H.

In certain embodiments both $-X^A-$ are of formula (x-1), in particular of formula (x-1')



wherein the dashed line marked with the asterisk indicates attachment to $-L^2-$ and the unmarked
30 dashed line indicates attachment to the remainder of $-P-$. In certain embodiments the dashed line marked with the asterisk indicates attachment to a moiety of formula (x-2) of $-L^2-$.

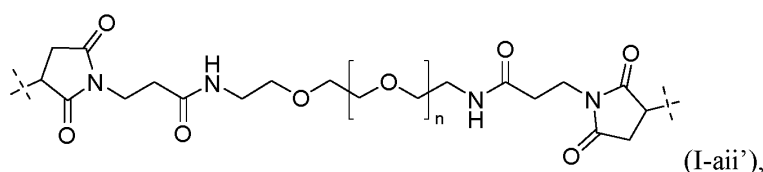
In certain embodiments -P- of formula (I-a) or (I-a') is of formula (I-aii)



wherein

- 5 dashed lines indicate attachment to -L²-;
- each b is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16;
- each c is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and
- 10 n is used as defined for n of formula (I-ai).

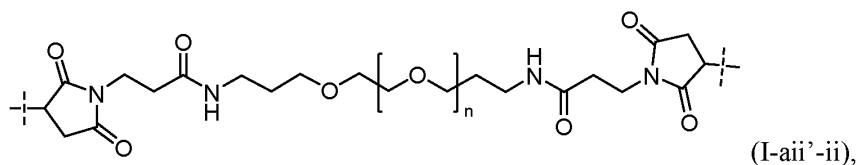
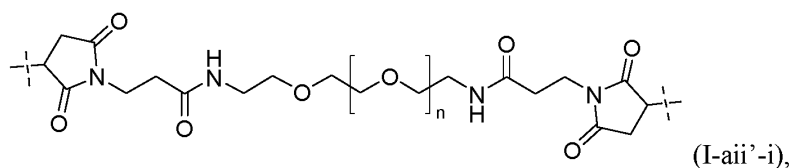
In certain embodiments -P- of formula (I-a) or (I-a') is of formula (I-aii')

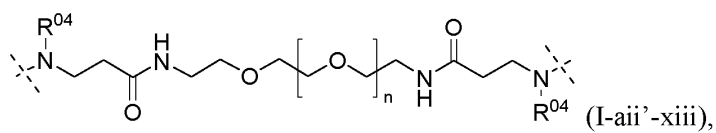
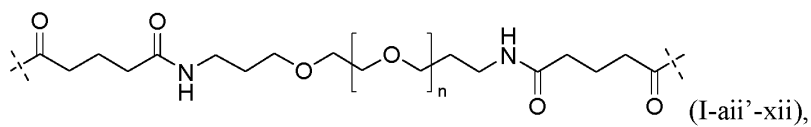
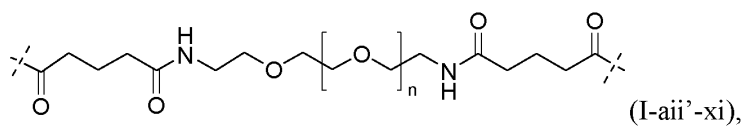
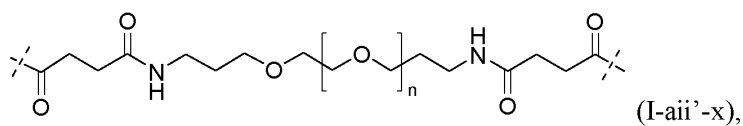
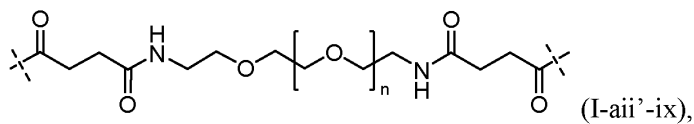
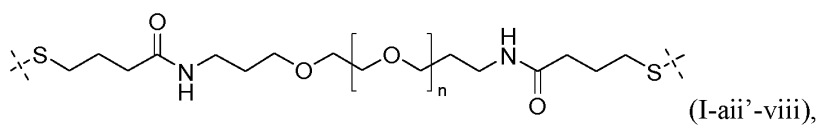
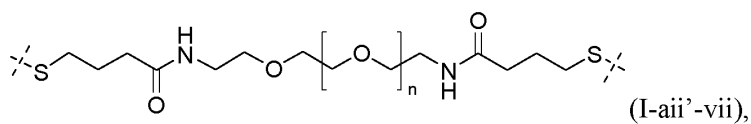
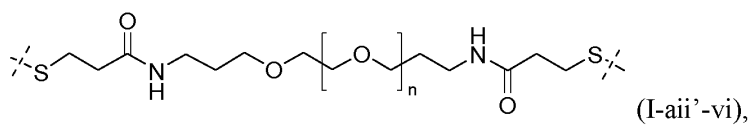
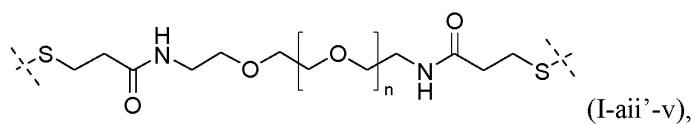
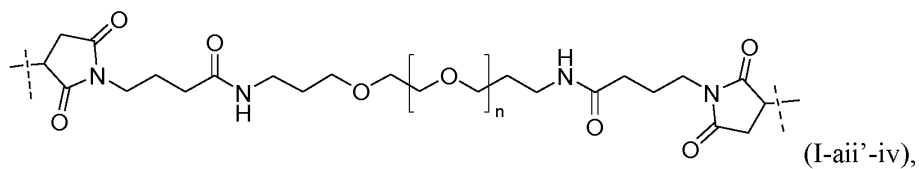
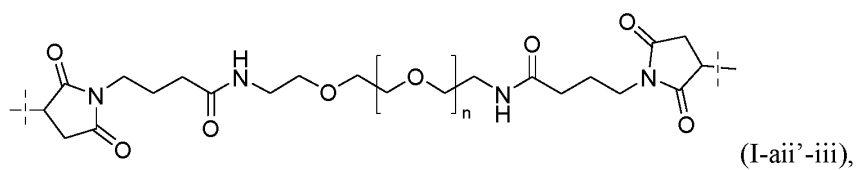


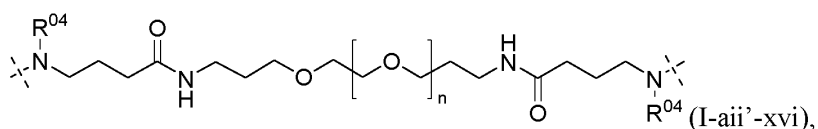
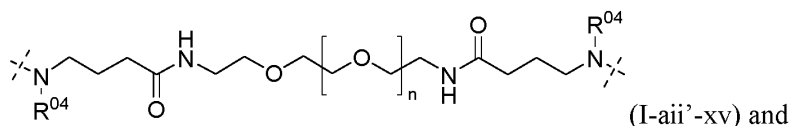
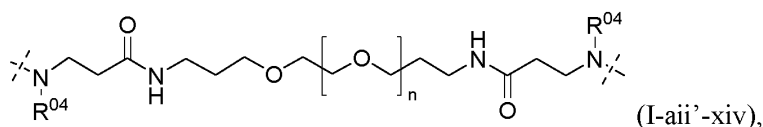
wherein

- 15 dashed lines indicate attachment to -L²-; and
- n is an integer such that the molecular weight of the PEG moiety ranges from about 1 about 20 kDa.

In certain embodiments -P- of formula (I-a) or (I-a') is selected from the group consisting of







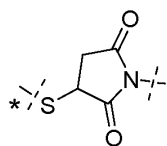
wherein

- 5 dashed lines indicate attachment to $-L^2-$;
 $-R^{04}$ is defined as above; and
 n is an integer such that the molecular weight of the PEG moiety ranges from about 1
 about 20 kDa.

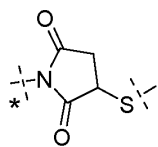
- 10 In certain embodiments $-R^{04}$ of formula (I-aii'-xiii), (I-aii'-xiv), (I-aii'-xv) or (I-aii'-xvi) is -H.

- In certain embodiments n of formulas (I-aii'-i), (I-aii'-ii), (I-aii'-iii), (I-aii'-iv), (I-aii'-v), (I-aii'-vi), (I-aii'-vii), (I-aii'-viii), (I-aii'-ix), (I-aii'-x), (I-aii'-xi), (I-aii'-xii), (I-aii'-xiii), (I-aii'-xiv), (I-aii'-xv) and (I-aii'-xvi) ranges from 2 to 22, i.e., n is in certain embodiments
 15 selected from the group consisting of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 32 and 22.

- A dashed line in any one of formulas (I-aii'-i), (I-aii'-ii), (I-aii'-iii) and (I-aii'-vi) suitably indicates attachment to $-L^2-$ via a moiety of formula (x-2), resulting in a moiety of formula (x-
 20 162')

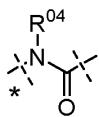


A dashed line in any one of formulas (I-aii'-v), (I-aii'-vi), (I-aii'-vii) and (I-aii'-viii) suitably indicates attachment to $-L^2-$ via a moiety of formula (x-1), resulting in a moiety of formula (x-162'')



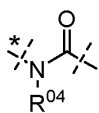
- (x-162''), wherein the dashed line marked with the asterisk indicates attachment to the remainder of $-L^2-$ and the unmarked dashed line indicates attachment to the remainder of $-P-$.

A dashed line in any one of formulas (I-aii''-ix), (I-aii''-x), (I-aii''-xi) and (I-aii''-xii) suitably indicates attachment to $-L^2-$ via a moiety of formula (x-13), resulting in a moiety of formula (x-12')



(x-12'), wherein the dashed line marked with the asterisk indicates attachment to the remainder of $-L^2-$ and the unmarked dashed line indicates attachment to the remainder of $-P-$, with $-R^{04}$ being used as defined in formula (I-ai-i). Suitably, $-R^{04}$ of formula (x-12') is $-H$.

- A dashed line in any one of formulas (I-aii''-xiii), (I-aii''-xiv), (I-aii''-xv) and (I-aii''-xvi) suitably indicates attachment to $-L^2-$ via a moiety of formula (x-14), resulting in a moiety of formula (x-12'')



- (x-12''), wherein the dashed line marked with the asterisk indicates attachment to the remainder of $-L^2-$ and the unmarked dashed line indicates attachment to the remainder of $-P-$, with $-R^{04}$ being used as defined in formula (I-ai-i). Suitably, $-R^{04}$ of formula (x-12'') is $-H$.

- In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety ranges from 1 to 15 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety ranges from 1 to 10 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 1 kDa. In certain embodiments n of

formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 2 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 2.5 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 3 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 4 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 5 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 7.5 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 10 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 15 kDa. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer such that the molecular weight of the PEG moiety is about 20 kDa.

In general, the conversion of the molecular weight of a PEG moiety to the number of ethylene glycol units, such as n in formula (I-ai), (I-ai-i), (I-aii), (I-aii'), (I-aii'-i), (I-aii'-ii), (I-aii'-iii), (I-aii'-iv), (I-aii'-v), (I-aii'-vi), (I-aii'-vii), (I-aii'-viii), (I-aii'-ix), (I-aii'-x), (I-aii'-xi), (I-aii'-xii), (I-aii'-xiii), (I-aii'-xiv), (I-aii'-xv) and (I-aii'-xvi), can easily be made by dividing the molecular weight of the PEG moiety in kDa by 0.044 (molecular weight of one ethylene glycol unit: 44 Da).

In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer ranging from and including about 22 to about 450. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is about 22. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii) or (I-aii') is about 23. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is about 45. In certain embodiments n of formula (I-ai) is about 57. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is about 68. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is about 90. In certain embodiments n of formula (I-ai) is about 113. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii')

or (I-aii'-i) to (I-aii'-xvi) is about 170. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is about 230. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is about 340. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is about 450.

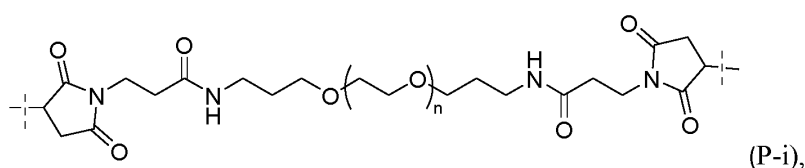
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In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is an integer ranging from and including 2 to 21. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is 2. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is 2. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is 3. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is 4. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is 5. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is 6. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is 7. In certain embodiments n of formula (I-ai), (I-ai-i), (I-aii), (I-aii') or (I-aii'-i) to (I-aii'-xvi) is 2.

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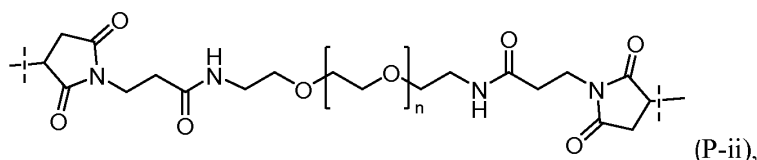
In certain embodiments -P- of formula (I-a) or (I-a') is of formula (P-i)



wherein

20 dashed lines indicate attachment to -L²-, and
n ranges from 50 to 200.

In certain embodiments -P- of formula (I-a) or (I-a') is of formula (P-ii)



25

wherein

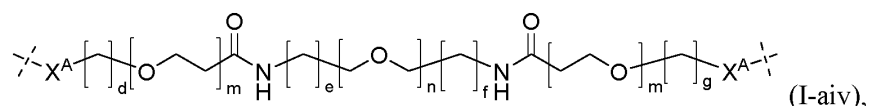
dashed lines indicate attachment to -L²-; and
n ranges from 50 to 200.

In certain embodiments n of formula (P-i) and (P-ii) ranges 60 to 180, from 70 to 160, from 80 to 160, from 90 to 140, from 95 to 130 or from 100 to 125. In certain embodiments n of formula (P-i) and (P-ii) n is selected such that P has a molecular weight of about 5 kDa.

- 5 In certain embodiments n of formulas (P-i) or (P-ii) ranges from 2 to 22, i.e., n is in certain embodiments 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22.

- In certain embodiments n of formulas (P-i) or (P-ii) ranges from 23 to 49, i.e., n is in certain embodiments 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43,
10 44, 45, 46, 47, 48 or 49.

In certain embodiments -P- of formula (I-a) or (I-a') is of formula (I-aiv)



wherein

- 15 the dashed lines indicate attachment to -BP-;
each -X^A- is independently used as defined in formula (I-ai-i);
d, e, f and g are independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;
each m is independently an integer ranging from 1 to 100; and
20 n is an integer such that the molecular weight of the PEG moiety ranges from about 1 about 20 kDa.

- In certain embodiments d of formula (I-aiv) is an integer ranging from 1 to 8. In certain embodiments d of formula (I-aiv) is an integer ranging from 1 to 6. In certain embodiments d of formula (I-aiv) is 1. In certain embodiments d of formula (I-aiv) is 2. In certain embodiments d of formula (I-aiv) is 3. In certain embodiments d of formula (I-aiv) is 4. In certain embodiments d of formula (I-aiv) is 5. In certain embodiments d of formula (I-aiv) is 6.

- In certain embodiments g of formula (I-aiv) is an integer ranging from 1 to 8. In certain embodiments g of formula (I-aiv) is an integer ranging from 1 to 6. In certain embodiments g of formula (I-aiv) is 1. In certain embodiments g of formula (I-aiv) is 2. In certain embodiments g of formula (I-aiv) is 3. In certain embodiments g of formula (I-aiv) is 4. In certain embodiments g of formula (I-aiv) is 5. In certain embodiments g of formula (I-aiv) is 6.

g of formula (I-aiv) is 3. In certain embodiments g of formula (I-aiv) is 4. In certain embodiments g of formula (I-aiv) is 5. In certain embodiments g of formula (I-aiv) is 6.

5 In certain embodiments d and g of formula (I-aiv) are the same integer. In certain embodiments both d and g of formula (I-aiv) are 1. In certain embodiments both d and g of formula (I-aiv) are 2. In certain embodiments both d and g of formula (I-aiv) are 3. In certain embodiments both d and g of formula (I-aiv) are 4.

10 In certain embodiments e of formula (I-aiv) is an integer ranging from 1 to 8. In certain embodiments e of formula (I-aiv) is an integer ranging from 1 to 6. In certain embodiments e of formula (I-aiv) is 1. In certain embodiments e of formula (I-aiv) is 2. In certain embodiments e of formula (I-aiv) is 3. In certain embodiments e of formula (I-aiv) is 4. In certain embodiments e of formula (I-aiv) is 5. In certain embodiments e of formula (I-aiv) is 6.

15 In certain embodiments f of formula (I-aiv) is an integer ranging from 1 to 8. In certain embodiments f of formula (I-aiv) is an integer ranging from 1 to 6. In certain embodiments f of formula (I-aiv) is 1. In certain embodiments f of formula (I-aiv) is 2. In certain embodiments f of formula (I-aiv) is 3. In certain embodiments f of formula (I-aiv) is 4. In certain embodiments f of formula (I-aiv) is 5. In certain embodiments f of formula (I-aiv) is 6.

20

In certain embodiments e and f of formula (I-aiv) are the same integer. In certain embodiments both e and f of formula (I-aiv) are 1. In certain embodiments both e and f of formula (I-aiv) are 2. In certain embodiments both e and f of formula (I-aiv) are 3. In certain embodiments both e and f of formula (I-aiv) are 4.

25

In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety ranges from 1 to 15 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety ranges from 1 to 10 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 1 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 2 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 2.5 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 3 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the

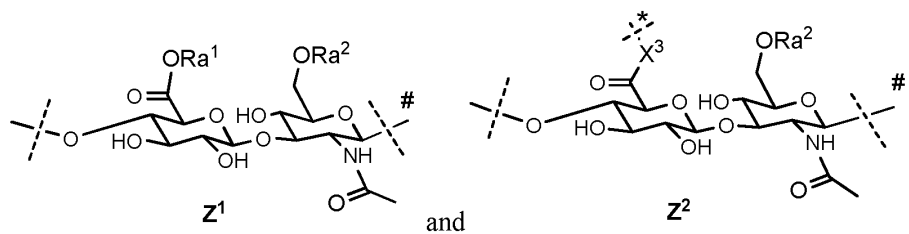
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molecular weight of the PEG moiety is about 4 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 5 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 7.5 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 10 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 15 kDa. In certain embodiments n of formula (I-aiv) is an integer such that the molecular weight of the PEG moiety is about 20 kDa.

In certain embodiments n of formula (I-aiv) is an integer ranging from and including about 22 to about 450. In certain embodiments n of formula (I-aiv) is about 22. In certain embodiments n of formula (I-aiv) is about 23. In certain embodiments n of formula (I-aiv) is about 45. In certain embodiments n of formula (I-ai) is about 57. In certain embodiments n of formula (I-aiv) is about 68. In certain embodiments n of formula (I-aiv) is about 90. In certain embodiments n of formula (I-ai) is about 113. In certain embodiments n of formula (I-aiv) is about 170. In certain embodiments n of formula (I-aiv) is about 230. In certain embodiments n of formula (I-aiv) is about 340. In certain embodiments n of formula (I-aiv) is about 450.

In certain embodiments the at least one polymeric moiety is a linear polymeric moiety -P- comprising a first and a second end and the at least two moieties of formula (I) and/or the at least one moiety of formula (I') is/are conjugated to -P- at sites selected from the group consisting of internal sites, the first end and the second end.

In certain embodiments the at least one polymeric moiety of the compounds of the present invention comprises a plurality of linearly connected units selected from the group consisting of



wherein

- an unmarked dashed line indicates a point of attachment to an adjacent unit at a dashed line marked with # or to a hydrogen,
- a dashed line marked with # indicates a point of attachment to an adjacent unit at an unmarked dashed line or to a hydroxyl;
- 5 a dashed line marked with the asterisk indicates attachment to $-L^2$;
- the total number of units Z^2 in $-P-$ is at least 2;
- the total number of units Z^1 and Z^2 is at least 5;
- $-Ra^1$ and $-Ra^2$ are each independently selected from the group consisting of hydrogen; C_{1-4} alkyl; an alkali metal ion, an ammonium ion, an alkaline earth metal ion, or other
- 10 suitable counterion;
- $-X^3-$ is selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{y1})-$, $-S(O)_2N(R^{y1})-$, $-S(O)N(R^{y1})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{y1})S(O)_2N(R^{y1a})-$, $-S-$, $-N(R^{y1})-$, $-OC(OR^{y1})(R^{y1a})-$, $-N(R^{y1})C(O)N(R^{y1a})-$, $-OC(O)N(R^{y1})-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{y3})-$, $-S(O)_2N(R^{y3})-$, $-S(O)N(R^{y3})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{y3})S(O)_2N(R^{y3a})-$, $-S-$, $-N(R^{y3})-$, $-OC(OR^{y3})(R^{y3a})-$, $-N(R^{y3})C(O)N(R^{y3a})-$, and $-OC(O)N(R^{y3})-$;
- 15 $-R^{y1}$ and $-R^{y1a}$ are independently of each other selected from the group consisting of $-H$, $-T$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different, and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-C(O)O-$,
- 20 $-O-$, $-C(O)-$, $-C(O)N(R^{y4})-$, $-S(O)_2N(R^{y4})-$, $-S(O)N(R^{y4})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{y4})S(O)_2N(R^{y4a})-$, $-S-$, $-N(R^{y4})-$, $-OC(OR^{y4})(R^{y4a})-$, $-N(R^{y4})C(O)N(R^{y4a})-$, and $-OC(O)N(R^{y4})-$;
- each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more $-R^{y2}$, which are the same or different;
- 25 each $-R^{y2}$ is independently selected from the group consisting of halogen, $-CN$, oxo ($=O$), $-COOR^{y5}$, $-OR^{y5}$, $-C(O)R^{y5}$, $-C(O)N(R^{y5}R^{y5a})$, $-S(O)_2N(R^{y5}R^{y5a})$,
- 30

-S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}),
 -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a},
 -N(R^{y5})C(O)OR^{y5a}, -N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}), and C₁₋₆ alkyl; wherein
 C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or
 5 different; and
 each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently selected from the group
 consisting of -H, and C₁₋₆ alkyl, wherein C₁₋₆ alkyl is optionally substituted with one or
 more halogen, which are the same or different.

10 In certain embodiments -X³- is selected from the group consisting of -T-, -C(O)O-,
 -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-,
 -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-,
 -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₂₀ alkyl, C<sub>2-
 20</sub> alkenyl, and C₂₋₂₀ alkynyl are optionally substituted with one or more -R^{y2}, which are
 15 the same or different and wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are
 optionally interrupted by one or more groups selected from the group consisting
 of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-,
 -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-,
 and -OC(O)N(R^{y3})-;

20 -R^{y1} and -R^{y1a} are independently of each other selected from the group consisting
 of -H, -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl; wherein -T, C₁₋₁₀ alkyl, C₂₋₁₀
 alkenyl, and C₂₋₁₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the
 same or different, and wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally
 interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-,
 25 -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-,
 -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-,
 and -OC(O)N(R^{y4})-;

each T is independently selected from the group consisting of phenyl, naphthyl, indenyl,
 indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered
 30 heterobicycyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered
 heteropolycyclyl; wherein each T is independently optionally substituted with one or
 more -R^{y2}, which are the same or different;

-R^{y2} is selected from the group consisting of halogen, -CN, oxo
 (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a}), -S(O)₂N(R^{y5}R^{y5a}),

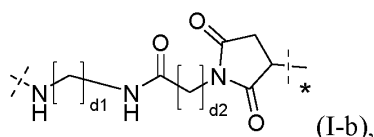
-S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}),
 -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)O
 R^{y5a}, -N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is
 optionally substituted with one or more halogen, which are the same or different; and
 5 each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently of each other selected
 from the group consisting of -H, and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally
 substituted with one or more halogen, which are the same or different.

In certain embodiments -X³- is selected from the group consisting of -T-, -C(O)O-,
 10 -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-,
 -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-,
 -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl;
 wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with
 one or more -R^{y2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl,
 15 and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the
 group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-,
 -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-,
 -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;
 -R^{y1} and -R^{y1a} are independently selected from the group consisting of -H, -T, C₁₋₁₀ alkyl,
 20 C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl;
 each T is independently selected from the group consisting of phenyl, naphthyl, indenyl,
 indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered
 heterobicyclyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered
 heteropolycyclyl;
 25 each -R^{y2} is independently selected from the group consisting of halogen, and C₁₋₆ alkyl;
 and
 each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently of each other selected
 from the group consisting of -H, and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally
 substituted with one or more halogen, which are the same or different.

30 In certain embodiments the total number of units Z¹ and Z² is such that -P- has a molecular
 weight ranging from about 1 about 20 kDa. In certain embodiments the total number of units
 Z¹ and Z² is such that -P- has a molecular weight ranging from about 1 about 15 kDa. In certain
 embodiments the total number of units Z¹ and Z² is such that -P- has a molecular weight of

about 1 kDa. In certain embodiments the total number of units Z^1 and Z^2 is such that -P- has a molecular weight of about 2 kDa. In certain embodiments the total number of units Z^1 and Z^2 is such that -P- has a molecular weight of about 3 kDa. In certain embodiments the total number of units Z^1 and Z^2 is such that -P- has a molecular weight of about 4 kDa. In certain
 5 embodiments the total number of units Z^1 and Z^2 is such that -P- has a molecular weight of about 5 kDa. In certain embodiments the total number of units Z^1 and Z^2 is such that -P- has a molecular weight of about 7.5 kDa. In certain embodiments the total number of units Z^1 and Z^2 is such that -P- has a molecular weight of about 10 kDa. In certain embodiments the total
 10 number of units Z^1 and Z^2 is such that -P- has a molecular weight of about 15 kDa. In certain embodiments the total number of units Z^1 and Z^2 is such that -P- has a molecular weight of about 20 kDa.

In certain embodiments $-X^3-$ is of formula (I-b)



15 wherein

the unmarked dashed line indicates attachment to the carbonyl of Z^2 ;

the dashed line marked with the asterisk indicates attachment to $-L^2-$;

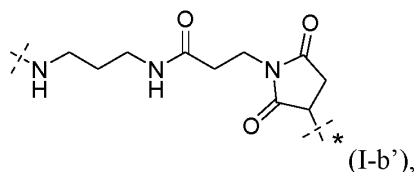
d_1 is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16;

20 d_2 is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

In certain embodiments d_1 of formula (I-b) is 1. In certain embodiments d_1 of formula (I-b) is 2. In certain embodiments d_1 of formula (I-b) is 3. In certain embodiments d_1 of formula (I-b)
 25 is 4. In certain embodiments d_1 of formula (I-b) is 5. In certain embodiments d_1 of formula (I-b) is 6.

In certain embodiments d_2 of formula (I-b) is 1. In certain embodiments d_2 of formula (I-b) is 2. In certain embodiments d_2 of formula (I-b) is 3. In certain embodiments d_2 of formula (I-b)
 30 is 4. In certain embodiments d_2 of formula (I-b) is 5. In certain embodiments d_2 of formula (I-b) is 6.

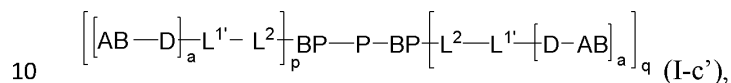
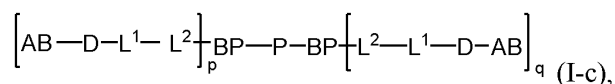
In certain embodiments -X³- is of formula (I-b')



wherein

- 5 the unmarked dashed line indicates attachment to the carbonyl of Z²; and
the dashed line marked with the asterisk indicates attachment to -L²-.

In certain embodiments the compound is of formula (I-c) or (I-c')



wherein

- each -L²- is independently a spacer moiety or is absent;
each -L¹- is independently a linker moiety that is covalently and reversibly conjugated
15 to -D-;
each -L^{1'}- is independently a linker moiety that is covalently and reversibly conjugated
to -D-;
each -D- is independently a drug moiety;
each -AB is independently an albumin-binding moiety;
20 -P- is a polymeric moiety;
each BP is independently a branching point;
each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6,
7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and
p and q are independently an integer selected from the group consisting of 2, 3, 4, 5, 6,
25 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

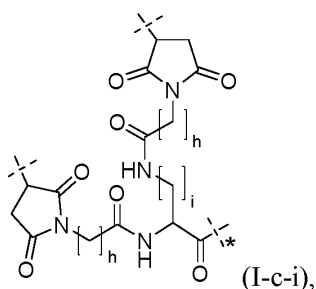
In certain embodiments the compound is of formula (I-c). In certain embodiments the compound is of formula (I-c').

It is understood that a moiety $-L^1-$ is conjugated to more than one moiety $-D-$ and that all linkages between $-L^1-$ and a moiety $-D-$ are covalent and reversible.

- In certain embodiments both a of formula (I-c') are the same integer. In certain embodiments both a of formula (I-c') are 2. In certain embodiments both a of formula (I-c') are 3. In certain embodiments both a of formula (I-c') are 4. In certain embodiments both a of formula (I-c') are 5. In certain embodiments both a of formula (I-a') are 6. In certain embodiments both a of formula (I-c') are 7. In certain embodiments both a of formula (I-c') are 8. In certain embodiments both a of formula (I-c') are 9. In certain embodiments both a of formula (I-c') are 10. In certain embodiments both a of formula (I-c') are 11. In certain embodiments both a of formula (I-c') are 12. In certain embodiments both a of formula (I-c') are 13. In certain embodiments both a of formula (I-c') are 14. In certain embodiments both a of formula (I-c') are 15. In certain embodiments both a of formula (I-c') are 16.
- 15 In certain embodiments p and q of formula (I-c) or (I-c') are the same integer. In certain embodiments p and q of formula (I-c) or (I-c') are a different integer.

Embodiments for $-P-$ are as described for formula (I-a) and (I-a') elsewhere herein.

- 20 Each BP of formula (I-c) and (I-c') is independently a branching point. In certain embodiments both BP are identical. In certain embodiments both BP are different. BP point may be a single atom, such as a nitrogen or carbon atom, or may be a group of atoms, such as a di-, tri- or tetraamino acid. A diamino acid may be selected from the group consisting of lysine, ornithine, 2,3-diaminopropionic acid and 2,4-diaminobutyric acid, each either in R- and S-configuration.
- 25 In certain embodiments BP of formula (I-c') comprises a lysine, in particular a lysine in S-configuration. In certain moieties both moieties BP of formula (I-c') comprise a lysine, in particular a lysine in S-configuration.
- 30 In certain embodiments both moieties BP have the structure of formula (I-c-i)



wherein

the unmarked dashed lines indicate attachment to $-L^2-$;

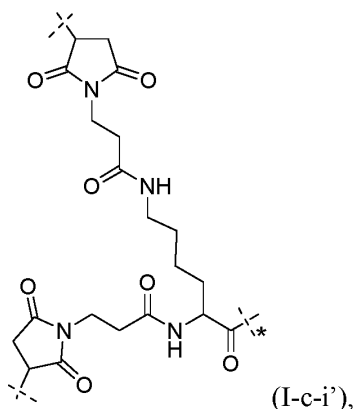
the dashed line marked with the asterisk indicates attachment to $-P-$; and

- 5 each h is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10; and

each i is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.

- 10 In certain embodiments both h of formula (I-c-i) are the same integer. In certain embodiments both h of formula (I-c-i) are 2 and i of formula (I-c-i) is 4. In certain embodiments both h of formula (I-c-i) are 3 and i of formula (I-c-i) is 4. In certain embodiments both h of formula (I-c-i) are 4 and i of formula (I-c-i) is 4.

- 15 In certain embodiments both moieties BP have the structure of formula (I-c-i')



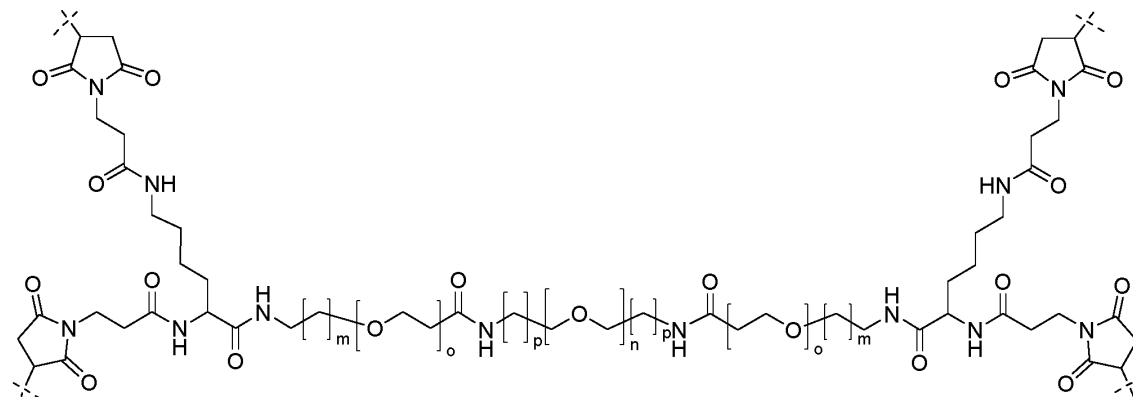
wherein

the unmarked dashed lines indicate attachment to $-L^2-$; and

the dashed line marked with the asterisk indicates attachment to $-P-$.

In certain embodiments one BP of formula (I-c') is lysine, in particular lysine in S configuration. In certain embodiments both moieties BP of formula (I-c') are lysine, in particular lysine in S configuration.

- 5 In certain embodiments the moiety BP-P-BP is of formula (I-d')



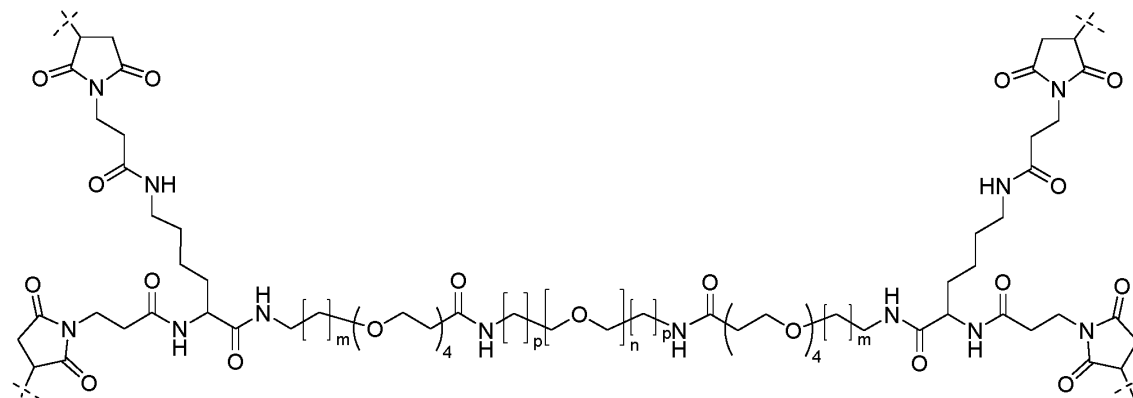
(I-d'),

wherein

the dashed lines indicate attachment to -L²-;

- 10 each m is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7 and 8;
- n is an integer ranging from 2 to 200;
- each o is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7 and 8; and
- 15 each p is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7 and 8.

In certain embodiments the moiety BP-P-BP is of formula (I-d)



(I-d),

wherein

the dashed lines indicate attachment to $-L^2-$;

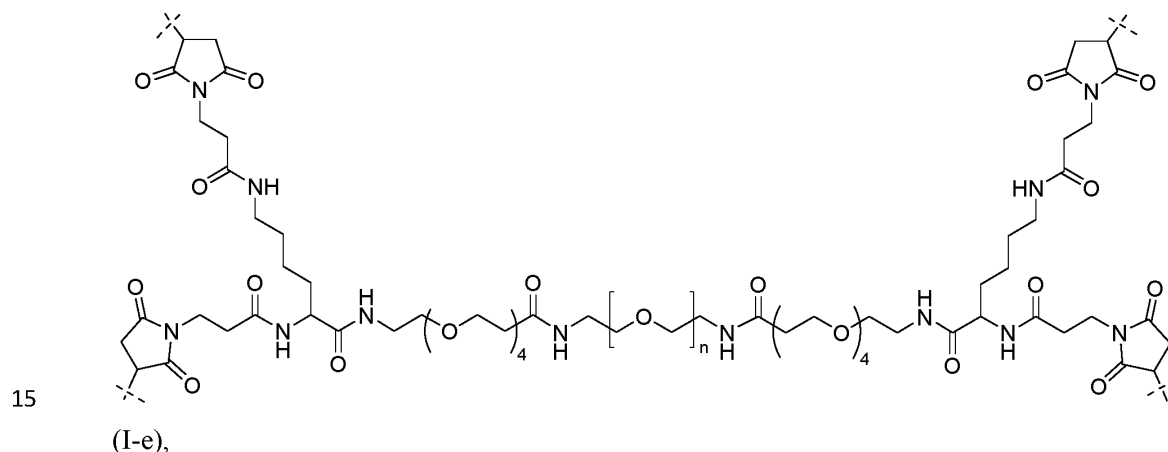
each m is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7 and 8;

each p is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7 and 8; and

n is an integer ranging from 2 to 200.

- 10 In certain embodiments n of formula (I-d) and (I-d') ranges 60 to 180, from 70 to 160, from 80 to 160, from 90 to 140, from 95 to 130 or from 100 to 125. In certain embodiments n of formula (I-d) and (I-d') is selected such that P has a molecular weight of about 5 kDa.

In certain embodiments the moiety BP-P-BP is of formula (I-e)



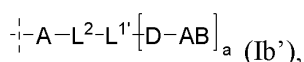
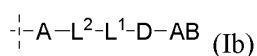
wherein dashed lines indicate attachment to $-L^2-$; and

n is an integer ranging from 2 to 200.

- 20 In certain embodiments n of formula (I-e) ranges 60 to 180, from 70 to 160, from 80 to 160, from 90 to 140, from 95 to 130 or from 100 to 125. In certain embodiments n of formula (I-e) is selected such that P has a molecular weight of about 5 kDa.

- 25 In certain embodiments the at least one polymeric moiety of the compound of the present invention is a multi-arm polymeric moiety. Such multi-arm polymeric moiety comprises at least one branching point. Accordingly, in certain embodiments the compound comprises at

least one branching point B, to which at least two moieties of formula (Ib) and/or at least one moiety of formula (Ib') are conjugated, wherein formula (Ib) and (Ib') are



5 wherein

the dashed line indicates attachment to a branching point B;

-A- is a polymeric moiety

each -L²- is independently a spacer moiety or is absent;

10 each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

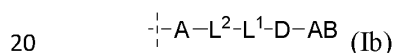
each -L^{1'}- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -D- is independently a drug moiety;

each -AB is independently an albumin-binding moiety; and

15 each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

In certain embodiments the compound comprises at least one branching point B, to which at least two moieties of formula (Ib) are conjugated, wherein formula (Ib) is



wherein

the dashed line indicates attachment to a branching point B;

-A- is a polymeric moiety

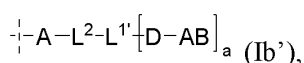
each -L²- is independently a spacer moiety or is absent;

25 each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -D- is independently a drug moiety; and

each -AB is independently an albumin-binding moiety.

30 In certain embodiments the compound comprises at least one branching point B, to which at least one moiety of formula (Ib') is conjugated, wherein formula (Ib') is



wherein

the dashed line indicates attachment to a branching point B;

-A- is a polymeric moiety

each -L²- is independently a spacer moiety or is absent;

5 each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -D- is independently a drug moiety;

each -AB is independently an albumin-binding moiety; and

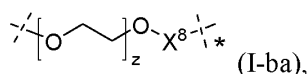
each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6,
10 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

The moiety -A- of formula (Ib) or (Ib') comprises one or more polymer, such as a polymer selected from the group consisting of 2-methacryloyl-oxyethyl phosphoyl cholins, poly(acrylic acids), poly(acrylates), poly(acrylamides), poly(alkyloxy) polymers, poly(amides),
15 poly(amidoamines), poly(amino acids), poly(anhydrides), poly(aspartamides), poly(butyric acids), poly(glycolic acids), poly(butylene terephthalates), poly(caprolactones), poly(carbonates), poly(cyanoacrylates), poly(dimethylacrylamides), poly(esters), poly(ethylenes), poly(ethyleneglycols), poly(ethylene oxides), poly(ethyl phosphates), poly(ethyloxazolines), poly(glycolic acids), poly(hydroxyethyl acrylates), poly(hydroxyethyl-
20 oxazolines), poly(hydroxymethacrylates), poly(hydroxypropylmethacrylamides), poly(hydroxypropyl methacrylates), poly(hydroxypropyloxazolines), poly(iminocarbonates), poly(lactic acids), poly(lactic-co-glycolic acids), poly(methacrylamides), poly(methacrylates), poly(methyloxazolines), poly(organophosphazenes), poly(ortho esters), poly(oxazolines), poly(propylene glycols), poly(siloxanes), poly(urethanes), poly(vinyl alcohols), poly(vinyl
25 amines), poly(vinylmethylethers), poly(vinylpyrrolidones), silicones, celluloses, carbomethyl celluloses, hydroxypropyl methylcelluloses, chitins, chitosans, dextrans, dextrans, gelatins, hyaluronic acids and derivatives, functionalized hyaluronic acids, mannans, pectins, rhamnogalacturonans, starches, hydroxyalkyl starches, hydroxyethyl starches and other carbohydrate-based polymers, xylans, and copolymers thereof.

30

In certain embodiments -A- of formula (Ib) or (Ib') comprises a PEG-based polymer or a hyaluronic acid-based polymer. In certain embodiments -A- of formula (Ib) or (Ib') comprises a PEG-based polymer. In certain embodiments -A- of formula (Ib) or (Ib') comprises a hyaluronic acid-based polymer.

In certain embodiments -A- of formula (Ib) or (Ib') is of formula (I-ba)



wherein

5 the unmarked dashed line indicates attachment to the branching point B;

the dashed line marked with the asterisk indicates attachment to -L²-;

z is an integer selected such that the molecular weight of -A- ranges from about 0.5 kDa to about 10 kDa;

-X⁸- is selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;

-R^{y1} and -R^{y1a} are independently of each other selected from the group consisting of -H-, -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different, and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-, -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-, and -OC(O)N(R^{y4})-;

each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more -R^{y2}, which are the same or different;

each -R^{y2} is independently selected from the group consisting of halogen, -CN, oxo (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a}), -S(O)₂N(R^{y5}R^{y5a}), -S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}), -N

O₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)OR^{y5a},
 5 -N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently selected from the group consisting of -H, and C₁₋₆ alkyl, wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.

In certain embodiments -X⁸- is selected from the group consisting of -T-, -C(O)O-, -O-,
 10 -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-,
 15 -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;

-R^{y1} and -R^{y1a} are independently of each other selected from the group consisting of -H, -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl; wherein -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different, and wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-, -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-,
 20 and -OC(O)N(R^{y4})-;

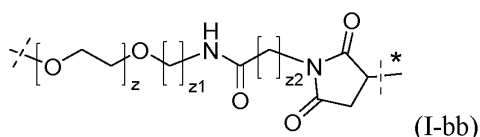
each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more -R^{y2}, which are the same or different;

-R^{y2} is selected from the group consisting of halogen, -CN, oxo (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a}), -S(O)₂N(R^{y5}R^{y5a}), -S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}), -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)OR^{y5a},

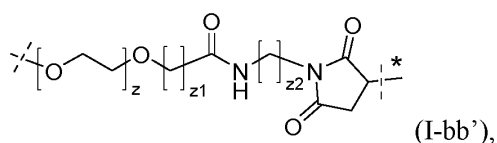
-N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently of each other selected from the group consisting of -H, and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.

In certain embodiments -X⁸- is selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-; -R^{y1} and -R^{y1a} are independently selected from the group consisting of -H, -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl; each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; each -R^{y2} is independently selected from the group consisting of halogen, and C₁₋₆ alkyl; and each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently of each other selected from the group consisting of -H, and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.

In certain embodiments -A- of formula (Ib) or (Ib') is of formula (I-bb) or (I-bb')



30



wherein

the unmarked dashed line indicates attachment to the branching point B;

5 the dashed line marked with the asterisk indicates attachment to $-L^2-$;

z is an integer selected such that the molecular weight of -A- ranges from about 0.5 kDa to about 10 kDa;

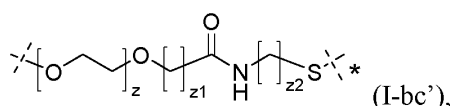
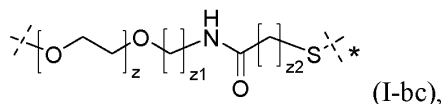
z1 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and

10 z2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

In certain embodiments -A- of formula (Ib) or (Ib') is of formula (I-bb). In certain embodiments -A- of formula (Ib) or (Ib') is of formula (I-bb').

15

In certain embodiments -A- of formula (Ib) or (Ib') is of formula (I-bc) or (I-bc')



20 wherein

the unmarked dashed line indicates attachment to the branching point B;

the dashed line marked with the asterisk indicates attachment to $-L^2-$;

z is an integer selected such that the molecular weight of -A- ranges from about 0.5 kDa to about 10 kDa;

25 z1 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and

z2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

In certain embodiments -A- of formula (Ib) or (Ib') is of formula (I-bc). In certain embodiments -A- of formula (Ib) or (Ib') is of formula (I-bc').

- 5 In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 1. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 2. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 3. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 4. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 5. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 6. In certain
10 embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 7. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 8. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 9. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 10. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 11. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 12. In certain embodiments z1
15 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 13. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 14. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 15. In certain embodiments z1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 16.

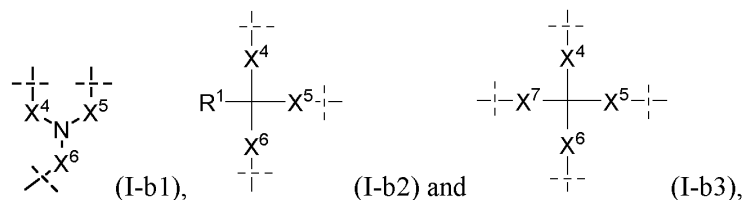
- In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 1. In certain
20 embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 2. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 3. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 4. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 5. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 6. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 7. In certain
25 formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 8. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 9. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 10. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 11. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 12. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 13. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 14. In certain
30 embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 15. In certain embodiments z2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 16.

In certain embodiments z_1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 3 and z_2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 2. In certain embodiments z_1 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 2 and z_2 of formula (I-bb), (I-bb'), (I-bc) or (I-bc') is 2.

- 5 In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- ranges from and includes about 0.5 kDa to about 10 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 0.5 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 1 kDa. In certain embodiments of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 1.5 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 2 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 2.5 kDa. In certain
10 embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 3 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 3.5 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 4 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 5 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 6 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 7 kDa. In certain embodiments of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 8 kDa. In certain
25 embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 9 kDa. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer such that the molecular weight of the -A- is about 10 kDa.
- 30 In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer ranging from and including about 11 to about 230. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is an integer ranging from and including about 11 to about 225. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 11. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 12. In certain

embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 22. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 23. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 34. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 45. In certain
 5 embodiments z of formula (I-ba), (I-bb) or (-I-bc) is about 57. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 68. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 79. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 90. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 102. In certain embodiments z of formula (I-ba), (I-bb), (I-
 10 bb'), (I-bc) or (I-bc') is about 113. In certain embodiments z of formula (I-bb) or (I-bc) is about 135. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 160. In certain embodiments z of formula (I-bb) or (I-bc) is about 180. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 205. In certain embodiments z of formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 225. In certain embodiments z of
 15 formula (I-ba), (I-bb), (I-bb'), (I-bc) or (I-bc') is about 230.

In certain embodiments the compound comprises one branching point B, such as a branching point selected from the group consisting of



20 wherein

dashed lines indicate attachment to -A- of formula (Ib);

-R¹ is used as defined for the term “substituent”; and

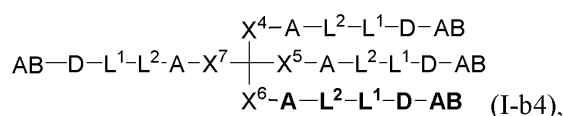
-X⁴-, -X⁵-, -X⁶- and -X⁷- are independently used as defined for -X¹- and -X²- of formula
 25 (I-ai).

In certain embodiments -X⁴-, -X⁵- and -X⁶- of formula (I-b1) and (I-b2) are identical. In certain embodiments -X⁴-, -X⁵- and -X⁶- of formula (I-b1) and (I-b2) are identical and are selected from the group consisting of -CH₂-, -CH₂CH₂- and -CH₂CH₂CH₂-.

In certain embodiments the compound comprises one branching point of formula (I-b1). In certain embodiments the compound comprises one branching point of formula (I-b2). In certain embodiments the compound comprises one branching point of formula (I-b3). In certain
 5 wherein $-X^4-$, $-X^5-$, $-X^6-$ and $-X^7-$ are identical. In certain embodiments the compound comprises one branching point of formula (I-b3), wherein $-X^4-$, $-X^5-$, $-X^6-$ and $-X^7-$ are selected from the group consisting of $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$ and $-\text{CH}_2\text{CH}_2\text{CH}_2-$. In certain embodiments the compound comprises one branching point of formula (I-b3), wherein $-X^4-$, $-X^5-$, $-X^6-$ and $-X^7-$ are $-\text{CH}_2-$.

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In certain embodiments the compound is of formula (I-b4)



wherein

each $-A-$ is a polymeric moiety;

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each $-L^2-$ is independently a spacer moiety or is absent;

each $-L^1-$ is independently a linker moiety that is covalently and reversibly conjugated to $-D-$;

each $-D-$ is independently a drug moiety;

each $-AB$ is independently an albumin-binding moiety;

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$-X^4-$, $-X^5-$, $-X^6-$ and $-X^7-$ are independently of each other selected from the group consisting of $-T-$, $-\text{C}(\text{O})\text{O}-$, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{N}(\text{R}^{y1})-$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{y1})-$, $-\text{S}(\text{O})\text{N}(\text{R}^{y1})-$, $-\text{S}(\text{O})_2-$, $-\text{S}(\text{O})-$, $-\text{N}(\text{R}^{y1})\text{S}(\text{O})_2\text{N}(\text{R}^{y1a})-$, $-\text{S}-$, $-\text{N}(\text{R}^{y1})-$, $-\text{OC}(\text{OR}^{y1})(\text{R}^{y1a})-$, $-\text{N}(\text{R}^{y1})\text{C}(\text{O})\text{N}(\text{R}^{y1a})-$, $-\text{OC}(\text{O})\text{N}(\text{R}^{y1})-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are

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optionally substituted with one or more $-\text{R}^{y2}$, which are the same or different and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-\text{C}(\text{O})\text{O}-$, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{N}(\text{R}^{y3})-$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{y3})-$, $-\text{S}(\text{O})\text{N}(\text{R}^{y3})-$, $-\text{S}(\text{O})_2-$, $-\text{S}(\text{O})-$, $-\text{N}(\text{R}^{y3})\text{S}(\text{O})_2\text{N}(\text{R}^{y3a})-$, $-\text{S}-$, $-\text{N}(\text{R}^{y3})-$, $-\text{OC}(\text{OR}^{y3})(\text{R}^{y3a})-$, $-\text{N}(\text{R}^{y3})\text{C}(\text{O})\text{N}(\text{R}^{y3a})-$, and $-\text{OC}(\text{O})\text{N}(\text{R}^{y3})-$;

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$-\text{R}^{y1}$ and $-\text{R}^{y1a}$ are independently of each other selected from the group consisting of $-\text{H}$, $-T$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-\text{R}^{y2}$, which are the

same or different, and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-, -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-, and -OC(O)N(R^{y4})-;

each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more -R^{y2}, which are the same or different;

each -R^{y2} is independently selected from the group consisting of halogen, -CN, oxo (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a}), -S(O)₂N(R^{y5}R^{y5a}), -S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}), -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)OR^{y5a}, -N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and

each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently selected from the group consisting of -H, and C₁₋₆ alkyl, wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.

In certain embodiments -X⁴-, -X⁵-, -X⁶- and -X⁷- of formula (I-b4) are independently of each other selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;

-R^{y1} and -R^{y1a} are independently of each other selected from the group consisting of -H, -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl; wherein -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different, and

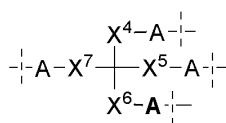
- wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-, -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-, and -OC(O)N(R^{y4})-;
- 5 each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more -R^{y2}, which are the same or different;
- 10 -R^{y2} is selected from the group consisting of halogen, -CN, oxo (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a}), -S(O)₂N(R^{y5}R^{y5a}), -S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}), -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)OR^{y5a}, -N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different;
- 15 each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently of each other selected from the group consisting of -H, and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.
- 20 In certain embodiments -X⁴-, -X⁵-, -X⁶- and -X⁷- of formula (I-b4) are independently of each other selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;
- 25 -R^{y1} and -R^{y1a} are independently selected from the group consisting of -H, -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl;
- each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl;

each $-R^{y2}$ is independently selected from the group consisting of halogen, and C_{1-6} alkyl; and each $-R^{y3}$, $-R^{y3a}$, $-R^{y4}$, $-R^{y4a}$, $-R^{y5}$, $-R^{y5a}$ and $-R^{y5b}$ is independently of each other selected from the group consisting of $-H$, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

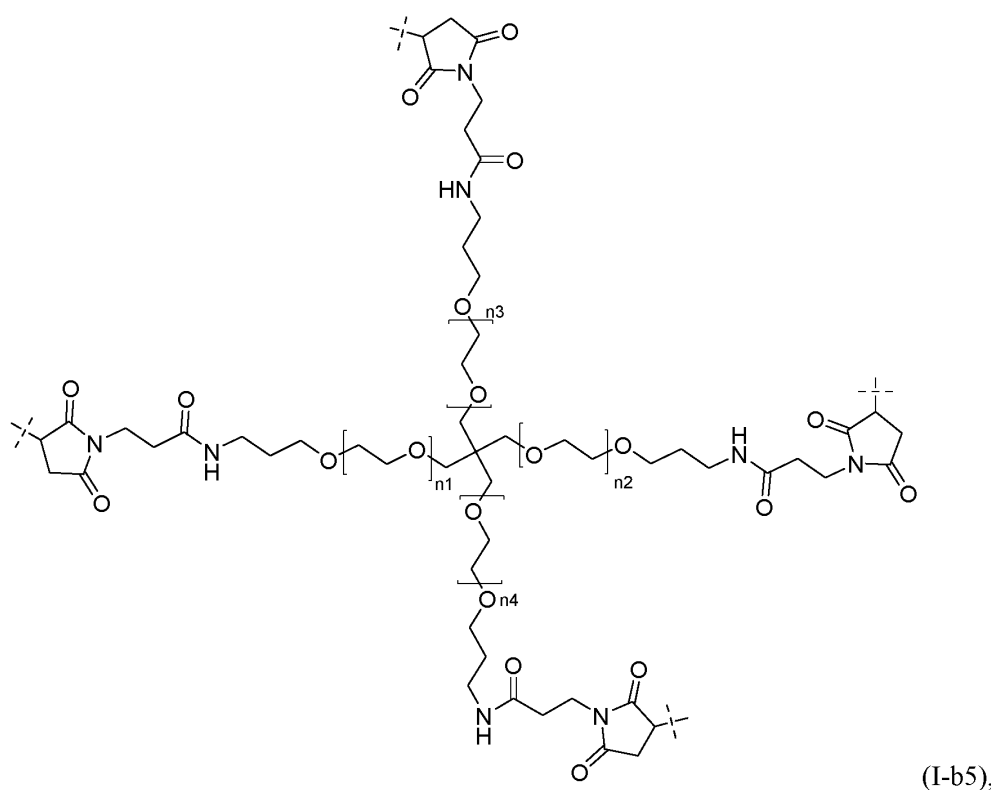
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In certain embodiments $-X^4$ -, $-X^5$ -, $-X^6$ - and $-X^7$ - of formula (I-b3) and (I-b4) are identical. In certain embodiments $-X^4$ -, $-X^5$ -, $-X^6$ - and $-X^7$ - of formula (I-b3) and (I-b4) are identical and are selected from the group consisting of $-CH_2-$, $-CH_2CH_2-$ and $-CH_2CH_2CH_2-$.

10 In certain embodiments the moiety



is of formula (I-b5)

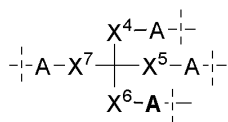


wherein

15 dashed lines indicate attachment to $-L^2$; and

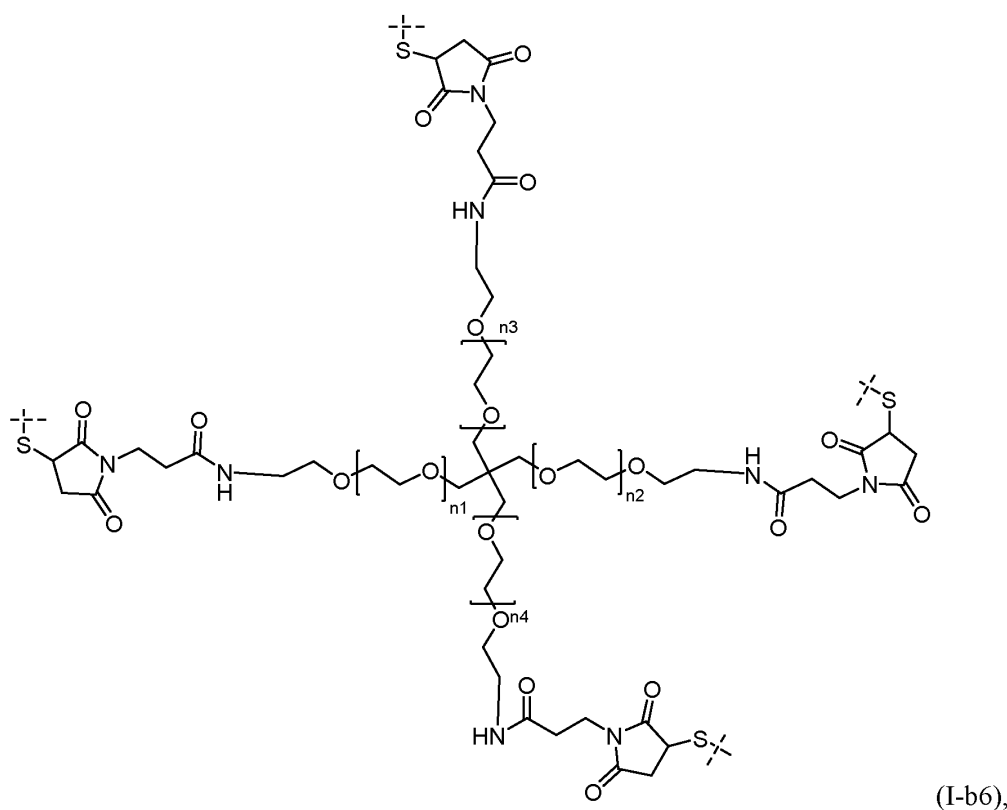
n1, n2, n3 and n4 are independently an integer ranging from and including about 10 to about 300, in certain embodiments from and including about 10 to about 230.

In certain embodiments the moiety



5

is of formula (I-b6)



wherein

dashed lines indicate attachment to $-L^2-$; and

10 n1, n2, n3 and n4 are independently an integer ranging from and including about 10 to about 230.

In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are the same integer. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 11. In certain
15 embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 12. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 22. In certain embodiments n1, n2, n3

and n4 of formula (I-b5) or (I-b6) are about 23. . In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 28. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 29. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 34. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 45. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 56. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 68. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 80. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 90. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 100. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 115. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 135. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 160. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 180. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 200. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 225. In certain embodiments n1, n2, n3 and n4 of formula (I-b5) or (I-b6) are about 230.

In certain embodiments the compound comprises more than one branching point B, such as two or more branching points selected from the group consisting of (I-b1), (I-b2) and (I-b3).

In certain embodiments -D- is a drug moiety selected from the group consisting of small molecule drug moieties, medium size molecule drug moieties, oligonucleotide drug moieties, peptide nucleic acid drug moieties, peptide drug moieties and protein drug moieties.

In certain embodiments -D- is a peptide drug moiety. In certain embodiments -D- is a small molecule drug moiety. In certain embodiments -D- is a medium size drug moiety. In certain embodiments -D- is an oligonucleotide drug moiety. In certain embodiments -D- is a peptide nucleic acid drug moiety. In certain embodiments -D- is a protein drug moiety.

In certain embodiments -D- or -D-AB is a GLP-1 receptor agonist moiety. Accordingly, the compound of the present invention may be a GLP-1 receptor agonist compound.

In certain embodiments -D- or -D-AB is a mono agonist of the GLP-1 receptor, i.e., only activates the GLP-1 receptor.

In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and an agonist of a further receptor, i.e., -D- or -D-AB is a dual GLP-1 receptor agonist. Such further receptor may be selected from the group consisting of the GIP receptor, the GCG receptor, an amylin receptor, a PYY receptor and the GLP-2 receptor.

5

In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and of the GIP receptor. In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and of the GCG receptor. In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and of an amylin receptor. In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and of a PYY receptor. In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and of the GLP-2 receptor.

In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and growth/differentiation factor 15 (GDF15). In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and fibroblast growth factor 21 (FGF21).

In certain embodiments -D- or -D-AB is an agonist of the GLP-1 receptor and an agonist of two further receptors, i.e., -D- or -D-AB is a triple GLP-1 receptor agonist. These further receptors are in certain embodiments selected from the group consisting of the GIP receptor (GIPR), the GCG receptor (GCGR), an amylin receptor, a PYY receptor (PYYR) and the GLP-2 receptor (GLP2R).

In certain embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that activates the GLP-1 receptor, the GIP receptor and the GCG receptor. In certain embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that activates the GLP-1 receptor, the GIP receptor and an amylin receptor. In certain embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that activates the GLP-1 receptor, the GIP receptor and a PYY receptor. In certain embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that activates the GLP-1 receptor, the GIP receptor and the GLP-2 receptor. In certain embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that activates the GLP-1 receptor, the GCG receptor and an amylin receptor. In certain embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that activates the GLP-1 receptor, the GCG receptor and a PYY receptor. In certain embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that activates the GLP-1 receptor, the GCG receptor and the GLP-2 receptor. In certain embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that

activates the GLP-1 receptor, an amylin receptor and a PYY receptor. In certain
embodiments -D- or -D-AB is a triple GLP-1 receptor agonist that activates the GLP-1 receptor,
the amylin receptor and the GLP-2 receptor. In certain embodiments -D- or -D-AB is a triple
GLP-1 receptor agonist that activates the GLP-1 receptor, a PYY receptor and the GLP-2
5 receptor.

In certain embodiments -D- is a human GLP-1 of SEQ ID NO:1:

HAEGTFTSDVSSYLEGQAAKEFIAWLVRGRG.

10 In certain embodiments -D- is human GLP-1 analog of SEQ ID NO:1, which peptide sequence
may comprise one or more amino acid changes compared to SEQ ID NO:1. Such amino acid
changes may be the addition of one or more amino acid residues, the deletion of one or more
amino acid residues, the substitution of one or more amino acid residues or may be any
combination thereof. Such amino acid change may be at the N-terminus, the C-terminus and/or
15 at an internal site of the GLP-1 of SEQ ID NO:1. In certain embodiments such human GLP-1
analog has a maximum of 3 amino acid changes compared to SEQ ID NO:1, i.e., a maximum
of three amino acids are added to, deleted from or substituted compared to the sequence of SEQ
ID NO:1.

20 In certain embodiments -D- has the sequence
HX₁EGTFTSDVSSYLEGQAAKEFIAWLVRGRG (SEQ ID NO:2),
wherein X₁ is 2-aminoisobutyric acid (Aib).

In certain embodiments -D- has the sequence
25 HX₁EGTFTSDVSSYLEGQAAKEFIAWLVRGRG (SEQ ID NO:3),
wherein X₁ is Aib and the C-terminal glycine, i.e., the glycine at position 31, is amidated as a
C-terminal primary amide.

In certain embodiments -D- is exenatide. Exenatide has the sequence
30 HEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS (SEQ ID NO:4).

In certain embodiments -D- has the sequence
HEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS (SEQ ID NO:5),

wherein the C-terminal serine, i.e., the serine at position 39, is amidated as a C-terminal primary amide.

In certain embodiments -D- is lixisenatide. Lixisenatide has the sequence

- 5 HEGTFTSDLSKQMEEEEAVRLFIEWLKNGGPSSGAPPSKKKKKK (SEQ ID NO:6),
wherein the C-terminal lysine, i.e., the lysine at position 44, is amidated as a C-terminal primary amide.

In certain embodiments -D- has the sequence

- 10 HEGTFTSDLSKQMEEEEAVRLFIEWLKNGGPSSGAPPSKKKKKK (SEQ ID NO:7).

In certain embodiments -D- has the sequence

HX₁EGTFTSDLSKQX₂EEEAVRLFIEWLKQGGPSSGAPPPC (SEQ ID NO:8),
wherein X₁ is D-alanine and X₂ is norleucine (Nle).

15

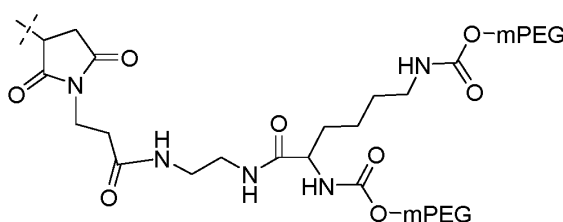
In certain embodiments -D- has the sequence

HX₁EGTFTSDLSKQX₂EEEAVRLFIEWLKQGGPSSGAPPPC (SEQ ID NO:9),
wherein X₁ is D-alanine, X₂ is Nle and the C-terminal cysteine, i.e., the cysteine at position 39,
is amidated as a C-terminal primary amide.

20

In certain embodiments -D- is PEG-loxenatide. PEG-loxenatide has the sequence

HX₁EGTFTSDLSKQX₂EEEAVRLFIEWLKQGGPSSGAPPPC (SEQ ID NO:10),
wherein X₁ is D-alanine; X₂ is Nle; the cysteine at position 39 is chemically modified through
conjugation to the thiol group of the cysteine side-chain with



25

wherein

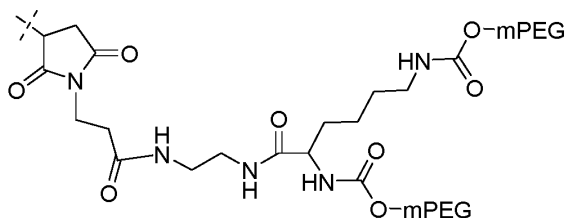
the dashed line indicates attachment to the thiol group of the cysteine side chain of the
cysteine at position 39, and each mPEG is methoxypoly(ethylene glycol) with a
molecular weight of approx. 20 kDa.

30

In certain embodiments -D- has the sequence

HX₁EGTFTSDLKQX₂EEEEAVRLFIEWLKQGGPSSGAPPPC (SEQ ID NO:11),

wherein X₁ is D-alanine; X₂ is Nle; the cysteine at position 39 is chemically modified through conjugation to the thiol group of the cysteine side-chain with



wherein

the dashed line indicates attachment to the thiol group of the cysteine side chain of the cysteine at position 39, each mPEG is methoxypoly(ethylene glycol) with a molecular weight of approx. 20 kDa, and the C-terminal cysteine, i.e., the cysteine at position 39, is amidated as a C-terminal primary amide.

In certain embodiments -D- has the sequence

HAEGTFTSDVSSYLEGQAAKEFIWLVRGRG (SEQ ID NO:12).

15 In certain embodiments -D- has the sequence

HAEGTFTSDVSSYLEGQAAKEFIWLVRGRG (SEQ ID NO:13),

and the C-terminal glycine, i.e., the glycine at position 31, is amidated as a C-terminal primary amide.

20 In certain embodiments -D- has the sequence

HVEGTFTSDVSSYLEEQAAAREFIKWLVGRGRG (SEQ ID NO:14).

In certain embodiments -D- has the sequence

HVEGTFTSDVSSYLEEQAAAREFIKWLVGRGRG (SEQ ID NO:15),

25 and the C-terminal glycine, i.e., the glycine at position 31, is amidated as a C-terminal primary amide.

In certain embodiments -D- has the sequence

HGEGTFTSDVSSYLEGQAAKEFIWLVRGRG (SEQ ID NO:16).

30

In certain embodiments -D- has the sequence
HGEFTFTSDVSSYLEGQAAKEFIAWLVRGRG (SEQ ID NO:17),
and the C-terminal glycine, i.e., the glycine at position 31, is amidated as a C-terminal primary
amide.

5

In certain embodiments -D- has the sequence
HX₁EGTFTSDVSSYLEGQAAKEFIAWLVRGRGL (SEQ ID NO:18),
wherein X₁ is Aib.

10 In certain embodiments -D- has the sequence
HX₁EGTFTSDVSSYLEGQAAKEFIAWLVRGRGL (SEQ ID NO:19),
wherein X₁ is Aib and the C-terminal leucine, i.e., the leucine at position 32, is amidated as a
C-terminal primary amide.

15 In certain embodiments -D- has the sequence
YX₁EGTFTSDYSIX₂LDKIAQKAFVQWLIAGGPSSGAPPPS (SEQ ID NO:20),
wherein X₁ is Aib, X₂ is Aib and the C-terminal serine, i.e., the serine at position 39, is amidated
as a C-terminal primary amide.

20 In certain embodiments -D- has the sequence
YX₁EGTFTSDYSIX₂LDKIAQKAFVQWLIAGGPSSGAPPPS (SEQ ID NO:21),
wherein X₁ is Aib and X₂ is Aib.

In certain embodiments -D- has the sequence
25 HSQGTFTSDKSEYLDSEARDFVAWLEAGG (SEQ ID NO:22).

In certain embodiments -D- has the sequence
HSQGTFTSDKSEYLDSEARDFVAWLEAGG (SEQ ID NO:23),
wherein the C-terminal glycine, i.e., the glycine at position 30, is amidated as a C-terminal
30 primary amide.

In certain embodiments -D- has the sequence
HX₁QGTFTSDYSKYLDERAADKDFIKWLESA (SEQ ID NO:24),

wherein X₁ is 1-amino-cyclobutanecarboxylic acid (Ac4c); and the C-terminal alanine, i.e. the alanine at position 29, is amidated as a C-terminal primary amide.

In certain embodiments -D- has the sequence

5 HX₁QGTFTSDYSKYLDERAAKDFIKWLESA (SEQ ID NO:25),

wherein X₁ is 1-amino-cyclobutanecarboxylic acid (Ac4c).

In certain embodiments -D- has the sequence

HX₁QGTFTSDYSKYLDEKAAKEFIQWLLQT (SEQ ID NO:26),

10 wherein X₁ is Aib and the glutamic acid at position 16 and the lysine at position 20 are connected via a lactam bridge.

In certain embodiments -D- has the sequence

HX₁QGTFTSDYSKYLDEKAAKEFIQWLLQT (SEQ ID NO:27),

15 wherein X₁ is Aib, the glutamic acid at position 16 and the lysine at position 20 are connected via a lactam bridge and the C-terminal threonine, i.e., the threonine at position 29, is amidated as a C-terminal primary amide.

In certain embodiments -D- has the sequence

20 HX₁QGTFTSDYSKYLDEKKAKEFVEWLLEGGPSSG (SEQ ID NO:28),

wherein X₁ is Aib and the C-terminal glycine, i.e., the glycine at position 34, is amidated as a C-terminal primary amide.

In certain embodiments -D- has the sequence

25 HX₁QGTFTSDYSKYLDEKKAKEFVEWLLEGGPSSG (SEQ ID NO:29),

wherein X₁ is Aib.

In certain embodiments -D- has the sequence

HX₁EGSFTSELATILDKQAARDFIAWLIQHKITD (SEQ ID NO:30),

30 wherein X₁ is Aib.

In certain embodiments -D- has the sequence

HX₁EGSFTSELATILDKQAARDFIAWLIQHKITD (SEQ ID NO:31),

wherein X₁ is Aib and the C-terminal aspartic acid, i.e., the aspartic acid at position 33, is amidated as a C-terminal primary amide.

In certain embodiments -D- has the sequence

5 YX₁QGTFTSDYSIX₂LDKKAQX₃AFIEYLLEGGPSSGAPPPS (SEQ ID NO:32),
wherein X₁ is Aib, X₂ is α -methyl-leucine (α MeL), X₃ is Aib; and the C-terminal serine, i.e. the serine at position 39, is amidated as a C-terminal primary amide.

In certain embodiments -D- has the sequence

10 YX₁QGTFTSDYSIX₂LDKKAQX₃AFIEYLLEGGPSSGAPPPS (SEQ ID NO:33),
wherein X₁ is Aib, X₂ is α -methyl-leucine (α MeL) and X₃ is Aib.

In certain embodiments -D- has the sequence

15 HX₁EGTFTSDVSSYLEEEAAKEFIAWLVRGGPSSGAPPPSK (SEQ ID NO:54),
wherein X₁ is Aib.

In certain embodiments -D- has the sequence

HX₁EGTFTSDVSSYLEEQAAKEFIAWLVRGGG (SEQ ID NO:55),
wherein X₁ is Aib.

20

In certain embodiments -D- has the sequence

HX₁EGTFTSDVSSYLEEQAAKEFIAWLVRGGGGAQPGAQPGAQPGAQPGAQPGAQPGAQPGAQPGAQPGQKP (SEQ ID NO:56),
wherein X₁ is Aib.

25

In certain embodiments -D- has the sequence

HX₁EGTFTSDVSSYLEEQAAKEFIAWLVRGGGGAQPGAQPGAQPGAQPGAQPGAQPGAQPGAQPGAQPGQKP (SEQ ID NO:56),
wherein X₁ is Aib.

30

In certain embodiments -D- is a drug selected from the group consisting of insulins; amylin and amylin/calcitonin; PYY; GIP; MSH; C5a binders; GDF15; PCSK9 I; immune stimulants; urocortin2; MIC-1; IL-1R antagonists; leptin; gastrin; glucagon; exendin-4; GLP-1; GLP-2; and GIP.

In certain embodiments -D- is a drug moiety selected from the group consisting of insulin; insulin analogues; amylin; dual amylin/calcitonin agonists; PYY; GIP; MSH; C5 inhibitors or modulators; GDF15; PCSK9 inhibitors; immune stimulants; urocortin II; MIC-1; IL-1R
5 antagonists; leptin; gastrin; glucagon; oxyntomodulin; neurokinin A; tachykinin/neurokinin receptor 2 (NK2R) agonists; neurokinin receptor (NKR) agonists and GLP-2.

In certain embodiments -D- is an insulin, such as insulin detemir, insulin degludec and insulin. In certain embodiments -D- is amylin and amylin/calcitonin, such as for example cagrilintide.
10 In certain embodiments -D- is PYY, such as NNC0165-1875. In certain embodiments -D- is GIP. In certain embodiments -D- is MSH. In certain embodiments -D- is a C5a binder, such as zilucoplan. In certain embodiments -D- is GDF15, such as NN LA-GDF15. In certain embodiments -D- is PCSK9 i. In certain embodiments -D- is an immune stimulant, such as romurtide or mifamurtide. In certain embodiments -D- is muramyl dipeptide. In certain
15 embodiments -D- is urocortin2. In certain embodiments -D- is MIC-1. In certain embodiments -D- is an IL-1R antagonist. In certain embodiments -D- is leptin. In certain embodiments -D- is gastrin.

