Claims

1. A controlled-release C-type natriuretic peptide ("CNP") agonist, wherein said controlled-release CNP agonist releases one or more CNP agonist with a release half-life of at least 6 hours under physiological conditions, wherein the controlled-release CNP agonist is a conjugate comprising a CNP agonist moiety which is covalently and reversibly conjugated to a carrier moiety via a reversible prodrug linker moiety and from which the CNP agonist is released in the form of the corresponding free CNP agonist, wherein the carrier is a branched carrier having a molecular weight of at least 10 kDa, 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 agonist and wherein the CNP agonist is CNP having 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 agonist.

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 agonist.

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 agonist 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 agonist 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 agonist 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 8, wherein the controlled-release CNP agonist is selected from the group consisting of crystals, nanoparticles, microparticles, nanospheres and microspheres.

10. The controlled-release CNP agonist of any one of claims 1 to 9, wherein the controlled-release agonist is a vesicle comprising at least one CNP agonist and wherein said vesicle is a micelle, liposome or polymersome.

11. The controlled-release CNP agonist of any one of claims 1 to 10, wherein the controlled-release CNP agonist is water-soluble.

12. The controlled-release CNP agonist of any one of claims 1 to 11, 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.

13. A pharmaceutical composition comprising the controlled-release CNP agonist of any one of claims 1 to 12 and at least one excipient.

14. The controlled-release CNP agonist of any one of claims 1 to 12 or the pharmaceutical composition of claim 13 for use as a medicament.

15. The controlled-release CNP agonist or the pharmaceutical composition for use as a medicament of claim 14, wherein the medicament is used in the treatment of achondroplasia.

16. Use of the controlled-release CNP agonist of any one of claims 1 to 12 or the pharmaceutical composition of claim 13 for the manufacture of a medicament for treating a disease 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, metatrophic dysplasia, spondyloepimetaphyseal dysplasia, neurofibromatosis, Legius syndrome, LEOPARD syndrome, Noonan syndrome, hereditary gingival fibromatosis, neurofibromatosis type 1, Legius syndrome, 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.

17. The use of claim 16, wherein the disease is achondroplasia.