Claims

1. A controlled-release C-type natriuretic peptide ("CNP") agonist, wherein said controlled-release CNP agonist releases one or more CNP with a release half-life of at least 6 hours ~~under~~ in ~~physiological conditions~~aqueous buffer at pH 7.4 and 37 °C, wherein the controlled-release CNP agonist is a conjugate comprising a CNP moiety which is covalently and reversibly conjugated to a carrier moiety via a reversible prodrug linker moiety and from which the CNP is released in the form of the corresponding free CNP, wherein the CNP comprises a ring moiety of the amino acid sequence of SEQ ID NO:96, the ring moiety being between two cysteine residues forming a disulfide bridge, wherein the carrier is a branched or multi-arm PEG-based polymer ~~branched carrier~~ having a molecular weight of at least 10 kDa, and conjugated via the linker moiety to the ring moiety of the CNP, or wherein the carrier is a hydrogel, ~~and~~ wherein the controlled-release CNP agonist has an at least 5-fold longer degradation half-life in an *in vitro* NEP degradation assay than the corresponding released CNP, and ~~wherein~~ CNP has the sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID

NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94 or SEQ ID NO:95.

2. The controlled-release CNP agonist of claim 1, wherein the controlled-release CNP agonist has an at least 15-fold longer degradation half-life in an in vitro NEP degradation assay than the corresponding released CNP.

3. The controlled-release CNP agonist of claim 1 or 2, wherein the controlled-release CNP agonist has an at least 25-fold longer degradation half-life in an in vitro NEP degradation assay than the corresponding released CNP.

4. The controlled-release CNP agonist of any one of claims 1 to 3, wherein the carrier has a molecular weight of at least 15 kDa.

5. The controlled-release CNP agonist of any one of claims 1 to 4, wherein the controlled-release CNP agonist releases at least one CNP in aqueous buffer at pH 7.4 and 37 °C~~under physiological conditions~~ with a release half-life of at least 24 hours.

6. The controlled-release CNP agonist of any one of claims 1 to 5, wherein the controlled-release CNP agonist releases at least one CNP in aqueous buffer at pH 7.4 and 37 °C~~under physiological conditions~~ with a release half-life of at least 48 hours.

7. The controlled-release CNP agonist of any one of claims 1 to 6, wherein the controlled-release CNP agonist releases at least one CNP in aqueous buffer at pH 7.4 and 37 °C ~~under physiological conditions~~ with a release half-life of at least 168 hours.

8. The controlled-release CNP agonist of any one of claims 1 to 7, wherein the controlled-release CNP agonist is water-insoluble.

9. The controlled-release CNP agonist of any one of claims 1 to 7, wherein the controlled-release CNP agonist is water-soluble.

~~10. The controlled-release CNP agonist of any one of claims 1 to 9, wherein the carrier comprises a C_{8-24} alkyl moiety or 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), 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, 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.~~

~~11.~~10. A pharmaceutical composition comprising the controlled-release CNP agonist of any one of claims 1 to ~~10~~ 9 and at least one excipient.

~~12.~~11. The controlled-release CNP agonist of any one of claims 1 to ~~10~~ 9 or the pharmaceutical composition of claim ~~11~~ 10 for use as a medicament.

~~13.~~12. The controlled-release CNP agonist or the pharmaceutical composition for use as a medicament of claim ~~12~~11, wherein the medicament is to be used in the treatment of achondroplasia.

~~14.~~13. Use of the controlled-release CNP agonist of any one of claims 1 to ~~10~~ 9 or the pharmaceutical composition of claim ~~11~~ 10 for the manufacture of a medicament for treating a disease that can be treated with CNP, wherein the disease is selected from the group consisting of achondroplasia, hypochondroplasia, short stature, dwarfism, osteochondrodysplasias, thanatophoric dysplasia, osteogenesis imperfecta,

achondrogenesis, chondrodysplasia punctata, homozygous achondroplasia, camptomelic dysplasia, congenital lethal hypophosphatasia, perinatal lethal type of osteogenesis imperfecta, short-rib polydactyly syndromes, rhizomelic type of chondrodysplasia punctata, Jansen-type metaphyseal dysplasia, spondyloepiphyseal dysplasia congenita, atelosteogenesis, diastrophic dysplasia, congenital short femur, Langer-type mesomelic dysplasia, Nievergelt-type mesomelic dysplasia, Robinow syndrome, Reinhardt syndrome, acrodysostosis, peripheral dysostosis, Kniest dysplasia, fibrochondrogenesis, Roberts syndrome, acromesomelic dysplasia, micromelia, Morquio syndrome, Kniest syndrome, metatropic dysplasia, spondyloepimetaphyseal dysplasia, neurofibromatosis, Legius syndrome, LEOPARD syndrome, Noonan syndrome, hereditary gingival fibromatosis, neurofibromatosis type 1, cardiofaciocutaneous syndrome, Costello syndrome, SHOX deficiency, idiopathic short stature, growth hormone deficiency, osteoarthritis, cleidocranial dysostosis, craniosynostosis, dactyly, brachydactyly, camptodactyly, polydactyly, syndactyly, dyssegmental dysplasia, enchondromatosis, fibrous dysplasia, hereditary multiple exostoses, hypophosphatemic rickets, Jaffe-Lichtenstein syndrome, Marfan syndrome, McCune-Albright syndrome, osteopetrosis and osteopoikilosis.

~~15.~~14. The use of claim ~~14~~13, wherein the disease is achondroplasia.