In certain embodiments -D- is selected from the list consisting of growth hormones, such as
20 human growth hormone; FGF21; EGF(a); and coagulations factors.

In certain embodiments -D- is a growth hormone, such as a human growth hormone, such as somapacitan. In certain embodiments -D- is FGF21, such as NNC0194 0499. In certain
embodiments -D- is EGF(a). In certain embodiments -D- is a coagulation factor.

25

In certain embodiments -D- is selected from cytotoxic small molecule drugs; chemotherapy small molecule drugs; and immune activating small molecule drugs.

In certain embodiments -D- is a cytotoxic small molecule drug. In certain embodiments -D- is
30 a chemotherapy small molecule drug. In certain embodiments -D- is and immune activating small molecule drug, such as telratolimod.

In certain embodiments -D- is paclitaxel. In certain embodiments -D- is doxorubicin. In certain
embodiments -D- is 5-FU.

In certain embodiments -D- is a PTH moiety.

In certain embodiments -AB is a fatty acid-based albumin-binding moiety.

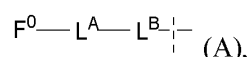
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A moiety -AB binds to albumin, such as human albumin, under physiological conditions (aqueous buffer pH 7.4, 37°C).

10 A moiety -D- may be conjugated to one moiety -AB. A moiety -D- may be conjugated to more than one moiety -AB. In certain embodiments the linkage between -D- and a moiety -AB is a stable linkage. In case a moiety -D- comprises two moieties -AB, the linkage between -D- and a first moiety -AB may be reversible and the linkage between -D- and a second moiety -AB may be stable. Alternatively, in case a moiety -D- comprises two moieties -AB, the linkage between -D- and both moieties -AB may be stable.

15

In certain embodiments -AB is of formula (A):

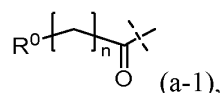


wherein

the dashed line indicates attachment to -D-;

20

-F⁰ is of formula (a-1)

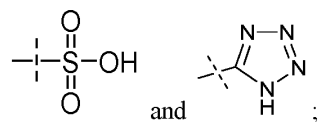


wherein

the dashed line indicates attachment to -L^A-;

-R⁰ is selected from the group consisting of -CR¹R^{1a}R^{1b}, -COOR¹,

25

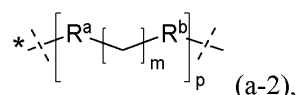


-R¹, -R^{1a} and -R^{1b} are selected from the group consisting of -H, methyl, ethyl, propyl and isopropyl;

n is an integer ranging from and including 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 and 22;

30

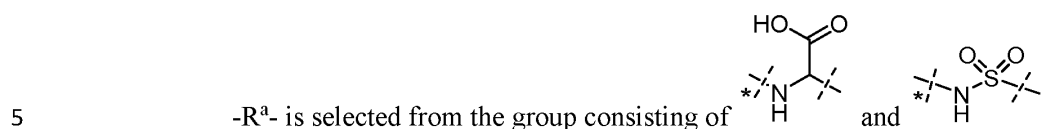
-L^A- is absent or is of formula (a-2)



wherein

the unmarked dashed line indicates attachment to $-\text{L}^B$ -;

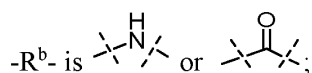
the dashed line marked with the asterisk indicates attachment to $-\text{F}^0$;



wherein

the dashed line marked with the asterisk indicates attachment to $-\text{F}^0$;

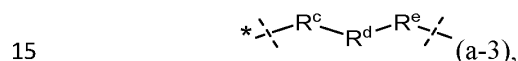
the unmarked dashed line indicates attachment to the remainder of $-\text{L}^A$;



10 m is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10

p is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;

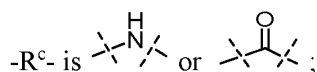
$-\text{L}^B$ - is absent or is of formula (a-3)



wherein

the unmarked dashed line indicates attachment to $-\text{D}$ -;

the dashed line marked with the asterisk indicates attachment to $-\text{L}^A$;

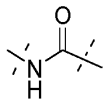


20 $-\text{R}^d$ - is selected from the group consisting of C_{1-50} alkyl, C_{2-50} alkenyl and C_{2-50} alkynyl, wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl may be substituted with one or more $-\text{R}^1$, which may be the same or different, and which C_{1-50} alkyl, C_{2-50} alkenyl or C_{2-50} alkynyl may be interrupted by one or more groups selected from the group consisting of $-\text{T}$ -, $-\text{C}(\text{O})\text{O}$ -, $-\text{O}$ -, $-\text{C}(\text{O})$ -,
 25 $-\text{C}(\text{O})\text{N}(\text{R}^2)$ -, $-\text{S}(\text{O})_2\text{N}(\text{R}^2)$ -, $-\text{S}(\text{O})\text{N}(\text{R}^2)$ -, $-\text{S}(\text{O})_2$ -, $-\text{S}(\text{O})$ -,
 $-\text{N}(\text{R}^2)\text{S}(\text{O})_2\text{N}(\text{R}^{2a})$ -, $-\text{S}$ -, $-\text{N}(\text{R}^2)$ -, $-\text{OC}(\text{OR}^2)(\text{R}^{2a})$ -, $-\text{N}(\text{R}^2)\text{C}(\text{O})\text{N}(\text{R}^{2a})$ -,
 and $-\text{OC}(\text{O})\text{N}(\text{R}^2)$ -;

each -T- is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each -T- may independently be substituted with one or more -R¹, which may be the same or different;

each -R¹ is independently selected from the group consisting of halogen, -CN, oxo (=O), -COOR³, -OR³, -C(O)R³, -C(O)N(R³R^{3a}), -S(O)₂N(R³R^{3a}), -S(O)N(R³R^{3a}), -S(O)₂R³, -S(O)R³, -N(R³)S(O)₂N(R^{3a}R^{3b}), -SR³, -N(R³R^{3a}), -NO₂, -OC(O)R³, -N(R³)C(O)R^{3a}, -N(R³)S(O)₂R^{3a}, -N(R³)S(O)R^{3a}, -N(R³)C(O)OR^{3a}, -N(R³)C(O)N(R^{3a}R^{3b}), -OC(O)N(R³R^{3a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different;

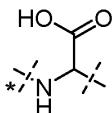
each -R², -R^{2a}, -R³, -R^{3a} and -R^{3b} is independently selected from the group consisting of -H, and C₁₋₆ alkyl, wherein C₁₋₆ alkyl may be substituted with one or more halogen, which may be the same or different; and

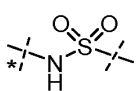
-R^c- is selected from the group consisting of -CH₂-,  and .

If -R^b- is  and -L^B- is not absent, then -R^c- is  and if -R^b- is  and -L^B- is

not absent, then -R^c- is .

In certain embodiments -L^A- is of formula (a-2), i.e., is not absent. In certain embodiments -L^A- is absent.

In certain embodiments -R^a- is , wherein the dashed line marked with the asterisk indicates attachment to -F⁰ and the unmarked dashed line indicates attachment to the remainder of -L^A-.

In certain embodiments $-R^a-$ is , wherein the dashed line marked with the asterisk indicates attachment to $-F^0$ and the unmarked dashed line indicates attachment to the remainder of $-L^A-$.

5 In certain embodiments $-R^b-$ is . In certain embodiments $-R^b-$ is .

In certain embodiments m of formula (a-2) is 1. In certain embodiments m of formula (a-2) is 2. In certain embodiments m of formula (a-2) is 3. In certain embodiments m of formula (a-2) is 4. In certain embodiments m of formula (a-2) is 5. In certain embodiments m of formula (a-2) is 6. In certain embodiments m of formula (a-2) is 7. In certain embodiments m of formula (a-2) is 8. In certain embodiments m of formula (a-2) is 9. In certain embodiments m of formula (a-2) is 10.

In certain embodiments p of formula (a-2) is 1. In certain embodiments p of formula (a-2) is 2. In certain embodiments p of formula (a-2) is 3. In certain embodiments p of formula (a-2) is 4. In certain embodiments p of formula (a-2) is 5. In certain embodiments p of formula (a-2) is 6. In certain embodiments p of formula (a-2) is 7. In certain embodiments p of formula (a-2) is 8. In certain embodiments p of formula (a-2) is 9. In certain embodiments p of formula (a-2) is 10.

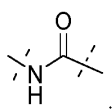
20

In certain embodiments $-L^B-$ is of formula (a-3). In certain embodiments $-L^B-$ is absent. If $-L^B-$ is absent, the unmarked dashed line in formula (a-2) indicates attachment to $-D-$.

25

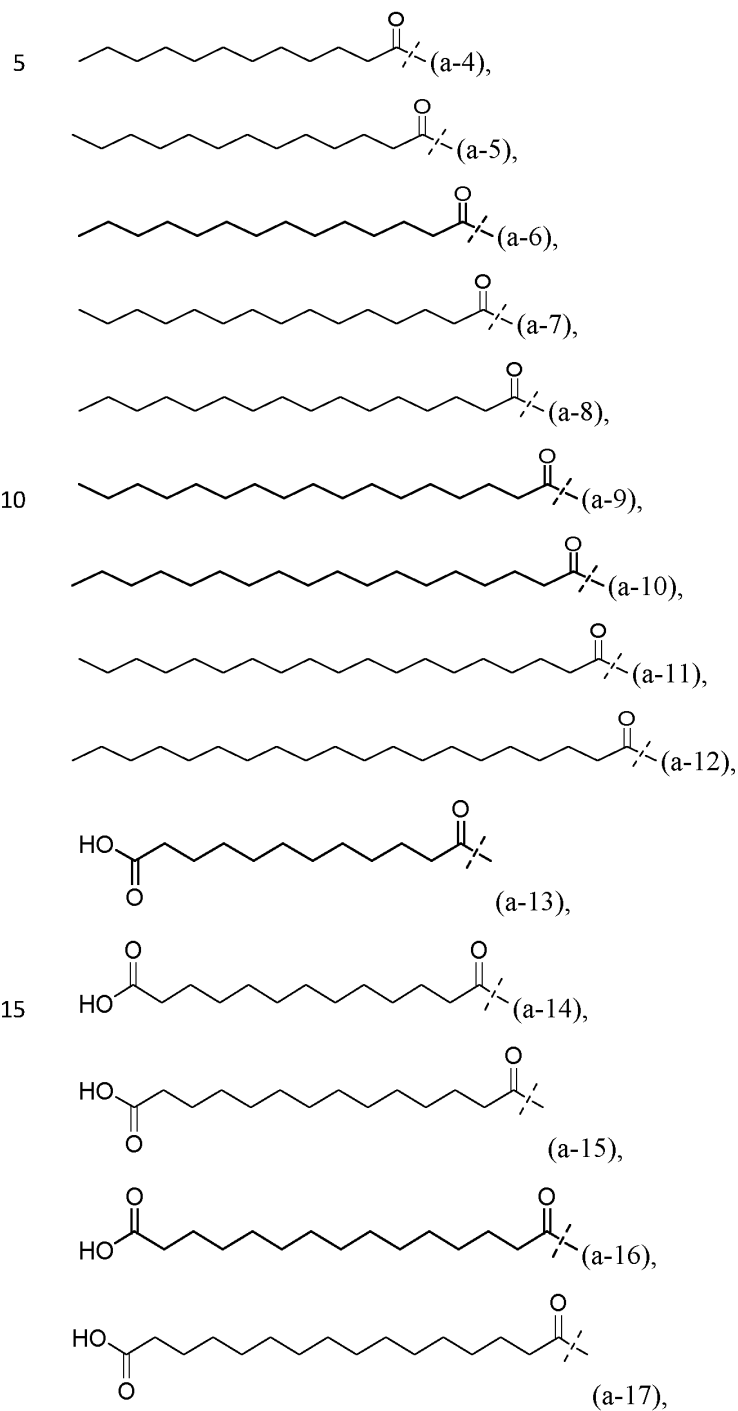
In certain embodiments $-R^c-$ is . In certain embodiments $-R^c-$ is .

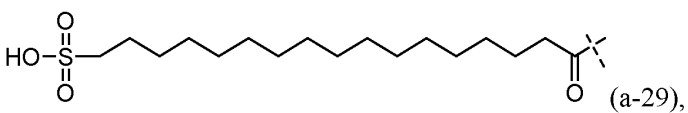
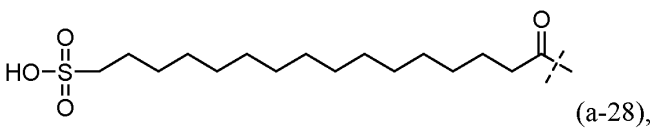
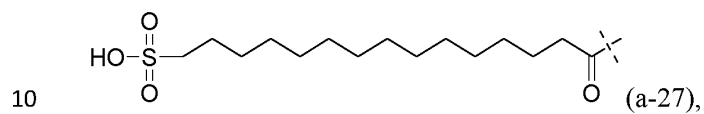
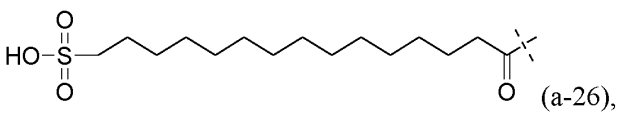
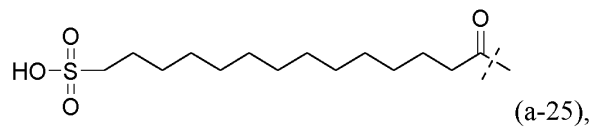
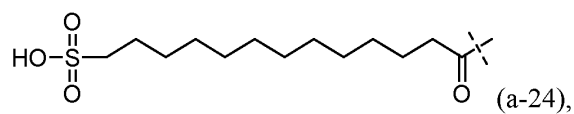
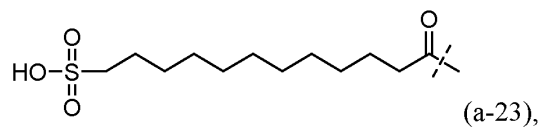
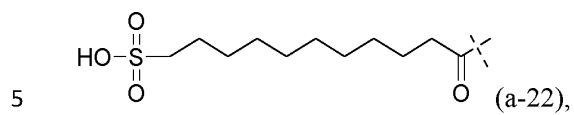
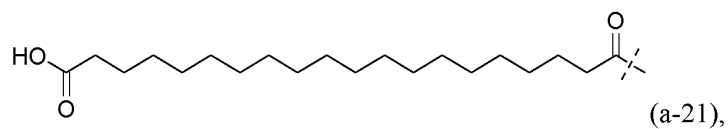
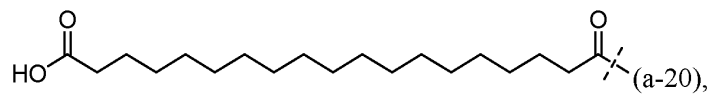
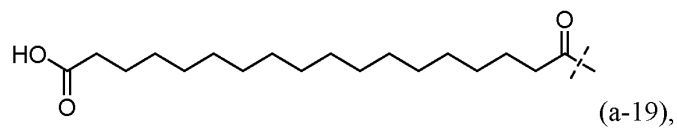
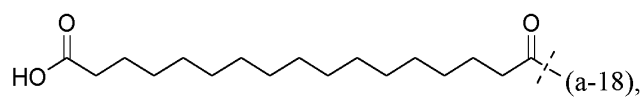
In certain embodiments $-R^e-$ is $-\text{CH}_2-$. In certain embodiments $-R^e-$ is . In certain

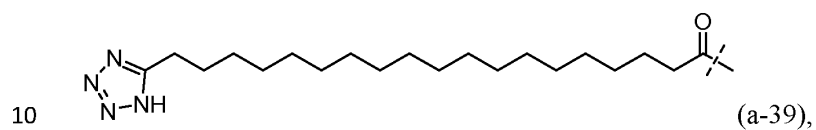
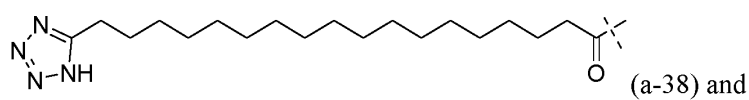
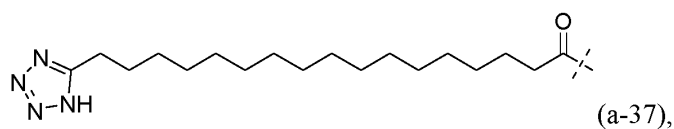
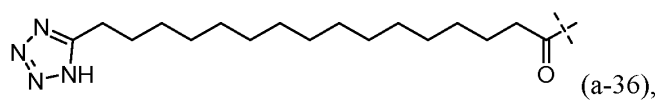
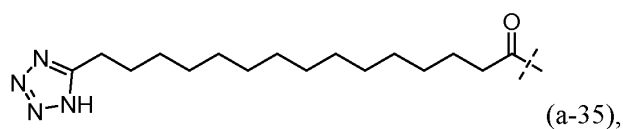
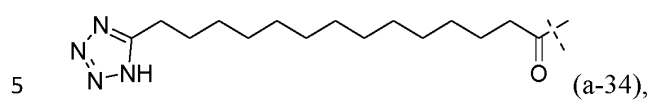
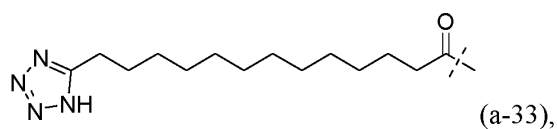
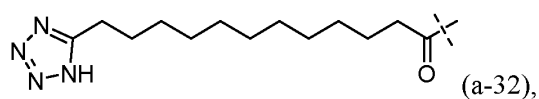
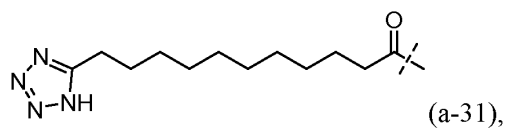
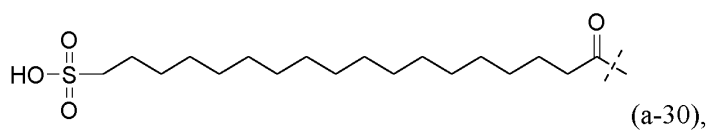
embodiments $-R^e-$ is .

In certain embodiments both $-L^A-$ and $-L^B-$ are absent. If both $-L^A-$ and $-L^B-$ are absent, the dashed line in formula (a-1) indicates attachment to $-D-$.

In certain embodiments $-F^0$ is selected from the group consisting of







wherein dashed lines indicate attachment to $-L^A-$.

If $-L^A-$ is absent, the dashed line in formulas (a-4) to (a-39) indicates attachment to $-L^B-$. If both $-L^A-$ and $-L^B-$ are absent, the dashed line in formulas (a-4) to (a-39) indicates attachment

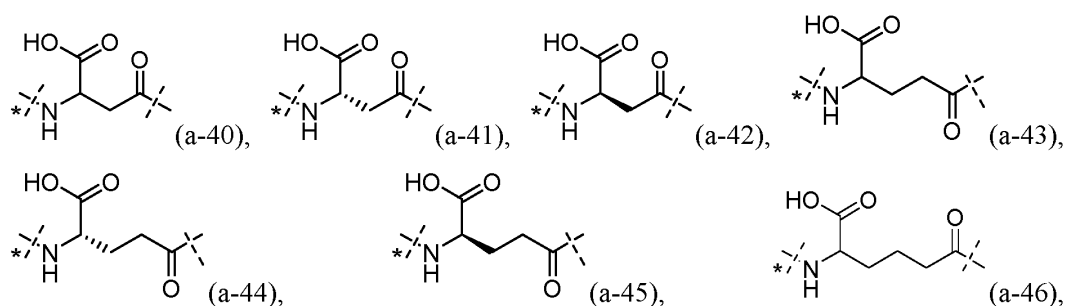
15 to $-D-$.

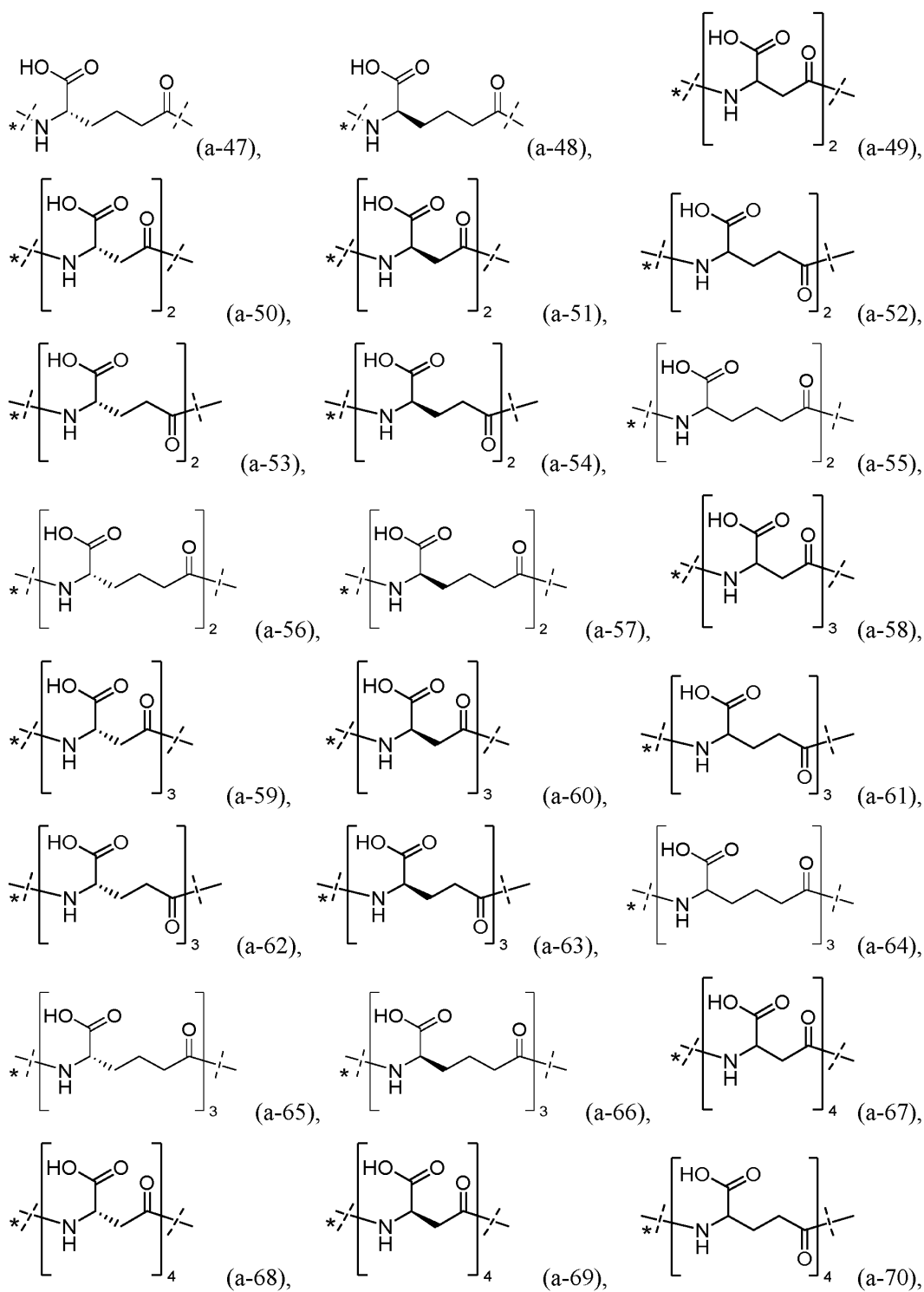
In certain embodiments -F⁰ is of formula (a-4). In certain embodiments -F⁰ is of formula (a-5). In certain embodiments -F⁰ is of formula (a-6). In certain embodiments -F⁰ is of formula (a-7). In certain embodiments -F⁰ is of formula (a-8). In certain embodiments -F⁰ is of formula (a-9). In certain embodiments -F⁰ is of formula (a-10). In certain embodiments -F⁰ is of formula (a-11). In certain embodiments -F⁰ is of formula (a-12). In certain embodiments -F⁰ is of formula (a-13). In certain embodiments -F⁰ is of formula (a-14). In certain embodiments -F⁰ is of formula (a-15). In certain embodiments -F⁰ is of formula (a-16). In certain embodiments -F⁰ is of formula (a-17). In certain embodiments -F⁰ is of formula (a-18). In certain embodiments -F⁰ is of formula (a-19). In certain embodiments -F⁰ is of formula (a-20). In certain embodiments -F⁰ is of formula (a-21). In certain embodiments -F⁰ is of formula (a-22). In certain embodiments -F⁰ is of formula (a-23). In certain embodiments -F⁰ is of formula (a-24). In certain embodiments -F⁰ is of formula (a-25). In certain embodiments -F⁰ is of formula (a-26). In certain embodiments -F⁰ is of formula (a-27). In certain embodiments -F⁰ is of formula (a-28). In certain embodiments -F⁰ is of formula (a-29). In certain embodiments -F⁰ is of formula (a-30). In certain embodiments -F⁰ is of formula (a-31). In certain embodiments -F⁰ is of formula (a-32). In certain embodiments -F⁰ is of formula (a-33). In certain embodiments -F⁰ is of formula (a-34). In certain embodiments -F⁰ is of formula (a-35). In certain embodiments -F⁰ is of formula (a-36). In certain embodiments -F⁰ is of formula (a-37). In certain embodiments -F⁰ is of formula (a-38). In certain embodiments -F⁰ is of formula (a-39).

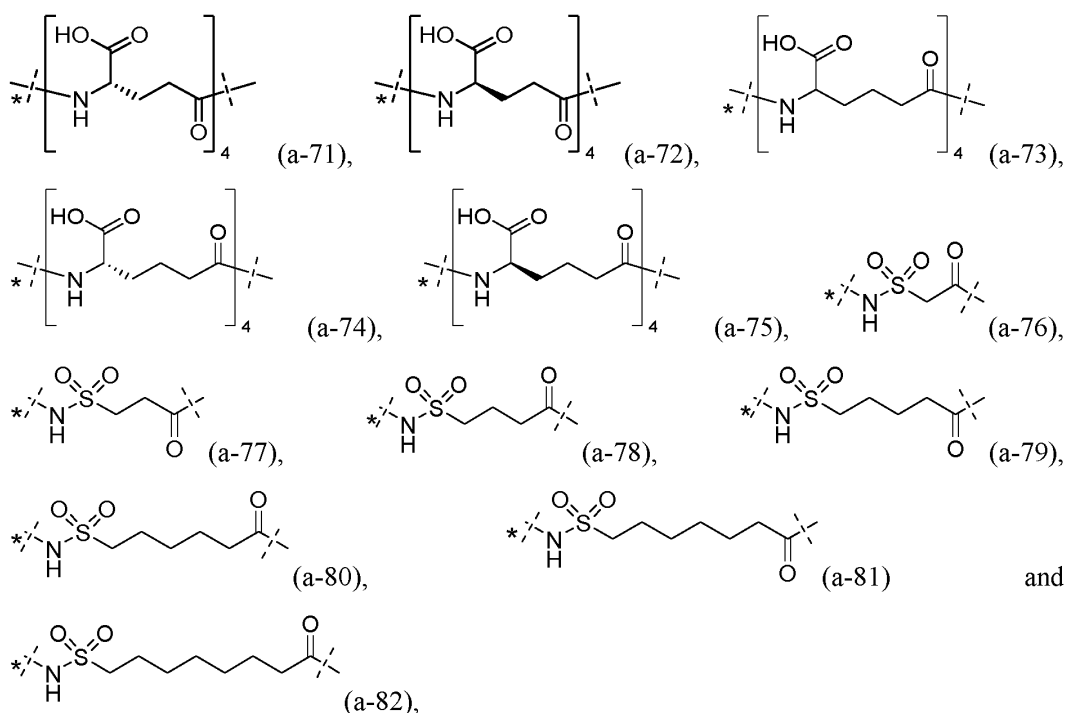
In certain embodiments $-F^0$ is of formula (a-4) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-5) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-6) and both $-L^A$ - and $-L^B$ - are absent. In certain
25 embodiments $-F^0$ is of formula (a-7) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-8) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-9) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-10) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-11) and both $-L^A$ - and $-L^B$ - are absent. In certain
30 embodiments $-F^0$ is of formula (a-12) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-13) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-14) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-15) and both $-L^A$ - and $-L^B$ - are absent. In certain
embodiments $-F^0$ is of formula (a-16) and both $-L^A$ - and $-L^B$ - are absent. In certain

embodiments $-F^0$ is of formula (a-17) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-18) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-19) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-20) and both $-L^A-$ and $-L^B-$ are absent. In certain
5 embodiments $-F^0$ is of formula (a-21) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-22) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-23) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-24) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-25) and both $-L^A-$ and $-L^B-$ are absent. In certain
10 embodiments $-F^0$ is of formula (a-26) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-27) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-28) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-29) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-30) and both $-L^A-$ and $-L^B-$ are absent. In certain
15 embodiments $-F^0$ is of formula (a-31) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-32) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-33) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-34) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-35) and both $-L^A-$ and $-L^B-$ are absent. In certain
20 embodiments $-F^0$ is of formula (a-36) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-37) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-38) and both $-L^A-$ and $-L^B-$ are absent. In certain
embodiments $-F^0$ is of formula (a-39) and both $-L^A-$ and $-L^B-$ are absent.

25 In certain embodiments $-L^A-$ is selected from the group consisting of





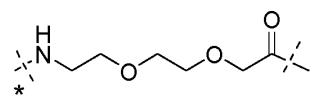


wherein a dashed line marked with an asterisk indicates attachment to $-F^0-$ and an unmarked dashed line indicates attachment to $-L^B-$. If $-L^B-$ is absent an unmarked dashed indicates attachment to $-D-$.

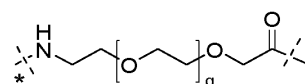
- 10 In certain embodiments $-L^A-$ is of formula (a-40). In certain embodiments $-L^A-$ is of formula (a-41). In certain embodiments $-L^A-$ is of formula (a-42). In certain embodiments $-L^A-$ is of formula (a-43). In certain embodiments $-L^A-$ is of formula (a-44). In certain embodiments $-L^A-$ is of formula (a-45). In certain embodiments $-L^A-$ is of formula (a-46). In certain embodiments $-L^A-$ is of formula (a-47). In certain embodiments $-L^A-$ is of formula (a-48). In certain embodiments $-L^A-$ is of formula (a-49). In certain embodiments $-L^A-$ is of formula (a-50). In certain embodiments $-L^A-$ is of formula (a-51). In certain embodiments $-L^A-$ is of formula (a-52). In certain embodiments $-L^A-$ is of formula (a-53). In certain embodiments $-L^A-$ is of formula (a-54). In certain embodiments $-L^A-$ is of formula (a-55). In certain embodiments $-L^A-$ is of formula (a-56). In certain embodiments $-L^A-$ is of formula (a-57). In certain embodiments $-L^A-$ is of formula (a-58). In certain embodiments $-L^A-$ is of formula (a-59). In certain embodiments $-L^A-$ is of formula (a-60). In certain embodiments $-L^A-$ is of formula (a-61). In certain embodiments $-L^A-$ is of formula (a-62). In certain embodiments $-L^A-$ is of formula (a-63). In certain embodiments $-L^A-$ is of formula (a-64). In certain embodiments $-L^A-$ is of formula (a-65). In certain

embodiments -L^A- is of formula (a-66). In certain embodiments -L^A- is of formula (a-67). In certain embodiments -L^A- is of formula (a-68). In certain embodiments -L^A- is of formula (a-69). In certain embodiments -L^A- is of formula (a-70). In certain embodiments -L^A- is of formula (a-71). In certain embodiments -L^A- is of formula (a-72). In certain
 5 embodiments -L^A- is of formula (a-73). In certain embodiments -L^A- is of formula (a-74). In certain embodiments -L^A- is of formula (a-75). In certain embodiments -L^A- is of formula (a-76). In certain embodiments -L^A- is of formula (a-77). In certain embodiments -L^A- is of formula (a-78). In certain embodiments -L^A- is of formula (a-79). In certain
 10 embodiments -L^A- is of formula (a-80). In certain embodiments -L^A- is of formula (a-81). In certain embodiments -L^A- is of formula (a-82).

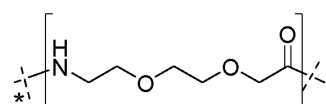
In certain embodiments -L^B- is selected from the group consisting of



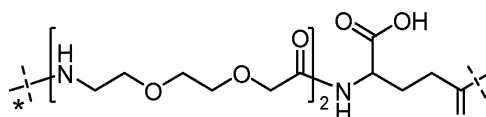
(a-83),



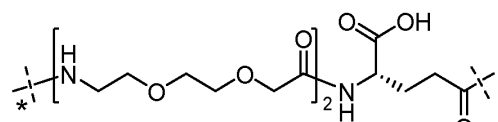
(a-84),



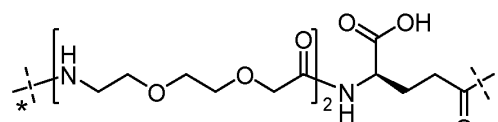
(a-85),



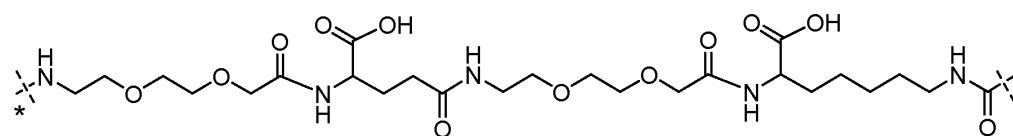
(a-86),



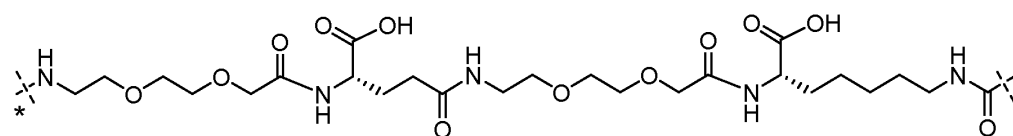
(a-87),



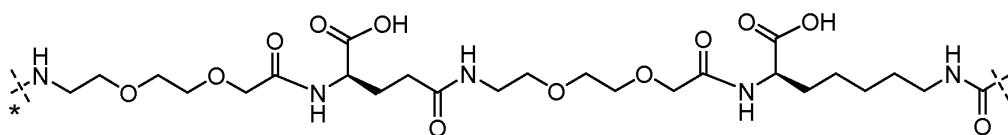
(a-88),



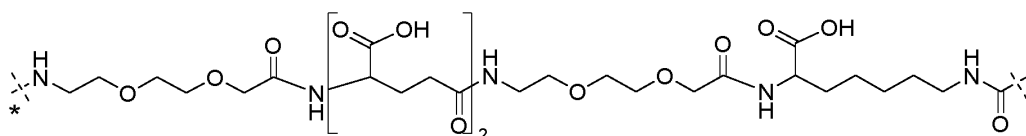
(a-89),



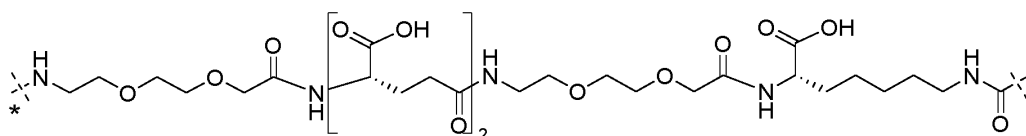
(a-90),



(a-91),

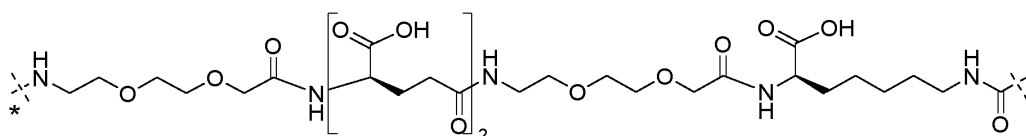


(a-92),



(a-93)

and



(a-94),

wherein

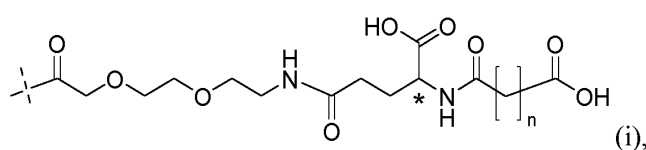
the dashed line marked with the asterisk indicates attachment to -L^A-;
the unmarked dashed line indicates attachment to -D-; and
q is an integer ranging from and including 2 to 50.

If -L^A- is absent, the dashed line marked with the asterisk in formulas (a-83) to (a-94) indicates attachment to -F⁰.

In certain embodiments q of formula (a-84) is an integer ranging from and including 3 to 45.
In certain embodiments q of formula (a-84) is an integer ranging from and including 4 to 40.
In certain embodiments q of formula (a-84) is an integer ranging from and including 5 to 35.
20 In certain embodiments q of formula (a-84) is an integer ranging from and including 6 to 30.
In certain embodiments q of formula (a-84) is an integer ranging from and including 7 to 25.
In certain embodiments q of formula (a-84) is an integer ranging from and including 10 to 20.
In certain embodiments q of formula (a-84) is 23.

In certain embodiments $-L^B$ - is of formula (a-83). In certain embodiments $-L^B$ - is of formula (a-84). In certain embodiments $-L^B$ - is of formula (a-84) with $q = 23$. In certain embodiments $-L^B$ - is of formula (a-85). In certain embodiments $-L^B$ - is of formula (a-86). In certain embodiments $-L^B$ - is of formula (a-87). In certain embodiments $-L^B$ - is of formula (a-88). In certain embodiments $-L^B$ - is of formula (a-89). In certain embodiments $-L^B$ - is of formula (a-90). In certain embodiments $-L^B$ - is of formula (a-91). In certain embodiments $-L^B$ - is of formula (a-92). In certain embodiments $-L^B$ - is of formula (a-93). In certain embodiments $-L^B$ - is of formula (a-94).

10 In certain embodiments -AB is of formula (i)



wherein the dashed line indicates attachment to $-D-$;

n is an integer ranging from and including 14 to 22; and

the stereocenter marked with the asterisk is either in S- or R-configuration.

15

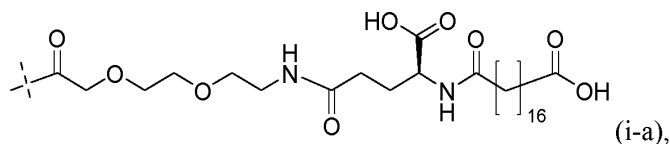
In certain embodiments -AB is of formula (i) and n is 14. In certain embodiments -AB is of formula (i) and n is 15. In certain embodiments -AB is of formula (i) and n is 16. In certain embodiments -AB is of formula (i) and n is 17. In certain embodiments -AB is of formula (i) and n is 18. In certain embodiments -AB is of formula (i) and n is 19. In certain embodiments -AB is of formula (i) and n is 20. In certain embodiments -AB is of formula (i) and n is 21. In certain embodiments -AB is of formula (i) and n is 22.

In certain embodiments -AB is of formula (i) and n is 14 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (i) and n is 15 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (i) and n is 16 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (i) and n is 17 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (i) and n is 18 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (i) and n is 19 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (i) and n is 20 and the stereocenter marked with the

asterisk is in R-configuration. In certain embodiments -AB is of formula (i) and n is 21 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (i) and n is 22 and the stereocenter marked with the asterisk is in R-configuration.

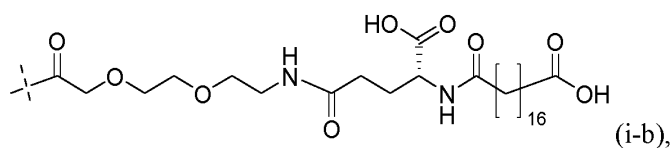
- 5 In certain embodiments -AB is of formula (i) and n is 14 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (i) and n is 15 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (i) and n is 16 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (i) and n is 17 and the stereocenter marked with the asterisk is in S-configuration.
- 10 asterisk is in S-configuration. In certain embodiments -AB is of formula (i) and n is 18 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (i) and n is 19 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (i) and n is 20 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (i) and n is 21 and the stereocenter marked with the asterisk is in S-configuration.
- 15 formula (i) and n is 22 and the stereocenter marked with the asterisk is in S-configuration.

In certain embodiments -AB is of formula (i-a):



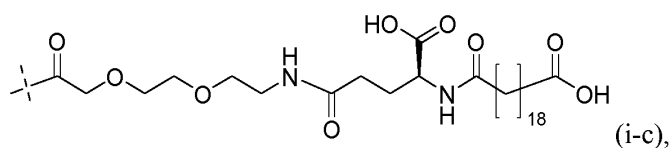
- 20 wherein
the dashed line indicates attachment to -D-.

In certain embodiments -AB is of formula (i-b):



- 25 wherein
the dashed line indicates attachment to -D-.

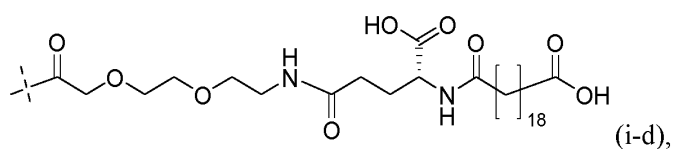
In certain embodiments -AB is of formula (i-c):



wherein

the dashed line indicates attachment to -D-.

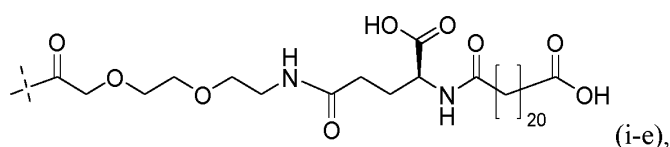
- 5 In certain embodiments -AB is of formula (i-d):



wherein

the dashed line indicates attachment to -D-.

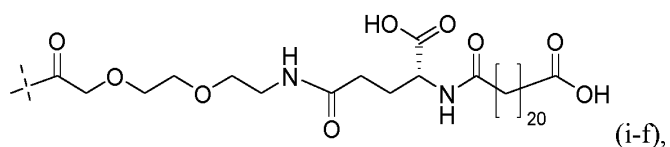
- 10 In certain embodiments -AB is of formula (i-e):



wherein

the dashed line indicates attachment to -D-.

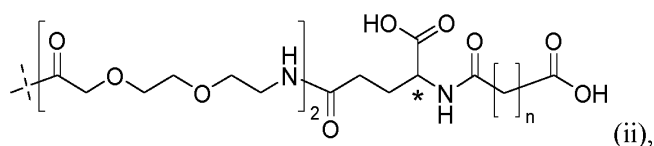
- 15 In certain embodiments -AB is of formula (i-f):



wherein

the dashed line indicates attachment to -D-.

- 20 In certain embodiments -AB is of formula (ii)



wherein the dashed line indicates attachment to -D-;

n is an integer ranging from 14 to 22; and
the stereocenter marked with the asterisk is either in S- or R-configuration.

5 In certain embodiments -AB is of formula (ii) and n is 14. In certain embodiments -AB is of formula (ii) and n is 15. In certain embodiments -AB is of formula (ii) and n is 16. In certain embodiments -AB is of formula (ii) and n is 17. In certain embodiments -AB is of formula (ii) and n is 18. In certain embodiments -AB is of formula (ii) and n is 19. In certain embodiments -AB is of formula (ii) and n is 20. In certain embodiments -AB is of formula (ii) and n is 21. In certain embodiments -AB is of formula (ii) and n is 22.

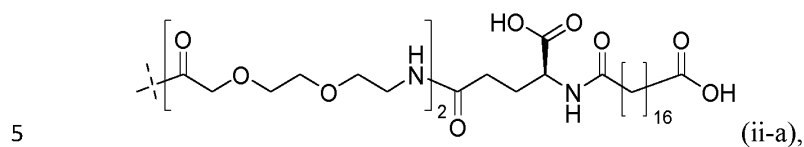
10

In certain embodiments -AB is of formula (ii) and n is 14 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (ii) and n is 15 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (ii) and n is 16 and the stereocenter marked with the asterisk is in R-configuration.
15 In certain embodiments -AB is of formula (ii) and n is 17 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (ii) and n is 18 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (ii) and n is 19 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (ii) and n is 20 and the stereocenter marked with the asterisk is in R-configuration.
20 In certain embodiments -AB is of formula (ii) and n is 21 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (ii) and n is 22 and the stereocenter marked with the asterisk is in R-configuration.

In certain embodiments -AB is of formula (ii) and n is 14 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (ii) and n is 15 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (ii) and n is 16 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (ii) and n is 17 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (ii) and n is 18 and the stereocenter marked with the asterisk is in S-configuration.
25 In certain embodiments -AB is of formula (ii) and n is 19 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (ii) and n is 20 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (ii) and n is 21 and the
30 In certain embodiments -AB is of formula (ii) and n is 22 and the stereocenter marked with the asterisk is in S-configuration.

stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (ii) and n is 22 and the stereocenter marked with the asterisk is in S-configuration.

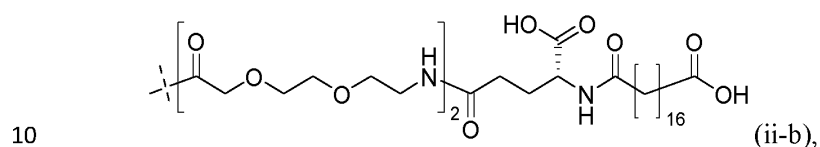
In certain embodiments -AB is of formula (ii-a):



wherein

the dashed line indicates attachment to -D-.

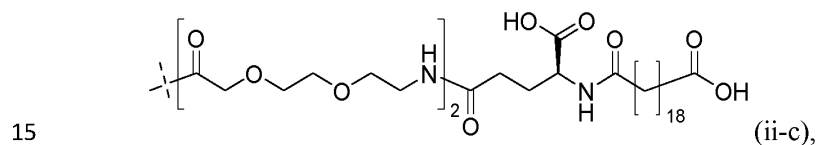
In certain embodiments -AB is of formula (ii-b):



wherein

the dashed line indicates attachment to -D-.

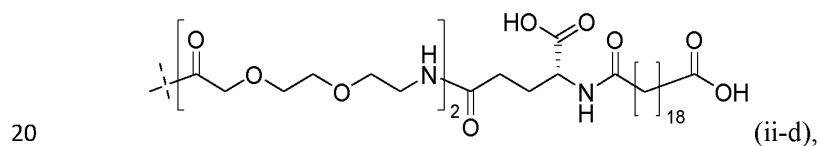
In certain embodiments -AB is of formula (ii-c):



wherein

the dashed line indicates attachment to -D-.

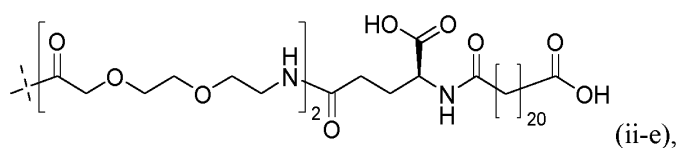
In certain embodiments -AB is of formula (ii-d):



wherein

the dashed line indicates attachment to -D-.

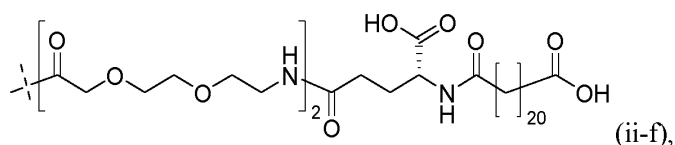
In certain embodiments -AB is of formula (ii-e):



wherein

the dashed line indicates attachment to -D-.

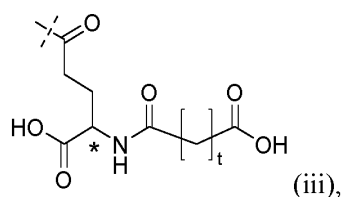
- 5 In certain embodiments -AB is of formula (ii-f):



wherein

the dashed line indicates attachment to -D-.

- 10 In certain embodiments -AB is of formula (iii)



wherein

the dashed line indicates attachment to -D-;

t is an integer ranging from and including 14 to 22; and

- 15 the stereocenter marked with the asterisk is either in S- or R-configuration.

- In certain embodiments -AB is of formula (iii) and t is 14. In certain embodiments -AB is of formula (iii) and t is 15. In certain embodiments -AB is of formula (iii) and t is 16. In certain embodiments -AB is of formula (iii) and t is 17. In certain embodiments -AB is of formula (iii) and t is 18. In certain embodiments -AB is of formula (iii) and t is 19. In certain embodiments -AB is of formula (iii) and t is 20. In certain embodiments -AB is of formula (iii) and t is 21. In certain embodiments -AB is of formula (iii) and t is 22.

- In certain embodiments -AB is of formula (iii) and t is 14 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (iii) and t is 15 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is

of formula (iii) and t is 16 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (iii) and t is 17 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (iii) and t is 18 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (iii) and t is 19 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (iii) and t is 20 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (iii) and t is 21 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (iii) and t is 22 and the stereocenter marked with the asterisk is in R-configuration.

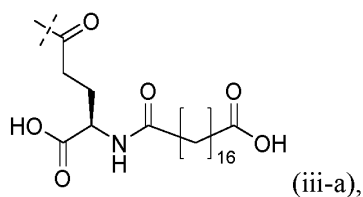
10

In certain embodiments -AB is of formula (iii) and t is 14 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (iii) and t is 15 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (iii) and t is 16 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (iii) and t is 17 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (iii) and t is 18 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (iii) and t is 19 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (iii) and t is 20 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (iii) and t is 21 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (iii) and t is 22 and the stereocenter marked with the asterisk is in S-configuration.

20

In certain embodiments -AB is of formula (iii-a)

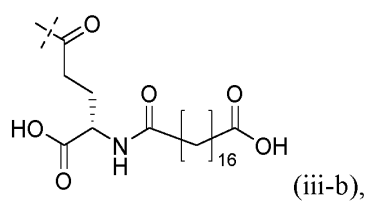
25



wherein

the dashed line indicates attachment to -D-.

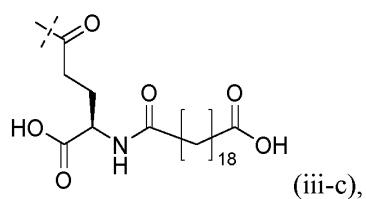
In certain embodiments -AB is of formula (iii-b)



wherein

the dashed line indicates attachment to -D-;

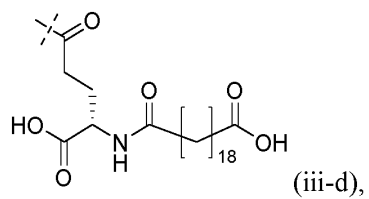
- 5 In certain embodiments -AB is of formula (iii-c)



wherein

the dashed line indicates attachment to -D-.

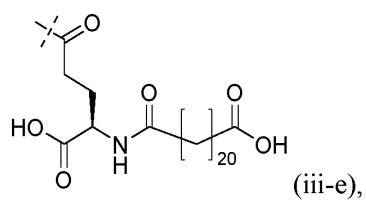
- 10 In certain embodiments -AB is of formula (iii-d)



wherein

the dashed line indicates attachment to -D-.

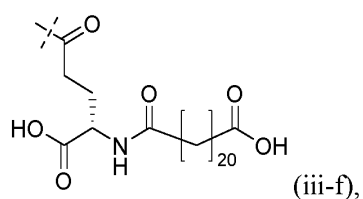
- 15 In certain embodiments -AB is of formula (iii-e)



wherein

the dashed line indicates attachment to -D-.

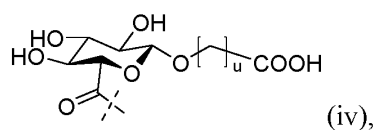
- 20 In certain embodiments -AB is of formula (iii-f)



wherein

the dashed line indicates attachment to -D-.

- 5 In certain embodiments -AB is of formula (iv)



wherein

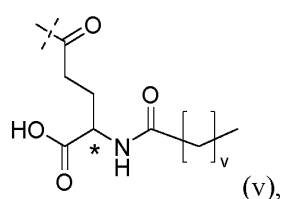
the dashed line indicates attachment to -D-, and

u is an integer ranging from and including 14 to 22.

10

- In certain embodiments -AB is of formula (iv) and u is 14. In certain embodiments -AB is of formula (iv) and u is 15. In certain embodiments -AB is of formula (iv) and u is 16. In certain embodiments -AB is of formula (iv) and u is 17. In certain embodiments -AB is of formula (iv) and u is 18. In certain embodiments -AB is of formula (iv) and u is 19. In certain
- 15 embodiments -AB is of formula (iv) and u is 20. In certain embodiments -AB is of formula (iv) and u is 21. In certain embodiments -AB is of formula (iv) and u is 22.

In certain embodiments -AB is of formula (v)



20

wherein

the dashed line indicates attachment to -D-;

v is an integer ranging from and including 14 to 22; and

the stereocenter marked with the asterisk is either in S- or R-configuration.

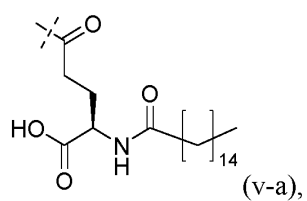
In certain embodiments -AB is of formula (v) and v is 14. In certain embodiments -AB is of formula (v) and v is 15. In certain embodiments -AB is of formula (v) and v is 16. In certain embodiments -AB is of formula (v) and v is 17. In certain embodiments -AB is of formula (v) and v is 18. In certain embodiments -AB is of formula (v) and v is 19. In certain
5 embodiments -AB is of formula (v) and v is 20. In certain embodiments -AB is of formula (v) and v is 21. In certain embodiments -AB is of formula (v) and v is 22.

In certain embodiments -AB is of formula (v) and v is 14 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (v) and v is 15 and
10 the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (v) and v is 16 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (v) and v is 17 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (v) and v is 18 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is
15 of formula (v) and v is 19 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (v) and v is 20 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (v) and v is 21 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (v) and v is 22 and the stereocenter marked with the asterisk is in R-configuration.

20

In certain embodiments -AB is of formula (v) and v is 14 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (v) and v is 15 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (v) and v is 16 and the stereocenter marked with the asterisk is in S-configuration. In
25 certain embodiments -AB is of formula (v) and v is 17 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (v) and v is 18 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (v) and v is 19 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (v) and v is 20 and the stereocenter marked with the
30 asterisk is in S-configuration. In certain embodiments -AB is of formula (v) and v is 21 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (v) and v is 22 and the stereocenter marked with the asterisk is in S-configuration.

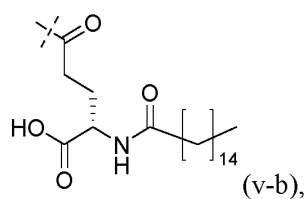
In certain embodiments -AB is of formula (v-a)



wherein

the dashed line indicates attachment to -D-.

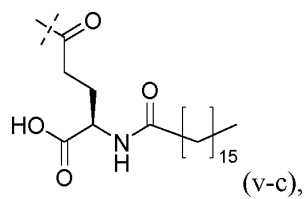
- 5 In certain embodiments -AB is of formula (v-b)



wherein

the dashed line indicates attachment to -D-;

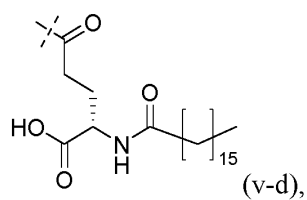
- 10 In certain embodiments -AB is of formula (v-c)



wherein

the dashed line indicates attachment to -D-.

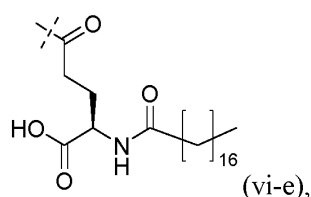
- 15 In certain embodiments -AB is of formula (v-d)



wherein

the dashed line indicates attachment to -D-.

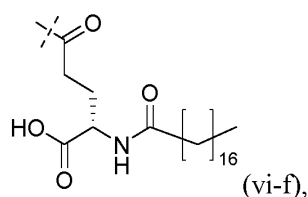
- 20 In certain embodiments -AB is of formula (vi-e)



wherein

the dashed line indicates attachment to -D-.

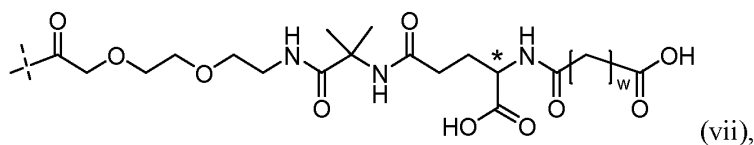
- 5 In certain embodiments -AB is of formula (vi-f)



wherein

the dashed line indicates attachment to -D-.

- 10 In certain embodiments -AB is of formula (vii)



wherein the dashed line indicates attachment to -D-;

w is an integer ranging from and including 14 to 22; and

the stereocenter marked with the asterisk is either in S- or R-configuration.

15

- In certain embodiments -AB is of formula (vii) and w is 14. In certain embodiments -AB is of formula (vii) and w is 15. In certain embodiments -AB is of formula (vii) and w is 16. In certain embodiments -AB is of formula (vii) and w is 17. In certain embodiments -AB is of formula (vii) and w is 18. In certain embodiments -AB is of formula (vii) and w is 19. In certain
- 20 embodiments -AB is of formula (vii) and w is 20. In certain embodiments -AB is of formula (vii) and w is 21. In certain embodiments -AB is of formula (vii) and w is 22.

- In certain embodiments -AB is of formula (vii) and w is 14 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (vii) and w is 15
- 25 and the stereocenter marked with the asterisk is in R-configuration. In certain

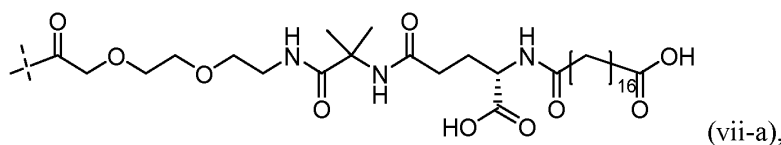
embodiments -AB is of formula (vii) and w is 16 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (vii) and w is 17 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (vii) and w is 18 and the stereocenter marked with the asterisk is in R-configuration.

- 5 In certain embodiments -AB is of formula (vii) and w is 19 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (vii) and w is 20 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (vii) and w is 21 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (vii) and w is 22 and the stereocenter marked with the asterisk is in R-configuration.
- 10

- In certain embodiments -AB is of formula (vii) and w is 14 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (vii) and w is 15 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (vii) and w is 16 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (vii) and w is 17 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (vii) and w is 18 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (vii) and w is 19 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (vii) and w is 20 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (vii) and w is 21 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (vii) and w is 22 and the stereocenter marked with the asterisk is in S-configuration.
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- 20

25

In certain embodiments -AB is of formula (vii-a):

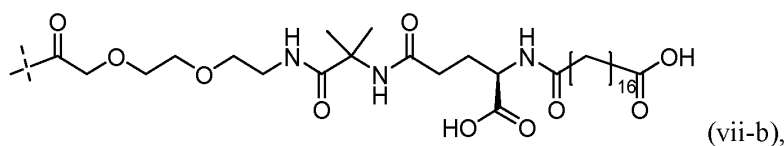


wherein

the dashed line indicates attachment to -D-.

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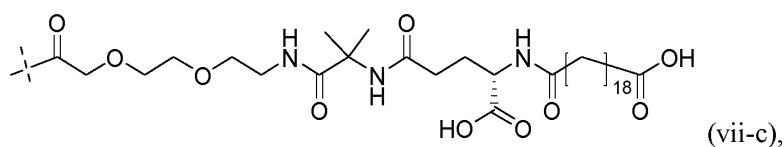
In certain embodiments -AB is of formula (vii-b):



wherein

the dashed line indicates attachment to -D-.

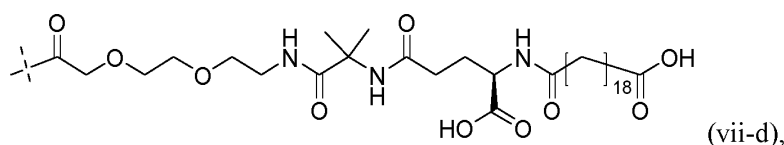
- 5 In certain embodiments -AB is of formula (vii-c):



wherein

the dashed line indicates attachment to -D-.

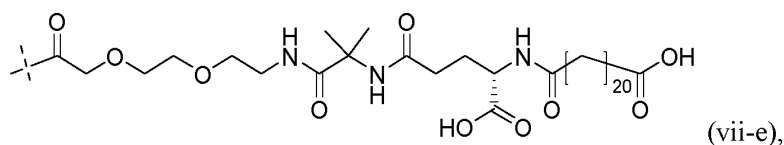
- 10 In certain embodiments -AB is of formula (vii-d):



wherein

the dashed line indicates attachment to -D-.

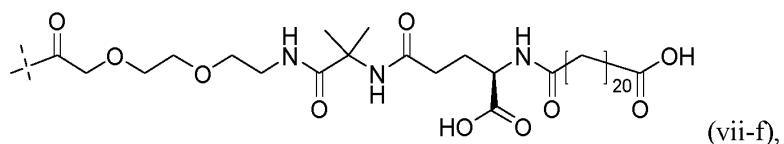
- 15 In certain embodiments -AB is of formula (vii-e):



wherein

the dashed line indicates attachment to -D-.

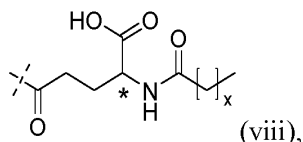
- 20 In certain embodiments -AB is of formula (vii-f):



wherein

the dashed line indicates attachment to -D-.

In certain embodiments -AB is of formula (viii)



- 5 wherein the dashed line indicates attachment to -D-;
w is an integer ranging from and including 14 to 22; and
the stereocenter marked with the asterisk is either in S- or R-configuration.

10 In certain embodiments -AB is of formula (viii) and x is 14. In certain embodiments -AB is of formula (viii) and x is 15. In certain embodiments -AB is of formula (viii) and x is 16. In certain embodiments -AB is of formula (viii) and x is 17. In certain embodiments -AB is of formula (viii) and x is 18. In certain embodiments -AB is of formula (viii) and x is 19. In certain embodiments -AB is of formula (viii) and x is 20. In certain embodiments -AB is of formula (viii) and x is 21. In certain embodiments -AB is of formula (viii) and x is 22.

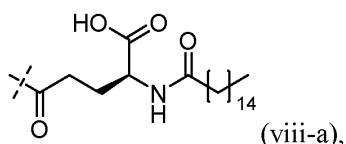
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In certain embodiments -AB is of formula (viii) and x is 14 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (viii) and x is 15 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (viii) and x is 16 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (viii) and x is 17 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (viii) and x is 18 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (viii) and x is 19 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (viii) and x is 20 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (viii) and x is 21 and the stereocenter marked with the asterisk is in R-configuration. In certain embodiments -AB is of formula (viii) and x is 22 and the stereocenter marked with the asterisk is in R-configuration.

30 In certain embodiments -AB is of formula (viii) and x is 14 and the stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of formula (viii) and x is 15

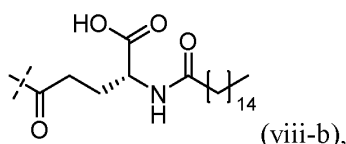
and the stereocenter marked with the asterisk is in S-configuration. In certain
embodiments -AB is of formula (viii) and x is 16 and the stereocenter marked with the asterisk
is in S-configuration. In certain embodiments -AB is of formula (viii) and x is 17 and the
stereocenter marked with the asterisk is in S-configuration. In certain embodiments -AB is of
5 formula (viii) and x is 18 and the stereocenter marked with the asterisk is in S-configuration.
In certain embodiments -AB is of formula (viii) and x is 19 and the stereocenter marked with
the asterisk is in S-configuration. In certain embodiments -AB is of formula (viii) and x is 20
and the stereocenter marked with the asterisk is in S-configuration. In certain
embodiments -AB is of formula (viii) and x is 21 and the stereocenter marked with the asterisk
10 is in S-configuration. In certain embodiments -AB is of formula (viii) and x is 22 and the
stereocenter marked with the asterisk is in S-configuration.

In certain embodiments -AB is of formula (viii-a)



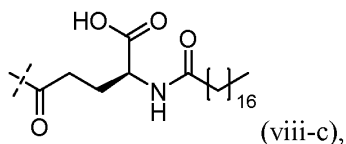
15 wherein the dashed line indicates attachment to -D-.

In certain embodiments -AB is of formula (viii-b)



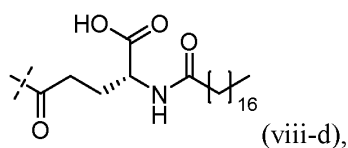
20 wherein the dashed line indicates attachment to -D-.

In certain embodiments -AB is of formula (viii-c)



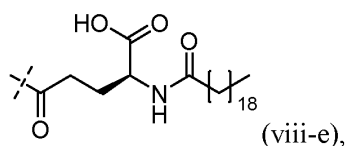
25 wherein the dashed line indicates attachment to -D-.

In certain embodiments -AB is of formula (viii-d)



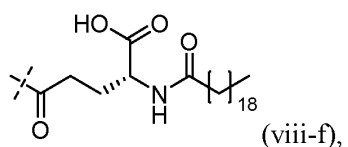
wherein the dashed line indicates attachment to -D-.

In certain embodiments -AB is of formula (viii-e)



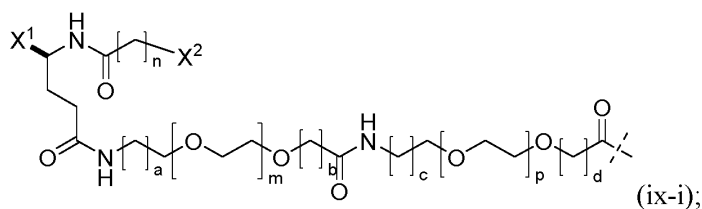
wherein the dashed line indicates attachment to -D-.

In certain embodiments -AB is of formula (viii-f)

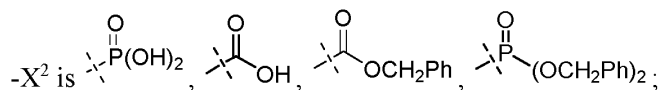
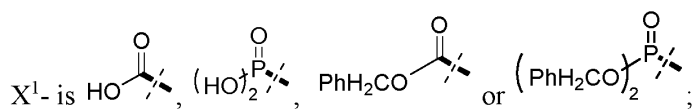


wherein the dashed line indicates attachment to -D-.

In certain embodiments -AB is of formula (ix-i)



wherein



with Ph being phenyl,

a is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

b is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

d is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

m is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10;

n is 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 or 24 ;

p is 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10.

- 5 In certain embodiments -AB is of formula (ix-i) with a being 1, b being 1, c being 1, d being 1, m being 1, n being 18 and m being 1.

In certain embodiments -AB is of formula (ix-i) and X^1 - is $\text{HO}-\text{C}(=\text{O})-$ and $-X^2$ is $-\text{P}(\text{OH})_2$. In

certain embodiments -AB is of formula (ix-i) and X^1 - is $\text{PhH}_2\text{CO}-\text{C}(=\text{O})-$ and $-X^2$ is

$-\text{P}(\text{O})(\text{OCH}_2\text{Ph})_2$. In certain embodiments -AB is of formula (ix-i) and X^1 - is $\text{PhH}_2\text{CO}-\text{C}(=\text{O})-$

- 10 and $-X^2$ is $-\text{P}(\text{OH})_2$. In certain embodiments -AB is of formula (ix-i) and X^1 - is $\text{HO}-\text{C}(=\text{O})-$ and $-X^2$

is $-\text{P}(\text{O})(\text{OCH}_2\text{Ph})_2$. In certain embodiments -AB is of formula (ix-i) and X^1 - is $(\text{PhH}_2\text{CO})_2-\text{P}(=\text{O})-$

and $-X^2$ is $-\text{C}(=\text{O})\text{OCH}_2\text{Ph}$. In certain embodiments -AB is of formula (ix-i) and X^1 - is

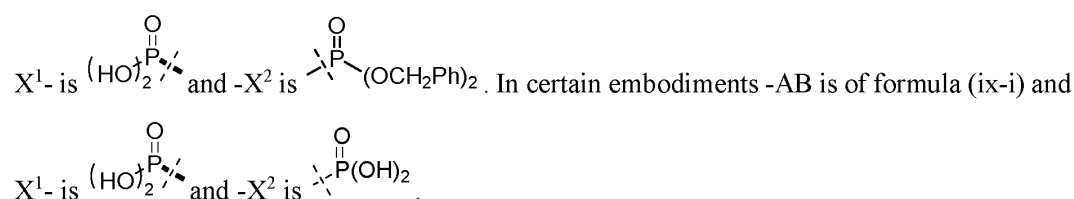
$(\text{PhH}_2\text{CO})_2-\text{P}(=\text{O})-$ and $-X^2$ is $-\text{C}(=\text{O})\text{OH}$. In certain embodiments -AB is of formula (ix-i) and X^1 - is

$(\text{HO})_2-\text{P}(=\text{O})-$ and $-X^2$ is $-\text{C}(=\text{O})\text{OCH}_2\text{Ph}$. In certain embodiments -AB is of formula (ix-i) and X^1 - is

- 15 $(\text{HO})_2-\text{P}(=\text{O})-$ and $-X^2$ is $-\text{C}(=\text{O})\text{OH}$. In certain embodiments -AB is of formula (ix-i) and X^1 - is

$(\text{PhH}_2\text{CO})_2-\text{P}(=\text{O})-$ and $-X^2$ is $-\text{P}(\text{O})(\text{OCH}_2\text{Ph})_2$. In certain embodiments -AB is of formula (ix-i) and

X^1 - is $(\text{PhH}_2\text{CO})_2-\text{P}(=\text{O})-$ and $-X^2$ is $-\text{P}(\text{OH})_2$. In certain embodiments -AB is of formula (ix-i) and



In certain embodiments -AB is a peptidic albumin-binding moiety.

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If -D- is a peptide or protein drug moiety, such peptidic moiety -AB may be fused to the N- or C-terminus of -D-, either directly or with a peptidic spacer between -D- and -AB.

In certain embodiments -AB is selected from the group consisting of

10 WVEQDRDWDFDVFGGGTP (SEQ ID NO:34);

DICLPRWGCLW (SEQ ID NO:35),

wherein the cysteines at position 3 and 9 are connected via a disulfide bridge;

RLIEDICLPRWGCLWEDD (SEQ ID NO:36),

wherein the cysteines at position 7 and 13 are connected via a disulfide bridge;

15 LAEAKVLANRELDKYGVSDFYKRLINKAKTVEGVEALKLHILAALP (SEQ ID NO:37);

IAEAKAANAELDSYGVSDFYKRLIDKAKTVEGVEALKDAILAALP (SEQ ID NO:38);

and

X_1EYEX_2EYE (SEQ ID NO:39),

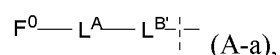
wherein X_1 is fluorescein-(AEEA), X_2 is K(palmitate), and AEEA is 2-(2-(2-aminoethoxy)acetyl.

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In certain embodiments -AB is of SEQ ID NO:34. In certain embodiments -AB is of SEQ ID NO:35. In certain embodiments -AB is of SEQ ID NO:36. In certain embodiments -AB is of SEQ ID NO:37. In certain embodiments -AB is of SEQ ID NO:38. In certain embodiments -AB is of SEQ ID NO:39.

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In certain embodiments -AB is of formula (A-a):



wherein

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the dashed line indicates attachment to -D-;

$-F^0$ and $-L^A$ are used as defined in formula (A),

-L^{B'} - is a polymeric moiety.

The moiety -L^{B'} - is a polymeric moiety, meaning that it comprises at least one polymer moiety. In certain embodiments the one or more polymer moiety has a molecular weight of at least 450 Da. In certain embodiments the one or more polymer moiety has a molecular weight of at least 1 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of at least 1.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of at least 2 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of at least 2.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of at least 3 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of at least 3.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of at least 4 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of at least 5 kDa. In certain embodiments the one or more polymer moiety has a maximum molecular weight of 160 kDa. In certain embodiments the one or more polymer moiety has a maximum molecular weight of 120 kDa. In certain embodiments the one or more polymer moiety has a maximum molecular weight of 100 kDa. In certain embodiments the one or more polymer moiety has a maximum molecular weight of 80 kDa. In certain embodiments the one or more polymer moiety has a maximum molecular weight of 70 kDa. In certain embodiments the one or more polymer moiety has a maximum molecular weight of 60 kDa. In certain embodiments the one or more polymer moiety has a maximum molecular weight of 50 kDa. In certain embodiments the one or more polymer moiety has a maximum molecular weight of 40 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 450 Da. In certain embodiments the one or more polymer moiety has a molecular weight of about 1 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 1.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 2 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 2.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 3 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 3.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 4 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 4.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 5.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight

of about 6 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 6.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 7 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 7.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 8 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 8.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 9 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 9.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 10 kDa. It is understood that if $-L^{B'}$ comprises one polymer moiety the minimum and maximum molecular weights provided above apply to this one polymer moiety and if $-L^{B'}$ comprises more than one polymer moiety the minimum and maximum molecular weights provided above refer to the minimum and maximum molecular weight of all polymer moieties together.

In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 1.2 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 1.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 2 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 2.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 3 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 3.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 4 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 4.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of at least 5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 200 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 175 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 150 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 125 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 100 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 75 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 50 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 45 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no

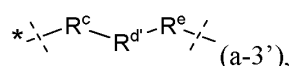
more than 40 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 35 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of no more than 30 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 1.2 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 1.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 2 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 2.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 3 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 3.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 4 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 4.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 5.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 6 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 6.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 7 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 8.5 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 9 nm. In certain embodiments the one or more polymer moiety of $-L^{B'}$ has a Flory radius of about 10 nm. It is understood that if $-L^{B'}$ comprises one polymer moiety the Flory radius provided above applies to this one polymer moiety and if $-L^{B'}$ comprises more than one polymer moiety the Flory radius provided above refers to the Flory radius of all polymer moieties together.

$-L^{B'}$ comprises one or more polymer moiety, such as polymer moiety selected from the group consisting of poly(2-methacryloyl-oxyethyl phosphoyl cholins), poly(acrylic acids), poly(acrylates), poly(acrylamides), poly(alkyloxy) polymers, poly(amides), poly(amidoamines), poly(amino acids), poly(anhydrides), poly(aspartamides), poly(butyric acids), poly(glycolic acids), polybutylene terephthalates, poly(caprolactones), poly(carbonates), poly(cyanoacrylates), poly(dimethylacrylamides), poly(esters), poly(ethylenes), poly(ethyleneglycols), poly(ethylene oxides), poly(ethyl phosphates), poly(ethyloxazolines), poly(glycolic acids), poly(hydroxyethyl acrylates), poly(hydroxyethyl-oxazolines), poly(hydroxymethacrylates), poly(hydroxypropylmethacrylamides), poly(hydroxypropyl methacrylates), poly(hydroxypropyloxazolines), poly(iminocarbonates),

poly(lactic acids), poly(lactic-co-glycolic acids), poly(methacrylamides), poly(methacrylates), poly(methyloxazolines), poly(organophosphazenes), poly(ortho esters), poly(oxazolines), poly(propylene glycols), poly(siloxanes), poly(urethanes), poly(vinyl alcohols), poly(vinyl amines), poly(vinylmethylethers), poly(vinylpyrrolidones), silicones, celluloses, carbomethyl
 5 celluloses, hydroxypropyl methylcelluloses, chitins, chitosans, dextrans, dextrans, gelatins, hyaluronic acids and derivatives, functionalized hyaluronic acids, alginate, mannans, pectins, rhamnogalacturonans, starches, hydroxyalkyl starches, hydroxyethyl starches and other carbohydrate-based polymers, xylans, and copolymers thereof.

10 In certain embodiments $-L^{B'}$ comprises a PEG-based polymer. In certain embodiments $-L^{B'}$ comprises a hyaluronic acid-based polymer. In certain embodiments $-L^{B'}$ comprises a random coil polymer. In certain embodiments $-L^{B'}$ comprises a poly-sarcosine polymer.

15 In certain embodiments $-L^{B'}$ of formula (A-a) is of formula (a-3')



wherein

the unmarked dashed line indicates attachment to $-D$;

the dashed line marked with the asterisk indicates attachment to $-L^A$;

20 $-R^c$ is $\text{---}N\text{---}$ or $\text{---}C(=O)\text{---}$;

$-R^d$ is a polymeric moiety; and

$-R^e$ is selected from the group consisting of $-\text{CH}_2-$, $\text{---}C(=O)\text{---}$ and $\text{---}N\text{---}$.

If $-R^b$ of formula (A-a) is $\text{---}N\text{---}$ then $-R^c$ of formula (a-3') is $\text{---}C(=O)\text{---}$ and if $-R^b$ of formula

25 (A-a) is $\text{---}C(=O)\text{---}$ then $-R^c$ of formula (a-3') is $\text{---}N\text{---}$.

The moiety $-R^d$ of formula (a-3') is a polymeric moiety, meaning that it comprises at least one polymer moiety. In certain embodiments the one or more polymer moiety has a molecular weight of at least 450 Da. In certain embodiments the one or more polymer moiety has a

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more polymer moiety has a molecular weight of about 8.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 9 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 9.5 kDa. In certain embodiments the one or more polymer moiety has a molecular weight of about 10 kDa. It is understood that if $-R^{d'}$ of formula (a-3') comprises one polymer moiety the minimum and maximum molecular weights provided above apply to this one polymer moiety and if $-R^{d'}$ of formula (a-3') comprises more than one polymer moiety the minimum and maximum molecular weights provided above refer to the minimum and maximum molecular weight of all polymer moieties together.

10

In certain embodiments the one or more polymer moiety of $-R^{d'}$ of formula (a-3') has a Flory radius of at least 1.2 nm. In certain embodiments the one or more polymer moiety has a Flory radius of at least 1.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of at least 2 nm. In certain embodiments the one or more polymer moiety has a Flory radius of at least 2.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of at least 3 nm. In certain embodiments the one or more polymer moiety has a Flory radius of at least 3.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of at least 4 nm. In certain embodiments the one or more polymer moiety has a Flory radius of at least 4.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of at least 5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 200 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 175 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 150 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 125 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 100 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 75 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 50 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 45 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 40 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 35 nm. In certain embodiments the one or more polymer moiety has a Flory radius of no more than 30 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 1.2 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 1.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of

30

about 2 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 2.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 3 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 3.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 4 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 4.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 5.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 6 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 6.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 7 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 8.5 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 9 nm. In certain embodiments the one or more polymer moiety has a Flory radius of about 10 nm. It is understood that if $-R^d-$ of formula (a-3') comprises one polymer moiety the Flory radius provided above applies to this one polymer moiety and if $-R^d-$ of formula (a-3') comprises more than one polymer moiety the Flory radius provided above refers to the Flory radius of all polymer moieties together.

$-R^d-$ of formula (a-3') comprises one or more polymer moiety, such as polymer moiety selected from the group consisting of poly(2-methacryloyl-oxyethyl phosphoyl cholins), poly(acrylic acids), poly(acrylates), poly(acrylamides), poly(alkyloxy) polymers, poly(amides), poly(amidoamines), poly(amino acids), poly(anhydrides), poly(aspartamides), poly(butyric acids), poly(glycolic acids), poly(butylene terephthalates), poly(caprolactones), poly(carbonates), poly(cyanoacrylates), poly(dimethylacrylamides), poly(esters), poly(ethylenes), poly(ethyleneglycols), poly(ethylene oxides), poly(ethyl phosphates), poly(ethyloxazolines), poly(glycolic acids), poly(hydroxyethyl acrylates), poly(hydroxyethyl-oxazolines), poly(hydroxymethacrylates), poly(hydroxypropylmethacrylamides), poly(hydroxypropyl methacrylates), poly(hydroxypropyloxazolines), poly(iminocarbonates), poly(lactic acids), poly(lactic-co-glycolic acids), poly(methacrylamides), poly(methacrylates), poly(methyloxazolines), poly(organophosphazenes), poly(ortho esters), poly(oxazolines), poly(propylene glycols), poly(siloxanes), poly(urethanes), poly(vinyl alcohols), poly(vinyl amines), poly(vinylmethylethers), poly(vinylpyrrolidones), silicones, celluloses, carbomethyl celluloses, hydroxypropyl methylcelluloses, chitins, chitosans, dextrans, dextrins, gelatins, hyaluronic acids and derivatives, functionalized hyaluronic acids, alginate, mannans, pectins,

rhamnogalacturonans, starches, hydroxyalkyl starches, hydroxyethyl starches and other carbohydrate-based polymers, xylans, and copolymers thereof.

In certain embodiments -R^d- of formula (a-3') comprises a PEG-based polymer. In certain
5 embodiments -R^d- of formula (a-3') comprises a hyaluronic acid-based polymer. In certain
embodiments -R^d- of formula (a-3') comprises a random coil polymer. In certain
embodiments -R^d- of formula (a-3') comprises a poly-sarcosine polymer.

In certain embodiments the distance between any two moieties -AB of a compound is such that
10 they can bind to two different binding sites on the same albumin molecule or to two different
albumin molecules. All or some moieties -AB may bind to different albumin molecules and/or
two or more moieties -AB may bind to one albumin molecule. In general, if a compound has x
moieties -AB they may bind to up to x albumin molecules. It is understood that not all
moieties -AB of a compound may be bound to an albumin molecule at any given time.

15

Binding to two or more different albumin molecules increases the molecular weight of the
compound significantly, which has an advantageous effect on circulation half-life.

In certain embodiments -D- is a protein or peptide drug moiety and -AB is conjugated to a
20 functional group of -D- provided by the N-terminal amine, the C-terminal carboxyl or a side
chain of an amino acid residue. In certain embodiments -AB is conjugated to the N-terminal
amine functional group of -D-. In certain embodiments -AB is conjugated to the C-terminal
carboxyl functional group. In certain embodiments -AB is conjugated to a functional group
provided by an amino acid residue of -D-, such as by a lysine, serine, aspartic acid, glutamic
25 acid, arginine, histidine, threonine, glutamine, asparagine, cysteine, proline, tyrosine or
tryptophan. In certain embodiments -AB is conjugated to the functional group of the side chain
of a lysine of -D-. In certain embodiments -AB is conjugated to the functional group of the side
chain of a serine of -D-. In certain embodiments -AB is conjugated to the functional group of
the side chain of an aspartic acid of -D-. In certain embodiments -AB is conjugated to the
30 functional group of the side chain of a glutamic acid of -D-. In certain embodiments -AB is
conjugated to the functional group of the side chain of an arginine of -D-. In certain
embodiments -AB is conjugated to the functional group of the side chain of a histidine of -D-.
In certain embodiments -AB is conjugated to the functional group of the side chain of a
threonine of -D-. In certain embodiments -AB is conjugated to the functional group of the side

chain of a glutamine of -D-. In certain embodiments -AB is conjugated to the functional group of the side chain of an asparagine of -D-. In certain embodiments -AB is conjugated to the functional group of the side chain of a cysteine of -D-. In certain embodiments -AB is conjugated to the functional group of the side chain of a proline of -D-. In certain embodiments
5 -AB is conjugated to the functional group of the side chain of a tyrosine of -D-. In certain embodiments -AB is conjugated to the functional group of the side chain of a tryptophan of -D-.

In certain embodiments -D-AB is selected from the group consisting of semaglutide, liraglutide, ecnoglutide, GZR18, GL0034, tirzepatide, cotadutide, BI-456906, pemvidutide, 10 mazdutide, dapiglutide and retatrutide.

In certain embodiments -D-AB is selected from the group consisting of semaglutide, liraglutide, ecnoglutide, GZR18 and GL0034.

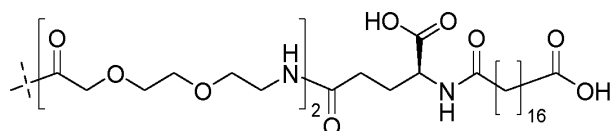
15 In certain embodiments -D-AB is semaglutide. Semaglutide is a compound of formula

HX₁EGTFTSDVSSYLEGQAAKEFIAWLVRGRG (SEQ ID NO:40),

wherein

X₁ is α-aminoisobutyric acid (Aib); and

the lysine at position 20 is chemically modified through conjugation to the epsilon-amine
20 group of the lysine side-chain with



wherein

the dashed line indicates attachment to the epsilon-amine group of the lysine side chain of the lysine at position 20.

25

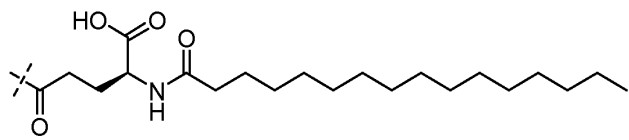
Semaglutide may be prepared using methods known to those skilled in the art, such as those described in WO2006/097537.

In certain embodiments -D-AB is liraglutide. Liraglutide is a compound of formula

HAEGTFTSDVSSYLEGQAAKEFIAWLVRGRG (SEQ ID NO:41),

wherein

the lysine at position 20 is chemically modified through conjugation to the epsilon-amine group of the lysine side chain with



5 wherein

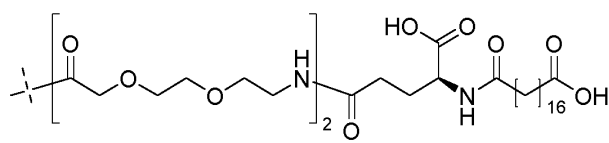
the dashed line indicates attachment to the epsilon-amine group of the lysine side chain of the lysine at position 20.

In certain embodiments -D-AB is ecnoglutide. Ecnoglutide is a compound of formula

10 HVEGTFTSDVSSYLEEQAAREFIKWLVGRG (SEQ ID NO:42),

wherein

the lysine at position 24 is chemically modified through conjugation to the epsilon-amine group of the lysine side chain with



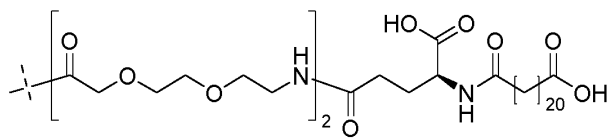
15 wherein the dashed line indicates attachment to the epsilon-amine group of the lysine side chain of the lysine at position 24.

In certain embodiments -D-AB is GZR18. GZR18 is a compound of formula

20 HEGTFTSDVSSYLEGQAAKEFIAWLVGRG (SEQ ID NO:43),

wherein

the lysine at position 20 is chemically modified through conjugation to the epsilon-amine group of the lysine side-chain with



25 wherein the dashed line indicates attachment to the epsilon amine group of the lysine side chain of the lysine at position 20.

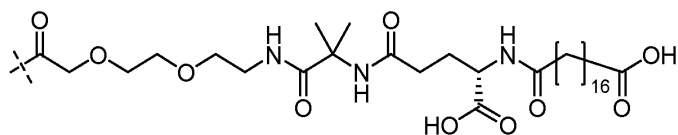
In certain embodiments -D-AB is GL0034. GL0034 is also known as utreglutide and is a compound of formula

HX₁EGTFTSDVSSYLEGQAAKEFIAWLVRGRGL (SEQ ID NO:44),

wherein

5 X₁ is Aib; and

the lysine at position 20 is chemically modified through conjugation to the epsilon-amine group of the lysine side-chain with



10 wherein the dashed line indicates attachment to the epsilon amine group of the lysine side chain of the lysine at position 20.

In certain embodiments -D- or -D-AB is a dual GLP-1 receptor agonist selected from the group consisting of tirzepatide, cotadutide, BI-456906, pemvidutide and mazdutide.

15 In certain embodiments -D-AB is a dual GLP-1 receptor agonist that activates the GLP-1 receptor and the GIP receptor. An example for such dual GLP-1 receptor agonist is tirzepatide.

In certain embodiments -D-AB is tirzepatide. Tirzepatide is a compound of formula

YX₁EGTFTSDYSIX₂LDKIAQKAFVQWLIAGGPSSGAPPPS (SEQ ID NO:45),

wherein

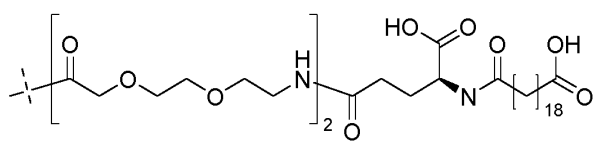
20 X₁ is Aib;

X₂ is Aib;

the lysine at position 20 is chemically modified through conjugation to the epsilon-amine group of the lysine side-chain with ([2-(2-amino-ethoxy)-ethoxy]-acetyl)₂-(γGlu)₁-CO-(CH₂)₁₈-CO₂H; and

25 the C-terminal serine, i.e. the serine at position 39, is amidated as a C-terminal primary amide.

The moiety ([2-(2-amino-ethoxy)-ethoxy]-acetyl)₂-(γGlu)₁-CO-(CH₂)₁₈-CO₂H has the following structure



wherein the dashed line indicates attachment to -D-.

In certain embodiments -D-AB is a dual GLP-1 receptor agonist that activates the GLP-1
 5 receptor and the glucagon receptor selected from the group consisting of cotadutide, BI-456906, pemvidutide and mazdutide.

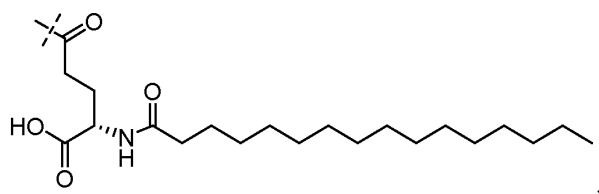
In certain embodiments -D-AB is cotadutide. Cotadutide is a compound of formula

HSQGTFTSDKSEYLDSEARDFVAWLEAGG (SEQ ID NO:46),

10 wherein

the lysine at position 10 is chemically modified through conjugation to the epsilon-amine group of the lysine side-chain with γ -Glu-palmitoyl.

The moiety γ -Glu-palmitoyl has the following structure:



15

wherein the dashed line indicates attachment to -D-.

In certain embodiments -D-AB is BI-456906. BI-456906 is also known as survodutide and is
 a compound of formula

20 $HX_1QGTFTSDYISKYLDERRAAKDFIKWLESA$ (SEQ ID NO:47),

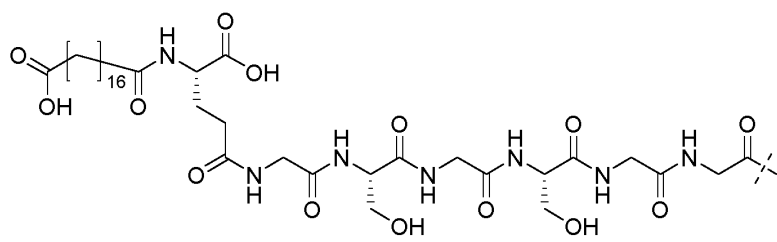
wherein

X_1 is 1-amino-cyclobutanecarboxylic acid (Ac4c);

the lysine at position 24 is chemically modified through conjugation to the epsilon-amine group of the lysine side-chain with [17-carboxy-heptadecanoyl]-isoGlu-GSGSGG; and

25 the C-terminal alanine, i.e. the alanine at position 29, is amidated as a C-terminal primary amide.

The moiety [17-carboxy-heptadecanoyl]-isoGlu-GSGSGG has the following structure:



wherein the dashed line indicates attachment to -D-.

In certain embodiments -D-AB is pemvidutide. Pemvidutide is a compound of formula

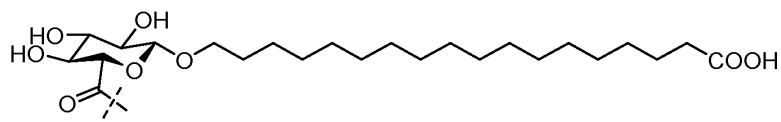
5 HX₁QGTFTSDYSKYLDEKAAKEFIQWLLQT (SEQ ID NO:48),

wherein

X₁ is Aib;

the glutamic acid at position 16 and the lysine at position 20 are connected via a lactam bridge;

10 the lysine at position 17 is chemically modified through conjugation to the epsilon-amine group of the lysine side-chain with glucuronic acid C-18, which is a moiety of formula



wherein

the dashed line indicates attachment to the epsilon-amine group of the lysine at position 17; and

15 the C-terminal threonine, i.e. the threonine at position 29, is amidated as a C-terminal primary amide

In certain embodiments -D-AB is mazdutide. Mazdutide is a compound of formula

20 HX₁QGTFTSDYSKYLDEKKAKEFVEWLLEGGPSSG (SEQ ID NO:49),

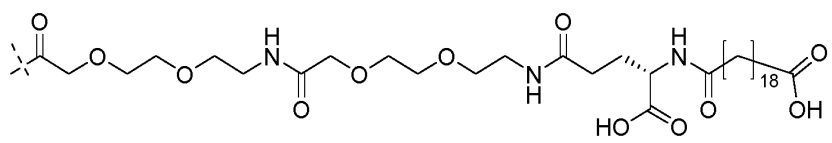
wherein

X₁ is Aib,

the lysine at position 20 is chemically modified by conjugation of the epsilon-amine group of the lysine side chain with ([2-(2-amino-ethoxy)-ethoxy]-acetyl)₂-(γ-Glu)-CO-(CH₂)₁₈-CO₂H; and

25 the C-terminal glycine, i.e. the glycine at position 34, is amidated.

The moiety ([2-(2-amino-ethoxy)-ethoxy]-acetyl)₂-(γ -Glu)-CO-(CH₂)₁₈-CO₂H has the following structure:



wherein the dashed line indicates attachment to -D-.

5

In certain embodiments -D-AB is a dual GLP-1 receptor agonist that activates the GLP-1 receptor and the GLP-2 receptor, such as dapiglutide. Dapiglutide is a compound of formula

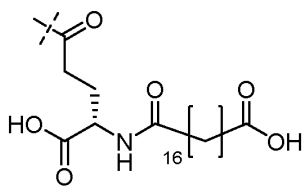
HX₁EGSFTSELATILDKQAARDFIAWLIQHKITD (SEQ ID NO:50),

wherein

10 X₁ is Aib; and

the lysine in position 16 is chemically modified by conjugation of the epsilon-amino-group of the lysine side chain with [17-carboxy-heptadecanoyl]-isoGlu.

The moiety [17-carboxy-heptadecanoyl]-isoGlu has the following structure:



15

wherein the dashed line indicates attachment to -D-.

In certain embodiments -D-AB is retatrutide, which is a triple GLP-1 receptor agonist that activates the GLP-1 receptor, the GIP receptor and the GCG receptor. Retatrutide is a compound of formula

20

YX₁QGTFTSDYSIX₂LDKKAQX₃AFIEYLLEGGPSSGAPPPS (SEQ ID NO:51),

wherein

X₁ is Aib;

X₂ is α -methyl-leucine (α MeL);

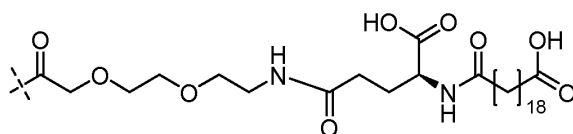
25 X₃ is Aib;

the lysine at position 17 is chemically modified by conjugation of the epsilon-amine group of the lysine side chain with (2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)-(γ -Glu)-CO-(CH₂)₁₈-CO₂H; and

the C-terminal serine, i.e. the serine at position 39, is amidated.

Retatrutide can also be described as Y-Aib-QGTFTSDYSI- α MeL-LDKK ((2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)-(γ Glu)-CO-(CH₂)₁₈-CO₂H) AQ-Aib-AFIEYLLEGGPSSGAPPS-NH₂ (SEQ ID NO:51).

The moiety (2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)-(γ Glu)-CO-(CH₂)₁₈-CO₂H has the following structure:



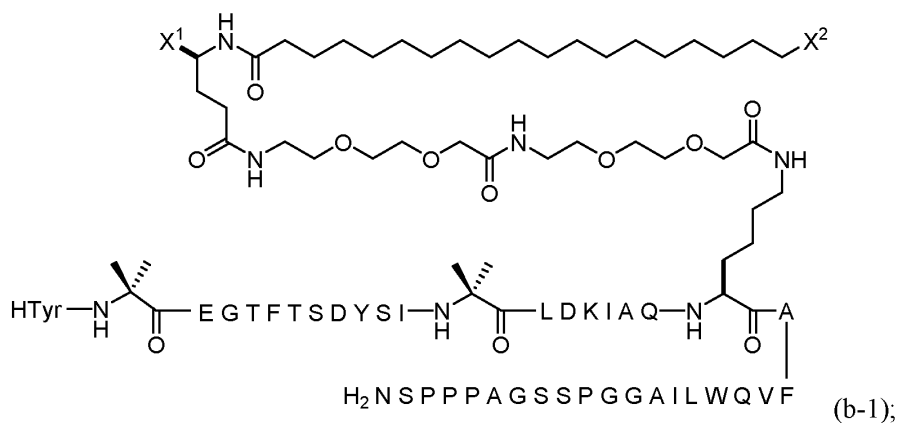
10

In certain embodiments -D-AB is noiglutide, also known as SHR20004.

In certain embodiments -D-AB is ZT002.

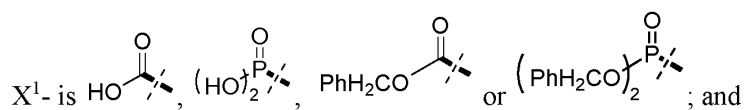
15 In certain embodiments -D-AB is selected from the group consisting of semaglutide, liraglutide, ecnoglutide, GZR18, GL0034, tirzepatide, cotadutide, BI-456906, pemvidutide, mazdutide, dapiglutide and retatrutide.

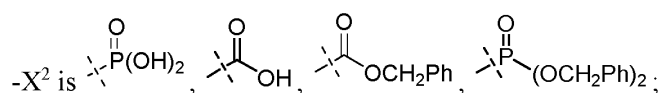
In certain embodiments -D-AB is of formula (b-1)



20

wherein





with Ph being phenyl.

The moiety -D- of formula (b-1) has the sequence of SEQ ID NO:57

5 YX₁EGTFTSDYSIX₂LDKIAQKAFVQWLIAGGPSSGAPPPS,

with X₁ and X₂ being Aib.

The compounds of formula (b-1) are disclosed in WO2022159395 and WO2023/044290, the content of which is herewith incorporated by reference in its entirety.

10

In certain embodiments -D-AB is of formula (b-1) and X¹- is $\text{HO}-\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \end{array}$ and -X² is $\begin{array}{c} \text{O} \\ \parallel \\ \text{---P}(\text{OH})_2 \end{array}$. In

certain embodiments D-AB is of formula (b-1) and X¹- is $\text{PhH}_2\text{CO}-\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \end{array}$ and -X² is

$\begin{array}{c} \text{O} \\ \parallel \\ \text{---P} \end{array} (\text{OCH}_2\text{Ph})_2$. In certain embodiments D-AB is of formula (b-1) and X¹- is $\text{PhH}_2\text{CO}-\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \end{array}$

and -X² is $\begin{array}{c} \text{O} \\ \parallel \\ \text{---P}(\text{OH})_2 \end{array}$. In certain embodiments D-AB is of formula (b-1) and X¹- is $\text{HO}-\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \end{array}$

15 and -X² is $\begin{array}{c} \text{O} \\ \parallel \\ \text{---P} \end{array} (\text{OCH}_2\text{Ph})_2$. In certain embodiments D-AB is of formula (b-1) and X¹- is

$(\text{PhH}_2\text{CO})_2-\begin{array}{c} \text{O} \\ \parallel \\ \text{---P} \end{array}$ and -X² is $\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \end{array} \text{OCH}_2\text{Ph}$. In certain embodiments D-AB is of formula (b-1) and

X¹- is $(\text{PhH}_2\text{CO})_2-\begin{array}{c} \text{O} \\ \parallel \\ \text{---P} \end{array}$ and -X² is $\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \end{array} \text{OH}$. In certain embodiments D-AB is of formula (b-1)

and X¹- is $(\text{HO})_2-\begin{array}{c} \text{O} \\ \parallel \\ \text{---P} \end{array}$ and -X² is $\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \end{array} \text{OCH}_2\text{Ph}$. In certain embodiments D-AB is of formula (b-1)

and X¹- is $(\text{HO})_2-\begin{array}{c} \text{O} \\ \parallel \\ \text{---P} \end{array}$ and -X² is $\begin{array}{c} \text{O} \\ \parallel \\ \text{---C} \end{array} \text{OH}$. In certain embodiments D-AB is of formula (b-1) and

X^1 - is $(\text{PhH}_2\text{CO})_2\text{P}(=\text{O})$ and $-X^2$ is $\text{P}(=\text{O})(\text{OCH}_2\text{Ph})_2$. In certain embodiments D-AB is of formula

(b-1) and X^1 - is $(\text{PhH}_2\text{CO})_2\text{P}(=\text{O})$ and $-X^2$ is $\text{P}(=\text{O})(\text{OH})_2$. In certain embodiments D-AB is of

formula (b-1) and X^1 - is $(\text{HO})_2\text{P}(=\text{O})$ and $-X^2$ is $\text{P}(=\text{O})(\text{OCH}_2\text{Ph})_2$. In certain embodiments D-AB is

of formula (b-1) and X^1 - is $(\text{HO})_2\text{P}(=\text{O})$ and $-X^2$ is $\text{P}(=\text{O})(\text{OH})_2$.

5

In certain embodiments -D-AB is a compound of formula

$\text{k}(\gamma\text{E}-(\text{miniPEG})_2-\gamma\text{E}-\text{COC}_{16}\text{H}_{32}\text{CO}_2\text{H})(\text{N-Me})\text{GSVSEIQLMHNLGKHLNSMERVIEW}$
 $\text{LRKKLQDVHK}(\gamma\text{E}-(\text{miniPEG})_2-\gamma\text{E}-\text{COC}_{16}\text{H}_{32}\text{CO}_2\text{H})-\text{OH}$ (SEQ ID NO:52),

wherein

10 k is d-Lys;

γE is the l-isomer of gamma, glutamic acid;

miniPEG is $\text{COCH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{NH}_2$;

$\text{COC}_{16}\text{H}_{32}\text{CO}_2\text{H}$ is C18 diacid;

(N-Me)G is sarcosine;

15 K is l-isomer of lysine; and

-OH designates the C-terminal amino acid has a terminal carboxylic acid.

In certain embodiments -D-AB is a compound of formula

$\text{k}(\gamma\text{E}-(\text{miniPEG})_2-\gamma\text{E}-\text{COC}_{16}\text{H}_{32}\text{CO}_2\text{H})(\text{N-Me})\text{GSVSEIQLMHNLGKHLNSMERVIEW}$
 20 $\text{LRKKLQDVHK}(\gamma\text{E}-(\text{miniPEG})_2-\gamma\text{E}-\text{COC}_{16}\text{H}_{32}\text{CO}_2\text{H})-\text{OH}$ (SEQ ID NO:53),

wherein

k is d-Lys;

γE is the l-isomer of gamma, glutamic acid;

(miniPEG)₂ is $\text{COCH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{NH}_2$;

25 $\text{COC}_{16}\text{H}_{32}\text{CO}_2\text{H}$ is C18 diacid;

(N-Me)G is sarcosine;

K is l-isomer of lysine; and

-OH designates the C-terminal amino acid has a terminal carboxylic acid.

If -D- is a peptide or protein drug moiety, -L¹- is either conjugated to a functional group of a side chain of an amino acid residue of -D-, to the N-terminal amine functional group or to the C-terminal carboxyl functional group of -D- or to a nitrogen atom in the backbone chain of -D-.

5

If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of -D- selected from the group consisting of carboxylic acid, primary amine, secondary amine, maleimide, thiol, sulfonic acid, carbonate, carbamate, hydroxyl, aldehyde, ketone, hydrazine, isocyanate, isothiocyanate, phosphoric acid, phosphonic acid, haloacetyl, alkyl halide, acryloyl, aryl fluoride, hydroxylamine, sulfate, disulfide, vinyl sulfone, vinyl ketone, diazoalkane, oxirane, guanidine and aziridine. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of -D- selected from the group consisting of hydroxyl, primary amine, secondary amine and guanidine. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of -D- selected from the group consisting of primary amine and secondary amine. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a primary amine of -D-.

If -D- is a peptide or protein drug moiety, -L¹- may be conjugated to a functional group of the side chain of an amino acid residue of -D-, which may be a proteinogenic amino acid residue or a non-proteinogenic amino acid residue.

If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of the side chain of a proteinogenic amino acid residue of -D-. In certain embodiments such amino acid residue is selected from the group consisting of histidine, lysine, tryptophan, serine, threonine, tyrosine, aspartic acid, glutamic acid and arginine. In certain embodiments such amino acid residue is selected from the group consisting of lysine, aspartic acid, arginine and serine. In certain embodiments such amino acid residue is selected from the group consisting of lysine, arginine and serine.

30

If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of a lysine residue of -D-. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of a histidine residue of -D-. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group

of a tryptophan residue of -D-. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of a serine residue of -D-. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of a threonine residue of -D-. If -D- is a peptide or protein drug moiety, -L¹- is in certain
5 embodiments conjugated to a functional group of a tyrosine residue of -D-. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of an aspartic acid residue of -D-. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of a glutamic acid residue of -D-. If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group
10 of an arginine residue of -D-.

If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to a functional group of the side chain of a non-proteinogenic amino acid residue of -D-.

15 It is understood that not every peptide or protein drug moiety -D- may comprise all of these amino acid residues.

If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to the N-terminal amine functional group of -D-.

20

If -D- is a peptide or protein drug moiety, -L¹- is in certain embodiments conjugated to the C-terminal functional group of -D-.

The moiety -L¹- may be connected to -D- through any type of linkage, provided that it is reversible. In certain embodiments -L¹- is connected to -D- through a linkage selected from the group consisting of amide, ester, carbamate, acetal, aminal, imine, oxime, hydrazone, disulfide and acylguanidine. In certain embodiments -L¹- is connected to -D- through a linkage selected from the group consisting of amide, ester, carbamate and acylguanidin. It is understood that some of these linkages *per se* are not reversible, but that in the present invention neighboring
25 groups present in -L¹- render these linkages reversible.

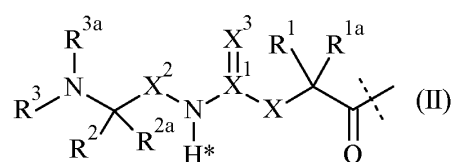
30

In certain embodiments -L¹- is connected to -D- through an amide linkage. In certain embodiments -L¹- is connected to -D- through a carbamate linkage. In certain

embodiments -L¹- is connected to -D- through an ester linkage. In certain embodiments -L¹- is connected to -D- through an acylguanidine linkage.

The moiety -L¹- is a reversible prodrug linker from which the drug, i.e., H-D-AB, is released in its free form, i.e. it is a traceless prodrug linker. It is understood that the “H-“ in “H-D-AB” is a hydrogen. Suitable prodrug linkers are known in the art, such as for example the reversible prodrug linker moieties disclosed in WO 2005/099768 A2, WO 2006/136586 A2, WO 2011/089216 A1 and WO 2013/024053 A1, which are incorporated by reference herewith.

In certain embodiments -L¹- is disclosed in WO 2009/095479 A2. Accordingly, in certain embodiments the moiety -L¹- is of formula (II):



wherein the dashed line indicates attachment to a nitrogen, hydroxyl or thiol of -D-;

-X¹- is selected from the group consisting of -C(R⁴R^{4a})-; -N(R⁴)-; -O-; -C(R⁴R^{4a})-C(R⁵R^{5a})-; -C(R⁵R^{5a})-C(R⁴R^{4a})-; -C(R⁴R^{4a})-N(R⁶)-; -N(R⁶)-C(R⁴R^{4a})-; C(R⁴R^{4a})-O-; -O-C(R⁴R^{4a})-; and -C(R⁷R^{7a})-;

X¹ is selected from the group consisting of C; and S(O);

-X²- is selected from the group consisting of -C(R⁸R^{8a})-; and -C(R⁸R^{8a})-C(R⁹R^{9a})-;

=X³ is selected from the group consisting of =O; =S; and =N-CN;

-R¹, -R^{1a}, -R², -R^{2a}, -R⁴, -R^{4a}, -R⁵, -R^{5a}, -R⁶, -R⁸, -R^{8a}, -R⁹, and -R^{9a} are independently selected from the group consisting of -H; and C₁₋₆ alkyl;

-R³, and -R^{3a} are independently selected from the group consisting of -H; and C₁₋₆ alkyl, provided that in case one of -R³, -R^{3a} or both are other than -H they are connected to N to which they are attached through an SP³-hybridized carbon atom;

-R⁷ is selected from the group consisting of -N(R¹⁰R^{10a}); and -NR¹⁰-(C=O)-R¹¹;

-R^{7a}, -R¹⁰, -R^{10a}, and -R¹¹ are independently of each other selected from the group consisting of -H; and C₁₋₆ alkyl;

optionally, one or more of the pairs -R^{1a}/R^{4a}, -R^{1a}/R^{5a}, -R^{1a}/R^{7a}, -R^{4a}/R^{5a}, and -R^{8a}/R^{9a} form a chemical bond;

optionally, one or more of the pairs -R¹/R^{1a}, -R²/R^{2a}, -R⁴/R^{4a}, -R⁵/R^{5a}, -R⁸/R^{8a},

and $-R^9/-R^{9a}$ are joined together with the atom to which they are attached to form a C_{3-10} cycloalkyl; or 3- to 10-membered heterocyclyl;

optionally, one or more of the pairs $-R^1/-R^4$, $-R^1/-R^5$, $-R^1/-R^6$, $-R^1/-R^{7a}$, $-R^4/-R^5$, $-R^4/-R^6$, $-R^8/-R^9$, and $-R^2/-R^3$ are joined together with the atoms to which they are attached to form a ring A;

optionally, R^3/R^{3a} are joined together with the nitrogen atom to which they are attached to form a 3- to 10-membered heterocycle;

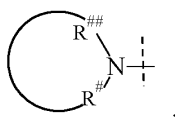
A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C_{3-10} cycloalkyl; 3- to 10-membered heterocyclyl; and 8- to 11-membered heterobicyclyl; and

wherein $-L^1-$ is substituted with at least one $-L^2-$ and wherein $-L^1-$ is optionally further substituted, provided that the hydrogen marked with the asterisk in formula (II) is not replaced by $-L^2-$ or a substituent.

In certain embodiments $-L^1-$ of formula (II) is substituted with one moiety $-L^2-$.

In certain embodiments $-L^1-$ of formula (II) is not further substituted.

It is understood that if $-R^3/-R^{3a}$ of formula (II) are joined together with the nitrogen atom to which they are attached to form a 3- to 10-membered heterocycle, only such 3- to 10-membered heterocycles may be formed in which the atoms directly attached to the nitrogen are sp^3 -hybridized carbon atoms. In other words, such 3- to 10-membered heterocycle formed by $-R^3/-R^{3a}$ together with the nitrogen atom to which they are attached has the following structure:



wherein

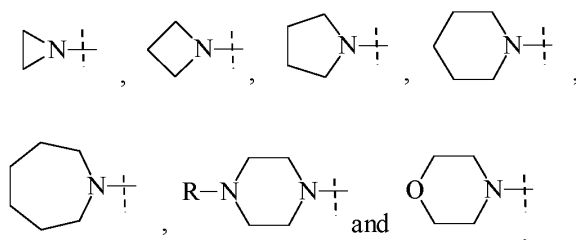
the dashed line indicates attachment to the rest of $-L^1-$;

the ring comprises 3 to 10 atoms comprising at least one nitrogen; and

$R^{\#}$ and $R^{\#\#}$ represent an sp^3 -hybridized carbon atom.

It is also understood that the 3- to 10-membered heterocycle may be further substituted.

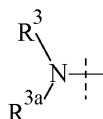
Exemplary embodiments of suitable 3- to 10-membered heterocycles formed by $-R^3/-R^{3a}$ of formula (II) together with the nitrogen atom to which they are attached are the following:



wherein

- 5 dashed lines indicate attachment to the rest of the molecule; and
 -R is selected from the group consisting of -H and C_{1-6} alkyl.

- L¹- of formula (II) may optionally be further substituted. In general, any substituent may be used as far as the cleavage principle is not affected, i.e., the hydrogen marked with the asterisk
 10 in formula (II) is not replaced and the nitrogen of the moiety



of formula (II) remains part of a primary, secondary or tertiary amine, i.e., $-R^3$ and $-R^{3a}$ are independently of each other -H or are connected to $-N<$ through an sp^3 -hybridized carbon atom.

- 15 In one embodiment $-R^1$ or $-R^{1a}$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^2$ or $-R^{2a}$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^3$ or $-R^{3a}$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^4$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^5$ or $-R^{5a}$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^6$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^7$
 20 or $-R^{7a}$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^8$ or $-R^{8a}$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^9$ or $-R^{9a}$ of formula (II) is substituted with $-L^2$ -. In another embodiment $-R^{10}$ is substituted with $-L^2$ -. In another embodiment $-R^{11}$ is substituted with $-L^2$ -. In certain embodiments $-R^3$ of formula (II) is substituted with $-L^2$ -.
 25 In certain embodiments $-X$ - of formula (II) is selected from the group consisting of $-C(R^4R^{4a})$ -, $-N(R^4)$ - and $-C(R^7R^{7a})$ -. In certain embodiments $-X$ - of formula (II) is $-C(R^4R^{4a})$ -. In certain embodiments $-X$ - of formula (II) is $-C(R^7R^{7a})$ -.

In certain embodiments $-R^7$ of formula (II) is $-NR^{10}-(C=O)-R^{11}$.

5 In certain embodiments $-R^{7a}$ of formula (II) is selected from -H, methyl and ethyl. In certain embodiments $-R^{7a}$ of formula (II) is -H.

In certain embodiments $-R^{10}$ is selected from -H, methyl and ethyl. In certain embodiments $-R^{10}$ is methyl.

10 In certain embodiments $-R^{11}$ is selected from -H, methyl and ethyl. In certain embodiments $-R^{11}$ is -H. In certain embodiments $-R^{11}$ is substituted with $-L^2$.

In certain embodiments $-X-$ of formula (II) is $-N(R^4)-$.

15 In certain embodiments $-R^4$ is selected from the group consisting of -H, methyl and ethyl. In certain embodiments $-R^4$ is -H.

In certain embodiments X^1 of formula (II) is C.

20 In certain embodiments $=X^3$ of formula (II) is =O.

In certain embodiments $-X^2-$ of formula (II) is $-C(R^8R^{8a})-$.

25 In certain embodiments $-R^8$ and $-R^{8a}$ of formula (II) are independently selected from the group consisting of -H, methyl and ethyl. In certain embodiments at least one of $-R^8$ and $-R^{8a}$ of formula (II) is -H. In certain embodiments both $-R^8$ and $-R^{8a}$ of formula (II) are -H.

In certain embodiments $-R^1$ and $-R^{1a}$ of formula (II) are independently selected from the group consisting of -H, methyl and ethyl.

30

In certain embodiments at least one of $-R^1$ and $-R^{1a}$ of formula (II) is -H. In certain embodiments $-R^1$ and $-R^{1a}$ of formula (II) are -H.

In certain embodiments at least one of $-R^1$ and $-R^{1a}$ of formula (II) is methyl. In certain embodiments both $-R^1$ and $-R^{1a}$ of formula (II) are methyl.

In certain embodiments $-R^2$ and $-R^{2a}$ of formula (II) are independently selected from the group consisting of -H, methyl and ethyl. In certain embodiments at least one of $-R^2$ and $-R^{2a}$ of formula (II) is -H. In certain embodiments both $-R^2$ and $-R^{2a}$ of formula (II) are H.

In certain embodiments $-R^3$ and $-R^{3a}$ of formula (II) are independently selected from the group consisting of -H, methyl, ethyl, propyl and butyl.

10

In certain embodiments at least one of $-R^3$ and $-R^{3a}$ of formula (II) is methyl. In certain embodiments $-R^3$ of formula (II) is methyl and $-R^{3a}$ of formula (II) is -H.

15

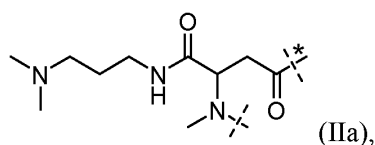
In certain embodiments $-R^3$ and $-R^{3a}$ of formula (II) are both -H.

In certain embodiments -D- is connected to $-L^1$ - through a nitrogen by forming an amide bond.

In certain embodiments $-L^1$ - is of formula (II), wherein X is $-C(R^7R^{7a})-$; X^1 is C; $-X^2$ - is $-C(R^8R^{8a})-C(R^9R^{9a})-$; $=X^3$ is =O; $-R^1$ and $-R^{1a}$ are -H; $-R^2$ and $-R^{2a}$ are -H; $-R^3$ and $-R^{3a}$ are methyl; $-R^7$ is $-N(R^{10}R^{10a})$; $-R^{7a}$ is -H; $-R^8$, $-R^{8a}$, $-R^9$ and $-R^{9a}$ are -H; and $-R^{10}$ is methyl and $-R^{10a}$ is -H.

20

In certain embodiments $-L^1$ - is of formula (IIa)

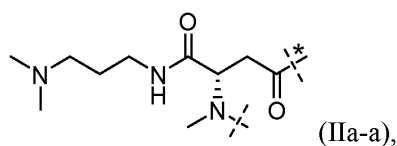


25

wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and the unmarked dashed line indicates attachment to $-L^2$ -.

In certain embodiments $-L^1$ - is of formula (IIa-a)

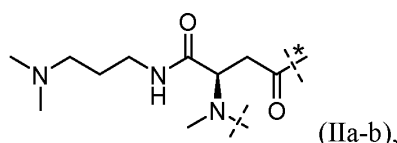


wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and
the unmarked dashed line indicates attachment to -L²-.

5

In certain embodiments -L¹- is of formula (IIa-b)



wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and
the unmarked dashed line indicates attachment to -L²-.

10

The moiety of formula (IIa), (IIa-a) and (IIa-b) is connected to -D- via an amide bond formed by a nitrogen of an amine functional group and the carbonyl to the left of the dashed line marked with the asterisk.

15

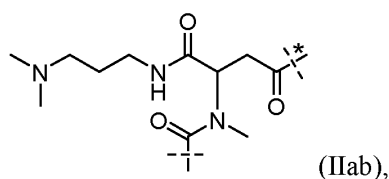
In certain embodiments -L¹- is of formula (II), wherein X is -C(R⁷R^{7a})-; X¹ is C; -X²- is -C(R⁸R^{8a})-C(R⁹R^{9a})-; =X³ is =O; -R¹ and -R^{1a} are -H; -R² and -R^{2a} are -H; -R³ and -R^{3a} are methyl; -R⁷ is -NR¹⁰-(C=O)-R¹¹; -R^{7a} is -H; -R⁸, -R^{8a}, -R⁹ and -R^{9a} are -H; and -R¹⁰ is methyl and -R¹¹ is -H.

20

In certain embodiments -L¹- is of formula (II), wherein X is -C(R⁷R^{7a})-; X¹ is C; -X²- is -C(R⁸R^{8a})-C(R⁹R^{9a})-; =X³ is =O; -R¹ and -R^{1a} are -H; -R² and -R^{2a} are -H; -R³ and -R^{3a} are methyl; -R⁷ is -NR¹⁰-(C=O)-R¹¹; -R^{7a} is -H; -R⁸, -R^{8a}, -R⁹ and -R^{9a} are -H; and -R¹⁰ is -H and -R¹¹ is -H.

25

In certain embodiments -L¹- is of formula (IIab)



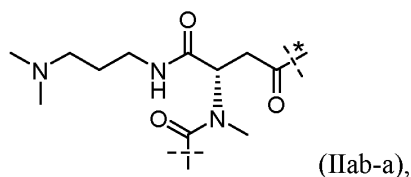
wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and

the unmarked dashed line indicates attachment to -L²-.

5

In certain embodiments -L¹- is of formula (IIab-a)

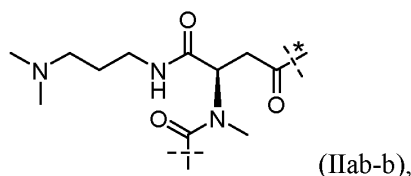


wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and

10 the unmarked dashed line indicates attachment to -L²-.

In certain embodiments -L¹- is of formula (IIab-b)



wherein

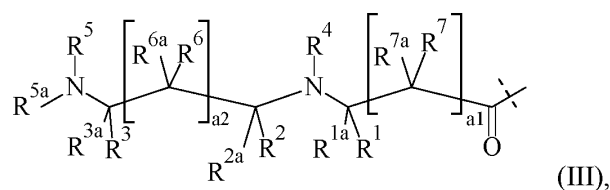
15 the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and

the unmarked dashed line indicates attachment to -L²-.

The moiety of formula (IIab), (IIab-a) and (IIab-b) is connected to -D- via an amide bond formed by a nitrogen of an amine functional group and the carbonyl to the left of the dashed line marked with the asterisk.

20

In certain embodiments -L¹- is disclosed in WO2016/020373A1. Accordingly, in certain embodiments the moiety -L¹- is of formula (III):



wherein

the dashed line indicates attachment to a primary or secondary amine or hydroxyl of -D- through an amide or ester linkage, respectively;

5 $-R^1, -R^{1a}, -R^2, -R^{2a}, -R^3$ and $-R^{3a}$ are independently of each other selected from the group consisting of $-H, -C(R^8R^{8a}R^{8b}), -C(=O)R^8, -C\equiv N, -C(=NR^8)R^{8a}, -CR^8(=CR^{8a}R^{8b}), -C\equiv CR^8$ and $-T$;

-R⁴, -R⁵ and -R^{5a} are independently of each other selected from the group consisting of -H, -C(R⁹R^{9a}R^{9b}) and -T;

10 a1 and a2 are independently of each other 0 or 1;

each -R⁶, -R^{6a}, -R⁷, -R^{7a}, -R⁸, -R^{8a}, -R^{8b}, -R⁹, -R^{9a}, and -R^{9b} are independently of each other selected from the group consisting of -H, halogen, -CN, -COOR¹⁰, -OR¹⁰, -C(O)R¹⁰, -C(O)N(R¹⁰R^{10a}), -S(O)₂N(R¹⁰R^{10a}), -S(O)N(R¹⁰R^{10a}), -S(O)₂R¹⁰, -S(O)R¹⁰, -N(R¹⁰)S(O)₂N(R^{10a}R^{10b}), -SR¹⁰, -N(R¹⁰R^{10a}), -NO₂, -OC(O)R¹⁰, -N(R¹⁰)C(O)R^{10a}, -N(R¹⁰)S(O)₂R^{10a}, -N(R¹⁰)S(O)R^{10a}, -N(R¹⁰)C(O)OR^{10a}, -N(R¹⁰)C(O)N(R^{10a}R^{10b}), -OC(O)N(R¹⁰R^{10a}), -T, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl; wherein -T, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally substituted with one or more -R¹¹, which are the same or different and wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R¹²)-, -S(O)₂N(R¹²)-, -S(O)N(R¹²)-, -S(O)₂-, -S(O)-, -N(R¹²)S(O)₂N(R^{12a})-, -S-, -N(R¹²)-, -OC(OR¹²)(R^{12a})-, -N(R¹²)C(O)N(R^{12a})-, and -OC(O)N(R¹²)-;

each -R¹⁰, -R^{10a}, and -R^{10b} is independently selected from the group consisting of -H, -T, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl; wherein -T, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally substituted with one or more -R¹¹, which are the same or different and wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R¹²)-, -S(O)₂N(R¹²)-, -S(O)N(R¹²)-, -S(O)₂-,

-S(O)-, -N(R¹²)S(O)₂N(R^{12a})-, -S-, -N(R¹²)-, -OC(OR¹²)(R^{12a})-, -N(R¹²)C(O)N(R^{12a})-, and -OC(O)N(R¹²)-;

each T is independently of each other selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, and 8- to 11-membered heterobicycyl; wherein each T is independently optionally substituted with one or more -R¹¹, which are the same or different;

each -R¹¹ is independently of each other selected from halogen, -CN, oxo (=O), -COOR¹³, -OR¹³, -C(O)R¹³, -C(O)N(R¹³R^{13a}), -S(O)₂N(R¹³R^{13a}), -S(O)N(R¹³R^{13a}), -S(O)₂R¹³, -S(O)R¹³, -N(R¹³)S(O)₂N(R^{13a}R^{13b}), -SR¹³, -N(R¹³R^{13a}), -NO₂, -OC(O)R¹³, -N(R¹³)C(O)R^{13a}, -N(R¹³)S(O)₂R^{13a}, -N(R¹³)S(O)R^{13a}, -N(R¹³)C(O)OR^{13a}, -N(R¹³)C(O)N(R^{13a}R^{13b}), -OC(O)N(R¹³R^{13a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different;

each -R¹², -R^{12a}, -R¹³, -R^{13a}, and -R^{13b} is independently selected from the group consisting of -H, and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different;

optionally, one or more of the pairs -R¹/-R^{1a}, -R²/-R^{2a}, -R³/-R^{3a}, -R⁶/-R^{6a}, and -R⁷/-R^{7a} are joined together with the atom to which they are attached to form a C₃₋₁₀ cycloalkyl or a 3- to 10-membered heterocyclyl;

optionally, one or more of the pairs -R¹/-R², -R¹/-R³, -R¹/-R⁴, -R¹/-R⁵, -R¹/-R⁶, -R¹/-R⁷, -R²/-R³, -R²/-R⁴, -R²/-R⁵, -R²/-R⁶, -R²/-R⁷, -R³/-R⁴, -R³/-R⁵, -R³/-R⁶, -R³/-R⁷, -R⁴/-R⁵, -R⁴/-R⁶, -R⁴/-R⁷, -R⁵/-R⁶, -R⁵/-R⁷, and -R⁶/-R⁷ are joint together with the atoms to which they are attached to form a ring A;

A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C₃₋₁₀ cycloalkyl; 3- to 10-membered heterocyclyl; and 8- to 11-membered heterobicycyl;

wherein -L¹- is substituted with at least one -L²- and wherein -L¹- is optionally further substituted.

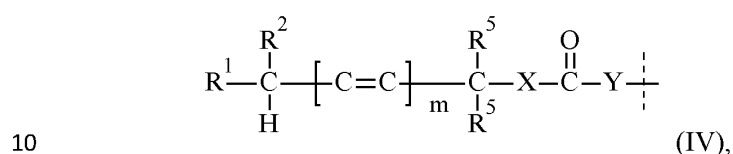
30 The optional further substituents of -L¹- of formula (III) are in certain embodiments as described above.

In certain embodiments -L¹- of formula (III) is substituted with one moiety -L²-.

In certain embodiments -L¹- of formula (III) is not further substituted.

In certain embodiments -L¹- is as disclosed in EP1536334B1, WO2009/009712A1, WO2008/034122A1, WO2009/143412A2, WO2011/082368A2, and US8618124B2, which
5 are herewith incorporated by reference in their entirety.

In certain embodiments -L¹- is as disclosed in US8946405B2 and US8754190B2, which are herewith incorporated by reference in their entirety. Accordingly, in certain embodiments -L¹- is of formula (IV):



wherein

the dashed line indicates attachment to -D- and wherein attachment is through a functional group of -D- selected from the group consisting of -OH, -SH and -NH₂; m is 0 or 1;

15 at least one or both of -R¹ and -R² is/are independently of each other selected from the group consisting of -CN, -NO₂, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkenyl, optionally substituted alkynyl, -C(O)R³, -S(O)R³, -S(O)₂R³, and -SR⁴,

one and only one of -R¹ and -R² is selected from the group consisting of -H, 20 optionally substituted alkyl, optionally substituted arylalkyl, and optionally substituted heteroarylalkyl;

-R³ is selected from the group consisting of -H, optionally substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, -OR⁹ and -N(R⁹)₂;

25 -R⁴ is selected from the group consisting of optionally substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, and optionally substituted heteroarylalkyl;

each -R⁵ is independently selected from the group consisting of -H, optionally substituted alkyl, optionally substituted alkenylalkyl, optionally substituted alkynylalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl;

30

-R⁹ is selected from the group consisting of -H and optionally substituted alkyl;

-Y- is absent and -X- is -O- or -S-; or

-Y- is -N(Q)CH₂- and -X- is -O-;

5 Q is selected from the group consisting of optionally substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl and optionally substituted heteroarylalkyl;

optionally, -R¹ and -R² may be joined to form a 3 to 8-membered ring; and

optionally, both -R⁹ together with the nitrogen to which they are attached form a heterocyclic ring;

10 wherein -L¹- is substituted with at least one -L²- and wherein -L¹- is optionally further substituted.

Only in the context of formula (IV) the terms used have the following meaning:

15 The term “alkyl” as used herein includes linear, branched or cyclic saturated hydrocarbon groups of 1 to 8 carbons, or in certain embodiments 1 to 6 or 1 to 4 carbon atoms.

The term “alkoxy” includes alkyl groups bonded to oxygen, including methoxy, ethoxy, isopropoxy, cyclopropoxy, cyclobutoxy, and similar.

20

The term “alkenyl” includes non-aromatic unsaturated hydrocarbons with carbon-carbon double bonds.

25 The term “alkynyl” includes non-aromatic unsaturated hydrocarbons with carbon-carbon triple bonds.

30 The term “aryl” includes aromatic hydrocarbon groups of 6 to 18 carbons, such as 6 to 10 carbons, including groups such as phenyl, naphthyl, and anthracenyl. The term “heteroaryl” includes aromatic rings comprising 3 to 15 carbons containing at least one N, O or S atom, such as 3 to 7 carbons containing at least one N, O or S atom, including groups such as pyrrolyl, pyridyl, pyrimidinyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, quinolyl, indolyl, indenyl, and similar.

In some instance, alkenyl, alkynyl, aryl or heteroaryl moieties may be coupled to the remainder of the molecule through an alkylene linkage. Under those circumstances, the substituent will be referred to as alkenylalkyl, alkynylalkyl, arylalkyl or heteroarylalkyl, indicating that an alkylene moiety is between the alkenyl, alkynyl, aryl or heteroaryl moiety and the molecule to which the alkenyl, alkynyl, aryl or heteroaryl is coupled.

The term “halogen” includes bromo, fluoro, chloro and iodo.

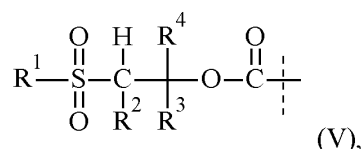
The term “heterocyclic ring” refers to a 4 to 8 membered aromatic or non-aromatic ring comprising 3 to 7 carbon atoms and at least one N, O, or S atom. Examples are piperidinyl, piperazinyl, tetrahydropyranyl, pyrrolidine, and tetrahydrofuranlyl, as well as the exemplary groups provided for the term “heteroaryl” above.

When a ring system is optionally substituted, suitable substituents are selected from the group consisting of alkyl, alkenyl, alkynyl, or an additional ring, each optionally further substituted. Optional substituents on any group, including the above, include halo, nitro, cyano, -OR, -SR, -NR₂, -OCOR, -NRCOR, -COOR, -CONR₂, -SOR, -SO₂R, -SONR₂, -SO₂NR₂, wherein each R is independently alkyl, alkenyl, alkynyl, aryl or heteroaryl, or two R groups taken together with the atoms to which they are attached form a ring.

In certain embodiments -L¹- of formula (IV) is substituted with one moiety -L²-.

In certain embodiments -L¹- of formula (IV) is not further substituted.

In certain embodiments -L¹- is as disclosed in WO2013/036857A1, which is herewith incorporated by reference in its entirety. Accordingly, in certain embodiments -L¹- is of formula (V):



wherein

the dashed line indicates attachment to -D- through an amine functional group of -D-;

- R¹ is selected from the group consisting of optionally substituted C₁-C₆ linear, branched, or cyclic alkyl; optionally substituted aryl; optionally substituted heteroaryl; alkoxy; and -NR⁵₂;
- R² is selected from the group consisting of -H; optionally substituted C₁-C₆ alkyl; optionally substituted aryl; and optionally substituted heteroaryl;
- R³ is selected from the group consisting of -H; optionally substituted C₁-C₆ alkyl; optionally substituted aryl; and optionally substituted heteroaryl;
- R⁴ is selected from the group consisting of -H; optionally substituted C₁-C₆ alkyl; optionally substituted aryl; and optionally substituted heteroaryl;
- each -R⁵ is independently of each other selected from the group consisting of -H; optionally substituted C₁-C₆ alkyl; optionally substituted aryl; and optionally substituted heteroaryl; or when taken together two -R⁵ can be cycloalkyl or cycloheteroalkyl;
- wherein -L¹- is substituted with at least one -L²- and wherein -L¹- is optionally further substituted.

Only in the context of formula (V) the terms used have the following meaning:

- “Alkyl”, “alkenyl”, and “alkynyl” include linear, branched or cyclic hydrocarbon groups of 1-8 carbons or 1-6 carbons or 1-4 carbons wherein alkyl is a saturated hydrocarbon, alkenyl includes one or more carbon-carbon double bonds and alkynyl includes one or more carbon-carbon triple bonds. Unless otherwise specified these contain 1-6 C.
- “Aryl” includes aromatic hydrocarbon groups of 6-18 carbons, such as 6-10 carbons, including groups such as phenyl, naphthyl, and anthracene “Heteroaryl” includes aromatic rings comprising 3-15 carbons containing at least one N, O or S atom, such as 3-7 carbons containing at least one N, O or S atom, including groups such as pyrrolyl, pyridyl, pyrimidinyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, quinolyl, indolyl, indenyl, and similar.
- The term “substituted” means an alkyl, alkenyl, alkynyl, aryl, or heteroaryl group comprising one or more substituent groups in place of one or more hydrogen atoms. Substituents may generally be selected from halogen including F, Cl, Br, and I; lower alkyl including linear, branched, and cyclic; lower haloalkyl including fluoroalkyl, chloroalkyl, bromoalkyl, and iodoalkyl; OH; lower alkoxy including linear, branched, and cyclic; SH; lower alkylthio

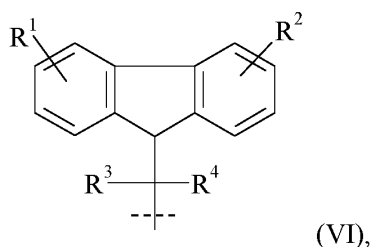
including linear, branched and cyclic; amino, alkylamino, dialkylamino, silyl including alkylsilyl, alkoxysilyl, and arylsilyl; nitro; cyano; carbonyl; carboxylic acid, carboxylic ester, carboxylic amide, aminocarbonyl; aminoacyl; carbamate; urea; thiocarbamate; thiourea; ketone; sulfone; sulfonamide; aryl including phenyl, naphthyl, and anthracenyl; heteroaryl
 5 including 5-member heteroaryls including as pyrrole, imidazole, furan, thiophene, oxazole, thiazole, isoxazole, isothiazole, thiadiazole, triazole, oxadiazole, and tetrazole, 6-member heteroaryls including pyridine, pyrimidine, pyrazine, and fused heteroaryls including benzofuran, benzothiophene, benzoxazole, benzimidazole, indole, benzothiazole, benzisoxazole, and benzisothiazole.

10

In certain embodiments -L¹- of formula (V) is substituted with one moiety -L²-.

In certain embodiments -L¹- of formula (V) is not further substituted.

15 In certain embodiments -L¹- is as disclosed in US7585837B2, which is herewith incorporated by reference in its entirety. Accordingly, in certain embodiments -L¹- is of formula (VI):



wherein

the dashed line indicates attachment to -D- through an amine functional group of -D;

20 R¹ and R² are independently selected from the group consisting of hydrogen, alkyl, alkoxy, alkoxyalkyl, aryl, alkaryl, aralkyl, halogen, nitro, -SO₃H, -SO₂NHR⁵, amino, ammonium, carboxyl, PO₃H₂, and OPO₃H₂;

R³, R⁴, and R⁵ are independently selected from the group consisting of hydrogen, alkyl, and aryl;

25 wherein -L¹- is substituted with at least one -L²- and wherein -L¹- is optionally further substituted.

Suitable substituents for formulas (VI) are alkyl (such as C₁₋₆ alkyl), alkenyl (such as C₂₋₆ alkenyl), alkynyl (such as C₂₋₆ alkynyl), aryl (such as phenyl), heteroalkyl, heteroalkenyl, heteroalkynyl, heteroaryl (such as aromatic 4 to 7 membered heterocycle) or halogen moieties.

5 Only in the context of formula (VI) the terms used have the following meaning:

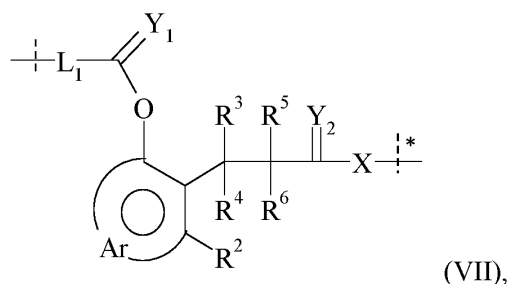
The terms “alkyl”, “alkoxy”, “alkoxyalkyl”, “aryl”, “alkaryl” and “aralkyl” mean alkyl radicals of 1-8, such as 1-4 carbon atoms, e.g. methyl, ethyl, propyl, isopropyl and butyl, and aryl radicals of 6-10 carbon atoms, e.g. phenyl and naphthyl. The term “halogen” includes bromo,
 10 fluoro, chloro and iodo.

In certain embodiments -L¹- of formula (VI) is substituted with one moiety -L²-.

In certain embodiments -L¹- of formula (VI) is not further substituted.

15

A further preferred embodiment for -L¹- is disclosed in WO2002/089789A1, which is herewith incorporated by reference in its entirety. Accordingly, a preferred moiety -L¹- is of formula (VII):



20

wherein

the dashed line indicates attachment to -D- through an amine functional group of -D-;
 L₁ is a bifunctional linking group,

Y₁ and Y₂ are independently O, S or NR⁷;

R², R³, R⁴, R⁵, R⁶ and R⁷ are independently selected from the group consisting of
 25 hydrogen, C₁₋₆ alkyls, C₃₋₁₂ branched alkyls, C₃₋₈ cycloalkyls, C₁₋₆ substituted alkyls,
 C₃₋₈ substituted cycloalkyls, aryls, substituted aryls, aralkyls, C₁₋₆ heteroalkyls,
 substituted C₁₋₆ heteroalkyls, C₁₋₆ alkoxy, phenoxy, and C₁₋₆ heteroalkoxy;

Ar is a moiety which when included in formula (VII) forms a multisubstituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

X is a chemical bond or a moiety that is actively transported into a target cell, a hydrophobic moiety, or a combination thereof,

y is 0 or 1;

wherein $-L^1-$ is substituted with at least one $-L^2-$ and wherein $-L^1-$ is optionally further substituted.

Only in the context of formula (VII) the terms used have the following meaning:

The term “alkyl” shall be understood to include, e.g., straight, branched, substituted C_{1-12} alkyls, including alkoxy, C_{3-8} cycloalkyls or substituted cycloalkyls, etc.

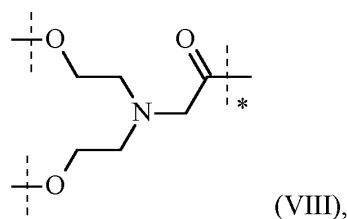
The term “substituted” shall be understood to include adding or replacing one or more atoms contained within a functional group or compounds with one or more different atoms.

Substituted alkyls include carboxyalkyls, aminoalkyls, dialkylaminos, hydroxyalkyls and mercaptoalkyls; substituted cycloalkyls include moieties such as 4-chlorocyclohexyl; aryls include moieties such as naphthyl; substituted aryls include moieties such as 3-bromo-phenyl; aralkyls include moieties such as toluyl; heteroalkyls include moieties such as ethylthiophene; substituted heteroalkyls include moieties such as 3-methoxythiophene; alkoxy includes moieties such as methoxy; and phenoxy includes moieties such as 3-nitrophenoxy. Halo- shall be understood to include fluoro, chloro, iodo and bromo.

In certain embodiments $-L^1-$ of formula (VII) is substituted with one moiety $-L^2-$.

In certain embodiments $-L^1-$ of formula (VII) is not further substituted.

In certain embodiments $-L^1-$ comprises a substructure of formula (VIII)



wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D- through an amide bond;

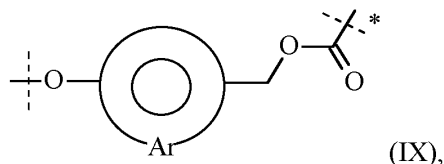
the unmarked dashed lines indicate attachment to the remainder of -L¹-; and

- 5 wherein -L¹- is substituted with at least one -L²- and wherein -L¹- is optionally further substituted.

In certain embodiments -L¹- of formula (VIII) is substituted with one moiety -L²-.

- 10 In certain embodiments -L¹- of formula (VIII) is not further substituted.

In certain embodiments -L¹- comprises a substructure of formula (IX)



wherein

- 15 the dashed line marked with the asterisk indicates attachment to a nitrogen of -D- through a carbamate bond;

the unmarked dashed lines indicate attachment to the remainder of -L¹-; and

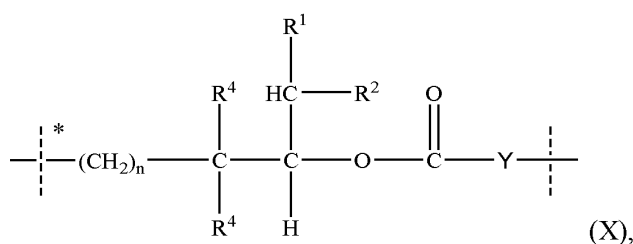
wherein -L¹- is substituted with at least one -L²- and wherein -L¹- is optionally further substituted.

20

In certain embodiments -L¹- of formula (IX) is substituted with one moiety -L²-.

In certain embodiments -L¹- of formula (IX) is not further substituted.

- 25 In certain embodiments -L¹- has a structure as disclosed in WO2020/206358 A1. Accordingly, in certain embodiments the moiety -L¹- is of formula (X):



wherein

the unmarked dashed line indicates attachment to -D-;

the dashed line marked with the asterisk indicates attachment to -L²-;

5 n is an integer selected from the group consisting of 0, 1, 2, 3, 4, 5 and 6;

-R¹ and -R² are independently an electron-withdrawing group, alkyl, or -H, and wherein at least one of -R¹ or -R² is an electron-withdrawing group;

each -R⁴ is independently C₁-C₃ alkyl or the two -R⁴ are taken together with the carbon atom to which they are attached to form a 3- to 6-membered ring; and

10 -Y- is absent when -D- is a drug moiety connected through an amine, or -Y- is -N(R⁶)CH₂- when -D- is a drug moiety connected through a phenol, alcohol, thiol, thiophenol, imidazole, or non-basic amine; wherein -R⁶ is optionally substituted C₁-C₆ alkyl, optionally substituted aryl, or optionally substituted heteroaryl.

15 In certain embodiments n of formula (X) is an integer selected from 1, 2, 3, 4, 5 and 6. In certain embodiments n of formula (X) is an integer selected from 1, 2 and 3. In certain embodiments n of formula (X) is an integer from 0, 1, 2 and 3. In certain embodiments n of formula (X) is 1. In certain embodiments n of formula (X) is 2. In certain embodiments n of formula (X) is 3.

20 In certain embodiments the electron-withdrawing group of -R¹ and -R² of formula (X) is selected from the group consisting of -CN; -NO₂; optionally substituted aryl; optionally substituted heteroaryl; optionally substituted alkenyl; optionally substituted alkynyl; -COR³, -SOR³, or -SO₂R³, wherein -R³ is -H, optionally substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, -OR⁸ or -NR⁸₂, wherein each -R⁸ is independently -H or optionally substituted alkyl, or both -R⁸ groups are taken together with the nitrogen to which they are attached to form a heterocyclic ring; or -SR⁹, wherein -R⁹ is optionally substituted alkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, or optionally substituted heteroarylalkyl.

25

In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is $-\text{CN}$. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is $-\text{NO}_2$. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is optionally substituted aryl comprising 6 to 10 carbons. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is optionally substituted phenyl, naphthyl, or anthracenyl. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is optionally substituted heteroaryl comprising 3 to 7 carbons and comprising at least one N, O, or S atom. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is optionally substituted pyrrolyl, pyridyl, pyrimidinyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, quinolyl, indolyl, or indenyl. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is optionally substituted alkenyl containing 2 to 20 carbon atoms. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is optionally substituted alkynyl comprising 2 to 20 carbon atoms. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is $-\text{COR}^3$, $-\text{SOR}^3$, or $-\text{SO}_2\text{R}^3$, wherein $-\text{R}^3$ is $-\text{H}$, optionally substituted alkyl comprising 1 to 20 carbon atoms, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, optionally substituted heteroarylalkyl, $-\text{OR}^8$ or $-\text{NR}^8_2$, wherein each $-\text{R}^8$ is independently $-\text{H}$ or optionally substituted alkyl comprising 1 to 20 carbon atoms, or both $-\text{R}^8$ groups are taken together with the nitrogen to which they are attached to form a heterocyclic ring. In certain embodiments the electron-withdrawing group of $-R^1$ and $-R^2$ of formula (X) is $-\text{SR}^9$, wherein $-\text{R}^9$ is optionally substituted alkyl comprising 1 to 20 carbon atoms, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, or optionally substituted heteroarylalkyl.

In certain embodiments at least one of $-R^1$ or $-R^2$ of formula (X) is $-\text{CN}$, $-\text{SOR}^3$ or $-\text{SO}_2\text{R}^3$. In certain embodiments at least one of $-R^1$ and $-R^2$ of formula (X) is $-\text{CN}$ or $-\text{SO}_2\text{R}^3$. In certain embodiments at least one of $-R^1$ and $-R^2$ of formula (X) is $-\text{CN}$ or $-\text{SO}_2\text{R}^3$, wherein $-\text{R}^3$ is optionally substituted alkyl, optionally substituted aryl, or $-\text{NR}^8_2$. In certain embodiments at least one of $-R^1$ and $-R^2$ of formula (X) is $-\text{CN}$, $-\text{SO}_2\text{N}(\text{CH}_3)_2$, $-\text{SO}_2\text{CH}_3$, phenyl substituted with $-\text{SO}_2$, phenyl substituted with $-\text{SO}_2$ and $-\text{Cl}$, $-\text{SO}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$, $-\text{SO}_2\text{CH}(\text{CH}_3)_2$, $-\text{SO}_2\text{N}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, or $-\text{SO}_2\text{N}(\text{CH}_2\text{CH}_2\text{OCH}_3)_2$.

In certain embodiments each $-R^4$ of formula (X) is independently C_1 - C_3 alkyl. In certain embodiments both $-R^4$ are methyl.

In certain embodiments $-Y-$ of formula (X) is absent. In certain embodiments $-Y-$ of formula
5 (X) is $-N(R^6)CH_2-$.

In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is $-CN$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is $-SO_2N(CH_3)_2$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is
10 SO_2CH_3 , $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is $-SO_2N(CH_2CH_2)_2CHCH_3$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is phenyl substituted with $-SO_2$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is phenyl substituted with $-SO_2$ and $-Cl$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X),
15 wherein n is 1, $-R^1$ is $-SO_2N(CH_2CH_2)_2O$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is $-SO_2CH(CH_3)_2$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is $-SO_2N(CH_3)(CH_2CH_3)$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is $-SO_2N(CH_2CH_2OCH_3)_2$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain
20 embodiments $-L^1-$ is of formula (X), wherein n is 1, $-R^1$ is phenyl substituted with $-SO_2$ and $-CH_3$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$.

In certain embodiments $-L^1-$ is of formula (X), wherein n is 2, $-R^1$ is $-CN$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 2, $-R^1$ is $-SO_2N(CH_3)_2$, $-R^2$
25 is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 2, $-R^1$ is SO_2CH_3 , $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 2, $-R^1$ is $-SO_2N(CH_2CH_2)_2CHCH_3$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 2, $-R^1$ is phenyl substituted with $-SO_2$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 2, $-R^1$ is phenyl substituted with $-SO_2$ and $-Cl$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X),
30 wherein n is 2, $-R^1$ is $-SO_2N(CH_2CH_2)_2O$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 2, $-R^1$ is $-SO_2CH(CH_3)_2$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula (X), wherein n is 2, $-R^1$ is $-SO_2N(CH_3)(CH_2CH_3)$, $-R^2$ is $-H$, and $-R^4$ is $-CH_3$. In certain embodiments $-L^1-$ is of formula

(X), wherein n is 2, -R¹ is -SO₂N(CH₂CH₂OCH₃)₂, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 2, -R¹ is phenyl substituted with -SO₂ and -CH₃, -R² is -H, and -R⁴ is -CH₃.

- 5 In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is -CN, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is -SO₂N(CH₃)₂, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is SO₂CH₃, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is -SO₂N(CH₂CH₂)₂CHCH₃, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is phenyl substituted with -SO₂, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is phenyl substituted with -SO₂ and -Cl, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is -SO₂N(CH₂CH₂)₂O, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is -SO₂CH(CH₃)₂, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is -SO₂N(CH₃)(CH₂CH₃), -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is -SO₂N(CH₂CH₂OCH₃)₂, -R² is -H, and -R⁴ is -CH₃. In certain embodiments -L¹- is of formula (X), wherein n is 3, -R¹ is phenyl substituted with -SO₂ and -CH₃, -R² is -H, and -R⁴ is -CH₃.

20

Only in the context of formula (X) the terms used have the following meaning:

- The term "alkyl" refers to linear, branched, or cyclic saturated hydrocarbon groups of 1 to 20, 1 to 12, 1 to 8, 1 to 6, or 1 to 4 carbon atoms. In certain embodiments an alkyl is linear or branched. Examples of linear or branched alkyl groups include methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, isobutyl, sec-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, n-nonyl, and n-decyl. In certain embodiments an alkyl is cyclic. Examples of cyclic alkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclopentadienyl, and cyclohexyl.

- 30 The term "alkoxy" refers to alkyl groups bonded to oxygen, including methoxy, ethoxy, isopropoxy, cyclopropoxy, and cyclobutoxy.

The term "alkenyl" refers to non-aromatic unsaturated hydrocarbons with carbon-carbon double bonds and 2 to 20, 2 to 12, 2 to 8, 2 to 6, or 2 to 4 carbon atoms.

The term "alkynyl" refers to non-aromatic unsaturated hydrocarbons with carbon-carbon triple bonds and 2 to 20, 2 to 12, 2 to 8, 2 to 6, or 2 to 4 carbon atoms.

- 5 The term "aryl" refers to aromatic hydrocarbon groups of 6 to 18 carbons, preferably 6 to 10 carbons, including groups such as phenyl, naphthyl, and anthracenyl. The term "heteroaryl" refers to aromatic rings comprising 3 to 15 carbons comprising at least one N, O or S atom, preferably 3 to 7 carbons comprising at least one N, O or S atom, including groups such as pyrrolyl, pyridyl, pyrimidinyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 10 quinolyl, indolyl, and indenyl.

In certain embodiments alkenyl, alkynyl, aryl or heteroaryl moieties may be coupled to the remainder of the molecule through an alkyl linkage. Under those circumstances, the substituent will be referred to as alkenylalkyl, alkynylalkyl, arylalkyl or heteroarylalkyl, indicating that an 15 alkylene moiety is between the alkenyl, alkynyl, aryl or heteroaryl moiety and the molecule to which the alkenyl, alkynyl, aryl or heteroaryl is coupled.

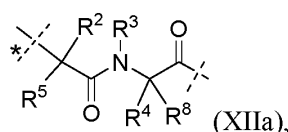
The term "halogen" or "halo" refers to bromo, fluoro, chloro and iodo.

- 20 The term "heterocyclic ring" or "heterocyclyl" refers to a 3- to 15-membered aromatic or non-aromatic ring comprising at least one N, O, or S atom. Examples include piperidiny, piperazinyl, tetrahydropyranyl, pyrrolidine, and tetrahydrofuranly, as well as the exemplary groups provided for the term "heteroaryl" above. In certain embodiments a heterocyclic ring or heterocyclyl is non-aromatic. In certain embodiments a heterocyclic ring or heterocyclyl is 25 aromatic.

The term "optionally substituted" refers to a group may be unsubstituted or substituted by one or more (e.g., 1, 2, 3, 4 or 5) of the substituents which may be the same or different. Examples of substituents include alkyl, alkenyl, alkynyl, halogen, -CN, -OR^{aa}, 30 -SR^{aa}, -NR^{aa}R^{bb}, -NO₂, -C=NH(OR^{aa}), -C(O)R^{aa}, -OC(O)R^{aa}, -C(O)OR^{aa}, -C(O)NR^{aa}R^{bb}, -OC(O)NR^{aa}R^{bb}, -NR^{aa}C(O)R^{bb}, -NR^{aa}C(O)OR^{bb}, -S(O)R^{aa}, -S(O)₂R^{aa}, -NR^{aa}S(O)R^{bb}, -C(O)NR^{aa}S(O)R^{bb}, -NR^{aa}S(O)₂R^{bb}, -C(O)NR^{aa}S(O)₂R^{bb}, -S(O)NR^{aa}R^{bb}, -S(O)₂NR^{aa}R^{bb}, -P(O)(OR^{aa})(OR^{bb}), heterocyclyl, heteroaryl, or aryl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, heteroaryl, and aryl are each independently optionally substituted

by $-R^{cc}$, wherein $-R^{aa}$ and $-R^{bb}$ are each independently $-H$, alkyl, alkenyl, alkynyl, heterocyclyl, heteroaryl, or aryl, or $-R^{aa}$ and $-R^{bb}$ are taken together with the nitrogen atom to which they attach to form a heterocyclyl, which is optionally substituted by alkyl, alkenyl, alkynyl, halogen, hydroxyl, alkoxy, or $-CN$, and wherein: each $-R^{cc}$ is independently alkyl, alkenyl, alkynyl, halogen, heterocyclyl, heteroaryl, aryl, $-CN$, or $-NO_2$.

In certain embodiments $-L^1$ has a structure as disclosed in formula I of WO2021/242756 A1. Accordingly, in certain embodiments the moiety $-L^1$ is of formula (XIIa):



wherein

the unmarked dashed line indicates attachment to $-D$;

the dashed line marked with the asterisk indicates attachment to $-L^2$;

$-R^2$, $-R^4$ and $-R^8$ are independently selected from the group consisting of $-H$ or C_{1-4} alkyl;

$-R^3$ is C_{1-4} alkyl or $-R^3$ and $-R^4$ together with the atoms to which they are attached form a 5- or 6-membered heterocyclic ring;

$-R^5$ is $-NH_2$;

with the proviso that when $-R^4$ and $-R^3$ together with the atoms to which they are attached from a 5- or 6-membered heterocyclic ring $-R^2$ is not $-H$; and

wherein the $-L^1$ of formula (XIIa) is optionally substituted.

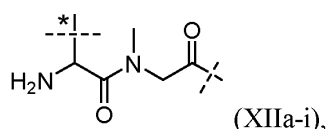
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In certain embodiments both $-R^4$ and $-R^8$ of formula (XIIa) are $-H$.

In certain embodiments $-R^3$ is methyl. In certain embodiments $-R^3$ is $-H$.

25 In certain embodiments $-R^2$ is $-H$.

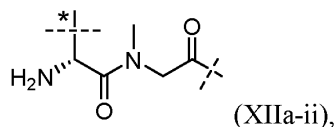
In certain embodiments $-L^1$ is of formula (XIIa-i)



the unmarked dashed line indicates attachment to $-D$; and

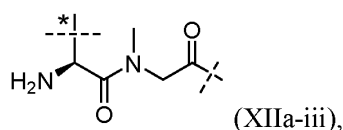
the dashed line marked with the asterisk indicates attachment to $-L^2$.

In certain embodiments $-L^1$ is of formula (XIIa-ii)



- 5 the unmarked dashed line indicates attachment to $-D$ -; and
the dashed line marked with the asterisk indicates attachment to $-L^2$.

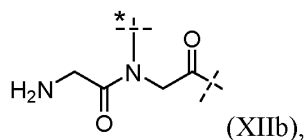
In certain embodiments $-L^1$ is of formula (XIIa-iii)



- 10 the unmarked dashed line indicates attachment to $-D$ -; and
the dashed line marked with the asterisk indicates attachment to $-L^2$.

In certain embodiments $-L^1$ has a structure as disclosed in formula II of WO2022/096636 A1.

Accordingly, in certain embodiments the moiety $-L^1$ is of formula (XIIb):



- 15 wherein
the unmarked dashed line indicates attachment to $-D$ -; and
the dashed line marked with the asterisk indicates attachment to $-L^2$.

- 20 In certain embodiments $-L^2$ is absent.

- In certain embodiments $-L^2$ is a spacer moiety, in particular selected from the group consisting of $-T$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{y1})$ -, $-S(O)_2N(R^{y1})$ -, $-S(O)N(R^{y1})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{y1})S(O)_2N(R^{y1a})$ -, $-S$ -, $-N(R^{y1})$ -, $-OC(OR^{y1})(R^{y1a})$ -, $-N(R^{y1})C(O)N(R^{y1a})$ -, $-OC(O)N(R^{y1})$ -, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T$ -, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are
- 25

optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;

- 5 -R^{y1} and -R^{y1a} are independently of each other selected from the group consisting of -H, -T, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different, and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-, -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-, and -OC(O)N(R^{y4})-;
- 10 each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl;
- 15 wherein each T is independently optionally substituted with one or more -R^{y2}, which are the same or different;

- each -R^{y2} is independently selected from the group consisting of halogen, -CN, oxo (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a}), -S(O)₂N(R^{y5}R^{y5a}), -S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}), -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)OR^{y5a}, -N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and
- 20 each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently selected from the group consisting of -H, and C₁₋₆ alkyl, wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.
- 25

- In certain embodiments -L²- is selected from -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, and C₂₋₂₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-,
- 30

- S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;
- R^{y1} and -R^{y1a} are independently of each other selected from the group consisting of -H, -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl; wherein -T, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different, and wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, and C₂₋₁₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-, -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-, and -OC(O)N(R^{y4})-;
- each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more -R^{y2}, which are the same or different;
- R^{y2} is selected from the group consisting of halogen, -CN, oxo (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a}), -S(O)₂N(R^{y5}R^{y5a}), -S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}), -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)OR^{y5a}, -N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently of each other selected from the group consisting of -H, and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.
- In certain embodiments -L²- is selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;

$-R^{y1}$ and $-R^{y1a}$ are independently selected from the group consisting of -H, -T, C_{1-10} alkyl, C_{2-10} alkenyl, and C_{2-10} alkynyl;

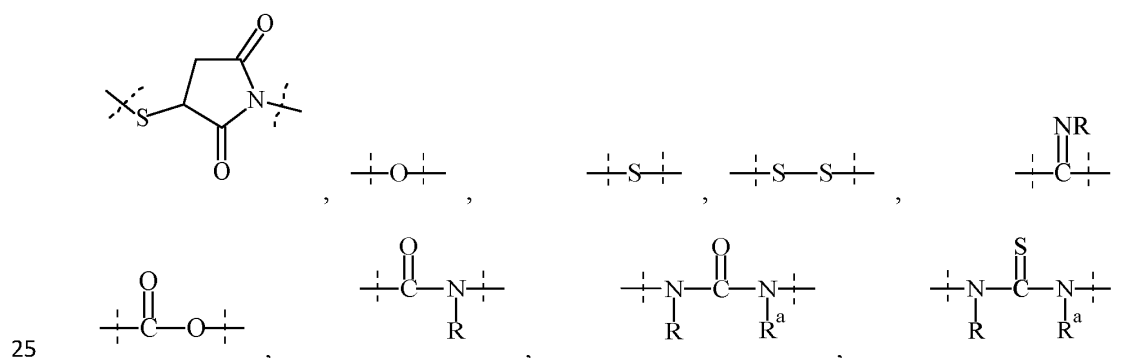
each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl;

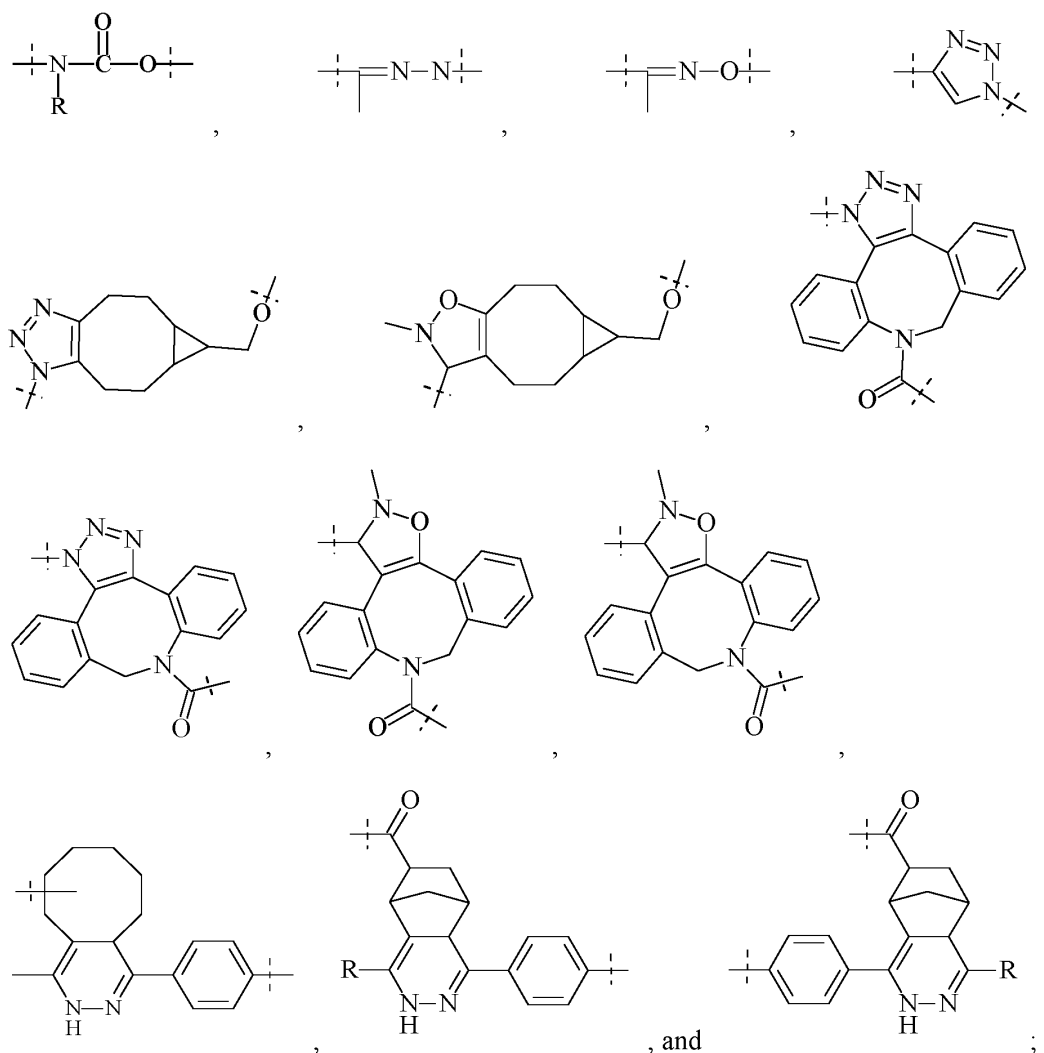
each $-R^{y2}$ is independently selected from the group consisting of halogen, and C_{1-6} alkyl; and each $-R^{y3}$, $-R^{y3a}$, $-R^{y4}$, $-R^{y4a}$, $-R^{y5}$, $-R^{y5a}$ and $-R^{y5b}$ is independently of each other selected from the group consisting of -H, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

In certain embodiments $-L^2-$ is a C_{1-20} alkyl chain, which is optionally interrupted by one or more groups independently selected from -O-, -S-, -T- and $-C(O)N(R^{y1})-$; and which C_{1-20} alkyl chain is optionally substituted with one or more groups independently selected from -OH, -T and $-C(O)N(R^{y6}R^{y6a})$; wherein $-R^{y1}$, $-R^{y6}$, $-R^{y6a}$ are independently selected from the group consisting of H and C_{1-4} alkyl and wherein T is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl.

In certain embodiments $-L^2-$ has a molecular weight in the range of from 14 g/mol to 750 g/mol.

In certain embodiments $-L^2-$ comprises a moiety selected from





5 wherein

-R and -R^a are independently of each other selected from the group consisting of -H, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl.

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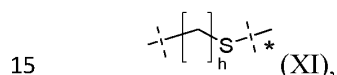
In certain embodiments -L²- has a chain length of 1 to 20 atoms. In certain embodiments -L²- has a chain length of 2 to 10 atoms.

In certain embodiments -L²- has a chain length of at least 35 atoms. In certain

15 embodiments -L²- has a chain length of at least 50 atoms. In certain embodiments -L²- has a

chain length of at least 75 atoms. In certain embodiments -L²- has a chain length of at least 100 atoms. In certain embodiments -L²- has a chain length of at least 150 atoms. In certain embodiments -L²- has a chain length of at least 200 atoms. In certain embodiments -L²- has a chain length of at least 250 atoms. In certain embodiments -L²- has a chain length of at least 300 atoms. In certain embodiments -L²- has a chain length of at most 3000 atoms. In certain embodiments -L²- has a chain length of at most 2500 atoms. In certain embodiments -L²- has a chain length of at most 2000 atoms. In certain embodiments -L²- has a chain length of at most 1500 atoms. In certain embodiments -L²- has a chain length ranging from 35 to 3000 atoms. In certain embodiments -L²- has a chain length ranging from 50 to 2500 atoms. In certain embodiments -L²- has a chain length ranging from 75 to 2000 atoms. In certain embodiments -L²- has a chain length ranging from 100 to 1500 atoms. In certain embodiments -L²- has a chain length ranging from 125 to 1000 atoms.

In certain embodiments -L²- is of formula (XI)



wherein

the unmarked dashed line indicates attachment to -L¹;

the dashed line marked with the asterisk indicates attachment to the at least one polymeric moiety;

20 h is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

In certain embodiments -L²- is of formula (XI) and h is 1. In certain embodiments -L²- is of formula (XI) and h is 2. In certain embodiments -L²- is of formula (XI) and h is 3. In certain embodiments -L²- is of formula (XI) and h is 4. In certain embodiments -L²- is of formula (XI) and h is 5. In certain embodiments -L²- is of formula (XI) and h is 6. In certain embodiments -L²- is of formula (XI) and h is 7. In certain embodiments -L²- is of formula (XI) and h is 8. In certain embodiments -L²- is of formula (XI) and h is 9. In certain embodiments -L²- is of formula (XI) and h is 10. In certain embodiments -L²- is of formula (XI) and h is 11. In certain embodiments -L²- is of formula (XI) and h is 12. In certain embodiments -L²- is of formula (XI) and h is 13. In certain embodiments -L²- is of formula (XI) and h is 14. In certain embodiments -L²- is of formula (XI) and h is 15.

In certain embodiments $-L^2-$ has a molecular weight of at least 450 Da. In certain embodiments $-L^2-$ has a molecular weight of at least 1 kDa. In certain embodiments $-L^2-$ has a molecular weight of at least 1.5 kDa. In certain embodiments $-L^2-$ has a molecular weight of at least 2 kDa. In certain embodiments $-L^2-$ has a molecular weight of at least 2.5 kDa. In certain
5 embodiments $-L^2-$ has a molecular weight of at least 3 kDa. In certain embodiments $-L^2-$ has a molecular weight of at least 3.5 kDa. In certain embodiments $-L^2-$ has a molecular weight of at least 4 kDa. In certain embodiments $-L^2-$ has a molecular weight of at least 5 kDa. In certain
embodiments $-L^2-$ has a maximum molecular weight of 160 kDa. In certain
embodiments $-L^2-$ has a maximum molecular weight of 120 kDa. In certain
10 embodiments $-L^2-$ has a maximum molecular weight of 100 kDa. In certain
embodiments $-L^2-$ has a maximum molecular weight of 80 kDa. In certain
embodiments $-L^2-$ has a maximum molecular weight of 70 kDa. In certain
embodiments $-L^2-$ has a maximum molecular weight of 60 kDa. In certain
embodiments $-L^2-$ has a maximum molecular weight of 50 kDa. In certain
15 embodiments $-L^2-$ has a maximum molecular weight of 40 kDa. In certain
embodiments $-L^2-$ has a molecular weight of about 450 Da. In certain embodiments $-L^2-$ has a
molecular weight of about 1 kDa. In certain embodiments $-L^2-$ has a molecular weight of about
1.5 kDa. In certain embodiments $-L^2-$ has a molecular weight of about 2 kDa. In certain
embodiments $-L^2-$ has a molecular weight of about 2.5 kDa. In certain embodiments $-L^2-$ has a
20 molecular weight of about 3 kDa. In certain embodiments $-L^2-$ has a molecular weight of about
3.5 kDa. In certain embodiments $-L^2-$ has a molecular weight of about 4 kDa. In certain
embodiments $-L^2-$ has a molecular weight of about 4.5 kDa. In certain embodiments $-L^2-$ has a
molecular weight of about 5 kDa. In certain embodiments $-L^2-$ has a molecular weight of about
5.5 kDa. In certain embodiments $-L^2-$ has a molecular weight of about 6 kDa. In certain
25 embodiments $-L^2-$ has a molecular weight of about 6.5 kDa. In certain embodiments $-L^2-$ has a
molecular weight of about 7 kDa. In certain embodiments $-L^2-$ has a molecular weight of about
7.5 kDa. In certain embodiments $-L^2-$ has a molecular weight of about 8 kDa. In certain
embodiments $-L^2-$ has a molecular weight of about 8.5 kDa. In certain embodiments $-L^2-$ has a
molecular weight of about 9 kDa. In certain embodiments $-L^2-$ has a molecular weight of about
30 9.5 kDa. In certain embodiments $-L^2-$ has a molecular weight of about 10 kDa.

In certain embodiments $-L^2-$ comprises a polymeric moiety, meaning that it comprises at least one polymer moiety. It is understood that if $-L^2-$ comprises one polymer moiety the minimum and maximum molecular weights provided above apply to this one polymer moiety and

if -L²- comprises more than one polymer moiety the minimum and maximum molecular weights provided above refer to the minimum and maximum molecular weight of all polymer moieties together.

- 5 In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 1.2 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 1.5 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 2 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 2.5 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 3 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 3.5 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 4 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 4.5 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of at least 5 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 200 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 175 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 150 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 125 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 100 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 75 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 50 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 45 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 40 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 35 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of no more than 30 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of about 1.2 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of about 1.5 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of about 2 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of about 2.5 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of about 3 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of about 3.5 nm. In certain embodiments the one or more polymer moiety of -L²- has a Flory radius of about

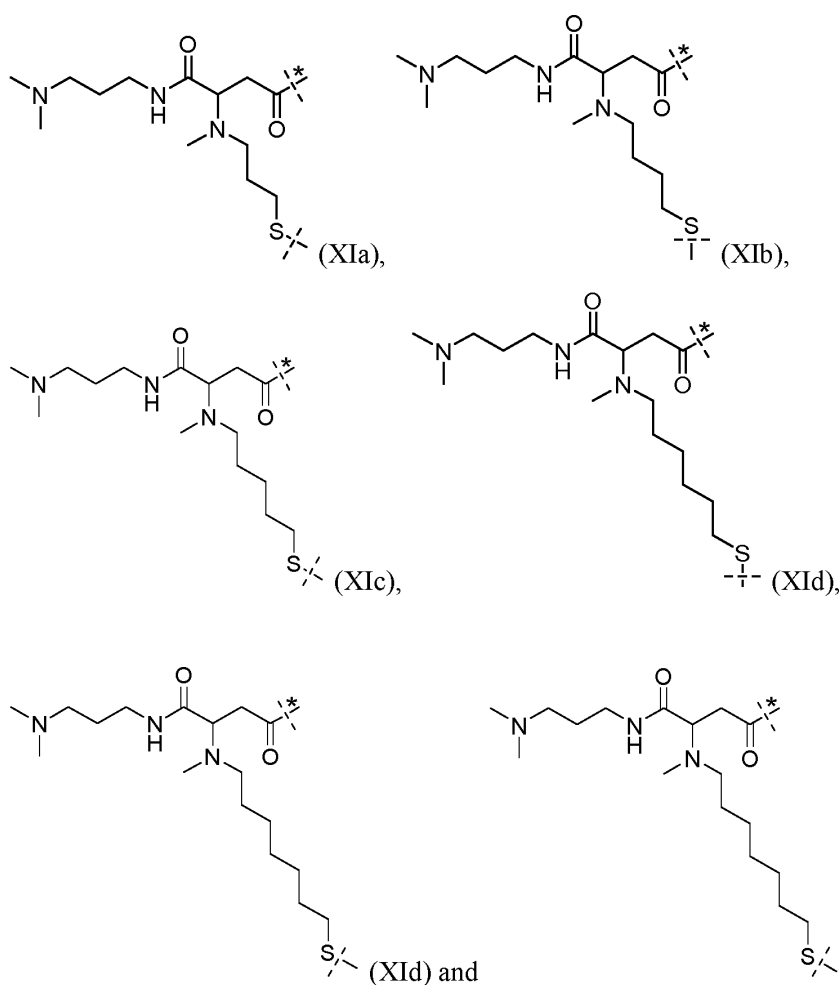
- 4 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 4.5 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 5 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 5.5 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 6 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 6.5 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 7 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 8.5 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 9 nm. In certain embodiments the one or more polymer moiety of $-L^2-$ has a Flory radius of about 10 nm. It is understood that if $-L^2-$ comprises one polymer moiety the Flory radius provided above applies to this one polymer moiety and if $-L^2-$ comprises more than one polymer moiety the Flory radius provided above refers to the Flory radius of all polymer moieties together.
- $-L^2-$ comprises one or more polymer moiety, such as polymer moiety selected from the group consisting of poly(2-methacryloyl-oxyethyl phosphoyl cholins), poly(acrylic acids), poly(acrylates), poly(acrylamides), poly(alkyloxy) polymers, poly(amides), poly(amidoamines), poly(amino acids), poly(anhydrides), poly(aspartamides), poly(butyric acids), poly(glycolic acids), poly(butylene terephthalates), poly(caprolactones), poly(carbonates), poly(cyanoacrylates), poly(dimethylacrylamides), poly(esters), poly(ethylenes), poly(ethyleneglycols), poly(ethylene oxides), poly(ethyl phosphates), poly(ethyloxazolines), poly(glycolic acids), poly(hydroxyethyl acrylates), poly(hydroxyethyl-oxazolines), poly(hydroxymethacrylates), poly(hydroxypropylmethacrylamides), poly(hydroxypropyl methacrylates), poly(hydroxypropyloxazolines), poly(iminocarbonates), poly(lactic acids), poly(lactic-co-glycolic acids), poly(methacrylamides), poly(methacrylates), poly(methyloxazolines), poly(organophosphazenes), poly(ortho esters), poly(oxazolines), poly(propylene glycols), poly(siloxanes), poly(urethanes), poly(vinyl alcohols), poly(vinyl amines), poly(vinylmethylethers), poly(vinylpyrrolidones), silicones, celluloses, carbomethyl celluloses, hydroxypropyl methylcelluloses, chitins, chitosans, dextrans, dextrins, gelatins, hyaluronic acids and derivatives, functionalized hyaluronic acids, alginate, mannans, pectins, rhamnogalacturonans, starches, hydroxyalkyl starches, hydroxyethyl starches and other carbohydrate-based polymers, xylans, and copolymers thereof.

In certain embodiments -L²- comprises a PEG-based polymer. In certain embodiments -L²- comprises a hyaluronic acid-based polymer. In certain embodiments -L²- comprises a random coil polymer. In certain embodiments -L²- comprises a poly-sarcosine polymer.

5

In certain embodiments the albumin-binding moieties of a compound disclosed herein bind to one albumin, such as via different binding domains. Suitably, the albumin-binding moieties of a compound disclosed herein bind to at least two albumins, such as to two albumins.

10 In certain embodiments -L¹-L²- is selected from the group consisting



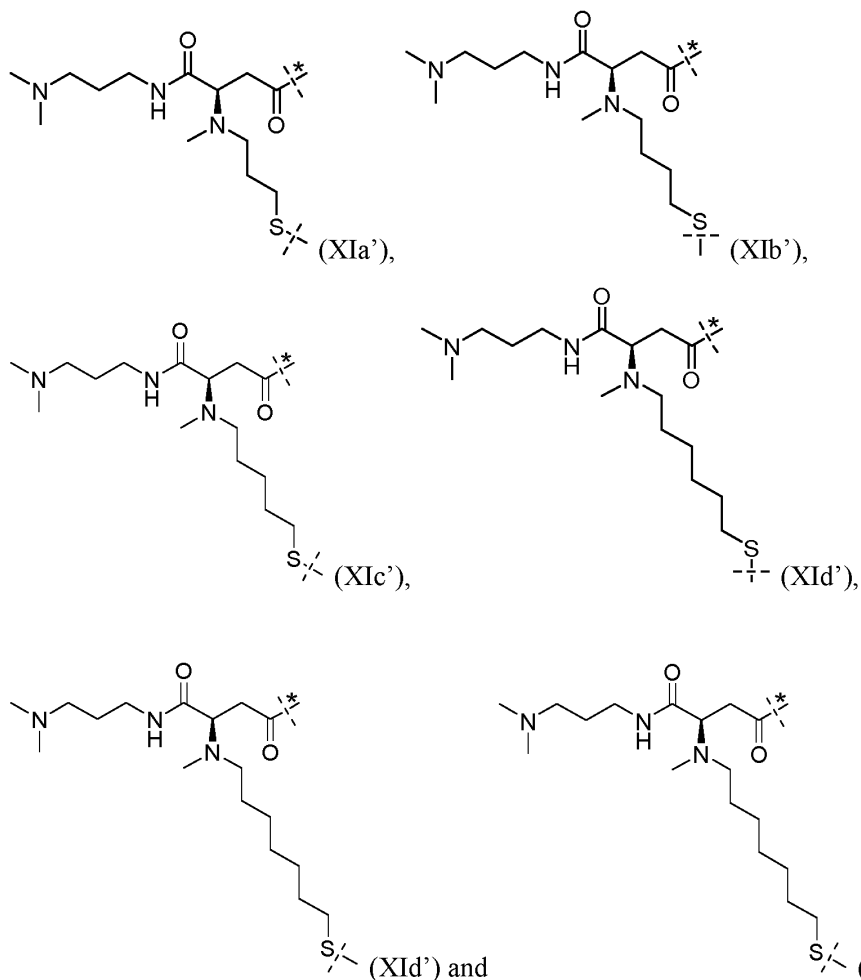
15

wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and the unmarked dashed line indicates attachment to the at least one polymeric moiety.

- In certain embodiments $-L^1-L^2-$ is of formula (XIa). In certain embodiments $-L^1-L^2-$ is of formula (XIb). In certain embodiments $-L^1-L^2-$ is of formula (XIc). In certain embodiments $-L^1-L^2-$ is of formula (XIe).
 5 In certain embodiments $-L^1-L^2-$ is of formula (XIe).

In certain embodiments $-L^1-L^2-$ is selected from the group consisting



10

wherein

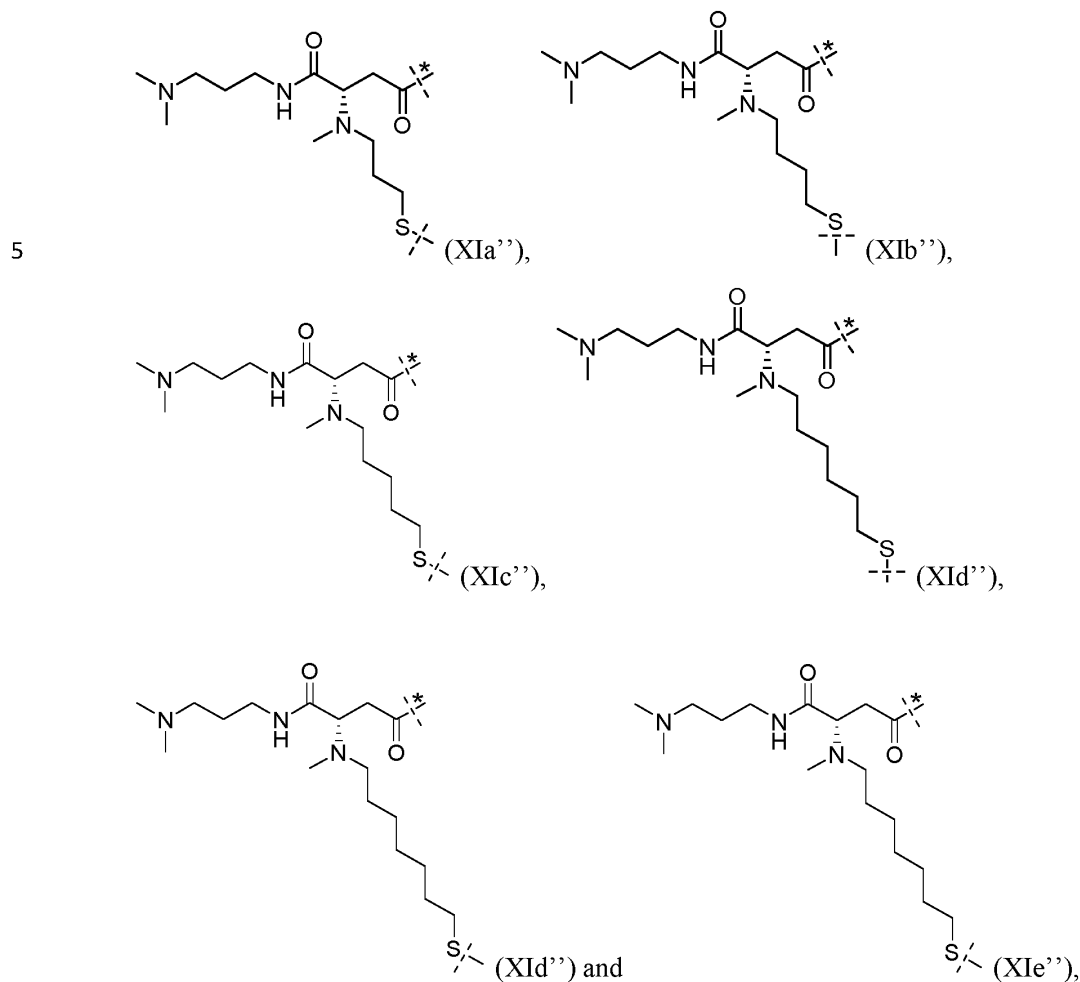
the dashed line marked with the asterisk indicates attachment to a nitrogen of $-D-$; and
 the unmarked dashed line indicates attachment to the at least one polymeric moiety.

15

In certain embodiments $-L^1-L^2-$ is of formula (XIa'). In certain embodiments $-L^1-L^2-$ is of formula (XIb'). In certain embodiments $-L^1-L^2-$ is of formula (XIc'). In certain

embodiments -L¹-L²- is of formula (XI^{d'}). In certain embodiments -L¹-L²- is of formula (XI^{e'}).
In certain embodiments -L¹-L²- is of formula (XI^{f'}).

In certain embodiments -L¹-L²- is selected from the group consisting

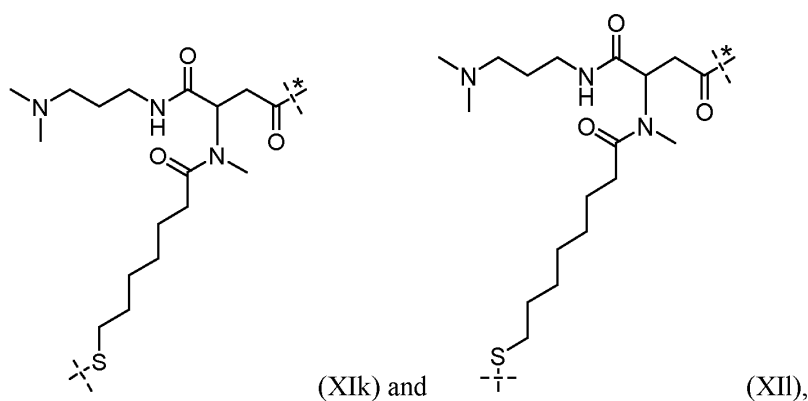
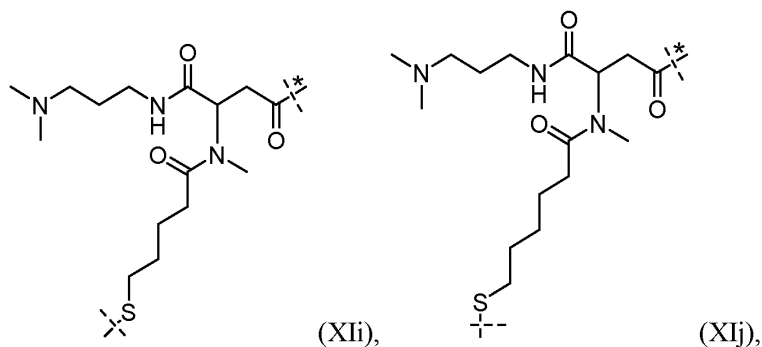
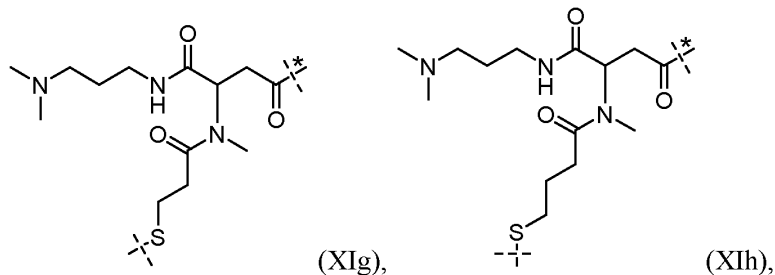


wherein

- 10 the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and
the unmarked dashed line indicates attachment to the at least one polymeric moiety.

- 15 In certain embodiments -L¹-L²- is of formula (XI^{a''}). In certain embodiments -L¹-L²- is of formula (XI^{b''}). In certain embodiments -L¹-L²- is of formula (XI^{c''}). In certain embodiments -L¹-L²- is of formula (XI^{d''}). In certain embodiments -L¹-L²- is of formula (XI^{e''}). In certain embodiments -L¹-L²- is of formula (XI^{f'}).

In certain embodiments $-L^1-L^2-$ is selected from the group consisting



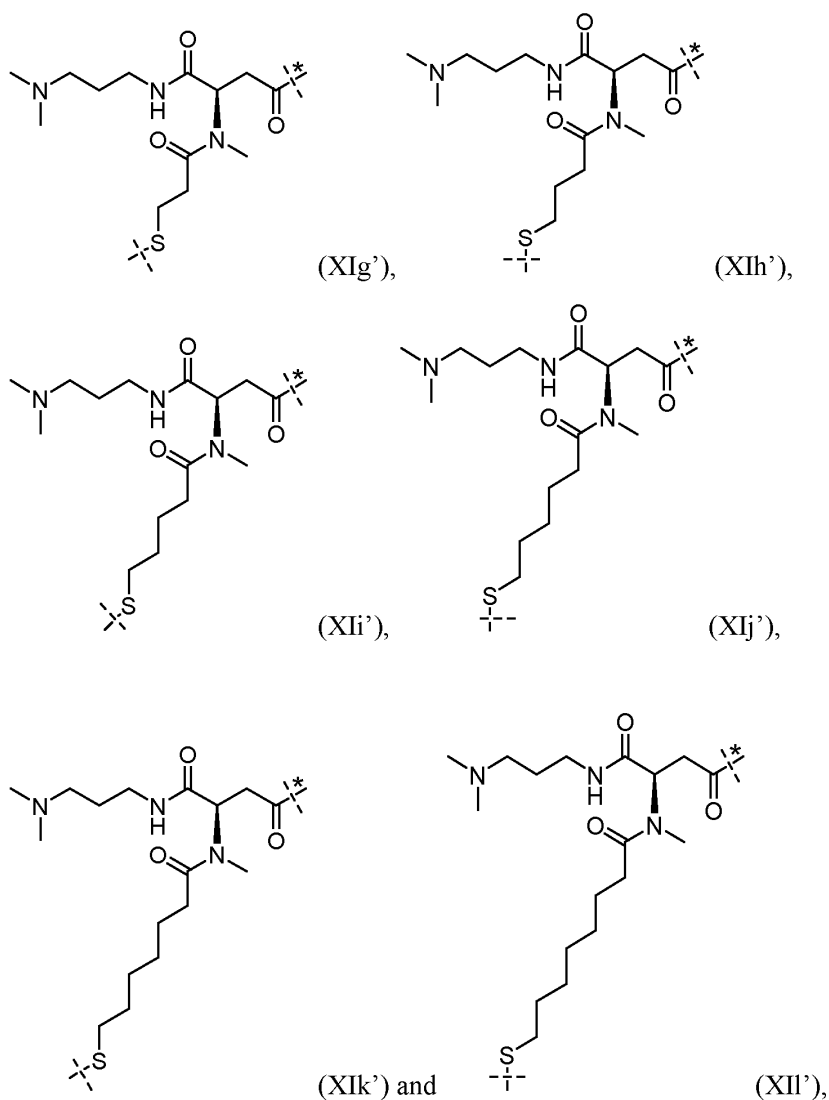
5

wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of $-D-$; and
the unmarked dashed line indicates attachment to the at least one polymeric moiety.

10 In certain embodiments $-L^1-L^2-$ is of formula (XIg). In certain embodiments $-L^1-L^2-$ is of formula (XIh). In certain embodiments $-L^1-L^2-$ is of formula (XIi). In certain embodiments $-L^1-L^2-$ is of formula (XIj). In certain embodiments $-L^1-L^2-$ is of formula (XIk). In certain embodiments $-L^1-L^2-$ is of formula (XII).

15 In certain embodiments $-L^1-L^2-$ is selected from the group consisting

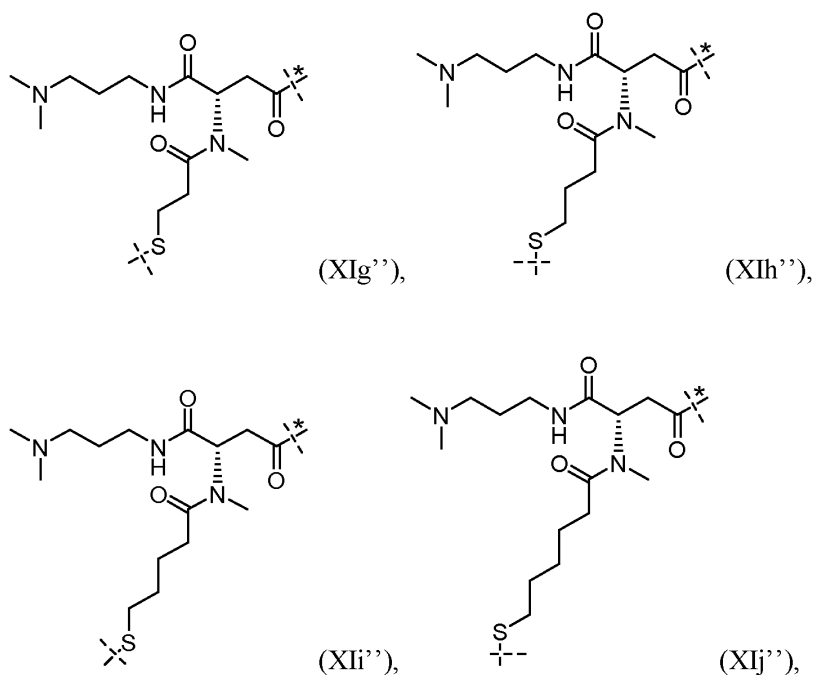


5 wherein

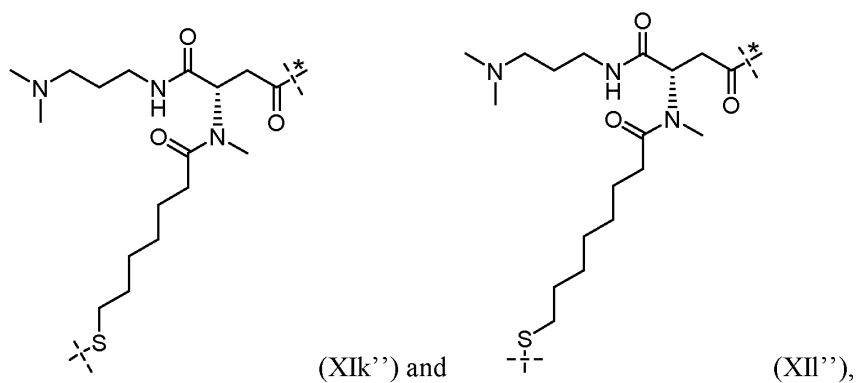
the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and
the unmarked dashed line indicates attachment to the at least one polymeric moiety.

In certain embodiments -L¹-L²- is of formula (XIg'). In certain embodiments -L¹-L²- is of
10 formula (XIh'). In certain embodiments -L¹-L²- is of formula (XII'). In certain
embodiments -L¹-L²- is of formula (XIj'). In certain embodiments -L¹-L²- is of formula (XIk').
In certain embodiments -L¹-L²- is of formula (XII').

In certain embodiments -L¹-L²- is selected from the group consisting



5



wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-; and
the unmarked dashed line indicates attachment to the at least one polymeric moiety.

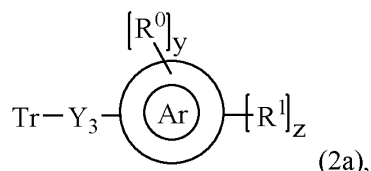
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In certain embodiments -L¹-L²- is of formula (XIg''). In certain embodiments -L¹-L²- is of formula (XIh''). In certain embodiments -L¹-L²- is of formula (XIi''). In certain embodiments -L¹-L²- is of formula (XIj''). In certain embodiments -L¹-L²- is of formula (XIk''). In certain embodiments -L¹-L²- is of formula (XIl'').

15

In certain embodiments $-L^1-$ is a multi-release linker, i.e., a linker from which more than one drug is released. An exemplary class of such multi-release linker is described in the following sections.

- 5 In certain embodiments $-L^1-$ is of formula (2a)



wherein

$-\text{Tr}$ is a cleavable triggering moiety;

$-\text{Y}_3-$ is independently selected from the group consisting of $-\text{O}-$, $-\text{S}-$ and $-\text{N}(\text{R}^6)-$;

10 z is selected from the group consisting of 2 and 3;

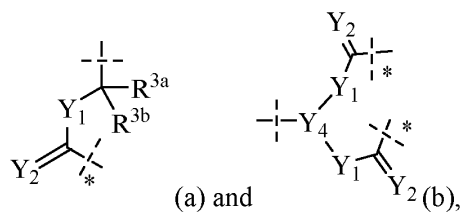
y is selected from the group consisting of 0, 1, 2, 3, 4 and 5;

$-\text{Ar}-$ is a ring selected from the group consisting of monocyclic or bicyclic aryl and heteroaryl, provided that $-\text{Ar}-$ is connected to $-\text{Y}_3-$ and $-\text{R}^1$ via carbon atoms; wherein said monocyclic or bicyclic aryl and heteroaryl are optionally substituted with $-\text{R}^0$, which are the same or different;

15 each $-\text{R}^0$ is independently selected from the group consisting of $-\text{C}(\text{O})\text{OH}$, $-\text{halogen}$, $-\text{NO}_2$, $-\text{CN}$, C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl; wherein C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl are optionally substituted with one or more $-\text{R}^4$, which are the same or different; and wherein

20 C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-\text{T}-$, $-\text{C}(\text{O})\text{O}-$, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{N}(\text{R}^5)-$, $-\text{S}(\text{O})_2\text{N}(\text{R}^5)-$, $-\text{S}(\text{O})\text{N}(\text{R}^5)-$, $-\text{S}(\text{O})_2-$, $-\text{S}(\text{O})-$, $-\text{N}(\text{R}^5)\text{S}(\text{O})_2\text{N}(\text{R}^{5a})-$, $-\text{S}-$, $-\text{N}(\text{R}^5)-$, $-\text{OC}(\text{OR}^5)(\text{R}^{5a})-$, $-\text{N}(\text{R}^5)\text{C}(\text{O})\text{N}(\text{R}^{5a})-$ and $-\text{OC}(\text{O})\text{N}(\text{R}^5)-$;

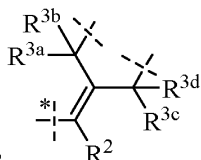
each $-\text{R}^1$ is independently selected from the group consisting of



wherein

an unmarked dashed line indicates attachment to $-\text{Ar}-$;

a dashed lined marked with an asterisk indicates attachment to -D-;
 the total number of moieties -D- in the compound ranges from 2 to 6;
 each -Y₁- is independently selected from the group consisting of -O- and -S-;
 each =Y₂ is independently selected from the group consisting of =O and =S;



5 -Y₄- is , wherein the dashed line marked with the asterisk indicates attachment to -Ar- and the unmarked dashed lines indicate attachment to -Y₁-;

each -R² is independently selected from the group consisting of -H, -C(O)OH, -halogen, -NO₂, -CN, C₁₋₃₀ alkyl, C₂₋₃₀ alkenyl and C₂₋₃₀ alkynyl; wherein C₁₋₃₀ alkyl, C₂₋₃₀ alkenyl and C₂₋₃₀ alkynyl are optionally substituted with one or more -R⁴, which are the same or different; and wherein C₁₋₃₀ alkyl, C₂₋₃₀ alkenyl and C₂₋₃₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R⁵)-, -S(O)₂N(R⁵)-, -S(O)N(R⁵)-, -S(O)₂-, -S(O)-, -N(R⁵)S(O)₂N(R^{5a})-, -S-, -N(R⁵)-, -OC(OR⁵)(R^{5a})-, -N(R⁵)C(O)N(R^{5a})- and -OC(O)N(R⁵)-;

each -R^{3a}, -R^{3b}, -R^{3c}, -R^{3d} are independently selected from the group consisting of -H, -C(O)OH, -F, -NO₂, -CN, C₁₋₃₀ alkyl, C₂₋₃₀ alkenyl and C₂₋₃₀ alkynyl; wherein C₁₋₃₀ alkyl, C₂₋₃₀ alkenyl and C₂₋₃₀ alkynyl are optionally substituted with one or more -R⁴, which are the same or different; and wherein C₁₋₃₀ alkyl, C₂₋₃₀ alkenyl and C₂₋₃₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R⁵)-, -S(O)₂N(R⁵)-, -S(O)N(R⁵)-, -S(O)₂-, -S(O)-, -N(R⁵)S(O)₂N(R^{5a})-, -S-, -N(R⁵)-, -OC(OR⁵)(R^{5a})-, -N(R⁵)C(O)N(R^{5a})- and -OC(O)N(R⁵)-;

each -T- is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl, wherein each -T- is independently optionally substituted with one or more -R⁴, which are the same or different;

-R⁴ is selected from the group consisting of -NO₂, -OCH₃, -CN, -N(R⁵)(R^{5a}), -OH, -C(O)OH and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different;

$-R^5$ and $-R^{5a}$ are independently selected from the group consisting of $-H$ and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

5 each $-R^6$ is independently selected from the group consisting of $-H$ and C_{1-6} alkyl;

and wherein $-L^1$ is substituted with one moiety $-L^2$.

In certain embodiments all $-R^1$ of formula (2a) are of formula (a).

10 In certain embodiments all $-R^1$ of formula (2a) are of formula (b).

In certain embodiments z of formula (2a) is 2. In certain embodiments z of formula (2a) is 3.

In certain embodiments z of formula (2a) is 2 and both $-R^1$ are of formula (a). In certain
embodiments z of formula (2a) is 2 and both $-R^1$ are of formula (b). In certain embodiments z
15 is of formula (2a) is 2 and one $-R^1$ is of formula (a) and one $-R^1$ is of formula (b).

In certain embodiments z of formula (2a) is 3 and all $-R^1$ are of formula (a). In certain
embodiments z of formula (2a) is 3 and all $-R^1$ are of formula (b). In certain embodiments z of
formula (2a) is 3 and one $-R^1$ is of formula (a) and two $-R^1$ are of formula (b). In certain
20 embodiments z of formula (2a) is 3 and two $-R^1$ are of formula (a) and one $-R^1$ is of formula
(b).

In certain embodiments y of formula (2a) is 0. In certain embodiments y of formula (2a) is 1.
In certain embodiments y of formula (2a) is 2. In certain embodiments y of formula (2a) is 3.
25 In certain embodiments y of formula (2a) is 4. In certain embodiments y of formula (2a) is 5.

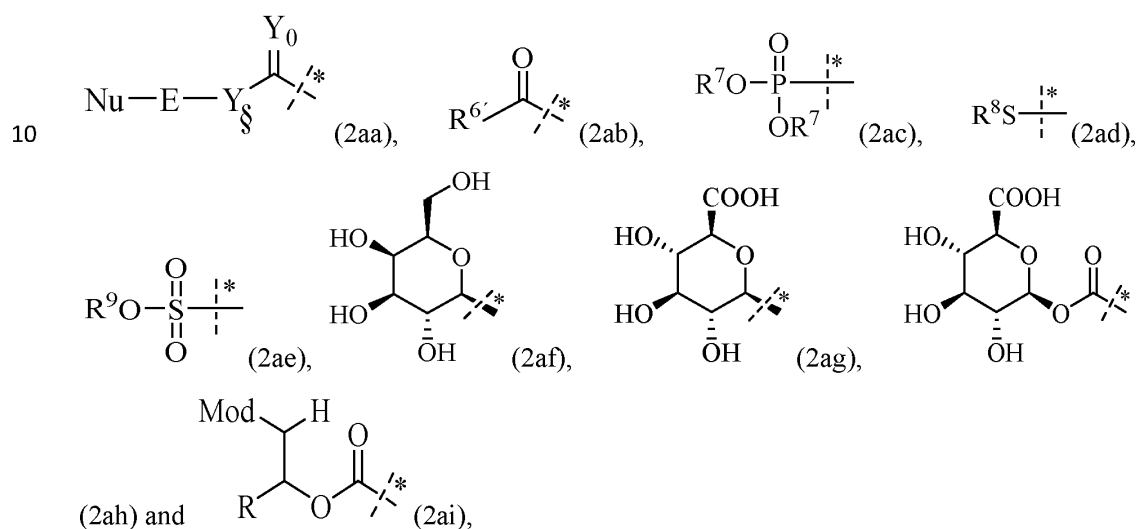
In certain embodiments z of formula (2a) is 2, both $-R^1$ of formula (2a) are of formula (a) and
 y of formula (2a) is 0. In certain embodiments z of formula (2a) is 3, all $-R^1$ of formula (2a) are
of formula (a) and y of formula (2a) is 0. In certain embodiments z of formula (2a) is 3, two $-$
30 R^1 are of formula (a), one $-R^1$ of formula (2a) is of formula (b) and y of formula (2a) is 0.

In certain embodiments $-Y_1$ of formula (2a) is $-O-$. In certain embodiments $-Y_1$ of formula
(2a) is $-S-$.

In certain embodiments $=Y_2$ of formula (2a) is $=O$. In certain embodiments $=Y_2$ of formula (2a) is $=S$.

In certain embodiments $-Y_3-$ of formula (2a) is $-O-$. In certain embodiments $-Y_3-$ of formula (2a) is $-S-$. In certain embodiments $-Y_3-$ of formula (2a) is $-N(R^6)-$, wherein $-R^6$ is as described elsewhere within the section covering the exemplary multi-release linker.

In certain embodiments $-Tr$ of formula (2a) is selected from the group consisting of a peptidyl moiety;



wherein

the dashed line marked with an asterisk indicates attachment to $-Y^3-$;

15 $-\text{Nu}$ is a nucleophile;

$-Y_8-$ is selected from the group consisting of $-O-$, $-C(R^{10})(R^{10a})-$, $-N(R^6)-$ and $-S-$;

$=Y_0$ is selected from the group consisting of $=O$, $=S$ and $=N(R^5)$;

20 $-E-$ and $-R$ are independently selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl and $-Q-$; wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl are optionally substituted with one or more $-R^{11}$, which are the same or different; and wherein C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-Q-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{12})-$, $-S(O)_2N(R^{12})-$, $-S(O)N(R^{12})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{12})S(O)_2N(R^{12a})-$, $-S-$, $-N(R^{12})-$, $-OC(OR^{12})R^{12a}$, $-N(R^{12})C(O)N(R^{12a})-$ and $-OC(O)N(R^{12})-$;

-Mod is selected from the group consisting of CF_3PhSO_2 -, ClPhSO_2 -, PhSO_2 -, MePhSO_2 -, MeOPhSO_2 -, $2,4,6\text{-Me}_3\text{PhSO}_2$ -, MeSO_2 -, $\text{O}(\text{CH}_2\text{CH}_2)_2\text{N-SO}_2$ -, CN- and Et_2NSO_2 -;

$-\text{R}^6$ is selected from the group consisting of $-\text{H}$ and C_{1-6} alkyl;

5 $-\text{R}^{5'}$, $-\text{R}^{6'}$, $-\text{R}^7$, $-\text{R}^8$, $-\text{R}^9$, $-\text{R}^{10}$, $-\text{R}^{10a}$ are independently selected from the group consisting of $-\text{H}$, C_{1-20} alkyl, C_{2-20} alkenyl, C_{2-20} alkynyl and $-\text{Q}$; wherein C_{1-20} alkyl, C_{2-20} alkenyl and C_{2-20} alkynyl are optionally substituted with one or more $-\text{R}^{11}$, which are the same or different; and wherein C_{1-20} alkyl, C_{2-20} alkenyl and C_{2-20} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-\text{Q-}$, $-\text{C}(\text{O})\text{O-}$,
10 $-\text{O-}$, $-\text{C}(\text{O})$ -, $-\text{C}(\text{O})\text{N}(\text{R}^{12})$ -, $-\text{S}(\text{O})_2\text{N}(\text{R}^{12})$ -, $-\text{S}(\text{O})\text{N}(\text{R}^{12})$ -, $-\text{S}(\text{O})_2$ -, $-\text{S}(\text{O})$ -, $-\text{N}(\text{R}^{12})\text{S}(\text{O})_2\text{N}(\text{R}^{12a})$ -, $-\text{S-}$, $-\text{N}(\text{R}^{12})$ -, $-\text{OC}(\text{OR}^{12})\text{R}^{12a}$ -, $-\text{N}(\text{R}^{12})\text{C}(\text{O})\text{N}(\text{R}^{12a})$ - and $-\text{OC}(\text{O})\text{N}(\text{R}^{12})$ -;

each Q is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl, wherein each Q is independently optionally substituted with one or more $-\text{R}^{11}$, which are the same or different; and
15

$-\text{R}^{11}$ is selected from the group consisting of C_{1-6} alkyl and $-\text{N}_3$, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different; and

$-\text{R}^{12}$ and $-\text{R}^{12a}$ are independently selected from the group consisting of $-\text{H}$ and C_{1-6} alkyl;
20 wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

$-\text{Nu}$ of formula (2aa) is a nucleophile that may be selected from the group consisting of primary, secondary, or tertiary amine and amide. In certain embodiments $-\text{Nu}$ of formula (2aa) is
25 selected from the group consisting of secondary and tertiary amine. In certain embodiments $-\text{Nu}$ of formula (2aa) is a primary amine. In certain embodiments $-\text{Nu}$ of formula (2aa) is a secondary amine. In certain embodiments $-\text{Nu}$ of formula (2aa) is a tertiary amine. In certain embodiments $-\text{Nu}$ of formula (2aa) is an amide.

30 In certain embodiments $-\text{Y}_8$ - of formula (2aa) is selected from the group consisting of $-\text{O-}$, $-\text{C}(\text{R}^{10})(\text{R}^{10a})$ - and $-\text{N}(\text{R}^6)$ -, wherein $-\text{R}^{10}$, $-\text{R}^{10a}$ and $-\text{R}^6$. In certain embodiments $-\text{Y}_8$ - of formula (2aa) is $-\text{O-}$.

In certain embodiments -Y_§- of formula (2aa) is -C(R¹⁰)(R^{10a})-, wherein -R¹⁰, -R^{10a} are independently selected from the group consisting of -H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₂₋₂₀ alkynyl and -Q; wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl and C₂₋₂₀ alkynyl are optionally substituted with one or more -R¹¹, which are the same or different; and wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl and C₂₋₂₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -Q-, -C(O)O-, -O-, -C(O)-, -C(O)N(R¹²)-, -S(O)₂N(R¹²)-, -S(O)N(R¹²)-, -S(O)₂-, -S(O)-, -N(R¹²)S(O)₂N(R^{12a})-, -S-, -N(R¹²)-, -OC(OR¹²)R^{12a}-, -N(R¹²)C(O)N(R^{12a})- and -OC(O)N(R¹²)-;

each Q is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl, wherein each Q is independently optionally substituted with one or more -R¹¹, which are the same or different; and

-R¹¹ is selected from the group consisting of C₁₋₆ alkyl and -N₃, wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and

-R¹² and -R^{12a} are independently selected from the group consisting of -H and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different

In certain embodiments -Y_§- of formula (2aa) is -N(R⁶)-, wherein -R⁶ is selected from the group consisting of -H and C₁₋₆ alkyl.

In certain embodiments =Y₀ of formula (2aa) is selected from the group consisting of =O and =S. In certain embodiments =Y₀ of formula (2aa) is =O. In certain embodiments =Y₀ of formula (2aa) is =S.

In certain embodiments =Y₀ of formula (2aa) is =N(R^{5'}), wherein -R^{5'} is selected from the group consisting of -H, C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl, C₂₋₂₀ alkynyl and -Q; wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl and C₂₋₂₀ alkynyl are optionally substituted with one or more -R¹¹, which are the same or different; and wherein C₁₋₂₀ alkyl, C₂₋₂₀ alkenyl and C₂₋₂₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -Q-, -C(O)O-, -O-, -C(O)-, -C(O)N(R¹²)-, -S(O)₂N(R¹²)-, -S(O)N(R¹²)-, -S(O)₂-, -S(O)-, -N(R¹²)S(O)₂N(R^{12a})-, -S-, -N(R¹²)-, -OC(OR¹²)R^{12a}-, -N(R¹²)C(O)N(R^{12a})- and -OC(O)N(R¹²)-;

each Q is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered

heterobicycyl, wherein each Q is independently optionally substituted with one or more -R¹¹, which are the same or different; and

-R¹¹ is selected from the group consisting of C₁₋₆ alkyl and -N₃, wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and

- 5 -R¹² and -R^{12a} are independently selected from the group consisting of -H and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different

- In certain embodiments -E- of formula (2aa) is selected from the group consisting of C₁₋₆ alkyl, C₂₋₆ alkenyl and C₂₋₆ alkynyl. In certain embodiments -E- of formula (2aa) is C₁₋₆ alkyl. In
10 certain embodiments -E- of formula (2aa) is C₂₋₆ alkenyl. In certain embodiments -E- of formula (2aa) is C₂₋₆ alkynyl. In certain embodiments -E- of formula (2aa) is -Q-, which in certain embodiments is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered
15 heterobicycyl. In certain embodiments Q is phenyl. In certain embodiments Q is naphthyl. In certain embodiments Q is indenyl. In certain embodiments Q is indanyl. In certain embodiments Q is tetralinyl. In certain embodiments Q is C₃₋₁₀ cycloalkyl. In certain embodiments Q is 3- to 10-membered heterocyclyl. In certain embodiments Q is 8- to 11-membered heterobicycyl. In certain embodiments Q is substituted with one or more -R¹¹.
20 In certain embodiments Q is not substituted with -R¹¹.

- In certain embodiments -R^{5'} of formula (2aa) is selected from the group consisting of -H, C₁₋₆ alkyl, C₂₋₆ alkenyl and C₂₋₆ alkynyl. In certain embodiments -R^{5'} of formula (2aa) is selected from the group consisting of -H and C₁₋₆ alkyl. In certain embodiments -R^{5'} of formula (2aa) is
25 -H. In certain embodiments -R^{5'} of formula (2aa) is C₁₋₆ alkyl.

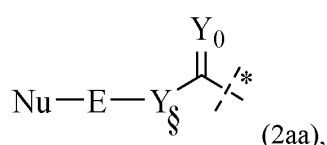
- In certain embodiments -R^{6'}, -R⁷, -R⁸, -R⁹, -R¹⁰, -R^{10a} as used in the various embodiments for Tr are independently selected from the group consisting of -H, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, C₂₋₁₀ alkynyl and -Q, wherein -Q is as defined elsewhere within the section covering the exemplary
30 multi-release linker.

In certain embodiments -R⁷ and -R⁹ as used in the various embodiments for Tr are independently selected from the group consisting of -H and C₁₋₆ alkyl. In certain embodiments

both -R⁷ and -R⁹ are -H. In certain embodiments -R⁷ is -H. In certain embodiments -R⁷ is C₁₋₆ alkyl. In certain embodiments -R⁹ is -H. In certain embodiments -R⁹ is C₁₋₆ alkyl.

In certain embodiments -R¹⁰ and -R^{10a} of formula (2aa) are independently selected from the group consisting of -H and C₁₋₆ alkyl. In certain embodiments both -R¹⁰ and -R^{10a} of formula (2aa) are -H. In certain embodiments -R¹⁰ of formula (2aa) is -H. In certain embodiments -R¹⁰ of formula (2aa) is C₁₋₆ alkyl. In certain embodiments -R^{10a} of formula (2aa) is -H. In certain embodiments -R^{10a} of formula (2aa) is C₁₋₆ alkyl.

10 In certain embodiments -Tr of formula (2a) is of formula (2aa)



wherein

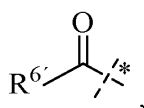
the dashed line marked with an asterisk indicates attachment to -Y₃-; and

-Nu, -E-, -Y_{\S}- and =Y₀ are as defined elsewhere within the section covering the exemplary multi-release linker herein.

It is understood that in this instance the release of the drug is not triggered by an enzyme, and that the drug is released in its unmodified, pharmacologically active form in the absence of an enzyme.

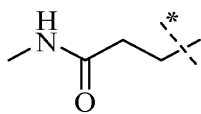
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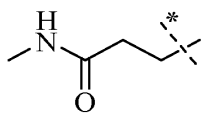
In certain embodiments -Tr of formula (2a) is



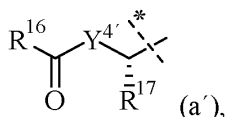
wherein and the dashed line marked with an asterisk indicates attachment to -Y³-; and

-R^{6'} is as defined elsewhere within the section covering the exemplary multi-release linker herein.



In certain embodiments $-R^{6'}$ is , wherein the dashed line marked with the asterisk indicates attachment to the carbon atom substituted by the oxygen atom.

In certain embodiments $-R^{6'}$ is of formula (a'):



5

wherein $-Y^{4'}$ is selected from the group consisting of C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl, which are optionally substituted with one or more $-R^{18}$ which are the same or different;

$-R^{16}$ and $-R^{17}$ are independently selected from the group consisting of $-H$, C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl; wherein C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl are optionally substituted with one or more $-R^{18}$ which are the same or different; and wherein C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-A'$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{19})$ -, $-S(O)_2N(R^{19})$ -, $-S(O)N(R^{19})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{19})S(O)_2N(R^{19a})$ -, $-S$ -, $-N(R^{19})$ -, $-OC(OR^{19})R^{19a}$ -, $-N(R^{19})C(O)N(R^{19a})$ -, $-OC(O)N(R^{19})$ - and $-N(R^{19})C(NH_2)N(R^{19a})$;

15

each A' is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl, wherein each A' is independently optionally substituted with one or more $-R^{18}$ which are the same or different;

20

wherein $-R^{18}$, $-R^{19}$ and $-R^{19a}$ are independently selected from the group consisting of $-H$ and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different; and

wherein the dashed line marked with an asterisk indicates attachment to the rest of $-Tr$.

25

In certain embodiments $-Y^{4'}$ is selected from the group consisting of C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl. In certain embodiments $-Y^{4'}$ is C_{3-10} cycloalkyl. In certain embodiments $-Y^{4'}$ is 3- to 10-membered heterocyclyl. In certain embodiments $-Y^{4'}$ is 8- to 11-membered heterobicyclyl. In certain embodiments $-Y^{4'}$

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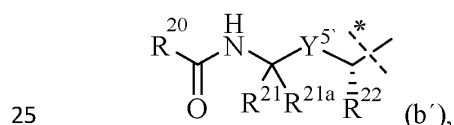
is substituted with one or more $-R^{18}$ which are the same or different. In certain embodiments $-Y^{4'}$ is not substituted with $-R^{18}$.

In certain embodiments $-R^{16}$ and $-R^{17}$ are selected from the group consisting of C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl. In certain embodiments $-R^{16}$ is C_{1-10} alkyl. In certain embodiments $-R^{16}$ is C_{2-10} alkenyl. In certain embodiments $-R^{16}$ is C_{2-10} alkynyl. In certain embodiments $-R^{17}$ is C_{1-10} alkyl. In certain embodiments $-R^{17}$ is C_{2-10} alkenyl. In certain embodiments $-R^{17}$ is C_{2-10} alkynyl.

In certain embodiments A' is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicycyl. In certain embodiments A' is phenyl. In certain embodiments A' is naphthyl. In certain embodiments A' is indenyl. In certain embodiments A' is indanyl. In certain embodiments A' is tetralinyl. In certain embodiments A' is C_{3-10} cycloalkyl. In certain embodiments A' is 3- to 10-membered heterocyclyl. In certain embodiments A' is 8- to 11-membered heterobicycyl. In certain embodiments A' is substituted with one or more $-R^{18}$, which are the same or different. In certain embodiments A' is not substituted with $-R^{18}$.

In certain embodiments $-R^{18}$, $-R^{19}$ and $-R^{19a}$ are selected from the group consisting of $-H$ and C_{1-6} alkyl. In certain embodiments $-R^{18}$ is $-H$. In certain embodiments $-R^{18}$ is C_{1-6} alkyl. In certain embodiments $-R^{19}$ is $-H$. In certain embodiments $-R^{19}$ is C_{1-6} alkyl. In certain embodiments $-R^{19a}$ is $-H$. In certain embodiments $-R^{19a}$ is C_{1-6} alkyl.

In certain embodiments $-R^{6'}$ is of formula (b'):



wherein $-Y^{5'}$ is selected from the group consisting of $-Q'$, C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl; wherein C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl are optionally substituted with one or more $-R^{23}$, which are the same or different; and wherein C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-Q'$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{24})-$, $-S(O)_2N(R^{24})-$, $-S(O)N(R^{24})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{24})S(O)_2N(R^{24a})-$, $-S-$, $-N(R^{24})-$,

$-\text{OC}(\text{OR}^{24})\text{R}^{24a}$ -,
 $-\text{N}(\text{R}^{24})\text{C}(\text{O})\text{N}(\text{R}^{24a})$ -, $-\text{OC}(\text{O})\text{N}(\text{R}^{24})$ - and $-\text{N}(\text{R}^{24})\text{C}(\text{NH}_2)\text{N}(\text{R}^{24a})$ -;
 $-\text{R}^{20}$, $-\text{R}^{21}$, $-\text{R}^{21a}$ and $-\text{R}^{22}$ are independently selected from the group consisting of -H, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl and C₂₋₁₀ alkynyl; wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl and C₂₋₁₀ alkynyl are optionally substituted with one or more -R²³ which are the same or different; and wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl and C₂₋₁₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -Q'-, -C(O)O-, -O-, -C(O)-, -C(O)N(R²⁴)-, -S(O)₂N(R²⁴)-, -S(O)N(R²⁴)-, -S(O)₂-, -S(O)-, -N(R²⁴)S(O)₂N(R^{24a})-, -S-, -N(R²⁴)-, $-\text{OC}(\text{OR}^{24})\text{R}^{24a}$ -, $-\text{N}(\text{R}^{24})\text{C}(\text{O})\text{N}(\text{R}^{24a})$ -, $-\text{OC}(\text{O})\text{N}(\text{R}^{24})$ - and $-\text{N}(\text{R}^{24})\text{C}(\text{NH}_2)\text{N}(\text{R}^{24a})$ -;
each Q' is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl, wherein each Q' is independently optionally substituted with one or more -R²³, which are the same or different;
wherein -R²³, -R²⁴ and -R^{24a} are independently selected from the group consisting of -H and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different;
optionally, the pair -R²¹/-R^{21a} is joined together with the atoms to which is attached to form a C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl or an 8- to 11-membered heterobicyclyl; and
wherein the dashed line marked with an asterisk indicates attachment to the rest of -Tr.

In certain embodiments -Y^{5'}- is selected from the group consisting of -Q'-, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl and C₂₋₁₀ alkynyl. In certain embodiments -Y^{5'}- is -Q'-. In certain embodiments -Y^{5'}- is C₁₋₁₀ alkyl. In certain embodiments -Y^{5'}- is C₂₋₁₀ alkenyl. In certain embodiments -Y^{5'}- is C₂₋₁₀ alkynyl.

In certain embodiments Q' is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl. In certain embodiments Q' is phenyl. In certain embodiments Q' is naphthyl. In certain embodiments Q' is indenyl. In certain embodiments Q' is indanyl. In certain embodiments Q' is C₃₋₁₀ cycloalkyl. In certain embodiments Q' is 3- to 10-membered heterocyclyl. In certain embodiments Q' is 8- to 11-membered heterobicyclyl. In certain

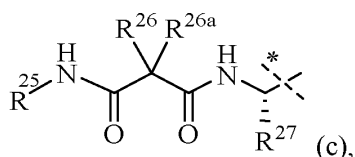
embodiments Q' is substituted with one or more -R²³ which are the same or different. In certain embodiments Q' is not substituted with -R²³.

In certain embodiments -R²⁰, -R²¹, -R^{21a} and -R²² are selected from the group consisting of
 5 -H, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl and C₂₋₁₀ alkynyl. In certain embodiments -R²⁰ is -H. In certain
 embodiments -R²⁰ is C₁₋₁₀ alkyl. In certain embodiments -R²⁰ is C₂₋₁₀ alkenyl. In certain
 embodiments -R²⁰ is C₂₋₁₀ alkynyl. In certain embodiments -R²¹ is -H. In certain embodiments
 -R²¹ is C₁₋₁₀ alkyl. In certain embodiments -R²¹ is C₂₋₁₀ alkenyl. In certain embodiments -R²¹ is
 C₂₋₁₀ alkynyl. In certain embodiments -R^{21a} is -H. In certain embodiments -R^{21a} is C₁₋₁₀ alkyl.
 10 In certain embodiments -R^{21a} is C₂₋₁₀ alkenyl. In certain embodiments -R^{21a} is C₂₋₁₀ alkynyl. In
 certain embodiments -R²² is -H. In certain embodiments -R²² is C₁₋₁₀ alkyl. In certain
 embodiments -R²² is C₂₋₁₀ alkenyl. In certain embodiments -R²² is C₂₋₁₀ alkynyl.

In certain embodiments -R²³, -R²⁴ and -R^{24a} are selected from the group consisting of -H and
 15 C₁₋₆ alkyl. In certain embodiments -R²³ is -H. In certain embodiments -R²³ is C₁₋₆ alkyl. In
 certain embodiments -R²⁴ is -H. In certain embodiments -R²⁴ is C₁₋₆ alkyl. In certain
 embodiments -R^{24a} is -H. In certain embodiments -R^{24a} is C₁₋₆ alkyl.

In certain embodiments the pair -R²¹/R^{21a} is joined together with the atoms to which is attached
 20 to form a C₃₋₁₀ cycloalkyl.

In certain embodiments -R^{6'} is of formula (c)



wherein

25 -R²⁵, -R²⁶, -R^{26a} and -R²⁷ are independently selected from the group consisting of -H, C₁₋₁₀
 alkyl, C₂₋₁₀ alkenyl and C₂₋₁₀ alkynyl; wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl and C₂₋₁₀
 alkynyl are optionally substituted with one or more -R²⁸ which are the same or different;
 and wherein C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl and C₂₋₁₀ alkynyl are optionally interrupted by one
 or more groups selected from the group consisting of -Q*, -C(O)O-, -O-, -C(O)-,
 30 -C(O)N(R²⁹)-, -S(O)₂N(R²⁹)-, -S(O)N(R²⁹)-, -S(O)₂-, -S(O)-, -N(R²⁹)S(O)₂N(R^{29a})-, -S-,

$-N(R^{29})-$, $-OC(OR^{29})R^{29a}-$, $-N(R^{29})C(O)N(R^{29a})-$, $-OC(O)N(R^{29})-$ and $-N(R^{29})C(NH_2)N(R^{29a})-$;

each Q^* is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl, wherein each Q^* is independently optionally substituted with

one or more $-R^{28}$, which are the same or different;

wherein $-R^{28}$, $-R^{29}$ and $-R^{29a}$ are independently selected from the group consisting of $-H$ and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

optionally, the pair $-R^{26}/-R^{26a}$ is joined together with the atoms to which is attached to form a C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl or an 8- to 11-membered heterobicyclyl; and

wherein the dashed line marked with an asterisk indicates attachment to the rest of $-Tr$.

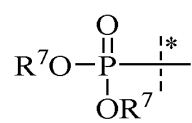
In certain embodiments $-R^{25}$, $-R^{26}$, $-R^{26a}$ and $-R^{27}$ are selected from the group consisting of $-H$, C_{1-10} alkyl, C_{2-10} alkenyl and C_{2-10} alkynyl. In certain embodiments $-R^{25}$ is $-H$. In certain embodiments $-R^{25}$ is C_{1-10} alkyl. In certain embodiments $-R^{25}$ is C_{2-10} alkenyl. In certain embodiments $-R^{25}$ is C_{2-10} alkynyl. In certain embodiments $-R^{26}$ is $-H$. In certain embodiments $-R^{26}$ is C_{1-10} alkyl. In certain embodiments $-R^{26}$ is C_{2-10} alkenyl. In certain embodiments $-R^{26}$ is C_{2-10} alkynyl. In certain embodiments $-R^{26a}$ is $-H$. In certain embodiments $-R^{26a}$ is C_{1-10} alkyl. In certain embodiments $-R^{26a}$ is C_{2-10} alkenyl. In certain embodiments $-R^{26a}$ is C_{2-10} alkynyl. In certain embodiments $-R^{27}$ is $-H$. In certain embodiments $-R^{27}$ is C_{1-10} alkyl. In certain embodiments $-R^{27}$ is C_{2-10} alkenyl. In certain embodiments $-R^{27}$ is C_{2-10} alkynyl.

In certain embodiments Q^* is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl. In certain embodiments Q^* is phenyl. In certain embodiments Q^* is naphthyl. In certain embodiments Q^* is indenyl. In certain embodiments Q^* is indanyl. In certain embodiments Q^* is tetralinyl. In certain embodiments Q^* is C_{3-10} cycloalkyl. In certain embodiments Q^* is 3- to 10-membered heterocyclyl. In certain embodiments Q^* is 8- to 11-membered heterobicyclyl. In certain embodiments Q^* is substituted with one or more $-R^{28}$, which are the same or different. In certain embodiments Q^* is not substituted with $-R^{28}$.

In certain embodiments $-R^{28}$, $-R^{29}$ and $-R^{29a}$ are selected from the group consisting of $-H$ and C_{1-6} alkyl. In certain embodiments $-R^{28}$ is $-H$. In certain embodiments $-R^{28}$ is C_{1-6} alkyl. In certain embodiments $-R^{29}$ is $-H$. In certain embodiments $-R^{29}$ is C_{1-6} alkyl. In certain embodiments $-R^{29a}$ is $-H$. In certain embodiments $-R^{29a}$ is C_{1-6} alkyl.

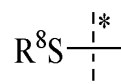
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In certain embodiments the pair $-R^{26}/-R^{26a}$ is joined together with the atoms to which is attached to form a C_{3-10} cycloalkyl. In certain embodiments the pair $-R^{26}/-R^{26a}$ is joined together with the atoms to which is attached to form a cyclobutyl.

10 In certain embodiments $-Tr$ is

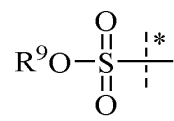
, wherein the dashed line marked with an asterisk indicates attachment to $-Y^3-$ and $-R^7$ is defined as elsewhere within the section covering the exemplary multi-release linker herein. In this instance the release of the drug may be triggered by an enzyme, such as phosphatase.

15

In certain embodiments $-Tr$ is

, wherein the dashed line marked with an asterisk indicates attachment to $-Y^3-$ which is $-S-$ and $-R^8$ is as defined elsewhere within the section covering the exemplary multi-release linker herein.

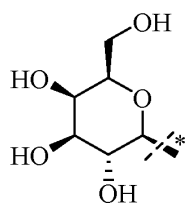
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In certain embodiments $-Tr$ is

, wherein the dashed line marked with an asterisk indicates attachment to $-Y^3-$ and $-R^9$ is as defined elsewhere within the section covering the exemplary multi-release linker herein. In this instance the release of the drug may be triggered by an enzyme, such as sulfatase.

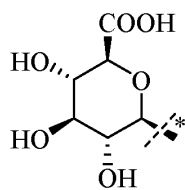
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In certain embodiments $-Tr$ is



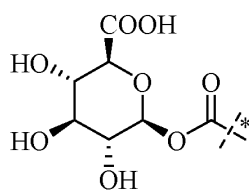
, wherein the dashed line marked with an asterisk indicates attachment to -Y³. In this instance the release of the drug may be triggered by an enzyme, such as α -galactosidase.

- 5 In certain embodiments -Tr is



, wherein the dashed line marked with an asterisk indicates attachment to -Y³. In this instance the release of the drug may be triggered by an enzyme, such as β -glucuronidase.

- 10 In certain embodiments -Tr is



, wherein the dashed line marked with an asterisk indicates attachment to -Y³. In this instance the release of the drug may be triggered by an enzyme, such as β -glucuronidase.

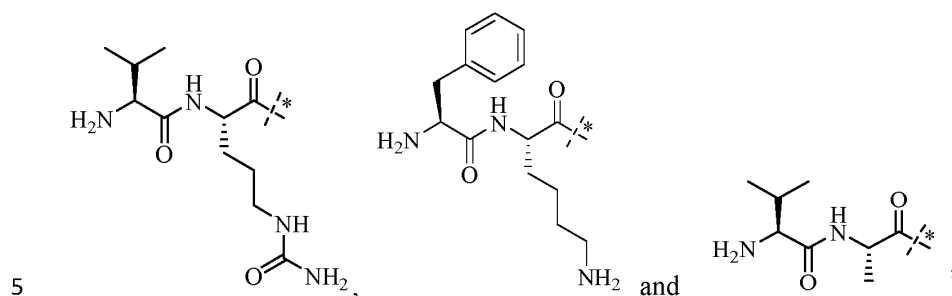
- 15 In certain embodiments -Tr is a peptidyl moiety. It is understood that if -Tr is a peptidyl moiety, then the release of the -D- may be triggered by an enzyme, such as protease. In certain embodiments the protease is selected from the group consisting of cathepsin B and cathepsin K. In certain embodiments the protease is cathepsin B. In certain embodiments the protease is cathepsin K.

20

In certain embodiments -Tr is a peptidyl moiety, such as a dipeptidyl, tripeptidyl, tetrapeptidyl, pentapeptidyl or hexapeptidyl moiety. In certain embodiments -Tr is a dipeptidyl moiety. In certain embodiments -Tr is a tripeptidyl moiety. In certain embodiments -Tr is a tetrapeptidyl

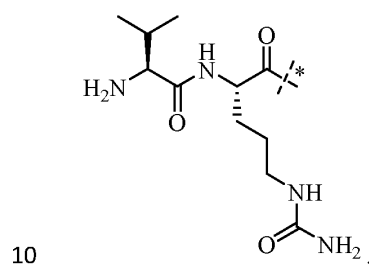
moiety. In certain embodiments -Tr is a pentapeptidyl moiety. In certain embodiments -Tr is a hexapeptidyl moiety.

In certain embodiments -Tr is a peptidyl moiety selected from the group consisting of:

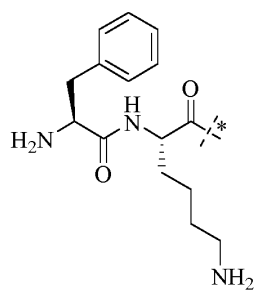


wherein the dashed line marked with an asterisk indicates attachment to -Y³.

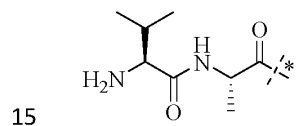
In certain embodiments -Tr is



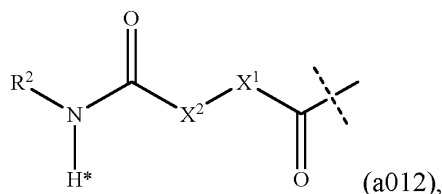
In certain embodiments -Tr is



In certain embodiments -Tr is



In certain embodiments -Y₃- is -N(R⁶)- and -Tr has the structure of -L¹- as disclosed in WO 2011/012722 A1, which is herewith incorporated by reference. Accordingly, In certain embodiments -Tr is of formula (a012):



- 5 wherein the dashed line indicates attachment -Y₃-;
 -X¹- is -C(R¹R^{1a})- or a cyclic fragment selected from C₃₋₇ cycloalkyl, 4 to 7 membered heterocyclyl, phenyl, naphthyl, indenyl, indanyl, tetralinyl, or 9 to 11 membered heterobicycyl,
 wherein in case -X¹- is a cyclic fragment, said cyclic fragment is incorporated into the moiety of formula (a012) via two adjacent ring atoms and the ring atom of -X¹-, which
 10 is adjacent to the carbon atom of the amide bond, is also a carbon atom;
 -X²- is a chemical bond or selected from -C(R³R^{3a})-, -N(R³)-, -O-, -C(R³R^{3a})-C(R⁴R^{4a})-, -C(R³R^{3a})-N(R⁴)-, -N(R³)-C(R⁴R^{4a})-, -C(R³R^{3a})-O-, or -O-C(R³R^{3a})-,
 wherein in case -X¹- is a cyclic fragment, -X²- is a chemical
 15 bond, -C(R³R^{3a})-, -N(R³)- or -O-;
 optionally, in case -X¹- is a cyclic fragment and -X²- is -C(R³R^{3a})-, the order of the -X¹- fragment and the -X²- fragment within the moiety of formula (a012) may be changed and the cyclic fragment is incorporated into the moiety of formula (a012) via two adjacent ring atoms;
 20 -R¹, -R³ and -R⁴ are independently selected from the group consisting of -H, C₁₋₄ alkyl and -N(R⁵R^{5a});
 -R^{1a}, -R², -R^{3a}, -R^{4a} and -R^{5a} are independently selected from the group consisting of -H, and C₁₋₄ alkyl;
 -R⁵ is -C(O)R⁶;
 25 -R⁶ is C₁₋₄ alkyl; and
 optionally, one of the pairs -R^{1a}/R^{4a}, -R^{3a}/R^{4a} or -R^{1a}/R^{3a} form a chemical bond.

In certain embodiments -Tr and -Y₃- form together a functional group selected from the group consisting of

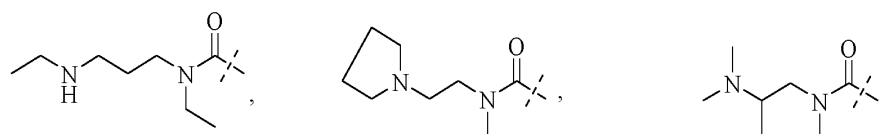
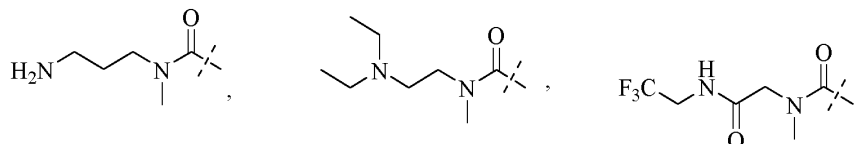
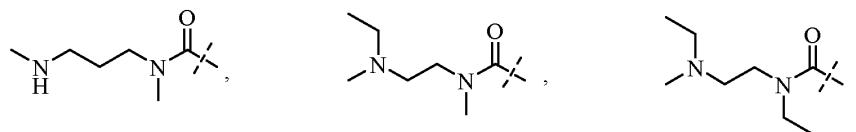
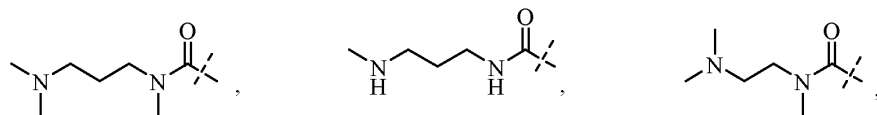
$\text{O}=\text{N}-\text{O}-\text{C}(\text{---})^*$ and $\text{N}^+=\text{N}^+=\text{N}-\text{C}(\text{---})^*$, wherein the dashed line marked with the asterisk indicates attachment to -Ar-.

In certain embodiments -Tr is

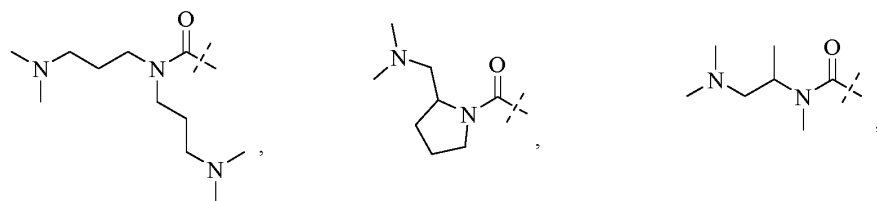
5 $\text{Mod}-\text{CH}(\text{H})-\text{CH}(\text{R})-\text{O}-\text{C}(=\text{O})-\text{C}(\text{---})^*$, wherein -Mod and -R are as defined elsewhere within the section covering the exemplary multi-release linker herein.

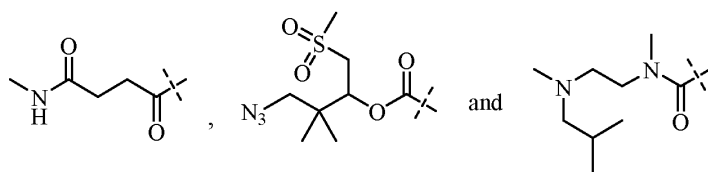
Suitably, -Mod is MeSO_2- .

10 In certain embodiments -Tr is selected from the group consisting of



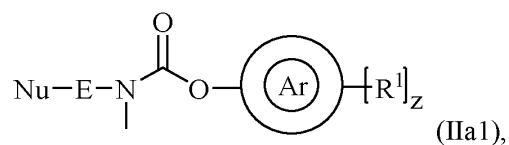
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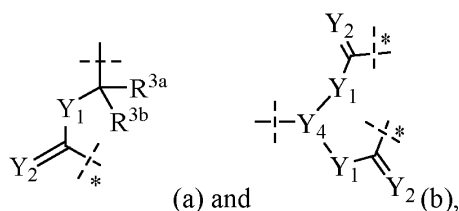
, wherein the dashed line indicates attachment to $-Y^3-$ as defined elsewhere within the section covering the exemplary multi-release linker herein.

- 5 In certain embodiments $-L^{1'}$ is of formula (IIa1):



wherein

each $-R^1$ is independently selected from the group consisting of



- 10 wherein

an unmarked dashed line indicates attachment to $-Ar-$;

a dashed line marked with an asterisk indicates attachment to $-D-$;

the total number of moieties $-D-$ within the compound is ranging from 2 to 6;

z is selected from the group consisting of 2 and 3;

- 15 each $-Y_1-$ is $-O-$;

each $=Y_2$ is $=O$;

$-Nu$ and $-E$ are used as defined in formula (2aa), and

$-Ar-$, $-Y_4-$, $-R^{3a}$ and $-R^{3b}$ are used as defined in formula (2a); and

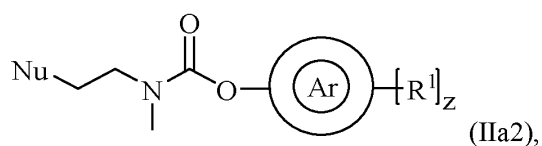
wherein $-L^{1'}$ is substituted with one moiety $-L^2-$.

- 20

In certain embodiments all $-R^1$ of formula (IIa1) are of formula (a).

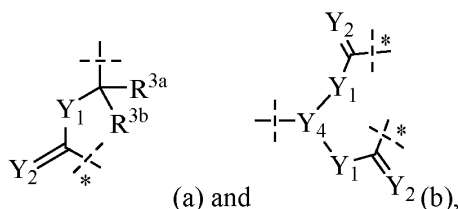
In certain embodiments all $-R^1$ of formula (IIa1) are of formula (b).

- 25 In certain embodiments $-L^{1'}$ is of formula (IIa2):



wherein

each -R¹ is independently selected from the group consisting of



5 wherein

the unmarked dashed line indicates attachment to -Ar-;

a dashed line marked with an asterisk indicates attachment to -D-;

z is selected from the group consisting of 2 and 3;

the total number of moieties -D- within the compound ranges from 2 to 6;

10 -Nu is a secondary or tertiary amine functional group;

each -Y₁- is -O-;

each =Y₂ is =O;

-Ar-, -Y₄-, -R^{3a} and -R^{3b} are used as defined in formula (2a); and

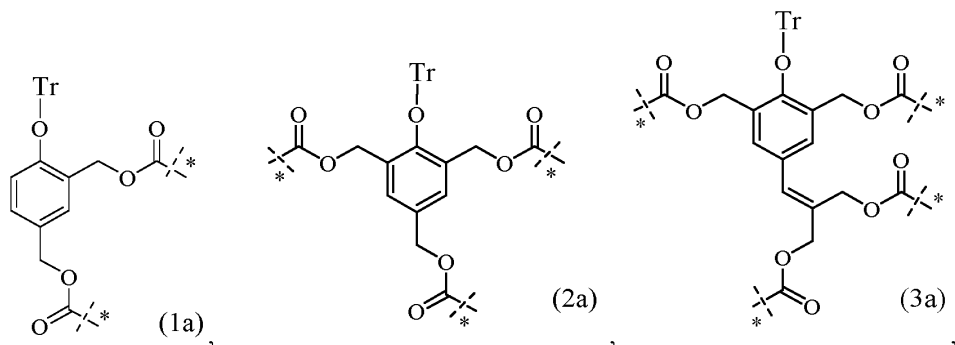
wherein -L¹- is substituted with one moiety -L²-.

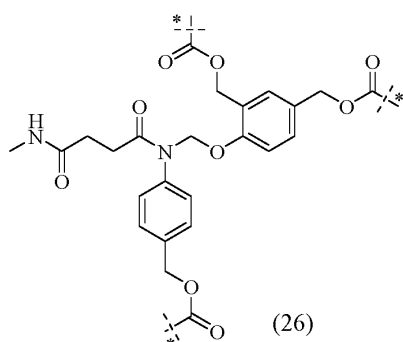
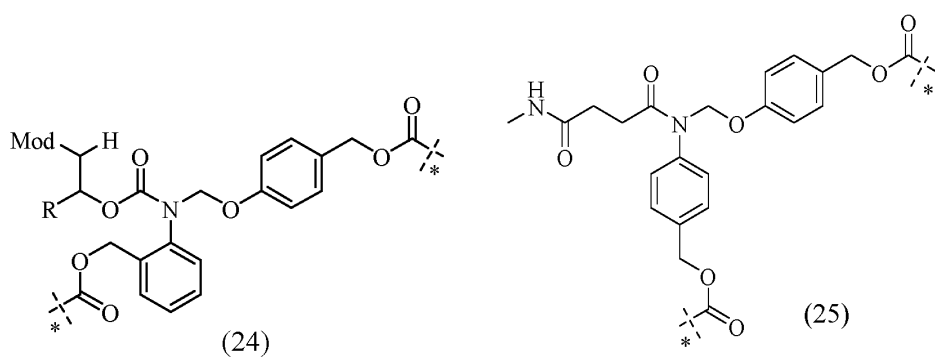
15

In certain embodiments all -R¹ of formula (IIa2) are of formula (a).

In certain embodiments all -R¹ of formula (IIa2) are of formula (b).

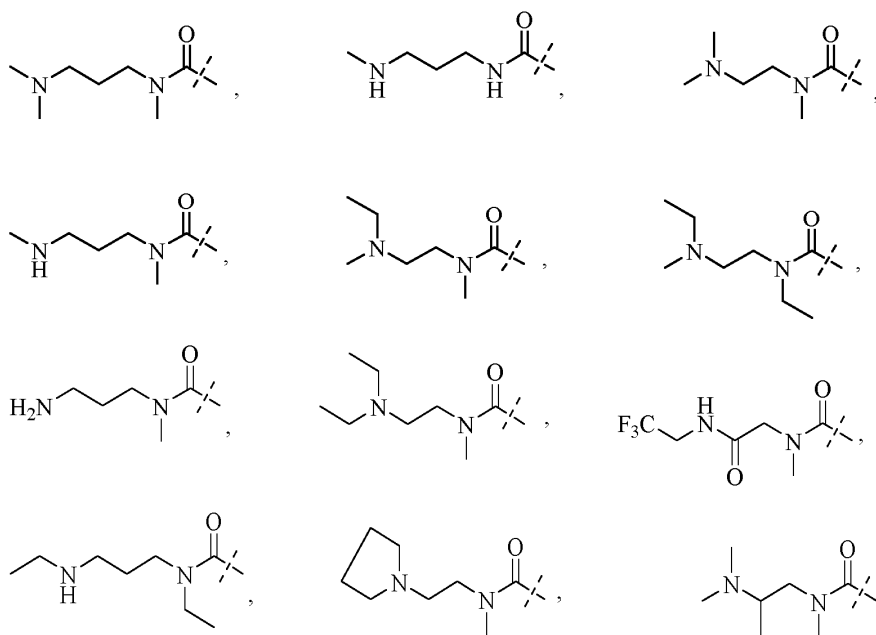
20 In certain embodiments -L¹- is selected from the group consisting of



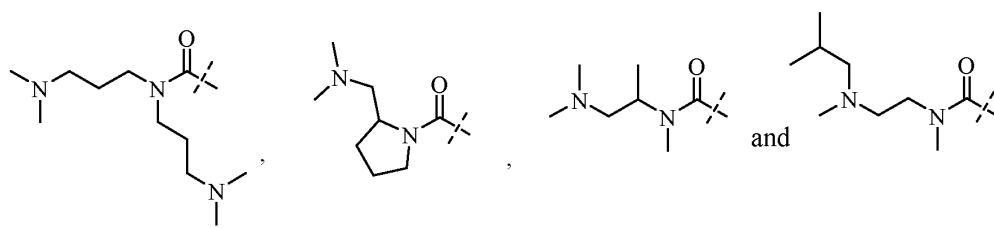


wherein

- 5 a dashed line marked with an asterisk indicates attachment to -D-;
 -R and -Mod are used as described for formula (2ai); and
 -Tr is selected from the group consisting of

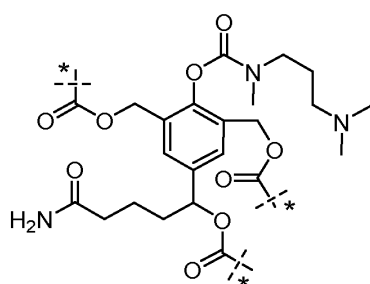


10



wherein the dashed line indicates attachment to the oxygen atom.

- 5 In certain embodiments -L^{1'}- is of formula (2b)



(2b),

wherein

the dashed lines marked with the asterisk indicate attachment to -D-; and

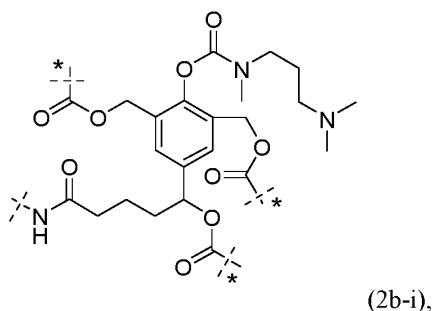
-L^{1'}- is substituted with -L²-.

10

In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to semaglutide. In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to lixisenatide. In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to PEG-loxenatide. In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to liraglutide. In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to ecnoglutide. In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to GZR18. In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to GL0018. In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to tirzepatide. In certain embodiments the moiety -L^{1'}- is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to cotadutide. In certain embodiments the moiety -L^{1'}- is of formula (2b)

and the dashed lines marked with the asterisk indicate attachment to BI-456906. In certain embodiments the moiety $-L^{1'}$ is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to pemvidutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to mazdutide. In certain
 5 embodiments the moiety $-L^{1'}$ is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to dapiglutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to retatrutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:52. In certain embodiments the
 10 moiety $-L^{1'}$ is of formula (2b) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:53.

In certain embodiments $-L^{1'}$ is of formula (2b-i)

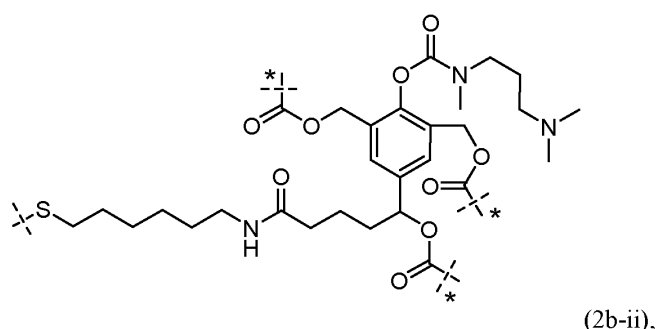


15 wherein
 the dashed lines marked with the asterisk indicate attachment to $-D-$; and
 the unmarked dashed line indicates attachment to $-L^2-$.

In certain embodiments the moiety $-L^{1'}$ is of formula (2b-i) and the dashed lines marked with
 20 the asterisk indicate attachment to semaglutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to lixisenatide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to PEG-loxenatide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to
 25 liraglutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to ecnoglutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to GZR18. In certain embodiments the moiety $-L^{1'}$ is of formula (2b-i) and the

dashed lines marked with the asterisk indicate attachment to GL0018. In certain embodiments the moiety $-L^1-$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to tirzepatide. In certain embodiments the moiety $-L^1-$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to cotadutide. In certain
 5 embodiments the moiety $-L^1-$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to BI-456906. In certain embodiments the moiety $-L^1-$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to pemvidutide. In certain
 10 embodiments the moiety $-L^1-$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to mazdutide. In certain embodiments the moiety $-L^1-$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to dapiglutide. In certain
 15 embodiments the moiety $-L^1-$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:52. In certain embodiments the moiety $-L^1-$ is of formula (2b-i) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:53.

In certain embodiments $-L^2-L^1-$ is of formula (2b-ii)



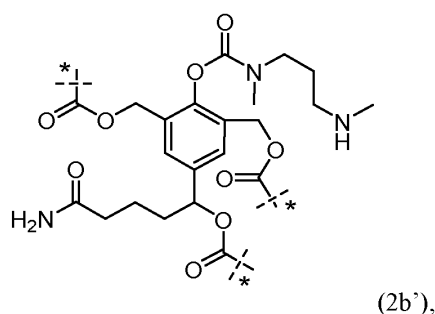
wherein

20 the dashed lines marked with the asterisk indicate attachment to $-D-$; and
 the unmarked dashed line indicates attachment to the at least one polymeric moiety, to formula (I-ai), to formula (I-a ii) or to formula (I-a iii).

In certain embodiments the unmarked dashed line in formula (2b-ii) indicates attachment to the at least one polymeric moiety. In certain embodiments the unmarked dashed line in formula (2b-ii) indicates attachment to formula (I-ai). In certain embodiments the unmarked dashed line in formula (2b-ii) indicates attachment to formula (I-a ii). In certain embodiments the unmarked dashed line in formula (2b-ii) indicates attachment to formula (I-a iii).

In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to semaglutide, in particular attachment to the N-terminal amine functional group of semaglutide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to lixisenatide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to PEG-loxenatide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to liraglutide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to ecnoglutide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to GZR18. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to GL0018. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to tirzepatide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to cotadutide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to BI-456906. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to pemvidutide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to mazdutide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to dapiglutide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to retatrutide. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:52. In certain embodiments the moiety $-L^2-L^{1'}$ is of formula (2b-ii) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:53.

In certain embodiments $-L^{1'}$ is of formula (2b')



wherein

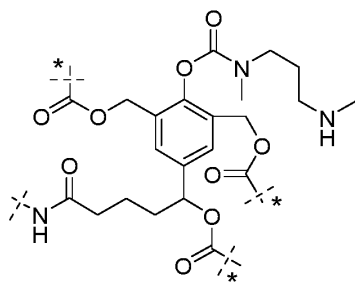
the dashed lines marked with the asterisk indicate attachment to -D-; and
 -L^{1'} - is substituted with -L^{2'} -.

5

In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to semaglutide, in particular attachment to the N-terminal amine functional group of semaglutide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to lixisenatide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to PEG-loxenate. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to liraglutide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to ecnoglutide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to GZR18. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to GL0018. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to tirzepatide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to cotadutide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to BI-456906. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to pemvidutide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to mazdutide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to dapiglutide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to retatrutide. In certain embodiments the moiety -L^{1'} - is of formula (2b') and the dashed lines marked with the asterisk

indicate attachment to the compound of SEQ ID NO:52. In certain embodiments the moiety $-L^{1'}$ is of formula (2b') and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:53.

- 5 In certain embodiments $-L^{1'}$ is of formula (2b'-i)



(2b'-i),

wherein

the dashed lines marked with the asterisk indicate attachment to $-D-$; and

the unmarked dashed line indicates attachment to $-L^2-$.

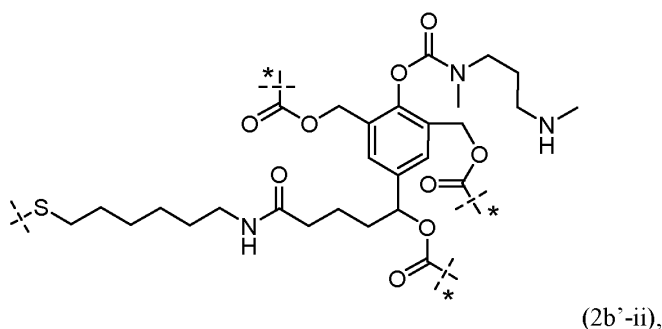
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- In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to semaglutide, in particular attachment to the N-terminal amine functional group of semaglutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to lixisenatide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to PEG-loxenate. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to liraglutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to ecnoglutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to GZR18. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to GL0018. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to tirzepatide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to cotadutide. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to BI-456906. In certain embodiments the moiety $-L^{1'}$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to

pemvidutide. In certain embodiments the moiety $-L^1-$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to mazdutide. In certain embodiments the moiety $-L^1-$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to dapiglutide. In certain embodiments the moiety $-L^1-$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to retatrutide. In certain embodiments the moiety $-L^1-$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:52. In certain embodiments the moiety $-L^1-$ is of formula (2b'-i) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:53.

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In certain embodiments $-L^2-L^1-$ is of formula (2b'-ii)



wherein

the dashed lines marked with the asterisk indicate attachment to $-D-$; and

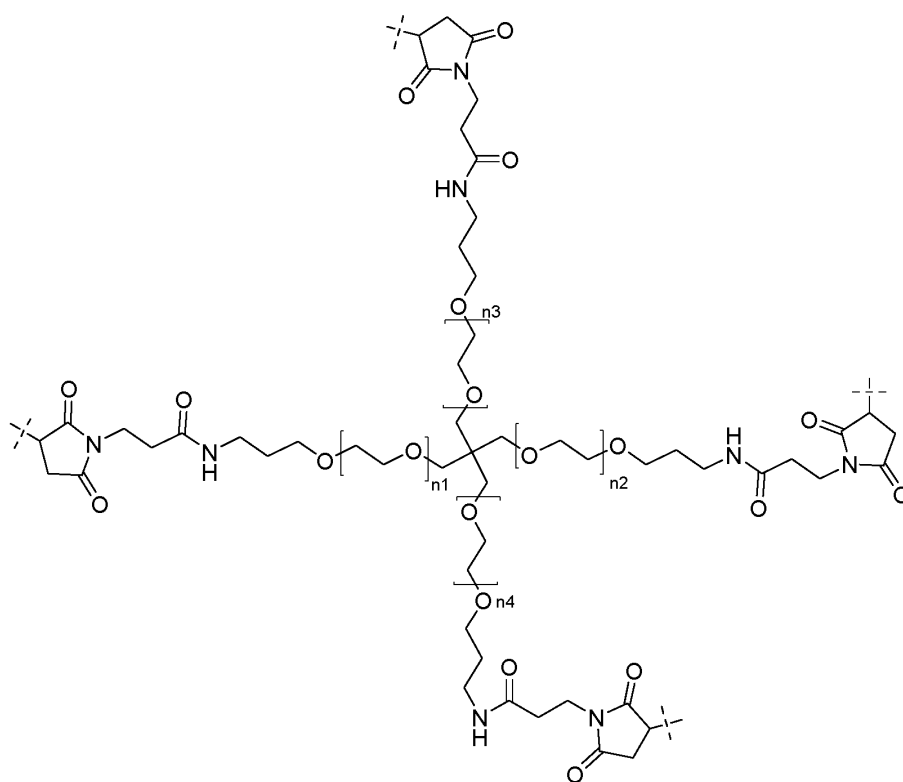
the unmarked dashed line indicates attachment to the at least one polymeric moiety, to formula (I-ai), to formula (I-aii) or to formula (I-aiii).

In certain embodiments the unmarked dashed line in formula (2b'-ii) indicates attachment to the at least one polymeric moiety. In certain embodiments the unmarked dashed line in formula (2b'-ii) indicates attachment to formula (I-ai). In certain embodiments the unmarked dashed line in formula (2b'-ii) indicates attachment to formula (I-aii). In certain embodiments the unmarked dashed line in formula (2b'-ii) indicates attachment to formula (I-aiii).

In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to semaglutide, in particular attachment to the N-terminal amine functional group of semaglutide. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to lixisenatide. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed

lines marked with the asterisk indicate attachment to PEG-loxenatide. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to liraglutide. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to ecnoglutide. In certain
5 embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to GZR18. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to GL0018. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to tirzepatide. In certain embodiments the
10 moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to cotadutide. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to BI-456906. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to pemvidutide. In certain embodiments the moiety $-L^2-L^1-$ is of
15 formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to mazdutide. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to dapiglutide. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to retatrutide. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and
20 the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:52. In certain embodiments the moiety $-L^2-L^1-$ is of formula (2b'-ii) and the dashed lines marked with the asterisk indicate attachment to the compound of SEQ ID NO:53.

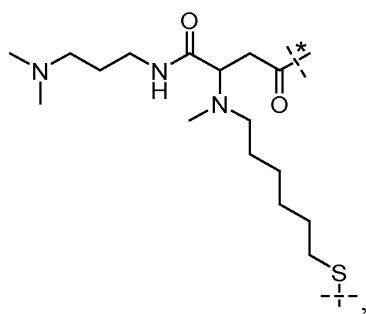
In certain embodiments the compound is of formula (2c)



wherein

n_1 , n_2 , n_3 and n_4 are independently an integer ranging from about 11 to about 115;

dashed lines indicate attachment to a moiety



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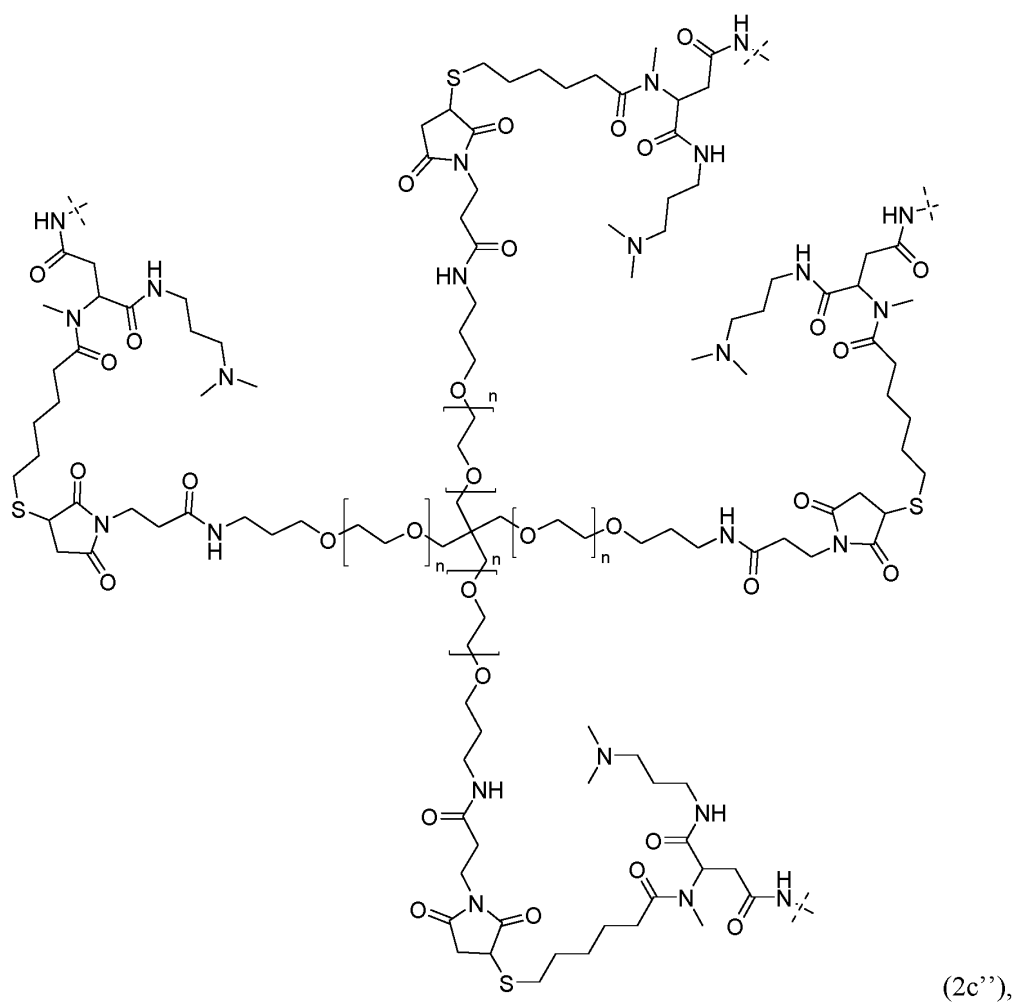
wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2c); and

the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

10

In certain embodiments the compound is of formula (2c'')

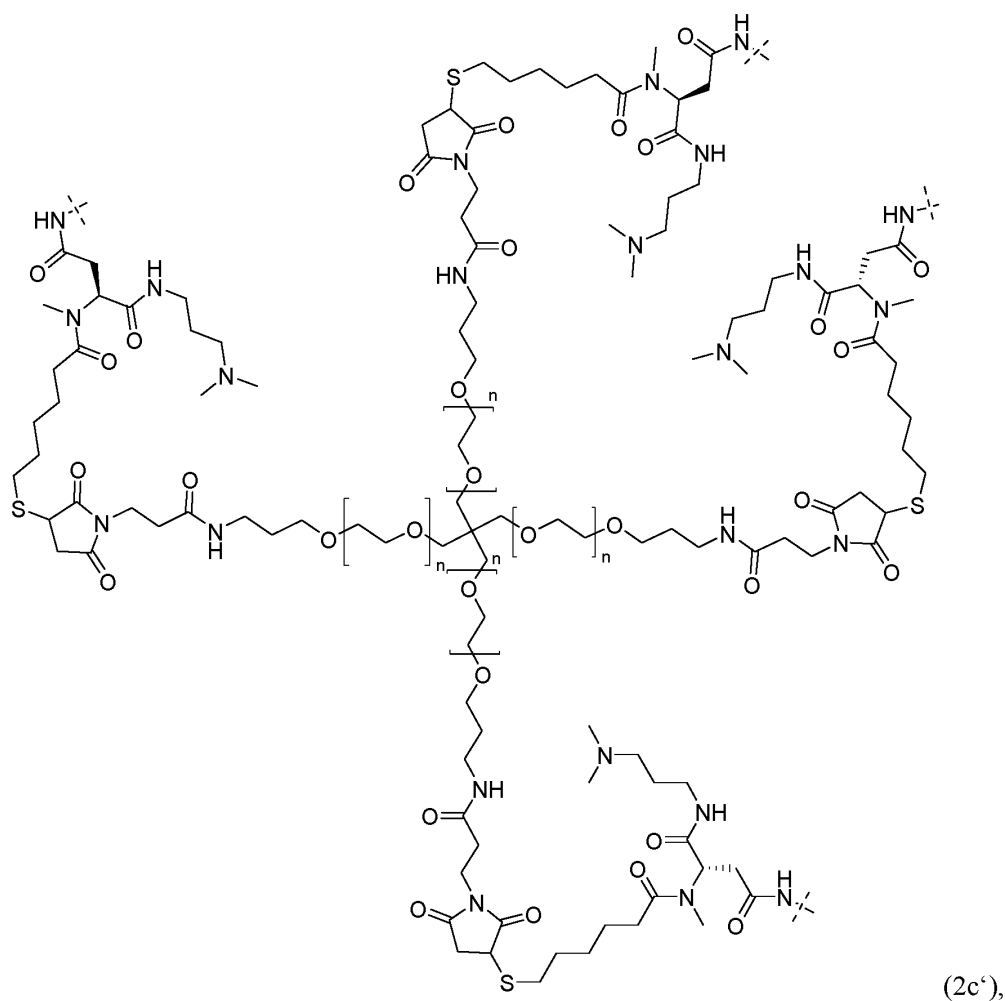


wherein

the dashed line indicates attachment to the N-terminal amine functional group of semaglutide; and

5 n1, n2, n3 and n4 are independently an integer ranging from about 11 to about 115.

In certain embodiments the compound is of formula (2c')



wherein

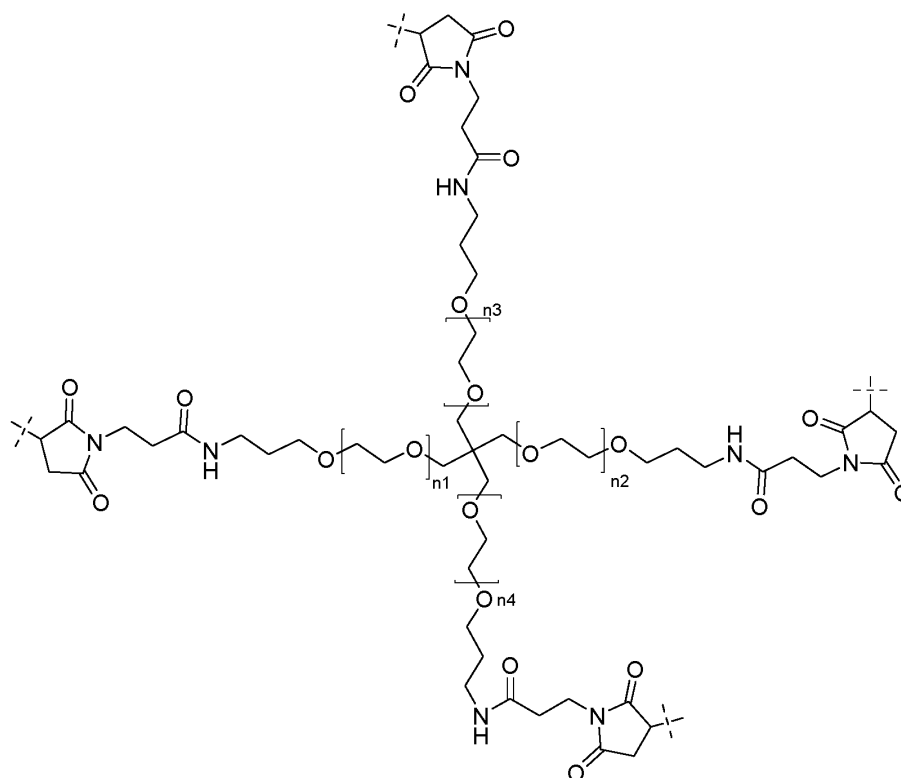
the dashed line indicates attachment to the N-terminal amine functional group of semaglutide; and

5 n1, n2, n3 and n4 are independently an integer ranging from about 11 to about 115.

In certain embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 22. In certain embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 23. In certain
 10 embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 28. In certain
 embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 34. In certain
 embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 45. In certain
 embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 56. In certain
 embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 68. In certain
 embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 80. In certain

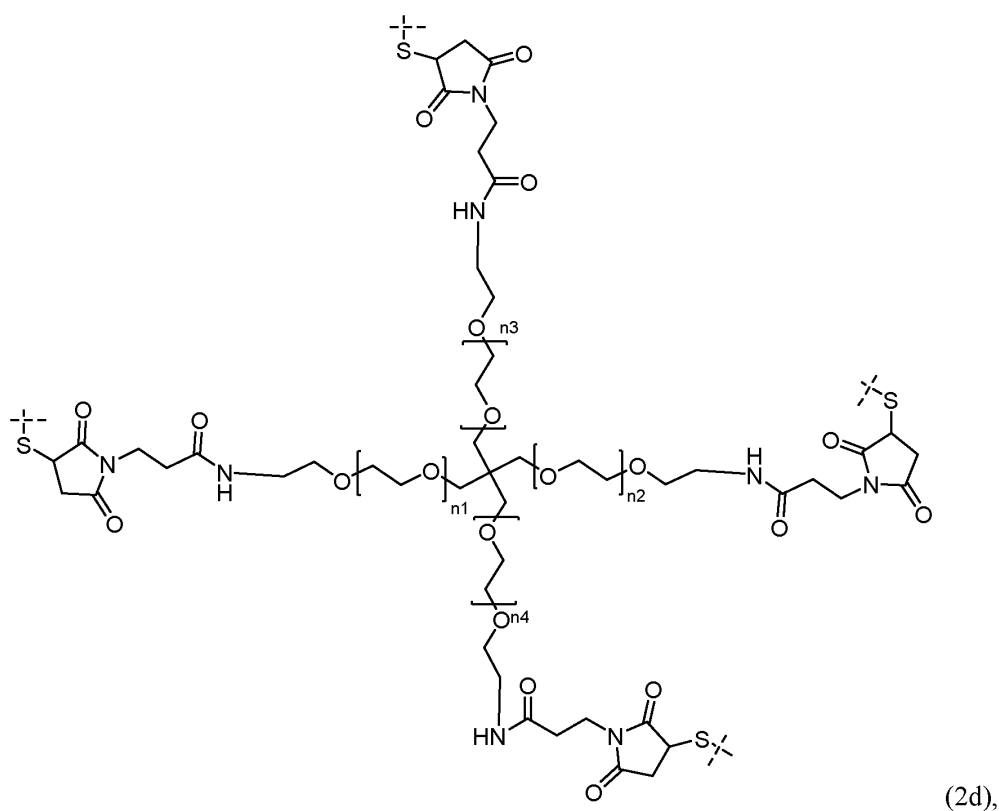
embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 90. In certain embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 100. In certain embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are about 115.

- 5 In certain embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are selected such that the total molecular weight of the moiety



- ranges from 7 to 13 kDa, such as from 8 to 12, from 9 to 11 kDa or is about 10 kDa. In certain embodiments n1, n2, n3 and n4 of formula (2c), (2c') and (2c'') are selected such that the total
10 molecular weight of this moiety ranges from 4 to 6 kDa or is about 5 kDa.

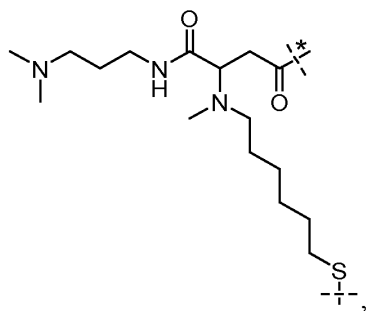
In certain embodiments the compound is of formula (2d)



wherein

n_1 , n_2 , n_3 and n_4 are independently an integer ranging from about 11 to about 115;

dashed lines indicate attachment to a moiety



5

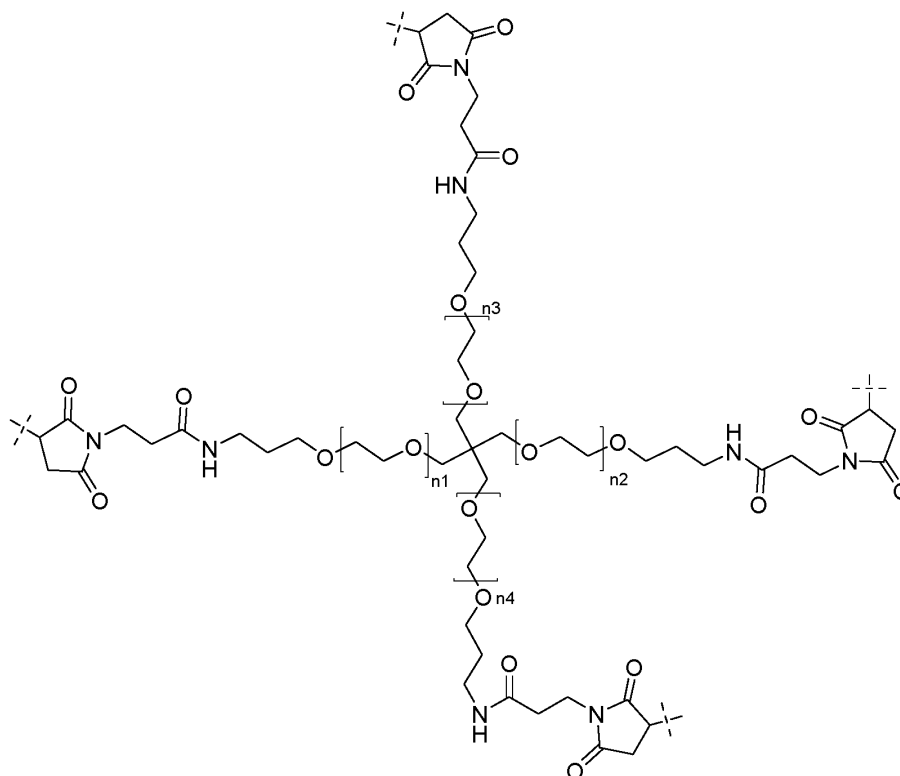
wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2d); and

the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

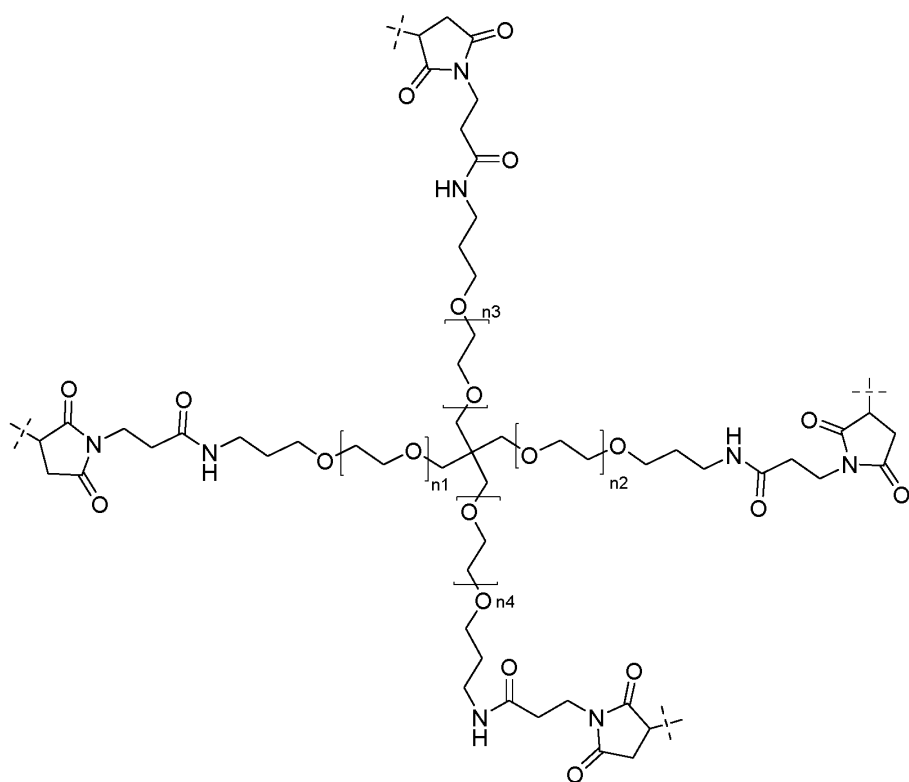
10

- In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 22. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 23. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 34. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 45. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 56. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 68. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 80. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 90. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 100. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are about 115.
- 10 In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2d) are selected such that the total molecular weight of the moiety



ranges from 7 to 13 kDa, such as from 8 to 12, from 9 to 11 kDa or is about 10 kDa.

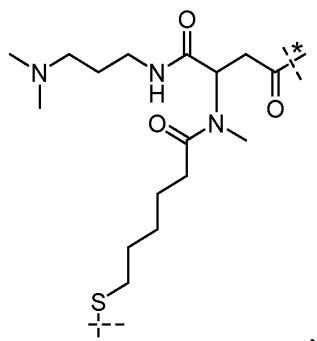
- 15 In certain embodiments the compound is of formula (2e)



wherein

n1, n2, n3 and n4 are independently an integer ranging from about 11 to about 115;

dashed lines indicate attachment to a moiety



5

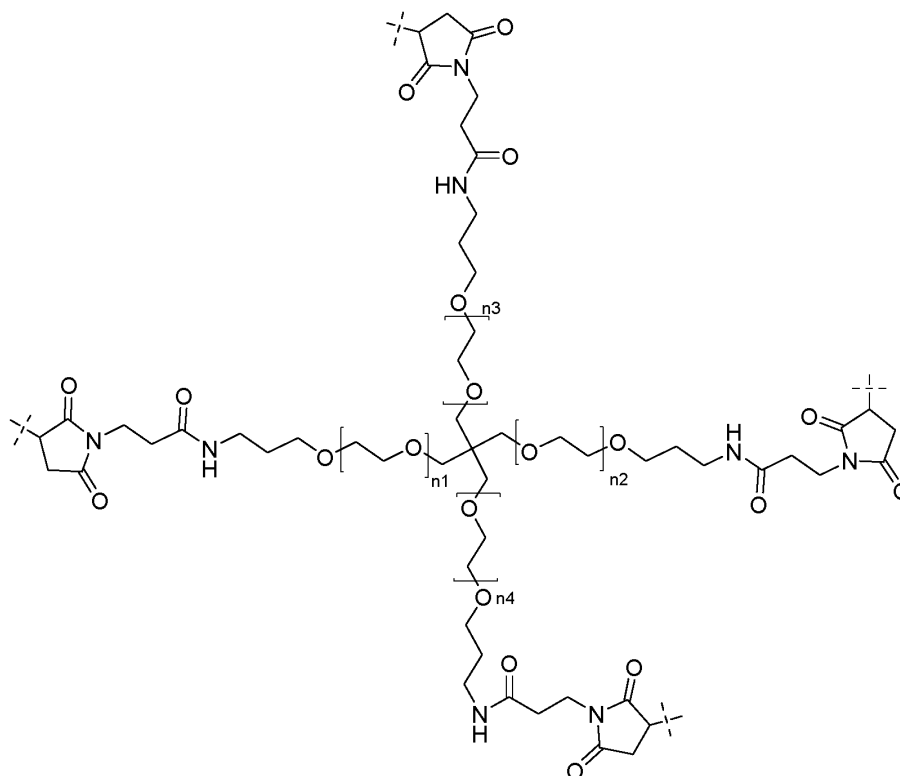
wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2e); and

the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

10

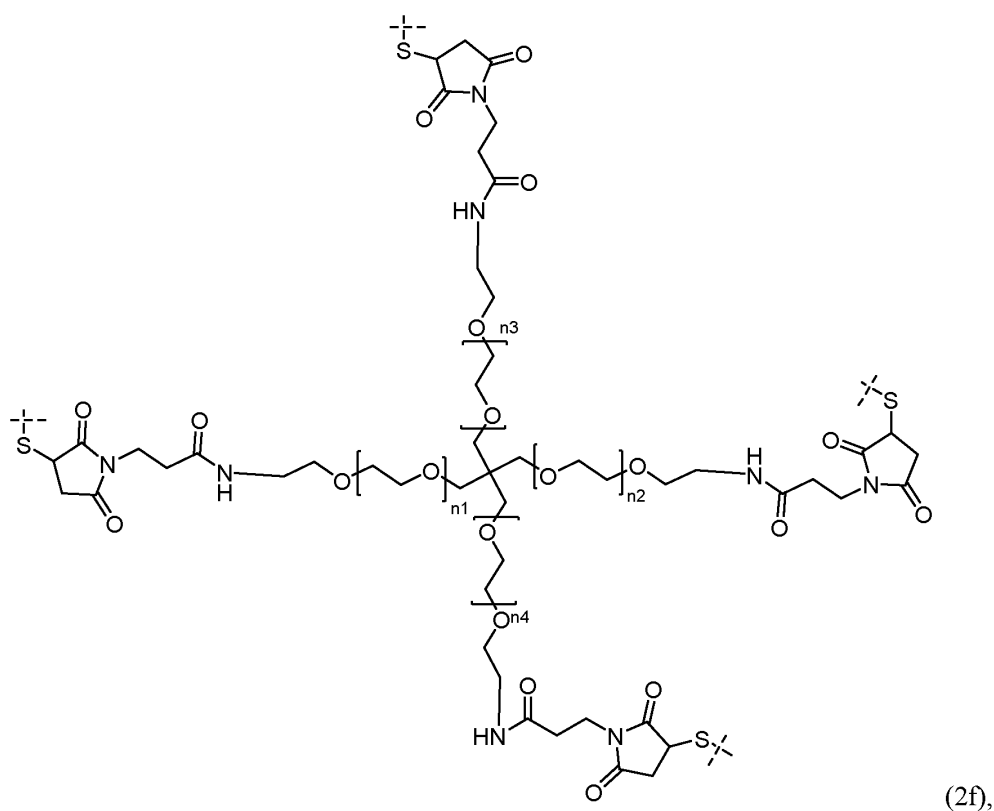
- In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 22. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 23. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 34. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 45. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 56. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 68. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 80. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 90. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 100. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are about 115.
- 10 In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2e) are selected such that the total molecular weight of the moiety



ranges from 7 to 13 kDa, such as from 8 to 12, from 9 to 11 kDa or is about 10 kDa. In certain embodiments the total molecular weight of this moiety is about 5 kDa.

15

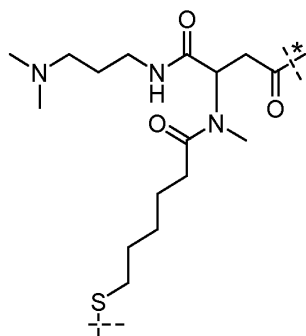
In certain embodiments the compound is of formula (2f)



wherein

n1, n2, n3 and n4 are independently an integer ranging from about 11 to about 115;

dashed lines indicate attachment to a moiety



5

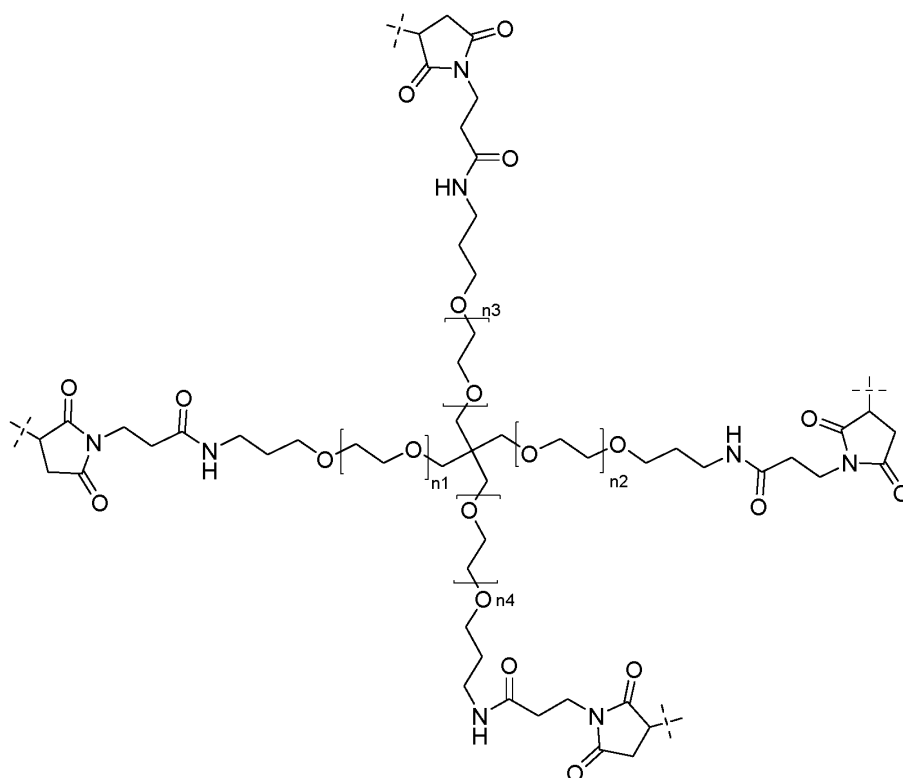
wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2f); and

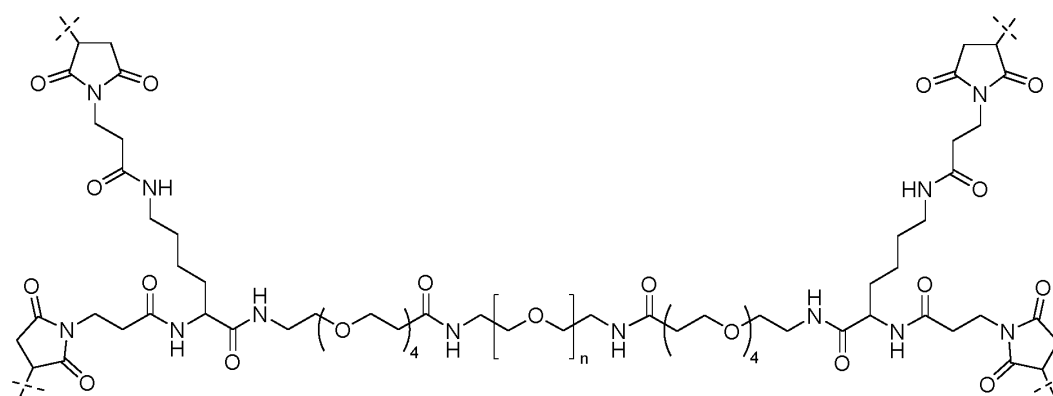
the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

10

- In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 22. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 23. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 34. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 45. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 56. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 68. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 80. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 90. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 100. In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are about 115.
- 10 In certain embodiments n_1 , n_2 , n_3 and n_4 of formula (2f) are selected such that the total molecular weight of the moiety



- ranges from 7 to 13 kDa, such as from 8 to 12, from 9 to 11 kDa or is about 10 kDa. In certain embodiments the total molecular weight of this moiety is about 5 kDa.
- 15 In certain embodiments the compound is of formula (2g)

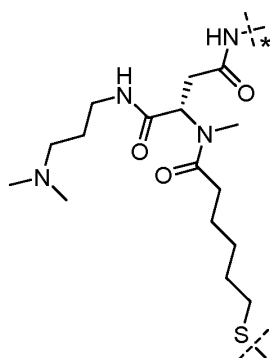


(2g),

wherein

n is independently an integer ranging from about 22 to about 230;

5 dashed lines indicate attachment to a moiety

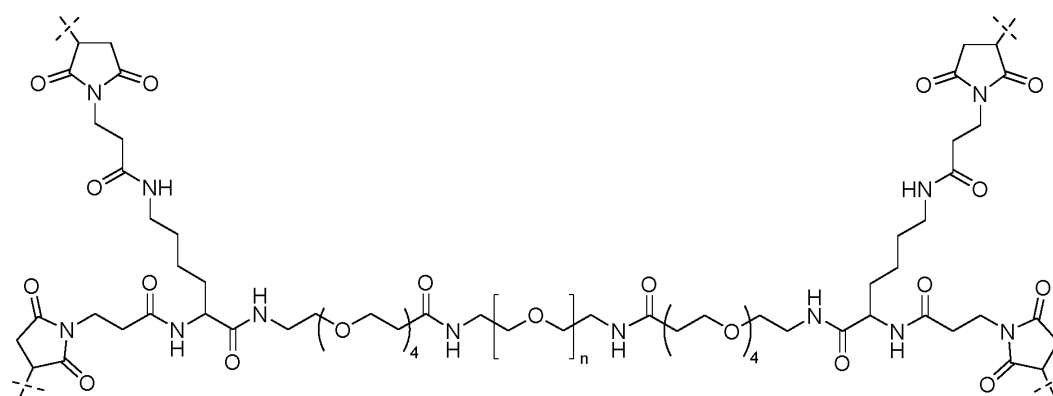


wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2g); and

10 the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

In certain embodiments the compound is of formula (2g')

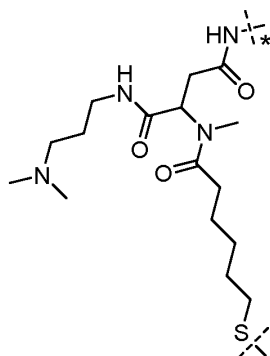


(2g'),

wherein

n is independently an integer ranging from about 22 to about 230;

5 dashed lines indicate attachment to a moiety



wherein

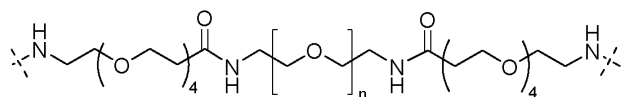
the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2g'); and

10 the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

In certain embodiments n of formula (2g) and (2g') is about 44. In certain embodiments n of formula (2g) and (2g') is about 46. In certain embodiments n of formula (2c) is about 68. In
 15 certain embodiments n of formula (2g) and (2g') is about 90. In certain embodiments n of formula (2g) and (2g') is about 112. In certain embodiments n of formula (2g) and (2g') is about 90. In certain embodiments n of formula (2g) and (2g') is about 113. In certain
 embodiments n of formula (2g) and (2g') is about 136. In certain embodiments n of formula (2g) and (2g') is about 160. In certain embodiments n of formula (2g) and (2g') is about 180.

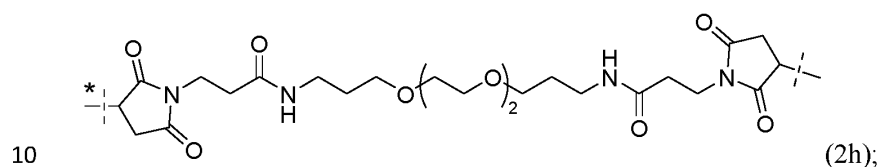
In certain embodiments n of formula (2g) and (2g') is about 200. In certain embodiments n of formula (2g) and (2g') is about 230.

In certain embodiments n of formula (2g) is selected such that the total molecular weight of the moiety



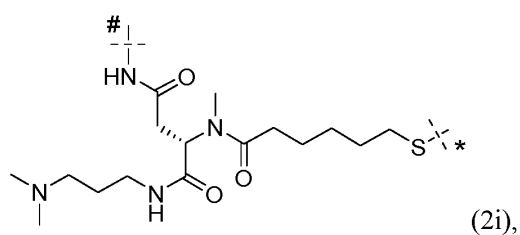
ranges from 3 to 7 kDa, such as from 4 to 6, from 4.5 to 5.5 kDa or is about 5 kDa.

In certain embodiments the compound is of formula (2h)



wherein

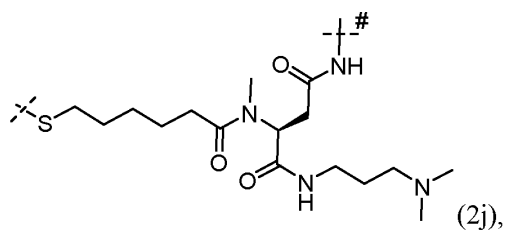
the dashed line marked with the asterisk indicates attachment to the dashed line of a moiety of formula (2i)



15 wherein

the dashed line marked with the # indicates attachment to the N-terminal amine functional group of semaglutide;

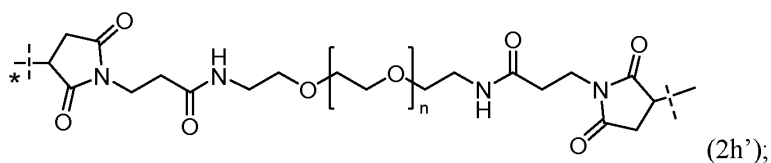
and wherein the unmarked dashed line of formula (2h) indicates attachment to the unmarked dashed line of formula (2j)



wherein

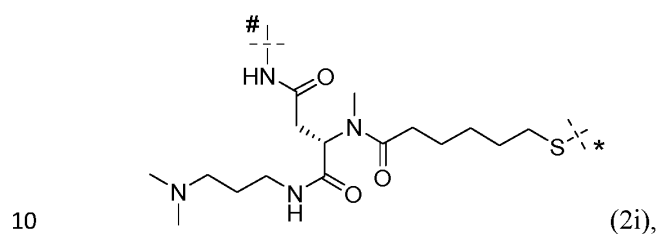
the dashed line marked with the # indicates attachment to the N-terminal amine functional group of semaglutide.

- 5 In certain embodiments the compound is of formula (2h')



wherein

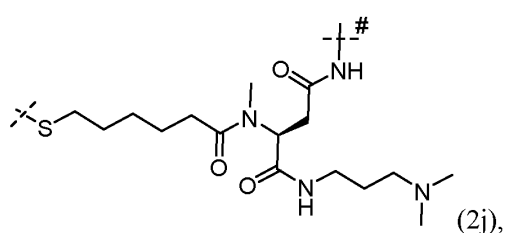
the dashed line marked with the asterisk indicates attachment to the dashed line marked with the asterisk of a moiety of formula (2i)



wherein

the dashed line marked with the # indicates attachment to the N-terminal amine functional group of semaglutide;

- 15 wherein the unmarked dashed line of formula (2h') indicates attachment to the unmarked dashed line of formula (2j)

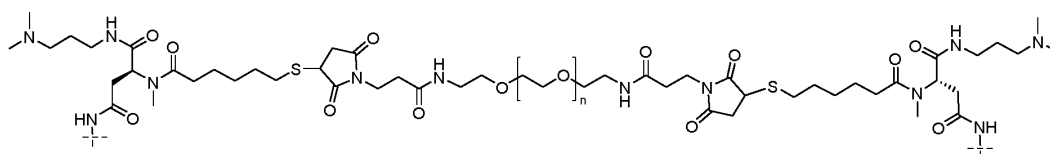


wherein

- 20 the dashed line marked with the # indicates attachment to the N-terminal amine functional group of semaglutide;

and wherein n is an integer ranging from about 22 to about 230.

In certain embodiments the compound is of formula (2h'')



(2h''),

wherein

a dashed line indicates attachment to the N-terminal amine functional group of semaglutide.

In certain embodiments n of formula (2h') is about 44. In certain embodiments n of formula (2h') is about 46. In certain embodiments n of formula (2h') is about 68. In certain embodiments n of formula (2h') is about 90. In certain embodiments n of formula (2h') is about 112. In certain embodiments n of formula (2h') is about 113. In certain embodiments n of formula (2h') is about 136. In certain embodiments n of formula (2h') is about 160. In certain embodiments n of formula (2h') is about 180. In certain embodiments n of formula (2h') is about 200. In certain embodiments n of formula (2h') is about 230.

In certain embodiments the half-life of the drug released from the compound is it at least 1.5-fold higher than the corresponding free drug's half-life. In certain embodiments the half-life of the drug released from the compound is it at least 2.5-fold higher than the corresponding free drug's half-life. In certain embodiments the half-life of the drug released from the compound is it at least 5-fold higher than the corresponding free drug's half-life. In certain embodiments the half-life of the drug released from the compound is it at least 7.5-fold higher than the corresponding free drug's half-life. In certain embodiments the half-life of the drug released from the compound is it at least 10-fold higher than the corresponding free drug's half-life.

In certain embodiments the release half-life of the compound is at least the circulation half-life of the corresponding free drug. In certain embodiments the release half-life of the compound is at least 2-fold higher than the circulation half-life of the corresponding free drug. In certain embodiments the release half-life of the compound is at least 3-fold higher than the circulation half-life of the corresponding free drug.

In certain embodiments the distance between two moieties -AB is such that they are capable of binding to a binding domain of two different albumins or to two different binding domains of

the same albumin. In certain embodiments the distance between two moieties -AB is such that they are capable of binding to a binding domain of two different albumins. In certain embodiments the distance between two moieties -AB is such that they are capable of binding to two different binding domains of the same albumin.

5

In another aspect the present invention relates to a pharmaceutical composition comprising at least one compound of the present invention or a pharmaceutically acceptable salt thereof and at least one excipient.

10 In another aspect the present invention relates to a compound of the present invention or a pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention for use as a medicament, optionally in combination with one or more additional therapeutically active compounds.

15 The present invention also relates to a compound or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention for use as a medicament.

The present invention also relates to a compound or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention for use in the manufacture of a
20 medicament.

Such medicament may be used in the treatment or prevention of a disease that can be treated or prevented with H-D-AB.

25 Another aspect of the present invention relates to a compound of the present invention or a pharmaceutically acceptable salt thereof or a pharmaceutical composition comprising said compound of the present invention for use in a method of treating or preventing a disease that can be treated or prevented with H-D-AB or its pharmaceutically acceptable salt thereof, optionally in combination with one or more additional therapeutically active compounds.

30

In another aspect the present invention relates to a method of treating a patient having a disease that can be treated or prevented with H-D-AB, wherein the method comprises the step of administering a pharmaceutically acceptable amount of a compound or a pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention to a patient in

need thereof, optionally in combination with one or more additional therapeutically active compounds.

Administration of a compound, a pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention may be via external application, injection or infusion, including intraarticular, periarticular, intradermal, subcutaneous, intramuscular, intravenous, intraosseous, intraperitoneal, intrathecal, intracapsular, intraorbital, intravitreal, intratympanic, intravesical, intracardiac, transtracheal, subcuticular, subcapsular, subarachnoid, intraspinal, intraventricular, intrasternal injection and infusion; direct delivery to the brain via implanted device allowing delivery of the invention or the like to brain tissue or brain fluids (e.g., Ommaya Reservoir), direct intracerebroventricular injection or infusion, injection or infusion into brain or brain associated regions, injection into the subchoroidal space, retro-orbital injection and ocular instillation. In certain embodiments the medicament is for subcutaneous injection, which may be done with a pen injector or via a syringe.

A compound, in which -D-AB is a GLP-1 receptor agonist, or its pharmaceutically acceptable salt thereof or a pharmaceutical composition comprising such compound may be used in the treatment or prevention of a disease selected from the group consisting of (i) all forms of diabetes, (ii) obesity, (iii) non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), (iv) cardiovascular disease, (v) neurodegenerative disorders, (vi) chronic kidney disease (CKD), (vii) diabetic kidney disease (DKD), (viii) peripheral arterial disease (PAD), and/or (ix) heart failure (HF).

Exemplary cardiovascular diseases may be selected from the group consisting of syndrome X, atherosclerosis, myocardial infarction, coronary heart disease, reperfusion injury, stroke, cerebral ischemia, an early cardiac or early cardiovascular disease, left ventricular hypertrophy, coronary artery disease, hypertension, essential hypertension, acute hypertensive emergency, cardiomyopathy, heart insufficiency, exercise intolerance, acute and/or chronic heart failure, arrhythmia, cardiac dysrhythmia, syncope, angina pectoris, cardiac bypass and/or stent reocclusion, intermittent claudication (atherosclerosis obliterans), diastolic dysfunction, and/or systolic dysfunction; and reduction of blood pressure, such as reduction of systolic blood pressure.

A compound, in which -D-AB is a GLP-1 receptor agonist, or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention may be also used in the treatment or prevention of dyslipidemia and/or diseases where one or more of the following clinical outcomes are the treatment goal: lowering total serum lipids; increasing HDL; lowering
5 small, dense LDL; lowering VLDL; lowering triglycerides; lowering cholesterol; lowering plasma levels of lipoprotein a (Lp(a)) in a human; inhibiting generation of apolipoprotein A (apo(A)).

Exemplary neurodegenerative disorders may be selected from the group consisting of
10 Alzheimer's disease and Parkinson's disease.

Exemplary forms of HF may be selected from the group consisting of heart failure with reduced ejection fraction (HFrEF), heart failure with mid-range ejection fraction (HFmrEF) and heart failure with preserved ejection fraction (HFpEF).

15

In certain embodiments the compound or pharmaceutically acceptable salt thereof of the present invention is used for the treatment of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH).

20 A compound, in which -D-AB is a GLP-1 receptor agonist, or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention may be also used in the treatment of obesity and/or eating disorders, where one or more of the following clinical outcomes are the treatment goal: decreasing food intake, increasing energy expenditure, reducing body weight, suppressing appetite, inducing satiety.

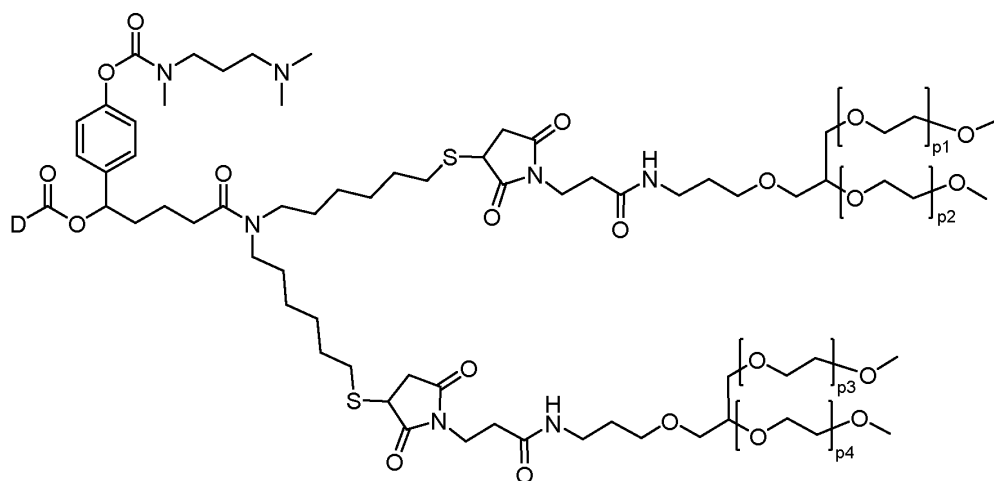
25

A compound, in which -D-AB is a GLP-1 receptor agonist, or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention may also be combined with one or more additional drugs, such as drugs selected from cardiovascular agents, antidiabetic agents, and/or anti-obesity agents. Examples of these pharmacologically active
30 substances are: inotropes, beta adrenergic receptor blockers, HMG-CoA reductase inhibitors, angiotensin II receptor antagonists, angiotensin converting enzyme inhibitors, calcium channel blockers, endothelin antagonists, renin inhibitors, diuretics, aldosterone receptor blockers, endothelin receptor blockers, aldosterone synthase inhibitors, CETP inhibitor, relaxin, PCSK9 inhibitors, BNP and NEP inhibitors, GLP-1 analogues, insulin, sulphonylureas, biguanides,

meglitinides, glucosidase inhibitors, glucagon antagonists, DPP-IV inhibitors, SGLT2 inhibitors. The treatment with the compound or pharmaceutically its pharmaceutically acceptable salt or the pharmaceutical composition of the present invention may also be combined with heart surgery.

5

A compound, in which -D-AB is a GLP-1 receptor agonist, or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention may also be administered in combination with a growth hormone, such as a human growth hormone. Such human growth hormone may be in the form of an unmodified drug, such as the human growth hormone of SEQ ID NO:58, or as a conjugate or complex comprising human growth hormone. Suitably, the compound, in which -D-AB is a GLP-1 receptor agonist, is administered to a patient in a co-treatment with lonapegsomatropin, which has the following structure:



wherein

15 D is a human growth hormone polypeptide of SEQ ID NO:58 connected to the rest of the molecule through an amine functional group provided by a lysine side chain; and each p1, p2, p3, p4 is independently an integer ranging from 210 to 240.

SEQ ID NO:58 has the following sequence:

20 FPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPKEQKYSFLQNPQTSLCFSESIP
TPSNREETQQKSNLELLRISLLLIQSWLEPVQFLRSVFANSLVYGASDSNVYDLLKDL
EEGIQTLMGRLEDGSPRTGQIFKQTYSKFDTNSHNDDALLKNYGLLYCFRKDMDKV
ETFLRIVQCRSVEGSCGF

In such co-treatment the compound, in which -D-AB is a GLP-1 receptor agonist, may be administered prior to, at the same time or after administration of the unmodified human growth hormone, the conjugate or complex comprising human growth hormone.

- 5 A compound, in which -D-AB is a PTH, such as the compound of SEQ ID NO:52 or SEQ ID NO:53, or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention may be used in the treatment or prevention of a disease selected from the group consisting of of hypoparathyroidism, hyperphosphatemia, osteoporosis, fracture repair, osteomalacia, osteomalacia and osteoporosis in patients with hypophosphatasia, steroid-
10 induced osteoporosis, male osteoporosis, arthritis, osteoarthritis, osteogenesis imperfecta, fibrous dysplasia, rheumatoid arthritis, Paget's disease, humoral hypercalcemia associated with malignancy, osteopenia, periodontal disease, bone fracture, alopecia, chemotherapy-induced alopecia, thrombocytopenia, chronic periodontitis, osteonecrosis of jaw and poorly healing fractures due to ALPL gene mutations.

15

In certain embodiments, said disease is hypoparathyroidism.

- In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment. In certain embodiments, said disease is hypoparathyroidism induced by
20 immune checkpoint inhibitor treatment targeting CTLA-4 (cytotoxic T-lymphocyte-associated protein 4), PD-1 (programmed cell death protein 1), PD-L1 (programmed death-ligand 1), PD-L2 (programmed death-ligand 2), KIR (killer-cell immunoglobulin-like receptor), B7-H3, B7-H4, BTLA (B- and T-lymphocyte attenuator), LAG3 (lymphocyte-activation gene 3), TIM-3 (T-cell immunoglobulin and mucin-domain containing-3), VISTA (V-domain Ig
25 suppressor of T cell activation), ILT2/LILRB1 (Ig-like transcript 2/leukocyte Ig-like receptor 1), ILT3/LILRB4 (Ig-like transcript 3/leukocyte Ig-like receptor 4), ILT4/LILRB2 (Ig-like transcript 4/leukocyte Ig-like receptor 2), TIGIT (T cell immunoreceptor with Ig and ITIM domains), NKG2A, PVRIG or combinations thereof.

- 30 In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting CTLA-4, PD-1, PD-L1 or combinations thereof. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting CTLA-4 with immune checkpoint inhibitors such as ipilimumab, tremelimumab, MK-1308, FPT155, PRS010, BMS-986249, BPI-002, CBT509, JS007,

ONC392, TE1254, IBI310, BR02001, CG0161, KN044, PBI5D3H5, BCD145, ADU1604, AGEN1884, AGEN1181, CS1002 or CP675206. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting PD-1 with immune checkpoint inhibitors such as pembrolizumab, nivolumab, pidilizumab, AMP-224, 5 BMS-936559, cemiplimab or PDR001. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting PD-L1 with immune checkpoint inhibitors such as MDX-1105, MEDI4736, atezolizumab, avelumab, BMS-936559 or durvalumab. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting PD-L2. In certain embodiments, 10 said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting KIR with immune checkpoint inhibitors such as lirilumab (IPH2102) or IPH2101. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting B7-H3 with immune checkpoint inhibitors such as MGA271. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting B7-H4 with immune checkpoint inhibitors such as FPA150. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting BTLA. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting LAG3 with immune checkpoint inhibitors such as IMP321 (eftilagimod alpha), relatlimab, MK-4280, 20 AVA017, BI754111, ENUM006, GSK2831781, INCAGN2385, LAG3Ig, LAG525, REGN3767, Sym016, Sym022, TSR033, TSR075 or XmAb22841. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting TIM-3 with immune checkpoint inhibitors such as LY3321367, MBG453 or TSR-022. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting VISTA with immune checkpoint inhibitors such as JNJ-61610588. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting ILT2/LILRB1. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting ILT3/LILRB4. In certain embodiments, said disease is hypoparathyroidism induced by 30 immune checkpoint inhibitor treatment targeting ILT3/LILRB2 with immune checkpoint inhibitors such as MK-4830. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting TIGIT with immune checkpoint inhibitors such as MK-7684, PTZ-201, RG6058 or COM902. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting

NKG2A with immune checkpoint inhibitors such as IPH-2201. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting PVRIG with immune checkpoint inhibitors such as COM701. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment targeting both PD-1 and CTLA-4. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment with nivolumab. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment with ipilimumab. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment with pembrolizumab. In certain embodiments, said disease is hypoparathyroidism induced by immune checkpoint inhibitor treatment with a combination of nivolumab and ipilimumab.

In certain embodiments, said disease is rheumatoid arthritis induced by immune checkpoint inhibitor treatment. In certain embodiments, said disease is rheumatoid arthritis induced by immune checkpoint inhibitor treatment targeting PD-1 or PD-L1. In certain embodiments, said disease is rheumatoid arthritis induced by immune checkpoint inhibitor treatment targeting PD-1. In certain embodiments, said disease is rheumatoid arthritis induced by immune checkpoint inhibitor treatment targeting PD-L1. In certain embodiments, said disease is rheumatoid arthritis induced by immune checkpoint inhibitor treatment with nivolumab. In certain embodiments, said disease is rheumatoid arthritis induced by immune checkpoint inhibitor treatment with pembrolizumab. In certain embodiments, said disease is rheumatoid arthritis induced by immune checkpoint inhibitor treatment with a combination of nivolumab and ipilimumab. In certain embodiments, said disease is rheumatoid arthritis which recurred after immune checkpoint inhibitor treatment.

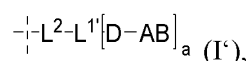
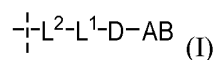
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A compound or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention may be administered, such as via subcutaneous administration, once a week, every two weeks, every three weeks or once a month.

30 In certain embodiments the compound or its pharmaceutically acceptable salt thereof or a pharmaceutical composition of the present invention may be administered once a week, every two weeks, every three weeks or once a month.

The invention is further described by the following non-limiting items.

1. A compound or a pharmaceutically acceptable salt thereof, wherein the compound comprises at least one polymeric moiety, to which at least two moieties of formula (I) are conjugated and/or to which at least one moiety of formula (I') is conjugated, wherein formula (I) and (I') are



wherein

each $-\text{L}^2-$ is independently a spacer moiety or is absent;

each $-\text{L}^1-$ is independently a linker moiety that is covalently and reversibly conjugated to $-\text{D}-$;

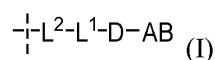
each $-\text{L}^1-$ is independently a linker moiety that is covalently and reversibly conjugated to $-\text{D}-$;

each $-\text{D}-$ is independently a drug moiety;

each $-\text{AB}$ is independently an albumin-binding moiety; and

each a is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

2. The compound or a pharmaceutically acceptable salt thereof of item 1, wherein the compound comprises at least one polymeric moiety, to which at least two moieties of formula (I) are conjugated, wherein formula (I) is



wherein

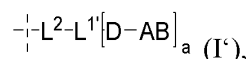
each $-\text{L}^2-$ is independently a spacer moiety or is absent;

each $-\text{L}^1-$ is independently a linker moiety that is covalently and reversibly conjugated to $-\text{D}-$;

each $-\text{D}-$ is independently a drug moiety; and

each $-\text{AB}$ is independently an albumin-binding moiety.

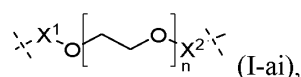
3. The compound or a pharmaceutically acceptable salt thereof of item 1, wherein the compound comprises at least one polymeric moiety, to which at least one moiety of formula (I') is conjugated, wherein formula (I') is



wherein

- each -L²- is independently a spacer moiety or is absent;
 each -L^{1'}- is independently a linker moiety that is covalently and reversibly conjugated to -D-;
 each -D- is independently a drug moiety;
 5 each -AB is independently an albumin-binding moiety; and
 each a is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.
4. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 3, wherein the at least one polymeric moiety of the compound is a linear polymeric moiety -P-.
- 10 5. The compound or a pharmaceutically acceptable salt thereof of item 4, wherein a moiety of formula (I) or (I') is conjugated to each of the two ends of such linear moiety -P-.
6. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 5, wherein the compound is of formula (I-a) or (I-a')
- 15
$$AB-D-L^1-L^2-P-L^2-L^1-D-AB \quad (I-a)$$
- $$\left[AB-D \right]_a L^{1'}-L^2-P-L^2-L^{1'} \left[D-AB \right]_a \quad (I-a'),$$
- wherein
- each -L²- is independently a spacer moiety or is absent;
 20 each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;
 each -L^{1'}- is independently a linker moiety that is covalently and reversibly conjugated to -D-;
 each -D- is independently a drug moiety;
 25 each -AB is independently an albumin-binding moiety;
 -P- is a polymeric moiety; and
 each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.
7. The compound or a pharmaceutically acceptable salt thereof of item 6, wherein the compound is formula (I-a).
- 30 8. The compound or a pharmaceutically acceptable salt thereof of item 6, wherein the compound is of formula (I-a').

9. The compound or a pharmaceutically acceptable salt thereof of item 6 or 8, wherein both a are 2.
10. The compound or a pharmaceutically acceptable salt thereof of item 6 or 8, wherein both a are 3.
- 5 11. The compound or a pharmaceutically acceptable salt thereof of item 6 or 8, wherein both a are 4.
12. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 11, wherein -P- comprises one or more polymer selected from the group consisting of poly(2-methacryloyl-oxyethyl phosphoyl cholines), poly(acrylic acids),
 10 poly(acrylates), poly(acrylamides), poly(alkoxy) polymers, poly(amides), poly(amidoamines), poly(amino acids), poly(anhydrides), poly(aspartamides), poly(hydroxybutyrate), poly(glycolic acids), poly(butylene terephthalates), poly(caprolactones), poly(carbonates), poly(cyanoacrylates), poly(dimethylacrylamides), poly(esters), poly(ethylenes), poly(ethyleneglycols),
 15 poly(ethylene oxides), poly(ethylene phosphates), poly(ethyloxazolines), poly(glycolic acids), poly(hydroxyethyl acrylates), poly(hydroxyethyl-oxazolines), poly(2-hydroxyethyl methacrylates), poly(N-(2-hydroxypropyl)methacrylamides), poly(hydroxypropyl methacrylates), poly(hydroxypropyloxazolines), poly(iminocarbonates), poly(lactic acids), poly(lactic-co-glycolic acids),
 20 poly(methacrylamides), poly(methacrylates), poly(methyloxazolines), poly(organophosphazenes), poly(ortho esters), poly(oxazolines), poly(propylene glycols), poly(siloxanes), poly(urethanes), poly(vinyl alcohols), poly(vinyl amines), poly(vinylmethylethers), poly(vinylpyrrolidones), celluloses, carboxymethyl celluloses, hydroxypropyl methylcelluloses, chitins, chitosans, dextrans, dextrans,
 25 gelatins, hyaluronic acids and derivatives, functionalized hyaluronic acids, mannans, pectins, rhamnogalacturonans, starches, hydroxyalkyl starches, hydroxyethyl starches and other carbohydrate-based polymers, xylans, and copolymers thereof.
13. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 12, wherein -P- is a PEG-based or hyaluronic acid-based moiety.
- 30 14. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 13, wherein -P- is a PEG-based polymer.
15. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 14, wherein -P- is of formula (I-ai)



wherein

dashed lines indicate attachment to $-\text{L}^2$;

n is an integer such that the molecular weight of the PEG moiety ranges from about 1 about 20 kDa;

$-\text{X}^1$ - and $-\text{X}^2$ - are independently of each other selected from the group consisting of $-\text{T}-$, $-\text{C}(\text{O})\text{O}-$, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{N}(\text{R}^{y1})-$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{y1})-$, $-\text{S}(\text{O})\text{N}(\text{R}^{y1})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{R}^{y1})\text{S}(\text{O})_2\text{N}(\text{R}^{y1a})-$, $-\text{S}-$, $-\text{N}(\text{R}^{y1})-$, $-\text{OC}(\text{OR}^{y1})(\text{R}^{y1a})-$, $-\text{N}(\text{R}^{y1})\text{C}(\text{O})\text{N}(\text{R}^{y1a})-$, $-\text{OC}(\text{O})\text{N}(\text{R}^{y1})-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-\text{T}-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-\text{R}^{y2}$, which are the same or different and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-\text{T}-$, $-\text{C}(\text{O})\text{O}-$, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{N}(\text{R}^{y3})-$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{y3})-$, $-\text{S}(\text{O})\text{N}(\text{R}^{y3})-$, $-\text{S}(\text{O})_2-$, $-\text{S}(\text{O})-$, $-\text{N}(\text{R}^{y3})\text{S}(\text{O})_2\text{N}(\text{R}^{y3a})-$, $-\text{S}-$, $-\text{N}(\text{R}^{y3})-$, $-\text{OC}(\text{OR}^{y3})(\text{R}^{y3a})-$, $-\text{N}(\text{R}^{y3})\text{C}(\text{O})\text{N}(\text{R}^{y3a})-$, and $-\text{OC}(\text{O})\text{N}(\text{R}^{y3})-$;

$-\text{R}^{y1}$ and $-\text{R}^{y1a}$ are independently of each other selected from the group consisting of $-\text{H}$, $-\text{T}$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-\text{T}$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-\text{R}^{y2}$, which are the same or different, and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-\text{T}-$, $-\text{C}(\text{O})\text{O}-$, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{N}(\text{R}^{y4})-$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{y4})-$, $-\text{S}(\text{O})\text{N}(\text{R}^{y4})-$, $-\text{S}(\text{O})_2-$, $-\text{S}(\text{O})-$, $-\text{N}(\text{R}^{y4})\text{S}(\text{O})_2\text{N}(\text{R}^{y4a})-$, $-\text{S}-$, $-\text{N}(\text{R}^{y4})-$, $-\text{OC}(\text{OR}^{y4})(\text{R}^{y4a})-$, $-\text{N}(\text{R}^{y4})\text{C}(\text{O})\text{N}(\text{R}^{y4a})-$, and $-\text{OC}(\text{O})\text{N}(\text{R}^{y4})-$;

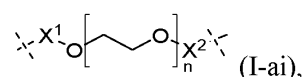
each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more $-\text{R}^{y2}$, which are the same or different;

each $-\text{R}^{y2}$ is independently selected from the group consisting of halogen, $-\text{CN}$, oxo ($=\text{O}$), $-\text{COOR}^{y5}$, $-\text{OR}^{y5}$, $-\text{C}(\text{O})\text{R}^{y5}$, $-\text{C}(\text{O})\text{N}(\text{R}^{y5}\text{R}^{y5a})$, $-\text{S}(\text{O})_2\text{N}(\text{R}^{y5}\text{R}^{y5a})$, $-\text{S}(\text{O})\text{N}(\text{R}^{y5}\text{R}^{y5a})$, $-\text{S}(\text{O})_2\text{R}^{y5}$, $-\text{S}(\text{O})\text{R}^{y5}$, $-\text{N}(\text{R}^{y5})\text{S}(\text{O})_2\text{N}(\text{R}^{y5a}\text{R}^{y5b})$, $-\text{SR}^{y5}$, $-\text{N}(\text{R}^{y5}\text{R}^{y5a})$, $-\text{NO}_2$, $-\text{OC}(\text{O})\text{R}^{y5}$, $-\text{N}(\text{R}^{y5})\text{C}(\text{O})\text{R}^{y5a}$, $-\text{N}(\text{R}^{y5})\text{S}(\text{O})_2\text{R}^{y5a}$, $-\text{N}(\text{R}^{y5})\text{S}(\text{O})\text{R}^{y5a}$, $-\text{N}(\text{R}^{y5})\text{C}(\text{O})\text{OR}^{y5a}$, $-\text{N}(\text{R}^{y5})\text{C}(\text{O})\text{N}(\text{R}^{y5a}\text{R}^{y5b})$, $-\text{OC}(\text{O})\text{N}(\text{R}^{y5}\text{R}^{y5a})$,

and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and

each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently selected from the group consisting of -H, and C₁₋₆ alkyl, wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.

16. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 1 kDa;
17. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 2 kDa.
18. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 3 kDa.
19. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 4 kDa.
20. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 5 kDa.
21. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 6 kDa.
22. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 7 kDa.
23. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 8 kDa.
24. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 9 kDa.
25. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 10 kDa.
26. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 15 kDa.
27. The compound or a pharmaceutically acceptable salt thereof of item 15, wherein n is an integer such that the molecular weight of the PEG moiety is about 20 kDa.
28. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 14, wherein -P- is of formula (I-ai)



wherein

dashed lines indicate attachment to $-L^2-$;

n is an integer selected from the group consisting of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 and 22;

$-X^1-$ and $-X^2-$ are independently of each other selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{y1})-$, $-S(O)_2N(R^{y1})-$, $-S(O)N(R^{y1})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{y1})S(O)_2N(R^{y1a})-$, $-S-$, $-N(R^{y1})-$, $-OC(OR^{y1})(R^{y1a})-$, $-N(R^{y1})C(O)N(R^{y1a})-$, $-OC(O)N(R^{y1})-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T-$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{y3})-$, $-S(O)_2N(R^{y3})-$, $-S(O)N(R^{y3})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{y3})S(O)_2N(R^{y3a})-$, $-S-$, $-N(R^{y3})-$, $-OC(OR^{y3})(R^{y3a})-$, $-N(R^{y3})C(O)N(R^{y3a})-$, and $-OC(O)N(R^{y3})-$;

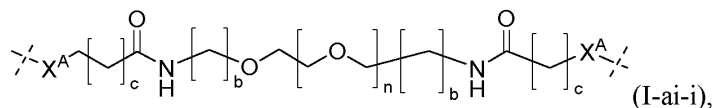
$-R^{y1}$ and $-R^{y1a}$ are independently of each other selected from the group consisting of $-H-$, $-T$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{y2}$, which are the same or different, and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{y4})-$, $-S(O)_2N(R^{y4})-$, $-S(O)N(R^{y4})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{y4})S(O)_2N(R^{y4a})-$, $-S-$, $-N(R^{y4})-$, $-OC(OR^{y4})(R^{y4a})-$, $-N(R^{y4})C(O)N(R^{y4a})-$, and $-OC(O)N(R^{y4})-$;

each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more $-R^{y2}$, which are the same or different;

each $-R^{y2}$ is independently selected from the group consisting of halogen, $-CN$, oxo ($=O$), $-COOR^{y5}$, $-OR^{y5}$, $-C(O)R^{y5}$, $-C(O)N(R^{y5}R^{y5a})$, $-S(O)_2N(R^{y5}R^{y5a})$, $-S(O)N(R^{y5}R^{y5a})$, $-S(O)_2R^{y5}$, $-S(O)R^{y5}$, $-N(R^{y5})S(O)_2N(R^{y5a}R^{y5b})$, $-SR^{y5}$, $-N(R^{y5}R^{y5a})$, $-NO_2$, $-OC(O)R^{y5}$, $-N(R^{y5})C(O)R^{y5a}$, $-N(R^{y5})S(O)_2R^{y5a}$, $-N(R^{y5})S(O)R^{y5a}$, $-N(R^{y5})C(O)OR^{y5a}$, $-N(R^{y5})C(O)N(R^{y5a}R^{y5b})$, $-OC(O)N(R^{y5}R^{y5a})$, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different; and

each $-R^{y3}$, $-R^{y3a}$, $-R^{y4}$, $-R^{y4a}$, $-R^{y5}$, $-R^{y5a}$ and $-R^{y5b}$ is independently selected from the group consisting of $-H$, and C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

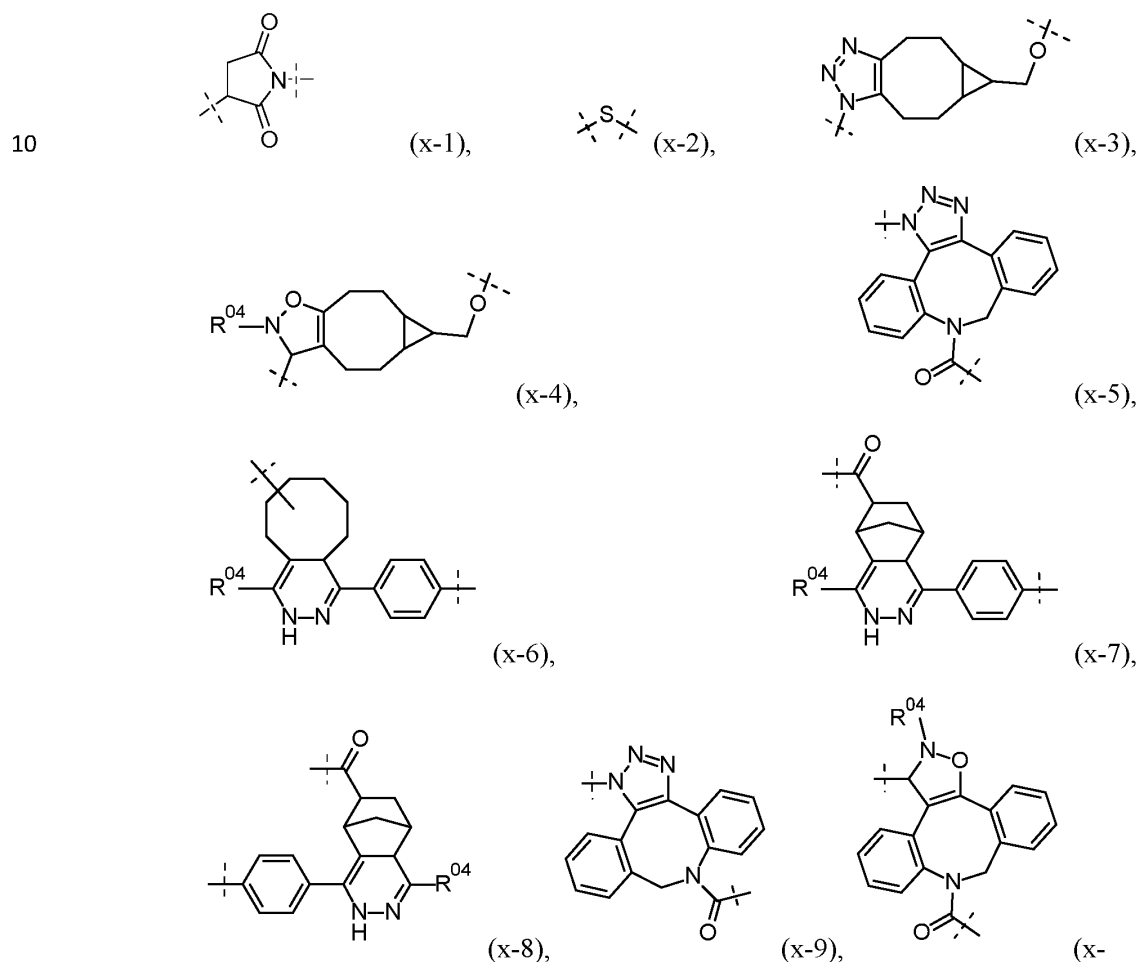
29. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 14, wherein $-P-$ is of formula (I-ai-i)

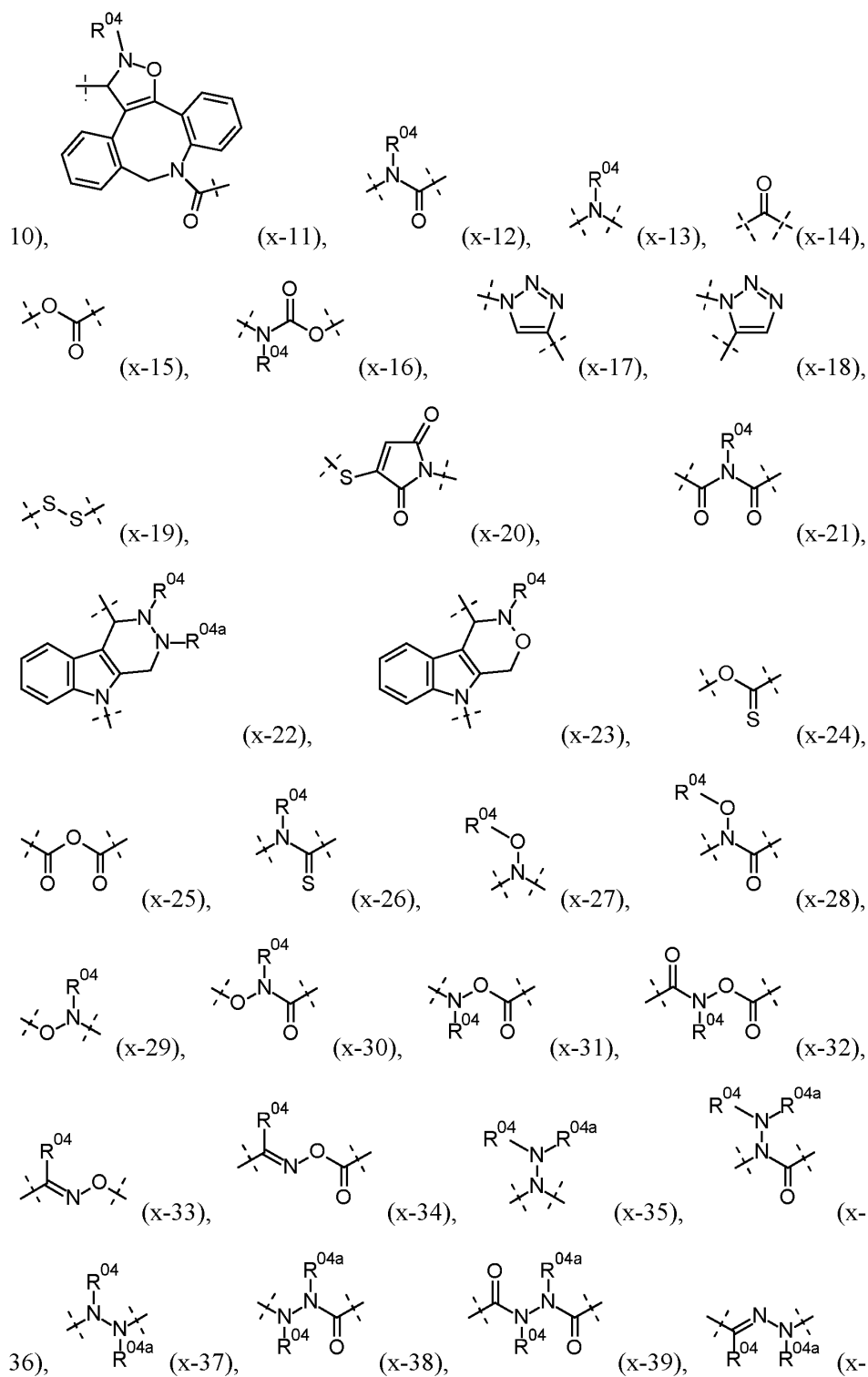


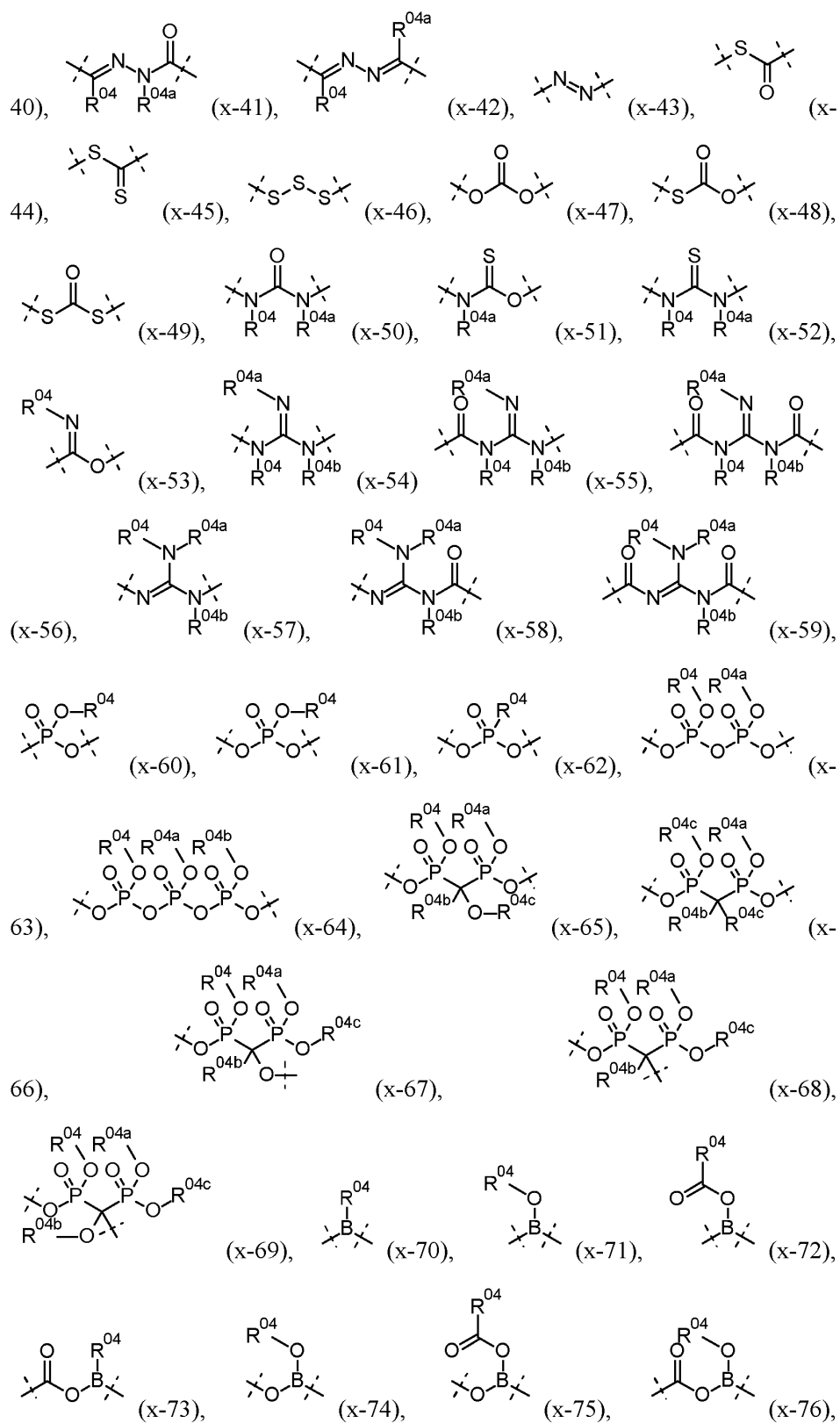
wherein

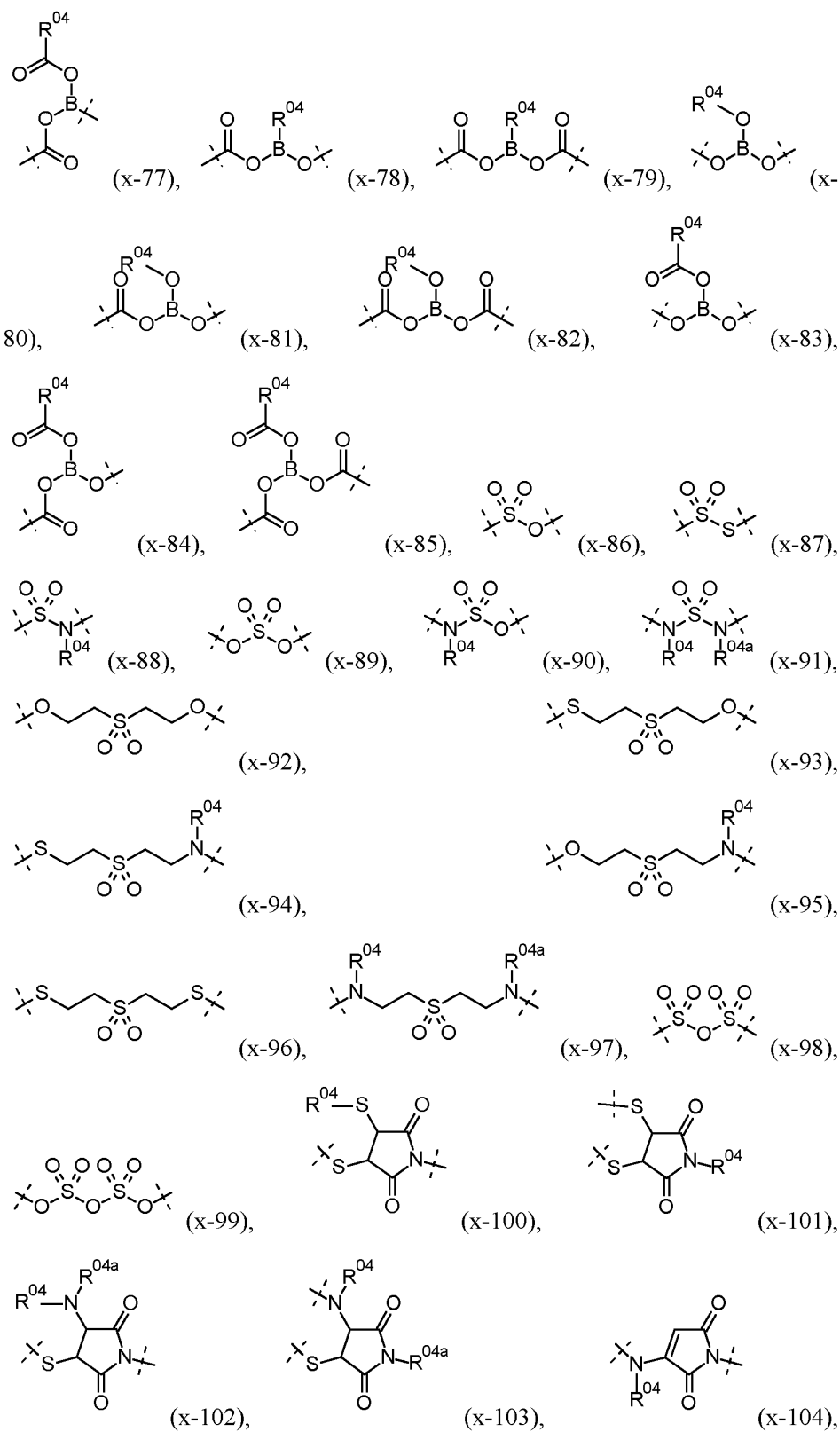
dashed lines indicate attachment to $-L^2-$;

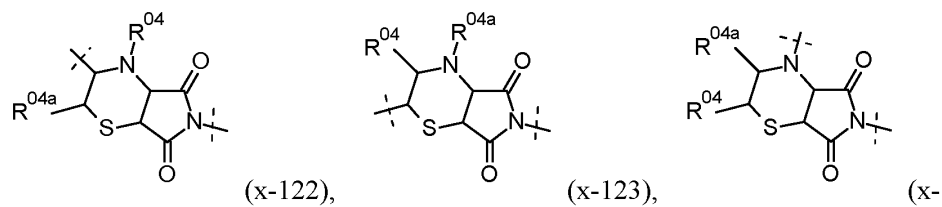
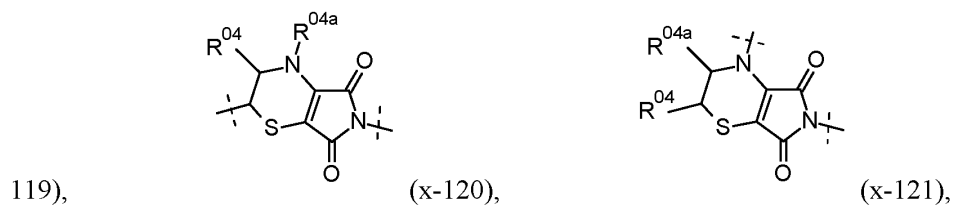
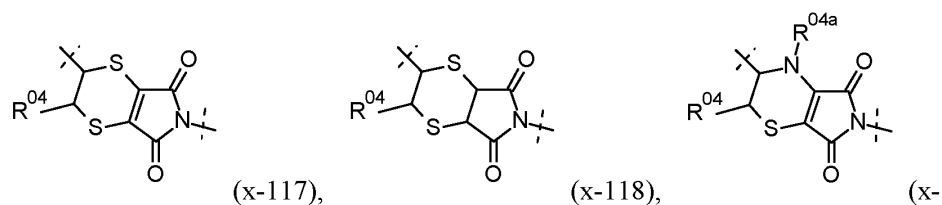
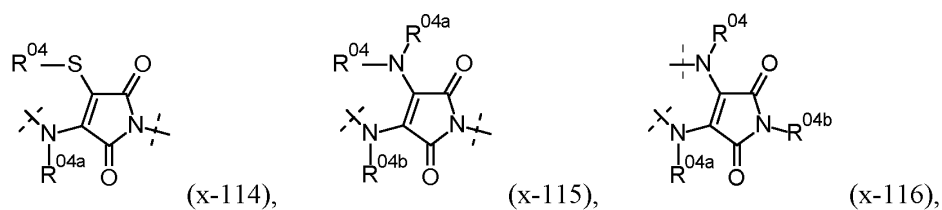
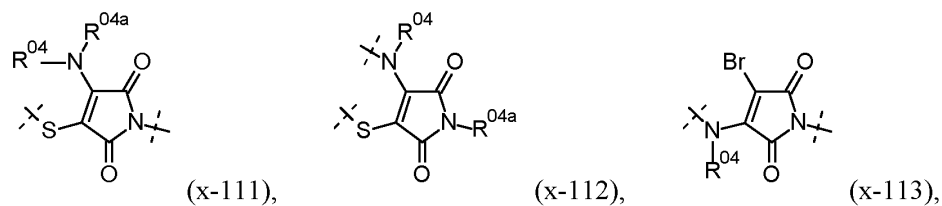
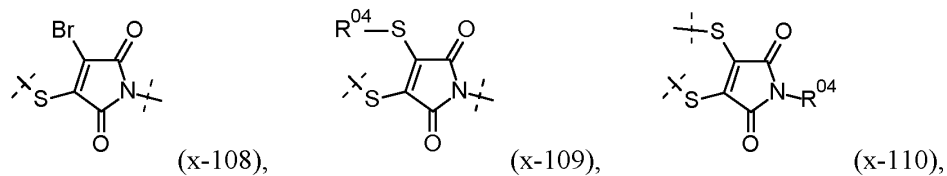
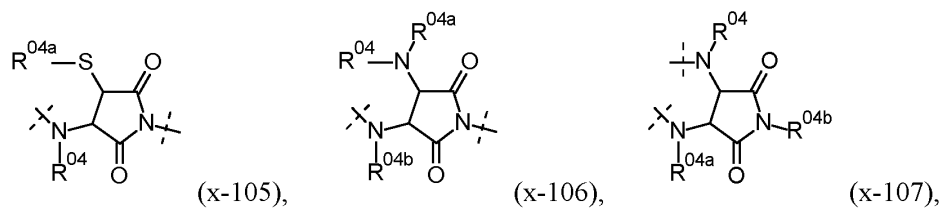
each $-X^A-$ is independently selected from the group consisting of

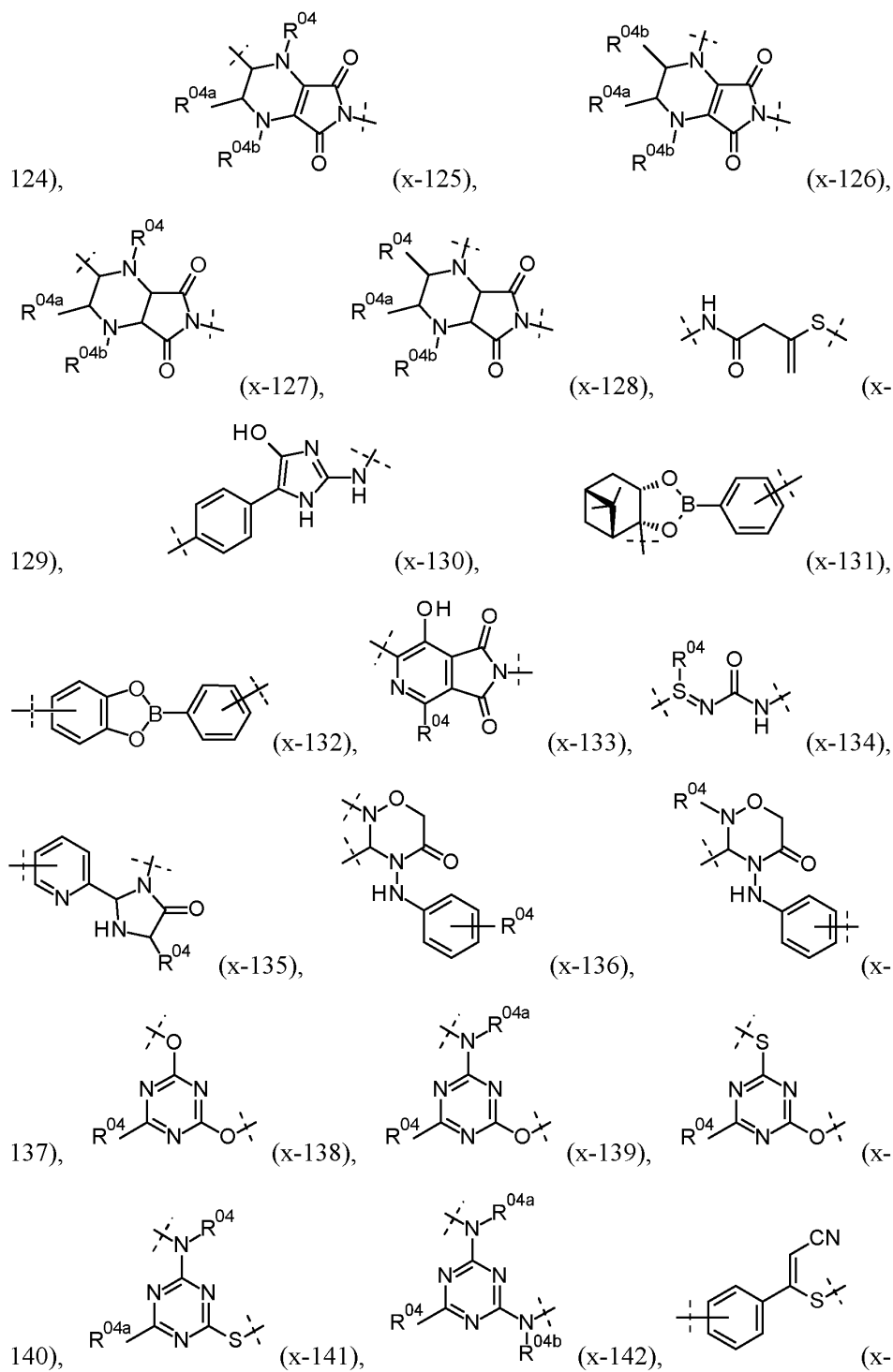


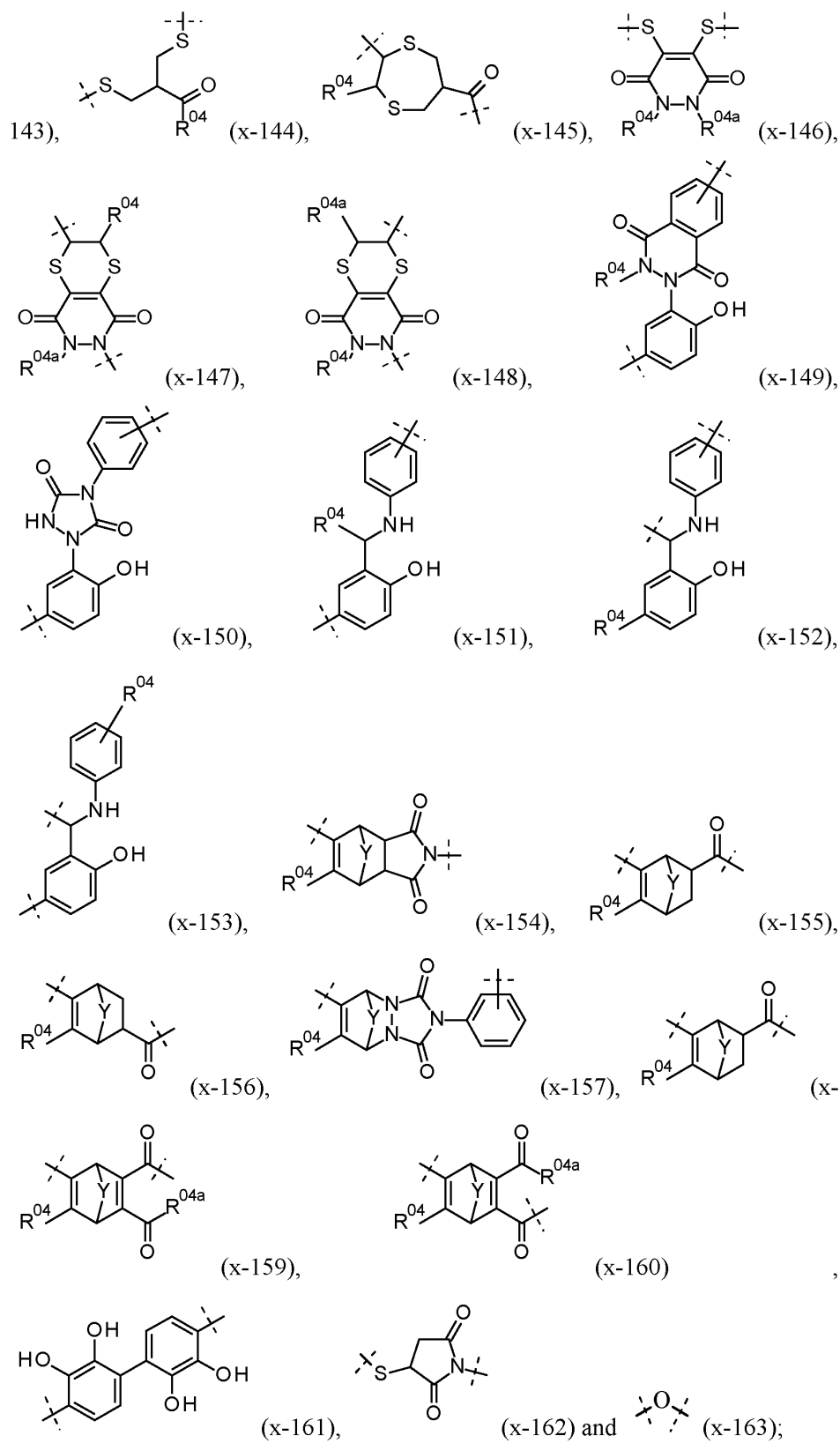












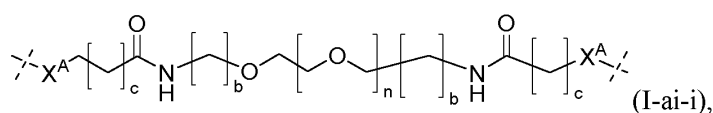
wherein

a dashed line indicates attachment to $-L^2-$ or the remainder of the moiety of formula (I-ai-i);

- each $-R^{04}$, $-R^{04a}$, $-R^{04b}$ and $-R^{04c}$ is independently selected from the group consisting of halogen, $-H$, $-CN$, $-T^0$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein $-T^0$, C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more $-R^{06}$, which are the same or different, and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T^0-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^{07})-$, $-S(O)_2N(R^{07})-$, $-S(O)N(R^{07})-$, $-S(O)_2-$, $-S(O)-$, $-N(R^{07})S(O)_2N(R^{07a})-$, $-S-$, $-N(R^{07})-$, $-OC(OR^{07})(R^{07a})-$, $-N(R^{07})C(O)N(R^{07a})-$, and $-OC(O)N(R^{07})-$; each T^0 is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, and 8- to 11-membered heterobicyclyl; wherein each T^0 is independently optionally substituted with one or more $-R^{06}$, which are the same or different; and each $-R^{06}$, $-R^{07}$ and $-R^{07a}$ is independently selected from the group consisting of $-H$ and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

- each b is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16;
- each c is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and
- n is an integer such that the molecular weight of the PEG moiety ranges from about 1 kDa to about 20 kDa.

30. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 14, wherein $-P-$ is of formula (I-ai-i)

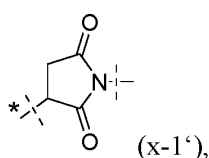


wherein

- 30 dashed lines indicate attachment to $-L^2-$;
- each $-X^A-$ is independently used as defined in item 30;
- each b and each c are independently used as defined in item 30;

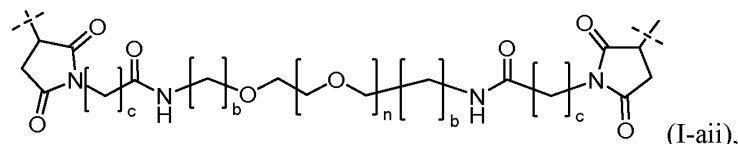
n is selected from the group consisting of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 and 22.

31. The compound or a pharmaceutically acceptable salt thereof of item 29 or 30, wherein both moieties $-X^A-$ are identical.
- 5 32. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 31, wherein $-X^A-$ is selected from the group consisting of formula (x-1), (x-2), (x-3), (x-5), (x-12), (x-13), (x-14), (x-15), (x-16), (x-17) and (x-18).
33. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 32, wherein both $-X^A-$ are of formula (x-1).
- 10 34. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 33, wherein both $-X^A-$ are of formula (x-1')



wherein the dashed line marked with the asterisk indicates attachment to $-L^2-$ and the unmarked dashed line indicates attachment to the remainder of $-P-$.

- 15 35. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 14, wherein $-P-$ is of formula (I-aii)



wherein

dashed lines indicate attachment to $-L^2-$;

- 20 each b is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16;

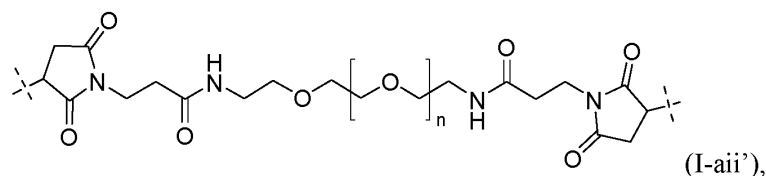
each c is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and

- 25 n is an integer such that the molecular weight of the PEG moiety ranges from about 1 about 20 kDa.

36. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 1 kDa;

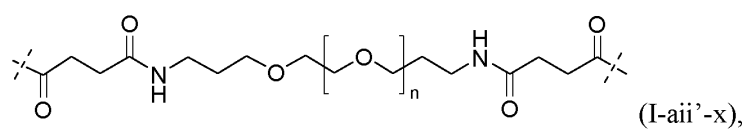
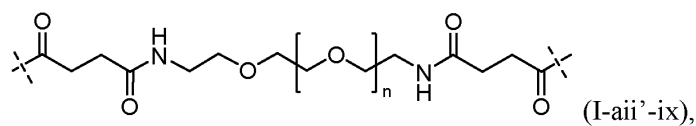
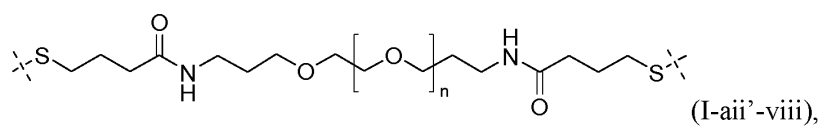
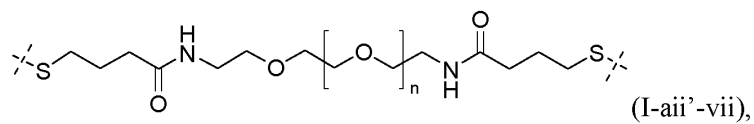
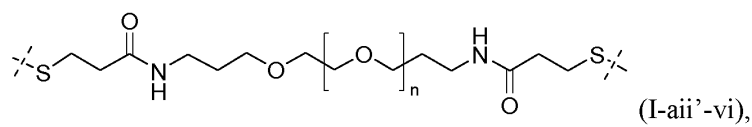
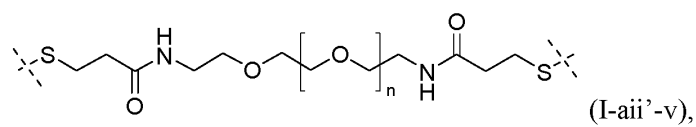
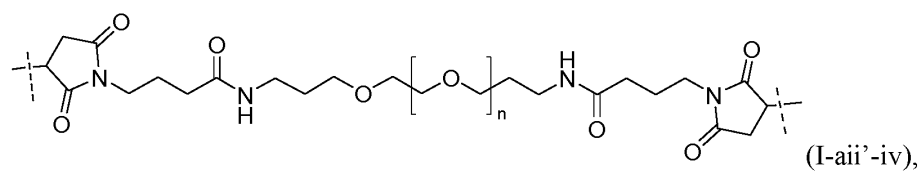
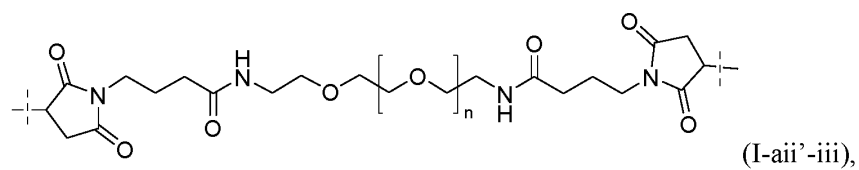
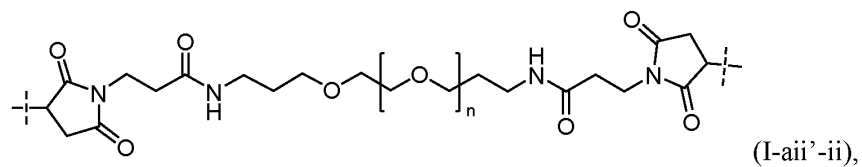
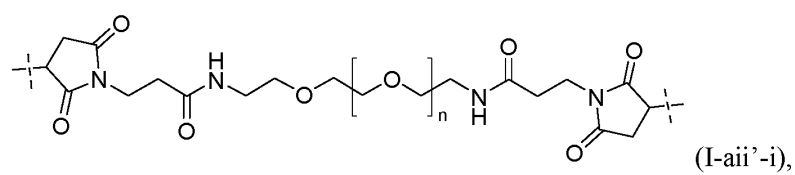
37. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 2 kDa.
- 5 38. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 3 kDa.
39. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 4 kDa.
- 10 40. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 5 kDa.
41. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 6 kDa.
- 15 42. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 7 kDa.
43. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 8 kDa.
- 20 44. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 9 kDa.
- 25 45. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 10 kDa.
46. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 15 kDa.
- 30 47. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 or 31 to 35, wherein n is an integer such that the molecular weight of the PEG moiety is about 20 kDa.

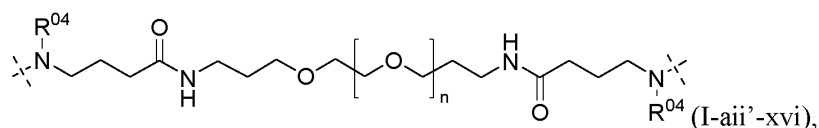
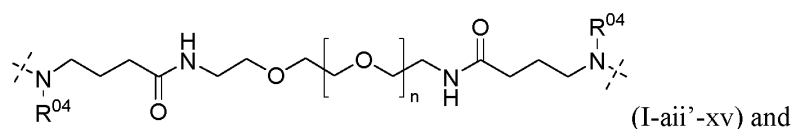
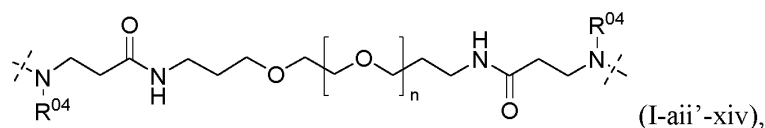
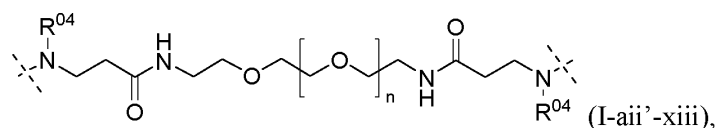
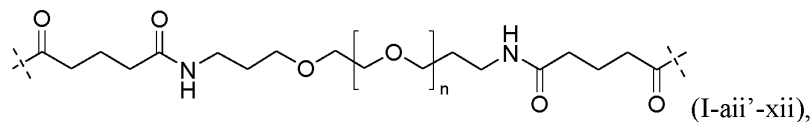
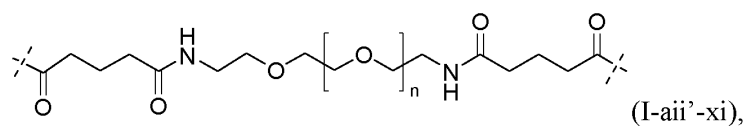
48. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 47, wherein b is 1.
49. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 47, wherein b is 2.
- 5 50. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 47, wherein b is 3.
51. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 47, wherein b is 4.
52. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 10 47, wherein b is 5.
53. The compound or a pharmaceutically acceptable salt thereof of any one of items 29 to 52, wherein c is 1.
54. The compound or a pharmaceutically acceptable salt thereof of any one of items 21 to 52, wherein c is 2.
- 15 55. The compound or a pharmaceutically acceptable salt thereof of any one of items 21 to 52, wherein c is 3.
56. The compound or a pharmaceutically acceptable salt thereof of any one of items 21 to 52, wherein c is 4.
57. The compound or a pharmaceutically acceptable salt thereof of any one of items 21 to 20 52, wherein c is 5.
58. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 14, wherein -P- is of formula (I-aii')



wherein

- 25 dashed lines indicate attachment to $-L^2-$; and
- n is an integer such that the molecular weight of the PEG moiety ranges from about 1 about 20 kDa.
59. The compound or a pharmaceutically acceptable salt thereof of any one of items 6 to 14, wherein -P- is selected from the group consisting of





wherein

dashed lines indicate attachment to $-L^2-$;

$-R^{04}$ is used as defined in item 29; and

10 n is an integer such that the molecular weight of the PEG moiety ranges from about 1 to about 20 kDa.

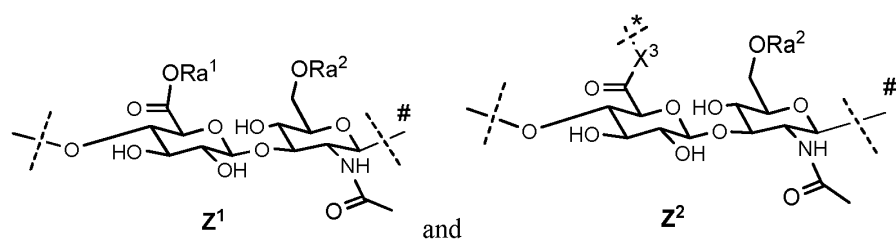
60. The compound or a pharmaceutically acceptable salt thereof of any one of item 58 or 59, wherein n is an integer such that the molecular weight of the PEG moiety ranges from 1 to 15 kDa.

15 61. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 60, wherein n is an integer such that the molecular weight of the PEG moiety ranges from 1 to 10 kDa.

62. The compound or a pharmaceutically acceptable salt thereof of item 58 or 59, wherein n is an integer ranging and including about 22 to about 450.

20 63. The compound or a pharmaceutically acceptable salt thereof of any one of items 58, 59 or 62, wherein n is about 22.

64. The compound or a pharmaceutically acceptable salt thereof of any one of items 58, 59 or 62, wherein n is about 23.
65. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61, wherein n is about 45.
- 5 66. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61, wherein n is about 57.
67. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61, wherein n is about 68.
68. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61 wherein n is about 90.
- 10 69. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61, wherein n is about 113.
70. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61, wherein n is about 170.
- 15 71. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61, wherein n is about 230.
72. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61, wherein n is about 340.
73. The compound or a pharmaceutically acceptable salt thereof of any one of items 58 to 61, wherein n is about 450.
- 20 74. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 4, wherein the compound of the present invention comprises a plurality of linearly connected units selected from the group consisting of



25

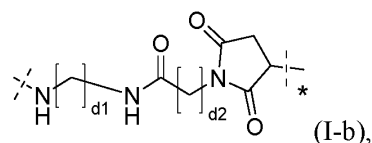
wherein

an unmarked dashed line indicates a point of attachment to an adjacent unit at a dashed line marked with # or to a hydrogen,

a dashed line marked with # indicates a point of attachment to an adjacent unit at an unmarked dashed line or to a hydroxyl;

a dashed line marked with the asterisk indicates attachment to $-L^2-$;
 the total number of units Z^2 in $-P-$ is at least 2;
 the total number of units Z^1 and Z^2 is at least 5;
 $-Ra^1$ and $-Ra^2$ are each independently selected from the group consisting of
 hydrogen; C_{1-4} alkyl; an alkali metal ion, an ammonium ion, an alkaline earth metal
 ion, or other suitable counterion;
 $-X^3-$ is used as defined for $-X^1-$ and $-X^2-$ of formula (I-ai) in item 11.

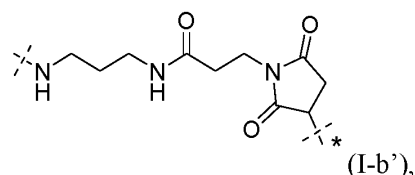
75. The compound or a pharmaceutically acceptable salt thereof of item 74, wherein $-X^3-$ is of formula (I-b)



wherein

the unmarked dashed line indicates attachment to the carbonyl of Z^2 ;
 the dashed line marked with the asterisk indicates attachment to $-L^2-$;
 $d1$ is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6,
 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16;
 $d2$ is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6,
 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

76. The compound or a pharmaceutically acceptable salt thereof of item 74 or 75, wherein $-X^3-$ is of formula (I-b')

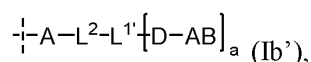
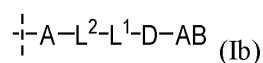


wherein

the unmarked dashed line indicates attachment to the carbonyl of Z^2 ; and
 the dashed line marked with the asterisk indicates attachment to $-L^2-$.

77. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 3,
 wherein the at least one polymeric moiety of the compound of the present invention is
 a multi-arm polymeric moiety.
78. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 4
 or 77, wherein the compound comprises at least one branching point B, to which at least

two moieties of formula (Ib) and/or at least one moiety of formula (Ib') are conjugated, wherein formula (Ib) and (Ib') are



5

wherein

the dashed line indicates attachment to a branching point B;

-A- is a polymeric moiety

each -L²- is independently a spacer moiety or is absent;

10

each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -D- is independently a drug moiety;

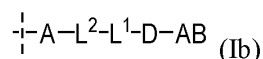
each -AB is independently an albumin-binding moiety; and

15

each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

79. The compound or a pharmaceutically acceptable salt thereof of any one of items 1, 2, 4, 77 or 78, wherein the compound comprises at least one branching point B, to which at least two moieties of formula (Ib) are conjugated, wherein formula (Ib) is

20



wherein

the dashed line indicates attachment to a branching point B;

-A- is a polymeric moiety

each -L²- is independently a spacer moiety or is absent;

25

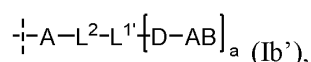
each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -D- is independently a drug moiety; and

each -AB is independently an albumin-binding moiety..

80. The compound or a pharmaceutically acceptable salt thereof of any one of items 1, 3, 4, 77 or 78, wherein the compound comprises at least one branching point B, to which at least one moiety of formula (Ib') is conjugated, wherein formula (Ib') is

30



z is an integer selected such that the molecular weight of -A- ranges from about 0.5 kDa to about 10 kDa;

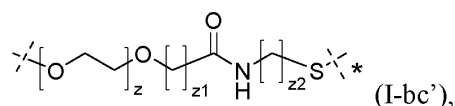
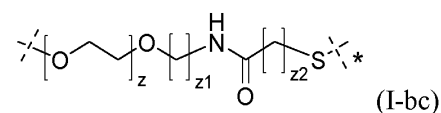
z1 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and

5 z2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

84. The compound or a pharmaceutically acceptable salt thereof of item 83, wherein -A- is of formula (I-bb).

85. The compound or a pharmaceutically acceptable salt thereof of item 83, wherein -A- is of formula (I-bb').

10 86. The compound or a pharmaceutically acceptable salt thereof of any one of items 78 to 82, wherein -A- is of formula (I-bc) or (I-bc')



15

wherein

the unmarked dashed line indicates attachment to the branching point B;

the dashed line marked with the asterisk indicates attachment to -L²-;

20 z is an integer selected such that the molecular weight of -A- ranges from about 0.5 kDa to about 10 kDa;

z1 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16; and

z2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

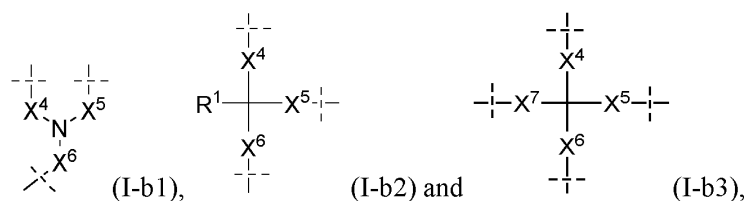
25 87. The compound or a pharmaceutically acceptable salt thereof of item 85, wherein -A- is of formula (I-bc).

88. The compound or a pharmaceutically acceptable salt thereof of item 85, wherein -A- is of formula (I-bc').

89. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 30 88, wherein z is an integer ranging from and including about 11 to about 230.

90. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 89, wherein z is an integer ranging from and including about 11 to about 225.
91. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 11.
- 5 92. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 12.
93. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 22.
94. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 10 90, wherein z is about 23.
95. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 34.
96. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 45.
- 15 97. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 57.
98. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 68.
99. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 20 90, wherein z is about 79.
100. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 90.
101. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 102.
- 25 102. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 113.
103. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 135.
104. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 30 90, wherein z is about 160.
105. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 180.
106. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 205.

107. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 230.
108. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 90, wherein z is about 270.
- 5 109. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 108, wherein z1 is 1.
110. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 108, wherein z1 is 2.
111. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 10 108, wherein z1 is 3.
112. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 108, wherein z1 is 4.
113. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 108, wherein z1 is 5.
- 15 114. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 108, wherein z1 is 6.
115. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 115, wherein z2 is 1.
116. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 20 115, wherein z2 is 2.
117. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 115, wherein z2 is 3.
118. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 115, wherein z2 is 4.
- 25 119. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 115, wherein z2 is 5.
120. The compound or a pharmaceutically acceptable salt thereof of any one of items 82 to 115, wherein z2 is 6.
121. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 4 30 or 77 to 121, wherein the compound comprises one branching point B selected from the group consisting of



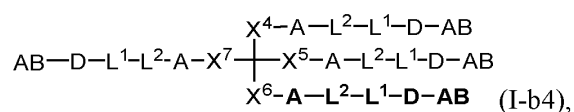
wherein

dashed lines indicate attachment to -A- of formula (Ib);

-R¹ is used as defined for the term “substituent”; and

5 -X⁴-, -X⁵-, -X⁶- and -X⁷- are independently used as defined for -X¹- and -X²- of formula (I-ai).

122. The compound or a pharmaceutically accepted salt thereof of item 121, wherein B is of formula (I-b1).
123. The compound or a pharmaceutically accepted salt thereof of item 121, wherein B is of formula (I-b2).
- 10 124. The compound or a pharmaceutically accepted salt thereof of item 121, wherein B is of formula (I-b3).
125. The compound or a pharmaceutically accepted salt thereof of item 122 or 123, wherein -X⁴-, -X⁵- and -X⁶- are identical.
- 15 126. The compound or a pharmaceutically accepted salt thereof of any one of items 122, 123 or 125, wherein -X⁴-, -X⁵- and -X⁶- are selected from the group consisting of -CH₂-, -CH₂CH₂- and -CH₂CH₂CH₂-.
127. The compound or a pharmaceutically accepted salt thereof of any one of items 122, 123, 125 or 126, wherein -X⁴-, -X⁵- and -X⁶- are -CH₂-.
- 20 128. The compound or a pharmaceutically accepted salt thereof of item 124, wherein -X⁴-, -X⁵-, -X⁶- and -X⁷- are identical.
129. The compound or a pharmaceutically accepted salt thereof of item 124 or 128, wherein -X⁴-, -X⁵-, -X⁶- and -X⁷- are selected from the group consisting of -CH₂-, -CH₂CH₂- and -CH₂CH₂CH₂-.
- 25 130. The compound or a pharmaceutically accepted salt thereof of any one of items 124, 128 or 129, wherein -X⁴-, -X⁵-, -X⁶- and -X⁷- are -CH₂-.
131. The compound or a pharmaceutically acceptable salt thereof of any one of items 1, 2, 4 to 7, 10 to 33 or 35 to 59, wherein the compound is of formula (I-b4)



wherein

$-X^4-$, $-X^5-$, $-X^6-$ and $-X^7-$ are independently used as defined for $-X^1-$ and $-X^2-$ of formula (I-ai) in item 15;

each $-A-$ is a polymeric moiety;

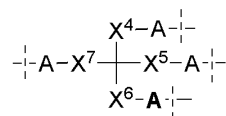
5 each $-L^2-$ is independently a spacer moiety or is absent;

each $-L^1-$ is independently a linker moiety that is covalently and reversibly conjugated to $-D-$;

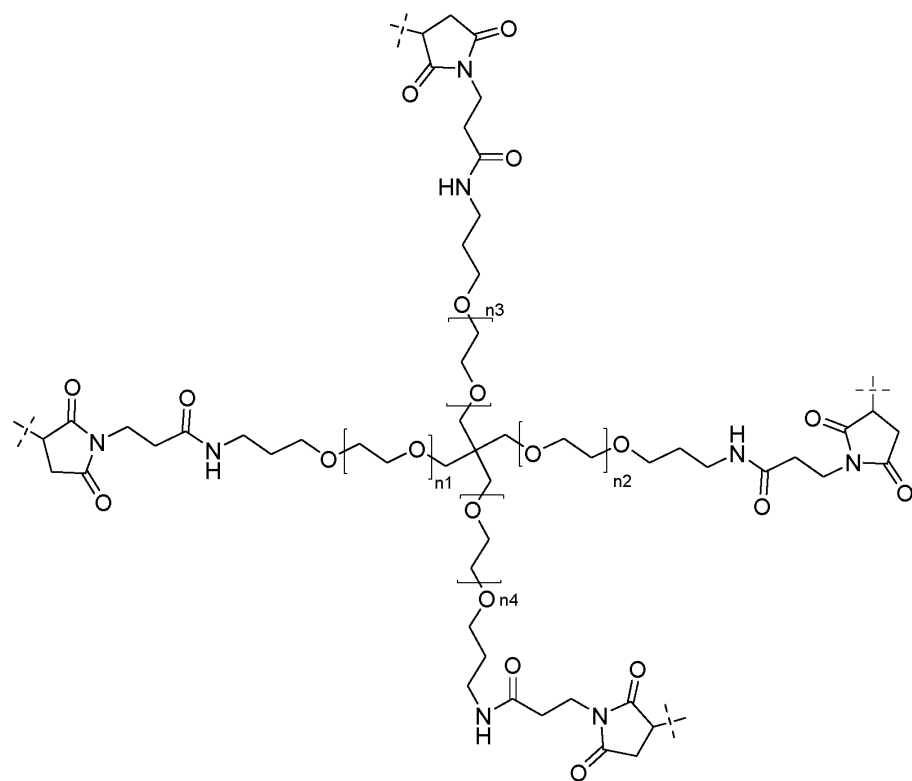
each $-D-$ is independently a drug moiety;

each $-AB$ is independently an albumin-binding moiety.

10 132. The compound or a pharmaceutically acceptable salt thereof of item 131, wherein the moiety



is of formula (I-b5)



(I-

15

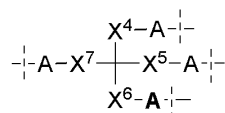
b5),

wherein

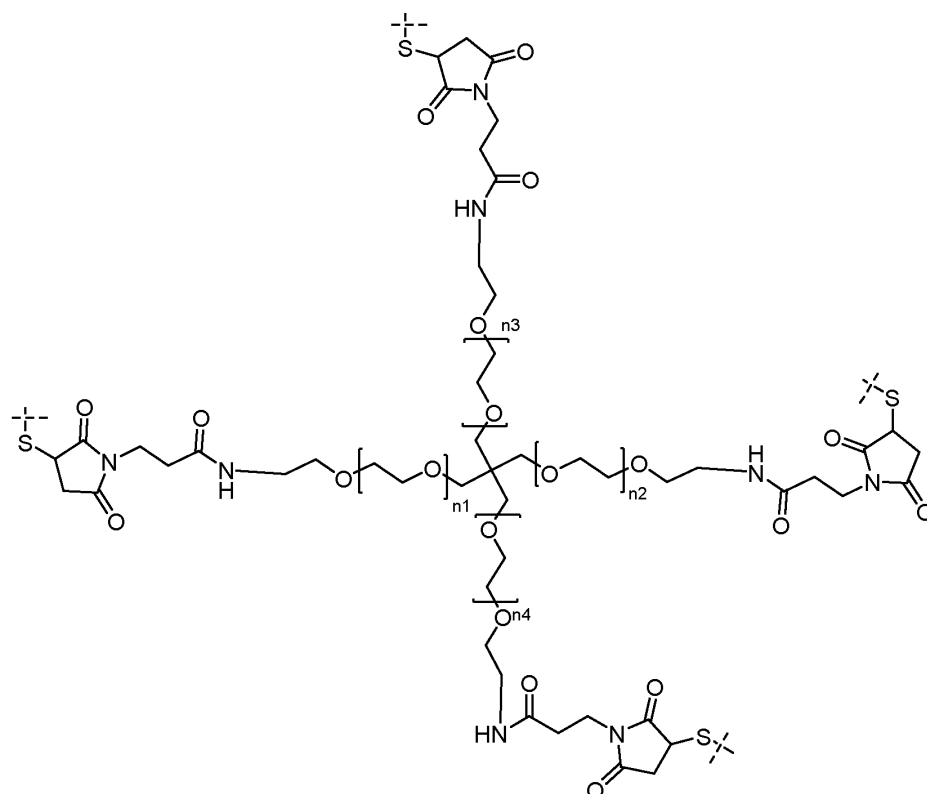
dashed lines indicate attachment to $-L^2-$; and

n_1 , n_2 , n_3 and n_4 are independently an integer ranging from and including about 10 to about 450.

133. The compound or a pharmaceutically acceptable salt thereof of item 131, wherein the moiety



is of formula (I-b6)



(I-b6),

wherein

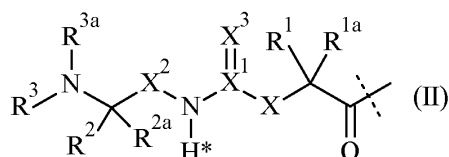
dashed lines indicate attachment to $-L^2-$; and

n_1 , n_2 , n_3 and n_4 are independently an integer ranging from and including about 10 to about 230.

134. The compound or a pharmaceutically acceptable salt thereof of item 132 or 133, wherein n_1 , n_2 , n_3 and n_4 are an integer ranging from and including about 11 to about 225.

135. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 11.
136. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 12.
- 5 137. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 22.
138. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 23.
139. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 10 134, wherein n_1 , n_2 , n_3 and n_4 are about 28.
140. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 29.
141. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 45.
- 15 142. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 56.
143. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 68.
144. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 20 134, wherein n_1 , n_2 , n_3 and n_4 are about 80.
145. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 90.
146. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 100.
- 25 147. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 115.
148. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 135.
149. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 30 134, wherein n_1 , n_2 , n_3 and n_4 are about 160.
150. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 180.
151. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n_1 , n_2 , n_3 and n_4 are about 200.

152. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n1, n2, n3 and n4 are about 225.
153. The compound or a pharmaceutically acceptable salt thereof of any one of items 132 to 134, wherein n1, n2, n3 and n4 are about 230.
- 5 154. The compound or a pharmaceutically acceptable salt thereof of any one of items 1, 2, 4 to 7, 12 to 79 or 81 to 153, wherein -L¹- is of formula (II):



- wherein the dashed line indicates attachment to a nitrogen, hydroxyl or thiol of -D-;
- X- is selected from the group consisting of -C(R⁴R^{4a})-; -N(R⁴)-; -O-; -C(R⁴R^{4a})-C(R⁵R^{5a})-; -C(R⁵R^{5a})-C(R⁴R^{4a})-; -C(R⁴R^{4a})-N(R⁶)-; -N(R⁶)-C(R⁴R^{4a})-; C(R⁴R^{4a})-O-; -O-C(R⁴R^{4a})-; and -C(R⁷R^{7a})-;
- X¹ is selected from the group consisting of C; and S(O);
- X²- is selected from the group consisting of -C(R⁸R^{8a})-; and -C(R⁸R^{8a})-C(R⁹R^{9a})-;
- =X³ is selected from the group consisting of =O; =S; and =N-CN;
- 15 -R¹, -R^{1a}, -R², -R^{2a}, -R⁴, -R^{4a}, -R⁵, -R^{5a}, -R⁶, -R⁸, -R^{8a}, -R⁹, and -R^{9a} are independently selected from the group consisting of -H; and C₁₋₆ alkyl;
- R³ and -R^{3a} are independently selected from the group consisting of -H; and C₁₋₆ alkyl, provided that in case one of -R³, -R^{3a} or both are other than -H they are connected to N to which they are attached through an SP³-hybridized carbon atom;
- 20 -R⁷ is selected from the group consisting of -N(R¹⁰R^{10a}); and -NR¹⁰-(C=O)-R¹¹;
- R^{7a}, -R¹⁰, -R^{10a}, and -R¹¹ are independently of each other selected from the group consisting of -H; and C₁₋₆ alkyl;
- optionally, one or more of the pairs -R^{1a}/R^{4a}, -R^{1a}/R^{5a}, -R^{1a}/R^{7a}, -R^{4a}/R^{5a}, and -R^{8a}/R^{9a} form a chemical bond;
- 25 optionally, one or more of the pairs -R¹/R^{1a}, -R²/R^{2a}, -R⁴/R^{4a}, -R⁵/R^{5a}, -R⁸/R^{8a}, and -R⁹/R^{9a} are joined together with the atom to which they are attached to form a C₃₋₁₀ cycloalkyl; or 3- to 10-membered heterocyclyl;
- optionally, one or more of the pairs -R¹/R⁴, -R¹/R⁵, -R¹/R⁶, -R¹/R^{7a}, -R⁴/R⁵, -R⁴/R⁶, -R⁸/R⁹, and -R²/R³ are joined together with the atoms to which they are attached to form a ring A;
- 30

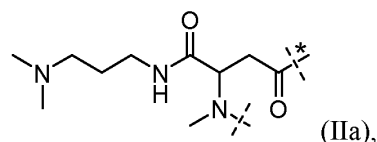
optionally, R^3/R^{3a} are joined together with the nitrogen atom to which they are attached to form a 3- to 10-membered heterocycle;

A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C_{3-10} cycloalkyl; 3- to 10-membered heterocyclyl; and 8- to 11-membered heterobicyclyl; and

wherein $-L^1-$ is substituted with at least one $-L^2-$ and wherein $-L^1-$ is optionally further substituted, provided that the hydrogen marked with the asterisk in formula (II) is not replaced by $-L^2-$ or a substituent.

155. The compound or a pharmaceutically acceptable salt thereof of item 154, wherein $-R^3$ and $-R^{3a}$ are both -H.
156. The compound or a pharmaceutically acceptable salt thereof of item 154, wherein $-R^3$ and $-R^{3a}$ are both methyl.
157. The compound or a pharmaceutically acceptable salt thereof of item 154, wherein $-R^3$ is methyl and $-R^{3a}$ is -H.
158. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 157, wherein $-X^2-$ is $-C(R^8R^{8a})-$.
159. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 157, wherein $-X^2-$ is $-C(R^8R^{8a})-C(R^9R^{9a})-$.
160. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 159, wherein $-R^8$ and $-R^{8a}$ are both -H.
161. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 160, wherein $-R^9$ and $-R^{9a}$ are both -H.
162. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 161, wherein $-R^2$ and $-R^{2a}$ are both -H.
163. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 162, wherein X^1 is C.
164. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 163, wherein $=X^3$ is =O.
165. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 164, wherein $-R^1$ and $-R^{1a}$ are both -H.
166. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 164, wherein $-R^1$ and $-R^{1a}$ are both methyl.
167. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 164, wherein $-R^1$ is -H and $-R^{1a}$ is methyl.

168. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 167, wherein -X- is -C(R⁴R^{4a})-.
169. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 167, wherein -X- is -C(R⁴R^{4a})-C(R⁵R^{5a})-.
- 5 170. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 167, wherein -X- is -C(R⁷R^{7a})-.
171. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 170, wherein -R⁷ is -N(R¹⁰R^{10a}).
172. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 10 170, wherein both -R¹⁰ and -R^{10a} are -H.
173. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 170, wherein both -R¹⁰ and -R^{10a} are methyl.
174. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 170, wherein -R¹⁰ is -H and -R^{10a} is methyl.
- 15 175. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 170, wherein -R⁷ is -NR¹⁰-(C=O)-R¹¹.
176. The compound or a pharmaceutically acceptable salt thereof of item 175, wherein -R¹¹ is -H.
177. The compound or a pharmaceutically acceptable salt thereof of any one of items 154 to 20 172, wherein -R¹¹ is methyl.
178. The compound or a pharmaceutically acceptable salt thereof of any one of items 175 to 177, wherein -R¹⁰ is -H.
179. The compound or a pharmaceutically acceptable salt thereof of any one of items 175 to 177, wherein -R¹⁰ is methyl.
- 25 180. The compound or a pharmaceutically acceptable salt thereof of item 154, wherein X is -C(R⁷R^{7a})-; X¹ is C; -X²- is -C(R⁸R^{8a})-C(R⁹R^{9a})-; =X³ is =O; -R¹ and -R^{1a} are -H; -R² and -R^{2a} are -H; -R³ and -R^{3a} are methyl; -R⁷ is -N(R¹⁰R^{10a}); -R^{7a} is -H; -R⁸, -R^{8a}, -R⁹ and -R^{9a} are -H; and -R¹⁰ is methyl and -R^{10a} is -H.
181. The compound or a pharmaceutically acceptable salt thereof of item 154 or 180, 30 wherein -L¹- is of formula (IIa)



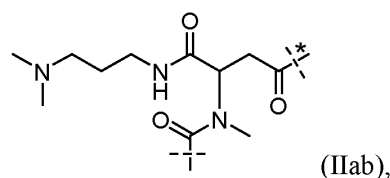
wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-;
and

the unmarked dashed line indicates attachment to -L²-.

- 5 182. The compound or a pharmaceutically acceptable salt thereof of item 154, wherein -L¹- is of formula (II), wherein X is -C(R⁷R^{7a})-; X¹ is C; -X²- is -C(R⁸R^{8a})-C(R⁹R^{9a})-; =X³ is =O; -R¹ and -R^{1a} are -H; -R² and -R^{2a} are -H; -R³ and -R^{3a} are methyl; -R⁷ is -NR¹⁰-(C=O)-R¹¹; -R^{7a} is -H; -R⁸, -R^{8a}, -R⁹ and -R^{9a} are -H; and -R¹⁰ is methyl and -R¹¹ is -H.

- 10 183. The compound or a pharmaceutically acceptable salt thereof of item 154 or 182, wherein -L¹- is of formula (IIab)

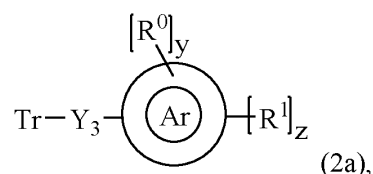


wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-;
and

the unmarked dashed line indicates attachment to -L²-.

- 15 184. The compound or a pharmaceutically acceptable salt thereof of any one of items 1, 3, 4 to 6, 8 to 78, 80 to 183, wherein -L¹- is of formula (2a)



20 wherein

-Tr is a cleavable triggering moiety;

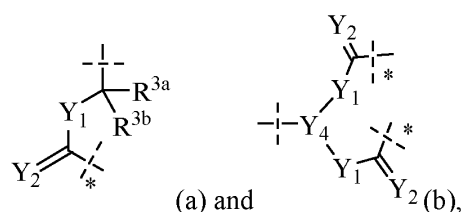
-Y₃- is independently selected from the group consisting of -O-, -S- and -N(R⁶)-;

z is selected from the group consisting of 2 and 3;

y is selected from the group consisting of 0, 1, 2, 3, 4 and 5;

- 25 -Ar- is a ring selected from the group consisting of monocyclic or bicyclic aryl and heteroaryl, provided that -Ar- is connected to -Y₃- and -R¹ via carbon atoms; wherein said monocyclic or bicyclic aryl and heteroaryl are optionally substituted with -R⁰, which are the same or different;

each $-R^0$ is independently selected from the group consisting of $-C(O)OH$, $-halogen$, $-NO_2$, $-CN$, C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl; wherein C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl are optionally substituted with one or more $-R^4$, which are the same or different; and wherein C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^5)-$, $-S(O)_2N(R^5)-$, $-S(O)N(R^5)-$, $-S(O)_2-$, $-S(O)-$, $-N(R^5)S(O)_2N(R^{5a})-$, $-S-$, $-N(R^5)-$, $-OC(OR^5)(R^{5a})-$, $-N(R^5)C(O)N(R^{5a})-$ and $-OC(O)N(R^5)-$; each $-R^1$ is independently selected from the group consisting of



wherein

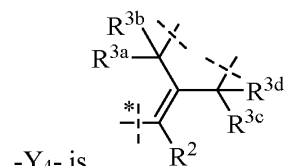
an unmarked dashed line indicates attachment to $-Ar-$;

a dashed lined marked with an asterisk indicates attachment to $-D-$;

the total number of moieties $-D-$ in the compound ranges from 2 to 6;

each $-Y_1-$ is independently selected from the group consisting of $-O-$ and $-S-$;

each $=Y_2$ is independently selected from the group consisting of $=O$ and $=S$;

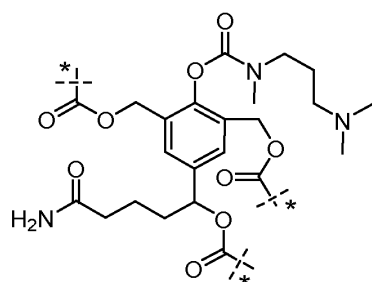


$-Y_4-$ is , wherein the dashed line marked with the asterisk indicates attachment to $-Ar-$ and the unmarked dashed lines indicate attachment to $-Y_1-$;

each $-R^2$ is independently selected from the group consisting of $-H$, $-C(O)OH$, $-halogen$, $-NO_2$, $-CN$, C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl; wherein C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl are optionally substituted with one or more $-R^4$, which are the same or different; and wherein C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^5)-$, $-S(O)_2N(R^5)-$, $-S(O)N(R^5)-$, $-S(O)_2-$, $-S(O)-$, $-N(R^5)S(O)_2N(R^{5a})-$, $-S-$, $-N(R^5)-$, $-OC(OR^5)(R^{5a})-$, $-N(R^5)C(O)N(R^{5a})-$ and $-OC(O)N(R^5)-$;

- each $-R^{3a}$, $-R^{3b}$, $-R^{3c}$, $-R^{3d}$ are independently selected from the group consisting of $-H$, $-C(O)OH$, $-F$, $-NO_2$, $-CN$, C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl; wherein C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl are optionally substituted with one or more $-R^4$, which are the same or different; and wherein
- 5 C_{1-30} alkyl, C_{2-30} alkenyl and C_{2-30} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T-$, $-C(O)O-$, $-O-$, $-C(O)-$, $-C(O)N(R^5)-$, $-S(O)_2N(R^5)-$, $-S(O)N(R^5)-$, $-S(O)_2-$, $-S(O)-$, $-N(R^5)S(O)_2N(R^{5a})-$, $-S-$, $-N(R^5)-$, $-OC(OR^5)(R^{5a})-$, $-N(R^5)C(O)N(R^{5a})-$ and $-OC(O)N(R^5)-$;
- each $-T-$ is independently selected from the group consisting of phenyl, naphthyl,
- 10 indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl and 8- to 11-membered heterobicyclyl, wherein each $-T-$ is independently optionally substituted with one or more $-R^4$, which are the same or different;
- $-R^4$ is selected from the group consisting of $-NO_2$, $-OCH_3$,
- 15 $-CN$, $-N(R^5)(R^{5a})$, $-OH$, $-C(O)OH$ and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;
- $-R^5$ and $-R^{5a}$ are independently selected from the group consisting of $-H$ and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;
- 20 each $-R^6$ is independently selected from the group consisting of $-H$ and C_{1-6} alkyl;
- and wherein $-L^{1'}$ is substituted with one moiety $-L^2-$.

185. The compound or a pharmaceutically acceptable salt thereof of item 184, wherein $-L^{1'}$ is of formula (2b)



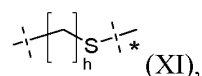
(2b),

wherein

the dashed lines marked with the asterisk indicate attachment to $-D-$; and

$-L^{1'}$ is substituted with $-L^2-$.

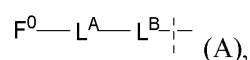
186. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 185, wherein $-L^2-$ is of formula (XI)



wherein

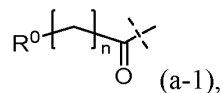
- 5 the unmarked dashed line indicates attachment to $-L^1-$;
the dashed line marked with the asterisk indicates attachment to the at least one polymeric moiety;
h is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

- 10 187. The compound or a pharmaceutically acceptable salt thereof of item 185, wherein h is 3.
188. The compound or a pharmaceutically acceptable salt thereof of item 185, wherein h is 4.
189. The compound or a pharmaceutically acceptable salt thereof of item 185, wherein h is
15 5.
190. The compound or a pharmaceutically acceptable salt thereof of item 185, wherein h is 6.
191. The compound or a pharmaceutically acceptable salt thereof of item 185, wherein h is 7.
20 192. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 191, wherein $-AB$ is of formula (A):



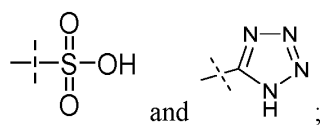
wherein

- the dashed line indicates attachment to $-D-$;
25 $-F^0$ is of formula (a-1)



wherein

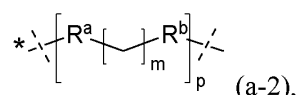
- the dashed line indicates attachment to $-L^A-$;
 $-R^0$ is selected from the group consisting of $-\text{CR}^1\text{R}^{1a}\text{R}^{1b}$, $-\text{COOR}^1$,



$-\text{R}^1$, $-\text{R}^{1a}$ and $-\text{R}^{1b}$ are selected from the group consisting of -H, methyl, ethyl, propyl, isopropyl;

n is an integer ranging from and including 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 and 22;

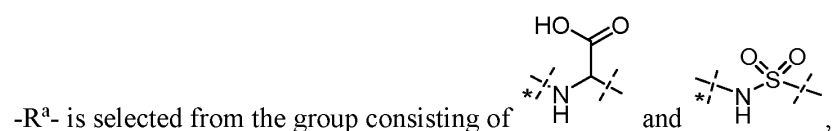
$-\text{L}^A$ - is absent or is of formula (a-2)



wherein

the unmarked dashed line indicates attachment to $-\text{L}^B$;

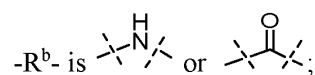
the dashed line marked with the asterisk indicates attachment to $-\text{F}^0$;



wherein

the dashed line marked with the asterisk indicates attachment to $-\text{F}^0$;

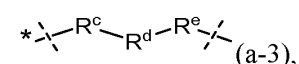
the unmarked dashed line indicates attachment to the remainder of $-\text{L}^A$;



m is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10

p is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;

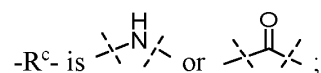
$-\text{L}^B$ - is absent or is of formula (a-3)



wherein

the unmarked dashed line indicates attachment to $-\text{D}$;

the dashed line marked with the asterisk indicates attachment to $-\text{L}^A$;



$-\text{R}^d$ - is selected from the group consisting of C_{1-50} alkyl, C_{2-50} alkenyl or C_{2-50} alkynyl,

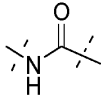
wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl may be substituted with one or more $-\text{R}^1$, which may be the same or different, and which C_{1-50} alkyl, C_{2-50} alkenyl

or C₂₋₅₀ alkynyl may be interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R²)-, -S(O)₂N(R²)-, -S(O)N(R²)-, -S(O)₂-, -S(O)-, -N(R²)S(O)₂N(R^{2a})-, -S-, -N(R²)-, -OC(OR²)(R^{2a})-, -N(R²)C(O)N(R^{2a})-, and -OC(O)N(R²)-;

each -T- is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each -T- may independently be substituted with one or more -R¹, which may be the same or different;

each -R¹ is independently selected from the group consisting of halogen, -CN, oxo (=O), -COOR³, -OR³, -C(O)R³, -C(O)N(R³R^{3a}), -S(O)₂N(R³R^{3a}), -S(O)N(R³R^{3a}), -S(O)₂R³, -S(O)R³, -N(R³)S(O)₂N(R^{3a}R^{3b}), -SR³, -N(R³R^{3a}), -NO₂, -OC(O)R³, -N(R³)C(O)R^{3a}, -N(R³)S(O)₂R^{3a}, -N(R³)S(O)R^{3a}, -N(R³)C(O)OR^{3a}, -N(R³)C(O)N(R^{3a}R^{3b}), -OC(O)N(R³R^{3a}), and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different;

each -R², -R^{2a}, -R³, -R^{3a} and -R^{3b} is independently selected from the group consisting of -H, and C₁₋₆ alkyl, wherein C₁₋₆ alkyl may be substituted with one or more halogen, which may be the same or different; and

-R^e- is selected from the group consisting of -CH₂-,  and .

193. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-4).

194. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-5).

195. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-6).

196. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-7).

197. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-8).

198. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-9).
199. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-10).
- 5 200. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-11).
201. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-12).
202. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-13).
- 10 203. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-14).
204. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-15).
- 15 205. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-16).
206. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-17).
207. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-18).
- 20 208. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-19).
209. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-20).
- 25 210. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-21).
211. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-22).
212. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-23).
- 30 213. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-24).
214. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-25).

215. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-26).
216. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-27).
- 5 217. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-28).
218. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-29).
219. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-30).
- 10 220. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-31).
221. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-32).
- 15 222. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-33).
223. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-34).
224. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-35).
- 20 225. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-36).
226. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-37).
- 25 227. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-38).
228. The compound or a pharmaceutically acceptable salt thereof of item 192, wherein -F⁰ is of formula (a-39).
229. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228, wherein -L^A- is absent.
- 30 230. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229, wherein -L^B- is absent.
231. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-40).

232. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-41).
233. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-42).
- 5 234. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-43).
235. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-44).
236. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 10 228 or 230, wherein -L^A- is of formula (a-45).
237. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-46).
238. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-47).
- 15 239. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-48).
240. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-49).
241. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 20 228 or 230, wherein -L^A- is of formula (a-50).
242. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-51).
243. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-52).
- 25 244. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-53).
245. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-54).
246. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 30 228 or 230, wherein -L^A- is of formula (a-55).
247. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-56).
248. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-57).

249. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-58).
250. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-59).
- 5 251. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-60).
252. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-61).
253. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 10 228 or 230, wherein -L^A- is of formula (a-62).
254. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-63).
255. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-64).
- 15 256. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-65).
257. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-66).
258. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 20 228 or 230, wherein -L^A- is of formula (a-67).
259. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-68).
260. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-69).
- 25 261. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-70).
262. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-71).
263. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 30 228 or 230, wherein -L^A- is of formula (a-72).
264. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-73).
265. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein -L^A- is of formula (a-74).

266. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein $-L^A-$ is of formula (a-75).
267. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein $-L^A-$ is of formula (a-76).
- 5 268. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein $-L^A-$ is of formula (a-77).
269. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein $-L^A-$ is of formula (a-78).
270. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 10 228 or 230, wherein $-L^A-$ is of formula (a-79).
271. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein $-L^A-$ is of formula (a-80).
272. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein $-L^A-$ is of formula (a-81).
- 15 273. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein $-L^A-$ is of formula (a-82).
274. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 228 or 230, wherein $-L^A-$ is of formula (a-82).
275. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 20 229 or 231 to 274, wherein $-L^B-$ is of formula (a-83).
276. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein $-L^B-$ is of formula (a-84).
277. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein $-L^B-$ is of formula (a-85).
- 25 278. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein $-L^B-$ is of formula (a-86).
279. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein $-L^B-$ is of formula (a-87).
280. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 30 229 or 231 to 274, wherein $-L^B-$ is of formula (a-88).
281. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein $-L^B-$ is of formula (a-89).
282. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein $-L^B-$ is of formula (a-90).

283. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein -L^B- is of formula (a-91).
284. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein -L^B- is of formula (a-92).
- 5 285. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein -L^B- is of formula (a-93).
286. The compound or a pharmaceutically acceptable salt thereof of any one of items 192 to 229 or 231 to 274, wherein -L^B- is of formula (a-94).
287. The compound or a pharmaceutically acceptable salt thereof of item 276, wherein q is
10 an integer ranging from and including 3 to 45.
288. The compound or a pharmaceutically acceptable salt thereof of item 276 or 287, wherein q is an integer ranging from and including 4 to 40.
289. The compound or a pharmaceutically acceptable salt thereof of any one of items 276, 287 or 288, wherein q is an integer ranging from and including 5 to 35.
- 15 290. The compound or a pharmaceutically acceptable salt thereof of any one of items 276 or 287 to 289, wherein q is an integer ranging from and including 6 to 30.
291. The compound or a pharmaceutically acceptable salt thereof of any one of items 276 or 287 to 290, wherein q is an integer ranging from and including 7 to 25.
292. The compound or a pharmaceutically acceptable salt thereof of any one of items 276 or
20 287 to 291, wherein q is an integer ranging from and including 10 to 20.
293. The compound or a pharmaceutically acceptable salt thereof of any one of items 276 or 287 to 292, wherein q is 23.
294. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 293, wherein -D- is a drug moiety selected from the group consisting of small molecule
25 drug moieties, medium size molecule drug moieties, oligonucleotide drug moieties, peptide nucleic acid drug moieties, peptide drug moieties and protein drug moieties.
295. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 294, wherein -D- is a small molecule drug moiety.
296. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to
30 294, wherein -D- is a medium size drug moiety.
297. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 294, wherein -D- is an oligonucleotide drug moiety.
298. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 294, wherein -D- is a peptide nucleic drug moiety.

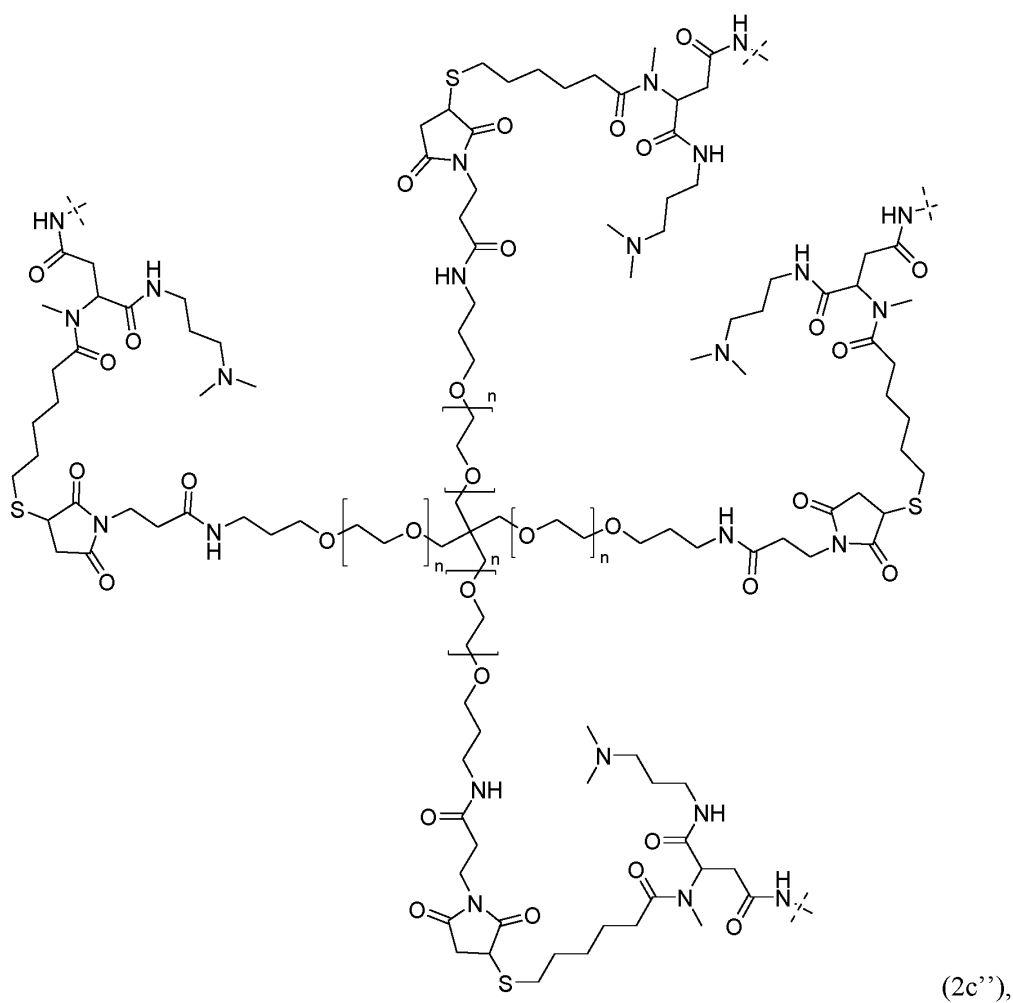
299. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 294, wherein -D- is a peptide drug moiety.
300. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 294, wherein -D- is a protein drug moiety.
- 5 301. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 294, wherein -D- or -D-AB is a GLP-1 receptor agonist moiety.
302. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:1.
303. The compound or a pharmaceutically acceptable salt thereof of any item 301,
10 wherein -D- is SEQ ID NO:2.
304. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:3.
305. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:4.
- 15 306. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:5.
307. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:6.
308. The compound or a pharmaceutically acceptable salt thereof of any item 301,
20 wherein -D- is SEQ ID NO:7.
309. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:8.
310. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:9.
- 25 311. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:10.
312. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:11.
313. The compound or a pharmaceutically acceptable salt thereof of any item 301,
30 wherein -D- is SEQ ID NO:12.
314. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:13.
315. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:14.

316. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:15.
317. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:16.
- 5 318. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:17.
319. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:18.
320. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:19.
- 10 321. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:20.
322. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:21.
- 15 323. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:22.
324. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:23.
325. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:24.
- 20 326. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:25.
327. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:26.
- 25 328. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:27.
329. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:28.
330. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:29.
- 30 331. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:30.
332. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:31.

333. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:32.
334. The compound or a pharmaceutically acceptable salt thereof of any item 301, wherein -D- is SEQ ID NO:33.
- 5 335. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 294 or 301, wherein -D- or -D-AB is a mono agonist of the GLP-1 receptor.
336. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 294 or 301, wherein -D- or -D-AB is a dual GLP-1 receptor.
337. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 10 294 or 301, wherein -D- or -D-AB is a triple GLP-1 receptor.
338. The compound or a pharmaceutically acceptable salt thereof of item 336, wherein the dual agonist is a GLP-1 receptor agonist and an agonist of a further receptor selected from the group consisting of the GIP receptor, the GCG receptor, an amylin receptor, a PYY receptor and the GLP-2 receptor.
- 15 339. The compound or a pharmaceutically acceptable salt thereof of item 338, wherein the further receptor is the GIP receptor.
340. The compound or a pharmaceutically acceptable salt thereof of item 338, wherein the further receptor is GCG receptor.
341. The compound or a pharmaceutically acceptable salt thereof of item 338, wherein the 20 further receptor is an amylin receptor.
342. The compound or a pharmaceutically acceptable salt thereof of item 338, wherein the further receptor is a PYY receptor.
343. The compound or a pharmaceutically acceptable salt thereof of item 338, wherein the further receptor is the GLP-2 receptor.
- 25 344. The compound or a pharmaceutically acceptable salt thereof of item 337, wherein the triple agonist is a GLP-1 receptor agonist and an agonist of two further receptors selected from the group consisting of the GIP receptor, the GCG receptor, an amylin receptor, a PYY receptor and the GLP-2 receptor.
345. The compound or a pharmaceutically acceptable salt thereof of item 337 or 344, 30 wherein the triple agonist is an agonist of the GLP-1 receptor, the GIP receptor and the GCG receptor.
346. The compound or a pharmaceutically acceptable salt thereof of item 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, the GIP receptor and an amylin receptor.

347. The compound or a pharmaceutically acceptable salt thereof of 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, the GIP receptor and a PYY receptor.
348. The compound or a pharmaceutically acceptable salt thereof of 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, the GIP receptor and the GLP-2 receptor.
- 5 349. The compound or a pharmaceutically acceptable salt thereof of 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, the GCG receptor and an amylin receptor.
350. The compound or a pharmaceutically acceptable salt thereof of 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, the GCG receptor and a PYY receptor.
- 10 351. The compound or a pharmaceutically acceptable salt thereof of 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, the GCG receptor and the GLP-2 receptor.
- 15 352. The compound or a pharmaceutically acceptable salt thereof of 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, an amylin receptor and a PYY receptor.
353. The compound or a pharmaceutically acceptable salt thereof of 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, an amylin receptor and the GLP-2 receptor.
- 20 354. The compound or a pharmaceutically acceptable salt thereof of 337 or 344, wherein the triple agonist is an agonist of the GLP-1 receptor, a PYY receptor and the GLP-2 receptor.
355. The compound or a pharmaceutically acceptable salt thereof of item 301, 303 or 335, wherein -D-AB is semaglutide.
- 25 356. The compound or a pharmaceutically acceptable salt thereof of item 301, 313 or 335, wherein -D-AB is liraglutide.
357. The compound or a pharmaceutically acceptable salt thereof of item 301, 315 or 335, wherein -D-AB is ecnoglutide.
- 30 358. The compound or a pharmaceutically acceptable salt thereof of item 301, 317 or 335, wherein -D-AB is GZR18.
359. The compound or a pharmaceutically acceptable salt thereof of item 301, 319 or 335, wherein -D-AB is GL0034.

360. The compound or a pharmaceutically acceptable salt thereof of item 301, 321 or 336, wherein -D-AB is tirzepatide.
361. The compound or a pharmaceutically acceptable salt thereof of item 301, 323 or 336, wherein -D-AB is cotadutide.
- 5 362. The compound or a pharmaceutically acceptable salt thereof of item 301, 325 or 336, wherein -D-AB is BI-456906.
363. The compound or a pharmaceutically acceptable salt thereof of item 301, 327 or 336, wherein -D-AB is pemvidutide.
364. The compound or a pharmaceutically acceptable salt thereof of item 301, 329 or 336,
10 wherein -D-AB is mazdutide.
365. The compound or a pharmaceutically acceptable salt thereof of item 301, 331 or 336, wherein -D-AB is dapiglutide.
366. The compound or a pharmaceutically acceptable salt thereof of item 301, 333 or 337, wherein -D-AB is retatrutide.
- 15 367. A compound or a pharmaceutically acceptable salt thereof of formula (2c'')

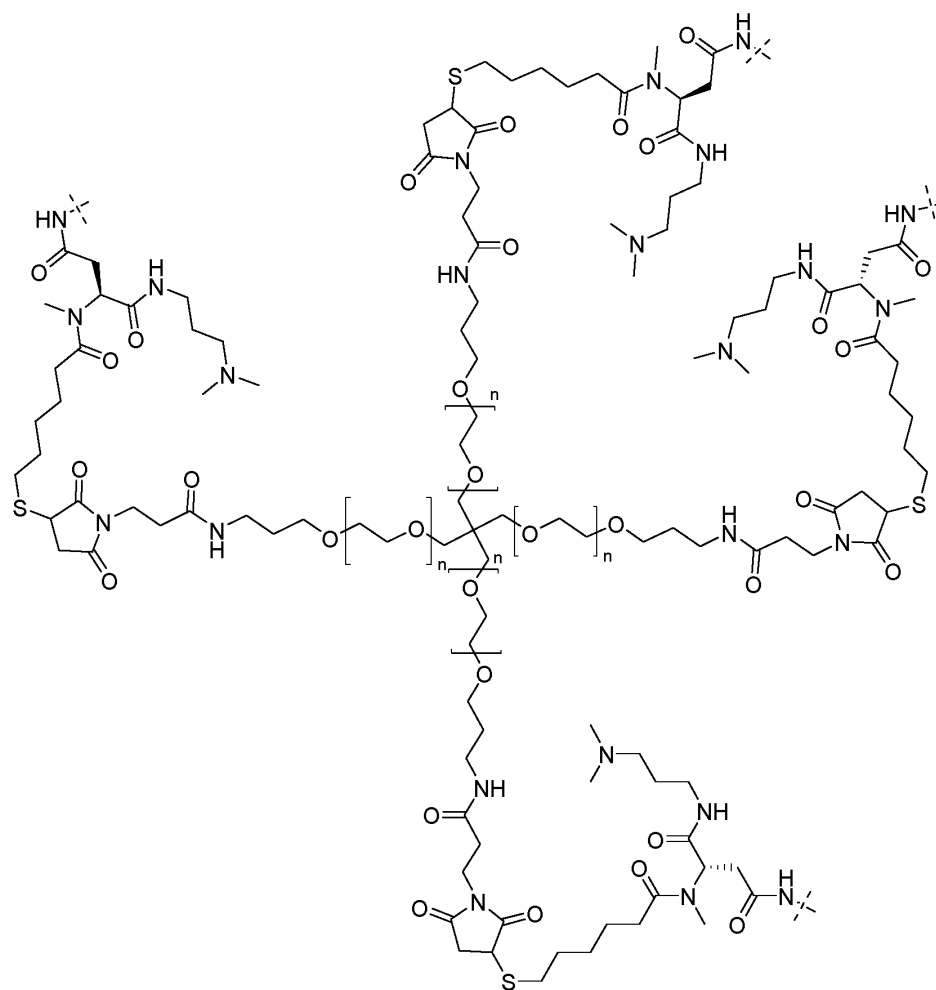


wherein

the dashed line indicates attachment to the N-terminal amine functional group of semaglutide; and

5 n1, n2, n3 and n4 are independently an integer ranging from about 11 to about 115.

368. A compound or a pharmaceutically acceptable salt thereof of formula (2c').



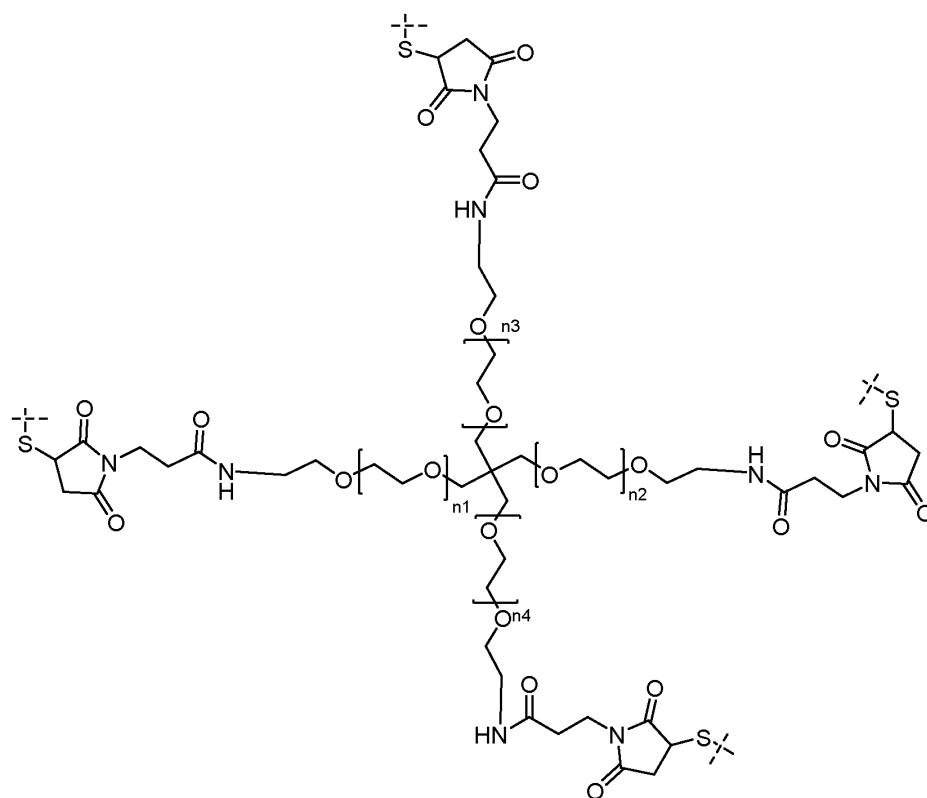
(2c'),

wherein

a dashed line indicates attachment to the N-terminal amine functional group of semaglutide; and

n1, n2, n3 and n4 independently range from about 11 to about 115.

369. A compound or a pharmaceutically acceptable salt thereof of formula (2d)

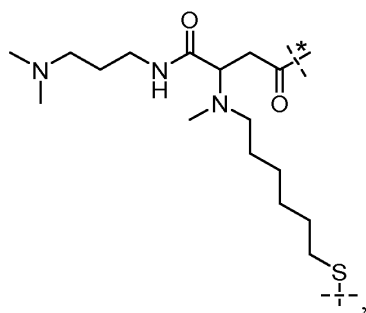


(2d),

wherein

n_1 , n_2 , n_3 and n_4 independently range from about 11 to about 115;

5 dashed lines indicate attachment to a moiety

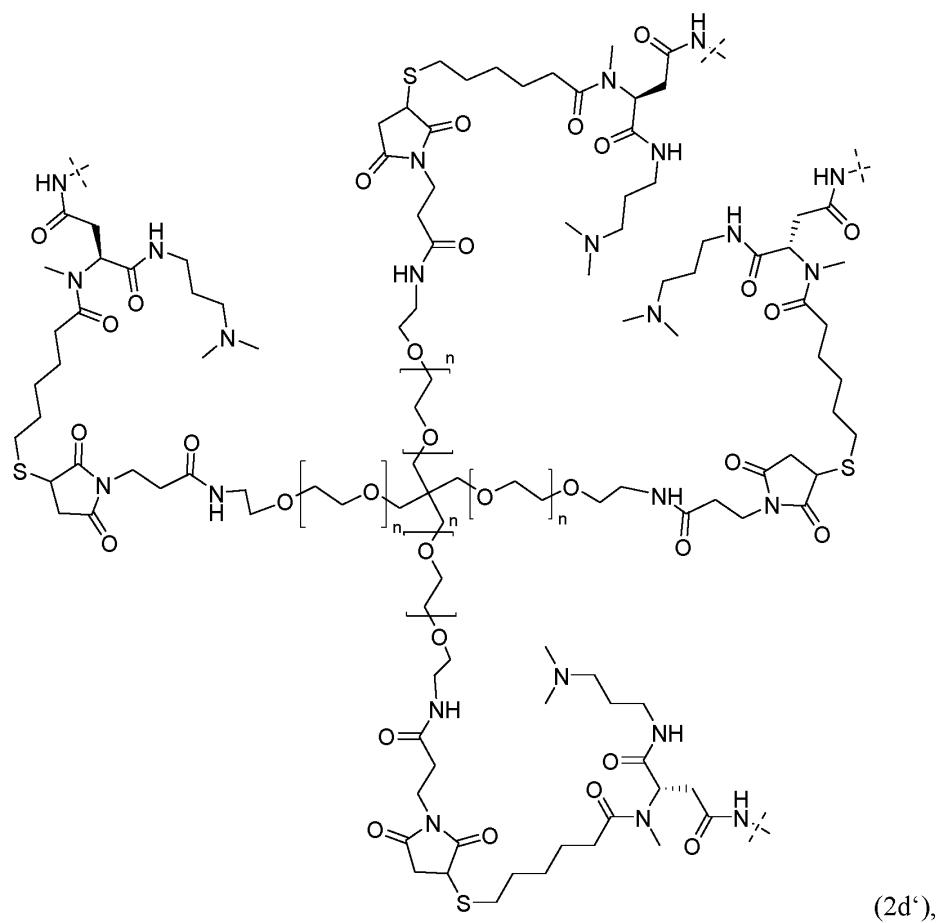


wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2d); and

10 the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

370. A compound or a pharmaceutically acceptable salt thereof of formula (2c')

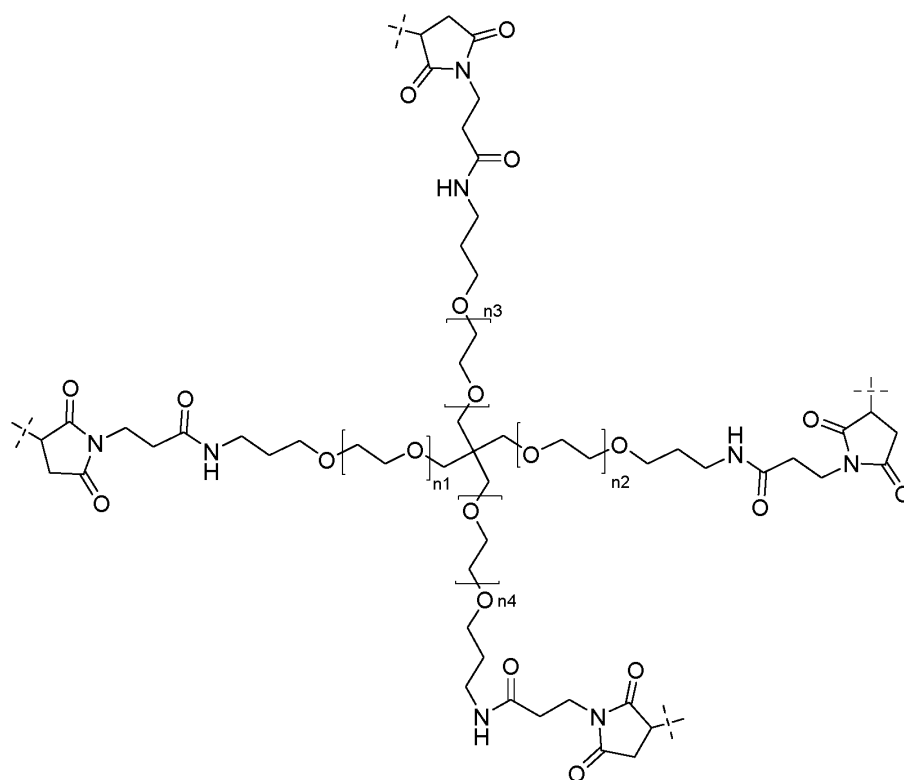


wherein

a dashed line indicates attachment to the N-terminal amine functional group of semaglutide; and

5 n1, n2, n3 and n4 independently range from about 11 to about 115.

371. A compound or a pharmaceutically acceptable salt thereof of formula (2e)

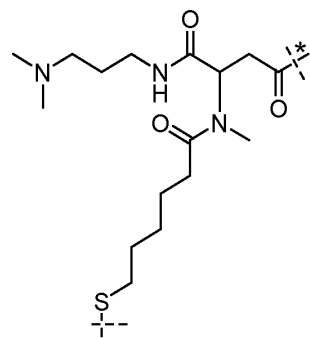


(2e),

wherein

n1, n2, n3 and n4 independently range from about 11 to about 115;

dashed lines indicate attachment to a moiety

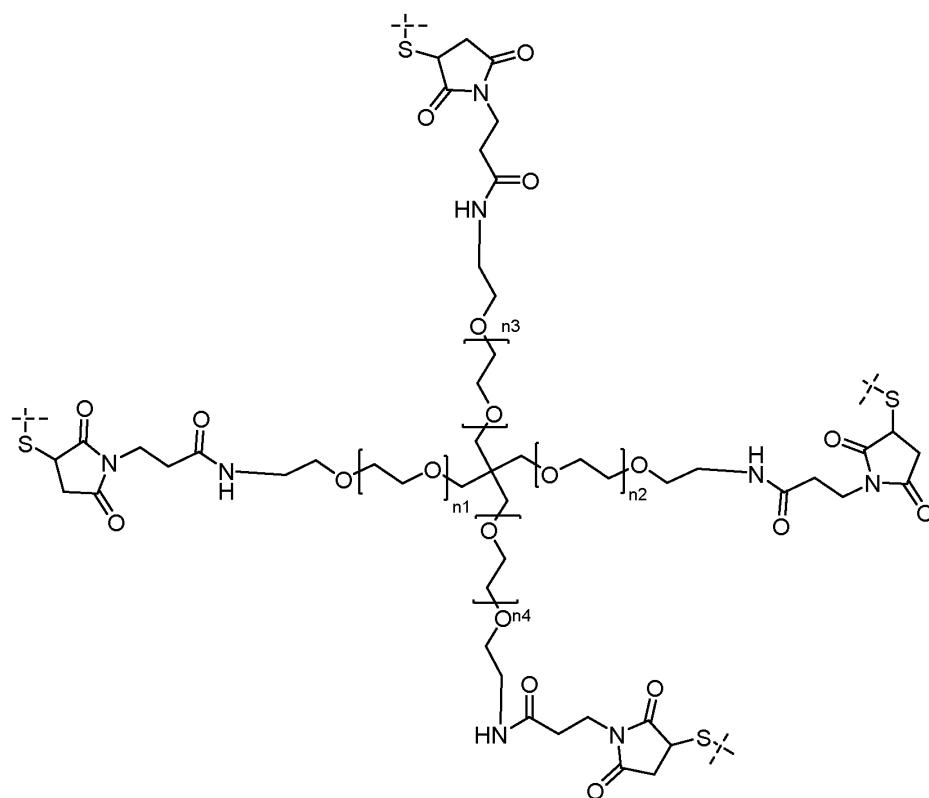


wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2e); and

the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

372. A compound or a pharmaceutically acceptable salt thereof of formula (2f)

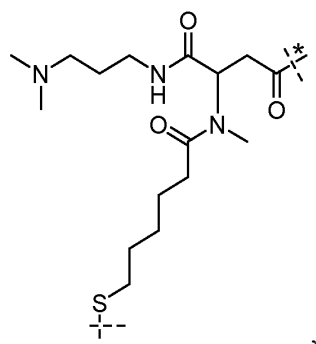


(2f),

wherein

n_1 , n_2 , n_3 and n_4 independently range from about 11 to about 115;

5 dashed lines indicate attachment to a moiety

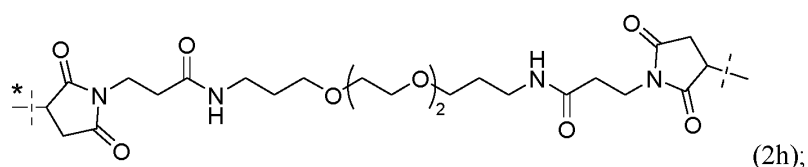


wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2f); and

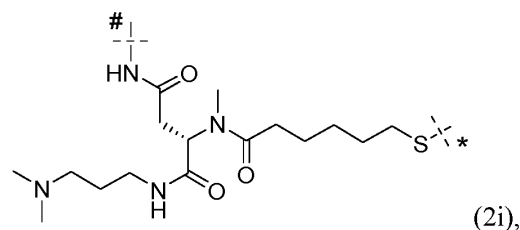
10 the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

373. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 372, wherein n1, n2, n3 and n4 are about 22.
374. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 372, wherein n1, n2, n3 and n4 are about 23.
- 5 375. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 372, wherein n1, n2, n3 and n4 are about 28.
376. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 372, wherein n1, n2, n3 and n4 are about 45.
377. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 10 372, wherein n1, n2, n3 and n4 are about 56.
378. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 372, wherein n1, n2, n3 and n4 are about 68.
379. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 372, wherein n1, n2, n3 and n4 are about 80.
- 15 380. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 372, wherein n1, n2, n3 and n4 are about 90.
381. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 372, wherein n1, n2, n3 and n4 are about 100.
382. The compound or a pharmaceutically acceptable salt thereof of any one of items 367 to 20 372, wherein n1, n2, n3 and n4 are about 115.
383. A compound or a pharmaceutically acceptable salt thereof of formula (2h)



wherein

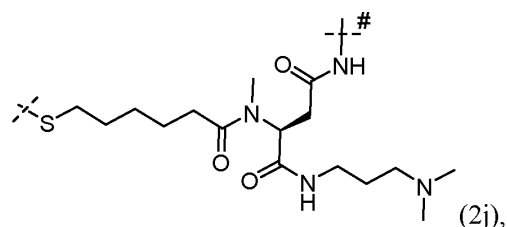
the dashed line marked with the asterisk indicates attachment to the dashed line of a moiety of formula (2i)



wherein

the dashed line marked with the # indicates attachment to the N-terminal amine functional group of semaglutide;

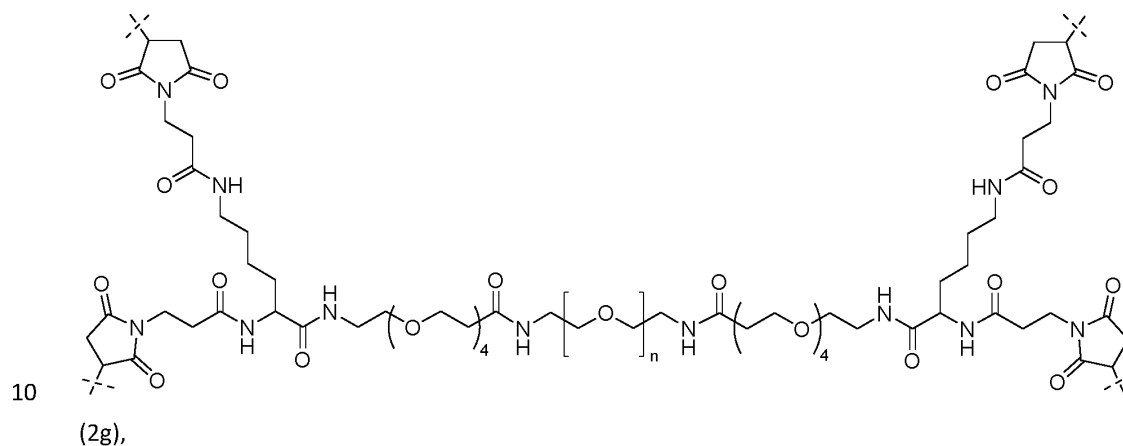
and wherein the unmarked dashed line of formula (2h) indicates attachment to the unmarked dashed line of formula (2j)



wherein

the dashed line marked with the # indicates attachment to the N-terminal amine functional group of semaglutide.

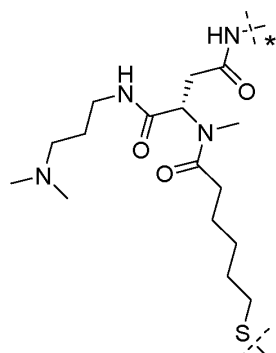
384. A compound or a pharmaceutically acceptable salt thereof of formula (2g)



wherein

n is an integer ranging from about 22 to about 230;

dashed lines indicate attachment to a moiety

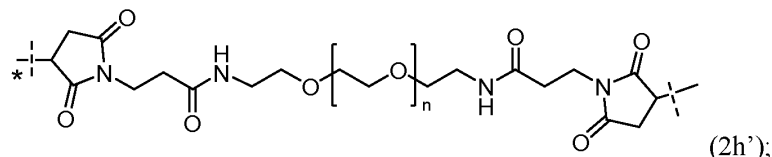


wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2g); and

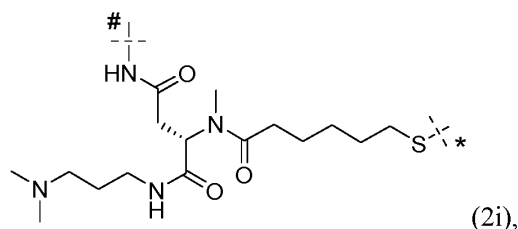
the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

- 5 385. A compound or a pharmaceutically acceptable salt thereof of formula (2h')



wherein

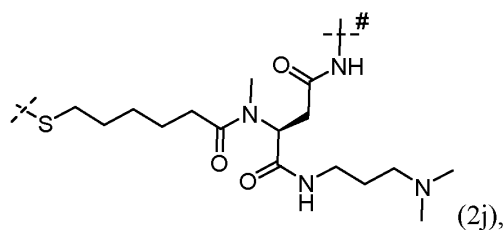
the dashed line marked with the asterisk indicates attachment to the dashed line marked with the asterisk of a moiety of formula (2i)



wherein

the dashed line marked with the # indicates attachment to the N-terminal amine functional group of semaglutide;

and wherein the unmarked dashed line of formula (2h') indicates attachment to the unmarked dashed line of formula (2j)



wherein

the dashed line marked with the # indicates attachment to the N-terminal amine functional group of semaglutide;

- 20 and wherein n is an integer ranging from about 22 to about 230.

386. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 44.

387. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 46.
388. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 68.
- 5 389. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 90.
390. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 112.
391. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385,
10 wherein n is about 113.
392. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 136.
393. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 160.
- 15 394. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 180.
395. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385, wherein n is about 200.
396. The compound or a pharmaceutically acceptable salt thereof of item 384 or 385,
20 wherein n is about 230.
397. The compound or a pharmaceutically acceptable salt thereof of any one of item 1 to 396, wherein the half-life of the drug released from the compound is it at least 1.5-fold higher than the corresponding free drug's half-life.
398. The compound or a pharmaceutically acceptable salt thereof of any one of item 1 to
25 397, wherein the half-life of the drug released from the compound is it at least 2.5-fold higher than the corresponding free drug's half-life.
399. The compound or a pharmaceutically acceptable salt thereof of any one of item 1 to 398, wherein the half-life of the drug released from the compound is it at least 5-fold higher than the corresponding free drug's half-life.
- 30 400. The compound or a pharmaceutically acceptable salt thereof of any one of item 1 to 399, wherein the half-life of the drug released from the compound is it at least 7.5-fold higher than the corresponding free drug's half-life.

401. The compound or a pharmaceutically acceptable salt thereof of any one of item 1 to 400, wherein the half-life of the drug released from the compound is at least 10-fold higher than the corresponding free drug's half-life.
- 5 402. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 401, wherein the release half-life of the compound is at least the circulation half-life of the corresponding free drug.
403. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 402, wherein the release half-life of the compound is at least 2-fold higher than circulation half-life of the corresponding free drug.
- 10 404. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 403, wherein the release half-life of the compound is at least 3-fold higher than circulation half-life of the corresponding free drug.
405. A pharmaceutical composition comprising at least one compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 404.
- 15 406. A pharmaceutical composition comprising at least one compound or a pharmaceutically acceptable salt thereof of any one of items 301 to 396.
407. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 405 or the pharmaceutical composition of item 374 for use as a medicament.
408. The compound or a pharmaceutically acceptable salt thereof of any one of items 301 to 396 or the pharmaceutical composition of item 406 for use as a medicament for the treatment of a disease that can be treated with a GLP-1 receptor agonist.
- 20 409. The compound or a pharmaceutically acceptable salt thereof of any one of items 1 to 404 or the pharmaceutical composition of item 405 for use in the treatment of a disease.
410. The compound or a pharmaceutically acceptable salt thereof of any one of items 301 to 396 or the pharmaceutical composition of item for use in the treatment of a disease that can be treated with a GLP-1 receptor agonist.
- 25 411. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of item 408 or 410, wherein the disease that can be treated with a GLP-1 receptor agonist is selected from the group consisting of (i) all forms of diabetes, (ii) obesity, (iii) non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), (iv) cardiovascular disease, (v) neurodegenerative disorders, (vi) chronic kidney disease (CKD), (vii) diabetic kidney disease (DKD), (viii) peripheral arterial disease (PAD), and/or (ix) heart failure (HF).
- 30

412. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition use of item 411, wherein the cardiovascular disease is selected from the group consisting of syndrome X, atherosclerosis, myocardial infarction, coronary heart disease, reperfusion injury, stroke, cerebral ischemia, an early cardiac or early cardiovascular disease, left ventricular hypertrophy, coronary artery disease, hypertension, essential hypertension, acute hypertensive emergency, cardiomyopathy, heart insufficiency, exercise intolerance, acute and/or chronic heart failure, arrhythmia, cardiac dysrhythmia, syncope, angina pectoris, cardiac bypass and/or stent reocclusion, intermittent claudication (atherosclerosis obliterans), diastolic dysfunction, and/or systolic dysfunction; and reduction of blood pressure, such as reduction of systolic blood pressure.
413. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of item 408 or 410, wherein the disease that can be treated with a GLP-1 receptor agonist is selected from the list consisting of dyslipidemia and/or diseases where one or more of the following clinical outcomes are the treatment goal: lowering total serum lipids; increasing HDL; lowering small, dense LDL; lowering VLDL; lowering triglycerides; lowering cholesterol; lowering plasma levels of lipoprotein a (Lp(a)) in a human; inhibiting generation of apolipoprotein A (apo(A)).
414. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of item 411, wherein the neurodegenerative disorder is selected from the group consisting of Alzheimer's disease and Parkinson's disease.
415. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of item 411, wherein the heart failure is selected from the group consisting of heart failure with reduced ejection fraction (HFrEF), heart failure with mid-range ejection fraction (HFmrEF) and heart failure with preserved ejection fraction (HFpEF).
416. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of item 411, wherein the disease that can be treated with a GLP-1 receptor agonist is non-alcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH).
417. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of item 408 or 410, wherein the disease that can be treated with a GLP-1 receptor agonist is obesity and/or eating disorders, where one or more of the

following clinical outcomes are the treatment goal: decreasing food intake, increasing energy expenditure, reducing body weight, suppressing appetite, inducing satiety.

418. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of any one of items 407 to 417, wherein the treatment is a co-treatment with one or more additional drugs.
419. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of 408 or 410 to 417, wherein the treatment is a co-treatment with one or more additional drugs.
420. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of item 419, wherein the one or more additional drugs is selected from the group consisting of inotropes, beta adrenergic receptor blockers, HMG-CoA reductase inhibitors, angiotensin II receptor antagonists, angiotensin converting enzyme inhibitors, calcium channel blockers, endothelin antagonists, renin inhibitors, diuretics, aldosterone receptor blockers, endothelin receptor blockers, aldosterone synthase inhibitors, CETP inhibitor, relaxin, PCSK9 inhibitors, BNP and NEP inhibitors, GLP-1 analogues, insulin, sulphonylureas, biguanides, meglitinides, glucosidase inhibitors, glucagon antagonists, DPP-IV inhibitors, SGLT2 inhibitors.
421. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of any one of items 408, 410 to 417, 419 or 420, wherein the treatment is combined with heart surgery.

Materials and methods

Chemicals

All materials were obtained from commercial vendors except where stated otherwise.

Semaglutide was purchased as the free acid from AdipoGen AG (Füllinsdorf, Switzerland).

Tirzepatide hydrochloride was purchased from MedChemExpress (New Jersey, USA)

Pentaerythritol tetra{[3-3(3-maleimido-1-oxopropyl)amino]propyl} polyoxyethylene (alternative name: 4-arm 10kDa-PEG tetramaleimide) was purchased from NOF Corporation.

Bis-Mal-Lysine-PEG4-TFP ester, Amine-PEG-amine, MW 5,000 and Mal-PEG-Mal, MW 5,000 were purchased from Broadpharm, San Diego, CA. mal-dPEG(3)-mal was purchased from Iris Biotech GmbH, Marktredwitz, Germany. 4-arm PEG-Mal, 5 kDa was purchased from Creative PEGWorks.

The number of ethylene glycol units “n” in a PEG reagent varies from batch to batch due to the polydispersity of polymeric moieties. All values for “n” are thus calculated based on the nominal molecular weight of a PEG reagent as provided by the manufacturer.

5 Reactions

Generally, reactions were stirred at room temperature and monitored by LCMS.

RP-HPLC purification

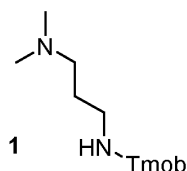
Preparative RP-HPLC purifications were performed with a Waters 600 controller with a 2487
10 Dual Absorbance Detector, an Agilent 1260 Infinity II preparative system, or a Knauer Azura Preparative gradient system. A Waters XBridge BEH300 Prep C18 10 μ m, 150 x 30 mm column or XSelect CSH Prep C18 10 μ m 150 x 30 mm column were used as stationary phase. Products were detected at 215 nm, 254 nm or 280 nm. Linear gradients of solvent system A (water containing 0.1% TFA v/v) and solvent system B (acetonitrile containing 0.1% TFA v/v)
15 were used. HPLC fractions containing product were pooled and lyophilized if not stated otherwise.

UPLC-MS analysis

Analytical ultra-performance LC (UPLC)-MS was performed on a Waters Acquity system or
20 an Agilent 1290 Infinity II equipped with a Waters BEH300 C18 column (2.1 x 50 mm, 1.7 μ m particle size or 2.1 x 100 mm, 1.7 μ m particle size) or with a XSelect CSH C18 (2.1 x 50 mm, 2.5 μ m particle size); solvent A: water containing 0.04% TFA (v/v), solvent B: acetonitrile containing 0.05% TFA (v/v) coupled to a Waters Micromass ZQ, Waters SQ Detector 2 or to an Agilent Single Quad MS system.

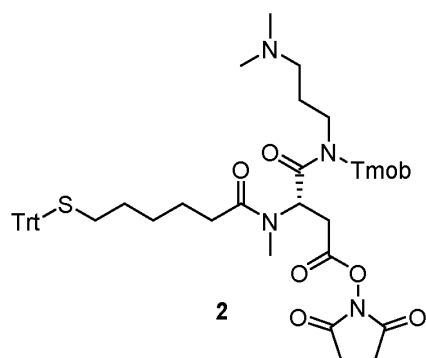
25

Example 1



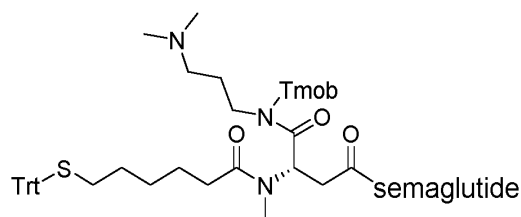
Compound 1 was prepared following the procedure described in WO2020064847 (example 11).

30 MS: m/z , 283.15 = $[M+H]^+$, (calculated $[M+H]^+$ = 283.20).

Example 2

Compound **2** was prepared as the TFA salt from **1** according to the procedure described in WO2020064847 (example 11).

- 5 MS: m/z , 881.36 = $[M+H]^+$, (calculated $[M+H]^+ = 881.42$).

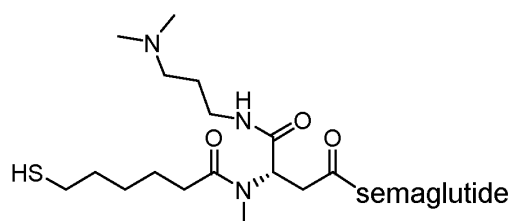
Example 3**3** Conjugated via His1 N α

- Semaglutide (5 mg, 1.0 eq., 1.22 μ mol) was dissolved in a mixture of 100 mM pH 8 borate buffer (0.5 mL) and acetonitrile (0.5 mL). To this was added **2** (7.3 mg, 6.0 eq., 7.29 μ mol) dissolved in acetonitrile (73 μ L). After stirring at rt for 21 h, the reaction was quenched by addition of 10% aq. TFA (20 μ L) and purified directly by preparative RP-HPLC to give **3** as the TFA salt.
- 10

Yield: 1.6 mg (25%, TFA salt)

- 15 MS: m/z 1627.74 = $[M+3H]^{3+}$, (calculated $[M+3H]^{3+} = 1627.17$).

Example 4



4 Conjugated via His1 Na

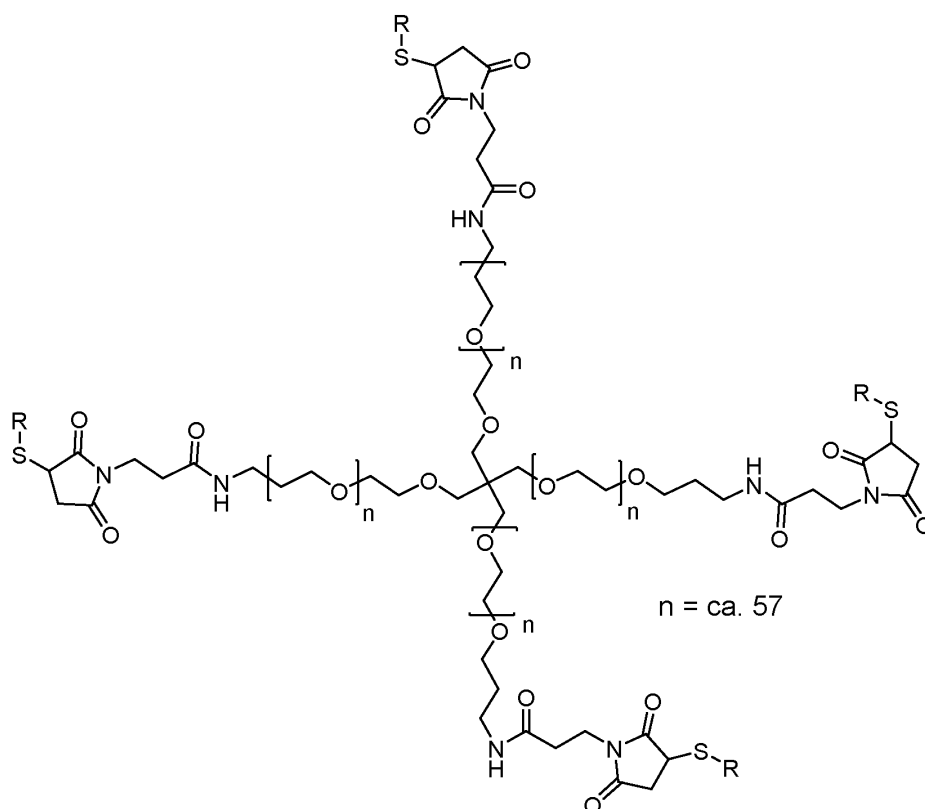
The protected conjugate **3** (1.6 mg, 1.0 eq., 0.30 μmol) was treated with 80 μL of HFIP/TES/water/DTT (39/1/5/2.5) then 20 μL of TFA. The mixture was shaken at rt for 55 min before addition of 1 mL of ice-cold diethyl ether. The mixture was vortexed, centrifuged, and the supernatant removed. The resulting precipitate was washed twice more with 1 mL of ice-cold diethyl ether. The crude conjugate was then purified via preparative RP-HPLC to give **4** as the TFA salt.

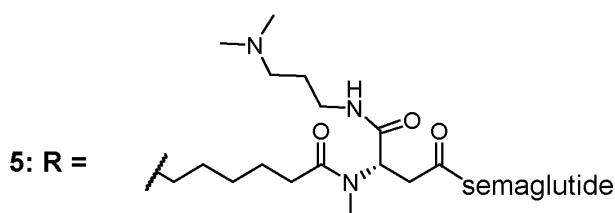
Yield: 1.1 mg (75%, TFA salt)

MS: m/z 1486.94 = $[\text{M}+3\text{H}]^{3+}$, (calculated $[\text{M}+3\text{H}]^{3+}$ = 1486.45).

10

Example 5





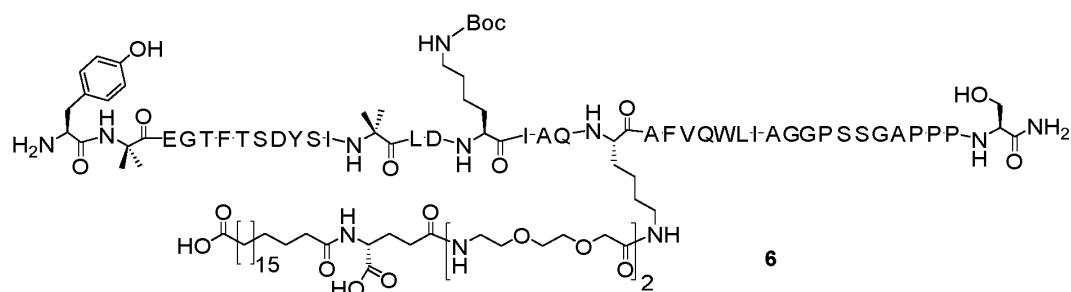
Conjugated via His1 Na

To a solution of 4-arm 10kDa-PEG tetramaleimide (0.38 mg, 1.0 eq., 0.037 μ mol) in 250 mM pH 7.4 phosphate buffer (38 μ L) was added conjugate **4** (0.37 mg, 2.0 eq, 0.075 μ mol) in 250 mM pH 7.4 phosphate buffer (50 μ L), acetonitrile (50 μ L), and water (25 μ L). After shaking at rt for 20 mins at rt, conjugate **4** (0.37 mg, 2.0 eq, 0.075 μ mol) in 250 mM pH 7.4 phosphate buffer (50 μ L), acetonitrile (50 μ L), and water (25 μ L) were added to the reaction mixture. After a further 20 mins shaking at rt, conjugate **4** (0.19 mg, 1.0 eq, 0.037 μ mol) in 250 mM pH 7.4 phosphate buffer (25 μ L), acetonitrile (25 μ L), and water (13 μ L) were added to the reaction mixture. After a further 95 mins, the reaction was quenched by addition of TFA (5 μ L) and the mixture was purified by preparative RP-HPLC to give **5** as a TFA salt.

Yield: 0.6 mg (54%, TFA salt)

Example 6

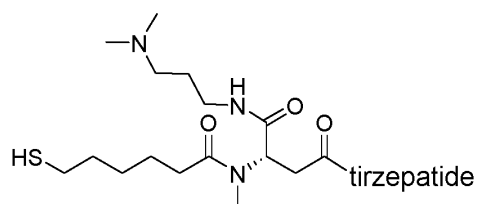
Preparation of [Lys(Boc)16]tirzepatide



Tirzepatide hydrochloride (2.0 mg, 1.0 eq., 0.41 μ mol) was dissolved in water (19 μ L), 1 M aq. NaHCO_3 solution (5.5 μ L) and DMF (56 μ L). To this was added N-(tert-butoxycarbonyloxy)succinimide (0.09 mg, 1.0 eq., 0.41 μ mol) in DMF (1.8 μ L). The solution was shaken in an Eppendorf tube at rt for 160 min before quenching with 400 μ L 1:1 acetonitrile/water (+0.1% TFA), TFA (1 μ L) and water (200 μ L). The crude product was then purified by preparative RP-HPLC to give **6** as a white solid.

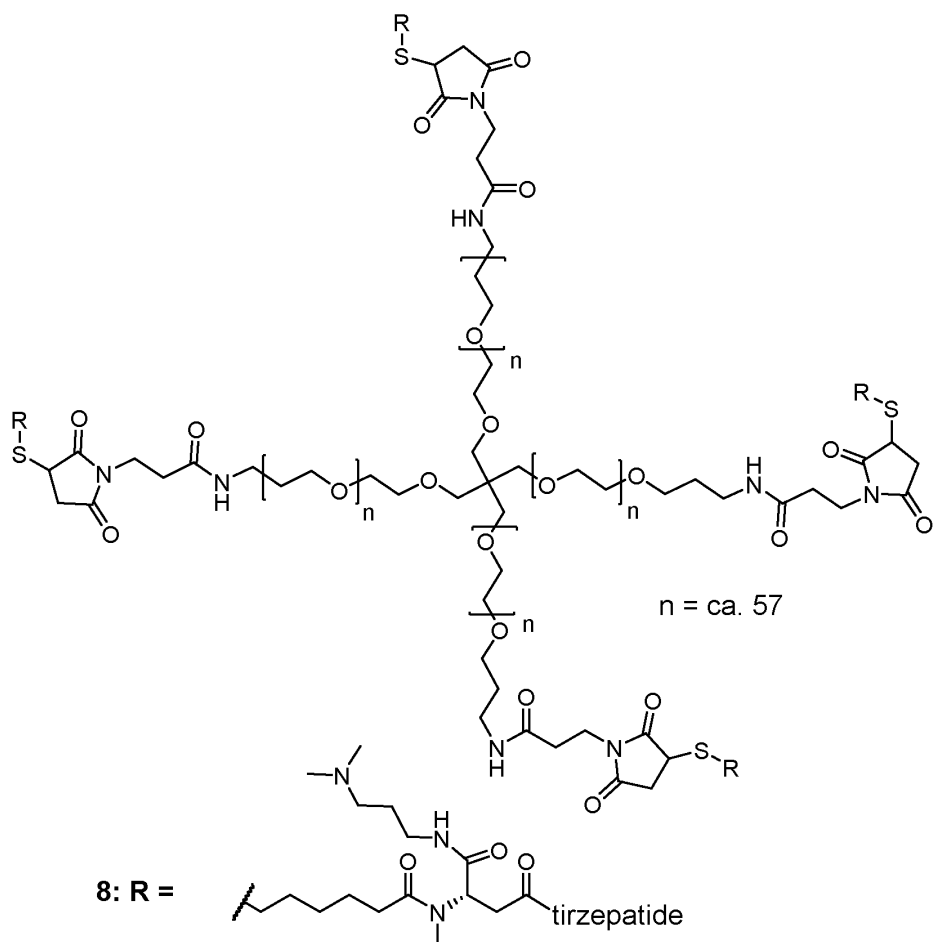
Yield: 1.2 mg (58%, TFA salt)

MS: m/z 1638.91 = $[\text{M}+3\text{H}]^{3+}$, (calculated for $[\text{M}+3\text{H}]^{3+}$ = 1638.53).

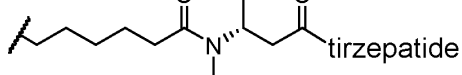
Example 7**7** Conjugated via Tyr1 Na

Conjugate 7 is prepared from 6 as per example 3 and 4.

5

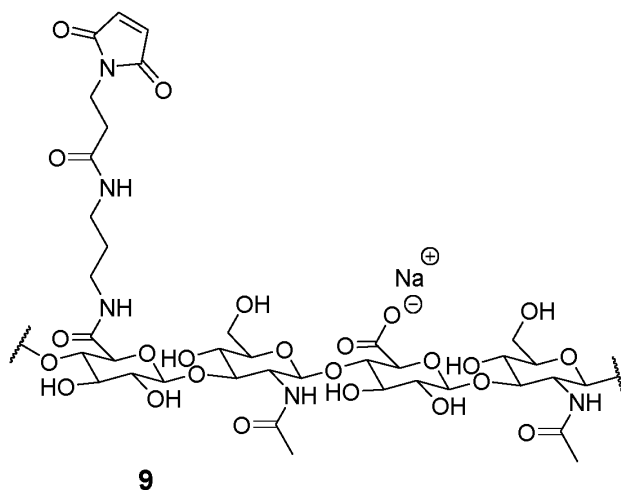
Example 8

8: R =

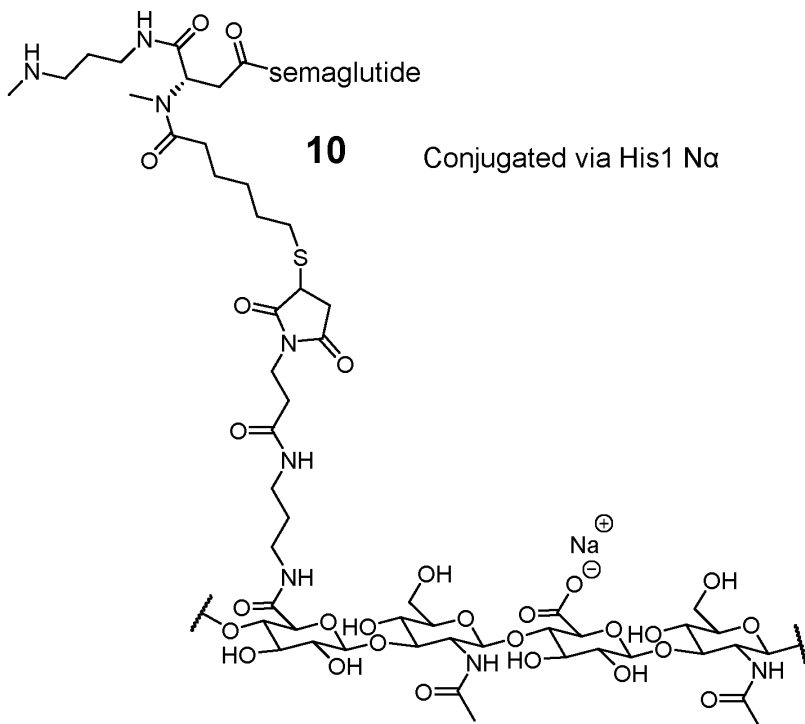


Conjugated via Tyr1 Na

Compound 8 is prepared from 7 and 4-arm 10kDa-PEG tetramaleimide as per example 5.

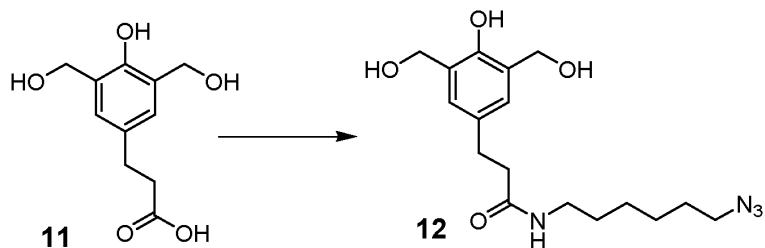
Example 9**Maleimide functionalized hyaluronic acid**

- 5 Maleimide functionalized hyaluronic acid **9** is prepared from hyaluronic acid (8 kDa) as described in WO2018175788 (example 2B). A degree of functionalization is achieved that gives between 2 and 6 maleimide groups per molecule.

Example 10

Maleimide functionalized hyaluronic acid **9** is conjugated to compound **4** as per example 5, except that the resulting conjugate **10** is purified by centrifugal filtration using a membrane with a 5 kDa molecular weight cut-off.

5 **Example 11**



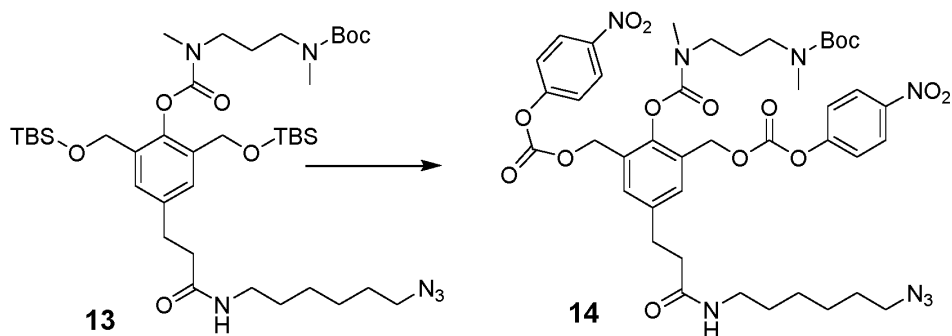
Compound **11**:

Compound **11** is prepared as described in US3689540 (example 1).

10 Compound **12**:

Compound **12** is prepared by coupling compound **11** with 6-azidohexan-1-amine using HATU and DIPEA in DMF.

Compound **13**:

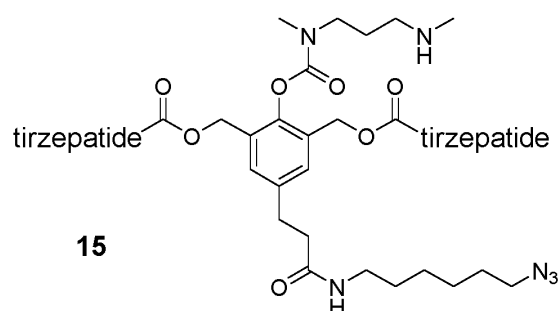


15

Compound **13** is prepared from **12** and 1,1-dimethylethyl N-methyl-N-[3-(methylamino)propyl]carbamate using a protocol similar to that described in *Angewandte Chemie International Edition* 2005, 44 (5), 716-720.

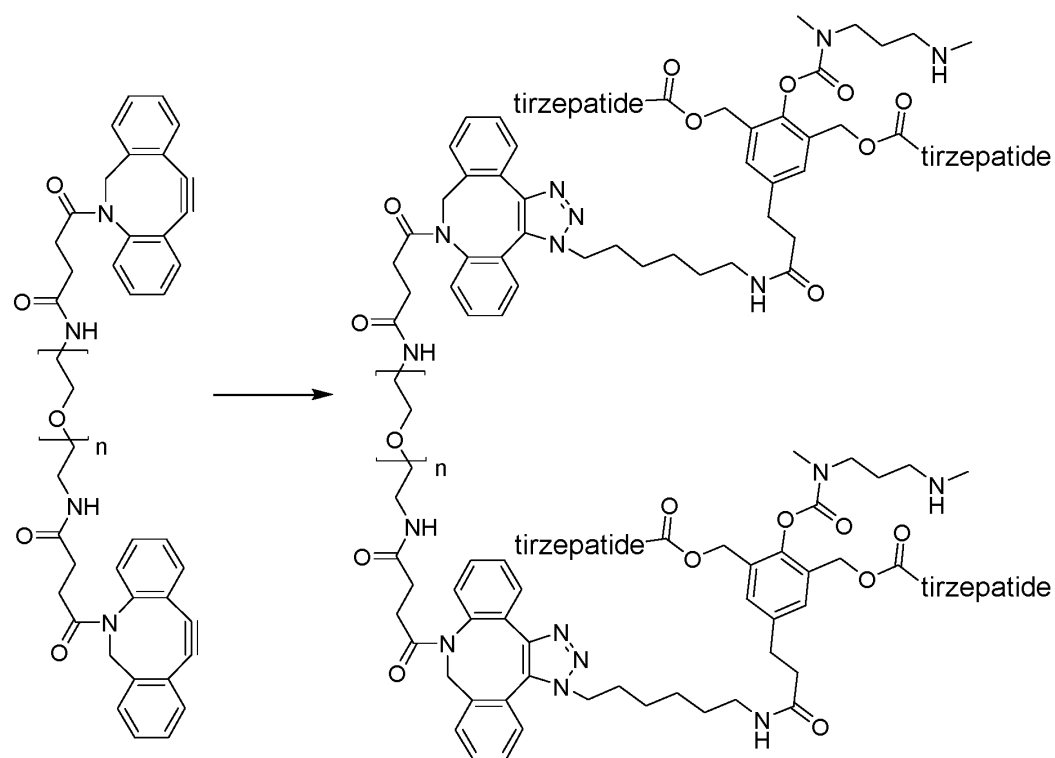
20 Compound **14**:

Compound **14** is prepared from **13** using a protocol similar to that described in *Angewandte Chemie International Edition* 2005, 44 (5), 716-720.

Example 12

Conjugated via Tyr1 Na

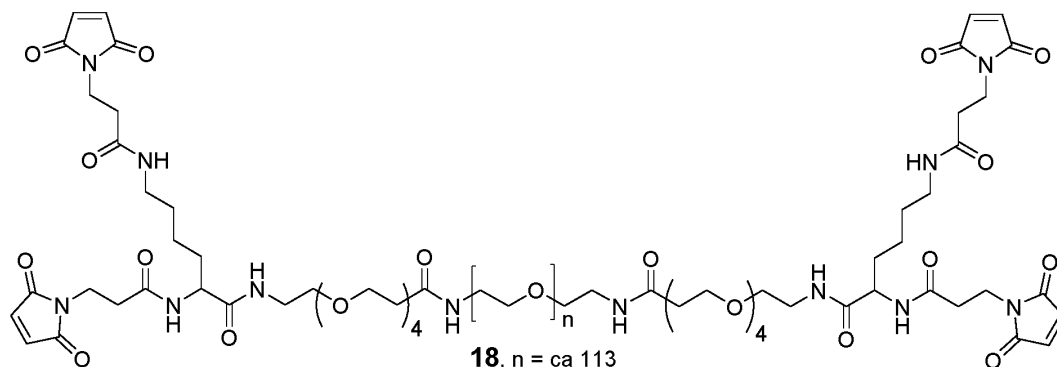
- To [Lys(Boc)**16**]tirzepatide **6** (2.25 eq.) in pH 7.0 phosphate buffer is added compound **14** in DMF. After stirring for 1 h, the mixture is diluted with water and lyophilized. The crude mixture is treated with HFIP/TES/water/DTT (39/1/5/2.5) then TFA. The conjugate is isolated by precipitation with ice-cold ether and is then purified by preparative RP-HPLC to give **15**.

Example 13

Conjugated via Tyr1 Na

To the commercially available bis-functional 10 kDa PEG **16** is added **15** in 1:1 buffer/DMF. After stirring at rt for 2 h, the crude material is purified directly by preparative RP-HPLC to give **17**.

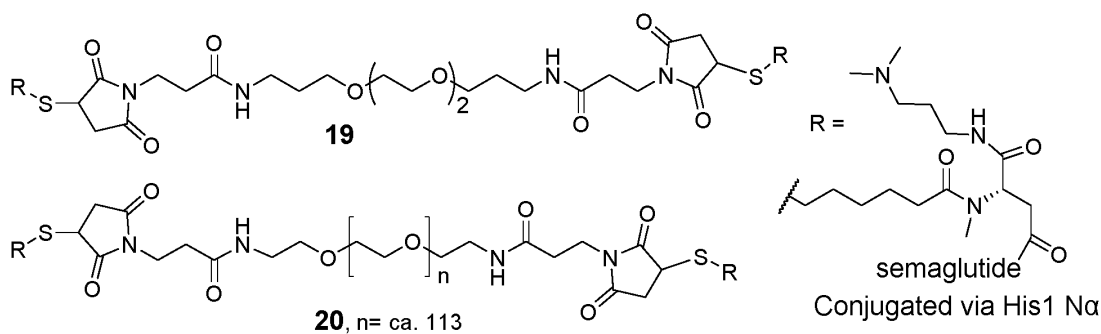
5 Example 14

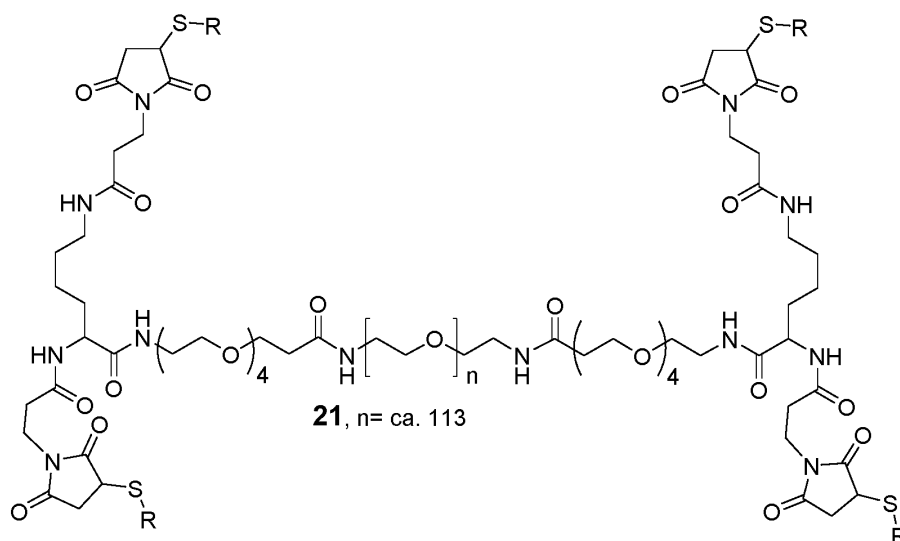


Bis-Mal-Lysine-PEG4-TFP ester (20.8 mg, 2.5 eq, 24.7 μmol) was dissolved in 1 mL acetonitrile / water (3:1 v/v). Amine-PEG-amine, MW 5,000 (50.0 mg, 1 eq, 9.88 μmol) dissolved in 1 mL acetonitrile / water (3:1 v/v) was added, followed by DIPEA (2.55 mg, 3.44 μL , 2 Eq, 19.8 μmol). The clear solution was stirred at rt. After 30 min the reaction was quenched with 3 μL TFA and the product purified by preparative RP-HPLC to give **18** as colorless solid.

Yield: 35 mg (55%)

15 Example 15





An excess of **4** in acetonitrile / water was added to 1 eq of the respective PEG maleimide portion-wise. The pH of the reaction was adjusted by addition of pH 7.0 or 7.4 sodium phosphate buffer. The reaction solution was shaken at rt and monitored by LC/MS. Upon completion the reaction was acidified with TFA. The product was purified by preparative RP-HPLC.

Synthesis of **19**: 1.0 eq mal-dPEG(3)-mal (0.6 mg),
 2.2 eq **4** (11.0 mg), pH 7.4: yield: 8.80 mg (75%, 8x TFA salt),
 10 MS: m/z 1349.31 = $[M+7H]^{7+}$, (calculated $[M+7H]^{7+} = 1349.12$)

Synthesis of **20**: 1 eq Mal-PEG-Mal, MW 5,000 (11.7 mg),
 2.0 eq **4** (21.4 mg), pH 7.0: yield: 18.4 mg (56%, 8x TFA salt)

15 Synthesis of **21**: 1 eq **18** (2.90 mg), 4.5 eq **4** (10.0 mg), pH 7.4: yield: 7.1 mg (60%, 16x TFA salt)

Example 16: PK study in Sprague Dawley rats

The objective of the study was to determine the pharmacokinetic (PK) characteristics of **5** when
 20 administered once by the intravenous (IV) or the subcutaneous (SC) route to the adult male Sprague Dawley rat. A semaglutide IV and SC group was included as comparator.

The Study design is shown in Table 1. Blood samples were processed to plasma and provided for PK analysis of semaglutide released from **5**.

Table 1: Design of Study

5 (Dose is in mg semaglutide equivalents/kg)

Group	Test item	n	Dose (mg/kg)	Administration Route	Blood sampling timepoints (hours post dose)
1	Semaglutide	3	0.030	IV	Predose, 0.25, 0.5, 1, 2, 4, 6, 24, 48
2	Semaglutide	3	0.030	SC	Predose, 1, 3, 4, 6, 8, 12, 24, 48
3	5	3	0.222	IV	0.25, 3, 8, 24, 36, 48, 72, 168, 264
4	5	3	0.222	SC	3, 6, 10, 24, 36, 48, 72, 168, 264

Example 17: PK study in Sprague Dawley rats

The objective of the study was to determine the PK characteristics of **19** and **20** when administered once by the IV or the SC route to the adult male Sprague Dawley rat. A semaglutide SC group was included as comparator and a vehicle SC group was included as control.

The Study design is shown in Table 2. Blood samples were processed to plasma and provided for PK analysis of released semaglutide (except from group F).

15

Table 2: Design of Study

(Dose is in mg semaglutide equivalents/kg)

Group	Test item	n	Dose (mg/kg)	Administration Route	Blood sampling timepoints (hours post dose) ^b
A	20	3	0.45	IV	0.25, 3, 8, 24, 36, 48, 72, 120, 168 and 264
B	19	3	0.45	IV	0.25, 3, 8, 24, 36, 48, 72, 120, 168 and 264
C	20	3	0.45	SC	3, 6, 10, 24, 36, 48, 72, 96, 168 and 264
D	19	3	0.45	SC	3, 6, 10, 24, 36, 48, 72, 96, 168 and 264
E	Semaglutide	3	0.030	SC	1, 2, 4, 6, 8, 12, 24, 48 and 58

F	Vehicle control	3	0	SC	3, 6, 10, 24, 36, 48, 72, 96, 168 and 264
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Example 18: PK analysis of semaglutide released from compounds 5, 19, 20 compared to semaglutide and PK analysis of semaglutide released from 22 and 24 in Sprague Dawley rats

- 5 The PK of semaglutide and semaglutide released from **5, 19, 20, 22** or **24** was determined after IV or SC administration of semaglutide and of **5, 19, 20, 22** or **24** to rats according to the study described in example 16, example 17 and example 29.

Blood samples were collected from all animals according to Table 1, Table 2 and Table 8.

- 10 Plasma samples were analyzed for semaglutide.

Semaglutide and semaglutide released from **5, 19, 20, 22** and **24** was quantified in Sprague Dawley rat K₃EDTA plasma via LC-MS/MS after plasma protein precipitation. Samples containing semaglutide were pipetted into the wells of a 96-well plate, followed by the addition of internal standard (d₈-semaglutide). Plasma protein precipitation was carried out using a mixture of acetonitrile and water (85/15, v/v). The precipitate was centrifuged at 4 °C and a fraction of the supernatant was transferred to a new 96-well plate, evaporated to dryness under a stream of heated nitrogen and reconstituted in water containing 0.2 % formic acid.

- 20 Chromatography was performed on a Waters Acquity UPLC Peptide BEH C18 analytical column (1.7 µm particle size; pore size 300 Å; column dimensions 50 x 2.1 mm). Water (UPLC grade) containing 0.1 % formic acid (v/v) was used as mobile phase A and acetonitrile (UPLC grade) with 0.1 % formic acid as mobile phase B. Multiple reaction monitoring (MRM) was performed for semaglutide and the internal standard and quantification was based on peak area and linear regression with 1/x² weighting.

A summary of the individual and mean PK parameters for semaglutide and semaglutide released from **5, 19, 20, 22** and **24** in rat plasma are shown below in Table 3, Table 4 and Table 5.

30

Table 3: Summary of the Mean PK Parameters of semaglutide and semaglutide released from **5** in rat plasma in study described in example 16.

Dose group	Test Item	ROA	Dose level (µg/kg)	C _{max} (ng/mL) ^a	t _{max} (h) ^b	t _{last} (h) ^b	AUC _{last} (h*ng/mL) ^a	t _{1/2} (h) ^a
1	semaglutide	IV	30	570 ^c	0.25	48	5,400 ^c	10 ^c
2	semaglutide	SC	30	130±26	6	48	3,000±620	11±1.3
3	5	IV	222	34±1.3	24	168	2,500±660	43±2
4	5	SC	222	24±3	24	72	1,100±120	30±0.9

^a mean value±SD; ^b median value; ^c n = 2

Table 4: Summary of the mean PK parameters of semaglutide and semaglutide released from **19** or **20** in rat plasma in example 17.

Dose group	Test Item	ROA	Dose level (µg/kg)	C _{max} (ng/mL) ^a	t _{max} (h) ^b	t _{last} (h) ^b	AUC _{last} (h*ng/mL) ^a	t _{1/2} (h) ^a
A	20	IV	450	56±7.1	24	120	3,400±250	28±2.2
B	19	IV	450	37±0.9	8	72	1,800±60	23±2.1
C	20	SC	450	50±1	24	96	2,500±460	27±2.6
D	19	SC	450	40±5.2	24	96	1,700±320	20±1.9
E	semaglutide	SC	30	110±21	8	58	3,100±560	12±0.2

5 ^a mean value±SD; ^b median value

Note: group F served as vehicle control and was not dosed with an active compound

Table 5: Summary of the Mean PK Parameters of semaglutide and semaglutide released from **22** and **24** in rat plasma in study described in example 29.

Dose group	Test Item	ROA	Dose level (µg/kg)	C _{max} (ng/mL) ^a	t _{max} (h) ^b	t _{last} (h) ^b	AUC _{last} (h*ng/mL) ^a	t _{1/2} (h) ^a
1	22	IV	450	58±3.0	24	120	3,800±170	29±1.0
2	24	IV	450	35±1.8	8	72	1,300±190	18±0.96

10 ^a mean value±SD; ^b median value

Example 19: PK study in cynomolgus monkey

The objective of the study was to determine the PK characteristics of **5** when administered once by the IV or SC route to the cynomolgus monkey.

15

The Study design is shown in Table 6. Blood samples were processed to plasma and provided for PK analysis of semaglutide released from **5**.

Table 6: Design of Study

20 Dose is in mg semaglutide equivalents/kg

Group No.	Test item	No. of Animals		Dose (mg/kg)	Administration Route	Blood sampling time points (hours post dose)
		Males	Females			
1	5	1	1	0.15	IV	Predose, 0.25, 2, 6, 12, 24, 48, 72, 96, 120, 144, 168, 216, 264, 288 and 336
2	5	1	1	0.15	SC	Predose, 3, 6, 10, 16, 24, 36, 48, 72, 96, 120, 144, 168, 216, 264, 288 and 336

Example 20: PK analysis of semaglutide released from 5 in cynomolgus monkeys

The PK of semaglutide released from 5 was determined after IV or SC administration of 5 to monkeys in the study described in example 19.

5

Semaglutide released from 5 was quantified in cynomolgus monkey K₃EDTA plasma via LC-MS/MS after plasma protein precipitation. Samples containing semaglutide were pipetted into the wells of a 96-well plate, followed by the addition of internal standard (d₈- semaglutide) solution containing 4 % formic acid. Plasma protein precipitation was carried out using a mixture of acetonitrile and water (85/15, v/v). The precipitate was centrifuged at 4 °C and a fraction of the supernatant was transferred to a new 96-well plate, evaporated to dryness under a stream of heated nitrogen and reconstituted in water containing 0.2 % formic acid.

10

Chromatography was performed on a Waters Acquity UPLC Peptide BEH C18 analytical column (1.7 µm particle size; pore size 300 Å; column dimensions 50 x 2.1 mm). Water (UPLC grade) containing 0.1 % formic acid (v/v) was used as mobile phase A and acetonitrile (UPLC grade) with 0.1 % formic acid as mobile phase B. Multiple reaction monitoring (MRM) was performed for semaglutide and the internal standard and quantification was based on peak area and linear regression with 1/x² weighting.

20

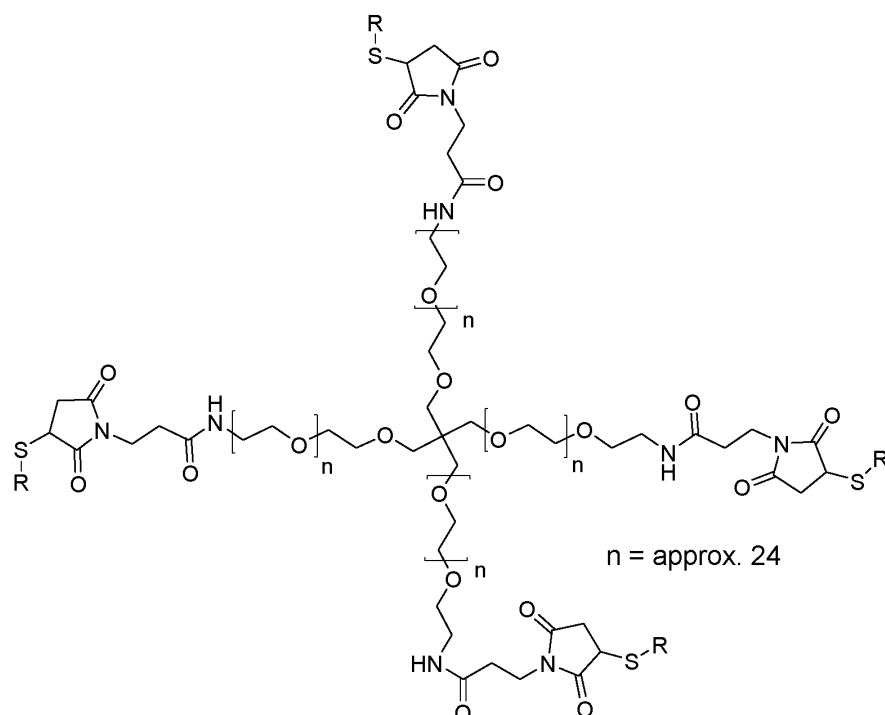
A summary of the individual and mean PK parameters for semaglutide released from 5 in monkey plasma are shown below in Table 7.

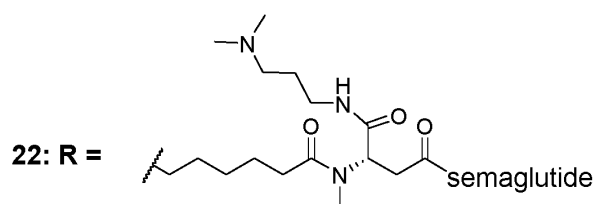
No sex-specific differences between the male and female animal within each group could be observed. $C_{\max}$ and area under the curve (AUC) were slightly lower for the SC group than for the IV group, but the half-life was comparable in both groups.

- 5 Table 7: Summary of the individual and mean PK parameters of semaglutide released from **5** in monkey Plasma in study described in example 19.

Dose group	Test Item	ROA	Dose level ($\mu\text{g/kg}$)	Animal	$C_{\max}$ (ng/mL)	$t_{\max}$ (h)	t_{last} (h)	AUC_{last} (h*ng/mL)	$t_{1/2}$ (h)
1	5	IV	150	m	84	72	336	19,000	123
				f	92	72	336	20,000	123
				mean	88			20,000	123
				median		72	336		
2	5	SC	150	m	68	120	336	16,000	144
				f	71	72	336	16,000	130
				mean	69			16,000	137
				median		96	336		

Example 21



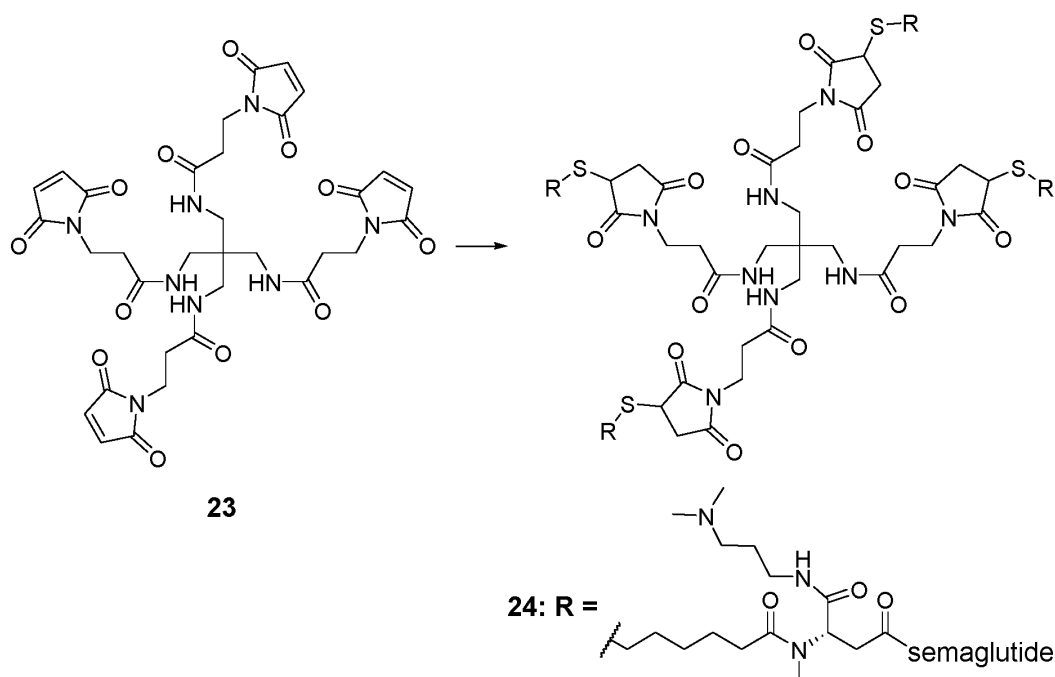


Conjugated via His1 N α

To a solution of 4-arm 5kDa-PEG tetramaleimide (5.0 mg, 1.0 eq., 0.98 μ mol) in acetonitrile (150 μ L) was added conjugate **4** (4.8 mg, 1.0 eq, 0.98 μ mol) in 1:1 acetonitrile/water (200 μ L) followed by 250 mM pH 7.4 phosphate buffer (200 μ L). After shaking at rt for 20 min, conjugate **4** (9.6 mg, 2.0 eq, 1.96 mmol) in 1:1 acetonitrile/water (400 μ L) was added. After a further 15 min shaking at rt, conjugate **4** (7.2 mg, 1.5 eq, 1.47 mmol) in 1:1 acetonitrile/water (300 μ L) was added followed by additional 1:1 acetonitrile/water (3 mL). After a further 75 min, the reaction was quenched by addition of 10 % TFA in water (50 μ L) and the mixture was purified by preparative RP-HPLC to give **22** as a TFA salt.

Yield: 10.2 mg (42 %)

Example 22



Conjugated via His1 N α

Compound **23**:

2,2-bis(aminomethyl)propane-1,3-diamine tetrahydrochloride (10.0 mg, 1.0 eq, 36.0 μ mol) was dissolved in acetonitrile (2.0 mL), DIPEA (23.2 mg, 31.3 μ L, 5.0 eq, 180 μ mol) and water (0.4 mL). 3-(Maleimido)propionic acid N-hydroxysuccinimide ester (47.9 mg, 5.0 eq, 180 μ mol) was added, followed by DIPEA (23.2 mg, 31.3 μ L, 5.0 eq, 180 μ mol). After stirring at rt for 25 min, the reaction was quenched by addition of TFA (20 μ L), and the mixture was purified by preparative RP-HPLC to give **23**.

Yield: 23.8 mg (90 %)

MS: m/z , 737.48 = $[M+H]^+$, (calculated $[M+H]^+ = 737.25$).

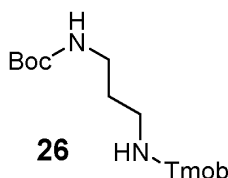
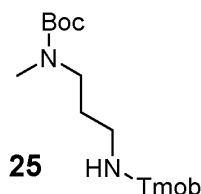
10 Compound **24**:

To a solution of conjugate **4** (30.0 mg, 4.5 eq, 6.11 μ mol) in 1:1 acetonitrile/water (2.0 mL) was added a solution of compound **23** (1.00 mg, 1 eq, 1.36 μ mol) in acetonitrile (0.1 mL), followed by 250 mM pH 7.4 phosphate buffer (0.5 mL). After stirring at rt for 45 min, the reaction was quenched by addition of TFA (5 μ L). The mixture was diluted with 1:1 acetonitrile/water (1 mL) and 250 mM pH 7.4 phosphate buffer (0.5 mL) and purified by preparative RP-HPLC to give **24** as a TFA salt.

Yield: 16.6 mg (60 %)

MS: m/z , 1857.80 = $[M+10H]^{10+}$, (calculated $[M+10H]^{10+} = 1857.52$).

20 Example 23



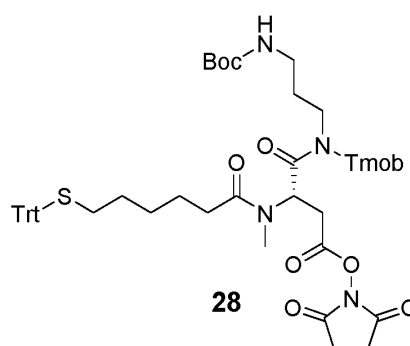
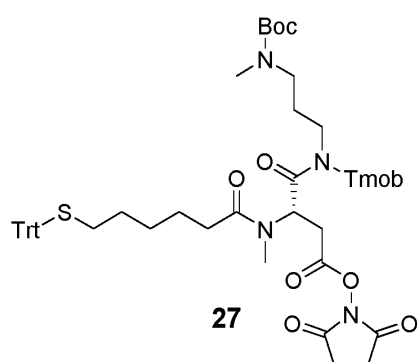
A solution of the respective amine (1.5 eq, see below) in acetic acid was added to a solution of 2,4,6-trimethoxybenzaldehyde (1.0 eq) in acetic acid. The reaction solution was stirred at rt and monitored by LCMS. After complete imine formation an excess of sodium borohydride was added portion wise. The reaction solution was stirred at rt and monitored by LCMS. After the reaction was complete it was quenched by addition of 1 N HCl. The mixture was stirred for 20 min and then added into water. The aqueous phase was washed with dichloromethane. The pH of the aqueous phase was adjusted to 14 using 12.5 N NaOH and extracted with dichloromethane. The organic phase was dried over sodium sulfate, evaporated and dried under high vacuum.

Synthesis of **25**: 1.0 eq tert-butyl N-(3-aminopropyl)-N-methylcarbamate (1.41 g), 1.2 eq sodium borohydride (229 mg), yield: 2.14 g (100 %, 86 % purity), m/z 369.42 = $[M+H]^+$, (calculated $[M+H]^+ = 369.47$).

5

Synthesis of **26** 1.0 eq N-Boc-1,3-diaminopropane (1.31 g), 15. eq sodium borohydride (286 mg), yield: 2.16 g (100 %, 82 % purity), m/z 355.40 = $[M+H]^+$, (calculated $[M+H]^+ = 355.45$).

10 Example 24



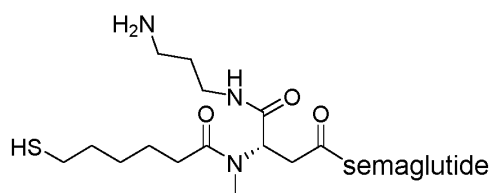
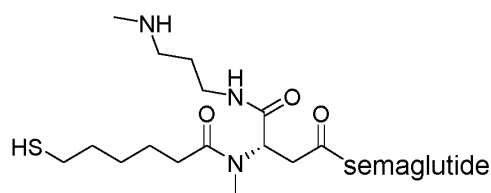
Compound **27** was prepared according to example 2 using compound **25** instead of **1**

MS: m/z , = 967.95 $[M+H]^+$, (calculated $[M+H]^+ = 968.19$).

Compound **28** was prepared according to example 2 using **26** instead of **1**

15 MS: m/z , = 953.90 $[M+H]^+$, (calculated $[M+H]^+ = 954.16$).

Example 25



Compound **29** was prepared as TFA salt according to examples 3 and 4 starting from compound **27** instead of **2**.

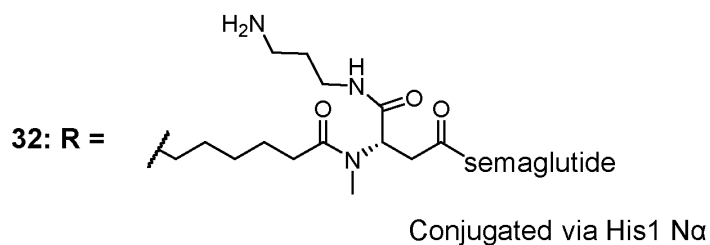
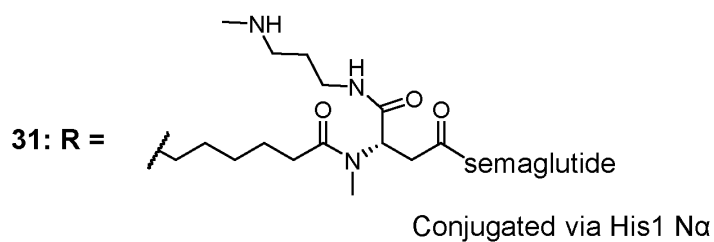
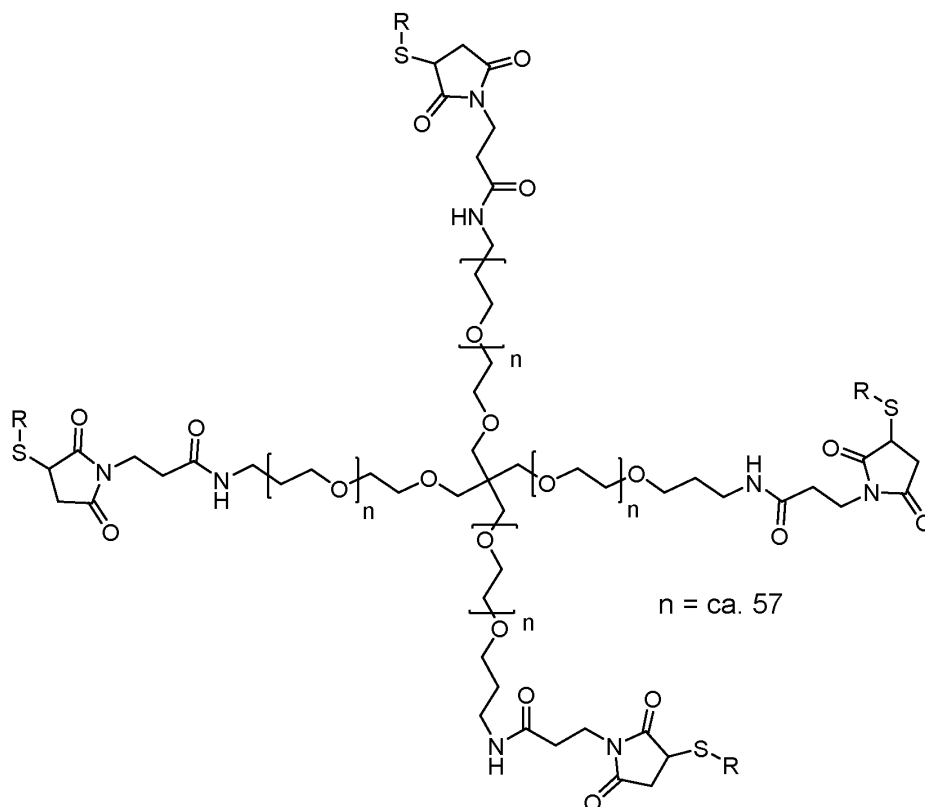
20

MS: m/z , = 1481.92 $[M+3H]^{3+}$, (calculated $[M+3H]^{3+} = 1482.03$).

Compound **30** was prepared as TFA salt according to examples **3** and **4** starting from compound **28** instead of **3**.

MS: m/z = 1477.97 $[M+3H]^{3+}$, (calculated $[M+3H]^{3+}$ = 1477.36).

5 Example 26



A solution of 4-arm 10 kDa-PEG tetramaleimide (1.0 eq) in acetonitrile was added to a solution of the respective conjugate (4.5 eq, **29** or **30**) in 1:1 acetonitrile/water. 250 mM pH 7.4 phosphate buffer was added and the reaction solution was stirred at rt and monitored by LCMS. Upon completion the reaction was acidified by addition of TFA and purified by preparative

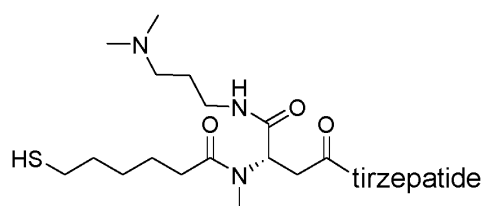
5 RP-HPLC.

Synthesis of **31**: 4.5 eq **29** (2.0 mg), yield: 1.0 mg (35 %, TFA salt)

Synthesis of **32**: 4.5 eq **30** (2.6 mg), yield: 3.9 mg (57 %, TFA salt)

Example 27:

10 Alternative synthesis of compound **7**



7 Conjugated via Tyr1 Na

[Lys(Boc)16]tirzepatide **6** (1.2 mg, 1.0 eq, 0.24 μmol) was dissolved in a mixture of 120 μL acetonitrile and 120 μL 60 mM pH 8 phosphate buffer. To this was added a solution of **2** (1.43 mg, 6.0 eq, 1.43 μmol) in acetonitrile (14.3 μL). After stirring at rt for 2 d the solution
 15 was diluted with 1:1 acetonitrile/water + 0.1 % TFA (250 μL) and quenched with TFA (1 μL). The crude mixture was purified by preparative RP-HPLC to give of the protected conjugate as TFA salt.

Yield: 0.5 mg (36 %),

MS: m/z 1421.07 = $[\text{M}+4\text{H}]^{4+}$, (calculated $[\text{M}+4\text{H}]^{4+} = 1420.91$).

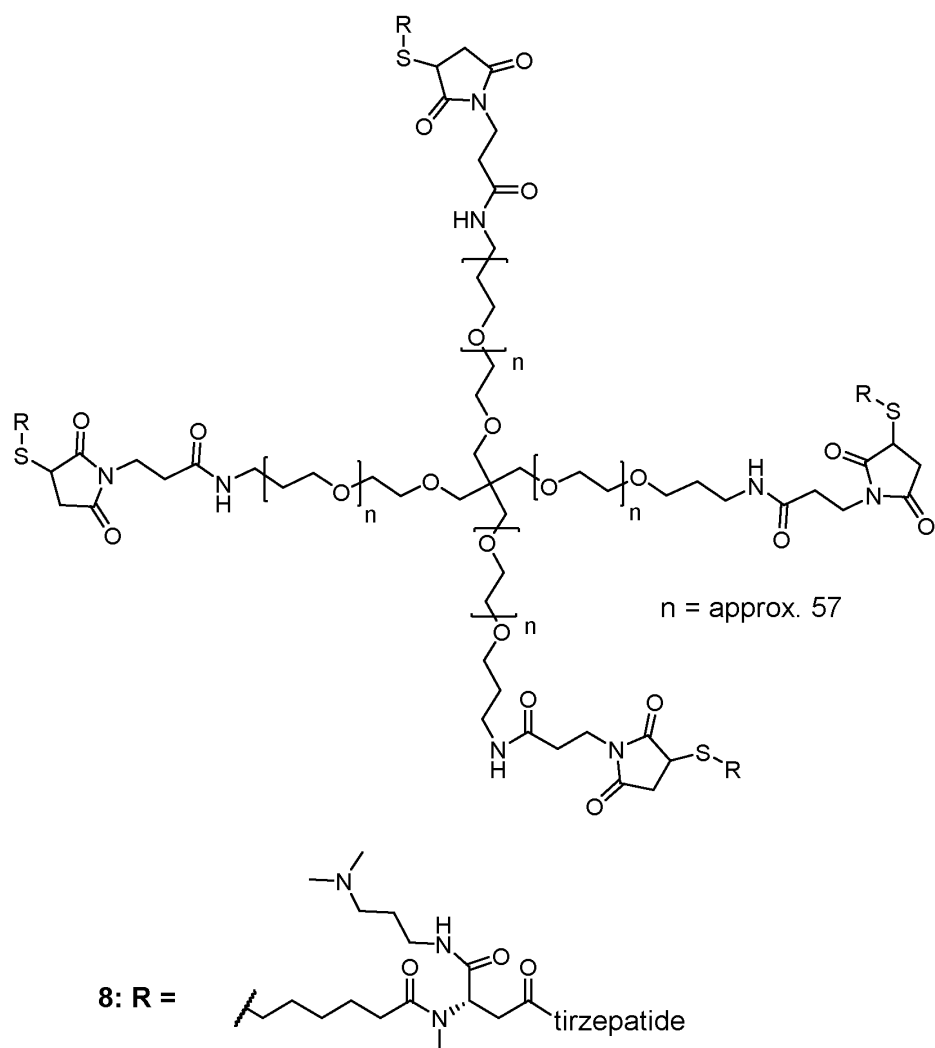
20 The protected conjugate (0.5 mg, 1.0 eq, 0.086 μmol) was dissolved in HFIP/TES/water/DTT (39/1/5/2.5) (80 μL) and TFA (20 μL) was added. After stirring for 65 min the product was precipitated by addition of 1 mL ice-cold diethyl ether. The precipitate was washed with ice-cold diethyl ether and purified by preparative RP-HPLC to give **7** as the TFA salt.

Yield: 0.2 mg (43 %),

25 MS: m/z 1720.15 = $[\text{M}+3\text{H}]^{3+}$, (calculated $[\text{M}+3\text{H}]^{4+} = 1720.00$).

Example 28:

Alternative synthesis of compound **8**



Conjugated via Tyr1 N α

A solution of **7** (0.2 mg, 4.5 eq, 0.037 μ mol) in 1:1 acetonitrile/water (225 μ L) was prepared. 100 μ L of the solution of **7** (2.0 eq) were added to a solution of 4-arm 10 kDa-PEG tetramaleimide (91 μ g, 1.0 eq, 8.3 nmol) in 1:1 acetonitrile/water (9.1 μ L), followed by 250 mM pH 7.4 phosphate buffer (10 μ L). After shaking at rt for 15 min, 100 μ L of the solution of **7** (2.0 eq) were added. After a further 15 min shaking at rt, 25 μ L of the solution of **7** (0.5 eq) were added. After a further 50 min, the reaction was quenched by addition of TFA (1 μ L), and the mixture was purified by preparative RP-HPLC to give **8** as a TFA salt.

10

Example 29: PK study in Sprague Dawley rats

The objective of the study was to determine the PK characteristics of **22** and **24** when administered once by the IV route to the adult male Sprague Dawley rat.

The Study design is shown in Table 8. Blood samples were processed to plasma and provided for PK analysis of released semaglutide.

5

Table 8: Design of Study

(Dose is in mg semaglutide equivalents/kg)

Group	Test item	n	Dose (mg/kg)	Blood sampling timepoints (hours post dose)
1	22	3	0.45	0.25, 3, 8, 24, 36, 48, 60, 72, 120 and 168
2	24	3	0.45	0.25, 3, 8, 24, 36, 48, 60, 72, 120 and 168

10 Abbreviations:

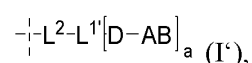
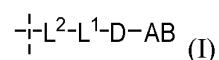
aq.	Aqueous
AUC	area under the curve
Boc	<i>tert</i> -butyloxycarbonyl
DIPEA	diisopropylethylamine
15 DMF	dimethylformamide
dPEG	discrete PEG
DTT	dithiothreitol
eq	equivalent
HATU	O-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium-
20	hexafluorophosphat
HFIP	1,1,1,3,3,3-hexafluoroisopropanol
HPLC	high performance liquid chromatography
IV	intravenous
LCMS	liquid chromatography mass spectrometry
25 mal	maleimide
MS	mass spectrometry
PEG	polyethylene glycol
PK	phaemacokinetics
ROA	Route of administration

	RP	reversed phase
	rt	room temperature
	sat.	saturated
	SC	subcutaneous
5	SD	standard deviation
	TBS	<i>tert</i> -butyl(dimethyl)silyl
	TES	triethylsilane
	TFA	trifluoroacetic acid
	TFP	tetrafluorophenyl
10	Tmob	2,4,6-Trimethoxybenzyl
	Trt	trityl
	UPLC	ultra performance liquid chromatography
	UPLC-MS	ultra performance liquid chromatography coupled to mass spectrometry

15

Claims

1. A compound or a pharmaceutically acceptable salt thereof, wherein the compound comprises at least one polymeric moiety, to which at least two moieties of formula (I) are conjugated and/or to which at least one moiety of formula (I') is conjugated, wherein formula (I) and (I') are

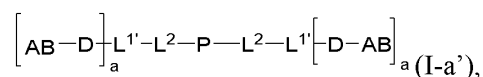
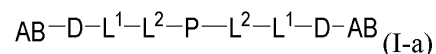


wherein

- each $\text{---}\text{L}^2\text{---}$ is independently a spacer moiety or is absent;
 each $\text{---}\text{L}^1\text{---}$ is independently a linker moiety that is covalently and reversibly conjugated to $\text{---}\text{D---}$;
 each $\text{---}\text{L}^1\text{---}$ is independently a linker moiety that is covalently and reversibly conjugated to $\text{---}\text{D---}$;
 each $\text{---}\text{D---}$ is independently a drug moiety;
 each $\text{---}\text{AB}$ is independently an albumin-binding moiety; and
 each a is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

2. The compound or a pharmaceutically acceptable salt thereof of claim 1, wherein the at least one polymeric moiety of the compounds of the present invention is a linear polymeric moiety $\text{---}\text{P---}$.

3. The compound or a pharmaceutically acceptable salt thereof of claim 1 or 2, wherein the compound is of formula (I-a) or (I-a')



wherein

- each $\text{---}\text{L}^2\text{---}$ is independently a spacer moiety or is absent;
 each $\text{---}\text{L}^1\text{---}$ is independently a linker moiety that is covalently and reversibly conjugated to $\text{---}\text{D---}$;

each -L^{1'}- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -D- is independently a drug moiety;

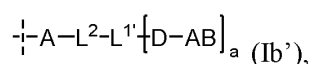
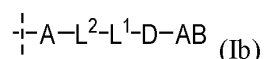
each -AB is independently an albumin-binding moiety;

5 -P- is a polymeric moiety; and

each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

4. The compound or a pharmaceutically acceptable salt thereof of claim 1, wherein the at least one polymeric moiety of the compound of the present invention is a multi-arm polymeric moiety.

5. The compound or a pharmaceutically acceptable salt thereof of claim 1 or 4, wherein the compound comprises at least one branching point B, to which at least two moieties of formula (Ib) and/or at least one moiety of formula (Ib') are conjugated, wherein formula (Ib) and (Ib') are



wherein

20 the dashed line indicates attachment to a branching point B;

-A- is a polymeric moiety

each -L²- is independently a spacer moiety or is absent;

each -L¹- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

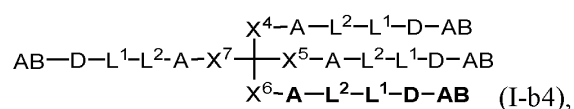
25 each -L^{1'}- is independently a linker moiety that is covalently and reversibly conjugated to -D-;

each -D- is independently a drug moiety;

each -AB is independently an albumin-binding moiety; and

30 each a is independently an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

6. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1, 4 or 5, wherein the compound is of formula (I-b4)



wherein

- X⁴-, -X⁵-, -X⁶- are independently of each other selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-,
 5 -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-,
 -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl;
 wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted
 with one or more -R^{y2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀
 alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected
 10 from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-,
 -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-,
 -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;
 -R^{y1} and -R^{y1a} are independently of each other selected from the group consisting
 of -H-, -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀
 15 alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which
 are the same or different, and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are
 optionally interrupted by one or more groups selected from the group consisting
 of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-,
 -S(O)-,
 20 -N(R^{y4})S(O)₂N(R^{y4a})-, -S-,
 -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-, and -OC(O)N(R^{y4})-;
 each T is independently selected from the group consisting of phenyl, naphthyl,
 indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to
 11-membered heterobicyclyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-
 membered heteropolycyclyl; wherein each T is independently optionally substituted
 25 with one or more -R^{y2}, which are the same or different;
 each -R^{y2} is independently selected from the group consisting of halogen, -CN, oxo
 (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a})-, -S(O)₂N(R^{y5}R^{y5a})-,
 -S(O)N(R^{y5}R^{y5a})-, -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b})-, -SR^{y5},
 -N(R^{y5}R^{y5a})-, -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a},
 30 -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)OR^{y5a}, -N(R^{y5})C(O)N(R^{y5a}R^{y5b})-, -OC(O)N(R^{y5}R^{y5a})-,
 and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen,
 which are the same or different; and

each $-R^{y3}$, $-R^{y3a}$, $-R^{y4}$, $-R^{y4a}$, $-R^{y5}$, $-R^{y5a}$ and $-R^{y5b}$ is independently selected from the group consisting of $-H$, and C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

each $-A-$ is a polymeric moiety;

5 each $-L^2-$ is independently a spacer moiety or is absent;

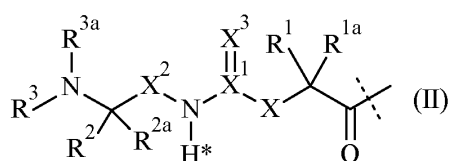
each $-L^1-$ is independently a linker moiety that is covalently and reversibly conjugated to $-D-$;

each $-D-$ is independently a drug moiety; and

each $-AB$ is independently an albumin-binding moiety.

10

7. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 6, wherein $-L^1-$ is of formula (II):



wherein the dashed line indicates attachment to a nitrogen, hydroxyl or thiol of $-D-$;

15 $-X-$ is selected from the group consisting of $-C(R^4R^{4a})-$; $-N(R^4)-$; $-O-$; $-C(R^4R^{4a})-C(R^5R^{5a})-$; $-C(R^5R^{5a})-C(R^4R^{4a})-$; $-C(R^4R^{4a})-N(R^6)-$; $-N(R^6)-C(R^4R^{4a})-$; $C(R^4R^{4a})-O-$; $-O-C(R^4R^{4a})-$; and $-C(R^7R^{7a})-$;

X^1 is selected from the group consisting of C ; and $S(O)$;

$-X^2-$ is selected from the group consisting of $-C(R^8R^{8a})-$; and $-C(R^8R^{8a})-C(R^9R^{9a})-$;

20 $=X^3$ is selected from the group consisting of $=O$; $=S$; and $=N-CN$;

$-R^1$, $-R^{1a}$, $-R^2$, $-R^{2a}$, $-R^4$, $-R^{4a}$, $-R^5$, $-R^{5a}$, $-R^6$, $-R^8$, $-R^{8a}$, $-R^9$, and $-R^{9a}$ are independently selected from the group consisting of $-H$; and C_{1-6} alkyl;

$-R^3$, and $-R^{3a}$ are independently selected from the group consisting of $-H$; and C_{1-6} alkyl, provided that in case one of $-R^3$, $-R^{3a}$ or both are other than $-H$ they are connected to N to which they are attached through an SP^3 -hybridized carbon atom;

25

$-R^7$ is selected from the group consisting of $-N(R^{10}R^{10a})$; and $-NR^{10}-(C=O)-R^{11}$;

$-R^{7a}$, $-R^{10}$, $-R^{10a}$, and $-R^{11}$ are independently of each other selected from the group consisting of $-H$; and C_{1-6} alkyl;

optionally, one or more of the pairs $-R^{1a}/-R^{4a}$, $-R^{1a}/-R^{5a}$, $-R^{1a}/-R^{7a}$, $-R^{4a}/-R^{5a}$, and $-R^{8a}/-R^{9a}$ form a chemical bond;

30

optionally, one or more of the pairs $-R^1/-R^{1a}$, $-R^2/-R^{2a}$, $-R^4/-R^{4a}$, $-R^5/-R^{5a}$, $-R^8/-R^{8a}$, and $-R^9/-R^{9a}$ are joined together with the atom to which they are attached to form a C_{3-10} cycloalkyl; or 3- to 10-membered heterocyclyl;

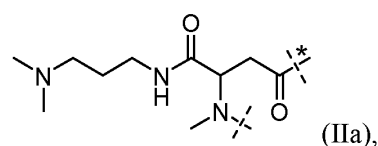
optionally, one or more of the pairs $-R^1/-R^4$, $-R^1/-R^5$, $-R^1/-R^6$, $-R^1/-R^{7a}$, $-R^4/-R^5$, $-R^4/-R^6$, $-R^8/-R^9$, and $-R^2/-R^3$ are joined together with the atoms to which they are attached to form a ring A;

optionally, R^3/R^{3a} are joined together with the nitrogen atom to which they are attached to form a 3- to 10-membered heterocycle;

A is selected from the group consisting of phenyl; naphthyl; indenyl; indanyl; tetralinyl; C_{3-10} cycloalkyl; 3- to 10-membered heterocyclyl; and 8- to 11-membered heterobicycyl; and

wherein $-L^1-$ is substituted with at least one $-L^2-$ and wherein $-L^1-$ is optionally further substituted, provided that the hydrogen marked with the asterisk in formula (II) is not replaced by $-L^2-$ or a substituent.

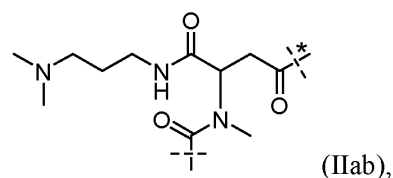
8. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 7, wherein $-L^1-$ is of formula (IIa)



wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of $-D-$; and
the unmarked dashed line indicates attachment to $-L^2-$.

9. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 7, wherein $-L^1-$ is of formula (IIab)



wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D-;
and

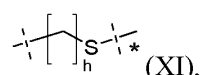
the unmarked dashed line indicates attachment to -L²-.

- 5 10. The compound of any of claims 1 to 9, wherein -L²- is a spacer moiety selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;
- 10 -R^{y1} and -R^{y1a} are independently of each other selected from the group consisting of -H-, -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different, and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-, -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-, and -OC(O)N(R^{y4})-;
- 15 each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more -R^{y2}, which are the same or different;
- 20 each -R^{y2} is independently selected from the group consisting of halogen, -CN, oxo (=O), -COOR^{y5}, -OR^{y5}, -C(O)R^{y5}, -C(O)N(R^{y5}R^{y5a}), -S(O)₂N(R^{y5}R^{y5a}), -S(O)N(R^{y5}R^{y5a}), -S(O)₂R^{y5}, -S(O)R^{y5}, -N(R^{y5})S(O)₂N(R^{y5a}R^{y5b}), -SR^{y5}, -N(R^{y5}R^{y5a}), -NO₂, -OC(O)R^{y5}, -N(R^{y5})C(O)R^{y5a}, -N(R^{y5})S(O)₂R^{y5a}, -N(R^{y5})S(O)R^{y5a}, -N(R^{y5})C(O)OR^{y5a}, -N(R^{y5})C(O)N(R^{y5a}R^{y5b}), -OC(O)N(R^{y5}R^{y5a}),
- 25
- 30

and C₁₋₆ alkyl; wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different; and

each -R^{y3}, -R^{y3a}, -R^{y4}, -R^{y4a}, -R^{y5}, -R^{y5a} and -R^{y5b} is independently selected from the group consisting of -H, and C₁₋₆ alkyl, wherein C₁₋₆ alkyl is optionally substituted with one or more halogen, which are the same or different.

11. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 10, wherein L²- is of formula (XI)



wherein

the unmarked dashed line indicates attachment to -L¹-;

the dashed line marked with the asterisk indicates attachment to the at least one polymeric moiety;

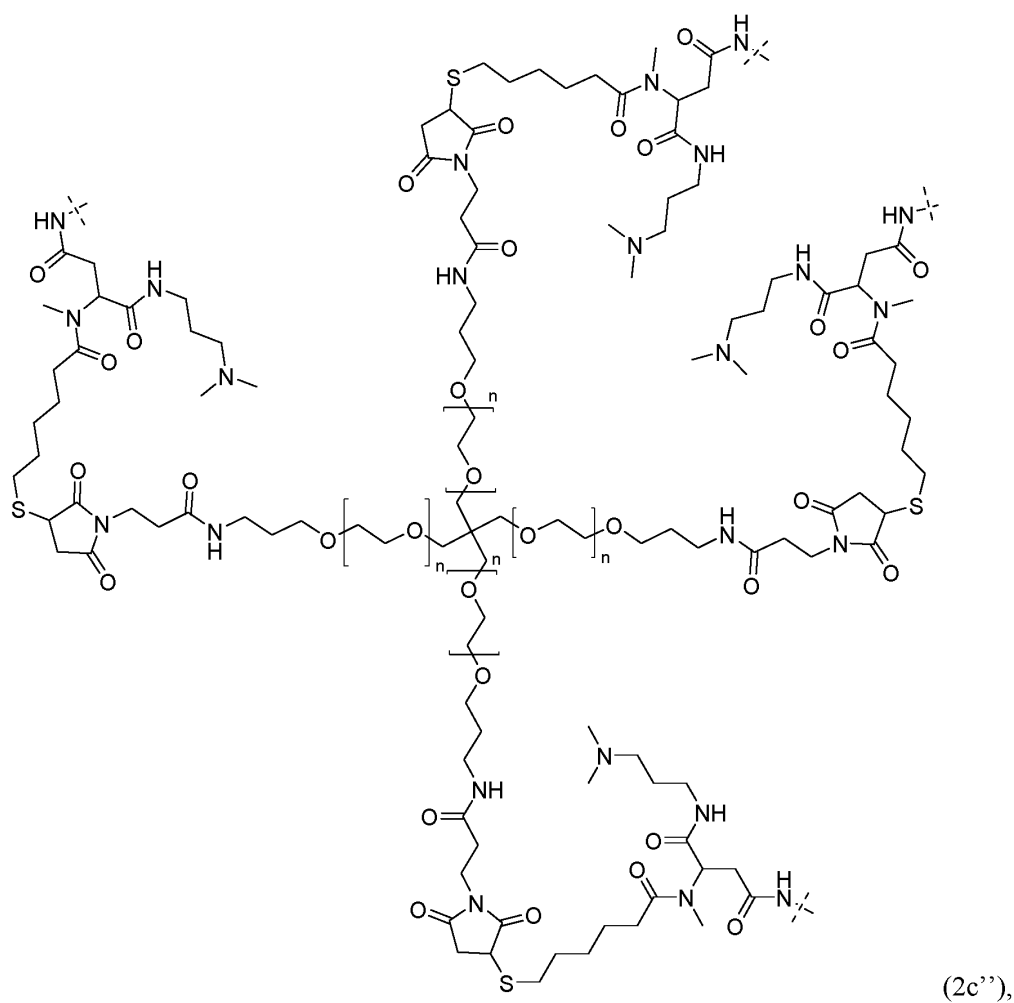
h is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16.

12. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 11, wherein -D-AB is a GLP-1 receptor agonist moiety.

13. The compound or a pharmaceutically acceptable salt thereof of claim 12, wherein the GLP-1 receptor agonist moiety is selected from the group consisting of semaglutide, liraglutide, ecnoglutide, GZR18, GL0034, tirzepatide, cotadutide, BI-456906, pemvidutide, mazdutide, dapiglutide and retatrutide.

14. The compound or a pharmaceutically acceptable salt thereof of any claim 12 or 13, wherein -D-AB is semaglutide.

15. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 or 4 to 14, wherein the compound is of formula (2c'')

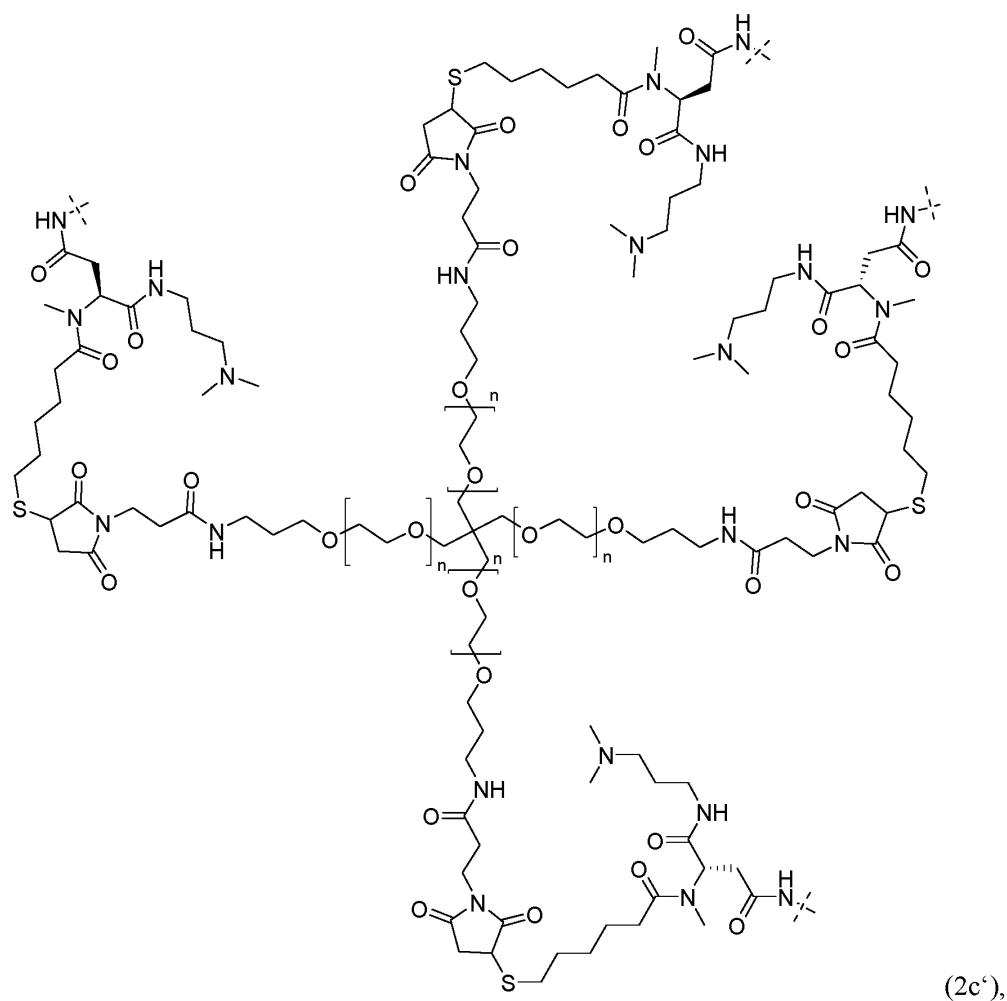


wherein

the dashed line indicates attachment to the N-terminal amine functional group of semaglutide; and

5 n_1 , n_2 , n_3 and n_4 are independently an integer ranging from about 11 to about 115.

16. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 or 4 to 15, wherein the compound is of formula (2c')



wherein

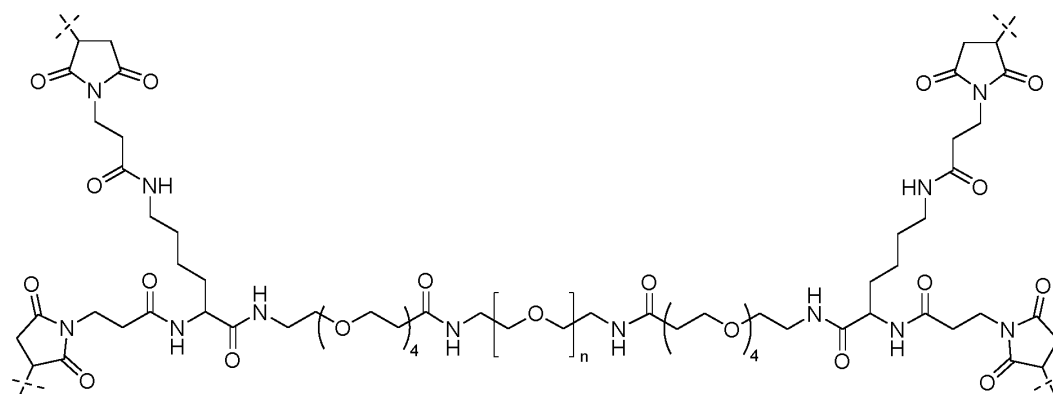
the dashed line indicates attachment to the N-terminal amine functional group of semaglutide; and

5 n_1 , n_2 , n_3 and n_4 are independently an integer ranging from about 11 to about 115.

17. The compound or a pharmaceutically acceptable salt thereof of claim 15 or 16, wherein n_1 , n_2 , n_3 and n_4 are independently an integer of about 28.

10 18. The compound or a pharmaceutically acceptable salt thereof of claim 15 or 16, wherein n_1 , n_2 , n_3 and n_4 are independently an integer of about 56.

19. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1, 2 or 7 to 14, wherein the compound is of formula (2g')

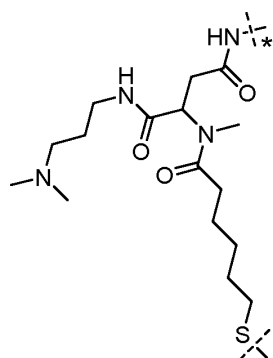


(2g'),

wherein

n is independently an integer ranging from about 22 to about 230;

5 dashed lines indicate attachment to a moiety



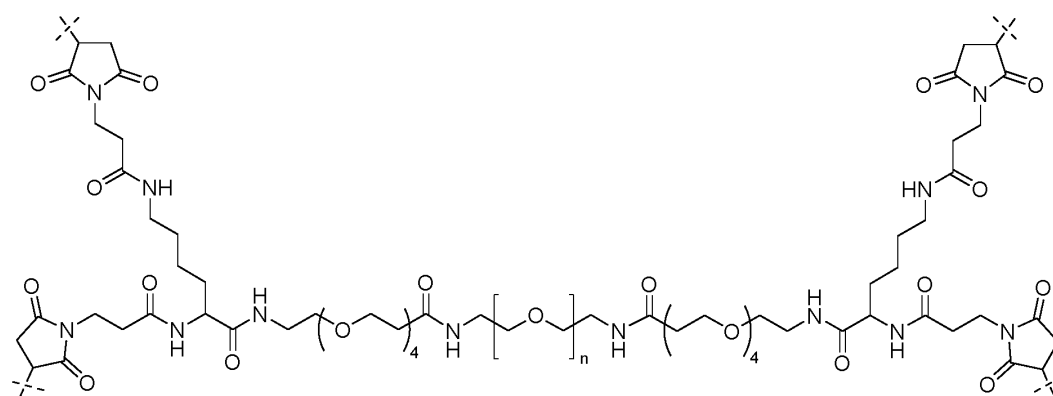
wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of
formula (2g'); and

10 the dashed line marked with the asterisk indicates attachment to the N-terminal
amine functional group of semaglutide.

20. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1, 2
or 7 to 14, wherein the compound is of formula (2g)

15

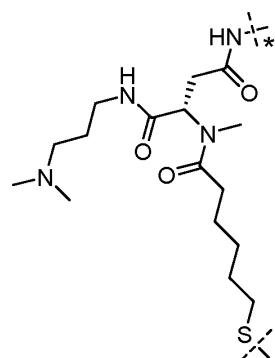


(2g),

wherein

n is independently an integer ranging from about 22 to about 230;

dashed lines indicate attachment to a moiety



wherein

the unmarked dashed line indicates attachment to an unmarked dashed line of formula (2g); and

the dashed line marked with the asterisk indicates attachment to the N-terminal amine functional group of semaglutide.

21. The compound or a pharmaceutically acceptable salt thereof of claim 19 or 20, wherein n is about 112.

22. A pharmaceutical composition comprising one or more of the compounds or a pharmaceutically acceptable salt thereof of any one of claims 1 to 21.

23. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 21 or the pharmaceutical composition of claim 22 for the manufacture of a medicament.

24. The compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 21 or the pharmaceutical composition of claim 22 for use in a treatment of a disease that can be treated with -D-AB.
- 5
25. The compound or a pharmaceutically acceptable salt thereof of any one of claims 12 to 21 or a pharmaceutically composition comprising one or more compounds of any one of claims 12 to 21 for use in the treatment of a disease selected from the group consisting of (i) all forms of diabetes, (ii) obesity, (iii) non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), (iv) cardiovascular disease, (v) neurodegenerative disorders, (vi) chronic kidney disease (CKD), (vii) diabetic kidney disease (DKD), (viii) peripheral arterial disease (PAD), and/or (ix) heart failure (HF).
- 10
26. The compound or a pharmaceutically acceptable salt thereof of any one of claims 12 to 21 or a pharmaceutically composition comprising one or more compounds of any one of claims 12 to 21 for use in the treatment of a disease selected from the group consisting of syndrome X, atherosclerosis, myocardial infarction, coronary heart disease, reperfusion injury, stroke, cerebral ischemia, an early cardiac or early cardiovascular disease, left ventricular hypertrophy, coronary artery disease, hypertension, essential hypertension, acute hypertensive emergency, cardiomyopathy, heart insufficiency, exercise intolerance, acute and/or chronic heart failure, arrhythmia, cardiac dysrhythmia, syncope, angina pectoris, cardiac bypass and/or stent reocclusion, intermittent claudication (atherosclerosis obliterans), diastolic dysfunction, and/or systolic dysfunction; and reduction of blood pressure, such as reduction of systolic blood pressure.
- 15
- 20
- 25
27. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of claim 25 or 26, wherein the compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition are administered in combination with a growth hormone.
- 30
28. The compound or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of claim 27, wherein the growth hormone is lonapegsomatropin.